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Nucleophilic Ring-Substitution Reactions of Unsymmetrical Quadridentate Schiff Base and Its Complex of Nickel(II) or Copper(II) with Ethyl Mercaptoacetate

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The nucleophilic replacement of halogen on the methine carbon of a Schiff base complex of nickel(II) or copper(II) by ethyl mercaptoacetate in dichloromethane proceeds via a four-centered intermediate, in which two polarizable atoms, such as bromine and sulfur, may stabilize strained bond angles. In the case of a free Schiff base ligand, a relatively stable adduct was spectrophotometrically confirmed. The adduct is thought to have a configuration analogous to that of a spiro compound containing a five-membered ring. Free ligands show no absorption bands in the wavelength region longer than 340 nm, while the adduct shows band at 375 nm assignable to a n-π* transition.

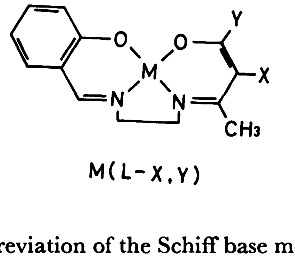
Many electrophilic substitutions of coordinated ligands have been reported; e.g. the methine protons of β-diketonato metal complexes have been replaced by such electrophiles as bromine, iodine, acyl derivatives, and sulfur.[1] The substitutions have also been reported on a quadridentate Schiff base complex of nickel(II) or copper(II), and those kinetics have been investigated.[2–4] On the other hand, only a few nucleophilic substitutions have been reported; the further conversion of the halogeno-substituted methine carbon of the β-diketone or a quadridentate Schiff base complex was been carried out with such nucleophiles as benzenethiol, its derivatives, and ethyl mercaptoacetate.[5–7] In this paper, we wish to report further studies of the nucleophilic substitution mechanism of the unsymmetrical quadridentate Schiff base and its complex of nickel(II) or copper(II) with ethyl mercaptoacetate, $HSCH_2CO_2C_2H_5$. The complexes used in this study are shown in Fig. 1.

Results and Discussion

The Substitution Reaction of the Nickel(II) or Copper(II) Complex. By the addition of ethyl mercaptoacetate, the spectrum of Ni(L-Br, CH_3) in dichloromethane changed to that of Ni(L-$SCH_2CO_2C_2H_5$, CH_3), with an isosbestic point at 288 nm (Fig. 2). The rate of reaction (1) was determined by means of the absorbance change at 385 nm by the use of a pseudo- first-order method:

$$\mathrm{Ni(L\text{-}Br,\ CH_3) + HSCH_2CO_2C_2H_5 \longrightarrow Ni(L\text{-}SCH_2CO_2C_2H_5,\ CH_3) + HBr} \tag{1}$$

The plot of $-\ln(A_\infty - A_t)$ vs. the time was linear to at least 80% completion, where A_t and A_∞ represent the absorbances at time t and infinity respectively. The pseudo- first-order rate constant (k_{obsd}) was estimated from its slope. The rate was also measured at



M(L-X,Y)

Fig. 1. Abbreviation of the Schiff base metal complexes.

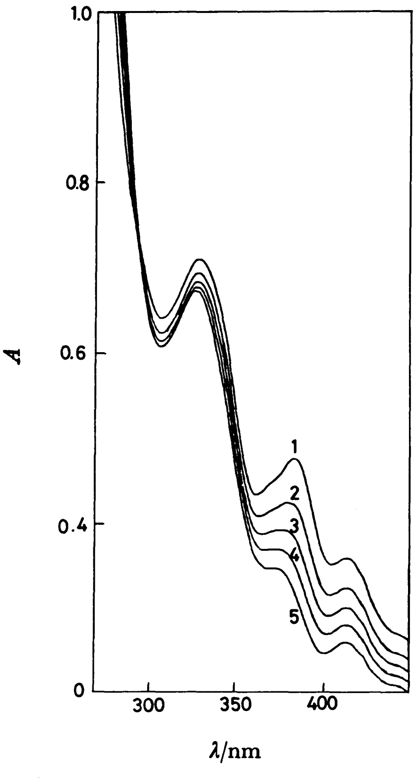


Fig. 2. Spectral change during the reaction of Ni(L-Br, CH_3) with ethyl mercaptoactate in dichloromethane at 20 °C: $[\mathrm{Ni(L\text{-}Br,CH_3)}]_0 = 1.50\times10^{-4}$ mol dm^{-3}, $[\mathrm{HSCH_2CO_2C_2H_5}]_0 = 3.00\times10^{-3}$ mol dm^{-3}. 1: 30 s, 2: 10 min, 3: 30 min, 4: 45 min, and 5: 80 min after the reaction.

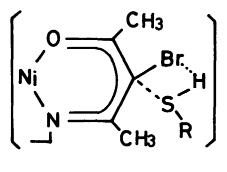
Table 1. The Rate Constants for the Reactions of the Nickel(II) and Copper(II) Complexes with Ethyl Mercaptoacetate in Dichloromethane

Run	$k^{a)}{}_{\mathrm{obsd}}/10^{-3}\ \mathrm{s}^{-1}$	Conditions
1	2.45±0.35	Ni(L-Br, CH_3) + $HSCH_2CO_2C_2H_5$ (2.25×10^{-3} mol dm^{-3})
2	2.71±0.55	(3.30×10^{-3} mol dm^{-3})
3	3.12±0.52	(3.75×10^{-3} mol dm^{-3})
4	4.44±0.63	(4.50×10^{-3} mol dm^{-3})
5	4.76±0.41	(5.25×10^{-3} mol dm^{-3})
	$k^{b)}/\mathrm{mol}^{-1}\ \mathrm{dm}^3\ \mathrm{s}^{-1}$	
6	$(9.20\pm0.98)\times10^{-1}$	Ni(L-Br, CH_3) + $HSCH_2CO_2C_2H_5$
7	$(1.12\pm0.15)\times10^{-3}$	Ni(L-Cl, CH_3) + $HSCH_2CO_2C_2H_5$
8	4.40±0.51	Ni(L-Br, C_6H_5) + $HSCH_2CO_2C_2H_5$
9	$(5.30\pm1.20)\times10$	Cu(L-Br, CH_3) + $HSCH_2CO_2C_2H_5$
	$k^{a,c)}{}_{\mathrm{obsd}}/10^{-2}\ \mathrm{s}^{-1}$	Ni(L-Br, CH_3) + $HSCH_2CO_2C_2H_5$
10	0.53±0.11	$[\mathrm{EtOH}]_0$ = 0.2%(v/v)
11	0.91±0.14	0.4%
12	1.25±0.18	0.6%
13	1.63±0.13	0.8%
14	1.94±0.21	1.0%
15	3.57±0.24	1.5%
16	4.33±0.28	2.0%

a) The first-order rate constants. b) The second-order rate constants. c) $[HSCH_2CO_2C_2H_5]_0=3.00\times10^{-3}$ mol dm^{-3}. $[\mathrm{complex}]_0=1.50\times10^{-4}$ mol dm^{-3}.

327 nm. Both values were the same (within the limit of experimental error), showing no wavelength-dependence of the rate. The value of k_{obsd} was proportional to the concentration of ethyl mercaptoacetate, indicating that the reaction order is first in the concentration of the nucleophile (Runs 1—5 in Table 1).

Ni(L-Br, CH_3) did not react with ethyl hydroxyacetate under the same conditions as those used for ethyl mercaptoacetate. This corresponds to the finding that acetylacetone complexes of aluminum(III), chromium(III), iron(III), and cobalt(III) react with benzenethiols, but not with phenols.[5] The rate constant of the reaction for Ni(L-Cl, CH_3) was very small compared with that for Ni(L-Br, CH_3)(Runs 6 and 7). It has also been reported that the substitution for Ni(L-Br, C_6H_5) is performed with *N*-bromosuccinimide, but not with *N*-chlorosuccinimide.[8] That is, at least two polarizable atoms, such as sulfur and bromine, are required to promote the reaction facilely. The following four-centered intermediate might be proposed in view of the results concerning a solvent effect to be discussed later:



Scheme 1.

where R is $CH_2CO_2C_2H_5$.

A sulfur atom of the nucleophile is more polarizable than an oxygen atom; thus, the clouds of valence electrons about the sulfur atom are more easily distorted by methine carbon than those about the oxygen atom. A bromine atom might play the same role in the intermediate. Then, the polarizable sulfur and bromine atoms must stabilize the strained intermediate. By the addition of ethanol (>2% v/v) to the dichloromethane solution of Ni(L-Br, CH_3) and ethyl mercaptoacetate, the reaction was strongly depressed. Ethanol destabilizes the intermediate, with the formation of a hydrogen bond. However, the rate was increased up to 2% of ethanol (Runs 10—16). Probably, ethyl mercaptoacetate forms a dimer in a nonpolar solvent such as dichloromethane; thus, the concentrations of the monomer species which is active for the reaction might be increased by the addition of adequate amounts of ethanol.

A similar intermediate has been proposed for the nucleophilic substitution of the bromo-substituted methine carbon of the *β*-diketonato metal complexes for thiophenols; the reaction occurred in dichloromethane, but was depressed in a polar solvent, such as ethanol, acetone or ethyl ether. The reaction was also inhibited by the addition of small amounts of pyridine or piperidine.[5]

The rate constant for Ni(L-Br, C_6H_5) was about six times that for Ni(L-Br, CH_3) (Runs 6 and 8). A phenyl group attracts an electron from the chelate ring, promoting the nucleophilic substitution on the methine carbon. The rate constant for Cu(L-Br, CH_3)

is about fifty times that for Ni(L-Br, CH_3) (Runs 6 and 9). The electronegativities of the nickel(II) and copper(II) ions are almost the same,[9] which might exclude the inductive effect of the central metal ion on the reaction rate. The same tendency has been reported for the case of the electrophilic substitution reactions of M(L-H, CH_3), where M is H_2, Cu(II), or Ni(II), for *N*-chlorosuccinimide; e.g., the copper(II) complex shows an extremely large rate constant as compared with the nickel(II) complex and the free ligand.[4] As has been proposed for the electrophilic substitution, the copper(II) ion may catalyze the reaction via the formation of an ethyl mercaptoacetate adduct. However, the details are not known at present.

The Substitution Reaction of the Free Ligand. The spectral change of the free ligand, H_2(L-Br, CH_3) with ethyl mercaptoacetate is shown in Fig. 3. At first, the absorption band of H_2(L-Br, CH_3) at 328 nm was decreased, and then new peaks appeared at 284 and 375 nm; isosbestic points were found at 242, 263, 311, and 352 nm. Subsequently, both bands were gradually decreased, followed by the appearance of the band at 316 nm, where isosbestic points were not observed, probably because of the presence of side reactions. However, the final spectrum is consistent with that of hydrobromide of H_2(L-$SCH_2CO_2C_2H_5$, CH_3), the preparation of which will be discussed later. That is, a relatively stable adduct might be formed in the reaction of the free ligand and ethyl mercaptoacetate.

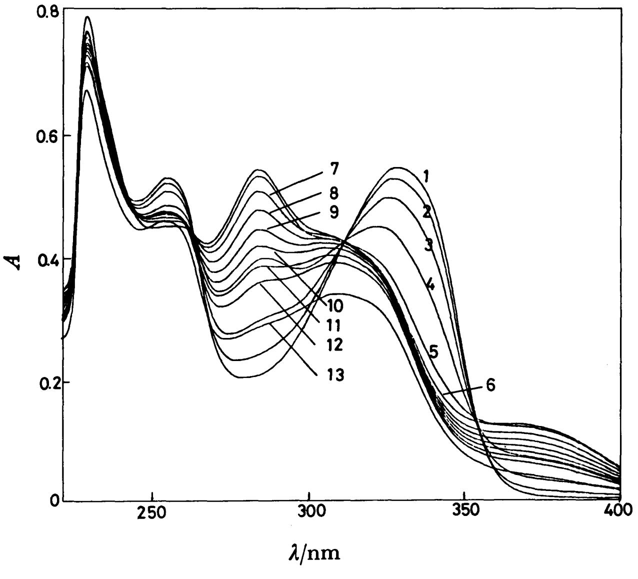
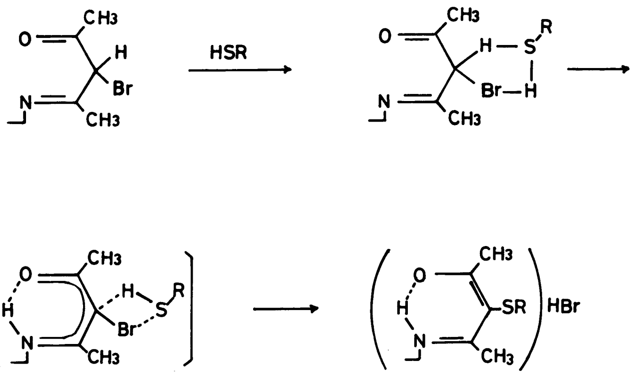


Fig. 3. Spectral change during the reaction of H_2(L-Br,CH_3) with ethyl mercaptoacetate in dichloromethane at 20 °C; $[H_2(\text{L-Br},CH_3)]_0 = 1.00 \times 10^{-4}$ mol dm^{-3}, $[HSCH_2CO_2C_2H_5]_0 = 2.50 \times 10^{-4}$ mol dm^{-3}. 1: 1 min, 2: 30 min, 3: 1 h, 4: 1 h 30 min, 5: 2 h, 6: 2 h 30 min, 7: 3 h 30 min, 8: 4 h 30 min, 9: 5 h 50 min, 10: 7 h 10 min, 11: 10 h 20 min, 12: 11 h 20 min, and 13: 19 h 40 min after the reaction. The intensiry of absorption at 284 nm was increased in time courses from 1 to 6, whereas it was decreased from 7 to 13.

To elucidate the reaction mechanism, a few further experiments were carried out. The formation rate of the adduct in benzene was faster than that in dichloromethane, but the spectrum of H_2(L-Br, CH_3) did not change upon the addition of the nucleophile in ethanol. The spectrum of the free ligand also did not change with ethyl hydroxyacetate. In addition, the spectrum of H_2(L-H, CH_3) and H_2(L-Cl, CH_3) showed no change with ethyl mercaptoacetate. Thus, two polarizable atoms must be required to form the adduct. Attempts to isolate the adduct were unsuccessful because of decomposition during purification. As *p*-toluenethiol has been reported to act as a nucleophile toward a Schiff base nickel(II) complex,[7] it was added to the dichloromethane solution of the free ligand. The spectral change was similar to that of ethyl mercaptoacetate; e.g., at first, a band appeared around 375 nm, but subsequently its intensity was decreased. By the addition of 1-butanethiol, similar spectral change was also observed. That is, only the SH group of the nucleophile must play an important role in the formation of the adduct. The band at 375 nm disappeared in polar solvents, such as methanol, ethanol, and acetone. The free ligands, such as H_2(L-H, CH_3), H_2(L-Cl, CH_3), H_2(L-Br, CH_3), and H_2(L-$SCH_2CO_2C_2H_5$, CH_3), exhibit no band at wavelengths longer than 340 nm. Therefore, the new band may be ascribed to a n-π^* transition in the adduct.

It is known that the free Schiff base ligand has three tautomeric forms: The Schiff base, the keto enamine, and the imino enol.[10] Although the keto-enamine form exists predominantly in solution,[10] with the nucleophile, the Schiff base type might form an adduct with a five-membered ring system (see the following reaction Scheme). Because the strains of the bond angles must be less than those in the four-centered system, the free Schiff base ligand at first forms a relatively stable spiro-type adduct with the nucleophiles. On the other hand, the metal complex can not form the adduct because of the lack of the enol hydrogen atom.

The nucleophilic-substituted ligand was also prepared; pale yellow precipitates were immediately obtained by the reaction of H_2(L-Br, CH_3) and ethyl mercaptoacetate in a benzene solution, but could not be characterized because of their decomposition to a brownish, tarry material. A test of silver nitrate was positive for the precipitates, showing the presence of bromide. To characterize the precipitates, nickel(II) acetate was added to their methanol solution; the orange nickel(II) complex was thus obtained and identified as Ni(L-$SCH_2CO_2C_2H_5$, CH_3) by means of an elemental analysis and ^{1}H NMR measurements. Thus, the precipitates might be confirmed to be hydrobromide of H_2(L-$SCH_2CO_2C_2H_5$, CH_3). In the ^{1}H NMR spectrum of the salt, an additional proton signal appeared in the low magnetic field (δ=11.02), probably arising from a -CH=N$\underline{H}^+$- proton. By the addition of an adequate amount of triethylamine to the salt, hydrogen bromide was liberated, resulting in an oily H_2(L-$SCH_2CO_2C_2H_5$, CH_3) compound which showed no band at 375 nm in dichloromethane. That is, the reaction might proceed as follows:



Scheme 2.

Consequently, the reaction of the Schiff base metal complex with ethyl mercaptoacetate proceeds via the four-centered intermediate, in which two polarizable atoms are required to stabilize the strained bond angles. On the other hand, the free Schiff base ligand at first forms the adduct with the five-membered ring system which shows the characteristic absorption band at 375 nm. Subsequently, the adduct slowly changes to the final product via the above intermediate.

Experimental

The Cu(L-Br, C_6H_5), Cu(L-Cl, C_6H_5), Ni(L-$SCH_2CO_2C_2H_5$, CH_3), and Ni(L-$SCH_2CO_2C_2H_5$, CH_3) complexes were prepared by the method described before.[4]

The Preparation of Cu(L-$SCH_2CO_2C_2H_5$, CH_3). A complex was prepared in a manner similar to those used for the nickel(II) complexes and was recrystallized with a mixture of methanol and water. Found: C, 50.37; H, 5.39; N, 6.61%. Calcd for $C_{18}H_{22}O_4SCu$: C, 50.75; H, 5.22; N, 6.57%. UV(CH_2Cl_2)λ_{max}(log ε) 268 (4.26), 328 (4.04), 384 (3.66), and 554 (2.65) nm. IR (ν CO) 1730 cm^{-1}.

The Preparation of Hydrobromide of H_2(L-$SCH_2CO_2C_2H_5$, CH_3). A benzene solution (20 cm^3) of 0.21 cm^3 (2.0 mmol) $HSCH_2CO_2C_2H_5$ was added to 50 cm^3 of a benzene solution containing 0.67 g (2.0 mmol) H_2(L-Br, CH_3); the mixture was then stirred at room temperature for 20 min. The pale yellow precipitates were filtered off and dried in a nitrogen atmosphere. The compound was sealed in a sample tube which had been purged with a nitrogen gas to prevent its decomposition into the brownish tarry material in air. ^{1}H NMR (DMSO-d_6) δ=1.39 (3H, t, CH_3), 2.67 (6H, s, CH_3), 3.43 (2H, s, SCH_2), 3.96—4.62 (6H, m, CH_2CH_2, C$\underline{H}_2$CH$_3$), 7.59—8.48 (4H, m, C_6H_4), 9.34 (H, s, -C$\underline{H}$=NH$^+$-), and 11.02 (H, s, -CH=N$\underline{H}^+$-) ppm.

The Preparation of H_2(L-$SCH_2CO_2C_2H_5$, CH_3). Adequate amounts of triethylamine were added to a dichloromethane suspension of the tarry hydrobromide salt, which then immediately dissolved. The hydrobromide of triethylamine was extracted with water for a few times, and the remaining dichloromethane solution was dehydrated on anhydrous sodium carbonate. When the solution was then concentrated under a reduced pressure, an oily material was obtained. ^{1}H NMR ($CDCl_3$) δ=1.25 (3H, t, CH_3), 2.34 (6H, d, CH_3), 3.33 (2H, s, SCH_2), 3.94 (4H, m, CH_2CH_2), 4.16—4.46 (2H, q, C$\underline{H}_2$CH$_3$), 7.44—8.09 (4H, m, C_6H_4), and 9.17 (H, s, CH=N) ppm. The orange nickel(II) complex was derived by adding an aqueous solution of nickel(II) acetate to the methanol solution of the oily material; it was then recrystallized with methanol. Found: C, 51.12; H, 4.95; N, 6.34%. Calcd for $C_{18}H_{22}N_2O_4SNi$: C, 51.33; H, 5.28; N, 6.65%. ^{1}H NMR ($CDCl_3$) δ=1.42 (3H, t, CH_3), 2.54 (3H, s, CH_3), 2.57 (3H, s, CH_3), 3.33—3.70 (6H, m, SCH_2, CH_2CH_2), 4.36—4.52 (2H, m, C$\underline{H}_2$CH$_3$), 7.16—7.99 (4H, m, C_6H_4), and 8.51 (H, s, CH=N) ppm. IR (ν CO) 1739 cm^{-1}.

Measurements. The ^{1}H NMR spectra were recorded with a JEOL-MH 100 spectrophotometer at a frequency of 100 MHz. The chemical shifts were determined in ppm, using TMS as the internal standard. The electronic spectra in solution and the infrared spectra using KBr pellets were measured on a Hitachi 124 spectrophotometer and a Hitachi 215 spectrophotometer respectively.

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