^{14}N Nuclear Quadrupole Coupling in Glycyl-Glycine and Related Peptides

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An ab initio calculation of double zeta quality on glycyl-glycine at the crystal structure yielded nuclear quadrupole coupling constants at the peptide centres very close to experiment; $\chi_{zz} - 3.03$, $\chi_{yy} + 2.14$, $\chi_{xx} + 0.89$ MHz. The first two couplings lie in the local π-direction, and along the C−N bond, respectively. At the $NH_3^{\oplus}$ centre the values were less satisfactory, but the (low) positive value of χ_{zz} was obtained, and lies relatively close to the N−C bond. The results suggest that similar calculations may be successful for other H-bonded systems, provided that aromatic systems are not involved.

Introduction

Recently we have shown that ^{14}N nuclear quadrupole coupling constants (NQCC) observed in the microwave spectra of various azoles and azines, hydrazines etc. [1, 2] can be almost quantitatively obtained from *ab initio* SCF calculations of double zeta (DZ) quality. In many instances the NQCC from the condensed phase by nuclear quadrupole resonance show substantial changes from the free molecule [1, 2]; however, we found that groups of 3 or 4 azole molecules, at the crystal orientation, allowed a good account of the variations in NQCC between the two phases [3, 4]. Recent work with a number of azoles shows the generality of that approach [5]. The biologically important α-amino-acids (**1**) normally exist in the solid and other states as the corresponding zwitterion (**2**); the lack of volatility associated with this structure accounts for the absence of gas phase NQCC data, but there is a considerable amount of polycrystalline NQR data, especially under double resonance (NQDR) conditions [6]. Normally both NQR and NQDR do not yield the tensor sign, but only give the principal axis magnitudes. Single crystal NMR studies, using cross-polarisation and magic angle spinning (CP-MAS), of the adjacent ^{13}C nucleus show splitting (or broadening) arising from the ^{14}N quadrupolar interaction [7]. The asymmetry of the observed splitting can be related to the sign of the NQCC in these zwitterions [8–10].

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$NH_2-CHR-CO_2H$ **1** $\overset{\oplus}{N}H_3-CHR-CO_2^{\ominus}$ **2**

$N(\overset{\oplus}{1})H_3-CH_2-CO-N(2)H-CH_2-CO_2^{\ominus}$

3

$N(\overset{\oplus}{1})H_3-CH_2-CO-N(2)H-CH_2-CO-N(3)H-CH_2-CO_2^{\ominus}$

4

Combination of the NQDR/CP-MAS results for glycine (1) (R = H) (GLY), alanine (R = Me) (ALA and serine (R = CH_2OH) (SER) shows that the largest principal axis (PA) value is relatively small (ca. 1.2 MHz) and *positive* [6, 8–10]. The dipeptides, glycyl-glycine (GLY-GLY) (**3**) and glycyl-alanine (GLY-ALA), have a similar small value (1.24 and 1.28 MHz) attributed to the NH_3^+ group, and a larger value (3.03 and 3.25 MHz with $\eta = 0.40$ in both cases) attributable to the peptide bond nitrogen (CO−NH−CHR) [6]. The single study of a tripeptide GLY-GLY-GLY (**4**) [11] shows that two values are very similar to the $NH_3^{\oplus}$ and peptide groups above and hence are N(1) and N(2). Comparison with poly-glycine (3.097 MHz), $\eta = 0.76$), which shows a single NQCC [12], which must come from the back-bone N atoms, can be used to assign the central peptide N(2) of GLY-GLY-GLY.

The variations in these NQCC and asymmetry parameters call for theoretical interpretation, to obtain the directions, signs and magnitudes of all the principal axis components of the tensor.

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In the present paper we are concerned with the dipeptide GLY-GLY; the x-ray [13, 14] and neutron diffraction studies [15, 16] show that the molecules adopt a layer-like structure, with individual molecules having an "extended-W" type of conformation. The N/C/O skeleton is thus close to planar [13]. A single molecule (centre, C, Fig. 1) has 4 neighbours in the layer (left, L; right, R; top, T; bottom, B), with two further molecules in adjacent layers (up U, and down D). Each H atom of the $NH_3^{\oplus}$ group is H-bonded (at a distance of 2.72 Å) to a different $CO_2^{\ominus}$ group, and the O atoms of the latter to two different $NH_3^{\oplus}$ groups. The only other H-bonds are from the −NH− (molecule C) to adjacent −CO− (molecule T), but at a rather longer distance 2.97 Å (N … O).

It was clearly impracticable for GLY-GLY to consider a complete environmental set of molecules, such as we had done for imidazole [3]. Since each H of the $NH_3^{\oplus}$ group was H-bonded relatively similarly to oxygen, this was taken as a common factor, which would have a relatively small effect upon the NQCC at the corresponding N(1) atom (see below). Similarly, the longer (NH…O−C) distance, relative

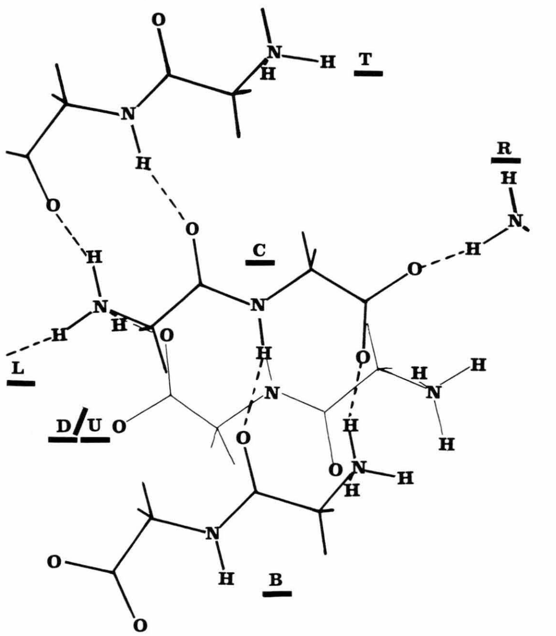


Fig. 1a. Portion of the GLY-GLY crystal structure; molecules in the same plane (C, T, B, R) in heavy lines; molecules above or below (U, D) in light lines. H-bonded centres are dotted.

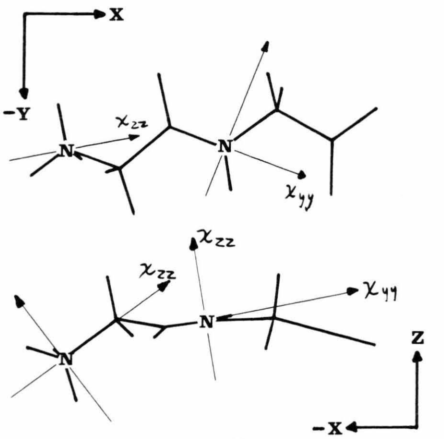


Fig. 1b. Principal axis [14]N NQCC in *xz* and *xy*-planes.

to (N … N) in imidazole (2.86 Å), and the absence of genuine resonance possibilities in the GLY-GLY case, was succient to justify the study of the single GLY-GLY molecule. We used the Dunning double zeta contraction [4s 2p] [17] of the Huzinaga (9s 5p) basis [18], leading to a total of 106 basis functions. The calculation was carried out on a CRAY-1s computer using the Atmol-3 suite of programs; integrals evaluation took approximately 40 minutes, SCF 6 minutes and electric field gradients for the NQCC 1 minute.

Results

(i) *The principal energy and population analysis results* are given in Table 1. The virial theorem results shows the adequate character of the basis set (theoretical value −2.0°). The total atomic populations reflect the usual electronegativity relationships O > N > C > H, and the group charges are more informative; thus the classical zwitterionic character of the molecule is largely adhered to. Within the groups, the large positive character of NH_3, and lesser values on CH_2, obscure the fact that the H-atoms are the major source of positive charge (although in the crystal some further intermolecular charge transfer can be expected), with the heavy atoms being negative in all cases except C in the CO/CO_2 groups. The C=O groups are highly polar (± 0.4 e).

(ii) *Nuclear Quadrupole Coupling Constants.* The computed electric field gradients and derived [1]

Table 1. Glycyl-glycine total energy and atomic populations.

Total energy − 489.38039 a.u. Virial theorem − 1.99934

Atomic populations

	C1(β)	C2(O)	C3(α)	C4(O_2)	N(1)	N(2)	
s	3.2894	3.0117	3.2398	2.9786	3.5650	3.5557	
p	2.9189	2.5849	2.8707	2.6722	3.9753	3.9778	
Total	6.2083	5.5966	6.1105	5.6508	7.5403	7.5315	
	01	02	03	3H(N)	2H(C)	H(N)	2H(C)
s	3.8320	3.8164	3.8183	1.8505	1.5218	0.6856	1.6304
p	4.6476	4.8131	4.7464	–	–	–	–
Total	8.4795	8.6295	8.5647	1.8505	1.5218	0.6856	1.6304

Group charges

NH_3(1)	CH_2(β)	CO(1)	NH(2)	CH_2(α)	CO_2(2, 3)
+ 0.6180	+ 0.2699	− 0.0761	− 0.2171	+ 0.2591	− 0.8450

Table 2. Principal axis electric field gradients and ^{14}N NQCC.

Centre	N(H_3)	N(H)
Field gradient ($10^{16} \times$ ESU cm^{-3})		
$\langle z^2 \rangle$	− 0.0316	0.2699
$\langle y^2 \rangle$	0.0255	− 0.1862
$\langle x^2 \rangle$	0.0061	− 0.0837
^{14}N NQCC (MH$_2$) calculated		
$\langle z^2 \rangle$	+ 0.344	− 2.935
$\langle y^2 \rangle$	− 0.277	2.025
$\langle x^2 \rangle$	− 0.066	0.910
η	0.614	0.380
^{14}N NQCC (MHz) observed (ref. [11])		
χ_{zz}	$\pm$1.218	$\mp$3.030
χ_{yy}	$\mp$0.864	$\pm$2.139
χ_{xx}	$\mp$0.354	$\pm$0.891
η	0.418	0.412

NQCC for ^{14}N and ^{2}H are given in Table 2. The numerical agreement between the magnitudes calculated and the observed values [11] for the −NH− group is excellent. The sign of the experimental principal value ($e^2 Q q_{zz} \equiv \chi_{zz}$) can be safely concluded as negative, i.e. χ_{zz} is −3.030 MHz. The principal value χ_{zz} at the peptide bond is locally π-in type, i.e. normal to the local (O)CNH plane. The direction of χ_{yy} is almost superimposed upon the C(O)−N(H) bond direction, with χ_{xx} about 30° away from the N−H bond. McDowell et al. [10], who attempted a fit with 6-different choices of principal axes for the peptide bond framework to the CP-MAS data, arrived at a similar result, except that χ_{xx} for GLY-GLY was fixed along the N−H bond. These results amply justify the Townes and Dailey analysis for simple amides R−CONH$_2$ in which the choice of axes were: χ_{zz} locally out-of-plane, with χ_{yy} along the C−N bond [19]. It thus appears that the sign, magnitude and direction of χ_{zz} at the GLY-GLY peptide bonds is similar to that of urea and thiourea [19]. This may prove to be generally true for peptides.

Whilst the present calculations correctly predict that the NQCC at NH_3^+ are much lower than at −NH−, the overall magnitudes are smaller than the experimental ones by 0.3 to 0.9 MHz. This probably arises from the additional polarity of the NH_3^+ portion, and the interaction with adjacent carboxylate anions in the crystal. None-the-less the general conclusions at this centre, smaller magnitudes and χ_{zz} positive, are consistent with the observations [8−10] at simple mono-amino acids. The direction pf χ_{zz}, virtually identical to the N(H_3)−C(H_2) bond, in the xz-projection (Fig. 2) but distorted towards CO in the yz-projection, is con-

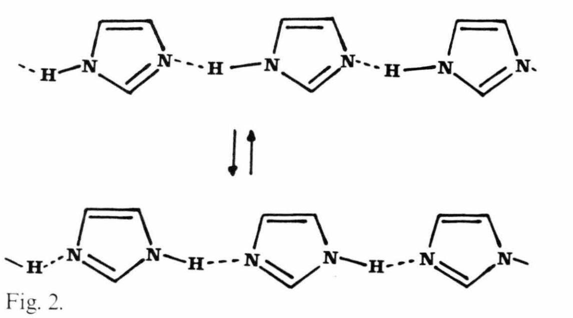


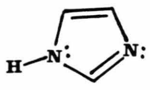
Fig. 2.

sistent with that derived for L-alanine (ALA) from the CP-MAS results [9]. The H-bonding to adjacent carboxylate is very similar to that in GLY-GLY. In both systems, although the H-bonding to non-equivalent carboxylate anions is unsymmetrical, the NQCC is more dominated by the local −O … H− systems, and hence is relatively close to C_{3v} (χ_{xx} and χ_{yy} differ by 0.5 MHz, and would be equal under C_{3v}).

Conclusions

The present work on GLY-GLY suggests that DZ calculations of NQCC may yield satisfactory explanations of variations in magnitude of NQR data in H-bonded systems where no resonance type interactions are occurring. Thus it may prove feasible to obtain the signs and directions of the tensor more easily by this method, than experimentally with single crystals.

The critical difference between the present type of H-bonding and our previous work on azoles is shown in Figure 1a. Although H-bonding occurs, it is relatively weak compared with full proton transfer. In contrast, the aromatic azole system, as in imidazole, allows a much higher level of delocalisation of charge (Figure 2). Thus a higher degree of "bond switching" can occur. An increased con-



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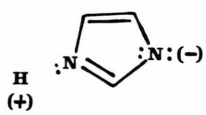

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tribution of the canonical form **6** relative to the non-ionic species **5**, occurs in the solid state. The −NQCC's at N(1) and N(3) in free imidazole are − 2.59 and + 2.29 MHz, respectively. In the solid state the molecule shows unsymmetrical H-bonds, with NN length 1.81 Å and NHN angle near 173° (neutron diffraction) [20]; the corresponding π-NQCC's are − 1.39 (N(1)) and + 1.47 MHz (N(3)), respectively; this shows the numerical decrease expected from a partial averaging of the two NQCC. Similar effects occur in the lone pair and radial NQCC [3].

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