

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

André Buzas* and Catherine Retourné

Laboratoire de Synthèse Organique, U.E.R. Sciences,
45100 Orléans-La Source

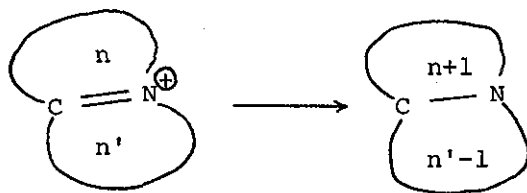
Jean-Pierre Jacquet and Gilbert Lavielle

Laboratoires Sauba, 260 rue de Rosny, 93104,
Montreuil-Sous-Bois

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 expansions¹ or
contractions² depending on the specific case.

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



Scheme 1

Such was the case with the enamine 1³, 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 3a⁵ isolated with a yield of 60%.

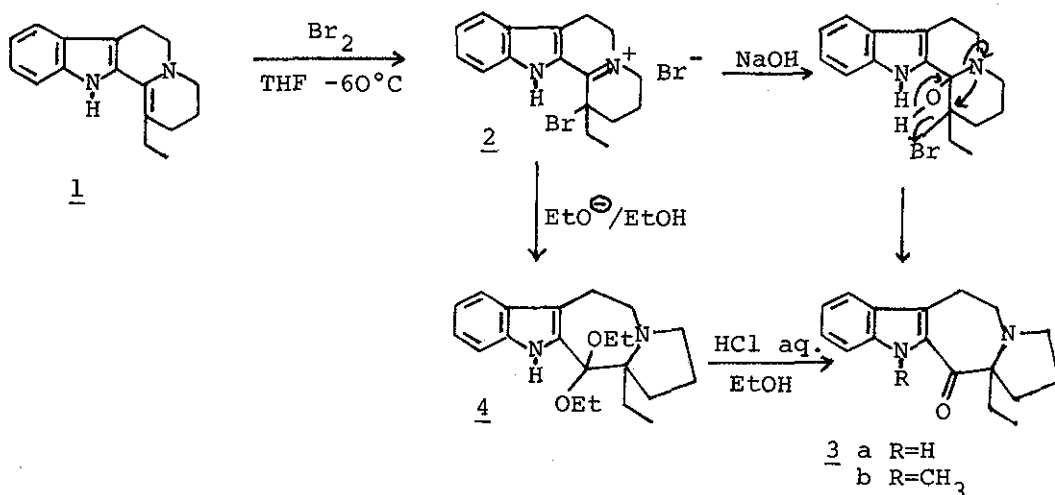
3a : mp = 170° C, IR (KBr) $\bar{\nu}$: 3310, 1610 cm⁻¹; ¹H NMR (CDCl₃) δ 8.3 (1H, s, NH indole), 7.2 (4H, m, aromatic protons), 3.5 (4H, m, CH₂), 3 (2H, m, CH₂), 2 (6H, m, CH₂), 0.9 (3H, t, CH₃); ¹³C-NMR (DMSO d₆)⁶ δ 8.28 (-CH₃), 20.8, 24, 27.9, 33.5, 42.8, 47.9 (-CH₂-), 74.5 ($\overset{|}{\text{C}}^-$), 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) $\bar{\nu}$: 3470, 1620 cm⁻¹; ¹H NMR (CDCl₃) δ 8.5 (1H, s, NH indole), 7.2 (4H, m, aromatic protons), 3.2 (10H, m, CH₂), 1.6 (6H, m, CH₂), 1 (9H, m, CH₃).

The compound 3a is an acyl indole, whose ketone carbon clearly appears in the ¹³C-NMR spectrum. Moreover, the alkylation of 3a (tBuOK-HMPT; CH₃I) 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

1. M. Takeda, H. Inoue, M. Konda and H. Kugita, J. Org. Chem., 1972, 37, 2677.
2. L. Duhamel and J.M. Poirier, Tetrahedron Letters, 1976, 2437.
3. E. Wenkert and B. Wickberg, J. Amer. Chem. Soc., 1962, 84, 4914.
4. a) M.C. Thal, T. Sevenet, H.P. Husson and P. Potier, C.R. Acad. Sci., 1972, 275C, 1295; b) Cs. Szantay, L. Szabo and G. Kalas, Tetrahedron Letters, 1973, 191; c) A. Buzas, C. Herisson and G. Lavielle, C.R. Acad. Sci., 1976, 283C, 763.

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.
 $\delta \text{ TMS} = \delta (\text{DMSO } d_6) + 39.5 \text{ ppm.}$

Received, 1st June, 1977