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Enhanced Activity of Sterically Crowded *N,N'*-Ethylenebis-(salicylideneaminato)cobalt(II) Derivatives as Catalysts for Oxygenation of 3-Methylindole

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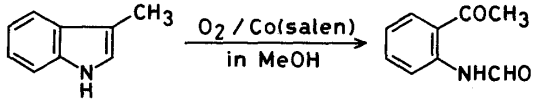
Six derivatives of *N,N'*-ethylenebis(3-*tert*-butylsalicylideneaminato)cobalt(II), abbreviated as Co(Busalen), were prepared by varying the diamine moiety with ethylenediamine, (*R*)-1,2-propanediamine, (2*S*,3*S*)-2,3-butanediamine, *meso*-2,3-butanediamine, (1*R*,2*R*)-1,2-cyclohexanediamine, and *cis*-1,2-cyclohexanediamine. The spectral and electrochemical properties of the complexes are reported. These complexes and four derivatives of *N,N'*-ethylenebis(salicylideneaminato)cobalt(II), Co(salen), were used as catalysts for the oxygenation of 3-methylindole. With increasing steric hindrance of the metal complex catalyst, the rate of the steady-state consumption of the substrate increased, and the induction period increased with increasing steric hindrance at the apical region of Co(Busalen) derivatives. A linear relationship was found between the logarithm of the rate constants and the half-wave potentials for $Co^{II/III}$ couples: $\log(10^2 k/\mathrm{mol^{-1}\,dm^{-3}\,s^{-1}}) = a(E_{1/2}/\mathrm{V}) + b$, where a and b are 5.2 and -0.56 for the Co(Busalen) series, and 5.5 and -1.25 for the Co(salen) series, respectively. Based on these observations, it is concluded that the catalysis is controlled by the redox potential and *tert*-butyl groups of the Co(Busalen) derivatives, and the activation of the substrate, not dioxygen, is the critical step of this reaction.

Keywords——*N,N'*-ethylenebis(salicylideneaminato)cobalt(II) derivative; 3-methylindole; oxygenation; catalysis; half-wave potential; structure–activity relationship

Oxygenation of 3-methylindole to 2-formylaminoacetophenone has been reported to



proceed in the presence of *N,N'*-ethylenebis(salicylideneaminato)cobalt(II), Co(salen), by Nishinaga.[1] This reaction is analogous to that catalyzed by tryptophan-2,3-dioxygenase[2] and the role of the catalyst is thus of interest in relation to the action of the enzyme. Several systems have since been reported to act as catalysts; CuCl–pyridine,[3] manganese phthalocyanine,[4] and cobalt and manganese porphyrin complexes.[5]

Although much attention has been paid to the interaction of dioxygen with Co(salen) derivatives, which show reversible absorption of dioxygen,[6] there have been few investigations of oxygenation reactions based upon the systematic modification of catalysts.[7] Such modification of catalysts should enable us to study the relationship between the structure of the catalysts and the catalytic activity, and should provide information useful for the design of more active and more selective catalysts. Two series of cobalt(II) Schiff-base chelates, Co(salen) and Co(Busalen) derivatives, of which the latter are derived from 3-*tert*-butylsalicylaldehyde instead of salicylaldehyde in the former, were prepared by varying the diamine moiety in order to investigate the steric effect on the catalytic activity for the

oxygenation of 3-methylindole. Furthermore, the relationship between the redox potentials of Co(salen) derivatives and the catalytic activities was investigated by cyclic voltammetry.

Experimental

Materials——Commercial 1,2-propanediamine was resolved as described by Dwyer *et al.* and (*R*)-1,2-propanediamine was obtained.[8] A mixture of *cis*- and *trans*-1,2-cyclohexanediamine was treated by the method of Kidani and Saito to separate the *cis*-isomer (*cis*-chxn).[9] (1*R*, 2*R*)-1,2-Cyclohexanediamine was obtained by resolution according to the method of Jaeger and Bijkerk.[10] (2*S*, 3*S*)-2,3-Butanediamine was prepared according to the method of Cooley *et al.*[11] *meso*-2,3-Butanediamine was prepared by hydrogenation of dimethylglyoxime with Raney nickel according to the method of Dickey *et al.*[12] 3-*tert*-Butylsalicylaldehyde was prepared according to the method of Duff[13] and by a slight modification of the method reported for 4-hydroxy-3,5-dimethoxybenzaldehyde.[14] Methanol was dehydrated by distillation over magnesium methoxide. All the other materials were purchased and used without further purification.

Preparation of Derivatives of *N,N'*-Ethylenebis(salicylideneimine)——*N,N'*-Ethylenebis(salicylideneimine) ($salenH_2$), *N,N'*-[(*R*)-1,2-propanediyl]bis(salicylideneimine) (sal-*R*-pnH_2), *N,N'*-[(1*R*, 2*R*)-1,2-cyclohexylene]bis-(salicylideneimine) (sal-*R*-chxnH_2), and *N,N'*-(*cis*-1,2-cyclohexylene)bis(salicylideneimine) (sal-*cis*-chxnH_2) were prepared according to the literature.[15]

***N,N'*-Ethylenebis(3-*tert*-butylsalicylideneimine) (BusalenH_2)**——A methanol solution of ethylenediamine (0.86 g, 14 mmol) was added to a solution of 3-*tert*-butylsalicylaldehyde (5.11 g, 28 mmol) in 30 cm^3 of methanol with constant stirring. The mixture was stirred for 30 min at 50—60 °C and then cooled on an ice-water bath. The yellow crystals that separated were collected on a filter, washed with small amounts of ice-cold methanol and dried *in vacuo*. Yield, 4.82 g (88%). These crystals were recrystallized from a 1 : 1 mixture of methanol and chloroform. The elemental analysis and melting point are shown in Table I, along with those of other compounds.

***N,N'*-[(*R*)-1,2-Propanediyl]bis(3-*tert*-butylsalicylideneimine) (Busal-*R*-pnH_2)**——A methanol solution of (*R*)-1,2-propanediamine (3.7 g, 0.05 mol) was added to a solution of 3-*tert*-butylsalicylaldehyde (17.8 g, 0.1 mol) in 110 cm^3 of methanol under stirring. The mixture was stirred for 30 min at 50—60 °C, then concentrated with a rotary evaporator to a yellow oil. This was dissolved in a minimum amount of methanol and the solution was filtered. The filtrate was left to stand in a refrigerator. Yellow crystals separated from the filtrate over 2 d. Yield, 14.8 g (75%).

***N,N'*-[(2*S*, 3*S*)-2,3-Butanediyl]bis(3-*tert*-butylsalicylideneimine) (Busal-*S*-bnH_2)**——A methanol solution of (2*S*,3*S*)-2,3-butanediamine (0.88 g, 10 mmol in 10 cm^3) was added to a methanol solution of 3-*tert*-butylsalicylaldehyde (3.56 g, 20 mmol). After being stirred at 50—60 °C for 30 min, the yellow solution was left to stand in a refrigerator for 3 d. The yellow crystals that separated were collected. Yield, 1.6 g (39%). This product was recrystallized from methanol.

***N,N'*-(*meso*-2,3-Butanediyl)bis(3-*tert*-butylsalicylideneimine) (Busal-*meso*-bnH_2)**——A methanol solution of *meso*-2,3-butanediamine (0.88 g, 10 mmol in 10 cm^3) was added to a methanol solution of 3-*tert*-butylsalicylaldehyde (3.56 g, 20 mmol). The mixture was stirred for 30 min at 50—60 °C. Yellow crystals that separated on cooling to room

Table I. Elemental Analyses and Melting Points of the Synthesized Compounds

	Elemental analyses (%)						mp (°C)
	C		H		N		
	Found	Calcd	Found	Calcd	Found	Calcd	
BusalenH_2	75.68	75.75	8.35	8.48	7.42	7.36	143.5—145
Busal-*R*-pnH_2	76.25	76.10	8.67	8.69	7.12	7.10	67—69
Busal-*meso*-bnH_2	76.23	76.43	8.73	8.88	6.57	6.86	131—133
Busal-*S*-bnH_2	76.65	76.43	8.96	8.88	6.97	6.86	81—83
Busal-*R*-chxnH_2	77.45	77.38	8.62	8.81	6.42	6.45	66—68
Busal-*cis*-chxnH_2	77.53	77.38	8.63	8.81	6.66	6.45	154—156
Co(Busalen)	65.67	65.90	6.86	6.91	6.47	6.40	
Co(Busal-*R*-pn)	66.42	66.51	7.10	7.14	6.43	6.20	
Co(Busal-*meso*-bn)	66.57	67.09	7.19	7.36	6.01	6.02	
Co(Busal-*S*-bn)·Me_2CO	66.34	66.52	7.72	7.70	5.57	5.35	
Co(Busal-*R*-chxn)	68.44	68.42	7.39	7.38	5.89	5.70	
Co(Busal-*cis*-chxn)	68.31	68.42	7.22	7.38	5.80	5.70	

temperature were collected on a filter, washed with a small amount of cold methanol, and recrystallized from methanol. Yield, 1.07 g (26%).

***N,N'*-[(1*R*,2*R*)-1,2-Cyclohexylene]bis(3-*tert*-butylsalicylideneimine) (Busal-*R*-chxnH_2)**——A mixture of 3-*tert*-butylsalicylaldehyde (17.8 g, 0.1 mol) and (1*R*,2*R*)-1,2-cyclohexanediamine (5.7 g, 0.05 mol) in 200 cm^3 of methanol was refluxed for 20 min. The yellow oil that separated was solidified on slow cooling to room temperature and the crude crystals were collected. Yield, 20.7 g (95%). The crude product was recrystallized from 420 cm^3 of methanol. Yield, 11.7 g (54%). A further crop was obtained by reducing the volume of the mother liquor. Yield, 5.83 g (27%).

***N,N'*-(*cis*-1,2-Cyclohexylene)bis(3-*tert*-butylsalicylideneimine) (Busal-*cis*-chxnH_2)**——A mixture of 3-*tert*-butylsalicylaldehyde (17.8 g, 0.1 mol) and *cis*-1,2-cyclohexanediamine (5.7 g, 0.05 mol) in 200 cm^3 of methanol was refluxed for 20 min. The yellow crystals that separated were collected on a filter. Yield, 19.8 g (91%). This product was recrystallized from an equivolume mixture of methanol and chloroform (300 cm^3). Yield, 15.7 g (72%).

Preparation of Cobalt(II) Complexes——Preparation of cobalt(II) complexes was carried out with a method analogous to that used for preparing *N,N'*-(1,1,2,2-tetramethylethylene)bis(3-*tert*-butylsalicylideneaminato)-cobalt(II), Co(Busal-Me_4en), as described by Schaefer *et al.*[16]

Co(Busalen): A methanolic solution of NaOH (0.12 g, 3 mmol in 7 cm^3) was added to the mixture of BusalenH_2 (0.55 g, 1.4 mmol) and $Co(OCOCH_3)_2 \cdot 4H_2O$ (0.36 g, 1.4 mmol) in 19 cm^3 of methanol under a nitrogen atmosphere. The red crystals that separated were washed with 5 cm^3 of methanol. Yield, 0.61 g (97%). This product was recrystallized from acetone.

Co(Busal-*R*-pn): A methanolic solution of NaOH (0.19 g, 4.8 mmol in 7.5 cm^3) was added to a mixture of Busal-*R*-pnH_2 (0.99 g, 2.5 mmol) and $Co(OCOCH_3)_2 \cdot 4H_2O$ (0.62 g, 2.5 mmol) in 15 cm^3 of methanol under a nitrogen atmosphere. The crystals that separated were washed twice with cold methanol. Yield, 1.05 g (93%). This product was recrystallized from 2-propanol.

Co(Busal-*R*-chxn): A mixture of Busal-*R*-chxnH_2 (4.34 g, 10 mmol) and methanol (70 cm^3) was heated to boiling and flushed with nitrogen. A methanol solution of $Co(OCOCH_3)_2 \cdot 4H_2O$ (2.49 g, 10 mmol in 25 cm^3) was then added with stirring. To the boiling mixture, a methanol solution of NaOH (0.8 g, 20 mmol in 30 cm^3 saturated with nitrogen) was added dropwise. The whole was kept at reflux for another 30 min then cooled to 0 °C. The crystals that separated were collected on a filter and washed with methanol (30 cm^3). Yield, 4.2 g (85%). These crystals were recrystallized from acetone.

Co(Busal-*cis*-chxn): Crude red crystals were obtained by the same method as described above, but with Busal-*cis*-chxnH_2 as the ligand. Yield, 3.57 g (73%). This product was recrystallized from 2-propanol.

Co(Busal-*S*-bn)·$(CH_3)_2CO$: This was obtained by the same method as above. The crude product was recrystallized from acetone.

Oxidation of 3-Methylindole——Oxygen saturated with dry methanol was passed into a methanol solution (20 cm^3) of 3-methylindole (3.5×10^{-2} mol dm^{-3}) in a reaction vessel at a flow rate of 23—25 cm^3 min^{-1} at 25±0.2 °C. The oxygenation was initiated by addition of weighed amounts of solid cobalt(II) complex (8.7×10^{-3} mol dm^{-3}). The decrease in amount of 3-methylindole was followed by gas liquid chromatography (GLC) (10% PEG20M + 5% KOH/celite, column temp. 200 °C) using biphenyl as an internal standard.

The oxygen uptake was independently measured using a gas buret which was connected to a reaction vessel at 1 atm (1 atm = 1.013×10^5 Pa). The reaction mixture was stirred magnetically.

Products Analysis——The reaction products were analyzed by high-performance liquid chromatography (HPLC) (column, Shodex Silicapak E-411, 0.46 (i.d.) × 15 cm; eluent, hexane : 2-propanol = 100 : 1.5; flow rate, 1.0 cm^3 min^{-1}) using biphenyl as an internal standard. An aliquot of 10×10^{-6} dm^3 of the reaction mixture was diluted with the eluent and subjected to analysis. The elution was monitored with a Toyo Soda UV-8 model II spectrophotometric detector operating at 250 nm.

Physical Measurements——Electronic spectra were recorded on a Shimadzu UV-210A spectrophotometer. Circular dichroism (CD) spectra were recorded on a Jasco J-40 recording polarimeter. Pyridine solutions of cobalt(II) complexes were well contacted with air and were incorporated in quartz capillaries and the electron spin resonance (ESR) spectra were recorded on a Varian E-112 at room temperature. Cyclic voltammograms were obtained with a Bioanalytical Systems CV-1B cyclic voltammetry instrument and recorded with a Riken Denshi F-3EH XY recorder. The electrode system consisted of an Ag/AgCl reference electrode and the working and auxiliary electrodes made from a platinum plate and a platinum wire, respectively. Measurements were made on methanol solutions of the cobalt complex (5.0×10^{-4} mol dm^{-3}) using 0.05 mol dm^{-3} tetraethylammonium perchlorate as the supporting electrolyte, and nitrogen was passed for 20 min prior to the measurements.

Results and Discussion

Two series of Schiff base cobalt(II) chelates, Co(salen) and Co(Busalen) derivatives, were examined for catalytic action in the oxygenation of 3-methylindole. One of these series, the Co(Busalen) derivatives, was newly prepared from 3-*tert*-butylsalicylaldehyde; the prepara-

tion and spectral properties of these compounds in relation to the stereochemistry are described first.

Preparation and Properties of Catalysts

A series of derivatives of *N*, *N'*-ethylenebis(3-*tert*-butylsalicylideneimine) was prepared from a variety of diamines and 3-*tert*-butylsalicylaldehyde. Cobalt(II) complexes were obtained by a method similar to that used for preparing Co(Busal-Me_4en).[16] The electronic spectra in chloroform solution of the cobalt(II) complexes prepared in this study showed a shoulder and two maxima in the visible region, *e.g.* at 480 (3150), 417 (13900), and 355 (12200) nm for Co(Busal-*R*-pn), where the molar absorption coefficients are shown in parentheses.

The CD spectra of chloroform solutions of optically active compounds, Co(Busal-*R*-pn), Co(Busal-*R*-chxn), and Co(Busal-*S*-bn) are shown in Fig. 1. The CD spectra of these Co(Busalen) derivatives have the same features as those of Co(salen) derivatives: the CD spectrum of Co(Busal-*R*-pn) is almost the mirror image of those of Co(Busal-*S*-bn) and Co(Busal-*R*-chxn).[17] The maxima in the CD spectra of Co(Busalen) derivatives move to lower energy by *ca.* 10 nm and their magnitudes are smaller than those of Co(salen) derivatives.[18a] Based on the CD spectra of Co(sal-*R*-pn), Co(sal-*S*-bn) and Co(sal-*R*-chxn), the methyl groups in the former two chelates have been assumed to adopt axial positions with respect to the chelate ring of a square planar complex,[18] as confirmed by X-ray crystallography.[19] The CD spectra show that the structures around the metal ion are a little altered by the presence of the two *tert*-butyl groups.

Further confirmation of the planar structure of Co(Busalen) derivatives was derived from the ESR spectra of the oxygenated pyridine adducts. The complexes were dissolved in pyridine and were well contacted with air and incorporated in capillaries. An eight-line signal was observed at $g=2.02$, with $a_{Co}=1.58$, 1.30, 1.22, and 1.18 mT for Co(Busalen), Co(Busal-

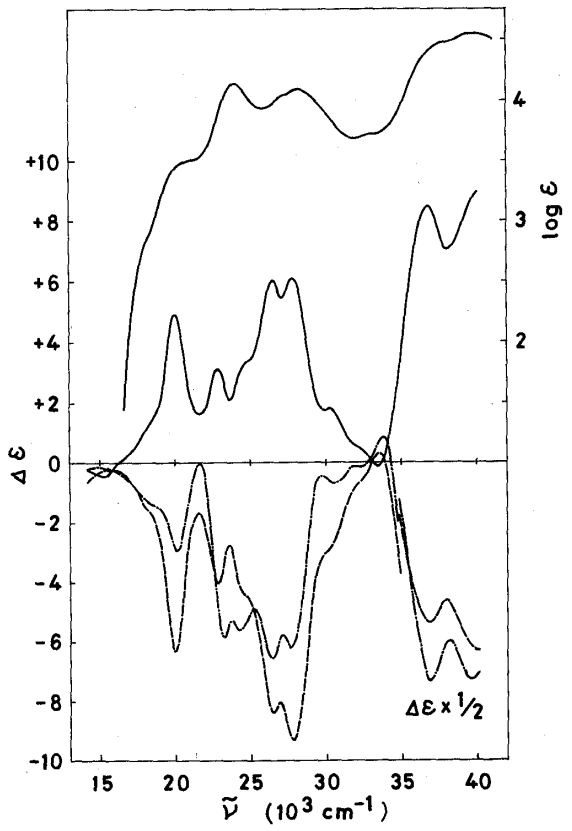


Fig. 1. Absorption and CD Spectra of Co^{II}-(Busal-*R*-chxn) (—·—), Co^{II}(Busal-*S*-bn) (– – –), and Co^{II}(Busal-*R*-pn) (——) in Chloroform

Absorption spectrum: $[Co(II)]=5\times10^{-5}$ mol dm^{-3}. CD spectra: $[Co(II)]=1\times10^{-4}$ mol dm^{-3}.

R-chxn), Co(Busal-*meso*-bn), and Co(Busal-*cis*-chxn), respectively, at room temperature. These ESR parameters are in agreement with those for O_2^-–Co(salen)pyr[20] and support the view that the monooxygenated structure is not significantly different from that of Co(salen).

On the basis of these spectral results, the prepared complexes have the following structural features: the *tert*-butyl substituents introduce steric crowdedness at the end of salen, but do not deform the planar arrangement of Co(salen) derivatives. As regards the diamine moiety, *R*-chxn introduces the cyclohexyl group as an extension of the plane of the chelate ring, while *R*-pn introduces a small degree of steric crowdedness in the apical region. One of the methyl groups of Co(Busal-*meso*-bn) takes the equatorial position while both methyl groups of Co(Busal-*S*-bn) take axial positions with respect to the chelate ring. *cis*-Chxn introduces substantial steric crowdedness in the apical position. The structure of Co(sal-*cis*-chxn) is such that the cyclohexane ring adopts a chair structure and occupies the apical region.[21] These structures are illustrated in Fig. 2.

Half-wave potentials of the prepared complexes were determined in methanol by cyclic voltammetry. Quasi-reversible cathodic and anodic peaks ($E_a - E_c = 0.07$ V) were observed in the range between 0.0 V and 0.3 V *vs.* Ag/AgCl, where the scan rate was changed from 0.1 to 0.4 V s^{-1}. The half-wave potentials ($E_{1/2} = (E_a + E_c)/2$) are tabulated in Table II along with the values for Co(salen) derivatives in pyridine solution reported by Puxeddu and Costa.[22] The redox potential moves to the anodic side when the substituents are orientated toward the apical position.

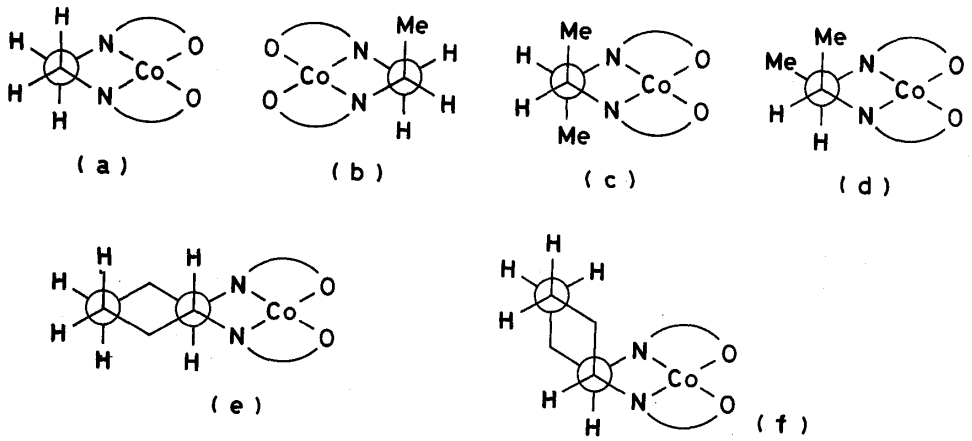


Fig. 2. Schematic Representation of the Orientation of Substituents in the Diamine Moiety in Co^{II}(salen) Derivatives

(a), Co(salen); (b), Co(sal-*R*-pn); (c), Co(sal-*S*-bn); (d), Co(sal-*meso*-bn); (e), Co(sal-*R*-chxn); (f), Co(sal-*cis*-chxn).

TABLE II. Half-Wave Potentials of Co(salen) Complexes for $Co^{II/III}$

Diamine	$E_{1/2}$/V Busalen[a]	$E_{1/2}$/V salen[a]	salen[b]
en	+0.11	+0.15	−0.395
pn	+0.15		−0.357
meso-bn	+0.17		−0.285
S-bn	+0.23		−0.364
R-chxn	+0.08	+0.11	−0.360
cis-chxn	+0.18	+0.19	−0.253

a) In methanol, *vs.* Ag/AgCl, present study. *b*) In pyridine, *vs.*saturated calomel electrode (SCE), from ref. 22.

Oxygenation of 3-Methylindole

The oxygenation of 3-methylindole by oxygen was initiated by the addition of catalysts depicted in Fig. 2. The catalysts dissolved gradually and the solution changed in color from orange to dark brown. For the reaction using Co(Busal-*cis*-chxn), a long induction period was observed and the dissolution of the catalyst accomplished at the end of the induction period. The intact complex separated out on cooling the reaction mixture after completion of the reaction.

The oxygenation of 3-methylindole has been reported to be catalyzed by Co(salen), yielding 2-formylaminoacetophenone as the main product, by Nishinaga,[1] and 2-aminoacetophenone has been reported as a minor product.[4] The oxygenation products were analyzed by HPLC and the results are shown in Table III. The main product was found to be 2-formylaminoacetophenone, irrespective of the catalyst employed, and a small amount of 2-aminoacetophenone was obtained.[23] Since the distribution of the products did not change significantly, it is likely that the same mechanism operates, irrespective of the catalyst used.

The time course of the reaction was followed by measuring the decrease in 3-methylindole by GLC. The amounts of 3-methylindole were plotted against reaction time in Figs. 3 and 4, for the reactions catalyzed by Co(salen) derivatives and Co(Busalen) derivatives, respectively. The reactions did not follow simple paths, since the reaction rates changed at some period after the initiation of the reaction. In the cases of Co(Busal-*cis*-chxn),

TABLE III. Products of the Oxygenation of 3-Methylindole Catalyzed by Various Co(salen) Derivatives

Catalyst	Reaction time (h)	Consumption of 3-methylindole (%)	Product yield (%)	
			2-Formylamino-acetophenone	2-Amino-acetophenone
Co(salen)	7.4	52	52	7
Co(sal-*R*-chxn)	8.3	42	36	11
Co(sal-*cis*-chxn)	8.4	71	42	10
Co(Busalen)	8.0	64	72	4
Co(Busal-*R*-pn)	7.4	94	54	4
Co(Busal-*meso*-bn)	5.2	96	54	6
Co(Busal-*S*-bn)	5.5	99	55	—
Co(Busal-*R*-chxn)	11.8	84	57	6
Co(Busal-*cis*-chxn)	5.0	98	55	1

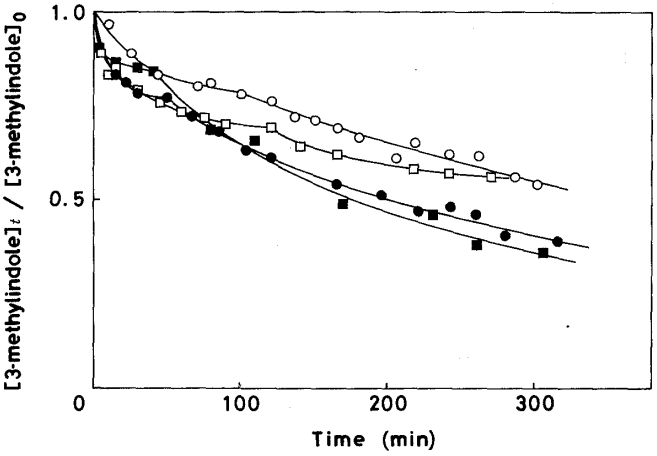


Fig. 3. Time Courses of the Consumption of 3-Methylindole in the Presence of Co(salen) Derivatives

Co(salen), ○; Co(sal-*R*-pn), ●; Co(sal-*R*-chxn), □; Co(sal-*cis*-chxn), ■.

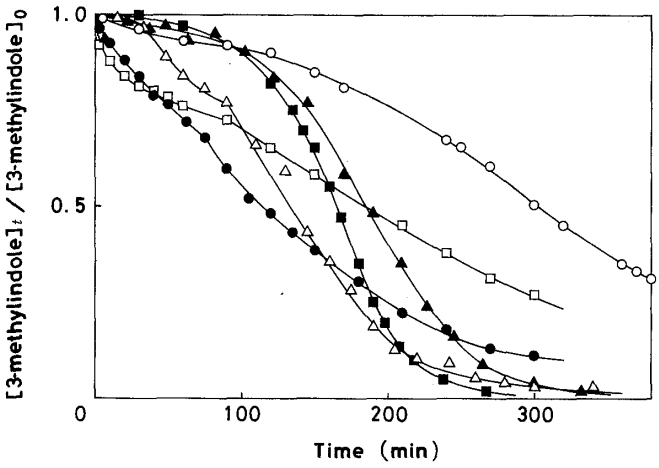


Fig. 4. Time Courses of the Consumption of 3-Methylindole in the Presence of Co(Busalen) Derivatives

Co(Busalen), ○; Co(Busal-*R*-pn), ●; Co(Busal-*meso*-bn), △; Co(Busal-*S*-bn), ▲; Co(Busal-*R*-chxn), □; Co(Busal-*cis*-chxn), ■.

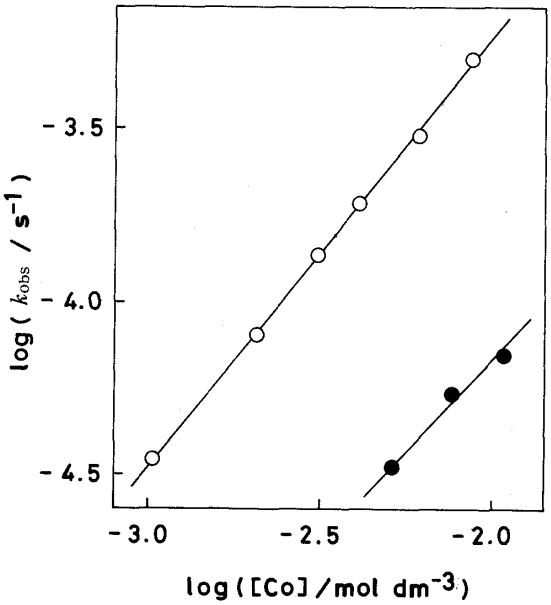


Fig. 5. log–log Plots of Observed First-Order Rate Constants *versus* Concentrations of Catalyst

Co(sal-*cis*-chxn), ●; Co(Busal-*cis*-chxn), ○.

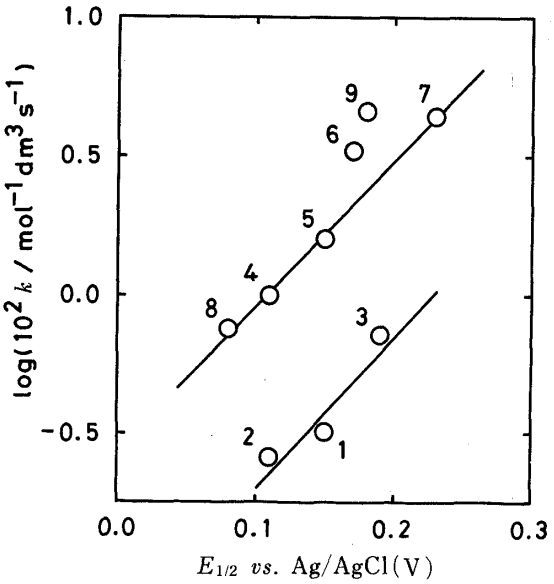


Fig. 6. Linear Relationship between Rate Constants and Half-Wave Potentials for $Co^{II/III}$ with Various Catalysts

1, Co(salen); 2, Co(sal-*R*-chxn); 3, Co(sal-*cis*-chxn); 4, Co(Busalen); 5, Co(Busal-*R*-pn); 6, Co(Busal-*meso*-bn); 7, Co(Busal-*S*-bn); 8, Co(Busal-*R*-chxn); 9, Co(Busal-*cis*-chxn).

TABLE IV. The Second-Order Rate Constants for Oxygenation of 3-Methylindole with Co(salen) Derivatives[a)]

Diamine	$k/10^{-2}$ mol^{-1} dm^3 s^{-1}	
	salen	Busalen
en	0.32	1.0
R-pn	0.53	1.6
meso-bn		3.3
S-bn		4.4
R-chxn	0.26	0.76
cis-chxn	0.72	4.6

a) [3-methylindole]$_0$ = 3.5×10^{-2} mol dm^{-3}, [Co complex] = 8.7×10^{-3} mol dm^{-3} in methanol at 25 °C.

Co(Busal-*S*-bn), and Co(Busalen), steady consumptions of the substrate were observed after long induction periods, the lengths of which increased with increase of the steric hindrance at the apical region of the metal complexes. With the other complexes, the consumptions showed two distinct phases: an amount equivalent to that of the catalyst was consumed rather rapidly prior to the steady consumption.[24] Plots of the natural logarithm of the amount of substrate against time yield a straight line for each catalyst after the induction period. The apparent first-order rate constant was obtained from the slope of the line. The consumption curve of oxygen was consistent with the consumption of an equimolar amount of substrate, 3-methylindole.

For the steady reaction region, the apparent first-order rate constant is proportional to the amount of catalyst employed, as shown in Fig. 5. The second-order rate constants derived from Eq. 1 are summarized in Table IV.

$$k_{obs}=k[Co^{II}] \quad (1)$$

Relationship between the Steady-State Catalytic Activity and the Structure of the Catalyst

The rate constants were larger for Co(Busalen) derivatives than Co(salen) derivatives, and decreased in the following order of diamine moiety for both series: *cis*-chxn > *S*-bn > *meso*-bn > *R*-pn > en > *R*-chxn, as shown in Table IV. These results show that the catalytic activity in the steady state is enhanced by steric hindrance in the apical region of the metal complex catalysts. This is rather surprising, because steric hindrance would be expected to retard the coordination of the substrate and/or dioxygen.

One possible explanation is that if the oxygenation of 3-methylindole proceeds *via* an autoxidation mechanism, the rates of the oxygenation catalyzed by more sterically crowded metal complexes will be observed to be larger because these metal complexes have less interaction with the substrate than non-substituted Co(salen). However, addition of pyridine (three equivalents to the catalysts) completely stopped the reaction.[24] Thus the oxygenation requires coordination of the substrate to the metal center.

One of the measures of the steric hindrance in the Co(salen) derivatives is the redox potential. The relationship between the structure of Co(salen) derivatives and redox potential has been investigated by Averill and Broman,[25] and Puxeddu and Costa.[22] They reported that the half-wave potential shifts in a positive direction when the substituents are situated in the axial position, which is in agreement with the present results (Table II). These shifts are ascribed to the increase in steric repulsion accompanying the change from four-coordinate cobalt(II) to six-coordinate cobalt(III).

As shown in Fig. 6, a linear relationship between $\log(k)$ and $E_{1/2}$ was found for each series. The straight lines shown are expressed by Eqs. 2 and 3 for Co(salen) and Co(Busalen)

$$\log(10^2 k/\mathrm{mol}^{-1}\,\mathrm{dm}^3\,\mathrm{s}^{-1}) = 5.5(E_{1/2}/\mathrm{V}) - 1.25 \quad (2)$$

$$\log(10^2 k/\mathrm{mol}^{-1}\,\mathrm{dm}^3\,\mathrm{s}^{-1}) = 5.2(E_{1/2}/\mathrm{V}) - 0.56 \quad (3)$$

derivatives, respectively. The steady-state reaction is governed partly by the ease of reduction of cobalt(III) to the cobalt(II) state, as represented by the coefficients of 5.5 and 5.2. Thus the catalytic function seems to arise from the oxidation of the substrate by the metal center in the trivalent state.[26] The different intercepts, -1.25 and -0.56, show that the *tert*-butyl groups play some role in the rate-determining step despite the fact that they have little effect on the redox potential.

The Co(salen) derivatives can form dioxygen adducts and it was assumed that oxygen activated by coordination to the metal ion, presumably O_2^-, is responsible for the catalytic oxygenation. The steric and conformational effects on the formation of dioxygen adducts of Co(salen) derivatives have been studied by Puxeddu and Costa.[22] They have reported on the

basis of polarographic studies that the rate constants for the oxygenation reaction in pyridine decrease in the following order: en > (+)-pn > (−)-chxn > *meso*-bn > *S*-bn > *cis*-chxn. This order is almost the reverse of that for the steady-state catalytic activity. Therefore the dioxygen adducts do not participate in the steady-state reaction and this catalysis involves an activation not of dioxygen but of the substrate.

Substrate selectivity, especially non-reactivity toward *N*-methylindole, has been reported by several groups[1,3,4] for a variety of catalysts, and is considered to reflect a requirement for the coordination of the substrate to the metal center prior to the oxidation. The catalytic activity should involve (i) the coordination of the substrate, (ii) oxidation at the reactive site, and (iii) departure of the products from the catalyst.

The existence of process (i) is confirmed by the complete inhibition by addition of pyridine and the ineffectiveness of *N*-methylindole as a substrate. However, this process does not contribute significantly to the rate of the oxygenation, because the steric hindrance does not retard the reaction. The process (ii) is important because the sterically hindered complex accelerates the reaction partly due to its high redox potential between the cobalt(II) and cobalt(III) states. The results represented in Fig. 6 show that a complex with a higher potential is a better catalyst and this fact is in agreement with the ease of electron transfer from the coordinated substrate to the cobalt(III) center. The process (iii) plays some role in determining the rate of oxygenation, because the *tert*-butyl group has an accelerating effect though it has little effect on the redox potential.

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