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The unusual solid state structure of heroin hydrochloride monohydrate and its selective detection using NQR spectroscopy

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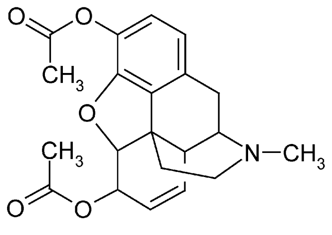
Heroin hydrochloride monohydrate, the normal crystalline form of this material, has been studied by X-ray crystallography, nuclear quadrupole resonance spectroscopy, and theoretical calculations. The X-ray data at 120 K could be refined in either of the two space groups $P4_1$ or $P4_12_12$ with the latter higher symmetry form being the more likely, but for the NQR spectra at 4.2 K the doublet structure suggests that a slight symmetry breaking has ocurrred, which lowers the symmetry to $P4_1$. The crystals have the unusual unit cell dimensions of $a = b = 7.5335(2)$ Å, $c = 71.976(4)$ Å, with $Z = 8$ (and $Z' = 2$ in $P4_1$); the molecules are arranged on a four-fold helix of pitch 72.0 Å with its axis parallel to the c axis, requiring a total of eight molecules in order to complete one turn. As in the free base the nitrogen ring system of the N-protonated heroin molecule has a chair conformation; in $P4_1$ the N–H hydrogen is bonded to a Cl^- with N–H···Cl distances of 3.056(15) and 3.095(14) Å and each Cl^- ion is also hydrogen bonded to two water molecules. ^{14}N and ^{35}Cl quadrupole resonance frequencies have been observed in both the pure material and material from a drugs seizure by two double resonance techniques; in cross-relaxation spectra, a broad $^{35,37}Cl$ resonance is found near 1.95 MHz at room temperature and an analysis of the line shape predicts an average quadrupole coupling constant for the two ions of 3.817 MHz and an asymmetry parameter of 0.4. In double resonance by level crossing experiments, ^{14}N doublets are observed near 0.965 and 1.035 MHz at 4.2 K, predicting a mean quadrupole coupling constant of 1.333 MHz and an asymmetry parameter of 0.158. A doublet ^{35}Cl signal is also observed at 1.965 MHz. The doublet patterns observed are consistent with a $P4_1$ space group at 4.2 K. The similarity of the NQR data from the pure sample and the seizure confirms that the illicit sample is of the helical monohydrate, suggesting that these methods can be used to detect the narcotic in real situations. Theoretical calculations with Gaussian at the HF/6-31+G* level for two molecules at the configurations they adopt in the solid state are in reasonable agreement with these conclusions for ^{14}N and one of the ^{35}Cl ions.

Introduction

Heroin (diacetylmorphine, **1**) is a class A drug, closely related to morphine and codeine, and derived from the opium poppy.



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It is produced by acetylation of morphine extracted from poppy latex, followed by treatment with HCl to give the hydrochloride, which is recrystallised from ethanol and diethyl ether to give heroin hydrochloride monohydrate. The monohydrate can be dried to give an anhydrous form. While simple colorimetric tests exist to detect the presence of drugs such as heroin hydrochloride, a simple quantitative, portable and non-destructive method for selectively identifying heroin in the presence of closely related compounds such as acetylcodeine is highly desirable. The ratio of acetylcodeine to heroin is, for example, often used as an indication of the origin of illicit drugs. In this paper, we have determined the unusual crystal structure of heroin hydrochloride monohydrate and from this result calculated the ^{14}N and ^{35}Cl nuclear quadrupole resonance (NQR) frequencies using Gaussian (method: HF/6-31+G*). Using these values as a guide, we then detected both ^{14}N and ^{35}Cl quadrupole resonance signals by double resonance and cross-relaxation techniques. Signals have been observed at identical frequencies in a sample of illicit heroin hydrochloride monohydrate taken from a drug seizure.

Experimental

Materials

A sample of diamorphine hydrochloride BP was obtained from Macfarlen-Smith and used in the double resonance NQR experiments. The loss on drying was stated to be 3.7%,

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compared to 4.3% expected for the pure monohydrate. For the X-ray studies, a sample was recrystallised from ethanol as in the common illicit production process. The sample of illicit heroin hydrochloride was obtained from the Forensic Science Service in the UK; its purity was estimated to be 85% as base, or 97.5% as the hydrochloride monohydrate.

X-Ray crystallography

The X-ray measurements were conducted on a Nonius $^{\mathrm{Kappa}}$CCD diffractometer using MoK$_\alpha$ radiation and a sample temperature of 120 K. Approximate unit cell dimensions were determined by the Nonius Collect program from 20 index frames of width 0.5° in ϕ using a Nonius $^{\mathrm{Kappa}}$CCD diffractometer, with a detector-to-crystal distance of 60 mm. The Collect program was then used to calculate a data collection strategy to 99.5% completeness for $\theta = 25°$ using a combination of 0.3° ϕ and ω scans of 120 s deg^{-1} exposure time. Crystals were indexed using the DENZO-SMN package and positional data were refined along with diffractometer constants to give the final unit cell parameters. Integration and scaling (DENZO-SMN, Scalepack) resulted in unique data sets corrected for Lorentz and polarisation effects and for the effects of crystal decay and absorption by a combination of averaging of equivalent reflections and an overall volume and scaling correction. Structures were solved using SHELXS-97[1] and developed *via* alternating least squares cycles and difference Fourier synthesis (SHELXL-97[2]) with the aid of the program XSeed[3] as an interface to the SHELX programs, from which the figures were prepared. All non-hydrogen atoms were modelled anisotropically, while hydrogen atoms were placed in calculated positions, assigned an isotropic thermal parameter 1.2 times that of the parent atom (1.5 for terminal atoms) and allowed to ride. Acidic protons were located on the final difference Fourier map and included as riding atoms with fixed isotopic thermal parameters as described above.

Because of extensive twinning there was some difficulty in establishing the correct space group for the crystal at 120 K; the X-ray data could be refined in either $P4_1$ or $P4_12_12$ with some preference for the latter. The problem lies in the lack of a firm absence condition for the 2_1 screw axis in the (0*k*0) reflections, the average intensity of which was 1.9 times the standard uncertainty. The refinement in either space group proved essentially identical with two apparently independent but highly correlated molecules, so there are no strong crystallographic grounds to assign a symmetry lower than $P4_12_12$ at 120 K. Collection of a further data set at 30 K gave no further evidence for a phase change to $P4_1$. However, the doublet structure of the NQR spectra taken at 4.2 K (see Fig. 8 below) suggests that $P4_1$ is the correct space group, at least at 4.2 K, implying that slight symmetry breaking occurs between 30 and 4.2 K, lowering the symmetry to $P4_1$. It is this latter structure that has been used in the theoretical calculations of the NQR parameters and for which X-ray structural data are reported in the remainder of the paper.

Crystal data for $C_{21}H_{26}ClNO_6$:† M = 423.88, 0.30 × 0.25 × 0.10 mm^3, tetragonal, space group $P4_1$ (No. 76), $a = b$ = 7.5335(2), c = 71.976(4) Å, U = 4084.9(3) Å^3, Z = 8, D_c = 1.378 g cm^{-3}, F_{000} = 1792, 3475 unique reflections. Final GoF = 1.024, R_1 = 0.0726, wR_2 = 0.1011, R indices based on 1729 reflections with $I > 2\sigma(I)$ (refinement on F^2), 530 parameters, 25 restraints (on displacement parameters). LP and absorption corrections applied, μ = 0.225 mm^{-1}. Absolute structure parameter: –0.22(19).[4] In $P4_12_12$ (No. 92) the crystal data are much the same except there were 2808 unique reflections (R_{int} = 0.0854). Final GoF = 1.000, R_1 = 0.0778, wR_2 = 0.0943, R indices based on 1328 reflections with $I > 2\sigma(I)$ (refinement on F^2), 273 parameters, 0 restraints, LP and absorption corrections applied. Absolute structure parameter: −0.3(2).[4]

NQR measurements

Double resonance by level crossing (DRLC) experiments[5] were performed at 4.2 K by means of the magnetic field cycle illustrated in Fig. 1. The polarising field B_{pol} was typically 0.8 to 1 T with a polarisation time of 30 to 60 s; the NMR observation field B_{nmr} was 0.627 T (^{1}H frequency of 26.7 MHz) and the residual field B_{res} lay between 1.5 and 2.0 mT. The magnetic field was provided by a superconducting solenoid of low inductance (L = 0.023 H) continuously powered by a fast switching power supply rated at 15 V and 160 A so that the magnetic field was proportional to the instantaneous current. The maximum field-ramping rate of the system was 10 T s^{-1}, but in these experiments the system was routinely operated at 8 T s^{-1}. The superconducting magnet system incorporated a variable temperature helium cryostat for the sample. Sample temperatures, measured by a calibrated Cernox resistance thermometer, were stable to within 0.05 K. The ^{1}H NMR signal was detected by an NMR coil tuned to 26.7 MHz. The 90° pulse employed to record the signal had a duration of 1 µs and the total dead-time was 4 µs. The broadband secondary rf irradiation used to drive the quadrupolar transitions was provided by a pair of Helmholtz coils comprising approximately 8 turns. The secondary rf field amplitude at the sample was approximately 0.2 mT, with irradiation times of typically 400 ms.

Cross-relaxation (CR) NQR spectra were recorded at room temperature using pneumatic transfer of the sample from high field to the cross-relaxation field.[6] In these experiments, B_{nmr} in Fig. 1 was set to equal to B_{pol}, both being supplied by a permanent magnet of 0.472 T field (^{1}H NMR frequency of 20.10 MHz). The sample was polarised in high field for 10 s, after which the ^{1}H NMR signal was recorded by means of a 90° pulse, and then transferred to the cross-relaxation field B_{res} for approximately 70 ms. No rf radiation was applied in this experiment, but the CR spectrum was obtained by stepping B_{res} between successive ^{1}H NMR signals from 0 to 3000 kHz in steps of 4.58 kHz. The spectrum was scanned twice and the two data sets added. The spectrum was corrected for a frequency offset caused by the stray field from the permanent magnet. The curved base line typical of cross-relaxation spectra was eliminated by applying a manual polynomial correction. The data were smoothed using a damping algorithm; a new smoothed point is calculated from the raw data by allowing it to change the previous point in the smoothed data set by 20% of their difference. This is quite a severe smoothing but does not affect the line shape because of its broadness (for chlorine) compared to the frequency step used.

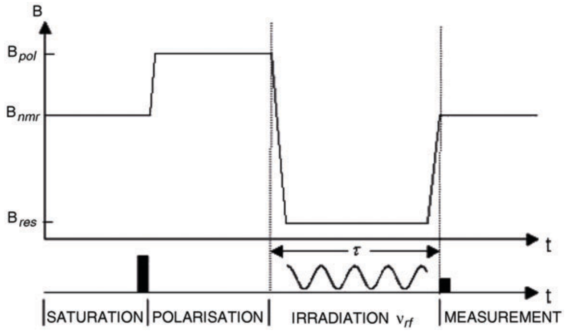

Fig. 1 Magnetic field cycle in the double resonance experiments.

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† CCDC reference number 242245. See http://www.rsc.org/suppdata/nj/b4/b401797h/ for crystallographic data in .cif or other electronic format.

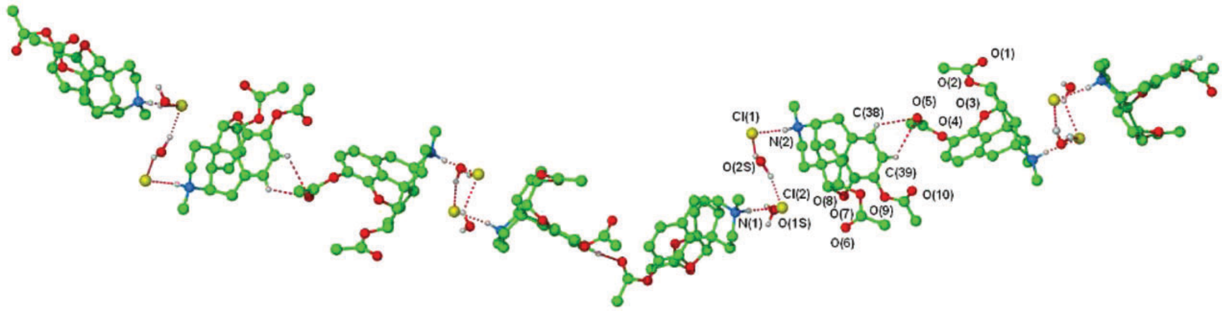

Fig. 2 Helical crystal packing along the *c* axis in heroin hydrochloride monohydrate showing labelling of the atoms (in $P4_1$).

Results and discussion

X-Ray crystal structure

Surprisingly, no details of the X-ray crystal structure of heroin hydrochloride monohydrate have been reported previously, despite the fact that it is readily crystallised. In fact, the structure determination proved challenging with even relatively large crystals showing weak scattering, partially because the compound displays a highly asymmetric plate-type morphology with extensive twinning and there is a long crystallographic *c* axis (Fig. 2) and hence potential problems of peak overlap in the detector.

The water and chlorine ions form an infinite hydrogen-bonded chain perpendicular to the 4_1 helical axis (*c* axis) with each water molecule hydrogen bonding to both chlorine ions. Hydrogen bond distances and angles are given in Table 1. The chlorine ions also form short, charge-assisted hydrogen bonds to the NH groups of the heroin cations (Fig. 3) with the interaction N(1)···Cl(2) being significantly longer than its symmetry independent counterpart in $P4_1$, N(2)···Cl(1) (Table 1). However, the D–H distances in Table 1 are subject to considerable unspecified errors; most are too short, as expected from X-ray measurements, but O(2S)–H(2S1) is anomalously long.

The most remarkable feature of the structure is the four-fold helix of pitch 72.0 Å, which requires a total of eight molecules in order to complete one turn (and hence one repeat of the crystallographic *c* axis). The molecules stack in face-to-face pairs interacting *via* the water/anion layers as described above. Each pair then propagates the helix to the neighbouring pair *via* a series of CH···O interactions[7] involving the ester carbonyl atoms O(5) and O(10) (Fig. 4). We have previously reported several helical structures brought about by weak hydrogen-bonding interactions and shown that in one case at least, helical packing of a resolved chiral compound necessitates a $Z = 2$ structure.[8,9]

Nuclear quadrupole resonance spectra

The asymmetric hydrogen bonding around each chlorine ion in the X-ray crystal structure leads to a non-zero quadrupole interaction at this nucleus and a finite nuclear quadrupole resonance (NQR) frequency, clearly shown in DRLC spectra near 1.965 MHz (Fig. 5) and as a broad dip near 1.9 MHz in the CR spectrum (Fig. 6). Since Cl(1) and Cl(2) are crystallographically non-equivalent in $P4_1$, two ^{35}Cl frequencies are expected and these are apparently resolved in DRLC spectra collected with smaller frequency steps (Fig. 7) at frequencies of 1.950 and 1.965 MHz, consistent with a slight symmetry breaking, reducing the space group symmetry to $P4_1$ at the lower temperature of 4.2 K used for the NQR experiments. No other signals assignable to ^{35}Cl were observed in frequency sweeps up to 4 MHz and none for ^{37}Cl. An almost identical ^{35,37}Cl CR spectrum was observed from a sample of street heroin hydrochloride monohydrate under the same experimental conditions, suggesting that in the solid state both had the same structure. This material also had the same ^{1}H NMR spectrum in solution as the pure material.

For a spin 3/2 nucleus such as ^{35}Cl and ^{37}Cl, the single frequency observed for each nucleus is given by the equation

$$\nu_Q = \frac{1}{2}\left(\frac{e^2qQ}{h}\right)\left(1+\frac{\eta^2}{3}\right)^{1/2} \qquad (1)$$

where

$$\left(\frac{e^2qQ}{h}\right)$$

is the nuclear quadrupole coupling constant (NQCC) in frequency units, q being the maximum principal component of the electric field gradient, Q the nuclear electric quadrupole moment and η the asymmetry parameter. From the two DRLC ^{35}Cl frequencies, which were excited in low or zero magnetic fields, it is impossible to deduce the quadrupole coupling constants and asymmetry parameters separately from eqn. (1). However, in CR spectra, the dips are generated in a non-zero magnetic field, and the Zeeman broadening of the observed

Table 1 Hydrogen bonds in heroin hydrochloride monohydrate

D–H···A	d(D–H)/Å	d(H···A)/Å	d(D···A)/Å	∠DHA/°
O(1S)–H(1S1)···Cl(1)	0.98	2.15	3.119(11)	167.5
N(1)–H(1)···Cl(2)	0.93	2.17	3.095(14)	172.1
N(2)–H(2)···Cl(1)	0.93	2.14	3.056(15)	169.0
O(2S)–H(2S1)···Cl(2)	1.16	2.01	3.103(11)	154.9
O(2S)–H(2S2)···Cl(1)	0.94	2.29	3.174(11)	158.1
O(1S)–H(1S2)···Cl(2)	0.96	2.46	3.153(11)	128.9

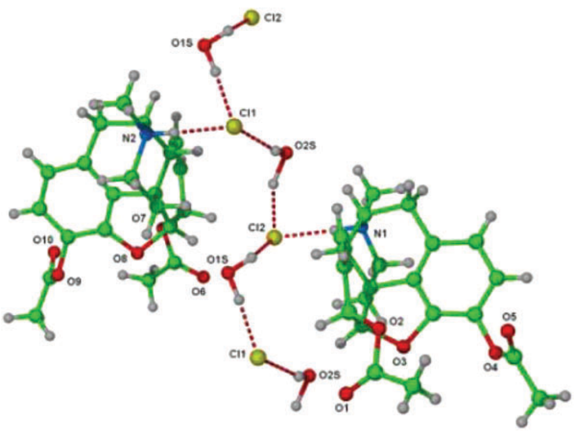

Fig. 3 Projection of two independent molecules on the *ab* plane, showing the N–H···Cl$^-$ and Cl$^-$···OH$_2$ hydrogen bonding.

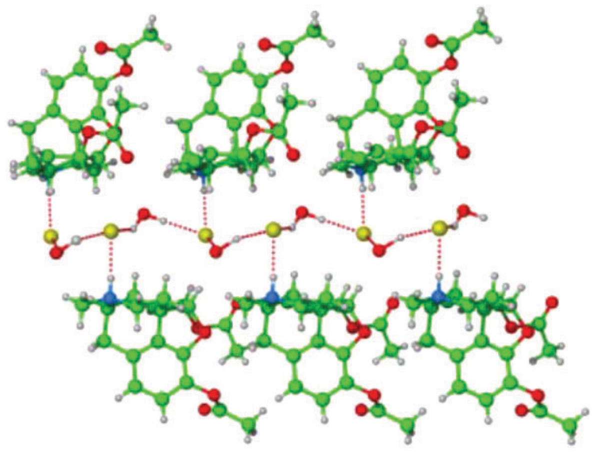

Fig. 4 Aryl and methyl CH···O interactions between the helices. Aryl C···O 3.270 Å, CH_3 C···O 3.200 Å.

lines allows both quantities to be estimated by building up simulated spectra in much the same way as the experiment. The proton frequency is incremented (usually in 10 kHz steps) from low frequency to a point where the proton Zeeman splitting exceeds any quadrupole splitting. At each proton frequency, the Zeeman interaction for the chlorine can be obtained from its gyromagnetic ratio (compared to that of protons). The Zeeman interaction and quadrupole interaction of the chlorine are then used to calculate the energies and wavefunctions of the quadrupole levels. This is repeated for 400 crystal orientations. The proton frequency is then incremented. During this cycle, data relevant to building up the final spectrum are stored for later use. Data is stored on the following basis: cross relaxation only occurs efficiently when the splitting of the proton Zeeman levels is of a similar magnitude to the splitting of a pair of quadrupole levels. As the frequency mismatch increases the efficiency is assumed to decrease as a Gaussian function with a time constant of approximately 50 µs so only splittings that have a mismatch of less than 70 kHz need to be stored.

Energy exchange between the two systems is facilitated by dipolar coupling between the two nuclei. This energy exchange is only allowed if the change in quantum number for the quadrupolar nuclei is ±1 or zero (from inspection of the dipolar Hamiltonian). The transition probability for the energy exchange between the two pairs of levels is calculated on this basis and stored so that when the program ends a large amount of data has been stored in the format: proton frequency, frequency mismatch, transition probability. This contains all the information necessary to build up a cross-relaxation spectrum as a histogram of block size 10 kHz.

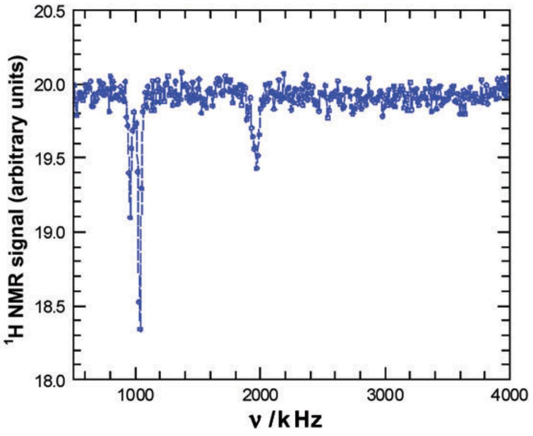

Fig. 5 Double resonance by level crossing (DRLC) spectrum of heroin hydrochloride monohydrate at 4.2 K; experimental conditions are given in the text.

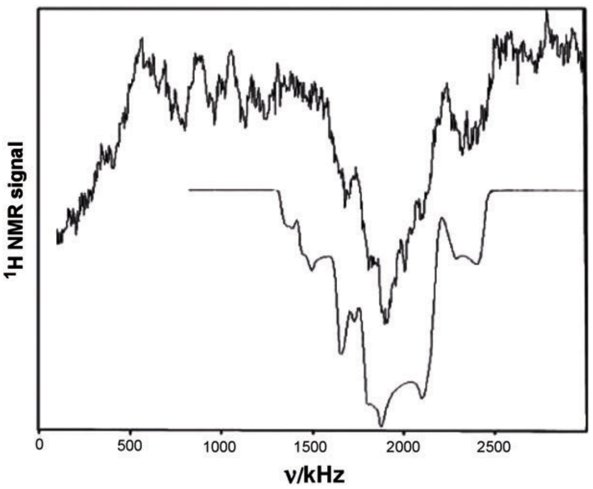

Fig. 6 Cross-relaxation (CR) spectrum of pure heroin hydrochloride monohydrate at room temperature with a residence time in high field of 10 s and in low field of 70 ms. The lower curve is a theoretical fit for a ^{35}Cl quadrupole coupling constant of 3.817 MHz and asymmetry parameter of 0.4.

The chlorine cross-relaxation spectrum is further complicated by overlapping contributions from the two chlorine isotopes, 35 and 37. The line shape for each isotope is calculated separately and the two added, in proportion to their natural abundances, to give the final spectrum. The lower abundance ^{37}Cl contributes quite significantly to the line shape because of its smaller gyromagnetic ratio. Also, ^{37}Cl has a smaller quadrupole interaction, by a factor of 1.269, which causes the cross-relaxation condition to be realized at lower fields, also reducing the Zeeman broadening and hence increasing its relative intensity.

Inspection of the experimental spectrum suggested a zero field resonance frequency of around 2000 kHz (for ^{35}Cl). Refinement of this value was achieved by calculating a series of cross-relaxation spectra using this value and an asymmetry parameter of 0.0 to 1.0 in steps of 0.2. The best fit was with $\eta = 0.4$ (lower line in Fig. 6). The fit was further improved by offsetting the two spectra by 50 kHz, suggesting that the ^{35}Cl NQR lines in zero field should be seen around 1950 kHz, in good agreement with the DRLC values. Combining the DRLC frequencies of 1.950 and 1.965 MHz at 4.2 K with the CR estimate of the asymmetry parameter (assumed to be the same for both lines) gives quadrupole coupling constants of 3.801 and 3.830 MHz.

The ^{35}Cl frequencies lie between two values previously published in hydrochlorides, *viz.* ^{35}Cl/^{37}Cl frequencies at

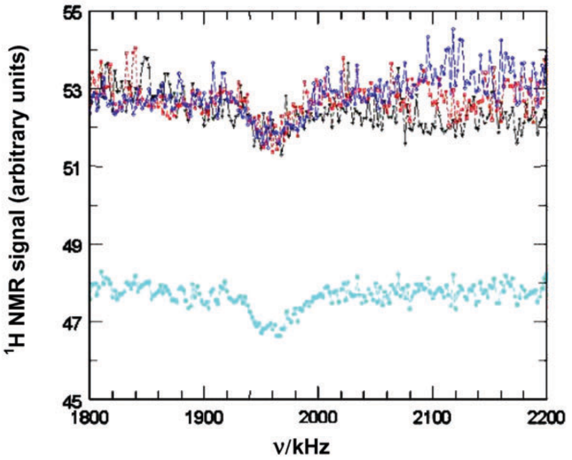

Fig. 7 The ^{35}Cl DRLC spectrum at 4.2 K with frequency steps of 2 kHz; the lower spectrum is an average of the upper spectra.

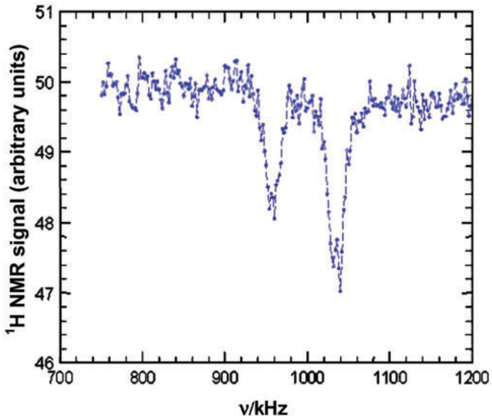

Fig. 8 ^{14}N DRLC NQR spectrum at 4.2 K with 2 kHz frequency steps.

1.215/0.860 MHz for decylamine hydrochloride[10] and 5.524/4.366 MHz for pyridine hydrochloride;[11] they are lower than the corresponding frequencies of 2.53/1.99 MHz reported for cocaine hydrochloride near 295 K[12,13] and the ^{35}Cl frequency of 2.712 MHz observed in ecstasy (MDMA hydrochloride)[13] at similar temperatures. These differences reflect important changes in the hydrogen bonding; in cocaine hydrochloride,[14] for example, the Cl^{-} ion is hydrogen bonded to just one N–H group with an N–H···Cl bond length of 3.06(9) Å, and the same is true in pyridine hydrochloride, where the hydrogen bond length is shorter at 2.95 Å.[15] In contrast, in heroin hydrochloride monohydrate, the Cl^{-} ion is hydrogen bonded not only to NH, with hydrogen bond lengths of 3.065(15) and 3.095(14) Å, but also to two O–H groups from two neighbouring water molecules. It is clear from these results that CR and NQR measurements of the ^{35}Cl signals provide a means of detecting these drugs and of distinguishing between them.

The ^{14}N DRLC spectrum is readily assigned if the observed doublets near 0.957 and 1.035 MHz, shown under higher resolution in Fig. 8, are assigned to ν_{-} and ν_{+}, respectively; for spin 1 nuclei; these are related to the quadrupole coupling constant and asymmetry parameter by the equation

$$\nu_{\pm} = \frac{3}{4}\left(\frac{e^2qQ}{h}\right)\left(1 \pm \frac{\eta^2}{3}\right)^{1/2} \qquad (2)$$

Note that once again the doublet structure predicted by the X-ray crystal structure analysis in $P4_1$ is clearly resolved, with splittings of 6.5 kHz for ν_{+} and 5.7 kHz for ν_{-}. It is impossible from these measurements alone to say which component of each doublet goes with the other; on the rather arbitrary basis of intensities, we pair off the frequencies (in MHz at 4.2 K) as (0.960, 1.039) and (0.954, 1.032), giving from eqn. (2) the two sets of quadrupole coupling constants (in MHz) and asymmetry parameters (1.333, 0.119) and (1.324, 0.118). The alternative assignment gives (1.328, 0.108) and (1.329, 0.128). These results are not inconsistent with the CR spectrum (Fig. 6) in which features assigned to ^{14}N are observed close to 926 (ν_{-}) and 1085 (ν_{+}) kHz. The higher frequency is close to previous double resonance measurements that located a broad signal near 1080 kHz at 15 K.[16]

Theoretical calculations

The NQR parameters have been related to the $P4_1$ X-ray crystal structure by means of theoretical calculations. The nitrogen-containing piperidine ring systems in the two protonated heroin molecules have the bond lengths and angles shown in Table 2, which are similar to those observed in cocaine hydrochloride,[14] with one significant difference in the C–N–C bond angle, which is close to 104° in the cocaine ion and has a mean value of 113.7° in the heroin ion.

In heroin hydrochloride monohydrate, C6, C7, C9 and C10 in the piperidine ring system in molecule 1 lie in the plane

$$-1.522x + 1.812y + 68.33z = 54.69 \qquad (3)$$

with an rms deviation of 0.048 Å, with N1 lying at 0.617 Å and C11 at −0.772 Å from this plane; in molecule 2, C27, C28, C30 and C31 lie in the plane

$$1.543x + 1.705y + 68.54z = 60.06 \qquad (4)$$

with an rms deviation of 0.031 Å, N2 lying at −0.693 Å and C32 at 0.719 Å from this plane. Both conformations are therefore chair, as in cocaine hydrochloride[14] and the free bases.[17–19]

The molecular dimensions for both molecules from the X-ray crystal structure analysis have been used to calculate the quadrupole parameters for both ^{14}N and ^{35}Cl using Gaussian[20] (HF/6-31+G*), with three corrections. Both N–H bond lengths have been lengthened from 0.93 to 1.04 Å, one of the O–H bond lengths [O(2S)–H(2S1)···Cl(2)] shortened from 1.16 to 0.98 Å and the others set to the same value, to be more consistent with acceptable values. Nuclear electric quadrupole moments of +20.44(3) mB for ^{14}N and −81.65(80) mB for ^{35}Cl were used[21] and the quadrupole coupling constants calculated using the equation.[22]

$$\text{NQCC (in MHz)} = 234.9647Qq \qquad (5)$$

where Q is the nuclear electric quadrupole moment in Barn (10^{-28} m^2) and q is q_{zz}, the maximum principal component, in atomic units (from Gaussian).

To simulate the effects of the solid state, the calculations for heroin hydrochloride monohydrate were performed for the two hydrogen-bonded molecules in the $P4_1$ structure shown in Fig. 3, each chlorine ion, Cl(1) and Cl(2), being hydrogen bonded to one N–H group and two water molecules, O(1S) and O(2S). Several different basis sets were used in the calculations, the general conclusion being that the larger split sets with the inclusion of polarization (*e.g.*, 3d functions for Cl) such as 6-31+G* gave better agreement with experiment. These results are summarised in Table 3. For ^{14}N, the two sets of results are in reasonable agreement, bearing in mind that thermal motion effects have been neglected and that the experimental assignment for the observed doublets has been made to optimise the agreement between the asymmetry parameters rather than the quadrupole coupling constants.

Table 2 Bond lengths and angles in the nitrogen ring system of heroin hydrochloride monohydrate

Molecule 1				Molecule 2			
Bond	Length/Å	Bond	Angle/°	Bond	Length/Å	Bond	Angle/°
N1–C9	1.459(15)	N1–C9–C10	114.0(12)	N2–C30	1.551(16)	N2–C30–C31	106.6(12)
C9–C10	1.493(17)	C9–C10–C11	110.9(12)	C30–C31	1.537(17)	C30–C31–C32	111.5(13)
C10–C11	1.546(18)	C10–C11–C6	107.2(13)	C31–C32	1.52(2)	C31–C32–C27	110.2(14)
C11–C6	1.531(19)	C11–C6–C7	106.7(12)	C32–C27	1.51(2)	C32–C27–C28	108.8(14)
C6–C7	1.55(2)	C6–C7–N1	108.1(13)	C27–C28	1.52(2)	C27–C28–N2	105.5(12)
C7–N1	1.536(18)	C7–N1–C9	113.2(12)	C28–N2	1.529(18)	C28–N2–C30	114.1(12)

Table 3 Comparison of theoretical and experimental values of the ^{14}N and ^{35}Cl quadrupole parameters in heroin hydrochloride monohydrate

	Theory		Experiment[a]	
Atom	NQCC/MHz	η	NQCC/MHz	η
N(1)	−1.575	0.098	1.328	0.108
N(2)	−1.399	0.142	1.329	0.128
Cl(1)	−4.076	0.311	3.801	0.4
Cl(2)	5.388	0.827	3.830	0.4

[a] At 4.2 K.

Table 4 Principal components of the ^{14}N quadrupole tensor in MHz and their directions with respect to the N–H bond

N atom & bond	$e^2q_{zz}Q/h$	$\theta/°$	$e^2q_{yy}Q/h$	$\theta/°$	$e^2q_{xx}Q/h$	$\theta/°$
N(1)–H(1)	−1.575	2.86	0.865	90.0	0.710	87.1
N(2)–H(2)	−1.399	2.79	0.799	90.0	0.600	87.2

The predicted NQR frequencies (ν_+ at 1.220 and 1.099 MHz, ν_- at 1.142 and 1.000 MHz) were sufficiently close to experiment (doublets close to 1.035 and 0.957 MHz), bearing in mind the neglect of temperature effects, to be used as preliminary estimates when frequency searching for unknown resonances. For ^{35}Cl, the agreement is less satisfactory, largely because the electric field gradients at this ion are governed by the positions of hydrogen-bonded hydrogen atoms, which are imprecisely located in the X-ray crystal structure analysis. The main uncertainty lies in the position of the O(2S)–H(2S1) hydrogen atom, which strongly affects the electric field gradient at Cl(2); the X-ray value for the O(2S)···H(2S1) bond length (1.16 Å) is anomalously long and suggests that the H coordinates are unreliable. The quadrupole parameters at Cl(1) are better reproduced and predict an NQR frequency of 2.071 MHz compared with mean values of 1.965 and 1.950 MHz from experiment at 4.2 K and room temperature, respectively, which should be regarded as unexpectedly good agreement.

As well as calculating the magnitude of q_{zz}, it is also useful to know the direction of the electric field gradient by calculating the direction cosines. It can be shown that the electric field gradient at the origin, due to a charge e at point (x, y, z) distance r away is

$$\frac{e}{r^5}\begin{bmatrix} 3x^2 - r^2 & 3xy & 3zx \\ 3xy & 3y^2 - r^2 & 3yz \\ 3zx & 3yz & 3z^2 - r^2 \end{bmatrix}$$

The values for the field gradient tensor were extracted from the Gaussian results and the direction cosines calculated. The eigenvalues were compared with the Gaussian-produced values to check the calculation. The position of the maximum principal component (q_{zz}) with respect to a bond within the molecule was then established (Table 4).

The direction cosine results for heroin hydrochloride monohydrate were as expected for ^{14}N, with a small angle between the N–H bond and the maximum principal component of the electric field gradient. This is chemically predictable, as the asymmetry parameter of ^{14}N is low, and q_{zz} would therefore be expected to be close to the N–H bond.

Conclusions

The X-ray crystal structure analysis of heroin hydrochloride monohydrate reveals an unusual structure in which eight molecules form a four-fold helix of pitch 72 Å, the repeat unit containing just one independent molecule at 120 K. There is no evidence for a space group of lower symmetry than $P4_12_12$ at 120 or 30 K, whereas the doublet structure of the NQR spectra recorded at 4.2 K implies two independent molecules more consistent with the space group $P4_1$ at this lower temperature. A sample of the same material from a drug seizure is shown to have the same ^{35}Cl spectrum. A theoretical calculation for a hydrogen-bonded pair of molecules with the dimensions found from the X-ray analysis gives good agreement for the ^{14}N quadrupole parameters but less so for ^{35}Cl, whose quadrupole parameters depend sensitively on the imprecisely located hydrogen atoms in the two water molecules to which they are hydrogen bonded. The unique structure of heroin hydrochloride hydrate is reflected in the NQR data and hence suggests that NQR cross-relaxation methods could form the basis for a sensitive method for the selective detection of this material in the presence of other closely related compounds.

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