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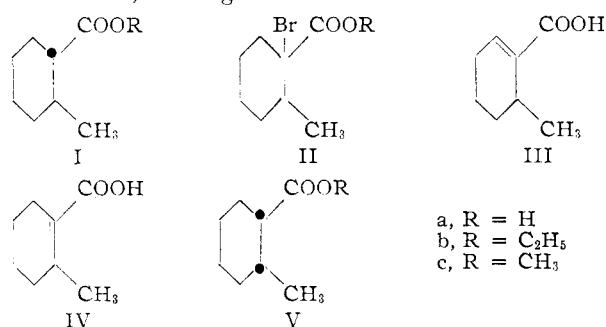
The Stereochemistry of Bromination of *o*-Substituted Cyclohexanecarboxylic Acids<sup>1</sup>BY JOSEPH KLEIN AND GERSHON LEVIN<sup>2</sup>

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Bromination of the chloride of *trans*-2-methylcyclohexane-1-carboxylic acid (Ia) and subsequent esterification gives predominantly that isomer of the  $\alpha$ -bromoester (IIc) in which the methyl and carboxyl groups are *cis* to each other. This was shown by stereoselective catalytic hydrogenolysis of the C-Br bond in IIc leading to methyl *cis*-2-methylcyclohexane-1-carboxylate (Vc). On the other hand, bromination of the chloride of *trans*-2-phenylcyclohexane-1-carboxylic acid (VIa) leads to the isomer of VIIb in which the phenyl and carboxyl groups are *trans* to each other.

Whilst *trans*-*o*-substituted cyclohexanecarboxylic acids are easily available by the Diels-Alder reaction of butadiene and *trans*- $\beta$ -substituted acrylic acids and subsequent hydrogenation, the *cis* isomers can be obtained only in those cases in which the *cis* form of the acrylic acids are accessible and no isomerization occurs under the conditions of the Diels-Alder condensation. Another route for the preparation of the *cis* isomers uses the Diels-Alder reaction between 1-substituted butadienes and acrylic acid; however, this reaction gives at low temperatures a low yield of the desired product and at higher temperatures increasing amounts of the *trans* isomers.<sup>3,4</sup> Furthermore, the *o*-acids obtained in the latter reaction are contaminated by the *m*-isomers.

It was thought possible to convert the *trans* into the *cis* forms by bromination and subsequent hydrogenolysis of the carbon-bromine bond formed: the bromine is likely to approach the intermediate enol from the side opposite to the *o*-substituent and thus give a product in which the carboxyl would be *cis* and the bromine atom *trans* to the shielding *o*-substituent. As the bromo-acid would no longer be enolizable, it was expected that it would not be capable of stereoisomerization. Hydrogenolysis of the C-Br bond under conditions under which the configuration of the carbon atom is retained, would give the desired acid.



The chloride of *trans*-2-methylcyclohexane-1-carboxylic acid (Ia) was brominated and the bromo-chloride converted into ethyl 1-bromo-2-methylcyclohexane-1-carboxylate (IIb). The *cis* position of the methyl and carboxyl groups in this compound follows from the dehydrobromination of IIc (see below) with pyridine, which after hydro-

lysis led to the known 6-methylcyclohex-1-ene-1-carboxylic acid (III), identified by its melting point and that of its anilide; dehydrobromination with pyridine is a bimolecular reaction and, therefore, proceeds by a *trans* mechanism. The formation of III would then imply, according to Saytzev's rule (which is known to apply to the dehydrohalogenation in cyclic systems),<sup>5,6</sup> that the bromine and hydrogen atoms in the positions 1 and 2, respectively, are in *cis* to each other; if they and, therefore, also the methyl and the carboxyl groups in IIc were *trans* to each other, 2-methylcyclohex-1-ene-1-carboxylic acid (IV) would have been formed, which is not the case.

Reduction of IIb with zinc and hydrochloric acid in acetic acid led to an ethyl 2-methylcyclohexane-1-carboxylate, converted by treatment with anilinomagnesium bromide<sup>7</sup> into an anilide of m.p. 110–112°. For the anilide of *cis*-2-methylcyclohexane-1-carboxylic acid (Va) melting points varying from 67 to 110° have been recorded in the older literature.<sup>8</sup> A study carried out by Macbeth, *et al.*,<sup>8</sup> revealed that all the compounds formerly described as *cis*-acids (Va) had been contaminated by the *trans* isomer Ia and that the pure *cis*-acid Va is partially isomerized when heated with thionyl chloride. At room temperature, at which no isomerization occurs, the pure *cis*-anilide, m.p. 126°, can be obtained *via* the chloride. The anilide obtained in the present study was obviously a mixture of the isomers and does not provide conclusive information as to the stereochemical purity of the corresponding acid.

In order to ascertain the steric identity of the product obtained, the pure acids Ia and Va were esterified with diazomethane to give the methyl esters Ic and Vc. On the other hand, the product of the bromination of the acid chloride of Ia was converted with methanol to the ester IIc. This ester was debrominated catalytically with hydrogen to give a methyl 2-methylcyclohexane-1-carboxylate. Its steric composition was then determined by comparing its refractive index with those of Ic and Vc; it contained 83% of the *cis* isomer Vc. When analogously the infrared spectra of the three preparations were compared, a *cis* content of 80 and 87%, respectively, for  $\lambda = 7.3$  and  $8.0 \mu$  was found. If we assume with Brewster<sup>9</sup> that cat-

(1) Presented before the International Congress of Pure and Applied Chemistry, Paris, 1957.

(2) From the M.Sc. thesis of G. Levin, Hebrew University, Jerusalem.

(3) J. S. Meek, B. T. Poon, R. T. Merrow and S. J. Cristol, *THIS JOURNAL*, **74**, 2669 (1952).

(4) K. Alder, H. Vagt and W. Vogt, *Ann.*, **565**, 135 (1949).

(5) W. Hueckel, W. Tappe and G. Legutke, *ibid.*, **544**, 191 (1940).

(6) E. D. Hughes, C. K. Ingold and J. B. Rose, *J. Chem. Soc.*, 3839 (1953).

(7) D. V. N. Hardy, *ibid.*, 398 (1936).

(8) For a review see A. K. Macbeth, J. A. Mills and D. A. Simmonds, *ibid.*, 1011 (1949).

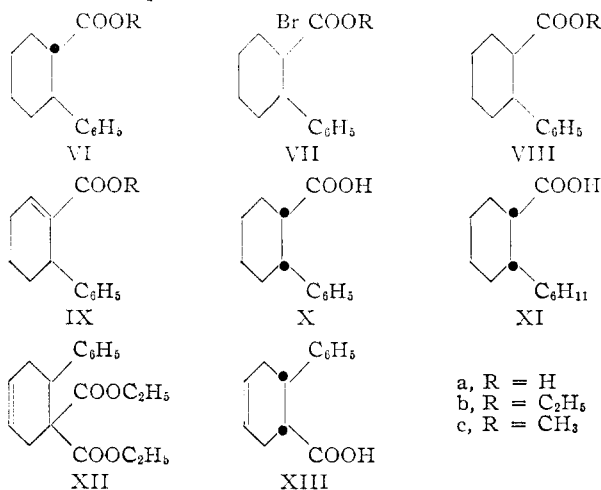
(9) J. H. Brewster, *THIS JOURNAL*, **76**, 6361 (1954); **78**, 4061 (1956).

alytic hydrogenolysis of the C-Br bond in the bromoester IIc proceeds stereoselectively with retention of configuration, one has to conclude that the bromination product of the acid chloride of Ia contains about 83% of II with the bromine atom *trans* to the methyl group.

As the phenyl group, being much bulkier than methyl, was expected to exert a more powerful shielding effect during the bromination, the bromination of *trans*-2-phenylcyclohexane-1-carboxylic acid (VIa) was studied. In the synthesis of VIa we have been able to obtain much higher yields than Alder, *et al.*,<sup>4</sup> by the use of an excess of butadiene and application of higher reaction temperatures. Compound VIa was converted into the acid chloride and the latter brominated, the bromination being markedly slower than in the case of Ia. The reaction of the brominated chloride with absolute ethanol gave ethyl 1-bromo-2-phenylcyclohexane-1-carboxylate (VIIb). Dehydrobromination of VIIb with pyridine led to a mixture of the two unsaturated esters, ethyl 2-phenylcyclohex-1-ene-1-carboxylate (VIIIb) and ethyl 6-phenylcyclohex-1-ene-1-carboxylate (IXb) in a ratio of 40:60, determined by comparison of the ultraviolet absorption spectrum of the mixture with those of the pure compounds IXa and Xa.<sup>10</sup> For the mixture of the acids VIIIa and IXa, obtained by saponification of the mixture of the unsaturated esters, a ratio of 46:54 was found by the same procedure. One can hardly assume that the direction of the elimination is controlled by the electromeric effect, since in this case both possible  $\alpha$ -bromo esters should have given only the fully conjugated ester VIIIb, in parallel to the formation of the conjugated 1-phenylcyclohex-1-ene by a *cis* elimination reaction from *trans*-2-phenylcyclohexyl-1-trimethylammonium hydroxide.<sup>11</sup> The dehydrobromination is, therefore, evidently sterically controlled and proceeds by *trans* elimination; consequently, at least 40% of the bromination product VII has, unexpectedly, the bromine atom *cis* to the phenyl group. The unexpected acid VIIIa is formed directly, as the isomer IXa is not transformed into VIIIa under the operating conditions.<sup>10</sup> Hydrogenation of VIIIa gave *cis*-2-phenylcyclohexane-1-carboxylic acid (X) or, under more drastic conditions, *cis*-2-cyclohexylcyclohexane-1-carboxylic acid (XI).

In fact, VII appears to consist mainly of the isomer which contains the bromine atom and the phenyl group in *cis* to each other. This can be shown by the following reasoning: Hydrogenolysis of the carbon-bromine bond in VIIb with zinc and hydrochloric acid in acetic acid gave an ester which formed with anilinomagnesium bromide the anilide of the *trans*-acid VIa; in this last reaction isomerization is not likely to occur.<sup>12</sup> Hydrogenolysis

with zinc and acid is generally assumed to proceed through the enol stage,<sup>9</sup> in which case the configuration of the final product would depend on the steric mechanism of proton addition in the ketonization step. Zimmerman<sup>13</sup> found that the keto-



nization of enols of *o*-substituted ketones proceeds with addition of the proton from the less hindered side, giving the kinetically controlled product, *viz.*, the *cis*-ketone. The same is true for the decarboxylation of *o*-substituted alicyclic 1,1-dicarboxylic acids, which according to Zimmerman also proceeds through an enol intermediate. We have shown this for the case of the condensation product XII of butadiene and diethyl benzylidenemalonate which, upon hydrolysis and decarboxylation, gave as the only product that could be isolated, *cis*-2-phenylcyclohex-4-ene-1-carboxylic acid (XIII). In a recent paper, Zimmerman<sup>14</sup> reported that the product of the decarboxylation of the analogous saturated 2-phenylcyclohexane-1,1-dicarboxylic acid contains 69% of the *cis*-acid. Consequently, we have to assume that in the debromination of VII the *enol* is not an intermediate and that the reaction proceeds through a direct displacement of the bromine atom by hydrogen, with retention of configuration. This has been observed recently in other cases also.<sup>15</sup> Hence, the bromination step is responsible for the configuration of the acid VIa, *i.e.*, for the *cis* position of the bromine atom and the phenyl group.<sup>16</sup> This configuration of the bromination product was, indeed, unexpected. One of two conclusions appears unavoidable. Either the bromination introduces the bromine atom *directly cis* to the phenyl group, or it leads initially to the isomer which contains bromine and phenyl in the *trans* position, but which is isomerized subsequently by some mechanism to give the more stable product having both the phenyl and carboxyl groups in equatorial position. Perhaps the relatively long reaction time required for the bromination of VIa is conducive to such an isomerization.

(13) H. E. Zimmerman, *J. Org. Chem.*, **20**, 549 (1955); *This Journal*, **78**, 1168 (1956).

(14) H. E. Zimmerman and J. Giallombardo, *ibid.*, **78**, 6259 (1956).

(15) E. J. Corey and R. A. Sneed, *ibid.*, **78**, 6269 (1956).

(16) It is worthy of note that the configuration was also retained during the debromination of IIc with zinc in acetic acid. The product had the same refractive index as that formed in the catalytic hydrogenolysis of IIc.

(10) W. E. Parham, W. N. Moulton and A. Zuckerbaum, *J. Org. Chem.*, **21**, 72 (1956); *cf.* W. N. Moulton, Thesis, University of Minnesota, 1954.

(11) J. Weinstock and F. G. Bordwell, *This Journal*, **77**, 6706 (1955).

(12) In order to verify that the formation of the anilide of the debromination product of VIIb is not attended by isomerization, the anilide was prepared from the bromination product of the acid chloride of VIa and aniline (in this case, isomerization is not possible, as the carbon atom alpha to the carbonyl does not bear hydrogen) and catalytically hydrogenolyzed. Thus, the anilide of the *trans*-acid VIa, m.p. 166°, was obtained (the anilide of the *cis*-acid melts at 123°).

We wish to express our gratitude to Prof. E. D. Bergmann for his aid during this study.

### Experimental

*trans*-2-Methylcyclohexane-1-carboxylic acid (Ia) was prepared by the method of Diels and Alder,<sup>17</sup> m.p. 52°.

**Ethyl 1-Bromo-2-methylcyclohexane-1-carboxylate (IIb).**—A solution of 30 g. of *trans*-2-methylcyclohexane-1-carboxylic acid in 70 ml. of thionyl chloride was kept for 12 hours at room temperature and refluxed for one hour. The thionyl chloride was then distilled off *in vacuo*, and to the residue was added 32 g. of bromine during three hours at 70°. The solution was heated at 80° for one hour, cooled and diluted with 50 ml. of absolute ethanol, which was added dropwise, with stirring and cooling. The solution was allowed to stand for five hours, then diluted with 400 ml. of water and extracted with ether, and the ether layer was washed with 5% aqueous sodium carbonate and water. Distillation gave 36 g. of an oil boiling at 127–129° (20 mm.),  $n_D^{20}$  1.4869.

*Anal.* Calcd. for  $C_{10}H_{17}BrO_2$ : C, 48.2; H, 6.8. Found: C, 48.6; H, 6.9.

**Debromination of IIb.**—To a solution of 2 g. of IIb in 15 ml. of acetic acid, 4 g. of zinc powder and then, during one hour, 3 ml. of concentrated hydrochloric acid were added, dropwise and with stirring. The mixture was stirred for three more hours, diluted with water and extracted with ether. The ether layer was washed with 5% aqueous sodium carbonate solution and water and the ether distilled off. The residue gave a negative Beilstein test for halogen. It was dissolved in ether and added to an excess of a solution of anilinomagnesium bromide.<sup>7</sup> The solution was refluxed for 30 minutes and decomposed with dilute hydrochloric acid. After distillation of the ether, 1.2 g. of an anilide of m.p. 110–112° was obtained.

**Methyl 1-Bromo-2-methylcyclohexane-1-carboxylate (IIc).**—This ester was obtained analogously to IIb. From 45 g. of the acid Ia, there was obtained 60 g. of an oil boiling at 121–122° (20 mm.),  $n_D^{20}$  1.4940.

*Anal.* Calcd. for  $C_9H_{16}BrO_2$ : C, 46.0; H, 6.4. Found: C, 46.2; H, 6.2.

**Dehydrobromination and Hydrolysis of IIc.**—To 10 g. of IIc was added 40 ml. of pyridine and the solution refluxed for 4 hours. The reaction mixture was cooled, acidified with dilute hydrochloric acid and extracted with ether. The ether solution was washed with 5% hydrochloric acid and water. Distillation gave 5 g. of a colorless oil, boiling at 87–88° (15 mm.).

To 4 g. of the ester so obtained, there were added 50 ml. of a 20% aqueous solution of potassium hydroxide and 10 ml. of ethanol. The mixture was refluxed for 3 hours, the ethanol distilled from the clear solution on the water-bath and the remaining liquid cooled and acidified with 10% sulfuric acid. Thus, 3.7 g. of a white precipitate, melting at 78–88°, was obtained. Recrystallization from petroleum ether gave 1.5 g. of 6-methylcyclohex-1-ene-1-carboxylic acid (III), m.p. 105–106°,<sup>18</sup> anilide m.p. 107°.

**Debromination of IIc.**—To a solution of 3 g. of the bromo-ester IIc in 50 ml. of acetic acid, 1.1 g. of sodium acetate and 0.5 g. of palladium-charcoal was added and the mixture hydrogenated at room temperature. After absorption of 210 ml. of hydrogen, the hydrogenation stopped. The reaction mixture was diluted with water and extracted with ether, and the ether solution washed with 10% aqueous sodium carbonate and water. Distillation afforded 1.6 g. (81%) of methyl 2-methylcyclohexane-1-carboxylate, b.p. 75° (15 mm.),  $n_D^{20}$  1.4479.

*Anal.* Calcd. for  $C_9H_{16}O_2$ : C, 69.2; H, 10.2. Found: C, 69.5; H, 10.4.

This ester gave with anilinomagnesium bromide an anilide of m.p. 107–109° and, after recrystallization from ligroin, m.p. 111–112°.

**Methyl *trans*-2-Methylcyclohexane-1-carboxylate (Ic).**—To 2 g. of Ia, dissolved in 50 ml. of anhydrous ether, a solution of 1 g. of diazomethane in 50 ml. of ether was added and the solution allowed to stand for 14 hours. Distillation gave 1.8 g. of a colorless oil, b.p. 95° (50 mm.),  $n_D^{20}$  1.4424.

(17) O. Diels and K. Alder, *Ann.*, **470**, 62 (1929).

(18) W. S. Rapson and R. G. Shuttleworth, *J. Chem. Soc.*, 636 (1940).

*Anal.* Calcd. for  $C_9H_{16}O_2$ : C, 69.2; H, 10.2. Found: C, 69.4; H, 10.0.

***cis*-2-Methylcyclohexane-1-carboxylic acid (Va)** was prepared from *o*-toluic acid<sup>19</sup> by the method of Macbeth.<sup>8</sup> The melting point of the piperazine salt obtained did not change upon recrystallization from acetone. The acid gave an anilide of m.p. 127°.<sup>8</sup>

**Methyl *cis*-2-Methylcyclohexane-1-carboxylate (Vc).**—To a solution of 2.5 g. of the *cis*-acid Va in 50 ml. of ether a solution of 1 g. of diazomethane in 50 ml. of ether was added and the solution left at room temperature for 14 hours. Distillation afforded 1.7 g. of a colorless oil, b.p. 85° (30 mm.),  $n_D^{20}$  1.4490.

*Anal.* Calcd. for  $C_9H_{16}O_2$ : C, 69.2; H, 10.2. Found: C, 69.1; H, 10.0.

***trans*-2-Phenylcyclohex-4-ene-1-carboxylic Acid.**—A mixture of 130 g. of *trans*-cinnamic acid, 170 g. of butadiene, 250 ml. of benzene and 1 g. of hydroquinone was heated in an autoclave at 190–200° for 24 hours. The resulting solution was extracted with 10% aqueous sodium carbonate solution, which gave on acidification 135 g. of an acid of m.p. 85–87°. Recrystallization from ligroin yielded a product of m.p. 99–100°.<sup>4</sup>

***trans*-2-Phenylcyclohexane-1-carboxylic Acid (VIa).**—Hydrogenation of 135 g. of the above unsaturated acid in 400 ml. of acetic acid in the presence of 1.5 g. of palladium-charcoal gave 97 g. of the saturated acid VIa, m.p. 108° (from ligroin).<sup>4</sup>

**Ethyl 1-Bromo-2-phenylcyclohexane-1-carboxylate (VIIb).**—To 60 g. of VIa, 100 ml. of thionyl chloride was added and the mixture allowed to stand overnight. It was then refluxed for one hour and the excess of thionyl chloride distilled off *in vacuo* on the water-bath. The acid chloride solidified; a sample was distilled at 124° (2 mm.) and melted at 85–86°.

To the acid chloride, 18 ml. of bromine was added dropwise during 5 hours at 85–90° and the mixture heated at 100° for one hour. The product was cooled and treated with 150 ml. of absolute ethanol. The solution so obtained was allowed to stand overnight at room temperature; then 500 ml. of water was added, the product extracted with ether, and the ether layer washed with 5% aqueous sodium carbonate solution and water. Distillation afforded 42 g. (42%) of the bromo-ester, b.p. 152–154° (0.3 mm.).

*Anal.* Calcd. for  $C_{15}H_{19}BrO_2$ : C, 58.1; H, 5.9. Found: C, 57.9; H, 6.1.

**Dehydrobromination of VIIb.**—A solution of 10 g. of potassium hydroxide in 30 ml. of methanol was added to 10 g. of the bromo-ester VIIb and the mixture refluxed for 3 hours, diluted with 150 ml. of water and extracted with ether. The alkaline solution gave, on acidification, an oily precipitate which was extracted with ether and, on distillation, afforded 2.2 g. of an oil, b.p. 153° (0.5 mm.), which solidified spontaneously. Recrystallization from aqueous acetic acid gave a product melting at 115° which, after two crystallizations from ligroin, afforded 1.5 g. of 2-phenylcyclohex-1-ene-1-carboxylic acid (VIIIa), m.p. 132–133°<sup>10</sup>. Its ultraviolet spectrum ( $\lambda_{max}$ , 245 m $\mu$ ,  $\log \epsilon$  3.87) was identical with that reported in the literature.<sup>10</sup>

*Anal.* Calcd. for  $C_{15}H_{19}O_2$ : C, 77.2; H, 6.9. Found: C, 77.3; H, 7.1.

***cis*-2-Phenylcyclohexane-1-carboxylic Acid (X).**—A solution of 150 mg. of VIIIa in 10 ml. of acetic acid was hydrogenated in the presence of palladium-charcoal. After 15 minutes, the hydrogen absorption stopped. On filtration and addition of 25 ml. of water, 120 mg. of the saturated *cis*-acid, m.p. 75°,<sup>4</sup> precipitated.

***cis*-2-Cyclohexylcyclohexane-1-carboxylic Acid (XI).**—A solution of 1 g. of VIIIa in 30 ml. of acetic acid was hydrogenated in the presence of platinum oxide at room temperature and 3 atm. pressure for 5 hours. After filtration and dilution with water, a product precipitated, melting at 83°. Recrystallization from petroleum ether raised the m.p. to 84–85°.<sup>20</sup>

*Anal.* Calcd. for  $C_{13}H_{22}O_2$ : C, 74.3; H, 10.5. Found: C, 74.6; H, 10.3.

**Dehydrobromination of VIIb with Pyridine.**—A solution of 10 g. of the bromoester VIIb in 35 ml. of pyridine was

(19) "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 820.

(20) J. Ranedo and A. Leon, *C. A.*, **19**, 1703 (1925).

refluxed for 6 hours, acidified with dilute hydrochloric acid and extracted with ether. The ether layer was washed with 5% hydrochloric acid and 5% sodium carbonate solution. Distillation gave 5.5 g. of an oil boiling at 122–125° (1 mm.),  $\lambda_{\text{inf}} 245 \text{ m}\mu$  ( $\log \epsilon 3.48$ ).

To the solution of 4.5 g. of this product in 30 ml. of ethanol, 50 ml. of a 25% aqueous potassium hydroxide solution was added and the mixture refluxed for 3 hours. The alkaline solution was then cooled, extracted with ether, boiled with charcoal, filtered and acidified and the precipitated oily acid extracted with ether. The ether residue (1.8 g.) solidified; it melted at 110–125°, and after recrystallization from ligroin at 118–123°,  $\lambda_{\text{inf}} 245 \text{ m}\mu$  ( $\log \epsilon 3.54$ ).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{14}\text{O}_2$ : C, 77.2; H, 6.9. Found: C, 77.1; H, 7.1.

**Debromination of Ethyl 1-Bromo-2-phenylcyclohexane-1-carboxylate (VIIb).**—To a stirred suspension of 4 g. of zinc powder in a solution of 1.5 g. of the bromo-ester VIIb in 30 ml. of acetic acid, 5 ml. of concentrated hydrochloric acid was added dropwise during 3 hours. The reaction mixture was diluted with 100 ml. of water and extracted with ether, and the ethereal extract washed with a 5% aqueous sodium carbonate solution and water. Distillation afforded 0.5 g. of an oil, b.p. 145° (15 mm.), which gave a negative Beilstein test for halogen, and yielded with anilinemagnesium bromide 0.6 g. of an anilide of m.p. 155–157° and, after recrystallization from ligroin, m.p. 165°. <sup>4</sup>

**Diethyl 2-Phenylcyclohex-4-ene-1,1-dicarboxylate.**—A mixture of 50 g. of diethyl benzylidenemalonate, <sup>21</sup> 50 g. of butadiene in 150 ml. of benzene and 0.5 g. of hydroquinone was heated at 180–190° for 24 hours. Distillation of the product gave 28 g. (46%) of an oil of b.p. 150–152° (0.02 mm.), and after a second distillation 18 g. of b.p. 150° (0.02 mm.).

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{22}\text{O}_4$ : C, 71.5; H, 7.3. Found: C, 71.0; H, 7.3.

***cis*-2-Phenylcyclohex-4-ene-1-carboxylic Acid.**—To 12 g. of the preceding ester in 15 ml. of ethanol, 40 ml. of a 30% aqueous solution of potassium hydroxide was added and the mixture refluxed for 4 hours, cooled and acidified. The oily product was decarboxylated, without previous purification, by heating it at 180° for 45 minutes and at 200° for 5 minutes. Trituration of the melt with ligroin gave 2 g. of a solid which on recrystallization from nitromethane and then from cyclohexane afforded 1.5 g. of the desired acid, m.p. 133°. <sup>4</sup>

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{14}\text{O}_2$ : C, 77.2; H, 6.9. Found: C, 77.6; H, 6.6.

**Reduction.**—To 300 mg. of the acid in 15 ml. of acetic acid, 100 mg. of palladium-charcoal was added and the mixture hydrogenated at room temperature. After filtration from the catalyst, distillation of 13 ml. of the solvent and addition of water, the colorless *cis*-2-phenylcyclohexane-1-carboxylic acid, m.p. 77°, was obtained.

**Anilide of 1-Bromo-2-phenylcyclohexane-1-carboxylic Acid.**—A quantity of 10 g. of VIa was converted into the acid chloride and brominated as described above. The bromochloride so obtained (8.5 g.) boiled at 165–170° (1.5 mm.). A solution of 5 g. of the product in 15 ml. of benzene was added to a solution of 5.1 g. of aniline in 15 ml. of benzene. The precipitate formed (4.0 g., m.p. 175–190°) was collected after one hour and washed with dilute hydrochloric acid, 5% sodium carbonate and water. After two

recrystallizations from toluene and *t*-butyl alcohol, 1.0 g. of a product melting at 214–215° was obtained.

*Anal.* Calcd. for  $\text{C}_{19}\text{H}_{20}\text{BrNO}$ : C, 63.7; H, 5.6, N, 3.9. Found: C, 64.1; H, 5.3; N, 3.7.

By stepwise evaporation of the filtrate, 0.4 g. of m.p. 205–210°, 0.4 g. of m.p. 193–200°, 0.4 g. of m.p. 175–193° and 0.9 g. of m.p. 155–165° were obtained.

All these anilide fractions were hydrogenolyzed under the following standard conditions: To the solution of 0.25 g. of the product in 20 ml. of ethanol, a solution of 0.25 of crystalline sodium acetate in 1 ml. of water and 0.1 g. of palladium-charcoal were added, and the mixture was hydrogenated until the absorption of hydrogen ceased. The resulting solution was heated to the boiling point and filtered from the catalyst, and some of the ethanol was distilled off, water was added, and the precipitate formed collected and washed with water. Thus the following products were obtained

M.p. of bromo-anilide, °C.	M.p. of crude anilide produced, °C.
214–215	166
205–210	166
193–200	164–165
175–193	163–165
155–165	145–153

The melting points of all these products were not depressed by the admixture of the anilide of pure *trans*-2-phenylcyclohexane-1-carboxylic acid (VIa).

**Determination of the Composition of the Product of the Hydrogenolysis of IIc. A. Refractive Index.**—The relative quantities of *cis*- and *trans*-2-methylcyclohexane-1-carboxylic acids were calculated from the formula

$$100n_m = n_c C + n_T T; C + T = 100$$

where  $n_c$ ,  $n_T$  and  $n_m$  are the refractive indices, respectively, of the pure Vc (*cis*), of the pure Ic (*trans*) and of the hydrogenolysis mixture, and  $C$  and  $T$  the percentages of Vc and Ic in the mixture. That the change of the refractive index of the mixture with the change in its composition is linear was shown by experiments with three artificially prepared mixtures containing 23, 37 and 49%, respectively, of the *trans* isomer. The deviation from linearity did not exceed 1.5%.

**B. Infrared Absorption.**—All measurements were carried out in a 0.5-mm. thick sodium chloride cell with chloroform solutions containing 20 mg./ml. of the product. The base-line method<sup>22</sup> for the determination of the percentage composition of the mixture of isomers was applied to the wave lengths 7.3  $\mu$  (sharp band) and 8  $\mu$  (broad band). In four artificially prepared mixtures of the two isomers, containing 20, 40, 60 and 80% of the *trans* compound Ic, deviations not larger than 5% were obtained. The formulas

$$100D_m = D_T T + D_C C; C = 100 - T$$

were used, where  $C$  and  $T$  are the percentages of Vc and Ic and  $D_C$ ,  $D_T$  and  $D_m$  the optical base-line densities of the pure Vc, pure Ic and of the mixture, all taken at the above concentration.

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(22) J. J. Hegl, M. F. Bell and J. U. White, *Anal. Chem.*, **19**, 293 (1947)

(21) Reference 19, p. 377.