

formed when dihydroxyacetone polymerized to the dimolecular form.⁴ To this end, three condensation products were isolated from dihydroxyacetone which had stood for many months. Each of these products exhibited characteristic x-ray diffraction patterns (Columns C, D and E, Table I). As far as could be determined by the diffraction patterns, these condensation products were not present in the dihydroxyacetone which had stood for thirty days. The latter was readily soluble in isopropanol, a further proof of the absence of the slightly soluble condensation products.

TABLE I

INTERPLANAR SPACINGS OF DIHYDROXYACETONE

Patterns were obtained by exposure of powdered crystalline material to the $K\alpha$ radiation of molybdenum. The interplanar spacings are reported in Ångström units. Intensity designations are: s, strong; m, medium; w, weak; v, very.

M. p., 72° (A)	M. p., 78-81° (B)	M. p., 130-133° (C)	M. p., 230-260° dec. (D)	M. p., 230-250° dec. (E)
5.5 m-s	6.8 w-m	6.4 w	6.3 w	5.10 vs
5.1 w	5.2 vs	5.1 vs	5.2 vs	4.25 m
4.6 m-s	4.6 vs	4.8 vs	4.8 vs	
4.3 m-s	4.2 m-s	4.3 vs	4.25 vs	
3.70 m	4.0 w	3.58 w	3.90 ?	
3.58 vw	3.65 w	3.25 w	3.55 w	
3.48 vw	3.32 vw	3.00 w	3.30 w	
3.30 vs	3.15 s	2.90 w	2.98 w	
3.18 w	2.98 w	2.75 w-m	2.76 w	

(4) Levene and Walti, *J. Biol. Chem.*, **78**, 23 (1928); Spoehr and Strain, *ibid.*, **89**, 507 (1930).

2.94 vw	2.90 w	2.57 w	2.57 w
2.75 w	2.75 w	2.47 w	2.48 ?
2.58 m-s	2.60 vw	2.30 w	2.12 w
2.42 m-s	2.48 w-m	2.12 w	1.90 w-m
2.28 m	2.40 w-m	2.01 w	1.80 w
2.17 m	2.30 m	1.91 m	
2.12 m	2.20 m	1.80 w	
2.05 vw	2.10 m	1.70 w	
1.96 vw	2.05 w		
1.87 vw	2.01 w		
1.78 w-m	1.96 w		
1.73 w	1.85 w		
	1.82 vw		
	1.75 m		
	1.68 vw		
	1.62 w		
	1.58 w		
	1.53 ?		
	1.40 ?		
	1.30 w		
	1.25 w		

Typical x-ray diffraction patterns for monomolecular, dimolecular and polymolecular dihydroxyacetone are shown in Fig. 1. The stronger lines which are given in the lists of Table I may be identified by their sequence in the respective patterns.

Summary

Crystalline monomolecular dihydroxyacetone rapidly polymerizes to dimolecular dihydroxyacetone.

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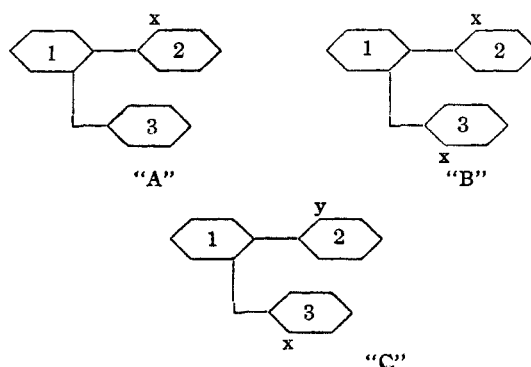
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Ortho Phenyl Biphenyls and "Synchronized Rotation"

By A. M. SADLER AND G. POWELL

"Synchronized rotation" has been suggested as a possible cause for the non-resolution of certain ortho substituted biphenyls.^{1,2} We have attempted to gain evidence concerning this postulated motion by a study of the substituted *o*-phenylbiphenyls. In this series any argument concerning the obstructive effect or shape of the substituent group is buttressed by the results already known in the simple biphenyl series from an examination in the same way. In addition, the

calculated amount of obstruction is very large. We have chosen the following types for study.



(1) Abstracted from a thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Columbia University, New York, N. Y., 1934.

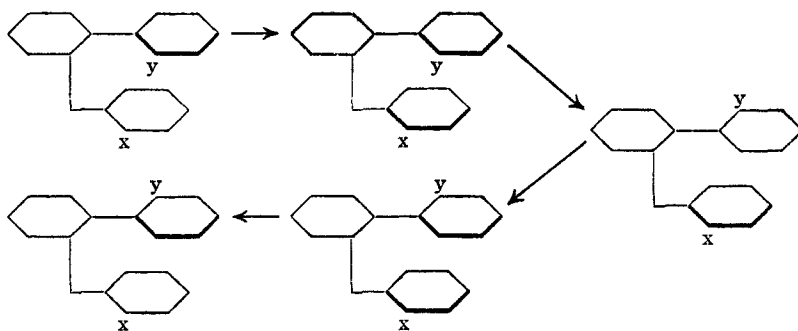
(2) Adams and Yuan, *Chem. Rev.*, **12**, 261 (1933); Maclean and Adams, *This Journal*, **55**, 4683 (1933).

Assuming no distortion of the valence bonds, these types show a minimum obstructive value of 0.43 Å. in the planar position, C-H distance being taken as 0.94 Å.³ Such a position can be considered impossible and indeed even some of the positions in which the phenyl groups (2 and 3) are perpendicular to each other would appear to be improbable. Thus when X or Y are groups comparable in size to the methyl group, the non-planar position in which X or Y is directed toward the perpendicular phenyl group would show an interference value of about 0.28 Å. when the benzene ring is treated as an hexagonal prism of uniform height 1.45 Å.

Compounds of type "A" and type "B" are analogous to certain compounds already described in the literature. Corbellini⁴ has described 2-dimethylhydroxymethyl-2'-carboxybiphenyl as giving mutarotating salts. Lesslie⁵ has described a biphenyl 2,2'-disulfonic acid which was resolved. Maclean² has described 3,3'-diaminodimesityl-methane which could not be resolved. In all these cases an interference value large enough to preclude existence in the planar form would be anticipated. It has been suggested² that the non-resolution of the last mentioned compound should be ascribable to synchronization of rotation of the phenyl groups or to distortion of the valence bonds. However, all these compounds, as well as compounds of type "A" and type "B," exhibit, in model, a certain non-planar position which has a plane of symmetry: a position involving no abnormal valence angles or interatomic distances. A model of type "A," for instance, has a plane of symmetry when the plane of group 3 is perpendicular to the plane of groups 1 and 2. Non-resolution of any such compounds could, conceivably, be due to the adoption of such a form by the molecule. Lesslie and Turner⁵ ascribe their successful resolution of the disulfonic acid to the "dynamic" effect of the sulfonic group in preventing the adoption of the symmetrical configuration. We have prepared a compound of type "A" (2-phenyl-6'-carboxybiphenyl) but so far have not succeeded in resolving it.

A compound of type "C" differs from the fore-

going compounds in that it possesses no mirror element of symmetry in any permissible position of no strain: inactivity in this type of molecule cannot, therefore, be ascribed to the adoption of any preferred non-planar form which is coincident with its mirror image. If the valence bonds are given their normal directions, and if the large interference value is sufficient to preclude the planar form, inactivity must be due to "synchronized rotation." We have prepared an example of type "C" (2-*o*-tolyl-6'-carboxybiphenyl). This, also, has not been resolved as yet. We propose to seek evidence concerning the direction of the valence bonds in this type of compound. In dealing with a model of type "C," the passage from a "d" to the "l" form can be demonstrated in the series of movements illustrated below.



Experimental

2-Phenyl-6'-carboxybiphenyl (Type A).—Ullmann condensations were done in a large test-tube, the contents being stirred with a thermometer. Eighty grams of 2-iododiphenyl was mixed with 133 g. of ethyl *o*-bromobenzoate in a metal bath kept at 270°. Seventy-five grams of copper bronze (Naturkupper C) was added rapidly with stirring. The temperature rose to 275°. An additional 50 g. of copper was added in the course of fifteen minutes. The cooled mixture was extracted with hot benzene, the solvent removed and the residue distilled. The fraction at 169–175° (1 mm.) was hydrolyzed with potassium hydroxide in 50% alcohol. The alcohol was evaporated and the residual water solution made acid with acetic acid. Ten grams of crude product was precipitated, leaving about 10 g. of diphenic acid in solution. The diphenic acid could be obtained, after filtration, by the addition of hydrochloric acid. The crude product was crystallized twice from 50% acetic acid, giving a pure product of m. p. 143–144.5°. The other by-product, 2,6'-diphenylbiphenyl boils at 193–195° (1 mm.), m. p. 117–119°, and could be obtained in the higher fractions of distillate. 2-Phenyl-6'-carboxybiphenyl is soluble in alcohol, acetone and petroleum ether.

Anal. Calcd.: C, 83.21; H, 5.14. Found: C, 83.10; H, 5.39.

The silver salt, on heating, gives a hydrocarbon of m. p.

(3) Stanley and Adams, *THIS JOURNAL*, **52**, 1200 (1930).

(4) Corbellini and Angeletti, *Atti. Accad. Lincei*, **18**, 968 (1932).

(5) Lesslie and Turner, *J. Chem. Soc.*, 1588 (1933).

56°, presumably *o*-phenylbiphenyl as described by Bachmann and Clarke.⁶ A strychnine salt was obtained from absolute alcohol, m. p. 215°. All fractions gave $[\alpha]_{D}^{25}$ -42 to -43° in chloroform.

Anal. Calcd. for $C_{10}H_{10}O_4N_2$: C, 77.63; H, 5.87. Found: C, 77.35; H, 5.96.

On decomposition of the salt the recovered acid gave no indications of activity.

A phenylethylamine salt was obtained from dilute alcohol, m. p. 115–116°, giving $[\alpha]_{D}^{25}$ -4.1° in alcohol for all crops. On decomposition of the salt, no evidence of activity of the free acid was obtained.

With brucine, morphine, cinchonine or quinine, in various solvents, no satisfactory results were obtained.

2-Nitro-6'-methylbiphenyl was obtained in 25% yield by the addition of a mixture of 125 g. of *o*-iodonitrobenzene and 100 g. of copper to 100 g. of *o*-iodotoluene in the course of one hour, bath temperature 220°. The bath was raised to 260° for half an hour more. Extraction and distillation gave 9 g. of b. p. 150–155° (2 mm.) and 14 g. of b. p. 155–175° (2 mm.). The second fraction was redistilled, and collected at 150–155° (2 mm.). The combined fractions at 150–155° were crystallized from absolute alcohol. The product has m. p. 64–65°, which is 7° higher than that reported for the same product by Mascarelli and Gatti.⁷

Anal. Calcd.: C, 73.40; H, 4.92. Found: C, 73.24; H, 5.16.

2,6'-Di-(*o*-tolyl)-biphenyl.—Eight grams of 2-iodo-6'-methylbiphenyl of m. p. 38–39° was heated to 265°. As before, 10 g. of copper was slowly added, the bath temperature being then raised to 285° for fifteen minutes. Extraction with ether and evaporation of the solvent gave a sticky solid. Washed with methyl alcohol, crystallized from methyl alcohol, the product gave m. p. 113–114°, yield 70%.

Anal. Calcd.: C, 93.36; H, 6.64. Found: C, 93.33; H, 6.81.

2-(*o*-Tolyl)-6'-carboxybiphenyl (Type C).—115 g. of 2-iodo-6'-methylbiphenyl, prepared by the method of Mascarelli and Gatti⁷ and 175 g. of ethyl *o*-bromobenzoate were mixed, the temperature of the bath being 275°, internal temperature 255°; 150 g. of copper was added slowly. The bath was raised to 290° for half an hour. Extraction with benzene and distillation gave a fraction of 35 cc. at 165–175° (1 mm.) from which a trace of the desired product could be obtained. The fraction 180–185° gave, on hydrolysis as before, removal of any hydrocarbons by extraction with ether, acidification with acetic acid, 6 g. of crude product. This was redissolved in ammonia and again precipitated with acetic acid after filtration. Crystallized twice from 50% acetic acid, 3 g. of product was obtained of m. p. 130.5–131.5°, soluble in alcohol, acetone and petroleum ether.

Anal. Calcd.: C, 83.33; H, 5.55. Found: C, 83.07; H, 5.34.

A strychnine salt could be obtained from absolute alcohol, shrinking at 85°, melting at 210°. All crops gave $[\alpha]_{D}^{25}$ -46.5° in chloroform.

(6) Bachmann and Clarke, *THIS JOURNAL*, **49**, 2089 (1927).

(7) Mascarelli and Gatti, *Atti Accad. Lincei*, **15**, 89 (1932).

Anal. Calcd. for $C_{14}H_{10}O_4N_2 \cdot C_2H_5OH$: C, 79.34; H, 6.9. Found: C, 79.27; H, 6.72.

On decomposition of the salt no evidence of activity could be obtained in the free acid.

A phenylethylamine salt from aqueous alcohol, m. p. 123–126°, gave crops all of $[\alpha]_{D}^{25}$ -3.5° in chloroform. On decomposition, no evidence of activity could be obtained in the free acid.

No results were obtained with brucine, cinchonine or morphine, in various solvents.

2-Methyl-6-nitrobiphenyl.—Fifty grams of 3-nitro-2-bromotoluene was mixed with 60 g. of iodobenzene. With bath temperature at 175°, 60 g. of copper was added in the course of half an hour. The bath temperature was then raised to 230° for half an hour more. Extraction with chloroform and distillation gave a fraction at 150–170° (3 mm.). Crystallized from absolute alcohol, the product gave b. p. 155° (3 mm.) and m. p. 105–106°; yield, 30%.

Anal. Calcd.: C, 73.24; H, 5.36. Found: C, 73.12; H, 5.33.

2-Methyl-6-aminobiphenyl.—Twenty grams of 2-methyl-6-nitrobiphenyl in 800 cc. of warm 95% alcohol were slowly added, with stirring, to 125 g. of stannous chloride dissolved in 100 cc. of concentrated hydrochloric acid at 40°. The alcohol was evaporated and the tin salt decomposed with excess of sodium hydroxide solution. The amine was extracted with chloroform and dried with sodium sulfate. Evaporation of the solvent gave an oil solidifying at m. p. 43–44°, b. p. 144–145° (2 mm.); yield, 70%.

Anal. Calcd. for hydrochloride: Cl, 16.17. Found: Cl, 16.16.

2-Methyl-6-iodobiphenyl.—From the amine, above, by the Sandmeyer reaction, b. p. 135° (1 mm.), crystallizing from petroleum ether, m. p. 29–30°.

Anal. Calcd.: I, 42.80. Found: I, 42.43.

2-Nitro-6'-carboxybiphenyl.—Twenty-three grams of ethyl *o*-bromobenzoate and 30 g. of *o*-iodonitrobenzene were mixed. With the bath at 250°, 30 g. of copper was added slowly, the internal temperature rising to 280°. The bath was kept at 285° for an additional half hour. Extraction with chloroform and distillation gave a fraction at 190–200° (4 mm.), which, on hydrolysis as before, and precipitation with acetic acid, gave 6 g. of a product of m. p. 165–166.5°.

Anal. Calcd.: C, 64.19; H, 3.74. Found: C, 64.27; H, 3.78.

2-Nitro-6-carboxybiphenyl.—Thirty grams of iodobenzene was placed in the test-tube, the bath temperature being 200°; 45 g. of methyl 3-nitro-2-bromobenzoate, intimately mixed with 50 g. of copper, was added slowly. The internal temperature rose to 225°. The bath was kept at 250° for an additional half hour. Extraction with benzene and distillation gave a fraction at 180–188° (3 mm.). This was hydrolyzed by refluxing with 70% sulfuric acid for half an hour. On cooling, needles came out; crystallized twice from 50% acetic acid, the product, in colorless needles, showed m. p. 187–188°.

Anal. Calcd.: C, 64.19; H, 3.74. Found: C, 64.38; H, 3.66.

Summary

Some *o*-phenylbiphenyls have been examined for optical activity; they have not been resolved. A

discussion of their suitability for an examination of the postulate of "synchronized rotation" is given.

NEW YORK, N. Y.

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[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

The Mechanism of Walden Inversion in Sugars: The Inversion of *p*-Toluenesulfonyl Esters of Rhamnose

BY IRVING E. MUSKAT¹

It has been observed that an inversion of the hydroxyl groups in the sugars may occur in the course of reactions in which there is the possibility of the formation of anhydro compounds as intermediates. Thus, Ohle and Vargha² obtained 5,6-anhydromonoacetone glucose on treating 6-*p*-toluenesulfonyl-monoacetone-glucose with sodium methylate. On hydrolyzing the anhydro compound they recovered about 50% of the expected monoacetone-glucose together with a mixture of products from which they isolated some monoacetone-*L*-idose—the inverted compound. From this they concluded that the ethylene oxide linkage could absorb not only in the *cis* position but also in the *trans* position, thus giving rise to a Walden inversion.

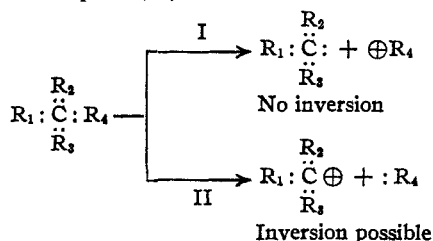
Fischer, Bergmann and Schotte³ showed that on treating 2-chloromethylmannoside (or glucoside?) with ammonia, an amino-sugar derivative was formed which they designated as "methyl-epiglucosamine." It was later shown⁴ that this "methyl-epiglucosamine" had the structure of 3-aminomethylaltroside and was formed through an intermediate anhydro compound. Bodycote, Haworth and Hirst⁵ adduced evidence to show also that 2-*p*-toluenesulfonyl- β -methylglucoside is converted by means of ammonia to the same "methyl-epiglucosamine"—the inverted product. Here again it was shown that an anhydro compound probably was formed as an intermediate, and the ethylene oxide linkage underwent scission in such a way as to give rise to an inverted product.

Mathers and Robertson⁶ studied the alkaline-hydrolysis of 2,3-di-*p*-toluenesulfonyl-4,6-dimethyl- α -methylglucopyranoside. They found that an

inversion had occurred during the hydrolysis but did not prove definitely the structures of their products.

In these investigations the sugar derivatives chosen permitted the formation of anhydro compounds and it was necessary to determine experimentally which carbon atom was involved in the inversion. On the other hand, in the research now reported it was possible to cause an inversion of the hydroxyl groups without the possibility of the intermediate formation of anhydro compounds. This greatly simplifies the problem and it should be possible to cause the inversion of any hydroxyl group the *p*-toluenesulfonyl ester of which can be prepared. Since the *p*-toluenesulfonyl esters of sugars are readily prepared, this procedure may lead to a simple method for the preparation of the rarer sugars, and their derivatives, from the more commonly occurring sugars.

It is logical to assume⁷ that a Walden inversion is most likely to occur in those reactions in which one of the groups attached to the asymmetric carbon atom is removable together with the bonding electron pair (II).⁸



It is not suggested that a Walden inversion will necessarily occur in all reactions of type (II), but

(7) F. C. Whitmore, *THIS JOURNAL*, **54**, 3436 (1932); Wallis, *ibid.*, **55**, 2598 (1933); *ibid.*, **56**, 491 (1934); see also A. R. Olson, *J. Chem. Phys.*, **1**, 418 (1933); Bergmann, Polyani and Szabo, *Z. physik. Chem.*, **B20**, 161 (1933).

(8) The plus and minus signs do not imply a complete transfer of an electron from one atom to another. They indicate merely a displacement of the electrons from their central positions. The circled plus and minus signs are being used to differentiate them from ionic charges.

(1) National Research Fellow in Chemistry.

(2) Ohle and Vargha, *Ber.*, **62**, 2435 (1929).

(3) Fischer, Bergmann and Schotte, *ibid.*, **53**, 509 (1920).

(4) Levene and Meyer, *J. Biol. Chem.*, **55**, 221 (1923); Freudenberg, Burkhart and Braun, *Ber.*, **59**, 714 (1926).

(5) Bodycote, Haworth and Hirst, *J. Chem. Soc.*, 151 (1934).

(6) Mathers and Robertson, *ibid.*, 1077 (1933).