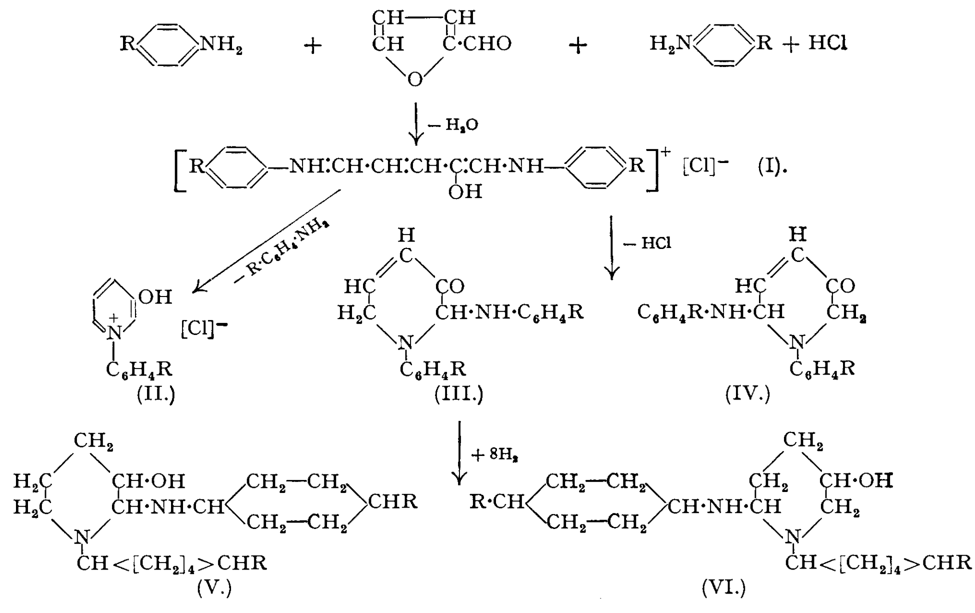
165. *The Preparation of Bases from the Coloured Compounds formed by Condensation of Furfuraldehyde with Aromatic Amines.*

By J. C. McGowan.

Crystalline compounds have been prepared by the action of sodium hydroxide on the coloured condensation products from aniline or *p*-toluidine with furfuraldehyde and hydrochloric acid. These compounds which are almost colourless are reconverted into the coloured compounds by mineral acids. They form monoacetates, contain a reactive methylene group, and have been catalytically reduced with the uptake of 8 mols. of hydrogen. Their reactions seem to indicate one of the formulæ (III) or (IV).

In 1870, Stenhouse (*Annalen*, **156**, 197) found that aniline, aniline hydrochloride, and furfuraldehyde reacted together to form a deep purple compound. Since then this type of compound has been the subject of a number of investigations (Schiff, *Annalen*, 1880, **201**, 356; 1887, **239**, 349; König, *J. pr. Chem.*, 1905, **72**, 555; Dieckmann and Beck, *Ber.*, 1905, **38**, 4122; Riegel and Hathaway, *J. Amer. Chem. Soc.*, 1941, **63**, 1835; Williams and Wilson, *J.*, 1942, 506) and evidence has steadily accumulated in favour of formula (I) first suggested by Zincke and Mühlhausen (*Ber.*, 1905, **38**, 3824), who discovered that the coloured condensation compounds were converted into 3-hydroxy-*N*-phenylpyridinium salts (II) when their solutions in alcohol or glacial acetic acid were boiled for a short time. Stenhouse (*loc. cit.*), who treated the condensation compounds from aniline and from *p*-toluidine with concentrated ammonia, obtained amorphous free bases. These bases were soluble in ether and on treatment with mineral acids re-formed the coloured crystalline salts. Zincke and Mühlhausen (*loc. cit.*) also obtained a resinous non-crystalline base from the condensation compound prepared from aniline. Details are now given for the preparation of crystalline bases from the aniline and *p*-toluidine condensation compounds. These bases are colourless and the purple compounds are regenerated when the bases are treated with mineral acids, but the full colour does not develop at once.



The reactions of the bases appear to indicate that the one derived from the aniline condensation compound (I; R = H) is either 2- (III; R = H) or 6-*anilino-3-keto-*N*-phenyl-1 : 2 : 3 : 6-tetrahydropyridine* (IV; R = H) and the other derived from the *p*-toluidine condensation compound (I; R = CH_3) is either 2- or 6-p*-toluidino-3-keto-*N-p*-tolyl-1 : 2 : 3 : 6-tetrahydropyridine*. Only one hydrogen in the bases can be acetylated. Crystalline *monobenzoyl* and *monoacetyl* derivatives were prepared from the *p*-toluidino-compound. The aniline compound readily gave a crystalline *benzylidene* and a *furfurylidene* derivative, indicating the presence of a reactive methylene group. Under vigorous conditions of catalytic hydrogenation, 8 moles of hydrogen were taken up by both bases and the products (V or VI), isolated as *perchlorates*, were diacidic bases and had no ketonic properties. In addition, from the reduction of the *p*-toluidine compound a *product* corresponding to the uptake of 2 moles of hydrogen was isolated. This product also had no ketonic properties. Finally, the ultra-violet absorption spectra of solutions of the toluidine base and its benzoate in methyl alcohol indicate little conjugation and support the formulæ given above.

EXPERIMENTAL.

2(*or* 6)-*Anilino-3-keto-*N*-phenyl-1 : 2 : 3 : 6-tetrahydropyridine* (III or IV; R = H).—The coloured condensation compound of furfuraldehyde, aniline, and aniline hydrochloride (Stenhouse, *loc. cit.*) (40 g.) was shaken with 3N-sodium hydroxide (100 c.c.) and ether (300 c.c.) in a separating funnel. When all the solid had dissolved the aqueous layer was separated and the ethereal layer was washed twice with water (a little sodium chloride was added if difficulty was experienced in obtaining separation of the layers during washing). The ethereal solution was dried (Na_2SO_4), and the ether distilled off. The residue (32 g.) was allowed to stand with a little acetone until it crystallised. The crystals were filtered off, washed with ethyl alcohol, and recrystallised from this solvent. The compound thus prepared forms colourless plates, m. p. 144° (decomp.; rapid heating); yield 8 g. (Found: C, 78·2, 76·7; H, 6·0, 6·0; N, 10·0; *M*,* 273. $C_{17}H_{16}ON_2$ requires C, 77·2; H, 6·1; N, 10·6%; *M*, 264·1). The *compound* is almost insoluble in water and in sodium hydroxide solution, sparingly soluble in light petroleum, and soluble in alcohol, benzene, and acetic acid. The colourless solutions in alcohol and acetic acid become red on addition of hydrochloric acid, and the colour deepens rapidly.

Acetylation. The base (2 g.) was dissolved in dry pyridine (100 c.c.) and acetic anhydride (10 c.c.) was added. After standing for 48 hours at room temperature, the mixture was poured into water. The *acetyl* derivative separated as an oil which soon crystallised. It was filtered off, washed well with water, and purified by two recrystallisations from alcohol and one from benzene; m. p. 128° (Found: N, 9·3, 8·9. $C_{19}H_{18}O_2N_2$ requires N, 9·15%).

Attempted benzoylation. The base (4·5 g.) was dissolved in dry pyridine (150 c.c.), and benzoyl chloride (35 c.c.) added. After standing for 48 hours at room temperature the mixture was poured into water, but the oil which separated could not be made to crystallise.

Benzylidene derivative. The base (0·85 g.) and benzaldehyde (1 g.) were added to a solution of potassium hydroxide (0·8 g.) in methyl alcohol (10 c.c.). The mixture was well stirred and after 2 hours the bright yellow solid was filtered off, washed with methyl alcohol, and dried (yield 0·67 g.). This *benzylidene* derivative was sparingly soluble in ethyl alcohol, readily soluble in 1 : 4-dioxan, and was decomposed by hot glacial acetic acid. It was purified by recrystallisation first from 1 : 4-dioxan and then from ethyl alcohol; small yellow needles darkening and decomposing at 195° without melting (Found: C, 81·6; H, 5·7; N, 8·1. $C_{24}H_{20}ON_2$ requires C, 81·8; H, 5·7; N, 8·0%).

Furfurylidene derivative. This derivative, prepared as above using furfuraldehyde in place of benzaldehyde, formed orange needles from alcohol, decomposing at 160° without melting (Found: N, 8·3. $C_{22}H_{18}O_2N_2$ requires N, 8·2%).

2(*or* 6)-p*-Toluidino-3-keto-*N-p*-tolyl-1 : 2 : 3 : 6-tetrahydropyridine* (III or IV; R = CH_3).—The first part of this preparation was carried out with the condensation compound of furfuraldehyde, *p*-toluidine, and *p*-toluidine hydrochloride (Stenhouse, *loc. cit.*) (40 g.), 3N-sodium hydroxide (100 c.c.), and ether (300 c.c.), as described above for the preparation of the corresponding aniline derivative. After the ether had been distilled off from the dry ethereal extract, the residue was stirred with a small quantity of ether. Crystallisation commenced, and after the mixture had stood for 48 hours the crystalline material (12 g.) was filtered off. It was purified by several recrystallisations from either alcohol or acetone (yield 6 g.). The colourless prisms had m. p. 175° (decomp.; rapid heating) (Found: C, 77·0; H, 6·8; N, 9·75; *M*, determined as described above, 277. $C_{19}H_{20}ON_2$ requires C, 78·0; H, 6·9; N, 9·6%; *M*, 292·2). This *compound* is soluble in ether, acetic acid, hot alcohol, and hot acetone. The colourless solutions in alcohol and acetic acid develop a deep purple colour after the addition of a little concentrated hydrochloric acid.

Acetylation. By the same procedure as for the anilino-analogue an oil was obtained which crystallised after some hours. The crystals were filtered off, dried over sulphuric acid in a vacuum desiccator, and purified by concentrating a solution in ether to half its bulk and leaving it to crystallise. This purification process was carried out three times. The *acetyl* derivative forms colourless prisms, m. p. 98°, very soluble in most organic solvents (Found: N, 8·2. $C_{21}H_{22}O_2N_2$ requires N, 8·4%).

Benzoylation. The base (2 g.) was dissolved in dry pyridine (100 c.c.) and benzoyl chloride (10 c.c.) was added. After standing for 48 hours at room temperature the mixture was poured into water. The crystalline material was filtered off and recrystallised several times from alcohol; rhombic prisms, m. p. 170° (Found: C, 79·3; H, 6·1; N, 7·2. $C_{26}H_{24}O_2N_2$ requires C, 78·8; H, 6·1; N, 7·1%). The ultra-violet absorption curves for this *benzoyl* derivative and for the original toluidino-compound itself are shown in the figure.

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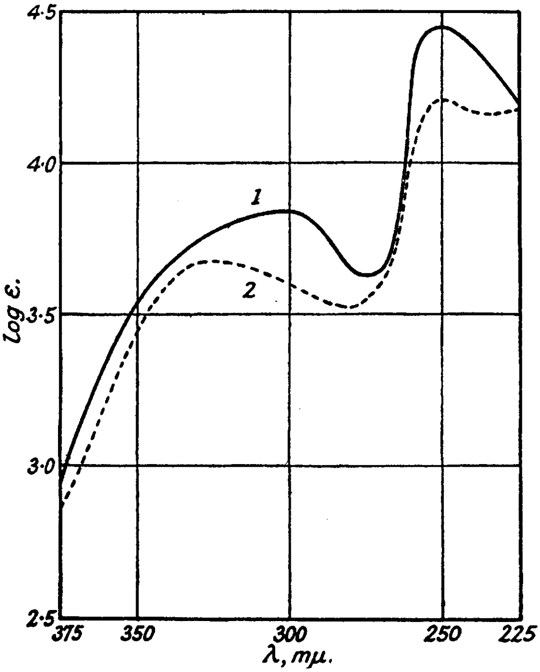
* Determined by comparing solutions in pyridine with solutions of acetanilide, using Emich's modification ("Microchemical Laboratory Manual," New York, 1932, 136) of Barger's micromethod (*Ber.*, 1904, **37**, 1754).

The acetate prepared from the aniline condensation compound and the benzoate from the toluidine compound gave solutions which remained colourless for 24 hours when small quantities were treated with equal volumes of concentrated hydrochloric acid and ethyl alcohol, although both the unsubstituted compounds when thus treated at once formed purple solutions.

Reduction of Condensation Products.—(i) 2(*or* 6)-*Anilino*-3-*keto*-N-*phenyl*-1 : 2 : 3 : 6-*tetrahydropyridine*. Reduction was carried out by dissolving 5 g. of the substance in alcohol (300 c.c.) and treating it with hydrogen at 75 atm. and 100° for 4 hours in the presence of Raney nickel (5 g.). The catalyst was filtered off, and the alcohol removed by distillation. Perchloric acid (50 c.c.; 15% wt./wt.) was added to the residue. The solid perchlorate was filtered off and dried in a vacuum over potassium hydroxide (yield 5·7 g.). The *perchlorate* of the reduced base was recrystallised twice from water and dried in a vacuum over phosphoric oxide at 100°; colourless plates (Found: C, 42·7, 43·1; H, 7·3, 7·1; N, 5·8; Cl, 13·7, 14·8. $C_{17}H_{32}ON_2,2HClO_4$ requires C, 42·4; H, 7·1; N, 5·8; Cl, 14·7%). Attempts to acetylate and benzoylate the base failed to give crystalline products.



Absorption spectra of:
(1) *Toluidine base.* (2) *Benzoate of toluidine base.*

(ii) 2(*or* 6)-p-*Toluidino*-3-*keto*-N-p-*tolyl*-1 : 2 : 3 : 6-*tetrahydropyridine*. Reduction was effected by dissolving 13·4 g. in ethyl alcohol (250 c.c.) and treating the solution with hydrogen at 90 atm. and 100° in the presence of Raney nickel (10 g.) for 3 hours. When the catalyst and solvent were removed a gum remained. A little alcohol was added and crystals were obtained. These were filtered off and recrystallised twice from alcohol; colourless plates (0·7 g.), m. p. 133° (Found: C, 76·6; H, 8·2; N, 9·5; *M*, 268. $C_{19}H_{24}ON_2$ requires C, 77·0; H, 8·2; N, 9·5%; *M*, 296·3). The formation of this *compound* has involved the uptake of 2 mols. of hydrogen.

The alcoholic mother-liquors were mixed with excess of dilute aqueous perchloric acid. The crystalline *perchlorate* that separated was recrystallised twice from water and dried in a vacuum over potassium hydroxide at 100°; yield 2·5 g. (Found: C, 44·7; H, 7·5; N, 5·4; Cl, 14·1. $C_{19}H_{36}ON_2,2HClO_4$ requires C, 44·8; H, 7·5; N, 5·5; Cl, 13·9%). An attempt to prepare a benzoate of the free base by the action of excess of sodium hydroxide solution and benzoyl chloride gave no solid product.

The reduced compounds gave no colours with mineral acids and did not react with semicarbazide, with 2 : 4-dinitrophenylhydrazine, or with salicylaldehyde in sulphuric acid.

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