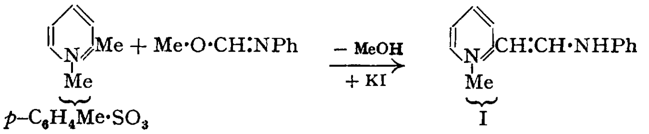
34. *Reactions of Alkyl*iso*formanilides. Part II. Reactions with Pyridinium Salts.*

By Edward B. Knott.

Alkyl*iso*formanilides will react with quaternary salts of mono- and poly-methylpyridines thereby converting the 2- and 4-methyl group to a β-anilinovinyl group. 2 : 6-Dimethylpyridinium salts also yield 2 : 6-*di-β-anilinovinylpyridinium salts.*

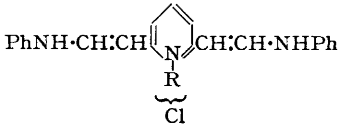
The preparation of β-acetanilidovinyl or β-anilinovinyl derivatives of cyclic quaternary ammonium salts, useful as intermediates in the preparation of photographic sensitising dyes, is usually achieved by the condensation of the ammonium salt containing a reactive methyl group with diphenylformamidine in acetic anhydride or by fusion (Piggott and Rodd, B.P. 344,409). Various examples of such compounds have been described in this and other patents, but only a few analogous compounds derived from homologues of pyridine have been described. α-Picolinium salts react readily on fusion with diphenylformamidine (Ogata, *J. Chem. Soc. Japan*, 1934, **55**, 394), giving the desired derivative, but before this application was attempted a more satisfactory alternative method of preparing such β-anilinovinyl derivatives had been found. Kuhn and Kern (B.P. 334,706) described the condensation of quaternary ammonium salts containing a reactive methyl group with substances of the general type, $R{\cdot}N{:}CR'X$ (I), where R and R′ represent hydrogen, alkyl, aralkyl or aryl groups and X is amino, alkoxy, acyloxy or halogen. Such substances are said to yield acetamidovinyl or acetanilidovinyl or substituted derivatives of the quaternary salt, on condensation in acetic anhydride. In the final specification, however, Kuhn and Kern restricted the general formula, (I), to substances where R and R′ are hydrogen, presumably because the larger general formula included substances which either do not condense or do not give the desired product. Included in this larger group are the alkyl*iso*formanilides (I; R = Ph, R′ = H; X = alkoxy). When these substances were allowed to react with quaternary salts of quinaldine, 2-methylbenzthiazole and similarly constituted bases in acetic anhydride the only products obtainable were carbocyanine dyes. When acetic anhydride–acetic acid was employed as solvent, as recommended in the above patent, the required β-acetanilidovinyl derivatives were obtained; this was not unexpected since, as has been shown in Part I (*J.*, **1945**, p. 687) an alkyl*iso*formanilide is converted rapidly and probably quantitatively into diphenylformamidine acetate on contact with acetic acid. The formation of the acetanilidovinyl derivative then results from the reaction of the quaternary salt and the above acetate as indicated in B.P. 344,409. With α-picolinium salts the use of acetic anhydride–acetic acid gave only a low yield of the β-acetanilidovinyl derivative. It was found, however, that reaction in a solvent which did not react with the anilino group, *e.g.* alcohols, gave very high yields of the required 2-β-anilinovinyl derivatives of benzoxazolium, benzthiazolium, naphthathiazolium and other salts. This reaction was applied to the quaternary salts of pyridines containing reactive methyl groups. On refluxing in ethyl alcohol a molar mixture of 2-methylpyridine metho-*p*-toluenesulphonate and methyl*iso*formanilide the reaction mixture yielded the required 2-β-anilinovinylpyridine methiodide (II) on treatment with potassium iodide.



(II.)

The corresponding *ethiodide* was formed in the same way. The yields, however, were *ca.* 30%. These low yields were due to a low reaction temperature and, on changing the solvent to *n*-butyl alcohol or pyridine, the yield was raised to 50%. In *n*-amyl alcohol the yield was 60% and, finally by fusion at 160°, the yield was raised to over 70%. By dissolving in hot acetic anhydride the anilino group was readily acetylated yielding 2-β-*acetanilidovinylpyridine alkiodides* which are extremely soluble in water. The isomeric 4-β-*anilinovinylpyridine alkiodides* obtained in the same way from γ-picoline alkyl *p*-toluenesulphonates were similar in colour to the 2-isomers (maximum absorption at 405 and 400 mμ respectively) but were more water-soluble.

In the preparation of mono-β-anilinovinyl derivatives from pyridines containing more than one reactive methyl group the mildest possible condensation conditions, compatible with a reasonable yield, are necessary in order to avoid the simultaneous formation of di-β-anilinovinyl derivatives. The formation of the mono-derivative is aided, however, in the case of pyridines containing 2- and 4-methyl groups by the higher reactivity of the former. In the case of 2 : 6-dimethylpyridine the two methyl groups are of identical reactivity. The best reaction temperature was found to be that of boiling *n*-butyl alcohol. By the use of this solvent the 2-β-*anilinovinyl*-6-*methylpyridinium* salts were obtained and isolated as their p-*toluenesulphonates* which are less soluble than the chlorides. 2-β-*Anilinovinyl*-4-*methylpyridinium* salts gave the p-*toluenesulphonates* as oils, but the *methobromide* was crystalline. 2-β-*Anilinovinyl*-4 : 6-*dimethylpyridinium* salts were isolated as their *metho*-p-*toluenesulphonates* and *ethiodides*. The position of the β-anilinovinyl group was determined by conversion of the derivative to dimethinmerocyanine dyes in the usual way, and a comparison of the absorption of these dyes with those obtained from the 2- and 4-β-anilinovinylpyridinium salts. The dye obtained from 3-ethylrhodanine and 4-β-anilinovinylpyridinium ethiodide had a maximum absorption at 563 mμ whilst similar dyes obtained from 2-methyl-, 2 : 4-dimethyl- and 2 : 4 : 6-trimethyl-pyridinium ethiodides had maximum absorptions at 538, 546, and 543 mμ respectively.



(III.)

Attempts to prepare di-β-anilinovinyl derivatives were successful only from 2 : 6-dimethylpyridine. 2 : 6-*Di*-β-*anilinovinylpyridine methochloride* (III; R = Me) and *ethochloride* (III; R = Et) were readily obtained on fusing the reactants at 170—200°. Their alcoholic solutions showed an intense green fluorescence. The methochloride crystallised in long threads giving a gel-like consistency to the crystallising liquor. Acetylation of the methochloride gave 2 : 6-*di*-β-*acetanilidovinylpyridine methochloride* in a crystalline state on adding ether to the acetic anhydride solution. The corresponding ethochloride was not obtained crystalline.

EXPERIMENTAL.

(Analyses are by Drs. Weiler and Strauss, Oxford; m. ps. are uncorrected.)

2-*β*- *and* 4-*β*-*Anilinovinylpyridinium Salts.*—2-Methylpyridine or 4-methylpyridine (3·72 g., 0·04 mol.) and methyl *p*-toluenesulphonate (7·44 g., 0·04 mol.) or ethyl *p*-toluenesulphonate (8·0 g., 0·04 mol.) were fused for 15 minutes at 100°. Methyl*iso*formanilide (5·4 g., 0·04 mol.) or ethyl*iso*formanilide (6·0 g.) was added and fused at 160° for 30 minutes. Alcohol was evolved and the melt turned orange. Alcohol (10 c.c.) was added to give a mobile liquid which was then poured into aqueous potassium iodide. The methiodide and ethiodide of the 2-isomer crystallised immediately as did also the methiodide of the 4-isomer. The ethiodide of the latter isomer separated as an oil which solidified slowly. 2-*β*-Anilinovinylpyridine methiodide, recrystallised from water, formed long glistening yellow needles, m. p. 210—212°

softening at 204° (Found : N, 8·6; I, 37·4. Calc. for $C_{14}H_{15}N_2I$: N, 8·3; I, 37·55%). Ogata (*loc. cit.*) gives m. p. 203°. The *perchlorate*, from water, formed orange needles, m. p. 196—197° (Found : N, 8·85. $C_{14}H_{13}O_4N_2Cl$ requires N, 9·0%).

2-β-Acetanilidovinylpyridine methiodide was obtained by refluxing the methiodide in acetic anhydride for 15 minutes and precipitating with ether. From aqueous potassium iodide, it formed pale yellow clusters of needles, m. p. 204°, containing water of crystallisation, removed by drying at 150° for 3 hours. Ogata (*loc. cit.*) gives m. p. 177° (Found : I, 33·5. Calc. for $C_{16}H_{17}ON_2I$: I, 33·4%). The *methoperchlorate* from water formed jagged, orange plates, m. p. 198—200° (Found : N, 7·95. $C_{16}H_{17}O_5N_2Cl$ requires N, 7·95%). 2-*β-Anilinovinylpyridine ethiodide* was obtained as the *monohydrate* from water, m. p. 206—207°, with previous shrinking (Found : N, 7·65. $C_{15}H_{19}N_2I,H_2O$ requires N, 7·55%). Dried at 137° over potassium hydroxide at 20 mm., the *anhydrous* salt was obtained, m. p. 206—207° (Found : N, 8·05; I, 35·95. $C_{15}H_{17}N_2I$ requires N, 7·9; I, 35·85%). The *ethoperchlorate* formed yellow needles, m. p. 161—162°, from water (Found : N, 8·5. $C_{15}H_{17}O_4N_2Cl$ requires N, 8·65%). The acetylated methiodide formed an oil which solidified under dry ether. It was not purified.

4-*β-Anilinovinylpyridine methiodide*, recrystallised from water, formed glistening flat yellow needles, m. p. 196° (Found : I, 37·4. $C_{14}H_{15}N_2I$ requires I, 37·55%). 4-*β-Anilinovinylpyridine ethiodide trihydrate* was difficult to purify. The crude solid was washed with a little *iso*propyl alcohol–ice water (5 : 1) to remove a dark colouring matter, dissolved in water at 20° and sufficient aqueous potassium iodide added to give a slight turbidity. On cooling to 5°, it crystallised as glistening flat yellow needles, m. p. 64—66° (Found : I, 31·15. $C_{15}H_{17}N_2I,3H_2O$ requires I, 31·25%).

2-*β-Anilinovinyl Derivatives of Polymethylpyridines*.—The pyridine (1 mol.) and alkyl *p*-toluenesulphonate (1 mol.) were fused at 100° for 15 minutes. Methyl*iso*formanilide (1 mol.) and sufficient *n*-butyl alcohol for solution were added and refluxed for 1 hour. The mixture was then poured into water or aqueous potassium bromide or iodide, shaken well and precipitated with ether. 2-*β-Anilinovinyl*-6-*methylpyridine metho*-p-*toluenesulphonate* crystallised from water and formed shining, flat, yellow needles with a pink reflex, m. p. 234° (Found : N, 7·05. $C_{22}H_{24}O_3N_2S$ requires N, 7·05%). 2-*β-Acetanilidovinyl*-6-*methylpyridine methoperchlorate* crystallised from alcohol in large, flat, rectangular aggregates of needles, m. p. 210° (Found : N, 7·85; Cl, 9·9. $C_{17}H_{19}O_5N_2Cl$ requires N, 7·65; Cl, 9·7%). 2-*β-Anilinovinyl*-6-*methylpyridine etho*-p-*toluenesulphonate monohydrate* crystallised from alcohol in flat orange needles, m. p. 148—150° (effervescence) (Found : N, 6·55. $C_{23}H_{26}O_3N_2S,H_2O$ requires N, 6·55%). 2-*β-Anilinovinyl*-4-*methylpyridine methobromide* crystallised from *iso*propyl alcohol in clusters of yellow needles, m. p. 236° (Found : Br, 26·4. $C_{15}H_{17}N_2Br$ requires Br, 26·2%). 2-*β-Anilinovinyl*-4 : 6-*dimethylpyridine metho*-p-*toluenesulphonate* formed bright orange feathery needles, m. p. 235°, from water (Found : N, 6·9. $C_{23}H_{26}O_3N_2S$ requires N, 6·8%). The *ethiodide dihydrate* formed flat orange needles, m. p. 265° (Found : I, 30·65. $C_{17}H_{21}N_2I,2H_2O$ requires I, 30·5%). The *anhydrous* salt, m. p. 265°, was obtained on heating the hydrate for 3 hours at 150°/20 mm. over potassium hydroxide (Found : I, 33·75. $C_{17}H_{21}N_2I$ requires I, 33·4%).

2 : 6-*Di-β-anilinovinylpyridine methochloride dihydrate* was obtained by refluxing at 200° in an oil bath, 2 : 6-dimethylpyridine metho-*p*-toluenesulphonate (1 mol.) and methyl*iso*formanilide (2 mol.) for 30 minutes. The melt was dissolved in hot alcohol and poured into an aqueous solution of ammonium chloride. The orange solid was well washed with cold alcohol, dissolved in hot alcohol and chilled in ice. The liquor set to a chrome-yellow gel. It formed matted yellow threads, m. p. 272°, with previous shrinking. It darkened appreciably in direct sunlight (Found : Cl, 8·85. $C_{22}H_{22}N_3Cl,2H_2O$ requires Cl, 8·85%). When dried over potassium hydroxide at 150°/20 mm., it gave the *anhydrous* salt, m. p. 272° (Found : Cl, 10·05. $C_{22}H_{22}N_3Cl$ requires Cl, 9·75).

2 : 6-*Di-β-acetanilidovinylpyridine methochloride* was precipitated on adding ether to the acetic anhydride solution of the above. Repeatedly dissolved in acetic anhydride and precipitated with ether it formed pale yellow needles, m. p. 106—108° (Found : Cl, 7·25. $C_{26}H_{26}O_2N_3Cl$ requires Cl, 7·9%).

2 : 6-*Di-β-anilinovinylpyridine ethochloride monohydrate.* Proceeding as for the methochloride this substance formed feathery bronze needles from alcohol, m. p. 240—245° (decomp.), with previous shrinking (Found : Cl, 8·8. $C_{23}H_{24}N_3Cl,H_2O$ requires Cl, 8·95%). When dried over potassium hydroxide at 150°/20 mm., it gave the *anhydrous* salt, m. p. 242—245° (Found : Cl, 9·05. $C_{23}H_{24}N_3Cl$ requires Cl, 9·4%).

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