

Solvent Effects on Oxygen-17 Chemical Shifts in Methyl Formate: Linear Solvation Shift Relationships

Dora G. de Kowalewski,^{*1} Valdemar J. Kowalewski,^{*1} Ruben H. Contreras,^{*1} Ernesto Díez,^{†2} Jorge Casanueva,[‡] Jesús San Fabián,[‡] Angel L. Esteban,[‡] and Maria P. Galache[‡]

^{*}Departamento de Física, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires and CONICET (LANAIS RMN-500), Pabellón I, Ciudad Universitaria, Buenos Aires 1428, Argentina; [†]Departamento de Química Física Aplicada, Facultad de Ciencias C2, Universidad Autónoma de Madrid, E-28049 Madrid, Spain; and [‡]Departamento de Química Física, Facultad de Ciencias, Universidad de Alicante, E-03080 Alicante, Spain

Received February 22, 2000; revised August 28, 2000

A multiple linear regression analysis has been carried out using the Kamlet–Abboud–Taft solvatochromic parameters in order to quantify the solvent effects on the ¹⁷O chemical shifts of methyl formate (MF). The influence of the solvents upon the carbonyl oxygen chemical shifts is smaller for MF than for *N*-methylformamide (NMF). The influence (in parts per million) of the solvent polarity–polarizability reduces from $-21.9\pi^*$ in amides to $-9.6\pi^*$ in MF. The influence of the solvent hydrogen-bond-donor acidities reduces from -42.0α in formamides to -16.9α in MF. The solvent effects upon the dicoordinated oxygen chemical shifts of MF are smaller in magnitude and opposite in direction, i.e., $4.8\pi^*$ and 2.6α , than those for the carbonyl oxygen. ¹⁷O hydration shifts have been calculated for the NMF + (H₂O)₆ and MF + (H₂O)₅ complexes by the *ab initio* GIAO method at the 6-311 + G** level. The hydration shifts calculated for the carbonyl oxygens of NMF and MF and for the dicoordinated oxygen of MF, -102.4 , -64.7 , and 17.6 ppm, respectively, show the same trend as the corresponding empirical hydration shifts, -101.7 , -42.0 , and 14.2 ppm. © 2001 Academic Press

Key Words: solvent effect; oxygen-17 chemical shifts; linear solvation shift relationships; *ab initio* hydration shift; methyl formate.

INTRODUCTION

¹⁷O chemical shifts $\delta(^{17}\text{O})$ are extremely sensitive, in general, to both solvation and substituent effects (1–3). Recently, a satisfactory model for the quantitative description of the solvent effects and determination of the substituent effects upon the $\delta(^{17}\text{O})$ chemical shifts of amides was proposed by Díez *et al.* (4). This model was derived from a multiple-linear-regression analysis (MLRA) using the Kamlet–Abboud–Taft (KAT) solvatochromic parameters (5–8). The same approach is applied in this work to the description of the solvent effects upon the $\delta(^{17}\text{O})$ chemical shifts of methyl formate (MF) with the aim of comparing the behavior of carbonyl oxygen in ester

and amide groups and of the dicoordinated oxygen O_c with the carbonyl oxygen O_c in MF (see Fig. 1).

Models for describing the solvent effects on the $\delta(^{17}\text{O})$ chemical shifts of amides were proposed first by Burgar and colleagues (9, 10) and then by Gerothanassis and co-workers (3, 11). The later model was reduced to a more quantitative basis (4) by application of the KAT parameters using linear solvation shift relationships. The chemical shifts of the four amides analyzed in (4) (*N*-methylformamide, NMF; *N,N*-dimethylformamide, DMF; *N*-methylacetamide, NMA, and *N,N*-dimethylacetamide, DMA) show the same dependence (in ppm) on the solvent polarity–polarizability, i.e., $-21.9\pi^*$. On the other hand, the influence of the solvent hydrogen-bond-donor (HBD) acidities is slightly larger for the acetamides NMA and DMA, i.e., -47.5α , than for the formamides NMF and DMF, i.e., -42.0α . The influence of the solvent HBD acidity is expected to be related to solute hydrogen-bond-acceptor (HBA) basicity, as measured by the β scale, and the influence of the solvent polarity/polarizability is expected to be related to the solute polarity/polarizability, as measured by the π^* scale. Unfortunately, these relations cannot be quantified from the amide results since the π^* and β parameters are available only for DMF and DMA, being close for both molecules the corresponding values of π^* , 0.88 and 0.85, and of β , 0.69 and 0.76. On the contrary, for the MF molecule the π^* value, 0.55, and the β value, 0.37, differ from those of DMF and DMA, providing the present study of the solvent effects on $\delta(^{17}\text{O}_c)$ chemical shifts of MF the pertinent results for elucidating the trends of the relationships between the influence of the solvent upon the $\delta(^{17}\text{O}_c)$ chemical shifts and the solute solvatochromic parameters β and π^* .

The application of MLRA using the KAT parameters (5–8) to the quantitative description of the solvent effects upon the $\delta(^{17}\text{O})$ chemical shifts provides less satisfactory results for MF than for amides (4). With the aim of clarifying some of the difficulties found in these analyses, comparative *ab initio* studies have been performed for NMF and MF comprising calcu-

¹ Member of CONICET.

² To whom correspondence should be addressed. Fax: 3413974187. E-mail: ernesto.diez@uam.es.

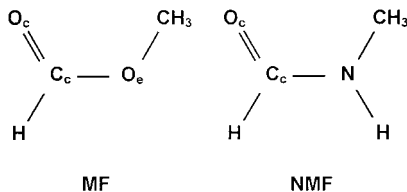


FIG. 1. Chemical formulas of methyl formate (MF) and *N*-methylformamide (NMF).

lations of shielding constants for the free molecules, hydration shifts, and solvent reaction field shifts.

LINEAR SOLVATION SHIFT RELATIONSHIPS (4–8)

A discussion of *ab initio* methods for the calculation of the NMR shieldings has been given in a recent review (12) where the authors stress that there is no systematic *ab initio* theory of NMR parameters in interacting atomic or molecular systems. Reliable supermolecule calculations, where some neighboring solvent molecules are explicitly included in the calculation together with the solvent molecule, only can be carried out when the solvent molecule is small. This approach has been applied in the present work to the calculation of hydration shifts of oxygen in NMF and MF. On the other hand, the solute–solvent hydrogen bond effects are not accounted for in the continuum models developed for describing the electrostatic effects of a surrounding dielectric medium. Therefore, this approach, which has also been used in the present work, only may be applied for solvents where the hydrogen bond contributions are negligible. A proper treatment of the solvent effects requires the combined use of quantum chemistry and molecular dynamics approaches, but efficient techniques for performing this kind of calculations have not been developed yet (12).

The development of empirical solvent scales (5–8, 13, 14) was originally prompted by the need to quantify solvent effects which were beyond the reach of theoretical tools. Using this framework, a linear dependence upon solvent parameters is assumed for describing a solute property such as a chemical shift (5). Of the many solvent scales that have been proposed, the KAT ones (5–8) have been found to be very successful. The application of the KAT formalism to the analysis of the solvent effects on ^{17}O chemical shifts is scarce (4, 15). On the contrary, the application of this formalism to the chemical shifts of the other nuclei (^1H , ^{13}C , ^{19}F , . . .) is frequent (5). In particular, the solvent effects on nitrogen NMR shieldings have been thoroughly studied by Witanowski and colleagues (16–19 and references quoted therein).

According to the KAT formalism, the observed chemical shift, δ_Y^X , of oxygen X (X equal to c or e for carbonyl or dicoordinated oxygens, respectively) at infinite dilution in solvent Y would be given by the relationship

$$\delta_Y^X = \delta_{\text{CH}}^X + s^X(\pi_Y^* + d^X\delta_Y) + a^X\alpha_Y + b^X\beta_Y, \quad [1]$$

where the solvent effects are described by the solvent parameters π_Y^* , δ_Y , α_Y , and β_Y . The π^* scale is an index of solvent dipolarity/polarizability, which measures the ability of the solvent to stabilize a charge or a dipole due to its dielectric effect. The α scale of solvent hydrogen-bond-donor acidities describes the ability of the solvent to donate a proton in a solvent-to-solute hydrogen bond. The β scale of hydrogen-bond-acceptor basicities measures the ability of the solvent to accept a proton (i.e., to donate an electron pair) in a solute-to-solvent hydrogen bond. The δ parameter is a polarizability correction term for polychlorinated ($\delta = 0.5$) and aromatic ($\delta = 1.0$) solvents. The coefficients s^X , a^X , and b^X in Eq. [1] define, respectively, the sensitivity of δ_Y^X to solvent dipolarity–polarizability, acidity, and basicity. The product of coefficients s^Xd^X defines the sensitivity of δ_Y^X for the polarizability correction term.

The term δ_{CH}^X in Eq. [1] is the chemical shift of oxygen X measured in cyclohexane, since this reference solvent does not form hydrogen bonds ($\alpha_{\text{CH}} = \beta_{\text{CH}} = 0$) and was selected to define the origin of the π^* scale ($\pi_{\text{CH}}^* = 0$). The term $s^X(\pi_Y^* + d^X\delta_Y)$ accounts for the difference between the contributions to δ_Y^X in solvent Y and in cyclohexane from the solute–solvent interactions other than hydrogen bonding. The terms $a^X\alpha_Y$ and $b^X\beta_Y$ represent the contributions from hydrogen bonds of methyl formate with solvents HBD and HBA, respectively.

Taking into account the fact that in cyclohexane solution the hydrogen bonding interactions are absent, the chemical shift δ_0^X for the isolated molecule could be estimated as

$$\delta_0^X = \delta_{\text{CH}}^X + s^X\pi_0^*, \quad [2]$$

where π_0^* is the π^* value in vacuum (i.e., for a bulk dielectric constant ϵ equal to 1). On the basis of vapor-phase electronic spectra of eight solvatochromic indicators, the π_g^* ($\approx \pi_0^*$) value of the gas phase was reported by Abboud and colleagues (20) to be -1.06 ± 0.1 . Recently, a refined value of -1.23 was reported (8) for π_g^* .

The solvent parameters π^* , α , and β used in the present work for Eq. [1] are given in Table 1. The used solvents were chosen taking into account the three constraints on MLRA suggested (7) by Abraham *et al.*: (i) there must be enough data points taken, (ii) the explanatory variables must cover as wide a range as possible, and (iii) the explanatory variables must not be linearly dependent. For these solvents, the polarizability correction parameter δ_Y is, in principle, equal to zero. For this reason, the term $d^X\delta_Y$ should be excluded from Eq. [1]. On the other hand, MF is a HBA base, ($\alpha = 0$, $\beta = 0.37$). For this reason, the term $b^X\beta_Y$ should be also excluded from Eq. [1] which reduces to

$$\delta_Y^X = \delta_{\text{CH}}^X + s^X\pi_Y^* + a^X\alpha_Y. \quad [3]$$

TABLE 1
Solvatochromic Parameters (π^* , α , β) Used in Eq. [1]

Solvent <i>Y</i>	π^*	α	β
1, perfluorohexane	-0.48	0.00	0.00
2, perfluoromethylcyclohexane	-0.48	0.00	0.00
3, perfluoromethyldecalin	-0.34	0.00	0.00
4, hexane	-0.11	0.00	0.00
5, cyclohexane	0.00	0.00	0.00
6, decalin	0.09	0.00	0.00
7, diethyl ether	0.24	0.00	0.47
8, triethyl amine	0.09	0.00	0.71
9, tetrahydrofuran	0.55	0.00	0.55
10, dimethyl sulfoxide	1.00	0.00	0.76
11, acetonitrile	0.66	0.19	0.37
12, 2-propanol	0.48	0.76	0.95
13, methanol	0.60	0.93	0.62
14, water	1.09	1.17	0.18
15, trifluoroethanol	0.73	1.51	0.00
16, hexafluoroisopropanol	0.65	1.96	0.00
Solute			
MF	0.55	0.00	0.37
DMF	0.88	0.00	0.69
DMA	0.85	0.00	0.76

Our set of 16 data points is ample for the three-parameter regressions to Eq. [3]. The perfluorinated solvents **1–3** and the nonaromatic hydrocarbons **4–6** are non-hydrogen-bonding solvents, ($\alpha = 0$, $\beta = 0$). For these solvents, Eq. [3] reduces to

$$\delta_Y^X = \delta_{\text{CH}}^X + s^X \pi_Y^* \quad [4]$$

For the HBA bases **7–10**, ($\alpha = 0$, $\beta \neq 0$), Eq. [4] should also be applicable, raising the number of data points available for

determining the parameters δ_{CH}^X and s^X to 10. For the amphiprotic solvents **11–14**, ($\alpha \neq 0$, $\beta \neq 0$) and the HBD acids **15** and **16** ($\alpha \neq 0$, $\beta = 0$), Eq. [3] must be applied. Therefore, there are 6 data points which are useful for determining the parameter a^X .

EXPERIMENTAL

NMR Measurements

All compounds used in this work were available commercially and when necessary they were purified by distillation. Their identities and purities were checked from their ^1H and ^{13}C spectra.

The ^{17}O NMR spectra were recorded with a Bruker AM-500 spectrometer operating to 67.801 MHz from 0.5 M solutions of methyl formate in 16 different solvents with D_2O as external standard. Sample temperatures were established at 298 K using the instrument's temperature control. Spectra were taken with the following parameters: memory size, 4K; spectral width, 62,500 Hz; acquisition time, between 0.03 and 0.06 s; digital resolution, between 15 and 30 Hz per point; pulse width 20 μs ; and number of sweeps, between 50,000 and 120,000. No relaxation delay Gaussian multiplication was used in the water solution to separate the H_2O – D_2O signals.

The ^{17}O chemical shifts reported in Table 2 for the carbonyl oxygen, O_c , and in Table 3 for the dicoordinated oxygen, O_e , are the average values of at least three independent measurements. They were corrected for the magnetic susceptibility effects according to

$$\delta_{\text{cor}} = \delta_{\text{obs}} - (4\pi/3)(\chi_s - \chi_r) \times 10^6, \quad [5]$$

TABLE 2
Solvent Effects on the ^{17}O Chemical Shifts δ_Y^c (ppm) of MF Carbonyl Oxygen and Differences d_Y^i between Calculated and Experimental Values for the Corresponding *i* Fits

Solvent <i>Y</i>	δ_Y^c	d_Y^1	d_Y^2	d_Y^3	d_Y^4	d_Y^5	d_Y^6
1, perfluorohexane	372.45	+2.2	+1.9	—	+0.8	+0.6	+1.0
2, perfluoromethylcyclohexane	372.36	+2.2	+2.0	—	+0.9	+0.7	+1.0
3, perfluoromethyldecalin	372.00	+1.4	+1.5	—	+0.5	-0.7	+0.1
4, hexane	373.98	-2.7	-2.0	+0.1	—	-0.2	-0.5
5, cyclohexane	373.51	-3.2	-2.2	-0.5	—	-1.1	-1.0
6, decalin	372.67	-3.1	-2.0	-0.5	—	-1.3	-1.0
7, diethyl ether	370.06	+0.8	-0.3	+0.7	-1.0	+1.3	+0.3
8, triethyl amine	372.01	+1.6	-1.3	+0.2	-2.1	+2.2	-0.3
9, tetrahydrofuran	368.16	+0.4	-0.3	-0.4	-0.9	-0.3	-0.6
10, dimethyl sulfoxide	363.83	+2.0	+1.2	-0.4	+0.7	-0.7	-0.4
11, acetonitrile	362.34	+1.4	+1.5	+1.2	+1.0	+1.1	+1.3
12, 2-propanol	361.12	-0.9	—	—	—	-0.1	—
13, methanol	359.82	-5.2	—	—	—	-3.7	—
14, water	342.55	+1.6	+1.5	+0.3	+1.5	+2.7	+2.3
15, trifluoroethanol	342.28	-1.1	-1.9	-1.7	-1.9	-2.8	-2.8
16, hexafluoroisopropanol	332.66	+2.5	+0.4	+1.0	+0.5	+2.3	+0.7

TABLE 3
Solvent Effects on the ^{17}O Chemical Shifts δ_Y^e (ppm) of MF Dicoordinated Oxygen and Differences d_Y^i between Calculated and Experimental Values for the Corresponding i Fits

Solvent Y	δ_Y^e	d_Y^1	d_Y^2	d_Y^3	d_Y^4
1, perfluorohexane	136.70	+0.5	+0.5	—	+0.1
2, perfluoromethylcyclohexane	136.89	+0.3	+0.3	—	-0.1
3, perfluoromethyldecalin	137.07	+0.8	+0.8	—	+0.4
4, hexane	140.01	-0.9	-1.0	-0.4	—
5, cyclohexane	140.31	-0.7	-0.8	-0.3	—
6, decalin	140.47	-0.4	-0.6	-0.1	—
7, diethyl ether	140.78	-0.2	-0.1	+0.1	-0.4
8, triethyl amine	139.68	+0.0	+0.2	+0.6	-0.1
9, tetrahydrofuran	142.01	+0.1	+0.1	+0.1	-0.1
10, dimethyl sulfoxide	145.00	-0.7	-0.7	-1.2	-0.9
11, acetonitrile	142.87	+0.3	+0.3	+0.2	+0.1
12, 2-propanol	143.94	-0.5	-0.2	+0.0	-0.3
13, methanol	143.33	+1.3	+1.4	+1.5	+1.4
14, water	146.82	+1.1	+0.9	+0.5	+1.0
15, trifluoroethanol	146.43	+0.6	+0.5	+0.5	+0.5
16, hexafluoroisopropanol	149.26	-1.5	-1.6	-1.4	-1.5

where δ_{obs} and δ_{cor} are the observed and the corrected chemical shifts in units of parts per million, and χ_s and χ_r are the volume magnetic susceptibilities of the sample and the reference solutions, respectively (21). The susceptibilities of solutions were estimated by adding the susceptibilities of the pure components multiplied by their volume fractions. The chemical shifts extrapolated to infinite dilution in hexane, cyclohexane, and tetrahydrofuran differ less than 0.6 ppm for O_c and 0.3 ppm for O_e , from those given in Tables 2 and 3 corresponding to 0.5 M solutions.

MO Calculations

The ^{17}O shielding constants have been calculated using the noncorrelated gauge independent atomic orbital method GIAO (22) at the 6-311 + G** level with the Gaussian 94 program (23). For the free molecules also, the correlated second-order LORG method SOLO (24) has been used with the RPAC program (25) interfaced to the GAMESS program (26).

The shielding constants for the free molecules of NMF and MF were calculated using full gradient optimized MP2/6-31G* molecular geometries. The hydration shifts were calculated using full gradient optimized structures for the complexes $\text{NMF} + (\text{H}_2\text{O})_4$ and $\text{MF} + (\text{H}_2\text{O})_4$. The *ab initio* optimizations have been performed at the SCF level for basis sets of double zeta plus polarization quality (27). These basis sets were constructed as 3,1 contractions of the shared-exponent valence basis sets of Stevens *et al.* (28). The H basis was the scaled Dunning DZ basis (29). The exponents used with polarization functions were $\alpha_p(\text{H}) = 1.0$, $\alpha_d(\text{O}) = 0.80$, $\alpha_d(\text{N}) = 0.77$, and $\alpha_p(\text{C}) = 0.75$. In all calculations, the 1s core electrons of carbon, nitrogen, and oxygen were replaced by compact effective potentials CEP (28), which results in a decrease in the

basis set superposition error relative to comparable all electron calculations (27, 30). The structures were restricted to C_s symmetry during the optimization.

The solvent reaction field shifts were evaluated by means of a shielding constant GIAO calculation performed at the 6-311 + G** level in the presence of a solvent, using the self-consistent reaction field (SCRF) approach (31, 32), as it is implemented in the DALTON program (33). The solvent response to the presence of the solute was represented by a multipole expansion including all terms up to $L = 10$ (33). In the SCRF model the solute is placed in a spherical cavity and surrounded by the dielectric medium; the cavity radii of FM ($a_0 = 3.41 \text{ \AA}$) and NMF ($a_0 = 3.68 \text{ \AA}$) were estimated by a gas-phase molecular volume calculation using the Gaussian 94 program (23). Full gradient optimized molecular geometries of MF and NMF surrounded by the dielectric medium were used in these calculations. The *ab initio* optimizations were performed at the SCF level using the same basis sets of double zeta plus polarization quality (27) as for the hydration complexes.

RESULTS AND DISCUSSION

Carbonyl Oxygen

Several linear equations including different sets of terms from Eq. [1] have been applied to the analysis of the complete set of 16 experimental carbonyl oxygen chemical shifts δ_Y^e of MF as well as to some subsets from this. Least-squares-fitted estimates for the MF parameters from the corresponding fits are given in Table 4. Differences d_Y^i between calculated and experimental chemical shifts for each fit i are reported in Table 2.

Although in our case the general Eq. [1] with five terms

TABLE 4
Least-Squared-Fitted MF Parameters for Eq. [1] from a Series of Fits of Carbonyl Oxygen Chemical Shifts δ_Y^c (ppm)

Parameter	Values for the following fits					
	1	2	3	4	5	6
δ_{CH}^c	370.3 ± 1.0	371.3 ± 0.5	373.0 ± 0.4	370.5 ± 0.5	372.5 ± 1.1	372.5 ± 0.6
δ_0^c	—	—	—	—	—	—
s^c	-8.9 ± 2.1	-6.3 ± 1.1	-9.6 ± 0.8	-5.9 ± 0.9	-12.4 ± 2.0	-9.0 ± 1.4
$s^c d^c$	—	—	—	—	-10.7 ± 3.6	-6.9 ± 2.7
a^c	-15.0 ± 1.5	-17.4 ± 0.9	-16.9 ± 0.5	-17.1 ± 0.7	-12.3 ± 1.4	-15.2 ± 1.1
b^c	5.8 ± 2.6	—	—	—	4.1 ± 2.1	—
Statistics ^a						
σ	2.5	1.7	0.9	1.3	1.8	1.3
ρ	0.983	0.993	0.998	0.996	0.991	0.996
n	16	14	11	11	16	14
m	4	3	3	3	5	4

^a Root-mean-squared deviation (σ), correlation coefficient (ρ), number of data points (n), and number of parameters (m).

would be reduced to Eq. [3] with three terms, an initial fit 1 was performed to an equation with four terms: the three terms in Eq. [3] and the term $b^X \beta_Y$ from Eq. [1]. This term was added to Eq. [3] in order to check whether a negligible value is obtained for b^c according to the fact that MF is an HBA base. The statistical quality of correlation for fit 1 can be considered satisfactory (see Table 4) for a MLRA using the KAT parameters, but the resulting value of 5.8 ± 2.6 ppm for the parameter b^c (see Table 4) is not negligible. When the term $b^X \beta_Y$ is not added to Eq. [3] the statistical quality of correlation for the fit decreases slightly: the correlation coefficient ρ decreases from 0.983 to 0.975 and the root-mean-squared deviation σ increases from 2.5 to 3.0 ppm. The change in σ is related mainly to the increase of the deviations d_Y between the calculated and the experimental $\delta(^{17}\text{O}_c)$ chemical shifts for 2-propanol, **12**, and methanol, **13**, solvents which goes from, respectively, -0.9 and -5.2 ppm in fit 1 up to -4.7 and -7.0 ppm in the fit to Eq. [3]. A fit to the same equation as fit 1, but excluding these two alcohols from the data set, improves the statistical quality of correlation ($\rho = 0.993$; $\sigma = 1.7$) and provides a negligible value of 1.1 ± 2.8 ppm for b^c . Taking into account these results, the alcohols **12** and **13** were excluded from the data set in the following fits except in fit 5.

A good statistical quality of correlation is obtained for fit 2 to Eq. [3], excluding the alcohols **12** and **13** from the data set. However, there is a shortcoming in the resulting d_Y^2 deviations between calculated and experimental values given in Table 2: the average of the d_Y^2 deviations is $+1.8$ ppm for the perfluorinated solvents **1–3** and -2.1 ppm for the hydrocarbons **4–6**. The difference of ca. 4 ppm between these two figures is excessive since the only solvent effect operative in this case is described by the term $s^X \pi_Y^*$. The values of the π^* parameter for solvents **1–3** are negative and larger in magnitude than those for solvents **4–6**; see Table 1. Accordingly, the calculated $\delta(^{17}\text{O})$ chemical shifts are larger for the first than for the second

group of solvents contrary to the experimental behavior. Alternatively, the discussed shortcoming could be attributed to an anomalous behavior of solvents **1–3** or of solvents **4–6**. In order to elucidate this question, two additional fits to Eq. [3] were performed excluding solvents **1–3** from the data set in fit 3 and excluding solvents **4–6** in fit 4. The smaller value of σ for fit 3, 0.9 ppm, than for fit 4, 1.3 ppm, suggests an anomalous behavior of perfluorinated solvents. This suggestion is also supported by the fact that the average of the d_Y^4 deviations for solvents **1–3** in fit 4 is positive, $+0.7$ ppm, as it is in fit 2. In this context it is interesting to note that studies of solvatochromic indicators in perfluorinated solvents (34, 35) showed that π^* values for these materials are significantly indicator-dependent.

The results from the fits 2 to 4 relative to the perfluorinated solvents **1–3** suggest that for polyfluorinated solvents, like for polychlorinated solvents, the polarizability correction term $d^X \delta_Y$ of Eq. [1] should be retained in the fits. The statistical quality of correlation for the corresponding fit 5 to Eq. [1], including the five terms and taking $\delta_Y = 0.5$ for the polyfluorinated solvents **1, 2, 3, 15**, and **16** and $\delta_Y = 0.0$ for the remaining solvents, is better than that for fit 1 where the term $d^X \delta_Y$ was excluded from Eq. [1]. However, the resulting value of -10.7 ± 3.6 for the parameter $s^c d^c$ is clearly too large in comparison with the value of 2.5 ± 1.1 ppm found in amides (4). When the term $b^X \beta_Y$ is excluded from Eq. [1] the magnitude of deviations d_Y for alcohols **12** and **13** increase up to -2.4 and -4.7 , respectively. When these two alcohols are excluded from the data set the results of fit 6 are obtained. The magnitude of the $s^c d^c$ parameter decreases to -6.9 ± 2.7 ppm but this figure seems still to be by far too large. Comparison of the results in Tables 2 and 4 for fit 6 with those for fit 3 shows that both fits are near equivalents. When the alcohols **12** and **13** are excluded from the data set, the results obtained by including the term $d^X \delta_Y$ into the equation, fit 6, are close to those

TABLE 5
Least-Squared-Fitted MF Parameters for Eq. [1] from a Series of Fits of Dicoordinated Oxygen Chemical Shifts δ_Y^c (ppm)

Parameter	Values for the following fits			
	1	2	3	4
δ_{CH}^c	139.6 \pm 0.3	139.5 \pm 0.3	140.0 \pm 0.4	139.2 \pm 0.3
δ_0^c	—	—	—	—
s^c	5.0 \pm 0.7	4.8 \pm 0.5	3.8 \pm 0.8	5.0 \pm 0.5
$s^c d^e$	—	—	—	—
a^e	2.5 \pm 0.5	2.6 \pm 0.4	2.7 \pm 0.4	2.7 \pm 0.4
b^e	-0.5 \pm 0.8	—	—	—
Statistics ^a				
σ	0.81	0.82	0.80	0.77
ρ	0.978	0.977	0.967	0.983
n	16	16	13	13
m	4	3	3	3

^a Root-mean-squared deviation (σ), correlation coefficient (ρ), number of data points (n), and number of parameters (m).

obtained without this term but excluding the perfluorinated solvents 1–3 from the data set, fit 3. Anyway, these solvents are not useful for estimating the chemical shifts δ_0^c of the isolated molecule of MF despite the fact that their negative π^* values are closest to that of the gas phase. Differences between the values of the parameters δ_{CH}^c , s^c , and a^e for fits 3 and 6 are small but we prefer to use hereafter the results for fit 3, which seem to be more physically meaningful.

Dicoordinated Oxygen

The solvent effects upon the dicoordinated oxygen chemical shifts δ_Y^c of MF are much smaller and opposite in direction than for the carbonyl oxygen chemical shifts δ_Y^c . While the range of δ_Y^c values in Table 2 is of 41.3 ppm, from 373.98 to 332.66 ppm, the range of δ_Y^c values in Table 3 is of 12.6 ppm, from 136.70 to 149.26 ppm.

The initial fit 1 to Eq. [3] enlarged with the term $b^e \beta_Y$ provides a negligible value of 0.5 \pm 0.8 ppm for the parameter b^e . When the term $b^e \beta_Y$ is not added to Eq. [3], fit 2, the results barely differ from those for fit 1; see Tables 5 and 3. As in the case of the carbonyl oxygen, the d_Y^2 deviations between calculated and experimental chemical shifts, given in Table 3, are positive for perfluorinated solvents 1–3 and negative for hydrocarbons 4–6 with average values of +0.5 and -0.8 ppm, respectively. When the hydrocarbons are excluded from the data set, fit 3, the statistical quality of correlation is slightly worse than when the perfluorinated solvents are excluded from the data set, fit 4; see Tables 5 and 3. Since the differences between the values of parameters δ_{CH}^c , b^e , and a^e for fits 2 and 4 are small, we prefer to use hereafter the results of fit 2 for the complete data set.

The inclusion into the equations of a polarizability correc-

tion term $d^X \delta_Y$ for polyfluorinated solvents seems to be unnecessary in the case of the δ_Y^c chemical shifts of MF. The fit of the complete data set to Eq. [1] provides small values of -1.1 ± 1.5 for $s^e d^e$ and of 0.7 ± 0.9 for b^e . When the term $b^e \beta_Y$ is excluded from Eq. [1] a value of 0.7 ± 1.4 results for $s^e d^e$.

Comparison of Results for MF and Amides

The first point to be considered is the relationship between the solute parameters in Eq. [1] for the $\delta(^{17}\text{O}_c)$ chemical shifts and the respective solvatochromic parameters π^* and β for these same solutes. Both sets of parameters are only available for MF, DMF, and DMA. The solvatochromic parameters for these molecules are given in Table 1. The least-squares-fitted solute parameters for Eq. [1] are compiled in Table 6 for the $\delta(^{17}\text{O}_c)$ chemical shifts of MF and NMF, as well as for the $\delta(^{17}\text{O}_c)$ chemical shifts of MF, together with the corresponding values of the chemical shifts for the free molecules, δ_0^X , and for solutions in cyclohexane, δ_{CH}^X , and water, $\delta_{\text{H}_2\text{O}}^X$.

In principle, the larger the HBA basicity as solvent of a substance is, i.e., larger β value, the larger the sensitivity of this substance to solvent acidity is, i.e., larger a values. Accordingly, the magnitude of the a^c values for MF, -16.9, DMF, -42.0, and DMA, -47.5, increases with the respective values of β for these substances: 0.37, 0.69, and 0.76. However, the sensitivity a^c of the $\delta(^{17}\text{O}_c)$ chemical shifts to solvent acidity is not proportional to the solute HBA basicity β . The magnitude of the ratio a^c/β of -46 for MF, -61 for DMF, and -63 for DMA seems to increase with β . On the other hand, the sensitivity s^c of the $\delta(^{17}\text{O}_c)$ chemical shifts to solvent dipolarity/polarizability seems to increase with the solute π^* value, but the s^c values for MF, -9.6, DMA, -21.9, and DMF, -21.9, are not proportional to the respective π^* values of 0.55, 0.85, and 0.88. The corresponding ratios s^c/π^* are 18, 26, and 25. The small difference between the values of the ratio s^c/π^* , and also of the ratio a^c/β , for DMF and DMA is not significant. The elucidation of the functional relationships between a^c and β and between s^c and π^* requires additional studies of the

TABLE 6
Least-Squared-Fitted Solute Parameter (s , a , b) from Fits to Eq. [1] of $\delta(^{17}\text{O}_c)$, in NMF and MF, and of $\delta(^{17}\text{O}_c)$, in MF; Chemical Shifts (ppm) for Free Molecules (δ_0^X) and for Solutions in Cyclohexane (δ_{CH}^X) and Water ($\delta_{\text{H}_2\text{O}}^X$)

	$\delta(^{17}\text{O}_c)$ in NMF		$\delta(^{17}\text{O}_c)$ in MF		$\delta(^{17}\text{O}_c)$ in MF	
	Fit	Exp.	Fit 3	Exp.	Fit 2	Exp.
s	-21.9	—	-9.6	—	4.8	—
a	-42.0	—	-16.9	—	2.6	—
b	-9.4	—	—	—	—	—
δ_0^X	376.3	—	384.8	—	133.6	—
δ_{CH}^X	349.4	—	373.0	373.5	139.5	140.3
$\delta_{\text{H}_2\text{O}}^X$	274.6	272.4	342.8	342.6	147.7	146.8

TABLE 7

Shieldings σ_M^X (ppm) for the Carbonyl ($X = c$) and Dicoordinated ($X = e$) Oxygens of NMF and MF, Calculated at the GIAO ($M = G$) and SOLO ($M = S$) Levels^a: Relative Energies ΔE (kcal/mol) Calculated for Three Orientations of Methyl Groups^b

ϕ^b	NMF			MF				
	σ_G^c	σ_S^c	ΔE	σ_G^c	σ_S^c	σ_G^e	σ_S^e	ΔE
0°	-67.6	-77.3	0.00	-98.9	-100.6	173.2	163.9	1.09
90°	-77.3	-87.7	0.02	-106.6	-109.3	169.6	159.7	0.57
180°	-84.5	-94.6	0.08	-112.7	-116.3	166.5	155.9	0.00
Average ^c	-76.4	-86.5		-109.1	-112.1	168.3	158.1	

^a The 6-311 + G** basis set was used with optimized MP2/6-31G* molecular geometries.

^b An angle $\phi = \text{H-C-X-C}$, with $X = \text{N}$ for NMF and $X = \text{O}$ for MF, defines the methyl group orientation.

^c Average value weighted with the displayed energies ΔE .

solvent effects on $\delta(^{17}\text{O}_c)$ chemical shifts of adequately chosen solutes.

The second point to be considered is the reliability of the empirically estimated δ_0^X chemical shifts for free molecules and the differences $\delta_0^X - \delta_0^Y$ between them. These estimates are important for comparison with results of *ab initio* calculations of $\delta(^{17}\text{O})$ chemical shifts. The δ_0^X are estimated by means of Eq. [2] where the value to be used for π_0^* is under dispute (7). On the other hand, the anomalous behavior of perfluorinated solvents in the case of the $\delta(^{17}\text{O}_c)$ chemical shifts of MF questions the fitness of Eq. [2]. Studies of solvent effects upon $\delta(^{17}\text{O})$ chemical shifts for molecules measured in gas phase and/or accurate *ab initio* calculations of $\delta(^{17}\text{O})$ can elucidate this problem. The differences $\delta_0^X - \delta_0^Y$ between the $\delta(^{17}\text{O})$ chemical shifts for free molecules can be empirically estimated and theoretically calculated more accurately than the δ_0^X values. In the case of the amides NMF, NMA, DMF, and DMA the values of s^c to be used in Eq. [2] is the same, -21.9 , for all four molecules. Therefore, the estimated differences $\delta_0^X - \delta_0^Y$ for the free amide molecules are the same as the differences $\delta_{\text{CH}}^X - \delta_{\text{CH}}^Y$ measured in cyclohexane solution. However, when comparing data for MF and NMF, the estimated difference $\delta_0^{\text{c, MF}} - \delta_0^{\text{c, NMF}}$ in gas phase, 8.5 ppm, is 15.1 ppm smaller than the measured difference $\delta_{\text{CH}}^{\text{c, MF}} - \delta_{\text{CH}}^{\text{c, NMF}}$ in cyclohexane solution, 23.6 ppm. The reason for this disagreement is the different values of s^c for MF, -9.6 , and NMF, -21.9 . The true value for $\delta_0^{\text{c, MF}} - \delta_0^{\text{c, NMF}}$ is probably between 8.5 and 23.6 ppm. Likewise, the estimated difference $\delta_0^c - \delta_0^e$ for MF, 251.2 ppm, is 17.7 ppm larger than the measured difference $\delta_{\text{CH}}^c - \delta_{\text{CH}}^e$, 233.5 ppm, because the different values of s^c , -9.6 and of s^e , 4.8.

Calculations of ^{17}O Shielding Constants

Reliable *ab initio* calculations of $\sigma(^{17}\text{O})$ shielding constants could contribute to the clarification of some of the difficulties found in the previous analysis of the $\delta(^{17}\text{O})$ chemical shifts of MF by using linear solvation shift relationships. With this aim, three kinds of such calculations have been performed for MF

and NMF: $\sigma(^{17}\text{O})$ shieldings of the free molecules, hydration shifts, and solvent reaction field shifts.

The $\sigma(^{17}\text{O})$ shielding constants of MF, like that of NMF (36, 37), show a large variation with the conformation of the methyl group. The calculated values for both molecules with three different orientations of the methyl group appear in Table 7. The 6-311 + G** basis set was used at the noncorrelated GIAO (22) and at the correlated SOLO (24) levels. The difference $\sigma_M^c - \sigma_M^e$ between the two average oxygen shieldings of MF calculated at the GIAO level, 277.4 ppm, is larger than that calculated at the SOLO level, 270.2 ppm. The decrease in the calculated difference of 7.2 ppm from electron correlation effects is too small for bringing off the SOLO figure in agreement with the corresponding empirically estimated difference $\delta_0^c - \delta_0^e$ of chemical shifts for the free molecule, 251.2 ppm. The agreement is still worse for the difference $\delta_{\text{CH}}^c - \delta_{\text{CH}}^e$ of chemical shifts measured in cyclohexane solution, 233.5 ppm. On the other hand, the difference between the average carbonyl oxygen shieldings σ_M^c of NMF and MF calculated at the GIAO level, 32.7 ppm, is larger than that calculated at the SOLO level, 25.6 ppm. The decrease in the calculated difference of 7.1 ppm from electron correlation effects brings the calculated SOLO value in good agreement with the corresponding difference $\delta_{\text{CH}}^{\text{c, MF}} - \delta_{\text{CH}}^{\text{c, NMF}}$ of carbonyl oxygen chemical shifts measured in cyclohexane solution, 23.6 ppm. However, this agreement seems to be fortuitous and does not prove that the empirical estimates of chemical shifts δ_0^X for the free molecules by using Eq. [2] are unreliable since the estimated difference $\delta_{\text{CH}}^{\text{c, MF}} - \delta_{\text{CH}}^{\text{c, NMF}}$, 8.5 ppm, differs only by 17.1 ppm from the corresponding calculated SOLO value, while the measured difference $\delta_{\text{CH}}^c - \delta_{\text{CH}}^e$ for MF differs by 36.7 ppm. Therefore, in order to get significative results, the *ab initio* calculation should be improved to bring the calculated difference of shieldings $\sigma_M^c - \sigma_M^e$ for MF (270.2 ppm at the SOLO level with the 6-311 + G** basis set) in good agreement with the empirically estimated difference $\delta_0^c - \delta_0^e$ for the free molecule, 251.2 ppm. These expensive improvements require not only the use of larger basis sets, higher electron correlation levels, and better

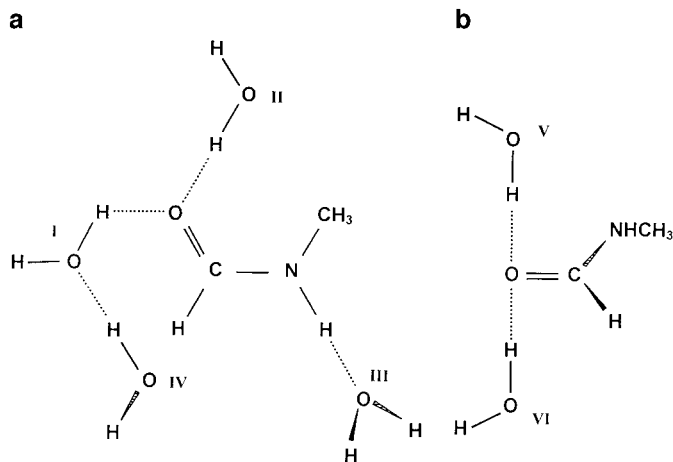


FIG. 2. (a) Drawing of the NMF + (H₂O)₄ system with four in-plane water molecules; (b) drawing of the NMF + (H₂O)₂ system with two out-of-plane water molecules.

molecular equilibrium geometries but also the calculation of rovibrational and large amplitude out-plane deformation corrections.

Previous studies of hydration in amides (4, 27, 38–44) support the conclusion that the first hydration shell of the carbonyl oxygen includes four solvent water molecules: two in-plane (molecules **I** and **II** in Fig. 2a) and two out-of-plane (molecules **V** and **VI** in Fig. 2b). Accordingly, the $\sigma(^{17}\text{O})$ shielding constants for the corresponding MF + (H₂O)₄ and NMF + (H₂O)₄ complexes were calculated at the GIAO level using the 6-311 + G** basis set. The calculated hydration chemical shifts δW^X for these complexes and for others, obtained from them after eliminating some water molecules, are given in Table 8. In this table also appears the empirically estimated hydration shifts $\delta_{\text{H}_2\text{O}}^X - \delta_0^X$ of NMF and MF together with the corresponding contributions from solvent dipolarity/polarizability ($s\pi_0^*$ and $s\pi_{\text{H}_2\text{O}}^*$), HBD acidity ($a\alpha_{\text{H}_2\text{O}}$), and HBA basicity ($b\beta_{\text{H}_2\text{O}}$). In the case of the NMF there is another water molecule in the first hydration shell hydrogen bonded to the N–H proton (molecule **III** in Fig. 2a), which changes the carbonyl oxygen hydration shift by -15.6 ppm. In the second hydration shell there is a water molecule to be considered (4) (molecule **IV** in Fig. 2a), which changes the hydration shift by -6.2 ppm. The total hydration shift calculated for the NMF + (H₂O)₆ complex, -102.4 ppm, is close to the empirical value of -101.7 ppm. In the case of the MF there are only four water molecules in the first hydration shell and the water molecule **IV** in the second hydration shell changes the carbonyl oxygen hydration shift by only -2.3 ppm and the dicoordinated oxygen hydration shift by $+0.9$ ppm. For the MF + (H₂O)₅ complex, the magnitude of the total hydration shift calculated for the carbonyl oxygen, -64.7 ppm, is larger than the empirical value of -42.0 ppm. That calculated for the dicoordinated oxygen, 17.6 ppm, is close to the empirical one, 14.2 ppm. The total hydration shifts calculated for the largest complexes stud-

ied in this work reproduce the empirical trends. The fact that the hydration shift calculated for the carbonyl oxygen of NMF is close to the empirical value while the magnitude of that calculated for the carbonyl oxygen of MF is larger than the magnitude of the empirical value is likely to be related to the fact that the interaction energy for the NMF + (H₂O)₄ complex, -16.2 kcal/mol, is larger in magnitude than that for the MF + (H₂O)₄ complex, -12.0 kcal/mol. The modeling of complete hydration of NMF and MF via statistical mechanical methods could clarify this supposition. Statistical mechanical computer simulations of diluted aqueous solution could be performed from expressions describing the dependence of the $\delta(^{17}\text{O})$ chemical shifts of NMF and MF with the orientation and distance of an H₂O molecule since the nonadditivity for the calculated chemical shifts given in Table 8 of complexes with two, three, and four molecules of water are not too severe. The corresponding figures are $+5.7$, $+0.3$, and -2.2 ppm for the carbonyl oxygen of NMF, $+4.7$, -4.1 , and -3.8 ppm for the carbonyl oxygen of MF, and 0.0 , $+0.1$, and $+0.2$ ppm for the dicoordinated oxygen of MF. On the other hand, when the total interaction energies ΔE of complexes with two, three, and four water molecules in Table 8 are calculated as the sum of the interaction energies for all the dimers, the nonadditivity devi-

TABLE 8
Hydration Shifts δW^X (ppm) for the Carbonyl ($X = \text{c}$) and Dicoordinated ($X = \text{e}$) Oxygens of NMF and MF, Calculated at the GIAO Level^a; Interaction Energies^b ΔE (kcal/mol); Contributions (in ppm) to the Hydration Shifts ($s\pi_0^*$, $s\pi^*$, $a\alpha$, $b\beta$) from Terms in Eqs. [1] and [2]

	NMF		MF		
	δW^c	ΔE	δW^c	δW^e	ΔE
Water positions ^c					
I	-29.4	-6.4	-24.9	1.0	-5.0
II	-32.1	-6.9	-25.8	8.1	-5.7
V	-15.2	-3.7	-10.8	3.9	-2.4
I + II	-57.2	-12.5	-47.9	9.1	-10.1
I + II + V	-67.0	-14.4	-55.4	12.9	-11.3
I + II + V + VI	-80.6	-16.2	-62.4	16.7	-12.0
Largest complexes ^d	-102.4	—	-64.7	17.6	—
Empirical values					
$\delta_{\text{H}_2\text{O}}^X - \delta_0^X$	-101.7	—	-42.0	14.2	—
$s\pi_0^*$	-26.9	—	-11.8	5.9	—
$s\pi_{\text{H}_2\text{O}}^*$	-23.9	—	-10.5	5.2	—
$a\alpha_{\text{H}_2\text{O}}$	-49.2	—	-19.7	3.1	—
$b\beta_{\text{H}_2\text{O}}$	-1.7	—	0.0	0.0	—

^a The 6-311 + G** basis set was used with structures optimized as described under Experimental.

^b Energy of complex minus sum of energies for free molecules.

^c See Fig. 2 for water positions in the complex.

^d Complex NMF + (H₂O)₆ with water molecules in positions **I + II + III + IV + V + VI** and complex MF + (H₂O)₅ with water molecules in positions **I + II + IV + V + VI**.

ations amount, respectively, to -0.1 , -1.0 , and -1.6 kcal/mol for NMF and 0.0 , -0.7 , and -1.7 kcal/mol for MF.

The solvent reaction field shifts $\delta^X(\epsilon) - \delta_0^X$ calculated at the GIAO level using the 6-311 + G** basis set show quadratic dependences on the dielectric constant ϵ function $\phi(\epsilon)$,

$$\phi(\epsilon) = (\epsilon - 1)/(2\epsilon + 1), \quad [6]$$

given by

$$\delta^{c,\text{NMF}}(\epsilon) - \delta_0^{c,\text{NMF}} = -50.7\phi(\epsilon) - 12.6\phi(\epsilon)^2, \quad [7]$$

$$\delta^{e,\text{MF}}(\epsilon) - \delta_0^{e,\text{MF}} = -35.9\phi(\epsilon) - 12.9\phi(\epsilon)^2, \quad [8]$$

$$\delta^{e,\text{MF}}(\epsilon) - \delta_0^{e,\text{MF}} = 7.6\phi(\epsilon) + 4.3\phi(\epsilon)^2. \quad [9]$$

The linear term is the main term in these equations. The coefficients of the linear terms, (-50.7 , -35.9 , and 7.6) follow the same trends that the corresponding coefficients s of the solvent polarity–polarizability parameter π^* in Eq. [1] given in Table 6 (-21.9 , -9.6 , and 4.8). However, the variations of carbonyl and dicoordinated oxygen chemical shifts of MF for solvents **1** to **10**, where the hydrogen-bond contributions are negligible, differ from those predicted by Eqs. [8] and [9]. On the other hand, the $\delta^X(\epsilon) - \delta_0^X$ values for cyclohexane ($\epsilon = 2.02$) provided by Eqs. [7] to [9] (-10.8 , -7.8 , and 1.7 ppm, respectively) are smaller in magnitude than the corresponding empirical contributions $s\pi_0^*$ given in Table 8 (-26.9 , -11.8 , and 5.9 ppm).

CONCLUSIONS

Application of MLRA using the KAT parameters to the quantitative description of the solvent effects upon the carbonyl oxygen chemical shifts of MF and amides shows that the magnitudes for the sensitivities a^c to the solvent acidities and s^c to the solvent dipolarity/polarizabilities increase with the solute β and π^* parameters, respectively; see Eq. [1]. However, neither is a^c proportional to β nor is s^c proportional to π^* . On the other hand, the magnitudes of the sensitivities a^c and s^c for the dicoordinated oxygen chemical shift of MF are smaller in magnitude and have opposite sign than the respective sensitivities, a^c and s^c , for the carbonyl oxygen.

The results of the fits for the carbonyl oxygen chemical shifts to the linear solvation shift relationship (Eq. [1]) on the KAT parameters provide less satisfactory results for MF than for amides. In the case of MF, the data for the two amphiprotic alcohol solvents (2-propanol and methanol) should be excluded from the fits in order to obtain a negligible value for the sensitivity b^c to the solvent basicity, as expected from the fact that MF is a HBA base. In addition, the behavior of the perfluorinated solvents seems to be anomalous. This questions the fitness of Eq. [2] for estimating the chemical shift δ_0^c of the isolated molecule of MF. The fact that Eq. [1] works better for

amides than for MF could be due to the larger values of the parameters π^* and β for amides and/or to the use of two different sets of solvents.

The results of *ab initio* calculations of oxygen chemical shifts by the electron correlated SOLO method at the 6-311 + G** level using MP2/6-31G* optimized molecular geometries of MF and NMF do not clarify the question about the reliability of the chemical shifts for the isolated molecules obtained from Eq. [2]. Expensive improvement in the *ab initio* calculations seems to be necessary in order to get conclusive results. On the other hand, the hydration shifts calculated for the NMF + (H₂O)₆ and MF + (H₂O)₅ complexes by the noncorrelated GIAO method with the 6-311 + G** basis set reproduce the empirical trends. However, the carbonyl oxygen hydration shift calculated for MF, -64.7 ppm, is larger than the empirical value, -42.0 ppm, suggesting the usefulness of performing statistical mechanics computer simulations for hydration shifts.

ACKNOWLEDGMENTS

This work was supported in part by the Comisión Interministerial de Ciencia y Tecnología of Spain (Projects PB96-0332 and PB98-0069). The Argentine authors thank CONICET, ANPCyT (PICT-604), and UBACYT for financial support.

REFERENCES

1. J. P. Kintzinger, in "NMR—Basic Principles and Progress" (P. Diehl, E. Fluck, and R. Dosfeld, Eds.), Vol. 17, pp. 1–64, Springer-Verlag, Berlin, 1981.
2. D. W. Boykin (Ed.), ¹⁷O NMR Spectroscopy in Organic Chemistry," CRC Press, Boston, 1991.
3. I. P. Gerathanassis, *Prog. NMR Spectrosc.* **26**, 171 (1994).
4. E. Diez, J. SanFabian, I. P. Gerathanassis, A. L. Esteban, J-L. M. Abboud, R. H. Contreras, and D. G. Kowalewski, *J. Magn. Reson.* **124**, 8 (1997).
5. M. J. Kamlet, J-L. M. Abboud, and R. W. Taft, *Prog. Phys. Org. Chem.* **13**, 485 (1981).
6. M. J. Kamlet, J-L. M. Abboud, M. H. Abraham, and R. W. Taft, *J. Org. Chem.* **48**, 2877 (1983).
7. M. H. Abraham, P. L. Grellier, J-L. M. Abboud, R. M. Doherty, and R. W. Taft, *Can. J. Chem.* **66**, 2673 (1988).
8. C. Laurence, P. Nicolet, M. T. Daleti, J-L. M. Abboud, and R. Notario, *J. Phys. Chem.* **98**, 5807 (1994).
9. M. I. Burgar, T. E. St. Amour, and D. Fiat, *J. Phys. Chem.* **85**, 502 (1981).
10. B. Valentine, A. Steinschneider, D. Dhawan, M. I. Burgar, T. St. Amour, and D. Fiat, *Int. J. Pept. Protein Res.* **25**, 26 (1985).
11. I. P. Gerathanassis and C. Vakka, *J. Org. Chem.* **59**, 2341 (1994).
12. T. Helgaker, M. Jaszunski, and K. Ruud, *Chem. Rev.* **99**, 293 (1999).
13. Y. Marcus, *Chem. Soc. Rev.*, 409 (1993).
14. J-L. M. Abboud and R. Notario, *Pure Appl. Chem.* **71**, 645 (1999).
15. M. A. P. Martins, G. M. Siqueira, A. F. C. Flores, N. Zanatta, and H. G. Bonaccorso, *Spect. Lett.* **32**, 973 (1999).
16. M. Witanowski, Z. Biedrzycka, W. Sicinska, and G. A. Webb, *J. Mol. Struct.* **516**, 107 (2000).

17. M. Witanowski, Z. Biedrzycka, and Z. Grabowski, *Magn. Reson. Chem.* **38**, 580 (2000).
18. M. Witanowski, Z. Biedrzycka, W. Sicinska, and G. A. Webb, *J. Chem. Soc. Perkin Trans. 2*, 533 (1997).
19. M. Witanowski, Z. Biedrzycka, W. Sicinska, Z. Grabowski, and G. A. Webb, *J. Magn. Reson.* **124**, 127 (1997).
20. M. Essfar, G. Guiheneuf, and J-L. M. Abboud, *J. Am. Chem. Soc.* **104**, 6786 (1982).
21. J. Homer, *Appl. Spec. Rev.* **9**, 1 (1975).
22. R. Ditchfield, *Mol. Phys.* **27**, 789 (1974).
23. Gaussian 94, Revision D.4, M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Pittsburgh, PA, 1995.
24. T. D. Bouman and A. E. Hansen, *Chem. Phys. Lett.* **175**, 292 (1990).
25. T. D. Bouman and A. E. Hansen, "RPAC Molecular Properties Package, Version 9.0," Southern Illinois Univ., Edwardsville, IL, 1991.
26. M. W. Schmidt, K. K. Baldrige, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. J. Su, T. L. Windus, M. Dupuis, and J. A. Montgomery, *J. Comput. Chem.* **14**, 1347 (1993).
27. P. G. Jasien and W. J. Stevens, *J. Chem. Phys.* **84**, 3271 (1986).
28. W. J. Stevens, H. Basch, and M. Krauss, *J. Chem. Phys.* **81**, 6026 (1984).
29. T. H. Dunning, *J. Chem. Phys.* **53**, 2823 (1970).
30. W. Kolos, *Theor. Chim. Acta* **51**, 219 (1979).
31. K. V. Mikkelsen, E. Dalgaard, and P. Swanstrom, *J. Phys. Chem.* **91**, 3081 (1987).
32. K. V. Mikkelsen, H. Agren, H. J. Aa. Jensen, and T. Helgaker, *J. Chem. Phys.* **89**, 3086 (1988).
33. DALTON, an *ab initio* electronic structure program, Release 1.0 (1997), written by T. Helgaker, H. J. Aa. Jensen, P. Jorgensen, J. Olsen, K. Ruud, H. Ågren, T. Andersen, K. L. Bak, V. Bakken, O. Christiansen, P. Dahle, E. K. Dalskov, T. Enevoldsen, B. Fernandez, H. Heiberg, H. Hettema, D. Jonsson, S. Kirpekar, R. Kobayashi, H. Koch, K. V. Mikkelsen, P. Norman, M. J. Packer, T. Saue, P. R. Taylor, and O. Vahtras.
34. J. E. Brady and P. W. Carr, *Appl. Chem.* **54**, 1751 (1982).
35. V. Bekárek and J. Jurina, *Collect. Czech. Chem. Commun.* **47**, 1060 (1982).
36. F. Ribas Prado, C. Giessner-Prettre, A. Pullman, J. F. Hinton, D. Horspool, and K. R. Metz, *Theor. Chim. Acta* **59**, 55 (1981).
37. R. H. Contreras, R. R. Biekofsky, A. L. Esteban, E. Diez, and J. San Fabian, *Magn. Reson. Chem.* **34**, 447 (1996).
38. I. P. Gerothanassis, I. N. Demetropoulos, and C. Vakka, *Biopolymers* **36**, 415 (1995).
39. I. N. Demetropoulos, I. P. Gerothanassis, C. Vakka, and C. Kakkavas, *J. Chem. Soc. Faraday Trans.* **92**, 921 (1996).
40. G. Alagona, A. Pullman, E. Scrocco, and J. Tomasi, *Int. J. Pept. Protein Res.* **5**, 251 (1973).
41. F. T. Marchese, P. K. Mehrotra, and D. L. Beveridge, *J. Phys. Chem.* **88**, 5692 (1984).
42. W. L. Jorgensen and C. J. Swenson, *J. Am. Chem. Soc.* **107**, 1489 (1985).
43. A. Johansson, P. Kollman, S. Rothenberg, and J. McKelvey, *J. Am. Chem. Soc.* **96**, 3794 (1974).
44. A. Pullman, H. Berthod, C. Giessner-Prette, J. F. Hinton, and D. Harpool, *J. Am. Chem. Soc.* **100**, 3991 (1978).