acid, only unchanged starting material was obtained on chloroform extraction; recovery, 0.91 g. (91%), m.p. 72–75°, no depression when mixed with starting material.

4-Iodo-2,2,6,6-tetramethyltetrahydrothiapyran 1,1-Dioxide (XVII).—A solution of 1.30 g. of XIV in 13 ml. of 47% hydriodic acid was refluxed for four hours and was then evaporated almost to dryness on the steam-bath. The semi-crystalline residue was washed with dilute sodium bisulfite solution and with water, filtered, and dried to afford 1.11 g. (51%) of colorless crystals, m.p. 146–149° with previous sintering. On recrystallization from dilute aqueous acetic acid the pure product was obtained in the form of silky needles melting at 150–151°.

Anal. Calcd. for $C_9H_{17}IO_2S$: C, 34.18; H, 5.42. Found: C, 34.32; H, 5.30.

The same compound was obtained when a solution of 0.20 g. of XVI in 1.0 ml. of 47% hydriodic acid was refluxed for three hours. The crystalline precipitate which appeared on dilution with water was collected, washed with water and dried to yield 0.08 g. (52%) of crude product; m.p. 149–151° after recrystallization from aqueous acetic acid, no depression when mixed with the iodosulfone described above.

Ultraviolet Absorption Spectra.—The spectra were determined with a Beckman quartz spectrophotometer, model DU, using an approximately constant spectral band width of 1–2 mμ down to wave lengths in the neighborhood of 220 mμ. Readings at shorter wave lengths were obtained by using the 0.1 switch position and balancing the galvanometer for 100% transmission with the solvent in position before the phototube. Absolute ethanol was used as the solvent.

SWARTHMORE, PENNA. RECEIVED SEPTEMBER 22, 1950

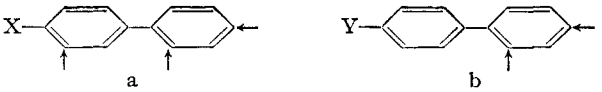
[CONTRIBUTION FROM THE MARION EDWARDS PARK LABORATORY OF BRYN MAWR COLLEGE]

The Dissociation Constants of Substituted 4-Biphenylcarboxylic Acids[1]

BY ERNST BERLINER AND ELIZABETH A. BLOMMERS

The dissociation constants of ten substituted 4-biphenylcarboxylic acids have been determined potentiometrically and compared with the dissociation constants of substituted benzoic acids. The dissociation constants fall on a line when plotted against Hammett's sigma values. The rho value is +0.37 (benzoic acids +1). These results show that the effect of substituents is transmitted through the biphenyl system, but that it is quantitatively less than in benzoic acids.

The problem of the conjugation of the two benzene rings in biphenyl in chemical reactions was last summarized in 1928 by Le Fevre and Turner who concluded that the two rings in biphenyl act independently.[2] This conclusion was drawn almost exclusively from the orientation characteristics of substituted biphenyls in electrophilic substitution. An activating group in one of the rings directs an electrophilic reagent into the ortho–para positions of the second ring (Fig. 1a),[3] but a meta directing substituent also directs the entering group into the ortho and para positions of the other ring (Fig. 1b). 4′-Nitrobiphenyl on nitration produces 37% of 2,4′- and 63% of 4,4′-dinitrobiphenyl.[4] Similar results are obtained if the nitro group is in position 2′ or 3′, or if two nitro groups, or other meta directing groups, are present in one of the rings.[5] The supposition that the two rings act independently in substitution reactions is therefore amply documented experimentally as far as the *direction* of electrophilic substitution is concerned, and the rule that one phenyl group is ortho–para directing irrespective of its substituent appears to be a valid one. This rule has also been invoked in one case of nucleophilic displacement, where a 4′-nitro group was found not to activate a bromine atom in the 4-position.[6] It would appear then that the resonance structures which are responsible for meta substitution in nitrobenzene cannot be extended across the bond joining the two benzene rings and into the second ring.



(X, ortho–para directing) (Y, meta directing)

Fig. 1.

There is, on the other hand, a wealth of data on physical and physico–chemical measurements which can best be explained on the basis of resonance interaction of the two benzene rings in biphenyl. Indeed, on the basis of dipole measurements Le Fevre concluded in 1936 that "the lack of conjugation is not as complete as previously stated."[7] Thermochemical data (and from them the derived resonance energies).[8] X-ray measurements,[9] quantum-mechanical calculations,[10] the inferences drawn from the existence of diradicals[11] and particularly the measurements of absorption spectra[12] indicate

(1) Taken from a dissertation submitted by Miss E. A. Blommers to the Graduate School of Bryn Mawr College in partial fulfillment of the requirements for the Ph.D. degree.

(2) (a) R. J. W. Le Fevre and E. E. Turner, *J. Chem. Soc.*, 245 (1928); (b) D. Vorländer, *Ber.*, **58**, 1893 (1925). For a discussion of the problem see also: (c) G. N. Burckhardt, C. Horrex and D. I. Jenkins, *J. Chem. Soc.*, 1654 (1936); (d) A. E. Gillem and D. A. Hey, *ibid.*, 1170 (1939).

(3) For instance: (a) F. Bell and J. Kenyon, *ibid.*, 3044 (1926); F. Bell, J. Kenyon and P. H. Robinson, *ibid.*, 1242 (1926); 1127 (1927); J. Kenyon and P. H. Robinson, *ibid.*, 3050 (1926); (b) H. A. Scarborough and W. A. Waters, *ibid.*, 557 (1926); 89, 1133 (1927); (c) W. S. M. Grieve and D. H. Hey, *ibid.*, 2245 (1932).

(4) H. C. Gull and E. E. Turner, *ibid.*, 491 (1929).

(5) Ref. 2b; F. Bell and J. Kenyon, *J. Chem. Soc.*, 2705 (1926); W. Blakely and H. A. Scarborough, *ibid.*, 3000 (1927); W. S. M. Grieve and D. A. Hey, *ibid.*, 970 (1933); A. H. Popkin and G. B. McVea, THIS JOURNAL, **66**, 796 (1944).

(6) N. Campbell, W. Anderson and J. Gilmore, *J. Chem. Soc.*, 446 (1940). See also H. Burton and J. Kenner, *ibid.*, **121**, 489 (1922). A case where such activation does occur has now been observed. Unpublished results with Miss T. Riaboff.

(7) R. J. W. Le Fevre and C. G. Le Fevre, *ibid.*, 1130 (1936).

(8) (a) G. W. Wheland, "The Theory of Resonance and Its Application to Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 69 ff.; (b) L. Pauling and J. Sherman, *J. Chem. Phys.*, **1**, 606, 676 (1933); (c) M. Szwarc, *Nature*, **161**, 890 (1948).

(9) J. Dhar, *Indian J. Phys.*, **7**, 43 (1932); *Proc. Natl. Inst. Sci. India*, **15**, 11 (1949) (*C. A.*, **43**, 4655 (1949)); ref. 8a, p. 108.

(10) Ref. 8a, p. 81; ref. 8b; J. E. Lennard-Jones and J. Turkevich, *Proc. Roy. Soc. (London)*, **A158**, 297 (1937); Y. K. Syrkin and M. Dyatkina, *Acta Physicochem. U. R. S. S.*, **21**, 641 (1946); C. A. Coulson and J. Jacobs, *J. Chem. Soc.*, 2805 (1949); E. Hückel, *Z. Elektrochem.*, **43**, 752 (1937).

(11) Ref. 8a, p. 203.

(12) L. W. Pickett, G. F. Walter and H. France, THIS JOURNAL, **58**, 2296 (1936); R. N. Jones, *ibid.*, **63**, 1658 (1941); B. Williamson and W. H. Rodebush, *ibid.*, **63**, 3018 (1941). Also ref. 2d.

conjugation across the joining bond in biphenyl. The question of the shortening of this bond is one that cannot be considered settled, X-ray and electron diffraction data giving different results.[13]

In considering this conflicting evidence it has to be recognized that the *direction* of substitution is only one aspect of the reactivity of aromatic compounds and only one way of showing the transmission of the effect of substituents through the aromatic system. The "independence" of the two nuclei may only be a characteristic of the directive influence of substituents in electrophilic substitution. Other types of reactions may confirm the existence of an interaction as evidenced by the physical data. The dissociation of properly substituted biphenylcarboxylic acids is such a reaction, particularly since the results can be viewed in the light of Hammett's equation.[14] In this way, not only can one obtain a qualitative picture as to whether or not interaction occurs, but also a quantitative estimation of the extent of transmission as compared to other systems such as, for instance, benzoic acids.

The relative dissociation constants of ten biphenylcarboxylic acids of the type shown in Fig. 2 were determined potentiometrically in 50% (by

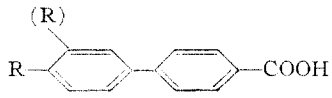


Fig. 2.

volume) aqueous butyl cellosolve. This solvent was chosen because of the low solubility of some of the acids. For purposes of comparison the dissociation constants of six benzoic acids were also determined in the same solvent. The solvent was 0.05 *M* in lithium chloride. Since no corrections were made for activities, the experimental figures are not the true dissociation constants. The results are listed in Tables I and II. The *pK*'s in the biphenyl series represent the average of at least three determinations. The average deviation of all data is 0.008 in the biphenyl series and 0.005 in the benzene series. Some of the results were checked after more than half a year with completely new solutions and standards.

TABLE I

APPARENT DISSOCIATION CONSTANTS OF SUBSTITUTED BIPHENYLCARBOXYLIC ACIDS IN 50% (BY VOLUME) AQUEOUS BUTYL CELLOSOLVE

Substituent	pK_{25}	n^a	Mean dev.
p-NO_2	5.25	4	0.007
m-NO_2	5.35	3	.013
p-Br	5.47	3	.010
m-Br	5.49	3	.003
p-Cl	5.47	4	.005
p-H	5.66	5	.012
p-CH_3	5.69	3	.003
p-OCH_3	5.75	3	.007
p-OH[b]	5.92	3	.003
p-NH_2	6.00	3	.017

[a] *n* denotes number of determinations. [b] Sigma value calculated for *p*-OH group is −0.53.

(13) I. L. Karle and L. O. Brockway, THIS JOURNAL, **66**, 1974 (1944).

(14) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, Inc., New York and London, 1940, Chapter VII.

TABLE II

APPARENT DISSOCIATION CONSTANTS OF SUBSTITUTED BENZOIC ACIDS IN 50% (BY VOLUME) AQUEOUS BUTYL CELLOSOLVE

Substituent	pK_{25}	n^a	Mean dev.
p-NO_2	4.44	2	0.005
m-NO_2	4.75	2	.005
p-Cl	5.24	3	.000
p-Br	5.24	2	.010
p-H	5.65	3	.010
p-OCH_3	5.99	2	.000

[a] *n* denotes number of determinations.

Sigma Values.—Figure 3 shows a plot of the *pK*'s of the biphenyl carboxylic acids (and benzoic acids) against Hammett's sigma values. The points are seen to follow a linear relationship. The median deviation of the sigma values from the least square line is 0.08.

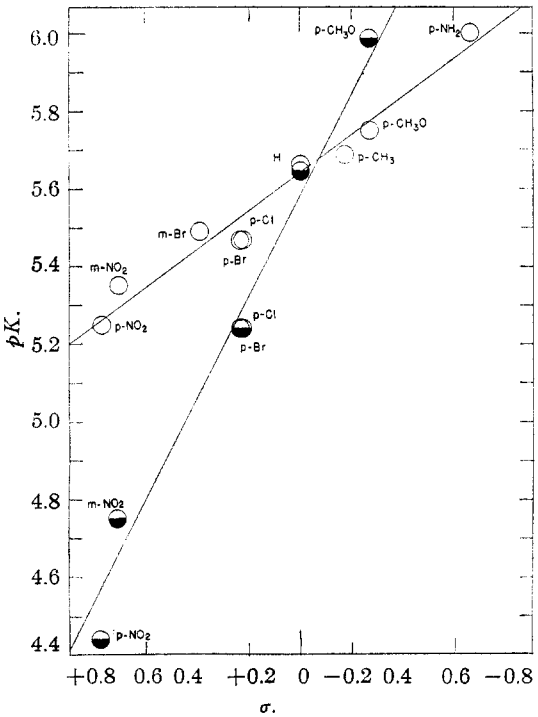


Fig. 3.—Plot of *pK* values against Hammett's σ values: O, biphenylcarboxylic acids; ◒, benzoic acids.

It can be concluded that the different substituents in biphenyl influence the dissociation constants in a predictable manner, *i.e.*, a methoxy group in one ring increases the electron density on the carboxyl group in the other ring and thereby raises the *pK*, while a nitro group withdraws electrons and has the opposite effect on the *pK*.

The Rho Value.—The rho value, which is a measure of the extent to which an electronic effect is transmitted through the aromatic system, has the magnitude +0.49 for the biphenylcarboxylic acids, with a median deviation of 0.03. The rho value for benzoic acids in the same medium is +1.32, with a median deviation of 0.06. This rho value for the benzoic acids is close to the value obtained for the dissociation constants of benzoic

acids in 50% ethanol.[15] The rho value for the dissociation constants of biphenylcarboxylic acids is considerably less than that of the benzoic acids. Compared to rho = 1 (benzoic acids in water), rho for the biphenyl acids is +0.37. The linear relationship does not necessarily imply a resonance interaction between the two rings. The sigma values are empirical numbers into which both electrostatic and resonance effects enter. The same combination of effects that determines the strength of substituted benzoic acids must also be responsible for the variations in the strength of the biphenylcarboxylic acids, at least as far as the ring carrying the substituent is concerned. The effects brought about by substituents in one ring could be transmitted into the other ring by an electrostatic effect (Fig. 4a), rather than by resonance (Fig. 4b), just as is probably the case with phenylpropionic acids. It is likely that in the presence of a perfectly

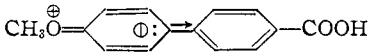


Fig. 4a.

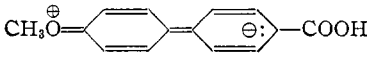


Fig. 4b.

reasonable resonating system, such as the second ring, such an effect would be transmitted through resonance rather than through induction. But the important point is that the electronic effect of groups *is* transmitted and that the two phenyl groups are therefore *not* isolated in the sense in which they appear to be on the basis of the orientation data. The linear relationship *per se* only means that the substituents in one ring of biphenyl influence the dissociation constants of the carboxyl group in the other ring qualitatively in the same way in which the same substituents affect the dissociation constants of benzoic acids. However, only a fraction of the effect, *i.e.*, one-third, operative in the benzoic acids is transmitted through the biphenyl system. It appears then that the benzene ring is a much better conductor than the biphenyl system as far as electronic effects are concerned. The power of transmission in biphenyl is less than in phenylacetic acids (rho, +0.471) and also less than in cinnamic acids (rho, +0.466), but somewhat greater than in phenylpropionic acids (rho, +0.212).[14] The greater rho value of the cinnamic acids is perhaps due to the greater polarizability of the double bond as compared to a benzene ring, but the generally rather low value of rho for the biphenyl acids may in part be connected with the necessity for coplanarity, or near coplanarity, of the benzene rings for conjugation to occur and to be most effective. The data on the dissociation constants of certain aminobiphenyls with and without restricted rotation around the pivot point toward such a requirement and have been interpreted as indicating blocking of resonance through non-coplanarity. They are a further indication of the transmission of the effects of substituents across the biphenyl system.[16] The large distance of the substituent from the reacting center will lower the effectiveness of transmission of any inductive influences.

It thus appears very likely that substituents in one ring in biphenyl will relay their effects into the other ring, but still, the same substituent will not cause meta *orientation* (if electron attracting) in direct electrophilic substitution. This can be explained by considering the stabilization of the transition state in aromatic substitution. If substitution should occur meta, resonance with the second ring is not possible. If the substitution is ortho–para to the second ring, the transition state resonance includes both rings and the positive charge in electrophilic substitution is spread over a much wider area (Fig. 5). The explanation is similar to that given for the substitution characteristics

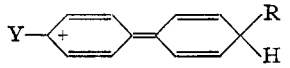


Fig. 5.

of cinnamic acids, ω-nitrostyrene, etc., which are all ortho–para directing.[17] From the experimental data one would have to conclude that the resonance stabilization of the transition state is a more important factor than the unfavorable charge distribution created in the second ring by the nitro or other deactivating group. The nitro group, although it cannot prevent ortho–para substitution, should hinder the reaction despite the ortho–para orientation, and the only available kinetic evidence shows that nitrobiphenyl is brominated 1/500 as rapidly as biphenyl itself.[18] In view of the low rho value both activation and deactivation of the second ring must be expected to be less than in benzene. It is presumably for that reason that 4-dimethylaminobiphenyl fails to couple with diazotized aniline in the 4′-position,[2b] does not react with benzaldehyde[19] and is not nitrosated in the unsubstituted ring. All of these reactions proceed readily with dimethylaniline. On the other hand, Friedel and Crafts reactions can be carried out on nitrobiphenyl,[20] but fail with nitrobenzene.

Experimental[21]

Syntheses and Purifications of Acids.—Except in two instances, the biphenylcarboxylic acids were prepared through oxidation of the corresponding methyl ketones. The benzoic acids were best commercial samples, recrystallized.

***p*-Phenylbenzoic Acid.**—*p*-Phenylacetophenone[22,23] was oxidized with sodium hypochlorite to *p*-phenylbenzoic acid according to directions given for the preparation of β-

(15) J. D. Roberts, E. A. McElhill and R. Armstrong, THIS JOURNAL, **71**, 2923 (1949).

(16) D. W. Sherwood and M. Calvin, *ibid.*, **64**, 1350 (1942); L. W. Pickett, M. Groth, S. Duckworth and J. Cunliffe, *ibid.*, **72**, 44 (1950); see also R. Kuhn and F. Zumstein, *Ber.*, **59**, 488 (1926).

(17) F. G. Bordwell and K. Rhode, THIS JOURNAL, **70**, 1191 (1948); C. K. Ingold and F. R. Shaw, *J. Chem. Soc.*, 575 (1949); Ref. 8a, p. 266: F. Seel, *Angew. Chem.*, **61**, 89 (1949). See R. Robinson and A. Zaki, *J. Chem. Soc.*, 2485 (1927), for an earlier but similar explanation.

(18) I. Hartman and P. W. Robinson, *ibid.*, 891 (1945); see also E. E. Turner, *Rec. trav. chim.*, **48**, 821 (1929).

(19) A. G. Banus and J. F. Thomas, *Anal. Fis. Quim.*, **19**, 293 (1921) [*Chem. Zentr.*, **94**, III, 1220 (1923)]. See also F. Bell, J. Kenyon and P. H. Robinson, *J. Chem. Soc.*, 1239 (1926), for the failure of derivatives of aminobiphenyl to undergo the usual migration reactions from side chain to (second) nucleus.

(20) W. S. M. Grieve and D. H. Hey, ref. 5. See also Experimental part of this paper.

(21) All melting points corrected unless otherwise stated.

(22) L. M. Long and H. R. Henze, THIS JOURNAL, **63**, 1939 (1941).

(23) We are indebted to Dr. D. T. Mowry of the Monsanto Chemical Company, Dayton, Ohio, for generous samples of *p*-acetyldiphenyl and *p*-chlorodiphenyl.

naphthoic acid.[24] White needle-like crystals[25] of *p*-phenylbenzoic acid separated from ethanol, m.p. 224.7–225.8° (lit. 222, 224 and 228°).

4-Methoxy-4′-acetobiphenyl.[26]—The crude ketone was crystallized from methanol–benzene instead of isopropyl alcohol; white plates, m.p. 154.6–155.5° (lit. 153–154°).

4-Methoxybiphenyl-4′-carboxylic Acid.[26]—The crude product was crystallized from glacial acetic acid until shiny, white plates were obtained, m.p. 245–247° (uncor.) (lit. 247–248°).

4-Hydroxybiphenyl-4′-carboxylic Acid.[27]—The acid, purified through its methyl ester (m.p. 227.4–228.8°), separated from peroxide-free dioxane and cyclohexane as shining white needles,[25] m.p. 295.2–297.2°[28] (lit. 293–294°).

4-Bromobiphenyl-4′-carboxylic Acid.—4-Bromo-4′-acetobiphenyl[29a] was oxidized to 4-bromobiphenyl-4′-carboxylic acid by the procedure utilized in the preparation of 4-methoxybiphenyl-4′-carboxylic acid.[26] The acid, purified through its methyl ester (m.p. 144.5–145.5°) (lit. 130–131°[29b]), separated from glacial acetic acid as a white powder,[25] m.p. 303.2–305.5°[28] (lit. 303–305°).[30]

4-Chlorobiphenyl-4′-carboxylic Acid.[23]—4-Chloro-4′-acetobiphenyl[31] was oxidized to 4-chlorobiphenyl-4′-carboxylic acid by the sodium hypobromite method.[26] The crude acid was crystallized from glacial acetic acid until white snow-flake crystals[25] were obtained, m.p. 289.8–290.8°[28] (lit. 290–293°).[30]

4-Nitrobiphenyl-4′-carboxylic Acid.—4-Nitro-4′-acetobiphenyl, prepared by the method of Grieve and Hey,[5] was oxidized with sodium hypobromite to 4-nitrobiphenyl-4′-carboxylic acid. The acid, purified through its ethyl ester (m.p. 110–115.5° even after repeated crystallizations from ligroin and absolute ethanol; on retake 112.2–112.5°; lit 112°), separated from preheated glacial acetic acid as a pale yellow powder,[25] m.p. 336.2–339.2°[28] (lit. 336–338°).

4-Aminobiphenyl-4′-carboxylic acid was prepared essentially by the method utilized in the preparation of *p*-aminophenylacetic acid.[32,33] After precipitation by glacial acetic acid, 4-aminobiphenyl-4′-carboxylic acid (95% yield) was crystallized twice from ethanol and then swirled four separate times with carbon disulfide (to remove sulfur). The residue, crystallized repeatedly from ethanol, afforded yellowish-orange granules, m.p. 227–236° (uncor.) (lit. 239°).[30] The melt solidified at 245° and this may be the reason for the wide range in melting point.

4-Methylbiphenyl-4′-carboxylic acid[34] separated as a white powder[25] from glacial acetic acid, m.p. 243–245°[28] (uncor.) (lit. 245°).[35]

3-Bromo-4′-acetobiphenyl.—To a solution of 8.1 g. of practical acetyl chloride and 14 g. (0.06 mole) of 3-bromobiphenyl[36,37] in 60 ml. of carbon disulfide in a three-necked round-bottom flask, equipped with a mercury sealed stirrer and condenser, was added 10.2 g. of aluminum chloride. Stirring was continued for ten minutes after the addition was complete. The mixture was refluxed for one-half hour longer and then allowed to stand overnight. The red addition complex was decomposed in the usual way, and the residue was taken up in ether. The ether extract was dried and the ether removed. The ketone was extracted from the liquid residue by heating the residue with 30–40° petroleum ether and decanting the petroleum ether solution from the undissolved oil. After the extraction process had been carried out several times, the extract was concentrated until a few oil droplets appeared. The solution was then decanted and concentrated again until it became milky. Refrigeration of this mixture brought about crystallization. From seven extractions of the initial liquid residue white plates totaling 8 g. (50% yield) were obtained, m.p. 37–41°. Recrystallization afforded white needles, m.p. 40.3–40.9°.

Anal. Calcd. for $C_{14}H_{11}OBr$: C, 61.11; H, 4.03. Found: C, 61.22; H, 4.20.

The 2,4-dinitrophenylhydrazone of 3-bromo-4′-acetobiphenyl, prepared by standard procedure,[38] formed tiny red plates from a mixture of alcohol and chloroform, m.p. 234.7–236.5°.

Anal. Calcd. for $C_{20}H_{15}O_4BrN_4$: C, 52.76; H, 3.32. Found: C, 53.06; H, 3.58.

3-Bromobiphenyl-4′-carboxylic acid was obtained through oxidation with sodium hypobromite of 3-bromo-4′-acetobiphenyl. Repeated crystallization from glacial acetic acid afforded shining, practically white plates,[25] m.p. 252.9–254.4°.[28]

Anal. Calcd. for $C_{13}H_9O_2Br$: C, 56.34; H, 3.27. Found: C, 56.06; H, 3.52.

The ethyl ester of 3-bromobiphenyl-4′-carboxylic acid forms white sheaths from 30–40° petroleum ether, m.p. 69.3–70.1°.

Anal. Calcd. for $C_{15}H_{13}O_2Br$: C, 59.03; H, 4.29. Found: C, 59.28; H, 4.41.

3-Nitro-4′-acetobiphenyl.—To a solution of 24 g. of aluminum chloride and 6 g. (0.03 mole) of 3-nitrobiphenyl[39] in 90 ml. of carbon disulfide was gradually added 7.2 g. of acetyl chloride. The red solution was heated at reflux for 12 hours and allowed to stand for 12 hours more. The reaction product (56% yield) formed yellow needles after several crystallizations from ethanol, m.p. 109.0–110.0°.

Anal. Calcd. for $C_{14}H_{11}O_3N$: C, 69.70; H, 4.60. Found: C, 69.86; H, 4.90.

The 2,4-dinitrophenylhydrazone of 3-nitro-4′-acetobiphenyl separated as red prisms from ethanol–chloroform, m.p. 234.7–236.3°.

Anal. Calcd. for $C_{20}H_{15}O_6N_5$: C, 57.01; H, 3.59. Found: C, 56.89; H, 3.72.

3-Nitrobiphenyl-4′-carboxylic acid was prepared from 3-nitro-4′-acetobiphenyl by the bromoform reaction. Recrystallization from glacial acetic acid afforded practically white plates,[25] m.p. 313–315.1°[28] (lit. 301°).[40] Without correction the melting point is 302.5–304.6°, and presumably this acid is identical with the acid isolated by Hey and Walker. The ethyl ester of 3-nitrobiphenyl-4′-carboxylic acid formed white needles from ethanol, m.p. 113.7–114.4°.

Anal. Calcd. for $C_{15}H_{13}O_4N$: C, 66.41; H, 4.83. Found: C, 66.26; H, 4.98.

Proof of Structure of 3-Nitrobiphenyl-4′-carboxylic Acid and 3-Bromobiphenyl-4′-carboxylic Acid.—3-Nitro-4′-acetobiphenyl was reduced to 3-amino-4′-acetobiphenyl. The amine was then divided into two parts: one part was converted into 3-bromo-4′-acetobiphenyl and the other was deaminated to *p*-phenylacetophenone. The Friedel and Crafts acetylations of 3-nitrobiphenyl and 3-bromobiphenyl resulted, therefore, in substitution para to a phenyl ring. Since the nitro group is a strong deactivating group as well as a meta directing group, it is assumed that substitution occurred in both cases in the 4′-positions. The 4-position is not impossible, but highly improbable.

Reduction of 3-Nitro-4′-acetobiphenyl.—The reduction was carried out with tin and concentrated hydrochloric acid, with ethanol as a solvent. The amine was recovered through

(24) M. S. Newman and H. L. Holmes, "Organic Syntheses," Coll. Vol. II, 1943, p. 428.

(25) Dried in an oven at 50°.

(26) W. S. Johnson, C. D. Gutsche and R. D. Offenhauer, THIS JOURNAL, **68**, 1648 (1946).

(27) L. F. Fieser and C. K. Bradsher, THIS JOURNAL, **58**, 1738 (1936).

(28) In a copper block.

(29) (a) B. R. Carpenter and E. E. Turner, *J. Chem. Soc.*, 869 (1934); (b) H. Gilman, W. Langham and F. W. Moore, THIS JOURNAL, **62**, 2327 (1940).

(30) I. G. Farben, French Patent, 735,846 [*Chem. Zentr.*, **104**, I, 1999 (1933)].

(31) D. T. Mowry, M. Renoll and W. F. Huber, THIS JOURNAL, **68**, 1105 (1946).

(32) G. R. Robertson, "Org. Syntheses," Coll. Vol. I, 52 (1943).

(33) We are indebted to Dr. H. E. Schroeder of E. I. du Pont de Nemours and Co., Wilmington, Delaware for generous samples of 4-biphenylcarboxylic acid and 4-nitrobiphenyl-4′-carboxylic acid.

(34) Prepared by Miss Liang Huang.

(35) T. Carnelley, *J. Chem. Soc.*, **32**, 654 (1877).

(36) W. F. Huber, M. Renoll, A. G. Rossow and D. T. Mowry, THIS JOURNAL, **68**, 1109 (1946).

(37) An 83% yield of 3-bromobiphenyl was obtained by deamination of 2-amino-5-bromobiphenyl by hypophosphorous acid. See N. Kornblum in "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 295.

(38) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1940, p. 143.

(39) J. Elks, J. W. Haworth and D. H. Hey, *J. Chem. Soc.*, 1284 (1940).

(40) D. H. Hey and E. W. Walker, *ibid.*, 2219 (1948).

neutralization of the acid solution and crystallized from ethanol. Yellow plates of 3-amino-4'-acetobiphenyl separated, m.p. 154–159° (uncor.). Repeated crystallizations gave a m.p. of 147.4–150.5°.

Anal. Calcd. for $C_{14}H_{13}ON$: C, 79.59; H, 6.20. Found: C, 79.63; H, 6.50.

Preparation of 3-Bromo-4'-acetobiphenyl.—The procedure followed was that for the preparation of *o*-chlorobromobenzene from *o*-chloroaniline.[41] White needles formed from 30–40° petroleum ether, m.p. 39–40°. Mixed with 3-bromo-4'-acetobiphenyl (m.p. 40–41.2°) prepared from acetyl chloride and 3-bromobiphenyl, it melted at 39–40.9°.

Deamination of 3-Amino-4'-acetobiphenyl.—The procedure was the same as that used to deaminate 2-amino-5-bromobiphenyl.[37] The crude product was crystallized from alcohol and then 60–70° ligroin; white needles separated, m.p. 120–121°. A mixed melting point with *p*-phenylacetophenone (crystallized from ligroin, m.p. 121.0–121.6°) melted at 120.5–121.5°.

Measurements.—A quarter-millimole sample of acid (a tenth-millimole sample in the cases of the nitrobiphenylcarboxylic acids) was weighed into a 250-ml. beaker and dissolved in 50 ml. of purified butyl cellosolve,[42] b.p. 166.8–167.2° (uncor.) at 750 mm. Fifty milliliters of a 0.1 *M* aqueous solution of lithium chloride (anhydrous Merck and Co., Inc., Reagent) was then stirred into the cellosolve so that a 50% (by volume) aqueous butyl cellosolve solution (μ = 0.05) was obtained. The lithium chloride was added to the acid solutions to increase the dielectric constant of the medium as well as to decrease any error arising from small changes in ionic strength.[43]

The 0.05 *N* carbonate-free sodium hydroxide used in the titrations was made up in the following way. One hundred milliliters of standard, approximately 0.1 *N* carbonate-free sodium hydroxide was run as quickly as possible into a brown bottle containing 100 ml. of carbonate-free butyl cellosolve. The usual siphon connections were then made to a 5-ml. buret, graduated in 0.01 ml., and the solution was well mixed.[44] The exact normality of the solution did not need to be known since the half-neutralization point of all titrations was determined from the end-point of the titration, not from the amount of acid weighed out.

The apparatus used in the potentiometric titrations consisted of a Leeds and Northrup glass electrode, calomel electrode, Type K potentiometer, 2420-c galvanometer and a Westinghouse thermionic amplifier. The sensitivity of the galvanometer (0.001 volt) limited *p*H readings to ±0.01 unit. The asymmetry correction of the glass electrode was determined with a biphthalate buffer (*p*H 4.008), an acetate buffer (*p*H 4.648) and a phosphate buffer (*p*H 6.857).[45] A manually operated thermostat maintained the temperature of the acid solution at 25 ± 0.5°.

E.m.f. measurements were made at various intervals during a titration, but in the half-neutralization range e.m.f. determinations were made after each 0.1 ml. of base added, while near the equivalence point measurements were taken after each 0.05 ml. of base added. For acids weaker than benzoic acid a stream of nitrogen was blown over the surface of the solutions throughout the final part of the titration. The end-point was reached when ΔE for each 0.05 ml. of base passed through a maximum. The *p*H at half-neutralization was then obtained graphically. The relationship between e.m.f. measurements and *p*H values found to hold for aqueous solutions was assumed to hold for 50% (by volume) aqueous butyl cellosolve solutions.

The *pK* values reported are the *p*H measurements at half-neutralization,[46] and, therefore, are of significance only in a relative sense. Representative results for two acids follow: 4-nitrobiphenyl-4'-carboxylic acid, *pK* = 5.25, 5.24, 5.26, 5.26; 4-methylbiphenyl-4'-carboxylic acid, 5.69, 5.69, 5.70.

Acknowledgment.—We gratefully acknowledge the assistance afforded by a Frederick Gardner Cottrell Grant of the Research Corporation.

(41) J. L. Hartwell, *Org. Syntheses*, **24**, 22 (1944).

(42) See the purification of butyl "carbitol," J. O. Halford, THIS JOURNAL, **53**, 2944 (1931).

(43) L. A. Wooten and L. P. Hammett, *ibid.*, **57**, 2289 (1935).

(44) This solution was assumed to deteriorate after ten days.

(45) D. I. Hitchcock and A. C. Taylor, THIS JOURNAL, **59**, 1812 (1937).

(46) Unit activity coefficients and equality of *p*H with logarithm of reciprocal of hydrogen ion concentration were assumed.

BRYN MAWR, PENNA. RECEIVED SEPTEMBER 26, 1950

[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE COLLEGE]

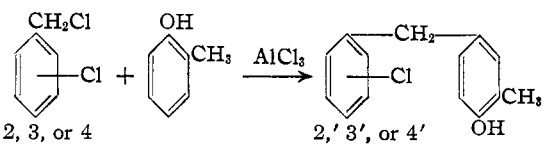
Chloro Substituted Diphenylmethanes, Phenyl Benzyl Ethers and Benzophenones Prepared from Ortho- or Para-cresol[1,2]

BY RALPH C. HUSTON AND KENNETH R. ROBINSON[3]

A series of halogenated phenolic derivatives of diphenylmethane have been prepared in this Laboratory, many of which show interesting bactericidal properties. In order to extend the series, the three monochlorobenzyl chlorides were condensed with *o*- and *p*-cresol. Eight of the nine resulting diphenylmethane derivatives were also prepared by reduction of the corresponding benzophenones which had in turn been prepared from the six possible methylphenyl chlorobenzoates obtainable from *o*- and *p*-cresol. Reduction of 2'-chloro-2-hydroxy-5-methylbenzophenone gave 2-methylxanthene. Six new methylphenyl chlorobenzyl ethers were obtained as by-products.

It has been recently been shown that a series of substituted diphenylmethanes prepared in this Laboratory[4] possess promising specific bactericidal activity. The present investigation was undertaken in order to extend this series to include nine additional chloro substituted diphenylmethanes. The nine corresponding substituted benzophenones and six substituted phenyl benzyl ethers were also prepared.

Two methods of direct alkylation of *o*- and *p*-cresol were used. When the condensation was carried out using an acidic catalyst ($AlCl_3$) *p*-alkylation of *o*-cresol took place.[5]



When the direct alkylation was carried out using basic conditions, in a non-dissociating solvent, carbon alkylation took place exclusively in the ortho position to the hydroxyl group of the phenol. In addition to the carbon alkylation some oxygen alkylation also occurred.

(1) From a thesis submitted by Kenneth R. Robinson to the Graduate School of Michigan State College in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Presented before the Division of Organic Chemistry at the 118th Meeting of the American Chemical Society, Chicago, Ill., September 3–9, 1950.

(3) Film Division, E. I du Pont de Nemours and Co., Inc., Buffalo, N. Y.

(4) R. C. Huston, *et al.*, THIS JOURNAL, **55**, 2146, 3639 (1933).

(5) R. C. Huston, *ibid.*, **46**, 2775 (1924).