HETEROCYCLES, Vol 27, No 10, 1988

4-DIMETHYLAMINOPYRIDINE N-OXIDE AS AN EXCELLENT CATALYST FOR THIONE TO THIOL REARRANGEMENT OF XANTHATES

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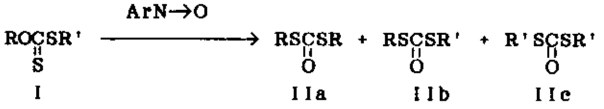
Abstract - 4-Dimethylaminopyridine N-oxide effectively catalyzes the thione to thiol rearrangement of O,S-dialkyl dithiocarbonates (xanthates) to provide S,S-dialkyl dithiocarbonates.

Interest in the chemistry of thione to thiol rearrangement of xanthates[1] has led to a continuing search for effective catalysts that can be used in the one-pot synthesis of thiols. Previously we have reported that pyridine N-oxides catalyzed the rearrangement of O,S-dialkyl dithiocarbonates (xanthates) (I) to provide S,S-dialkyl dithiocarbonates (IIa-c) in good yields (Scheme 1).[2] In the reaction, we found that the use of pyridine N-oxides having electron-donating substituents such as 3,5-dimethylpyridine N-oxide showed high catalytic reactivity toward xanthates.

- Scheme 1 -



$$\underset{\mathbf{I}}{\mathrm{RO}\underset{\underset{\displaystyle \mathrm{S}}{\|}}{\mathrm{C}}\mathrm{SR'}} \xrightarrow{\mathrm{ArN\rightarrow O}} \underset{\mathbf{IIa}}{\mathrm{RS}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{SR}} + \underset{\mathbf{IIb}}{\mathrm{RS}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{SR'}} + \underset{\mathbf{IIc}}{\mathrm{R'S}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{SR'}}$$

On the basis of the previous study and molecular orbital calculation data,[3] we concluded that the ideal catalyst for the thione to thiol rearrangement would have a high-lying highest occupied molecular orbital (HOMO) energy level.

We now wish to report on catalytic behavior of 4-dimethylaminopyridine N-oxide (4-DMAPNO)[4] toward xanthates.

First of all, we determined the optimum amount of the catalyst by using O-methyl

S-benzyl xanthate as a substrate. The rearrangement of the xanthate was carried out by warming a mixture of the xanthate and various amounts of 4-DMAPNO in DMSO-d_6 at 40 ℃. The product mixture was analyzed by ^{1}H-nmr using a JEOL GX-400 spectrometer and 4-DMAPNO as the internal standard.

Table I. Effect of Reactant/Catalyst Ratio on the Yield of II in the Reaction of *O-Methyl S-Benzyl Xanthate*[a)]

Exp. No.	Xanthate:4-DMAPNO	Time (h)	Yield (%)
1	50 : 1	5.0	79
2	40 : 1	4.0	85
3	20 : 1	2.5	88
4	10 : 1	1.5	93
5	5 : 1	2.5	77
6	2 : 1	2.5	14[b)]

a) The reactions were carried out in DMSO-d_6 at 40 ℃.

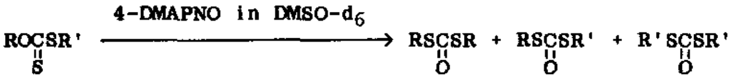
b) Benzyl methyl sulfide was observed by glc.

As can be seen in Table I, the reaction is sensitive to reactant/catalyst ratio and the best yield was obtained at a reactant to catalyst molar ratio of 10 (Exp. No. 4). When a large amount of catalyst was used (Exp. No. 6), a significant decrease of the yield was observed, a consequence of formation of benzyl methyl sulfide. It is noteworthy that the reaction can be carried out with trace of 4-DMAPNO in fairly good yield (Exp. No. 1, 2).

The applications of this rearrangement with 4-DMAPNO as catalyst to several xanthates are shown in Table II. As shown in Table II, primary O-alkyl xanthates easily underwent the thione to thiol rearrangement to give the mixtures of the dithiol esters in high yields. On the other hand, secondary ones required more severe reaction conditions. The order of reactivity of xanthates (Bz>Me>Et>n-Pr>iso-Pr) is consistent with the relative rates of S_N2-type reactions.

In the case of secondary O-alkyl xanthates, intensive colorations due to charge transfer phenomena between the substrate and catalyst were observed. This may be unfavorable for the rearrangement due to a stabilization of the ground state. These facts indicate that the reaction proceeds via the S_N2-type nucleophilic attack of the oxygen atom of 4-DMAPNO to the O-alkyl group of xanthates.

Table II. Catalytic Rearrangement of Xanthates by 4-DMAPNO[a]



$$\mathrm{RO}\underset{\substack{\| \\ \mathrm{S}}}{\mathrm{C}}\mathrm{SR'} \xrightarrow{\text{4-DMAPNO in DMSO-}d_6} \mathrm{RS}\underset{\substack{\| \\ \mathrm{O}}}{\mathrm{C}}\mathrm{SR} + \mathrm{RS}\underset{\substack{\| \\ \mathrm{O}}}{\mathrm{C}}\mathrm{SR'} + \mathrm{R'S}\underset{\substack{\| \\ \mathrm{O}}}{\mathrm{C}}\mathrm{SR'}$$

I IIa IIb IIc

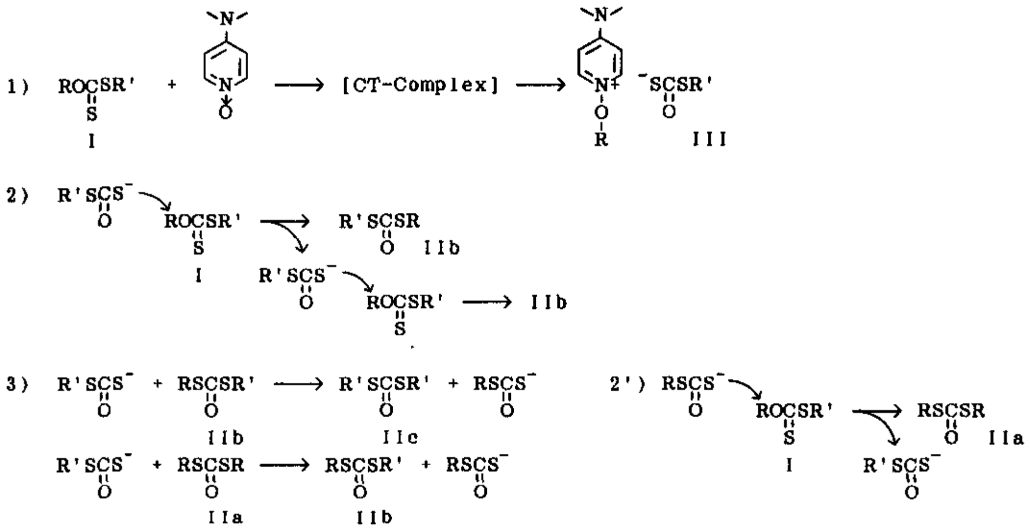
R	R'	Reaction Conditions		Yield(%)[b]
		Temp.(℃)	Time(h)	IIa + IIb + IIc
Me	Me	40	2.0	99
		60	0.5	95
Me	Bz	40	1.5	93
Et	Me	70	7.0	83
		80	3.0	83
Et	Et	80	3.0	88
n-Pr	Me	80	6.0	87
n-Bu	Me	80	6.0	94
n-Decyl	Me	90	3.0	83
Bz	Me	40	1.0	92
i-Pr	Me	110	10.0	71
		130	3.0	80
cyclohexyl	Me	130	20.0	18

a) The ratio of xanthate to 4-DMAPNO was 10:1 in all cases.

b) IIa:IIb:IIc=1:2:1

Inspection of the ^{1}H-nmr spectrum of the reaction mixture indicated the presence of an intermediacy ascribable to the structure of III. The aromatic protons (C_2-H and C_6-H) showed a pattern nearly identical with the ones observed for 1-alkoxy-4-dimethylaminopyridinium iodides. The resulted $^-$SCOSR' anion then undergoes nucleophilic attack on ROCSSR' to give RSCOSR' and $^-$SCOSR' followed by transesterification[5] with RSCOSR' to give the mixed dithiol esters as shown in Scheme 2.

- Scheme 2 -



Combination of this rearrangement with a procedure described previously (heating II in ethanolamine) is of synthetic value for a short synthesis of thiols from alcohols.[6]

In connection with a possible role of charge-transfer complexs, a detailed mechanistic investigation of the reaction is now in progress.

REFERENCES AND NOTES

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   b) K. Harano and T. Taguchi, Tetrahedron Lett., 1974, 4479.
   c) K. Harano, K. Miyoshi, and T. Hisano, Chem. Pharm. Bull., 33, 1861(1985).
2. K. Harano, I. Shinohara, and T. Hisano, Heterocycles, 26, 2583(1987).
3. The MNDO energy levels (eV) for the reactants are as follows: O,S-Dimethyl xanthate HOMO; -9.843, LUMO,-0.506. Pyridine N-oxide; HOMO, -8.769, LUMO, -0.474. 4-Aminopyridine N-oxide; HOMO, -8.018, LUMO, -0.355, NLUMO, -0.148.
4. A. R. Katritzky, J. Chem. Soc., 1957, 1769.
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Received, 30th May, 1988