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(Cyclopentadienone)iron-Catalyzed Transfer Dehydrogenation of Symmetrical and Unsymmetrical Diols to Lactones

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ABSTRACT

Air-stable iron carbonyl compounds bearing cyclopentadienone ligands with varying substitution were explored as catalysts in dehydrogenative diol lactonization reactions using acetone as both the solvent and hydrogen acceptor. Two catalysts with trimethylsilyl groups in the 2- and 5-positions—[2,5-$(SiMe_3)_2$-3,4-$(CH_2)_4(\eta^4$-$C_4C{=}O)]Fe(CO)_3$ (**1**) and [2,5-$(SiMe_3)_2$-3,4-$(CH_2)_3(\eta^4$-$C_4C{=}O)]Fe(CO)_3$ (**2**)—were found to be the most active, with **2** being the most selective in the lactonization of diols containing both primary and secondary

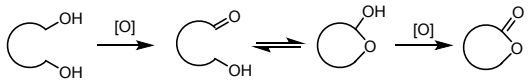
alcohols. Lactones containing five-, six-, and seven-membered rings were successfully synthesized, and no over-oxidations to carboxylic acids were detected. The lactonization of unsymmetrical diols containing two primary alcohols occurred with catalyst **1**, but selectivity was low based on alcohol electronics and modest based on alcohol sterics. Evidence for a transfer dehydrogenation mechanism was found, and insight into the origin of selectivity in the lactonization of 1°/2° diols was obtained. Additionally, spectroscopic evidence for a trimethylamine-ligated iron species formed in solution during the reaction was discovered.

INTRODUCTION

Lactones are common structural features found in natural products and biologically active compounds,[1,2] and they can also be used as monomers in the synthesis of biodegradable polyesters using ring-opening polymerizations.[3] One efficient way to access these versatile compounds is through the oxidation of diols (Scheme 1), and various methods using stoichiometric oxidants—including Cr(VI) species,[4,5] manganese oxides,[6,7] sodium bromite,[8] Raney nickel,[9] and silver carbonate[10]—have been developed. Additionally, oxidative lactonizations of diols using organic or metal-based catalysts with terminal oxidants such as bleach,[11] peroxides,[12,13] hypervalent iodine,[14,15] or molecular oxygen,[16–21] are also known. There are a few examples of acceptorless dehydrogenations[22,23] of diols to lactones catalyzed by Ru,[24,25] Ir,[26,27] Fe,[28,29] and Co,[30] which typically require high temperatures and/or strong bases or have a limited substrate scope. A majority of the catalytic approaches use strong oxidants, but there are concerns about safety and selectivity when organic compounds are treated with them either alone or as terminal oxidants in

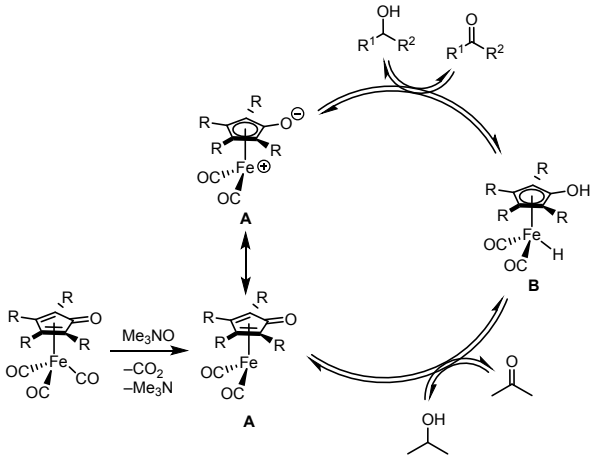
catalytic reactions. Transfer dehydrogenations avoid strong oxidants by employing less reactive organic hydrogen acceptors, and simple carbonyl compounds have been used as both the solvent and terminal oxidant in iridium-catalyzed[31] and ruthenium-catalyzed[32–37] lactonizations of diols. While these processes avoid strong oxidants, they use rare metals. Long-term environmental and economic sustainability are of growing importance, so new catalytic methods using earth-abundant metals are desirable.

Scheme 1. Oxidative lactonization of a diol.



Recently, it has been shown that (cyclopentadienone)iron carbonyl compounds can catalyze transfer dehydrogenations of alcohols to carbonyl compounds using acetone as the stoichiometric oxidant (i.e., Oppenauer-type oxidation), and even a few simple diols have been lactonized.[38–44] Scheme 2 illustrates the activation of the catalyst with trimethylamine *N*-oxide to form unsaturated species **A** and the reversibility of the catalytic cycle. In addition to being based on iron—the second most-abundant metal in the earth's crust—these compounds do not require a base to be activated, they have air-stable pre-catalysts, and even during catalysis they are not moisture sensitive.[45–47] Additionally, they react chemoselectively and tolerate the presence of a variety of functional groups, including nitro groups, esters, alkenes, alkynes, aryl halides, ethers, aliphatic epoxides, and cyclopropanes.[40,42,48] Due to their desirable properties and ease of use, we explored the reactivity of a selection of (cyclopentadienone)iron carbonyl compounds in the transfer dehydrogenation of symmetrical and unsymmetrical diols to lactones (Figure 1).

Scheme 2. Transfer dehydrogenation of alcohols and transfer hydrogenation of carbonyls with (cyclopentadienone)iron carbonyl compounds.



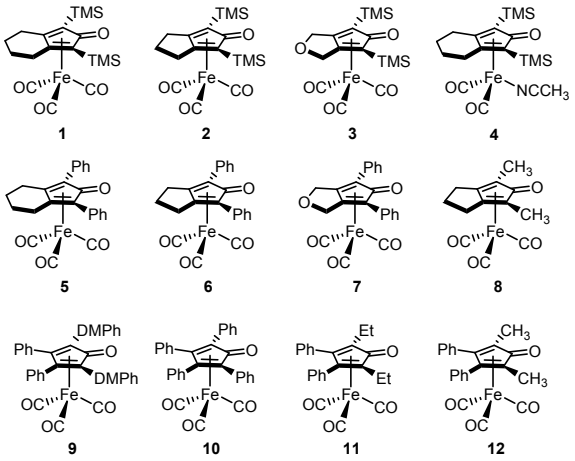
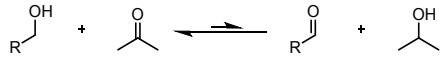


Figure 1. Iron catalysts examined in this study. TMS = trimethylsilyl; DMPh = 3,5-dimethylphenyl.

RESULTS AND DISCUSSION

We expected the process outlined in Scheme 1 to occur with (cyclopentadienone)iron carbonyl compounds: one primary alcohol would be oxidized to the aldehyde, the lactol

would reversibly form, and it would undergo a second dehydrogenation to form the lactone. A major advantage of using a transfer dehydrogenation catalyst was that no over-oxidation of the aldehyde to the carboxylic acid would occur.[49] We chose acetone as both the solvent and hydrogen acceptor because it ranks favorably in health, safety, and environmental considerations,[50–52] but its relatively low oxidation potential meant the equilibrium between a primary alcohol/acetone and aldehyde/isopropanol would favor the alcohol/acetone side (eq. 1).[49,53] Unfortunately, the oxidation of a primary alcohol to an aldehyde was the first step in the desired transformation (Scheme 1). This challenge could be overcome if lactone formation was irreversible, and (cyclopentadienone)iron carbonyl compounds do not reduce esters, which suggested lactones could also be unreactive.[42,44,54]



(1)

Lactonization of symmetrical diols. Modifications to the cyclopentadienone substitution affect the reactivity of this class of catalysts.[40,41,43,44,55–60] Therefore, we examined a collection of twelve known iron tricarbonyl compounds with varying cyclopentadienone substitution (Figure 1) in the dehydrogenative lactonization of 1,5-pentanediol (**13a**), and the results are shown in Figure 2. Trimethylamine *N*-oxide was added to activate the catalyst by oxidatively removing a carbonyl ligand (Scheme 2).[40] Catalysts **1**, **2**, **4**, and **9**, which have sterically bulky TMS or 3,5-dimethylphenyl groups adjacent to the cyclopentadienone carbonyl, were the most active. The substitution in the 3- and 4-positions of the cyclopentadienone also had a large effect on catalyst reactivity, as can be seen when comparing lactone yields with catalysts **5**, **6**, **7**, and **10**. Catalysts with oxygen atoms in the fused ring were less reactive than those without (**3** and **7** vs. **2** and **6**, respectively). No aldehydes or lactols were observed

by ^{1}H NMR spectroscopy in the crude reaction mixtures after 24 h, which is consistent with the disfavored equilibrium illustrated in equation 1.

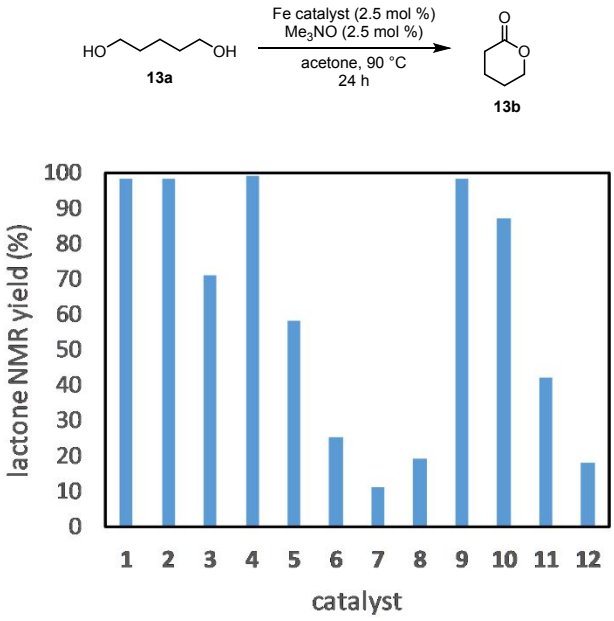
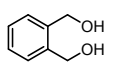
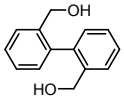
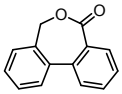
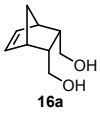
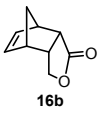


Figure 2. Lactonization of 1,5-pentanediol (**13a**) with (cyclopentadienone)iron tricarbonyl catalysts. Reaction conditions: 1,5-pentanediol (1 equiv; 0.5 M in acetone), Fe catalyst (0.025 equiv), anhydrous trimethylamine *N*-oxide (0.025 equiv), and acetone at 90 °C for 24 h in a sealed, thick-walled test tube. Lactone yield determined by ^{1}H NMR spectroscopy.

The activity of **1**, **2**, **4**, and **9** in the lactonization of a few other diols was examined (Table 1). The TMS-containing catalyst **1** and its acetonitrile derivative **4** afforded the desired lactones in the highest yields. Compound **4** is activated by heat—the nitrile ligand dissociates and unsaturated species **A** (Scheme 2) is generated in solution. While **1** and **4** have similar activities, an extra synthetic step is required to access **4**, so **1** was used in subsequent reactions. When the reactions were run at the reflux temperature of acetone, the yields were reduced. It has been observed that **9** has alcohol dehydrogenation activity equal to or greater than **1**, but it may be decomposing under the elevated temperature required

for diol lactonization (see below).[44] Iron compound **1** has successfully catalyzed redox transformations at temperatures >100 °C.[46,61,62]

Table 1. Comparison of 1, 2, 4, and 9 in diol lactonizations.[a]

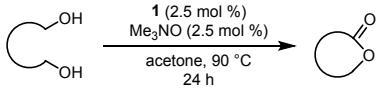
diol	lactone	lactone NMR yield (%)			
		1	**2**	**4**	**9**
 **14a**	 **14b**	>98 (87)	>98	>98	62
 **15a**	 **15b**	>98 (43)	70	95	32
 **16a**	 **16b**	>98 (87)	93	96	10

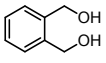
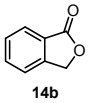
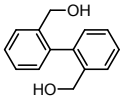
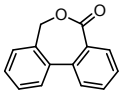
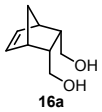
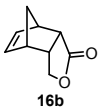
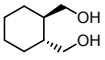
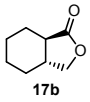
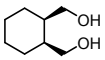
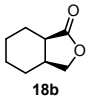
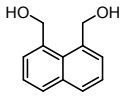
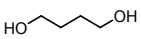
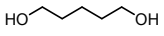
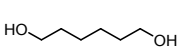
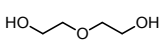
[a]Reaction conditions: diol (1 equiv; 0.5 M in acetone), Fe catalyst (0.025 equiv), anhydrous trimethylamine *N*-oxide (0.025 equiv), and acetone at 90 °C for 24 h in a sealed, thick-walled test tube. Lactone yield determined by ^{1}H NMR spectroscopy. Values in parentheses are for reactions run at reflux (oil bath at 60 °C) in an open vessel under N_2.

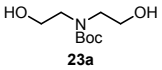
Table 2 illustrates the scope of symmetrical diols lactonized by **1**. Lactones composed of five-, six-, and seven-membered rings could be generated using this procedure. In some cases, 5 mol % of catalyst was required to achieve high yields (Table 2, entries 5, 6). Diols with unrestricted rotation (Table 2, entries 7–11) were lactonized as well as those with less conformational freedom (Table 2, entries 1–6), although seven-membered lactone **21b** was challenging to form with 2.5 mol % of **1**. Lactones bearing coordinating functional groups (Table 2, entries 10 and 11) were isolated in low yields, which could be due either to coordination to the catalyst—decreasing catalyst activity—or a decrease in the reduction potential of the primary alcohols due to the inductively withdrawing oxygen or BOC-protected nitrogen in **22a** and **23a**, respectively.[53] The tricarbonyl compound **1** was the superior catalyst with most substrates, but yields of lactones bearing coordinating functional groups were a few percent higher when the nitrile-ligated catalyst **4** was used (Table 2,

entries 10 and 11).[42] A possible explanation for the small increase in yield relates to the acetonitrile ligand. If the substrate coordinated to unsaturated species **A**, the nitrile ligand could assist in dissociating it from the iron, regenerating the catalytically active species. Again, no aldehydes or lactols were observed in the ^{1}H NMR spectra of the crude reaction mixtures after 24 h.

Table 2. Symmetrical diols lactonized by 1.[a]



entry	diol	lactone	yield (%)[b]
1	 **14a**	 **14b**	92
2	 **15a**	 **15b**	87
3	 **16a**	 **16b**	89
4	 **17a**	 **17b**	95
5[c]	 **18a**	 **18b**	87
6[d]	 **19a**	 **19b**	88
7	 **20a**	 **20b**	77[e]
8	 **13a**	 **13b**	90
9	 **21a**	 **21b**	~21[e]
10[f]	 **22a**	 **22b**	34

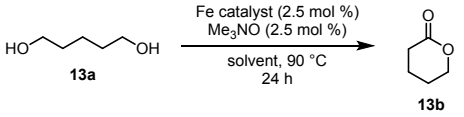
11[f]	 **23a**	 **23b**	38

[a]Reaction conditions: unless otherwise noted, diol (1 equiv, 0.5 M in acetone), **1** (0.025 equiv), anhydrous trimethylamine *N*-oxide (0.025 equiv), and acetone at 90 °C for 24 h in a sealed, thick-walled test tube. [b]Isolated yield. [c]**2** and trimethylamine *N*-oxide loadings of 0.05 equiv (5 mol %) were used. [d]**1** and trimethylamine *N*-oxide loadings of 0.05 equiv (5 mol %) were used. [e]Isolated with small amounts of impurities, including **1**; see Experimental Section for details. [f]Catalyst **4** (2.5 mol %) with no trimethylamine *N*-oxide was used.

A series of reactions was performed to provide evidence for the proposed mechanism shown in Scheme 2, and Table 3 summarizes the results from the control experiments. When no iron species was added, no lactone formed (Table 3, entry 1). Trimethylamine *N*-oxide is an oxidant and could react similarly to TEMPO—which catalyzes diol lactonizations in the presence of hypervalent iodine—but no evidence for even stoichiometric alcohol oxidation was found in the absence of iron.[14] At elevated temperature, it is possible for the cyclopentadienone ligand to dissociate, and the remaining $Fe(CO)_x$ species could be catalytically active. The fact that cyclopentadienone substitution affected catalyst activity suggested this was not the case, but a control experiment was done using $Fe(CO)_5$ as the catalyst (Table 3, entry 2). No lactone was detected, which is consistent with the need for a cyclopentadienone ligand. Finally, evidence for a transfer dehydrogenation mechanism was targeted. When toluene was used in place of acetone as the solvent, 12% of the lactone formed indicating a few catalyst turnovers (Table 3, entry 3). It is highly unlikely toluene served as a hydrogen acceptor, so hydrogen gas may be directly released under these conditions (i.e., an acceptorless dehydrogenation occurred). Shvo's catalyst, a diruthenium bridging hydride structurally similar to this class of iron compounds, is known to perform acceptorless dehydrogenations.[63,64] To distinguish between transfer and acceptorless dehydrogenation mechanisms under the typical conditions, the lactonization of **14a** was run

in acetone-d_6 and a ^{1}H NMR spectrum was taken. The reaction went to 92% conversion, and a signal at 3.87 ppm indicated the presence of isopropanol-d_6 in a 2:1 molar ratio relative to the lactone (Figure 3). This evidence strongly supports the transfer dehydrogenation mechanism where two oxidations are required for lactone formation.

Table 3. Control experiments.[a]



entry	catalyst	solvent	NMR yield (%)
1	none	acetone	ND
2[b]	$Fe(CO)_5$	acetone	ND
3	**1**	toluene	12

[a]Reaction conditions: unless otherwise noted, diol (1 equiv, 0.5 M in acetone), catalyst (0.025 equiv), anhydrous trimethylamine *N*-oxide (0.025 equiv), and acetone at 90 °C for 24 h in a sealed, thick-walled test tube. NMR yields determined by peak areas in the ^{1}H NMR spectrum relative to biphenyl as an internal standard. ND = none detected. [b]Trimethylamine *N*-oxide loading of 0.05 equiv (5 mol %) was used.

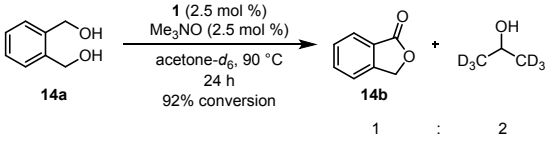
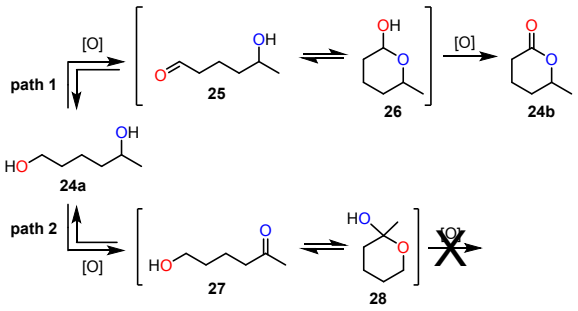


Figure 3. Evidence for a transfer dehydrogenation mechanism.

Lactonization of unsymmetrical diols. We also explored how this class of catalysts reacted with unsymmetrical diols, including substrates with two primary alcohols and those with one primary and one secondary alcohol. These diols were expected to be challenging substrates due to selectivity issues. For example, in the dehydrogenation of 1,5-hexanediol (**24a**), an initial oxidation of the primary alcohol would lead to the desired product (**24b**,

Scheme 3, path 1), but oxidation of the secondary alcohol would not afford lactone (Scheme 3, path 2). Unfortunately, secondary alcohols are typically more readily oxidized than primary alcohols in transfer dehydrogenations with acetone as the hydrogen acceptor,[65] but the equilibrium-driven nature of most steps in the process could lead to high yields of lactone if they were truly reversible, the catalyst remained active, and lactonization was irreversible.

Scheme 3. Possible reaction pathways in the oxidative lactonization of an unsymmetrical diol.



The same twelve iron tricarbonyl compounds were explored in the lactonization of **24a** (Figure 4). Reaction outcomes were determined by gas chromatography, and both diol consumption (conversion) and lactone formation (yield) were tracked. Quite a few catalysts dehydrogenated the diol, but only the TMS-containing catalysts (**1**–**4**) afforded lactone **24b** in >50% yield, with **2** outperforming the rest. Structural changes to the 3- and 4-positions of the cyclopentadienone again affected catalyst activity (catalysts **5**, **6**, **7**, and **10** in Figure 4). To gain insight into what other products were forming, ^{1}H NMR spectra of the crude reaction mixtures generated using catalysts **5**, **7**, **9**, **10**, and **12** were analyzed. In all cases the major products were a mixture of 6-hydroxy-2-hexanone (**27**) and its lactol **28**, indicating that path 2 in Scheme 3 was being followed when many of the catalysts were used.[66–68] The presence of these compounds is consistent with this class of catalysts being generally selective for oxidizing secondary alcohols over primary.[39,40,44]

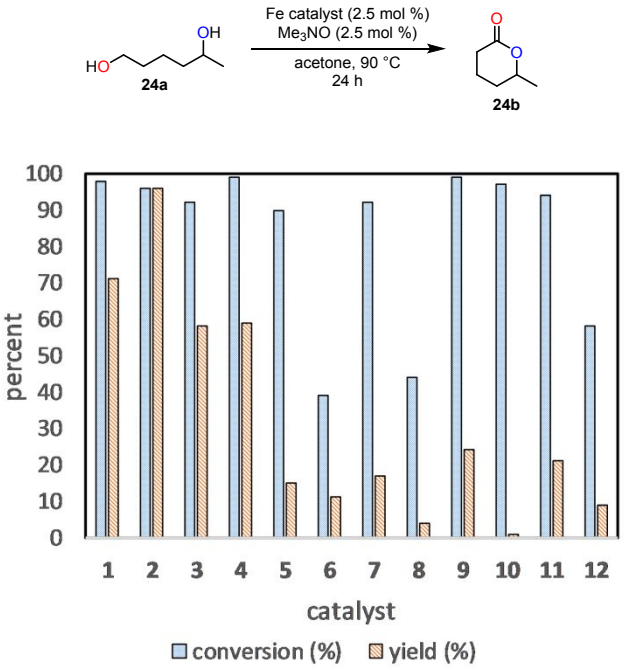


Figure 4. Lactonization of 1,5-hexanediol with (cyclopentadienone)iron tricarbonyl catalysts. Reaction conditions: 1,5-hexanediol (1 equiv, 0.5 M in acetone), Fe catalyst (0.025 equiv), anhydrous trimethylamine *N*-oxide (0.025 equiv), biphenyl (0.25 equiv), and acetone at 90 °C for 24 h in a sealed, thick-walled test tube. Diol conversion and lactone yield determined by gas chromatography relative to biphenyl.

Many of the catalyst systems that selectively form lactones from 1°/2° diols are also selective for the oxidation of primary alcohols over secondary alcohols.[14,18,34,35] (Cyclopentadienone)iron carbonyl compounds dehydrogenate secondary alcohols efficiently but afford low yields of aldehydes from primary alcohols when acetone is used as the hydrogen acceptor, presumably due to the disfavored equilibrium (eq. 1).[39,40,42,44] The selectivity of **1**–**4** for path 1 in Scheme 3 may be due to the sterically bulky TMS groups decreasing the rate of secondary alcohol dehydrogenation relative to primary alcohols and the irreversibility of the dehydrogenation leading to lactone formation. To gain insight into the origins of selectivity, lactol **26**[69] (as a mixture of stereoisomers) was treated with catalysts **2** and **10** under the established reaction conditions. One equivalent of isopropanol relative to **26** was added because it would be present in solution under normal conditions

after the dehydrogenation of the first alcohol. As shown in Figure 5, lactol **26** was converted into lactone **24b** with a small amount of ketone **27** and no detectable starting material with both catalysts. Alternatively, ketone **27** was the major product when diol **24a** was treated with tetraphenyl catalyst **10** (Scheme 3, path 2). These results are consistent with the initial oxidation of the diol acting as the selectivity-determining step, because once lactol **26** forms (from the oxidation of the primary alcohol of diol **24a**), it goes on to form lactone with both catalysts. As noted above, the bulky TMS groups on the 2- and 5-positions of the cyclopentadienone ring of **2** may decrease the rate of secondary alcohol oxidation and initially favor the oxidation of the primary alcohol (Scheme 3, path 1). As shown in Figure 5, the resulting lactol would then preferentially form lactone. With catalyst **10**, it is likely that lactol **26** does not form; instead, the secondary alcohol is oxidized directly to ketone **27**. The fact that a small amount of ketone **27** was present when both catalysts were used shows that lactol formation from the diol was reversible, but formation of lactone from lactol was favored.

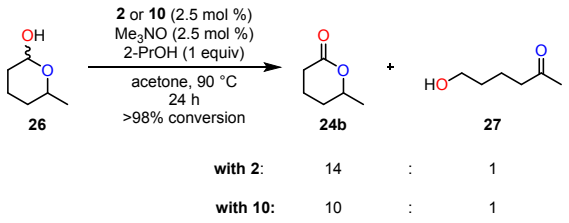
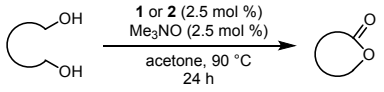


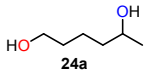
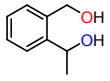
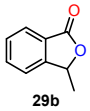
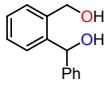
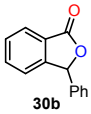
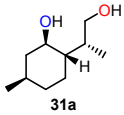
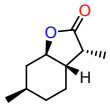
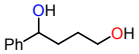
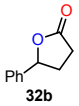
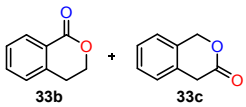
Figure 5. Dehydrogenation of lactol **26** to lactone **24b** with catalysts **2** and **10**.

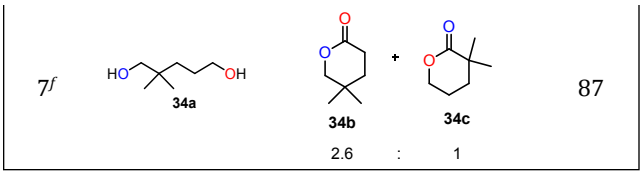
The activity and selectivity of catalysts **1** and **2** in the lactonization of other unsymmetrical diols were explored (Table 4). Lactonizations of diols with both primary and secondary alcohols using catalyst **2** remained selective for the lactone when both alcohols were either benzylic or aliphatic (Table 4, entries 1–4). When a diol with a secondary benzylic and primary aliphatic alcohol was dehydrogenated, the lactone (**32b**) was the major

product but the ketone from secondary alcohol oxidation also formed formed (Table 4, entry 5). Unsymmetrical diols bearing two primary alcohols were also dehydrogenated using **1**. Table 4, entry 6 illustrates that selectivity based on diol electronics was low when it contained both a benzylic and an aliphatic primary alcohol—only a slight excess of lactone from the initial dehydrogenation of the benzylic alcohol occurred. Steric hindrance close to one of the primary alcohols led to modest selectivity that favored the lactone formed by dehydrogenation of the less hindered alcohol (Table 4, entry 7). Catalyst systems based on Ru, W, Ir, and Cu all showed higher selectivity (>9:1) for **34b** over **34c** when using diol **34a**.[12,20,31–33]

Table 4. Unsymmetrical diols lactonized by **1** and **2**.[a]



entry	diol	lactone	yield (%)[b]
1	 **24a**	 **24b**	69[c]
2	 **29a**	 **29b**	86
3[d]	 **30a**	 **30b**	77
4[d]	 **31a**	 **31b**	88
5	 **32a**	 **32b**	72[e]
6[f]	 **33a**	 **33b** : **33c** 1.3 : 1	91



[a]Reaction conditions: unless otherwise noted, diol (1 equiv, 0.5 M in acetone), **2** (0.025 equiv), anhydrous trimethylamine *N*-oxide (0.025 equiv), and acetone at 90 °C for 24 h in a sealed, thick-walled test tube. [b]Isolated yields. [c]Isolated with small amounts of impurities, including **2**; see Experimental Section for details. [d]Catalyst **2** and trimethylamine *N*-oxide loadings of 0.04 equiv (4 mol %) were used. [e]The minor reaction product was 4-hydroxy-1-phenyl-1-butanone. [f]Catalyst **1** and trimethylamine *N*-oxide (2.5 mol % of both) were used.

Catalyst stability and active species. Cyclopentadienone structure dramatically affects catalyst activity, but the origin of the effect is not clear. A series of NMR experiments was performed to gain insight into catalyst structure under the reaction conditions (Figure 6). First, ^{1}H and ^{13}C NMR spectra were taken of solutions of **1**, trimethylamine *N*-oxide, and either diol **13a** or **14a** in a 1:1:5 molar ratio in acetone-d_6 at 80 °C. The solutions were held at 80 °C in the spectrometer for approximately 10–15 minutes before spectral data were collected. The reaction solutions were then cooled to 50 °C and additional spectra were taken.

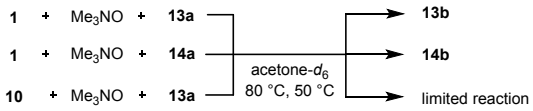


Figure 6. NMR experiments performed; catalyst:Me_3NO:diol ratio = 1:1:5.

Diol lactonization occurred at 80 °C with catalyst **1**; peaks corresponding to both lactone **13b** or **14b** were observed along with isopropanol-d_6. With **13a**, the ratio of diol to lactone **13b** was ~1:3; with **14a**, the diol:lactone ratio was 1.1:1. No signal from trimethylamine *N*-oxide (singlet at 3.16 ppm in acetone-d_6) was observed, which is consistent with it reacting rapidly with **1** to form unsaturated species **A**.[40] Alcohols are known to bind to **A**, but those compounds are only stable below room temperature.[70] There

was no evidence for alcohol-bound species for either **13a** or **14a** because no shift in the signals representing the HO-$\boldsymbol{CH_2}$ carbons or hydrogens were observed, which would occur upon binding to iron.

There were multiple peaks in the 0–0.4 ppm range of the ^{1}H NMR spectra indicating different types of TMS-containing species. The spectra at 80 °C had one major singlet at 0.27 ppm, and at 50 °C there was a second singlet at 0.28 ppm. These signals occurred in reactions with both **13a** and **14a**. There were also two sets of signals corresponding to the $(CH_2)_4$ ring on the cyclopentadienone of **1**: one set at approximately 2.65 ppm and 1.87 ppm, and a second set at 2.27 ppm and 1.61 ppm. The former are consistent with the spectrum of **1** in acetone-d_6. The only cyclopentadienone signals that appeared in the ^{13}C NMR spectrum at 80 °C also matched those found in **1**. The latter set of signals for the $(CH_2)_4$ hydrogens were shielded and had chemicals shifts similar to those found on the nitrile-ligated compound **4**.[42] A singlet at 2.62 ppm was present in all ^{1}H NMR spectra using **1**, but it was larger in the spectra at 50 °C relative to those taken at 80 °C. Additionally, the peak at 1.1 ppm in the ^{13}C NMR spectra was also larger at 50 °C. Finally, a small signal at 105 ppm in the ^{13}C NMR spectrum of the reaction with **13a** at 50 °C appeared and was consistent with the spectrum of the iron-bound cyclopentadienone in **4**.[42] Together, these signals have been assigned to the trimethylamine-ligated compound **35** (Figure 7). Replacement of the strongly pi-accepting carbonyl ligand with an amine would be expected to have a similar electronic effect to substituting it with a nitrile ligand. The singlet at 2.62 ppm in the ^{1}H NMR spectrum was assigned to the methyl groups of the bound trimethylamine ligand, and the chemical shift was similar to those of the methyl groups in $[CpFe(CO)_2(NMe_3)]Tf_2N$.[71] At lower temperatures, the equilibrium favored the bound species **35** based on the relative heights of

the peak at 2.62 ppm at 50 °C and 80 °C. At higher temperatures, trimethylamine dissociated, giving less of compound **35**. A spectrum of **1**, trimethylamine *N*-oxide, and **13a** taken at room temperature—the solution was never heated—showed no lactone **13b**, no trimethylamine *N*-oxide, and a large singlet at 2.62, which is consistent with **35** forming in solution and being favored at lower temperatures. Trimethylamine is volatile, but these reactions were performed in sealed vessels where it was trapped.

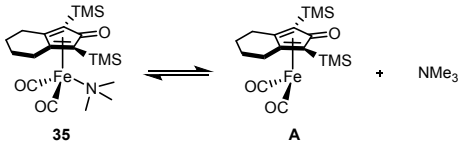


Figure 7. Proposed catalyst resting state **35** and its reversible dissociation of trimethylamine.

As noted above, multiple TMS signals appeared in the ^{1}H NMR spectra. In the ^{13}C NMR spectra, only three TMS signals appeared. While peaks corresponding to **1** and **35** were found, no peaks corresponding to the non-TMS atoms of the cyclopentadienone ligand on other species were present. Additionally, only one signal for CO ligands was observed in all ^{13}C NMR spectra and was assigned to **1**. In the ^{1}H NMR spectra of the reaction with **14a**, signals at –12 ppm were observed and are consistent with iron hydride **B** derived from **1** (Scheme 2), which has a chemical shift of –11.62 in C_6D_6.[45] Based on the integrations, there was only a small amount of iron hydride present at both 50 °C and 80 °C. While iron species other than **1**, **35**, and the iron hydride may be present during catalysis, they would need to be present in small quantities because of the lack of peaks in the NMR spectra. These studies are consistent with the cyclopentadienone retaining its hapticity and not dissociating when the CO ligand is removed by trimethylamine *N*-oxide, but they do not rule out the possibility of other catalytically active species forming in small amounts. The reaction of **13a** with $Fe(CO)_5$ (Table 3, entry 2) showed that the presence of cyclopentadienone is important for

catalytic activity, but the exact nature of how the cyclopentadienone is bound to the iron during catalysis is still unknown.

Attempts to do the same experiments with catalyst **10** were less successful (Figure 6). Upon heating an acetone-d_6 solution of **10**, trimethylamine *N*-oxide, and **13a** to 80 °C, almost no lactonization occurred and a precipitate formed, which caused dramatic peak broadening in the spectra. No trimethylamine *N*-oxide was present indicating that it had reacted with the iron compound, but no peaks similar to the trimethylamine-ligated iron compound **35** appeared. No iron hydrides were observed out to –30 ppm. Upon dilution, the precipitate dissolved, but the solution was too dilute to get a ^{13}C NMR spectrum where cyclopentadienone signals could be observed. It is important to note that no precipitate formed when the reaction was run under normal conditions (i.e., more dilute) in a sealed vessel. The main conclusion that can be drawn from this experiment is that the initial rate of the lactonization of **13a** with **10** is much slower than with **1**. Peak broadening due to precipitate formation limited the information available about cyclopentadienone coordination.

CONCLUSION

The catalytic activity of a series of (cyclopentadienone)iron carbonyl compounds in the dehydrogenative lactonization of diols was explored. Catalyst **1** and its acetonitrile-ligated derivative **4** were the most active in the lactonization of symmetrical diols, and catalyst **2** afforded lactones selectively from diols containing both 1° and 2° alcohols. Catalyst loadings between 2.5–5 mol % were discovered to be optimal. Five-, six-, and seven-membered ring lactones were formed, and no over-oxidations of primary alcohols were observed. The presence of two equivalents of isopropanol-d_6 in a diol lactonization supports

the proposed transfer dehydrogenation mechanism. The lactonizations of simple diols with catalysts **1** and **10** were observed by NMR spectroscopy, and reactions with **1** occurred significantly more quickly. The presence of trimethylamine-ligated iron compound **35** was proposed based on the spectral data, and its concentration decreased as the temperature increased. No analogous compound generated from **10** was observed, but peak broadening in the NMR spectra and the formation of a precipitate limited the amount of information that could be collected. (Cyclopentadienone)iron carbonyl compounds other than **2** reacted with 1°/2° diols, but only small amounts of lactone were detected. With catalysts **5**, **7**, **9**, **10**, and **12**, the major products arose from the oxidation of the secondary alcohol. Both of the most active catalysts contained trimethylsilyl groups in the 2- and 5-positions of their cyclopentadienone ligands; results from reactions with a lactol intermediate suggest these sterically bulky groups decrease the rate of secondary alcohol oxidation relative to primary alcohol oxidation and lead to the higher selectivity observed in the 1°/2° diols. Steric bulk around one of the alcohols in a diol with two primary alcohols led to the lactone where the least hindered primary alcohol was dehydrogenated as the major product, but the selectivity was modest. These results show that lactones derived from symmetrical diols and 1°/2° diols can be synthesized efficiently using air-stable (cyclopentadienone)iron carbonyl compounds and acetone as both the solvent and the hydrogen acceptor.

EXPERIMENTAL SECTION

General Information. All ^{1}H and ^{13}C NMR spectra were collected at ambient temperature at 400 MHz and 100 MHz, respectively. ^{13}C NMR spectra were proton decoupled. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), sextet

(sext), septet (sept), multiplet (m), and broad (br). Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Visualization was performed with UV light and/or phosphomolybdic acid stain. Flash column chromatography was performed using silica gel 60 (230-400 mesh). Reagent grade acetone was degassed by bubbling nitrogen through it for at least 15 minutes prior to use, but no attempts were made to dry it. All reactions were performed under a nitrogen atmosphere unless otherwise noted. All commercial chemicals were used as received. The following (cyclopentadienone)iron carbonyl compounds were prepared by known methods: **1–2**,[72,73] **3**,[73] **4**,[42] **5–6**,[74] **7**,[41] **8**,[75] **9–12.**[44] The following diols were prepared by known methods: racemic **17a** and **18a**,[76] **23a**,[77] **29a** and **33a**,[29] **30a** and **32a**,[26] **31a**,[78] **34a**.[79] Lactol **26** was prepared as a mixture of stereoisomers by DIBAL reduction of δ-hexalactone.[69,80]

General procedure for diol lactonization: A solution of diol (0.5 M in acetone), (cyclopentadienone)iron carbonyl compound, and anhydrous trimethylamine *N*-oxide in degassed acetone in a thick-walled, screw-top tube was placed in a 90 °C oil bath. After stirring for 24 hours, the reaction solution cooled to room temperature, the solvent was evaporated under reduced pressure, and the crude product was purified by flash chromatography.

Phthalide (14b). Following the general procedure, 1,2-benzendimethanol (**14a**) (198 mg, 1.43 mmol, 1 equiv), **1** (15 mg, 0.036 mmol, 0.025 equiv), and trimethylamine *N*-oxide (2.7 mg, 0.036 mmol, 0.025 equiv) in acetone (2.9 mL) afforded 177 mg (92%) of **14b** as a pale yellow solid after purification by flash chromatography (80% hexanes/20% ethyl acetate, R_f = 0.30). ^{1}H NMR ($CDCl_3$, ppm): δ 7.92 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.55 (d, J = 8.0

Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 5.34 (s, 2H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, ppm): δ 171.1, 146.6, 134.0, 129.0, 125.7, 122.2, 69.7. Spectral data matched those found in the literature.[20,81]

Dibenzo[c,e]oxepin-5(7H)-one (15b). Following the general procedure, 2,2'-biphenyldimethanol (**15a**) (307 mg, 1.43 mmol, 1 equiv), **1** (15 mg, 0.036 mmol, 0.025 equiv), and trimethylamine *N*-oxide (2.7 mg, 0.036 mmol, 0.025 equiv) in acetone (2.9 mL) afforded 261 mg (87%) of **15b** as a pale yellow solid after purification by flash chromatography (80% hexanes/20% ethyl acetate, R_f = 0.50). ^{1}H NMR ($CDCl_3$, ppm): δ 7.99 (d, *J* = 7.2 Hz, 1H), 7.70–7.61 (m, 3H), 7.57–7.51 (m, 2H), 7.48–7.42 (m, 2H), 5.02 (d, *J* = 23.2 Hz, 2H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, ppm): δ 170.3, 139.0, 137.3, 134.9, 132.6, 132.0, 130.7, 130.2, 128.74, 128.71, 128.6, 128.5, 69.2. Spectral data matched those found in the literature.[20]

3,4,7,7-Tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (16b). Following the general procedure, 5-norbornene-2-*endo*,3-*endo*-dimethanol (**16a**) (221 mg, 1.43 mmol, 1 equiv), **1** (15 mg, 0.036 mmol, 0.025 equiv), and trimethylamine *N*-oxide (2.7 mg, 0.036 mmol, 0.025 equiv) in acetone (2.9 mL) afforded 191 mg (89%) of **16b** as a colorless oil after purification by flash chromatography (80% hexanes/20% ethyl acetate, R_f = 0.29). ^{1}H NMR ($CDCl_3$, ppm): δ 6.32–6.27 (m, 2H), 4.29 (dd, *J* = 9.6, 8.4 Hz, 1H), 3.80 (dd, *J* = 3.2, 9.6 Hz, 1H), 3.33–3.36 (m, 1H), 3.26 (dd, *J* = 4.4, 9.2 Hz, 1H), 3.14–3.07 (m, 2H), 1.65 (dt, *J* = 1.6, 7.2 Hz, 1H), 1.47 (d, *J* = 8.4 Hz, 1H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, ppm): δ 178.1, 136.9, 134.4, 70.3, 51.8, 47.6, 46.1, 45.8, 40.3. Spectral data matched those found in the literature.[20]

***trans*-Hexahydroisobenzofuran-1(3H)-one (17b).** Following the general procedure, racemic **17a** (207 mg, 1.43 mmol, 1 equiv), **1** (15 mg, 0.036 mmol, 0.025 equiv), and

trimethylamine *N*-oxide (2.7 mg, 0.036 mmol, 0.025 equiv) in acetone (2.9 mL) afforded 190 mg (95%) of **17b** as a pale yellow oil after purification by flash chromatography (85% hexanes/15% ethyl acetate, R_f = 0.30). ^{1}H NMR ($CDCl_3$, ppm): δ 4.36 (dd, *J* = 6.4, 8.4 Hz, 1H), 3.85 (dd, *J* = 8.4, 10.8 Hz, 1H), 2.19–2.14 (m, 1H), 2.04–1.84 (m, 5H), 1.32–1.23 (m, 4H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 177.6, 72.2, 45.2, 43.6, 28.1, 25.5, 24.9, 24.8. Spectral data matched those found in the literature.[31]

***cis*-Hexahydroisobenzofuran-1(3H)-one (18b).** Following the general procedure, racemic **18a** (230 mg, 1.60 mmol, 1 equiv), **2** (32 mg, 0.080 mmol, 0.05 equiv), and trimethylamine *N*-oxide (6.0 mg, 0.080 mmol, 0.05 equiv) in acetone (3.2 mL) afforded 195 mg (87%) of **18b** as a pale yellow oil after purification by flash chromatography (85% hexanes/15% ethyl acetate, R_f = 0.30). ^{1}H NMR ($CDCl_3$, ppm): δ 4.20 (dd, *J* = 4.8, 8.8 Hz, 1H), 3.95 (d, *J* = 8.8 Hz, 1H), 2.66–2.62 (m, 1H), 2.50–2.43 (m, 1H), 2.14–2.10 (m, 1H), 1.85–1.81 (m, 1H), 1.67–1.59 (m, 3H), 1.30–1.18 (m, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 178.5, 71.8, 39.5, 35.4, 27.2, 23.4, 22.9, 22.5. Spectral data matched those found in the literature.[31]

1H,3H-Benzo[de]isochromen-1-one (19b). Following the general procedure, 1,8-naphthalenedimethanol (**19a**) (270 mg, 1.43 mmol, 1 equiv), **1** (30 mg, 0.072 mmol, 0.05 equiv), and trimethylamine *N*-oxide (5.4 mg, 0.072 mmol, 0.05 equiv) in acetone (2.9 mL) afforded 232 mg (88%) of **19b** as a pale yellow solid after purification by flash chromatography (85% hexanes/15% ethyl actate, R_f = 0.26). ^{1}H NMR ($CDCl_3$, ppm): δ 8.41 (dd, *J* = 0.8, 7.2 Hz, 1H), 8.12 (dd, *J* = 0.8, 8.0 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.67 (dd, *J* = 7.6, 8.0 Hz, 1H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.38 (dd, *J* = 1.2, 7.2 Hz, 1H), 5.84 (s, 2H). ^{13}C{^{1}H} NMR

(benzene-d_6, ppm): δ 163.1, 132.8, 132.1, 128.8, 128.5, 127.8, 126.5, 126.3, 126.2, 121.2, 121.1, 69.4. Spectral data matched those found in the literature.[29]

γ-Butyrolactone (20b). Following the general procedure, 1,4-butanediol (**20a**) (144 mg, 1.60 mmol), **1** (17 mg, 0.040 mmol, 0.025 equiv), and trimethylamine *N*-oxide (3 mg, 0.04 mmol, 0.025 equiv) in acetone (3.2 mL) afforded 119 mg (89 wt. % of **20b**; 77% yield) of a mixture of **20b** and **1** in a 40:1 ratio as a yellow oil after purification by flash chromatography on a 1.8 cm wide column with 7–8 cm of silica gel. Attempts to visualize **20b** on the TLC plate using standard stains ($KMnO_4$, anisaldehyde, vanillin, phosphomolybdic acid, ceric ammonium molybdate, and I_2) were unsuccessful, so it was purified by eluting with approximately 30 mL of 95% cyclohexane/5% MTBE until a yellow band came off, followed by elution with 100 mL of 40% cyclohexane/40% dichloromethane/20% MTBE. The 40/40/20 fraction was evaporated to afford **20b**, which contained small amounts of impurities. ^{1}H NMR ($CDCl_3$, ppm): δ 4.36 (t, J = 7.2 Hz, 2H), 2.51 (t, J = 8.0 Hz, 2H), 2.28 (quint, J = 7.6 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 177.8, 68.6, 27.8, 22.1. Spectral data matched those found in the literature.[20]

δ-Valerolactone (13b). Following the general procedure, 1,5-pentanediol (**13a**) (166 mg, 1.60 mmol), **1** (17 mg, 0.040 mmol, 0.025 equiv), and trimethylamine *N*-oxide (3 mg, 0.04 mmol, 0.025 equiv) in acetone (3.2 mL) afforded 144 mg (90%) of **13b** as a pale yellow solid after purification by flash chromatography on a 1.8 cm wide column with 7–8 cm of silica gel. Attempts to visualize **13b** on the TLC plate using standard stains ($KMnO_4$, anisaldehyde, vanillin, phosphomolybdic acid, ceric ammonium molybdate, and I_2) were unsuccessful, so it was purified by eluting with approximately 30 mL of 95% cyclohexane/5% MTBE until a yellow band came off, followed by elution with 100 mL of 40% cyclohexane/40%

dichloromethane/20% MTBE. The 40/40/20 fraction was evaporated to afford **13b**. ^{1}H NMR ($CDCl_3$, ppm): δ 4.35 (t, *J* = 6.0 Hz, 2H), 2.56 (t, *J* = 6.8 Hz, 2H), 1.96-1.83 (m, 4H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, ppm): δ 171.5, 69.5, 29.8, 22.3, 19.1. Spectral data matched those found in the literature.[20]

ε-Caprolactone (21b). Following the general procedure, 1,6-hexanediol (**21a**) (189 mg, 1.60 mmol), **1** (17 mg, 0.040 mmol, 0.025 equiv), and trimethylamine *N*-oxide (3 mg, 0.04 mmol, 0.025 equiv) in acetone (3.2 mL) afforded 42 mg (approximately 90 wt. % of **21b**; approximately 21% yield) of a mixture of **21b** and **1** in a 33:1 ratio (as well as other small impurities) as a yellow oil after purification by flash chromatography on a 1.8 cm wide column with 7–8 cm of silica gel. Attempts to visualize **21b** on the TLC plate using standard stains ($KMnO_4$, anisaldehyde, vanillin, phosphomolybdic acid, ceric ammonium molybdate, and I_2) were unsuccessful, so it was purified by eluting with approximately 30 mL of 95% cyclohexane/5% MTBE until a yellow band came off, followed by elution with 100 mL of 40% cyclohexane/40% dichloromethane/20% MTBE. The 40/40/20 fraction was evaporated to afford **21b**. ^{1}H NMR ($CDCl_3$, ppm): δ 4.23 (t, *J* = 4.8 Hz, 2H), 2.66-2.63 (m, 2H), 1.87-1.76 (m, 6H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, ppm): δ 176.2, 69.3, 34.6, 29.3, 29.0, 22.9. Spectral data matched those found in the literature.[20]

1,4-Dioxan-2-one (22b). Following the general procedure, diethylene glycol (**22a**) (148 mg, 1.39 mmol) and **4** (15 mg, 0.035 mmol, 0.025 equiv) in acetone (2.8 mL) afforded 49 mg (34%) of **22b** as a yellow oil after purification by flash chromatography on a 1.8 cm wide column with 7–8 cm of silica gel. Attempts to visualize **22b** on the TLC plate using standard stains ($KMnO_4$, anisaldehyde, vanillin, phosphomolybdic acid, ceric ammonium molybdate, and I_2) were unsuccessful, so it was purified by eluting with approximately 30 mL of 95%

cyclohexane/5% MTBE until a yellow band came off, followed by elution with 100 mL of 40% cyclohexane/40% dichloromethane/20% MTBE. The 40/40/20 fraction was evaporated to afford **22b**. ^{1}H NMR ($CDCl_3$, ppm): δ 4.50 (t, *J* = 4.8 Hz, 2H), 4.37 (s, 2H), 3.88 (t, *J* = 4.8 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 166.6, 68.6, 66.3, 62.6. Spectral data matched those found in the literature.[20]

***tert*-Butyl 2-oxomorpholine-4-carboxylate (23b).** Following the general procedure, **23a** (285 mg, 1.39 mmol) and **4** (15 mg, 0.035 mmol, 0.025 equiv) in acetone (2.8 mL) afforded 107 mg (38%) of **23b** as a light yellow, waxy solid after purification by flash chromatography on a 1.8 cm wide column with 7–8 cm of silica gel. Attempts to visualize **23b** on the TLC plate using standard stains ($KMnO_4$, anisaldehyde, vanillin, phosphomolybdic acid, ceric ammonium molybdate, and I_2) were unsuccessful, so it was purified by eluting with approximately 30 mL of 95% cyclohexane/5% MTBE until a yellow band came off, followed by elution with 100 mL of 40% cyclohexane/40% dichloromethane/20% MTBE. The 40/40/20 fraction was evaporated to afford **23b**. ^{1}H NMR ($CDCl_3$, ppm): δ 4.42 (br t, *J* = 4.4 Hz, 2H), 4.25 (s, 2H), 3.65 (t, *J* = 5.2 Hz, 2H), 1.48 (s, 9H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 153.5, 81.3, 67.5 (br), 46.0 (br), 39.8 (br), 28.3; the lactone carbonyl carbon was lost in the baseline. Spectral data matched those found in the literature.[20]

δ-Hexalactone (24b). Following the general procedure, 1,5-hexanediol (**24a**) (189 mg, 1.60 mmol), **2** (16 mg, 0.040 mmol, 0.025 equiv), and trimethylamine *N*-oxide (3 mg, 0.04 mmol, 0.25 equiv) in acetone (3.2 mL) afforded 150 mg (87 wt. % **24b**, 69% yield) of a 42/2.8/1 mixture of **24b**, 6-hydroxy-2-hexanone (**27**), and **1** as a yellow oil after purification by flash chromatography on a 1.8 cm wide column with 7–8 cm of silica gel. Attempts to visualize **24b** on the TLC plate using standard stains ($KMnO_4$, anisaldehyde, vanillin,

phosphomolybdic acid, ceric ammonium molybdate, and I_2) were unsuccessful, so it was purified by eluting with approximately 30 mL of 95% cyclohexane/5% MTBE until a yellow band came off, followed by elution with 100 mL of 40% cyclohexane/40% dichloromethane/20% MTBE. The 40/40/20 fraction was evaporated to afford **24b**, which contained small amounts of impurities. ^{1}H NMR ($CDCl_3$, ppm): δ 4.50-4.40 (m, 1H), 2.62-2.52 (m, 1H), 2.40-2.50 (m, 1H), 1.82-1.98 (m, 3H), 1.49-1.59 (m, 1H), 1.38 (d, *J* = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 171.9, 76.9, 29.5, 29.2, 21.7, 18.5. Spectral data matched those found in the literature.[20]

3-Methylisobenzofuran-1(3H)-one (29b). Following the general procedure, **29a** (226 mg, 1.48 mmol, 1 equiv), **2** (15 mg, 0.037 mmol, 0.025 equiv), and trimethylamine *N*-oxide (2.8 mg, 0.037 mmol, 0.025 equiv) in acetone (3.0 mL) afforded 189 mg (86%) of **29b** as a colorless oil after purification by flash chromatography (80% hexanes/20% ethyl acetate, R_f = 0.30). ^{1}H NMR ($CDCl_3$, ppm): δ 7.90 (d, *J* = 7.6 Hz, 1H), 7.68 (td, *J* = 1.2, 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.45 (dd, *J* = 0.4, 7.6 Hz, 1H), 5.57 (q, *J* = 6.4 Hz, 1H), 1.65 (d, *J* = 6.4, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 170.5, 151.2, 134.1, 129.1, 125.74, 125.65, 121.6, 77.8, 20.4. Spectral data matched those found in the literature.[20]

3-Phenylisobenzofuran-1(3H)-one (30b). Following the general procedure, **30a** (285 mg, 1.33 mmol, 1 equiv), **2** (22 mg, 0.053 mmol, 0.04 equiv), and trimethylamine *N*-oxide (4.0 mg, 0.053 mmol, 0.04 equiv) in acetone (2.7 mL) afforded 216 mg (77%) of **30b** as a pale yellow solid after purification by flash chromatography (85% hexanes/15% ethyl acetate, R_f = 0.30).^{1}H NMR ($CDCl_3$, ppm): δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.65 (td, *J* = 0.8, 7.6 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.40–7.33 (m, 4H), 7.29-7.27 (m, 2H), 6.41 (s, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm):

δ 170.5, 149.7, 136.4, 134.4, 129.4, 129.3, 129.0, 127.0, 125.64, 125.59, 122.9, 82.7. Spectral data matched those found in the literature.[82]

(3R,3aS,6R,7aR)-3,6-Dimethylhexahydrobenzofuran-2(3H)-one (31b). Following the general procedure, **31a** (250 mg, 1.45 mmol, 1 equiv), **2** (23.5 mg, 0.058 mmol, 0.04 equiv), and trimethylamine *N*-oxide (4.4 mg, 0.058 mmol, 0.04 equiv) in acetone (2.9 mL) afforded 214 mg (88%) of **31b** as a colorless oil after purification by flash chromatography (87% hexanes/13% ethyl acetate, R_f = 0.37). ^{1}H NMR ($CDCl_3$, ppm): δ 4.00 (td, *J* = 3.6, 11.2 Hz, 1H), 2.64 (quint, *J* = 7.6 Hz, 1H), 2.25 (dt, *J* = 3.6, 11.2 Hz, 1H), 1.98–1.89 (m, 1H), 1.83–1.74 (m, 2H), 1.66–1.53 (m, 1H), 1.38–1.20 (m, 2H), 1.15 (d, *J* = 7.6 Hz, 3H), 1.11–1.04 (m, 1H), 1.02 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 180.3, 81.4, 47.1, 38.7, 34.2, 31.3, 23.8, 22.0, 9.6. Note that two peaks in the ^{13}C NMR spectrum are overlapping at 38.7 ppm, which is consistent with reports of two peaks with almost identical chemical shifts.[20,83]

5-Phenyldihydrofuran-2(3H)-one (32b). Following the general procedure, **32a** (266 mg, 1.60 mmol, 1 equiv), **2** (16 mg, 0.040 mmol, 0.025 equiv), and trimethylamine *N*-oxide (3 mg, 0.04 mmol, 0.025 equiv) in acetone (3.2 mL) afforded 187 mg (72%) of **32b** as a pale yellow oil after purification by flash chromatography (75% cyclohexane/25% ethyl acetate, R_f = 0.34). ^{1}H NMR ($CDCl_3$, ppm): δ 7.40-7.31 (m, 5H), 5.50 (dd, *J* = 6.4, 8.0 Hz, 1H), 2.70-2.61 (m, 3H), 2.24-2.12 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 177.0, 139.4, 128.8, 128.5, 125.3, 81.3, 31.0, 29.0. Spectral data matched those found in the literature.[84]

Isochroman-1-one (33b) and isochroman-3-one (33c). Following the general procedure, **33a** (243 mg, 1.60 mmol, 1 equiv), **1** (16.7 mg, 0.040 mmol, 0.025 equiv), and trimethylamine *N*-oxide (3.0 mg, 0.040 mmol, 0.025 equiv) in acetone (3.2 mL) afforded 216 mg (91%) of a 1.3:1 mixture of **33b** and **33c**, respectively, as a colorless oil after purification by flash

chromatography (80% cyclohexane/20% ethyl acetate, R_f = 0.26; both compounds had the same R_f value). Spectral data for **33b** and **33c**: ^{1}H NMR ($CDCl_3$, ppm): δ 8.08 (dd, *J* = 1.2, 8.0 Hz, 1H, **33b**), 7.54 (td, *J* = 1.6, 7.6 Hz, 1H, **33b**), 7.41-7.21 (m, 6H, **33b** and **33c**), 5.31 (s, 2H, **33c**), 4.53 (t, *J* = 6.0 Hz, 2H, **33b**), 3.71 (s, 2H, **33c**), 3.06 (t, *J* = 6.0 Hz, 2H, **33b**). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 170.8, 165.2, 139.6, 133.7, 131.6, 131.0, 130.3, 128.8, 127.7, 127.4, 127.3, 127.1, 125.3, 124.7, 70.1, 67.3, 36.2, 27.8. Spectral data matched literature values for **33b**[85] and **33c**.[86]

5,5-Dimethyltetrahydro-2H-pyran-2-one (34b) and 3,3-dimethyltetrahydro-2H-pyran-2-one (34c). Following the general procedure, **34a** (212 mg, 1.60 mmol, 1 equiv), **1** (16.8 mg, 0.040 mmol, 0.025 equiv), and trimethylamine *N*-oxide (3.0 mg, 0.040 mmol, 0.025 equiv) in acetone (3.2 mL) afforded 179 mg (87%) of a 2.6:1 mixture of **34b** and **34c**, respectively, as a colorless oil after purification by flash chromatography (20% hexanes, 80% ethyl acetate, R_f = 0.25). Spectral data for **34b**: ^{1}H NMR ($CDCl_3$, ppm): δ 3.98 (s, 2H), 2.56 (t, *J* = 7.6 Hz, 2H), 1.70 (t, *J* = 7.6 Hz, 2H), 1.06 (s, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 171.4, 78.7, 32.9, 29.4, 27.3, 24.8. Spectral data for **34c**: ^{1}H NMR ($CDCl_3$, ppm): δ 4.35 (t, *J* = 5.6 Hz, 2H), 1.94–1.88 (m, 2H), 1.78–1.75 (m, 2H), 1.31 (s, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, ppm): δ 177.1, 70.6, 38.7, 35.1, 27.8, 20.6. Spectral data for **34b**[20] and **34c**[12] matched those found in the literature.

Evidence of transfer dehydrogenation mechanism (Figure 3). A solution of 1,2-benzenedimethanol **14a** (207 mg, 1.50 mmol), **1** (15.7 mg, 0.0375 mmol), and anhydrous trimethylamine *N*-oxide (2.8 mg, 0.038 mmol) in 3.0 mL of degassed acetone-d_6 was stirred at 90 °C for 24 h in a sealed, thick-walled test tube. After cooling to rt, the yellow reaction solution was filtered through celite, and a ^{1}H NMR spectrum was taken of 0.7 mL of the

filtrate. The integrals of the signals corresponding to phthalide **14b** (s, 5.38 ppm, CH_2), unreacted **14a** (s, 4.69 ppm, 2 x CH_2), and isopropanol-d_6 (s, 3.87 ppm, CH) were used to determine that 92% of **14b** formed and the **14b** to isopropanol-d_6 ratio was 1:2.

Dehydrogenation of lactol 26 (Figure 5). A 50 μL aliquot of a solution of lactol **26** (185 mg, 1.60 mmol) and biphenyl (62 mg, 0.40 mmol; internal standard) in 3.2 mL of acetone was taken, the solvent was removed by evaporation, and a ^{1}H NMR spectrum labeled "time 0" was collected. Catalyst **2** or **10** (0.04 mmol), isopropanol (96 mg, 0.12 mL, 1.6 mmol), and anhydrous trimethylamine *N*-oxide (3.0 mg, 0.04 mmol) were added to the remaining solution, the thick-walled test tube was sealed with a PTFE cap, and it was stirred at 90 °C. After 24 h, 0.2 mL of the reaction solution was added to 1 mL of cyclohexane. The resulting solution was added to a glass pipet half filled with silica gel, and it was eluted with 4 mL of ethyl acetate. The filtrate from the pipet column was evaporated under reduced pressure, and a ^{1}H NMR spectrum ($CDCl_3$) was taken. The integrals of the signals corresponding to lactone **24b** (m, 4.46–4.42 ppm, CH) and ketone **27** (t, 3.63 ppm, CH_2) were used to determine the relative amounts of the two compounds.

NMR experiment with 1 and 13a at rt. A solution of **1** (25 mg, 0.060 mmol), trimethylamine *N*-oxide (4.5 mg, 0.060 mmol), and 1,5-pentanediol (**13a**) (12.4 mg, 0.12 mmol) in 1 mL of acetone-d_6 was stirred at room temperature under nitrogen for 5 minutes. The solution was transferred to a screw-cap NMR tube under nitrogen, and ^{1}H and ^{13}C NMR spectra were collected.

NMR experiment with 1 and 13a at elevated temperature. A solution of **1** (60 mg, 0.143 mmol), trimethylamine *N*-oxide (10.8 mg, 0.143 mmol), and 1,5-pentanediol (**13a**) (74.7 mg, 0.72 mmol) in 1 mL of acetone-d_6 was stirred at room temperature under nitrogen for 5

minutes. The orange solution was transferred to a J. Young NMR under nitrogen, sealed, and placed in the NMR spectrometer, which had been preheated to 80 °C. After approximately 10–15 minutes, ^{1}H and ^{13}C NMR spectra were collected. The temperature of the probe was changed to 50 °C, and ^{1}H and ^{13}C NMR spectra were collected again.

NMR experiment with 1 and 14a at elevated temperature. A solution of **1** (25 mg, 0.060 mmol), trimethylamine *N*-oxide (4.5 mg, 0.060 mmol), and 1,2-benzenedimethanol (**14a**) (41.3 mg, 0.30 mmol) in 0.75 mL of acetone-d_6 was stirred at room temperature under nitrogen for 5 minutes. The orange solution was transferred to a J. Young NMR under nitrogen, sealed, and placed in the NMR spectrometer, which had been preheated to 80 °C. After approximately 10–15 minutes, a ^{1}H NMR spectrum was collected. The temperature of the probe was changed to 50 °C, and another ^{1}H NMR spectrum was collected.

NMR experiment with 10 and 13a at elevated temperature. A solution of **10** (75 mg, 0.143 mmol), trimethylamine *N*-oxide (10.8 mg, 0.143 mmol), and 1,5-pentanediol (**13a**) (74.7 mg, 0.72 mmol) in 0.75 mL of acetone-d_6 was stirred at room temperature under nitrogen for 5 minutes. The orange solution was transferred to a J. Young NMR under nitrogen, sealed, and placed in the NMR spectrometer, which had been preheated to 80 °C. After approximately 10 minutes, ^{1}H and ^{13}C NMR spectra were collected. The temperature of the probe was changed to 50 °C and ^{1}H and ^{13}C NMR spectra were taken again, but the peaks were very broad and a precipitate was present in the tube. Attempts to take more spectra at 80 °C were unsuccessful due to peak broadening.

ASSOCIATED CONTENT

NMR spectra for all isolated lactones

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Notes

The authors declare no competing financial interest.

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