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1,3- AND 1,4- SHIFTS OF A METHYL GROUP DURING FISCHER INDOLE SYNTHESIS

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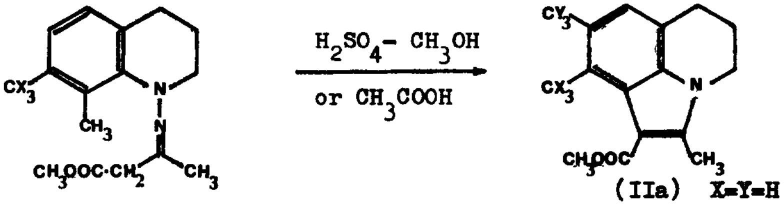
In a previous paper(1) we described an example of a 1,3- alkyl group shift occurring during a Fischer indole synthesis. We have now observed an analogous migration of a methyl group during indolization of the hydrazone (Ia), which gave the indole compound (IIa) (80% yield), the structure of which has been confirmed by independent synthesis(2).



(Ia) X=H
(Ib) X=D

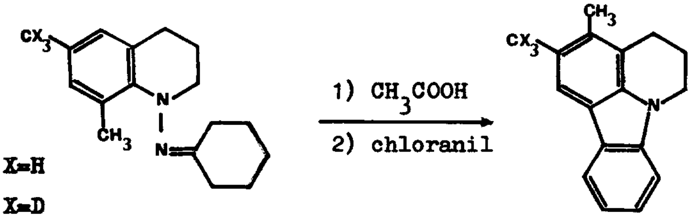
(IIa) X=Y=H
(IIb) X=H Y=D
(IIc) X=D Y=H

In order to distinguish whether the mechanism of this rearrangement is a sigmatropic 1,3- shift or the result of two subsequent 1,2- methyl group shifts, we repeated the same reaction on the deuterium labelled hydrazone (Ib)(3).

The p.m.r. spectrum (CS_2) of the reaction product revealed the presence of both the indole derivatives (IIb) and (IIc) in about 1:1 ratio; in fact, two signals (7.62 and 7.75τ, each about 1.5 H) related to both the methyl groups on the benzene ring in (IIb) and (IIc) were present.

This result is clearly consistent only with a reaction mechanism involving a double 1,2- shift of the methyl group.

We also succeeded in demonstrating the second case(4) in chemical literature of a 1,4- methyl group shift, during our study on the Fischer rearrangement of the hydrazone (IIIa). Besides some other products, the reaction afforded the compound (IVa), the structure of which was proved through its independent synthesis(5).



(IIIa) X=H
(IIIb) X=D

(IVa) X=H
(IVb) X=D

On repeating the same reaction sequence on the labelled hydrazone (IIIb)(6), we obtained only the carbazole (IVb); the p.m.r. spectrum (CS_2, only one signal for a methyl group at 7.35τ, 3 H) excluded the presence of the isomer having the methyl and the trideuteromethyl groups in inverted positions(7).

This fact demonstrated that this 1,4- migration is not the result of three subsequent 1,2- methyl group shifts, as other Authors have suggested(8).

We are forced to admit that this migration does not involve the formation of σ bonds between the migrating group and other carbon atoms of the ring at the level of reaction intermediates.

The experimental evidence about this 1,4- alkyl group migration on an aromatic ring, which is an extremely rare reaction in organic chemistry, is consistent with the hypothesis of a transition state with the migrating methyl halfway between the 1 and 4 carbon atoms of a boat cyclohexadiene system, in agreement with Carlin's hypothesis.

REFERENCES AND NOTES

1) R.Fusco and F.Sannicolò, Gazz.Chim.Ital., 103, 197(1973).
2) Synthesis was achieved starting from 1,2,3,4-tetrahydro-6,7-dimethyl quinoline through a standard reaction sequence; see reference 1.
3) 2-Methyl-3-trideuteromethyl aniline, starting material for the synthesis of (Ib), was prepared by reducing methyl 2-methyl-3-amino benzoate with $LiAlD_4$, followed by conversion of the resulting benzyl alcohol into the corresponding bromide with 48% HBr and its subsequent reduction with DCl in D_2O solution.
4) The first example has been reported by R.B.Carlin and M.S.Moores (J.Amer.Chem. Soc., 84, 4107(1962)) in the case of the mesithylhydrazone of cyclohexanone.
5) Synthesis of (IVa) started from 1,2,3,4-tetrahydro-5,6-dimethyl quinoline, obtained by reduction with H_2 and 10% Pd/C of 5,6-dimethyl-8-chloro quinoline.
6) 2-Methyl-4-trideuteromethyl aniline, starting material for the synthesis of (IIIb), was prepared by reacting methyl 3-methyl-4-amino benzoate with $LiAlD_4$ at 130° in diglyme solution.
7) In this case a signal at 7.64τ should have been present.
8) M.J.S.Dewar, "Molecular rearrangements" by P.de Mayo, Interscience, I, 305(1963).