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Pyridine *N*-Oxide Catalyzed Thione-to-Thiol Rearrangement of Xanthates. MO Analysis of the Reaction Mechanism

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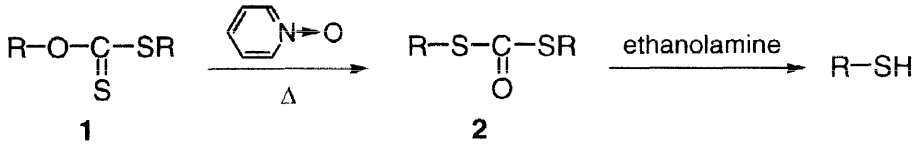
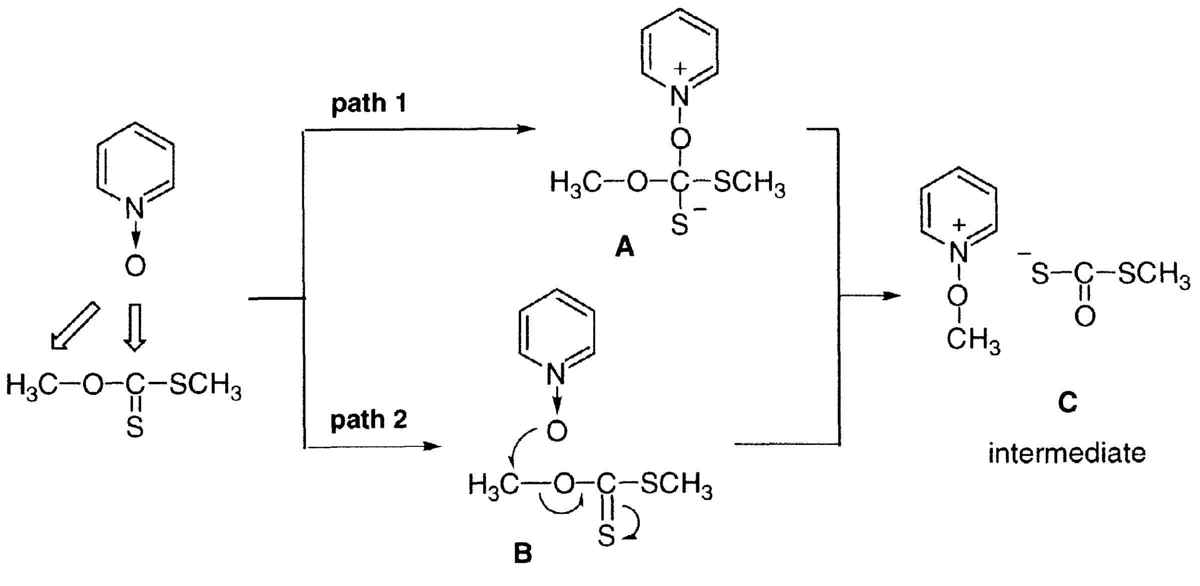
Abstract: The pyridine *N*-oxide-catalyzed thione-to-thiol rearrangement of *O,S*-dialkyl xanthates was analyzed by semiempirical and *ab initio* molecular orbital methods. The transition-structure analyses indicate that the attack of pyridine *N*-oxide toward xanthates proceeds through an S_N2 mechanism to give the dithiolcarbonate anion ($RSCOS^-$) which acts as actual catalyst.

In the previous paper,[1a] it was reported that heating of *O,S*-dialkyl dithiocarbonates (xanthates, **1**) in the presence of pyridine *N*-oxides gave *S,S*-dialkyl dithiocarbonates (dithiolcarbonate, **2**). The rearrangement products (**2**) are important precursors of the thiols which can be generated upon heating of **2** with ethanolamine.[1d]



Scheme 1

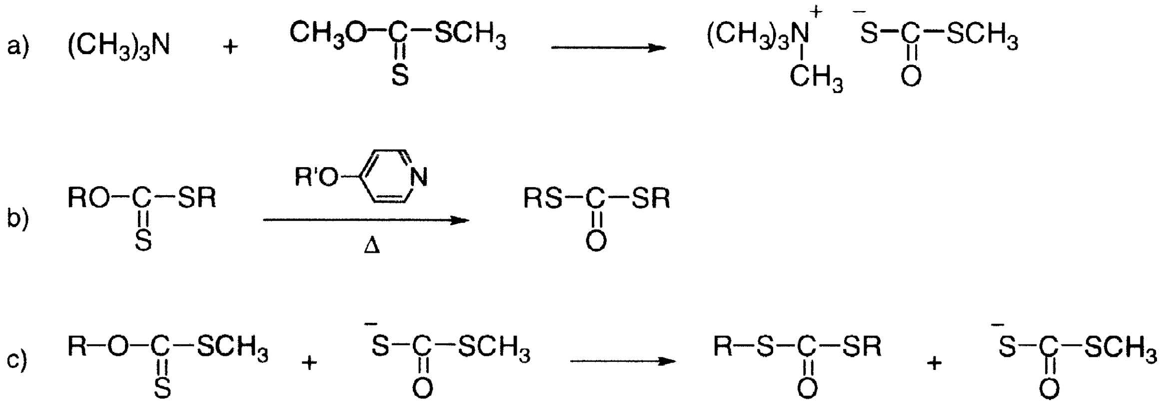
The rearrangement rates were found to be proportional to the concentration of pyridine *N*-oxides and the reactions were remarkably accelerated by electron-donating substituents on pyridine *N*-oxide. From these results, we previously proposed a reaction pathway (Path 1) shown in Scheme 2.



Scheme 2

PII: S0040-4020(98)00578-X

On the other hand, it was reported that *O*,*S*-dimethyl xanthate reacted with trimethylamine to give the tetramethylammonium dithiocarbonate.[2] In this connection, we found that the rearrangement occured by using catalytic amounts of 4-alkoxy- or 4-dialkylaminopyridine,[1b] indicating that alkyldithiolcarbonate anion ($RSCOS^-$) is actual catalyst which attacks *O*,*S*-dialkyl xanthates to give the dithiol ester with regeneration of $RSCOS^-$.[1c]



Scheme 3

Thus, pyridine *N*-oxide is considered to act as a trigger to generate the dithiolcarbonate anion. However, Path 1 passing through the intermediate **A** seems to be questionable because the subsequent reaction must involve energetically unfavorable 1,3-shift of the alkyl group. In order to get a theoretical evidence for the presence of the intermediate **A**, we have performed molecular orbital (MO) calculations on the thione-to-thiol rearrangement of *O*,*S*-dialkyl xanthates. The results are discussed here in the light of newly obtained data to clarify the overall character of the reactions.

EXPERIMENTAL

The UV-Vis spectral data were taken with a Hitachi 150-20 spectrophotometer.

Materials ------ Xanthates and 4-donor-substituted pyridine *N*-oxides were prepared according to the previously reported methods.[1a]

Calculation --- Semiempirical MO calculations (AM1[3a] and PM3[3b]) were run through the ANCHOR II interface using MOPAC6.0[3] on a Fujitsu S4/2 work station (WS). These calculations were done *in vacuo*, and structures were optimized with use of the EF and TS routines. The *ab initio* calculations were performed with GAUSSIAN94[4] program package using 3-21G* and 6-31G* basis sets on a Scientists' Paradise Dragon AXP5A/433 computer or a Convex Exemplar SPP-1000 parallel computer. The stationary points calculated by PM3 method were used as starting geometries for the *ab initio* calculations. All transition states were confirmed by the presence of only one negative eigenvalue of the Hessian.

The heats of formation (ΔH_f) for PM3 calculations and energies (E) for *ab initio* calculation are summarized in Tables 1 and 2.

RESULTS AND DISCUSSION

First of all, we tried to calculate the **A**-type intermediate by PM3 or AM1 method[3] using various molecular complex models in which the oxygen atom of pyridine *N*-oxide was placed just above the thione carbonyl carbon at separation of 2.1-2.5Å.

Table 1. Energetics of Reactants and Transition States involved in the Pyridine *N*-oxide-Catalyzed Rearrangement of *O,S*-Dialkyl Xanthate

Geometry	Method	ΔH_f a)	E b)
GS for *O,S*-dimethyl xanthate			
	AM1	-17.36	
	PM3	-0.80 c)	
	RHF/3-21G*		-982.2143
	RHF/6-31G*		-986.9635
GS for methyldithiolcarbonate anion			
	AM1	-71.40	
	PM3	-70.19	
	RHF/3-21G*		-942.8606
GS for pyridine *N*-oxide			
	AM1	39.52	
	PM3	27.31	
	RHF/3-21G		-319.6711
	RHF/6-31G*		-321.4738
GS for complex of *O,S*-dimethyl xanthate and pyridine *N*-oxide (See Fig. 2)			
	AM1	18.35	
	PM3	22.87	
	RHF/3-21G		-1301.9003
	RHF/6-31G*		-1308.4449
TS for pyridine *N*-oxide-catalyzed Rearrangement (See Figs. 1 and 3)			
S_Ni	AM1	87.78	
	PM3	92.36	
	RHF/3-21G*		-1301.8011
	RHF/6-31G*		-1308.3430
S_N2	AM1	60.87	
	PM3	71.36	
	RHF/3-21G*		-1301.8584
	RHF/6-31G*		-1308.3922
TS for methyldithiolcarbonate-catalyzed Rearrangement (See Fig. 5)			
S_Ni	AM1	-56.78	
	PM3	-40.71	
	RHF/3-21G*		-1924.9964
	RHF/6-31G*		-1934.2953
S_N2	AM1	-88.07	
	PM3	-63.85	
	RHF/3-21G*		-1925.0611
	RHF/6-31G*		-1934.3568
GS for dithiol ester exchange reaction (See Fig. 6)			
	PM3	-107.69	
TS for dithiol ester exchange reaction (See Fig. 6)			
	PM3	-86.70	

a) Kcal/mol. b) Hartree. 1 hartree=627.5 kcal/mol c) See ref. 5

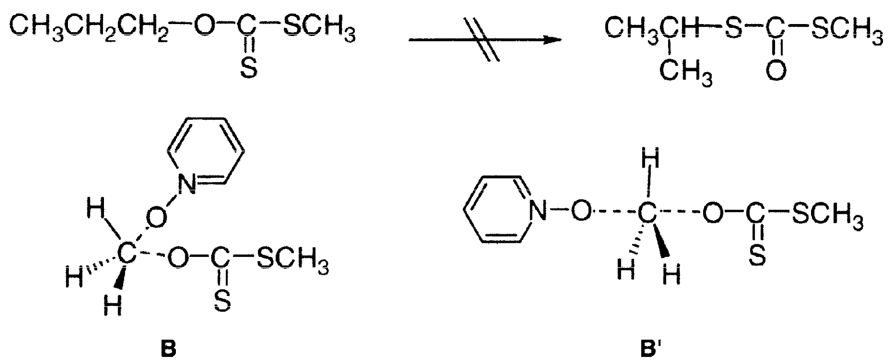
Table 2. Reaction Barriers

Reaction calculated	Method	$\Delta\Delta H_f$ a)	ΔE a)
Pyridine *N*-oxide-catalyzed Rearrangement			
S_Ni	AM1	65.62	
	PM3	65.85	
	RHF/6-31G*		59.17
S_N2	AM1	38.71	
	PM3	44.85	
	RHF/6-31G*		28.30
Methyldithiolcarbonate-catalyzed Rearrangement			
S_Ni	AM1	31.98	
	PM3	48.05	
	RHF/3-21G*		49.26
S_N2	AM1	0.69	
	PM3	7.14	
	RHF/3-21G*		8.66
Dithiol ester exchange reaction			
	PM3	20.99	

a) Kcal/mol.

However, we could not obtain any stationary geometries corresponding to the ground-state (**GS**) structure of the intermediate (**A**). The structure optimization led to dissociation of the molecular complex or epoxidation of the thiocarbonyl moiety, indicating that the stabilization could not occur by the interaction between the >N→O and >C=S groups. Inspection of the PM3-calculated net charges of *O,S*-dimethyl xanthate indicates that the thiocarbonyl carbon has small negative charge (-0.055), suggesting that the attractive coulombic interaction between the >C=S and N→**O** is negligible at an initial stage of the reaction.

In the catalytic rearrangement of *O*-(*n*-propyl) *S*-methyl xanthate, a sizable rate retardation was observed in *O*-(secondary alkyl) xanthates and the *n*-propyl moiety did not isomerize to the isopropyl one. The order of reactivity of *O*-alkyl *S*-methyl xanthates (Et > *n*-Pr > *iso*-Pr > cyclohexyl) is consistent with the relative rates of S_N2-type reactions. Based on these facts, we considered that xanthates directly alkylates the oxygen atom of pyridine *N*-oxides (Path 2) and the thione-to-thiol rearrangement would proceed *via* an S_Ni or S_N2 mechanism rather than a free ion mechanism. Along this assumption, we tried to locate the possible transition structures (**B** and **B'**).



Scheme 4

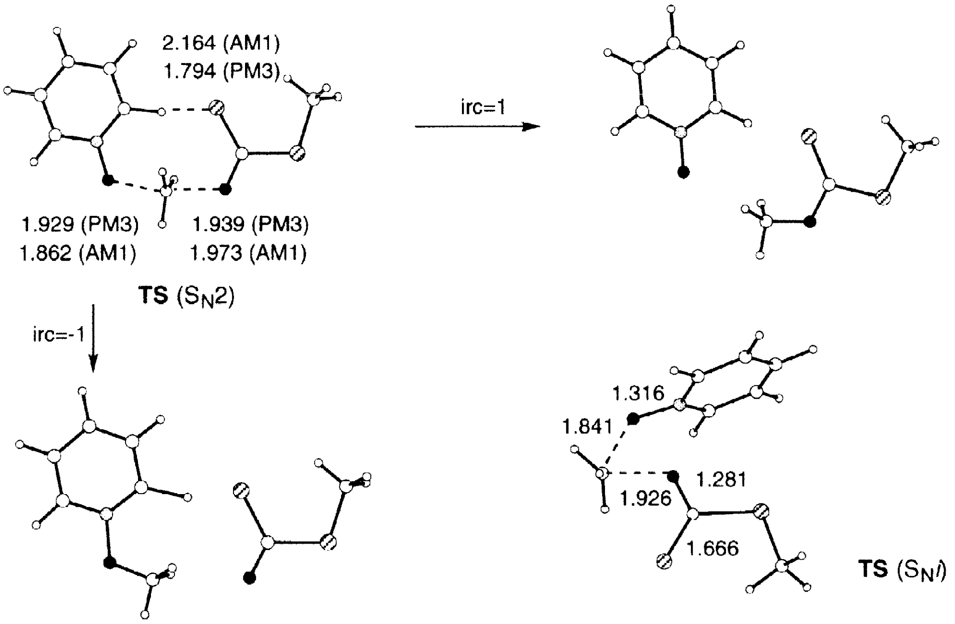


Fig. 1. PM3 Transition Structures for the Reaction of *O,S*-Dimethyl Xanthate with Pyridine *N*-Oxide and Products derived from the IRC Calculations

Consequently, we successfully located both types of the transition structures. The PM3-calculated transition structure with the geometries from the intrinsic reaction coordinate (IRC) calculations are depicted in Fig. 1. The heat of formation of the S_N2-type transition structure is *ca.* 20 kcal/mol more stable than that of the S_Ni-type (Fig. 2). As shown in Fig. 1, the interacting H_3C---O(C=S)- and >N→O---CH_3O- bond distances are 1.939 and 1.929Å, respectively. The IRC calculations[6] starting from the transition state confirmed the presence of 1-methoxypyridinium methyldithiolcarbonate at the end of IRC. The weakly-united molecular complex of the reactants has been obtained at the other end of IRC. The AM1 calculations gave similar results.

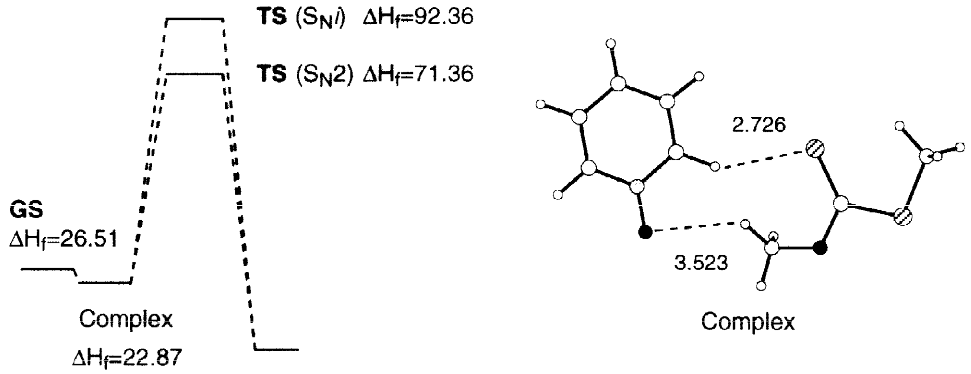


Fig. 2. PM3 Energy Profile and Molecular Complex for the Reaction of *O,S*-Dimethyl Xanthate with Pyridine *N*-Oxide

In order to confirm the result of the semiempirical MO calculations, we performed the *ab initio* calculations[4] of the transition structure at 3-21G* and 6-31G* levels. The transition structures are depicted in Fig. 3. The *ab initio* calculated transition structures are found to be loosely united, in which the interacting distances are longer than those from the semiempirically-derived geometries having a strong hydrogen bond between the 2-hydrogen of pyridine *N*-oxide and the thiocarbonyl sulfur of *O,S*-dimethyl xanthate. The 3-21G* and 6-31G* transition structures of the S_N2-type reaction are more stable than those of the S_Ni type reactions by 35.96 and 30.87 kcal/mol, respectively.

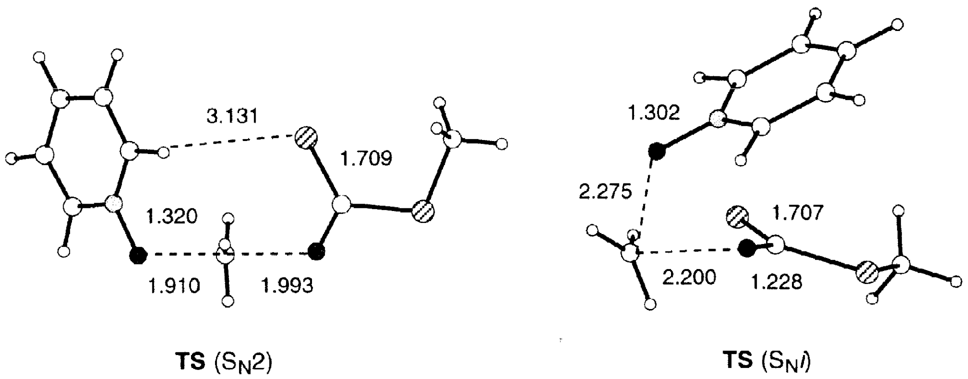


Fig. 3. Transition Structures of the Reaction of *O,S*-Dimethyl Xanthate with Pyridine *N*-Oxide Calculated by *Ab Initio* at RHF/6-31G* Levels

The formation of the salt **C** is considered to be supported by the fact that the CT absorption band[7] was observed in an early stage of the reaction of 4-donor-substituted pyridine *N*-oxide with xanthates (Fig. 4).

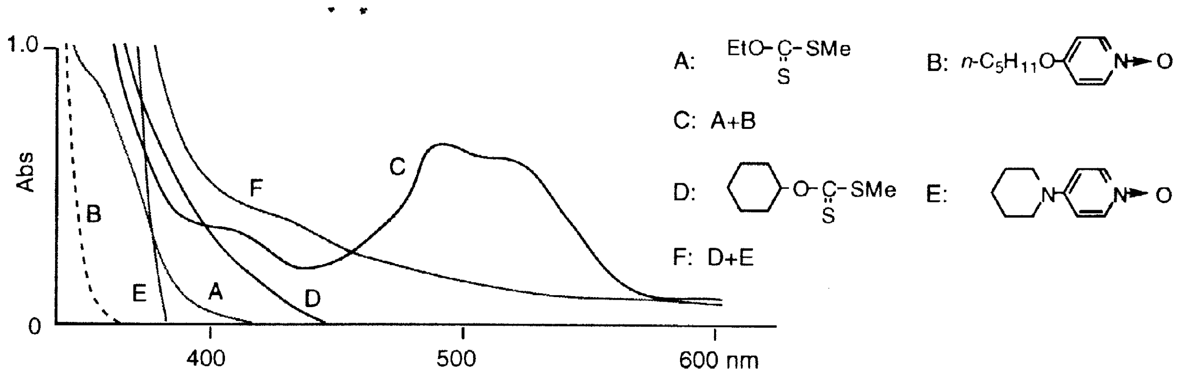


Fig. 4. CT Absorption Bands of the Mixtures of Some Xanthates and 4-Donor-substituted Pyridine *N*-Oxides

Next, we performed the MO calculations on the transition structure of the reaction of *O*,*S*-dimethyl xanthate with the dithiolcarbonate anion (MeSCOS$^-$). The calculated transition structures are shown in Fig. 5. The S_N2-type transition state is remarkably stable than the S_Ni-type one. The reaction barrier of S_N2-type substitution is very low (8.66 kcal/mol for RHF/3-21G*), indicating that the reaction spontaneously occurs at room temperature.

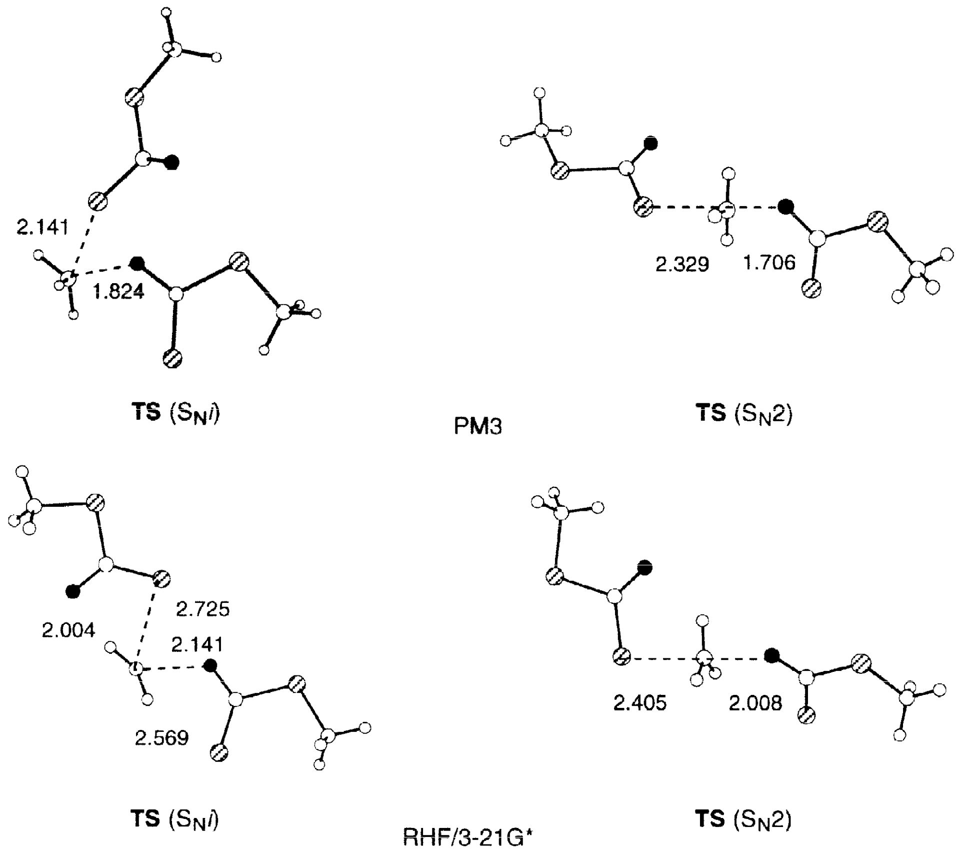
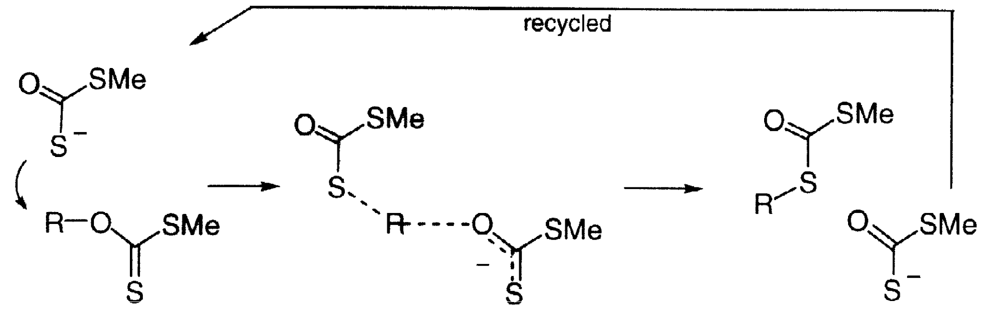


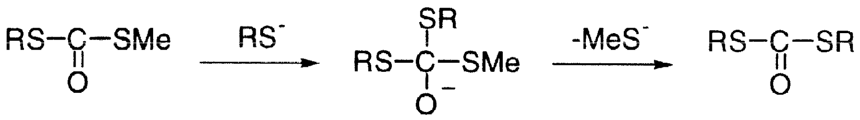
Fig. 5. Transition Structures of the Reaction of *O*,*S*-Dimethyl Xanthate with Methyldithiolcarbonate Anion Calculated by PM3 and *Ab Initio* at RHF/3-21G* Level

The thione-to-thiol rearrangement mechanism of *O*-alkyl *S*-methyl xanthates can be shown in Scheme 5. Xanthates alkylates the dithiolcarbonate anion to give the *S*,*S*-dialkyl dithiocarbonate and the dithiolcarbonate anion which again reacts with the xanthate. Thus, the dithiocarbonate anion acts as catalyst in recycling procedure.



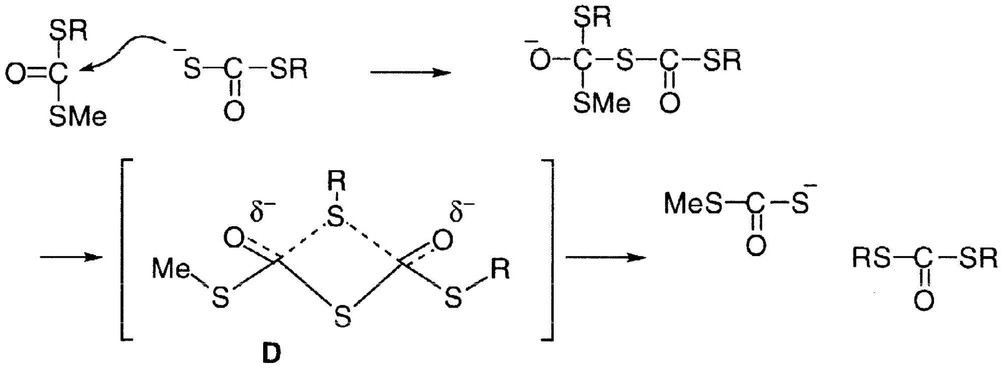
Scheme 5

The catalytic rearrangement reaction of an unsymmetrical xanthate gave a mixture of the dithiol esters. At first, we considered that the mixture was formed from an equilibrium reaction between the corresponding rearrangement product and the thiol anions (RS^-) derived from the decomposition reaction of the alkyldithiol-carbonate anion ($RSCOS^- \rightarrow RS^- + COS$). However, during the reaction, evolusion of COS gas could not be recognized, indicating that there is no possibility of the equilibrium reaction with RS^-.



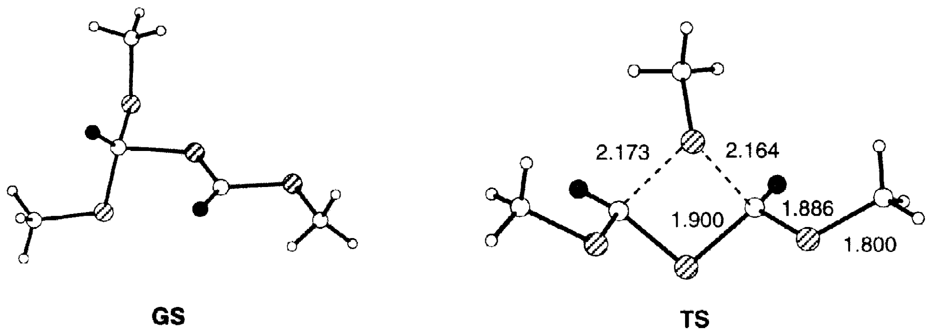
Scheme 6

The dithiol esters are assumed to be formed from an equilibrium reaction of the rearrangement product with the dithiolcarbonate anion. The transition structure of the exchange reaction was calculated assuming that the dithiolcarbonate anion would attack the carbonyl carbon of the dithiol ester to give the intermediate followed by the migration of the alkylthio group.



Scheme 7

The TS structure of the **D**-type intermediate calculated at PM3 level is shown in Fig. 6. The PM3-calculated activation energy is 21 kcal/mol, indicating that this type of migration is plausible.



GS

TS

Fig. 6. Ground-state and Transition-state Structures for the Reaction of the Methyldithiolcarbonate Anion with *S,S*-Dimethyl Dithiocarbonate Calculated by PM3

In conclusion, the MO analyses of pyridine *N*-oxide-catalyzed thione-to-thiol rearrangement of xanthates to the corresponding dithiol esters provide a theoretical evidence of the formation mechanism of 1-methoxypyridinium methyldithiolcarbonate which acts as actual catalyst. The calculated reaction mechanisms are considered to be modified in the solvent used. However, taking into consideration that the reactions occur without polar solvents, the reaction mechanism is assumed to be not very far from the calculated one.

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5. The PM3 calculation of dimethyl xanthate showed the existence of two local minimum conformations. The methyl groups lie within a plane of -O(C=S)S- group with *syn/anti* dispositions with regard to the C=S bond. The *anti* conformation which is global minimum is *ca.* 1.6 kcal/mol more stable than the *syn* conformation. However *ab initio* calculation (RHF/6-31G*) gave opposite prediction (*syn*). This structure is in accordance with those observed in the X-ray crystal structures of the analogous compounds. Abrahamson, S.; Innes, M. *Acta Crystallogr. Sc.*, **1974**, *30*, 721; B. Dahlen, *Acta. Chem. Scand. Ser.*, **1977**, *31*, 407.
6. To save the CPU time, the time-consuming IRC calculations were performed by PM3 and AM1 methods.
7. Similar CT bands were observed in the UV-Vis absorption spectra of *N*-alkylpyridinium iodide in various solvents. Kosower, E. M. *J. Am. Chem. Soc.*, **1958**, *80*, 3253, 3261, 3267.