ated through the same column to yield 3 g. (15%) of 2-acetoxy-$\Delta^{9(10)}$-octalin (IIh), b.p. 130–131° (12 mm.), $n^{25}$D 1.4940.

*Anal.* Calcd. for $C_{12}H_{18}O_2$: C, 74.23; H, 9.27. Found: C, 74.48; H, 9.48.

**1,4,5,6,7,8-Hexahydronaphthalene-2,3-dicarboxylic Acid (IVb).**—After a mixture of 10.8 g. (0.10 mole) of 1,2-dimethylenecyclohexane (I) and 14.2 g. (0.10 mole) of dimethyl acetylenedicarboxylate in 25 ml. of ether had been heated under reflux for 1 hr., the solvent was removed by distillation under reduced pressure. The residue was fractionated through an 8-inch, helix-packed column to yield 20 g. (80%) of dimethyl 1,4,5,6,7,8-hexahydronaphthalene-2,3-dicarboxylate (IVa), b.p. 168° (3 mm.), $n^{25}$D 1.5110.

A mixture of 1 g. of IVa and 20 ml. of 10% alcoholic potassium hydroxide was heated under reflux for 2 hr. The reaction mixture was acidified with concentrated hydrochloric acid, and the precipitated acid was removed by filtration. Recrystallization from 50 ml. of 70% ethanol produced 0.55 g. (62%) of 1,4,5,6,7,8-hexahydronaphthalene-2,3-dicarboxylic acid (IVb), m.p. 223–225°.

*Anal.* Calcd. for $C_{12}H_{14}O_4$: C, 64.86; H, 6.35. Found: C, 64.70; H, 6.59.

**1,4,5,6,7,8-Hexahydronaphthalene-2-carboxylic Acid (IVd).**—After 5.0 g. (0.021 mole) of ethyl 1,4,5,6,7,8-hexahydronaphthalene-2-carboxylate (IVc)[5] had been saponified with 50 ml. of 10% alcoholic potassium hydroxide, the solution was acidified with concentrated hydrochloric acid. The resulting precipitate was removed by filtration and recrystallized from acetic acid to yield 3 g. (78%) of 1,4,5,6,7,8-hexahydronaphthalene-2-carboxylic acid (IVd), m.p. 165–166°.

*Anal.* Calcd. for $C_{11}H_{14}O_2$: C, 74.16; H, 7.87. Found: C, 73.90; H, 7.67.

DETROIT 1, MICHIGAN

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, CHAS. PFIZER AND CO., INC.]

# Stereochemistry of the Itaconic Acid–Cyclopentadiene Adduct

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The adduct of itaconic acid and cyclopentadiene prepared in refluxing aqueous isopropyl alcohol is a mixture of isomers. The isomers were converted to the iodolactones which were separated by recrystallization. Treatment of the iodolactones with zinc and acetic acid regenerated the isomeric acids. The ratio of the isomer with an *exo*-carboxyl to that with the *endo*-carboxyl was about three.

The reaction of itaconic anhydride and cyclopentadiene was reported in 1928.[1] The resulting adduct, which was hydrolyzed to the acid but was not investigated further, appeared to consist of a single isomer.[2] The present paper describes the preparation of the adduct from cyclopentadiene and itaconic acid and the separation of the product *via* the iodolactones into two geometric isomers for which structures are assigned. The adduct I was obtained in 84% yield by heating the reactants in aqueous isopropyl alcohol. The wide melting range of I, even after several recrystallizations, indicated that it was a mixture. The neutral equivalent and hydrogen uptake of the product indicated it was a mixture of isomers.

Acid-catalyzed lactonization[3] of the mixture in an attempt to prepare the lactones IIa and IIb gave a viscous non-crystallizing sirup which exhibited a five-membered lactone band[4] at 5.63 $\mu$, and a possible six-membered lactone band[4] at 5.83 $\mu$. An attempt to prepare the bromolactones (IIIa and IIIb)[3,5] also resulted in a viscous sirup which did not crystallize. The infrared spectrum indicated a mixture similar to that obtained in lactonization, since five- and possibly six-membered lactone bands were observed at 5.57 and 5.78 $\mu$. The possible occurrence of Wagner–Meerwein rearrangements during these reactions makes the evidence inconclusive as to the nature of the components of the original acid adduct.[3,5b,6]

The iodolactonization reaction which is milder than the bromolactonization reaction,[7] has been utilized as a method for characterization of unsaturated acids[8] and for separation of *exo–endo* isomers.[9] When the acid adduct I was treated with iodine in alkaline solution, two crystalline iodolactones were obtained. The major isomer, which melted at 208–209°, was isolated in about three times the amount of the minor isomer, which melted at 168–169°. Some infrared spectral data for these compounds are summarized in Table I. The data collected there indicate the important effect of the phase in which these compounds are examined. In potassium bromide the six-membered lactone band and the acid band of IVa absorb at the expected wave lengths,[4] while in dioxane only a single broad band appears, presumably from a shift of the acid carbonyl absorption. Isomer IVb in potassium bromide exhibits a poorly resolved doublet, while in dioxane both the five-membered lactone and the acid bands are observed.

The unrearranged lactone formulas IVa and IVb have been proposed for the two substances obtained from the iodolactonization reaction. In these structures the adjacent iodo- and ester oxygen

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[1] O. Diels and K. Alder, *Ann.*, **460**, 117 (1928).

[2] Dr. R. Hill and Mr. T. van Auken at Princeton University have also observed the formation of a single isomer from itaconic anhydride and cyclopentadiene (private communication). The iodolactone resulting from this isomer was apparently identical to our IVa.

[3] K. Alder and G. Stein, *Ann.*, **514**, 7 (1934).

[4] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 152–163.

[5] (a) K. Alder and G. Stein, *Ann.*, **504**, 216 (1933); (b) R. B. Woodward and H. Baer, THIS JOURNAL, **70**, 1161 (1948); (c) H. Kwart and L. Kaplan, *ibid.*, **76**, 4078 (1954); (d) J. A. Berson, *ibid.*, **76**, 5748 (1954); (e) K. Alder and F. Brochhagen, *Chem. Ber.*, **87**, 167 (1954).

[6] (a) K. Alder, F. W. Chambers and W. Trimborn, *Ann.*, **566**, 27 (1950); (b) S. Beckmann, R. Schaber and R. Bamberger, *Chem. Ber.*, **87**, 997 (1954); (c) see also, J. A. Berson and R. Swidler, THIS JOURNAL, **76**, 4060 (1954), and ref. 2 for a summary of rearrangements in other bicyclic systems.

[7] C. D. Ver Nooy and C. S. Rondestvedt, Jr., THIS JOURNAL, **77**, 3583 (1955).

[8] (a) J. Bougault, *Ann. chim. et phys.*, **14**, 145 (1908); **15**, 296 (1908); (b) E. E. van Tamelen and M. Shamma, THIS JOURNAL, **76**, 2315 (1954).

[9] C. D. Ver Nooy and C. S. Rondestvedt, Jr., *ibid.*, **77**, 4878 (1955).

TABLE I

INFRARED CARBONYL ABSORPTION OF IODOLACTONIZATION PRODUCTS

| Compound | M.p., °C. | Band position (μ) | Phase | Band identification |
|---|---|---|---|---|
| IVa | 208–209 | 5.77 | KBr | 6-Membered lactone[a] |
| | | 5.88 | | Acid[b] |
| | | 5.73(broad) | Dioxane | 6-Membered lactone[a] and acid[c] |
| IVb | 168–169 | 5.68–5.76[e] | KBr | |
| | | 5.57 | Dioxane | 5-Membered lactone[d] |
| | | 5.76 | | Acid[b] |

[a] Ref. 4; ref. 8b. [b] Ref. 4, p. 140. [c] Ref. 4, p. 143. [d] Ref. 4; ref. 8b; J. A. Berson, THIS JOURNAL, **76**, 4975 (1954). [e] Poorly resolved doublet.

atoms are in the *trans* position suitable for eliminations regenerating the unsaturated acids. Typical Wagner–Meerwein rearrangements, should they occur during iodolactonization, would lead to structures where elimination would be unlikely. An attempt to bring about a reversal of the reaction by which the iodolactones were formed with excess iodide ion was unsuccessful. The eliminations were finally accomplished by treating the iodolactones with zinc and acetic acid.[5e] The lactones IVa and IVb gave the acids Ia and Ib, respectively, in good yields. Each of the regenerated acids absorbed the theoretical amount of hydrogen in the presence of a platinum catalyst. The isomers resulting from the Diels–Alder reaction have thus been separated *via* the iodolactones. The ratio of isomers Ia/Ib = 3, is probably close to the equilibrium value under these conditions.[10]

The apparent dissociation constants, $pK_a$, of the acids are listed in Table II. Benzoic acid is included for standardization of our method of determining acidities. The $pK_a$ of benzoic acid in 50% aqueous ethanol is listed in the literature as 5.73.[11]

TABLE II

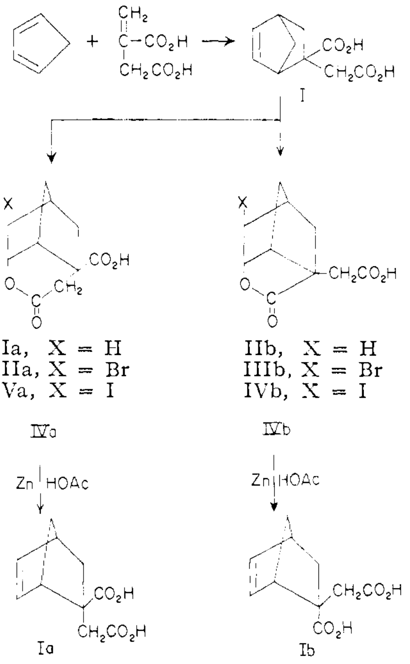
APPARENT DISSOCIATION CONSTANTS OF ACIDS AT ROOM TEMPERATURE IN 48% AQUEOUS ETHANOL

| Compound | $pK_a^I$ | $pK_a^{II}$ |
|---|---|---|
| IVa | 4.7 | |
| IVb | 5.4 | |
| Ia | 5.1 | 8.2 |
| Ib | 5.2 | 8.0 |
| Benzoic acid | 5.5 | |

The higher acidity of IVa as compared with IVb must be due to the field effect of the iodine and lactone functions. Roberts and Moreland[12] showed the pronounced effects on the acid strengths of substituents in 4-substituted bicyclo[2.2.2]-octane-1-carboxylic acids. Replacing a 4-hydrogen by a 4-bromine changes the $pK_a$ from 6.75 to 6.08 in 50% aqueous ethanol at room temperature. The considerably greater acidity of IVa compared with these compounds must be due to the combined effects and closer proximity of the negative groups in the iodolactone. While the acidities of the isomeric dicarboxylic acids Ia and Ib are very similar, the slight differences are consistent with the observation of Bode[13] that an *endo* carboxylic group is a somewhat stronger acid than an *exo* group.

**Acknowledgment.**—We are indebted to Miss N. De Filippi for her very capable assistance during this investigation. We should like to thank Dr. R. Wagner, Jr., and Mr. T. Toolan and their staffs for the spectral and titration data and for the microanalyses. We are grateful to Professor E. J. Corey for several interesting discussions.

REACTION CHART



## Experimental

**1-Carboxy-2,5-endomethylene-3-cyclohexene-1-acetic Acid.**—To a suspension of 774 g. (5.95 moles) of itaconic acid in 1.00 l. of water was added a solution of 473 g. (7.15 moles) of freshly prepared cyclopentadiene in 1.25 l. of isopropyl alcohol. The mixture was heated under reflux with stirring for 5.25 hours. The solvent was removed *in vacuo* and the remaining crude product was recrystallized from 1.5–2.0 l. of benzene using a hot filtration. After drying, the adduct weighed 987 g. (84.5%) and melted at 121–131°.

Repeated fractional crystallization from benzene, from water, and from these solvents alternately resulted in little separation of isomers as indicated by the melting points. A sample which had been recrystallized alternately from water and benzene several times melted at 140–141° after drying at 78° (0.5 mm.).

*Anal.* Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17; neut. equiv., 196. Found: C, 61.58; H, 6.13; neut. equiv., 200.

**1-Carboxy-2,5-endomethylenecyclohexane-1-acetic Acid.**—Thirty grams (0.153 mole) of the above unsaturated acid which had been recrystallized several times was dissolved in 100 ml. of ethanol and 20 ml. of water. Platinum oxide catalyst (0.75 g.) was prereduced and the above solution was subjected to hydrogenation at 50 lb. pressure. Approximately 0.15 mole of hydrogen was absorbed. After filtration, evaporation of the solvent *in vacuo*, and recrystallization from water, 24.7 g. (82%) of saturated acid was obtained. The major portion of this material, 14.6 g., melted at 133–134°. After two additional recrystallizations

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(10) J. A. Berson, R. D. Reynolds and W. J. Jones, THIS JOURNAL, **78**, 6049 (1956). See ref. 4 of this paper for a summary of studies on *endo*—*exo* equilibrations.

(11) F. G. Bordwell and G. D. Cooper, *ibid.*, **74**, 1058 (1952).

(12) J. D. Roberts and W. T. Moreland, Jr., *ibid.*, **75**, 2167 (1953).

(13) H. Bode, *Ber.*, **70**, 1167 (1937); *Z. physik. Chem.*, **B170**, 231 (1934).

from benzene and drying at 80° (1 mm.), the melting point was 136.8–137.3°.

*Anal.* Calcd. for $C_{10}H_{14}O_4$: C, 60.60; H, 7.12; neut. equiv., 198. Found: C, 60.67; H, 7.19; neut. equiv., 200.

**The Lactonization of 1-Carboxy-2,5-endomethylene-3-cyclohexene-1-acetic Acid.**—The recrystallized acid adduct, 19.6 g. (0.10 mole), was dissolved in 350 ml. of chloroform which had been dried and distilled. Hydrogen chloride was passed into the solution slowly over a one-hour period. The solution stood at room temperature for 16 hours after which the hydrogen chloride and chloroform were removed *in vacuo*. The oil which remained amounted to 16.9 g. By treating the oil with boiling benzene 2.74 g. of unreacted acid was recovered. The remaining material did not crystallize. The infrared spectrum of the material in chloroform showed a carbonyl band at 5.63 $\mu$ and a broad band at 5.83 $\mu$.

**Attempted Preparation of the Bromolactones of 1-Carboxy-2,5-endomethylene-3-cyclohexene-1-acetic Acid.**—A suspension of 19.6 g. (0.100 mole) of the recrystallized acid in 150 ml. of water was neutralized with 13.2 g. (0.200 mole) of 85% potassium hydroxide in 100 ml. of water. While the solution of the potassium salt was stirred in an ice-bath, 20.0 g. (0.125 mole) of liquid bromine was added dropwise. The mixture warmed to room temperature over a 2-hour period after which excess bromine was removed with formic acid. The solution was acidified with concentrated hydrochloric acid and the organic material was extracted with ether. After removal of the ether, the sirup remaining was examined by infrared absorption in chloroform. It exhibited absorption bands at 5.59 and 5.80 $\mu$.

**Iodolactones of 1-Carboxy-2,5-endomethylene-3-cyclohexene-1-acetic Acid.**—To a suspension of 200 g. (1.02 moles) of the once-recrystallized itaconic acid–cyclopentadiene adduct in 1.60 l. of water was added a solution of 90 g. (2.2 moles) of 99% sodium hydroxide in 700 ml. of water. The mixture was cooled and stirred until all the solid dissolved. After the addition of 52 g. (0.62 mole) of sodium bicarbonate a solution of 258 g. (1.02 moles) of iodine and 285 g. (1.90 moles) of sodium iodide in 1.20 l. of water was added slowly with stirring over a 30-minute period. The mixture was stirred three additional hours at room temperature and then acidified to *p*H 1 with concentrated hydrochloric acid while cooling in an ice-bath. The precipitated crude material, after filtration and drying, amounted to 305 g. (93%), m.p. 149–195° dec. By concentrating the filtrate and extracting continuously with ether 6.35 g. of additional iodolactone, m.p. 173–174° dec., was obtained.

Ten grams of the crude first crop of iodolactone was recrystallized from 75 ml. of hot water. The impure high-melting lactone, which was insoluble, amounted to 5.88 g., m.p. 176–179° dec. From the filtrate crystallized 2.11 g. of crude low-melting iodolactone which decomposed below 130° in a melting point capillary. From the filtrate was obtained by evaporation to dryness 1.82 g. of an impure mixture of isomers. By recrystallization of the high-melting lactone from 50% aqueous ethanol and the low-melting lactone from benzene was obtained 4.39 g. of iodolactone, m.p. 209–210° dec., 1.43 g. of iodolactone, m.p. 148–160°, and 2.68 g. of a very impure mixture which according to the infrared spectrum probably contained more of the low-melting isomer. The infrared spectrum and carbon and hydrogen analyses of the material melting at 148–160° indicate it was composed almost entirely of low-melting iodolactone in spite of the wide melting point range. It was difficult to purify, but fractional recrystallization from water followed by benzene gave pure material melting at 169.4–170.0°.

*Anal.* Calcd. for $C_{10}H_{11}O_4I$: C, 37.27; H, 3.44; I, 39.38; neut. equiv., 322. Found: C, 37.40; H, 3.72; I, 39.46; neut. equiv., 325.

The melting point of the high-melting lactone varied somewhat with the rate of heating. An analytical sample placed in the bath at 200° and heated at one degree per minute melted with decomposition at 209–210°.

*Anal.* Calcd. for $C_{10}H_{11}O_4I$: C, 37.27; H, 3.44; I, 39.38; neut. equiv., 322. Found: C, 37.23; H, 3.55; I, 39.66; neut. equiv., 322.

**Regeneration of 1-Carboxy-(*exo*)-2,5-endomethylene-3-cyclohexene-1-acetic Acid (Ia) from IVa.**—To 8.53 g. (0.0264 mole) of the lactone IVa and 100 ml. of glacial acetic acid was added 15.0 g. of zinc dust. The mixture was stirred for one hour. Two more portions of zinc of 15.0 g. each were added with the reaction mixture being stirred for one hour after each addition. The zinc was removed by filtration and washed several times with acetic acid. The acetic acid was removed *in vacuo* and the remaining oil was treated with 45 ml. of water, 50 ml. of ether and 9 ml. of concentrated hydrochloric acid to break up the zinc salts. The aqueous layer was extracted twice more with ether. The combined ether extracts were washed with water, dried over anhydrous magnesium sulfate and the ether was boiled off. The crude acid remaining amounted to 3.91 g. (75.5%) and melted at 156–158°. After two recrystallizations from water 2.07 g. of analytical material melting at 153.6–154.6° was obtained.

*Anal.* Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17; neut. equiv., 196. Found: C, 61.07; H, 6.26; neut. equiv., 200.

A 0.2567-g. sample of the acid, when reduced in 95% ethanol with a platinum catalyst, absorbed 29.4 ml. of hydrogen (corrected to standard conditions) or 100% of the theoretical amount.

**Regeneration of 1-Carboxy-(*endo*)-2,5-endomethylene-3-cyclohexene-1-acetic Acid (Ib) from IVb.**—To 8.60 g. (0.0267 mole) of the iodolactone IVb, m.p. 169.0–169.5°, and 100 ml. of glacial acetic acid was added 10.0 g. of zinc dust. The mixture was stirred for one hour. Two additional portions of zinc of 10.0 g. each were added with a one-hour stirring period after each addition. The zinc was removed by filtration and washed well with acetic acid. The acetic acid was removed *in vacuo* and 45 ml. of cold water, 50 ml. of ether and 5 ml. of concentrated hydrochloric acid were added to the remaining sirup. The ether layer was removed and the aqueous layer was extracted three times with 25-ml. portions of ether. The combined ether extracts were washed once with water and dried over Drierite. The solution was filtered and the ether was boiled off leaving 4.19 g. (80%) of acid melting with decomposition at 161–163°. One recrystallization from a benzene–acetone mixture gave analytical material melting at 165.7–166.3° dec. A mixed melting point with the acid Ia was 140–148°.

*Anal.* Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17; neut. equiv., 196. Found: C, 61.31; H, 6.26; neut. equiv., 201.

A 0.2450-g. sample of the acid when reduced in 95% ethanol over a platinum catalyst absorbed 27.7 ml. (corrected) of hydrogen or 99% of the theoretical amount.

**Apparent Dissociation Constants.**—Acidities were measured during determination of neutral equivalents with the glass electrode in solutions consisting of 50% by volume water and 50% by volume 95% alcohol. The figures reported as $pK_a^{I}$ and $pK_a^{II}$ are the *p*H values for the half-neutralized first and second carboxyl groups, respectively.

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