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A NEW REARRANGEMENT OF ARYLHYDRAZONES OF AROMATIC ALDEHYDES AND DIARYLKETONES

R. Fusco and F. Sannicolo'
Istituto di Chimica Industriale dell'Universita'
CNR Centro di studio sulla sintesi e stereochimica di speciali sistemi organici
Via Golgi, 19 - 20133 Milano

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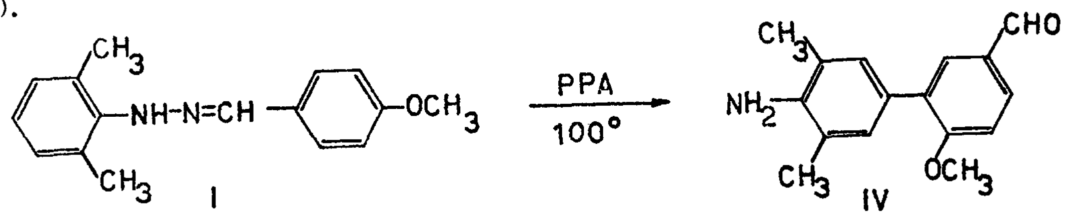
Within the framework of our research on the Fischer indole synthesis[1], we decided to verify the behaviour of non-indolizable arylhydrazones, like those arising from aromatic aldehydes and diarylketones, with Lewis acids.

This preliminary account summarizes the results of an investigation on the reaction with polyphosphoric acid (PPA) of 2,6-dimethylphenylhydrazones of 4-methoxybenzaldehyde (I), 4,4'-dimethoxybenzophenone (II) and fluorenone (III).

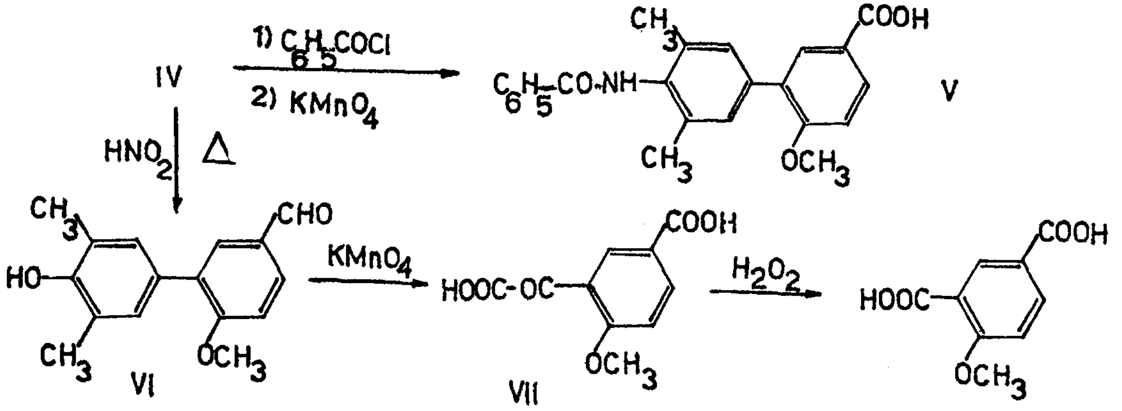
We have been able to demonstrate that all these substrates undergo a completely new kind of rearrangement.

The 2,6-dimethyl-phenylhydrazone of anisaldehyde (I) (m.p.=50°C from iso-propylalcohol) was heated at 100°C for 30 minutes with PPA (ten times its weight) with vigorous stirring. The basic products, (extracted with $CHCl_3$ after addition to water and correction of the pH to 6 with ammonium hydroxide) were chromatographed on a silica gel column to give a viscous oily substance (yield=35%), to which the structure of 4-amino-3'-formyl-6'-methoxy-3,5-dimethylbiphenyl (IV) was assigned. NMR[2]: 0.48 (1H, s, CHO); 2.3 and 3.0 (2H and 3H respectively, 2m, aromatic); 6.16 (3H, s, OCH_3); 6.5 (2H, broad s exchangeable with D_2O, NH_2); 7.80 (6H, s, $2CH_3$); p-nitrophenylhydrazone : m.p. = 226°C (iso-propylalcohol).



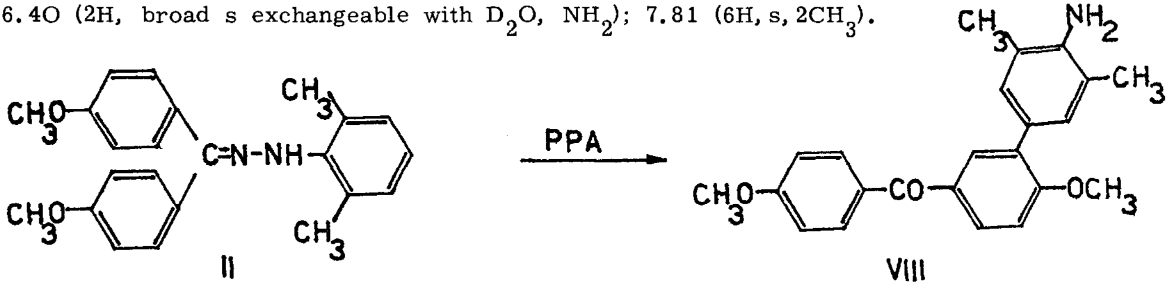
The benzoyl derivative of (IV) (m.p.=221°C from benzene) gave upon oxidation with $KMnO_4$ in a water-acetic acid solution a benzoyl-aminoacid (V) (m.p. : above 250°C from acetic acid).

Thermal decomposition of the diazocompound obtained from (IV) afforded a phenolic aldehyde (VI) (p-nitrophenylhydrazone: m.p.=219°C from acetic acid), which was oxidized with alkaline $KMnO_4$ at 60°C, to give 2-methoxy-5-carboxyphenylglyoxylic acid (VIII): m.p.=130°C dec. from dioxane (p-nitrophenylhydrazone : m.p. = above 260°C from acetic acid). The latter could be oxidized in turn to 4-methyoxyisophthalic acid[3] with H_2O_2 in alkali.

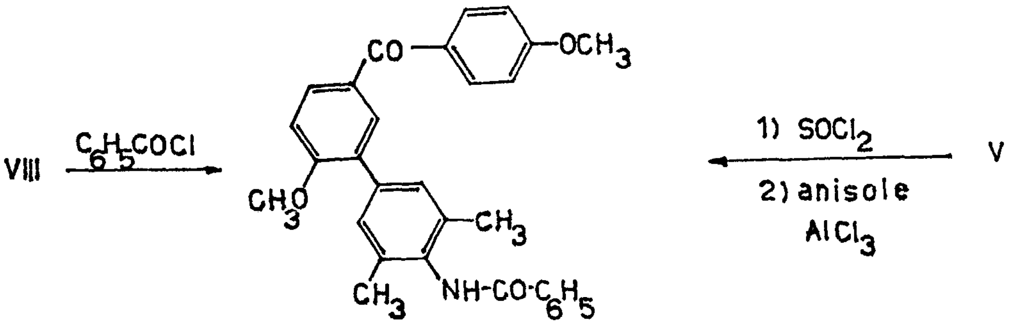


This shows that the attack occurred in position "ortho" to the methoxy group; furthermore the coincidence in the NMR spectrum of (IV) of the methyl group signals and the equivalence of the aromatic hydrogens of the dimethylanilino group indicate that the latter has a substituent para to the nitrogen atom.

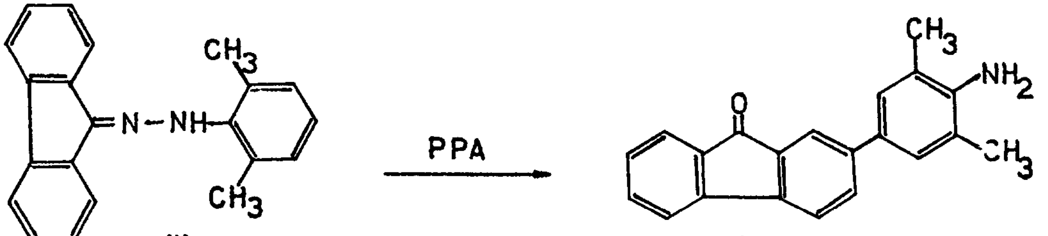
Analogous treatment of the <u>2,6-dimethylphenylhydrazone of 4,4'-dimethoxybenzophenone</u> (II) with PPA gave <u>4,4'-dimethoxy-3-(4-amino-3,5-dimethylphenyl)benzophenone</u> (VIII): m.p. =148-9°C. NMR: 2.3 and 3.0 (4 and 5H respectively, 2m, aromatic); 6.18 (6H, s, $2OCH_3$); 6.40 (2H, broad s exchangeable with D_2O, NH_2); 7.81 (6H, s, $2CH_3$).



This structural assignment was confirmed by the synthesis of the benzoyl derivative of (VIII) (m.p. = 215°C from benzene) starting from the benzoyl-amino-acid (V), through the condensation of the corresponding acylchloride with anisole in the presence of $AlCl_3$.



The rearrangement of the 2, 6-dimethylphenylhydrazone of fluorenone (III) in PPA gave a red product (m.p. = 152°C from iso-propylalcohol), to which the structure of 2-(4-amino-3, 5-dimethylphenyl) fluorenone (IX) was assigned on the basis of analytical and spectral data. NMR: 2.5 (9H, m, aromatic); 6.32 (2H, broad s exchangeable with D_2O, NH_2); 7.78 (2H, s, $2CH_3$).

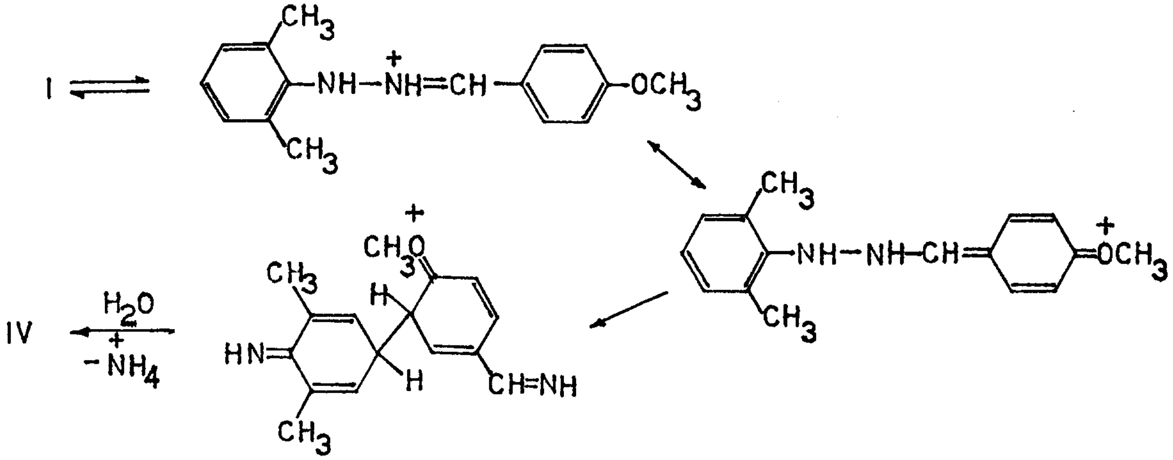


III

IX

The position of attack of the dimethylanilino group to the fluorenone system was confirmed by oxidation of (IX) with $KMnO_4$ in dilute acetic acid, which afforded fluorenone-2-carboxylic acid, already known in literature[4]. The identity of this acid and the methyl ester was confirmed by comparison with authentic samples[4, 5]. In this case also, the NMR spectrum of (IX) (only one signal for both the methyl groups) showed that the fluorenone residue was located para to the amino group.

The reaction mechanism we propose for this new reaction involves a [5,5] sigmatropic rearrangement of the protonated arylhydrazones; for example:



This reaction, for which we have given only a few examples, seems to be of general applicability: research is in progress in order to ascertain its scope and to clarify the influence of the nature and position of substituents on its course.

REFERENCES AND NOTES

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105, 465, 1105 (1975); 106, 85 (1976).
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2) Chemical shifts are given in τ (TMS as internal standard and $CDCl_3$ as solvent) and refer to the centre of the signal. s=singlet, m=multiplet; accuracy is about ± 0.03 τ.

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all new products gave correct elemental analyses.