Probing the solvent-induced tautomerism of a redox-active ureidopyrimidinone.

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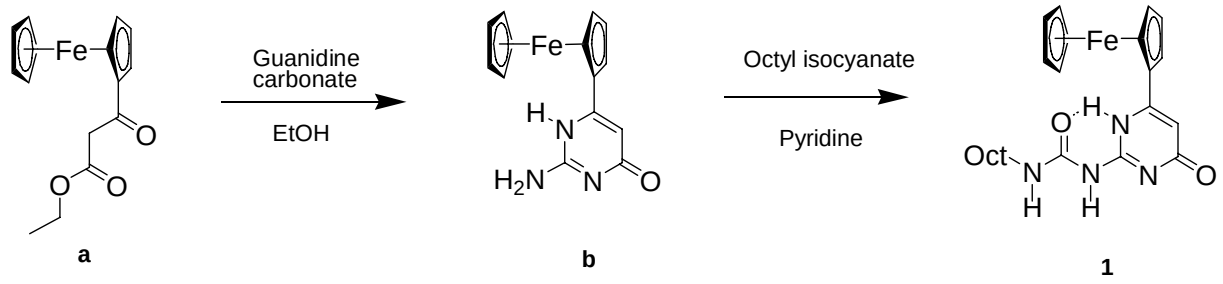
1. Synthesis of 3

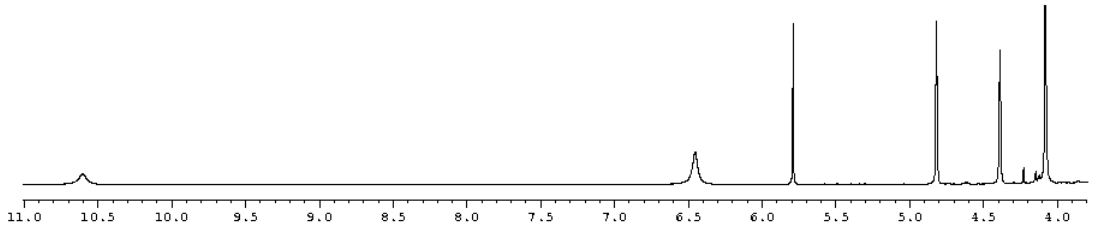


a **b** **1**

Compound **a** was synthesized according to the literature method.[1]

Compound b.

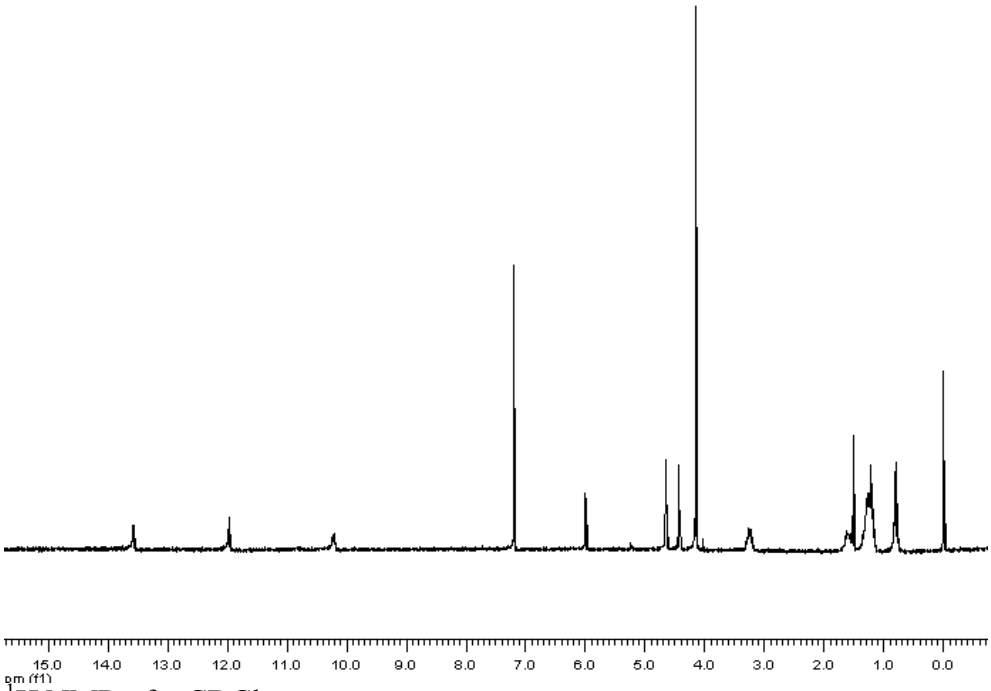
A solution of compound **a** (2.0 g, 6.7 mmol) and guanidine carbonate (0.65g, 3.6 mmol) were heated in a solution of ethanol (100 ml) overnight. The solution was concentrated under reduced pressure and purified using column chromatography (eleuent: acetone) to afford compound **b** as an orange/brown solid (1.2 g, 61 %). Mp 175°C (dec). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.54 (s, 1 H), 6.46 (br. s, 2 H), 5.79 (s, 1 H), 4.82 (s, 2 H), 4.37 (s, 2 H), 4.08 (s, 5 H). ^{13}C NMR (400MHz, DMSO-d_6) δ 166.57, 162.85, 155.14, 96.04, 81.55, 69.99, 69.55, 67.62. IR (NaCl, cm^{-1}): 3589, 3005, 1709, 1422, 1363, 1222, 1092. MS (EI): m/z 295 (M^+). Anal. calcd. for $C_{14}H_{13}N_3OFe$: C, 56.95; H, 4.41; N, 14.24. Found: C, 56.75; H, 4.43, N, 14.28 %.



^{1}H NMR of compound **b** in DMSO-d_6

Compound 1.

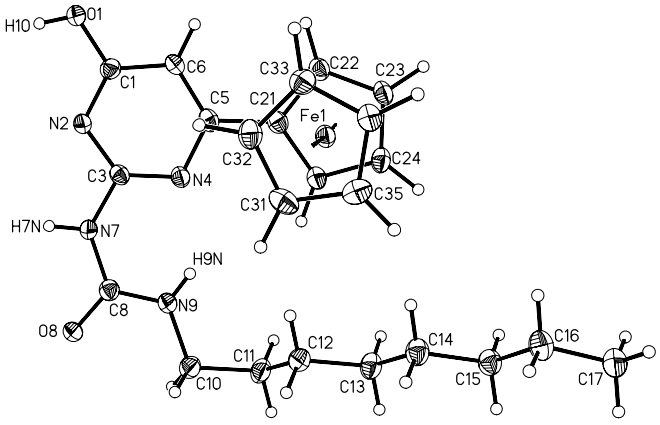
A mixture of octyl isocyanate (0.53 g, 3.4 mmol) and compound **b** (1.0 g, 3.4 mmol) were heated under reflux in pyridine (50 ml) for 3h. The solvent was evaporated under reduced pressure and the mixture was purified using column chromatography (eluent: CH_2Cl_2/acetone 8:2, v/v) to afford **1** as an orange solid (1.3 g, 85 %). Mp 216-219°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 13.50 (s, 1 H), 11.98 (s, 1 H), 10.20 (t, 1 H), 6.02 (s, 1 H), 4.66 (t, 2 H), 4.48 (t, 2 H), 4.15 (s, 5H), 3.25 (q, 2H), 1.65 (m, 2H), 1.28, (m, 10H), 0.85 (t, 3H). MS (EI): m/z 450 (M^+). Anal. calcd. for $C_{23}H_{30}N_4O_2Fe$: C, 61.33; H, 6.66; N, 12.44. Found: C, 61.22; H, 6.69; N, 12.24 %.



^{1}H NMR of **1** $CDCl_3$

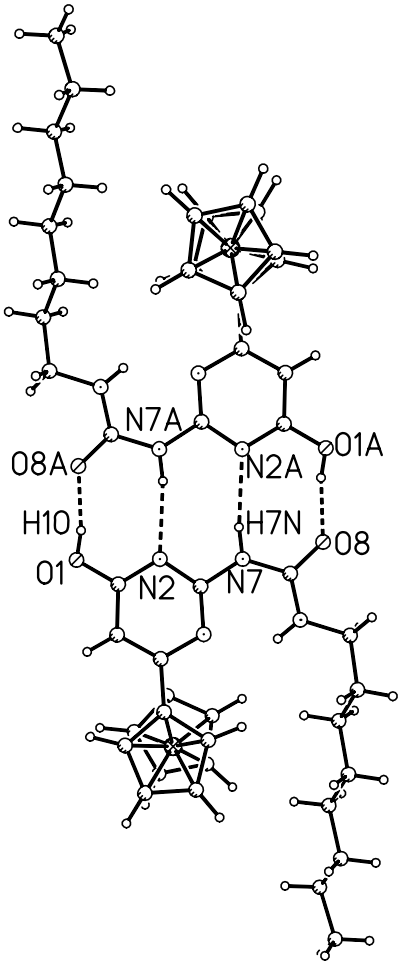
1. "Encapsulation of an Electroactive Guest in a Dynamically Self-Assembled Polymer" F. Ilhan, T. Galow, G. Cooke, V. Rotello *J. Am. Chem. Soc.,* **2000**, *122*, 3595-3598.

2. X-ray crystallography data for 1



General features:

Molecules of **1** pack as a centrosymmetric dimers, composed of two NH…N and two OH…O hydrogen bonds. The planes containing the hydrogen bonding atoms pack in a staggered arrangement parallel to the a axis and lie nearly parallel to the cp rings in the same stack. Additionally π–π interactions also exist in dimeric arrangements where one cp rings lies 3.3 Å from the heterocycle, although just two carbon atoms (C23, C24) from the cp ring lie directly overhead.



Intensity data were collected on a single crystal 0.22 x 0.08 x 0.02 mm^3 coated in Paratone-N oil and mounted with vacuum grease onto glass fibers, on a Bruker Nonius X8Apex 2 diffractometer with Mo Kα radiation at 100K, cooled by an Oxford Cryosystems Cryostream. Structures were solved by direct methods and refined by full matrix least squares refinement with F^2 data using the SHELXTL suite of programs.

Hydroxyl hydrogen atom H1O, N-bound H atoms H7N and H9N located in the difference Fourier map and its coordinates freely refined. All other hydrogen atoms were constrained to ideal geometries and displacement parameters of all H atoms were treated at riding on the bound atom.

Crystal data and structure refinement for **1**.

Empirical formula	C23 H30 Fe N4	
O2		
Formula weight	450.36	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 6.8841(6) Å	α= 102.073(7)°.
	b = 10.4063(10) Å	β= 94.324(5)°.
	c = 16.1990(13) Å	γ = 109.281(5)°.
Volume	1057.95(16) $Å^3$	
Z	2	
Density (calculated)	1.414 Mg/m^3	
Absorption coefficient	0.740 mm^{-1}	
F(000)	476	

Crystal size	0.22 x 0.08 x 0.02 mm^3
Theta range for data collection	2.77 to 26.68°.
Index ranges	-8<=h<=8, -13<=k<=13, -20<=l<=20
Reflections collected	32280
Independent reflections	4424 [R(int) = 0.0808]
Completeness to theta = 25.00°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9853 and 0.8541
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4424 / 0 / 281
Goodness-of-fit on F^2	1.007
Final R indices [I>2sigma(I)]	R1 = 0.0408, wR2 = 0.0813
R indices (all data)	R1 = 0.0689, wR2 = 0.0912
Largest diff. peak and hole	0.372 and -0.588 e.$Å^{-3}$

Table 2. Bond lengths [Å] and angles [°] for **3**.

C(1)-O(1)	1.329(3)	C(1)-N(2)	1.340(3)	C(1)-C(6)	1.395(3)
O(1)-H(1O)	0.82(3)	N(2)-C(3)	1.349(3)	C(3)-N(4)	1.326(3)
C(3)-N(7)	1.386(3)	N(4)-C(5)	1.366(3)	C(5)-C(6)	1.375(3)
C(5)-C(21)	1.467(3)	C(6)-H(6)	0.9500	N(7)-C(8)	1.381(3)
N(7)-H(7N)	0.88(3)	C(8)-O(8)	1.254(3)	C(8)-N(9)	1.331(3)
N(9)-C(10)	1.459(3)	N(9)-H(9N)	0.81(3)	C(10)-C(11)	1.521(3)
C(10)-H(10A)	0.9900	C(10)-H(10B)	0.9900	C(11)-C(12)	1.519(3)
C(11)-H(11A)	0.9900	C(11)-H(11B)	0.9900	C(12)-C(13)	1.526(3)
C(12)-H(12A)	0.9900	C(12)-H(12B)	0.9900	C(13)-C(14)	1.523(3)
C(13)-H(13A)	0.9900	C(13)-H(13B)	0.9900	C(14)-C(15)	1.523(3)
C(14)-H(14A)	0.9900	C(14)-H(14B)	0.9900	C(15)-C(16)	1.524(3)
C(15)-H(15A)	0.9900	C(15)-H(15B)	0.9900	C(16)-C(17)	1.519(3)
C(16)-H(16A)	0.9900	C(16)-H(16B)	0.9900	C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800	C(17)-H(17C)	0.9800	Fe(1)-C(22)	2.034(2)
Fe(1)-C(21)	2.044(2)	Fe(1)-C(32)	2.041(3)	Fe(1)-C(34)	2.048(2)
Fe(1)-C(33)	2.046(2)	Fe(1)-C(25)	2.048(2)	Fe(1)-C(31)	2.049(3)
Fe(1)-C(23)	2.053(2)	Fe(1)-C(35)	2.057(2)	Fe(1)-C(24)	2.059(2)
C(21)-C(22)	1.434(3)	C(21)-C(25)	1.440(3)	C(22)-C(23)	1.423(3)
C(22)-H(22)	1.0000	C(23)-C(24)	1.422(3)	C(23)-H(23)	1.0000

C(24)-C(25)	1.419(3)	C(24)-H(24)	1.0000	C(25)-H(25)	1.0000
C(31)-C(35)	1.417(4)	C(31)-C(32)	1.424(4)	C(31)-H(31)	1.0000
C(32)-C(33)	1.421(3)	C(32)-H(32)	1.0000	C(33)-C(34)	1.420(3)
C(33)-H(33)	1.0000	C(34)-C(35)	1.417(3)	C(34)-H(34)	1.0000
C(35)-H(35)	1.0000				

O(1)-C(1)-N(2)	118.8(2)	O(1)-C(1)-C(6)	118.5(2)	N(2)-C(1)-C(6)	122.7(2)
C(1)-O(1)-H(1O)	110.9(19)	C(1)-N(2)-C(3)	114.9(2)	N(4)-C(3)-N(2)	127.6(2)
N(4)-C(3)-N(7)	118.9(2)	N(2)-C(3)-N(7)	113.4(2)	C(3)-N(4)-C(5)	115.9(2)
N(4)-C(5)-C(6)	121.4(2)	N(4)-C(5)-C(21)	116.0(2)	C(6)-C(5)-C(21)	122.5(2)
C(5)-C(6)-C(1)	117.3(2)	C(8)-N(7)-C(3)	129.9(2)	C(8)-N(7)-H(7N)	113.8(16)
C(3)-N(7)-H(7N)	116.2(16)	O(8)-C(8)-N(9)	121.5(2)	O(8)-C(8)-N(7)	118.6(2)
N(9)-C(8)-N(7)	119.9(2)	C(8)-N(9)-C(10)	120.2(2)	C(8)-N(9)-H(9N)	117.2(19)
C(10)-N(9)-H(9N)	122.6(19)	N(9)-C(10)-C(11)	112.9(2)	C(12)-C(11)-C(10)	115.4(2)
C(11)-C(12)-C(13)	112.1(2)	C(14)-C(13)-C(12)	113.9(2)	C(15)-C(14)-C(13)	114.4(2)
C(14)-C(15)-C(16)	113.0(2)	C(17)-C(16)-C(15)	113.9(2)	C(22)-Fe(1)-C(21)	41.19(9)
C(22)-Fe(1)-C(32)	117.62(10)	C(21)-Fe(1)-C(32)	105.81(10)	C(22)-Fe(1)-C(34)	124.14(10)
C(21)-Fe(1)-C(34)	161.02(10)	C(32)-Fe(1)-C(34)	68.22(10)	C(22)-Fe(1)-C(33)	104.76(10)
C(21)-Fe(1)-C(33)	123.29(10)	C(32)-Fe(1)-C(33)	40.69(10)	C(34)-Fe(1)-C(33)	40.60(10)
C(22)-Fe(1)-C(25)	68.99(10)	C(21)-Fe(1)-C(25)	41.21(9)	C(32)-Fe(1)-C(25)	126.10(10)
C(34)-Fe(1)-C(25)	156.54(10)	C(33)-Fe(1)-C(25)	162.15(9)	C(22)-Fe(1)-C(31)	153.66(10)
C(21)-Fe(1)-C(31)	119.89(10)	C(32)-Fe(1)-C(31)	40.75(10)	C(34)-Fe(1)-C(31)	68.14(10)
C(33)-Fe(1)-C(31)	68.49(10)	C(25)-Fe(1)-C(31)	109.28(10)	C(22)-Fe(1)-C(23)	40.75(9)
C(21)-Fe(1)-C(23)	68.83(9)	C(32)-Fe(1)-C(23)	152.76(10)	C(34)-Fe(1)-C(23)	107.75(10)
C(33)-Fe(1)-C(23)	118.51(10)	C(25)-Fe(1)-C(23)	68.35(10)	C(31)-Fe(1)-C(23)	164.97(10)
C(22)-Fe(1)-C(35)	162.61(10)	C(21)-Fe(1)-C(35)	155.95(10)	C(32)-Fe(1)-C(35)	68.14(10)
C(34)-Fe(1)-C(35)	40.41(10)	C(33)-Fe(1)-C(35)	68.20(10)	C(25)-Fe(1)-C(35)	122.39(10)
C(31)-Fe(1)-C(35)	40.39(10)	C(23)-Fe(1)-C(35)	127.29(10)	C(22)-Fe(1)-C(24)	68.52(10)
C(21)-Fe(1)-C(24)	68.73(10)	C(32)-Fe(1)-C(24)	164.47(10)	C(34)-Fe(1)-C(24)	121.59(10)
C(33)-Fe(1)-C(24)	154.48(10)	C(25)-Fe(1)-C(24)	40.44(9)	C(31)-Fe(1)-C(24)	128.24(10)
C(23)-Fe(1)-C(24)	40.47(10)	C(35)-Fe(1)-C(24)	110.57(10)	C(22)-C(21)-C(25)	107.1(2)
C(22)-C(21)-C(5)	127.0(2)	C(25)-C(21)-C(5)	125.8(2)	C(22)-C(21)-Fe(1)	69.06(14)
C(25)-C(21)-Fe(1)	69.54(13)	C(5)-C(21)-Fe(1)	124.07(17)	C(23)-C(22)-C(21)	108.3(2)
C(23)-C(22)-Fe(1)	70.34(14)	C(21)-C(22)-Fe(1)	69.75(13)	C(24)-C(23)-C(22)	108.2(2)
C(24)-C(23)-Fe(1)	69.97(14)	C(22)-C(23)-Fe(1)	68.91(14)	C(25)-C(24)-C(23)	108.3(2)

C(25)-C(24)-Fe(1)	69.36(14)	C(23)-C(24)-Fe(1)	69.56(14)	C(24)-C(25)-C(21)	108.2(2)
C(24)-C(25)-Fe(1)	70.20(14)	C(21)-C(25)-Fe(1)	69.25(14)	C(35)-C(31)-C(32)	107.8(2)
C(35)-C(31)-Fe(1)	70.10(14)	C(32)-C(31)-Fe(1)	69.33(14)	C(31)-C(32)-C(33)	108.2(2)
C(31)-C(32)-Fe(1)	69.93(14)	C(33)-C(32)-Fe(1)	69.85(14)	C(34)-C(33)-C(32)	107.6(2)
C(34)-C(33)-Fe(1)	69.76(14)	C(32)-C(33)-Fe(1)	69.46(14)	C(35)-C(34)-C(33)	108.3(2)
C(35)-C(34)-Fe(1)	70.14(14)	C(33)-C(34)-Fe(1)	69.64(14)	C(34)-C(35)-C(31)	108.1(2)
C(34)-C(35)-Fe(1)	69.45(14)	C(31)-C(35)-Fe(1)	69.51(14		

Table 3. Torsion angles [°] for 3.

O(1)-C(1)-N(2)-C(3)	-177.4(2)	C(6)-C(1)-N(2)-C(3)	2.4(3)
C(1)-N(2)-C(3)-N(4)	-2.4(4)	C(1)-N(2)-C(3)-N(7)	177.5(2)
N(2)-C(3)-N(4)-C(5)	0.6(4)	N(7)-C(3)-N(4)-C(5)	-179.4(2)
C(3)-N(4)-C(5)-C(6)	1.3(3)	C(3)-N(4)-C(5)-C(21)	-177.4(2)
N(4)-C(5)-C(6)-C(1)	-1.1(4)	C(21)-C(5)-C(6)-C(1)	177.4(2)
O(1)-C(1)-C(6)-C(5)	179.1(2)	N(2)-C(1)-C(6)-C(5)	-0.8(4)
N(4)-C(3)-N(7)-C(8)	5.4(4)	N(2)-C(3)-N(7)-C(8)	-174.6(2)
C(3)-N(7)-C(8)-O(8)	-179.7(2)	C(3)-N(7)-C(8)-N(9)	0.4(4)
O(8)-C(8)-N(9)-C(10)	1.0(4)	N(7)-C(8)-N(9)-C(10)	-179.1(2)
C(8)-N(9)-C(10)-C(11)	158.5(2)	N(9)-C(10)-C(11)-C(12)	75.7(3)
C(10)-C(11)-C(12)-C(13)	178.8(2)	C(11)-C(12)-C(13)-C(14)	177.7(2)
C(12)-C(13)-C(14)-C(15)	176.3(2)	C(13)-C(14)-C(15)-C(16)	178.2(2)
C(14)-C(15)-C(16)-C(17)	173.7(2)	N(4)-C(5)-C(21)-C(22)	-174.3(2)
C(6)-C(5)-C(21)-C(22)	7.1(4)	N(4)-C(5)-C(21)-C(25)	2.2(4)
C(6)-C(5)-C(21)-C(25)	-176.5(2)		

Table 4. Hydrogen bonds for 3 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1O)...O(8)#1	0.82(3)	1.77(3)	2.583(2)	168(3)
N(9)-H(9N)...N(4)	0.81(3)	2.07(3)	2.713(3)	136(2)
N(7)-H(7N)...N(2)#1	0.88(3)	2.14(3)	3.013(3)	171(2)

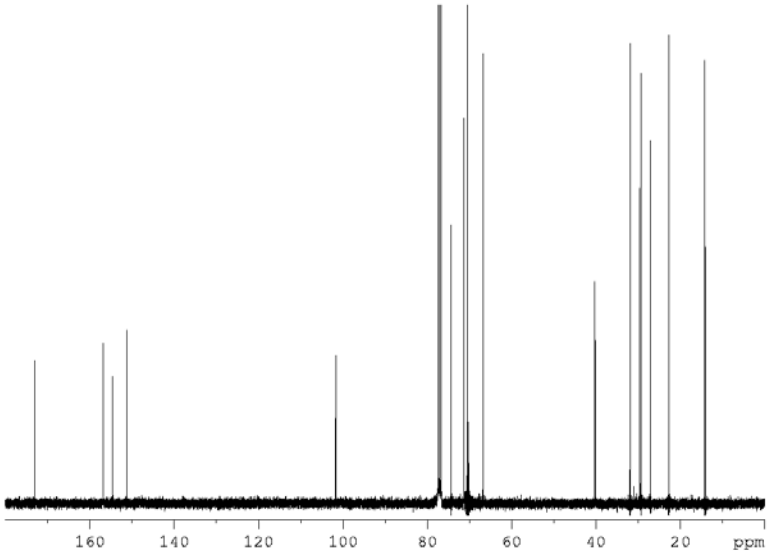
Symmetry transformations used to generate equivalent atoms:

#1 -x-1,-y+1,-z+1

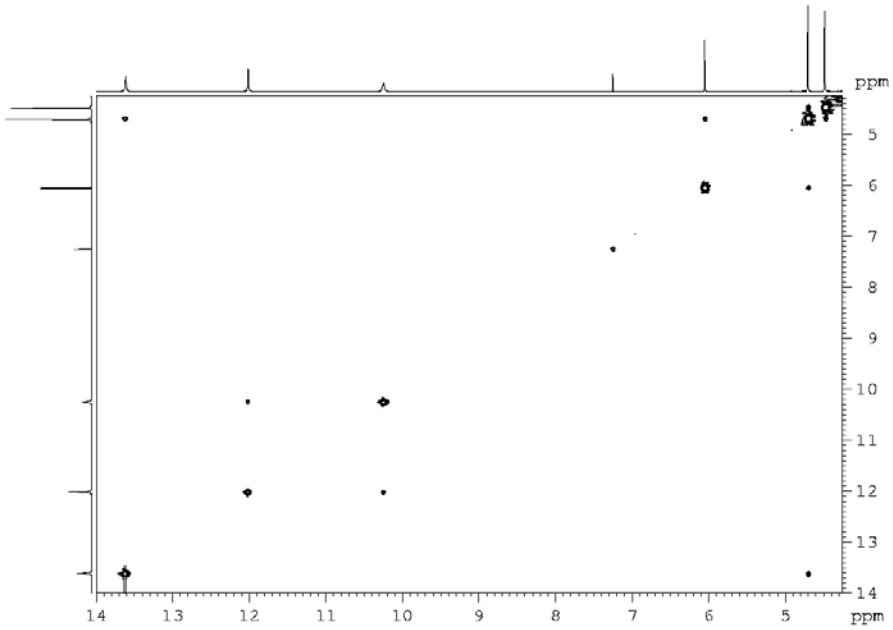
The crystal structure presented in this manuscript was prepared using Mercury (The Cambridge Crystallographic Data Centre).

3. NMR data

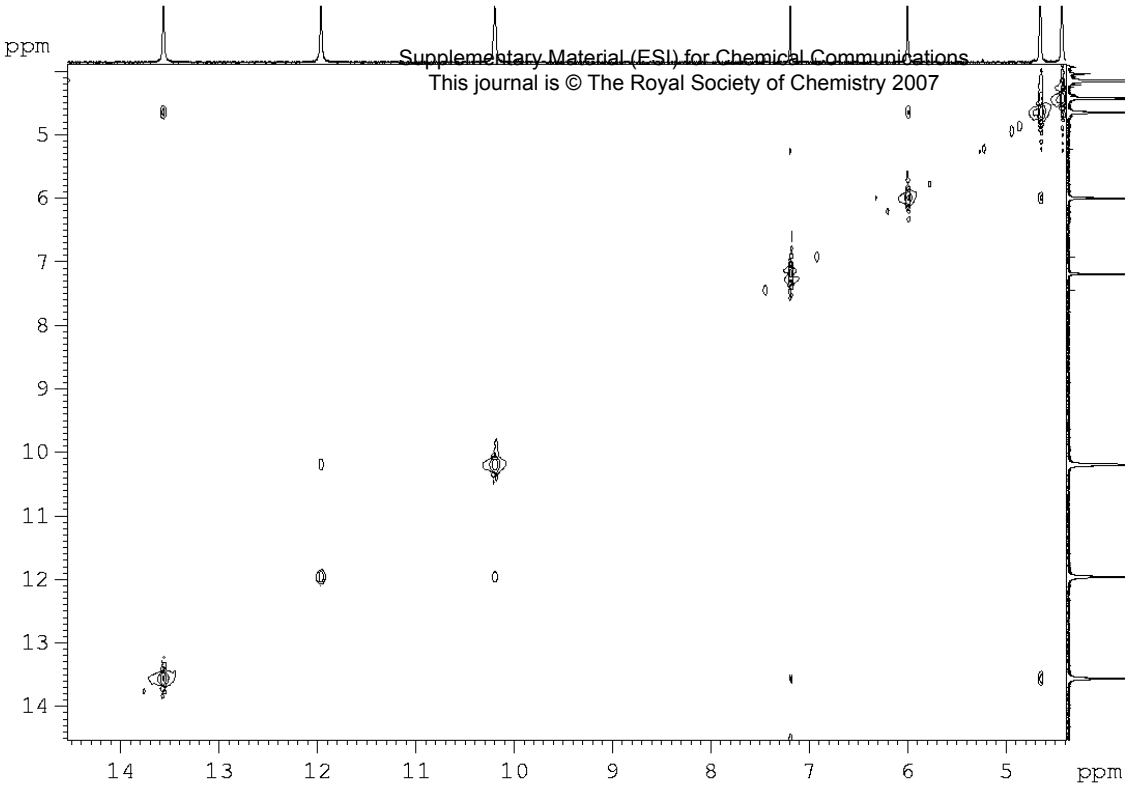
(a) Solution data in $CDCl_3$



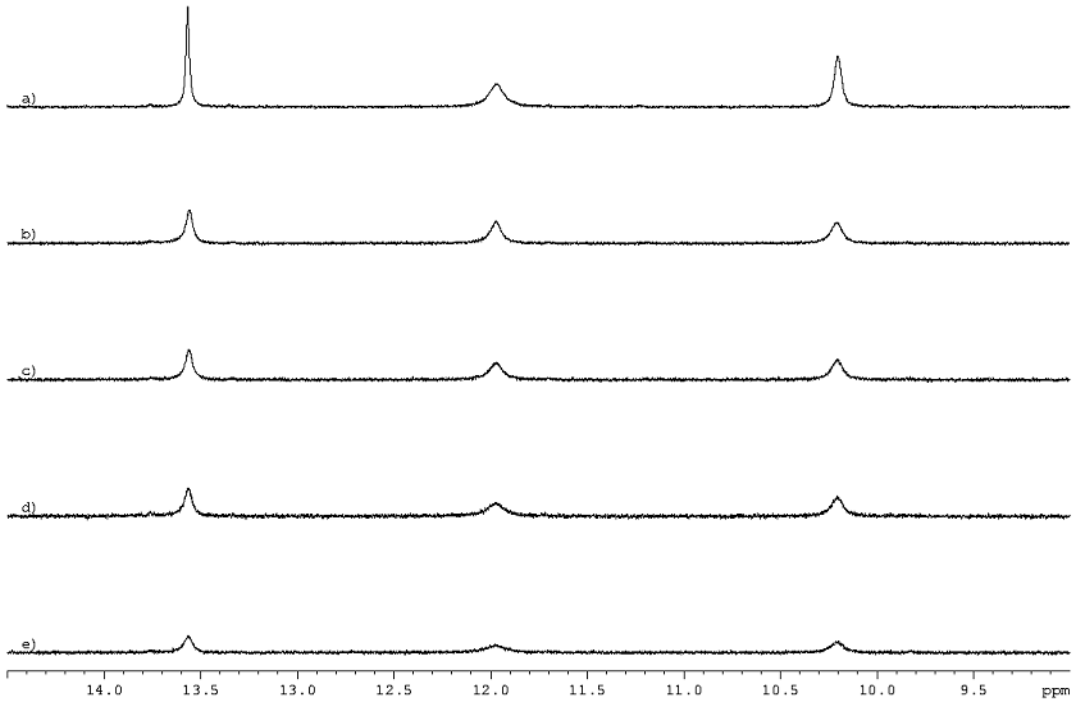
^{13}C NMR of **1** $CDCl_3$



ROESY spectrum of **1** recorded in $CDCl_3$ at 298 K.

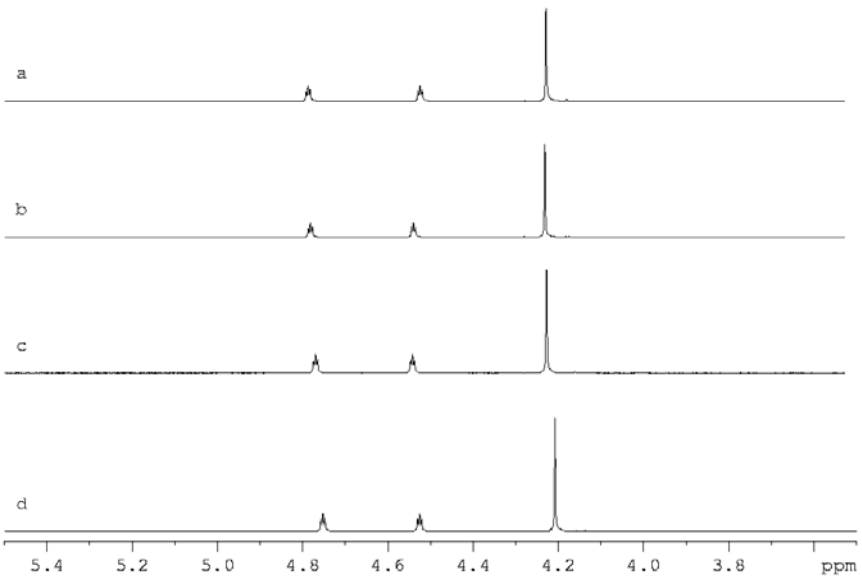


^{1}H - ^{1}H NOESY (400 MHz) spectrum of **1** recorded in $CDCl_3$ at 298 K.

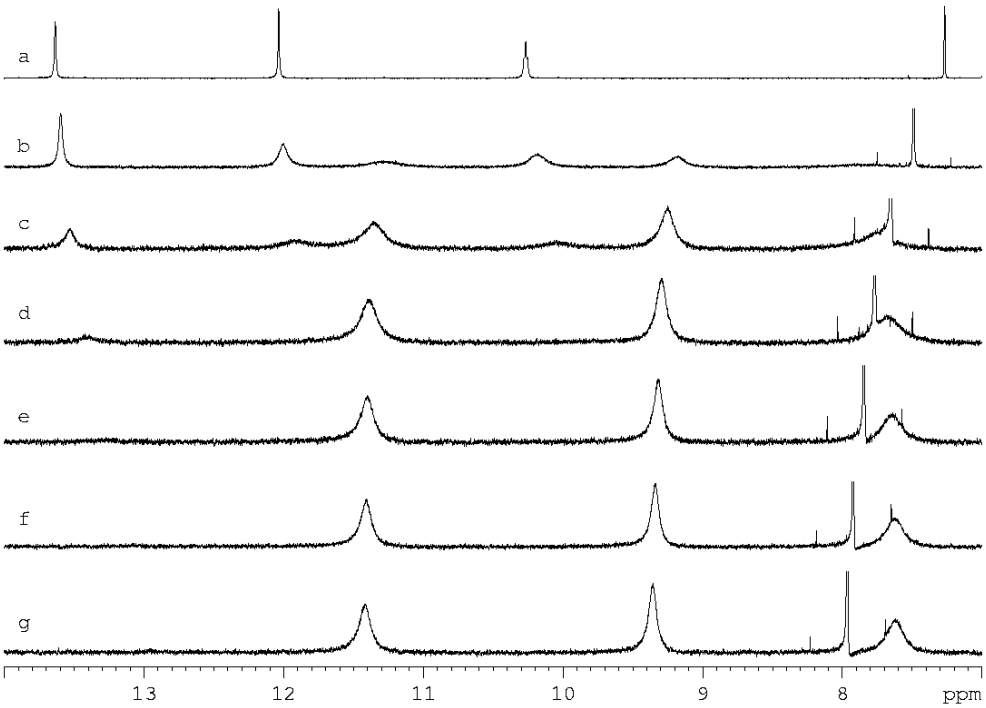


Selected ^{1}H NMR (400 MHz) dilution studies of compound **1** ($CDCl_3$).

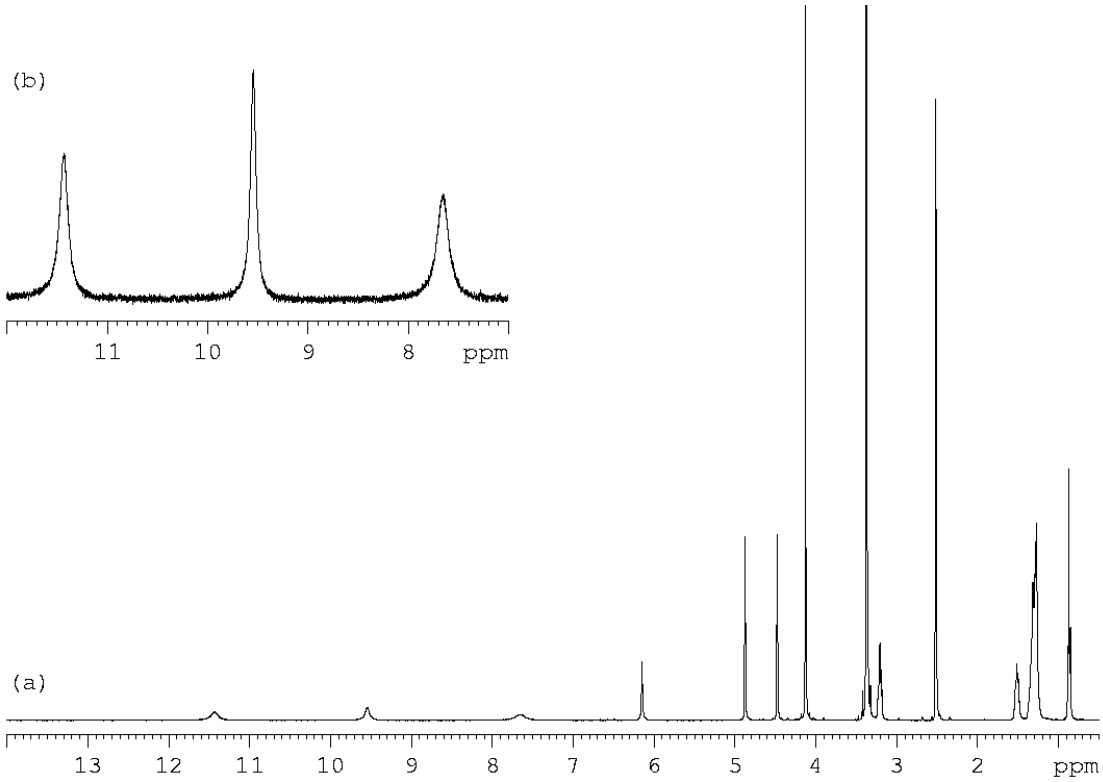
a) 13.3×10^{-3} mol^{-1}
b) 8.87×10^{-3} mol^{-1}
c) 6.65×10^{-3} mol^{-1}
d) 5.32×10^{-3} mol^{-1}
e) 4.43×10^{-3} mol^{-1}



^{1}H NMR spectrum (400 MHz) of acetyl ferrocene in $CDCl_3$ (~1.6 X 10^{-2} M) upon the addition of aliquots of DMSO-*d6*. (a) 0% DMSO-*d6*, (b) 10% DMSO-*d6*, (c) 20% DMSO-*d6*, (d) 30 % DMSO-*d6*. Referenced to TMS = 0 PPM.



^{1}H NMR spectrum (400 MHz) of **1** in $CDCl_3$ (~1.6 X 10^{-2} M) upon the addition of aliquots of DMSO-*d6*. (a) 0% DMSO-*d6*, (f) 30 % DMSO-*d6*. Referenced to TMS = 0 PPM.



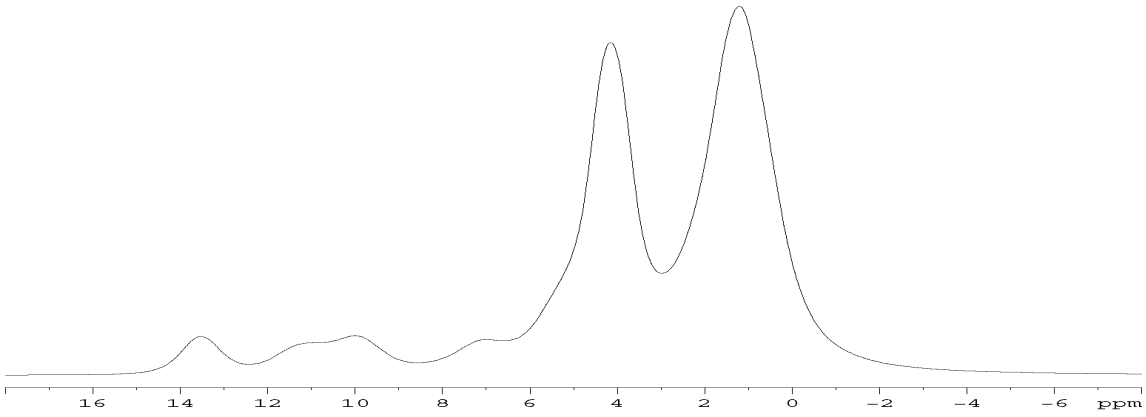
(a) ^{1}H NMR (400 MHz) of compound **1** in DMSO-d_6 (~1.6 X 10^{-2} M). (b) Expansion between 12-9 ppm)

(b) Solid-state NMR data

Solid-state ^{1}H NMR data was recorded on a Bruker Avance II+ spectrometer operating at Larmor frequencies of 850.27 MHz. The experiments were carried out using a commercial Bruker 2.5 mm double resonance MAS probe with spinning frequencies of 30 kHz, typical $\pi/2$-pulse lengths of 2 μs and recycle delays of 10 s. All spectra are referenced to solid tetrakis(trimethylsilyl)silane[1] and were collected at 320 K. ^{1}H-^{1}H dipolar double quantum (DQ) experiments were performed employing the compensated back-to-back (BaBa) recoupling sequence with an excitation time equal to one rotor period.[2] The States-TPPI method[3] was applied for phase sensitive detection in the t_1 dimension.

1. J. V. Muntean, L. M. Stock, R. E. Botto, *J. Magn. Reson.* **1998**, *76*, 540-542.
2. M. Feike, D. E. Demco, R. Graf, J. Gottwald, S. Hafner, H. W. Spiess, *J. Magn. Reson. A* **1996**, *122*, 214-221.

3. D. Marion, M. Ikura, R. Tschudin, A. Bax, *J. Magn. Reson.* **1989**, *85*, 393-399.

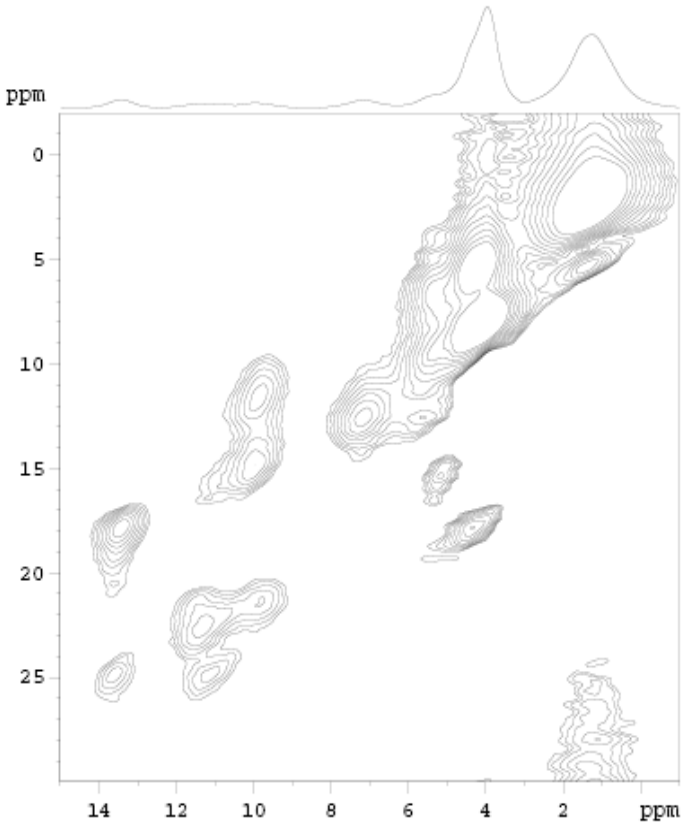


^{1}H MAS NMR spectrum of **1**

Observed shifts (ppm)	**assignment**
13.5(2)	H_a (ol-proton)
11.1(7)	H_b (inner NH-proton)
9.9(1)	H_c (outer NH-proton)
7.0(1)	H´ (aromatic proton)
4.1(6)	Cp-protons
1.2(2)	aliphatic sidechain

Table 1.

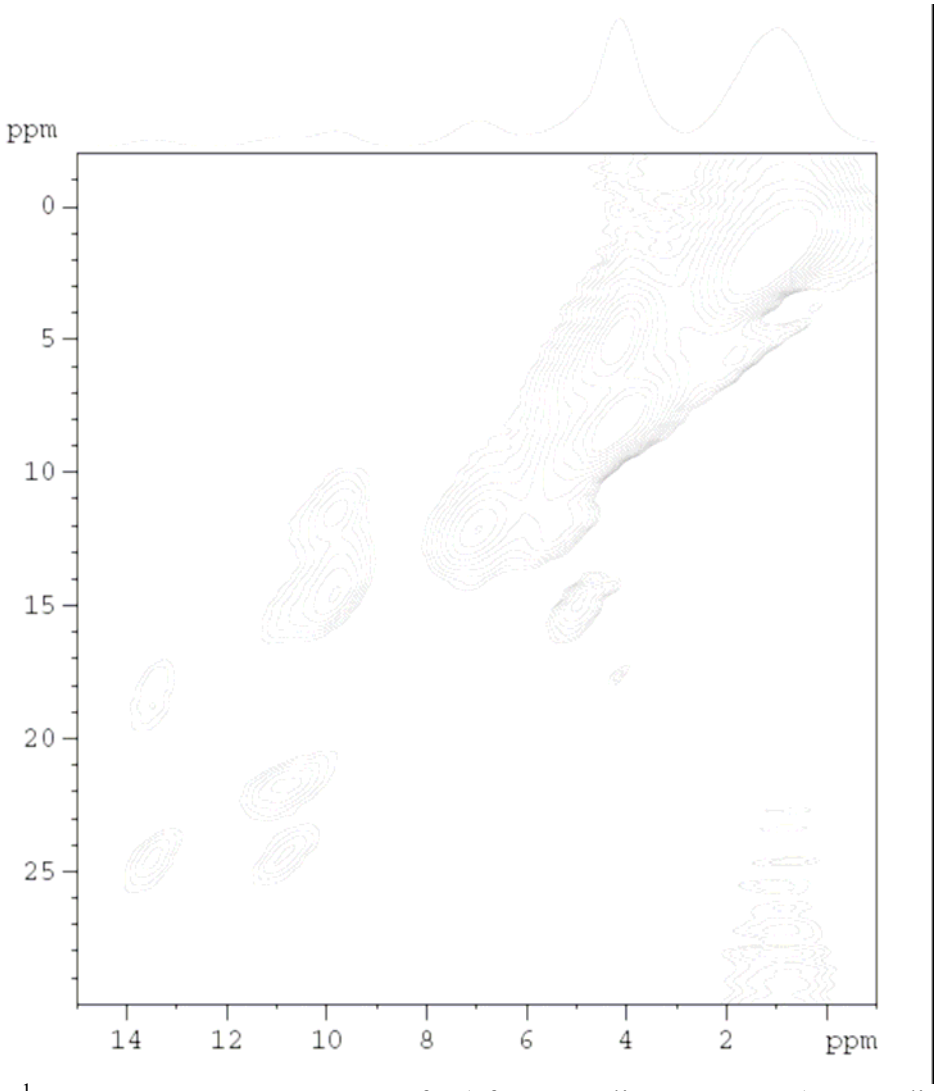
For protons that are involved in hydrogen-bonded structures, the ^{1}H chemical shift qualitatively depends on the strength of the hydrogen bond. Typically, ^{1}H chemical shifts in the range of 8-20 ppm are observed. Therefore, an inspection of the ^{1}H MAS spectrum of **1** reveals the formation of a dimeric species that is stabilized by hydrogen bonds. In order to analyze the presence of particular tautomers in **1**, we employed ^{1}H-^{1}H double-quantum (DQ) MAS NMR. Here, we use the fact that for short dipolar recoupling times the intensity of the observed DQ signal is proportional to D_{ij}^2 or r_{ij}^{-6}, respectively (D_{ij} is the dipolar coupling constant, r_{ij} the internuclear distance). Hence, the presence of strong DQ contact peaks at the shortest applicable dipolar recoupling time of one rotor period (τ_R = 33.3 μs) reflects nearest spatial proximities.



^{1}H-^{1}H DQ MAS NMR spectrum of **1** at $1t_R$ dipolar recoupling time.

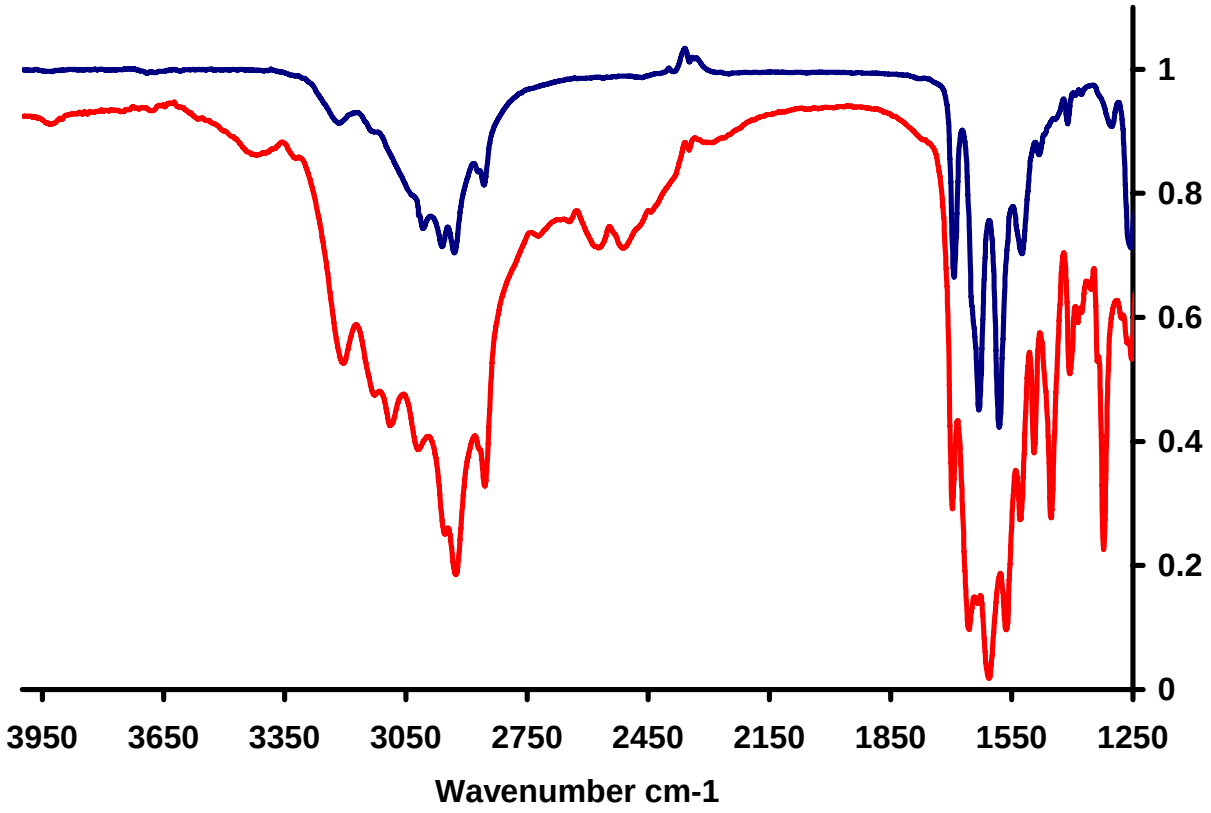
The DQ cross peak pattern observed for compound **1** is highly reminiscent of that previously reported for ureido-pyrimidinone moieties[4]. The presence of the characteristic signatures (*cross*peak between H_a and H_b protons and an *auto*peak of H_b protons as well as the *cross*peak between H_b and H_c protons) clearly evidences that the solid compound **1** is a mixture of both –one and –ol tautomers. Based on the intensities of the observed DQ signals, a slight excess of the –one tautomer is found in the nascent compound (approx. 52% –one / 48% –ol). However, upon prolonged annealing (at e.g. 391.5 K), the –one tautomer rearranges into the –ol form, which is illustrated by the corresponding DQ MAS NMR spectrum (see below).

4. I. Schnell, B. Langer, S. H. M. Söntjens, R. P. Sijbesma, M. H. P. van Genderen, H. W. Spiess, *Phys. Chem. Chem. Phys.* **2002**, *4*, 3750-3758.



^{1}H-^{1}H DQ MAS NMR spectrum of **1** (after annealing at 391.5 K) at $1t_R$ dipolar recoupling time.

4. IR data



FT-IR transmittance spectra of **1** (—) in chloroform (10mg in 1ml) and as a KBr disk (—)

5. Electrochemistry

All electrochemical experiments were performed using a CH Instruments 620A electrochemical workstation. The electrolyte solution (0.1 M) was prepared from recrystallised Bu_4NPF_6 using dry CH_2Cl_2 and DMSO. A three electrode configuration was used with a platinum disc working electrode, a platinum wire counter electrode and a Ag/AgCl reference electrode. The solution purged with nitrogen prior to recording the electrochemical data, and all measurements were recorded under a nitrogen atmosphere.