reaction mixture was refluxed with water for 3 hours to ensure complete hydrolysis of the residual benzoyl chloride. The ethylene dichloride was removed and the products were taken up in carbon disulfide. The infrared spectrum was examined and compared with that of a standard solution of *p*-phenylbenzophenone in carbon disulfide; bands at 8.50, 11.72 μ. A yield of 92.2% *p*-phenylbenzophenone was indicated.

Acetylation of Biphenyl.—Aluminum chloride, 0.0800 *M*, was dissolved in excess acetyl chloride, 0.1600 *M*, in ethylene dichloride at 0°. Controlled quantities of these freshly prepared solutions were added to the vigorously stirred solutions of biphenyl and toluene in ethylene dichloride at 25.0° over a period of 10 minutes, giving a total volume of 50 ml. After an additional 10 minutes, the reaction mixtures were quenched with an ice–sodium hydroxide solution; 8 ml. of a standard solution of benzophenone, 0.300 *M*, was added as an internal standard.

The organic layer was washed with water and the solvent removed by distillation through a short column. The residues were analyzed using a 5-ft. column with a silicone substrate operated at 190°. The amount of acetotoluene and acetobiphenyl relative to the concentration of benzophenone introduced was determined. The data are summarized in Table I.

Biphenyl was acetylated under the usual kinetic conditions and the product isolated as described above. It was dissolved in carbon disulfide and analyzed for *p*-phenylacetophenone content by comparison of the infrared spectrum with that of a standard solution of *p*-phenylacetophenone at 8.42, 11.84 and 12.04 μ. The analysis indicated the formation of 97.3% of *p*-phenylacetophenone.

Acetylation of Fluorene.—Standard solutions of aluminum chloride in acetyl chloride dissolved in ethylene dichloride were added to standard solutions of fluorene and prehnitene or *o*-xylene in ethylene dichloride. After the reaction mixture was quenched, 8.00 ml. of a 0.300 *M* solution of *p*-phenylacetophenone was added, as an internal standard, and the reaction mixture was analyzed on a silicone column operated at 220°. The data are summarized in Table II.

The gross reaction product obtained from the acetylation of fluorene in carbon disulfide was compared by infrared with a standard solution of 2-acetylfluorene in the same solvent. The yield was almost 100%.

[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY, LAFAYETTE, IND., AND THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO, CHICAGO, ILL.]

Relative Rates and Isomer Distributions in the Bromination of Biphenyl and Fluorene in Acetic Acid. Partial Rate Factors for the Bromination Reaction[1-3]

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The relative rates for the non-catalytic bromination of fluorene, biphenyl and benzene in acetic acid solvents were determined to be 2.11×10^6, 1.00×10^3 and 1.00, respectively. The isomer distribution for the bromination of biphenyl was established as 2.5% *o*- and 97.5% *p*-bromobiphenyl by infrared spectroscopy. A qualitative examination of the products of the bromination of fluorene indicated 2-bromofluorene as the only detectable product. Partial rate factors calculated from these observations are o_f^{Ph} 37.5, p_f^{Ph} 2920 and 2-Fl_f 6.33×10^6. In contrast to the partial rate data previously reported for ethylation, mercuration and acylation, bromination *para* to a phenyl group is more activated than substitution *para* to a methyl group, p_f^{Me} 2420. It is suggested that under the strong electron demand of the bromination reaction, a reaction of very high selectivity, the two benzene rings of the biphenyl molecule achieve a closer approach to coplanarity with an improved possibility for electron supply from the phenyl substituent to the electron-deficient center. The high value observed for 2-Fl_f is attributed to the coplanarity of the two benzene rings brought about by the methylene bridge.

Introduction

In 1953, it was suggested that a linear free energy relationship might be applicable to the electrophilic substitution reactions of monosubstituted benzenes.[5] Since this suggestion was made, data have been accumulated for a rigorous test of the Selectivity Relationship.[6]

In recent papers, the application of the treatment to the substitution reactions of toluene,[7] *t*-butylbenzene[8] and anisole[9] have been examined. The approach has proved quite satisfactory for these aromatics. However, shortly after the initial suggestion of the possible utility of a linear free energy treatment,[5] de la Mare pointed out the existence of a serious discrepancy in an attempted correlation of the available data on the nitration and chlorination of biphenyl.[10]

In view of this situation, it appeared desirable to subject the behavior of biphenyl in electrophilic substitutions to critical scrutiny. Accordingly, data were obtained for the mercuration,[11a] ethylation[11b] and acylation[11c] of biphenyl. In addition to these reactions and others which have since become available it appeared desirable to investigate the highly selective non-catalytic bromination of biphenyl in acetic acid.[12] In the course of this work, it became apparent that the reactivity of fluorene would have a considerable bearing on possi-

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(1) Directive Effects in Aromatic Substitution. XLVIII.

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(3) Based in part upon a thesis submitted by Leon M. Stock in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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(5) H. C. Brown and K. L. Nelson, *J. Am. Chem. Soc.*, **75**, 6292 (1953).

(6) H. C. Brown and C. R. Smoot, *ibid.*, **78**, 6255 (1956).

(7) (a) F. R. Jensen, G. Marino and H. C. Brown, *ibid.*, **81**, 3303 (1959); (b) H. C. Brown and G. Marino, *ibid.*, **81**, 3308 (1959); (c) H. C. Brown, G. Marino and L. M. Stock, *ibid.*, **81**, 3310 (1959); (d) S. U. Choi and H. C. Brown, *ibid.*, **81**, 3315 (1959); (e) H. C. Brown and B. A. Bolto, *ibid.*, **81**, 3320 (1959); (f) L. M. Stock and H. C. Brown, *ibid.*, **81**, 3323 (1959).

(8) (a) H. C. Brown and M. Dubeck, *ibid.*, **81**, 5608 (1959); (b) H. C. Brown and G. Marino, *ibid.*, **81**, 5611 (1959); (c) L. M. Stock and H. C. Brown, *ibid.*, **81**, 5613 (1959); (d) **81**, 5621 (1959).

(9) (a) H. C. Brown and M. Dubeck, *ibid.*, **82**, 1939 (1960); (b) L. M. Stock and H. C. Brown, *ibid.*, **82**, 1942 (1960).

(10) P. B. D. de la Mare, *J. Chem. Soc.*, 4450 (1954).

(11) (a) H. C. Brown, M. Dubeck and G. Goldman, *J. Am. Chem Soc.*, **84**, 1229 (1962); (b) H. C. Brown and A. Neyens, *ibid.*, **84**, 1233 (1962); (c) H. C. Brown and G. Marino, *ibid.*, **84**, 1236 (1962).

(12) Since this study was completed, two independent investigations of the bromination of biphenyl have been reported, ref. 13 and 14.

(13) S. F. Mason, *J. Chem. Soc.*, 4329 (1958).

(14) E. Berliner and J. C. Powers, *J. Am. Chem. Soc.*, **83**, 905 (1961); E. Berliner, G. L. Zimmerman and G. C. Pearson, *J. Org. Chem.*, **26**, 1633 (1961).

ble interpretations of the results. Consequently, the bromination of this aromatic was also examined.

Results

The relative rates for the bromination of biphenyl and fluorene compared to benzene were determined through a comparison of the time required for 10 and 20% reaction under standardized conditions. This technique was adopted in order to avoid the kinetic difficulties associated with the bromination reaction.[14-16] The limited solubility of biphenyl in 85% acetic acid prevented measurement of the reaction rate at the concentrations employed previously for benzene and the methylbenzenes.[16] Accordingly, toluene and biphenyl were examined at concentration 0.150 *M* with a variable concentration of bromine. This procedure enabled an estimate of the reaction time by two independent techniques. Thus, it was possible to employ the kinetic observation to calculate the reaction interval for a selected concentration, 0.02 *M*, and to check the result by graphical extrapolation.

Aqueous acetic acid was not a satisfactory medium for a study of the bromination of fluorene because of its insolubility and high reactivity. Previously it had been established that the absolute rate of bromination of aromatics was decreased by a factor of 150 in anhydrous acetic acid without appreciably altering the relative reactivity.[16] We took advantage of this characteristic of the bromination reaction and examined the bromination of fluorene in the anhydrous solvent. Since a new batch of solvent was employed in these experiments, the bromination of *m*-xylene was re-examined to provide a direct comparison with the earlier measurements.

The kinetic observations are summarized in Table I.

TABLE I

REACTION INTERVALS REQUIRED FOR 10 AND 20% REACTION FOR THE BROMINATION OF TOLUENE, *m*-XYLENE, BIPHENYL AND FLUORENE IN ACETIC ACID SOLVENTS AT 25°

Aromatic	Concentration, *M* [ArH]	Concentration, *M* [Br_2]	Reacn. interval examined, min. Obsd. t_{10}	Obsd. t_{20}	Corr.[a] t_{10}	Corr.[a] t_{20}
Toluene[b]	0.150	0.0265	304	762	402	1008
		.0228	360	907	410	1032
		.0197	460	1095	454	1078
		.0195	482	1120	470	1097
Biphenyl[b]	0.150	.0281	191	487	268	680
		.0248	215	560	266	692
		.0233	221	582	247	648
		.0211		660		696
		.0209	246	596	257	608
		.0205		685		702
m-Xylene[c,d]	0.0200	.0106	1280		1330	
		.0105	1400		1440	
Fluorene[c]	0.0200	.00965	355		358	
		.0101	290		316	

[a] Corrected to 0.0200 *M* bromine by application of third-order expression. [b] In 85% aqueous acetic acid. [c] In 100% acetic acid. [d] The value, t_{10}, determined previously[16] was 1290 min.

The relative rates estimated from these data are summarized in Table II.

TABLE II

RELATIVE RATES ESTABLISHED BY 10 AND 20% REACTION TIMES FOR BROMINATION IN ACETIC ACID AT 25°

Aromatic	Reacn. interval, min. t_{10}	t_{20}	Relative rate
Benzene[a]			1.00
Toluene[a]			0.605×10^3
Toluene[b]	458	1085	
Biphenyl[b]	255	697	
Toluene[c]	434	1053	
Biphenyl[c,d]	260	671	1.00×10^{3c}
m-Xylene[a,c]	1385		5.14×10^5
Fluorene[c]	337		2.11×10^6

[a] Relative rate based on earlier results.[16] [b] Based on extrapolated t_{10} and t_{20} observations. [c] Based on mean value of corrected t_{10} and t_{20} observations, Table I. [d] Relative rate for biphenyl based on average of 4 comparisons. [e] A value of 1100 has been reported for 85% acetic acid[13] and 1400 for 50% acid.[14]

The isomer distribution for the bromination of biphenyl was determined by spectroscopic analysis of the product mixture obtained for reaction under kinetic conditions. Excess biphenyl was removed by fractionation. Preliminary experiments revealed substitution, as expected, predominantly in the *para* position. In order to achieve a satisfactory analysis for the *ortho* isomer, it was necessary to remove the large excess of *p*-bromobiphenyl from the analytical solution. The selective removal of the *para* isomer was readily achieved by successive crystallizations of the *para* isomer from ethanol, providing a solution sufficiently enriched in the *ortho* isomer to permit satisfactory analysis.

The results of this analysis for the isomer distribution are summarized in Table III.

TABLE III

ISOMER DISTRIBUTION IN THE BROMINATION OF BIPHENYL IN 85% ACETIC ACID AT 25°

	Bromobiphenyl, % *o*-	*p*-
Detmn. A	2.29	97.71
Detmn. B	2.73	97.21
Mean value	2.5 ± 0.2	97.5 ± 0.2[a]

[a] Reported[14] as 93.9 ± 2.4% of product in 50% acetic acid.

The infrared spectrum of the analytical solution, enriched in the *ortho* isomer and other possible products of the reaction, failed to reveal absorption bands for materials other than *o*- and *p*-bromobiphenyl. No additional bands were observed when the residual *para* isomer was blanked out by the addition of the pure isomer to the reference cell of the double beam instrument. The product mixture was thus shown to be free of significant concentrations (>1%) of *m*- and *p,p'*-substitution products.

Although it appeared certain from observations in the literature that the bromination of fluorene yielded predominantly the 2-isomer, the products of the reaction were examined qualitatively. In earlier studies, 2-bromofluorene was separated from the hydrocarbon by recrystallization. In this operation small quantities of the 4-bromo isomer would have been removed with the hydrocar-

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(15) For a review and other applications of the technique, see P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution," Butterworths Scientific Publications, London, 1959, Chap. 9.

(16) H. C. Brown and L. M. Stock, *J. Am. Chem. Soc.*, **79**, 1421 (1957).

bon. Accordingly, we examined the infrared spectrum of a crude mixture of fluorene and the bromofluorene isolated from the reaction solvent. The spectrum did not reveal any absorption bands other than those identified with fluorene and 2-bromofluorene. The addition of fluorene to the reference cell effected the resolution of two bands for 2-bromofluorene in the 13 μ region, but did not introduce any other bands. In particular, the absorption band for 4-bromofluorene at 12.9 μ was not detected in any of the spectra. On the basis of these observations, it appears safe to conclude that the bromination of fluorene proceeds predominantly (>95%) to the formation of 2-bromofluorene.

Discussion

The relative rate k_{BP}/k_B of 1000 is in reasonably good agreement with the value 1100 obtained by comparison of kinetic rate constants in 85% acetic acid.[13] The result obtained here is somewhat smaller than that reported for 50% acid, 1400, by Berliner and Powers.[14] However, the deviation is not major in view of the different solvents employed.

Several qualitative investigations of the isomer distribution in the bromination of biphenyl indicate predominant *para* substitution. In carbon disulfide, *p*-bromobiphenyl[17] with lesser amounts of the *o*- and *p,p'*-derivatives[18] have been reported for the reaction. These early observations are supported by the finding that *p,p'*-dibromobiphenyl could be isolated in 90% yield from the non-catalytic bromination in refluxing acetic acid.[19] These results are consistent with very low *ortho* substitution.

More recently, an isotopic dilution analysis of the products of bromination in 50% aqueous acetic acid indicated *p*-bromobiphenyl accounted for 93.9 ± 2.4% of the product.[14] Our results are within experimental uncertainty of this latter observation.

Combining the value for the relative rate with the isomer distribution leads to the partial rate factors o_f^{Ph} 37.5 and p_f^{Ph} 2920. A value of m_f^{Ph} 0.3 was estimated from the relative rates of bromination of *p*-phenylanisole and *p*-methylanisole.[9b]

On the basis of this value for m_f^{Ph}, the concentration of *m*-bromobiphenyl in the reaction mixture is calculated to be 0.02%.

The partial rate factor for *ortho* substitution, o_f^{Ph} 37.5, is considerably less than that for toluene, o_f^{Me} 600. In part this factor is doubtless the result of the operation of the larger steric requirements of the phenyl substituent and its electron-withdrawing inductive effect. However, a contributing factor may also be the loss of a considerable portion of the resonance stabilization of the phenyl substituent in the conformation required for the introduction of the bromine substituent in the transition state.[20]

The agreement achieved between the present study and the results of several independent investigations in other laboratories argues that the *para* partial rate factor, p_f^{Ph} 2920, must be free of major error. Significantly, the results of other investigations indicate this value to be even somewhat greater. The unusual feature of this observation is the greater reactivity of the *para* position in biphenyl compared to bromination *para* to the methyl group in toluene, p_f^{Me} 2420.[16] All other quantitative studies of the substitution reactions of biphenyl and toluene reveal the *p*-methyl partial rate factor to be greater than for biphenyl.

A detailed discussion of this question is presented in the following paper.[21] However, it may be pointed out here that the lower reactivity in the *para* position of biphenyl as compared to toluene has been attributed[11] to the non-coplanar phenyl nuclei in biphenyl with reduced resonance contributions. The high selectivity of the bromination reaction, $\rho = -12$, suggests an explanation for the reversal. The large electron demand in the bromination process and the increased energy requirements possibly allow the rings to achieve a closer approach to coplanarity. In this situation the phenyl substituent may make a greater contribution to the electron-deficient center of the transition state.

The kinetics of bromination of fluorene has not been examined previously. The relative rate, fluorene to benzene, evaluated from the 10% reaction intervals, Table I, is 2.11×10^6.

The experimental evidence indicates the bromination to proceed practically completely to 2-bromofluorene. Earlier investigations of the bromination of fluorene also pointed to essentially exclusive substitution in the 2-position. Thus, in chloroform at 0–5°, the reaction is reported to yield 90% of 2-bromofluorene.[22] Bromination with dioxane dibromide in dioxane is reported to provide a quantitative yield of the same product.[23]

Combining the relative rate with the value of 100% substitution in the 2-position leads to the partial rate factor, 2-Fl_f 6.33×10^6. It is evident that the coplanar conformation of the biphenyl system enforced by the methylene bridge has resulted in a marked activation of the position corresponding to the *para* position of the biphenyl system.

A detailed discussion of the significance of these results to the Selectivity treatment is presented in the following paper.

Experimental Part

Materials.—The preparation of solvents and bromine have been described previously.[16] Biphenyl, fluorene, the pure isomeric bromobiphenyls and 2- and 4-bromofluorene were available from a concurrent study.[11]

Kinetic Measurements.—The tenth- and fifth-lives were determined in reaction flasks with narrow necks as previously reported.[16] The kinetic experiments with fluorene were carried out in a batch of pure acetic acid different from that employed in earlier experiments. The observations made are reported in Table I and a typical run is summarized in Table IV.

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[17] G. Schultz, *Ann.*, **174**, 201 (1874).

[18] W. Schlenk, *Ber.*, **46**, 1475 (1913).

[19] R. E. Buckles, E. A. Hausman and N. G. Wheeler, *J. Am. Chem. Soc.*, **72**, 2494 (1950). Only 71% had been obtained in an earlier examination of the reaction under these conditions; R. Scholl and W. Neovius, *Ber.*, **44**, 1075 (1911).

[20] This question has been discussed in detail by de la Mare and Ridd, ref. 15, Chap. 12.

[21] L. M. Stock and H. C. Brown, *J. Am. Chem. Soc.*, **84**, 1242 (1962).

[22] C. Courtot and C. Vignati, *Bull. soc. chim. France*, **[4] 41**, 58 (1927).

[23] A. P. Terent'ev, L. I. Belen'kiĭ and L. A. Yanovskaya, *Zhur. Obshch. Khim.*, **24**, 1265 (1954).

TABLE IV

TYPICAL DATA FOR THE BROMINATION OF FLUORENE IN THE DARK IN DRY ACETIC ACID AT 25°

Time, min.	Titer[a] of 0.0108 N $Na_2S_2O_3$	Reaction,[b] %
0.0	8.91	0.00
89	8.65	2.9
184	8.45	5.2
289	8.19	8.1
422	7.86	11.8
522	7.54	15.4

[a] For 5-ml. sample of reaction mixture. [b] Initial concentration, fluorene, 0.0205 M; bromine 0.00965 M.

Isomer Distribution.—The non-catalytic bromination of biphenyl was carried out in 85% acetic acid in the dark. In order to avoid disubstitution, the aromatic hydrocarbon was kept in large excess. In a typical experiment, 26.73 g. of biphenyl was dissolved in 1000 ml. of 85% acetic acid. To this solution 5.83 g. of bromine was added. The reaction was allowed to proceed in the dark for 39 days. An aliquot of the reaction mixture was analyzed for residual bromine indicating 0.632 g. remained and a theoretical yield of 7.57 g. of bromobiphenyls. The reaction mixture was then transferred to a continuous liquid–liquid extractor and water added. The organic materials were extracted into carbon disulfide over a 30-hour interval. The extraction solvent was stripped off by distillation through a short column. Biphenyl was removed by fractionation under vacuum in the presence of tetraglyme (tetraethylene glycol dimethyl ether) which possesses a vapor pressure intermediate between biphenyl and the bromobiphenyls. The column was then washed down with carbon disulfide and the residual tetraglyme removed by extraction into water. The water layer was subsequently washed with carbon disulfide. The carbon disulfide solutions were combined, concentrated and reextracted with water. This procedure was repeated. After drying, the final solution was concentrated by distillation. The column was washed down with absolute alcohol and the ethanol solution cooled to precipitate *p*-bromobiphenyl. The mother liquor was concentrated and additional *p*-bromobiphenyl recovered. These solid fractions were recrystallized from fresh ethanol to yield two batches of the solid *para* isomer, 4.563 g. (m.p. 90–91°) and 0.719 g. (m.p. 86–89°). The latter material contained a trace of biphenyl as indicated by subsequent infrared analysis and a correction was applied. The infrared spectra of the first batch indicated no contamination by biphenyl and both proved to be free of the *ortho* isomer. The washings and mother liquors were combined and taken up in carbon disulfide. The alcohol was removed by a procedure identical to that described for tetraglyme above. The excess carbon disulfide was distilled providing a slightly yellow 10-ml. solution for infrared analysis.

The infrared spectra of this solution revealed that both *o*- and *p*-bromobiphenyl were present. In these experiments, the absorption bands 13.45 and 12.10 μ were employed for the *o*- and *p*-bromo isomers, respectively.

The concentration of the *p*-bromo isomer was established by the examination of 2 ml. of the resultant solution diluted to 10 ml. Analysis of this solution indicated 1.01 g. of *p*-bromobiphenyl in the total sample. The undiluted sample was analyzed for the *o*-bromo isomer. The absorption band was resolved by the addition of *p*-bromobiphenyl to the reference cell of the double beam instrument. Known mixtures of variable concentration of the *o*-bromo isomer in the presence of 1.0 g. of the *para* isomer were employed to standardize the method. The *ortho* content of this solution was determined by this procedure to be 0.176 g. The total amounts of each isomer are thus established as 0.176 g. of *o*- and 6.294 g. of *p*-bromobiphenyl. The yield was 85.5%. Another experiment carried out in the same manner provided confirmatory results; Table III.

Prior to the utilization of this technique for unknown mixtures, it was tested through the analysis of synthetic mixtures of biphenyl and the bromobiphenyls. These mixtures were treated in the manner described above. Analysis indicated that the found concentration of the *ortho* isomer tended to be low by approximately 20%.

The non-catalytic bromination of fluorene was carried out in dry acetic acid in the dark. Fluorene, 0.500 g., was dissolved in 50 ml. of acetic acid and 50 ml. of a solution of bromine, 0.045 M, in acetic acid added rapidly. The contents were mixed and the reaction allowed to proceed in the dark. After 45 days, analysis indicated 90% of the available bromine had been consumed. An aliquot of the reaction mixture was transferred to a separatory funnel and the excess bromine destroyed with aqueous sodium borohydride. Excess water was added and the organic material extracted into carbon disulfide. The solution was dried over calcium sulfate, filtered and evaporated to dryness. The residual solid was taken up in 10 ml. of carbon disulfide and the solution examined by infrared spectroscopy. From the spectra[24] of pure samples of fluorene, 2-, 4- and 9-bromofluorene, it was apparent that the 4- and 9-bromo isomers were not present in significant concentration in the unknown samples. The addition of fluorene to the reference cell of the instrument resolved the 13.0 μ doublet for the 2-isomer, but no other bands appeared in the spectra. Moreover, the intensity ratio of the 13.0 μ doublet for 2-bromofluorene in the unknown was within experimental error of the ratio calculated from the relative intensities for these bands as exhibited by the pure compound in carbon disulfide.

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[24] We are indebted to Dr. John H. Weisburger for the spectra of pure 4- and 9-bromofluorene.