Conformational and Electronic Interaction Studies of α-Substituted Carbonyl Compounds. Part 9.[1] ω-Hetero-substituted Acetophenones

Paulo R. Olivato * and **Sandra A. Guerrero**
Instituto de Química, Universidade de São Paulo, Caixa Postal 20780, 01498 São Paulo, SP, Brazil
Yoshiyuki Hase and Roberto Rittner
Instituto de Química, Universidade Estadual de Campinas, Caixa Postal 6154, 13081 Campinas, SP, Brazil

ν_{CO} frequencies and intensities, $n \rightarrow \pi^*_{CO}$ transition energies and α-methylene carbon chemical shifts were measured for some ω-hetero-substituted acetophenones ($\varphi COCH_2X$: X = F, OMe, NMe$_2$, NEt$_2$, Cl, Br, SEt, and I), and their conformations were estimated with the help of molecular-mechanics calculations. The stability of the *gauche* rotamers is discussed in terms of hyperconjugative interactions between σ_{CX} and π^*_{CO} orbitals. The carbonyl frequency shifts of the *cis* rotamers are interpreted as due to the substituent field effect, while the corresponding shifts for the *gauche* rotamers have been ascribed to an interplay of the inductive and hyperconjugative effects. The abnormal negative ν_{CO} *gauche* shifts and the $n \rightarrow \pi^*_{CO}$ band bathochromic shifts of the ω-fluoro- and ω-methoxy-acetophenones, and the observed shielding effect on the α-methylene carbon atom of the studied acetophenones, are discussed in terms of π^*_{CO}/σ_{CX} and π^*_{CO}/X_{1p} orbital overlapping. The higher stabilization of the ω-ethylthioacetophenone *gauche* rotamer, the largest negative ν_{CO} *gauche* shift, and the lower shielding effect for its methylene carbon have been interpreted as due to the simultaneous occurrence of π^*_{CO}/σ_{CS} and π_{CO}/σ^*_{CS} orbital interactions.

Previous work from this laboratory on some α-heterosubstituted acetones [2,3] have suggested that a π_{CO}/σ_{CX} hyperconjugative interaction occurs both in the ground as in the excited state for their *gauche* rotamers, and from the IR data for the corresponding acetamides [4] a similar interaction also occurs in the ground state. Our recent reports [1,5,6] on some ω-halo-*p*-substituted acetophenones (Hal: Cl, Br, and I) also indicate the existence of this hyperconjugative interaction, although ^{13}C NMR data of some ω-ethylthio-*p*-substituted acetophenones [7] have shown that, in the ground state, charge transfer from the π_{CO} to the 3d sulphur orbital should also occur. Moreover, the conformational analysis of some ω-heterosubstituted acetophenones by IR, UV, NMR, and electric dipole moment studies [8-16] have already been reported, but no systematic studies have been performed for the whole series.

As an extension of our previous work on α-heterosubstituted acetones,[2] this paper describes the investigation of the electronic interactions in some ω-heteroacetophenones (*i.e.* substituted at the ω-position by representative elements from the first to the fourth rows of the Periodic Table), using IR, UV, and ^{13}C NMR data and molecular-mechanics calculation (MMC).

Results and Discussion

cis/gauche *Rotational Isomerism.*—Table 1 shows the carbonyl stretching frequencies and the corresponding apparent molar absorptivities, for some ω-heterosubstituted acetophenones (2)–(9) and the parent compound (1) in n-hexane, carbon tetrachloride and chloroform. Compounds (2), (3), and (6)–(9) show two overlapped carbonyl bands in all solvents, while the parent compound (1) presents just a single carbonyl band. Both the dimethylamino- (4) and the diethylaminoacetophenone (5) exhibit an overlapped triplet in n-hexane and carbon tetrachloride, which loses its central component in chloroform solutions.

The molar absorption coefficient ratio between the higher and lower frequency components for compounds (2), (3), and

(6)–(8), and between the higher and the sum of the lower frequency components for compounds (4) and (5), increases progressively from n-hexane to carbon tetrachloride, and from these to chloroform solutions, *i.e.* in the same way as the solvent polarity increases. These solvent effects and the occurrence of two or three overlapped carbonyl bands in the first overtone region (Table 2) strongly indicate that compounds (2)–(9) display a *cis* (I)/*gauche* (II) rotational isomerism.[17,18] Thus, it

(I)   (II)
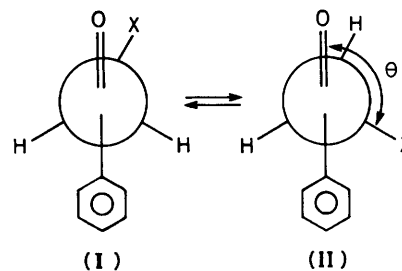
may be assumed that the higher frequency band corresponds to the more polar *cis* rotamer (I) and the lower frequency band to the less polar *gauche* rotamer (II); for compounds (2), (3), (6)–(9), and for compounds (4) and (5) the two lower frequency bands correspond to the two *gauche* rotamers. As it is impossible to determine the apparent molar absorption coefficients for the *pure cis* and *gauche* rotamers, it was assumed that the molar absorption coefficients for both rotamers were the same, and then the ratio of two rotamers was estimated from that of the apparent molar absorption coefficient at the absorption maxima of the two carbonyl band components ($\varepsilon_c/\varepsilon_g$) (see Table 1).

For the ω-hetero-substituted acetophenones (2)–(9), in chloroform, the $\varepsilon_c/\varepsilon_g$ ratios follow the order: F ~ O > N > Cl > Br > S > I, which is the same as that observed for the corresponding α-heterosubstituted acetones.[2] In the less polar solvents, n-hexane and carbon tetrachloride, the same trend was observed, except for the nitrogen derivatives (4) and (5),

Table 1. Frequencies and intensities[a] of the carbonyl stretching bands in the IR spectra of ω-heterosubstituted acetophenones φCOCH₂X.

Compound	X	n-C₆H₁₄ v/cm⁻¹	ε/dm³ mol⁻¹ cm⁻¹	εc/εg[b]	CCl₄ v/cm⁻¹	ε/dm³ mol⁻¹ cm⁻¹	εc/εg	CHCl₃ v/cm⁻¹	ε/dm³ mol⁻¹ cm⁻¹	εc/εg
(1)	H[c]	1 696	642	—	1 691	670		1 683	472	
(2)	F	1 720	(264)[d]		1 716	(307)		1 709	390[f]	
		1 691	(246)	(1.07)[e]	1 687	(228)	— (1.35)	1 684	104	3.75
(3)	OMe	1 710	(244)		1 709	(278)		1 702	361	
		1 691	(225)	1.08	1 686	(218)	— (1.28)	1 684	94	3.84
(4)	NMe₂	1 709	120		1 704	114(160)		1 697	268	
		1 699	96		1 695	57(170)		—		
		1 691	328	0.28[g]	1 686	366	0.27(0.30)[h]	1 682	141	1.90
(5)	NEt₂	1 709	61		1 703	96(126)		1 697	192	
		1 699	77		1 695	50(161)		—		
		1 690	326	0.15[g]	1 684	316	0.26(0.26)[h]	1 679	123	1.56
(6)	Cl	1 718	134		1 715	191(213)		1 707	252	
		1 697	353	0.38	1 694	351	0.54(0.61)	1 690	176	1.43
(7)	Br[i]	1 713	81		1 711	90(107)		1 704	99	
		1 692	601	0.13	1 689	572	0.16(0.19)	1 684	344	0.29
(8)	SEt[j]	1 700	41		1 698	45(76)		1 692	50	
		1 681	469	0.09	1 677	581	0.08(0.13)	1 673	293	0.17
(9)	I[k]	1 705	44		1 702	40(57)		1 699	36	
		1 687	722	0.06	1 682	694	0.06(0.08)	1 677	442	0.08

[a] Expressed by ε, the apparent molar absorption coefficient. [b] Subscripts c and g indicate *cis* and *gauche* rotamers respectively. [c] Parent compound. [d] All intensity data in brackets were measured directly from the unresolved bands. [e] Ratio of the high and low frequency components of the unresolved doublet. [f] All unbracketed intensity data were measured at the maxima of the graphically decomposed bands. [g] Ratio of the high and the sum of the low frequencies components of the resolved triplet. [h] Same as f, for the unresolved triplet (for details see the Experimental section). [i] From ref. 1. [j] From ref. 7. [k] From ref. 5.

Table 2. Frequencies and intensities[a] of the carbonyl stretching bands in the first overtone region of the ω-heterosubstituted acetophenones φ-COCH₂X, in CCl₄.

Compound	X	v/cm⁻¹	ε/10⁻¹ dm³ mol⁻¹ cm⁻¹	εc/εg[b]
(1)	H[c]	3 358	60	—
(2)	F	3 411	(15)[d]	
		3 356	(11)	(1.36)[e]
(3)	OMe	3 391	(47)	
		3 351	(37)	(1.27)
(4)	NMe₂	3 376	(15)	
		3 365	(15)	
		3 343	(23)	(0.39)
(5)	NEt₂	3 387	(9)	
		3 370	(13)	
		3 348	(22)	(0.26)
(6)	Cl	3 404	(21)	
		3 362	(34)	(0.62)
(7)	Br[f]	3 393	(11)	
		3 352	(55)	(0.20)
(8)	SEt	3 372	(5.5)	
		3 338	(42)	(0.13)
(9)	I[g]	3 375	(6)	
		3 341	(61)	(0.10)

[a–e] (See footnotes of Table 1). [f] From ref. 1. [g] From ref. 5.

Table 3. Carbon–heteroatom mean polarizabilities[a] (ᾱ) and σ_{C–X} vertical ionization energies[b] (E_i).

Group	ᾱ/Å³	E_i/eV
F	0.67	16.2[c]
OMe	0.60	15.1[d]
NMe₂	0.65	14.4[e]
Cl	2.53	14.4[c]
Br	3.61	13.5[c]
SEt	1.75	13.7[d]
I	5.40	12.5[c]

[a] ᾱ refers to the carbon–heteroatom bond, and the ᾱ values were taken from ref. 19(b). [b] E_i refers to the vertical ionization energy for the σ_{CX} molecular orbital of the heterosubstituted methane. [c] H. Schmidt and A. Schweig, *Angew. Chem., Int. Ed. Engl.*, 1973, 12, 307. [d] H. Ozata, H. Omizuka, Y. Nikei, and H. Yamada, *Bull. Chem. Soc. Jpn.*, 1973, 46, 3036. [e] K. Kimura and K. Osafune, *Mol. Phys.*, 1975, 29, 1073.

which may be attributed to their less precise ε_g values, obtained from the sum of two ε_g values.

It is well established that there is a close relationship between the C–X bond polarizability and the reciprocal of the σ_{C–X} bond ionization energy[19a,20] (Table 3). So, it became of interest to compare the *cis/gauche* ratios for the ω-heteroacetophenones, with the corresponding C–X bond polarizabilities. As in the case

of the α-heteroacetones, the progressive decrease of the *cis/gauche* ratio on going from fluoro- (2) to iodo-acetophenone (9) is followed by an increase of the C–X bond polarizability. With the exception of the amino-derivatives *i.e.* compounds (4) and (5), good correlations between log(εc/εg)* and C–X bond polarizabilities (ᾱ) are obtained in all solvents. For example, when the solvent is n-hexane, equation (1) is obtained (Figure 1).

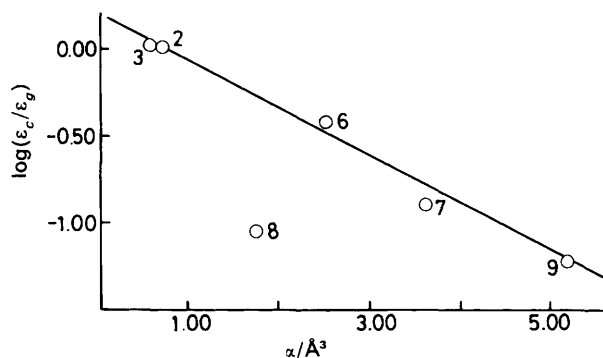$$\log(\varepsilon_c/\varepsilon_g) = -0.27\,\bar{\alpha} + 0.20 \qquad (1)$$

$$(n = 5; r = 0.993; s = 0.07)$$

However, in the case of the polar solvent chloroform a reasonably good correlation is also obtained, even with dimethylamino-derivative (4), as shown by equation (2).
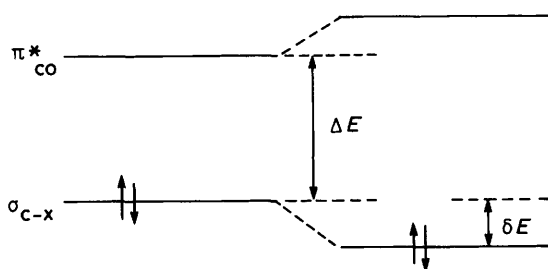
$$\log(\varepsilon_c/\varepsilon_g) = -0.33\,\bar{\alpha} + 0.73 \qquad (2)$$

$$(n = 6; r = 0.967; s = 0.19)$$

* log(εc/εg) is roughly proportional to ΔG of the two rotamers, for ΔG = −RT ln(c_c/c_g) and (εc/εg) ~ (c_c/c_g).

Figure 1. Plot of the log of the *cis/gauche* ratio, estimated in n-hexane, against the C–X bond polarizability, for the ω-heterosubstituted acetophenones (**2**), (**3**), (**6**), (**7**), (**8**), and (**9**) ($r = 0.993$).

Figure 2. Qualitative energy levels diagram for the σ_{C-X} and π^*_{CO} orbitals of the ω-heteroacetophenones, showing the stabilization of the *gauche* conformation due to the π^*_{CO}/σ_{C-X} hyperconjugation.

As illustrated in Figure 1, the sulphur derivative (**8**) deviates strongly from the straight line, and, therefore, it was excluded from all correlations for the reasons outlined below. It should be noted that the good correlation between $\log(\varepsilon_c/\varepsilon_g)$ and $\bar{\alpha}_{C-X}$ for the heteroacetophenones are similar to those obtained for the heteroacetones, for which a dipolar hyperconjugative structure has been proposed to account for the stability of the *gauche* rotamers with the increasing polarizability of the C–X bonds. Thus, *it seems reasonable to suggest for the heteroaceto-phenones (in the valence bond terminology) that the enhance-ment of the C–X bond polarizability can be correlated with an increasing contribution of the dipolar hyperconjugative struc-ture* (**III**), and this trend is supported by molecular-orbital


(III)
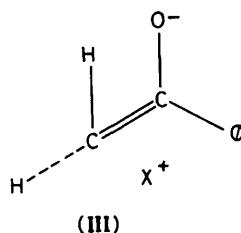
perturbation theory.[21] It is found that the smaller the bonding character of the σ_{C-X} orbital, the closer the energy levels of the unperturbed σ_{C-X} and π^*_{CO} molecular orbitals (Table 3). Therefore, larger interactions between these orbitals will occur leading to a progressive stabilization of the σ_{C-X} orbital by δE (Figure 2). Hence, this π^*_{CO}/σ_{C-X} hyperconjugative interaction may be responsible for the increasing stabilization of the *gauche* rotamers, on going from fluoro- (**2**) to iodo-acetophenone (**9**), but exerts only a minor influence in the case of the sulphur derivative (**8**). The large stabilization of the *gauche* rotamer of the latter compound (see Table 1) is neither accompanied by a corresponding higher C–S bond polarizability nor by a lower ionization energy of σ_{C-S} orbital.

Carbonyl Stretching Frequency Shifts.—Table 4 shows the

frequency shifts (Δv), in carbon tetrachloride, for the *cis* and *gauche* rotamers of the ω-heterosubstituted acetophenones (**2**)–(**9**), in comparison with the parent compound (**1**). Both the carbonyl frequency shifts for the *cis* rotamers (Δv_c) as for the *gauche* rotamers (Δv_g) are reasonably close and well correlated (Δv_c: $r = 0.958$; $s = 2.0$ cm⁻¹; Δv_g: $r = 0.999$; $s = 0.4$ cm⁻¹) to those previously obtained for the corresponding α-hetero-acetones[2] (**10**)–(**16**), which are also included in Table 4. However, the *gauche* shifts for the fluoro-(**2**) and methoxy-acetophenone (**3**) deviate significantly from the straight line and were excluded from the latter correlation. The *gauche* shift for the central component of the triplet, *i.e.*, for the first *gauche* rotamer of the dimethylamino-(**4**) and for the diethylamino-acetophenone (**5**) also deviate from that correlation. The observed correlations seem to indicate that both ketone series exhibit a similar behaviour,[2] and that they may be closely compared. It can be noted (Table 4) that the carbonyl frequency shifts for the *cis* rotamers (Δv_c) of compounds (**2**)–(**9**) are all positive ($+24$ to $+7$ cm⁻¹). The positive *cis* shifts and the observed Δv_c trend for the whole heteroacetophenones series can both be attributed to the repulsive field effect between the CO and CX dipoles, combined with the inductive effect of the ω-substituent.

The *gauche* shifts (Δv_g) vary from positive to negative values within the range from $+4$ to -14 cm⁻¹ (Table 4) and they may be ascribed to a competition between the inductive and hyperconjugative effects (see below). In order to explain the abnormal carbonyl *gauche* shifts for the ω-fluoroacetophone (**2**) (Δv_g -4 cm⁻¹) and for the ω-methoxyacetophenone (**3**) (Δv_g -5 cm⁻¹) in relation to those for the α-fluoroacetone (**10**) (Δv_g $+12$ cm⁻¹) and for the α-methoxyacetone (**11**) (Δv_g $+4$ cm⁻¹), it seems appropriate to compare the geometries of the *gauche* rotamers of the heteroacetophenones (**2**) and (**3**), to those of the corresponding heteroacetones (**10**) and (**11**). An inspection of the molecular models shows that in the α-fluoroacetone the fluorine atom may be in the *trans* conformation (**IV**) ($\theta = 180°$)

(IV)   (V)
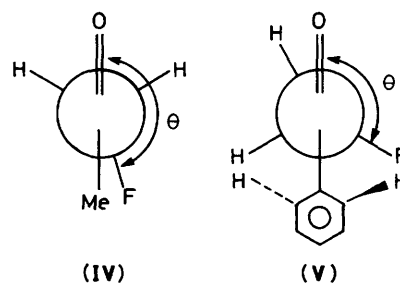
without any degree of steric strain in relation to the acetyl methyl group; however for the ω-fluoroacetophenone in the *trans* conformation, there is a strong steric repulsion between the fluorine atom and the *ortho* hydrogen atom of the phenacyl group. This latter leads, consequently, to a smaller dihedral angle θ, in order to relieve the steric strain [rotamer (**V**)]. The same reasoning may be applied to the ω-methoxyacetophenone considering the larger steric repulsion between the more bulky methoxyl group (whose Charton steric parameter[22] v is 0.36) and the *ortho* hydrogen atom of the phenacyl group, leading to a smaller dihedral angle θ for the *gauche* rotamer of this compound, in relation to the same rotamer of the ω-fluoroacetophenone where[22] $v = 0.27$.

In order to have more precise geometries for the con-formations of the heteroacetophenones series in comparison with those of the corresponding heteroacetones, molecular-mechanics calculations were performed for both ketones series, the latter bearing, in the ω- and α-positions, simple substituents such as the halogen atoms F, Cl, Br, and I. The data obtained (Table 5) show there is a good agreement between the com-

Table 4. Carbonyl frequency shifts [a,b] for the *cis* (Δv_c) and *gauche* (Δv_g) rotamers of the ω-hetero-substituted acetophenones φCOCH$_2$X, and of the α-heterosubstituted acetones MeCOCH$_2$X; computed carbonyl frequency shifts,[c] induced by the hyperconjugative (Δv_H) effects of the substituents.

X	Compound	φCOCH$_2$X		Compound	MeCOCH$_2$X		
		Δv_c/cm^{-1}	Δv_g/cm^{-1}		Δv_c/cm^{-1}	Δv_g/cm^{-1}	Δv_H/cm^{-1}
F	(2)	+24	−4	(10)	+28	+12	0
OMe	(3)	+18	−5	(11)	+18	+4	−2.1
NMe$_2$	(4)	+13	+4 −5	(12)	+12	−3	−4.2
NEt$_2$	(5)	+12	+4 −7				
Cl	(6)	+24	+3	(13)	+31	+3	−8.1
Br	(7)	+20	−2	(14)	+23	−1	−11.6
SEt	(8)	+7	−14	(15)	+10	−11	−15.5
I	(9)	+11	−9	(16)	+14	−7	−16.2

[a] In CCl$_4$. [b] Δv_c and Δv_g, refers to the difference: ν(substituted ketone) − ν(parent compound), for the *cis* and *gauche* rotamers, respectively. [c] From ref. 2.

Table 5. Calculated molecular-mechanics energies, electric dipole moments, dihedral angles for the minimum energy conformations, and the relative rotamer populations of ω-haloacetophenones φCOCH$_2$X and α-haloacetones MeCOCH$_2$X.

X	Compound	φCOCH$_2$X[a]					Compound	MeCOCH$_2$X				
		Conf.[b]	θ[c]	μ/D	E/kcal mol^{-1}	c/g[d]		Conf.	θ	μ/D	E/kcal mol^{-1}	c/g (t)
F	(2)	c	0	4.073	0[e]	0.89	(10)	c	0	4.239	2.07	0.03
		g	130	1.952	0.34	(1.07)[f]		t	180	1.144	0	(0.07)[g]
Cl	(6)	c	0	4.099	0	1.08	(13)	c	0	4.271	0.89	0.22
		g	111	2.491	0.46	(0.38)		t	180	0.965	0	(0.22)
Br	(7)	c	0	3.978	1.01	0.09	(14)	c	0	4.153	1.28	0.23
		g	103	2.662	0	(0.13)		g	119	2.367	0	(0.18)
I	(9)	c	0	3.588	1.29	0.04	(16)	c	0	3.762	1.47	0.05
		g	100	2.615	0	(0.06)		g	100	2.773	0	(0.07)

[a] The computed dihedral angle Ψ between the carbonyl group and the benzene ring in the phenacyl group was found to be nearly 0° for the whole series. [b] c, g, and t refers to the *cis, gauche,* and *trans* conformations respectively. [c] Dihedral angle θ (in degrees), as defined for rotamer (II). [d] Relative rotamer populations (for details see text). [e] Zero energy corresponds to the minimum-energy conformation. [f] Relative rotamer populations taken from IR data in n-hexane, from Table 1. [g] Relative rotamer populations taken from IR data in n-hexane, from ref. 2. 1D = 10^{-30} C m.

puted *cis/gauche* (or *cis/trans*) population ratios and the corresponding values obtained from the IR spectral data, in n-hexane, for both ketone series, except for the chloro-acetophenone.

The *cis/gauche* population ratio for the ω-fluoroaceto-phenone is much larger than the corresponding ratio for the α-fluoroacetone. While both *cis* rotamers are destabilized by a strong electrostatic repulsive interaction between the CO and CX dipoles (field effect), the *trans* and *gauche* rotamers are stabilized by different attractive interactions, *i.e.* a fluorine–acetyl–methyl attractive interaction (mainly electrostatic) for the *trans* rotamer of the α-fluoroacetone and a weak fluorine–benzene ring attractive van der Waals interaction for the *gauche* rotamer of the ω-fluoroacetophenone. Table 5 also indicates that the *cis* rotamers for both haloacetophenones (2), (6), (7), (9), and haloacetones (10), (13), (14), (16) exhibit a dihedral angle θ equal to 0°, and, as expected, they have higher electric dipole moments than the corresponding *gauche* or *trans* rotamers. For the *gauche* (or *trans*) rotamers, the dihedral angle θ decreases progressively from the fluoro- to the iodo-derivative both in the haloacetophenones (θ, 130–100°) as in the haloacetones (θ, 180–100°).

The molecular-mechanics geometry for the less polar rotamer is *gauche* (V) (θ 130°) for the ω-fluoroacetophenone (2), and *trans* (IV) (θ 180°) for the α-fluoroacetone (20), which is the same as that previously obtained by microwave spectroscopy.[23] For the α-heterosubstituted acetones the carbonyl frequency shifts induced by the hyperconjugative effect (Δv_H) were

previously[2] estimated taking into account that the fluoro-acetone geometry is *trans*, for which the π^*_{CO}/σ_{CF} hypercon-jugative interaction should be negligible ($\Delta v_H = 0$), and by assuming the carbonyl frequency shift of +12 cm^{-1} to be due only to the inductive effect of the fluorine atom ($\Delta v_I = +12$ cm^{-1}). Therefore, the Δv_I values for the remaining hetero-substituted acetones were computed from the substituents inductive parameters (σ_I), assuming that there is a simple proportionality between both sets. Since the frequency shifts for the *gauche* rotamers (Δv_g) should be the result of summing up the inductive and hyperconjugative effects ($\Delta v_I + \Delta v_H$), the Δv_H values could be obtained, once the Δv_I values were known (Table 4). Although it is not possible to compute the carbonyl frequency shifts induced by the hyperconjugative effect (Δv_H), for the whole heteroacetophenone series (2)–(9), it seems obvious that the good correlation obtained between the carbonyl *gauche* shifts (Δv_g) for the heteroacetophenones (3)–(9) and for the corresponding heteroacetones (12)–(16), (*i.e.* with the exception of the fluoro-(1) and methoxy-(2) derivatives), is a good indication that the heteroacetophenones (3)–(9) may have practically the same Δv_H parameters as the corresponding heteroacetones.

The smaller dihedral angle for the *gauche* rotamer of the ω-fluoroacetophenone (2) may lead to a π^*_{CO}/σ_{CF} orbital overlap (hyperconjugative effect), while in the *trans* rotamer of the α-fluoroacetone (10) this overlap will not occur. Therefore, the fluorine atom should induce a decrease in the carbonyl force constant, and then a decrease in the carbonyl stretching

Table 6. UV data for the carbonyl $n{\rightarrow}\pi^*$ transition of the ω-hetero-substituted acetophenones $\varphi COCH_2X$, in n-hexane.

Compound	X	λ_{max}/nm	$\log(\varepsilon/dm^3\ mol^{-1}\ cm^{-1})$
(1)	H	317	1.63
(2)	F	320	1.72
(3)	OMe	328	1.70
(4)	NMe$_2$	327[a]	1.94
(5)	NEt$_2$	328[a]	2.43
(6)	Cl	324	1.88
(7)	Br	328	2.17
(8)	SEt	339	2.67
(9)	I	337	2.43

[a] Shoulder.

Table 7. Experimental[a,b] and calculated α-methylene carbon ^{13}C NMR chemical shifts (δ_C in ppm), for ω-heterosubstituted acetophenones, $\varphi COCH_2X$, in CCl_4–Me$_4$Si.

Compound	X	$\alpha_X{}^a$	Exp.	Calc.	$\Delta\delta^d$
(1)	H	0.0	28.7	—	—
(2)	F	70.5	84.1	96.9	−12.8
(3)	OMe	59.5	75.9	85.9	−10.0
(4)	NMe$_2$	46.4	66.3	74.2	−7.9
(5)	NEt$_2$	40.1	60.4	66.5	−6.1
(6)	Cl	31.5	45.3	57.9	−12.6
(7)	Br	20.0	30.1	46.4	−16.3
(8)	SEt	18.6	36.6	45.0	−8.4
(9)	I	−10.5	1.3	15.9	−14.6

[a] From ref. 26. [b] $\Delta\delta = \delta_{Exp} - \delta_{Calc}$.

frequency for the *gauche* rotamer of the ω-fluoroacetophenone (**2**) in relation to the parent compound (**1**) ($\Delta\nu_g = -4\ cm^{-1}$), in contrast with the positive shift observed for the *trans* rotamer of the α-fluoroacetone (**10**) ($\Delta\nu_g = +12\ cm^{-1}$) (Table 4). A similar explanation may be given to justify the *gauche* shift for the ω-methoxyacetophenone (**3**) ($\Delta\nu_g = -5\ cm^{-1}$), which differs by 9 cm^{-1} from the *gauche* shift of the α-methoxyacetone (**11**) ($\Delta_g = +4\ cm^{-1}$). In fact, from a molecular models analysis, the dihedral angle θ for the *gauche* rotamer of compound (**3**) will be smaller than the one for the *gauche* rotamer of compound (**11**).

Carbonyl n$\rightarrow\pi^*$ Transition Energies and Intensities.—Table 6 shows the $n{\rightarrow}\pi^*_{CO}$ transition energies and the corresponding band intensities for compounds (**1**)–(**9**), in n-hexane. The $n{\rightarrow}\pi^*$ transition band displays a bathochromic shift and hyperchromic effect, which progressively increase, on going from fluoro-(**2**) to iodoacetophenone (**9**). These trends can be attributed to a hyperconjugative interaction between the π^*_{CO} and σ^*_{CX} orbitals, which occurs for the *gauche* rotamers whereas for the *cis* rotamers there is not any significant effect. This behaviour is similar to that observed for the α-heterosubstituted acetones,[2] except for the fluoro-derivative. Whereas for the ω-fluoroacetophenone (**2**) a small bathochromic shift (*ca.* 3 nm) and a hyperchromic effect are observed, (which is also the case for the axial conformer of 4-t-butyl-2-fluorocyclohexanone),[24] for the α-fluoroacetone (**10**) the $n{\rightarrow}\pi^*$ transition has almost the same energy (wavelength) as the parent compound, and so exhibits only a small hypochromic effect.[2] Furthermore, in the case of the ω-methoxyacetophenone (**2**) a still larger bathochromic shift and hyperchromic effect are also observed (Table 6), in comparison with that for the corresponding methoxyacetone.[2] Therefore the UV data corroborate the existence of a better $\pi^*_{CO}/\sigma^*_{C-F(C-O)}$ orbital overlap in the excited state due to a smaller dihedral angle between the C=O and C–X bonds.

α-Methylene Carbon Chemical Shifts.—Table 7 shows both the experimental and the calculated α-methylene chemical shifts, in carbon tetrachloride, for the ω-heterosubstituted acetophenones (**2**)–(**9**), as well as the difference ($\Delta\delta$) between both values, *i.e.*, the non-additivity effects[25] (NAE) of the substituent parameters. The calculated chemical shifts, which are downfield in relation to the experimental values, were obtained through equation (3), where α_X is the α-effect of an X-substituent in

$$\delta_{CH_2} = -2.3 + \alpha_A + \alpha_X \qquad (3)$$

linear alkanes,[26] and α_A is that of the phenacyl group [estimated from the α-methyl chemical shifts of the unsubstituted acetophenone (**1**), (Table 7)], and −2.3 is the chemical shift for the methane carbon atom. The additional shielding on the α-methylene carbon may be ascribed, as suggested by

Nesmeyanov,[27] to an increase in the double bond character between the α-methylene carbon and the carbonyl group due to the π^*_{CO}/σ_{CX} hyperconjugation [structure (**III**)]. This may suggest that the $\Delta\delta$ values should correlate with the $\Delta\nu_H$ shifts. However, as the $\Delta\nu_H$ shifts for the ω-heteroacetophenones cannot be estimated (see above), the $\Delta\nu_H$ shifts for the very similar α-heteroacetones were used instead (Table 4), and a quite reasonable correlation ($r = 0.827$; $s = 2.20$ ppm) was found, though the fluoro-(**2**) and ethylthio-(**8**) derivatives deviate strongly from the correlation (see below). However, it should be noted that the $\Delta\delta$ values were obtained from average chemical shifts for both conformers of the ω-hetero-substituted acetophenones, the *cis/gauche* ratios of which are in range 0.06–1.35 (Table 1).

As outlined above, the hyperconjugative shift ($\Delta\nu_H$) for the ω-fluoroacetophenone (**2**) will be larger than that of the α-fluoroacetone (**10**), for which $\Delta\nu_H = 0$. However, as the *cis* rotamer, in the *cis/gauche* equilibrium for the ω-fluoroacetophenone (**2**), is predominant (*ca.* 1.35 times), the abnormal NAE value of *ca.* 13 ppm seems too high to be justified by the π^*_{CO}/σ_{CF} hyperconjugative interaction alone, considering that the σ_{C-F} bond has one of the highest ionization energies (16.2 eV, Table 3). Therefore, it seems reasonable to suggest, as proposed by Salem[28] for the fluoroacetaldehyde, that in the *gauche* rotamer of the ω-fluoroacetophenone, a significant overlap between one of the 2p fluorine lone pairs and the low-lying π^*_{CO} orbital should occur [structure (**VI**)], as well as the

(**VI**)
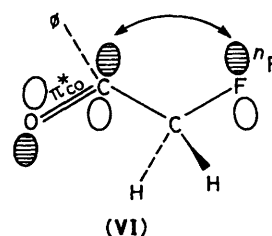
π^*_{CO}/σ_{C-F} hyperconjugation. The π^*_{CO}/n_F interaction should stabilize the *gauche* conformation and should also lead to a decrease in the carbonyl bond order, and consequently to a lowering in the carbonyl frequency (Table 3). This latter interaction may also cause an increase in the electron density on the α-methylene carbon atom, and consequently a higher shielding, as observed for the α-methylene carbon of the ω-fluoroacetophenone (**2**).

Finally, the deviation from the above correlation of the ethylthioderivative (**8**) is in agreement with our recent studies,[7] which indicated that in α-alkylthio-carbonyl compounds, besides the π^*_{CO}/σ_{C-S} hyperconjugation, there is also a π_{CO}/σ^*_{C-S} interaction leading to a decrease in the non-additivity effect for the SEt substituent. It seems evident that the computed $\Delta\nu_H$

value for the ethylthio substituent in the heteroacetone series[2] (Table 4), overestimated the π^*_{CO}/σ_{C-S} hyperconjugative contribution. In fact, both the larger stabilization of the *gauche* conformations of ethylthioacetophenone and ethylthioacetone,[2] and the higher Δv_H value for the ethylthio substituent, in relation to the expected value, should result from the sum of two contributions, *i.e.*, the π^*_{CO}/σ_{C-S} and π_{CO}/σ^*_{C-S} orbitals interactions. As a consequence, these combined interactions should result in a larger stabilization of the *gauche* rotamers of the ethylthio ketones and a smaller carbonyl force constant, and therefore produce the lowest observed carbonyl frequencies for the *gauche* rotamers within the two ketones series, both for the ω-ethylthioacetophenone (**8**) (Table 4) and for the α-ethylthioacetone[2] (**15**).

Calculations

Molecular-mechanics Calculations.—The MMC for the α-haloacetones were performed on an IBM-PC/XT compatible computer with the MM2 (1977) force field,[29] using the PC-version of MM2 program. For the ω-haloacetophenones, the same 1977 force field was also utilized to perform the MM2 calculations with a 'mechanical' treatment of the planar benzene ring,[30] rather than the time-consuming MMp-type calculations. In this treatment, the force-field parameters related to the benzene ring carbon atoms C_ϕ were taken as the same as those for the sp[2] hybrid carbon atoms C_{sp^2}, except for the special parameters of the $C_\phi-C_\phi$ bond ($k_s = 7.00$ mdyn Å^{-1} and $l_0 = 1.397$ Å), which were estimated to reproduce structure parameters of the free benzene molecule. The torsional constants, for the $C_\phi-C_{CO}-C_{sp^3}-X$ (X = F, Cl, Br, I) dihedral angles, were assumed to be $V_1 = V_2 = V_3 = 0.0$ kcal mol^{-1}.*

Rotamer Population Ratios.—The *cis/gauche* (or *trans*) rotamer population ratios were determined[31] by the energy difference between them, using the relation:

$$\Delta G° = -RT\ln K$$

where the symbols have their customary meaning. For the case of the α-haloacetophenones and α-haloacetones the equilibrium:

$$cis \rightleftharpoons gauche \text{ (or } trans)$$

may be determined, from the fact that there are two enantiomeric *gauche*, one *cis* and one *trans* rotamers for the entropy of mixing. For instance, for the chloroacetophenone at 27 °C or 300 K, the *cis/gauche* equilibrium has $\Delta H° = +0.46$ kcal mol^{-1} (see Table 5). Since there are two enantiomeric *gauche* rotamers, the free energy is related to the enthalpy change, by an entropy of mixing:

$$\Delta S° = R\ln 2$$
$$\Delta G° = \Delta H° - T\Delta S°$$
$$\Delta G° = 0.46 - 0.41 = 0.05 \text{ kcal mol}^{-1}$$
$$K = \frac{C_g}{C_c} = 0.928 \text{ or } \frac{C_c}{C_g} = 1.08$$

Therefore the *cis/gauche* rotamer population ratio for the title compound is 1.08 (see Table 5).

Experimental

Materials.—All solvents for spectrometric measurements were spectrograde and were used without further purification. Commercial acetophenone and methoxyacetophenone were purified as described elsewhere.[32] Commercial chloro- and bromo-acetophenones were purified by recrystallization from ethanol. Fluoro-,[33] dimethylamino-,[34] diethylamino-,[35] ethylthio-,[36] and iodo-acetophenones[37] were prepared by literature procedures.

IR Measurements.—The IR spectra were recorded on a Perkin-Elmer model 283 grating spectrometer at room temperature. The spectral slit width was 2.0 and 3.5 cm^{-1} in the fundamental and in the first overtone carbonyl frequency regions, respectively. The carbonyl frequencies, in the fundamental region, were measured in the transmittance scale mode for *ca.* 2.0×10^{-2} mol dm^{-3} solutions in n-hexane, carbon tetrachloride and chloroform, using a pair of 0.5 mm sodium chloride matched cells. In the first overtone, *ca.* 2.0×10^{-2} mol dm^{-3} solutions in carbon tetrachloride were measured using a pair of 1.00 cm quartz matched cells. Further dilution did not affect the spectra. The spectra were calibrated with polystyrene film at 1 601.4 and 2 850.7 cm^{-1}. The carbonyl frequencies for the more and less intense components of the doublet, in the fundamental region, are accurate to ± 0.5 and ± 1 cm^{-1}, respectively. In the first overtone region the frequencies are accurate to ± 1 cm^{-1} and ± 2 cm^{-1}, respectively. The *cis/gauche* ratios for compounds (**2**)–(**9**) were obtained from the spectra recorded in the 1 800–1 550 cm^{-1} interval, in the absorbance scale mode. The *cis/gauche* relative concentrations for compounds (**4**)–(**9**) were estimated from the ratio of the apparent molar absorption coefficients of the two or three components of the graphically decomposed bands,[38] assuming, as an approximation, equality of the molar absorption coefficients of the two or three rotamers (see the text). As the intensities of the higher and the lower frequency components of the two superimposed carbonyl bands for compounds (**2**) and (**3**), (in n-hexane and in CCl$_4$), were not significantly different (see Table 1), the graphical decomposition of these bands was not performed and the intensities were directly measured at the maxima of the overlapped bands. The other bracketed intensities values (in CCl$_4$) for compounds (**4**)–(**9**) in Table 1 were measured directly at the maxima or at the inflexion points of the overlapped carbonyl bands, in order to compare their *cis/gauche* intensities ratios with those corresponding ratios for the unresolved carbonyl bands in the first overtone region (Table 2).

The UV spectra of (10^{-3}–10^{-2} mol dm^{-3}) solutions in n-hexane, and ^{13}C NMR spectra of the 0.3 mol dm^{-3} solutions of the title compounds (**1**)–(**9**), in CCl$_4$, were obtained as previously described.[2,39]

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