Asymmetric Cyclopropanation Catalyzed by Chiral Cobalt(II) Complexes from (1R)-3-Hydroxymethylene-Bornane-2-Thione.

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Abstract: The Co(II) complex **3**, derived from (1R)-3-hydroxymethylene-bornane-2-thione and ethylenediamine was used as chiral catalyst for the asymmetric cyclopropanation of styrene and 1-octene by ethyl diazoacetate.

Some years ago Nakamura and Otsuka¹ reported the asymmetric cyclopropanation of conjugated olefins by diazoalkane derivatives and chiral bis(α -camphorquinonedi-oximate) cobalt(II) or related complexes; unconjugated olefins or vinyl ethers failed to react. The Japanese authors interpreted the experimental data with metal carbene-metalocyclobutane intermediates though the unusual reactivity may be inferred from an alternative mechanism.²

To the best of our knowledge no other reports have been published on the catalytic activity and application of cobalt(II)-camphor derivative complexes. On the other hand extensive research has been developed for performing asymmetric cyclopropanations of olefins with chiral copper³ or rhodium⁴ catalysts.

For some time our group has been interested in the synthesis, spectroscopical characterization and stereochemistry of metal complexes **1** derived from the condensation of (1R)-3-hydroxymethylene-bornane-2-thione and diamines.⁵

Figure 1

In this paper we report our preliminary results on the asymmetric cyclopropanation of styrene and 1-octene by ethyl diazoacetate and the cobalt(II) complex **3**.

The ligand **2** was prepared as previously described by us.⁵ By reacting compound **2** with cobalt(II) dichloride hexahydrate in degassed ethanol under argon atmosphere, the complex **3** was isolated in nearly quantitative yields.

Scheme 1

The cyclopropanation reactions of styrene and 1-octene with ethyl diazoacetate were run at 35 °C with a 3% molar amount, relative to ethyl diazoacetate, of the catalyst **3**. The cyclopropane derivatives **4**, **5**, **6** and **7** were isolated from the reaction mixture in 50-60% yield. Table 1 reports the diastereoisomeric ratio and the enantiomeric excess of compounds **4**, **5**, **6** and **7**.

Scheme 2

As depicted in Table 1, the results in terms of enantioselectivity are opposite for styrene (75%ee for the cis isomer) and 1-octene (97% for the trans isomer). While further investigations are necessary to interpret these experimental data, the unprecedented reactivity with excellent enantioselectivity of the complex **3** towards simple olefins such as 1-octene is noteworthy.

Table I. Asymmetric cyclopropanation of styrene and 1-octene by ethyl diazoacetate and the Co(II) complex 3

Diastereoselectivity ^a	Enantioselectivity (%ee) ^{b,c}	
4 + 5	4	5
1.8 : 1	20	75
6 + 7 ^d	6	7
1.8 : 1	97	18

^aThe diastereoisomeric ratio was determined by both ¹H-NMR spectroscopy on the crude reaction mixture and capillary GLC analysis.

^bThe enantiomeric excess was determined by ¹H-NMR spectroscopy in the presence of Eu(hfc)₃ on the methyl esters obtained by hydrolysis of compounds 4-7 and subsequent treatment with diazomethane. The enantiomeric excess was also verified by ¹⁹F-NMR spectroscopy of the Mosher esters obtained by reduction of compounds 4-7 by LiAlH₄ and reaction of the corresponding alcohols with (+)-MTPACl.

^cThe absolute configuration of compounds 4 and 5 was shown to be 1S, 2S and 1S, 2R, respectively, by chiroptical comparison with reported values (reference 3). The absolute configuration of compounds 6-7 was not determined.

^dThe relative configuration of compounds 6 and 7 was established by comparison with the reported ¹H-NMR data of the analogous derivatives of 1-heptene (reference 3).

Having in hand the copper complex 1 (R=CH₂CH₂, M=Cu(II))⁵, we reacted styrene with ethyl diazoacetate in the presence of this catalyst; while the chemical yields were superior (70-80%), the enantiomeric excess of the *trans* and *cis* diastereoisomers was 43% and 35%, respectively.⁶

The chiral complexes such as 1 represent simple and potentially versatile catalysts for asymmetric synthesis. Further study is under way in our laboratory.

Typical procedure: Synthesis of the Co(II) complex 3 and asymmetric cyclopropanation of styrene and 1-octene.

To a solution of the ligand 2 (0.416 g, 1 mmol) in degassed ethanol (5 ml) was added sodium hydroxide (1M methanolic solution, 2 ml) at room temperature and under argon atmosphere. After 1h, and at the same temperature, a solution of Co(II) dichloride hexahydrate (0.237 g, 1 mmol) in degassed ethanol (5 ml) was added dropwise. A brown solid separated out immediately. The reaction mixture was left for 30 min under stirring. The microcrystalline solid was filtered under argon atmosphere and dried *in vacuo*. The thus obtained complex 3 (0.465 g, nearly quantitative yields) was submitted to elemental and spectroscopical analyses without further purification [Found: C, 60.12; H, 7.03; N, 6.09. Calc. for C₂₄H₃₄CoN₂S₂: C, 60.89; H, 7.19; N, 5.92. IR (Nujol mull, cm⁻¹): 1638 w, 1551 s, 1493 s, 1201 m, 721 m. UV (MeOH), λ/nm (ε/dm³ mol⁻¹ cm⁻¹): 268 (2500), 312 (1460), 336 (1200), 358 (1100), 388 (1350), 438 (1500)]

A solution of ethyl diazoacetate (0.905 g, 7.95 mmol) in the appropriate alkene (1 ml) was added, via a syringe pump, to a solution of complex 3 (0.116 g, 0.24 mmol) in alkene (2 ml) over a 16h period at 35°C under argon atmosphere. The reaction mixture was stirred at the same temperature until the complete disappearance of ethyl diazoacetate [TLC: light petroleum-ethyl acetate 9:1; 24h for styrene; 48h for 1-octene]. After cooling at room temperature, the reaction mixture was chromatographed on silica gel, eluting with light petroleum first and then with light petroleum/ethyl acetate 9:1. The mixture of the *trans* and *cis* diastereoisomers was obtained in 50-60% yield.

Pure *trans* and *cis* diastereoisomers were obtained by preparative TLC (light petroleum/ethyl acetate 19:1).

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References and Notes

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