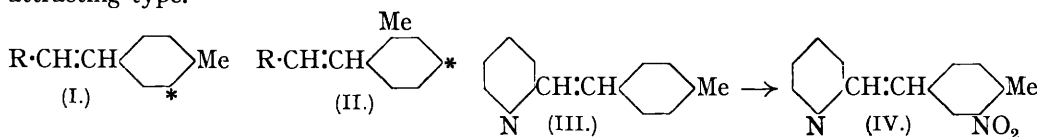


## 68. The Nitration of $\beta$ -Phenylethylpyridines and Related Compounds. Part II.

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THE inversion of the relative directive powers of pairs of *o/p*-directing groups (X, Y) attached to the benzene nucleus, as indicated by the position of entry of a third group, when X is (1) ortho and (2) para to Y, is a well-known phenomenon, which has been attributed (a) to differences of the *o/p* ratios characteristic of each group as indicated by substitution in  $C_6H_5X$  and  $C_6H_5Y$  respectively (*e.g.*, *Ann. Reports*, 1930, 138); (b) to differences of the inductive and direct effects (Ingold and Vass, J., 1928, 417); (c) to differences of the inductive and tautomeric effects (Baddeley and Bennett, J., 1933, 267). In addition, it is probable (d) that the phenomenon would be observed when one substituent is especially bulky (Le Fèvre, J., 1933, 980), but no data are available, *e.g.*, for *o*-cymene. Although explanation (a) is less fundamental than (b), (c), or (d), the evidence cited (below) indicates that it is not always valid, and it is therefore more than a mere re-statement of the phenomenon.

An example is afforded by the data for the nitration of various *p*- and *o*-methylstyrenes (I and II; \* = position of entry of the nitro-group), R being a substituent of the electron-attracting type.



Only 3-nitration has been detected in 4-methylcinnamic acid and its methyl ester (I, R = CO<sub>2</sub>H and CO<sub>2</sub>Me) and in *p*-tolylvinyl methyl ketone (I, R = CO·CH<sub>3</sub>) (Hanzlik and Bianchi, *Ber.*, 1899, **32**, 2287; Gatterman, *Annalen*, 1906, **347**, 360), so that in these compounds the influence of the methyl group predominates. On the other hand, only 4-nitration has been detected in 2-methylcinnamic acid (II, R = CO<sub>2</sub>H), and the rate of substitution is greater than in 4-methylcinnamic acid (Franzen and Schneider, *J. pr. Chem.*, 1914, **90**, 547), so that here the influence of the  $\omega$ -substituted vinyl radical predominates. It is possible that a mutual interaction of the external effects of the  $\omega$ -substituent and the methyl group, as well as the remoteness of the 4-position, contributes to this result. In these reactions the yields of pure products were poor (10–35%), but the indications are now confirmed for (I) by the nitration of 4'-methyl-2-stilbazole (III), which gives in 93% yield a product of which 65% is 3'-nitro-4'-methyl-2-stilbazole (IV). No other product was isolated.

Space models of  $\omega$ -substituted 4-methylstyrenes do not indicate pronounced volume influence (d) by either substituent. The *o/p* ratios for nitration of the compounds  $C_6H_5 \cdot CH:CHR$ , where R = CO<sub>2</sub>H, CO<sub>2</sub>Me, or 2-pyridinium, are greater than 0.9, so that factor (a) cannot be preponderant. The phenomenon may be ascribed, therefore, to electronic effects, such as (b) or (c). The unsubstituted vinyl group is regarded by Ingold (*Rec. trav. chim.*, 1929, **48**, 797) as exerting + *I* + *T* effects. The above data are consistent with the hypothesis that the net effect of the vinyl group containing an  $\omega$ -substituent of the electron-attracting type is - *I* + *T* (contrast Shoppee, J., 1933, 1118). The fact that *m*-substitution in  $\omega$ -substituted styrenes is probably not appreciable, and is certainly less than in toluene, indicates that the *T* effect is positive. The observed deactivation of the *o*-positions must therefore be due to the - *I* effect of the  $\omega$ -substituent, and the absence of *m*-substitution indicates that this effect acts principally through space (- *D*).

Owing to partial oxidation and resinification, 4-stilbazole (4-styrylpyridine) is nitrated less smoothly than 2-stilbazole, so that sufficient evidence for a similar variation of the *o/p* ratio with conditions (Part I; Shaw and Wagstaff, J., 1933, 79) was not available. The *o/p* ratio (1.05) was somewhat higher than for 2-stilbazole (0.93) under the same conditions. This is consistent with the relative remoteness of the pyridinium nitrogen in 4-stilbazole.

The nitration of 2:6-distyrylpyridine and 4-β-phenylethylpyridine is described. 2-β-4'-Nitrophenylethylpyridine, when further nitrated, gives the 2':4'-dinitro-compound almost exclusively.

Temporary deep colours were developed during all the nitrations described in this paper, and in Part I.

#### EXPERIMENTAL.

The *nitrate* of 4'-methyl-2-stilbazole (J., 1933, 78) formed yellow needles, m. p. 147°, from chloroform (Found: C, 64.8; H, 5.4.  $C_{14}H_{13}N_2.HNO_3$  requires C, 65.1; H, 5.4%). The salt (2 g.) was added to nitric acid (*d* 1.48; 20 g.) at -10° or to sulphuric acid (17 g.) at 0°. After 6 hours, the solution was diluted and basified. The product, crystallised from alcohol, gave the 3'-nitro-compound (yield, 58%), leaving an oil which yielded no other pure substance as such or as picrate. A smell of *p*-tolualdehyde, the yield (89—93%), and the isolation of acids (4%; not investigated) indicated that some oxidation had occurred. The results for the nitration of the nitro-2-stilbazoles (Part I) showed that the 2'-nitro-compound was least readily oxidised, so that in the present case the proportion of 3'-nitro-compound was probably higher than that stated. Attempts to nitrate the salt with stronger or weaker nitric acid resulted in increased oxidation. 3'-Nitro-4'-methyl-2-stilbazole, yellow needles, m. p. 137° (Found: C, 70.0; H, 5.0.  $C_{14}H_{12}O_2N_2$  requires C, 70.0; H, 5.0%) (picrate, m. p. 223°), was oxidised with 1% permanganate solution to nitroterephthalic acid, and with nitric acid (*d* 1.2) to 3-nitro-4-methylbenzoic acid.

*Preparation of 4-Stilbazole and the Nitro-4-stilbazoles.*—A mixture of mono- and di-methylpyridines, b. p. 139—146° (after two distillations through a 1.5-metre Dufton column), was heated for 10 hours at 220° in an autoclave with benzaldehyde (1 mol.) and zinc chloride (0.1 mol.; contrast Bailey and McElvain, *J. Amer. Chem. Soc.*, 1930, 52, 1635). The product was acidified and steam-distilled, whereby benzaldehyde was removed. The residue was basified and the unchanged bases (Z) were distilled in steam. The residual non-volatile bases were converted into a mixture of soluble and insoluble hydrochlorides by treatment with excess of hydrochloric acid. 2:6-Distyrylpyridine was isolated from the insoluble hydrochloride by the method of Shaw (J., 1924, 125, 2363). The soluble hydrochloride, when treated with excess of sodium hydroxide solution, gave bases which after several recrystallisations from benzene or pyridine yielded 4-stilbazole as white prisms, m. p. 131° (Found: C, 85.9; H, 6.1; N, 7.7. Calc. for  $C_{13}H_{11}N$ : C, 86.2; H, 6.1; N, 7.7%). From the mother-liquors were isolated 2-stilbazole and 2-styryl-6-methylpyridine.

The unchanged bases (Z) were dried and (40 g.) were heated with a nitrobenzaldehyde (100 g.) and acetic anhydride (20 g.) in closed glass vessels for 10 hours at 200°. The product in each case was extracted with warm hydrochloric acid. The insoluble hydrochloride (yield, 20%) was decomposed with hot pyridine, giving 2:6-di-(2', 3', or 4')-nitrostyrylpyridine, which was recrystallised from pyridine. The soluble hydrochloride when basified gave (2', 3', or 4')-nitro-4-stilbazole (yield, 40%) (which was recrystallised from chloroform and alcohol), and unchanged bases rich in 3-picoline. 4-Stilbazole was prepared similarly from benzaldehyde.

2:6-Di-2'-nitrostyrylpyridine, m. p. 140° (Found: C, 67.8; H, 3.9.  $C_{21}H_{15}O_4N_3$  requires C, 67.6; H, 4.0; N, 11.3%), 2:6-di-3'-nitrostyrylpyridine, m. p. 216° (Found: C, 67.5; H, 4.2%), and 2:6-di-4'-nitrostyrylpyridine, m. p. 258° (Found: C, 67.9; H, 3.8; N, 11.5%) (picrate, m. p. 294°), all formed yellow prisms. The last compound was also prepared from 2:6-distyrylpyridine (5 g.) by treatment with nitric acid (*d* 1.46; 129 g.) at 0° for 6 hours. The product was thrice recrystallised from pyridine. The remainder of the nitration product was not investigated. 2:6-Di-4'-nitrostyrylpyridine was oxidised with permanganate solution or nitric acid (*d* 1.25) to *p*-nitrobenzoic acid (yield, 20% and 83% respectively. The poor yield in the former case was due to the insolubility of the base). The substance, m. p. 168—169° (picrate, m. p. 246°), described by Werner (*Ber.*, 1903, 36, 1683) as 2:6-di-4'-nitrostyrylpyridine was possibly 4'-nitro-4-stilbazole, since he rejected his insoluble hydrochlorides.

2'-Nitro-4-stilbazole formed yellow prisms, m. p. 105° (Found: N, 12.5. Calc. for

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$C_{13}H_{10}O_2N_2$ : C, 69.0; H, 4.4; N, 12.4%), and 3'-nitro-4-stilbazole buff crystals, m. p. 144°. 4'-Nitro-4-stilbazole formed yellow prisms, m. p. 171° (Found: C, 69.4; H, 4.2%). Baumert (*Ber.*, 1906, **39**, 2971) gives m. p. 119°. The hydrochloride had m. p. 308°, and the picrate, m. p. 249°.

The following data were obtained for mixtures of 2'- and 4'-nitro-4-stilbazoles.

<i>o/p</i> Ratio .....	0.67	1.00	1.33	1.66	1.99
Initial setting point .....	128.0°	116.8°	108.8°	99.1°	92.0°
Eutectic .....	77.9°	78.7°	79.2°	80.2°	80.0°

*Nitration of 4-Stilbazole.*—The *nitrate* (pale yellow prisms, m. p. 160°. Found: C, 64.0; H, 4.7.  $C_{13}H_{11}N, HNO_3$  requires C, 63.9; H, 4.9%) was added to nitric or sulphuric acid, as for 2-stilbazole (Part I). The nitration products (yield, 86—96%) had eutectic points which were 4—10° (nitration in nitric acid) or 10—15° (nitration in sulphuric acid) lower than those of *o/p* binary mixtures and were raised by the addition of either pure component. The nitration products, when fractionally crystallised from alcohol, gave 2'- and 4'-nitro-4-stilbazoles and smaller quantities of brown resins. The best nitration was effected by adding the nitrate (2 g.) to nitric acid (*d* 1.485; 17 g.) at  $-10^\circ$ . After 3 hours the solution was poured on ice and basified. The product (A; yield, 95.6%) (Found: C, 68.8; H, 4.4. Calc. for  $C_{13}H_{10}O_2N_2$ : C, 69.0; H, 4.4%) had initial setting point 113.2°; eutectic, 75.1°. When a correction is applied, as in Part I, these values correspond to an *o/p* ratio of *ca.* 1.05. After addition (to 1.000 g.) of pure 4'-nitro-4-stilbazole (0.309 g.) the i.s.p. was 128.0°; eutectic 76.7°; corresponding to an *o/p* ratio for A, 1.05. The *o/p* ratio for 2-stilbazole under the same conditions is 0.93.

A solution of 4-stilbazole (3 g.) in nitric acid (*d* 1.42; 50 g.) was heated for 3 hours on a water-bath, diluted with water to 80 c.c., cooled, and filtered. The residue was *p*-nitrobenzoic acid, m. p. 230°. The yield (24%) was lower than that obtained from 2-stilbazole (37%). This was due either to a higher *o/p* ratio or to the inferior protection against oxidation afforded by the 4-, compared with the 2-, pyridinium radical. Copper acetate precipitated copper *isonicotinate* (yield, 75%) from the neutralised filtrate.

*Nitration of 4- $\beta$ -Phenylethylpyridine.*—The base was nitrated in nitric acid (*d* 1.42 or 1.52). The product, when crystallised from alcohol, readily gave 4- $\beta$ -4'-nitrophenylethylpyridine (yield, 50%) as colourless prisms, m. p. 85° (Found: C, 68.6; H, 5.3.  $C_{13}H_{12}O_2N_2$  requires C, 68.4; H, 5.3%). The remainder of the nitration product was not investigated. The methiodide, m. p. 155°, gave *p*-nitrobenzoic acid when oxidised with aqueous permanganate.

*Nitration of 2- $\beta$ -4'-Nitrophenylethylpyridine.*—A solution of the 4'-nitro-compound (5 g.) in nitric acid (*d* 1.505; 75 g.) was kept for 12 hours at 20°, poured on ice, and partly neutralised with sodium hydroxide solution. 2- $\beta$ -2': 4'-Dinitrophenylethylpyridine *nitrate* (yield, 83%) separated as colourless prisms, m. p. 160° (decomp.) after recrystallisation from alcohol (Found: C, 46.7; H, 3.3;  $HNO_3$ , by titration in presence of chloroform, 21.5.  $C_{13}H_{11}O_4N_3, HNO_3$  requires C, 46.4; H, 3.6;  $HNO_3$ , 21.6%). The filtrate was basified, and the product crystallised from alcohol; 2- $\beta$ -2': 4'-dinitrophenylethylpyridine (Found: N, 15.5.  $C_{13}H_{11}O_4N_3$  requires N, 15.4%) separated as colourless prisms, m. p. 78° (slight decomp.) after sintering at 58°. This base was best prepared by shaking its nitrate with aqueous sodium hydroxide and chloroform and evaporating the chloroform layer. The total yield of dinitro-compound was 94%. Attempted further purification as picrate (m. p. 160°) or perchlorate (m. p. 174°) failed to alter the m. p. Unlike the corresponding dinitrobenzyl compound (Tschitschibabin, Kuindshi, and Benewolenskaja, *Ber.*, 1925, **58**, 1580), this substance does not exhibit phototropy. The *methiodide*, prepared with excess of methyl iodide at 100°, crystallised from alcohol in yellow needles, m. p. 210° (Found: C, 40.7; H, 3.3; I, 31.0.  $C_{14}H_{14}O_4N_3I$  requires C, 40.5; H, 3.4; I, 30.6%), and when oxidised with permanganate gave 2 : 4-dinitrobenzoic acid (yield, 76%).

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