[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Cyclic Polyolefins. XX. Cycloöctatetraenecarboxylic Acid[1]

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Cycloöctatetraenyllithium has been prepared by a halogen–metal interchange reaction between bromocycloöctatetraene and *n*-butyllithium, and converted into cycloöctatetraenecarboxylic acid (58% yield) by carbonation. Cycloöctatetraenecarboxylic acid also has been obtained in low yield (4.4%) by ozonization of vinylcycloöctatetraene and decomposition of the ozonide with silver oxide. The structure of the acid has been established by hydrogenation to cycloöctene-1-carboxylic acid and to cycloöctanecarboxylic acid. Attempts to resolve cycloöctatetraenecarboxylic acid were unsuccessful.

Among substitution products of cycloöctatetraene, the carboxylic acid may be regarded as having particular importance, both for possible resolution (if monosubstitution leads to asymmetry[4]), and as an intermediate for the preparation of other derivatives. Cycloöctatetraenecarboxylic acid has been obtained in 4.4% yield by the ozonization of vinylcycloöctatetraene[5] at -70° followed by treatment of the ozonide with silver oxide. A much better synthesis consisted in the reaction of bromocyclooctatetraene[6] and *n*-butyllithium at -55°,[7] forming *n*-butyl bromide and cycloöctatetraenyllithium (another versatile intermediate for the synthesis of cycloöctatetraene derivatives). Carbonation of the lithium derivative formed cycloöctatetraenecarboxylic acid in 58% yield.

Cycloöctatetraenecarboxylic acid as purified by recrystallization from ether or by sublimation under reduced pressure was a yellow crystalline solid melting at 72–73°. The acid appeared to be relatively stable, although it contains structural elements permitting intra- or intermolecular Diels–Alder reactions, with bridging or polymerization. Its acidity was determined by electrometric titration; pK_A 4.4. The ultraviolet and infrared spectra of the acid are shown in Figs. 1 and 2, respectively. Treatment of cycloöctatetraenecarboxylic acid with diazomethane formed a liquid methyl es-

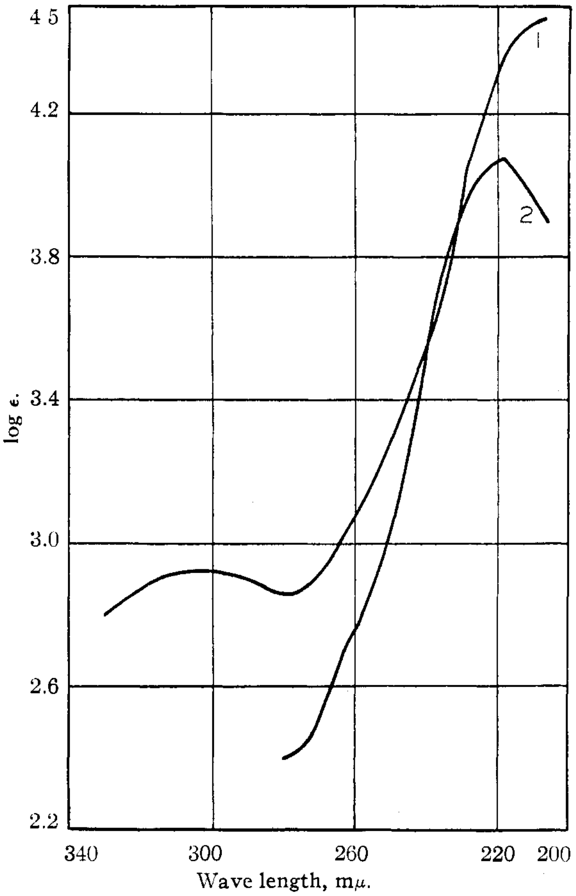

Fig. 1.—Ultraviolet absorption spectra: curve 1, cyclooctatetraenecarboxylic acid; curve 2, cycloöctene-1-carboxylic acid, both in 95% ethanol.

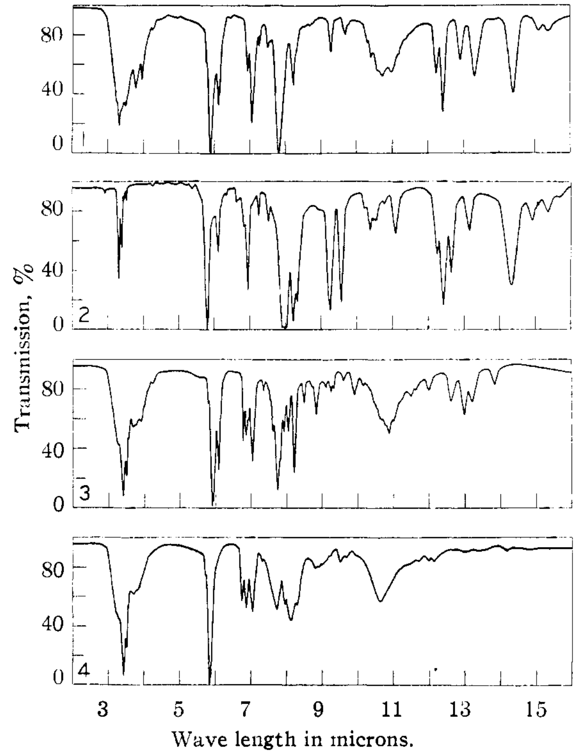

Fig. 2.—Infrared absorption spectra for solutions in carbon tetrachloride in the region 2–8μ and in carbon disulfide in the region 8–16μ: curve 1, cycloöctatetraenecarboxylic acid (50 mg./ml.); curve 2, methyl cycloöctatetraenecarboxylate (100 mg./ml.); curve 3, cycloöctene-1-carboxylic acid (50 mg./ml.); curve 4, cycloöctanecarboxylic acid (50 mg./ml.).

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(4) See A. C. Cope and M. R. Kinter, THIS JOURNAL, **73**, 3424 (1951).

(5) A. C. Cope and S. W. Fenton, *ibid.*, **73**, 1195 (1951); L. E. Craig and C. E. Larrabee, *ibid.*, **73**, 1191 (1951).

(6) A. C. Cope and M. Burg, *ibid.*, **74**, 168 (1952).

(7) Halogen–metal interchange between substituted vinyl bromides and alkyllithium compounds forming substituted vinyllithium derivatives has been described by D. Y. Curtin and E. E. Harris, *ibid.*, **73**, 2716 (1951).

ter (89% yield), from which the acid was reformed by saponification with dilute sodium hydroxide. The infrared spectrum of the ester is shown in Fig. 2.

Conclusive evidence for the structure of cyclooctatetraenecarboxylic acid was obtained by catalytic hydrogenation. The acid absorbed three moles of hydrogen rapidly in the presence of a palladium catalyst in ethanol, forming principally cycloöctene-1-carboxylic acid, which after recrystallization melted at 102–103°. The reduction product was identical in melting point, mixed melting point, ultraviolet absorption spectrum (Fig. 1) and infrared spectrum with an authentic sample. Carbonation of 1-cycloöctenyllithium (prepared from 1-bromocycloöctene and lithium[8]) yielded the authentic sample (30%).

Hydrogenation of cycloöctene-1-carboxylic acid (prepared from cycloöctenyllithium), or prolonged reduction of cycloöctatetraenecarboxylic acid in the presence of Adams platinum catalyst in acetic acid with the absorption of four molar equivalents of hydrogen, yielded cycloöctanecarboxylic acid. The structure of this liquid acid was proved by comparison of its infrared spectrum with the spectrum of an authentic sample prepared by carbonation of cycloöctylmagnesium bromide, and by the identity (mixed melting point) of crystalline amides derived from the two samples.

Cycloöctatetraenecarboxylic acid formed crystalline salts with *d*- and *l*-β-phenylisopropylamine and with quinine. The rotations and melting points of these salts were unchanged by repeated recrystallization, and the acid recovered from the salts was optically inactive. This result indicates either that the structure of the acid is not asymmetric, that rapid racemization occurs (see ref. 4), or that the salts were not suitable for the resolution under the conditions investigated. Preliminary attempts to prepare crystalline salts from cycloöctatetraenecarboxylic acid and brucine, strychnine and thebaine were unsuccessful.

Experimental[9]

Cycloöctatetraenecarboxylic Acid (a) Preparation from Cycloöctatetraenyllithium.—To a stirred solution of *n*-butyllithium[10] prepared from 5.2 g. (0.038 mole) of *n*-butyl bromide and 0.52 g. (0.076 g. atom) of lithium wire in 95 ml. of dry ether, under dry nitrogen and cooled to −60° with a bath of Dry Ice and trichloroethylene, 5.85 g. (0.032 mole) of bromocycloöctatetraene[6] in 20 ml. of dry ether was added during 2 minutes at −60 to −54°. The orange mixture was stirred for 1.5 hours at a reaction temperature of −60 to −54° and then was siphoned onto powdered Dry Ice. After adding 100 ml. of water to the yellow, turbid mixture, the ether layer was washed with two 50-ml. portions of water. The combined aqueous layers were acidified to *p*H 3 with hydrochloric acid with cooling in an ice-bath, and extracted with four 50-ml. portions of pentane. The extracts were dried over magnesium sulfate and concentrated, yielding 3.8 g. of crude I as a yellow solid. One recrystallization from ether yielded 2.74 g. (58.5%) of pure cycloöctatetraenecarboxylic acid as yellow needles, m. p. 72–73°.

Anal. Calcd. for $C_9H_8O_2$: C, 72.96; H, 5.44; neut. equiv., 148. Found: C, 72.80; H, 5.65; neut. equiv., 147.

Conditions for the halogen–metal interchange between bromocycloöctatetraene and *n*-butyllithium were varied in development of the method described above. Yields of cycloöctatetraenecarboxylic acid were 10, 20, 26.5 and 51% when the interchange was conducted at −40° for 7 minutes, −50 to −60° for 35 minutes, −50 to −55° for 10 minutes and −60° for 3 hours, respectively.

(b) **Preparation from Vinylcycloöctatetraene.**—A stream of oxygen delivering 10 mg. of ozone per minute was passed into a solution of 1.30 g. of vinylcycloöctatetraene[5] in 50 ml. of pentane cooled to −70° with a bath of Dry Ice and acetone for 50 minutes. The resulting mixture was stirred with 3 g. of moist, freshly prepared silver oxide for 1 hour at 0° and 2 hours at 26°. After careful acidification with cold, dilute sulfuric acid, the mixture was extracted with three 50-ml. portions of ether. The extracts were concentrated, and the yellow, crystalline residue was sublimed at 0.1 mm. with a heating block temperature of 50–100°. The crude product (0.103 g., m. p. 69–72°) was recrystallized twice from ether–petroleum ether, and yielded 64.7 mg. (4.4%) of analytically pure cycloöctatetraenecarboxylic acid, m. p. 72–73°, which was identical with a sample prepared by procedure (a) in neutral equivalent, mixed melting point and infrared spectrum.

Properties and Structure of Cycloöctatetraenecarboxylic Acid.—Titration of cycloöctatetraenecarboxylic acid using a *p*H meter with a glass electrode and carbonate-free sodium hydroxide gave pK_A 4.4. The ultraviolet absorption spectrum (Fig. 1, curve 1), determined in 95% ethanol with a Beckman model DU quartz ultraviolet spectrophotometer, contained a maximum at 306 mμ (ϵ 830).

Hydrogenation of a solution of 0.444 g. of cycloöctatetraenecarboxylic acid in 4 ml. of acetic acid in the presence of 100 mg. of prereduced platinum oxide resulted in the absorption of three molar equivalents of hydrogen in 1.5 hours and a total of 99.9% of four molar equivalents in 6.5 hours. After filtering, the acetic acid was removed by gradually reducing the pressure to 0.3 mm., and the oily residue was distilled through a semi-micro column,[11] yielding 0.45 g. (96%) of cycloöctanecarboxylic acid, b. p. 98–99° (0.28 mm.), $n^{25}\text{D}$ 1.4778.[12] Comparison of the infrared spectrum of the acid with the spectrum of an authentic sample showed them to be identical. A sample of cycloöctanecarboxylic acid prepared from cycloöctatetraenecarboxylic acid was converted through the acid chloride to the amide, m.p. and mixed m.p. with a known sample, 192.4–195.8° (sublimation and dec.) (Godchot and Cauquil, ref. 12, report m.p. 191°).

Hydrogenation of a solution of 0.444 g. of cycloöctatetraenecarboxylic acid in 4 ml. of 95% ethanol in the presence of 0.1 g. of 10% palladium-on-Norit was complete in 50 minutes and 99.8% of three molar equivalents of hydrogen was absorbed. After filtration and dilution with 90 ml. of water, extraction with six 5-ml. portions of ether and concentration of the extracts yielded 0.45 g. (97.5%) of a crude acid, m. p. 89–97°. Several recrystallizations from ether yielded 0.30 g. of cycloöctene-1-carboxylic acid, m.p. 102–103°.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15; neut. equiv., 154. Found: C, 70.04; H, 9.16; neut. equiv., 153.

Cycloöctene-1-carboxylic Acid.—1-Bromocycloöctene[13] (5.7 g.) was added with stirring during 0.5 hour to 0.414 g. of lithium wire in 50 ml. of dry ether under nitrogen. The mixture was stirred for 15 minutes after the addition was completed, and then was siphoned onto powdered Dry Ice. After addition of 10 ml. of water and extraction of the ether

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[8] Analogous to the preparation of 1-cyclohexenyllithium described by E. A. Braude and J. A. Coles, *J. Chem. Soc.*, 2014 (1950).

[9] Melting points are corrected and boiling points are uncorrected. We are indebted to Mr. S. M. Nagy and his associates for analyses and for the infrared spectra, which were determined with a Baird Double Beam Infrared Recording Spectrometer, Model B, fitted with a sodium chloride prism.

[10] Prepared by the procedure of H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn and L. S. Miller, This Journal, **71**, 1499 (1949).

[11] C. W. Gould, Jr., G. Holzman and C. Niemann, *Anal. Chem.*, **20**, 361 (1948).

[12] An authentic sample was prepared by carbonation of cycloöctylmagnesium bromide by the procedure of M. Godchot and G. Cauquil, *Chimie et industrie*, Special No., 1019 (June, 1933); *C. A.*, **28**, 468 (1934), who report b.p. 150° (19 mm.), $n^{22}\text{D}$ 1.4779.

[13] Prepared by the procedure of E. P. Kohler, M. Tishler, H. Potter and H. T. Thompson, This Journal, **61**, 1057 (1939).

layer with two additional 10-ml. portions of water, the combined aqueous layers were acidified with hydrochloric acid. The colorless crystalline acid was extracted with ether, and the extracts were dried over magnesium sulfate and concentrated, yielding 2.2 g. of cycloöctene-1-carboxylic acid as a white solid, m.p. 98.6–101.6°. Recrystallization from ether yielded 1.40 g. (30%) of the acid, m.p. 101.8–102.6°. This sample of the acid was identical with the sample prepared from cycloöctatetraenecarboxylic acid (mixed melting point and comparison of the infrared spectra). The ultraviolet spectrum (Fig. 1, curve 2), determined in 95% ethanol with a Beckman model DU quartz ultraviolet spectrophotometer, also was identical with the spectrum of the acid derived from cycloöctatetraenecarboxylic acid and contained a maximum at 218 mμ (ϵ 12,100). This maximum may be compared with the maximum at 212 mμ (ϵ 11,000) reported for cyclohexene-1-carboxylic acid.[8]

Hydrogenation of a solution of 0.444 g. of cycloöctene-1-carboxylic acid (prepared from 1-cycloöctenyllithium) in 4 ml. of glacial acetic acid in the presence of 0.1 g. of prereduced platinum oxide was complete in 3 hours and resulted in absorbtion of 101% of one molar equivalent of hydrogen. The cycloöctanecarboxylic acid formed was isolated by the procedure described above; 0.35 g. (78%), b.p. 90–92° (0.10 mm.), n^{25}_{D} 1.4782, and had an infrared spectrum identical with the authentic sample.[12]

Methyl Cycloöctatetraenecarboxylate.—An ethereal solution (25 ml.) containing the diazomethane prepared from 2.0 g. of nitrosomethylurea was added to a solution of 1.0 g. of cycloöctatetraenecarboxylic acid in 20 ml. of ether. After nitrogen evolution ceased, glacial acetic acid was added dropwise to decompose the excess diazomethane, and the solution was washed with two 10-ml. portions of saturated sodium bicarbonate solution and dried over magnesium sulfate. After concentration, the residue was distilled through a semi-micro column, and yielded 0.976 g. (89%) of methyl cycloöctatetraenecarboxylate as a yellow liquid, b.p. 75–76.2° (5 mm.), n^{25}_{D} 1.5398, d^{25}_{4} 1.092.

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.23; sapn. equiv., 162. Found: C, 74.06; H, 6.42; sapn. equiv., 161.

Saponification of 0.105 g. of the ester with very dilute aqueous sodium hydroxide containing a little ethanol at about 80° for 2 hours yielded 0.078 g. (81%) of cycloöctatetraenecarboxylic acid, m.p. and mixed m.p. 72–73°.

Quinine Salt of Cycloöctatetraenecarboxylic Acid.—A solution of 1.00 g. of cycloöctatetraenecarboxylic acid in 100 ml. of ether was added to 2.6 g. of quinine hydrate in 200 ml. of ether. The yellow, crystalline salt which separated slowly weighed 2.89 g. (91%) after drying. The salt melted at 200.6–202° (dec.) and had $[\alpha]^{28°}_{\mathrm{D}}$ −122.5° (1. = 1, *c* 2.0 in 95% ethanol). After one recrystallization from ethyl acetate and three from water, these physical constants were unchanged.

Anal. Calcd. for $C_{29}H_{32}N_2O_4$: C, 73.55; H, 7.02; N, 5.92. Found: C, 73.57; H, 6.94; N, 6.00.

1-β-Phenylisopropylamine Salt of Cycloöctatetraenecarboxylic Acid.—A solution of l-β-phenylisopropylamine was prepared by neutralizing 1.88 g. of the sulfate with 0.64 g. of sodium hydroxide in 50 ml. of water and extracting the base with 50 ml. of ether. This solution was added to 1.00 g. of cycloöctatetraenecarboxylic acid in 25 ml. of ether. Yellow needles of the salt separated slowly, which after drying weighed 1.85 g. (97%); m.p. 155.6–157.2°, $[\alpha]^{28}_{\mathrm{D}}$ +1.4° (1. = 1, *c* 2.0 in 95% ethanol). After two recrystallizations from ethyl acetate and two from water, the melting point and rotation were unchanged.

Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.06; H, 7.44; N, 4.98.

***d*-β-Phenylisopropylamine Salt of Cycloöctatetraenecarboxylic Acid.**—This salt was prepared by the procedure described for the salt of the *l*-base in a yield of 1.73 g., m.p. 155.9–157.2°, $[\alpha]^{28}_{\mathrm{D}}$ −0.5° (1. = 1, *c* 2.0 in 95% ethanol). Three crystallizations from ethyl acetate and two from water did not change these physical constants.

Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.29; H, 7.42; N, 4.92.

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Cyclic Polyolefins. XXI. Alkylcycloöctatetraenes and Alkylcycloöctatrienes from Cycloöctatetraene and Alkyllithium Compounds

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The reaction of typical *n*-alkyllithium compounds (ethyllithium and *n*-butyllithium) with cycloöctatetraene in ether proceeds by addition, followed by the equivalent of lithium hydride transfer to another molecule of cycloöctatetraene. The products formed are the *n*-alkylcycloöctatetraenes and a mixture of 1,3,5- and 1,3,6-cycloöctatrienes, plus small amounts of the alkylcycloöctatrienes. Reaction of *n*-butyllithium and *s*-butyllithium with cycloöctatetraene in pentane results only in addition, and yields the alkylcycloöctatrienes.

This paper reports an extension of the preparation of arylcycloöctatetraenes from cycloöctatetraene and aryllithium compounds[2] to the synthesis of alkylcycloöctatetraenes. *n*-Butyllithium and ethyllithium were investigated as typical *n*-alkyllithium derivatives. Both reacted with cycloöctatetraene in ether, and after hydrolysis the hydrocarbons isolated were the alkylcycloöctatetraenes (I and II), alkylcycloöctatrienes (III and IV), a mixture of 1,3,5- and 1,3,6-cycloöctatrienes (V) and recovered cycloöctatetraene. The mixtures were separated by a combination of fractional distillation and differential extraction with silver nitrate. The reactions presumably follow the same course as the reaction of cycloöctatetraene with aryllithium compounds, which formed similar products.[2]

The hydrocarbons formed from *n*-butyllithium were separated by an initial differential extraction with aqueous silver nitrate. Extraction with 20–25% silver nitrate separated recovered cycloöctatetraene (38%), while 50% silver nitrate extracted *n*-butylcycloöctatetraene and the isomeric cycloöctatrienes (V). After regeneration of the hydrocarbons from the 50% silver nitrate extract by treatment with an excess of sodium chloride, fractional distillation separated *n*-butylcycloöctatetraene (14.5%) from the cycloöctatrienes (11.5%). A small amount (3%) of *n*-butylcycloöctatriene (III) was isolated by distillation of the fraction that was insoluble in aqueous silver nitrate.

The products formed from ethyllithium were separated by the more advantageous procedure of an initial distillation to separate (1) a mixture of cycloöctatetraene and cycloöctatrienes from (2) a mixture of ethylcycloöctatetraene and ethylcyclo-

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[1] du Pont Fellow, 1949–1950.

[2] A. C. Cope and M. R. Kinter, THIS JOURNAL, **72**, 630 (1950); **73**, 3424 (1951).