119. *The Formation of Osazones. Part IV.* A Quantitative Study of the Reaction of Benzoin Phenylhydrazone with Phenylhydrazine.*

By G. J. Bloink and K. H. Pausacker.

A new mechanism for osazone formation has been proposed, based on the relative amounts of ammonia formed and phenylhydrazine consumed in the reaction of benzoin phenylhydrazone with phenylhydrazine. Aqueous acetic acid was used as solvent and the rate of acetylation of phenylhydrazine by this medium was also measured.

The most commonly accepted mechanism for osazone formation may be illustrated as follows, with benzoin :

Mechanism (I)

$$\mathrm{HO{\cdot}CHPh{\cdot}CPh{:}O + Ph{\cdot}NH{\cdot}NH_2 \overset{(A)}{\rightleftharpoons} HO{\cdot}CHPh{\cdot}CPh{:}N{\cdot}NHPh + H_2O}$$

$$\mathrm{HO{\cdot}CHPh{\cdot}CPh{:}N{\cdot}NHPh + Ph{\cdot}NH{\cdot}NH_2 \xrightarrow{(B)} O{:}CPh{\cdot}CPh{:}N{\cdot}NHPh + Ph{\cdot}NH_2 + NH_3}$$

$$\mathrm{O{:}CPh{\cdot}CPh{:}N{\cdot}NHPh + Ph{\cdot}NH{\cdot}NH_2 \xrightarrow{(C)} NHPh{\cdot}N{:}CPh{\cdot}CPh{:}N{\cdot}NHPh + H_2O}$$

The most difficult stage of this mechanism to understand is stage (*B*) where phenylhydrazine acts in the unusual role of an oxidising agent. In order to explain this, Weygand (*Ber.*, 1940, **73**, 1284; *Chem. Ber.*, 1949, **82**, 438) assumed an Amadori rearrangement. Now, it has already been shown (Kenner and Knight, *Ber.*, 1936, **69**, 341; Bloink and Pausacker, *J.*, 1950, 1328) that osazone formation is favoured when substituted phenylhydrazines possess an electron-attracting group and is hindered when they possess an electron-repelling group, whereas the rate of hydrazone formation would be affected in the reverse order by these substituents (Conant and Bartlett, *J. Amer. Chem. Soc.*, 1932, **54**, 2881; Ardagh, Kellam, Rutherford, and Walstaff, *ibid.*, p. 721). In the Amadori rearrangement, each molecule of phenylhydrazine reacts with a carbonyl (or imine) group so that this explanation of stage (*B*) is incorrect. Recently, Braude and Forbes (*J.*, 1951, 1763) have overcome this objection by their ingenious and satisfactory explanation of stage (*B*).

Before mechanism (1) is accepted, another that has not been proposed previously should be considered.

---

* Part III, *J.*, 1951, 2212.

Mechanism (II)

$$\mathrm{HO{\cdot}CHPh{\cdot}CPh{:}O + Ph{\cdot}NH{\cdot}NH_2 \overset{(D)}{\rightleftharpoons} HO{\cdot}CHPh{\cdot}CPh{:}N{\cdot}NHPh + H_2O}$$

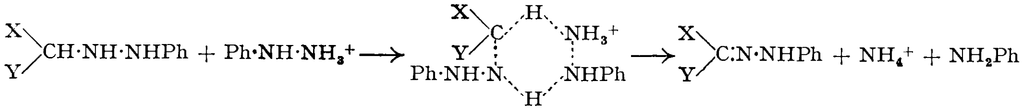
$$\mathrm{HO{\cdot}CHPh{\cdot}CPh{:}N{\cdot}NHPh + Ph{\cdot}NH{\cdot}NH_2 \overset{(E)}{\rightleftharpoons} NHPh{\cdot}NH{\cdot}CHPh{\cdot}CPh{:}N{\cdot}NHPh + H_2O}$$

$$\mathrm{NHPh{\cdot}NH{\cdot}CHPh{\cdot}CPh{:}N{\cdot}NHPh + Ph{\cdot}NH{\cdot}NH_2 \xrightarrow{(F)} NHPh{\cdot}N{:}CPh{\cdot}CPh{:}N{\cdot}NHPh + Ph{\cdot}NH_2 + NH_3}$$

The first stage (*D*) of this mechanism is the same as stage (*A*) of mechanism (I). The second stage (*E*) is supported by the work of Cowper and Stevens (*J.*, 1940, 347), who found that aniline condenses with benzoins with the formation of keto-amines; the mechanism of this stage could be represented as follows (cf. Cowper and Stevens, *loc. cit.*; Smith and Anderson, *J. Org. Chem.*, 1951, **16**, 963) :

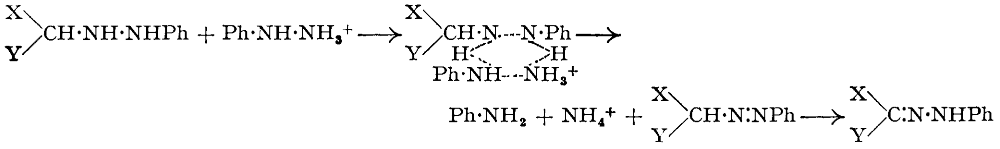
$$\mathrm{HO{\cdot}CHPh{\cdot}CPh{:}N{\cdot}NHPh \rightleftharpoons HO{\cdot}CPh{:}CPh{\cdot}NH{\cdot}NHPh \rightleftharpoons O{:}CPh{\cdot}CHPh{\cdot}NH{\cdot}NHPh}$$
$$\mathrm{\xrightleftharpoons{Ph{\cdot}NH{\cdot}NH_2} NHPh{\cdot}N{:}CPh{\cdot}CHPh{\cdot}NH{\cdot}NHPh}$$

The third stage (*F*) could be represented in a manner analogous to that suggested by Braude and Forbes (*loc. cit.*) for stage (*B*) :



(X = Ph; Y = CPh:N·NHPh)

An alternative scheme, based on the fact that Franzen and Fürst (*Annalen*, 1917, **412**, 29) found that 1-*o*-aminophenyl-2-benzylhydrazine is converted into benzaldehyde *o*-aminophenylhydrazone, benzylamine, and *o*-phenylenediamine, is as follows :



However, this does not explain the formation of osazones with 1-methyl-1-phenylhydrazine, as an intermediate azo-compound would not be possible.

By measuring the value of the ratio between phenylhydrazine consumed and ammonia formed during the reaction of benzoin phenylhydrazone with phenylhydrazine, it should be possible to distinguish between mechanisms (I) and (II). With mechanism (I) this value should be initially less than two, whereas with mechanism (II) it should be initially greater than two. Both should, of course, approach two at infinite time.

The investigation of this reaction was complicated by two factors : (*a*) the reaction was carried out in aqueous acetic acid (30% water) and it was found that phenylhydrazine was appreciably acetylated under the conditions used; (*b*) benzoin phenylhydrazone dissolved but slowly in the aqueous acetic acid and a precipitate of benzil bisphenylhydrazone (identified by m. p. and mixed m. p., 241°) was obtained, owing to the fact that benzoin phenylhydrazone co-exists in the solution in equilibrium with benzoin and phenylhydrazine.

The reaction of phenylhydrazine with the aqueous acetic acid was therefore investigated separately and the reaction was found to be of first order, owing to the large excess of acetic acid. In addition, 1-acetyl-2-phenylhydrazine was completely without action on benzoin phenylhydrazone under the same conditions. These results were then used to calculate the amount of phenylhydrazine consumed by acetylation during the reaction with benzoin phenylhydrazone. The amount of phenylhydrazine consumed in osazone formation (denoted by *P*) was taken to be the difference between the total amount of phenylhydrazine consumed and that consumed by acetylation. *P* is obviously too small as no account has been taken of the phenylhydrazine that is present in the medium owing to the reversible dissociation of the hydrazone. In addition, the amount of phenylhydrazine consumed by acetylation has been calculated without consideration of the simultaneous reaction to form osazone, so that its value is slightly large.

Despite the fact that P is too small, the value of the ratio between P and ammonia formed exceeds 2 initially in all the reactions investigated. It then falls below 2 and finally begins to approach 2 again (see Table 3). These results are not in accord with mechanism (I), and so mechanism (II) is favoured. The values much greater than 2 are obtained after short reaction times during which it is assumed that the equilibrium

$$\mathrm{Ph{\cdot}NH{\cdot}N{:}CPh{\cdot}CHPh{\cdot}OH + H_2O \rightleftharpoons O{:}CPh{\cdot}CHPh{\cdot}OH + Ph{\cdot}NH{\cdot}NH_2}$$

has not been established. As the reaction proceeds, the phenylhydrazine thus produced causes the value to fall below 2, but its effect will be less marked as the reaction proceeds and the value of the ratio should once again approach 2.

When benzoin phenylhydrazone alone was allowed to react with the aqueous acetic acid at 49·1°, it was found that 0·273 mole of ammonia per mole of hydrazone was formed at infinite time. Benzil bisphenylhydrazone was also isolated (see above). If the reaction involved is assumed to be

$$\mathrm{3Ph{\cdot}NH{\cdot}N{:}CPh{\cdot}CHPh{\cdot}OH + H_2O \longrightarrow Ph{\cdot}NH{\cdot}N{:}CPh{\cdot}CPh{:}N{\cdot}NHPh + 2O{:}CPh{\cdot}CHPh{\cdot}OH + Ph{\cdot}NH_2 + NH_3}$$

then 0·333 mole of ammonia per mole of hydrazone should be produced. This difference (0·060 mole of ammonia) may be ascribed to the amount of phenylhydrazine lost by acetylation. Fortunately, 1-acetyl-2-phenylhydrazine can be separated quantitatively from a synthetic mixture with benzoin and benzil bisphenylhydrazone owing to its solubility in warm water. In the above reaction it was found that 0·108 mole of 1-acetyl-2-phenylhydrazine per mole of benzoin phenylhydrazone was formed. This corresponds to a decrease of 0·036 mole of ammonia below that expected from the above equation (viz., 0·297 mole), in good agreement with the experimental value (0·273 mole). By contrast, Theilacker and Tröster (*Annalen*, 1951, **572**, 114) found that benzoin phenylhydrazone reacted as follows :

$$\mathrm{HO{\cdot}CHPh{\cdot}CPh{:}N{\cdot}NHPh + H_2O \longrightarrow \underset{(74\%)}{O{:}CPh{\cdot}CPh{:}O} + \underset{(52\%)}{Ph{\cdot}NH_2} + NH_3}$$

It should be noted, however, that these authors used aqueous acetic acid at 100°. On the other hand, benzil monophenylhydrazone was quantitatively recovered unchanged, under our conditions, in agreement with Theilacker and Tröster.

The reaction of phenylhydrazine with benzoin was also investigated at 39·7°, and it was found that the rates of production of ammonia and aniline were almost identical, which supports stage (F).

EXPERIMENTAL

Benzoin.—Commercial benzoin was crystallised four times from absolute alcohol (twice with charcoal), giving cream-coloured needles, m. p. 134—136°.

Benzoin Phenylhydrazone.—Benzoin (3·0 g., 0·014 mole) was heated with pure phenylhydrazine (1·5 g., 0·014 mole) on the water-bath until all the benzoin had dissolved. Alcohol was added and the product allowed to crystallise. The benzoin phenylhydrazone was then recrystallised from absolute alcohol, giving colourless needles, m. p. 106°. Smith (*Amer. Chem. J.*, 1899, **22**, 199) gives m. p. 106°.

Acetic Acid.—Excess of liquid was removed from crystalline acetic acid which was then refluxed (3 hours) with chromium trioxide (1·5% by wt.), and the product distilled twice. Water (*ca.* 30% by wt.) was added until the d^{20} was 1·070.

Phenylhydrazine.—Commercial phenylhydrazine was distilled *in vacuo*, and the distillate frozen at 7°. The oily portion was then decanted and the residue redistilled, the constant-boiling fraction being reserved. Owing to the difficulty of preventing aerial oxidation, it was converted into its hydrochloride, which is quite stable (cf. Ardagh, Kellam, Rutherford, and Walstaff, *loc. cit.*). The product was free from ammonium chloride.

Procedure.—Benzoin phenylhydrazone was dissolved in 30% aqueous acetic acid (*ca.* 25—30 ml.), at the temperature of the bath, in a 50-ml. flask. Phenylhydrazine hydrochloride and the exact amount of 1·000N-sodium hydroxide required to neutralise the phenylhydrazine hydrochloride were then added and the solution made up to the mark with the aqueous acetic acid. At determined times, 5-ml. aliquots were withdrawn, added to 5 ml. of 0·5N-hydrochloric acid, and extracted with ether. The ethereal layer was then well washed with distilled water, and the washings were added to the aqueous extract. The aqueous layer was then analysed as follows: Ammonium ion was determined by the use of a standard micro-Kjeldahl apparatus (phenolphthalein); separate experiments showed that the addition of aniline and phenylhydrazine did not interfere. Phenylhydrazine present was determined by Ardagh and Williams's iodometric method (*J. Amer. Chem. Soc.*, 1925, **47**, 2976); addition of aniline and

TABLE 1.

Wt. of $Ph\cdot NH\cdot NH_2,HCl$ = 0·4281 g. (29·67 × 10^{-4} mole). Concn. of $CH_3\cdot CO_2H$ = 12·31 mole $l.^{-1}$ (const.). Temp. = 59·7°.

Time (min.)		150	250	350	450	550
$Ph\cdot NH\cdot NH_2$ consumed (10^{-4} mole)	obs.	7·40	10·74	13·60	16·40	18·80
	calc.	7·10	10·43	14·00	16·61	18·80

$k = 2{\cdot}47 \times 10^{-6}$ mole^{-1} l. sec.$^{-1}$.

TABLE 2.

Temp.:	39·7°	49·1°	59·7°
10^7k (mole^{-1} l. sec.$^{-1}$)	1·83, 2·06, 1·85	7·04, 6·96, 6·88	23·4, 24·7, 23·8
(Average)	1·91	6·96	24·0

The bimolecular constants obey the Arrhenius equation as shown by the following data, where the calculated values are given by $k = 8{\cdot}70 \times 10^{11}e^{-26,600/RT}$.

Temp.:		39·7°	49·1°	59·7°
10^7k	obs.	1·91	6·96	24·0
	calc.	1·95	6·75	25·1

TABLE 3. *Reaction of phenylhydrazine with benzoin phenylhydrazone.*

Wt. of $Ph\cdot NH\cdot NH_2,HCl$ = 0·2882 g. (19·94 × 10^{-4} mole).
Wt. of benzoin phenylhydrazone = 0·2716 g. (8·99 × 10^{-4} mole).

Temp.	Time (min.)	NH_3 formed (10^{-4} mole)	Total $Ph\cdot NH\cdot NH_2$ used (10^{-4} mole)	$Ph\cdot NH\cdot NH_2$ used by acetylation (× 10^{-4} mole)	P (× 10^{-4} mole)	P/NH_3 formed
39·7°	100	1·39	3·87	0·23	3·64	2·62
	200	2·48	4·77	0·48	4·29	1·73
	500	3·71	7·07	1·05	6·02	1·62
	1000	4·72	10·01	1·90	8·11	1·72
	1600	5·30	12·55	2·62	9·93	1·87
	3100	5·96	15·00	3·67	11·33	1·90
49·1	100	1·69	5·12	0·88	4·24	2·50
	200	2·70	7·37	1·47	5·90	2·18
	300	3·36	8·99	2·07	6·92	2·06
	400	3·78	10·14	2·67	7·47	1·98
	500	4·12	11·13	3·08	8·05	1·96
	∞	4·58	—	—	—	—
59·7	100	3·09	9·06	2·65	6·41	2·07
	200	3·77	11·03	4·38	6·65	1·76
	300	3·90	12·83	5·88	6·95	1·78
	400	4·04	14·48	6·92	7·56	1·87
	∞	4·60	—	—	—	—

TABLE 4. *Reaction of phenylhydrazine with benzoin.*

Wt. of $Ph\cdot NH\cdot NH_2,HCl$ = 0·4275 g. (29·59 × 10^{-4} mole).
Wt. of benzoin = 0·1905 g. (8·99 × 10^{-4} mole). Temp. = 39·7°.

t (min.)	200	400	1000	1400	2000
NH_3 formed (10^{-4} mole)	2·48	3·28	4·72	5·12	5·49
$Ph\cdot NH_2$ formed (10^{-4} mole)	2·44	3·17	4·52	5·07	5·35

ammonium ion was independently found to have no effect on this estimation. Aniline was determined by prior destruction of the phenylhydrazine with a warm aqueous acetic acid solution of cupric sulphate, and titration with bromine solution by Pamfilov's method (*Ind. Eng. Chem.*, 1926, **18**, 763); methyl-red was a better indicator than indigo-carmine; ammonium ion did not interfere.

The acetylation of phenylhydrazine and also its reaction with benzoin were also measured. All the reactions were performed in a stream of nitrogen.

The results (all obtained in duplicate) are shown in the following tables. The temperatures were accurate to ±0·1°.

Reaction of Phenylhydrazine with 30% *Aqueous Acetic Acid.*—A typical example is given in Table 1. Results are summarised in Table 2.

We thank Drs. N. V. Riggs and C. C. J. Culvenor for helpful discussion.

University of Melbourne, N.3,
Victoria, Australia.

[*Received, October* 15*th*, 1951.]