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Hydrogen Bonding Effects on the ^{13}C NMR Chemical Shift Tensors of Some Amino Acids in the Solid State

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The influence of hydrogen bonding (HB) on the ^{13}C chemical shift tensors in four solid amino acids was studied by the *ab initio* gauge-included atomic orbital (GIAO) approach. The results of the present calculations were compared with those predicted previously and with the experimentally observed shieldings. The RMS error (without HB) found on comparing the calculated and observed principal components of the shielding tensor for the four carboxyl carbons is 35.3 ppm, whereas when the HB effects are included, the RMS error is reduced to 19.6 ppm. This clearly demonstrates the importance of including HB effects in the calculation of the ^{13}C shieldings for the carboxyl carbons, especially for the δ_{22} component; this also agrees with published experimental results. © 1997 by John Wiley & Sons, Ltd.

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INTRODUCTION

In a recent paper, the calculated principal values of the ^{13}C chemical shift tensors of some amino acids were reported.[1] It was shown that for the carboxyl carbons there are large root-mean-square (RMS) errors when the calculated and experimental values are compared. For instance, in the case of the δ_{22} principal component in α-Gly the difference between the predicted and observed values is as large as 50.3 ppm. All of the calculations given in Ref. 1 failed to predict the principal values for the carboxyl carbons correctly even though the predicted isotropic chemical shifts are close to the experimental values.

Intermolecular effects have been investigated in the solid state by de Dios *et al.*;[2] with a charge-field perturbation they achieved more accurate results. By considering the effects of hydrogen bonding, they also successfully studied the shieldings of carbonyl carbons in peptides and proteins.[3] Experimentally, Ando and co-workers[4–6] investigated the effects of hydrogen bonding and observed a linear dependence, in a series of peptides in the solid state, between the carbonyl ^{13}C chemical shifts and the measured hydrogen bond length (R_{N-O}). In addition, quantum-chemical calculations of the ^{13}C shieldings within the finite perturbation theory–intermediate neglect of differential overlap (FPT–INDO) method gave results which were qualitatively in agreement with the experimental results on taking into account the effects of hydrogen bonding.

In this paper, new quantum chemical calculations including hydrogen bonding effects are presented to explain the results of the experimental measurements of the ^{13}C chemical shift tensors in four amino acids (α-Gly, L-Ala, L-Ser and DL-Ser).

CALCULATION

We studied the influence of hydrogen bonding on the ^{13}C chemical shifts of four amino acids. Shielding calculations were performed with the GIAO approach.[7–9] The basis set used was 6–311G**,[10] which includes polarization functions (p orbitals for the hydrogen atom and d orbitals for other atoms). To include the effects of hydrogen bonding, the two closest molecules of glycine were included in the isolated molecule model. The molecular structure of glycine showing the hydrogen bonding interactions is given in Fig. 1, where we use the distances and angles between the glycine and its first neighbours obtained from experimental geometries.[11] The neighbours are replaced by NH_3 groups to simplify the calculations (similarly to the method used by Facelli *et al.*[12] and Malkin *et al.*[13]). Calculations on the other three amino acids were performed in a similar way; the molecular geometrical parameters used were taken from x-ray diffraction data for L-Ala,[14] L-Ser[15] and DL-Ser.[15] All of the calculated ^{13}C chemical shifts are converted to the TMS scale using the value of 195.05 ppm.[1]

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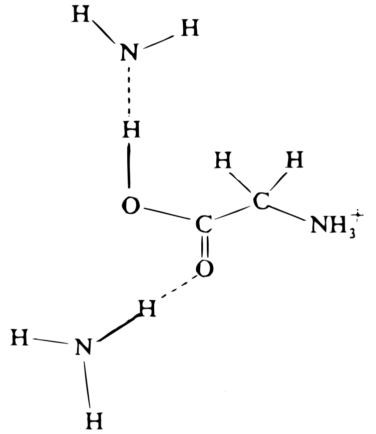

Figure 1. Molecular structure of glycine showing the hydrogen bonding interactions.

The calculations reported were performed on an Indigo/Entry work-station at the Wuhan Institute of Physics.

RESULTS AND DISCUSSION

The calculated principal components of the ^{13}C chemical shift tensors for the four amino acids are listed in Table 1. All of the predicted values, obtained without hydrogen bonding (HB) effects, in Table 1 fail to reproduce the experimental results for the carboxyl carbons. Comparison of the present calculations with the former calculation[1] and with the experimentally observed shieldings[16] show that the RMS error (without HB effects) of the 12 principal components for the four carboxyl carbons is 35.3 ppm, whereas the RMS error is reduced to 19.6 ppm when HB is introduced. This successfully explains most of the differences between the predicted and observed results for the carboxyl carbons in the previous report.[1] The results presented in this paper clearly imply the importance of including hydrogen bonding effects in the calculation of ^{13}C chemical shieldings for the carboxyl carbons.

From Table 1, we can also see that hydrogen bonding effects play a more important role in the anisotropic values of the shieldings of the carboxyl carbons, less important for the C-α and C-β carbons. In addition, the three principal shielding components of the carboxyl carbons demonstrate different hydrogen bonding effects: the δ_{33} (perpendicular to the $CO_2{}^-$ plane) and δ_{11} (in the $CO_2{}^-$ plane, normal to the C=O bond) values decrease in magnitude when HB effects are considered, whereas the intermediate element, δ_{22} (in the $CO_2{}^-$ plane, along the C=O direction), experiences a dramatic decrease in shielding (about 40 ppm) if HB effects are introduced. It is shown that the δ_{22} component is very sensitive to hydrogen bonding effects, which agrees with the experimental results of Gu *et al.*[17] They suggested that by using the value of the intermediate component δ_{22}, the approximate hydrogen bonding strength can be determined.

Table 1. Calculated and experimental ^{13}C chemical shifts of four amino acids[a]

Amino acid	Carbon	δ_{11}	δ_{22}	δ_{33}	δ_{iso}
α-Gly	C-0	246	179	106	176.2
		(283.3)	(128.7)	(108.7)	(173.6)
		[268.6]	[174.0]	[102.8]	[181.8]
	C-α	61	46	24	43.5
		(67.0)	(45.8)	(16.5)	(43.1)
		[63.9]	[48.4]	[19]	[43.8]
L-Ala	C-0	239	184	106	176.8
		(280.0)	(140.7)	(107.6)	(176.1)
		[273.1]	[177.6]	[101.7]	[184.1]
	C-α	63	56	30	50.9
		(71.7)	(58.8)	(23.6)	(51.4)
		[69.7]	[61.3]	[27.4]	[52.8]
	C-β	31	19	7	19.8
		(35.2)	(20.5)	(−1.8)	(18.0)
		[31.9]	[19.8]	[−1.7]	[16.7]
L-Ser	C-0	238	175	113	175.1
		(277.9)	(130.4)	(107.6)	(172.0)
		[274.0]	[169.6]	[102.3]	[182.0]
	C-α	69	59	39	55.6
		(71.8)	(53.0)	(26.9)	(50.6)
		[69.9]	[53.4]	[28.5]	[50.6]
	C-β	87	66	35	62.9
		(75.4)	(57.2)	(28.2)	(53.6)
		[73.8]	[54.5]	[22.9]	[50.7]
DL-Ser	C-0	238	175	113	175.1
		(284.4)	(133.3)	(108.8)	(175.5)
		[274.7]	[182.3]	[100.0]	[185.7]
	C-α	69	59	39	55.6
		(74.9)	(52.2)	(28.3)	(51.8)
		[74.0]	[54.9]	[45.8]	[58.2]
	C-β	87	66	35	62.9
		(69.2)	(52.0)	(14.8)	(45.3)
		[75.5]	[62.5]	[34.3]	[57.4]

[a] Values with no brackets are experimental results taken from Ref. 16, those in parentheses are theoretical values taken from Ref. 1 and those in square brackets are values calculated in this work including HB effects.

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