The Diazotisation of 3,4,5,6-Tetrachloroanthranilic Acid: A Convenient Synthesis of 2,3,4,5-Tetrachlorophenol[1]

By R. Howe

Diazotisation of 3,4,5,6-tetrachloroanthranilic acid in concentrated sulphuric acid solution and subsequent steam distillation of the diazonium sulphate solution gives 2,3,4,5-tetrachlorophenol in 77% yield and 3,4,5,6-tetrachlorosalicylic acid as a minor product. Diazotisation in glacial acetic acid solution gives a mixture of 1,2,3,4,5,6,7,8-octachloroacridone, 3,4,5,6,2′,3′,4′,5′-octachlorodiphenylamine-2-carboxylic acid, and 2,3,4,5-tetrachlorophenyl acetate. Mechanisms are suggested for the formation of these products.

2,3,4,5-TETRACHLOROPHENOL can be prepared from 3,4,5,6-tetrachloroanthranilic acid[2,3] *via* 2,3,4,5-tetrachloroaniline in 39% yield.[3,4] The yield (70%) of 2,3,4,5-tetrachloroaniline obtained by heating 3,4,5,6-tetrachloroanthranilic acid above its melting point[3] was improved to 90% by adding sufficient diethanolamine to form a homogeneous solution at 180°. The diazotisation[4] of 2,3,4,5-tetrachloroaniline was unreliable and never gave more than 43% yield of 2,3,4,5-tetrachlorophenol. The alternative route from 3,4,5,6-tetrachloroanthranilic acid *via* 3,4,5,6-tetrachlorosalicylic acid was therefore investigated.

3,4,5,6-Tetrachloroanthranilic acid in concentrated sulphuric acid solution was smoothly diazotised by treatment with sodium nitrite at 25°. When the resulting diazonium sulphate solution was added slowly to a small volume of boiling copper sulphate solution, 2,3,4,5-tetrachlorophenol steam distilled in 77% yield. A small amount of non-steam-volatile 3,4,5,6-tetrachlorosalicylic acid (5% yield) was usually carried over mechanically. Some of the 2,3,4,5-tetrachlorophenol was no doubt formed by decarboxylation of 3,4,5,6-tetrachlorosalicylic acid under the strongly acidic conditions, 90% sulphuric acid at 170°, which were finally attained. However, some 2,3,4,5-tetrachlorophenol must have been formed by a different route because it began to steam distil at the beginning of the addition of the diazonium sulphate solution, when the sulphuric acid concentration was very low and the temperature

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[1] B.P. 924,299/1963.

[2] W. R. Orndorff and E. H. Nichols, *Amer. Chem. J.*, 1912, **48**, 473.

[3] V. Villiger and L. Blangey, *Ber.*, 1909, **42**, 3549.

[4] G. J. Tiessens, *Rec. Trav. chim.*, 1931, **50**, 112.

was 100°. In a control experiment 3,4,5,6-tetrachlorosalicylic acid only began to decarboxylate appreciably at a sulphuric acid concentration of 32% and a temperature of 110°.

3,4,5,6-Tetrachlorosalicylic acid could not be isolated as the major product from the diazotisation. When the diazonium sulphate solution was added more quickly to copper sulphate solution, care being taken to ensure that the concentration of sulphuric acid remained below 32%, 3,4,5,6-tetrachlorosalicylic acid was isolated in 11% yield. The other reaction products were 2,3,4,5-tetrachlorophenol (33%) and tar (∼25%). Thus the major part of the 2,3,4,5-tetrachlorophenol must have arisen by a route which does not involve 3,4,5,6-tetrachlorosalicylic acid.

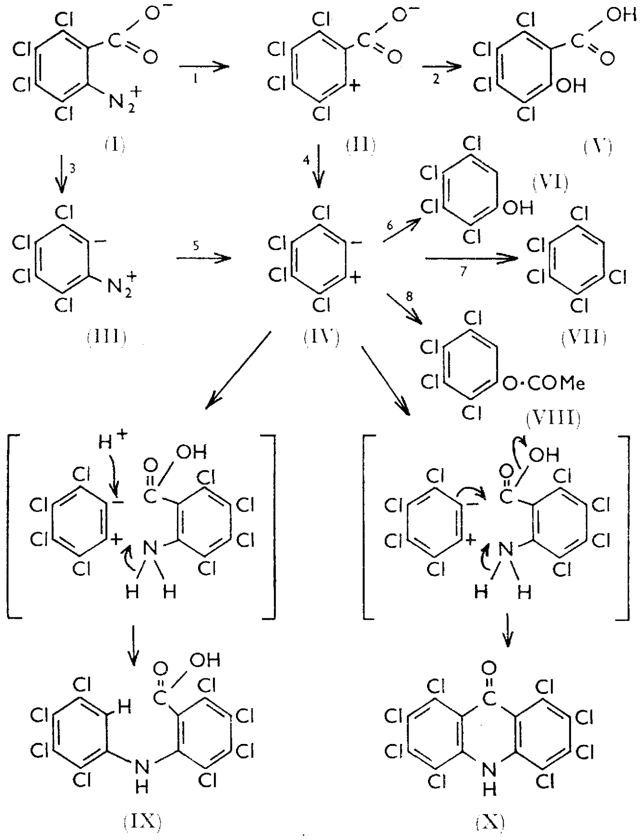
Diazotisation of 3,4,5,6-tetrachloroanthranilic acid in concentrated hydrochloric acid is difficult and incomplete.[5] It is also incomplete in 18% hydrochloric acid after 19 hr. Steam distillation of the resulting diazonium chloride solution gives a mixture of pentachlorobenzene (13%) and 2,3,4,5-tetrachlorophenol (3%).

Addition of sodium nitrite to a solution of 3,4,5,6-tetrachloroanthranilic acid in glacial acetic acid at 25° caused a brisk evolution of nitrogen and carbon dioxide, and after a few minutes 1,2,3,4,5,6,7,8-octachloroacridone, m. p. 370°, separated in 10% yield. This compound, of m. p. 340°, has previously been obtained by the action of antimony pentachloride on acridone.[6] The other products isolated from the diazotisation were 3,4,5,6,2′,3′,4′,5′-octachlorodiphenylamine-2-carboxylic acid (∼20% yield) and 2,3,4,5-tetrachlorophenyl acetate (∼40% yield).

The octachloroacridone did not arise from preformed octachlorodiphenylamine-2-carboxylic acid because the latter was not cyclised by heating under reflux with glacial acetic acid or by sodium nitrite in glacial acetic acid at 25°. It could be cyclised to octachloroacridone by concentrated sulphuric acid at 100°. It was not cyclised by thionyl chloride but formed the acid chloride, from which the amide and *NN*-diethylamide were prepared.

The formation of benzyne intermediates from aryldiazonium-2-carboxylates has previously been reported.[7,8] Five of the six products obtained by diazotisation of 3,4,5,6-tetrachloroanthranilic acid appear to have been formed *via* tetrachlorobenzyne (IV) as shown in the chart.

Only 11% of tetrachlorosalicylic acid (V) could be obtained from the diazotisation of tetrachloroanthranilic acid in sulphuric acid, and so decarboxylation of tetrachlorobenzenediazonium-2-carboxylate (I) to give (III) must have proceeded more readily than expulsion of nitrogen to give (II). None of the products isolated from the diazotisation of tetrachloroanthranilic acid in glacial acetic acid was formed by the minor route of decomposition of tetrachlorobenzenediazonium-2-carboxylate (I). The formation of tetrachlorophenol (VI), pentachlorobenzene (VII), and tetrachlorophenyl acetate (VIII) by the addition of water, hydrogen chloride, and acetic acid respectively to tetrachlorobenzyne (IV) is straightforward. Octachlorodiphenylamine-2-carboxylic acid (IX) is presumably formed by the addition of the amino-group of undiazotised tetrachloroanthranilic acid to tetrachlorobenzyne. A concerted reaction in which both the amino-group and carboxyl group of tetrachloroanthranilic acid react with tetrachlorobenzyne would give octachloroacridone (X). The formation of an acridone by diazotisation of an anthranilic acid appears to be new.



Reagents: 1, Minor route, $-N_2$; 2, H_2O; 3, Major route, $-CO_2$; 4, $-CO_2$; 5, $-N_2$; 6, H_2O; 7, HCl; 8, AcOH.

3,4,5,6-Tetrachlorosalicylic acid, hitherto unknown, and reported not to be obtained by chlorination of salicylic acid,[9] has been characterised.

EXPERIMENTAL

Diazotisation of 3,4,5,6-*Tetrachloroanthranilic Acid in Concentrated Sulphuric Acid*.—(*a*) Sodium nitrite (27 g., 0·39 mol.) was added during ½ hr. to a stirred solution of 3,4,5,6-tetrachloroanthranilic acid (100 g., 0·36 mol.) in concentrated sulphuric acid (850 c.c.) at 25°. After 16 hr. the diazonium sulphate solution was added during 5 hr. to a boiling solution of copper sulphate (10 g.) in water

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[5] R. Lesser and R. Weiss, *Ber.*, 1913, **46**, 3939.

[6] A. Eckert and K. Steiner, *Ber.*, 1914, **47**, 2628.

[7] M. Stiles, R. G. Miller, and U. Burckhardt, *J. Amer. Chem. Soc.*, 1963, **85**, 1792, 1798.

[8] L. Friedman and F. M. Logullo, *J. Amer. Chem. Soc.*, 1963, **85**, 1549.

[9] L. H. Farinholt, A. P. Stuart, and D. Twiss, *J. Amer. Chem. Soc.*, 1940, **62**, 1237.

(100 c.c.) through which a fast current of steam was passing. The steam distillate was collected. It was arranged by suitable heating that at the end of the addition the distillation flask contained ~90% by weight of sulphuric acid. The solid (74·3 g.), recovered from the steam distillate by ether extraction, was repeatedly extracted with light petroleum (b. p. 40—60°). The extract furnished 2,3,4,5-tetrachlorophenol (65 g., 77%), as needles, m. p. 117°.

The material (5 g.), which was not extracted into light petroleum, was purified by solution in 5% aqueous sodium hydrogen carbonate and precipitation with hydrochloric acid. 3,4,5,6-*Tetrachlorosalicylic acid* formed needles, m. p. 208° (from methanol–water) (Found: C, 30·9; H, 0·7; Cl, 51·2. $C_7H_2Cl_4O_3$ requires C, 30·4; H, 0·7; Cl, 51·5%). The acid gives a purple colour with ferric chloride. The *acetyl derivative* formed needles, m. p. 132—134° (from light petroleum, b. p. 60—80°) (Found: C, 34·2; H, 1·1. $C_9H_4Cl_4O_4$ requires C, 34·0; H, 1·25%).

(*b*) Diazonium sulphate solution prepared from 3,4,5,6-tetrachloroanthranilic acid (30 g.) was added during ½ hr. to a boiling solution of copper sulphate (10 g.) in water (1500 c.c.) through which steam was passing. Care was taken to ensure that the sulphuric acid concentration in the distillation flask did not rise above 25% by weight. As soon as the addition of diazonium sulphate solution was complete the distillation flask was cooled, and the contents were extracted with ether. The ether extract was separated into (i) 3,4,5,6-tetrachlorosalicylic acid (3·3 g., 11%), m. p. 205—206°, soluble in 5% aqueous sodium hydrogen carbonate, (ii) 2,3,4,5-tetrachlorophenol (2·25 g., 9%), m. p. 116°, insoluble in 5% aqueous sodium hydrogen carbonate solution but soluble in 5% aqueous sodium hydroxide, and (iii) alkali-insoluble tar (7·5 g.). 2,3,4,5-Tetrachlorophenol (6·0 g., 24%), m. p. 116°, was recovered from the steam distillate.

Diazotisation of 3,4,5,6-*Tetrachloroanthranilic Acid in Hydrochloric Acid*.—Sodium nitrite (1·35 g.) was added to a stirred suspension of 3,4,5,6-tetrachloroanthranilic acid (5 g.) in hydrochloric acid (200 c.c., 50% by volume) at 25°. After 16 hr., water (150 c.c.) was added and stirring was continued for 3 hr. The mixture was filtered to remove unchanged starting material (2 g.) and then the filtrate was steam distilled. The solid (0·43 g.), m. p. 74—76°, recovered from the steam distillate by ether extraction, was separated into (*a*) 2,3,4,5-tetrachlorophenol (75 mg., 3%), m. p. 115°, which was soluble in aqueous sodium hydroxide and (*b*) pentachlorobenzene (0·35 g., 13%), m. p. 85° (Found: C, 29·1; H, 0·5; Cl, 70·5. Calc. for C_6HCl_5: C, 28·7; H, 0·4; Cl, 70·9%).

Diazotisation of 3,4,5,6-*Tetrachloroanthranilic Acid in Acetic Acid*.—Sodium nitrite (5 g., 0·073 mol.) was added in one portion to a stirred solution of 3,4,5,6-tetrachloroanthranilic acid (20 g., 0·073 mol.) in glacial acetic acid (1250 c.c.) at 25°. Carbon dioxide and nitrogen were briskly evolved, and after a few minutes a yellow solid began to separate. The mixture was stirred for 16 hr. and then filtered, the filtrate being retained. The residual yellow solid (1·9 g.) consisted of 1,2,3,4,5,6,7,8-octachloroacridone which formed needles, m. p. 370° (from chlorobenzene) (Found: C, 33·2; H, 0·3; N, 3·0; Cl, 60·1. Calc. for $C_{13}HCl_8NO$: C, 33·1; H, 0·2; N, 3·0; Cl, 60·25%).

The filtrate retained above was evaporated at reduced pressure to remove acetic acid and the residue was stirred with ether (150 c.c.). The mixture was filtered, and the solid residue washed with ether (50 c.c.), the filtrate being retained. The solid residue (10·7 g.) was digested with hot water (100 c.c.) to remove sodium acetate and then the mixture was filtered. The dried residue (4·5 g.) consisted of 3,4,5,6,2′,3′,4′,5′-*octachlorodiphenylamine*-2-*carboxylic acid* which formed needles, m. p. 254—255° (from benzene) (Found: C, 31·8; H, 0·6; N, 2·9; Cl, 56·9. $C_{13}H_3Cl_8NO_2$ requires C, 31·9; H, 0·6; N, 2·85; Cl, 58·0%).

The ether filtrate retained above was evaporated and the residual gum (12·9 g.) was heated at 100° with 10% aqueous sodium hydroxide (100 c.c.) for 2 hr. The mixture was acidified with hydrochloric acid and then steam distilled. 2,3,4,5-Tetrachlorophenol (6·8 g., 40%), m. p. 114—115°, was recovered from the steam distillate.

In another experiment the above ether filtrate was not evaporated but was washed with dilute sodium hydroxide solution and then with water. The dried ether solution was evaporated and the residue was repeatedly extracted with light petroleum (b. p. 40—60°). The material extracted was 2,3,4,5-*tetrachlorophenyl acetate* which formed needles, m. p. 66—67° (from methanol–water) (Found: C, 35·3; H, 1·2; Cl, 52·1. $C_8H_4Cl_4O_2$ requires C, 35·0; H, 1·45; Cl, 51·9%).

1,2,3,4,5,6,7,8-*Octachloroacridone*.—3,4,5,6,2′,3′,4′,5′-Octachlorodiphenylamine-2-carboxylic acid (0·5 g.) and concentrated sulphuric acid (8 c.c.) were heated at 100° for 2 hr. The cooled solution was poured on to ice. The solid 1,2,3,4,5,6,7,8-octachloroacridone which separated formed yellow needles, m. p. and mixed m. p. 370°.

3,4,5,6,2′,3′,4′,5′-*Octachlorodiphenylamine*-2-*carbonyl Chloride*.—The acid (5 g.) and thionyl chloride (50 c.c.) were heated under reflux for 2 hr. and then the excess of thionyl chloride was evaporated. The residual *acid chloride* formed needles, m. p. 180—181° (from light petroleum, b. p. 60—80°) (Found: C, 31·2; H, 0·4; N, 2·8; Cl, 62·6. $C_{13}H_2Cl_9NO$ requires C, 30·75; H, 0·4; N, 2·75; Cl, 62·95%).

2-(NN-*Diethylcarbamoyl*)-3,4,5,6,2′,3′,4′,5′-*octachlorodiphenylamine*.—Diethylamine (5 c.c.) was added to a stirred solution of the above acid chloride (2·2 g.) in dry ether (200 c.c.). After 16 hr. the mixture was filtered, and the solid residue washed with water to remove diethylamine hydrochloride. The residual solid consisted of 2-(NN-*diethylcarbamoyl*)-3,4,5,6,2′,3′,4′,5′-*octachlorodiphenylamine* which formed prisms, m. p. 272—273° (from benzene) (Found: C, 37·3; H, 2·0; N, 5·3; Cl, 52·7. $C_{17}H_{12}Cl_8N_2O$ requires C, 37·5; H, 2·2; N, 5·15; Cl, 52·2%).

2-*Carbamoyl*-3,4,5,6,2′,3′,4′,5′-*octachlorodiphenylamine*.—A stirred solution of the acid chloride (2·2 g.) in dry ether (200 c.c.) was saturated with ammonia. After 16 hr. the mixture was filtered and the solid residue washed with water to remove ammonium chloride. The residual solid, 2-*carbamoyl*-3,4,5,6,2′,3′,4′,5′-*octachlorodiphenylamine* formed prisms, m. p. 298° (from chlorobenzene) (Found: C, 32·0; H, 1·0; N, 5·6; Cl, 58·0. $C_{13}H_4Cl_8N_2O$ requires C, 31·9; H, 0·8; N, 5·75; Cl, 58·2%).

Imperial Chemical Industries Ltd.,
Pharmaceuticals Division,
Alderley Park, Macclesfield,
Cheshire.

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