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DIPOLE MOMENTS OF SOME SUBSTITUTED ACETOPHENONES

INFLUENCE OF ORTHO SUBSTITUENTS ON THE POSITION OF THE ACETYL GROUP

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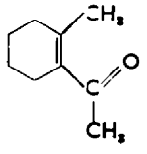
Abstract—The electric dipole moments of a number of substituted acetophenones, with at least one substituent (methyl, halo, nitro or amino) in the *ortho* position, have been measured in benzene solution and compared with the values calculated for free rotation as well as for *s-trans* and *s-cis* orientations of the acetyl group. 2-Methylacetophenones have a greater proportion of the *s-cis* isomer while 2-haloacetophenones have a greater proportion of the *s-trans* isomer. With increase in temperature there is an increase in the proportion of the less stable isomer. The observed dipole moment of *o*-aminoacetophenone indicates that the molecule exists predominantly in the *s-cis* configuration stabilized by intramolecular hydrogen bonding.

OF THE many rotational isomers possible for 1-acetyl-2-methylcyclohex-1-ene the *s-cis* (I) and *s-trans* (II) forms[1] are two isomers in which the acetyl and methyl groups are co-planar. Turner and Voitle[2] have shown that this compound exists predominantly in the *s-cis* form from a comparison of its absorption properties with



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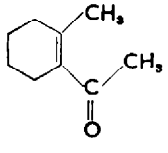

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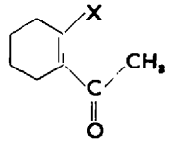


III

those of α,β-unsaturated ketones of the *s-cis* type. They thought that their conclusion was consistent with the lesser hindrance of the *s-cis* form.

While predicting the relative stabilities of the *s-cis* and *s-trans* configurations of 2-substituted 1-acetylcyclohex-1-enes, we have to consider not only the sizes of the groups in the 1,2-positions but also the polarity of these groups. The electrostatic repulsion between the two methyl groups renders the *s-trans* configuration unstable. On the other hand such a configuration would be favoured in 1-acetyl-2-halocyclohex-1-enes (III, X = Halogen), irrespective of the size of the halogen atom, due to the opposite polarities of the methyl group and the halogen atom.

[1] The terms *s-cis* and *s-trans* were first employed by R. S. Mulliken [(*Rev. Mod. Phys.* **14**, 265 (1942)] to designate *cis* and *trans* isomers about a single bond possessing some double bond character.
[2] R. B. Turner and D. M. Voitle, *J. Amer. Chem. Soc.* **73**, 1403 (1951).

These considerations have prompted us to study the structures of some *ortho*-substituted acetophenones from measurements of their dipole moments. The dipole moment, being a vector quantity, should give valuable information regarding the spatial disposition of the *ortho* groups.

Dipole moments

The dielectric constants and densities of benzene solutions were measured at 30°. In the case of some compounds they were also measured at 50°. Definitions of symbols used here and the method of calculating dipole moments were given in a previous paper.[3] Observations and results of the present work are summarized in Tables 1 and 2.

TABLE 1. POLARIZATION DATA AT 30°

Acetophenone	α	β	P_2 (ml)	R_D (ml)	μ (D)	Previous values
o-Methyl	2·473	0·136	182·4	41·1	2·65	2·60[a]
p-Methyl	3·575	0·126	246·8	41·4	3·19	3·23[b]
o-Amino	1·336	0·204	114·4	41·9	1·90	—
o-Nitro	6·441	0·258	499·4	42·3	4·77	—
p-Nitro	3·082	0·323	257·2	42·8	3·26	3·29[c]
o-Chloro	3·032	0·273	240·0	41·0	3·15	—
p-Chloro	1·767	0·273	155·8	41·7	2·38	2·40[c]
o-Bromo	2·487	0·411	253·0	43·9	3·22	—
2,5-Dichloro	1·805	0·351	188·7	46·3	2·66	—
2,5-Dibromo	1·238	0·542	191·4	52·3	2·63	—
5-Chloro-2-methyl	1·158	0·254	126·9	46·0	2·01	—
5-Bromo-2-methyl	0·898	0·402	125·8	48·9	1·96	—
5-Iodo-2-methyl	0·760	0·494	130·0	54·4	1·94	—
2-Methyl-5-nitro	2·319	0·294	221·7	47·0	2·95	—

[a] J. W. Smith, *J. Chem. Soc.* 4050 (1957).
[b] J. B. Bentley, K. B. Everard, R. J. B. Marsden and L. E. Sutton, *J. Chem. Soc.* 2957 (1949).
[c] B. Eda and K. Ito, *Bull. Chem. Soc. Japan* **30**, 164 (1957); *Chem. Abstr.* **51**, 14346 (1957).

TABLE 2. POLARIZATION DATA AT 50°

Acetophenone	α	β	P_2 (ml)	R_D (ml)	μ (D)
o-Chloro	2·878	0·279	234·8	41·0	3·21
o-Bromo	2·331	0·433	243·7	43·9	3·26
2,5-Dichloro	1·672	0·382	179·7	46·3	2·66
5-Chloro-2-methyl	1·119	0·234	127·6	46·0	2·08
5-Bromo-2-methyl	0·862	0·388	125·8	48·9	2·02
5-Iodo-2-methyl	0·727	0·467	131·0	54·4	2·02
2-Methyl-5-nitro	2·235	0·288	220·6	47·0	3·03

[3] V. Baliah and M. Uma, *Tetrahedron* **19**, 455 (1963).

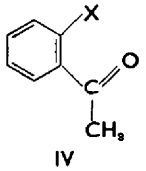
DISCUSSION

Whether or not there is inhibition of free rotation of groups in *ortho*-substituted acetophenones can be ascertained by comparing the observed dipole moments with those calculated by the vector addition of group moments, assuming free rotation of the groups. When there is inhibition of free rotation the observed moments should be significantly different from the calculated moments. Such a calculation requires a knowledge of the direction along which the moment of —$COCH_3$ group acts with reference to its axis of rotation. Assuming the moments of —$COCH_3$ and —Cl to be the same as the moments of acetophenone and chlorobenzene, respectively, and using the moments of *p*-chloroacetophenone (2·38 D), acetophenone (2·90 D)[3] and chlorobenzene (1·57 D)[3] the angle which the moment of —$COCH_3$ makes with its axis of rotation (the axis being directed towards the group) was found to be 55°. A similar calculation from the moments of *p*-nitroacetophenone (3·26 D), nitrobenzene (3·95 D)[3] and acetophenone showed the angle to be 54½°. So the angle was assumed to be 55°. The dipole moments of all the *ortho*-substituted acetophenones, whose configurations have been examined in the present investigation, were then calculated from group moments.[3] The calculated as well as the observed moments are given in Table 3.

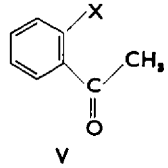
TABLE 3. OBSERVED AND CALCULATED DIPOLE MOMENTS OF ORTHO-SUBSTITUTED ACETOPHENONES

Acetophenone	μ_{obs} (D) at 30°	μ_{calc} (D) for		
		free rotation	*s-cis* form	*s-trans* form
o-Methyl	2·65	2·82	2·53	3·08
5-Chloro-2-methyl	2·01	2·99	0·99	4·12
5-Bromo-2-methyl	1·96	2·98	1·00	4·10
5-Iodo-2-methyl	1·94	2·92	1·21	3·96
2-Methyl-5-nitro	2·95	4·46	1·45	6·14
o-Chloro	3·15	3·67	4·47	2·65
o-Bromo	3·22	3·66	4·42	2·65
2,5-Dichloro	2·66	2·90	2·90	2·90
2,5-Dibromo	2·63	2·90	2·90	2·90
o-Amino	1·90	3·01	2·20	3·64
o-Nitro	4·77	5·53	6·84	3·79

The observed dipole moments are seen to be appreciably different from the values calculated from free rotation. This can be taken as a definite indication of restriction to free rotation of the acetyl group. The values calculated for the *s-cis** (IV) and *s-trans** (V) configurations are also given in Table 3. The observed moments of acetophenones, which have a methyl group *ortho* to the acetyl group, do not agree



IV



V

* This nomenclature is based on the Kekule structure having a double bond between the carbon atoms to which the *ortho* substituents are attached.

with the moments calculated for either the *s-cis* or *s-trans* configuration but they are closer to the *s-cis* values. We may then say that at the equilibrium position, the acetyl group orients itself in such a way as to impart the molecule an *s-cis*-like configuration (IV, X = CH_3), the acetyl group not being planar to the benzene ring.* Alternatively we may say that more molecules of the *s-cis* configuration will be present in the equilibrium mixture. The ratio of the number of molecules, $N_{s\text{-}trans}$, in the *s-trans* configuration to the number, $N_{s\text{-}cis}$, in the *s-cis* configuration may be evaluated from the equation[4]

$$\mu^2 = \frac{\mu^2_{s\text{-}cis} + \mu^2_{s\text{-}trans} \times N_{s\text{-}trans}/N_{s\text{-}cis}}{1 + N_{s\text{-}trans}/N_{s\text{-}cis}}$$

where μ is the observed moment and $\mu_{s\text{-}cis}$ and $\mu_{s\text{-}trans}$ are the calculated moments for the *s-cis* and *s-trans* configurations. The ratios obtained for the 2-methyl compounds are given in Table 4.

TABLE 4. RELATIVE PROPORTION OF ROTATIONAL ISOMERS

Acetophenone	$\frac{N_{s\text{-}trans}}{N_{s\text{-}cis}}$
o-Methyl	0·25
5-Chloro-2-methyl	0·24
5-Bromo-2-methyl	0·22
5-Iodo-2-methyl	0·19
2-Methyl-5-nitro	0·23

The lower proportion of the *s-trans* isomer is to be expected because there will be electrostatic repulsion between the two methyl groups. The electronic nature of the oxygen atom is no less important for the observed configurational preference. The nucleophilic oxygen atom takes a position adjacent to the electrophilic *ortho* methyl group.

The existence of molecules with preferred configurations has been recognized for a long time. Pauling[5] suggested that the splitting of IR spectral absorption lines in the 7000 cm^{-1} region in some *ortho*-substituted phenols like *o*-chlorophenol can be attributed to the existence of molecules of two different configurations. From the area of the two absorption peaks at 7050 cm^{-1} (*trans* form) and 6910 cm^{-1} (*cis* form) Pauling calculated that *o*-chlorophenol in carbon tetrachloride solution consists of about 91% *cis* and 9% *trans* molecules. The *cis* configuration is stabilized by the

* E. A. Braude and F. Sondheimer [*J. Chem. Soc.* 3754 (1955)] had concluded from a study of electronic spectra and dipole moments that 2-methylacetophenones have non-coplanar conformations. They even calculated the interplanar angle. In another paper E. A. Braude and C. J. Timmons [*J. Chem. Soc.* 3766 (1955)] stated that *s-cis-trans*-isomerism need not be considered for 2-methylacetophenone unless a high degree of symmetry in the electron-distribution in the benzenoid ring is postulated.

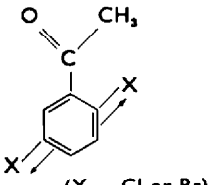
[4] N. Watanabe, S. Mizushima and Y. Morino, *Sci. Papers Inst. Phys. Chem. Research* (Tokyo) **39**, 401 (1942).

[5] L. Pauling, *J. Amer. Chem. Soc.* **58**, 94 (1936).

weak intramolecular hydrogen bonding between hydrogen and chlorine. This was corroborated from dipole moment studies by Anzilloti and Curran.[6]

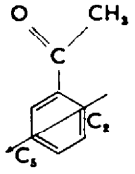
The existence of molecules with both *s-cis* and *s-trans* configurations in *ortho*-substituted acetophenones has been shown from IR absorption spectral studies of *o*-chloro-, *o*-bromo- and *o*-nitro-acetophenone by Jones *et al.*[7] They observed a doublet in the 1700 cm^{-1} region and attributed it to an equilibrium between the *s-trans* and *s-cis* isomers.

We may next consider the dipole moments of 2-haloacetophenones. 2,5-Dichloro- and 2,5-dibromo-acetophenone should have the same moment as acetophenone if the C-X moments in the *para* positions (VI) cancel each other. On account of proximity



(X = Cl or Br)

VI



VII

of the halogen atom and the acetyl group, the moments due to them will be reduced by mutual induction. There may thus be a small moment acting along the C_2-C_5 axis (VII). This, in combination with the reduced acyl moment, may account for the lower value observed (2,5-dichloroacetophenone, 2·66 D; 2,5-dibromoacetophenone, 2·63 D) relative to that of acetophenone (2·90 D).

The configurational preference of the acetyl group in 2-haloacetophenones might be expected to depend upon two factors; (1) polar repulsive interaction between the contiguous dipoles at the ortho positions and (2) the usual steric interaction. The relative importance of these two factors can be known from an analysis of the dipole moments of *o*-chloro- and *o*-bromo-acetophenone. The relevant data are found in Table 3. The observed dipole moments are close to the value calculated for the *s-trans* configuration (V, X = Cl or Br). This is to be expected. The *s-cis* configuration would be destabilized due to polar repulsive interactions between the group moments of C=O and C—Halogen at close range. Similar observations have been made in the study of the dipole moments of 2-halocyclohexanones[8] in which the halogen is oriented axially to a greater extent, contrary to normal conformational preference.

While comparing the dipole moments of *o*-chloro- and *o*-bromo-acetophenone, one would expect that the two compounds will have very nearly the same moment because C—Br and C—Cl have almost the same group moments. But from a consideration of the size of the two groups, there will be greater steric hindrance to the *s-trans* configuration in the bromo than in the chloro compound. Such an effect should result in an increase in the moment of *o*-bromoacetophenone compared to that of *o*-chloro-acetophenone. This is indeed the case. Thus the bulkier bromine atom

[6] W. F. Anzilloti and B. C. Curran, *J. Amer. Chem. Soc.* **65**, 607 (1943).
[7] R. N. Jones, W. F. Forbes and W. A. Mueller, *Can. J. Chem.* **35**, 504 (1957).
[8] N. L. Allinger, J. Allinger and N. A. LeBel, *J. Amer. Chem. Soc.* **82**, 2926 (1960).

reduces the proportion of molecules with the *s-trans* configuration (see Table 5). This finding is consistent with the observation of Jones *et al.*[7] who found, from the

TABLE 5

	$N_{s\text{-}trans}/N_{s\text{-}cis}$
o-Chloroacetophenone	3·40
o-Bromoacetophenone	2·74

intensities of IR absorption of the two ketones, that in the doublet of the carbonyl stretching absorption in the 1700 cm^{-1} region, the band of lower frequency (1694 cm^{-1}) is more intense for the chloro compound, but the higher frequency component (1706 cm^{-1}) is stronger for the bromo compound.

Intramolecular hydrogen bonding exists[9] in *o*-aminoacetophenone and this would be possible only in the *s-cis* configuration. The observed dipole moment of *o*-aminoacetophenone is 1·90 D. Estimation of the moment from group moments is not easy because the actual position of the groups and the effect of hydrogen bonding on group moments are not known with certainty. Four possibilities have been considered: (1) *s-cis* orientation and (2) *s-trans* orientation of the acetyl group with respect to a freely rotating amino group, (3) free rotation of the two groups independent of each other, and (4) *s-cis* orientation with the amino group fixed such that the two hydrogen atoms are symmetrically oriented with the possibility of both entering into hydrogen bonding. The calculated values for these four possibilities are 2·20, 3·64, 3·01 and 2·07 D, respectively. Since the observed moment is 1·90 D, the *s-trans* configuration and free rotation of the two groups may be excluded from consideration. We may then take the view that the molecule exists predominantly in the *s-cis* configuration stabilized by intramolecular hydrogen bonding.

The effect of temperature on the dipole moments of some 2-substituted acetophenones has also been studied. The values obtained at 50° are given in Table 6. For comparison the moments at 30° are also given. There is a definite increase in the value of the dipole moment with increase in temperature for all the ketones except

TABLE 6. EFFECT OF TEMPERATURE ON DIPOLE MOMENTS AND ISOMER RATIO

Acetophenone	μ_{obs} (D) at		$N_{s\text{-}trans}/N_{s\text{-}cis}$ ratio at	
	30°	50°	30°	50°
o-Chloro	3·15	3·21	3·40	2·95
o-Bromo	3·22	3·36	2·74	2·47
2,5-Dichloro	2·66	2·66	—	—
5-Chloro-2-methyl	2·01	2·08	0·24	0·26
5-Bromo-2-methyl	1·96	2·02	0·22	0·24
5-Iodo-2-methyl	1·94	2·02	0·19	0·23
2-Methyl-5-nitro	2·95	3·03	0·23	0·25

[9] A. E. Lutskii and V. V. Dorofeev, *Zuhr. Fig. Khim.* **33**, 331 (1959); *Chem. Abstr.* **53**, 20982 (1959).

for 2,5-dichloroacetophenone. The reason for the absence of temperature effect in this compound is obvious. The $N_{s\text{-}trans}/N_{s\text{-}cis}$ ratios at 50° (Table 6) indicate that there is a greater proportion of the less stable isomer at 50° than at 30°.

EXPERIMENTAL

Materials

All the known aryl methyl ketones were prepared as described in the literature. The physical constants of the liquids are given in Table 7.

TABLE 7. PHYSICAL CONSTANTS OF SUBSTITUTED ACETOPHENONES

Acetophenone	B.p.	n_D^{30}	d_4^{30}
o-Methyl	68°/7 mm	1·5280	1·007
p-Methyl	77°/7 mm	1·5300	1·001
o-Amino	108°/8 mm	1·6074	1·114
o-Nitro	133°/9 mm	1·5415	1·228
o-Chloro	81°/4 mm	1·5390	1·180
p-Chloro	93°/5 mm	1·5506	1·181
o-Bromo	100°/6 mm	1·5623	1·471
2,5-Dichloro	118°/12 mm	1·5595	1·321
5-Bromo-2-methyl	130°/17 mm	1·5685	1·426

5-Chloro-2-methylacetophenone. To a solution of methyl magnesium iodide prepared from magnesium (2·4 g) and methyl iodide (6·5 ml) in dry ether (50 ml) was added gradually a solution of 5-chloro-2-methylbenzonitrile[10] (5·2 g) in dry ether (30 ml). The mixture was refluxed for 11 hr and allowed to stand overnight at room temp. It was then poured into crushed ice, treated with 20% H_2SO_4 (60 ml) and heated on a water bath for 3 hr. The oil that separated was extracted with ether. The ethereal solution was washed successively ($NaHSO_3$ aq., dil. alkali and water). It was then dried ($CaCl_2$), the ether was removed and the fraction distilling at 121–122°/7 mm was collected. Yield 96%; n_D^{30} 1·5452; d_4^{30} 1·159 (Found: C, 64·42; H, 5·61. C_9H_9OCl requires: C, 64·10; H, 5·38%).

5-Iodo-2-methylbenzonitrile. 5-Amino-2-methylbenzonitrile[11] (13·2 g) was dissolved in 10% H_2SO_4 (200 ml) and diazotized at 0° with $NaNO_2$ (7 g in 30 ml of water). The solution was treated with KI (20 g in 20 ml water) and allowed to attain the room temp. It was then heated on a water bath for 1 hr and steam-distilled after adding enough $NaHSO_3$ to remove any iodine that may be formed. The distillate was extracted with ether and the extract was dried ($CaCl_2$) after washing with dil. NaOH aq. Evaporation of ether gave a solid (11·5 g) which crystallized from light petroleum (b.p. 60–80°) and melted at 72–73°. (Found: C, 39·79; H, 2·64. C_8H_6NI requires: C, 39·53; H, 2·49%).

5-Iodo-2-methylacetophenone was prepared in the same way as 2-methyl-5-chloroacetophenone. The yield was almost quantitative; b.p. 134–135°/5 mm; n_D^{30} 1·6110; d_4^{30} 1·659. (Found: C, 41·83; H, 3·79. C_9H_9OI requires: C, 41·56; H, 3·49%).

Physical measurements. The dielectric constants of the benzene solutions were measured with the apparatus described in ref. 3. In the case of liquids the molar refraction was calculated from the density and refractive index measurements. In the case of solids R_D was estimated from measurements made on benzene solutions with a Bellingham and Stanley refractometer of the Pulfrich type.

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[10] K. von Auwers and L. Harres, *Z. Physik. Chem.* A **143**, 1 (1929).
[11] W. Borsche and A. Herbert, *Liebigs Ann.* **546**, 277 (1941).