THE REACTION OF INDOLES WITH SUCCINIMIDO-SULFONIUM SALTS I.
A CONVENIENT SYNTHESIS OF INDOLE-3-THIOETHERS

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Reaction of indoles with succinimido-dialkyl- or alkylarylsulfonium chlorides, prepared from dialkyl or alkylaryl sulfides and N-chlorosuccinimide, afforded indole-3-dialkyl- or alkylarylsulfonium chlorides which gave 3-alkylthio- or arylthioindoles on pyrolysis.

Succinimido-dimethylsulfonium chloride, prepared from N-chlorosuccinimide and dimethylsulfides, have been known to react with some nucleophiles such as amines, phenols, alcohols, carbanions and enamines. In this paper, we report a new reaction of the sulfonium salts with indole compounds.

To a solution of succinimido-diethylsulfonium chloride in dichloromethane or chloroform, prepared by the addition of diethylsulfide (Ia) to a solution of N-chlorosuccinimide at 0°C, was added equimolar amount of indole (IIa) in the same solvent at -20°C under an atmosphere of nitrogen. The temperature of the mixture was raised gradually to 20°C during 1 hour. After removal of the solvent, 3-diethylsulfoniumindole (IIIa) and succinimide were obtained quantitatively: (IIIa); mp 148-149°C
(decomp. methanol-tetrahydrofuran), NMR (60 Mc, in D$_2$O); δ 1.19 (6H, t, J=7 Hz, -CH$_2$-CH$_3$), 3.65 (4H, q, J=7 Hz, S$^+$-CH$_2$-CH$_3$), 7.25-7.90 (4H, m, aromatic protons), 8.15 (1H, s, indole α-H).

When the salt (IIIa) was heated at 150°C in nitrogen atmosphere or refluxed in xylene for 30 min, 3-ethylthioindole (IVa) was obtained as a light yellow oil in 80% yield: NMR (in CDCl$_3$); δ 1.16 (3H, t, J=8 Hz, -CH$_2$-CH$_3$), 2.70 (2H, q, J=8 Hz, S-CH$_2$-CH$_3$), 7.10-7.80 (5H, m, aromatic protons), 8.2 (1H, br., NH). IR$^\text{liq}$: 3430 cm$^{-1}$ (NH). Mass spectrum; m/e 177 (M$^+$).

Likewise, with some other dialkylsulfides (Ib-e), 3-alkythioindoles (IVb-g) were prepared in good yields via the intermediate (IIib-g). (Scheme 1)

The reaction of indole with the succinimido-sulfonium salt of tetrahydrothiophene gave the corresponding 3-sulfonium chloride quantitatively which afforded 3-ω-chloro-n-butylthioindole on pyrolysis in 90% yield: NMR (in CDCl$_3$); δ 1.70 (4H, m, -CH$_2$-CH$_2$-), 2.63 (2H, t, J=7 Hz, S-CH$_2$-CH$_2$-), 3.43 (2H, t, J=7 Hz, -CH$_2$-CH$_2$-Cl), 7.05-7.80 (6H, m, aromatic protons and NH). This finding suggests that the indole-3-thioethers (IV) are formed by the nucleophilic attack of the Cl$^-$ on the α-carbons of the alkyl groups in the sulfonium salts (III).

Therefore phenylmethylsulfide presented 3-phenylthioindole, mp 151-3°C, in 50% overall yield as the sole product, expectedly. The usual way for the synthesis of indole-3-alkylthioethers is the alkylation of indolethiols$^{3a}$ or the direct formation by the indole synthesis.$^{3b}$ Indole-3-aryltioethers have been formed by the latter method.$^{3c}$ The present reaction
provides a simpler and more efficient way to approach both alkyl- and arylthioethers.

Synthetic application of this new reaction will be shown in the subsequent papers.

Scheme 1

\begin{align*}
I &\quad R = \text{C}_2\text{H}_5 & II &\quad R' = \text{H}, R'' = \text{H} & III, IV &\quad R = \text{C}_2\text{H}_5 & R' = \text{H}, R'' = \text{H} \\
b &\quad \text{CH}_3 & b &\quad \text{R'} = \text{H}, \text{R''} = \text{CH}_3 & b &\quad \text{CH}_3 & " \\
c &\quad \text{nC}_3\text{H}_7 & c &\quad \text{R'} = \text{CH}_3, \text{R''} = \text{H} & c &\quad \text{nC}_3\text{H}_7 & " \\
\hat{a} &\quad \text{nC}_4\text{H}_9 & \hat{a} &\quad \text{nC}_4\text{H}_9 & \hat{a} &\quad \text{nC}_4\text{H}_9 & " \\
e &\quad \text{nC}_6\text{H}_{17} & e &\quad \text{nC}_8\text{H}_{17} & e &\quad \text{nC}_8\text{H}_{17} & " \\
f &\quad \text{C}_2\text{H}_5 & f &\quad \text{R'} = \text{H}, \text{R''} = \text{CH}_3 \\
g &\quad " & g &\quad \text{R'} = \text{CH}_3, \text{R''} = \text{H} 
\end{align*}
REFERENCES


Received, 9th January, 1976