earlier references in the series; (c) G. Neif and R. Weichert, *Chem. Ber.*, **109**, 3025 (1976); (d) U. Eder, H. Gibian, G. Haffer, G. Neef, G. Sauer, R. Wiechert, *Chem. Ber.*, **109**, 2948 (1976); (e) T. Kametani, H. Nemoto, H. Ishikawa, K. Shiroyama, and K. Fukumoto, *J. Am. Chem. Soc.*, **98**, 3378 (1976); (f) A. R. Daniewski and M. Kocor, *J. Org. Chem.*, **40**, 3136 (1975), and earlier references in the series; (g) G. Sauer, U. Eder, G. Haffer, G. Neef, and R. Wiechert, *Angew. Chem., Int. Ed. Engl.*, **14**, 417 (1975); (h) R. A. Micheli, Z. G. Hajos, N. Cohen, D. R. Parrish, L. A. Portland, W. Sciamanna, M. A. Scott, and P. A. Wehrle, *J. Org. Chem.*, **40**, 675 (1975); (i) N. Cohen. B. L. Banner, W. F. Eichel, D. R. Parrish, G. Saucy, J. M. Cassal, W. Meier, and A. Furst, *ibid.*, **40**, 681 (1975).
(3) For a few early examples, see (a) W. Cole and P. L. Julian, *J. Am. Chem. Soc.*, **67**, 1369 (1945); (b) A. Romeo and R. Williotti, *Ann. Chim. (Rome)*, **47**, 618 (1957); (c) K. Tsuda and K. Sakai, *Chem. Pharm. Bull.*, **9**, 529 (1961); (d) U. Kerb, G. Schulz, P. Hocks, R. Wiechert, A. Furlenmeier, A. Furst, A. Langemann, and G. Waldvogel, *Helv. Chim. Acta*, **49**, 1601 (1966). For a few recent examples, see (e) S. C. Eyley and D. H. Williams, *J. Chem. Soc.*, *Perkin Trans. 1*, 727 (1976); (f) W. Suerow and W. Littmann, *Chem. Ber.*, **109**, 2884 (1976).
(4) J. J. Partridge, V. Toome, and M. R. Uskokovic, *J. Am. Chem. Soc.*, **98**, 3739 (1976).
(5) (a) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. McLamore, *J. Am. Chem. Soc.*, **74**, 4223 (1952); (b) H. M. E. Cardwell, J. W. Cornforth, S. R. Duff, H. Holtermann, and R. Robinson, *J. Chem. Soc.*, 361 (1953); (c) W. S. Johnson, J. A. Marshall, J. F. W. Keana, R. W. Franck, D. G. Martin, and V. J. Bauer, *Tetrahedron, Suppl.*, **8** (2), 541 (1966).
(6) P. Kurath and M. Capezzuto, *J. Am. Chem. Soc.*, **78**, 3527 (1956).
(7) (a) J. P. Schmit, M. Piraux, and J. F. Pilette, *J. Org. Chem.*, **40**, 1586 (1975); (b) T. C. McMorris and S. R. Schow, *ibid.*, **41**, 3759 (1976); (c) W. R. Nes, T. E. Varkey, and K. Krevitz, *J. Am. Chem. Soc.*, **99**, 260 (1977).
(8) J. Wicha and K. Ba, *J. Chem. Soc., Chem. Commun.*, 968 (1975).
(9) I. J. Bolton, R. G. Harrison, and B. Lythgoe, *J. Chem. Soc. C*, 2950 (1971).
(10) For a preliminary report of a portion of this work, see B. M. Trost and T. R. Verhoeven, *J. Am. Chem. Soc.*, **98**, 630 (1976).
(11) Cf (a) A. M. Krubiner and E. P. Oliveto, *J. Org. Chem.*, **31**, 24 (1966); (b) A. Krubiner, N. Gottfried, and E. Oliveto, *ibid.*, **33**, 1715 (1968).
(12) B. M. Trost and P. E. Strege, *Tetrahedron Lett.*, 2603 (1974).
(13) (a) H. C. Volger, *Recl. Trav. Chim. Pays-Bas*, **88**, 225 (1969); (b) K. Vireze, H. C. Volger, and P. W. N. M. van Leeuwen, *Inorg. Chim. Acta Rev.*, **3**, 109 (1969); (c) J. W. Faller, M. E. Thomsen, and M. J. Mattina, *J. Am. Chem. Soc.*, **93**, 2642 (1971).
(14) B. M. Trost and L. Weber, *J. Am. Chem. Soc.*, **97**, 1611 (1975).

(15) B. M. Trost and T. J. Fullerton, *J. Am. Chem. Soc.*, **95**, 292 (1973).
(16) For a review see J. E. McMurry, *Org. React.*, **24**, 187 (1976).
(17) Adapted from a procedure of W. S. Johnson, private communication.
(18) K. E. Atkins, W. E. Walker, and R. M. Manyik, *Tetrahedron Lett.*, 3821 (1970); K. Takahashi, A. Miyake, and G. Hata, *Bull. Chem. Soc. Jpn.*, **45**, 230 (1972); H. Onoue, I. Moritani, and S. I. Murahashi, *Tetrahedron Lett.*, 121 (1973).
(19) (a) B. M. Trost and T. R. Verhoeven, *J. Org. Chem.*, **41**, 3215 (1976); (b) B. M. Trost and P. E. Strege, *J. Am. Chem. Soc.*, **99**, 1649 (1977); (c) B. M. Trost and Y. Matsumura, *J. Org. Chem.*, **42**, 2036 (1977).
(20) A. C. Cope and J. K. Heeren, *J. Am. Chem. Soc.*, **87**, 3125 (1965), and earlier references; J. K. Crandall and L. C. Lin, *J. Org. Chem.*, **33**, 2375 (1968), and earlier references; C. L. Kissel and B. Rickborn, *J. Org. Chem.*, **37**, 2060 (1972).
(21) For differential regioselectivity, see B. M. Trost and S. Kurozumi, *Tetrahedron Lett.*, 1929 (1974); A. Yasuda, S. Tanaka, K. Oshima, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **96**, 6514 (1974); C. G. Pitt, M. S. Fowler, S. Sathe, S. C. Srivastava, and D. L. Williams, *ibid.*, **97**, 3798 (1975).
(22) (a) V. T. Bhalerao and H. Rapoport, *J. Am. Chem. Soc.*, **93**, 4835 (1971); (b) for a review, see N. Rabjohn, *Org. React.*, **24**, 261 (1976); (c) also see D. Arigoni, A. Vasella, K. B. Sharpless, and H. P. Jensen, *J. Am. Chem. Soc.*, **95**, 7917 (1973).
(23) B. M. Trost, H. C. Arndt, P. E. Strege, and T. R. Verhoeven, *Tetrahedron Lett.*, 3477 (1976).
(24) T. J. Scallen and W. Kreuger, *J. Lipid Res.*, **9**, 120 (1968).
(25) P. E. Strege and T. R. Verhoeven, unpublished work in these laboratories.
(26) Cf. K. S. Y. Law, P. K. Wong, and J. K. Stille, *J. Am. Chem. Soc.*, **98**, 5832 (1976); J. K. Stille and K. S. Y. Law, *ibid.*, **98**, 5841 (1976); A. V. Kramer, J. A. Labinger, J. S. Bradley, and J. A. Osborn, *ibid.*, **96**, 7145 (1974); A. V. Kramer and J. A. Osborn, *ibid.*, **96**, 7832 (1974).
(27) For information of the first stable olefin–palladium(0) complex, see R. van der Linde and R. O. de Jongh, *Chem. Commun.*, 563 (1971).
(28) K. Vrieze, "Dynamic NMR Spectroscopy", Academic Press, New York, N.Y., 1975, p 441.
(29) The rate of this reaction relative to the rate of alkylation is clearly substrate dependent. If interconversion requires formation of a σ bond to a tertiary carbon, interconversion is slow relative to alkylation.[19a] On the other hand, such is not the case if formation of a σ bond to a secondary carbon is involved (T. R. Verhoeven, unpublished results).
(30) B. M. Trost and Y. Matsumura, submitted for publication.
(31) D. J. Vanderah and C. Djerassi, *Tetrahedron Lett.*, 683 (1977).
(32) L. F. Fieser and M. Fieser, "Steroids", Reinhold New York, N.Y., 1959.

A Highly Enantioselective Synthesis of Cyclopropane Derivatives through Chiral Cobalt(II) Complex Catalyzed Carbenoid Reaction.[1] General Scope and Factors Determining the Enantioselectivity

Akira Nakamura,*[2a] Akira Konishi,[2b] Yoshitaka Tatsuno,[2b] and Sei Otsuka*[2b]

Contribution from the Department of Polymer Science, Faculty of Science, and the Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka, Japan 560. Received May 23, 1977

Abstract: Optically active cyclopropane derivatives, e.g., *cis*- and *trans*-2-phenylcyclopropanecarboxylic acid, were prepared by carbenoid type reactions between olefins and diazoalkanes catalyzed by bis[(−)-camphorquinone-α-dioximato]cobalt(II). A high enantioselectivity (maximum 88% optical yield) was achieved with a high chemical yield (90–95%) for the preparation of neopentyl *trans*-2-phenylcyclopropanecarboxylate, using a 3 mol % catalyst concentration at 0 °C. The reaction occurs selectively at a terminal double bond conjugated with a vinyl, aryl, or alkoxycarbonyl group. Diazo compounds containing electron-attracting groups (CO_2R, COR, or CN) can be used. The (1*S*) enantiomer was always in large excess (60–80% ee) in the 2-substituted cyclopropanecarboxylates thus obtained with this catalyst.

Optically active cyclopropane derivatives have been prepared,[3] for example, by the reaction of olefins with stoichiometric amounts of chiral sulfonium ylides (maximum optical yield 30%),[4] by the Simmons–Smith reactions (CH_2X_2/Zn) employing chiral substrates (optical yield 9.3%),[5] or by catalytic olefin cyclopropanation with diazoalkanes under the influence of chiral copper complexes (maximum optical yield 8%).[6,7] In the course of our study on the interaction of diazo compounds with transition metal compounds,[8] we have been interested in the asymmetric carbenoid reaction of diazo

compounds catalyzed by chiral metal complexes. Among many complexes examined, bis(α-camphorquinonedioximato)-cobalt(II) was found to be an active catalyst for the formation of optically active cyclopropanes with over 80% optical yield. The chemical yield is often in the range 80–95% and only a small amount (1 mol % relative to diazo compound) of catalyst is required. The ready availability of the chiral camphorquinonedioxime ligand from natural sources is also an advantage. Recently, communications[9] have appeared describing cyclopropanation of 2,5-dimethyl-2,4-hexadiene with various chiral

Table I. Asymmetric Synthesis of Ethyl 2-Phenylcyclopropanecarboxylate with Co(α-cqd)$_2$·H$_2$O as Catalyst

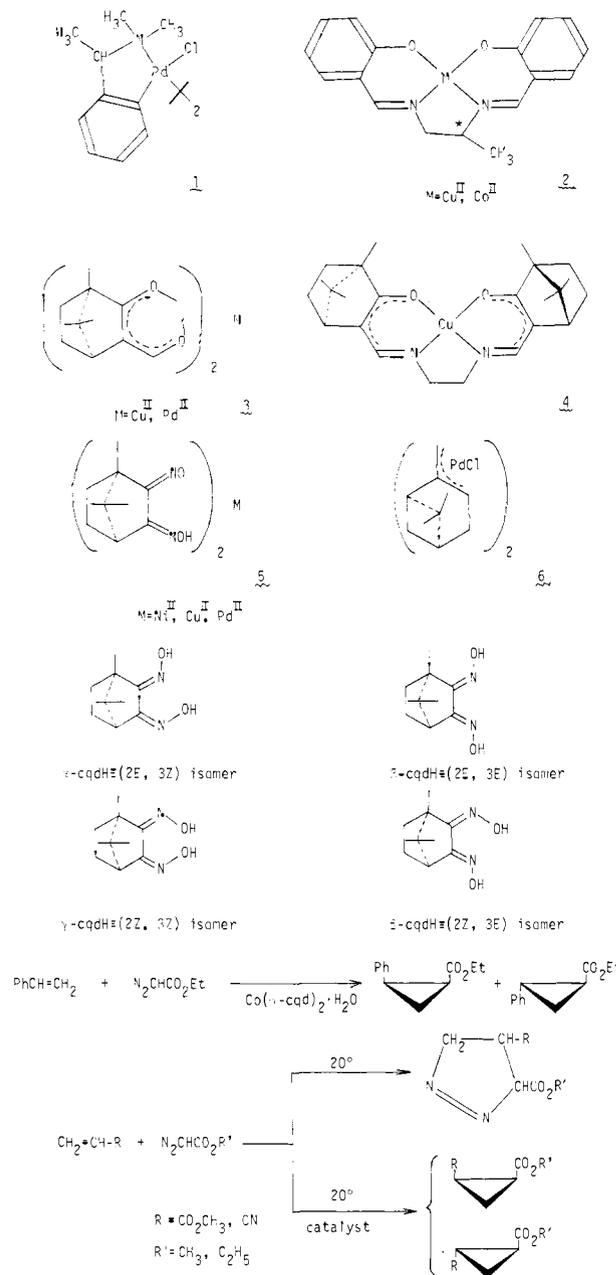| Catalyst[b] mol %	Temp, °C	Yield,[b] %	Trans/cis[c]	[α]$_D$, deg		Optical yield,[d] %	
				Trans	Cis	Trans	Cis
3	99	95	1.3	+102	+2.9	33	16
3	24	93	0.98	+236	+11	75	61
3	0	92	0.85	+236	+12	75	67
3	−15	80	0.95	+239	+13	76	72
1	0	87	0.75	+233	+12	74	67
0.5	0	51	0.95	+186	+9.6	59	53

[a] Reaction was performed in neat styrene. [b] Based on ethyl diazoacetate. [c] Ratio of area in the GLC peaks. [d] The product was hydrolyzed to the corresponding acid and optical yield was calculated from the specific rotation, cis acid [α]$_D$ +30°, A. Aratani, Y. Nakanishi, and H. Nozaki, *Tetrahedron*, **26**, 1675–1684 (1970); trans acid [α]$_D$ +381°, Y. Inouye, T. Sugita, and H. W. Walborsky, *Tetrahedron*, **20**, 1695–1699 (1964).

copper chelates with a highly complex ligand (enantioselectivity, 90% max ee).

Since the usefulness of cobalt(II) chelates for catalyzing carbenoid cyclopropanation has been unexplored, we mostly confined our investigations to a cobalt(II) complex of camphorquinonedioxime (cqdH)[10] which is now the best enantioselective catalyst for preparation of *cis*- and *trans*-2-phenylcyclopropanecarboxylic acid. The preparation of the catalyst, details of the reaction, and its general scope and limitations are described in this pyrazoline formed from the acrylate sets in above 60 °C yielding racemic dimethyl cyclopropanedicarboxylate. In the presence of the highly active cyclopropanation catalysts Co(α-cqd)$_2$·H$_2$O, the reaction in part catalyzed at 22 °C gives a mixture of the cyclopropane and the pyrazoline. Optically active dimethyl *trans*-cyclopropanedicarboxylate was obtained in low yields by distillation of the mixture at 34 °C. Chiral catalysts of lower activity (e.g., Cu[sal(−)pn]) did not give the optically active cyclopropane by direct carbenoid reaction because the uncatalyzed pyrazoline formation occurs first. A similar reaction of acrylonitrile with ethyl diazoacetate at 47–49 °C also proceeds simultaneously via catalyzed and uncatalyzed paths to give mixed *cis*-/*trans*-2-cyanocyclopropanecarboxylate (13% yield) and the corresponding pyrazoline, respectively.

Butadiene or isoprene is cyclopropanated using the same catalyst in an autoclave or in glass pressure tubes to give a cis/trans mixture of 2-vinyl- or 2-isopropenyl cyclopropanecarboxylates (Table II) which are not readily separable by GLC. The reaction of *trans*-1-phenyl-1,3-butadiene with ethyl diazoacetate in the presence of Co(α-cqd)$_2$·H$_2$O also gave a mixture of *cis*- and *trans*-2-(*trans*-2′-phenylvinyl)cyclopropanecarboxylate in good yields. The absence of the cyclopropanation products at the inner double bond is confirmed by the GLC and ^{1}H NMR data (see Experimental Section), indicating high regioselectivity. Similar cyclopropanation of isoprene is not very regioselective and a 3:1 mixture of the products involving cyclopropanation at the methylvinyl and vinyl moieties was obtained. Optical yields and absolute configurations of these products from butadiene, isoprene, and *trans*-1-phenyl-1,3-butadiene are unknown, but the [α]$_D$ values (see Table III) are relatively large, suggesting a high degree of enantioselectivity in the catalysis.

The enantioselective cyclopropanation can be extended to other diazoalkanes (cf. Table III). The ester group of the diazoacetate can be varied without any serious effect. An increase in the size of the ester group (methyl, ethyl, isopropyl, neopentyl) gave important information regarding the enantioselection mechanism which is discussed separately in another paper. Diazomethane, diazoacetophenone, and dicyanodiazomethane are catalytically decomposed at 20–40 °C with Co(α-cqd)$_2$·H$_2$O. Even highly reactive diazomethane does cyclopropanation selectively with terminal olefins, e.g., styrene, in the presence of Co(α-cqd)$_2$·H$_2$O. The similar reaction in

1

2

3

4

5

6

M=Ni^{II}, Cu^{II}, Pd^{II}

ε-cqdH≡(2E, 3Z) isomer

γ-cqdH≡(2Z, 3Z) isomer

?-cqdH≡(2E, 3E) isomer

ε-cqdH≡(2Z, 3E) isomer

$$PhCH=CH_2 \ + \ N_2CHCO_2Et \ \xrightarrow{Co(\alpha\text{-cqd})_2\cdot H_2O} \ Ph\text{-}CO_2Et \ + \ Ph\text{-}CO_2Et$$

trans-1-phenyl-1-propene, however, gave only polymethylene. Bulky diazo compounds such as Ph$_2$CN$_2$ or 9-diazofluorene are not decomposed even above 60 °C. The reaction of dicyanodiazomethane with styrene proceeded at 35 °C to give 2-phenyl-1,1-dicyanocyclopropane in 20% yield. The enantioselectivity was only 4.6% and side reactions predominated.

Table II. Asymmetric Cyclopropanation of Various Olefins with Ethyl Diazoacetate[a]

Olefin substrate	Catalyst[b] mol %	Temp, °C	Yield,[b] %	Product	Configuration	Optical yield,[c] % ([α]D)
PhCH=CH2	3.0	0	92	Ph CO2Et	(1S,2R)[d]	67[d]
				CO2Et / Ph	(1S,2S)[d]	75[d]
Ph2C=CH2	2.5	5	95	Ph CO2Et / Ph	(1S)[e]	70[e]
Ph(MeO2C)C=CH2	2.1	0	92	MeO2C CO2Et / Ph	(1R,2S)[f]	37[f]
				Ph CO2Et / CO2Me	(1S,2S)[f]	71[f]
Ph(Me)C=CH2	2.4	0	97	Ph CO2Et / Me	g	(+35.4°)
				Me CO2Et / Ph	g	(+145°)
H(MeO2C)C=CH2[h]	2.0	22	11	CO2Me / CO2Me	(1S,2S)[i]	33[i]
H(NC)C=CH2	3.7	47–49	13	CN CO2Et	g	(+1.7°)
				CO2Et / CN	g	(+13.6°)
H2C=CH–CH=CH2	1.7	40	87	CO2Et / H2C=CH	g	(+120°)[j]
H2C=C(CH3)–CH=CH2				CO2Et / H2C=C—CH3	g	(+115°)[j]
				H3C CO2Et / H2C=CH	g	(+145°)[j]
Ph–CH=CH–CH=CH2	2.9	20–22	92	Ph CO2Et	g	(−13.8°)
				CO2Et / Ph	g	(+213°)

[a] Reaction was performed in each neat olefin. [b] Based on ethyl diazoacetate. [c] Based on the highest specific rotation of the corresponding acid unless otherwise noted. [d] Cf. Table I, footnote *d*. [e] H. W. Walborsky, L. Barash, A. E. Young, and F. J. Impastato, *J. Am. Chem. Soc.*, **84**, 4831–4838 (1962). The highest value, [α]D +230 ± 5°. [f] K. Nishiyama, J. Oda, and Y. Inouye, *Bull. Chem. Soc. Jpn.*, **47**, 3175–3176 (1976). The highest value, cis [α]D +212°; trans [α]D +92.8°. [g] The absolute configuration is unknown. [h] Methyl diazoacetate was used instead of ethyl diazoacetate. [i] Y. Inouye, T. Sugita, and H. W. Walborsky, *Tetrahedron*, **20**, 1695–1699 (1964). Based on the highest specific rotation of the dimethyl ester, [α]D −333°. [j] Value obtained for a trans/cis mixture which could not be separated by GLC; hence the structural assignment has not been made.

Diazoacetophenone and styrene also give a mixture of *cis*- and *trans*-2-phenyl-1-benzoylcyclopropane (cf. Table III). The trans isomer was obtained in an optical yield of 20%, which is considerably lower than the value obtained with diazoacetates.
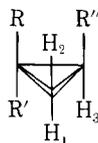
The optical rotation and configuration of the optically pure cis isomer are unknown.

Although most of the reactions have been performed in neat olefin, it is possible to dilute the reaction mixture with usual

Table III. Asymmetric Cyclopropanation of Styrene with Various Diazo Compounds

Diazo compd	Catalyst[b] mol %	Temp, °C	Yield,[b] %	Product	Configuration	Optical yield, % ([α]D)
N₂CHCO₂-neo-Pent	3.1	0	87	Ph CO₂-Pent	(1S,2R)[c]	81[c]
				CO₂-Pent / Ph	(1S,2S)[c]	88[c]
N₂C(CN)₂	5.6	30–35	20	Ph CN / CN	(2S)[d]	4.6[d]
N₂CHCOPh	9.4	45–50	44	Ph COPh	e	(−18.2°)
				COPh / Ph	(1S,2S)[f]	20[f]

[a] Reaction was performed in neat styrene. [b] Based on the diazo compound. [c] Cf. Table 1, footnote d. [d] E. W. Yankee, B. Spencer, N. E. Howe, and D. J. Cram, *J. Am. Chem. Soc.*, **95**, 4220–4230 (1973). The highest value, [α]₅₄₆ +227° (acetone). [e] The absolute configuration is unknown. [f] C. R. Johnson and C. W. Schroeck, *J. Am. Chem. Soc.*, **90**, 6852–6854 (1968). The highest value, [α]D +390.5°.

Table IV. ¹H NMR Data of Various Dissymmetric Cyclopropane Derivatives[a]

	R	R'	R''	R	R'	R''		H₁	H₂	H₃
1	Ph	H	CO₂H	7.19 s	2.54 q	11.22 s		1.26 mc	1.59 mc	1.94 mc
2	H	Ph	CO₂H	2.63 mc	7.24 mc	11.36 s		1.40 mc	1.66 mc	1.90 p
3	Ph	Ph	CO₂H	7.23 mc[c]		10.07 s		(1.61 q	2.88 t)	2.45 q
4	Ph	CH₃	CO₂C₂H₅	7.30 s	1.52 s	4.24 q	0.95 t	1.14 mc	1.98 mc[c]	
5	CH₃	Ph	CO₂C₂H₅	1.52 s	7.30 s	4.24 q	1.28 t	1.40 mc[c]		1.98 mc
6	CO₂CH₃	Ph	CO₂C₂H₅	3.64 s	7.38 mc	4.20 q	1.28 t	(1.50 mc	2.08 mc)[b]	2.20 mc
7	Ph	CO₂CH₃	CO₂C₂H₅	7.28 s	3.52 s	3.88 q	0.96 t	(1.88 mc	2.00 mc)[b]	2.75 mc
8	CN	H	CO₂C₂H₅		1.76 mc	4.26 q	1.30 t	1.48 mc	1.80 mc	2.08 mc
9	H	CN	CO₂C₂H₅	2.20 mc		4.21 q	1.28 t	1.46 mc	1.56 mc	1.90 mc
10	CN	CN	Ph			7.40 mc		2.20 mc[c]		3.30 mc
11	Ph	H	COPh	7.19 s	2.86 mc[c]	7.96 mc	7.46 mc	(1.39 mc	2.09 mc)[b]	2.86 mc[c]
12	H	Ph	COPh	2.70 mc[b]	7.26 mc	7.52 mc	8.06 mc	(1.55 mc	1.92 mc)[b]	2.90 mc[b]

[a] (δ ppm, from internal Me₄Si, 100 MHz, in CDCl₃): s, singlet; t, triplet; q, quartet; p, pentuplet; mc, multiplet center. [b] The assignment may be interchangeable. [c] Unresolvable.

Table V. Solvent Effect on Asymmetric Synthesis[a] of Ethyl 2-Phenylcyclopropanecarboxylate

	Yield,[b]		[α]D,[d] deg	
Solvent	%	Trans/cis[c]	Cis	Trans
None	92	0.85	+12	+236
Acetone	81	1.3	+5.4	+197
Ethyl acetate	92	1.0	+11	+222
Di-n-butyl ether	88	0.67	+12	+199
n-Hexane	67	0.85	+13	+223
Acetophenone	95	0.95	+11	+200

[a] Reaction was performed at 0 °C with 3 mol % of the catalyst (based on ethyl diazoacetate) with styrene concentration 2.6–2.9 M (in twofold molar excess). [b] Based on ethyl diazoacetate. [c] Ratio of area in the GLC peaks. [d] Measured in CHCl₃ with a cell (0.5 dm).

organic solvents, such as ethyl acetate to an extent of ~3 M for the olefin concentration. Further dilution deactivates the catalyst and retards very much the reaction rate. The results in Table V show that the enantioselectivity does not decrease appreciably in most cases. Use of more strongly coordinating solvents such as pyridine or picolines decreases the activity and selectivity. Effects of these additives will be fully described separately.

Discussion

Scope and Limitation. Although much remains to be elucidated in this cyclopropanation, it is important that the optical yield near room temperature is as high as 88%. This value constitutes a great improvement over other existing chiral cyclopropanation catalysts. Simple recrystallization of the product, e.g., 2-phenylcyclopropanecarboxylic acid, easily raises the optical purity to nearly 100% without appreciable loss of material. In addition, the yields of cyclopropane products are often very high (90–95%), side reactions being suppressed. Considering the ready availability of natural d-camphor, the Co(α-cqd)₂ catalyst is promising for large-scale single-step preparations of optically active cyclopropanes.

The application to simple monoolefins is, however, limited. Mono-, di-, or trialkylethylenes, cycloolefins or -dienes, sterically hindered conjugated dienes, and vinyl ethers cannot be cyclopropanated with ethyl diazoacetate using Co(α-cqd)₂.

H_2O as catalyst. Therefore, we conclude that $Co(\alpha\text{-cqd})_2$-catalyzed cyclopropanation is fairly regioselective to a terminal double bond which is in conjugation with such a group as an aryl, carbonyl, or olefinic bond. The method also fails for allenes (e.g., PhC_3H_3) and acetylenes (e.g., $PhC\equiv CH$). Perhaps the catalyst is deactivated by these acetylenes or allenes.

Enantioface Selection with $Co(\alpha\text{-cqd})_2$ Catalyst. There are two different sites in enantioface selection in cyclopropanation of olefins with singlet carbenes or metal carbenoids. One is enantioface selection of prochiral olefins (e.g., $RCH=CH_2$) and the other is of prochiral carbenes ($=CHR$) or carbenoids ($M=CHR$). In the $Co(\alpha\text{-cqd})_2$-catalyzed reaction, we have found that the prochirality of olefin is not always necessary in inducing the enantioselection. Thus, 1,1-diphenylethylene, a nonprochiral olefin, gave an optically active cyclopropane by the catalyzed reaction with ethyl diazoacetate in 70% optical yield. When nonprochiral carbenoid is generated from, e.g., $N_2C(CN)_2$, an only marginally optically active (4% optical yield) 1,1-dicyano-2-phenylcyclopropane was obtained by reaction with neat styrene.

Importance of enantioface selection of the carbene side is also demonstrated in the reaction of a prochiral olefin, e.g., styrene, with a prochiral carbenoid, e.g., ethyl diazoacetate. The major enantiomer of the cyclopropanation products, ethyl *cis-* and *trans*-2-phenylcyclopropanecarboxylate (molar ratio ca. 1:1), have $(1S,2R)$ and $(1S,2S)$ configurations, respectively. It is noteworthy to observe the S configuration of the carbon at C-1 position which is derived from the carbenoid species. This stereochemical result indicates the enantioface selection of the carbenoid side. Our result with the other olefins also showed that the predominating enantiomers of chiral cyclopropanes have S configuration at the carbon derived from the carbenoid component (see Figure 1).

If enantioselection of prochiral olefins and prochiral carbenoids both occurs, only one geometrical isomer (cis or trans) must be formed in large excess. This is not occurring with the $Co(\alpha\text{-cqd})_2$ catalyst since about equal amounts of cis and trans isomers are usually found.

These results suggest a cobalt–carbene complex as intermediate in the carbenoid cyclopropanation. A similar cobalt(II)–carbene complex has been proposed by Johnson[11] in the reaction of octaethylporphinatocobalt(II) with ethyl diazoacetate. Formation of carbene complexes has been observed for reactions of some metal complexes with diazoalkanes, e.g., $[Rh(CO)(CPh_2)Cl]_n$[12] or $(\eta^5\text{-}CH_3C_5H_4)Mn(CO)_2[C(Ph)\text{-}COPh]$.[13] The rhodium complex was found to have a bridging carbene ligand by an x-ray analysis.[14]

It is interesting to note that the formation of carbene dimers or azines is almost completely suppressed in the cyclopropanation. This specificity may arise from the sterically congested bischelate structure of the Co(II) catalyst. The correlation between the complex structure and the enantioselectivity will be the subject of a subsequent paper.

Although proper choice of olefins and diazo compounds is a crucial factor in realization of highly enantioselective cyclopropanation, this one-step preparation of various cyclopropanecarboxylates or of cyclopropyl ketones in high optical purity is regarded as an asymmetric synthetic method of considerable potential.

Experimental Section

The spectroscopic measurements were carried out by a Jeol MH-100 for ^1H NMR and Hitachi EPS-3T for electronic spectra. Optical rotation was measured with a JASCO DIP-SL. The carbenoid reactions and the physical measurements of Co(II) complexes were performed in a pure nitrogen atmosphere with degassed or N_2-saturated reagents and solvents.

Preparation of $(-)$-Camphorquinone-α- and -β-dioxime. Essentially the same procedure as reported by Forster[10] was used with some im-

provement. Isonitrosocamphor (Claisen mixture[15]) (80.4 g) prepared from *d*-camphor was dissolved in ethanol (400 mL) to which hydroxylamine hydrochloride (64.3 g) and sodium acetate (128.6 g) dissolved in water (420 mL) were added. From the clear solution, after 12 weeks at room temperature, pale brown crystals (73.4 g) were separated. On extracting the crystal four times with boiling acetone (each 300 mL), a white powder of the β-dioxime (16.5 g) remained. The crude β-dioxime was purified further by washing twice with boiling acetone (300 mL). When the hot acetone solution was cooled, pale yellow crystals of the α-dioxime (9.1 g) were separated. Colorless needles of the pure α-dioxime were obtained (6 g) by recrystallization from ethyl acetate (1000 mL). The β-dioxime melted with decomposition at 272–273 °C (lit. mp 248 °C). The melting point (201 °C) of the α-dioxime and the optical rotation of α-, $[\alpha]^{22}_D$ $-61.9°$ (c 1.87, ethanol), and β-dioxime, $[\alpha]^{22}_D$ $-24.1°$ (c 0.465, 2% aqueous NaOH), agree with the data reported by Forster.[10] The structures of camphorquinone dioximes proposed by Forster[10] have been revised by Daniel and Pavia,[16] who determined their structures with the aid of the ^1H NMR spectrum. Our samples had the same ^1H NMR data as reported by them.

Preparation of $(+)$-Camphorquinone-δ-dioxime. Repeated recrystallization of the residue remained upon extraction of α- and β-cqdH gave only 1.6 g of the δ isomer ($[\alpha]^{22}_D$ $+77°$, c 2.71, ethanol) based on 80.4 g of isonitrosocamphor. An improved method[10] for the preparation is as follows. A clear aqueous solution (1000 mL) of isonitrosocamphor (100 g), sodium hydroxide (90 g), and hydroxylamine hydrochloride (100 g) was kept at room temperature for 3 weeks. The solution was extracted with ether and the water layer was acidified with dilute sulfuric acid until no color change with aqueous $FeSO_4$ was observed. The aqueous solution was decanted to remove pale yellow gummy precipitates containing the γ and δ isomers and acidified further to give about 24 g of white γ-cqdH crystals. The optically pure δ isomer (10 g, $[\alpha]^{23}_D$ $+79°$, c 2.74, ethanol) was obtained from thermal isomerization of the γ isomer (24 g) under reflux in ethanol for 8 h and after three recrystallizations from methanol.

Preparation of Bis[(−)-camphorquinone-α-dioximato]cobalt(II) Hydrate. To a suspension of (−)-camphorquinone-α-dioxime (α-cqdH) (1.02 g, 5.22 mmol) and cobalt(II) chloride 6-hydrate (0.621 g, 2.61 mmol) in ethanol (40 mL) was added, with stirring, an aqueous solution of NaOH (0.209 g in 0.4 mL). After standing overnight, water (70 mL) was added to the brown solution. The brown powder precipitated was filtered, washed twice with water (10 mL), and dried in vacuo at room temperature to give the title compound (0.86 g, 73% yield), mp 240–241 °C (under N_2), λ_{sh} 400 nm(ϵ 3000 in ethanol). Anal. ($C_{20}H_{32}N_4O_5Co$) C, H, N.

Preparation of Bis[(−)-camphorquinone-β-dioximato]cobalt(II) Hydrate. This compound was prepared by the same method as described above for $Co(\alpha\text{-cqd})_2\cdot H_2O$: brown microcrystals, mp 295–296 °C (under N_2), λ_{max} 477 nm (ϵ 3100 in ethanol). Anal. ($C_{20}H_{32}N_4O_5Co$) C, H, N.

Preparation of Bis[(+)-camphorquinone-δ-dioximato]cobalt(II) Hydrate. This compound was prepared similarly using δ-cqdH: brown microcrystals, mp 252–253 °C (under N_2), λ_{sh} 400 nm (ϵ 3100 in ethanol). Anal. ($C_{20}H_{32}N_4O_5Co$) C, H, N.

Asymmetric Carbenoid Reaction with $Co(\alpha\text{-cqd})_2\cdot H_2O$ as Catalyst. Since all the asymmetric carbenoid reactions were carried out by similar procedures, only typical examples will be described. Experimental conditions and product characteristics are summarized in Tables II and III.

(1) Reaction of Ethyl Diazoacetate with Styrene. A solution of ethyl diazoacetate (1.81 g, 1.74 mmol) in styrene (2 mL) was added dropwise to a styrene (4 mL) solution of $Co(\alpha\text{-cqd})_2\cdot H_2O$ (0.231 g, 0.494 mmol) with stirring at −15 °C for 5 h. After nitrogen as evolution had ceased (2 h), the reaction mixture was distilled under reduced pressure (85–87 °C, 2 mm) to give a mixture of ethyl *cis-* and *trans*-2-phenylcyclopropanecarboxylate (2.6 g, 80% yield, cis/trans = 1:0.95). They were separated by GLC (Apiezon grease L). Each pure stereoisomer was then hydrolyzed with alkaline aqueous ethanol (1:1) at room temperature (during 24 h) to give *cis-* and *trans*-2-phenylcyclopropanecarboxylic acid.

The following optically active cyclopropanes were prepared by essentially the same procedure: ethyl 2,2-diphenylcyclopropanecarboxylate, ethyl 2-methyl-2-phenylcyclopropanecarboxylate, 1-methyl-2-ethyl 1-phenylcyclopropane-1,2-dicarboxylate, ethyl 1-methyl-2-vinylcyclopropanecarboxylate, and ethyl 2-(isopropenyl)-cyclopropanecarboxylate. For the chemical and optical yields and the
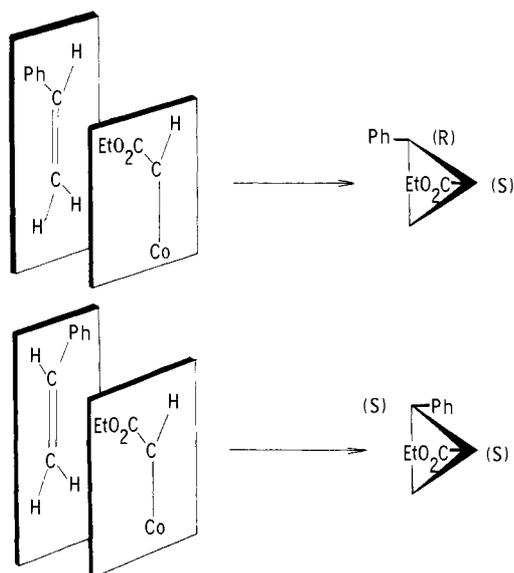
Figure 1.

¹H NMR data, see Tables II–IV.


¹H NMR data, see Tables II–IV.

(2) Reaction of Methyl Diazoacetate with Methyl Acrylate. Methyl diazoacetate (2.59 g, 25.9 mmol) was added dropwise to a methyl acrylate (5.8 mL) solution of Co(α-cqd)₂·H₂O (0.239 g, 0.431 mmol) at 22 °C for 1 h. The reaction mixture was distilled under reduced pressure (32–34 °C, 1 mm) to give dimethyl *trans*-cyclopropane-1,2-dicarboxylate (0.44 g, 11% yield), which was purified by GLC to give an analytically pure sample.

(3) Reaction of Diazoacetophenone with Styrene. A solution of di-azoacetophenone (0.82 g, 5.6 mmol) in styrene (2 mL) was added dropwise to a styrene (2 mL) solution of Co(α-cqd)₂·H₂O (0.247 g, 0.528 mmol) with stirring at 40–50 °C for 1 h. The reaction mixture was distilled under reduced pressure (155–160 °C, 1 mm) to give a mixture of *cis*- and *trans*-1-benzoyl-2-phenylcyclopropane (0.44 g, 44% yield, cis/trans = 1:1.6). The mixture was separated into pure components by GLC (Apiezon grease L).

(4) Reaction of Ethyl Diazoacetate with 1,3-Butadiene. A 100-mL autoclave chilled in a dry ice–methanol bath was charged with a 1,3-butadiene solution (29 g) of ethyl diazoacetate (9.18 g, 80.4 mmol) and Co(α-cqd)₂·H₂O (0.642 g, 0.137 mmol). The autoclave was shaken at 40 °C for 10 h after which period the pressure rose up to 24 kg/cm². The reaction mixture was distilled under reduced pressure (40–41 °C, 3 mm) to give a mixture of *cis*- and *trans*-vinylcyclopropanecarboxylate (9.56 g, 85% yield) which was purified to give an analytically pure sample.

(5) Reaction of Ethyl Diazoacetate with *trans*-1-Phenyl-1,3-butadiene. A solution of ethyl diazoacetate (3.16 g, 27.7 mmol) in *trans*-1-phenyl-1,3-butadiene was added dropwise to a *trans*-1-phenyl-1,3-butadiene (3.8 g) solution of Co(α-cqd)₂·H₂O (0.380 g, 0.813 mmol) with stirring at 20–22 °C for 4 h. After nitrogen evolution had ceased, the reaction mixture was distilled under reduced pressure (117–122 °C, 1.5 mm) to give a mixture of ethyl *cis*- and *trans*-2-(*trans*-2′-phenylvinyl)cyclopropanecarboxylate (5.16 g, 92% yield, trans/cis = 0.79:1). The mixture was separated into the pure isomers by GLC (Apiezon grease L, 10%, 1.5 m, 185 °C). The optical rotation: cis isomer, [α]²⁰D −13.8° (c 1.45, CHCl₃); trans isomer, [α]²⁰D +213° (c 1.30, CHCl₃). Anal. (C₁₃H₁₅O₂) C, H (for both isomers).
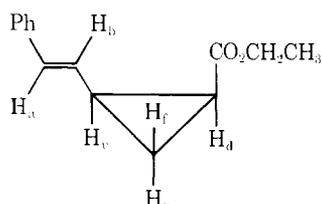
¹H NMR (CDCl₃) δ 7.29 (mc, aromatic), 6.63 (d, Hₐ), 6.25 (q, H_b), 4.17 (q, CH₂, J = 6.5 Hz), 2.10 (mc, H_c, H_d), 1.35 (mc, H_e, H_f), 1.25 (t, CH₃, J = 6.5 Hz)
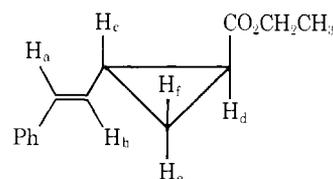
δ 7.13 (mc, aromatic), 6.56 (d, Hₐ), 5.77 (q, H_b), 4.18 (q, CH₂, J = 7 Hz), 2.19 (mc, H_c), 1.78 (mc, H_d), 1.50 (mc, H_e), 1.27 (t, CH₃, J = 7 Hz), 1.06 (mc, H_f)

Reactions of Ethyl Diazoacetate with Styrene Catalyzed by Several Other Complexes. Typical results are listed in an order of (1) catalyst, (2) catalyst concentration (mol % based on ethyl diazoacetate), (3) reaction temperature, (4) yield (based on ethyl diazoacetate), (5) trans/cis ratio, and (6) [α]D value (in CHCl₃).

(a) (1) Di-μ-chloro-bis[(−)-*N*,*N*-dimethyl-α-phenethylamine-2-*C*,*N*]-dipalladium(II)[17] (1), (2) 4 mol %, (3) −20 °C, (4) 37%, (5) 2.0, (6) cis ≃0°, trans +1.2°.

(b) (1) Bis[salicylaldehyde-(+)-propylenediiminato]cobalt(II) (2), (2) 4 mol %, (3) 27 °C, (4) 90%, (5) 1.8, (6) cis +0.8°, trans +8.1°.

(c) (1) Bis[salicylaldehyde-(−)-propylenediiminato]copper(II) (2), (2) 2 mol %, (3) 53–56 °C, (4) 79%, (5) 2.7, (6) cis +3.2°, trans +29°.

(d) (1) Bis[(+)-hydroxymethylenecamphorato]copper(II)[18] (3), (2) 18 mol %, (3) 55–56 °C, (4) 72%, (5) 2.2, (6) cis +0.2°, trans +2.3°.

(e) (1) Bis[(+)-hydroxymethylenecamphorato]palladium(II) (3), (2) 13 mol %, (3) −10 °C, (4) 57%, (5) 2, (6) cis ≃0°, trans ≃0°.

(f) (1) (1*R*,1*R*′)-3,3′-[Ethylenebis(iminomethyl)]dibornan-2-onocopper(II) (4), (2) 2 mol %, (3) 55 °C, (4) 66%, (5) 2.3, (6) cis −0.4°, trans +6.9°.

(g) (1) Bis[(−)-camphorquinone-α-dioximato]copper(II) (5), (2) 1 mol %, (3) 52–54 °C, (4) 56%, (5) 2.5, (6) mixture of cis and trans −2.0°.

(h) (1) Bis[(−)-camphorquinone-α-dioximato]palladium(II) (5), (2) 2 mol %, (3) 45 °C, (4) 45%, (5) —, (6) mixture of cis and trans −0.1 °C.

(i) (1) Bis[chloro-(7,1,2-η³-(−)-pinene)]palladium(II)[19] (6), (2) 2 mol %, (3) −30 to −35 °C, (4) 37%, (5) —, (6) mixture of cis and trans +1.7°.

References and Notes

(1) Part of this paper has been communicated before: Y. Tatsuno, A. Konishi, A. Nakamura, and S. Otsuka, *J. Chem. Soc., Chem. Commun.*, 588–589 (1974).
(2) (a) Faculty of Science; (b) Faculty of Engineering Science.
(3) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions", Prentice-Hall, Englewood Cliffs, N.J., 1971, pp 241–252.
(4) C. R. Johnson and C. W. Shroeck, *J. Am. Chem. Soc.*, **95**, 7418–7423 (1973).
(5) S. Sawada, K. Takehana, and Y. Inouye, *J. Org. Chem.*, **33**, 1767–1770 (1968).
(6) H. Nozaki, H. Takaya, S. Moriuti, and R. Noyori, *Tetrahedron*, **24**, 3655–3669 (1968).
(7) W. R. Moser, *J. Am. Chem. Soc.*, **91**, 1135–1140, 1141–1146 (1969).
(8) S. Otsuka, A. Nakamura, T. Koyama, and Y. Tatsuno, *Justus Liebigs Ann. Chem.*, 626–635 (1975).
(9) T. Aratani, Y. Yoneyoshi, and T. Nagase, *Tetrahedron Lett.*, 1707–1710 (1975); 2599–2602 (1977).
(10) M. O. Forster, *J. Chem. Soc.*, **83**, 514–536 (1903); **103**, 662–669 (1913).
(11) A. W. Johnson and D. Ward, *J. Chem. Soc., Perkin Trans 1*, 2076–2085 (1975).
(12) P. Hong, N. Nishii, K. Sonogashira, and N. Hagihara, *J. Chem. Soc., Chem. Commun.*, 993 (1972).
(13) W. A. Herrmann, *Chem. Ber.*, **108**, 485–499 (1975).
(14) H. Ueda, Y. Kai, N. Yasuoka, and N. Kasai, 21st Symposium on Organometallic Chemistry, Japan, Abstract 214, 1974; T. Yamamoto, A. R. Garber, J. R. Wilkinson, C. B. Boss, W. Streib, and L. J. Todd, *J. Chem. Soc., Chem. Commun.*, 354–356 (1974).
(15) L. Claisen and O. Manasse, *Justus Liebigs Ann. Chem.*, **274**, 71–98 (1893).
(16) A. Daniel and A. A. Pavia, *Tetrahedron Lett.*, **13**, 1145–1148 (1967).
(17) S. Otsuka, A. Nakamura, T. Kano, and K. Tani, *J. Am. Chem. Soc.*, **93**, 4301–4303 (1971).
(18) R. L. Lintvedt and A. M. Fatta, *Inorg. Chem.*, **7**, 2489–2495 (1968).
(19) K. Dunne and F. J. McQuillin, *J. Chem. Soc. C*, 2200–2203 (1970).