[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

A Synthesis of Diisopropylidene Ethylenetetracarboxylate[1]

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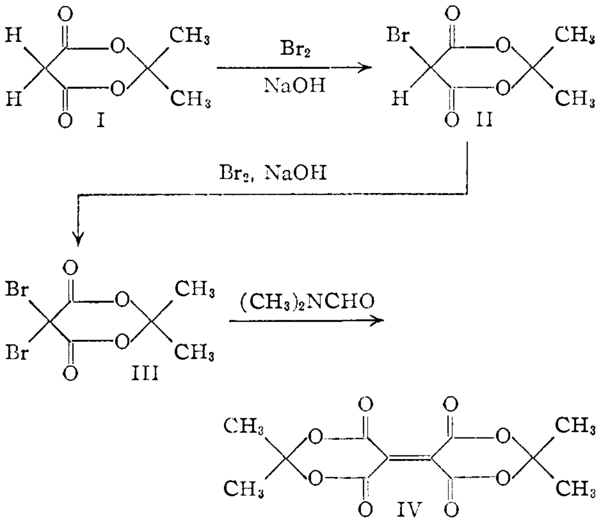
Diisopropylidene ethylenetetracarboxylate has been synthesized by debromination of isopropylidene dibromomalonate in dimethylformamide. Infrared and nuclear magnetic resonance spectra of isopropylidene malonate and isopropylidene bromomalonate are consistent with substituted 4,6-diketo-1,3-dioxane structures.

The synthesis of diisopropylidene ethylenetetracarboxylate (IV) was undertaken as part of an investigation of certain derivatives of isopropylidene malonate (I). Isopropylidene bromomalonate (II) and isopropylidene dibromomalonate (III) were the intermediates chosen since the literature abounds with examples of preparations of olefins by dehydrohalogenation and dehalogenation of halo derivatives of active methylene compounds. Although attempts to dehydrobrominate isopropylidene bromomalonate and to debrominate isopropylidene dibromomalonate by methods analogous to those used for the preparation of tetraethyl ethylenetetracarboxylate[3-6] and tetracyanoethylene[7] failed, the debromination of isopropylidene dibromomalonate was accomplished in dimethylformamide to produce diisopropylidene ethylenetetracarboxylate in moderate (32%) yield.



Isopropylidene malonate and isopropylidene bromomalonate have been known for nearly fifty years,[8,9] but their correct structures were not recognized until 1948.[10] They were previously thought to be β,β-dimethyl-β-propiolactone-α-carboxylic acid and its α-bromo derivative. Isopropylidene dibromomalonate has not been reported previously. It was prepared by bromination of isopropylidene malonate in the presence of two moles of potassium or sodium hydroxide. High-melting complex salts containing the alkali metal bromide precipitated from the aqueous solutions. These salts may be similar to those which have been reported from dibromomalononitrile and alkali metal halides.[11] The complex salts of isopropylidene dibromomalonate dissociate rapidly in organic solvents such as ether, benzene or acetone. Isopropylidene dibromomalonate is a crystalline, white solid which undergoes decomposition over a period of a few days at room temperature to produce lachrymatory products. In the presence of a base it generates carbon tetrabromide.

The infrared spectra of chloroform solutions of isopropylidene malonate, isopropylidene bromomalonate and isopropylidene dibromomalonate confirm the absence of a carboxyl group. The split carbonyl bands occur at 1787, 1760; 1780, 1767 and 1790, 1768 cm.$^{-1}$, respectively. If the enol forms of isopropylidene malonate and isopropylidene bromomalonate are present in chloroform or acetone solutions, the quantities are too slight to be detected in. the infrared and nuclear magnetic resonance spectra. The NMR spectrum of isopropylidene malonate in 50% acetone has only two peaks in addition to the peak which results from the six equivalent hydrogen atoms of the solvent, and they occur at +57 and +139 cycles relative to the hydrogen atoms of water in the approximate area ratio of 1:3. The corresponding bands for isopropylidene bromomalonate are at −35 and +137 cycles; the ratio is approximately 1:6.

Isopropylidene bromomalonate is more acidic than isopropylidene malonate, as shown by the fact that the conjugate base of isopropylidene malonate reacts with isopropylidene bromomalonate not by displacement of bromide ion but by removal of a proton to produce the conjugate base of isopropylidene bromomalonate. Attempts to prepare diisopropylidene ethylenetetracarboxylate by the treatment of isopropylidene bromomalonate with bases such as potassium carbonate, sodium methoxide, ammonia and aniline failed. The potassium, sodium, ammonium and anilinium salts of isopropylidene bromomalonate were obtained. Attempts to prepare diisopropylidene ethylenetetracarboxylate by treatment of isopropylidene dibromomalonate with copper in benzene or with sodium iodide in acetone also failed. The dibromide was recovered in the first instance; the sodium iodide treatment produced isopropylidene malonate in 60% yield after decolorization with sulfurous acid.

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(1) The material here reported is taken from a dissertation submitted by C. W. Kruse to the Graduate College of the University of Illinois in partial fulfillment of the requirements for the degree of Doctor of Philosophy, February, 1958.

(2) Phillips Petroleum Co. Fellow, 1956–1957.

(3) R. Malachowski and Z. Sienkiewiczowa, *Ber.*, **68B**, 29 (1935).

(4) H. Finkelstein, *ibid.*, **43**, 1532 (1910).

(5) M. Conrad and C. Bruckner, *ibid.*, **24**, 3004 (1891).

(6) M. Conrad and M. Guthzeit, *Ann.*, **214**, 76 (1882).

(7) T. Cairns, *et al.*, THIS JOURNAL, **79**, 2340 (1957).

(8) A. Meldrum, *J. Chem. Soc.*, **93**, 598 (1908).

(9) E. Ott, *Ann.*, **401**, 159 (1913).

(10) D. Davidson and S. Bernhard, THIS JOURNAL, **70**, 3426 (1948).

(11) L. Ramberg and S. Wideqvist, *Arkiv Kemi, Mineral. Geol.*, **12A**, No. 22, 12 (1937); *C. A.*, **32**, 2511 (1938).

When a solution of isopropylidene dibromomalonate in dimethylformamide was allowed to stand at room temperature for 20 hours, a high-melting, white product crystallized. The infrared spectrum of this compound, empirical formula $C_3H_3O_2$ and molecular weight 301 (ebullioscopic in nitroethane), possessed noticeable similarities to spectra of isopropylidene malonate and its derivatives. The new compound was shown to be diisopropylidene ethylenetetracarboxylate[12] by hydrolysis to ethylenetetracarboxylic acid, by methanolysis to a 1,2-dimethyl ester of ethylenetetracarboxylic acid and by addition of hydrogen to the double bond. The methanolysis product, which may have been *cis* or *trans* or a mixture of both, was converted to tetramethyl ethylenetetracarboxylate with a limited amount of diazomethane, and also was converted to tetramethyl ethanetetracarboxylate by hydrogenation over platinum followed by reaction with diazomethane.

The carbonyl bands in the infrared spectrum of a Nujol mull of diisopropylidene ethylenetetracarboxylate occur at approximately 1770 and 1755 cm.$^{-1}$. These values are higher than expected for an α,β-unsaturated derivative of isopropylidene malonate. The carbonyl bands of isopropylidene cyclohexylidenemalonate occur at 1755 and 1730 cm.$^{-1}$ as compared to 1787 and 1760 cm.$^{-1}$ for isopropylidene malonate. Similarly, the expected shift to lower frequencies of the carbonyl absorption bands has been reported not to occur for tetraethyl ethylenetetracarboxylate and for diethyl 1,2-dicyanoethylene-1,2-dicarboxylate.[13] Models of diisopropylidene ethylenetetracarboxylate indicate that there is considerable steric interference between the carbonyl functions, and that coplanarity of the atoms in the conjugated system is not possible. There is a possibility that the isopropylidene malonate rings accentuate the carbonyl interference to the extent that stereoisomers result. These could be geometric (*cis–trans*) isomers if the double bond remains untwisted or optical isomers if the molecule is twisted along the axis of the double bond. The lack of solubility in any of the common organic solvents or water indicates that diisopropylidene ethylenetetracarboxylate possesses an unusually stable crystal lattice. Diisopropylidene ethylenetetracarboxylate is not appreciably soluble in refluxing benzene, ethanol, chloroform, dioxane or methyl ethyl ketone. Recrystallization was accomplished from 1-nitropropane, in which it is soluble to the extent of 0.5% at the boiling point. Diisopropylidene ethylenetetracarboxylate decomposes with gas evolution at 215–225° in a capillary tube, but when small crystals are observed under the microscope, they darken between 200 and 240° but do not appear to melt below 350°.

The mode by which debromination in dimethylformamide occurs has not been established, but there is the possibility that it may involve dehydrobromination of isopropylidene bromomalonate. Dehydrobromination in dimethylformamide has been reported in the literature.[14] The production of diisopropylidene ethylenetetracarboxylate in dimethylformamide is accompanied by the formation of carbon tetrabromide and highly lachrymatory products which are believed to be bromoacetones. A measure of support for the postulation of dehydrobromination was obtained by reaction of isopropylidene bromomalonate with dimethylformamide. Diisopropylidene ethylenetetracarboxylate was obtained, but the yield was less than 1%. Repeated attempts gave erratic results.

Experimental[15–19]

Isopropylidene malonate was prepared according to the procedures described by Davidson and Bernhard[10] and isopropylidene bromomalonate by Ott's procedure.[9]

Isopropylidene Dibromomalonate.—To a solution, prepared at 0–10° by dissolving 14.4 g. (0.1 mole) of isopropylidene malonate in 100 ml. of 2 *N* sodium hydroxide, was added dropwise with stirring at 0–10° over a 10-min. period 32 g. (0.2 mole) of bromine. The slurry was stirred for 20 min. at 0° and then filtered. The crystalline product was washed with two 25-ml. portions of ice-water. The yield was 29 g. of a slightly yellow, complex salt containing sodium bromide, water and isopropylidene dibromomalonate. It was shaken with 200 ml. of benzene, and the aqueous phase was removed. By concentration of the solution to dryness under reduced pressure, 22 g. (72%) of isopropylidene dibromomalonate, m.p. 75–76°, was obtained. An analytical sample, which was prepared by bromination of isopropylidene bromomalonate under similar conditions, had the same melting point, 75–76°, after two recrystallizations from carbon tetrachloride.

Anal. Calcd. for $C_6H_6O_4Br_2$: C, 23.87; H, 2.00; Br, 52.94. Found: C, 23.68; H, 2.23; Br, 52.38.

Diisopropylidene Ethylenetetracarboxylate.—A solution of 0.2 g. (0.66 mmole) of isopropylidene dibromomalonate in 3 ml. of dry dimethylformamide upon standing at room temperature for 20 hr. deposited 11.5 mg. (12%) of diisopropylidene ethylenetetracarboxylate, fragmentation at 170–190°.[20] Recrystallization from 1-nitropropane produced an analytical sample, sublimation near 200°, decomposition with gas evolution in a capillary tube at 215–225°.

Anal. Calcd. for $C_{12}H_{12}O_8$: C, 50.71; H, 4.26; mol. wt., 284. Found: C, 50.80; H, 4.25; mol. wt. (ebullioscopic in nitroethane), 301.

A yield of 32% was obtained from a solution of 1 g. of isopropylidene dibromomalonate in enough dimethylformamide to cover the bottom of a 125-ml. erlenmeyer flask to a depth of 0.65 cm. after two days at room temperature.

Hydrolysis of Diisopropylidene Ethylenetetracarboxylate.—To a solution of 0.31 g. (5.6 mmoles) of potassium hydroxide in 0.5 ml. of water was added in small portions 0.2 g. (0.7 mmole) of diisopropylidene ethylenetetracarboxylate with stirring at 40–50° until solution was complete. After 2 hr. at room temperature, the excess potassium hydroxide was neutralized with glacial acetic acid and 1 ml. of ethanol was added. The dipotassium salt of ethylenetetracarboxylic

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[12] Two structural formulas can be written for diisopropylidene ethylenetetracarboxylate. Structure IV is the expected product from the manner of synthesis. Isomerization to a compound in which the isopropylidene groups bridge 1,2-carboxyl groups is considered unlikely.

[13] D. Felton and S. Orr, *J. Chem. Soc.*, 2170 (1955).

[14] R. Holysz, THIS JOURNAL, **75**, 4432 (1953).

[15] Melting points on a Kofler micro hot-stage unless otherwise indicated.

[16] Analyses by J. Nemeth, Miss Claire Higham, Mrs. Ruby Ju and Mrs. M. Stingl.

[17] Infrared spectra by P. McMahon, J. Brader and B. Cloonan from Perkin-Elmer model 21 double beam recording spectrophotometers equipped with sodium chloride optics.

[18] Nuclear magnetic resonance spectra by B. Shoulders from a Varian Associates model V4300-2 high resolution NMR spectrometer with super stabilizer.

[19] Molecular weight determination by E. Pierron of the Clark Microanalytical Laboratory, Urbana, Ill.

[20] This phenomenon is very likely associated with the release of trapped dimethylformamide since the infrared spectra of the analytical sample and of a sample which had been heated to 200° do not possess an absorption band at 1675 cm.$^{-1}$ which appears in the spectrum of the crude product.

acid was removed by filtration and washed with 95% ethanol. A benzene slurry of the salt was treated with hydrogen chloride gas, evaporated to dryness, and the residue was extracted with ether. Evaporation of the ether left 0.07 g. (50%) of impure ethylenetetracarboxylic acid, m.p. 155–165° dec. Comparison of the infrared spectrum of this sample with one of an authentic sample of pure ethylenetetracarboxylic acid[3] left no doubt that the spectra are of the same compound.

Methanolysis of Diisopropylidene Ethylenetetracarboxylate.—A methanol solution, which was obtained after 5 hr. at reflux temperature from a slurry of 1.0 g. (3.5 mmoles) of diisopropylidene ethylenetetracarboxylate in 25 ml. of absolute methanol to which a trace of hydrogen chloride gas had been added, was decanted from a trace of undissolved material and concentrated to dryness under vacuum. The residue was dissolved in a minimum amount of 2 *N* potassium bicarbonate, filtered, and acidified with 12 drops of concentrated hydrochloric acid. The product was extracted with ten 5-ml. portions of ether, and the solution was dried over calcium chloride. Evaporation left 0.86 g. of waxy, white 1,2-dimethyl ester of ethylenetetracarboxylic acid, m.p. 189–190° with gas evolution, after recrystallization from an ether–chloroform mixture. The stereochemistry is not known.

Anal. Calcd. for $C_8H_8O_8$: C, 41.39; H, 3.47. Found: C, 41.14; H, 3.54.

Treatment of 0.1 g. of the dimethyl ester with excess diazomethane produced a liquid, but reaction with a limited amount produced tetramethyl ethylenetetracarboxylate, m.p. 121°[21] (lit.[2] m.p. 121°).

Reduction of 33 mg. (0.14 mmole) of the dimethyl ester with hydrogen over platinum in methanol at room temperature, followed by treatment with diazomethane, produced tetramethyl ethanetetracarboxylate, m.p. 137–138°. A mixed melting point with an authentic sample[21] was not depressed.

Hydrogenation of Diisopropylidene Ethylenetetracarboxylate.—The reduction of 0.284 g. (1 mmole) of diisopropylidene ethylenetetracarboxylate in 300 ml. of benzene over platinum under 3400 lb. hydrogen pressure at 85° for about 1 hr. produced a solution which, after evaporation, left a crystalline material and an oil. The oil was later found to be an impurity in the benzene. The residue was slurried with chloroform. By filtration, 45 mg. (16%) of diisopropylidene ethanetetracarboxylate, m.p. 198–200° from benzene, was obtained.

Anal. Calcd. for $C_{12}H_{14}O_8$: C, 50.35; H, 4.93. Found: C, 50.65; H, 4.90.

Isopropylidene Cyclohexylidenemalonate.—A solution of 1.44 g. (10 mmoles) of isopropylidene malonate and 0.98 g. (10 mmoles) of cyclohexanone in 5 ml. of dimethylformamide stood at room temperature for 24 hr. Isopropylidene cyclohexylidenemalonate (0.4 g., 18%) crystallized when the solution was poured into about 20 ml. of ice-water. A preliminary purification was accomplished by pouring a saturated acetone solution of it into water. A product, m.p. 85–86°, was obtained by filtration. An analytical sample, m.p. 87–87.5°, was obtained by recrystallization from methanol.

Anal. Calcd. for $C_{13}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.55; H, 7.39.

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[21] C. Bischoff, *Ber.*, **29**, 1283 (1896).

[CONTRIBUTION FROM THE OLIN MATHIESON CHEMICAL CORPORATION, HIGH ENERGY FUELS ORGANIZATION]

Concerted Displacement Reactions: The Reaction of Catechol with Acyl Halides[1a,b]

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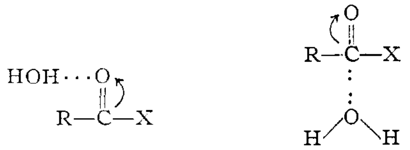
The rates of reaction of catechol with several acyl halides were determined in 95% acetone. The results indicate that the reaction proceeds by a concerted attack of the monocatecholate ion on the acyl halide with the formation of the monoacyl ester of catechol. Benzenesulfonyl fluoride and benzoic anhydride appear to react with catechol by a similar concerted mechanism. Resorcinol, hydroquinone and phenol are, relative to catechol, unreactive toward acyl halides.

Introduction

The rates of hydrolysis and alcoholysis of acyl halides in inert solvents have been claimed to vary with the square of the concentration of water or alcohol.[2a,b]

$$\text{rate of reaction} = k(H_2O)^2\ (\text{acyl halide})$$

Water or alcohol can act by virtue of their amphoteric character either as electrophilic or nucleophilic reagents in the solvolysis of acyl halides.



electrophilic attack nucleophilic attack

The possibility that the reaction in such systems involves a simultaneous electrophilic and nucleophilic attack on the substrate was recognized by Lowry and Faulkner[3] in their study of the mutarotation of tetramethylglucose. In inert solvents a mixture of pyridine and cresol markedly increased the rate of mutarotation even though both reagents were relatively ineffective by themselves. The hypothesis of a termolecular reaction mechanism was, therefore, advanced. Swain used the term "concerted displacement" to describe the phenomenon.[4,5] A concerted mechanism in general gives rise to third-order kinetics. The observed third-order kinetics can also arise from two consecutive bimolecular reactions.

$$A + B \underset{k_2}{\overset{k_1}{\rightleftharpoons}} C$$

$$C + D \xrightarrow{k_3} E$$

If k_3 is the rate-determining step, the rate of reaction is

$$\frac{k_1k_3}{k_2}\,(A)\,(B)\,(D)$$

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[1] (a) This document is based upon work performed under Contract Number DA-18-108-CML-5635 for the Chemical Corps, Department of the Army; (b) presented before the 132nd Meeting of the American Chemical Society, New York, N. Y., September, 1957.

[2] (a) G. Zimmerman and C. Yuan, THIS JOURNAL, **77**, 332 (1955); V. Gold and J. Hilton, *J. Chem. Soc.*, 838 (1955), disagree with Z and Y. (b) A. A. Ashdown, THIS JOURNAL, **52**, 268 (1930).

[3] T. Lowry and I. J. Faulkner, *J. Chem. Soc.*, **127**, 2883 (1925).

[4] C. G. Swain, THIS JOURNAL, **70**, 1124 (1948).

[5] C. G. Swain, *ibid.*, **72**, 4678 (1950).