215. *Constitutional Factors controlling Prototropic Changes in Carbonyl Compounds. Part V. A Relationship between the Polar Characters of Substituent Groups and the Activation Energies of Proton Addition.*

By W. S. Nathan and H. B. Watson.

Although the observed velocities of certain bimolecular reactions in solution are smaller by several powers of ten than those calculated on the simple collision theory (Christiansen, *Z. physikal. Chem.*, 1924, **113**, 35; Norrish and Smith, J., 1928, 129; Moelwyn-Hughes and Hinshelwood, J., 1932, 230), a considerable number of changes nevertheless proceed at speeds which are approximately in harmony with the assumption that reaction occurs (as in gases) whenever two molecules collide with the necessary increment of energy (Moelwyn-Hughes, *Chem. Reviews*, 1932, **10**, 241; *Phil. Mag.*, 1932, **14**, 112). It has further been pointed out by Grant and Hinshelwood (this vol., p. 258) that in nearly all known processes of the latter type one of the reactants is an ion, and they suggest that, in general, "reactions between an organic compound and an ion in solution tend to take place at approximately the rate given by the simple kinetic equation." The conclusions outlined below have been arrived at by an examination, in the light of this suggestion, of our previous results for the velocities of prototropic change of certain *p*-substituted acetophenones (Part III, this vol., p. 217) and of some new data for *p*-substituted ω-chloroacetophenones.

The order of the velocities of acid-catalysed prototropic change of $CH_3{\cdot}CO{\cdot}C_6H_4X$ (*p*-Me$>$H$>$*p*-I$>$*p*-Br$>$*p*-Cl$>$*p*-NO_2, Part III) demonstrated that the governing factor in these changes is the co-ordination of carbonyl oxygen with the acid catalyst. This, indeed, was already evident from the observation (Parts I and II, Hughes, Watson, and Yates, J., 1931, 3318; 1932, 1207) that substituent halogen atoms reduce the efficiency of acid catalysts, and from a comparison of the results of various workers who had examined the prototropy of such compounds as acetaldehyde, acetone, and pyruvic acid. Only a simple assumption was then necessary (Part III) to relate the velocity of the acid-catalysed prototropic change with the speed of addition of proton to the ketone molecule by the expression

$$v = \text{const.} \times k_{\text{ass.}} [\text{ketone}] [H^{\cdot}] \quad . \quad . \quad . \quad . \quad (1)$$

If the concentrations of ketone and hydrogen ion remain constant, the expression becomes

$$v = \text{const.} \times k_{\text{ass.}} . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

i.e., the relative velocities of prototropic change are determined by the speeds of addition of proton to the ketone. According to Grant and Hinshelwood's suggestion, the rate of the latter change should be in harmony with the simple kinetic equation.

For two different reacting species, this equation is given by Moelwyn-Hughes (*loc. cit.*) as

$$k = 5{\cdot}71 \times 10^{25} \,.\, T^{\frac{1}{2}} \,.\left(\frac{M_1 + M_2}{M_1 M_2}\right)^{\frac{1}{2}}\left(\frac{\sigma_1 + \sigma_2}{2}\right)^2 . \, e^{-E/RT} \quad . \quad . \quad (3)$$

where σ_1 and σ_2 are the molecular diameters of the reactants. This expression does not take into account the "free-space," "phase," and "steric" corrections. The first, according to Jowett (*Phil. Mag.*, 1929, **8**, 1059), increases the collision rate by a factor of the order 10, which is constant for a given medium at one temperature, while the product of the two last-named has been found constant for the halogenation of a series of phenolic ethers (Bradfield, Jones, and Spencer, J., 1931, 2907). In the consideration of the *relative* speeds of prototropic change of *p*-substituted acetophenones in a given medium and at the same temperature, it may safely be assumed that these corrections will cancel out. For our present purpose, then, the kinetic equation may be written

$$k = \text{const.}\left(\frac{M_1 + M_2}{M_1 M_2}\right)^{\frac{1}{2}}\left(\frac{\sigma_1 + \sigma_2}{2}\right)^2 . \, e^{-E/RT}$$

$$\text{or} \quad E = c - RT \log_e \frac{k}{[(M_1 + M_2)/M_1 M_2]^{\frac{1}{2}}[(\sigma_1 + \sigma_2)/2]^2} \quad . \quad . \quad (4)$$

The velocities of prototropic change were determined (Part III) by measurements of speeds of bromination, and the results were expressed as fall of $N/50$-thiosulphate titre per minute for 20 c.c. of $0{\cdot}1M$-solutions of ketone. In accordance with equation (2), these quantities are a measure of the velocity of addition of proton to the ketone, *i.e.*, of k in equation (4), concentration terms appearing in the constant c; E is the energy of activation of the process $CH_3{\cdot}CO{\cdot}C_6H_4X + H^{\cdot} \longrightarrow CH_3{\cdot}C(OH^{\cdot}){\cdot}C_6H_4X$, *i.e.*, of the formation of a bond between proton and carbonyl oxygen. The different values of E for various substituted acetophenones are clearly due to the different contributions of the substituent groups X to the critical energy increment.

In the absence of better means of computing molecular diameters, values have usually been derived from molecular volumes by the use of a formula such as $\sigma = 1{\cdot}33 \times 10^{-8} V_m^{\frac{1}{3}}$ (compare Moelwyn-Hughes, *loc. cit.*). We have employed Sugden's parachor values, since parachors give a measure of molecular volumes under comparable conditions, and the atomic and structural constants are known with a fair degree of accuracy. In the case of acetophenone itself, the parachor has actually been measured, and the value 292·4 (Hammick and Andrew, J., 1929, 754) is in reasonably good agreement with that got by summation of Sugden's constants, *viz.*, 294·1. The molecular collision area is given by $10^{-16}P^{\frac{2}{3}}/2{\cdot}42$ (Sugden, "The Parachor and Valency," 1930, p. 32), and the molecular diameter may then be taken as $2\sqrt{10^{-16}P^{\frac{2}{3}}/2{\cdot}42\,\pi} = 0{\cdot}725 \times 10^{-8}P^{\frac{1}{3}}$. In Table I the values of the quantity $z = [(M_1 + M_2)/M_1M_2]^{\frac{1}{2}}[(\sigma + \sigma_2)/2]^2$ are calculated for collision of the ketone molecule with the oxonium ion. For the parachor of the oxonium ion the value is taken as $P = 3 \times 17{\cdot}1\ (3H) + 20\ (O) - 1{\cdot}6$ (co-ordinate bond) $= 69{\cdot}7$. The corresponding value for the molecular diameter (σ_2) is $2{\cdot}982 \times 10^{-8}$. The quantity $\log_e k/z$, the only variable term in the expression for E (equation 4), is referred to as E'.

If E_0 and E'_0 are the values of E and E' for unsubstituted acetophenone, it is evident from equation (4) that

$$E - E_0 = -RT(E' - E_0') \quad . \quad . \quad . \quad . \quad (5)$$

The largest value of $E - E_0$ (where E refers to *p*-nitroacetophenone) is 425 cals. per g.-mol.

The most striking result of the present work is the observation of a quantitative relationship between the critical increments of the reactions of hydrogen ion with the ketones of the series $CH_3{\cdot}CO{\cdot}C_6H_4X$ and the dipole moments of C_6H_5X. It was pointed out in Part III that the velocities of prototropic change follow the order of dipole moments.

TABLE I.

Reaction of $CH_3{\cdot}CO{\cdot}C_6H_4X$ *with oxonium ion.*

(1) Calculation of z.

X.	P.	$10^8\sigma_1$.	$10^{16}[(\sigma_1 + \sigma_2)/2]^2$.	$[(M_1 + M_2)/M_1M_2]^{\frac{1}{2}}$.	$10^{16}z$.
CH_3	333·1	5·024	16·02	0·2451	3·926
H	294·1	4·820	15·22	0·2469	3·758
I	368·0	5·195	16·72	0·2381	3·978
Br	345·0	5·084	16·26	0·2401	3·904
Cl	331·3	5·016	15·99	0·2431	3·887
NO_2	350·0	5·109	16·36	0·2423	3·964

(2) Values of E' for reactions in 75% acetic acid.

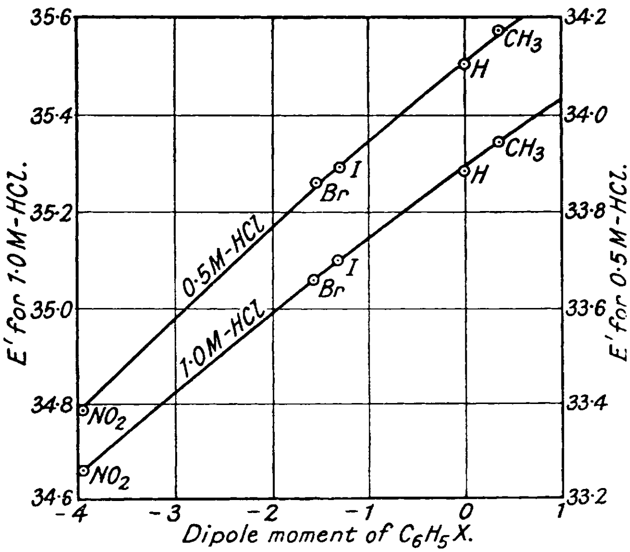
	HCl = 0·5M.		HCl = 1·0M.	
X.	k.	$E' - 32$.	k.	$E' - 32$.
CH_3	0·273	2·175	0·876 *	3·341
H	0·243	2·105	0·793	3·286
I	0·208	1·891	0·696	3·098
Br	0·197	1·855	0·656	3·059
NO_2	0·125	1·385	0·446	2·657

(3) Values of E' for reactions in 50% acetic acid.

	HCl = 1·0M.		HCl = 2·0M.	
CH_3	0·335	2·380	1·068	3·539
H	0·297	2·304	0·954	3·470
Br	0·217	1·952	0·737	3·174
Cl	0·216	1·951	0·727	3·165

* The value 0·964 recorded in Part III was due to an error in copying, and overlooked in the proofs. The correct value is here given.

FIG. 1.



It now becomes evident that the values of E', when calculated on the assumption that reaction is with the oxonium ion, bear an almost linear relationship with the dipole moments of C_6H_5X (see Fig. 1). Deviation from the linear is hardly perceptible over the range of moments extending from 0·39 to —1·56 (CH_3 to Cl), but becomes obvious when the moment is of the magnitude —3·97 (NO_2). The exact relationship in Debye units is

$$E' = E_0' + x\,(\mu - 0{\cdot}032\mu^2) \quad (6)$$

The values of E' calculated for reaction with the unsolvated proton (whatever parachor value be assumed from zero up to 17·1, the constant for combined hydrogen) do not bear a definite relationship with the dipole moments; for different concentrations of acid the curves are not of identical form. This fact favours the hypothesis of reaction with the oxonium ion, as would be anticipated.

Combining equations (5) and (6), we have the relationship:

$$E - E_0 = -RTx\,(\mu - 0{\cdot}032\mu^2) = -\,C\,(\mu - 0{\cdot}032\mu^2) \quad . \quad . \quad (7)$$

The critical increment of the reaction of a p-substituted acetophenone $CH_3{\cdot}CO{\cdot}C_6H_4X$ with oxonium ion thus differs from that of the corresponding reaction of the unsubstituted ketone under identical conditions by a quantity proportional to (μ —$0{\cdot}032\mu^2$), where μ is

TABLE II.

Values of E′ — 32, (a) *observed, and* (b) *calculated from equation* (6).

		In 75% acetic acid.				In 50% acetic acid.			
		HCl = 0·5*M*.		HCl = 1·0*M*.		HCl = 1·0*M*.		HCl = 2·0*M*.	
		(x = 0·161.)		(x = 0·1407.)		(x = 0·212.)		(x = 0·185.)	
X.	μ.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
CH_3	0·39	2·175	2·171	3·341	3·343	2·380	2·380	3·539	3·540
H	0	2·105	2·108	3·286	3·286	2·304	2·299	3·470	3·469
I	− 1·30	1·891	1·891	3·098	3·096	—	—	—	—
Br	− 1·53	1·855	1·850	3·059	3·061	1·952	1·958	3·174	3·172
Cl	− 1·56	—	—	—	—	1·951	1·951	3·165	3·166
NO_2	− 3·97	1·385	1·388	2·657	2·657	—	—	—	—

(The dipole moments are those obtained by Tiganik, *Z. physikal. Chem.*, 1931, *B*, **13**, 452, except for iodine, where the value 1·30 is due to Bergmann, Engel, and Sandor, *ibid.*, 1930, *B*, **10**, 115.)

the dipole moment of C_6H_5X. As is to be expected, the magnitude of the influence of the dipole moment (*i.e.*, the x term in equations 6 and 7) varies with the medium; its variation with the acid concentration may also be a medium effect, or it may perhaps be due to reaction occurring with a varying small proportion of covalent hydrogen chloride. For the purpose of the present discussion, the important fact is the constancy of the relationship for a series of ketones reacting under identical conditions.

Additional data have now been obtained by measurement of the velocities of prototropic change of ω-chloroacetophenone and some of its *p*-substituted derivatives (general formula $ClCH_2{\cdot}CO{\cdot}C_6H_4X$). 0·1*M*-Solutions of the ketones in 90% acetic acid were employed, this solvent being chosen on account of the small solubility of the ketones in more dilute media. The concentration of hydrogen chloride was 0·4167*M*. The relationship expressed in equation (6) has again been observed (see Table III). It should be clearly understood that, although these measurements are comparable among themselves, yet they provide no information regarding the effect of the ω-chlorine atom, since the medium conditions were vastly different from those obtaining in the experiments with *p*-substituted acetophenones.

TABLE III.

Values of E′ *for reaction of* $ClCH_2{\cdot}CO{\cdot}C_6H_4X$ *with oxonium ion.*

X.	P.	$10^8\sigma_1$.	$10^{16}\left(\frac{\sigma_1+\sigma_2}{2}\right)^2$.	$\left(\frac{M_1+M_2}{M_1M_2}\right)^{\frac{1}{2}}$.	$10^{16}z$.	k.	E'.	E', calc. (x=0·135.)
CH_3	370·3	5·206	16·76	0·2420	4·055	0·0560	32·559	32·556
H	331·3	5·017	16·00	0·2431	3·890	0·0506	32·500	32·502
Br	282·2	5·261	16·99	0·2386	4·054	0·0426	32·286	32·285
NO_2	387·2	5·283	17·08	0·2401	4·101	0·0292	31·897	31·898

In the derivation of the relationship $E - E_0 = C\,(\mu - a\mu^2)$ it has been assumed that the velocity of addition of proton to the ketone molecule may be found from the measured velocity of prototropic change in accordance with equation (1), and that it follows the simple kinetic equation. There is little reason to doubt the truth of either assumption. The argument would stand on a much firmer foundation, however, if a similar relationship were found for other reactions where the first assumption, particularly, is not involved. The necessary confirmation has been obtained by an inspection of the dissociation constants of a number of substituted acetic acids. The available data are admittedly somewhat inaccurate, but since the values range over several powers of ten the inaccuracies are *relatively* small. On the basis of the free energy equation $A = RT\,.\log K$, Derick (*J. Amer. Chem. Soc.*, 1911, **33**, 1152, 1167, 1181) has expressed the "positivity" or "negativity" of a substituent as $-1000/\log K$, and his "polaric constants" are clearly equivalent to present-day "inductive effects," and should be replaceable by some function of the dipole moment. On examining the necessary data, we find that the dissociation constants of a number of acids of general formula $X{\cdot}CH_2{\cdot}CO_2H$ are given by the expression $\log K = \log K_0 - 2{\cdot}4(\mu + 0{\cdot}032\mu^2)$ where K_0 is the dissociation constant of acetic acid, and μ is the dipole moment of CH_3X (see Fig. 2 and Table IV).

In any discussion of the dissociation constants of acids, we are dealing with the equilibrium $HA + H_2O \rightleftarrows H_3O^{\cdot} + A'$, and, on the assumption that both dissociation and association processes are in harmony with the kinetic equation, an expression is obtained which is similar to that derived for addition of hydrogen ion to ketones. As a first approximation, the factor z involving the molecular weights and diameters may be regarded as the same for the direct and the reversed reactions. For the unsubstituted acid, equation (4) then becomes

$$E_{0(\text{diss.})} = c_{\text{diss.}} - RT \log k_{0(\text{diss.})}/z_0$$

and $$E_{0(\text{ass.})} = c_{\text{ass.}} - RT \log k_{0(\text{ass.})}/z_0,$$

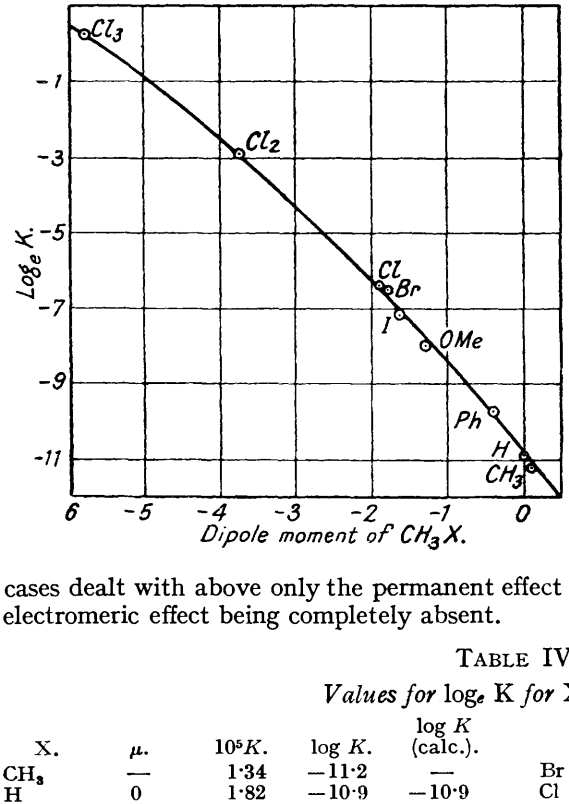
whence $$E_{0(\text{diss.})} - E_{0\,(\text{ass.})} = c - RT \log K_0.$$

Similarly for $X{\cdot}CH_2{\cdot}CO_2H$,

$$E_{\text{diss.}} - E_{\text{ass.}} = c - RT \log K = c - RT\,[\log K_0 - 2{\cdot}4\,(\mu + 0{\cdot}032\,\mu^2)].$$

Hence, $[E_{\text{diss.}} - E_{\text{ass.}}]-[E_{0(\text{diss.})} - E_{0(\text{ass.})}] = 2{\cdot}4\,RT\,(\mu + 0{\cdot}032\,\mu^2)$. The difference between the critical increments of the dissociation and the association process is thus related to the dipole moment of CH_3X by the expression $E - E_0 = C\,(\mu + a\mu^2)$. The identity of the numerical value of a here and in the equations for the acetophenones is probably fortuitous, and the reason for the change in the sign of the term in μ^2 is not immediately obvious. The similarity, indeed almost identity, of the two expressions derived from completely distinct sets of data is strong evidence for their correctness, and this relationship between the critical increment and the polar character of the substituent may prove to be applicable to a large number of reactions of organic compounds.

FIG. 2.



The existence of electronic displacements not connected with any permanent separation of charges (electromeric effect) would render the relationship inapplicable, and there is therefore good reason for supposing that in the cases dealt with above only the permanent effect of the substituent group is operative, the electromeric effect being completely absent.

TABLE IV.

Values for $\log_e$ K *for* $X{\cdot}CH_2{\cdot}CO_2H$.

X.	μ.	10^5K.	log K.	log K (calc.).	X.	μ.	10^5K.	log K.	log K (calc.).
CH_3	—	1·34	−11·2	—	Br	−1·80	138	−6·59	−6·83
H	0	1·82	−10·9	−10·9	Cl	−1·88	155	−6·47	−6·66
Ph	−0·39	5·6	− 9·8	−10·0	Cl_2	−3·76	5,140	−2·97	−2·96
MeO	−1·29	33·5	− 8·0	− 7·9	Cl_3	−5·64	121,000	0·19	0·17
I	−1·63	75	− 7·19	− 7·19					

(Values of K are mainly due to Ostwald. Dipole moments are from those tabulated by Sutton, *Proc. Roy. Soc.*, 1931, *A*, **133**, 685. Values for $>CCl_2$ and $-CCl_3$ are twice and three times respectively the moment for CH_3Cl and not the observed moments of CH_2Cl_2 and $CHCl_3$. In the case of CH_3, the curve indicates a moment of about 0·1.)

EXPERIMENTAL.

p-Methyl- and *p*-bromo-ω-chloroacetophenones were prepared by the Friedel–Crafts method, chloroacetyl chloride being used with the appropriate benzene derivative. Owing to the small solubility of the ketones in ether, extraction with methyl ethyl ketone was resorted to, hydrogen chloride being then removed from the extract by shaking with concentrated sodium acetate solution containing a little sodium carbonate and then with calcium chloride solution, with which the methyl ethyl ketone is practically immiscible. The product was finally crystallised several times from 90% acetic acid; m. p.'s 67° and 115·5° respectively. ω-Chloro- and *p*-nitro-ω-chloro-acetophenones were prepared by chlorination of acetophenone and its *p*-nitro-derivative respectively in glacial acetic acid, and crystallised from 90% acetic acid; m. p.'s 54·5° and 85·5° respectively. The nitro-compound is not reported in the literature; from 9 g. of *p*-nitro-acetophenone, 5·5 g. of the pure compound were obtained as pale yellow crystals.

The 90% acetic acid was prepared for the velocity measurements by diluting 900 c.c. (at 25°) of previously purified acid to 1 litre at 25°. Very small changes in the composition of this medium have a marked influence upon the velocities, and great accuracy is therefore necessary in its preparation.

The measurements were carried out as in Part III. The velocities recorded are the mean of those obtained for the initial and the final halves of the reaction; since there is ultimately a 5% fall in concentration of ketone (mols. ketone/mols. Br = 20 initially), the figures refer actually to a ketone concentration of 0·0975*M*. An accurately reproducible quantity of bromine can be added by the use of a small " pipette " constructed from the inner tube of a broken thermometer drawn to a capillary end. The necessity of an initial titre is thus removed.

We express our thanks to Messrs. Imperial Chemical Industries for a substantial grant.

THE TECHNICAL COLLEGE, CARDIFF. [*Received, June* 17*th*, 1933.]