[Contribution from the George Herbert Jones Laboratory, University of Chicago, Chicago, Ill.]

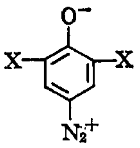
# The Formation of Biphenyls from Derivatives of Benzene-1,4-diazooxide. Electrophilic Substitution[1]

By Michael J. S. Dewar[2] and K. Narayanaswami

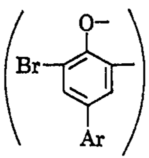
Received January 16, 1964

Earlier work[3] had shown that the thermal decomposition of derivatives of benzene-1,4-diazooxides in benzene, or in derivatives of benzene, in the presence of catalytic amounts of alcohol gives derivatives of 4-hydroxybiphenyl in good yield. We have re-examined this reaction in detail and have shown that, contrary to an earlier suggestion,[3] it does not involve a free radical mechanism. Decomposition of the diazooxide gives a carbene which attacks the aromatic substrate. The process is essentially an electrophilic substitution, the first step in which is the formation of a $\pi$-complex or spiran. The bearing of this on the mechanism of electrophilic aromatic substitution is discussed.

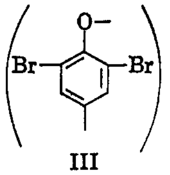
Previous work[3] had shown that the thermal decomposition of 3,5-dibromobenzene-1,4-diazooxide (Ia) in chlorobenzene, *o*- or *m*-dichlorobenzene, or bromobenzene, gives polymers together with free bromine, and that the polymers are copolymers of the repeating units II and III. This was interpreted in terms of a mechanism in which Ia decomposes to the biradical IV. One of the unpaired electrons in IV occupies a $\pi$-MO similar to that occupied by the odd electron in a phenoxy radical, while the other occupies an in-plane $\sigma$-type AO which is not mesomerically stabilized. The unstabilized radical center should show the same reactivity as that in a free aryl radical; attack on the solvent accounts for the incorporation of solvent molecules in the polymer. The second radical center should be much less reactive; however, it can apparently displace a bromine atom from some other molecule, forming an oxide bridge together with free bromine. The feasibility of this process was established by experiments with bromophenols. Thus oxidation of 2,4,6-tribromophenol gave a polymer together with free bromine, the polymer presumably being a polyphenylene oxide formed by an attack of intermediate aryloxy radicals on the tribromophenol. Various polymers of this kind were prepared in this way from other phenol derivatives, and Staffin and Price[4] have also independently prepared such materials by an analogous route.



Ia, X = Br
b, X = Cl



II



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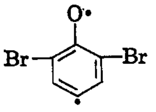
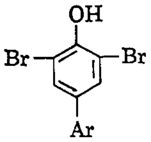


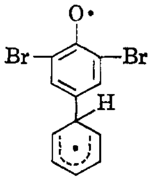
IV



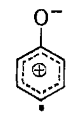
V

Entirely different results were obtained when compound I was heated in benzene, or in anisole, fluorobenzene, N,N-dimethylaniline, methyl benzoate, or benzonitrile. In these cases little or no polymer was formed, no bromine was evident, and the product was a mixture of isomeric 4-hydroxybiphenyls (V), the yields being excellent. It was then found that similar biphenyl derivatives could also be obtained from the chlorinated or brominated benzenes if the reaction were carried out in presence of a little alcohol; as little as 1% of methanol or ethanol was sufficient to repress the polymerization completely, and to give a biphenyl derivative in excellent yield.

Competitive experiments showed that different benzene derivatives reacted at very similar rates-with Ia in the presence of alcohols, seeming to suggest that the biaryl synthesis also involved a free-radical mechanism. It was therefore postulated that both the polymerization and the biaryl synthesis involve a preliminary attack by IV on the solvent, the resulting biradical VI either stabilizing itself by a hydrogen transfer giving V or undergoing conversion to polymers. It was suggested that the remarkable effect of alcohols might be due to their acting as hydrogen transfer agents *via* intermediate radicals such as $\cdot CH_2OH$. The orientation of the products from chlorobenzene indicated that the attack was electrophilic in nature, the product being a mixture of 2′- and 4′-chloro-2,6-dibromo-4-hydroxybiphenyls (V, Ar = 2- or 4-chlorophenyl); however, this observation did not in itself exclude a radical mechanism for the reaction since it has been shown[5] that phenyl radicals carrying electron-withdrawing substituents behave as electrophilic reagents. Polarization of the $\pi$-electrons in IV should make it approximate to VII; one might therefore expect IV to show a strong electrophilic tendency when it acts as an arylating agent.



VI



VII

This biaryl synthesis is clearly of interest both as a possible practical route to biaryls and also from a theoretical standpoint. If it does indeed involve a free radical substitution process, it would provide an excellent system for studying orientation and reactivity in such reactions; for no other radical substitution reaction has

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(1) This work was supported by the Office of Naval Research through Contract Nonr 2121-21 and by a grant from the National Science Foundation.

(2) Correspondence should be addressed to Department of Chemistry, The University of Texas, Austin, Texas.

(3) M. J. S. Dewar and A. N. James, *J. Chem. Soc.*, 917, 4265 (1958).

(4) G. D. Staffin and C. C. Price, *J. Am. Chem. Soc.*, **82**, 3632 (1960).

(5) J. I. G. Cadogan, D. H. Hey, and G. H. Williams, *J. Chem. Soc.*, 1425 (1955).

given such good yields of product. We have therefore re-examined the reactions of diazooxides with benzene derivatives in some detail. Our work has been carried out mostly with 3,5-dichlorobenzene-1,4-diazooxide (Ib) which has been shown[3] to react in much the same way as the dibromide Ia.

Decomposition of I in a benzene derivative $C_6H_5X$ can give three biaryl derivatives (V) in which the substituent X occupies an *o*-, *m*-, or *p*-position. Our object was to determine the partial rate factors for attack in each position of $C_6H_5X$. For this we needed to know the rates of over-all reaction of $C_6H_5X$ relative to benzene, and the proportions of the three isomers in the product; in order to do this we had to synthesize the various biphenyl derivatives independently since most of them were at that time unknown.

## Experimental

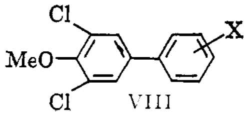
The reactions of I were carried out in an excess of the benzene derivative as solvent at 70°; the substrates used were benzene, fluorobenzene, chlorobenzene, bromobenzene, anisole, methyl benzoate, and benzonitrile. When evolution of nitrogen had ceased (usually after 6 hr.) the excess solvent was steam distilled and the biphenyl derivative V isolated with alkali and methylated with diazomethane in ether.

Preliminary work had shown that the best way of analyzing the product was by vapor phase chromatography of the methyl ethers, and that the methylation of V to the ether was quantitative under the conditions we used. Chromatography on silicone gum rubber at 300° very easily separated compounds derived from different benzene derivatives, and it also separated the *o*-isomer from the *m*- and *p*-isomers in each case. The inseparable mixtures of *m*- and *p*-isomers were analyzed by infrared spectroscopy, using the spectra of the pure compounds which we prepared independently. The reactivities of the benzene derivatives relative to benzene were determined by a competitive method, using a mixture of benzene and $C_6H_5X$ as solvent.

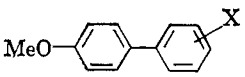
Nearly all our work was carried out with the dichlorodiazooxide Ib since the biphenyl derivatives V derived from Ia tended to decompose during chromatography. We also looked for a possible isotope effect in the reaction of Ib with 1,3,5-trideuteriobenzene; in this case the product was analyzed by mass spectrometry.[6]

The role of alcohol in the reaction was studied by using α,α-dideuterioethanol as catalyst; the fate of the deuterium was established by infrared and n.m.r. spectroscopy.

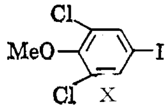
**Synthesis of Reference Compounds.**—We required a series of X'-substituted 3,5-dichloro-4-hydroxybiphenyls (VIII) containing fluorine, chlorine, bromine, methoxyl, methoxycarbonyl, or cyano in each of the three possible positions (2', 3', 4'). Most of these compounds were prepared either by an Ullmann reaction of an X-substituted iodobenzene and *p*-iodoanisole to form an X'-substituted 4-methoxybiphenyl (IX), which was then chlorinated to VIII, or directly by an Ullmann reaction of the appropriate iodobenzene with 2,6-dichloro-4-iodoanisole (X). Full details are given below.



VIII



IX



X

VIII, X = F, Cl, Br, MeO, MeOOC, CN; IX, X as in VIII

**3,5-Dibromo-2'-chloro-4-hydroxybiphenyl.**—Bromine (0.4 ml.) in acetic acid (5 ml.) was added to a solution of 2-chloro-4'-hydroxybiphenyl (0.71 g.) in acetic acid (3 ml.). Precipitation with water and recrystallization from petroleum ether (b.p. 30–35°) gave the dibromochlorohydroxybiphenyl (1.50 g., 79%) as needles, m.p. 132–134° (lit.[3] 124–126°).

**3,5-Dibromo-4'-chloro-4-hydroxybiphenyl** was prepared likewise from 4'-chloro-4-hydroxybiphenyl in 75% yield, m.p. 166–167° (lit.[3] 167.5–168.5°).

**3,4',5-Trichloro-4-methoxybiphenyl.**—The calculated amount of chlorine was passed into a solution of 4-chloro-4'-hydroxybiphenyl (0.68 g.) in acetic acid (7 ml.) and carbon tetrachloride (12 ml.) at room temperature. Excess chlorine was removed with a current of air and the solution evaporated under vacuum. The residue of 3,4',5-trichloro-4-hydroxybiphenyl crystallized from petroleum ether (b.p. 60–65°) in white needles (0.756 g., 90%), m.p. 148–149°. Methylation with diazomethane in ether gave **3,4',5-trichloro-4-methoxybiphenyl** in almost quantitative yield, m.p. 98–99°.

*Anal.* Calcd. for $C_{13}H_9OCl_3$: C, 54.29; H, 3.15; Cl, 36.99. Found: C, 54.64; H, 3.35; Cl, 37.23.

**3,3',5-Trichloro-4-methoxybiphenyl** was prepared likewise by chlorination of 3-chloro-4'-hydroxybiphenyl to 3,3',5'-trichloro-4'-hydroxybiphenyl, m.p. 121–122°, followed by methylation; m.p. 91–92°.

*Anal.* Found: C, 54.57; H, 3.24; Cl, 36.98.

**2,3',5'-Trichloro-4'-methoxybiphenyl** was prepared likewise *via* the phenol, m.p. 106–107°; m.p. 83–84°.

*Anal.* Found: C, 54.78; H, 3.21; Cl, 36.96.

**Methyl 3',5'-Dichloro-4'-methoxybiphenyl-4-carboxylate.**—A mixture of 2,6-dichloro-4-iodoanisole (7.0 g.), methyl 4-iodobenzoate (5.0 g.), and copper bronze (4.5 g.) was heated 7 hr. at 165°. The residue was extracted with chloroform and the extract chromatographed on alumina from benzene–light petroleum (1:1). The first and last fractions consisted, respectively, of methyl biphenyl-4,4'-dicarboxylate (0.5 g., m.p. 214°) and 3,3',5,5'-tetrachloro-4,4'-dimethoxybiphenyl (3.0 g., m.p. 185–186°). The middle fraction of **methyl 3',5'-dichloro-4'-methoxybiphenyl-4-carboxylate** (1.0 g.) had m.p. 132–133°.

*Anal.* Calcd. for $C_{15}H_{12}O_3Cl_2$: C, 57.90; H, 3.89; Cl, 22.79. Found: C, 58.01; H, 4.03; Cl, 22.80.

**Methyl 3',5'-dichloro-4'-methoxybiphenyl-3-carboxylate** was prepared likewise from 2,6-dichloro-4-iodoanisole (9.8 g.) and methyl 3-iodobenzoate (7.0 g.); 2.6 g., m.p. 115–116°.

*Anal.* Found: C, 58.00; H, 3.86.

**Methyl 3',5'-dichloro-4'-methoxy-2-carboxylate** was prepared likewise from 2,6-dichloro-4-iodoanisole (7.0 g.) and methyl 2-bromobenzoate (5.0 g.); the ester (2.15 g.) had m.p. 87–88°.

*Anal.* Found: C, 58.02; H, 3.91; Cl, 22.67.

**3,5-Dichloro-4'-fluoro-4-methoxybiphenyl** was prepared likewise from *p*-fluoroiodobenzene (10.0 g.), 2,6-dichloro-4-iodoanisole (13.6 g.), and copper bronze (8.9 g.); 1.35 g., m.p. 94–95°.

*Anal.* Calcd. for $C_{13}H_9OCl_2F$: C, 57.59; H, 3.35; Cl, 26.16. Found: C, 57.95; H, 3.50; Cl, 25.80.

**3,5-Dichloro-3'-fluoro-4-methoxybiphenyl** was prepared likewise; 1.57 g., m.p. 100–102°.

*Anal.* Found: C, 57.25; H, 3.52; Cl, 26.92.

**3,5-Dichloro-2'-fluoro-4-methoxybiphenyl** was prepared likewise; 0.87 g., m.p. 86–87°.

*Anal.* Found: C, 57.56; H, 3.22; Cl, 26.42.

**3,5-Dichloro-4,4'-dimethoxybiphenyl.**—Copper bronze (9.0 g.) was added over 20 min. to a stirred mixture of *p*-iodoanisole (7.0 g.) and 2,6-dichloro-4-iodoanisole (12.0 g.) at 195° and heating continued for 12 hr. The **dichlorodimethoxybiphenyl** (2.51 g.) was isolated as before and after crystallization from methanol had m.p. 60–61°.

*Anal.* Calcd. for $C_{14}H_{12}O_2Cl_2$: C, 59.38; H, 4.27; Cl, 25.04. Found: C, 59.39; H, 4.46; Cl, 25.08.

**3,5-Dichloro-2',4-dimethoxybiphenyl** was prepared likewise from 2,6-dichloro-4-iodoanisole (7.0 g.) and *m*-iodoanisole (5.0 g.); 2.5 g., m.p. 66–67°.

*Anal.* Found: C, 59.39; H, 4.50; Cl, 25.18.

**Nitration of 3,5-Dichloro-4-methoxybiphenyl.**—Nitration of 3,5-dichloro-4-methoxybiphenyl with nitric acid in acetic anhydride gave a mixture of mononitro derivatives which was separated by fractional crystallization from methanol into **3,5-dichloro-4-methoxy-2'-nitrobiphenyl**, m.p. 101°, and **3,5-dichloro-4-methoxy-4'-nitrobiphenyl**, m.p. 155–156°, the over-all yields being 32 and 46%, respectively.

*Anal.* Calcd. for $C_{13}H_9NO_3Cl_2$: C, 52.37; H, 3.04; N, 4.70; Cl, 23.79. Found for 2'-isomer: C, 52.75; H, 2.90; N, 4.76; Cl, 23.60. Found for 4'-isomer: C, 52.45; H, 3.15; N, 4.88; Cl, 23.78.

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(6) We are very grateful to Dr. S. Meyerson of the American Oil Co. for carrying out these determinations.

**4-Amino-3′,5′-dichloro-4′-methoxybiphenyl.**—Reduction of the nitro compound with iron filings in acetic acid gave the amine in almost theoretical yield, crystallizing from petroleum ether (b.p. 60–68°) in needles, m p. 78°.

*Anal.* Calcd. for $C_{13}H_{11}NOCl_2$: C, 58.23; H, 4.14; N, 5.22; Cl, 26.45. Found: C, 58.60; H, 3.91; N, 5.47; Cl, 26.51.

**3,5-Dichloro-2′-hydroxy-4-methoxybiphenyl.**—Reduction of 3,5-dichloro-4-methoxy-2′-nitrobiphenyl as above gave the crude amine as a viscous oil (4.65 g.) which was diazotized; the diazonium solution on pouring into boiling dilute sulfuric acid gave **3,5-dichloro-2′-hydroxy-4-methoxybiphenyl** which separated from petroleum ether (b.p. 60–68°) in needles (3.5 g., 75%), m.p. 118–119°.

*Anal.* Calcd. for $C_{13}H_{10}O_2Cl_2$: C, 58.02; H, 3.75; Cl, 26.35. Found: C, 58.07; H, 3.86; Cl, 26.27.

**3,5-Dichloro-2′,4-dimethoxybiphenyl.**—Methylation of the above hydroxybiphenyl (3.0 g.) with dimethyl sulfate (3.0 g.) in aqueous potassium hydroxide (5 ml. of 20%) gave the ether which crystallized from petroleum ether (b.p. 30–35°) in needles (3.0 g., 95%), m.p. 38°.

*Anal.* Calcd. for $C_{14}H_{12}O_2Cl_2$: C, 59.38; H, 4.27; Cl, 25.04. Found: C, 59.41; H, 4.32; Cl, 25.04.

**3,5-Dichloro-2′-cyano-4-methoxybiphenyl** was prepared in the usual way from the corresponding amine by diazotization and treatment with cuprous cyanide; the nitrile after crystallization from petroleum ether (b.p. 60–68°) had m.p. 176–177°.

*Anal.* Calcd. for $C_{14}H_9NOCl_2$: C, 60.46; H, 3.26; N, 5.04; Cl, 25.50. Found: C, 60.25; H, 3.34; N, 4.84; Cl, 25.79.

**3,5-Dichloro-4′-cyano-4-methoxybiphenyl** was prepared likewise; m.p. 147–148°.

*Anal.* Found: C, 61.00; H, 3.10; N, 4.90; Cl, 25.49.

**2-Bromo-3′,5′-dichloro-4′-methoxybiphenyl** was prepared in an analogous manner from the amine by diazotization and treatment with cuprous bromide; the **bromodichlorodimethoxybiphenyl** crystallized from petroleum ether in needles (yield 85%), m.p. 80–81°.

*Anal.* Calcd. for $C_{13}H_9OBrCl_2$: C, 47.02; H, 2.73; Br, 24.07; Cl, 21.36. Found: C, 47.00; H, 2.70; Br, 24.05; Cl, 21.20.

**4-Bromo-3′,5′-dichloro-4′-methoxybiphenyl** was prepared likewise; the compound crystallized from petroleum ether (b.p. 60–68°) in needles (yield 47%), m.p. 92°.

*Anal.* Found: C, 47.40; H, 2.57; Br, 24.15; Cl, 21.22.

**4-Acetamido-3′,5′-dichloro-4′-methoxybiphenyl** was prepared from the amine and acetic anhydride; after crystallization from ethanol, m.p. 218°.

*Anal.* Calcd. for $C_{15}H_{13}NOCl_2$: N, 4.76. Found: N, 4.61.

**4-Acetamido-3′,5′-dichloro-4′-methoxy-3-nitrobiphenyl.**—Nitration of the above acetamidobiphenyl gave the nitro derivative in almost theoretical yield, crystallizing from acetic acid in yellow flakes, m.p. 213°.

*Anal.* Calcd. for $C_{15}H_{12}N_2O_3Cl_2$: N, 8.26. Found: N, 8.06.

**4-Amino-3′,5′-dichloro-4′-methoxy-3-nitrobiphenyl.**—Hydrolysis of the acetyl derivative gave the **aminodichloromethoxynitrobiphenyl** which separated from ethanol in bright red crystals (yield 99%), m.p. 212°, depressed by the acetyl derivative.

*Anal.* Calcd. for $C_{13}H_{10}N_2O_3Cl_2$: N, 8.95. Found: N, 9.11.

**3,5-Dichloro-4-methoxy-3′-nitrobiphenyl.**—The amine (2.0 g.) was diazotized in dilute sulfuric acid and the diazonium solution added to cold hypophosphorous acid (20 ml. of 30%). Next day the **dichloromethoxynitrobiphenyl** was isolated with ether and crystallized from ethanol, forming a yellow powder (1.89 g., 95%), m.p. 161°.

*Anal.* Calcd. for $C_{13}H_{19}NO_3Cl_2$: N, 4.70. Found: N, 4.60.

**3-Amino-3′,5′-dichloro-4′-methoxybiphenyl.**—Reduction of the nitro compound as before gave the amine which was isolated as its hydrochloride, needles from ethanol–ether, m p. 228°.

*Anal.* Calcd. for $C_{13}H_{12}NOCl_3$: N, 5.47. Found: N, 5.32.

**3,5-Dichloro-3′-cyano-4-methoxybiphenyl** was prepared as before from the amine by a Sandmeyer reaction; m.p. 165–166°.

*Anal.* Calcd. for $C_{14}H_9NOCl_2$: C, 60.46; H, 3.26; N, 5.04. Found: C, 59.90; H, 3.03; N, 5.06.

## Results

The relative rate constants for the over-all reactions of Ib with the various substituted benzenes are shown in Table I, together with the corresponding values for nitration with nitric acid in acetic anhydride[7] and for phenylation by phenyl radicals.[8]

TABLE I

RELATIVE RATE CONSTANTS FOR OVER-ALL SUBSTITUTION OF BENZENE DERIVATIVES BY VARIOUS AGENTS

| X in $C_6H_4X^-$ | Relative rates of substitution by: Ib | $HNO_3 + Ac_2O$ | Ph |
|---|---|---|---|
| H | 1 | 1 | 1 |
| F | 0.388 | 0.15 | 1.35 |
| Cl | .429 | .033 | 1.44 |
| Br | .345 | .03 | 1.75 |
| MeO | 1.276 | .. | 2.5 |
| MeOOC | 0.522 | 0.0037[a] | .. |
| CN | 0.335 | .. | 3.6 |

[a] Value for ethyl benzoate.

The proportions of isomers in the products from Ib are shown in Table II; note that in the case of chlorobenzene or bromobenzene, one product was 2,6-dichloro-4-phenylanisole (VIII, X = H), formed by displacement of chlorine or bromine from the substrate.

TABLE II

PROPORTIONS OF PRODUCTS FROM REACTION OF Ib WITH PhX

| X in PhX | Proportions of products, %: Unsubstd.[a] | *ortho* | *meta* | *para* |
|---|---|---|---|---|
| F | 0 | 62.1 | 0[b] | 37.8 |
| Cl | 6 | 62 | 0[b] | 32 |
| Br | 26 | 42.3 | 0[b] | 31.6 |
| MeO | 0 | 72.8 | 0[b] | 27.25 |
| MeOOC | 0 | 35.1 | 47.2 | 17.7 |
| CN | 0 | 45.0 | 16.5 | 38.5 |

[a] *I.e.*, 2,6-dichloro-4-phenylanisole (VIII, X = H). [b] Less than 0.5% of the *m*-isomer could have been detected in each case.

Table III compares the partial rate factors for substitution by Ia in the various benzene derivatives with those for nitration in acetic anhydride[7] and for phenylation by phenyl radicals.[8]

TABLE III

PARTIAL RATE FACTORS FOR SUBSTITUTION IN PhX BY VARIOUS AGENTS

| Compound | Position | Partial rate factor for reaction with: Ib | $HNO_3 + Ar_2O$ | Ph |
|---|---|---|---|---|
| PhF | *o* | 0.72 | 0.056 | 2.19 |
| | *m* | 0 | 0 | 1.5 |
| | *p* | 0.88 | 0.79 | 1.23 |
| PhCl | *o* | 0.85 | .029 | 2.6 |
| | *m* | 0 | .0009 | 1.12 |
| | *p* | 0.88 | .137 | 1.19 |
| PhBr | *o* | 0.59 | .033 | 2.09 |
| | *m* | 0 | .0011 | 1.8 |
| | *p* | 0.88 | .112 | 1.83 |
| PhOMe | *o* | 2.78 | ... | .. |
| | *m* | 0 | ... | .. |
| | *p* | 2.09 | ... | .. |
| PhCOOMe | *o* | 0.55 | .0026[a] | .. |
| | *m* | .49 | .0079[a] | .. |
| | *p* | .37 | .001[a] | .. |
| PhCN | *o* | .45 | ... | .. |
| | *m* | .17 | ... | .. |
| | *p* | .77 | ... | .. |

[a] Values for PhCOOEt.

Reaction of 1,3,5-trideuteriobenzene with Ib can give either 3′,5′-dideuterio- (XX) or 2′,4′,6′-trideuterio-

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(7) C. K. Ingold and M. S. Smith, *J. Chem. Soc.*, 905 (1938); M. L. Bird and C. K. Ingold, *ibid.*, 918 (1938).

(8) D. H. Hey, *et al.*, *ibid.*, 1974, 2094 (1952); 44, 3412 (1953); 794, 3352 (1954); 6 (1955); 1463 (1956).

TABLE IV

PROPORTIONS OF ISOTOPIC SPECIES IN 1,3,5-TRIDEUTERIOBENZENE AND IN THE REACTION PRODUCT OF Ib WITH A MIXTURE OF IT WITH NORMAL BENZENE

| Compound | Proportion (%) containing various numbers of deuterium atoms<br>0 | 1 | 2 | 3 |
|---|---|---|---|---|
| 1,3,5-Trideuteriobenzene | 1.25 | 0.05 | 2.6 | 96.1 |
| Reaction product | 83.2 | 0.7 | 7.9 | 8.1 |

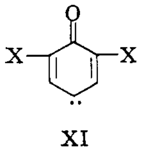
2,6-dichloro-4-hydroxybiphenyl (XIX). The reaction was carried out with a mixture of normal benzene and 1,3,5-trideuteriobenzene (5:1 w./w). Table IV shows the deuterium content[6] of the 1,3,5-trideuteriobenzene, and of the mixture of methyl ethers formed by methylation of the reaction product.

## Discussion

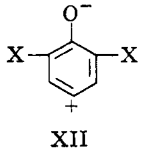
The most salient feature of the results listed in Tables II and III is the complete absence of *m*-isomer in the products from anisole, chlorobenzene, or bromobenzene. Examination of synthetic mixtures showed that 0.5% of the *m*-isomer could easily have been detected in each case. This seems to rule out completely a radical mechanism for the reaction; no aryl radical could possibly show selectivity of so high an order as this. The reaction of Ib indeed shows an even greater selectivity than does nitration with nitric acid in acetic acid; both chlorobenzene and bromobenzene give about 1% of *m*-nitrohalobenzene under these conditions. It had been reported[3] previously that Ia attacks chlorobenzenes exclusively in the *o*- and *p*-positions; however, the analytical procedure used in that investigation was less accurate than the method adopted here and the earlier conclusions were consequently less definite.

The radical mechanism[3] for the biaryl synthesis suffers from the further defect of not explaining why some benzene derivatives give polymers with I whereas others give biphenyl derivatives. The distinction certainly does not depend on the electronic nature of the substituents; thus fluorobenzene, dimethylaniline, and methyl benzoate give biphenyl derivatives almost exclusively, whereas chlorobenzene and bromobenzene give only polymers. The only difference between the two classes of substrates seems to be that the ones giving polymers contain heavy atoms (Cl, Br). There seems to be only one way in which these facts can be explained.

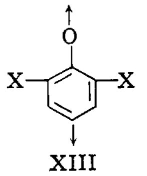
Decomposition of I can give four different types of product; a carbene (XI), a zwitterion (XII), or a biradical which can exist in either a singlet (XIII) or triplet (XIV) state. The three species differ in the distribution of electrons between the $\pi$-MO's and the in-plane $\sigma$-AO of the carbon atom *para* to oxygen. In XI there are six $\pi$-electrons and two electrons in the $\sigma$-AO; in XII there are eight $\pi$-electrons and none in the $\sigma$-AO; in XIII or XIV there are seven $\pi$-electrons and one electron in the $\sigma$-AO.



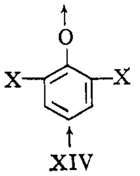
XI



XII



XIII



XIV

The electronic wave functions of XI and XII have the same total symmetry; consequently XI and XII are not chemically distinct species, but possible resonance structures of one single species. Presumably this will approximate closely to the neutral carbene structure XI. The wave function of XIII differs in symmetry from XI or XII; it is antisymmetric for reflection in the nodal plane, whereas those of XI and XII are symmetric. Hence XIII is a chemically distinct species from XI or XII rather than a mere resonance structure; XIII will exist in equilibrium with (XI ↔ XII)—although of course the interconversion of the two forms would be expected to be extremely fast. The triplet structure XIV is also a chemically distinct species; the conversion of XIII to XIV may be quite slow since it involves an intersystem crossing and it should be greatly facilitated by heavy atoms in the vicinity of the odd electron.

The initial thermal decomposition of I should produce the intermediate initially in a singlet state which should approximate the carbene structure XI. Now this is a vinylog of an acyl carbene, and carbenes carrying +E substituents (such as acyl) are little stabilized by resonance since the *p*-orbital of the divalent carbon atom is empty. Carbenes are the conjugate bases of carbonium ions and are likewise stabilized best by electron-releasing (−E, −I) substituents. For this reason carbenes carrying +E substituents are comparable with carbene itself in reactivity; carbethoxycarbene and cyanocarbene[9] react with benzene to form derivatives of cycloheptatriene or norcaradiene. It is therefore tempting to attribute the biphenyl synthesis to a reaction of this kind between XI and the aromatic substrate; in this case the product would be a curious spiran that would be expected to isomerize very easily to a derivative of biphenyl.

The formation of polymers from I in solvents containing chlorine or bromine must then involve the free radical IV. If we are right in supposing that XI reacts with benzene derivatives as a carbene, and that XI is in very rapid tautomeric equilibrium with the singlet biradical XIII, we must suppose the polymerization to involve the triplet biradical XIV. The role of solvents containing chlorine or bromine is then to accelerate the formation of XIV from XI; the ability of solvents containing heavy atoms to accelerate intersystem crossings of this kind has been well recognized since a classic investigation by Kasha.[10]

It may at first sight seem strange that the solvent should have so great an effect, given that the carbene itself contains two heavy atoms. These, however, are remote from the critical orbital (the in-plane $\sigma$-AO *para* to oxygen) which contains the electron whose spin is to be reversed. This electron could only reach the heavy atom if there were a strong resonance coupling between the $\sigma$-AO and the $\pi$-MO's and couplings of this kind are known to be small.

These conclusions have been supported by further studies of the effect of alcohol on the reaction between I and chlorobenzene. If the alcohol acts as a hydrogen carrier, as suggested previously,[3] then in the first place there should be an exchange between the $\alpha$-hydrogen atoms of the alcohol and the hydroxyl group

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(9) M. J. S. Dewar and R. Pettit, *J. Chem. Soc.*, 2026 (1956).

(10) M. Kasha, *Discussions Faraday Soc.*, **9**, 14 (1950); *J. Chem. Phys.*, **20**, 71 (1952).

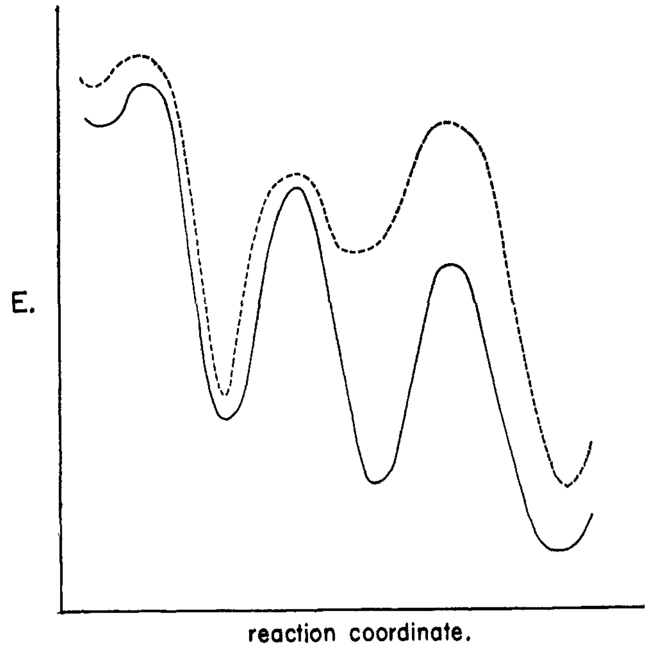


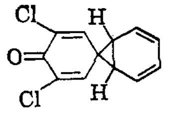
Fig. 1.—Potential energy diagram for the reaction of XI with benzene: (a) rate of isomerization of XV slower than final proton transfer (———); (b) rate of final proton transfer slower than rate of isomerization (- - - - -).

of the 4-hydroxybiphenyl formed in the reaction, and in the second place tertiary alcohols should fail to act as catalysts. When, however, we used $\alpha,\alpha$-dideuterioethanol as catalyst in the reaction, no such exchange took place, for the infrared spectrum of the product showed it to be free from deuterium while the n.m.r. spectrum of the recovered alcohol showed no $\alpha$-hydrogen. Moreover it has been found[11] that *t*-butyl alcohol is an active catalyst although it contains no $\alpha$-hydrogen, while diphenylamine is not, although it contains a hydrogen atom that can very easily be extracted by radicals.

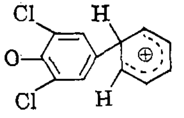
The most likely explanation of the action of alcohols seems to be that they form strong hydrogen-bonded complexes with the carbene XI, but not with the biradical XIV. This seems reasonable for the carbene must in fact be represented as a hybrid of the unchanged structure XI and the zwitterionic structure XII, whereas there are no unexcited ionic structures for the biradical XIV. The oxygen atom in the latter should therefore be less negatively charged and so should form weaker hydrogen bonds. Hydrogen bonding may affect the relative rates of attack by XI on the solvent, and of isomerization of XI to XIV, in two ways. First, such solvation should increase the electrophilicity of XI and so increase the rate of attack on the solvent; second, the extra energy of solvation may conceivably make the carbene more stable than the biradical, or at least reduce the rate of isomerization by making it less exothermic.

Our conclusion then is that the biaryls are formed through attack by the carbene XI on the substrate; the observed orientation of the products moreover shows the over-all reaction to be an electrophilic substitution. We now have to explain why it is that XI shows very high selectivity (greater than nitric acid in acetic acid) in choosing between the positions in a given substrate molecule PhX, but very little selectivity in choosing between different substrate molecules PhX, PhY. This certainly runs entirely counter to Brown's "selectivity rule",[12] a rule which can be shown by a simple MO treatment[13] to follow from the conventional Wheland[14] mechanism for substitution.

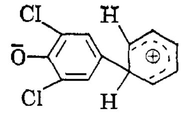
The only explanation seems to be that XI reacts with PhX by a very exothermic reaction with very low activation energy to form an intermediate which can be written as a spiran (XV). The spiran can isomerize to one or other of two benzenonium ions XVI, XVII, by rupture of one or the other of the bonds in the three-membered ring; these in turn form the final reaction products by shift of a proton from the substrate ring to oxygen. If the formation of XV has a very low activation energy, changes in the substrate will affect its rate but little. This can be seen very easily from an argument[15] based on the use of potential curves, a type of argument first introduced by Bell, Evans, and Polanyi some time ago.[16] It is easily shown that the rate of a highly exothermic reaction with a small activation energy should vary little with structural changes in the reactants. This general principle has been rediscovered from time to time by various authors; the original application[15] was to explain the different products that may form when a mesomeric anion reacts with electrophilic agents of varying reactivity. In the present case the argument is still clearer; for both the substrate PhX and the spiran XV are even alternant hydrocarbons, and so the heat of formation of XV from PhX should vary little with the nature of X, the resonance energy for the interaction between a substituent X and an even alternant hydrocarbon being small.[17] The heats of isomerization of XV to the benzenonium ions XVI or XVII will, however, differ greatly if X is a substituent with a selective stabilizing or destabilizing effect on carbonium ions[17]; if the isomerization has an appreciable activation energy, there may then be very significant rate differences for the conversion of XV into one or other of the possible isomeric benzenonium ions. At the same time the *formation* of XV may still be the rate-controlling step of the over-all process, provided that this reaction is so exothermic that the transition state for the isomerization of XV remains lower in energy than that for the formation of XV. These relations are illustrated in Fig. 1. The second step can have a large activation energy even though the first step is still rate determining. In these circumstances there may be large differences in rate for the formation of the various possible products from a given substrate PhX, but little between the rates of attack on different substrates PhX, PhY.



XV



XVI



XVII

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(11) Unpublished work in this laboratory by Dr. J. Blackwell and by Mrs. N. L. Sabelli.

(12) H. C. Brown and K. L. Nelson, *J. Am. Chem. Soc.*, **75**, 6293 (1953); **77**, 2300 (1955).

(13) M. J. S. Dewar, T. Mole, and E. W. T. Warford, *J. Chem. Soc.*, 3581 (1956).

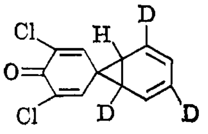
(14) G. W. Wheland, *J. Am. Chem. Soc.*, **64**, 900 (1942).

(15) M. J. S. Dewar, *Discussions Faraday Soc.*, **2**, 261 (1947).

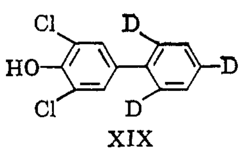
(16) *Cf.* M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **32**, 1340 (1936); R. P. Bell, *Proc. Roy. Soc.* (London), **A154**, 414 (1936).

(17) M. J. S. Dewar, *J. Am. Chem. Soc.*, **74**, 3341, 3345, 3350, 3353, 3355, 3357 (1952).

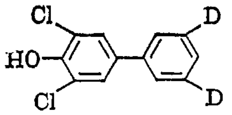
One final point needs to be settled. The conversion of XV to the product involves two steps, isomerization to XVI or XVII, and loss of a proton from carbon to form the product. Either of these last two steps might be rate determining; indeed, there is a third alternative, that ring opening and deprotonation occur synchronously by an EN2 mechanism. In order to distinguish between these mechanisms, we studied the reaction of Ib with 1,3,5-trideuteriobenzene. Here the intermediate is XVIII, and the final product can be either XIX or XX. If the loss of the proton occurs in the slow step, there should be a primary isotope effect favoring the formation of XIX.



XVIII



XIX



XX

As a matter of convenience we carried out the experiment with a mixture of 1,3,5-trideuteriobenzene and normal benzene; in this way we could get a free check on any possible isotope effect on the over-all reaction The results in Table IV show that benzene and trideuteriobenzene react at essentially identical rates with XI, and that XIX and XX are formed in equal amounts. Table V compares the observed proportions of undeuterated, dideuterated, and trideuterated dichlorophenylhydroxybiphenyls in the reaction product with those calculated assuming zero isotope effects. The values agree within the limits of experimental error, showing that the product-determining step in the conversion of XV to the final product is the isomerization of XV to XVI or XVII. The course of the reaction is that indicated by the solid line in Fig. 1.

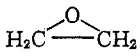
TABLE V

COMPARISONS OF OBSERVED AND PREDICTED PROPORTIONS OF ISOTOPIC SPECIES FROM THE REACTION OF Ib WITH BENZENE CONTAINING 1,3,5-TRIDEUTERIOBENZENE (5:1 w./w.)

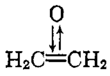
| Deuterium atoms in product | 0 | 2 | 3 |
|---|---|---|---|
| Proportion of products obsd., % | 83.8 | 8.0 | 8.2 |
| Proportion of products calcd. assuming zero isotopic effect | 84.0 | 8.0 | 8.0 |

**Mechanism of Electrophilic Substitution.**—The results discussed here have a bearing on the mechanism of electrophilic aromatic substitution. Some time ago one of us[18] suggested that the first step in such reactions might be the formation of a $\pi$-complex from the substrate and the electrophile, this in turn isomerizing to the benzenonium intermediate postulated by Wheland. If this is so, one can distinguish two cases. In the first, the $\pi$-complex is formed irreversibly in the rate-determining step. In the second, the $\pi$-complex is formed reversibly and the slow step is its isomerization to one or other of the possible benzenonium ion intermediates. One can see at once that only the first case is chemically significant; in the second, the formation of the $\pi$-complex can have no effect either on the over-all rate of reaction or on the proportions of isomers formed.

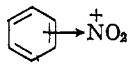
Our biphenyl synthesis is an electrophilic substitution of the former type, where formation of the complex is rate determining. It may seem at first sight that the spiran intermediate XV is far removed in structure from a $\pi$-complex, but this is not in fact the case. Just as the classical (XXI) and $\pi$-complex (XXII) forms of ethylene oxide are closely related, depending only on the state of hybridization of the carbon atoms, so also is XV related to an analogous $\pi$-complex in which the benzene ring essentially retains its integrity. Olah and his collaborators[19] have observed similar relationships in the nitration of a variety of alkylbenzenes by the free nitronium ion; they have interpreted their results in terms of the $\pi$-complex mechanism. These reactions seem to follow the course indicated by the potential curves of Fig. 1a (solid line), the formation of the $\pi$-complex being rate determining; here again one can write the intermediate either as a $\pi$-complex (XXIII) or with a three-membered ring (XXIV).



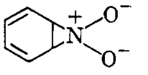
XXI



XXII



XXIII



XXIV

Our case is particularly striking in the complete lack of selectivity shown by XI to different benzene derivatives; anisole and methyl benzoate would undergo nitration at rates differing by many orders of magnitude while their rates of reaction with XI differ less than threefold. Yet XI shows greater selectivity between the different positions in chlorobenzene than does nitric acid in acetic anhydride! These results suggest that the possibility that $\pi$-complex formation may be rate determining should always be kept in mind when studying reactions involving electrophilic substitution.

Recent investigations by Kunitake and Price[20] and by Stille, Cassidy, and Plummer[21] support the general mechanism suggested above. These authors independently studied the thermal and photochemical decomposition of 3,5-dimethylbenzene-1,4-diazooxide in chlorobenzene,[20] nitrobenzene,[22] and tetrahydrofuran.[20,21] In the first case only biphenyl derivatives were formed, in the second nitrosobenzene and 2,6-dimethylbenzoquinone (*cf.* 3), in the third a polymer. These reactions were interpreted in terms of an electrophilic attack on the solvent by an intermediate formulated as a carbene (XI, X = Me) or zwitterion (XII, X = Me), in complete agreement with the mechanism suggested here.

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[18] M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Clarendon Press, Oxford, 1949.

[19] G. A. Olah, S. J. Kuhn, and S. H. Flood, *J. Am. Chem. Soc.*, **83**, 4571, 4581 (1961).

[20] T. Kunitake and C. C. Price, *ibid.*, **85**, 761 (1963).

[21] J. K. Stille, P. Cassidy, and L. Plummer, *ibid.*, **85**, 1318 (1963).