

The column filtrate containing the material which had given rise to the orange zone was also evaporated to dryness in an inert atmosphere and the residue (40 mg.) crystallized from benzene and isopropyl ether. Clusters of scarlet blades were obtained sintering at 184°; the color<sup>18</sup> agrees well with the formulation of this substance as a derivative of an  $\alpha,\beta$  unsaturated ketone (VI).

*Anal.* Calcd. for  $C_{14}H_{14}N_4O_4$ : C, 55.62; H, 4.67; N, 18.54. Found: C, 55.67; H, 4.97; N, 18.93.

**Investigation of Basic Products.**<sup>19</sup>—The ether solution obtained by continuous extraction of the liberated bases from the pyrolysis distillate was carefully distilled to remove solvent and the residue fractionated in special equipment. Because of the small amounts of material available (0.4 cc.) accurate separations were not achieved. The unsaturated base, 1-dimethylaminocyclobutene-1 (III) was not isolated nor could any characteristic derivative be obtained. However, cyclobutanone (identified as semi-

(18) According to a generalization formulated by Dr. C. E. Redemann (based on unpublished observations made in this Laboratory), when the parent carbonyl compound has a double bond conjugated with the carbonyl group, the 2,4-dinitrophenylhydrazone is colored red; a few exceptions are known. The method used above to prepare the dinitrophenylhydrazones of (V) and (VI) is based on a procedure recommended by Redemann.

(19) In one pyrolysis carried out at 350–400°, the contents of the hydrochloric acid wash bottle were combined with the pyrolysis distillate and the neutral material removed with ether. The acid solution was then evaporated to dryness *in vacuo*, taken up in a small amount of water and slowly added to potassium hydroxide pellets in an apparatus arranged for distillation. Volatile amines were removed at a bath temperature of 60° and the oily top layer remaining allowed to stand for 24 hours in contact with the concentrated base. During this time the oily layer had been transformed to an amorphous non-volatile solid, difficultly soluble in water and ether, soluble in alcohol and pyridine; it was easily soluble in dilute hydrochloric acid and from the resulting solution was reprecipitated by addition of alkali. Evidently dimethylamine had added to condensation products of cyclobutanone to give high molecular weight bases.

carbazone) was recovered from the fraction boiling at 90–110°. 1,2-bis-(Dimethylamino)-cyclobutane (II) was shown to be present in the appropriate fraction (ca. 0.25 cc.) by conversion to its characteristic dipicrate, dimethiodide and (from this latter) dimethopicrate. The properties of these derivatives agreed with those found above.

The contents of the hydrochloric acid wash bottle were evaporated to dryness *in vacuo* at 100°, giving 12.4 g. of a mixture of the hydrochlorides of dimethylamine and of trimethylamine. The former was identified by its benzenesulfonyl derivative, m. p. 47°<sup>20</sup> from isopropyl ether, and the latter by its picrate, yellow needles from aqueous alcohol, m. p. 224–225°.<sup>21</sup> A comparison of the amount of benzenesulfonyl derivative obtained, with that formed under identical conditions in control experiments from mixtures of dimethylamine and trimethylamine of known composition indicated that these had been formed during the pyrolysis in the ratio of approximately 1 to 5.

### Summary

Cyclobutadiene was not detected among the products of thermal decomposition of *trans*-1,2-cyclobutane-*bis*-(trimethylammonium) hydroxide. Dimethylamine, trimethylamine, *trans*-1,2-*bis*-(dimethylamino)-cyclobutane, cyclobutanone and condensation products of the latter were identified as products of the pyrolysis. 1-Dimethylaminocyclobutene-1 is postulated as an unstable intermediate in the reaction.

(20) Beilstein, "Handbuch der organischen Chemie," 4th ed., 1928, Vol. XI, p. 40.

(21) Beilstein, "Handbuch der organischen Chemie," 4th ed., 1923, Vol. VI, p. 280.

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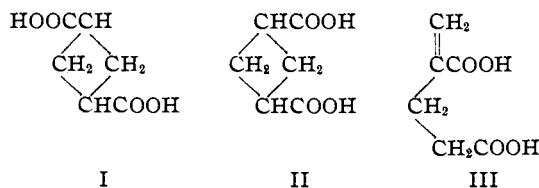
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## Cyclobutane Derivatives. III. *cis*-1,3-Cyclobutanedicarboxylic Acid

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In 1890 Markownikoff<sup>1</sup> converted *trans*-1,3-cyclobutanedicarboxylic acid (I) into an isomeric acid to which the *cis*-structure (II) was later assigned by E. Haworth and Perkin, Jr.<sup>2</sup> These



(1) Markownikoff, *J. Russ. Phys.-Chem. Soc.*, **22**, 279 (1890) [*Ber.*, **23**, 432 (1890)].

(2) Haworth and Perkin, *J. Chem. Soc.*, **73**, 330 (1898).

latter authors also reported<sup>2</sup> that they were able to isolate (II) from the mother liquors resulting from the preparation<sup>3</sup> of (I) and from the product of the action of alkali on polymeric methylenemalonic ester. The preparation of (II) by related reactions (from formaldehyde and malonic ester or their equivalents) was claimed in further studies<sup>4</sup> by Perkin, Jr., and co-workers. Although the acid obtained in this way yielded,<sup>4c</sup> under relatively mild conditions, products having an open

(3) From the action of sodium ethylate on ethyl  $\alpha$ -chloropropionate, Markownikoff and Krestownikoff, *Ann.*, **208**, 333 (1881).

(4) (a) Bottomley and Perkin, *J. Chem. Soc.*, **77**, 294 (1900); (b) Simonsen, *ibid.*, **93**, 1777 (1908); (c) Perkin and Simonsen, *ibid.*, **95**, 1166 (1909).

chain, the assigned structure has not previously been questioned.<sup>5</sup>

In connection with researches involving the preparation of considerable amounts of cyclobutanedicarboxylic acids, the above syntheses were reexamined. It was found that (II) may be obtained both from the *trans*-isomer (I) as had been demonstrated by Markownikoff<sup>1</sup> and as a by-product in the preparation of (I) as shown by Haworth and Perkin.<sup>2</sup> Its structure was substantiated by the fact that it was found possible (see Experimental) to reconvert it to (I).

However the acid obtained by a variety of methods<sup>2,4</sup> from formaldehyde and malonic ester does not possess the cyclic structure and is, in fact, identical with the well characterized<sup>6</sup>  $\alpha$ -methylene-glutaric acid (III). Its properties when made by the English investigators' methods<sup>2,4</sup> coincided with the literature data<sup>6</sup> on this substance; the constitution was confirmed by direct comparison with (III) of known structure made from methyl acrylate.<sup>6b</sup>

There is a fortuitous physical resemblance between (II) and (III) and between some of their derivatives which accounts for the mistake in identity. Chemically the two acids can easily be distinguished; (II) has saturated properties consistent with its formula while (III) reacts instantaneously with alkaline permanganate,<sup>6b,c</sup> adds hydrobromic acid<sup>4c,6b,c,7</sup> and with diazomethane readily gives a pyrazoline derivative.

### Experimental<sup>8</sup>

*cis*-1,3-Cyclobutanedicarboxylic Acid (II).—Following the procedure of Markownikoff,<sup>1</sup> the silver salt of the *trans*-acid (I) was treated with acetyl chloride to give the mixed anhydride, distillation of which at 2 mm. yielded the anhydride of (II), rosetts of colorless blades from absolute ether, m. p. 47.5–48.0°.

*Anal.* Calcd. for C<sub>6</sub>H<sub>8</sub>O<sub>3</sub>: C, 57.14; H, 4.80. Found: C, 56.89; H, 4.97.

The mixed anhydride was more conveniently prepared by refluxing (I) with ten molecular proportions of acetyl chloride<sup>9</sup> for five hours. After removal of solvent by distillation, the residue was treated as above to give the anhydride of (II).

The *cis*-acid (II) was obtained from its anhydride by

(5) Compare Wassermann, *Helv. Chim. Acta*, **13**, 223 (1930); see also Clemo and Welch, *J. Chem. Soc.*, 2621 (1928).

(6) (a) Weidel, *Monatsh.*, **11**, 513 (1890); [*Ber.*, **24B**, 148 (1891)]; (b) von Pechmann and Röhm, *ibid.*, **34**, 428 (1901); (c) Fichter and Beisswenger, *ibid.*, **36**, 1202 (1903).

(7) The product obtained by Perkin and Simonsen<sup>4c</sup> must be formulated as  $\alpha$ -(bromomethyl)-glutaric acid. The other supposed products of ring splitting retain their previously assigned formulas.

(8) All melting points are corrected.

(9) Haworth and Perkin<sup>2</sup> employed acetic anhydride.

evaporating a solution in five times its weight of 6 *N* hydrochloric acid to dryness on a steam-bath and recrystallizing the residue from hydrochloric acid and finally from water, m. p. 143.0–143.5°.

*Anal.* Calcd. for C<sub>6</sub>H<sub>8</sub>O<sub>4</sub>: C, 50.00; H, 5.60. Found: C, 50.20; H, 5.85.

Crude diethyl ester<sup>3</sup> b. p. 123–130° at 28 mm. was refluxed for twenty-four hours with 6.5 times its weight of 6 *N* hydrochloric acid and the resulting solution evaporated on a steam-bath. The residue, consisting of crude crystalline *trans*-acid (I) and a dark oil was pressed on porous tile and the tile extracted with ether. After removal of solvent, seeding and allowing to stand at about 0°, a small amount of crude crystalline (II) was obtained which, after two recrystallizations from hydrochloric acid, melted at 143° and gave no depression when mixed with (II) made from the anhydride. Further larger amounts of (II) were obtained from the mother liquors; treatment of these with acetyl chloride, distillation and refractionation of the distillate gave a portion boiling at about 104° at 4 mm. which crystallized on cooling and was hydrolyzed to (II) as above.

Alkaline permanganate was not decolorized by (II) at room temperature. The dimethyl ester was prepared by refluxing (II) with methyl alcohol and a small amount of sulfuric acid, b. p. 110–111° at 20 mm.

*Anal.* Calcd. for C<sub>8</sub>H<sub>12</sub>O<sub>4</sub>: C, 55.80; H, 7.03. Found: C, 55.94; H, 7.09.

The dihydrazide was formed by heating the dimethyl ester for five hours at 130° with the theoretical amount of 85% hydrazine hydrate, clusters of colorless prisms or plates from alcohol-water, m. p. 172–174°.

*Anal.* Calcd. for C<sub>6</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub>: C, 41.85; H, 7.02; N, 32.54. Found: C, 41.98; H, 6.85; N, 32.37.

The *p*-bromophenacyl ester was made from the disodium salt of (II) in the usual manner, colorless needles from absolute alcohol, m. p. 121.2–121.7°.

*Anal.* Calcd. for C<sub>22</sub>H<sub>18</sub>Br<sub>2</sub>O<sub>8</sub>: C, 49.09; H, 3.37. Found: C, 49.24; H, 3.33.

**Reconversion of *cis*-Acid (II) to *trans*-Acid (I).**<sup>10</sup>—Attempts to effect this change by heating (II) for five to six hours at 180° with concentrated hydrochloric acid in a sealed tube were unsuccessful. Extensive destruction<sup>11</sup> of (II) took place with formation of carbonized material and sirups; no (I) could be detected among the reaction products.

The effect of heat on (II) was also studied. When heated for five hours from a bath at 200°, complete conversion to its anhydride was observed. Heating at higher temperatures also gave no (I).

To a solution of sodium methylate prepared from 0.25 g. of sodium in 50 cc. of methanol, 5 g. of the dimethyl ester of (II) was added and the mixture refluxed for one hour. After distilling off the solvent, the product was washed with water and hydrolyzed by evaporating to dryness on the steam-bath with 10 volumes of 6 *N* hydrochloric

(10) Compare conversion of *cis*-1,2-cyclobutanedicarboxylic acid to the *trans*-isomer, Buchman, Reims, Skei and Schlatter, *This Journal*, **64**, 2696 (1942).

(11) The instability of (II) toward hydrochloric acid was apparently first noted<sup>2</sup> by Haworth and Perkin.

acid. The residue was recrystallized from water, m. p. and mixed m. p. with an authentic sample of (I) 172.0–173.0°.

**$\alpha$ -Methyleneglutaric Acid (III).**—Samples of (III) made by various methods were shown to be identical by mixed melting point determinations; all samples reacted instantaneously at room temperature with alkaline permanganate. Substantial depressions of the melting point were observed when (III) and (II) or corresponding derivatives (anhydride, *p*-bromophenacyl ester) were mixed.

(III) was prepared in small yield from polymerized methyl acrylate, <sup>4b</sup> from methoxymethylmalonic ester, <sup>4b,5</sup> from crude 1-methoxy-2,2,4,4-tetracarboethoxybutane <sup>4c</sup> (b. p. 180–185° at 3 mm.), from diethyl methylenemalonate, <sup>4a,12</sup> and in somewhat better yield (21%) from "ethylparamethylenemalonate."<sup>2,4a</sup>

A superior method for preparation of (III) was developed starting from formaldehyde and malonic ester. To 192 g. (1.2 moles) of the latter in a flask surrounded by an ice-bath was added 100 g. (1.33 moles) of 40% formaldehyde and 3.4 g. of piperidine. After two hours the mixture was removed from the ice-bath and allowed to stand at room temperature for twelve hours. The heavier organic layer (220 g.) was separated and added to 100 g. (2.5 moles) of sodium hydroxide<sup>14</sup> in one liter of methanol in a flask surrounded by an ice-bath. The mixture slowly turned to a white pasty mass, was then removed from the ice-bath and permitted to stand at room temperature overnight; it was again cooled to 0° and 2 liters (6 moles) of 3 *N* hydrochloric acid added. After standing for two hours the methanol was distilled off, 500 cc. (6 moles) of concentrated hydrochloric acid added and the mixture refluxed for twelve hours. The residue obtained on evaporating the mixture to dryness on a steam-bath was extracted with absolute alcohol, the solvent removed and the material again evaporated with 500 cc. of water to hydrolyze any ester which might have formed. The oil remaining was allowed to crystallize for several days in the ice-box and the crude crystals recrystallized from water, yield 17.9 g. (20% yield from malonic ester) of (III), m. p. 131.0–132.0°, b. p. 175° at 3.5 mm.

*Anal.* Calcd. for C<sub>6</sub>H<sub>8</sub>O<sub>4</sub>: C, 50.00; H, 5.60. Found: C, 50.07; H, 5.71.

The mother liquors from several preparations of (III) by essentially the above method were combined and esterified with ethanol in the presence of hydrochloric acid and the esters carefully fractionated.<sup>15</sup> The ethyl esters of glutaric acid (a major product), b. p. 104–105° at 8 mm., of  $\alpha$ -methyleneglutaric acid (III), b. p. 111–113° at 8 mm. and of 1,3,5-pentanetricarboxylic acid, b. p. approx. 128–132° at 2 mm.<sup>16</sup> were isolated and identified by con-

(12) Made in poor yield both by distillation of the polymer and also by the method of Bachman and Tanner, *J. Org. Chem.*, **4**, 493 (1939).

(13) These relative amounts appeared to give optimum yields of (III).

(14) It was not found possible to work out as convenient a method employing potassium hydroxide.

(15) From the forerun (up to 80° at 2 mm.) a small amount of a crystalline material containing ionic halogen separated on standing, m. p. 220.0–220.5° from alcohol, easily soluble in water, quite insoluble in ether, acid to litmus. The analysis (Found: C, 49.79; H, 8.36; N, 7.77; Cl<sup>-</sup>, 18.43) points to the formula C<sub>8</sub>H<sub>10</sub>ClNO<sub>2</sub> (Calcd.: C, 49.61; H, 8.33; N, 7.23; Cl<sup>-</sup>, 18.31); the substance is obviously derived from the piperidine used as catalyst.

(16) Kay and Perkin, *J. Chem. Soc.*, **89**, 1647 (1906).

version to the corresponding acids.<sup>17</sup> From a fraction present in small amount, boiling at about 103° at 2 mm., on hydrolysis with 6 *N* hydrochloric acid, a new acid,  $\alpha, \alpha'$ -dimethyleneglutaric acid,<sup>18</sup> was obtained which after recrystallization from water melted at 152.0–153.0°.

*Anal.* Calcd. for C<sub>7</sub>H<sub>8</sub>O<sub>4</sub>: C, 53.84; H, 5.16. Found: C, 53.90; H, 5.23.

When the acid (III) was esterified with ethanol in the presence of hydrochloric acid there was a substantial loss due to polymerization. The diethyl ester, obtained in 43% yield, b. p. 132–133° at 23 mm., on treatment with hydrazine hydrate gave no crystalline dihydrazide. The anhydride was prepared in the usual fashion,<sup>2,4c</sup> b. p. 112–115° at 2 mm., large colorless prisms from anhydrous ether, m. p. 51.0–51.5° (analysis).

On treatment with 10% excess of thionyl chloride and distillation at reduced pressure, (III) gave the acid chloride, b. p. 82–83° at 5 mm., and smaller amounts of the anhydride. A portion of the acid chloride dissolved in ether was saturated with excess of dry ammonia, the ether evaporated and the residue extracted with chloroform. The diamide was obtained from the chloroform extract, m. p. 164.0–165.0° from absolute alcohol.

*Anal.* Calcd. for C<sub>6</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>: C, 50.69; H, 7.09; N, 19.71. Found: C, 50.63; H, 7.38; N, 19.82.

The *p*-bromophenacyl ester crystallized in colorless needles from 96% alcohol, m. p. 121.6–121.7°.

*Anal.* Calcd. for C<sub>22</sub>H<sub>18</sub>Br<sub>2</sub>O<sub>6</sub>: C, 49.09; H, 3.37. Found: C, 49.11; H, 3.33.

An excess of diazomethane in ether was added to 1 g. of (III), the ether removed and the residual oil heated in a sealed tube at 100° for twenty hours with 20 cc. of an alcoholic ammonia solution (saturated at 0°). After evaporation of the solvent on a steam-bath the remaining oil crystallized, m. p. 145.0–145.5° from absolute alcohol. The analysis indicates that this substance is the diamide of the pyrazoline<sup>19</sup> resulting from the addition of diazomethane to the double bond in (III).

*Anal.* Calcd. for C<sub>7</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub>: C, 45.64; H, 6.57; N, 30.42. Found: C, 45.92; H, 6.67; N, 30.42.

## Summary

In accord with literature claims, *cis*-1,3-cyclobutanedicarboxylic acid may be obtained from the *trans*-isomer or as a by-product in the preparation of the latter. It has properties consistent with its structure.

The compound obtained from formaldehyde and malonic ester or their equivalents and reported as *cis*-1,3-cyclobutanedicarboxylic acid is  $\alpha$ -methyleneglutaric acid.

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(17) 1,3,5-Pentanetricarboxylic acid, m. p. 112.5–113.0° (analysis); compare ref. 4a.

(18) This structure is in accord with the method of formation from malonic ester and formaldehyde. All of the products isolated could be formed from a common intermediate, methylenedimalonic ester; compare Welch, *J. Chem. Soc.*, 257 (1930).

(19) Regarding its probable structure see von Auwers and Cauer, *Ann.*, **470**, 284 (1929); von Auwers and König, *ibid.*, **496**, 27 (1932).