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

The Selectivity Relationship. An Examination of the Electrophilic Substitution, Electrophilic Side-chain and Hammett Side-chain Reactions of Toluene and Tolyl Derivatives[1-3]

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The available data for forty-seven electrophilic substitution reactions of toluene have been examined by conventional statistical methods for adherence to the Selectivity Relationship and related equations. The fit of the data to these equations is excellent, with an average percentage error in the reaction constant of 7.3%. Electrophilic side-chain and the normal Hammett side-chain reactions have been investigated similarly. In these cases the deviations from the least squares regression lines are somewhat larger, 17.2 and 18.5%, respectively. The statistical analysis of the complete series of electrophilic substitution reactions yields a value of −0.280 ± 0.04 for the *p*-methyl electrophilic substituent constant, in reasonable agreement with the value, −0.311, derived from the *t*-cumyl solvolysis data.

Introduction

In 1953, it was pointed out that the apparent anomaly concerning the formation of high proportions of the *m*-alkyltoluene in the Friedel–Crafts alkylation reaction under kinetically controlled conditions could be resolved in terms of the high reactivity and low selectivity of the electrophilic reagent.[5] At the same time, although the data for other electrophilic substitution reactions of toluene were scanty and of variable quality, its examination indicated a possible correlation through the linear relation

$$\log p_f = b \log (p_f/m_f) \qquad (1)$$

The partial rate factors[6] then available were insufficient to provide a clear test of the proposed linear relationship. Indeed, several authors have noted their skepticism that such a relationship should exist.[7-9]

More recently, it has been shown that this expression (1) is the direct result of a Hammett free energy relationship.[10,11] Furthermore, it was possible to derive three equations from the Hammett equation and to evaluate the slope, *b*, of each in terms of σ-constants (2,3,4)[11,12]

$$\log p_f = \frac{\sigma_p}{\sigma_m} \log m_f \qquad (2)$$

$$\log p_f = \frac{\sigma_p}{\sigma_p - \sigma_m} \log (p_f/m_f) = \frac{\sigma_p}{\sigma_p - \sigma_m} S_f \qquad (3)$$

$$\log m_f = \frac{\sigma_m}{\sigma_p - \sigma_m} \log (p_f/m_f) = \frac{\sigma_m}{\sigma_p - \sigma_m} S_f \qquad (4)$$

In recent years the availability of powerful research techniques such as infrared spectroscopy and isotopic dilution methods have permitted intensive investigations of these substitution reactions. The observations provided by these studies now allow a rigid test of the validity of the Selectivity Relationship[6,12] for toluene. Accordingly, the results of previous investigations have been compiled and the adherence to a linear free energy relationship examined by statistical methods.

Certain electrophilic side-chain reactions, *e.g.*, the ionization of substituted triarylmethyl alcohols[13] and the solvolysis of substituted phenyldimethylcarbinyl chlorides,[14,15] have been proposed as models for aromatic substitution. These reactions provide a convenient method for the establishment of σ-constants for reactions involving electron deficient intermediates. Hence, it was desirable to compare the results of these studies with the Selectivity Relationship. Finally, it appeared desirable to compare the applicability and precision of this proposed relationship for electron deficient systems with that of the long established Hammett equation[10] for the so-called normal side-chain reactions of *m*- and *p*-tolyl derivatives.

Compiled Data and Statistical Evaluation.—For convenience, the data under examination have been divided into four reaction series. The first series is composed of 47 different substitution reactions of toluene, Table I. To our knowledge, this includes all data in the literature, with but one omission. The reaction omitted, deuterium exchange in aqueous perchloric acid,[16] provides partial rate factors considerably at variance with the observations of two other investigations (Table I, entries

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(3) Based 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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TABLE I[a]

ELECTROPHILIC SUBSTITUTION REACTIONS OF TOLUENE

	Reaction[b]	o_f	m_f	p_f	S_f	$\frac{\log p_f}{\log m_f}$	$-\rho$	$\Delta\rho$	Ref.
1	Deuterium exchange, DBr, 25°	1000	6.0	6000	3.000	4.86	12.39	1.10	50
2*	Bromination, Br_2, 85% HOAc, 25°	600	5.5	2420	2.644	4.57	11.40	0.68	18
3	Chlorination,[c] Cl_2, HOAc, 24°	600	5.0	870	2.241	4.21	10.32	.18	40–42
4*	Chlorination, Cl_2, HOAc, 25°	617	4.95	820	2.219	4.19	10.24	.17	19
5	Bromination,[c] Br_2, HOAc, 25°		4.72	534	2.053	4.05	9.66	.08	43
6*	Benzoylation, C_6H_5COCl, $AlCl_3$, $C_6H_5NO_2$, 25°	32.6	5.0	831	2.221	4.18	10.28	.15	20
7*	Benzoylation, C_6H_5COCl, $AlCl_3$, 25°	30.7	4.8	589	2.090	4.07	9.88	.01	21
8*	Benzoylation, C_6H_5COCl, $AlCl_3$, $C_2H_4Cl_2$, 25°	32.6	4.9	626	2.107	4.05	10.00	.01	22
9*	Acetylation, CH_3COCl, $AlCl_3$, $C_2H_4Cl_2$, 25°	4.5	4.8	749	2.192	4.22	10.07	.19	23
10	Basicity,[c] HF, 20°	145	3.6	414	2.061	4.71	8.71	.64	44, 29
11*	Deuteration, D_2O, CF_3CO_2H, 70°	253	3.8	421	2.044	4.52	8.89	.48	38
12	Deuteration, CF_3CO_2H, 25°	263	3.57	350	1.992	4.61	8.54	.54	51
13*	Chloromethylation, CH_2O, HCl, $ZnCl_2$, HOAc, 60°	117	4.37	430	1.993	4.11	9.35	.06	5
14	Basicity,[c] HF, BF_3, n-C_7H_{16}, 20°	103	3.1	145	1.670	4.40	7.42	.30	45–47
15	Iodination,[c] ICl, $ZnCl_2$, HOAc, 25°	144	6.58	230	1.544	2.89	10.14	1.71	48
16	Deuteration, 68%, H_2SO_4, 25°	83	1.9	83	1.640	6.88	5.45	1.40	9
17	Tritiation, 80.8% H_2SO_4, 25°	70	2.2	63	1.457	5.26	5.69	0.73	17
18*	Bromination, HOBr, $HClO_4$, 50% dioxane, 25°	76	2.5	59	1.373	4.45	6.05	.27	24
19*	Chlorination, HOCl, $HClO_4$, H_2O, 25°	134	4.0	82	1.311	3.18	7.77	.94	25
20*	Brominolysis, $ArB(OH)_2$, Br_2, 20% HOAc, 25°		3.3	78.5	1.373	3.63	7.17	.40	39
21*	Nitration, HNO_3, 90% HOAc, 45°	42	2.5	58	1.366	4.43	6.04	.26	26
22*	Nitration, $AcONO_2$, Ac_2O, 0°	47.3	3.56	60.3	1.229	3.23	7.05	.95	27
23*	Nitration, $AcONO_2$, Ac_2O, 30°	40.4	3.04	51.2	1.226	3.54	6.47	.53	27
24*	Nitration, HNO_3, CH_3NO_2, 30°	36.6	2.33	46.1	1.297	4.53	5.63	.31	27
25*	Sulfonylation, $C_6H_5SO_2Cl$, $AlCl_3$, 25°	6.8	2.09	30.2	1.160	4.63	4.97	.32	28
26*	Detrimethylsilylation, $ArSiMe_3$, Br_2, 98.5% HOAc, 25°		3.2	49	1.185	3.35	6.68	.65	33
27*	Mercuration, $Hg(OAc)_2$, $HClO_4$, HOAc, 25°	4.98	2.25	32.9	1.165	4.31	5.26	.16	29
28*	Mercuration, $Hg(OAc)_2$, $HClO_4$, HOAc, 50°	4.20	2.41	28.8	1.077	3.82	5.38	.17	29
29*	Mercuration, $Hg(OAc)_2$, $HClO_4$, HOAc, 70°	3.24	2.23	24.5	1.041	3.99	5.00	.04	29
30*	Detrimethylsilylation, $ArSiMe_3$, $HClO_4$, 50% MeOH, 51.2°		2.3	21.2	0.964	3.66	5.00	.26	34
31*	Detrimethylsilylation, $ArSiMe_3$, HCl, HOAc, 25°		2.14	20.1	.973	3.95	4.72	.07	35
32*	Mercuration, $Hg(OAc)_2$, HOAc, 25°	5.71	2.23	23.0	1.014	3.91	4.95	.09	30
33*	Mercuration, $Hg(OAc)_2$, HOAc, 50°	4.60	1.98	16.8	0.928	4.12	4.17	.13	30
34*	Mercuration, $Hg(OAc)_2$, HOAc, 70°	4.03	1.83	13.5	.867	4.30	3.78	.03	30
35*	Mercuration, $Hg(OAc)_2$, HOAc, 90°	3.51	1.70	11.2	.819	4.56	3.84	.51	30
36*	Detrimethylsilylation, $ArSiMe_3$, p-$C_7H_7SO_3H$, HOAc, 25°	17.5	2.0	16.5	.917	4.05	4.10	.27	36
37*	Detrimethylsilylation, $ArSiMe_3$, p-$C_7H_7SO_3H$, H_2O, HOAc, 25°	15.7	2.19	14.3	.815	3.40	4.53	.41	37
38*	Detrimethylsilylation, $ArSiMe_3$, 0.02 M $Hg(OAc)_2$, HOAc, 25°	10.8	1.99	11.5	.762	3.55	4.06	.27	37
39	Detrimethylsilylation, $ArSiMe_3$, 0.4 M $Hg(OAc)_2$, HOAc, 25°	11.3	2.15	12.3	.758	3.29	4.35	.46	37
40*	Methylation, CH_3Br, $GaBr_3$, ArH, 25°	9.51	1.7	11.8	.842	4.66	3.06	.27	12, 31
41*	Ethylation, C_2H_5Br, $GaBr_3$, ArH, 25°	2.84	1.56	6.02	.587	4.04	2.66	.15	12, 31
42*	Isopropylation, i-C_3H_7Br, $GaBr_3$, ArH, 25°	1.52	1.41	5.05	.554	4.72	2.54	.38	32
43	Methylation, CH_3Br, $AlBr_3$, ArH, 0–5°	6.07	1.96	6.56	.525	2.80	3.39	.87	52
44	Methylation, CH_3Br, $AlBr_3$, ArH, 27–32°	4.41	1.85	5.19	.448	2.68	3.21	.66	52
45	Methylation, CH_3I, $AlBr_3$, ArH, −1 to 2°	7.02	1.73	11.0	.807	4.39	3.59	.14	52
46	Methylation, CH_3Br, $AlBr_3$, 1,2,4-$C_6H_3Cl_3$, 25°	8.60	1.81	9.80	.733	3.84	3.64	.10	53
47	Benzylation, $C_6H_5CH_2Br$, $GaBr_3$, ArH, 25°	4.91	2.32	9.43	.609	2.66	4.39	.91	54

[a] An asterisk indicates that the partial rate factors are known with some confidence. [b] Electrophilic reaction is given first, then the molecule examined if other than toluene followed by the electrophilic reagent, catalyst, solvent and temperature in that order. [c] Partial rate factors calculated from rate data for the polymethylbenzenes.

16 and 17) for the exchange reaction carried out under similar conditions.[9,17]

The second group was gathered by the critical examination of the substitution data in the first series. Those included in the selected second series are substitution reactions whose partial rate factors have been obtained through a careful examination of the isomer distribution and for which either a kinetic or thoroughly tested com-

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TABLE II

SIDE-CHAIN ELECTROPHILIC REACTIONS

Reaction	o_f	m_f	p_f	S_f	$\frac{\log p_f}{\log m_f}$	$\sigma^+_{p\text{-CH}_3}$[a]	Ref.
Ionization, Ar_3COH, H_2SO_4, 25°		1.24	10.5	0.927	10.97	−0.24[b]	13, 57
Ionization, Ar_3CCl, SO_2, 0°	20.2	2.32	22.4	.984	3.69	.26	58
Migration aptitude, $(Ar_2COH)_2$		1.94	15.7	.908	4.15	.29	59
Rearrangement, $ArCHOHCH{=}CHCH_3$	2.00	1.21	8.99	.871	11.49	.73	60
Solvolysis, $ArCMe_2Cl$, 90% acetone, 25°	3.63	2.00	26.0	1.113	4.70	.31	61
Solvolysis, Ar_2CHCl, 66.7% acetone, 0°		1.72	32.1	1.280	6.40	.44	62
Solvolysis, Ar_2CHCl, 70% acetone, 0°		1.76	32.5	1.266	6.20	.43	62
Solvolysis, Ar_2CHCl, 80% acetone, 0°		1.79	32.9	1.265	6.02	.42	62
Solvolysis, Ar_2CHCl, 90% C_2H_5OH, 0°		1.93	30.9	1.204	5.21	.36	62
Solvolysis, Ar_2CHCl, C_2H_5OH, 25°	2.9	2.1	16.2	0.888	3.76	.26	63
Solvolysis, $ArCH_2OTs$, HOAc, 40°		2.6	56.5	1.337	4.22	.29	64
Solvolysis, $ArCH_2OTs$, 76.6% acetone, 25.3°		1.79	29.8	1.221	5.83	.40	65
Solvolysis, $ArCH_2Cl$, 48% C_2H_5OH, 30°	4.95	1.30	9.37	0.858	8.53	.59	66
Solvolysis, $ArCH_2Cl$, 48% C_2H_5OH, 83°	4.78	1.39	10.6	.877	7.26	.50	66
Solvolysis, $ArCH_2Cl$, 50% acetone, 30°	4.36	1.24	7.7	.794	9.50	.66	67
Solvolysis, $ArCH_2Cl$, 50% acetone, 60°	4.11	1.20	8.7	.860	11.86	.82	67
Solvolysis, $ArC(CH_3)_2CH_2OBs$, HOAc, 75°		1.93	7.27	.576	3.01	.21	68

[a] Calculated from log p_f/log m_f with $\sigma_{m\text{-CH}_3}$ − 0.069 unless otherwise indicated. [b] Published value of Deno and Evans, ref. 13.

petitive procedure has been employed to determine the relative rate, toluene to benzene.[18–32] Further data included in this group are derived from kinetic studies of replacement reactions, detrimethylsilylation,[33–37] entries 26, 30, 31, 36-39; deuterium exchange,[38] entry 11; and brominolysis of arylboronic acids,[39] entry 20. On the other hand, those reactions whose relative rate or equilibrium constants depend on the calculation of partial rate factors from observations on the higher methylbenzenes,[40–48] entries 3, 5, 10, 14, 15; where serious steric factors or the relative stability of π-complexes may be important,[18,48,49] in addition to other deuterium exchange reactions,[9,17,50,51] entries 1, 12, 16, 17; and those reactions which are subject to major kinetic errors due to difficult experimental problems,[52–55] entries 43–47, have been omitted from this preferred group. These restrictions result in the selection of 32 reactions for which the partial rate factors are known with considerable confidence. These selected reactions are indicated by an asterisk in Table I.

The third series of reactions is composed of those side-chain reactions of *m*- and *p*-tolyl derivatives in which an electron deficient intermediate or transition state may be expected to have a significant role in the determination of relative reactivity, Table II.[56–68]

The fourth sequence of reactions was from typical side-chain reactions of the Hammett type. For this purpose, the reactions of *m*- and *p*-tolyl deriva-

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TABLE III

HAMMETT SIDE-CHAIN REACTIONS OF *m*- AND *p*-TOLYL DERIVATIVES

	Reaction	log m_t	log p_t	log (p_t/m_t)	$\frac{\log p_t}{\log m_t}$	Ref.
1	Solvolysis of benzyl fluorides in ethanol at 76°	−0.024	−0.899	−0.875	37.5	[a]
2	Decomposition of benzoyl peroxides in dioxane at 80°	.020	.165	0.145	8.25	[b]
3	Acid hydrolysis of arylsulfuric acids at 78.6°	− .020	− .149	− .129	7.45	[c]
4	Ionization of anilinium ions in water at 25°	− .090	− .490	− .400	5.44	[d]
5	2-Methylbenzoic acids with phenyldiazomethane at 30°	− .040	− .172	− .132	4.30	[e]
6*	Anilines with formic acid in pyridine–water at 100°	.050	.193	.143	3.86	[f]
7*	Hydrolysis of formanilides in pyridine–water at 100°	− .0035	− .123	− .120	3.51	[g]
8*	Ionization of benzoic acids in water at 25°	− .040	− .140	− .100	3.50	[h]
9*	Benzoic acids with cyclohexanol at 65°	− .043	− .150	− .107	3.49	[i]
10*	Phenolate ions with propylene oxide in 98% ethanol at 70°	.069	.229	.160	3.32	[j]
11	Anilines with dinitrochlorobenzene in ethanol at 25°	.128	.398	.270	3.11	[k]
12*	Alkaline methanolysis of *l*-menthyl benzoates at 40°	.124	.364	.240	2.94	[l]
13*	Hydrolysis of benzoyl chlorides in acetone–water at 0°	.165	.461	.296	2.79	[m]
14	Anilines with dinitrochloronaphthalene in ethanol at 25°	.216	.545	.329	2.52	[k]
15*	Anilines with formic acid in pyridine–water at 100°	.071	.173	.102	2.44	[g]
16	Anilines with dinitrochlorobenzene in ethanol at 100°	.170	.390	.220	2.29	[k]
17*	Ionization of phenols in 48% ethanol at 20–22°	− .150	− .330	− .180	2.20	[n]
18*	Ionization of 2-methylbenzoic acids in 50% ethanol at 25°	− .161	− .320	− .159	1.99	[e]
19*	Phenolate ions with sodium methylsulfate in water at 100°	.050	.099	.049	1.98	[o]
20*	Phenolate ions with ethyl iodide in ethanol at 25°	.062	.117	.055	1.89	[p]
21	Ionization of phenols in water at 25°	− .130	− .240	− .110	1.85	[q]
22*	Alkaline hydrolysis of benzamides in water at 100°	− .099	− .181	− .082	1.83	[r]
23*	Ethanolysis of benzoyl chlorides at 25°	− .069	− .118	− .049	1.71	[s]
24*	Hydrolysis of ethyl benzoates in 51% acetone at 25°	− .235	− .403	− .168	1.71	[t]
25*	Ionization of pyridinium ions in water at 25°	− .510	− .850	− .340	1.67	[u]
26*	Ionization dimethylanilinium ions in 50% ethanol at 20°	− .450	− .730	− .280	1.62	[v]
27*	Ionization of thiophenols in 95% ethanol at 20°	− .240	− .380	− .140	1.58	[n]
28*	Alkaline hydrolysis of ethyl phenylacetates in 56% acetone at 25°	− .152	− .226	− .074	1.49	[t]
29*	Alkaline hydrolysis of benzyl acetates in 56% acetone at 25°	− .109	− .152	− .043	1.39	[t]
30*	Ionization of thiophenols in 48.9% ethanol at 20–22°	− .210	− .290	− .080	1.38	[w]
31*	Phenolate ions with ethylene oxide in 98% ethanol at 70.4°	.096	.132	.036	1.38	[j]
32*	Ionization of phenylpropionic acids in water at 25°	− .018	− .024	− .006	1.33	[x]
33	Decomposition of benzoyl peroxides in acetophenone at 80°	.139	.135	− .004	.971	[y]
34	Acetophenones with bromine in 75% acetic acid at 25°	.085	.049	− .036	.565	[z]
35	Ionization of phenylboronic acids in 25% ethanol at 25°	− .290	− .150	.140	.517	[aa]
36	Alkaline hydrolysis of formanilides in pyridine–water at 100°	− .067	− .028	.039	.418	[f]
37	Alkaline hydrolysis of ethylbenzoates in 87.36% ethanol at 25°	− .151	− .330	− .179	.330	[bb]
38	Acid-catalyzed esterification of benzoic acids in ethanol at 25°	− .054	.012	− .042	.220	[cc]
39	Acid hydrolysis of benzyl acetates in 56% acetone at 25°	− .043	.012	.055	− .279	[t]
40	Acid hydrolysis of phenyl acetates in 56% acetone at 25°	− .013	.025	.038	− 1.92	[t]
41	Methanolysis of benzoyl chlorides at 0°	.062	− .158	− .220	− 2.55	[s]
42	Acid hydrolysis of benzamides in water at 100°	.002	− .048	− .050	−24.0	[r]

[a] W. T. Miller and J. Bernstein, THIS JOURNAL, **70**, 3600 (1948). [b] C. G. Swain, W. H. Stockmayer and J. T. Clarke, *ibid.*, **72**, 5426 (1950). [c] G. N. Burkhardt, C. Horrex and D. I. Jenkens, *J. Chem. Soc.*, 1654 (1936). [d] N. F. Hall and M. R. Sprinkle, THIS JOURNAL, **54**, 3469 (1932); M. Kilpatrick and C. A. Arenberg, *ibid.*, **75**, 3812 (1953). [e] J. D. Roberts and J. A. Yancey, *ibid.*, **73**, 1011 (1951). [f] O. C. M. Davis, *Z. physik. Chem.*, **78**, 353 (1912). [g] O. C. M. Davis and R. W. Rixon, *J. Chem. Soc.*, **107**, 728 (1915). [h] G. Briegleb and A. Bieber, *Z. Elektrochem.*, **55**, 250 (1951). J. F. J. Dippy, *Chem. Revs.*, **25**, 151 (1939). [i] R. J. Hartman, H. M. Hoogsteen and J. A. Moede, THIS JOURNAL, **66**, 1714 (1944). [j] D. R. Boyd and E. R. Marle, *J. Chem. Soc.*, **105**, 2117 (1914). [k] H. J. Van Opstall, *Rec. trav. chim.*, **52**, 901 (1933). [l] R. W. Taft, M. S. Newman and F. H. Verhoek, THIS JOURNAL, **72**, 4511 (1950). [m] G. Berger and S. C. J. Olivier, *Rec. trav. chim.*, **46**, 516 (1927). [n] G. Schwarzenbach and E. Rudin, *Helv. Chim. Acta*, **22**, 360 (1939). [o] G. H. Green and J. Kenyon, *J. Chem. Soc.*, 1589 (1950). [p] L. J. Goldsworthy, *ibid.*, 1254 (1926). [q] F. G. Bordwell and G. D. Cooper, THIS JOURNAL, **74**, 1058 (1952). G. E. Spengling and C. W. Lewis, *ibid.*, **75**, 5709 (1953); C. M. Judson and M. Kilpatrick, *ibid.*, **71**, 3115 (1949). [r] E. E. Reid, *Am. Chem. J.*, **21**, 284 (1899); **24**, 397 (1900). [s] J. F. Norris and H. H. Young, THIS JOURNAL, **57**, 1420 (1935). [t] E. Tommila and C. N. Hinshelwood, *J. Chem. Soc.*, 1801 (1938). [u] H. C. Brown and D. H. McDaniel, THIS JOURNAL, **77**, 3752 (1955); H. C. Brown and X. R. Mihm, *ibid.*, **77**, 1723 (1955). [v] R. A. Benkeser and H. R. Krysiak, *ibid.*, **75**, 2421 (1953); W. C. Davies and H. W. Addis, *J. Chem. Soc.*, 1622 (1937). [w] G. Schwarzenbach and H. Egli, *Helv. Chim. Acta*, **17**, 1183 (1934). [x] J. F. J. Dippy and J. E. Page, *J. Chem. Soc.*, 357 (1938). [y] A. T. Blomquist and A. J. Buselli, THIS JOURNAL, **73**, 3883 (1951). [z] W. S. Nathan and H. B. Watson, *J. Chem. Soc.*, 217 (1933); D. P. Evans, V. G. Morgan and H. B. Watson, *ibid.*, 1167 (1935). [aa] J. F. J. Dippy, *Chem. Revs.*, **25**, 151 (1939). [bb] K. Kindler, *Ann.*, **450**, 1 (1926). [cc] R. J. Hartman and A. M. Borders, THIS JOURNAL, **59**, 2107 (1937).

tives tabulated by Jaffé have been utilized.[69] Jaffé lists 42 reactions for which both m_t and p_t are known. In order to examine the data in critical detail those reactions involving radicals, polysubstituted aromatic compounds, nucleophilic substitutions and data obtained in two or more different laboratories were rejected prior to further

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(69) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953). We are indebted to Mr. A. Tsukamoto for the compilation of the original data from the literature cited by Jaffé.

examination. These considerations eliminated 10 reactions. Surprisingly, for the remaining reactions the log p_f/log m_f ratio varied from 37.5 to −1.92. This variation is due in part, if not entirely, to the errors accompanying the determination of small differences in the rate of equilibrium constants in these systems. In order to provide a series of reactions which would agree reasonably well with an equation of the Hammett type, we have arbitrarily discarded those few results for which the log p_f/log m_f value is greater than 4.0 or less than 1.0. The selected reactions are indicated by an asterisk in Table III.

Each reaction series has been examined statistically for fit to equations 2, 3 and 4. The results of the least squares analysis and the σ-constant calculated from the slope are reported in Table IV.

TABLE IV

STATISTICAL CONSTANTS FOR INDICATED REACTION SERIES

	Reaction series[a]	Correlation equation	b[b]	r[c]	s[d]	n[e]	$\sigma^+_{p\text{-CH}_3}$[f]
1	All electrophilic substitution reactions	2	4.026	0.916	0.320	47	−0.278
		3	1.316	.999	.102	47	− .287
		4	0.316	.978	.103	47	− .285
2	Thirty two selected substitution reactions	2	4.019	.999	.208	32	− .277
		3	1.325	.999	.069	32	− .282
		4	0.325	.990	.068	32	− .281
3	Electrophilic side-chain reactions	2	4.858	.853	.408	17	− .335
		3	1.223	.997	.099	17	− .378
		4	0.223	.929	.098	17	− .378
4	Hammett side-chain reactions	2	1.724	.976	.076	23	− .119
		3	2.052	.963	.094	23	− .134
		4	1.054	.874	.093	23	− .134

[a] See text for basis of selection. [b] Least square regression line slope. [c] Correlation coefficient. [d] Standard deviation from regression line. [e] Number of reactions examined in each series. [f] Calculated from slope, b, and $\sigma_{m-\text{CH}_3}$ −0.069.

The correlation coefficient may be unambiguously interpreted and following Jaffé's suggestion $r > 0.99$ indicates excellent, > 0.95 satisfactory and > 0.90 fair fit to the developed regression equations.[69] However, the standard deviation, s, does not lend itself to simple interpretation since it depends on the absolute magnitude of the data included in the correlation.[69] It appeared desirable then to examine the precision of the equations by another method. This was accomplished by the adoption of the σ-values, σ_m −0.069 and σ_p^+ −0.280, and the computation of ρ for both the m- and p-positions.

$$\rho_m = (\log m_f)/\sigma_m \qquad (5)$$

$$\rho_p = (\log p_f)/\sigma_p^+ \qquad (6)$$

The ρ-values for each reaction were averaged and the percentage difference determined. This variation in ρ is then a direct measure of the variation in the log of the appropriate partial rate factor or in the difference in free energy for the process. The percentage error in ρ was then averaged over all the data in the reaction series. This value is reported in Table V together with the σ-values utilized for the computation.

TABLE V

PERCENTAGE ERROR IN ρ FOR EACH REACTION SERIES

	Reaction series[a]	σ_p^+	σ_m	n[b]	Average % error in ρ
1	All electrophilic substn.	−0.280	−0.069	47	7.25
2	Thirty two selected substn.	− .280	− .069	32	5.36
3	Electophilic side-chain	− .378	− .069	17	17.2
		− .280	− .069	17	24.9
4	Hammett side-chain	− .129	− .069	23	18.5
		− .170	− .069	23	20.8

[a] See text for basis of selection. [b] Number of reactions in each series.

Discussion

Evaluation of the Linear Free Energy Relationship.—On the basis of the statistical constants developed from the least squares analysis in accord with the conditions (stated above) as specified by Jaffé,[69] the second series of 32 critically selected electrophilic substitution reactions indicates excellent agreement with a linear free energy relationship for each equation (2, 3, 4), Table IV. The log p_f/log m_f ratio is quite constant 4.04 ± 0.37. A plot of the data, log p_f vs. log(p_f/m_f) Fig. 1 (closed circles), also reveals this excellent agreement. This treatment is equivalent to a plot of log p_f against log m_f. As Gold and Satchell have pointed out, the linearity of such a diagram provides an excellent test of a linear free energy relationship.[9] Furthermore, the average percentage error in ρ is only 5.36. These 32 reactions then fulfill all the requirements by which a free energy relationship may be tested. It is clear that such a relationship does apply to the experimental observations.

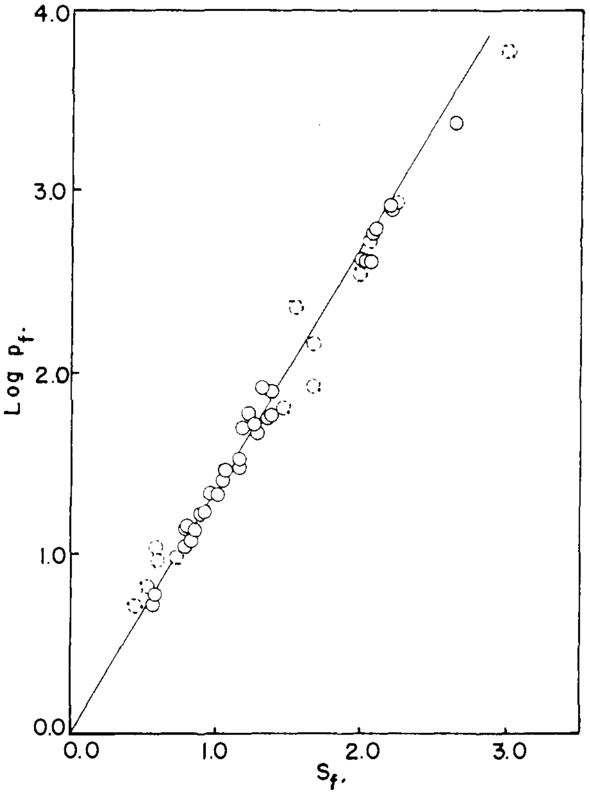

Fig. 1.—Relationship between log p_f and Selectivity Factor, S_f, for electrophilic substitution reactions of toluene. Points which are established with confidence are indicated by closed circles.

Consideration of the complete first series, comprised of all the electrophilic substitution data, reveals that equations, 2, 3 and 4 provide fair, excellent and satisfactory agreement with a linear free energy relationship as measured by the correlation coefficient. When the experimental difficulties and potential errors involved in the evaluation of m_f are considered, the agreement must be regarded as somewhat more than satisfactory. For the purpose of this discussion, the ratio log p_f/log m_f provides a valuable measure of the adherence to the Selectivity Relationship. For the entire series this ratio is 4.04 ± 0.55 and identical to the value obtained for the selected reactions.

The higher limit for this ratio, 6.88, was obtained by Gold and Satchell[9] for the deuterium exchange reaction, entry 16, Table I. Indeed, the various measurements concerning these exchange reactions, entries 1, 11, 12, 16 and 17, provide varying observations, log p_f/log m_f ratio ranging between 6.88 and 4.52. It would be highly desirable to establish whether these variations are real or merely the consequence of the relatively difficult technique involved in these measurements.

The minimum value for log p_f/log m_f has been obtained in the reaction of toluene with benzyl bromide catalyzed by gallium bromide,[54] entry 47. Low values of this ratio also are reported for other alkylation experiments.[52,53] A characteristic of such reactions is their sensitivity to isomerization and disproportionation under the influence of the electrophilic catalysts. The relative rate data established for the systems noted above could be determined only through the employment of competitive flow reactor techniques. Furthermore, in the case of methylations, the competitive procedure was complicated by the presence of toluene as both a reactant and a product. These difficulties present a barrier to the achievement of precise experimental data. Other alkylations, entries 40–42, methylation,[31] ethylation[31] and isopropylation,[32] in which these experimental difficulties were not encountered, provide partial rate factors which are in agreement with the linear relationship. The values of log p_f/log m_f for the above reactions are 4.66, 4.04 and 4.72, respectively.

Other data which have been discarded from the selected series were developed from polymethylbenzene substitution or equilibrium data, entries 3, 5, 10, 14, 15. Although much of this information conforms to the relationship, it has been discarded on a formal basis, since the full applicability of the approximations utilized has not yet been established.

When the probable experimental deviations are recognized, the agreement realized must be considered highly satisfactory. The average percentage error in the reaction constant for this series, 7.25, is only moderately larger than the value observed in the series of selected reactions.

On a theoretical basis, serious deviations from the relationship might have been anticipated for reactions which were either highly selective (large absolute ρ) or relatively non-selective (small absolute ρ) due to the change in resonance contribution of the *p*-methyl group as a function of the energy requirements of the reactants. It is apparent that the highly selective reactions, *e.g.*, halogenation, Friedel–Crafts acylation, obey the relationship, as do the less selective reactions, mercuration and Friedel-Crafts alkylation. Since the scatter throughout the range of activity thus far examined is random, a relation between the reaction constant and the log p_f/log m_f ratio is not substantiated.

Examination of the available data on electrophilic side-chain reactions reveals a much less satisfactory fit to the Selectivity Relationship (Fig. 2). Experimental uncertainties and discrepancies exist in several cases and a portion of the apparent deviations may be attributed to this factor. Indeed, re-examination of some of the systems listed in Table II has yielded values of log p_f/log m_f in far better agreement with the values for this quantity which are observed in aromatic substitution[70] (Table I). We hope to report these results shortly.

Least squares analysis of the data (Table II) yields a regression line significantly different from that obtained for the aromatic substitutions, Table IV. In the case of the side-chain reactions, the average value of log p_f/log m_f is both larger and more variable, 6.64 ± 2.33, than in the former series, 4.04 ± 0.55. Utilizing a σ^+-value for *p*-methyl of -0.378 results in an average error in the reaction constant, ρ, for these reactions of 17.2% (Table V). Adoption of the value derived from the substitution reactions, -0.280, gives rise to an average error of 24.9% in ρ.

These errors would appear to be greater than could be tolerated in a really satisfactory quantitative relationship. In view of the discrepancies that we have already observed in certain of the data used in this analysis, it is probably desirable to reserve judgment for the present as to the degree of the correlation which may be realized utimately between side-chain electrophilic reactions and the Selectivity Relationship.

The side-chain reactions of *m*- and *p*-tolyl derivatives typical of those reactions correlated by the Hammett equation have also been examined for their fit to the correlations utilized for the electrophilic reactions. Somewhat unexpectedly, the fit realized in the Selectivity plot (Fig. 3), reveals considerable scatter, easily as large as that observed with the electrophilic side-chain data (Fig. 2). The statistical analysis (Table IV) confirms this conclusion. The correlation revealed by these data is far less satisfactory than that exhibited by the electrophilic substitution results, and even less satisfactory than that shown by the electrophilic side-chain reactions. Utilization of the best value of $\sigma_{p\text{-Me}}$, -0.129, results in an average error in the reaction constant of 18.5%. This is increased to 20.8% if the value, -0.170, based on the ionization of the benzoic acid is used. It is therefore apparent that the effects of methyl substituents on electrophilic reactions are correlated more satisfactorily than are the effects of these groups on the so-called normal side-chain reactions.

Evaluation of Electrophilic Substituent Constants.

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[70] Unpublished results of Dr. Y. Okamoto and research in progress by Dr. S. Nishida.

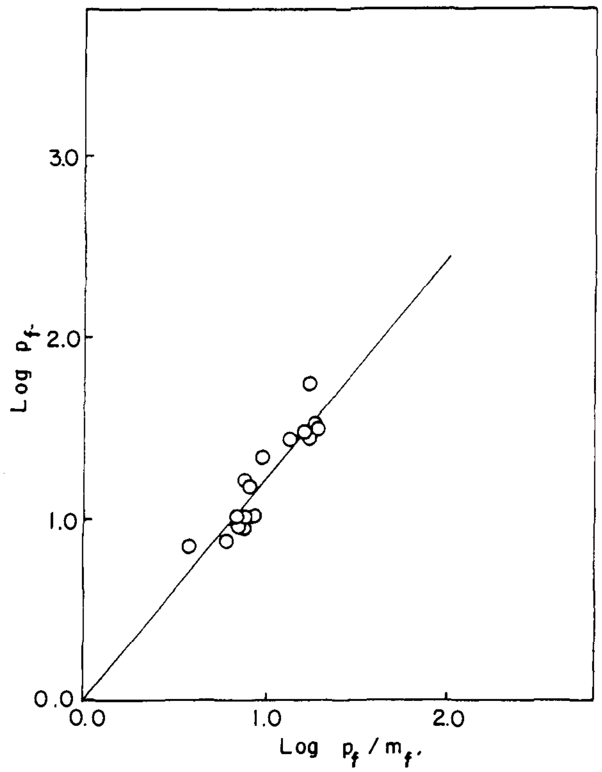

Fig. 2.—Relationship between log p_f and log p_f/m_f for electrophilic side-chain reactions.

—The available data on the substitution of toluene clearly follow the Selectivity Relationship. Consequently, $\sigma^+_{p\text{-Me}}/\sigma^+_{m\text{-Me}}$ must be a constant. It has been observed that excellent linear relationships are realized between log k for m-substituted derivatives and the Hammett σ constants for these substituents. On this basis, it is reasonable to equate $\sigma^+_{m\text{-Me}}$ with $\sigma_{m\text{-Me}}$ (-0.069). It follows that the electronic contributions of p-methyl in electrophilic substitutions can be represented by a constant with a high degree of precision.

Ideally, such electrophilic substituent constants should be based on substitution data. An attempt to derive these constants from substitution data proved unsatisfactory because of the paucity and uncertainty of the available data.[11] In the absence of such data, the solvolysis of t-cumyl chlorides was adopted as a convenient alternative route to electrophilic substituent constants. It results in the value -0.311 for p-methyl.[14,15]

It is now possible to calculate $\sigma^+_{p\text{-Me}}$ from the substitution data. For these reactions, log p_f/log m_f = $\sigma^+_{p\text{-Me}}/\sigma_{m\text{-Me}}$ is 4.04 ± 0.55. Adopting the value, $\sigma_{m\text{-Me}}$ -0.069, this approach yields a value for $\sigma^+_{p\text{-Me}}$ of -0.280 ± 0.04. Consequently, in the case of the methyl substituent the value of the electrophilic constant from the t-cumyl series agrees with the value based on the many substitution results, within the experimental uncertainty in these data.

The applicability of the Selectivity Relationship to the substitution reactions of toluene now appears to have been established with considerable certainty. Moreover, the electrophilic substituent constant derived from substitution data appears to be in satisfactory agreement with the value based on the solvolysis of the t-cumyl chlorides.

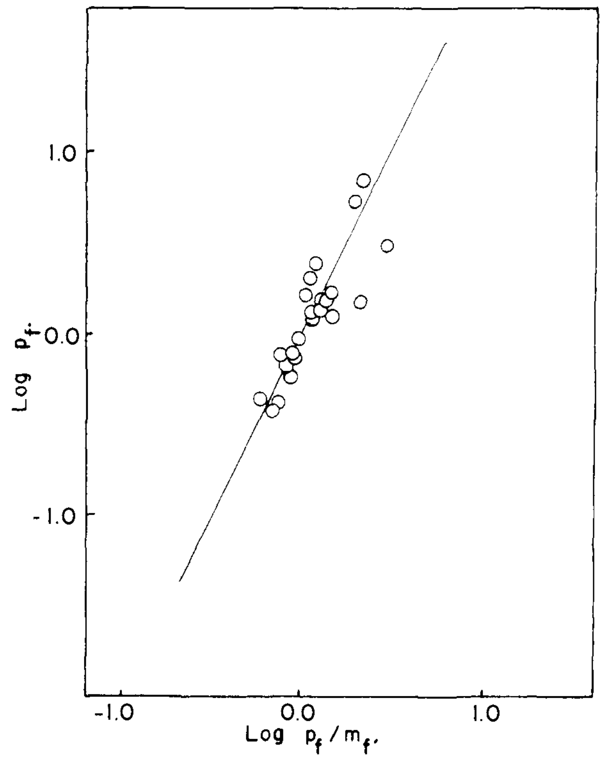

Fig. 3.—Relationship between log p_f and log p_f/m_f for Hammett type side-chain reactions.

The question as to whether this treatment can be extended to correlate the substitution reactions of other benzene derivatives with equal precision cannot now be examined satisfactorily, because of the paucity of the available data. In order to obtain such data, we are studying typical substitution reactions of t-butylbenzene, anisole and biphenyl. These results should permit a decision as to whether this approach, which has proved so successful in the case of toluene, can be extended to other monosubstituted benzenes. It should then also be possible to test rigorously the validity of our original assumption that the electrophilic constants, based upon the solvolysis of t-cumyl chloride derivatives, should be applicable to the correlation of electrophilic aromatic substitutions.

Although we are exercising caution in extending this approach to other substituents, the available data appear highly promising for the development of a truly quantitative treatment of aromatic substitution.

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