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In Situ Generation of the Coates Catalyst: A Practical and Versatile Catalytic System for the Carbonylation of *meso*-Epoxides

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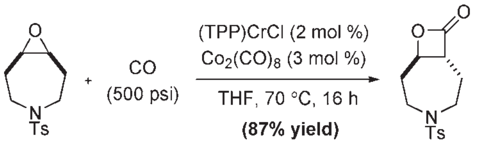
ABSTRACT



12 additional examples: *meso*-epoxide/(TPP)CrCl as low as 1000:1

A highly active catalytic system for the carbonylation of *meso*- and terminal epoxides to β-lactones is described. The active catalyst, analogous to Coates' catalyst, is generated *in situ* from commercially available (TPP)CrCl and $Co_2(CO)_8$. This practical system circumvents the preparation of air sensitive cobaltate salts, operates at low catalyst loadings, and allows the carbonylation of functionalized, sterically demanding and heterocyclic *meso*-epoxides.

The carbonylation of epoxides[1] is an industrially relevant process that provides direct access to versatile synthons such as β-hydroxy esters,[2] β-hydroxy amides,[3] and β-lactones.[4] Well into the 1990s, the carbonylation of epoxides to β-lactones was the subject of limited studies due to the lack of catalysts that selectively produce β-lactones without competing polymerization to poly(β-hydroxyalkanoate)s or isomerization of the starting epoxides to ketones. The disclosure of a patent by Drent in 1994 claiming that a catalytic system comprised of $Co_2(CO)_8$ and 3-hydroxypyridine could give rise to high ratios of β-lactones to polyesters from terminal epoxides reinvigorated interest in this reaction.[5] In subsequent studies, Alper developed a system based on the cobaltate salt [PPN][Co(CO)$_4$] (PPN $=$ $PPh_3{=}N{=}PPh_3$) which in combination with $BF_3 \cdot Et_2O$ activation selectively produced β-lactones from a series of terminal epoxides.[6] This system incorporates a Lewis acid (LA) induced activation of the epoxide in conjunction with a ring-opening nucleophilic attack of $[Co(CO)_4]^-$, a phenomenon first studied in detail by Heck.[7]

Cobaltate salts as a concept were further elaborated by the Coates group who designed well-defined catalysts of the general form $[LA]^+[Co(CO)_4]^-$ that incorporate Lewis acidic, oxophilic counterions such as the depicted $[(porphyrin)Cr]^+$ salts **1**/**2** and $[(salph)Al/Cr]^+$ salts **3a**/**b** (Figure 1).[8]

In a different approach, Rieger reported on a catalytic system comprising $Co_2(CO)_8$ and $AlMe_3$ that proved highly active for terminal epoxides. Using detailed *in situ*

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[1] For reviews, see: (a) Church, T. L.; Getzler, Y. D. Y. L.; Byrne, C. M.; Coates, G. W. *Chem. Commun.* **2007**, 657–674. (b) Nakano, K.; Nazoki, K. *Top. Organomet. Chem.* **2006**, *18*, 223–238.

[2] (a) Deng, F.-G.; Hu, B.; Sun, W.; Chen, J.; Xia, C.-G. *Dalton. Trans.* **2007**, 4262–4267. (b) Denmark, S. E.; Ahmad, M. *J. Org. Chem.* **2007**, *72*, 9630–9634. (c) Kim, H. S.; Bae, J. Y.; Lee, J. S.; Jeong., C., II; Choi, D. K.; Kang, S. O.; Cheong, M. *Appl. Catal., A: Gen.* **2006**, *301*, 75. (d) Hinterding, K.; Jacobsen *J. Org. Chem.* **1999**, *64*, 2164–2165.

[3] (a) Goodman, S. N.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2002**, *41*, 4703–4705. (b) Watanabe, Y.; Nishiyama, K.; Zhang, K.; Okuda, F.; Kondo, T.; Tsuji, Y. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 879–882.

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[5] Drent, E.; Kragtwijk, E. Eur. Pat. Appl. 577206, 1994; *Chem. Abstr.* **1994**, *120*, 191517c.

[6] Lee, J. T.; Thomas, P. J.; Alper, H. *J. Org. Chem.* **2001**, *66*, 5424–5426.

[7] Heck, R. F. *J. Am. Chem. Soc.* **1963**, *85*, 1460–1463.

[8] (a) Kramer, J. W.; Lobkovsky, E. B.; Coates, G. W. *Org. Lett.* **2006**, *8*, 3709–3712. (b) Schmidt, J. A. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2005**, *127*, 11426–11435. (c) Schmidt, J. A. R.; Mahadevan, V.; Getzler, Y. D. Y. L.; Coates, G. W. *Org. Lett.* **2004**, *6*, 373–376. (d) Mahadevan, V.; Getzler, Y. D. Y. L.; Coates, G. W. *Angew. Chem., Int. Ed.* **2002**, *41*, 2781–2784. (f) Getzler, Y. D. Y. L.; Mahadevan, V.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 1174–1175.

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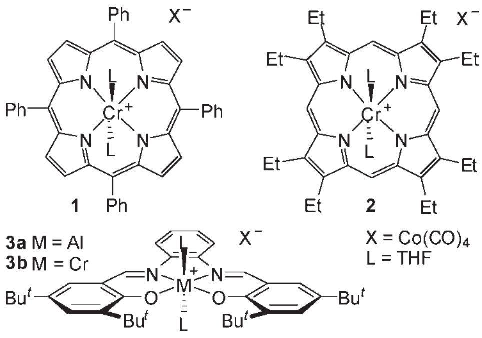


Figure 1. Coates' catalysts for epoxide carbonylation.

IR studies, the *in situ* generated cobaltate salt $[Me_2Al(diglyme)]^+[Co(CO)_4]^-$ was identified as the active catalyst.[9]

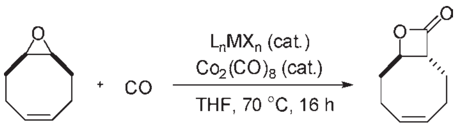
Most of the catalytic systems described above show high activity for terminal epoxides; however, only salts **1** and **2** display high activity with 1,2-disubstituted *meso*-epoxides. Catalysts **1** and **2** are air sensitive and require the use of glovebox and Schlenk-line techniques for their synthesis and handling, which impedes their general use within nonspecialized laboratories.

We report here on a catalytic system comprised of commercially available components that circumvents the preparation and handling of air sensitive cobaltate salts. Moreover, it displays activities similar or higher than the best catalysts described to date for both *meso*- and terminal epoxides.

It is well-documented that Lewis bases (LBs) disproportionate $Co_2(CO)_8$ to form homonuclear ion pairs (HNIPs).[10] However, the disproportionation of $Co_2(CO)_8$ by halide sources has been the subject of a relatively few publications.[11] In particular, a report by Braterman caught our attention, where it was shown that free or complexed halide sources could catalyze the disproportionation of $Co_2(CO)_8$ to generate the nucleophilic $[Co(CO)_4]^-$ ion.[11a]

Our group is interested in utilizing Lewis acidic metal halides as multifunctional reagents, for instance, simultaneously as an LA and a halide source.[12] We hypothesized that the use of a Lewis acidic metal halide in conjunction with $Co_2(CO)_8$ could form *in situ* a catalyst that would combine LA activation of the epoxide with halide-assisted generation of the nucleophilic $[Co(CO)_4]^-$ ion. In order to test our hypothesis, we examined metal halides of varying Lewis acidity in the carbonylation of cyclooctene oxide.

Table 1. Screening of Lewis Acidic Metal Halides[a]



entry	L_nMX_n	L_nMX_n (mol %)	$Co_2(CO)_8$ (mol %)	P(CO) (psi)	conv[b] (%)
1	–	–	5.0	900	0
2	$AlCl_3$	1.0	1.0	900	0
3	$ZnCl_2$	1.0	1.0	900	0
4	$ZrCl_4$	1.0	1.0	900	0
5	Cp_2TiCl_2	1.0	1.0	900	trace
6	$(^iPrO)_2TiCl_2$	1.0	1.0	900	trace
7	$TiBr_4$	1.0	1.0	900	24
8	(TPP)CrCl	1.0	1.0	900	≥98
9	(TPP)AlCl	1.0	1.0	900	18
10	(TPP)FeCl	1.0	1.0	900	trace
11	(TPP)CoCl	1.0	1.0	900	0
12	(TPP)CrCl	0.5	0.5	900	≥98
13	(TPP)CrCl	0.5	0.5	500	≥98
14	(TPP)CrCl	0.5	0.5	400	91
15	(TPP)CrCl	0.5	0.5	100	59
16	(TPP)CrCl	0.1	0.1	500	22

[a] Reaction conditions: epoxide (2 mmol), THF (3 mL, 0.67 M). [b] Determined by ^1H NMR spectroscopy of the crude material.

For initial catalyst screening we employed 1 mol % of a metal halide and equimolar amounts of $Co_2(CO)_8$ under 900 psi of CO pressure, with reactions run at 70 °C and a reaction time of 16 h. A control experiment with 5 mol % of $Co_2(CO)_8$ failed to give any product (Table 1, entry 1). $AlCl_3$, $ZnCl_2$, and $ZrCl_4$ as precatalysts gave no conversion (entries 2–4), while Cp_2TiCl_2 and $(^iPrO)_2TiCl_2$ gave only traces of the product (entries 5 and 6). We were pleased to find that $TiBr_4$ gave a 24% conversion to the product confirming our hypothesis that an *in situ* generated catalyst from a Lewis acidic metal halide can catalyze the carbonylation of epoxides (entry 7). We examined (TPP)CrCl next, which has been reported to form the strongly Lewis acidic $[(TPP)Cr(L)_2]^+$ ion in the presence of epoxides,[13] and were delighted to find that cyclooctene oxide was completely converted to the *β*-lactone (entry 8). In comparison, (TPP)AlCl gave a conversion of 18%, whereas (TPP)FeCl produced only traces of the product, with (TPP)CoCl being inactive (entries 9–11). These findings are in agreement with Coates' work and underline the uniqueness of the chromium porphyrin systems.[8b,c] Subsequent reaction parameter optimization using (TPP)CrCl showed that lowering the (TPP)CrCl and $Co_2(CO)_8$ loading to 0.5 mol % (entry 12) and the CO pressure to 500 psi

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(9) (a) Molnar, F.; Luinstra, G. A.; Allmendinger, M.; Rieger, B. *Chem.—Eur. J.* **2003**, *9*, 1273–1280. (b) Allmendinger, M.; Eberhardt, R.; Luinstra, G. A.; Molnar, F.; Rieger, B. *Z. Anorg. Allg. Chem.* **2003**, *629*, 1347–1352.

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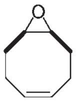
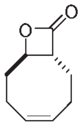
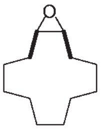
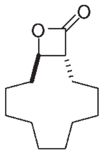
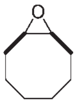
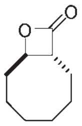
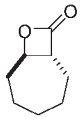
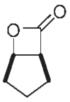
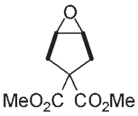
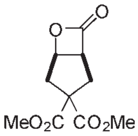
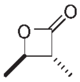
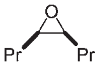
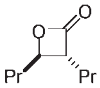
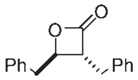
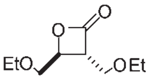
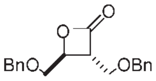
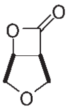
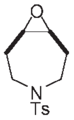
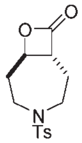
(12) (a) Akula, R.; Galligan, M. J.; Ibrahim, H. *Chem. Commun.* **2009**, 6991–6993. (b) Akula, R.; Galligan, M. J.; Ibrahim, H. *Synthesis* **2011**, 347–351.

(13) Chen, P.; Malcolm, H. C.; Gallucci, J. C.; Zhang, X.; Zhou, Z. *Inorg. Chem.* **2005**, *44*, 2588–2595.

Table 2. (TPP)CrCl/$Co_2(CO)_8$ Catalyzed Carbonylation of *meso*-Epoxides (cat. = (TPP)CrCl)[a]

ent	substrate	s/cat.	β-lactone	conv[b] (%)
1		200		≥98 (91)
2		1000		≥98 (91)
3		200		≥98 (87)
4		200		≥98 (89)
5		200		≥98 (84)
6		100		78 (74)
7		200		≥98 (95)
8		200		≥98 (94)
9		20		76 (68)
10		200		≥98 (84)
11		200		62 (47)
12		200		≥98 (91)
13		50		≥98 (87)

[a] Reaction conditions: epoxide (2 mmol), THF (3 mL, 0.67 M), (TPP)CrCl/$Co_2(CO)_8$ = 1:1.5, CO (500 psi), 70 °C, 16 h. [b] Determined by ^1H NMR spectroscopy of the crude material; yield of isolated β-lactone is given in parentheses.

(entry 13) still gave complete conversion to the product. However, a further decrease in CO pressure (entries 14 and 15) and or catalyst loading (entry 16) had a detrimental effect on the conversion.

With the optimized conditions from Table 1, entry 13 in hand, we set out to carbonylate a series of *meso*-epoxides (Table 2). Our system proved highly active in the carbonylation of 12-, 8-, 7-, and 5-membered carbocyclic epoxides with an epoxide/(TPP)CrCl loading of 200:1 (Table 2, entries 2–5). Moreover, lowering the catalyst loading to 1000:1 in the case of the 12-membered epoxide still gave full conversion to the β-lactone (entry 2).[14] Dicarboxylate cyclopentene oxide was less reactive and a loading of 100:1 was needed for a good conversion (entry 6). We then examined carboacyclic *meso*-epoxides and found that they displayed similar activities (entries 7–11). However, 2,3-dibenzyl and 2,3-benzyloxymethyl ethylene oxide proved less reactive and a higher loading of 20:1 was required for a good conversion with the former (entry 9).

We have also subjected epoxides derived from heterocycles to our carbonylation conditions and were delighted to find that they gave heterocyclic-fused β-lactone products in high yields. The epoxide derived from 2,5-dihydrofuran was carbonylated in 91% yield under the standard loading of 200:1 (entry 12), whereas a higher loading of 50:1 was required to carbonylate the 1-tosyl-2,3,6,7-tetrahydro-1*H*-azepine derived epoxide, which was obtained in 87% yield (entry 13). An X-ray structure determination confirmed the *trans*-stereochemistry of the tetrahydro-1*H*-azepine derived β-lactone (Figure 2).

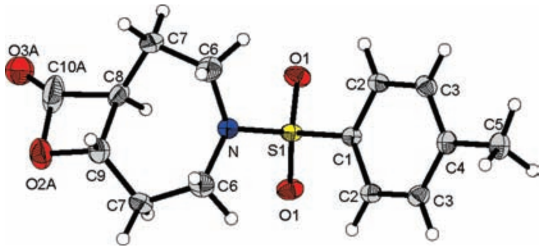


Figure 2. Tetrahydro-1*H*-azepine derived β-lactone with its crystal structure drawn with 50% thermal ellipsoids.

In order to demonstrate the synthetic utility of these heterocycle-fused β-lactones, we choose to convert the tetrahydrofuran β-lactone into the literature known transpentacin analogue *trans*-4-aminotetrahydrofuran-3-carboxylic acid.[15] Thus, S_N2 opening of the β-lactone with NaN_3 followed by azide reduction furnished the *trans* β-amino acid in 56% overall yield (Scheme 1).[16]

With our catalytic system displaying high activity with *meso*-epoxides, we were interested in examining the

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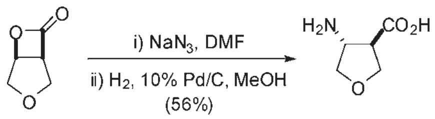
[14] Both, a synthesized and a purchased sample from Strem Chemicals of (TPP)CrCl gave complete conversion to the product at a loading of 1000:1.

[15] Bunnage, M. E.; Davies, S. G.; Roberts, P. M.; Smith, A. D.; Withey, J. M. *Org. Biomol. Chem.* **2004**, *2*, 2763–2776.

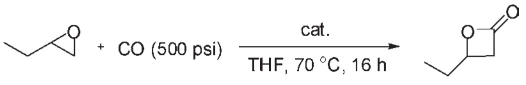
[16] Yokota, Y.; Cortez, G. S.; Romo, D. *Tetrahedron* **2002**, *58*, 7075–7080.

Scheme 1. Conversion of Tetrahydrofuran-Fused β-Lactone into the *trans*-4-Aminotetrahydrofuran-3-carboxylic Acid



catalytic activity with terminal epoxides. As expected, our (TPP)CrCl/$Co_2(CO)_8$ system proved highly active with 1,2-epoxybutane (EB) as substrate, displaying unprecedented TONs (Scheme 2).

Scheme 2. Catalytic Carbonylation of 1,2-Epoxybutane with the (TPP)CrCl/$Co_2(CO)_8$ System



EB/(TPP)CrCl/$Co_2(CO)_8$	10000:1:1.5	100% conv
EB/(TPP)CrCl/$Co_2(CO)_8$	20000:1:1.5	80% conv

On a 100 mmol scale and with an EB/(TPP)CrCl loading of 10000:1, EB was fully converted to β-valerolactone, as judged by ^{1}H NMR spectroscopy (Scheme 1). Lowering the EB/(TPP)CrCl loading even further to 20000:1 on the same scale still gave a conversion of 80%.

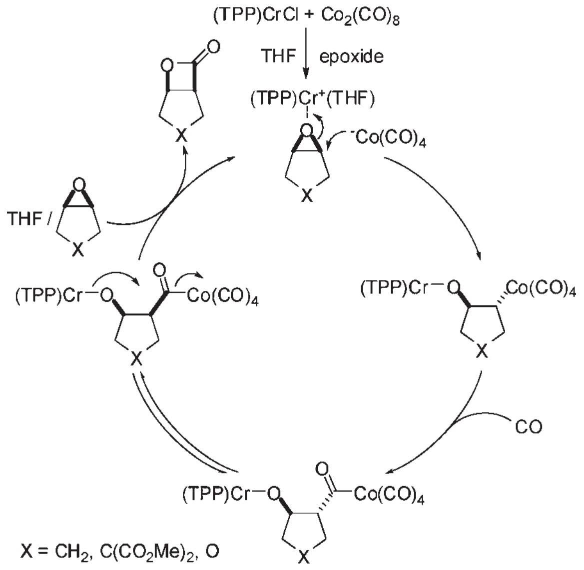
We believe that, in the presented catalytic system, a catalyst analogous to Coates' chromium cobaltate complex **1** is generated *in situ* by a chloride-assisted disproportionation of $Co_2(CO)_8$ according to eq 1, where L = THF or epoxide.[11]

$$\frac{3}{2}Co_2(CO)_8 + 2(TPP)CrCl \xrightarrow{4\,L} 2[(TPP)Cr(L)_2]^+[Co(CO)_4]^- + CoCl_2 + 4CO \qquad (1)$$

However, as this reaction occurs in the presence of epoxide and CO, we propose that a very fast ring opening of the epoxide by $[Co(CO)_4]^-$ occurs within the ion pair $[(TPP)Cr(L)(epoxide)]^+[Co(CO)_4]^-$, followed by an immediate CO insertion, leading to a neutral chromium alkoxide/cobalt acyl intermediate.[17]

Finally, the observed *cis* stereochemistry in the case of five-membered ring β-lactones (Table 2, entries 5, 6, and 12) raises the possibility of an alternative mechanistic pathway in operation to that of larger rings (Scheme 3).

Scheme 3. Proposed Mechanism for the Carbonylation of Five-Membered Ring Epoxides



In addition to the cationic mechanism proposed by Coates,[8b] we propose that a ring closure preceding epimerization of the neutral chromium alkoxide/cobalt acyl intermediate is feasible under the Lewis acidic reaction conditions. The exact nature of this epimerization is not clear at present.

In conclusion, we have disclosed an *in situ* generated catalytic system that allows the ring-expansive carbonylation of epoxides using low precatalyst loadings. Our unique approach to catalyst generation permits the use of commercially available air stable components thereby eliminating the need for glovebox and Schlenk-line techniques required for the preparation and handling of air sensitive cobaltate salts. We anticipate that our new approach could greatly expand the general utility of this important transformation.

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Supporting Information Available. Experimental carbonylation procedures and analytical data of all β-lactones. This material is available free of charge via the Internet at http://pubs.acs.org.

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[17] For detailed mechanistic studies with aluminum complex **3a**, see: Church, T. L.; Getzler, Y. D. Y. L.; Coates, G. W. *J. Am. Chem. Soc.* **2006**, *128*, 10125–10133.