Infrared C-D Stretching and ^{2}H NMR Spectra of Isopropyl-2-*d* 1-(*p*-Substituted Phenyl)ethyl Ketones. Evidence for the Hydrogen Bond-Like Interaction between C-D Group and Aromatic π-Electrons

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(Received May 9, 1986)

Isopropyl-2-*d* 1-(*p*-X-phenyl)ethyl ketones (where, X=H, NO_2, Br, Cl, C_2H_5, CH_3, and NH_2) were shown to have two absorption bands in the C-D stretching region. The absorption band at the higher frequency (ca. 2177 cm^{-1}) is assigned to the C-D···π approached conformer, and the high frequency shift is ascribed to the effect of steric compression. Weak C-D···π hydrogen bond was shown to occur by the measurement of the substituent effect on the formation constant and the relative enthalpy of the C-D···π approached conformer.

Through the recent investigations of ours[1-5] and several other authors,[6,7] it has been clarified that an alkyl group often prefers to take a position close to an aromatic ring in certain molecules. Thus, 2-alkyl-1-arylethanes Ar-CHR-CHXR′ generally take preferably a conformation in which the aryl (Ar) and the alkyl (R′) groups are gauche to each other.[2,3,8] In addition, 1-arylethyl *t*-butyl sulfides and sulfoxides have similar preferred conformations. To account for the preferred conformations of these compounds, weak attractive force is assumed to operate between the aryl and the alkyl groups and named sometimes CH···π interaction, while the nature of the weak interaction remains to be explored. At first, the authors[9,10] tentatively explained this as being originated from weak hydrogen bonding between CH group and aromatic π-electrons similar to the intermolecular interaction between chloroform and benzene.[11,12] However, this interpretation is hypothetical and nothing renders a confident support on it. Alternatively, the observed conformational preferences were reproduced nearly quantitatively by molecular force field calculations.[8,13] The preference for alkyl/aryl approached (gauche) conformations in the series of $ArCH_2CHXR'$ cannot be rationalized without taking into account an attractive interaction between aryl and alkyl groups. Dispersion force is the only general attractive force included in the calculation. Therefore, the CH···π interaction should be ascribed to dispersive force to a large extent.

In spite of this conclusion, presence of weak CH···π hydrogen bonding cannot be excluded completely. On the contrary, the minor contribution of CH···π hydrogen bonding to the stabilization of the alkyl/aryl gauche conformers of 1-aryl-2-alkylethanes is suggested from LIS measurements on this series of compounds.[2-4] Ab initio (4—31G) calculation on 1-phenyl-2-propanol gives small but definitely positive bond population between methyl hydrogen atom and aromatic carbon atoms.[14] However, the absolute values of the bond populations are about one tenth of those for OH···π interaction ((O)-H···C bond populations). If the hydrogen bond-like CH···π interaction does exist, the interaction is expected to become strong when the C-H group is linked to an electronegative atom. Thus, the possibility of such an interaction was examined in the series of 1-phenylalkyl ketones. In order to observe the behavior of the particular hydrogen atom participating in CH···π hydrogen bonding separately, isopropyl-2-*d* 1-(substituted phenyl)ethyl ketones in which the hydrogen atom is replaced by deuterium were prepared, and their infrared and ^{2}H NMR spectra were measured and discussed.

Experimental

Preparation of 1-Aryl Isopropyl-2-*d* Ketones. Appropriately substituted 2-phenylpropionaldehyde was prepared by the method reported by Nerdel and Frohlich[15,16] and reacted with (isopropyl-2-*d*)magnesium bromide in ether. The alcohol obtained as the product was then oxidized by sodium dichromate-sulfuric acid mixture to give the ketone **2**. Other ketones (**3**—**9**) were also prepared by a similar method. Nitro ketone **2b** was prepared by nitrating ketone **2a**. Reduction of **2b** gives amino ketone **2g**.

All ketones and intermediate alcohols were identified by comparing their boiling points with the reported boiling points of unlabeled ketones[16] and also by their NMR, infrared, and mass spectra.

Measurement of Spectra. ^{2}H NMR spectra were recorded on a JEOL FX 90Q spectrometer in acetone or dimethyl sulfoxide solutions. Infrared spectra were recorded on a Hitachi 225 spectrophotometer using an NaCl cell of 2 cm optical path length in carbon tetrachloride or chloroform solutions. Temperature studies were performed with the carbon tetrachloride solutions.

Results and Discussion

Infrared C-D Stretching Absorptions and Their Assignment. The C-H stretching absorption of methine (isolated C-H) group is known to be very weak in comparison with those of CH_2 and CH_3

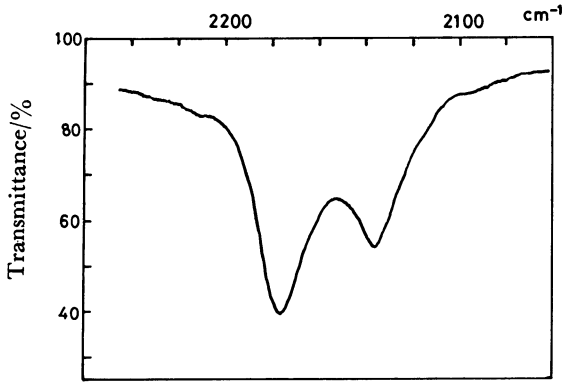
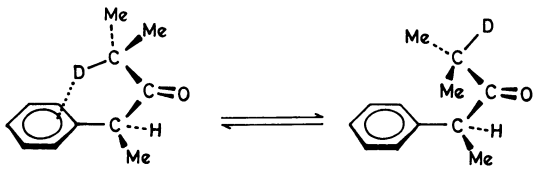


Fig. 1. Infrared C–D stretching absorption of isopropyl-2-*d* 1-phenylethyl ketone in CCl_4 solution.

groups,[17] which would make the recognition of the C–H band of isopropyl group extremely difficult. In fact, the C–H band of isopropyl group could not be identified in the spectrum of isopropyl 1-phenylethyl ketone (**1**) probably because of the interference caused by stronger overlapping bands. Thus, the deuterium-labeled analogs, isopropyl-2-*d* 1-(substituted phenyl)-ethyl ketones **2a—g**, were prepared and their infrared spectra in the C–D stretching frequency region (2300—2000 cm^{-1}) were measured.

As shown in Fig. 1, ketone **2a** has two absorption maxima at 2177 and 2136 cm^{-1} in this frequency region. The absorption bands can be characterized in spite of their very low intensity, since both the ketone and the solvent (carbon tetrachloride or chloroform) do not absorb the light of this frequency region.

Since the ketone **2a** has only a C–D bond, two absorption bands should be assigned to two different isomers, most probably rotamers in this case. Fermi resonance and related vibrational couplings might not operate in these circumstances, though they cannot be excluded completely. Temperature dependence measurement decribed later will support the conclusion, showing the presence of two energetically unequal isomers rapidly converting to each other. The sterical structures of the two conformers were estimated by molecular mechanics (MM2) calculations,[8] and the two conformers were tentatively assigned to the most and the next stable conformations (I and II, respectively) from the calculations.



(I) (II)

Table 1. C–D Stretching Absorptions of Isopropyl-2-*d* Ketones R–C–CD(CH_3)$_2$

No.	R	ν/cm^{-1}	No.	R	ν/cm^{-1}
3	Ph	2191	**6**	CMe_3	2195
		2156			2182
2a	PhCHMe	2177	**7**	$CDMe_2$	2182
		2136			2154
4	$PhCH_2$	2153	**8**	CH_2CH_3	2168
					2130
5	$PhCH_2CH_2$	2157	**9**	CH_3	2167
		2130			2130

The absorption frequencies of the two bands are rather higher than estimated from the reported methine C–H frequency 2890±10 cm^{-1}.[18] This frequency can be converted to 2121 cm^{-1} in the C–D stretching region if we assume the band to arise from a pure C–H (or C–D) stretching mode of molecular vibration. As revealed by examining the molecular models and more confidently by the C–H···C(Ar) distance in the most stable conformation(I) estimated from MM2 calculations on ketone **1**, some compression of the C–H bond length is expected to occur with the isopropyl methine group of ketone **1** due to the steric congestion around the bond.[18,19] Therefore, the high frequency shift of the C–D bands of ketones **2a—g** are ascribable to the shortening of the C–D bonds due to the steric compression.

In order to prove the effect of steric compression experimentally, the C–D stretching absorptions of several isopropyl-2-*d* ketones $RCOCDMe_2$ (**3—9**) were measured and given in Table 1. In cases of methyl and ethyl ketones (**8** and **9**), as well as 2-phenylethyl ketone (**5**), no steric congestion was expected around the C–D bond in problem. The C–D absorption frequencies of the two series of ketones in Table 1 clearly shows that the high frequency shift is caused by the steric crowdedness, the most crowded *t*-butyl and phenyl ketones (**3** and **6**, respectively) absorbing at the highest frequency in both series. In line with the prediction from MM2 calculations, the C–D bond in one conformer (which absorbs at 2177 cm^{-1} of **2a** is suspected from its high absorption frequency to suffer a considerable compression sterically.[20,21] MM2 calculations further revealed that the C–D bond is located very close and nearly perpendicular to the plane of the aromatic ring of 1-phenylethyl group in this conformer(I), and the nonbonded H(D)·····C_{Ar} distance was calculated to be as close as 2.65 A. The distance is too close to have an optimum van der Waals contact with each other and results in a weak repulsive nonbond interaction between H(D) and C_{Ar}. In accord with the above reasonings, the band at the higher frequency (2177 cm^{-1}) was tentatively assigned to the C–D···π approached conformation(I) and the one at the lower frequency to the conformation(II)

Table 2. C-D Stretching Absorptions of the Ketones *p*-XC$_6$H$_4$CHMeCOCDMe$_2$ (**2**) in CCl_4. (2 cm NaCl Cell; Concentration, ca. 0.05 mol dm^{-3})

No.	X	ν_I/cm^{-1}	ε_I/l mol^{-1} cm^{-1}	ν_{II}/cm^{-1}	ε_{II}/l mol^{-1} cm^{-1}	$\varepsilon_I/\varepsilon_{II}$
2b	NO_2	2174	4.94	2135	4.99	1.10
2c	Br	2174	5.26	2135	4.07	1.29
2d	Cl	2175	6.48	2136	4.59	1.41
2a	H	2177	6.54	2136	4.12	1.59
2e	C_2H_5	2176	5.07	2136	3.30	1.54
2f	CH_3	2176	6.34	2136	3.98	1.59
2g	NH_2	2175	5.65	2135	3.44	1.64

which is estimated to be the next stable from the MM2 calculations.

Possibility of Intramolecular C-D···π Hydrogen Bonding. In turn, C-D···π hydrogen bonding is expected to be favorably formed in the C-D···π approached conformation(I). Ab initio calculations on a more simplified model compound $PhCH_2CH$-(OH)Me also gave a small but definitely positive bond populations between the methyl H and aromatic C atoms opposing in close distances (CH_3 and C_1 or C_2 of phenyl group in a conformer).[14]

Both the unusually short distance from MM2 and the positive bond populations from ab initio MO suggest the occurrence of an intramolecular hydrogen bond-like interaction between the CH and the aromatic π system. If such an interaction is assumed to be present, the formation constant of the intramolecular hydrogen bond could be estimated from the ratio of the absorption intensities (ε_I and ε_{II}) of the two C-D bands assigned to the conformations I and II by Eq. 1.

$$K = a\frac{\varepsilon_I}{\varepsilon_{II}} \text{ or } a\frac{\varepsilon_{int}}{\varepsilon_{free}} \quad (1)$$

As the intrinsic molar extinction coefficients of the C-D···π interacted and the free (non-interacted) conformers (ε_I^0 and ε_{II}^0, respectively) are not necessarily equal, proportionality constant a which is equal to their ratio was introduced. Here, ε_I and ε_{II} are appearent extinction coefficients and related to the intrinsic extinction coefficients by $\varepsilon_I = X_I\varepsilon_I^0$ and $\varepsilon_{II} = X_{II}\varepsilon_{II}^0$, where X_I and X_{II} are molar fractions of conformers I and II.

Since the more electron-rich π system acts as a stronger hydrogen acceptor in forming hydrogen bond, negative slope is expected with the logarithm of the formation constant vs. σ plot for a series of isopropyl-2-*d* 1-(substituted phenyl)ethyl ketones (**2a**—**2g**). Thus the $\log(\varepsilon_I/\varepsilon_{II})$ vs. σ plot was drawn by employing the intensities in Table 2. As expected, the slope of the plot (in Fig. 2) becomes negative, and the above assignment was supported experimentally.

In general, intramolecular hydrogen bonds are cleaved when a stronger hydrogen-donating solvent

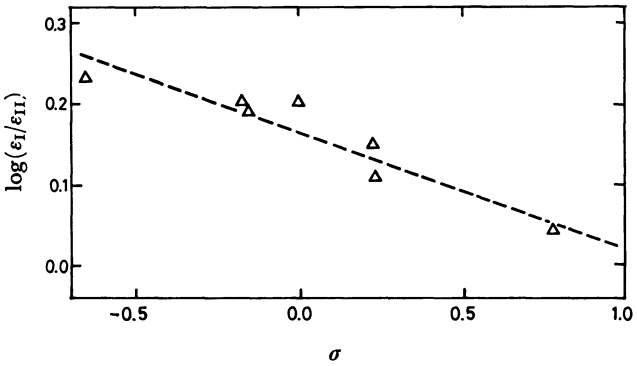
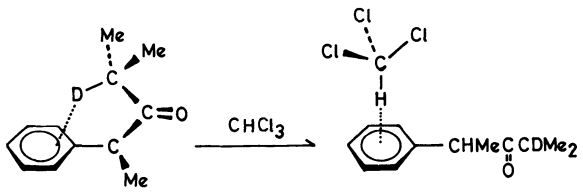


Fig. 2. Substituent effect on the ratios of absorption intensities of the two C-D bands. The $\varepsilon_I/\varepsilon_{II}$ vs. σ plot.

coexists. Therefore, the spectra of these ketones were measured in chloroform-*d* which is known as a typical C-H hydrogen donor in C-H···π hydrogen bonding.[11,12,22]



(I) (III)

The results are shown in Table 3. The observed $\varepsilon_I/\varepsilon_{II}$ ratios in Table 3 are significantly smaller than those in carbon tetrachloride. This reveals the fact that conformer I has been converted to the associated species III due to the solvation by forming intermolecular C-H···π hydrogen bond in chloroform. At present, we have no experimental evidence on whether the associated species III takes a conformation similar to the conformer II or not. However, the C-D bond of the associated species must not be very congested judging from its absorption frequency. Thus, the solvent effect on $\varepsilon_I/\varepsilon_{II}$ ratio again supports the above assignment of the C-D stretching bands and the presence of intramolecular hydrogen bonds.

Table 3. C-D Stretching Absorptions of the Ketones p-$XC_6H_4CHMeCOCDMe_2$ (**2**) in $CDCl_3$. (2 cm NaCl Cell; Concentration, ca. 0.05 mol dm^{-3})

No.	X	ν_I/cm^{-1}	ε_I/l mol^{-1} cm^{-1}	ν_{II}/cm^{-1}	ε_{II}/l mol^{-1} cm^{-1}	$\varepsilon_I/\varepsilon_{II}$
2b	NO_2	2167	3.00	2131	3.42	0.88
2d	Cl	2163	2.24	2133	3.00	0.75
2a	H	2163	2.84	2132	3.74	0.76
2f	CH_3	2163	2.25	2131	2.92	0.77

Table 4. ^2H NMR Spectra of the Ketones p-XC_6H_4-$CHMeCOCDMe_2$ (**2**) in Acetone[a)]

No.	X	δ_D(ppm) from $CDCl_3$
2b	NO_2	−5.298
2c	Br	−5.357
2d	Cl	−5.357
2a	H	−5.367
2e	C_2H_5	−5.371
2f	CH_3	−5.378

a) A small amount of LiBr for internal lock signal and $CDCl_3$ for reference were added.

Another evidence comes from ^2H NMR spectra of the ketones **2a—g**. The deuterium atom is located just above and very close to the plane of aromatic ring in conformer I and expected to resonate at a higher frequency than the one in conformer II due to the anisotropy effect of strongly diamagnetic aromatic ring. This implies that the electron-donating substituent on the aromatic ring favors the conformation I and, hence, causes a high field shift of the ^2H chemical shift. ^2H NMR of ketones **2** are given in Table 4. Due to the limitations from the solubility of LiBr for internal locking (since LiBr is sparingly soluble in CCl_4), the measurements were carried out in acetone containing a small amount of chloroform-*d* as an internal reference. As anticipated, the ^2H chemical shifts tend to move towards high fields in the order of decreasing electron-withdrawing ability and increasing electron-donating ability of the substituent, i.e., in the order of decreasing σ value.[23,24]

In conclusion, the C-D bond is sterically enforced to oppose the aromatic ring to have a considerable overlap of its antibonding orbital with the aromatic π-MO and is favorable in forming a C-D···π hydrogen bond. Judging from the substituent electronic effect and the solvent effect discussed above, the existence of the intramolecular hydrogen bonding between the isopropyl methine group and π-electrons on the aromatic ring becomes confident.

Substituent Effect on the Enthalpy of the C-D···π Interacted Conformer. As is remarked briefly in relation to the assignment of the C-D stretching bands, the intensities of the two C-D absorption bands

Table 5. Temperature Dependence of the C-D Absorption Intensities of p-$XC_6H_4CHMeCOCDMe_2$

X	T/K	$\varepsilon_I/\varepsilon_{II}$	ΔH/kJ mol^{-1}
NO_2	291.1	1.095	1.26
	300.4	1.110	
	310.0	1.126	
	320.1	1.145	
	329.0	1.162	
Br	293.5	1.289	0.92
	300.7	1.303	
	302.9	1.308	
	310.1	1.308	
	314.1	1.320	
	318.7	1.321	
	324.2	1.334	
	330.1	1.345	
Cl	297.6	1.413	0.88
	304.0	1.427	
	311.8	1.438	
	317.4	1.441	
	319.2	1.453	
	329.8	1.461	
H	293.7	1.586	0.80
	301.4	1.593	
	310.8	1.618	
	321.0	1.634	
	323.2	1.634	
	329.6	1.642	
C_2H_5	293.6	1.553	0.67
	303.2	1.546	
	313.1	1.565	
	320.3	1.582	
	329.9	1.595	
CH_3	292.4	1.594	0.55
	300.5	1.612	
	311.3	1.617	
	319.7	1.629	
	330.3	1.638	
NH_2	291.4	1.639	0.42
	301.4	1.640	
	307.4	1.657	
	317.4	1.650	
	329.1	1.673	

are temperature dependent. This provides us with a clue to elucidate the nature of the intramolecular interaction, since we can estimate the relative enthalpies of the C-D···π interacted conformers by measuring the formation constant K (given by Eq. 1) as a function of temperature. The measurements were carried out with carbon tetrachloride solutions of ketones **2a—g**, and the results are given in Table 5. The differences in enthalpy between the two conformers (ΔH) were calculated by Eq. 2 from the slope of $\log K$ vs. T^{-1} plots obtained by least squares calculation.[25]

$$\log K = -(\Delta H/R)T^{-1} + \Delta S/R \quad (2)$$

Here, K could be substituted by $\varepsilon_I/\varepsilon_{II}$ since a (in Eq. 1) affects only the entropy term in Eq. 2.

The relative enthalpies ΔH ($=H_I-H_{II}$) in Table 5 showed that the C-D···π interacted conformer(I) is not the most stable. This conclusion on the conformational preference does not agree with the prediction from MM2. However, the difference in enthalpy is less than 2 kJ mol^{-1} (or 0.5 kcal† mol^{-1}) which is known to be the maximal deviation from the experiment in MM2 calculations on hydrocarbons.[26]

If we assume that the substituent on the aromatic ring does not affect the stability of the free conformer(II), the relative enthalpy (ΔH) should give the relative stability of the C-D···π interacted conformer(I). The assumption seems entirely reasonable since the C-D bond is separated by a saturated carbon and a carbonyl carbon atoms from the aromatic ring, and the electronic effect is not likely to be transmitted through them. After all, the ΔH value can be a measure of the enthalpy of the C-D···π hydrogen-bond formation.

The C-D···π hydrogen bond is expected to be strengthened in the increasing order of π-electron density on the aromatic carbon atoms. Hence, electron-donating substituent on the aromatic ring should favor the hydrogen bond and stabilize the C-D···π interacted conformer. This leads to the conclusion that the ΔH should be lower when the substituent is more electron-donating. As easily seen from the ΔH vs. σ plot in Fig. 3, the relative enthalpies in Table 5 are in line with the theoretical consequences on the substituent effect, giving a straight line with a positive ρ value (ρ=+0.605 kJ mol^{-1}). In other words, the C-D···π interacted conformer becomes more stabilized with ketone 2 carrying an electron-donating substituent and less stabilized with ketone 2 carrying an electron-withdrawing substituent. Without an exception, hydrogen-bonded system previously investigated were shown to behave similarly towards the effect of polar

† 1 cal=4.184 J.

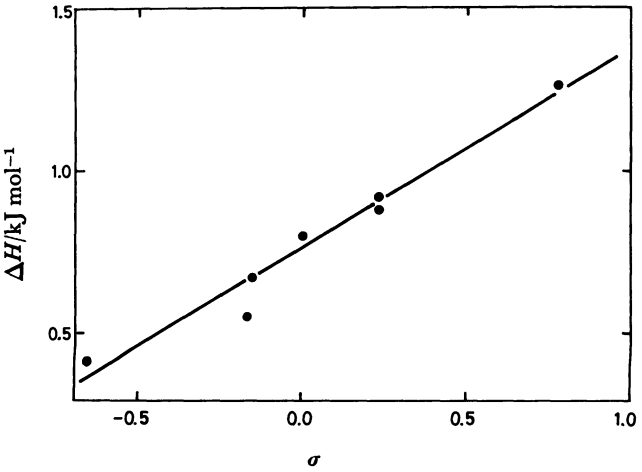


Fig. 3. Substituent effect on the relative enthalpies of the C-D···π interacted conformers. The ΔH vs. σ plot.

substituents.[27] Thus, the substituent effect on the ΔH's renders another support on the C-D···π hydrogen bonding in isopropyl-2-*d* 1-arylethyl ketones (**2**).

This research was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture to which the authors are grateful.

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