Chloromethyl Bis-(*p*-chlorophenyl)-carbinols

BY J. M. PEPPER[1] AND MARSHALL KULKA

The heretofore unknown monochloromethyl (III) and dichloromethyl bis-(*p*-chlorophenyl)-carbinol (IV) have now been prepared from *p*-chlorophenylmagnesium bromide and the corresponding ω-chlorinated *p*-chloroacetophenones I and II.[2] Dehydration of the carbinols III and IV with concentrated sulfuric acid resulted in the ethenes V and VI.[3]

$$p\text{-ClC}_6\text{H}_4\text{MgBr} + p\text{-ClC}_6\text{H}_4\text{COCHR}_1\text{R}_2 \longrightarrow$$

$$(\text{I}, \text{R}_1 = \text{H}, \text{R}_2 = \text{Cl})$$
$$(\text{II}, \text{R}_1 = \text{R}_2 = \text{Cl})$$

$$(p\text{-ClC}_6\text{H}_4)_2\text{C(OH)CHR}_1\text{R}_2 \longrightarrow (p\text{-ClC}_6\text{H}_4)_2\text{C}{=}\text{CR}_1\text{R}_2$$

$$\begin{array}{ll} (\text{III}, \text{R}_1 = \text{H}, \text{R}_2 = \text{Cl}) & (\text{V}, \text{R}_1 = \text{H}, \text{R}_2 = \text{Cl}) \\ (\text{IV}, \text{R}_1 = \text{R}_2 = \text{Cl}) & (\text{VI}, \text{R}_1 = \text{R}_2 = \text{Cl}) \end{array}$$

An attempt to prepare trichloromethyl bis-(*p*-chlorophenyl)-carbinol by the same method failed. The reaction product of *p*-chlorophenylmagnesium bromide and ω,ω,ω,*p*-tetrachloroacetophenone[2] was a low-boiling mixture of compounds (b. p. at 12 mm., 90–140°) one of which was identified as ω,ω,*p*-trichloroacetophenone (II). The formation of II must be attributed to the reducing action of the Grignard reagent.

Experimental

Chloromethyl Bis-(*p*-chlorophenyl)-carbinol (III).—A mixture of magnesium turnings (4 g.), *p*-chlorobromobenzene (28.8 g.), a crystal of iodine, and dry ether (150 cc.) was heated under reflux until no more magnesium dissolved (two hours). Then a solution of ω,*p*-dichloroacetophenone[2] (I) (23 g.) in dry ether (300 cc.) was added over a period of fifteen minutes with stirring and cooling on a water-bath. The resulting reaction mixture was heated under gentle reflux for ten minutes, poured into a mixture of cracked ice (200 g.) and concentrated hydrochloric acid (15 cc.), and shaken in a separatory funnel. The ether layer was separated, washed well with water and the solvent removed. The residue was distilled yielding a viscous liquid b. p. (0.06 mm.) 162–165°, yield, 31 g. or 85%.

Anal. Calcd. for $C_{14}H_{11}OCl_3$: C, 55.72; H, 3.65; Cl, 35.33. Found: C, 56.36, 56.28; H, 3.70, 3.88; Cl, 35.21, 35.37.

1-Chloro-2,2-bis-(*p*-chlorophenyl)-ethene (V).—The crude carbinol III (1.0 g.) was added to concentrated sulfuric acid (10 cc.) and the reaction mixture stirred for four and one-half hours. The dark solution was poured on ice, the white solid filtered, washed with water, dried and crystallized from methanol, m. p. 60–63°, yield, 0.80 g. Further crystallization from methanol or petroleum ether raised the melting point to 63–64°.

Anal. Calcd. for $C_{14}H_9Cl_3$: C, 59.25; H, 3.17; Cl, 37.56. Found: C, 59.75, 59.60; H, 3.40, 3.38; Cl, 37.73, 37.53.

Dichloromethyl Bis-(*p*-chlorophenyl)-carbinol (IV).—This was prepared from ω,ω,*p*-trichloroacetophenone[2] (II) and *p*-chlorobromobenzene by the same method as was III, b. p. (1 mm.) 200–210°, m. p. 108–109° from petroleum ether (60–80°), yield 52%.

Anal. Calcd. for $C_{14}H_{10}OCl_4$: C, 50.01; H, 2.98; Cl, 42.23. Found: C, 50.49, 50.25; H, 3.61, 3.25; Cl, 42.58, 42.64.

1,1-Dichloro-2,2-bis-(*p*-chlorophenyl)-ethene (VI).—This was prepared by dehydration of IV with sulfuric acid (see V above); yield, 90%; m. p. 86–87°, no depression when mixed with an authentic sample of 1,1-dichloro-2,2-bis-(*p*-chlorophenyl)-ethene.[3]

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[2] Gautier, *Ann. chim.*, [6] **14**, 395, 402, 403 (1888).

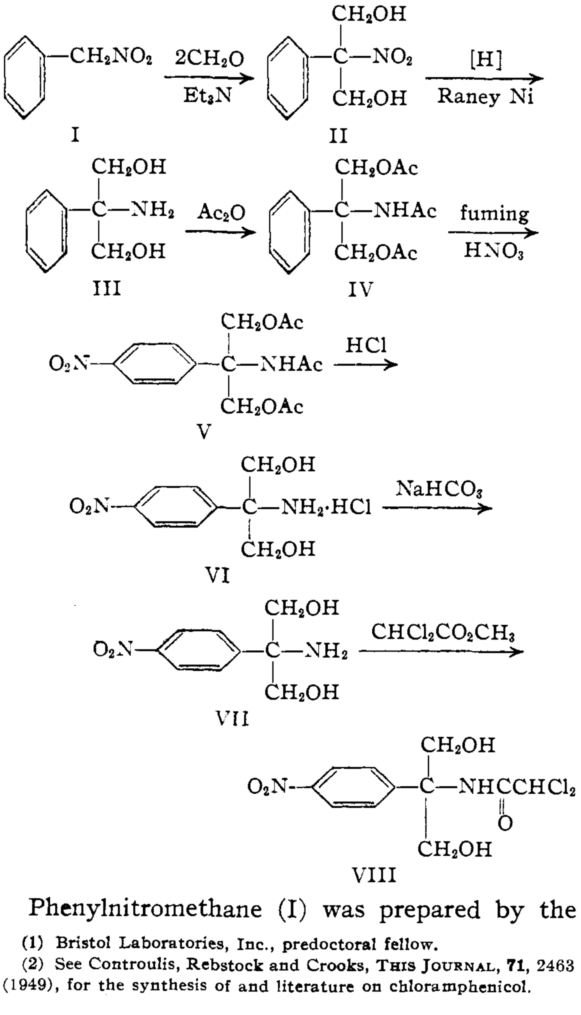
[3] Grummitt, Buck and Becker, THIS JOURNAL, **67**, 2265 (1945).

Synthesis of 2-Dichloroacetamido-2-*p*-nitrophenyl-1,3-propanediol, a Position Isomer of Chloramphenicol

BY P. M. RUOFF AND J. ROBERT MILLER[1]

In view of the marked activity against epidemic typhus, scrub typhus, typhoid fever and Rocky Mountain spotted fever reported for the antibiotic chloramphenicol,[2] D-*threo*-2-dichloroacetamido-1-*p*-nitrophenyl-1,3-propanediol, it appeared of interest to synthesize for biological screening a position isomer in which the *p*-nitrophenyl group was attached to the 2-position.

The synthesis of this isomer, 2-dichloroacetamido-2-nitrophenyl-1,3-propanediol, was carried out as illustrated in the following sequence of reactions



Phenylnitromethane (I) was prepared by the

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[2] See Controulis, Rebstock and Crooks, THIS JOURNAL, **71**, 2463 (1949), for the synthesis of and literature on chloramphenicol.