The Chlorination of Aldehyde and Ketone Phenylhydrazones

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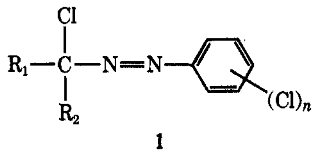
Azo compounds have been prepared by reaction of aldehyde and ketone phenylhydrazones with chlorine. Chlorination of propionaldehyde (2,4,6-trichlorophenyl)hydrazone or propionaldehyde phenylhydrazone gave 1′,1′,2,4,6-pentachlorobenzeneazopropane (**3**). The product, an orange liquid, was thermally stable up to 250° and was stable in acidic or basic media at room temperature. Chlorination of acetone (2,4,6-trichlorophenyl)hydrazone gave 1′,2,4,6-tetrachloro-1′-methylbenzeneazoethane (**9**). Nucleophilic displacement of the 1′-chlorine substituent in **9** by cyanide and acetate gave the corresponding azo cyanide (**10**) and azo acetate (**11**). The azo products obtained by chlorination of other ketone phenylhydrazones are described.

We have recently found that chlorination of aldehyde and ketone phenylhydrazones affords a convenient synthesis for the 1′-chlorobenzeneazoalkanes of structure **1**. The azo compounds formed from aldehyde phenylhydrazones are stable compounds, whereas those formed from ketone phenylhydrazones are somewhat unstable, reactive chemicals. The chlorination of benzaldehyde phenylhydrazones to benzoyl chloride phenylhydrazones and ketone phenylhydrazones to the corresponding ring chlorinated ketone phenylhydrazones has been reported,[1,2] but little was reported concerning the formation of azo compounds in these reactions.[3]



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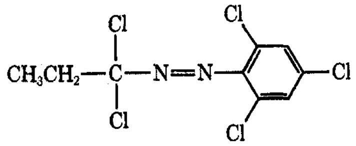
R_1 = alkyl or phenyl
R_2 = alkyl, phenyl, or chlorine
For nature of *n*, see text.

Treatment of a solution of propionaldehyde (2,4,6-trichlorophenyl)hydrazone in benzene with chlorine followed by distillation of the reaction product afforded 1′,1′,2,4,6-pentachlorobenzeneazopropane (**3**) in high yield (76%). The same orange-colored liquid was obtained by chlorination of propionaldehyde phenylhydrazone in chloroform. That the product was the azo compound **3** and not the isomeric *N*-chloro compound **4** was indicated by spectral comparisons with 2,4,6-trichloro-1′-methylbenzeneazoethane[4] (**5**), prepared from acetone (2,4,6-trichlorophenyl)hydrazone.



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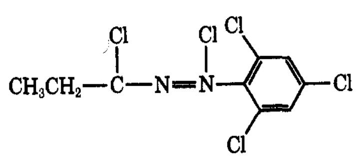

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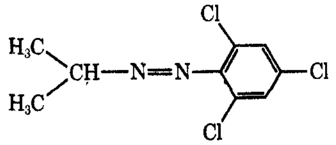

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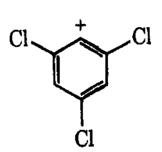
Compounds **3** and **5** showed a weak intensity absorption near 405 $m\mu$ (ϵ 100–400) characteristic of the phenylazo linkage[5] and also showed strong ir bands at 1550 and 1570 cm^{-1} that appear characteristic for the (2,4,6-trichlorophenyl)azo structure.[6] The mass spectra of **3** and **5** show, in addition to the molecular ion, major peaks for ions **6** and **7**. Similar mass spectral fragmentation has been reported for azobenzenes,[7a] while phenylhydrazones show instead **8** as a major ion.[7b]



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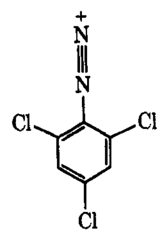

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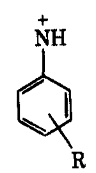

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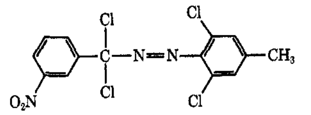
[1] J. E. Humphries, H. Humble, and R. Evans, *J. Chem. Soc.*, **127**, 1304 (1925).

[2] (a) F. D. Chattaway and A. B. Adamson, *ibid.*, 843 (1930); (b) J. M. Burgess and M. S. Gibson, *ibid.*, 1500 (1964).

[3] We believe that the initial product obtained on chlorination of *m*-nitrobenzoyl chloride (2,6-dichloro-*p*-tolyl)hydrazone[2a] is 1′,1′,2,6-tetrachloro-4-methyl-1′-(*m*-nitrophenyl)benzeneazomethane (**2**) and not the



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isomeric *N*-chloro compound reported by Chattaway. While we have not repeated this reaction, Mr. V. L. Rizzo of these laboratories has observed that benzoyl chloride (2,4,6-trichlorophenyl)hydrazone reacts slowly (*ca.* 24 hr) with chlorine in carbon tetrachloride with formation of 1′,1′,2,4,6-pentachloro-1′-phenylbenzeneazomethane. The compound was purified by chromatography on silica gel; the nmr, ir, and uv spectral data were consistent with the proposed structure. The structure of a second compound described by Chattaway[2a] was recently revised; see M. S. Gibson, *ibid.*, 2270 (1962). The *N*-chloro compounds reported in ref 2b are also probably azo compounds; all show the low-intensity band near 410 $m\mu$ expected for the azo structure.

[4] The details of the synthesis are given in the Experimental Section. 1′-Methylbenzeneazoethane has been prepared by the same method; see R. C. Goodwin and J. R. Bailey, *J. Amer. Chem. Soc.*, **47**, 167 (1925).

[5] A. E. Gillam and E. S. Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," E. Arnold, London, 1958, p 127; A. Burawoy, *J. Chem. Soc.*, 1177 (1939).

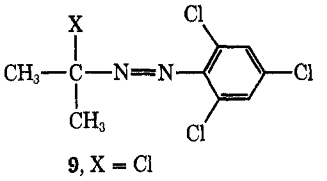
[6] We have prepared a large number of compounds containing the (2,4,6-trichlorophenyl)azo group. Additional examples are given in an accompanying paper. All the compounds prepared show the two characteristic ir bands at about 1550 and 1570 cm^{-1}.

[7] (a) J. H. Bowie, G. E. Lewis, and R. G. Cooks, *J. Chem. Soc. B*, 621 (1967); (b) W. D. Crow, J. L. Occolowitz, and R. K. Solly, *Aust. J. Chem.*, **21**, 761 (1968).

Compound **3** was thermally stable up to 250°. Above this temperature it decomposed with evolution of 1 molar equiv of gas, presumably nitrogen, leaving a viscous residue. The azo compound was stable at room temperature in ethanolic solutions of hydrochloric acid or sodium hydroxide.[8]

Several azo compounds were formed by chlorination of ketone phenylhydrazones. They were all unstable to chromatography on silica gel and some decomposed when stored at room temperature for several months.

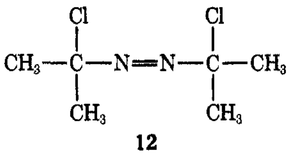
A solution of acetone (2,4,6-trichlorophenyl)hydrazone in chloroform reacted with chlorine to give 1′,2,4,6-tetrachloro-1′-methylbenzeneazoethane (**9**). Compound **9** showed the uv and ir bands found characteristic for the azo products **3** and **5** and a similar mass spectral fragmentation pattern. Unlike **3**, **9** is a reactive compound, the 1′-chlorine substituent being readily displaced by nucleophiles. Thus, **9** reacted with potassium cyanide to give **10** and with sodium acetate in acetic acid to give **11**.[9] Such reactivity has been observed by Benzing[10] for the related azo product **12** prepared by chlorination of acetone azine.



9, X = Cl

10, X = CN

11, X = $O-\underset{\underset{O}{\|}}{C}-CH_3$



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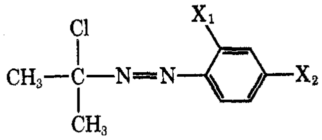
Acetone (2,4-dichlorophenyl)hydrazone gave a single azo product **13**, when chlorinated, while acetone phenylhydrazone gave a mixture of products, mainly **13**, **14**, and **15**, upon chlorination.[11] This mixture of products could be separated only by vpc, and was characterized by vpc comparison with the azo mixtures obtained by chlorination of the three isomeric acetone monochlorophenylhydrazones. The nmr spectra of all the azo mixtures show a characteristic singlet methyl absorption at about δ 1.90 and the expected aromatic absorption patterns.



13, $X_1 = X_2 = Cl$

14, $X_1 = H$; $X_2 = Cl$

15, $X_1 = Cl$; $X_2 = H$

Chlorination of the (2,4,6-trichlorophenyl)hydrazones of acetophenone and benzophenone gave the crystalline azo derivatives 1′,2,4,6-tetrachloro-1′-phenylbenzeneazoethane and 1′,2,4,6-tetrachloro-1′,1′-diphenylbenzeneazomethane, respectively. We have extended our studies to include other classes of phenylhydrazones and have found that azo compounds are usually formed during the chlorination reactions. A part of this work is reported in an accompanying paper.[12]

Experimental Section[13]

The apparatus used for the chlorination reactions was routinely fitted with a condenser cooled with a mixture of Dry Ice and acetone to prevent loss of chlorine but allow hydrogen chloride generated in the reaction to escape. Chlorination was effected by condensing a measured volume of liquid chlorine in a separate container and allowing it to pass by evaporation into the reaction vessel.

1′,1′,2,4,6-Pentachlorobenzeneazopropane (3). Method A.—A mixture of (2,4,6-trichlorophenyl)hydrazine (48 g, 0.23 mol) and propionaldehyde (17.5 g, 0.30 mol) in benzene (300 ml) was refluxed for 1 hr, a Dean and Stark apparatus being used to remove the water formed by the reaction. The solution of propionaldehyde (2,4,6-trichlorophenyl)hydrazone thus obtained was cooled to 0° and stirred while chlorine (35 ml liquid, 0.74 mol) was added. After 2 hr the benzene was removed under reduced pressure, Skellysolve B (500 ml) was added to the residual oil, and the solution was filtered to remove a small quantity of insoluble tar. After removal of the Skellysolve B the residue was distilled to give 56 g (76%) of 1′,1′,2,4,6-pentachlorobenzeneazopropane: bp 145° (0.4 mm); ir (film) 1550 (s) and 1570 cm^{-1} (s); nmr ($CDCl_3$) δ 1.25 (t, 3, CH_3), 2.64 (q, 2, CH_2), and 7.30 (s, 2, ArH); λ_{max}^{hexane} 236 mμ (shoulder, ε 7300), 280 (5000), and 408 (317); mass spectrum m/e for ^{35}Cl (rel intensity, number of Cl atoms in ion) 318 (2, 5), 283 (8, 4), 207 (100, 3), and 179 (65, 3).

Anal. Calcd for $C_9H_7Cl_5N_2$: C, 33.73; H, 2.20; Cl, 55.32; N, 8.74. Found: C, 33.80; H, 2.18; Cl, 55.60; N, 8.98.

Method B.—A mixture of phenylhydrazine (54 g, 0.5 mol) and propionaldehyde (35 g, 0.6 mol) in benzene (300 ml) was refluxed for 1 hr, a Dean and Stark apparatus being used to remove the water formed by the reaction. Evaporation of the benzene gave a residue of propionaldehyde phenylhydrazone which was dissolved in chloroform (500 ml). Chlorine (190 ml liquid, 4.1 mol) was added to the stirred reaction solution while maintaining the temperature at −40°. The solution was allowed to warm and held at 10° for 3 hr. The solvents were removed under reduced pressure, Skellysolve B (500 ml) was added, and the solution was filtered to remove the insoluble tars. After removal of the Skellysolve B, the residue was distilled to give 109.6 g (68%) of 1′,1′,2,4,6-pentachlorobenzeneazopropane, bp 145-150° (0.4 mm); the product was identical with that obtained by method A by ir, vpc, nmr, and tlc analysis.

Stability of Compound 3.—Two solutions of **3** (1 g) in ethanol (50 ml) were prepared. To one of these was added a solution of sodium hydroxide (1.0 g) in water (5 ml). To the second solution was added concentrated hydrochloric acid (3 ml). After 2 hr at 25° the reaction mixtures were diluted and extracted with chloroform. In each case evaporation of the chloroform gave an oil (85-90% recovery), identified as unchanged **3** by nmr, ir, and tlc analysis.

2,4,6-Trichloro-1′-methylbenzeneazoethane (5).—Platinum oxide (1 g) was added to a solution of acetone (2,4,6-trichlorophenyl)hydrazone (25 g, 0.1 mol) in ethanol (180 ml) containing concentrated hydrochloric acid (10 ml). The solution was hydrogenated for 15 min until 0.12 mol of hydrogen had been absorbed. The solution was filtered, the filtrate was diluted with ice–water, and concentrated hydrochloric acid (10 ml) was added. A solution of sodium nitrite (7.5 g, 0.11 mol) in water was added to the

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[8] Stability to base would be unexpected if the structure of the chlorination product was the acid chloride phenylhydrazone **4**.

[9] Azo acetates related to **11** have previously been prepared by reaction of acetone phenylhydrazones with lead tetraacetate; see D. C. Iffland, L. Salisbury, and W. R. Schafer, *J. Amer. Chem. Soc.*, **83**, 749 (1961).

[10] E. Benzing, *Justus Liebigs Ann. Chem.*, **631**, 10 (1960).

[11] A recent publication describes the preparation of the fluoro azo compound 1′-fluoro-1′-methylbenzeneazoethane by action of lead diacetate difluoride on acetone phenylhydrazone; see J. Bornstein and L. Skarlos, *J. Org. Chem.*, **35**, 1230 (1970).

[12] M. W. Moon, *J. Org. Chem.*, **37**, 386 (1972).

[13] Melting points were taken in open capillary tubes using a Thomas-Hoover melting point apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer Model 137 spectrophotometer and the uv spectra on a Cary Model 15 spectrophotometer. The nmr spectra were recorded on a Varian A-60A spectrometer; chemical shifts are reported in δ units using $CDCl_3$ as solvent and tetramethylsilane as the internal standard. (In nmr descriptions s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet.) Vpc data were obtained using a Micro Tek gas chromatograph Model 220, a column (45 cm × 3 mm i.d.) of 3% QF-1 on 100-120 mesh Gas-Chrom Q, a helium carrier gas (flow rate 85 ml/min), and a hydrogen flame ionization detector. The mass spectra were recorded at 70 eV on an LKB 9000A gas chromatograph–mass spectrometer using a column of 3% QF-1 (4 ft × 3 mm i.d.) maintained at 95°.

stirred reaction mixture. After 10 min an unstable solid (13.4 g) was filtered off. Nmr analysis indicated that this was the *N*-nitroso derivative of 1-isopropyl 2-(2,4,6-trichlorophenyl)hydrazine: nmr ($CDCl_3$) δ 1.60 [d, 6, $(CH_3)_2$], 4.44 (m, 1, CH), 7.30 (s, 2, ArH), and 7.90 (s, 1, NH).

The above solid was dissolved in Skellysolve B (80 ml) at 25°; it decomposed with evolution of nitrous fumes within 1 hr. The solution was applied to a column (50 × 2 cm diameter) of silica gel which was eluted with benzene. The fractions containing the yellow azo compound were pooled and the solvent was removed at 110° (5 mm) to give 8.4 g of 2,4,6-trichloro-1′-methylbenzeneazoethane: ir (film) 1550 (s), and 1570 cm^{-1} (s); nmr ($CDCl_3$) δ 1.44 [d, 6, $(CH_3)_2$], 4.16 (m, 1, CH), and 7.34 (s, 2, ArH); λ_{max}^{hexane} 247 mμ (ϵ 7600), 275 (shoulder, 2400), and 403 (169); mass spectrum *m/e* for ^{35}Cl (rel intensity, number of Cl atoms in ion) 250 (5, 3), 207 (79, 3), 179 (54, 3), and 43 (100, 0).

Anal. Calcd for $C_9H_9Cl_3N_2$: C, 42.97; H, 3.60; Cl, 42.29; N, 11.14. Found: C, 43.47; H, 3.65; Cl, 42.62; N, 11.04.

1′,2,4,6-Tetrachloro-1′-methylbenzeneazoethane (9).—Chlorine (10 ml liquid, 0.22 mol) was added to a stirred solution of acetone (2,4,6-trichlorophenyl)hydrazone (37.5 g, 0.1 mol) in chloroform (200 ml) at −40°. The reaction solution was held at 0° for 1 hr and was then evaporated under reduced pressure to 41.0 g of 1′,2,4,6-tetrachloro-1′-methylbenzeneazoethane. A portion (10 g) of the product was distilled to give the analytical sample: bp 120–122° (0.15 mm); ir (film) 1550 (s) and 1570 cm^{-1} (s); nmr ($CDCl_3$) δ 1.98 [s, 6, $(CH_3)_2$] and 7.34 (s, 2, ArH); λ_{max}^{hexane} 242 mμ (ϵ 7850), 272 (3800), and 403 (232); mass spectrum *m/e* for ^{35}Cl (rel intensity, number of Cl atoms in ion) 207 (75, 3), 194 (37, 3), 179 (45, 3), 74 (100, 0), and 41 (96, 0).

Anal. Calcd for $C_9H_8Cl_4N_2$: C, 37.79; H, 2.82; Cl, 49.59; N, 9.80. Found: C, 37.97; H, 2.90; Cl, 49.05; N, 9.43.

2-Methyl-2-[(2,4,6-trichlorophenyl)azo]propionitrile (10).—Potassium cyanide (10 g, 0.15 mol) in water (50 ml) was added to a stirred solution of 1′,2,4,6-tetrachloro-1′-methylbenzeneazoethane (7.5 g, 0.026 mol) in ethanol (100 ml). After 15 min the precipitate was filtered off, washed well with water, and air dried to give 5.3 g (74%) of 2-methyl-2-[(2,4,6-trichlorophenyl)azo]propionitrile, mp 72–76°. Two recrystallizations from petroleum ether (bp 30–60°) gave the analytical sample: mp 76–78°; ir (Nujol) 1555 (s) and 1575 cm^{-1} (s); nmr ($CDCl_3$) δ 1.81 [s, 6, $(CH_3)_2$] and 7.28 (s, 2, ArH); λ_{max}^{hexane} 288 mμ (ϵ 5320) and 414 (362).

Anal. Calcd for $C_{10}H_8Cl_3N_3$: C, 43.43; H, 2.91; Cl, 38.35. Found: C, 43.55; H, 3.07; Cl, 38.47.

1′-Acetoxy-2,4,6-trichloro-1′-methylbenzeneazoethane (11).—1′-2,4,6-Tetrachloro-1′-methylbenzeneazoethane (7.5 g, 0.026 mol) was added to a stirred suspension of anhydrous sodium acetate (10 g, 0.12 mol) in acetic acid (40 ml). After 1 hr water was added and the precipitate was filtered off, washed well with water, and air dried to give 7.7 g (96%) of 1′-acetoxy-2,4,6-trichloro-1′-methylbenzeneazoethane, mp 44–48°. Two recrystallizations from petroleum ether gave the analytical sample: mp 48–50°; ir (Nujol) 1750 (vs, C=O), 1545 (s), and 1565 cm^{-1} (s); nmr δ 1.72 [s, 6, $(CH_3)_2$], 2.08 (s, 3, CH_3C=O), and 7.24 (s, 2, ArH).

Anal. Calcd for $C_{11}H_{11}Cl_3N_2O_2$: C, 42.67; H, 3.58; Cl, 34.35; N, 9.05. Found: C, 42.97; H, 3.86; Cl, 34.55; N, 8.74.

1′,2,4-Trichloro-1′-methylbenzeneazoethane (13).—Chlorine (10.5 ml liquid, 0.23 mol) was added to a stirred solution of acetone (2,4-dichlorophenyl)hydrazone (18.8 g, 0.087 mol) in chloroform (200 ml) at −40°. The reaction solution was warmed to 0° for 1 hr and was then concentrated to give 20.8 g of red oil. This was distilled to give 1′,2,4-trichloro-1′-methylbenzeneazoethane in high yield: bp 114–116° (0.30 mm); ir (film) 1575 (s), 1530 (m), and 1510 cm^{-1} (m); nmr δ 1.88 [s, 6, $(CH_3)_2$] with aromatic hydrogens at 7.08 (d of d, *J* = 2 and 8 Hz), 7.30 (d, 1, *J* = 8 Hz), and 7.37 (d, 1, *J* = 2 Hz).

Anal. Calcd for $C_9H_9Cl_3N_2$: C, 42.98; H, 3.61; Cl, 42.29; N, 11.14. Found: C, 42.78; H, 3.59; Cl, 42.52; N, 11.28.

Chlorination of Acetone Phenylhydrazone.—Chlorine (20 ml liquid, 0.43 mol) was added to a stirred solution of acetone phenylhydrazone (14.8 g, 0.1 mol) in chloroform (100 ml) at −40°. The solution was warmed to 10° for 30 min and was then concentrated to a gum. Skellysolve B (200 ml) was added and the solution was filtered to remove insoluble tars. Evaporation of the Skellysolve B gave 13.1 g of dark red oil which was characterized as a mixture of **13**, **14**, and **15** by nmr and vpc methods. The nmr spectrum showed a singlet methyl absorption at δ 1.89 and about four aromatic hydrogens absorbing between δ 7.0 and 7.8. Vpc[11] showed the presence of **14** and **15** (retention times at 75°, 2.2 and 2.6 min, respectively) and **13** (retention time 5.4 min at 75°); the ratio of (**14** and **15**):**13** was 56:44.

Acetone phenylhydrazones were not present in the reaction products. Vpc retention times for the various acetone phenylhydrazones at 75° were as follows: phenylhydrazone, 3.4 min; (*o*-chlorophenyl)hydrazone, 3.4 min; (*m*-chlorophenyl)hydrazone, 13.0 min; (*p*-chlorophenyl)hydrazone, 12.6 min; (2,4-dichlorophenyl)hydrazone, 9.6 min.

Under the conditions used for the chlorination of acetone phenylhydrazone (a) acetone (*p*-chlorophenyl)hydrazone gave a mixture of **13** (25%) and **14** (75%); (b) acetone (*o*-chlorophenyl)-hydrazone gave a mixture of **13** (25%) and **15** (75%); (c) acetone (*m*-chlorophenyl)hydrazone gave a product showing peaks with retention times of 2.4 (50%) and 6.2 min (50%), presumably 1′,3-dichloro-1′-methylbenzeneazoethane and the related trichloroazo compound.

1′,2,4,6-Tetrachloro-1′-phenylbenzeneazoethane.—A stirred mixture of acetophenone (2,4,6-trichlorophenyl)hydrazone (9 g, 0.029 mol) and chlorine (2.5 ml, 0.055 mol) in chloroform (100 ml) was kept at −20° for 1 hr and the solvent was then evaporated under reduced pressure. The residual oil was crystallized from petroleum ether to give 7.7 g of 1′,2,4,6-tetrachloro-1′-phenylbenzeneazoethane, mp 41–44°. Recrystallization from the same solvent gave the analytical sample: mp 40–44°; nmr δ 2.33 (s, 3, CH_3) and 7.28–7.80 (m, 7, ArH).

Anal. Calcd for $C_{14}H_{10}Cl_4N_2$: C, 48.31; H, 2.90; Cl, 40.75; N, 8.05. Found: C, 48.38; H, 3.00; Cl, 41.08; N, 8.02.

1′,2,4,6-Tetrachloro-1′,1′-diphenylbenzeneazomethane.—Chlorine (5 ml liquid, 0.11 mol) was added to a stirred solution of benzophenone (2,4,6-trichlorophenyl)hydrazone (18.75 g, 0.05 mol) in carbon tetrachloride (200 ml) at −10°. After 30 min the solvent was evaporated and the residual oil was crystallized from Skellysolve B to give 18.5 g of 1′,2,4,6-tetrachloro-1′,1′-diphenylbenzeneazomethane, mp 76°. Recrystallization from the same solvent gave the analytical sample, mp 74–76°.

Anal. Calcd for $C_{19}H_{12}Cl_4N_2$: C, 55.64; H, 2.95; Cl, 34.58; N, 6.83. Found: C, 55.62; H, 3.27; Cl, 34.56; N, 6.61.

Registry No.—**3**, 32974-64-4; **5**, 32974-65-5; **9**, 32974-66-6; **10**, 32974-67-7; **11**, 32974-68-8; **13**, 32974-69-9; 1′,2,4,6-tetrachloro-1′-phenylbenzeneazoethane, 32974-70-2; 1′,2,4,6-tetrachloro-1′,1′-diphenylbenzeneazomethane, 32974-71-3.

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