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

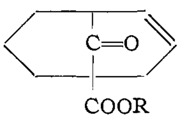
Cyclic Polyolefins. XXXV. Cycloöct-1-ene-1,5-dicarboxylic Acid and Cycloöctane-*cis*- and *trans*-1,5-Dicarboxylic Acids

BY ARTHUR C. COPE, ERIC S. GRAHAM AND DAVID J. MARSHALL

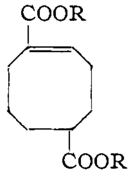
RECEIVED APRIL 8, 1954

Ethyl bicyclo[3.3.1]non-3-ene-9-one-1-carboxylate (I) has been shown to undergo a reverse acetoacetic ester condensation in the presence of sodium ethoxide to yield diethyl cycloöct-1-ene-1,5-dicarboxylate (III, 58%). Catalytic hydrogenation of cycloöct-1-ene-1,5-dicarboxylic acid yielded a mixture of *cis* and *trans* isomers of cycloöctane-1,5-dicarboxylic acid, which were separated by fractional crystallization from water. Reaction of the ester I with magnesium methoxide in methanol resulted in Meerwein–Ponndorff reduction and yielded methyl bicyclo[3.3.1]non-3-ene-9-ol-1-carboxylate (VI, 77%). Lithium aluminum hydride reduction of 1-bromobicyclo[3.3.1]nonan-9-one (IX) has been shown to result in molecular rearrangement, forming bicyclo[3.3.0]octane-1-methanol (XI).

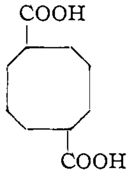
As part of a study of the utilization of carbonyl-bridged intermediates for the synthesis of cyclooctapolyenes, the preparation of ethyl bicyclo-[3.3.1]non-3-ene-9-one-1-carboxylate (I) was reported.[1] It now has been found that this α,α-disubstituted β-ketoester will undergo a reverse acetoacetic ester condensation[2] in the presence of sodium ethoxide to yield diethyl cycloöct-1-ene-1,5-dicarboxylate (III, 58%). Evidence for the structure of III was obtained from analysis and the saponification equivalent, which showed it to be a dicarboxylic ester, and from the ultraviolet spectrum, which showed a maximum at 221 $m\mu$ (ϵ 9820) consistent with the formulation of III as an α,β-unsaturated ester.



I, R = C_2H_5
II, R = H



III, R = C_2H_5
IV, R = H

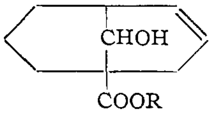


V

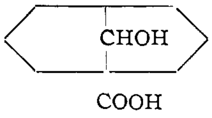
Saponification of III led to the dicarboxylic acid IV, which was hydrogenated quantitatively to cycloöctane-1,5-dicarboxylic acid (V). The latter was obtained as a mixture of *cis* and *trans* isomers that was separated into its components by crystallization from water. Isomer A, which crystallized first, melted at 169.0–171.0°, while isomer B, which tended to concentrate in the mother liquors, melted at 170.8–172.1°. A mixed melting point was depressed a small but significant amount, to 166.0–168.5°. Infrared spectra of the two acids were similar but not identical. Since the spectra were determined for Nujol mulls of the solids because of their insolubility in suitable solvents, the differences could have been due either to stereoisomerism or to differences in crystal structure (polymorphism). Dr. David P. Shoemaker has kindly examined the two acids by the Debye–Scherrer powder photographic X-ray diffraction method, and concluded that they have significantly different crystal structures, and almost certainly correspond to different chemical species. Monobenzylamine salts of the two acids had very similar melting points and showed only a small depression in mixed melting points. However, the di-*p*-bromophenacyl esters differed in melting point by 20° and had distinctly different solubilities. These data support the conclusion that the two forms A and B are stereoisomers rather than polymorphous forms of the same substance. The two acids could be sublimed unchanged under reduced pressure at temperatures below their melting points, but on heating with acetic anhydride both formed the same intramolecular anhydride. No attempt was made to assign configurations (*cis* and *trans*) to the two stereoisomers.

When the unsaturated dicarboxylic ester III was allowed to react with N-bromosuccinimide, an allylic bromide (or a mixture of isomeric allylic bromides) was formed. However, preliminary attempts to dehydrobrominate this product by heating with triethylamine, tri-*n*-butylamine or collidine in order to introduce a second double bond into the eight-membered ring were unsuccessful.

In one of a series of experiments designed to determine optimum conditions for the alcoholysis of the β-ketoester I, magnesium methoxide was used as the base. In this case a Meerwein–Ponndorff type of reduction took place, and a 77% yield of the β-hydroxyester VI was obtained (the methyl ester being formed by alcohol interchange with the methanol solvent). The hydroxyester VI was saponified to the corresponding acid VII, and the latter was hydrogenated to bicyclo[3.3.1]-nonan-9-ol-1-carboxylic acid (VIII), the melting point of which was not depressed on admixture with a known sample. The authentic sample of VIII was obtained by hydrogenation of the β-ketoacid II. Magnesium ethoxide is reported[3] to give poor results in the Meerwein–Ponndorff reduction due to its tendency to cause aldol condensation to occur. The effectiveness of magnesium methoxide in the present case undoubtedly is due to the fact that I cannot undergo self-condensation.



VI, R = CH_3
VII, R = H



VIII

A recent study[4] of the reactions of 1-bromobicyclo[3.3.1]nonan-9-one (IX) (obtained by hy-

---

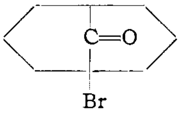
[1] A. C. Cope and M. E. Synerholm, THIS JOURNAL, **72**, 5228 (1950).

[2] See C. R. Hauser and B. E. Hudson, in "Organic Reactions," Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 269.

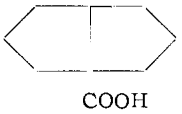
[3] H. Meerwein and R. Schmidt, *Ann.*, **444**, 221 (1925).

[4] A. C. Cope and E. S. Graham, THIS JOURNAL, **73**, 4702 (1951).

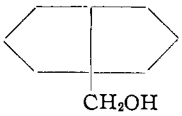
drogenation of the carbon–carbon double bond of the ketoacid II, formation of the silver salt, and treatment of the latter with bromine[1]) has shown that this compound undergoes a number of reactions involving rearrangement of the carbon skeleton. For example, IX gives an immediate precipitate of silver bromide with ethanolic silver nitrate with the concomitant formation of a mixture of bicyclo[3.3.0]octane-1-carboxylic acid (X) and the corresponding ethyl ester. In the present work, it was found that reduction of IX with lithium aluminum hydride yielded a very volatile solid alcohol that was shown to have the structure XI by comparison with a sample obtained by lithium aluminum hydride reduction of the acid X. The two samples of the alcohol XI were compared through their 3,5-dinitrobenzoates, which proved to be identical. The rearrangement of the carbon skeleton of IX in its conversion to the alcohol XI can be interpreted by a "push-pull" mechanism analogous to the one proposed previously to account for some of the other reactions of IX.[4] The transfer of a hydride ion from aluminohydride ion to the carbonyl carbon atom of IX[5] and a shift of the electron pair of the C_5–C_9 bond to form the C_5–C_1 bond supply the "push," and removal of the bromine aided by aluminum hydride, the solvent, or ion pairs present in the solution supplies the "pull." The intermediate aldehyde XII would then be reduced to the alcohol XI in the normal manner.



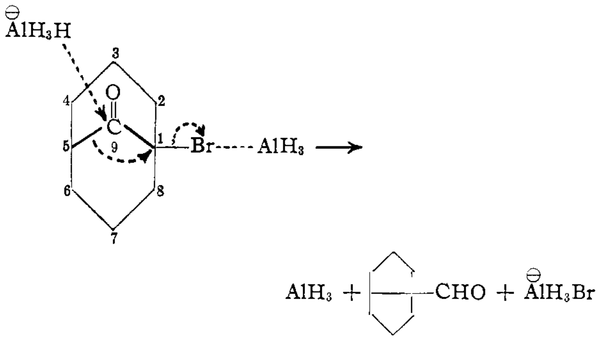
IX



X



XI



XII

Experimental[6]

Diethyl Cycloöct-1-ene-1,5-dicarboxylate (III).—To a solution of sodium ethoxide prepared from 0.287 g. (0.0125 mole, 52 mole %) of sodium and 50 ml. of absolute ethanol was added 5.00 g. (0.024 mole) of ethyl bicyclo[3.3.1]non-3-ene-9-one-1-carboxylate (I).[1] The mixture was heated under reflux for 21 hours, poured into 250 ml. of water, acidified with hydrochloric acid and extracted with four 50-ml. portions of ether. The ether extracts were washed with 5% sodium bicarbonate solution and dried over magnesium sulfate. The ether was removed and the residue was distilled through a semimicro column,[7] and yielded 3.50 g. (58%) of diethyl cycloöct-1-ene-1,5-dicarboxylate (III) as a colorless oil, b.p. 115–118° (0.37 mm.), $n^{25}\text{D}$ 1.4789, d^{25}_4 1.061. A sample from a similar preparation having $n^{25}\text{D}$ 1.4803 was analyzed; $\lambda_{\max}$ 221 mμ (ϵ 9820) in 95% ethanol.

Anal. Calcd. for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72; sapon. equiv., 127.2. Found: C, 65.85; H, 8.65; sapon. equiv., 130.0.

When I was heated with 15 mole % of sodium ethoxide for 18 hours, 33 mole % for 5 hours, and 50 mole % for 2.5 hours, the yields of III were 38, 50 and 42%, respectively.

Cycloöct-1-ene-1,5-dicarboxylic Acid (IV).—To 0.290 g. of the ester III was added 12.70 ml. of 0.5126 *N* sodium hydroxide and 3–4 ml. of water, and the mixture was heated under reflux for 18 hours. After cooling, the mixture was neutralized with 35.88 ml. of 0.1193 *N* hydrochloric acid. Removal of most of the solvent by a stream of air gave white crystals of cycloöct-1-ene-1,5-dicarboxylic acid (IV), m.p. 217.5–219.5°. Extraction of the residual solution with ether and evaporation of the ether gave a white solid that was sublimed at 270° (0.3 mm.), yielding an additional 10 mg., m.p. 216–218°. The total yield of IV was 0.173 g. (77%), melting at 218.8–220.0° after recrystallization from water.

Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12; neut. equiv., 99.1. Found: C, 60.43; H, 7.29; neut. equiv., 100.6.

Cycloöctane-1,5-dicarboxylic Acid (V) (*cis* **and** *trans* **Isomers**).—Cycloöct-1-ene-1,5-dicarboxylic acid (IV) (3.18 g.) was hydrogenated in 100 ml. of glacial acetic acid in the presence of 400 mg. of pre-reduced platinum oxide catalyst. After reduction was complete (7 hours), separation of the catalyst and removal of the solvent left 3.13 g. (98%) of crude cycloöctane-1,5-dicarboxylic acid (V) as a colorless solid, m.p. 153–165°. Two grams of this solid was dissolved in 100 ml. of boiling water, and the hot solution was filtered and allowed to cool slowly undisturbed. The colorless needles so obtained (1.3 g., m.p. 164–167°) were recrystallized four times from water to yield pure isomer A melting at 169.0–171.0°. Further recrystallization did not change the melting point.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.99; H, 8.06. Found: C, 59.96; H, 8.21.

The mother liquor from the original crystallization was concentrated to about 25 ml. On cooling, colorless plates (0.33 g.) were obtained, m.p. 171–172.5°. After three recrystallizations from water, pure isomer B was obtained melting at 170.8–172.1°; further recrystallization did not change the melting point. A mixed melting point of isomers A and B was 166.0–168.5°.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.99; H, 8.06. Found: C, 60.09; H, 8.26.

The monobenzylamine salt of isomer A was prepared by dissolving 50 mg. of the acid in boiling ethyl acetate and adding 0.06 ml. of benzylamine. The salt, which precipitated immediately, was recrystallized from acetonitrile and then melted at 192.4–193.4° (nitrogen-filled sealed capillary).

Anal. Calcd. for $C_{17}H_{25}NO_4$: C, 66.42; H, 8.20; N, 4.56. Found: C, 66.35; H, 8.42; N, 4.49.

The monobenzylamine salt of isomer B was prepared as described above for isomer A. After recrystallization from acetonitrile it melted at 192.6–193.6° (nitrogen-filled sealed capillary). A mixed melting point with the corresponding salt of isomer A was 188.5–192° (nitrogen-filled sealed capillary).

Anal. Calcd. for $C_{17}H_{25}NO_4$: C, 66.42; H, 8.20; N, 4.56. Found: C, 66.44; H, 8.28; N, 4.56.

The di-*p*-bromophenacyl ester[8] **of isomer A** crystallized from ethyl acetate as colorless needles, m.p. 172–174.5°.

Anal. Calcd. for $C_{26}H_{26}Br_2O_6$: C, 52.54; H, 4.41; Br, 26.89. Found: C, 52.33; H, 4.17; Br, 27.25.

The di-*p*-bromophenacyl ester of isomer B crystallized from ethyl acetate as colorless needles, m.p. 194.0–195.5°, much less soluble than the corresponding derivative of isomer A. A mixed m.p. with the derivative of isomer A was 171–185°.

---

(5) See W. G. Brown, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 471, for a discussion of the mechanism of lithium aluminum hydride reductions.

(6) Melting points are corrected and boiling points are uncorrected. We are indebted to Dr. S. M. Nagy and his associates for analyses.

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

(8) Prepared by the general method described by R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 157.

Anal. Calcd. for $C_{26}H_{26}Br_2O_6$: C, 52.54; H, 4.41; Br, 26.89. Found: C, 52.60; H, 4.48; Br, 27.24.

Cycloöctane-1,5-dicarboxylic Anhydride.—A solution of 200 mg. of isomer A in 6 ml. of acetic anhydride was heated under reflux for 4 hours. The solvent was removed under reduced pressure and the residue was sublimed at a heating block temperature of 140–170° and a pressure of 0.01 mm. The colorless solid was resublimed and then crystallized from benzene–petroleum ether to yield 102 mg. of cyclooctane-1,5-dicarboxylic anhydride as blunt, colorless needles, m.p. 138.0–139.5°.

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.61; H, 7.65.

By the same procedure isomer B yielded the same anhydride, m.p. and mixed m.p. 138.0–139.5°.

Methyl Bicyclo[3.3.1]non-3-ene-9-ol-1-carboxylate (VI).—To a solution of magnesium methoxide prepared from 0.585 g. (0.024 mole) of magnesium and 50 ml. of dry methanol was added 5.00 g. (0.024 mole) of ethyl bicyclo[3.3.1]-non-3-ene-9-one-1-carboxylate (I). The mixture was heated under reflux for 3 hours and poured into 250 ml. of water. Sufficient 20% hydrochloric acid was added to dissolve the magnesium hydroxide, and the mixture was extracted with three 50-ml. portions of ether. After drying over magnesium sulfate, the ether was removed and the residue was distilled through a semimicro column,[6] yielding 3.62 g. (77%) of methyl bicyclo[3.3.1]non-3-ene-9-ol-1-carboxylate (VI) as a colorless oil, b.p. 86–89° (0.61 mm.), n^{25}_{D} 1.5044.

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.33; H, 8.22; sapon. equiv., 196. Found: C, 66.87; H, 8.26; sapon. equiv., 193.

Bicyclo[3.3.1]non-3-ene-9-ol-1-carboxylic Acid (VII).—A mixture of 1 g. of the ester VI and 30 ml. of 0.5 *N* sodium hydroxide was heated under reflux for 1.5 hours. After cooling, the solution was acidified with concentrated hydrochloric acid and extracted with ether. Removal of the ether and recrystallization of the residue from water yielded bicyclo[3.3.1]non-3-ene-9-ol-1-carboxylic acid (VII) as a colorless solid, m.p. 119.3–121.1°.

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.79; H, 7.78.

Bicyclo[3.3.1]nonan-9-ol-1-carboxylic Acid (VIII).—The acid VII (0.239 g.) was hydrogenated in 20 ml. of 95% ethanol in the presence of 120 mg. of 10% palladium-on-Norit. Reduction was complete in 50 minutes with the absorption of 99% of 1 molar equivalent of hydrogen. After separation of the catalyst, the solvent was removed under reduced pressure. The residue was sublimed by heating at 0.2 mm., yielding 0.212 g. (88%) of bicyclo[3.3.1]nonan-9-ol-1-carboxylic acid (VIII), m.p. 122.6–123.1°, undepressed on admixture with the authentic sample described below.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 65.32; H, 8.70.

An authentic sample of VIII was obtained by the hydrogenation of 0.278 g. of bicyclo[3.3.1]non-3-ene-9-one-1-carboxylic acid (II) in 20 ml. of glacial acetic acid in the presence of 107 mg. of pre-reduced platinum oxide catalyst. Hydrogen absorption amounted to 100% of 2 molar equivalents in 1 hour. Sublimation of the crude product remaining after removal of catalyst and solvent by heating at 0.2 mm. yielded 0.243 g. (85%) of VIII, m.p. 117–121°. Resublimation followed by recrystallization from methylcyclohexane raised the melting point to 122.4–122.8°.

Bicyclo[3.3.0]octane-1-methanol (XI).—To 1.00 g. (0.0262 mole) of lithium aluminum hydride in 70 ml. of dry ether was added a solution of 2.00 g. (0.0092 mole) of 1-bromobicyclo[3.3.1]nonan-9-one (IX)[1,4] in 25 ml. of ether, with stirring under an atmosphere of nitrogen. After heating under reflux for 1 hour, the mixture was cooled to 0° and hydrolyzed with dilute hydrochloric acid. The aqueous layer was extracted with two 40-ml. portions of ether, and the combined ether solutions were dried over magnesium sulfate. Removal of the ether left a slightly yellow oil that was sublimed at 130° (0.3 mm.), yielding 1.13 g. (88%) of bicyclo[3.3.0]octane-1-methanol (XI) as a white solid, m.p. 44–52°, with a strong camphor-like odor. Resublimation at 50° (30 mm.) gave 1.06 g. of XI as long needles, m.p. 52–54°. Three more sublimations, the last two being conducted at room temperature and atmospheric pressure onto a cold-finger condenser, yielded an analytical sample of XI, m.p. 54–55°, and the melting point did not change on further sublimation.

Anal. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.62; H, 11.43.

An authentic sample of XI was prepared by adding dropwise a solution of 1.3 g. of bicyclo[3.3.0]octane-1-carboxylic acid (II) in 50 ml. of ether to 0.6 g. of lithium aluminum hydride in 50 ml. of ether. After heating under reflux for 3 hours, water and dilute hydrochloric acid were added. The water layer was extracted with two 20-ml. portions of ether and the combined ether solutions were washed with dilute sodium bicarbonate solution and dried over magnesium sulfate. Removal of the ether left an oil that was sublimed at 100° (30 mm.), yielding 0.99 g. of XI, m.p. 38–41°. The alcohol was difficult to purify and was converted to the 3,5-dinitrobenzoate for comparison with the sample obtained from IX.

Bicyclo[3.3.0]octane-1-methanol 3,5-dinitrobenzoate was prepared by adding 0.22 g. of 3,5-dinitrobenzoyl chloride to 0.11 g. of XI in 1 ml. of dry pyridine and boiling the mixture for 1 minute. The solution was cooled, poured into 5 ml. of water, and the solid derivative was recrystallized to constant melting point from 95% ethanol; m.p. and mixed m.p. with a known sample (prepared from the authentic sample of XI described above) 82.2–83.2°.

Anal. Calcd. for $C_{16}H_{16}N_2O_6$: C, 57.47; H, 5.43; N, 8.38. Found: C, 57.61; H, 5.54; N, 8.37.

Cambridge, Massachusetts