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Catalytic Dehydrogenation of 1,2- and 1,3-Diols

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Abstract:

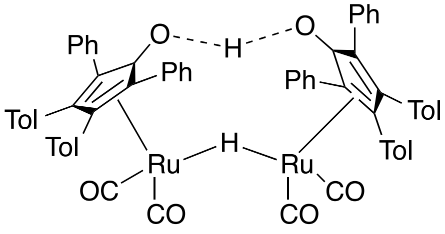
Described are studies of the dehydrogenation of 1,2- and 1,3-diols in homogenous solutions catalyzed by $\{[2,5\text{-diphenyl-}3,4\text{-ditoluyl-}(\eta^5\text{-}C_4CO)]_2H\}Ru_2(CO)_4(\mu\text{-}H)$ (otherwise known as the Casey/Shvo catalyst). Both in the presence and absence of a dihydrogen acceptor, these reactions led to the analogous α-hydroxyketone as the only organic product. Isotopic labeling studies indicate that this product arises from reversible dehydrogenation/hydrogenation reactions, resulting in formation of the thermodynamically favored α-hydroxyketone. When this catalytic dehydrogenation was carried out in the presence of the rhodium decarbonylation catalyst $Rh(dppp)_2Cl$ (dppp = 1,3-bis(diphenylphosphino)propane), modest amounts of carbon monoxide result, suggesting that the dehydrogenation does generate at least some aldehydes that are intercepted by this catalyst. However, the efficiency of the latter reaction is poor.

[#] Taken in part from the M.S. Dissertation of MAW, University of California, Santa Barbara, 2011.

Introduction

In the context of sustainability, there is a growing interest in developing chemical methodology for utilizing non-food biomass, mostly lignocellulose, as a carbon neutral, renewable feedstock for production of organic chemicals and liquid fuels [1,2]. Lignocellulose is composed of three primary components lignin, cellulose and hemicellulose. All three are highly functionalized, so the petrochemical methods that have evolved over the past century for converting fossil carbon into these key products are not well suited for biomass conversion. Thus, it has been necessary to establish new approaches that may be sensitive to multiple functional groups for the chemical transformations of such feedstocks to higher value materials [3].

One approach toward biomass utilization is to convert it to synthesis gas ($CO + H_2$) via various hydrothermal methodologies [4]. Although this transformation is endothermic, syngas and the hydrogen that one can derive from it have myriad uses. This transformation requires catalytic pathways that can both dehydrogenate and decarbonylate such substrates. A common functional group motif for each of the lignocellulose components is the vicinal diol. The present study was initiated in order to explore how the mechanistically well-characterized homogeneous catalyst for alcohol dehydrogenation, {[2,5-diphenyl-3,4-ditoluyl-(η^5-C_4CO)]$_2$H}$Ru_2(CO)_4(\mu$-H), commonly known as the Casey/Shvo catalyst (**1**) [5,6], is affected by the additional -OH functionality of a 1,2-diol or 1,3-diol. Furthermore, we will describe studies using this dehydrogenation catalyst acting in tandem with a decarbonylation catalyst on a vicinal diol. Earlier studies [7-9] have shown that such tandem catalysis can dehydrogenate/decarbonylate primary alcohols.



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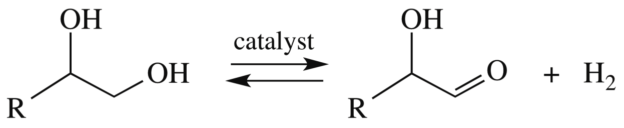
The goal of the present study was to delineate the major reaction pathways that occur in the catalytic dehydrogenation of polyfunctional compounds. Prior research has shown that the Casey/Shvo catalyst achieves higher dehydrogenation rates with primary alcohols than with secondary alcohols [10], thus, it seems likely that the major product of the dehydrogenation reactions will be an α-hydroxyaldehyde (α-HA), formed by dehydrogenation at the primary alcohol (eq. 1) [10,11]. However, since dehydrogenations with this catalyst are reversible [10], it is likely the flux of products will lead to the more stable α-hydroxyketone (α-HK, eq. 2). Described here are studies focused on evaluating these pathways in 1,2- and 1,3-diols.



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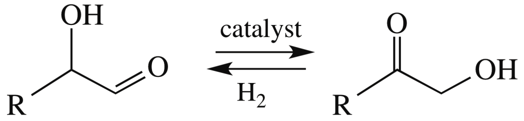

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Experimental Section

***Materials**:*

The solvents decane, toluene and diglyme were purchased from Aldrich, and the diglyme was distilled over sodium using benzophenone as an indicator. Deuterated dimethyl sulfoxide was purchased from Cambridge Isotope Laboratory, Inc. Argon was purchased from Praxair. The substrates 1,2-propanediol, anhydrous 1,3-butanediol, 1,3-propanediol, 1-phenyl-1,2-ethanediol and cyclohexanone were purchased from Aldrich, and 1,2-butanediol was purchased from TCI America. The deuterated substrates 1,2-butanediol-d_2 and 2,2',6,6'-cyclohexanone-d_4 were prepared by previously reported procedures [12,13]. The Casey-Shvo catalyst (**1**)[10] and the Rh(dppp)$_2$Cl catalyst (**2,** dppp = 1,3-bis(diphenylphosphino)propane) [14] were synthesized according to literature procedures.

Analytical methods:

Gas chromatography was performed on an Agilent 6890 gas chromatograph with a 10 m Carbosieve packed column and a thermal conductivity detection (TCD). Samples were typically 500 μL injections. The oven temperature (T) was programmed to begin at 50 ^{o}C from which it was ramped to 250 ^{o}C in 10 min, then ramped to 290 ^{o}C during the following 10 min at which T it was maintained for 45 min. GC-mass spectrometric analysis used a Hewlett Packard 5890 gas chromatograph with a Hewlett Packard 5970 series mass selective detector. Samples were dissolved in methanol and injected at a column temperature of 50 ^{o}C, which was then increased to 300 ^{o}C over the next 18 min, and then held for another 6 min. Proton and carbon NMR spectra were obtained using a Varian Unity Inova 400 MHz NMR spectrometer or a Varian Unity Inova 500 MHz NMR spectrometer. ^{1}HNMR spectra were obtained at room temperature (rt) with samples dissolved in DMSO-d_6. ^{13}CNMR spectra were obtained at rt either as neat samples or as samples dissolved in DSMO-d_6. Products were identified by comparing to NMR spectra of authentic samples or to the spectra in the SDBS database [15]. Quantities of product were determined by integration of ^{1}HNMR spectra using either benzene or mesitylene as an internal standard.

Reactivity studies with the Casey-Shvo catalyst (1).

Neat diol: A solution of **1** dissolved in 1,2-propanediol was added to a 80 mL Fisher Porter bottle fitted with a pressure gauge. The system was sealed, degassed by five freeze, pump, thaw (fpt) cycles and then back-filled with argon (1 atm). The mixture was heated to 150 ^{o}C and stirred for ~18 h after which the reaction was quenched by rapid cooling and the gas phase was collected. Liquid products were separated by vacuum distillation.

Open system experiments with solvent(s): (a) A solution of 1,2-propanediol and **1** was was prepared by dissolving these in toluene under a flow of argon. This solution was heated to reflux (115 ^{o}C) for 24 h, after which the solution was cooled to room temperature and concentrated by vacuum. Products were evaluated by examining the ^{1}HNMR spectrum in DMSO-d_6. (b) Under a flow of argon, an analogous solution of 1,2-propanediol and **1** was prepared in dry diglyme. The mixture was degassed by two fpt cycles and then refluxed at 162 ^{o}C under flowing argon. After 18 h the mixture was cooled to rt. Products were separated by vacuum distillation, dissolved in DMSO-d_6 and the ^{1}HNMR spectra recorded.

Reaction with a hydrogen acceptor: A solution of 1,2-butanediol (2.0 mmol), cyclohexanone (4.0 mmol) and **1** (2.3 μmol) was added to a NMR tube equipped with a J.

Young valve, and degassed by five fpt cycles. The sealed tube was then heated in an oil bath at 150 °C for 30 min then rapidly quenched by cooling to rt in a bath. The ^{1}H NMR spectrum was obtained for the reaction mixture dissolved in DMSO-d_6. Analogous procedures were used for the substrates 1,3-butanediol, 1,3-propanediol and 1-phenyl-1,2-ethanediol.

Deuterium transfer studies:

Using cyclohexanone-d_4: A solution of 1,2-butanediol-d_2 (2.01 mmol), cyclohexanone-d_4 (5.02 mmol) and **1** (2.7 μmol) was charged into a NMR tubes with a J. Young valve, which was degassed by 5 fpt cycles and then heated to 150 °C for 30 min. The system was rapidly cooled and a ^{13}C NMR spectrum was recorded. The reaction system was then again heated at 150 °C for another 30 min, and a second set of ^{13}C NMR spectra were acquired.

Using acetone-d_6: A solution of 1,2-butanediol-d_2 (2.49 mmol), acetone-d_6 (8.20 mmol) and **1** (3.0 μmol) was charged in a NMR tube equipped with a J. Young valve. The mixture was degassed by five fpt cycles and then heated at 55 °C. The reaction was monitored by ^{13}C NMR spectroscopy after 1.5, 6, 15 and 19 h.

Tandem catalysis studies with Rh(dppp)$_2$Cl (2).

Using 1,2-butanediol: 1,2-butanediol (2.14 mmol), cyclohexanone (4.12 mmol), **1** (2.3 μmol), and **2** (3.6 μmol) were combined in a NMR tube adapted with a J. Young valve and degassed by 5 ftp cycles. The mixture was heated to 150 °C for 19.5 h, after which the tube was cooled to rt, and a ^{13}C NMR spectrum recorded. The gas phase in the headspace was analyzed by GC-TCD, and an aliquot of the liquid was dissolved in DMSO-d_6 and the ^{1}H NMR spectrum recorded.

Using 1-phenyl-1,2-ethanediol: 1-phenyl-1,2-ethanediol (1.44 mmol), cyclohexanone (6.23 mmol), **1** (1.6 μmol), and **2** (2.1 μmol) were combined in a NMR tubes equipped with a J. Young valve and degassed by 5 ftp cycles. The mixture was heated to 150 °C for 19.5 h, then the tube was cooled to rt and a ^{13}C NMR spectrum recorded. An aliquot of the liquid mixture was dissolved in DMSO-d_6 and the ^{1}H NMR spectrum was recorded. The headspace gases were sampled and analyzed by GC TCD with quantities determined by peak integration calibrated against authentic samples.

In order to improve the GC analysis of less volatile products, some liquid products were treated with *tert*-butyldimethylsilyl chloride to convert alcohols (ROH) to more the volatile silyl ethers $^tBuMe_2SiOR$ for GC-MS analysis. Liquid product mixtures were dissolved in 30 mL of dichloromethane under argon and cooled to 0 ^oC, and to this solution, *tert*-butyldimethylsilyl chloride (0.397 g, 2.644 mmol, 1.3 equiv.) and imidazole (0.224 g, 3.30 mmol, 1.5 equiv.) were added. The mixture was warmed to rt and allowed to stir overnight with monitoring by thin layer chromatography. The reaction mixture was then either filtered through celite and concentrated, or washed with water (2x) then brine (1x), dried over anhydrous Na_2SO_4, and concentrated. An aliquot of the mixture was dissolved in DMSO-d_6 and a proton NMR recorded to confirm conversion of the hydroxide groups to silyl ethers. A second aliquot was dissolved in MeOH and analyzed by GC MS methods. After silylation the diols typically gave two GC peaks, representing mono- and di- silylated derivatives.

Results and Discussion

The following diols were studied: 1,2-butanediol, 1,2-propanediol, 1-phenyl-1,2-ethanediol, 1,3-butanediol, and 1,3-propanediol. Dehydrogenations were carried out: (a) with neat substrate in a closed system: (b) with a hydrogen acceptor to increase catalysis turnover; (c) with deuterated substrates to probe potential isomerization mechanisms (d) with the rhodium decarbonylation catalyst **2** to evaluate whether aldehyde intermediates could be intercepted.

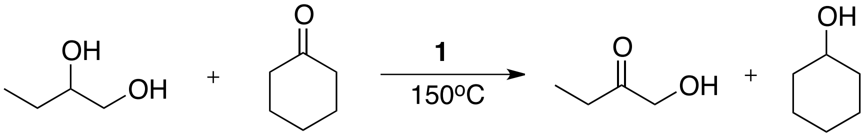
Acceptor-free dehydrogenation of 1,2-propanediol:

A deaerated solution of **1** (6.9 mg, 12 μmol) in neat 1,2-propanediol (11.1 g, 0.146 mol) was stirred at 150 ^oC in a Fisher-Porter bottle for 18 h. The solution color was initially a golden yellow but turned lighter and browner as the reaction progressed. GC-TCD analysis of the gas phase display a negative peak eluting at 1.72 min (H_2), integration of which demonstrated that 0.37 mmol of H_2 was produced. This corresponded to 31 catalyst turnovers, but only to 0.25% conversion of the diol. Distillation of the reaction mixture yielded a clear liquid. The ^{1}HNMR spectrum in DMSO-d_6 (Supporting information Figure S-1) showed that this liquid to be largely unreacted 1,2-propanediol but also showed resonances at δ = 2.05 (s, *CH_3*(CO)CH_2OH), 4.04 (d, CH_3(CO)*CH_2*OH) and 5.09 (t, CH_3(CO)CH_2*OH*) consistent with the α-HK product 1-hydroxyacetone as confirmed by comparison with the spectrum listed in the SDBS database [15]. There was no indication of the α-HA product 2-hydroxypropanal over the 9-11 ppm region characteristic of an aldehyde proton.

Dehydrogenation was then attempted by heating in an open system so that any H_2 formed was released. In the first experiment, a solution prepared from 1,2-propanediol (0.381 g, 5 mmol) and **1** (5.7 mg, 10 μmol) in toluene (6.7 mL) was refluxed (115 ^oC) for 24 h during which time the solution remained bright yellow. After removing the solvent by distillation, the ^1H NMR spectrum of the product showed only a small amount of the α-HK (1.3 % yield based on NMR integration, corresponding to ~7 catalyst turnovers) plus the unreacted diol. (SI Figure S-2). When the analogous open system reaction was carried out for 18 h in refluxing diglyme (~162 ^oC), the yield of the α-HK increased to ~40%. No products were apparent in the absence of catalyst.

Reactions of vicinal diols with a hydrogen acceptor:

A solution of 1,2-butanediol (0.180 g, 2.0 mmol), the hydrogen acceptor cyclohexanone (0.396 g, 4.0 mmol) and **1** (1.3 mg, 2.3 μmol) was added to a J. Young valve adapted NMR tube. This was degassed by fpt cycles then sealed, after which the tube heated in an oil bath at 150 ^oC for 30 min, after which the system was quenched by cooling to ambient temperature. The ^{13}C NMR spectrum of the neat solution showed resonances at δ = 211.026 (C=O), 67.598 (CH_2OH), 31.105 (CH_2), and 7.019 (CH_2) ppm (SI Figure S-3) consistent with the formation of the α-HK 1-hydroxybutanone (eq. 3), The ^1H NMR spectrum of this product mixture dissolved in DMSO-d_6 (δ= 5.03 (t, -CH_2*OH*), 4.05 (d, -*CH_2*OH), 2.41 (q, CH_3*CH_2*-) and 0.93 (t, *CH_3*CH_2-) ppm, SI Figure S-4) confirmed formation of 1-hydroxybutanone as the major dehydrogenation product according to the SBDS database [15]. Integration of the ^1H NMR spectrum, using benzene as an internal standard, revealed 1.16 mmol of the ketone formed, corresponding to 56% conversion and 510 catalyst turnovers. Peaks at δ = 4.55 (d, *OH*CH-), 3.25 (m, OH*CH*-), 1.45 (m, -C_5H_{10}) and 1.16 (m, -C_5H_{10}) ppm in the ^1H NMR spectrum corresponded to formation of 1.41 mmol of cyclohexanol. Resonances indicating the presence of unreacted 1,2-butanediol and cyclohexanone were apparent, and the spectra of these last three components were confirmed by comparison to the spectra of these compounds in DMSO-d_6 (SI Figures S-4 & S-5).



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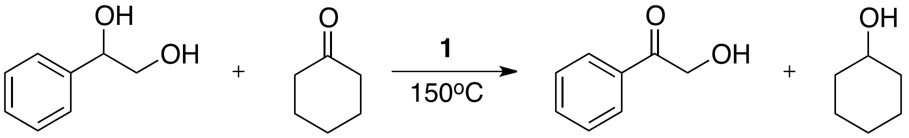
An identical sample was heated at 150 °C for 10 min intervals, and monitored by recording the ^{13}C NMR spectra. After the first interval, it was determined that 64% conversion had occurred. However, no additional conversion was observed as the heating continued, so a steady state was apparently reached. From these data it is apparent that the hydrogen transfer process indicated by eq. 3 occurs with much greater net catalytic activity than does the acceptorless dehydrogenation.

The vicinal diol 1-phenyl-1,2-ethanediol was studied similarly. This substrate (0.215 g, 1.56 mmol), cyclohexanone (0.602 g, 6.14 mmol) and **1** (0.9 mg, 1.5 μmol) were heated together in a J. Young valve adapted NMR tube at 150 °C for 30 min. The ^{13}C NMR spectrum of the resulting solution (δ = 197.927 (C=O), 133.468 (C_6H_5), 132.934 (C_6H_5), 127.165 (C_6H_5), 126.232 (C_6H_5) and 64.833 (CH_2OH) ppm) as well as the ^{1}H NMR spectrum in DMSO-d6 (δ = 7.93 (d, -C_6H_5), 7.64 (t, -C_6H_5), 7.53 (t, -C_6H_5), 4.53 (t, -(CO)CH_2*OH*), 3.42 (t, -(CO)*CH_2*OH)) (SI Figures S-6 & S-7) indicated the formation of 1-hydroxyacetophenone (eq. 4). The ^{1}H NMR spectrum of this product was confirmed by comparison to the SDBS database.[15] Integration of these proton resonances, referenced to a mesitylene standard, indicated formation of 0.79 mmol of this product (70 % conversion and 562 catalyst turnovers). The ^{13}C and ^{1}H NMR spectra also indicated the presence of cyclohexanol, unreacted 1-phenyl-1,2-ethanediol and cyclohexanone in the reaction mixture.



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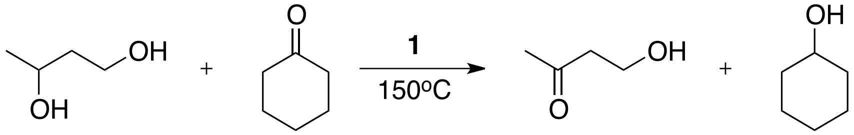
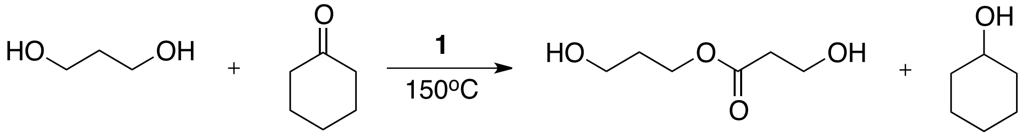
Dehydrogenation of 1,3-diols using a hydrogen acceptor.

In an analogous experiment anhydrous 1,3-butanediol (0.19 mL, 2.12 mmol), cyclohexanone (0.402 g, 4.10 mmol) and **1** (1.5 mg, 2.6 μmol) were combined, degassed, and heated to 150 ^{0}C in a J. Young valve adapted NMR tube for 30 min. The ^{13}C NMR spectrum (peaks at δ= 208.65 (C=O), 57.80 (CH_2OH), 46.66 (CH_2) and 30.38 (CH_3) ppm, SI Figure S-8) indicated formation of the β-HK 4-hydroxybutanone as the only C_4 product (eq. 5). The ^{1}H NMR spectrum (peaks at δ = 4.65 (t, *OH*CH_2CH_2-), 3.625 (q, OH$\mathit{CH_2}$$CH_2$-), 2.53 (t, $OHCH_2$$\mathit{CH_2}$-), and 2.09 (s, -(CO)$\mathit{CH_3}$) ppm, SI Figure S-9) confirmed the formation of this product according to the SDBS database [15]. Integration of proton resonances, calibrated to a benzene standard, gave the 4-hydroxybutanone yield as 1.44 mmol (68 % conversion and 746 catalyst turnovers). Resonances for cyclohexanol, 1,3-butanediol and cyclohexanone were also evident in the ^{13}C and ^{1}H NMR spectra. Integration of proton resonances gave a 1.87 mmol yield for the hydrogen transfer product cyclohexanol. The ^{1}H NMR spectrum of 1,3-butanediol in DMSO-d_6 is shown in SI Figure S-9.



(5)

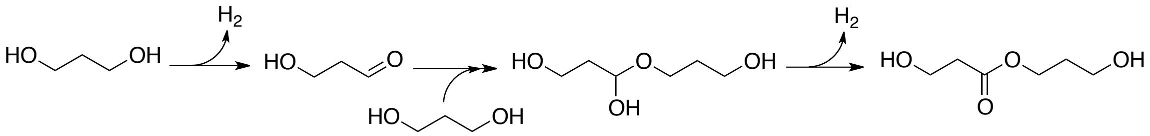
Dehydrogenation of 1,3-propanediol should not give a ketone product without major isomerization. This substrate (0.157 g, 2.26 mmol), cyclohexanone (0.414 g, 4.23 mmol), and **1** (1.5 mg, 2.3 μmol) were combined in a J. Young valve adapted NMR tube and heated to 150 ^{o}C for 30 min. The ^{13}C NMR spectrum of the product mixture (SI Figure S-10) showed the formation of cyclohexanol as well as peaks at δ = 172.62 (C=O), 62.14 (CH_2O), 58.86 (CH_2OH), 58.34 (CH_2OH), 38.28 (CH_2), and 32.30 (CH_2) ppm that we attribute to the ester 3-hydroxypropyl 3-hydroxyproponate (eq. 6). The latter is a type of product often seen in the dehydrogenative oxidation of primary alcohols [16,17]. Formation of the ester, rather than an aldehyde, was confirmed by DEPT-NMR, which showed that the 172.62 ppm peak (not seen by this method) corresponds to a carbon without protons. The ^{1}H NMR spectrum (δ = 4.67 (t, *OH*CH_2-), 4.51 (t, *OH*CH_2-), 4.08 (t, -$\mathit{CH_2}$O(CO)-), 3.64 (q, -(CO)$CH_2$$\mathit{CH_2}$OH), 2.42 (t, -(CO)$\mathit{CH_2}$$CH_2OH$), and 1.71 (m, $OHCH_2$$\mathit{CH_2}$$CH_2O$-) ppm, SI Figure S-11) confirmed the ester as the primary dehydrogenation product. Integration of these peaks, compared to a mesitylene standard, a yield of 0.45 mmol (19.4% conversion, 302 catalyst turnovers). Unreacted 1,3-propanediol and cyclohexanone are also evident in the product NMR spectra.



(6)

The bimolecular ester presumably results from dehydrogenation of 1,3-propanediol since the carbon backbone is too short to form a stable lactone. It is likely that 3-hydroxy propanal is formed as an intermediate, but this reacts with a second 1,3-propanediol to form a hemiacetal. Further dehydrogenation (Scheme 1) would give the ester [16,17]. Close inspection of the ^{1}H NMR spectrum in SI Figure S-11 showed several, very small, unidentified peaks, indicating the presence of other, minor products.

Scheme 1: Proposed formation of an ester via the hemiacetal



Summary of dehydrogenation experiment

The results of the above dehydrogenations are summarized in Table 1. The reaction in a closed vessel without an acceptor produced dihydrogen but the yield was quite small as was also found for catalysis with an open system where any H_2 formed would dissipate. Thus, these results must be attributed to the low reactivity of the catalyst under these conditions. This is consistent with slow H_2 release from 1, which is greatly accelerated by the presence of a hydrogen acceptor [6].

Less obvious is the explanation for formation of the α-HKs from the vicinal diols and the 4-hydroxybutanone from 1,3-butane diol as the only products detectable by NMR. Literature precedents that primary alcohols are dehydrogenated at a faster rate than secondary alcohols suggest that hydroxyaldehyde products would be kinetically favored. However, even if primary OH dehydrogenation occurs preferentially, this may followed by isomerization to the more stable

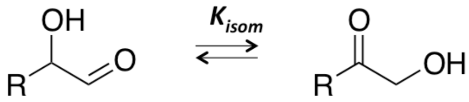
Table 1: Diol dehydrogenation reactions with and without a hydrogen acceptor.

	Diol (mmol)	**Cyclohexanone (mmol)**	**1 (μmol)**	**Product identified**	**Product Yield (mmol)**	**Turnover Number**
1,2-propanediol[a]	146	-	12.0	H_2	0.37	36
1,2-butanediol[b]	2.09	4.0	2.30	1-hydroxy butanone	1.61	509
1-phenyl-1,2-ethanediol[b]	2.33	4.15	2.63	1-hydroxy acetophenone	0.79	562
1,3-butanediol[b]	2.12	4.27	2.63	4-hydroxy butanone	1.44	746
1,3-propanediol[b]	1.13	6.52	1.5	3-hydroxy-propyl-3-hydroxypropionate	0.45	302

[1] Reaction at 150 °C for 24 h

[2] Reaction at 150 °C for 30 min

ketone. While we do not have comparative heats of formation for all likely products from the diol reactions, the HK isomers should be significantly more stable than the respective HA isomers, given that the ΔH for isopropanol dehydrogenation is 13 kJ/mol more favorable than the analogous reaction for n-propanol [18]. Assuming an analogous free energy difference between the HA and HK isomers, equilibrium between these (eq. 7) would favor the HKs by 40-fold at 150 °C.

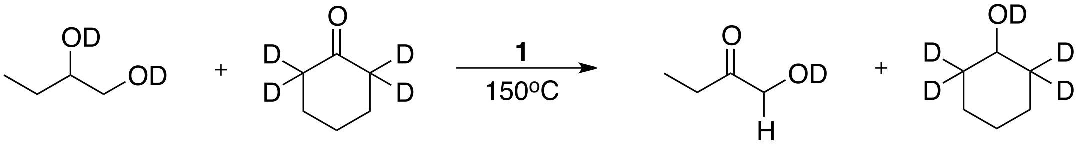


(7)

For a α-HA, such isomerization might be an intra-molecular process via an enolate intermediate catalyzed the traces of acid or base, although it is more difficult to visualize an analogous isomerization for the β-HA formed by dehydrogenation of the 1,3-butanediol. Another pathway would be reversible dehydrogenation/hydrogenation of the functionalized carbons as previously described for mono-ol systems (Scheme 3) [6]. This would be consistent with the observation that, even with a hydrogen acceptor, the diol dehydrogenations do not go to completion, but instead reach an apparent steady state.

Deuterium labeling experiments:

Isotopically labeled 1,2-butanediol-d$_2$ ($CH_3CH_2CH(OD)CH_2OD$) and cyclohexanone-d$_4$ ($C_6H_6D_4O$), prepared by exchanging acidic hydrogens on the two compounds, were used in reactions analogous to those above. A degassed mixture of the diol (0.181g, 2.01 mmol), cyclohexanone-d$_4$ (0.492 g, 5.02 mmol) and **1** (1.52 mg, 2.7 μmol) in a J. Young valve adapted NMR tube was heated to 150 °C for 30 min, after which the ^{13}C NMR spectrum was recorded. Although the carbonyl carbon was not detected, peaks at δ = 68.67 (CHOH(D)), 32.20 (CH_2) and 8.18 (CH_3) ppm were consistent with those expected for the 1-hydroxybutanone. The cyclohexanol product displayed resonances at δ = 74.40 (CHOH(D)), 35.64 (m, CD_2), 27.33 (CH_2) and 25.24 (CH_2) ppm (SI Figure S-12). 1,2-butanediol-d$_2$ and cyclohexanone-d$_4$ were also present. All H-decoupled ^{13}C resonances attributed to the diol or the hydroxyketone appeared as singlets, suggesting that there was no deuterium exchange onto the carbon atoms of the dehydrogenation product (eq. 8).

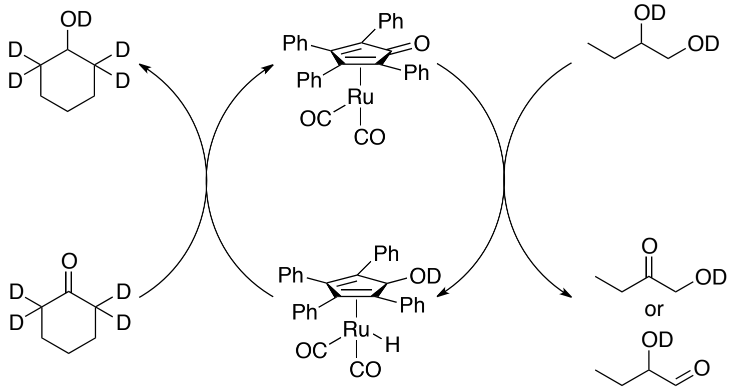


(8)

In a similar experiment at lower T, 1,2-butanediol (0.224 g, 2.49 mmol), acetone-d$_6$ (0.475 g, 8.20 mmol) and **1** (1.7 mg, 3.0 μmol) were combined in a J. Young adapted NMR tube and heated to 55 °C. The ^{13}C NMR spectra were recorded after 1.5, 6, 15 and 19 h. Singlets at 207.843 (C=O), 63.662 (CHOH), 31.370 (CH_2) and 7.548 (CH_3) ppm (SI Figure S-13) confirmed the formation of the α-hydroxyketone with no deuteration of the carbons. A septuplet at δ = 68.01 ppm confirmed the presence of isopropanol-d$_6$. Unreacted 1,2-butanediol and acetone-d$_6$ were also present. After 19 h, conversion to the α-HK had reached 25.7% (216 turnovers). This and isopropanol-d$_6$ were the only products detected.

These observations are consistent with the regiospecific, concerted hydride and proton transfer mechanism proposed by Casey et al (Scheme 2) [6]. If α-HA is first formed then isomerizes to the α-HK via an enolate intermediate, C-H(D) exchange should be evident as a triplets in the ^{13}C NMR spectrum. Instead all peaks were singlets, with the exception of the deuterated carbons of hydrogen acceptors, thus this pathway is not important.

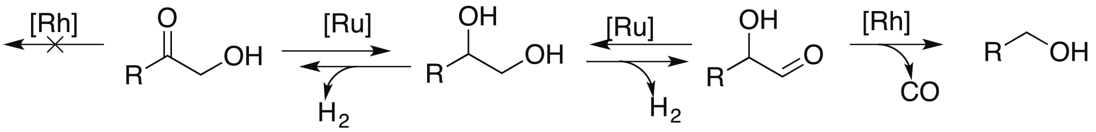
Scheme 2: Proposed mechanism for butanediol dehydrogenation at primary or secondary sites according to literature precedent [6].



Tandem catalysis studies with 1,2-diols

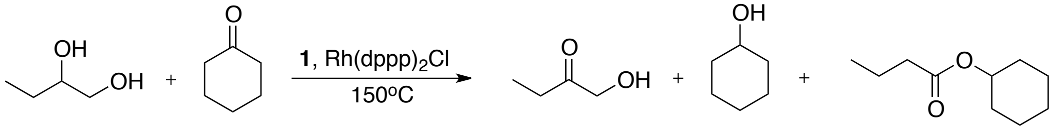
The question remains whether a HA is first formed then is converted to the HK product by reversible, regiospecific hydrogenation/dehydrogenation steps, since the experiments described above neither confirm nor exclude the formation of α-hydroxy-aldehydes in 1,2-diols dehydrogenations. This led us to explore the possibility of a tandem catalytic scheme using the rhodium complex **2**, which is effective for aldehyde decarbonylation [19]. Thus, if an α-HA were formed by primary alcohol dehydrogenation by **1**, this may be intercepted *in situ* by decarbonylation (Scheme 3). For examples, Monrad and Madsen have used the same catalyst to decarbonylate the linear forms of several sugars [7], and Morton and Cole-Hamilton[9] have used similar tandem catalysis to decarbonylate acetaldehyde formed during dehydrogenation of ethanol. Although the latter researchers found that the resulting CO poisoned the dehydrogenation catalyst, **1** is not inhibited by CO.

Scheme 3: Detecting a hydroxy-aldehyde intermediate via decarbonylation of the aldehyde.



1,2-butanediol. In the first example, a degassed mixture of 1,2-butanediol (0.192 g, 2.14 mmol), cyclohexanone (0.403 g, 4.12 mmol), **1** (1.3 mg, 2.3 μmol), and **2** (3.6 mg, 3.6 μmol) in a J. Young valve adapted NMR tube was heated at 150 ^{o}C for 19.5 h. Analysis of the headspace gas by GC-TCD showed peaks at retention times 2.1, 8.35, 12.57 and 21.11 min, corresponding to H_2, CO, CO_2 and ethane with the respective yields 2.45, 20.9, 8.50 and 2.46 μmol. Observation of CO is consistent with the formation and decarbonylation of an aldehyde intermediate; however, the CO_2 was a bit more surprising. (This was not an artifact of the GC analysis; injection of pure CO gave no CO_2 signal).

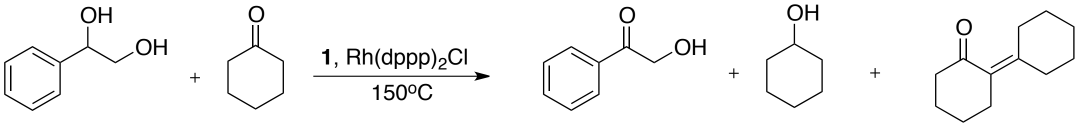
GC-MS analysis of the liquid mixture after silylation was used to identify the major organic products (eq. 9). The product mixtures included cyclohexanone, which eluted at 5.3 min and the silylated form of cyclohexanol, which eluted at 8.52 min. Some chromatograms also showed the non-silylated cyclohexanol eluting at 5.5 min. (Notably, the molecular ion *m/z* values of the silylated alcohols do not include the ^{t}Bu group, which was lost upon ionization.) As seen in the absence of **2**, the major dehydrogenation product was the α-HK, the silylated form of which eluted at 8.12 min with a molecular ion peak of 145 *m/z*. The ^{13}C NMR (211.03 (C=O), 67.66 (CHOC), 31.18 (CH_2), and 7.12 (CH_3) ppm,) and ^{1}H NMR (5.05 (t, -CH_2*OH*), 4.04 (d-(CO)*CH_2*OH), 2.38 (q, CH_3*CH_2*(CO)-), and 0.93 (t, *CH_3CH_2*-) ppm (SI Figure S-14) spectra confirmed the identity of this product (0.41 mmol). A component that eluted at 8.23 min with a molecular ion 170 *m/z* in the GC-MS spectrum corresponds to the ester cyclohexyl butyrate. The ^{1}H NMR spectra displayed resonances at 3.96 (q) and 0.86 (t) ppm for the tertiary proton and the terminal methyl of the butyl chain. Integration revealed that 0.51 mmol of this species and 1.42 mmol of cyclohexanol were produced. Propanol, the expected product from dehydrogenation at the primary -OH followed by decarbonylation, was not found in the reaction mixture, nor were 1- or 2-butanol, although a number of smaller peaks were visible in the ^{13}C NMR spectrum but not identified.



(9)

Based on the quantity of **1** present, the cyclohexanol formed (plus the small amount of H_2) corresponds to 618 turnovers of the dihydrogen transfer catalyst. Noting that the formation of the ester requires two dehydrogenation steps, the formation of the α-HK plus the ester correspond to 622 catalyst turnovers, a agreement that seems fortuitous given the likely contributions of other side reactions. The CO and CO_2 combined are only a small fraction (~2%) of these dehydrogenation processes.

1-phenyl-1,2-ethanediol: In this case, a solution of 1-phenyl-1,2-ethanediol (0.199 g, 1.44 mmol), cyclohexanone (0.611 g, 6.23 mmol), **1** (0.9 mg, 1.6 μmol) and **2** (2.0 mg, 2.1 μmol) in a J. Young valve adapted NMR tube was heated to 150 ^{o}C for 19.5 h. The color, initially bright yellow, turned to a dark, but homogenous, brown. Gas phase analysis by GC-TCD showed the formation of H_2 (1.83 μmol), CO (3.67 μmol) and CO_2 (3.02 μmol). The main components in the liquid phase of the reaction were identified by GC/MS after silylation of the mixture. Peaks that eluted at 11.55 and 12.84 min. correspond to the mono- and di-silylated diol, while a peak eluting at 11.68 min (193 *m/z*) corresponds to the silylated α-hydroxyketone. The latter species was confirmed in both the ^{13}C NMR (δ = 199.28 (C=O), 134.88 (C_6H_5), 134.39 (C_6H_5), 129.48 (C_6H_5), 128.38 (C_6H_5), 127.56 (C_6H_5) and 66.24 (CH_2OH) ppm) and ^{1}H NMR (δ = 7.93 (C_6H_5), 7.64 (C_6H_5), and 7.52 (C_6H_5) ppm) spectra (SI Figure S-15). A third product, which eluted at 9.76 min and had a mass of 178 *m/z* in the GC MS analysis was concluded to be 2-cyclohexylidene cyclohexanone, the product of cyclohexanone self condensation. This product was not further quantified. Neither benzyl alcohol nor benzene, logical products from decarbonylation, were evident in the reaction mixture, but concentrations would have been likely too low for detection. The observation of CO as a reaction argues that aldehydes are likely as dehydrogenation products, although too reactive to be isolated under these conditions



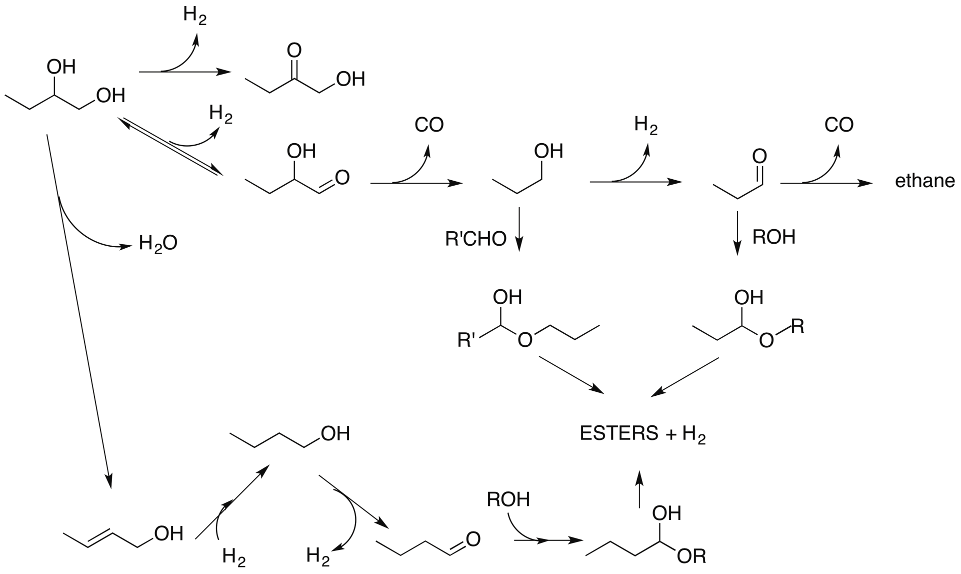
(10)

In order to evaluate mass balance for the reactions, the full ^{1}H spectra of the products from the two tandem catalysis reactions were integrated versus a non-reactive internal standard (benzene or mesitylene). The moles of protons from this integration were then compared to the total moles of protons added at the started of the reaction. For the runs with 1,2-butanediol and 1-phenyl-1,2-ethanediol, the integrated values were 92and 113% of the protons calculated to have been added to the system. Although the experimental uncertainty is substantial, this does show that the large majority of protons can be accounted for even if the products are not all identified.

Overview and Summary.

Introducing a second catalyst and the longer reaction times employed led to a more complex suite of products. Scheme 7 proposes a series of reactions that may contribute to this complexity. This scheme does not account for CO_2 formation, although a likely source would be the water gas shift reaction [20], since these systems were not rigorously dried and some H_20 may be generated by alcohol dehydration.

Scheme 7: The three main pathways that appear in the tandem reactions: dehydrogenation at the secondary hydroxide, dehydrogenation at the primary hydroxide and dehydration to form butanol. The last two pathways have the possibility of forming hemiacetals and esters.



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Supporting information:

Figures (15) showing NMR spectra of reaction products.

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