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The Development and Application of Gold(I)-Catalyzed Cyclization Cascades

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The Development and Application of Gold(I)-Catalyzed Cyclization Cascades

by

Steven Gregory Sethofer

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University of California, Berkeley

Committee in charge:

Professor F. Dean Toste, Chair
Professor Richmond Sarpong
Professor Benito de Lumen

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Steven Gergory Sethofer

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The formation of saturated carbon-carbon bonds in a precise and controlled manner is arguably the principal objective of organic synthesis. Carbocyclic ring systems comprise the underlying structure for the preponderance of natural products and pharmaceutical agents. Therefore, synthetic methods capable of selectively initiating polycyclization processes in the presence of spectating functionality are of significant value, particularly so when multiple stereocenters are formed enantioselectively.

The emergence of phosphine gold(I) catalysis over the past decade has opened up new avenues to carbocycle formation via π activation of alkynes occurring under exceedingly mild conditions and with excellent chemoselectivity. The research described herein describes the use of homogenous gold(I) complexes to initiate electrophilic cyclization cascades. Through rational substrate design, carbocationic centers may be generated in a predictable manner and employed in subsequent intramolecular cyclization processes.

Chapter 1 introduces the unique reactivity observed in complexes of gold imparted by its relativistically accelerated valence electrons. One consequence of this perturbation is the linear geometry maintained by gold(I) complexes, minimizing the influence of ligand-based chirality on reactions occurring at coordinated alkynes. In spite of this challenge, moderate levels of enantioselectivity were achieved in the desymmetrization of dienynes by cycloisomerization using chiral bisphosphite gold(I) catalysts.

Ultimately, we were able to achieve selectivities up to 98% *ee* using hindered chiral bisphosphine gold(I) catalysts during the evaluation of another enyne cycloisomerization reaction, described in chapter 2. In this process, an initial regioselective cyclization was used to generate a carbocationic species poised to undergo intramolecular trapping. Consistently high enantioselectivity was maintained using various pendant oxygen, carbon and nitrogen nucleophiles. The diastereomerically pure bi- and tricyclization products obtained provided support for a concerted polyene cyclization mechanism as predicted by the Stork-Eschenmoser postulate.

Chapter 3 describes another tandem process exploiting the transient cationic species arising from gold(I)-promoted enyne cycloisomerization. In this case, a gold(I)-initiated tandem cyclopentannulation reaction was employed in the total synthesis of the novel triquinane ventricosene. A cyclopropanol unit embedded in the enyne substrate underwent a semipinacol rearrangement in response to the carbocation, leading cleanly to bicyclo[3.2.0]heptan-6-one products. For cyclopentenyl substrates, the hindered all-carbon quaternary center and all of the ring fusions of the angular triquinane ring system were formed at once. The choice of a hydrocarbon target highlighted the utility of gold(I) catalysts as selective activators of carbon unsaturation; throughout the synthesis only a single heteroatom was present.

This work concludes by extending the scope gold(I)-catalyzed carbocyclization reactions which generate useful cationic intermediates. The gold(I)-catalyzed Rautenstrauch rearrangement forms a cyclopentene-based cationic species which was shown to undergo efficient trapping by pendant arenes to give a saturated 5,6-ring fusion comprising a chiral benzylic quaternary center. The chirality transfer observed in the parent process was found to be conserved in the tandem process. Interestingly, cyclization of racemic substrates by chiral bisphosphine digold catalysts was found to proceed with moderate enantioselectivity, suggesting a competing mechanism is in effect which proceeds through an achiral intermediate.

for the Ole Mule

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Accursed thirst for gold! What dost thou not compel mortals to do?

-Virgil, The Aeneid

Acknowledgements

In order to express my gratitude to those who have helped me achieve the most significant goal of my life, I must begin here on an awkwardly metaphysical note. During a period of confusion in my youth regarding the purpose life in what I had come to see as an infinitely complex yet coldly purposeless universe, I found comfort in the self-correcting and internally consistent mass of knowledge called science. Guided by the ideas of people much smarter than myself, I was led to the only rational explanation for existence: that from its infinite complexity, the universe had produced the human mind in order to understand itself. While helping little with the absurdities and struggles in day-to-day life, this understanding has given me to an appreciation for and desire to contribute to the body of scientific knowledge. Therefore, I would like to begin by acknowledging the efforts of scientists in general.

One scientist to whom I am particularly grateful is my advisor, Dean Toste. There are moments in either formal education or daily experience, prized particularly by inquisitive children and scientists, where an understanding comes as little rush, the thrill we get when something resonates by virtue of its intuitive *rightness*. Dean is a living manifestation these little euphorias of comprehension, he represents to me an embodiment of the 'cool factor' that makes the study of nature so rewarding. As an advisor he employs enthusiasm and encouragement rather than intimidation and pressure to motivate his students, as a human being he is a genuinely nice guy who is fun to be around.

I have always been impressed with the support provided by the group in general. Sort of flowing from Dean's example, there is a of mob mentality of education in the Toste labs. You never know what kind of insight will come from conversations when out searching for a reagent or piece of glassware. The group attracts good people that are fun to work with, in a self-reinforcing manner.

To single out individuals for acknowledgment seems almost too challenging, but I will make an attempt. Steve and Olivia were instrumental in getting me functional in the group. Once I found my home in 611, my roommates Britt, Greg and Nate provided support, friendship and amusement. To say we had excellent chemistry would be both an awful pun and a major understatement. In addition to Greg, my other classmates Asa and Pete provided critical support in the most challenging times. Other people whose help and friendship I am grateful for include Cole, Yiming, Iain, Pablo and my collaborator Timo. I cannot neglect to thank those from my 'former life', my parents Nick and Liba, all my friends. Most of all, I am grateful to my precious bride Sarah who gave all she had to give, showing me in the process how much one person can take in the name of love.

Vi veri veniversum vivus vici.

Chapter 1.
A Primer on the Reactivity of Gold(I) Catalysts

Relativistic Alteration of Relative Orbital Energy Levels in Gold

Over the past decade, developments in the field of homogenous gold catalysis have led to an intriguing diversity of new transformations, which serve to affirm the role of gold as a superior Lewis acid for activation of unsaturated carbon bonds. Of particular significance is the preference of electrophilic gold(I) complexes to impart electrophilic reactivity to coordinated alkynes, even in the presence of water and various heteroatom-containing functionality.[1]

The characteristic catalytic activity exhibited by complexes of gold is attributed to the effects of a trend toward increasing velocity of electrons in 4th row transition metals, which is at a maximum with the electronic configuration of gold. The relativistic speeds of the 6*s* and 6*p* electrons cause significant mass gain, leading to contraction of the orbitals. This, in turn, has the effect of shielding the nuclear charge and causing expansion of the 5*d* orbitals.[2]

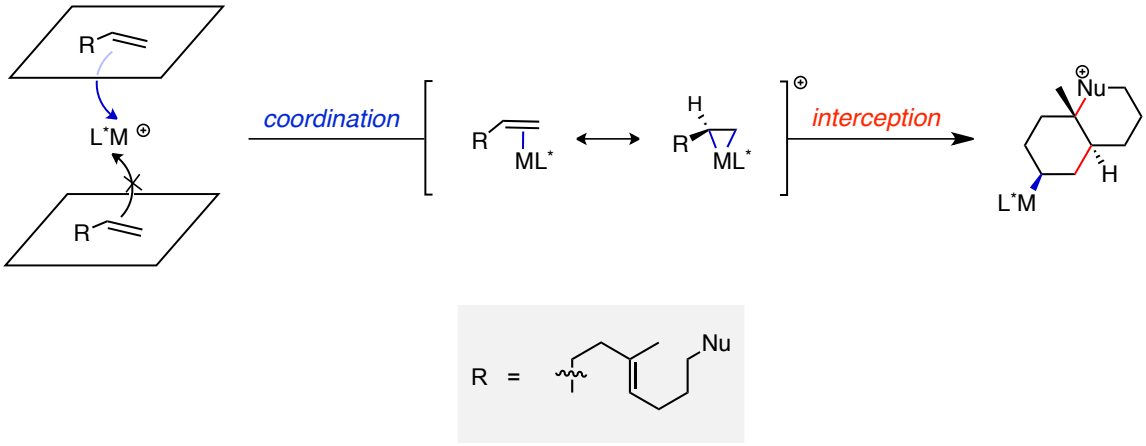
This perturbation to orbital energies has profound influences over the chemistry of gold. For example, the contracted valence orbitals correspond to a lower-energy lowest unoccupied molecular orbital thus explaining the increased lewis acidity and electrophilicity of gold. On the other hand, electrons occupying the expanded 5*d* orbitals experience less Pauli repulsion, significantly raising their oxidation potential through ground state stabilization.[2]

The diminished extent of electron back donation from gold *d* orbitals into ligand antibonding orbitals[3] via the Chatt-Dewar-Duncanson model[4] in the π–coordinated cationic gold(I) complex corresponds to a more electron-deficient ligand prone to nucleophilic attack, accounting for gold's tendency toward π activation. On the other hand, donation of electrons from the lower-energy, contracted *d* orbitals into more accessible, nonbonding *p* orbitals provides rationalization for the carbenoid reactivity often observed in gold(I) complexes. A recent theoretical analysis has correlated attenuated back donation in gold(I) π complexes with an increased sensitivity to electronic effects in the ancillary ligand, as well structural features in the reactive complex[5] while maintaining an essentially constant level of σ donation from the ligand.[6]

Another consequence of relativistic effects on the complexes of gold(I) having significant implications for enantioselective catalysis is the preference to

adhere to a linear, bicoordinate geometry.[7] As a result, ligand-based chirality is positioned at 180° with respect to the metal center. Taken together with the predilection of gold(I) complexes towards selective activation of alkynes over olefins, a significant challenge emerges to asymmetric induction by chiral phosphinegold(I) catalysts.

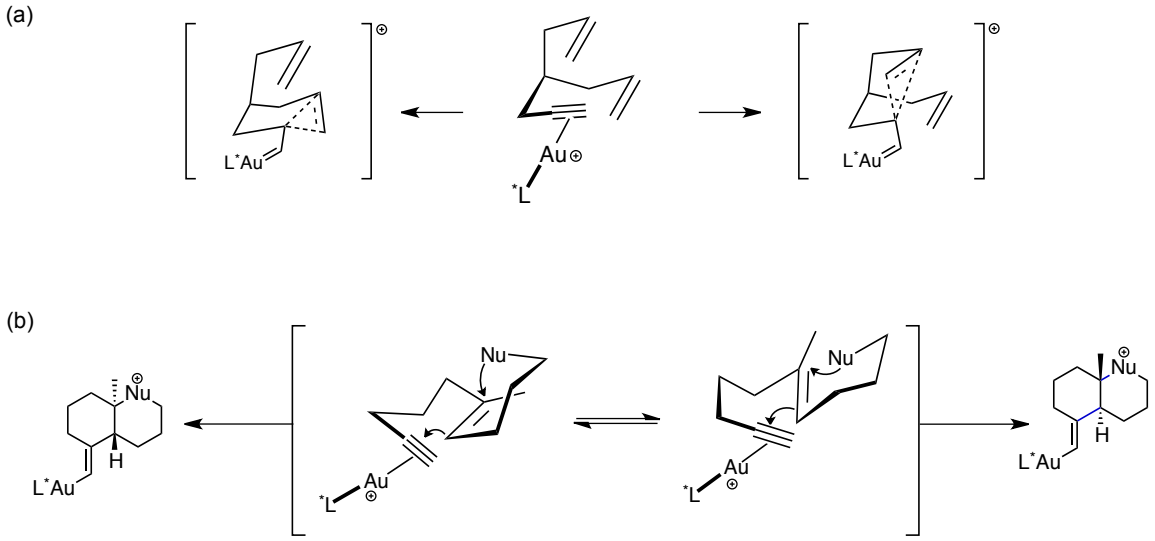
Figure 1.1. Ligand-Based Enantioselectivity in Transition Metal Mediated Enantiofacial Discrimination of Olefins.



Discrimination of prochiral faces in enantioselective olefin activation processes involves selective coordination by a chiral metal complex. Subsequent formation of chiral centers by intramolecular nucleophilic attack then occurs as a diastereoselective step, as depicted in Figure 1.1 for a generalized polyene cyclization process.

On the other hand, asymmetric induction cannot be achieved by facial discrimination in the π activation of alkynes, which belong to the D_{∞} symmetry group and are thus not prochiral. In such transformations, long-range enantioselectivity with regard to the incoming nucleophile is required, for example in desymmetrizing (Figure 1.2a) or cascade (Figure 1.2b) enyne cyclization processes. In spite of the relative remoteness of the chiral ligand in these processes from the incipient chiral centers, examples of enantioselective alkyne activation by gold(I) complexes were known at the time.[8] We were therefore interested in exploring the potential for asymmetric induction in the processes depicted in Figure 1.1.

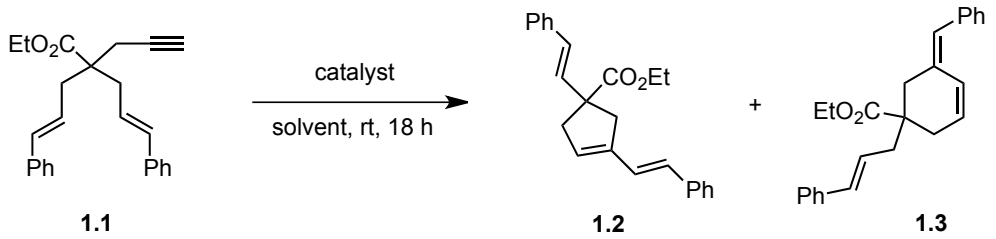
Figure 1.2. Ligand-Based Enantioselectivity in Gold(I)-Catalyzed Desymmetrization and Intercepted Enyne Cycloisomerization Processes.



Evaluation of Chiral Gold(I) Catalysts in the Desymmetrizing Cycloisomerization of Dienynes.

We began with studies directed at the desymmetrization of dienynes by a gold(I)-catalyzed cycloisomerization processs. Table 1.1 summarizes the results obtained for cyclization of substrate **1.1** by various chiral digold(I) catalysts, which provided a mixture of isomeric trienes **1.2** and **1.3** in varying ratios. Using Binap(AuCl)$_2$ as precatalyst gave 25% and 15% *ee* for the 5-*exo* (**1.2**) and 6-*endo* (**1.3**) products, respectively in a 9:1 ratio (entry 1).[9] Repeating the reaction using a dicationic catalyst generated using 2 equiv. $AgSbF_6$ abolished the enantioselectivity and reduced the regioselectivity of the cycloisomerization (entry 2). No significant improvement in enantioselectivity was observed using various bisphosphine digold(I) precatalysts (entries 3-6). A significant improvement was obtained, however, when the hindered bisphosphite ligand (R,R)-chiraphite was employed, giving respectively 45% and 57% *ee* for **1.2** and **1.3**, which were formed in a 1:1 ratio (entry 7).

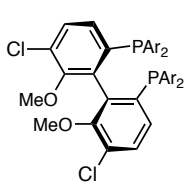
Table 1.1. Screening of Ligand and Solvent Effects on the Au(I)-Catalyzed Desymmetrization of Dienyne **1.1**.



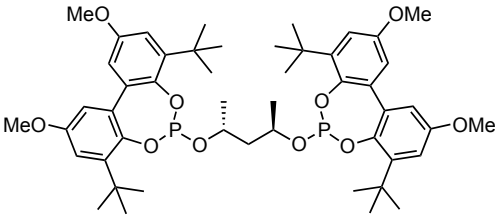
1.1 **1.2** **1.3**

Entry	Ligand	Solvent	Ratio 1.2 / 1.3	*ee 1.2 (%)*	*ee 1.3 (%)*
1	(R)-Binap	CH_2Cl_2	9:1	25	15
2	(R)-Binap [b]	CH_2Cl_2	2:1	5	0
3	(R)-DTBM-Segphos	CH_2Cl_2	5:1	29	10
4	(R)-Cl,MeO-Biphep	CH_2Cl_2	2:1	19	14
5	(R)-*tol*-Binap	CH_2Cl_2	9:1	23	19
6	(R)-Difluorophos	CH_2Cl_2	3:1	13	20
7	(R,R)-Chiraphite	CH_2Cl_2	1:1	45	57
8	(R,R)-Chiraphite	CH_3CN	NR	--	--
9	(R,R)-Chiraphite	benzene	1:1	17	45
10	(R,R)-Chiraphite	THF	2:1	10	31
11	(R,R)-Chiraphite	CH_3NO_2	2:1	37	63
12	(R,R)-Chiraphite[c]	CH_2Cl_2	2:1	51	65

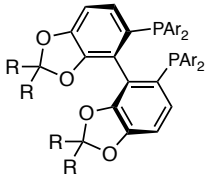
[a] Reaction Conditions: 3 mol % catalyst used. Unless otherwise indicated, catalyst generated from Ligand$(AuCl)_2$ and $AgSbF_6$ in a 1:1 ratio. Product ratios determined by ^1H NMR. [b] 2 equiv. $AgSbF_6$ used, relative to precatalyst. [c] 1 equiv. $NaBArF_{24}$ used, 96 h. required for full conversion.



(R)-Cl,MeO-Biphep



(R,R)-Chiraphite



(R)-DTBM-Segphos; R= H,
Ar = 3,5-(^{t}Bu)$_2$-4-MeO-C_6H_2
(R)-Difluorophos; R = F, Ar = C_6H_5

We next evaluated solvent effects using (R,R)-chiraphite as ligand in anticipation of further optimizing the enantioselectivity of the cycloisomerization reaction. No conversion was observed in acetonitrile, possibly due to catalyst inhibition by the solvent (entry 8). Reduced enantioselectivity was obtained using benzene and THF, relative to CH_2Cl_2 (entries 9 and 10). With nitromethane as solvent, however, a slight increase in the enantioselectivity of minor 6-*endo* product **1.3** was obtained along with a diminished enantioselectivity in product **1.2** (entry 11). Finally, while more coordinating counterions gave no reaction, switching the counterion source from $AgSbF_6$ to sodium tetrakis[(3,5-trifluoromethyl)phenyl]borate ($NaBArF_{24}$) resulted in improved enantioselectivity for both products, albeit requiring a prolonged reaction time (entry 12).

At this point in the project, we turned our attention to the transformation outlined in Figure 1.2b, the enantioselective polycyclization of enynes initiated by gold(I)-catalyzed cycloisomerization, which is outlined in full detail in chapter 2.

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5. Benitez, D.; Shapiro, N. D.; Tkatchouk, E.; Wang, Y.; Goddard, W. A.; Toste, F. D., *Nat. Chem.* **2009,** *1*, 482.
6. Salvi, N.; Belpassi, L.; Tarantelli, F., *Chem. Eur. J.* **2010,** *16*, 7231.
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8. Munoz, M. P.; Adrio, J.; Carretero, J. C.; Echavarren, A. M., *Organometallics* **2005,** *24*, 1293.
9. A discussion of the mechanistic details of this transformation may be found on page 176.

Chapter 2.

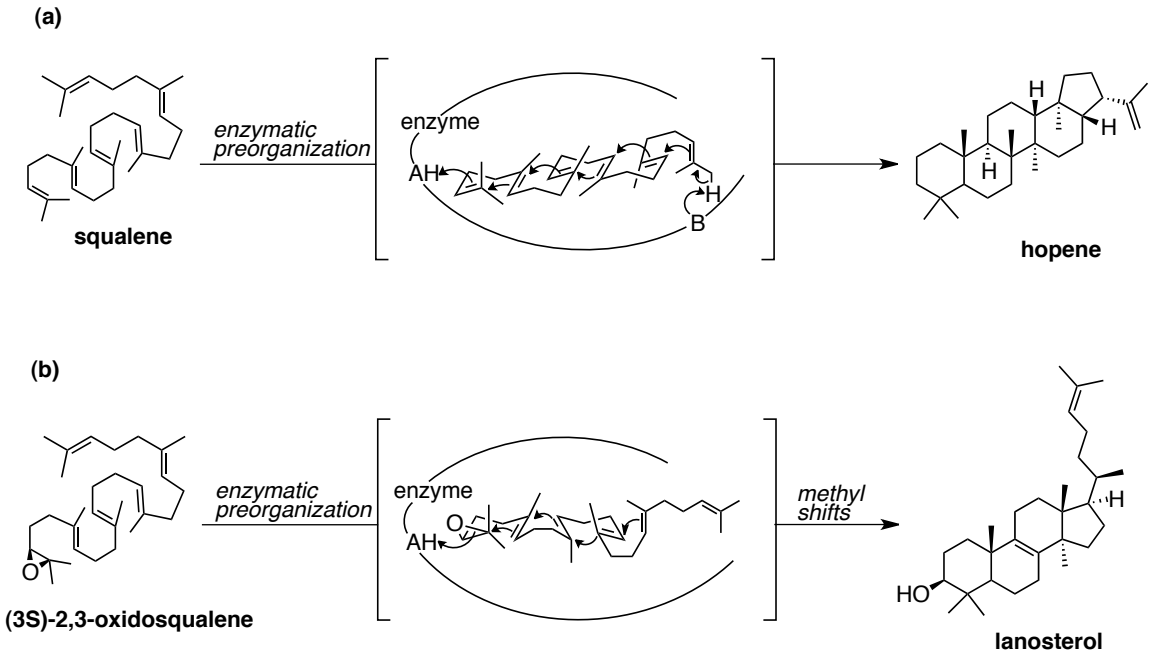
Development of Enantioselective Polycyclizations Through Interception of Gold(I)-Catalyzed Eynyne Cycloisomerization.

Chapter 2 details the development of a gold(I)-catalyzed method for enantioselective polyolefin cyclization cascades. The cycloisomerization of 1,6-enynes substituted with a pendant nucleophile serves to initiate a polycyclization process adhering to the Stork-Eschenmoser postulate. In addition to being one of only a handful of polyene cyclization processes capable of achieving high enantioselectivity, the present transformation represents the first such method originating in selective alkyne activation. Procedurally convenient, the method employs air- and moisture-stable chiral bisphosphine digold(I) chlorides as catalyst, easily prepared from commercial ligands. Treatment of the enyne substrate with a cationic gold(I) complex generates species with significant carbocationic character *requiring no protective measures* such as exclusion of moisture. The optimized catalyst and solvent conditions were broadly applicable to a variety of nucleophilic terminators, providing a number of hetero- and carbocyclic systems in nearly quantitative yield. Furthermore, the same conditions were successfully applied to dienyne substrates, triggering a tricyclization process and the diastereospecific formation of four contiguous stereocenters with excellent enantioselectivity. This research was conducted with the assistance of Timo Meyer and has been published in part (Sethofer, S. G.; Mayer, T.; Toste, F. D. *J. Am. Chem. Soc.* **2010**, *132*, 8276 – 8277).

Introduction

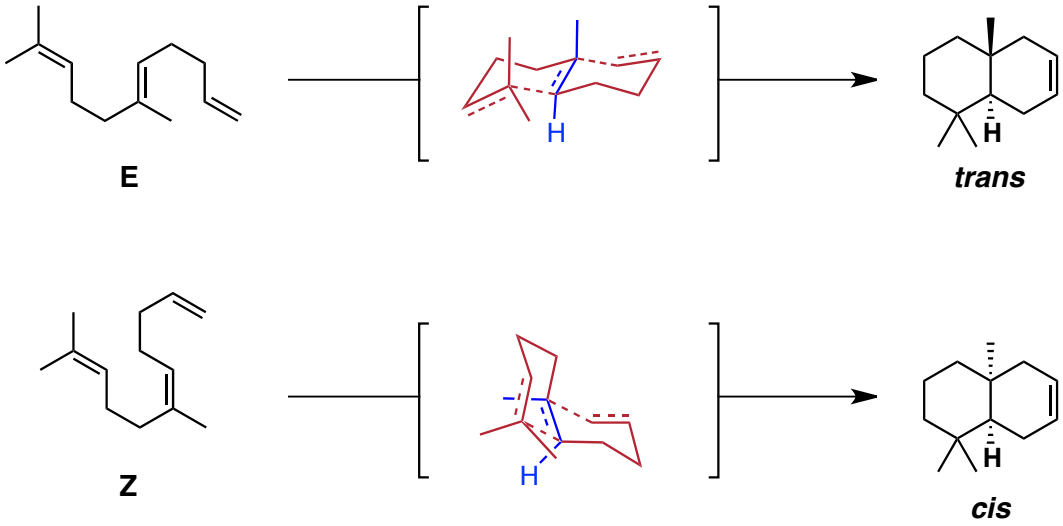
The biochemical cyclizations of polyisoprenoids have served as fertile ground for the development of synthetic methodology capable of rapidly producing molecular complexity.[1] The cyclization of squalene to hopene in bacteria (Figure 2.1a), along with oxidosqualene to lanosterol (Figure 2.1b) in vertebrates and fungi by squalene cyclase enzymes serve as prototypical examples.[2]

Figure 2.1. Biosynthesis of Hopene and Lanosterol.

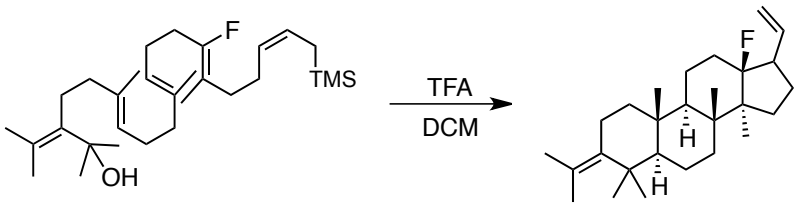


In these transformations, the inherent diastereoselectivity of the polyene cyclization is governed by the Stork-Eschenmoser postulate (Scheme 2.1).[3] The geometry of the alkene undergoing addition determines the relative stereochemistry of the resulting ring junction. The origin of this selectivity lies in the anti-periplanar relationship necessary[4] for a concerted addition across the π-system of an alkene. This alignment of electron donor and acceptor is accommodated in a chairlike transition state with E and Z olefins transforming into *trans* and *cis* ring fusions, respectively.

Scheme 2.1. The Stork-Eschenmoser Postulate for Polyolefin Cyclization.



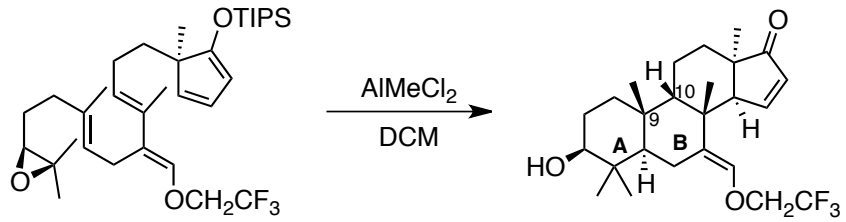
In biosynthetic processes, the cyclase enzyme exerts additional influence over the substrate-mediated reactivity depicted in Scheme 2.1. The features of this enzymatic control correspond to key features of a successful biomimetic catalytic system. For example, initiation by the presence of a suitably acidic proton within the active site occurs regiospecifically at terminal olefin of the polyisoprenoid, a significant challenge for chemical synthesis when multiple olefins of similar reactivity must be distinguished. The reactive cationic intermediate typically experiences stabilizing interactions within the enzyme, preventing premature termination pathways. In cases when cyclization must proceed through non-chair conformations (Figure 2.1b) the enzyme must adequately stabilize the higher-energy conformer. Termination should then occur in a regiospecific manner, releasing product as a single isomer.



(2.1)

2.1

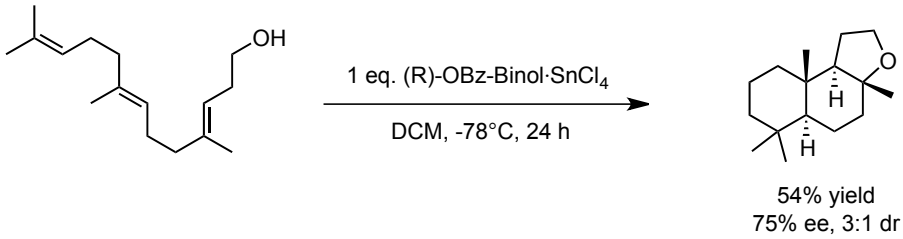
The tetracyclization cascade employed by Johnson *et al.* in the synthesis of dammarenediol[5] illustrates the use of the vinyl fluoride group to stabilize α-cationic charge density,[6] resulting in significantly improved yields of **2.1** (eq. 2.1). The cation stabilizing carbon-fluorine bond was reduced to hydrocarbon with retention of stereochemistry in good yield with Na / K alloy.



2.2 (2.2)

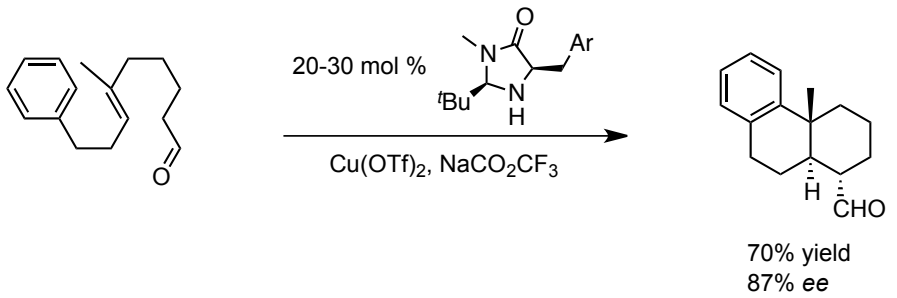
In 1996, Corey reported the cyclization of an epoxy-terminated polyene to give polycycle **2.2** using a Lewis acidic catalyst (eq. 2.2).[7] A vinyl trifluoroethyl ether auxiliary was used to override the standard *trans-anti-trans* triterpene folding, instead inducing cyclization via a boatlike transition state for the nascent **B** ring, providing **A/B**-*trans* 9,10-*syn* product **2.2**.

Perhaps the most impressive feat performed by cyclase enzymes is their ability to produce complex polycyclic systems as single enantiomers. While numerous examples of diastereoselective polyene cyclizations are known, relatively few enantioselective versions have been reported. Yamamoto *et al.* reported the first such system in 2000, some 45 years after the formulation of the Stork-Eschenmoser postulate.[8] He utilized his chiral Lewis acid-assisted Brønsted acid methodology to provide a chiral proton source of suitable acidity to initiate cyclization (eq. 2.3).



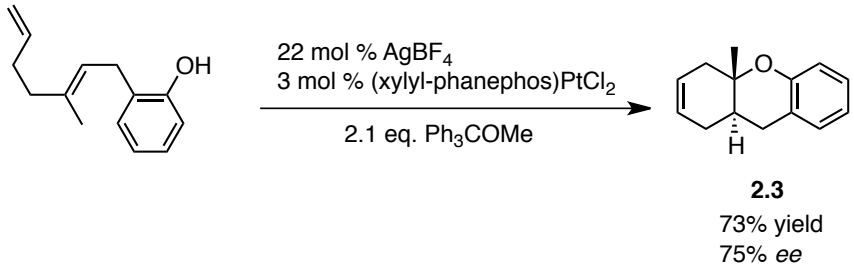
54% yield
75% ee, 3:1 dr (2.3)

More recently, MacMillan *et al.* developed an enantioselective radical polycyclization using SOMO catalysis (eq. 2.4).[9] The process involves selective oxidation of a chiral enamine generated by the organocatalyst to initiate a radical cascade, which proceeded under mild conditions and tolerated a range of both electron-poor and electron-rich functionality.



(2.4)

Late transition metal complexes[10] and electrophlic halide sources[8] have been used to catalyze enantioselective polycyclizations by π-activation. For instance, Gagne found the phenoxy-terminated cyclization of dienes[11] catalyzed by cationic *xyl*-phanephos platinum(II) chloride complex proceeded in 73% yield to give **2.3** in 75% *ee* (eq. 2.5). Cyclization onto the terminal olefin-coordinated platinum species led to a σ-alkyl complex which underwent β-hydride elimination. Trityl methyl ether served dual purpose as a proton scavenger and then hydride acceptor, permitting turnover of the cationic platinum catalyst.

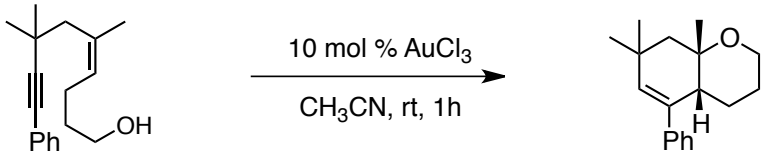


(2.5)

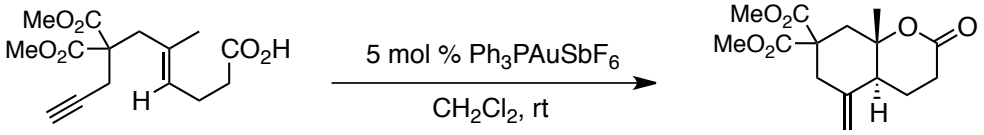
We were interested in the potential for an enantioselective, alkyne-initiated polycyclization reaction mediated by chiral gold catalysts. Precedent for the highly regio- and diastereoselective tandem enyne cycloisomerization/annulation is presented in Scheme 2.2. Kozmin[12] and Furstner[13] described the interception of cationic intermediates in the gold(I)-catalyzed cycloisomerization of 1,5- and 1,6-enynes, respectively (Scheme 2.2). These highly regio- and diastereoselective cyclizations provided precedent for the utilization of cations arising from olefin attack onto gold-activated alkynes in subsequent cyclization processes (Scheme 2.2).

Based on previous examples of asymmetric enyne cycloisomerization reactions, we hypothesized that the application of chiral bisphosphinegold(I) catalysts would lead to enantioselective, multi-ring forming transformations proceeding with high chemoselectivity and tolerance of functionality.

Scheme 2.2. Gold(I)-Catalyzed Diastereoselective Polycyclizations.



2.4
90% yield

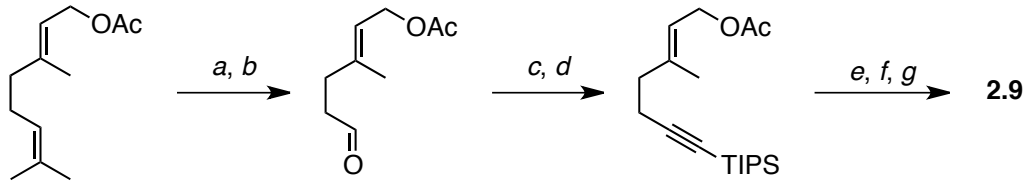


2.5 **2.6**
80% yield

Enantioselective Polycyclization of 1,5-Enynes

Given that most asymmetric cationic polycyclization reactions were induced by an endocyclic process, we decided to first evaluate the use of chiral phosphinegold(I) complexes in a 6-*endo*-dig initiated polycyclization of 1,5-enynes. Substrate **2.9** was prepared as depicted in Scheme 2.3. In this approach, the requisite (E)-trisubstituted olefin was derived in isomerically pure form from geranyl acetate. The prenyl terminus was regioselectively dihydroxylated and oxidatively cleaved to give acetoxy aldehyde **2.7**. Alkynylation was accomplished using the Bestmann-Ohira reaction conditions,[14] followed by protection of the acetylenic proton. Arylation of the allylic bromide obtained from **2.8** was achieved by treatment with sodium phenoxide in refluxing ether. Deprotection using TBAF in THF provided the desired substrate 1,5-enyne **2.9**.

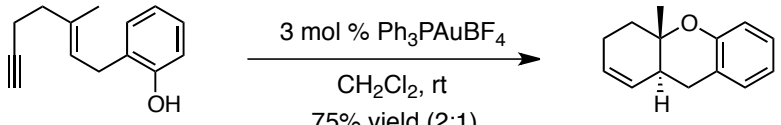
Scheme 2.3. Synthesis of Phenolic 1,5-Enyne Substrate from Geranyl Acetate.[a]



2.7 **2.8**

[a] *Reagents and Conditions:* (a) AD-mix β, $MsNH_2$, 1:1 ^tBuOH / H_2O, 93% (b) $NaIO_4$ / SiO_2, CH_2Cl_2, 85% (c) Bestmann's reagent, K_2CO_3, MeOH, 75% (d) LDA, TIPS-Cl, 82% (e) LiOH, 1:1 H_2O / THF, 86% (f) $SOCl_2$, CH_2Cl_2, 83% (g) PhOH, Na^0, Et_2O, reflux 18h, then TBAF / THF, 42%.

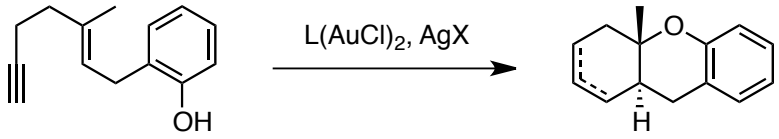
A solution of **2.9** in CH_2Cl_2 was treated with Ph_3PAuBF_4, generated by sonication of Ph_3PAuCl and $AgBF_4$ in CH_2Cl_2, followed by filtration through a glass microfiber filter. Upon stirring 24 hours at room temperature, a 1:2 mixture of olefin isomers was obtained in 75% yield (eq 2.6).[15] Participation of the pendant nucleophile during the cycloisomerization event was evidenced by the isolation of a mixture of **2.10** and **2.3**, each in diastereomerically pure form as determined by ^1H NMR analysis. It was found that upon standing at room temperature, **2.10** became completely isomerized to **2.3** in one week.



2.9 **2.10** (2.6)

Cyclization of **2.9** catalyzed by chiral bisphosphinegold(I) complexes proceeded similarly to catalysis by Ph_3PAuBF_4 (Table 2.1). The product distribution remained unchanged except for cases when the reaction time was prolonged.

Table 2.1. Evaluation of Asymmetric Induction in 1,5-Enyne Substrate **2.9**.[a]



2.9

Entry	Ligand	AgX[b]	*ee* (%)	Yield (%)
1	(R)-*tol*-Binap	$AgSbF_6$	10	81
2	(R)-*tol*-Binap	$AgBF_4$	9	83
3	(R)-*tol*-Binap	AgOPNB	4	42
4	(R)-*tol*-Binap	$AgSbF_6$[c]	8	74
5	(R)-DTBM-Segphos	$AgSbF_6$	13	73
6	(R)-*tol*-SDP	$AgSbF_6$	9	80
7	(S)-H_8-Binap	$AgSbF_6$	9	65
8	(R)-DTBM-MeO-Biphep	$AgSbF_6$	3	76

[a] Reaction Conditions: 5 mol % catalyst, CH_2Cl_2, rt, 5h. Product isolated in ca. 2:1 ratio of **2.3** and **2.10** in all cases. [b] Unless otherwise indicated, catalyst and AgX used in a 1:1 ratio. [c] 2 eq. silver salt used, relative to catalyst.

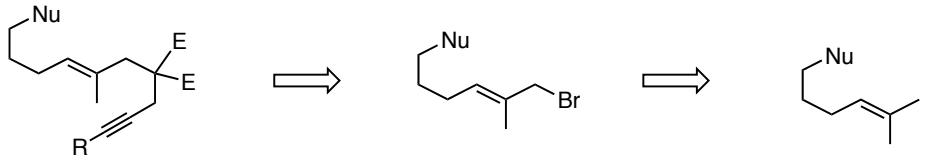
Initially, we used the cationic species derived from (R)-*tol*-Binap$(AuCl)_2$ as a catalyst, resulting in products of 10% *ee*. This result demonstrated that, in principle, induction can be achieved in the present system by chiral bisphosphinegold(I) complexes (entry 1). The use of tetrafluoroborate as counterion had no effect on the yield and enantioselectivity of the reaction (entry 2). With the more coordinating *p*-nitrobenzoate ion, conversion of **2.9** required 72 hours and led to diminished yield and enantioselectivity. The enantioselectivity was not improved by variation of the ligand scaffold (entries 5-8), nor through the use of a fully ionized digold(I) catalyst (entry 4).

At this point, we decided to examine substrates comprising a 1,6-enyne. Enantioselectivity in the cyclization of these systems had recently been demonstrated using gold(I) catalysis.[16] Owing to the highly regiocontrolled cyclization of **2.5** reported by Furstner[13] under gold(I) catalysis (Scheme 2.2), we

decided to begin our study with the carboxylate-terminated cycloisomerization of 1,6-enynes.

First, however, a route to 1,6-enynes was needed[17,18] which would generate the stereodefined *trans* trisubstituted olefin[19] and was amenable to the incorporation of different terminating groups (Scheme 2.4). The alkylation of propargyl malonates with allylic halides provided a convenient entry to 1,6-enynes. Incorporation of a nucleophile into the allylic halide would allow for rapid diversification of the propargylic substituent. Preparation of a suitable terminator-containing fragment would be possible starting with a *gem*-dimethyl olefin of type **2.11**, by means of a selective *trans*-allylic hydroxylation and bromination.

Scheme 2.4. General Approach to Nucleophile-Substituted 1,6-Enynes.

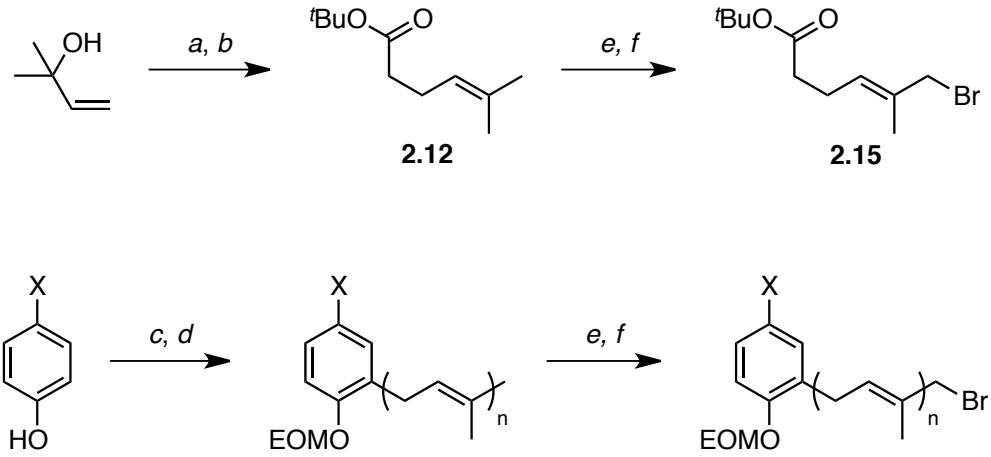


2.11

Commonly encountered in natural products chemistry and biochemistry,[20] numerous means exist for manipulation of the prenyl group. In particular, the Claisen rearrangement and related [3,3]-sigmatropic processes have been applied to the synthesis of compounds of type **2.11**.[21] The SeO_2-mediated allylic oxidation is well-suited for establishment of the *trans*-trisubstituted olefin linker owing to its stereospecific oxidation of *gem*-dimethyl olefins.[22] Thus, allyl bromides **2.15** and **2.16** were prepared from prenyl compounds **2.12** and **2.13** by treatment with SeO_2 in the presence of *tert*-butanol followed by reaction with CBr_4 / PPh_3 at low temperature (Scheme 2.5).

Prenyl ester **2.12** was furnished by a Johnson-Claisen rearrangement of 2-methylbut-3-en-2-ol and transesterification with excess *tert*-butyl acetate and catalytic sodium *tert*-butoxide under vacuum.[23] Prenylated phenol acetal **2.13a** was prepared by the regioselective *ortho* allylation of phenol with prenyl chloride over sodium[24] followed by a standard protection protocol. Despite the rather harsh conditions, this transformation could be extended to the synthesis of diene **2.14** by the use of geranyl chloride.

Scheme 2.5. Preparation of Nucleophile-Containing Coupling Fragments.[a]



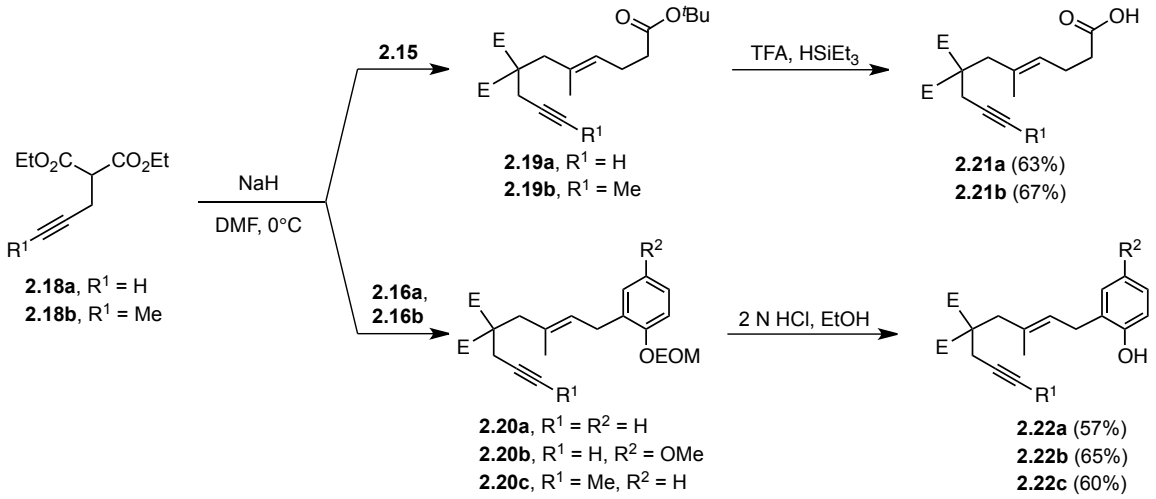
2.13a, X = H; n = 1 **2.16a**
2.13b, X = OMe; n = 1 **2.16b**
2.14, X = H; n = 2 **2.17**

[a] *Reagents and Conditions:* (a) $H_3CC(OEt)_3$, cat. $EtCO_2H$, 140°C, 18h, 83%. (b) Cat. KO^tBu, ^tBuOAc, THF, vac., 72%. (c) Na^0 (4 eq.), Allyl chloride, Et_2O, reflux 18h, 70-72% (d) $ClCH_2OEt$, $^iPrNEt_2$, CH_2Cl_2, 79%. (e) Cat. SeO_2, TBHP, CH_2Cl_2, rt, 18h, (66% from **2.12**, 52% from **2.13a**). (f) CBr_4, Ph_3P, TEA, CH_2Cl_2, -78°C, 2h. (66% for **2.15**, 72% for **2.16a**)

As depicted in Scheme 2.6 for bromides **2.15**, **2.16a** and **2.16b**, 1,6-enynes were prepared by alkylation of propargyl malonates containing both terminal and internal alkynes. Ester cleavage with trifluoroacetic acid in the presence of a cation scavenger proceeded at room temperature to provide **2.21a** and **2.21b**.[20] The phenols **2.22a**, **2.22b**, and **2.22c** were obtained by deacetalization with ethanolic hydrogen chloride at room temperature.

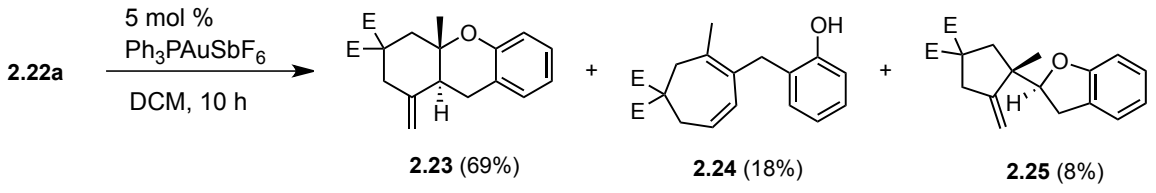
Our study of 1,6-enyne polycyclization reactions began with phenol **2.22a**. An initial trial was conducted with 5 mol % of $Ph_3PAuSbF_6$. In contrast to the purely Stork-Eschenmoser mode of reactivity reported by Furstner for carboxylic acid **2.5**,[13] the isolation of two other products suggested competing pathways were in effect for **2.22a**.[25] Thus, hexahydroxanthene **2.23** was isolated in 69% yield, along with substituted cycloheptadiene **2.24** and dihydrobenzofuran **2.25** in a 7:2:1 ratio (Scheme 2.7). The olefin geometry of **2.22a** and relative stereochemistry of **2.23** were confirmed by NOESY.

Scheme 2.6. Coupling of Subsituted Allyl Bromides with Propargyl Malonates.

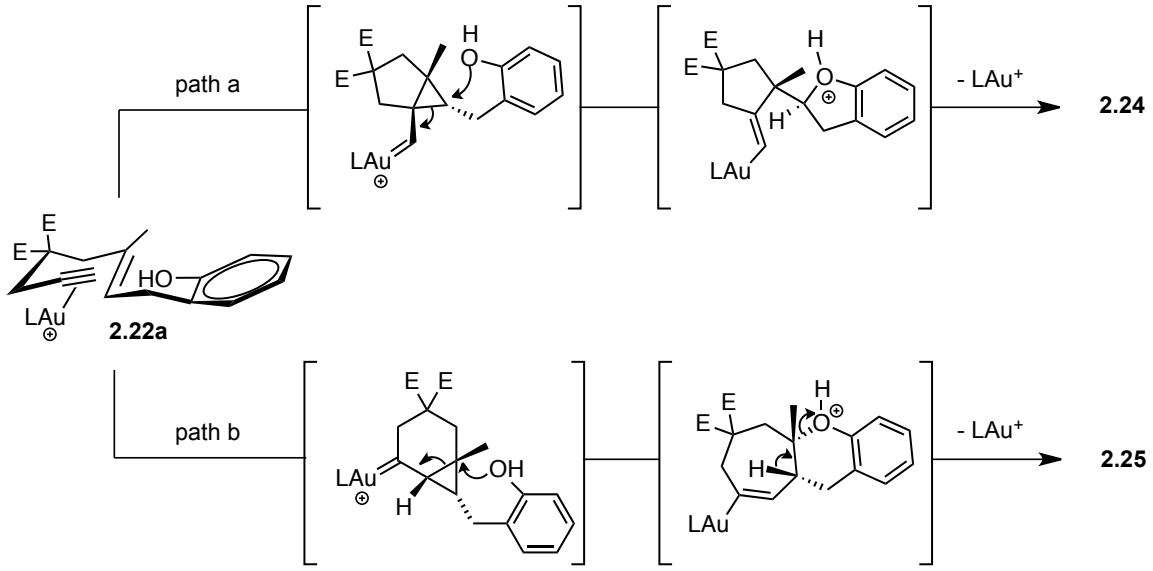


The deviation in reactivity of **2.22a** from the organized, decalin-like transition state typical of Brønsted acid-catalyzed carbocationic polyene cyclizations leading to **2.23** may be rationalized by involvement of the low-lying *d* electrons on gold (Scheme 2.8). Specifically, the 5-*exo*-dig product **2.25** corresponds to interception of the cationic intermediate by the phenolic trap at the less substituted carbon atom, standing at odds with the Stork-Eschenmoser postulate. Opening of a gold-stabilized cyclopropyl atom, on the other hand, would reasonably occur at the less crowded carbon atom (Scheme 2.8, path a).[13]

Scheme 2.7. Product Distribution of the Cyclization of Phenol **2.22a**.

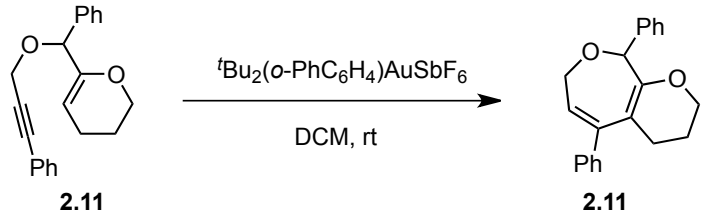


Scheme 2.8. Rationale for the formation of minor products **2.24** and **2.25**.



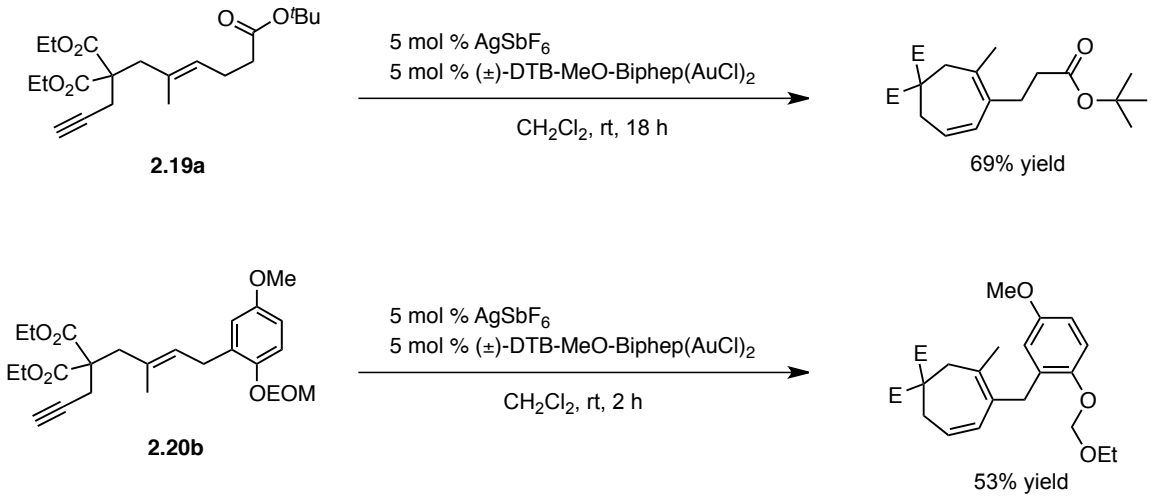
Likewise, stabilization by the phenol oxygen of the delocalized cation arising from an initial 6-*endo* cyclization (path b) followed by elimination, rather than carbon-oxygen bond formation, would plausibly lead to cycloheptadiene **2.25**.

In studies on the cycloisomerization of alkynyl enol ethers, Echavarren observed[26] similar reactivity using cationic gold and platinum complexes of electron-rich phosphines (eq. 2.7). It would appear from these examples that, regardless of the degree of gold carbenoid character in the transition state, the 7-*endo*-dig mode of cyclization for gold(I)-catalyzed cycloisomerization of 1,6-enynes is promoted by anchimeric donation toward the positively-charged olefinic carbon.



(2.7)

Scheme 2.9. Cyclization of Protected Substrates **2.19a** and **2.20b**.



Further support for this idea comes from experiments involving cyclization of protected substrates **2.19a** and **2.20b** by cationic, electron-rich bisphosphine di(gold chloride) catalysts (Scheme 2.9). In these examples, the electron-rich pendant functionality is less prone to covalent bond formation but is still capable of anchimeric interaction with the developing positive charge on carbon. The major product[27] in both cases arose from cyclization by the 7-*endo* pathway as opposed to the typical products of simple 1,6-enyne cycloisomerization.

Control experiments were conducted using 5 mol % of either $HN(Tf)_2$ or $AgSbF_6$ analyzed by ^1H NMR with an internal standard. The relatively slow, nonselective Brønsted-catalyzed cyclization of **2.22a** in CH_2Cl_2 proceeded with 60% conversion within 36 h to a complex mixture with no trace of the desired product. Treatment of **2.22a** with a suspension of $AgBF_4$ in CH_2Cl_2 gave 35% conversion at 36h, accompanied by deposition of the reduced metal. Products **2.23** and **2.24** were detected in a 2:1 ratio, accounting together for ca. 10% of the mass balance. However, when the heterogeneous mixture was sonicated in CH_2Cl_2 and then filtered into a solution of the substrate, no reaction was observed.

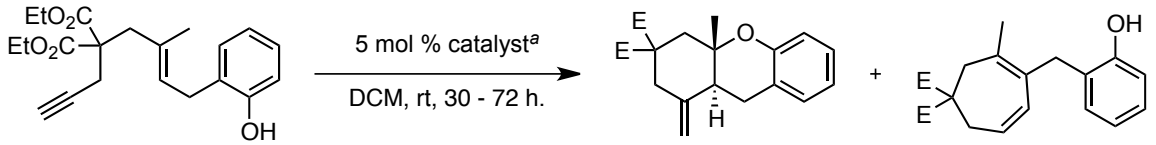
Optimization

In an initial evaluation of enantioselectivity for the formation of **2.23,** a number of chiral bisphosphine ligands were examined in the gold(I)-catalyzed cyclization of **2.22a**. In particular, attention was paid to sterically hindered ligands[28] which reports from the Toste lab[29] and others[30] cite as key to obtaining high

enantioselectivity in gold(I)-catalyzed cycloisomerizations. Relative to the 5-*endo*-dig cyclization of 1,5-enyne **2.9**, enantioselectivities were generally improved.

Representative examples from the ligand screen for the gold-catalyzed reaction of **2.22a** are given in Table 2.2. Starting out with (R)-Binap$(AuCl)_2$ led to a somewhat disappointing initial *ee* of 26% (entry 1). A distinct improvement, however, was achieved when the *p*-tolyl analog of Binap was employed as ligand (entry 2).

Table 2.2. Initial Study of Ligand, Solvent and Counterion Effects in the Enantioselective Cyclization of **2.22a**.



2.22a **2.23a** **2.24**

Entry	Ligand	X	Solvent	*ee*	Yld 2.23 (2.24) (%)
1	(R)-Binap	SbF_6	CH_2Cl_2	-26	62 (24)
2[b]	(R)-*tol*-Binap	SbF_6	CH_2Cl_2	-54	65 (30)
3	(R)-*tol*-Binap	BF_4	CH_2Cl_2	-44	61 (26)
4	(R)-*tol*-Binap	OPNB	CH_2Cl_2	-30	52 (36)
5	(R)-*tol*-Binap	SbF_6	CH_3CN	-37	35 (36)
6	(R)-*tol*-Binap	SbF_6	THF	-31	60 (20)
7	(R)-*tol*-SDP	SbF_6	CH_2Cl_2	9	56 (27)
8	(R)-MeO-Biphep	SbF_6	CH_2Cl_2	-23	55 (23)
9	(R)-DTBM-MeO-Biphep	SbF_6	CH_2Cl_2	-47	55 (23)
10	(R)-Segphos	SbF_6	CH_2Cl_2	-51	44 (28)
11	(R)-DTBM-Segphos	SbF_6	CH_2Cl_2	-5	32 (20)

[a] Catalyst prepared by salt metathesis of 1:1 Ligand$(AuCl)_2$ and silver salt followed by filtration. [b] Use of the dicationic catalyst had no effect on selectivity and lowered the yield to 40%.

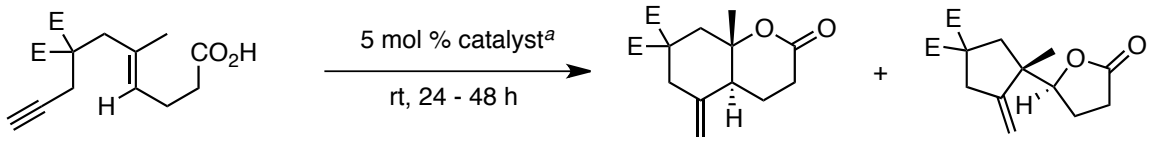
The use of the corresponding dicationic catalyst[31] did not influence selectivity, whereas evaluation of counterion effects showed erosion of the enantioselectivity on going to a less cationic gold species (entries 3-5) and to more polar reaction media (entries 6, 7). Other chiral ligand scaffolds examined (*e.g.*, entries 7-11) failed to surpass *tol*-Binap with regard to enantioselectivity. The more hindered *xyl*-Binap did, however, deliver **2.23** in 64 % *ee* (Table 2.4, entry 1).

We next turned our attention to the carboxylate-terminated substrate **2.21a**. The conditions reported by Furstner for analog **2.5** were first employed to prepare racemic **2.26** 90% yield (Table 2.3, entry 1). Proceeding with evaluation of chiral ligands in the enantioselective cyclization, a moderate decrease in yield accompanied the use of bisphosphine ligands in CH_2Cl_2 (entries 2-8). As with **2.22a**, the Binap ligands gave better selectivities with increasing substitution at the arylphosphine rings (entries 2-4).

Ultimately, ligand evaluation studies identified MeO-DTBM-Biphep as the optimal ligand for cyclization of **2.21a** in CH_2Cl_2 (entry 8). In contrast with trends in alkyl substitution within the Binap and Biphep series of ligands, using DTBM-Segphos$(AuCl)_2$ for both **2.22a** (Table 2.2, entry 5) and **2.21a** (Table 2.3, entry 9) provided racemic product, whereas **2.23** was formed in 51% *ee* using the unsubstituted Segphos ligand (Table 2.2, entry 10).

Studies aimed at optimization of the cyclization of carboxylic acid **2.21a** using MeO-DTBM-Biphep$(AuCl)_2$ (Table 2.3, entries 8 – 12) revealed a significant solvent effect on enantioselectivity. Specifically, while solvents more polar than CH_2Cl_2 had little or no effect (entry 9), a consistent increase in *ee* accompanied changing the reaction media to benzene, then toluene, reaching 87% with *m*-xylene (entries 10-12). Finally, with the more lipophilic bisphosphine MeO-DTB-Biphep ligand (**2.28**), we observed formation of **2.26** in 92% *ee* with a catalyst loading as low as 1 mol % (entry 13). Moreover, use of **2.28**$(AuCl)_2$ as a catalyst eliminated the formation of minor side-products observed with other bisphosphines; analysis of the crude ^{1}H NMR spectrum revealed the essentially quantitative conversion of **2.21a** to a mixture of **2.26** and **2.27** in 86% and 11% yield, respectively. A single crystal of the complex **2.28**$(AuCl)_2$ was obtained from a pentane solution, providing the x-ray structure presented in Figure 2.2.

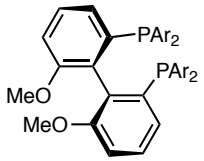
Table 2.3. Optimization of Conditions for Enantioselective Lactonization of **2.21a**.



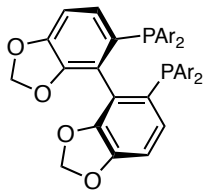
2.21a **2.26a** **2.27**

Entry	Ligand	Solvent	*ee* (%)	Yld. 2.26 (2.27) (%)
1	Ph_3P	CH_2Cl_2	--	90 (4)
2	(S)-Binap	CH_2Cl_2	-17	83 (7)
3	(R)-*tol*-Binap	CH_2Cl_2	23	72 (8)
4	(R)-*xyl*-Binap	CH_2Cl_2	40	70 (10)
5	(R)-DTBM-Segphos	CH_2Cl_2	2	81 (8)
6	(R)-MeO-DM-Biphep	CH_2Cl_2	36	67 (9)
8	(R)-MeO-DTBM-Biphep	CH_2Cl_2	46	71 (7)
9	(R)-MeO-DTBM-Biphep	$MeNO_2$	47	72 (3)
10	(R)-MeO-DTBM-Biphep	benzene	83	76 (8)
11	(R)-MeO-DTBM-Biphep	toluene	85	77 (9)
12	(R)-MeO-DTBM-Biphep	*m*-xylene	87	76 (12)
13	(R)-MeO-DTB-Biphep (**2.28**)	*m*-xylene	92[b]	86 (11)

[a] Catalyst prepared by salt metathesis of Ligand$(AuCl)_2$ and equimolar $AgSbF_6$ followed by filtration. [b] Identical results were obtained using 1 mol % catalyst.

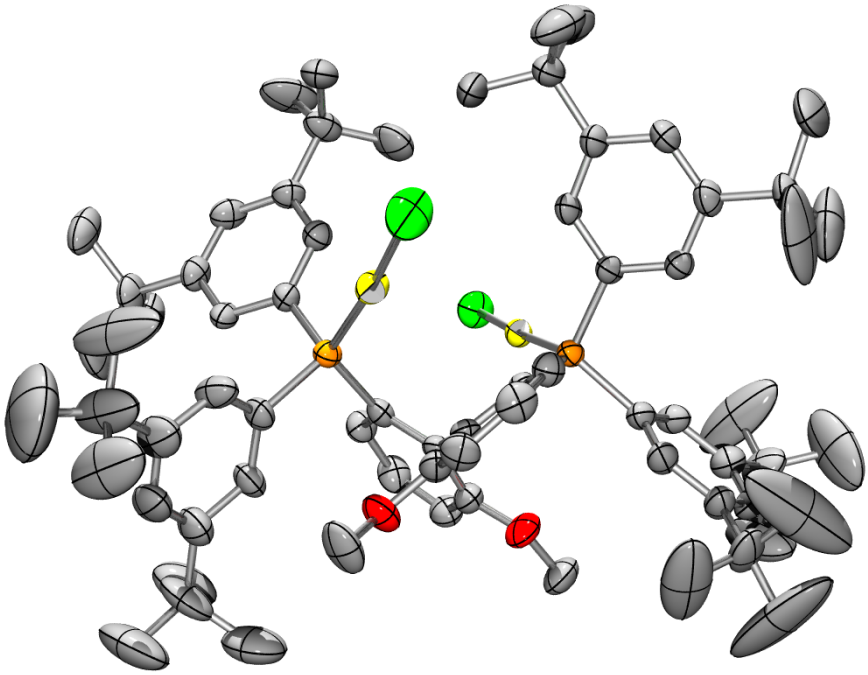


MeO-DTBM-Biphep, Ar = 3,5-(^{t}Bu)$_2$-4-MeO-C_6H_2
MeO-DTB-Biphep (**2.28**), Ar = 3,5-(^{t}Bu)$_2C_6H_3$

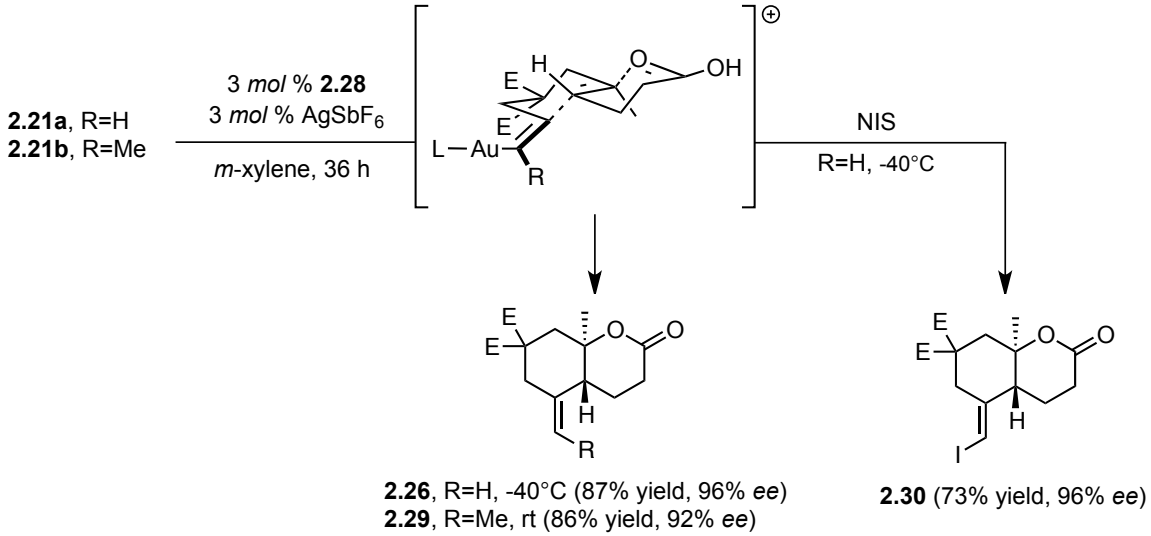


DTBM-Segphos, Ar = 3,5-(^{t}Bu)$_2$-4-MeO-C_6H_2

Figure 2.2. X-Ray Diffraction Structure of Optimized Catalyst **2.28**$(AuCl)_2$.



Scheme 2.10. Optimized conditions for asymmetric lactonization.



Enantioselectivity in the lactonization of **2.21a** was further improved to 96% by lowering the reaction temperature to -40°C (Scheme **2.10**).[32] We anticipated that catalyst turnover by iododeauration could outcompete protonolysis and thereby make accessible synthetically useful enantioenriched vinyl iodides.[33] Thus, it was found that repeating the cyclization in the presence of a slight excess N-iodosuccinimide led to isolation of iodide **2.30** in 73% yield. In accord with the proposed mechanism, the resulting vinylgold intermediate would plausibly be reactive toward the electrophilic iodine source. This notion was supported by the identical enantiomeric ratios obtained for **2.26** and **2.30** (Scheme 2.10).

Nonterminal alkynes underwent slower conversion to product, however, the degree of enantioselectivity was unchanged. For example, no reaction was observed with **2.21b** after several days at -40°C with 3 mol % catalyst, but at room temperature the encumbered alkene **2.29** was obtained in 86% yield and 92% *ee*.

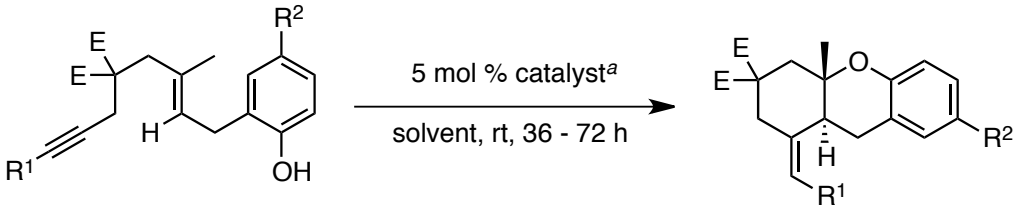
Substrate Scope

In light of the above results, we were interested in exploring the influence of aromatic solvents on the cyclization of phenol substrates (Table **2.4**). Cyclization of **2.22a** in CH_2Cl_2 using *xyl*-Binap$(AuCl)_2$ gave **2.23a** in 64% *ee* (entry 1); however no reaction was observed when **2.22a** was treated with a filtered benzene solution prepared by sonication of (S)-*xyl*-Binap$(AuCl)_2$ and $AgSbF_6$, even with prolonged periods of salt metathesis. Formation of the catalyst *in situ* resulted in the slow and nonselective formation of **2.23a (**15% yield, 32% *ee*) along with increased side-reaction products. On the other hand, addition of the catalyst formed in CH_2Cl_2 to **2.21a** in the same volume of xylene (entry 2), gave 72% *ee* along with a slight increase in yield (65%).

As illustrated by the selectivity of Reetz' helical, C_3-symmetric monophosphite ligand **2.31**[34] in benzene (80% *ee*, entry 3) as opposed to CH_2Cl_2 (60% *ee*, entry 4), this cooperative effect is not restricted to MeO-Biphep ligands, or even C_2-symmetric bisphosphines in general. The lipophilicity of the ligand, and thus it's ability to support homogeneous cationic gold(I) complexes in apolar media appears to play a role in the observed solvent effect.

The conditions optimized for cyclization of carboxylic acid **2.22a** (Table 2.3, entry 13) were successfully extended to phenol-terminated cyclizations. Thus, cyclization of **2.21a** in xylene using precatalyst **2.28**$(AuCl)_2$ gave **2.23** in 96% *ee* and 94% yield (entry 5). Similar results were obtained using non-terminal alkyne **2.21b** (entry 6) and methoxyaryl substrate **2.21c** (entry 7).

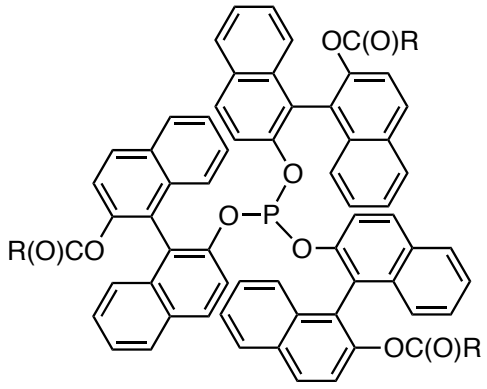
Table 2.4. Solvent and Catalyst Effects on the Enantioselective Cyclization of Phenol Substrates.



2.22a, $R^1 = R^2 = H$ **2.23a**
2.22b, $R^1 = H$, $R^2 = OMe$ **2.23b**
2.22c, $R^1 = Me$, $R^2 = H$ **2.23c**

Entry	Ligand	R^1	R^2	Solvent	*ee* (%)	Yield (%)
1	(S)-xyl-Binap	H	H	CH_2Cl_2	64	52
2	(S)-xyl-Binap	H	H	1:1 CH_2Cl_2 / *m*-xylene[b]	72	65
3	(R)-**2.31**	H	H	CH_2Cl_2	-60	53
4	(R)-**2.31**	H	H	*m*-xylene	-80	67
5	(R)-**2.28**	H	H	*m*-xylene	96	93
6	(R)-**2.28**	Me	H	*m*-xylene	93	93
7	(R)-**2.28**	H	OMe	*m*-xylene	98	94

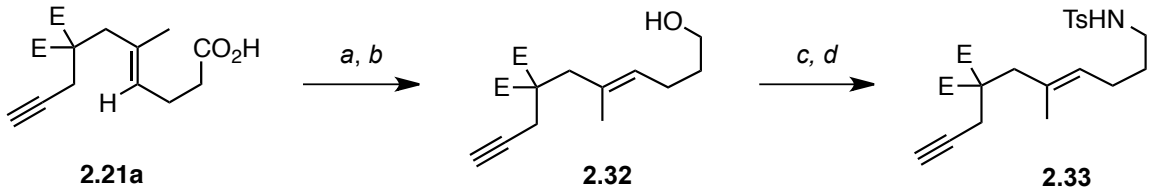
[a] Catalyst prepared by salt metathesis of the gold chloride precatalyst and $AgSbF_6$ (1:1) followed by filtration. [b] No reaction was observed when catalyst generation was performed in either *m*-xylene or benzene.



2.31, R = 1-adamantyl

The cooperative effect of the hindered chiral ligand **2.28** with aromatic solvents consistently provided high enantioselectivity and yield for 1,6-enynes, insensitive to modification of the terminator or alkylation at the alkyne terminus. For example, phenolic substrates **2.21b** and **2.21c**, both cyclized with the same degree of induction as the parent **2.21a**, despite having structural features expected to perturb the reaction stereoelectronics.

Scheme 2.11. Synthesis of Tosylamide Substrate.



2.21a **2.32** **2.33**

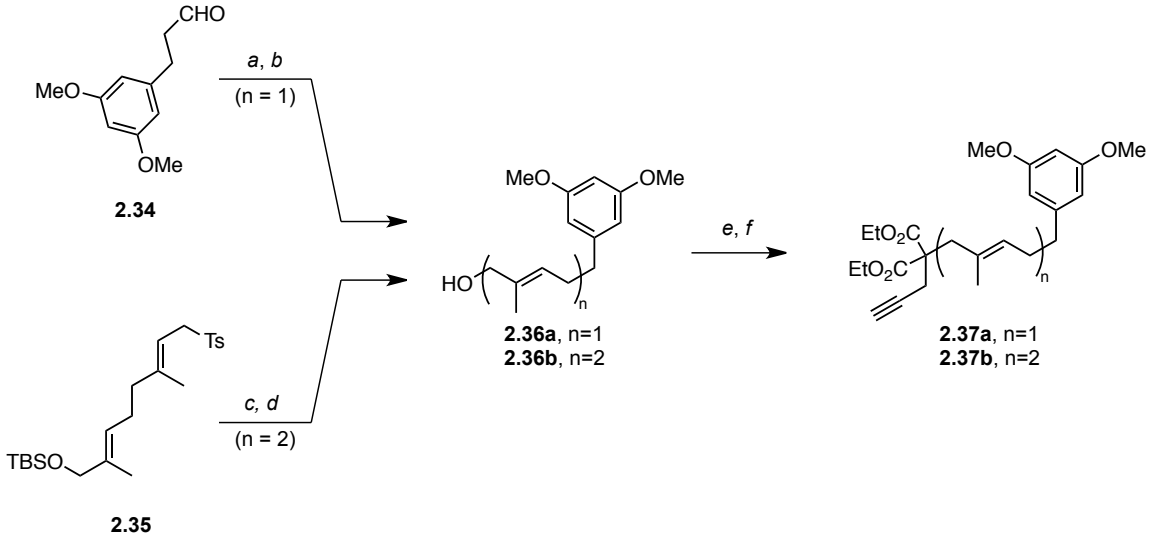
Reagents and Conditions: (a) ^{i}BuOCOCl, NMM, THF, 0°C (b) $NaBH_4$, MeOH, 0°C, 3h, 73% from **2.21a**. (c) DIAD, Ph_3P, TsNHBoc, THF, rt, 18h (d) DMSO, 170°C, 30 min, 69% from **2.32**.

We therefore continued with our efforts establishing the scope of the enantioselective bicyclization process with regard to the nature of the terminating group. A surplus of carboxylic acid substrate **2.22a** made a fine starting point for preparation of tosylamide substrate **2.33** (scheme 2.11).

The acid functionality of **2.22a** was selectively reduced to the primary alcohol **2.32** in 73% yield, through initial reaction with ethyl chloroformate then reduction of the crude mixed anhydride by $NaBH_4$ in ethanol.[35] The tosylamide functionality was conveniently introduced by a Mitsunobu reaction of **2.32** with *tert*-butyl tosylcarbamate followed by pyrolysis in degassed DMSO at 170°C, providing a 69% yield of **2.33** over the two-step sequence.

Scheme **2.12** depicts the synthesis of arene-terminated substrate **2.37a** and homolog **2.37b**. Allylic alcohol **2.36a** was prepared by initial olefination of aldehyde **2.34** with 2-(triphenylphosphoranylidene)propanal in 71% yield.[36] The crude aldehyde was reduced in methanolic sodium borohydride for one hour at 0°C to give **2.36a**, which was elaborated to substrate **2.37a**.

Scheme 2.12. Synthesis of Arene-Terminated Substrates **2.37a** and **2.37b**.

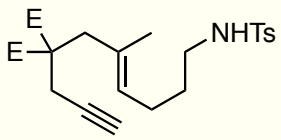
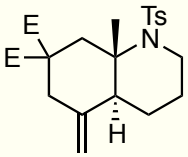
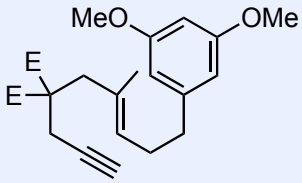
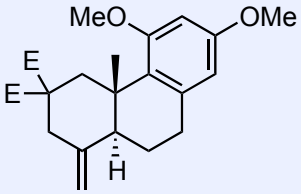
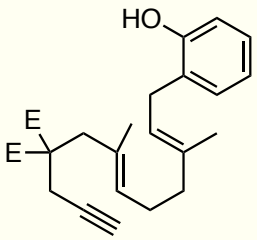
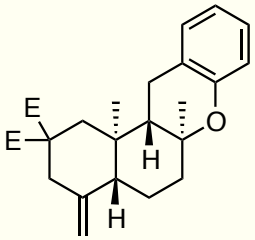
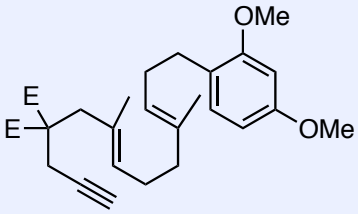
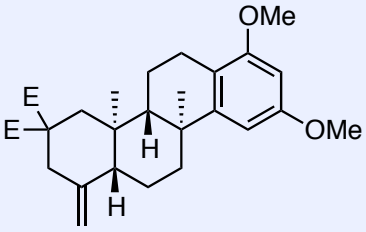


(a) $Ph_3P{=}C(CH_3)CHO$, benzene, 90°C, 18h, 71%. (b) $NaBH_4$, MeOH, 0°C, 1h, 92%. (c) *n*BuLi, 3,5-$(MeO)_2$-$C_6H_4CH_2Br$**,** THF, -78°C to 0°C, 2h then $Pd(Oac)_2$/dppb, $LiEt_3BH$, 1h, rt. (d) TBAF, THF, 0°C, 52% from **2.35**. (e) CBr_4, Ph_3P, TEA, CH_2Cl_2, -78°C, 2h. (f) Na^-**2.18a**, DMF, 0°C, 63% (**2.37a**), 66% (**2.37b**).

The apparent insensitivity to the nature of the trapping group suggests that the enantioselectivity is determined in the cycloisomerization event with some degree of asynchronicity, permitting chiral information to be propagated to additional chiral centers due to the diastereoselectivity described by the Stork-Eschenmoser postulate.[37] As a consequence, we anticipated that selectivity would be maintained if a second olefin were introduced between the initiating alkyne and trapping groups.[38] This would result in the simultaneous formation of four contiguous stereocenters in a gold(I)-catalyzed tricyclization process, assuming continued adherence to the Stork-Eschenmoser postulate.[37]

Bisfunctionalized linker **2.35**, encompassing the full diene system of substrate **2.37b**, was prepared by selective oxidation of geranyl tosyl sulfone[39] using SeO_2/TBHP.[40] The lithium salt of **2.35** was alkylated by 3,5-dimethoxybenzyl chloride and then desulfonylated using Overman's modification[41] of the one pot process reported by Orita.[42] Deprotection of the silyl ether and application of the usual malonate alkylation sequence gave 26dd26yne **2.37b** in 66% yield from **2.36b**. A second tricyclization substrate, diene **2.38**, was prepared from geranyl bromide **2.14**.

Table 2.5. Scope of the Optimized Asymmetric Au(I)-Catalyzed Polycyclization.[a]

Entry	Enyne	Polycycle	*ee* (%)	Yield (%)
1			92	75
	2.33	**2.39**		
2			96	94
	2.37a	**2.40**		
3			88	50
	2.38	**2.41**		
4			97	61
	2.37b	**2.42**		

[a] Cyclization conditions: 3 mol % catalyst derived from salt metathesis of 1:1 (R)-**2.28**$(AuCl)_2$ and $AgSbF_6$.

Figure 2.3. X-Ray Structure of **2.26**.

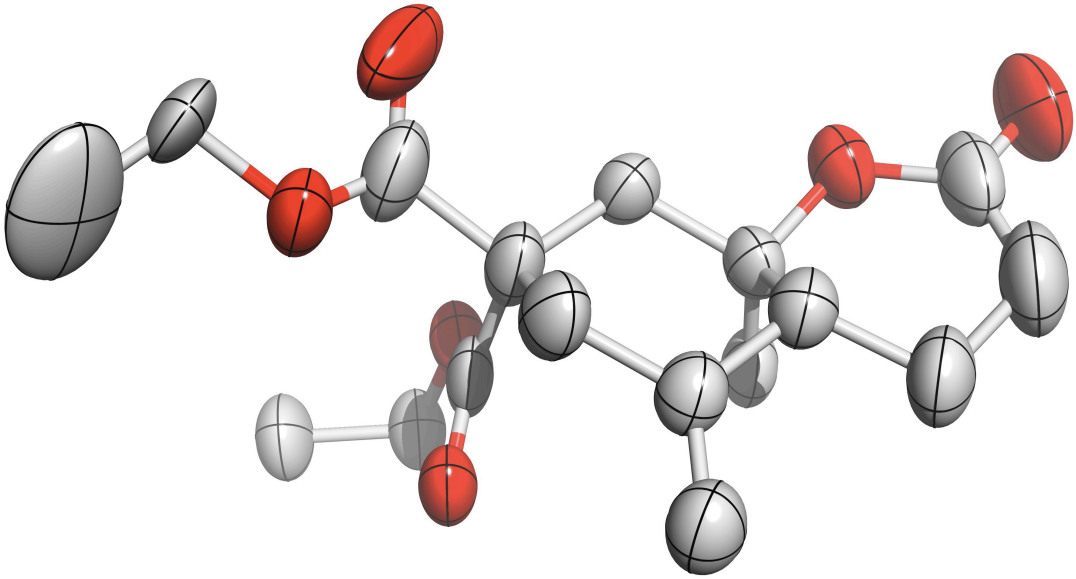
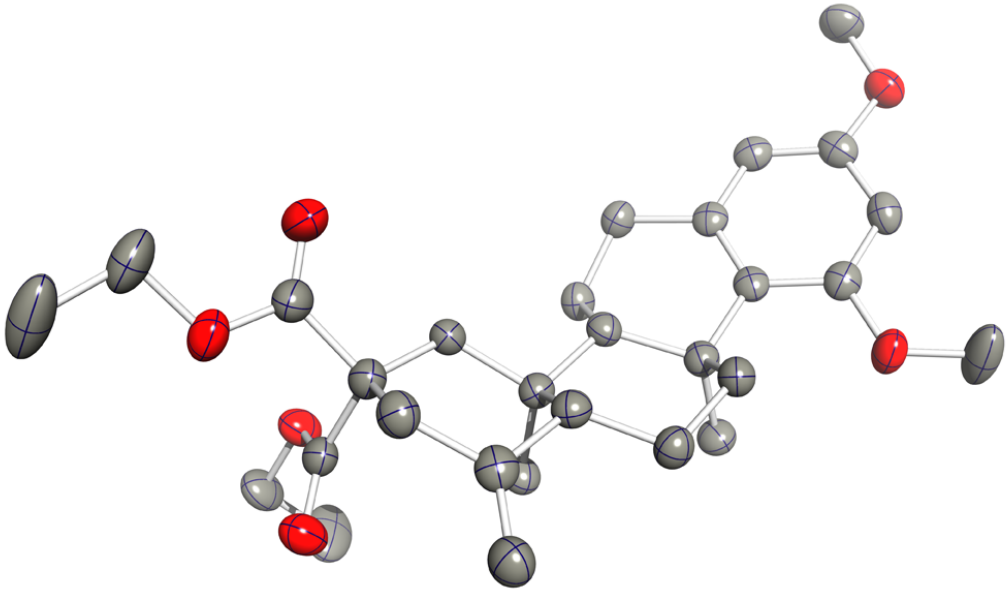


Figure 2.4. X-Ray Structure of **2.42**.

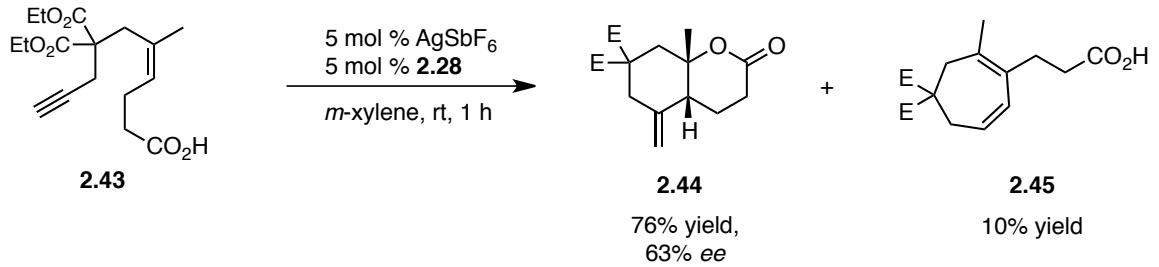


Cyclization of enynes **2.33** and **2.37a** using precatalyst **2.28**$(AuCl)_2$ resulted in the formation of the anticipated cyclization products both in greater than 90% *ee* (Table 2.5, entries 1 and 2). Tosylamide **2.33** furnished bicycle **2.39** in 75% yield. The angular tricycle **2.40** produced from substrate **2.37a** demonstrates the formation of a fully carbocyclic system encompassing a hindered, benzylic quaternary center with no negative effects on yield or selectivity.

Subjection of ynedienes **2.38** and **2.37b** to the optimized conditions for asymmetric cyclization gave diastereomerically pure **2.41** and **2.42** as the sole tricyclization product in each case (entries 3 and 4). The mixture of mono- and bicyclic untrapped byproducts formed in both cases reflects the increased entropic cost of preorganization associated with transition states leading to **2.41** or **2.42**. X-ray structures were obtained from crystals of **2.26** (Figure 2.3) and **2.42** (Figure 2.4) and provide structural confirmation and assignment of absolute stereochemistry. Notably, the same sense of chirality was induced by (R)-**2.28** ligand in both cases.

Finally, substrate **2.43** was prepared to examine the cyclization of a *cis* olefin-containing enyne (Scheme 2.13). Cyclization under the optimized conditions using (R)-**2.28**$(AuCl)_2$ gave the anticipated *syn*-fused ring system **2.44** in 76% yield and 63% *ee*. Notably, 10% of the expected yield was accounted for by cycloheptadiene **2.45**, which was only observed in trace amounts in the cyclization of (E)-olefin **2.21a**.

Scheme 2.13. Synthesis of *cis*-Lactone from (Z)-Olefin Substrate.



Conclusion

With the development of the methodology described in Chapter 2, we have uncovered the first example of an asymmetric polyene cyclization initiated by an alkyne. Excellent enantioselectivities were obtained in both bi- and tricyclization reactions of 1,6-enynes catalyzed by monocationic biphep-derived bisphosphine digold complexes. Diastereospecific cyclization of various oxygen, carbon and nitrogen traps proceeded with consistently high enantioselectivity and yield when using aromatic solvents such as *m*-xylene.

Supporting Information

General Information

Unless otherwise stated, all commercial materials were used without further purification. Solvents were purchased from EM-Science and were dried by passage through activated alumina, except *meta*-xylene. Solvents used in polycyclization reactions were stored over 4Å molecular sieves. Silver tetrafluoroborate ($AgBF_4$), silver perchlorate ($AgClO_4$) and silver hexafluoroantimonate ($AgSbF_6$) were obtained from Aldrich Chemical Company and stored in the dark under an inert atmosphere. Silver salts kept under argon in a sealed vial and protected from light could be used several times before succumbing to deliquescence. Bisphosphine ligands were obtained from Solvias and Takasago. $AuCl_3$ was provided by Johnson Matthey. Chiral digold chloride complexes were prepared as previously described by previous work from this lab.[43] Complexes used for ligand optimization provided spectra in agreement with those previously described.[44] Except for the inhomogeneous mixture arising in the synthesis of **2c**, small scale reactions were not stirred beyond a brief mixing upon addition of the catalyst. Thin layer chromatography (TLC) analysis of reaction mixtures was performed on Merck silica gel 60 F_{254} TLC plates and flash chromatography was carried out on Sorbent Technologies 40-63 D 60 Å silica gel. ^1H and ^{13}C NMR spectra were recorded with Bruker AVQ-400, AVB-400, AV-500 or AV-600 spectrometers using either $CDCl_3$ or C_6D_6, and are internally referenced to residual protio solvent signals. ^1H NMR multiplicities are reported as follows: m = multiplet; s = singlet; d = doublet; t = triplet; q = quartet. All ^{13}C NMR spectra were obtained with proton decoupling. Enantiomeric ratios were measured by chiral HPLC employing a Shimidzu VP Series instrument equipped with SPD-M10A microdiode array detector using a Chiral PAK AD-H column.

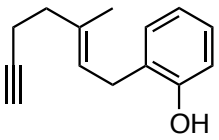
General Procedure for Enantioselective Polycyclizations.

A mixture of $AgSbF_6$ (0.8 mg, 2.2 μmol) and the bisphosphine digold(I) chloride complex (3.32 mg, 2.22 μmol) is suspended in 300 μL of *m*–xylene in a sealed vial, and sonicated or stirred magnetically for 15 min at room temperature). The resulting suspension is filtered through a glass microfiber plug directly into a solution of substrate (15 mg, 0.044 mmol) in 600 μl of *m*-xylene,

thorough mixing is ensured and the resulting homogenous solution is allowed stand until such time as the substrate was fully consumed as judged by TLC or ^{1}H NMR analysis. Determination of yield was made by calibration with an internal standard (9-bromophenanthrene) prior to addition of catalyst. Upon consumption of the starting material, an aliquot containing ca. 4 mg. of crude product was concentrated under a stream of N_2 until a thick oil was obtained. This was dissolved in 100 μL C_6D_6 and concentrated under flowing N_2 twice, providing a residual oil free from excessive *m*-xylene which was subsequently analyzed by ^{1}H NMR. The product was isolated in analytically pure form by evaporation of the reaction mixture to a volume of ca. 100 μL which was then eluted through a short silica column. Products **2a** and **15** provided crystals suitable for x-ray analysis (see below for details) permitting assignment of the absolute stereochemistry. Notably, cyclization by the catalyst derived from (R)-DTB,MeO-Biphep$(AuCl)_2$ proceeded with the same sense of enantioselectivity in both cases. Crystallographic data provided.

Experimental Details

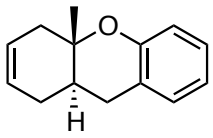
(E)-2-(3-methylhept-2-en-6-yn-1-yl)phenol (2.9).[11]



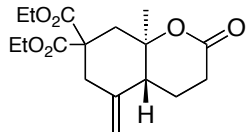
The synthesis and characterization of this compound has been reported by Gagne et al. All spectral data were in accord with those previously reported.

(4aS,9aR)-4a-methyl-4,4a,9,9a-tetrahydro-1H-xanthene (2.3).[11]

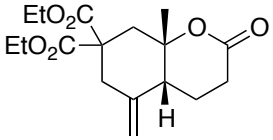
Prepared from **2.9** in accord with the general procedure for cyclization. The characterization of this compound has been reported by Gagne et al. All spectral data were in accord with those previously reported.



(4R,8R)-Diethyl-8-methyl-5-methylene-2-oxohexahydro-2*H*-chromene-7,7(3*H*)-dicarboxylate (2.26a).



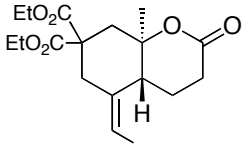
Prepared from **2.21a** in accord with the general procedure for cyclization. Chromatography (1:1 hexanes : diethyl ether) provided a clear oil which was recrystallized by slow evaporation (3:2 dichloromethane : hexanes) to provide transparent needles suitable for x-ray analysis, crystallographic data provided. **^{1}H NMR** (600 MHz, C_6D_6): δ 7.07 (dd, *J* = 7.0, 1.4 Hz, 2H), 6.97 (d, *J* = 7.6 Hz, 1H), 6.87-6.85 (m, 1H), 5.16 (d, *J* = 1.0 Hz, 1H), 4.73 (d, *J* = 1.1 Hz, 1H), 3.97-3.83 (m, 4H), 3.38 (dd, *J* = 13.5, 2.2 Hz, 1H), 3.16 (dd, *J* = 13.6, 2.1 Hz, 1H), 2.74 (d, *J* = 13.7 Hz, 1H), 2.58 (dd, *J* = 16.0, 12.8 Hz, 1H), 2.36 (dd, *J* = 16.1, 4.6 Hz, 1H), 2.24 (s, 1H), 1.04 (s, 3H), 0.86 (t, *J* = 8.0 Hz, 6H). **^{13}C NMR** (151 MHz, C_6D_6): δ 170.67, 169.91, 152.81, 142.91, 129.65, 121.06, 120.0`4, 117.39, 111.03, 99.96, 76.53, 61.29, 60.84, 54.51, 43.92, 43.16, 40.00, 24.38, 17.24, 13.49. **MS** HRMS (ESI) calc. for $[C_{21}H_{27}O_5]^+$: 359.1850, found: 358.1853. **HPLC** (95:5 hexanes : isopropanol, 0.7 mL/min, λ_{max}= 205 nm). T_R 27.58 min (major), 25.31 (minor): 91% *ee.*



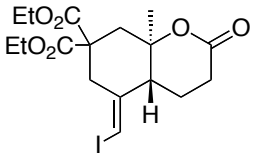
(4R,8S)-diethyl 8a-methyl-5-methylene-2-oxohexahydro-2H-chromene-7,7(3H)-dicarboxylate (2.44).

Prepared from **2.43** in accord with the general procedure for cyclization. **1H-NMR** (600 MHz, C6H6): δ 5.15 (s, 1H), 4.67 (d, *J* = 0.4 Hz, 1H), 4.23-4.11 (m, 2H), 3.93 (qt, *J* = 7.2, 3.6 Hz, 2H), 3.06 (d, *J* = 13.9 Hz, 1H), 2.79 (dd, *J* = 14.7, 1.8 Hz, 1H), 2.36-2.26 (m, 3H), 1.91 (ddd, *J* = 18.7, 8.9, 5.0 Hz, 1H), 1.58 (t, *J* = 5.1 Hz, 1H), 1.46 (ddt, *J* = 14.2, 8.8, 5.2 Hz, 1H), 1.25 (33dd, *J* = 14.4, 8.9, 7.3, 5.2 Hz, 1H), 1.05 (t, *J* = 7.1 Hz, 3H), 0.95 (s, 3H), 0.89 (t, *J* = 7.1 Hz, 3H). **13C-NMR** (151 MHz, C6H6): δ 170.68, 169.38, 167.62, 141.04, 114.00, 81.14, 61.35, 61.11, 53.38, 42.62, 40.95, 37.96, 27.33, 26.14, 18.91, 13.66, 13.53. **MS** HRMS (ESI) calc. for $[C_{21}H_{27}O_5]^+$: 359.1850, found: 358.1855.

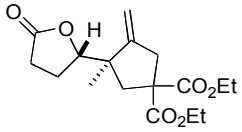
(4R,8R,Z)-diethyl-5-ethylidene-8a-methyl-2-oxohexahydro-2H-chromene-7,7(3H)-dicarboxylate (2.29).

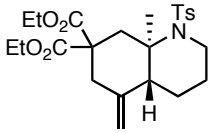


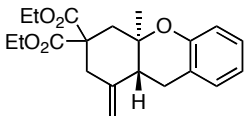
Prepared from **2.21b** in accord with the general procedure for cyclization. Flash chromatography (1:1 hexanes : diethyl ether) provided the lactone as a clear oil. **^{1}H-NMR** (600 MHz, C_6D_6): δ 5.55 (t, *J* = 7.0 Hz, 1H), 5.30 (td, *J* = 7.0, 1.2 Hz, 1H), 5.27 (d, *J* = 6.9 Hz, 1H), 4.04-3.93 (m, 4H), 3.38 (s, 5H), 3.23 (s, 2H), 3.14 (d, *J* = 2.7 Hz, 2H), 2.63 (dt, *J* = 16.8, 8.2 Hz, 2H), 2.10 (q, *J* = 7.3 Hz, 2H), 2.04 (t, *J* = 7.5 Hz, 2H), 1.77 (dt, *J* = 5.4, 2.7 Hz, 1H), 1.61 (s, 3H), 1.52 (s, 3H), 0.93 (t, *J* = 7.1 Hz, 6H). **^{13}C-NMR** (150 MHz, C_6D_6): δ 170.59, 169.81, 167.36, 131.57, 124.38, 82.75, 61.50, 60.91, 55.01, 48.10, 43.88, 43.61, 30.73, 21.35, 21.22, 13.61, 13.24. **MS** HRMS (ESI) calc. for $[C_{18}H_{27}O_6]^+$**:** 339.1802, found: 339.1809. **HPLC** (95:5 hexanes : isopropanol, 0.4 mL/min, λ_{ax}= 205 nm). T_R 26.86 min (major), 25.46 min (minor): 92% *ee.*



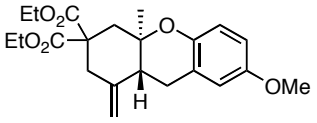
(4R,8R,E)-diethyl-5-(iodomethylene)-8a-methyl-2-oxohexahydro-2H-chromene-7,7(3H)-dicarboxylate (2.30). Prepared from **2.21a** in accord with the general procedure for cyclization with the following modification: Immediately before the addition of catalyst, 2.1 equivalents of N-iodosuccinimide were added at -40°C, and this temperature was maintained for 18 hours with rapid stirring. Purified by flash chromatography (1:1 hexanes : Et_2O) to provide the lactone as a slightly tan oil. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 5.29-5.26 (m, 1H), 4.16 (qq, *J* = 10.1, 7.0 Hz, 4H), 2.75 (s, 2H), 2.68 (d, *J* = 2.5 Hz, 2H), 2.36-2.29 (m, 4H), 1.74 (t, *J* = 2.5 Hz, 3H), 1.23 (d, *J* = 14.2 Hz, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 170.36, 170.34, 169.50, 143.95, 82.27, 78.29, 62.47, 62.04, 54.51, 47.77, 43.02, 40.54, 29.14, 21.00, 19.09, 14.21, 14.11. **MS** HRMS (EI) calc. for $[C_{17}H_{23}O_6I]^+$: 473.0432, found: 473.0438. **HPLC** (95:5 hexanes : isopropanol, 0.4 mL/min, λ_{ax}= 225 nm). T_R 65.14 min (major), 59.83 min (minor): 96 % *ee.*

(R)-diethyl 3-methyl-4-methylene-3-((S)-5-oxotetrahydrofuran-2-yl)cyclopentane-1,1-dicarboxylate (2.27).  Prepared from **2.21a** in accord with the general procedure for cyclization, isolated by flash chromatography (2:3 diethyl ether : hexanes) as a minor product along with **2.26a.** Analytically pure material was obtained from the cyclization of triester **2.19a**, providing **2.27** as the major isolable product along with **2.26a** as further purified by trituration with cold pentane isolation of the supernate. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 4.93 (t, *J* = 2.0 Hz, 1H), 4.73 (dd, *J* = 2.6, 1.6 Hz, 1H), 4.03-3.92 (m, 4H), 3.73 (t, *J* = 7.9 Hz, 1H), 3.21 (t, *J* = 2.6 Hz, 1H), 3.20 (d, *J* = 1.3 Hz, 1H), 2.59 (d, *J* = 14.0 Hz, 1H), 2.44 (dd, *J* = 14.0, 1.1 Hz, 1H), 1.90-1.84 (m, 1H), 1.72 (dt, *J* = 17.4, 10.3 Hz, 1H), 1.20-1.14 (m, 3H), 0.94-0.89 (m, 11H). **^{13}C-NMR** (125 MHz, $CDCl_3$): δ 175.73, 172.20, 171.84, 154.60, 108.52, 85.63, 62.19, 61.99, 58.57, 48.37, 43.38, 42.76, 29.33, 24.33, 23.52, 14.45, 14.45. **MS** HRMS (ESI) calc. for $[C_{17}H_{24}O_6Na]^+$: 347.1465, found: 347.1463.

(4R,8R)-diethyl-8a-methyl-5-methylene-1-tosyloctahydroquinoline-7,7(1H)-dicarboxylate (2.39).  Prepared from **2.33** in accord with the general procedure for cyclization. Purified by flash chromatography (1:1 hexanes : diethyl ether), providing the title compound as a clear oil. **^{1}H-NMR** (500 MHz, C_6D_6): δ 7.87 (d, J = 8.3 Hz, 2H), 6.84 (d, J = 7.9 Hz, 2H), 5.13 (d, J = 1.3 Hz, 1H), 4.59 (d, J = 1.5 Hz, 1H), 4.06 (dt, J = 13.1, 3.5 Hz, 1H), 4.03-3.80 (m, 5H), 3.33 (dd, J = 13.3, 1.9 Hz, 1H), 2.90 (td, J = 12.5, 3.6 Hz, 1H), 2.71 (d, J = 14.0 Hz, 1H), 2.13 (d, J = 13.4 Hz, 1H), 1.87-1.84 (m, 4H), 1.37-1.25 (m, 2H), 1.20-1.16 (m, 1H), 1.07 (q, J = 6.0 Hz, 4H), 0.95 (t, J = 7.1 Hz, 3H), 0.84 (t, J = 7.1 Hz, 3 H). **^{13}C-NMR** (100 MHz, C_6D_6): δ 178.83, 171.49, 171.21, 143.69, 143.12, 140.47, 129.80, 127.40, 112.64, 63.64, 62.11, 61.63, 55.14, 50.42, 43.66, 41.98, 40.27, 25.76, 22.52, 21.86, 14.67, 14.31, 14.22. **MS** HRMS (ESI) calc. for $[C_{24}H_{34}NO_6S]^+$: 464.2101, found: 464.2105. **HPLC** (95:5 hexanes : isopropanol, 1 mL/min, λ_{max}= 206 nm). T_R min 20.26 (major), 15.71 min (minor): 90% ee.

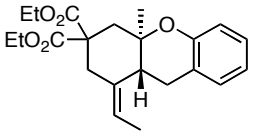


(4R,9R)-diethyl 4-methyl-1-methylene-4,4,9,9-tetrahydro-1H-xanthene-3,3(2*H*)-dicarboxylate (2.23). Prepared from **2.22a** in accord with the general procedure for cyclization. Purified by flash chromatography (4:1 hexanes : diethyl ether), providing the title compound as a clear oil. **^{1}H NMR** δ (600 MHz, C_6H_6): δ 7.09-7.02 (m, 2H), 6.97 (d, J = 7.6 Hz, 1H), 6.86 (td, J = 6.9, 2.6 Hz, 1H), 5.16 (d, J = 1.0 Hz, 1H), 4.73 (d, J = 1.1 Hz, 1H), 3.98-3.82 (m, 4H), 3.38 (dd, J = 13.5, 2.2 Hz, 1H), 3.16 (dd, J = 13.6, 2.1 Hz, 1H), 2.74 (d, J = 13.7 Hz, 1H), 2.58 (dd, J = 16.0, 12.8 Hz, 1H), 2.36 (dd, J = 16.1, 4.6 Hz, 1H), 2.23 (d, J = 13.5 Hz, 1H), 2.09-2.06 (m, 1H), 1.04 (s, 3H), 0.86 (t, J = 8.0 Hz, 6H). **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 170.67, 169.91, 152.81, 142.91, 129.65, 121.06, 120.04, 117.39, 111.03, 99.96, 76.53, 61.29, 60.84, 54.51, 43.92, 43.16, 40.00, 24.38, 17.24, 13.53, 13.49. **MS** HRMS (ESI) calc. for $[C_{21}H_{27}O_5]$+ : 359.1853, found: 359.1850. **HPLC** Chiralpak AD-H column (98:2 hexanes : ethanol, 0.5 mL/min) t_R 19.84 min (major), 14.95 min (minor): 92% *ee*.



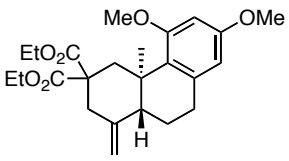
(4R,9R)-diethyl 7- methoxy-4-methyl-1-methylene-4,4,9,9-tetrahydro-1H-xanthene-3,3(2H)-dicarboxylate (2.23b). Prepared from **2.22b** in accord with the general procedure for cyclization. (4:1 hexanes : diethyl ether), providing the title compound as a clear oil. **^{1}H-NMR** (400 MHz, CDCl): δ 6.75-6.69 (m, 2H), 6.65 (d, *J* = 2.4 Hz, 1H), 5.16 (s, 1H), 4.91 (s, 1H), 4.26-4.10 (m, 4H), 3.75 (s, 3H), 3.20 (dd, *J* = 13.7, 2.1 Hz, 1H), 2.81-2.73 (m, 2H), 2.65 (dd, *J* = 16.3, 4.8 Hz, 1H), 2.45 (d, *J* = 13.7 Hz, 1H), 2.38 (dd, *J* = 12.1, 4.5 Hz, 1H), 2.32 (d, *J* = 13.7 Hz, 1H), 1.26 (td, *J* = 7.1, 3.4 Hz, 7H), 0.92 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 171.05, 170.56, 153.15, 146.31, 142.73, 121.66, 117.73, 114.09, 113.68, 111.48, 76.38, 61.90, 61.40, 55.67, 54.53, 44.13, 42.75, 40.00, 24.80, 17.06, 14.01, 13.92. **MS** HRMS (ESI) calc. for $[C_{22}H_{28}O_6Na]^+$: 411.1778, found: 411.1782. **HPLC** (98:2 hexanes : ethanol, 0.5 mL/min, λ_{max}= 226) t_r 18.62 min (major), 16.40 min (minor): 93% *ee*

(4*R*,9*R*,*Z*)-diethyl 1-ethylidene-4-methyl-4,4,9,9-tetrahydro-1*H*-xanthene-3,3(2*H*)-dicarboxylate (2.23c).

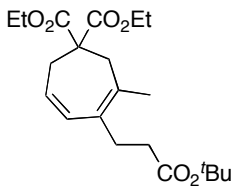


Prepared from **2.22c** in accord with the general procedure for cyclization. Purified by flash chromatography (4:1 hexanes : diethyl ether), providing the title compound as a clear oil. **^{1}H-NMR** (600 MHz, C_6D_6) δ 7.06 (dt, J = 18.8, 8.8 Hz, 2H), 6.95 (d, J = 7.5 Hz, 1H), 6.85 (t, J = 7.3 Hz, 1H), 5.69 (q, *J* = 7.4 Hz, 1H), 4.00 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.94-3.84 (m, 3H), 3.19 (ddd, *J* = 13.3, 8.1, 1.7 Hz, 2H), 3.14 (d, *J* = 14.5 Hz, 1H), 2.76-2.71 (m, 2H), 2.36 (t, *J* = 13.4 Hz, 2H), 1.57 (d, *J* = 7.4 Hz, 3H), 1.21 (s, 3H), 0.87 (dt, *J* = 17.9, 7.1 Hz, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 170.91, 170.06, 152.69, 132.02, 129.58, 124.32, 121.24, 119.84, 117.30, 77.29, 65.61, 61.31, 60.77, 55.05, 45.95, 43.80, 27.19, 18.80, 15.29, 13.62, 13.61. **MS** HRMS (EI) calc. for $[C_{22}H_{28}O_5Na]^+$: 395.1829, found: 395.1826. **HPLC** (99:1 hexanes : ethanol, 0.3 mL/min, λ_{ax}= 274 nm). T_R 25.82 min (major), 30.62 min (minor): 93% *ee*

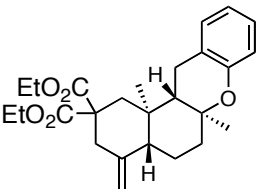
(4*R*,10*R*)-diethyl-5,7-dimethoxy-4-methyl-1-methylene-1,2,4,4,10,10-hexahydrophenanthrene-3,3(9*H*)-dicarboxylate (2.40). Prepared from **2.37a** in



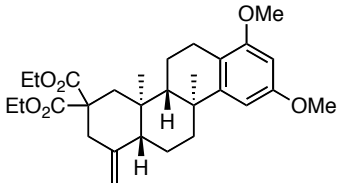
accord with the general procedure for cyclization. Purified by flash chromatography (4:1 hexanes : diethyl ether), providing the title compound as a clear oil. **^{1}H-NMR** (600 MHz,C_6D_6): δ 6.32 (d, *J* = 2.4 Hz, 1H), 6.24 (d, *J* = 2.4 Hz, 1H), 5.33 (d, *J* = 1.1 Hz, 1H), 4.41 (dd, *J* = 14.1, 1.9 Hz, 1H), 4.16-4.08 (m, 2H), 3.94-3.83 (m, 2H), 3.61 (dd, *J* = 13.3, 1.9 Hz, 1H), 3.42 (s, 3H), 3.28 (s, 3H), 2.78-2.72 (m, 1H), 2.62 (dt, *J* = 16.9, 3.3 Hz, 1H), 2.45 (dd, *J* = 37.6, 13.8 Hz, 2H), 2.23 (t, *J* = 7.1 Hz, 1H), 1.65-1.61 (m, 2H), 1.34 (s, 3H), 1.05 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 172.28, 172.14, 159.58, 158.08, 145.47, 137.99, 126.70, 109.94, 104.80, 97.27, 61.31, 60.86, 55.11, 54.99, 54.93, 50.44, 40.36, 39.70, 39.07, 31.89, 20.63, 17.72, 13.86, 13.84. **MS** HRMS (ESI) calc. for $[C_{24}H_{32}O_6Na]^+$: 439.2091, found: 439.2091. **HPLC** (99:1 hexanes : ethanol, 0.85 mL/min, λ_{max}= 208 nm). T_R 19.216 min (major), 22.57 min (minor): 94% *ee*



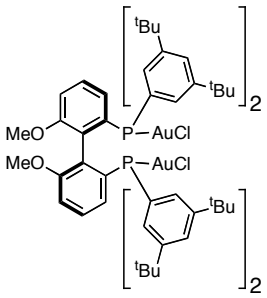
diethyl 4-(3-tert-butoxy-3-oxopropyl)-3-methylcyclohepta-3,5-diene-1,1-dicarboxylate (2.46). Prepared from **10** in accord with the general procedure for cyclization. Purified by flash chromatography (5:1 hexanes : diethyl ether). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.27 (d, J = 15.6 Hz, 1H), 5.46 (dt, J = 15.0, 7.3 Hz, 1H), 3.97 (sextet, J = 6.4 Hz, 4H), 3.43 (s, 2H), 3.22 (s, 2H), 2.33 (q, J = 7.1 Hz, 2H), 2.17 (d, J = 7.4 Hz, 2H), 1.50 (s, 3H), 1.37 (d, J = 0.8 Hz, 9H), 0.91 (t, J = 7.1 Hz, 6H). **13C-NMR** (150 MHz, C_6D_6): δ 185.92, 172.11, 171.85, 132.70, 131.19, 129.19, 125.06, 79.65, 79.65, 61.37, 57.65, 46.78, 41.76, 35.53, 29.04, 28.17, 14.04, 13.33. **MS** HRMS (ESI) calc. for $[C_{21}H_{32}O_6Na]^+$: 403.2091, found: 403.2095.



(4*R*,6*S*,12*S*,12*R*)-diethyl-6,12b-dimethyl-4-methylene-3,4,4,5,6,6,12,12a-octahydro-1*H*-benzo[*a*]xanthene-2,2(12b*H*)-dicarboxylate (2.41). Prepared from **12** in accord with the general procedure for cyclization. Purified by flash chromatography (4:1 hexanes : diethyl ether), providing the title compound as a clear oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.11 (t, *J* = 6.2 Hz, 2H), 6.86 (td, *J* = 7.5, 1.0 Hz, 1H), 6.81 (d, *J* = 8.2 Hz, 1H), 5.31 (t, *J* = 7.3 Hz, 2H), 5.24 (s, 1H), 4.19 (qq, *J* = 10.9, 7.2 Hz, 4H), 3.37 (d, *J* = 7.1 Hz, 1H), 2.79-2.77 (m, 4H), 2.16-2.06 (m, 4H), 1.99 (t, *J* = 2.7 Hz, 1H), 1.76 (s, 3H), 1.53 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 6H). **^{13}C-NMR** (151 MHz, C_6D_6): δ 171.52, 171.00, 153.62, 144.90, 129.78, 127.94, 121.98, 119.72, 117.16, 109.54, 76.02, 61.16, 60.81, 54.65, 51.05, 49.87, 43.10, 40.41, 39.31, 38.26, 29.82, 22.98, 21.44, 20.71, 13.60, 13.03. **MS** HRMS (ESI) calc. for $[C_{26}H_{34}O_5Na]^+$: 449.2298, found: 449.2300. **HPLC** (98:2: hexanes:isopropanol, 0.6 mL/min, λ_{ax}= 205 nm). T_{Rs} 11.37 min (major), 16.88 min (minor). 88 % *ee.*



(4*R*,4*S*,10*S*,12*R*)-diethyl-7,9-dimethoxy-4,10b-dimethyl-1-methylene-1,2,4,4,5,6,10b,11,12,12a-decahydrochrysene-3,3(4*H*)-dicarboxylate (2.42). Prepared from **14** in accord with the general procedure for cyclization. Purified by flash chromatography (5:1 hexanes : diethyl ether) to give a clear oil which solidified on standing. A solution of this material crystallized on slow evaporation of a solution in 3:2 MTBE : pentanes. **^{1}H-NMR** (600 MHz, C_6D_6): δ 6.37 (d, J = 2.0 Hz, 1H), 6.20 (d, J = 1.9 Hz, 1H), 5.25 (s, 1H), 4.84 (s, 1H), 4.12-4.01 (m, 2H), 3.98-3.87 (m, 2H), 3.55 (d, J = 13.4 Hz, 1H), 3.42 (s, 3H), 3.28 (s, 3H), 3.06 (d, J = 13.6 Hz, 1H), 2.74-2.63 (m, 2H), 2.37 (d, J = 13.4 Hz, 1H), 2.04 (d, J = 13.7 Hz, 1H), 1.84-1.78 (m, 2H), 1.73 (qd, J = 12.9, 2.6 Hz, 1H), 1.60-1.58 (m, 1H), 1.45 (s, 2H), 1.43-1.40 (m, 1H), 1.36 (t, J = 5.6 Hz, 3H), 1.01 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.1 Hz, 3H), 0.86 (s, 3H).**^{13}C-NMR** (100 MHz, C_6D_6): δ 171.99, 171.42, 159.50, 158.33, 145.87, 138.43, 130.15, 108.88, 105.02, 97.91, 61.09, 60.79, 55.11, 54.91, 54.43, 54.25, 51.68, 43.94, 40.46, 39.59, 39.51, 36.83, 33.37, 29.87, 21.37, 21.15, 18.65, 14.53, 13.65. **MS** HRMS (ESI) calc. for $C_{29}H_{40}O_6Na$: 507.2717, found: 507.2708. **HPLC** (99:1 hexanes : isopropanol, 0.65 mL/min, λ_{ax}= 207 nm). T_R 20.60 min (major), 42.16 min (minor). 96% *ee.*



(R)-DTB,MeO-biphep(AuCl)$_2$. Prepared from treatment of the commercially available ligand with AuCl, generated *in-situ* from $AuCl_3$ and thiodiglycol, as described recently by this group.[1] The crude product, as an oil concentrated from benzene, was recrystallized from a concentrated solution of 5% benzene in pentane, layered underneath a fivefold excess of pentane and kept at 0°C for ten days. The crystalline material thus obtained proved suitable for x-ray analysis, crystallographic data provided. **^{1}H-NMR** (400 MHz, CD_2Cl_2): δ 7.59 (q, *J* = 1.8 Hz, 3H), 7.55 (dd, *J* = 8.2, 2.5 Hz, 2H), 7.52 (q, *J* = 1.7 Hz, 2H), 7.41 (dd, *J* = 14.1, 1.8 Hz, 4H), 7.12 (dd, *J* = 14.2, 1.6 Hz, 4H), 6.97 (ddd, *J* = 10.7, 7.8, 0.8 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 2.61 (s, 6H), 1.26 (d, *J* = 8.5 Hz, 73H). **^{13}C-NMR** (100 MHz, CD_2Cl_2): δ 158.96, 158.83, 151.68, 151.19, 151.08, 130.34-130.16, 129.67, 129.50, 129.45-129.40, 129.08, 128.87, 128.80, 128.72, 128.66-128.57, 128.44, 128.29, 128.25, 128.19, 128.15, 125.74, 125.27, 113.21, 34.96, 31.05. **^{31}P-NMR** (162 MHz; C_6D_6): δ 24.96. **MS** HRMS (ESI) calc. for $[C_{70}H_{96}O_2Au_2Cl]^+$: 1459.5900, found: 1459.5902.

Substrate Synthesis

Triethyl but-3-yne-1,1,1-tricarboxylate (2.47)[45]

To a suspension of NaH (60% dispersion in mineral oil, 1.67 g, 41.75 mmol, 1.1 equiv.) in DMF (80 mL) was added triethyl methanetricarboxylate (8.81 g, 37.98 mmol) dropwise at 0 °C. The resulting mixture was stirred at room temperature for 15 min, then a solution of propargyl bromide (80 wt. % in xylene, 5.08 mL, 45.53 mmol, 1.2 equiv.) in toluene (30 mL) was added dropwise. The reaction mixture was heated to 80 °C and stirred at this temperature for 14 h. After cooling to room temperature, it was poured into saturated aqueous $NaHCO_3$ (60 mL), diluted with H_2O (200 mL) and extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with H_2O, followed by saturated aqueous NaCl; then dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography (hexanes/EtOAc = 9/1) yielded the desired product **2.47** (8.10g, 29.97 mmol, 79%) as a colorless oil. All spectral data were in accord with those previously published.

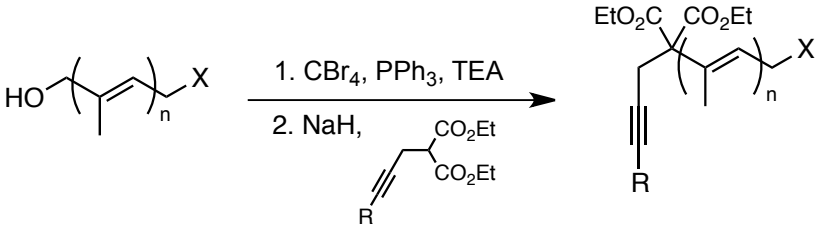
Diethyl prop-2-ynylmalonate (2.18)[45]

A solution of tricarboxylate **2.47** (8.00 g, 29.60 mmol) in THF (130 mL) was added to a suspension of KOEt (2.99 g, 35.52 mmol, 1.2 equiv.) in THF (170 mL) at 0 °C. The resulting mixture was stirred at room temperature overnight. After quenching with 1 M aqueous Hcl, the mixture was stirred for 20 min, then extracted with EtOAc (3 × 100 mL). The combined organic phases were washed successively with saturated aqueous $NaHCO_3$, H_2O and saturated aqueous NaCl; then dried ($MgSO_4$), filtered and concentrated under reduced pressure. Flash chromatography (hexanes/EtOAc = 10/1) provided the desired product (3.75 g, 18.92 mmol, 64%) as a colorless oil. . All spectral data were in accord with those previously published.

Triethyl pent-4-yne-1,1,1-tricarboxylate (2.18b)[45]

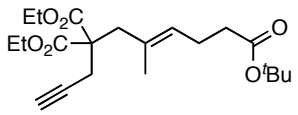
Prepared in a manner analogous to **2.18a**, all spectral data were in accord with those previously published.

General Procedure for Allylation of Malonate Derivitives



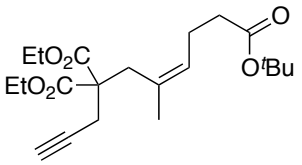
To a solution of the allyl alcohol (3.04 mmol), carbon tetrabromide (1.2 equiv., 3.65 mmol), and triethylamine (0.25 equiv., 0.76 mmol) in CH_2Cl_2 (18 mL) held at -78°C was added dropwise triphenylphosphine (1.1 equiv., 3.34 mmol) in CH_2Cl_2 (2 mL). The resulting solution was allowed to warm slowly to 0°C over 3 hours and was then concentrated, triturated with diethyl ether, filtered and concentrated (3 x 35 mL). The resulting crude allyl bromide was passed through a plug of silica gel with hexane, concentrated and used immediately in the next step.

To a solution of 1 equiv. diethyl 2-(prop-2-yn-1-yl)malonate (R = H) or diethyl 2-(but-2-yn-1-yl)malonate (R = CH_3) in dry DMF (10 mL) at 0°C was added NaH (1.15 equiv.). Upon stirring 30 minutes at this temperature, the allyl bromide in dry DMF (4 mL) was added dropwise and the reaction mixture was allowed to warm to room temperature at stir for 18 hours. The reaction mixture was quenched with saturated $NaHCO_3$ (5 mL), diluted with water (10 mL) and extratcted with ether (2 x 20 mL). The organic fractions were washed with water (2 x 20 mL), brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The resulting resuidue was purified by flash chromatography to give the desired enyne product.



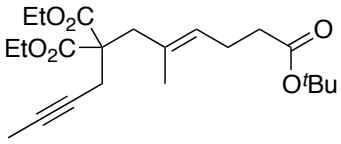
(E)-1-tert-butyl 6,6-diethyl 4-methylnon-3-en-8-yne-1,6,6-tricarboxylate (2.48).

Purified by flash chromatography (9:1 Hexanes:Et_2O), 83%. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 5.30 (t, J = 6.4 Hz, 1H), 4.18 (qq, J = 10.5, 7.1 Hz, 5H), 2.77 (d, J = 4.4 Hz, 2H), 2.29-2.20 (m, 4H), 2.00 (d, J = 2.6 Hz, 1H), 1.43 (s, 9H), 1.24 (t, J = 7.1 Hz, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 172.47, 170.18, 130.47, 129.18, 80.13, 79.40, 71.57, 61.54, 56.50, 41.21, 35.27, 28.06, 23.76, 22.41, 16.80, 13.99. **MS** HRMS (ESI) calc. for $[C_{21}H_{32}O_6Na]^+$: 403.2091, found: 403.2089.



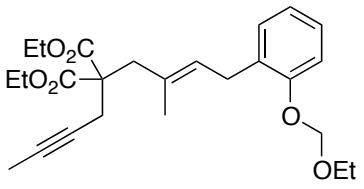
(Z)-1-tert-butyl 6,6-diethyl 4-methylnon-3-en-8-yne-1,6,6-tricarboxylate (2.49).

Purified by flash chromatography (9:1 Hexanes:Et_2O), 82%. **1H-NMR** (600 MHz, CDCl3): δ 5.30 (t, *J* = 7.2 Hz, 1H), 4.25-4.13 (m, 4H), 2.89 (s, 2H), 2.76 (d, *J* = 2.6 Hz, 2H), 2.36 (q, *J* = 7.3 Hz, 2H), 2.22 (t, *J* = 7.6 Hz, 2H), 2.00 (t, *J* = 2.6 Hz, 1H), 1.59 (s, 3H), 1.42 (d, *J* = 30.5 Hz, 9H), 1.25 (t, *J* = 7.1 Hz, 6H). **13C-NMR** (151 MHz, CDCl3): δ 172.48, 170.35, 130.26, 130.01, 80.04, 79.55, 71.53, 61.66, 56.41, 35.72, 33.90, 28.08, 24.13, 23.97, 22.61, 13.95. **MS** HRMS (ESI) calc. for $[C_{21}H_{32}O_6Na]^+$: 403.2097, found: 403.2099.

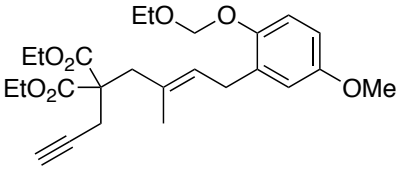


(E)-1-tert-butyl 6,6-diethyl 4-methyldec-3-en-8-yne-1,6,6-tricarboxylate (2.50).

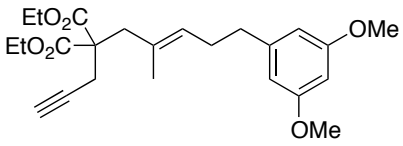
Purified by flash chromatography (9:1 Hexanes:Et_2O), 87%. **^{1}H NMR** (400 MHz, $CDCl_3$): d = 1.24 (t, *J* = 7.1 Hz, 6H), 1.43 (s, 9H), 1.55 (s, 3H), 1.74 (t, *J* = 2.6 Hz, 3H), 2.18–2.28 (m, 4H), 2.69 (q, *J* = 2.5 Hz, 2H), 2.75 (s, 2H), 4.10–4.24 (m, 4H), 5.24–5.30 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): d = 3.5, 14.0, 16.9, 22.8, 23.8, 28.1, 35.3, 41.2, 56.9, 61.4, 73.9, 78.9, 80.1, 128.8, 130.8, 170.5, 172.6. **MS** HRMS (ESI) calc. for $[C_{22}H_{34}O_6Na]^+$: 417.2253, found: 417.2256.



(E)-diethyl 2-(but-2-yn-1-yl)-2-(4-(2-(ethoxymethoxy)phenyl)-2-methylbut-2-en-1-yl)malonate (2.51).
Purified by flash chromatography (9:1 Hexanes:Et_2O), 84%. **1H-NMR** (400 MHz, C6H6): δ 7.31-7.26 (m, 2H), 7.13 (td, *J* = 7.8, 1.8 Hz, 1H), 7.13 (td, *J* = 7.8, 1.8 Hz, 1H), 6.98 (td, *J* = 7.4, 1.1 Hz, 1H), 5.89 (t, *J* = 7.2 Hz, 1H), 5.09 (s, 2H), 4.08-3.98 (m, 4H), 3.60-3.55 (m, 4H), 3.37 (s, 2H), 3.29 (q, *J* = 2.5 Hz, 2H), 1.87 (d, *J* = 0.5 Hz, 3H), 1.49 (t, *J* = 2.5 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.1 Hz, 6H). **13C-NMR** (101 MHz, C6H6): δ 170.68, 156.03, 131.17, 130.35, 130.03, 129.57, 127.59, 122.08, 114.44, 93.54, 79.44, 74.94, 64.38, 61.42, 57.89, 42.27, 29.53, 23.98, 17.48, 15.42, 14.13, 3.40. **MS** HRMS (ESI) calc. for $[C_{25}H_{34}O_6]^+$: 430.2355, found: 430.2350.

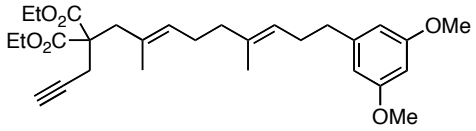


(E)-diethyl 2-(4-(2-(ethoxymethoxy)-5-methoxyphenyl)-2-methylbut-2-en-1-yl)-2-(prop-2-yn-1-yl)malonate (2.52).
Purified by flash chromatography (9:1 Hexanes:Et_2O), 82%. **1H-NMR** (400 MHz, CDCl3): δ 7.06-6.94 (m, 1H), 6.68 (dt, *J* = 12.5, 4.1 Hz, 2H), 5.51 (td, *J* = 7.1, 1.4 Hz, 1H), 5.16 (s, 2H), 4.22-4.12 (m, 4H), 3.76 (s, 3H), 3.73 (q, *J* = 7.1 Hz, 2H), 3.32 (d, *J* = 7.3 Hz, 2H), 2.85 (s, 2H), 2.82 (d, *J* = 2.7 Hz, 2H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.65 (t, *J* = 0.5 Hz, 3H), 1.23 (td, *J* = 7.1, 1.1 Hz, 10H). **13C-NMR** (101 MHz, CDCl3): δ 170.28, 154.48, 149.34, 131.38, 130.60, 128.83, 115.59, 115.18, 111.56, 94.11, 79.49, 71.70, 64.13, 61.61, 56.73, 55.67, 41.42, 28.83, 22.66, 17.01, 15.19, 14.04. **MS** HRMS (ESI) calc. for $[C_{25}H_{35}O_7]^+$: 447.2377, found: 447.2390.



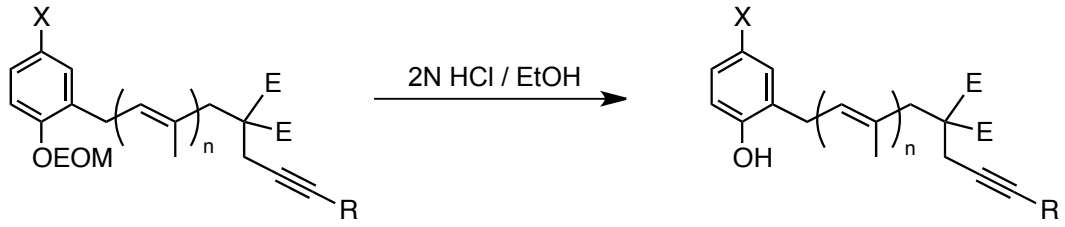
(E)-diethyl 2-(5-(3,5-dimethoxyphenyl)-2-methylpent-2-en-1-yl)-2-(prop-2-yn-1-yl)malonate (2.37a).

Purified by flash chromatography (9:1 Hexanes:Et_2O), 88%. **1H-NMR** (400 MHz, CDCl3): δ 6.42 (d, *J* = 2.3 Hz, 2H), 6.37 (t, *J* = 2.2 Hz, 1H), 5.45 (t, *J* = 6.8 Hz, 1H), 4.25 (qq, *J* = 11.4, 7.2 Hz, 4H), 3.85 (s, 6H), 2.86 (s, 2H), 2.81 (d, *J* = 2.6 Hz, 2H), 2.65 (t, *J* = 7.8 Hz, 2H), 2.36 (t, *J* = 7.6 Hz, 2H), 2.09 (t, *J* = 2.6 Hz, 1H), 1.59 (d, *J* = 0.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 6H). **13C-NMR** (101 MHz, C6H6): δ 170.27, 160.69, 144.40, 130.09, 129.94, 106.43, 97.81, 79.51, 71.58, 61.55, 56.56, 55.25, 41.29, 35.95, 29.83, 22.43, 16.86, 14.01.



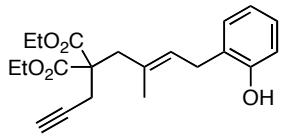
diethyl 2-((2*E*,6*E*)-9-(3,5-dimethoxyphenyl)-2,6-dimethylnona-2,6-dienyl)-2-(prop-2-ynyl)malonate (2.37b).

Purified by flash chromatography (95:5 Hexanes:Et_2O), 79%. **^{1}H-NMR** (600 MHz, C_6D_6): δ 6.53 (d, *J* = 2.3 Hz, 2H), 6.49 (t, *J* = 2.2 Hz, 1H), 5.56-5.54 (m, 1H), 5.30 (t, *J* = 7.1 Hz, 1H), 4.04-3.93 (m, 4H), 3.39 (d, *J* = 1.8 Hz, 1H), 3.23 (d, *J* = 2.7 Hz, 2H), 3.14 (d, *J* = 2.7 Hz, 2H), 2.64 (t, *J* = 7.8 Hz, 2H), 2.39 (q, *J* = 7.5 Hz, 2H), 2.10 (t, *J* = 7.3 Hz, 2H), 2.05-2.02 (m, 2H), 1.77 (t, *J* = 2.7 Hz, 1H), 1.67 (d, *J* = 1.3 Hz,), 1.61 (s, 3H), 1.53-1.50 (m, 3H), 0.93 (t, *J* = 7.1 Hz, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 171.21, 143.42, 142.82, 140.22, 129.51, 127.12, 112.34, 63.37, 61.82, 61.34, 54.87, 50.14, 43.37, 41.71, 39.99, 25, 22.24, 21.56, 14.41, 14.02, 13.93. **MS** HRMS (ESI) calc. for $[C_{29}H_{40}O_6Na]^+$: 507.2717, found: 507.2716.



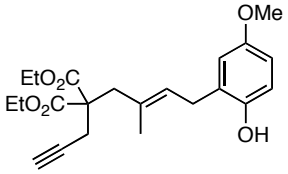
General Procedure for Deprotection of Ethoxymethyl Phenols

To a solution of acetal (0.349 mmol) in EtOH (3 mL) at room temperature was added 2N HCl (2.5 equiv., 435 µL) and the reaction was well mixed. Upon completion, the reaction was quenched with 3 mL saturated $NaHCO_3$, then 4 mL saturated NH_4Cl. The reaction mixture was diluted with water (20 mL) and extracted with EtOAc (2 x 20 mL). The organic fractions were washed with brine and dried over $MgSO_4$. Upon concentration, the crude product was purified by flash chromatography.

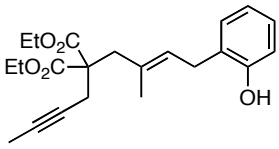


(*E*)-diethyl 2-(4-(2-hydroxyphenyl)-2-methylbut-2-enyl)-2-(prop-2-ynyl)malonate (2.22a).

Purified by flash chromatography (85:15 Hexanes:EtOAc), 82%. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.73 (d, *J* = 8.5 Hz, 1H), 6.65 (td, *J* = 8.5, 3.0 Hz, 2H), 5.48 (t, *J* = 7.0 Hz, 1H), 3.76 (s, 3H), 3.31 (d, *J* = 7.2 Hz, 2H), 2.87 (s, 2H), 2.81 (d, *J* = 2.6 Hz, 2H), 2.02 (t, *J* = 2.6 Hz, 1H), 1.70 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 170.20, 153.84, 131.73, 129.86, 128.21, 127.41, 126.73, 120.86, 115.65, 79.29, 71.75, 61.64, 56.84, 41.32, 29.29, 22.78, 17.16, 13.95. **MS** HRMS (ESI) calc. for $[C_{21}H_{26}O_5Na]^+$: 381.1672, found: 381.1676.

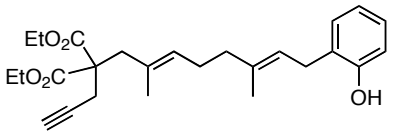


(*E*)-diethyl 2-(4-(2-hydroxy-5-methoxyphenyl)-2-methylbut-2-enyl)-2-(prop-2-ynyl)malonate (2.22b). Purified by flash chromatography (85:15 Hexanes:EtOAc), 84%. **1H-NMR** (400 MHz, CDCl3): δ 7.02 (d, *J* = 8.7 Hz, 1H), 6.68 (dt, *J* = 12.5, 4.1 Hz, 2H), 5.51 (td, *J* = 7.3, 1.2 Hz, 1H), 5.16 (s, 2H), 4.17 (qq, *J* = 11.3, 7.1 Hz, 4H), 3.76 (s, 3H), 3.70 (s, 2H), 3.32 (d, *J* = 7.3 Hz, 2H), 2.85 (s, 2H), 2.82 (d, *J* = 2.7 Hz, 2H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.65 (t, *J* = 0.5 Hz, 3H), 1.23 (td, *J* = 7.1, 1.1 Hz, 10H). **13C-NMR** (101 MHz, CDCl3): δ 170.00, 154.24, 148.09, 131.53, 128.64, 128.28, 116.23, 115.41, 112.34, 79.47, 72.03, 61.30, 57.18, 55.11, 41.67, 29.36, 23.14, 17.04, 13.67. **MS** HRMS (ESI) calc. for $[C_{22}H_{28}O_6Na]^+$: 411.1778, found: 411.1774



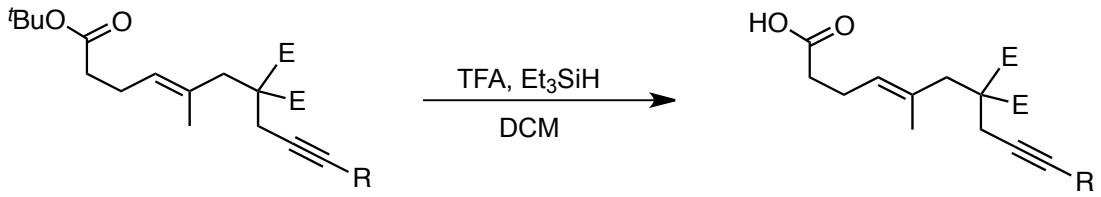
(*E*)-diethyl 2-(but-2-ynyl)-2-(4-(2-hydroxyphenyl)-2-methylbut-2-enyl)malonate (2.22c).

Purified by flash chromatography (85:15 Hexanes:EtOAc), 88%. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.73 (d, *J* = 8.5 Hz, 1H), 6.65 (td, *J* = 8.5, 3.0 Hz, 2H), 5.48 (t, *J* = 6.8 Hz, 1H), 4.56 (s, 1H), 4.16 (qq, *J* = 12.3, 7.0 Hz, 4H), 3.76 (s, 3H), 3.31 (d, *J* = 7.2 Hz, 2H), 2.87 (s, 2H), 2.81 (d, *J* = 2.6 Hz, 2H), 2.02 (t, *J* = 2.6 Hz, 1H), 1.70 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 6H). **^{13}C-NMR** (10\1 MHz, $CDCl_3$): δ 170.20, 153.84, 131.73, 129.86, 128.21, 127.41, 126.73, 120.86, 115.65, 79.29, 71.75, 61.64, 56.84, 41.32, 29.29, 22.78, 17.16, 13.95. **MS** HRMS (EI) calc. for $[C_{22}H_{28}O_5Na]^+$: 395.1829, found: 395.1831.



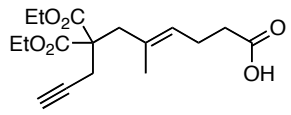
diethyl 2-((2*E*,6*E*)-8-(2-hydroxyphenyl)-2,6-dimethylocta-2,6-dienyl)-2-(prop-2-ynyl)malonate (2.38).

Purified by flash chromatography (9:1 Hexanes:EtOAc), 84%. **^{1}H-NMR** (600 MHz, C_6D_6):6.37 (d, J = 2.0 Hz, 1H), 6.20 (d, J = 1.9 Hz, 1H), 5.25 (s, 1H), 4.84 (s, 1H), 4.12-4.01 (m, 2H), 3.98-3.87 (m, 2H), 3.55 (d, J = 13.4 Hz, 1H), 3.42 (s, 3H), 3.28 (s, 3H), 3.06 (d, J = 13.6 Hz, 1H), 2.74-2.63 (m, 2H), 2.37 (d, J = 13.4 Hz, 1H), 2.04 (d, J = 13.7 Hz, 1H), 1.84-1.78 (m, 2H), 1.73 (qd, J = 12.9, 2.6 Hz, 1H), 1.60-1.58 (m, 1H), 1.45 (s, 2H), 1.43-1.40 (m, 1H), 1.36 (t, J = 5.6 Hz, 3H), 1.01 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.1 Hz, 3H), 0.86 (s, 3H).**^{13}C-NMR** (100 MHz, C_6D_6): δ 171.99, 171.42, 159.50, 158.33, 145.87, 138.43, 130.15, 108.88, 105.02, 97.91, 61.09, 60.79, 55.11, 54.91, 54.43, 54.25, 51.68, 43.94, 40.46, 39.59, 39.51, 36.83, 33.37, 29.87, 21.37, 21.15, 18.65, 14.53, 13.65. **MS** HRMS (ESI) calc. for $[C_{29}H_{40}O_6Na]^+$: 507.2717, found: 507.2708.



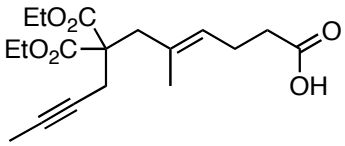
General Procedure for the Deprotection of *tert*-Butyl Esters.

To a solution of the *tert*-butyl ester (196 mg, 0.50 mmol) in DCM (1.1 mL) was added triethylsilane (0.2 mL, 1.25 mmol, 2.5 eq.), followed by trifluoroacetic acid (0.48 mL, 6.48 mmol, 13.0 eq.). The mixture was stirred at room temperature for 3 h, then concentrated under a stream of nitrogen. The residue was dissolved in toluene and concentrated under nitrogen, and the resulting crude product was purified by column chromatography to give the carboxylic acid as a colorless oil.

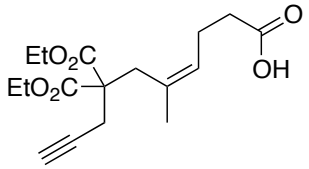


(*E*)-7,7-bis(ethoxycarbonyl)-5-methyldec-4-en-9-ynoic acid (2.21a). Purified by flash chromatography (1:1 to 1:3 hexanes:Et_2O), 80%. **^{1}H NMR (400 MHz,** $CDCl_3$**):** δ 1.24 (t, *J* = 7.2 Hz, 6H), 1.55–1.57 (m, 3H), 2.00–2.02 (m, 1H), 2.26–2.34 (m, 2H), 2.35–2.41 (m, 2H), 2.75 (d, *J* = 2.7 Hz, 2H), 2.79 (s, 2H), 4.11–4.25 (m, 4H), 5.29–5.34 (m, 1H). **^{13}C-NMR** (100 MHz, $CDCl_3$**):** δ 179.0, 170.2, 131.2, 128.5, 79.3, 71.6, 61.6, 56.5, 41.2, 33.7, 23.3, 22.4, 16.8, 14.0. **MS** HRMS (ESI) calc. for $[C_{17}H_{24}O_6Na]^+$: 347.1465, found: 347.1467.

(*E*)-7,7-bis(ethoxycarbonyl)-5-methylundec-4-en-9-ynoic acid (2.21b).

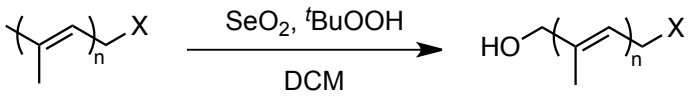


Purified by flash chromatography (1:1 to 1:3 hexanes:Et_2O), 85%. **^{1}H NMR** (400 MHz, $CDCl_3$**)**: δ 1.23 (t, *J* = 7.1 Hz, 6H), 1.56 (s, 3H), 1.74 (t, *J* = 2.6 Hz, 3H), 2.25–2.34 (m, 2H), 2.34–2.40 (m, 2H), 2.69 (q, *J* = 2.4 Hz, 2H), 2.76 (s, 2H), 4.10–4.23 (m, 4H), 5.28 (t, *J* = 6.5 Hz, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$**):** δ 3.4, 14.0, 16.9, 22.8, 23.3, 33.8, 41.1, 57.0, 61.4, 73.8, 79.0, 128.1, 131.5, 170.5, 179.2. **MS** HRMS (ESI) calc. for $[C_{18}H_{26}O_6Na]^+$: 361.1622, found: 361.1624.



(Z)-7,7-bis(ethoxycarbonyl)-5-methyldec-4-en-9-ynoic acid (2.43).

Purified by flash chromatography (1:1 to 1:3 hexanes:Et_2O), 83%. **1H-NMR** (600 MHz, C6H6): δ 5.17 (t, *J* = 7.3 Hz, 1H), 4.00 (dq, *J* = 10.8, 7.1 Hz, 2H), 3.92 (dq, *J* = 10.8, 7.1 Hz, 2H), 3.20 (s, 2H), 2.99 (d, *J* = 2.7 Hz, 2H), 2.43 (q, *J* = 7.4 Hz, 2H), 2.14 (t, *J* = 7.5 Hz, 2H), 1.76 (q, *J* = 2.6 Hz, 1H), 1.60 (s, 3H), 0.91 (t, *J* = 7.1 Hz, 6H). **13C-NMR** (101 MHz, CDCl3): δ 179.60, 170.04, 131.06, 129.60, 79.65, 71.89, 61.36, 56.61, 34.18, 34.00, 24.10, 23.58, 22.99, 13.66. **MS** HRMS (ESI) calc. for $[C_{17}H_{24}O_6]^+$: 324.1573, found: 324.1575.

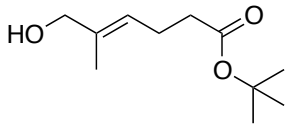


General Procedure for Regiospecific Allylic Oxidation

TBHP (90% purity, 6.44 mL, 57.9 mmol, 3.5 equiv.), followed by selenium dioxide (920 mg, 8.3 mmol, 0.5 equiv.), was added to a solution of prenyl compound (16.6 mmol) in DCM (12 mL) at 0°C. The reaction mixture was stirred at 0 °C for 1 h, then warmed to room temperature and stirred for additional 4 h. Saturated aqueous $NaHCO_3$ (20 mL) was added, and, after separation, the aqueous phase was extracted with DCM (3 × 20 mL). The combined organic layers were washed with brine (20 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford crude alcohol.

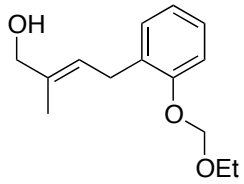
In some cases, significant over oxidation to the unsaturated aldehyde occurred and a subsequent reduction step was carried out. The crude aldehyde / alcohol mixture was dissolved in MeOH (30 mL), and $NaBH_4$ (630 mg, 16.6 mmol, 1.0 equiv.) was slowly added at 0 °C. The resulting mixture was stirred for 1 h, then quenched with saturated aqueous NH_4Cl (30 mL) and diluted with H_2O (20 mL). After extraction with DCM (3 × 25 mL), the combined organic phases were washed with saturated aqueous NaCl (2 × 10 mL), then dried ($MgSO_4$), filtered and concentrated *in vacuo*.

The crude product was then purified by flash chromatography using the solvent system described below.



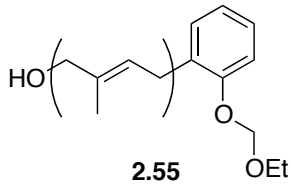
***tert*-Butyl (4*E*)-6-hydroxy-5-methylhex-4-enoate (2.53).**

Purified by flash chromatography (Hexanes/EtOAc = 4/1 to 2/1), 66%. **^{1}H NMR** (400 MHz, $CDCl_3$): d = 1.43 (s, 9H), 1.66 (s, 3H), 1.87 (s, 1H,), 2.22–2.34 (m, 4H), 3.93 (d, *J* = 5.1 Hz, 2H), 5.34–5.39 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): d = 13.6, 23.3, 28.0, 35.3, 68.5, 80.2, 123.9, 135.9, 172.7. **MS** HRMS (ESI) calc. for $[C_{11}H_{21}O_3]^+$: 201.1489, found: 201.1487.



(E)-4-(2-(ethoxymethoxy)phenyl)-2-methylbut-2-en-1-ol (2.54).

Purified by flash chromatography (9:1 hexanes:Et_2O), 63%. **1H-NMR** (500 MHz, CDCl3): δ 7.18-7.13 (m, 2H), 7.09 (d, *J* = 7.5 Hz, 1H), 6.93 (td, *J* = 7.4, 0.9 Hz, 1H), 5.59 (td, *J* = 7.4, 1.2 Hz, 1H), 5.26 (s, 2H), 4.04 (s, 2H), 3.73 (q, *J* = 7.1 Hz, 2H), 3.39 (d, *J* = 7.3 Hz, 2H), 1.79 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). **13C-NMR** (151 MHz, CDCl3): δ 155.37, 135.71, 130.17, 129.87, 127.47, 124.61, 121.87, 114.26, 93.42, 69.21, 64.54, 28.69, 15.40, 14.00. **MS** HRMS (ESI) calc. for $[C_{14}H_{20}O_3Li]^+$: 243.1567, found: 243.1569.

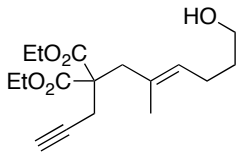


2.55

(2E,6E)-8-(2-(ethoxymethoxy)phenyl)-2,6-dimethylocta-2,6-dien-1-ol (2.55).

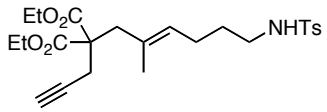
Purified by flash chromatography (95:5 hexanes: Et_2O), 69%. **1H-NMR** (600 MHz, CDCl3): δ 7.16-7.14 (m, 2H), 7.09-7.07 (m, 1H), 6.93 (td, *J* = 7.4, 1.1 Hz, 1H), 5.38 (td, *J* = 7.0, 1.3 Hz, 1H), 5.32 (td, *J* = 7.3, 1.3 Hz, 1H), 5.25 (s, 2H), 3.97 (d, *J* = 4.4 Hz, 2H), 3.74 (q, *J* = 7.1 Hz, 2H), 3.35 (d, *J* = 7.3 Hz, 2H), 2.18-2.15 (m, 2H), 2.08 (t, *J* = 7.6 Hz, 2H), 1.72 (s, 3H), 1.65 (s, 3H), 1.57 (s, 1H), 1.23 (t, *J* = 7.1 Hz, 4H). **13C-NMR** (151 MHz, CDCl3): δ 155.31, 135.67, 135.05, 130.95, 129.67, 127.13, 126.16, 123.11, 121.78, 114.31, 93.44, 69.21, 64.42, 39.52, 28.72, 26.28, 16.23, 15.33, 13.87. **MS** HRMS (ESI) calc. for $[C_{19}H_{29}O_3]^+$: 305.2111, found: 305.2119.

(E)-diethyl 2-(6-hydroxy-2-methylhex-2-en-1-yl)-2-(prop-2-yn-1-yl)malonate (2.32).



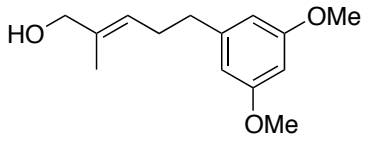
To a solution of carboxylic acid **2.21a** (310 mg, 1 mmol) in THF (10 mL) at 0°C was added *tert*-butyl chloroformate (1.2 mmol, 287.9 mg, 1.2 equiv.) and N-methyl morpholine (1.2 mmol, 121.4 mg, 1.2 equiv.) and the resulting solution was allowed to warm to room temperature over 2 hours. The reaction mixture was then concentrated *in vacuo*, triturated with Et_2O and filtered (3 x 20 mL) to give the crude mixed anhydride, which was used without further purification. To a solution of the anhydride in methanol (10 mL) at 0°C was added $NaBH_4$ (75.9 mg, 2 mmol, 2 equiv.) with stirring and the temperature was maintained for 3 h. The reaction mixture was then warmed to room temperature, quenched with water (2 mL) and made acidic with sat. NH_4Cl (10 mL) then diluted with water (25 mL) and extracted with EtOAc (3 x 15 mL). **1H-NMR** (500 MHz, CDCl3): δ 5.35 (td, *J* = 7.2, 1.0 Hz, 1H), 4.19 (qq, *J* = 12.5, 7.1 Hz, 4H), 3.64 (t, *J* = 6.5 Hz, 2H), 2.80 (s, 2H), 2.78 (d, *J* = 2.7 Hz, 2H), 2.08 (q, *J* = 7.3 Hz, 2H), 2.03 (t, *J* = 2.7 Hz, 1H), 1.61 (quintet, *J* = 7.1 Hz, 2H), 1.56 (d, *J* = 0.6 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 6H). **13C-NMR** (101 MHz, CDCl3): δ 170.73, 130.79, 130.43, 79.92, 72.05, 62.97, 62.03, 57.13, 41.78, 32.90, 24.88, 23.02, 17.32, 14.48. **MS** HRMS (ESI) calc. for $[C_{17}H_{26}O_5Li]^+$: 317.1935, found: 317.1933.

(*E*)-diethyl 2-(2-methyl-6-(4-methylphenylsulfonamido)hex-2-enyl)-2-(prop-2-ynyl)malonate (2.33).

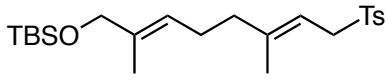


To a solution of Ph_3P (314.4 mg, 1.2 mmol). *tert*-butyl tosylcarbamate (325 mg, 1.2 mmol) and **2.33** (310.2 mg, 1 mmol) in THF (6 mL) was added DIAD (242.6 mg.,1.2 mmol) to give an orange solution which was stirred 18 hours, concentrated *in vacuo* passed through a short silica gel column (2% benzene in hexanes) to give the crude carbamate as a pale yellow oil (590 mg). This material was dissolved in DMSO which had been degassed by flowing N_2 for 20 minutes (2 mL) and heated under N_2 to 170°C for 30 minutes, during which a subtle evolution of gas was observed. The reaction mixture was loaded onto silica gel and purified by flash chromatography (8:2 hexanes:EtOAc) to provide **2.33** as a clear oil (319.5 mg, 69%) (**1H-NMR** (400 MHz, CDCl3): δ 7.77-7.75 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.23 (t, *J* = 7.1 Hz, 1H), 4.40 (td, *J* = 6.2, 0.3 Hz, 1H), 4.26-4.12 (m, 4H), 2.93 (d, *J* = 6.7 Hz, 2H), 2.77 (s, 2H), 2.72 (d, *J* = 2.7 Hz, 2H), 2.44 (s, 3H), 2.02-1.97 (m, 3H), 1.53-1.50 (m, 5H), 1.26 (t, *J* = 7.1 Hz, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 170.18, 143.36, 142.23, 136.90, 130.63, 129.69,

129.33, 127.08, 79.33, 71.65, 61.59, 56.54, 42.77, 41.18, 29.39, 25.07, 22.47, 21.51, 16.86, 14.00. **MS** HRMS (ESI) calc. for $[C_{24}H_{34}NO_6S]^+$: 464.2101, found: 464.2103.

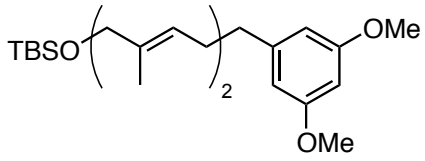


(E)-5-(3,5-dimethoxyphenyl)-2-methylpent-2-en-1-ol (2.56). A stirred suspension 3-(3,5-dimethoxyphenyl)propanal (248 mg., 1.3 mmol) and 2-(triphenylphosphoranylidene)propanal (497 mg., 1.56 mmol, 1.2 equiv.) in benzene (10 mL) was heated 90°C in a sealed tube for 18 hours to give a clear solution. Upon cooling to room temperature, the reaction mixture was concentrated *in vacuo*, and the crude aldehyde was dissolved in methanol (10 mL) at 0°C and treated with $NaBH_4$ (58.9 mg, 1.56 mmol, 1.2 equiv.) Upon stirring at this temperature for 1 h, the reaction mixture was quenched with water (50 mL) and extracted with EtOAc (3 x 20 mL). The combined organic fractions were washed with brine (30 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (8:2 Hexanes : EtOAc) to give **2.56** as a clear oil (276 mg, 92%). **1H-NMR** (400 MHz, CDCl3): δ 6.36 (d, *J* = 2.2 Hz, 2H), 6.31 (t, *J* = 2.2 Hz, 1H), 5.45 (td, *J* = 7.1, 1.0 Hz, 1H), 3.99 (s, 2H), 3.78 (s, 6H), 2.61 (t, *J* = 7.8 Hz, 2H), 2.35 (q, *J* = 7.6 Hz, 2H), 1.64 (s, 3H), 1.48-1.45 (m, 1H). **13C-NMR** (101 MHz, CDCl3): δ 161.11, 144.84, 135.91, 125.59, 106.94, 98.11, 69.26, 55.69, 36.41, 29.71, 14.13. **MS** HRMS (ESI) calc. for $[C_{14}H_{20}O_3Li]^+$: 243.1567, found: 243.1568.



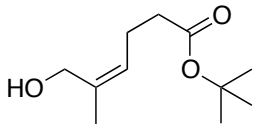
tert-butyl(((2E,6E)-2,6-dimethyl-8-tosylocta-2,6-dien-1-yl)oxy)dimethylsilane (2.35).[39]

This compound was prepared as described in the literature, all spectral data were in accord with those previously published.



(2E,6E)-9-(3,5-dimethoxyphenyl)-2,6-dimethylnona-2,6-dien-1-ol (2.57).

To a solution of **2.35** (500 mg, 1.27 mmol) in anhydrous THF (8 mL) at -78°C was added dropwise nBuLi (580 µL of a 2.5 M solution in hexanes, 1.33 mmol) and the resulting solution was warmed to -30°C and stirred at that temperature for 1 hour and then cooled again to -78°C. A solution of 3,5-dimethoxybenzyl bromide (294 mg., 1.27 mmol) was added dropwise, the reaction mixture was allowed to warm to room temperature and stirred for 45 minutes. The reaction mixture was then cooled to 0°C and a solution of $Pd(OAc)_2$ (14.2 mg., 0.13 mmol) and 1,3-bis(diphenylphosphino)propane (26.2 mg., 0.065 mmol) in THF (2 mL) was added dropwise to give a brilliant red solution to which was added a solution of $LiBHEt_3$ (1.27 mL of a 1 M solution in THF, 1.27 mmol) dropwise and the solution was allowed to slowly warm to room temperature. After stirring 10 hours at room temperature, the reaction mixture was diluted with Et_2O (25 mL), washed with sat. $NaHCO_3$ (30 mL), brine (30 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The resulting red oil was purified by flash chromatography (95:5 hexanes:Et_2O) to give **2.57** as a clear oil (449 mg, 85%). **1H-NMR** (600 MHz, CDCl3): δ 6.36 (d, *J* = 2.3 Hz, 2H), 6.30 (t, *J* = 2.2 Hz, 1H), 5.37 (d, *J* = 1.2 Hz, 1H), 5.19-5.19 (m, 1H), 4.00 (s, 2H), 3.78 (s, 6H), 2.58 (t, *J* = 7.9 Hz, 2H), 2.29 (d, *J* = 7.9 Hz, 2H), 2.11 (dd, *J* = 7.8, 7.3 Hz, 2H), 2.03-2.00 (m, 2H), 1.59 (s, 3H), 1.58 (s, 3H), 1.55 (s, 1H), 0.91 (s, 10H), 0.06 (s, 6H). **13C-NMR** (151 MHz, CDCl3): δ 160.66, 144.84, 135.60, 134.33, 124.29, 123.69, 107.79-105.62, 97.68, 68.63, 55.21, 39.36, 36.41, 29.73, 26.16, 25.95, 18.41, 15.97, 13.40, -5.26. **MS** HRMS (ESI) calc. for $[C_{25}H_{42}O_3Si]^+$: 418.2903, found: 418.2908.

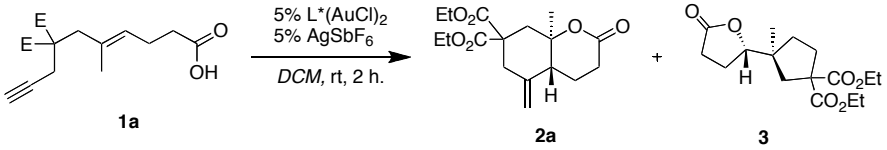


(Z)-tert-butyl 6-hydroxy-5-methylhex-4-enoate (2.58).

To a suspension of tert-butyl 4-tertbutoxycarbonylbutyltriphenylphosphonium bromide (3.06 g., 6.33 mmol) in anhydrous THF (30 mL) at -78°C was added KHMDS (12.4 mL of a 0.5 M solution in toluene, 6.20 mmol). After 35 minutes stirring at this temperature, a transparent orange solution was obtained. A solution of 1-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-one (1.0 g, 6.33 mmol) in Et_2O was added dropwise and the solution was allowed to warm to room temperature. After 7 hours, the reaction was quenched with water (45 mL), extracted with Et_2O (3 x 45 mL) and the combined organic fractions washed with sat. $NaHCO_3$, (45 mL), water (45 mL) and brine (45 mL). The solution wad dried over $MgSO_4$, concentrated *in vacuo* and the resulting residue was dissolved in MeOH (50 mL) and stirred 3 hours in the presence of TsOH (100 mg). The reaction mixture was poured into 100 mL sat $NaHCO_3$, extracted with EtOAc (3 x 50 mL) and the resulting organic fractions were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude allylic alcohol was purified by flash chromatography (7:3 hexanes:Et_2O) to give **2.58** as a clear oil (1.10 g., 85%). **1H-NMR** (500 MHz, CDCl3): δ 5.25-5.22 (m, 1H), 4.13 (s, 2H), 2.38-2.30 (m, 4H), 2.17-2.06 (m, 1H), 1.81 (t, *J* = 1.2 Hz, 3H), 1.45 (s, 9H). **13C-NMR** (101 MHz, CDCl3): δ 173.10, 136.31, 126.31, 80.67, 61.58, 35.20, 28.17, 23.10, 21.78. **MS** HRMS (ESI) calc. for $[C_{11}H_{21}O_3]^+$: 201.1489, found: 201.1485

Additional Optimization Data

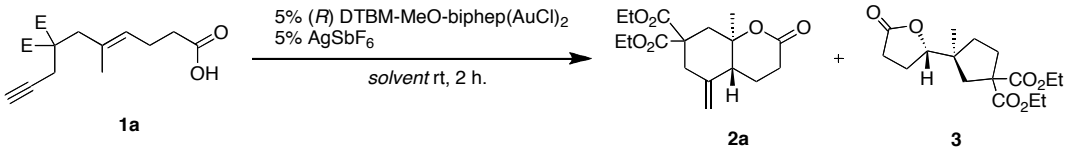
Table S1: Catalyst Optimization



entry	ligand	ee (%)	yield 2a (%)	yield 3 (%)
1	(*R*)-DTBM-MeO-biphep	-46	81	10
2	*(R)-xyl*-MeO-BIPHEP	-36	66	11

3	*(R)-xyl*-BINAP	-40	71	12
4	*(R)-tol*-BINAP	-23	75	10
5	*(S)*-BINAP	13	81	8
6	*(R)*-C_3-Tunephos	7	72	8
7	*(R)*-SEGPHOS	-3	88	6
8	*(S)*-Difluorphos	-3	80	-
9	*(R)*-DTBM-SEGPHOS	-2	78	10

Table S2: Solvent Optimization



1a **2a** **3**

entry	solvent	ee (%)	yield 2a (%)	yield 3 (%)
1	DCM	-46	81	10
2	benzene	-83	83	11
3	toluene	-85	81	11
4	*m*-xylene	-87	83	14
5	fluorobenzene	-73	88	7
6	nitromethane	-47	79	3
7	THF	-58	83	13

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4. This process is the reverse of an E2 elimination and is therefore subject to the same stereochemical requirements.
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15. NMR analysis indicated the remaining mass balance was comprised of 5% unreacted **2.9** and 15% of a mixture of phenolic compounds displaying diastereotopic protons, likely arising from competition by the standard decomposition pathways for enyne cycloisomerization.
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17. While the acid **2.5** is known, its synthesis was unfortunately not described.
18. E.g. those bearing methyl and tert-butyl groups on the peripheral arylphosphine rings.
19. Aldehyde olefination with 2-phosphorylpropanoate esters provided ca. 10% of the cis isomer which was exceedingly difficult to separate by flash chromatography.
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27. Furthermore, significant amounts of deprotected cycloheptadienes were detected in both reaction mixtures.
28. Specifically, those ligands bearing alkyl substituents on the peripheral arylphosphine rings.
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31. Formed from the digold(I) chloride complex by treatment with 2 eq. of silver salt.
32. In all other examples, the enantioselectivity was identical at rt and -40°C.
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38. I.e., by replacing the prenyl group with its geranyl homolog.
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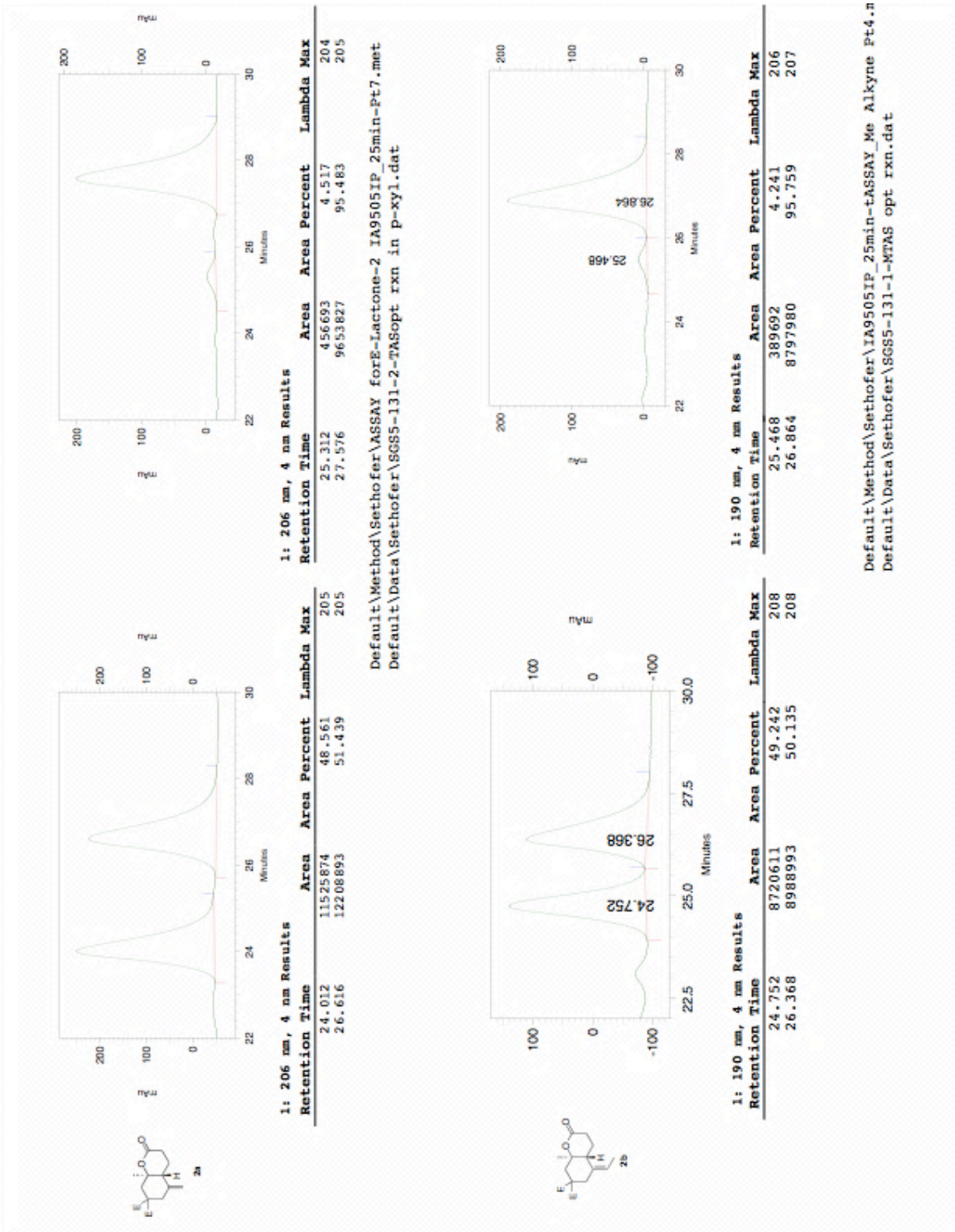
Spectral Data for Chapter 2

HPLC Data



1: 206 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
24.012	11525874	48.561	205
26.616	12208893	51.439	205

1: 206 nm, 4 nm Results

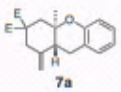
Retention Time	Area	Area Percent	Lambda Max
25.312	456693	4.517	204
27.576	9653827	95.483	205

1: 190 nm, 4 nm Results

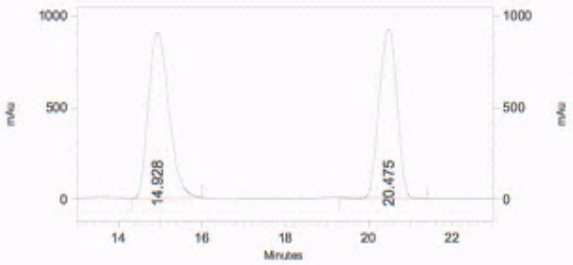
Retention Time	Area	Area Percent	Lambda Max
24.752	8720611	49.242	208
26.368	8988993	50.135	208

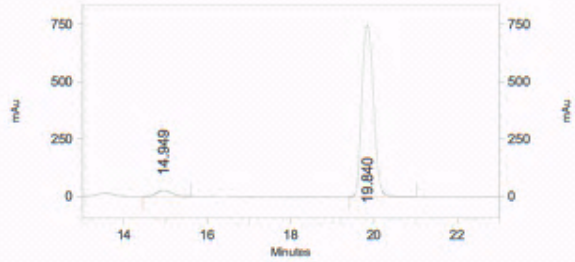
1: 190 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
25.468	389692	4.241	206
26.864	8797980	95.759	207



7a





1: 220 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
14.928	30539390	52.958	273
20.475	27127825	47.042	273

1: 280 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
14.949	668535	4.419	273
19.840	14458483	95.581	273

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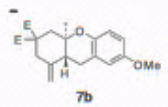
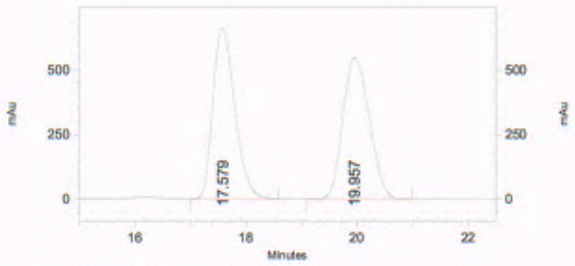
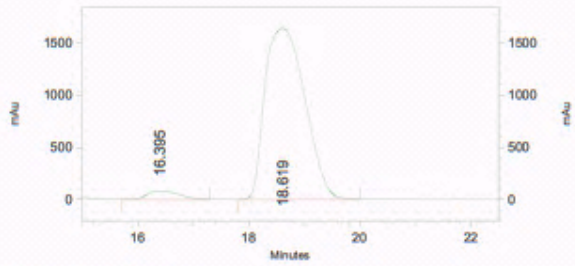


7b





1: 221 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
17.579	18255094	49.989	226
19.957	18263309	50.011	226

1: 221 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
16.395	3161662	3.72	226
18.619	81826924	96.28	226

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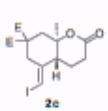
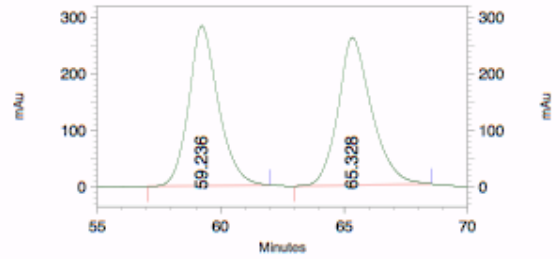
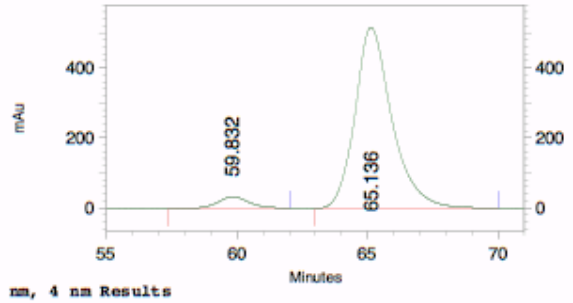




1: 225 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
59.236	23701724	48.979	225
65.328	24689862	51.020	225



1: 236 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
59.83	837322	2.036	232
65.14	40284356	97.964	225

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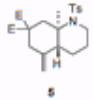
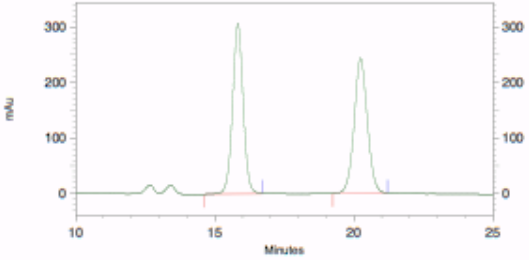
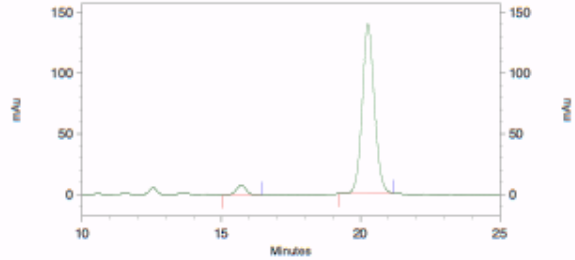
60.116
65.704





1: 207 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
15.828	8092698	50.168	206
20.232	8038556	49.832	206



1: 207 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
15.712	199233	4.488	206
20.264	4240282	95.512	206

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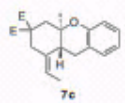
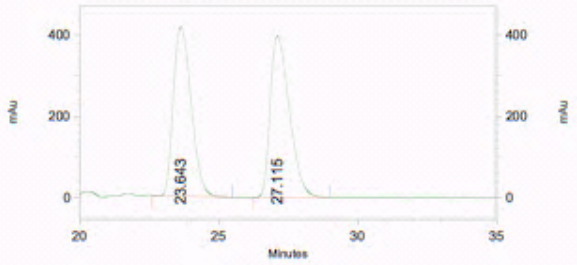
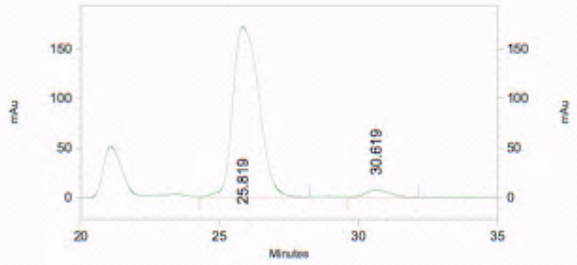




2: 280 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
23.643	18537834	49.290	274
27.115	19071776	50.710	274



2: 280 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
25.819	11156281	96.404	274
30.619	416116	3.596	272

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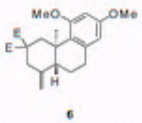
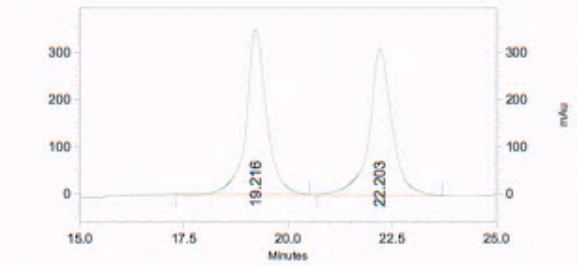
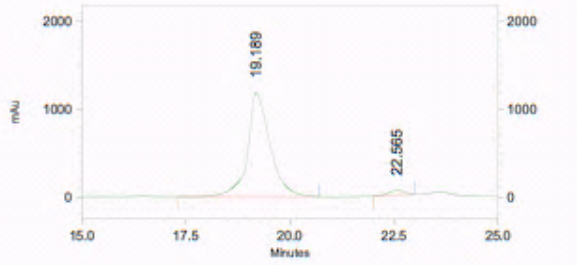




1: 217 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
19.216	11863681	50.198	208
22.203	11770065	49.802	208



1: 217 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
19.189	35727132	96.895	208
22.565	1462552	3.185	208

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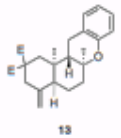
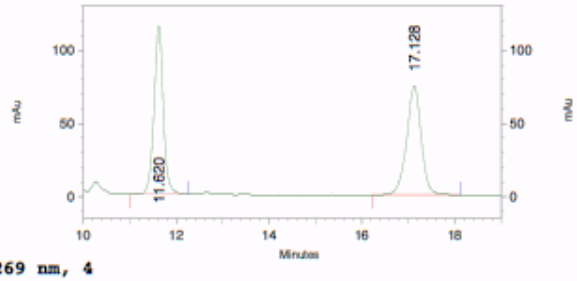


13



2: 269 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
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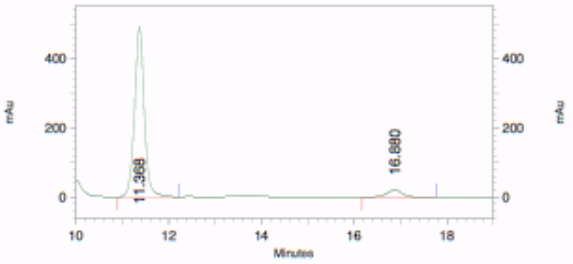

2: 269 nm, 4 nm Results

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16.880	465708	6.092	204

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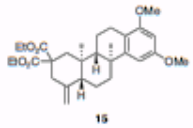

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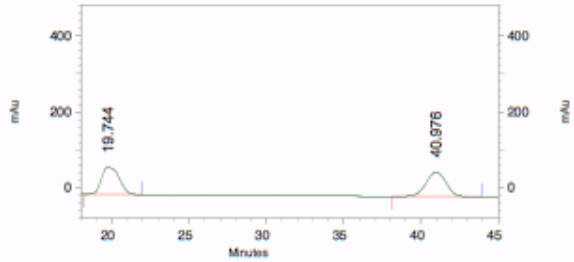
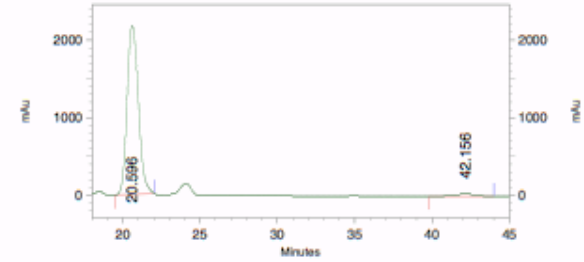


1: 214 nm, 4 nm Results

Retention Time	Area	Area Percent	Lambda Max
19.744	5682768	49.536	207
40.976	5789122	50.464	207



1: 214 nm, 4 nm Results

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20.596	110283653	97.966	208
42.156	2289649	2.034	208

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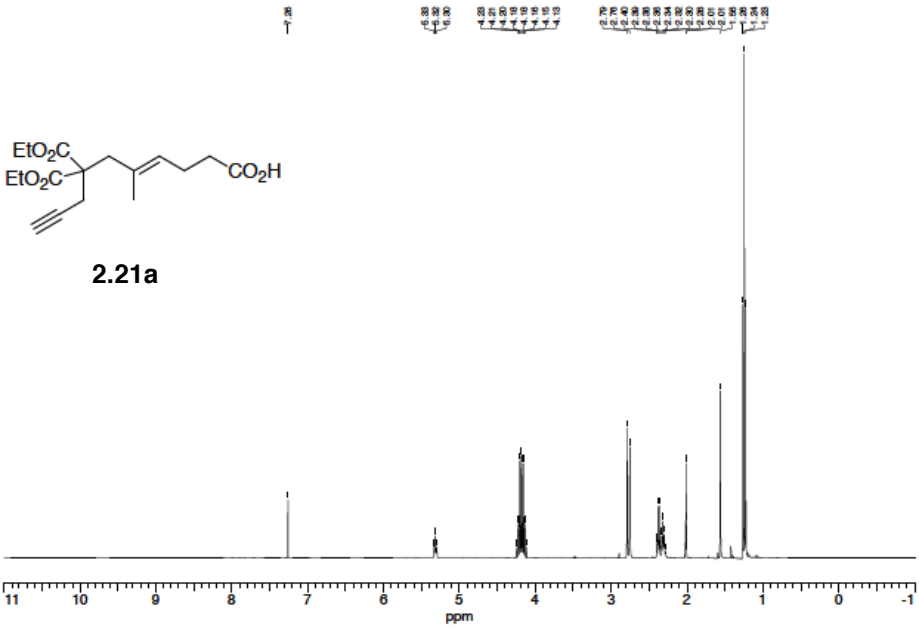
NMR spectra



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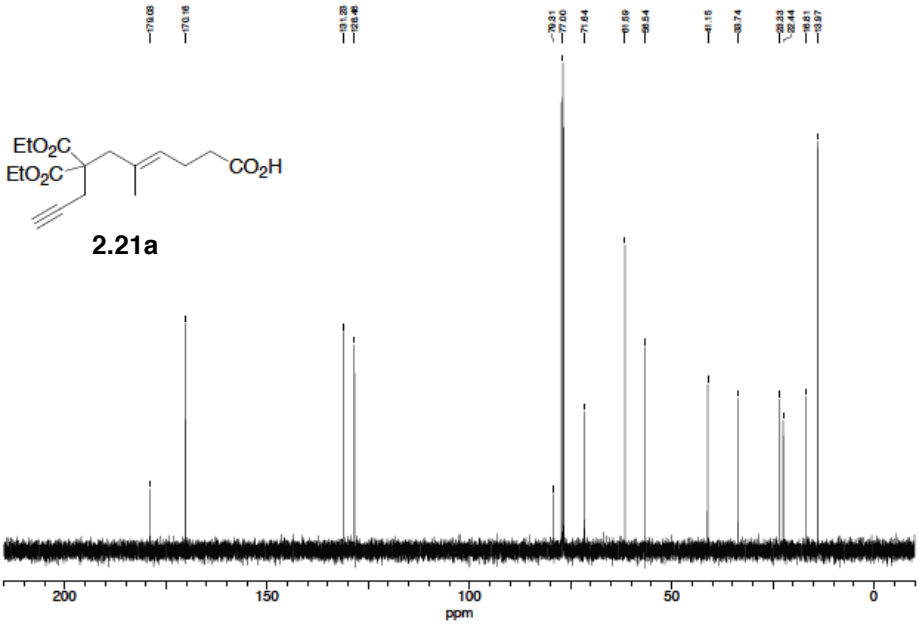
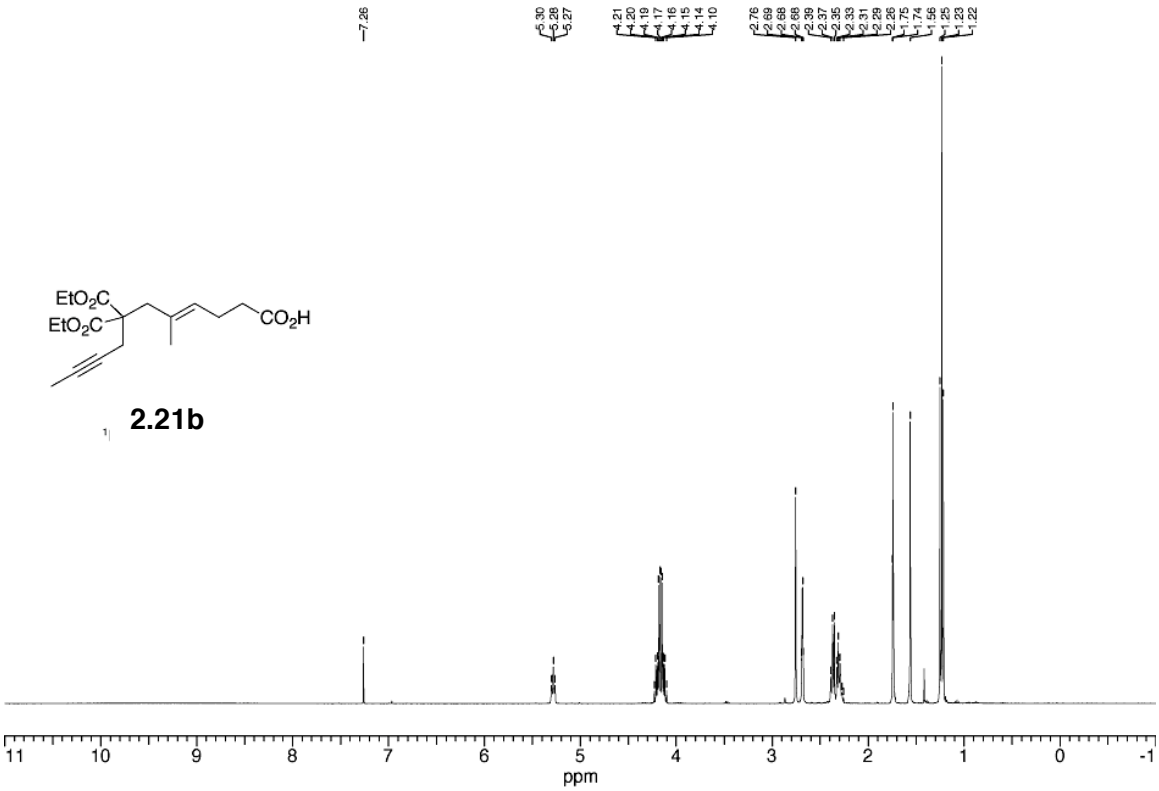


2.21a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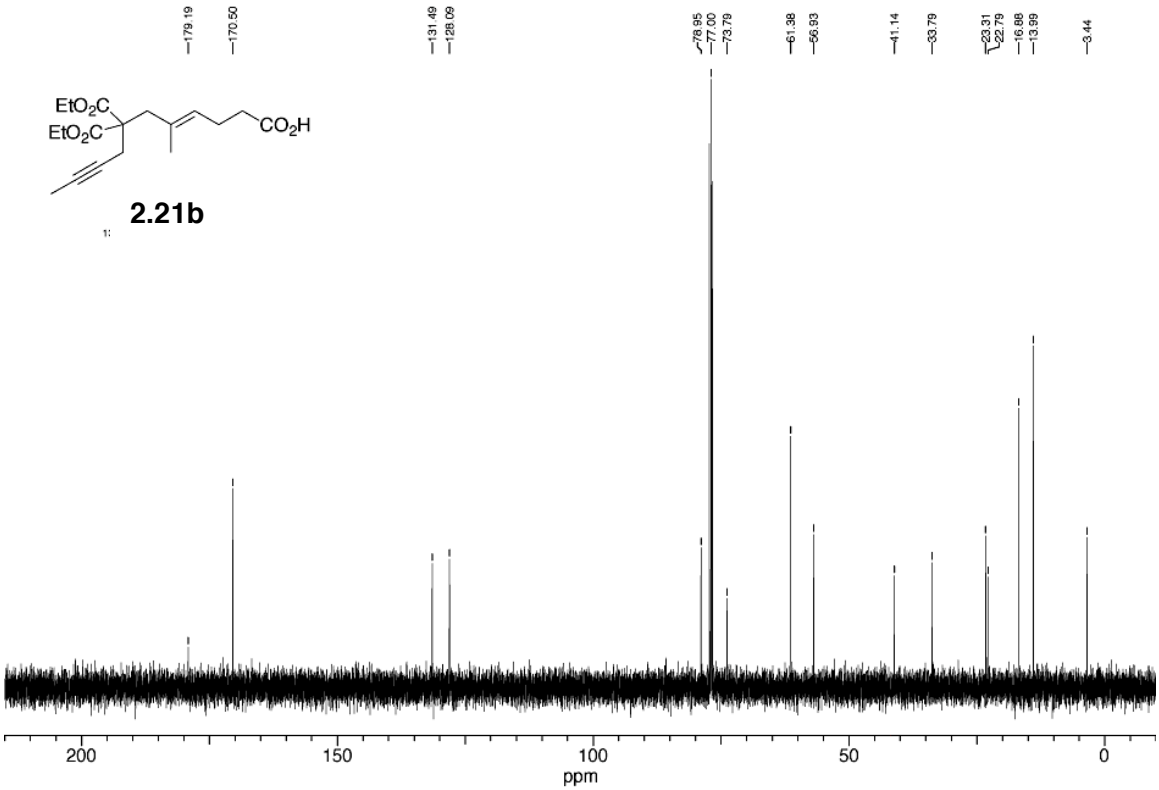
2.39
2.37
2.35
2.33
2.31
2.29
2.26
1.75
1.74
1.56
1.25
1.23
1.22
EtO2C
EtO2C
CO2H
2.21b
11
10
9
8
7
6
5
4
3
2
1
0
-1
ppm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131.49
128.09
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77.00
73.79
61.38
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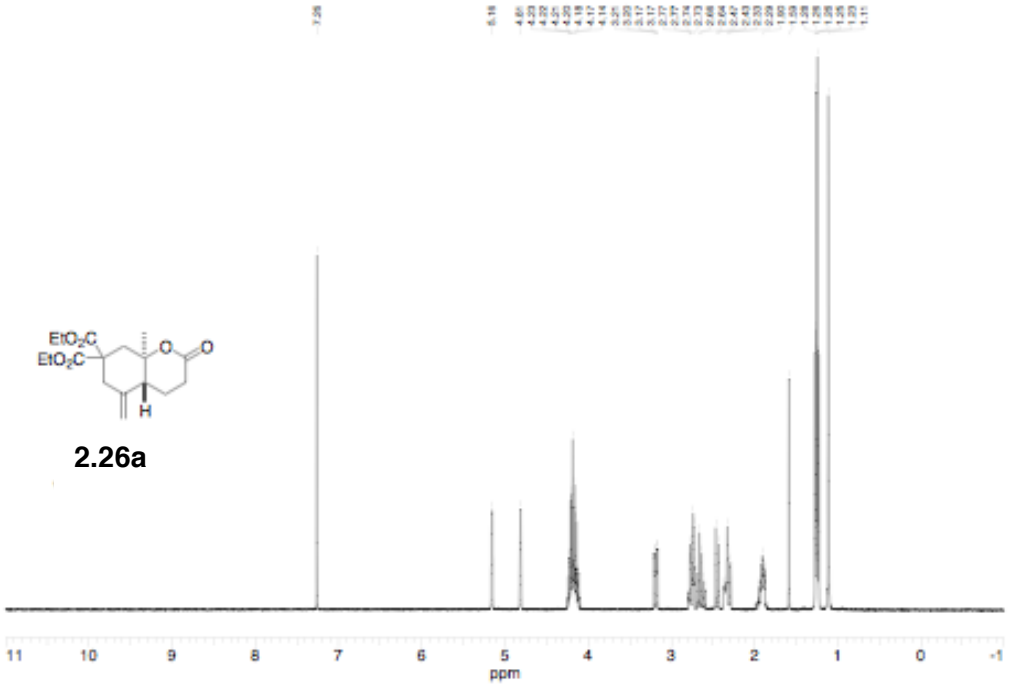
41.14
33.79
23.31
22.79
16.88
13.99
3.44
EtO2C
EtO2C
CO2H
2.21b
200
150
100
50
0
ppm


EtO2C
EtO2C
O
O
H
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10
9
8
7
6
5
4
3
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1
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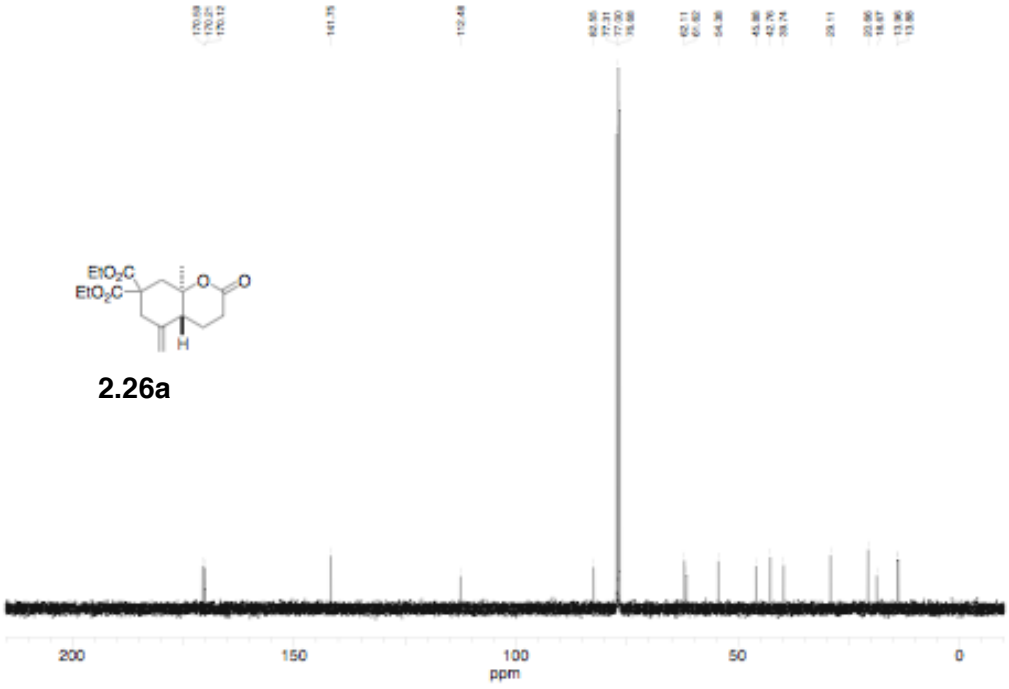
ppm

2.26a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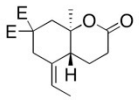
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E
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O
H

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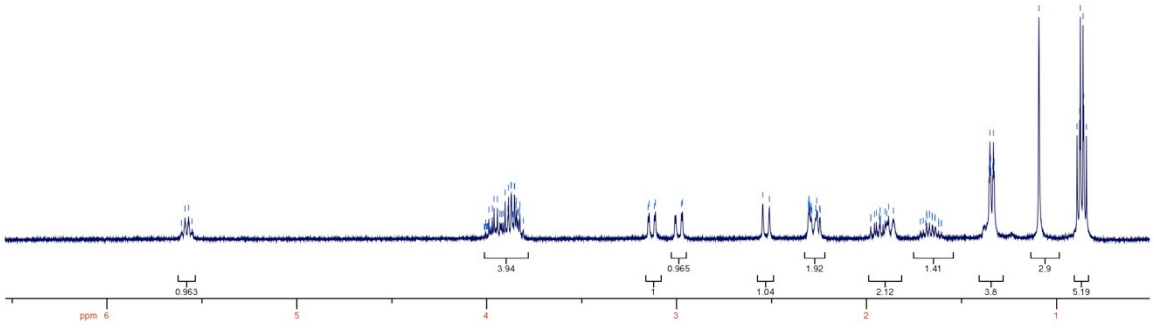
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ppm 6
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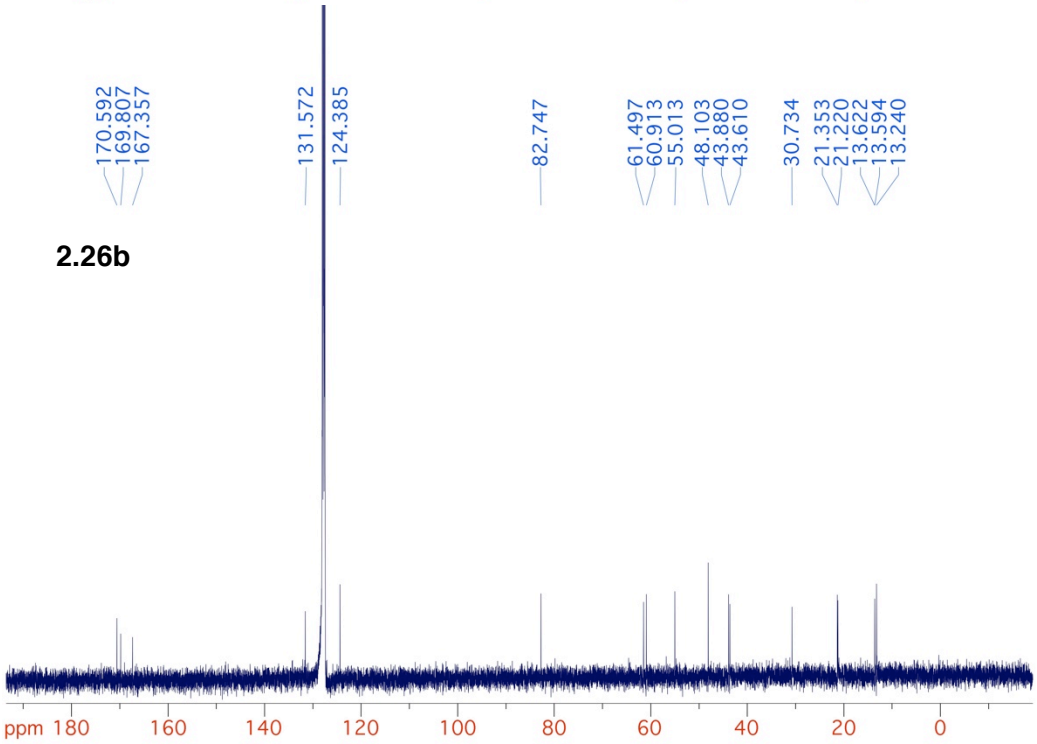
4
3
2
1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167.357
131.572
124.385
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61.497
60.913
55.013
48.103
43.880
43.610
30.734
21.353
21.220
13.622
13.594
13.240
ppm 180
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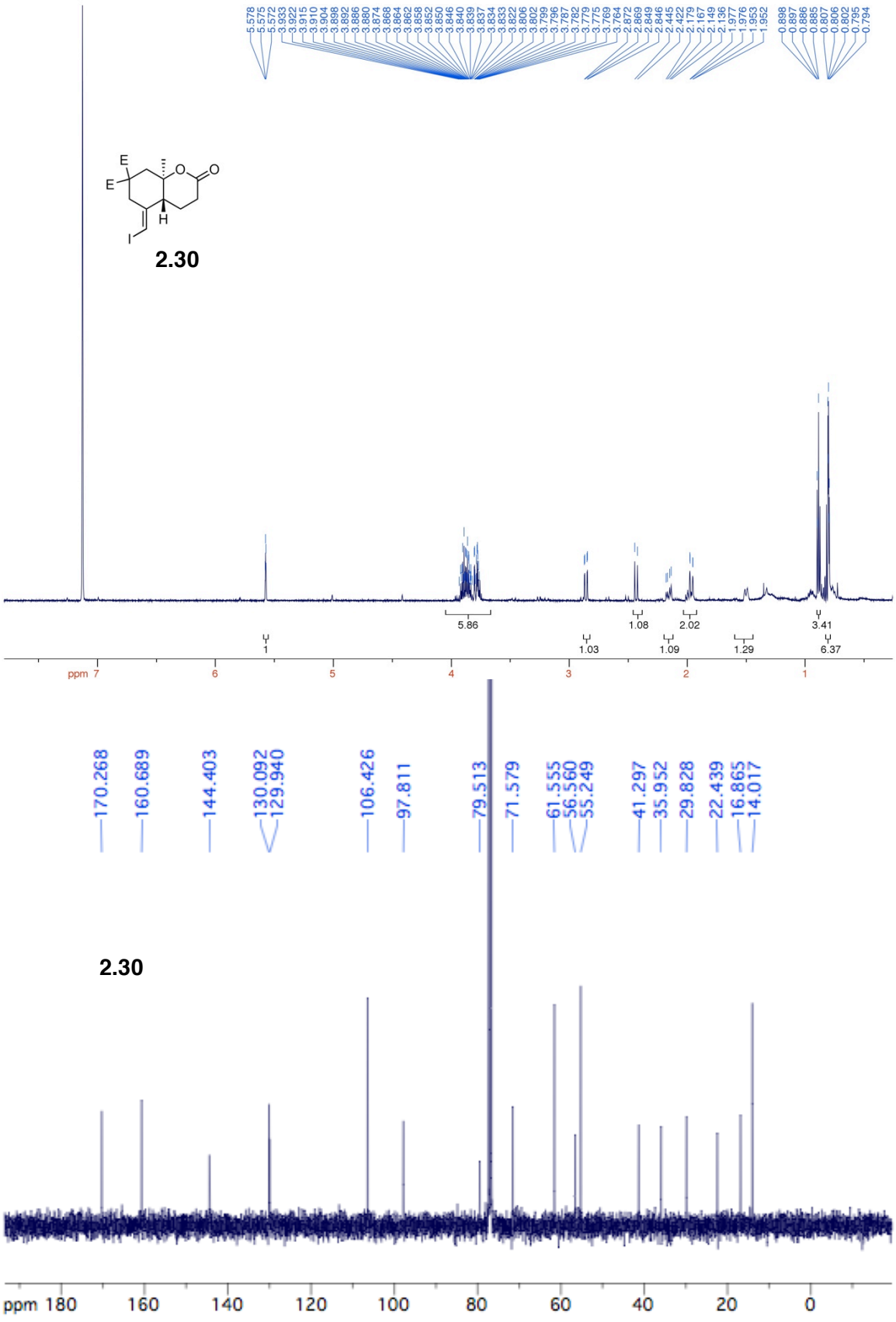
140
120
100
80
60
40
20
0

2.26b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5.575
5.572
5.933
3.922
3.915
3.910
3.904
3.898
3.892
3.886
3.880
3.874
3.868
3.864
3.862
3.858
3.852
3.850
3.846
3.840
3.839
3.837
3.834
3.833
3.822
3.806
3.802
3.799
3.796
3.787
3.782
3.779
3.775
3.769
3.764
2.872
2.869
2.849
2.846
2.445
2.422
2.179
2.167
2.149
2.136
1.977
1.976
1.953
1.952
0.898
0.897
0.886
0.885
0.807
0.806
0.802
0.795
0.794
E
E
O
O
H
I
2.30
5.86
1.08
2.02
3.41
1
1.03
1.09
1.29
6.37
ppm 7
6
5
4
3
2
1
170.268
160.689
144.403
130.092
129.940
106.426
97.811
79.513
71.579
61.555
56.560
55.249
41.297
35.952
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16.865
14.017
2.30
ppm 180
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140
120
100
80
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40
20
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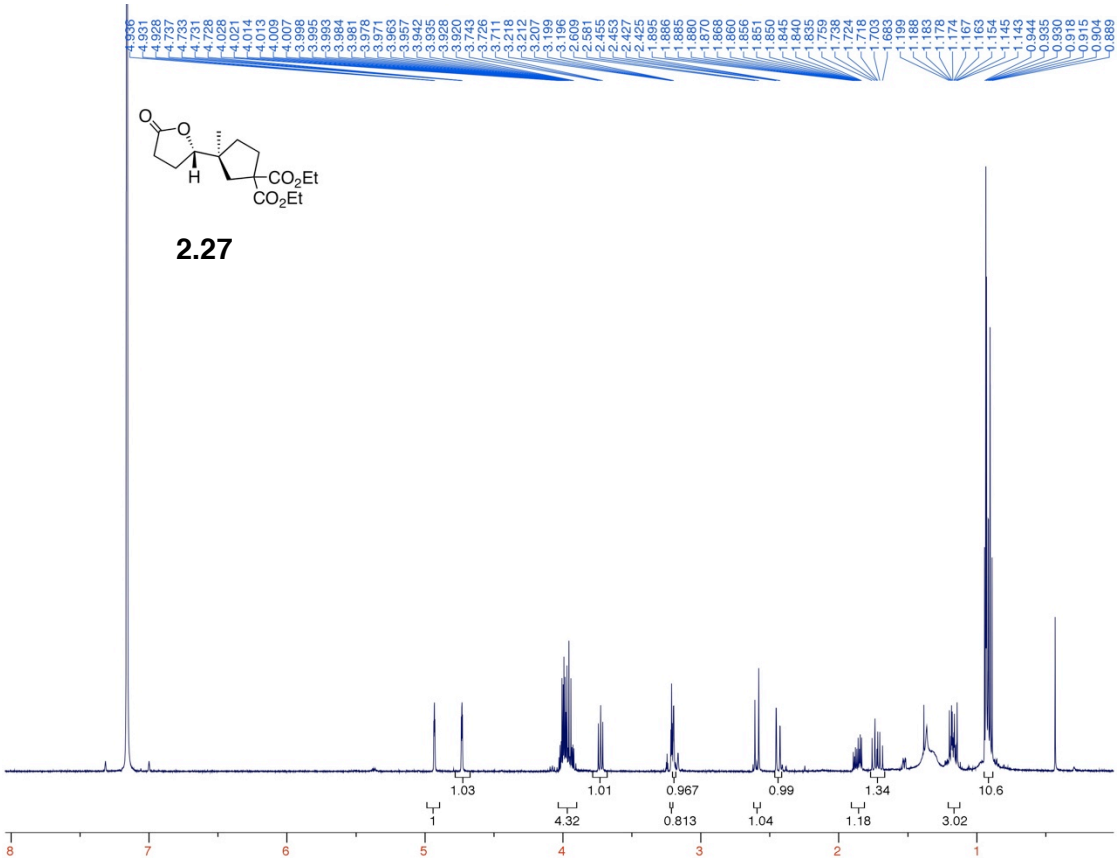
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CO2Et
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1.01
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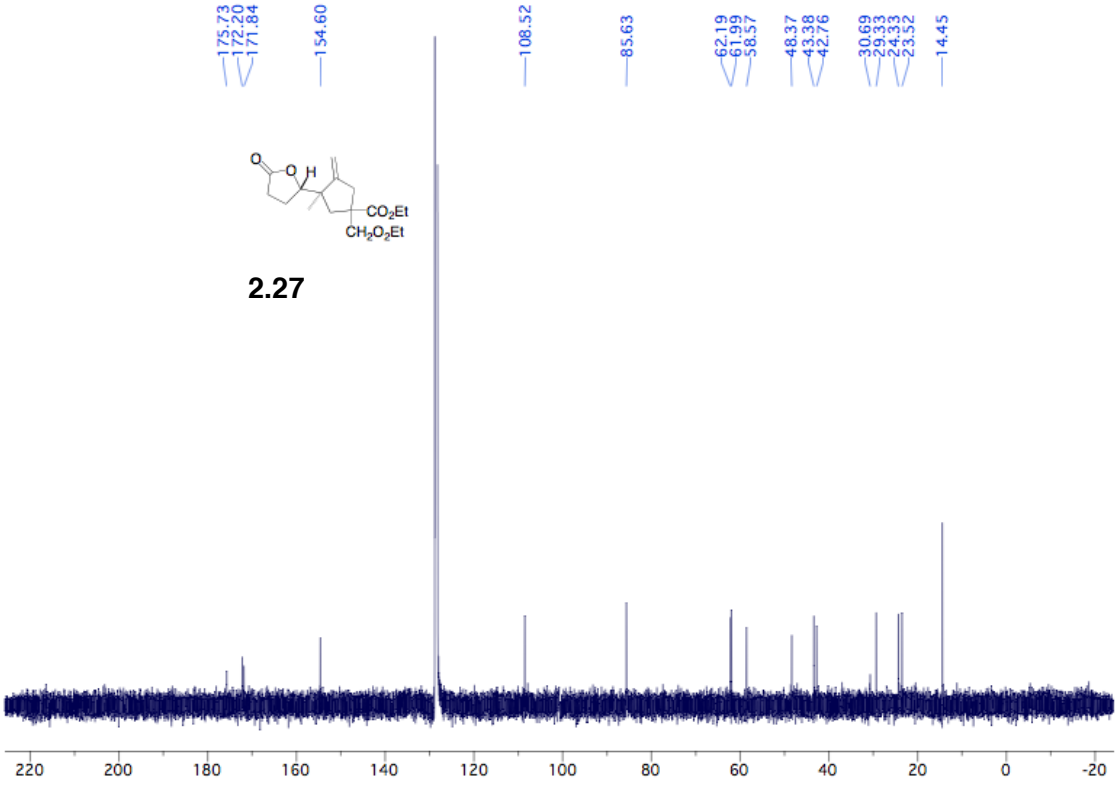
0.99
1.34
10.6
1
4.32
0.813
1.04
1.18
3.02

2.27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172.20
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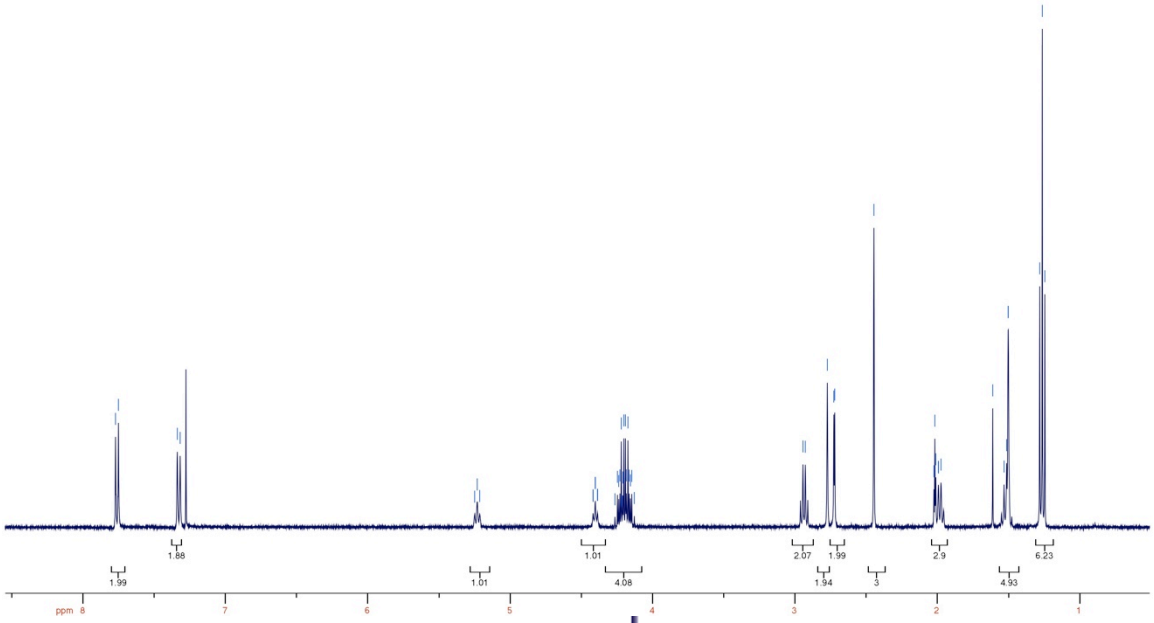
154.60
108.52
85.63
62.19
61.99
58.57
48.37
43.38
42.76
30.69
29.33
24.33
23.52
14.45
CO2Et
CH2O2Et

2.27


EtO2C
EtO2C
NHTs

2.33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1.99
1.01
1.01
4.08
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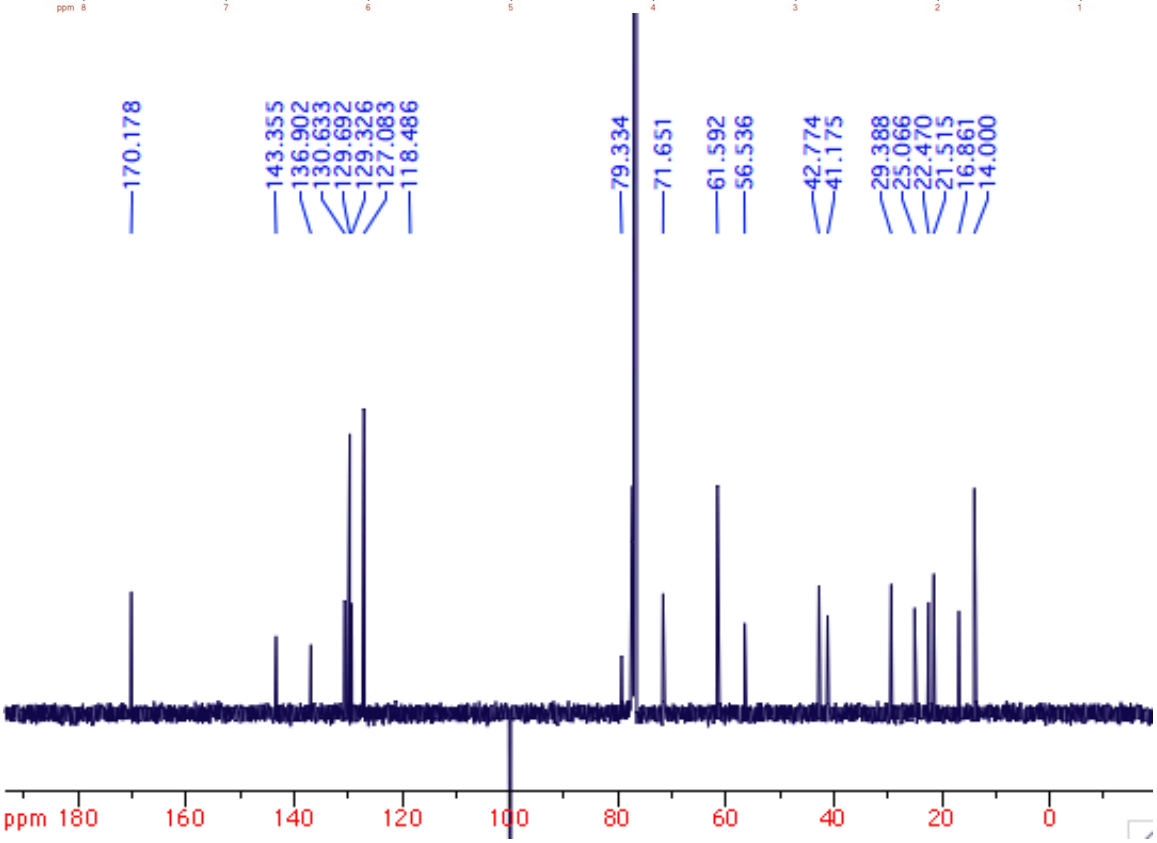
1.94
3
2.9
4.93
6.23
ppm 8
7
6
5
4
3
2
1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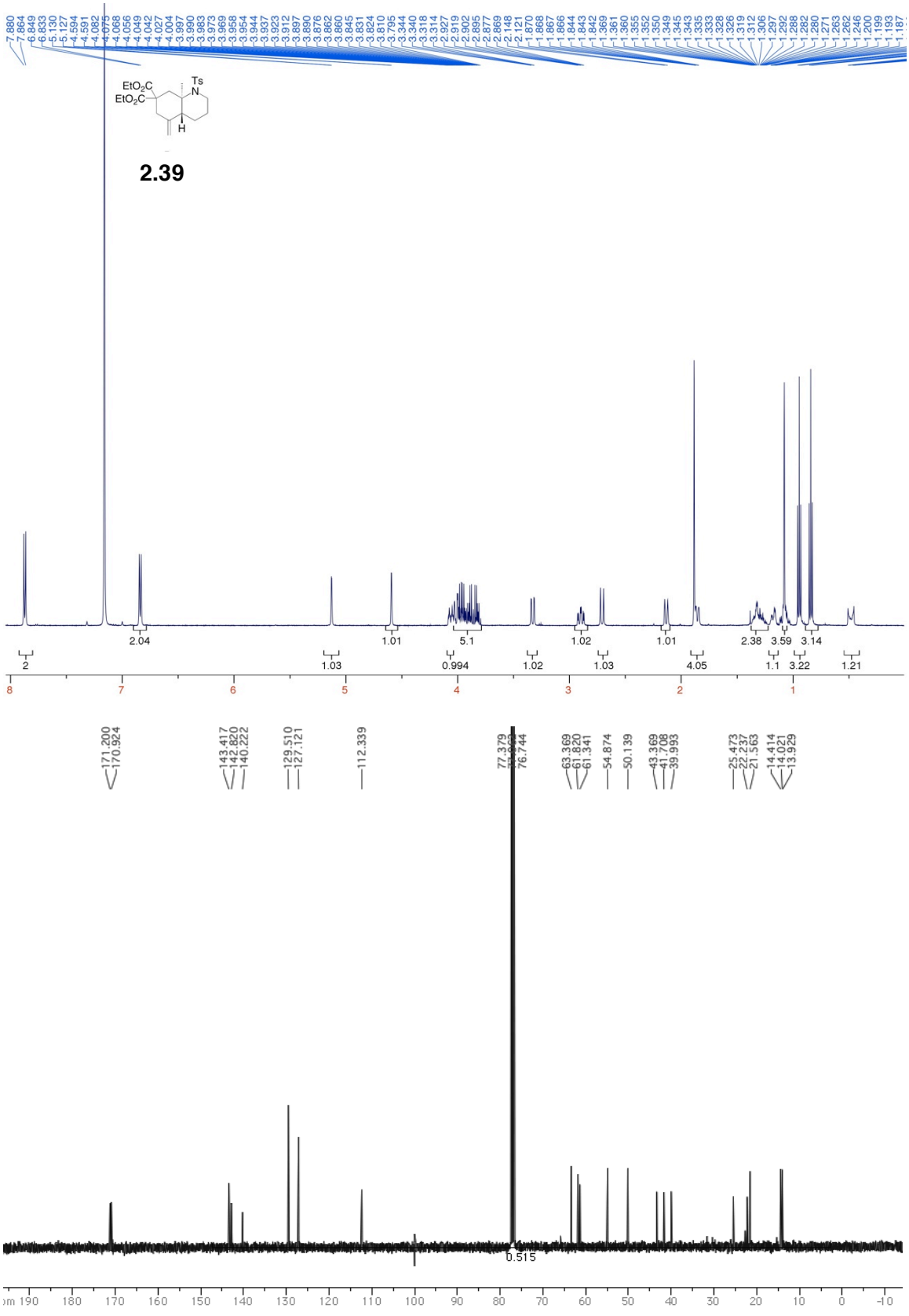
136.902
130.633
129.692
129.326
127.083
118.486
79.334
71.651
61.592
56.536
42.774
41.175
29.388
25.066
22.470
21.515
16.861
14.000
ppm 180
160
140
120
100
80
60
40
20
0


EtO2C
EtO2C
Ts
N
H
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2.04
1.01
5.1
1.02
1.01
2.38
3.59
3.14
2
1.03
0.994
1.02
1.03
4.05
1.1
3.22
1.21
171.200
170.924
143.417
142.820
140.222
129.510
127.121
112.339
77.379
76.744
63.369
61.820
61.341
54.874
50.139
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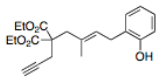
41.708
39.993
25.473
22.237
21.563
14.414
14.021
13.929
0.515


EtO2C
EtO2C
OH

2.22a

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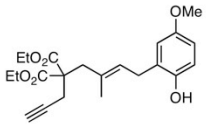
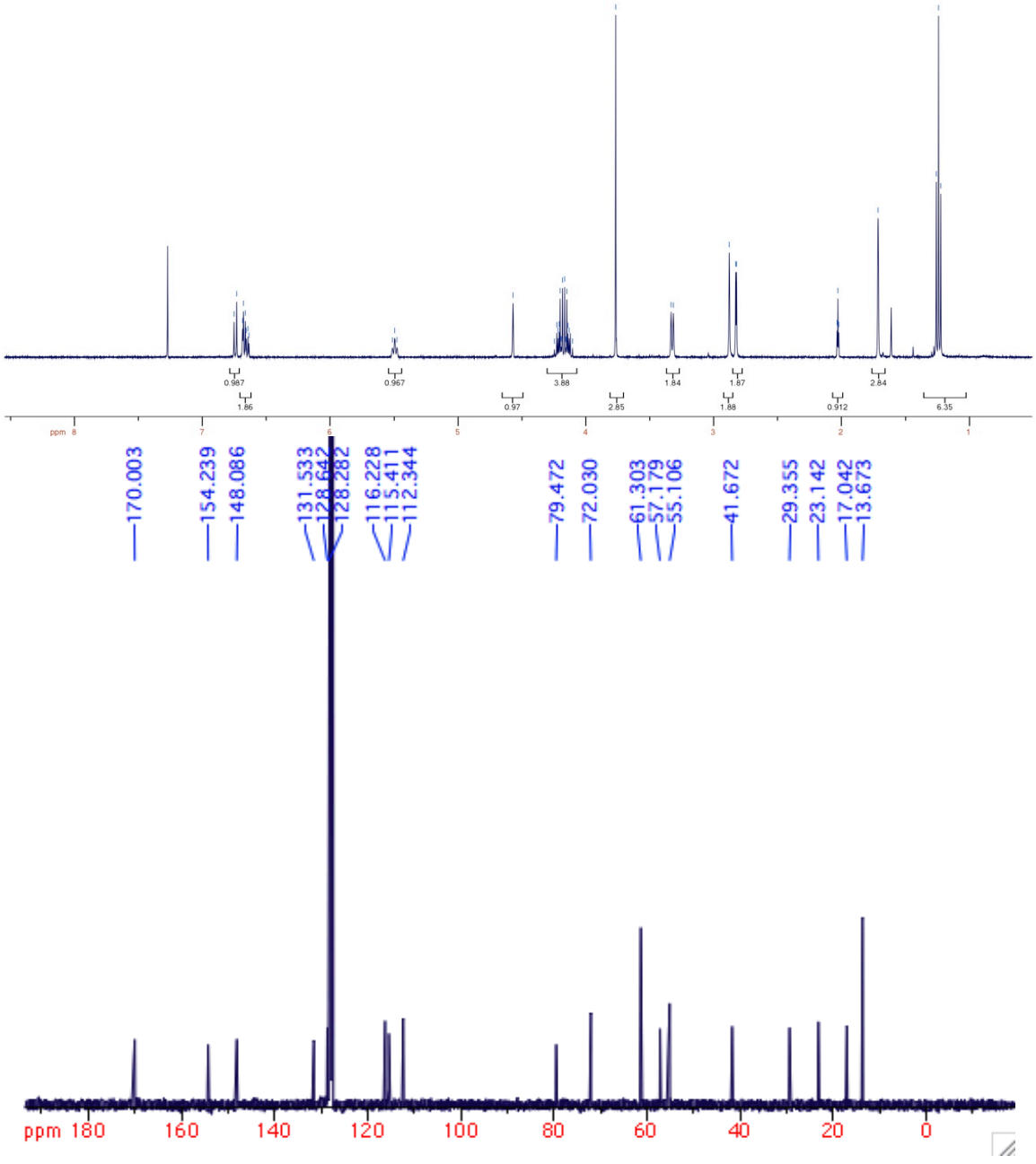
5.505
4.943
4.930
4.220
4.209
4.202
4.197
4.191
4.185
4.179
4.167
4.164
4.152
4.146
4.141
4.134
4.123
4.111
3.350
3.338
2.871
2.819
2.814
2.017
2.013
2.008
1.712
1.244
1.232
1.220
0.956
1
3.86
1.95
0.859
5.79
1.88
0.914
0.926
1.95
1.93
2.88
170.666
169.914
152.813
142.907
129.646
121.063
120.038
117.392
111.031
99.967
99.961
76.533
61.289
60.836
54.513
43.924
43.156
40.005
24.375
17.240
13.531
13.457
ppm 180
160
140
120
100
80
60
40
20
0


OMe
EtO2C
EtO2C
OH

2.22b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115.411
112.344
79.472
72.030
61.303
57.179
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29.355
23.142
17.042
13.673
ppm 180
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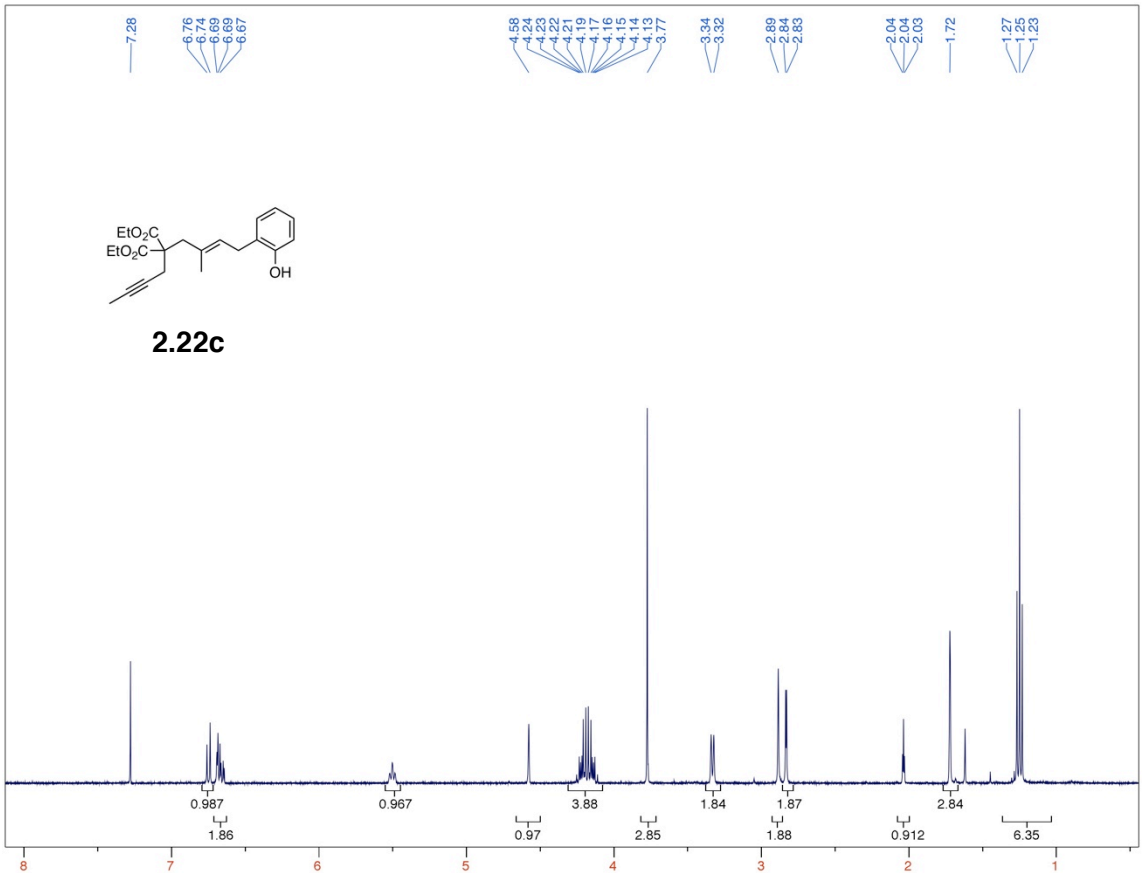
140
120
100
80
60
40
20
0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6.74
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6.69
6.67
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4.24
4.23
4.22
4.21
4.19
4.17
4.16
4.15
4.14
4.13
3.77
3.34
3.32
2.89
2.84
2.83
2.04
2.04
2.03
1.72
1.27
1.25
1.23
EtO2C
EtO2C
OH
0.987
1.86
0.967
0.97
3.88
2.85
1.84
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1.88
2.84
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6.35
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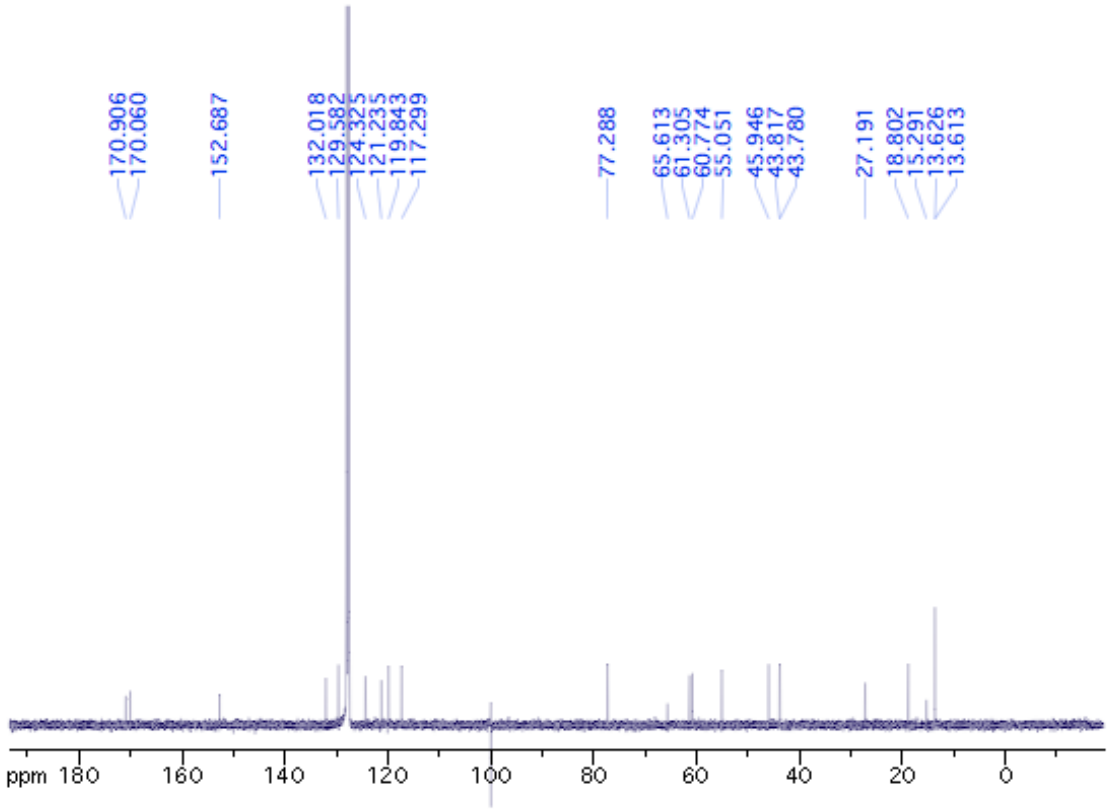
7
6
5
4
3
2
1

2.22c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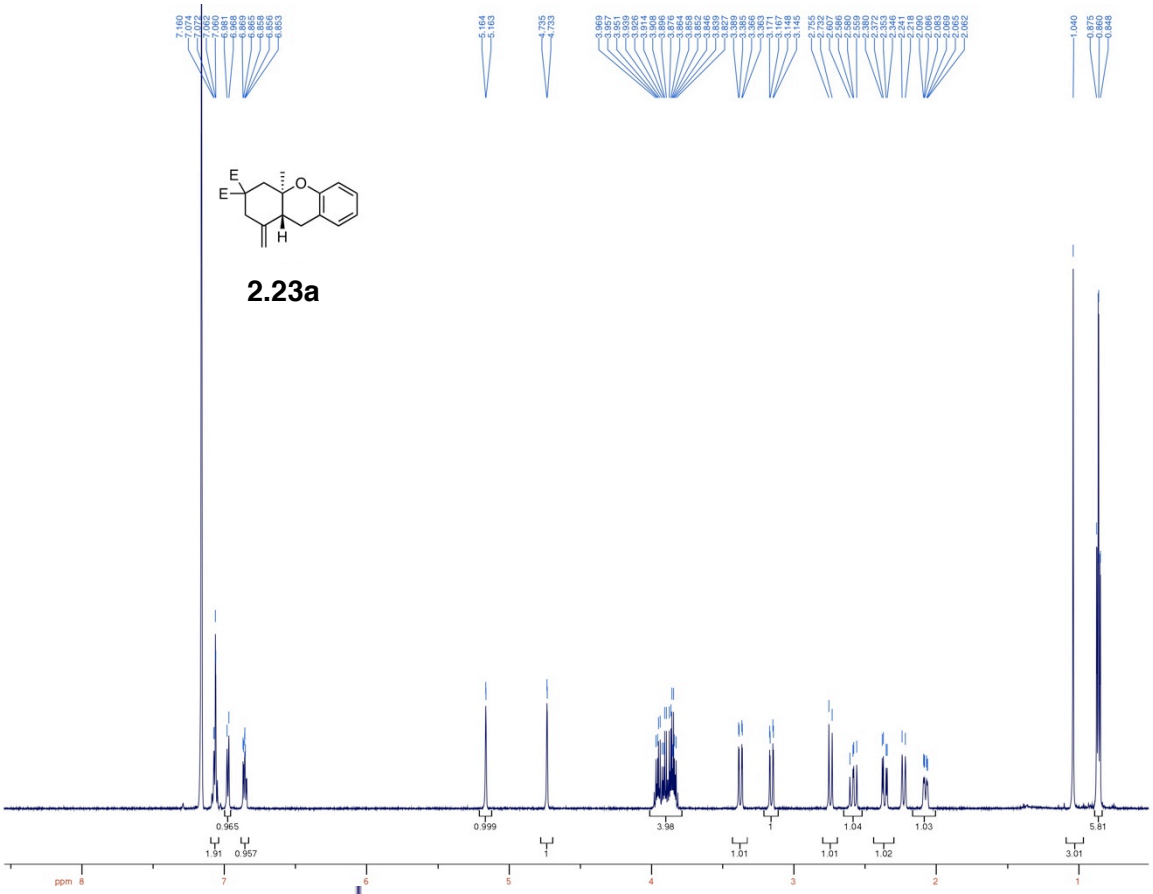
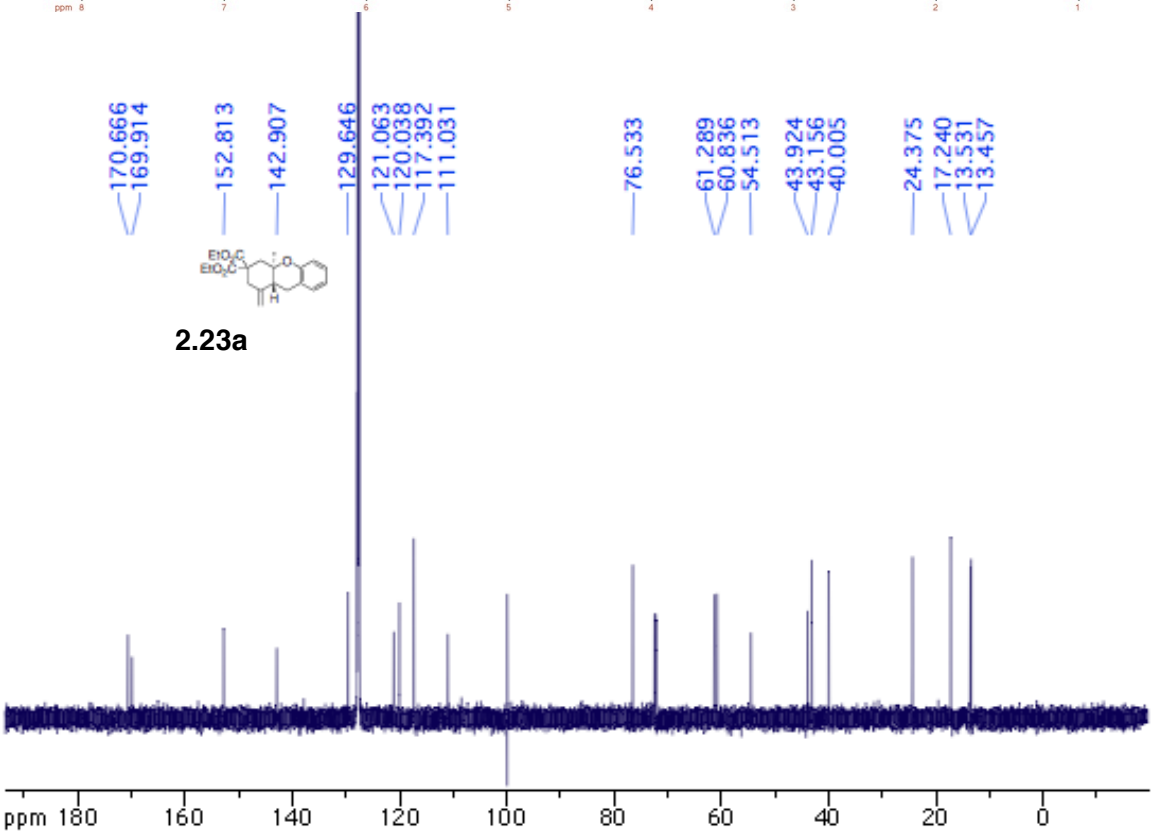
170.060
152.687
132.018
129.582
124.325
121.235
119.843
117.299
77.288
65.613
61.305
60.774
55.051
45.946
43.817
43.780
27.191
18.802
15.291
13.626
13.613
ppm 180
160
140
120
100
80
60
40
20
0


E
E
O
H
2.23a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152.813
142.907
129.646
121.063
120.038
117.392
111.031
76.533
61.289
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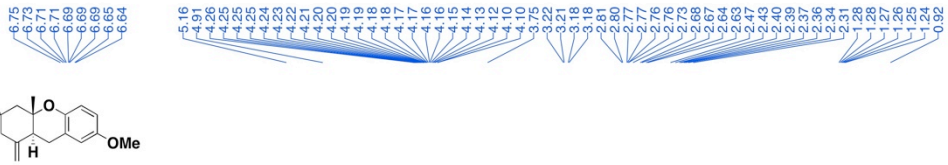
54.513
43.924
43.156
40.005
24.375
17.240
13.531
13.457
EtO2C
EtO2C
O
H
2.23a
ppm 180
160
140
120
100
80
60
40
20
0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6.71
6.69
6.69
6.69
6.65
6.64
5.16
4.91
4.26
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4.25
4.24
4.23
4.22
4.21
4.20
4.20
4.19
4.19
4.18
4.18
4.17
4.17
4.16
4.16
4.15
4.14
4.13
4.12
4.10
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3.21
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2.47
2.43
2.40
2.39
2.37
2.36
2.34
2.31
1.28
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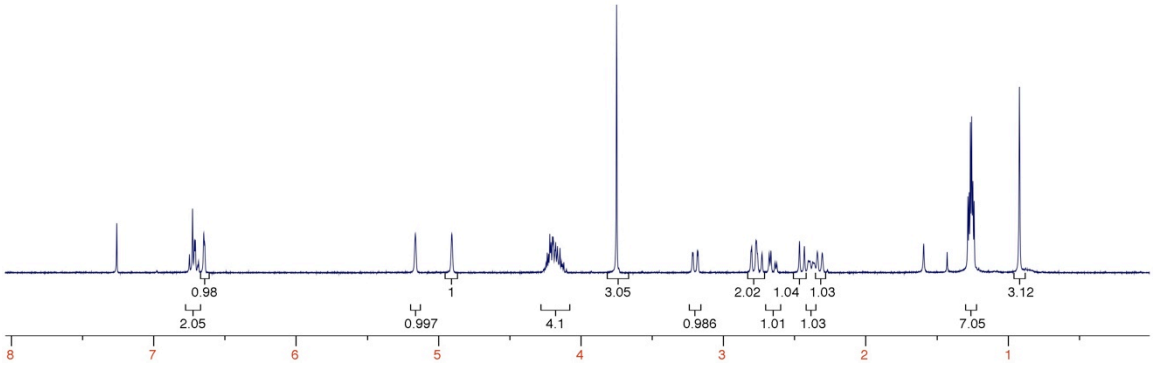
1.25
1.24
0.92

EtO2C
EtO2C
O
H
OMe

2.23b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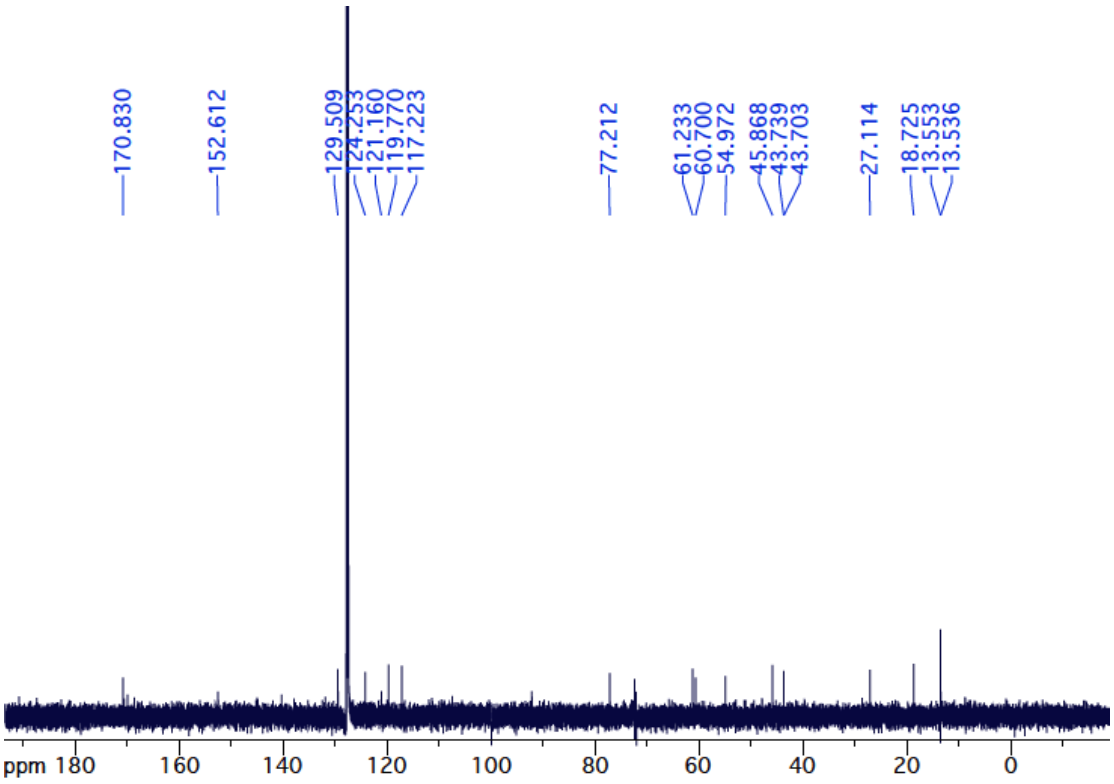
1.01
1.03
1.03
3.12
7.05
8
7
6
5
4
3
2
1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77.212
61.233
60.700
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45.868
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43.703
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18.725
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13.536
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140
120
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80
60
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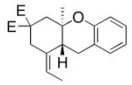
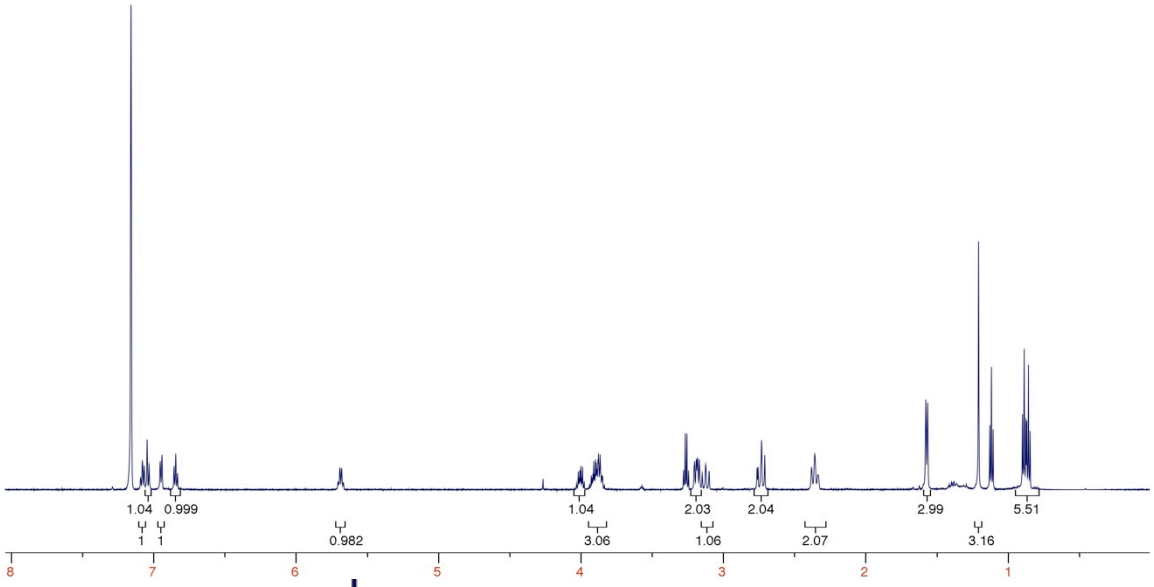
20
0



2.23c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1
1
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1.06
2.04
2.07
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3.16
5.51
8
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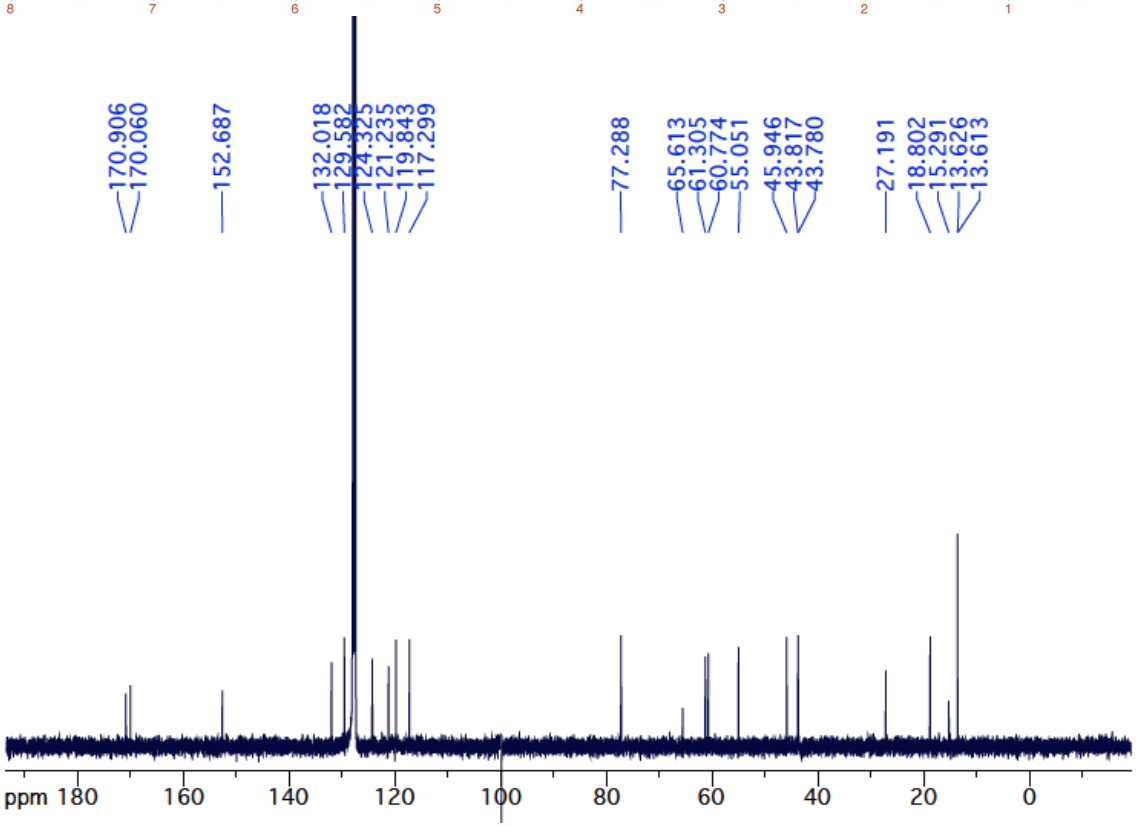
6
5
4
3
2
1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170.060
152.687
132.018
129.582
124.325
121.235
119.843
117.299
77.288
65.613
61.305
60.774
55.051
45.946
43.817
43.780
27.191
18.802
15.291
13.626
13.613
ppm 180
160
140
120
100
80
60
40
20
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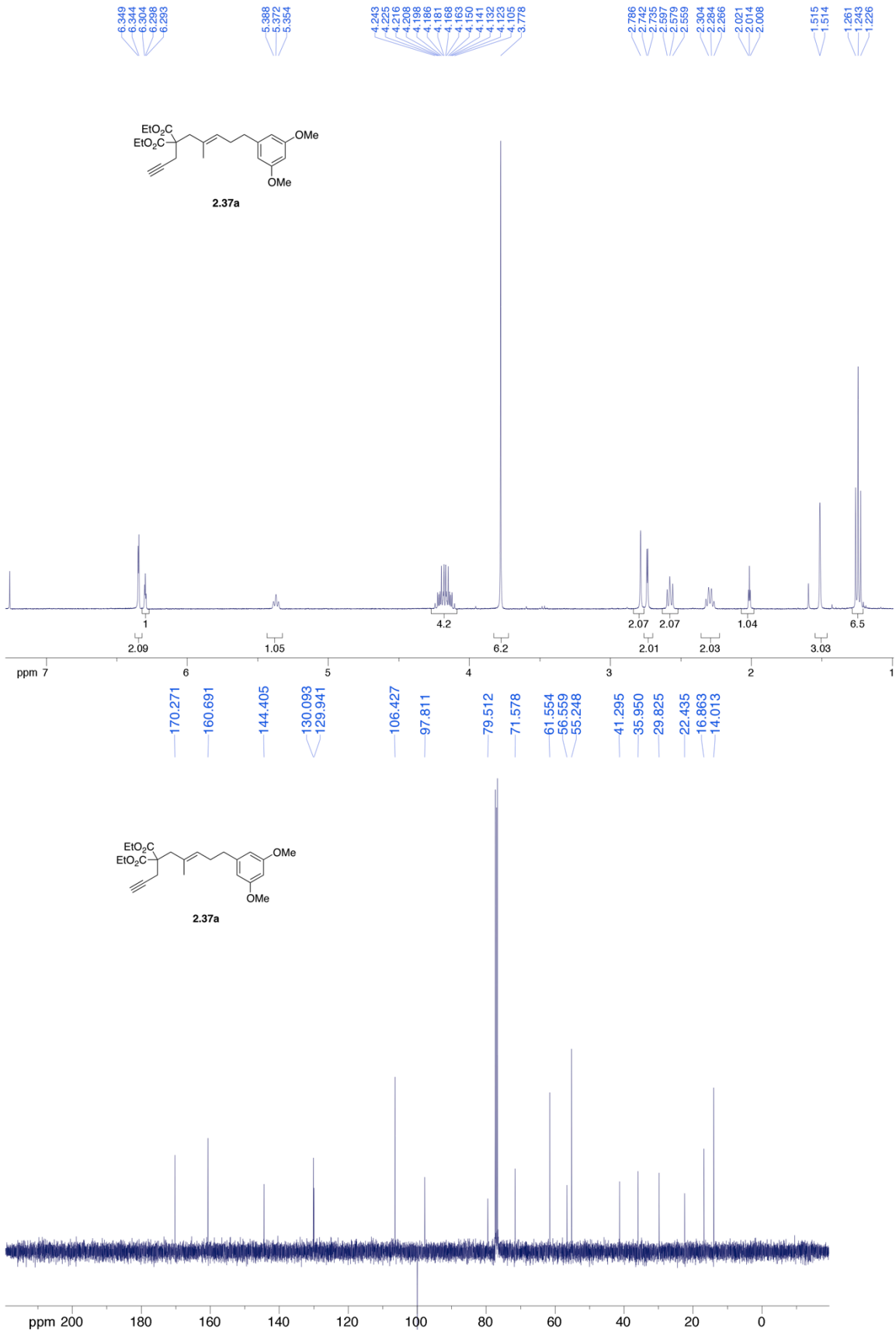
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4.225
4.216
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4.198
4.186
4.181
4.168
4.163
4.150
4.141
4.122
4.105
3.778
2.786
2.742
2.735
2.597
2.570
2.559
2.304
2.284
2.266
2.021
2.014
2.008
1.515
1.514
1.261
1.243
1.226
EtO2C
EtO2C
OMe
OMe
2.37a
1
4.2
2.07
2.07
1.04
6.5
2.09
1.05
6.2
2.01
2.03
3.03
ppm 7
6
5
4
3
2
1
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130.093
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79.512
71.578
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56.559
55.248
41.295
35.950
29.825
22.435
16.863
14.013
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EtO2C
OMe
OMe
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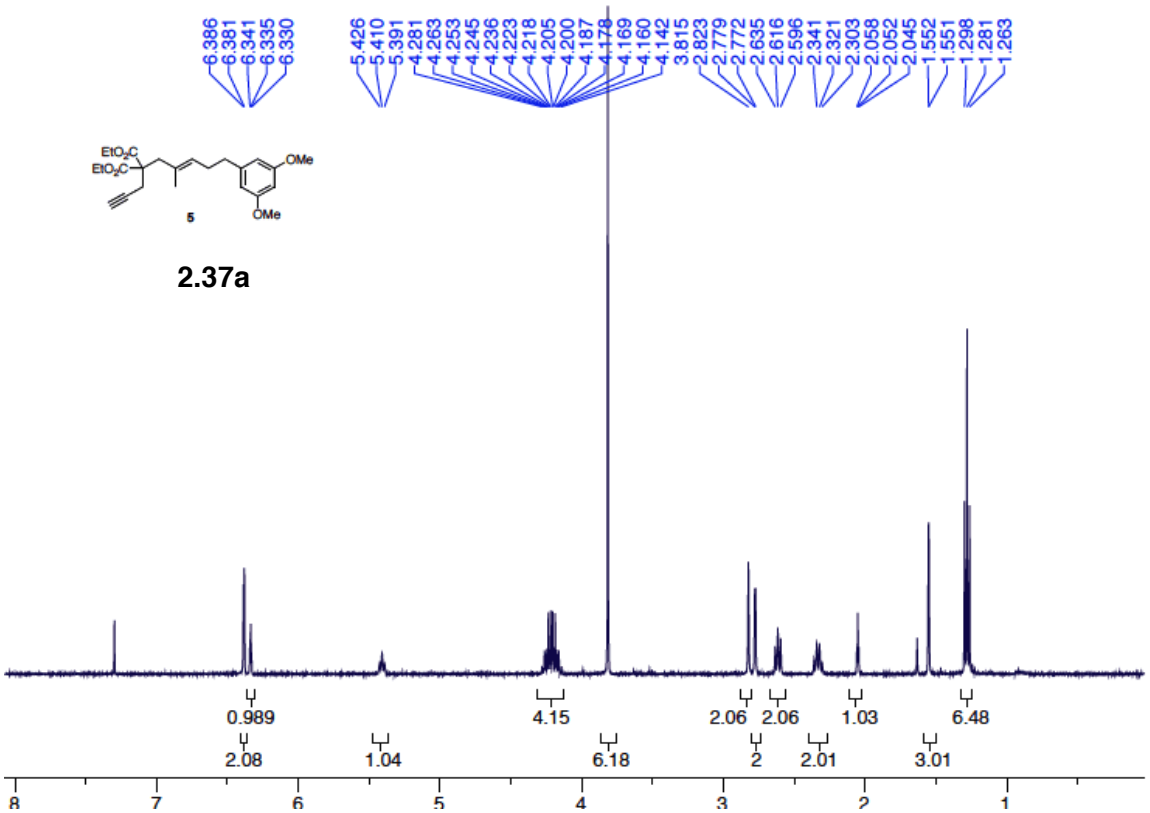
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4.236
4.223
4.218
4.205
4.200
4.187
4.178
4.169
4.160
4.142
3.815
2.823
2.779
2.772
2.635
2.616
2.596
2.341
2.321
2.303
2.058
2.052
2.045
1.552
1.551
1.298
1.281
1.263
EtO2C
EtO2C
OMe
OMe
5
0.989
4.15
2.06
2.06
1.03
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1.04
6.18
2
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3.01
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6
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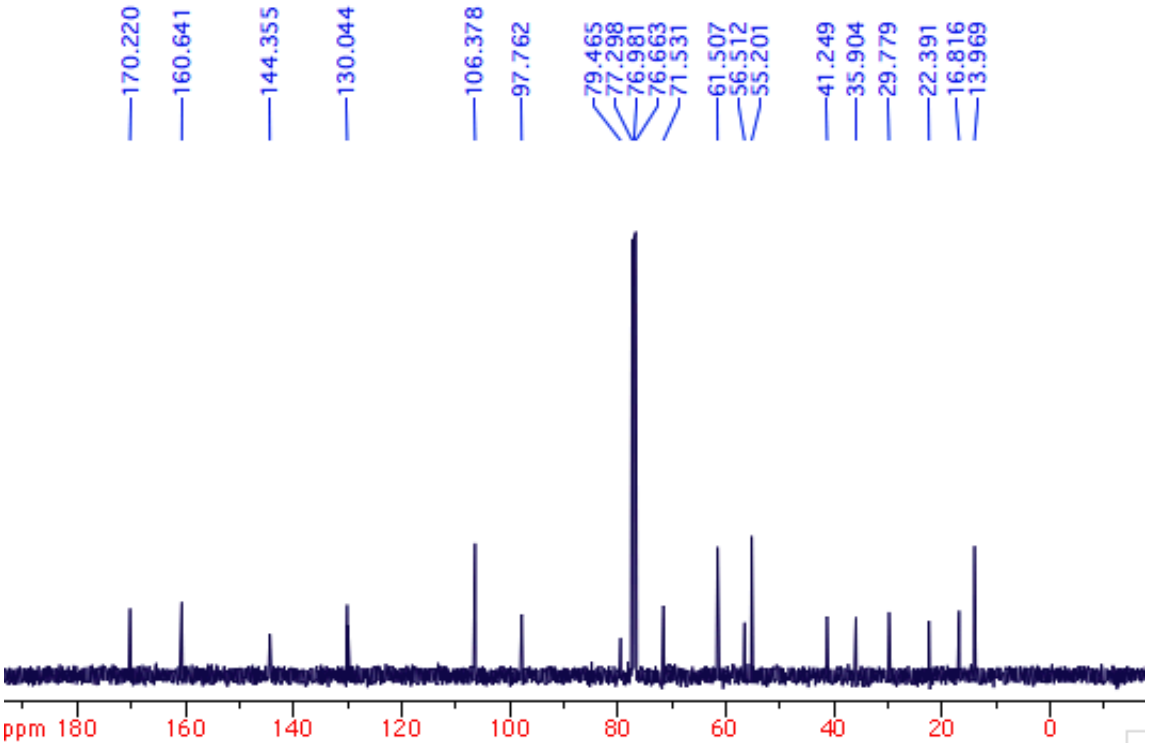
3
2
1

2.37a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130.044
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97.762
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77.298
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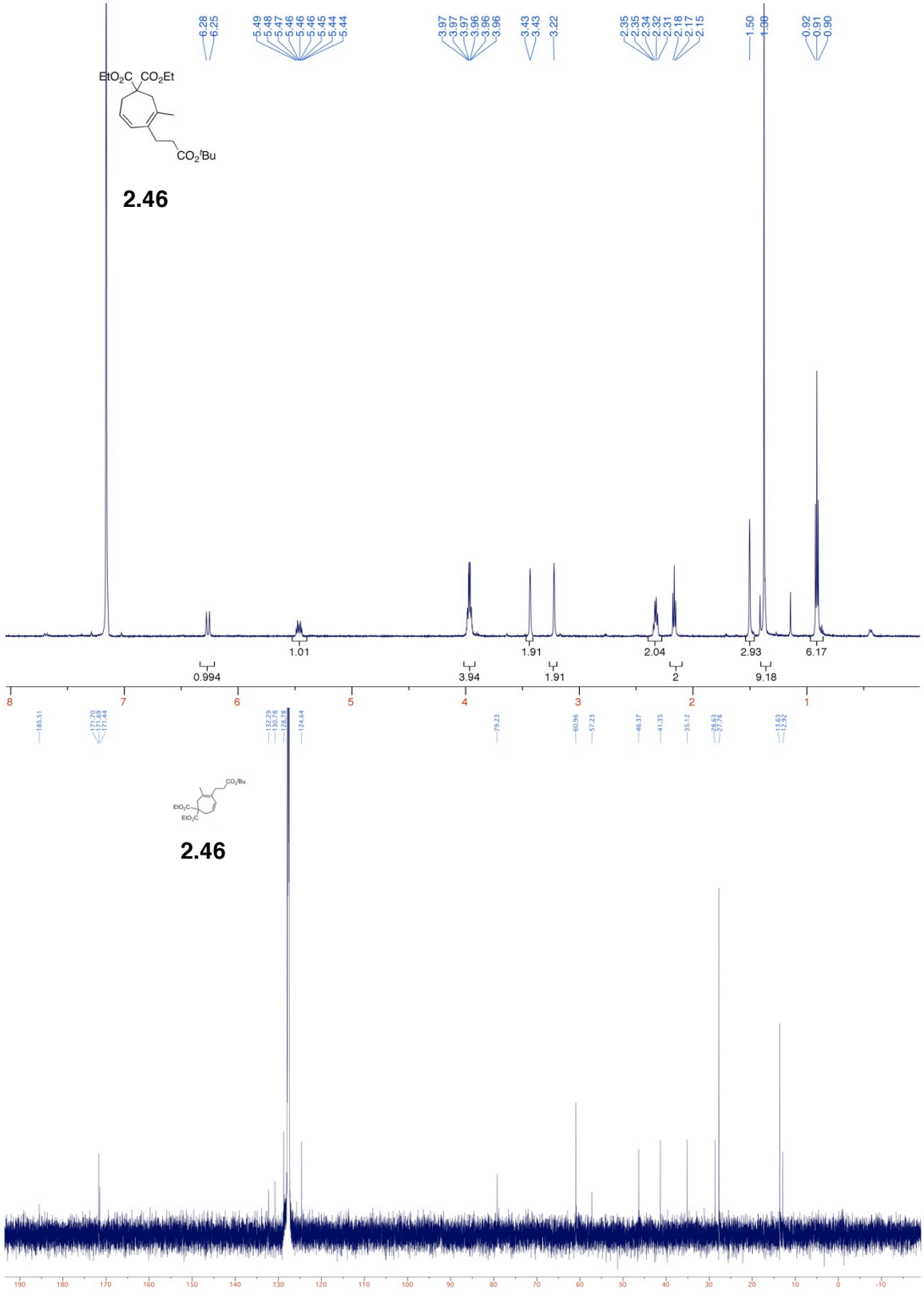
76.663
71.531
61.507
56.512
55.201
41.249
35.904
29.779
22.391
16.816
13.969
ppm 180
160
140
120
100
80
60
40
20
0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5.44
5.44
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3.97
3.96
3.96
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3.43
3.22
2.35
2.35
2.34
2.32
2.31
2.18
2.17
2.15
1.50
1.38
0.92
0.91
0.90
EtO2C CO2Et
CO2tBu
2.46
1.01
0.994
1.91
3.94
1.91
2.04
2
2.93
9.18
6.17
8
7
6
5
4
3
2
1
185.51
171.70
171.69
171.44
132.29
130.78
129.76
124.64
79.23
60.96
57.23
46.37
41.35
35.12
28.63
27.76
13.63
12.92
CO2tBu
EtO2C
EtO2C
2.46
190
180
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140
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120
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100
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50
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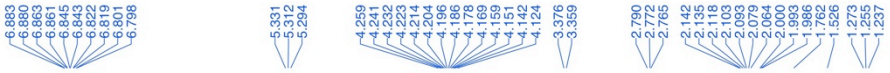
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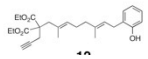
1.237



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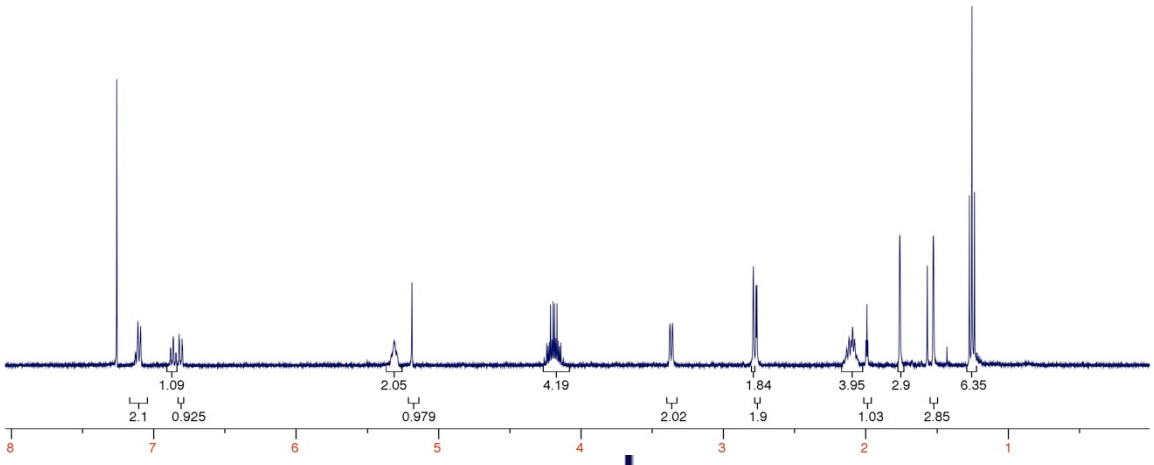
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2.05
4.19
1.84
3.95
2.9
6.35
2.1
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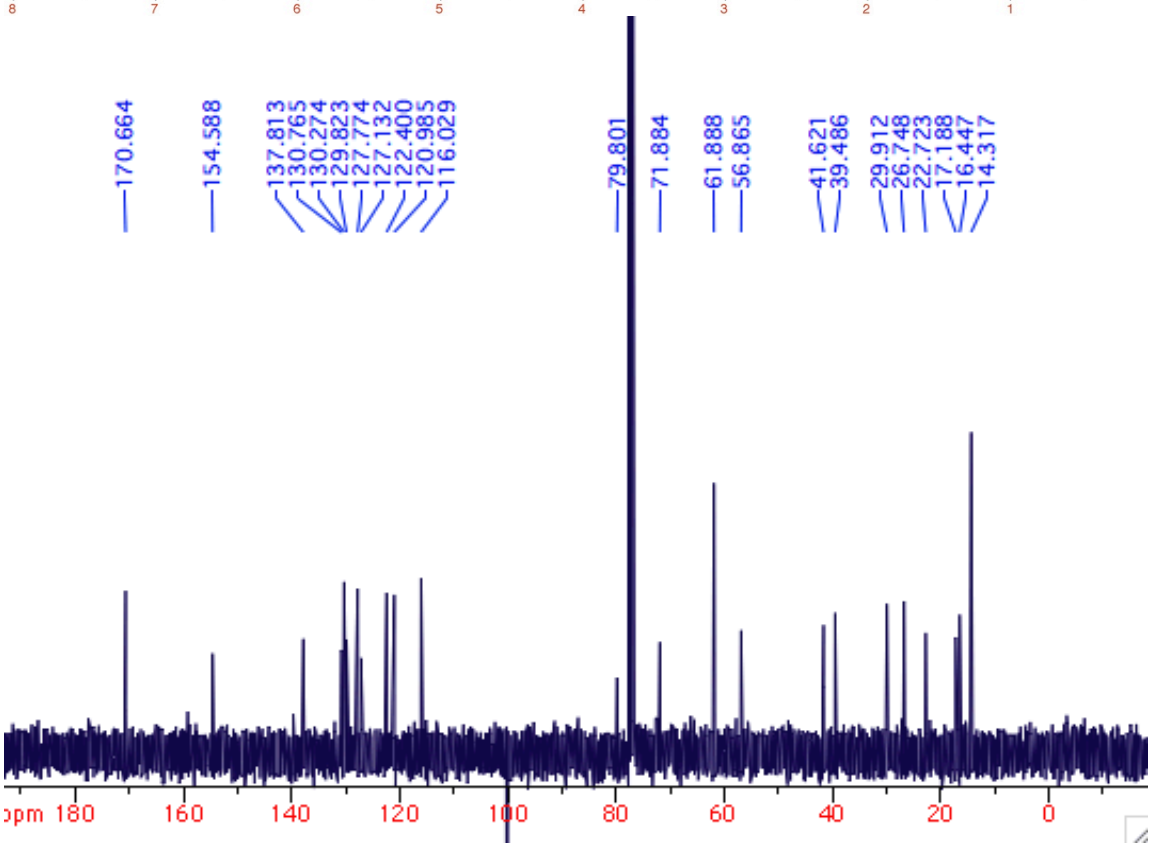
0.979
2.02
1.9
1.03
2.85
8
7
6
5
4
3
2
1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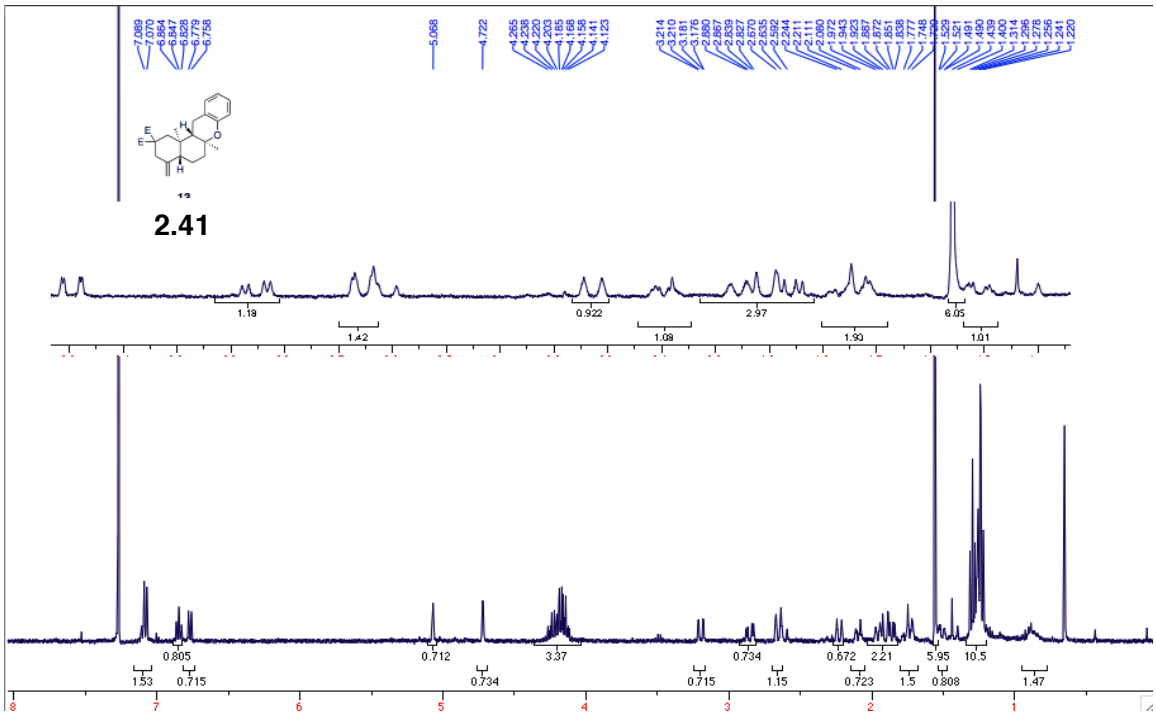
137.813
130.765
130.274
129.823
127.774
127.132
122.400
120.985
116.029
79.801
71.884
61.888
56.865
41.621
39.486
29.912
26.748
22.723
17.188
16.447
14.317
ppm 180
160
140
120
100
80
60
40
20
0



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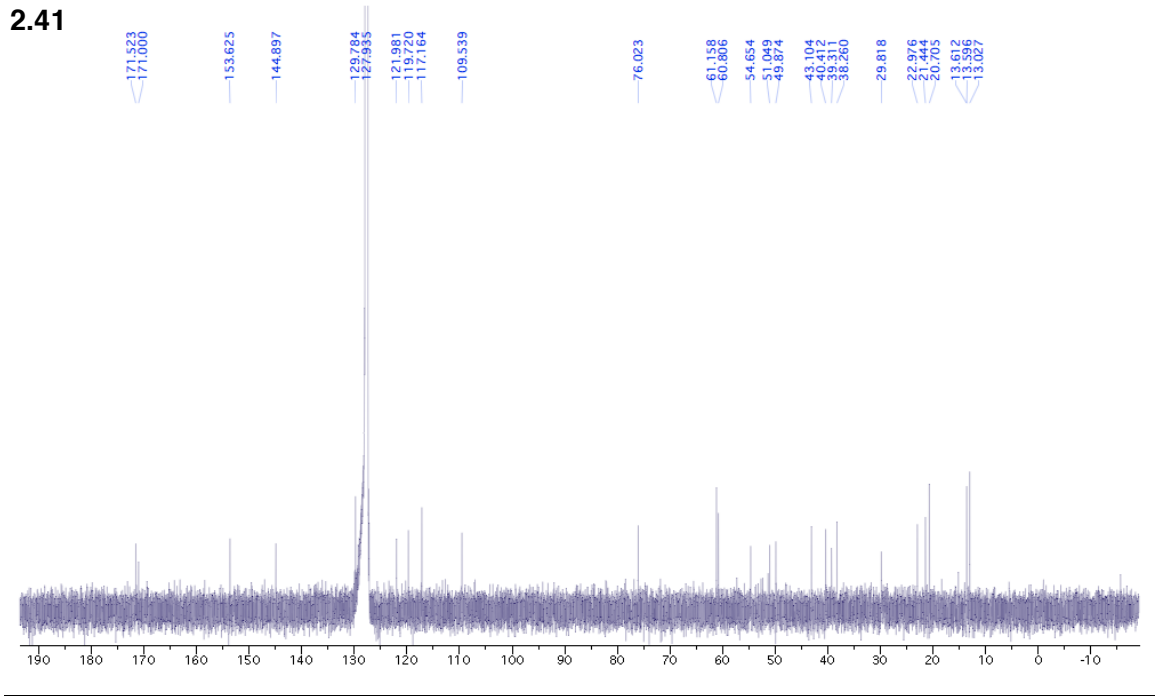

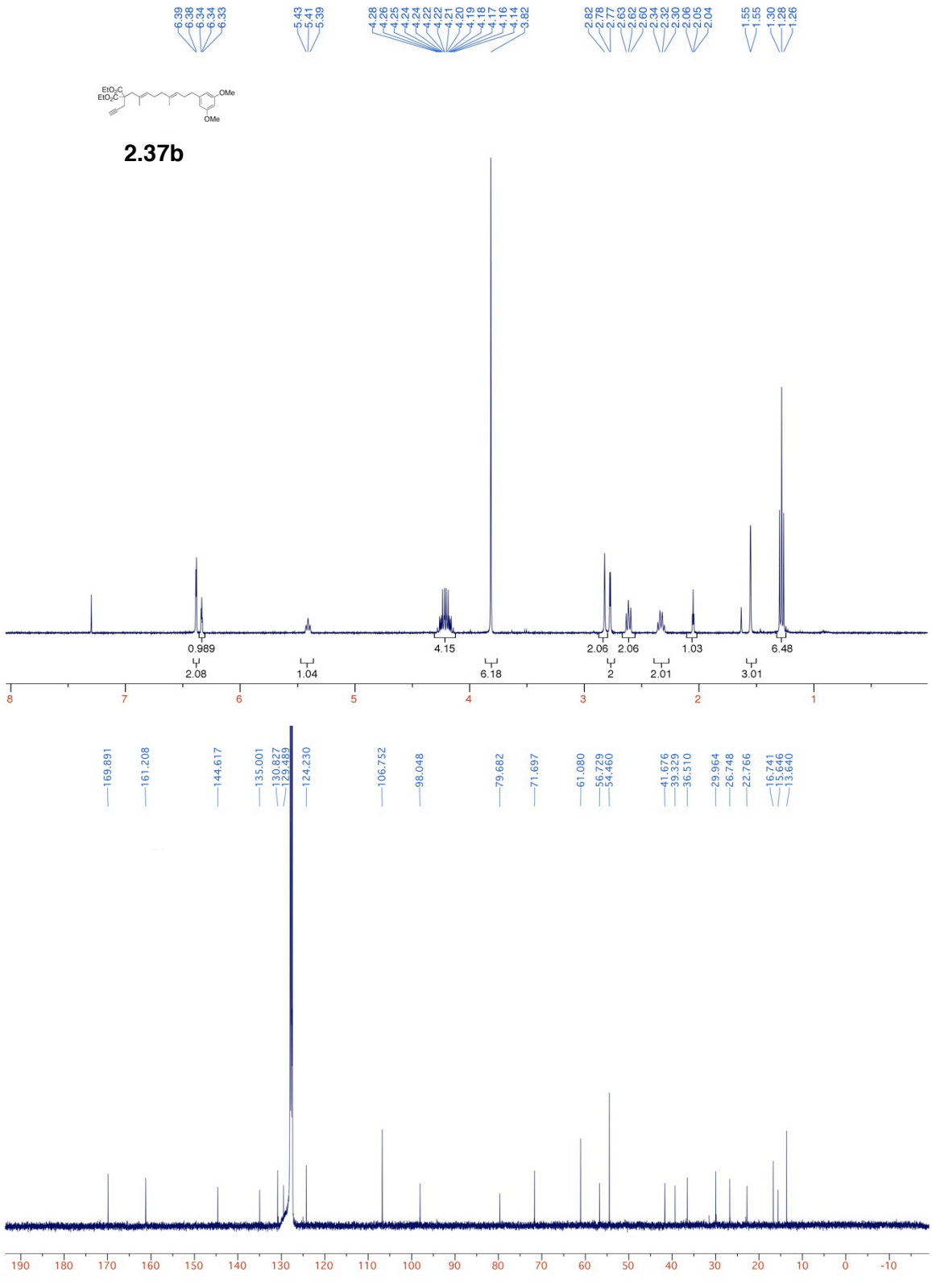
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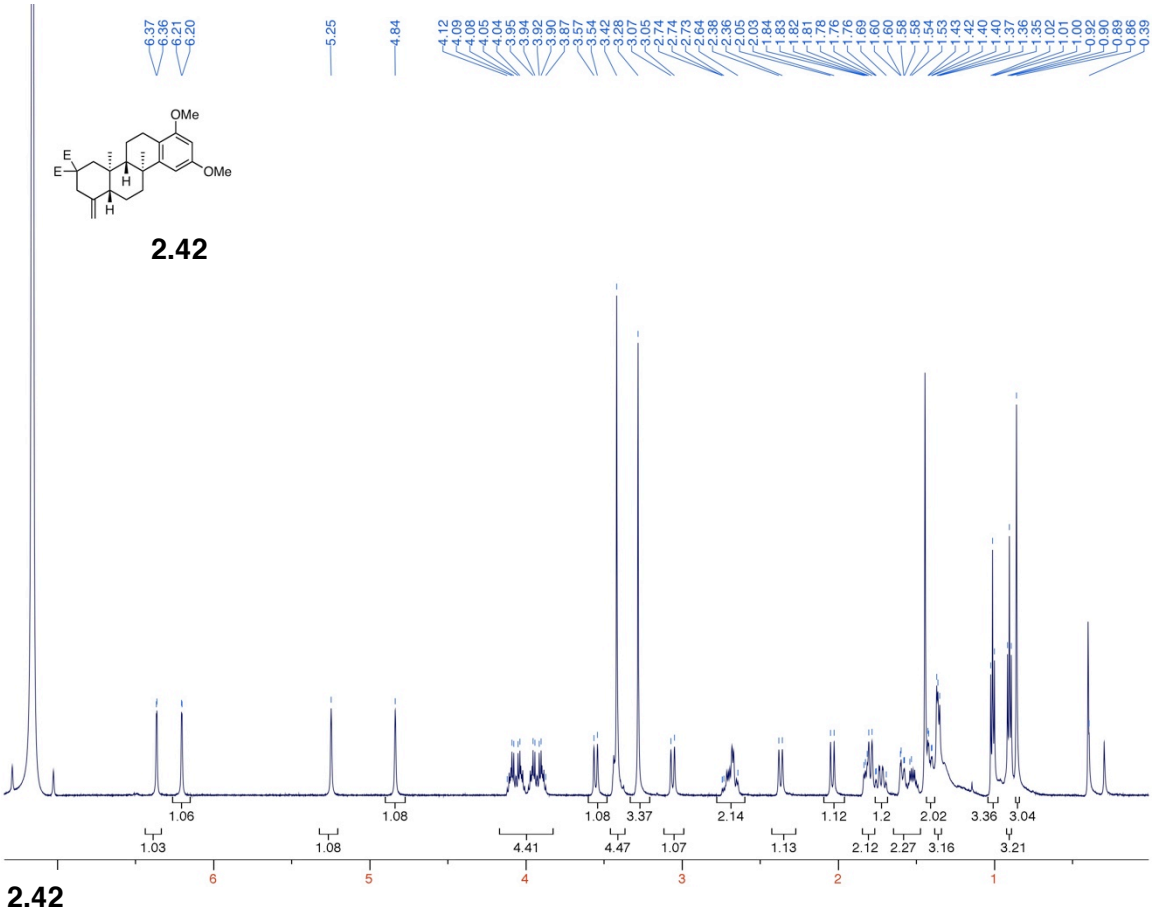
6.38
6.34
6.34
6.33
5.43
5.41
5.39
4.28
4.26
4.25
4.24
4.24
4.22
4.22
4.21
4.20
4.19
4.18
4.17
4.16
4.14
3.82
2.82
2.78
2.77
2.63
2.62
2.60
2.34
2.32
2.30
2.06
2.05
2.04
1.55
1.55
1.30
1.28
1.26
EtO2C
EtO2C
OMe
OMe
0.989
2.08
1.04
4.15
6.18
2.06
2.06
2
1.03
2.01
6.48
3.01
8
7
6
5
4
3
2
1
169.891
161.208
144.617
135.001
130.827
129.489
124.230
106.752
98.048
79.682
71.697
61.080
56.729
54.460
41.676
39.329
36.510
29.964
26.748
22.766
16.741
15.446
13.640
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

2.37b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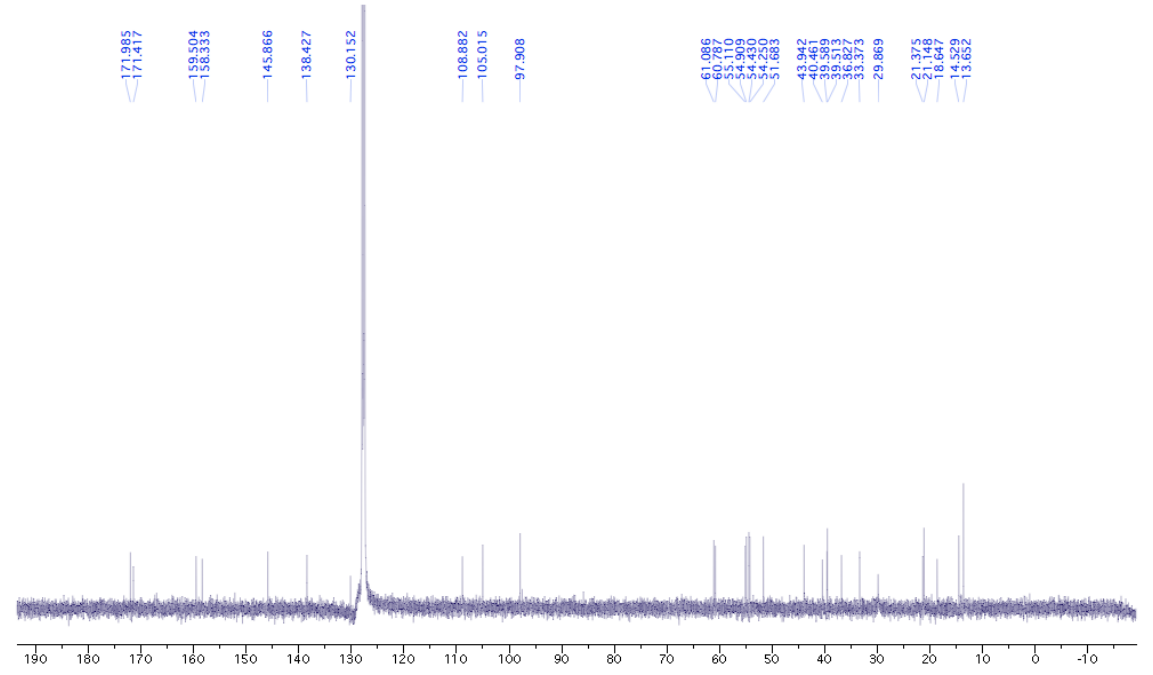
6.36
6.21
6.20
5.25
4.84
OMe
OMe
E
E
H
H
1.06
1.08
1.08
3.37
2.14
1.12
1.2
2.02
3.36
3.04
1.03
1.08
4.41
4.47
1.07
1.13
2.12
2.27
3.16
3.21
6
5
4
3
2
1

2.42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159.504
158.333
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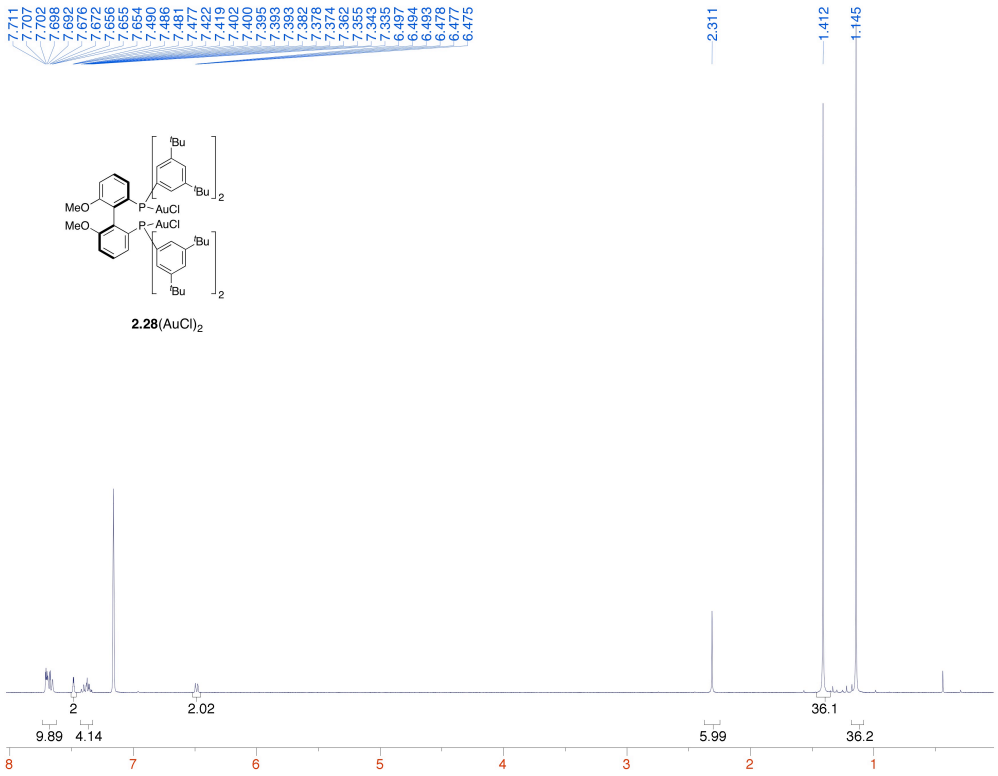
138.427
130.152
108.882
105.015
97.908
61.086
60.787
55.910
54.430
54.250
51.683
43.942
40.461
39.513
36.827
33.373
29.869
21.375
21.148
18.647
14.529
13.652
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

2.42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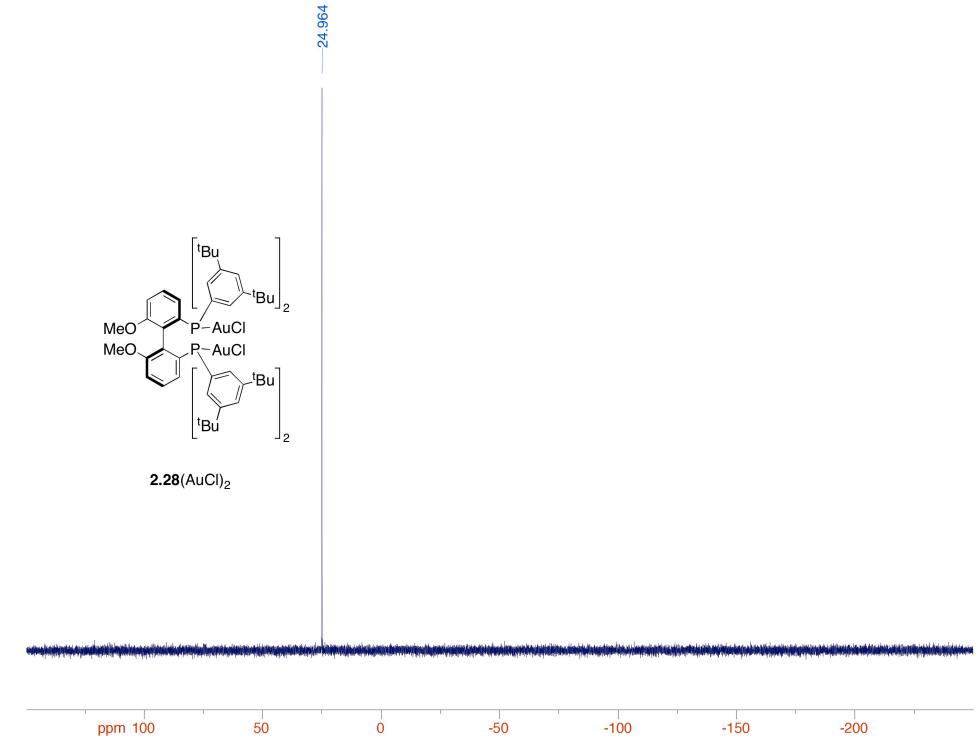
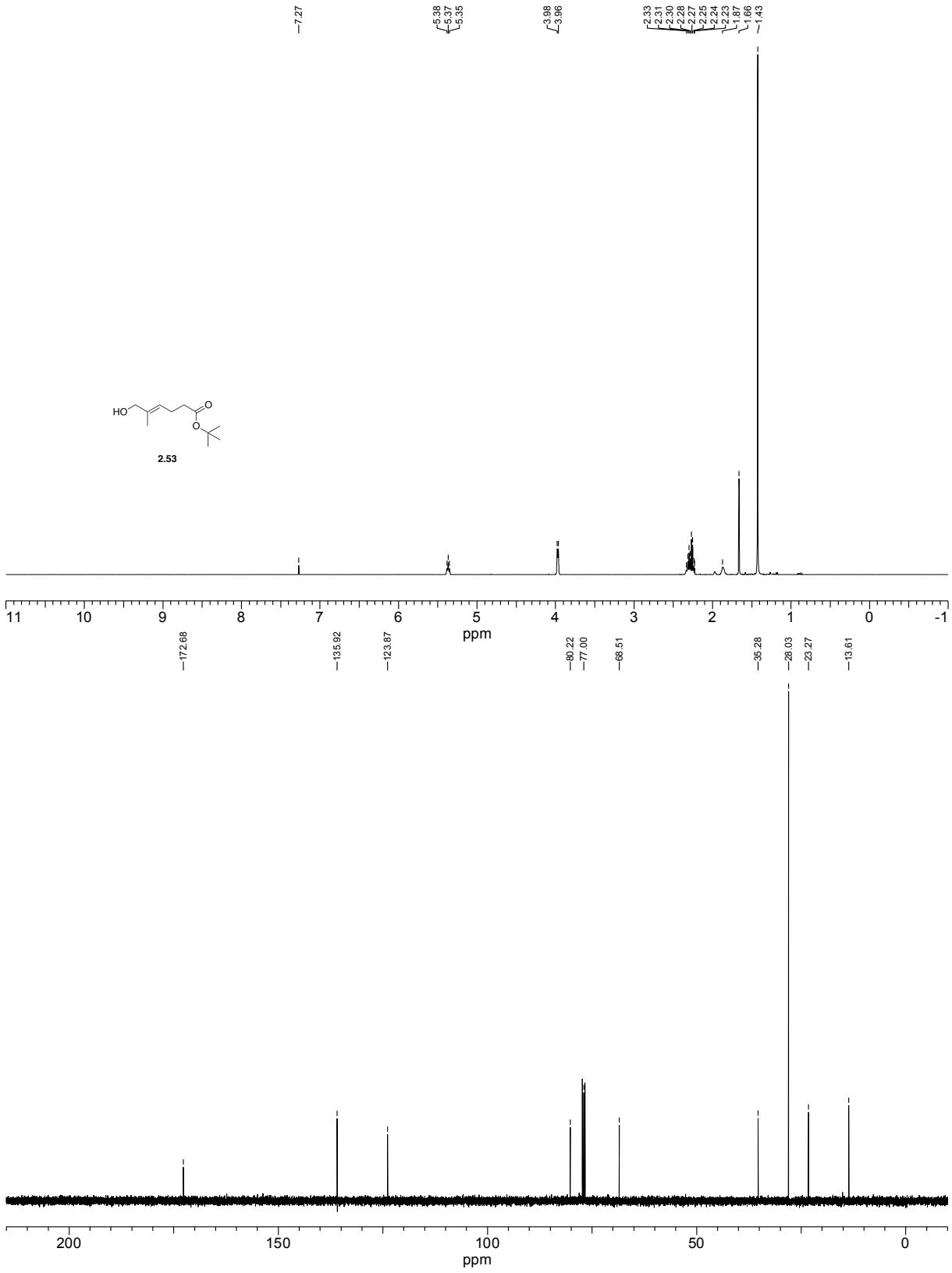
7.707
7.702
7.698
7.692
7.676
7.672
7.656
7.655
7.654
7.490
7.486
7.481
7.477
7.422
7.419
7.402
7.400
7.395
7.393
7.393
7.382
7.378
7.374
7.362
7.355
7.343
7.335
6.497
6.494
6.493
6.478
6.477
6.475
2.311
1.412
1.145
tBu
tBu
MeO
MeO
P–AuCl
P–AuCl
tBu
tBu
2
2
2.28(AuCl)2
2
2.02
36.1
9.89
4.14
5.99
36.2
8
7
6
5
4
3
2
1


24.964
tBu
tBu
MeO
MeO
P–AuCl
P–AuCl
tBu
tBu
2
2
2.28(AuCl)2
ppm 100
50
0
-50
-100
-150
-200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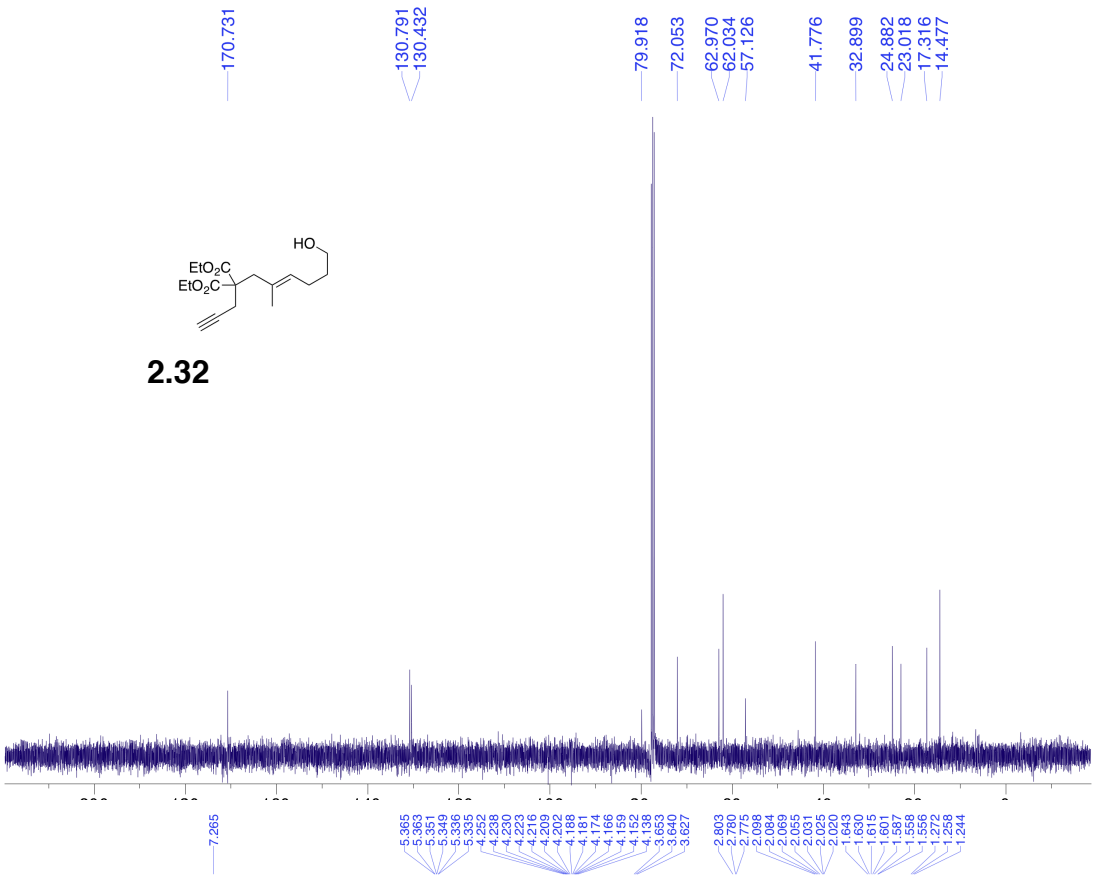
5.38
5.37
5.35
3.98
3.96
2.33
2.31
2.30
2.28
2.27
2.25
2.24
2.23
1.87
1.86
1.43
HO
O
O
2.53
11
10
9
8
7
6
5
4
3
2
1
0
-1
ppm
172.68
135.92
123.87
80.22
77.00
68.51
35.28
28.03
23.27
13.61
200
150
100
50
0
ppm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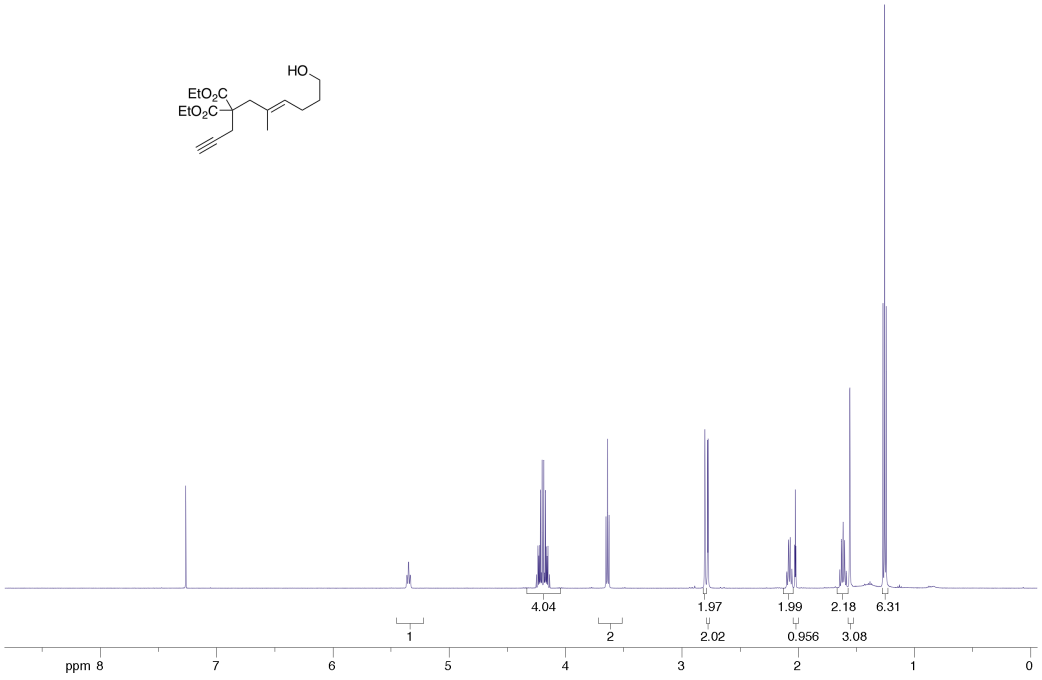
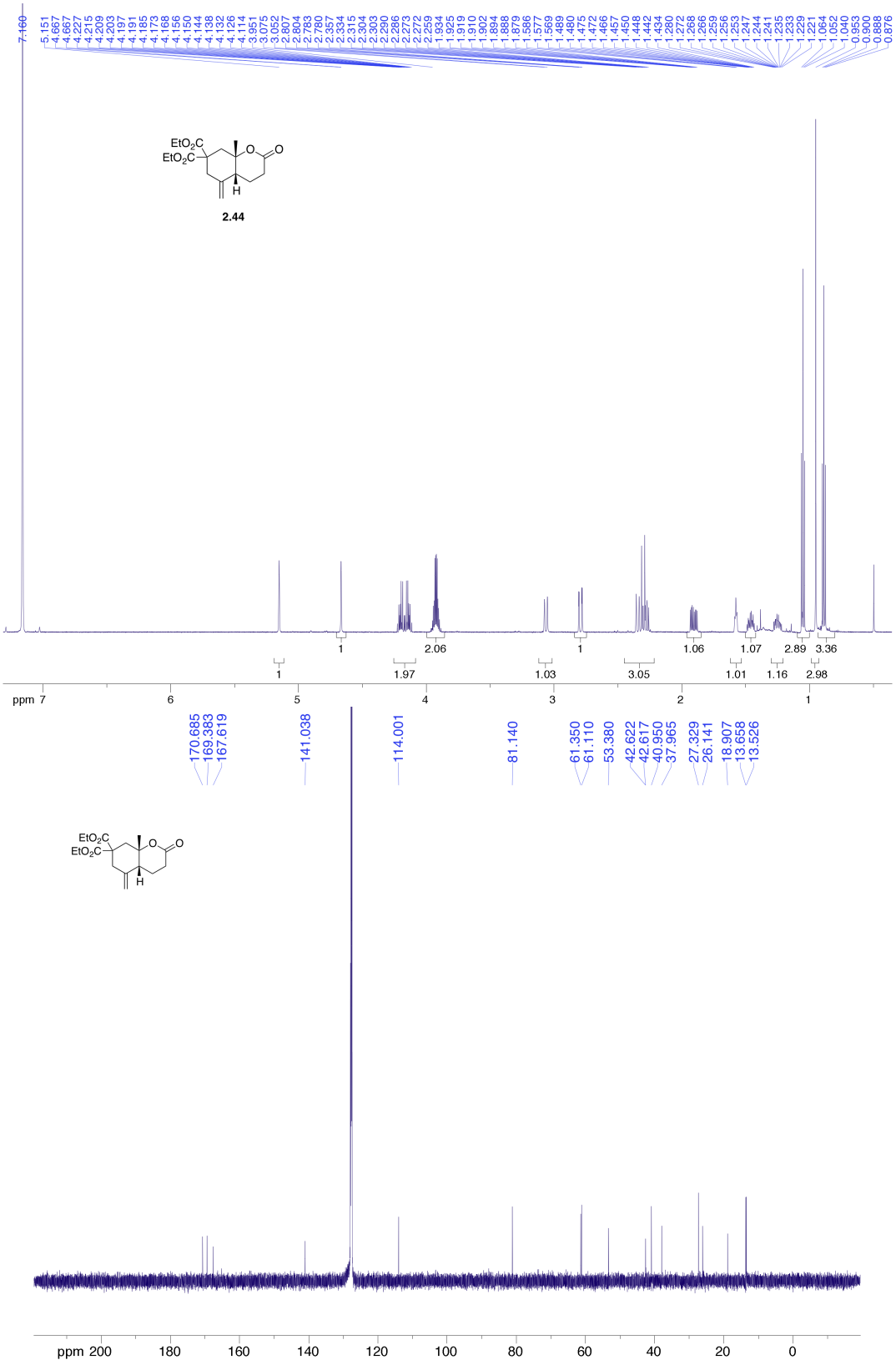
130.432
79.918
72.053
62.970
62.034
57.126
41.776
32.899
24.882
23.018
17.316
14.477
HO
EtO2C
EtO2C
7.265
5.365
5.363
5.351
5.349
5.336
5.335
4.252
4.238
4.230
4.223
4.216
4.209
4.202
4.188
4.181
4.174
4.166
4.159
4.152
4.138
3.653
3.640
3.627
2.803
2.780
2.775
2.098
2.084
2.069
2.055
2.031
2.025
2.020
1.643
1.630
1.615
1.601
1.587
1.558
1.555
1.272
1.258
1.244

2.32


HO
EtO2C
EtO2C
4.04
1.97
1.99
2.18
6.31
1
2
2.02
0.956
3.08
ppm 8
7
6
5
4
3
2
1
0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5.151
4.667
4.667
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4.215
4.209
4.203
4.197
4.191
4.185
4.173
4.168
4.156
4.150
4.144
4.138
4.132
4.126
4.114
3.951
3.075
3.052
2.807
2.804
2.783
2.780
2.357
2.334
2.315
2.304
2.303
2.290
2.286
2.273
2.272
2.259
1.934
1.925
1.919
1.910
1.902
1.894
1.888
1.879
1.586
1.577
1.569
1.489
1.480
1.475
1.472
1.466
1.457
1.450
1.448
1.442
1.434
1.280
1.272
1.268
1.266
1.259
1.255
1.253
1.247
1.244
1.241
1.235
1.233
1.229
1.221
1.064
1.052
1.040
0.953
0.900
0.888
0.876
EtO2C
EtO2C
O
O
H
2.44
1
2.06
1
1.06
1.07
2.89
3.36
1
1.97
1.03
3.05
1.01
1.16
2.98
ppm 7
6
5
4
3
2
1
170.685
169.383
167.619
141.038
114.001
81.140
61.350
61.110
53.380
42.622
42.617
40.950
37.965
27.329
26.141
18.907
13.658
13.526
EtO2C
EtO2C
O
O
H
ppm 200
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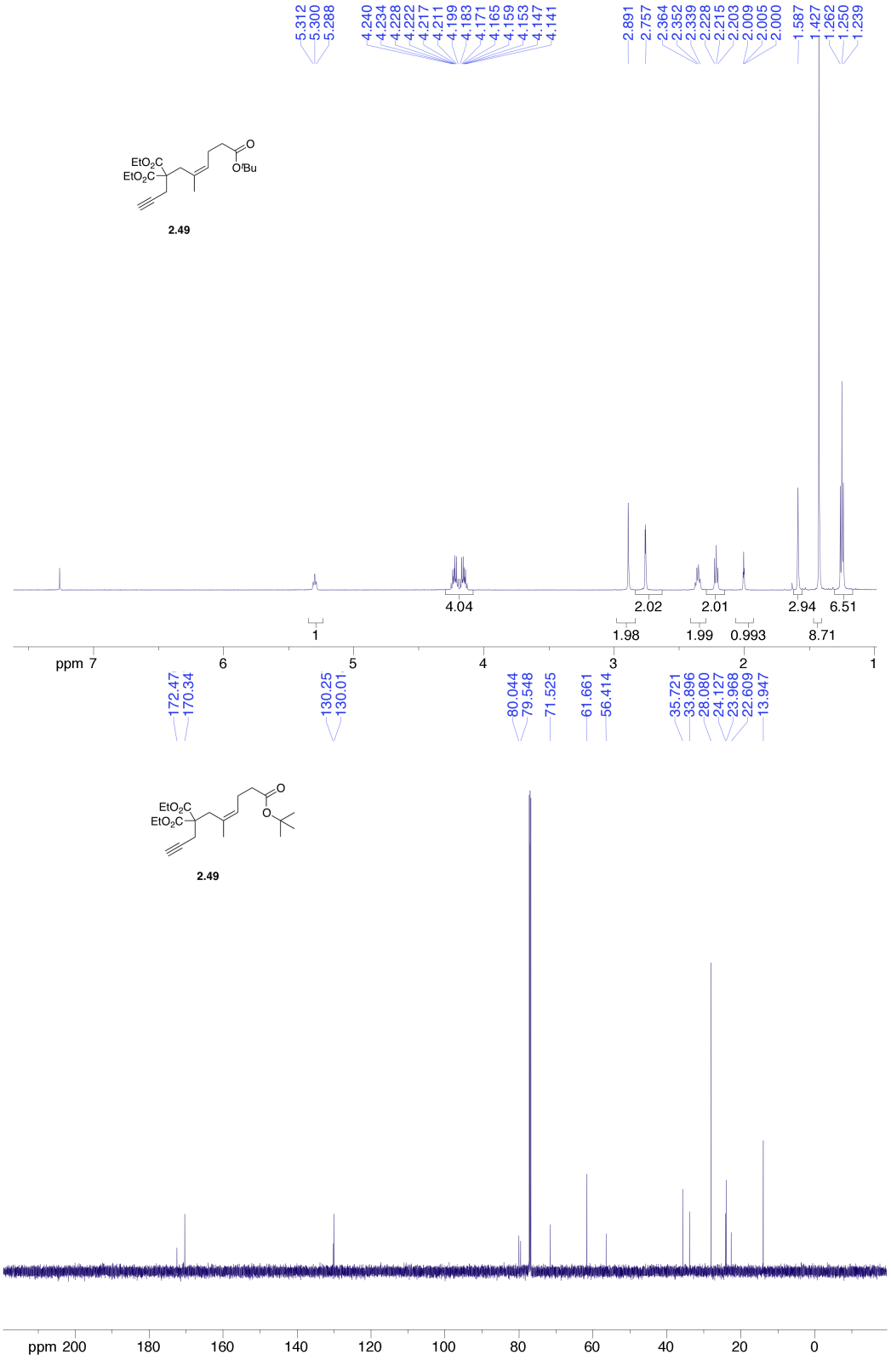
160
140
120
100
80
60
40
20
0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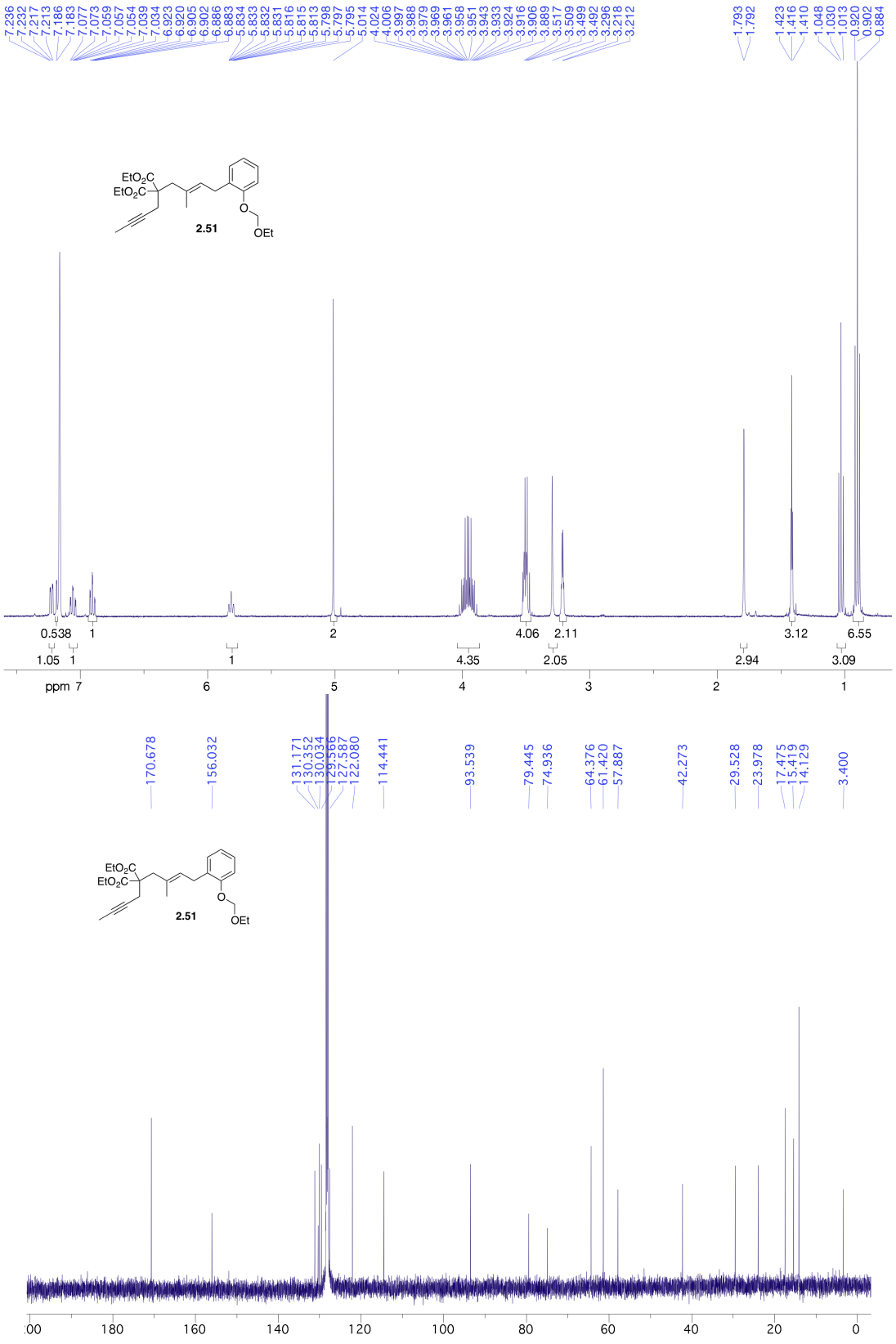
4.234
4.228
4.222
4.217
4.211
4.199
4.183
4.171
4.165
4.159
4.153
4.147
4.141
2.891
2.757
2.364
2.352
2.339
2.228
2.215
2.203
2.009
2.005
2.000
1.587
1.427
1.262
1.250
1.239
EtO2C
EtO2C
O
OtBu
2.49
4.04
2.02
2.01
2.94
6.51
1
1.98
1.99
0.993
8.71
ppm 7
6
5
4
3
2
1
172.47
170.34
130.25
130.01
80.044
79.548
71.525
61.661
56.414
35.721
33.896
28.080
24.127
23.968
22.609
13.947
EtO2C
EtO2C
O
O
2.49
ppm 200
180
160
140
120
100
80
60
40
20
0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7.183
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7.073
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7.057
7.054
7.039
7.034
6.923
6.920
6.905
6.902
6.886
6.883
5.834
5.833
5.832
5.831
5.816
5.815
5.813
5.798
5.797
5.795
5.014
4.024
4.006
3.997
3.988
3.979
3.969
3.961
3.958
3.951
3.943
3.933
3.924
3.916
3.906
3.889
3.517
3.509
3.499
3.492
3.296
3.218
3.212
1.793
1.792
1.423
1.416
1.410
1.048
1.030
1.013
0.920
0.902
0.884
EtO2C
EtO2C
O
OEt
2.51
0.538
1
2
4.06
2.11
3.12
6.55
1.05
1
1
4.35
2.05
2.94
3.09
ppm 7
6
5
4
3
2
1
170.678
156.032
131.171
130.352
130.034
129.586
127.587
122.080
114.441
93.539
79.445
74.936
64.376
61.420
57.887
42.273
29.528
23.978
17.475
15.419
14.129
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EtO2C
EtO2C
O
OEt
2.51
00
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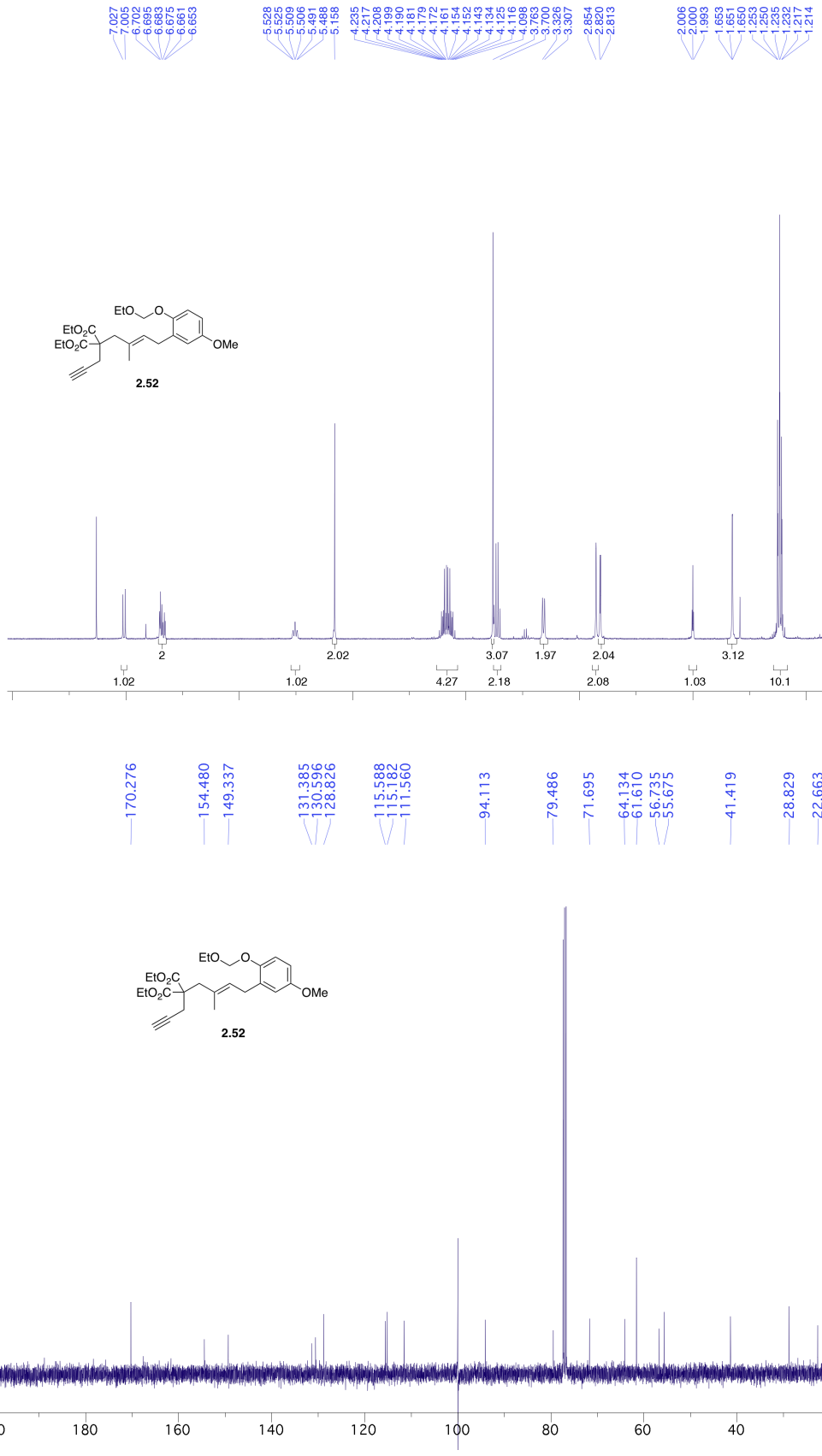
160
140
120
100
80
60
40
20
0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5.525
5.509
5.506
5.491
5.488
5.158
4.235
4.217
4.208
4.199
4.190
4.181
4.179
4.172
4.161
4.154
4.152
4.143
4.134
4.125
4.116
4.098
3.763
3.700
3.326
3.307
2.854
2.820
2.813
2.006
2.000
1.993
1.653
1.651
1.650
1.253
1.250
1.235
1.232
1.217
1.214
EtO
O
EtO2C
EtO2C
OMe
2.52
2
2.02
3.07
1.97
2.04
3.12
1.02
1.02
4.27
2.18
2.08
1.03
10.1
170.276
154.480
149.337
131.385
130.596
128.826
115.588
115.182
111.560
94.113
79.486
71.695
64.134
61.610
56.735
55.675
41.419
28.829
22.663
17.011
15.194
14.038
EtO
O
EtO2C
EtO2C
OMe
2.52
00
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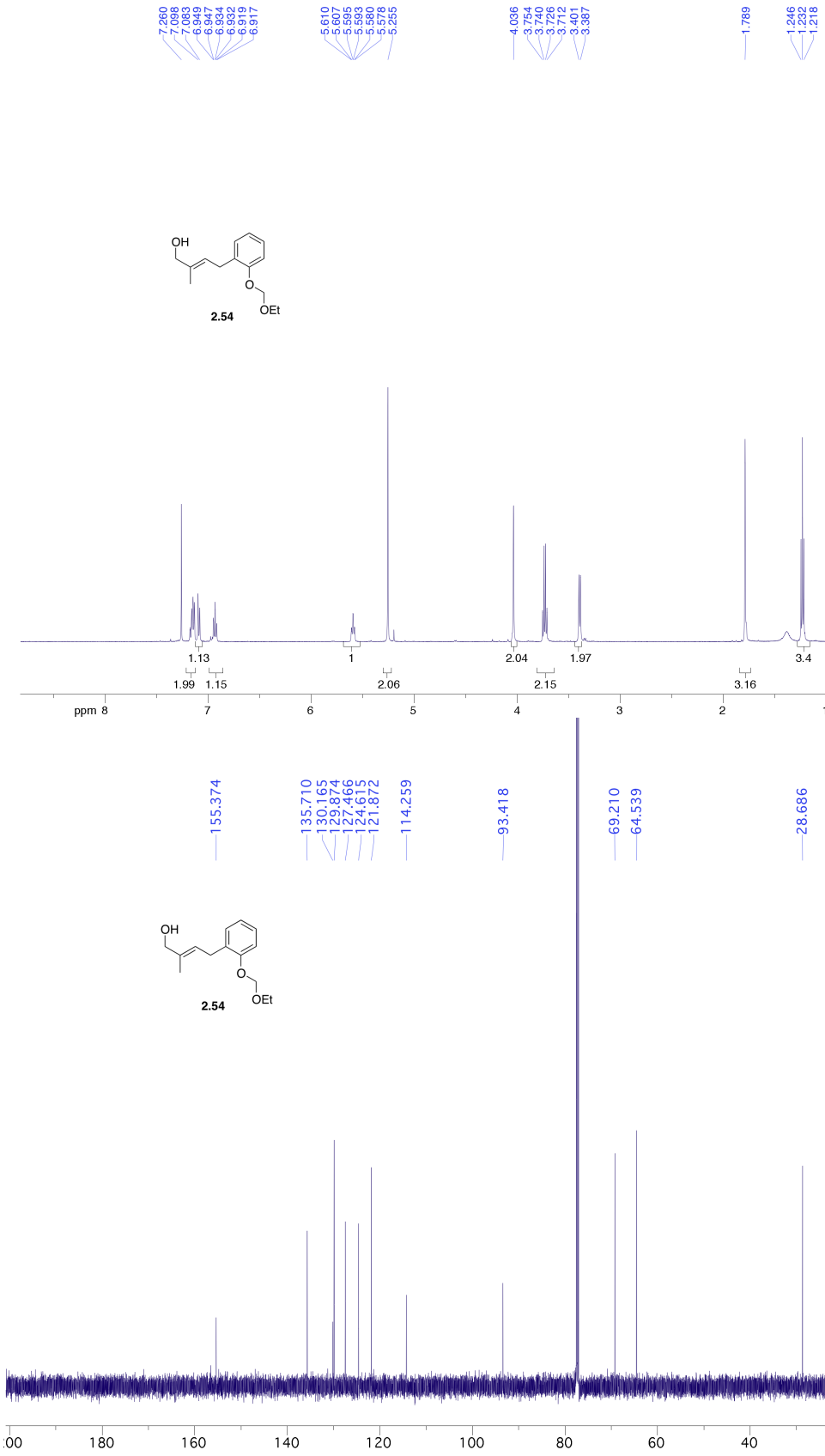
160
140
120
100
80
60
40
20
0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6.934
6.932
6.919
6.917
5.610
5.607
5.595
5.593
5.580
5.578
5.255
4.036
3.754
3.740
3.726
3.712
3.401
3.387
1.789
1.246
1.232
1.218
OH
O
OEt
2.54
1.13
1.99
1.15
1
2.06
2.04
2.15
1.97
3.16
3.4
ppm 8
7
6
5
4
3
2
1
0
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135.710
130.165
129.874
127.466
124.615
121.872
114.259
93.418
69.210
64.539
28.686
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14.003
OH
O
OEt
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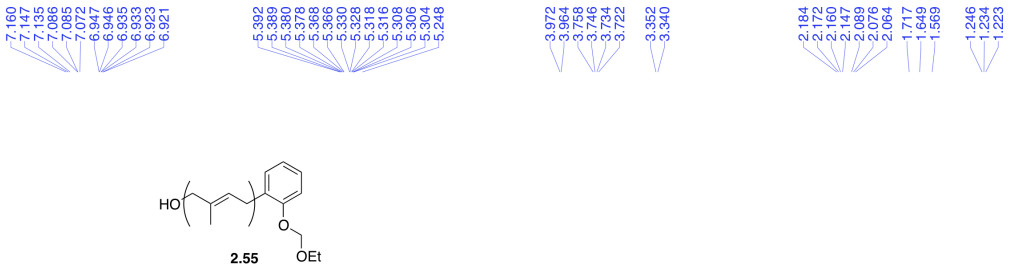
140
120
100
80
60
40
20
0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7.085
7.072
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6.946
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6.933
6.923
6.921
5.392
5.389
5.380
5.378
5.368
5.366
5.330
5.328
5.318
5.316
5.308
5.306
5.304
5.248
3.972
3.964
3.758
3.746
3.734
3.722
3.352
3.340
2.184
2.172
2.160
2.147
2.089
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1.717
1.649
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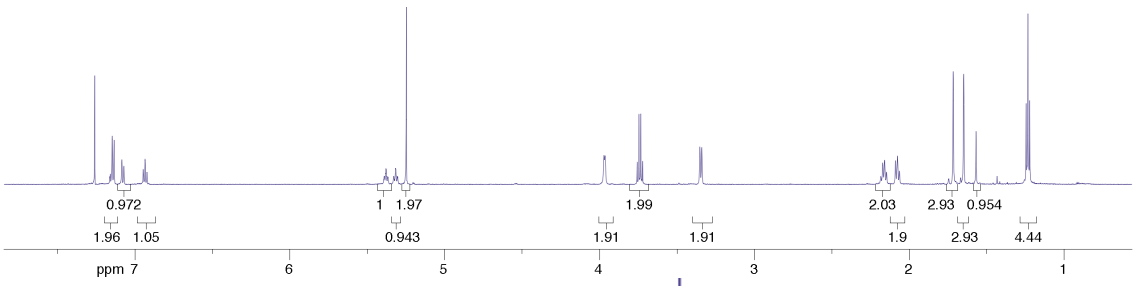
1.234
1.223
HO
O
OEt
2.55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1
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0.943
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1.91
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1.9
2.93
0.954
2.93
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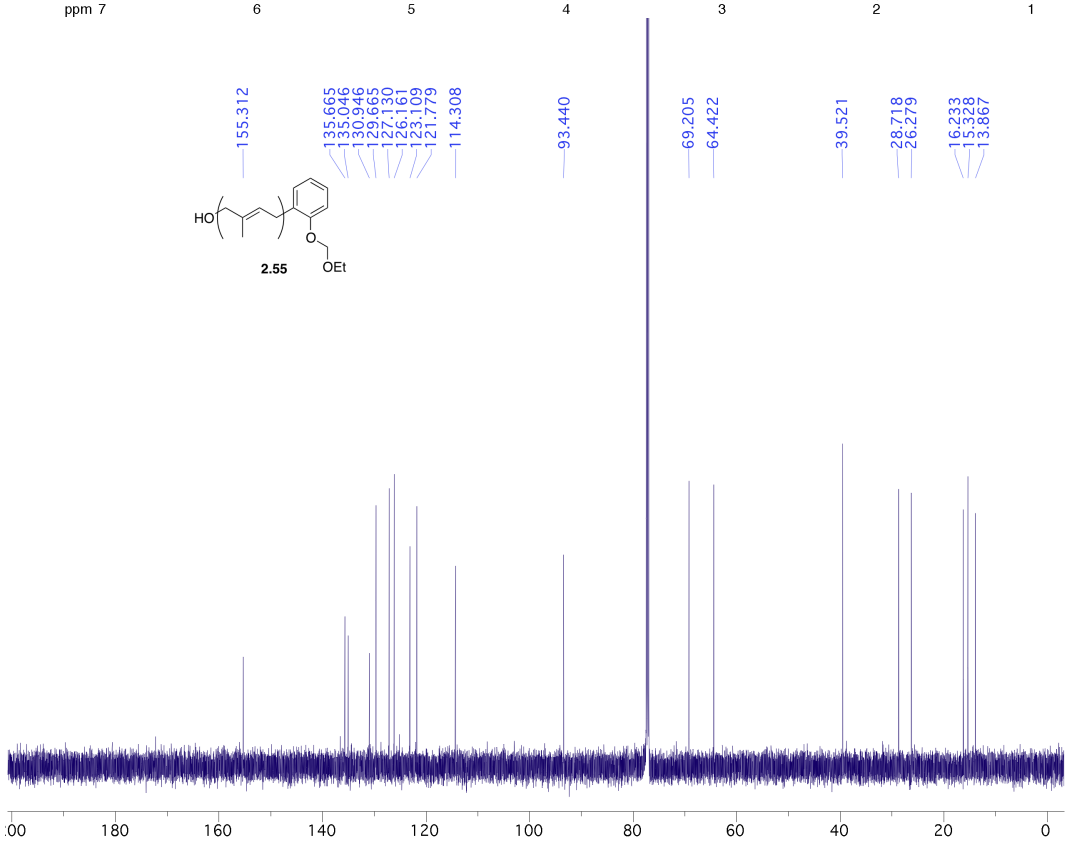
ppm 7
6
5
4
3
2
1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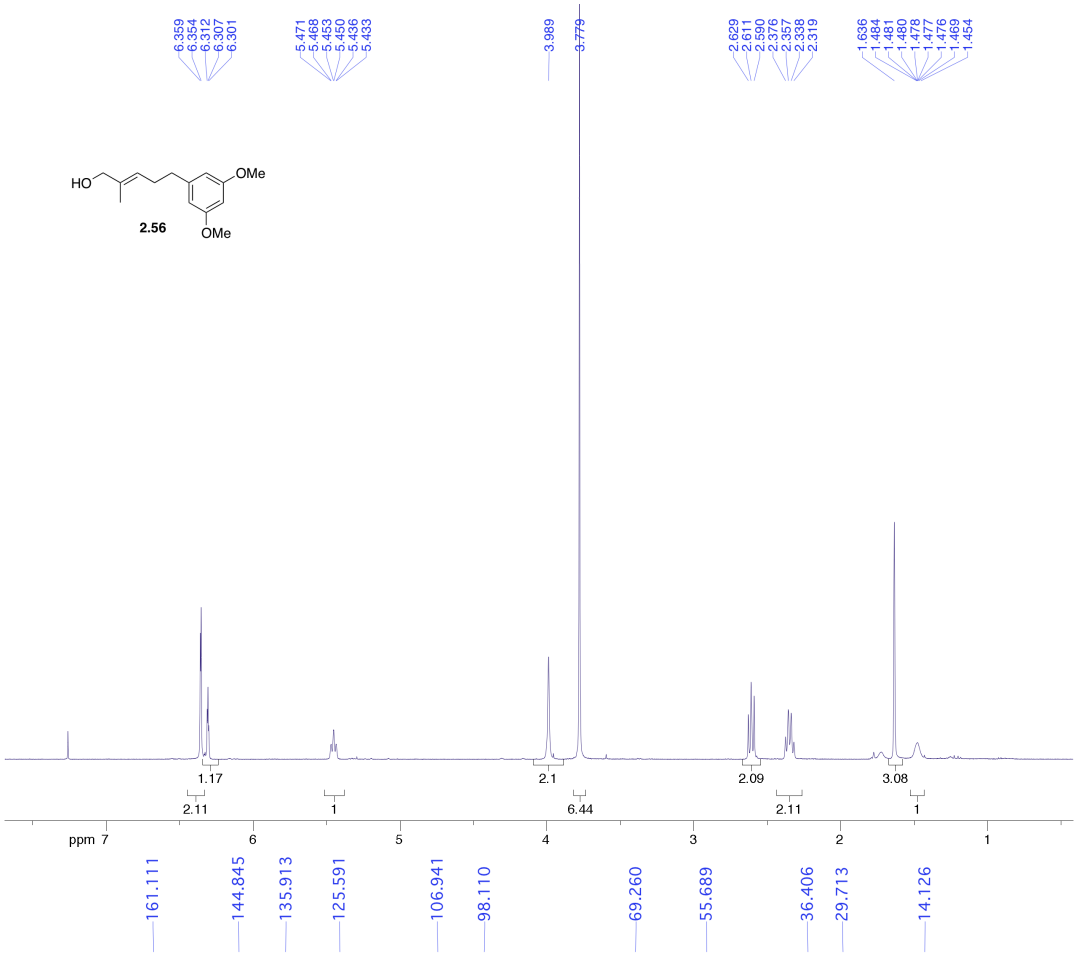
126.161
123.109
121.779
114.308
93.440
69.205
64.422
39.521
28.718
26.279
16.233
15.328
13.867
HO
O
OEt
2.55
200
180
160
140
120
100
80
60
40
20
0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5.453
5.450
5.436
5.433
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3.779
2.629
2.611
2.590
2.576
2.357
2.338
2.319
1.636
1.484
1.481
1.480
1.478
1.477
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OMe
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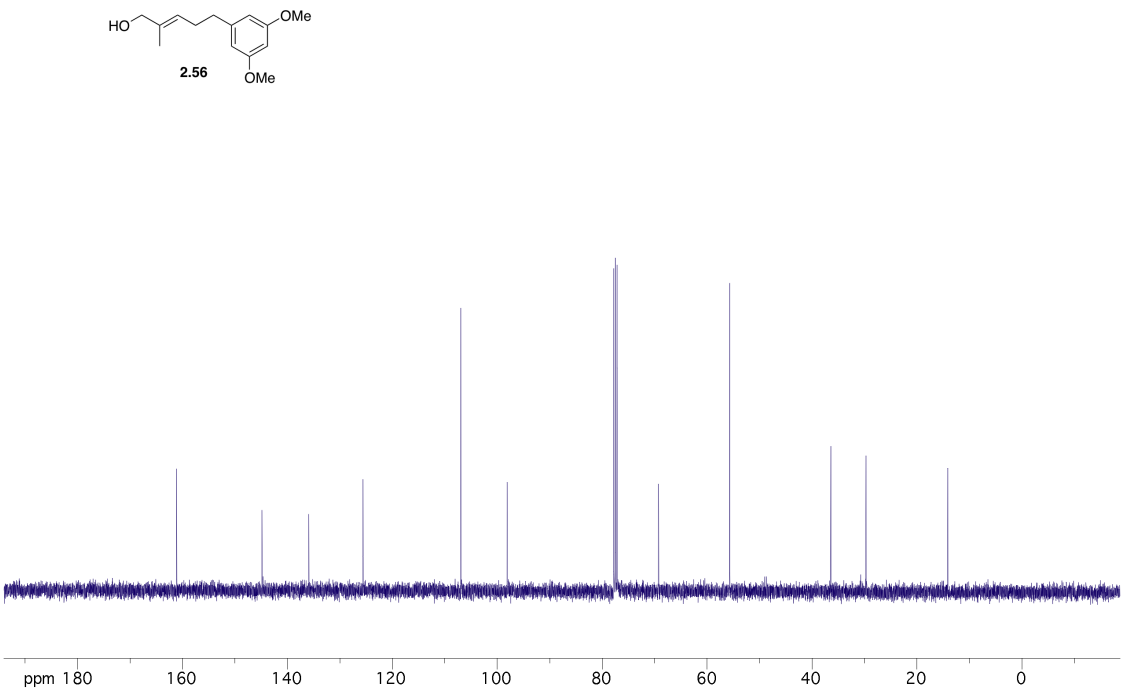
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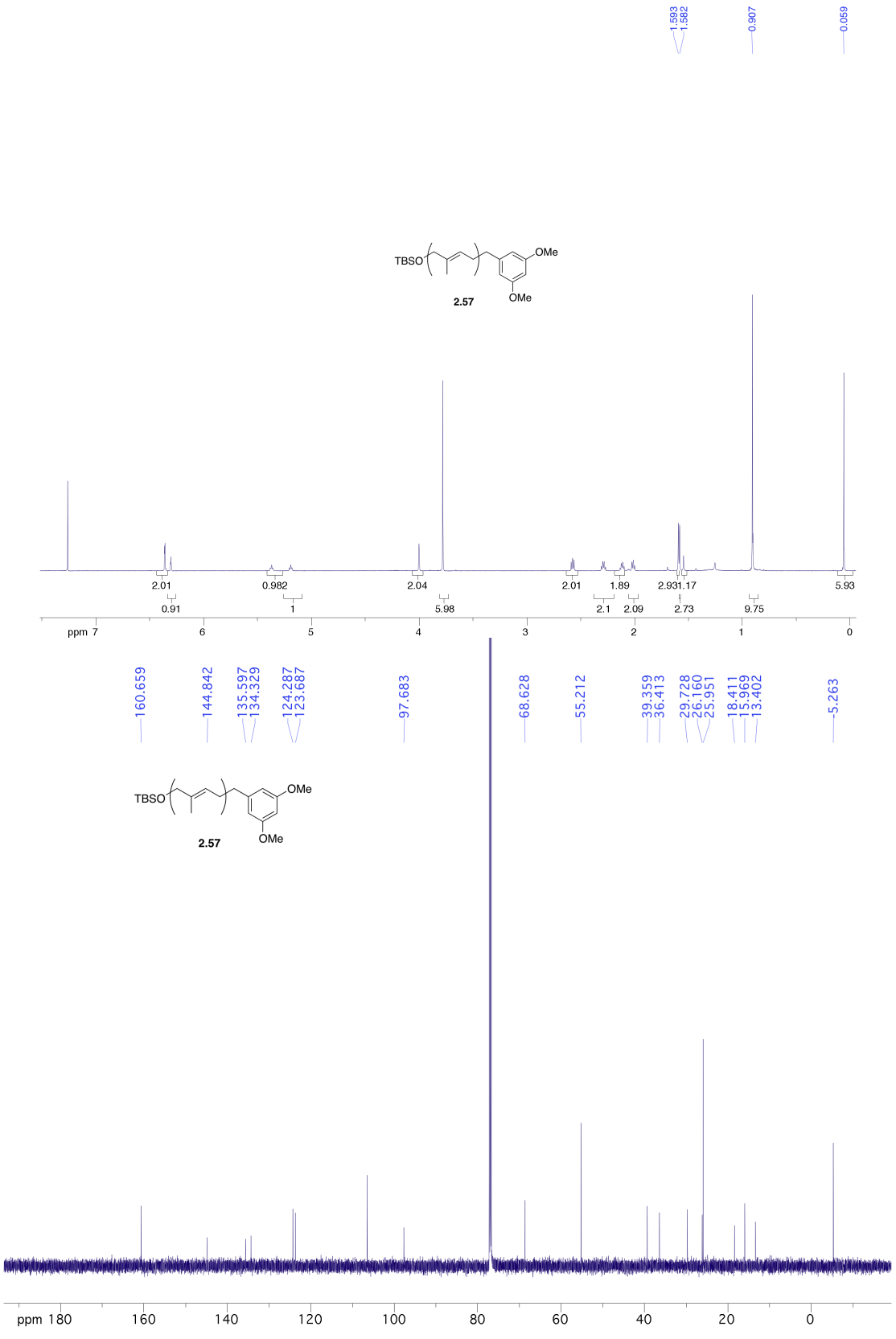
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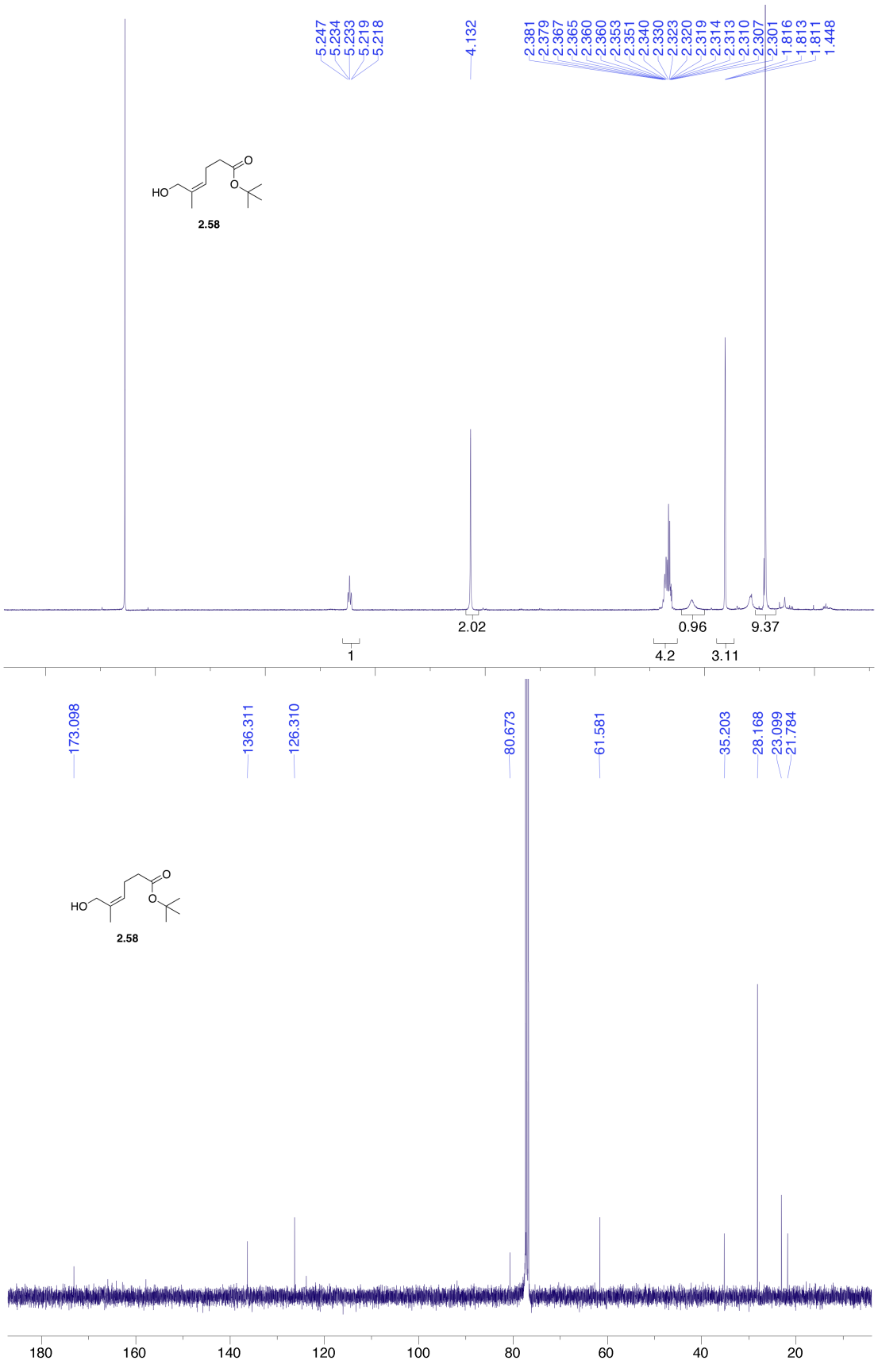
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1.813
1.811
1.448
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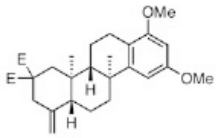
20

X-Ray Crystallography Data



2.42

A colorless block 0.12 x 0.10 x 0.10 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using phi and omega scans. Crystal-to-detector distance was 60 mm and exposure time was 5 seconds per frame using a scan width of 1.0°. Data collection was 99.0% complete to 67.00° in q. A total of 22065 reflections were collected covering the indices, -11<=*h*<=11, -10<=*k*<=11, -16<=*l*<=16. 4471 reflections were found to be symmetry independent, with an R_{int} of 0.0166. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P2(1) (No. 4). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SIR-2004) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-97). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-97. Absolute stereochemistry was unambiguously determined to be *S*, *S*, and *R* at C1, C10, and C11 respectively.

Table 1. Crystal data and structure refinement for toste18.

X-ray ID	toste18
Sample/notebook ID	SGS5-151
Empirical formula	C29 H40 O6
Formula weight	484.61
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 9.6322(6) Å a= 90°.
	b = 9.7408(6) Å b= 91.456(2)°.
	c = 14.0139(9) Å g = 90°.
Volume	1314.43(14) $Å^3$
Z	2
Density (calculated)	1.224 Mg/m^3
Absorption coefficient	0.678 mm^{-1}
F(000)	524
Crystal size	0.12 x 0.10 x 0.10 mm^3
Crystal color/habit	colorless block
Theta range for data collection	3.15 to 67.94°.
Index ranges	-11<=h<=11, -10<=k<=11, -16<=l<=16
Reflections collected	22065
Independent reflections	4471 [R(int) = 0.0166]
Completeness to theta = 67.00°	99.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9353 and 0.9230
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4471 / 1 / 322
Goodness-of-fit on F^2	1.094
Final R indices [I>2sigma(I)]	R1 = 0.0296, wR2 = 0.0830
R indices (all data)	R1 = 0.0298, wR2 = 0.0832
Absolute structure parameter	0.00(12)
Largest diff. peak and hole	0.264 and -0.307 $e.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)
for toste18. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

x	y	z	U(eq)	
C(1)	1279(1)	10261(1)	140(1)	20(1)
C(2)	-79(1)	10315(1)	-476(1)	19(1)
C(3)	-58(1)	10454(1)	-1485(1)	22(1)
C(4)	-1256(1)	10624(1)	-2034(1)	23(1)
C(5)	-2547(1)	10627(1)	-1601(1)	23(1)
C(6)	-2621(1)	10394(2)	-635(1)	22(1)
C(7)	-1397(1)	10228(1)	-82(1)	20(1)
C(8)	-1590(1)	9930(1)	971(1)	22(1)
C(9)	-253(1)	9449(2)	1466(1)	22(1)
C(10)	869(1)	10483(2)	1204(1)	20(1)
C(11)	2071(1)	10681(1)	1955(1)	19(1)
C(12)	1400(1)	11175(2)	2889(1)	21(1)
C(13)	2414(1)	11719(2)	3674(1)	23(1)
C(14)	3494(1)	12735(2)	3268(1)	24(1)
C(15)	4087(1)	12244(1)	2339(1)	23(1)
C(16)	2981(1)	11885(1)	1599(1)	20(1)
C(17)	3475(1)	11641(2)	588(1)	22(1)
C(18)	2236(1)	11480(2)	-111(1)	21(1)
C(19)	2000(1)	8881(2)	-68(1)	24(1)
C(20)	1260(2)	10387(2)	-2911(1)	42(1)
C(21)	-4980(1)	10993(2)	-1791(1)	31(1)
C(22)	2916(1)	9369(1)	2147(1)	23(1)
C(23)	1561(1)	12544(2)	4391(1)	26(1)
C(24)	1720(2)	13890(2)	5792(1)	38(1)
C(25)	2760(2)	14157(3)	6581(1)	52(1)
C(26)	3155(1)	10579(2)	4239(1)	24(1)
C(27)	2820(2)	8517(2)	5113(1)	31(1)
C(28)	3113(2)	7360(2)	4458(1)	51(1)
C(29)	5439(2)	12196(2)	2202(1)	28(1)
O(1)	1220(1)	10410(1)	-1900(1)	27(1)
O(2)	-3656(1)	10856(1)	-2208(1)	28(1)
O(3)	372(1)	12866(2)	4283(1)	45(1)
O(4)	2350(1)	12918(1)	5142(1)	32(1)
O(5)	4390(1)	10504(1)	4372(1)	30(1)
O(6)	2239(1)	9689(1)	4585(1)	27(1)

Table 3. Bond lengths [Å] and angles [°] for toste18.

C(1)-C(19)	1.5448(19)	C(17)-C(18)	1.5324(17)
C(1)-C(18)	1.5486(18)	C(17)-H(17A)	0.9900
C(1)-C(2)	1.5497(16)	C(17)-H(17B)	0.9900
C(1)-C(10)	1.5680(16)	C(18)-H(18A)	0.9900
C(2)-C(7)	1.4001(17)	C(18)-H(18B)	0.9900
C(2)-C(3)	1.4203(18)	C(19)-H(19A)	0.9800
C(3)-O(1)	1.3754(15)	C(19)-H(19B)	0.9800
C(3)-C(4)	1.3804(18)	C(19)-H(19C)	0.9800
C(4)-C(5)	1.3974(19)	C(20)-O(1)	1.4181(16)
C(4)-H(4)	0.9500	C(20)-H(20A)	0.9800
C(5)-O(2)	1.3664(16)	C(20)-H(20B)	0.9800
C(5)-C(6)	1.3775(19)	C(20)-H(20C)	0.9800
C(6)-C(7)	1.4025(17)	C(21)-O(2)	1.4225(17)
C(6)-H(6)	0.9500	C(21)-H(21A)	0.9800
C(7)-C(8)	1.5201(17)	C(21)-H(21B)	0.9800
C(8)-C(9)	1.5217(18)	C(21)-H(21C)	0.9800
C(8)-H(8A)	0.9900	C(22)-H(22A)	0.9800
C(8)-H(8B)	0.9900	C(22)-H(22B)	0.9800
C(9)-C(10)	1.5289(18)	C(22)-H(22C)	0.9800
C(9)-H(9A)	0.9900	C(23)-O(3)	1.1931(18)
C(9)-H(9B)	0.9900	C(23)-O(4)	1.3328(17)
C(10)-C(11)	1.5563(16)	C(24)-O(4)	1.4568(18)
C(10)-H(10)	1.0000	C(24)-C(25)	1.496(2)
C(11)-C(22)	1.5353(18)	C(24)-H(24A)	0.9900
C(11)-C(12)	1.5505(16)	C(24)-H(24B)	0.9900
C(11)-C(16)	1.5543(18)	C(25)-H(25A)	0.9800
C(12)-C(13)	1.5468(17)	C(25)-H(25B)	0.9800
C(12)-H(12A)	0.9900	C(25)-H(25C)	0.9800
C(12)-H(12B)	0.9900	C(26)-O(5)	1.2015(16)
C(13)-C(26)	1.5304(19)	C(26)-O(6)	1.3366(18)
C(13)-C(23)	1.5400(18)	C(27)-O(6)	1.4633(17)
C(13)-C(14)	1.5532(19)	C(27)-C(28)	1.486(3)
C(14)-C(15)	1.5130(18)	C(27)-H(27A)	0.9900
C(14)-H(14A)	0.9900	C(27)-H(27B)	0.9900
C(14)-H(14B)	0.9900	C(28)-H(28A)	0.9800
C(15)-C(29)	1.322(2)	C(28)-H(28B)	0.9800
C(15)-C(16)	1.5086(17)	C(28)-H(28C)	0.9800
C(16)-C(17)	1.5248(17)	C(29)-H(29A)	0.9500
C(16)-H(16)	1.0000	C(29)-H(29B)	0.9500
C(19)-C(1)-C(18)	110.55(10)	C(18)-C(1)-C(2)	110.27(10)
C(19)-C(1)-C(2)	107.57(10)	C(19)-C(1)-C(10)	115.13(11)

C(18)-C(1)-C(10)	106.02(10)	C(13)-C(12)-C(11)	115.99(10)
C(2)-C(1)-C(10)	107.22(9)	C(13)-C(12)-H(12A)	108.3
C(7)-C(2)-C(3)	115.73(11)	C(11)-C(12)-H(12A)	108.3
C(7)-C(2)-C(1)	122.64(11)	C(13)-C(12)-H(12B)	108.3
C(3)-C(2)-C(1)	121.63(11)	C(11)-C(12)-H(12B)	108.3
O(1)-C(3)-C(4)	120.82(11)	H(12A)-C(12)-H(12B)	107.4
O(1)-C(3)-C(2)	116.96(11)	C(26)-C(13)-C(23)	106.90(10)
C(4)-C(3)-C(2)	122.22(11)	C(26)-C(13)-C(12)	113.39(11)
C(3)-C(4)-C(5)	119.94(12)	C(23)-C(13)-C(12)	107.76(10)
C(3)-C(4)-H(4)	120.0	C(26)-C(13)-C(14)	110.13(11)
C(5)-C(4)-H(4)	120.0	C(23)-C(13)-C(14)	106.28(12)
O(2)-C(5)-C(6)	125.44(12)	C(12)-C(13)-C(14)	111.97(11)
O(2)-C(5)-C(4)	114.88(11)	C(15)-C(14)-C(13)	112.66(11)
C(6)-C(5)-C(4)	119.67(12)	C(15)-C(14)-H(14A)	109.1
C(5)-C(6)-C(7)	119.86(12)	C(13)-C(14)-H(14A)	109.1
C(5)-C(6)-H(6)	120.1	C(15)-C(14)-H(14B)	109.1
C(7)-C(6)-H(6)	120.1	C(13)-C(14)-H(14B)	109.1
C(2)-C(7)-C(6)	122.23(11)	H(14A)-C(14)-H(14B)	107.8
C(2)-C(7)-C(8)	121.90(11)	C(29)-C(15)-C(16)	124.96(12)
C(6)-C(7)-C(8)	115.87(11)	C(29)-C(15)-C(14)	122.10(12)
C(7)-C(8)-C(9)	112.31(10)	C(16)-C(15)-C(14)	112.90(11)
C(7)-C(8)-H(8A)	109.1	C(15)-C(16)-C(17)	116.34(10)
C(9)-C(8)-H(8A)	109.1	C(15)-C(16)-C(11)	110.44(10)
C(7)-C(8)-H(8B)	109.1	C(17)-C(16)-C(11)	111.84(11)
C(9)-C(8)-H(8B)	109.1	C(15)-C(16)-H(16)	105.8
H(8A)-C(8)-H(8B)	107.9	C(17)-C(16)-H(16)	105.8
C(8)-C(9)-C(10)	106.38(11)	C(11)-C(16)-H(16)	105.8
C(8)-C(9)-H(9A)	110.5	C(16)-C(17)-C(18)	110.75(10)
C(10)-C(9)-H(9A)	110.5	C(16)-C(17)-H(17A)	109.5
C(8)-C(9)-H(9B)	110.5	C(18)-C(17)-H(17A)	109.5
C(10)-C(9)-H(9B)	110.5	C(16)-C(17)-H(17B)	109.5
H(9A)-C(9)-H(9B)	108.6	C(18)-C(17)-H(17B)	109.5
C(9)-C(10)-C(11)	115.91(10)	H(17A)-C(17)-H(17B)	108.1
C(9)-C(10)-C(1)	109.52(11)	C(17)-C(18)-C(1)	113.06(11)
C(11)-C(10)-C(1)	117.33(9)	C(17)-C(18)-H(18A)	109.0
C(9)-C(10)-H(10)	104.1	C(1)-C(18)-H(18A)	109.0
C(11)-C(10)-H(10)	104.1	C(17)-C(18)-H(18B)	109.0
C(1)-C(10)-H(10)	104.1	C(1)-C(18)-H(18B)	109.0
C(22)-C(11)-C(12)	109.94(10)	H(18A)-C(18)-H(18B)	107.8
C(22)-C(11)-C(16)	112.53(10)	C(1)-C(19)-H(19A)	109.5
C(12)-C(11)-C(16)	106.66(10)	C(1)-C(19)-H(19B)	109.5
C(22)-C(11)-C(10)	113.44(11)	H(19A)-C(19)-H(19B)	109.5
C(12)-C(11)-C(10)	106.87(9)	C(1)-C(19)-H(19C)	109.5
C(16)-C(11)-C(10)	107.02(10)	H(19A)-C(19)-H(19C)	109.5

H(19B)-C(19)-H(19C)	109.5
O(1)-C(20)-H(20A)	109.5
O(1)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
O(1)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
O(2)-C(21)-H(21A)	109.5
O(2)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
O(2)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(11)-C(22)-H(22A)	109.5
C(11)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(11)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
O(3)-C(23)-O(4)	123.65(13)
O(3)-C(23)-C(13)	125.52(13)
O(4)-C(23)-C(13)	110.74(11)
O(4)-C(24)-C(25)	107.11(14)
O(4)-C(24)-H(24A)	110.3
C(25)-C(24)-H(24A)	110.3
O(4)-C(24)-H(24B)	110.3
C(25)-C(24)-H(24B)	110.3
H(24A)-C(24)-H(24B)	108.5
C(24)-C(25)-H(25A)	109.5
C(24)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
C(24)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
O(5)-C(26)-O(6)	124.37(14)
O(5)-C(26)-C(13)	124.82(13)
O(6)-C(26)-C(13)	110.79(10)
O(6)-C(27)-C(28)	110.82(12)
O(6)-C(27)-H(27A)	109.5
C(28)-C(27)-H(27A)	109.5
O(6)-C(27)-H(27B)	109.5
C(28)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	108.1
C(27)-C(28)-H(28A)	109.5
C(27)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
C(27)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
C(15)-C(29)-H(29A)	120.0
C(15)-C(29)-H(29B)	120.0
H(29A)-C(29)-H(29B)	120.0
C(3)-O(1)-C(20)	118.04(11)
C(5)-O(2)-C(21)	117.04(11)
C(23)-O(4)-C(24)	115.69(12)
C(26)-O(6)-C(27)	116.22(11)

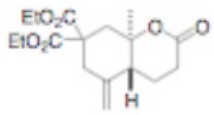
Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for toste18. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	21(1)	19(1)	19(1)	-1(1)	0(1)	1(1)
C(2)	24(1)	15(1)	20(1)	-1(1)	-1(1)	1(1)
C(3)	24(1)	18(1)	23(1)	-1(1)	2(1)	-2(1)
C(4)	31(1)	20(1)	19(1)	1(1)	-2(1)	-2(1)
C(5)	25(1)	18(1)	25(1)	-2(1)	-5(1)	-1(1)
C(6)	22(1)	18(1)	26(1)	-2(1)	1(1)	-1(1)
C(7)	23(1)	14(1)	21(1)	-3(1)	0(1)	0(1)
C(8)	23(1)	24(1)	21(1)	-1(1)	2(1)	-1(1)
C(9)	24(1)	23(1)	20(1)	1(1)	0(1)	-2(1)
C(10)	21(1)	19(1)	19(1)	1(1)	-1(1)	2(1)
C(11)	19(1)	20(1)	19(1)	0(1)	1(1)	1(1)
C(12)	20(1)	25(1)	19(1)	0(1)	-1(1)	2(1)
C(13)	22(1)	26(1)	20(1)	-3(1)	0(1)	1(1)
C(14)	26(1)	24(1)	23(1)	-2(1)	-2(1)	-2(1)
C(15)	26(1)	18(1)	24(1)	0(1)	-1(1)	-2(1)
C(16)	20(1)	20(1)	22(1)	0(1)	0(1)	1(1)
C(17)	21(1)	24(1)	21(1)	-1(1)	2(1)	-2(1)
C(18)	22(1)	23(1)	19(1)	1(1)	0(1)	1(1)
C(19)	26(1)	23(1)	24(1)	-3(1)	0(1)	4(1)
C(20)	32(1)	72(1)	21(1)	-8(1)	5(1)	-16(1)
C(21)	24(1)	36(1)	34(1)	0(1)	-5(1)	2(1)
C(22)	25(1)	21(1)	23(1)	1(1)	-2(1)	3(1)
C(23)	28(1)	29(1)	22(1)	0(1)	1(1)	4(1)
C(24)	45(1)	41(1)	28(1)	-12(1)	11(1)	-3(1)
C(25)	45(1)	76(2)	36(1)	-29(1)	16(1)	-26(1)
C(26)	23(1)	29(1)	19(1)	-5(1)	-1(1)	3(1)
C(27)	30(1)	38(1)	26(1)	11(1)	-3(1)	4(1)
C(28)	77(1)	38(1)	36(1)	9(1)	-4(1)	23(1)
C(29)	26(1)	32(1)	25(1)	-2(1)	-3(1)	-2(1)
O(1)	26(1)	37(1)	18(1)	-3(1)	3(1)	-2(1)
O(2)	25(1)	32(1)	26(1)	0(1)	-5(1)	1(1)
O(3)	36(1)	68(1)	32(1)	-16(1)	-5(1)	23(1)
O(4)	30(1)	41(1)	24(1)	-11(1)	2(1)	0(1)
O(5)	22(1)	38(1)	31(1)	3(1)	-3(1)	1(1)
O(6)	22(1)	31(1)	27(1)	6(1)	-2(1)	2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3)
for toste18.

x	y	z	U(eq)	
H(4)	-1202	10737	-2705	28
H(6)	-3499	10346	-342	26
H(8A)	-2310	9214	1036	27
H(8B)	-1920	10772	1289	27
H(9A)	-2	8518	1245	27
H(9B)	-363	9422	2167	27
H(10)	375	11387	1198	24
H(12A)	728	11912	2725	25
H(12B)	870	10401	3157	25
H(14A)	3045	13638	3164	29
H(14B)	4261	12860	3744	29
H(16)	2352	12700	1558	25
H(17A)	4053	10801	576	26
H(17B)	4054	12424	389	26
H(18A)	2586	11343	-762	26
H(18B)	1685	12337	-114	26
H(19A)	1545	8144	283	36
H(19B)	2980	8934	135	36
H(19C)	1934	8688	-754	36
H(20A)	702	9616	-3156	63
H(20B)	2222	10279	-3108	63
H(20C)	882	11249	-3167	63
H(21A)	-5234	10124	-1489	47
H(21B)	-5675	11226	-2288	47
H(21C)	-4943	11722	-1310	47
H(22A)	3602	9538	2662	34
H(22B)	3395	9103	1567	34
H(22C)	2291	8628	2335	34
H(24A)	859	13501	6051	45
H(24B)	1486	14755	5453	45
H(25A)	2886	13324	6965	79
H(25B)	2426	14902	6986	79
H(25C)	3648	14422	6309	79
H(27A)	2154	8214	5597	37
H(27B)	3689	8798	5450	37
H(28A)	2248	7068	4134	76
H(28B)	3505	6589	4825	76

H(28C)	3778	7658	3982	76
H(29A)	5777	11918	1601	33
H(29B)	6073	12439	2705	33



2.26a

A colorless needle 0.10 x 0.04 x 0.04 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using phi and omega scans. Crystal-to-detector distance was 60 mm and exposure time was 5 seconds per frame using a scan width of 1.0°. Data collection was 96.3% complete to 67.00° in q. A total of 11108 reflections were collected covering the indices, -12<=*h*<=12, -8<=*k*<=7, -14<=*l*<=14. 2767 reflections were found to be symmetry independent, with an R_{int} of 0.0147. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P2(1) (No. 4). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SIR-2004) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-97). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-97. Absolute stereochemistry was unambiguously determined to be *S*, *R*, and *R* at C1, C4, and C8, respectively.

Table 1. Crystal data and structure refinement for toste14.

X-ray ID	toste14
Sample/notebook ID	TM-148
Empirical formula	C17 H24 O6
Formula weight	324.36
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 10.0705(7) Å a= 90°.
	b = 7.5860(6) Å b= 114.183(3)°.
	c = 11.9468(9) Å g = 90°.
Volume	832.58(11) $Å^3$
Z	2
Density (calculated)	1.294 Mg/m^3
Absorption coefficient	0.809 mm^{-1}
F(000)	348
Crystal size	0.10 x 0.04 x 0.04 mm^3
Crystal color/habit	colorless needle
Theta range for data collection	4.06 to 68.15°.
Index ranges	-12<=h<=12, -8<=k<=7, -14<=l<=14
Reflections collected	11108
Independent reflections	2767 [R(int) = 0.0147]
Completeness to theta = 67.00°	96.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9684 and 0.9235
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2767 / 1 / 238
Goodness-of-fit on F^2	1.064
Final R indices [I>2sigma(I)]	R1 = 0.0253, wR2 = 0.0666
R indices (all data)	R1 = 0.0260, wR2 = 0.0672
Absolute structure parameter	0.02(14)
Largest diff. peak and hole	0.174 and -0.134 $e.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)
for toste14. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

x	y	z	U(eq)	
C(1)	6416(1)	7988(2)	7875(1)	27(1)
C(2)	5561(1)	9507(2)	7014(1)	29(1)
C(3)	6419(1)	10312(2)	6361(1)	26(1)
C(4)	6868(2)	8995(2)	5635(1)	27(1)
C(5)	7697(2)	9723(2)	4925(1)	34(1)
C(6)	8052(2)	8224(3)	4239(1)	42(1)
C(7)	8202(2)	6384(2)	4749(1)	35(1)
C(8)	7772(1)	7520(2)	6493(1)	25(1)
C(9)	6927(1)	6668(2)	7160(1)	26(1)
C(10)	6716(2)	12013(2)	6428(1)	32(1)
C(11)	9305(1)	8091(2)	7356(1)	26(1)
C(12)	7652(1)	8744(2)	9018(1)	25(1)
C(13)	9726(2)	8059(2)	10824(1)	31(1)
C(14)	9223(2)	8215(2)	11847(1)	35(1)
C(15)	5365(2)	7060(2)	8321(2)	35(1)
C(16)	4303(2)	7448(3)	9808(2)	29(1)
C(17)	2970(4)	8624(8)	9223(4)	37(1)
C(16A)	3572(7)	7272(9)	9022(8)	35(2)
C(17A)	3186(18)	8560(30)	9685(14)	66(5)
O(1)	7939(1)	6059(1)	5752(1)	32(1)
O(2)	8496(1)	5143(2)	4267(1)	49(1)
O(3)	7792(1)	10287(1)	9281(1)	30(1)
O(4)	8534(1)	7469(1)	9693(1)	27(1)
O(5)	4720(1)	5729(2)	7893(1)	52(1)
O(6)	5385(3)	7973(2)	9351(2)	25(1)
O(6A)	4765(8)	7973(6)	8749(8)	33(1)

Table 3. Bond lengths [Å] and angles [°] for toste14.

C(1)-C(12)	1.5334(19)	C(11)-H(11B)	0.9800
C(1)-C(9)	1.5346(19)	C(11)-H(11C)	0.9800
C(1)-C(15)	1.5372(19)	C(12)-O(3)	1.2049(19)
C(1)-C(2)	1.550(2)	C(12)-O(4)	1.3373(17)
C(2)-C(3)	1.5109(19)	C(13)-O(4)	1.4623(16)
C(2)-H(2A)	0.9900	C(13)-C(14)	1.5079(19)
C(2)-H(2B)	0.9900	C(13)-H(13A)	0.9900
C(3)-C(10)	1.320(2)	C(13)-H(13B)	0.9900
C(3)-C(4)	1.509(2)	C(14)-H(14A)	0.9800
C(4)-C(5)	1.5164(19)	C(14)-H(14B)	0.9800
C(4)-C(8)	1.5387(19)	C(14)-H(14C)	0.9800
C(4)-H(4)	1.0000	C(15)-O(6A)	1.166(5)
C(5)-C(6)	1.527(2)	C(15)-O(5)	1.196(2)
C(5)-H(5A)	0.9900	C(15)-O(6)	1.405(3)
C(5)-H(5B)	0.9900	C(16)-O(6)	1.461(2)
C(6)-C(7)	1.506(3)	C(16)-C(17)	1.523(5)
C(6)-H(6A)	0.9900	C(16)-H(16A)	0.9900
C(6)-H(6B)	0.9900	C(16)-H(16B)	0.9900
C(7)-O(2)	1.202(2)	C(17)-H(17A)	0.9800
C(7)-O(1)	1.3516(18)	C(17)-H(17B)	0.9800
C(8)-O(1)	1.4705(16)	C(17)-H(17C)	0.9800
C(8)-C(11)	1.5258(18)	C(16A)-C(17A)	1.41(2)
C(8)-C(9)	1.5274(18)	C(16A)-O(6A)	1.467(7)
C(9)-H(9A)	0.9900	C(16A)-H(16C)	0.9900
C(9)-H(9B)	0.9900	C(16A)-H(16D)	0.9900
C(10)-H(10A)	0.9500	C(17A)-H(17D)	0.9800
C(10)-H(10B)	0.9500	C(17A)-H(17E)	0.9800
C(11)-H(11A)	0.9800	C(17A)-H(17F)	0.9800
C(12)-C(1)-C(9)	113.94(10)	C(10)-C(3)-C(2)	121.82(13)
C(12)-C(1)-C(15)	106.54(11)	C(4)-C(3)-C(2)	113.53(12)
C(9)-C(1)-C(15)	109.25(12)	C(3)-C(4)-C(5)	116.36(13)
C(12)-C(1)-C(2)	109.89(12)	C(3)-C(4)-C(8)	109.44(10)
C(9)-C(1)-C(2)	109.76(11)	C(5)-C(4)-C(8)	109.07(12)
C(15)-C(1)-C(2)	107.21(11)	C(3)-C(4)-H(4)	107.2
C(3)-C(2)-C(1)	111.26(11)	C(5)-C(4)-H(4)	107.2
C(3)-C(2)-H(2A)	109.4	C(8)-C(4)-H(4)	107.2
C(1)-C(2)-H(2A)	109.4	C(4)-C(5)-C(6)	109.42(14)
C(3)-C(2)-H(2B)	109.4	C(4)-C(5)-H(5A)	109.8
C(1)-C(2)-H(2B)	109.4	C(6)-C(5)-H(5A)	109.8
H(2A)-C(2)-H(2B)	108.0	C(4)-C(5)-H(5B)	109.8
C(10)-C(3)-C(4)	124.64(13)	C(6)-C(5)-H(5B)	109.8

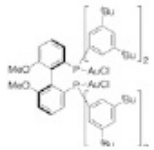
H(5A)-C(5)-H(5B)	108.2
C(7)-C(6)-C(5)	118.69(13)
C(7)-C(6)-H(6A)	107.6
C(5)-C(6)-H(6A)	107.6
C(7)-C(6)-H(6B)	107.6
C(5)-C(6)-H(6B)	107.6
H(6A)-C(6)-H(6B)	107.1
O(2)-C(7)-O(1)	117.26(16)
O(2)-C(7)-C(6)	122.42(14)
O(1)-C(7)-C(6)	120.26(13)
O(1)-C(8)-C(11)	106.71(10)
O(1)-C(8)-C(9)	102.75(11)
C(11)-C(8)-C(9)	113.17(10)
O(1)-C(8)-C(4)	109.21(10)
C(11)-C(8)-C(4)	113.72(12)
C(9)-C(8)-C(4)	110.56(11)
C(8)-C(9)-C(1)	113.56(11)
C(8)-C(9)-H(9A)	108.9
C(1)-C(9)-H(9A)	108.9
C(8)-C(9)-H(9B)	108.9
C(1)-C(9)-H(9B)	108.9
H(9A)-C(9)-H(9B)	107.7
C(3)-C(10)-H(10A)	120.0
C(3)-C(10)-H(10B)	120.0
H(10A)-C(10)-H(10B)	120.0
C(8)-C(11)-H(11A)	109.5
C(8)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(8)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
O(3)-C(12)-O(4)	124.59(13)
O(3)-C(12)-C(1)	124.18(13)
O(4)-C(12)-C(1)	111.22(12)
O(4)-C(13)-C(14)	110.64(11)
O(4)-C(13)-H(13A)	109.5
C(14)-C(13)-H(13A)	109.5
O(4)-C(13)-H(13B)	109.5
C(14)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	108.1
C(13)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
O(6A)-C(15)-O(5)	113.6(3)
O(6A)-C(15)-O(6)	31.5(4)
O(5)-C(15)-O(6)	126.98(15)
O(6A)-C(15)-C(1)	115.7(3)
O(5)-C(15)-C(1)	124.63(15)
O(6)-C(15)-C(1)	108.26(14)
O(6)-C(16)-C(17)	108.7(2)
O(6)-C(16)-H(16A)	110.0
C(17)-C(16)-H(16A)	110.0
O(6)-C(16)-H(16B)	110.0
C(17)-C(16)-H(16B)	110.0
H(16A)-C(16)-H(16B)	108.3
C(16)-C(17)-H(17A)	109.5
C(16)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(16)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(17A)-C(16A)-O(6A)	108.3(8)
C(17A)-C(16A)-H(16C)	110.0
O(6A)-C(16A)-H(16C)	110.0
C(17A)-C(16A)-H(16D)	110.0
O(6A)-C(16A)-H(16D)	110.0
H(16C)-C(16A)-H(16D)	108.4
C(16A)-C(17A)-H(17D)	109.5
C(16A)-C(17A)-H(17E)	109.5
H(17D)-C(17A)-H(17E)	109.5
C(16A)-C(17A)-H(17F)	109.5
H(17D)-C(17A)-H(17F)	109.5
H(17E)-C(17A)-H(17F)	109.5
C(7)-O(1)-C(8)	120.58(12)
C(12)-O(4)-C(13)	115.24(12)
C(15)-O(6)-C(16)	116.60(17)
C(15)-O(6A)-C(16A)	120.0(5)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for toste14. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}	
C(1)	26(1)	24(1)	35(1)	1(1)	16(1)	0(1)
C(2)	23(1)	26(1)	36(1)	-2(1)	11(1)	2(1)
C(3)	22(1)	24(1)	26(1)	3(1)	4(1)	1(1)
C(4)	25(1)	26(1)	25(1)	1(1)	6(1)	-2(1)
C(5)	35(1)	38(1)	27(1)	4(1)	12(1)	-1(1)
C(6)	47(1)	53(1)	29(1)	0(1)	17(1)	1(1)
C(7)	27(1)	48(1)	29(1)	-9(1)	10(1)	0(1)
C(8)	26(1)	22(1)	26(1)	-4(1)	9(1)	1(1)
C(9)	26(1)	20(1)	29(1)	0(1)	8(1)	-3(1)
C(10)	32(1)	28(1)	32(1)	4(1)	8(1)	1(1)
C(11)	24(1)	28(1)	27(1)	1(1)	11(1)	1(1)
C(12)	29(1)	24(1)	30(1)	1(1)	19(1)	-1(1)
C(13)	29(1)	35(1)	28(1)	-2(1)	11(1)	0(1)
C(14)	37(1)	39(1)	30(1)	-3(1)	16(1)	-1(1)
C(15)	28(1)	34(1)	44(1)	7(1)	17(1)	-1(1)
C(16)	23(1)	32(1)	36(1)	4(1)	18(1)	-1(1)
C(17)	19(1)	43(2)	51(2)	17(2)	17(1)	7(1)
C(16A)	25(3)	33(4)	51(5)	-5(3)	19(4)	-14(2)
C(17A)	67(8)	40(6)	90(11)	40(9)	32(8)	6(5)
O(1)	36(1)	29(1)	30(1)	-5(1)	13(1)	2(1)
O(2)	50(1)	54(1)	46(1)	-16(1)	24(1)	5(1)
O(3)	37(1)	25(1)	33(1)	-2(1)	20(1)	-2(1)
O(4)	31(1)	25(1)	28(1)	-1(1)	14(1)	1(1)
O(5)	50(1)	66(1)	38(1)	-4(1)	15(1)	-34(1)
O(6)	24(1)	28(1)	29(1)	0(1)	15(1)	-3(1)
O(6A)	32(3)	28(2)	44(4)	-4(2)	21(3)	-5(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3)
for toste14.

x	y	z	U(eq)	
H(2A)	4625	9048	6401	35
H(2B)	5341	10427	7502	35
H(4)	5958	8442	5025	32
H(5A)	8608	10289	5497	40
H(5B)	7100	10624	4333	40
H(6A)	7283	8201	3393	51
H(6B)	8976	8525	4176	51
H(9A)	7552	5770	7737	31
H(9B)	6066	6055	6551	31
H(10A)	7248	12486	5999	39
H(10B)	6397	12765	6905	39
H(11A)	9767	7153	7953	39
H(11B)	9250	9167	7789	39
H(11C)	9881	8319	6880	39
H(13A)	10085	9217	10684	37
H(13B)	10540	7206	11060	37
H(14A)	8443	9094	11627	52
H(14B)	10041	8582	12602	52
H(14C)	8857	7071	11979	52
H(16A)	4712	7570	10712	34
H(16B)	4026	6199	9598	34
H(17A)	2234	8282	9521	55
H(17B)	2568	8493	8329	55
H(17C)	3250	9856	9442	55
H(16C)	2725	6991	8249	42
H(16D)	3887	6178	9511	42
H(17D)	2406	8097	9895	98
H(17E)	2847	9620	9184	98
H(17F)	4036	8843	10440	98



2.28

A colorless prism 0.17 x 0.15 x 0.15 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 143(2) K using phi and omega scans. Crystal-to-detector distance was 60 mm and exposure time was 10 seconds per frame using a scan width of 0.3°. Data collection was 99.8% complete to 25.00° in q. A total of 118617 reflections were collected covering the indices, -27<=*h*<=27, -36<=*k*<=46, -14<=*k*<=15. 21127 reflections were found to be symmetry independent, with an R_{int} of 0.0344. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P2(1)2(1)2 (No. 18). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SIR-2004) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-97). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-97.

Table 1. Crystal data and structure refinement for toste09.

X-ray ID	toste09
Sample/notebook ID	SGS5-4
Empirical formula	C70 H96 Au2 Cl2 O2 P2
Formula weight	1496.24
Temperature	143(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2
Unit cell dimensions	a = 22.632(3) Å a= 90°.
	b = 38.947(5) Å b= 90°.
	c = 13.0122(16) Å g = 90°.
Volume	11469(2) $Å^3$
Z	6
Density (calculated)	1.300 Mg/m^3
Absorption coefficient	3.981 mm^{-1}
F(000)	4524
Crystal size	0.17 x 0.15 x 0.15 mm^3
Crystal color/habit	colorless prism
Theta range for data collection	2.39 to 25.44°.
Index ranges	-27<=h<=27, -36<=k<=46, -14<=l<=15
Reflections collected	118617
Independent reflections	21127 [R(int) = 0.0344]
Completeness to theta = 25.00°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.5866 and 0.5509
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	21127 / 0 / 1092
Goodness-of-fit on F^2	1.050
Final R indices [I>2sigma(I)]	R1 = 0.0326, wR2 = 0.0827
R indices (all data)	R1 = 0.0415, wR2 = 0.0869
Absolute structure parameter	-0.009(4)
Largest diff. peak and hole	1.061 and -0.965 $e.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)
for toste09. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

x	y	z	U(eq)	
C(1)	7713(2)	7462(2)	3076(4)	36(1)
C(2)	7407(2)	7173(2)	2774(4)	39(1)
C(3)	6980(3)	7028(2)	3393(5)	43(2)
C(4)	6866(3)	7189(2)	4338(5)	46(2)
C(5)	7178(3)	7477(2)	4669(4)	45(2)
C(6)	7597(2)	7615(2)	4021(4)	38(1)
C(7)	6620(3)	6704(2)	3065(5)	56(2)
C(8)	5989(4)	6813(3)	2855(8)	85(3)
C(9)	6636(5)	6429(3)	3942(8)	99(4)
C(10)	6889(5)	6532(3)	2121(8)	114(5)
C(11)	7079(3)	7633(2)	5739(5)	55(2)
C(12)	6555(7)	7472(4)	6302(9)	168(8)
C(13)	6934(7)	8017(3)	5622(8)	127(5)
C(14)	7617(6)	7577(5)	6365(8)	167(8)
C(15)	8483(2)	8043(2)	2757(4)	38(1)
C(16)	8188(3)	8342(2)	2547(5)	45(2)
C(17)	8342(3)	8642(2)	3036(6)	54(2)
C(18)	8812(3)	8629(2)	3745(6)	56(2)
C(19)	9112(3)	8335(2)	3960(5)	50(2)
C(20)	8949(3)	8040(2)	3447(5)	45(2)
C(21)	8028(4)	8987(2)	2832(8)	73(2)
C(22)	7495(7)	8949(3)	2125(17)	207(11)
C(23)	7780(7)	9140(4)	3812(13)	174(8)
C(24)	8445(6)	9253(3)	2390(15)	158(7)
C(25)	9622(3)	8326(3)	4750(7)	75(3)
C(26)	9392(6)	8269(9)	5724(11)	340(20)
C(27)	9922(8)	8655(4)	4830(20)	283(17)
C(28)	10088(5)	8092(4)	4400(12)	180(9)
C(29)	8878(2)	7354(2)	2287(4)	32(1)
C(30)	8972(3)	7199(2)	3250(5)	42(2)
C(31)	9489(3)	7013(2)	3414(5)	51(2)
C(32)	9911(3)	6980(2)	2662(5)	50(2)
C(33)	9817(2)	7128(2)	1713(5)	42(2)
C(34)	9284(2)	7309(2)	1496(4)	35(1)
C(35)	10720(3)	6907(3)	1050(7)	75(3)
C(36)	8986(2)	7264(2)	-372(4)	34(1)
C(37)	8874(3)	7424(2)	-1310(5)	41(2)
C(38)	8991(3)	7766(2)	-1439(5)	48(2)

C(39)	9224(3)	7960(2)	-650(6)	49(2)
C(40)	9321(3)	7807(2)	293(5)	42(2)
C(41)	9199(2)	7457(2)	459(4)	32(1)
C(42)	9615(4)	8330(2)	1091(6)	63(2)
C(43)	9611(2)	6639(2)	-788(5)	41(2)
C(44)	9977(3)	6851(2)	-1345(5)	50(2)
C(45)	10508(3)	6726(2)	-1759(7)	63(2)
C(46)	10634(3)	6390(2)	-1589(8)	77(3)
C(47)	10288(3)	6170(2)	-1034(8)	75(3)
C(48)	9762(3)	6310(2)	-628(7)	59(2)
C(49)	10906(4)	6972(3)	-2387(9)	97(4)
C(50)	10569(5)	7136(4)	-3214(9)	116(5)
C(51)	11096(5)	7277(3)	-1640(11)	121(5)
C(52)	11473(5)	6824(4)	-2660(13)	153(7)
C(53)	10457(4)	5795(3)	-858(17)	153(7)
C(54)	10532(11)	5644(5)	-1974(18)	246(12)
C(55)	9991(5)	5589(3)	-381(18)	197(10)
C(56)	11031(5)	5780(3)	-284(15)	154(7)
C(57)	8374(2)	6686(2)	-1270(5)	37(1)
C(58)	8556(3)	6593(2)	-2261(4)	38(1)
C(59)	8145(3)	6510(2)	-3003(4)	43(2)
C(60)	7549(3)	6519(2)	-2735(5)	47(2)
C(61)	7356(2)	6609(2)	-1753(5)	41(2)
C(62)	7776(3)	6690(2)	-1027(5)	40(1)
C(63)	8329(3)	6419(2)	-4102(5)	52(2)
C(64)	8159(4)	6716(2)	-4800(6)	73(2)
C(65)	8005(5)	6093(2)	-4488(6)	77(3)
C(66)	9011(4)	6354(3)	-4180(6)	89(3)
C(67)	6701(3)	6600(2)	-1433(5)	53(2)
C(68)	6298(3)	6554(3)	-2371(8)	102(4)
C(69)	6612(3)	6298(2)	-716(7)	68(2)
C(70)	6535(3)	6939(2)	-903(7)	74(3)
C(71)	3463(3)	5258(2)	11209(6)	48(2)
C(72)	3337(3)	5602(2)	11161(6)	52(2)
C(73)	2898(3)	5753(2)	11734(7)	66(2)
C(74)	2577(3)	5538(3)	12363(7)	70(2)
C(75)	2674(3)	5189(3)	12464(7)	66(2)
C(76)	3138(3)	5053(2)	11885(6)	60(2)
C(77)	2767(4)	6138(2)	11689(9)	85(3)
C(78)	2178(5)	6210(4)	11420(20)	267(16)
C(79)	2883(14)	6293(6)	12740(20)	320(20)
C(80)	3223(7)	6328(4)	11150(20)	244(15)
C(81)	2280(5)	4958(3)	13147(7)	88(3)
C(82)	2509(6)	4583(3)	13218(9)	114(4)

C(83)	1675(5)	4952(4)	12694(11)	144(6)
C(84)	2283(6)	5123(3)	14251(9)	127(5)
C(85)	3568(3)	4863(2)	9384(6)	51(2)
C(86)	2984(3)	4780(2)	9514(7)	59(2)
C(87)	2656(3)	4636(2)	8718(7)	64(2)
C(88)	2922(3)	4582(2)	7786(7)	66(2)
C(89)	3508(3)	4670(2)	7617(6)	56(2)
C(90)	3830(3)	4804(2)	8416(6)	55(2)
C(91)	2004(3)	4553(3)	8904(10)	90(3)
C(92)	1726(4)	4362(4)	8105(12)	164(8)
C(93)	1973(4)	4286(4)	9872(14)	154(7)
C(94)	1699(4)	4856(3)	9288(10)	102(4)
C(95)	3785(4)	4631(2)	6545(7)	73(2)
C(96)	4432(7)	4683(9)	6523(14)	286(18)
C(97)	3610(11)	4336(5)	6006(16)	290(18)
C(98)	3600(20)	4901(6)	5925(15)	430(30)
C(99)	4372(3)	4746(2)	11113(6)	53(2)
C(100)	4159(3)	4408(2)	11130(8)	70(2)
C(101)	4407(4)	4164(2)	11732(8)	82(3)
C(102)	4867(4)	4244(2)	12387(8)	73(3)
C(103)	5102(3)	4573(2)	12381(6)	55(2)
C(104)	4864(3)	4825(2)	11723(6)	47(2)
C(105)	5838(4)	4432(3)	13599(7)	85(3)
O(1)	10201(2)	7109(1)	911(3)	55(1)
O(2)	9530(2)	7971(1)	1143(4)	53(1)
O(3)	5555(2)	4682(2)	12975(4)	66(2)
P(1)	8246(1)	7640(1)	2172(1)	33(1)
P(2)	8909(1)	6800(1)	-289(1)	33(1)
P(3)	4005(1)	5076(1)	10358(2)	47(1)
Cl(1)	7320(1)	7806(1)	-843(1)	55(1)
Cl(2)	8500(1)	6246(1)	2653(2)	91(1)
Cl(3)	5090(1)	5883(1)	8778(3)	113(1)
Au(1)	7817(1)	7711(1)	650(1)	34(1)
Au(2)	8689(1)	6551(1)	1200(1)	45(1)
Au(3)	4574(1)	5469(1)	9605(1)	58(1)

Table 3. Bond lengths [Å] and angles [°] for toste09.

C(1)-C(2)	1.380(8)	C(17)-C(21)	1.546(11)
C(1)-C(6)	1.392(8)	C(18)-C(19)	1.359(10)
C(1)-P(1)	1.822(6)	C(18)-H(18)	0.9500
C(2)-C(3)	1.379(8)	C(19)-C(20)	1.381(9)
C(2)-H(2)	0.9500	C(19)-C(25)	1.545(9)
C(3)-C(4)	1.403(9)	C(20)-H(20)	0.9500
C(3)-C(7)	1.562(9)	C(21)-C(24)	1.516(14)
C(4)-C(5)	1.394(9)	C(21)-C(23)	1.514(17)
C(4)-H(4)	0.9500	C(21)-C(22)	1.525(16)
C(5)-C(6)	1.378(8)	C(22)-H(22A)	0.9800
C(5)-C(11)	1.535(8)	C(22)-H(22B)	0.9800
C(6)-H(6)	0.9500	C(22)-H(22C)	0.9800
C(7)-C(8)	1.515(11)	C(23)-H(23A)	0.9800
C(7)-C(10)	1.526(11)	C(23)-H(23B)	0.9800
C(7)-C(9)	1.565(13)	C(23)-H(23C)	0.9800
C(8)-H(8A)	0.9800	C(24)-H(24A)	0.9800
C(8)-H(8B)	0.9800	C(24)-H(24B)	0.9800
C(8)-H(8C)	0.9800	C(24)-H(24C)	0.9800
C(9)-H(9A)	0.9800	C(25)-C(26)	1.388(16)
C(9)-H(9B)	0.9800	C(25)-C(27)	1.453(17)
C(9)-H(9C)	0.9800	C(25)-C(28)	1.466(14)
C(10)-H(10A)	0.9800	C(26)-H(26A)	0.9801
C(10)-H(10B)	0.9800	C(26)-H(26B)	0.9801
C(10)-H(10C)	0.9800	C(26)-H(26C)	0.9801
C(11)-C(14)	1.480(12)	C(27)-H(27A)	0.9800
C(11)-C(12)	1.529(12)	C(27)-H(27B)	0.9800
C(11)-C(13)	1.538(14)	C(27)-H(27C)	0.9800
C(12)-H(12A)	0.9800	C(28)-H(28A)	0.9800
C(12)-H(12B)	0.9800	C(28)-H(28B)	0.9800
C(12)-H(12C)	0.9800	C(28)-H(28C)	0.9800
C(13)-H(13A)	0.9800	C(29)-C(34)	1.392(8)
C(13)-H(13B)	0.9800	C(29)-C(30)	1.406(8)
C(13)-H(13C)	0.9800	C(29)-P(1)	1.818(6)
C(14)-H(14A)	0.9800	C(30)-C(31)	1.392(9)
C(14)-H(14B)	0.9800	C(30)-H(30)	0.9500
C(14)-H(14C)	0.9800	C(31)-C(32)	1.374(10)
C(15)-C(16)	1.370(9)	C(31)-H(31)	0.9500
C(15)-C(20)	1.385(8)	C(32)-C(33)	1.379(10)
C(15)-P(1)	1.826(6)	C(32)-H(32)	0.9500
C(16)-C(17)	1.375(10)	C(33)-O(1)	1.359(7)
C(16)-H(16)	0.9500	C(33)-C(34)	1.425(8)
C(17)-C(18)	1.409(10)	C(34)-C(41)	1.480(8)

C(35)-O(1)	1.425(8)	C(53)-C(56)	1.500(18)
C(35)-H(35A)	0.9800	C(53)-C(54)	1.58(3)
C(35)-H(35B)	0.9800	C(54)-H(54A)	0.9800
C(35)-H(35C)	0.9800	C(54)-H(54B)	0.9800
C(36)-C(37)	1.393(8)	C(54)-H(54C)	0.9800
C(36)-C(41)	1.402(8)	C(55)-H(55A)	0.9800
C(36)-P(2)	1.822(7)	C(55)-H(55B)	0.9800
C(37)-C(38)	1.368(10)	C(55)-H(55C)	0.9800
C(37)-H(37)	0.9500	C(56)-H(56A)	0.9800
C(38)-C(39)	1.378(10)	C(56)-H(56B)	0.9800
C(38)-H(38)	0.9500	C(56)-H(56C)	0.9800
C(39)-C(40)	1.382(10)	C(57)-C(62)	1.390(8)
C(39)-H(39)	0.9500	C(57)-C(58)	1.400(8)
C(40)-O(2)	1.361(8)	C(57)-P(2)	1.814(6)
C(40)-C(41)	1.408(9)	C(58)-C(59)	1.380(8)
C(42)-O(2)	1.412(8)	C(58)-H(58)	0.9500
C(42)-H(42A)	0.9800	C(59)-C(60)	1.394(9)
C(42)-H(42B)	0.9800	C(59)-C(63)	1.530(9)
C(42)-H(42C)	0.9800	C(60)-C(61)	1.394(9)
C(43)-C(48)	1.340(10)	C(60)-H(60)	0.9500
C(43)-C(44)	1.376(9)	C(61)-C(62)	1.377(8)
C(43)-P(2)	1.827(6)	C(61)-C(67)	1.540(8)
C(44)-C(45)	1.403(9)	C(62)-H(62)	0.9500
C(44)-H(44)	0.9500	C(63)-C(64)	1.519(11)
C(45)-C(46)	1.355(12)	C(63)-C(65)	1.549(11)
C(45)-C(49)	1.549(12)	C(63)-C(66)	1.569(11)
C(46)-C(47)	1.368(13)	C(64)-H(64A)	0.9800
C(46)-H(46)	0.9500	C(64)-H(64B)	0.9800
C(47)-C(48)	1.414(10)	C(64)-H(64C)	0.9800
C(47)-C(53)	1.526(14)	C(65)-H(65A)	0.9800
C(48)-H(48)	0.9500	C(65)-H(65B)	0.9800
C(49)-C(52)	1.451(14)	C(65)-H(65C)	0.9800
C(49)-C(50)	1.467(15)	C(66)-H(66A)	0.9800
C(49)-C(51)	1.594(17)	C(66)-H(66B)	0.9800
C(50)-H(50A)	0.9800	C(66)-H(66C)	0.9800
C(50)-H(50B)	0.9800	C(67)-C(69)	1.516(11)
C(50)-H(50C)	0.9800	C(67)-C(70)	1.535(12)
C(51)-H(51A)	0.9800	C(67)-C(68)	1.535(10)
C(51)-H(51B)	0.9800	C(68)-H(68A)	0.9800
C(51)-H(51C)	0.9800	C(68)-H(68B)	0.9800
C(52)-H(52A)	0.9800	C(68)-H(68C)	0.9800
C(52)-H(52B)	0.9800	C(69)-H(69A)	0.9800
C(52)-H(52C)	0.9800	C(69)-H(69B)	0.9800
C(53)-C(55)	1.462(19)	C(69)-H(69C)	0.9800

C(70)-H(70A)	0.9800	C(87)-C(88)	1.371(12)
C(70)-H(70B)	0.9800	C(87)-C(91)	1.529(11)
C(70)-H(70C)	0.9800	C(88)-C(89)	1.387(11)
C(71)-C(72)	1.371(10)	C(88)-H(88)	0.9500
C(71)-C(76)	1.397(10)	C(89)-C(90)	1.375(10)
C(71)-P(3)	1.799(8)	C(89)-C(95)	1.537(12)
C(72)-C(73)	1.375(11)	C(90)-H(90)	0.9500
C(72)-H(72)	0.9500	C(91)-C(92)	1.426(14)
C(73)-C(74)	1.376(12)	C(91)-C(94)	1.455(13)
C(73)-C(77)	1.528(12)	C(91)-C(93)	1.637(19)
C(74)-C(75)	1.385(13)	C(92)-H(92A)	0.9800
C(74)-H(74)	0.9500	C(92)-H(92B)	0.9800
C(75)-C(76)	1.396(11)	C(92)-H(92C)	0.9800
C(75)-C(81)	1.548(12)	C(93)-H(93A)	0.9800
C(76)-H(76)	0.9500	C(93)-H(93B)	0.9800
C(77)-C(78)	1.408(15)	C(93)-H(93C)	0.9800
C(77)-C(80)	1.451(19)	C(94)-H(94A)	0.9800
C(77)-C(79)	1.52(2)	C(94)-H(94B)	0.9800
C(78)-H(78A)	0.9800	C(94)-H(94C)	0.9800
C(78)-H(78B)	0.9800	C(95)-C(98)	1.39(2)
C(78)-H(78C)	0.9800	C(95)-C(97)	1.406(17)
C(79)-H(79A)	0.9811	C(95)-C(96)	1.477(18)
C(79)-H(79B)	0.9811	C(96)-H(96A)	0.9803
C(79)-H(79C)	0.9811	C(96)-H(96B)	0.9803
C(80)-H(80A)	0.9800	C(96)-H(96C)	0.9803
C(80)-H(80B)	0.9800	C(97)-H(97A)	0.9800
C(80)-H(80C)	0.9800	C(97)-H(97B)	0.9800
C(81)-C(83)	1.491(16)	C(97)-H(97C)	0.9800
C(81)-C(82)	1.552(16)	C(98)-H(98A)	0.9800
C(81)-C(84)	1.572(15)	C(98)-H(98B)	0.9800
C(82)-H(82A)	0.9800	C(98)-H(98C)	0.9800
C(82)-H(82B)	0.9800	C(99)-C(104)	1.400(9)
C(82)-H(82C)	0.9800	C(99)-C(100)	1.405(10)
C(83)-H(83A)	0.9800	C(99)-P(3)	1.819(8)
C(83)-H(83B)	0.9800	C(100)-C(101)	1.353(11)
C(83)-H(83C)	0.9800	C(100)-H(100)	0.9500
C(84)-H(84A)	0.9800	C(101)-C(102)	1.382(12)
C(84)-H(84B)	0.9800	C(101)-H(101)	0.9500
C(84)-H(84C)	0.9800	C(102)-C(103)	1.388(11)
C(85)-C(86)	1.372(9)	C(102)-H(102)	0.9500
C(85)-C(90)	1.411(11)	C(103)-O(3)	1.353(8)
C(85)-P(3)	1.809(7)	C(103)-C(104)	1.408(10)
C(86)-C(87)	1.392(11)	C(104)-C(104)#1	1.499(13)
C(86)-H(86)	0.9500	C(105)-O(3)	1.420(10)

C(105)-H(10D)	0.9800	P(3)-Au(3)	2.2244(18)
C(105)-H(10E)	0.9800	Cl(1)-Au(1)	2.2751(15)
C(105)-H(10F)	0.9800	Cl(2)-Au(2)	2.274(2)
P(1)-Au(1)	2.2230(14)	Cl(3)-Au(3)	2.263(2)
P(2)-Au(2)	2.2227(15)		

C(2)-C(1)-C(6)	120.4(5)	H(10A)-C(10)-H(10B)	109.5
C(2)-C(1)-P(1)	117.3(4)	C(7)-C(10)-H(10C)	109.5
C(6)-C(1)-P(1)	122.2(5)	H(10A)-C(10)-H(10C)	109.5
C(3)-C(2)-C(1)	121.3(5)	H(10B)-C(10)-H(10C)	109.5
C(3)-C(2)-H(2)	119.4	C(14)-C(11)-C(12)	108.2(11)
C(1)-C(2)-H(2)	119.3	C(14)-C(11)-C(5)	108.8(6)
C(2)-C(3)-C(4)	117.3(6)	C(12)-C(11)-C(5)	112.7(7)
C(2)-C(3)-C(7)	122.5(5)	C(14)-C(11)-C(13)	111.9(10)
C(4)-C(3)-C(7)	120.2(5)	C(12)-C(11)-C(13)	106.3(9)
C(5)-C(4)-C(3)	122.5(6)	C(5)-C(11)-C(13)	109.0(6)
C(5)-C(4)-H(4)	118.7	C(11)-C(12)-H(12A)	109.5
C(3)-C(4)-H(4)	118.8	C(11)-C(12)-H(12B)	109.5
C(6)-C(5)-C(4)	118.3(5)	H(12A)-C(12)-H(12B)	109.5
C(6)-C(5)-C(11)	120.0(6)	C(11)-C(12)-H(12C)	109.5
C(4)-C(5)-C(11)	121.7(6)	H(12A)-C(12)-H(12C)	109.5
C(5)-C(6)-C(1)	120.2(6)	H(12B)-C(12)-H(12C)	109.5
C(5)-C(6)-H(6)	119.9	C(11)-C(13)-H(13A)	109.5
C(1)-C(6)-H(6)	119.9	C(11)-C(13)-H(13B)	109.5
C(8)-C(7)-C(10)	110.8(8)	H(13A)-C(13)-H(13B)	109.5
C(8)-C(7)-C(3)	108.3(7)	C(11)-C(13)-H(13C)	109.4
C(10)-C(7)-C(3)	111.4(6)	H(13A)-C(13)-H(13C)	109.5
C(8)-C(7)-C(9)	110.2(7)	H(13B)-C(13)-H(13C)	109.5
C(10)-C(7)-C(9)	106.1(9)	C(11)-C(14)-H(14A)	109.5
C(3)-C(7)-C(9)	110.0(6)	C(11)-C(14)-H(14B)	109.5
C(7)-C(8)-H(8A)	109.5	H(14A)-C(14)-H(14B)	109.5
C(7)-C(8)-H(8B)	109.5	C(11)-C(14)-H(14C)	109.5
H(8A)-C(8)-H(8B)	109.5	H(14A)-C(14)-H(14C)	109.5
C(7)-C(8)-H(8C)	109.5	H(14B)-C(14)-H(14C)	109.5
H(8A)-C(8)-H(8C)	109.5	C(16)-C(15)-C(20)	120.6(6)
H(8B)-C(8)-H(8C)	109.5	C(16)-C(15)-P(1)	120.2(5)
C(7)-C(9)-H(9A)	109.5	C(20)-C(15)-P(1)	119.1(5)
C(7)-C(9)-H(9B)	109.5	C(15)-C(16)-C(17)	120.3(6)
H(9A)-C(9)-H(9B)	109.5	C(15)-C(16)-H(16)	119.8
C(7)-C(9)-H(9C)	109.5	C(17)-C(16)-H(16)	119.8
H(9A)-C(9)-H(9C)	109.5	C(16)-C(17)-C(18)	117.7(7)
H(9B)-C(9)-H(9C)	109.5	C(16)-C(17)-C(21)	122.9(7)
C(7)-C(10)-H(10A)	109.5	C(18)-C(17)-C(21)	119.4(7)
C(7)-C(10)-H(10B)	109.5	C(19)-C(18)-C(17)	122.8(7)

C(19)-C(18)-H(18)	118.6	C(25)-C(27)-H(27A)	109.5
C(17)-C(18)-H(18)	118.6	C(25)-C(27)-H(27B)	109.5
C(18)-C(19)-C(20)	117.9(6)	H(27A)-C(27)-H(27B)	109.5
C(18)-C(19)-C(25)	122.1(7)	C(25)-C(27)-H(27C)	109.5
C(20)-C(19)-C(25)	120.0(7)	H(27A)-C(27)-H(27C)	109.5
C(19)-C(20)-C(15)	120.6(7)	H(27B)-C(27)-H(27C)	109.5
C(19)-C(20)-H(20)	119.7	C(25)-C(28)-H(28A)	109.5
C(15)-C(20)-H(20)	119.7	C(25)-C(28)-H(28B)	109.5
C(24)-C(21)-C(23)	106.3(11)	H(28A)-C(28)-H(28B)	109.5
C(24)-C(21)-C(22)	109.3(12)	C(25)-C(28)-H(28C)	109.4
C(23)-C(21)-C(22)	104.7(12)	H(28A)-C(28)-H(28C)	109.5
C(24)-C(21)-C(17)	112.0(8)	H(28B)-C(28)-H(28C)	109.5
C(23)-C(21)-C(17)	111.7(9)	C(34)-C(29)-C(30)	120.4(5)
C(22)-C(21)-C(17)	112.5(8)	C(34)-C(29)-P(1)	122.3(4)
C(21)-C(22)-H(22A)	109.5	C(30)-C(29)-P(1)	117.1(4)
C(21)-C(22)-H(22B)	109.5	C(31)-C(30)-C(29)	119.1(6)
H(22A)-C(22)-H(22B)	109.5	C(31)-C(30)-H(30)	120.5
C(21)-C(22)-H(22C)	109.4	C(29)-C(30)-H(30)	120.4
H(22A)-C(22)-H(22C)	109.5	C(32)-C(31)-C(30)	121.6(6)
H(22B)-C(22)-H(22C)	109.5	C(32)-C(31)-H(31)	119.2
C(21)-C(23)-H(23A)	109.5	C(30)-C(31)-H(31)	119.2
C(21)-C(23)-H(23B)	109.5	C(31)-C(32)-C(33)	119.4(6)
H(23A)-C(23)-H(23B)	109.5	C(31)-C(32)-H(32)	120.3
C(21)-C(23)-H(23C)	109.5	C(33)-C(32)-H(32)	120.3
H(23A)-C(23)-H(23C)	109.5	O(1)-C(33)-C(32)	124.4(6)
H(23B)-C(23)-H(23C)	109.5	O(1)-C(33)-C(34)	114.5(6)
C(21)-C(24)-H(24A)	109.5	C(32)-C(33)-C(34)	121.0(6)
C(21)-C(24)-H(24B)	109.5	C(29)-C(34)-C(33)	118.3(5)
H(24A)-C(24)-H(24B)	109.5	C(29)-C(34)-C(41)	122.7(5)
C(21)-C(24)-H(24C)	109.5	C(33)-C(34)-C(41)	118.9(5)
H(24A)-C(24)-H(24C)	109.5	O(1)-C(35)-H(35A)	109.5
H(24B)-C(24)-H(24C)	109.5	O(1)-C(35)-H(35B)	109.5
C(26)-C(25)-C(27)	104.6(17)	H(35A)-C(35)-H(35B)	109.5
C(26)-C(25)-C(28)	117.0(16)	O(1)-C(35)-H(35C)	109.5
C(27)-C(25)-C(28)	103.5(12)	H(35A)-C(35)-H(35C)	109.5
C(26)-C(25)-C(19)	109.4(8)	H(35B)-C(35)-H(35C)	109.5
C(27)-C(25)-C(19)	111.9(10)	C(37)-C(36)-C(41)	119.9(6)
C(28)-C(25)-C(19)	110.2(7)	C(37)-C(36)-P(2)	118.6(5)
C(25)-C(26)-H(26A)	109.4	C(41)-C(36)-P(2)	121.3(4)
C(25)-C(26)-H(26B)	109.5	C(38)-C(37)-C(36)	120.5(6)
H(26A)-C(26)-H(26B)	109.5	C(38)-C(37)-H(37)	119.8
C(25)-C(26)-H(26C)	109.5	C(36)-C(37)-H(37)	119.8
H(26A)-C(26)-H(26C)	109.5	C(37)-C(38)-C(39)	121.0(6)
H(26B)-C(26)-H(26C)	109.5	C(37)-C(38)-H(38)	119.5

C(39)-C(38)-H(38)	119.5	H(50A)-C(50)-H(50C)	109.5
C(38)-C(39)-C(40)	119.2(6)	H(50B)-C(50)-H(50C)	109.5
C(38)-C(39)-H(39)	120.4	C(49)-C(51)-H(51A)	109.5
C(40)-C(39)-H(39)	120.4	C(49)-C(51)-H(51B)	109.5
O(2)-C(40)-C(39)	125.1(6)	H(51A)-C(51)-H(51B)	109.5
O(2)-C(40)-C(41)	113.5(5)	C(49)-C(51)-H(51C)	109.5
C(39)-C(40)-C(41)	121.4(6)	H(51A)-C(51)-H(51C)	109.5
C(36)-C(41)-C(40)	117.9(5)	H(51B)-C(51)-H(51C)	109.5
C(36)-C(41)-C(34)	122.7(5)	C(49)-C(52)-H(52A)	109.5
C(40)-C(41)-C(34)	119.4(5)	C(49)-C(52)-H(52B)	109.5
O(2)-C(42)-H(42A)	109.5	H(52A)-C(52)-H(52B)	109.5
O(2)-C(42)-H(42B)	109.5	C(49)-C(52)-H(52C)	109.5
H(42A)-C(42)-H(42B)	109.5	H(52A)-C(52)-H(52C)	109.5
O(2)-C(42)-H(42C)	109.5	H(52B)-C(52)-H(52C)	109.5
H(42A)-C(42)-H(42C)	109.5	C(55)-C(53)-C(56)	113.1(16)
H(42B)-C(42)-H(42C)	109.5	C(55)-C(53)-C(47)	114.1(9)
C(48)-C(43)-C(44)	120.1(6)	C(56)-C(53)-C(47)	109.1(10)
C(48)-C(43)-P(2)	119.6(5)	C(55)-C(53)-C(54)	105.3(15)
C(44)-C(43)-P(2)	120.3(5)	C(56)-C(53)-C(54)	110.6(14)
C(43)-C(44)-C(45)	120.7(7)	C(47)-C(53)-C(54)	104.2(15)
C(43)-C(44)-H(44)	119.7	C(53)-C(54)-H(54A)	109.5
C(45)-C(44)-H(44)	119.7	C(53)-C(54)-H(54B)	109.5
C(46)-C(45)-C(44)	116.8(7)	H(54A)-C(54)-H(54B)	109.5
C(46)-C(45)-C(49)	124.1(7)	C(53)-C(54)-H(54C)	109.5
C(44)-C(45)-C(49)	119.0(8)	H(54A)-C(54)-H(54C)	109.5
C(45)-C(46)-C(47)	124.8(7)	H(54B)-C(54)-H(54C)	109.5
C(45)-C(46)-H(46)	117.6	C(53)-C(55)-H(55A)	109.5
C(47)-C(46)-H(46)	117.6	C(53)-C(55)-H(55B)	109.5
C(46)-C(47)-C(48)	115.8(8)	H(55A)-C(55)-H(55B)	109.5
C(46)-C(47)-C(53)	122.5(9)	C(53)-C(55)-H(55C)	109.5
C(48)-C(47)-C(53)	121.7(9)	H(55A)-C(55)-H(55C)	109.5
C(43)-C(48)-C(47)	121.8(7)	H(55B)-C(55)-H(55C)	109.5
C(43)-C(48)-H(48)	119.1	C(53)-C(56)-H(56A)	109.5
C(47)-C(48)-H(48)	119.1	C(53)-C(56)-H(56B)	109.5
C(52)-C(49)-C(50)	117.0(11)	H(56A)-C(56)-H(56B)	109.5
C(52)-C(49)-C(45)	113.4(10)	C(53)-C(56)-H(56C)	109.5
C(50)-C(49)-C(45)	110.8(8)	H(56A)-C(56)-H(56C)	109.5
C(52)-C(49)-C(51)	102.0(11)	H(56B)-C(56)-H(56C)	109.5
C(50)-C(49)-C(51)	105.2(11)	C(62)-C(57)-C(58)	119.9(5)
C(45)-C(49)-C(51)	107.3(8)	C(62)-C(57)-P(2)	119.1(5)
C(49)-C(50)-H(50A)	109.5	C(58)-C(57)-P(2)	120.9(4)
C(49)-C(50)-H(50B)	109.5	C(59)-C(58)-C(57)	120.4(5)
H(50A)-C(50)-H(50B)	109.5	C(59)-C(58)-H(58)	119.8
C(49)-C(50)-H(50C)	109.5	C(57)-C(58)-H(58)	119.8

C(58)-C(59)-C(60)	118.1(5)	H(68A)-C(68)-H(68B)	109.5
C(58)-C(59)-C(63)	121.7(6)	C(67)-C(68)-H(68C)	109.5
C(60)-C(59)-C(63)	120.2(6)	H(68A)-C(68)-H(68C)	109.5
C(61)-C(60)-C(59)	122.6(5)	H(68B)-C(68)-H(68C)	109.5
C(61)-C(60)-H(60)	118.7	C(67)-C(69)-H(69A)	109.5
C(59)-C(60)-H(60)	118.7	C(67)-C(69)-H(69B)	109.5
C(62)-C(61)-C(60)	118.0(5)	H(69A)-C(69)-H(69B)	109.5
C(62)-C(61)-C(67)	118.9(6)	C(67)-C(69)-H(69C)	109.5
C(60)-C(61)-C(67)	123.0(5)	H(69A)-C(69)-H(69C)	109.5
C(61)-C(62)-C(57)	120.9(6)	H(69B)-C(69)-H(69C)	109.5
C(61)-C(62)-H(62)	119.6	C(67)-C(70)-H(70A)	109.5
C(57)-C(62)-H(62)	119.6	C(67)-C(70)-H(70B)	109.5
C(64)-C(63)-C(59)	108.4(6)	H(70A)-C(70)-H(70B)	109.5
C(64)-C(63)-C(65)	108.0(6)	C(67)-C(70)-H(70C)	109.5
C(59)-C(63)-C(65)	111.4(6)	H(70A)-C(70)-H(70C)	109.5
C(64)-C(63)-C(66)	109.5(7)	H(70B)-C(70)-H(70C)	109.5
C(59)-C(63)-C(66)	111.5(6)	C(72)-C(71)-C(76)	118.6(7)
C(65)-C(63)-C(66)	108.1(7)	C(72)-C(71)-P(3)	119.8(6)
C(63)-C(64)-H(64A)	109.5	C(76)-C(71)-P(3)	121.5(6)
C(63)-C(64)-H(64B)	109.5	C(71)-C(72)-C(73)	122.9(7)
H(64A)-C(64)-H(64B)	109.5	C(71)-C(72)-H(72)	118.5
C(63)-C(64)-H(64C)	109.5	C(73)-C(72)-H(72)	118.5
H(64A)-C(64)-H(64C)	109.5	C(72)-C(73)-C(74)	116.3(8)
H(64B)-C(64)-H(64C)	109.5	C(72)-C(73)-C(77)	122.6(8)
C(63)-C(65)-H(65A)	109.5	C(74)-C(73)-C(77)	121.1(8)
C(63)-C(65)-H(65B)	109.5	C(73)-C(74)-C(75)	124.8(8)
H(65A)-C(65)-H(65B)	109.5	C(73)-C(74)-H(74)	117.6
C(63)-C(65)-H(65C)	109.5	C(75)-C(74)-H(74)	117.6
H(65A)-C(65)-H(65C)	109.5	C(74)-C(75)-C(76)	116.1(8)
H(65B)-C(65)-H(65C)	109.5	C(74)-C(75)-C(81)	122.3(8)
C(63)-C(66)-H(66A)	109.5	C(76)-C(75)-C(81)	121.5(9)
C(63)-C(66)-H(66B)	109.5	C(71)-C(76)-C(75)	121.2(8)
H(66A)-C(66)-H(66B)	109.5	C(71)-C(76)-H(76)	119.4
C(63)-C(66)-H(66C)	109.5	C(75)-C(76)-H(76)	119.4
H(66A)-C(66)-H(66C)	109.5	C(78)-C(77)-C(80)	116.7(15)
H(66B)-C(66)-H(66C)	109.5	C(78)-C(77)-C(73)	113.0(9)
C(69)-C(67)-C(70)	110.9(6)	C(80)-C(77)-C(73)	112.4(9)
C(69)-C(67)-C(68)	108.6(7)	C(78)-C(77)-C(79)	108.1(17)
C(70)-C(67)-C(68)	108.2(8)	C(80)-C(77)-C(79)	96.2(17)
C(69)-C(67)-C(61)	108.1(6)	C(73)-C(77)-C(79)	108.9(12)
C(70)-C(67)-C(61)	109.8(6)	C(77)-C(78)-H(78A)	109.4
C(68)-C(67)-C(61)	111.1(6)	C(77)-C(78)-H(78B)	109.5
C(67)-C(68)-H(68A)	109.5	H(78A)-C(78)-H(78B)	109.5
C(67)-C(68)-H(68B)	109.5	C(77)-C(78)-H(78C)	109.5

H(78A)-C(78)-H(78C)	109.5	C(88)-C(87)-C(86)	119.1(7)
H(78B)-C(78)-H(78C)	109.5	C(88)-C(87)-C(91)	122.1(7)
C(77)-C(79)-H(79A)	109.7	C(86)-C(87)-C(91)	118.8(8)
C(77)-C(79)-H(79B)	109.6	C(87)-C(88)-C(89)	121.5(7)
H(79A)-C(79)-H(79B)	109.4	C(87)-C(88)-H(88)	119.3
C(77)-C(79)-H(79C)	109.5	C(89)-C(88)-H(88)	119.3
H(79A)-C(79)-H(79C)	109.4	C(90)-C(89)-C(88)	118.8(8)
H(79B)-C(79)-H(79C)	109.4	C(90)-C(89)-C(95)	120.4(7)
C(77)-C(80)-H(80A)	109.5	C(88)-C(89)-C(95)	120.7(7)
C(77)-C(80)-H(80B)	109.4	C(89)-C(90)-C(85)	120.9(7)
H(80A)-C(80)-H(80B)	109.5	C(89)-C(90)-H(90)	119.5
C(77)-C(80)-H(80C)	109.5	C(85)-C(90)-H(90)	119.5
H(80A)-C(80)-H(80C)	109.5	C(92)-C(91)-C(94)	117.8(10)
H(80B)-C(80)-H(80C)	109.5	C(92)-C(91)-C(87)	114.9(9)
C(83)-C(81)-C(75)	108.2(9)	C(94)-C(91)-C(87)	109.9(8)
C(83)-C(81)-C(82)	108.3(11)	C(92)-C(91)-C(93)	102.0(11)
C(75)-C(81)-C(82)	112.8(9)	C(94)-C(91)-C(93)	103.5(10)
C(83)-C(81)-C(84)	111.9(10)	C(87)-C(91)-C(93)	107.2(8)
C(75)-C(81)-C(84)	106.5(9)	C(91)-C(92)-H(92A)	109.5
C(82)-C(81)-C(84)	109.1(10)	C(91)-C(92)-H(92B)	109.5
C(81)-C(82)-H(82A)	109.5	H(92A)-C(92)-H(92B)	109.5
C(81)-C(82)-H(82B)	109.5	C(91)-C(92)-H(92C)	109.5
H(82A)-C(82)-H(82B)	109.5	H(92A)-C(92)-H(92C)	109.5
C(81)-C(82)-H(82C)	109.5	H(92B)-C(92)-H(92C)	109.5
H(82A)-C(82)-H(82C)	109.5	C(91)-C(93)-H(93A)	109.5
H(82B)-C(82)-H(82C)	109.5	C(91)-C(93)-H(93B)	109.5
C(81)-C(83)-H(83A)	109.5	H(93A)-C(93)-H(93B)	109.5
C(81)-C(83)-H(83B)	109.5	C(91)-C(93)-H(93C)	109.5
H(83A)-C(83)-H(83B)	109.5	H(93A)-C(93)-H(93C)	109.5
C(81)-C(83)-H(83C)	109.5	H(93B)-C(93)-H(93C)	109.5
H(83A)-C(83)-H(83C)	109.5	C(91)-C(94)-H(94A)	109.5
H(83B)-C(83)-H(83C)	109.5	C(91)-C(94)-H(94B)	109.5
C(81)-C(84)-H(84A)	109.5	H(94A)-C(94)-H(94B)	109.5
C(81)-C(84)-H(84B)	109.5	C(91)-C(94)-H(94C)	109.5
H(84A)-C(84)-H(84B)	109.5	H(94A)-C(94)-H(94C)	109.5
C(81)-C(84)-H(84C)	109.5	H(94B)-C(94)-H(94C)	109.5
H(84A)-C(84)-H(84C)	109.5	C(98)-C(95)-C(97)	104.2(19)
H(84B)-C(84)-H(84C)	109.5	C(98)-C(95)-C(96)	101(2)
C(86)-C(85)-C(90)	118.5(7)	C(97)-C(95)-C(96)	112.5(15)
C(86)-C(85)-P(3)	123.4(6)	C(98)-C(95)-C(89)	109.3(10)
C(90)-C(85)-P(3)	118.0(5)	C(97)-C(95)-C(89)	114.5(9)
C(85)-C(86)-C(87)	121.2(8)	C(96)-C(95)-C(89)	114.2(9)
C(85)-C(86)-H(86)	119.4	C(95)-C(96)-H(96A)	109.5
C(87)-C(86)-H(86)	119.4	C(95)-C(96)-H(96B)	109.5

H(96A)-C(96)-H(96B)	109.4
C(95)-C(96)-H(96C)	109.5
H(96A)-C(96)-H(96C)	109.4
H(96B)-C(96)-H(96C)	109.4
C(95)-C(97)-H(97A)	109.5
C(95)-C(97)-H(97B)	109.5
H(97A)-C(97)-H(97B)	109.5
C(95)-C(97)-H(97C)	109.5
H(97A)-C(97)-H(97C)	109.5
H(97B)-C(97)-H(97C)	109.5
C(95)-C(98)-H(98A)	109.5
C(95)-C(98)-H(98B)	109.5
H(98A)-C(98)-H(98B)	109.5
C(95)-C(98)-H(98C)	109.4
H(98A)-C(98)-H(98C)	109.5
H(98B)-C(98)-H(98C)	109.5
C(104)-C(99)-C(100)	118.0(7)
C(104)-C(99)-P(3)	121.0(5)
C(100)-C(99)-P(3)	121.0(6)
C(101)-C(100)-C(99)	121.7(8)
C(101)-C(100)-H(100)	119.2
C(99)-C(100)-H(100)	119.2
C(100)-C(101)-C(102)	120.9(8)
C(100)-C(101)-H(101)	119.6
C(102)-C(101)-H(101)	119.6
C(101)-C(102)-C(103)	119.5(8)
C(101)-C(102)-H(102)	120.3
C(103)-C(102)-H(102)	120.3
O(3)-C(103)-C(102)	125.2(7)
O(3)-C(103)-C(104)	114.7(6)
C(102)-C(103)-C(104)	120.1(7)
C(99)-C(104)-C(103)	119.8(6)
C(99)-C(104)-C(104)#1	121.6(6)
C(103)-C(104)-C(104)#1	118.5(6)
O(3)-C(105)-H(10D)	109.5
O(3)-C(105)-H(10E)	109.5
H(10D)-C(105)-H(10E)	109.5
O(3)-C(105)-H(10F)	109.5
H(10D)-C(105)-H(10F)	109.5
H(10E)-C(105)-H(10F)	109.5
C(33)-O(1)-C(35)	117.4(6)
C(40)-O(2)-C(42)	118.2(6)
C(103)-O(3)-C(105)	116.9(7)
C(29)-P(1)-C(1)	103.6(3)
C(29)-P(1)-C(15)	105.1(3)
C(1)-P(1)-C(15)	104.6(3)
C(29)-P(1)-Au(1)	119.61(18)
C(1)-P(1)-Au(1)	109.50(17)
C(15)-P(1)-Au(1)	113.1(2)
C(57)-P(2)-C(36)	105.3(3)
C(57)-P(2)-C(43)	104.3(3)
C(36)-P(2)-C(43)	103.7(3)
C(57)-P(2)-Au(2)	111.0(2)
C(36)-P(2)-Au(2)	120.42(18)
C(43)-P(2)-Au(2)	110.8(2)
C(71)-P(3)-C(85)	103.8(3)
C(71)-P(3)-C(99)	104.9(3)
C(85)-P(3)-C(99)	107.7(3)
C(71)-P(3)-Au(3)	113.3(2)
C(85)-P(3)-Au(3)	108.9(3)
C(99)-P(3)-Au(3)	117.4(2)
P(1)-Au(1)-Cl(1)	175.54(6)
P(2)-Au(2)-Cl(2)	174.18(9)
P(3)-Au(3)-Cl(3)	175.68(8)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for toste09. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	31(3)	50(4)	26(3)	-5(3)	-2(2)	-9(3)
C(2)	38(3)	51(4)	27(3)	-8(3)	2(2)	-7(3)
C(3)	42(3)	52(4)	34(3)	-9(3)	2(2)	-8(3)
C(4)	45(3)	54(4)	40(3)	-5(3)	12(3)	-8(3)
C(5)	46(3)	57(4)	32(3)	-5(3)	2(3)	0(3)
C(6)	35(3)	45(4)	33(3)	-4(3)	-2(2)	-8(3)
C(7)	54(4)	66(5)	46(4)	-11(4)	13(3)	-22(4)
C(8)	64(5)	91(8)	100(7)	-11(6)	-19(5)	-28(5)
C(9)	128(8)	85(8)	85(7)	8(6)	-7(6)	-61(7)
C(10)	129(8)	109(9)	105(8)	-71(7)	72(7)	-78(7)
C(11)	68(4)	62(5)	34(3)	-13(3)	15(3)	-7(4)
C(12)	218(15)	187(15)	99(9)	-78(9)	112(10)	-112(12)
C(13)	221(15)	97(9)	65(6)	-27(6)	20(8)	22(9)
C(14)	166(12)	290(20)	48(6)	-75(9)	-46(6)	118(13)
C(15)	33(3)	45(4)	36(3)	-4(3)	1(2)	-9(3)
C(16)	36(3)	42(4)	56(4)	2(3)	0(3)	-7(3)
C(17)	52(4)	49(5)	60(4)	-3(4)	3(3)	-10(3)
C(18)	49(4)	50(5)	69(5)	-21(4)	1(3)	-14(3)
C(19)	35(3)	62(5)	53(4)	-20(3)	-4(3)	-4(3)
C(20)	34(3)	59(5)	42(3)	-11(3)	-5(2)	-4(3)
C(21)	72(5)	33(5)	115(7)	-4(5)	-12(5)	-2(4)
C(22)	181(14)	55(8)	380(30)	-26(12)	-167(18)	34(9)
C(23)	213(16)	120(12)	189(15)	38(11)	92(14)	105(12)
C(24)	117(10)	77(9)	280(20)	46(11)	71(12)	-7(8)
C(25)	52(4)	95(7)	78(6)	-44(5)	-21(4)	-4(4)
C(26)	92(9)	860(70)	67(8)	100(20)	-29(7)	-40(20)
C(27)	185(16)	121(13)	540(40)	-75(19)	-250(20)	0(12)
C(28)	90(8)	260(20)	193(14)	-131(15)	-88(9)	70(10)
C(29)	30(3)	36(4)	31(3)	-3(2)	-3(2)	-5(2)
C(30)	42(3)	47(4)	36(3)	0(3)	-3(2)	-3(3)
C(31)	56(4)	53(5)	44(4)	12(3)	-14(3)	0(3)
C(32)	36(3)	58(5)	55(4)	4(4)	-9(3)	5(3)
C(33)	29(3)	49(4)	48(4)	-9(3)	-3(2)	-3(3)
C(34)	27(2)	36(4)	41(3)	-4(3)	-4(2)	-8(3)
C(35)	43(4)	112(8)	71(5)	-4(5)	0(3)	35(4)
C(36)	26(2)	40(4)	35(3)	1(3)	4(2)	3(2)
C(37)	47(3)	44(4)	32(3)	5(3)	1(2)	-4(3)

C(38)	61(4)	46(5)	37(3)	13(3)	5(3)	5(3)
C(39)	54(4)	34(4)	58(4)	5(3)	9(3)	-6(3)
C(40)	39(3)	36(4)	50(4)	-5(3)	4(3)	-3(3)
C(41)	23(2)	37(3)	36(3)	1(3)	2(2)	-4(2)
C(42)	80(5)	47(5)	61(5)	-11(4)	0(4)	-22(4)
C(43)	30(3)	46(4)	48(3)	-4(3)	2(3)	6(3)
C(44)	40(3)	54(5)	55(4)	-1(3)	15(3)	4(3)
C(45)	49(4)	60(6)	80(5)	-4(4)	17(4)	7(4)
C(46)	38(4)	70(7)	122(8)	-19(5)	15(4)	6(4)
C(47)	45(4)	61(6)	119(8)	-3(5)	-3(4)	13(4)
C(48)	36(3)	43(4)	99(6)	5(4)	-4(4)	-2(3)
C(49)	60(5)	128(10)	102(8)	31(7)	43(5)	4(6)
C(50)	77(7)	171(13)	100(8)	49(8)	18(6)	-9(7)
C(51)	81(7)	116(11)	168(12)	37(10)	25(7)	-34(7)
C(52)	74(7)	151(13)	235(17)	54(12)	69(9)	1(7)
C(53)	49(5)	56(7)	350(20)	-14(11)	10(9)	16(5)
C(54)	320(30)	131(18)	280(30)	-75(19)	30(20)	55(19)
C(55)	84(7)	39(6)	470(30)	44(12)	-31(14)	0(5)
C(56)	94(8)	78(9)	290(20)	18(11)	-51(11)	23(7)
C(57)	39(3)	36(4)	35(3)	-3(3)	5(2)	-5(3)
C(58)	44(3)	38(4)	32(3)	-1(3)	9(2)	-13(3)
C(59)	55(4)	45(4)	31(3)	-1(3)	-2(3)	-4(3)
C(60)	46(3)	55(5)	39(3)	7(3)	-10(3)	-13(3)
C(61)	34(3)	46(4)	42(3)	3(3)	-5(2)	-6(3)
C(62)	39(3)	45(4)	36(3)	-3(3)	0(2)	-6(3)
C(63)	67(4)	61(5)	28(3)	-8(3)	3(3)	-2(4)
C(64)	119(7)	54(5)	45(4)	6(4)	11(4)	-8(5)
C(65)	129(7)	58(5)	43(4)	-11(4)	11(4)	-16(5)
C(66)	88(6)	133(10)	47(5)	-27(5)	22(4)	6(6)
C(67)	32(3)	78(6)	50(4)	3(4)	-2(3)	-10(3)
C(68)	45(4)	169(11)	91(7)	15(7)	-17(4)	-40(6)
C(69)	55(4)	73(6)	75(5)	-13(5)	22(4)	-27(4)
C(70)	37(3)	82(7)	103(7)	-1(5)	14(4)	8(4)
C(71)	45(3)	31(4)	68(4)	0(3)	-12(3)	-9(3)
C(72)	42(3)	36(4)	77(5)	-1(4)	1(3)	-9(3)
C(73)	58(4)	51(5)	89(6)	-11(4)	5(4)	-4(4)
C(74)	58(4)	74(7)	78(6)	-16(5)	0(4)	-9(4)
C(75)	56(4)	75(7)	66(5)	-2(4)	-1(4)	-16(4)
C(76)	62(4)	40(5)	77(5)	1(4)	-16(4)	-12(4)
C(77)	79(6)	41(5)	134(9)	-11(5)	27(6)	1(4)
C(78)	79(8)	87(11)	640(50)	74(19)	-117(17)	4(7)
C(79)	420(40)	160(20)	370(40)	-150(20)	-210(40)	120(30)
C(80)	142(13)	61(10)	530(50)	27(18)	120(20)	9(9)

C(81)	94(7)	95(8)	76(6)	5(5)	19(5)	-23(6)
C(82)	159(11)	78(9)	106(8)	27(7)	29(8)	-41(8)
C(83)	96(8)	189(16)	146(12)	8(11)	39(8)	-65(9)
C(84)	170(12)	124(11)	86(7)	-11(7)	41(8)	-32(9)
C(85)	37(3)	33(4)	83(5)	2(4)	-5(3)	-4(3)
C(86)	51(4)	44(4)	83(5)	-12(4)	-3(4)	-1(3)
C(87)	41(3)	57(5)	93(6)	-32(5)	-9(4)	6(3)
C(88)	52(4)	56(5)	88(6)	-20(4)	-18(4)	10(4)
C(89)	61(4)	32(4)	75(5)	2(4)	-9(4)	3(3)
C(90)	49(4)	31(4)	84(5)	4(4)	-9(4)	0(3)
C(91)	41(4)	92(8)	138(9)	-55(7)	3(5)	-9(4)
C(92)	54(6)	214(17)	225(16)	-143(14)	23(8)	-38(8)
C(93)	50(5)	126(12)	280(20)	-43(13)	30(9)	-26(6)
C(94)	48(4)	96(8)	161(11)	-48(8)	7(6)	10(5)
C(95)	79(6)	55(6)	84(6)	-3(4)	-7(5)	-7(4)
C(96)	130(13)	610(60)	118(13)	-100(20)	46(11)	-70(20)
C(97)	410(30)	220(20)	240(20)	-150(19)	220(20)	-200(20)
C(98)	900(80)	240(30)	146(17)	104(18)	260(30)	320(40)
C(99)	45(3)	39(4)	74(5)	2(4)	-5(3)	-4(3)
C(100)	54(4)	50(5)	105(6)	15(5)	-13(4)	-24(4)
C(101)	63(5)	43(5)	139(8)	36(5)	-31(5)	-18(4)
C(102)	68(5)	44(5)	109(7)	31(5)	-13(5)	-11(4)
C(103)	42(3)	52(5)	70(5)	9(4)	-1(3)	-6(3)
C(104)	37(3)	37(4)	68(4)	2(3)	8(3)	-5(3)
C(105)	65(5)	110(9)	79(6)	24(6)	-16(4)	-13(5)
O(1)	32(2)	76(4)	56(3)	0(2)	5(2)	7(2)
O(2)	69(3)	31(3)	60(3)	-1(2)	2(3)	-15(2)
O(3)	54(3)	67(4)	75(4)	18(3)	-10(2)	-5(3)
P(1)	28(1)	42(1)	29(1)	-3(1)	0(1)	-5(1)
P(2)	32(1)	37(1)	30(1)	1(1)	2(1)	-6(1)
P(3)	38(1)	30(1)	74(1)	3(1)	-6(1)	-8(1)
Cl(1)	53(1)	73(1)	38(1)	4(1)	-13(1)	-4(1)
Cl(2)	154(2)	78(2)	42(1)	14(1)	13(1)	-32(2)
Cl(3)	59(1)	50(1)	231(3)	54(2)	26(2)	-4(1)
Au(1)	31(1)	42(1)	30(1)	-2(1)	-1(1)	-3(1)
Au(2)	59(1)	45(1)	31(1)	2(1)	2(1)	-14(1)
Au(3)	40(1)	32(1)	102(1)	11(1)	0(1)	-7(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3)
for toste09.

x	y	z	U(eq)	
H(2)	7493	7071	2127	46
H(4)	6566	7097	4768	55
H(6)	7807	7816	4221	45
H(8A)	5982	6976	2283	127
H(8B)	5824	6922	3470	127
H(8C)	5752	6611	2677	127
H(9A)	6400	6229	3740	148
H(9B)	6473	6528	4574	148
H(9C)	7045	6357	4063	148
H(10A)	6665	6324	1955	172
H(10B)	7301	6471	2265	172
H(10C)	6875	6691	1538	172
H(12A)	6615	7223	6358	252
H(12B)	6191	7517	5918	252
H(12C)	6524	7571	6991	252
H(13A)	6903	8122	6304	191
H(13B)	6558	8043	5257	191
H(13C)	7249	8130	5232	191
H(14A)	7664	7331	6501	251
H(14B)	7579	7701	7017	251
H(14C)	7963	7662	5991	251
H(16)	7874	8342	2061	54
H(18)	8923	8834	4089	67
H(20)	9158	7832	3570	54
H(22A)	7246	9154	2177	310
H(22B)	7266	8746	2329	310
H(22C)	7630	8922	1414	310
H(23A)	8106	9200	4275	261
H(23B)	7522	8972	4148	261
H(23C)	7552	9347	3647	261
H(24A)	8614	9167	1747	238
H(24B)	8763	9299	2882	238
H(24C)	8227	9466	2254	238
H(26A)	9260	8030	5780	509
H(26B)	9056	8423	5840	509
H(26C)	9698	8314	6241	509

H(27A)	9646	8828	5089	425
H(27B)	10064	8724	4147	425
H(27C)	10258	8634	5299	425
H(28A)	9985	7856	4592	270
H(28B)	10463	8156	4724	270
H(28C)	10126	8108	3652	270
H(30)	8687	7222	3782	50
H(31)	9551	6906	4061	61
H(32)	10265	6857	2795	60
H(35A)	10969	7013	1579	113
H(35B)	10939	6896	401	113
H(35C)	10609	6675	1265	113
H(37)	8715	7295	-1863	49
H(38)	8911	7872	-2082	58
H(39)	9316	8195	-754	59
H(42A)	9944	8381	627	94
H(42B)	9705	8418	1779	94
H(42C)	9254	8439	833	94
H(44)	9870	7084	-1451	60
H(46)	10988	6302	-1877	92
H(48)	9508	6168	-231	71
H(50A)	10822	7301	-3577	174
H(50B)	10228	7257	-2922	174
H(50C)	10430	6961	-3698	174
H(51A)	11342	7186	-1083	182
H(51B)	10742	7385	-1349	182
H(51C)	11321	7448	-2029	182
H(52A)	11410	6627	-3119	230
H(52B)	11676	6747	-2036	230
H(52C)	11714	6996	-3011	230
H(54A)	10463	5396	-1960	369
H(54B)	10933	5690	-2221	369
H(54C)	10246	5753	-2436	369
H(55A)	10067	5345	-512	295
H(55B)	9608	5653	-675	295
H(55C)	9987	5631	361	295
H(56A)	10989	5899	376	232
H(56B)	11341	5893	-691	232
H(56C)	11140	5540	-163	232
H(58)	8965	6588	-2423	46
H(60)	7263	6463	-3241	56
H(62)	7656	6750	-351	48
H(64A)	7732	6754	-4760	109

H(64B)	8269	6660	-5510	109
H(64C)	8367	6924	-4581	109
H(65A)	7578	6134	-4489	115
H(65B)	8096	5900	-4032	115
H(65C)	8137	6039	-5187	115
H(66A)	9112	6289	-4887	134
H(66B)	9123	6167	-3712	134
H(66C)	9225	6563	-3992	134
H(68A)	6309	6314	-2595	152
H(68B)	6434	6702	-2931	152
H(68C)	5892	6616	-2186	152
H(69A)	6690	6084	-1087	101
H(69B)	6204	6297	-463	101
H(69C)	6885	6317	-133	101
H(70A)	6115	6934	-719	111
H(70B)	6610	7131	-1371	111
H(70C)	6773	6967	-280	111
H(72)	3564	5742	10712	62
H(74)	2268	5637	12756	84
H(76)	3234	4817	11952	72
H(78A)	2137	6202	10666	401
H(78B)	2072	6440	11661	401
H(78C)	1915	6040	11729	401
H(79A)	2884	6544	12682	473
H(79B)	3268	6215	12991	473
H(79C)	2573	6221	13216	473
H(80A)	3193	6283	10410	366
H(80B)	3612	6255	11397	366
H(80C)	3172	6574	11277	366
H(82A)	2233	4446	13629	171
H(82B)	2899	4581	13545	171
H(82C)	2539	4486	12526	171
H(83A)	1510	5184	12694	215
H(83B)	1421	4800	13104	215
H(83C)	1695	4866	11987	215
H(84A)	2091	5348	14226	190
H(84B)	2692	5149	14486	190
H(84C)	2069	4973	14728	190
H(86)	2800	4821	10159	71
H(88)	2700	4482	7243	79
H(90)	4236	4858	8316	65
H(92A)	1375	4246	8379	246
H(92B)	2003	4190	7838	246

H(92C)	1608	4517	7550	246
H(93A)	1569	4199	9944	230
H(93B)	2089	4405	10504	230
H(93C)	2243	4093	9747	230
H(94A)	1813	5057	8876	153
H(94B)	1808	4895	10007	153
H(94C)	1271	4822	9238	153
H(96A)	4631	4462	6629	429
H(96B)	4546	4843	7070	429
H(96C)	4548	4778	5855	429
H(97A)	3959	4221	5722	435
H(97B)	3343	4401	5446	435
H(97C)	3405	4179	6476	435
H(98A)	3701	4852	5208	643
H(98B)	3799	5113	6141	643
H(98C)	3172	4930	5990	643
H(100)	3832	4348	10708	84
H(101)	4263	3935	11703	98
H(102)	5022	4074	12839	88
H(10D)	5574	4366	14163	127
H(10E)	6204	4528	13881	127
H(10F)	5930	4229	13183	127

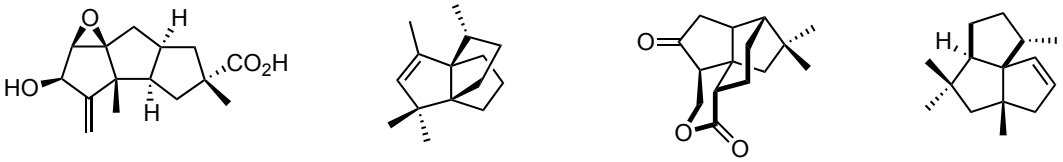
Chapter 3.
The Total Synthesis of Ventricosene

Triquinane natural products, comprised of multiple fused cyclopentane rings, have served as a proving ground for novel cyclopentannulation reactions. In chapter 3, a tandem enyne cycloisomerization / semipinacol ring expansion, catalyzed by cationic gold(I), serves as the key step in the total synthesis of ventricos-7(13)-ene. By positioning a cyclopropanol linker within a 1,6-enyne, the cationic species arising upon gold(I)-initiated cycloisomerization underwent a σ-bond migration, providing bicyclo[3.2.0]heptanone products. Much of the preliminary work was conducted by Steve Staben, including the development of the tandem gold(I)-catalyzed transformation, optimization of the cyclopropanation step as well as early studies of the second ring expansion. Portions of this work have been published (Sethofer, S. G.; Staben, S. T.; Hung O. Y.; Toste, F. D. Org Lett*, **2008**, 10, 4315-4318)*.

Introduction

Ever since the structural elucidation of hirsutic acid in 1965[1], the intricate structures of polyquinane natural products have inspired and challenged organic chemists.[2] Figure 3.1 depicts several important triquinane natural products. Modhephene, isolated from the goldenrod plant *Isocomoa wrightii* in 1978[3] and first synthesized in 1980 by Dreiding,[4] was the first natural product discovered containing the [3.3.3]-propellane skeleton. The fungus-derived diquinane (-)-quadrone and its congeners, which feature an uncommon tetracyclic structure and exhibit significant antitumor activity[5] have been the focus of numerous synthetic efforts.[6]

Figure 3.1. Representative Triquinane Natural Products.



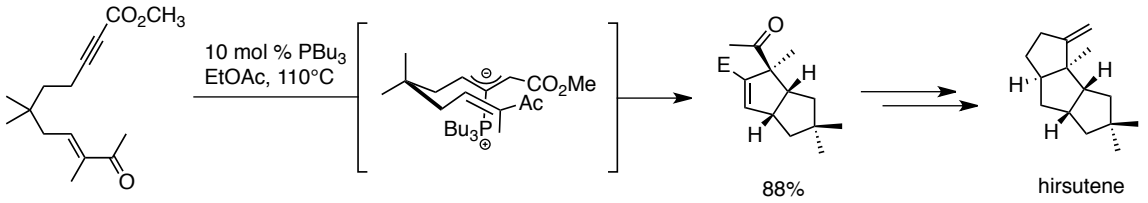
Hirsutic Acid | Modhephene | Quadrone | Silphinene

Synthetic approaches to this group of polycyclic terpenes have introduced a number of novel cyclopentannulation protocols[7] including radical-mediated cyclizations,[8] cycloadditions[9] and electrophilic transannulation processes.[10]

In the synthesis of hirsutene by Krische *et al*. in 2005,[11] for example, nucleophilic catalysis by tributyl phosphine generated a 1,3-dipole which underwent a diastereoselective intramolecular cycloaddition, forming a fused diquinane system and a quaternary carbon center in the process (Scheme 3.1).

The squarate ester cascade, developed in the Paquette labs, has been employed in the synthesis of a number[12] of natural products, including the highly oxygenated triquinane coriolin[13] (Scheme 3.2). The sequential addition of vinyllithium reagents initiated ring opening of the cyclobutene followed by a complex anionic skeletal rearrangement, provided the linear triquinane ring system of coriolin in 24% yield.

Scheme 3.1. Key [3+2] Dipolar Cycloaddition Reaction in the Synthesis of Hirsutene.



Angular triquinanes such as silphinene have attracted much attention as synthetic targets due to their distinct architectural features,[14] the most notable of which is the central spirocyclic quaternary carbon. Until recently, all angular triquinane natural products belonged to one of four structural types based on the arrangement of the four methyl groups around the periphery of the octahydro-cyclopenta[c]pentalene system (Figure 3.2). The isolation and characterization of ventricos-7(13)-ene (**3.1**, Scheme 3.3) from the liverwort *Lophozia ventricosa* in 2005 thus represented the first entry into a new family of angular triquinanes.[15]

Recently, a gold(I)-catalyzed process for the construction of four and five membered rings by ring expansion was developed by the Toste lab (Figure 3.3a);[16] we hypothesized that this transformation could be extended to a tandem process which could be applied to the construction of the ventricosene system.

Figure 3.3 illustrates the conceptual development of the tandem cycloisomerization / pinacol ring expansion. Initial coordination of cationic gold(I) to the alkyne generates an electron-deficient center and initiates a semipinacol ring expansion (path a) or attack of a pendant alkene upon the activated alkyne complex (path b). In the latter case, intermolecular cation trapping leads to an exo-methylene cyclohexane.

Scheme 3.2. Application of the Squarate Ester Cascade to the Synthesis of Coriolin.

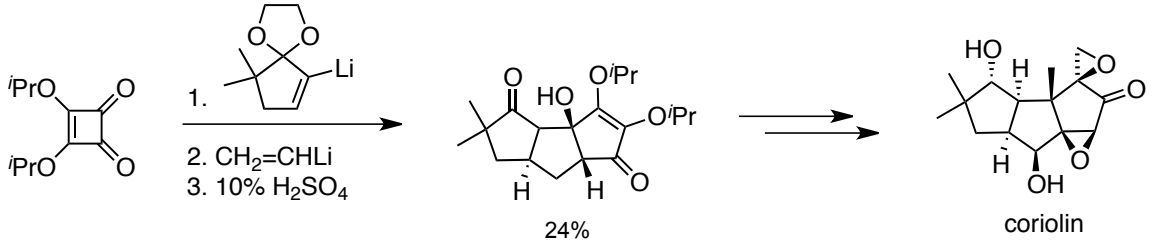
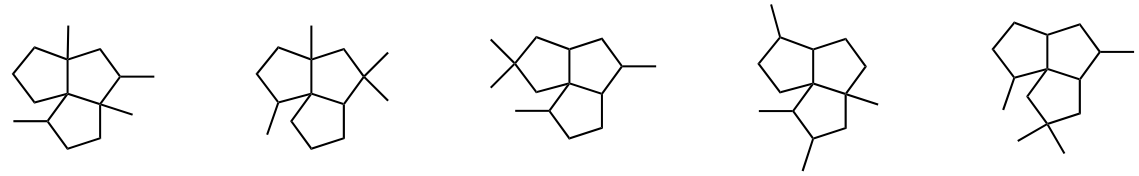


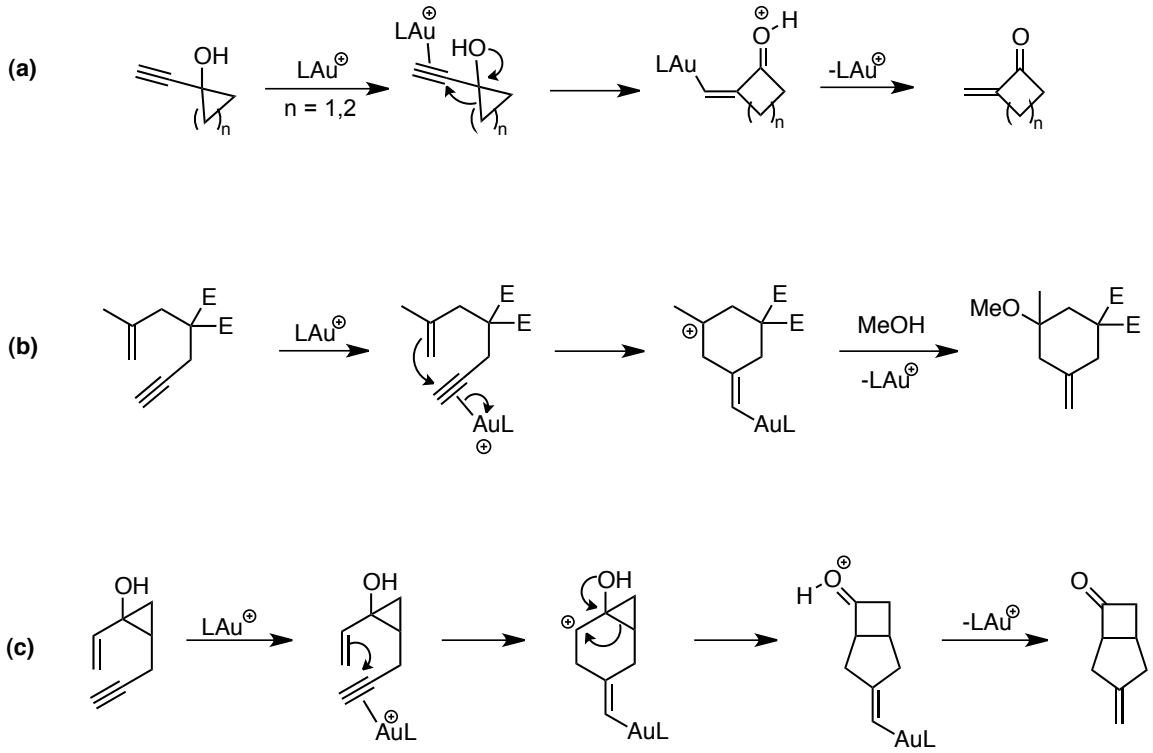
Figure 3.2. Skeletal Classes of the Angular Triquinane Natural Products.

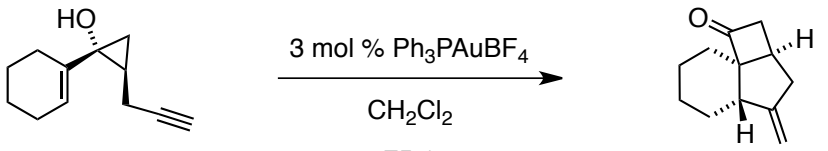


We anticipated that the cationic species arising in path b could be intercepted by a nucleophilic σ-bond in a process analogous to the ring expansion shown in path a. Thus, by coupling these two processes, the sequential cycloisomerization / semipinacol ring expansion was anticipated to provide access to fused bicyclo[3.2.0]heptanone products (path c).

An initial evaluation of the substrate scope[17] established that the pinacol-terminated cycloisomerization reaction proceeded with high diastereoselectivity for cyclic alkenes bearing a *cis*-dialkyl cyclopropanol (eq 1). This reaction could be used to generate the tricyclic core of ventricosene **3.1** by replacing the cyclohexene fragment with an appropriately substituted cyclopentene.

Figure 3.3. Tandem Gold(I)-Catalyzed Cycloisomerization / Ring Expansion.



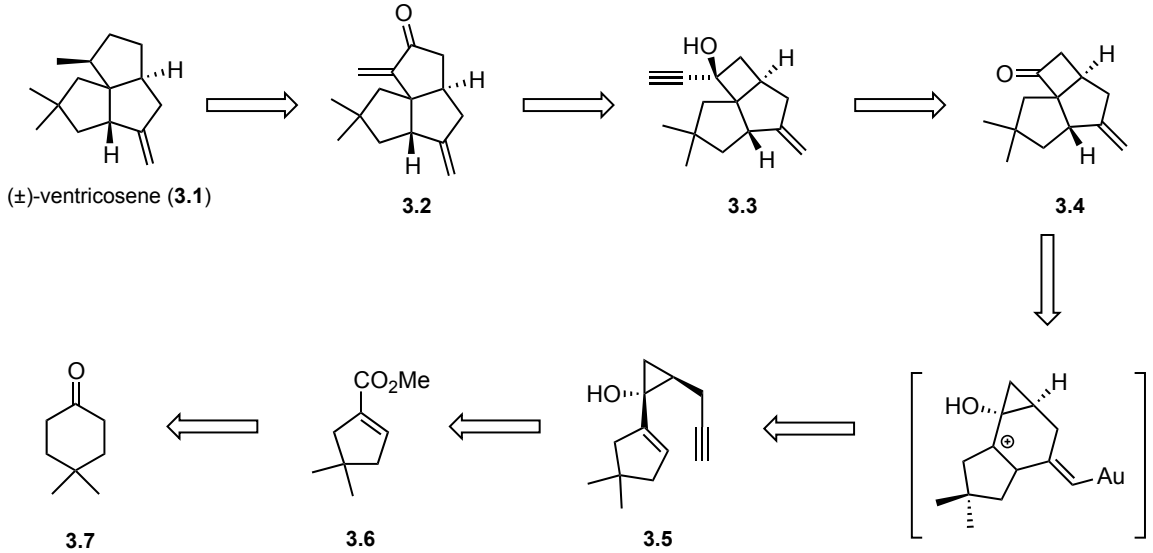


(3.1)

Results

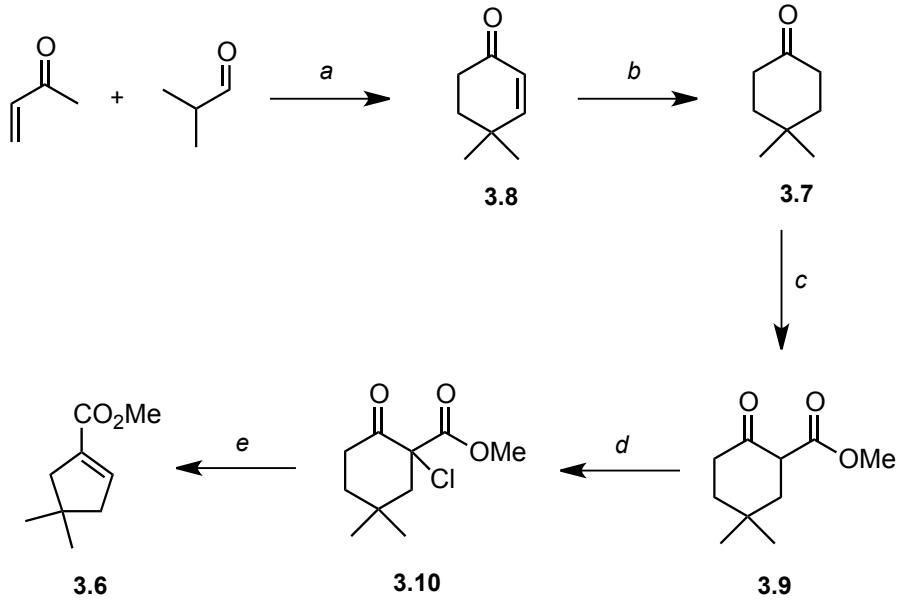
The retrosynthetic analysis for ventricosene is presented in Scheme 3.3. Ventricosene **3.1** could be obtained from exo-methylene ketone **3.2** by means of a diastereoselective conjugate reduction and subsequent deoxygenation. A diastereoselective 1,4-reduction of exo-methylene enone **3.2** followed by deoxygenation would yield **3.1**. We envisioned that **3.2** would arise from application of our gold(I)-catalyzed ring expansion to cyclobutanol **3.3**, which could, in turn be obtained by a few routine manipulations from ketone **3.4**. This tricycle is the expected product of the key cycloisomerization/semipinacol reaction. *Cis*-dialkyl cyclopropanol **3.5** was identified as the requisite substrate for this reaction.

Scheme 3.3. Retrosynthetic Analysis for Ventricosene.



The Kulinkovich cyclopropanation of esters,[18] which is known to exhibit an intrinsic *cis*-1,2-dialkyl selectivity,[19] was seen as the ideal means to prepare enyne **3.5**. This disconnection leads to enoate **3.6**, which is available from the symmetric ketone **3.7** by a ring-contraction sequence. In this manner, molecular complexity could be rapidly built up through a series of electrophilic skeletal rearrangements while at the same time taking advantage of the high diastereoselectivities of the Kulinkovich cyclopropanation and subsequent semipinacol-terminated enyne cycloisomerization.

Scheme 3.4. Synthesis of Methyl Cyclopentenoate **3.6**.[a]



[a] Reagents and conditions: (a) cat H_2SO_4, C_6H_6, 80 °C, 4h, 65%. (b) cat Pd / C, 45 psi H_2, EtOAc, 90%. (c) cat. KH, NaH (2.2 eq), $(MeO)_2CO$ (5.2 eq), THF, 65 °C, 3h, 82%. (d) cat. PhSeCl, NCS (1.1 eq), CH_3CN, rt, 1 h, 90%. (e) Na_2CO_3 (1.2 eq), *m-x*ylene, 150°C, 48 h, 76%.

In the synthesis of cyclopropanation substrate **3.6**, Büchi's method for ring contraction by dehydrochlorination-decarbonylation[20] was utilized to prepare a cyclopentenoate ester from the symmetric ketone **3.7** (Scheme 3.4). The synthesis began with an acid-catalyzed Robinson annulation of methyl vinyl ketone and isobutyraldehyde to give enone **3.8** in moderate yield on a mole scale.[21] Catalytic hydrogenation of **3.8** over palladium on charcoal at 45 psi H_2 gave an excellent yield of ketone **3.7**. This ketone was enolized with sodium

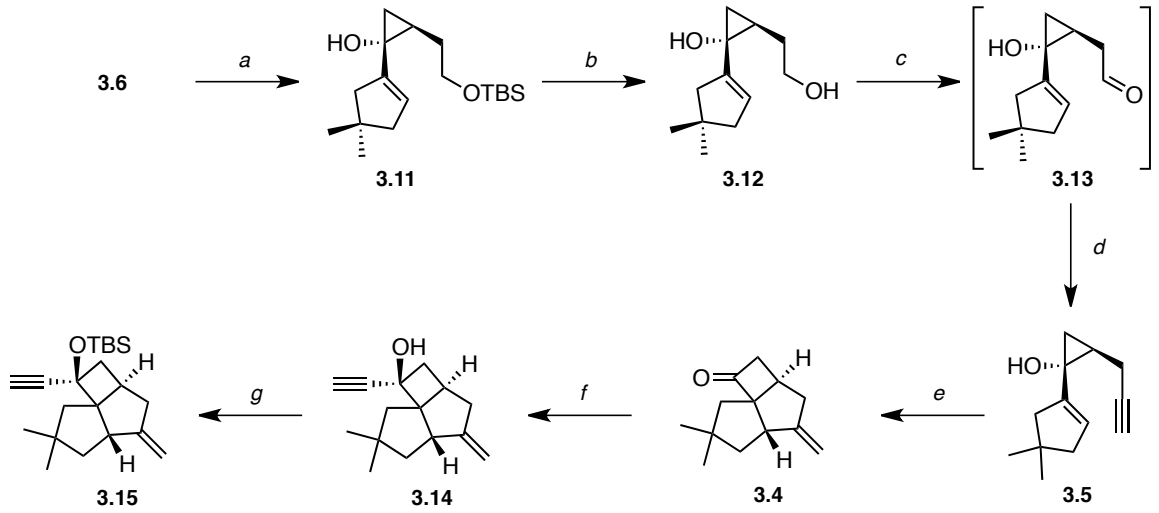
hydride and treated with dimethyl carbonate in the presence of catalytic potassium hydride, affording β-keto ester **3.9** in good yield. Introduction of the α-chloro group was accomplished with *N*-chlorosuccinimide and catalytic phenylselenyl chloride using the method of Wang[22] to give chloride **3.10** in good yield. Ring-contraction substrate **3.10** was converted to enoate **3.6** over 48 h in 76% yield in the presence of sodium carbonate at elevated temperatures under anhydrous conditions.

With the cyclopropanation substrate in had, we began construction of the fused tricyclic ring system of ventricosene (Scheme 3.5). In order to avoid known difficulties with Kulinkovich cyclopropanation of α,β-unsaturated esters, a modified version of this reaction was employed using a less oxophillic zirconium complex as mediator, rather than one of the traditional titanium complexes.[23] Treatment of zirconocene dichloride with two equivalents of a Grignard reagent generated a stoichiometric zirconacyclopropane reagent used to cyclopropanate unsaturated ester **3.6.** Thus, cyclopropanol **3.11** was prepared as a single diastereomer in 52% yield. Desilylation of this material was accomplished with TBAF in THF at room temperature to furnish diol **3.12** in good yield.

The conversion of primary alcohol **3.12** to alkyne **3.5** involved the intermediacy of aldehyde **3.13**, which was prone to undergo an intramolecular attack of the vinylcyclopropanol on the carbonyl functional group, particularly in the presence of acid or silica gel.[24] Swern oxidation[25] was chosen as the means to prepare **13.3** due to its nonacidic conditions. In spite of this, enyne **3.5** was obtained in only 36% yield from diol **3.12** after oxidation and immediate treatment of the crude aldehyde with the Bestmann-Ohira reagent and potassium carbonate in methanol.[26] Competitive formation of the methylthiomethyl ether from the tertiary alcohol during the Swern oxidation is another likely factor in the low yield of this sequence.[27]

With the vinylcyclopropanol and alkyne fragments in place, the stage was set for the key cycloisomerization reaction. Treatment of **3.5** with a pregenerated solution of 3 mol % Ph_3PAuBF_4 in CH_2Cl_2 at room temperature generated the cyclobutanone **3.4** in 81% yield as a single diastereomer. Addition of lithium trimethylsilylacetylide to ketone **3.4** followed by deprotection with methanolic potassium carbonate gave tertiary alcohol **3.14**. This material could be converted to silyl ether **3.15** with TBSOTf and 2,6-lutidene.

Scheme 3.5. Synthesis of cyclobutanol ring expansion substrates **3.14** and **3.15**.[a]

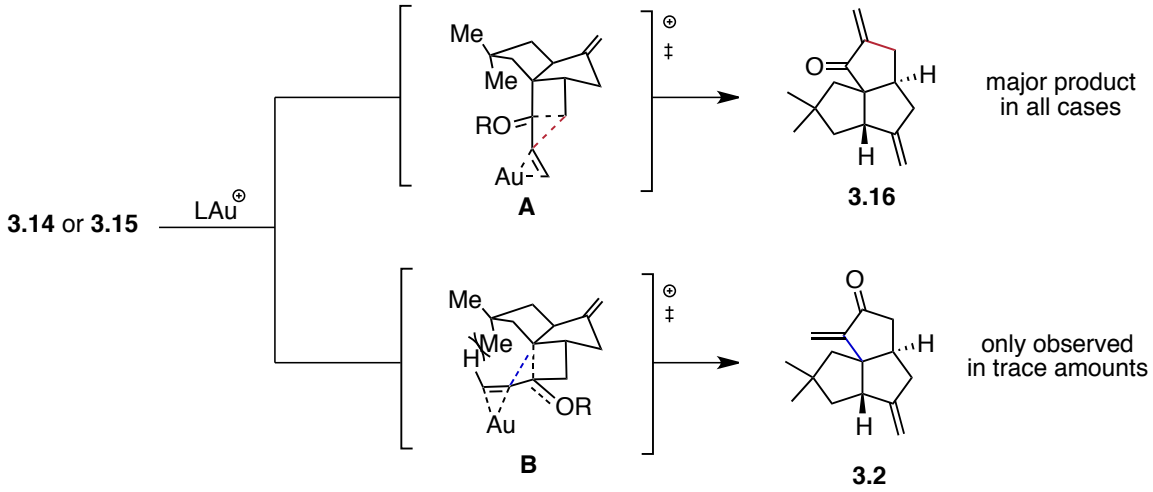


[a] Reagents and conditions: (a) $TBSO(CH_2)_4MgCl$ (4 eq), Cp_2ZrCl_2 (2 eq), 2:3 THF/PhMe, 0 °C, 2 h, 52%. (b) TBAF (1.2 eq), THF, rt, 3 h, 80%. (c) DMSO (1.8 eq), $(COCl)_2$ (1.2 eq), TEA (5.5 eq), -78 °C, 1 h. (d) Bestmann's reagent (1.5 eq), K_2CO_3 (2.4 eq), MeOH, 0 °C, 18 h, 36%. (e) Ph_3PAuBF_4 (3 mol %), CH_2Cl_2, rt, 2 h, 81%. (f) LiCCTMS (4 eq), THF, -78 °C then excess K_2CO_3 in MeOH, rt, 2h. (g) TBSOTf (1.2 eq), 2,6-lutidene (1.2 eq), CH_2Cl_2, rt, 92%.

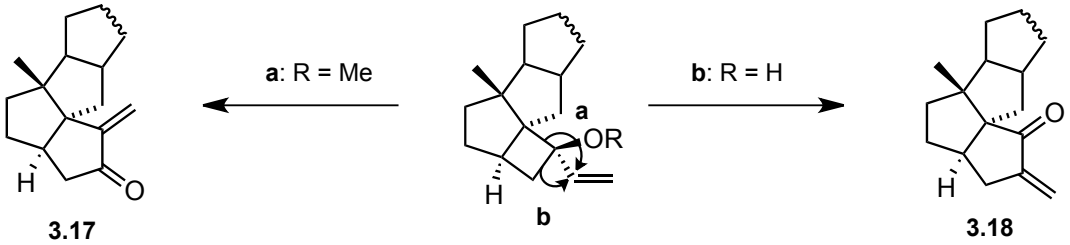
At this point, completion the angular triquinane ring system of ventricosene only required a ring expansion of the cyclobutane ring in a regiocontrolled manner. However, preliminary studies[17] of the alkynyl cyclobutanol ring expansion of related systems indicated σ-bond migration proceeded with regiochemistry opposite to that required for the synthesis of **3.1**. Indeed, in screening a variety of gold(I) catalysts, we found that the ring expansion of **3.14** and **3.15** yielded enone **3.16**[28] as the major product, with only traces of the desired product **3.2**.

A rationalization for the observed regioselectivity is presented in Scheme 3.6. Initial coordination of gold(I) to the alkyne group generates electron deficiency at the acetylinic carbons, typically facilitating migration of the more electron-rich carbon of the cyclobutane ring, as in transition state **B** (Scheme 3.6). The required orientation for this migration produces a steric interaction with the skeleton of the molecule, which is not present in alternative transition state **A,** which corresponds to migration of the methylene group. Thus, this typically electronically-controlled reaction proceeds along the more sterically favorable pathway in the case of **3.14** and **3.15**.

Scheme 3.6. Rationale for observed regiochemistry in the ring expansion of **14** and **15**.[17]

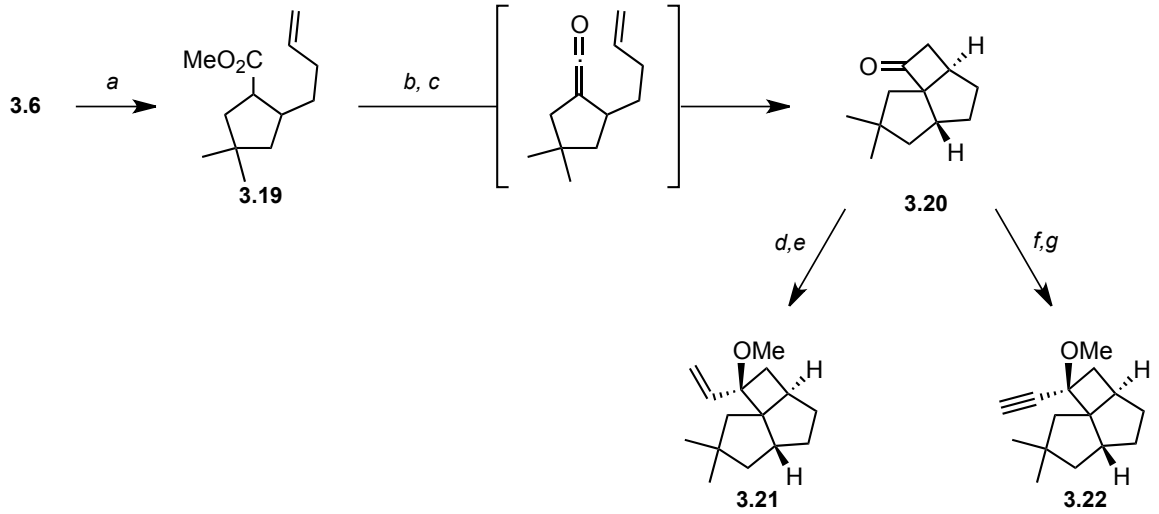


Scheme 3.7. Substrate Control in the Ring Expansion of 1-Vinylcyclobutanols.



Kočovský et al. have studied the related ring expansion of 1-vinylcyclobutanols in the synthesis of angular triquinanes.[29] Scheme 3.7 summarizes their results using 5 mol % of $(CH_3CN)_2PdCl_2$ with benzoquinone as a stoichiometric oxidant. In the case of the vinyl alcohol, ring expansion proceeded with migration of the less substituted carbon (path a, Scheme 3.7), providing enone **3.18** along with a minor amount of the isomeric alkene **3.17**. Interestingly, the migratory tendency of this system could be changed by alkylation of the hydroxyl group. Thus, the corresponding methyl ether underwent ring expansion via pathway *b*, giving a 75% yield of enone **3.17** as the sole product.[30] We decided to evaluate this ring expansion protocol using a model system related to ventricosene (**3.1**).

Scheme 3.8. Synthesis of Model System for Cyclobutane Ring Expansion.[a]

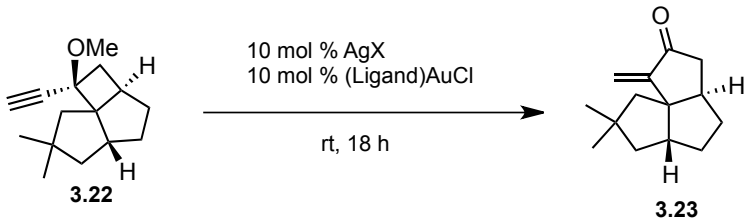


[a] Reagents and conditions: (a) CH_2=CH(CH_2)$_3$MgBr (5 eq), CuI (2.5 eq), HMPA (2.5 eq), TMSCl (5 eq), THF, -78 °C to rt. (b) KOH, 2:1 MeOH / H_2O, 70 °C, 3h. (c) cat DMAP, DIEA (5 eq), C_6H_6, 100 °C, 18 h (45%). (d) CH_2=CHMgBr (3 eq), $CeCl_3$ (3 eq), THF, -78 °C to rt. (e) NaH (1.1 eq), MeI (4 eq), THF, 45 °C, 4 h (49%). (f) *n*-BuLi (4 eq), TMSCCH (4 eq), TMEDA (4 eq), THF, -78 °C to rt. (g) NaH (1.1 eq), MeI (4 eq), THF, 45 °C, 4 h (61%).

A [2 + 2] ketene / olefin cycloaddition can be used to rapidly construct the model tricyclic ring system (Scheme 3.8).[31] Conjugate addition of but-3-enylmagnesium bromide to **3.6** mediated by CuI gave olefin **3.19**. Saponification followed by treatment with Hünig's base and DMAP at elevated temperatures generated a transient ketene, which underwent cycloaddition with the pendant olefin providing **3.20** in 45% yield from **3.6**. Vinyl ether **3.21** was prepared by cerium-mediated addition of vinylmagnesium bromide[32] to **20** followed by methylation of the resulting alcohol. Alkyne **22** was prepared in a similar fashion by addition of lithium trimethylsilylacetylide, basic deprotection and methylation.

We examined the gold(I)-catalyzed ring expansion of propargyl ether **3.22**, hoping to observe the same substrate-controlled regioselectivity reported by Kočovský (Table 1). Treatment of **3.22** with 10 mol % of $Ph_3PAuSbF_6$ gave **3.23** in 11% yield with none of the regioisomer present. Unfortunately, the use of several other cations (entries 1 - 3) or gold(I) complexes (entries 8 and 9) did not improve the yield, and decomposition of **3.23** occurred as evidenced by disappearance of the ^{1}H NMR signal of the methoxy group.

Table 3.1. Gold(I) Catalyzed Ring Expansion of Ether **3.22**.



3.22 **3.23**

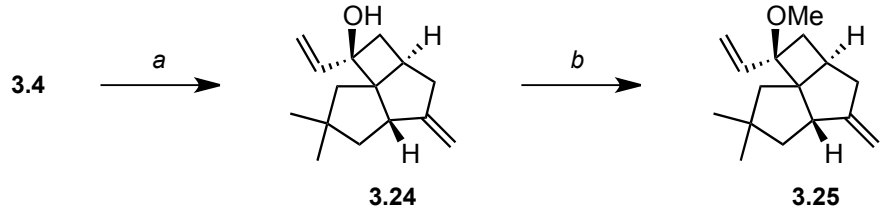
Entry	Ligand	X	Solvent	Conversion (%)[a]	Yield (%)[a]
1	Ph_3P	SbF_6	CD_2Cl_2	45	11
2	Ph_3P	BF_4	CD_2Cl_2	36[b]	6
3	Ph_3P	OTf	CD_2Cl_2	24[c]	0
4	Ph_3P	SbF_6	CD_3NO_2	100[c]	0
5	Ph_3P	SbF_6	CD_3CN	100[c]	0
6	Ph_3P	SbF_6	THF-d8	24	0
7	Ph_3P	SbF_6	C_6D_6	13	0
8	$(p\text{-}(CF_3)C_6H_4)_3P$	SbF_6	CD_2Cl_2	68	6
9	IMes	SbF_6	CD_2Cl_2	8	0

[a] Determined by ^{1}H NMR against an internal standard (pentamethylbenzene). [b] The regioisomeric enone was present in 8% yield. [c] A complex mixture containing no vinylic signals is observed by ^{1}H NMR after 3 h.

Varying the solvent resulted in either complete decomposition within 3 hours in more polar solvents (entries 4 and 5) or attenuated decomposition of **3.22** (entries 6 and 7). Of note is the presence of vinylic signals attributable to the regioisomeric enone when the counterion was changed to tetrafluoroborate (entry 2). In spite of the low yield of both enones, this apparent counterion-controlled regioselectivity is interesting and could warrant further study using simpler cyclobutyl methyl ethers.

Gratifyingly, treatment of **3.21** with 5 mol % of $(CH_3CN)_2PdCl_2$ and 2 equivalents of *p*-benzoquinone in THF at room temperature provided enone **3.23** in 54% yield.[33] We decided to proceed with the synthesis of ventricosene **3.1** using palladium catalysis to carry out the final ring-expansion step.

Scheme 3.9. Synthesis of Ring Expansion Substrate **3.25**.[a]



[a] Reagents and conditions: (a) CH_2=CHMgBr (3 eq), $CeCl_3$ (3 eq), THF, -78 °C to rt, 63%; (b) NaH (1.1 eq), MeI (4 eq), THF, 45 °C, 4 h, 50%

To that end, cyclobutanone **3.4** was converted to **3.25** by the same sequence used to prepare **3.21** (Scheme 3.9). Application of the palladium(II)-catalyzed ring-expansion protocol to **3.25** resulted in an exceedingly slow reaction relative to that of model **3.21**. After 18 hours, analysis of the crude ^{1}H NMR revealed **3.25** had undergone only 30% conversion. The only new set of vinylic signals present in the spectrum, however, corresponded to ring expansion with the desired regioselectivity. Changing the source of palladium to $Pd(OAc)_2$ or $Pd(PPh)_3$ resulted in no reaction after 36 hours.

It is possible that the change in conformation induced by the introduction of the exo-methylene group negatively impacts the facility of ring-expansion, or that a palladium species in the catalytic cycle becomes bound to the exo-methylene group. In light of the considerable formation bulk palladium metal observed, we hypothesized that slow oxidation was leading to removal of palladium from the catalytic cycle (Figure 3.4).

Replacement of 1,4-benzoquinone with DDQ, a more powerful oxidant, led to a significantly improved yield, providing enone **3.2** in 42% yield after 18 hours at room temperature (Figure 3.5). By refluxing the reaction mixture in THF for 8 hours, a 70% yield of enone **3.2** was isolated using DDQ as oxidant. With the triquinane ring system finally established, we turned our attention to manipulation of the *exo*-enone functionality.

Figure 3.4. Proposed Catalytic Cycle for Ring Expansion of **3.25**.

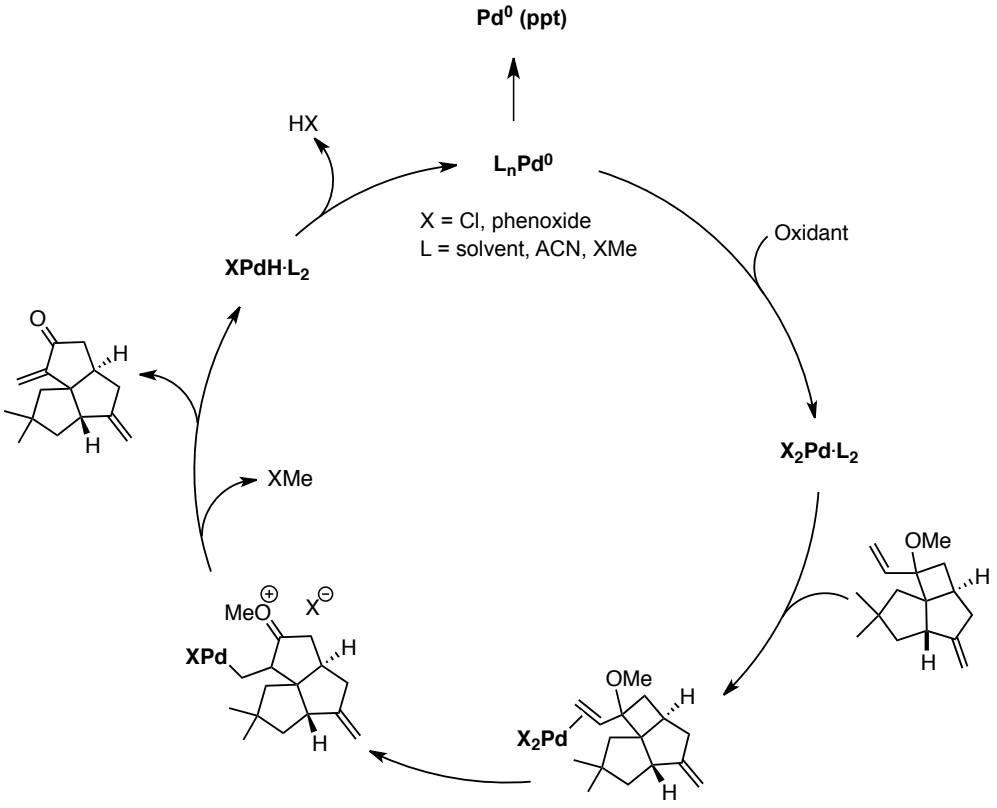
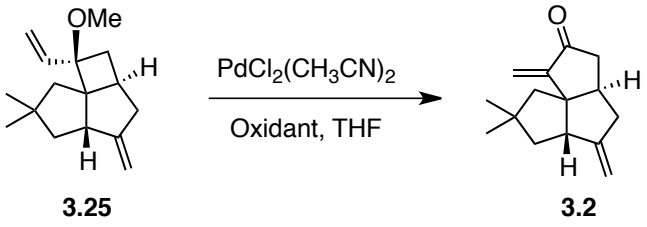
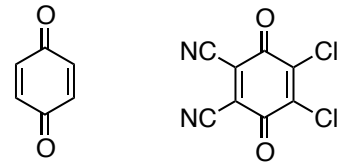


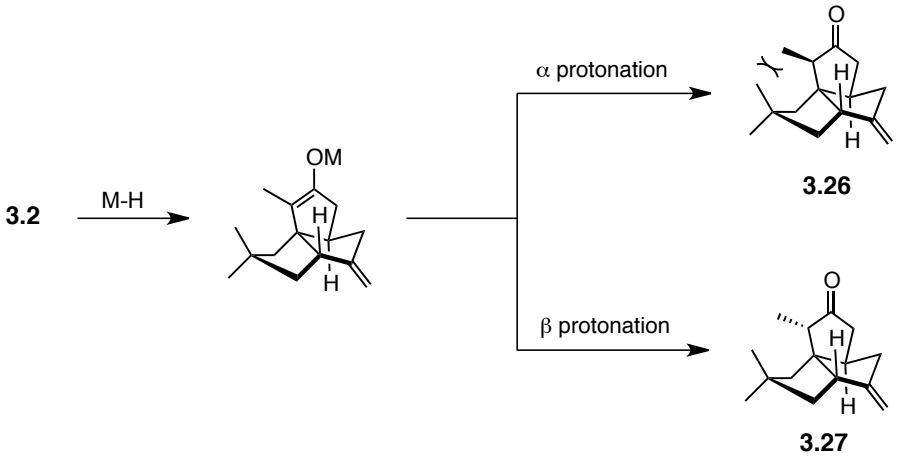
Figure 3.5. Optimization of Conditions for Pd-Catalyzed Ring Expansion of **3.25**.



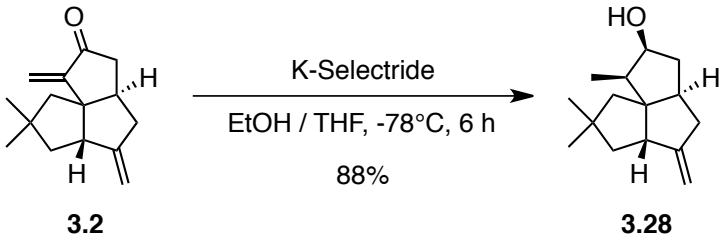


	Benzoquinone	**DDQ**
Yield, 23°C:	16%,18 h	42%, 6 h
Yield, 70°C:	22%,18 h	70%, 8 h

Scheme 3.10. Diastereoselective Protonation of Enolate Derived from **3.2**.

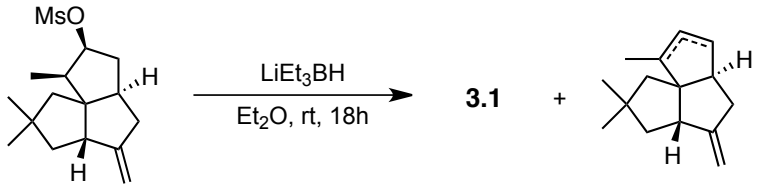


Our goal was to effect the regioselective 1,4 delivery of hydride to the enone, giving a metal enolate which would then undergo diastereoselective protonation from the less hindered alpha face to give kinetic product **3.26**, having the stereochemistry desired for ventricosene **1** (scheme 3.10). Considering the potential of ketone **2.26** to undergo epimerization to **3.27** due to steric interactions between the secondary methyl group and the skeleton of the molecule, we hoped to achieve a sequential twofold reduction under kinetically controlled conditions to the provide the more stable hydroxy compound.



(3.2)

To this end, enone **3.2** was smoothly reduced to secondary alcohol **3.28** in 88% yield using K-Selectride in a 1:1 mixture of ethanol and THF at low temperature (eq 3.2).[34] With hydroxyventricosene **3.28** in hand, we considered two approaches to removal of the hydroxyl group: displacement of a pseudohalide derivative by nucleophilic hydride and the radical deoxygenation of the corresponding xanthate ester by the Barton-McCombie reaction.

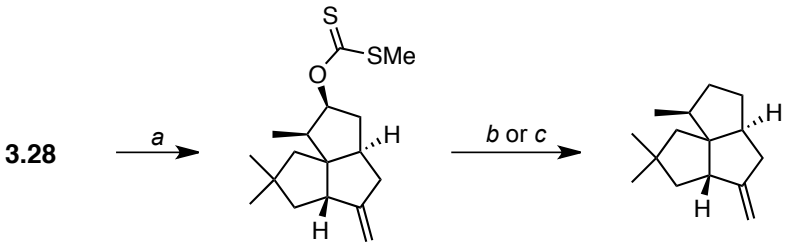


3.29 1 : 1 (3.3)

Difficulty in the purification and isolation of the natural product was anticipated, on account of the lipophilic and relatively volatile nature of **3.1**. Due to the use of stoichiometric organotin reagents in the radical process, we began by examining the polar reduction of mesylate **3.29**. Treatment of **3.29** with $LiEt_3BH$ in ether provided ventricosene **3.1** as a 1:1 mixture with two isomeric elimination products (eq. 3.3). Similar results were obtained with $LiAlH_4$ and $NaAlH_2(OC_2H_4OCH_3)_2$ (Red-Al). The reaction mixture components proved frustratingly inseparable using either silica gel chromatography or preparatory HPLC.

Turning our attention to the radical-mediated deoxygenation, alcohol **3.28** was converted to xanthate ester **3.30** as outlined in Scheme 3.11. In the final step, the use of tris(trimethylsilyl)silane[35] (TTMSS) as hydride source proved critical: the silane byproducts could be removed by treatment of the reaction mixture with TBAF at 0°C, whereas we were unable to adequately purify the natural product when using the conventional tributyltin hydride. Thus, **3.1** was formed in 54% yield[36] by ^{1}H NMR upon heating xanthate **3.30** with TTMSS and catalytic AIBN in benzene to 80°C.

Scheme 3.11. Radical-Mediated Deoxygenation to Ventricosene **3.1**.[a]



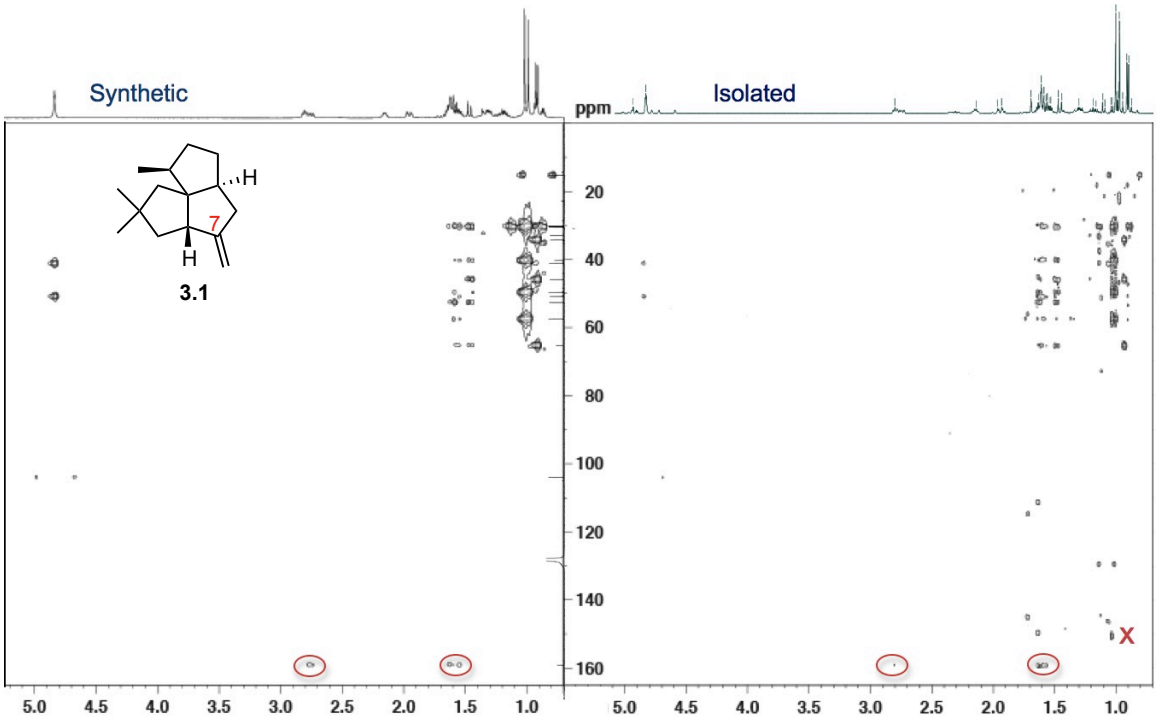
3.30 **3.1**

[a] Reagents and conditions: (a) NaH, DMF, rt, then CS_2, then MeI, 83%. (b) Bu_3SnH, AIBN, benzene, 80°C, intractable (c) $(TMS)_3SiH$, AIBN, benzene, 80°C, 54%.

Examination of the ^{1}H and ^{13}C NMR spectra of **3.1** revealed all but a single ^{13}C resonance matched the data published for the isolated natural product.[15] The signal in question, assigned to the olefinic C-7 position, appeared in the synthetic material at 159.00 ppm, whereas the literature reported a value of 150.07 ppm. Correspondence with the Koenig group revealed that due to poor signal to noise in the ^{13}C spectrum and the presence of impurities in the isolated material, the C-7 resonance was assigned based on the HMBC spectrum, which was kindly provided to us.

Figure 3.6 presents the HMBC spectra of **3.1** from both the isolated and synthetic sources. The carbon signal at 159.00 ppm is present in both spectra with identical coupling patterns, whereas the previously assigned signal at 150.07 ppm is absent in the synthetic material and is apparently due to an olefinic impurity.

Figure 3.6. HMBC Spectra of Synthetic and Isolated Ventricosene **3.1**.



The first total synthesis of ventricosene **3.1**, completed in 11 steps from ester **3.12**, illustrates the ever-increasing utility of gold-catalyzed enyne cycloisomerization as a tool for the rapid construction of carbocyclic systems. Through the use of a single heteroatom, the complex hydrocarbon structure of **3.1** was assembled over four steps by sequential application of gold- and palladium-mediated ring expansion reactions.

Experimental

General Information. All commercial materials were used without further purification. Solvents were purchased from EM-Science. THF and CH_2Cl_2 were dried by passage through a column of activated alumina, and triethylamine was distilled from CaH_2 prior to use. Unless otherwise noted, all transfers of liquid were performed via syringe, all reactions were run under a dry N_2 atmosphere and all glassware was dried in an oven at 150°C for at least 8 h TLC analysis of reaction mixtures was performed on Merck silica gel 60 F_{254} TLC plates. Chromatography was carried out on ICN SiliTech 32-63 D 60 Å silica gel. ^1H and ^{13}C NMR spectra were recorded with Bruker AVQ-400, AVB-400, and AV-300 spectrometers. Infrared spectra were obtained on a ThermoNicolet Avatar 370 FTIR spectrophotometer as thin films on a NaCl plate. Unless otherwise noted, NMR spectra were obtained in $CDCl_3$. ^1H NMR multiplicities are reported as follows: b = broad; m = multiplet; s = singlet; d = doublet; t = triplet; q = quartet. All ^{13}C NMR spectra were obtained with proton decoupling. Infrared spectra were obtained on a ThermoNicolet Avatar 370 FTIR spectrophotometer as thin films on a NaCl plate. Mass spectral data were obtained via the Micro-Mass/Analytical Facility operated by the College of Chemistry, University of California, Berkeley.

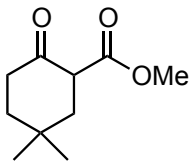
4,4-Dimethylcyclohex-2-enone (3.8)

This material was prepared from commerical isobutyraldehyde and methyl vinyl ketone via Robinson annulation according to the method of Flaugh.[21] The ^1H NMR and ^{13}C NMR spectra were consistent with those reported by Hopf.[37] IR (neat): 2960, 2868, 1684, 1470, 1375, 1235 cm^{-1}. **^1H NMR** (400 MHz) δ 6.56 (d, J = 10.0 Hz, 1H), 5.72 (d, J = 10.0 Hz, 1H), 2.34 (t, J = 6.8 Hz, 2H), 1.78 (t, J = 6.8 Hz, 2H), 1.07 (s, 6H). **^{13}C NMR** (100 MHz) δ 199.39, 159.76, 126.67, 35.92, 34.26, 32.69, 27.56.

4,4-Dimethylcyclohexanone (3.7)

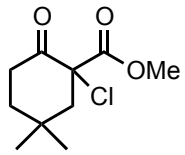
This material was prepared from enone **3.8** in accord with the procedure reported by Liu.[38] The ^1H NMR and ^{13}C NMR spectra were consistent with those reported by Hopf.[37] **^1H NMR** (400 MHz) δ 2.33 (t, J = 6.8 Hz, 4H), 1.66 (t, J = 6.8 Hz, 4H), 1.08 (s, 6H). **^{13}C NMR** (100 MHz) δ 39.05, 37.96, 29.83, 27.44.

Methyl 5,5-dimethyl-2-oxocyclohexanecarboxylate (3.9)[39]



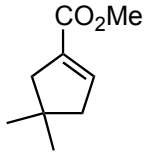
A 500 mL three-neck round-bottom flask equipped with a reflux condenser and addition funnel was flushed with dry N_2 and charged with NaH (17.4 g of a 60% dispersion in mineral oil, 434 mmol) and KH (600 mg, 15.0 mmol). The solids were washed twice with pentane and the supernatant was removed via syringe under positive N_2 pressure. The resulting solid was cooled to 0°C and suspended in 700 mL of THF. Dimethyl carbonate (86.6 mL, 1.03 mol) was added dropwise over 5 min and the resulting suspension was heated to 60°C. Cautiously, ketone **3.7** (24.9 g, 198 mmol) was added dropwise over 1 h and the reaction mixture was allowed to stir at this temperature for 6 h After cooling to room temperature, the reaction mixture was poured slowly into 500 mL of sat. aqueous NH_4Cl and extracted with ethyl acetate (2 x 300 mL). The combined organic extracts were washed with water (1 x 300 mL) and brine (1 x 300 mL), dried over $MgSO_4$ and concentrated. Chromatography (19:1 hexanes/ethyl acetate) gave 29.9 g (82%) of keto ester **3.9** as a pale yellow oil. IR (neat): 2956, 1748, 1716, 1655, 1618, 1442, 1283, 1231, 1207 cm^{-1}. **^{1}H NMR** (400 MHz) δ 12.11 (s, 1H), 3.71 (s, 3H), 2.25 (t, *J* = 6.6 Hz, 2H), 1.99 (s, 2H), 1.41 (t, *J* = 6.6 Hz, 2H), 0.92 (s, 6H); **^{13}C NMR** (100 MHz) δ 173.11, 171.20, 96.23, 51.24, 36.04, 34.30, 28.88, 27.76, 26.51. **MS** HRMS calc. for $C_{10}H_{16}O_3$: 184.1099, found: 184.1097

Methyl 1-chloro-5,5-dimethyl-2-oxocyclohexanecarboxylate (3.10)[40]



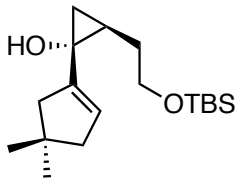
To a 250 ml round-bottom flask at room temperature was added sequentially acetonitrile (60 ml), **3.9** (5.44 g, 29.5 mmol), phenylselenyl chloride (364 mg, 1.2 mmol) and *N*-chlorosuccinimide (4.33 g, 32.4 mmol). The reaction mixture was stirred at room temperature 1h, diluted with water (100 mL) and extracted with ethyl acetate (2 x 100 mL). The organic fractions were washed with water (1 x 100 mL) and brine (1 x 100 mL), dried over $MgSO_4$ and concentrated. The residue was purified by chromatography (9:1 hexanes/ethyl acetate) to give 5.80 g (90%) of alkyl chloride **3.10** as an amber oil. **^{1}H NMR** (400 MHz) δ 3.74 (s, 3H), 2.69 (dd, *J* = 13.6, 2.6 Hz, 1H), 2.58 (m, 2H), 1.96 (dd, *J* = 13.5, 2.6 Hz, 1H), 1.66 (m, 2H), 1.013 (s, 3H), 0.971 (s, 3H). **^{13}C NMR** (100 MHz) δ 199.32, 168.60, 72.11, 51.76, 39.08, 36.22, 32.07, 30.70, 25.61. **MS** HRMS calc. for $C_{10}H_{15}ClO_3$: 218.0709, found: 218.0708

Methyl 4,4-dimethylcyclopent-1-enecarboxylate (3.6)[40]



To an oven-dried 250 mL round-bottom flask was added anhydrous Na_2CO_3 (557 mg, 5.26 mmol) and crushed glass (2.76 g) and the mixture heated to 150°C under high vacuum (approximately 6 mTorr) for 2 h The flask was allowed to cool to room temperature, fitted with a reflux condenser and xylenes (10 mL) and **3.10** (1.0 g, 4.57 mmol) were added. The resulting suspension was heated to 150°C for 40 h, cooled to room temperature and filtered through celite and the residue was rinsed with diethyl ether (75 mL). The solution was concentrated under reduced pressure to remove diethyl ether, loaded onto silica gel and purified by chromatography (hexanes to elute xylenes then 19:1 hexanes/ethyl acetate) to give 540 mg (76%) of **3.6** as a pale yellow oil. **IR** (neat): 2954, 1716, 1633, 1435, 1348, 1246 cm^{-1}. **^{1}H NMR** (400 MHz) δ 6.65 (t, *J* = 1.8 Hz, 1H), 3.71 (s, 3H), 2.38 (t, *J* = 2.0 Hz, 2H), 2.29 (t, *J* = 1.8 Hz, 2H), 1.10 (s, 6H). **^{13}C NMR** (400 MHz) δ 165.84, 142.53, 134.86, 51.29, 48.17, 46.17, 38.74, 29.51. **MS** HRMS calc. for $C_9H_{14}O_2$: 154.0993, found: 154.0990.

(*1R*,2R*)n*-2-(2-(*tert*-butyldimethylsilyloxy)ethyl)-1-(4,4-dimethylcyclopent-1-enyl)cyclopropanol (3.11)



A freshly prepared 1 M solution of (4-(*tert*-butyldimethylsilyloxy)butyl)magnesium chloride in THF (52.9 mL, 52.9 mmol) was added dropwise to a 250 mL round-bottom flask containing a suspension of zirconocene dichloride (7.58 g, 25.9 mmol) in toluene (50 mL) at 0°C. The resulting black solution was stirred for 30 min at this temperature and enoate **3.6** (2.00 g, 12.97 mmol) was added dropwise as a solution in toluene (5 mL). The reaction temperature was maintained at 0°C for 30 min, allowed to warm to room temperature and stirred for 4 s. Water (45 mL) was added and the resulting suspension was filtered through celite and extracted with diethyl ether (3 x 75 mL). The combined organic fractions were washed with water (2 x 125 mL) and brine (125 mL) and concentrated. The resulting residue was purified by chromatography (95:5 hexanes/ethyl acetate) to give 2.08 g (52%) of **3.11** as a pale yellow oil. **IR** (neat): 3307, 2953, 2857, 1471, 1255 cm^{-1}. **^{1}H NMR** (400 MHz) δ 5.41 (pentet, *J* = 2.8 Hz, 1H), 3.66 (t, *J* = 7.2 Hz, 2H), 2.42 (dq, *J* = 15.6, 2.8 Hz, 1H), 2.35-2.10 (m, 3H), 2.06 (br s, 1H), 1.67 (m, 1H), 1.32-1.17 (m, 2H), 1.15 (s, 3H), 1.11 (s, 3H), 0.98 (dd, *J* = 9.6, 5.2 Hz, 1H), 0.93 (s, 9H), 0.66 (m, 1H), 0.09 (s, 3H). **^{13}C NMR** (100 MHz) 142.30, 125.12, 63.06, 58.07, 48.34, 47.28, 38.74, 31.99, 29.98, 29.77, 26.01, 23.94, 18.39, 18.05, -3.55. **MS** HRMS calc. for $C_{18}H_{34}O_2Si$: 310.2328, found: 310.2334

(1*R,2*R**)-1-(4,4-Dimethylcyclopent-1-enyl)-2-(2-hydroxyethyl)cyclopropanol (3.12)**

Silyl ether **3.11** (2.02 g, 6.51 mmol) was dissolved in 45 mL of THF in a 250 mL round-bottom flask cooled to 0°C. The solution was treated with TBAF (7.81 mL of a 1 M solution in THF, 7.81 mmol) and allowed to stir 2 h at room temperature. The reaction mixture was poured into 250 mL of a 1:1 mixture of ethyl acetate and water. The aqueous phase was extracted with ethyl acetate (2 X 50 mL), and the combined organic extracts were washed with brine (100 mL) and concentrated. Purification of the resulting residue by chromatography (7:3 hexanes/ethyl acetate) gave 1.01 g (80%) of diol **3.12** as an amber oil. **^{1}H NMR** δ 5.25 (s, 1H), 3.50 (t, *J* = 8.0 Hz, 2H), 2.27 (d, *J* = 16.0 Hz, 1H), 2.17 – 1.94 (m, 3H), 1.41 (m, 1H), 1.28 – 1.08 (m, 2H), 1.00 (s, 3H), 0.96 (s, 3H), 0.85 (m, 1H), 0.51 (m, 1H). **^{13}C NMR** (100 MHz) δ 142.20, 124.89, 72.25, 57.66, 48.38, 47.23, 38.65, 31.45, 29.97, 29.71, 23.84, 17.91. **MS** HRMS calc. for $C_{12}H_{20}O_2$: 196.1463, found: 196.1464

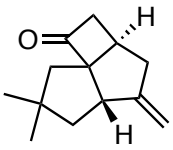
(1*R,2*R**)-1-(4,4-Dimethylcyclopent-1-enyl)-2-(prop-2-ynyl)cyclopropanol (3.5)**

A solution of oxalyl chloride (514 μL, 5.92 mmol) in CH_2Cl_2 (2 mL) at -78°C is treated dropwise with DMSO (660 μL, 9.27 mmol) in CH_2Cl_2 (4 mL). The reaction mixture was stirred at this temperature for 30 min, at which time a solution of diol **3.12** (1.012 g, 5.15 mmol) in CH_2Cl_2 (1 mL) was added. The resulting solution was stirred an additional 1.5 h at -78°C, TEA (3.94 mL, 28.3 mmol) was added and the reaction allowed to warm to room temperature over 45 min The reaction mixture was added to 100 mL of a rapidly stirring 1:1 mixture of CH_2Cl_2/water and extracted with CH_2Cl_2 (1 x 50 mL). The combined organic fractions were washed with water, dried over $MgSO_4$ and concentrated. Due to the anticipated instability of the aldehyde, the crude residue was immediately taken up in methanol (10 mL) at 0°C and treated sequentially with K_2CO_3 (1.71 g, 5.15 mmol) and Bestmann's reagent (dimethyl 1-diazo-2-oxopropylphosphonate, 1.48 g, 7.73 mmol). The reaction mixture was allowed to slowly warm to room temperature over 4 h at which time water (50 mL) and ethyl acetate (100 mL) were added. The aqueous fraction was extracted with ethyl acetate (2 x 50 mL) and the combined organic phases were washed with water (2 x 100 mL), dried over $MgSO_4$ and concentrated. The crude residue was purified by chromatography (9:1 hexanes/ethyl acetate) to afford 350 mg (36% from **3.12**) of enyne **3.5** as a pale

yellow oil. IR (neat): 3644, 3311, 3025, 2952, 2864, 2840, 2123, 1659, 1192, 630 cm^{-1}. **^{1}H NMR** (400 MHz) δ 5.45 (br s, 1H), 2.48 (m, 1H), 2.25-2.18 (m, 3H), 2.12 (m, 2H), 2.01 (t, *J* = 3.2 Hz, 1H), 1.82 (br s, 1H), 1.51 (m, 1H), 1.16 (s, 3H), 1.12 (s, 3H), 1.07 (m, 1H), 0.72 (m, 1H). **^{13}C NMR** (100 MHz) δ 141.38, 126.02, 83.75, 68.40, 58.23, 48.20, 47.27, 38.70, 30.03, 29.74, 25.53, 18.14, 17.77. **MS** HRMS calc. for $C_{13}H_{18}O$: 190.1357, found: 190.1361

***rel*-(4*R*,5*R*,8*S*)-2,2-Dimethyl-7-methyleneoctahydrocyclobuta[c]pentalen-9-one (3.4)**

A solution of $(PPh_3)AuBF_4$, generated by the addition of $(PPh_3)AuCl$ (33 mg, 0.067 mmol) and $AgBF_4$ (13 mg, 0.067 mmol) to 100 μL CH_2Cl_2, is added



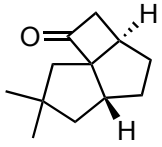
dropwise to a 25 mL round-bottom flask containing a solution of enyne **3.5** (425 mg, 2.23 mmol in CH_2Cl_2 (5 mL). The reaction mixture is stirred 2h at room temperature, concentrated to approx. 0.5 mL and loaded onto silica gel. Elution with 19:1 hexanes/ethyl acetate gave 345 mg (81%) of **3.4** as a clear oil. **IR** (neat): 3074, 2953, 2866, 1769, 1660, 1460, 1436, 1385, 1367, 1315, 1271, 1120, 1066, 1014, 889 cm^{-1}. **^{1}H NMR** (400 MHz) δ 5.03 (br s, 1H), 5.00 (br s, 1H), 3.23 (m, 1H), 2.99 (dd, *J* = 17.6, 8.0 Hz, 1H), 2.93 (m, 1H), 2.58 (dd, *J* = 17.6, 6.8 Hz, 1H), 2.46 (app q, *J* = 6.8 Hz, 1H), 2.37 (d, *J* = 15.2 Hz, 1H), 2.02 (dd, *J* = 13.6, 2.0 Hz, 1H), 1.74 (ddd, *J* = 12.4, 8.0, 2.4 Hz, 1H), 1.56 (d, *J* = 13.6 Hz, 1H), 1.38 (app t, *J* = 11.2 Hz, 1H), 1.08 (s, 3H), 1.05 (s, 3H). **^{13}C NMR** (100 MHz, CD_2Cl_2) δ 210.97, 152.81, 109.07, 81.21, 55.48, 48.38, 47.67, 46.05, 41.62, 38.05, 36.13, 28.10, 26.71. **MS** HRMS calc. for $C_{13}H_{18}O$: 190.1357, found: 190.1353

***rel*-(4R,5R,8R,9R)-9-Ethynyl-2,2-dimethyl-7-methyleneoctahydrocyclobuta[c]pentalen-9-ol (3.14)**

The synthesis and characterization of this material is reported in the doctoral dissertation of Staben.[17]

***rel*-(4R,5R,8R,9R)-9-Ethynyl-2,2-dimethyl-7-methylene-9-trimethylsiloxyoxy-octahydrocyclobuta[c]pentalene (3.15)**

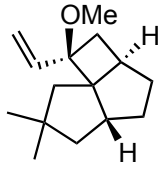
The synthesis and characterization of this material is reported in the doctoral dissertation of Staben.[17]



***rel*-(4R,5R,8R)-2,2-Dimethyloctahydrocyclobuta[c]pentalen-9-one (3.20)**

To a solution of freshly prepared but-3-enylmagnesium bromide (36.4 mL of a 1.1 M solution in THF, 40.0 mmol) at -78°C was

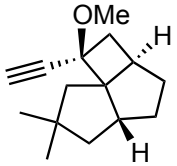
added anhydrous CuI (3.81 g, 20 mmol) and the resulting suspension was allowed to warm to -40°C for 20 min The reaction mixture was then cooled to -78°C and HMPA (3.48 mL, 20 mmol), TMSCl (5.39 mL, 40 mmol) and then **3.6** (1.31 g, 8.47 mmol) were added in succession. The cooling bath was removed and saturated aqueous NH_4Cl (75 mL) was added followed by ethyl acetate (100 mL). The aqueous phase was extracted with ethyl acetate (100 mL) and the combined organic extracts washed with water (2 x 100 mL) and brine (100 mL) and concentrated. The resulting residue was taken up in methanol (45 mL), added to aqueous KOH (2M, 33.0 mL, 66.0 mmol) in a 100 mL bomb flask and heated to 70°C for 3 h Upon cooling to room temperature, the reaction mixture was concentrated to remove methanol and the resulting solution was washed with diethyl ether (2 x 75 mL) and cooled to 0°C. The solution was acidified by the addition of aqueous HCl (6N, 15 mL) and extracted with CH_2Cl_2 (2 x 100 mL). The organic fractions were dried over $MgSO_4$ and concentrated to give 1.52 g of a pale green oil. To a solution of the crude acid in CH_2Cl_2 (25 mL) at 0°C was added oxalyl chloride (1.98 g, 23.3 mmol) and DMF (approx. 40 μL). The reaction mixture was stirred 2 h at this temperature and concentrated. The resulting residue was exposed to reduced pressure (approx. 6 mTorr) for 2 h and transferred to a sealed reaction vessel containing benzene (90 mL). *N*,*N*-Diisopropylethylamine (6.69 mL, 38.8 mmol) and then DMAP (191 mg, 1.56 mmol) were added and the resulting solution was heated to 100°C for 18 h, cooled to room temperature and added to water (150 mL). The organic fraction was diluted with ether (100 mL), washed with aqueous HCl (0.5 M, 2 x 75 mL) water (100 mL) and brine (100 mL), and dried over $MgSO_4$. Removal of solvent gave a crude oil which was purified by chromatography (99:1 hexanes/ethyl acetate) to afford 672 mg (45% from **3.6**) of **3.20** as a clear oil. **^{1}H NMR** (400 MHz) δ 2.90 (dd, *J* = 17.6 Hz, 8.8 Hz, 1H), 2.79 (dt, *J* = 11.6, 7.6 Hz, 1H), 2.54 (dd, *J* = 6.0, 2.0 Hz, 1H), 2.42 (m, 1 H), 2.04 (m, 1H), 1.98 – 1.89 (m, 2H), 1.79 (dd, *J* = 12.4, 6.4 Hz, 1H), 1.69 (dd, *J* = 13.2, 6.4 Hz, 1H), 1.52 (m, 1H), 1.43 (d, *J* = 13.5, 1H), 1.17 (m, 1H), 1.00 (s, 3H), 0.98 (s, 3H). **^{13}C NMR** (100 MHz) δ 213.83, 81.77, 50.07, 47.11, 46.84, 46.43, 40.99, 38.65, 30.40, 28.85, 28.29, 27.46. **MS** HRMS calc. for $C_{12}H_{18}O$: 178.1357, found: 178.1356



***rel*-(4R,5R,8R,9R)-9-Methoxy-2,2-dimethyl-9-vinyloctahydrocyclobuta[c]pentalene (3.21)**

A 50 mL round-bottom flask was flushed with dry N_2, cooled to -78°C and charged with anhydrous $CeCl_3$ (897 mg, 3.69 mmol) and THF (8mL). Vinylmagnesium bromide (3.64 mL of a commercial 1 M solution, 3.64 mmol) was added dropwise and the reaction mixture was stirred

1 h A solution of **3.20** (216 mg, 1.21 mmol) in THF (1 mL) was added and the reaction mixture was allowed to warm to room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl (100 mL) and extracted with ethyl acetate (3 x 75 mL). The combined organic fractions were washed with water (2 x 100 mL) and brine (100 mL), dried over $MgSO_4$, and concentrated. The resulting residue was passed through a short plug of silica gel with diethyl ether (50 mL) and concentrated. The crude alcohol was added to a 25 mL bomb flask (vented with N_2) containing a suspension of sodium hydride (46 mg of a 60% dispersion in mineral oil, 1.17 mmol) in THF (5 mL) at 0°C. The resulting solution was stirred at this temperature for 30 min and methyl iodide (28 μL, 0.46 mmol) was added. The flask was sealed and the reaction mixture heated to 50°C for 1 h, cooled to room temperature and poured into 50 mL of saturated aqueous NH_4Cl. The resulting suspension was extracted with diethyl ether (3 x 50 mL) and the combined organic fractions were washed successively with water (2 x 75 mL) and brine (100 mL) and then concentrated. The residue was purified by chromatography (49:1 hexanes/ethyl acetate) to afford 95 mg (49%) of **3.21** as a clear oil. **^{1}H NMR** (400 MHz) δ 5.78 (dd, *J* = 17.6, 11.2 Hz, 1 H), 5.23 (m, 2H), 3.05 (m, 4H), 2.06 (dd, *J* = 12.0, 8.4 Hz, 1H), 2.01 – 1.89 (br m, 2H), 1.74 (m, 2H), 1.60 – 1.43 (br m, 4H), 1.07 – 0.96 (m, 2H), 0.97 (s, 3H), 0.91 (s, 3H). **^{13}C NMR** (100 MHz) δ 141.73, 113.43, 78.82, 65.14, 50.61, 49.10, 48.35, 43.03, 40.02, 39.64, 30.24, 29.11, 28.77, 28.68, 26.94. **MS** HRMS calc. for $C_{15}H_{24}O$: 220.1827, found: 220.1824.



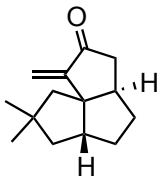
***rel*-(4R,5R,8R,9R)-9-Ethynyl-9-methoxy-2,2-dimethyloctahydrocyclobuta[c]pentalene (3.22)**

Ethynyltrimethylsilane (400 μL, 2.81 mmol) and TMEDA (339 μL, 2.24 mmol) were added to a 50 mL round-bottom flask containing THF (9 mL). The solution was cooled to -78°C and *n*-BuLi (896 μL of a 2.5 M solution in hexanes, 2.24 mmol) was added dropwise. The resulting solution was warmed to 0°C for 10 min and then cooled to -78°C at which time **3.20** (100 mg, 0.562 mmol) was added dropwise as a solution in THF (2 mL). The reaction mixture was stirred at -78°C for 2 h, allowed to warm to room temperature, and quenched with saturated aqueous NH_4Cl (50 mL). The resulting mixture was extracted with ethyl acetate (2 x 100 mL) and the organic fractions were washed with water (2 x 75 mL) and brine (100 mL). The resulting solution was dried over Na_2SO_4 and concentrated. The crude alcohol was dissolved in THF (1 mL) and added to a suspension of NaH (56 mg of a 60% dispersion in mineral oil, 1.14 mmol) in THF (8 mL) in a 25 mL bomb flask (vented with dry N_2) at 0°C. The suspension was warmed to room temperature and stirred for 30 min

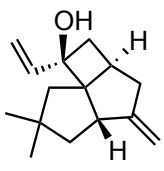
Methyl iodide (58 μL, 0.931 mmol) was added and the flask was sealed and warmed to 40°C for 2 h The reaction mixture was cooled to room temperature, quenched with saturated aqueous NH_4Cl (75 mL) and extracted with ethyl acetate (2 x 100 mL). The combined organic fractions were washed with water (2 x 75 mL) and brine (100 mL), dried over $MgSO_4$, and concentrated. The residue was taken up in methanol (5 mL) and K_2CO_3 (500 mg, 3.60 mmol) was added at room temperature. The resulting suspension was stirred 1 h, concentrated and dissolved in water (100 mL) and ethyl acetate (100 mL). The layers were separated and the aqueous fraction was extracted with ethyl acetate (100 mL). The organic fractions were washed with brine (100 mL), dried over $MgSO_4$, and concentrated. The residue was purified by chromatography (neat hexanes) to give 75 mg (61% from **3.20**) of **3.22** as a clear oil. **^{1}H NMR** δ 3.29 (s, 3H), 2.97 (dt, *J* = 11.4, 8.0 Hz, 1H), 1.60 (s, 1H), 2.25 – 2.10 (m, 3H), 1.91 (m, 1H), 1.77 (m, 1H), 1.63 – 1.58 (m, 2H), 1.51 (m, 2H), 1.40 (d, *J* = 13.6 Hz, 1H) 1.07 (t, *J* = 11.6 Hz, 1H), 0.98 (s, 3H), 0.93 (s, 3H**). ^{13}C HNMR** (100 MHz) δ 85.32, 74.59, 74.27, 64.83, 51.68, 51.36, 48.61, 42.88, 39.78, 34.19, 29.98, 29.05, 28.94, 27.38. **MS** HRMS calc. for $C_{15}H_{22}O$: 218.1670, found 218.166.

***rel*-(4R,5R,8R)-2,2-Dimethyl-9-methyleneoctahydrocyclopenta[c]pentalen-10-one (3.23)**

To a 20 mL vial is added a solution of ether **3.21** (31.5 mg, 133 μmol) in THF (2.5 mL) followed by a bis(acetonitrile)palladium(II) chloride (3.4 mg, 13.3 μmol) and DDQ (33.2 mg, 146 μmol). The reaction mixture was stirred at 50°C for 3 h, concentrated to an oil and loaded onto silica gel. Elution with 19:1 hexanes/ethyl acetate gave 20 mg (70%) of enone **3.23** as a clear oil. **^{1}H NMR** (400 MHz, C_6D_6) δ 6.14 (d, *J* = 0.8 Hz, 1H), 5.07 (d, *J* = 0.8 Hz, 1H), 2.30 (m, 1H), 2.23 (q, *J* = 10.0, 1H), 1.92 – 1.83 (m, 2H), 1.65 (app. pentet, *J* = 6.4 Hz, 1H), 1.57 – 1.47 (m, 3H), 1.29 – 1.22 (m, 1H), 1.07 – 1.19 (m, 3H), 0.96 (s, 3H), 0.93 (s, 3H). **^{13}C NMR** (100 MHz, C_6D_6) δ 206.00, 155.99, 116.31, 63.20, 56.90, 54.15, 49.15, 56.72, 42.16, 41.29, 32.26, 30.72, 29.68, 29.26. **MS** HRMS calc. for $C_{14}H_{20}O$: 204.1514, found: 204.1509.



***rel*-(4R,5R,8S)-2,2-Dimethyl-7-methylene-9-vinyloctahydrocyclobuta[c]pentalen-9-ol (3.24)**

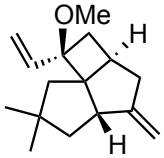


A 50 mL round-bottom flask was charged with anhydrous $CeCl_3$ (1.16 g, 4.73 mmol), THF (15 mL) was added and the resulting suspension was cooled to -78°C. Vinyl magnesium bromide (4.73 mL of a commercial 1M solution, 7.73 mmol) was added

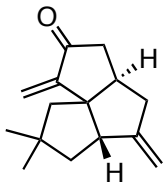
dropwise and the reaction mixture was warmed to 0°C for 1 h The reaction mixture was cooled to -78°C and a solution of cyclobutanone **3.4** (300 mg, 1.58 mmol) in THF (1 mL) was added dropwise. The suspension was allowed to warm to room temperature over 2 h and saturated aqueous NH_4Cl (45 mL) was added. The mixture was extracted with ethyl acetate (2 x 75 mL) and the combined organic fractions were washed with water (2 x 75 mL) and brine (100 mL), dried over $MgSO_4$ and concentrated. Purification of the residue by chromatography (9:1 hexanes/ethyl acetate) gave 217 mg (63%) of vinyl alcohol **3.24** as a clear oil. **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 6.05 (dd, *J* = 10.8, 17.2 Hz, 1H), 5.23 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.08 (dd, *J* = 10.8, 1.2 Hz, 1H), 4.91 (s, 1H), 4.86 (s, 1H), 3.89 (t, *J* = 9.2 Hz, 1H), 2.66 (m, 1H), 2.20 – 2.02 (m, 4H), 1.77 - 1.71 (m, 2H), 1.55 (dd, *J* = 8.0, 12.0 Hz, 1H), 1.31 – 1.18 (m, 2H), 0.95 (s, 3H), 0.87 (s, 3H). **^{13}C NMR** (100 MHz, CD_2Cl_2) δ 157.15, 143.37, 110.02, 107.05, 74.40, 66.52, 49.66, 49.20, 40.62, 37.57, 37.15, 36.88, 28.13, 26.55. **MS** HRMS calc. for $C_{15}H_{33}O$: 218.1670, found: 218.1665

***rel*-(4R,5R,8S)-9-Methoxy-2,2-dimethyl-7-methylene-9-vinyloctahydrocyclobuta[c]pentalene (3.25)**

To a 50 mL bomb flask (vented with dry N_2) was added sodium hydride (35 mg of a 60% dispersion in mineral oil, 0.894 mmol) and THF (3 mL). The resulting suspension was cooled to 0°C and a solution of alcohol **3.24** (135 mg, 0.619 mmol) in DMF (1.2 mL) was added dropwise. The flask was allowed to warm to room temperature over 1 h at which time evolution of gas had ceased. Methyl iodide (77 μL, 1.23 mmol) was added and the flask was sealed and warmed to 50°C for 3 h Upon cooling to room temperature, the reaction mixture was poured into 50 mL of saturated aqueous NH_4Cl and extracted with diethyl ether (3 x 50 mL). The combined organic phases were washed with brine (100 mL), dried over Na_2SO_4 and concentrated. Purification of the residue by chromatography (hexanes) gave 115 mg (83%) of ether **3.25** as a clear oil. **^{1}H NMR** (400 MHz) δ 5.82 (dd, *J* = 11.2, 17.6 Hz, 1H), 5.29 (d, *J* = 10.4, 1H), 5.27 (d, *J* = 17.6, 1H), 4.97 (s, 1H), 4.91 (s, 1H), 3.57 (t, *J* = 9.2 Hz), 3.08 (s, 3H), 2.76 (m, 1H), 2.18 – 2.10 (m, 2H), 1.96 (dd, *J* = 7.6, 14.4 Hz, 1H), 1.82 – 1.75 (m, 2H), 1.56 (dd, *J* = 8.4 Hz, 11.6), 1.25 – 1.16 (m, 2H), 0.99 (s, 3H), 0.93 (s, 3H). **^{13}C NMR** (100 MHz) δ 157.89, 141.09, 113.84, 106.95, 79.19, 65.63, 50.73, 49.41, 48.96, 48.60, 40.80, 37.82, 37.02, 30.17, 28.42, 26.57. **MS** HRMS calc for $C_{16}H_{24}O$: 232.1822, found: 232.1827

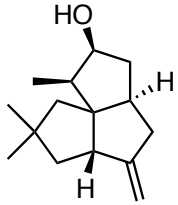


***rel*-(4R,5R,8R)-2,2-Dimethyl-9,7-dimethyleneoctahydrocyclopenta[c]pentalen-10-one (3.2)**



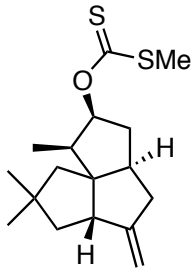
To a 20 mL vial is added a solution of ether **3.21** (31.5 mg, 133 μmol) in THF (2.5 mL) followed by a bis(acetonitrile)palladium(II) chloride (3.4 mg, 13.3 μmol) and DDQ (33.2 mg, 146 μmol). The reaction mixture was stirred at 50°C for 3 h, concentrated to an oil and loaded onto silica gel. Elution with 19:1 hexanes/ethyl acetate gave 20 mg (70%) of enone **3.2** as a clear oil. **^{1}H NMR** (400 MHz, C_6D_6) δ 6.21 (s, 1H), 5.06 (s, 1H), 4.84 (d, J = 1.2 Hz, 1H), 4.81 (d, J = 1.2 Hz, 1H), 2.84 (t, J = 6.8 Hz), 2.42 (dd, J = 15.6, 6.8 Hz, 1H), 2.25 (dd, J = 19.2, 9.2 Hz, 1H), 2.04 – 1.95 (m, 2H), 1.80 (dd, J = 15.6, 7.6 Hz, 1H), 1.73 (dd, J = 12.0, 7.6 Hz, 1H), 1.59 (s, 1H), 1.56 (s, 1H) 1.48 (m, 1H), 1.00 (s, 3H), 0.99 (s, 3H). **^{13}C NMR** (100 MHz, C_6D_6) δ 205.25, 154.93, 154.49, 116.77, 105.84, 63.19, 57.89, 56.01, 48.76, 44.77, 41.85, 41.78, 40.23, 29.58. **MS** HRMS calc. for $C_{15}H_{20}O$: 216.1514, found: 216.1515

***rel*-(4R,5R,8R)-2,2,9-Trimethyl-7-methyleneoctahydrocyclopenta[c]pentalen-10-ol (3.28)**



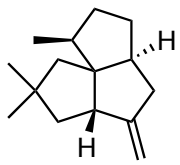
To a solution of **3.2** (34.0 mg, 157 μmol) in ethanol (700 μL) at -78ºC is added dropwise K-selectride (472 μL of a 1M solution, 472 μmol). Stirring is continuted at this temperature for 6 h at which time the reaction mixture was allowed to warm to 0ºC and aqueous NaOH was added (700 μL of a 3M solution) followed by the cautious dropwise addition of aqueous hydrogen peroxide (300 μL of a 30% solution). The reaction mixture was allowed to warm to room temperature and stirred for 6 h and then diluted with 50 mL Et_2O. The organic fraction was washed with water (2 x 50 mL) and brine (50 mL) and then the aqueous fractions were extracted with Et_2O (2 x 25 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Chromatography of the resulting residue (95:5 hexanes:ethyl acetate) gave 30.3 mg (88%) of **3.26** as a clear oil. **^{1}H NMR** (400 MHz) δ 4.87 (d, J = 1.2 Hz 1H), 4.83 (d, J = 1.2 Hz 1H), 3.94 (m, 1H), 2.94 (dd, J = 17.6, 8.4 Hz, 1H), 2.29 (tt, J = 10.0, 3.0 Hz, 1H), 2.19 – 2.11 (m, 1H), 2.06 (d, J = 15.6, 1H), 1.86 (dt, J = 12, 7.2 Hz, 1H), 1.79 (d, J = 13.6 Hz, 1H), 1.69 (ddd, J = 12.4, 8.0, 1.6 Hz 1H), 1.63 (dd, J = 13.6, 1.6 Hz, 1H), 1.58 (s, 2H), 1.52 – 1.44 (m, 1H), 1.40 (dt, J = 14, 3.2 Hz, 1H), 1.03 (s, 3H), 1.02 (d, J = 7.2, 3H), 0.98 (s, 3H). **^{13}C NMR** (100 MHz) δ 158.01, 106.26, 77.36, 64.80, 58.19, 51.31, 51.13, 50.04, 49.55, 42.02, 40.57, 40.03, 30.08, 29.61, 10.20. **MS** HRMS calc. for $C_{15}H_{24}O$: 220.1827, found: 220.1824

***rel*-S-methyl, O-((1R,2S,3R,5S)-1,7,7-trimethyl-5-methylenedecahydrocyclopenta[c]pentalen-2-yl) carbonodithioate (3.30)**



A suspension of NaH (15 mg of a 60% dispersion in mineral oil, 358 μmol) in THF (3 mL) was stirred for 15 minutes and the solvent decanted. The resulting solid was suspended in THF (1 mL) and cooled to 0°C. To this suspension was added imidazole (0.1 mg) and **3.2** (17 mg, 77 μmol) in 300 μL THF. The reaction mixture was stirred for 1 h at 0°C and then CS_2 (18.7 μL, 309 μmol) is added in 300 μL THF. The reaction was warmed to room temperature and stirred for 1 h at which time MeI (15 μL, 233 μmol) was added. After stirring an additional hour, the reaction was quenched by the addition of 5 mL sat. aq. NH_4Cl and 5 mL Et_2O at 0°C. The aqueous fraction was extracted with Et_2O (2 x 10 mL) and the combined organic fractions were washed with water (10 mL), brine (10 mL) and concentrated *in vacuo*. The residue was then purified by chromatography (neat hexanes) to afford 20 mg (83%) of xanthate **3.30** as a yellow oil. **^{1}H NMR** (400 MHz, C_6D_6) δ 5.83 (d, J = 5.2, 4 Hz, 1H), 4.87 (d, J = 2 Hz, 1H), 4.86 (d, J = 2 Hz, 1H), 3.03 (t, J = 4.8 Hz, 1H), 2.69 (qd, J = 9.2, 1.2 Hz, 1H), 2.14 (s, 3H), 2.10 – 2.03 (m, 1H), 2.01 – 1.79 (m, 3H), 1.68 (dt, J = 13.6, 3.6 Hz, 1H), 1.59 (dd, J = 12.4, 8.4 Hz, 1H), 1.48 (dd, J = 12.4, 5.6 Hz, 1H), 1.4 – 1.36 (m, 2H), 0.94 (s, 3H), 0.90 (s, 3H), 0.89 (d, J = 7.6 Hz, 3H). **^{13}C NMR** (100 MHz, C_6D_6) δ 215.66, 158.09, 105.17, 89.02, 64.81, 57.92, 51.02, 49.94, 49.88, 48.26, 41.04, 40.21, 37.92, 29.73, 29.37, 18.53, 10.12. **MS** HRMS calc. for $C_{17}H_{26}OS_2$: 310.1425, found: 310.1429

Ventricosene (3.1)



A solution of tris(trimethylsilyl) silane (23.9 μL, 77 μmol), AIBN (3.2 mg, 19 μmol), and **3.30** (20 mg, 64.5 μmol) in 1 mL C_6D_6 were heated to 80°C in a sealed tube for 2 h. Upon cooling to room temperature, the reaction mixture was treated with TBAF (185 μL of a 1M solution in THF, 185 μmol) and allowed to stir at room temperature for 25 minutes. The resulting solution was diluted with pentane (2 mL), washed with water (2 x 20 mL), brine (10 mL) and dried over $MgSO_4$. The solvent was removed by cautious kugelrohr distillation, providing a fragrant residue which was passed through a short plug of silica gel with pentane to provide 3.1 mg (23%) of ventricosene **3.1** as a clear oil smelling of patchouli. Repeating the reaction in the presence of an internal standard (pentamethylbenzene) gave a 54% yield by ^{1}H NMR. **^{1}H NMR** (500 MHz, C_6D_6) δ 4.84 (app triplet, J = 1.5 Hz, 2H), 2.81 (t, J = 6.5 Hz, 1H), 2.77 – 2.73 (m, 1H),

2.16 (m, 1H), 1.95 (m, 1H), 1.67 – 1.52 (m, 6H), 1.46 (d, J = 13.3 Hz, 1H), 1.36 – 1.29 (m, 1H), 1.22 – 1.16 (m, 1H), 1.02 (s, 3H), 0.99 (s, 3H), 0.92 (d, J = 6.9 Hz, 3H). **^{13}C NMR** (125 MHz, C_6D_6) δ 159.01, 103.82, 65.13, 57.31, 52.47, 50.72, 49.55, 45.75, 40.98, 40.07, 34.07, 32.77, 30.35, 30.01, 15.10. **MS** HRMS calc. for $[C_{15}H_{24}]^+$: 204.1878, found: 204.1877. All spectral data were in full accord with those reported for the isolated natural product[12] with the exception of a single ^{13}C resonance (159.01 ppm), which we hereby reassign.

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28. The regiochemistry of **3.2** was assigned based on the appearance of the vinylic protons of the enone in the ^{1}H NMR spectrum as a doublet of triplets exhibiting a coupling constant consistent with that of an allylic system (J = 2.4 Hz).
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30. This regiochemical control is attributed by Kocovsky *et. al.* to an interaction between palladium and the hydroxyl group which is disrupted upon methylation. This is supported by their report of the hydroxy compound undergoing expansion by path a when mediated by less oxophillic metals such as Hg(II) and Tl(III).

31. This approach was not deemed suitable for the synthesis of **3.1** due to concerns about Prins-type attack on the ketene by the second, more nucleophillic olefin which is absent in the model system.
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33. An impurity was isolated from the reaction mixture in ca 10% yield which we believe to be a dimer or oligomers resulting from enolization of **3.2** followed by Michael addition.
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36. Upon careful distillation of the solvent and elution through silica gel using pentane, ventricosene **3.1** was isolated in 23% yield.
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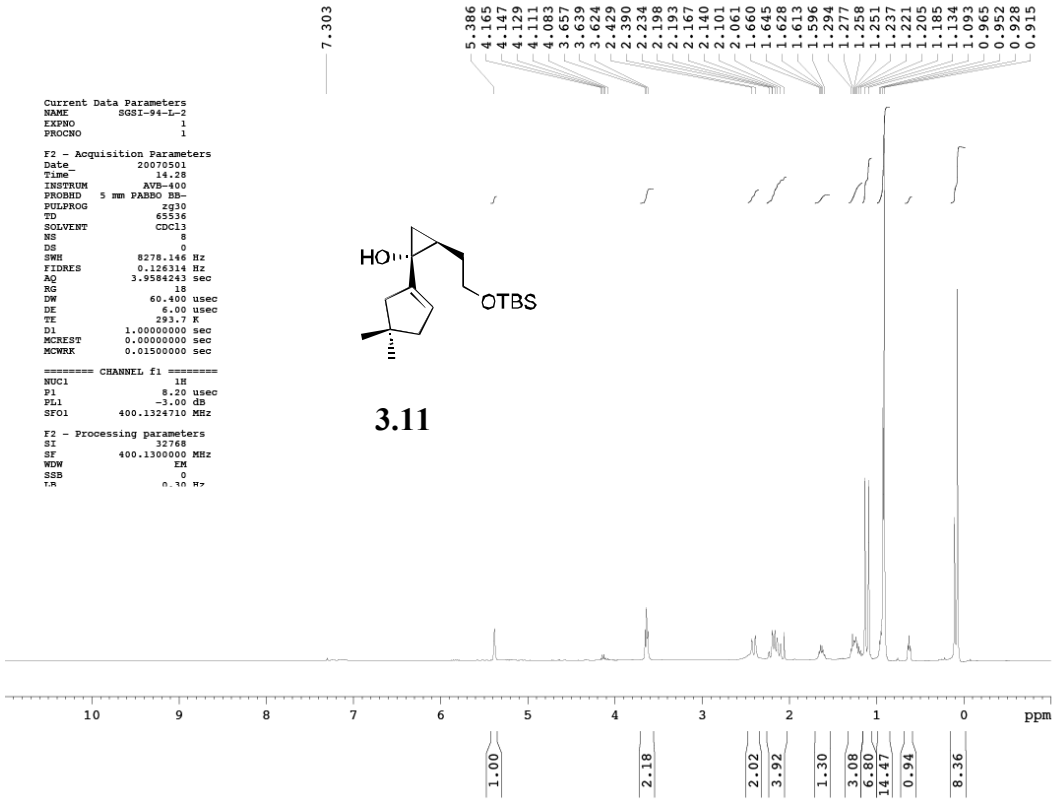
AVB-400 ZBO Proton starting parameters. 6/11/03 RN



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PROCNO 1

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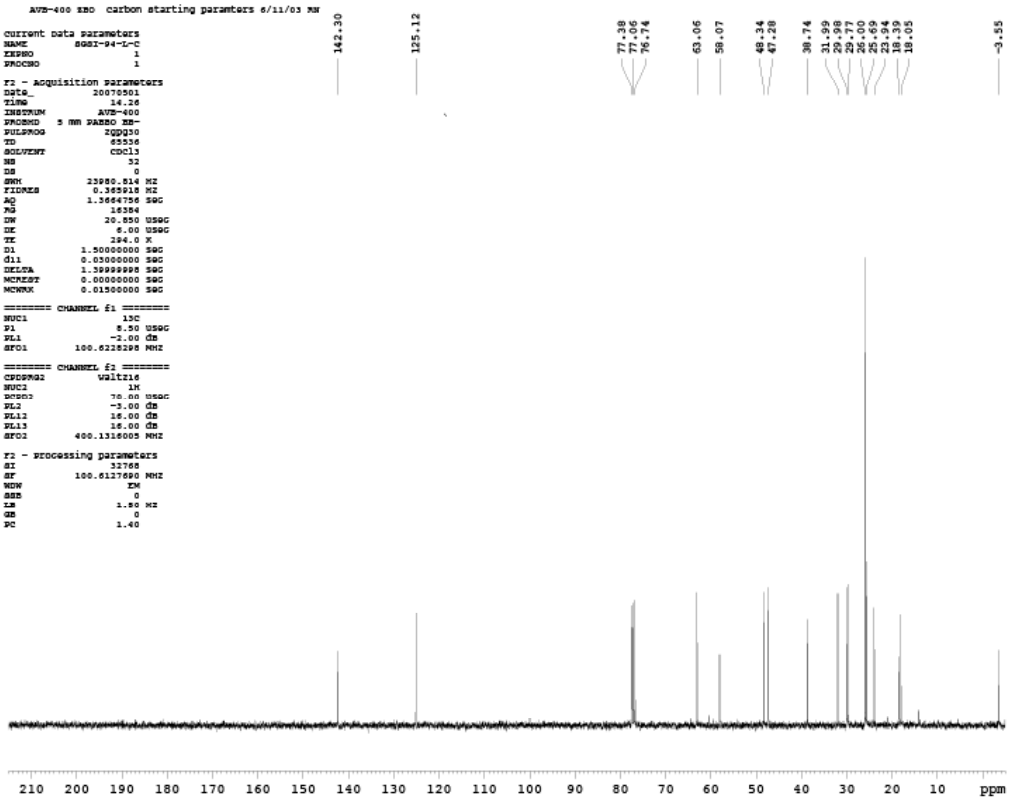
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 18
DW 60.400 usec
DE 6.00 usec
TE 293.7 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 8.20 usec
PL1 -3.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz

3.11

AVB-400 ZBO carbon starting parameters 6/11/03 RN



current data parameters
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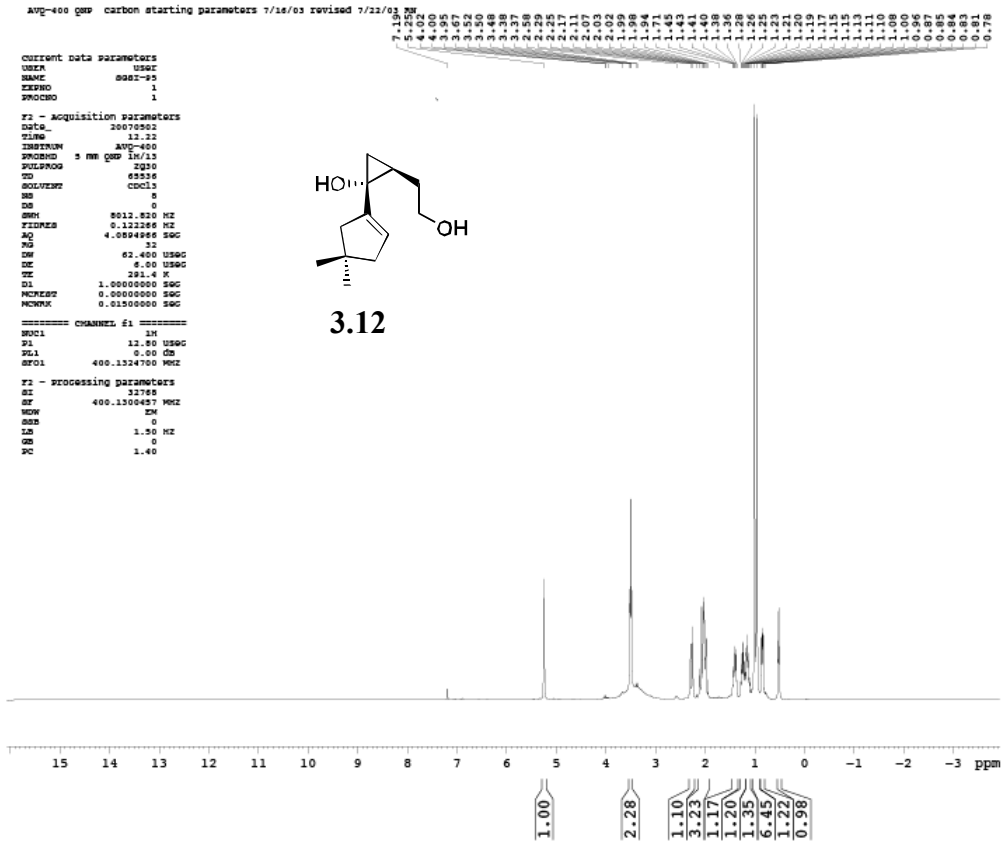
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 32
DS 0
SWH 23980.814 HZ
FIDRES 0.365918 HZ
AQ 1.3664756 SEC
RG 16384
DW 20.850 USEC
DE 6.00 USEC
TE 294.0 K
D1 1.50000000 SEC
d11 0.03000000 SEC
DELTA 1.39999998 SEC
MCREST 0.00000000 SEC
MCWRK 0.01500000 SEC

======== CHANNEL f1 ========
NUC1 13C
P1 8.50 USEC
PL1 -2.00 dB
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 78.00 USEC
PL2 -3.00 dB
PL12 18.00 dB
PL13 18.00 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.50 HZ
GB 0
PC 1.40



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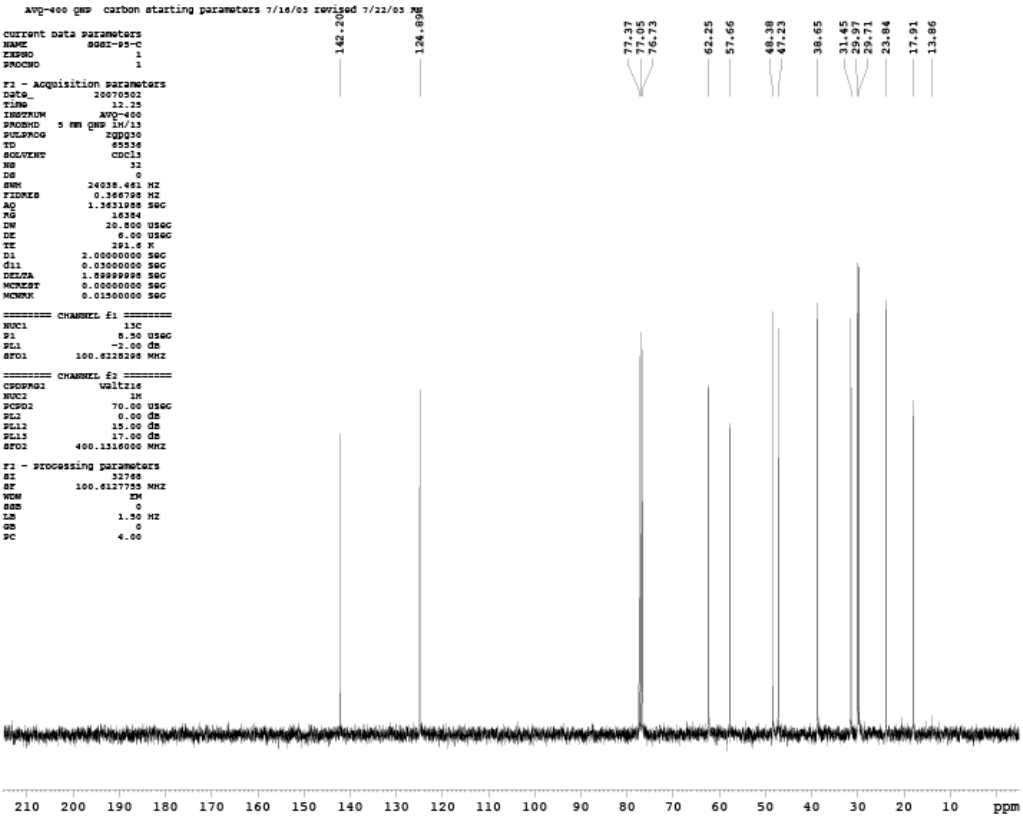

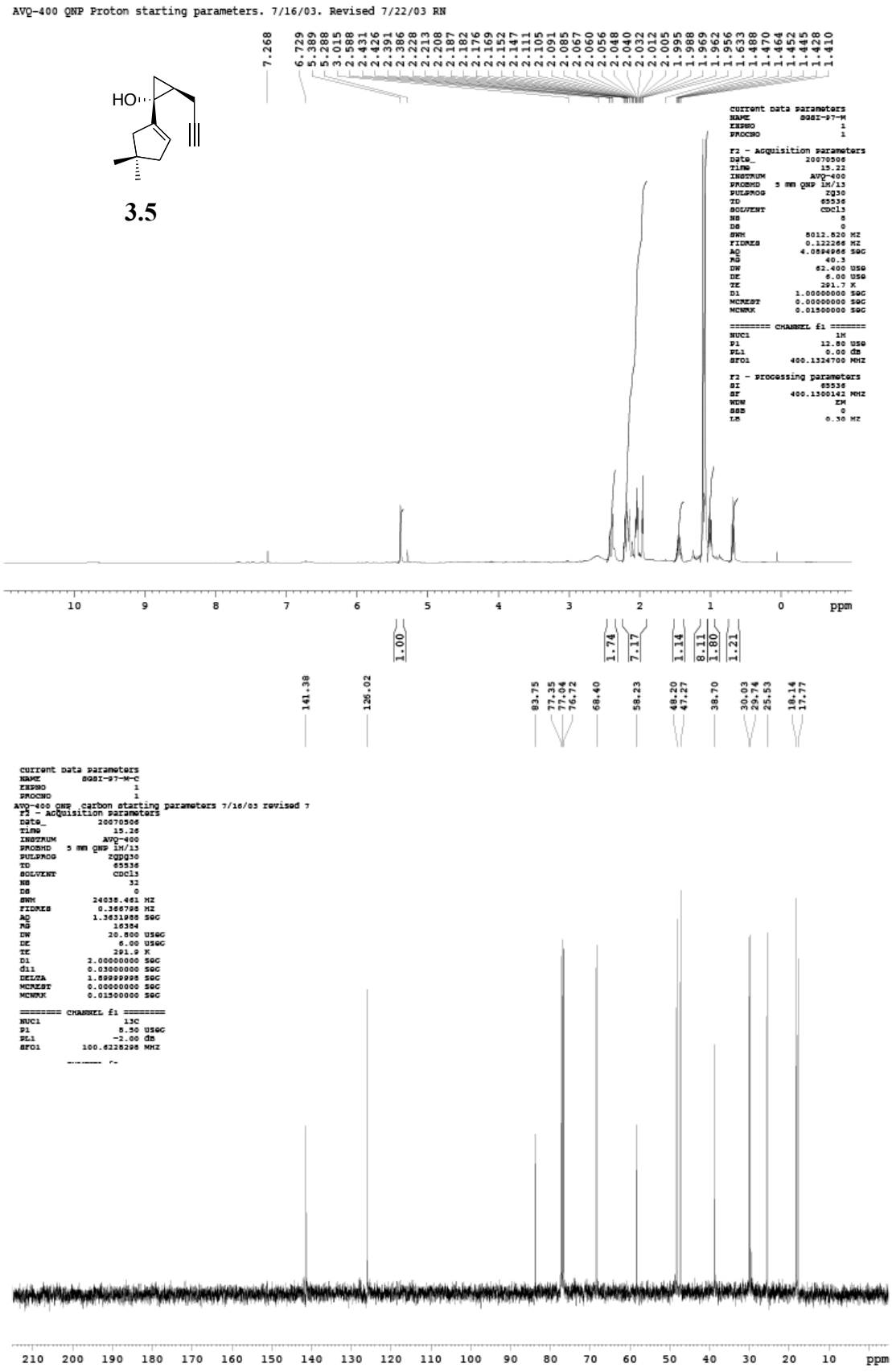
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3.5
7.268
6.729
5.389
5.288
3.015
2.588
2.431
2.426
2.391
2.386
2.228
2.213
2.208
2.187
2.182
2.176
2.169
2.152
2.147
2.111
2.105
2.091
2.085
2.067
2.060
2.056
2.048
2.040
2.032
2.012
2.005
1.995
1.988
1.969
1.962
1.956
1.633
1.488
1.470
1.464
1.452
1.445
1.428
1.410
current data parameters
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PROCNO 1
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Time 15.22
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PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 8012.820 HZ
FIDRES 0.122266 HZ
AQ 4.0894966 SEC
RG 40.3
DW 62.400 USEC
DE 6.00 USEC
TE 291.7 K
D1 1.00000000 SEC
MCREST 0.00000000 SEC
MCWRK 0.01500000 SEC
======== CHANNEL f1 ========
NUC1 1H
P1 12.80 USEC
PL1 0.00 dB
SFO1 400.1324700 MHZ
F2 - Processing parameters
SI 65536
SF 400.1300142 MHZ
WDW EM
SSB 0
LB 0.30 HZ
ppm
1.00
1.74
7.17
1.14
8.11
1.80
1.21
141.38
126.02
83.75
77.35
77.04
76.72
68.40
58.23
48.20
47.27
38.70
30.03
29.74
25.53
18.14
17.77
current data parameters
NAME 8GSI-97-M-C
EXPNO 1
PROCNO 1
AVQ-400 QNP carbon starting parameters 7/16/03 revised 7
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Date_ 20070506
Time 15.26
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PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 32
DS 0
SWH 24038.461 HZ
FIDRES 0.366798 HZ
AQ 1.3631988 SEC
RG 16384
DW 20.800 USEC
DE 6.00 USEC
TE 291.9 K
D1 2.00000000 SEC
d11 0.03000000 SEC
DELTA 1.89999998 SEC
MCREST 0.00000000 SEC
MCWRK 0.01500000 SEC
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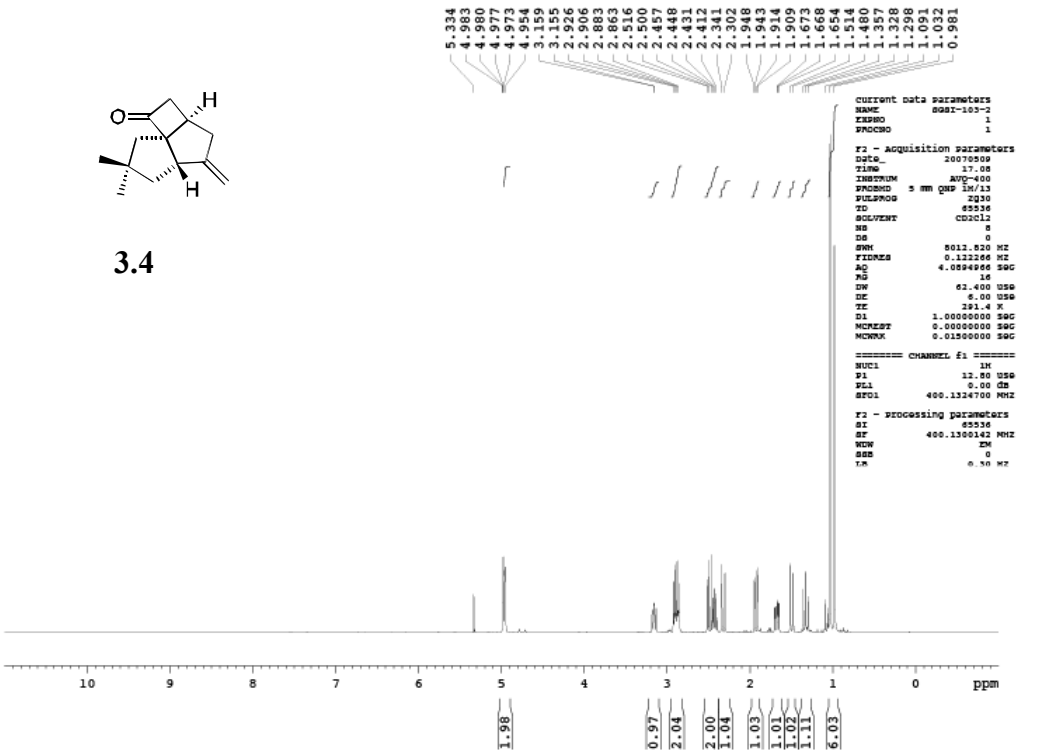
P1 8.50 USEC
PL1 -2.00 dB
SFO1 100.6228298 MHZ
ppm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4.980
4.977
4.973
4.954
3.159
3.155
2.926
2.906
2.883
2.863
2.516
2.500
2.457
2.448
2.431
2.412
2.341
2.302
1.948
1.943
1.914
1.909
1.673
1.668
1.654
1.514
1.480
1.357
1.328
1.298
1.091
1.032
0.981
O
H
H
3.4
current data parameters
NAME SQSI-103-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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TIME 17.08
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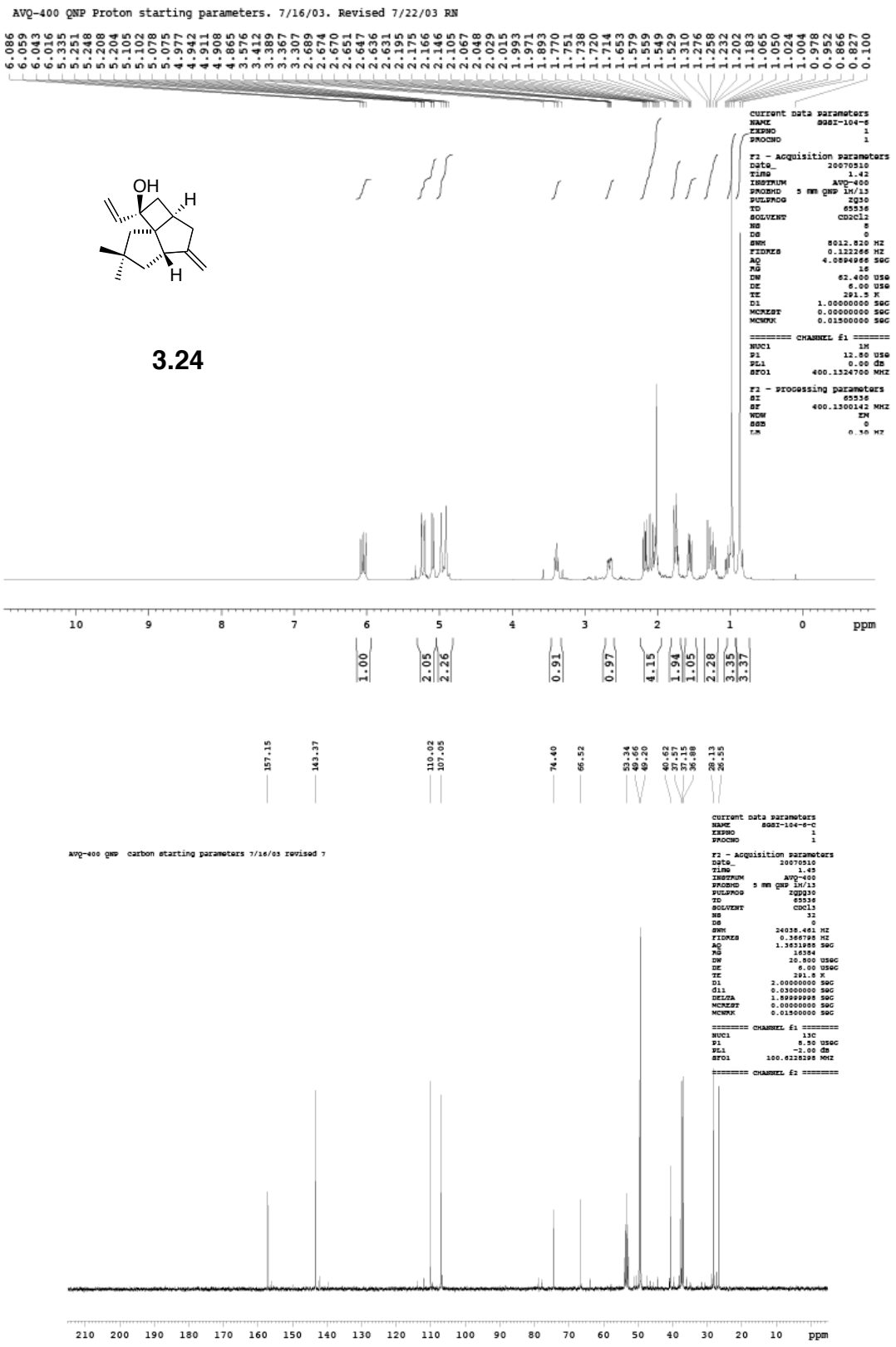
PROBHD 5 mm QNP 1H/13
PULPROG 2g30
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 5011.820 HZ
FIDRES 0.122266 HZ
AQ 4.0894966 SEC
RG 16
DW 62.400 USEC
DE 6.00 USEC
TE 291.4 K
D1 1.00000000 SEC
MCREST 0.00000000 SEC
MCWRK 0.01500000 SEC
======== CHANNEL f1 =======
NUC1 1H
P1 12.80 USEC
PL1 0.00 dB
SFO1 400.1324700 MHZ
F2 - Processing parameters
SI 65536
SF 400.1300142 MHZ
WDW EM
SSB 0
10
9
8
7
6
5
4
3
2
1
0
ppm
1.98
0.97
2.04
2.00
1.04
1.03
1.01
1.02
1.11
6.03
210.97
152.81
109.07
81.21
55.48
53.64
53.37
53.10
49.38
47.67
46.05
41.62
38.05
36.13
28.10
26.71
current data parameters
NAME SQSI-103-2-C
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070509
TIME 17.10
INSTRUM AVQ-400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 32
DS 0
SWH 24038.461 HZ
FIDRES 0.366795 HZ
AQ 1.3631988 SEC
RG 14384
DW 20.800 USEC
DE 6.00 USEC
TE 291.7 K
D1 2.00000000 SEC
d11 0.03000000 SEC
DELTA 1.89999998 SEC
MCREST 0.00000000 SEC
MCWRK 0.01500000 SEC
======== CHANNEL f1 ========
NUC1 13C
P1 8.50 USEC
PL1 -2.00 dB
SFO1 100.6228298 MHZ
======== CHANNEL f2 ========
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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H
H
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ppm
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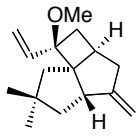
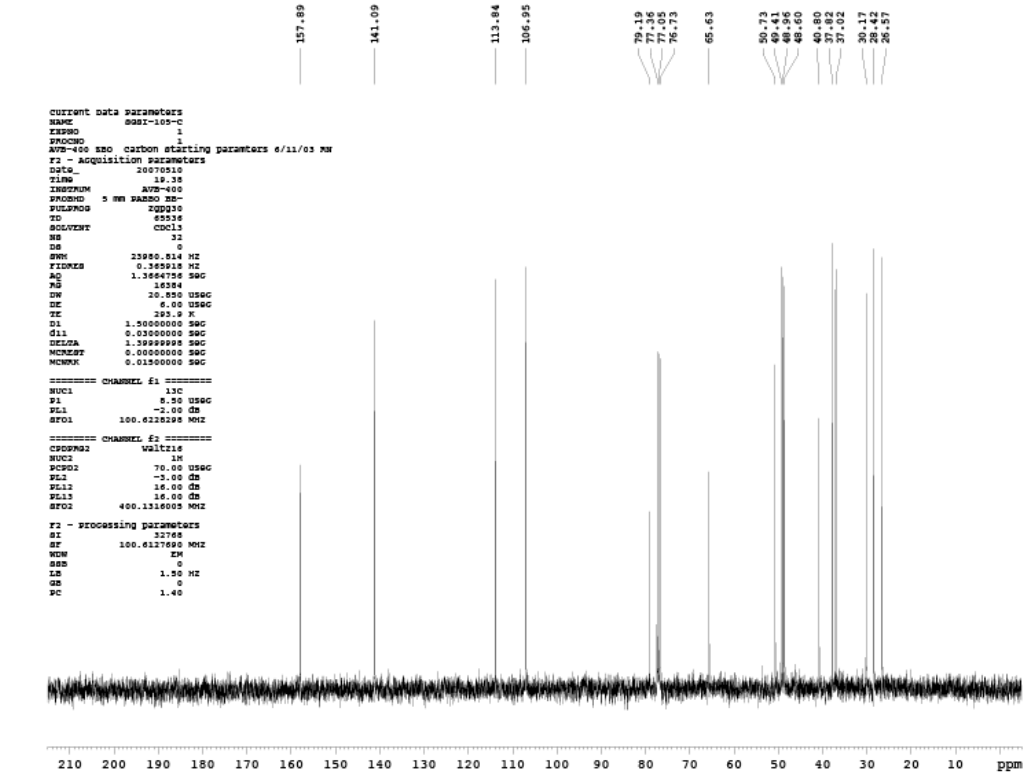
2.05
2.26
0.91
0.97
4.15
1.94
1.05
2.28
3.35
3.37
AVQ-400 QNP carbon starting parameters 7/16/03 revised 7
ppm

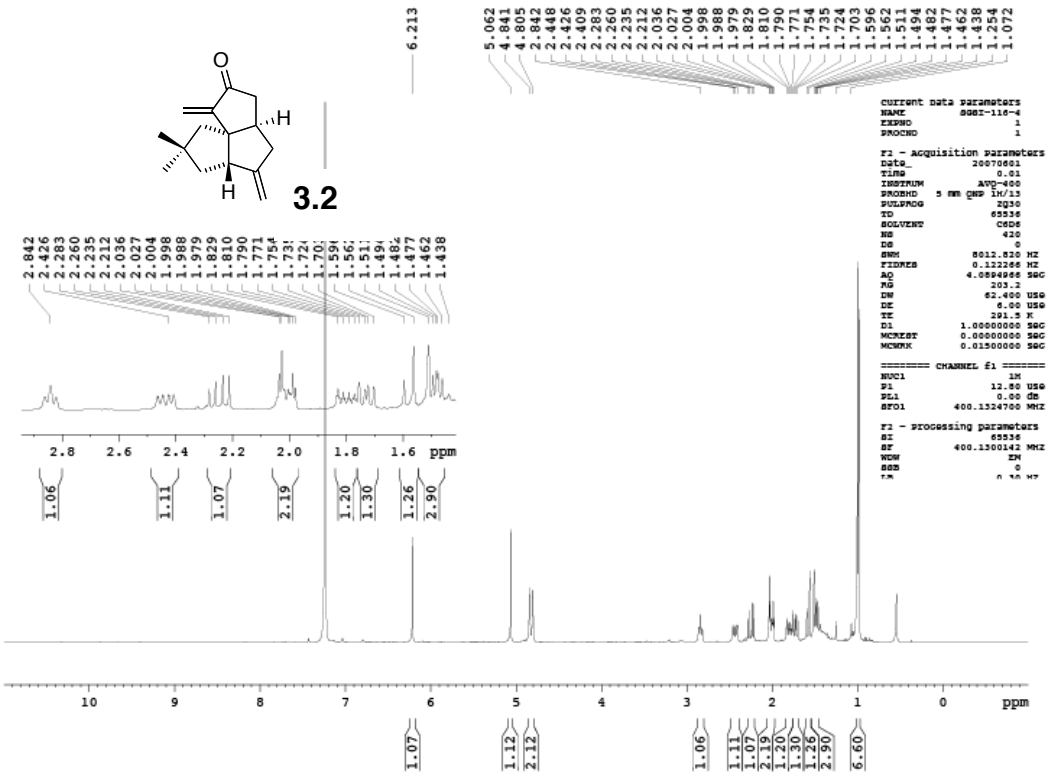
AVB-400 ZBO Proton starting parameters. 6/11/03 RN



3.25



AVQ-400 QNP Proton starting parameters. 7/16/03. Revised 7/22/03 RN



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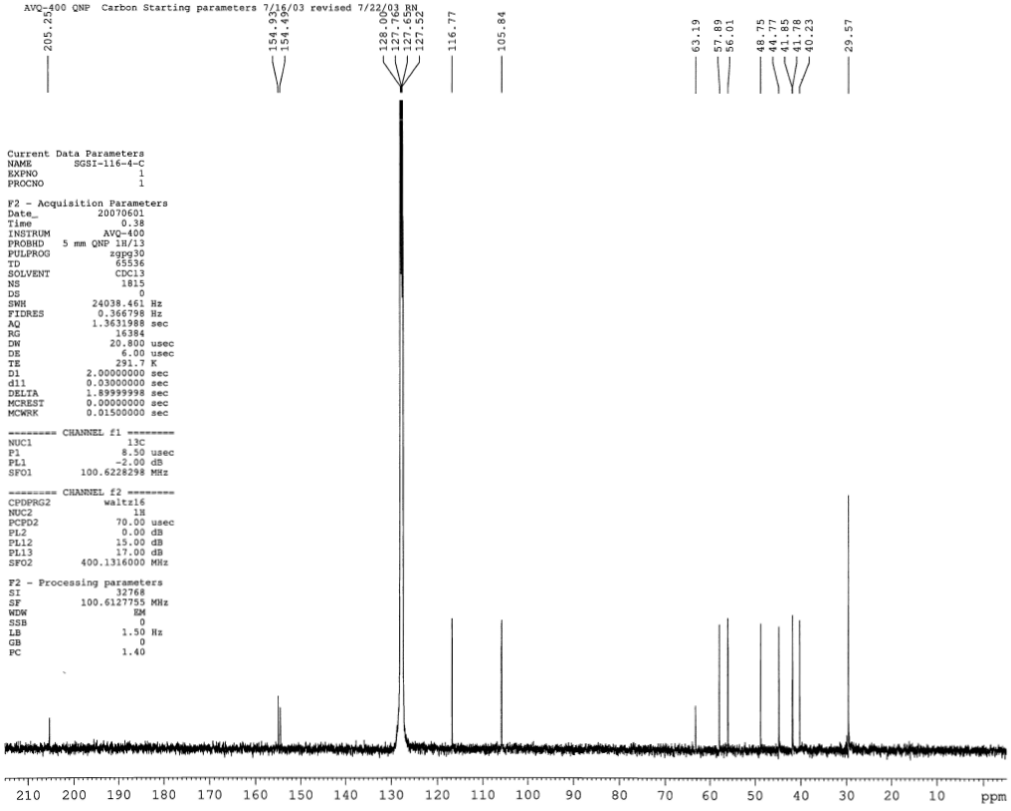

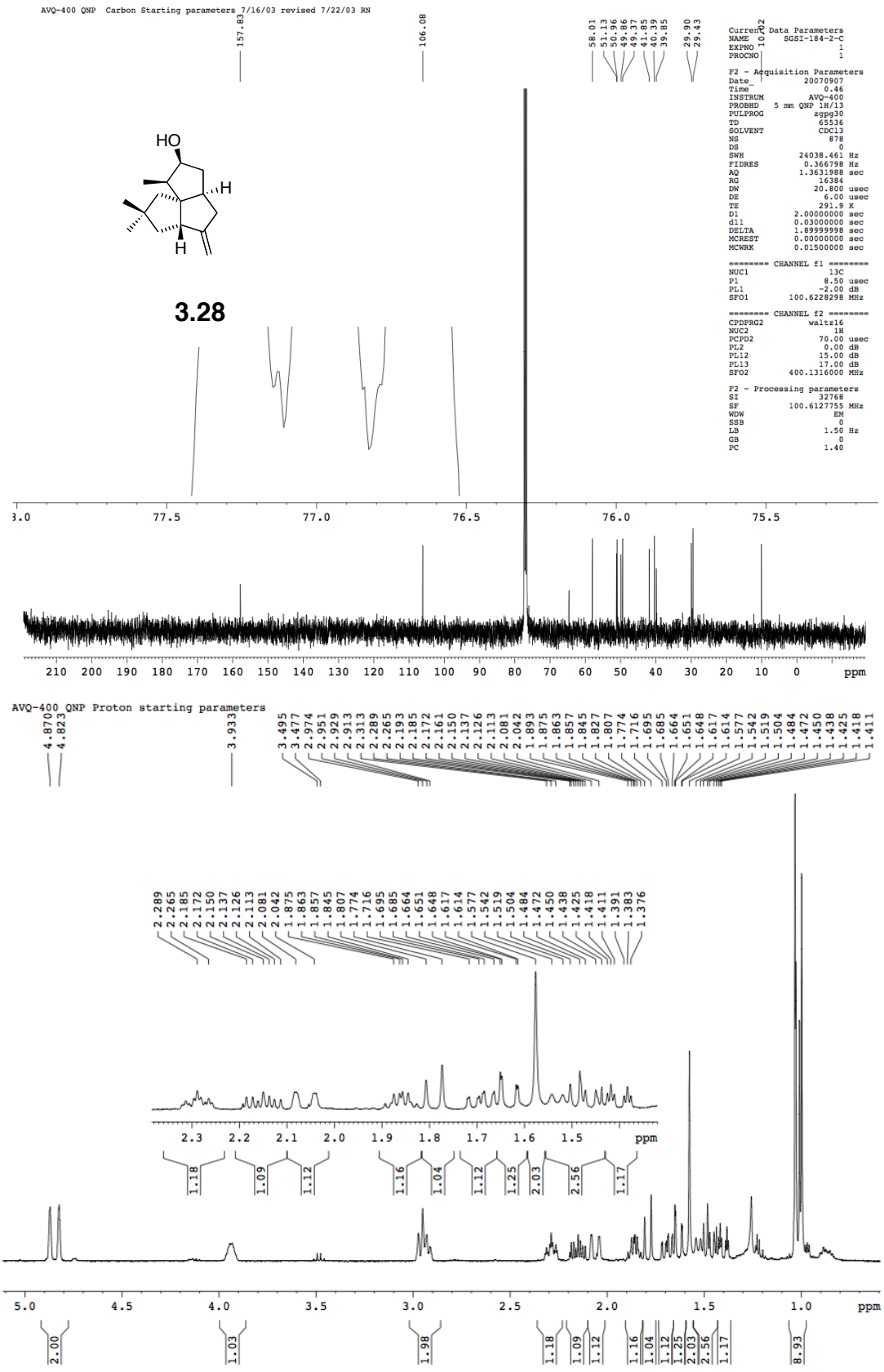
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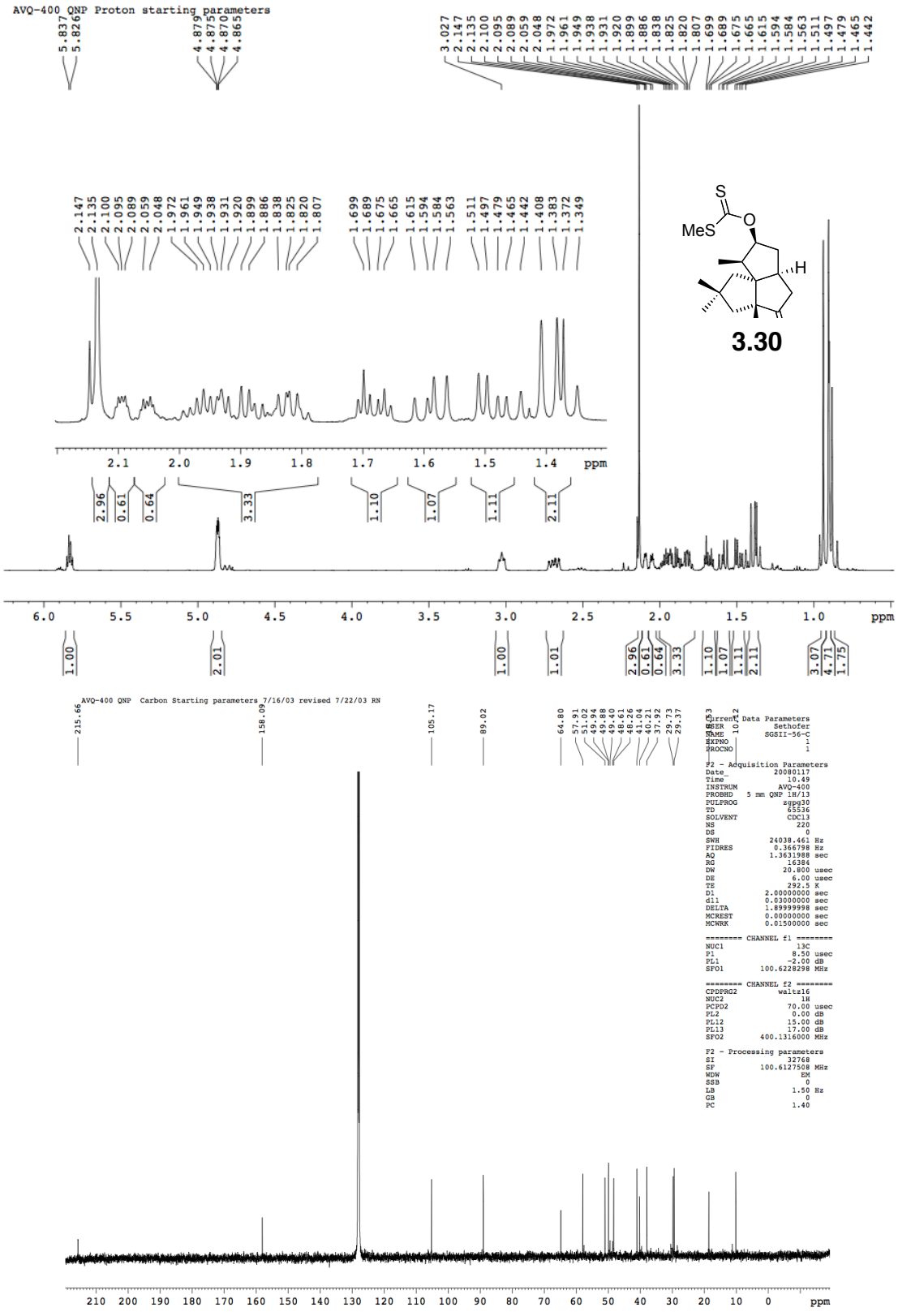
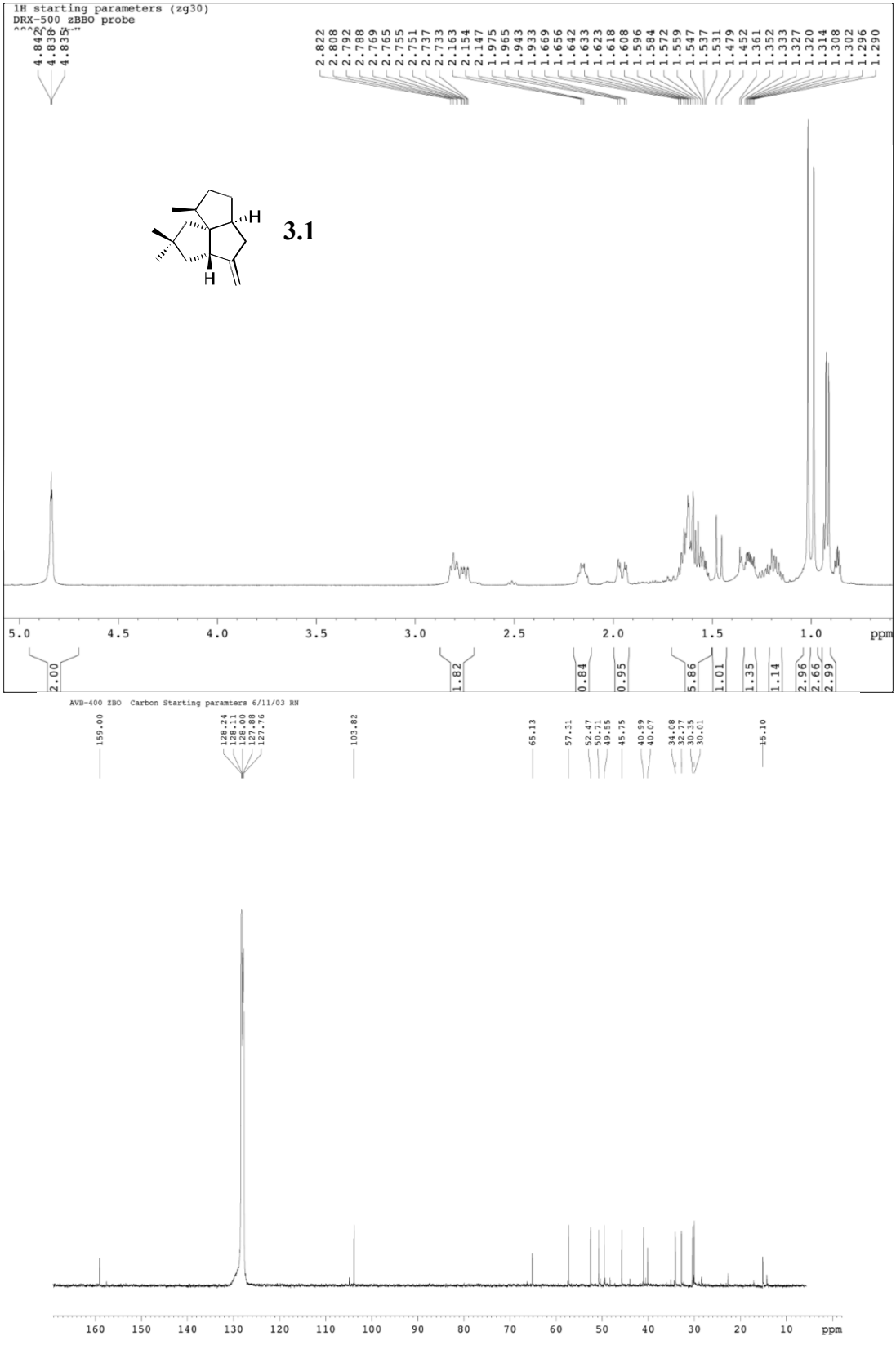
HO
H
H
3.28
AVQ-400 QNP Proton starting parameters
ppm


AVQ-400 QNP Proton starting parameters
MeS
S
O
H
3.30
ppm
AVQ-400 QNP Carbon Starting parameters 7/16/03 revised 7/22/03 RN


1H starting parameters (zg30)
DRX-500 zBBO probe
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4.838
4.835
2.822
2.808
2.792
2.788
2.769
2.765
2.755
2.751
2.737
2.733
2.163
2.154
2.147
1.975
1.965
1.943
1.933
1.669
1.656
1.642
1.633
1.623
1.618
1.608
1.596
1.584
1.572
1.559
1.547
1.537
1.531
1.479
1.452
1.361
1.352
1.333
1.327
1.320
1.314
1.308
1.302
1.296
1.290
H
H
3.1
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.00
1.82
0.84
0.95
5.86
1.01
1.35
1.14
2.96
2.66
2.99
AVB-400 ZBO Carbon Starting paramters 6/11/03 RN
159.00
128.24
128.11
128.00
127.88
127.76
103.82
65.13
57.31
52.47
50.71
49.55
45.75
40.99
40.07
34.08
32.77
30.35
30.01
15.10
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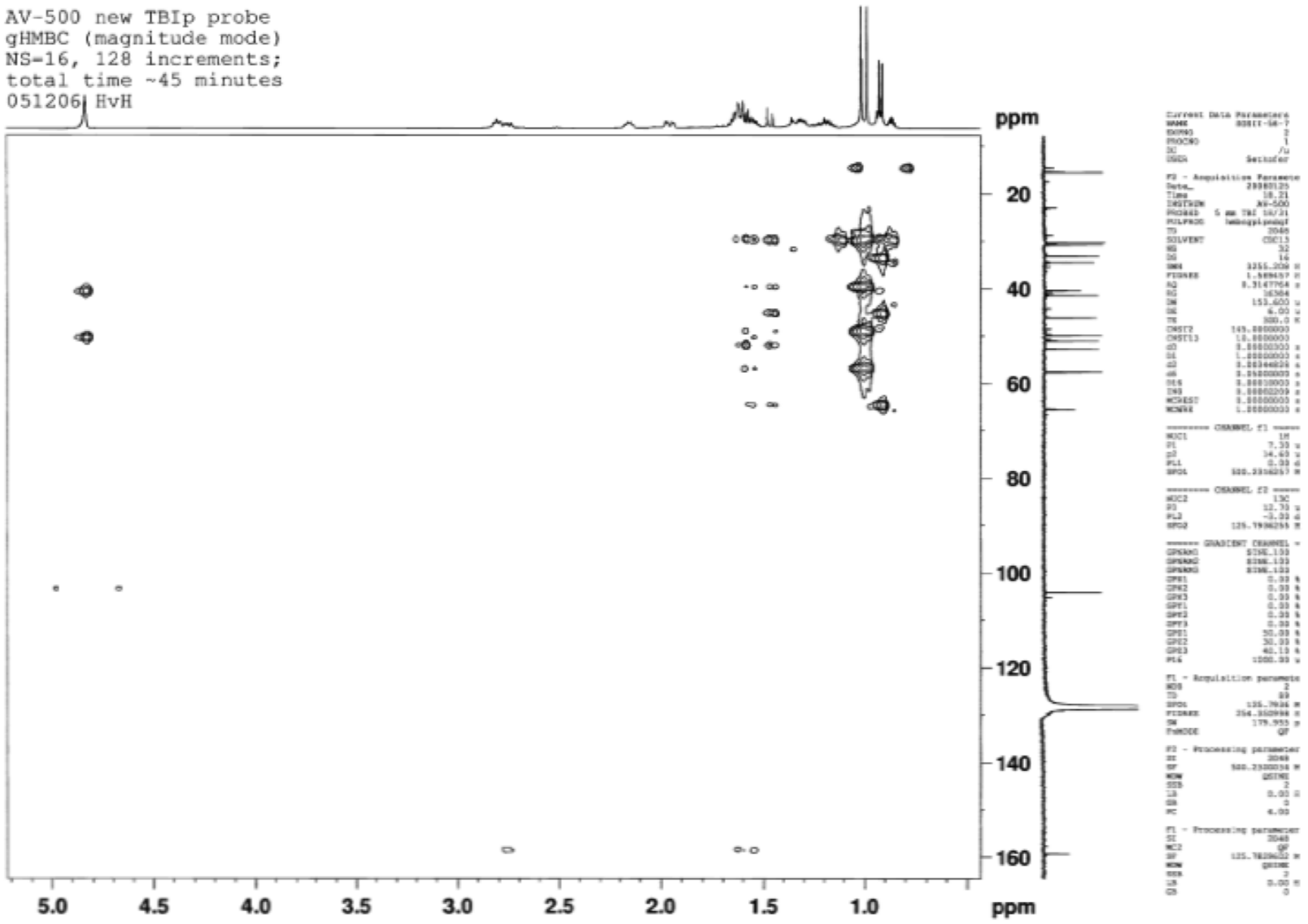
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


AV-500 new TBIp probe
gHMBC (magnitude mode)
NS=16, 128 increments;
total time ~45 minutes
051206 HvH
ppm
20
40
60
80
100
120
140
160
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

Chapter 4.

Interception of Reactive Intermediates Arising in the Gold(I)-Catalyzed Rautenstrauch Rearrangement

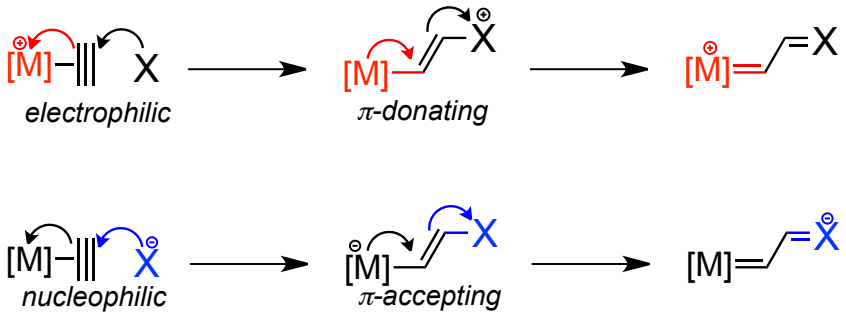
Chapter 4 describes efforts to expand the scope of the intramolecular trapping of cationic species generated by gold(I) complexes. The carbocationic intermediate arising in the gold(I)-catalyzed Rautenstrauch rearrangement of allyl propargyl esters was intercepted by pendant arene nucleophiles to generate diastereomerically pure functionalized hexahydro-1H-indene systems in excellent yields. The transformation proceeds with asymmetric induction when chiral bisphosphine gold(I) complexes are used as catalyst. Moreover, efficient chirality transfer was observed in the cyclization of enantioenriched substrates.

`

Introduction

Transition metal carbene complexes constitute an important class of organometallic reagents employed in a number of important transformations of both academic and industrial relevance. This includes olefin metathesis[1] and cyclopropanation[2] reactions, as well as various carbon-hydrogen functionalization[3] and intramolecular cascade processes.[3a, 4] While carbenoids are generally available through the decomposition of diazoalkanes by transition metal complexes,[2b, 5] limitations of diazo compounds such as competitive side-reactions, toxicity and their tendency to explode motivate research into alternative routes to metal carbene complexes.[6] One such approach to the *in-situ* generation of carbenoids which involves nucleophilic attack on carbon-carbon triple bonds activated by π-acidic transition metals with concomitant back-donation of electrons from the metal center (Scheme 4.1).[7]

Scheme 4.1. Cooperative Formation of Carbenes from Alkyne π-Complexes.



This pull-push mechanism has been proposed for the carbenoid reactivity displayed by a number of transition metals including tungsten,[8] rhodium,[9] ruthenium[10] and copper.[11] However, this mode of reactivity is most common in the post-lanthanide, late transition metals platinum and gold.[12] The reactivity pattern depicted in Scheme 4.1 is a consequence of the relativistic modification of orbital energies that is characteristic of the chemistry of gold, as discussed in Chapter 1.

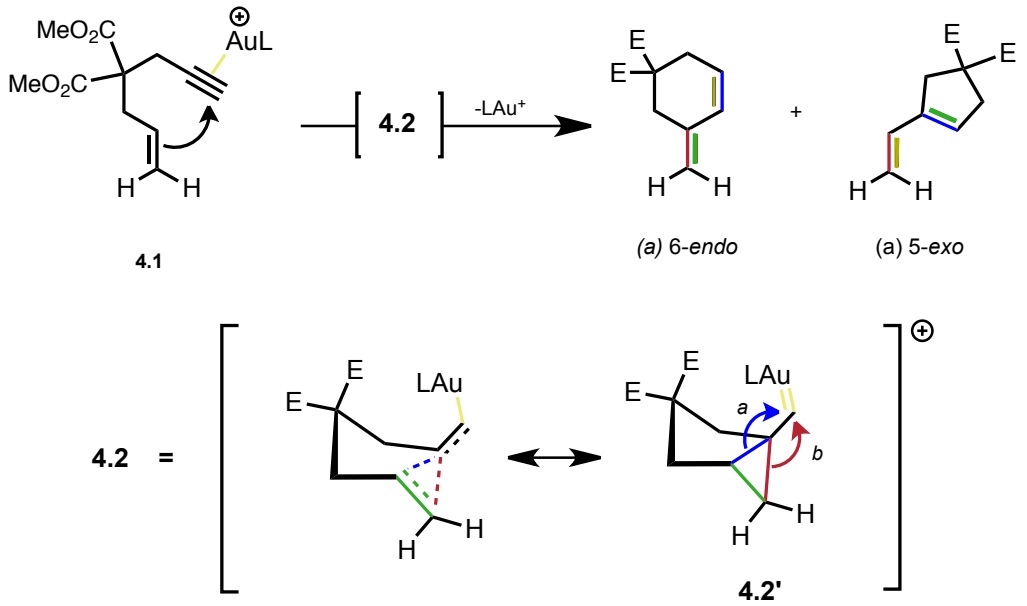
Tunable phosphinegold(I)[13] catalysts, in particular, capitalize on their tendency to induce electrophilic attack at hydrocarbon ligands, while stabilizing developing charge together with a reluctance to engage in reactivity involving formal oxidation state change.

Carbenoid Reactivity

In spite of the variety of mechanistic studies reported,[14] a detailed understanding of the carbenoid reactivity exhibited by gold complexes remains elusive. What is generally accepted, however, is the ability to tune the nature of phosphinegold(I) catalysts in response to their stereoelectronic environment[15]. Variation of the substrate,[14a] ancillary ligand,[13, 16] and other parameters, such as the choice of solvent,[17] can influence the reaction pathways catalyzed by gold.

The degree of carbenoid character exhibited by gold intermediates depends on a complementary electronic interaction by the nucleophilic component (Scheme 4.1). Nucleophiles with the capability to stabilize the donation of negative charge associated with the carbenoid π-bonding component stabilize carbenoid reactivity in organogold species, and hopefully will provide a means to develop new synthetic methodology.

Scheme 4.2. Enyne Cycloisomerization via Cyclopropyl Carbene Rearrangement.

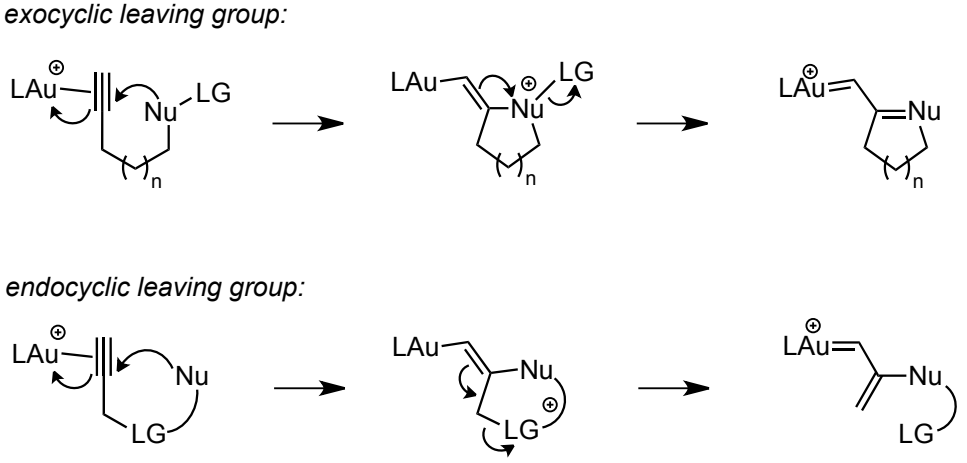


The enyne cycloisomerization reaction provides an example of the interaction of a gold π-complex with a simple olefin. Echavarren reported the conversion of enyne **4.1** to a 7:1 mixture of two cyclic dienes using $Ph_3PAuSbF_6$ (Scheme 4.2).[18] Intramolecular attack of the alkene generates a delocalized

carbocation with positive charge buildup at the olefinic carbons. The intermediate responsible for product formation is represented by resonance hybrid **4.2**, with limiting structure **4.2'** representing stabilization of the cation by the 5*d* orbitals on gold. The observed product distribution may be rationalized by σ-bond migration toward the electron poor carbon in **4.2'** by either path *a* or *b*, accompanied by fragmentation of the distal cyclopropane bond, in a net methylene transfer to the electrophilic carbenoid.[19] Protonation of the σ-bound gold(I) species then regenerates the catalyst and releases the diene product.

A number of more practical methods for exploiting the carbenoid reactivity of gold have been developed in recent years. The use of more polarized, heteroatom-containing nucleophiles to differentiate the σ-donating and π-accepting components allows for carbene formation in a more regiocontrolled manner. A suitable nucleofuge acting in concert with π-electron donation by gold coincides with gold carbene formation, as depicted schematically in Figure 4.1.[20]

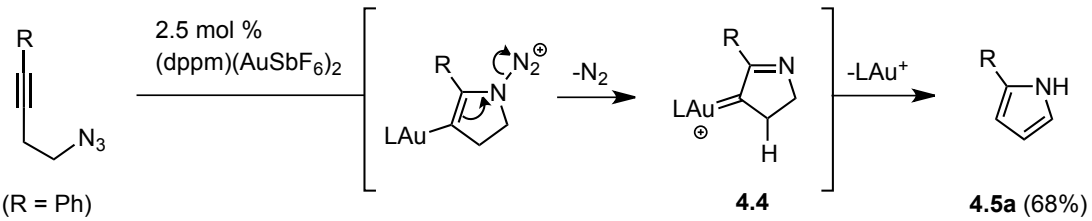
Figure 4.1. Au(I)-Carbene Formation Promoted by Bond Fragmentation.



In both examples, the vinylgold(I) species formed by intramolecular attack of a tethered nucleophile donates electrons through the π-system, terminating in a σ-bond cleavage with departure of two electrons. In the first case, an exocyclic leaving group bound directly to the nucleophile is displaced during the formation of a formal double bond to the nucleophilic atom. A second mode of carbene formation involves expulsion of a propargylic leaving group and concomitant olefin formation. When the nucleophile is tethered to the leaving group as in Figure 4.1, this process amounts to a net 1,2-migration of the propargylic substituent.

The acetylenic Schmidt rearrangement described by the Toste group[21] provides a particularly cogent example of this type of reactivity. Cyclization of homopropargyl azides **4.3a** - **4.3b** promoted by cationic gold(I) proceeds in good yield, providing substituted pyrroles under mild conditions. In this process, the azide group acts as a latent amine nucleophile bearing a dinitrogen leaving group. Attack upon the activated alkyne promotes loss of N_2 via backbonding by gold to give

Scheme 4.3. Gold(I)-Catalyzed Acetylenic Schmidt Rearrangement.



4.3a (R = Ph)
4.3b (R = 2-MeO-C_6H_4)
4.3c (R = ^{n}Hex)

4.4

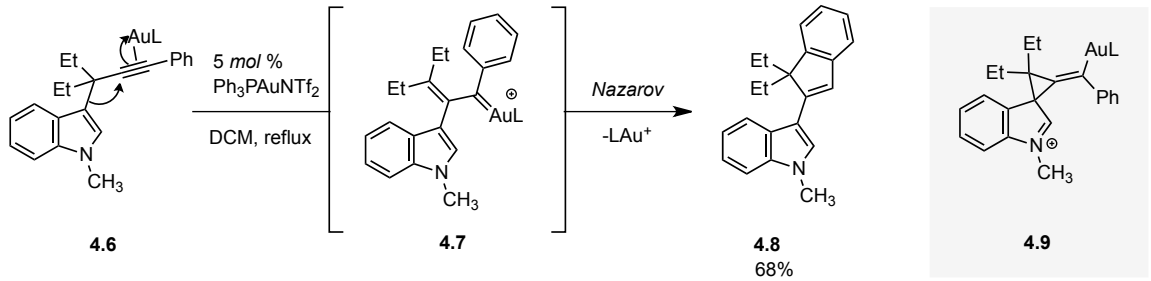
4.5a (68%)
4.5b (88%)
4.5c (76%)

imino carbene **4.4**. This intermediate relaxes by a 1,2-hydride shift / elimination process to an intermediate 2*H*-pyrrole, which then spontaneously isomerizes to the 1*H* isomer. As represented by products **4.5a** – **4.5c**, a variety of aryl and aliphatic groups are tolerated on the acetylene group, and furthermore, substitution at the methylene positions was also demonstrated.

An unusual 1,2-migration of 3-propargyl indoles was recently employed by Sanz *et al.* to generate key intermediate **4.7** in a tandem rearrangement / Nazarov cyclization process.[22] Initially, a mechanism was proposed involving cyclization of indole onto the activated alkyne to give **4.9,** followed by the gold-assisted rupture of the cyclopropane ring (Scheme 4.4).

The intermediacy of vinylidene spirocycle **4.9** was supported by density functional calculations.[23] However, based on the scarcity of 3-*exo*-dig cyclizations in the literature[24], the direct formation of **4.7** by a 1,2-Meerwein shift of **4.6** promoted by back donation from gold may provide a better representation of the process.

Scheme 4.4. Tandem 1,2-Indole Migration / Aura-Nazarov Cyclization.



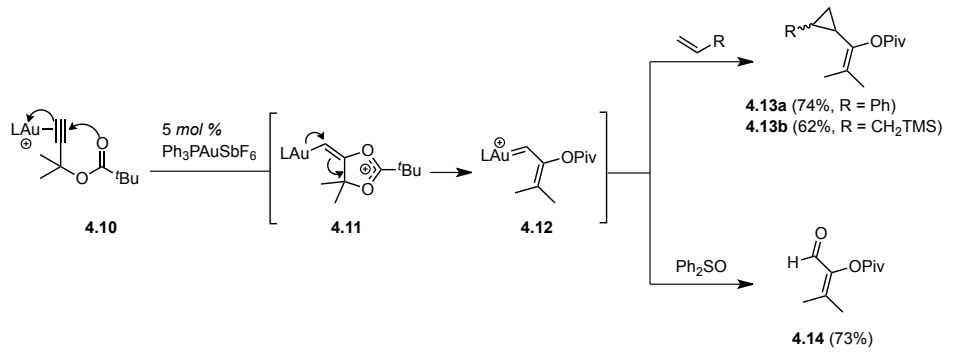
Gold(I)-Carbene Complexes from Propargylic Esters

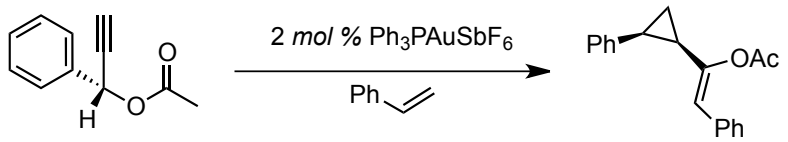
Propargylic esters have been widely employed to access carbenoid reactivity in platinum[25] and gold[26] catalysis. The intramolecular cyclopropanation of **4.10**, for example, was demonstrated by the Toste group for a variety of aromatic (**4.13a**) and aliphatic (**4.13b**) olefins.

The 5-*exo*-dig cyclization of the ester carbonyl oxygen onto the gold-activated alkyne and subsequent opening to give the rearranged ester **4.12** is proposed to involve charge stabilization by the transient carboxonium species **4.11**.[26b] Intramolecular carbene transfer from **4.12** to the olefin led to catalyst turnover and provided the rearranged cyclopropane product **4.13**.[27]

Additional support for intermediate **4.12** comes from experiments using diphenylsulfoxide to trap the carbenoid species in an oxygen transfer process, providing aldehyde **4.14** in 73% yield.[28] Furthermore, the complete racemization observed in the cyclization of enantiomerically enriched acetate **4.15** is consistent with full cleavage of the carbon-oxygen and thus a fully formed carbene. The diastereoselectivity of this process, evident in **4.16**, is in accord with previously reported models for cyclopropanation of olefins by transition metal carbene complexes.[29]

Scheme 4.5. Cyclopropanation and Oxidation of Gold(I) Carbene Complexes.





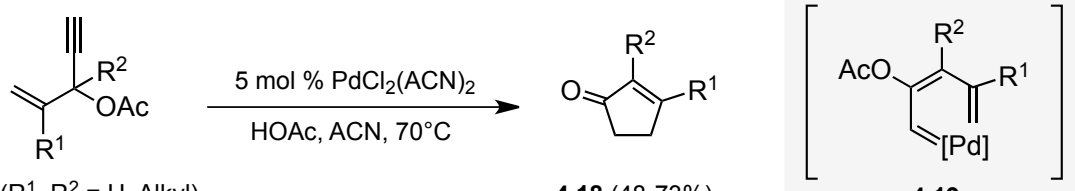
(4.1)

Cyclopentanones by the Gold(I)-Catalyzed Rautenstrauch Reaction

The small barrier to conformational exchange of cyclopentane relative to cyclohexane systems, and the lack of highly general preparatory methods comparable to the Diels-Alder reaction or the Robinson annulation contributes to the relative shortfall of stereocontrolled cyclopentannulation methodology. Substituted cyclopentanones are particularly attractive targets for asymmetric methodology development due to the synthetic versatility of the ketone functionality in subsequent diastereoselective transformations. Their presence in a wide range of natural products, such as triquinanes and various other terpenoids, cyclopentanoid antibiotics, the prostaglandin and prostacyclin eicosanoids, as well a number of anticancer therapeutic agents[30] further demonstrates the importance of enantioselective cyclopentanone-forming processes.

Several asymmetric versions of existing cyclopentanone formations have been developed, including the Pauson-Khand reaction[31,32] and Nazarov cyclization.[33,34] Another approach involves the [3+2] cycloaddition of 1,3-carbon dipoles.[35] While carbenes have been used to form cyclopentanones by carbon-hydrogen insertion of α-diazo carbonyl species,[36] the cyclization of olefins onto carbenes derived from alkynes has been more limited.

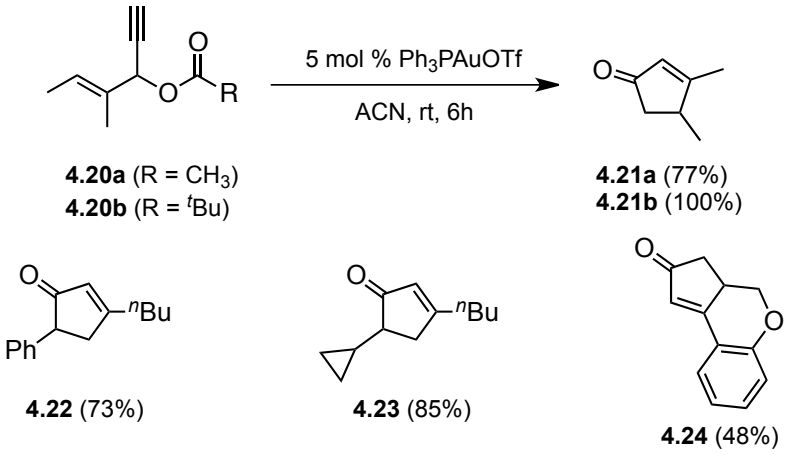
Scheme 4.6. The Rautenstrauch Rearrangement of Allyl Propargyl Acetates.



4.17 (R^1, R^2 = H, Alkyl) **4.18** (48-73%) **4.19**

In 1984, Rautenstrauch reported on the rearrangement of α-vinyl propargylic acetates **4.17** by palladium(II) complexes (Scheme 4.6). While this transformation was limited in scope to cyclopentanones substituted at the vinylic positions, it represented an efficient and mechanistically novel cyclization process. Rationalization was presented involving intermediate **4.19**, marking the first time a transition metal carbene arising from a 1,2-ester migration was proposed as a reaction intermediate. Attack of the pendant olefin at the electrophilic carbenoid center of **4.19** then conceivably leads to product formation.

Scheme 4.7. Au(I)-Catalyzed Rautenstrauch Rearrangement.



4.20a (R = CH_3)
4.20b (R = ^{t}Bu)

4.21a (77%)
4.21b (100%)

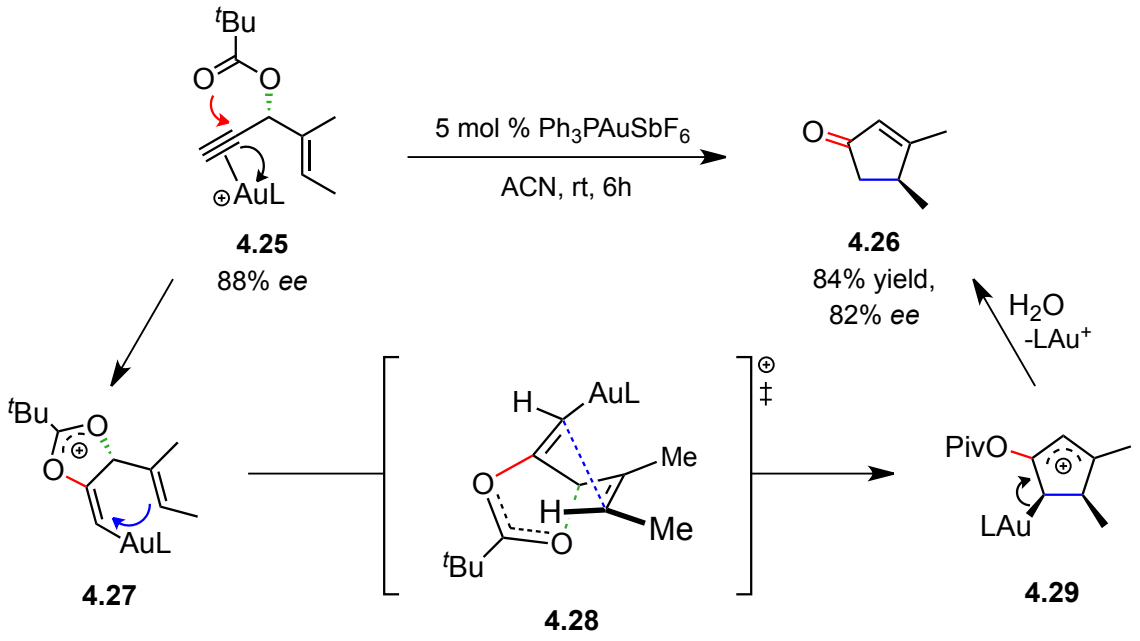
4.22 (73%) **4.23** (85%) **4.24** (48%)

In light of the similarity of **4.19** to intermediate **4.12** proposed for the intramolecular cyclopropanation process (Scheme 4.5), workers in the Toste lab began a study of the gold(I)-catalyzed Rautenstrauch rearrangement as part of efforts to uncover carbene reactivity in phosphinegold(I) complexes. Cyclization of acetate **4.20a** proceeded in the presence of 5 mol % $Ph_3PAuOTf$ in acetonitrile to give **4.21a** in 77% yield,[37] which was presumably generated by hydrolysis of the

intermediate vinyl ester by adventitious water. Using the more hindered pivalate ester gave quantitative conversion of **4.20b** to **4.21b**. The reaction was tolerant to substitution at the acetylenic (**4.22**) and both vinylic (**4.23**, **4.24**) positions (Scheme 4.7).

Efficient chirality transfer was observed in this process for enantioenriched pivalate esters. When a sample of substrate **4.25** of 88% *ee* was cyclized by $Ph_3PAuSbF_6$, the resulting enone **4.26** was formed in 84% *ee*. This observation casts doubt onto a mechanism involving a fully-formed gold carbene **4.30** (Scheme 4.8). More specifically, it implies that some degree of the initial carbon-oxygen bond from the chiral center of **4.25** remains in the transition state. Alternatively, if carbon-oxygen bond cleavage should occur first, cyclization must be faster than the rate of bond rotation.

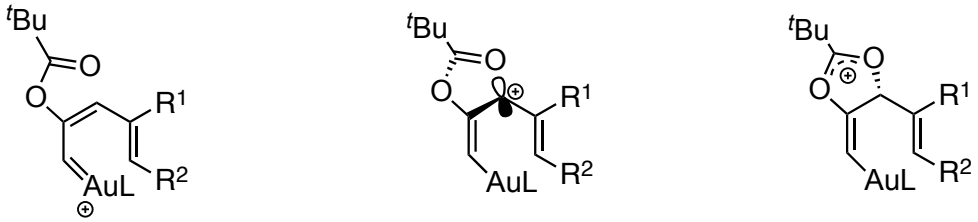
Scheme 4.8. Au(I)-Mediated Chirality Transfer in the Rautenstrauch Reaction.



Helical structure **4.28** was proposed to rationalize the transfer of chiral information in the formation of the methine group of **4.29**. Then, upon activation of the alkyne unit, a 1,2-pivalate migration is initiated, forming vinylgold(I) species **4.27**. Upon cyclization, cationic species **4.29** is formed and then undergoes elimination of gold to regenerate the catalyst. Spontaneous hydrolysis of the ester

and tautomerization then provides enantiomerically enriched product **4.26**. High levels of chirality transfer were demonstrated for various cyclic olefin substrates as well. In a subsequent theoretical analysis reported by Faza *et al.*,[38] cyclization was proposed to occur not from carboxonium **4.32,** but rather the short-lived, helically chiral free carbenium ion **4.31** in a center-to-helix-to-center transfer of chirality (Figure 4.2).

Figure 4.2. Possible Transition-State Structures for the Cyclization of **4.25**.



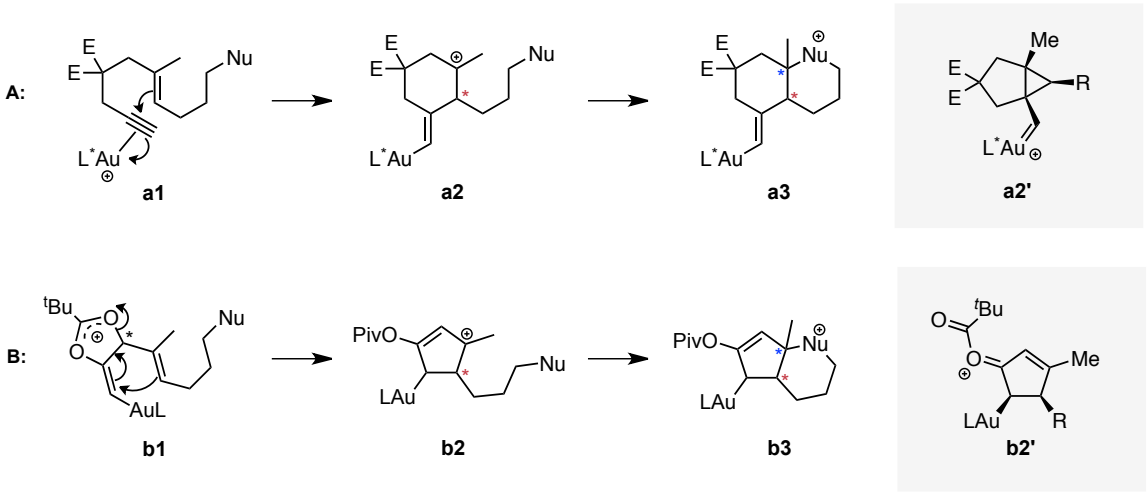
4.30 **4.31** **4.32**

Development of a Tandem Rautenstrauch / Friedel-Crafts Cyclization

We were interested in exploring the potential synthetic applications of the chirality transfer observed in the gold(I)-catalyzed Rautenstrauch rearrangement. Considering the relative ease of generating enantiomerically enriched secondary alcohols,[39] our goal was to achieve chirality transfer in a gold(I)-catalyzed method for cascade cyclization capable of forming multiple chiral centers.

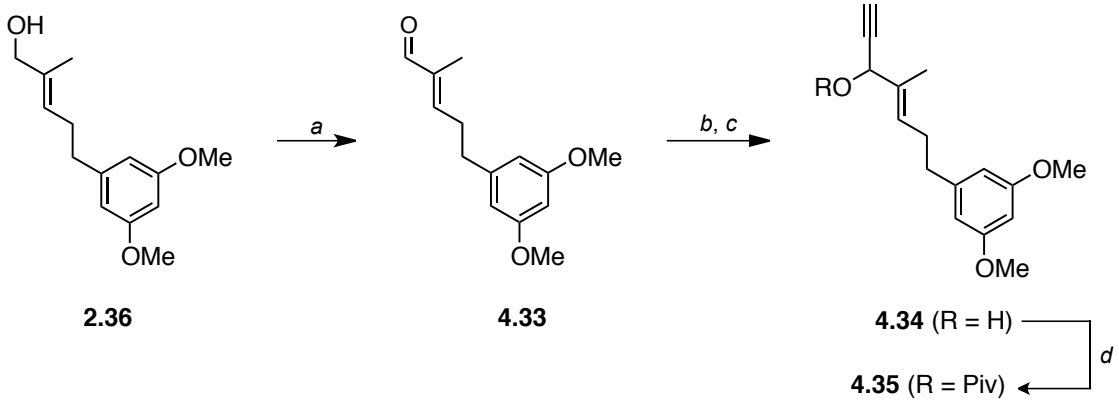
Figure **4.3-A** provides a schematic depiction of the tandem 1,6-enyne cyclization described in Chapter 2.[40] The cyclized pivaloxyallyl cation **4.29** (Scheme 4.8) may be envisioned in analogy (i.e. as **b2**) to the gold-stabilized cation **a2** arising from enyne **a1**. Thus, interception of **b2** by a suitable pendant trap should divert the reactivity depicted in Scheme 4.8 (**4.29 → 4.26**). We anticipated a stereospecific cyclization similar to **a2 → a3** would be operative for species **b2**, providing a mechanism for propagation of the chiral information in **b1** to a second prochiral carbon atom. The structures **a2** and **b2** represent relevant canonical forms corresponding to stabilized cations **a2'** and **b2'**, respectively.

Figure 4.3. Diastereoselectivity in Tandem Cyclization Processes



In order to evaluate the potential for a Rautenstrauch-initiated polycyclization, an appropriate substrate was prepared initially from an α,β-unsaturated aldehyde **2.36** (Scheme 4.9). Allylic oxidation provided unsaturated aldehyde **4.33**. Acetylide addition followed by deprotection with TBAF provided propargyl allylic alcohol **4.34**. Acylation with pivaloyl chloride catalyzed by DMAP provided substrate **4.35**.

Scheme 4.9. Preparation of Tandem Rautenstrauch / Freidel-Crafts Substrate.[a]

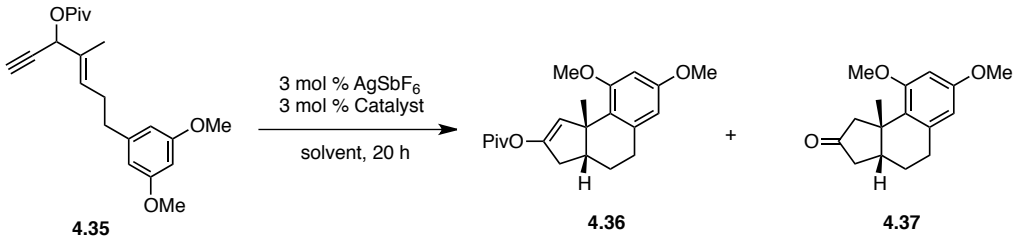


[a] Reagents and conditions: (a) 10 equiv. MnO_2, CH_2Cl_2, rt, 18 h, 92%. (b) LiCCTMS, THF, -78°C, 89% (c) TBAF, THF, 86%. (d) PivCl, DMAP, pyr, 92%.

Cyclization of **4.35** for 20 hours under the optimized conditions for the gold(I)-catalyzed Rautenstrauch produced angularly fused tricyclic pivalate **4.36**[41] in

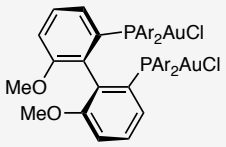
a 5:1 ratio with the corresponding hydrolysis product **4.37**, in contrast to the much more labile conjugated vinyl pivalate esters generated in the untrapped Rautenstrauch rearrangement (Figure 4.4).[42] Changing the solvent to dichloromethane gave similar yields of both **4.36** and **4.37**, requiring only 3 hours for full conversion. It was found that hydrolysis could be surpressed by treatment of a benzene solution of **4.35** with catalyst generated in DCM. Thus, **4.36** was formed in 84% yield within 3 hours.

Figure 4.4. Tandem Rautenstrauch / Friedel-Crafts Cyclization.



Solvent	Catalyst	Time (h)	% **4.36** (**4.37**)[a]
ACN	Ph_3PAuCl	20	75 (13)
DCM	Ph_3PAuCl	3	72 (10)
PhH / DCM[b]	Ph_3PAuCl	3	84 (<5)
PhH	(R)-**4.38**[c]	3	97 (0)

[a] Yields det. by ^1H NMR vs. 9-bromophenanthrene.
[b] In a 3:1 ratio. [c] Product formed in 34% *ee*.

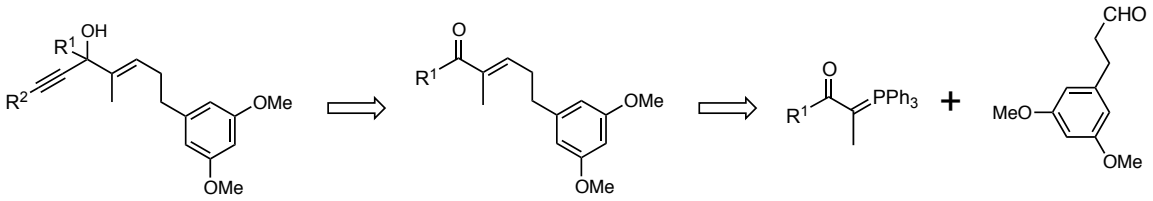


4.38, Ar = 3,5-(^{t}Bu)$_2$C$_6$H$_3$

Quantitative product formation was achieved using the cation derived from (R)-**4.38**, generating vinyl pivalate **4.36** in 34% *ee*. The observation of asymmetric induction arising from a chiral, racemic substrate corresponds to incomplete chirality transfer, suggesting an achiral pathway is operative under these conditions, presumably involving carbenoid intermediate **4.30** (Figure 4.2).

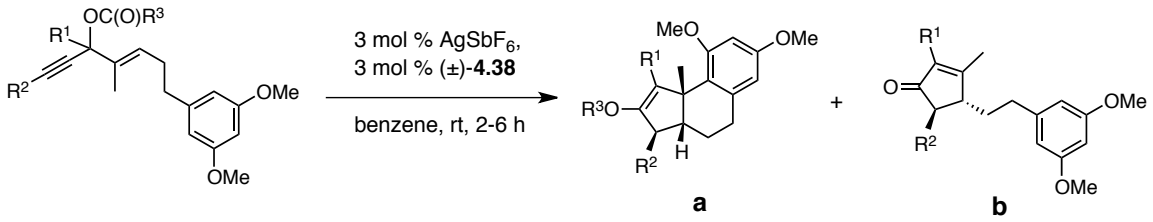
Several analogs of **4.35** were prepared to examine the effect of substitution on the cyclopentane ring (Scheme 4.10). The *trans*-selective coupling of preformed stabilized ylides with 3,5-dimethoxyphenylpropionaldehyde, followed by addition of acetylide ion provides a convenient approach to diversified allyl propargyl alcohols. Pivalate and benzoate formation proceeded without consequence for secondary alcohols, however, beyond the simple acetate, acylation of tertiary hydroxyl groups failed, even under anionic conditions.[43]

Scheme 4.10. Synthetic Approach to Arene-Terminated Rautenstrauch Substrates.



The substituent effects using catalyst **4.38** to prepare tricycle **a** are summarized in Table 1. The competing product **b** is the cyclopentenone arising from a failure to intercept the cationic Rautenstrauch intermediate. Somewhat surprisingly, changing the solvent from benzene (entry 1) to fluorobenzene (entry 2) led to the formation of cyclopentanone **b** as a significant side-product. The benzoate ester cyclized in benzene with exclusive cation interception (entry 3), although greater hydrolysis was observed, accounting for the reduced yield relative to pivalate **4.36**. Generally, nonterminal alkynes interfere with cation trapping. Poor yields of **a** were obtained for methyl (entry 5) and benzyl (entry 4) substituted alkynes; with the phenylacetylene providing only product **b** (entry 6). Finally, substitution at the α-carboxy position also hindered arene trapping, giving a 2:3 ratio of **a** to **b** (entry 7).

Table 4.1. Interception of Rautenstrauch Intermediate.

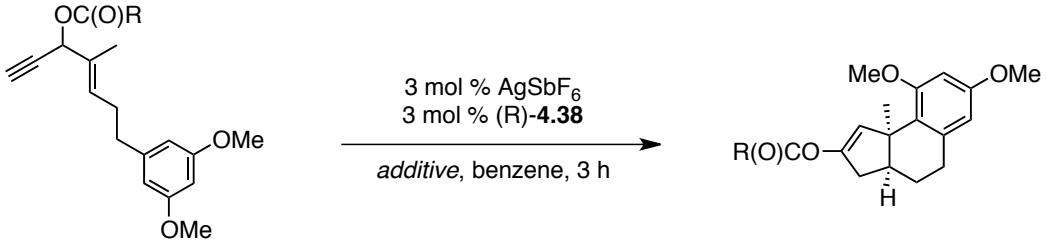


Entry	Solvent	R^1	R^2	R^3	Yield a (%)[a]	Yield b (%)[a]
1	benzene	H	H	^{t}Bu	97	0
2	fluorobenzene	H	H	^{t}Bu	61	36
3	benzene	H	H	Ph	75	0
4	benzene	H	Bn	^{t}Bu	13	71
5	benzene	H	Me	^{t}Bu	14	68
6	benzene	H	Ph	^{t}Bu	0	86
7	benzene	Me	H	Me	38	52

[a] Yields determined by ^{1}H NMR vs. 9-bromophenanthrene.

Proceeding with esters **4.35** and **4.39**, a study of the stereoselectivity of the Rautenstrauch polycyclization was initiated. The asymmetric induction observed using catalyst (R)-**4.38** and racemic **4.36** (Figure 4.4) was further examined. Catalyst **4.38** provided the best results in an evaluation of ligand effects on enantioselectivity, and no further improvement was observed by variation of solvent or counterion. The optimized conditions for the enantioselective cyclization of pivalate and benzoate esters is presented in Table 4.2. An increase in enantioselectivity was observed for **4.35** in the presence of 5 eq. trifluoroethanol, giving product in 52% *ee* (entry 2).[44] Reducing the amount of additive to 10 mol % provided the same result (entry 3). However, using increased amounts diminished the effect somewhat (entry 4). No change in selectivity was observed with either ethanol or phenol additives (entries 5 and 6).

Table 4.2. Additive Effects on Enantioselectivity.



4.35 (R = ^{t}Bu)
4.39 (R = Ph)

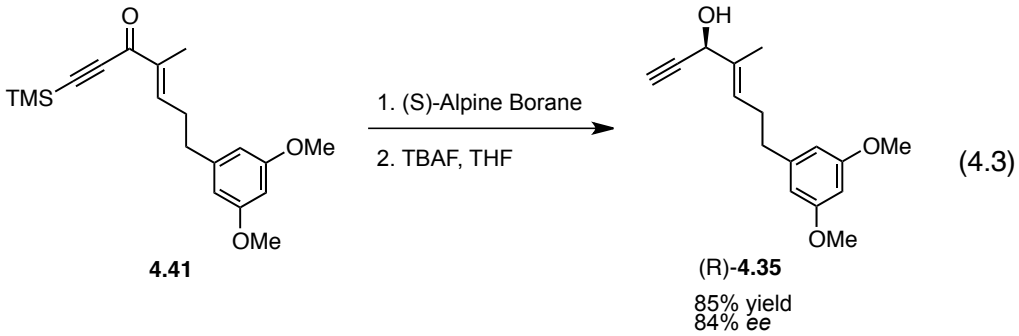
4.36 (R = ^{t}Bu)
4.40 (R = Ph)

Entry	R	Additive (eq.)	Eq.	*ee* (%)	Yield (%)[a]
1	^{t}Bu	--	--	36	93
2	^{t}Bu	CF_3CH_2OH	5	52	89
3	^{t}Bu	CF_3CH_2OH	10 mol %	50	90
4	^{t}Bu	CF_3CH_2OH	50	43	86
5	^{t}Bu	EtOH	2	38	88
6	^{t}Bu	PhOH	2	35	85
7	Ph	--	--	46	74
8	Ph	CF_3CH_2OH	2	48	72

[a] Yields determined by ^{1}H NMR vs. 9-bromophenanthrene.

The benzoate ester **4.39** underwent cyclization using precatalyst (R)-**4.38** with greater enantioselectivity than the pivalate (entry 7 vs. entry 1), however, no additive effects were observed using this substrate (entry 8).

Turning our attention to the prospects of chirality transfer in the present transformation, enantioenriched substrates[45] (R)-**4.35** and (R)-**4.39** were prepared in 84% *ee* (eq 4.2) by the enantioselective reduction of ketone **4.41** using the procedure of Midland *et al.* with (S)-(–)-B-isopinocampheyl-9-borabicyclo[3.3.1]nonane (Alpine Borane).[46,47]



4.41 (R)-**4.35**

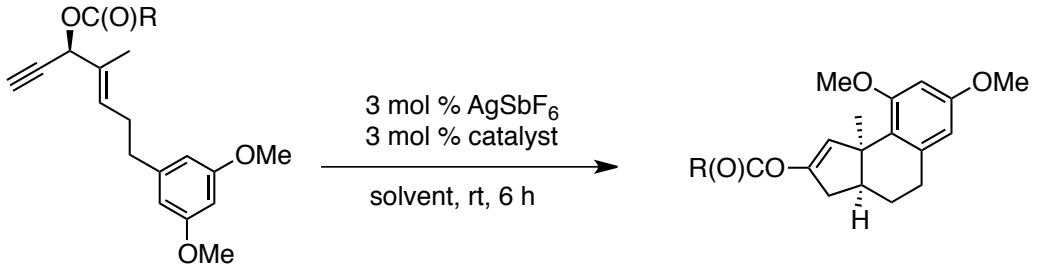
85% yield
84% *ee*

(4.3)

The results of chirality transfer experiments are summarized in Table 4.3. The pivalate substrate (R = ^{t}Bu, (R)-**4.35**) in 3:1 benzene / methylene chloride produced tricycle **4.36** in 74% *ee* with $Ph_3PAuSbF_6$ (entry 1). No improvement was observed when the solvent was changed to acetonitrile, neat dichloromethane or nitromethane (entries 2-4). The benzoate substrate (R = Ph, (R)-**4.39**) gave the cyclized product **4.40** in 66% *ee* (entry 5) under the same conditions employed for entry 1. Employing precatalyst (±)-**4.38**, enantioenriched pivalate (R)-**4.35** underwent cyclization to give **4.36** in 73% *ee* (entry 6). Using precatalyst (R)-**4.38** gave **4.36** in 73% *ee* (entry 7), whereas only racemic product was obtained using (S)-**4.38** (entry 8). Finally, for the benzoate (R)-**4.39**, the (R)-**4.38** catalyst provided **4.40** in 64% *ee*, while the (S) enantiomer of precatalyst **4.38** again provided only racemic product (entries 9 &10).

Scheme 4.11 presents a mechanistic hypothesis accounting for the observed *cis*-fused products in the present transformation. In contrast to the concerted mechanism proposed for cyclizations in Chapter 2, the intercepted Rautenstrauch reaction most likely proceeds with a stepwise mechanism. The steric hindrance about the olefin in species **a** would seem to preclude significant interaction of the pendant arene in the initial cyclization. Therefore, a discrete Rautenstrauch cyclization step followed by conformational interchange to **c** prior to trapping appears to best rationalize product formation, providing a rationalization for the increased tendency toward elimination products for this process.

Table 4.3. Cyclization of Enantioenriched Substrates.



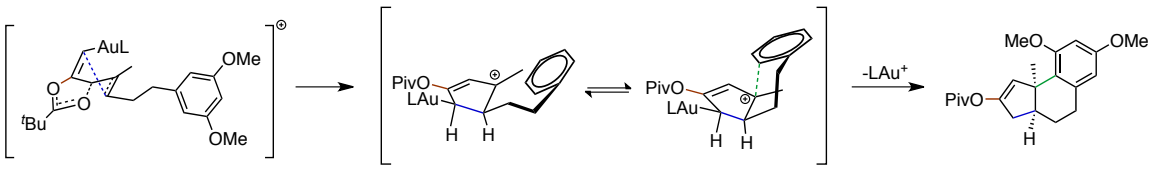
(R)-**4.35** (R = ^{t}Bu)
(R)-**4.39** (R = Ph)
84% *ee*

4.36 (R = ^{t}Bu)
4.40 (R = Ph)

Entry	R	Catalyst	Solvent	*ee* (%)	Yield (%)[a]
1	^{t}Bu	Ph_3PAuCl	PhH / DCM[b]	74	89
2	^{t}Bu	Ph_3PAuCl	ACN	64	66
3	^{t}Bu	Ph_3PAuCl	DCM	61	72
4	^{t}Bu	Ph_3PAuCl	$MeNO_2$	43	41
5	Ph	Ph_3PAuCl	PhH / DCM[b]	66	73
6	^{t}Bu	(±)-**4.38**	PhH	73	84
7	^{t}Bu	(R)-**4.38**	PhH	73	88
8	^{t}Bu	(S)-**4.38**	PhH	0	56
9	Ph	(R)-**4.38**	PhH	64	75
10	Ph	(S)-**4.38**	PhH	0	63

[a] Yields determined by ^{1}H NMR vs. 9-bromophenanthrene. [b] In a 3:1 ratio.

Scheme 4.11. Stepwise Mechanism for Formation of *cis* Ring Fusion.

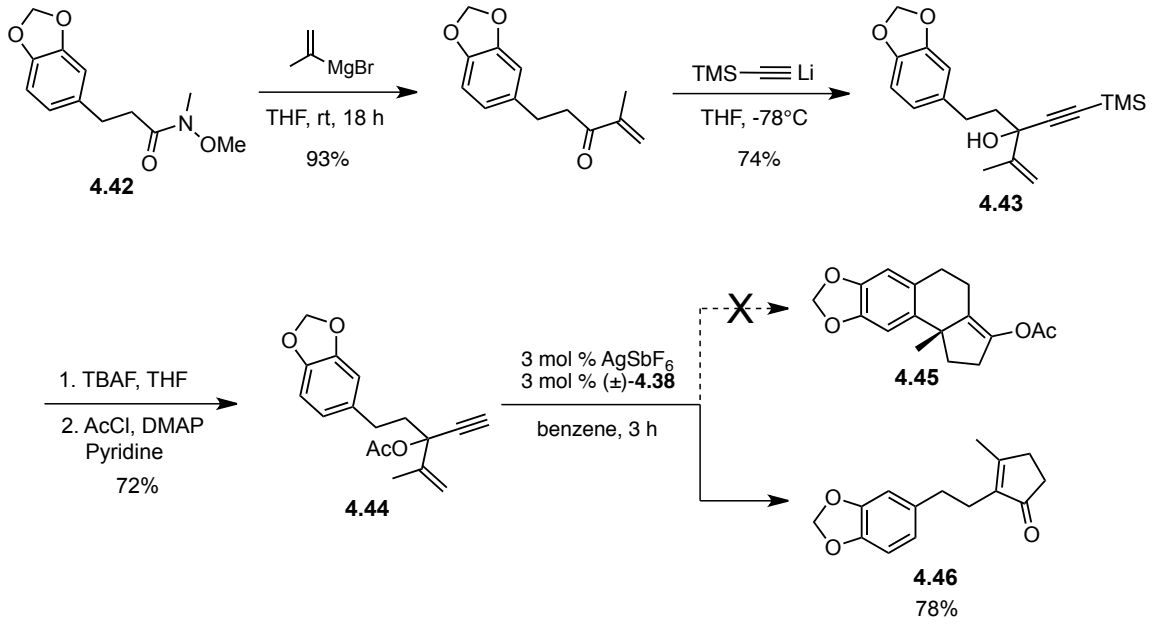


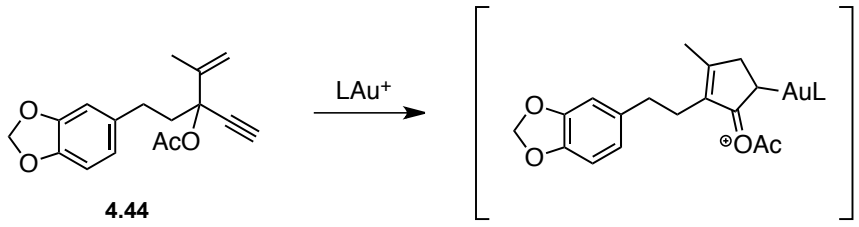
a b c

Substrate Scope

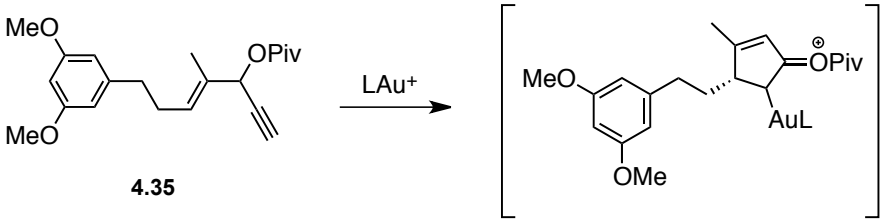
Synthetic efforts were directed toward new substrates in order to further investigate the scope of the reaction. Tertiary acetate **4.44** was prepared to examine an alternative point of attachment for the tethered nucleophile. Thus, Weinreb amide **4.42** was treated successively with isopropenylmagnesium bromide and lithium trimethylsilylacetylide to give tertiary alcohol **4.43**. Deprotection and esterification then provided acetate **4.44**. Treatment of **4.44** with the cation derived from complex **4.38** in benzene yielded exclusively monocycle **4.46** rather than the expected Friedel-Crafts product **4.45**. The observed failure of **4.43** to trap may be due to attachment of the arene tether to the endocyclic π-system in the cationic intermediate (eq. 4.3). In the corresponding cation derived from **4.35**, the side chain enjoys greater conformational mobility by virtue of attachment at an sp^3 carbon (eq. 4.4).

Scheme 4.12. Alternative Site of Nucleophilic Tether Substitution.





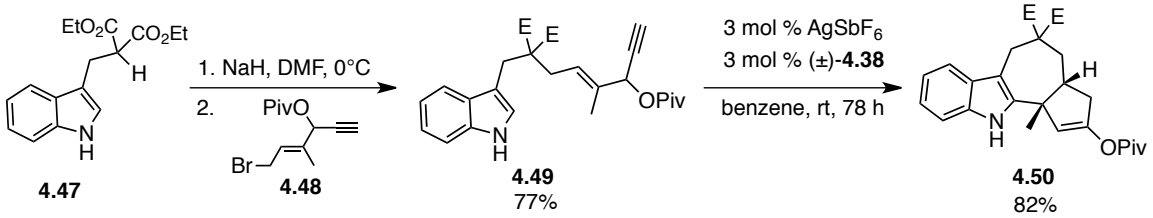
4.44 (4.3)



4.35 (4.4)

In order to demonstrate interception by indole and provide a scaffold for future substrate synthesis, allyl bromide **4.48** was prepared. The selective alkylation of known unprotected indolyl malonate **4.47** gave substrate **4.49** in 77% yield. Upon treatment of **4.49** with 3 mol % of the cation derived from **4.38**, tetracycle **4.50** was isolated in 82% yield as the sole detectable product.

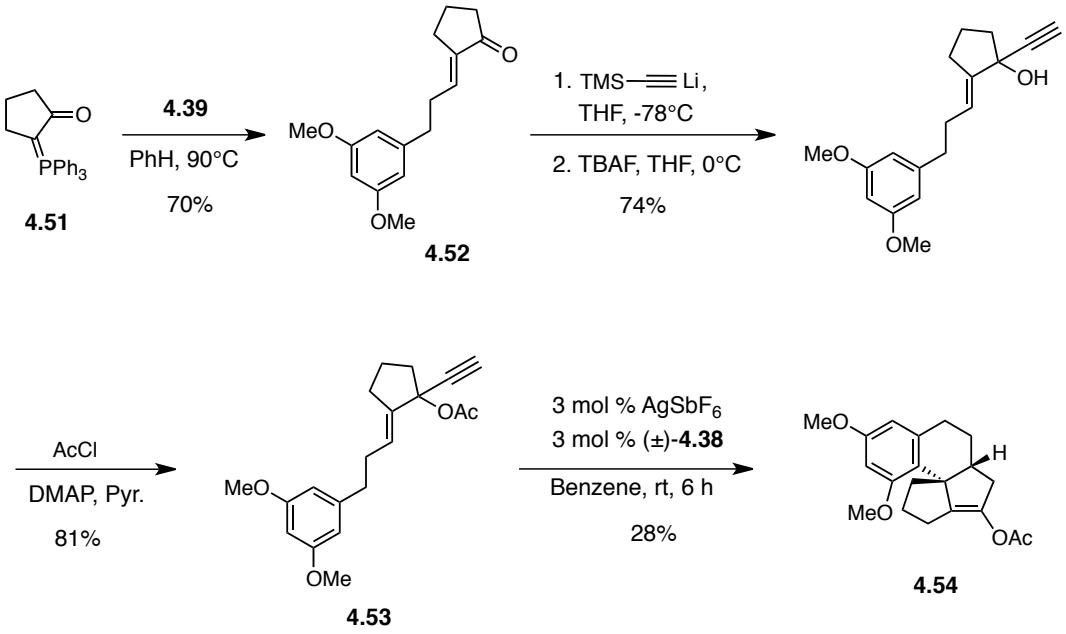
Scheme 4.13. Synthesis and Cyclization of Indole Substrate **4.49**.



4.47 **4.48** **4.49** 77% **4.50** 82%

Finally, cyclopentyl acetate **4.53** was prepared from cyclic stabilized phosphonium ylide **4.51** by olefination with **4.39** to give enone **4.52**, which was then converted to substrate as usual (Scheme 4.14). Cyclization of **4.53** using cationic **4.38** in benzene gave in 28% yield, hindered tetracycle **4.54**.

Scheme 4.14. Reaction of Substrate Incorporating a Cyclopentane Scaffold.

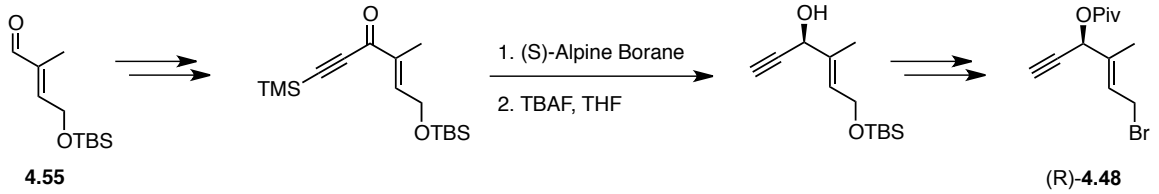


Conclusion

The tandem Rautenstrauch / annulation process described in chapter 4 represents a convenient approach to functionalized hexahydro-1*H*-indene systems, formed under mild conditions using gold(I) catalysis. As a conceptual extension of the cycloisomerization-initiated cascade described in chapter 2, the present transformation expands the range of gold-stabilized cationic species which can be incorporated into tandem reaction processes. The transformation is capable of proceeding with chirality transfer, as well as asymmetric induction using chiral bisphosphine digold precatalysts.

Future study of this transformation should be conducted with the goal of extending the scope of the chirality transfer observed, beginning with indole substrate **4.50**. To this end, enriched pivalate (R)-**4.48** could be prepared from known aldehyde **4.55** (scheme 4.15), and applied to the synthesis of (R)-**4.49** as per scheme 4.13. Additional substrates possessing diverse aromatic nucleophiles could also be generated from enantioenriched intermediate (R)-**4.48**.

Scheme 4.15. Proposed Approach to Enantioenriched Fragment for Use in Future Studies of Substrate Scope.

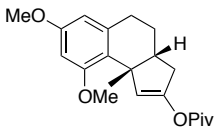


Experimental

Unless otherwise stated, all commercial materials were used without further purification. Solvents were purchased from EM-Science and were dried by passage through activated alumina, except *meta*-xylene. Solvents used in polycyclization reactions were stored over 4Å molecular sieves. Silver tetrafluoroborate ($AgBF_4$), silver perchlorate ($AgClO_4$) and silver hexafluoroantimonate ($AgSbF_6$) were obtained from Aldrich Chemical Company and stored in the dark under an inert atmosphere. Silver salts kept under argon in a sealed vial and protected from light could be used several times before succumbing to deliquescence. Bisphosphine ligands were obtained from Solvias and Takasago. $AuCl_3$ was provided by Johnson Matthey. Chiral digold chloride complexes were prepared as previously described by previous work from this lab.[48] Complexes used for ligand optimization provided spectra in agreement with those previously described. Gold(I)-catalyzed reactions were not stirred beyond a brief mixing upon addition of the catalyst. Thin layer chromatography (TLC) analysis of reaction mixtures was performed on Merck silica gel 60 F_{254} TLC plates and flash chromatography was carried out on Sorbent Technologies 40-63 D 60 Å silica gel. ^1H and ^{13}C NMR spectra were recorded with Bruker AVQ-400, AVB-400, AV-500 or AV-600 spectrometers using either $CDCl_3$ or C_6D_6, and are internally referenced to residual protio solvent signals. ^1H NMR multiplicities are reported as follows: m = multiplet; s = singlet; d = doublet; t = triplet; q = quartet. All ^{13}C NMR spectra were obtained with proton decoupling. Enantiomeric ratios were measured by chiral HPLC employing a Shimidzu VP Series instrument equipped with SPD-M10A microdiode array detector.

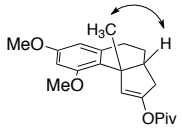
General Procedure for Gold(I)-Catalyzed Rautenstrauch Rearrangement.

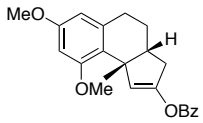
A mixture of $AgSbF_6$ (0.8 mg, 2.2 μmol) and the bisphosphine digold(I) chloride complex (3.32 mg, 2.22 μmol) is suspended in 300 μL of C_6D_6 in a sealed, screw-top vial, and sonicated or stirred magnetically for 15 min at room temperature). The resulting suspension is filtered through a glass microfiber plug directly into a solution of substrate (15 mg, 0.044 mmol) in 600 μl of C_6D_6, thorough mixing is ensured and the resulting homogenous solution is allowed to stand until such time as the substrate was fully consumed as judged by TLC or ^{1}H NMR analysis. Determination of yield was made by calibration with an internal standard (9-bromophenanthrene) prior to addition of catalyst. Upon consumption of the starting material, an aliquot containing ca. 4 mg. of crude product was concentrated under a stream of N_2 to a volume of ca. 100 μL which was then eluted through a short silica column.



7,9-dimethoxy-9b-methyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[a]naphthalen-2-yl pivalate (4.36).

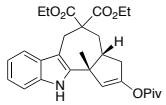
Formed in 97% yield based on ^{1}H NMR analysis. **1H-NMR** (600 MHz, C_6D_6): δ 6.41 (t, *J* = 1.6 Hz, 1H), 6.28 (d, *J* = 2.4 Hz, 1H), 6.19 (d, *J* = 2.5 Hz, 1H), 3.37 (s, 3H), 3.16 (s, 3H), 2.84 (ddd, *J* = 15.4, 7.9, 1.9 Hz, 1H), 2.57 (dt, *J* = 16.0, 5.7 Hz, 1H), 2.48 (td, *J* = 8.2, 6.1 Hz, 1H), 2.35 (ddd, *J* = 15.5, 4.8, 1.5 Hz, 1H), 2.18 (tt, *J* = 7.9, 5.3 Hz, 1H), 1.68-1.65 (m, 2H), 1.63 (s, 3H), 1.11 (s, 9H). **13C-NMR** (151 MHz, C_6D_6): δ 175.82, 159.76, 159.08, 150.03, 139.21, 128.51, 122.15, 105.46, 98.31, 54.98, 54.74, 46.69, 46.67, 39.23, 35.94, 29.79, 28.14, 27.37, 26.69. **MS** HRMS (EI) calc. for $C_{21}H_{28}O_4$: 344.1988, found: 344.1975. **HPLC** Chiralpak IB column (1% EtOAc in hexanes, 0.85 mL/min, λ_{ax}= 219 nm). t_{Rs} 12.72 min (major), 14.78 min (minor). 73 % *ee.* Important ^{1}H NOE correlations:





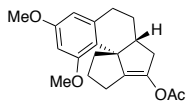
7,9-dimethoxy-9b-methyl-3a,4,5,9b-tetrahydro-3H-cyclopenta[a]naphthalen-2-yl benzoate (**4.40**)**.**

Formed in 75% yield based on ^{1}H NMR analysis. **1H-NMR** (600 MHz, C_6D_6): δ 8.12 (d, *J* = 7.9 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 7.7 Hz, 2H), 6.54 (s, 1H), 6.34 (d, *J* = 2.2 Hz, 1H), 6.24 (d, *J* = 2.3 Hz, 1H), 3.41 (s, 3H), 3.23 (s, 3H), 2.96 (ddd, *J* = 15.5, 7.9, 1.2 Hz, 1H), 2.63 (dt, *J* = 16.0, 5.7 Hz, 1H), 2.53 (dt, *J* = 15.5, 6.7 Hz, 1H), 2.45 (dd, *J* = 15.6, 4.8 Hz, 1H), 2.25 (tt, *J* = 7.8, 5.2 Hz, 1H), 1.74-1.71 (m, 2H), 1.69 (s, 3H). **13C-NMR** (151 MHz, CDCl3): δ 164.28, 159.72, 159.04, 149.83, 139.16, 133.16, 130.68, 130.28, 128.67, 128.43, 123.91, 122.68, 105.41, 98.28, 54.91, 54.70, 46.61, 35.94, 29.70, 28.05, 26.55. **MS** HRMS (EI) calc**.** for $C_{23}H_{24}O_4$: 364.1675, found: 364.1670 **HPLC** Chiralpak IB column (3% MTBE in hexanes, 1.0 mL/min, λ_{ax}= 196 nm). t_{Rs} 23.32 min (major), 28.81 min (minor). 68 % *ee*.



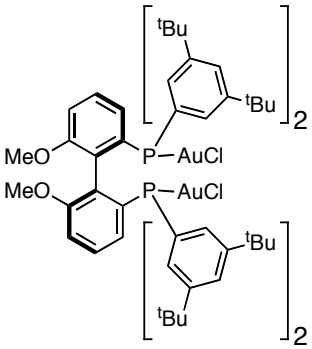
diethyl 11b-methyl-2-(pivaloyloxy)-3a,4,11,11b-tetrahydro-3H-azuleno[4,5-b]indole-5,5(6H)-dicarboxylate (**4.50**).

Formed in 82% yield based on ^{1}H NMR analysis. **1H-NMR** (600 MHz, C_6D_6): δ 7.87 (s, 1H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.21-7.18 (m, 3H), 5.88 (s, 1H), 4.86 (d, *J* = 1.2 Hz, 1H), 4.59 (s, 1H), 4.10 (dd, *J* = 9.2, 5.7 Hz, 1H), 4.00 (dtt, *J* = 10.8, 7.2, 3.6 Hz, 2H), 3.97-3.92 (m, 1H), 3.81 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.38 (dd, *J* = 15.6, 2.5 Hz, 1H), 2.99 (ddd, *J* = 13.1, 5.9, 1.6 Hz, 1H), 2.35 (dd, *J* = 13.1, 10.8 Hz, 1H), 1.56 (d, *J* = 1.1 Hz, 3H), 1.10 (s, 9H), 0.95 (t, *J* = 7.1 Hz, 3H), 0.79 (t, *J* = 7.1 Hz, 3H). **13C-NMR** (151 MHz, C_6D_6): δ 176.62, 171.45, 170.25, 152.05, 141.63, 136.87, 132.79, 128.01, 123.31, 121.88, 119.49, 118.24, 111.00, 108.70, 104.39, 61.25, 60.96, 54.85, 43.32, 38.72, 33.90, 27.53, 26.78, 14.77, 13.72, 13.60. **MS** HRMS (EI) calc. for $C_{28}H_{35}O_6NLi$: 488.2619, found: 488.2618.

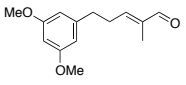


9,11-dimethoxy-2,3,5,5a,6,7-hexahydro-1H-pentaleno[6a,1-a]naphthalen-4-yl acetate (**4.54**).

Formed in 28% yield based on ^{1}H NMR analysis. **1H-NMR** (600 MHz, $CDCl_3$): δ 6.36 (d, J = 2.4 Hz, 1H), 6.34 (d, J = 2.4 Hz, 1H), 3.41 (s, 3H), 3.26 (s, 3H), 2.96 (td, J = 12.5, 1.9 Hz, 1H), 2.72-2.62 (m, 2H), 2.59 (ddd, J = 14.9, 7.3, 4.5 Hz, 1H), 2.54-2.44 (m, 3H), 2.15-2.09 (m, 1H), 1.93-1.83 (m, 3H), 1.68 (s, 3H), 1.62 (dt, J = 11.9, 8.0 Hz, 1H), 1.38-1.29 (m, 1H). **13C-NMR** (151 MHz, $CDCl_3$): δ 167.21, 159.40, 158.62, 141.94, 141.11, 139.16, 128.02, 123.99, 105.35, 98.13, 56.85, 54.95, 54.50, 51.63, 42.16, 40.66, 29.70, 28.40, 26.37, 26.09, 20.07. **MS** HRMS (EI) calc. for $C_{20}H_{24}O_4Li$: 335.1829, found: 335.1833



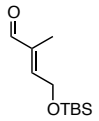
(R)-DTB,MeO-biphep(AuCl)$_2$.
See experimental details in chapter 2 for preparation and characterization of this complex (**2.28**)



(E)-5-(3,5-dimethoxyphenyl)-2-methylpent-2-enal (4.33).

A stirred suspension 3-(3,5-dimethoxyphenyl)propanal[49] (2.23 g., 11.73 mmol) and 2-(triphenylphosphoranylidene)propanal (4.48 g., 14.08 mmol, 1.2 equiv.) in benzene (80 mL) was heated 90°C in a sealed tube for 9 hours, giving a clear solution. Upon cooling to room temperature, the reaction mixture was concentrated *in vacuo*, triturated with cold ether, filtered and concentrated again to give the crude aldehyde. Purification by flash chromatography (95:5 to 8:2 hexanes:Et_2O) gave 1.86 g. of **4.33** as a clear oil (67%). **1H-NMR** (600 MHz, $CDCl_3$): δ 9.22 (s, 1H), 6.44 (t, J = 2.2 Hz, 1H), 6.36 (d, J = 2.2 Hz, 2H), 5.87 (td, J

= 7.2, 1.3 Hz, 1H), 3.35 (s, 6H), 2.35 (t, J = 7.6 Hz, 2H), 2.17 (q, J = 7.6 Hz, 2H), 1.56 (s, 3H). **13C-NMR** (151 MHz, $CDCl_3$): δ 195.20, 160.90, 153.20, 142.95, 139.82, 106.48, 97.99, 55.26, 34.64, 30.37, 9.21. **MS** HRMS (EI) calc. for $C_{14}H_{18}O_3$: 234.1256, found: 234.1259

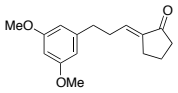


(E)-4-((tert-butyldimethylsilyl)oxy)-2-methylbut-2-enal (4.55)[50]

This material was prepared as reported in the literature. All spectral data were in accord with those previously published.

2-(triphenylphosphoranylidene)cyclopentanone (4.61)[51]

This material was prepared as reported in the literature. All spectral data were in accord with those previously published.

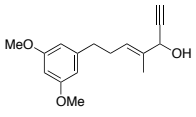


(E)-2-(3-(3,5-dimethoxyphenyl)propylidene)cyclopentanone (4.52)

A stirred suspension 3-(3,5-dimethoxyphenyl)propanal[49] (390 mg, 2.01 mmol) and **4.61** (765.9 mg, 2.21 mmol, 1.1 equiv.) in benzene (5 mL) was heated 90°C in a sealed tube for 9 hours to give a clear solution. Upon cooling to room temperature, the reaction mixture was concentrated *in vacuo*, triturated with cold ether, filtered and concentrated (3 x 25 mL Et_2O) to give the crude aldehyde. Purification by flash chromatography (8:2 hexanes : EtOAc) gave 420 mg. of **4.33** as a clear oil (80%). **1H-NMR** (600 MHz, $CDCl_3$): δ 6.78 (tt, *J* = 7.5, 2.7 Hz, 1H), 6.54 (t, *J* = 2.2 Hz, 1H), 6.48 (d, *J* = 2.2 Hz, 2H), 3.45 (s, 6H), 2.55 (t, *J* = 7.6 Hz, 2H), 2.27 (d, *J* = 7.7 Hz, 2H), 2.12 (d, *J* = 14.5 Hz, 2H), 2.05 (s, 2H), 1.42 (q, *J* = 7.5 Hz, 2H). **13C-NMR** (151 MHz, $CDCl_3$): δ 204.36, 161.27, 143.59, 137.82, 133.38, 106.63, 98.23, 54.53, 38.09, 34.90, 31.32, 26.34, 19.57. **MS** HRMS (EI) calc. for $C_{16}H_{20}O_3$: 260.1412, found: 260.1416

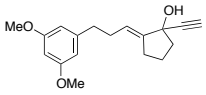
General Procedure for Acetylide Addition to Unsaturated Aldehydes.

To a solution of trimethylsilylacetylene (1.77 mL, 12.3 mmol, 1.23 equiv.) in anhydrous THF (80 mL) at -78°C was added dropwise nBuLi (4.6 mL of a 2.5 M solution in hexanes, 11.5 mmol, 1.15 equiv.) and the resulting solution was held at this temperature for 1 hour. A solution of **4.33** (1.67 g., 7.14 mmol) in THF (5 mL) was added dropwise with stirring, and the solution was allowed to reach room temperature slowly. After 12 hours, the reaction mixture was cooled to 0°C and quenched with sat. NH_4Cl (20 mL), diluted with water (100 mL) and extracted with Et_2O (3 x 40 mL). The combined organic fractions were washed with water (50 mL), brine (50 mL) and dried over $MgSO_4$. Upon concentration *in vacuo*, a residue was obtained which was passed through a short column of silica gel (9:1 hexanes : EtOAc), concentrated and dissolved in anhydrous THF (70 mL) at 0°C. To this solution was added TBAF (8.56 mL of a 1M solution in THF, 8.56 mmol, 1.2 equiv.) dropwise over 5 minutes with stirring. The temperature was maintained for 2 hours, at which time sat. NH_4Cl (10 mL) was added, followed by water (40 mL). The solution was extracted with Et_2O (3 x 40 mL) and the resulting organic fractions were washed with water (40 mL), brine (40 mL) and dried over $MgSO_4$. Upon concentration *in vacuo*, the crude alcohol was purified by flash chromatography using silica gel conditioned with triethylamine (3 % w/w).



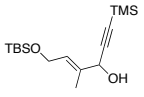
(E)-7-(3,5-dimethoxyphenyl)-4-methylhept-4-en-1-yn-3-ol (4.34).

Purified by flash chromatography (9:1 hexanes : EtOAc) to provide 2.66 g. of **4.34** as a clear oil (85%). **1H-NMR** (500 MHz, $CDCl_3$): δ 6.34 (d, *J* = 2.2 Hz, 2H), 6.30 (t, *J* = 2.2 Hz, 1H), 5.67 (t, *J* = 7.0 Hz, 1H), 4.74 (d, *J* = 4.7 Hz, 1H), 3.77 (s, 6H), 2.62 (t, *J* = 7.8 Hz, 2H), 2.53 (d, *J* = 2.2 Hz, 1H), 2.35 (q, *J* = 7.6 Hz, 2H), 1.72 (s, 3H). **13C-NMR** (101 MHz, $CDCl_3$): δ 160.77, 144.19, 134.55, 127.63, 106.56, 97.88, 83.14, 74.09, 67.83, 55.30, 35.72, 29.50, 12.22. **MS** HRMS (EI) calc. for $C_{16}H_{20}O_3$: 260.1412, found: 260.1415



(E)-2-(3-(3,5-dimethoxyphenyl)propylidene)-1-ethynylcyclopentanol (4.60).

Purified by flash chromatography (9:1 hexanes : EtOAc), 86%. **1H-NMR** (600 MHz, $CDCl_3$): δ 6.78 (tt, *J* = 7.5, 2.7 Hz, 1H), 6.54 (t, *J* = 2.2 Hz, 1H), 6.48 (d, *J* = 2.2 Hz, 2H), 3.45 (s, 6H), 2.55 (t, *J* = 7.6 Hz, 2H), 2.27 (q, *J* = 7.6 Hz, 2H), 2.12 (t, *J* = 7.2 Hz, 2H), 2.03 (t, *J* = 7.9 Hz, 2H), 1.41 (quintet, *J* = 7.5 Hz, 2H). **13C-NMR** (151 MHz, $CDCl_3$): δ 161.10, 147.22, 144.58, 124.58, 106.95, 98.26, 86.55, 75.10, 72.62, 55.63, 42.74, 35.92, 31.36, 27.22, 22.22. **MS** HRMS (EI) calc. for $C_{18}H_{22}O_3$: 286.1569, found: 286.1571

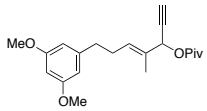


(E)-6-((tert-butyldimethylsilyl)oxy)-4-methyl-1-(trimethylsilyl)hex-4-en-1-yn-3-ol (**4.58**).

Purified by flash chromatography (9:1 hexanes : EtOAc) to provide **4.58** as a clear oil (74%). **1H-NMR** (400 MHz, $CDCl_3$): δ 5.77 (tt, *J* = 6.1, 1.2 Hz, 1H), 4.74 (s, 1H), 4.26 (d, *J* = 6.1 Hz, 2H), 1.75 (d, *J* = 1.0 Hz, 3H), 0.91 (s, 9H), 0.18 (s, 9H), 0.08 (s, 6H). **13C-NMR** (101 MHz, $CDCl_3$): δ 134.77, 127.75, 104.22, 90.99, 67.89, 60.06, 25.94, 18.36, 12.65, -0.20, -5.11. **MS** HRMS (EI) calc. for $C_{16}H_{32}O_2Si_2$: 312.1941, found: 312.1935.

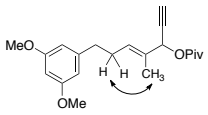
General Procedure for Acylation of Allylic Propargylic Alcohols.

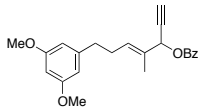
To a solution of the secondary alcohol (1 mmol) in pyridine (3 mL) at 0°C is added DMAP (10 mol %) then dropwise the appropriate acid chloride (1.2 equiv.) and the reaction mixture is allowed to warm to room temperature and stirred for and additional 8-16 hours until complete by TLC analysis. The resulting solution is diluted with water (15 mL) and extracted with Et_2O (3 x 15 mL). The combined organic fractions were washed with 10% $CuSO_4$ (5 x 10 mL, until no color change observed in aqueous fraction), then water (15 mL) and brine (15 mL). The solution was dried over $MgSO_4$, concentrated *in vacuo* and the resulting residue purified by flash chromatography.



(E)-7-(3,5-dimethoxyphenyl)-4-methylhept-4-en-1-yn-3-yl pivalate (4.35).

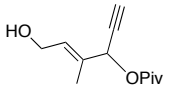
Purified by flash chromatography (8:2 hexanes:Et_2O) to provide **4.35** as a clear oil (86%). **1H-NMR** (400 MHz, $CDCl_3$): δ 6.34 (d, *J* = 2.3 Hz, 2H), 6.30 (t, *J* = 2.3 Hz, 1H), 5.75-5.72 (m, 2H), 3.78 (s, 6H), 2.63 (t, *J* = 7.7 Hz, 2H), 2.49 (d, *J* = 2.2 Hz, 1H), 2.37 (q, *J* = 7.7 Hz, 2H), 1.68 (s, 3H), 1.21 (s, 9H), 6.34 (d, *J* = 2.3 Hz, 2H), 6.30 (t, *J* = 2.3 Hz, 1H), 5.75-5.72 (m, 2H), 3.78 (s, 6H), 2.63 (t, *J* = 7.7 Hz, 2H), 2.49 (d, *J* = 2.2 Hz, 1H), 2.37 (q, *J* = 7.7 Hz, 2H), 1.68 (s, 3H), 1.21 (s, 9H). **13C-NMR** (101 MHz, $CDCl_3$): δ 177.29, 160.98, 144.30, 131.35, 129.78, 106.75, 98.12, 80.33, 74.40, 68.67, 55.49, 39.06, 35.83, 29.78, 27.23, 12.69. **MS** HRMS (EI) calc. for $C_{21}H_{28}O_4$: 344.1988, found: 344.1978. Important ^1H NOE correlations:





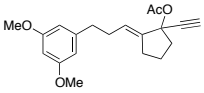
(E)-7-(3,5-dimethoxyphenyl)-4-methylhept-4-en-1-yn-3-yl benzoate (**4.39**).

Purified by flash chromatography (8:2 hexanes : Et_2O) to provide **4.39** as a clear oil (81%). **1H-NMR** (600 MHz, CDCl3): δ 8.22 (d, *J* = 7.7 Hz, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 2H), 6.56 (s, 1H), 6.50 (d, *J* = 1.9 Hz, 2H), 6.41 (s, 1H), 5.88 (t, *J* = 7.0 Hz, 1H), 3.46 (s, 6H), 2.53 (t, *J* = 7.7 Hz, 2H), 2.29 (q, *J* = 7.6 Hz, 2H), 2.19 (s, 1H), 1.80 (s, 3H). **13C-NMR** (151 MHz, CDCl3): δ 164.79, 161.24, 143.93, 132.73, 131.10, 130.38, 130.28, 129.78, 128.24, 128.02, 106.69, 98.28, 80.10, 74.72, 69.34, 54.52, 54.50, 35.55, 29.71, 12.31. **MS HRMS (EI) calc.** for $C_{23}H_{24}O_4$: 364.1675, found: 364.1677

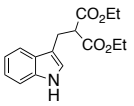


(E)-6-hydroxy-4-methylhex-4-en-1-yn-3-yl pivalate (4.59).

Prepared from **4.58** using the general procedure for acylation, followed by treatment of the crude pivalate with 2.4 eq. TBAF in THF at 0°C for 2 hours. Purified by flash chromatography (8:2 hexanes : EtOAc) to provide **4.59** as a clear oil (70%). **1H-NMR** (600 MHz, CDCl3): δ 5.92 (t, *J* = 6.4 Hz, 1H), 5.76 (s, 1H), 4.25 (t, *J* = 6.4 Hz, 2H), 2.51 (d, *J* = 1.9 Hz, 1H), 1.77 (s, 3H), 1.23 (s,9H). **13C-NMR** (151 MHz, CDCl3): δ 176.95, 133.30, 128.53, 79.47, 74.54, 67.69, 59.13, 38.82, 26.98, 12.80. **MS** HRMS (EI) calc. for $C_{12}H_{18}O_3$: 210.1256, found: 210.1256

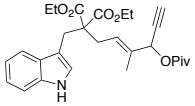


(E)-2-(3-(3,5-dimethoxyphenyl)propylidene)-1-ethynylcyclopentyl acetate (4.53). Purified by flash chromatography (8:2 hexanes : Et_2O) to provide **4.53** as a clear oil (81%). **1H-NMR** (600 MHz, CDCl3): δ 6.34 (d, *J* = 2.1 Hz, 2H), 6.30 (s, 1H), 5.76-5.74 (m, 1H), 3.78 (s, 6H), 3.21 (s, 1H), 2.65-2.60 (m, 1H), 2.54-2.49 (m, 3H), 2.42 (t, *J* = 7.6 Hz, 2H), 2.06 (s, 3H), 1.93-1.84 (m, 3H). **13C-NMR** (151 MHz, CDCl3): δ 170.13, 160.77, 149.70, 143.70, 120.29, 106.39, 97.99, 82.98, 79.31, 71.87, 55.25, 36.80, 34.27, 31.90, 31.84, 22.15, 20.97. **MS HRMS (EI) calc.** for $C_{20}H_{24}O_4Li$: 335.1829, found: 335.1835



diethyl 2-((1H-indol-3-yl)methyl)malonate (4.47)[52]

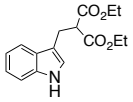
This material was prepared as reported in the literature. All spectral data were in accord with those previously published.



(E)-diethyl 2-((1H-indol-3-yl)methyl)-2-(3-methyl-4-(pivaloyloxy)hex-2-en-5-yn-1-yl)malonate (4.49).

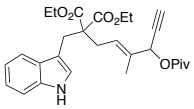
To a solution of the **4.59** (323 mg., 1.54 mmol), carbon tetrabromide (612 mg, 1.84 mmol, 1.2 equiv.), and triethylamine (54 µL, 0.39 mmol, 0.25 equiv.) in CH_2Cl_2 (7 mL) held at -78°C was added dropwise triphenylphosphine (443 mg, 1.69 mmol, 1.1 equiv.) in CH_2Cl_2 (1 mL). The resulting solution was allowed to warm slowly to 0°C over 3 hours and was then concentrated, triturated with diethyl ether, filtered and concentrated (3 x 15 mL). The resulting crude allyl bromide was passed through a plug of silica gel with hexane, concentrated and used immediately in the next step.

To a solution of **4.47** (469 mg, 1.62 mmol, 1.05 equiv.) in dry DMF (5 mL) at 0°C was added NaH (68 mg of a 60% suspension in mineral oil, 1.69 mmol, 1.1 equiv.). Upon stirring 30 minutes at this temperature, the allyl bromide in dry DMF (2 mL) was added dropwise and the reaction mixture was allowed to warm to room temperature at stir for 18 hours. The reaction mixture was quenched with saturated $NaHCO_3$ (5 mL), diluted with water (10 mL) and extratcted with ether (2 x 20 mL). The organic fractions were washed with water (2 x 20 mL), brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (2:2:1 benzene : DCM : hexanes) give **4.49** as a clear oil. **1H-NMR** (600 MHz, CDCl3): δ 7.78 (d, *J* = 7.7 Hz, 1H), 7.24 (dd, *J* = 14.2, 6.5 Hz, 2H), 7.07 (d, *J* = 7.7 Hz, 1H), 6.78 (br s, 1H), 6.74 (s, 1H), 6.14-6.11 (m, 2H), 4.09-3.97 (m, 4H), 3.79 (s, 2H), 2.99 (d, *J* = 7.0 Hz, 2H), 2.10 (s, 1H), 1.67 (s, 3H), 1.22 (s, 9H), 0.96 (td, *J* = 7.1, 3.9 Hz, 6H). **13C-NMR** (151 MHz, CDCl3): δ 176.03, 170.99, 170.97, 135.90, 133.94, 128.93-128.37, 124.33, 123.24, 121.86, 119.49, 119.12, 110.96, 110.01, 80.05, 74.37, 68.13, 60.92, 58.72, 38.59, 31.40, 28.50, 26.83, 13.70, 12.82. **MS** HRMS (EI) calc. for $C_{28}H_{35}O_6NNa$: 504.2357, found: 504.2366



diethyl 2-((1H-indol-3-yl)methyl)malonate (4.47)[52]

This material was prepared as reported in the literature. All spectral data were in accord with those previously published.



(E)-diethyl 2-((1H-indol-3-yl)methyl)-2-(3-methyl-4-(pivaloyloxy)hex-2-en-5-yn-1-yl)malonate (4.49).

To a solution of the **4.59** (323 mg., 1.54 mmol), carbon tetrabromide (612 mg, 1.84 mmol, 1.2 equiv.), and triethylamine (54 µL, 0.39 mmol, 0.25 equiv.) in CH_2Cl_2 (7 mL) held at -78°C was added dropwise triphenylphosphine (443 mg, 1.69 mmol, 1.1 equiv.) in CH_2Cl_2 (1 mL). The resulting solution was allowed to warm slowly to 0°C over 3 hours and was then concentrated, triturated with diethyl ether, filtered and concentrated (3 x 15 mL). The resulting crude allyl bromide was passed through a plug of silica gel with hexane, concentrated and used immediately in the next step.

To a solution of **4.47** (469 mg, 1.62 mmol, 1.05 equiv.) in dry DMF (5 mL) at 0°C was added NaH (68 mg of a 60% suspension in mineral oil, 1.69 mmol, 1.1 equiv.). Upon stirring 30 minutes at this temperature, the allyl bromide in dry DMF (2 mL) was added dropwise and the reaction mixture was allowed to warm to room temperature at stir for 18 hours. The reaction mixture was quenched with saturated $NaHCO_3$ (5 mL), diluted with water (10 mL) and extratcted with ether (2 x 20 mL). The organic fractions were washed with water (2 x 20 mL), brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (2:2:1 benzene : DCM : hexanes) give **4.49** as a clear oil. **1H-NMR** (600 MHz, CDCl3): δ 7.78 (d, *J* = 7.7 Hz, 1H), 7.24 (dd, *J* = 14.2, 6.5 Hz, 2H), 7.07 (d, *J* = 7.7 Hz, 1H), 6.78 (br s, 1H), 6.74 (s, 1H), 6.14-6.11 (m, 2H), 4.09-3.97 (m, 4H), 3.79 (s, 2H), 2.99 (d, *J* = 7.0 Hz, 2H), 2.10 (s, 1H), 1.67 (s, 3H), 1.22 (s, 9H), 0.96 (td, *J* = 7.1, 3.9 Hz, 6H). **13C-NMR** (151 MHz, CDCl3): δ 176.03, 170.99, 170.97, 135.90, 133.94, 128.93-128.37, 124.33, 123.24, 121.86, 119.49, 119.12, 110.96, 110.01, 80.05, 74.37, 68.13, 60.92, 58.72, 38.59, 31.40, 28.50, 26.83, 13.70, 12.82. **MS** HRMS (EI) calc. for $C_{28}H_{35}O_6NNa$: 504.2357, found: 504.2366

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37. Upon solvent optimization, moderate yields were obtained with a number of other solvents.
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40. A stepwise depiction is used here to emphasize the movement of chiral information. The cyclization probably occurs by a concerted asynchronous mechanism.
41. The *cis* ring fusion in the product was confirmed by proton nOe correlations, notably between the bridghead proton and methyl protons.
42. In fact, hydrolysis of the isolated pivalate required 36 h in 1:1 MeOH / 2 M NaOH.
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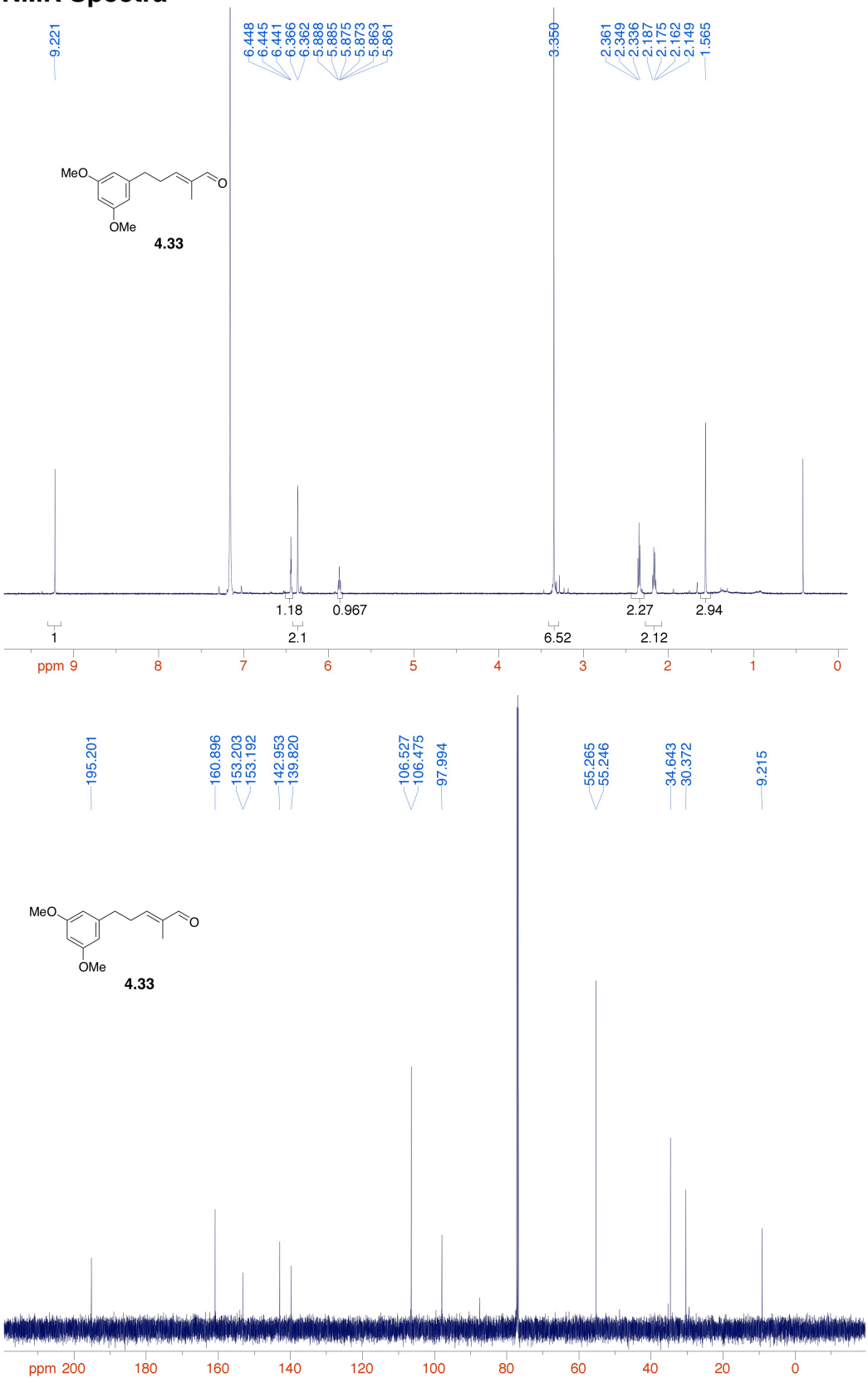
NMR Spectra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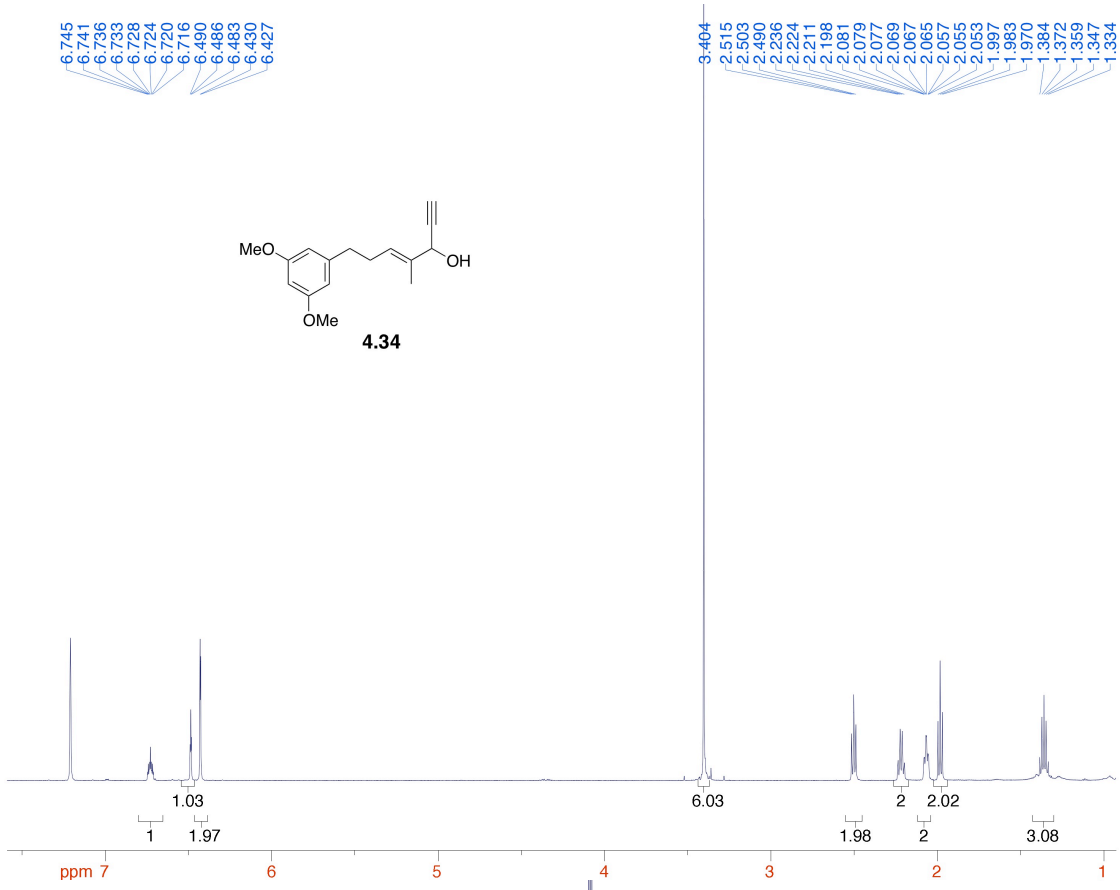
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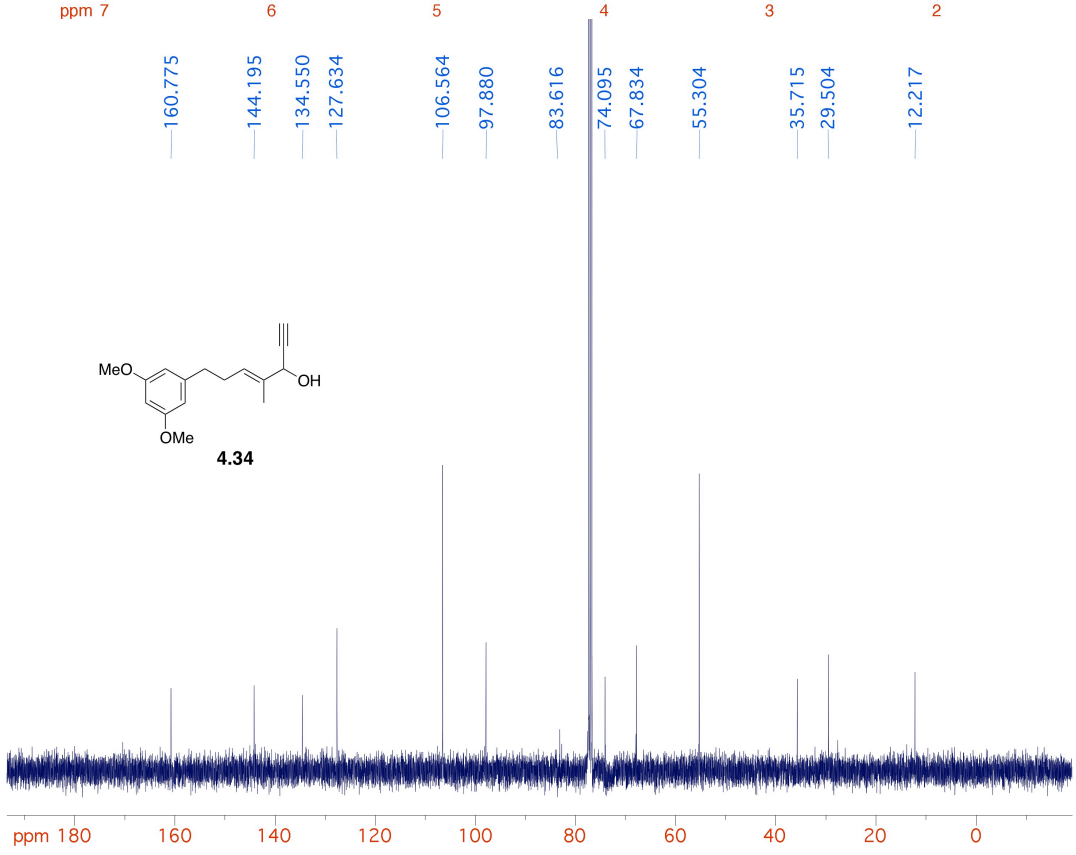
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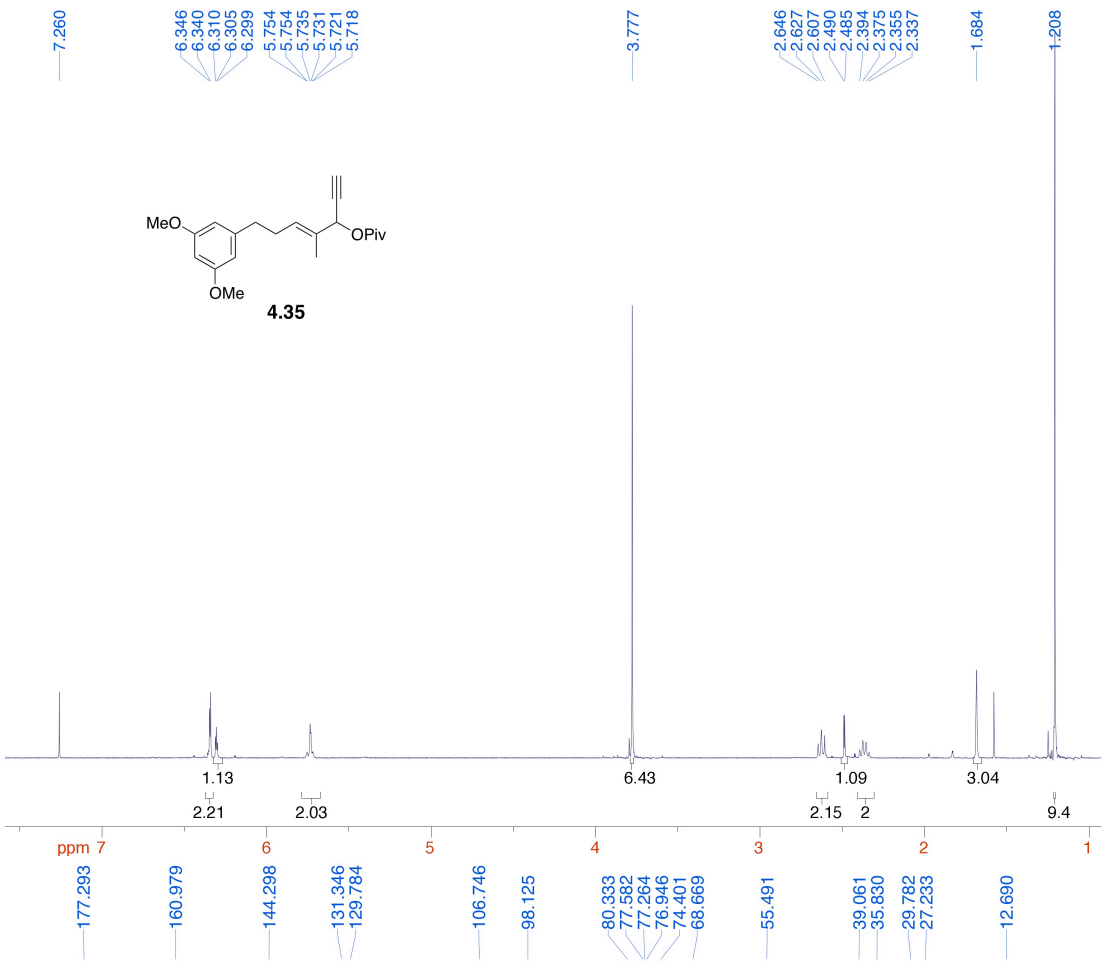
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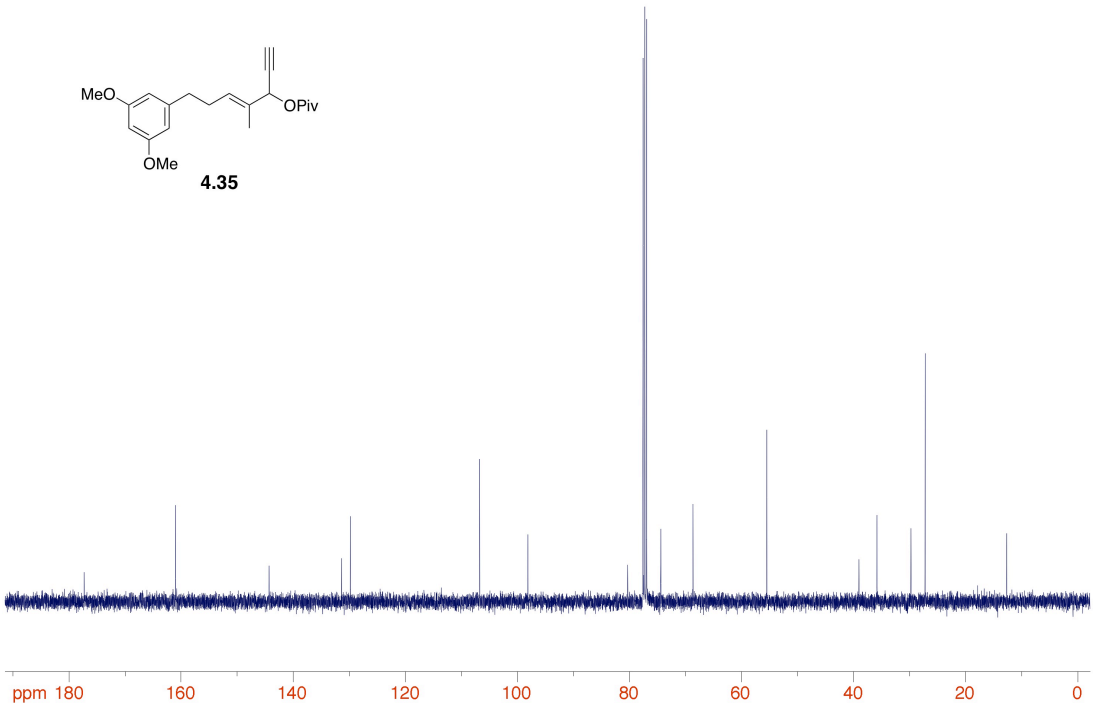
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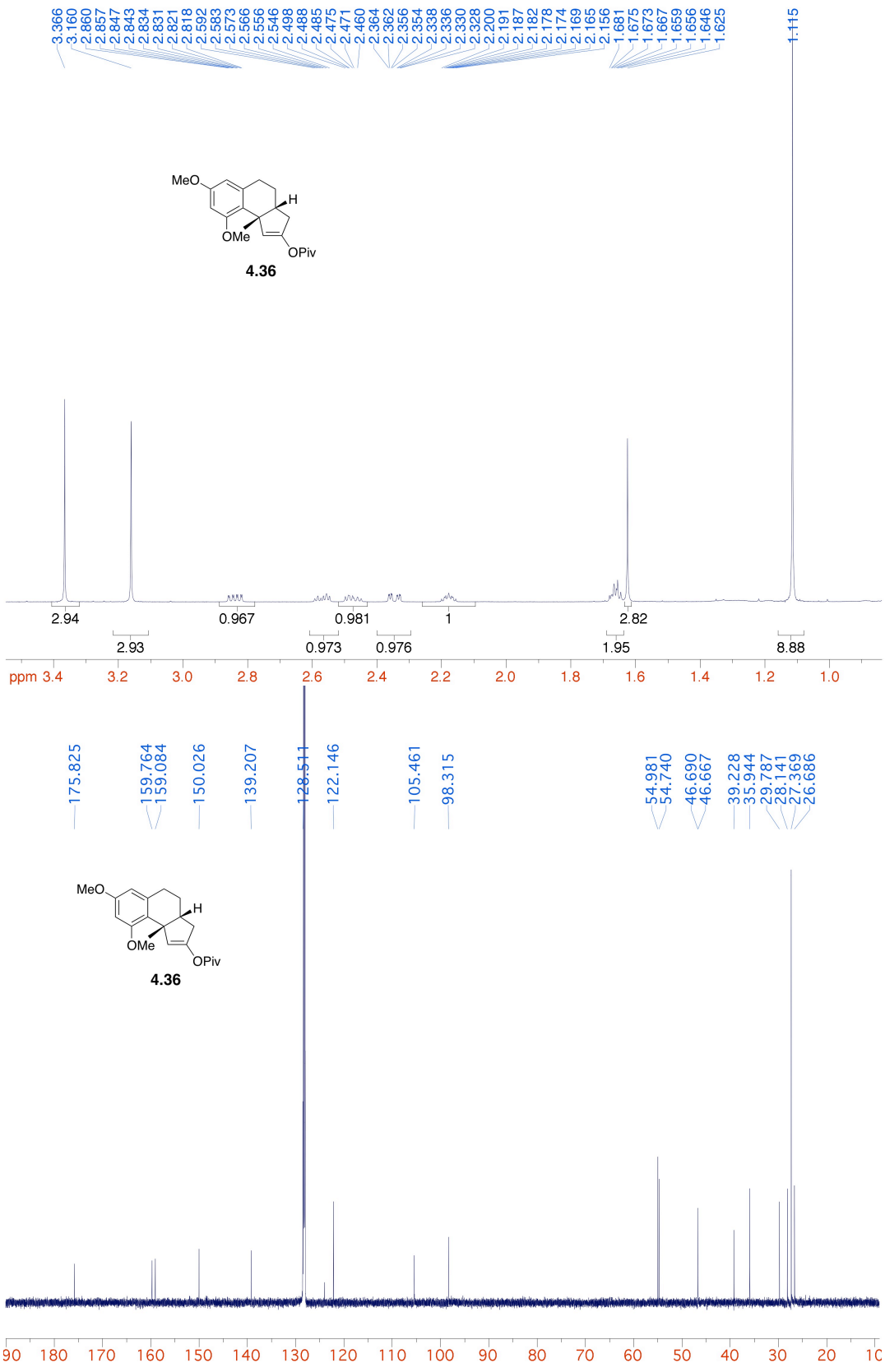
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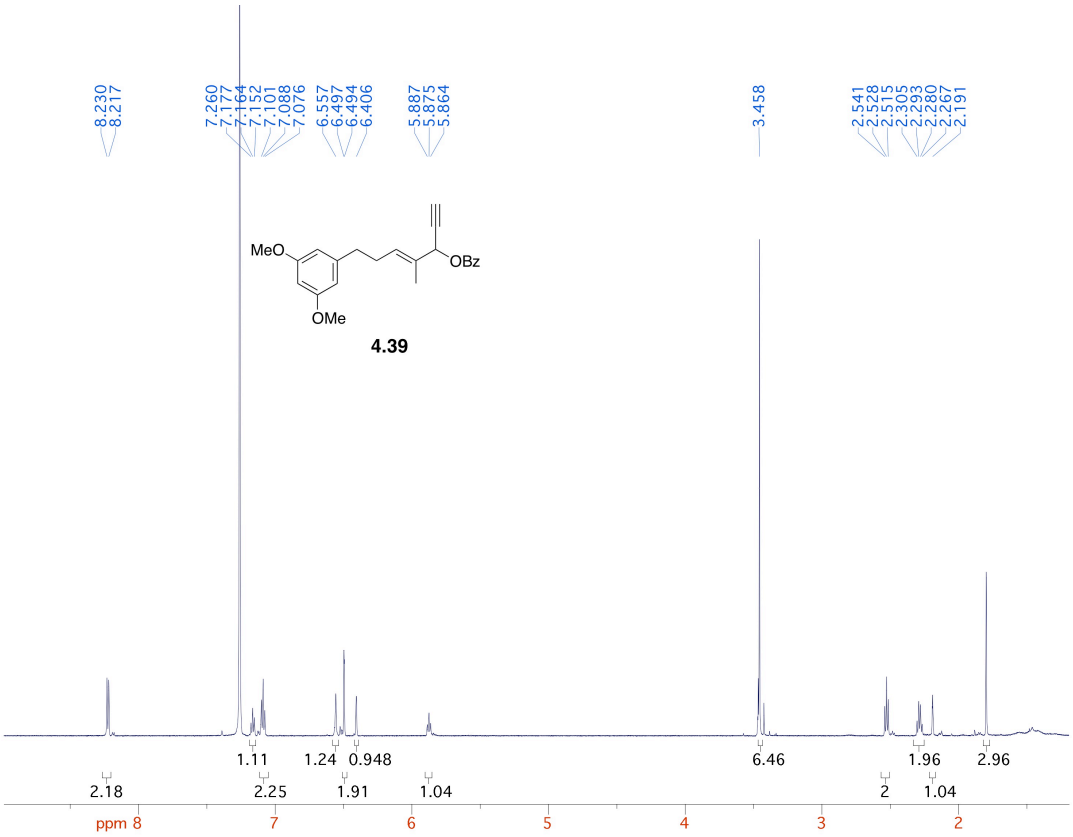
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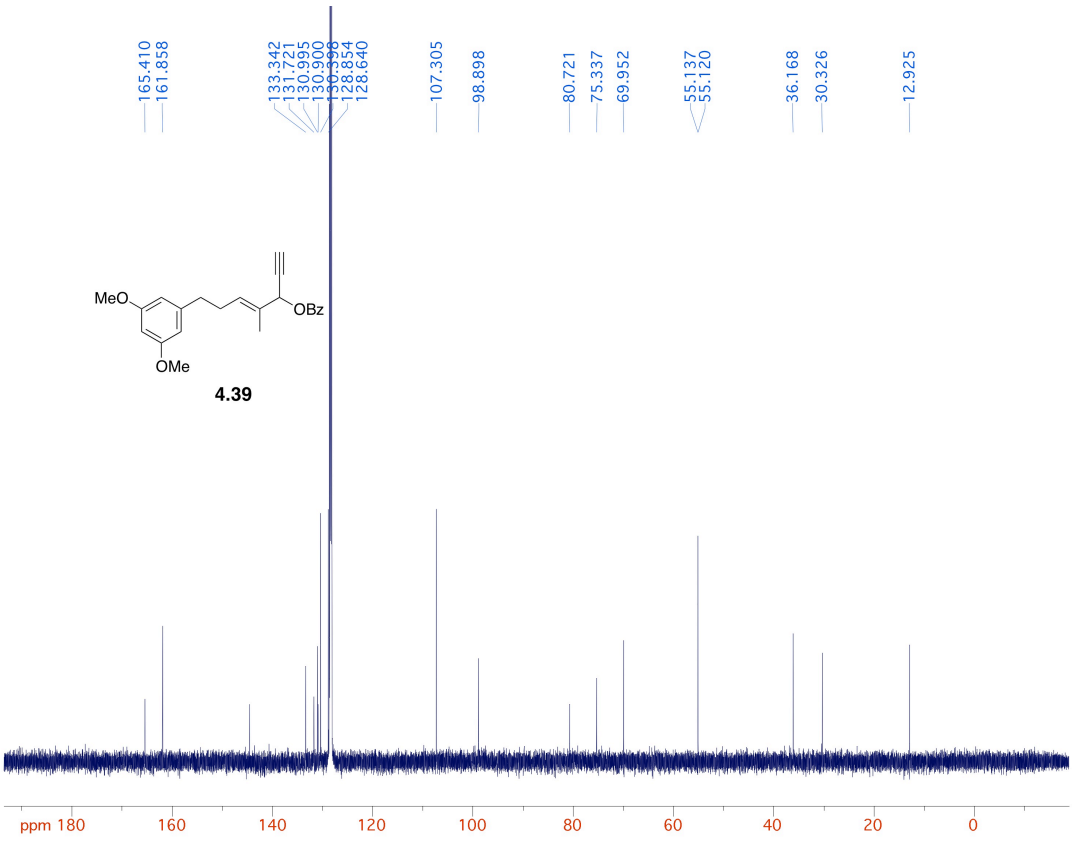
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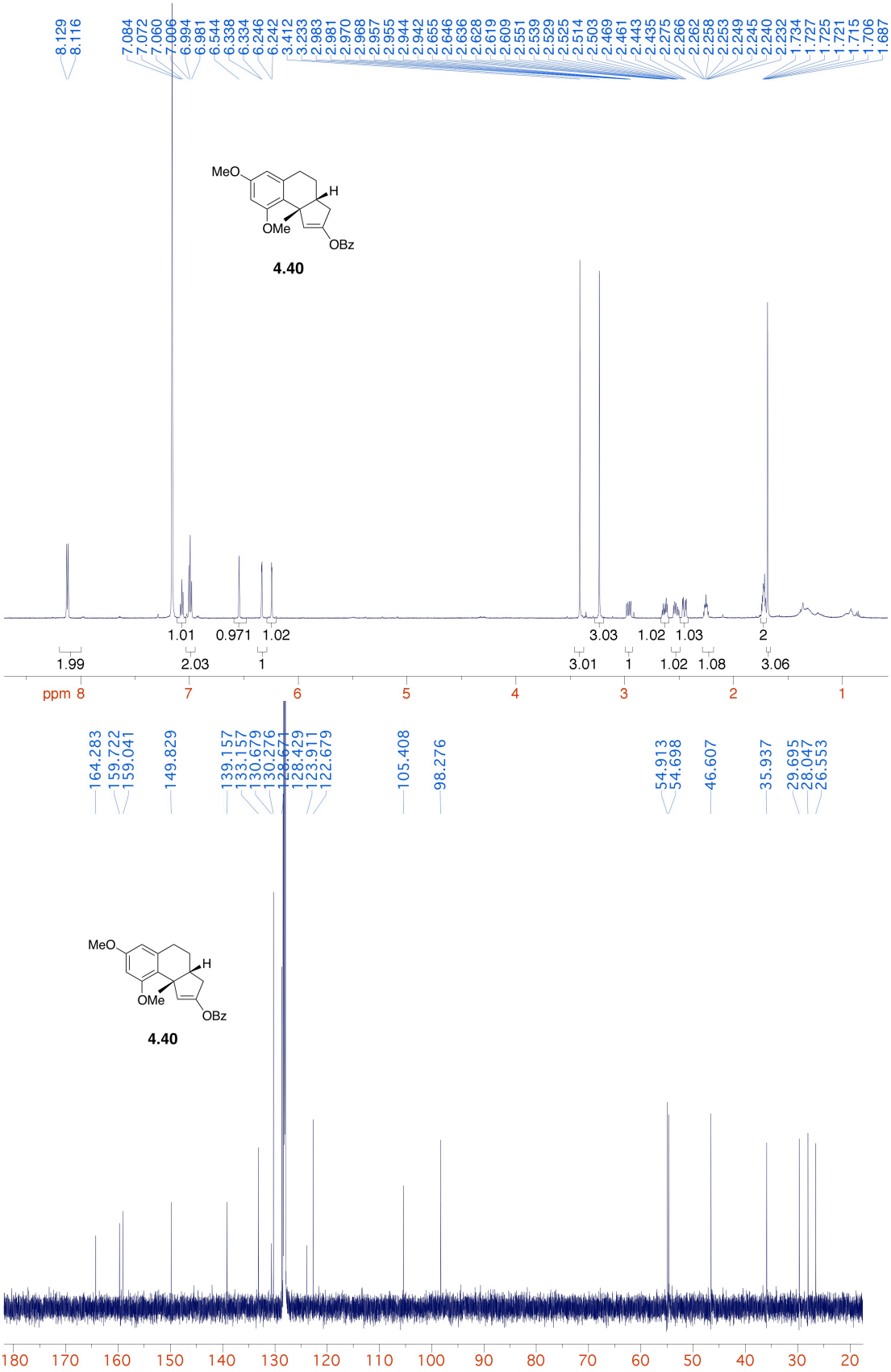
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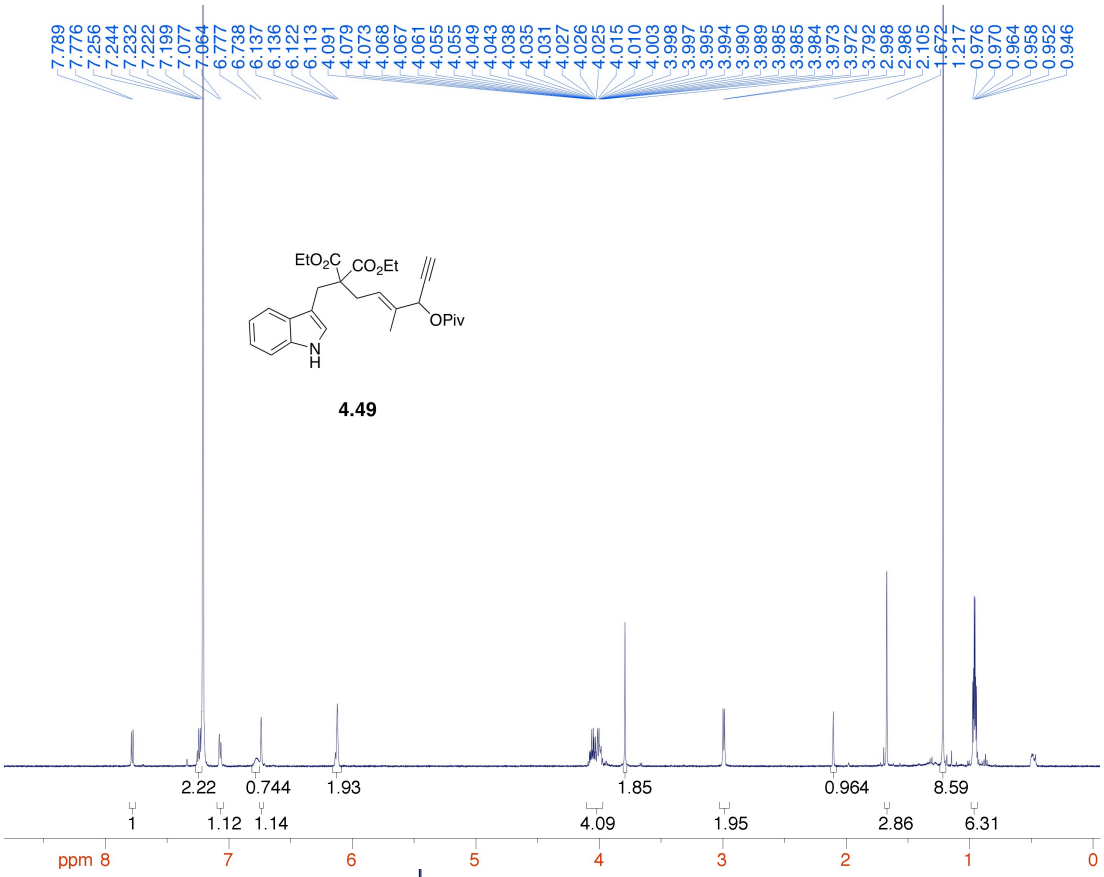
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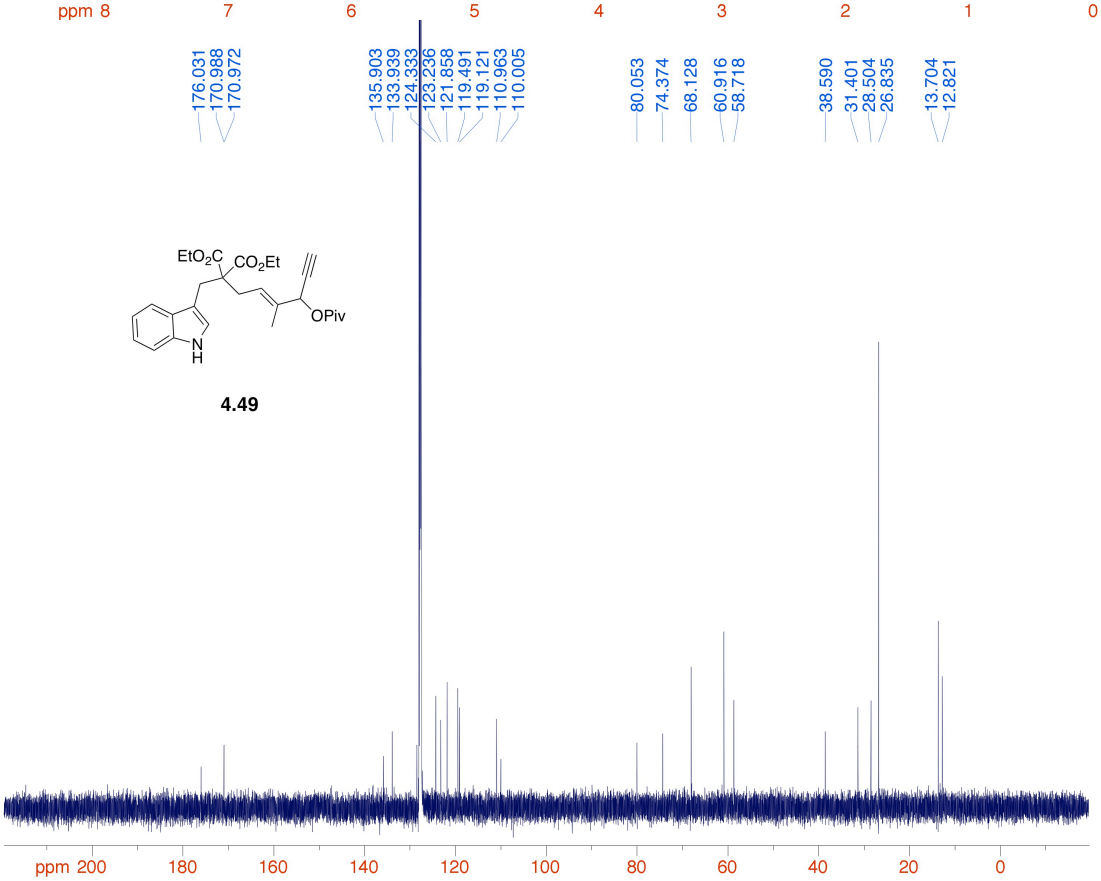
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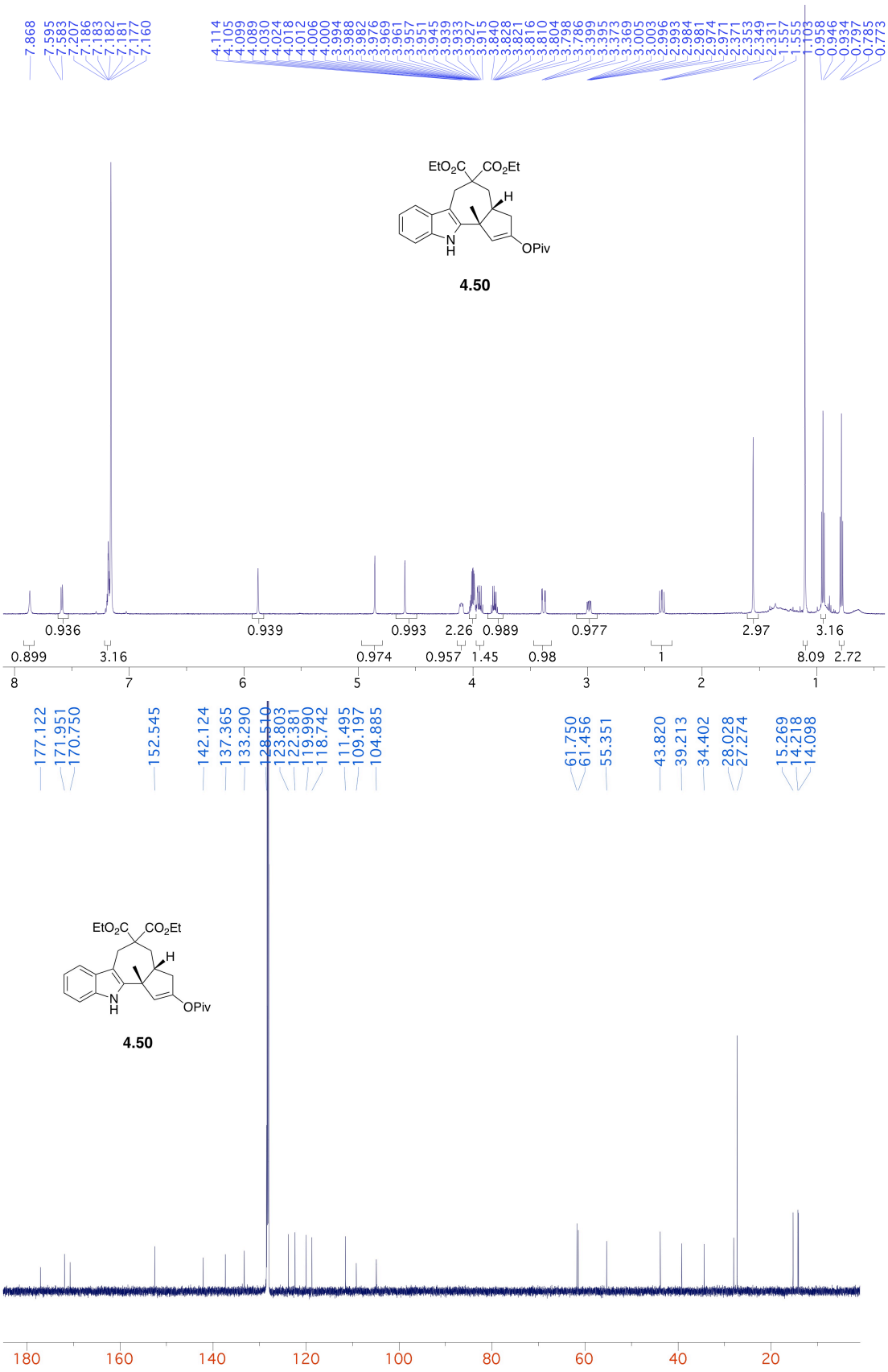
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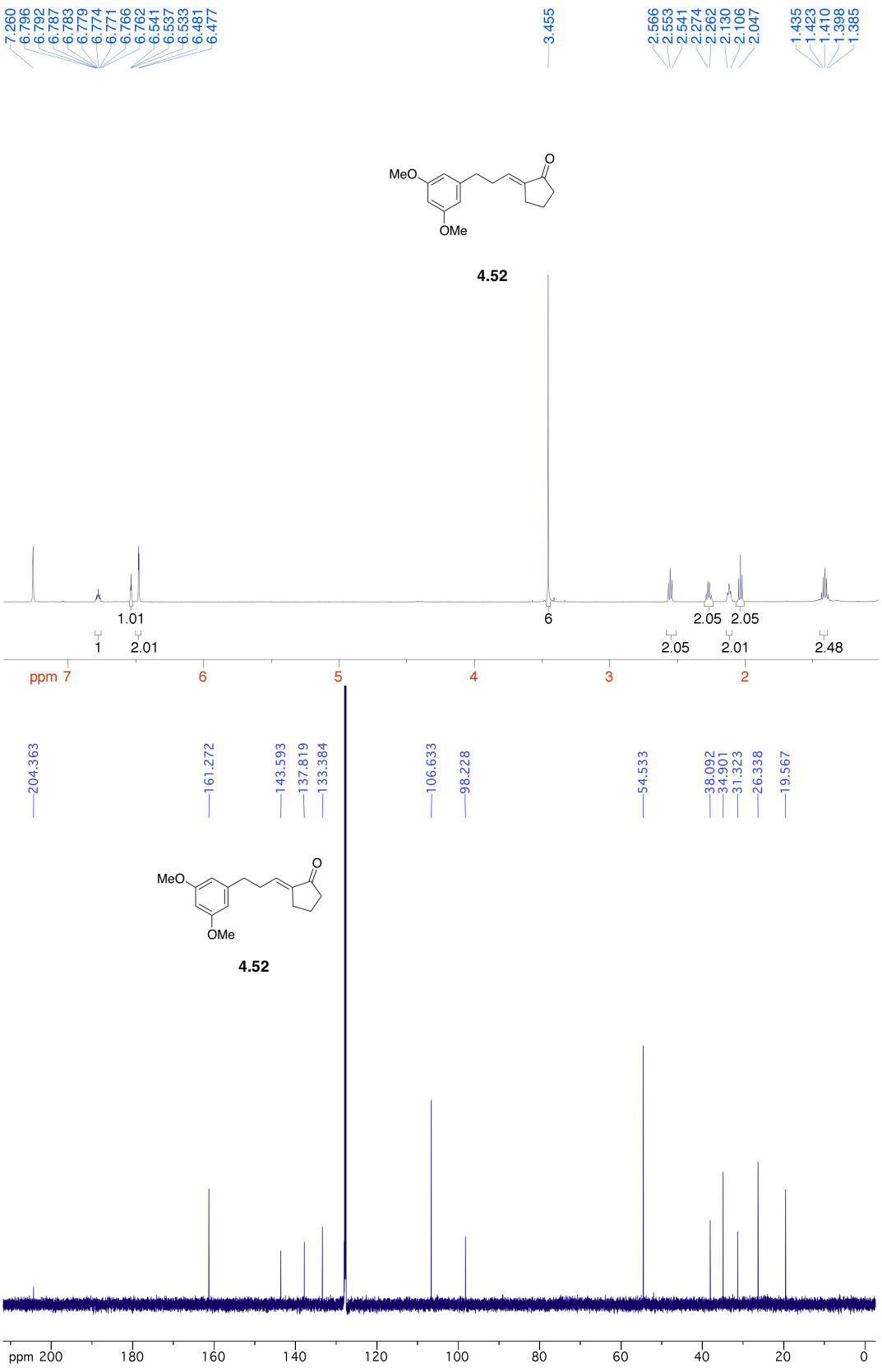
2.371
2.353
2.349
2.331
1.557
1.555
1.103
0.958
0.946
0.934
0.797
0.785
0.773
EtO2C
CO2Et
H
N
H
OPiv
4.50
0.936
0.939
0.993
2.26
0.989
0.977
2.97
3.16
0.899
3.16
0.974
0.957
1.45
0.98
1
8.09
2.72
8
7
6
5
4
3
2
1
177.122
171.951
170.750
152.545
142.124
137.365
133.290
128.510
123.803
122.381
119.990
118.742
111.495
109.197
104.885
61.750
61.456
55.351
43.820
39.213
34.402
28.028
27.274
15.269
14.218
14.098
EtO2C
CO2Et
H
N
H
OPiv
4.50
180
160
140
120
100
80
60
40
20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6.771
6.766
6.762
6.541
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6.533
6.481
6.477
3.455
2.566
2.553
2.541
2.274
2.262
2.130
2.106
2.047
1.435
1.423
1.410
1.398
1.385
MeO
OMe
O
4.52
1.01
6
2.05
2.05
1
2.01
2.05
2.01
2.48
ppm 7
6
5
4
3
2
204.363
161.272
143.593
137.819
133.384
106.633
98.228
54.533
38.092
34.901
31.323
26.338
19.567
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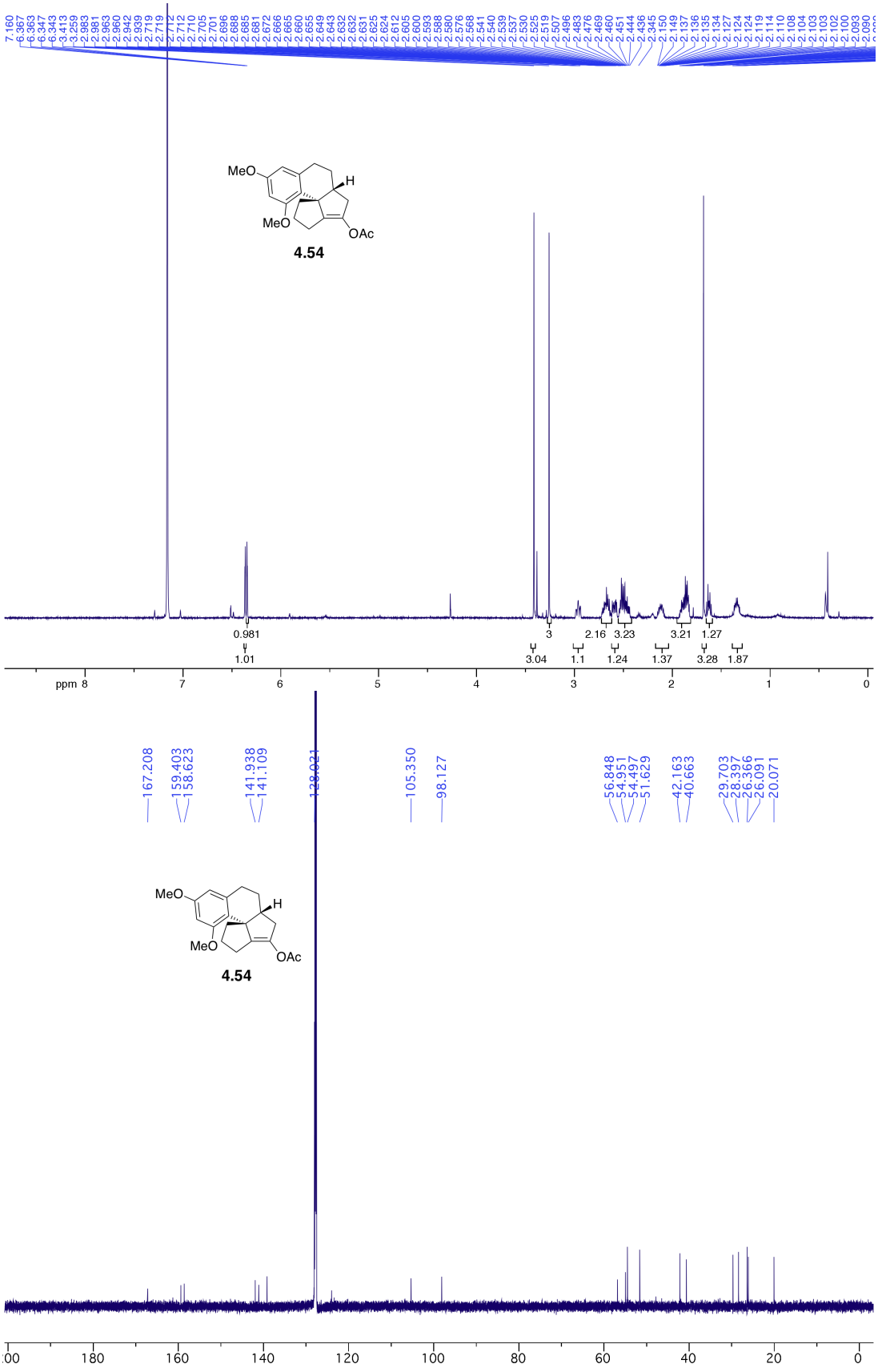
OMe
O
4.52
ppm 200
180
160
140
120
100
80
60
40
20
0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MeO
H
OAc
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1.01
3
3.04
2.16
1.1
3.23
1.24
3.21
1.37
1.27
3.28
1.87
ppm 8
7
6
5
4
3
2
1
0
167.208
159.403
158.623
141.938
141.109
128.021
105.350
98.127
56.848
54.951
54.497
51.629
42.163
40.663
29.703
28.397
26.366
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MeO
H
OAc
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140
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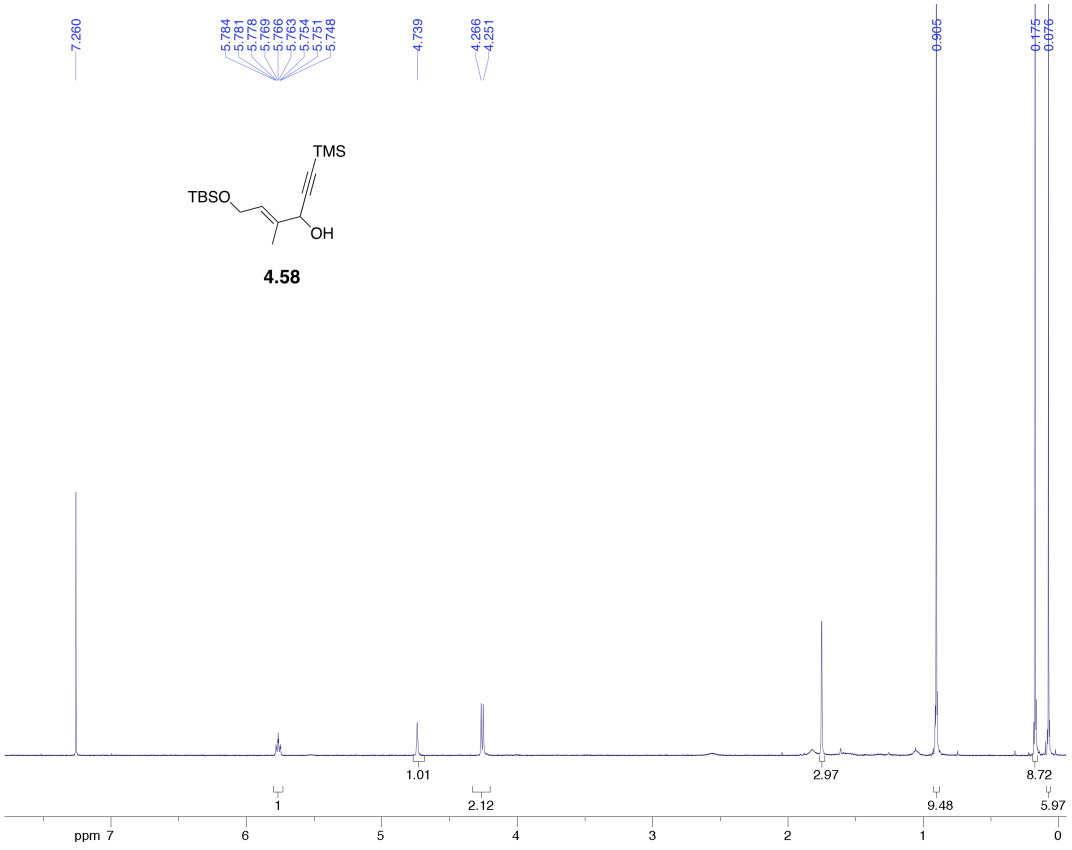
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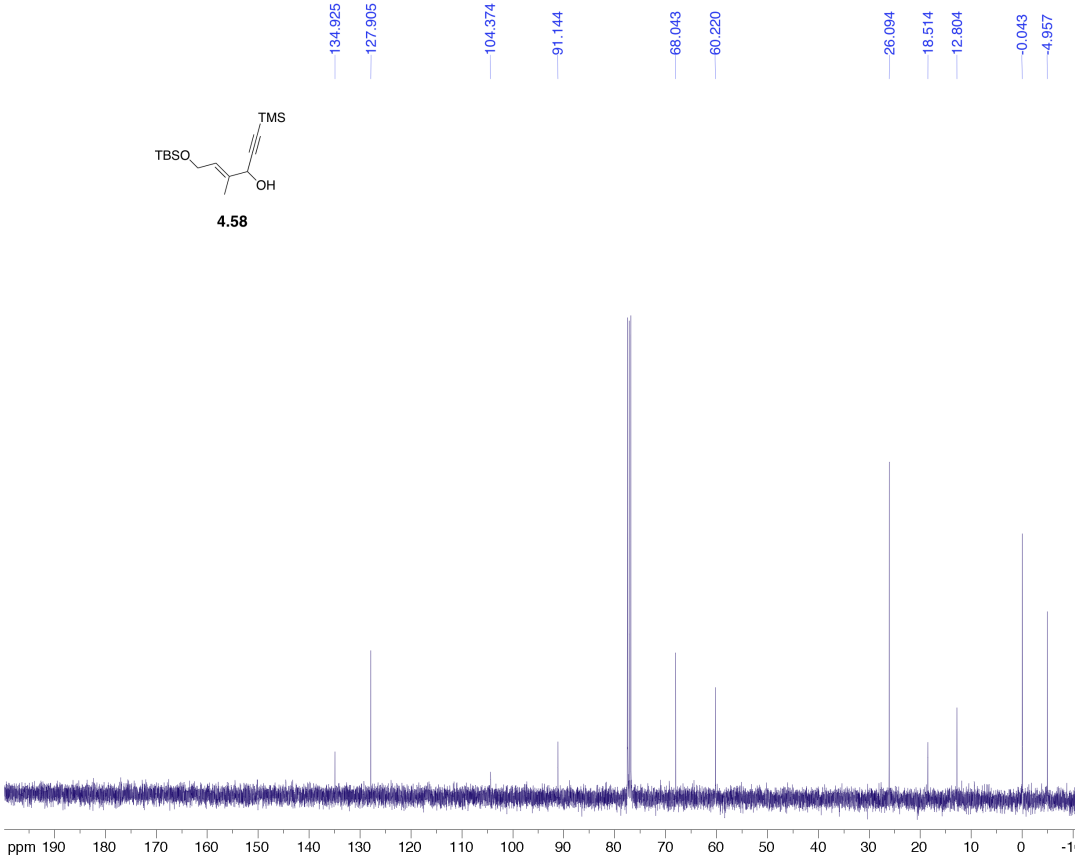
4.266
4.251
0.905
0.175
0.076
TMS
TBSO
OH
4.58
1.01
2.97
8.72
1
2.12
9.48
5.97
ppm 7
6
5
4
3
2
1
0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91.144
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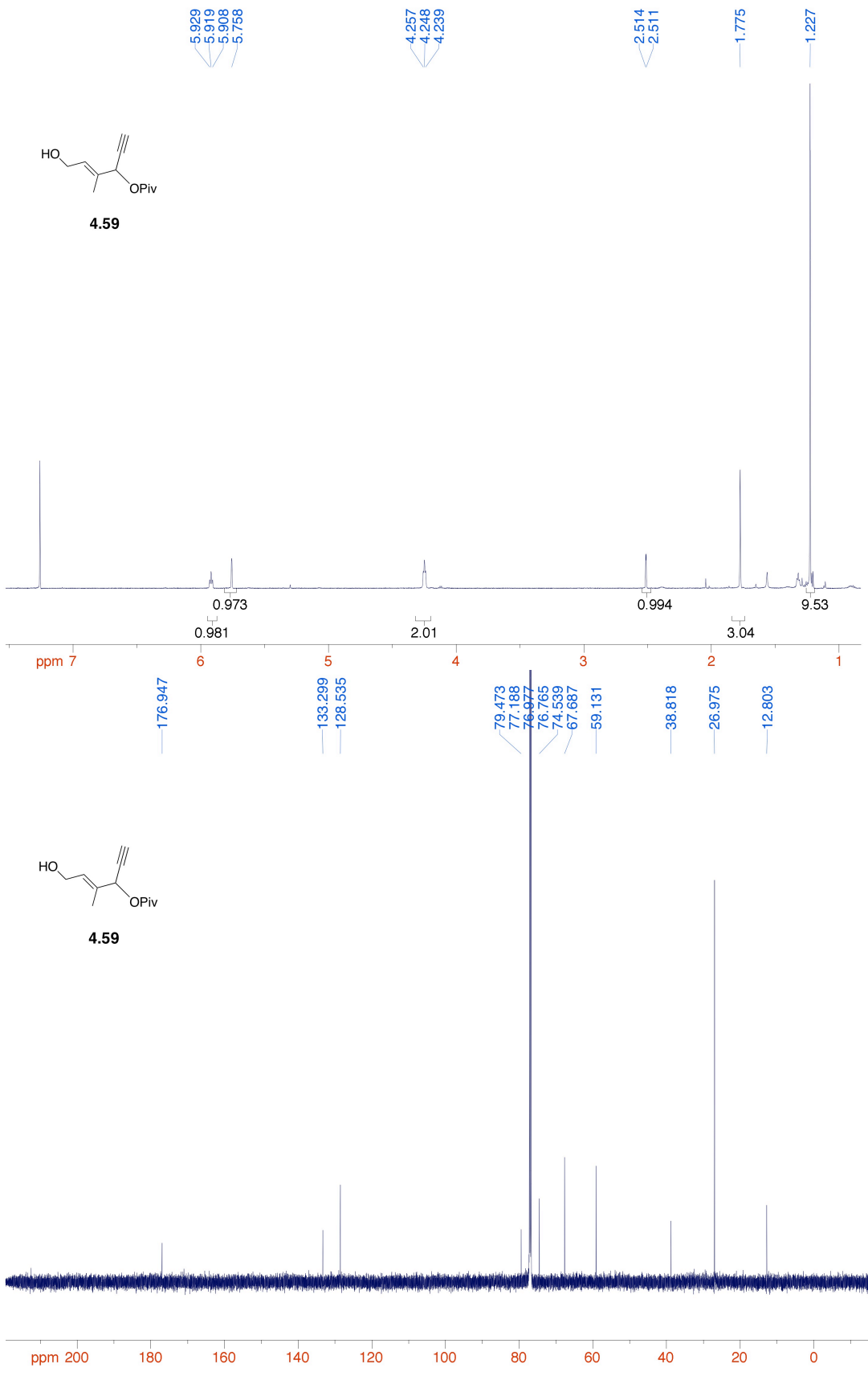
26.094
18.514
12.804
-0.043
-4.957
TMS
TBSO
OH
4.58
ppm 190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10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4.239
2.514
2.511
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1.227
HO
OPiv
4.59
0.973
0.994
9.53
0.981
2.01
3.04
ppm 7
6
5
4
3
2
1
176.947
133.299
128.535
79.473
77.188
76.977
76.765
74.539
67.687
59.131
38.818
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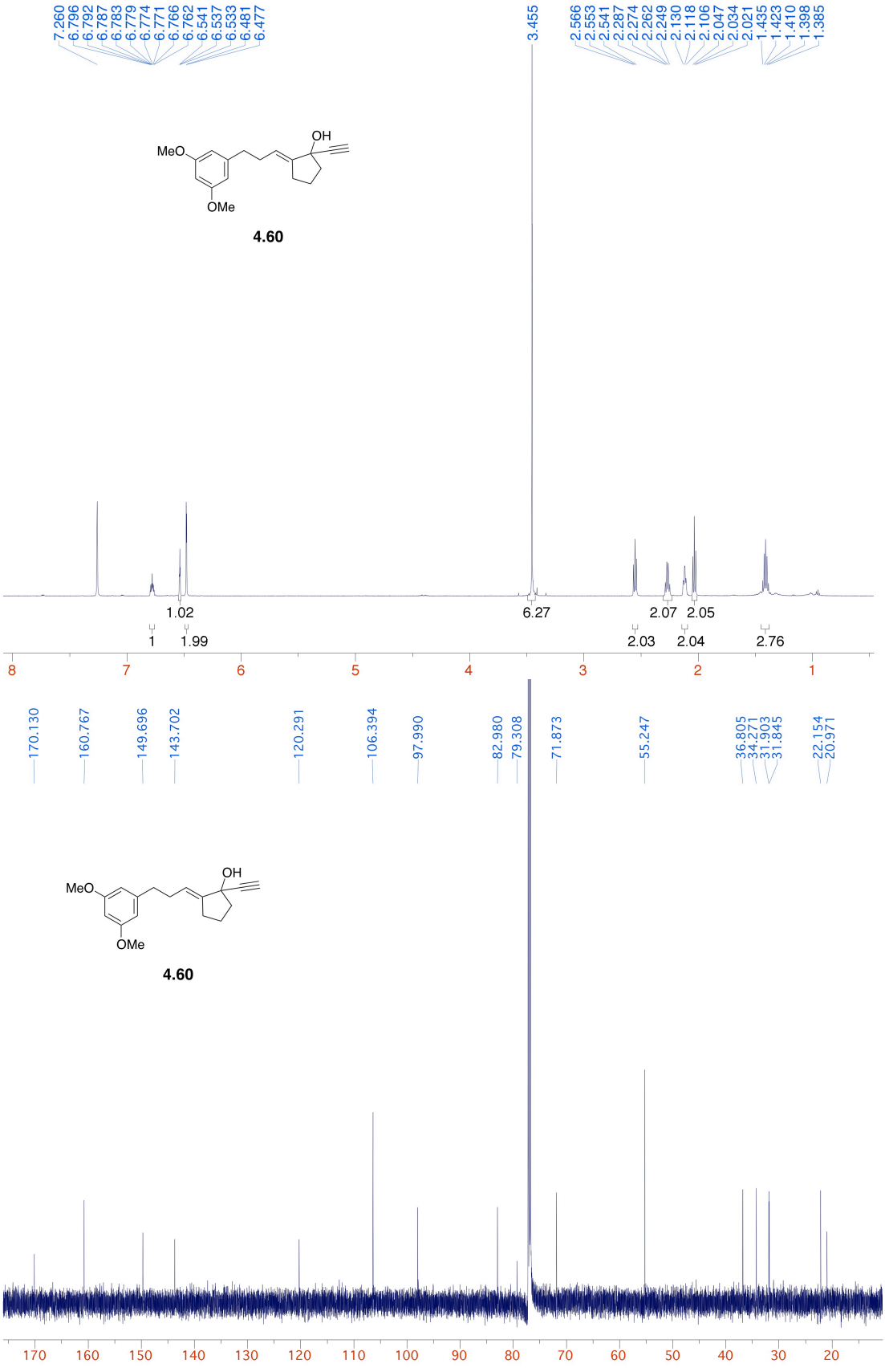
HO
OPiv
4.59
ppm 200
180
160
140
120
100
80
60
40
20
0


7.260
6.796
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6.481
6.477
3.455
2.566
2.553
2.541
2.287
2.274
2.262
2.249
2.130
2.118
2.106
2.047
2.034
2.021
1.435
1.423
1.410
1.398
1.385
MeO
OH
OMe
4.60
1.02
1.99
6.27
2.07
2.05
2.03
2.04
2.76
8
7
6
5
4
3
2
1
170.130
160.767
149.696
143.702
120.291
106.394
97.990
82.980
79.308
71.873
55.247
36.805
34.271
31.903
31.845
22.154
20.971
MeO
OH
OMe
4.60
170
160
150
140
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110
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90
80
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60
50
40
30
20

HPLC Spectra

RAC_ASSAY_FCRP
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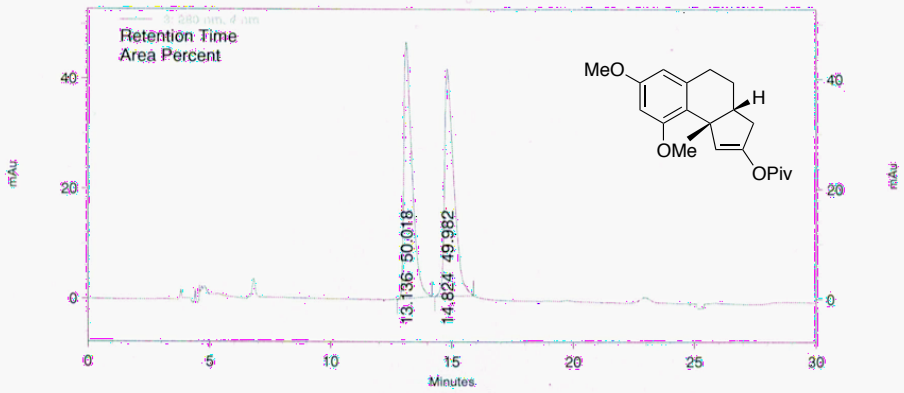

3: 280 nm, 4 nm
Results

Pk #	Retention Time	Area Percent	Lambda Max
1	13.136	50.018	219
2	14.824	49.982	219

SGS6-192-b-(+-)
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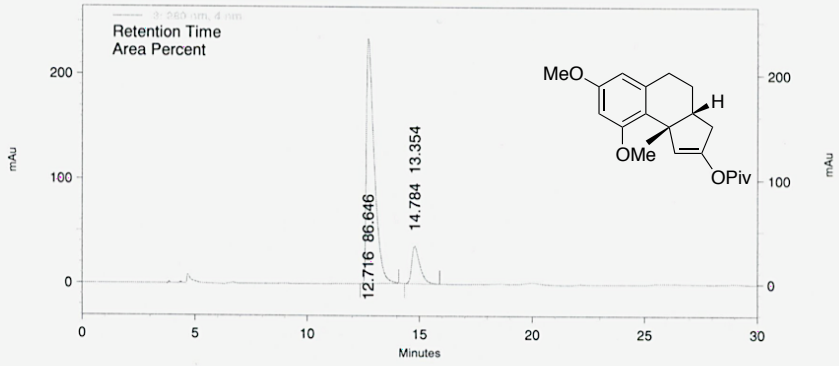

3: 280 nm, 4 nm
Results

Pk #	Retention Time	Area Percent	Lambda Max
1	12.716	86.646	221
2	14.784	13.354	219

SGS6-5-FCRPBz-RAC
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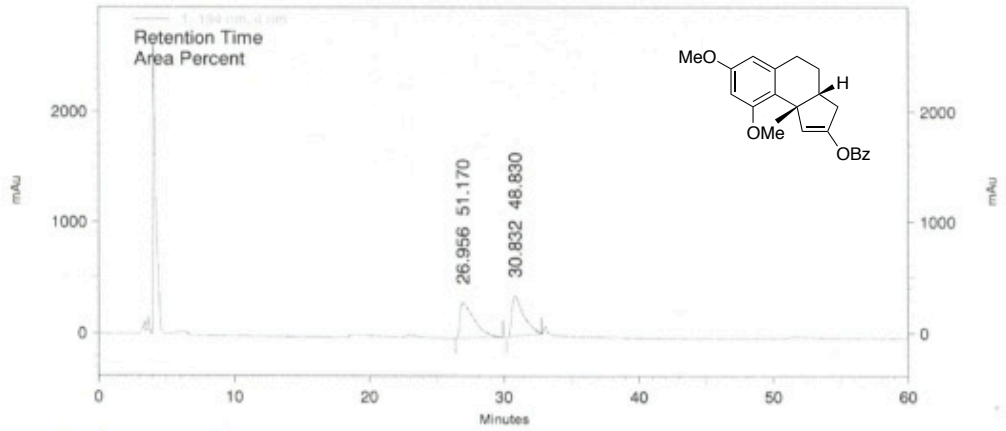

1: 194 nm, 4 nm
Results

Pk #	Retention Time	Area Percent	Lambda Max
1	26.956	51.170	199
2	30.832	48.830	199

SGS6-159-1-FCRPBz
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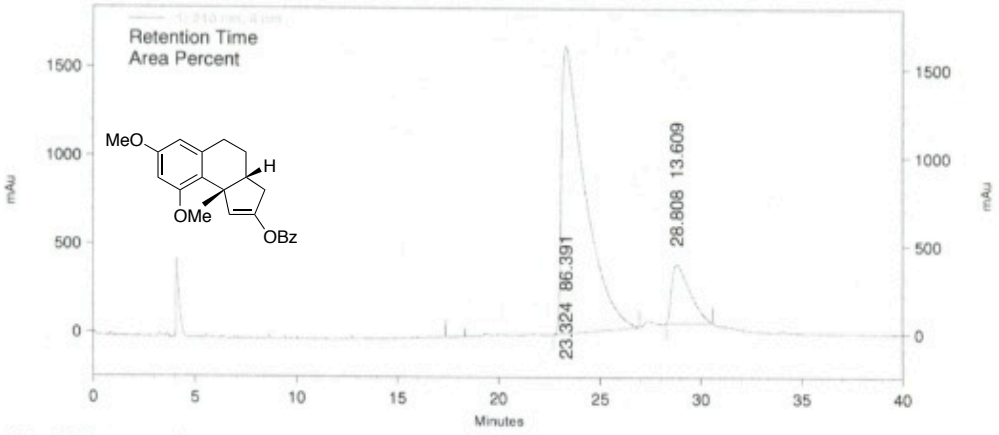

1: 210 nm, 4 nm
Results

Pk #	Retention Time	Area Percent	Lambda Max
1	23.324	86.391	196
2	28.808	13.609	226