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REARRANGEMENT OF A QUINOLIZIDINE TO PYRROLO-AZEPINE BY EXPANSION-CONTRACTION OF CYCLES. SYNTHESIS OF 2-ACYL-INDOLE

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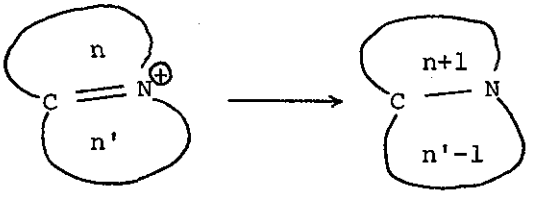
Bromination of 1-ethyl hexahydro indolo [2,3 a] quinolizidine followed by basic hydrolysis leads to a rearrangement giving a pyrrolo-azepine.

The bromination of heterocyclic enamines gives rise to rearrangements permitting either expansions[1] or contractions[2] depending on the specific case.

An examination of the mechanism of these rearrangements shows that by carefully selecting a bicyclic enamine, one can, by simple bromination, produce contraction and expansion of the cycles simultaneously. To achieve this result, it is necessary for the intermediate immonium to be formed at the junction of the two cycles (Scheme 1)



Scheme 1

Such was the case with the enamine 1[3], whose nucleophilic properties have been used in the synthesis of alkaloids of the vincamine[3,4] type. Thus, the bromination of 1 in THF at -60° C gives an immonium salt 2 which precipitates in the medium (Scheme 2). Treatment of the reaction with aqueous NaOH then produces the compound 3a[5] isolated with a yield of 60%.

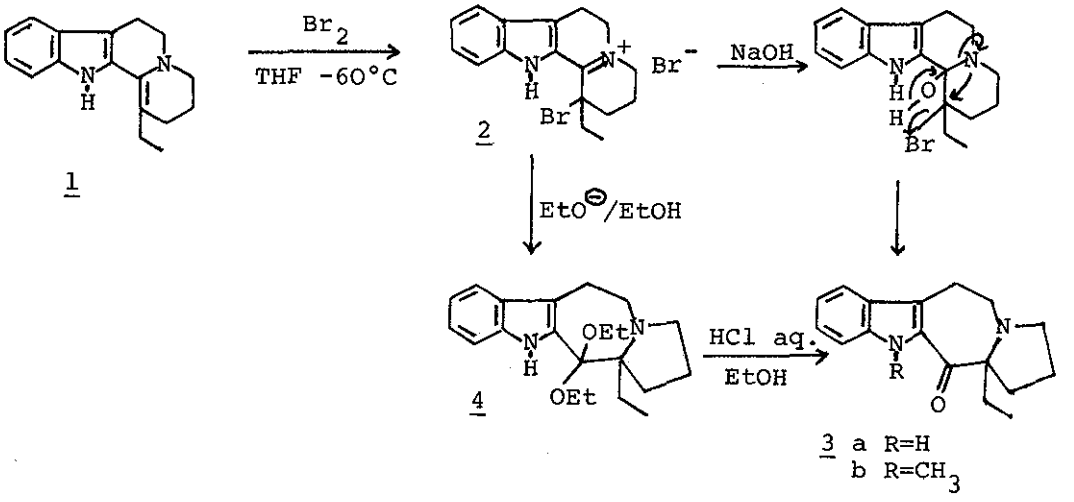
3a : mp = 170° C, IR (KBr)ν: 3310, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.3 (1H, s, NH indole), 7.2 (4H, m, aromatic protons), 3.5 (4H, m, CH_2), 3 (2H, m, CH_2), 2 (6H, m, CH_2), 0.9 (3H, t, CH_3); ^{13}C-NMR (DMSO d_6)[6] δ 8.28 ($-CH_3$), 20.8, 24, 27.9, 33.5, 42.8, 47.9 ($-CH_2-$), 74.5 ($\dot{C}-$), 113.4, 120, 121.6, 122, 126.7, 127.5, 132.9, 137.8 (=CH indole), 203 (C=O); MS m/e : 284 (M^+), 237, 227, 199 (100%), 143.

The immonium salt 2 is converted, in situ, in acetal 4 by the action of sodium ethylate in ethanol. Acidic hydrolysis of 4 again gives the compound 3a.

4 : Oil. IR (neat)ν: 3470, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.5 (1H, s, NH indole), 7.2 (4H, m, aromatic protons), 3.2 (10H, m, CH_2), 1.6 (6H, m, CH_2), 1 (9H, m, CH_3).

The compound 3a is an acyl indole, whose ketone carbon clearly appears in the ^{13}C-NMR spectrum. Moreover, the alkylation of 3a (tBuOK-HMPT; CH_3I) leads to a new compound 3b, whose ketone band appears in a normal position in ir spectrum.

3b : Oil. IR (neat) : 1650 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 7.3 (4H, m, aromatic protons), 3.85 (3H, s, $N-CH_3$), 3.5 (4H, m, CH_2), 3 (2H, m, CH_2), 1.8 (6H, m, CH_2), 0.9 (3H, t, CH_3).



Scheme 2

The application of this reaction to the synthesis of alkaloids possessing a pyrrolo-azepine pattern is under investigation.

REFERENCES AND NOTES

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5. The intermediate formation of an analogue of 3a was recently postulated without isolation of the product : G. Costa, C. Riche and J.P. Husson, Tetrahedron, 1977, 33, 315.
6. The δ are given in ppm in relations to TMS. δ TMS = δ (DMSO d_6)+39.5ppm.

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