Fluorocyclohexane ring inversion in a solid thiourea inclusion compound studied by fluorine-19 magic-angle spinning NMR with high-power proton decoupling

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Variable-temperature ^{19}F magic-angle spinning NMR experiments involving high-power proton decoupling are used to examine the conformational preference and ring-inversion kinetics in the fluorocyclohexane–thiourea inclusion compound.

One of the most interesting and potentially important aspects of solid-state inclusion chemistry is the fact that the behaviour of molecules constrained as guests within a solid host structure is often very different from the behaviour of the same molecules in other environments (such as in their pure crystalline phase, in dispersed phases, or as guests in other host structures). In this regard, the conformational properties of substituted cyclohexane guest molecules can provide a sensitive probe of the structural constraints imposed by a solid host structure, and form a basis for comparison between different types of host structure. Thiourea forms solid inclusion compounds with cyclohexane and certain substituted cyclohexanes. In such compounds, the thiourea (host) structure contains tunnels in which the guest molecules reside.[1,2] Thiourea inclusion compounds containing mono- and di-substituted cyclohexane guests have been the subject of a number of studies. Much of the interest concerns the conformational dependence of the cyclohexane ring in the thiourea tunnels upon the substituent (X). For monosubstituted cyclohexanes with X = Me, NH_2 and OH, the equatorial conformer predominates. In comparison, when X = Cl, Br and I, the axial conformer predominates. Many of these results have been obtained using solid-state ^{13}C NMR spectroscopy.[3–5] In this study we have used ^{19}F NMR, with high-power proton decoupling, to examine the fluorocyclohexane–thiourea inclusion compound. Previous studies[4,5] indicate that in this system, both conformations of fluorocyclohexane are present in equal proportions. Fluorine-19 NMR has a considerable advantage over ^{13}C NMR, namely its greatly superior sensitivity. However, because of the close proximity of the ^{1}H and ^{19}F frequencies (within 6%) and the high powers required for decoupling in the solid state, a specially designed 'HF' probe[6,7] is needed, so that until very recently ^{19}F MAS NMR has been little used for systems containing both fluorine and hydrogen.[8]

Fluorine-19 MAS NMR spectra were recorded with a Chemagnetics CMX 200 NMR spectrometer operating at 200.13 MHz for ^{1}H and 188.28 MHz for ^{19}F. A Chemagnetics HF double-resonance probe was used which accepts 4 mm o.d. zirconia rotors fitted with a Vespel end-cap, spacer and drive tip. Typical spectral conditions were: $\pi/2$ pulse duration, 3 μs; pulse delay, 60 s; ^{1}H decoupling power, 105 kHz; spin rate, 7.0 kHz. Variable-temperature operation involved passing cool nitrogen gas over the sample. Temperatures were calibrated using tetrakis(trimethylsilyl)silane soaked in liquid methanol.[9] Fluorine-19 chemical shifts were referenced externally, by rotor replacement, to hexafluorobenzene (δ −166.4 with respect to $CFCl_3$). The ^{19}F chemical shifts obtained from experiments involving ^{1}H decoupling have been corrected for the Bloch–Siegert effect.[10]

At room temperature, a single resonance was observed in the ^{19}F MAS NMR spectrum. However on lowering the temperature, this resonance broadened and then sharpened to give two peaks of approximately equal intensity at 177 K (Fig. 1). This can be attributed to the well documented ring-inversion process in cyclohexane type molecules. The resonances at δ −163.9 and −187.0 at 177 K can be assigned to the equatorial and axial conformers respectively using solution-state NMR data.[11] To investigate the kinetics of the ring-inversion process, bandshape analysis was carried out assuming a two-site exchange model. This involved comparing 'by eye' the simulated and experimental data. Bandshape analysis shows that upon increasing the temperature there is a very slight shift in the equilibrium position towards the axial conformer. To demonstrate that ring-inversion occurs on the NMR timescale at temperatures well below coalescence, a two-dimensional ^{19}F exchange[12] spectrum was recorded at 227 K. With a mixing time of 50 ms, all four peaks are of equal intensity, indicating that exchange is complete. Away from the coalescence temperature, bandshapes are insensitive to the ring-inversion rate constant, so ^{19}F selective polarisation inversion experiments[13] were carried out at 217, 197 and 177 K. The method for selectively inverting one of the resonances involved offsetting the transmitter from one peak by a frequency equal to the

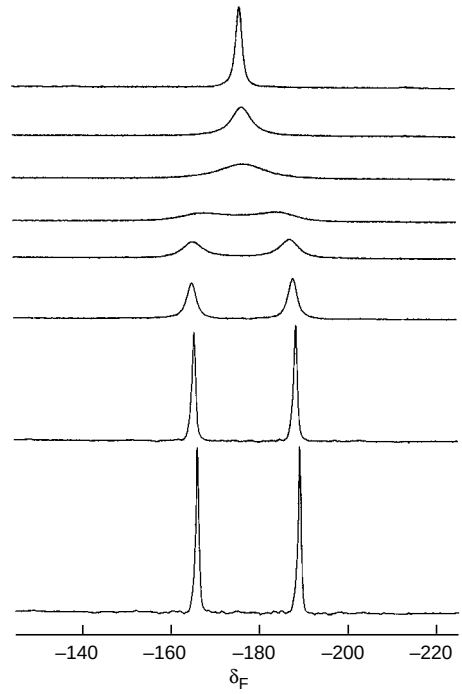

Fig. 1 Variable-temperature ^{19}F MAS NMR spectra, acquired with ^{1}H decoupling, of the fluorocyclohexane–thiourea inclusion compound. From bottom to top: 177, 217, 237, 247, 258, 268, 278, 300 K.

separation between the two peaks.[14] Exchange between the two sites was monitored by varying the mixing time, and the results of the experiment performed at 197 K are shown in Fig. 2.

The rate constants determined by the two methods were used to study the thermodynamics of the ring-inversion process. The average activation parameters obtained from an Eyring plot are: $\Delta H^{\ddagger} = 39.4 \pm 2.6$ kJ mol^{-1}, $\Delta S^{\ddagger} = -11.9 \pm 11.0$ J mol^{-1} K^{-1} and $\Delta G^{\ddagger}$ (263 K) = 42.5 ± 5.5 kJ mol^{-1}. The values that we have obtained for $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ differ from those reported using ^{13}C NMR in a previous study,[5] although data for $\Delta G^{\ddagger}$ (263 K) are comparable. However, we have studied the ring-inversion process over a wider temperature range (120 K) using the sensitivity advantage of ^{19}F NMR, and have obtained, with selective polarisation inverson, rate constants in the slow-exchange regime where bandshape analysis lacks precision. For this reason we believe that the studies reported here have led to significantly improved values for the activation parameters.

We have demonstrated that ^{19}F NMR can be used to probe the ring-inversion process in the fluorocyclohexane–thiourea inclusion compound in the same way that ^{13}C NMR has been used to investigate other substituted cyclohexane–thiourea inclusion compounds. However, the greater sensitivity of ^{19}F NMR in comparison to ^{13}C NMR enables spectra to be obtained in shorter times and hence two-dimensional experiments are more feasible, particularly at low temperatures.

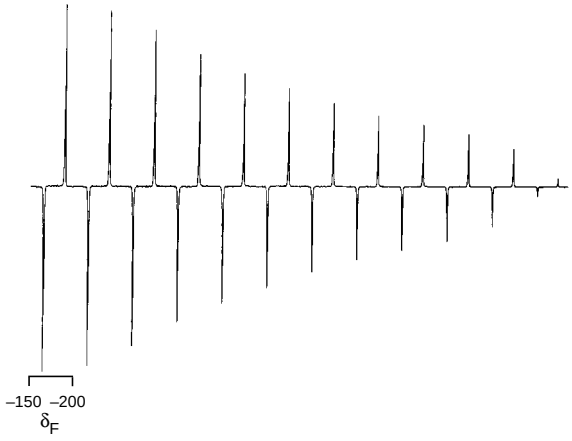

Fig. 2 Fluorine-19 selective polarisation inversion experiment at 197 K, with mixing times of: 0.001, 1.0, 5.0, 10.0, 15.0, 20.0, 25.0, 30.0, 35.0, 40.0, 50.0 and 100.0 ms (from left to right). A spin rate of 8.6 kHz was used and a time of 116 μs was used to create a phase difference of 180° between the two magnetisation vectors for the axial and equatorial spins.[15]

The fluorocyclohexane–thiourea inclusion compound was prepared by slowly cooling a solution containing fluorocyclohexane and thiourea in methanol. The crystals were collected and washed with 2,2,4-trimethylpentane to remove any fluorocyclohexane molecules adhering to their external surfaces. Powder X-ray diffraction studies at ambient temperature indicated that these crystals have the rhombohedral thiourea tunnel structure,[1] as found for thiourea inclusion compounds containing other cyclohexane-based guest molecules.

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Footnote

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