Summary

Ethyl methyl ketone and bleaching powder react to give propionic acid and chloroform. Furfuralacetone gives furylacrylic acid and chloroform. Difurfuralacetone does not react to produce furylacrylic acid. Ethyl acetoacetate gives rise to dichloroacetic acid but no chloroform.

Oxalic acid and ammonium tetroxalate are among the reaction products of dilute nitric acid on furfuralacetone.

EVANSTON, ILLINOIS

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

Stereochemistry of Diphenyls. XXX.[1] Preparation and Resolution of 2,2'-Diiodo-4,4'-dicarboxydiphenyl

BY N. E. SEARLE[2] AND ROGER ADAMS

In an earlier paper[3] in this series it was pointed out that on the basis of the studies already completed on 2,2',6 and 2,2',6,6'-substituted diphenyls, there appeared to be no reason why certain 2,2'-disubstituted diphenyls should not be resolved provided the groups were large enough. Moreover, the fact that a disubstituted dinaphthyl[4] was successfully resolved, although such a compound is not entirely comparable to the disubstituted diphenyls, does indicate the likelihood of the existence of resolvable 2,2'-disubstituted diphenyls.

On account of the size of the sulfonic acid group as roughly estimated from the x-ray data available, it was predicted that a 2,2'-disulfonic acid derivative of a diphenyl might be resolved. Diphenyl-2,2'-disulfonic acid and 4,4'-diaminodiphenyl-2,2'-disulfonic acid were prepared, but attempts to resolve them resulted in failure. In the same communication it was pointed out that possibly the 2,2'-dibromo and probably the 2,2'-disubstituted diiododiphenyl should be resolvable. By the system of calculation previously used, based on x-ray data and using a value of 2.20 Å. for the C–I distance,[5] the interference on each side of the molecule should be approximately 0.12 Å.

A diiodo compound has finally been obtained, namely, 2,2'-diiodo-4,4'-dicarboxydiphenyl (IV). It readily formed dialkaloidal salts from which

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[1] For paper XXIX see Patterson and Adams, THIS JOURNAL, **55**, 1069 (1933).

[2] Submitted as part of a thesis for the degree of Doctor of Philosophy at the University of Illinois.

[3] Stanley and Adams, THIS JOURNAL, **52**, 4471 (1930).

[4] Stanley, *ibid.*, **53**, 3104 (1931); Meisenheimer and Beisswenger, *Ber.*, **65**, 32 (1932); Corbellini, *Atti. R. Accad. Lincei (Roma), Rend.*, [6] **13**, 702 (1931).

[5] In a previous paper the aromatic internuclear distance C–I was calculated as 2.06–2.35 Å. [see Neuburger, *Z. Krist*, **80**, 118 (1931)]. The iodine atom has been demonstrated to be a polarizable atom in that its electron shell is easily distorted so that an average of the two limiting values given above seems a satisfactory approximation.

TABLE I

2,2'-Diiodo-4,4'-dicarboxydiphenyl	Wt.[a] in g.	Solvent at 25°	l	Rotation in degrees: Max. $[\alpha]_D$ by extrap.	Time[b] in min.	Initial α_D	Initial $[\alpha]_D$	Final α_D	Final $[\alpha]_D$	Av. K[d]	Av. dev. of K	Half-life period in min.
Brucine salt of *l*-acid	0.2023	Chloroform	2	−27.6	11	−0.68	−25.2	−0.09	−3.33	0.0043	±0.0002	70.0
Brucine salt of *d*-acid	.1522	Chloroform	2	+24.5	6	+0.47	+23.2	.00	0.00	.0042	± .0003	71.7
Brucine salt of *l*-acid	.1512	Dioxane	2	−50.5	11	−1.00	−49.5	− .52	−25.8	.0027	± .0004	111.5
l-Acid	.1515	Dioxane	1	−47.6	5	−0.48	−47.5	.00	0.0	.0033	± .0002	91.3
d-Acid	.0614	Dioxane	1	+51.5	6	+ .21	+51.3	.00	0.0	.0033	± .0003	91.3
l-Acid	.1529	Ethyl acetate	1	−41.7	8	− .41	−40.2	.00	0.0	.0024	± .0002	125.4
Na salt of *l*-acid	.0999	Water[c]	1	−39.3	7	− .25	−37.5	.00	0.0	.0021	± .0004	143.4

$$K = \frac{1}{t}\log\frac{\alpha_0 - \alpha_f}{\alpha_t - \alpha_f}\quad\left[\begin{array}{l}\text{Half-life period;}\\ T = (1/K)\log 2\end{array}\right]$$

[a] Made up to 15 cc. [b] Counted from time of adding solvent. [c] 0.1 N NaOH solution was used. [d] Average of six values. The brucine salt was insoluble in ethyl acetate. The free acid was insoluble in chloroform and glacial acetic acid at ordinary temperature. The sodium salt was insoluble in absolute alcohol.

the brucine was selected for study. Upon crystallization from ethyl alcohol only one form of the salt could be isolated, the salt of the *l*-acid. It is apparent, then, that the same phenomenon was in hand as obtained in the case of 2'-carboxy-6'-nitro-2-methoxydiphenyl and its derivatives as reported by Yuan and Adams.[6] The salt of the *d*-acid during evaporation of the solvent was obviously mutarotating to the salt of the *l*-acid which separated from solution.

When the salt was prepared in methanol, however, a first fraction was obtained which consisted of the salt of the *d*-acid and the other fractions the salt of the *l*-acid. By modifying the procedure it was also possible to obtain from the same solution two different types of crystal clusters which could be separated by hand. One, the smaller in amount, proved to be the salt of the *d*-acid, the other, in larger amount, the salt of the *l*-acid.

From Table I it may be seen that, as in previous racemization and mutarotation experiments, the solvent has a marked effect. The sodium salt in water racemizes more slowly than the free acid in organic solvents.

Two interesting articles by Lesslie and Turner[7] have just appeared in which the diphenyl ester of the 4,4'-diaminodiphenyl-2,2'-disulfonic acid (I) and the diphenyl-2,2'-disulfonic acid (II)

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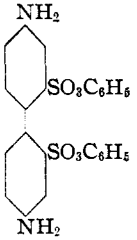
(6) Yuan and Adams, THIS JOURNAL, **54**, 4434 (1932).

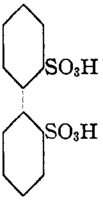
(7) Lesslie and Turner, *J. Chem. Soc.*, 2021 (1932); *ibid.*, 2394 (1932).

have been resolved. It is obvious that the experimental work of Stanley and Adams in connection with the latter compound did not result in the discovery of the proper conditions for resolution. The successful resolution by Lesslie and Turner demonstrates the correctness of the prediction of Stanley and Adams that such disulfonic acids should be resolvable.

Turner has also described the preparation and resolution of another 2,2′-disubstituted diphenyl, the mono-methiodide of 2,2′-*bis*-dimethylaminodiphenyl (III).[8] Corbellini has prepared and resolved 2-(diphenylhydroxymethyl)-2′-carboxydiphenyl (IIIa).[8a] With the 2,2′-diiodo-4,4′-dicarboxydiphenyl (IV) described in this communication, five 2,2′-disubstituted diphenyls have been resolved and the possibility of the resolution of many others may be anticipated.



I



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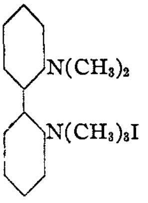

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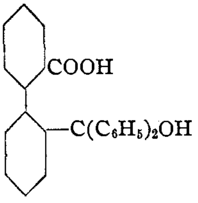
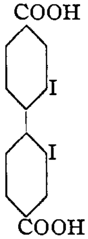


IIIa



IV

Lesslie and Turner[7] in their paper on the diphenyl ester of 4,4′-diaminodiphenyl-2,2′-disulfonic acid have discussed a procedure for estimating the resolution or non-resolution of substituted diphenyls. They have, at the same time, questioned the "theoretical justification" of the method for predicting resolvability or non-resolvability of such compounds, previously suggested by Stanley and Adams.[9] It may be stated merely that the assumptions made in connection with our calculations are fully recognized. On the basis of these calculations, predictions were made which conformed surprisingly well to the experimental results. The method of Lesslie and Turner is equally open to criticism since it involves arbitrary assumptions as to the effective diameter of certain atoms (*i. e.*, as to how close atoms can approach without interfering). The possibility of clarifying the diphenyl problem will depend primarily on the accumulation of additional pertinent experimental data.

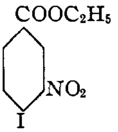
Experimental

The 2,2′-diiodo-4,4′-dicarboxydiphenyl (IV) was prepared through the following series of reactions. (V) was condensed with copper to (VI), the nitro group reduced to (VII), diazotization to (VIII), rearrangement to (IX) and saponification to (IV).

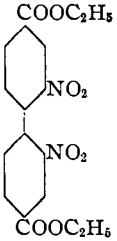
[8] Turner, *Nature*, **130**, 315 (1932).

[8a] Carbellini and Pizzi, *Atti. accad. Lincei* **15**, 287 (1932).

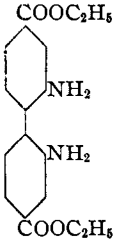
[9] Stanley and Adams, THIS JOURNAL, **52**, 1200 (1930).



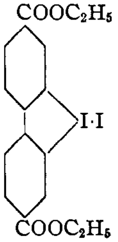
V



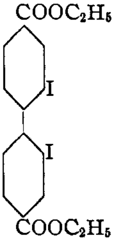
VI



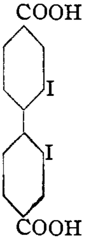
VII



VIII



IX



IV

Ethyl 4-Iodobenzoate.—A fine suspension of ethyl 4-aminobenzoate hydrochloride was prepared by adding 500 cc. of 6 *N* hydrochloric acid to 100 g. of ethyl 4-aminobenzoate, previously made into a thin paste with water. The suspension of the amine hydrochloride was cooled to zero degrees and diazotized with 48.2 g. of sodium nitrite dissolved in 100 cc. of water. During the diazotization about 100 g. of ice was added. To the diazotized solution, 160 g. of potassium iodide dissolved in 150 cc. of water was added with rapid stirring. On warming, a heavy black oil separated which was shaken with sodium bisulfite solution to remove excess iodine and distilled with superheated steam. The product was dried over anhydrous magnesium sulfate; yield, 122 g. (68.5% of theoretical); b. p., 281–283° at 760 mm.; 135° at 5 mm.; d^{20} 1.655; n_D^{25} 1.5854.

Anal. Calcd. for $C_9H_9O_2I$: C, 39.13; H, 3.26; I, 46.02. Found (micro): C, 39.63; H, 3.40; I, 46.28.

This product has been made previously by McCombie and Scarborough,[10] b. p. 153.5° at 14 mm., and by Schmidt and Schulz[11] by esterification of 4-iodobenzoic acid.

Ethyl 3-Nitro-4-iodobenzoate (V).—A cold mixture of 60 cc. of concentrated nitric acid (sp. gr. 1.42) and 60 cc. of concentrated sulfuric acid was added slowly to a solution of 122 g. of ethyl 4-iodobenzoate in 150 cc. of concentrated sulfuric acid kept at 5–6° with ice and salt. This required one-half hour with good mechanical stirring and efficient cooling. Then the solution was allowed to warm up to 15° and was kept at that temperature until a yellow precipitate appeared (about two hours). The mixture was stirred for twenty minutes more and poured onto cracked ice. The ethyl 3-nitro-4-iodobenzoate separated as a yellow solid and was crystallized from 95% ethyl alcohol; yield, 120 g. of fine yellow crystals melting at 89–90.5°. The compound has been described previously by Allen,[12] who prepared it by esterification of 3-nitro-4-iodobenzoic acid. He reports a melting point of 88–89.5°.

2,2'-Dinitro-4,4'-dicarboethoxydiphenyl (VI).—A solution of 120 g. of (V) in 120 cc. of redistilled nitrobenzene was placed in a flask fitted with air-cooled condenser and mechanical stirrer and heated on a metal bath until the solution just began to boil. Then copper bronze powder was added slowly with stirring, causing the solution to boil more vigorously. When all further action had ceased, the nitrobenzene solution was filtered from the cuprous iodide and excess copper and was steam distilled. The residue was twice crystallized from 95% ethyl alcohol. The product consisted of pale yellow scales that melted at 95–96°; yield, 50 g. (69%).

Anal. Calcd. for $C_{18}H_{16}O_8N_2$: C, 55.68; H, 4.16; N, 7.22. Found (micro): C, 55.99; H, 4.24; N, 7.38.

2,2'-Diamino-4,4'-dicarboethoxydiphenyl (VII).—A solution of 15 g. of the dinitro

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[10] McCombie and Scarborough, *J. Chem. Soc.*, **107**, 16 (1915).

[11] Schmidt and Schulz, *Ann.*, **207**, 334 (1881).

[12] Allen, *Ber.*, **26**, 1742 (1893).

compound (II) in 350 cc. of 95% ethyl alcohol and 0.3 g. of platinum oxide[13] was reduced with hydrogen at a pressure of 35–45 lbs. The theoretical amount was absorbed in one-half hour. After several treatments with norite the diamine was precipitated by diluting the solution with water. It was recrystallized from dilute methanol and melted at 99–100°; yield from two runs, 20 g. of pale yellow scales (79%).

Anal. Calcd. for $C_{18}H_{20}O_4N_2$: N, 8.54. Found (micro Dumas): N, 8.57.

2,2'-Diiodo-4,4'-dicarboethoxydiphenyl (VIII) and (IX).—The procedure for replacing the two amino groups with iodine was similar to that used by Mascarelli and Benati[14] for converting 2,2'-diaminodiphenyl to the corresponding diiodo compound.

A suspension of 15 g. of (VII) in a mixture of 50 cc. of concentrated hydrochloric acid and 50 cc. of water was cooled with ice and salt and diazotized with 8 g. of sodium nitrite dissolved in 10 cc. of water. The cold diazonium salt solution was then filtered and a solution of 22 g. of sodium iodide in 50 cc. of water was slowly added with stirring. Upon warming the solution, a dark solid separated which was decolorized by adding sodium bisulfite. The product, 4,4'-dicarboethoxydiphenylene iodonium iodide (VIII), consisted of 20 g. of fine, light yellow powder that melted at 218° and was very insoluble in the usual organic solvents. It had the expected salt-like properties.[14]

Eighteen grams of (VIII) was heated at 218° for five minutes. After cooling, the dark product was taken up in 150 cc. of hot methyl alcohol and filtered. The filtrate was treated with decolorizing charcoal (norite) several times and the 2,2'-diiodo-4,4'-dicarboethoxydiphenyl (IX) was precipitated by adding water. After recrystallizing twice with dilute alcohol, 8 g. of white microscopic crystals was obtained melting at 118°.

Anal. Calcd. for $C_{18}H_{16}O_4I_2$: C, 39.30; H, 2.94. Found: C, 39.32; H, 3.21.

2,2'-Diiodo-4,4'-dicarboxydiphenyl (IV).—The ester was saponified by warming with alcoholic potassium hydroxide. The free acid was obtained by acidification with dilute hydrochloric acid and was recrystallized twice from dilute methanol. From 7.5 g. of ester, 5.5 g. of product was obtained as fine white crystals, m. p. 339–341°.

Anal. Calcd. for $C_{14}H_8O_4I_2$: neut. equiv., 247; C, 34.05; H, 1.63; I, 51.44. Found: neut. equiv., 249; C, 34.33; H, 1.74; I, 51.80.

Resolution of 2,2'-Diiodo-4,4'-dicarboxydiphenyl. (First Method)

Brucine Salt.—A solution of 3 g. of 2,2'-diiodo-4,4'-dicarboxydiphenyl in 140 cc. of absolute methanol was added to a solution of 4.8 g. of anhydrous brucine in 60 cc. of absolute methanol. After standing for one-half hour the salt came down as an oil. This was redissolved by adding 500 cc. more of absolute methanol and boiling. The solution was then evaporated to 450 cc. on the steam-cone. On standing overnight at room temperature 1.35 g. of salt precipitated as a fine powder, m. p. 212–224°. This fraction was dextrorotatory and was the salt of the *d*-acid (for rotations see Table I).

Anal. Less soluble salt—salt of *d*-acid. Calcd. for $C_{14}H_8O_4I_2 \cdot 2C_{23}H_{26}O_4N_2$: N, 4.37. Found (micro Dumas): N, 4.07.

The mother liquor from the first fraction was allowed to evaporate slowly at room temperature. After standing four days, a second fraction of 1.95 g. of salt crystals deposited. By allowing the mother liquor to evaporate spontaneously for a week at room temperature a third fraction of 2.90 g. of crystals was obtained. The second and third fractions were found to be identical in melting point and rotation and were different from the first fraction. They were levorotatory and proved to be the salt of *l*-acid, m. p. 201–212° (for rotations see Table I).

Anal. Calcd. for $C_{14}H_8O_4I_2 \cdot 2C_{23}H_{26}O_4N_2$: N, 4.37. Found (micro Dumas): N, 4.45.

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[13] "Organic Syntheses," Collective Vol. I, 1932, p. 452.

[14] Mascarelli and Benati, *Gazz. chim. ital.*, **38**, (II) 624 (1908).

(Second Method.)—Two moles of anhydrous brucine in ethyl acetate and one mole of racemic acid in ethyl acetate were mixed and allowed to stand overnight. The salt precipitated gradually and quantitatively. The mixture of the two diastereoisomeric salts was treated as follows.

A. A solution of 2.75 g. of the mixed salts in 250 cc. of ordinary methanol was allowed to evaporate slowly to 100 cc. at room temperature. At first small hard hemispherical clusters of crystals formed but later clusters of larger, transparent prismatic crystals deposited. The mother liquor was poured off and the crystals washed with methanol. After drying, the two kinds of crystals were easily separated by hand. The hemispherical clusters that first appeared were in the smaller amount and were the salt of the *d*-acid. The prismatic crystals that formed later were in the larger amount and were the salt of the *l*-acid.

B. A solution of 4.3 g. of the salt obtained from the ethyl acetate process in 500 cc. of hot 95% ethyl alcohol deposited 1.72 g. of crystals on cooling. After standing overnight 0.99 g. more of salt crystallized out. Upon evaporating at room temperature a third fraction of 0.84 g. was obtained. All three fractions were identical in melting point and rotation and were the salt of the *l*-acid.

***d*-2,2′-Diiodo-4,4′-dicarboxydiphenyl.**—The *d*-salt was ground with ice-cold 6 *N* hydrochloric acid in a small porcelain mortar cooled by an ice-bath. The fine suspension thus produced was filtered on a sintered quartz filter and continuously washed with cold 6 *N* hydrochloric acid for four hours until the acid gave a negative test for brucine. After washing thoroughly with cold water it was dried *in vacuo* over sulfuric acid. From 0.65 g. of salt, 0.30 g. of active acid was obtained, m. p. 339–341° (for rotations and racemization see Table I).

***l*-2,2′-Diiodo-4,4′-dicarboxydiphenyl.**—The *l*-acid was obtained by the method used for the *d*-acid. From 3.0 g. of the *l*-salt, 1.1 g. of the active acid was obtained, m. p. 339–341° (for rotations and racemization see Table I).

Summary

2,2′-Diiodo-4,4′-dicarboxydiphenyl has been prepared and resolved. The brucine salt mutarotates and the active acids readily racemize at 25°. The iodine and hydrogen atoms in the 2,2′-positions of diphenyl are of sufficient size to interfere with each other.

URBANA, ILLINOIS

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