

UNUSUAL FRAGMENTATIONS UNDER POLONOVSKI REACTION CONDITIONS

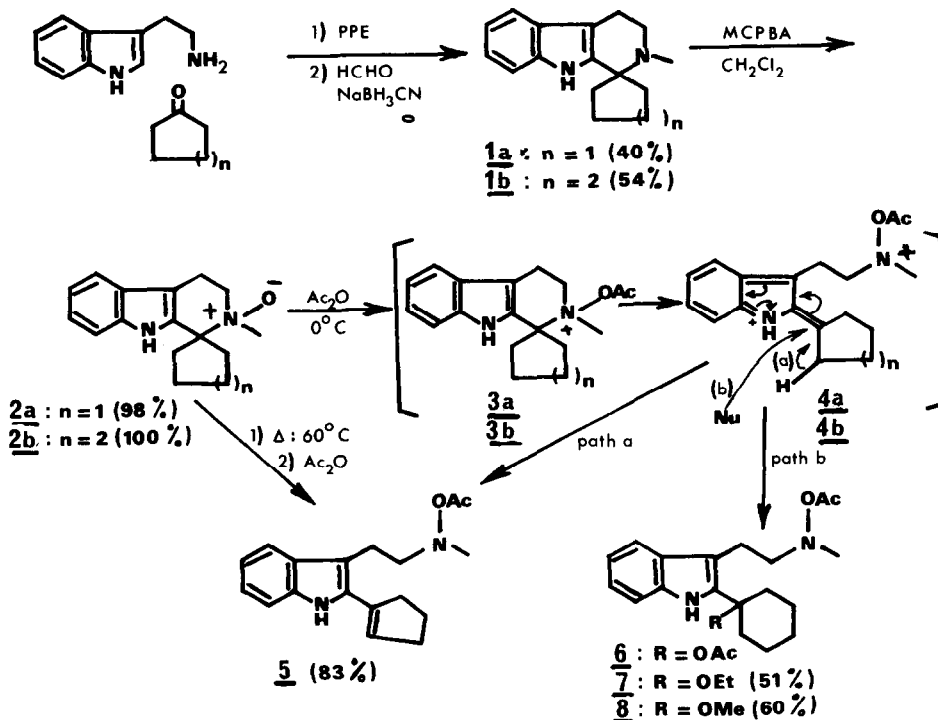
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Abstract : N_D -oxides 2a and 2b in the presence of acetic anhydride led to products 5, 7 or 8 with participation of the indole nucleus during the fragmentation reaction.

In connection with research oriented toward the total synthesis of indole alkaloids, we were interested to test the behaviour of tetrahydro- β -carboline N_D -oxides 2a or 2b under the POLONOVSKI reaction condition¹.

Compounds 1a and 1b have been prepared by the usual PICTET-SPINGLER cyclisation² followed by the N_D -methylation³ of the resulting spiro compounds (Scheme).



SCHEME

The corresponding N_b -oxides 2a and 2b when subjected to POLONOVSKI reaction conditions ($Ac_2O - CH_2Cl_2 - 0^\circ C$) led to two neutral products which could be isolated without sodium borohydride reduction :

- The Nb-oxide 2a gave rise to compound 5 which showed in u.v. a typical conjugated indole chromophore. Compound 5 was also obtained by an independent pathway from the N_b -oxide 2a via a COPE fragmentation, followed by acetylation.

- On the other hand, the N_b -oxide 2b, under POLONOVSKI condition, gave rise to the indole 7 after extraction with chloroform stabilized with ethanol (0.5 %). If the reaction medium was treated with anhydrous methanol the corresponding methoxy derivative 8 was obtained (Scheme).

The formation of compounds 5, and 7 or 8 can be rationalized by a fragmentation reaction involving the participation of the indole nucleus. This type of reaction is reminiscent of gramine fragmentation but is unknown under POLONOVSKI reaction condition ¹ in which the N_b -acetoxy of the acetoxy-ammonium intermediates 3a or 3b acts usually as a leaving group.

The difference of behaviour between the cyclopentane and cyclohexane derivatives 2a and 2b is worthy of note :

The immonium intermediate 4a led to the vinyl indole 5 by proton elimination (path a), whereas, under the same condition, the immonium salt 4b was submitted to nucleophilic attack leading to compounds 7 or 8 probably via the acetate intermediate 6 (path b).

In the presence of trifluoroacetic anhydride (POLONOVSKI-POTIER reaction) ¹, the N_b -oxides 2a and 2b were unreactive between $- 30^\circ C$ and $0^\circ C$. At higher temperature no well defined compounds have been isolated. The presence of nucleophilic species like acetoxy ions are probably necessary to induce the fragmentation reaction ⁴.

The same type of reaction with more strained indole derivatives in the spiro cyclobutane series is currently under investigation in our laboratory.

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Reference :

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