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Epoxide deoxygenation mediated by Salen complexes

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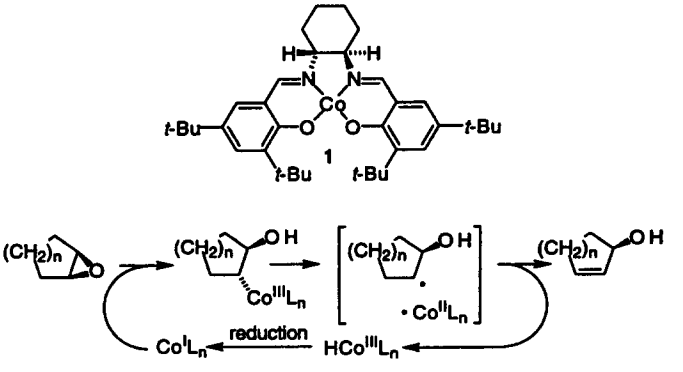
Abstract

N,N'-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminocobalt(II) (**1**) catalyzes the reductive deoxygenation of epoxides by Na(Hg) in THF, with 5–10 catalytic turnovers. The simpler *N,N'*-bis(salicylidene)-ethylenediaminocobalt(II) [$Co(Salen)_2$] (**16**) failed to catalyze deoygenations in THF but did in DMF.

Keywords: cobalt; cobalt compounds; catalysis; deoxygenation; epoxides.

Scheffold and co-workers showed that vitamin B_{12} catalyzes the enantioselective desymmetrization of *meso* epoxides,[1] aziridines[2] and activated cyclopropanes.[3] The accepted mechanism is illustrated in Scheme 1 for the desymmetrization of *meso* cyclic epoxides.



Scheme 1.

Although the B_{12}-catalyzed processes work well for some substrates, in general they are of limited scope. We decided to examine highly enantioenriched chiral B_{12} model compounds as possible

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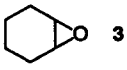
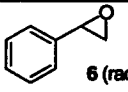
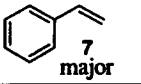
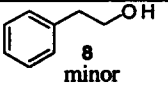
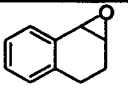
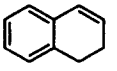
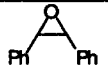
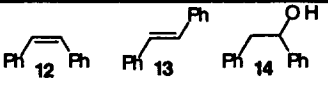
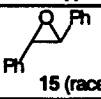
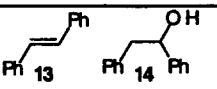
Table 1

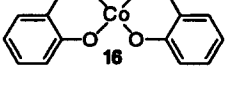
Entry	Substrate	Conditions	Results
1	 2	50 mM **2**, 20 mole % **1**, 10 mol equiv Na(Hg) in anaerobic THF-d_8 for 6 h (NMR tube experiment)	quantitative by ^{1}H NMR  4
2	**2**	as above but 10 mole % **1** for ~2 days	quantitative **4** by ^{1}H NMR
3	**2**	as above but 5 mole % **1** for ~2 days	incomplete (~ 48% **4**) by ^{1}H NMR
4	 3	50 mM **3**, 20 mole % **1**, 10 mol equiv Na(Hg) in anaerobic THF-d_8 for 6 h (NMR tube experiment)	quantitative by ^{1}H NMR  5
5	 6 (racemic)	14 mM **6**, 20 mole % **1**, 10 mol equiv Na(Hg) in anaerobic THF for 1 h	 7 major  8 minor
6	 9 (racemic)	14 mM **9**, 20 mole % **1**, 10 mol equiv Na(Hg) in anaerobic THF for 1 h	 10 ~quantitative
7	 11	14 mM **11**, 20 mole % **1**, 10 mole equiv Na(Hg) in anaerobic THF for 24 h	 12 13 14
8	 15 (racemic)	14 mM **15**, 20 mole % **1**, 10 mole equiv Na(Hg) in anaerobic THF for 24 h	 13 14

catalysts. We chose to study commercially available (*R,R*)-(−)-*N,N'*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminocobalt(II) (**1**),[4] which has been shown by Jacobsen and co-workers to be an excellent chiral Lewis acid catalyst for the opening of epoxides with nucleophiles.[5] To our surprise, **1** was not a catalyst for the conversion of epoxides to allylic alcohols; instead **1** was a catalyst for epoxide deoxygenation.[6]

Several examples are shown in Table 1. The catalyst **1** is essential for the reaction; no deoxygenation occurs if **1** is left out of an otherwise complete reaction. The strong reductant Na(Hg) is also essential; no deoxygenation occurs using Al(Hg) or $NaBH_4$.

To examine whether the deoxygenation reaction might be useful for enantioselective synthesis we attempted kinetic resolutions on racemic **6** and racemic **9**. Several reactions of each were run to partial completion. The reactions were worked up by filtration through silica gel then evaporation of THF. Unreacted **6** or **9** were examined by ^{1}H NMR using the chiral shift reagent europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] [Eu(hfc)$_3$]. In all cases the unreacted starting materials **6** or **9** were racemic. Thus, both enantiomers of **6** or **9** react at essentially the same rate.

To examine stereospecificity we studied *cis*-stilbene oxide (**11**) and *trans*-stilbene oxide (**15**). The reaction of 14 mM *cis*-stilbene oxide (**11**) with 10 mol equiv. Na(Hg) and 20 mol% **1** in anaerobic THF went to completion after 24 h, producing mixtures of *cis*-stilbene (**12**), *trans*-stilbene (**13**) and 1,2-diphenylethanol (**14**), in slightly varying ratios averaging **12**:**13**:**14**=1:10:3, as determined by ^{1}H NMR. The reaction of *trans*-stilbene oxide (**15**) under the same conditions led to a 1:4 mixture of **13** and **14**, as determined by ^{1}H NMR. Unfortunately, this information cannot be used to assess stereospecificity since a control reaction showed that the reaction conditions catalyze the isomerization of **12** to **13**.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The bulky *N,N'*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminocobalt(II) catalyst is essential for successful deoxygenations in THF. The simpler *N,N'*-bis(salicylidene)-ethylenediaminocobalt(II) [$Co(Salen)_2$] (**16**) failed to catalyze the deoxygenation of **2**, **3**, **6**, **9**, **11** or **15** in THF under standard reaction conditions used with **1**. Deoxygenations using **16** in DMF were attempted for the deoxygenation of **2**, **6** and **15** and were somewhat successful, but required longer reaction times, proceeded in low yields, were not completely reproducible and are thus not as good as the reactions using **1** in THF.

In conclusion, the deoxygenation of epoxides can be accomplished within a few hours at room temperature using 10–20 mol% **1** and Na(Hg) in anaerobic THF.

Acknowledgements

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