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BEHAVIOUR OF 2,6-DISUBSTITUTED ARYLHYDRAZIDES WITH PHOSPHORUS PENTACHLORIDE

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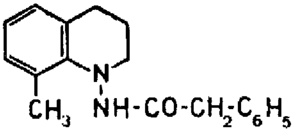
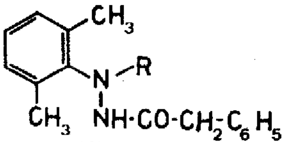
In the course of our previous research in the field of the Fischer rearrangement of 2,6-disubstituted arylhydrazones several reaction paths have been outlined: the simple(1) or the double(2) 1,2-shift, the 1,4-shift(3) and the loss(4) of an ortho substituent.

We then planned a few experiments to verify whether analogous phenomena could take place during the Kost synthesis of 2-aminoindoles(5) starting from N-acylderivatives of 2,6-disubstituted arylhydrazines.

Our current results show a completely different course for this reaction; the present paper reports a preliminary account of our observations on reacting the hydrazides (I) and (II) with PCl$_5$ (1:1 molar ratio) in refluxing benzene solution for two hours.


(I)

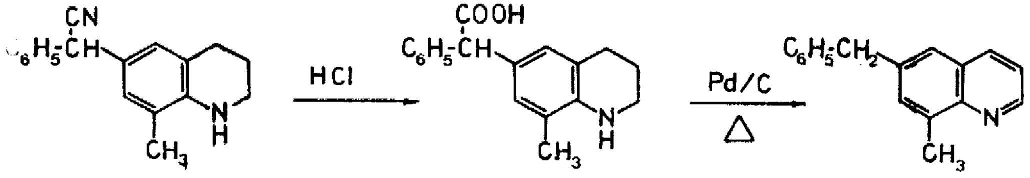

(II)

In the case of the hydrazide (I) (m.p. = 180°C from benzene), two products were isolated in fairly good yield after chromatography: an oily base (A) (b.p. = 226°C at 0.2 Torr; yield = 57%) and a less basic solid (B) (m.p. = 97°C; yield = 10%).

The structure of an α-cyanobenzyl-8-methyl-1,2,3,4-tetrahydroquinoline was assigned to (A) on the basis of its spectroscopic and analytic data. MW (mass spectroscopy) = 262. IR (film): ν_{NH} = 3448 and ν_{CN} = 2247 cm^{-1}. PMR (CDCl$_3$)(6): 2.68 (5H, m, C$_6$H$_5$); 3.20 (2H, s, aromatic on the tetrahydroquinoline ring); 5.05 (1H, s, C$_6$H$_5$-C$\underline{H}$-CN); 6.55 (1H, broad s exchangeable with D$_2$O, NH); 6.64 (2H, t, N - CH$_2$); 8.0 (5H, m with a s emerging at 7.96, CH$_2$ on saturated carbons and CH$_3$); 7.25 (2H, t, benzylic).

The hydrolysis of (A) in 20% hydrochloric acid solution at reflux for 24 hours gave the corresponding carboxylic acid; m.p. = 148°C. IR (nujol): ν_{NH} = 3333 and ν_{CO} = 1701 cm^{-1}. PMR ($CDCl_3$): 2.78 (7H, m with a s, exchangeable with D_2O, emerging at 7.85, C_6H_5 and NH - COOH); 3.23 (2H, s, aromatic on the tetrahydroquinoline ring); 5.16 (1H, s, C_6H_5-C$\underline{H}$-COOH); 6.68 (2H, t, N-CH_2); 7.29 (2H, t, benzylic); 8.1 (5H, m with a s emerging at 7.99, CH_2 on saturated carbons and CH_3). This acid easily underwent simultaneous decarboxylation and aromatization by three hour reflux in a xylene solution in the presence of 10% Pd on charcoal, giving a benzyl-8-methylquinoline (b.p. = 163°C at 0.3 Torr). PMR (CCl_4): 1.60 and 2.15 (each 1H, 2dd, aromatic in position 2 and 4 of the quinoline ring); 2.8 (8H, m, aromatic); 5.98 (2H, s, CH_2); and 7.28 (3H, s, CH_3).

In order to clarify the position of the benzyl group, we have synthesized the three possible benzylsubstituted 8-methylquinolines. We found that the 6-benzyl-8-methylquinoline(°) was identical to the sample resulting from (A) through the reaction sequence described before. On this basis structure (III) must be assigned to product (A).



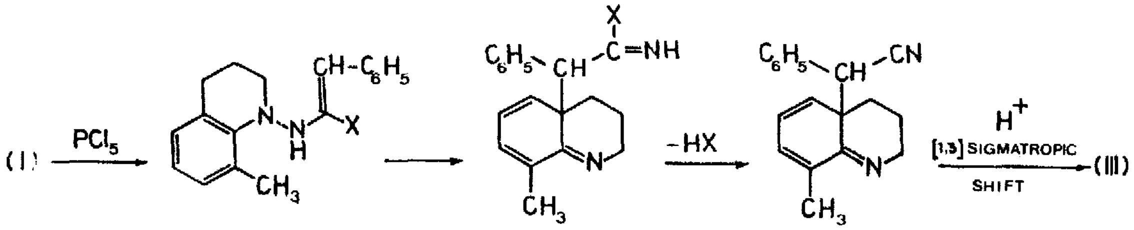
(III) (IV) (V)

(°) The 6-benzyl-8-methylquinoline was synthesized through the following reaction sequence, starting from the known 3-methyl-4-nitrobenzophenone; its reduction with $NaBH_4$ afforded an oily carbinol easily converted into the corresponding benzhydryl chloride with PCl_5 (b.p. = 155-160°C at 0.1 Torr.); the reaction of the latter with morpholine gave the N-(3-methyl-4-nitrobenzhydryl)morpholine (m.p. = 100°C) which was hydrogenated over Pd on charcoal to yield the 3-methyl-4-amino-diphenyl methane (m.p. = 58°C). The Skraup quinoline synthesis on the latter yielded (V). By an analogous reaction scheme the two other benzyl-8-methylquinolines were synthesized.

The PMR spectrum of the product (B), which is an isomer of (A) [MW (mass spectroscopy) = 262], is consistent with a diastereoisomeric mixture of the cyclohexadienoneimine (VI). PMR ($CDCl_3$): 2.5 (5H, m, C_6H_5); 3.0 (3H, m, aromatic); 4.48 (1H, s, C_6H_5-$C\underline{H}$-CN); 6.9 (2H, m resulting from the superimposition of 2 t, N-CH_2 of two diastereoisomers); 7.25 (2H, t, CH_2 in position 4 of the nitrogenated ring); 7.61 (3H, s, CH_3); 7.75 and 8.4 (2H, 2m, CH_2 in position 3 of the nitrogenated ring of two diastereoisomers).

By refluxing (B) with a 48% HBr solution the same aminoacid (IV) we had previously obtained from the hydrolysis of (A) was isolated.

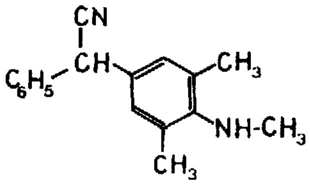
The mechanism which can be put forward for the origin of (A) and (B) from (I) is somewhat similar, at least in its initial steps, to the one which governs the formation of aminoindoles in the Kost synthesis, as summarized in the following scheme:



X = Cl, OPOCl$_2$ (VI)

The 2,6-dimethyl-phenylhydrazide of the phenylacetic acid (II, R = H) (m.p. = 135°C from diisopropylether) did not react with PCl_5 even under severe conditions (130°C without solvent), while the corresponding N'-methyl derivative (II, R = CH_3) (m.p. = 144°C from benzene) reacts more easily, yielding the 3,5-dimethyl-4-methylamino-benzhydrylcyanide (VII) as the only isolable product (b.p. = 175°C at 1 Torr). IR (film): ν_{NH} = 3390 and ν_{CN} = 2294 cm^{-1}. PMR (CCl_4): 2.83 (5H, m, C_6H_5); 3.21 (2H, s, aromatic); 5.18 (1H, s, C_6H_5-$C\underline{H}$-CN); 6.42 (1H, broad s exchangeable with D_2O, NH); 7.34 (3H, s, N-CH_3); 7.86 (6H, s, 2 CH_3).

The base (VII) arises from a cyclohexadienone intermediate analogous to (VI).



(VII)

A [1,3] sigmatropic shift of a benzyl group during the acid catalyzed rearrangement of a cyclohexadienone derivative has been recently reported(7).

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6) Chemical shifts are given in τ (TMS as internal standard) and refer to the centre of the signal; accuracy is about ± 0.03τ. s = singlet; d = doublet; t = triplet; m = multiplet; dd = doublet of doublets.

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