

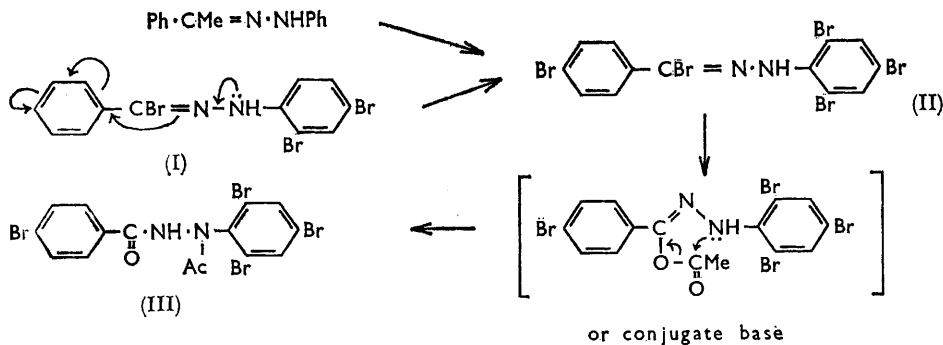
285. Hydrazones. Part V.¹ The Perhalogenation of Arylidene Arylhydrazones.

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Perbromination of *N*-arylidene-*N'*-arylhydrazines at elevated temperature involves (i) replacement of an α -methyl group (if present) by bromine, and (ii) *para*-substitution of the *C*-aryl group (unless deactivated).

By chlorination, *N'*-chloro-derivatives have been prepared in the α -methyl and *N'*-*o*-tolyl-series; unlike the *N'*-*p*-tolyl- analogues, these do not rearrange smoothly in boiling 95% acetic acid.

In the halogenation of benzaldehyde phenylhydrazone (*N*- α -benzylidene-*N'*-phenylhydrazone) in acetic acid, the α -position and the *N'*-phenyl group undergo substitution, the latter behaving as an aniline residue; *e.g.*, tribromination gives *N*- α -bromobenzylidene-*N'*-(2,4-dibromophenyl)hydrazone (I). From examination of several phenylhydrazones, the order of substitution in these reactions has emerged as $4 \geq \alpha \geq 2 > 6$, the last-mentioned having been observed only in chlorinations.² It was further found that a methyl group at C-2 or C-4 in the above series simply prevented substitution at the occupied position, the order remaining otherwise unchanged.³ A methyl group at the α -position might be expected to behave similarly, but halogenation of acetophenone phenylhydrazone, when conducted in carbon tetrachloride at low temperature, was found to give tarry products; working-up was complicated by hydrolysis of the hydrazones by liberated hydrogen halide, and only poor yields of acetophenone 4-bromo- and 2,4-dichloro-phenylhydrazones were obtained.⁴ We have obtained similar results in acetic acid, *e.g.*, monobromination giving a small yield of acetophenone 4-bromophenylhydrazone. When, however, a large excess of bromine was used, and the temperature raised, a sparingly soluble compound (II), C₁₃H₇Br₅N₂, resulted; the best yield was obtained at reflux temperature. The nuclear magnetic resonance spectrum of (II) showed that the methyl group had disappeared in the reaction, whilst the formation of an intense red colour on boiling with ethanolic phenylhydrazine² suggested that the compound, like (I) was an α -bromo-derivative. This was confirmed by reaction with acetate ion² to give the hydrazone (III);



acidic hydrolysis of (III) gave *p*-bromobenzoic acid, establishing the positions of two of the bromine atoms in the hydrazone (II). Compounds (II) and (III) thus appeared to be *N*-(4, α -dibromobenzylidene)-*N'*-(2,4,6-tribromophenyl)hydrazone and *N*-acetyl-*N'*-4-bromobenzoyl-*N'*-(2,4,6-tribromophenyl)hydrazone, respectively. These views were confirmed when it was found that high-temperature bromination of (I) also gave (II).

¹ Part IV, *Tetrahedron*, 1963, **19**, 1587.

² Chattaway and Walker, *J.*, 1925, **127**, 975, 1687, 2407.

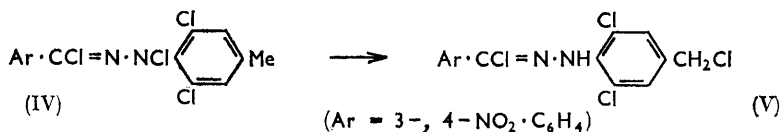
³ Chattaway and Adamson, *J.*, 1930, 157; 1931, 2787.

⁴ Humphries, Bloom, and Evans, *J.*, 1923, **123**, 1766; Humphries, Humble, and Evans, *J.*, 1925, **127**, 1304.

The observed *para*-substitution in what has hitherto been regarded as an unreactive benzene ring is of interest in showing that weak activation of that ring is possible once the other ring is 2,4,6-trisubstituted. Another example of this was found in the bromination of benzaldehyde *o*-tolylhydrazone with excess of bromine. This gave *N*-(4- α -dibromobenzylidene)-*N'*-(2,4-dibromo-6-methylphenyl)hydrazine, which was degraded to *p*-bromobenzoic acid as in the previous case. The acetylsis exemplified by (II) \rightarrow (III) is typical of these α -halogeno-compounds, and is not apparently susceptible to steric hindrance. The reaction probably involves the intermediate formation of the α -acetoxy-compound, which then undergoes *O* \rightarrow *N* acetyl migration (intramolecular acetylation) as shown.⁵

The mode of removal of the α -methyl group in the perbromination of acetophenone phenylhydrazone remains to be determined. Loss of the α -methyl group in such a reaction is probably general as the perbromination of *m*-nitroacetophenone phenylhydrazone similarly gave *N*-(α -bromo-3-nitrobenzylidene)-*N'*-(2,4,6-tribromophenyl)hydrazine; the structure of the latter follows from its preparation from *N*-(α -bromo-3-nitrobenzylidene)-*N'*-(2,4-dibromophenyl)hydrazine.

In the chlorination of *m*- and *p*-nitrobenzaldehyde *p*-tolylhydrazones, the highest chlorination products, obtained at 60°, have been *N*-chloro-*N'*-(α -chloro-3- and -4-nitrobenzylidene)-*N*-(2,6-dichloro-4-methylphenyl)hydrazines.⁶ These compounds (IV) rearrange smoothly in boiling 95% acetic acid to *N*-(α -chloro-3- and -4-nitrobenzylidene)-*N'*-(2,6-dichloro-4-chloromethylphenyl)hydrazines (V), respectively.^{6,7} The analogous *N*-chloro-*N'*-(α -methyl-3-nitrobenzylidene)-*N*-(2,4,6-trichlorophenyl)hydrazine and *N*-chloro-*N'*-(α -chloro-3-nitrobenzylidene)-*N*-(2,4-dichloro-6-methylphenyl)hydrazine have now been prepared. On attempted rearrangement (cf. above), much tar was formed and only small quantities of *m*-nitroacetophenone 2,4,6-trichlorophenylhydrazone and *N*-(α -chloro-3-nitrobenzylidene)-*N'*-(2,4-dichloro-6-methylphenyl)hydrazine, respectively, both resulting from de-*N*-chlorination, could be recovered. The Chattaway-Adamson rearrangement thus appears to be peculiar to the *p*-series.



EXPERIMENTAL

Microanalyses are by Mr. V. Manohin. Ultraviolet spectra were measured for ethanol solutions.

Perbromination of Acetophenone Phenylhydrazone.—Bromine (10 ml.) was added to a stirred suspension of acetophenone phenylhydrazone (5 g.) in glacial acetic acid (25 ml.), and the mixture was then heated under reflux for 1 hr. The solid dissolved, hydrogen bromide was evolved, and a solid began to separate. When cool, the product (5.3 g.) was collected, washed, and dried. Two crystallisations from acetic acid gave *N*-(4- α -dibromobenzylidene)-*N'*-(2,4,6-tribromophenyl)hydrazine as needles (2.65 g.), m. p. 180—181° (Found: Br, 67.5; N, 4.7. C₁₃H₇Br₃N₂ requires Br, 67.7; N, 4.7%). The compound gave a cherry-red colour on boiling with ethanolic phenylhydrazone due to the formation of the formazyl derivative.²

N-Acetyl-*N'*-4-bromobenzoyl-*N*-(2,4,6-tribromophenyl)hydrazine and its Hydrolysis.—A mixture of *N*-(4- α -dibromobenzylidene)-*N'*-(2,4,6-tribromophenyl)hydrazine (7 g.), anhydrous sodium acetate (7 g.), and glacial acetic acid (300 ml.) was boiled under reflux for 3½ hr., cooled and the solution poured into water (1 l.). The precipitate (4.25 g.) was collected, washed, and dried, *N*-Acetyl-*N'*-4-bromobenzoyl-*N*-(2,4,6-tribromophenyl)hydrazine separated as needles (from ethanol), m. p. 183—184° (Found: Br, 56.1; N, 4.9. C₁₅H₁₀Br₄N₂O₂ requires Br, 56.1; N, 4.9%); ν_{max} . (Nujol mull) 1700 and 1665 cm.⁻¹ (C=O).

⁵ Cf. Stevens and Munk, *J. Amer. Chem. Soc.*, 1958, **80**, 4065.

⁶ Chattaway and Adamson, *J.*, 1930, 843.

⁷ Gibson, *J.*, 1962, 2270.

The compound (4.25 g.) was heated under reflux for 3 hr. in a mixture of dioxan (22.5 ml.) and concentrated hydrochloric acid (15 ml.). The resulting solution was poured into water (150 ml.), treated with excess of sodium hydrogen carbonate, and insoluble material discarded. Acidification of the filtrate with hydrochloric acid yielded crude *p*-bromobenzoic acid (0.57 g.); after crystallisation from aqueous ethanol, the acid formed plates, m. p. and mixed m. p. 252—254°. The infrared spectrum was identical with that of the authentic specimen.

Bromination of N- α -Bromobenzylidene-N'-(2,4-dibromophenyl)hydrazine.—A suspension of *N*- α -bromobenzylidene-N'-(2,4-dibromophenyl)hydrazine² (4.3 g.) in acetic acid (35 ml.) and bromine (2.6 ml.) was boiled under reflux for 1½ hr., hydrogen bromide being evolved. When cool, the product (4.2 g.) was collected, washed, and dried. Crystallisation from acetic acid gave *N*-(4, α -dibromobenzylidene)-N'-(2,4,6-tribromophenyl)hydrazine as needles, m. p. and mixed m. p. 180—181°.

N-(4, α -Dibromobenzylidene)-N'-(2,4-dibromo-6-methylphenyl)hydrazine.—Bromine (7.5 ml.) was added in one portion to a stirred suspension of benzaldehyde *o*-tolylhydrazone (4.75 g.) in acetic acid (24 ml.). The temperature rose rapidly to 80°, hydrogen bromide was evolved, and a brown sludge formed. When cool, the product was collected, and washed well with acetic acid. Crystallisation from acetic acid gave *N*-(4, α -dibromobenzylidene)-N'-(2,4-dibromo-6-methylphenyl)hydrazine (6.5 g.) as needles, m. p. 143—144° (Found: C, 32.1; H, 2.1; Br, 60.8; N, 5.4. C₁₄H₁₀Br₄N₂ requires C, 31.9; H, 1.9; Br, 60.8; N, 5.3%). The compound gave a cherry-red colour when boiled with ethanolic phenylhydrazine, and showed λ_{\max} . 234 (4.21) and 319 m μ (4.14) (these and other values in parentheses are log ϵ).

The compound (900 mg.) was acetolysed by being boiled under reflux for 2 hr. with anhydrous sodium acetate (620 mg.) in acetic acid (12.5 ml.). The crude product (830 mg.) was then boiled with ethanol (6 ml.) and concentrated hydrochloric acid (6 ml.) for 2 hr. Isolated essentially as in the previous case, the acid fraction (80 mg.) afforded *p*-bromobenzoic acid as plates (from aqueous ethanol), m. p. and mixed m. p. 252—254°.

Perbromination of m-Nitroacetophenone Phenylhydrazine.—Bromine (10 ml.) was added to a stirred suspension of *m*-nitroacetophenone phenylhydrazine (5.5 g.) in acetic acid (25 ml.). The mixture was then heated under reflux for ½ hr., cooled, and poured into water (500 ml.). The solid was collected, washed, dried, and crystallised from acetic acid, giving *N*-(α -bromo-3-nitrobenzylidene)-N'-(2,4,6-tribromophenyl)hydrazine (1.1 g.) as pale yellow needles, m. p. 172—174° (Found: C, 27.9; H, 1.3; Br, 57.5; N, 7.6. C₁₃H₇Br₄N₃O₂ requires C, 28.0; H, 1.3; Br, 57.5; N, 7.5%). The compound gave a reddish-brown colour when boiled with ethanolic phenylhydrazine, and showed λ_{\max} . 314 m μ (4.16).

Bromination of N-(α -Bromo-3-nitrobenzylidene)-N'-(2,4-dibromophenyl)hydrazine.—A mixture of *N*-(α -bromo-3-nitrobenzylidene)-N'-(2,4-dibromophenyl)hydrazine² (2 g.), acetic acid (40 ml.), and bromine (1.3 ml.) was heated under reflux for 1 hr., the product separating. When cool, the solid was collected, washed, and crystallised from acetic acid, giving *N*-(α -bromo-3-nitrobenzylidene)-N'-(2,4,6-tribromophenyl)hydrazine (1.65 g.) as needles, m. p. and mixed m. p. 172—174°.

m-Nitroacetophenone 2,4,6-Trichlorophenylhydrazine.—The hydrazone, prepared from the ketone and 2,4,6-trichlorophenylhydrazine,⁸ formed needles (from butanol), m. p. 156—157° (Found: Cl, 29.7; N, 11.8. C₁₄H₁₀Cl₃N₃O₂ requires Cl, 29.8; N, 11.7%), λ_{\max} . 312 m μ (4.27).

N-Chloro-N'-(α -methyl-3-nitrobenzylidene)-N-(2,4,6-trichlorophenyl)hydrazine.—Chlorine was passed through a suspension of *m*-nitroacetophenone 2,4,6-trichlorophenylhydrazine (2.5 g.) in acetic acid (14 ml.) at room temperature for 15 min. After 18 hr., the *N*-chloro-compound (1.65 g.) was collected and dried; crystallisation from a small volume of acetic acid gave amber rhombohedra, m. p. 72—73.5° (Found: Cl, 36.3; N, 10.4. C₁₄H₉Cl₄N₃O₂ requires Cl, 36.1; N, 10.7%), λ_{\max} . 251 (4.10) and 417 m μ (2.34).

Reduction and Attempted Rearrangement of the N-Chloro-compound.—(a) A solution of sodium iodide (470 mg.) in water (1.5 ml.) and acetic acid (3 ml.) was added to a solution of the *N*-chloro-compound (650 mg.) in acetic acid (6 ml.) at 50—60°. Iodine was immediately liberated, and *m*-nitroacetophenone 2,4,6-trichlorophenylhydrazine (410 mg.) separated as a sandy solid. This was collected, washed with ethanol, and dried; crystallisation from butanol (charcoal) gave needles, m. p. and mixed m. p. 152—156°.

(b) A solution of the *N*-chloro-compound (1 g.) in acetic acid (8 ml.) and water (0.5 ml.) was

⁸ Chattaway and Irving, *J.*, 1931, 1740.

boiled for 10 min., the solution turning deep red. Cooling and scratching induced the separation of *m*-nitroacetophenone 2,4,6-trichlorophenylhydrazone (80 mg.) (needles, from butanol, m. p. and mixed m. p. 156—157°). Dilution of the reaction filtrate gave tar.

N-(α -Chloro-3-nitrobenzylidene)-*N'*-(2,4-dichloro-6-methylphenyl)hydrazine.—Chlorine was passed through a suspension of *m*-nitrobenzaldehyde *o*-tolylhydrazone (1 g.) in glacial acetic acid (20 ml.). An exothermic reaction occurred and soon the mixture set practically solid. Passage of chlorine was continued until the solid began to re-dissolve. The product (780 mg.) was then collected, washed, and dried. From acetic acid, *N*-(α -chloro-3-nitrobenzylidene)-*N'*-(2,4-dichloro-6-methylphenyl)hydrazine separated as pale yellow needles, m. p. 140—141° (Found: Cl, 29.7. $C_{14}H_{10}Cl_3N_3O_2$ requires Cl, 29.7%), λ_{max} . 315 μ (4.25). The compound gave a reddish-brown colour when boiled with ethanolic phenylhydrazine.

Perchlorination of m-Nitrobenzaldehyde o-Tolylhydrazone.—Chlorine was passed through a suspension of the hydrazone (5 g.) in acetic acid (50 ml.), the temperature rising to 50° as the yellow trichloro-derivative separated. The temperature was then raised to 60°, and passage of chlorine continued until an orange solution resulted (30 min.). This was kept overnight at room temperature, an orange granular precipitate (3.77 g.) slowly forming. *N*-Chloro-*N'*-(α -chloro-3-nitrobenzylidene)-*N*-(2,4-dichloro-6-methylphenyl)hydrazine crystallised from ethanol as orange rhombohedra, m. p. 76.5—78° (Found: Cl, 36.0; N, 10.8. $C_{14}H_9Cl_4N_3O_2$ requires Cl, 36.1; N, 10.7%), λ_{max} . 295 (3.99) and 418 μ (2.73).

Reduction and Attempted Rearrangement of the N-Chloro-compound.—(a) Reduction of the *N*-chloro-compound (400 mg.) as above with proportional quantities of potassium iodide and solvents gave *N*-(α -chloro-3-nitrobenzylidene)-*N'*-(2,4-dichloro-6-methylphenyl)hydrazine (320 mg.), m. p. (and mixed m. p.), 140—141°, after crystallisation from acetic acid.

(b) A solution of the *N*-chloro-compound (1 g.) in acetic acid (20 ml.) and water (1 ml.) was boiled for 10 min., the solution becoming dark brown. Cooling and scratching induced the separation of *N*-(α -chloro-3-nitrobenzylidene)-*N'*-(2,4-dichloro-6-methylphenyl)hydrazine (80 mg.) (needles, m. p. and mixed m. p. 140—141°, from acetic acid). Dilution of the reaction filtrate gave tar.

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