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Carbonylative Ring Opening of Terminal Epoxides at Atmospheric Pressure

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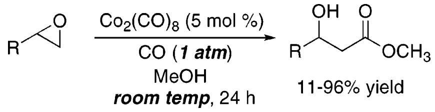

The carbonylative opening of terminal epoxides under mild conditions has been developed using $Co_2(CO)_8$ as the catalyst. Under 1 atm of carbon monoxide and at room temperature in methanol, propylene oxide is converted to methyl 3-hydroxybutanoate in up to 89% yield. This transformation is general for many terminal epoxides bearing alkyl, alkenyl, aryl, alkoxy, chloromethyl, phthalimido, and acetal functional groups. The opening takes place without epimerization at the secondary stereocenter.

Introduction

Given the environmental concerns in modern society, catalytic reactions that minimize waste and increase efficiency are in great demand. Accordingly, the development of atom-economic[1] and atom-efficient[2] reactions is of great interest. Obviously, the most atom-efficient processes are either molecular rearrangements or addition reactions that incorporate all of the starting materials into the products without generating a waste stream. Among the latter processes, those reactions that incorporate new functional groups and stereocenters are particularly useful. Catalytic carbonylative ring opening or ring expansion of epoxides represents an extremely efficient reaction, that affords high value-added products.[3] The carbonylative ring expansion of epoxides produces lactones[4] or succinic anhydrides[5] (by double carbonylation), whereas carbonylative ring opening with *N*- or *O*-nucleophiles affords β-hydroxyl amides[6] or esters, respectively (Scheme 1).[7]

Carbonylation chemistry is used extensively in industry as illustrated by the bulk production of carbonylation intermediates.[8] Of particular note is the industrial process for the synthesis of propane-1,3-diol, a useful pharmaceutical intermediate and polyester component.[9] The production of this diol from ethylene oxide (by hydroformylation followed by hydrogenation) has been studied intensively.[10] Landmark reports from Heck[11] and others[12] on the application of homonuclear ion pairs (HNIP's),

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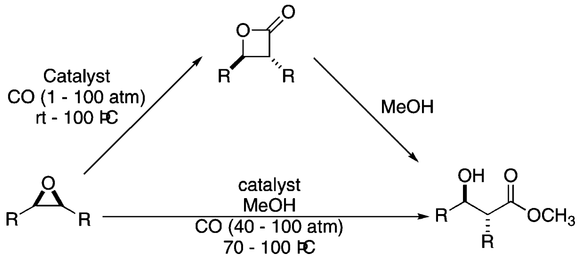
10.1021/jo7014455 CCC: $37.00

SCHEME 1



for carbonylative carbon−carbon bond forming reactions, set a milestone in carbonylation chemistry. Mechanistic studies by Marko and Faschinetti showed that HNIP's are generated from the disproportionation of $Co_2(CO)_8$ by Lewis bases.[13] The preparative advantages of HNIP's are clear, as this catalyst system requires only one metal. Upon interaction with a Lewis base the $Co_2(CO)_8$ disproportionates into an ionic species, $[LB_2Co(CO)_3]^+$ $[Co(CO)_4]^-$. The Lewis acidic cationic portion $[LB_2Co(CO)_3]^+$ is known to coordinate and activate the epoxide and the anionic $[Co(CO)_4]^-$ will attack the epoxide to make an organocobalt ate complex. Insertion of carbon monoxide to this cobalt ate species results in a cobalt acyl complex, which is intercepted by nucleophiles to give β-lactones or β-hydroxy esters and amides. In the early 1990s Drent and Kragtwijk reported an efficient HNIP catalytic system based on $Co_2(CO)_8$ and 3-hydroxypyridine (**3**) for the carbonylative ring opening of terminal aliphatic epoxides.[14] Hinterding and Jacobsen[7a] successfully exploited this transformation in the production of enantiopure β-hydroxy esters starting from enantiopure epoxides that are, in turn, easily prepared by hydrolytic kinetic resolution.[15] Although the reported carbonylation conditions are milder than those reported by Eisenmann,[16] they still required 40 bar of carbon monoxide and 65−70 °C.[17]

The disproportionation of $Co_2(CO)_8$ with other nucleophiles, for example, silyl amides, has been used for the carbonylative ring opening of epoxides to produce β-hydroxy amides under atmospheric pressure of carbon monoxide.[6] Moreover, Kim has shown that zinc Lewis acids such as $ZnBr_2(NC_5H_5)$ accelerate the carbonylative ring opening of ethylene oxide with $Co_2(CO)_8$.[18] Finally, Coates has developed a highly efficient bimetallic catalyst that allows the carbonylative ring expansion of epoxides under atmospheric pressure of CO and at room temperature.[19]

Although high-pressure reactions often provide interesting products, the need for specialized equipment represents a limitation for synthetic organic chemists. Thus, we have embarked on a program to develop novel Lewis bases to efficiently catalyze the formation of reactive HNIP's that are effective at opening epoxides and aziridines under mild conditions (1 atm of CO and room temperature). We targeted the carbonylation of epoxides because the β-hydroxy ester products are useful intermediates in organic and polymer chemistry[4e,20] and thus initiated studies on the carbonylative ring opening of propylene oxide (**1a**) in methanol as the test reaction. Much to our surprise we observed through preliminary control experiments that this reaction proceeded readily at atmospheric pressure of CO and room temperature in the absence of a Lewis basic catalyst! Because this unexpected observation contradicted the general practice for this important process we have extensively investigated the reaction and describe our results in full below.

Results and Discussion

1. Initial Discovery. The carbonylation of **1a** in MeOH/THF under CO pressure was selected as the model system. Initial studies involved a survey of CO pressure, temperature, time, solvent, and catalyst. Orienting experiments employed the conditions developed by Drent: 5 mol % of $Co_2(CO)_8$, 10 mol % of **3** in a 1:1 mixture of MeOH and THF under 41 bar of CO at 72 °C for 12 h. Under these conditions an 85% yield of methyl-3-hydroxybutyrate (**2a**) was obtained (Table 1, entry 1). As part of a series of standard, systematic control experiments, we performed the carbonylation of **1a**, in MeOH/THF (1:1), with 10 mol % of $Co_2(CO)_8$ and 20 mol % of **3** under atmospheric pressure of CO and at room temperature. Much to our surprise, **2a** was isolated in 40% yield (Table 1, entry 2).

2. Optimization and Control Experiments. This striking observation encouraged further investigation of this reaction. Remarkably, by lowering the loading of both $Co_2(CO)_8$ (to 5 mol %) and **3** (to 10 mol %) at atmospheric pressure of CO and room temperature, the yield of **2a** improved from 40% to 80% (Table 1, entries 2 and 3).[21] The next two controls showed that no reaction occurs without $Co_2(CO)_8$, but surprisingly, an 85% yield of **2a** was obtained in an experiment without **3** (Table 1, entries 4 and 5). Apparently, methanol alone is able to

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[17] Liu, J.; Chen, J.; Xia, C. *J. Mol. Catal. A*: *Chem.* **2006**, *250*, 232−236.

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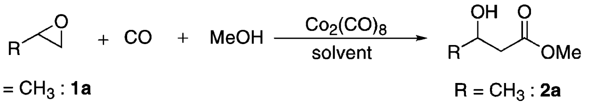
[21] The adverse effect of high carbon monoxide pressure and reaction temperature has been observed on the outcome of the cobalt-catalyzed carbonylation of cyclic ethers using *N*-silylamines by Watanabe et al. See: Watanabe, Y.; Nishiyama, K.; Zhang, K.; Okuda, F.; Kondo, T.; Tsuji, Y. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 879−882.

TABLE 1. Optimization of Carbonylative Ring Opening of Propylene Oxide[a]



entry	$Co_2(CO)_8$ (mol %)	**3**[b] (mol %)	solvent	CO (bar)	temp (°C)	time (h)	yield (%)[c]
1	5	10	MeOH/THF (1:1)[d]	41	72	12	85
2	10	20	MeOH/THF (1:1)[e]	1	rt	24	40
3	5	10	MeOH/THF (1:1)	1	rt	24	80
4	–	10	MeOH/THF (1:1)	1	rt	24	0
5	5	–	MeOH/THF (1:1)	1	rt	24	85
6[f]	5[g]	–	MeOH/THF (1:1)	1	rt	24	79
7[f]	5[g]	–	MeOH/THF (1:1)	1	rt	24	90
8	5[h]	10	MeOH/THF (1:1)	1	rt	24	72
9	5[h]	–	MeOH/THF (1:1)	1	rt	24	80
10	5[g]	10	MeOH/THF (1:1)[i]	1	rt	24	71
11	5[g]	10	MeOH/THF (1:1)	1[j]	rt	24	81
12	5[g]	–	MeOH/THF (1:1)	1	rt	24	ND[k]
13	5[g]	–	THF	1	rt	24	*l*
14	5[g]	–	MeOH	1	rt	24	89
15	5[g]	–	MeOH	1	rt	0.5	37
16	5[g]	–	MeOH	1	rt	1	55
17	5[g]	–	MeOH	1	rt	3	76
18	5[g]	–	MeOH	1	rt	6	83
19	5[g]	–	MeOH	1	rt	12	90

[a] 5 mmol of epoxide, 1 M. [b] 3-Hydroxypyridine. [c] Isolated yield. [d] 0.5 M. [e] 2 M. [f] Distilled **1a** (from CaH_2) was used. [g] Sublimed $Co_2(CO)_8$ was used. [h] Different bottle of $Co_2(CO)_8$. [i] THF and MeOH from freshly opened ACS Grade bottle. [j] New tank of CO. [k] No ethereal workup and passing through plug of silica gel. [l] *β*-Lactone formation in low yield by ^{1}H NMR analysis.

disproportionate the $Co_2(CO)_8$ to produce the HNIP that catalyzed the carbonylative ring opening of **1a**.[22]

Because of the dramatic differences between the conditions employed herein and those described in the literature for opening of **1a**, we suspected that a spurious contaminant could be catalyzing the formation of the HNIP's. Accordingly, we checked the source and purity of **1a**, $Co_2(CO)_8$, the solvents, and carbon monoxide. Thus, **1a** was redistilled, the $Co_2(CO)_8$ was sublimed,[23] and both were employed in the carbonylative ring opening with and without **3**. We were delighted to find that both reactions were reproducible: in the presence of **3** the yield of **2a** was 79% (compare entries 3 and 6 in Table 1) whereas in the absence of **3** the yield of **2a** was 90% (compare entries 5 and 7 in Table 1). To eliminate all possibility of adventitious catalysts, $Co_2(CO)_8$ from a different bottle was employed both with and without **3**. Once again, both reactions afforded **2a** in similar yields as before (compare entries 8 and 3, and entries 9 and 5 in Table 1). The next control experiment targeted the source of MeOH and THF (ACS grade). In these experiments, freshly opened bottles of solvent were used instead of the freshly purified MeOH (distilled from $Mg(OMe)_2$) or THF (dried through Al_2O_3). Under these conditions, a 71% yield of **2a** was obtained (Table 1, entry 10). The reaction also worked well with CO from a different cylinder,[24] affording and 81% yield of **2a** (Table 1, entry 11).

Having ruled out adventitious contaminants in the starting materials and the solvent as the source of accelerated reactions, we next investigated if the workup and purification were responsible for the carbonylation reaction. To exclude this possibility, a standard reaction was run for 24 h and then was filtered through a sintered glass frit. Careful evaporation of the solvent gave a pink oil that by ^{1}H NMR analysis (broad peaks observed because of cobalt present) confirmed the formation of **2a** (Table 1, entry 12).

In another series of control experiments, a survey of MeOH or THF alone as the solvent revealed that the carbonylative ring opening of **1a** runs smoothly in MeOH to afford an 89% yield of **2a**, whereas in THF, only *β*-lactone formation was observed (^{1}H NMR analysis) in extremely poor yield (Table 1, entries 13 and 14). Next, to test if the (arbitrarily chosen) 24 h reaction time was indeed necessary, a series of experiments under standard conditions were set up and quenched at 0.5, 1, 3, 6, and 12 h. After workup, the 0.5-h run afford a 37% yield of **2a**, whereas the reactions run for 1, 3, 6, and 12 h gave 55%, 75%, 76%, and 89% yield of **2a**, respectively (Table 1, entries 15–19). *Thus, on the basis of all the control experiments and foregoing studies, we conclude that the* $Co_2(CO)_8$*-catalyzed, carbonylative ring opening of* ***1a*** *in methanol/THF takes place at 1 atm of CO and room temperature*.

3. Demonstration of Scope. The ready carbonylative ring opening of **1a** with $Co_2(CO)_8$ in methanol under atmospheric pressure at room temperature stimulated a study of the general scope of this catalytic process for the synthesis of *β*-hydroxy esters. Thus, a wide range of functionalized, terminal epoxides bearing alkyl, alkenyl, alkyl-aryl, glycidyl, and carbonyl groups were subjected to the carbonylation conditions. In general, very good yields of *β*-hydroxy esters were obtained. Not surprisingly, simple aliphatic and olefinic terminal epoxides reacted well (Table 2, entries 1, 2, and 3). Terminal epoxides bearing aromatic residues are known to react slowly thus affording lower yields. Thus, 3-phenylpropylene oxide and 4-phenylbutene 1,2-oxide gave moderate yields with minor amounts of a methyl ketone side product (Table 2, entries 4 and 5). Ketone formation (particularly at lower CO pressure) finds ample precedent in related studies and arises from the non-carbonylative rearrangement of ring-open epoxide intermediate as proposed by Coates et al.[25] Heteroatom functionalized epoxides such as epichlorohydrin afforded a 73% yield of methyl 4-chloro-3-hydroxybutyrate (Table 2, entry 6). In addition, various glycidol ethers also reacted well to afford the *β*-hydroxy esters in good yields together with the minor amounts of a methyl ketone byproduct (Table 2, entries 7–9). Surprisingly, the TBS-protected glycidol **1j** did not react cleanly and gave an equivalent amount of the methyl ketone with lower conversion, whereas *N*-(2,3-epoxypropyl)pthalimide afforded the corresponding *β*-hydroxy ester in good yield (Table 2, entries 10 and 11). Functionally more diverse epoxides such as acetal, ester, and ketone-bearing oxiranes gave poor yields for the desired product (Table 2, entries 12–15). Presumably, carbonyl functional groups are not compatible with the HNIP generated from $Co_2(CO)_8$ and methanol. In a preliminary experiment with an internal epoxide, cyclohexane oxide **1p**, the *β*-hydroxy ester **2p** was formed in 20% yield.

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(22) Evidence for the existence of $[Co(CO)_4(ROH)]^+[Co(CO)_4]^-$ complexes from $Co_2(CO)_8$ and methanol at >25 °C has been provided; see: Tucci, E. R.; Gwynn, B. H. *J. Am. Chem. Soc.* **1964**, *86*, 4838–4841.

(23) Propylene oxide (Fischer Scientific) was heated at reflux over calcium hydride for 12 h, distilled, and stored in a Schlenk flask. Dicobalt octacarbonyl (Strem Chemicals) was sublimed in a 100 mL glass sublimation chamber at 35 °C (0.5 mmHg), using an acetone/dry ice cold finger.

(24) Compressed carbon monoxide from Matheson TRI.GAS, CP grade (CP = Chemically pure). Lot no. 1046405663B9

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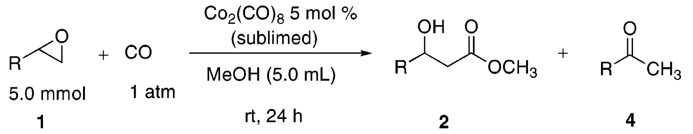
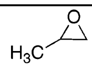
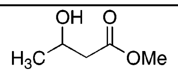
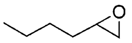
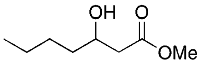
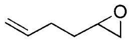
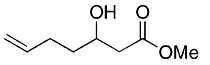
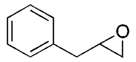
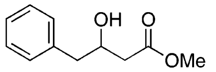
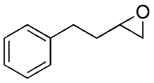
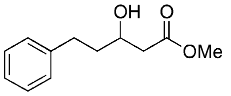
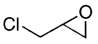
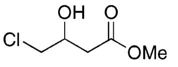
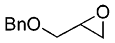
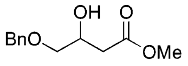
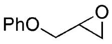
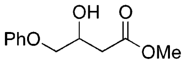
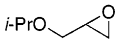
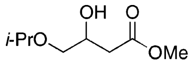
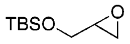
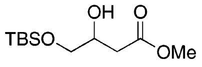
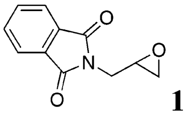
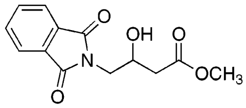
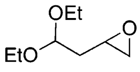
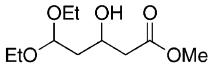
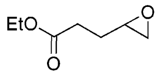
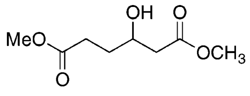
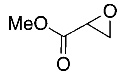
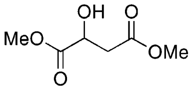
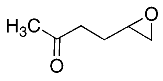
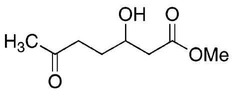
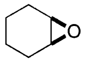
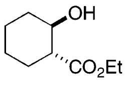
TABLE 2. Cobalt-Catalyzed Carbonylation of Epoxides[a]



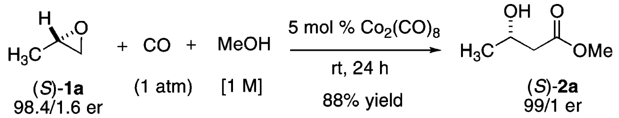
entry	epoxide	major product	yield of **2** (%)[b]	yield of **4** (%)[b]	recovered **1** (%)[b]	**2:4**[c]
1	 **1a**	 **2a**	89	-	-	-
2	 **1b**	 **2b**	89	-	-	-
3	 **1c**	 **2c**	96	-	-	-
4	 **1d**	 **2d**	54	5	38	92:8
5	 **1e**	 **2e**	64	8	-	89:11
6	 **1f**	 **2f**	73	-	-	-
7	 **1g**	 **2g**	83	9	-	90:10
8	 **1h**	 **2h**	86	9	-	90:10
9	 **1i**	 **2i**	80	-	-	-
10	 **1j**	 **2j**	22	15	60	58:42
11	 **1k**	 **2k**	76	5	-	96:4
12	 **1l**	 **2l**	11	-	85	-
13	 **1m**	 **2m**	18	-	80	-
14	 **1n**	 **2n**	35	-	58	-
15[d]	 **1o**	 **2o**	17	-	70	-
16	 **1p**	 **2p**	20	-	73	-

[a] Reactions run with 5 mmol of epoxide. [b] Yield of isolated, purified products. [c] Based on the yield of isolated products.

The catalytic, ring-opening carbonylation of terminal epoxides is known to proceed with retention of configuration.[7a] Under the mild conditions described in this report, (*S*)-**1a** (98.4/1.6 er) provided (*S*)-**2a** (>99/1 er) as well (Scheme 2).

Although the scope of the carbonylative ring opening under these conditions is somewhat limited, and therefore may not be of general preparative significance, we are nonetheless struck by the use of high pressure and temperature for simple terminal epoxides in the literature. Most importantly, we are encouraged in our pursuit to identify Lewis basic activators of the formation of HNIPs for the ligand-accelerated, catalytic carbonylation of epoxides of diverse structure.

SCHEME 2



Conclusion

We have demonstrated that carbonylative ring opening of terminal epoxides can be performed at atmospheric pressure of CO and room temperature under catalysis by $Co_2(CO)_8$. Modest to good yields are obtained with simple as well as functionalized epoxides and glycidols, but epoxides bearing carbonyl groups give lower yields. Enantiopure propylene oxide is opened with complete retention of configuration. Further studies on HNIP-based catalytic ring opening of aziridines and epoxides are in progress, and will be reported in due course.

Experimental Section

General Experimental Procedures. See the Supporting Information.

Ring Opening Carbonylation of Propylene Oxide: Preparation of Methyl 3-Hydroxybutanoate (2a) [Table 2, Entry 1]. In a glovebox, $Co_2(CO)_8$ (84.5 mg, 0.25 mmol, 0.05 equiv) was placed in a 100-mL Schlenk flask equipped with a magnetic stir bar. The flask was sealed with a rubber septum and was removed from the drybox. The flask was purged three times for 2 s with carbon monoxide (filled in a 5 in. latex balloon). Freshly distilled methanol (5.0 mL) was added and the mixture was stirred for 2 min before **1a** (350 μL, 5.0 mmol) was added in one portion and the reaction was allowed to stir at room temperature for 24 h. The carbon monoxide balloon was removed carefully and vented in a fume hood. The reaction mixture was diluted with ether (50 mL) and stirred for 30−60 min to precipitate the cobalt complex. The mixture was filtered through a plug of silica gel (5 g), using ether as the eluent, and upon careful removal of solvent under reduced pressure, 525 mg (89%) of **2a** was obtained as a clear colorless oil.[26] Data for **2a**: ^1H NMR (500 MHz, $CDCl_3$) δ 4.21−4.17 (m, 1 H), 3.70 (s, 3 H), 2.96 (d, 1 H), 2.49 (dd, $J = 16.0, 3.5$ Hz, 1 H), 2.42 (dd, $J = 16.2, 8.7$ Hz, 1 H), 1.22 (d, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 173.3, 64.2, 51.7, 42.5, 22.4.

Acknowledgment. We are grateful to the National Science Foundation for generous financial support (NSF CHE 0414440 and 0717989). Dr. Son T. Nguyen is thanked for the preparation of Jacobsen's catalyst.

Supporting Information Available: Full experimental procedures and characterization data for all carbomethoxylation products. This material is available free of charge via the Internet at http://pubs.acs.org.

JO7014455

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[26] (a) Deng, G-J.; Li, G-R.; Zhu, L-Y.; Zhou, H-F.; He, Yan-Mei.; Fan, Q-H.; Shuai, Z-G. *J. Mol. Catal.* **2006**, *244*, 118−123. (b) Bette, V.; Mortreux, A.; Lehmann, C. W.; Carpentier, J-F. *Chem. Commun.* **2003**, *3*, 332−333. (c) Baumhof, P.; Mazitschek, R.; Giannis, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 3672−3674.