Electronic Supplementary Material (ESI) for Chemical Communications

Supporting information

Hydrogen bonded supramolecular polymers in moderately polar solvents

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Solvent	δ_a ($MPa^{0.5}$)	**1**	**2**	**3**	**4**
cyclohexane	0.2	G	I	I	I
toluene	2.4	G	G	G	V
chloroform	6.5	S	S	G	S
dichloromethane	8.8	I	S	G	S
butyl acrylate		I	I	G	I
methyl methacrylate		I	I	G	-
ethyl acetate	8.9	I	S	G	I
tetrahydrofuran	9.8	S	S	G	-
methylethyl ketone	10.3	S	-	V	-
acetone	12.5	S	-	I	-
dimethylformamide	17.8	S	S	S	S
acetonitrile	19	I	I	I	I
dimethylsulfoxide	19.3	S	S	S	S
ethanol	21.3	S	S	S	S
water	45.2	I	I	I	I

Table S1. Solubility data: samples (10mM) were prepared by stirring *at room temperature*. G: clear, homogeneous gel; V: clear, viscous solution; S: clear, fluid solution; I: insoluble. Solvents are arranged according to their Hansen solubility parameter ($\delta_a = \sqrt{\delta_p{}^2 + \delta_h{}^2}$), which combines contributions from polar (δ_p) and hydrogen bonding (δ_h) interactions.[1,2]

a) t = 0 min

b) t = 1 min

c) t = 8 min

Fig. S1 Photographs of solutions of **3** in chloroform/DMSO mixtures ([**3**] = 40 mM = 18 g/L), at various delays after inverting the vials. From left to right: 0, 1, 2, 3, 5% DMSO.

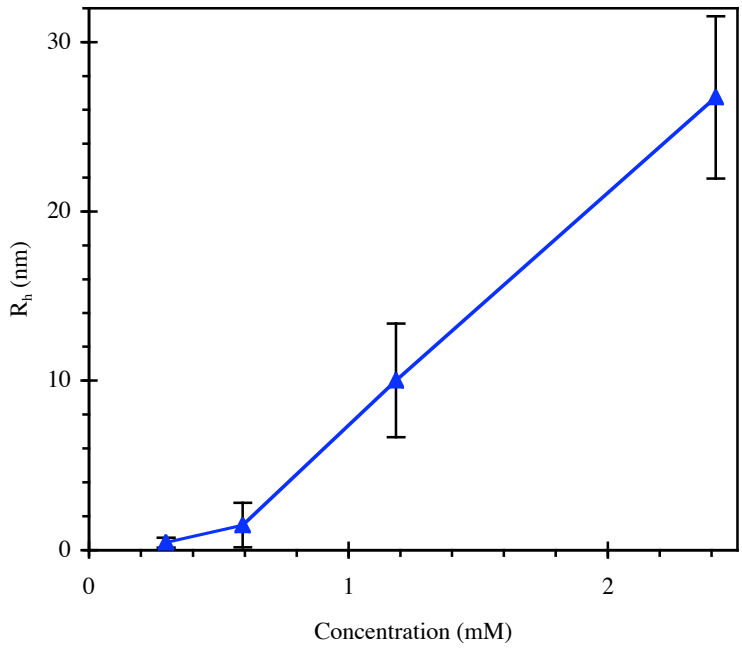


Fig. S2 Apparent hydrodynamic radius determined by dynamic light scattering for solutions of bis-urea **3** in ethyl acetate (25°C).

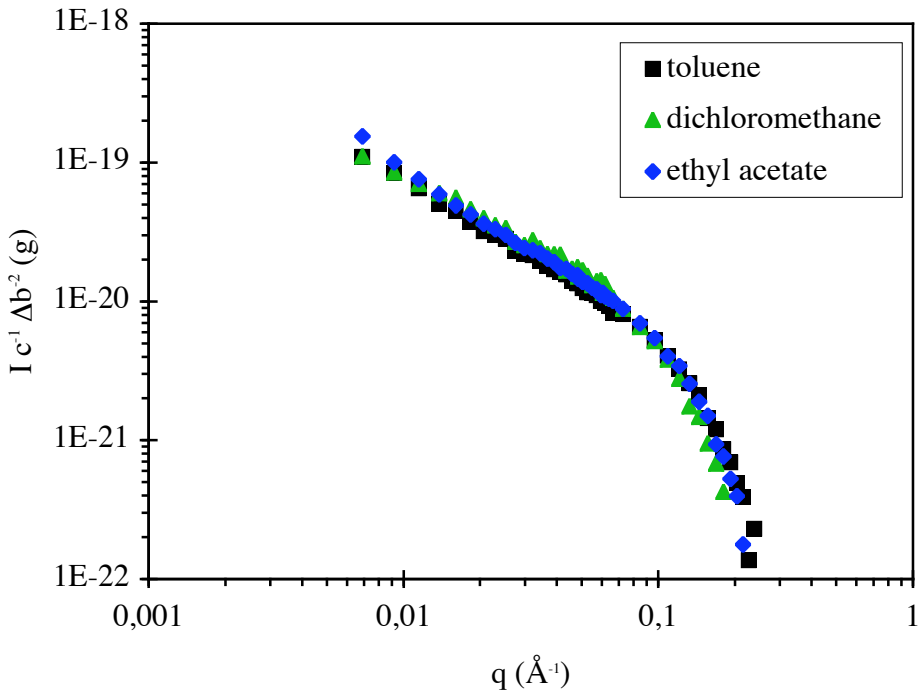


Fig. S3 SANS intensity, normalized by concentration (c) and specific contrast (Δb^2), versus scattering vector for 12 mM solutions of bis-urea **3** in d_8-toluene, d_2-dichloromethane or d_8-ethyl acetate (20°C).

Solvent	Δb^2 ($cm^2\ g^{-2}$)	diameter (Å)	linear density ($Å^{-1}$)
d_8-toluene	$1.84\ 10^{21}$	26	0.32
d_2-dichloromethane	$5.90\ 10^{20}$	31	0.37
d_8-ethyl acetate	$1.82\ 10^{21}$	28	0.36

Table S2. Calculated specific contrast for bis-urea **3** in several solvents and dimensions deduced from the fit of the curves in Fig. S3 by the form factor for infinitely long and rigid isolated fibrillar species with a circular cross-section and a uniform scattering length density profile.

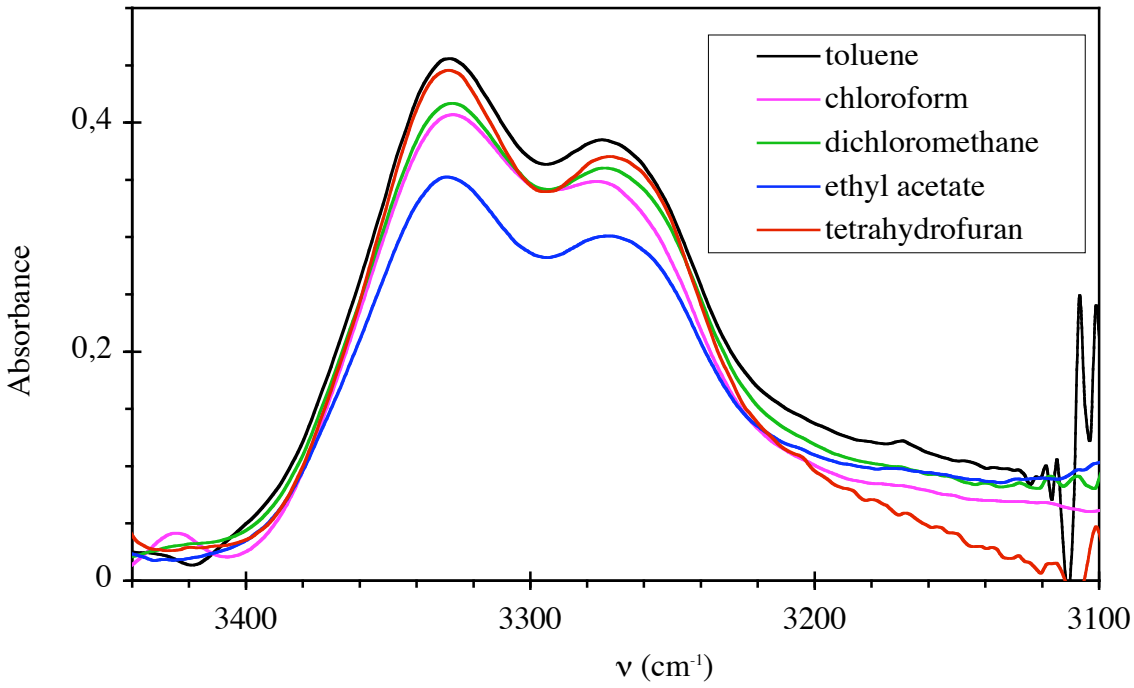


Fig. S4 FTIR spectra for solutions of **3** in several solvents at 10 mM at 20°C.

Experimental Section:

SANS. Measurements were made at the LLB (Saclay, France) on the Pace instrument, at two distance-wavelength combinations to cover the 6.9 10^{-3} to 0.37 $Å^{-1}$ q-range, where the scattering vector q is defined as usual, assuming elastic scattering, as $q = (4\pi/\lambda)\sin(\theta/2)$, where θ is the angle between incident and scattered beam. Data were corrected for the empty cell signal and the solute and solvent incoherent background. A light water standard was used to normalize the scattered intensities to cm^{-1} units.

Viscosimetry. Solutions were prepared under stirring at room temperature, at least 1 day prior to use. Capillary viscosity was measured at 25 ± 0.1°C with an automatic Anton-Paar AMVn viscometer (capillary internal diameter 1.8 mm ; ball diameter 1.5 mm). The measurements were performed with an angle of 50°, and repeated 6 times.

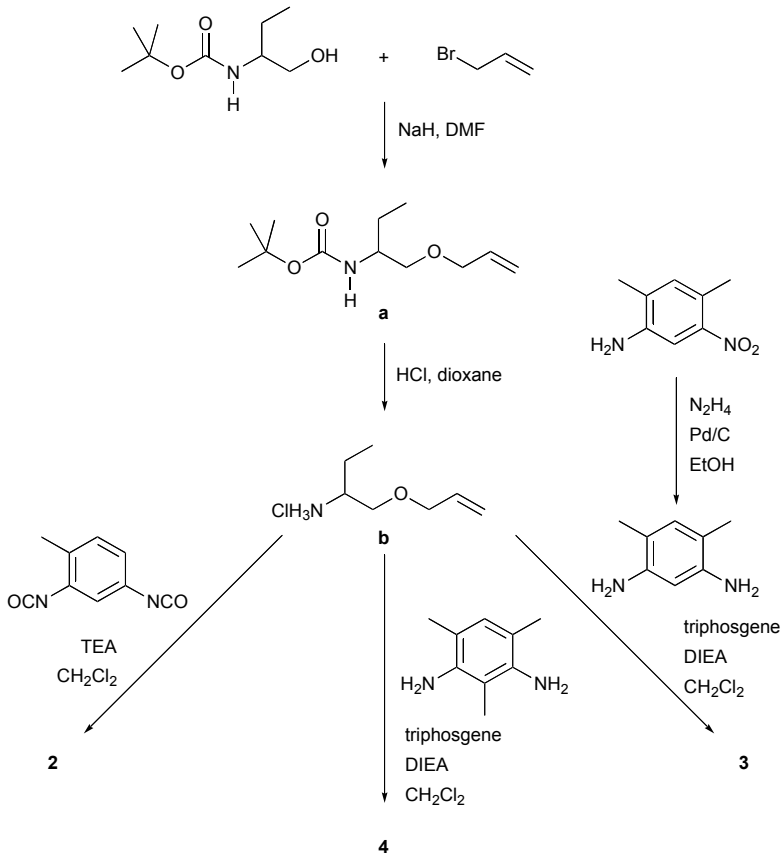
DLS. Dynamic Light Scattering experiments were undertaken using a Malvern Zetasizer Nano S90 from Malvern using a 5 mW He-Ne laser at 633 nm and a thermoelectric Peltier temperature controller. The measurements were made at a scattering angle of 90°.

FTIR. Infrared spectra were recorded on a Nicolet Avatar 320 spectrometer in KBr cells of 0.1 cm path length at 20°C.

ITC. Heats of dissociation were measured using a MicroCal VP-ITC titration microcalorimeter. The sample cell (1.435 mL) was filled with ethyl acetate. A 4 mM bis-urea **3** solution in ethyl acetate was placed in a 295 μL continuously stirred (310 rpm) syringe. A first 2 μL aliquot was injected, without taking into account the observed heat, to remove the effect of solute diffusion across the syringe tip during the equilibration period. Subsequent aliquots of the solution (4 μL) were automatically injected into the sample cell every 240 s, until the syringe was empty.

Synthesis. Chemicals and solvents (technical grade) were purchased from Acros Organics, TCI, Aldrich or Alfa Aesar and used as received unless otherwise stated. Solvents were dried on a solvent purification system (MBRAUN). NMR spectra were recorded on a Brüker AC200 (^{1}H, 200 MHz; ^{13}C, 50.31 MHz) or a Brüker AC250 (^{1}H, 250 MHz; ^{13}C, 62.89 MHz) spectrometer at 20°C and referenced using the residual solvent resonance (m = multiplet, s =

singlet, d = doublet, t = triplet, q = quadruplet, dd = doublet of doublets, ddt = doublet of doublet of triplets, br s = broad singlet). Elemental analyses were performed by the "Service de Microanalyses", SIARE (Service Interdisciplinaire d'Aide à la Recherche et l'Enseignement), UPMC Paris. (±)-2-(*N-tert*-Butoxycarbonylamino)butan-1-ol was prepared according to a literature procedure.[3]



Scheme S1

2-allyloxy-1-(*N-tert*-Butoxycarbonylamino-1-ethylethane (a). A solution of (±)-2-(*N-tert*-butoxycarbonylamino)butan-1-ol[3] (50 mmol) in dimethylformamide (50 mL) was cooled in an ice bath and NaH (150 mmol, 60% dispersion in mineral oil) was slowly added. After stirring 15 minutes at room temperature, allyl bromide (53 mmol) was added dropwise. After stirring overnight, the mixture was cooled in an ice bath and saturated NH_4Cl (50 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (3 x 60 mL), the combined organics were then dried over anhydrous $MgSO_4$ and filtered. The solvent was removed under reduced pressure. The crude product was purified by silica gel chromatography with pentane / ethyl acetate (8/2) mixture as eluent to give a colorless oil. Yield = 67 %. **^{1}H-NMR** (200 MHz,

$CDCl_3$): δ 0.91 (t, ^3J(HH) = 7.5 Hz, 3H, CH_2CH_3), 1.35-1.67 (m, 11H, $C(CH_3)_3$ and CH_2CH_3), 3.35-3.46 (m, 2H, $CH_2CHNHBoc$), 3.59 (br s, 1H, CHNHBoc), 3.93-4.00 (m, 2H, $CH_2CH=CH_2$), 4.68 (s, 1H, NHBoc), 5.12-5.31 (m, 2H, $CH_2=CH$), 5.88 (ddt, ^3J(HH) = 17.3 Hz, ^3J(HH) = 10.4 Hz, ^3J(HH) = 5.4 Hz, 1H, $CH_2=CH$). **$^{13}C\{^1H\}$ Jmod NMR** (50 MHz, $CDCl_3$): δ 10.6 (CH_3), 25.2 ($C(CH_3)_3$), 28.5 (CH_3), 51.9 (CHNHBoc), 71.6 (CH_2), 72.2 (CH_2), 117.0 ($CH_2=CH$), 134.8 ($CH_2=CH$), 155.9 (C=O). **HRMS (ESI)**: $[M+Na]^+$ 252.1576, calcd for $C_{12}H_{23}NO_3Na$ 252.1570.

2-allyloxy-1-amino-1-ethylethane hydrochloride (b). A solution of N-Boc-O-allyl-aminoalcohol **a** (40 mmol) in 1,4-dioxane (140 mL) was cooled in an ice bath and HCl 37% $_{(aq)}$ (400 mmol, 10 eq, 65 mL) was added dropwise. After stirring overnight at room temperature, the volatiles were evaporated under reduced pressure to obtain a colorless solid. Yield = 94 %. **^{1}H-NMR** (200 MHz, d_6-DMSO): δ 0.91 (t, J^3(HH) = 7.5 Hz, 3H, CH_2CH_3), 1.50-1.66 (m, 2H, CH_2CH_3), 3.09-3.22 (m, 1H, $CHNH_3^+$), 3.40-3.59 (m, 2H, $CH_2CHNH_3^+$), 3.92-4.10 (m, 2H, $CH_2CH=CH_2$), 5.14-5.23 (m, 1H, $CH_2=CH$), 5.32 (ddd, J^3(HH) = 17.3 Hz, J^2(HH) ≈ J^4(HH) = 1.8 Hz, 1H, $CH_2=CH$), 5.90 (ddt, J^3(HH) = 17.3 Hz, J^3(HH) = 10.4 Hz, J^3(HH) = 5.4 Hz, 1H, $CH_2=CH$), 8.04 (s, 3H, NH_3^+). **$^{13}C\{^1H\}$ Jmod NMR** (50 MHz, d_6-DMSO): δ9.7 (CH_3), 22.4 (CH_2CH_3), 51.7 ($CHNH_3^+$), 68.6 (CH_2), 71.3 (CH_2), 117.1 ($CH_2=CH$), 134.7 ($CH_2=CH$). **HRMS (ESI)**: $[M+Cl]^+$ 130.1222, calcd for $C_7H_{16}ON$ 130.1226.

Bisurea 2. A dry and argon flushed 100 mL flask, equipped with a magnetic stirrer and a septum, was charged with toluene diisocyanate (850 mg, 4.9 mmol) and dry CH_2Cl_2 (30 mL). A solution of 2-allyloxy-1-amino-1-ethylethane hydrochloride (1.773 g, 10.8 mmol) in dry CH_2Cl_2 (20 mL) was added via a canula to the diisocyanate solution. NEt_3 (2.7 mL, 19.6 mmol) was then added and the mixture was stirred overnight at room temperature. The organic phase was washed with saturated K_2CO_3 (40 mL) and water (3 x 40 mL). The organic phase was dried with anhydrous $MgSO_4$, filtered and evaporated *in vacuo*. The crude solid was recrystallized in acetonitrile to yield (1.264 g, 2.9 mmol) as a white solid. Yield = 60 %. The compound was stored in the dark and under vacuum in order to avoid slow degradation (otherwise, color changed from white to yellow over a few months). **^{1}H-NMR** (200 MHz, d_6-DMSO): δ 0.86 (t, ^3J(HH) = 7.2 Hz, 3H, CH_2CH_3), 0.89 (t, ^3J(HH) = 7.2 Hz, 3H, CH_2CH_3), 1.31-1.66 (m, 4H, CH_2CH_3), 2.08 (s, 3H, CH_3Ph), 3.26-3.46 (m, 4H, CH_2CHNH), 3.58-3.75 (m, 2H, CHNH), 3.94-3.98 (m, 4H, $CH_2CH=CH_2$), 5.12-5.32 (m, 4H, $CH_2=CH$), 5.79-6.00

(m, 3H, 2 x CH_2=C*H* and one NH), 6.51 (d, ^3J(HH) = 8.4 Hz, 1H, NH), 6.92 (d, ^3J(HH) = 8.2 Hz, 1H, CH arom.), 7.10 (dd, ^3J(HH) = 8.2 Hz, ^4J(HH) = 2.0 Hz, 1H, CH arom.), 7.57 (s, 1H, NH), 7.76 (d, ^4J(HH) = 2.0 Hz, 1H, CH arom.), 8.34 (s, 1H, NH). **^{13}C{^{1}H} Jmod NMR** (50 MHz, d_6-DMSO): δ 10.3 (CH_2CH_3), 10.4 (CH_2CH_3), 17.3 (CH_3Ph), 24.7 (CH_2CH_3), 50.0 (*C*HNH), 50.1 (*C*HNH), 71.2 (CH_2), 71.6 (CH_2), 109.6 (CH arom.), 111.2 (CH arom.), 116.4 (CH_2=CH), 116.5 (CH_2=CH), 118.7 (C arom.), 129.9 (CH arom.), 135.2 (CH_2=CH), 138.3 (C arom.), 138.6 (C arom.), 154.9 (C=O), 155.0 (C=O). **HRMS (ESI)**: $[M+Na]^+$ 455.2625, calcd for $C_{23}H_{36}O_4N_4Na$ 455.2629. **Anal.** Calcd for $C_{23}H_{36}O_4N_4$ (432.56): C, 63.86; H, 8.39; N, 12.95. Found: C, 63.93; H, = 8.57; N, 12.78.

1,3-diamino-4,6-dimethylbenzene. The synthesis was adapted from classic nitroarene hydrogenation. A 1L flask, equipped with a magnetic stirrer, was charged with 1-nitro-3-amino-4,6-dimethylbenzene (Apollo Scientific) (4.98 g, 30 mmol), Pd/C (10 wt. % loading) (500 mg) and ethanol (500 mL). A solution of hydrazine monohydrate 64-65% (24 mL, 500 mmol) was slowly added. After stirring 48 hours at refluxed temperature, the mixture was cooled and filtered through celite. The celite was washed with dichloromethane. The solvents were removed under reduced pressure. The crude product was solubilized in ethylacetate (200 mL), then washed with water (3x100 mL). The organic phase was dried over anhydrous $MgSO_4$ and filtered. The solvent was removed under reduced pressure to obtain the expected product as a white solid. Yield = 75%. **^{1}H NMR** (200 MHz, $CDCl_3$): δ 6.73 (s, 1H, Ar), 6.08 (s, 1H, Ar), 3.37 (br s, 4H, NH_2), 2.07 (s, 6H, CH_3). **^{13}C{^{1}H} Jmod NMR** (50 MHz, $CDCl_3$): δ 16.4 (CH_3), 102.5/132.5 (Ar, *C*H), 113.0 (Ar, *C*-CH_3), 143.3 (Ar, *C*-NH_2).

Bisurea 3. The synthesis was adapted from literature.[4,5] A dry and argon flushed 250 mL three-necked flask, equipped with a magnetic stirrer and a septum, was charged with triphosgene (870 mg, 2.9 mmol) and dry CH_2Cl_2 (50 mL). A solution of 4,6-diamino-1,3-*m*-xylene (600 mg, 4.4 mmol) and diisopropylethylamine (2.2 mL, 8.8 mmol) in dry CH_2Cl_2 (20 mL) was added with a syringe, with a pump controller at a low rate (5 mL per hour), at room temperature. Once the addition completed, the reaction mixture was stirred at room temperature during 1 hour. A solution of 2-allyloxy-1-amino-1-ethylethane hydrochloride **b** (1.6 g, 9.7 mmol) and diisopropylethylamine (2.2 mL, 8.8 mmol) in dry CH_2Cl_2 (15 mL) was added with a syringe at room temperature. After stirring during 48h at room temperature, the reaction mixture was evaporated *in vacuo* and recrystallized in acetonitrile to yield (1.08 g,

2.4 mmol) of a white solid. Yield = 55 %. The compound was stored in the dark and under vacuum in order to avoid slow degradation (otherwise, color changed from white to yellow over a few months). **^{1}H-NMR** (200 MHz, d_6-DMSO): δ0.88 (t, ^3J(HH) = 7.3 Hz, 6H, CH_2CH_3), 1.31-1.64 (m, 4H, CH_2CH_3), 2.06 (s, 6H, CH_3Ph), 3.27-3.45 (m, 4H, CH_2CHNH), 3.58-3.73 (m, 2H, CHNH), 3.96 (d, ^3J(HH) = 5.2 Hz, 4H, $CH_2CH=CH_2$), 5.15 (m, 2H, *cis*-CH_2=CH ^3J(HH) = 10.4 Hz), 5.27 (m, 2H, *trans*-CH_2=CH ^3J(HH) 17.2 Hz), 5.80-6.00 (m, 2H, $CH_2=CH$), 6.29 (d, ^3J(HH) = 8.4 Hz, 2H, NH), 6.84 (s, 1H, CH arom.), 7.53 (s, 1H, NH), 8.05 (s, 1H, CH arom.). **^{13}C{^{1}H} Jmod NMR** (50 MHz, d_6-DMSO): δ10.4 (CH_2CH_3), 17.3 (CH_3Ph), 24.8 (CH_2CH_3), 50.2 (CHNH), 71.2 (CH_2), 71.7 (CH_2), 114.9 (CH arom.), 116.5 (CH_2=CH), 121.6 (C arom.), 131.2 (CH arom.), 135.3 ($CH_2=CH$), 135.8 (C arom.), 155.1 (C=O). **HRMS (ESI)**: $[M+H]^+$ 447.2970, calcd for $C_{24}H_{39}O_4N_4$ 447.2966. **Anal**. Calcd for $C_{24}H_{38}O_4N_4$ (446.58): C, 64.55; H, 8.58; N, 12.55. Found: C, 65.84; H, 8.99; N, 11.70.

Bisurea 4. The synthesis was adapted from literature.[4,5] A dry and argon flushed 250 mL three-necked flask, equipped with a magnetic stirrer and a septum, was charged with triphosgene (870 mg, 2.9 mmol) and dry CH_2Cl_2 (50 mL). A solution of 1,3-diamino-2,4,6-trimethylbenzene (660 mg, 4.4 mmol) and diisopropylethylamine (2.2 mL, 8.8 mmol) in dry CH_2Cl_2 (20 mL) was added with a syringe pump at 5 mL per hour, at room temperature. Once the addition was completed, the reaction mixture was stirred at room temperature during 1 hour. A solution of 2-allyloxy-1-amino-1-ethylethane hydrochloride (1.6 g, 9.7 mmol) and diisopropylethylamine (2.2 mL, 8.8 mmol) in dry CH_2Cl_2 (15 mL) was added with a syringe at room temperature. After stirring during 48h at room temperature, the reaction mixture was evaporated *in vacuo* and the solid obtained was recrystallized in acetonitrile to yield (1.015 g, 2.2 mmol) of a white solid. Yield = 50 %. The compound was stored in the dark and under vacuum in order to avoid slow degradation (otherwise, color changed from white to yellow over a few months). **^{1}H-NMR** (200 MHz, d_6-DMSO): δ 0.87 (t, ^3J(HH) = 7.3 Hz, 6H, CH_2CH_3), 1.23-1.62 (m, 4H, CH_2CH_3), 1.98 (s, 3H, CH_3Ph), 2.09 (s, 6H, CH_3Ph), 3.20-3.45 (m, 4H, CH_2CHNH), 3.58-3.74 (m, 2H, CHNH), 3.95 (d, ^3J(HH) = 5.0 Hz, 4H, $CH_2CH=CH_2$), 5.12-5.30 (m, 4H, CH_2=CH), 5.78-5.98 (m, 4H, $CH_2=CH$ and NH), 6.87 (s, 1H, CH arom.), 7.40 (s, 1H, NH). **^{13}C{^{1}H} NMR** (50 MHz, d_6-DMSO): δ 10.4 (CH_2CH_3), 13.6 (CH_3Ph), 18.0 (CH_3Ph), 24.9 (CH_2CH_3), 50.4 (CHNH), 71.1 (CH_2), 72.0 (CH_2), 116.4 (CH_2=CH), 128.3 (CH arom.), 133.3 (C arom.), 133.9 (C arom.), 135.3 ($CH_2=CH$), 135.4 (C arom.), 156.1 (C=O).

HRMS (ESI): $[M+H]^+$ 461.3124, calcd for $C_{25}H_{41}O_4N_4$ 461.3122. **Anal**. Calcd for $C_{25}H_{40}O_4N_4$ (460.61): C, 65.19; H = 8.75; N = 12.16. Found: C, 64.89; H, 8.89; N, 12.11.

References:

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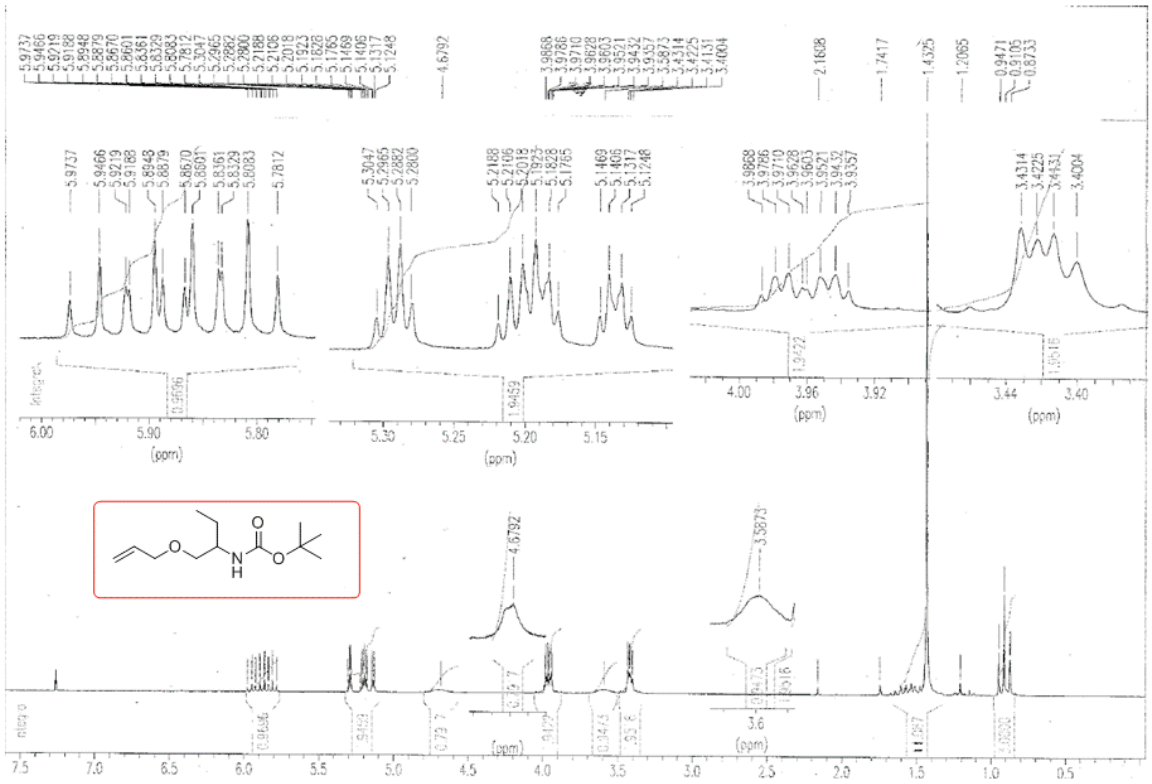
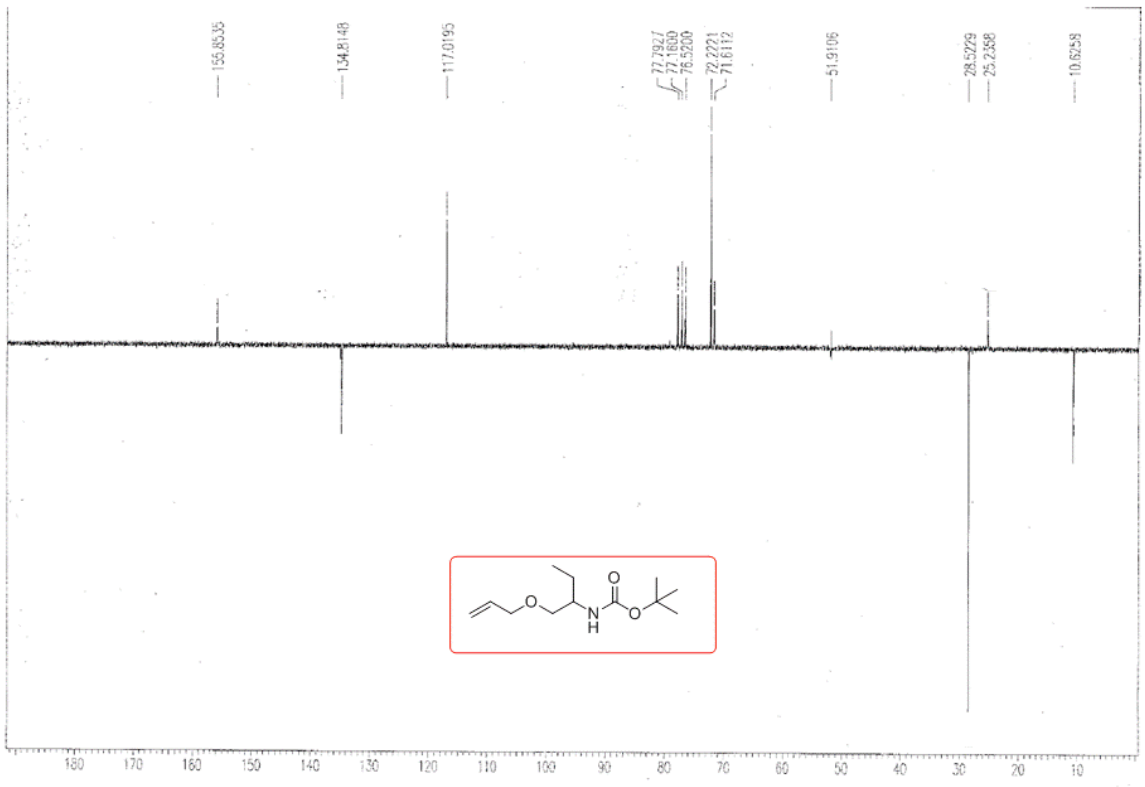
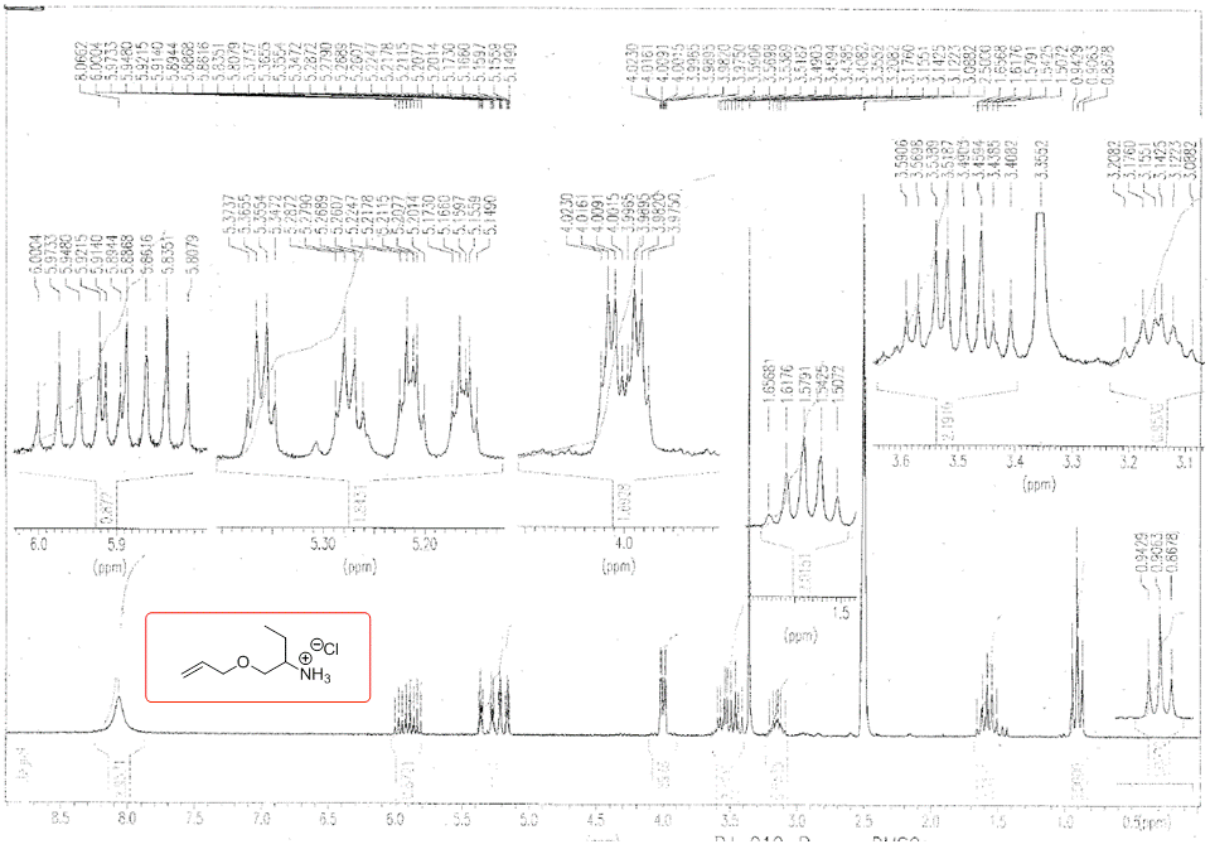
Compound a, ^{1}H-NMR, 200 MHz, $CDCl_3$



Compound a, ^{13}C {^{1}H} Jmod-NMR, 50 MHz, $CDCl_3$



Compound b, ^{1}H-NMR, 200 MHz, DMSO d^{6}



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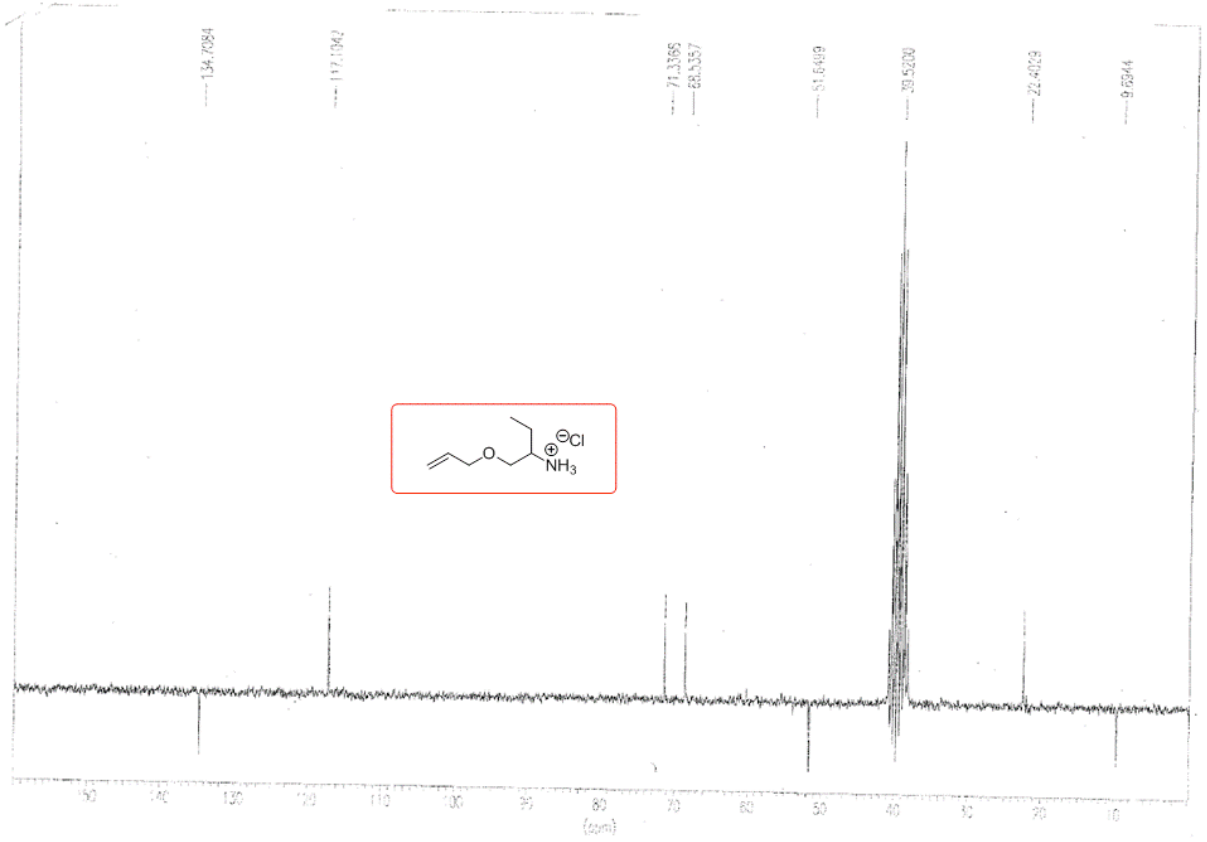
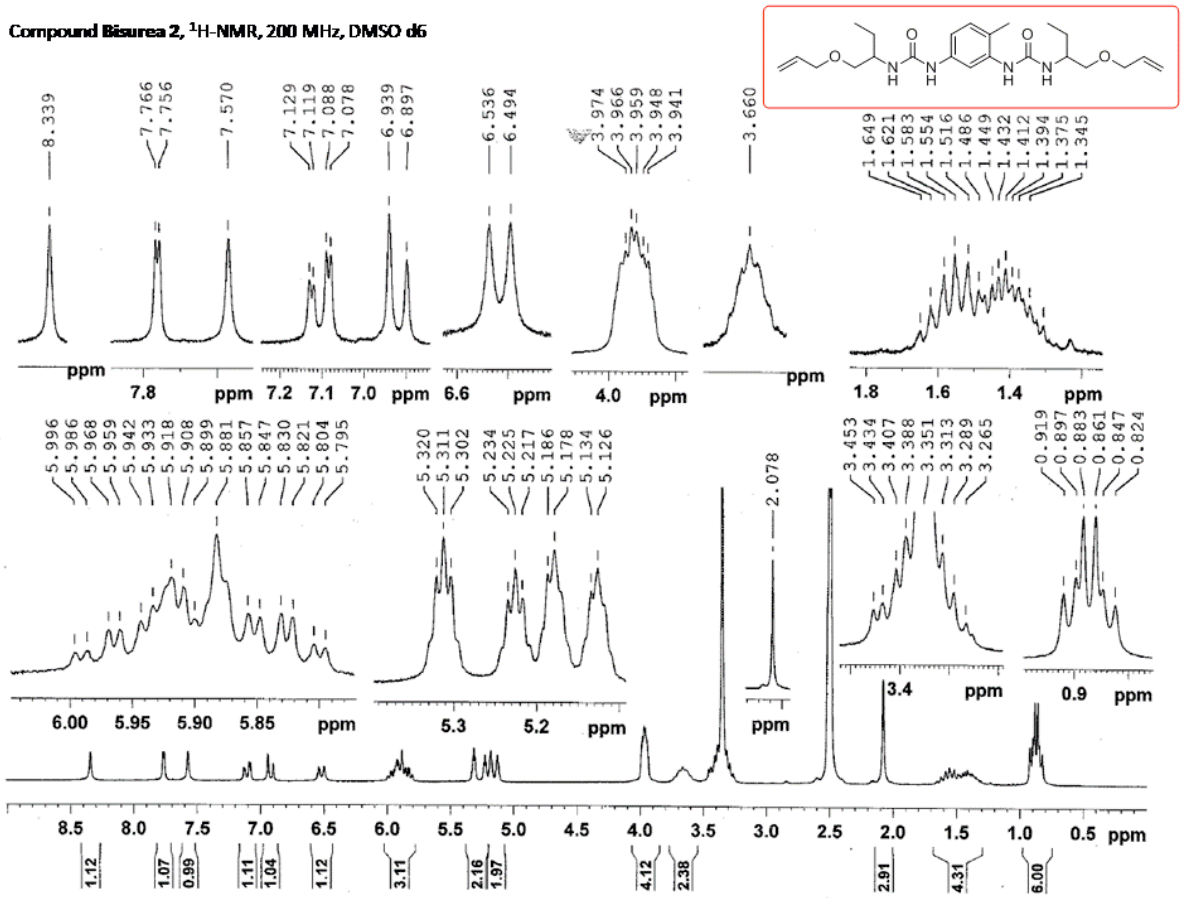


Compound Bisurea 2, ^{1}H-NMR, 200 MHz, DMSO d6



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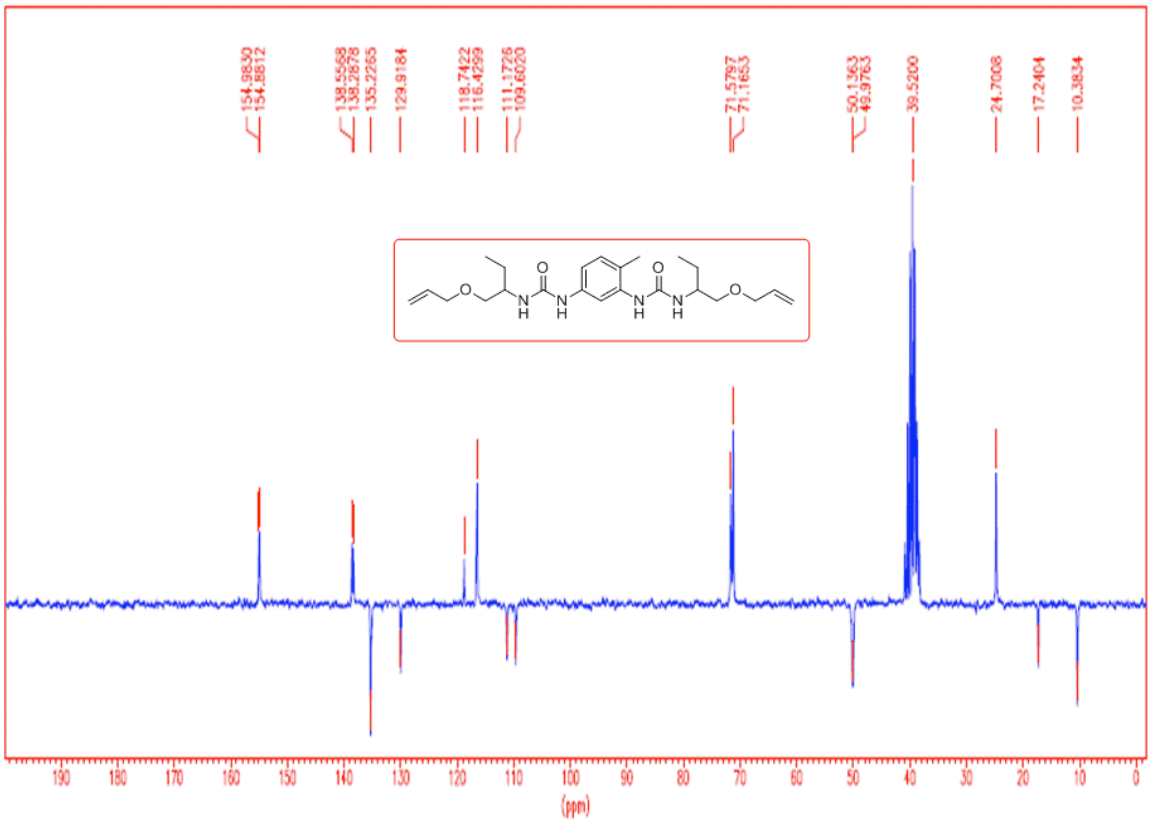
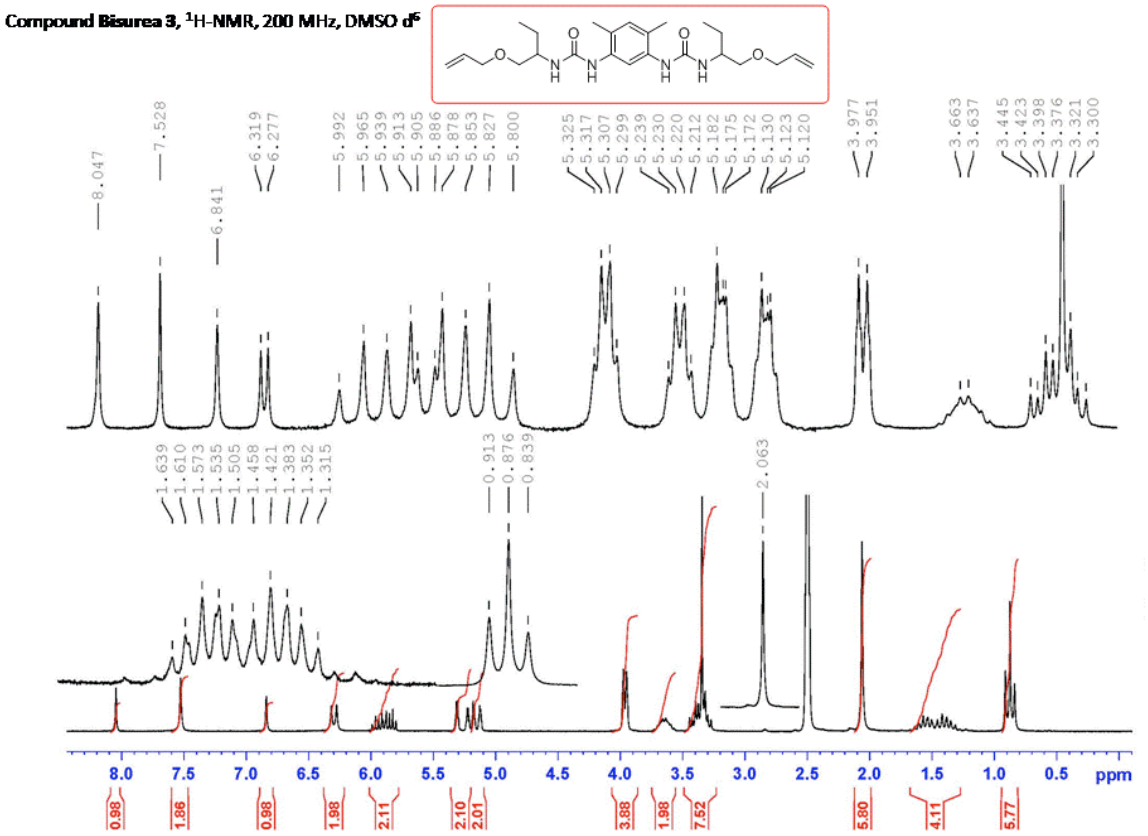
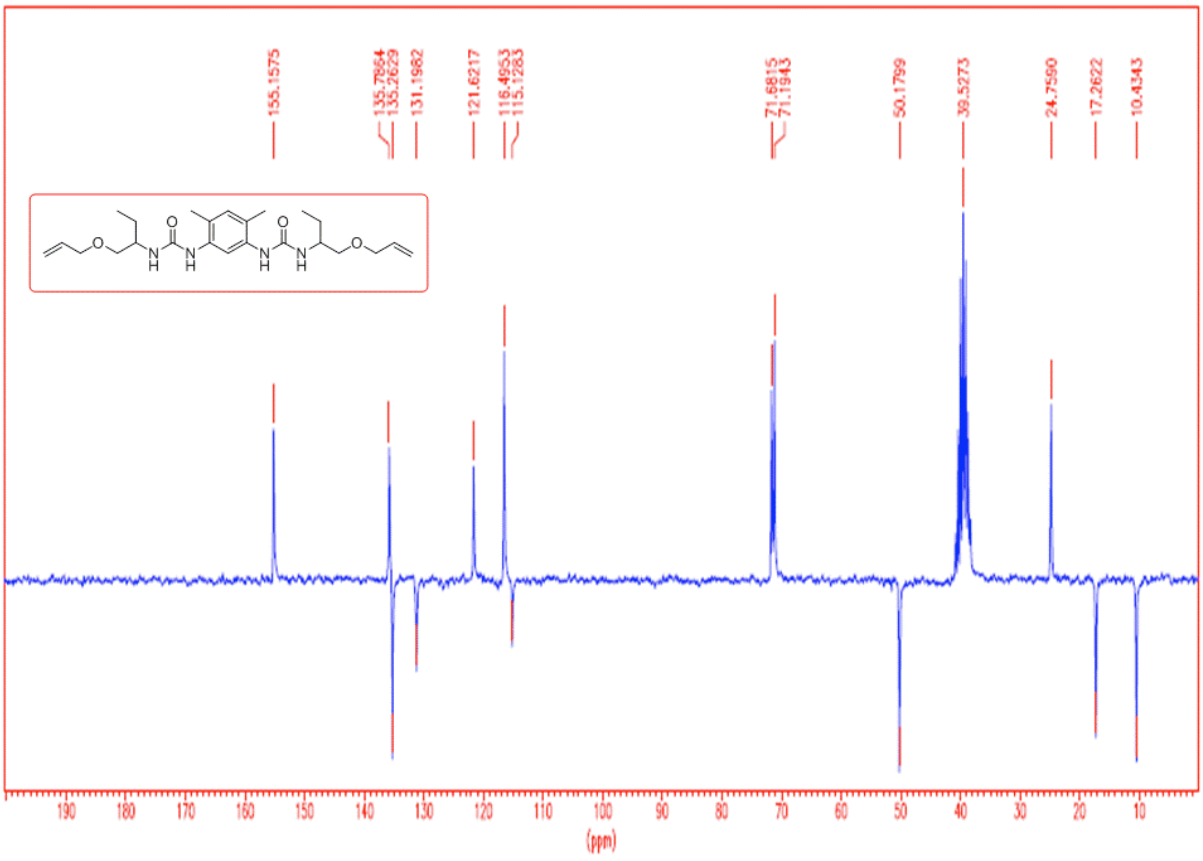


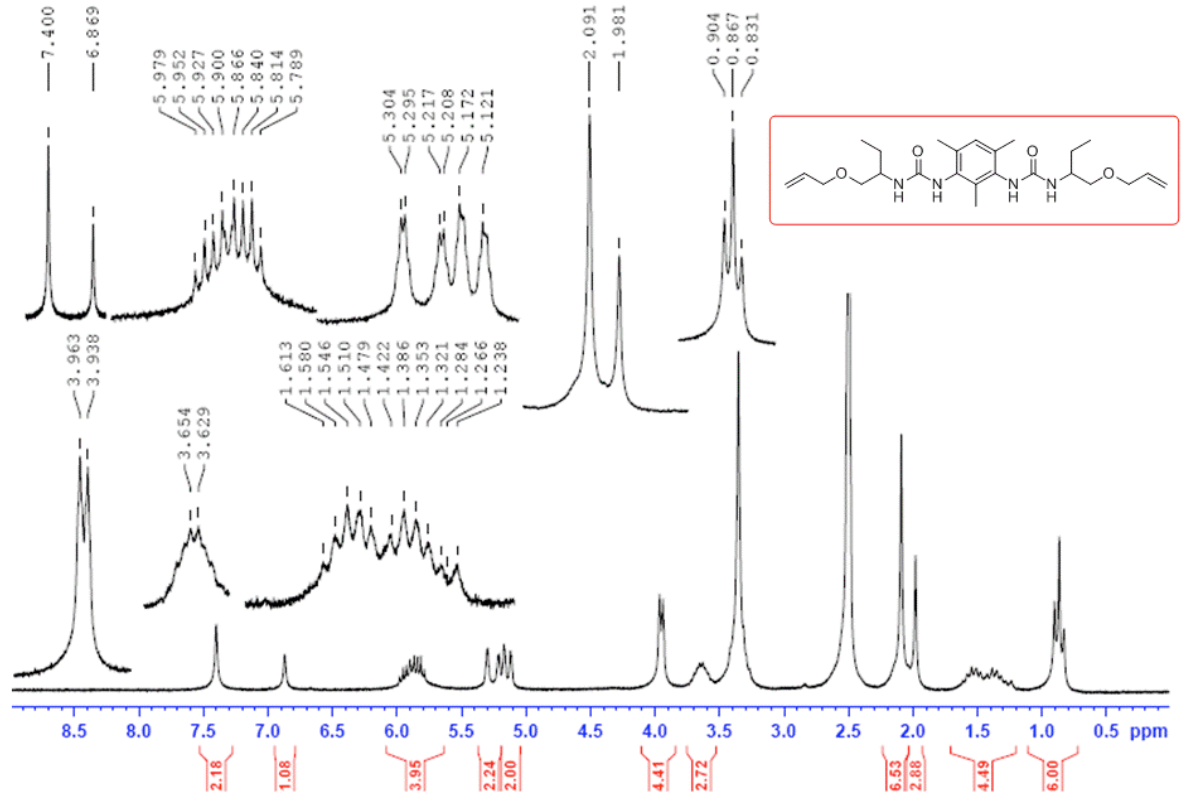
Compound Bisurea 3, ^{1}H-NMR, 200 MHz, DMSO d^{6}



Compound Bisurea 3, ^{13}C {^{1}H} Jmod -NMR, 50 MHz, DMSO d^{6}



Compound Bisurea 4, ^{1}H-NMR, 200 MHz, DMSO d^{6}



Compound Bisurea 4, ^{13}C {^{1}H} -NMR, 50 MHz, DMSO d6