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SYNTHESIS AND ALKALINE HYDROLYSIS OF 1,1-BIS(*N*-ACETYLINDOL-3-YL)ALKENES

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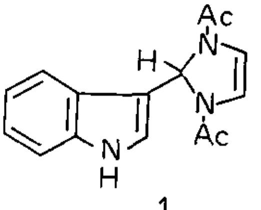
Abstract - 1,1-Bis(*N*-acetylindol-3-yl)alkenes are prepared by the reaction between indole and 2-alkyl-4,5-dihydrooxazoles/acetic anhydride in refluxing acetic anhydride. Alkaline hydrolysis of the products in ethanol/water resulted in a cleavage giving indole and a 3-acylindole. Only the 2-unsubstituted 1,1-bis(*N*-acetylindol-3-yl)alkene yielded the parent alkene.

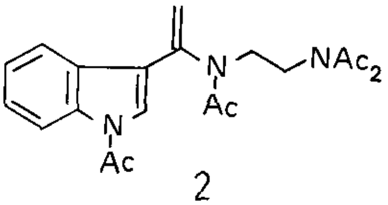
In some previous papers[1-3] we have shown that the reaction between 1,3-diazolium ions and reactive aromatic compounds (notably indoles), yields adducts such as 1, 2 and 3, which usually can be conveniently hydrolysed to the corresponding carbonyl compounds.

In an attempt to expand the scope of this synthesis, we have now studied the interaction of indole with a 2-alkyl-4,5-dihydrooxazole/acetic anhydride reagent, which yielded 1,1-bis(*N*-acetylindol-3-yl)alkenes (4), usually in crystalline form directly from the reaction mixture. Scheme 1 outlines the probable course of this reaction. In connection with these studies, it was also noted that direct acetylation of the reaction mixture obtained from acetyl chloride and 2-methylindole (containing 7, *cf.* refs 4 and 5) gave the monoacetylated alkene derivative 8 in 60% yield. The yields of 4a, 4b and 4c were in the range 70-90%.

Compound 4a was earlier obtained by Saxton[6] as a by-product (5-10 %) in connection with a synthesis of 1,3-diacetylindole. Saxton also noted that 4a could be readily hydrolysed to a product assigned the structure 5a, but later shown by Noland *et al.*[7] to be, in fact, the tautomer 6a. (For some further references to 1,1-di(3-indolyl)ethene derivatives, see ref. 5.) Recently 4a has also been obtained (66% yield) by treating tryptamine with hot acetic anhydride, acetic acid, and pyridine[8].



1



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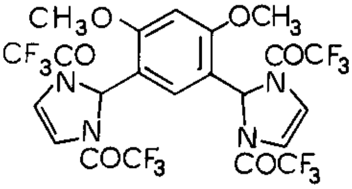

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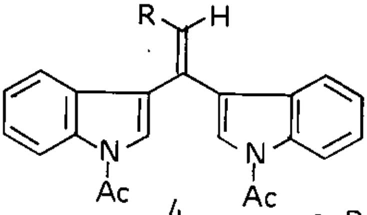
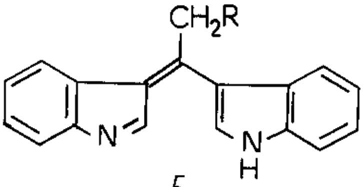


4

a R=H

b R=CH_3[9]

c R=C_2H_5[10]



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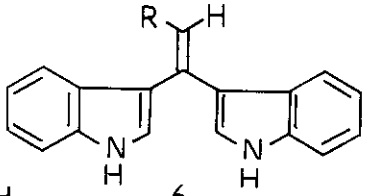
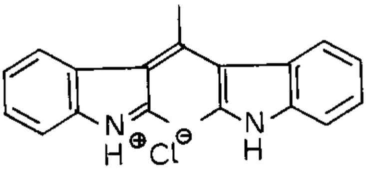


6

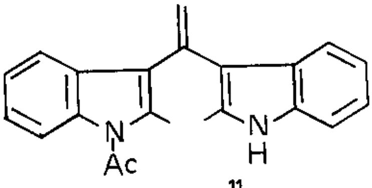
a R=H

b R=CH_3

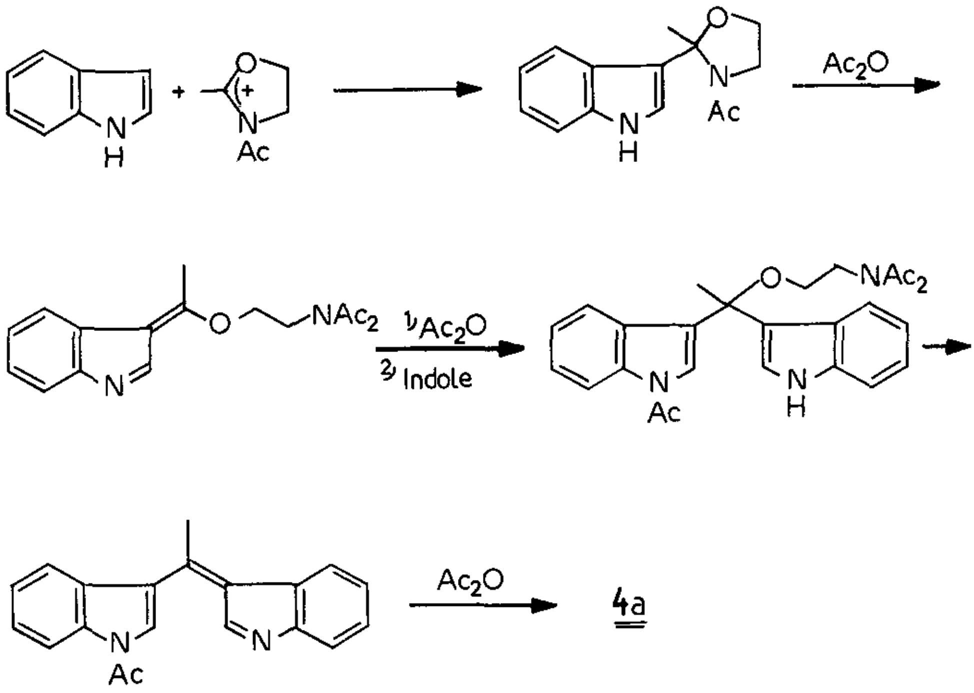
c R=C_2H_5



7

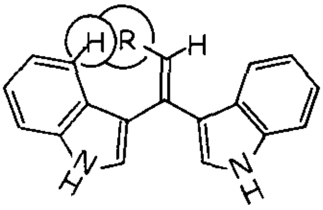


8[11]



Scheme 1

In agreement with the results reported by Saxton, compound 4a could readily be hydrolysed to 6a, which is inert to further hydrolysis. In dramatic contrast, the new compounds 4b and 4c were readily cleaved to indole and the appropriate 3-acylindole. The deacetylated compounds 6b and 6c could not be isolated even under very mild conditions. In explanation it is suggested that the tautomeric equilibrium 6 ⇄ 5 is forced to the indolenine side (5) in the cases of b and c due to severe steric interaction between the alkyl group and the hydrogen atom in the 2- or in the 4-position of the indole ring. The indolenine formed is then rapidly hydrolysed to the observed products (*cf.* refs 12 and 13).



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9. Compound **4b**, m.p. 254-256°C; MS *m/e* (% relative intensity): 357 (20), 356 (72), 315 (16), 314 (58), 273 (23), 272 (100), 271 (51), 258 (18), 257 (19), 256 (22) and 255 (12). Only peaks stronger than 10% of the base peak and above *m/e* 250 are given; ^{1}H NMR ($CDCl_3$, 200 MHz): δ= 1.88 (d, 3H, CH_3), 2.51, 2.59, 2.65 (s, 6H $COCH_3$), 6.54 (q, 1H, CH), 7.15-7.42 (m, 7H), 7.58 (dd, 1H) and 8.48 (dd, 2H).
10. Compound **4c**, m.p. 205-207°C; MS *m/e* (% relative intensity): 371 (27), 370 (100), 357 (16), 356 (54), 342 (25), 329 (17), 328 (59), 327 (14), 314 (53) and 313 (34). Only peaks stronger than 10% of the base peak and above *m/e* 300 are given; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.10 (t, 3H, CH_3), 2.26 (dq, 2H, CH_2), 2.48, 2.56, 2.64 (s, 6H $COCH_3$), 6.45 (t, 1H, CH), 7.14-7.42 (m, 7H), 7.61, 7.64 (1H) and 8.50 (d, 2H).
11. Compound **8**, m.p. 176-178°C; ^{1}H NMR ($DMSO_{d6}$, 200 MHz): δ = 2.22 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 2.70 (s, 3H, CH_3), 5.41 (d, $1H{=}\!<^{H_A)}_{H_B}$, 5.67 (d, $1H{=}\!<^{H_A)}_{H_B}$ 6.9-7.4 (m, 7H), 8.15 (d, 1H); J_{AB} = 1.95 Hz.
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