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

Stereochemistry of Diphenyls. XXXVIII. Resolution of 2,2'-Dibromo-4,4'-dicarboxydiphenyl[1]

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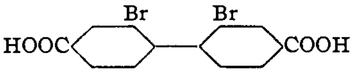
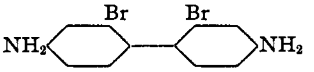
The resolution of 2,2'-diiodo-4,4'-dicarboxydiphenyl[3] which represents a 2,2'-disubstituted diphenyl with monatomic substituents was readily accomplished Two similar compounds containing the somewhat smaller bromine as substituents, 2,2'-dibromo-4,4'-dicarboxydiphenyl (I) and 2,2'-dibromo-4,4'-diaminodiphenyl (II), have now been prepared for comparison.



I



II

From I it was possible to isolate a mono- and dibrucine salt, both of which mutarotated. The former on decomposition yielded the dextro dibromo acid and the latter the levo modification. Both salts mutarotated faster than the salts of the diiodo acid and the active forms racemized much more rapidly than the corresponding iodine compound. In fact, to obtain data on the dibromo acids and their salts, it was necessary to determine racemization and mutarotation rates at 0° and to prepare the active acids by decomposition of the salts at −65°.

TABLE I

ROTATION OF ACIDS AND MUTAROTATION OF SALTS

2,2'-Dibromo-4,4'-dicarboxydiphenyl	Wt. in g. made up to 15 cc. $l = 1$	Solvent at 0°	Max. $[\alpha]_D$ by extrap.	Time[a] in min.	Initial		Final		Av. K[b]	Av. dev. of K	Half-life period in min.
					α_D	$[\alpha]_D$	α_D	$[\alpha]_D$			
Monobrucine	0.1579	Chloroform	+27.2	3.5	+0.22	+20.9	+0.02	+1.9	0.040	±0.002	7.5
salt of *d*-acid	.1014	7:3 Mixture dioxane and methanol	+34.7	5	+ .17	+25.2	+ .05	+7.40	.046	± .005	6.6
Dibrucine salt	.1568	Chloroform	−15.7	4	− .11	−10.5	.00	0.00	.036	± .003	8.4
of *l*-acid	.1249	7:3 Mixture dioxane and methanol	−12.7	3.5	− .09	−10.8	− .02	−2.4	.037	± .005	8.1
d-Acid	.0976	7:3 Mixture dioxane and methanol	+17.4	4	+ .09	+13.8	.00	0.00	.028	± .004	10.7
l-Acid	.1006	7:3 Mixture dioxane and methanol	−17.8	6	− .08	−11.9	.00	.00	.034	± .005	8.9

[a] Counted from time of adding solvent. [b] Average of five to seven values.

Although the 2,2'-dibromo-4,4'-diaminodiphenyl readily formed salts with camphorsulfonic and bromocamphorsulfonic acids, no mutarotation of the salts could be observed even at low temperatures and neither gave an active acid on decomposition. The non-resolution of this compound may be due to the fact that proper experimental conditions were not found for the resolution. On the other hand, the presence of the amino groups in place of the carboxyls in the 4,4'-positions may be an important factor. The rather marked effect on the rate of racemization of easily racemized active diphenyls of various groups in the 3,4,5 or 3',4',5' position has been noted in the study of substituted 2'-methoxy-2-nitro-6-carboxydiphenyl.[4] It was particularly noticeable that in the same position non-polar and polar groups differed materially in their effect. It is possible that in the 2,2'-dibromo-4,4'- substituted diphenyls the amino groups cause no change or a decrease in the rate of racemization as compared with 2,2'-dibromodiphenyl itself, and the carboxyl groups effect an increase in the rate.

The difference in the rate of racemization of the diiodo and the dibromo acids is greater than might be expected, based merely on the size of the atoms as determined by x-ray data. However, the tendency of the iodine and bromine atoms to become deformed is recognized. The 2,2'-disubstituted compounds[5] all show rather marked increased stability as compared with tri- and tetra-substituted diphenyls.

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(1) For a previous paper in this series see Knauf, Shildneck and Adams, THIS JOURNAL, **56**, 2109 (1934); also Adams and Yuan, *Chem. Rev.*, **12**, 261 (1933).

(2) Submitted as part of a thesis for the Degree of Doctor of Philosophy at the University of Illinois.

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

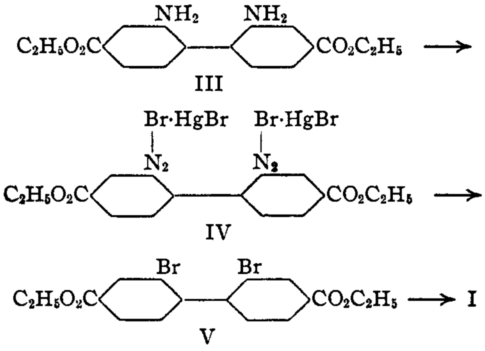
(4) Yuan and Adams, *ibid.*, **54**, 2966, 4434 (1932); Chien and Adams, *ibid.*, **56**, 1787 (1934).

(5) Stanley, *ibid.*, **53**, 3104 (1931); Corbellini, *Atti. accad. Lincei*, **13**, 702 (1931); Meisenheimer and Beisswenger, *Ber.*, **65**, 32 (1932); Lesslie and Turner, *J. Chem. Soc.*, 2021. 2394 (1932); Turner, *Chem. and Ind.*, **51**, 435 (1932); Shaw and Turner, *ibid.*, 135 (1933); Corbellini and Pizzi, *Atti. accad. Lincei*, **15**, 287 (1932); Corbellini and Angeletti, *ibid.*, **15**, 968 (1932).

Experimental

2,2'-Dibromo-4,4'-dicarboxydiphenyl (I) was made by the thermal decomposition of the dry 2,2'-bis-(diazonium-bromide-mercuric-bromide)-4,4'-dicarboethoxydiphenyl (IV). This latter compound was produced from 2,2'-diamino-4,4'-dicarboethoxydiphenyl (III).

2,2'-Dibromo-4,4'-diaminodiphenyl (II) was produced by the benzidine rearrangement of *m*-bromohydrazobenzene.



2,2'-Diamino-4,4'-dicarboethoxydiphenyl (III).—This compound was prepared by the catalytic reduction of 2,2'-dinitro-4,4'-dicarboethoxydiphenyl as previously described in this Journal.[3]

2,2'-Bis-(diazonium-bromide-mercuric-bromide)-4,4'-dicarboethoxydiphenyl (IV).—A solution of 5 g. of 2,2'-diamino-4,4'-dicarboethoxydiphenyl in 100 cc. of 1:1 sulfuric acid was cooled to 0° and diazotized with saturated sodium nitrite solution (starch-potassium iodide for end-point). This diazonium salt solution was poured slowly with stirring into a mixture consisting of a solution of 20 g. of hydrated mercuric nitrate in 1 liter of water to which had been added 40% hydrobromic acid (about 50 cc.) until the precipitate of mercuric bromide that first forms dissolved. The mercuric bromide double salt precipitated as a light yellow curd and was filtered off, washed thoroughly with ether, and sucked dry on a filter. A yield of 17.0 g. of dry salt was obtained (92.4% of theoretical) that decomposed without melting. On continued exposure to light, the yellow salt turned green, and when ground in a mortar it turned into a brown tar.

2,2'-Dibromo-4,4'-dicarboxydiphenyl (I).—An intimate mixture of 17 g. of the dry mercuric bromide double salt with 50 g. of fine dry potassium bromide was placed in a thin-walled tube 60 × 2.5 cm. and closed at one end. The mixture was shaken until it occupied about one-third of the cross-sectional area for the entire length of the tube and then clamped in a slightly sloping position. The open end was fitted with an air-cooled condenser. Starting at the upper end of the tube near the condenser the mixture was heated with a small Bunsen flame until decomposition had occurred in one place; then the adjacent portion of the mixture was heated to decomposition and so on down the tube until all of the material was decomposed.

After extracting with hot water, the dark decomposition product was taken up in ethyl alcohol, boiled twice with decolorizing charcoal, and saponified with aqueous alcoholic potassium hydroxide. (The ester could not be readily isolated in a pure state.) Dilution with water and subsequent acidification precipitated the acid, which was filtered off and recrystallized several times from dilute ethanol. The fourth crystallization yielded 1.5 g. of fine white crystals that melted at 310–312°.

This method was quite similar to the one used by Schwechten[6] in preparing 2,2'-dibromodiphenyl.

Anal. Calcd. for $C_{14}H_8O_4Br_2$: C, 42.00; H, 2.00; neut. equiv., 200. Found: C, 42.13; H, 2.06; neut. equiv., 202.

Resolution of 2,2'-Dibromo-4,4'-dicarboxydiphenyl

Brucine Salt.—This salt was prepared in ethyl alcohol by mixing 2.96 g. (2 moles) of brucine in 100 cc. of ethyl alcohol with 1.5 g. of 2,2'-dibromo-4,4'-dicarboxydiphenyl in 100 cc. of hot ethyl alcohol. After standing for two days, 3.2 g. of crystalline salt deposited and 1.11 g. more of the salt was obtained from the mother liquor by partial evaporation. The two fractions thus obtained were combined and were probably a mixture of mono- and dibrucine salts. Resolution could not be obtained in either methanol or ethanol.

A solution of 3.5 g. of the brucine salt just described, in 1500 cc. of hot ethyl acetate was allowed to evaporate spontaneously at room temperature. After standing for six days, a first fraction of 1.3 g. of acicular crystals deposited, which, by analysis, proved to be a dextro-rotatory monobrucine salt, m. p. 210–220° (for rotations see Table I).

Anal. Calcd. for $C_{14}H_8O_4Br_2 \cdot C_{23}H_{26}O_4N_2$: C, 55.80; H, 4.28; N, 3.53; Br, 20.15. Found: C, 56.47; H, 4.51; N, 3.77; Br, 20.14.

Upon standing a week longer, the mother liquor deposited not only a small amount of the needle-like crystals, but also several large coral-like clusters which, after decanting off the mother liquor, were easily separated by hand. These latter crystals amounted to 0.66 g. and proved to be a levo-rotatory dibrucine salt, m. p. 197–207°. A third fraction of 0.68 g. was obtained which proved to be the dibrucine salt just described.

Anal. Calcd. for $C_{14}H_8O_4Br_2 \cdot 2C_{23}H_{26}O_4N_2$: N, 4.71. Found: N, 4.74.

***d*-2,2'-Dibromo-4,4'-dicarboxydiphenyl.**—The free active acid was obtained from the salt by agitating 0.30 g. of the finely ground monobrucine salt with a 1:1 mixture of concentrated hydrochloric acid and ethyl alcohol kept at −65° with solid carbon dioxide for an hour, and then washing with water on a sintered glass filter until the test for brucine was negative; m. p. 311–313° (for rotations see Table I).

Anal. Calcd. for $C_{14}H_8O_4Br_2$: C, 42.00; H, 2.00. Found: C, 42.80; H, 2.50.

***l*-2,2'-Dibromo-4,4'-dicarboxydiphenyl.**—The *l*-acid was obtained from the dibrucine salt by the method used for preparing the *d*-acid from the monobrucine salt. From 0.4 g. of the brucine salt, 0.11 g. of the active acid was obtained, m. p. 311–313° (for rotations see Table I).

Anal. Calcd. for $C_{14}H_8O_4Br_2$: C, 42.00; H, 2.00. Found: C, 42.58; H, 2.51.

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[6] Schwechten, *Ber.*, **65**, 1605 (1932).

2,2′-Dibromo-4,4′-diaminodiphenyl (II).—This compound was previously made by Gabriel,[7] and by Dobbie, Fox and Gauge.[8] A solution of 100 g. of *m*-bromohydrazobenzene in 500 cc. of ether was dropped slowly with stirring into 700 cc. of cold, concentrated hydrochloric acid. The 2,2′-dibromo-4,4′-diaminodiphenyl hydrochloride precipitated out as fine white crystals; yield, 55 g.

The free base was obtained by adding sodium hydroxide solution to a solution of the hydrochloride. Recrystallization from dilute ethanol gave colorless crystals melting at 150–151.5°.

The *d*-Bromocamphorsulfonic Acid Salt.—To a solution of 9.85 g. of ammonium bromo-*d*-camphorsulfonate (0.030 mole) in 50 cc. of water was added 6 g. of 2,2′-dibromo-4,4′-diaminodiphenyl hydrochloride (0.145 mole) in 40 cc. of hot water. The salt came down as an oil (11.24 g.) which later solidified and was recrystallized from dilute methanol; m. p. 297–300°.

Anal. Calcd. for $C_{12}H_{10}Br_2 \cdot 2C_{10}H_{15}O_4SBr$: N, 2.89. Found: N, 3.15.

When a solution of 5 g. of the bromocamphorsulfonic acid salt in 100 cc. of methanol was allowed to evaporate slowly to 20 cc., 2.34 g. of large brownish crystals deposited, m. p. 297–300°. No mutarotation was observed either at 0° or at 25° in pyridine.

Rotation. 0.1510 g. in 15 cc. of pyridine gave α_D 0.63; $l = 1$; $[\alpha]^0_D$ +62.8°.

Similar results were obtained when the salt was slowly crystallized from an azeotropic mixture of chloroform and methanol and from a dilute methanol solution.

The *d*-Camphorsulfonic Acid Salt.—To a solution of 2.3 g. of the 2,2′-dibromo-4,4′-diaminodiphenyl (0.00673 mole) in 10 cc. of methanol was added 1.56 g. of *d*-camphorsulfonic acid (0.00673 mole) in 10 cc. of methanol. Almost at once 2.8 g. of the monocamphorsulfonate precipitated out while 0.7 g. was recovered from the mother liquor; m. p. 218–219°. The dicamphorsulfonate was not formed by using twice the molal quantity of *d*-camphorsulfonic acid.

Anal. Calcd. for $C_{12}H_{10}Br_2N_2 \cdot C_{10}H_{16}O_4S$: N, 4.88. Found: N, 4.80.

A solution of 3 g. of the salt in 2000 cc. of boiling water deposited no crystals upon cooling, but after standing for two weeks at room temperature, 1.65 g. of feathery crystals formed and were filtered off from 1700 cc. of solution; m. p. 215–217°. A second fraction of 0.8 g. of the crystals formed when the mother liquor from the first had stood for a week. Both fractions were identical in melting point and rotations and no mutarotation was observed either at 0 or at 25°.

Anal. Calcd. for $C_{12}H_{10}Br_2N_2 \cdot C_{10}H_{16}O_4S$: N, 4.88. Found: N, 5.08.

Rotation. 0.1519 g. of salt made up to 15 cc. with pyridine at 0° gave α_D 0.17; $l = 1$; $[\alpha]^0_D$ +14.80°.

In attempting to obtain mutarotating compounds, diacetyl-*d*-tartaric anhydride and *d*-menthoxyacetyl chloride were condensed with the 2,2′-dibromo-4,4′-diaminodiphenyl but in each case amorphous substances impossible to purify were obtained.

Decompositon of the *d*-Camphorsulfonate.—The salt was finely ground and placed in a 15-cc. wide-mouthed, glass-stoppered bottle with a few small glass balls. This was then cooled in solid carbon dioxide and 8 cc. of concentrated aqueous ammonia similarly cooled was added. The bottle was stoppered and mechanically shaken for half an hour while surrounded by dry ice. The contents were then poured into water, filtered, and washed. The free amine that was isolated melted at 151–152° but was inactive. From 0.6 g. of salt, 0.33 g. of amine was isolated.

Summary

1. 2,2′ - Dibromo - 4,4′ - dicarboxydiphenyl was synthesized and resolved into its active forms. The active compound racemizes readily and the salts mutarotate. The rate of racemization of the active form is much more rapid than that of the corresponding iodo compound.

2. 2,2′-Dibromo-4,4′-diaminodiphenyl could not be resolved.

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[7] Gabriel, *Ber.*, **9**, 1407 (1876).

[8] Dobbie, Fox and Gauge, *J. Chem. Soc.*, **99**, 1615 (1911).