(D). An experiment identical with (C), but in which the solution of heptanal and cholesterol was allowed to stand 30 min. at 25° after the addition of 0.25 ml. of 5*N* hydrochloric acid, was carried out. The crude product contained 8.5% of conjugated cholestenone (ϵ 1370 at 232 mμ); 49 mg. (10%) of cholesteryl heptanoate was obtained as before, and had m.p. and mixed m.p. 110–111°.

Oxidation of cetyl alcohol. A solution of 4.84 g. (0.02 mole) of cetyl alcohol in 20 ml. of acetic acid and 10 ml. of acetone at 15° was treated with 10 ml. of chromic–sulfuric acid solution over 15 min., and stirred a further 15 min. at 25°. Addition of 130 ml. of 10% sodium hydroxide solution at 0°, followed by working up as usual, gave 2.33–2.48 g. (48.5–51.5%) of cetyl palmitate, m.p. and mixed m.p. 49.5–50.5°, identical in infrared spectrum with an authentic specimen.

Oxidation of heptanal and methanol. (*A*). A mixture of 2.28 g. (0.02 mole) of heptanal and 0.64 g. (0.02 mole) of methanol in 5 ml. of acetic acid was treated at 10° with 10 ml. of chromic-sulfuric solution during 15 min. After a further 15 min. stirring at 10°, the mixture was worked up as usual. Distillation gave 2.3 g., b.p. 48–62° (12 mm.), n_D^{24} 1.4098, shown by gas chromatography to consist of 1.5 g. (65%) of recovered aldehyde and 0.8 g. (28% yield) of methyl heptanoate, identical in retention time with an authentic specimen.

(*B*). Repetition of the experiment with 6.4 g. (0.2 mole) of methanol gave 2 g. of product, b.p. 63–65° (12 mm.), n_D^{25} 1.4096, consisting of 0.5 g. (22%) of recovered aldehyde and 1.5 g. (52% yield) of the methyl ester.

(*C*). When a mixture of 2.28 g. (0.02 mole) of heptanal and 6.4 g. (0.2 mole) of methanol in 3 ml. of acetic acid was treated with 20 ml. of chromic-sulfuric acid solution at 10° during 20 min., (stirred for a further 10 min. at 10°), the product was 2.5 g., b.p. 56–66° (12 mm.), n_D^{24} 1.4097, consisting of 1.65 g. of methyl heptanoate (57%) and 0.85 g. (37%) of heptanal (by gas chromatography).

(*D*). Repetition of experiment (C) using 30 ml. of chromic-sulfuric acid solution (added over 30 min. at 10°), afforded 2.6 g. of product, n_D^{24} 1.4102, containing 1.75 g. (61%) of methyl ester and 0.85 g. (37%) of recovered aldehyde.

(*E*). When experiment (C) was repeated with only 5 ml. of chromic-sulfuric acid solution, the product was 2.45 g., b.p. 56–66° (12 mm.), n_D^{24} 1.4098, consisting of 1.7 g. of recovered aldehyde (*i.e.* 1.14 g. (0.01 mole) plus 0.56 g. (45% of 0.01 mole) and 0.75 g. (52% yield of 0.01 mole) of methyl heptanoate.

Oxidation of n-butyl alcohol. A solution of 14.8 g. (0.2 mole) of *n*-butyl alcohol in 10 ml. of acetic acid was cooled to 10°, and 100 ml. of chromic-sulfuric acid solution was added over 30 minutes at 10°. At 0–10°, 28 ml. of 50% sodium hydroxide solution was added, and the mixture was extracted with ether. The combined extracts were washed with 10% sodium hydroxide solution, with water, and dried over magnesium sulfate. Distillation through a short Vigreux column gave 8.2–8.8 g. (57–61%) of *n*-butyl butyrate, b.p. 164–166°, n_D^{25} 1.4032, identical in its infrared spectrum and retention time with an authentic sample.

BETHESDA, MD.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE SPRAGUE ELECTRIC CO.]

Polyfunctional Acids and Alcohols from Tetrachloro-*o*-xylene, Tetrachloro-*p*-xylene, and Trichloromesitylene

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Received March 4, 1960

Procedures are described for the ω-chlorination of tetrachloro-*o*-xylene, for the ω-bromination of tetrachloro-*o*-xylene, tetrachloro-*p*-xylene, and trichloromesitylene and for replacement of the bromine by hydroxyl (*via* the acetates), by carboxymethyl (*via* malonic ester alkylation), by phenyl (*via* the Friedel-Crafts reaction), and by *n*-propoxy (*via* reaction with sodium propoxide in *n*-propyl alcohol).

In connection with studies of condensation polymers, we have prepared the polyfunctional carboxylic acids and alcohols, which are described in the experimental section. The structural feature which these compounds have in common is a fully-substituted, highly chlorinated benzene ring. The aromatic ring, when properly inserted as an element in a polymer chain, is known to raise the melting point and increase the thermal stability of a polymer.[2] As these compounds are highly chlorinated, they also offer the possibility of conferring flame retarding properties on a polymer.

The synthetic approach adopted was to use the methyl groups in three known compounds, tetrachloro-*o*-xylene,[3] tetrachloro-*p*-xylene,[3a,c,4] and trichloromesitylene[3a,c,5], as handles for the introduction of either the alcohol or acid functions. When adapted to the xylenes, the general ring-chlorination procedure of Silberrad[6] proved more convenient than the methods described in the references above. Although we did succeed in preparing both 1-methyl-2-chloromethyl-3,4,5,6-tetrachlorobenzene and 1,2-bis(chloromethyl)-3,4,5,6-tetrachlorobenzene, and 1,4-bis(chloromethyl)-2,3,-5,6-tetrachlorobenzene was known,[4c] the synthetic

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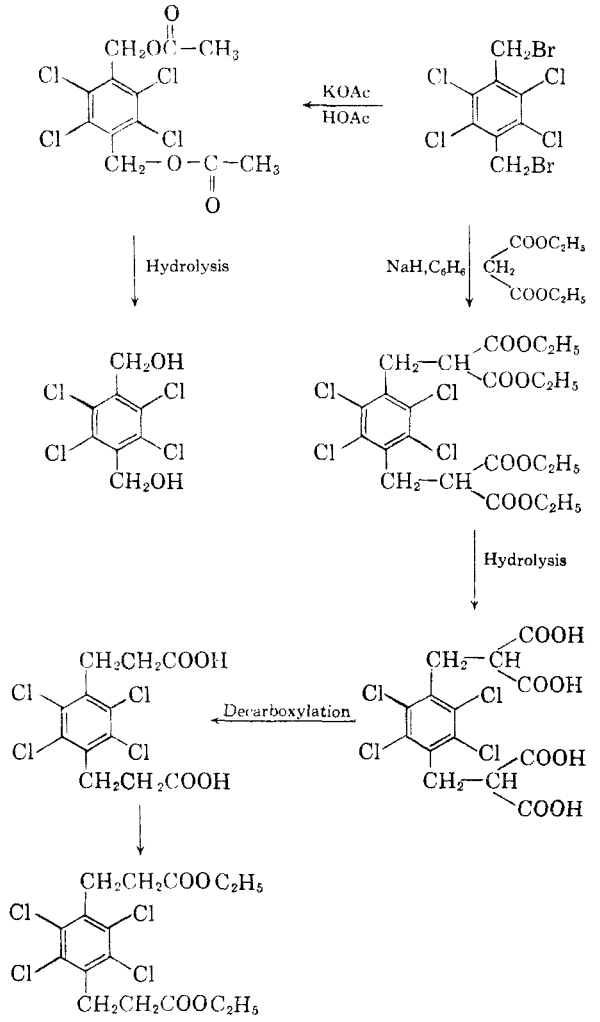
operations were carried out largely with the bromomethyl derivatives, as these could be obtained more cleanly and in better yields. The reactions involved are outlined below for 1,4-bis(bromomethyl)-2,3,5,6-tetrachlorobenzene.



EXPERIMENTAL[7,8]

3,4,5,6-Tetrachloro-o-xylene. A mixture of sulfur monochloride (12.8 g.) and sulfuryl chloride (1280 g.) was added dropwise with external cooling to a stirred suspension of aluminum chloride (10 g.) in *o*-xylene (212 g.; 2 moles). During the first half of the addition the temperature was maintained at 25–30°. When the temperature started to drop, heat was gradually applied until, in the last stages, the reflux temperature of the chlorinating mixture was attained. At the close of the reaction, the mixture was almost completely solid. The excess chlorinating reagents were removed with the water pump and water was added to decompose the aluminum chloride. The crude product was filtered, dried, and crystallized from trichloroethylene; yield, 226 g. (46.4%), m.p. 224–226°. Recrystallization from carbon tetrachloride raised the m.p. to 226.5–227.5°.

2,3,5,6-Tetrachloro-p-xylene. The Silberrad chlorination[6] carried out as above with sulfur monochloride (12.8 g., 0.095 mole), sulfuryl chloride (1280 g., 9.5 moles), and aluminum chloride (10 g.) on *p*-xylene (212 g., 2 moles) gave 361 g. (74%) of tetrachloro-*p*-xylene, m.p. 211–213°, from carbon tetrachloride.

1-Methyl-2-chloromethyl-3,4,5,6-tetrachlorobenzene. Tetrachloro-*o*-xylene (243.8 g., 1 mole) was chlorinated at 225° to a gain in weight of 34.5 g. The crude product was distilled at 10 mm. through a heated Vigreux column, yielding the following fractions: 1. b.p. to 182°; wt. 114 g.; 2. b.p. 182–186°; wt. 106 g.; 3. b.p. 186–195°; wt. 30 g. Fraction 1, on crystallization from trichloroethylene, gave 40.5 g. of tetrachloro-*o*-xylene and a second crop of material melting over a wide range. Fraction 2 gave a first crop of 53.5 g. melting from 96–99° and a second crop of 24.5 g. melting from 78–90°. A sample of this first crop crystallized for analysis three additional times from denatured alcohol-trichloroethylene (1:1) melted from 99.5–100°.

Anal. Calcd. for $C_8H_5Cl_5$: C, 34.70; H, 1.78. Found: C, 34.41, 34.48; H, 1.64, 1.80.

Fraction 3 on crystallization from trichloroethylene gave a first crop of 3.5 g. melting from 94–99° and a second crop of 9 g. melting from 65–82°. Repeated crystallization of this second crop from trichloroethylene-ethanol (1:2) gave finally pure 1,2-bis(chloromethyl)-3,4,5,6-tetrachlorobenzene, m.p. 83.5–84.5°, no depression of mixture melting point with an authentic sample.

1,2-Bis(chloromethyl)-3,4,5,6-tetrachlorobenzene. Reaction of tetrachloro-*o*-xylene (243.8 g., 1 mole), as above, with double the amount of chlorine, followed by fractionation first at 0.5 mm., then at 0.3 mm., and crystallization from trichloroethylene-ethanol (1:3) gave 56 g. of the bischloromethyl compound; m.p. 82–83° A sample crystallized for analysis three additional times melted from 83.5–84.5°.

Anal. Calcd. for $C_8H_4Cl_6$: C, 30.33; H, 1.28. Found: C, 30.73, 30.51; H, 1.22, 1.40.

1,2-Bis(bromomethyl)-3,4,5,6-tetrachlorobenzene. Bromine (640 g.; 4 moles) was added dropwise at room temperature to a stirred solution of tetrachloro-*o*-xylene (488 g., 2 moles) in carbon tetrachloride (1.5 l.) illuminated with a 500 watt bulb. When the bromine color disappeared, the solvent was distilled until the liquid temperature reached 110°. The crude product, which crystallized on cooling, was pressed dry on filter paper and crystallized from 2 l. of acetone-methanol (4:1). This gave 726 g. (94.8%) of the dibromide; m.p. 114.5–116°. A sample crystallized for analysis three time from denatured alcohol-carbon tetrachloride (2:1) and once from acetone melted at 115.5–116.5°.

Anal. Calcd. for $C_8H_4Cl_4Br$: C, 23.88; H, 1.00. Found: C, 23.99, 24.08; H, 1.01, 1.08.

1-Methyl-2-bromomethyl-3,4,5,6-tetrachlorobenzene. Treatment of tetrachloro-*o*-xylene (243.8 g., 1 mole) in carbon tetrachloride (300 cc.) and chloroform (700 cc.) with bromine (150 g., 0.94 mole), as above, gave a mixture of the starting material and the monobromide, which was separated by virtue of insolubility of tetrachloro-*o*-xylene in trichloroethylene. The yield of crude 1-methyl-2-bromomethyl-3,4,5,6-tetrachlorobenzene was 150 g. (46.5%), m.p. 90–94°. A sample crystallized for analysis three times from 95% alcohol melted from 100.5–101.5°.

Anal. Calcd. for $C_8H_5Cl_4Br$: C, 29.71; H, 1.55. Found: C, 29.42, 29.69; H, 1.50, 1.59.

1,4-Bis(bromomethyl)-2,3,5,6-tetrachlorobenzene. The reaction of tetrachloro-*p*-xylene (48.8 g., 0.2 mole) in carbon tetrachloride (400 cc.) with bromine (64 g., 0.4 mole) gave 66 g. (82%) of the dibromide; m.p. 215–216° from carbon tetrachloride.

Anal. Calcd. for $C_8H_4Br_2Cl_4$: C, 23.88; H, 1.00. Found: C, 23.70, 23.90; H, 1.21, 1.09.

1,3,5-Tris(bromomethyl)-2,4,6-trichlorobenzene. A solution of trichloromesitylene (24 g., 0.107 mole) in carbon tetrachloride (300 cc.) was treated with a solution of bromine (51.5 g., 0.321 mole) in carbon tetrachloride (100 cc.), as above. On cooling the product separated as white needles; yield 43 g (87%); m p. 184–185°.

Anal. Calcd. for $C_9H_6Cl_3Br_3$: C, 23.49; H, 1.31. Found: C, 23.01, 23.22; H, 1.09, 1.22.

(7) All analyses are by Clark Microanalytical Laboratories.

(8) The melting points are uncorrected.

1,2-Bis(acetoxymethyl)-3,4,5,6-tetrachlorobenzene. A mixture of 1,2-bis(bromomethyl)-3,4,5,6-tetrachlorobenzene (40.1 g., 0.1 mole), potassium acetate (100 g., 1 mole), and glacial acetic acid (300 cc.) was refluxed 24 hr. and then poured into water. The diacetate, which precipitated, was filtered and dried; yield, 34 g. (94%); m.p. 130–133.5°. A sample crystallized four times for analysis from denatured alcohol melted at 133.5–134.5°.

Anal. Calcd. for $C_{12}H_{10}O_4Cl_4$: C, 40.01; H, 2.80. Found: C, 39.69, 39.87; H, 2.62, 2.79.

1-Methyl-2-acetoxymethyl-3,4,5,6-tetrachlorobenzene. Treatment of 1-methyl-2-chloromethyl-3,4,5,6-tetrachlorobenzene, as above, gave a quantitative yield of the crude acetate; m.p. 83–86°. A sample crystallized for analysis five times from 95% alcohol melted from 91–92.5°.

Anal. Calcd. for $C_{10}H_8O_2Cl_4$: C, 39.80; H, 2.67. Found: C, 39.16, 39.30; H, 2.49, 2.61.

1,4-Bis(acetoxymethyl)-2,3,5,6-tetrachlorobenzene. Treatment of 1,4-bis(bromomethyl)-2,3,5,6-tetrachlorobenzene with sodium acetate and acetic acid, as above, yielded 80% of the diacetate; m.p. 218–220° from benzene.

Anal. Calcd. for $C_{12}H_{10}O_4Cl_4$: C, 40.01; H, 2.80. Found: C, 39.57, 39.80; H, 2.60, 2.48.

1,3,5-Tris(acetoxymethyl)-2,4,6-trichlorobenzene. The above procedure with 1,3,5-tris(bromomethyl)-2,4,6-trichlorobenzene gave an 81% yield of the triacetate; m.p. 135.5–136.5° from ethanol.

Anal. Calcd. for $C_{15}H_{15}O_6Cl_3$: Cl, 26.75. Found: Cl, 26.56.

1,2-Bis(hydroxymethyl)-3,4,5,6-tetrachlorobenzene. A mixture of 1,2-bis(acetoxymethyl)-3,4,5,6-tetrachlorobenzene (32 g., 0.089 mole), potassium hydroxide (11.2 g., 0.2 mole), water (100 cc.), and acetone (150 cc.) was refluxed 6 hr. and then poured into water. The crude glycol was filtered and dried; yield 23 g. (93%); m.p. 210–215°. Crystallization from denatured alcohol–carbon tetrachloride (3:1) gave 17 g. (69%) of the glycol; m.p. 222–225. A sample crystallized for analysis once from the above solvent pair and once from denatured alcohol melted at 226–227°.

Anal. Calcd. for $C_8H_6O_2Cl_4$: C, 34.80; H, 2.18. Found: C, 35.02, 34.83; H, 2.06, 1.89.

1-Methyl-2-hydroxymethyl-3,4,5,6-tetrachlorobenzene. Hydrolysis of 1-methyl-2-acetoxymethyl-3,4,5,6-tetrachlorobenzene by the procedure described above yielded the alcohol in 96% yield; m.p. 208–212°. A sample crystallized three times from benzene-ethanol (2:1) melted from 212–213.5°.

Anal. Calcd. for $C_8H_6OCl_4$: C, 36.96; H, 2.33. Found: C, 36.85, 36.68; H, 2.19, 2.35.

1,4-Bis(hydroxymethyl)-2,3,5,6-tetrachlorobenzene 1,4-Bis(acetoxymethyl)-2,3,5,6-tetrachlorobenzene, when hydrolyzed as above, gave the glycol in 68% yield; m.p. 229–230° from ethanol. Further crystallization raised the m.p. to 230–231°.

Anal. Calcd. for $C_8H_6O_2Cl_4$: Cl, 51.39. Found: Cl, 51.02.

1,3,5-Tris(hydroxymethyl)-2,4,6-trichlorobenzene. Hydrolysis of the triacetate, as above, gave the triol in 83% yield; m.p. 241–242°.

Anal. Calcd. for $C_9H_9O_3Cl_3$: Cl, 39.18. Found: Cl, 38.88.

1,4-Bis(ω,ω-dicarbethoxyethyl)-2,3,5,6-tetrachlorobenzene. A solution of diethyl malonate (17.5 g., 0.11 mole) in dry benzene (500 cc.) was added dropwise to a stirred suspension of sodium hydride (2.6 g., 0.11 mole) in benzene (50 cc.). When the evolution of hydrogen ceased, 1,4-bis(bromomethyl)-2,3,5,6-tetrachlorobenzene (15.1 g., 0.05 mole) in dry benzene (200 cc.) was added, and the mixture was refluxed 24 hours. The benzene solution was freed of sodium bromide by washing with water, dried, and concentrated. Addition of alcohol precipitated the product; yield 21 g. (75%); m.p. 111–112°. Three crystallizations from benzene-hexane (1:1) did not alter the melting point.

Anal. Calcd. for $C_{22}H_{26}Cl_4O_8$: C, 47.16; H, 4.68. Found: C, 47.33, 47.38; H, 5.00, 4.82.

1,4-Bis(ω,ω-dicarboxyethyl)-2,3,5,6-tetrachlorobenzene. A mixture of 1,4-bis(ω,ω-dicarbethoxyethyl)-2,3,5,6-tetrachlorobenzene (18.5 g., 0.033 mole), potassium hydroxide (10 g., 0.18 mole), water (10 cc.) and ethanol (150 cc.) was refluxed 15 hr. Ethanol (75 cc.) was removed by distillation. The residue was dissolved in cold water (100 cc.) and poured into a solution of sulfuric acid (15 cc.) in water (100 cc.). The product which precipitated was filtered, washed with water, and dried; yield 15 g. (97%); m.p. 269–274°. A sample crystallized for analysis from methanol-water melted at 269–271°.

Anal. Calcd. for $C_{14}H_{10}Cl_4O_8$: C, 37.53; H, 2.25; neut. equiv., 112. Found: C, 37.90, 38.08; H, 2.35, 2.13; neut. equiv., 115.6.

1,4-Bis(ω-carboxyethyl)-2,3,5,6-tetrachlorobenzene. The above tetracarboxylic acid (50 g., 0.11 mole) was heated with quinoline (75 cc.) until the evolution of carbon dioxide ceased (15 min.). The hot reaction mixture was poured into 500 cc. of water-concd. hydrochloric acid (1:1). The acid which precipitated was filtered, dried and crystallized from alcohol-water; yield 36 g. (90%); m.p. 271–274°. A sample crystallized several times from alcohol-benzene melted at 271–273°.

Anal. Calcd. for $C_{12}H_{10}Cl_4O_4$: C, 40.03; H, 2.77; neut. equiv., 180. Found: C, 40.38, 40.52; H, 2.91, 3.08; neut. equiv., 168.

1,4-Bis(ω-carbethoxyethyl)-2,3,5,6-tetrachlorobenzene. A solution of 1,4-bis(ω-carboxyethyl)-2,3,5,6-tetrachlorobenzene (35 g., 0.097 mole) and concd. sulfuric acid (1 cc.) in ethanol (1 l.) and benzene (200 cc.) was refluxed 5 hr. The ternary mixture of alcohol, benzene, and water (600 cc.) was then removed by distillation over a 4 hr. period. On cooling of the residue, the ester crystallized; yield 36 g. (86%); m.p. 141–144°. A sample recrystallized three times from alcohol-benzene melted at 146–147°.

Anal. Calcd. for $C_{16}H_{18}Cl_4O_4$: C, 46.18; H, 4.36. Found: C, 46.00, 45.84; H, 4.12, 4.15.

1,3,5-Tris(ω-carboxyethyl)-2,4,6-trichlorobenzene. Diethyl malonate (50 g., 0.315 mole) was added dropwise over a 30-min. period to a suspension of sodium hydride (7.6 g., 0.315 mole) in dry benzene (400 cc.). After an additional 30 min. the evolution of hydrogen slowed, and 1,3,5-tris(bromomethyl)-2,4,6-trichlorobenzene (44.8 g., 0.1 mole) was added. The mixture was brought to reflux temperature and an exothermic reaction set in. Refluxing was continued 20 hr. The cooled reaction mixture was washed with water to remove the sodium bromide. After drying, the benzene was evaporated leaving an oil which could not be induced to crystallize; yield 65 g. (94%).

The above condensation product (60 g., 0.086 mole) was refluxed with potassium hydroxide (40 g., 0.7 mole) in ethanol (250 cc.) and water (20 cc.). After 30 min., water (100 cc.) was added to dissolve the salts which precipitated, and refluxing was continued 18 hr. The alcohol was removed, and the remaining solution was acidified with sulfuric acid. The hexacarboxylic acid did not precipitate and was partially decarboxylated in the acid solution by refluxing 20 hr. As decarboxylation occurred, the acid precipitated. To complete the decarboxylation, the acid was filtered and refluxed 2 hr. in pyridine (100 cc.). The pyridine solution was poured into a hydrochloric acid–water (1:1) mixture (300 cc.). The product was filtered and dried; yield 27 g. (80%); m.p. 254–258°. A sample crystallized twice from alcohol-water melted at 254–256°.

Anal. Calcd. for $C_{15}H_{15}O_6Cl_3$: C, 45.30; H, 3.80. Found: C, 45.85, 45.64; H, 4.02, 4.01.

1,3,5-Tris(ω-carbethoxyethyl)-2,4,6-trichlorobenzene. The above tribasic acid (10 g., 0.025 mole) was dissolved in a mixture of absolute ethanol (100 cc.), benzene (50 cc.), and concd. sulfuric acid (0.5 cc.), and the solution was refluxed 15 hr. Most of the alcohol-benzene mixture was removed by distillation, and the residue was poured into water (150 cc.). The aqueous solution was extracted with ether, and the ether solution was washed with water and 5%

sodium bicarbonate. The ether was evaporated, and the residue was crystallized from hexane; yield 6 g. (50%); m.p. 60–63°. A sample crystallized three additional times from hexane melted at 63.5–64.5°.

Anal. Calcd. for $C_{21}H_{27}O_6Cl_3$: C, 52.34; H, 5.65. Found: C, 52.46, 52.39; H, 5.70, 5.76.

1,2-Dibenzyl-3,4,5,6-tetrachlorobenzene. 1,2-Bis(bromomethyl)-3,4,5,6-tetrachlorobenzene (40.1 g., 0.1 mole) in benzene (200 cc.) was added dropwise at room temperature to a stirred suspension of aluminum chloride (0.5 g.) in benzene (200 cc.). Stirring was continued 6 hr., and the reaction mixture was then left standing overnight. The crude product was isolated in the usual manner. Distillation at 0.09 mm. gave a middle fraction, b.p. 170–220°, 24 g. Crystallization of this fraction from ethanol-benzene gave 21 g. (53%); m.p. 161–164°. Two recrystallizations raised the m.p. to 164–165.5°.

Anal. Calcd. for $C_{20}H_{14}Cl_4$: C, 60.68; H, 3.56. Found: C, 60.79, 60.94; H, 2.94, 3.06.

1-Methyl-2-benzyl-3,4,5,6-tetrachlorobenzene. 1-Methyl-2-bromomethyl-3,4,5,6-tetrachlorobenzene, treated with benzene and aluminum chloride as above, gave the product in 78% yield; b.p. 155° at 0.9 mm.; m.p. 87–88° from benzene-ethanol (1:1). Recrystallization raised the m.p. to 87.5–89°.

Anal. Calcd. for $C_{14}H_{10}Cl_4$: C, 52.58; H, 3.15. Found: C, 52.60, 52.41; H, 3.02, 3.16.

1,2-Bis(n-propoxymethyl)-3,4,5,6-tetrachlorobenzene. A solution of sodium propoxide was prepared by treating sodium (27.6 g., 1.2 moles) with 1-propanol (750 cc.). To this was added 1,2-bis(bromomethyl)-3,4,5,6-tetrachlorobenzene (201 g., 0.5 mole), and the mixture was refluxed overnight. Water was added, and the organic layer was separated, washed with saturated sodium chloride solution, dried over magnesium sulfate, and filtered. The 1-propanol was removed by distillation, and the crude product was distilled at 0.3 mm. to yield 157 g. (87%) of the diether; b.p. 145–149°. A small sample redistilled for analysis boiled at 143.5° at 0.2 mm. and n_D^{25} 1.5378.

Anal. Calcd. for $C_{14}H_{18}O_2Cl_4$: C, 46.69; H, 5.04. Found: C, 46.74, 46.92; H, 5.00, 4.84.

1-Methyl-2-n-propoxymethyl-3,4,5,6-tetrachlorobenzene. Treatment of 1-methyl-2-bromomethyl-3,4,5,6-tetrachlorobenzene with sodium propoxide in 1-propanol as above gave the ether contaminated with some tetrachloro-*o*-xylene, which was probably present as an impurity in the starting bromide. The crude product was distilled at 7 mm. (b.p. 180–181°). The distillate was crystallized from ethanol containing a little trichloroethylene. The tetrachloro-*o*-xylene crystallized first, and concentration of the mother liquors gave the ether; yield, 58%; m.p. 38–40°. A sample crystallized for analysis four times from 95% ethanol melted from 42–43°.

Anal. Calcd. for $C_{11}H_{12}OCl_4$: C, 43.73; H, 4.00. Found: C, 43.08, 43.19; H, 3.80, 3.72.

Acknowledgment. This work was carried out, in part, under Contract No. DA-36-039-sc-15553 with the Signal Corps of the United States Army.

NORTH ADAMS, MASS.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF PENNSYLVANIA]

Synthesis of 5-Ketopipecolic Acid from Glutamic Acid

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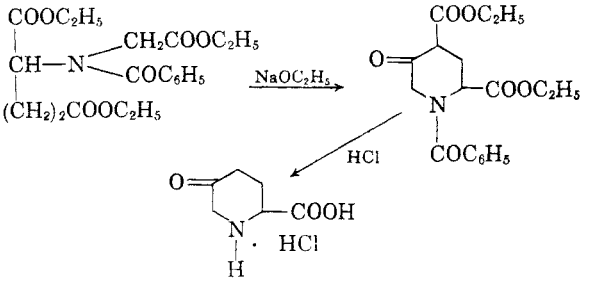
Received April 4, 1960

The synthesis of 5-keto-2-piperidinecarboxylic acid has been studied. It has been shown that an important by-product of this synthesis is diethyl 1-carboxymethylpyroglutamate. It was shown that the latter may be obtained in good yields from triethyl *N*-carboxymethylglutamate.

The synthesis of 5-ketopipecolic acid (5-keto-2-piperidinecarboxylic acid) from L-glutamic acid was first reported by King, King, and Warwick.[1] These workers isolated this compound as its hydrochloride salt containing one mole of methanol and one mole of acetone of crystallization. The over-all yield was rather low and they reported the formation of a by-product which they apparently did not identify.

These workers alkylated diethyl glutamate with ethyl bromoacetate to form diethyl *N*-carbethoxymethylglutamate. The latter compound was benzoylated in pyridine solution and the resulting *N*-benzoyl derivative treated with sodium ethoxide to form diethyl-1-benzoyl-5-ketopiperidine-2,4-dicarboxylate. In the last step, hydrolysis with hydrochloric acid gave 5-ketopipecolic acid.

5-Ketopipecolic acid was of interest to us for two reasons: (1) it appeared to be a useful starting material for the synthesis of other heterocyclic ring systems; and (2) it has been postulated that it might arise *in vivo* by intramolecular cyclization from 6-diazo-5-oxonorleucine.[2] It was decided, therefore, to study the reactions reported by the previous workers,[1] to study the properties of 5-ketopipecolic acid and to determine the nature of the by-product.



(1) F. E. King, T. J. King, and A. J. Warwick, *J. Chem. Soc.*, 3590 (1950).

(2) A. A. Patchett and B. Witkop, *J. Am. Chem. Soc.*, 79, 192 (1957).