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STUDIES ON THE FISCHER INDOLE SYNTHESIS. VI

TWO EXAMPLES OF 1, 5 - SHIFT OF A METHYL GROUP

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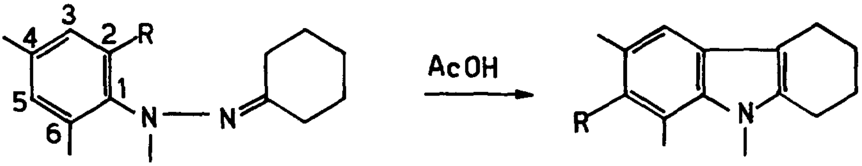
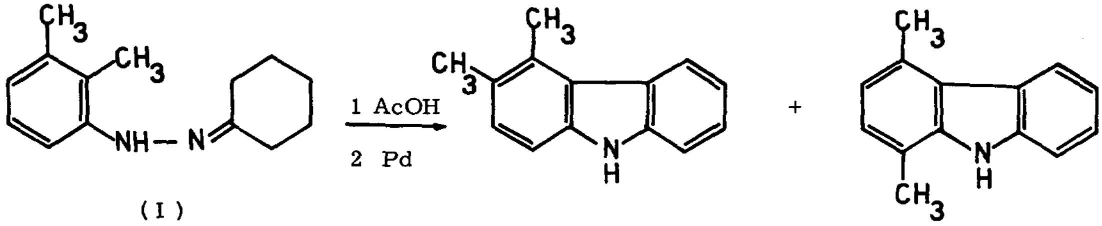
2, 6-Alkyldisubstituted phenylhydrazones undergo Fischer indolization either with loss (1) or simple (2) or double (3) 1, 2-shift of an alkyl group:in few cases an apparent 1, 4-shift of an alkyl substituent has been observed (4). We demonstrated that this last unusual migration does not develop along carbon atoms 3 and 4 of the ring (5), as it was previously believed: more recently Miller further suggested a triple 1, 2-shift in the opposite direction through the positions 1 and 6 (6).



We report in this paper results on the indolization of 2, 3-dimethyl and 2, 5-dimethyl phenylhydrazones of cyclohexanone (I) and (II), substrates we have chosen in consideration that "ortho" monosubstituted phenylhydrazones are known to give indoles resulting from attack to both the "ortho" position (7) and in our case the study of the structure of the indolization products was expected to shed some light on the mechanism of the apparent alkyl group 1, 4- migration.

After short refluxing in acetic acid solution, hydrazones (I) and (II) gave 1, 2 - and 1, 4-dimethyl-tetrahydrocarbazoles respectively, by far the predominant products, resulting from the expected attack to the "ortho" unsubstituted position:however, the mixture showed clear evidence for the formation of tetrahydrocarbazoles arising from the attack to the other "ortho" position carrying the methyl group. Careful chromatography, fractional crystallization and distillation of tetrahydrocarbazoles and carbazoles allowed us to obtain partial separation of each single side product and we have been able to identify them by comparative VPC and PMR (8) with authentic samples.

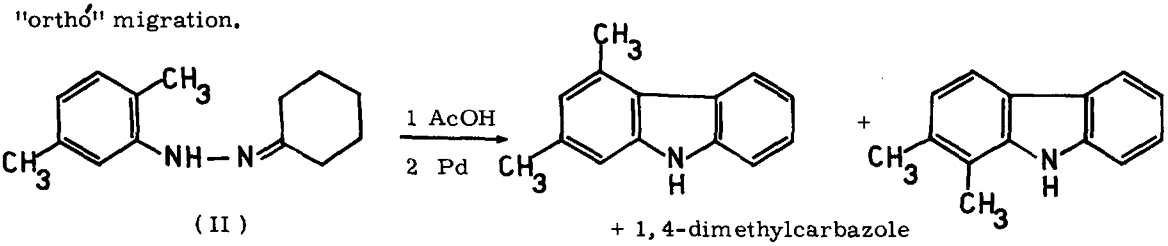
The side products from the indolization of hydrazone (I) were the 3, 4-dimethylcarbazole, resulting from a double 1, 2-shift of the methyl group and the 1, 4-dimethylcarbazole, arising from migration of the methyl group from an "ortho" to the other "ortho" position.



(I)

+ 1, 2-dimethylcarbazole

Hydrazone (II) analogously gave the 2, 4-dimethylcarbazole, arising from the 1, 2-shift of the methyl group, and the 1, 2-dimethylcarbazole, resulting again from an "ortho"-"ortho'" migration.



(II)

+ 1, 4-dimethylcarbazole

In order to explain this "ortho"-"ortho'" shift, two alternative reaction mechanisms can be considered: a [1, 5] sigmatropic shift(9) and a double 1, 2-shift of the methyl group. The latter should affect position 1 of the aromatic ring in agreement with Miller's hypothesis for the apparent 1, 4-alkyl group migration. At this stage, it does not seem easy however to devise experiments which would discriminate between these mechanistic possibilities.

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8) PMR spectra were recorded on a Varian ass. HA 100 D spectrometer. Table below reports the chemical shifts (δ, TMS) of the methyl groups of dimethylcarbazoles in 10% (w/v) C_6D_6 solution (except for the scarcely soluble 2, 3-dimethylcarbazole).

Dimethylcarbazoles		1, 2	1, 3	1, 4	2, 3	2, 4	3, 4
CH_3 position	1	1.93	2.06	2.09			
	2	2.27			2.30	2.41	
	3		2.39		2.30		2.33
	4			2.71		2.66	2.59

9) This possibility was apparently not considered by Miller (loc. cit.).

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