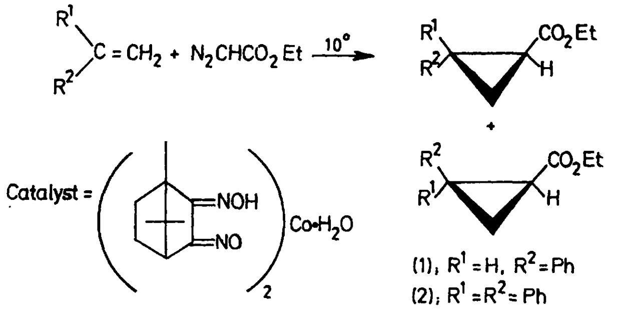
Enantioselective Synthesis of 2-Phenylcyclopropanecarboxylates through Chiral Cobalt Chelate Complex-catalysed Carbenoid Reactions

By Yoshitaka Tatsuno, Akira Konishi, Akira Nakamura, and Sei Otsuka*
(*Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka, Japan* 560)

Summary Enantioselective cyclopropanation (70% enantiomeric excess) through carbenoid reaction of diazoalkanes has been achieved using bis-[(+)-camphorquinonedioximato]cobalt(II) as catalyst.

Although optically active, substituted cyclopropanes have been prepared by carbenoid reactions of diazoalkanes catalyzed by metal complexes having chiral ligands, the stereoselectivity achieved was less than 10%.[1] We have found that optically active cyclopropanecarboxylic acid derivatives can be prepared in 90% yield with enantioselectivity as high as 70% by use of a chiral cobalt chelate complex.

The cobalt catalyst was prepared by reaction of (+)-camphorquinone-α-dioxime (α-CQDOH)[2] with cobalt(II) chloride in alkaline aqueous ethanol under nitrogen. An air-sensitive brown powder formulated as Co(α-CQDO)$_2$·H$_2$O, decomp. 240° (under nitrogen), was obtained (73%), and was soluble in most organic solvents. Ethyl diazoacetate was added dropwise to a styrene solution of the catalyst (2·6 mol %) at 10° under nitrogen, resulting in vigorous evolution of gas. After distillation of the crude carbenoid reaction product (91%), ethyl *cis*- and *trans*-2-phenylcyclopropanecarboxylate (**1**) were separated by preparative g.l.c. to give a nearly 1 : 1 mole ratio of the two isomers. The *trans*-acid formed by hydrolysis has $[\alpha]_D^{22}$ +266° (*c* 0·695, CHCl$_3$); this indicates an enantiomer with (1*S*, 2*S*) configuration[3] in 70% excess. The *cis*-acid has $[\alpha]_D^{21}$ +13·5° (*c* 1·72, CHCl$_3$) showing predominance of (1*S*, 2*R*) configuration[4] in 68% excess. Such high stereoselectivity has not been achieved for catalytic carbon–carbon bond formation apart from a few recent examples of nickel-catalyzed reactions.[5] Achiral olefins, *e.g.* Ph$_2$C=CH$_2$, gave optically active substituted cyclopropanes with



(1), R^1 = H, R^2 = Ph
(2); R^1 = R^2 = Ph

somewhat lower selectivity. Thus the reaction of 1,1-diphenylethylene with ethyl diazoacetate in the presence of the same catalyst gave ethyl 2,2-diphenylcyclopropanecarboxylate (**2**) (70%) with the (+)-(*S*) enantiomer[6] *ca.* 37% e.e. Higher stereoselectivity was obtained in the cyclopropanation with a diazo compound of type N_2CRR^1, *e.g.* N_2CHCO_2Et, than with symmetrical ones, *e.g.* $N_2C(CN)_2$. The reaction with styrene gave 1,1-dicyano-2-phenylcyclopropane (20%) with the (+)-(*R*) enantiomer[7] *ca.* 4·6% e.e. These results suggest that a cobalt–carbene complex is an important intermediate leading to asymmetric induction. A similar cobalt–carbene complex has been proposed[8] in the reaction of octaethylporphinatocobalt(II) with ethyl diazoacetate.

Cobalt catalyst systems comprising an achiral dioxime ligand, *e.g.* dimethylglyoxime or benzildioxime, and a chiral axial base, *e.g.* cinchonidine, gave totally optically inactive or slightly active 2-phenylcyclopropanecarboxylates. Apparently the chirality of the axial base is not effective in inducing dissymetry in the carbenoid reaction. The stereoselectivity also depends critically on the proper choice of metal species and ligands. Bis(hydroxymethylenecamphorato)palladium(II) or (*S*)-(*N*,*N*-dimethyl-α-methylbenzylamine-2-*C*,*N*)palladium chloride[9] vigorously decomposes ethyl diazoacetate in styrene to give 2-phenylcyclopropanecarboxylates only in a low e.e (maximum 1%).

In comparison with previous catalyst systems,[1] the present chiral chelate ligand system proved highly efficient in asymmetric carbenoid reactions. A reasonable mechanism accounting for the stereochemistry of the reaction can be suggested on the basis of the absolute configuration of the chelate ligand and the cyclopropanation products.[10] The catalyst system is easily preparable, and thus gives a route to chiral cyclopropane derivatives including naturally occurring ones.

(*Received*, 30*th April* 1974; *Com.* 492.)

---

[1] H. Nozaki, H. Takaya, S. Moriuti, and R. Noyori, *Tetrahedron*, 1968, **24**, 3655; W. R. Moser, *J. Amer. Chem. Soc.*, 1969, **91**, 1135, 1141.

[2] M. O. Forster, *J. Chem. Soc.*, 1903, **83**, 514.

[3] Y. Inoue, T. Sugita, and H. M. Walborsky, *Tetrahedron*, 1964, **20**, 1695.

[4] T. Aratani, Y. Nakanishi, and H. Nozaki, *Tetrahedron*, 1970, **26**, 1765.

[5] G. Wilke, G. Bogdanovič, B. Henc, and B. Meister, *Angew. Chem. Internat. Edn.*, 1972, **11**, 1023; G. Bogdanovič, B. Henc, A. Lösler, B. Meister, H. Pauling, and G. Wilke, *ibid.*, 1973, **12**, 954; Y. Kiso, K. Tamao, N. Miyake, K. Yamamoto, and M. Kumada, *Tetrahedron Letters*, 1974, 3.

[6] H. M. Walborsky, L. Barash, A. E. Young, and F. J. Impastato, *J. Amer. Chem. Soc.*, 1961, **83**, 2517.

[7] E. W. Yankee, B. Spencer, N. E. Howe, and D. J. Cram, *J. Amer. Chem. Soc.*, 1973, **95**, 4220.

[8] A. W. Johnson, in 'Organometallic Chemistry,' eds. F. G. A. Stone and M. I. Bruce, Butterworths, London, 1970, p. 381.

[9] S. Otsuka, A. Nakamura, T. Kano, and K. Tani, *J. Amer. Chem. Soc.*, 1971, **93**, 4301.

[10] S. Otsuka *et al.*, to be published.