Quantitative Structure–Reactivity–Temperature Correlations for Reactions of Diphenyldiazomethanes with Benzoic Acids in Toluene[1]

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Rate constants are reported for 23 reactions of diphenyldiazomethanes with benzoic acids in toluene at 25.01, 34.90, and 45.06°. It is shown that the reaction constant for *meta* or *para* substitution in diphenyldiazomethane, ρ_D, increases with increasing temperature, while the reaction constant for *meta* or *para* substitution in benzoic acid, ρ_B, decreases with increasing temperature. The equation, $\log k = (7.69 - 2857/T) - (0.338 + 378/T)\Sigma\sigma_D + (0.211 + 589/T)\Sigma\sigma_B$, provides an excellent quantitative structure–reactivity–temperature relationship for the 69 reported k-values. Values of E_a, $\log A$, ΔH^*, ΔS^*, and ΔF^* are reported for the 23 reactions. It is shown that variation in reaction rate within the diphenyldiazomethane–benzoic acid reaction series is due to changes in both ΔH^* and ΔS^* with ΔH^* varying nonlinearly with ΔS^*. For diphenyldiazomethane–benzoic acid reactions in which both reactants are simultaneously *meta* or *para* substituted, the rate effect of changes in enthalpy and entropy of activation caused by *meta* or *para* substitution in diphenyldiazomethane is independent of and additive to the rate effect of changes in enthalpy and entropy of activation resulting from *meta* or *para* substitution in benzoic acid. Similar considerations apply to the Arrhenius parameters, E_a and $\log A$. Structural changes in the diphenyldiazomethane–benzoic acid series result in larger changes in ΔF^* than in ΔH^* and $T\Delta S^*$.

Hammett proposed[2] that the reaction constant, ρ, varies inversely with the absolute temperature. Later, Jaffé showed[3] that there are many exceptions to this proposal. Moreover, for reaction series for which the enthalpy is a linear function of the entropy, Leffler has proposed[4] that ρ must reach zero and change its sign at the isokinetic temperature.

In view of the preceding discussion, it seemed desirable to make a study of quantitative temperature effects on structure–reactivity correlations for reactions of diphenyldiazomethanes with benzoic acids in toluene since this reaction series has already been studied[5,6] extensively at 25°.

Results and Discussion

Second-order rate constants for 23 reactions of diphenyldiazomethanes with benzoic acids in toluene at 25.01, 34.90, and 45.06° are shown in Table I. Rate constants for 18 of the 23 reactions at 25.01° have been reported previously, as indicated by footnotes. The other 51 rate constants were determined in the present study.

TABLE I

RATE CONSTANTS FOR 23 REACTIONS OF SUBSTITUTED DIPHENYLDIAZOMETHANES WITH SUBSTITUTED BENZOIC ACIDS IN TOLUENE

No.	Diphenyldiazomethane substituents	Benzoic acid substituents	Log k (k in l. mole^{-1} sec.$^{-1}$) 25.01°	34.90°	45.06°
1	4,4′-$(CH_3O)_2$	H	-0.777^a	-0.416	-0.220
2	4,4′-$(CH_3)_2$	H	-1.384^a	-1.120	-0.797
3	4-Cl	H	-2.282^a	-1.993	-1.642
4	4-Br	H	-2.317^a	-1.999	-1.688
5	4,4′-Cl_2	H	-2.587^a	-2.249	-1.918
6	3-NO_2	H	-2.999^a	-2.658	-2.360
7	3,3′-$(NO_2)_2$	H	-4.204^a	-3.861	-3.516
8	H	H	-1.969^b	-1.648	-1.339
9	H	3,5-$(NO_2)_2$	$+1.262$	$+1.413$	$+1.694$
10	H	3-NO_2	-0.380	-0.126	$+0.217$
11	H	3-Br	-0.963	-0.741	-0.468
12	H	3-CH_3	-2.171^b	-1.863	-1.538
13	H	4-$(CH_3)_3C$	-2.338^b	-2.010	-1.719
14	H	4-CH_3O	-2.606^b	-2.308	-1.963
15	H	4-CH_3	-2.312^b	-2.012	-1.747
16	4,4′-$(CH_3O)_2$	3-NO_2	$+0.942$	$+1.106$	$+1.380$
17	4,4′-$(CH_3)_2$	3-Br	-0.380^c	-0.184	$+0.069$
18	4,4′-$(CH_3O)_2$	4-CH_3	-1.091^b	-0.831	-0.456
19	4,4′-$(CH_3)_2$	4-$(CH_3)_3C$	-1.725^b	-1.464	-1.158
20	4,4′-Cl_2	4-CH_3	-2.922^b	-2.566	-2.235
21	3,3′-$(NO_2)_2$	3-Br	-3.411^b	-3.105	-2.732
22	3,3′-$(NO_2)_2$	4-CH_3	-4.542^b	-4.168	-3.788
23	3,3′-$(NO_2)_2$	4-CH_3O	-4.751	-4.462	-3.993

[a] Ref. 5. [b] Ref. 6. [c] J. F. Norris and W. H. Strain, *J. Am. Chem. Soc.*, **57**, 187 (1935).

Hammett Structure–Reactivity–Temperature Correlations.—For the first eight reactions in Table I, linear regression analysis[7a] of $\log k_D$ on $\Sigma\sigma_D$ (sum of the σ-values[8a] for the *meta* and *para* substituents in the diphenyldiazomethanes[9]) at each of the temperatures gives eq. 1 where $\log k_0$ is the regression intercept and

$$\log k_D = \log k_0 + \rho_D\Sigma\sigma_D \qquad 1)$$

ρ_D is the reaction constant[8b] for *meta* and *para* substitution in diphenyldiazomethane. The parameters of eq. 1 are shown in Table II along with corresponding values of the linear correlation coefficient, r, and of the standard deviation from regression, s. The values given in Table II indicate that the reaction constant for substitution in diphenyldiazomethane, ρ_D, in-

TABLE II

PARAMETERS OF EQUATION 1

Temp., °C.	Log k_0	ρ_D	r	s
25.01	-1.923	-1.58	-0.999	0.039
34.90	-1.604	-1.57	-0.999	0.055
45.06	-1.308	-1.52	-0.999	0.044

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[1] Abstracted in part from the M.S. thesis of E. F., Texas A & M University, Jan. 1961.

[2] L. P. Hammett, *J. Am. Chem. Soc.*, **59**, 96 (1937).

[3] H. H. Jaffé, *Chem. Rev.*, **53**, 218 (1953).

[4] J. E. Leffler, *J. Org. Chem.*, **20**, 1202 (1955).

[5] C. K. Hancock, R. F. Gilby, Jr., and J. S. Westmoreland, *J. Am. Chem. Soc.*, **79**, 1917 (1957).

[6] C. K. Hancock and J. S. Westmoreland, *ibid.*, **80**, 545 (1958).

[7] G. W. Snedecor, "Statistical Methods," 5th Ed., The Iowa State College Press, Ames, Iowa, 1956: (a) Chapter 6; (b) Chapter 14.

[8] (a) The σ-values given by L. P. Hammett ("Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 188) were used, except the σ-value of -0.361 given in ref. 5 for the p-CH_3O group was used; (b) *ibid.*, p. 186.

[9] Subscript D denotes values for reactions of substituted diphenyldiazomethanes with unsubstituted benzoic acid, subscript B denotes values for reactions of unsubstituted diphenyldiazomethane with substituted benzoic acids, and subscript DB denotes values for reactions of substituted diphenyldiazomethanes with substituted benzoic acids.

creases with increasing temperature which is contrary to Hammett's proposal.[2]

For reactions 8–15 in Table I, linear regression analysis of log k_B on $\Sigma\sigma_B$ (sum of the σ-values for the *meta* and *para* substituents in the benzoic acids[9]) at each of the temperatures gives eq. 2 where ρ_B is

$$\log k_B = \log k_0 + \rho_B\Sigma\sigma_B \qquad (2)$$

the reaction constant for *meta* and *para* substitution in benzoic acid. The parameters of eq. 2 along with corresponding *r*- and *s*-values are shown in Table III. The values given in Table III indicate that the reaction constant for *meta* and *para* substitution in benzoic acid, ρ_B, decreases with increasing temperature in accordance with Hammett's proposal.[2]

Table III

Parameters of Equation 2

Temp., °C.	Log k_0	ρ_B	r	s
25.01	−1.913	2.22	0.999	0.077
34.90	−1.620	2.13	0.999	0.059
45.06	−1.314	2.12	0.999	0.066

For all 23 reactions in Table I, multiple regression analysis[7b] of log k_{DB} on $\Sigma\sigma_D$ and $\Sigma\sigma_B$ at each of the temperatures gives eq. 3. The parameters of eq. 3

$$\log k_{DB} = \log k_0 + \rho_D\Sigma\sigma_D + \rho_B\Sigma\sigma_B \qquad (3)$$

with corresponding values of the multiple correlation coefficient, *R*, and of *s* are given in Table IV. The data of Table IV are based on more extensive data and confirm that, as the temperature increases, ρ_D increases while ρ_B decreases.

Table IV

Parameters of Equation 3

Temp., °C.	Log k_0	ρ_D	ρ_B	R	s
25.01	−1.882	−1.60	2.20	0.999	0.082
34.90	−1.591	−1.57	2.10	0.999	0.066
45.06	−1.278	−1.52	2.07	0.999	0.078

The analyses of the linear regressions of the parameters of eq. 3 (Table IV) on $1/T$ yield eq. 4–6.

$$\log k_0 = 7.69 - 2857/T,\ r = -0.999,\ s = 0.013 \qquad (4)$$

$$\rho_D = -0.338 - 378/T,\ r = -0.992,\ s = 0.007 \qquad (5)$$

$$\rho_B = 0.211 + 589/T,\ r = 0.957,\ s = 0.027 \qquad (6)$$

Substitution of eq. 4–6 in eq. 3 gives eq. 7. Values of

$$\log k_{DB} = (7.69 - 2857/T) - (0.338 + 378/T)\Sigma\sigma_D + (0.211 + 589/T)\Sigma\sigma_B \qquad (7)$$

log k_{DB} for the 69 reactions were calculated by eq. 7 and are plotted against experimental log k_{DB} values in Figure 1. The correlation coefficient between the calculated and experimental log k_{DB} values is 0.999 and the standard deviation of calculated log k_{DB} values from experimental log k_{DB} values is 0.073 log units. The standard deviation is only 1.1% of the range in experimental log k_{DB} values of 6.45 log units (2,800,000-fold range in *k*-values). Thus, it is evident that eq. 7 provides an excellent quantitative structure–reactivity–temperature relationship for simultaneous variation of *meta* and *para* substituents in benzoic acid and in diphenyldiazomethane and of temperature over the range of 25 to 45°.

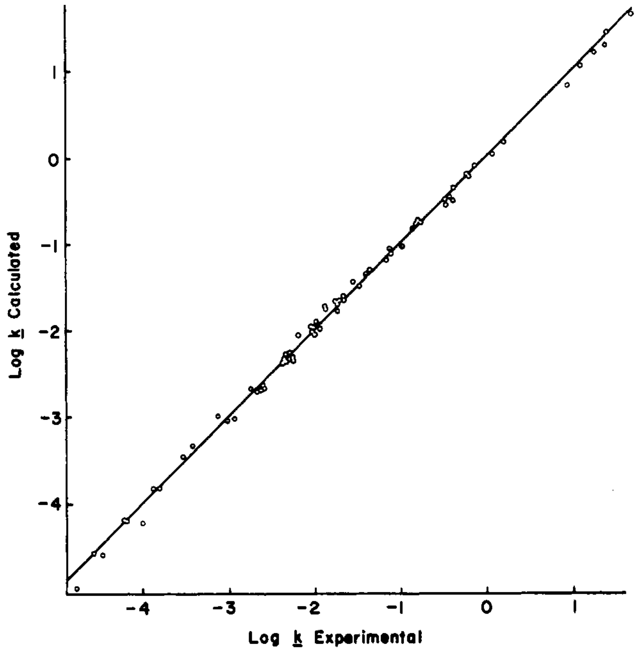

Figure 1.—The relationship between experimental log *k* values and log *k* values calculated from eq. 7 for 23 reactions of diphenyldiazomethanes with benzoic acids in toluene at 25.01, 34.90, and 45.06°.

Correlations Involving Activation Parameters.— For each of the 23 reactions, the analysis of the linear regression of log *k* on $1/T$ was carried out. The regression intercepts are recorded in Table V as log *A*. Values of E_a recorded in Table V were calculated by multiplying the regression slopes by $-2.3R$.

Also, for each of the 23 reactions, the analysis of the linear regression of log $[(kh)/(\kappa T)]$ on $1/T$[10] was carried out. Values of ΔS^* recorded in Table V were calculated by multiplying the regression intercepts by $2.3R$. Values of ΔH^* recorded in Table V were calculated by multiplying the regression slopes by $-2.3R$. Values of ΔF^* at 25° were calculated from $\Delta F^* = \Delta H^* - T\Delta S^*$, using the regression values of ΔH^* and ΔS^*. Calculated values of log $k^{25°}$ were obtained from the equations for the regression of log $[(kh)/(\kappa T)]$ on $1/T$.

In the above two alternate regression treatments, the average log *k* values from Table I were not used; instead, all replicate log *k* values at each of the three temperatures were used. It may be of interest that, for each of the 23 reactions, a slightly greater correlation coefficient was found for the regression of log *k* on $1/T$.

Bunnett[11] has listed the following causes of variation in reaction rate within a reaction series: (1) changes in ΔH^* only with ΔS^* being substantially constant, (2) changes in ΔS^* only with ΔH^* being substantially constant, (3) changes in both ΔH^* and ΔS^* with ΔH^* varying linearly with ΔS^*, and (4) changes in both ΔH^* and ΔS^* with ΔH^* varying nonlinearly with ΔS^*.

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(10) S. Glasstone, K. J. Laidler, and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p. 14.

(11) J. F. Bunnett, "Investigation of Rates and Mechanisms of Reactions," Vol. 8, Part 1, 2nd Ed., "Technique of Organic Chemistry," S. L. Friess, E. S. Lewis, and A. Weissberger, Ed., Interscience Publishers, Inc.; New York, N. Y., 1961, p. 205.

TABLE V

ACTIVATION PARAMETERS FOR 23 REACTIONS OF SUBSTITUTED DIPHENYLDIAZOMETHANES WITH SUBSTITUTED BENZOIC ACIDS IN TOLUENE AT 25.01, 34.90, AND 45.06°

No.[a]	Log $k^{25°}$ calcd.[b]	E_a, kcal./mole	Log A	ΔH^*, kcal./mole	ΔS^*, e.u.	ΔF^* at 25°, kcal./mole
1	−0.766	12.6	8.5	12.0 ± 0.5[c]	−21.9 ± 1.6[c]	18.5
2	−1.390	12.6	7.8	11.9 ± 0.2	−24.9 ± 0.7	19.3
3	−2.290	13.7	7.8	13.1 ± 0.3	−25.0 ± 0.9	20.6
4	−2.318	13.6	7.7	13.0 ± 0.1	−25.5 ± 0.3	20.6
5	−2.588	14.5	8.0	13.9 ± 0.1	−23.9 ± 0.3	21.0
6	−2.995	14.0	7.2	13.3 ± 0.2	−27.5 ± 0.6	21.5
7	−4.206	14.9	6.7	14.3 ± 0.3	−29.9 ± 0.8	23.2
8	−1.969	13.6	8.0	13.0 ± 0.1	−23.9 ± 0.4	20.1
9	+1.232	9.5	8.2	8.9 ± 0.7	−23.1 ± 2.2	15.8
10	−0.399	13.1	9.2	12.5 ± 0.5	−18.5 ± 1.5	18.0
11	−0.971	10.6	6.8	10.0 ± 0.2	−29.3 ± 0.8	18.8
12	−2.174	13.6	7.8	13.0 ± 0.1	−24.9 ± 0.4	20.4
13	−2.335	13.4	7.5	12.8 ± 0.1	−26.4 ± 0.5	20.6
14	−2.613	13.8	7.5	13.2 ± 0.3	−26.2 ± 1.0	21.0
15	−2.310	12.3	6.7	11.7 ± 0.1	−30.0 ± 0.4	20.6
16	+0.923	9.4	7.8	8.8 ± 0.6	−24.7 ± 1.8	16.2
17	−0.403	10.0	6.9	9.4 ± 0.4	−29.0 ± 1.2	18.0
18	−1.107	13.6	8.9	13.0 ± 0.5	−20.1 ± 1.8	19.0
19	−1.738	12.3	7.2	11.6 ± 0.3	−27.4 ± 1.0	19.8
20	−2.920	14.9	8.0	14.2 ± 0.3	−24.1 ± 0.9	21.4
21	−3.427	14.8	7.4	14.2 ± 0.4	−26.7 ± 1.2	22.1
22	−4.545	16.3	7.4	15.7 ± 0.2	−26.6 ± 0.5	23.7
23	−4.785	16.6	7.4	16.0 ± 1.0	−26.7 ± 3.4	24.0

[a] Refers to the reaction as given in Table I. [b] Values of log $k^{25°}$ were calculated from the regression of log $[(kh)/(\kappa T)]$ on $1/T$. [c] Standard error.

As shown below in Tables VI–IX and in eq. 8–11, the three subseries of reactions in Table V, *i.e.*, (1) reactions 1–8 between substituted diphenyldiazomethanes and unsubstituted benzoic acid, (2) reactions 8–15 between unsubstituted diphenyldiazomethane and substituted benzoic acids, and (3) reactions 16–23 between substituted benzoic acids and substituted diphenyldiazomethanes, all fall under the fourth case above; that is, variation in reaction rate within any of these subseries is due to changes in both ΔH^* and ΔS^* with ΔH^* varying nonlinearly with ΔS^*. For all three of these subseries: (1) the data of Table VI show that there is appreciable variation of both ΔH^* and ΔS^*, (2) the data of Tables VII and VIII show that log $k^{25°}$ (calcd.) is not a satisfactory linear function of either ΔH^* or ΔS^*, and (3) the data of Table IX show that there is no significant correlation between ΔH^* and ΔS^*.

TABLE VI

RANGE IN VALUES OF ΔS^*, ΔH^*, $T\Delta S^*$, AND ΔF^*

Reaction subseries[a]	Range in ΔS^*, e.u.	Range in kcal./mole		
		ΔH^*	$T\Delta S^*$ at 25°	ΔF^* at 25°
1–8	8.0	2.4	2.4	4.7
8–15	11.5	4.3	3.4	5.2
16–23	8.9	7.2	2.7	7.8

[a] Refers to the reactions as given in Table I.

TABLE VII

DATA FOR THE LINEAR REGRESSION OF LOG $k^{25°}$ (CALCD.) ON ΔH^*

Reaction subseries[a]	r	s
1–8	−0.923	0.430
8–15	−0.802	0.851
16–23	−0.956	0.640

[a] Refers to the reactions as given in Table I.

TABLE VIII

DATA FOR THE LINEAR REGRESSION OF LOG $k^{25°}$ (CALCD.) ON ΔS^*

Reaction subseries[a]	r	s
1–8	0.903	0.479
8–15	0.480	1.25
16–23	0.190	2.14

[a] Refers to the reactions as given in Table I.

TABLE IX

DATA FOR THE LINEAR REGRESSION OF ΔH^* ON ΔS^*

Reaction subseries[a]	r	s
1–8	−0.669	0.654
8–15	0.138	1.71
16–23	0.106	2.92

[a] Refers to the reactions as given in Table I.

For the three reaction subseries of Table V, the analyses of the multiple regression of log $k^{25.01°}$ from Table I on ΔH^* and ΔS^* from Table V give the near-perfect relationships shown in eq. 8–10. In these

$$\log k_D^{25.01°} = 12.77 - 0.733\Delta H_D^* + 0.218\Delta S_D^*,\ R = 0.99998,\ s = 0.007 \quad (8)$$

$$\log k_B^{25.01°} = 12.92 - 0.738\Delta H_B^* + 0.221\Delta S_B^*,\ R = 0.999994,\ s = 0.005 \quad (9)$$

$$\log k_{DB}^{25.01°} = 12.80 - 0.734\Delta H_{DB}^* + 0.218\Delta S_{DB}^*,\ R = 0.99999,\ s = 0.012 \quad (10)$$

three equations, the corresponding intercepts and coefficients of ΔH^* and of ΔS^* are almost identical and very closely approximate the theoretical values of log $(\kappa T/h)$, $-1/(2.3RT)$, and $1/(2.3R)$, respectively. In view of the origin of ΔH^* and ΔS^*, good correlations for these multiple regressions are to be expected; however, the very excellent correlations provided by

TABLE X

PARAMETERS OF EQUATION 11

Temp., °C.	Intercept	Coeff. of ΔH^*	Coeff. of ΔS^*	R	s
25.01	12.83	−0.734	0.219	0.99997	0.012
34.90	12.76	−0.709	0.217	0.99987	0.026
45.06	12.85	−0.688	0.219	0.99996	0.014

eq. 8–10 serve to substantiate the accuracy and consistency of both the experimental data and of the calculations. For the same three reaction subseries, relationships closely analogous to eq. 8–10 were found for $\log k^{34.90°}$ and $\log k^{45.06°}$.

Further, for all 23 reactions at each of the three temperatures, the analyses of the multiple regression of $\log k$ on ΔH^* and ΔS^* give the near-perfect relationships shown in eq. 11. The parameters of eq. 11 are given in Table X.

$$\mathrm{l\ og}\ k^T = \log (\kappa T/h) - \Delta H^*/(2.3RT) + \Delta S^*/(2.3R) \quad (11)$$

Thus, for changes of *meta* or *para* substituents in diphenyldiazomethane only or in benzoic acid only or in both of these reactants simultaneously, the accompanying changes in reaction rate cannot be accounted for satisfactorily by ΔH^* changes alone or by ΔS^* changes alone; instead, changes in both ΔH^* and ΔS^*, which are not linearly related, must be considered simultaneously.

It has been shown previously[6] and again by eq. 1–3 above that the rate effect of *meta* or *para* substitution on diphenyldiazomethane, $\rho_D\Sigma\sigma_D$, is independent of the rate effect of *meta* or *para* substitution on benzoic acid, $\rho_B\Sigma\sigma_B$, and that these two rate effects are directly additive. Equation 12 follows from eq. 1–3 since substitution of eq. 1 and 2 in eq. 12 gives eq. 3. For reactions 16–23 of Table V, values of $\log k_{DB}^{25.01°}$ were obtained by eq. 12. The average deviation of these eight calculated values from the corresponding values of $\log k_{DB}^{25.01°}$ given in Table I is only 0.06 log unit for a range in $\log k_{DB}^{25.01°}$ of 5.7 log units.[12]

$$\log k_{DB} = \log k_D + \log k_B - \log k_0 \quad (12)$$

Using theoretical values of the intercept and of the coefficients of ΔH^* and of ΔS^*, substitution of eq. 8 and 9 in eq. 12 gives eq. 13. For reactions 16–23 of Table V, values of $\log k_{DB}^{25.01°}$ were calculated by eq. 13. The average deviation of these eight calculated values from the corresponding experimental values of $\log k_{DB}^{25.01°}$ given in the fourth column of Table I is only 0.08 log unit for a range in $\log k_{DB}^{25.01°}$ of 5.7 log units.[13]

$$\log k_{DB}^{25.01°} = 27.55 - 0.733(\Delta H_D^* + \Delta H_B^*) + 0.218(\Delta S_D^* + \Delta S_B^*) \quad (13)$$

From the very close fit provided by eq. 13, for diphenyldiazomethane–benzoic acid reactions in which both reactants are simultaneously *meta* or *para* substituted, it may be concluded that the rate effect of changes in enthalpy and entropy of activation caused by *meta* or *para* substitution in diphenyldiazomethane is independent of and additive to the rate effect of changes in enthalpy and entropy of activation resulting from *meta* or *para* substitution in benzoic acid.

All of the above conclusions concerning quantitative relationships involving $\log k^{25.01°}$, ΔH^*, and ΔS^* apply in a similar manner to quantitative relationships involving $\log k^{25.01°}$, E_a, and $\log A$. For example, multiple regression analyses give eq. 14 and 15.

$$\log k_D^{25.01°} = 0.035 - 0.733\, E_{aD} + 0.996 \log A_D,\ R = 0.99998,\ s = 0.007 \quad (14)$$

$$\mathrm{og}\ k_B^{25.01°} = -0.001 - 0.738\, E_{aB} + 1.01 \log A_B,\ R = 0.999994,\ s = 0.005 \quad (15)$$

Using theoretical values of the intercept (zero) and of the coefficients of E_a and of $\log A$, substitution of eq. 14 and 15 into eq. 12 gives eq. 16, where $1.969 = -\log k_0^{25.01°}$. Equation 16 provides just as good a fit for the values of $\log k_{DB}^{25.01°}$ given in Table I for reactions 16–23 as does eq. 12 or eq. 13.

$$\log k_{DB}^{25.01°} = 1.00 \log (A_D A_B) - 0.733(E_{aD} + E_{aB}) + 1.969 \quad (16)$$

Wells[14] has discussed two reaction series (dissociation of benzoic acids and acid hydrolysis of benzyl acetates) that follow a Hammett $\rho\sigma$ relationship even though the enthalpy is not linear with the entropy; however, the Hammett relationship for the latter series is very poor. DeWolfe[15] found an excellent $\rho\sigma$ relationship for the acid hydrolysis rates of N,N'-diarylformamidines even though the enthalpy of activation is not linear with the entropy of activation.

Rearrangement of eq. 12 gives eq. 17, and, since $\Delta F^* = -RT \ln k$, eq. 18 follows from eq. 17. Both eq. 17 and 18 apply closely to the data of this study. Differentiating eq. 18 with respect to T gives eq. 19, and, since $\Delta F^* = \Delta H^* - T\Delta S^*$, eq. 20 follows from eq. 19. It has been found that neither eq. 19 nor eq. 20 is satisfied by the experimental data. Hence, although the additivity relationships of eq. 17 and 18 appear to hold over the temperature range 25–45°; they would not be expected to hold in general, *i.e.*, outside of this temperature range.

$$\log k_{DB} + \log k_0 = \log k_D + \log k_B \quad (17)$$

$$\Delta F_{DB}^* + \Delta F_0^* = \Delta F_D^* + \Delta F_B^* \quad (18)$$

$$\Delta S_{DB}^* + \Delta S_0^* = \Delta S_D^* + \Delta S_B^* \quad (19)$$

$$\Delta H_{DB}^* + \Delta H_0^* = \Delta H_D^* + \Delta H_B^* \quad (20)$$

There remains the question as to why the additivity relationships of eq. 17 and 18 are followed closely while those of eq. 19 and 20 show serious deviations.[16]

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[12] As an example of the calculations, for reaction 18, $\log k_D^{25.01°} = -0.777$ from reaction 1, $\log k_B^{25.01°} = -2.312$ from reaction 15, and $\log k_0^{25.01°} = -1.969$ from reaction 8. Substituting these values in eq. 12, a calculated value of −1.120 for $\log k_{DB}^{25.01°}$ for reaction 18 is obtained. This value agrees quite closely with the experimental value of −1.091 given in Table I.

[13] As an example of the calculations, for reaction 22, $\Delta H_D^* = 14.3$ and $\Delta S_D^* = -29.9$ from reaction 7 while $\Delta H_B^* = 11.7$ and $\Delta S_B^* = -30.0$ from reaction 15. Substituting these values in eq. 13, a calculated value of −4.57 for $\log k_{DB}^{25.01°}$ for reaction 22 is obtained. This value agrees quite closely with the experimental value of −4.54 given in the fourth column of Table I.

[14] P. R. Wells, *Chem. Rev.*, **63**, 171 (1963).

[15] R. H. DeWolfe, *J. Am. Chem. Soc.*, **82**, 1585 (1960).

[16] A referee has proposed that a perturbing interaction mechanism exists whose isokinetic temperature just happens to be near the mean experimental temperature, so that its effects are seen only in the enthalpy and entropy and not in the free energy. *Cf.* J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963.

Further experimental data, over a wider temperature range, if feasible, or in other solvents would seem desirable. It does not appear, from the standard error given in Table V, that the failure of eq. 19 and 20 is due to lack of precision in measurements of ΔH^* and ΔS^*. The largest standard errors in ΔH^* and ΔS^* were found for reaction 23. However, in all regression analyses involving reaction 23, no significant improvement was obtained by omitting the data for 23. Thus, it is indicated that the values of ΔH^* and ΔS^* for reaction 23 are fairly reliable.

Finally, it may be of interest that the ranges in values of the activation parameters given in Table VI show generally that structural changes in this reaction series result in larger changes in ΔF^* than in ΔH^* and $T\Delta S^*$.

Experimental

Materials.—The materials used in this study have been described previously,[5,6] except for 3,5-dinitrobenzoic acid which was obtained from a commercial source and was recrystallized from toluene until the melting point agreed with previously reported values (204–205°).

Rate Measurements.—A Beckman Model DU spectrophotometer was used to follow the reactions. The spectrophotometer was equipped with thermospacers and the cell compartment was thermostatted at the desired temperature by circulating water from a constant-temperature bath through the thermospacers. The reaction temperatures were maintained within ± 0.01° of the values given in Table I.

Due to low solubility in toluene, all reactions of 3,5-dinitro- and 3-nitrobenzoic acids were run in 10-cm. cells and all reactions of 3-bromo- and 4-methoxybenzoic acids were run in 5-cm. cells. All other reactions were run in 1-cm. cells. The reactant solutions were prepared and mixed as described previously[5,6] and then an aliquot of the mixture was transferred to the spectrophotometer cell which had been placed in the thermostatted cell compartment 2 hr. previously. The cell containing the reacting mixture was left in the thermostatted cell compartment until the reaction had proceeded through about 3 half-lives.

Otherwise, the rate measurements were made as described previously.[5,6]

Three to six rate determinations were made on each reaction at each temperature. The precision of the results is comparable to that reported previously.

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Hydration, Hydrate Acidity, and Aldolization of Isobutyraldehyde[1a]

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The equilibrium constants for the hydration and the aldolization of isobutyraldehyde in aqueous solution have been determined by n.m.r. and ultraviolet measurements. The acidity of isobutyraldehyde hydrate and the kinetics of the dealdolization of isobutyraldol have also been studied. From the kinetic study it appears that the combination of an isobutyraldehyde carbanion with an isobutyraldehyde molecule is comparable in rate to its protonation, so that the rate-controlling step in dealdolization may change with a change in the nature of the basic catalyst used.

In relation to a study of the α-hydrogen exchange of isobutyraldehyde it became desirable to investigate possible complications due to aldolization and hydration of the aldehyde, and the acidity of the aldehyde hydrate. The aldol condensation of acetaldehyde, which has been studied by a number of workers[2–5] has been found to be sufficiently irreversible that, even in relatively dilute aqueous solutions, the kinetics may be studied without allowance for reversibility (in the early part of the reaction, at least). The equilibrium constant for the aldolization of acetone at 25°, which climbs from about 0.023 M^{-1} in 4% water–96% acetone–diacetone alcohol to 0.037 M^{-1} in 80% water–20% acetone–diacetone alcohol,[6] is so unfavorable that the pure organic equilibrium mixture contains only about 13% diacetone alcohol and in dilute aqueous solution the dealdolization reaction can be run essentially to completion.[6–8]

Usherwood showed that the aldol condensation of isobutyraldehyde is reversible and reported that in the organic layer of the two-phase potassium carbonate catalyzed reaction about 5.5, 33.2, and 90.1% isobutyraldehyde is present at 13, 60, and 100°, respectively.[9] No measurements were made in aqueous solution, however, and the interpretation of the results obtained is complicated by the subsequent demonstration that the principal higher boiling constituent of the organic phase is not isobutyraldol but 2,6-diisopropyl-5,5-dimethyl-4-*m*-dioxanol, the product of the addition of a molecule of isobutyraldehyde to one of aldol.[10–12]

The extent of hydration of aldehydes and ketones in aqueous solution, ranging from more than 99% for chloral and formaldehyde to an amount too small to detect for acetone, has been measured or estimated by

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(1) (a) Abstracted in part from the Ph.D. thesis of James G. Houston, 1965. (b) National Defense Education Act Fellow, 1960–1963.

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