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

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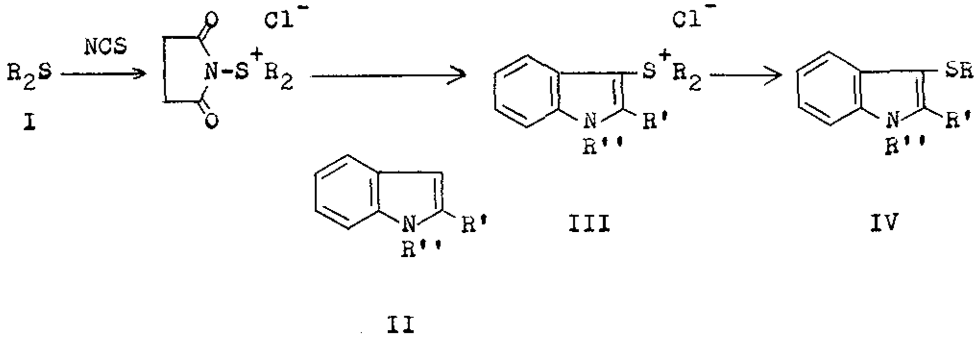
Reaction of indoles with succinimido-dialkyl- or alkylarylsulfonium chlorides, prepared from dialkyl or alkylaryl sulfides and N-chlorosuccinimide, afforded indole-3-dialkyl- or alkylarylsulfonium chlorides which gave 3-alkylthio- or arylthioindoles on pyrolysis.

Succinimido-dimethylsulfonium chloride, prepared from N-chlorosuccinimide and dimethylsulfides,$^{1)}$ have been known to react with some nucleophiles such as amines, phenols, alcohols, carbanions and enamines.$^{2)}$ 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_2O); δ 1.19 (6H, t, J=7 Hz, $-CH_2-C\underline{H}_3$), 3.65 (4H, q, J=7 Hz, $S^+-C\underline{H}_2-CH_3$), 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, $-CH_2-C\underline{H}_3$), 2.70 (2H, q, J=8 Hz, $S-C\underline{H}_2-CH_3$), 7.10-7.80 (5H, m, aromatic protons), 8.2 (1H, br., $N\underline{H}$). IR_{ν}^{liq}: 3430 cm^{-1} (NH). Mass spectrum; m/e 177 (M^+). Likewise, with some other dialkylsulfides (Ib-e), 3-alkylthioindoles (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, $-C\underline{H}_2-C\underline{H}_2-$), 2.63 (2H, t, J=7 Hz, $S-C\underline{H}_2-CH_2-$), 3.43 (2H, t, J=7 Hz, $-CH_2-C\underline{H}_2-Cl$), 7.05-7.80 (6H, m, aromatic protons and $N\underline{H}$). 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-arylthioethers 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

Ia	$R=C_2H_5$	IIa	$R'=R''=H$	III,IVa	$R=C_2H_5$	$R'=R''=H$
b	CH_3	b	$R'=H$, $R''=CH_3$	b	CH_3	"
c	nC_3H_7	c	$R'=CH_3$, $R''=H$	c	nC_3H_7	"
d	nC_4H_9			d	nC_4H_9	"
e	nC_8H_{17}			e	nC_8H_{17}	"
				f	C_2H_5	$R'=H$, $R''=CH_3$
				g	"	$R'=CH_3$, $R''=H$

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