

Thione–Thiol Rearrangement of Xanthates Catalyzed by Pyridine *N*-Oxides. Remarkably Enhanced Reactivity of 4-Dialkylaminopyridine *N*-Oxides

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Pyridine *N*-oxides bearing electron-donating substituents (III) are efficient catalysts for rearrangement of *O*-alkyl *S*-methyl dithiocarbonates (xanthates) (I) to the corresponding *S*-alkyl *S*-methyl dithiocarbonates (dithiolcarbonates) (II). Of the catalysts tested, 4-piperidinopyridine *N*-oxide (IIIh) is the best from the viewpoints of catalytic activity and solubility in I. Heating of I in the presence of catalytic amounts (0.02–0.05 molar eq) of IIIh gave II together with the symmetric *S,S*-dialkyl and *S,S*-dimethyl dithiocarbonates in good yields. The catalytic behavior of donor-substituted pyridine *N*-oxides is discussed on the basis of kinetic and molecular orbital calculation data. The complete calculation of the perturbation equation on the initial stage of the reaction was consistent with the experimentally observed activity of the catalysts.

Keywords *O,S*-dialkyl dithiocarbonate; *S,S*-dialkyl dithiocarbonate; 4-dialkylaminopyridine *N*-oxide; thione–thiol rearrangement; charge transfer; catalytic rearrangement; xanthate; MNDO

In the previous papers,¹⁾ we have reported that *O,S*-dialkyl dithiocarbonates (xanthates) (I) underwent rearrangement to *S,S*-dialkyl dithiocarbonates (dithiolcarbonates) (II), catalyzed by pyridine *N*-oxides (III). Combination of this reaction and aminolysis of II with ethanolamine²⁾ serves as an efficient method for the generation of thiols under neutral non-aqueous conditions [see Chart 1(a) and (b)].

On the basis of a kinetic study^{1a)} of the catalytic rearrangement of xanthates and the spectroscopic evidence

of formation of 1-methoxy-4-dimethylaminopyridinium methylthiolcarbonate (IVf in Chart 2), we proposed that the catalytic activity of pyridine *N*-oxides is probably a consequence of the formation of the intermediates IV (step 1). The resultant dithiolcarbonate anion ([−]SCSR₂) (IV) is alkylated by the xanthate (I) to produce the rearranged product (II) accompanied with generation of [−]SCSR₂ (step 2). This process will be repeated until all of the xanthate is consumed and the dithiol ester (II) is then converted into the equilibrium mixture of dithiol esters by the action of [−]SCSR₂ (step 3).

During the course of the study, we found that the catalytic activity of III increases with raising of the highest occupied molecular orbital (HOMO) energy level of pyridine *N*-oxides and the solubility of the catalyst in I is an additional important factor determining the reaction rate.

This paper deals with the catalytic behavior of pyridine *N*-oxides bearing electron-donating substituents (IIIb–h) (Chart 3).

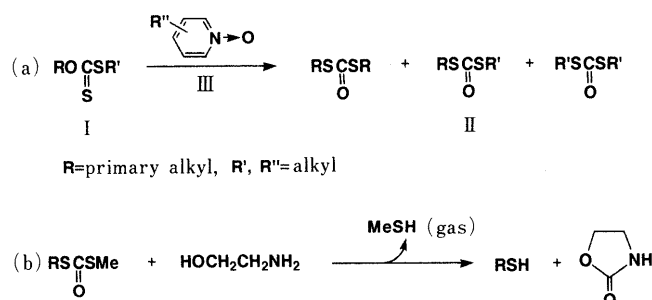


Chart 1

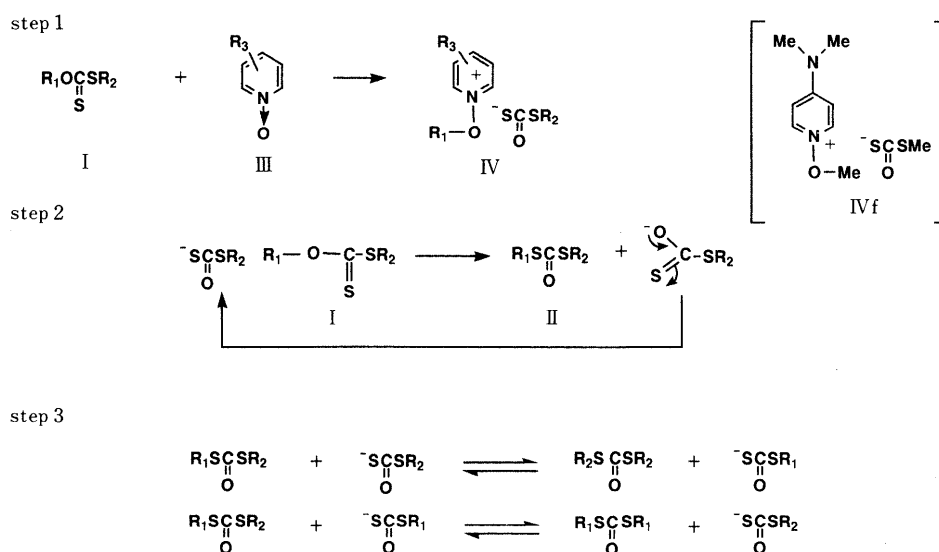


Chart 2

Results

4-Alkoxypyridine *N*-Oxides (IIIb–e) as Catalysts First of all, pyridine *N*-oxides (IIIb–e) bearing an alkoxy group at the 4-position were synthesized and their catalytic activities were investigated. Mixtures of *O*-ethyl *S*-methyl xanthate (Iba) and 0.1 eq of a pyridine *N*-oxide (III) were heated at 100°C until disappearance of Iba as judged by

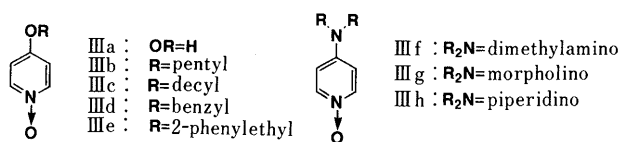


Chart 3

TABLE I. Conversion of *O*-Ethyl *S*-Methyl Xanthate (Iba) to the Dithiol Esters (IIaa, IIba, IIbb)^{a)} Catalyzed by 4-Alkoxypyridine *N*-Oxides (IIIb–e)^{b)}

 (III) R	Reaction conditions		Yields (%)			
	Temp. (°C)	Time (h)	IIaa	IIba	IIbb	Total
IIIa Unsubstituted	140	16	3	13	2	18) ^{c)}
IIIb Pentyl	100	6.5	18	26	13	57
IIIc Decyl	100	6	19	30	22	71
IIId Benzyl	100	6	19	31	13	63
IIIe 2-Phenylethyl	100	6	20	33	17	70

a) EtO(C=S)SMe (Iba) → (MeS)₂C=O (IIaa) + EtS(C=O)SMe (IIba) + (EtS)₂C=O (IIbb). b) The molar ratio (I/III) was 10.0. c) A standard for comparison.

TABLE II. Conversion of *O*-Ethyl *S*-Methyl Xanthate (Iba) to the Dithiol Esters (IIaa, IIba, IIbb) Catalyzed by 4-Dialkylaminopyridine *N*-Oxides (IIIf–h)^{a)} at 80°C

 (III) R ₂ N	Reaction conditions		Yields (%)			
	Solvent	Time (h)	IIaa	IIba	IIbb	Total
IIIf Dimethylamino	DMSO- <i>d</i> ₆	3	28	39	20	87
IIIg Morpholino	DMSO- <i>d</i> ₆	3	20	30	16	66
	No solvent	6	19	30	13	62
IIIh Piperidino	DMSO- <i>d</i> ₆	3	18	27	13	58
	No solvent	2	22	36	17	75

a) The molar ratio (I/III) was 10.0.

TABLE IV. Conversion of *O*-Alkyl *S*-Methyl Xanthates [RO(C=S)SMe] (I) to the Dithiol Esters (II) in the Presence of 4-Piperidinopyridine *N*-Oxide (IIIh)^{a)}

Substrate		Reaction conditions		Yields (%)			
I	R	Temp. (°C)	Time (h)	MeSCOSMe	RSCOSMe	RSCOSR	Total
Ica	<i>n</i> -Propyl	80	8	22 (IIaa)	37 (IIca)	15 (IIcc)	74
		90	4	21	35	14	70
Ida	<i>n</i> -Butyl	80	8	21 (IIaa)	36 (IIda)	11 (IIdd)	68
		90	4	21	33	13	67
Iea	Isopropyl	110	5	19 (IIaa)	28 (IIea)	6 (IIee)	53
		130	1.5	11	18	2	31
Ifa	Cyclohexyl	130	13	3 (IIaa)	10 (IIfa)	2 (IIff)	15
		150	9	3	9	0	12

a) The molar ratio (I/IIIh) was 10.0.

thin layer chromatography (TLC), giving mixtures of the dithiol esters, *S,S*-dimethyl (IIaa), *S*-ethyl *S*-methyl (IIba) and *S,S*-diethyl (IIbb) dithiocarbonates in 60–70% yield (total yield). The relative amounts of products formed were estimated by 400 MHz ¹H-nuclear magnetic resonance (¹H-NMR) integrations and comparison of the spectral data with those of authentic samples obtained from catalytic rearrangement of the corresponding xanthates by AlCl₃.³⁾ The reaction conditions and product compositions are summarized in Table I, in which the result for unsubstituted pyridine *N*-oxide (IIIa) is included as a standard.

As compared with the previously reported results^{1a)} for pyridine *N*-oxide (IIIa) and some alkyl-substituted pyridine *N*-oxides such as 3,5-dimethylpyridine *N*-oxide (IIIi), introduction of a long carbon chain (alkoxy group) onto the pyridine nucleus at the 4-position clearly raised the solubility in xanthates (I) and increased the reactivity toward I. Heating Iba at 140°C in the presence of 0.1 eq of IIIa for 16 h gave only an 18% yield of a mixture of the dithiol esters. By contrast, in the presence of 0.1 eq of IIIc, Iba was cleanly converted into the dithiol esters in 71% yield when heated to 100°C for 6 h.

However, the catalytic activity of 4-alkoxypyridine *N*-oxides (IIIb–e) is considered to be still lower than that found for 4-dimethylaminopyridine *N*-oxide (IIIf)^{1b)} (see also Table II).

4-Dialkylaminopyridine *N*-Oxides (IIIf–h) as Catalysts The preliminary study^{1b)} indicated that 4-dimethylaminopyridine *N*-oxide (IIIf) shows high catalytic activity for the rearrangement reaction. However, IIIf has a low solubility in xanthates (I). To improve this point, we prepared some 4-dialkylaminopyridine *N*-oxides (IIIg, h) including

TABLE III. Effect of Concentration of 4-Piperidinopyridine *N*-Oxide (IIIh) upon the Reaction of *O*-Ethyl *S*-Methyl Xanthate (Iba) at 80°C

Reaction conditions		Yields (%)			
Iba : IIIh	Time (h)	IIaa	IIba	IIbb	Total
50 : 1	12	21	40	16	77
40 : 1	11	24	35	18	77
20 : 1	8	22	39	17	78
10 : 1	2	22	36	17	75
5 : 1	1	22	34	16	72
2 : 1	2	21	29	19	69

a cyclic amine such as morpholine or piperidine. The results are summarized in Table II. The catalysts IIIg and IIIh showed high activity. The reactions occurred at 80 °C in the presence of 0.1 eq of the catalysts to give the rearranged products in high yields. In the case of IIIf, dimethyl sulfoxide (DMSO) was required for the manifestation of sufficient catalytic activity.

Next, the effect of the amount of III on the yield of II was studied in the reaction of Iba with IIIh. The results are summarized in Table III. The yields were 75–78% when Iba was heated at 80 °C in the presence of 0.02–0.1 eq of IIIh without solvent for 8–12 h.

Similarly, heating several *O*-(alkyl or cycloalkyl) *S*-methyl xanthates (Ica–fa) at 80–150 °C in the presence of IIIh gave mixtures of the dithiol esters (II) in good yields. The main products were the corresponding dithiol esters (IIca–fa). High yields were obtained when the *O*-alkyl group of I was primary, and branching at the *O*-alkyl strongly impeded the reaction. Skeletal rearrangement of the alkyl moiety, *e.g.* propyl to isopropyl, was not observed under the conditions used. The observed order of reactivity of *O*-alkyl *S*-methyl xanthates (Et > *n*-Pr = *n*-Bu > iso-Pr > cyclohexyl) is consistent with the relative rates of *S_N2*-type reactions,⁴⁾ suggesting that pyridine *N*-oxide catalyst is unsuitable for the thione–thiol rearrangement of *O*-cycloalkyl xanthates for steric reasons.

Kinetics To understand the pronounced reactivity of 4-dialkylaminopyridine *N*-oxides, we performed a kinetic study on the reactions of Iba with 4-dimethylaminopyridine *N*-oxide (IIIh), 4-piperidinopyridine *N*-oxide (IIIi) and 3,5-dimethylpyridine *N*-oxide^{1a)} (IIIi). However, the kinetic study could not be performed under common reaction conditions using a relatively nonpolar solvent or without solvent, because IIIf is hardly soluble in ordinary organic solvents. Therefore, we had to use high-boiling dipolar solvents, although the kinetic experimental conditions were widely different from the preparative ones.

The reactions of Iba with III in DMSO obeyed pseudo first-order kinetics. Relative reactivity is shown in Table V. The reactivity in DMSO seems to be inconsistent with that deduced from the preparative conditions. In DMSO, the rate for IIIf is larger than that for IIIh and the rate for IIIi seems to be greater than that estimated from the rate constant^{1a)} in the absence of DMSO. A plausible explanation for this discrepancy is that the solvent may assist the formation of the quaternary salt and have the ability to solvate the cation, separating it from the cation–dithiolcarbonate anion pair (IV) and leaving a free anion ([−]SCOSR) in the reaction mixture.

Based on the rate constants at 75–90 °C, the activation parameters (E_a , $\Delta S^\ddagger$) were calculated (see Table V). The activation energies (E_a) for the reaction of Iba with 4-dialkylaminopyridine *N*-oxides (IIIh, i) are considerably smaller than that for 3,5-dimethylpyridine *N*-oxide (IIIi). The activation entropies ($\Delta S^\ddagger$) for IIIh, i were calculated to be negative values, reflecting the highly ordered structures of the activated complexes. As regards the effect of the catalyst amount on the reaction rate, the rate constants were not directly proportional to the catalyst concentration (see Table VI). A possible explanation for this deviation is the influence of the charge-transfer complex (CT) formation in an early stage of the reaction.⁵⁾

TABLE V. Rate Constants and Activation Parameters for the Conversion Reaction of *O*-Ethyl *S*-Methyl Xanthate (Iba) by Catalysis of Some Pyridine *N*-Oxides in DMSO

Catalyst ^{a)}	$k \times 10^5$ (s ^{−1}) ^{b)}	E_a (kcal/mol)	$\Delta S^\ddagger$ (e.u.) ^{c)}
IIIi	ca. 1.2 ^{d)}	ca. 37 ^{d)}	
IIIh	26.5	17.1	−30
IIIi	18.7	17.1	−31

a) The molar ratio (Iba/III) was 10.0. b) Value at 90 °C. c) Value calculated at 90 °C. d) Crude value.

TABLE VI. Effect of the Amount of IIIh on the Reaction Rate of Iba at 80 °C

Molar ratio (IIIh/Iba) × 40	$k \times 10^5$ (s ^{−1})	Relative rate
1	3.21	1
2	6.67	2.08
4	8.16	2.54
6	14.2	4.42
8	25.5	7.94

Molecular Orbital Calculation To clarify the catalytic activity of donor-substituted pyridine *N*-oxides, modified neglect of diatomic overlap (MNDO)⁶⁾ calculations were carried out. As we have pointed out in the previous paper,^{1a)} inspection of the frontier molecular orbitals (FMO's)⁷⁾ of both reactants reveals that the dominant interaction occurs between the HOMO of IIIa, which acts as a donor, and the lowest unoccupied molecular orbital (LUMO) of Iaa, which behaves as an acceptor (see Chart 4 and Table IX). The perturbation theory⁸⁾ allows us to predict that the first bond would link the softest centers having the largest FMO coefficients, *i.e.*, the O atom of >N→O (*ca.* 0.65 in the HOMO) and the C atom of >C=S (*ca.* 0.78 in the LUMO), wherein the Coulombic interaction is also operative because the polar centers of the reactant molecules are identical with those having the largest FMO coefficients.

Based on this assumption, we tried to explain the catalytic activity of III in terms of the FMO method. The calculations were performed on some typical pyridine *N*-oxides, *i.e.*, 3,5-dichloropyridine *N*-oxide,^{1a)} pyridine *N*-oxide (IIIa),^{1a)} 3,5-dimethylpyridine *N*-oxide (IIIi),^{1a)} 4-methoxypyridine *N*-oxide and 4-dimethylaminopyridine *N*-oxide (IIIh). The interaction (stabilization) energies^{9b)} in the perturbation theory and the superdelocalizabilities^{9c)} of the oxygen atoms of several pyridine *N*-oxides were calculated based on the MNDO data. The order of the activity and several reactivity indexes are summarized in Tables VII, VIII and IX.

In the FMO theory, it has been proposed that the interaction energy involving charged molecules should be evaluated based on Eq. 2,^{9b)} in which the main contributors are extracted from the perturbation equation devised by Klopman and Salem (Eq. 1),¹⁰⁾ which not only treats interactions of all the occupied orbitals with all the unoccupied orbitals, but also takes account of closed-shell repulsions and polar effects (Coulombic effects).^{8,9a)}

First of all, we used Eq. 2 for the evaluation of the stabilization energies.

$$\Delta E = -E(\text{repulsion of occ/occ}) + E(\text{Coulombs}) + E(\text{attraction of occ/unocc}) \quad (1)$$

$$\Delta E = E(\text{Coulombs}) + E(\text{attraction of FMO}) \quad (2)$$

As can be seen in Table VII, in the early stage of the reaction (*ca.* 3 Å), the frontier term is negligible and the Coulombic term is operative. When the distance becomes less than 2.5 Å, the FMO interaction energies overcome the Coulombic energies. However, the calculation data for pyridine *N*-oxides could not account for the experimentally derived order of the catalytic activity. The total energy at 3.0 Å is narrowly consistent with the order of the reactivity.

In contrast, the complete calculations of Eq. 1 (Table VIII) support the order of the catalytic activity for all the distances used.¹⁰⁾ At the distance of 1.75 Å, which corresponds to the maximum σ -type overlap of the carbon *p*-atomic orbitals, the stabilization energy for 4-dimethylaminopyridine *N*-oxide (III_f) is calculated to be -22.7 kcal/mol, which is *ca.* 8 kcal/mol lower than the value for 3,5-dichloropyridine *N*-oxide.^{1a)} At the interacting distance of 3.0 Å, which corresponds to the weakly interacting complexes, the energy gained is *ca.* -4 kcal/mol.

Interestingly, a correlation between the catalytic activity of III and the superdelocalizability (S_r)^{9c)} of the oxygen atom of III is observed (see Table IX). This may be

because the magnitude of S_r bears an obvious relation to the third term of the perturbation equation (Eq. 1).^{8,9a)} As compared with S_r , the correlation for the electron density (ρ , Eq. 4) of the oxygen atom of III is poor. This may be due to the absence of the contribution of the orbital energy levels (see Eqs. 3 and 4).

$$S_r = k \sum c_j^2 / e_j \quad (3)$$

$$\rho = 2 \sum c_j^2 \quad (4)$$

These results suggest that the activity of III depends upon not only the coefficients of all the occupied orbitals but also their energy levels. Briefly speaking, pyridine *N*-oxides having the high-lying HOMO show high catalytic activity toward the thione-thiol rearrangement reaction.

Charge-Transfer Complex Formation Recently, we have demonstrated that some pyridine *N*-oxides show 1,3-dipolar cycloaddition reactivity toward active dipolarophiles, in which CT complexes play a significant role in determination of the reactivity and periselectivity.¹¹⁾

In the reaction of pyridine *N*-oxides with xanthates, we considered that xanthates might act as a 2π -source to give the cycloadduct (B).

To evaluate the cycloaddition reactivity of III toward I, we calculated the heat of formation of intermediates along

TABLE VII. The Coulomb and Frontier Orbital Interaction Energies^{a)} for the Reaction of *O,S*-Dimethyl Xanthate (Iaa)^{b)} with Some Pyridine *N*-Oxides (III) Using Eq. 2

Substituent of III	ΔE_{II+FMO} (kcal/mol)				
		3.0 Å	2.5 Å	2.0 Å	1.75 Å
3,5-Dichloro	Coul.	-3.59	-4.31	-5.39	-6.16
	FMO	-0.40	-3.05	-18.5	-37.8
	Total	-3.99	-7.36	-23.89	-43.96
Unsubstituted (IIIa)	Coul.	-3.84	-4.61	-5.76	-6.58
	FMO	-0.44	-3.37	-20.5	-41.7
	Total	-4.28	-7.98	-26.26	-48.28
3,5-Dimethyl (IIIi)	Coul.	-3.91	-4.70	-5.87	-6.71
	FMO	-0.44	-3.38	-20.5	-41.8
	Total	-4.35	-8.08	-26.37	-48.51
4-Methoxy	Coul.	-4.00	-4.79	-5.99	-6.85
	FMO	-0.43	-3.29	-20.0	-40.7
	Total	-4.43	-8.08	-25.99	-47.55
4-Dimethylamino (IIIf)	Coul.	-4.16	-4.99	-6.24	-7.13
	FMO	-0.39	-3.04	-18.4	-37.5
	Total	-4.55	-8.03	-24.64	-44.63

a) The details are given in ref. 10. b) The HOMO and LUMO energy levels are -9.820 and -0.705 eV, respectively. The LUMO coefficients of the C=S π -bond are 0.784 for carbon and -0.505 for sulfur. The net charges of the C and S atoms are 0.171 and -0.253, respectively.

TABLE VIII. The Perturbation Energy^{a)} for the Reaction of *O,S*-Dimethyl Xanthate (Iaa) with Some Pyridine *N*-Oxides Using Eq. 1

Substituent of III	$\Delta E_{I+II+III}$ (kcal/mol)				
		3.0 Å	2.5 Å	2.0 Å	1.75 Å
3,5-Dichloro	Repul	0.61	4.89	29.61	60.55
	Coul.	-3.59	-4.31	-5.39	-6.16
	Orb.	-0.72	-5.60	-33.97	-69.19
	Total	-3.70	-5.02	-9.75	-14.8
Unsubstituted	Repul	0.62	4.93	29.86	61.06
	Coul.	-3.84	-4.61	-5.76	-6.58
	Orb.	-0.76	-5.91	-35.87	-73.06
	Total	-3.98	-5.59	-11.77	-18.58
3,5-Dimethyl	Repul	0.62	4.95	29.99	61.33
	Coul.	-3.91	-4.70	-5.87	-6.71
	Orb.	-0.77	-5.98	-36.28	-73.88
	Total	-4.06	-5.73	-12.12	-19.26
4-Methoxy	Repul	0.62	4.98	30.17	61.70
	Coul.	-4.00	-4.79	-5.99	-6.85
	Orb.	-0.78	-6.07	-36.88	-75.10
	Total	-4.16	-5.88	-12.70	-20.25
4-Dimethylamino	Repul	0.63	5.03	30.45	62.27
	Coul.	-4.16	-4.99	-6.24	-7.13
	Orb.	-0.81	-6.29	-38.20	-77.80
	Total	-4.34	-6.25	-13.99	-22.66

a) The details of the calculations are given in ref. 10.

TABLE IX. Correlation between the Catalytic Activity and the Reactivity Indexes^{a)} of Several Pyridine *N*-Oxides (III)

Substituent on III	HOMO (eV)	HOMO coeff. >N→O	LUMO (eV)	Total electron density ^{b)}	ΔE_{II+FMO} kcal/mol at 2.5 Å	$\Delta E_{I+II+III}$ kcal/mol at 2.5 Å	$S_r \times 10^{-2}$ >N→O	Catalytic activity
3,5-Dichloro	-9.35	0.64	-1.150	-0.394	-7.36	-5.02	-6.97	Very small ↓ Very large
Unsubstituted	-8.77	0.65	-0.474	-0.421	-7.98	-5.59	-7.47	
3,5-Dimethyl	-8.74	0.65	-0.473	-0.429	-8.08	-5.73	-7.59	
4-Methoxy	-8.46	0.63	-0.467	-0.438	-8.08	-5.88	-7.75	
4-Dimethylamino	-8.07	0.59	-0.227	-0.456	-8.03	-6.25	-8.10	

a) Based on the MNDO data. b) Net charge. c) Constant includes β_{C-O} .

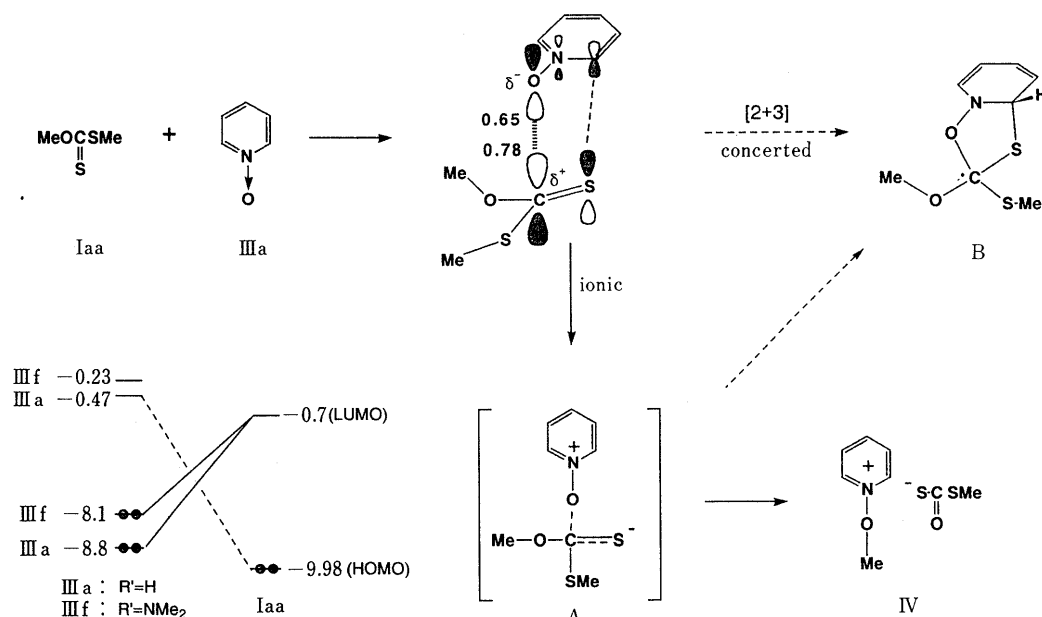


Chart 4

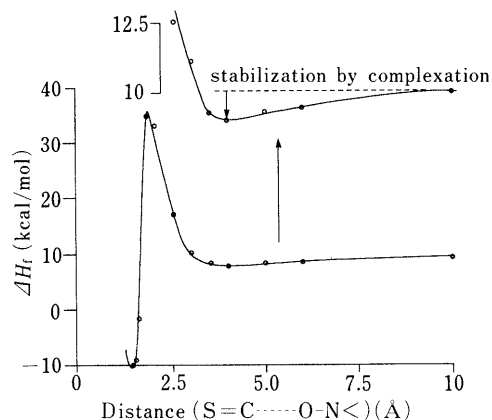
TABLE X. Interaction Energy for Reaction of Pyridine *N*-Oxide (IIIa) with *O,S*-Dimethyl Xanthate (Iaa)

Interacting distance (Å) S=C...O-N<	Heat of formation (ΔH_f) kcal/mol
50.0	10.294
20.0	10.258
10.0	9.948
6.0	9.372 ^{a)}
5.0	9.247
4.0	8.947 (CT-complexation) ^{a)}
3.5	9.227
3.0	11.070
2.5	17.951
2.0	33.786
1.8	35.525 (transition state) ^{a)}
1.6	-1.266
1.5	-8.836
1.4256	-9.823 (cycloaddition) ^{a)}

a) The optimized geometry is depicted in Fig. 2.

the reaction coordinates by using the MNDO approximation combined with geometrical optimization. In order to reduce the computation time as much as possible, the simplest model compounds [*O,S*-dimethyl xanthate (Iaa) and pyridine *N*-oxide (IIIa)] were used. In the initial stages of the reaction, the $\text{>N}\rightarrow\text{O}$ moiety was considered to approach the $\text{>C}=\text{S}$ moiety in such a way as to keep the dipoles lined up in an antiparallel manner and then the interacting distance ($\text{O}\cdots\text{C}$) was varied from 50.0 to 1.4 Å (Table X).

Heat of formation (ΔH_f) for the interaction of the two reactants slightly decreases with decrease of the distance (50—10 Å). Further decrease of the distance decreases the ΔH_f , stabilizing the reaction system to make a shallow minimum at *ca.* 4.0 Å, which is more stable by *ca.* 1.35 kcal/mol than the value at 50.0 Å. Then, the ΔH_f increases with decrease of the distance to reach the maximum value at *ca.* 1.8 Å. Further decrease of the distance causes sudden relaxation to give the 1,3-dipolar

Fig. 1. MNDO-Energy Profile for the Reaction of *O,S*-Dimethyl Xanthate (Iaa) and Pyridine *N*-Oxide (IIIa)

Heats of formation (kcal/mol) are given.

cycloadduct (B). The activation energy for formation of B is estimated to be about 25 kcal/mol ($\Delta\Delta H_f = \Delta H_{f,1.8\text{Å}} - \Delta H_{f,50.0\text{Å}}$) (Figs. 1 and 2).

Based on the above result, the possibility of the formation of the cycloadducts was carefully inspected. However, the ^1H -NMR spectra of the reaction products under various reaction conditions did not show any signals ascribable to the 1,3-dipolar cycloadduct.

In the catalytic reaction of electron-rich pyridine *N*-oxides, a coloration of the reaction mixture was recognized. For example, the visible absorption spectrum for 4-pentyloxy pyridine *N*-oxide (IIIb) showed absorption maxima at *ca.* 420 and 500 nm, characteristic of CT complexation (Fig. 3). In the reaction with III f, large bathochromic shifts occurred accompanying the introduction of the 4-dimethylamino group into the pyridine ring, showing absorption maxima at 450 and 620 nm,^{1a)} which gradually faded away with the progress of the reaction.

These findings together with the absence of CT complexation in alkyl-substituted pyridine *N*-oxides and the absence of the catalytic activity of aliphatic nitrones

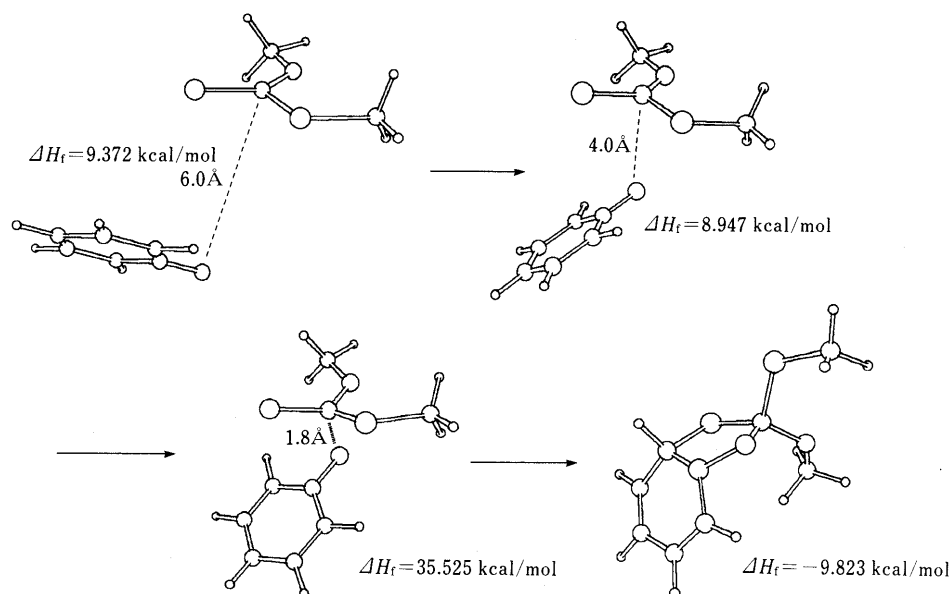


Fig. 2. MNDO Optimized Structures for Important Points along the Reaction Coordinates for the Reaction of *O,S*-Dimethyl Xanthate (Iaa) and Pyridine *N*-Oxide (IIIa)

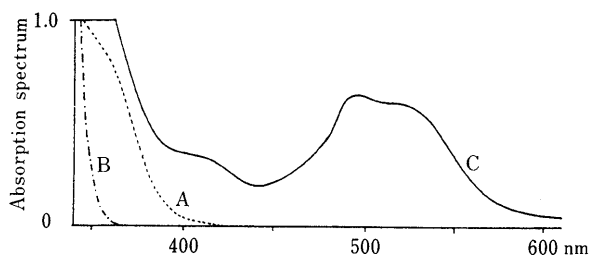
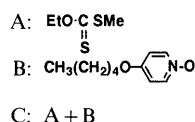


Fig. 3. Visible Absorption Spectrum of the Reaction Mixture of 4-Pentyloxypyridine *N*-Oxide (IIg) and *O*-Ethyl *S*-Methyl Xanthate (Iba) in DMSO Solution



suggest that the CT complexation depends on the π - π interaction affected by the HOMO energy level of III (Chart 4).

The MO simulation is assumed to be a gas phase reaction wherein solvation is not operative. Therefore, the MO prediction is considered to be quite different from the actual situation. In the reaction conditions used, the nonionic concerted nature of the reaction is assumed to be altered to an ionic reaction as a result of solvation or dipole-induced dipole-dipole interaction of the reactants. However, we may accept the involvement, at least in part, of the molecular complex, which then transforms to the quaternary salt (IV) *via* the betaine-type compound (A).

Discussion

As regards the reaction mechanism, the newly obtained data provide further support for the previously proposed mechanism.^{1a)} The marked difference between alkyl-substituted and alkoxy- or dialkylamino-substituted pyridine *N*-oxides reflects formation of the CT complexes (Chart 5). In the cases of 4-alkoxy- and 4-dialkylaminopyridine *N*-oxides (IIIb-h), the CT complexation was

observed. The MO simulation involving structure optimization supports the possibility of CT complexation prior to the reaction. Whether 1,3-dipolar cycloaddition occurs or not may depend upon the degree of charge transfer. The highly polarized HOMO's of I and III will be unfavorable for the synchronous bond formation required for the concerted cycloadditions. The O-C bond formation is more advanced than the C-S bond formation, raising the possibility that the CT complexes of I and III are betaine-like compounds (A)¹¹⁾ or more loosely combined molecular complexes, which may transform into the quaternary salt (IV)^{1a)} (see Chart 4). Another factor is substrate aromaticity. The loss of the aromatic energy of the pyridine nucleus prevents the occurrence of the concerted cycloaddition, leading to the formation of A after CT complexation.

As described in the previous paper,^{1a)} the formation of dithiol esters is favored by the use of dipolar aprotic solvents at elevated temperatures with high reactant concentration. However, under such reaction conditions, elimination reaction (Chugaev reaction)¹²⁾ or sulfide formation reaction is often observed and difficulty is frequently encountered in the separation of the products from the reaction mixture containing high-boiling solvents. Adding electron-donating substituents to the pyridine *N*-oxide ring markedly increases the catalytic activity and counteracts the disadvantages mentioned above. For example, in the reaction of 4-piperidinopyridine *N*-oxide (IIIh) with Iba, use of 1/50 eq of IIIh at 80 °C showed sufficient reactivity, in contrast to the case of alkyl-substituted pyridine *N*-oxides.^{1a)}

In conclusion, among the catalysts tested, IIIh is the best from the viewpoint of synthetic advantages (activity and solubility). In practical use, 0.1 eq of IIIh is recommended to be used without solvent. The superdelocalizability appears to provide a clue for quantitative assessment of the catalytic activity of III. The MO simulation predicted the occurrence of the 1,3-dipolar cycloaddition if reaction conditions suitable for the concerted reactions are chosen.

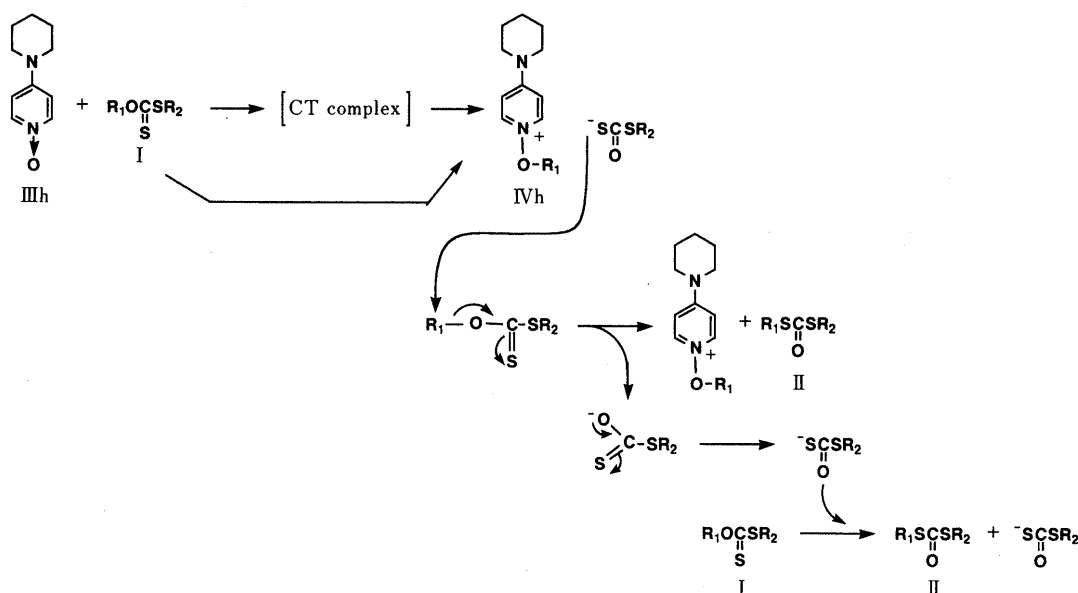


Chart 5

Experimental

All melting points are uncorrected. The infrared (IR) spectra were taken with a Hitachi 270-30 grating spectrophotometer. The ultraviolet (UV) and visible absorption spectra were determined by using a Hitachi 150-20 or a JASCO UVIDEK-220B digital spectrophotometer. The ^1H -NMR spectra were taken with a Hitachi R-600 (60 MHz) or a JEOL GX-400 (400 MHz) spectrometer using tetramethylsilane as an internal standard, and the chemical shifts are expressed in δ values. High-performance liquid chromatography (HPLC) was carried out on a Hitachi 655A-12 apparatus equipped with a 655A UV monitor and a Hitachi D-2000 integrator using a JASCO ODS-Finepack SIL C-18 column.

Molecular orbital calculations were performed on a FACOM M-780 computer at the Computer Center of Kumamoto University and the reaction simulations were executed on a Fujitsu S4/2 engineering workstation. Least-squares calculations and molecular graphics were performed on a Fujitsu FM-16 β HDII or FMR-60 HD microcomputer.

Pyridine *N*-Oxides Pyridine *N*-oxide^{13a)} (IIIa), 4-pentyloxy pyridine *N*-oxide^{13b)} (IIIb), 4-benzyloxy pyridine *N*-oxide^{13b)} (IIIc), 4-dimethylaminopyridine *N*-oxide^{13c)} (IIId), 4-morpholinopyridine *N*-oxide^{13c)} (IIIe), 4-piperidinopyridine *N*-oxide^{13c)} (IIIh) and 3,5-dimethylpyridine *N*-oxide^{13c)} (IIIi) were prepared according to the established method.

4-Decyloxy pyridine *N*-oxide (IIIc) and 4-(2-phenylethoxy) pyridine *N*-oxide (IIe) were prepared by the reaction of the corresponding sodium salts of alkanols with 4-nitropyridine *N*-oxide.^{13b)}

IIIc: mp 86–87°C (colorless needles). Yield 43%. MS m/z : 251 (M^+). Calcd for $\text{C}_{15}\text{H}_{25}\text{NO}_2$: 251.1885. Found: 251.188. IR (KBr): 1638(C=C), 1492(C-H), 1462(C=N), 1216(N-O) cm^{-1} . ^1H -NMR (400 MHz) δ : 0.88 (3H, t, $J=6.8$ Hz, Me), 1.28–1.46 (14H, m, $7\times\text{-CH}_2\text{-}$), 1.80 (2H, m, $\text{-CH}_2\text{-C-O-}$), 3.99 (2H, t, $J=6.6$ Hz, $\text{-CH}_2\text{O-}$), 6.80 (2H, ddd, $J=8.0$, 3.3, 2.6 Hz, $\text{C}_3\text{-H}$ and $\text{C}_5\text{-H}$), 8.12 (2H, ddd, $J=8.0$, 3.3, 2.6 Hz, $\text{C}_2\text{-H}$ and $\text{C}_6\text{-H}$).

IIIe: mp 98.5–100°C (colorless needles). Yield 67%. MS m/z : 215 (M^+). Calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_2$: 215.0946. Found: 215.0938. IR (KBr): 1624(C=C), 1486(C-H), 1456(C=N), 1198(N-O) cm^{-1} . ^1H -NMR (400 MHz) δ : 3.11 (2H, t, $J=6.96$ Hz, $\text{-CH}_2\text{O-}$), 4.20 (2H, t, $J=6.96$ Hz, $\text{Ph-CH}_2\text{-}$), 6.78 (2H, ddd, $J=7.8$, 3.3, 2.4 Hz, $\text{C}_3\text{-H}$ and $\text{C}_5\text{-H}$), 7.25–7.35 (5H, m, Ph), 8.10 (2H, ddd, $J=7.8$ Hz, 3.3, 2.4 Hz, $\text{C}_2\text{-H}$ and $\text{C}_6\text{-H}$).

***O,S*-Dialkyl Dithiocarbonates** *O*-Methyl (Iaa), *O*-ethyl (Iba), *O*-propyl (Ica), *O*-butyl (Ida), *O*-isopropyl (Iea), and *O*-cyclohexyl *S*-methyl (Ifa) dithiocarbonates were prepared according to the previously described method.³⁾

Rearrangement of I to II (General Procedure) A mixture of **I** (1 mol) and **III** (0.02–0.1 mol) was heated at 80°C until **I** was no longer detectable by TLC. After cooling, the reaction mixture was treated with *n*-hexane and the catalyst was removed by passing the *n*-hexane extract through a short column of silica gel. The *n*-hexane was evaporated off *in vacuo* by rotary evaporation, and the residue was purified by distillation to give **II**. The products were identified by comparison of the spectral

data with those of authentic samples.^{1,3)} The dithiol esters (**II**) commonly exhibited characteristic IR absorption bands at *ca.* 1640 and 870 cm^{-1} which can be ascribed to the -S(C=O)S- moiety.

Determination of the Compositions of the Product Mixtures in the Catalytic Conversion of I to II by Pyridine *N*-Oxides (III) A mixture of **I** (1 mmol) and **III** (0.02–0.5 mmol) was placed in a nuclear magnetic resonance (NMR) tube and heated at the desired temperature until completion of the reaction had been confirmed by TLC, then allowed to cool. $\text{DMSO-}d_6$ (0.4 ml) was introduced into the test tube. The samples were analyzed by 400 MHz ^1H -NMR using *o*-nitroanisole as an internal standard.

In the reactions using $\text{DMSO-}d_6$ as the solvent, the progress of the reactions was monitored by Fourier-transform (FT) pulse NMR spectroscopy (Hitachi R-600).

Kinetics A DMSO solution (10 ml) containing **I** (25 mmol), **III** (0.5–2.5 mmol) and *o*-nitroanisole (30 mmol) was placed in a test tube, which was sealed with a ground glass stopper and heated in a constant-temperature silicone oil bath controlled to $\pm 0.1^\circ\text{C}$. The rearrangement rate was followed at a given temperature by analyzing the decrease of the HPLC peak of **I** using *o*-nitroanisole as an internal standard [HPLC conditions: eluent $\text{MeOH-H}_2\text{O}$ (5:2), flow rate 0.2 ml/s, detection wavelength 350 nm]. The relative amounts of **I** left unreacted at each interval were estimated by HPLC digital integration. The output data were treated by means of a nonweighted least-squares program written in F-BASIC86 V2.0 (MS-DOS V3.1). The maximum error in integration was estimated to be about 1.3%. The rate constants (s^{-1}) for the reactions of **I** with **III**f and **III**h (0.1 eq) are as follows. $k \times 10^5$ for **III**f (0.1 eq): 75°C, 9.40; 80°C, 14.3; 90°C, 26.5. $k \times 10^5$ for **III**h (0.1 eq): 75°C, 6.92; 80°C, 8.16; 90°C, 18.7. The activation parameters and effect of the catalyst amount are listed in Tables V and VI, respectively.

Measurement of Visible Absorption Spectrum A mixture of **I**ba (2 mmol) and **II**g (0.2 mmol) was heated at 100°C for 3 h. A solution of the reaction mixture in CHCl_3 (2 ml) was used for the measurement using a 1 cm Pyrex cell. The visible absorption spectrum (320–650 nm) was measured on a Hitachi 150-20 spectrometer.

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$$\Delta E = -\sum (q_a + q_b) \beta_{ab} S_{ab} + \sum (Q_k Q_l / \epsilon R_{kl}) - \sum \sum - \sum \sum 2[\sum C_{ra} C_{sb} \beta_{ab}] / (E_r - E_s)$$

The first term of Eq. 1 is the closed shell repulsion term, the second term is the Coulombic repulsion or attraction term, and the third term represents the interaction of all the occupied orbitals of the one molecule with all the unoccupied orbitals of the other. In this equation, q_a and q_b are electron densities at the interacting atomic orbitals a and b respectively, and β_{ab} and S_{ab} are the resonance integral and the overlap integral for the atomic orbitals a and b, respectively. Q_k and Q_l are the total charges at the interacting atoms k and l, and R_{kl} is the distance between the atoms k and l. In this study, β_{ab} was taken from ref. 9e and S_{ab} was calculated by the CNDO/2 method. As the local dielectric constant (ϵ), the value of benzene was employed. C_{ra} and C_{sb} mean the coefficients of the atomic orbital a in the molecular orbital r and the atomic orbital b in the molecular orbital s, respectively, and E_r and E_s are the energies of the molecular orbitals r and s, respectively.
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