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Synthesis of β-Lactones: A Highly Active and Selective Catalyst for Epoxide Carbonylation

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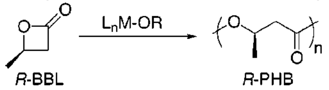
Poly((*R*)-β-hydroxybutyrate) (*R*-PHB, Scheme 1), a thermoplastic polyester found naturally in some bacteria, shares many of the physical and mechanical properties of poly(propylene) with the added feature of biodegradability.[1] Despite proven properties and ready applications, industrial production of *R*-PHB as a bulk polymer using biological methods has, to date, proven economically nonviable.[2] Potential alternate synthetic routes to this promising polymer include Baeyer−Villiger oxidation of an isotactic propylene/carbon monoxide copolymer,[3] asymmetric hydrogenation of the unsaturated polyester from ring opening polymerization (ROP) of ketene dimer[4] and ROP of (*R*)-β-butyrolactone[1a,5] (*R*-BBL, Scheme 1). While the first two routes involve postpolymerization modification of a polymer backbone, a difficult and unreliable task, the third uses the proven technology of lactone polymerization. Unfortunately *R*-BBL is not a readily available commodity[6,7] such as is required for polymer production.

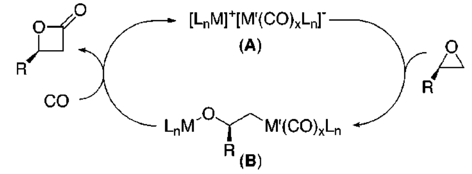
Scheme 1. Poly((*R*)-β-hydroxybutyrate) from (*R*)-β-Butyrolactone



R-BBL has been made from ketene and acetaldehyde,[8] from *rac*-BBL by enzymatic kinetic resolution,[9] and from the dimer of ketene via asymmetric hydrogenation.[10] The first two routes suffer chronically low ee's and yields, respectively, with hydrogenation showing the greatest promise of the three. A fourth approach is the catalytic synthesis of *R*-BBL from the cheap and abundant feedstocks, propylene oxide and carbon monoxide.[11,12] Herein we report discrete cationic Lewis-acid complexes of $Co(CO)_4^-$ that exhibit unprecedented activity and selectivity for epoxide carbonylation. Application of these catalysts with a variety of substrates is also addressed.

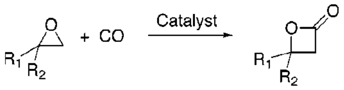
Although metal complexes have been reported for the carbonylation of epoxides, yields and selectivities are typically low.[13] Mixtures of dicobalt octacarbonyl [$Co_2(CO)_8$] and hydroxy-substituted pyridines are catalytically active for the carbonylation of a variety of simple epoxides (such as ethylene and propylene oxide) to produce mixtures of lactones and polyester oligomers, the ratio of which is dependent on reaction conditions employed.[14−16] It is established that neutral donor ligands (L) and [$Co_2(CO)_8$], engage in an equilibrium with $[L_2Co(CO)_3]^+[Co(CO)_4]^-$,[17] and we believe this ion pair is active in the epoxide carbonylation chemistry. In the proposed catalytic cycle (Scheme 2) we envision epoxide coordination and activation by a Lewis-acidic cation. Backside attack by $Co(CO)_4^-$ on the less hindered carbon would give the ring-opened species **B**.[18] Insertion of CO, ring extrusion and recoordination of CO to M′ complete the catalytic cycle. As a proposed mechanism it has been an important intellectual framework in our catalyst design process (vide infra). Alper and coworkers have recently demonstrated that the mixture $[Ph_3P{=}N{=}PPh_3]^+[Co(CO)_4]^-/BF_3{\bullet}Et_2O$ is effective for the carbonylation of epoxides (Table 1, entry 1), and it exhibits improved selectivity over $Co_2(CO)_8$ based catalysts.[15]

Scheme 2. Proposed Mechanism of Epoxide Carbonylation



Given the great strength of CO as a ligand for electron-rich late transition metals and the vital role of the anion in epoxide carbonylation[19] we looked to modification of the cation for mediation of catalytic activity. Our investigation of simple nonmetallic cations such as $^nBu_4N^+$ and Ph_4P^+, in combination with $Co(CO)_4^-$ anions, found them inactive for reaction of CO and propylene oxide (entries 2, 3). Under the premise that the cation must activate the epoxide we looked to metal-based cations. Although the simple complex [Na][$Co(CO)_4$] slowly produces 6% BBL from CO/propylene oxide (entry 4), it also produces an equal amount of acetone[20] as well as 40% PHB oligomers (2 mol % Co, 16 h). The complex [Cp_2Co][$Co(CO)_4$] was inactive for propylene oxide carbonylation (entry 5). Assuming that the inactivity of this complex was due to the coordinatively saturated 18e⁻ Cp_2Co^+ cation, we turned to oxophilic cations capable of ether coordination. Aluminum−salen complexes were chosen as they are easy to prepare and modify[21] and have previously shown activity as Lewis-acid catalysts.[22]

Table 1. Carbonylation of Epoxides



entry	catalyst	R_1	R_2	time (h)	yield (%)[d]
1	$[PPN][Co(CO)_4]/BF_3.Et_2O$[a]	H	Me	24	77[e]
2	$[^nBu_4N][Co(CO)_4]$[b]	H	Me	16	0
3	$[Ph_4P][Co(CO)_4]$[b]	H	Me	16	0
4	$[Na][Co(CO)_4]$[b]	H	Me	16	6[f]
5	$[Cp_2Co][Co(CO)_4]$[b]	H	Me	16	0
6	**1**[c]	H	Me	1	95
7	**1**[c]	H	(*R*)-Me	1	95[g]
8	**1**[c]	H	Et	2.5	>99
9	**1**[c]	H	CH_2Cl	9.5	73
10	**1**[c]	Me	Me	1	83[h]

[a] Reference 15; [PPN] = $[Ph_3P{=}N{=}PPh_3]^+$; 1 mol % Co, 900 psi, 80 °C, DME. [b] 2 mol % Co, 1000 psi, 80 °C, triglyme. [c] 1 mol % Co, 880 psi, 50 °C, neat substrate. [d] Determined by ^1H NMR for entries 2−10. [e] Reference 15; some α-methyl-β-propiolactone also produced. [f] Acetone (6%) and oligomers (40%) also produced. [g] Product = *R*-BBL [h] α,α-Dimethyl-β-propiolactone (7%) also produced.

The complex [(salph)Al$(THF)_2$][$Co(CO)_4$] (**1**; Figure 1) is prepared from the corresponding (salph)AlCl and $NaCo(CO)_4$. The highly crystalline ruby-red product, which has been fully characterized by NMR, IR, and X-ray crystallography, is isolated in 93%

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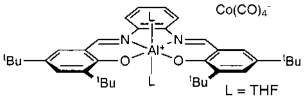
yield and is stable for prolonged periods under nitrogen. The X-ray structure of **1** reveals axially bound THF molecules in lieu of the ion-separated $Co(CO)_4^-$ anion, testament to its ability to coordinate cyclic ethers.



[(salph)Al(THF)$_2$][Co(CO)$_4$]; **1**

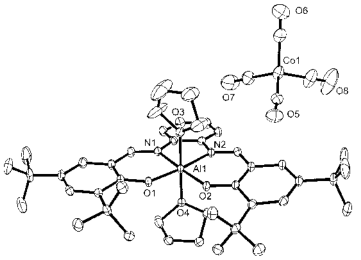


Figure 1. Structure of [(salph)Al(THF)$_2$][Co(CO)$_4$] (**1**) with displacement ellipsoids drawn at 40% probability.

Complex **1** carbonylates propylene oxide to 95% conversion in 1 h (entry 6). Although prior reported systems produce significant levels of α-methyl-*β*-propiolactone isomers, acetone and polymeric side-products in the carbonylation of propylene oxide, we observe only BBL. Since *R*-BBL is of particular interest for *R*-PHB synthesis, we investigated the use of (*R*)-propylene oxide, readily available through Jacobsen's hydrolytic kinetic resolution.[23] (*R*)-Propylene oxide is converted to *R*-BBL with >98% retention of configuration (entry 7).[24] The poly(hydroxyalkanoate) random copolymer composed of methyl and ethyl side chains is more easily processed than (*R*)-PHB;[1a] thus, an important feature of **1** is that it carbonylates 1-butene oxide to >99% conversion in 2.5 h (entry 8). This catalyst can also be used to carbonylate epichlorohydrin to 73% conversion in 9.5 h (entry 9).

The carbonylation of isobutylene oxide reaches 90% conversion in 1 h, producing a mixture of the two possible regioisomers (entry 10), suggesting different reaction pathways. We propose the primary sequence to involve nucleophilic attack of the activated epoxide at the less hindered site by $Co(CO)_4^-$ to give a *β*-substituted lactone. We believe the other could involve the cationic ring-opening of the epoxide by Lewis-acidic $[(salph)Al]^+$. Subsequent trapping of the more stable tertiary cation by $Co(CO)_4^-$ leads to the α-substituted lactone.

In summary, complex **1** exhibits unprecedented activity and selectivity for the carbonylation of a variety of epoxides. As opposed to previous epoxide carbonylation systems this one is composed of a discrete complex, which will facilitate future mechanistic studies. Furthermore the reactions may be run neat in substrate which reduces waste and facilitates purification.[25] Given the epoxide carbonylations presented here we believe catalysts of the general form $[\text{Lewis acid}]^+[M(CO)_x]^-$ can be applied to a broad array of heterocycle carbonylations. Most important is the utility of this catalyst in the quick and efficient synthesis, from inexpensive starting materials, of monomers for the production of poly(hydroxyalkanoate)s.

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Supporting Information Available: Synthesis and characterization of **1** and details of epoxide carbonylation (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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