PYRIDINE N-OXIDES AS CATALYSTS FOR THIONE-THIOL REARRANGEMENT

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Abstract - Pyridine N-oxides are efficient catalysts for rearrangement
of O,S-dialkyl dithiocarbonates to S,S-dialkyl dithiocarbonates.
A solid-phase copolymer of 4-vinylpyridine N-oxide (P4VPNO) is also a
useful catalyst, being nonvolatile and easily handled. The rearrange-
ment products are served as useful precursors of thiols.

In the previous papers,[1] we showed that the 1,3-dipolar cycloaddition of pyridine
N-oxides (III) to cumulenes such as phenyl isocyanates takes place by a concerted
process and the reactivity may result from both the frontier molecular orbital
(FMO) interaction and the relatively high degree of coulombic attraction arizing
from the highly polarized structures of addends. Based on these results, we
concluded that the reactive dipolarophile toward aromatic N-oxides should have a
polar structure and focused our attention on the 1,3-dipolar cycloaddition
behavior of thiocarbonyl compounds such as O,S-dialkyl dithiocarbonates (xan-
thates) (I). As the result, O,S-dialkyl dithiocarbonates (I) did not show cyclo-
addition reactivity toward pyridine N-oxides (III) but underwent rearrangement to
S,S-dialkyl dithiocarbonates (II) by catalysis of pyridine N-oxides (III).
We present here that the use of pyridine N-oxides (III) as catalyst allows the
conversion of O,S-dialkyl dithiocarbonates (I) into the corresponding S,S-dialkyl
dithiocarbonates (II) in fairly good yield under neutral non-aqueous conditions.
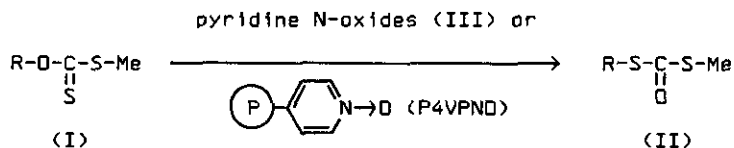
The starting materials are readily available from xanthation of the correspon-
ding alcohols using dimethyl sulfoxide (DMSO) as a solvent.[2] A typical procedure

for the synthesis of S.S-dialkyl dithiocarbonates is as follows: A mixture of pyridine N-oxide (IIIa) (5 mmol) and O-(n-propyl) S-methyl dithiocarbonate (Ic) (10 mmol) was heated at 100°C until disappearance of starting material as judged by TLC. The reaction mixture was then diluted with n-hexane and passed through a short column of silica gel to remove the catalyst. The product was purified by distillation to afford S-methyl S-(n-porpyl) dithiocarbonate (IIc) in 92% yield. Similarly, heating O-alkyl S-methyl dithiocarbonates (Ia-f) with pyridine N-oxide (IIIa) at 60-110°C gave the corresponding S-alkyl S-methyl dithiocarbonates (IIa-f) in good yields. Reaction conditions and yields are listed in Table I.

Table I. Rearrangement of O-Alkyl S-Methyl Dithiocarbonates (Ia-f) to
S-Alkyl S-Methyl Dithiocarbonates (IIa-f) in the Presence of
Pyridine N-Oxides (III) as Catalysts

R-OCS-CH$_3$ (Ix) S		Catalyst[b]	Reaction condition[a]		Yield(%)[c]
x	R		Temp.(°C)	Time(h)	
a	Me	H	65	5.0	95.6
		P4VPNO[d]	65	20.0	88.3
b	Et	H	110	2.5	98.6
	Et	3.5-dimethyl	110	1.0	91.7
	Et	2-phenyl	110	18.5	20.0
	Et	3.5-dibromo	110	18.5	31.6
	Et	P4VPNO[d]	110	10.0	86.0
c	n-Pr	H	110	9.0	92.4
d	iso-Pr	H	110	15.0	62.9
e	Bz	H	50	4.0	88.1
f	cyclohexyl	H	140	6.0	62.3

a) Mixtures of I and III in a 2:1 mole ratio were heated without solvent.
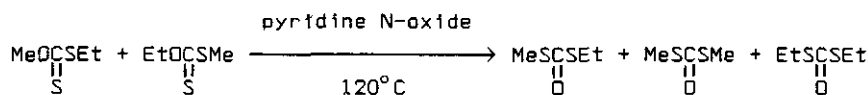
b) Substituents of pyridine N-oxide (ArN→O).

c) Determined by [1]H-nmr analyses.

d) A copolymer of 4-vinylpyridine N-oxide[3] (P4VPNO). A 2.0 mmol scale with 30 mg of the catalyst was employed.

The products were identified by comparison with the authentic samples obtained
from catalytic rearrangement of the corresponding alcohols by $AlCl_3$.[4]
Some important features of this reaction are noted: (a) Of pyridine N-oxides
(III), 3-methylpyridine (3-picoline) and 3,5-dimethylpyridine (3,5-lutidine) N-
oxides are effective catalysts, whereas pyridine N-oxides bearing electron-
attracting substituents or a substituent at the 2-position are far less active
than pyridine N-oxide.(b) Branching at R impedes the reaction. The order of
reactivity of I apparently parallels the ease of nucleophilic substitution at R.
However, S-secondary alkyl S-methyl dithiocarbonates (IId, f) were obtained in
better yields than the case of Lewis acids. (c) The skeleton rearrangement of the
alkyl moiety, e. g. n-propyl to isopropyl, was not observed in the condition used.
(d) The use of dipolar aprotic solvent such as N,N-dimethylformamide (DMF)
enhanced the reaction rate.[5]
When two esters having different O-alkyl groups and different S-alkyl groups were
allowed to rearrange in the same solution, a "cross product" was obtained
(Scheme 1).[6] This observation suggests that the reaction may be intermolecular
and ionic.

- Scheme 1 -

$$\text{MeOCSEt} + \text{EtOCSMe} \xrightarrow[\quad 120°C \quad]{\text{pyridine N-oxide}} \text{MeSCSEt} + \text{MeSCSMe} + \text{EtSCSEt}$$

The reaction is probably initiated by electrophilic attack[7] of the thiocarbonyl
carbon on the oxygen atom of pyridine N-oxide followed by formation of alkoxy-
ammonium salt intermediate. During the course of the reaction, isomerization of
thione to thiol[8] occurs and the resulting dithiol-type anion is considered to be
more nucleophilic and coupled with the alkyl group from the alkoxyammonium cation.

- Scheme 2 -
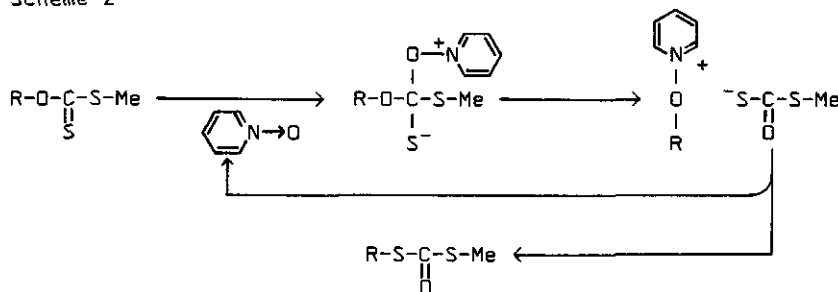
Use of a solid-phase copolymer (PVPNO)[3] of pyridine N-oxide as a catalyst for the reaction has the important advantage that the resins are insoluble in water and in organic solvents and can be removed by filtration. The catalysts may be used repeatedly by washing with a solvent (See Table I).

The reaction is of synthetic value for generation of thiols because of simplicity of operation. After completion of the rearrangement, the reaction mixture is heated with 2-aminoethanol (1 mole) to afford alkanethiol.[9]
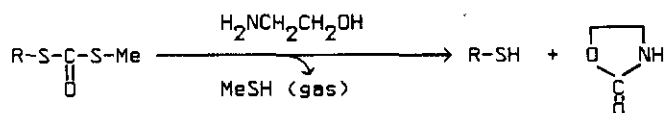
The procedures for the rearrangement of xanthates and the generation of thiols can be carried out in an only distilling flask.

REFERENCES AND NOTES

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5. The rate was followed by analyzing the [1]H-nmr spectrum of the S-Me groups. The pseudo first-order rate constants ($k \times 10^6$/sec. I: 3 mmol. II: 1.5 mmol) for Ic and Id at 110 C in DMSO-D_6 are 3.362 and 0.702 respectively.

6. The reaction mixture was analyzed by GLC.

7. The CNDO/2 calculation data are as follows: Coefficient of HOMO for II: O, -0.742; N, 0.190. Net charge ($\times 10^3$e) for II: O, -427; N, 300. Coefficient of LUMO for Ia: C, -0.493; S, 0.648. Net charge ($\times 10^3$e) for I: C, 185; S, -187.

8. Bond energy data indicate that isomerization is exothermic by ca. 24kcal/mol: F. N. Jones, *J. Org. Chem.*, **33**, 4290(1968).

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