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 rearrangement products are served as useful precursors of thiol.

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 arising 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 thiacarbonyl compounds such as O.S-dialkyl dithiocarbonates (xanthates) (I). As the result, O.S-dialkyl dithiocarbonates (I) did not show cycloaddition 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.

\[ \text{pyridine N-oxides (III) or} \]
\[ \text{R-O-C-S-Me} \]
\[ \text{S} \]
\[ \text{(I)} \]
\[ \text{P} \]
\[ \text{N} \]
\[ \text{D} \]
\[ \text{P4VPNO} \]
\[ \text{R-S-C-S-Me} \]
\[ \text{S} \]
\[ \text{II} \]

The starting materials are readily available from xanthation of the corresponding alcohols using dimethyl sulfoxide (DMSO) as a solvent.2 A typical procedure

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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-propyl) 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 (IIIa) as Catalysts

<table>
<thead>
<tr>
<th>R-OCS-CH₃ (IX) S</th>
<th>Catalyst</th>
<th>Reaction condition</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>R</td>
<td>Temp. (°C)</td>
<td>Time(h)</td>
</tr>
<tr>
<td>a</td>
<td>Me</td>
<td>H</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P4VPN³d)</td>
<td>65</td>
</tr>
<tr>
<td>b</td>
<td>Et</td>
<td>H</td>
<td>110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3,5-dimethyl</td>
<td>110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-phenyl</td>
<td>110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3,5-di-bromo</td>
<td>110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P4VPN³d)</td>
<td>110</td>
</tr>
<tr>
<td>c</td>
<td>n-Pr</td>
<td>H</td>
<td>110</td>
</tr>
<tr>
<td>d</td>
<td>iso-Pr</td>
<td>H</td>
<td>110</td>
</tr>
<tr>
<td>e</td>
<td>Bz</td>
<td>H</td>
<td>50</td>
</tr>
<tr>
<td>f</td>
<td>cyclohexyl</td>
<td>H</td>
<td>140</td>
</tr>
</tbody>
</table>

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 ¹H-nmr analyses.
d) A copolymer of 4-vinylpyridine N-oxide³ (P4VPN³). 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 AlCl₃.⁴

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 (IIId, 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 -

\[
\text{pyridine N-oxide} \quad \begin{array}{c}
\text{MeOCSe} + \text{EtOCSMe} \\
\hline
\text{O} & \text{S} \\
\hline
\text{O} & \text{S}
\end{array} \xrightarrow{120^\circ\text{C}} \text{MeSCSe} + \text{MeSCSMe} + \text{EtSCSe}
\]

The reaction is probably initiated by electrophilic attack⁷ of the thiocarbonyl carbon on the oxygen atom of pyridine N-oxide followed by formation of alkoxyammonium salt intermediate. During the course of the reaction, isomerization of thione to thiol⁸ 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 -

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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.\(^9\)

\[
\begin{align*}
R-S-C-S-Me &\xrightleftharpoons[H_2NCH_2CH_2OH]{MeSH \text{ (gas)}} R-SH + O\bigcirc\bigcirc\bigcirc\bigcirc\bigcirc\bigcirc\bigcirc\bigcirc\bigcirc\bigcirc\bigcirc[
\end{align*}
\]

The procedures for the rearrangement of xanthates and the generation of thiols can be carried out in an only distilling flask.

REFERENCES AND NOTES


5. The rate was followed by analyzing the \(^1\)H-nmr spectrum of the S-Me groups. The pseudo first-order rate constants \((x10^6/sec. I: 3 \text{ mmol}; II: 1.5 \text{ mmol})\) 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: 0. -0.742; N: 0.190. Net charge \((x10^3e)\) for II: O: -427; N: 300. Coefficient of LUMO for Ia: C: -0.493; S: 0.648. Net charge \((x10^3e)\) for I: C: 185; S: -187.


Received, 15th May, 1987