TABLE VIII

EQUILIBRIUM CONCENTRATIONS OF KETALS WITH VARIOUS 2,2-DIMETHYL-1,3-PROPANEDIOL–KETONE RATIOS

Init. concn. of dicarbonyl cpd.	Init. concn. of glycol	Equil. concn. of cyclohexanone ketal	Equil. concn. of 2-methylcyclopentanone ketal
1	1	0.57	0.03
1	2	.75	.06
1	3	.82	.09
1	4	.86	.11
1	4.5	.88	.12

Substituting for y in (5) and solving for x, we get

$$x^3 - 5.041x^2 + 6.122x - 2.041 = 0 \qquad (8)$$

This equation was solved by Horner's method[20] to yield a value $x = 0.573$, which leads to a value of 0.026 for y. In a similar way calculations can be made for other initial glycol concentrations. In Table VIII a few of these results are listed.

By differentiating equation 7, simplifying, and setting equal to 1 (because maximum separation can be obtained when $dy/dx = 1$) we get

$$\frac{dy}{dx} = 1 = \frac{50}{(50 - 49x)^2} \qquad (9)$$

On solving, we find that $x = 0.88$ and $y = 0.12$.

In order to find out what initial glycol concentration would be required to obtain maximum separation, substitute the following values in equation 3

initial ketone concentration	1
initial glycol concentration	z
cyclohexanone ketal concn. at equil.	0.88
water concn. at equilibrium	$0.88 + 0.12 = 1.00$
cyclohexanone concn. at equil.	$1.00 - 0.88 = 0.12$
glycol concn. at equilibrium	$z - 1$

On solving we find that $z = 4.5$ and hence maximum preferential blocking can be obtained when 4.5 moles of 2,2-dimethyl-1,3-propanediol is equilibrated with one mole of the hypothetic diketone A.

COLUMBUS 10, OHIO

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[20] I. S. and E. S. Sokolnikoff, "Higher Mathematics for Engineers and Physicists," McGraw-Hill Book Co., Inc., New York, N. Y., 1934, pp. 27–32.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF BRITISH COLUMBIA]

The Protonation of the Carbonyl Group. I. The Basicity of Substituted Acetophenones[1]

BY ROSS STEWART AND K. YATES[2]

RECEIVED JULY 9, 1958

The basicities of twenty *m*- and *p*-substituted acetophenones have been determined by a spectrophotometric method in sulfuric acid media. With the exception of hydroxy and alkoxy groups which, it is believed, hydrogen bond strongly to the solvent, a very good correlation exists between pK_{BH^+} and σ^+. A good correlation also exists between pK_{BH^+} and $\nu_{C=O}$, the carbonyl stretching frequencies in the ketones. The conjugate acid of 2-acetylfluorene is considerably more stable than that for *p*-phenylacetophenone and the theoretical consequences of this are discussed.

In connection with a study of the position of protonation of the carboxyl group, which will be reported later, we found it necessary to use compounds containing the carbonyl group as models. The protonation of the carboxyl group might occur at either the "carbonyl" or "ether" oxygen but there is one oxygen atom only available for protonation in a carbonyl compound. We have accordingly determined the effect of *m*- and *p*-substituents on the basicity of acetophenones and this information later will be correlated with the data obtained with substituted benzoic acids.

Hammett[3a,b,c] in his classical investigation of the strength of very weak bases determined the basicity of acetophenone and its *p*-CH_3 and *p*-Br derivatives by a spectrophotometric method in sulfuric acid solution. This approach, which we have followed, utilizes the concept of the H_0 acidity function and has the advantage of producing absolute values of basicities, *i.e.*, absolute insofar as they are based on dilute aqueous solution as the standard state. Pratt and Matsuda[4] determined relative basicities of some acetophenones in benzene solution by a distillation method. They observed as we do, that *p*-OMe and *p*-OEt have anomalously high basicities.

Experimental

Acetophenones.—Commercially available acetophenones were purified either by vacuum distillation or by several recrystallizations.

m-Methylacetophenone was prepared from *m*-bromotoluene by the method of Gilman and Nelson.[5] *m*-Chloro- and *m*-bromo-acetophenones were obtained by diazotization of *m*-aminoacetophenone followed by the standard Sandmeyer procedure. *p*-Fluoroacetophenone and 2-acetylfluorene were prepared by the standard Friedel-Crafts acylation of fluorobenzene and fluorene, respectively. The physical constants of the purified compounds are reported in Table I.

Sulfuric Acids.—Sulfuric acid–water solutions ranging from 44.0 to 95.5% acid were prepared by dilution of Fisher C.P. Reagent grade sulfuric acid (95.0% min.). Concentrations were determined by titration with standard base. The H_0 values of these were obtained by interpolation from a standard curve constructed using the values given by Paul and Long.[6] Further solutions up to 99.9% acid were prepared from 30% fuming sulfuric acid (Baker and Adamson reagent) and H_0 values of these determined by indicator methods.[3c] All H_0 values of solutions were checked periodically.

Measurement of pK_{BH^+}.—A sample of each ketone weighed on a microbalance was dissolved in acetone to make a 5×10^{-3} *M* stock solution from which 0.1-ml. aliquots were pipetted into standardized 10-ml. volumetric flasks. After the acetone had been removed at the pump, the flasks were made up to volume with the sulfuric acid–water mixtures, the resulting concentration of ketone being 5×10^{-5}

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[1] Presented at the San Francisco Meeting of the American Chemical Society, April 7–11, 1958.

[2] Holder of a National Research Council of Canada Studentship, 1957–1958.

[3] (a) L. A. Flexser, L. P. Hammett and A. Dingwall, THIS JOURNAL, **57**, 2103 (1935); (b) L. A. Flexser and L. P. Hammett, *ibid.*, **60**, 885 (1938); (c) L. P. Hammett and A. J. Deyrup, *ibid.*, **54**, 2721 (1932).

[4] E. F. Pratt and K. Matsuda, *ibid.*, **75**, 3739 (1953).

[5] H. Gilman and J. F. Nelson, *Rec. trav. chim.*, **55**, 520 (1936).

[6] M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 1 (1957).

TABLE I

PHYSICAL CONSTANTS OF ACETOPHENONES

Acetophenone	M.p., or b.p. (mm.) and refractive index	Reported value of physical constants
m-Methyl-	B.p. 116–117° (26), $n^{21.5}$D 1.53	B.p. 109° (12), n^{15}D 1.533[a]
m-Chloro-	B.p. 230°, semicarbazone m.p. 225–226°[c]	B.p. 227–229°, semicarbazone m.p. 232°[b]
m-Bromo-	B.p. 135–136° (26), n^{21}D 1.5755	B.p. 131–132° (17), n^{20}D 1.5755[c]
p-Fluoro-	B.p. 97–98° (23), n^{25}D 1.5085	B.p. 79° (10), n^{25}D 1.5081[d]
m-Methoxy-	B.p. 141° (23), n^{23}D 1.5371	B.p. 127–128° (16–17), n^{20}D 1.5410[e]
m-Ethoxy-	B.p. 254°	B.p. 255°[f]
p-Ethoxy-	M.p. 35.5°	M.p. 38–39°[e]
2-Acetylfluorene	M.p. 128–130°	M.p. 128–129°[g]

[a] F. Mauthner, *J. prakt. Chem.*, **103**, 394 (1922). [b] A. Wahl and J. Rolland, *Ann. chim.*, 10, 29 (1928). [c] C. S. Marvel, R. E. Allen and C. E. Overberger, THIS JOURNAL, **68**, 1088 (1946). [d] M. W. Renoll, *ibid.*, **68**, 1159 (1946). [e] K. v. Auwers, *Ann.*, **408**, 242 (1915). [f] S. v. Kostanecki and J. Tambor, *Ber.*, **34**, 1691 (1901). [g] F. E. Ray and G. Rieveschl, Jr., *Org. Syntheses*, **28**, 3 (1948).

M. In cases of sufficient water solubility, aqueous stock solutions were prepared and the acids added directly to the aliquots, eliminating removal of solvent and possible loss of ketone by evaporation. Necessary corrections were made for added water. The flasks were then maintained at 25 ± 0.1° by means of a constant temperature bath.

The extinction coefficients of the above solutions were determined at two wave lengths with quartz cells of 1-cm. path length using a Beckman model DU spectrophotometer whose cell compartment was maintained at the above temperature by means of thermospacers. The sulfuric acids were tested for optical clarity in the regions used and a solvent blank of the same concentration as that containing the ketone was used. Ultraviolet absorption spectra of the ketones in 44.0% and 95.5% acids measured with a Cary model 14 recording spectrophotometer were used where necessary to locate the wave lengths of maximal absorption of the unprotonated (λu) and protonated (λ_i) forms. These are listed in Table II.

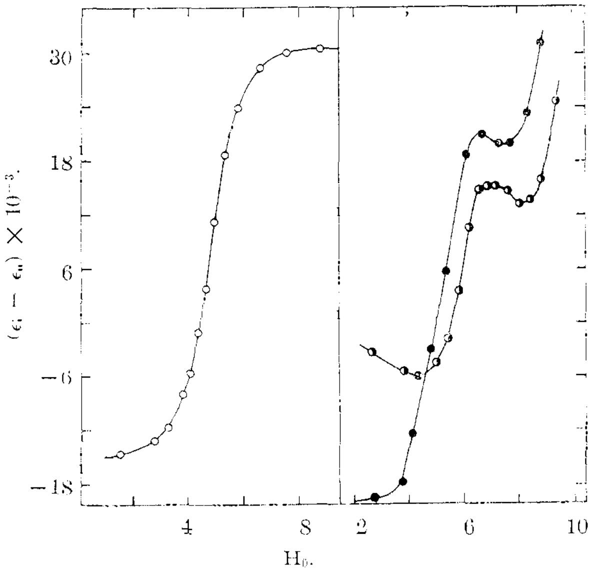

Fig. 1a (left).—The function $(\epsilon_i - \epsilon_u) \times 10^{-3}$ plotted against H_0 for *p*-methoxyacetophenone, O. Fig. 1b (right).—The function $0.5(\epsilon_i - \epsilon_u) \times 10^{-3}$ plotted against H_0 for 2-acetylfluorene, ●, and for *p*-phenylacetophenone, ◑.

The pK_{BH^+} values were determined by the method of Davis and Geissman[7] as described. The difference $[\epsilon(\lambda_i) - \epsilon(\lambda_u)]$ which is linearly related to the fraction ionized, was plotted against H_0. At the inflection point in this curve it can be shown that fraction ionized = fraction un-ionized and hence, $H_0 = pK_a$. The results of a typical determination are shown in Fig. 1a. In all cases, except *p*-phenylacetophenone and 2-acetylfluorene whose results are shown in Fig. 1b and discussed later, a sigmoid, titration-like curve was obtained and the inflection point taken as the mid-point of the "straight" portion. The advantages and limitations of this method of pK_a determination are discussed by the above authors. We feel too that in cases of complex absorption spectra, the second decimal in the pK_a value is of doubtful value.

TABLE II

pK_{BH^+} AND WAVE LENGTH MAXIMA FOR SUBSTITUTED ACETOPHENONES

Substituent	pK_{BH^+}	(44.0% H_2SO_4) mμ	(95.5% H_2SO_4) mμ
H[a]	6.15	250	290
m-CH_3	6.02	252	300
p-CH_3[b]	5.47	260[c]	310[d]
p-C_2H_5	5.61	260	315
m-OCH_3	6.70	253	296
p-OCH_3	4.81	282	340
m-OC_2H_5	6.70	253	296
p-OC_2H_5	4.90	284	350
m-OH	6.59	254	292
p-OH	4.73	280	330
p-F	6.06	250	299
m-Cl	7.01	248	295
p-Cl	6.52	258	315
m-Br	6.90	248	297
p-Br[b]	6.52	270[e]	330[d]
m-NO_2	7.62	232	278
p-NO_2	7.94	270	288
β-C_4H_4[f]	5.71	250	272
p-C_6H_5	..	288	349
2,3-C_7H_6[g]	..	316	379

[a] Identical with corrected value (ref. 6) of Flexser, Hammett and Dingwall (ref. 3). [b] Taken from ref. 3b, and corrected to ref. 6. [c] 52.0% H_2SO_4. [d] 96.0% H_2SO_4. [e] 60.1% H_2SO_4. [f] β-Naphthyl methyl ketone. [g] 2-Acetylfluorene.

Because of the possibility of rapid sulfonation found in the case of anisole the absorption spectra of the alkoxyacetophenones in 95.5% acid were repeated after one-hour standing. They were found to undergo no appreciable change and on subsequent dilution the resulting spectra reproduced closely those of control solutions in dilute acid. The spectra in dilute acid also resemble closely those in water. In all cases, the measurements were taken as rapidly as possible after the addition of the acids.

Results and Discussion

The values of pK_{BH^+} for the substituted acetophenones are listed in Table I and are plotted as a function of σ, the Hammett substituent constant, in Fig. 2. (The straight line in Fig. 2 was drawn with respect to the groups *p*-NO_2, *m*-NO_2, *m*-Cl, *m*-Br, H, *m*-Me; groups which should not be subject to either of the effects described below.) The positive and negative deviations from the

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(7) C. T. Davis and T. A. Geissman, THIS JOURNAL, **76**, 3507 (1954).

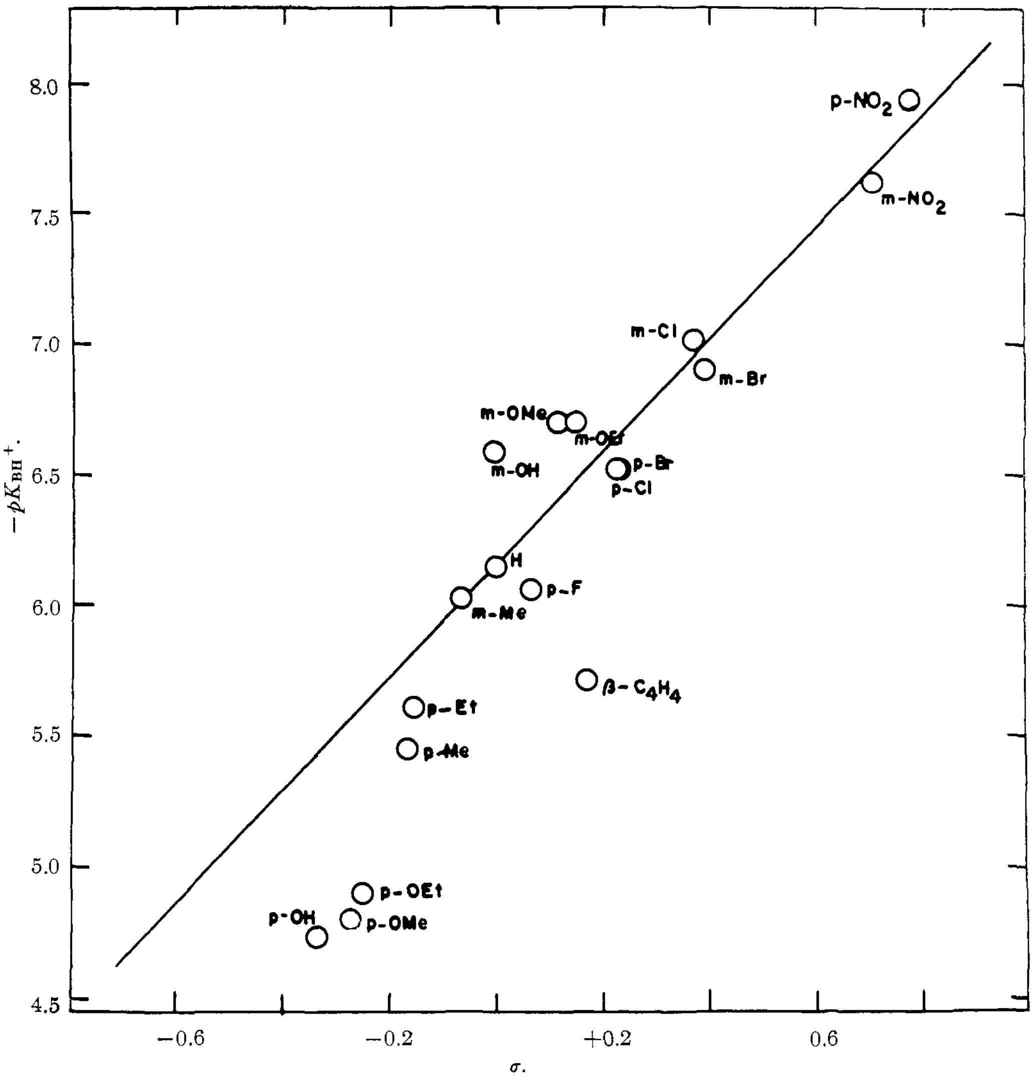
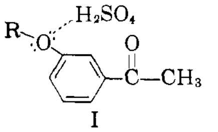


Fig. 2.— $-pK_{BH^+}$ for substituted acetophenones plotted against σ-values taken from Jaffé (ref. 8).

linear free energy relation which are so apparent in Fig. 2 can be considered separately.

Positive Deviations in Fig. 2.—Those points which fall considerably above the line in Fig. 2 are those representing *m*-HO, *m*-MeO and *m*-EtO. The σ-values of these groups have been determined for the most part using neutral solvents and one would expect that in sulfuric acid solution, solute–solvent hydrogen bonding as in I will be particularly strong at the alkoxyl and hydroxyl groups resulting in an actual increase in the values of σ for these groups in sulfuric acid and a consequent lowering of the basicity of the ketone.


I

Another possible cause of the deviations of the alkoxyl and hydroxyl groups was considered, *viz.*, that these groups protonate at lower acidities than the carbonyl group. The resulting groups, H_2O^+– and RHO^+–, would exert an electron-withdrawing effect in qualitative agreement with the deviations observed in Fig. 2, but this possibility was rejected for these several reasons: (i) The groups H_2O^+– and RHO^+– by analogy with NH_3^+– and RNH_2^+– would be expected to exert a much stronger electron-withdrawing effect than that actually observed. Thus $\sigma_{m\text{-}NH_2}$, which has a value of −0.16 changes by some 0.8 unit on protonation to give a value of +0.63 for $\sigma_{m\text{-}NH_3^+}$.[8] The change is even larger for the MeNH– group. There would be a difference of only 0.16 unit between the σ-values of *m*-MeO– and *m*-$MeOH^+$– if the latter was, in fact, the group present, assuming that it obeys the Hammett relation.[9] (ii) The spectral changes which occur when the alkoxy and hydroxy acetophenones are protonated are very similar to those obtained with the other acetophenones considered here, as can be seen in Table II, and involve a red shift of some magnitude. On the other hand, *m*-

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(8) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

(9) Strictly speaking, H_+ rather than H_0 should be used to determine the value of positively charged groups such as $MeHO^+$–, but there is evidence that H_0 and H_+ are close in H_2SO_4, probably not more than 0.3 unit apart (J. C. D. Brand, W. C. Horning and M. B. Thornley, *J. Chem. Soc.*, 1374 (1952)).

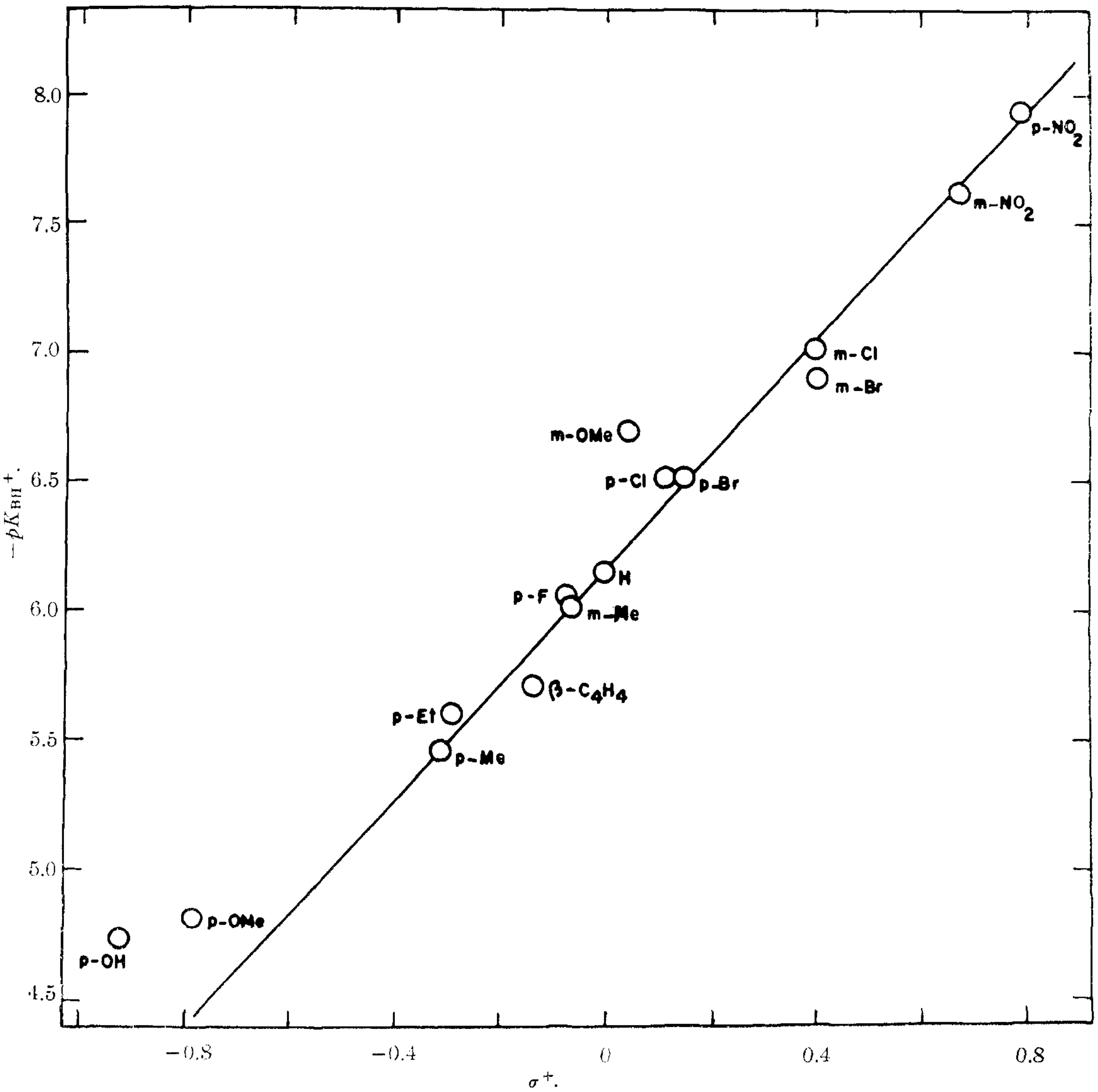
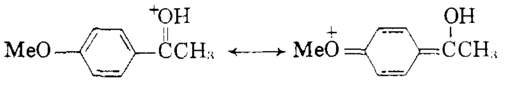


Fig. 3.—$-pK_{BH^+}$ for substituted acetophenones plotted against the σ^+-values of Brown and Okamoto (ref. 11.).

and *p*-aminoacetophenone which are unquestionably protonated more easily at the amino than at the carbonyl group, undergo a blue shift on protonation. This is expected since the positively charged substituent will oppose the dipole created in the excited state and thus raise its energy. (iii) Alkoxybenzenes are much less basic than aliphatic ethers. Although rapid sulfonation made an accurate determination of the pK_{BH^+} of anisole in sulfuric acid impossible, it appears to be less basic than acetophenone.

Negative Deviations in Fig. 2.—Those points which fall appreciably below the line in Fig. 2 represent in all cases *p*-substituents which are able to donate electrons by resonance. Several investigators have noted that substituents such as *p*-OMe are able to stabilize carbonium ions to a much greater extent than is indicated by their σ-values,[10] and Brown and Okamoto[11] among others[12] have derived σ^+-values for groups which can donate electrons by resonance for use in reactions in which a positive charge is developed in conjugation with the group. Figure 3 shows a plot of σ^+ against pK_{BH^+} for those substituted acetophenones for which σ^+-values are available.[13] An excellent linear relation is obtained if one disregards the points representing *p*-OMe and *m*-OMe. It should be noted that the *p*-OMe group here is strongly electron donating by resonance but is not quite as strong as the σ^+-value predicts, presumably because of the interaction with solvent discussed above.



The ρ-value for the σ^+–pK_{BH^+} curve, omitting the methoxy groups, is 2.17 (least squares calculations used throughout) and for the straight line in

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(10) (a) D. E. Pearson, J. F. Baxter and C. J. Martin, *J. Org. Chem.*, **17**, 1511 (1952); (b) J. K. Kochi and G. S. Hammond, THIS JOURNAL, **75**, 3445 (1953); (c) J. J. Jaruzelski, N. C. Deno and A. Schriesheim, *J. Org. Chem.*, **19**, 155 (1954).

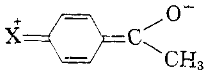
(11) H. C. Brown and Y. Okamoto, THIS JOURNAL, **79**, 1913 (1957).

(12) N. C. Deno and W. L. Evans, *ibid.*, **79**, 5804 (1957).

(13) D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

Fig. 2, is 2.22. The correlation coefficient for all 15 points in Fig. 3 is 0.983 whereas for the corresponding points in Fig. 2 the correlation coefficient is only 0.905.

Correlation with Infrared Spectra.—Several investigators have remarked on the fair correlation which exists between the carbon–oxygen stretching frequencies for substituted acetophenones and the corresponding σ-constants. Jones, Forbes and Mueller[14] recently have shown that a very good linear relation exists between $\tilde{\nu}_{C=O}$ and σ for *m*-substituted acetophenones but not for the *p*-substituted compounds. Their results indicated a considerable contribution from structures like II which would introduce more single bond character into the carbonyl group and hence lower its stretching frequency


II

Since the resonance effects of *p*-substituents are believed responsible for the deviations observed in both the infrared and the protonation experiments reported herein, it is of interest to see if a linear relation exists between $\tilde{\nu}_{C=O}$ and pK_{BH^+}. Figure 4 shows that this is the case, the correlation coefficient being 0.964. The stretching frequencies shown are mean values obtained by combining the results of several groups of investigators and in view of this the agreement is very satisfactory.[15]

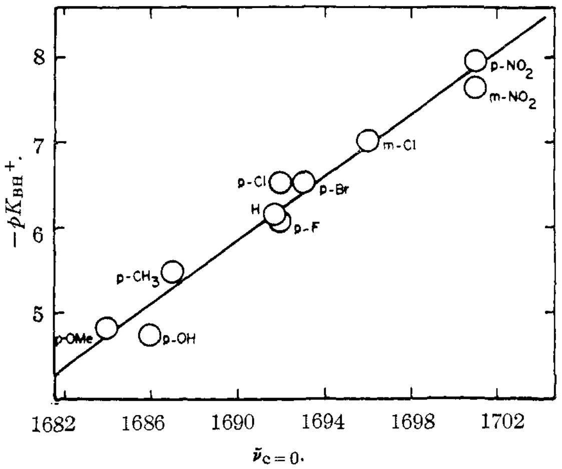
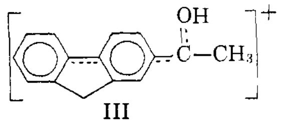


Fig. 4.— $-pK_{BH^+}$ shown as a function of the carbonyl stretching frequencies for substituted acetophenones.

***p*-Phenylacetophenone and 2-Acetylfluorene.**—As mentioned earlier, the only two ketones studied which gave unsatisfactory plots of $[\epsilon_{(\lambda i)} - \epsilon_{(\lambda u)}]$ *vs.* H_0 were *p*-phenylacetophenone and 2-acetylfluorene. The cause of the odd shaped plots in Figure 1b is probably the unusually large increase in extinction coefficient in going from the un-ionized to the ionized forms for these compounds (*p*-phenylacetophenone: $\epsilon_{288} = 9200$, $\epsilon_{349} = 27{,}800$; and 2-acetylfluorene: $\epsilon_{316} = 40{,}000$, $\epsilon_{379} = 72{,}2000$). Brown[16] has pointed out that phenyl substituents often provide unexpectedly low stability when substituted *para* in a benzene ring to a cationic center compared to the very great stability provided by a phenyl group α to a cationic center. He has suggested that this is because the two benzene rings in a biphenyl derivative are twisted at an angle of about 45° to one another thus greatly reducing the π-orbital overlap between the rings. On this basis, Brown has predicted that 2-fluorenyl derivatives in which the benzene rings are largely restricted to the same plane, should be much more effective in stabilizing carbonium ions. Although absolute determinations of pK_a for *p*-phenylacetophenone and 2-acetylfluorene were not possible, it can be seen from Fig. 1 that the fluorenyl curve is very similar to the curve for *p*-phenyl but that it is displaced some 0.3 logarithmic unit to the left indicating that the conjugate acid III is, in fact, considerably more stable than that for the *p*-phenyl compound.


III

Acknowledgment.—The financial support of the National Research Council of Canada is gratefully acknowledged.

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[14] R. N. Jones, W. F. Forbes and W. A. Mueller, *Can. J. Chem.*, **35**, 504 (1957).

[15] Only the values measured in carbon tetrachloride were used since the frequencies can change considerably on changing the dielectric constant of the solvent. These values were taken from ref. 14 and also from N. Fuson, M. L. Josien and G. M. Skelton, THIS JOURNAL, **76**, 2526 (1954); G. M. Barrow, *J. Chem. Phys.*, **21**, 2008 (1953); and L. J. Bellamy, *J. Chem. Soc.*, 4221 (1955).

[16] H. C. Brown, personal communication.