butylene glycols herein presented is somewhat unique in that reactions involving extensive racemization, namely, esterification and pyrolysis, were employed and, furthermore, the sign of rotation always indicated which active form was present. The symmetry of the glycol molecule containing two asymmetric centers permits the existence of only two active forms, the D- and L-, and on removing one of these centers by dehydration (or deacetylation of the diacetate), the methylvinylcarbinol (or its acetate) so produced also exists in only two active forms, D- or L-. As pointed out above, the active methylvinylcarbinol (or its acetate) must have the same configuration as the active glycol from which it was prepared.

Summary

In studying the conversion of optically active 2,3-butylene glycols to butadiene, the intermediate methylvinylcarbinols were isolated, each exhibiting the same sign of rotation as the glycol from which it was prepared. Hydrogenation to methylethylcarbinol also proceeded without change in sign. Since the configuration of dextrorotatory methylethylcarbinol had already been related to that of dextrorotatory lactic acid, which belongs to the L-series, the configuration of the active 2,3-butylene glycols was, therefore, established as D-(−)- and L-(+)−.

PEORIA, ILLINOIS RECEIVED FEBRUARY 17, 1944

[CONTRIBUTION FROM THE RESEARCH DIVISION OF THE GENERAL PRINTING INK CORPORATION]

Orientation in the Biphenyl System. The Preparation of 2- and 4-Aminobiphenyl-4′-sulfonamides[1]

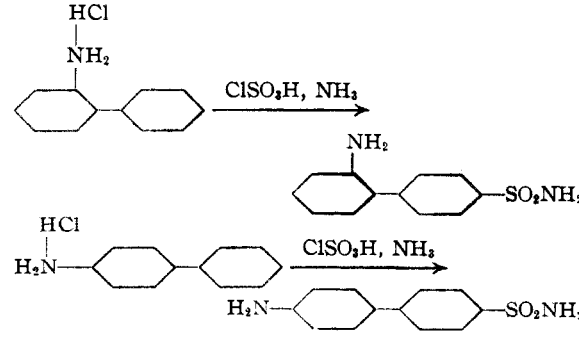
BY A. H. POPKIN AND G. B. MCVEA

Detailed studies[2] on orientation in the biphenyl system have been made in the past and several hypotheses have been proposed to explain the data obtained. These may be summarized as follows: (1) the usual directive influences ascribed to all simple groups when present in the benzene nucleus occur also in the biphenyl group; (2) those groups which normally orient ortho–para usually direct other groups into the same nucleus; conversely, meta-orienting groups direct further substitution into the adjacent ring; (3) the two nuclei of biphenyl act independently of each other.

Certain anomalous behaviors of the acetamido group which normally exhibits an ortho–para-orienting influence have been noted. The nitration of 2-acetamidobiphenyl[3] gave a 50% yield of 2-acetamido-4′-nitrobiphenyl instead of substitution into the five position of the same ring. Also the mononitration of diacetylbenzidine in concentrated sulfuric acid as solvent gave 2-nitrobenzidine instead of the expected 3-nitro-substitution.[4] More recently it was noted that the reaction of 2-acetamidobiphenyl with chlorosulfonic acid also gave substitution in the 4′-position.[5]

Bell[6] explained the anomalous behavior of the acetamido group stating that "this group enters into salt formation with a strong acid thereby being converted into a weakly orienting positive group so that further substitution naturally resembles that of 2-nitrodiphenyl."[7] This conclusion was substantiated by the work of Orton and Bradfield,[8] who showed that the velocity of chlorination of acetanilide was decreased with an increase of the concentration of hydrochloric acid which indicated a gradual shift of the acetamido group from ortho–para-orienting to a meta-orienting characteristic.

The present work confirms further the conclusions arrived at by Bell. The hydrochlorides of 2-aminobiphenyl and 4-aminobiphenyl were each treated with chlorosulfonic acid and ammonia. In each case, substitution was obtained in the 4′-position of the second ring, the products being 2-aminobiphenyl-4′-sulfonamide, 66% yield, and 4-aminobiphenyl-4′-sulfonamide, 88% yield.

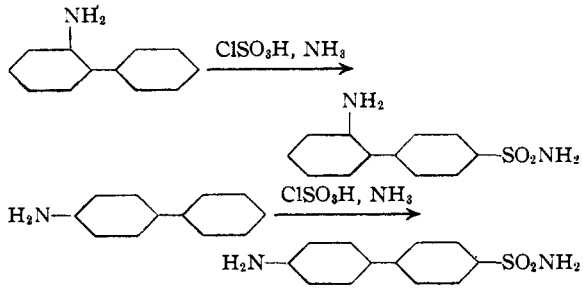


The purity of the materials isolated indicated strongly the absence of isomers which might arise from substitution in the five position of the first ring. This proves that the amino group, and by

(1) Presented before the Division of Organic Chemistry, Cleveland meeting of the American Chemical Society, April, 1944.
(2) *J. Chem. Soc.*, 1926–1931.
(3) Scarborough and Waters, *ibid.*, 89 (1927).
(4) Le Fèvre and Turner, *ibid.*, 2041 (1926).
(5) Popkin, THIS JOURNAL, **65**, 2043 (1943).
(6) Bell, *J. Chem. Soc.*, 2770 (1928).
(7) Dadwell and Kenner, *ibid.*, 1102 (1927); Le Fèvre and Turner, *ibid.*, 2043 (1926); Bell and Kenyon, *ibid.*, 2707 (1926).
(8) Orton and Bradfield, 986 (1927).

analogy the acetamido group, in combination with a mineral acid as a salt, exhibits a meta-orienting influence.

The reaction of 2-acetamidobiphenyl with chlorosulfonic acid to give 4'-substitution[5] suggested that the corresponding amino compound, being more basic, might react similarly and thereby make available a new and simplified preparation of the sulfonamide. This proved to be true. The reaction of 2-and 4-aminobiphenyls with chlorosulfonic acid and ammonia gave 2-aminobiphenyl-4'-sulfonamide, 55% yield, and 4-aminobiphenyl-4'-sulfonamide, 54% yield.



However, it was surprising to note that the unprotected amino compounds required a more vigorous treatment than either the corresponding acetamido compounds or the hydrochlorides. This was unexpected in the light of the established practice of protecting the amino groups for most substitution reactions.[9]

These reactions are now being applied to aniline, aniline hydrochloride and their various derivatives, and will be reported later.

Experimental

Preparation of 2- and 4-Aminobiphenyl Hydrochlorides.—A solution was made of 200 g. of the corresponding aminobiphenyl in three liters of benzene. Hydrogen chloride gas, generated by dropping concd. sulfuric acid into concd. hydrochloric acid, was bubbled into the solution. The colorless hydrochloride which formed was separated by suction filtration, washed with a liter of benzene and dried at 80°. In this manner, 2- and 4-aminobiphenyl hydrochlorides were prepared in 85–95% yields and substantially free of unconverted amine.

Reaction of 2-Aminobiphenyl Hydrochloride with Chlorosulfonic Acid and Ammonium Hydroxide.—Into a two-liter beaker was placed 1150 g. (650 cc., 9.86 moles) of chlorosulfonic acid. To this was added 410 g., 1.99 moles, of 2-aminobiphenyl hydrochloride during one hour and twenty minutes. The reaction temperature was kept below 10° during the addition. The resulting product was heated during three hours at 60° and then poured slowly and with agitation into 3200 cc. of concd. aqueous ammonium hydroxide. The temperature was kept at 8° during the latter addition. The precipitate was separated by suction filtration, the filter cake reslurried twice with two liters of water and then washed with distilled water until free of chloride and sulfate ions. The solid was dried at 55°; wt. 327 g., 66% yield; m. p. 178–182°. Solution in aqueous alkali and treatment with Norite gave purified 2-aminobiphenyl-4'-sulfonamide, m. p. 186–187°. A mixed m. p. with a sample of known material[5] showed no depression in the m. p.

(9) Smiles and Stewart, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1925, Vol. V, p. 3.

Reaction of 4-Aminobiphenyl Hydrochloride with Chlorosulfonic Acid and Ammonium Hydroxide.—This reaction was conducted in the manner just described using 50 g. of 4-aminobiphenyl hydrochloride. A crude product was obtained; wt. 53.7 g., 88% yield; m. p. 230–250°. Purification from methanol gave m. p. 248–250°. No depression in the melting point was obtained when this was mixed with a sample of known 4-aminobiphenyl-4'-sulfonamide.[10]

Reaction of 2-Aminobiphenyl with Chlorosulfonic Acid and Ammonium Hydroxide.—Into a 250-cc. beaker was placed 105 g. (60 cc., 0.9 mole) of chlorosulfonic acid. To this was added 32.3 g., 0.19 mole, of 2-aminobiphenyl (Monsanto Chemical Co.) during fifteen minutes. The reaction temperature was allowed to rise from 25° to 70° during the addition. The resulting product was heated during one and one-half hours at 90° and then poured slowly and with agitation into 300 cc. of concd. aqueous ammonium hydroxide. The temperature was kept below 20° during the latter addition. The precipitate was separated by suction filtration, the press cake reslurried twice with 50 cc. of water and then washed with distilled water until free of chloride and sulfate ions. The solid was dried at 80°; wt. 26.3 g., 55.4% yield; m. p. 176–182°. Crystallization from ethyl alcohol gave purified 2-aminobiphenyl-4'-sulfonamide, m. p. 186–187°. A mixed m. p. with a sample of known material[5] gave no depression in the m. p.

The above conditions were found to give the optimum yield of the sulfonamide. When 2-aminobiphenyl was heated with chlorosulfonic acid at 60° for three hours, unreacted 2-aminobiphenyl was obtained when the reaction product was poured into ammonium hydroxide. When 2-aminobiphenyl was heated with chlorosulfonic acid at 110° for one hour, only 9.3 g. of the sulfonamide was obtained. When heated for one hour at 100° and added to ammonium hydroxide at 25–50°, 8.2 g. of the sulfonamide resulted.

Reaction of 4-Aminobiphenyl with Chlorosulfonic Acid and Ammonium Hydroxide.—This reaction was conducted with the optimum conditions described above and starting with 129.2 g., 0.76 mole, of 4-aminobiphenyl (Monsanto Chemical Co.) and 420 g. (244 cc., 3.7 moles) of chlorosulfonic acid. A crude product was obtained; wt. 103.1 g., 54% yield, m. p. 233–250°. Purification gave m. p. 252–254°. No depression in the m. p. was obtained when this was mixed with a sample of known 4-aminobiphenyl-4'-sulfonamide.

Preparation of 4-Aminobiphenyl-4'-sulfonamide.—This was prepared from 4-acetamidobiphenyl without isolation of the intermediates 4-acetamidobiphenyl-4'-sulfonyl chloride and 4-acetamidobiphenyl-4'-sulfonamide. The reaction product of 4-acetamidobiphenyl and chlorosulfonic acid was poured upon ice water, the resulting solid treated with aqueous ammonium hydroxide and then with boiling hydrochloric acid. Crude 4-aminobiphenyl-4'-sulfonamide was obtained by treating the hydrochloride with ammonium hydroxide and purification effected by washing with boiling water and crystallization from ethyl alcohol; m. p. 255–256° with slight decomposition. Van Meter, Bianculli and Lowy[10] reported m. p. 261° with slight decomposition for a highly purified sample of the same compound.

Acknowledgment.—The authors are indebted to the General Printing Ink Corporation for permission to publish this work.

Summary

2- and 4-aminobiphenyl-4'-sulfonamides were prepared from 2- and 4-aminobiphenyls and their hydrochlorides by the action of chlorosulfonic acid and ammonia. This substantiates the hypothesis that the acetamido group in biphenyl exercises a meta-orienting influence in the presence

(10) Van Meter, Bianculli and Lowy, THIS JOURNAL, 62, 3146 (1940).

of a strong acid because of salt formation. The stability of the unprotected amines toward chlorosulfonic acid was unexpected.

NEW YORK, N. Y. RECEIVED FEBRUARY 7, 1944

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Dibenzofuran. XX. 2,3,7,8-Derivatives[1]

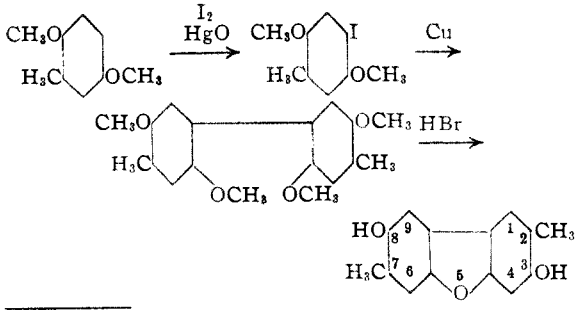
BY HENRY GILMAN, JACK SWISS, H. B. WILLIS AND F. A. YEOMAN

The present work is an extension of studies concerned with the bridging of the 1,9-positions. In an earlier paper,[2] the dibromination of 4,6-dimethoxydibenzofuran was reported. The structure of the resulting dibromo compound has not been definitely established, but it may possibly be 1,9-dibromo-4,6-dimethoxydibenzofuran.

We are now reporting the dibromination of 2,8-dimethoxydibenzofuran. From this reaction there resulted two isomeric dibromodimethoxydibenzofurans, one of m. p. 196–197°, and the other of m. p. 260–261°. The lower-melting isomer has been designated tentatively as 1,9-dibromo-2,8-dimethoxydibenzofuran, since it is known that 1-bromo-2-methoxydibenzofuran has a lower m. p. than the 3-bromo isomer.[3] However, it is possible that the spatial configuration of the dibenzofuran molecule is such that the 1- and 9-positions are in close proximity and simultaneous substitution of both positions by any large group or atom may, consequently, be very difficult. The 1,7-dibromo isomer is, therefore, a possibility not to be excluded from consideration.

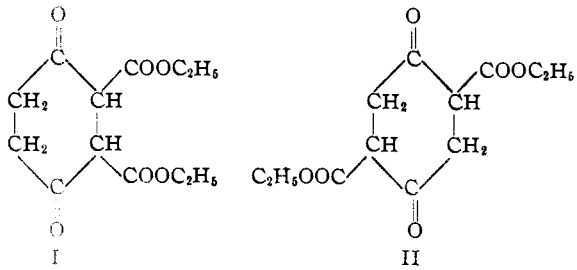
The higher-melting isomer is now shown to be 3,7-dibromo-2,8-dimethoxydibenzofuran. This structure was established by conversion to 3,7-dimethyl-2,8-dihydroxydibenzofuran and comparison of this compound with an authentic sample prepared by a synthesis involving ring closure.

The series of transformations resulting in the formation of 3,7-dimethyl-2,8-dihydroxydibenzofuran through ring closure is schematically represented below.



The iodination of toluhydroquinone dimethyl ether and the Ullmann coupling of the resulting iodo compound to give 2,2′,5,5′-tetramethoxy-4,4′-dimethylbiphenyl have been reported by Erdtman.[4] The same investigator also reported the nitration of toluhydroquinone dimethyl ether, but the position in which the substituent enters the ring does not appear to have been finally proved for either the iodination or the nitration.[5] If the iodine atom entered the ring in the position ortho to the methyl group, the product obtained from the above series of reactions would be 1,9-dimethyl-2,8-dihydroxydibenzofuran. Hence, it was necessary to establish definitely the position of iodination.

Nef[6] has reported the synthesis of 2,5-dimethoxyterephthalic acid and of its diethyl ester from ethyl succinylsuccinate. The latter compound was first prepared by Hermann[7] who believed it to have the structure (I) and oxidized it to the corresponding benzene derivative. Ebert, however, has shown that the symmetrical structure (II) is the correct one.[8]



I II

Accordingly, the iodination product of toluhydroquinone dimethyl ether was converted to 2,5-dimethoxyterephthalic acid by the following series of reactions.

The iodo compound was first converted to the corresponding nitrile by the method of Koelsch.[9]

(1) Paper XIX: Gilman, Swiss and Cheney, THIS JOURNAL, **62**, 1963 (1940). The present address of Jack Swiss is Research Laboratories, Westinghouse Electric and Manufacturing Co., East Pittsburgh, Pa., and that of H. B. Willis is Fine Chemicals Division, Gelatine Products Co., Detroit, Michigan.

(2) Gilman and Cheney, THIS JOURNAL, **61**, 3149 (1939).

(3) Gilman and P. R. Van Ess, *ibid.*, **61**, 1365 (1939).

(4) Erdtman, *Proc. Roy. Soc.* (London), **A143**, 191 (1933).

(5) In a private communication, Dr. Erdtman stated, "I don't think the structure of this compound (5-iodotoluhydroquinone dimethyl ether) has been rigorously proved, but it follows, I believe, conclusively from the analogous reactivity of toluquinol and hydroxyquinol." The present authors have been unable to find any record of an investigation of this type having been carried out on toluhydroquinone or hydroxyhydroquinone. We are grateful to Dr. Erdtman for a sample of the 5-iodotoluhydroquinone dimethyl ether prepared by him. The material proved identical with the iodination product prepared in this Laboratory.

(6) Nef, *Ann.*, **258**, 297 (1890).

(7) Hermann, *ibid.*, **211**, 306 (1882).

(8) Ebert, *ibid.*, **229**, 45 (1885).

(9) Koelsch, THIS JOURNAL, **58**, 1328 (1936).