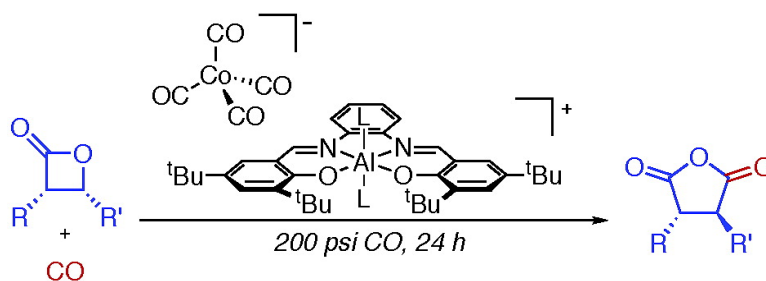## Communication

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Catalytic Carbonylation of β-Lactones to Succinic Anhydrides

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Due to the many uses of succinic anhydrides in organic and polymer chemistry,[1−3] the development of new synthetic routes to these versatile intermediates is an important scientific challenge. Succinic anhydrides and their derivatives have been synthesized by a variety of methods;[4−6] enantiomerically pure derivatives are accessible from either desymmetrization of meso succinic anhydrides or kinetic resolution of monosubstituted succinic anhydrides.[7]

Transition-metal-mediated ring expansive carbonylations have been used to produce a wide variety of heterocycles, including β-lactones,[8,9] β-lactams,[8b,10] and γ-lactones,[11] among others.[12] Mori and Tsuji have reported the carbonylation of β-propiolactone using $Co_2(CO)_8$ under harsh reaction conditions (1500 psi CO, 150 °C), giving a mixture of succinic anhydride and acrylic acid in relatively low yield.[13] In related chemistry, α-lactams have been carbonylated to give azetidine-2,4-diones,[14] styrene oxides have been doubly carbonylated to yield 3-hydroxy-2-oxo-4-phenyl-2,5-dihydrofurans,[15] and cyclic anhydrides have been decarbonylated to give β-substituted carboxylic acids.[16]

We recently reported the carbonylation of epoxides to β-lactones using a variety of discrete catalysts composed of a Lewis-acidic cation and the cobalt tetracarbonyl anion.[8] While investigating the carbonylation of *trans*-2,3-epoxybutane (**1**)[8b,e] using complex **2**, we purified the expected product, *cis*-2,3-dimethyl-β-propiolactone **3**, by distillation from the crude reaction mixture (Figure 1). Unexpectedly, a few small droplets of high-boiling material, left for some time to cool in the distillation apparatus, formed colorless crystals that contained carbonyl absorptions in the IR spectrum inconsistent with a β-lactone product.[17] X-ray crystallography unambiguously established the material as *trans*-2,3-dimethylsuccinic anhydride (**4**), the product of the unprecedented double carbonylation of *trans*-epoxide **1**, presumably via the β-lactone intermediate. This discovery was followed by initial experiments confirming the catalytic production of methylsuccinic anhydride from β-butyrolactone. Subsequent experiments revealed that the rate of β-lactone carbonylation increased in toluene and decreased in donor solvents such as ethers and esters. Since toluene slowed epoxide carbonylation, relative to donor solvents, we chose to study lactone carbonylation prior to attempting optimization of epoxide double carbonylation. Reported herein is the catalytic carbonylation of β-lactones to succinic anhydrides, as well as carbonylation of the related four-membered heterocycle oxetane.

Given recent advances in catalytic, stereoselective production of β-lactones,[8a−c,18] the carbonylation of these lactones to form succinic anhydrides is more than a serendipitous discovery—it is a potentially viable route to succinic anhydrides and their derivatives. We propose that the mechanism of this reaction (Scheme 1) is analogous to epoxide carbonylation.[8a,b] After the Lewis acid $[L_nAl]^+$ coordinates and activates the β-lactone, nucleophilic attack by $[Co(CO)_4]^-$ at the β-carbon of the lactone, with inversion, yields ring-opened species **B**. Migratory insertion of CO gives the aluminum carboxylate/cobalt acyl **C**. Intramolecular nucleophilic
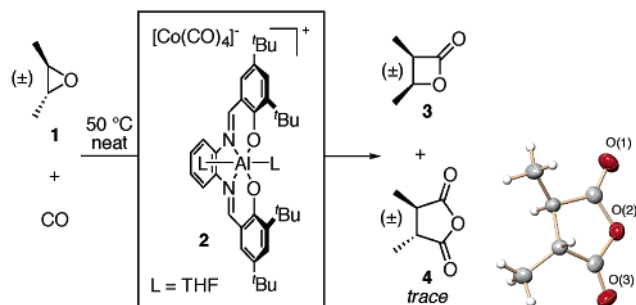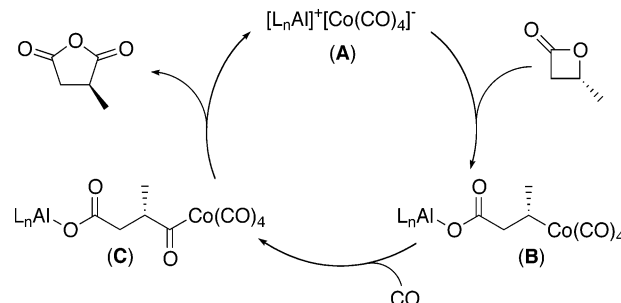

Figure 1. Epoxide double carbonylation by **2** and X-ray structure of **4**.

Scheme 1. Proposed Mechanism of β-Lactone Carbonylation

attack of the carboxylate on the acyl leads to anhydride formation and regeneration of **A** to complete the catalytic cycle.

Catalyst loadings were systematically varied in order to achieve yields of 90% or greater in 24 h (Table 1). In toluene at 80 °C, β-butyrolactone is converted to methylsuccinic anhydride at low loadings (0.45 mol %) of **2** (entry 1). There are no side products detected in this reaction, and it may be run longer than the time required for full conversion without detrimental effects. When (R)-β-butyrolactone is subjected to similar reaction conditions, (S)-methylsuccinic anhydride is produced (entry 2), consistent with our proposed mechanism. At 80 °C, however, some racemization occurs. We believe this is a function of the catalyst acting on the product; when independently prepared, enantiomerically pure (S)-methylsuccinic anhydride (**5**) was subjected to the reaction conditions (0.55 mol % **2**), partial racemization occurred (eq 1). At lower temperature (55 °C), (R)-β-butyrolactone is converted to (S)-methylsuccinic anhydride with 99% retention of enantiomeric purity (entry 3). Confirming our initial discovery, *cis*-β-lactone **3** is cleanly carbonylated to yield the *trans* anhydride **4** at 50 °C (entry 4).
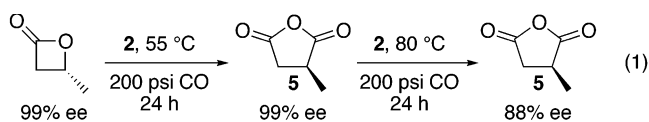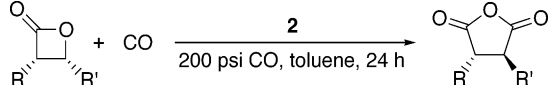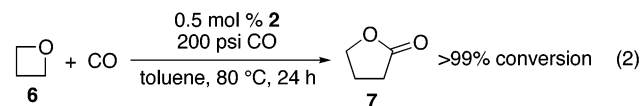
Table 1. Carbonylation of β-Lactones

entry	R	R′	T (°C)	lactone/catalyst[a]	yield[b] (%)
1	H	Me	80	220	95
2[c]	H	(R)-Me[e]	80	180	95
3[d]	H	(R)-Me[e]	55	110	94
4	Me	cis-Me	50	50	96
5	H	Et	80	120	93
6	H	$(CH_2)_9CH_3$	80	50	>99
7	H	CH_2O^nBu	80	50	90
8	H	$CH_2OSi(^tBu)Me_2$	80	20	97
9	H	$(CH_2)_2CH{=}CH_2$	80	20	90
10	H	H	24	300	98

[a] All reactions run in toluene (1.8 M lactone). [b] Anhydride yield determined from the ^1H NMR spectrum of reaction mixture; no other products detected. [c] Product is (S)-methylsuccinic anhydride, 95% ee (GC). [d] Product is (S)-methylsuccinic anhydride, 99% ee (GC). [e] Starting material is >99% ee (GC).

Lactones with bulkier substituents, such as ethyl and decyl, at the β-position are also converted to the corresponding anhydrides (entries 5 and 6). These substrates are generally slower to react and thus require higher catalyst loadings to reach the desired conversion in 24 h. Alkyl ether substitution is tolerated (entry 7), as is bulky, synthetically modifiable substitution such as a *tert*-butyldimethylsilyl ether (entry 8). Also synthetically useful is olefinic substitution (entry 9), which is tolerated. When unsubstituted at the β-position, the substrate is dramatically more reactive. For example, carbonylation of β-propiolactone reaches high conversion at the lowest catalyst loading, despite also being run at the lowest temperature (entry 10). This striking increase in reactivity as a function of decreased steric hindrance is consistent with the proposed nucleophilic attack on the β-carbon of the lactone (Scheme 1).

The carbonylation of thietanes and oxetanes to produce γ-lactones using other catalysts has been studied.[11b] When subjected to carbonylation in the presence of **2**, oxetane (**6**) is cleanly and selectively converted to γ-butyrolactone (**7**) (eq 2).

In summary, we have discovered that complex **2** is effective for the selective and efficient carbonylation of β-lactones to produce succinic anhydrides. As with epoxide carbonylation, we propose that other complexes of the general form [Lewis acid]⁺[metal carbonyl]⁻ have the potential to catalyze this carbonylation. The reaction rate is strongly dependent on the sterics of substitution at the β-carbon of the lactone, and the reaction proceeds with clean inversion of stereochemistry at this site. These data are consistent with nucleophilic attack by $[Co(CO)_4]^-$ at the β-carbon of the lactone. This discovery adds to a portfolio of single carbon heterocycle expansions, and we anticipate it will find broad utility in many areas of polymer and organic synthesis.

Supporting Information Available: General experimental procedures, spectral data for all new compounds, and X-ray data for **4** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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