26. *The Reaction between 2-Picoline and Aromatic Aldehydes.*

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STILBAZOLES of the formula $C_5H_4N{\cdot}CH{:}CH{\cdot}C_6H_4R$ (I) have usually been prepared by the interaction of equimolecular proportions of 2- or 4-picoline and aromatic aldehydes at 180—230° in presence of zinc chloride. Bennett and Pratt (J., 1929, 1465) used acetic anhydride as condensing agent in the preparation of 2′ : 4′-dinitro-2-stilbazole. This agent is now found to be generally applicable, and gives purer products than zinc chloride in higher yield. Small quantities of cinnamic acids are also formed, except with benzaldehyde and *p*-tolualdehyde. The formation of benzylidenediacetates was not detected. Moreover, *p*-nitrobenzylidenediacetate reacts much less readily (1% in 10 hr. at 135°) than *p*-nitrobenzaldehyde. The following yields were obtained by the use of 6 mols. of acetic anhydride during 10 hours at 135° : (sequence 1) *p*-methyl, 1; unsubstituted, 6; *o*-nitro, 39; *m*-nitro, 41; *p*-nitro, 51; 2 : 4-dinitro, 65% (in 1 hr.; 2 mols. Ac_2O). The reaction with 2-picoline resembles that with 2-methylquinoxaline (Bennett and Willis, J., 1928, 1960), for which the order of increasing efficacy is: unsubstituted < mononitro < 2 : 4-dinitro. In both reactions the relative reactivities of the nitrobenzaldehydes differ from those anticipated on theoretical grounds by Hinkel, Ayling, and Morgan (J., 1931, 1835), and, in contrast with the results of these authors for the Hantzsch pyridine condensation, all three nitrobenzaldehydes are much more reactive than benzaldehyde. This is usually so (see, *e.g.*, Lassar-Cohn, " Arbeitsmethoden," p. 430).

The formation of stilbazoles appears to proceed as follows: $C_5H_4N{\cdot}CH_3 + CHO{\cdot}C_6H_4R \overset{(a)}{\rightleftharpoons} C_5H_4N{\cdot}CH_2{\cdot}CH(OH){\cdot}C_6H_4R$ (II) $\xrightarrow{(b)} C_5H_4N{\cdot}CH{:}CH{\cdot}C_6H_4R + H_2O$. Alkines (II) are the principal products at 130—150° in presence of water (Bach, *Ber.*, 1901, **34**, 2223). The following yields of alkines have been obtained under standard conditions: (sequence 2) *p*-methyl, 5; unsubstituted, 11; *m*-nitro, 25; *o*-nitro, 37; *p*-nitro, 48%. Reaction (a) is reversible. The alkines, when heated with water at 140—200°, are in part converted into 2-picoline and the aldehydes. At 200° the *m*-nitro-alkine is also in part converted into the stilbazole. The stilbazoles are unchanged when heated with water at 140—230°.

The alkines, when heated with acetic anhydride, are converted into the corresponding stilbazoles (reaction b). The rates of reaction are in the order: (sequence 3) unsubstituted <*o*-nitro<*p*-nitro-<*m*-nitro. In all cases stage (b) proceeds rapidly compared with the net rate of formation of the stilbazoles in acetic anhydride, so that stage (a) is the rate-determining factor.

Although Räth (*Ber.*, 1925, **58**, 542) by dehydration of the *o*-amino- and *o*-nitro-alkines prepared the *cis*-forms of the corresponding stilbazoles, only the normal (? *trans*-)forms have been isolated under the conditions now described.

EXPERIMENTAL.

The order of reactivity was determined by heating the aldehyde (1 mol.) with 2-picoline (1 mol.) and Ac_2O (6 mols.) both in open vessels at 135° with exclusion of air and in thin-walled sealed tubes in an autoclave; both methods gave similar results. Sequence (1) is based upon 44 such expts.

The stilbazoles are best prepared at the b. p. of the solution, 1 mol. each of the aldehyde and 2-picoline being used. 2-Stilbazole, 4′-methyl-, and 2′-nitro-2-stilbazole were isolated by steam distillation and extraction from the dried residue with light petroleum. The other bases were extracted from the reaction mixture with dil. HCl aq. All m.p.'s are corrected.

Benzaldehyde: 0·5 mol. Ac_2O; 30 hr.; yield 87%.

o-*Nitrobenzaldehyde*: 1·5 mols. Ac_2O; 10 hr.; yield 80%. 2-Nitro-2-stilbazole forms lemon-yellow prismatic needles, m.p. 101°, $d_{4^\circ}^{20^\circ}$ 1·307. *Nitrate*, needles, m. p. 148° (Found: HNO_3 by titration, 21·7. $C_{13}H_{10}O_2N_2,HNO_3$ requires HNO_3, 21·7%); picrate, fibrous yellow needles, m. p. 220°, from acetone.

m- *and* p-*Nitrobenzaldehydes*: 1 mol. Ac_2O; 10 hr.; yield 90%. 3′-Nitro-2-stilbazole separates from EtOH in very pale yellow needles, m. p. 129°. 4′-Nitro-2-stilbazole forms lemon-yellow prisms from petroleum (b. p. 100—120°), m. p. 136°, $d_{4^\circ}^{20^\circ}$ 1·319; the sulphate, m. p. 274°, and nitrate, m. p. 155° (decomp.), are colourless, the picrate forms yellow needles, m. p. 272°, from EtOH.

2 : 4-*Dinitrobenzaldehyde*: 2 mols. Ac_2O; 1 hr.; yield 65%. Extensive resinification ensued on longer heating.

4′-*Methyl*-2-*stilbazole* was prepared by heating *p*-tolualdehyde, 2-picoline, and Ac_2O (1 mol. each) during 10 hr. at 200°, and formed white needles, m. p. 87°, from EtOH; yield, 80% (Found: C, 85·9; H, 6·5. $C_{14}H_{13}N$ requires C, 86·1; H, 6·7%).

Condensations using Zinc Chloride.—The yields of stilbazoles obtained after 10 hrs.' heating at 195° were: *o*-nitro, 64; *m*-nitro and *p*-nitro, 67%. Feist (*Arch. Pharm.*, 1902, **240**, 130) obtained yields *o*-, 70; *m*-, 60—70; *p*-, 50%.

Condensation with o-*Nitrobenzaldehyde in Acetic Acid*.—After 10 hr. at 135°, the yield was 79% with 1 mol. AcOH, and 48% with 3 mols.; with 12 mols., considerable decomp. ensued and no stilbazole was isolated.

Reaction in Absence of a Condensing Agent.—A mixture of the aldehyde and 2-picoline (1 mol. each) was boiled for 10 hr. The products were mixtures of the alkines and stilbazoles.

Preparation of the Alkines.—The results of sequence (2) were obtained by heating the aldehyde and 2-picoline (1 mol. each) with H_2O (4 mols.) in sealed tubes during 10 hr. at 140°. The mixtures were not homogeneous at room temp. The products were treated as in the prepn. of the corresponding stilbazoles. 2-Stilbazolealkine has m. p. 112°, and the *o*-nitro-compound, 139°. 4′-*Methyl*-2-*stilbazolealkine* forms colourless prisms, m. p. 96°, from light petroleum (Found: C, 78·7; H, 6·8. $C_{14}H_{15}ON$ requires C, 78·9; H, 7·0%). 3′-*Nitro*-2-*stilbazolealkine* separates from EtOH in nodules, m. p. 98° (Found: C, 63·7; H, 4·8. $C_{13}H_{12}O_3N_2$ requires C, 63·9; H, 4·9%).

Reversibility of the Alkine Condensation.—The alkines (1 g.) were heated with H_2O (2 g.) in sealed tubes at 140° during 10 hr. The unchanged alkine was weighed, and the aldehyde isolated both in the solid state and as 2 : 4-dinitrophenylhydrazone. The decomp. found was: unsubstituted, 60%; *o*-, *m*-, *p*-nitro, *ca.* 30%.

Dehydration of the Alkines.—The alkines (1 mol.) were heated with Ac_2O (4 mols.) during

0·5—3·0 hr. at 100°. Sequence (3) is based upon the setting points of the products and the isolation of pure compounds from them. When heated in boiling Ac_2O during 1 hr., the alkines gave the corresponding stilbazoles in almost pure condition.

The authors are indebted to Professor F. S. Kipping, F.R.S., for his interest in this work, to the Chemical Society for a grant, and to the South Metropolitan Gas Company for a gift of pyridine bases.

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[*Received, September* 26*th*, 1932.]