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Spectra and *Keto-Enol* Equilibrium of Benzoylacetanilides

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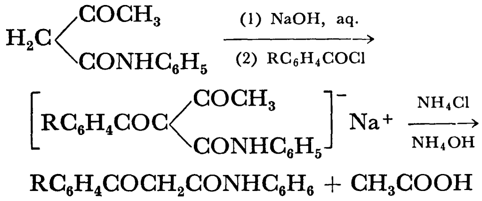
A series of twelve monosubstituted benzoylacetanilides have been prepared by condensation of acetoacetanilide with substituted benzoylchlorides. IR and UV spectral data are presented and discussed. The benzoyl CO stretching frequencies were correlated with σ^+($\bar{\nu}=34.97\sigma^+ + 1705$; $r=0.983$). The effect of substituents in the benzoyl moiety on the *keto-enol* equilibrium, has also been investigated. The data were correlated by the equation: $\log K=0.865\sigma^+ - 0.615$; $r=0.988$.

While several investigations on benzoylacetanilides have been made concerning their reactions[1] and acidities,[2] meagre data are available on their spectral characteristics. Furthermore, although there are several reports dealing with the effects of substituents on the *keto-enol* equilibria in systems such as benzoylacetones,[3] 2-benzoylcyclanones,[4] and ethyl benzoylacetates,[5] benzoylacetanilides (I) have not been included in these analyses.

In the present communication, we wish to present a convenient method for the preparation of substituted benzoylacetanilide together with their spectral (IR and UV) characteristics. This report also contains the results of a study of the *keto-enol* equilibrium of such compounds and the effect of substituents on it.

Synthesis. Of the various methods that have been reported[6] for the synthesis of aroylacetanilides, the only generally useful one has been the condensation of equimolecular amounts of ethyl aroylacetate with the appropriate arylamine at elevated temperatures. Since most of the ethyl esters of aroylacetic acids are not commercially available, it was of interest to find an alternate short and general method that could be employed for the synthesis of aroylacetanilides. The conversion of ethyl benzoylacetoacetate to ethyl benzoylacetate[7] with ammonium chloride and ammonium hydroxide suggests that acylation of acetoacetanilide and the decomposition of the resulting 2-aroylacetoacetanilide might be a general reaction which has been long overlooked. We have, in fact, found that aroylacetanilides (I) can be conveniently prepared from acetoacetanilide according to the reaction sequence outlined in Scheme 1. Twelve compounds (Ia—l), four of which are new, were prepared this way.



$$H_2C\begin{matrix}\diagup COCH_3 \\ \diagdown CONHC_6H_5\end{matrix} \xrightarrow[\text{(2) }RC_6H_4COCl]{\text{(1) NaOH, aq.}} \left[RC_6H_4COC\begin{matrix}\diagup COCH_3 \\ \diagdown CONHC_6H_5\end{matrix}\right]^- Na^+ \xrightarrow[NH_4OH]{NH_4Cl}$$

$$\underset{\text{I}}{RC_6H_4COCH_2CONHC_6H_6} + CH_3COOH$$

a, $R=4\text{-}CH_3O$
b, $R=4\text{-}CH_3$
c, $R=3\text{-}CH_3$
d, $R=H$
e, $R=3\text{-}CH_3O$
f, $R=4\text{-}Cl$
g, $R=4\text{-}Br$
h, $R=3\text{-}Cl$
i, $R=3\text{-}Br$
j, $R=4\text{-}CN$
k, $R=3\text{-}NO_2$
l, $R=4\text{-}NO_2$

Scheme 1

Infrared Spectra. The infrared absorption maxima of aroylacetanilides (Ia—l) and their assignments are given in Table 1. The most significant feature of these spectra is the presence and location of the carbonyl stretching bands. In the carbonyl region, benzoylacetanilide (Id) possesses two strong bands, one near 1705 and the second 1669 cm^{-1}. By analogy to acetoacetanilide[8] these bands are assigned to the benzoyl and anilide carbonyl groups, respectively. The appearance of the bonzoyl CO group and the complete absence of any OH band suggest that benzoylacetanilide and its substituted derivatives, under the conditions of measurement, exist almost in the *keto* form. The data indicate also that the position of the aroyl CO band depends, to a large extent, upon the nature of the substituent present. As shown in Table 1, as the character of the substituent (*meta* or *para* to the CO group) changes progressively from electron donating to electron withdrawing, the value of ν_{CO} increases.

Good correlations of carbonyl stretching frequencies with Hammett constants have been reported for acetophenones,[9] benzophenones,[10] benzoyl chlorides,[11] and chalcones.[12] The application of the Hammett

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TABLE 1. CHARACTERISTIC INFRARED BANDS (cm^{-1}) OF SUBSTITUTED BENZOYLACETANILIDES

Ia	Ib	Ic	Id	Ie	If	Ig	Ih	Ii	Ij	Ik	Il	Assignment
3260	3300	3300	3260	3290	3290	3290	3280	3270	3350	3375	3400	N–H stretch
3175	3185	3200	3200	3180	3200	3200	3120	3180	3120	3340	3320	
3045	3050	3050	3065	3060	3060	3040	3040	3040	3050	3075	3050	=C–H stretch
3020		3100	3045							3040		
2950	2920	2930	2900	2950	2925	2940	2940	2925	2925	2950	2930	–C–H stretch
2830	2850	2875	2840	2840	2850	2850	2830	2850	2910	2850	2850	
1683	1689	1700	1705	1703	1710	1710	1720	1722	1726	1730	1734	Aroyl CO
1666	1666	1666	1669	1668	1662	1662	1666	1665	1670	1652	1650	Amide-I
1600	1600	1590	1605	1604	1600	1609	1608	1600	1610	1608	1600	C=C skeletal
1580	1570	1575	1560		1570			1575		1560	1570	stretching
1510	1510	1515	1515	1500	1500	1500	1510	1500	1500	1500	1510	vibrations
1450	1460	1465	1450	1455	1455	1440	1450	1455	1450	1460		
1540	1540	1550	1550	1557	1541	1543	1550	1547	1550	1552	1563	Amide-II
1430	1420	1430	1415	1425	1415	1415	1420	1425	1425	1410	1410	C–H scissoring
1325	1300	1315	1310	1325	1300	1315	1310	1310	1315	1310	1315	Amide-III
1265	1265	1275	1265	1280	1275	1275	1220	1220	1250	1280	1290	
1225	1250	1225	1230		1225	1225			1225	1260	1215	
840					845	845				865	870	Aromatic C–H
835												bending
820	810				825	825			830		855	
	790	790		785			790	780		780	775	
760	760	755	755	765	760	760	770	750	765	750	762	
740			725		730	720	750	740		730	755	
	700		700	700			700		702		725	
695		695	690	690	069	690	685	960	695	698	700	

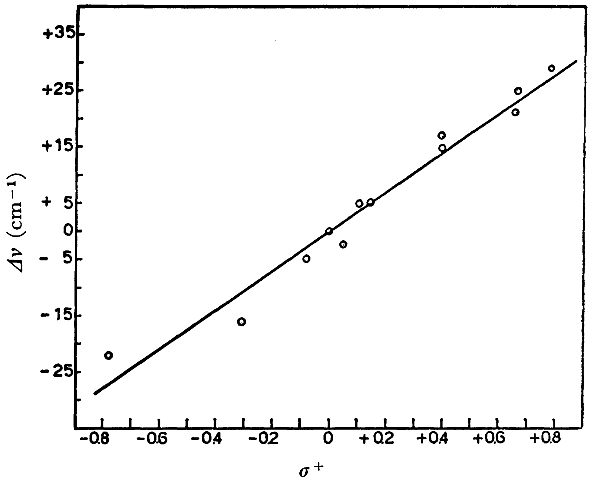


Fig. 1. Plot of $\Delta\nu$ *vs.* the substituent σ^+ for benzoylacetanilides.

TABLE 2. ULTRAVIOLET SPECTRA OF SUBSTITUTED BENZOYLACETANILIDES

Compound No.	Ethanol λ_{max}, nm(log ε) Band A	Ethanol λ_{max}, nm(log ε) Band B	Cyclohexane λ_{max}, nm (log ε) Band A	Cyclohexane λ_{max}, nm (log ε) Band B
Ia	323 (3.69)	272 (4.29)	318 (3.73)	278 (4.30)
Ib	311 (3.83)	251 (4.30)	309 (3.96)	254 (4.44)
Ic	310 (3.81)	244 (4.19)	303 (3.92)	244 (4.21)
Id	308 (3.97)	242 (4.35)	306 (4.07)	243 (4.37)
Ie	311 (4.13)	242 (4.35)	305 (3.97)	245 (4.11)
If	314 (4.06)	251 (4.30)	306 (4.24)	254 (4.30)
Ig	315 (4.08)	251 (4.29)	311 (4.23)	260 (4.24)
Ih	312 (4.07)	237 (4.24)	307 (4.14)	237 (4.16)
Ii	312 (4.06)	239 (4.24)	308 (4.15)	237 (4.21)
Ij	324 (4.12)	244 (4.26)	321 (4.16)	243 (4.20)
Ik	312 (4.14)	230 (4.29)	309 (3.95)	240 (3.98)
Il	345 (4.15)	257 (4.29)	334 (4.19)	248 (4.23)

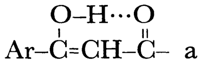
equation to the CO frequencies of aroylacetanilides (Ia—l) is shown in Fig. 1, in which $\Delta\bar{\nu}$ is plotted against σ^+ values; $\Delta\bar{\nu}=\bar{\nu}_R-\bar{\nu}_H$. The values of the slope and intercept were calculated by the least-squares method.[15] The best straight line fit corresponds to the equation:

$$\bar{\nu}=34.97\sigma^+ + 1705;\ r=0.983$$

The ρ of value ~35 obtained for benzoylacetanilides indicates a shift of ~35 cm^{-1} per unit of σ^+ constant, which is, within statistical limits, three times as much as the ρ for acetophenones series ($\rho=12.33$).[9,12] This relatively high sensitivity of the strength of the CO double bond to substituents suggests strongly that there is appreciable orbital overlap between the phenyl and carbonyl groups of the present series in solid state.

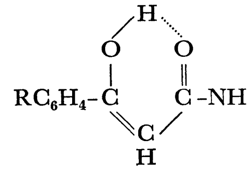
Ultraviolet Spectra. The ultraviolet spectral data for benzoylacetanilides in cyclohexane and ethanol are presented in Table 2. The absorption pattern was, in each case, characterized by the presence of two bands: Band A usually is located in the region of 305—350 nm, and Band B in the 240—280 nm region. The data also indicate that for the compounds studied Band A exhibits a bathochromic displacement as the solvent is varied from cyclohexane to ethanol.

It has been reported that λ_{max} values (log ε 4 to 5 in every case) for the chromophoric systems: Ar–C=C–C=O, Ar–CO–C=C–, Ar–CO–CH$_2$–CO–, and



$\overset{\text{O–H}\cdots}{\text{Ar–}\overset{|}{\text{C}}\text{=CH–}}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{–}$

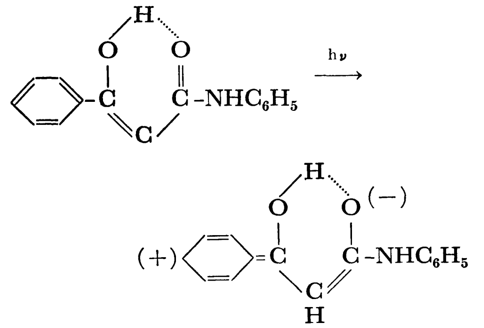
are 281—307, 248—283, 253 and 300 nm, respectively.[13] Accordingly, the A and B bands in the electronic absorption spectra of benzoylacetanilides can be assigned to the cinnamoyl and benzoyl chromophoric groups of the *enol* and *keto* forms respectively. Further, the fact that the λ_{max} values of the A bands are all larger than 300 nm provides evidence that the aroyl carbonyl rather than the anilide carbonyl is involved in enolization of the benzoylacetanilides as shown in structure II.



II

The position of λ_{max} of band A of benzoylacetanilides cannot be attributed to a bathochromic effect of the OH on the Ar–C=C–CO– system because it has been observed that the auxochromic effect of the OH and CH$_3$O groups on such a system does not shift λ_{max} beyond the 300 nm region.[13]

The shift of λ_{max} with a change of solvent is in the direction expected for a transition in which absorption produces a more polar excited state.



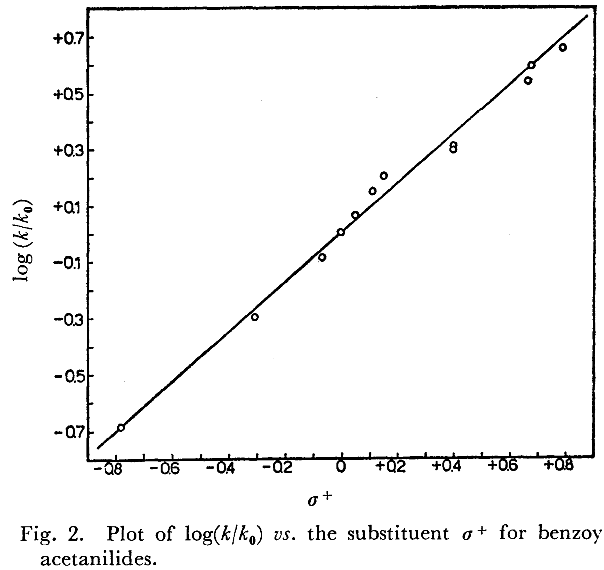


Fig. 2. Plot of log(k/k_0) *vs.* the substituent σ^+ for benzoylacetanilides.

TABLE 3. TAUTOMERIC EQUILIBRIUM AND SIGMA SUBSTITUENT CONSTANTS

Compound No.	*Enol*, %	K	log K/K_0	σ^+
Ia	5.00	0.0523	−0.690	−0.78
Ib	11.58	0.131	−0.294	−0.31
Ic	17.28	0.209	−0.088	−0.07
Id	20.40	0.256	0.000	0.00
Ie	18.20	0.222	−0.062	0.05
If	26.4	0.358	0.146	0.11
Ig	24.3	0.320	0.097	0.15
Ih	33.4	0.501	0.292	0.40
Ii	34.8	0.534	0.300	0.40
Ij	46.8	0.879	0.536	0.66
Ik	49.8	0.993	0.589	0.67
Il	54.06	1.176	0.662	0.79

The Keto-Enol *Equilibrium*. As expected, the lowest *enol* per cent (Table 3) is observed for the *p*-methoxyl group and the highest for the nitro group. The values of the equilibrium data as log(K/K_0) for the enolization reaction have been correlated with the substituent constant σ^+ as taken from Ritchie and Sager.[14] Figure 2 illustrates such a correlation. It is seen that the *meta-* and *para-*substituted benzoylacetanilides follow the Hammett equation closely.

A computer program was written to carry out the least-squares and statistical treatment of the date with the sigma constants according to the method of Jaffé.[15] The twelve values set of K in Table 3 best fit a straight line indicated by the equation: $\log K=0.865\,\sigma^+-0.615$; ($r=0.988$; $s=0.033$). The magnitude of the reaction constant ρ of value 0.865 is, within statistical limits, very close to the reaction constant for ethyl benzoylacetates (0.967).[5] This suggests that in the compounds studied the effects of coplanarity, resonance, inductive, and dipole interactions appear to be parallel to the same effects in ethyl benzoylacetate tautomeric equilibrium.

Furthermore, the data indicate that *enol* stability is determined by both mesomeric electronic delocalization[16a,b] and inductive electron withdrawal.[16c] From the value and sign of ρ, it is clear that electron donor substituents (methyl and methoxyl) lend more stability to the *keto* form than the enol form. It is logical, therefore, to conclude that the *enol* system is less electron deficient (electron demanding) than is the single carbonyl group.

Experimental

Melting points were determined on a Fischer-Johns hot stage. Elemental analyses were performed by microanalysis

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Laboratory, National Research Center, Dokki, Giza, Egypt. All solvents employed in this study were of spectral quality. Acetoacetanilide was prepared from ethyl acetoacetate and aniline by a method previously described[18] All yields reported relate to the recrystallized material.

Preparation of Aroylacetanilides. Acetoacetanilide (0.1 mol) was dissolved in 60 m*l* of 20% aqueous sodium hydroxide solution. The resulting solution was externally cooled by an ice bath and stirred by a magnetic stirrer. When the temperature of the solution reaches 2°C aroyl chloride (0.1 mol) was added from a dropping funnel, if liquid or in 0.1 g increments if solid, while the temperature of the reaction mixture was kept below 5°C. After all the acid chloride was added, the mixture was stirred for half an hour at 5°C; and for additional 30 min at room temperature. The reaction mixture was then diluted with 15 m*l* of 25% aqueous ammonium hydroxide solution containing 5.4 g (0.1 mol) of ammonium chloride and stirred for 5 minutes. The resulting mixture was heated to 40—50°C, left to stand overnight at room temperature, and filtered. Recrystallisation of the crude product from ethanol or dilute ethanol gave aroylacetanilide in 40—50% yield. The mp of the previously reported compounds agree with the literature values. The following aroylacetanilides ($RC_6H_4COCH_2CONHC_6H_5$) are new: R=4-Br, mp 144—145°C, Found: C, 56.61; H, 3.95; N, 4.10; Br, 24.98%. Calcd for $C_{15}H_{12}BrNO_2$: C, 56.60; H, 3.77; N, 4.40; Br, 25.16%. R=3-Cl, mp 127—128°C. Found: C, 66.17; H, 4.57; N, 5.20; Cl, 12.96%. Calcd for $C_{15}H_{12}ClNO_2$: C, 65.81; H, 4.39; N, 5.12; Cl, 12.98%. R=3-Br, mp 123—124°C, Found: C, 56.60; H, 3.90; N, 4.01; Br, 25.32%. Calcd for $C_{15}H_{12}BrNO_2$: C, 56.60; H, 3.77; N, 4.40; Br, 25.16%. R=4-CN, mp 140—142°C, Found: C, 72.75; H, 4.39; N, 10.58%. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.54; N, 10.60%.

Measurement of Spectra. The IR spectra were measured using a Perkin-Elmer model 377 double beam recording spectrophotometer, with sodium chloride optics. All compounds were recorded as potassium bromide pellets.

The UV spectra were determined using a Beckmann DK recording spectrophotometer. Matched quartz cells were used. Stock solutions for each compound were prepared by dissolving an accurately weighed amount of the sample in 50 m*l* of ethanol or cyclohexane. Solution with concentrations of 10^{-3} to 10^{-5} M were prepared by dilution of the stock solution using certified National Bureau of Standards 2- and 5-m*l* pipets and 10-m*l* volumetric flasks. In all cases solutions were allowed to equilibrate at least 24 hr in the dark before spectra were measured. Data determined are listed in Tables 1 and 2.

Determination of Percentage of Enol. The *enol* content was determined at equilibrium. A weighed sample of benzoylacetanilide (approximately 0.2 g) was dissolved in 50 m*l* of anhydrous absolute methanol. The solution was allowed to stand for 24 hr in a constant temperature water bath at 25±1°C in the dark. After this time, the modified bromine titration procedure[19] was used to determine the percentage of *enol*, with results given in Table 3. That the equilibrium is attained, is ensured by the fact that the *enol* per cent determined after extending the equilibrium time to 48 and 72 hr is similar to that determined after 24 hr. The maximum deviation of single determinations from the average of three to five determinations for each compounds was ±1 or less.

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