Note

Remarkably Accelerated Regioselective Hydrogenolysis of Terminal Epoxides in the Presence of $CoCl_2$ or $NiSO_4$[†]

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The rate of atmospheric pressure hydrogenolysis of terminal epoxides over palladium-charcoal to the corresponding methyl alcohols could be remarkably accelerated by introduction of CoCl2 or NiSO4.

Keywords   epoxides, hydrogenolysis, cobalt, nickel, ring-opening

Introduction

Reductive ring-opening of terminal epoxides to the corresponding methyl alcohols is a useful transformation of remarkable significance in organic synthesis.[1] In practice this type of conversion is usually realized through either metal hydride (such as $LiAlH_4$) reduction[2] or hydrogenolysis. The former, although rather frequently used in research laboratories nowadays, is expensive and bound to yielding stoichiometric quantities of waste. In comparison, hydrogenolysis[3] is much less costly and more environment-friendly. However, the regio-selectivity in the ring-openings of terminal epoxides by hydrgenolysis is far not always satisfactory. Primary alcohols, for instance, may form[4] as by-products. Usually slow conversion rate under atmospheric pressure is another shortcoming. To ensure a reasonably fast reaction, elevated[5] pressure of hydrogen appeared to be necessary. In an on-going project we needed some substituted methyl alcohols and entirely by accident discovered that pollution of traces of a cobalt salt led to dramatically enhanced hydrogenolysis rate. It is well-known that the ring-opening of epoxides by nucleophiles may be greatly facilitated[6] by addition of Lewis acids to the reaction mixture. However, we were not able to find any literature precedents of similar acceleration by Lewis acids in epoxide hydrogenolysis. Therefore, we subsequently tested a few other readily accessible terminal epoxides and found that the acceleration by cobalt salt appeared to be general. NiSO4 also showed similar effects. CuSO4, however, had no acceleration effects at all. Reported in this

Note are some of our findings along this line.

Experimental

General procedure: A mixture of the epoxide (1 mmol) in MeOH (5 mL) containing 10% Pd-C (10 mg per 100 mg of epoxide) and the Lewis acid (1 mol%) was stirred at 25 ℃ under H_2 (101 kPa) until absorption of hydrogen stopped. The catalyst was filtered off and the filtrate was concentrated on a rotary evaporator. The residue was chromatographed on silica gel (eluting with a mixture of EtOAc/hexanes) to give the resulting methyl alcohol. The Lewis acids ($CuSO_4 \cdot 5H_2O$, $NiSO_4 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$, $Co(OAc)_2 \cdot 4H_2O$) were all of reagent grade from commercial sources and used as received without any further treatment.

Results and discussion

Our preliminary results are summarized in Table 1. The effects of three Lewis acids were first examined under otherwise identical conditions using glycidyl phenyl ether as substrate. In the absence of any added Lewis acids, epoxide **1** gave **2** in only 15% yield after one hour's reaction (Entry 1). Addition of CuSO4 did not result in any facilitation (Entry 2). No **2** could be detected within 1 h. Introduction of NiSO4 or CoCl2 to the reaction system showed similar effects (Entries 3 and 4), leading to methyl alcohol **2** in 85% and 86% yield, respectively. It was noted that no primary alcohol was formed in these two experiments.
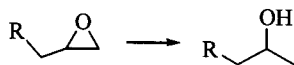
The catalytic effects of CoCl2 in hydrogenolysis of terminal epoxides was also clearly demonstrated by another pair of experiments conducted in parallel (Entries 5 and 6). In the presence of CoCl2 epoxide **3** was cleaved into corresponding methyl alcohol **4** in 92% yield. Without the

Table 1   Effects of some Lewis acids on the hydrogenolysis of terminal epoxides[a]

Entry	Epoxide	R	Lewis acid	Time (h)	Product (yield)
1	1	PhO	—	1	**2** (15%)
2	1	PhO	$CuSO_4$	1	No reaction
3	1	PhO	$NiSO_4$	1	**2** (85%)
4	1	PhO	$CoCl_2$	1	**2** (86%)
5	3	o-$MeOC_6H_4O$	—	3	**4** (24%)
6	3	o-$MeOC_6H_4O$	$CoCl_2$	3	**4** (92%)
7	5	1-Naphthoxy	$CoCl_2$	7	**6** (<5%)
8	7	p-$MeOC_6H_4O$	$CoCl_2$	1	**8** (<96%)
9	9	p-EtC_6H_4O	$CoCl_2$	3	**10** (94%)
10	11	$PhCO_2(CH_2)_2$	$Co(OAc)_2$	12	**12** (99%)[b]
11	13	$MeO_2C(CH_2)_7$	$CoCl_2$	10	**14** (65%)[c]

[a] The reactions were performed under otherwise the same conditions described in the *Experimental*. [b] Both **11** and **12** showed *ee* values > 99%. [c] About 20% **13** was recovered.

added $CoCl_2$, the yield of **4** dropped drastically to only 24%. Steric crowding around the oxirane appears to have significant influence on the reaction rate, because the presence of an *o*-methoxy group at the phenyl ring made the reaction time essentially tripled (Entries 4 and 6).

Encouraged by these observations, we next tested a few more other readily available terminal epoxides with $CoCl_2$ as catalyst. The alpha naphthol-derived epoxide **5** seemed to be rather resistant to the hydrogenolysis (Entry 7). After 7 hours' reaction, only trace of alcohol **6** was formed. Judging from the molecular structure we believe the steric crowding caused by the phenyl ring fused into the phenol ring was the most possible cause for the sluggish cleavage.

Other epoxides so far examined all could be cleaved smoothly into corresponding methyl alcohols in good to excellent yields, although longer reaction time was required for **11** and **13**. A chiral epoxide (Entry 10) did not loose any optical purity after fully cleaved into the methyl alcohol.

We also briefly looked into the possibility of kinetic resolution of racemic epoxides using a chiral cobalt complex salenCo(III), which was shown to be very efficient in nucleophilic ring-opening of epoxides by water (Jacobsen[7] kinetic hydrolytic resolution). With (R, R)-salenCo(III) in place of $CoCl_2$, epoxide **1** was indeed cleaved rapidly. In order to optimize the conditions for observing any potential kinetic resolution, we terminated the reaction at an early stage and isolated the alcohol. Thus, after 30 min's hydrogeoolysis, alcohol **2** was formed in 40% yield, together with 54% of recovered starting **1**. Unfortunately, chromatographic analysis on chiral column showed that **2** was completely racemic (Scheme 1). In another experiment with (R, R)-salenCo(II) rather than (R, R)-salenCo(III) as catalyst and racemic **11** as substrate, however, we isolated recovered epoxide **1** with partial optical activity (~11% *ee*). Although the level of enantiomeric differen-

tiation observed here is still low, it does show some hope for the future investigations.

Scheme 1
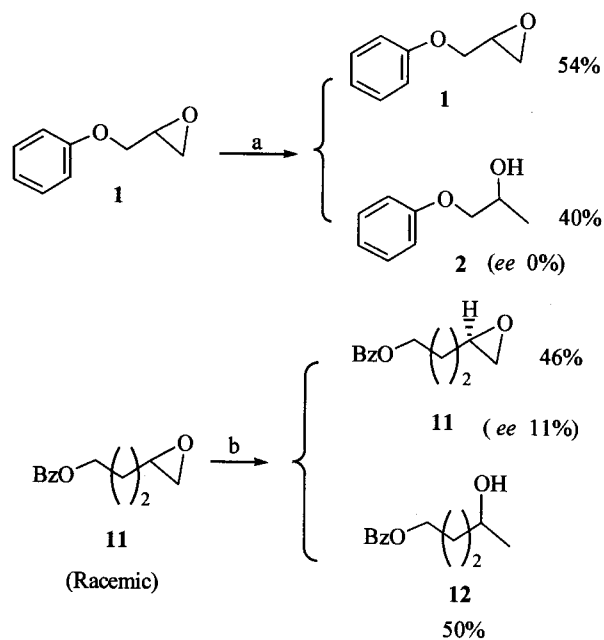
(a) H_2 (101 kPa)/Pd-C/(R, R)-salenCo(III)OAc (1 mol%), 25 °C, 30 min. (b) H_2 (101 kPa)/Pd-C/(R, R)-salenCo(II) (1 mol%), 25 °C, 3 h.

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