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Formal [4+2] Cycloadditions of Anhydrides and α,β-Unsaturated *N*-Tosyl Ketimines

By

NOAH PHILLIP BURLOW
THESIS

Submitted in partial satisfaction of the requirements for the degree of

MASTER OF SCIENCE

in

Chemistry

in the

OFFICE OF GRADUATE STUDIES

of the

UNIVERSITY OF CALIFORNIA

DAVIS

Approved:

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Jared T. Shaw, Chair

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Neil E. Schore

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Prof. Mark J. Kurth

Committee in Charge

2022

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ACKNOWLEDGEMENTS

First of all, I want to thank my family for their love and support. My mother Lori, grandmother Sandra, aunt Stephanie, uncles Phillip and Gary, as well as my cousin Spencer. Without them, none of this would be possible. I would also like to thank all Shaw lab members both past and present. In particular, Dr. Nina Howard for her contributions to the work described in this thesis, as well as Dr. Kellan Lamb for her mentorship during my early years in the lab. I would like to thank Prof. Neil Schore and Prof. Mark Kurth for their involvement in my thesis committee. And last but certainly not least, I want to thank my graduate advisor Prof. Jared Shaw. His support and patience has been invaluable during the many challenging times in my graduate school journey.

ABSTRACT

Herein is described a method for the diastereoselective synthesis of highly-substituted β-enamino ketones from anhydrides and ketone-derived imines. Cyclic, enolizable anhydrides undergo a base-promoted conjugate addition reaction with α,β-unsaturated *N*-tosyl ketimines, followed by an intramolecular acylation to give formal [4+2] cycloaddition products. The carboxylic acid-containing products are formed in modest selectivity for the cis-diastereomer and can be fully epimerized to the trans-diastereomer upon esterification.

1. Introduction

Cyclic anhydrides are useful dipolar synthons for the synthesis of complex organic molecules through formal cycloaddition reactions.[1] The most widely studied reaction of cyclic anhydrides involves the addition to imines to form lactams, recently referred to as the Castagnoli-Cushman reaction.[1b] Although most previous studies of this reaction employed *N*-alkyl imines, the reaction of *N*-sulfonyl imines was recently shown to proceed by base mediation[2] and rendered asymmetric using organocatalysts[3] (Figure 1). Although *N*-aryl imines are less commonly used, they exhibit excellent reactivity in a recently-reported catalytic reaction.[3b]
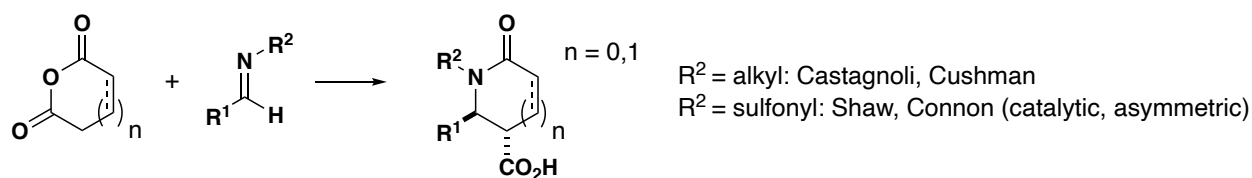

Figure 1. Previous reactions of imines and cyclic anhydrides

In parallel, Tamura has demonstrated that homophthalic anhydride undergoes base-mediated addition to alkynes to form, after decarboxylation, highly substituted naphthalenes.[4] Early studies included limited examples of addition to alkenes to form substituted tetralins[4-5] and more recently Connon developed an asymmetric variant of this process[6] (Figure 2).
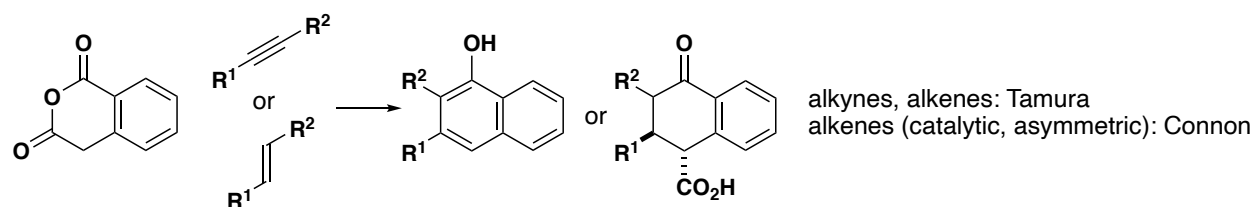

Figure 2. Reactions of homophthalic anhydride and alkenes/alkynes

We initiated a study of α,β-unsaturated ketimines, which have the potential to exhibit merged "Tamura-like" and "Cushman-like" reactivity. Thus, we refer to the reaction of these imines with anhydrides as the "aza-Tamura reaction." Herein we report the first reactions of cyclic anhydrides with electron-deficient unsaturated imines[7], which proceed in high diastereoselectivity and, for the first time, exhibit "Tamura-like" reactivity to form 5-membered ring products (Figure 3).
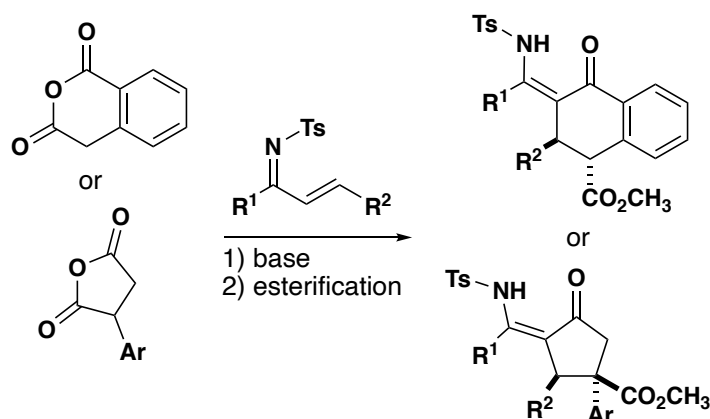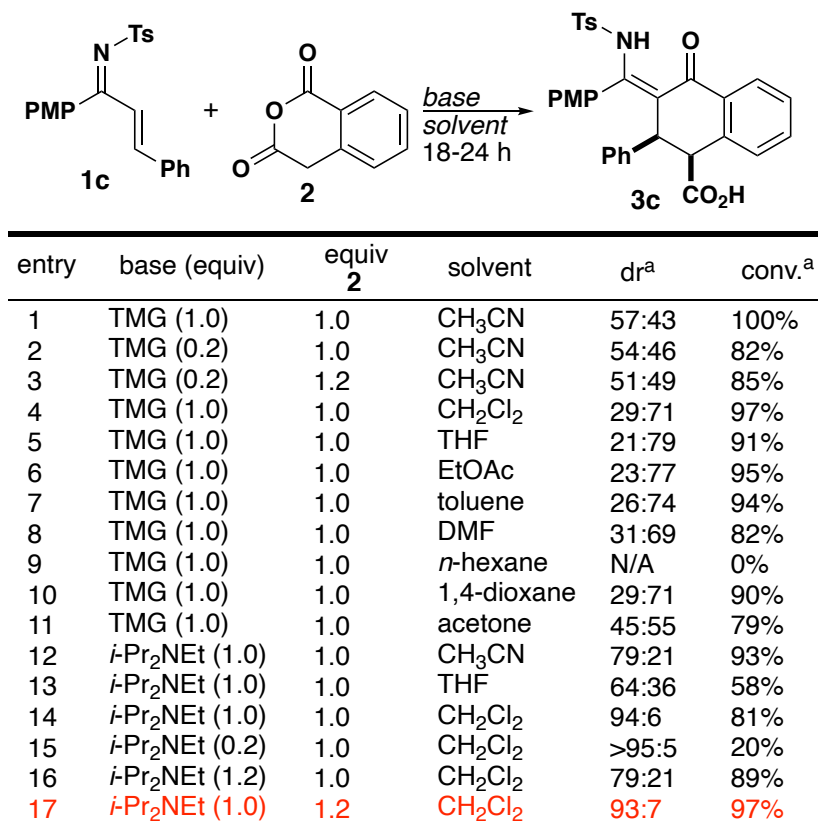

Figure 3. Our work on imine-anhydride formal [4+2] cycloadditions

2. Reaction Optimization

For our initial investigation of this reaction, we used the readily enolizable homophthalic anhydride and methoxy substituted chalcone imine **1c** (Figure 4). Chalcone-derived imines were chosen for their ease of synthesis and diversification.

entry	base (equiv)	equiv 2	solvent	dr[a]	conv.[a]
1	TMG (1.0)	1.0	CH$_3$CN	57:43	100%
2	TMG (0.2)	1.0	CH$_3$CN	54:46	82%
3	TMG (0.2)	1.2	CH$_3$CN	51:49	85%
4	TMG (1.0)	1.0	CH$_2$Cl$_2$	29:71	97%
5	TMG (1.0)	1.0	THF	21:79	91%
6	TMG (1.0)	1.0	EtOAc	23:77	95%
7	TMG (1.0)	1.0	toluene	26:74	94%
8	TMG (1.0)	1.0	DMF	31:69	82%
9	TMG (1.0)	1.0	*n*-hexane	N/A	0%
10	TMG (1.0)	1.0	1,4-dioxane	29:71	90%
11	TMG (1.0)	1.0	acetone	45:55	79%
12	*i*-Pr$_2$NEt (1.0)	1.0	CH$_3$CN	79:21	93%
13	*i*-Pr$_2$NEt (1.0)	1.0	THF	64:36	58%
14	*i*-Pr$_2$NEt (1.0)	1.0	CH$_2$Cl$_2$	94:6	81%
15	*i*-Pr$_2$NEt (0.2)	1.0	CH$_2$Cl$_2$	>95:5	20%
16	*i*-Pr$_2$NEt (1.2)	1.0	CH$_2$Cl$_2$	79:21	89%
17	*i*-Pr$_2$NEt (1.0)	1.2	CH$_2$Cl$_2$	93:7	97%

[a]Determined by ^{1}H NMR spectrum of unpurified reaction mixture

Figure 4. Reaction optimization with homopththalic anhydride and imine **1c**

Our favored conditions for the base-catalyzed anhydride-Mannich reaction (AMR), 1 equiv tetramethylguanidine (TMG) in acetonitrile, provided the desired product in full conversion but with virtually no diastereoselectivity (entry 1).[8] Similar results were observed with 20 mol% TMG with either 1.0 or 1.2 equiv of anhydride (entries 2-3). Switching the base to 1 equiv *i*-Pr$_2$NEt resulted in a reversal of selectivity to the *cis* isomer (entry 12) and performing the reaction in CH$_2$Cl$_2$ provided a diastereomer ratio (dr) of 94:6 (entry 14). Attempts at using sub-stoichiometric quantities of *i*-Pr$_2$NEt resulted in lower conversion (entry 15). We attribute the reduced reactivity in this case to the acidity of the *N*-tosyl vinylogous amide proton, which results in a catalyst inhibition by protonation.

3. Stereochemical Determination

Acid **3c** was converted to the corresponding methyl ester for ease of purification. Upon treatment with TMS-diazomethane, the diastereomer ratio of the resulting ester shifted to varying degrees, and with the addition of DBU seemed to invert completely. As such, we suspected that the configuration of the initially-formed acid was *cis* and as a result of base-mediated epimerization of the stereogenic center alpha to the carboxyl group, the configuration of the ester was *trans* (Figure 5).
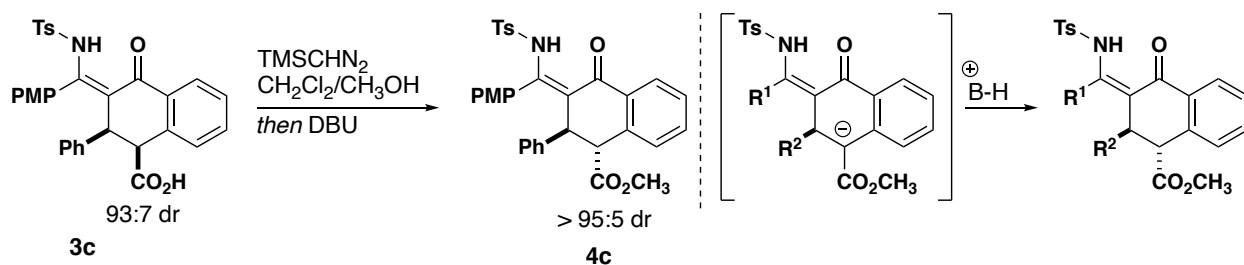
Figure 5. Esterification and epimerization of aza-Tamura products

To support our hypothesis, the ester **4c** was hydrolyzed back to the acid using LiOH. We hoped to obtain an X-ray crystal structure by converting the carboxylic acid to a benzyl amide. After examining several conditions for amide coupling, those of Knapp and coworkers resulted in the formation of a less polar product lacking the expected amide protons.[9] X-ray crystallography revealed that the nitrile had been formed, presumably through a von Braun-like mechanism proceeding through cleavage of the PMB amide[10] (Figure 6).
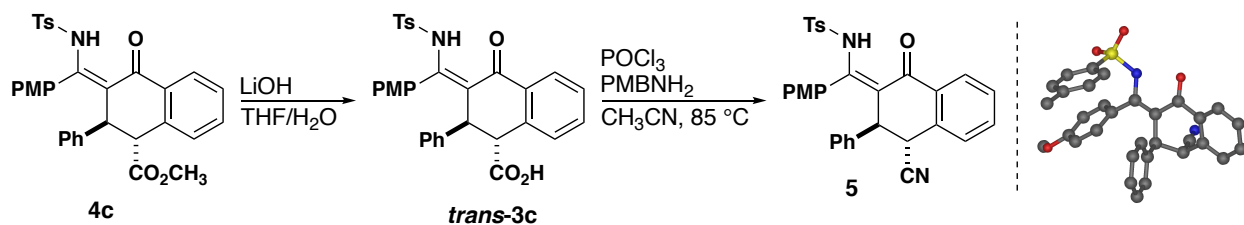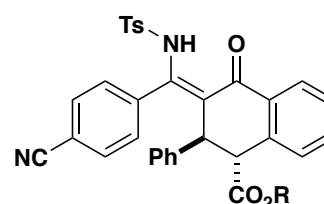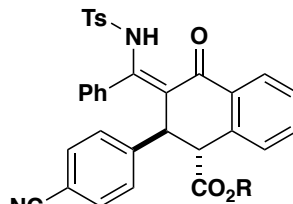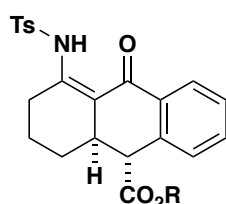
Figure 6. Synthesis and X-ray crystal structure of nitrile **5**

Additionally, this structure showed the relative stereochemistry of nitrile **5** to be *trans*. Given the similarity in coupling constants between ester **4c** and nitrile **5**, we conclude that both compounds have a *trans* configuration between the adjacent stereogenic centers.

4. Reaction Scope

Chalcone imines with a variety of substituents provided formal cycloaddition products in high yield (Figure 7). The electronics of the aryl ring adjacent to the imine had a noticeable effect on the diastereoselectivity of the reaction, with electron donating groups giving an improved dr for the *cis*-diastereomer. Alternatively, electron withdrawing grou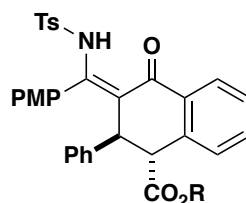ps resulted in an erosion of dr, which can be explained by a faster rate of epimerization to the *trans*-diastereomer under the reaction conditions. Enolizable imines **(1h)** and **(1i)** were tolerated under the reaction conditions as well.

Figure 7. Imine scope of the aza-Tamura reaction

Reaction scheme (top):

i-Pr$_2$NEt (1.0 equiv), CH$_2$Cl$_2$

1a-k + **2** → **3a-k** (CO$_2$H)

TMSCHN$_2$, CH$_2$Cl$_2$, CH$_3$OH, *then* DBU → **4a-k** (CO$_2$CH$_3$)

3a 15:85 dr[a]
4a >95:5 dr
94% yield[b]

3b 15:85 dr
4b >95:5 dr
92% yield

3c 7:93 dr
4c >95:5 dr
92% yield

3d 15:85 dr
4d >95:5 dr
84% yield

3e 20:80 dr
4e >95:5 dr
68% yield

3f 15:85 dr
4f >95:5 dr
84% yield

3g 35:65 dr
4g >95:5 dr
55% yield

3h 23:77 dr
4h >95:5 dr
57% yield

3i 85:15 dr
4i 85:15 dr
50% yield

3j 20:80 dr
4j >95:5 dr
89% yield

3k 47:53 dr
4k >95:5 dr
85% yield

[a] all diastereomer ratios refer to trans:cis
[b] all yields calculated over two steps

Methyl-substituted homophthalic anhydride and phenyl succinic anhydride also give formal cycloaddition products (Figure 8). Unfortunately, the scope of this reaction was limited to

anhydrides of similar reactivity to homophthtalic anhydride. Use of a more reactive anhydride such as cyano succinic anhydride resulted in base-promoted polymerization.
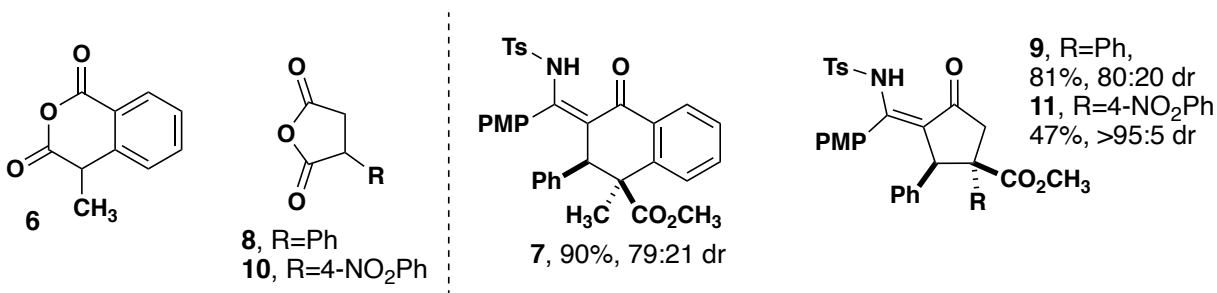
Figure 8. Anhydride scope of the aza-Tamura reaction

5. Mechanistic Hypothesis

We hypothesize that the mechanism for this reaction involves conjugate addition of the anhydride enolate to the imine, followed by an intramolecular acylation (Figure 9). The ambident enamine anion resulting from conjugate addition can undergo *N*-acylation to form a δ-lactam **(15)** or *C*-acylation followed by tautomerization to form a β-enamino cyclohexanone **(3a-i)**.
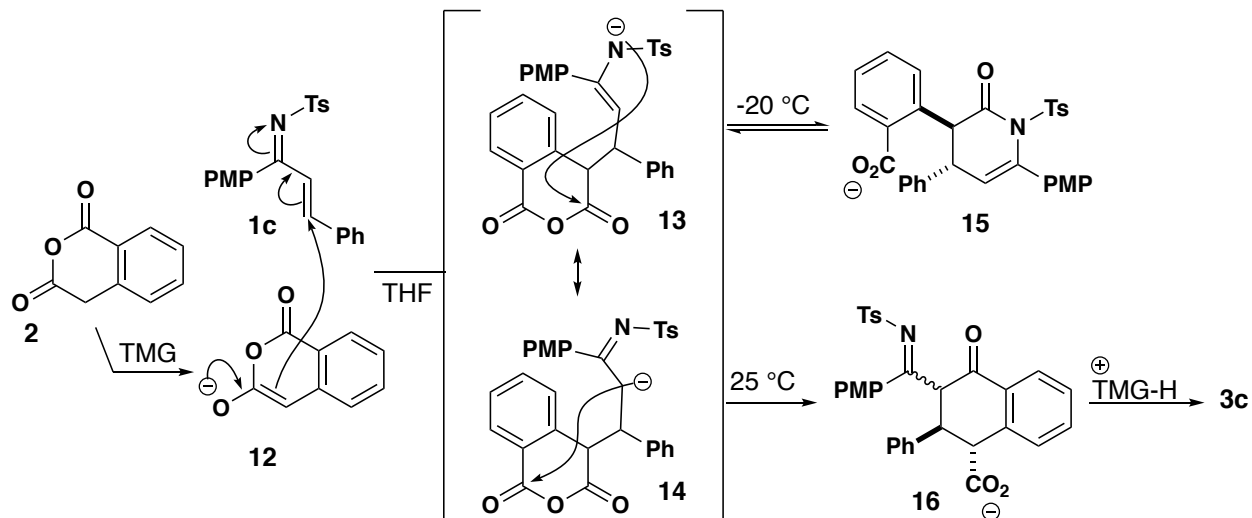
Figure 9. Proposed mechanism for the aza-Tamura reaction

We have observed the *N*-acylation product of type **15** in ^{1}H NMR studies as a transient, kinetically favored intermediate that converts to the β-enamino ketone over the course of the reaction. The reaction was set up in an NMR tube in deuterated chloroform and an NMR spectrum was collected every hour for 24 hours (Figure 10). After 2 hours the alkene proton of **15** can be seen at 5.05 ppm. Over time, this proton signal disappears while the proton signal at 4.45 ppm corresponding to **16** grows. This supports our hypothesis that **15** is formed first as the kinetic product, and over time converts to **16**. The structure of this intermediate was assigned based on comparison of ^{1}H NMR signals with similar molecules that have been previously synthesized by Smith and coworkers.[11]
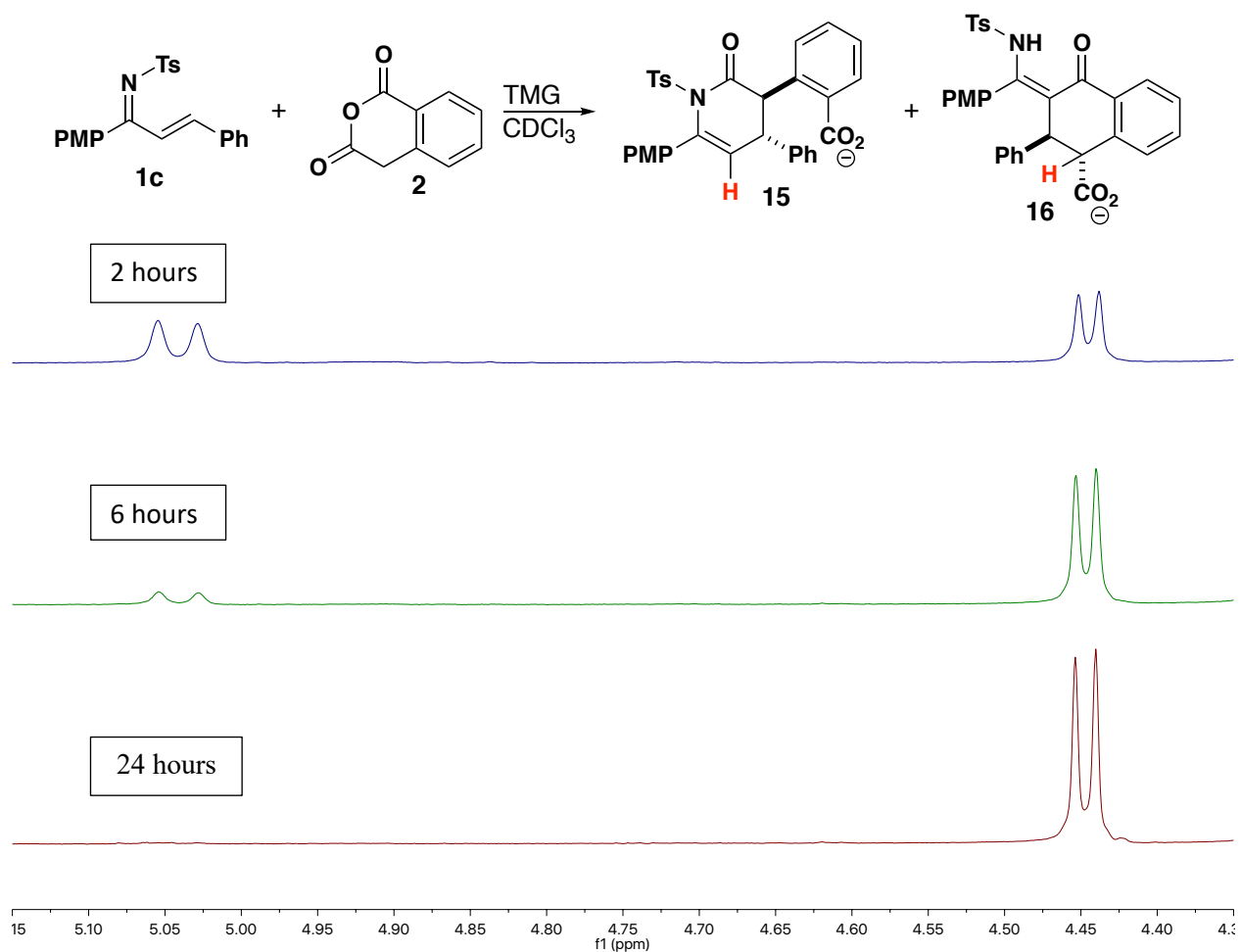
Figure 10. NMR kinetic studies

6. Product Derivatization

The *N*-Ts products can be cleanly detosylated by dissolution in neat sulfuric acid.[12] As exemplified with **4c**, the resulting β-enamino ketone **(17)** can then be acylated with various acid chlorides and reagents of similar reactivity (Figure 11). β-enamino ketones have been shown to undergo condensation reactions, however we found the carbonyl of our β-enamino cyclohexanone substrate to be inert to these conditions.[13]
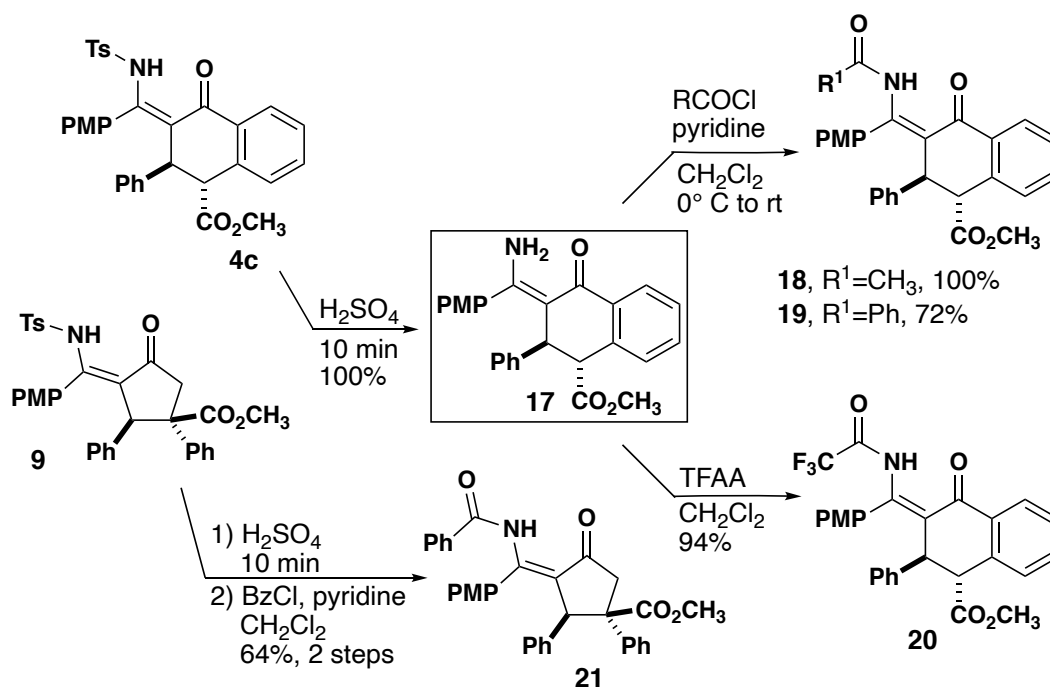
Figure 11. Derivatization of aza-Tamura products

7. Conclusion

In summary, we have developed a base-promoted reaction between α,β-unsaturated *N*-tosyl ketimines and cyclic, enolizable anhydrides. Although the reaction can be run catalytically with TMG, the use of stoichiometric Hünig's base provides higher yield and diastereomer ratio. Conversion to the methyl ester allows for full epimerization to the *trans*-diastereomer by subsequent treatment with DBU. The resulting β-enamino ketone products can be detosylated and derivatized with a variety of acylating reagents.

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9. Experimental Section

9.1. Materials and Instrumentation

Unless otherwise specified, all commercially available reagents were used as received. All reactions using dried solvents were carried out under an atmosphere of argon in flame-dried glassware with magnetic stirring. Dry solvent was dispensed from a solvent purification system that passes solvent through two columns of dry neutral alumina. ^{1}H NMR spectra and proton decoupled ^{13}C NMR spectra were obtained on a 400 MHz Bruker, 500 MHz Bruker, 600 MHz Bruker, or 600 MHz Varian NMR spectrometer at ambient temperature unless otherwise noted. ^{1}H Chemical shifts (δ) are reported in parts per million (ppm) relative to TMS (s, δ 0). Multiplicities are given as: s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), and m (multiplet). Complex splitting will be described by a combination of these abbreviations, i.e. dd (doublet of doublets). ^{13}C NMR chemical shifts are reported relative to CDCl$_3$ (t, δ 77.4) unless otherwise noted. High-resolution mass spectra were recorded on positive ESI mode unless otherwise noted. Melting points were taken on an EZ-melting apparatus and are uncorrected. Infrared spectra were taken on a Bruker Tensor 27 spectrometer. Chromatographic purifications were performed by flash chromatography with silica gel (Fisher, 40–63 μm) packed in glass columns. The eluting solvent for the purification of each compound was determined by thin-layer chromatography (TLC) on glass plates coated with silica gel 60 F254 and visualized by ultraviolet light.

9.2. Synthesis of Imines 1a-k

General Procedure A for N-Tosyl Imines

Following a modified literature procedure,[1] to a 0 °C solution of chalcone (1 equiv) and *p*-toluenesulfonamide (1 equiv) in CH_2Cl_2 (0.165 M) was added triethylamine (2 equiv). After 5 min, $TiCl_4$ (1 equiv, 1M in CH_2Cl_2) was added. The reaction was brought to reflux and stirred for 12 h, then quenched with 50 mL water. The aqueous layer was extracted with CH_2Cl_2 (3x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and solvent was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (70:30 hexanes/EtOAc) to yield imine product as an amorphous solid.

General Procedure B for N-Tosyl Imines

Following a modified literature procedure,[1] to a 0 °C solution of chalcone (1 equiv) and *p*-toluenesulfonamide (1 equiv) in CH_2Cl_2 (0.08 M) was added triethylamine (2.2 equiv). After 5 min, $TiCl_4$ (1.1 equiv, 1M in CH_2Cl_2) was added. The reaction was brought to reflux and stirred for 12 h, then quenched with 50 mL water. The aqueous layer was extracted with CH_2Cl_2 (3x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and solvent was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (70:30 hexanes/EtOAc) to yield imine product as an amorphous solid.
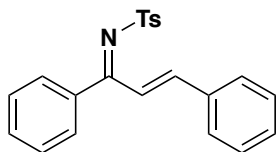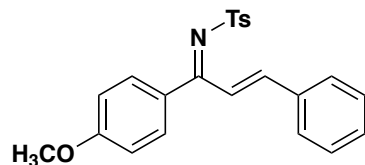
N-((1E,2E)-1,3-diphenylallylidene)-4-methylbenzenesulfonamide (1a): The title compound was synthesized according to general procedure **A** with *trans*-chalcone, (2.88 mmol, 0.600 g) to yield **1a** as a yellow amorphous solid (0.422 mg, 48%). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92 (d, *J* = 7.9 Hz, 2H), 7.65 (s, 2H), 7.59 – 7.51 (m, 3H), 7.42 (tdd, *J* = 8.9, 6.1, 2.8 Hz, 5H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 16.1 Hz, 1H), 2.42 (s, 3H). ^{1}H NMR spectrum is consistent with published data.[1]
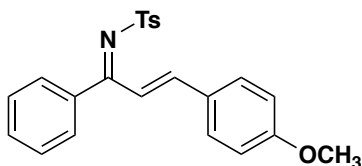
N-((1E,2E)-3-(4-methoxyphenyl)-1-phenylallylidene)-4-methylbenzenesulfonamide (1b): The title compound was synthesized according to general procedure **A** with (*E*)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one (2.1 mmol, 0.50 g) to yield **1b** as a yellow amorphous solid (1.88 g, 89%). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.94 (d, *J* = 8.2 Hz, 3H), 7.64 (s, 2H), 7.55 (tq, *J* = 5.6, 1.5 Hz, 3H), 7.45 (dd, *J* = 8.3, 6.9 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 16.0 Hz, 1H), 6.98 – 6.91 (m, 2H), 3.88 (s, 3H), 2.44 (s, 3H). ^{1}H NMR spectrum is consistent with published data.[1]
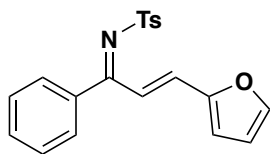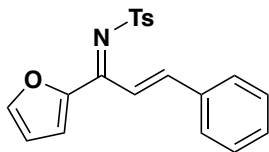
N-((1E,2E)-1-(4-methoxyphenyl)-3-phenylallylidene)-4-methylbenzenesulfonamide (1c): The title compound was synthesized according to general procedure **A** with (E)-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-one (0.25 g, 1.05 mmol) to yield **1c** as a yellow solid (0.295 g, 72%). ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.93 (d, J = 7.9 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.58 (dd, J = 6.6, 2.9 Hz, 2H), 7.42 (dd, J = 4.7, 2.0 Hz, 3H), 7.31 (d, J = 7.9 Hz, 2H), 7.05 (d, J = 16.1 Hz, 1H), 6.93 (d, J = 8.4 Hz, 2H), 3.87 (s, 3H), 2.42 (s, 3H). ^{1}H NMR spectrum is consistent with published data.[1]

N-((1E,2E)-3-(furan-2-yl)-1-phenylallylidene)-4-methylbenzenesulfonamide (1d): The title compound was synthesized according to general procedure **B** with (E)-3-(furan-2-yl)-1-phenylprop-2-en-1-one (1.01 mmol, 0.20 mg), to yield crude **1d** as a brown amorphous solid (0.230 g, 64%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92 (d, J = 7.9 Hz, 2H), 7.63 – 7.49 (m, 4H), 7.46 – 7.39 (m, 2H), 7.31 (dd, J = 8.0, 4.7 Hz, 3H), 6.83 (d, J = 15.7 Hz, 1H), 6.68 (d, J = 3.5 Hz, 1H), 6.51 (dd, J = 3.5, 1.8 Hz, 1H), 2.42 (s, 3H). ^{1}H NMR spectrum is consistent with published data.[1]

N-((1E,2E)-1-(furan-2-yl)-3-phenylallylidene)-4-methylbenzenesulfonamide (1e)

The title compound was synthesized according to general procedure **B** with (*E*)-1-(furan-2-yl)-3-phenylprop-2-en-1-one (0.403 mmol, 0.080 mg), which produced crude **1e** as a brown amorphous solid (0.013 g, 90%) The crude product was recrystallized in EtOH for characterization. Spectroscopic data was acquired at 110 °C: mp: 170-173 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.09 – 8.01 (m, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.72 – 7.59 (m, 3H), 7.59 – 7.44 (m, 5H), 7.40 (d, *J* = 8.0 Hz, 2H), 6.78 (d, *J* = 3.7 Hz, 1H), 2.40 (s, 3H).^{13}C NMR (126 MHz, DMSO-d_6) δ 162.0, 149.5, 148.8, 144.1, 142.6, 138.6, 134.3, 130.1, 128.9, 128.4, 127.7, 125.9, 121.9, 120.7, 112.8, 20.3. AMM (ESI-TOF) m/z calcd for $C_{20}H_{18}NO_3S^+$ [M+H]$^+$ 352.1002, found 352.1010.
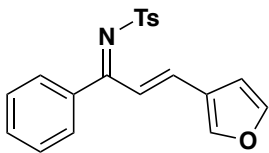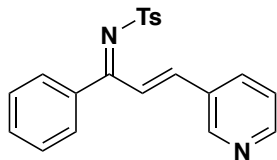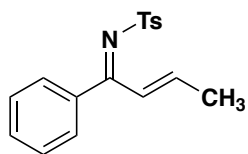

N-((1E,2E)-3-(furan-3-yl)-1-phenylallylidene)-4-methylbenzenesulfonamide (1f): The title compound was synthesized according to general procedure **B** with (*E*)-3-(furan-3-yl)-1-phenylprop-2-en-1-one (2.02 mmol, 0.40 g), which produced **1f** as a brown amorphous solid (0.450 g, 64%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.03 – 7.95 (m, 2H), 7.76 – 7.65 (m, 2H), 7.62 – 7.44 (m, 4H), 7.26 (d, *J* = 2.1 Hz, 1H), 6.71 (d, *J* = 2.0 Hz, 1H). ^{1}H NMR spectrum is consistent with published data.[1]

4-methyl-*N*-((1*E*,2*E*)-1-phenyl-3-(pyridin-3-yl)allylidene)benzenesulfonamide (1g): The title compound was synthesized according to general procedure **B** with (*E*)-1-phenyl-3-(pyridin-3-yl)prop-2-en-1-one (0.250 g, 1.19 mmol), which produced **1g** as a brown amorphous solid (0.182 g, 42%). The crude product was recrystallized in EtOH for characterization. Spectroscopic data was acquired at 108 °C. mp: 139.4 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.78 (d, J = 2.3 Hz, 1H), 8.62 (d, J = 4.7 Hz, 1H), 8.07 (d, J = 8.1, 2.1 Hz, 1H), 7.87 – 7.77 (m, 3H), 7.70 (d, J = 7.8 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.5 Hz, 2H), 7.48 (dd, J = 8.1, 4.8 Hz, 1H), 7.41 (d, J = 7.9 Hz, 2H), 7.15 (d, J = 16.3 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 176.0, 150.5, 149.0, 142.8, 142.7, 138.1, 135.7, 133.9, 131.4, 129.8, 128.9, 128.9, 127.8, 126.0, 124.8, 123.2, 20.2.; AMM (ESI-TOF) m/z calcd for $C_{21}H_{19}N_2O_2S^+$ [M+H]$^+$ 363.1162, found 363.1167.

4-methyl-*N*-((1*E*,2*E*)-1-phenylbut-2-en-1-ylidene)benzenesulfonamide (1h)

The title compound was synthesized according to general procedure **A** with (*E*)-1-phenylbut-2-en-1-one, (0.343 g, 2.34 mmol) to yield **1h** as a red oil (0.12 g, 17%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.98 – 7.84 (m, 2H), 7.64 – 7.53 (m, 2H), 7.49 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 7.9 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 6.43 (d, J = 13.8 Hz, 1H), 2.43 (s, 3H), 2.05 (d, J = 6.9 Hz, 3H). ^{1}H NMR spectrum is consistent with published data.[1]
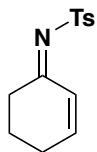
(*Z*)-*N*-(cyclohex-2-en-1-ylidene)-4-methylbenzenesulfonamide (1i): Following a modified literature procedure:[2] To a solution of TiCl4 and Ti(OEt)4 in toluene was added NEt3. The resulting mixture was stirred for 5 min at rt before TsNH2 was added, and the reaction mixture was stirred for 15 min under reflux. A solution of cyclohexenone in toluene was added dropwise over 15 min to the refluxing solution and was stirred for 4 hours. The reaction mixture was poured into a stirred and precooled (0 °C) suspension of NaHCO3 in acetone/water (200 mL 100:1), diluted with hexanes (100 mL), dried (MgSO4), and filtered. The filtrate was concentrated under *in vacuo*, and the crude product was purified by flash chromatography (70:30 Hexanes/EtOAc) to yield **1i** as an off white solid (0.35 g, 15%): ^{1}H NMR (400 MHz, CDCl3) δ 7.86 (dd, *J* = 8.4, 2.1 Hz, 2H), 7.35 – 7.28 (m, 2H), 6.94 (ddt, *J* = 12.2, 9.9, 4.1 Hz, 1H), 6.15 (dt, *J* = 10.0, 2.0 Hz, 1H), 3.22 – 3.13 (m, 1H), 2.57 – 2.51 (m, 1H), 2.43 (s, 3H), 2.36 (dddd, *J* = 14.3, 6.2, 4.2, 2.1 Hz, 2H), 1.96 (h, *J* = 6.4 Hz, 2H). ^{1}H NMR spectrum is consistent with published data.[2]
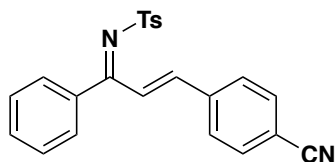
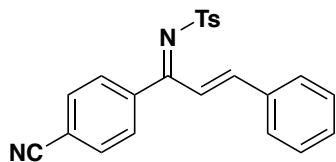**N-((1*E*,2*E*)-3-(4-cyanophenyl)-1-phenylallylidene)-4-methylbenzenesulfonamide (1j)**: The title compound was synthesized according to general procedure **A** with (*E*)-4-(3-oxo-3-phenylprop-1-en-1-yl)benzonitrile (2.14 mmol, 0.50 g), to yield **1j** as a pale yellow amorphous solid (0.51 g, 61%): ^{1}H NMR (600 MHz, CDCl3) δ 8.14 (d, *J* = 15.9 Hz, 1H), 7.97 – 7.87 (m, 2H), 7.75 – 7.62 (m, 6H), 7.60 – 7.54 (m, 1H), 7.49 – 7.43 (m, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 7.03 (d, *J*

= 16.1 Hz, 1H), 2.43 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 176.3, 144.8, 143.79, 138.8, 138.2, 136.7, 132.7, 132.5, 130.3, 129.5, 128.8, 128.6, 127.2, 125.7, 118.3, 113.8, 21.6.; AMM (ESI-TOF) m/z calcd for C$_{23}$H$_{19}$N$_2$O$_2$S$^+$ [M+H]$^+$ 387.1162, found 387.1166.

***N*-((1*E*,2*E*)-1-(4-cyanophenyl)-3-phenylallylidene)-4-methylbenzenesulfonamide (1k)**: The title compound was synthesized according to general procedure **A** with 4-cinnamoylbenzonitrile (1.28 mmol, 0.30 g), to yield **1k** as a yellow amorphous solid (0.30 g, 60%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.12 (d, *J* = 16.2 Hz, 1H), 7.98 – 7.85 (m, 2H), 7.81 – 7.69 (m, 4H), 7.66 – 7.52 (m, 2H), 7.50 – 7.39 (m, 3H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.01 (d, *J* = 15.9 Hz, 1H), 2.44 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 175.3, 149.6, 144.0, 141.4, 138.1, 134.0, 132.1, 131.7, 130.6, 129.6, 129.2, 128.9, 127.3, 121.8, 118.0, 115.2, 21.6.; IR: 1612, 2204, 2229, 2852, 2921, 3061 cm^{-1}.; AMM (ESI-TOF) m/z calcd for C$_{23}$H$_{19}$N$_2$O$_2$S$^+$ [M+H]$^+$ 387.1162, found 387.1170.

9.3. Synthesis of Enamines 4a-k, 5, 7, 9, 11, 17-22

Imine Scope:

Due to restricted rotation of nearby aromatic rings, the aromatic region of the NMR of the aza-Tamura products does not have defined peaks in CDCl$_3$ at room temperature. A proton NMR experiment was run on product **4a** in DMSO at 80 °C, which gave defined product peaks. We

expect that this example demonstrates the restricted rotation, and it can be extrapolated that other products would provide the same result.
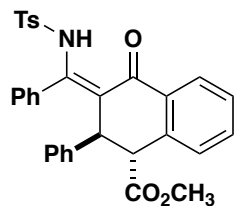
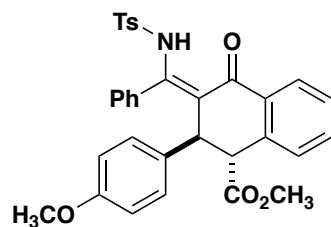**methyl (1*R*,2*S*,*Z*)-3-(((4-methylphenyl)sulfonamido)(phenyl)methylene)-4-oxo-2-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate (4a):** To a solution of imine **1a** (0.05 g, 0.14 mmol) and homophthalic anhydride (28 mg, 0.17 mmol) in dry CH_2Cl_2 (1.4 mL, 0.1 M) was added *i*-Pr$_2$NEt (0.024 mL, 0.14 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH_2Cl_2 (1.4 mL, 0.1 M) and CH_3OH (1 mL), and $TMSCHN_2$ solution (0.10 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.14 mL, 1M in CH_2Cl_2) was added. The reaction was stirred at 25 °C for 22 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (75:25 hexanes/EtOAc) to yield **4a** as a pale yellow amorphous solid (0.070 g, 94%): ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.61 (s, 1H), 8.06 – 8.00 (m, 1H), 7.46 (dtd, *J* = 24.6, 7.5, 1.5 Hz, 2H), 7.40 – 7.27 (m, 5H), 7.23 – 7.15 (m, 3H), 7.10 – 7.00 (m, 3H), 6.79 – 6.73 (m, 2H), 6.70 (d, *J* = 7.5 Hz, 2H), 4.22 (s, 1H), 4.10 (d, *J* = 2.2 Hz, 1H), 3.58 (s, 3H), 2.38 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 189.3, 171.9, 155.2, 143.9, 142.7, 137.6, 136.0, 134.1, 133.7, 130.9, 130.0, 129.4, 129.4, 129.1,

128.6, 128.4, 127.8, 127.7, 127.6, 127.5, 126.7, 111.3, 52.6, 52.1, 43.8, 21.7.; AMM (ESI-TOF) m/z calcd for $C_{32}H_{28}NO_5S^+$ $[M+H]^+$ 538.1683, found 538.1670.

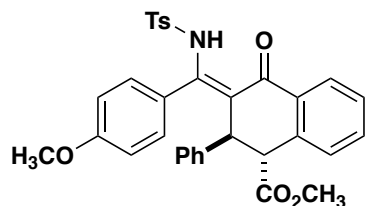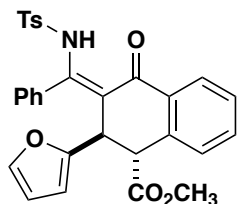**methyl (1R,2S,Z)-2-(4-methoxyphenyl)-3-(((4-methylphenyl)sulfonamido)(phenyl) methylene)-4-oxo-1,2,3,4-tetrahydronaphthalene-1-carboxylate (4b)** To a solution of imine **1b** (0.05 g, 0.128 mmol) and homophthalic anhydride (0.026 g, 0.154 mmol) in dry CH_2Cl_2 (1.28 mL, 0.1 M) was added *i*-Pr$_2$NEt (0.022 mL, 0.128 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH_2Cl_2 (1.28 mL, 0.1 M) and CH_3OH (1 mL), and TMSCHN$_2$ solution (0.128 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.128 mL, 1M in CH_2Cl_2) was added. The reaction was stirred at 25 °C for 22 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (70:30 hexanes/EtOAc) to yield **4b** as a pale yellow amorphous solid (0.067 g, 92%): ^1H NMR (600 MHz, CDCl$_3$) δ 13.86 (s, 1H), 8.19 – 8.13 (m, 1H), 7.45 – 7.37 (m, 2H), 7.34 – 7.27 (m, 4H), 7.14 – 7.08 (m, 3H), 7.07 – 7.02 (m, 2H), 6.61 – 6.52 (m, 5H), 4.03 (d, J = 2.1 Hz, 1H), 3.82 (d, J = 2.2 Hz, 1H), 3.67 (s, 3H), 3.59 (s, 3H), 2.37 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 189.2, 171.8, 158.0, 154.9, 143.7, 137.4, 136.0, 134.6, 134.0, 133.6, 130.8, 129.8, 129.3, 129.2,

128.9, 128.4, 128.3, 127.6, 127.6, 127.4, 113.5, 111.5, 55.0, 52.4, 52.1, 42.9, 21.6.; AMM (ESI-TOF) m/z calcd for $C_{33}H_{30}NO_6S^+$ [M+H]$^+$ 568.1788, found 568.1782.

methyl (1R,2S,Z)-3-((4-methoxyphenyl)((4-methylphenyl)sulfonamido)methylene)-4-oxo-2-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate (4c): To a solution of imine **1c** (0.5 g, 1.28 mmol) and homophthalic anhydride (0.250 g, 1.54 mmol) in dry CH$_2$Cl$_2$ (13 mL, 0.1 M) was added *i*-Pr$_2$NEt (0.223 mL, 1.28 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 20 mL of 1 M HCl solution. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 20 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH$_2$Cl$_2$ (6.5 mL) and CH$_3$OH (6.5 mL), and TMSCHN$_2$ solution (1.3 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.128 mL, 1M in CH$_2$Cl$_2$) was added. The reaction was stirred at 25 °C for 23 h and then quenched with 150 µL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (80:20 to 70:30 hexanes/EtOAc) to yield **4c** as a pale yellow amorphous solid (0.67 g, 92%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 13.80 (s, 1H), 8.18 – 8.11 (m, 1H), 7.42 – 7.36 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 7.06 – 6.98 (m, 4H), 6.73 – 6.50 (m, 6H), 4.17 (d, *J* = 2.1 Hz, 1H), 3.88 (d, *J* = 2.0 Hz, 1H), 3.79 (s, 3H), 3.59 (s, 3H), 2.37 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 189.1, 171.7, 160.3, 155.1, 143.6, 142.6, 137.3, 135.8, 134.0, 133.5, 130.5, 129.7, 129.2, 128.4,

128.2, 127.6, 127.6, 127.3, 126.5, 123.1, 112.8, 111.6, 55.2, 52.4, 52.0, 43.6, 21.5.; AMM (ESI-TOF) m/z calcd for $C_{33}H_{30}NO_6S^+$ [M+H]$^+$ 568.1788, found 568.1781.

methyl (1R,Z)-2-(furan-2-yl)-3-(((4-methylphenyl)sulfonamido)(phenyl)methylene)-4-oxo-1,2,3,4-tetrahydronaphthalene-1-carboxylate (4d)

To a solution of imine **1d** (0.05 g, 0.142 mmol) and homophthalic anhydride (0.028 g, 0.171 mmol) in dry CH_2Cl_2 (1.42 mL, 0.1 M) was added i-Pr$_2$NEt (0.025 mL, 0.142 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH_2Cl_2 (1.42 mL, 0.1 M) and CH_3OH (1 mL), and TMSCHN$_2$ solution (0.142 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.142 mL, 1M in CH_2Cl_2) was added. The reaction was stirred at 25 °C for 22 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (80:20 hexanes/EtOAc) to yield **4d** as a pale yellow amorphous solid (0.062 g, 84%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 13.71 (d, J = 2.2 Hz, 1H), 8.10 (d, J = 7.8 Hz, 1H), 7.42 (dt, J = 33.8, 7.5 Hz, 2H), 7.37 – 7.30 (m, 3H), 7.24 – 7.11 (m, 5H), 7.07 (s, 1H), 6.97 (d, J = 41.0 Hz, 2H), 6.02 (d, J = 2.6 Hz, 1H), 5.64 (d, J = 2.8 Hz, 1H), 4.17 (d, J = 2.4 Hz, 1H), 4.10 (s, 1H), 3.59 (d, J = 2.1 Hz, 3H), 2.39 (d, J = 2.0 Hz, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 188.6,

171.1, 154.9, 154.5, 143.8, 141.6, 137.4, 136.1, 133.5, 133.4, 130.4, 129.6, 129.5, 129.3, 129.0, 128.4, 127.7, 127.6, 127.5, 110.0, 109.5, 107.7, 52.4, 48.2, 38.3, 21.6.; AMM (ESI-TOF) m/z calcd for $C_{30}H_{26}NO_6S^+$ [M+H]$^+$ 528.1475, found 528.1473.
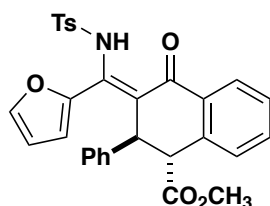
methyl (1R,2S,Z)-3-(furan-2-yl((4-methylphenyl)sulfonamido)methylene)-4-oxo-2-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate (4e)

To a solution of imine **1e** (0.05 g, 0.142 mmol) and homophthalic anhydride (0.028 g, 0.171 mmol) in dry CH_2Cl_2 (1.42 mL, 0.1 M) was added i-Pr$_2$NEt (0.025 mL, 0.142 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH_2Cl_2 (1.42 mL, 0.1 M) and CH$_3$OH (1 mL), and TMSCHN$_2$ solution (0.142 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.142 mL, 1M in CH_2Cl_2) was added. The reaction was stirred at 25 °C for 22 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (80:20 hexanes/EtOAc) to yield **4e** as a pale yellow amorphous solid (0.058 mg, 68%): ^{1}H NMR (600 MHz, CD$_3$CN) δ 12.95 (s, 1H), 7.98 (d, J = 7.7 Hz, 1H), 7.54 – 7.52 (m, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.46 (td, J = 7.5, 1.3 Hz, 1H), 7.40 (t, J = 7.8 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 7.5 Hz, 1H), 7.10 – 7.06 (m, 3H), 6.23 – 6.21 (m, 1H), 4.61 – 4.59 (m, 1H), 4.22 (d, J = 2.1 Hz, 1H), 3.54 (s, 3H), 2.40 (s, 3H).; ^{13}C NMR (151 MHz, CD$_3$CN) δ

191.0, 172.6, 146.2, 145.6, 144.8, 143.3, 143.0, 137.5, 137.2, 135.0, 134.9, 130.7, 130.6, 129.5, 129.5, 128.2, 128.2, 128.1, 127.7, 117.1, 116.3, 112.4, 53.1, 52.0, 44.6, 21.6.; AMM (ESI-TOF) m/z calcd for $C_{30}H_{26}NO_6S^+$ [M+H]$^+$ 528.1475, found 528.1481.
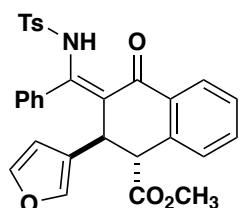
methyl (1R,2S,Z)-2-(furan-3-yl)-3-((((4-methylphenyl)sulfonamido)(phenyl)methy-lene)-4-oxo-1,2,3,4-tetrahydronaphthalene-1-carboxylate (4f)
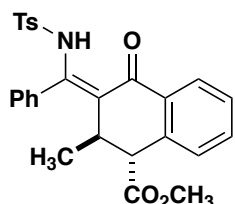
To a solution of imine **1f** (0.05 g, 0.142 mmol) and homophthalic anhydride (0.028 g, 0.171 mmol) in dry CH$_2$Cl$_2$ (1.42 mL, 0.1 M) was added i-Pr$_2$NEt (0.025 mL, 0.142 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 2 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH$_2$Cl$_2$ (1.42 mL, 0.1 M) and CH$_3$OH (1 mL), and TMSCHN$_2$ solution (0.142 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.142 mL, 1M in CH$_2$Cl$_2$) was added. The reaction was stirred at 25 °C for 22 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (80:20 hexanes/EtOAc) to yield **4f** as a pale yellow amorphous solid (0.062 g, 84%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 13.64 (d, J = 2.3 Hz, 1H), 8.13 (d, J = 7.8 Hz, 1H), 7.45 (dt, J = 28.1, 7.6 Hz, 2H), 7.37 (t, J = 7.6 Hz, 1H), 7.32 (dd, J = 8.3, 2.2 Hz, 2H), 7.17 (d, J = 7.5 Hz, 1H), 7.07 (s, 1H), 7.03 – 6.64 (m, 2H), 6.62 (s, 1H), 5.72 (s, 1H), 3.99 (s, 1H), 3.83 (s,

1H), 3.59 (d, J = 2.2 Hz, 3H), 2.38 (d, J = 2.1 Hz, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 188.7, 171.3, 154.0, 143.8, 142.9, 139.8, 137.4, 136.4, 133.6, 133.6, 130.6, 129.8, 129.5, 129.3, 129.2, 128.5, 127.8, 127.6, 127.5, 126.8, 111.7, 109.3, 52.4, 50.5, 35.5, 21.6.; AMM (ESI-TOF) m/z calcd for C$_{30}$H$_{26}$NO$_6$S$^+$ [M+H]$^+$ 528.1475, found 528.1464.
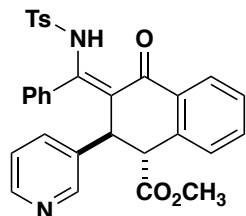
methyl (1R,2S,Z)-3-(((4-methylphenyl)sulfonamido)(phenyl)methylene)-4-oxo-2-(pyridin-3-yl)-1,2,3,4-tetrahydronaphthalene-1-carboxylate (4g) To a solution of imine **1g** (0.05 g, 0.138 mmol) and homophthalic anhydride (0.027 g, 0.166 mmol) in dry CH$_2$Cl$_2$ (1.42 mL, 0.1 M) was added i-Pr$_2$NEt (0.025 mL, 0.142 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 2 mL), followed by EtOAc (3x5 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH$_2$Cl$_2$ (1.38 mL, 0.1 M) and CH$_3$OH (2 mL), and TMSCHN$_2$ solution (0.138 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.138 mL, 1M in CH$_2$Cl$_2$) was added. The reaction was stirred at 25 °C for 22 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (80:20 hexanes/EtOAc) to yield **4g** as a pale yellow amorphous solid (0.041 g, 55%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 13.95 (s, 1H), 8.29 (t, J = 3.1 Hz, 1H), 8.20 – 8.15 (m, 1H), 7.90 (s, 1H), 7.48 – 7.41 (m, 2H), 7.33 (t, J = 7.4 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.13 – 7.05 (m, 4H), 6.95 (d, J = 3.4 Hz, 3H), 4.15 (s, 1H), 3.78 (s, 1H), 3.63 (s, 3H), 2.37 (s, 3H).; ^{13}C

NMR (151 MHz, CDCl$_3$) δ 188.7, 171.4, 156.1, 149.1, 148.2, 144.1, 138.2, 137.4, 135.3, 134.8, 134.0, 133.9, 130.5, 130.1, 129.7, 129.4, 129.0, 129.0, 128.0, 127.8, 127.7, 123.2, 109.9, 52.8, 51.7, 41.6, 21.7.; AMM (ESI-TOF) m/z calcd for C$_{32}$H$_2$NO$_6$S$^+$ [M+H]$^+$ 539.1635, found 539.1626.

methyl (1R,2R,Z)-2-methyl-3-(((4-methylphenyl)sulfonamido)(phenyl)methylene)-4-oxo-1,2,3,4-tetrahydronaphthalene-1-carboxylate (4h)
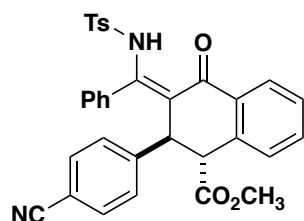
To a solution of imine **1h** (0.05 g, 0.167 mmol) and homophthalic anhydride (0.032 g, 0.200 mmol) in dry CH$_2$Cl$_2$ (1.67 mL, 0.1 M) was added *i*-Pr$_2$NEt (0.029 mL, 0.167 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 2 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH$_2$Cl$_2$ (1.67 mL, 0.1 M) and CH$_3$OH (1 mL), and TMSCHN$_2$ solution (0.167 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.167 mL, 1M in CH$_2$Cl$_2$) was added. The reaction was stirred at 25 °C for 22 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (85:15 hexanes/EtOAc) to yield **4h** as a pale yellow amorphous solid (0.045 mg, 57%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 13.64 (s, 1H), 8.15 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.52 (td, *J* = 7.5, 1.5 Hz, 1H), 7.45 (td, *J* = 7.6, 1.3 Hz, 1H), 7.38 (tt, *J* = 7.5, 1.3 Hz, 1H), 7.31 (d, *J* = 1.8 Hz, 1H), 7.27 (d, *J* = 7.7 Hz, 1H), 7.26 – 7.22 (m, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 6.97 (s, 2H), 3.55 (s, 3H), 3.51 (d, *J* = 2.1 Hz, 1H), 2.99 (qd, *J* = 7.1, 2.1 Hz, 1H), 2.38 (s, 3H), 0.82 (d, *J* = 7.1

Hz, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 188.68, 171.98, 152.64, 143.58, 137.56, 136.55, 133.51, 133.21, 130.89, 129.96, 129.23, 129.21, 129.18, 128.34, 127.95, 127.64, 127.51, 114.34, 52.16, 50.98, 33.23, 21.53, 21.25.; AMM (ESI-TOF) m/z calcd for C$_{27}$H$_{26}$NO$_5$S$^+$ [M+H]$^+$ 476.1526, found 476.1547.
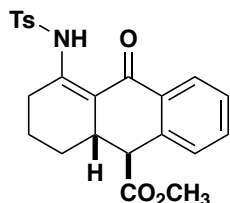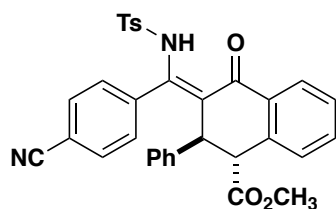

methyl 4-((4-methylphenyl)sulfonamido)-10-oxo-1,2,3,9,9a,10-hexahydroanthrace-ne-9-carboxylate (4i) To a solution of imine **1i** (0.05 g, 0.201 mmol) and homophthalic anhydride (0.039 g, 0.241 mmol) in dry CH$_2$Cl$_2$ (2.01 mL, 0.1 M) was added *i*-Pr$_2$NEt (0.035 mL, 0.142 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 2 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH$_2$Cl$_2$ (2.01 mL, 0.1 M) and CH$_3$OH (1 mL), and TMSCHN$_2$ solution (0.201 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.201 mL, 1M in CH$_2$Cl$_2$) was added. The reaction was stirred at 25 °C for 22 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (80:20 hexanes/EtOAc) to yield **4i** as a pale yellow amorphous solid (0.045 g, 55%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 14.08 (s, 1H), 8.09 – 8.03 (m, 1H), 7.83 – 7.77 (m, 2H), 7.51 – 7.40 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 7.7 Hz, 1H), 3.85 (s, 3H), 3.62 (d, *J* = 12.4 Hz, 1H), 3.07 – 2.96 (m, 1H), 2.80 (d, *J* = 19.7 Hz, 1H), 2.57 – 2.47 (m, 1H), 2.43 (s, 3H), 1.89 – 1.81 (m, 2H), 1.50 – 1.39 (m, 1H), 1.31 – 1.24 (m, 1H).;

^{13}C NMR (151 MHz, CDCl$_3$) δ 188.0, 173.5, 154.7, 144.2, 139.0, 137.7, 133.4, 133.0, 130.0, 128.1, 128.0, 127.3, 125.6, 109.5, 52.2, 52.2, 37.3, 27.5, 26.7, 21.6, 20.0.; AMM (ESI-TOF) m/z calcd for C$_{23}$H$_{24}$NO$_5$S$^+$ [M+H]$^+$ 426.1370, found 426.1358.

methyl (1R,2S,Z)-2-(4-cyanophenyl)-3-(((4-methylphenyl)sulfonamido)(phenyl) me-thyl-ene)-4-oxo-1,2,3,4-tetrahydronaphthalene-1-carboxylate (4j): To a solution of imine **1j** (0.05 g, 0.129 mmol) and homophthalic anhydride (0.025 g, 0.155 mmol) in dry CH$_2$Cl$_2$ (1.29 mL, 0.1 M) was added *i*-Pr$_2$NEt (0.032 mL, 0.129 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 2 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH$_2$Cl$_2$ (1.29 mL, 0.1 M) and CH$_3$OH (2 mL), and TMSCHN$_2$ solution (0.129 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.129 mL, 1M in CH$_2$Cl$_2$) was added. The reaction was stirred at 25 °C for 22 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (75:25 hexanes/EtOAc) to yield **4j** as a pale yellow amorphous solid (0.065 mg, 89%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 13.77 (s, 1H), 8.19 – 8.11 (m, 1H), 7.45 – 7.41 (m, 2H), 7.36 – 7.32 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.09 – 7.01 (m, 4H), 6.66 – 6.63 (m, 2H), 3.97 (d, *J* = 1.8 Hz, 1H), 3.85 (d, *J* = 1.8 Hz, 1H), 3.60 (d, *J* = 1.1 Hz, 3H), 2.40 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 189.1, 171.6, 152.2, 144.3, 142.0, 137.2, 135.7, 135.5, 134.0, 133.5, 131.2, 130.1,

129.9, 129.5, 128.7, 128.5, 127.7, 127.4, 127.2, 126.9, 118.2, 113.2, 111.8, 52.6, 51.8, 43.5, 21.6.;

AMM (ESI-TOF) m/z calcd for $C_{33}H_{27}N_2O_5S^+$ [M+H]$^+$ 563.1633, found 563.1633.

methyl (1R,2S,Z)-3-((4-cyanophenyl)((4-methylphenyl)sulfonamido)methylene)-4-oxo-2-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate (4k) To a solution of imine **1k** (0.050 g, 0.129 mmol) and homophthalic anhydride (0.025 g, 0.155 mmol) in dry CH_2Cl_2 (1.29 mL, 0.1 M) was added i-Pr$_2$NEt (0.032 mL, 0.129 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH_2Cl_2 (1.29 mL, 0.1 M) and CH_3OH (2 mL), and TMSCHN$_2$ solution (0.129 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 1 h and then DBU solution (0.129 mL, 1M in CH_2Cl_2) was added. The reaction was stirred at 25 °C for 22 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (70:30 hexanes/EtOAc) to yield **4k** as a pale yellow amorphous solid (0.062 g, 85%): ^{1}H NMR (600 MHz, Chloroform-d) δ 13.77 (s, 1H), 8.18 – 8.14 (m, 1H), 7.45 – 7.41 (m, 2H), 7.34 (d, J = 7.9 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 7.10 – 7.02 (m, 5H), 6.65 (d, J = 7.3 Hz, 2H), 3.97 (s, 1H), 3.85 (s, 1H), 3.60 (s, 3H), 2.40 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 189.1, 171.6, 152.2, 144.3, 141.9, 137.3, 135.7, 135.5, 134.0, 133.5, 131.2, 130.1, 129.9, 129.5, 128.7, 128.5, 127.7, 127.4, 127.2, 126.9, 118.2, 113.2, 111.8, 52.6, 51.8, 43.5, 21.6.; IR: 1576,1611, 2228,

2852, 3061 cm^{-1}.; AMM (ESI-TOF) m/z calcd for C$_{33}$H$_{27}$N$_2$O$_5$S$^+$ [M+H]$^+$ 563.1635, found 563.1622.
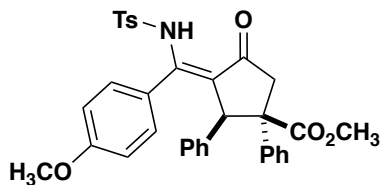
Anhydride Scope:
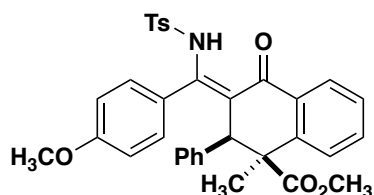
methyl (Z)-3-((4-methoxyphenyl)((4-methylphenyl)sulfonamido)methylene)-1-meth-yl-4-oxo-2-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate (7):
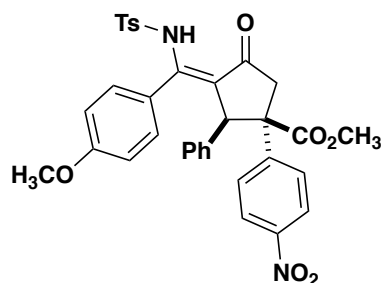
To a solution of imine **1c** (0.05 g, 0.13 mmol) and anhydride **6** (0.028 g, 0.16 mmol) in dry CH$_2$Cl$_2$ (1.3 mL, 0.1 M) was added *i*-Pr$_2$NEt (0.023 mL, 0.13 mmol). The reaction mixture was stirred for 18 h at 25 °C and then quenched with 2 mL of 1 M HCl solution. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 2 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH$_2$Cl$_2$ (1.3 mL) and CH$_3$OH (1 mL), and TMSCHN$_2$ solution (0.13 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 20 h and then quenched with 10 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (80:20 hexanes/EtOAc) to yield **7** as a pale yellow amorphous solid (0.067 g, 90%, 79:21 dr). A portion of the major diastereomer was isolated for characterization purposes: ^{1}H NMR (600 MHz, CDCl$_3$) δ 13.75 (s, 1H), 8.31 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.51 (td, *J* = 7.6, 1.6 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.02 (t, *J* = 7.3 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 2H), 6.42 (d, *J* = 7.6 Hz, 2H), 3.86 (s, 3H), 3.69 (s, 1H), 3.15 (s, 3H),

2.34 (s, 3H), 1.61 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 188.0, 174.1, 160.2, 154.8, 143.7, 142.8, 141.2, 137.3, 133.7, 132.6, 129.2, 129.1, 128.1, 127.9, 127.7, 127.6, 127.5, 126.8, 122.7, 113.0, 112.1, 55.3, 53.3, 52.3, 51.5, 29.9, 29.7, 21.5.; AMM (ESI-TOF) m/z calcd for C$_{34}$H$_{32}$NO$_6$S$^+$ [M+H]$^+$ 582.1950, found 582.1948.

methyl (Z)-3-((4-methoxyphenyl)((4-methylphenyl)sulfonamido)methylene)-4-oxo-1,2-diphenylcyclopentane-1-carboxylate (9): To a solution of imine **1c** (0.10 g, 0.26 mmol) and phenylsuccinic anhydride (0.55 g, 0.31 mmol) in dry CH$_2$Cl$_2$ (2.6 mL, 0.1 M) was added *i*-Pr$_2$NEt (0.045 mL, 0.26 mmol). The reaction mixture was stirred for 24 h at 40 °C and then quenched with 3 mL of 1 M HCl solution. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 3 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH$_2$Cl$_2$ (2.6 mL) and CH$_3$OH (1 mL), and TMSCHN$_2$ solution (0.26 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 5 h and then quenched with 20 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (80:20 hexanes/EtOAc) to yield **7** as a pale yellow amorphous solid (0.121 g, 81%, 80:20 dr). A portion of the major diastereomer was isolated for characterization purposes: ^{1}H NMR (600 MHz, CDCl$_3$) δ 11.51 (s, 1H), 7.36 – 7.33 (m, 2H), 7.30 – 7.22 (m, 2H), 7.16 (pd, J = 8.4, 7.8, 3.6 Hz, 5H), 7.09 – 7.07 (m, 2H), 6.76 – 6.73 (m, 2H), 6.67 (s, 5H), 4.30 (s, 1H), 3.81 (s, 3H), 3.76 (d, J = 18.4 Hz, 1H), 3.21 (s, 3H), 2.73 (dd, J = 18.4, 1.3 Hz, 1H), 2.43 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 205.18, 172.48, 160.98, 149.45,

143.89, 141.93, 141.32, 136.65, 130.62, 129.41, 128.88, 128.59, 128.17, 127.51, 127.44, 127.26, 126.17, 123.79, 120.24, 113.11, 58.96, 55.27, 52.56, 51.91, 49.00, 21.64.; AMM (ESI-TOF) m/z calcd for $C_{34}H_{32}NO_6S^+$ [M+H]$^+$ 582.1950, found 582.1947.
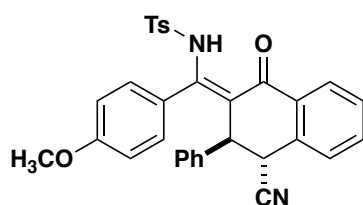

methyl (Z)-3-((4-methoxyphenyl)((4-methylphenyl)sulfonamido)methylene)-1-(4-nitrophenyl)-4-oxo-2-phenylcyclopentane-1-carboxylate (11):

To a solution of imine **1c** (0.20 g, 0.51 mmol) and *p*-nitrophenylsuccinic anhydride (0.137 g, 0.62 mmol) in dry CH_2Cl_2 (5 mL, 0.1 M) was added *i*-Pr$_2$NEt (0.09 mL, 0.52 mmol). The reaction mixture was stirred for 24 h at 25 °C and then quenched with 10 mL of 1 M HCl solution. The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The resulting crude carboxylic acid was dissolved in dry CH_2Cl_2 (2.5 mL) and CH_3OH (2.5 mL), and TMSCHN$_2$ solution (0.51 mL, 2M in hexanes) was added dropwise. The reaction was stirred at 25 °C for 10 h and then quenched with 30 μL of AcOH. The volatiles were concentrated *in vacuo*, and the crude mixture was purified by flash chromatography (85:25 hexanes/EtOAc) to yield **11** as a pale yellow amorphous solid (0.153 g, 47%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 11.52 (s, 1H), 8.14 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 2H), 7.23 – 7.16 (m, 5H), 6.79 – 6.75 (m, 2H), 6.71 – 6.59 (m, 4H), 4.27 (s, 1H), 3.83 (d, *J* = 18.3 Hz, 1H), 3.82 (s, 3H), 3.24 (s, 3H), 2.70 (d, *J* = 18.5 Hz, 1H), 2.44 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 203.8, 171.3, 161.2, 150.4, 149.1, 147.0, 144.2,

140.5, 136.5, 130.5, 129.5, 128.5, 128.4, 127.7, 127.5, 127.6, 124.0, 123.3, 118.9, 113.3, 59.2, 55.3, 52.9, 52.3, 48.5, 21.6.; AMM (ESI-TOF) m/z calcd for $C_{34}H_{31}N_2O_8S^+$ [M+H]$^+$ 627.1801, found 627.1776.

Aza-Tamura Derivatization:

***N*-(((3*S*,4*R*,*Z*)-4-cyano-1-oxo-3-phenyl-3,4-dihydronaphthalen-2(1*H*)-ylidene)(4-methoxyphenyl)methyl)-4-methylbenzenesulfonamide (5)** To a solution of **4c** (0.084 g, 0.15 mmol) in THF (0.4 mL) and H_2O (0.2 mL) was added LiOH (0.036 g, 1.5 mmol). The reaction mixture was stirred for 11 h at 25 °C and then another portion of LiOH (18 mg, 0.75 mmol) was added. After stirring for an additional 8 h the reaction mixture was diluted with H_2O (1 mL) and acidified with 1 M HCl. The aqueous layer was extracted with EtOAc (3 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and solvent was concentrated *in vacuo*. To a solution of the crude carboxylic acid in dry CH_3CN (2 mL, 0.08 M) was added 4-methoxybenzylamine (30 μL, 0.23 mmol) and POCl$_3$ (20 μL, 0.21 mmol). The reaction mixture was stirred for 18 h at 85 °C. The reaction was then cooled and quenched with ice water (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL) and the combined organic layers were dried over Na_2SO_4 and filtered. Solvent was concentrated *in vacuo* and the crude mixture was purified by flash chromatography (80:20 Hex/EtOAc) to yield **5** as a yellow solid: mp: 174-176

°C.; ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.20 (dd, J = 7.4, 1.8 Hz, 1H), 7.50 – 7.42 (m, 2H), 7.35 (d, J = 8.3 Hz, 2H), 7.14 (d, J = 8.1 Hz, 2H), 7.09 – 7.04 (m, 4H), 6.74 – 6.67 (m, 6H), 4.15 (d, J = 2.3 Hz, 1H), 4.06 (d, J = 2.3 Hz, 1H), 3.81 (s, 3H), 2.37 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 187.6, 160.6, 157.0, 144.1, 139.9, 137.0, 134.2, 133.6, 132.2, 130.6, 129.8, 129.4, 128.7, 128.6, 128.5, 127.6, 127.23, 127.2, 122.4, 119.0, 113.3, 109.4, 55.3, 43.9, 37.0, 21.6.; AMM (ESI-TOF) m/z calcd for C$_{32}$H$_{27}$N$_2$O$_4$S$^+$ [M+H]$^+$ 535.1692, found 535.1686.
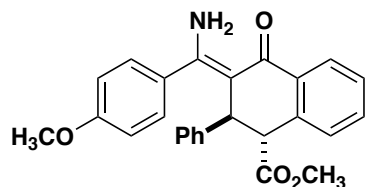
methyl (1R,2S,Z)-3-(amino(4-methoxyphenyl)methylene)-4-oxo-2-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate (17) A solution of **4c** (0.705 g, 1.24 mmol) in concentrated H$_2$SO$_4$ (9.2 mL, 0.13 M) was stirred for 10 min at 25 °C and then poured into 50 mL of ice water. The solution was allowed to warm to 25 °C, and then the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 30 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo* to yield **17** as a yellow amorphous solid (0.513 g, 100%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 11.12 (s, 1H), 8.11 (dd, J = 7.8, 1.3 Hz, 1H), 7.36 (td, J = 7.6, 1.2 Hz, 1H), 7.29 (td, J = 7.4, 1.4 Hz, 1H), 7.10 – 7.01 (m, 5H), 7.00 (dd, J = 7.5, 1.1 Hz, 1H), 6.92 (dd, J = 7.1, 1.8 Hz, 2H), 6.82 (d, J = 8.3 Hz, 2H), 5.28 (s, 1H), 4.39 (d, J = 2.0 Hz, 1H), 3.85 (d, J = 2.0 Hz, 1H), 3.80 (s, 3H), 3.61 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 186.4, 172.5, 164.2, 160.2, 144.4, 135.6, 134.9, 131.5, 129.6, 129.4, 128.5, 128.1, 128.0, 127.7, 126.4, 126.0, 113.7, 100.6, 55.2, 52.7, 52.3, 43.8.; AMM (ESI-TOF) m/z calcd for C$_{26}$H$_{24}$NO$_4$$^+$ [M+H]$^+$ 414.1705, found 414.1712.
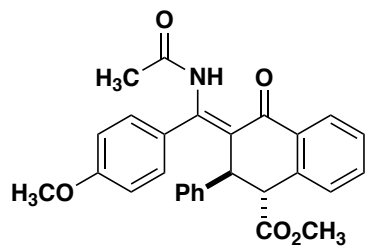
methyl (1*R*,2*S*,*Z*)-3-(acetamido(4-methoxyphenyl)methylene)-4-oxo-2-phenyl-1,2,-3,4-tetrahydronaphthalene-1-carboxylate (18) To a solution of **17** (0.05 g, 0.12 mmol) in dry CH$_2$Cl$_2$ (1.2 mL, 0.1 M) at 0 °C was added acetyl chloride (0.01 mL, 0.14 mmol) and pyridine (0.01 mL, 0.12 mmol). The solution was stirred for 21 h at 25 °C and then quenched with 2 mL of saturated NaHCO$_3$ solution. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 2 mL) and the combined organic layers were dried over Na$_2$SO$_4$ and filtered. Solvent was concentrated *in vacuo* and the crude mixture was purified by flash chromatography (70:30 hexanes/EtOAc) to yield **18** as a green oil (0.06 g, 100%): ^{1}H NMR (600 MHz, CDCl$_3$) δ 13.30 (s, 1H), 8.17 – 8.10 (m, 1H), 7.45 – 7.36 (m, 2H), 7.13 – 7.02 (m, 4H), 6.87 – 6.74 (m, 3H), 4.37 (d, *J* = 2.0 Hz, 1H), 3.95 (d, *J* = 2.0 Hz, 1H), 3.80 (s, 3H), 3.66 (s, 3H), 2.16 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 189.5, 172.0 168.5, 159.6, 154.7, 143.0, 135.8, 134.6, 133.4, 129.7, 128.4, 128.4, 128.3, 127.5, 127.4, 126.6, 126.5, 113.4, 111.2, 55.1, 52.5, 52.1, 43.6, 25.4.; AMM (ESI-TOF) m/z calcd for C$_{28}$H$_{26}$NO$_5^+$ [M+H]$^+$ 456.1811, found 456.1797.
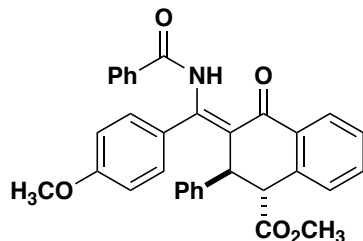
methyl (1*R*,2*S*,*Z*)-3-(benzamido(4-methoxyphenyl)methylene)-4-oxo-2-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate (19) To a solution of **17** (0.05 g, 0.12 mmol) in dry CH_2Cl_2 (1.2 mL, 0.1 M) was added pyridine (0.02 mL, 0.25 mmol) and benzoyl chloride (0.03 mL, 0.26 mmol). The solution was stirred for 22 h at 25 °C and then quenched with 2 mL of saturated $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL) and the combined organic layers were dried over Na_2SO_4 and filtered. Solvent was concentrated *in vacuo* and the crude mixture was purified by flash chromatography (80:20 hexanes/EtOAc) to yield **19** as a yellow solid (0.055 g, 87%): mp: 229-231 °C.; ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.22 – 8.17 (m, 1H), 8.14 – 8.06 (m, 3H), 7.63 – 7.46 (m, 4H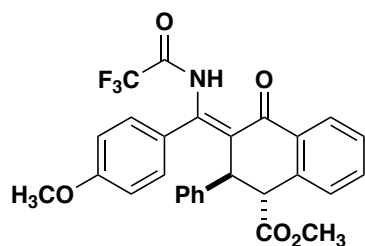), 7.44 – 7.39 (m, 2H), 7.13 – 7.05 (m, 4H), 6.87 (dd, *J* = 7.4, 1.9 Hz, 2H), 4.46 (d, *J* = 2.1 Hz, 1H), 3.98 (d, *J* = 2.1 Hz, 1H), 3.82 (s, 3H), 3.68 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 189.8, 172.0, 164.9, 159.6, 155.4, 143.0, 135.8, 134.7, 133.9, 133.7, 133.4, 132.5, 130.2, 129.7, 128.8, 128.4, 128.3, 128.14, 127.6, 126.9, 126.6, 113.4, 112.2, 55.1, 52.5, 52.2, 43.7.; AMM (ESI-TOF) m/z calcd for $C_{33}H_{28}NO_5^+$

[M+H]$^+$ 518.1967, found 518.1948.

methyl (1R,2S,Z)-3-((4-methoxyphenyl)(2,2,2-trifluoroacetamido)methylene)-4-oxo-2-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate (20) To a solution of **17** (0.03 g, 0.07 mmol) in dry CH₂Cl₂ (1 mL, 0.07M) at 0 °C was added trifluoroacetic anhydride (0.01 mL, 0.07 mmol). The solution was stirred for 22 h at 25 °C and then quenched with 2 mL of saturated NaHCO₃ solution. The aqueous layer was extracted with CH₂Cl₂ (3 x 2 mL) and the combined organic layers were dried over Na₂SO₄ and filtered. Solvent was concentrated *in vacuo* and the crude mixture was purified by flash chromatography (80:20 hexanes/EtOAc) to yield **23** as a yellow amorphous solid (0.035 g, 94%): ^{1}H NMR (600 MHz, CDCl₃) δ 8.18 (dd, J = 7.4, 1.8 Hz, 1H), 7.44 (pd, J = 7.4, 1.6 Hz, 3H), 7.14 – 7.07 (m, 4H), 7.04 – 6.89 (m, 2H), 6.89 – 6.78 (m, 4H), 4.44 (d, J = 1.9 Hz, 1H), 3.99 (d, J = 1.9 Hz, 1H), 3.81 (s, 3H), 3.68 (s, 3H).; ^{13}C NMR (151 MHz, CDCl₃) δ 190.2, 171.8, 160.2, 154.9, 151.0, 142.2, 136.1, 134.2, 133.8, 129.9, 128.7, 128.5, 128.0, 127.4, 126.9, 124.8, 116.5, 116.0, 114.5, 113.7, 55.2, 52.6, 51.8, 43.7.; AMM (ESI-TOF) m/z calcd for $C_{28}H_{23}F_3NO_5^+$ [M+H]$^+$ 510.1528, found 510.1537.
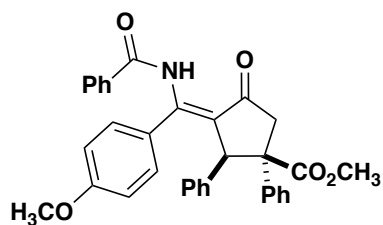
methyl (1*R*,2*S*,*Z*)-3-(benzamido(4-methoxyphenyl)methylene)-4-oxo-1,2-diphenylc-yclopentane-1-carboxylate (21) A solution of **9** (0.20 g, 0.34 mmol, 80:20 dr) in concentrated H_2SO_4 (2.6 mL, 0.13 M) was stirred for 10 minutes at 25 °C and then poured into 20 mL of ice water. The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and solvent was concentrated *in vacuo*. To a solution of the crude mixture in dry CH_2Cl_2 was added pyridine (60 µL, 0.74 mmol) and benzoyl chloride (80 µL, 0.69 mmol). The reaction mixture was stirred for 19 h at 25 °C and then quenched with 5 mL of saturated $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and filtered. Solvent was concentrated *in vacuo* and the crude mixture was purified by flash chromatography (80:20 to 100:0 CH_2Cl_2/hexanes) to yield **21** as a green oil (0.116 g, 64%, 80:20 dr). A portion of the major diastereomer was isolated for characterization purposes: ^{1}H NMR (600 MHz, CDCl3) δ 12.83 (s, 1H), 7.98 (d, *J* = 7.4 Hz, 3H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 3H), 7.35 (t, *J* = 7.6 Hz, 3H), 7.30 – 7.26 (m, 1H), 7.25 – 7.21 (m, 3H), 7.03 (d, *J* = 6.6 Hz, 3H), 6.92 (d, *J* = 8.1 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 4.52 (s, 1H), 3.97 (d, *J* = 18.3 Hz, 1H), 3.82 (s, 3H), 3.24 (s, 3H), 2.81 (d, *J* = 18.3, 1.3 Hz, 1H).; ^{13}C NMR (151 MHz, CDCl3) δ 205.5, 172.7, 164.6, 160.1, 150.6, 142.3, 141.5, 133.3, 132.6, 128.9, 128.8, 128.8, 128.5, 128.3, 128.0, 127.4, 127.3, 126.4, 126.3, 119.6, 113.5, 59.3, 55.2, 52.4, 51.9, 49.5.; AMM (ESI-TOF) m/z calcd for $C_{34}H_{30}NO_5^+$ [M+H]$^+$ 532.2124, found 532.2119.
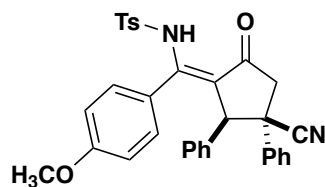
N-((Z)-((2R,3R)-3-cyano-5-oxo-2,3-diphenylcyclopentylidene)(4-methoxyphenyl)methyl)-4-methylbenzenesulfonamide (22) A solution of (1R,2S,Z)-3-((4-methoxyphenyl)((4-methylphenyl)sulfonamido)methylene)-4-oxo-1,2-diphenylcyclop-entane-1-carboxylic acid (0.16 g, 0.28 mmol, 80:20 dr) in SOCl$_2$ (0.85 mL, 0.33 M) was stirred for 2 h at reflux and then concentrated *in vacuo*. To a solution of the crude acid chloride in THF (1 mL, 0.28 M) at 0 °C was added 28% NH$_4$OH solution (1 mL). The reaction mixture was stirred for 18 h at 25 °C and then diluted with CH$_2$Cl$_2$ (10 mL). The organic layer was washed with H$_2$O (5 mL), saturated NaHCO$_3$ solution (5 mL) and brine (5 mL). The organic layer was dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. To a solution of the crude amide in dry CH$_2$Cl$_2$ (2.8 mL, 0.1 M) at 0 °C was added trifluoroacetic anhydride (0.12 mL, 0.85 mmol) and triethylamine (0.23 mL, 1.7 mmol). The reaction mixture was stirred at 0 °C for 15 minutes and then 2 h at 25 °C. The reaction mixture was quenched with 10 mL of saturated NaHCO$_3$ solution, and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 10 mL). The organic layers were dried over Na$_2$SO$_4$, filtered, and solvent was concentrated *in vacuo*. The crude mixture was purified by flash chromatography (80:20 hexanes/EtOAc) to yield **22** as a yellow solid (0.040 g, 26%, 90:10 dr). A portion of the major diastereomer was isolated for characterization purposes. mp: 206-208 °C.; ^{1}H NMR (600 MHz, CDCl$_3$) δ 11.76 (s, 1H), 7.37 – 7.27 (m, 7H), 7.24 – 7.15 (m, 4H), 6.83 – 6.78 (m, 2H), 6.51 (q, *J* = 8.4 Hz, 4H), 3.96 (s, 1H), 3.73 (s, 3H), 3.36 (d, *J* = 18.1 Hz, 1H), 3.11 (d, *J* = 18.1 Hz, 1H), 2.44 (s, 3H).; ^{13}C NMR (151 MHz, CDCl$_3$) δ 202.3, 161.0, 152.3, 144.2, 139.9, 139.3, 136.5,

130.6, 129.5, 129.3, 128.6, 128.5, 128.2, 128.0, 127.6, 125.6, 122.8, 120.6, 115.7, 113.0, 57.9, 55.2, 48.1, 29.7, 21.7.; AMM (ESI-TOF) m/z calcd for $C_{33}H_{29}N_2O_4S^+$ [M+H]$^+$ 549.1848, found 549.1863.

9.4. Experimental References

1. Espinosa, M.; Blay, G.; Cardona, L.; Pedro, J. R., *Chem. Eur. J.* **2013**, *19* (44), 14861-14866.

2. Hirner, S.; Westmeier, J.; Gebhardt, S.; Müller, C. H.; von Zezschwitz, P., *Synlett* **2014**, *25* (12), 1697-1700.