[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY, LAFAYETTE, IND.]

Rate Data and Isomer Distributions in Aluminum Chloride-catalyzed Acetylation and Benzoylation of Biphenyl and Fluorene in Ethylene Dichloride[1]

BY HERBERT C. BROWN AND GIANLORENZO MARINO[2]

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The second-order rate constant for the aluminum chloride-catalyzed benzoylation of biphenyl in ethylene dichloride at 25° was evaluated as 0.568×10^{-3} l. mole^{-1} sec.$^{-1}$. The reaction proceeded to form 92.2% *p*-phenylbenzophenone. The partial rate factor, p_f^{Ph}, calculated from these data is 245. The relative rate of the aluminum chloride-catalyzed acetylation of biphenyl to benzene was determined to be 85.1 by competitive experiments. Under these conditions 97.3% *p*-phenylacetophenone was formed. Combination of these observations provides the partial rate factor, p_f^{Ph} 248. The competitive acetylation of fluorene and biphenyl revealed the planar fluorene molecule to react 148 fold more rapidly. The only detectable product was 2-acetylfluorene yielding the partial rate factor, 2-Fl_f 38,000. The high yields of *para* isomer obtained in the acetylation and benzoylation of biphenyl are in accord with the steric factor observed for the acylation of toluene and related monoalkylbenzenes. The partial rate factors for acylation in the *para* position are significantly less than the corresponding values for toluene in agreement with the observations for mercuration and ethylation. The high reactivity of fluorene is attributed primarily to the large resonance stabilization of the transition state made possible by the coplanarity of the aromatic system.

Introduction

The available data for the electrophilic substitution of toluene,[3] *t*-butylbenzene[4] and anisole[5] are correlated with satisfactory precision by a linear free energy treatment, the Selectivity Relationship.[6] In extending the examination of the applicability of this treatment to biphenyl and fluorene, rate and isomer distribution data for the mercuration,[7a] ethylation,[7b] acylation and bromination[7c] were obtained. Results for the benzoylation[8] and acetylation[8c,9] reaction are reported in the present paper.

Results

Benzoylation of Biphenyl.—The kinetic procedure for determination of the rate of reaction of benzoyl chloride–aluminum chloride with biphenyl in ethylene dichloride at 25.0° was identical with that previously employed for toluene[8b] and *t*-butylbenzene.[8c] The second-order constant had been observed to increase slightly with an increase in the initial concentration of the acylating agent.[8a] Accordingly, the rate was determined with 0.10 *M* benzoyl chloride–aluminum chloride to provide data for direct comparison under the conditions of the earlier work.

The second-order rate constant was determined to be 0.568×10^{-3} l. mole^{-1} sec.$^{-1}$ at 25°. Comparison of this datum with earlier measurements revealed the relative rate of benzoylation of biphenyl compared to benzene is 90.3 and that for biphenyl compared to toluene is 0.74.

Infrared comparison of the reaction products with standard solutions of pure *p*-phenylbenzophenone indicated the formation of 92.2% of the *para* isomer.

Acetylation of Biphenyl.—The high velocity of the acetylation reaction made it impractical to attempt a direct determination of the rate of acetylation of biphenyl. Consequently, we had recourse to the competitive procedure previously utilized to determine the relative reactivities of the monoalkylbenzenes[8c] and the polymethylbenzenes.[10] Standard solutions of biphenyl and toluene in ethylene chloride at 25.0° were treated with a deficient quantity of the acetyl chloride–aluminum chloride complex in the same solvent. The reaction mixture was quenched and the reaction products analyzed by gas chromatography. A column with a silicone oil substrate operated at 190° proved to be satisfactory for the analysis. Benzophenone was used as an internal standard to establish the actual concentrations of the products formed in the reaction.

The results of several experiments, employing different concentrations of the reactants, are summarized in Table I.

TABLE I

BIPHENYL TO TOLUENE REACTIVITY RATIO FOR THE ALUMINUM CHLORIDE-CATALYZED ACETYLATION IN ETHYLENE DICHLORIDE AT 25.0°

Init. concn.,[a] *M*		Final concn., *M*		Reaction, %	Rel. rate, k_{BP}/k_T
[Biphenyl]	[Toluene]	[CH_3CO-$C_6H_4C_6H_5$]	[CH_3CO-$C_6H_4CH_3$]		
0.120	0.120	0.0336	0.0399	91.9	0.631
.180	.120	.0389	.0385	96.7	.681
.240	.120	.0470	.0327	99.6	.684

[a] 0.0800 *M* acetyl chloride–aluminum chloride and 0.0800 *M* acetyl chloride.

The rate of acetylation of biphenyl relative to toluene, 0.67, is similar to the value obtained in the benzoylation experiment, 0.74. The isomer distribution in biphenyl was established by acetylation under the same conditions as employed in the competitive experiments. Gas chromatographic examination of the product indicated only a single peak. The reaction product was subjected to infrared examination and compared with a standard solution of pure *p*-phenylacetophenone. The

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[1] Directive Effects in Aromatic Substitution. XLVII.

[2] Post-doctorate research associate, 1957–1959, on project no. AT(11-1)-170 supported by the Atomic Energy Commission.

[3] L. M. Stock and H. C. Brown, *J. Am. Chem. Soc.*, **81**, 3323 (1959).

[4] L. M. Stock and H. C. Brown, *ibid.*, **81**, 5621 (1959).

[5] L. M. Stock and H. C. Brown, *ibid.*, **82**, 1942 (1960).

[6] H. C. Brown and K. L. Nelson, *ibid.*, **75**, 6292 (1953).

[7] (a) H. C. Brown, M. Dubeck and G. Goldman, *ibid.*, **84**, 1229 (1962); (b) H. C. Brown and A. Neyens, *ibid.*, **84**, 1233 (1962); (c) H. C. Brown and L. M. Stock, *ibid.*, **84**, 1238 (1962).

[8] (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) **81**, 5611 (1959).

[9] H. C. Brown, G. Marino and L. M. Stock, *ibid.*, **81**, 3310 (1959).

[10] G. Marino and H. C. Brown, *ibid.*, **81**, 5929 (1959).

analysis indicated the formation of this isomer in 97.3% of the theoretical yield.

These data lead to the partial rate factor for the acetylation reaction, p_f^{Ph} 245.

Acetylation of Fluorene.—Preliminary experiments involving the competitive acetylation of fluorene and biphenyl indicated fluorene reacted 150–200 times faster. To minimize the errors involved in the competitive method for large reactivity ratios,[11] it was decided to compare biphenyl and fluorene *via* suitable aromatic derivatives of intermediate reactivity.

Prehnitene (rate relative to benzene, 7300[10]) and *o*-xylene (relative rate, 2130[10]) proved to be suitable reference compounds. Accordingly, competitive acetylations of fluorene and prehnitene or *o*-xylene were carried out under the standard conditions. The products were examined by gas chromatography. Results of these experiments are reported in Table II.

TABLE II

COMPETITIVE ACETYLATION OF FLUORENE AND PREHNITENE OR *o*-XYLENE IN ETHYLENE DICHLORIDE AT 25.0°

Init. concn., *M* [Fluorene]	Init. concn., *M* [Prehnitene]	Init. concn., *M* [*o*-Xylene]	Final concn., *M* [Acetylfluorene]	Final concn., *M* [CH_3COAr]	Rel. rates k_{Fl}/k_{ArH}	Rel. rates k_{Fl}/k_B
0.120[a]	0.120		0.03901	0.0239	1.77	12,900
.240[a]	0.120		.0464	.0147	1.64	12,000
.120[b]		0.120	.0579	.0123	6.1	13,000
					Mean value	12,600

[a] 0.063 *M* acetyl chloride–aluminum chloride, 0.063 *M* acetyl chloride. [b] 0.070 *M* acetyl chloride–aluminum chloride, 0.070 *M* acetyl chloride.

The product formed in the acetylation of fluorene was subjected to infrared comparison with a sample of 2-acetylfluorene. It was concluded that 2-acetylfluorene had been formed in essentially 100% yield. No other material could be detected.

Discussion

The relative rate data, isomer distributions and partial rate factors for the benzoylation and acetylation of biphenyl and fluorene are summarized in Table III.

TABLE III

PARTIAL RATE FACTORS FOR THE ALUMINUM CHLORIDE-CATALYZED ACYLATION OF BIPHENYL AND FLUORENE IN ETHYLENE DICHLORIDE AT 25.0°

Aromatic	Reaction	Rel. rate k_{ArH}/k_B	Partial rate factors			
			o_f	m_f	p_f	2-Fl_f
Toluene	Benzoyln.	117	32.6	4.9	626	
Biphenyl	Benzoyln.	90.3		(0.3)[a]	245	
Toluene	Acetyln.	128	4.5	4.8	749	
Biphenyl	Acetyln.	85.1		(0.3)[a]	248	
Fluorene	Acetyln.	12600				38,000

[a] Estimated from relative rate of acylation of *para* substituted anisoles, ref. 12.

The benzoylation of toluene provided 89.3% *p*-, 1.4% *m*- and 9.3% *o*-methylbenzophenone.[8] Acetylation, surprisingly, involves somewhat greater steric interactions in the transition state. This reaction yielded less *ortho* and more *para* isomer,[9] 97.5% *p*-, 1.3% *m*- and 1.2% *o*-methylacetophenone. In the present study no attempt to analyze for the minor products was made. The yields of *para* isomer spectroscopically identified are 92.2% *p*-phenylbenzophenone and 97.3% *p*-phenylacetophenone. The formation of more *ortho* isomer, as implied by the yield of *para* products, in the benzoylation is consistent with the observations for the corresponding acylations in toluene.

The analysis did not indicate the formation of any *meta* isomers. An estimate for m_f^{Ph} in the acetylation reaction may be calculated from the relative rates of acetylation of *p*-methylanisole and *p*-phenylanisole.[12] The value obtained, m_f^{Ph} 0.3, is in agreement with the formation of only traces of the *meta* isomer. The partial rate factor and experimental relative rate predict the formation of 0.2% *m*-acetylbiphenyl. This concentration is far too small to be detected by direct infrared analysis.

In the acylation reaction, as in the mercuration[7a], and ethylation[7b] reactions previously described, biphenyl is considerably less reactive than toluene.[13] As indicated by the partial rate factors, Table III, the same pattern of reactivity is maintained in the far more selective acylation reactions. That is, the inductive influence of the substitutent phenyl and methyl groups control relative rate in the *meta* position. On the other hand, the *para* position in both aromatics is activated toward electrophilic substitution with the methyl group possessing the ability to stabilize the activated complex to a slightly greater extent than *p*-phenyl.

Presumably, the consistent lower reactivity of the *p*-phenyl substituent in these reactions has a common physical basis. A lowered resonance contribution by the aryl group arising from the noncoplanar conformation of the biphenyl system provides an attractive explanation. The higher reactivity of fluorene, 2-Fl_f 38,000, is consistent with this view.[14]

Experimental Part

Materials.—Aluminum chloride, ethylene dichloride and acetyl chloride were purified as previously described.[8,9] Biphenyl and fluorene were available from a previous study.[7a] *p*-Phenylacetophenone was synthesized following the procedure of Long and Henze[15] and recrystallized twice from ethanol; m.p. 118.5–119.5°. *p*-Methylacetophenone (Eastman Kodak Co.) exhibited the presence of the *ortho* and *meta* isomers in the amounts realized in the direct acylation.[8c] The product was purified by conversion to the semicarbazone, repeated recrystallization, followed by hydrolysis to the ketone. Gas chromatographic examination of the product demonstrated the absence of the *ortho* and *meta* isomers. 2-Acetylfluorene (K. and K. Laboratories) was recrystallized from ethanol.

Benzoylation of Biphenyl.—The kinetics of benzoylation of biphenyl were followed by use of the procedures previously developed for determination of the rates of benzoylation of benzene and toluene.[8]

The following procedure was employed for the determination of the percentage of *p*-phenylbenzophenone formed in the reaction. The benzoylation of biphenyl was carried out under the same conditions as the kinetic experiments. The

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[11] See discussion by T. S. Lee in "Technique of Organic Chemistry," Vol. VIII, Interscience Publishers, Inc., New York, N. Y., 1953, p. 110.

[12] H. C. Brown and G. Marino, unpublished results.

[13] S. Komoto, *J. Pharm. Soc. Japan*, **75**, 727 (1955), has recently reported the relative rate of acetylation of biphenyl with respect to toluene at 48° in carbon disulfide is 3.2. He indicated that experimental difficulties decreased the precision of his measurements. However, his value is in serious disagreement wih the reactivity ratio, 0.67, reported here.

[14] For a detailed discussion of this question, with pertinent literature references, see the final paper of this group, L. M. Stock and H. C. Brown, *J. Am. Chem. Soc.*, **84**, 1242 (1962).

[15] L. M. Long and H. R. Henze, *ibid.*, **63**, 1939 (1941).

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]

BY HERBERT C. BROWN AND LEON M. STOCK[4]

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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.

[4] Department of Chemistry, University of Chicago. Monsanto Chemical Co. Fellow at Purdue University, 1957–1958.

[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).