

THE REACTION OF INDOLES WITH SUCCINIMIDO-SULFONIUM SALTS.II
A NEW SYNTHESIS OF 2-ALKYL AND ALLYL INDOLES

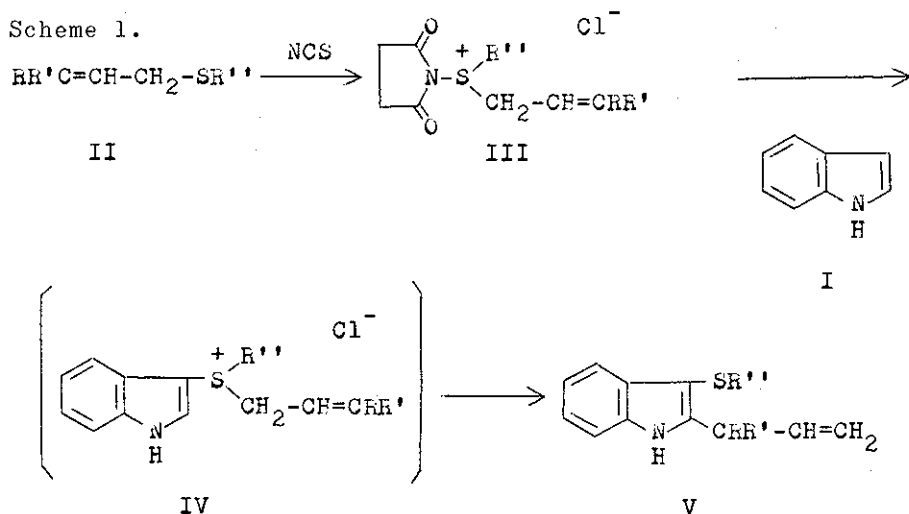
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Reaction of indole with succinimido-diallyl- or alkylallylsulfonium chlorides afforded 2-allyl-3-allylthio- or 2-allyl-3-alkylthioindoles which gave 2-alkyl- or 2-allylindoles by the reductive desulfurization with Raney Ni or Zn - acetic acid.

In the previous paper, we reported that indole compounds reacted with succinimido-dialkyl- or alkylarylsulfonium chlorides to give indole-3-sulfonium chlorides which were converted to 3-alkylthio- or arylthioindoles on pyrolysis.¹⁾ In this report, we report a new convenient method for the synthesis of 2-alkyl- and 2-allylindoles using succinimido-diallyl- or alkylallylsulfonium chlorides.

Indole (I) was added to a solution of succinimido-3,3-dimethylallyl ethylsulfonium chloride (IIIa), prepared from N-chlorosuccinimide and 3,3-dimethylallyl ethylsulfide (IIa), in dichloromethane at -30°C under an atmosphere of nitrogen. The temperature of the reaction mixture was raised gradually to 35°C during 1 hour. After removal of the solvent, the resulting

residue was submitted to column chromatography on Silica gel. Oily compound (Va) was obtained in 58% yield from the benzene eluent as the sole product and assigned as 2- α,α -dimethylallyl-3-ethylthioindole on the basis of spectral data: NMR (in CDCl_3); δ 1.10 (3H, t, $J=8$ Hz, $-\text{CH}_2-\text{CH}_3$), 1.66 (6H, s, $-\text{C}(\text{CH}_3)_2-$), 2.73 (2H, q, $J=8$ Hz, $-\text{S}-\text{CH}_2-\text{CH}_3$), 5.13, 5.16 (2H, 2dd, $-\text{CH}=\text{CH}_2$, $J_{\text{cis}}=12$ Hz, $J_{\text{trans}}=16$ Hz, $J_{\text{gem}}=1.5$ Hz), 6.25 (1H, dd, $J=12$ and 16 Hz, $-\text{CH}=\text{CH}_2$), 7.0-7.8 (4H, m, aromatic protons), 8.2 (1H, br., NH). Similarly, the reaction of some other diallyl or alkylallylsulfides (IIb-e) afforded 2-allyl-3-alkylthio- or 2-allyl-3-allylthioindoles (Vb-e) in 40-60% yield, as shown in Scheme 1.



Scheme 1

II, III, IV, Va, $\text{R}=\text{R}'=\text{CH}_3$, $\text{R}''=\text{C}_2\text{H}_5$

b, $\text{R}=\text{CH}_3$, $\text{R}'=\text{H}$, $\text{R}''=\text{C}_2\text{H}_5$

c, $\text{R}=\text{CH}_3$, $\text{R}'=\text{H}$, $\text{R}''=\text{CH}_2-\text{CH}=\text{CHCH}_3$

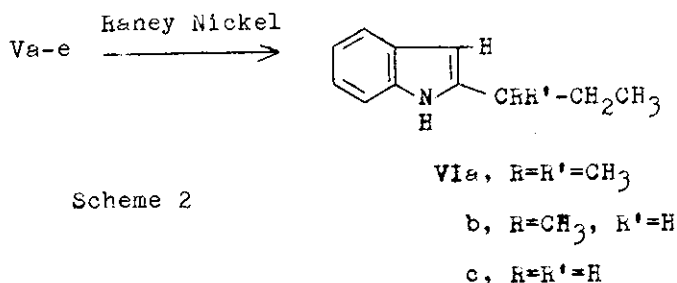
d, $\text{R}=\text{R}'=\text{H}$, $\text{R}''=\text{C}_2\text{H}_5$

e, $\text{R}=\text{R}'=\text{H}$, $\text{R}''=\text{CH}_2-\text{CH}=\text{CH}_2$

It is reasonable to consider that the compound (V) might be formed via sigmatropic rearrangement of the initially formed sulfonium salts (IV), since analogous sulfonium salts were isolated in the reaction of succinimido-dialkylsulfonium chlorides with indoles.¹⁾

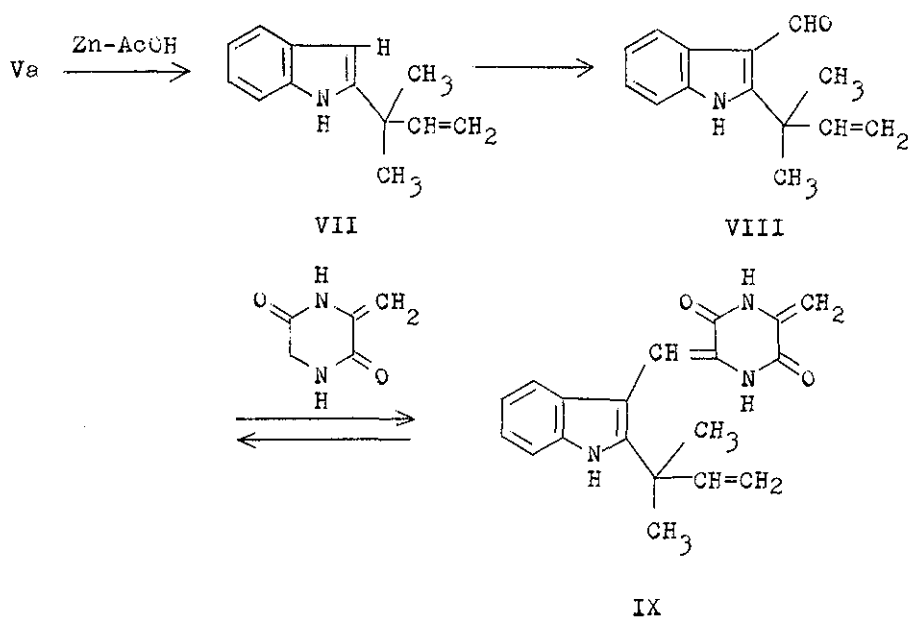
It seems attractive that the rearrangement proceeds with complete reversal of the allyl groups and no other products were obtained. Although many attempts concerning the introduction of allyl groups into the 2-position of the indole skeleton, especially α,α -dimethylallyl substituent, have been accumulated, in connection with the synthesis and biosynthesis of naturally occurring Echinulin series, the results have so far been almost failed.²⁾ Then reductive removal of the 3-substituents of the compounds (Va-e) were tried.

By the reduction of (Vd) with Raney-Nickel in ethanol at room temperature, 2-n-propylindole (VIc) was obtained in 85% yield; bp 120°C/1 mmHg, picrate mp 143°C, NMR (in CDCl₃); δ 0.95 (3H, t, J=7 Hz, -CH₂-CH₃), 1.70 (2H, sextet, J=7 Hz, -CH₂-CH₂-CH₃), 2.63 (2H, t, J=7 Hz, -CH₂-CH₂-), 6.20 (1H, d, J=2 Hz, β -H). Mass spectrum; m/e 159 (M⁺). Compounds (Va-c, e) also gave the 2-alkylindoles (VIa-c) in the same way. Scheme 2.



Scheme 2

On the other hand, when (Va) was treated with zinc powder in acetic acid at 60°C for 10 hrs, 2- α,α -dimethylallylindole (VII) was obtained in 61% yield: NMR (in CCl_4); δ 1.40 (6H, s, $-\text{C}(\text{CH}_3)_2-$), 5.00, 5.05 (2H, 2dd, $-\text{CH}=\text{CH}_2$, $J_{\text{cis}}=11$ Hz, $J_{\text{trans}}=17$ Hz, $J_{\text{gem}}=2$ Hz), 6.00 (1H, dd, $J=11$ and 17 Hz, $-\text{CH}=\text{CH}_2$), 6.9-7.8 (5H, m, aromatic protons and NH). Mass spectrum; m/e 185 (M^+). This is, we believe, the first practical synthesis of 2- α,α -dimethylallylindole from indole, which is an important intermediate for the synthesis of the natural products. Thus, (VII) was converted to the 3-formyl derivative (VIII), mp 186-187°C, by Vilsmeier reaction which had been connected with Neoechinulin B (IX).³⁾



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