

Supporting Information for

Rigid Urea and Self-healing Thiourea Ethanolamine Monolayers

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1. Synthesis

1.1 Synthesis of 1-dodecyl-3-(2-hydroxyethyl)urea (1)¹

Tridecanoic acid (0.86 g, 4.00 mmol), triethylamine (1.0 mL, 7.2 mmol) and diphenylphosphoryl azide (0.95 mL, 4.4 mmol) were dissolved in dry toluene (20 mL). The solution was refluxed for 3 h. Then the solution was cooled to 0 °C and ethanolamine (0.24 mL, 4.00 mmol) was added. The mixture was stirred overnight at 20 °C and then mixed with 70 mL of CH₂Cl₂ to be extracted with 100 mL of water containing 10 mL of NH₄OH (aq., 25%). The water phase was washed twice with 70 mL of CH₂Cl₂. After drying over MgSO₄, the organic solvents were evaporated and the crude product was purified by silica gel column (95 % CH₂Cl₂, 5% MeOH). A white powder (440 mg, 1.62 mmol, 40%) was obtained.

$R_f = 0.17$ (95% CH₂Cl₂, 5% MeOH) ¹H NMR (500 MHz, Methanol-d₄) δ 3.67 (t, $J = 5.3$ Hz, 2H), 3.58 (s, 2H), 3.46 (s, 2H), 1.65 – 1.47 (m, 2H), 1.30 (s, 18H), 0.90 (t, $J = 7.0$ Hz, 3H). ¹³C NMR (126 MHz, MeOD) δ 161.47 (s), 62.66 (s), 43.46 (s), 41.06 (s), 33.09 (s), 32.15 – 29.47 (m), 27.98 (s), 14.44 (s).

IR (cm⁻¹): 3340, 3317, 3030, 2955, 2921, 2849, 1619, 1591, 1462, 1268, 1057, 620 HRMS (ESI+) m/z calcd for C₁₅H₃₃N₂O₂ [M+H]⁺ 273.2536 found 273.2532

1.2. Synthesis of 1-dodecyl-3-(2-hydroxyethyl)thiourea (2)

Dodecyl isothiocyanate was first synthesized by variation of a procedure of Meijer et al.² DCC (2.9 g, 17 mmol) and CS₂ (7.20 mL, 119 mmol) were dissolved in dry diethyl ether (40 mL). Dodecyl amine (3.2 g, 17 mmol) was added at 0 °C. Then the mixture stirred overnight at room temperature. The precipitated solid was filtered off and washed with 60 mL of dry diethyl ether. The residual solvent was removed under reduced pressure and the isothiocyanate was used without further purification.

Ethanolamine (0.23 mL, 3.8 mmol) and triethylamine (0.61 mL, 4.37 mmol) were dissolved in dry THF (40 mL). Dodecyl isothiocyanate (1.0 mL, 3.8 mmol) was added dropwise at 0 °C. After stirring at 20 °C for 3.5 h, the mixture was added to CH₂Cl₂ (70 mL) to be extracted with 100 mL of water containing 10 mL of NH₄OH (aq., 25%). The water phase was washed twice with 70 mL of CH₂Cl₂. After drying over MgSO₄, the organic solvents were evaporated and the crude product was purified by silica gel column (95 % CH₂Cl₂, 5% MeOH). The product was recrystallized from dioxane/pentane (1:1) at 8 °C overnight. A white powder (850 mg, 2.95 mmol, 77%) was obtained.

$R_f = 0.28$ (95 % CH₂Cl₂, 5% MeOH), ¹H NMR (500 MHz, Methanol-d₄) δ 3.67 (t, $J = 5.3$ Hz, 2H), 3.58 (s, 2H), 3.46 (s, 2H), 1.65 – 1.47 (m, 2H), 1.30 (s, 18H), 0.90 (t, $J = 7.0$ Hz, 3H). ¹³C NMR (126 MHz, MeOD) δ 183.84, 61.82, 47.43, 45.39, 33.09, 30.79, 30.79, 30.49, 30.20, 27.99, 23.75, 14.45. IR (cm⁻¹):

¹ K. Dreger, B. Zou, Z. Mu, H. J. Galla, L. Chi, H. Fuchs, H. J. Schäfer, *Langmuir* **2006**, *22*, 1619–1625.

² U. Boas, A. J. Karlsson, B. F. M. de Waal, and E. W. Meijer, *J. Org. Chem.* **2001**, *66*, 2136–2145.

3293, 3233, 3071, 2918, 2849, 1565, 1471, 1461, 1294, 1276, 1255, 1210, 1163, 1059, 1034, 728, 650
HRMS (ESI+) m/z calcd for $C_{15}H_{33}N_2OS$ $[M+H]^+$ 289.2308 found 289.2305.

1.3. Synthesis of *N*-(2-hydroxyethyl)heptadecanamide (3)

Following a procedure of Quan and al.³ tetradecanoic acid (1.6 g, 5.9 mmol), pyridine (0.62 mL, 7.7 mmol) and methyl chloroformate (0.46 mL, 5.9 mmol) were mixed in dry CH_2Cl_2 (20 mL) at 15 °C. After 45 min at room temperature, ethanolamine (0.36 mL, 5.9 mmol) was added at 0 °C. After 2 h at 20 °C, the mixture was added to CH_2Cl_2 (70 mL) to be extracted with 100 mL of water containing 10 mL of NH_4OH (aq., 25%). The water phase was washed twice with 70 mL of CH_2Cl_2 . After drying over $MgSO_4$, the solvents were evaporated and the crude product was purified by silica gel column (95 % CH_2Cl_2 , 5% MeOH). A white powder (130 mg, 0.420 mmol, 7%) was obtained.

$R_f = 0.18$ (95 % CH_2Cl_2 , 5% MeOH) ¹H NMR (500 MHz, MeOD) δ 3.57 (t, $J = 5.9$ Hz, 2H), 3.27 (t, $J = 5.9$ Hz, 2H), 2.25 – 2.11 (m, 2H), 1.67 – 1.51 (m, 2H), 1.28 (s, 26H), 0.89 (t, $J = 7.0$ Hz, 3H). ¹³C NMR (126 MHz, MeOD) δ 176.67 (s), 61.64 (s), 42.91 (s), 37.12 (s), 33.08 (s), 31.11 – 29.50 (m), 27.00 (s), 23.74 (s), 14.43 (s). IR (cm^{-1}): 3296, 3092, 2917, 2849, 1640, 1559, 1462, 1379, 1304, 1264, 1218, 1126, 1044, 925, 718, 634. *HRMS (ESI+)* m/z calcd for $C_{19}H_{40}NO_2$ $[M+H]^+$ 314.3053 found 314.3054

1.4. Synthesis of 1-(2-hydroxyethyl)-3-pentadecylurea (4)

Pentadecyl isocyanate was synthesized using a variation of a procedure of de Feyter et al.⁴ palmitoyl chloride (5.6 mL, 18 mmol) and sodium azide (1.5 g, 23 mmol) were mixed in dry toluene (40 mL). The solution was refluxed over 5 h and was then used directly without further purification.

Ethanolamine (0.22 mL, 3.7 mmol) and dry Et_3N (1.04 mL, 7.42 mmol) were dissolved in dry THF (25 mL). 4.9 mL of the toluene solution of 1-isocyanatopentadecane (0.94 g, 3.70 mmol) in dry THF (10 mL) was added dropwise (30 min) to the solution at 0 °C and stirred 3 h at room temperature. Then the solution was treated with 10 mL NH_4OH (aq., 25%) in 100 mL water, and extracted with CH_2Cl_2 (4 x 50 mL). The solvents from the combined organic phases were dried over $MgSO_4$ and removed under reduced pressure. The crude product was purified by silica gel column (95% CH_2Cl_2 , 5% MeOH) to give a white powder (555 mg, 1.76 mmol, 48%).

$R_f = 0.20$ (95 % CH_2Cl_2 , 5% MeOH), ¹H NMR (500 MHz, $CDCl_3$ /Methanol- d_4 1:1) δ 3.56 (t, $J = 5.4$ Hz, 2H), 3.21 (t, $J = 5.3$ Hz, 2H), 3.07 (t, $J = 7.1$ Hz, 2H), 1.52 – 1.35 (m, 2H), 1.22 (s, 24H), 0.84 (t, $J = 7.0$ Hz, 3H). ¹³C NMR (126 MHz, $CDCl_3$ /Methanol- d_4 1:1) δ 159.66, 61.40, 41.98, 39.68, 31.40, 29.56, 29.15, 29.13, 29.11, 29.09, 28.87, 28.82, 26.37, 22.13, 13.29. IR (cm^{-1}): 3309, 3214, 3079, 2919, 2850, 1572, 1471, 1348, 1271, 1037, 718, 650. *HRMS (ESI+)* m/z calcd for $C_{18}H_{39}N_2O_2$ $[M+H]^+$ 315.3002 found 315.3006.

1.5. Synthesis of 1-(2-hydroxyethyl)-3-pentadecylthiourea (5)

Pentadecyl isothiocyanate was synthesized using a variation of a procedure by Meijer et al.² DCC (3.1 g, 15 mmol) and CS_2 (6.30 mL, 104 mmol) were dissolved in dry diethyl ether (40 mL). Pentadecyl amine (3.4 g, 15 mmol) was added to the mixture at 0 °C. The mixture was stirred overnight at room temperature. The precipitated solid was filtered off and washed with 60 mL of dry diethyl ether. The

³ L. Guan, D. Zhao, J. Xiu, X. Sui, H. Piao, Z. Quan, *Arch. Pharm. Chem. Life Sci.*, **2009**, *342*, 34–40.

⁴ S. De Feyter, M. Larsson, N. Schuurmans, B. Verkuijl, G. Zoriniants, A. Gesquière, M. M. Abdel - Mottaleb, J. van Esch, B. L. Feringa, J. van Stam, F. De Schryver, *Chem. Eur. J.*, **2003**, *9*, 1198–1206.

solvents were removed under reduced pressure and the isothiocyanate was used without further purification.

Ethanolamine (0.23 mL, 3.8 mmol) and dry Et₃N (1.0 mL, 7.4 mmol) were dissolved in dry THF (40 mL). Pentadecyl isothiocyanate (1.0 mL, 3.7 mmol) in dry THF (20 mL) was added dropwise over 1.5 h at 0 °C. After stirring at 20 °C for 4.5 h, the mixture was added to CH₂Cl₂ (70 mL) and extracted with 100 mL of water containing 10 mL of NH₄OH (aq., 25%). The water phase was washed twice with 70 mL of CH₂Cl₂. After drying over MgSO₄, the solvents were evaporated and the crude product was purified by silica gel column (95% CH₂Cl₂, 5% MeOH). The product was recrystallized from dioxane/pentane (1:4) at 8 °C overnight. A white powder (700 mg, 2.12 mmol, 57%) was obtained.

Rf = 0.36 (95 % CH₂Cl₂, 5% MeOH) ¹H NMR (300 MHz, CDCl₃) δ 3.92 – 3.76 (m, 2H), 3.68 (s, 2H), 3.37 (s, 2H), 1.69 – 1.49 (m, 2H), 1.25 (s, 24H), 0.88 (t, *J* = 6.5 Hz, 3H). ¹³C NMR (126 MHz, MeOD) δ 183.71, 61.82, 47.43, 45.39, 33.08, 30.78, 30.48, 30.20, 27.98, 23.74, 14.44. IR (cm⁻¹): 3228, 3073, 2915, 2848, 1567, 1470, 1365, 1293, 1276, 1216, 1049, 738, 720, 665 HRMS (*ESI*+) *m/z* calcd for C₁₈H₃₉N₂OS [M+H]⁺ 331.2777 found 331.2774

1.6. Synthesis of 1-(2-hydroxyethyl)-3-hexadecylthiourea (6)

Hexadecyl isothiocyanate was synthesized using a variation of a procedure by Meijer et al.² DCC (2.42 g, 14.5 mmol) and CS₂ (6.00 mL, 100 mmol) were dissolved in dry diethyl ether (40 mL). Hexadecyl amine (3.80 g, 14.2 mmol) was added to the mixture at 0 °C and the mixture was stirred overnight at room temperature. The precipitated solid was filtered off and washed with 60 mL of dry diethyl ether. The solvents were removed by evaporation and the isothiocyanate was used without further purification.

Aminoethanol (0.22 mL, 3.7 mmol) and dry Et₃N (1.0 mL, 7.4 mmol) were dissolved in dry THF (25 mL). 1-isothiocyanatohexadecane (1.0 mL, 3.7 mmol) in dry THF (15 mL) was added dropwise (1.5 h) to the solution at 0 °C and then stirred at room temperature for 3.5 h. Then the solution was treated with 10 mL NH₄OH (aq., 25%) in 100 mL water, and extracted with CH₂Cl₂ (4 x 50 mL). The solvents from the combined organic phases were dried over MgSO₄ and removed under reduced pressure. The crude product was purified by silica gel column (95% CH₂Cl₂, 5% MeOH) and then by recrystallisation (dioxane/pentane, 4:1) to give the product as a white powder (756 mg, 2.19 mmol, 59%).

Rf = 0.25 (95 % CH₂Cl₂, 5% MeOH) ¹H NMR (500 MHz, Methanol-d₄) δ 3.66 (t, *J* = 5.4 Hz, 2H), 3.57 (s, 2H), 3.43 (s, 2H), 1.64 – 1.47 (m, 2H), 1.29 (s, 26H), 0.90 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (126 MHz, MeOD) δ 183.01, 61.82, 47.45, 45.57, 33.08, 30.79, 30.73, 30.71, 30.48, 30.20, 27.98, 23.74, 14.44. IR (cm⁻¹): 3298, 3231, 3073, 2917, 2849, 1565, 1461, 1366, 1286, 1272, 1211, 1059, 1036, 728, 651. HRMS (*ESI*+) *m/z* calcd for C₁₉H₄₁N₂OS [M+H]⁺ 345.2930 found 345.2934.

1-dodecyl-3-(2-hydroxyethyl)urea (1)

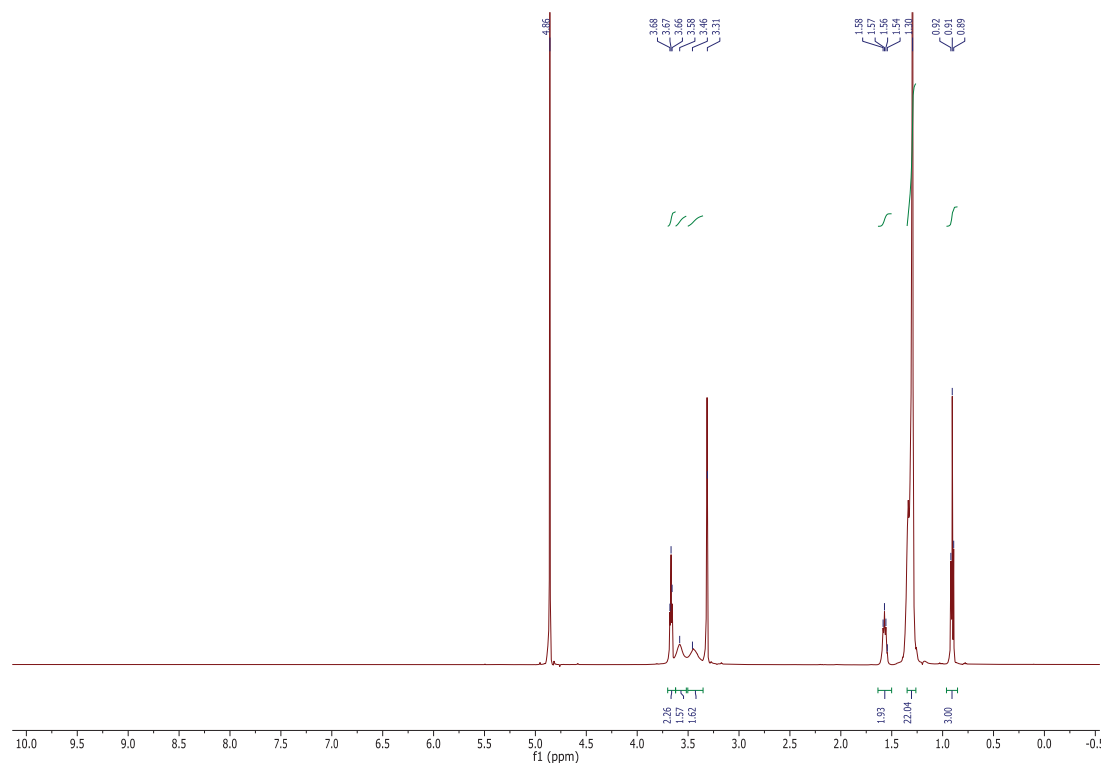
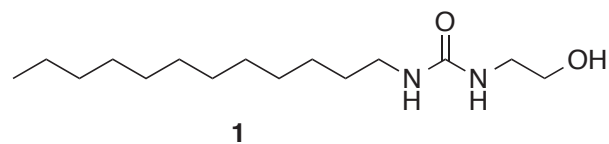


Figure S1. ^1H NMR spectra of 1-dodecyl-3-(2-hydroxyethyl)urea (**1**).

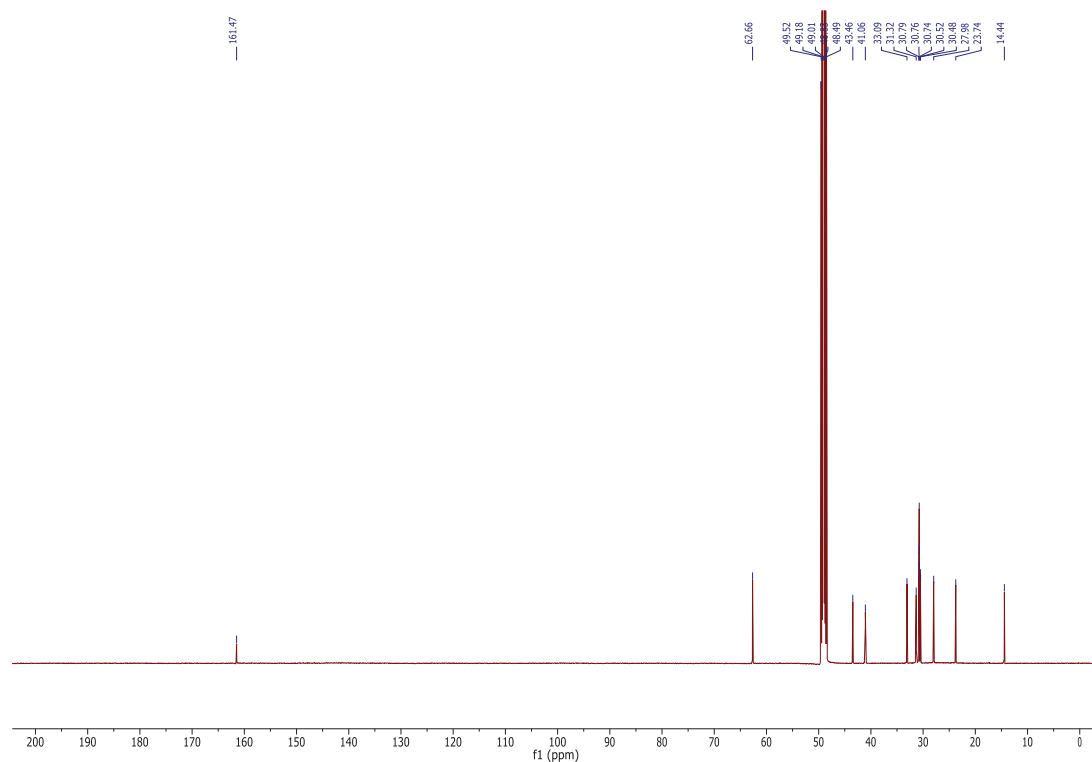
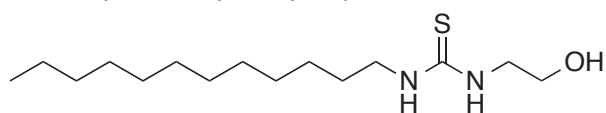


Figure S2. ^{13}C NMR spectra of 1-dodecyl-3-(2-hydroxyethyl)urea (**1**).

1-dodecyl-3-(2-hydroxyethyl)thiourea (2)



2

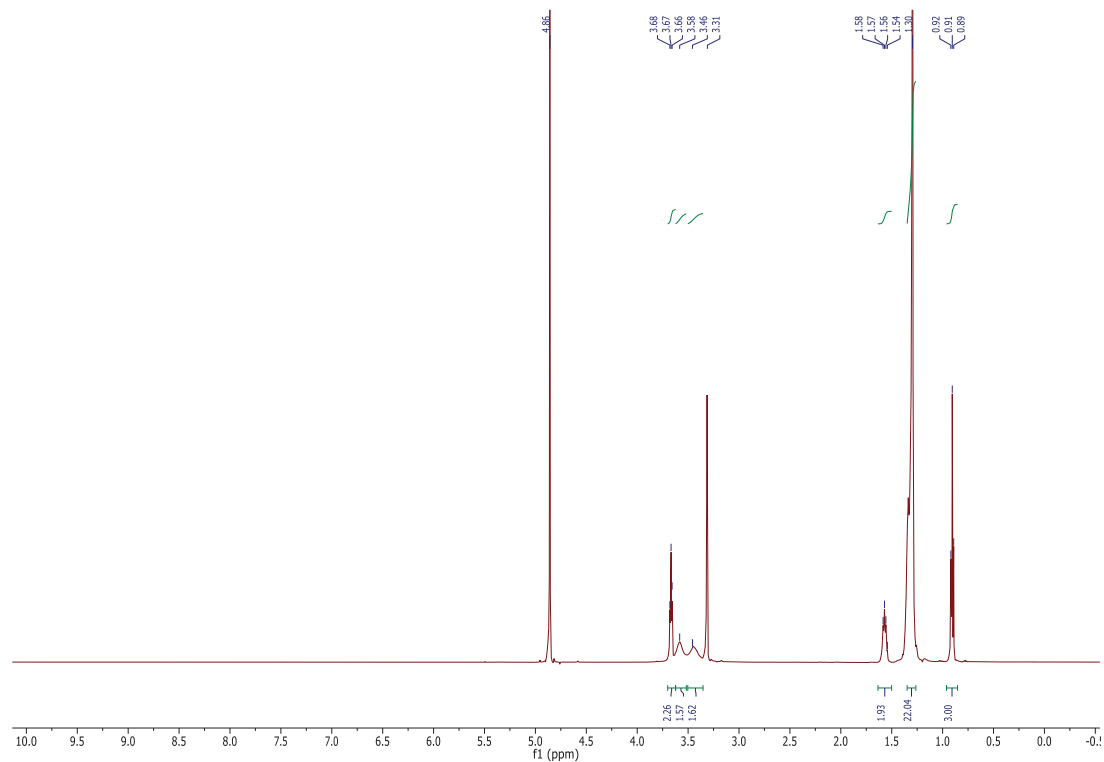


Figure S3. ¹H NMR spectra of 1-dodecyl-3-(2-hydroxyethyl)thiourea (2).

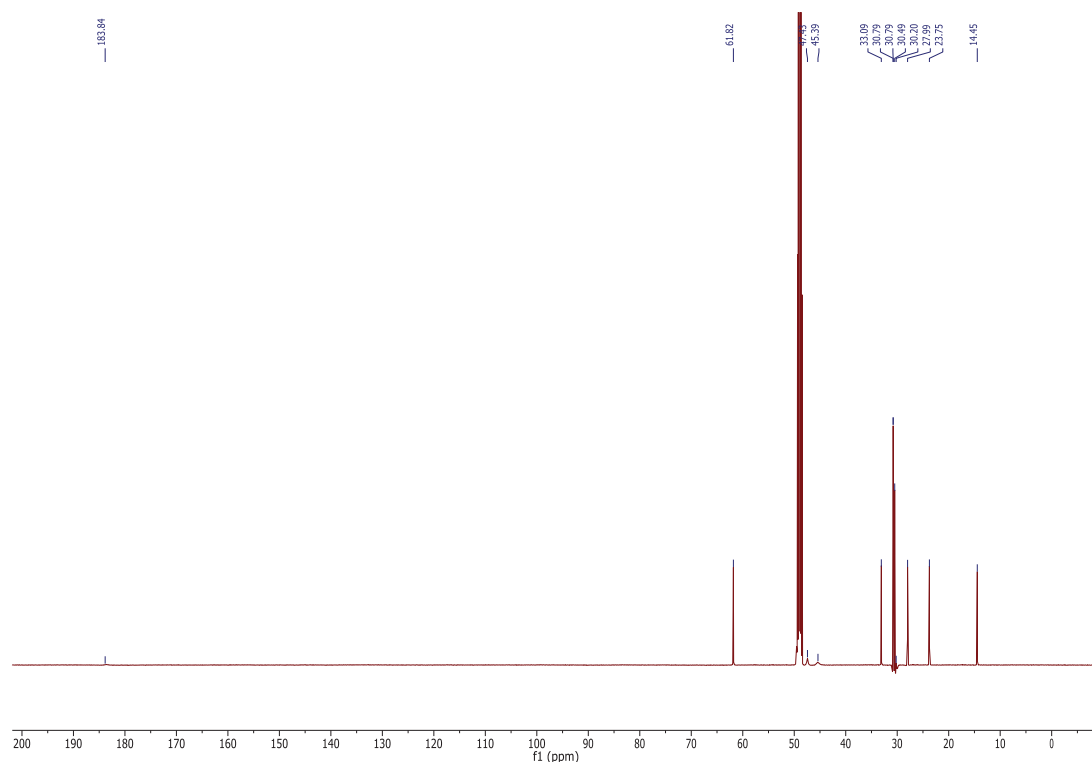


Figure S4. ¹³C NMR spectra of 1-dodecyl-3-(2-hydroxyethyl)thiourea (2).

N-(2-hydroxyethyl)heptadecanamide (**3**)

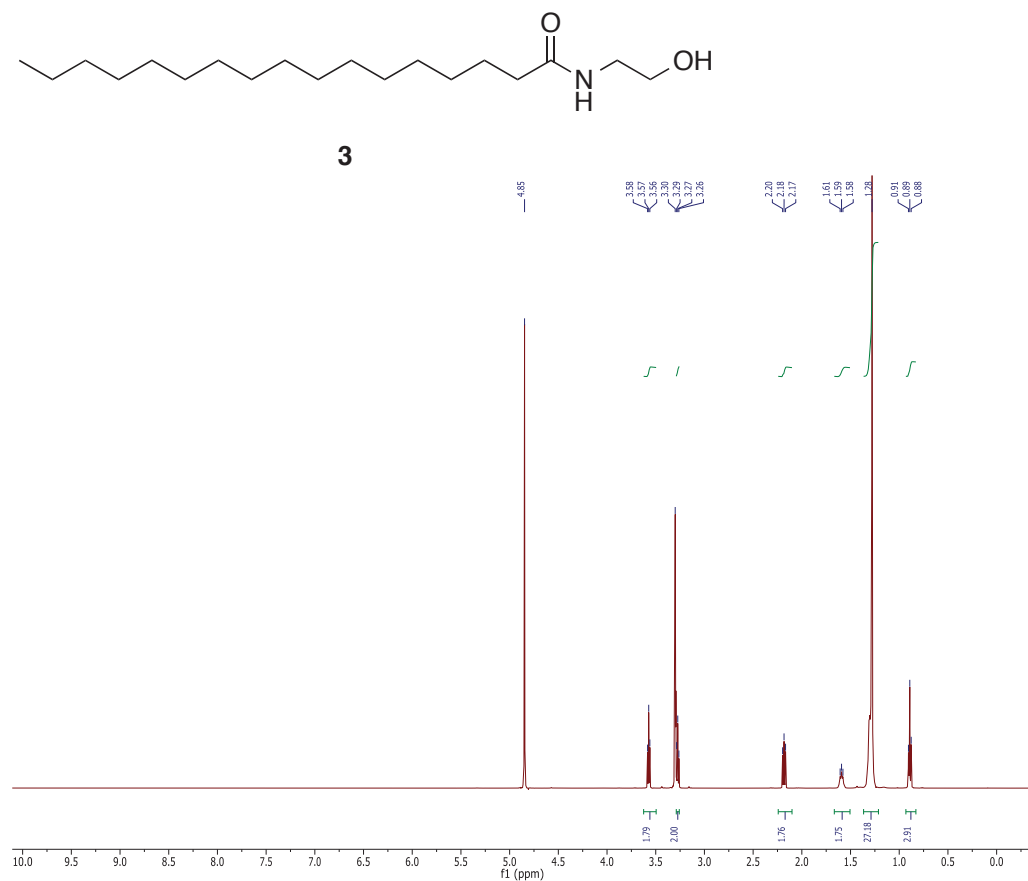


Figure S5. ¹H NMR spectra of *N*-(2-hydroxyethyl)heptadecanamide (**3**).

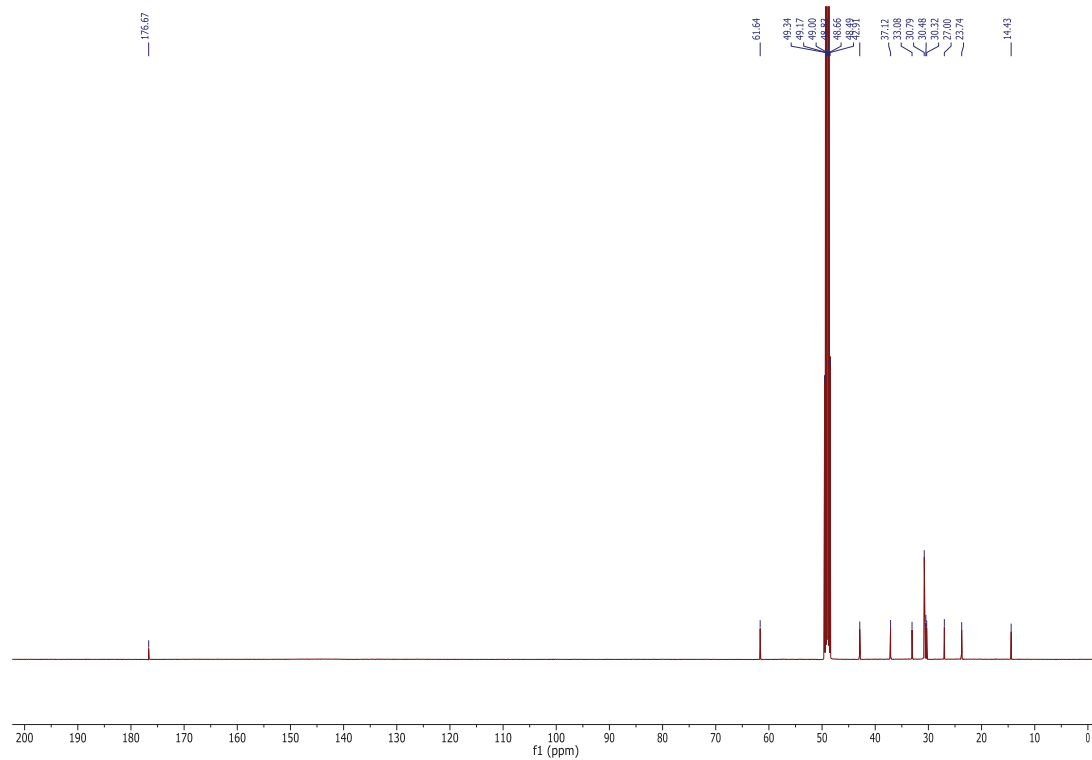
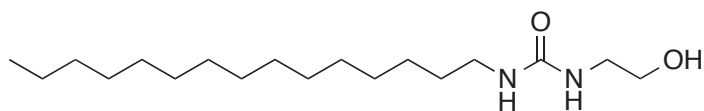


Figure S6. ¹³C NMR spectra of *N*-(2-hydroxyethyl)heptadecanamide (**3**).

1-(2-hydroxyethyl)-3-pentadecylurea (**4**)



4

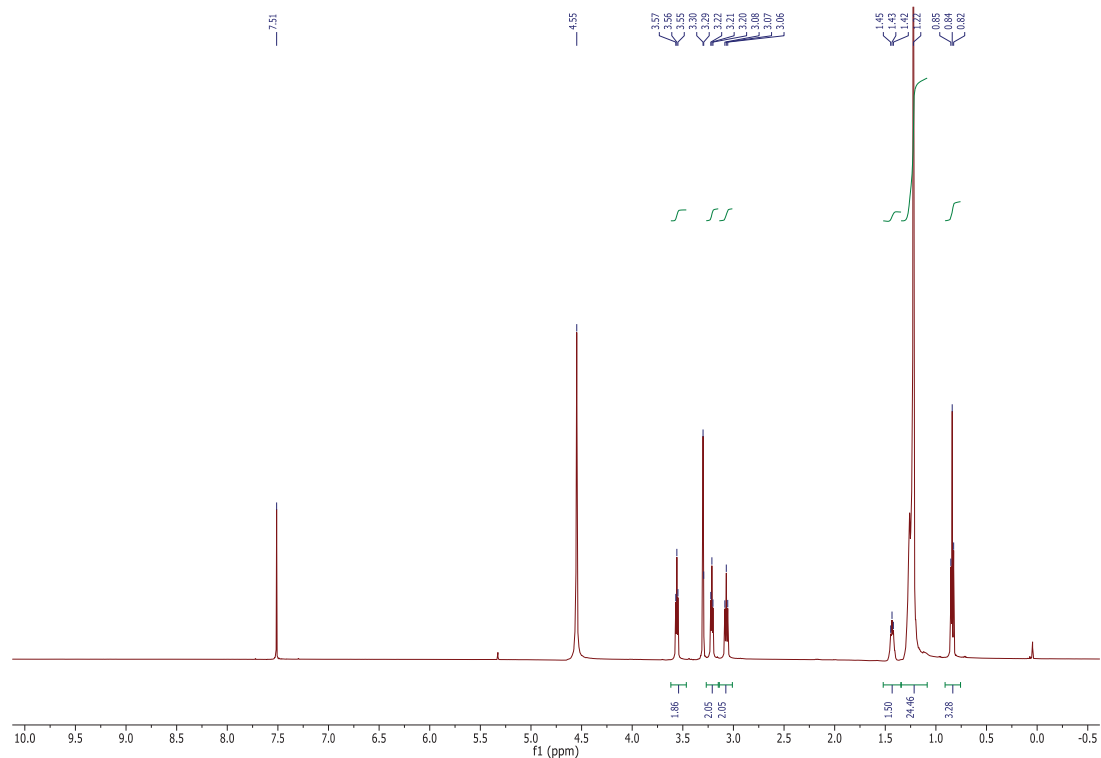


Figure S7. ^1H NMR spectra of 1-(2-hydroxyethyl)-3-pentadecylurea (**4**).

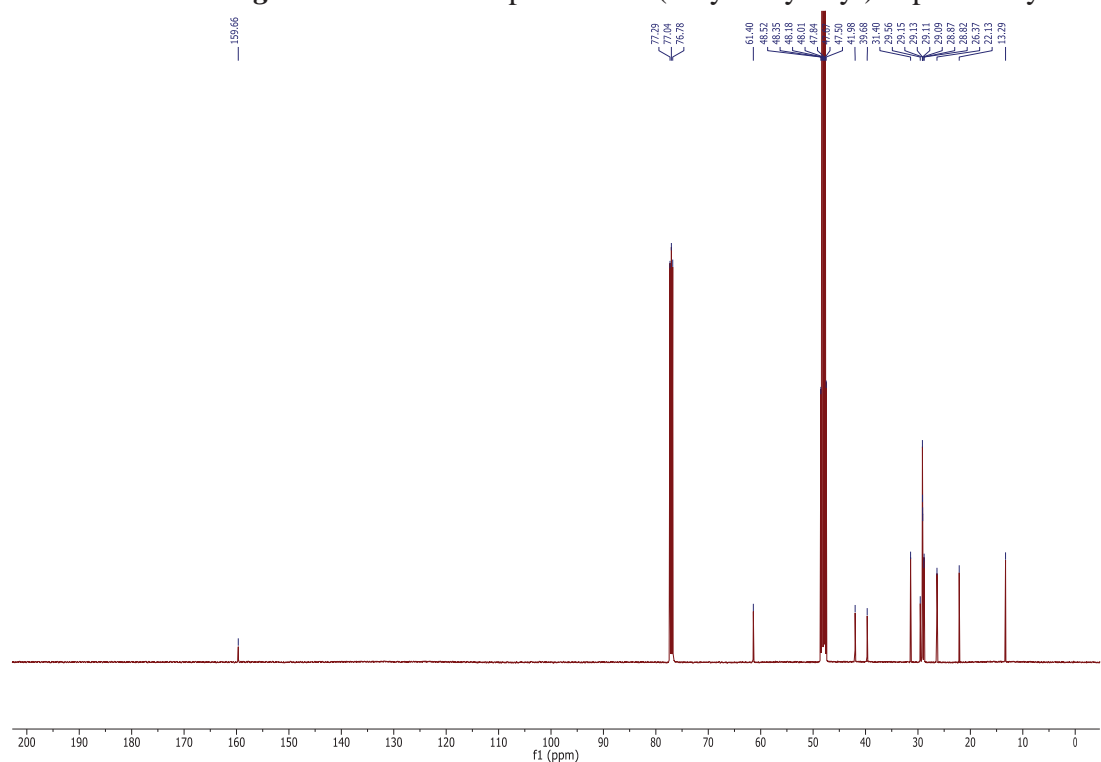


Figure S8. ^{13}C NMR spectra of 1-(2-hydroxyethyl)-3-pentadecylurea (**4**).

1-pentadecyl-3-(2-hydroxyethyl)thiourea (**5**)

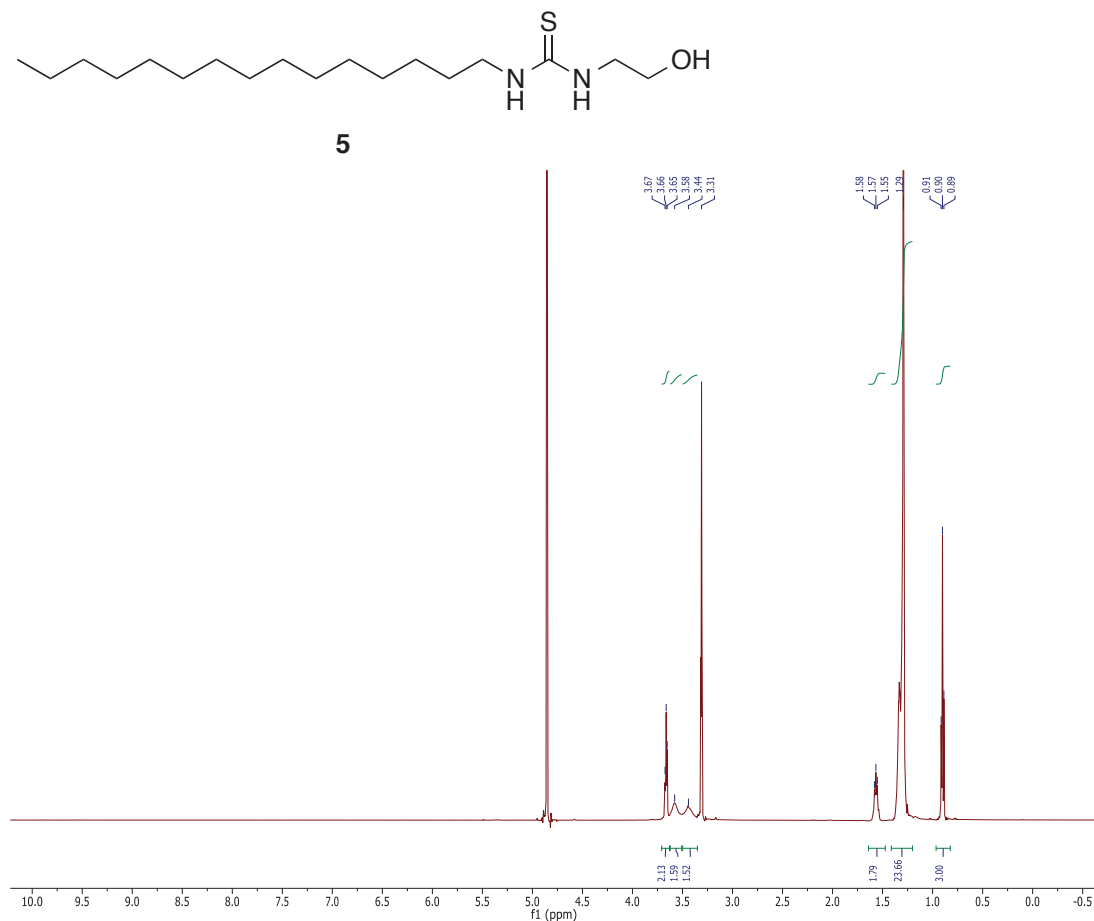


Figure S9. ¹H NMR spectra of 1-pentadecyl-3-(2-hydroxyethyl)thiourea (**5**).

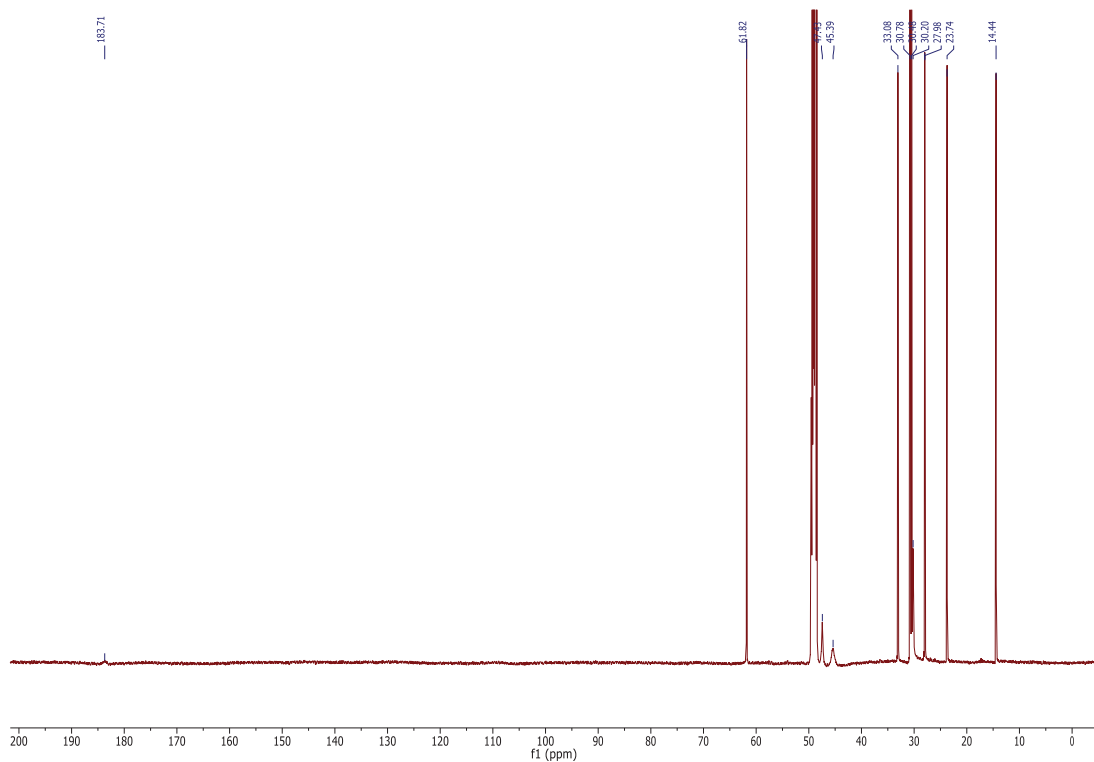


Figure S10. ¹³C NMR spectra of 1-pentadecyl-3-(2-hydroxyethyl)thiourea (**5**).

1-hexadecyl-3-(2-hydroxyethyl)thiourea (**6**)

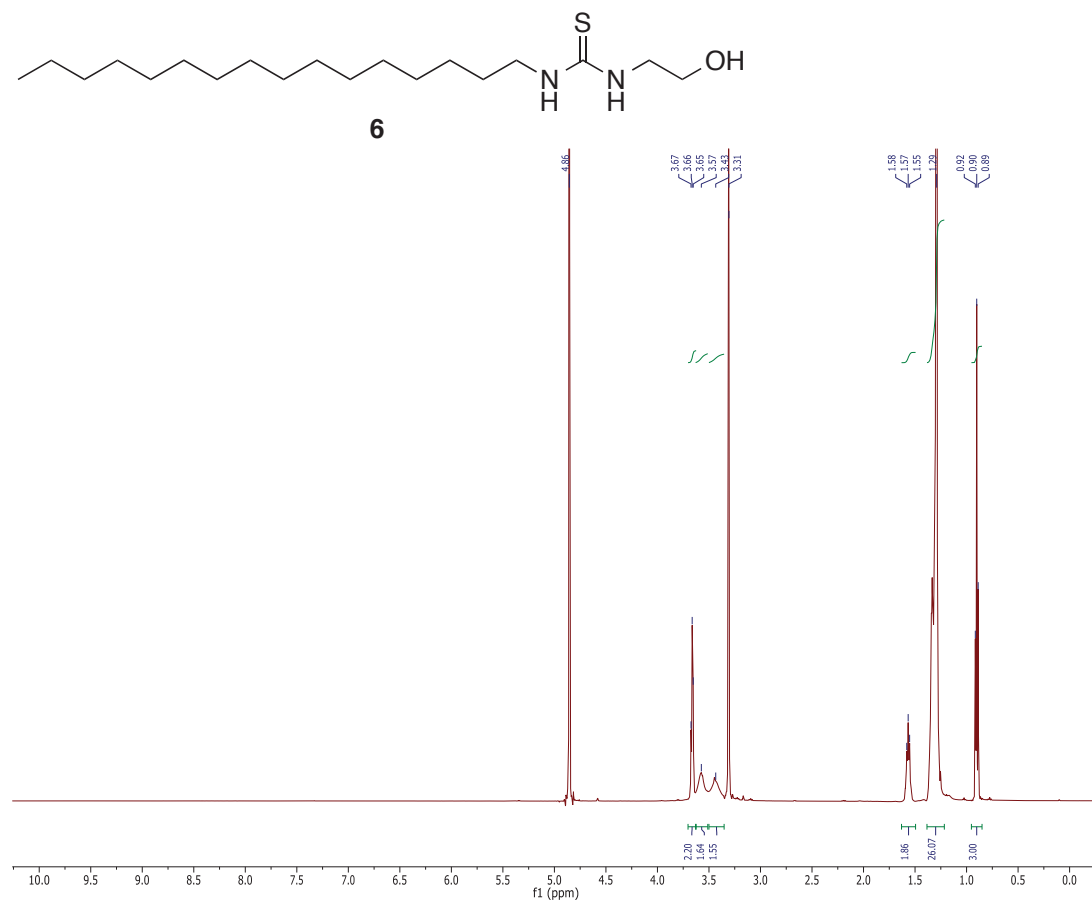


Figure S11. ¹H NMR spectra of 1-hexadecyl-3-(2-hydroxyethyl)thiourea (**6**).

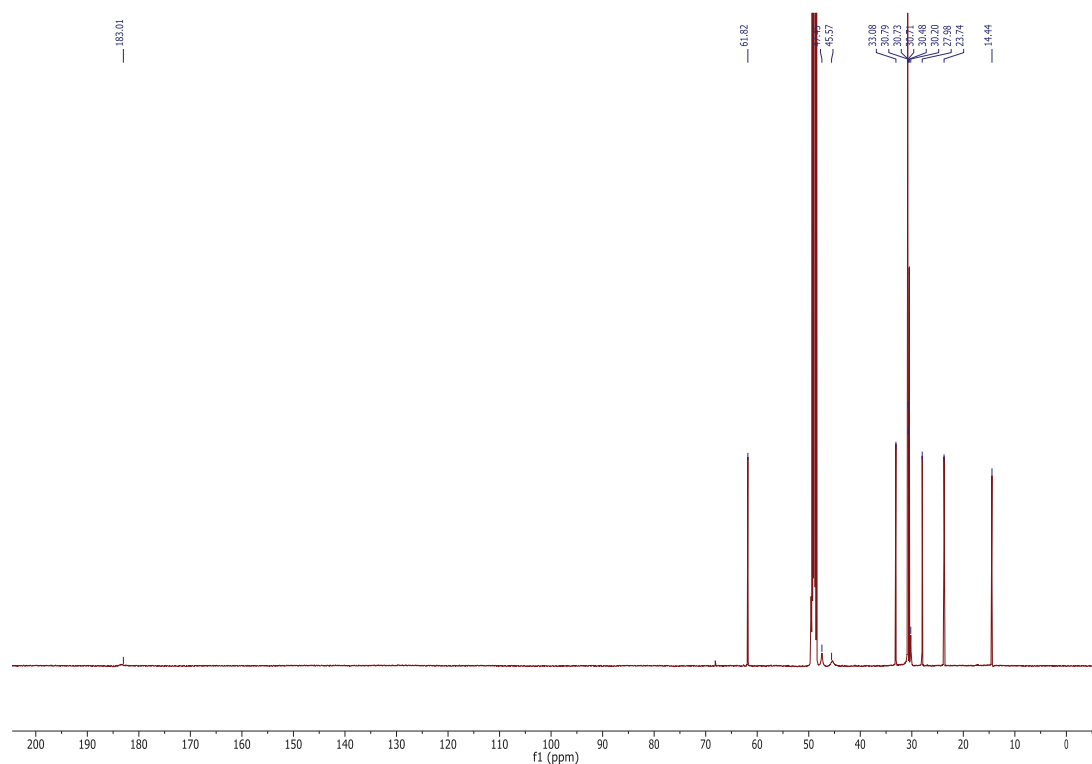


Figure S12. ¹³C NMR spectra of 1-hexadecyl-3-(2-hydroxyethyl)thiourea (**6**).

2. Isotherm measurements and GIXD data

2.1. Isotherms

The monolayers of urea and thiourea derivatives are extremely stiff. The high viscosity of the layer leads to the tilting of a small paper Wilhelmy plate on compression similar to observations made with highly viscous polymer monolayers. Only the use of a heavier and bigger glass plate results in reasonable pressure/area isotherms. The isotherms of compound **5** (Figure S13) at two different temperatures show a slight hysteresis between compression and expansion, and the lateral pressure does not return to zero after expansion to large molecular areas. The final value is with 0.5 mN/m still very small but shows that either the contact angle of the plate is changed by the interaction with the compound which remains attached to the Wilhelmy plate, or the extremely stiff island coexisting at zero pressure with the gaseous phase are not homogeneously distributed on the surface as after spreading but stay in closer contact to the plate.

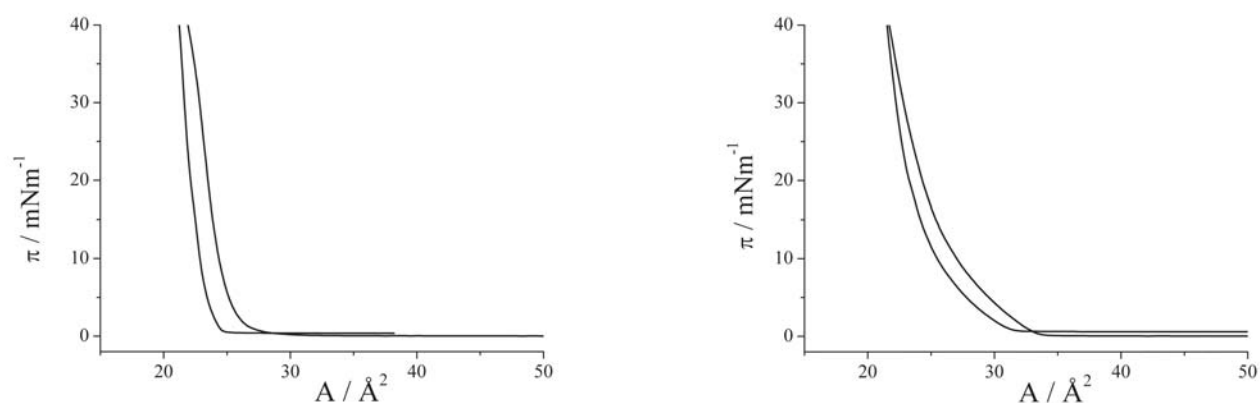


Figure S13. Lateral pressure π / molecular area A isotherms of thiourea **5** on water at 20 °C (left) and at 25 °C (right).

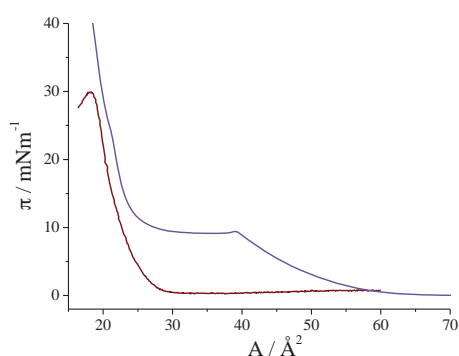


Figure S14. Lateral pressure π / molecular area A isotherms of amide amphiphiles (C14 - purple, 3 - brown) at 20 °C on water.

The temperature dependence of the π/A isotherms of thiourea **5** has been investigated in the minutest details (Figure S14). The first-order phase transition from the unstructured LE to the highly ordered LC phase is observed only above 29 °C.

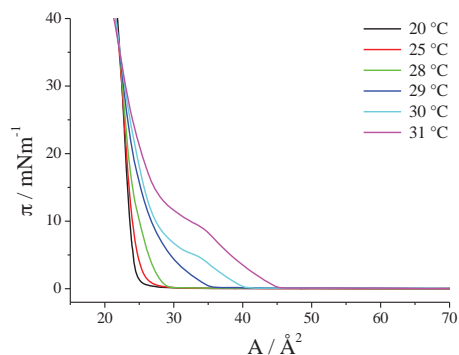


Figure S15. Lateral pressure π / molecular area A isotherms of thiourea **5** at different temperatures (indicated) on water.

2.2. GIXD data

π [mN/m]	Q_{xy1} [\AA^{-1}]	Q_{z1} [\AA^{-1}]	Q_{xy2} [\AA^{-1}]	Q_{z2} [\AA^{-1}]	Q_{xy3} [\AA^{-1}]	Q_{z3} [\AA^{-1}]
5	1.427	0.404	1.427	0.514	1.413	0.918
	0.012	0.28	0.012	0.28	0.021	0.28
30	1.430	0.402	1.430	0.499	1.416	0.901
	0.013	0.27	0.013	0.27	0.026	0.28

Table S1. GIXD results of monolayers of thiourea **5** on water at 20 °C: Bragg peak and rod positions and the corresponding full-widths at half-maximum (fwhm).

π [mN/m]	$a/b/c$ [\AA]	$\alpha/\beta/\gamma$ [$^\circ$]	distortion	tilt t [$^\circ$]	A_{xy} [\AA^2]	A_0 [\AA^2]
5	5.067	120.6	0.0131	33.07	22.5	18.9
	5.117	119.7				
	5.117	119.7				
30	5.057	120.6	0.01307	32.5	22.4	18.9
	5.107	119.7				
	5.107	119.7				

Table S2. GIXD results of monolayers of thiourea **5** on water at 20 °C: Lattice parameters a , b , c and α , β , γ of the unit cell, lattice distortion (d), chain tilt (t) from the surface normal, in plane area per alkyl chain (A_{xy}) and chain cross-sectional area (A_0).

Experimental	Calculated (orthorhombic in- plane lattice)	Deviation	Miller Indices (h, k)
1.244	1.244	0	(1,0)
1.416	1.416	0	(0, 2)
1.430	1.431	0.001	(1,1)
2.458	2.461	0.003	(1, 3)
2.481	2.488	0.007	(2, 0)
2.578	2.586	0.008	(2, 1)

Table S3. Calculated Bragg peak positions Q_{xy} (\AA^{-1}) compared to experimentally measured ones for thiourea **5** monolayers.

π [mN/m]	Q_{xy1} [\AA^{-1}]	Q_{z1} [\AA^{-1}]	Q_{xy2} [\AA^{-1}]	Q_{z2} [\AA^{-1}]
30mN/m	1.487	0.0	1.435	0.492
	0.027	0.27	0.09	0.27

Table S4. GIXD data revealing the non-equilibrium structure of monolayers of thiourea **5** at 30 mN/m and 10 °C; Bragg peak and rod positions and the corresponding full-widths at half-maximum (fwhm) are given.

π [mN/m]	$a/b/c$ [\AA]	$\alpha/\beta/\gamma$ [$^\circ$]	distortion	tilt t [$^\circ$]	A_{xy} [\AA^2]	A_0 [\AA^2]
30 mN/m	5.119	117.6	0.0480	21.8	21.6	20.0
	4.940	121.2				
	4.940	121.2				

Table S5. GIXD data of the non-equilibrium structure of thiourea **5** monolayers at 30 mN/m and 10 °C: Lattice parameters a, b, c and α, β, γ of the unit cell, lattice distortion (d), chain tilt (t) from the surface normal, in-plane area per alkyl chain (A_{xy}) and chain cross-sectional area (A_0).

π [mN/m]	Q_{xy1} [\AA^{-1}]	Q_{z1} [\AA^{-1}]	Q_{xy2} [\AA^{-1}]	Q_{z2} [\AA^{-1}]	Q_{xy3} [\AA^{-1}]	Q_{z3} [\AA^{-1}]
30	1.441	0.0	1.337	0.958		
	0.039	0.27	0.054	0.27		

Table S6. GIXD results of urea **4** monolayers on water at 10 °C: Bragg peak and rod positions and the corresponding full-widths at half-maximum (fwhm) are given.

π [mN/m]	a/b/c [Å]	$\alpha/\beta/\gamma$ [°]	distortion	tilt t [°]	A_{xy} [Å ²]	A_0 [Å ²]
30	5.578	114.8	0.1022	40.4	24.3	18.5
	5.176	122.6	NN			
	5.176	122.6				

Table S7. GIXD results of urea **4** monolayers on water at 10 °C: Lattice parameters a , b , c and α , β , γ of the unit cell, lattice distortion (d), chain tilt (t) from the surface normal, in plane area per alkyl chain (A_{xy}) and chain cross-sectional area (A_0).

3. Computational methods and strategy

Details of the density functional theory method (B3LYP⁵ and 6-31G* basis set⁶ as implemented in the Turbomole⁷ package) are described in the cited references. The Moller-Plesset⁸ methods are known to be more adequate in describing the interactions between aliphatic carbons than the B3LYP method, which on the other hand is quite adequate for describing potential energy surface of hydrogen-bonded molecules. Freezing the position of most of the aliphatic carbons in the hexamers not only allowed us to avoid nonphysical conformers due to deficiencies of B3LYP calculations in describing van der Waals interactions within the cluster but also reflect the constraints in the real quasi-infinite membrane arising from strong hydrophobic interactions and van der Waals attraction between aliphatic chains. Such a combined methodology allowed us to perform conformational searches of quite large systems (hexamers) because the B3LYP method is computationally less demanding than the Moller-Plesset one. The geometry of either of the studied complexes is not unique as several local minima are possible. We adopted a particular strategy to detect differences in conformational preferences of urea and thiourea clusters. The strategy consisted of the following steps. At first, a local minimum of one compound was determined. In the following step the sulfur atoms were *in silico* mutated into oxygen (or vice versa) and the geometry was optimized. The two sets of geometries were used to detect conformational preferences of each cluster. The final results discussed in the present work were obtained by applying the above procedure several times starting from different local minima. Only the most stable corresponding pair of conformers is discussed. In this pair, further mutations did not lead to any new minima.

⁵ A. D. Becke, *J.Chem.Phys.* **1993**, 98, 5648-5652.

⁶ P. C. Hariharan, J. A. Pople, *Theoret.Chim.Acta* **1973**, 28, 213-222.

⁷ <http://www.cosmologic.de/index.php?cosId=3010&crId=3>

⁸ C. Møller, M. S. Plesset, *Phys. Rev.* **1934**, 46, 618-622.

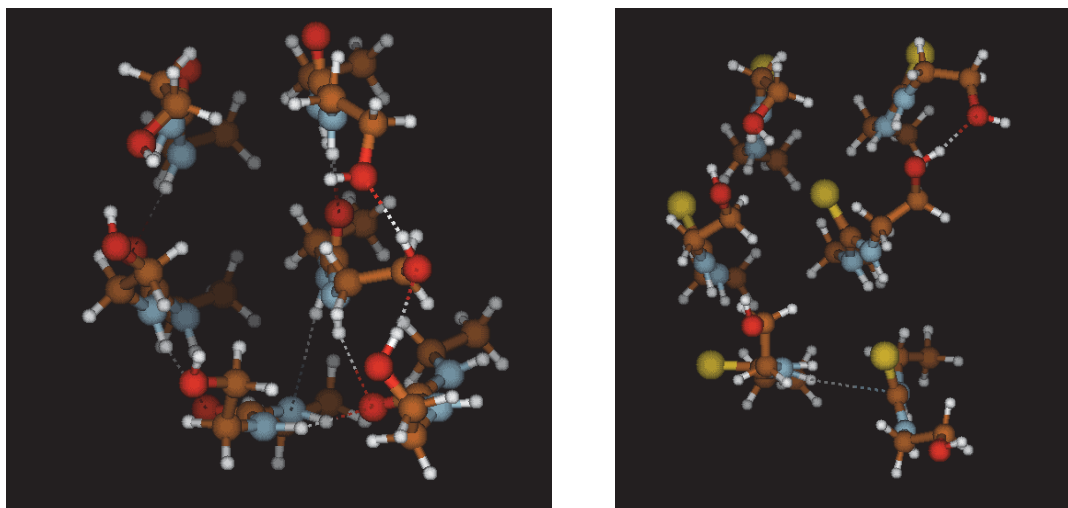


Figure S16. Lowest-energy hexamer structures. *Left:* calculated hexamer of urea head groups. *Right:* calculated hexamer of thiourea head groups. Red = O, yellow = S.