Enantioselective Carbenoid Cyclopropanation Catalyzed by Chiral *vic*-Dioximatocobalt(II) Complexes Prepared from Natural Camphor and β-Pinene. Mechanism and Stereochemistry

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Abstract: Three geometrical isomers of *vic*-dioximes derived from (1*R*,4*S*)-bornan-2-one (*d*-camphor), (2*E*,3*Z*) ($\equiv \alpha$-cqdH), (2*E*,3*E*) ($\equiv \beta$-cqdH), and (2*Z*,3*E*) ($\equiv \delta$-cqdH), and one (2*Z*,3*E*) dioxime ($\equiv \delta$-PrcqdH) of the 7-*anti*-(*n*-butyl) derivative of the bornanedione were prepared. Also prepared were (2*E*,3*E*) dioxime ($\equiv \beta$-nqdH) and (2*Z*,3*E*) dioxime ($\equiv \delta$-nqdH) of (1*R*,5*R*)-nopinane-2,3-dione. The α and δ isomers form N,O-six-membered chelated cobalt(II) complexes, while β isomers form N,N-five-membered chelated complexes. The enantioselective cyclopropanation of styrene (optical yield maximum 88%), 1,1-diphenylethylene, and others with diazoacetate effected with these chiral Co(II) complexes was investigated to elucidate the mechanism of enantioselection. From the visible spectrum, a weak interaction between ethyl diazoacetate and Co(α-cqd)$_2$·H$_2$O was detected at room temperature. The interaction leads to dinitrogen evolution producing the carbene dimers along with unidentified cobalt compounds resulting from intramolecular carbene attack. The dinitrogen evolution under the catalytic condition using excess olefin parallels with the cyclopropane production. The catalytic reaction rate in neat styrene is first order with respect to Co(α-cqd)$_2$·H$_2$O and diazoacetate while the zero-order dependence on styrene concentration approaches first order at low styrene concentration. The effects of the para-substituted styrenes, steric bulk of the ester group of diazoacetate, and base additives on the rate and the enantioselectivity were studied. The catalytic reaction involves (1) coordination of diazoacetate to Co(II), (2) formation of Co(II)-carbene species, (3) olefin attack to the Co(II)-carbene, and (4) decomposition of cobaltacyclobutane intermediate releasing the cyclopropane. The carbenoid cyclopropanation of *cis*-d_2-styrene revealed geometrical isomerization of the olefin component incorporated in the products; the extent is independent of the enantioselectivity at the carbon derived from the carbene. Factors affecting the enantioselectivity are discussed. Transition state structures which account for the observed product chiralities are proposed based on the stereochemical correlations between the products and catalyst structures; namely, (1*R*)- and (1*S*)-2-phenylcyclopropanecarboxylates were obtained respectively by Co(α-cqd)$_2$ and Co(δ-cqd)$_2$ or Co(δ-nqd)$_2$, which are quasi-enantiomeric. The stereochemical environment around the metal involving rather bulky peripheral groups is considered to be a requisite not only for the effective chiral recognition, but also for the high chemical yield and regioselectivity in the catalysis.

Introduction

As reported in the preceding paper,[2] the optical yield of the carbenoid cyclopropanation of styrene achieved by bis[(−)-camphorquinone-α-dioximato](aqua)cobalt(II), Co(α-cqd)$_2$·H$_2$O, exceeds 80%, an enantioselectivity much higher than any precedent. The remarkably unique ability of the cobalt catalyst in inducing chirality justifies a detailed mechanistic study.

Kinetic investigation of transition metal catalyzed carbenoid reactions is often hampered owing to the low chemical yields or the inhomogeneity of the reaction systems. Recently, Kochi et al.[3] have made a detailed kinetic study for the soluble copper(I) trifluoromethanesulfonate (triflate) catalyzed carbenoid reaction and suggested an intermediacy of either Cu(I)-carbene or Cu(I)-diazoalkane species. The present Co(II)-catalyzed reaction may also involve incipient formation of diazoalkane-Co(II) or carbene-Co(II) species.

In most of the previous studies of asymmetric cyclopropanation,[4,5] no persuasive mechanistic arguments have been made owing to the lack of detailed study. In particular, no unambiguous correlation could be made between the configuration of the prevailing enantiomer and that of the chiral center(s) of the catalyst, because of the structural freedom in the coordination sphere, a freedom arising from the coordination of monodentate chiral ligand(s) like tri(*l*-bornyl)-phosphite.[5] In the bidentate bis(dioximato)cobalt(II) system, such freedom is removed, thus providing a better template for the catalysis. Despite the high enantioselectivity, the present catalyst system still produces two geometrical isomers, e.g., *cis*- and *trans*-2-phenylcyclopropanecarboxylate in roughly comparable amounts. At first, this phenomenon may appear not to be compatible with the high enantioselection.

The main purpose of this paper is to derive a plausible transition state structure accounting for all these experimental observations including the formation of the enantiomeric and geometric isomers of the cyclopropanes produced. For this purpose, detailed mechanistic studies were carried out mainly for the Co(α-cqd)$_2$-catalyzed reactions. These results, when combined with the structural information on the Co(α-cqd)$_2$·H$_2$O and the cyclopropane products, lead us to propose a transition state geometry on the premise of a concerted mechanism. The argument based on a postulated configuration of an unisolated transient intermediate, Co(carbene)(α-cqd)$_2$, has received support from a stereochemical correlation between the catalyst and products. Namely, several new dioximatocobalt(II) compounds which are quasi-enantiomeric to Co(α-cqd)$_2$ produced the 2-phenylcyclopropanecarboxylate of opposite chirality to the one produced by Co(α-cqd)$_2$ catalyst. Unexpectedly, however, geometrical isomerization of the olefin component was found in the carbenoid cyclopropanation, which casts some doubt on the perfect concertedness. Intricate factors affecting the reaction stereochemistry and the nonlinear temperature dependence of the enantioselectivity will be discussed.

Results

Optically Active *vic*-Dioximatocobalt(II) Complexes. These were prepared with three geometrical isomers (α-, β-, and δ-) of camphorquinone dioxime (cqdH)[2] and employed as catalysts for the cyclopropanation. The original stereochemistry

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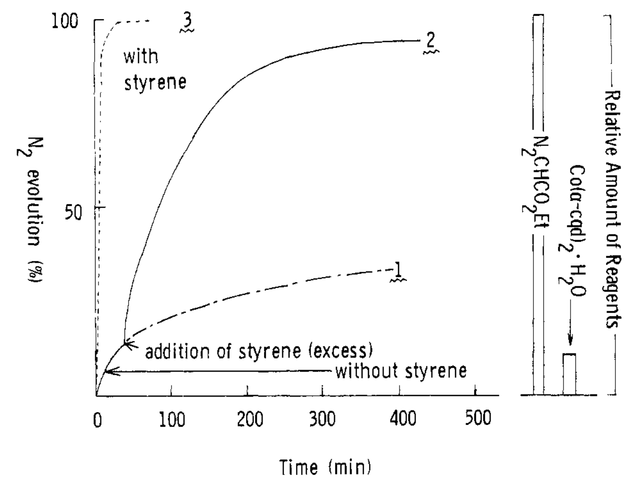
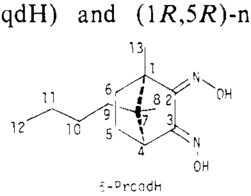


Figure 1. Decomposition of N_2CHCO_2Et with a catalytic amount of $Co(\alpha\text{-cqd})_2 \cdot H_2O$: 1, 2, toluene solution; 3, styrene solution. The details of the reaction conditions are described in the Experimental Section.

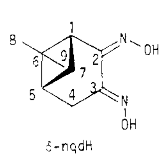
at the nitrogen atom of α-, β-, and δ-cqdH is preserved in the corresponding Co(II) complexes since geometrical isomerization of these dioximes was not observed in the reaction with transition metal ions such as Co^{2+} or Ni^{2+} as confirmed by IR spectra. Then α-cqd ((2*E*,3*Z*) isomer) or δ-cqd ((2*Z*,3*E*) isomer) coordination requires an N,O-chelation instead of an N,N-chelation which occurs with β-cqd ((2*E*,3*E*) isomer).

Attempts to detect η^2-coordination of an olefin like styrene and acrylonitrile to $Co(\alpha\text{-cqd})_2 \cdot H_2O$ using common physical methods, e.g., visible and infrared spectra and magnetic moment, were unsuccessful. The electronic spectrum (in ethanol) of $Co(\alpha\text{-cqd})_2 \cdot H_2O$ shows a strong charge transfer absorption tailing into the visible region which is featureless. A slight change (~5%) in intensity around 400 nm was discerned upon introduction of diazoacetate to the complex at 25 °C. The magnetic moment (3.6 μ_B) in neat α-methylstyrene at 35 °C is practically the same with that found in toluene at 35 °C (3.5 μ_B). Owing to the paramagnetism of the complex, the ^1H NMR spectrum of the Co(II) complex does not provide information on the ligation. The ESR spectrum was uninformative owing to the low intensity and broadness of the signals.

Two new chiral *vic*-dioximes, (1*R*,4*S*,7*R*)-7-*anti*-(*n*-butyl)-1,7-dimethylnorbornane-2,3-dione-2(*Z*)-3(*E*)-dioxime (δ-PrcqdH) and (1*R*,5*R*)-nopinane-2,3-dione-2(*Z*)-3(*E*)-dioxime (δ-nqdH), were prepared (see Experimental Section). Note that the carbon skeleton of PrcqdH is the same as that of cqdH except for the propyl group at C-9. From the mixture of geometrical isomers of Prcqd were isolated pure β and δ isomers in substantial yields by recrystallizations. Their ^1H NMR spectra are similar to those[6] of β- and δ-cqdH, except for the butyl group, indicating retention of the camphor skeleton. The nqdH (nopinoquinone dioxime) was prepared from (−)-β-pinene. The β (2*E*,3*E*) and δ isomer (2*Z*,3*E*) were separated by repeated recrystallizations and identified by the ^1H NMR spectra (Experimental Section).



δ-PrcqdH



δ-nqdH

Neutral cobalt(II) complexes of δ-Prcqd, δ-nqd, and β-nqd were prepared following essentially the same procedure as used for the α-cqd complex.[2] These complexes contain one coordinated water molecule as evidenced by elemental analysis. Studies on these novel six-membered N,O-chelated *vic*-dioximato metal compounds will be a subject of a separate paper.[7]

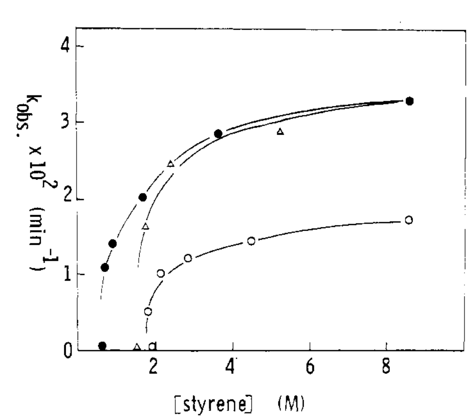


Figure 2. Dependence of observed pseudo-first-order rate constants in organic solvents. Reaction conditions: $Co(\alpha\text{-cqd})_2 \cdot H_2O$ 1.2 × 10^{-2} M, N_2CHCO_2Et 0.23 M; ●, in *trans*-1-phenyl-1-propene at 20 °; △, in ethyl acetate at 20 °C; ○, in toluene at 0 °C.

Kinetics of $Co(\alpha\text{-cqd})_2$-Catalyzed Reaction. Some features of reactivity of $Co(\alpha\text{-cqd})_2 \cdot H_2O$ are illustrated in Figure 1. Addition of an excess (10 mol) of ethyl diazoacetate to a toluene solution of the catalyst (1 mol) causes slow evolution of dinitrogen (curve 1). Addition of excess styrene to the solution effectively initiates the catalytic reaction as exhibited by the dinitrogen evolution (curve 2). Addition of ethyl diazoacetate to a mixture of the catalyst and a large excess of styrene causes an immediate vigorous evolution of dinitrogen (curve 3), suggesting an interaction of styrene with diazoalkane complex. The α-cqd complex does not initiate a radical polymerization of styrene, butadiene, isoprene, or *trans*-1-phenyl-1,3-butadiene at 20 °C.

A linear correlation between the amount of the cyclopropanation product and the volume of the evolved dinitrogen was established experimentally, and the dinitrogen evolution was utilized to monitor the reaction rate. Because of the air sensitivity of the catalyst, rigorous exclusion of air from the reaction system was necessary to obtain reproducible kinetic results. The rate was followed until over 80% reaction at 0-40 °C. The rate in neat styrene was first order with respect to both concentrations of ethyl diazoacetate (0.03-0.23 M) and the catalyst (6-24 mM). Dilution of the reaction mixture with usual organic solvents below 2 M greatly reduces the catalytic activity or often deactivates the complex completely. An unreactive internal olefin, *trans*-1-phenyl-1-propene, can be used as solvent. The dependence of the observed rate constant (rate = k_{obsd}[Diazo]) on styrene concentration in typical organic solvents is shown in Figure 2. The pseudo-first-order rate constants obtained below 2 M in such solvents as toluene or ethyl acetate are less reproducible. The deactivation becomes important in the concentration range (2.0-0.7 M) as manifested by the curvature in the first-order rate plots, which do not intercept the origin. The first-order rate constants (k_{obsd}) in *trans*-1-phenyl-1-propene are two- or threefold larger than those in other solvents (below 2 M).

Energetics of the overall carbenoid reaction were calculated from the data obtained in neat styrene at the temperature range 0-40 °C to give $E^a_{app} = 5.3$ kcal mol^{-1}, $\Delta S^{\ddagger}_{app} = -55$ eu. Since addition of a small amount of donor molecules such as β- or γ-picoline greatly influences the enantioselectivity (vide infra), the rate was studied in the presence of these donors. The cyclopropanation rate was reduced most remarkably by addition of 1 molar equiv of β- or γ-picoline and remained almost unchanged on further addition of the base until 2.6 mol. The kinetic parameters are compared in Table I. The retardation by triphenylphosphine and 4-methyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane was insignificant.

Table I. Kinetic Parameters of the Cyclopropanation of Styrene with Ethyl Diazoacetate in the Presence of Co(α-cqd)$_2$ as Catalyst[a]

	H_2O	α-Picoline[b]	β-Picoline[b]
$k_{obsd} \times 10^2$, min^{-1}	5.1[c]	4.3[c]	2.6[c]
E^a_{app}, kcal/mol	5.3 ± 0.3[d]	9.1 ± 0.1[e]	12 ± 1.6[f]
$\Delta S^\ddagger_{app}$, eu	-55 ± 1[g]	-34 ± 2[g]	-27 ± 5[g]

[a] [Co(α-cqd)$_2$·H_2O], 1.2×10^{-2} M; [N_2CHCO_2Et], 0.23 M in neat styrene. [b] Base/Co(α-cqd)$_2$·H_2O = 2.6. [c] Measured at 30 °C. [d] At 0–40 °C. [e] At 0–50 °C. [f] At 30–60 °C. [g] At 30 °C.

Table II. Effects of the Para-Substituted Styrene and of the Ester Group of Diazoacetate on the Relative Rates of the Cyclopropanation with Co(α-cqd)$_2$

A. Effect of X in p-$XC_6H_4CH{=}CH_2$[a]

X in p-$XC_6H_4CH{=}CH_2$	k_{obsd}, min^{-1}
CH_3O	2.5×10^{-2}
CH_3	2.0×10^{-2}
H	1.7×10^{-2}
Cl	3.8×10^{-3}

B. Effect of R Group in N_2CHCO_2R[b]

R in N_2CHCO_2R	k_{obsd}, min^{-1}
Me	2.5×10^{-2}
Et	1.7×10^{-2}
i-Pr	1.4×10^{-2}
i-Bu	8.4×10^{-3}
neo-Pent	1.2×10^{-3}

[a] Reaction conditions: 0 °C, [Co(α-cqd)$_2$·H_2O], 1.2×10^{-2} M; [N_2CHCO_2Et], 0.24 M in neat olefin. [b] 0 °C, [Co(α-cqd)$_2$·H_2O], 1.2×10^{-2} M, [N_2CHCO_2R], 0.23 M in neat styrene.

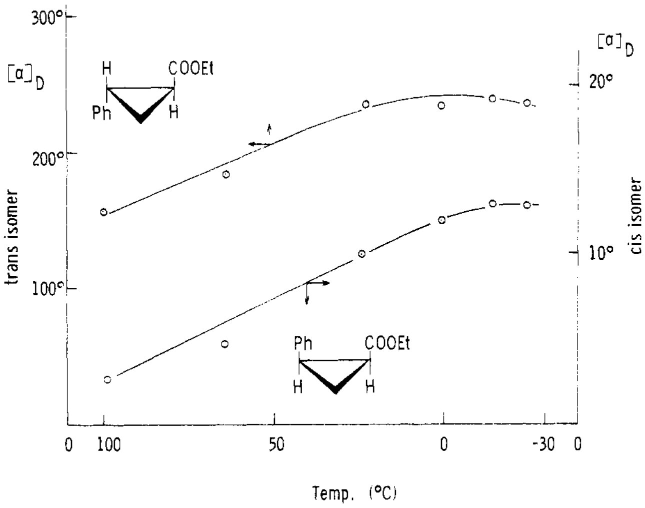


Figure 3. Temperature dependence of the enantioselectivity. The details of the reaction conditions are described in the Experimental Section.

Table III. Cyclopropanation[a] of Styrene with Various Alkyl Diazoacetates (N_2CHCO_2R) in the Presence of Co(α-cqd)$_2$·H_2O

R in N_2CHCO_2R	Yield,[b] %	Trans/cis[c]	$[\alpha]^{23}_D$,[d] Cis	Trans	OY[e] of trans acid, %
Me	94	0.69	+21	+231	61
Et	92	0.85	+21	+286	75
i-Pr	91	1.15	+22	+320	84
i-Bu	94	0.92	+21	+302	80
neo-Pent	87	2.34	+24	+335	88
c-Hex	72	1.46	+22	+298	78

[a] Reaction was performed in neat styrene at 0 °C with 3 mol % catalyst (based on alkyl diazoacetate). [b] Based on alkyl diazoacetate. [c] Ratio of area in the GLC peaks. [d] Value of the corresponding acid obtained after alkaline hydrolysis of the ester. Measured at 23 °C in $CHCl_3$ with a cell (0.5 dm). Concn: cis, c 5.07–5.20; trans, c, 1.00–1.20. [e] Optical yield was calculated from the highest specific rotation of the trans acid, $[\alpha]_D$ +381°.

Electron-donating substituents, CH_3O and CH_3, on the styrene enhance the rate (Table II), although no simple correlation exists between the Hammett constants and the rates. Consistently a competitive reaction of styrene and methyl acrylate with diazoacetate catalyzed by Co(α-cqd)$_2$·H_2O at 0 °C produced only ethyl 2-phenylcyclopropanecarboxylate.

The steric bulk of the ester group of the diazo component retards the rate (Table II).

In the catalytic decomposition of diazoacetate using [Pd(η^3-allyl)Cl]$_2$,[8] the rate of catalysis, giving carbene dimers, is very fast, exceeding that of the deactivation of the complex catalyst. The present cobalt(II) chelates are less stable, compared to [Pd(η^3-allyl)Cl]$_2$, in the absence of olefins as reflected by the very low yields (8–16%) of carbene dimers, e.g., dialkyl fumarate and maleate. The ratio of geometrical isomers of the carbene dimers appears to be sensitive to the steric crowding at the metal center. Thus, the cis/trans ratio of the carbene dimer is largest (~5) for Co(α-cqd)$_2$·H_2O and lowest (0.2) for [Pd(η^3-allyl)Cl]$_2$.

In order to study the fate of the carbene moiety (=$CHCO_2Et$), a deep brown solid residue precipitated in the stoichiometric reaction of Co(α-cqd)$_2$ was examined by IR spectroscopy. The spectrum shows very strong absorptions due to an ester carbonyl group, indicating incorporation of the (=$CHCO_2Et$) moiety into the deactivated catalyst. Several possible sites for the attachment of the (=$CHCO_2Et$) moiety exist but the exact location could not be determined. Degradation of the solid residue by concentrated sulfuric acid liberated camphorquinone in reasonable yields confirming the persistence of camphor skeleton in this intramolecular carbenoid reaction.

Factors Influencing Enantioselectivity. Since the best enantioselective catalyst was found to be Co(α-cqd)$_2$·H_2O, these factors were investigated primarily with this catalyst as described below.

The present cyclopropanation reaction belongs to a kinetically controlled reaction type. The energetic information on the diastereomeric transition states leading to (1S)- or (1R)-2-phenylcyclopropanecarboxylates may be obtained from the plot of the optical yields vs. temperature (Figure 3). The optical yield obtained with ethyl diazoacetate reaches a ceiling value of 78% when the reaction temperature approaches −15 °C (Figure 3). The free energy difference $\Delta\Delta G^\ddagger$ was calculated on the basis of the Curtin-Hammett principle[9] for a temperature range (25–100 °C), where a linear correlation of ln (c_S/c_R) with $1/T$ holds.

$$\Delta\Delta G^\ddagger_{S\text{-}R} = -RT \ln \frac{c_S}{c_R}$$

$$= -RT \ln \frac{1-P}{1-P} = \Delta\Delta H^\ddagger - T\Delta\Delta S^\ddagger$$

c_S and c_R: mole fractions of S and R enantiomers

P: optical yield

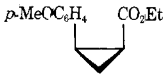
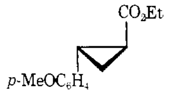
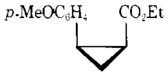
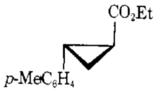
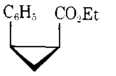
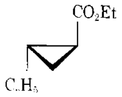
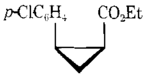
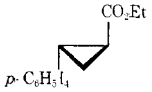
As shown in Table III, the enantioselectivity increases with an increase in bulkiness of the ester group of diazoacetate. The value of $\Delta\Delta G^\ddagger_{S\text{-}R}$ increases accordingly (Table IV). Both values of $\Delta\Delta H^\ddagger_{S\text{-}R}$ and $\Delta\Delta S^\ddagger_{S\text{-}R}$ increase simultaneously. The trans/

Table IV. Energetics of the Enantioselection in the Cyclopropanation of Styrene with Various Diazoacetates[a]

R in N_2CHCO_2R	$\Delta\Delta G^{\ddagger}_{S-R}$ (at 25 °C), kcal/mol	$\Delta\Delta H^{\ddagger}_{S-R}$, kcal/mol	$\Delta\Delta S^{\ddagger}_{S-R}$, eu
Me	0.91	3.1	7.4
Et	1.2	3.8	8.8
i-Pr	1.4	5.4	13.3

[a] Parameters are obtained for *trans*-2-phenylcyclopropanecarboxylic acid formed by reactions at 25-100 °C (see Experimental Section).

Table V. Cyclopropanation[a] of Para-Substituted Styrene with Ethyl Diazoacetate in the Presence of Co(α-cqd)$_2$·H_2O

X in *p*-$XC_6H_4CH{=}CH_2$	Yield,[b] %	*Trans*/cis[c]	Product[d]	$[\alpha]_D$,[e] deg
MeO	96	0.97		−5.1
				+245
Me	91	1.0		+2.2
				+234
H	92	0.85		+13
				+236
Cl	96	0.83		−4.9
				+219

[a] Reaction was performed in neat olefin at 0 °C with 3 mol % catalyst (based on ethyl diazoacetate). [b] Based on ethyl diazoacetate. [c] Ratio of area in the GLC peaks. [d] The absolute configurations of ethyl 2-phenylcyclopropanecarboxylate are known and those of other para-substituted derivatives are inferred from the CD spectra. [e] Measured in $CHCl_3$ with a cell (0.5 dm).

Table VI. Effect of an Axial Base on Asymmetric Synthesis[a] of Ethyl 2-Phenylcyclopropanecarboxylate

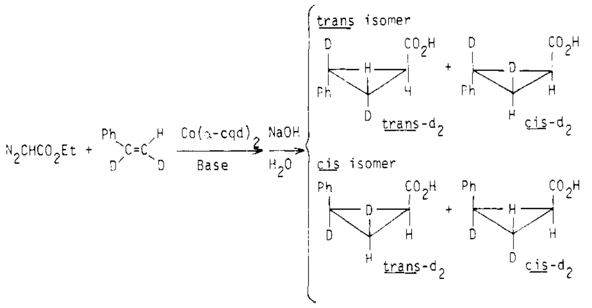
Axial base	Yield,[b] %	Trans/ cis[c]	$[\alpha]_D$,[d] deg Cis	Trans
H_2O	92	0.85	+13	+236
Pyridine	70	1.4	+1.4	+60.6
α-Picoline	91	0.74	+3.1	+248
β-Picoline	67	1.4	−0.4	+36.6
γ-Picoline	67	1.1	−1.9	+17.9
2,6-Lutidine	86	0.72	+10	+187
3,5-Lutidine	84	1.3	−1.8	+12.8
$CH_3C(CH_2O)_3P$[e]	89	1.1	+7.0	+232
Triphenylphosphine	86	0.69	+12	+211

[a] Reaction was performed at 0 °C in neat styrene with 3 mol % of the catalyst (based on ethyl diazoacetate) and a base (2.5-fold molar ratio to the catalyst). [b] Based on ethyl diazoacetate. [c] Ratio of area in the GLC peaks. [d] Measured in $CHCl_3$ with a cell (0.5 dm). [e] 4-Methyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane.

cis ratio also shows the same trend; the bulkier the ester group, the higher is the trans/cis ratio (see Table III).

The chemical yields and selectivities in cyclopropanation on para-substituted styrenes are shown in Table V. The same absolute configuration of C-1 was found in all these substituted phenylcyclopropanes by means of the CD spectra.

Addition of a donor molecule to the cobalt(II) catalyst causes a marked effect on the enantioselectivity as shown in Table VI. The most dramatic effect occurs with addition of a sterically unhindered strong base, e.g., γ-picoline. The optical rotation of the cis ester ranges from +13 to −1.9° with a considerable decrease in the chemical yield. Interestingly the configuration of the prevailing enantiomer of the cis ester is *reversed* by addition of β- or γ-picoline. The coordination of pyridine to Co(α-cqd)$_2$ was examined in benzene by the visible spectrum. An increased absorption around 400 nm indicates an adduct formation. The CD spectrum of Co(α-cqd)$_2$·H_2O reveals an extremum at 497 nm ($\Delta\epsilon$ −0.92) and a shoulder at 546 nm ($\Delta\epsilon$ −0.42). By adding pyridine, the spectrum changes exhibiting an extremum at 545 nm ($\Delta\epsilon$ −0.91) and a shoulder at 470 nm ($\Delta\epsilon$ −0.57).

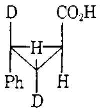
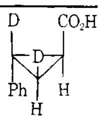
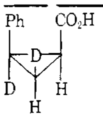
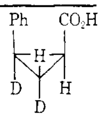


Utilizing *cis*-d_2-styrene, we found that the olefin undergoes geometrical isomerization upon carbenoid cyclopropanation. Thus nearly a quarter of the *trans*-cyclopropane isomer is trans-d_2 and the *cis*-cyclopropane isomer contains even more of a trans-d_2 component as estimated by the ^1H NMR (see Figure 4 and Table VII). This is rather astonishing in view of the high enantioselectivity. The addition of β-picoline causes an increase in the trans-d_2 component in the trans isomer but such an effect is hardly discernible in the *cis*-cyclopropane isomer. The geometrical isomerization does not reach the equilibrium value (50%). The presence of an axial base, e.g., β-picoline, reduces the optical yield dramatically: 65 to 9.0% for the trans isomer.

Effects of *vic*-Dioximato Ligand Structures. The carbenoid cyclopropanation of styrene and 1,1-diphenylethylene with ethyl diazoacetate was carried out at 0-5 °C to compare results with various Co(II) catalysts (Tables VIII and IX). A conspicuous feature emerges. The C-1 configuration in 2-phenylcyclopropanecarboxylates produced with Co(δ-cqd)$_2$·H_2O and Co(δ-nqd)$_2$·H_2O is always *R*, whereas the Co(α-cqd)$_2$·H_2O catalyst produces the (1*S*) cyclopropane. A nonprochiral olefin, 1,1-diphenylethylene, also gives, upon cyclopropanation with Co(δ-cqd)$_2$·H_2O, Co(δ-nqd)$_2$·H_2O, and Co(δ-Prcqd)$_2$·H_2O, the (1*R*) cyclopropane (Table IX). An exception is the case with Co(δ-Prcqd)$_2$·H_2O, which produces *cis*-(1*S*)-2-phenylcyclopropanecarboxylate (Table VIII). It is perplexing to find inferior optical yields for Co(δ-Prcqd)$_2$·H_2O, which carries an additional chiral center at C-7. Two five-membered N,N-chelated Co(II) complexes, Co(β-cqd)$_2$·H_2O and Co(β-nqd)$_2$·$2H_2O$, proved not to be effective chiral catalysts, although the chemical yields are high (Table VIII).

Cyclopropanation of methyl atropate with ethyl diazoace-

Table VII. Results of the Cyclopropanation with *cis*-d_2-Styrene and Optical Yields[a]

		Trans isomer		Cis isomer				
							Optical yield, %	
Temp, °C	Base	*trans*-d_2	*cis*-d_2	*trans*-d_2	*cis*-d_2	Trans/cis	Trans	Cis
30	H_2O	24	76	37	63	0.73	41	35
0	H_2O	23	77	37	63	0.72	65	63
0	β-Picoline	37	63	38	62	1.32	9.0	7.2

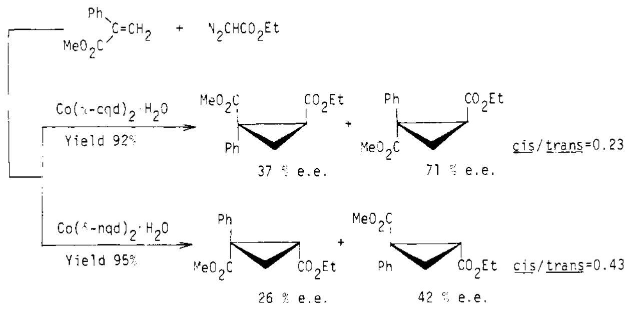
[a] The values are averages of two independent reactions and accurate to ±3%. See Experimental Section for the reaction conditions.

Table VIII. Asymmetric Synthesis of Ethyl 2-Phenylcyclopropanecarboxylate with Various Co(II) Catalysts[a]

			Cis isomer			Trans isomer		
Catalyst	Yield,[b] %	Trans/cis[c]	[α]D, deg	Confign	OY,[d] %	[α]D, deg	Confign	OY,[d] %
Co(α-cqd)$_2$·H_2O	92	0.85	+12	(1*S*,2*R*)	66	+236	(1*S*,2*S*)	75
Co(δ-cqd)$_2$·H_2O	62	0.65	−11	(1*R*,2*S*)	63	−202	(1*R*,2*R*)	64
Co(δ-Prcqd)$_2$·H_2O	78	0.60	+4.4	(1*S*,2*R*)	24	−82	(1*R*,2*R*)	26
Co(δ-nqd)$_2$·H_2O	83	0.91	−3.7	(1*R*,2*S*)	21	−237	(1*R*,2*R*)	74
Co(β-cqd)$_2$·H_2O	81	2.2	−5.6	(1*R*,2*S*)	31	+29	(1*S*,2*S*)	9
Co(β-nqd)$_2$·$2H_2O$	80	8.0	+0.6[e]	(1*S*,2*R*)	4	−0.6[e]	(1*R*,2*R*)	0.2

[a] Reaction was performed in neat styrene at 0 °C with 3 mol % catalyst (based on ethyl diazoacetate). [b] Based on ethyl diazoacetate. [c] Ratio of area in the GLC peaks. [d] Each ester was hydrolyzed to the corresponding acid and optical yield was calculated from the highest specific rotation of the acid: the cis acid, [α]D 18°; the trans acid, [α]D 381°. [e] Observed rotation was 0.01° with a 0.5-dm cell.

tate was carried out with Co(α-cqd)$_2$·H_2O and Co(δ-nqd)$_2$·H_2O. The reaction proceeds at comparable rates giving *cis*- and *trans*-1-phenylcyclopropane-1,2-dicarboxylates in good yields (>90%). These products are readily identified by their ¹H NMR spectra and the enantiomeric excess is assessed from the reported maximum specific rotation.[10] Interestingly, the configurations of the predominant enantiomers obtained by Co(α-cqd)$_2$·H_2O are (1*R*,2*S*) and (1*S*,2*S*), respectively, for the cis and trans products, whereas those obtained by Co(δ-nqd)$_2$·H_2O are (1*S*,2*R*) and (1*R*,2*R*). The optical yields are better for Co(α-cqd)$_2$·H_2O than Co(δ-nqd)$_2$·H_2O and they are also better for the trans products than for the cis products. The same reaction was attempted with Co(δ-Prcqd)$_2$·H_2O and Co(δ-cqd)$_2$·H_2O. The carbenoid reaction was negligible, giving the products only in trace amounts, insufficient for the optical measurement.



A brief kinetic study was made at 0 °C for the Co(δ-nqd)$_2$·H_2O and Co(δ-cqd)$_2$·H_2O catalyzed reaction of styrene with ethyl diazoacetate. A similar first-order dependence of the rate on ethyl diazoacetate concentrations was found as for the Co(α-cqd)$_2$·H_2O catalyzed reaction. The observed pseudo-first-order rate constants (k_{obsd}) in neat styrene are compared for three Co(II) complexes catalysts in Table X. The temperature dependence of the optical yield was also examined. In the case of Co(δ-cqd)$_2$·H_2O, the temperature dependence is linear for the range 25–100 °C; the optical yield reaches a maximum around 20 °C and further lowering of the temperature does not improve the optical yield. In the case of Co(δ-nqd)$_2$·H_2O, a linear dependence is observed over the range 0–65 °C. However, above 65 °C, a marked deviation from linearity is observed and the optical yield asymptotically approaches zero. Assuming the Curtin–Hammett principle, the energetic parameters of enantioselection were calculated within the temperature range where the linear dependence is observed and are listed in Table X.

Table IX. Asymmetric Synthesis of Ethyl 1,1-Diphenylcyclopropanecarboxylate with Various Co(II) Catalysts[a]

Catalyst	Yield,[b] %	[α]D, deg	Confign	Optical yield,[c] %
Co(α-cqd)$_2$·H_2O	95	+156	(1*S*)	70
Co(δ-cqd)$_2$·H_2O	77	−112	(1*R*)	50
Co(δ-Prcqd)$_2$·H_2O	68	−61	(1*R*)	27
Co(δ-nqd)$_2$·H_2O	87	−118	(1*R*)	54

[a] Reaction was performed in neat 1,1-diphenylethylene at 5 °C with 2.2–2.9 mol % catalyst (based on ethyl diazoacetate). [b] Based on ethyl diazoacetate. [c] Ester was hydrolyzed to the corresponding acid and optical yield was calculated from the highest specific rotation of the acid, [α]D 230 ± 5°.

The stoichiometric reaction of ethyl diazoacetate with Co(δ-nqd)$_2$·H_2O and Co(δ-cqd)$_2$·H_2O was also briefly studied as for the Co(α-cqd)$_2$·H_2O catalyst. The products identified were the carbene dimer formed in very low yield (7–17%). The fumarate/maleate ratio was larger in these cases than in the case of Co(α-cqd)$_2$·H_2O (see Experimental Section).

Discussion

Metal complex catalysts for asymmetric synthesis containing monodentate chiral ligands generally create a problem, stereochemical ambiguity, owing to the ligand dissociation and/or rotation of the metal–ligand bond. The present cobalt catalyst, being assisted by chelation, precludes such an ambiguity, a feature particularly amenable for discussion of catalysis. Another aspect adding an important element to these discussions is the product chirality. The disubstituted cyclo-

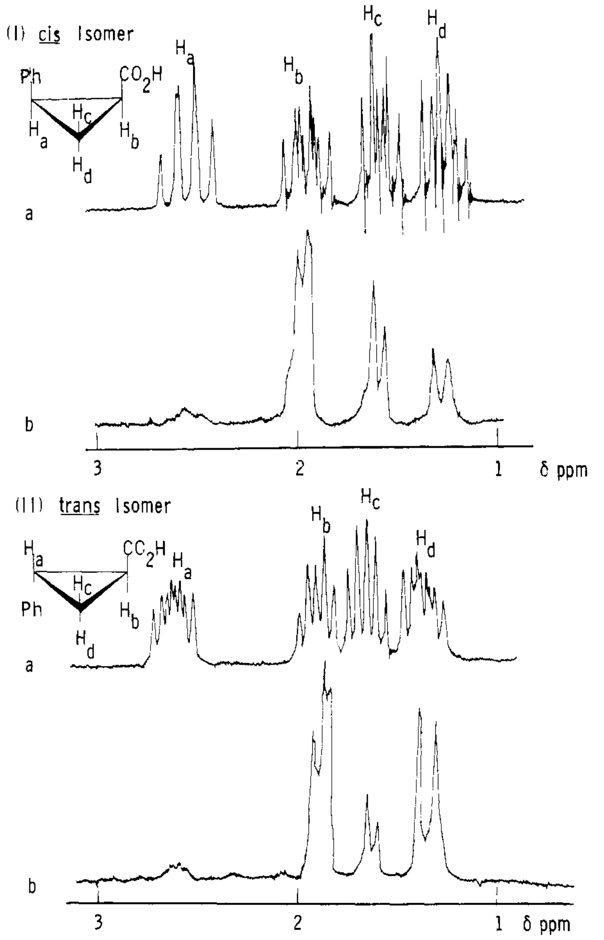
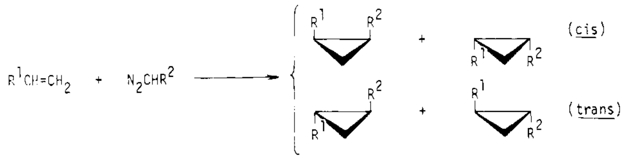


Figure 4. ^1H NMR spectra of the nondeuterated and 2,3-dideuterated 2-phenylcyclopropanecarboxylic acid (Me_4Si as internal standard in $CDCl_3$): (a) nondeuterated; (b) 2,3-dideuterated. The details of the reaction conditions are described in the Experimental Section.

propanes with two chiral centers have four stereoisomers. The isomer distribution reflecting the stereochemical as well as the kinetic factors of the catalysis should provide much more mechanistic information compared to nonchiral reaction systems.



Catalytically Active Species and Reaction Pathways. In many metal complex catalysis of the cyclopropanation, ligand-free metal species are sometimes extremely active and any elaborate modification of the ligands is meaningless. This was the case with Pd complexes with chiral ligands, e.g., 1,2,7-η^3-pinenyl ligand.[8] Our study on these Pd complex catalyses indicated that the active site contains halide ligands but not the chiral ligands.[8] Consequently the optical yield is either very low or null. The observed high enantioselectivity of the present Co(α-cqd)$_2$ catalyst indicates retention of the chiral ligand throughout the catalysis.

In the conventional copper catalysis, the oxidation state of the metal in the active species is debatable.[11] In the present case, [Co^{III}(β-cqd)$_2$Cl(py)] was found totally inactive and the catalytic activity of [Co^I(α-cqd)$_2$]$^-$ was lower by an order of magnitude than the Co^{II} analogue. The active species must be a cobalt(II) species. The ^1H NMR of the reaction mixture, after the cobalt(II)-catalyzed carbenoid reaction, indicated persistence of paramagnetism. Therefore, the oxidation state appears to remain intact during the reaction.

Table X. Relative Rates[a] and Enantioselection Energetics[b] of the Cyclopropanation of Styrene with Ethyl Diazoacetate Catalyzed by Various Co(II) Complexes

Catalyst	k_{obsd}, min^{-1}	$\Delta\Delta G^\ddagger$ (25 °C), kcal/mol	$\Delta\Delta H^\ddagger$, kcal/mol	$\Delta\Delta S^\ddagger$, eu
Co(α-cqd)$_2$·H_2O	1.7×10^{-2}	1.2[c]	3.8[c]	8.8[c]
Co(δ-nqd)$_2$·H_2O	4.1×10^{-3}	0.80[d]	4.2[d]	11.4[d]
Co(δ-cqd)$_2$·H_2O	1.6×10^{-3}	1.1[c]	4.6[c]	11.8[c]

[a] Reaction conditions: [catalyst], 1.2×10^{-2} M; [N_2CHCO_2Et], 0.24 M; at 0 °C in neat styrene. [b] Reaction was performed in neat styrene at 0, 25, 65, and 100 °C with 3 mol % catalyst (based on ethyl diazoacetate). Parameters were obtained for *trans*-2-phenylcyclopropanecarboxylic acid. [c] Calculated from the data at 25-100 °C. [d] Calculated from the data at 0-65 °C.

Kinetic rate equations were reported for catalytic decomposition of diazoalkanes by LiCl[12] and copper(I) trifluoromethanesulfonate.[3] In the absence of olefin, the rates for both cases showed first-order dependence both on diazoalkane and the catalyst concentration. At high olefin concentrations, the rates by the Cu(I) catalyst showed reciprocal first-order dependence on the olefin concentration suggestive of strong affinity of olefin toward Cu(I).

In the absence of olefins, the Co(α-cqd)$_2$ complex slowly decomposes diazoacetate at 20 °C and dies in a few hours. A stationary catalytic cyclopropanation cycle is obtained only with a large excess of some particular olefins. Therefore, most of our kinetic data has been obtained under pseudo-first-order conditions with a large excess of styrene. In neat styrene, the reaction rate depends on both concentrations of catalyst and diazoacetate. As the styrene concentration becomes low (below 3M), the rate dependency on the concentration approaches first order (Figure 2). The catalyst thus interacts with both reactants in kinetically important steps. The relative affinity of the two reactants toward the metal complex was examined. The featureless visible spectrum of Co(α-cqd)$_2$·H_2O in ethanol was changed by addition of diazoacetate, whereas no influence on the spectrum was observed upon addition of styrene. This indicates that coordination of the diazoacetate to the catalyst is stronger than that of styrene. However, the cyclopropanation rate is not retarded by a high diazoacetate concentration implying the noncompetitive nature of the diazo compound with respect to styrene. Consistently the first-order dependence on concentration of diazoacetate was observed throughout the whole range (0.5-8 M) of styrene concentration. Thus, a reaction scheme involving a one-step termolecular intermediate formation is excluded and a multistep mechanism must be considered. The diazoacetate complex is apparently kinetically unstable, readily eliminating dinitrogen as confirmed by the stoichiometric reaction between the diazoacetate and the cobalt complex. It seems then reasonable to postulate formation of a metal-carbene complex.[13] Since the interaction with diazoacetate is strong as described above, the initial attack of diazoacetate on the catalyst is expected to initiate the catalytic cycle. When the step involving styrene becomes slow, at low styrene concentrations, the metal-carbene intermediate tends to accumulate because of the irreversibility of N_2 elimination from the metal-diazoacetate.

In an unreactive olefin like *trans*-1-phenyl-1-propene, the rate equation can be expressed as

$$\text{rate} = k\,\frac{[\text{catalyst}][\text{diazo}][\text{styrene}]}{1 + K[\text{styrene}]}$$

because the deactivation at low styrene concentration (0.8-2.0 M) is avoided (Figure 2). This equation indicates first-order rate dependence on the styrene concentrations at the low styrene concentrations. The reactive metal-carbene complex formed under these conditions seems to be stabilized to some extent, presumably through a reversible interaction with a double bond of this special internal olefin. In other words, the irreversible deactivation by intramolecular carbenoid reactions is prevented by this interaction. An exchange of this coordinated internal olefin with styrene leads to cyclopropanation.

An alternative mechanism is a catalyzed decomposition of substituted pyrazoline initially formed from diazoacetate and styrene. Since Co(α-cqd)$_2$·H$_2$O does not decompose the preformed pyrazoline, this possibility is excluded.

Thus, the following sequence of elementary steps may be proposed: (1) interaction of diazoacetate with the catalyst leading to a Co(II)-diazoacetate complex, (2) transformation of the diazoacetate complex to a carbene complex, (3) the reaction of the carbene complex with an olefin to give a cobaltacyclobutane intermediate, (4) elimination of a cyclopropane derivative regenerating the original catalyst, and (5) deactivation of the catalysis (k_d) or formation of the carbene dimers with regeneration of the catalyst.

$$\mathrm{N_2CHCO_2R} + \text{“}\mathrm{Co(\alpha\text{-}cqd)_2(L)}\text{”} \xrightleftharpoons[k_{-1}]{k_1} \mathrm{Co(\alpha\text{-}cqd)_2(L)(N_2CHCO_2R)} \quad (1)$$

$$\mathrm{Co(\alpha\text{-}cqd)_2(L)(N_2CHCO_2R)} \xrightarrow{k_2} \mathrm{Co({=}CHCO_2R)(\alpha\text{-}cqd)_2(L)} + \mathrm{N_2} \quad (2)$$

$$\mathrm{Co({=}CHCO_2R)(\alpha\text{-}cqd)_2(L)} + \mathrm{PhCH{=}CH_2} \xrightleftharpoons[k_{-3}]{k_3} \mathrm{Co({=}CHCO_2R)(PhCH{=}CH_2)(\alpha\text{-}cqd)_2} + \mathrm{L} \quad (3)$$

$$\mathrm{Co({=}CHCO_2R)(PhCH{=}CH_2)(\alpha\text{-}cqd)_2} \xrightarrow{k_4} \text{“}\mathrm{Co(\alpha\text{-}cqd)_2(L)}\text{”} + \mathrm{Ph}\underbrace{\mathrm{CH{-}CH_2{-}CH}}\mathrm{CO_2R} \quad (4)$$

$$\mathrm{Co({=}CHCO_2R)(\alpha\text{-}cqd)(L)} \begin{array}{l} \xrightarrow{k_d} \text{catalytically inactive species} \\ \xrightarrow{k_5} \mathrm{({=}CHCO_2R)_2} + \text{“}\mathrm{Co(\alpha\text{-}cqd)_2(L)}\text{”} \end{array} \quad (5)$$

L = base (e.g., H$_2$O, pyridine, etc.)

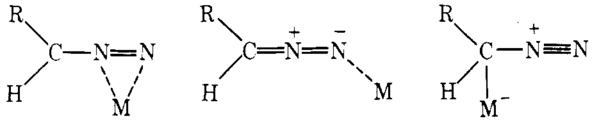
The observed kinetic features in various solvents can be rationalized when the following conditions are met: (a) k_1[N$_2$CHCO$_2$Et] $< k_{-1} + k_2$ and (b) k_3[styrene] $\leq k_{-3} + k_4$. In neat styrene, the k_3[styrene][carbene complex] is larger than the term k_1[N$_2$CHCO$_2$Et][catalyst] and the rate equation is approximated as k_1[N$_2$CHCO$_2$Et][catalyst]. When the styrene concentration is low, the competing reactions of the carbene complex override the cyclopropanation, i.e., $k_d + k_5 > k_3$ [styrene].

In this case, the plot of [styrene] vs. rate does not come to the origin (Figure 2) and the reaction rate cannot be described by a simple expression. As shown in Figure 1, a delayed addition of styrene (curve 2) does not revive the original catalytic activity found in neat styrene. Since cyclopropanation of internal olefins is possible only with sterically less bulky cobalt(II) chelates, e.g., Co(dmg)$_2$ and Co(α-nqd)$_2$, the prevention of catalyst deterioration by *trans*-1-phenyl-1-propene is ascribed to the steric effect arising from the bulk of both cqd ligands and the olefin. The Co(α-cqd)$_2$-catalyzed cyclopropanation in *trans*-1-phenyl-1-propene solution, therefore, probably involves nonproductive interaction of the olefin with a reactive cobalt-carbene species. Only the interaction with styrene is productive and leads to rapid cyclopropanation.

It is likely that the catalyst deactivation is caused by an intramolecular carbenoid reaction of cobalt-carbene complex. There are precedents. For example, Sato observed formation of carbene-addition products in a stoichiometric reaction between Cu(acac)$_2$ and N$_2$CHCO$_2$Et.[14] Teyssié et al. also found a reaction of acetylacetone with N$_2$CHCO$_2$Et in the presence of Rh(I) giving a furan derivative.[15] A reaction of N$_2$CHCO$_2$Et with porphyrinatocobalt(II) was recently reported to give a carbene (CHCO$_2$Et) insertion product at one of the Co-N bonds.[16]

Let us examine each step. A weak interaction between the olefin and the metal is invoked to account for the rate-accelerating effect (Figure 1). The attack of diazoacetate at the Co(II) center may be facilitated by simultaneous dissociation of a weakly coordinated olefin or water molecule. Thus, this acceleration could be due to an effect similar to a solvation effect, preventing a large decrease in the entropy of activation upon coordination of the diazoalkane in step 1.

Three modes are conceivable for coordination of a diazoalkane molecule to a metal atom. Recently, authentic η^2-diazoalkane complexes have been made and the structure involving η^2-coordination through two N atoms is verified by an x-ray analysis of Ni(η^2-diazofluorene)(t-BuNC)$_2$.[17] Our study[18] of the reactivity of this η^2 complex revealed that this mode of coordination stabilizes the diazoalkane against N$_2$ evolution and thereby hinders carbene complex formation. Considering the electropositive character of Co(II) in Co(α-cqd)$_2$·H$_2$O, the η^2(N,N) complexation is not expected in step 1. The ligation with the terminal nitrogen atom (η^1(N) species), which will be formed by interaction with the positive metal center at low temperature, is sterically preferred but will not lead to N$_2$ evolution. Sterically hindered diazoalkanes, Ph$_2$CN$_2$ or 9-diazofluorene, are decomposed by Co(dmg)$_2$ but not by Co(α- or β-cqd)$_2$·H$_2$O. Probably, the ligand bulk of Co(cqd)$_2$ only allows these diazoalkanes the η^1(N) coordination mode, which does not induce the C-N$_2$ bond cleavage. Since examination of the MOs[19] of the η^1(C) coordination indicates weakening of the C-N$_2$ bond, the η^1(C)-coordinated diazoalkane must be kinetically unstable and readily eliminates dinitrogen molecule to give the corresponding carbene complex.[20] It is known that the carbon-nitrogen bond of diazoalkane is readily cleaved upon interaction with a Lewis acid such as BF$_3$, etc. The Lewis acidity at the Co(II) coordination center probably causes similar σ-acid-base interaction with the nucleophilic sp^2 carbon of diazoalkane. Considering the catalytic activity of low-valent Rh or Pd complexes for decomposition of diazoalkanes, the σ-acid-base interaction does not seem to be the sole factor for the nitrogen evolution. In these low-valent transition metal catalyses, a σ-donative interaction of a filled metal orbital with the antibonding π^* molecular orbital (3B$_1$)[19] of diazoalkane is possible. However, the metal in Co(α-cqd)$_2$ is probably not such a strongly electron-donating center. The lack of electron-donating substituents on the carbene also results in the instability of the carbene-metal bond and facilitates a nucleophilic olefin attack.



η^2(N,N) complex η^1(N) complex η^1(C) complex

As discussed above, the reaction of diazoalkane with the metal compound leads to a metal carbene species. Although we were unable to obtain direct evidences for the intermediacy owing to the instability, there is ample indirect evidence,

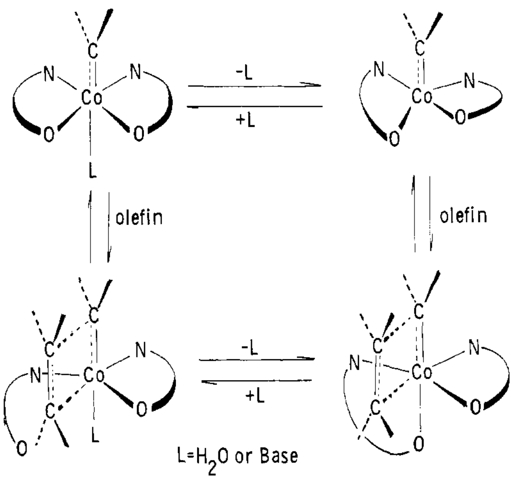


Figure 5. A postulated mechanism of the reaction of an olefin with the cobalt-carbene intermediate.

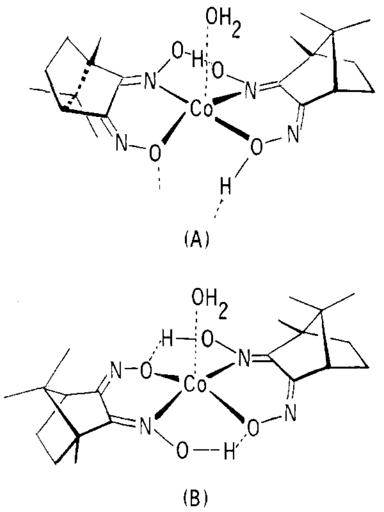


Figure 6. Possible structures of $Co(\alpha\text{-cqd})_2 \cdot H_2O$.

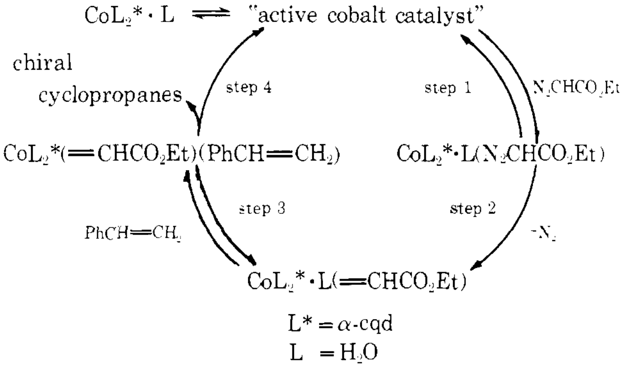
namely, (1) the formation of carbene dimers in the absence of excess olefin, (2) a sudden death of the catalytic activity at low olefin substrate concentrations which is due to an intramolecular carbenoid reaction, and (3) the remarkably high stereoselectivity in the formation of one cyclopropane enantiomer which can be explained by the effective selection of the enantiofaces of the carbene-metal species.

Step 3 is an olefin attack on the carbene complex. The electronic effect of the olefin component on the rate (Table II) suggests an electropositive character of the carbene carbon attached to Co(II). Consistently, a competitive cyclopropanation using a mixture of styrene and methyl acrylate gave only cyclopropanation products of styrene. It is worth noting that the α- and δ-dioximato complexes produce *cis*-2-phenylcyclopropanecarboxylate in relatively high yield (Tables III, V, and VIII). This is remarkable since the $Co(dmg)_2$-catalyzed reaction gives a high trans/cis ratio (~5). The copper-catalyzed reaction also gives the trans isomer in large excess. The steric interaction between the two reactants (olefin and cobalt-carbene moiety) should favor the formation of the trans cyclopropanes. The factor is apparently overcome in the far more congested transition state (step 3) of the present system (olefin, cobalt carbenoid moiety plus bulky ligands). The preferential formation of the cis olefin, maleate, in the stoichiometric decomposition of the diazoacetate by these cobalt complexes (Experimental Section) also reflects the congestion. This steric effect could be a factor preventing the side reaction of carbenoids in the cyclopropanation catalysis. The observed regioselectivity[2] with respect to the olefin may also be due to this steric congestion.

Step 4 is a release of the cyclopropane from the hypothetical cobaltacyclobutane intermediate. The process is accompanied to some extent by epimerization as will be discussed later. Thus, step 4 constitutes a stereochemically important but kinetically less important process.

In general, hexacoordinate Co(II) complexes are labile[21] and react with nucleophilic reagents through a dissociative mechanism. In the hexacoordinated metal-carbene intermediate, $Co(\alpha\text{-cqd})_2(\text{carbene})(L)$, a strongly coordinating ligand L should prevent the olefin approach. Indeed a retarding effect of an added axial base was observed (Table I). The accommodation of an olefin in the carbene-metal species may be achieved through either dissociation of a weakly coordinated ligand like a water molecule or detachment of one of the coordinating atoms of the chelate (see Figure 5). The latter process is less likely but cannot be excluded. Here, a two-center interaction is postulated in which the metal allows the olefin approach only through the unsubstituted terminal carbon atom. The large negative $\Delta S^{\ddagger}_{\text{app}}$ value for the reaction involving a base (Table I) is interpreted in terms of the dissociation effect and is thus consistent with the proposed reaction scheme (Figure 5). A perfect concert, however, is not alleged, as will become evident from consideration of the epimerization (vide infra).

Scheme I



The catalytic cycle is shown in Scheme I.

Catalyst Structure and Mechanism of Enantioface Selection. Our first task was to determine the catalyst structure. Unfortunately, unambiguous structural determination of the pentacoordinate compound, $Co(\alpha\text{-cqd})_2 \cdot H_2O$, could not be made, because attempts to obtain a single crystal appropriate for x-ray analysis were unsuccessful. The structure was conjectured mainly on the basis of molecular weight determination, the electronic spectrum, and the magnetic property. It is dimeric in benzene. This fact provides an important clue for the geometry of the first coordination sphere. Of two possible geometrical alignments of α-cqd ligands (A and B in Figure 6), the cis form A is more likely in view of the incapability of the trans form B to form the dimer through hydrogen bonds as revealed by the molecular model (in structure B, intramolecular hydrogen bonds are possible). Since the steric bulk of two α-cqd ligands prevents association in axial direction through bridging of coordinating oxygen atoms, the dimer formation must be achieved by two intermolecular hydrogen bonds possible only through the coordinating O atoms but not through the uncoordinated O atoms of the α-cqd ligands. The latter are involved in a puckered six-membered chelate ring Co-NO—HON.[7]

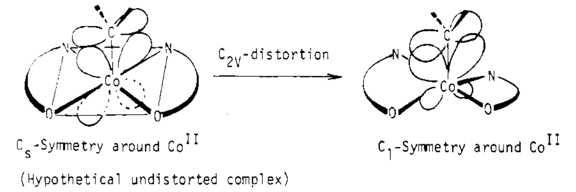
Usually, bis N,O-chelated Co(II) complex, $Co(N\text{-}O)_2 \cdot L$, forms a square pyramidal structure. The molecular model of A (Figure 6) indicates C_{2v} distortion from the planar ar-

Table XI. Percentages of Carbon *S* Configuration at C-1 and C-2 in Total Cyclopropanation Product, *cis*- and *trans*-$Ph^2\underline{CH^3CH_2{}^1C}HCO_2R$, Obtained with Co($\alpha$-cqd)$_2$·H$_2$O Catalyst

	C-1		C-2	
R	Total 1*S* %[a]	Excess % (confign)[b]	Total 2*S* %[a]	Excess % (confign)[b]
Me	83	66 (*S*)	42	16 (*R*)
Et	86	72 (*S*)	48	4 (*R*)
i-Pr	90	80 (*S*)	55	10 (*S*)
c-Hex	89	78 (*S*)	58	16 (*S*)
neo-Pent	93	86 (*S*)	69	38 (*S*)

[a] Values of 1*S* % calculated by the following equations, where P_{cis} and P_{trans} are the optical yields of the cis and trans isomers, respectively, and Y is the trans/cis ratio: total $1S(\%) = 1S_{cis} + 1S_{trans} = (1S,2S) + (1S,2R)$ (1); $1S_{cis}/1R_{cis} = (100 + P_{cis})/(100 - P_{cis})$ (2); $1S_{cis} + 1R_{cis} = 100/(1 + Y)$ (3); $1S_{trans}/1R_{trans} = (100 + P_{trans})/(100 - P_{trans})$ (4); $1S_{trans} + 1R_{trans} = 100Y/(1 + Y)$ (5). Similarly was obtained 2*S* %. [b] Excess % = total *S* (%) − total *R* (%).

rangement (C_s) of the two sets of chelated N,O atoms owing to the proximity of the two uncoordinated O atoms. The distortion will be more enhanced in the assumed Co(II)–carbene complex by the orbital interaction between the vacant p orbital of the carbene and the filled d orbital of Co(II). A similar C_{2v} distortion in a pentacoordinated mixed-ligand metal complexes with one axial π-acid ligand has recently been suggested by Hoffmann et al.[22] This geometrical feature is considered to be most important for the enantiofacial selection on the metal-carbene plane. The dramatic effect of an added pyridine base on the optical yield (Table VI) is now understood as arising from hexacoordination which has local C_s symmetry. Note that chirality still exists in the hexacoordinated complex molecule, Co(α-cqd)$_2$(carbene)(base), as a whole.



With respect to the carbene moiety, there are two conformations, C and D (Figure 7). The ratio of the two conformations will be determined by the steric environment and preferential formation of one comformer is necessary for the enantioselection. The observed high stereoselectivity lends indirect support for the assumed structure A rather than B, since the available space in A opens toward the two coordinated-oxygen atoms like an opened clam shell, while in B the coordinating nitrogen and oxygen atoms assume trans alignments, and the walls around Co(II) are more or less parallel (see Figure 6).

Let us examine the product stereochemistry. Distribution of four stereoisomers of 2-phenylcyclopropanecarboxylic esters, i.e., (1*S*,2*S*), (1*S*,2*R*), (1*R*,2*R*), and (1*R*,2*S*), in the total cyclopropanation product can be calculated from the trans/cis values and the optical yields of each trans and cis isomers (cf. Table III). The combined amounts of (1*S*) products, i.e., (1*S*,2*S*) + (1*S*,2*R*), and (2*S*) products ((1*S*,2*S*) + (1*R*,2*S*)) are listed in Table XI which shows enantioselection for the *S* configuration at C-1 but not at C-2. Note that the predominant C-2 configuration changes from *R* to *S* as the ester size increases. The result implies that the enantiofacial selection of the prochiral olefin plane is virtually absent when the carbene substituent is small. The increase in *S* configuration at C-2 with an increase in bulkiness of the ester group is related to the increase of the trans cyclopropane product.

A discussion of the enantioselection mechanism is now in order. A prochiral diazoalkane gives, upon η^1(C) coordination, two diastereomeric cobalt-diazoalkane complexes which go on to the cobalt-carbene complexes (C and D in Figure 7). Consideration by molecular models reveals that the sterically preferred conformation of Co(carbene)(α-cqd)$_2$(L) is C rather than D (Figure 7). It is possible that one of the diastereomeric diazoalkane complexes transforms stereospecifically to the less preferred conformation D. However, even in this case, the rotation of the cobalt-carbene bond would convert D to the preferred one C. Thus rotation could equilibrate two carbene-cobalt conformers whose ratio is subject to their sterical environments. When the preference of C is assumed, the olefin will predominantly approach to the si face of the Co(II)-carbene plane due to the congestion in the re face. The *S* configuration of C-1 of the predominant enantiomer of the cyclopropanecarboxylates can be ascribed to this transition state geometry.

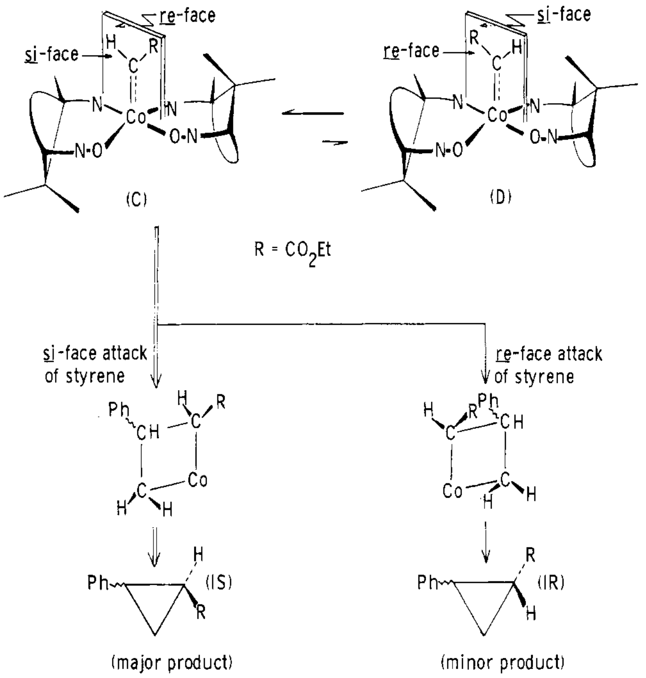
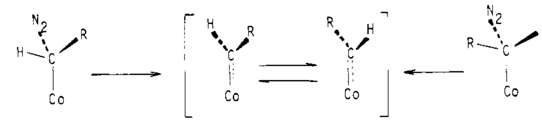


Figure 7. A proposed mechanism of the preferential si-face attack in the enantioselective cyclopropanation by Co(α-cqd)$_2$.



The above discussion, based purely on the steric aspect, may be an oversimplification. In the cis alignment of the coordinating atoms of Co(α-cqd)$_2$, the different electronegativity of O and N atoms should produce a polarization in the first coordinating sphere. Hydrogen bond formation would occur preferentially between the coordinated oxygen atoms of α-cqd and the carbonyl oxygen atom of the ester group of alkoxycabonylcarbene. This could be an assisting factor for stabilizing the preferred carbene conformation C.

In the first coordination sphere, both Co(δ-cqd)$_2$·H$_2$O and Co(δ-nqd)$_2$·H$_2$O are identical. The reverse Cotton effect[7] with maxima of comparable intensities indicates that the two δ-dioximato complexes are effectively enantiomeric to Co(α-cqd)$_2$·H$_2$O, only minor peripheral modification being involved (Figure 8). The structural relationships may be regarded as *quasi-enantiomeric.*[23] It is obvious then that an attacking styrene is allowed to approach the re face of the Co(=CHCO$_2$R) moiety (Figure 9) to form the cyclopropanes of (1*R*) configuration. The high optical yields and the opposite

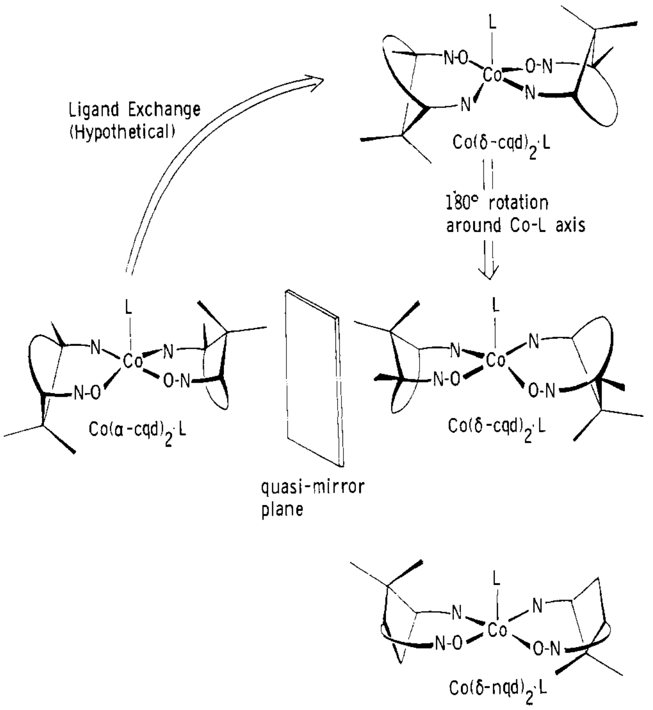


Figure 8. Chiral environment of Co(α-cqd)$_2$·L, Co(δ-cqd)$_2$·L, and Co(δ-nqd)$_2$·L.

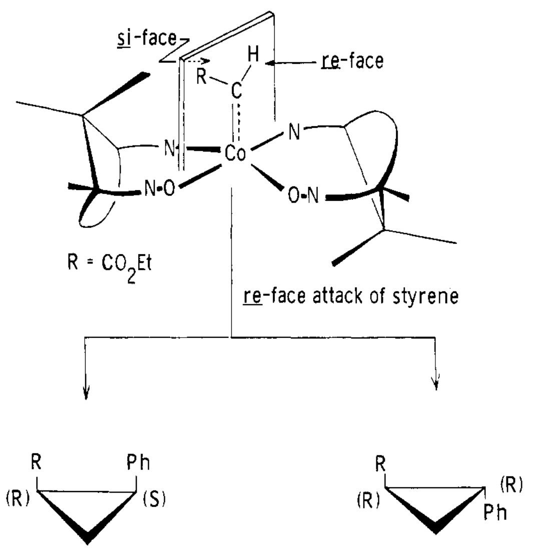


Figure 9. A proposed mechanism of the preferential re-face attack in the enantioselective cyclopropanation by Co(δ-cqd)$_2$.

chiralities of the products strongly support the proposed enantioselection mechanism based on the cobalt-carbene complexes.

Co(δ-Prcqd)$_2$·H$_2$O is assumed to have the same coordination geometry as Co(δ-cqd)$_2$·H$_2$O based on the similar CD spectra.[7] The optical yields produced by this complex are unexpectedly low. This may be due to contamination by geometrically isomeric complexes.

Co(β-cqd)$_2$·H$_2$O assumes an ordinary five-membered N,N-chelation around the metal where the C_{2v} distortion does not create chirality in the first coordination sphere and the local symmetry of the first coordination sphere including the carbene ligand (a pentacoordination) belongs to C_s symmetry. As was the case with the catalysis with an added pyridine base, the relatively low optical yield may reflect this factor. Caution is necessary here, however, The diamagnetic Co(III) species, CoCl(β-cqd)$_2$·py (py = pyridine),[7] was found to be a mixture of structural isomers. Similarly, one syn and two anti isomers are possible for Co(β-cqd)$_2$·L (Figure 10). Thus the complex Co(β-cqd)$_2$·H$_2$O obtained could also be an isomer mixture. This could also be the case for Co(β-nqd)$_2$·2H$_2$O. Unfortunately, we could not determine the isomer ratio in these β-dioximatocobalt(II) compounds. The results (Table VII) obtained with these β-dioximato complexes are therefore inadequate for discussion of the reaction stereochemistry.

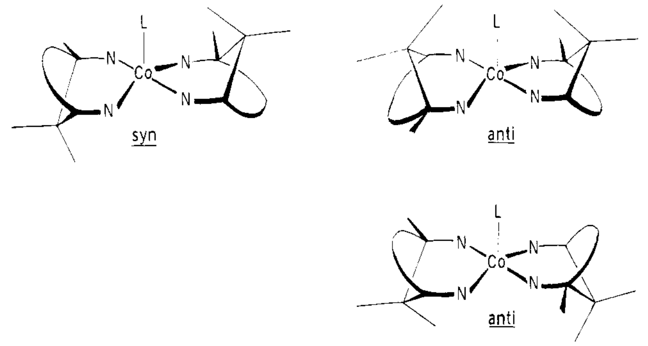
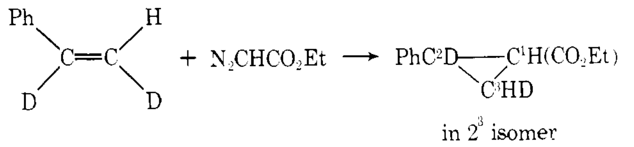


Figure 10. Schematic drawings of possible structures of Co(β-cqd)$_2$·L.

The foregoing argument is based on a concerted multicenter mechanism. However, the epimerization at one ring carbon atom found by the experiment using *cis*-d_2-styrene (Table VII) is incompatible with a perfectly concerted multicenter mechanism. In the cyclopropanation of *cis*-d_2-styrene with ethyl diazoacetate, three asymmetric carbons are generated. Eight stereoisomers are possible. It is possible that the enantioselection at C-1 is independent from the selection at C-2 and C-3.



$$\text{PhDC=CHD} + \text{N}_2\text{CHCO}_2\text{Et} \longrightarrow \text{PhC}^2\text{D}\!-\!\text{C}^1\text{H(CO}_2\text{Et)}\!-\!\text{C}^3\text{HD}$$

in 2^3 isomer

The recovery of the original *cis*-d_2-styrene from the reaction indicates no isomerization prior to the cyclopropanation and the occurrence of geometrical isomerization of the olefin double bond (epimerization at C-3) during the ring contraction step (step 4; see Table VII). The isomerization could occur either prior to or during the ring closure. Since the steric bulk of the Co(α-cqd)$_2$ is expected to result in the regioselective formation of a cobaltacyclobutane intermediate (Co–C^1–C^2–C^3) containing the terminal olefinic carbon as C-3, a bond formation between C-1 and C-3 is most probable for the cyclopropane formation step. The epimerization at C-1 in a cobaltacyclobutane intermediate, (1*S*,2*S*,3*S*)-Co-CH(CO$_2$R)-CHD-CDPh (step 4), if it occurs, gives (1*R*,2*S*,3*S*)-cyclopropane and lowers the optical yield of the prevailing (1*S*,2*S*,3*S*) isomer. Although the epimerization cannot be directly estimated from the optical yields of the cyclopropanation, the extent should become minor when a bulky group is attached to C-1 (see Table III). Thus the higher optical yield obtained with a bulkier ester group (Table III) could be a result arising from the steric effect exerted on several stereochemically important steps (step 2, 3, and 4). The epimerization at C-3 is not strongly temperature dependent as the geometrical isomerization persists at low reaction temperature (see Table VII). A small activation energy is thus implicated for this process probably because of the small size of the -CHD- group. If the Co–carbene bond is regarded as a two centers-two electrons bond, the cobaltacyclobutane formation is formally a cycloaddition reaction which requires either a symmetry-allowed process [2$_s$ + 2$_a$] or a biradical intermediate.[24] A rationale for the facile epimerization can then be given on this basis, if one ignores the participation of d orbitals.

The nonlinear temperature dependence of enantioselection (see Figure 3) merits discussion. The energetics shown in Table IV were obtained only for a limited temperature range where a linear correlation of ln (c_S/c_R) with temperature holds. Therefore caution is necessary to interpret these data. Obviously, an enantioselection mechanism involving only one diastereomeric transition state is not adequate here. In the present catalysis, the formation of a diastereomeric complex from the carbene-metal and styrene (step 3) is the most stereochemically important step as revealed by the steric effect of both components. There is another stereochemically important step (epimerization) affecting the stereochemical integrity at C-1 (step 4). A large entropy contribution will seriously affect the energy profile of a reaction coordinate on changing the temperature greatly (100 to −25 °C) leading to a non-Arrhenius relation. A negative activation entropy is expected for the bimolecular reaction of step 3 while a positive value is expected for the unimolecular process of step 4. It follows that while the energy barrier at step 3 is reduced to some extent, say, a few kilocalories upon lowering temperature by 100 °C, a reversed situation is expected for step 4. Step 4 will then become important at low temperatures. In such cases, a maximum could be observed in the plot of optical yields vs. temperature. In some catalytic asymmetric reactions[25] such a nonlinear behavior has been observed but no interpretation attempted. The maximum point depends on the energetic terms of each step involved. Although the presently available energetic data are not sufficient for a quantitative assessment, the nonlinear dependence is qualitatively explicable in terms of multistep processes in which the energy profile is susceptible to a temperature change.

Conclusions

Thus far the unique properties of Co(α-cqd)$_2$·H$_2$O in the carbenoid reaction have been amply demonstrated. The complex is far superior to the conventional catalysts in the activity at low temperature, chemical yield, enantioselectivity, and regioselectivity. The contribution to organic synthesis is obvious. The mechanistic study reveals an intriguing sequence of elemental reactions: carbene complex formation, enantiofacial selection upon olefin attack, and epimerization during the cyclization.

The established correlation between the chirality of cyclopropane products and the catalyst structure enable us to produce selectively the desired enantiomer of the cyclopropanes. For the preparation of the other enantiomer in excess, the catalyst systems are not necessarily required to be exactly enantiomeric. A *quasi-enantiomeric* catalyst fulfills the task. In the present case, for example, we do not require the cobalt complex to be made from (−)-camphor of limited accessibility. The results should contribute to the design of a chiral catalyst for not only the carbenoid reaction but also possibly for many other synthetic reactions.

Experimental Section

Isopropyl, isobutyl, cyclohexyl, and neopentyl diazoacetate were obtained in the same manner as for ethyl diazoacetate[26] and characterized by elemental analysis, ^{1}H NMR spectra, and boiling points: *i*-Pr, bp 26–27 °C (4 mm); *i*-Bu, bp 42–43 °C (25 mm); c-Hex, bp 52–53 °C (1 × 10^{-2} mm); neo-Pen, bp 26–27 °C (3 × 10^{-1} mm).

(1*R*,4*S*,7*R*)-7-*anti*-(*n*-Butyl)-1,7-dimethylnorbornane-2,3-dione-2,3-dioxime (PrcqdH). The reaction (35–40 °C, 48 h) of [Ni(η^3-C$_3$H$_5$)Br]$_2$ (0.731 mol) with 9-bromocamphor[27] (0.710 mol) in dimethylformamide (500 mL) gave, after usual workup[28] and vacuum distillation (89–94 °C, 1.5 mm), the coupling product in 78% yield (based on 9-bromocamphor): MS *m/e* 192; $[\alpha]^{24}{}_D$ +92.2° (*c* 3.55, ethanol); ^{1}H NMR (CDCl$_3$) δ 0.86 (s, 3 H), 0.93 (s, 3 H), 1.00–2.44 (m, 11 H), 4.84–5.14 (m, 2 H), 5.60–6.04 (m, 1 H). Anal. (C$_{13}$H$_{20}$O) C, H.

The coupling product (0.547 mol) was catalytically hydrogenated (5% Pd/C, 25 °C) in ethyl acetate (250 mL) to give quantitatively the saturated product, (1*R*,4*R*,7*R*)-7-*anti*-(*n*-butyl)-1,7-dimethylnorbornan-2-one: MS *m/e* 194; $[\alpha]^{24}{}_D$ +83.6° (*c* 4.47, ethanol); ^{1}H NMR (CDCl$_3$) δ 0.84 (s, 3 H), 0.93 (s, 3 H), 0.94 (t, 3 H), 1.00–2.44 (m, 13 H). Anal. (C$_{13}$H$_{22}$O) C, H.

The monoketone (0.44 mol) was converted into the isonitroso derivative (28%) by the same method used for isonitrosocamphor.[29] The crude isonitroso compound (ca. 0.12 mol), a yellow, viscous oil, was dissolved in ethanol (20 mL), and then treated with a hot aqueous solution (4 mL) of NH$_2$OH·HCl (0.25 mol) and NaOAc (0.26 mol). A pale yellow precipitate was obtained. The precipitate was recrystallized several times from ethyl acetate to give a pure (1*R*,4*S*,7*R*)-7-*anti*-(*n*-butyl)-1,7-dimethylnorbornane-2,3-dione-2(*E*)-3(*E*)-dioxime (β-PrcqdH) (8.4 mmol): mp 223–224 °C $[\alpha]^{23}{}_D$ +42.5° (*c* 0.870, Me$_2$SO); ^{1}H NMR (Me$_2$SO-d_6) δ 0.83 (s, 3 H), 0.90 (t, 3 H), 1.35 (s, 3 H), 0.90–1.84 (m, 10 H), 3.10 (d, 1 H), 10.57 (s, 1 H), 10.61 (s, 1 H). Anal. (C$_{13}$H$_{22}$N$_2$O$_2$) C, H, N.

Upon concentration of the mother liquid, a mixture of α, (2*E*,3*Z*), β, (2*E*,3*E*), and δ isomer, (2*Z*,3*E*), was obtained as a sticky solid. Several recrystallizations from methanol gave an analytically and optically pure sample of the δ-PrcqdH (6.3 mmol): mp 165–167 °C; $[\alpha]^{22}{}_D$ + 85.3° (*c* 1.55, ethanol); ^{1}H NMR (Me$_2$SO-d_6) δ 0.73 (s, 3 H), 0.89 (t, 3 H), 0.99 (s, 3 H), 0.90–1.80 (m, 10 H), 3.14 (d, 1 H), 10.85 (s, 1 H), 11.01 (s, 1 H). Anal. (C$_{13}$H$_{22}$N$_2$O$_2$) C, H, N. The presence of α isomer was detected by a ^{1}H NMR spectrum of the mixture. The amount was too small to be isolated.

Nopinoquinonedioxime (nqdH). (+)-Nopinone, α_D +14.5°, was prepared according to the known method[30] from (−)-β-pinene, α_D −17.2° (optical purity 93%; a generous gift of Takasago Perfumery Co. Ltd.). Following the conventional method[29] using isoamyl nitrite, isonitrosonopinone was obtained in 33% yield from (+)-nopinone. Crude isonitrosonopinone (ca. 0.39 mol) dissolved in 100 mL of ethanol was treated with an aqueous solution (10 mL) of NH$_2$OH·HCl (0.81 mol) and NaOAc (0.86 mol) at 80–90 °C for 2–3 days. The solid product precipitated from the cooled reaction mixture was recrystallized four times from ethyl acetate to give an analytically and optically pure sample of the δ isomer (0.066 mol): mp 214.5–216 °C; $[\alpha]^{20}{}_D$ +10° (*c* 1.42, methanol); ^{1}H NMR (Me$_2$SO-d_6) δ 0.74 (s, 3 H), 1.20 (mc, 1 H), 1.31 (s, 3 H), 2.10 (mc, 1 H), 2.44–2.78 (m, 4 H), 12.08 (s, 1 H), 12.30 (s, 1 H). Anal. (C$_9$H$_{14}$N$_2$O$_2$) C, H.

The mother liquid was concentrated in vacuo to one-half of the original volume to give a mixture of δ and β isomer as the first crop which was discarded. Further concentration, removing ethanol completely, gave crude β isomer as a colorless solid. Recrystallization from aqueous ethanol gave the pure β isomer (0.176 mol): mp 210–211 °C; $[\alpha]^{21}{}_D$ +40° (*c* 1.09, methanol); ^{1}H NMR (Me$_2$SO-d_6) δ 0.74 (s, 3 H), 1.07 (d, 1 H), 1.30 (s, 3 H), 2.05 (mc, 1 H), 2.48–2.74 (m, 3 H), 3.47 (t, 1 H), 10.72 (s, 1 H), 11.09 (s, 1 H).

Bis[(+)-(1*R*,4*S*,7*R*)-7-*anti*-(*n*-butyl)-1,7-dimethylnorbornane-2,3-dione-2(*Z*)-3(*E*)-dioximato]cobalt(II) Hydrate, Co(δ-Prcqd)$_2$·H$_2$O. This was prepared with the same method as previously described for Co(α-cqd)$_2$·H$_2$O using δ-PrcqdH as a brown, microcrystalline solid, mp 241–243 °C. Anal. (C$_{26}$H$_{44}$N$_4$O$_5$Co) C, H, N.

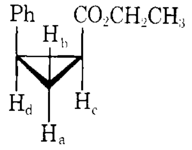
Bis[(+)-nopinoquinone-δ-dioximato]cobalt(II) Hydrate, Co(δ-nqd)$_2$·H$_2$O. This was prepared similarly using δ-nqdH as a brown, microcrystalline solid, mp >250 °C dec. Anal. (C$_{18}$H$_{28}$N$_4$O$_5$Co) C, H, N.

Decomposition of Ethyl Diazoacetate in the Presence of Co(I) or Co(III) cqd Complex. Co(α-cqd)$_2$·H$_2$O (0.492 g) was reduced with 1% Na amalgam (9.5 g) in tetrahydrofuran (13.5 g) under nitrogen until the brown color had changed to green. The Co(I) complex was immediately used for decomposition of ethyl diazoacetate after removal of the amalgam, evaporation of the solution, and dissolution of the almost black residue in toluene. The rate of decomposition of ethyl diazoacetate (k_{obsd}) was measured in toluene under the following condition: [Co(I) complex], 1.2 × 10^{-2} M; [N$_2$CHCO$_2$Et], 0.23 M; [PhCH=CH$_2$], 4.4 M; at 0 °C to obtain k_{obsd}, 2.1 × 10^{-3} min^{-1}. The k_{obsd} was about $^1/_7$ of the value obtained in the reaction with Co(α-cqd)·H$_2$O as catalyst.

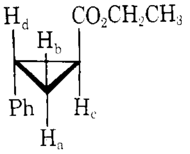
Ethyl diazoacetate was not decomposed even at 60 °C in styrene in the presence of the Co(III) complexes, e.g., [Co(α-cqd)$_2$(OH)$_n$], CoCl(β-cqd)$_2$py, or CoCH$_3$(β-cqd)$_2$py.[7]

Decomposition of Ethyl Diazoacetate with a Catalytic Amount of Co(α-cqd)$_2$ in the Absence or Presence of Styrene. (1) Ethyl diazoacetate (0.40 g, 3.5 mmol) was added to a toluene solution (5 mL) of Co(α-cqd)$_2$·H$_2$O (0.19 g, 0.43 mmol) at 21–23 °C and the nitrogen

Chart I



	CH_3	H_a	H_b	H_c	H_d	CH_2
δ, ppm	0.96 t	1.30 mc	1.70 mc	2.06 mc	2.58 mc	3.88 q
$\Delta\delta$, ppm	3.3	3.1	6.3	9.2	4.1	9.1



	CH_3	H_a	H_b	H_c	H_d	CH_2
δ, ppm	1.26 t	1.30 mc	1.86 mc	2.52 mc	2.52 mc	4.18 q
$\Delta\delta$, ppm	3.3	4.0	7.7	8.5	8.3	10.8

gas evolution was monitored for 6 h (see Figure 1, curve 1). Diethyl fumarate and diethyl maleate were detected by GLC among the products. (2) After the gas evolution amounted to 1 molar equiv of the catalyst at the same condition as (1), styrene (4 mL) was added to the reaction mixture (Figure 1, curve 2). Then nitrogen evolution resumed. (3) The catalytic decomposition of ethyl diazoacetate was performed in styrene solution at the same condition as (1) (Figure 1, curve 3). The reaction immediately occurred and was almost completed in 20 min.

Kinetics of the Co(α-cqd)$_2$-Catalyzed Reaction of Ethyl Diazoacetate with Styrene. A 50-mL Erlenmeyer flask with a 10/20 female joint, which had two small side necks, one near the top and the other fitted with a rubber stopper, was connected to a measuing part which also serves as a vacuum take-off and nitrogen take-in. Nitrogen evolution was measured by a gas buret filled with decalin. The reaction temperature was maintained to ±0.2 °C with a water bath. The contents of the vessel was magnetically stirred. Reagent grade styrene, ethyl diazoacetate, and solvents were freshly distilled under nitrogen. A standard solution of the catalyst (0.048 M) was prepared by dissolving Co(α-cqd)$_2$·H_2O in styrene under nitrogen. The air in the reaction vessel was displaced with pure nitrogen and then the catalyst solution (2.5 mL) was charged through the side neck with a syringe. To the vessel immersed in a constant temperature bath, an ethyl diazoacetate solution (0.92 M, 2.5 mL) was added with vigorous stirring through the side neck with a syringe. Nitrogen evolution commenced immediately. The quantity of nitrogen gas evolved was measured to an accuracy of ±0.08 mL at atmospheric pressure. A typical experiment in neat styrene at 0.0 ± 0.2 °C gave an apparent pseudo-first-order rate constant of 2.1×10^{-2} min^{-1} until 80% reaction. The rate constants in various solvents are listed below in an order of solvent, styrene concentration (M), and rate constants ($\times 10^{-2}$ min^{-1}): toluene (at 0 °C), 4.6, 1.4; 2.1, 0.98; 1.8, 0.52. Ethyl acetate (at 20 °C), 5.2, 2.8; 2.4, 2.5; 1.4, 0.44. 1-Phenyl-1-propene (at 20 °C), 8.5, 3.2; 3.6, 2.8; 1.7, 2.0; 0.90, 1.4; 0.70, 1.1; 0.54, 0.90. None (at 20 °C), 3.2.

Asymmetric Kinetic Parameters in the Cyclopropanation of Styrene with Various Diazoacetates. The molar ratio of catalyst and reagents was kept constant (Co(α-cqd)$_2$·$H_2O/N_2CHCO_2R/PhCH{=}CH_2$ = 3/100/300, R = Me, Et, *i*-Pr) throughout. The reactions of each alkyl diazoacetate were carried out at 0, 25, 65, and 100 °C. The mixture of alkyl *cis*- and *trans*-2-phenylcyclopropanecarboxylate obtained from each reaction was separated into the pure isomer by GLC and each hydrolyzed to the acid for evaluation of the optical activity (cf. Figure 3). The energy parameters are calculated for the trans isomer formed by reactions at 24–100 °C and shown in Table IV.

Geometrical Isomerization of an Olefin Component in the Cyclopropanation. *cis*-d_2-Styrene was prepared by hydrogenation of phenylacetylene with deuterium catalyzed with Lindlar catalyst (the ratio of *cis*-d_2- to *trans*-d_2-styrene thus obtained was 80/20). The catalytic carbenoid reaction of ethyl diazoacetate with *cis*-d_2-styrene in the presence of Co(α-cqd)$_2$·H_2O was performed in the same manner as in the carbenoid reaction in styrene, which was previously described.[2] The ^1H NMR spectra of each isomer of 2,3-dideuterio-*cis*- and -*trans*-2-phenylcyclopropanecarboxylic acid are shown in Figure 4. The value of the isomer distribution (cf. Table VII) have been corrected by assuming the stereochemical purity of the original *cis*-d_2-styrene. The ^1H NMR examination indicated that the stereochemical purity of the *cis*-d_2-styrene recovered after the reaction had not changed. To assign ^1H NMR of each isomer of ethyl *cis*- and *trans*-2-phenylcyclopropanecarboxylates, tris(heptafluorodimethyloctanedionate)europium(III) (Eu(fod)$_3$) was used as a shift reagent. The Eu-shifted ^1H NMR spectra were measured in $CDCl_3$ at molar ratios, ester/Eu(fod)$_3$, of 0.05, 0.1, and 0.2. The δ and $\Delta\delta$ values of each esters in $CDCl_3$ are listed below (δ values are observed ones in the absence of Eu(fod)$_3$ and $\Delta\delta$ values are the difference between the δ and the calculated values for the 1:1 mixture, i.e., the ester/Eu(fod)$_3$ = 1). The $\Delta\delta$ values led to the assignment shown in Chart I.

Stoichiometric Reaction of Ethyl Diazoacetate with Bisdioximatocobalt(II) Complexes. To a benzene solution (5 mL) of 1.34 mmol of a cobalt complex (vide infra) was added 1.19 mmol of ethyl diazoacetate at room temperature with stirring. The diazo compound being completely decomposed (ca. 4 h), the reaction mixture was analyzed by GLC (PEG-20M, 160 °C) for diethyl fumarate and maleate to give the results listed in the order of the cobalt(II) complex, the total yield of these esters based on the diazoacetate, and the fumarate/maleate ratio: Co(α-cqd)$_2$·H_2O, 7%, 0.18; Co(δ-nqd)$_2$·H_2O, 17%, 0.37; Co(δ-cqd)$_2$·H_2O, 10%, 0.66.

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Quinol Intermediates in the Reaction of π-Allylnickel Bromides with Quinones

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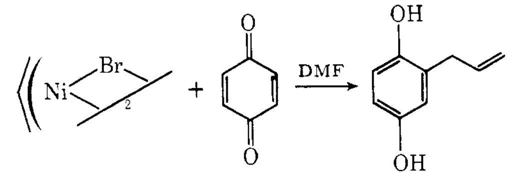
Abstract: The reaction of π-allylnickel bromide complexes with quinones was shown to proceed through relatively unstable allylquinol intermediates, which were isolated and characterized for the first time. Rearrangements of these allylquinols under a variety of conditions were studied, and their role in the production of allylquinones from the above reactions was elucidated.

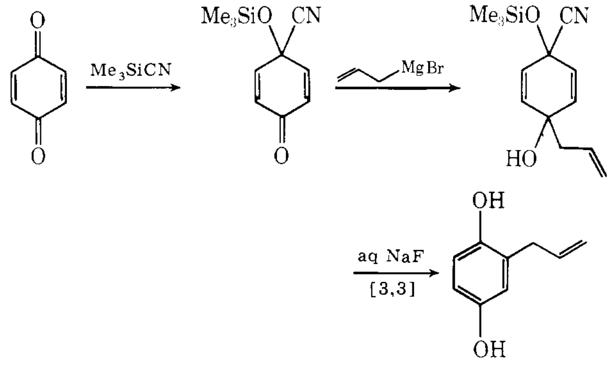
Introduction

The reaction of π-allylnickel bromide complexes with quinones produces allylhydroquinones in fair yield (eq 1).[1] With



(1)

unsymmetrical quinones under standardized reaction and isolation conditions high regioselectivity is observed, the allyl group being introduced at the ring site of highest spin density in the corresponding quinone radical anion.[2] However, alteration of reaction and isolation procedure leads to changes in the site of allylation, allowing a variety of differently substituted allylquinones and enediones to be prepared.[3] An alternate approach to allylquinones involving a protection, allylation, deprotection, and rearrangement sequence has recently been developed (eq 2).[4] Although allylquinols were never detected, they were implicated as intermediates and were thought to proceed to products via a facile [3,3] sigmatropic rearrangement. Since π-allylnickel halide complexes are known to react with ketones to produce homoallylic alcohols,[5] and since the products from eq 1 and 2 are identical, evidence for the intermediacy of allylquinols in the reaction of eq 1 was sought.



(2)

Results and Discussion

Isolation and Characterization of Allylquinols from the Reactions of π-Allylnickel Bromide Complexes with Quinones.

Since the standard reaction and isolation procedures for the reaction of π-allylnickel bromides with quinones involve stirring the reaction mixture for 12 h at 22 °C followed by partitioning between ether and 1.2 N HCl, quinols, if initially formed, would probably not survive these conditions. Hence the reactions were run under milder conditions (−10 to 0 °C) and isolated using a neutral partition between water and ether to facilitate detection of quinols. While no quinols were detectable in the reactions of simple alkyl quinones, quinols were *isolable* from reactions involving naphthoquinone, 2-methylnaphthoquinone, and 2,3-dimethoxy-5-methylbenzoquinone. This is the first time, to our knowledge, that allylquinols have been isolated and characterized. Once removed from the reaction mixture and purified these quinols were relatively stable, particularly those of dimethoxymethylbenzoquinone. Thus, treatment of this quinone with π-2-methylallylnickel bromide in DMF at −60 °C followed by slow warming to −10 °C, partitioning of the cold reaction mixture between ether and saturated NaCl solution, and separation by preparative layer chromatography gave both possible quinols (**1** and **2**) as well as rearrangement products thereof (eq 3). Quinols **1** and **2** had characteristic NMR spectra with well-separated signals for the two different OMe groups. They were differentiated by the relative chemical shifts of the ring methyl and hydrogen signals, δ 1.84 and 6.41, respectively, for **1** and δ 2.06 and 5.93 for **2**. In a similar fashion quinols **5**–**8** were prepared. All of these were relatively stable once purified, but underwent rapid rearrangement at 22 °C in the reaction mixture.

Quinol **1** was also prepared by the method described in eq 2. The protected quinol underwent deprotection *without* subsequent rearrangement upon treatment with aqueous NaF. The quinol of 2,5-dimethylbenzoquinone, prepared by the same route, was detected by NMR during the deprotection step but proved too unstable to isolate. Quinols **5** and **6** could not be prepared by this method since coupling of the allyl Grignard always occurred at the tertiary carbon of the allyl system,[4] in contrast to the primary coupling observed with π-allylnickel bromide complexes. Quinol **2** was also unavailable by eq 2 because of the regiospecificity of the protection reaction.

Behavior of the Pure Quinols. Isolation of substantial quantities of quinols from the above π-allylnickel bromide–quinone reactions suggests that quinols play an important role. To clarify this role, the behavior of the pure quinols was investigated first. Upon standing for periods (~2 weeks) at room

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