27. *The Nitration of β-Phenylethylpyridines and Related Compounds. Part I.*

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2-β-PHENYLETHYLPYRIDINE (I), 2-stilbazole (II), and 2-phenylacetylenylpyridine (III) have been nitrated, and the products investigated quantitatively (Table I).

TABLE I.

Nitration in Sulphuric Acid. Nitro-isomerides isolated, %.

	(I) $C_5H_4N{\cdot}CH_2{\cdot}CH_2Ph$.	(II) $C_5H_4N{\cdot}CH{:}CHPh$.	(III) $C_5H_4N{\cdot}C{\vdots}CPh$.
Ortho-	16·0	40·1	28·7
Meta-	3·4	nil	0·6
Para-	64·5	49·0	62·7
Total	83·9	89·1	92·0

The proportions of *m*-nitration of 2-phenylpyridine (Forsyth and Pyman, J., 1926, 2912), 2-benzylpyridine (Bryans and Pyman, J., 1929, 549; cf. Tschitschibabin, Kuindshi, and Benewolenskaja, *Ber.*, 1925, **58**, 1580), and 2-β-phenylethylpyridine (I) under similar conditions are 34·9, 10·4, and 3·4% respectively. These values support the principle that the successive intercalation of methylene groups between a *m*-orienting radical and a benzene nucleus progressively decreases the proportion of *m*-substitution.

Baurath (Inaug.-Dissert., Kiel, 1888; cf. Bach, *Ber.*, 1901, **34**, 2223) failed to nitrate 2-stilbazole (II). This has now been effected, and the product shown by the thermal method to be almost entirely a mixture of 2′- and 4′-nitro-2-stilbazoles. The *op*-ratio varies considerably (0·75—1·12) with the composition of the nitration medium (Table II). Increase in the concentration, combined with decrease in the quantity, of the nitric acid employed decreases the *op*-ratio. Varying the temperature appears to have a slight influence, but its effect was not disentangled satisfactorily, owing to the occurrence of side reactions, from that of varying the quantity of acid, which also is small. Addition of soluble nitrates (expt. 12) or acetic acid (expt. 15) to the nitric acid increases the *op*-ratio, but to a less extent than an equal weight of water. Nitration in sulphuric acid (expts. 18—21) gives *op*-ratios (0·85—0·93) equal to those obtained with 87—92% nitric acid.

The products of nitration of (I) and (III) are not susceptible to thermal analysis, but separation of the isomerides indicates that a similar variation of the *op*-ratio exists for (III), and that the variation for (I), if existent, is much smaller. These variations may be ascribed with some probability to the base–salt–ion equilibria. The strengths of the bases are in the order I>II>III; the amounts of *op*-variation are in the order III>II>I. Any slight difference between the proportion of the quaternary forms present in solutions of (I), (II), and (III) will be magnified by the relative slowness of substitution in these forms.

The *op*-ratio for 2-stilbazole (0·8—1·1) is higher than that for the ethane (I) (0·25) or for the acetylene (III) (0·4—0·55). This agrees with the hypothesis of Lapworth and Robinson (*Mem. Manchester Phil. Soc.*, 1928, **72**, 43), according to which a modification in the constitution of a side chain resulting in a greater or less attraction for electrons would respectively decrease or increase the *op*-ratio. That a greater attraction for electrons is exerted

TABLE II.

Nitration of 2-Stilbazole in Nitric and Sulphuric Acids.

W and *w* = g. of HNO_3 and H_2SO_4, respectively, per g. of 2-stilbazole nitrate.
Δ = amount by which f. p. of eutectic is lower than that of binary mixture.

No. of expt.	*W*.	$d_{4^\circ}^{15^\circ}$ of HNO_3.	*w*.	Time, hr.	Temp.	Yield, %.	Initial f. p.	Δ.	*op*-Ratio.
1	2·7	1·525	—	0·2	−15°	97·4	100·8°	3·6°	0·78
2	4·6	1·516	—	1·2	−15	98·7	101·0	5·1	0·75
3	4·0	1·507	—	1·5	−12	96·8	99·5	6·5	0·78
4	3·7	1·497	—	1·5	−12	98·4	100·2	0·2	0·85
5	3·7	1·494	—	1·0	−12	97·0	98·7	4·0	0·85
6	14·5	1·475	—	4·0	−12	96·1	95·8	1·6	1·00
7	32·0	1·464	—	3·5	0	94·5	94·2	0·8	1·08
8	34·0	1·452	—	16·0	−10	97·5	94·0	3·0	1·04
9	34·0	1·452	—	3·0	20	89·2	90·0	3·0	(*a*)
10	17·0	1·452	—	3·5	20	97·5	94·5	2·0	1·04
11	17·0	1·452	—	42·0	− 5	78·3	89·6	4·0	(*a*)
12	20·0	(*b*)	—	1·5	−12	96·1	97·5	2·8	0·92
13	22·0	1·440	—	13·5	0	98·5	94·8	1·1	1·06
14	40·0	1·438	—	15·0	0	97·0	94·1	0·8	1·09
15	22·0	(*c*)	—	3·0	− 5	95·2	95·7	2·8	1·00
16	27·0	1·425	—	6·0	20	95·5	92·3	2·0	1·12
17	100·0	1·398	—	80·0	0	45·1	—	—	(*a*)
18	—	—	6·5	8·0	− 5	97·2	98·2	2·0	0·88
19	—	—	6·0	4·0	−10	96·6	96·9	2·3	0·93
20	—	—	3·6	2·0	−10	94·0	80·5	(*d*) 4·0	0·85
21	—	—	4·5	4·0	− 5	97·3	83·4	(*e*) 2·0	0·88

(*a*) Extensive oxidation occurred. (*b*) Contained HNO_3, 76·5; H_2O, 3; NH_4NO_3, 13·5; KNO_3, 7%. (*c*) Contained HNO_3, 74; H_2O, 1; AcOH, 25%. (*d*) Residue from separation of 36·3% *p*-. (*e*) Residue from separation of 40·3% *p*-.

by the side chain of compounds (I) and (III) is indicated by the occurrence of *m*-substitution and, in the case of (III), by the relative slowness of nitration. No difference in the rates of nitration of (I) and (II) was detected.

The other available data for a comparison of the orienting influence of the side chains $CH_2{\cdot}CH_2R$, CH:CHR, and C⋮CR are limited to the case where R = CO_2H and, except those for phenylpropiolic acid, are unsatisfactory. In this series also the *op*-ratio for the ethylene is higher than for the ethane or for the acetylene.

2-Phenylacetylenylpyridine (III) was nitrated by addition of its nitrate to nitric and sulphuric acids. The proportion of *m*-substitution (0·6%), although a minimum value, is less than that detected by Baker, Cooper, and Ingold (J., 1928, 426; cf. Reich, *Compt. rend.*, 1916, **162**, 129) for phenylpropiolic acid (8%) and its ethyl ester (6%). The value is, however, higher than that found for 2-stilbazole (nil).

2-Stilbazole when heated with 70% nitric acid gave a mixture of acids, from which *p*-nitrobenzoic acid was isolated in 37% yield, indicating that nitration largely precedes oxidation. A similar observation was made by Koenigs and von Bentheim (*Ber.*, 1905, **38**, 3907) for 2 : 6-di- and 2 : 4 : 6-tri-styrylpyridines.

2′- and 4′-Nitro-2-stilbazoles when further nitrated gave 2′ : 4′-dinitro-2-stilbazole. Attempts to nitrate 3′-nitro-2-stilbazole resulted in extensive oxidation; 3′ : 4′-dinitro-2-stilbazole was isolated in 15% yield.

EXPERIMENTAL.

2-β-*Phenylethylpyridine*.—A mixture of 2-stilbazole (45 g.), red P (20 g.), I (50 g.), H_2O (20 g.), and AcOH (200 c.c.) was boiled for 24 hr., and the product purified by Baurath's method (*Ber.*, 1888, **21**, 818); m. p. − 3°. The *nitrate*, recryst. from $CHCl_3$–petroleum and from EtOH, formed colourless striated prisms, m. p. 91° (Found : C, 63·1; H, 5·7; *M*, by titration, 243. $C_{13}H_{13}N,HNO_3$ requires C, 63·4; H, 5·7%; *M*, 246) : it dissolved readily in $CHCl_3$, and after a few min. the solution deposited a bulky white solid, m. p. (air-dried) *ca.* 60°, which slowly lost $CHCl_3$. The methiodide, deep yellow needles, m. p. 189°, from EtOH, and the perchlorate, white plates, m. p. 98°, were also prepared.

Nitration.—(A) *In sulphuric acid.* The nitrate (5 g.) was added during 1 hr. to H_2SO_4

(*d* 1·84; 20 g.) at − 12° in a rotating flask. After 2 hr. further, the solution was warmed to 20° (1 hr.) and poured on ice (250 g.).

(B) *In nitric acid.* The nitrate (3 g.) was added (15—30 min.) to HNO_3 (*d* 1·39—1·525, 150—12 g.). With acid of $d > 1·42$, a red-brown colour, disappearing within 5 min., was developed after each addition [similar colours were observed for (II) and (III)]. The product was poured on ice.

The nitro-compounds (yield, 99—101%) were pptd. with NaOH aq., either fractionally or completely, and fractionally crystallised from EtOH, giving *p*-nitro-compound (62—66%) and an oil (X). The setting point of the crude nitration product also indicated that the variation in the proportion of *p*-nitro-compound was not large.

The oil X (Found : C, 67·4; H, 5·3. $C_{13}H_{12}O_2N_2$ requires C, 68·4; H, 5·3%) slowly deposited *ca.* 1% each of *m*- (dense prisms) and *p*-nitro-compound (fibrous needles), but was usually converted into derivatives. The weight of *o*-nitro-compound pptd. as picrate from acetone under standard conditions ranged from 48—55% of X, indicating that the proportion of *o*-nitro-compound formed in nitration did not vary extensively. The remaining picrates when fractionally cryst. from EtOH (30 crops) gave *o*-, 16·0%; *m*-, 3·4%; *p*-, 1·6% : 62·9% of *p*- had been previously separated. Fractional crystn. as methiodides from EtOH gave *o*-, 15·0%; *m*-, 2·4% : 62·5% of *p*- had been previously separated.

2-β-o-*Nitrophenylethylpyridine*, prepared by shaking the picrate, m. p. 156°, from the oil X, with $CHCl_3$ and NaOH aq., had m. p. 36° (Found : C, 68·2; H, 5·2%). The methiodide, yellow needles, m. p. 184°, from EtOH, gave *o*-nitrobenzoic acid when oxidised with $KMnO_4$ aq.

2-β-p-*Nitrophenylethylpyridine* crystallised from EtOH in white prisms, m. p. 96° (Found : C, 68·3; H, 5·3%). It was markedly stable towards $KMnO_4$ aq. and HNO_3 aq., a considerable proportion being recovered after several days' boiling. The methiodide, deep yellow needles, m. p. 198°, from EtOH, gave *p*-nitrobenzoic acid when oxidised with $KMnO_4$ aq. at 20°. The picrate, yellow needles, m. p. 171°, from acetone, the perchlorate, white needles, m. p. 150°, and the nitrate, colourless prisms, m. p. 138° (decomp.), from EtOH, were also prepared.

Preparation of the Amino-β-*phenylethylpyridines.*—The nitro-2-stilbazole (10 g.) was heated with red P (5 g.) and HI (*d* 1·7; 45 c.c.) at 160° for 5 hr. Much PH_3 was generated. The isolated base was recrystallised from petroleum (b. p. 40—60°). 2-β-o-*Aminophenylethylpyridine* formed long colourless needles, m. p. 61° (Found : C, 78·6; H, 7·2. $C_{13}H_{14}N_2$ requires C, 78·8; H, 7·1%), hydrobromide, white needles, m. p. 295°. 2-β-m-*Aminophenylethylpyridine* formed colourless needles, m. p. 72° (Found : C, 78·7; H, 7·1%). 2-β-p-*Aminophenylethylpyridine* formed colourless prisms, m. p. 57° (Found : C, 78·6; H, 7·0%) (mononitrate, m. p. 224°), and was also prepared by reduction with red P and HI of 4′-amino-2-stilbazole, prepared by Feist's method (*Ber.*, 1901, **34**, 465).

Preparation of 2-β-m-*Nitrophenylethylpyridine.*—The *p*-amino-compound (2·5 g.) was heated with Ac_2O (3 c.c.) for 1 hr. at 100°. The crude acetyl derivative was treated with HNO_3 (*d* 1·49; 20 g.) at − 10° (3 hr.). The base (yield, 80%; m. p. 147°), obtained by hydrolysis of the nitration product with conc. HCl, when cryst. from EtOH gave 2-(β-3′-*nitro*-4′-*aminophenylethyl*)-*pyridine*, deep yellow needles, m. p. 150° (Found : C, 63·9; H, 5·1. $C_{13}H_{13}O_2N_3$ requires C, 64·2; H, 5·3%). This substance was diazotised in alc. H_2SO_4, and the solution heated at 100°. The crude product (yield, 55%; m. p. 71°), when recryst. from petroleum, gave 2-β-m-*nitrophenylethylpyridine*, in colourless feathery aggregates, m. p. 76° (Found : C, 68·1; H, 4·8%). This substance was also prepared (yield, 15%) by Sandmeyer's reaction from the *m*-amino-compound.

Preparation of 2-*Stilbazole.*—The crude product prepared by Shaw's method (J., 1924, **125**, 1930) contained small quantities of stilbene and ferrous compounds. These were shown to result from the action of Ph·CHO on the Fe autoclave by heating Ph·CHO with Fe filings, stilbene being produced, together with other compounds not yet investigated. 2-*Stilbazole nitrate*, matted needles, m. p. 89° (Found : *M*, by titration, 279. $C_{13}H_{11}N,HNO_3,2H_2O$ requires *M*, 280), from dil. HNO_3, when kept in vac. at 60°, slowly gave the anhyd. *salt*, m. p. 123° (decomp.) (Found : C, 63·5; H, 4·7. $C_{13}H_{11}N,HNO_3$ requires C, 63·9; H, 4·9%). The methosulphate had m. p. 160°; the picrate, m. p. 212°.

Thermal Analysis.—Mixtures (total wt., 1·2 g.) of 2′- and 4′-nitro-2-stilbazole (see preceding paper) were melted in the usual apparatus. Consistent results (Table III) were obtained for the required *op*-ranges. Weighed quantities (20—100 mg.) of 2-stilbazole, 3′-nitro-, and 2′ : 4′-dinitro-2-stilbazole were added (20 expts.) to various *op*-mixtures (1·0 g.). The ratio of the depression of the initial setting point to that of the eutectic point was less for 2′ : 4′-dinitro-2-stilbazole (0·45) than for the other compounds (0·75). In nitration expts. 1—5 (Table II) the initial setting point was corrected on the assumption that the impurity was the dinitro-compound. In expts. 6—21 it was assumed that the impurity was 2-stilbazole and/or the 3′-nitro-compound. These assumptions were based on the experimental conditions, and supported by analyses (below). The corrections (usually 0·1—1·5) are not large.

Nitration of 2-*Stilbazole*.—(1) The nitrate (1·2 g.) was added to HNO_3 (Table II). The basified solution yielded a product [Found (expts. 1, 4, and 16) : C, 68·6, 68·9, 69·4; H, 4·1, 4·4, 4·7. $C_{13}H_{10}O_2N_2$ requires C, 69·0; H, 4·4%], which was thermally analysed.

TABLE III.

Mixtures of 2′- and 4′-Nitro-2-stilbazoles.

% 2′-Nitro-	0·0	2·5	3·1	30·0	45·0	45·0	50·0	55·0	55·0	60·0
Initial s. p.	134·0°	130·7°	130·0°	114·7°	101·6°	101·2°	97·5°	91·3°	91·5°	85·2°
Eutectic	—	—	—	—	81·5°	81·5°	81·5°	81·6°	81·5°	81·3°
% 2′-Nitro-	63·5	67·0	69·5	71·5	73·2	74·5	75·1	80·5	87·5	100·0
Initial s. p.	82·3°	81·3°	81·4°	80·4°	81·5°	83·0°	83·3°	86·5°	90·0°	98·1°
Eutectic	81·3°	81·3°	81·3°	81·3°	81·3°	81·2°	81·1°	80·4°	77·5°	—

(2) *In sulphuric acid.* The nitrate (5 g.) was added during 1 hr. to H_2SO_4 (Table II). Solution was complete after 1 hr. further. After 1—5 hr. the mixture was warmed to 20° (1 hr.) and poured on ice (120 g.).

(Expts. 18 and 19.) The suspension of sulphates was basified, and the ppt. thermally analysed (Table II) [Found (expt. 18) : C, 68·8; H, 4·3%].

(Expts. 20 and 21.) The suspension of sulphates was filtered. The residue when basified gave the 4′-nitro-compound. The filtrate yielded bases (Y) (expt. 21) (Found for Y : C, 69·0; H, 4·4%). To Y (0·800 g.) was added pure 4′-nitro-compound (0·518 g.); the s.p. was now 98·5°; eutectic, 80·2°; indicating *o* : *p*, 47·1 : 52·9; calc., 47·6 : 52·4). Y (3 g.) was fractionally crystallised from EtOH. At first pure 2′-nitro-compound separated (2 crops, 1·0 g.). Further separation (30 crops) was facilitated by the fact that the 2′-nitro-isomeride formed dense prisms on the walls of the vessel, whereas the 4′-compound formed felted needles. No 3′-nitro-compound was detected in the later crops. The total nitration product was thus separated into *o*-, 40·1; *p*-, 49·0%.

Combined Nitration and Oxidation.—2-Stilbazole (3 g.) was heated for 1 hr. at 90° with HNO_3 (*d* 1·42; 40 g.), and diluted to 80 c.c. with H_2O. The ppt. was *p*-nitrobenzoic acid (yield, 37%). Copper picolinate (yield, 70%) was isolated from the filtrate.

Further Nitration.—2′ (or 4′)-Nitro-2-stilbazole (2 g.) was treated (4 hr.) with HNO_3 (*d* 1·515; 60 g.) at − 12°. The diluted product yielded bases, m. p. 155° [yields : from 2′-, 87%; from 4′-, 63%; from the *op*-mixture Y (expt. 21), 83%], which when recryst. from EtOH gave 2′ : 4′-dinitro-2-stilbazole, m. p. and mixed m. p. 166°.

3-Nitro-2-stilbazole (5 g.) was treated with HNO_3 (*d* 1·515; 150 g.) at − 5°. After 12 hr. the solution was basified. The pptd. bases (G, 1·0 g., m. p. 145°) when fractionally cryst. from EtOH gave 3′-nitro- (1%) and 3′ : *4′-dinitro-2-stilbazole* (15%), deep yellow needles, m. p. 168° (Found : C, 57·4; H, 3·2. $C_{13}H_9O_4N_3$ requires C, 57·6; H, 3·3%), which when warmed with $KMnO_4$ aq. gave 3 : 4-dinitrobenzoic acid. *m*-Nitrobenzaldehyde (25%) was isolated from the filtrate from G.

Nitration of 2-*Phenylacetylenylpyridine*.—(1) The *nitrate* (5 g.) [white prisms, m. p. 85° (decomp.), from $CHCl_3$ (Found : C, 64·1; H, 4·0. $C_{13}H_9N,HNO_3$ requires C, 64·4; H, 4·1%)] was added (1 hr.) to conc. H_2SO_4 (20 g.) at − 5°. After 1 hr. the solution was warmed to 10° (1 hr.) and poured on ice. The product was pptd. with NaOH aq. The first two crops (52%) were the pure 4′-nitro-compound. The third crop (22%), m. p. 50—130°, when cryst. from EtOH gave 4′- (10%) and 2′-nitro-compound (10%). The fourth crop (11%), m. p. 51°, was nearly pure 2′-compound. The final crop (13%, m. p. 42°) (total yield, 97·7%), when cryst. from petroleum (b. p. 40—60°), gave 2′-nitro-compound (5%), and curved crystals (1·5%, m. p. 40—70°), which were purified as the picrate. The recovered base (0·3%) was the 3′-nitro-compound, m. p. and mixed m. p. 92°. Further small quantities of 2′- and 3′-nitro-compound were isolated as picrates (total yields, see Table I).

(2) *In nitric acid.* The nitrate was added (15—30 min.) to HNO_3. The proportion of 4′-nitro-compound isolated from the product by crystn. from EtOH is given in Table IV. The oxidation which took place in addition to nitration was possibly selective, so that the *p*-variation is best shown by expts. 2, 5, and 6, in which the oxidation was slight. The product in expts. 3, 7, and 8 was oily. A clean solid product was obtained by further treatment with HNO_3 (*d* 1·470).

TABLE IV.

Nitration of 2-Phenylacetylenylpyridine in Nitric Acid.

No. of expt.	*d* of HNO_3.	G. HNO_3 per g. nitrate.	Temp.	Time, hr.	Yield (X %).	*p*- isolated (% of X).
1	1·516	3·0	−12°	1·0	91·0	68·7
2	1·504	5·0	−12	4·0	100·1	67·3
3	1·492	6·7	−12	2·5	(incomplete nitration)	
4	1·492	8·0	−12	6·0	96·2	68·0
5	1·477	24·0	−12	8·0	100·2	62·0
6	1·470	23·0	−10	6·5	97·0	62·3
7	1·453	30·0	− 5	23·0	(incomplete nitration)	
8	1·422	30·0	− 5	10·0	(incomplete nitration)	

2-o-*Nitrophenylacetylenylpyridine*, colourless needles, m. p. 55° (Found: C, 69·4; H, 3·5. $C_{13}H_8O_2N_2$ requires C, 69·6; H, 3·6%), from light petroleum, became brown in daylight, and when oxidised with $KMnO_4$ aq. gave *o*-nitrobenzoic acid. The picrate had m. p. 175° (decomp.).

A mixture of 3′-nitro-2-stilbazole dibromide (4 g.), KOH (1·8 g.), and dry EtOH was distilled (3 hr.), diluted with H_2O, and extracted with petroleum. The bases were fractionally pptd. with NaOH aq. from dil. HCl solution. The first crop (25%, m. p. 90°), when recryst. from petroleum, gave 2-m-*nitrophenylacetylenylpyridine*, pale yellow feathers, m. p. 93° (Found: C, 69·3; H, 3·6%) (picrate, m. p. 199°). Later crops gave 3′-nitro-2-stilbazole.

2-p-*Nitrophenylacetylenylpyridine* crystallised from EtOH in colourless needles, m. p. 157° (Found: C, 69·5; H, 3·6%) [picrate, m. p. 206° (decomp.)], and when oxidised with $KMnO_4$ aq. gave *p*-nitrobenzoic acid.

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