^{79,81}Br-, ^{127}I-NQR, and Crystal Structure of Glycyl-l-alanine Hydrobromide Monohydrate and Hydroiodide Monohydrate

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The crystal structures of glycyl-l-alanine hydrobromide monohydrate, **1**, and glycyl-l-alanine hydroiodide monohydrate, **2**, were determined and the temperature dependence of the ^{127}I NQR frequencies was investigated in the temperature range $77 \leqq T/\mathrm{K} \leqq 370$. The ^{127}I NQR frequencies are strongly influenced by hydrogen bonds and this is proved by the frequency shift of the H ⇆ D exchange. By deuteration the nuclear quadrupole coupling constant $e^2qQh^{-1}(^{127}\mathrm{I})$ of **2** is shifted downwards 2.72 MHz at room temperature.

The title compounds are isotype, and at room temperature they crystallize monoclinic with the space group C_2^2–$P2_1$, with two molecules in the unit cell. The lattice constants for **1** are $a = 1068.7$ pm, $b = 614.1$ pm, $c = 762.0$ pm, and $\beta = 108.55°$ and for **2** are $a = 1093.3$ pm, $b = 637.1$ pm, $c = 770.9$ pm, and $\beta = 107.29°$.

Introduction

Hydrogen bonds play a crucial role in intra- and intermolecular interactions of peptides. A simple model for the study of such interactions is the hydrogen bond in the hydrohalides of amino acids and low molecular weight peptides. It turns out that ^{79,81}Br and ^{127}I nuclear quadrupole resonance, NQR, is quite sensitive to the hydrogen bond in such compounds as it is in case of simple ammonium salts $R-NH_3^+X^-$, R = phenyl or substituted phenyl and X = Br, I [1–7].

It was observed that the ^{79}Br NQR frequencies of crystalline amino acid hydrobromides are found in the range $12 < \nu(^{79}\mathrm{Br})/\mathrm{MHz} < 18.5$ as long as there are only hydrogen bonds $N-H\cdots Br^-$ present. Additional hydrogen bonds $O-H\cdots Br^-$ shift the ^{79}Br NQR frequencies to the range $24.8 < \nu(^{79}\mathrm{Br})/\mathrm{MHz} < 27$ [8, 9]. This frequency shift is found, of course, for the ^{81}Br NQR, too (in the frequency band given by the ratio $Q(^{79}\mathrm{Br})/Q(^{81}\mathrm{Br}) = 1.1971$). Iodine is an $I = 5/2$ nucleus, and therefore two transitions, $m = \pm 1/2 \leftrightarrows m = \pm 3/2$ and $m = \pm 3/2 \leftrightarrows m = \pm 5/2$ occur, from which the nuclear quadrupole coupling constant (NQCC) e^2qQh^{-1} (e = unit charge, $eq = \Phi_{zz}$ main principal axis of the electric field gradient tensor ($\Phi_{xx}, \Phi_{yy}, \Phi_{zz}$), eQ = nuclear electric quadrupole moment, h = Planck's constant) and the asymmetry parameter $\eta = |\Phi_{xx} - \Phi_{yy}|/|\Phi_{zz}|$ ($|\Phi_{xx}| \leqq |\Phi_{yy}| \leqq |\Phi_{zz}|$) are available. If NQCC of ^{127}I of the crystalline amino acid hydroiodides at room temperature is found in the range $70 < e^2qQh^{-1}(^{127}\mathrm{I})/\mathrm{MHz} < 125$, $N-H\cdots I^-$ hydrogen bonds only are present in the crystal [9].

In the following we report on ^{127}I NQR results and on the crystal structure of glycyl-l-alanine hydrobromide monohydrate, **1**, glycyl-l-alanine hydroiodide monohydrate, **2**. In Fig. 1 the molecular structure and the atomic assignment of **1** and **2** are shown.

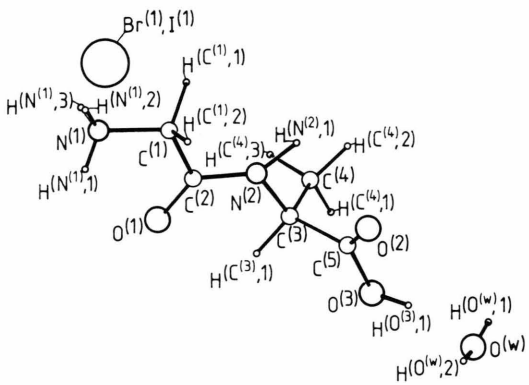

Fig. 1. The structure formula and the numbering of the atoms of Gly-l-Ala · HX · H_2O (X = Br, I).

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Table 1. Characterization of the compounds investigated.

No.	Substance[a]	T_m/K	Habitus; Colour	Chemical analysis (in weight%)							
				C		N		H		X[d]	
				calc.	found	calc.	found	calc.	found	calc.	found
1	Gly-l-Ala · HBr · H_2O	396[c]	six sided plates; colourless	24.50	24.21	11.43	11.31	5.35	5.33	32.61	32.59
2	Gly-l-Ala · HI · H_2O	387	six sided plates; colourless	20.56	20.43	9.59	9.49	4.35	4.49	43.45	43.68

[a] Gly-l-Ala · HBr · H_2O[b]: Glycyl-l-alanine hydrobromide monohydrate, $NH_2-CH_2-CO-NH-CH(CH_3)-COOH \cdot HBr \cdot H_2O$, $(ND_2-CH_2-CO-ND-CH(CH_3)-COOD \cdot DBr \cdot D_2O)$;
Gly-l-Ala · HI · H_2O[b]: Glycyl-l-alanine hydroiodide monohydrate, $NH_2-CH_2-CO-NH-CH(CH_3)-COOH \cdot HI \cdot H_2O$, $(ND_2-CH_2-CO-ND-CH(CH_3)-COOD \cdot DI \cdot D_2O)$.

[b] In parentheses: Deuterated compound, gained by dissolution of the protonated compound in D_2O and evaporating of D_2O in vacuum; several cycles. – [c] Decomposition temperature. – [d] $X = Br^-, I^-$.

Table 2. Experimental conditions for the structure determination and crystal structure data of glycyl-l-alanine hydrobromide monohydrate and glycyl-l-alanine hydroiodide monohydrate[a]. In this table, as in the following ones, the error is written in parentheses.

	Gly-l-Ala · HBr · H_2O	Gly-l-Ala · HI · H_2O
Formula	$C_5H_{10}N_2O_3 \cdot HBr \cdot H_2O$	$C_5H_{10}N_2O_3 \cdot HI \cdot H_2O$
Crystal habitus, size	six sided prism, $(0.2 \cdot 0.5 \cdot 1.0)$ mm^3	elliptic plate, $(0.16 \cdot 0.5 \cdot 0.7)$ mm^3
Diffractometer	Stoe-Stadi 4	Stoe-Stadi 4
Wavelength/pm (Mo-Kα)	71.069	71.069
Monochromator	Graphite (002)	Graphite (002)
T/K	300	299
Absorption coefficient/m^{-1}	4290	3090
Scan	$\omega/2\Theta$	$\omega/2\Theta$
$(\sin\Theta/\lambda)_{max}$/pm^{-1}	0.007367	0.007367
Number of reflexions measured	5202	3746
Symmetry independent reflexions	2634	2956
Reflexions considered	2608	2938
Number of free parameters	140	140
$R(F)$	0.0302	0.0216
$R_w(F)$	0.0289	0.0229
Point position	all atoms in 2a $x, y, z; \bar{x}, 1/2+y, \bar{z}$	all atoms in 2a $\bar{x}, y, z; x, 1/2+y, \bar{z}$
Lattice constants		
a/pm	1068.7 (3)	1093.3 (3)
b/pm	614.1 (2)	637.1 (2)
c/pm	762.0 (2)	770.9 (2)
β/°	108.55 (1)	107.29 (1)
Volume of the unit cell $V \cdot 10^{-6}$/pm^3	474.10	512.66
Space group	$C_2^2-P2_1$	$C_2^2-P2_1$
Formula units per unit cell	2	2
ϱ_{calc}/Mg · m^{-3}	1.716 ($T = 300$ K)	1.892 ($T = 299$ K)
ϱ_{pykn}/Mg · m^{-3}	1.73 ($T = 296$ K)	1.90 ($T = 296$ K)

[a] The structure formula with the numbering of the atoms is shown in Figure 1.

Experimental

1 and **2** were synthesized from benzyloxycarbonyl-glycyl-l-alanine methyl ester, which in turn was synthesized from benzyloxycarbonyl-glycine and alanine methyl ester hydrochloride by the mixed anhydride method [10, 11]. The hydrolysis of benzyloxycarbonyl-glycyl-l-alanine methyl ester with an excess of 48% HBr or 57% HI at 300–310 K and evaporation to dryness gave **1** or **2**, respectively, in high yield (95–99%). The white, crystalline products were recrystallized from water. In Table 1 the results of the chemical analysis (C, H, N, X), colour, habitus, and melting temperature are listed.

The crystal structures of **1** and **2** were determined by single crystal techniques at room temperature, using MoKα radiation. The experimental conditions are listed in Table 2 together with the crystallographic data.

The ^{79}Br and ^{127}I NQR spectra were measured via a superregenerative oscillator type spectrometer. The temperature of the sample under investigation was controlled by thermostates with oil ($300 \leqq T/K \leqq 420$), and methanol ($195 \leqq T/K \leqq 300$), respectively, as coolants, and by a temperature regulated stream of nitrogen gas ($120 \leqq T/K \leqq 200$). To achieve $T = 77$ K, the sample was immersed in liquid nitrogen. The measurement of the temperature at the sample site was accurate to ± 0.5 K. The accuracy of the measured NQR frequencies is ± 5 kHz.

Results

Crystal Structure

From the X-ray diffraction intensity data, the systematic extinctions, and the calculations of Patterson

Table 3. Positional and thermal parameters of glycyl-l-alanine hydrobromide monohydrate. The temperature factor is of the form

$$T=\exp\{-2\pi^2(U_{11}h^2a^{*2}+U_{22}k^2b^{*2}+U_{33}l^2c^{*2}+2U_{12}hka^*b^*+2U_{13}hla^*c^*+2U_{23}klb^*c^*)\}.$$

The U_{ij} are given in pm^2; U is the isotropic mean for the hydrogen atoms.

Atom [a]	x/a	y/b	z/c	U_{11}, U	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
$Br^{(1)}$	0.9734(0)	0.5000(0)	0.1857(0)	343(1)	285(1)	370(1)	23(1)	95(1)	28(2)
$C^{(1)}$	0.8432(2)	0.9999(8)	0.2995(3)	370(11)	320(12)	260(10)	−118(18)	108(8)	−40(20)
$C^{(2)}$	0.7425(2)	0.8358(4)	0.3224(4)	255(10)	232(12)	276(12)	10(9)	93(9)	−24(10)
$C^{(3)}$	0.6653(3)	0.6442(5)	0.5486(4)	339(13)	318(15)	283(13)	− 86(11)	99(11)	−19(11)
$C^{(4)}$	0.7391(4)	0.4400(6)	0.6400(6)	687(24)	333(21)	627(24)	57(14)	319(20)	44(15)
$C^{(5)}$	0.6036(3)	0.7561(5)	0.6780(4)	292(12)	324(14)	248(12)	− 36(10)	66(9)	42(11)
$N^{(1)}$	0.8415(2)	1.0013(7)	0.1062(3)	342(9)	339(11)	296(9)	− 60(16)	131(8)	− 5(17)
$N^{(2)}$	0.7523(2)	0.7926(5)	0.4963(3)	310(11)	396(15)	238(11)	−117(10)	69(9)	−30(10)
$O^{(1)}$	0.6587(2)	0.7576(4)	0.1853(3)	281 (8)	371(11)	286(10)	− 40(8)	38(7)	−24(9)
$O^{(2)}$	0.6399(2)	0.9295(4)	0.7516(3)	436(11)	342(12)	393(12)	− 66(8)	143(10)	−36(9)
$O^{(3)}$	0.5070 (3)	0.6395(5)	0.7025(4)	449(12)	473(15)	553(15)	−153(11)	282(11)	−54(12)
$O^{(w)}$	0.3955(3)	0.8104(5)	0.9339(4)	362(14)	392(11)	441(13)	30(10)	84(10)	14(11)
$H^{(C^{(3)},\,1)}$	0.5881(3)	0.5955(5)	0.4245(4)	600					
$H^{(C^{(1)},\,1)}$	0.9404(2)	0.9550(8)	0.3884(3)	600					
$H^{(C^{(1)},\,2)}$	0.8187(2)	1.1602(8)	0.3370(3)	600					
$H^{(C^{(4)},\,1)}$	0.6674(4)	0.3263(6)	0.6592(6)	600					
$H^{(C^{(4)},\,2)}$	0.8114(4)	0.4758(6)	0.7724(6)	600					
$H^{(C^{(4)},\,3)}$	0.7876(4)	0.3694(6)	0.5491(6)	600					
$H^{(N^{(1)},\,1)}$	0.7653(34)	1.0424(68)	0.0302(49)	365(95)					
$H^{(N^{(1)},\,2)}$	0.9025(61)	0.9011(122)	0.0699(92)	1035(232)					
$H^{(N^{(1)},\,3)}$	0.8786(40)	1.1193(71)	0.0911(59)	297(90)					
$H^{(N^{(2)},\,1)}$	0.8021(38)	0.8539(73)	0.5728(56)	425(110)					
$H^{(O^{(3)},\,1)}$	0.4789(52)	0.6989(103)	0.7949(71)	743(157)					
$H^{(O^{(w)},\,1)}$	0.4669(61)	0.8429(110)	1.0153(94)	865(193)					
$H^{(O^{(w)},\,2)}$	0.3671(54)	0.9151(102)	0.8920(80)	805(204)					

[a] For the numbering, see Figure 1.

Table 4. Positional and thermal parameters of glycyl-l-alanine hydroiodide monohydrate. The temperature factor is of the form

$$T=\exp\{-2\pi^2(U_{11}h^2a^{*2}+U_{22}k^2b^{*2}+U_{33}l^2c^{*2}+2U_{12}hka^*b^*+2U_{13}hla^*c^*+2U_{23}klb^*c^*)\}.$$

The U_{ij} are given in pm^2; U is the isotropic mean for the hydrogen atoms.

Atom [a]	x/a	y/b	z/c	U_{11}, U	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
$I^{(1)}$	0.9715(0)	0.5000(0)	0.1954(0)	369(1)	311(1)	390(1)	34(1)	116(1)	28(1)
$C^{(1)}$	0.8235(2)	0.9974(9)	0.2873(4)	408(11)	353(11)	283(12)	−100(21)	118(10)	−13(24)
$C^{(2)}$	0.7284(2)	0.8346(5)	0.3139(4)	270(10)	310(12)	275(14)	37(9)	101(10)	− 8(11)
$C^{(3)}$	0.6564(3)	0.6472(5)	0.5416(4)	399(14)	364(14)	255(14)	− 99(11)	92(12)	− 4(12)
$C^{(4)}$	0.7294(5)	0.4502(6)	0.6273(7)	797(27)	403(23)	626(28)	68(16)	357(23)	67(17)
$C^{(5)}$	0.5993(3)	0.7556(5)	0.6750(5)	295(11)	359(14)	295(14)	− 34(10)	77(11)	46(12)
$N^{(1)}$	0.8228(2)	1.0016(8)	0.0971(3)	393(10)	382(10)	306(11)	− 73(19)	138(9)	− 6(21)
$N^{(2)}$	0.7394(2)	0.7925(5)	0.4846(4)	339(11)	466(14)	252(13)	−126(10)	61(10)	− 4(11)
$O^{(1)}$	0.6470(2)	0.7590(4)	0.1815(3)	306(9)	427(11)	270(11)	− 45(8)	54(8)	−31(10)
$O^{(2)}$	0.6367(2)	0.9217(4)	0.7474(4)	485(12)	396(11)	419(14)	− 78(9)	181(11)	−48(10)
$O^{(3)}$	0.5054(3)	0.6452(5)	0.7029(5)	527(13)	545(16)	639(20)	−188(13)	349(14)	−51(15)
$O^{(w)}$	0.3998(2)	0.8172(5)	0.9381(4)	399(12)	448(14)	475(17)	38(10)	91(12)	17(12)
$H^{(C^{(3)},\,1)}$	0.5802(3)	0.5990(5)	0.4235(4)	600					
$H^{(C^{(1)},\,1)}$	0.9184(2)	0.9579(9)	0.3724(4)	600					
$H^{(C^{(1)},\,2)}$	0.7970(2)	1.1503(9)	0.3249(4)	600					
$H^{(C^{(4)},\,1)}$	0.6531(5)	0.3516(6)	0.6431(7)	600					
$H^{(C^{(4)},\,2)}$	0.7996(5)	0.4735(6)	0.7580(7)	600					
$H^{(C^{(4)},\,3)}$	0.7743(5)	0.3756(6)	0.5361(7)	600					
$H^{(N^{(1)},\,1)}$	0.7630(39)	1.0580(67)	0.0309(60)	459(125)					
$H^{(N^{(1)},\,2)}$	0.8552(54)	0.8785(107)	0.0610(84)	670(180)					
$H^{(N^{(1)},\,3)}$	0.8686(42)	1.1178(77)	0.0952(63)	332(104)					
$H^{(N^{(2)},\,1)}$	0.8060(43)	0.8498(79)	0.5805(69)	455(109)					
$H^{(O^{(3)},\,1)}$	0.4825(52)	0.7227(96)	0.7733(75)	642(157)					
$H^{(O^{(w)},\,1)}$	0.4931(59)	0.8129(108)	1.0424(85)	857(179)					
$H^{(O^{(w)},\,2)}$	0.3840(52)	0.9198(90)	0.9139(84)	780(211)					

[a] For the numbering, see Figure 1.

Table 5. Bond length and bond angles of glycyl-l-alanine hydrobromide monohydrate and glycyl-l-alanine hydroiodide monohydrate; $X = Br^-, I^-$.

Atoms	Gly-l-Ala $\cdot HBr \cdot H_2O$ length/pm	Gly-l-Ala $\cdot HI \cdot H_2O$ length/pm
$N^{(1)}-C^{(1)}$	146.7 (3)	146.4 (3)
$C^{(1)}-C^{(2)}$	152.4 (4)	152.5 (5)
$C^{(2)}-O^{(1)}$	123.6 (3)	123.5 (3)
$C^{(2)}-N^{(2)}$	132.3 (3)	131.3 (4)
$N^{(2)}-C^{(3)}$	144.6 (3)	145.3 (4)
$C^{(3)}-C^{(4)}$	152.6 (5)	152.8 (5)
$C^{(3)}-C^{(5)}$	151.4 (4)	151.8 (5)
$C^{(5)}-O^{(2)}$	120.8 (4)	121.0 (4)
$C^{(5)}-O^{(3)}$	131.7 (3)	131.4 (4)
$X^{(1)} \cdots N^{(1)}$	334.5	354.5
$X^{(1)} \cdots N'^{(1)}$	336.0	356.3
$X^{(1)} \cdots N'^{(2)}$	340.1	363.2
$O'^{(2)} \cdots N^{(1)}$	290.4	289.9
$O^{(1)} \cdots O^{(w)}$	287.4	281.9
$O'^{(1)} \cdots O^{(w)}$	289.2	295.9
$O^{(w)} \cdots O^{(3)}$	264.0	265.8
	angle/deg.	angle/deg.
$N^{(1)}-C^{(1)}-C^{(2)}$	109.5 (0.3)	110.2 (0.3)
$C^{(1)}-C^{(2)}-N^{(2)}$	114.4 (0.2)	114.3 (0.2)
$C^{(1)}-C^{(2)}-O^{(1)}$	120.6 (0.2)	120.4 (0.3)
$O^{(1)}-C^{(2)}-N^{(2)}$	125.0 (0.2)	125.3 (0.3)
$C^{(2)}-N^{(2)}-C^{(3)}$	123.4 (0.2)	123.6 (0.3)
$N^{(2)}-C^{(3)}-C^{(4)}$	111.1 (0.3)	111.1 (0.3)
$N^{(2)}-C^{(3)}-C^{(5)}$	110.1 (0.2)	109.6 (0.3)
$C^{(4)}-C^{(3)}-C^{(5)}$	110.1 (0.3)	110.4 (0.3)
$C^{(3)}-C^{(5)}-O^{(2)}$	124.1 (0.2)	124.0 (0.3)
$C^{(3)}-C^{(5)}-O^{(3)}$	111.6 (0.3)	111.5 (0.3)
$O^{(2)}-C^{(5)}-O^{(3)}$	124.3 (0.3)	124.5 (0.3)
$H^{(O^{(w)},1)}-O^{(w)}-H^{(O^{(w)},2)}$	105.3 (6.1)	109.1 (6.0)
$H^{(O^{(3)},1)}-O^{(3)}-C^{(5)}$	110.7 (3.7)	101.0 (4.0)

Table 6. Scheme of the hydrogen bonds of glycyl-l-alanine hydrobromide monohydrate and glycyl-l-alanine hydroiodide monohydrate.

	Gly-l-Ala $\cdot HBr \cdot H_2O$ length/pm	Gly-l-Ala $\cdot HI \cdot H_2O$ length/pm
$H^{(N^{(1)},2)} \cdots Br^{I}, I^{I}$	264.5	277.9
$H^{(N^{(1)},3)} \cdots Br^{II}, I^{II}$	255.9	269.7
$H^{(N^{(2)},1)} \cdots Br^{III}, I^{III}$	267.2	270.6
$H^{(N^{(1)},1)} \cdots O'^{(2)\,IV}$	223.0	237.6
$H^{(O^{(w)},1)} \cdots O^{(1)\,V}$	211.2	174.0
$H^{(O^{(w)},2)} \cdots O'^{(1)\,VI}$	217.8	227.6
$H^{(O^{(3)},1)} \cdots O^{(w)\,VII}$	172.8	186.5
Symmetry code		
Br^{I}, I^{I}	x y	z
Br^{II}, I^{II}	x $y+1$	z
Br^{III}, I^{III}	$-x+2$ $y+1/2$	$-z+1$
$O'^{(2)\,IV}$	x y	$z-1$
$O^{(1)\,V}$	x y	$z+1$
$O'^{(1)\,VI}$	$-x+1$ $y+1/2$	$-z+1$
$O^{(w)\,VII}$	x y	z
	angle/deg.	angle/deg.
$O^{(3)}-H \cdots O^{(w)}$	168.4	160.7
$O^{(1)} \cdots H^{(O^{(w)},1)}-O^{(w)}$	150.5	167.5
$O'^{(1)} \cdots H^{(O^{(w)},2)}-O^{(w)}$	163.1	172.7
$X^{(1)} \cdots H^{(N^{(2)},1)}-N^{(2)}$	163.6	167.2
$X^{(1)} \cdots H^{(N^{(1)},2)}-N^{(1)}$	128.7	142.0
$X'^{(1)} \cdots H^{(N^{(1)},3)}-N^{(1)}$	154.1	158.2
$O^{(2)} \cdots H^{(N^{(1)},1)}-N^{(1)}$	133.9	125.0

and Fourier maps, the space group $C_2^2-P2_1$ was found for both title compounds. The Patterson method (SHELX-86) was used to determine the heavy atom position, and from the Fourier synthesis all atoms could be located.

The structure parameters were refined by means of full matrix least squares method (SHELX-76). The positions of the hydrogen atoms, which are involved in the hydrogen bonds, were taken from difference Fourier maps, and they were refined by least squares cycles. In Table 2 the space group, lattice constants etc. of the two title compounds are listed together with further crystallographic data. Table 3 contains the positional and thermal parameters of **1**, whereas these parameters for **2** are given in Table 4. The reliability factors for **1** and **2** are 0.0302 and 0.0216, respectively. In Table 5 we list bond- and intermolecular distances and bond angles. Table 6 gives the hydrogen bond scheme and the symmetry code. Table 7 shows the values of the torsion angles of the peptide backbone. The notation followed in the description of the conformational parameters is that of the IUPAC-IUB Comission on Biochemical Nomenclature [12].

Bromine and Iodine NQR

The temperature dependence of the ^{79}Br NQR frequency of **1** was reported in [9]. In Fig. 2 the ^{127}I NQR frequencies of **2** are shown as functions of temperature. From the two frequencies ν_1 ($m = \pm 1/2 \leftrightarrows m = \pm 3/2$) and ν_2 ($m = \pm 3/2 \leftrightarrows m = \pm 5/2$), $e^2 q Q h^{-1}$ and η were calculated, using the method given in [13]. In Fig. 3 the NQCC and the asymmetry parameter η are plotted as functions of temperature. In Table 8 the ^{79}Br and ^{127}I NQR frequencies of **1** and **2** are listed for $T = 77$ K and $T \approx 273$ K. This table contains also the ^{79}Br and ^{127}I NQR frequencies for the deuterated compounds Gly-l-Ala $\cdot$ DBr $\cdot$ D_2O and

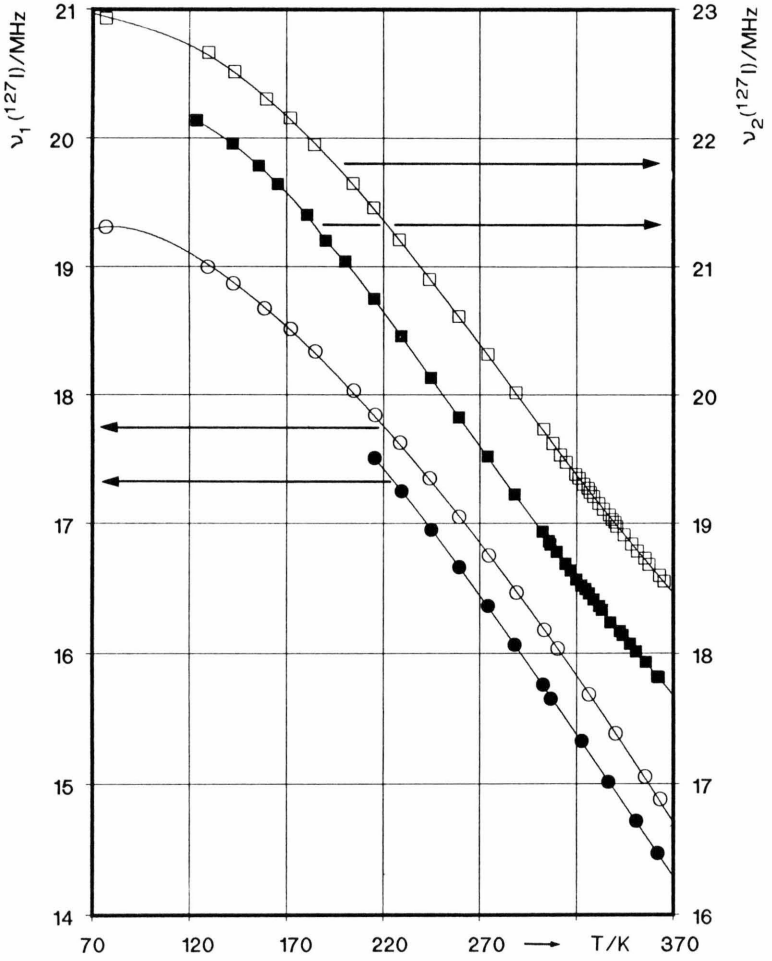

Fig. 2. ^{127}I NQR frequencies of glycyl-l-alanine hydroiodide monohydrate as functions of temperature.
○ $\nu_1(m=\pm1/2 \leftrightarrows m=\pm3/2)$ Gly-l-Ala · HI · H_2O;
● $\nu_1(m=\pm1/2 \leftrightarrows m=\pm3/2)$ Gly-l-Ala · DI · D_2O;
□ $\nu_2(m=\pm3/2 \leftrightarrows m=\pm5/2)$ Gly-l-Ala · HI · H_2O;
■ $\nu_2(m=\pm3/2 \leftrightarrows m=\pm5/2)$ Gly-l-Ala · DI · D_2O.

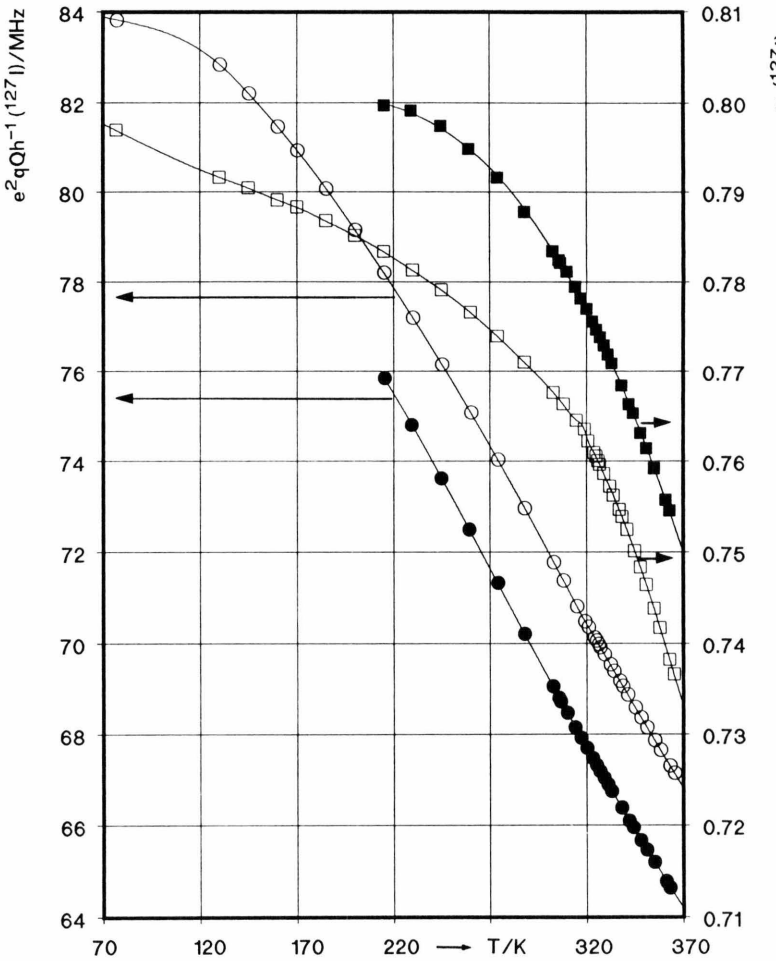

Fig. 3. $e^2qQh^{-1}(^{127}I)$ and $\eta(^{127}I)$ of glycyl-l-alanine hydroiodide monohydrate as functions of temperature.
○ e^2qQh^{-1} of Gly-l-Ala · HI · H_2O;
● e^2qQh^{-1} of Gly-l-Ala · DI · D_2O;
□ η of Gly-l-Ala · HI · H_2O;
■ η of Gly-l-Ala · DI · D_2O.

Table 7. Torsion angles of the peptide backbone. The angles are defined in the following way [12]. Looking along the line atom 2 → atom 3, atom 1 is positionated at 0° in a 360° scale. In this projection, the angle between atom 1 and atom 4 is counted clockwise from 0° to 180°. If the angle in this way is larger than 180°, one counts anticlockwise with a minus sign. For example for ψ: Looking along $C^{(1)}-C^{(2)}$, $N^{(1)}$ is at zero degrees. $N^{(2)}$ is in the projection then at 168.41°, 168.13°, −173.95°, and −163.54° in Gly-l-Ala · HBr · H_2O, Gly-l-Ala · HI · H_2O, Gly-l-Ala · HCl, and Gly-l-Ala, respectively.

	Gly-l-Ala · HBr · H_2O	Gly-l-Ala · HI · H_2O	Gly-l-Ala-HCl [17]	Gly-l-Ala [18]
$\psi = N^{(1)}-C^{(1)}-C^{(2)}-N^{(2)}$	168.41	168.13	−173.95	−163.54
$\omega = C^{(1)}-C^{(2)}-N^{(2)}-C^{(3)}$	178.97	177.88	169.34	−173.94
$\varphi = C^{(2)}-N^{(2)}-C^{(3)}-C^{(5)}$	−126.03	−126.27	− 72.42	− 78.36
$\psi_1 = N^{(2)}-C^{(3)}-C^{(5)}-O^{(2)}$	− 11.92	− 12.94	− 0.98	− 35.88
$\psi_2 = N^{(2)}-C^{(3)}-C^{(5)}-O^{(3)}$	169.20	167.78	180.00	149.99

Table 8. The NQR frequencies of ^{79}Br in Gly-l-Ala · HBr · H_2O and of ^{127}I in Gly-l-Ala · HI · H_2O at $T \approx 273$ K and $T = 77$ K. $d\nu/dT$ is the temperature coefficient at $T = 273$ K.

No.	Substance	T/K	ν/MHz [a]	$\frac{d\nu}{dT}\frac{K}{kHz}$	S/N [b]	$\frac{(e^2qQh^{-1})}{MHz}$ [c]	η [d]	Lit.
1a	Gly-l-Ala · HBr · H_2O	273.7	13.735	14	90			[9]
		77	15.443					
1b	Gly-l-Ala · DBr · D_2O	273.8	13.322	14	25			[9]
		77	15.249					
2a	Gly-l-Ala · HI · H_2O							
	$m = \pm 3/2 \leftrightarrows m = \pm 1/2$	274.5	16.758	20	50	74.04	0.774	[e]
	$m = \pm 5/2 \leftrightarrows m = \pm 3/2$	274.2	20.311	20	70			
	$m = \pm 3/2 \leftrightarrows m = \pm 1/2$	77	19.312			83.82	0.797	
	$m = \pm 5/2 \leftrightarrows m = \pm 3/2$	77	22.927					
2b	Gly-l-Ala · DI · D_2O							
	$m = \pm 3/2 \leftrightarrows m = \pm 1/2$ [f]	273.9	16.371	21	8	71.34	0.792	[e]
	$m = \pm 5/2 \leftrightarrows m = \pm 3/2$	273.9	19.521	21	17			
	$m = \pm 5/2 \leftrightarrows m = \pm 3/2$	77	22.474					

[a] Mean deviation ±0.005. – [b] Signal to noise ratio by use of lock in, recorder and a time constant of 10 s.
[c] Mean deviation ±0.01. – [d] Mean deviation ±0.004. – [e] This paper.
[f] The transition $m = \pm 1/2 \leftrightarrows m = \pm 3/2$ was undetectable at $T = 77$ K.

Table 9. Power series expansion of $\nu_{1,2}(^{127}I) = f(T)$. $\nu_{1,2}(^{127}I) = a_0 + a_1 \cdot T + a_{-1} \cdot T^{-1} + a_2 \cdot T^2$.

No.	Substance	a_0/MHz	$a_1 \cdot 10^2$/MHz · K^{-1}	a_{-1}/MHz · K	$a_2 \cdot 10^5$/MHz · K^{-2}	$\overline{\Delta\nu}$/kHz [a]	m	ΔT/K
2a	Gly-l-Ala- · HI · H_2O							
	$m = \pm 3/2 \leftrightarrows m = \pm 1/2$	21.350	−1.040	− 87.172	−1.870	13.1	19	77–366
	$m = \pm 5/2 \leftrightarrows m = \pm 3/2$	25.802	−1.476	−128.178	−1.281	10.1	20	77–324
	$m = \pm 5/2 \leftrightarrows m = \pm 3/2$	13.966	0.566	1626.301	−1.447	5.9	18	321–366
2b	Gly-l-Ala · DI · D_2O							
	$m = \pm 3/2 \leftrightarrows m = \pm 1/2$	30.963	−4.873	−919.824	−2.814	8.0	12	215–363
	$m = \pm 5/2 \leftrightarrows m = \pm 3/2$	29.387	−3.576	−382.980	1.778	9.0	19	123–315
	$m = \pm 5/2 \leftrightarrows m = \pm 3/2$	23.865	−2.590	410.683	1.680	7.4	18	309–363

[a] Mean error $\overline{\Delta\nu} = \left(\frac{\sum(\nu_{mea} - \nu_{calc})^2}{m-n}\right)^{1/2}$; m = number of measurements $\nu = f(T)$; n = number of parameters in the power series.

Gly-l-Ala · DI · D_2O. Some values of the NQCC and η are listed, too. The curves $\nu_{1,2}(^{127}I) = f(T)$ can be described by a power series

$$\nu_{1,2}(^{127}I) = \sum_{i=-1}^{2} a_i \cdot T^i. \quad (1)$$

For the coefficients a_i see Table 9.

Discussion

Both peptide hydrohalides crystallize monoclinic with the space group C_2^2–$P2_1$, and so they are isomorphous with the homologous glycyl-l-alanine hydrochloride monohydrate [14]. The lattice constants of the hydrobromide are in good agreement with those reported by Tranter [14–16]. The observed intramolecular bond distances and bond angles of glycyl-l-alanine hydrobromide monohydrate, **1**, and glycyl-l-alanine hydroiodide monohydrate, **2**, are nearly the same as in glycyl-l-alanine hydrochloride [17] and glycyl-l-alanine [18], and there is no significant deviation from the normal value of bond lengths and bond angles among different atoms observed [19, 20].

The atoms $C^{(1)}$, $C^{(2)}$, $O^{(1)}$, $N^{(2)}$, and $C^{(3)}$ constitute the peptide group. The dimensions of the peptide group are in good agreement with the values reported by Benedetti [20] for a large number of peptides.

For peptides, the torsion angles are very important to rationalize the molecular conformation. In case of a dipeptide there are five torsion angles, one angle ψ with respect to the bond $C^{(1)}$–$C^{(2)}$, one angle ω with respect to the bond $C^{(2)}$–$N^{(2)}$, one angle φ with respect to the bond $N^{(2)}$–$C^{(3)}$, and two angles ψ_1 and ψ_2 with respect to the bond $C^{(3)}$–$C^{(5)}$.

The corresponding torsion angles of **1** and **2** are nearly the same. From Table 7 one finds, that the torsion angles besides φ are similar to that of Gly-l-Ala · HCl [17] and Gly-l-Ala [18]. For the N-terminal end of a peptide there is no angle φ and only one angle ψ, which can be both, positive or negative for a glycyl residue [12]. Because the peptide bonding in **1** and **2**, like in many other peptides, has trans-configuration, ω should have values near 180° [12] and this we find. Although the conformational angles φ and $\psi_{1,2}$ lie in the allowed region of the φ, ψ diagram for peptide configurations [12, 21, 22], the torsion angle φ has a different value like in other, chemically similar peptides [17, 18]. This seems to be due to the forming of the short hydrogen bond between the hydroxyl group of the carboacid group and the water molecule.

Figure 4 shows the unit cell of **1** projected along the *c*-axis. In this projection it is easy to see, that the peptide backbone $N^{(1)}$–$C^{(1)}$–$C^{(2)}$–$N^{(2)}$–$C^{(3)}$ is nearly planar. The carboacid group $C^{(5)}$–$O^{(2,3)}$ and the methyl group $C^{(4)}$–$H^{(C^{(4)},1,2,3)}$, of the alanyl group are oriented away from this pseudoplane. The torsion angles given in Table 7 show this qualitatively. The polar axis $2_1 \parallel \boldsymbol{b}$ is easily recognized in this projection, too. Assuming a partial electrical dipole direction along $C^{(4)}$–$C^{(3)}$–$C^{(5)}$, the dipoles point in the same direction, inclined by an angle of ~30° to the ***b***-axis. Another partial dipole is formed by the backbone $N^{(1)}$–$C^{(1)}$–$C^{(2)}$–$N^{(2)}$–$C^{(3)}$ again unidirectional and inclined by 45° against ***b*** (see Figure 4).

The peptide molecules (ions) build, together with H_2O, double layers parallel to the ac-plane as seen in Figure 5. Within each single layer the Gly-l-Ala molecules are antiparallel and they are involved by hydrogen bonds as are the double layers formed by such bonds. The halogen ions (Br^-, I^-) form layers parallel to the dipole, too, at $x = 0 \pm \delta$. Hydrogen bonds $N-H \cdots X^-$ connect the peptide double layers via the halogen atoms. In this way a threedimensional network of hydrogen bonds is formed in **1** and **2**.

Seven hydrogen atoms are present in the molecule Gly-l-Ala · H_2O, which can interact in hydrogen bonds and all of them do so, see Figure 5. The water molecule forms two hydrogen bonds with $O^{(1)}$ and $O^{(1')}$. A short hydrogen bond exists between the hydroxy group $O^{(3)}$–H of the carboacid group and the water molecule as hydrogen bond acceptor. The ion X (Br^-, I^-) is involved in three hydrogen bonds; two hydrogen bonds are formed by two different amino groups, but only one bond is shown in Figure 5. The second bond $NH_3^+ \cdots X$ is coming from the amino group above or below, respectively, of the neighbouring unit cells. The third hydrogen bond to the ion X is formed by the nitrogen atom of the peptide group. The third hydrogen atom of the free amino group forms a hydrogen bond with $O^{(2)}$ of the carboacid group. The structure therefore confirms Donohue's postulate [23] about the maximum use of the hydrogen bonding capacities of the N–H and O–H groups present in the molecule for structures of this type.

The $^{79,81}Br$ and ^{127}I NQR-spectra are in agreement with the crystal structure. Br^- and I^- occupy one point position (2a in $P2_1$), and therefore there is

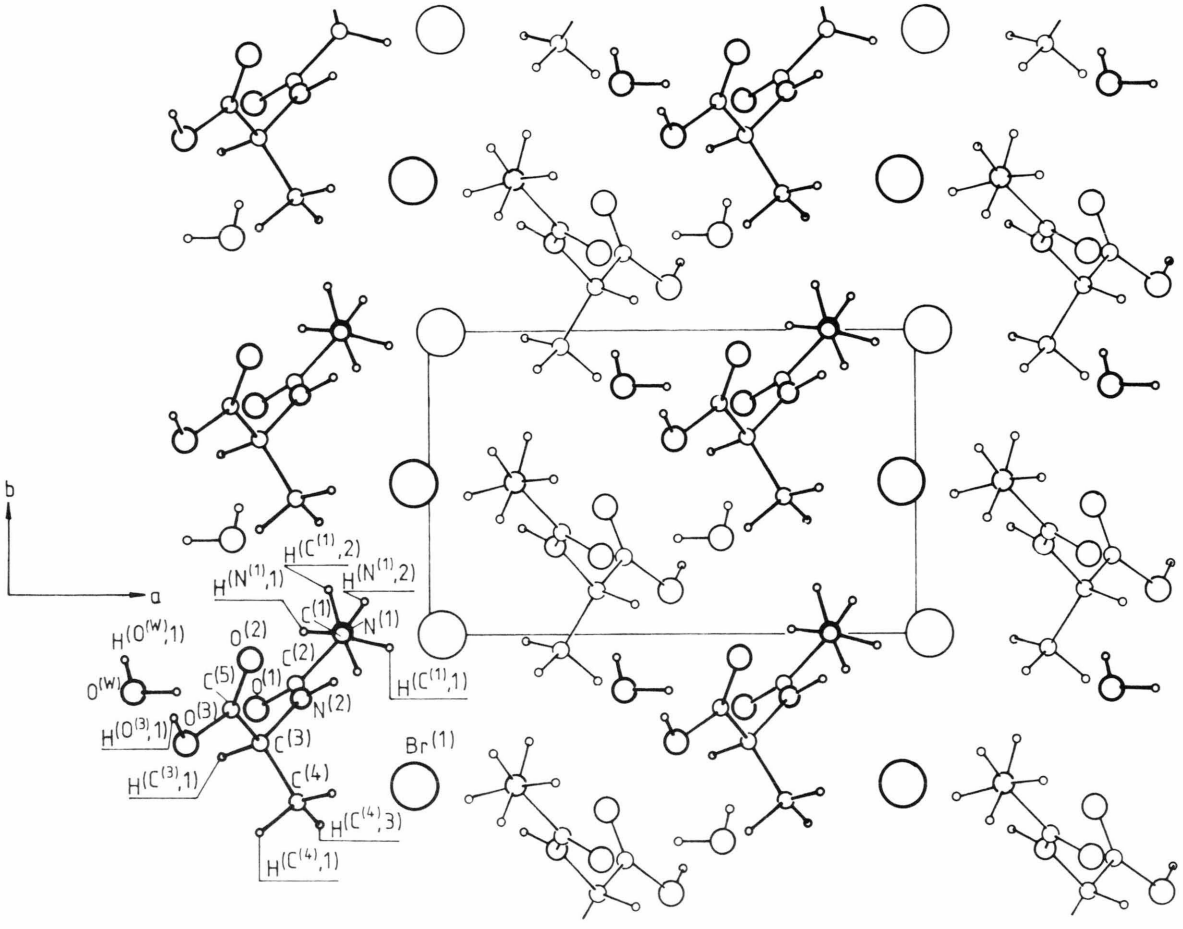

Fig. 4. Projection of the crystal structure of glycyl-l-alanine hydrobromide monohydrate along *c* onto the *ab*-plane. The molecules are drawn with different line gauge, which means that they are in different altitudes of the unit cell.

Table 10. Influence of deuteration on the ^{127}I NQR; $\Delta\nu_1 = \nu_1^H - \nu_1^D$ (transition $m = \pm 1/2 \leftrightarrows m = \pm 3/2$); $\Delta\nu_2 = \nu_2^H - \nu_2^D$ (transition $m = \pm 3/2 \leftrightarrows m = \pm 5/2$); $\Delta(e^2 q Q h^{-1}) = (e^2 q Q h^{-1})^H - (e^2 q Q h^{-1})^D$; $\Delta\eta = \eta^H - \eta^D$.

Substance	T / K	$\Delta\nu_1$ / kHz	$\Delta\nu_2$ / MHz	$\Delta(e^2 q Q h^{-1})$ / MHz	$\Delta\eta$	Lit.
$EtNH_2 \cdot HI$	77	265	520	1.65	−0.009	[24]
	293	370	690	2.38	−0.004	
$4F-C_6H_4-NH_2 \cdot HI$	77	502	1059	3.48	−0.005	[3]
	293	467	1078	3.54	−0.013	
$4Cl-C_6H_4-NH_2 \cdot HI$	77	399	813	2.7	−0.003	[3]
	295	451	897	3.0	0.0	
$C_6H_5-NH_2 \cdot HI$	77	323	628	2.10	−0.002	[4]
	295	281	732	2.36	−0.014	
Gly-l-Ala · HI · H_2O	215	336	691	2.36	−0.016	This
	303	419	795	2.72	−0.017	paper

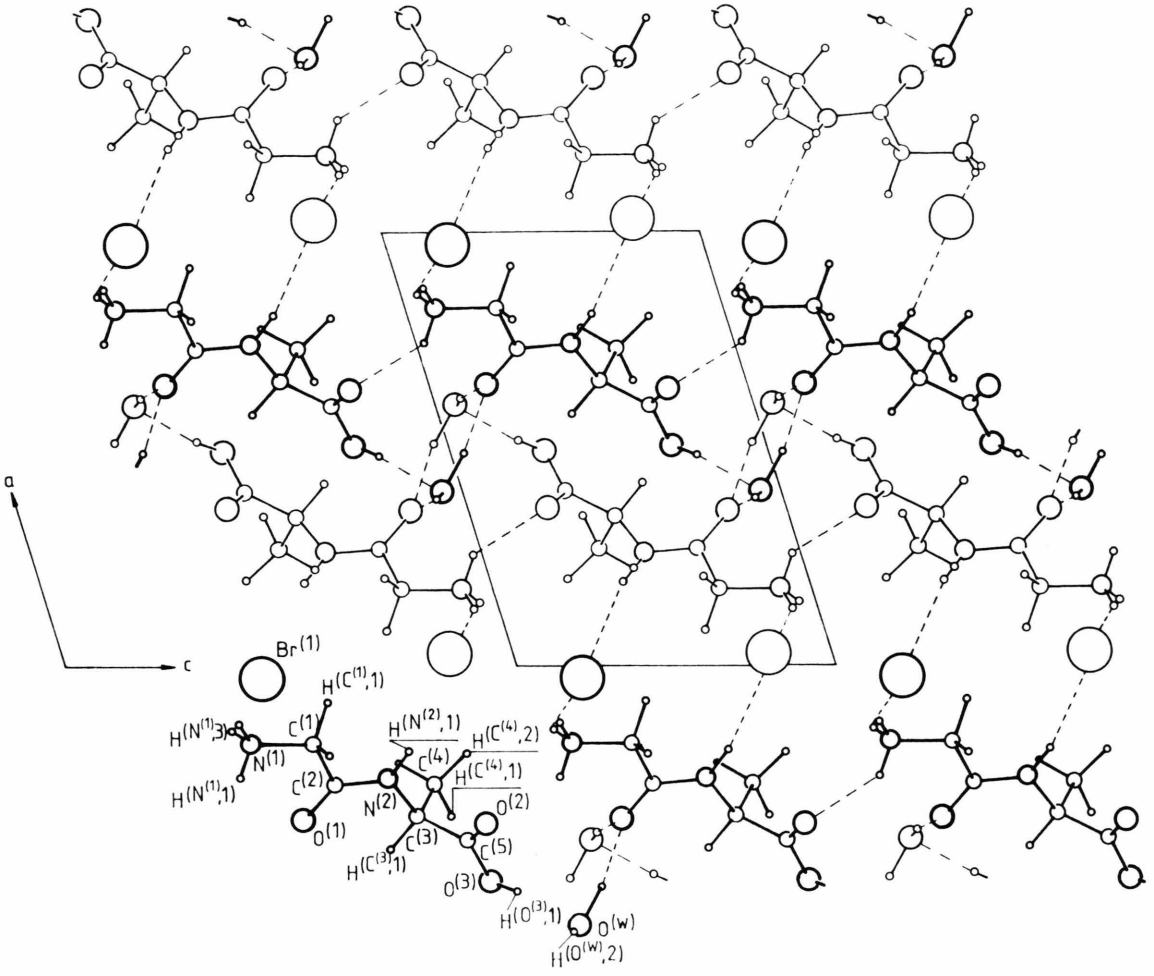

Fig. 5. Projection of the crystal structure of glycyl-l-alanine hydrobromide monohydrate along *b* onto the *ac*-plane. The dashed lines symbolize hydrogen bonds. The molecules are drawn with different line gauge, which means that they are in different altitudes of the unit cell.

only one resonance for ^{79}Br, one for ^{81}Br, and two for ^{127}I (two transitions) observed.

The resonance frequency of **1** is in the range $12 \leqq \nu/\mathrm{MHz} \leqq 19$, in accordance with a correlation between the ^{79}Br NQR frequencies and the type of the involved hydrogen bonds observed by Fleck and Weiss [8]. It states that this frequency range is connected with $\mathrm{N-H \cdots Br^-}$ hydrogen bonds only around the bromine ion for salts of amino acids. Since in **2** the iodine ion is involved in $\mathrm{N-H \cdots I^-}$ hydrogen bonds only, the nuclear quadrupole coupling constant at $T \approx 274$ K should be in the range $70 \leqq e^2 q Q h^{-1}/\mathrm{MHz} \leqq 125$ [9] and this is found, too.

The negative frequency shift $\Delta\nu$ of the ^{127}I NQR frequencies induced by deuteration is also a qualitative proof for the high degree of hydrogen bonding in the crystal structure. The ratio of the shifts of the resonance by deuteration, $\Delta\nu_1/\Delta\nu_2$ ($\Delta\nu_{1,2} = \nu^{\mathrm{H}}_{1,2} - \nu^{\mathrm{D}}_{1,2}$) is nearly 1:2. In Table 10 the values of **2** are compared with a few data from literature [3, 4, 24]. There is a discontinuity in the plot of $\nu_{1,2}(^{127}\mathrm{I})$ versus T, which is only detectable in the higher transition $\nu_2(^{127}\mathrm{I})$ at $T = 321 \pm 2$ K. The same effect can be seen by the deuterated compound at $T = 315 \pm 2$ K, but in both cases by differential thermal analysis (DTA) no phase transition was detectable.

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