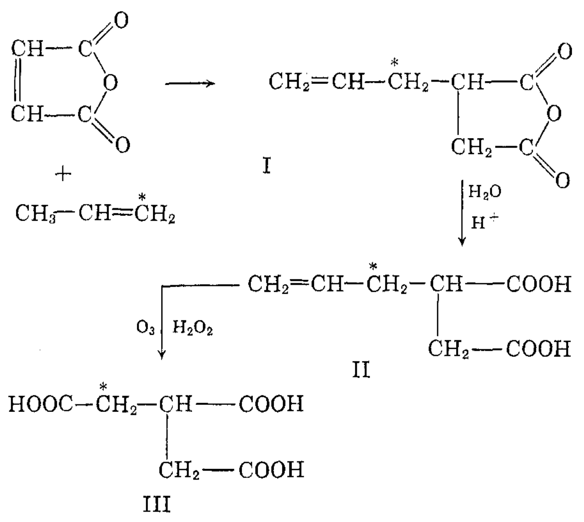

agreement with a concerted mechanism since any long-lived independent ionic or free radical species of propene would be expected to distribute the isotopic carbon between the one and three positions of the propene. For the same reason, it is evident that no isomerization of propene occurred under the reaction conditions (250°, 4300 p.s.i.).

## EXPERIMENTAL

*Propene-1-$C^{14}$*. Propionic acid-1-$C^{14}$ was obtained by carbonation of ethylmagnesium iodide as described by Ostwald[9] for the preparation of acetic acid-1-$C^{14}$. Reduction of the acid with lithium aluminum hydride gave propanol-1-$C^{14}$ in 65% yield which was converted to propene-1-$C^{14}$ *via* the quaternary ammonium hydroxide using the method of Fries and Calvin.[10]

*Allylsuccinic anhydride.* In an autoclave of 50-ml. capacity was placed 33 ml. of benzene and 1.8 g. of maleic anhydride. After cooling the autoclave in Dry Ice-acetone and evacuating, 16 g. of propene-1-$C^{14}$ was added. The reaction vessel was heated to 250° with shaking for 12 hr.; a maximum pressure of 4300 p.s.i. was recorded. After removal of the benzene, 0.81 g. of allylsuccinic anhydride was obtained on distillation as a colorless oil, b.p. 133–140°/16 mm.

*Allylsuccinic acid.* The product obtained in the previous experiment was hydrolyzed by warming with 50 ml. of 10% sodium hydroxide, acidifying with hydrochloric acid, and extracting with ether. The residue remaining after removal of the ether was recrystallized twice from ethyl acetate–ligroin. A yield of 0.76 g. of allylsuccinic acid-$C^{14}$ melting at 96–97° was obtained.

*Anal.* Calcd. for $C_7H_{10}O_4$: C, 53.19; H, 6.73. Found: C, 53.50, 53.28; H, 6.52, 6.29. Radioactive assay: 5.48 ± 0.01 mc./mole.

*Oxidation of allylsuccinic acid to 3-carboxyglutaric acid.* The ozonolysis of 0.4 g. of allylsuccinic acid was carried out in the usual manner using ethyl acetate as a solvent. The ethyl acetate was then removed under diminished pressure while simultaneously adding acetic acid until all ethyl acetate had been distilled and the ozonide was contained in 30 ml. of acetic acid. This solution was added dropwise with stirring to a mixture of 0.7 g. sulfuric acid, 7 g. water, and 7 g. of 30% hydrogen peroxide. The reaction temperature was slowly raised to reflux during the course of the addition, and reflux maintained for 2 hr. After dilution to twice the reaction volume with water, the mixture was extracted twice with ether, and the ether extract discarded. To remove the sulfuric acid, the solution was made basic to sodium hydroxide and reacidified with hydrochloric acid. After evaporation to dryness under diminished pressure, the residual solid was extracted in a Soxhlet extractor with ethyl acetate. The product which remained after removal of the solvent and four recrystallizations from acetonitrile melted 157–158°. A mixed melting point with authentic 3-carboxyglutaric acid gave no depression.

*Anal.* Calcd. for $C_6H_8O_6$: C, 40.91; H, 4.54. Found: C, 40.73; H, 4.52. Radioactive assay: 5.45 ± 0.01 mc./mole.

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[9] R. Ostwald, *J. Biol. Chem.*, **173**, 207 (1948).

[10] B. A. Fries and M. Calvin, *J. Am. Chem. Soc.*, **70**, 2235 (1948).

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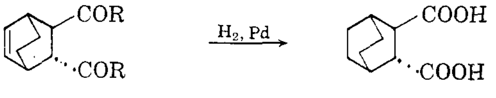
# Convenient Synthesis of Bicyclo[2.2.2]-octane-*trans*-2,3-dicarboxylic Acid

JOHN B. CLEMENTS[1]

*Received November 17, 1960*

In another connection, a considerable quantity of bicyclo[2.2.2]octane-*trans*-2,3-dicarboxylic acid (II) was required. Previous syntheses[2–4] have been tedious, multi-step processes and did not appear to lend themselves to the preparation of this acid in the quantities needed. Acid II is easily prepared in the required amounts by taking advantage of the facile condensation of 1,3-cyclohexadiene with fumaryl chloride to give acid chloride Ia which is hydrolyzed to bicyclic acid Ib. This acid was previously reported by Alder and Stein[5] but no yield or analytical data were given. Catalytic hydrogenation of Ib affords the desired acid in good yields. This method has the advantage of convenience in manipulation and very good over-all yields (85%).



Ia. R = Cl
Ib. R = OH

II

## EXPERIMENTAL[6]

*Bicyclo[2.2.2]octene-5-trans-dicarbonyl chloride* (Ia). To 168.3 g. (1.10 mole) of fumaryl chloride was added 80.1 g. (1.00 mole) of 1,3-cyclohexadiene[7] dropwise with stirring while controlling the mildly exothermic reaction at 40–45°. The reaction mixture was allowed to stand at room tempera-

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[1] Present address: Chemstrand Research Center, Inc., P. O. Box 731, Durham, N. C.

[2] O. Diels and K. Alder, *Ann.*, **478**, 137 (1930).

[3] K. H. McNeely, A. Rodgman, and G. F. Wright, *J. Org. Chem.*, **20**, 714 (1955).

[4] R. C. Cookson and N. S. Wariyar, *Chem. & Ind.* (*London*), **1955**, 915.

[5] K. Alder and G. Stein, *Ann.*, **514**, 1 (1934).

[6] All melting points are corrected. Analyses are by Mr. Grant Gustin of our analytical department.

[7] C. S. Marvel and G. E. Hartzell, *J. Am. Chem. Soc.*, **81**, 448 (1959).

ture overnight, then vacuum distilled to give 214.5 g. (92.0%) of adduct boiling at 87-89°/0.25 mm.

The *diamide*, prepared from the above diacid chloride and excess concentrated ammonium hydroxide, was recrystallized from ethanol for analysis. It melted at 261–262°.

*Anal.* Calcd. for $C_{10}H_{14}N_2O_2$: C, 61.84; H, 7.27; N, 14.43. Found: C, 61.6, 61.4; H, 7.07, 7.17; N, 14.3, 14.3.

*Bicyclo[2.2.2]octene-5-trans-2,3-dicarboxylic acid* (Ib). A mixture of 176.3 g. (0.75 mole) of bicyclo[2.2.2]octene-5-*trans*-2,3-dicarbonyl chloride and 1 l. of water was allowed to stand at room temperature overnight. The resulting white solid, after filtering, washing well with water, and drying, weighed 141.4 g. (96.2%) and melted at 213–215°. For analysis it was recrystallized from water and it then melted at 214–215°. Alder and Stein[5] reported a melting point of 211°.

*Anal.* Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.4, 61.4; H, 6.17, 6.07.

*Bicyclo[2.2.2]octane-trans-2,3-dicarboxylic acid* (II). A solution of 78.4 g. (0.40 mole) of bicyclo[2.2.2]octene-5-*trans*-2,3-dicarboxylic acid and 650 ml. of 10% sodium carbonate was hydrogenated using 0.78 g. of 10% palladium-on-charcoal. After the theoretical amount of hydrogen was consumed, the catalyst was filtered and the product precipitated with concentrated hydrochloric acid. The white solid, after filtering and drying, weighed 76.8 g. (92.2%) and melted at 234–235.5°. After recrystallizing from 1:1 methanol-water the melting point was 234–235°. A mixture with authentic bicyclo[2.2.2]octane-*trans*-2,3-dicarboxylic acid[2] melted at 233–234.5°. The authentic diacid and the present acid have identical infrared spectra (Nujol mull).

*Anal.* Calcd. for $C_{10}H_{14}O_4$: C, 60.60; H, 7.12. Found: C, 60.3, 60.5; H, 7.28, 7.31.

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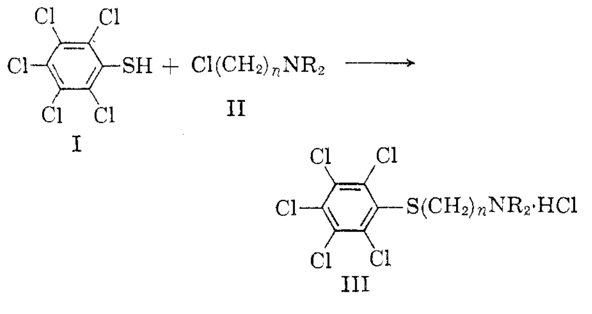
# Dialkylaminoalkyl Pentachlorophenyl Sulfides

James H. Short

*Received November 28, 1960*

The availability of pentachlorothiophenol (I) prompted the synthesis of a few dialkylaminoalkyl pentachlorophenyl sulfides (III). The desired compounds were prepared by the condensation of I with dialkylaminoalkyl chlorides (II).



One compound, 3-dimethylaminopropyl pentachlorophenyl sulfide (III. $n = 3$, R = $CH_3$), was quaternized with methyl iodide and *o*-bromobenzyl bromide.

The six compounds were tested for various pharmacological and chemotherapeutic activities including effect on blood pressure, anti-serotonin activity, monamine oxidase inhibition, psychopharmacological activity, and anticancer activity. They were tested for ability to inhibit growth of various gram-negative bacteria such as *E. coli*, and for their effect on parasites such as *S. obvelata*, *E. tenella*, *S. mansoni*, *T. cruzi* and *H. nana*. No particularly outstanding activity was observed.

## EXPERIMENTAL[1]

*3-Dimethylaminopropyl pentachlorophenyl sulfide hydrochloride.* To a mixture of 14 g. (0.05 mole) of pentachlorobenzenethiol and 8 g. (0.05 mole) of dimethylaminopropyl chloride hydrochloride in 350 ml. of 2-propanol was added a solution of 6.6 g. (0.1 mole) of 85% potassium hydroxide in 10 ml. of water. The resulting solution was refluxed overnight. The reaction mixture was poured into 1.0 l. of water, extracted with ether, and dried. Alcoholic hydrogen chloride was added to give 12.6 g. (63%) o fine, white leaflets, m.p. 229–230.5°. Recrystallization twice from dry ethanol raised the melting point to 230.5–231°.

*Anal.* Calcd. for $C_{11}H_{12}Cl_5NS \cdot HCl$: C, 32.70; H, 3.24; Cl, 52.66; N, 3.47; S, 7.93. Found: C, 32.95; H, 3.35; Cl, 52.73; N, 3.54; S, 8.08.

*2-Dimethylaminoisopropyl pentachlorophenyl sulfide hydrochloride.* Pentachlorobenzenethiol, 14 g. (0.05 mole), and 8.0 g. (0.05 mole) of dimethylaminoisopropyl chloride hydrochloride were allowed to react and the reaction worked up as described above, to yield 9.1 g. (45%) of material melting at 184–190°. Three recrystallizations from ethanol-acetone raised the melting point to 198–200°.

*Anal.* Calcd. for $C_{11}H_{12}Cl_5NS \cdot HCl$: C, 32.70; H, 3.24; Cl, 52.66; N, 3.47; S, 7.93. Found: C, 32.87; H, 3.24; Cl, 52.89; N, 3.58; S, 8.03.

*2-Dimethylaminoethyl pentachlorophenyl sulfide hydrochloride.* A mixture of 14 g. (0.05 mole) of pentachlorobenzenethiol, 5.4 g. (0.05 mole) of 2-dimethylaminoethyl chloride in an equal weight of xylene, and 2.7 g. (0.05 mole) of sodium methoxide in 400 ml. of dry ethanol was heated under reflux overnight. After working up as described above, 13.6 g. (70%) of product was obtained, m.p. 228–231°. One recrystallization from dry ethanol, with the aid of charcoal, raised the melting point to 232–234°.

*Anal.* Calcd. for $C_{10}H_{10}Cl_5NS \cdot HCl$: C, 30.80; H, 2.84; Cl, 54.55; N, 3.59; S, 8.22. Found: C, 30.86; H, 3.00; Cl, 54.26; N, 3.50; S, 8.26.

*2-Di-n-butylaminoethyl pentachlorophenyl sulfide hydrochloride.* Pentachlorobenzenethiol, 14 g. (0.05 mole), and 9.6 g. (0.05 mole) of di-*n*-butylaminoethyl chloride in an equal weight of xylene were allowed to react, and then worked up as described above. It was necessary to add ether to the alcoholic solution in order to induce the product to precipitate. The yield was 20.5 g. (86.5%), m.p. 121–124°. Recrystallization from ethanol-ether with the aid of charcoal gave white needles, and did not raise the melting point.

*Anal.* Calcd. for $C_{16}H_{22}Cl_5NS \cdot HCl$: C, 40.53; H, 4.89; Cl, 44.87; N, 2.95; S, 6.76. Found: C, 40.52; Y, 5.08; Cl, 44.79; N, 3.29; S, 6.87.

*[3-(Pentachlorophenylthio)propyl]trimethylammonium iodide.* 3-Dimethylaminopropyl pentachlorophenyl sulfide was prepared as described above on a 0.05 mole scale. The ether solution was taken to dryness, and the residual oil dissolved in 100 ml. of acetone. Methyl iodide, 42 g. (0.3 mole), was added and the solution was allowed to stand at room temperature for 6 hr., during which time a cream-colored solid precipitated. The solid weighed 25 g. (98%)

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[1] Microanalyses are due to Mr. Elmer Shelberg and staff of the Abbott Microanalytical Laboratory.