

Simultaneous solution of equations (20) and (21) gives equation (22).

$$\ln \left[\frac{1}{\omega} (\ln E_{d_0} - \chi Z - \ln Z) \right] = \ln E_{D_0} - \omega Z - \frac{\psi}{\omega} (\ln E_{d_0} - \chi Z - \ln Z) \quad (22)$$

Since the constants E_{d_0} , E_{D_0} , χ , ψ and ω are all determined by the previous choices of the force constants, van der Waals potentials, etc., equation (22) can be solved numerically for Z ; subsequently, either equation (20) or (21) can be solved numerically for Y . From equations (10), (14), (17), (18) and (19) it follows that

$$E^0 = Z^2\chi + Y^2\psi + 2ZY\omega + 2Y + 2Z \quad (23)$$

The strain energy for diiodobenzene can also be determined by methods similar to those already presented^{1,2}; this energy is found to be

$$E_{\text{ortho}} = \frac{Y'^2}{2\rho'^2} \sum_i \frac{C_i^2}{a_i} + Y' \quad (24)$$

where

$$Y' = E_{D_0} \exp \left(-\frac{1}{\rho'} \sum_i C_i^2/a_i \right) \quad (25)$$

For the calculations of Y' , the iodine-iodine interactions were assumed to be the same as those used in the calculations of E^0 . However, as previously noted, it was necessary to use an exponential approximation to the van der Waals potential different from that used in determining the value of the strain energy for the tetraiodo acid; this statement follows at once from the fact that the iodine atoms are further apart in

diiodobenzene than they are in the activated complex for the racemization of the tetraiodo acid. The exponential approximations used in determining the strain energy for diiodobenzene are given in Table III.

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VII. Summary

J. E. Mayer and one of the authors recently developed a method for calculating the activation energies for the racemization of optically active derivatives of biphenyl. This theory emphasizes the importance of the bending of valence bonds, as well as overlap of atoms, as a major element in steric strain.

To test this theory, activation energies have been measured and calculated for the racemization of 2,2'-diiodo-5,5'-dicarboxybiphenyl and for 2,2',3,3'-tetraiodo-5,5'-dicarboxybiphenyl. For the latter compound, the iodine atoms in the 3- and 3'-positions "buttress" those in the 2- and 2'-(ortho) positions, and thereby retard the racemization process. In agreement with the qualitative argument presented above and with the quantitative calculations, the experimentally determined activation energy for the tetraiodo acid exceeds that for the diiodo acid by about 6.4 kcal./mole.

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The Preparation and Resolution of 2,2'-Diiodo-5,5'-dicarboxybiphenyl and of 2,2',3,3'-Tetraiodo-5,5'-dicarboxybiphenyl

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In the preceding article,¹ the calculated and observed activation energies for the racemization of 2,2'-diiodo-5,5'-dicarboxybiphenyl (the "diiodo acid") and of 2,2',3,3'-tetraiodo-5,5'-dicarboxybiphenyl (the "tetraiodo acid") are reported. In this paper, the methods of preparing and resolving these compounds are described.

The general plan of the preparations is shown in Fig. 1. The central compound of this series is the dimethyl ester, XI, of 2,2'-diamino-5,5'-dicarboxybiphenyl. Both amino groups of this ester can be diazotized, and the resulting tetrazonium salt converted (by way of the iodonium iodide, XIII) to the ester, XIV, of the "diiodo acid." Alternatively, the amino ester, XI, can be iodinated to form the diiododiamino ester, XVI, which can then be converted (by way of the

corresponding tetrazonium salt and the iodonium iodide, XVII) to the ester, XVIII, of the "tetraiodo acid." It has been assumed that, in the iodination of 2,2'-diamino-5,5'-dicarbomethoxybiphenyl (XI), the iodine atoms are introduced into the 3 and 3' positions. Since, in the diamino ester, XI, the position para and one of the positions ortho to each amino group are blocked, it is expected that the iodination will occur as indicated above.

The precursor for the diamino ester, XI, is the dinitro ester, V. The latter compound had previously been prepared by Case and Koft.² The first step in their synthesis was the nitration of *o*-tolidine (VI) to form a dinitro-*o*-tolidine to which they (as well as earlier workers) ascribe the structure VII. On deamination, this dinitro-*o*-tolidine yields a dinitroditolyl to which these

* Harvard University Ph.D. 1935.

(1) Rieger and Westheimer, **72**, 19 (1950).

(2) Case and Koft, *THIS JOURNAL*, **63**, 508 (1941).

toluidine was carried over with 35 l. of distillate. The semi-solid, water-insoluble product was triturated twice with 5% sodium hydroxide solution, and then with water. The yields of 3-bromo-4-nitrotoluene (needles from methanol, m. p. 35–36°) averaged 131 g. or 37%.

2,2'-Dinitro-5,5'-dimethylbiphenyl (VIII).—Ten grams of commercial copper powder was added with stirring, over a period of twenty minutes, to fifteen grams of 3-bromo-4-nitrotoluene, which had previously been heated to 215°. The temperature of the mixture was kept below 235°. When the reaction was complete, the mixture was cooled, taken up in 100 cc. of benzene, and filtered to remove copper and copper salts. The benzene solution was treated twice with Norite, and allowed to evaporate slowly. The product (6.9 g. of 2,2'-dinitro-5,5'-dimethylbiphenyl) separated as large crystals, m. p. 160–161°.

Alternatively, this biphenyl was prepared by the deamination of 2,2'-dinitro-*o*-toluidine.² Although Case and Koft obtained a yield of 53% on reduction of the diazonium salt with alcohol, the maximum yield (39%) we obtained was by reduction with hypophosphorous acid.⁶ Fifteen grams of 2,2'-dinitro-*o*-toluidine (VII) was added to 75 cc. of concentrated hydrochloric acid. The resulting white paste was mixed with 75 cc. of water, stirred, and kept below 10° while a saturated solution of 10 g. of sodium nitrite in water was slowly added. The clear solution of the tetrazonium salt was poured in a slow stream with stirring into 200 cc. of 30% hypophosphorous acid previously chilled to 0°. The mixture was allowed to stand at 4° for eight hours and at room temperature for an additional twelve hours. Crude 2,2'-dinitro-5,5'-dimethylbiphenyl (VIII) separated from the solution during this period as a yellow-brown solid. The biphenyl derivative was recrystallized from glacial acetic acid; it did not depress the melting point of the compound prepared by the Ullmann synthesis.

Methyl 3-Bromo-4-nitrobenzoate (IV).—Chromium trioxide (150 g.) was added in small portions over a period of an hour to 130 g. of 3-bromo-4-nitrotoluene, dissolved in 1000 cc. of boiling glacial acetic acid. The mixture was refluxed for six hours, poured into 9 liters of ice-water, and allowed to stand for forty-eight hours. Most of the supernatant liquid was then decanted, and the residual greenish-white precipitate filtered. The wet filter cake was stirred at 80° with a liter of 5% sodium hydroxide solution, and the hot solution acidified with concentrated hydrochloric acid. The resultant slurry was chilled thoroughly and filtered. The solid so obtained was suspended with stirring in 500 cc. of water, and enough 10% sodium hydroxide added to make the solution distinctly alkaline. Twenty grams of filter-cel was stirred into the solution, which was then filtered. To the clear filtrate, 300 cc. of methanol was added, and after the resulting solution had been heated to boiling, it was acidified with excess hydrochloric acid. The white precipitate consisted of 90 g. (60% of theory) of 3-bromo-4-nitrobenzoic acid, m. p. 194–195° (cor.); the pure material melts⁷ at 197°.

Ninety grams of this crude acid was dissolved in 700 cc. of boiling methanol, and dry hydrogen chloride was passed into the refluxing mixture for four hours. The hot solution, which contained some solid, was poured over 1500 g. of crushed ice. A white precipitate appeared and was filtered, washed with water, and triturated twice with 10% sodium bicarbonate. The solid remaining consisted of 92 g. of yellow-white ester, melting at 70–72°. Several recrystallizations of a small amount of this solid from methanol produced pale yellow needles of methyl-3-bromo-4-nitrobenzoate, m. p. 75–76° (cor.).

Anal. Calcd. for C₈H₆O₄Br: Br, 30.65. Found: Br, 30.35.

2,2'-Dinitro-5,5'-dicarbomethoxybiphenyl (V).—Methyl 3-bromo-4-nitrobenzoate (61 g.) was dissolved in 80 cc. of boiling nitrobenzene. Small portions of commercial copper bronze (45 g.) were added over a period of

twenty minutes to the well-stirred solution. After all the copper had been added, the mixture was maintained at 205° for another ten minutes, cooled and taken up in 600 cc. of boiling benzene. The slurry was filtered to remove cuprous bromide and excess copper. The filtrate was steam distilled until the odor of nitrobenzene was no longer detectable; the brownish-black solid residue was air dried, dissolved in 200 cc. of benzene and treated with Norite. The resulting deep brown benzene solution was evaporated to 75 cc., and then 150 cc. of hot methanol was added. The brownish-yellow material, which separated when the benzene-methanol solution was cooled, was recrystallized from acetone-methanol; 34 g. (81%) of 2,2'-dinitro-5,5'-dicarbomethoxybiphenyl, melting at 174–175° (cor.) was obtained. The melting point of this ester was not depressed when the material was mixed with some prepared according to the procedure of Case and Koft.²

Alternatively, the 2,2'-dinitro-5,5'-dicarbomethoxybiphenyl can be prepared by the esterification of the corresponding acid, which in turn can be made by the oxidation of 2,2'-dinitro-5,5'-dimethylbiphenyl. The oxidation procedure of Case and Koft, and several variations of this procedure were tried, but in no case could we obtain a yield of the dicarboxylic acid greater than 20%. (Case and Koft report 31%.) In addition to this low yield of the dicarboxylic acid, 15–20% of the starting material was recovered. Furthermore, fractional crystallization of the acidic oxidation products from acetic acid gave a small yield (ca. 5%) of a new acid, presumably 2,2'-dinitro-5-methyl-5'-carboxybiphenyl. This monocarboxylic acid, which is more soluble in acetic acid than the dicarboxylic acid, melts at 234–235° (cor.).

Anal. Calcd. for C₁₄H₁₀O₆H₂: N, 9.28; neut. equiv., 302. Found: N, 9.23, 9.46; neut. equiv., 305.

2,2'-Diamino-5,5'-dicarbomethoxybiphenyl (XI).—Twenty-eight grams of 2,2'-dinitro-5,5'-dicarbomethoxybiphenyl (V) was dissolved in 700 cc. of hot methanol; to this hot solution, 70 cc. of glacial acetic acid was added. Fifty-six grams of iron powder was added over a period of twenty minutes to the stirred solution and the resulting mixture stirred and refluxed for two hours. The hot reaction mixture was filtered rapidly, using filter-cell as a filtration aid; the filter cake was washed twice with 200-cc. portions of boiling acetone. The filtrate and washings were combined and poured into 4 liters of ice-water; the resulting pink precipitate was filtered and washed with warm (50°) water until almost all the pink color had disappeared. The almost colorless remaining solid was air dried and then recrystallized from a mixture of benzene and methanol, yielding 17 g. (73% of theory) of 2,2'-diamino-5,5'-dicarbomethoxybiphenyl, m. p. 208–209° (cor.).

Anal. Calcd. for C₁₆H₁₆O₄N₂: N, 9.35. Found: N, 9.33, 9.37.

Alternatively, but less efficiently, the diamino ester, XI, could be prepared by catalytic reduction of the dinitro ester, V. Fifteen grams of 2,2'-dinitro-5,5'-dicarbomethoxybiphenyl was dissolved in 200 cc. of methyl acetate and reduced (over a period of forty-five minutes) by the theoretical amount of hydrogen (3-atm. pressure) in the presence of 0.1 g. of Adams catalyst. After the catalyst had been removed by filtration, 100 cc. of methyl acetate was distilled from the greenish-brown solution, and 100 cc. of methanol added. The solution was treated with Norite, diluted further with methanol and cooled; a brownish white solid appeared. This solid was dissolved in 150 cc. of 15% hydrochloric acid and fractionally precipitated with 20% sodium hydroxide solution. The first material which precipitated was brownish-yellow. On recrystallization from acetone-methanol, 2 g. of yellow needles, m. p. 224–225°, could be obtained. This yellow compound was unaffected by nitrous acid or Tollens reagent; presumably it is 2,9-dicarbomethoxybenzo(C)-cinnoline (XII).

Anal. Calcd. for C₁₅H₁₂O₄N₂: N, 9.56. Found: N, 9.56.

After the cinnoline had been removed in the fractional precipitation procedure referred to above, the residual al-

(6) Kornblum, in Adams, "Organic Reactions," John Wiley and Sons, New York, N. Y., 1944, pp. 262–340.

(7) Claus and Scheulen, *J. prakt. Chem.*, **43**, 200 (1891).

most colorless acidic solution was made distinctly basic, whereupon 4.9 g. (39%) of the diamino ester, XI, was obtained.

2,2'-Diido-5,5'-dicarbomethoxybiphenyl (XIV).—The amino groups of the diamino ester, XI, were replaced by iodine atoms by a procedure which parallels that used by Searle and Adams⁸ for the preparation of 2,2'-diido-4,4'-dicarbomethoxybiphenyl.

Ten grams of 2,2'-diamino-5,5'-dicarboxybiphenyl (XI) was dissolved in 150 cc. of 15% hydrochloric acid. The compound was tetrazotized, at a temperature below 10°, with a solution of 5 g. of sodium nitrite in 10 cc. of water. The resulting deep orange solution was filtered and poured with stirring into an ice-cold solution of 35 g. of potassium iodide in 50 cc. of water. The mixture, which foamed violently, was warmed on the steam-bath for one hour; while it was still warm, it was treated with a solution of 4 g. of sodium bisulfite in 30 cc. of water. Filtration of this mixture yielded 18 g. of a pale brown solid which melted from 250 to 270°, and which was insoluble in alcohol, benzene, acetone, ether and carbon tetrachloride. This material was not purified for analysis, but was assumed to consist primarily of 2,8-dicarbomethoxydibenziodolum iodide (XIII). Seventeen grams of this material was melted in a large test-tube and then kept at 230–240° for one minute. When the melt had cooled, a black glassy material was obtained; it was dissolved in hot benzene and treated three times with Norite. Methanol was added to the benzene solution, whereupon a brown solid separated; this solid was twice recrystallized from benzene and methanol, and yielded 4.2 g. (24% of theory) of 2,2'-diido-5,5'-dicarbomethoxybiphenyl, m. p. 179.5–180.5 (cor.).

Anal. Calcd. for $C_{16}H_{12}O_4I_2$: I, 48.65; sapn. equiv., 261. Found: I, 48.85; sapn. equiv., 257.

2,2'-Diido-5,5'-dicarboxybiphenyl (XV) (The "Diido Acid").—Five grams of 2,2'-diido-5,5'-dicarbomethoxybiphenyl was refluxed in a mixture of 100 cc. of ethanol and 20 cc. of 10% aqueous sodium hydroxide for three hours. The resulting clear hot solution was acidified with 10 cc. of concentrated hydrochloric acid. When this mixture was cooled, and when an additional 50 cc. of water was added, a white solid crystallized. The acid, after recrystallization from aqueous alcohol, separated in small, shiny, almost white crystals melting at 346–348°. The yield on this saponification was 4.5 g. (95%).

Anal. Calcd. for $C_{14}H_8O_4I_2$: C, 34.10; H, 1.66; I, 51.42; neut. equiv., 247. Found: C, 34.23; H, 1.72; I, 51.20; neut. equiv., 246.

2,2'-Diamino-3,3'-diido-5,5'-dicarbomethoxybiphenyl (XVI).—Twelve grams of 2,2'-diamino-5,5'-dicarbomethoxybiphenyl was dissolved in 400 cc. of 80% acetic acid at 80°. Twenty-six grams of iodine monochloride was poured in a steady stream into the hot, vigorously stirred solution. During this period, a dark solid settled to the bottom of the flask. The formation of this material was disregarded, and the whole hot mixture poured rapidly into 500 cc. of ice-cold 10% sodium hydroxide solution, which contained 30 g. of sodium sulfite. A heavy black crystalline material and a flocculent white one separated out. All the solid material present in the mixture was removed by filtration, air dried, dissolved in hot benzene treated with charcoal, and finally crystallized from benzene solution by the addition of methanol. Recrystallization from benzene-methanol mixtures yielded 15 g. (68% of theory) of 2,2'-diamino-3,3'-diido-5,5'-dicarbomethoxybiphenyl which crystallized in large, slightly pink crystals melting at 246–247.5°.

Anal. Calcd. for $C_{16}H_{14}O_4N_2I_2$: I, 45.97. Found: I, 46.21.

2,2',3,3'-Tetraido-5,5'-dicarbomethoxybiphenyl (XVIII).—The tetrazotization of 2,2'-diamino-3,3'-diido-5,5'-dicarboxybiphenyl, and the replacement of the diazonium groups by iodine atoms, exactly paralleled the corresponding preparation, already described for these re-

actions of 2,2'-diamino-5,5'-dicarbomethoxybiphenyl. From 14.5 g. of 2,2'-diamino-3,3'-diido-5,5'-dicarbomethoxybiphenyl, tetrazotized with 4 g. of sodium nitrite, 15 g. of a dry, red-orange solid melting at 235–255° was obtained; this solid was assumed to consist largely of the idonium iodide XVII. The idonium iodide was dissolved in 50 cc. of hot nitrobenzene, which was refluxed for fifteen minutes. After the nitrobenzene had cooled, 200 cc. of methanol was added; the tetraidoester crystallized from the reaction mixture and was separated from a less soluble orange impurity by crystallization from benzene and methanol. Finally, 7.3 g. (30%) of almost colorless crystals of 2,2',3,3'-tetraido-5,5'-dicarbomethoxybiphenyl, melting at 224.5–225.5° (cor.) was obtained.

Anal. Calcd. for $C_{16}H_{10}O_4I_4$: I, 65.60; mol. wt., 773. Found: I, 65.23; mol. wt. (Rast), 754.

2,2',3,3'-Tetraido-5,5'-dicarboxybiphenyl (XIX) (The "Tetraido Acid").—Seventy-five cc. of hydroiodic acid (sp. gr. 1.5) was added to a solution of 7.1 g. of the tetraido methyl ester, XVIII, in 200 cc. of hot glacial acetic acid. This mixture was refluxed and stirred for twenty hours, cooled and poured into 2 l. of ice-water. The white precipitate that formed was filtered, washed with water and redissolved in 50 cc. of 5% sodium hydroxide solution. This alkaline solution was then poured into a hot mixture of 175 cc. of ethanol and 25 cc. of concentrated hydrochloric acid. The acid precipitated as a gel which coagulated when the suspension was boiled. The suspension was cooled, the solid removed by filtration and recrystallized from ethanol and a little water. The acid separated in small shiny crystals melting (with decomposition) at 392–396°; the yield was 6.8 g. (98% of theory).

Anal. Calcd. for $C_{14}H_6O_4I_4$: C, 22.54; H, 0.81; I, 68.05; neut. equiv., 373. Found: C, 22.85; H, 0.71; I, 68.25; neut. equiv., 372, 373.

Resolution of 2,2'-Diido-5,5'-dicarboxybiphenyl.—The resolution of the diido acid was carried out through the monobrucine salt. Only levorotatory diido acid was isolated, and this enantiomorph was obtained in a yield considerably higher than 50% of the optically inactive starting material. Apparently an asymmetric transformation occurred. This is not surprising, since the half-life for the racemization of the diido acid at the boiling point of alcohol is of the order of one minute. Attempts to accomplish a resolution through the dibrucine salt failed; the monobrucine salt resulted when two moles of brucine was used for one mole of the acid. On the other hand, no crystals were obtained in attempts to prepare the monobrucine salt from one mole of acid and one mole of brucine.

The procedure followed is described below. Three grams (0.00608 mole) of 2,2'-diido-5,5'-dicarboxybiphenyl was added to 600 cc. of boiling 95% ethyl alcohol. To the resulting clear solution was added 4.8 g. (0.01216 mole) of brucine. Boiling was continued until the volume had been reduced to 200 cc. The hot solution was filtered rapidly into a flask which had previously been placed in a large Dewar filled with water at 80°. The solution was allowed to cool slowly. Best results were obtained if the solution was not disturbed at all during the cooling time. Usually some crystals appeared when the solution stopped boiling; fifteen hours later, when the mixture had cooled to 30–40°, the liquid contained clusters of needles. The yield was 3.4 g. of the monobrucine salt of the levorotatory acid; the salt melted with decomposition at 290–295°.

Anal. Calcd. for $C_{14}H_8O_4I_2 \cdot C_{21}H_{25}O_4N_2$: N, 3.16; I, 28.57. Found: N, 3.23; I, 28.64.

To recover the free acid from the salt, 3 g. of the latter was dissolved in 30 cc. of 1% alcoholic sodium hydroxide, to which 30 g. of crushed ice had been added. The resulting solution was filtered and then poured slowly with rapid stirring into a mixture of 40 cc. of 95% ethyl alcohol, 30 g. of cracked ice, and 15 cc. of concentrated hydrochloric acid. If this operation was carried out properly, a white solid precipitated, and could be filtered easily. In some experiments the acid did not precipitate at all, and in others the acid precipitated as a gel. In the first instance

(8) Searle and Adams, *THIS JOURNAL*, **55**, 1649 (1933).

the stirring was continued and more water was added; in the second the stirring was continued and more ethyl alcohol was added. The solid acid was filtered and washed with 500 cc. of cold 5% hydrochloric acid, followed by 500 cc. of cold water. The acid did not give a positive test for brucine with concentrated nitric acid, and did not have a bitter taste. After drying, the resolved acid weighed 1.5 g., and melted at 349–352°.

Anal. Calcd. for $C_{14}H_8O_4I_2$: C, 34.10; H, 1.66; neut. equiv., 247. Found: C, 34.42; H, 1.90; neut. equiv., 244.

No attempt was made to prepare an optically pure sample of this acid (0.1062 g. of diiodo acid, neutralized by sodium hydroxide in 38% alcohol, 2-dm. tube, α_{obs} . -0.518°, $[\alpha]^{25D}$ -24.3°).

Resolution of 2,2',3,3'-Tetraiodo-5,5'-dicarboxybiphenyl.—The resolution of the tetraiodo acid was accomplished both through the monobrucine salt of the levo acid and through the dibrucine salt of the dextro acid. The two salts mentioned above are of comparable solubility in ethyl alcohol, and only from alcohol were successful resolutions accomplished. Numerous attempts at resolution were carried through before satisfactory seed crystals were obtained; subsequent resolutions were relatively easy. The resolution may be accomplished as follows:

1.5 g. of the tetraiodo acid was suspended in 25 cc. of 95% alcohol and exactly neutralized with a solution of potassium hydroxide in 95% alcohol. The solution of the salt was filtered, using filter-cell as a filtration aid. A solution of 1.58 g. of recrystallized brucine in 25 cc. of absolute alcohol was likewise filtered and added to the solution of the tetraiodo acid. The solution was heated to boiling, and an excess (above that needed to neutralize the potassium hydroxide) of a 95% alcoholic solution of acetic acid added to the hot, clear solution, which was then seeded with the monobrucine salt of the levo acid. The erlenmeyer containing the mixture was stoppered and placed in a dewar flask containing water at 80°. After fifteen hours, 0.3–0.4 g. of the monobrucine salt of the levo acid usually separated. If no crystals separated, absolute alcohol (in which the salts are much less soluble than they are in 95% alcohol) was added, and the attempt to crystallize repeated. The monobrucine salt consisted of hexagonal plates, which could be recrystallized from absolute alcohol. For analysis, the finely ground sample was dried at 145°.

Anal. Calcd. for $C_{14}H_8O_4I_4 \cdot C_{23}H_{26}O_4N_2$: N, 2.46; I, 44.52. Found: N, 2.48; I, 44.38, 44.84.

After the monobrucine salt of the levo acid had separated, the mother liquors were decanted and seeded with the dibrucine salt of the dextro acid. The latter crystallized as clusters of fine needles.

Anal. Calcd. for $C_{14}H_8O_4I_4 \cdot 2C_{23}H_{26}O_4N_2$: N, 3.65; I, 33.08. Found: N, 3.65; I, 32.98.

Not infrequently, despite all precautions, both salts crystallized together, and the recovered acid was either racemic or only slightly optically active. On one occasion,

crystals were obtained which may have been an impure sample of the dibrucine salt of the levo acid.

The recovery of the free tetraiodo acid from the salts was carried out as follows: 1.3 g. of salt was dissolved in a mixture of 25 cc. of aqueous 5% sodium hydroxide and 25 cc. of ethyl alcohol. The resulting solution was filtered and warmed rapidly to the boiling point. Thirty cc. of a mixture of concentrated hydrochloric acid and ethyl alcohol was added, and the boiling continued until all the precipitated gel had coagulated into small particles. After cooling, the solid acid was filtered, washed with lukewarm 5% hydrochloric acid and then with warm water. The remaining solid was brucine-free (nitric acid test). Whenever the specific rotation of the sodium salt of the resolved acid was less than 65°, the resolution was repeated. The maximum specific rotation observed was $[\alpha]^{25D}$ -112°. The measurements of optical activity were made by dissolving the acid in an equivalent amount of aqueous sodium hydroxide and diluting to volume with a 1% solution of sodium bicarbonate (0.203 g. of levo acid in 10 cc. of NaOH-NaHCO₃ solution, 2-dm. tube, α_{obs} . -4.58°, $[\alpha]^{25D}$ -112°; 0.1217 g. of dextro acid in 10 cc. of NaOH-NaHCO₃ solution, 2-dm. tube, α_{obs} . +2.52°, $[\alpha]^{25D}$ +104°). The identity of the resolved acids was demonstrated by melting point and analysis. The melting points of the resolved acids were essentially identical with that of the racemic acid, presumably due to racemization during heating. A sample of the levo acid was specially purified for analysis; the dextro acid was analytically pure as recovered.

Dextro acid, $[\alpha]^{25D}$ +84°. *Anal.* Calcd. for $C_{14}H_8O_4I_4$: C, 22.54; H, 0.85; neut. equiv., 373. Found: C, 22.74; H, 1.00; neut. equiv., 379.

Levo acid, $[\alpha]^{25D}$ -94°. *Anal.* Calcd. for $C_{14}H_8O_4I_4$: C, 22.54; H, 0.85; I, 78.05; neut. equiv., 373. Found: C, 22.81; H, 0.81; I, 77.7; neut. equiv., 375.

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Summary

2,2'-Diiodo-5,5'-dicarboxybiphenyl has been synthesized in nine steps from 3-bromo-4-aminotoluene in an over-all yield of 2.8%. 2,2',3,3'-Tetraiodo-5,5'-dicarboxybiphenyl has been synthesized in ten steps from the same starting material in an over-all yield of 2.5%. Both acids have been resolved through their brucine salts. These acids were needed for a study, reported in the preceding paper, of the "buttressing" effect on the rate of racemization of optically active derivatives of biphenyl.

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