Electronic Supplementary Material (ESI) for ChemComm.

Substrate Selective Amide Coupling driven by Encapsulation of a Coupling Agent within a Self-Assembled Hexameric Capsule

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Reagents and Materials.

General

^{1}H NMR were recorded at 298 K, unless otherwise stated, on a Bruker AVANCE 300 spectrometer operating at 300.15 MHz. δ values in ppm are relative to SiMe4. GC analysis were performed on HP SERIES II 5890 equipped with a HP5 column (30 m, I. D. 0.25 m, film 0.25 μm) using He as gas carrier and FID. GC-MS analyses were performed on a GC Trace GC 2000 equipped with a HP5-MS column (30 m, I.D. 0.25 mm, film 0.25 μm) using He gas carrier and coupled with a quadrupole MS Thermo Finnigan Trace MS with *Full Scan* method.

Solvents and reactants were used as received; otherwise they were purified as reported in the literature.[1] TLC analysis were performed on TLC Polygram ® Sil G/UV254 of 0.25 mm thickness and flash-chromatography separations were performed on silica gel Merk 60, 230-400 mesh.[2]

Substrates and capsule

All carboxylic acids **3** and amines **4** as well as the coupling agent 1-ethyl-3-(-3-dimethylaminopropyl) carbodiimide hydrochloride **2** are all commercially available products (Aldrich) and were used as received without any further purification. Resorcin[4]arene **1** was prepared as reported in the literature.[3] Amide products **5** were determined by GC-MS analysis.

Catalytic Studies

*Catalytic reactions of amide coupling between acids **3** with amines **4** mediated by the carbodiimide **2** in the presence of the capsule $\mathbf{1}_6 \cdot 8H_2O$*

Water saturated solvent was prepared by shaking chloroform-d with bidistilled water at room temperature in a separation funnel. Resorcin[4]arene **1** (6.6 equivalents, 81.4 mM) was placed in a screw-capped vial equipped with silicone septum and dissolved in the water saturated chloroform-d (1 mL) stirring for few minutes. To this solution, 1-ethyl-3-(-3-dimethylaminopropyl) carbodiimide hydrochloride **2** (1 equivalent, 13.2 mM) was added, followed after few minutes stirring, by octane, decane, dodecane, tetradecane, or docosane as GC-MS standard (3.3 mM), a series of carboxylic acids (0.5 equivalents each, 6.7 mM) and a series of amines (0.5 equivalents each, 6.7 mM). The reaction was then left at 60°C under vigorous stirring for 2 days and the reaction progress was monitored by GC-MS analysis by periodically sampling directly from the reaction mixtures. Conversion, product assignment and distribution were determined by direct GC-MS analysis of the reaction mixture as the average of three experiments.

GC-MS analyses were performed on a GC Trace GC 2000 coupled with a quadrupole MS Thermo Finnigan Trace MS with *Full Scan* method. Experimental conditions are reported in the following table.

Experimental conditions for GC-MS analysis	
Capillary column:	HP5-MS 30 m, 0.25 mm x 0.25 μm
Initial T, °C:	80°C for 5 min
Rate, °C/min:	30°C/min
Final T, °C:	280°C for 30 min
Injector T (split), °C:	280°C
Gas carrier flow, mL/min.	0.8 mL/min
Injected volume, μL	0.8-1 μL
Solvent delay, min.	4 min.
Mass range, amu:	35-500 amu
Detector voltage, V:	350 V
Interface T, °C	280°C
Source T, °C:	200°C

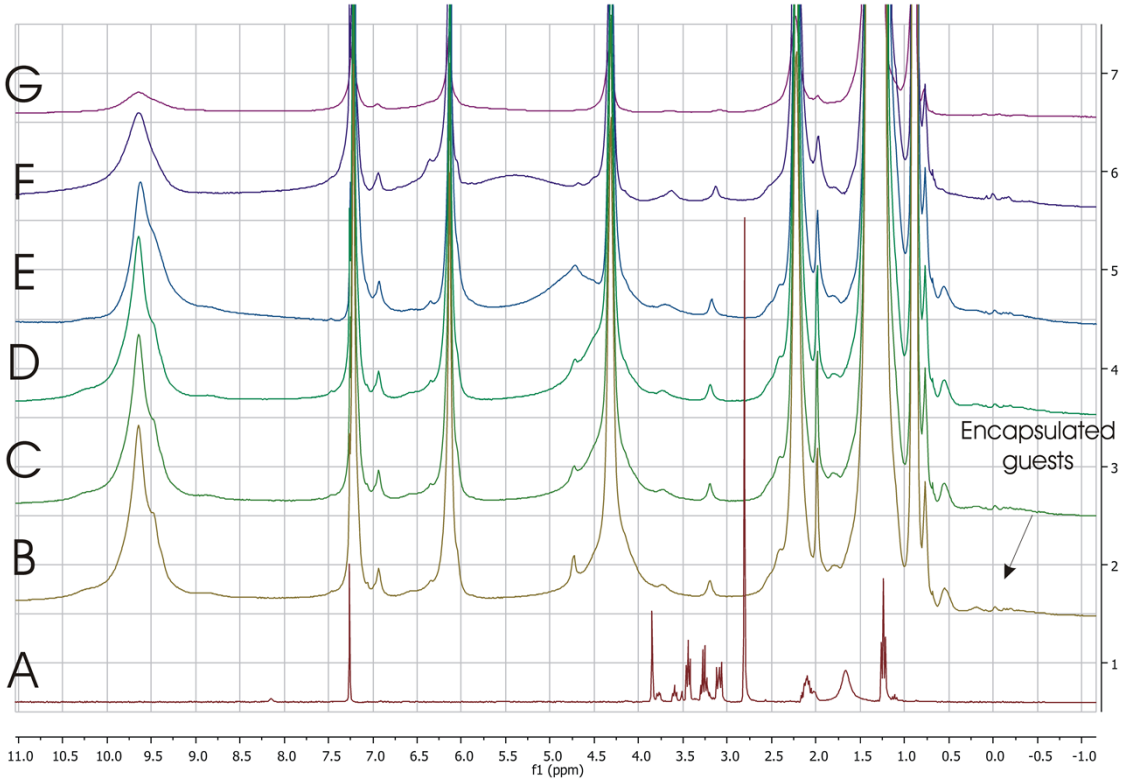


Figure S1. ^{1}H NMR spectra in water saturated chloroform-d: A) 1-ethyl-3-(-3-dimethylaminopropyl) carbodiimide hydrochloride **2** (26.5 mM), B) **2** (26.5 mM) and $\mathbf{1}_6 \cdot 8H_2O$ (26.5 mM) after mixing; C) **2** (26.5 mM) and $\mathbf{1}_6 \cdot 8H_2O$ (26.5 mM) after 15 min; D) **2** (26.5 mM) and $\mathbf{1}_6 \cdot 8H_2O$ (26.5 mM) after 30 min; E) **2** (26.5 mM) and $\mathbf{1}_6 \cdot 8H_2O$ (26.5 mM) after 2 h; F) **2** (26.5 mM) and $\mathbf{1}_6 \cdot 8H_2O$ (26.5 mM) after 3 days; G) **2** (26.5 mM) and $\mathbf{1}_6 \cdot 8H_2O$ (26.5 mM) after 11 days.

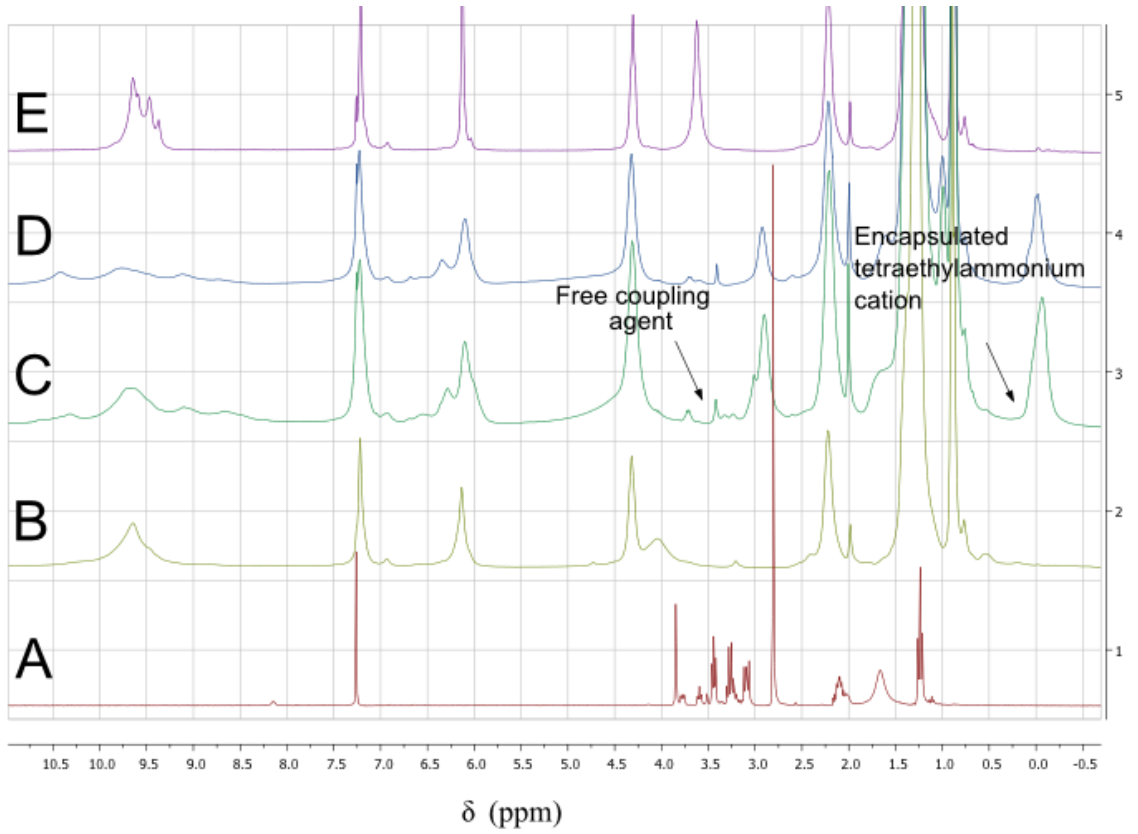


Figure S2. ^{1}H NMR spectra in water saturated chloroform-d: A) 1-ethyl-3-(-3-dimethylaminopropyl) carbodiimide hydrochloride **2** (26.5 mM), B) **2** (26.5 mM) and $\mathbf{1}_6 \cdot 8H_2O$ (26.5 mM) C) **2** (26.5 mM) and $\mathbf{1}_6 \cdot 8H_2O$ (26.5 mM) and tetraethylammonium tetrafluoroborate **6** (265.3 mM); D) **2** (26.5 mM) and $\mathbf{1}_6 \cdot 8H_2O$ (26.5 mM) and tetraethylammonium tetrafluoroborate **6** (265.3 mM) after 3 days; E) Hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM).

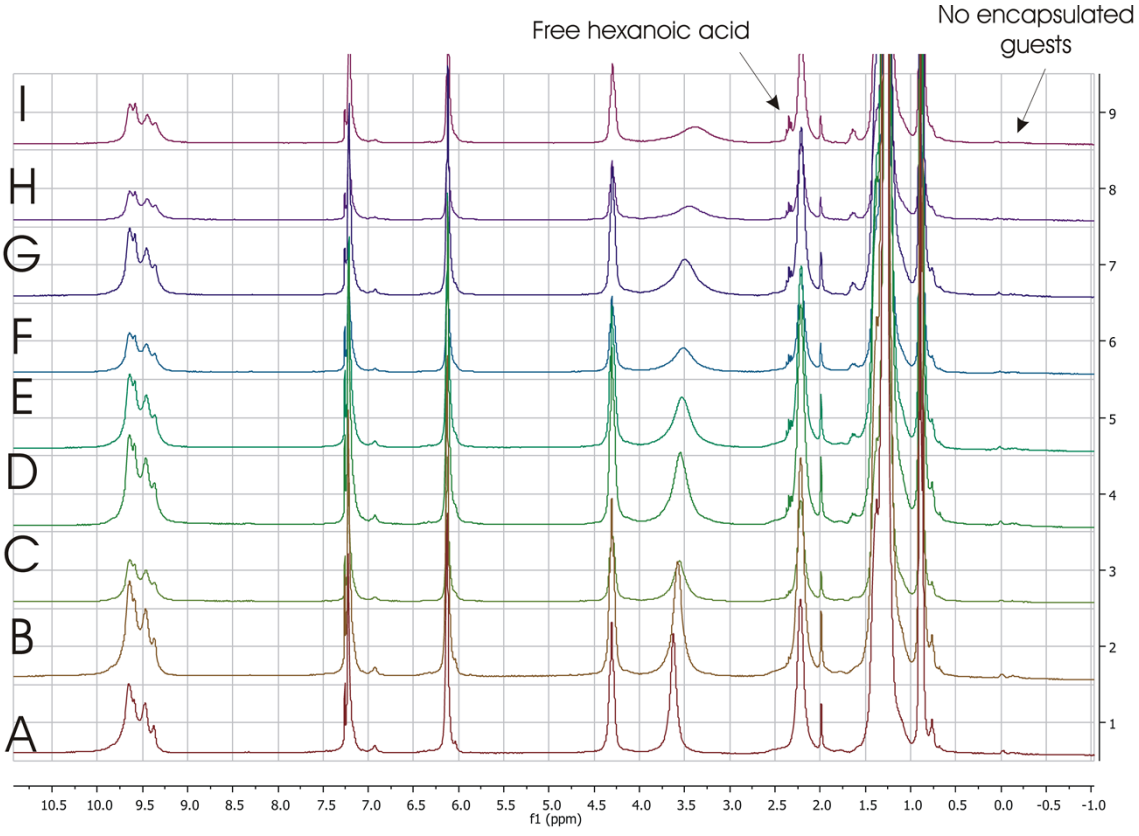


Figure S3. ^{1}H NMR spectra in water saturated chloroform-d: A) Hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM); B) $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) with 0.2 eq. of hexanoic acid; C) $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) with 0.4 eq. of hexanoic acid; D) $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) with 0.6 eq. of hexanoic acid; E) $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) with 0.8 eq. of hexanoic acid; F) $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) with 1.0 eq. of hexanoic acid; G)

1$_6$·8H_2O (13.5 mM) with 1.2 eq. of hexanoic acid; H) **1**$_6$·8H_2O (13.5 mM) with 1.6 eq. of hexanoic acid; I) **1**$_6$·8H_2O (13.5 mM) with 2.0 eq. of hexanoic acid.

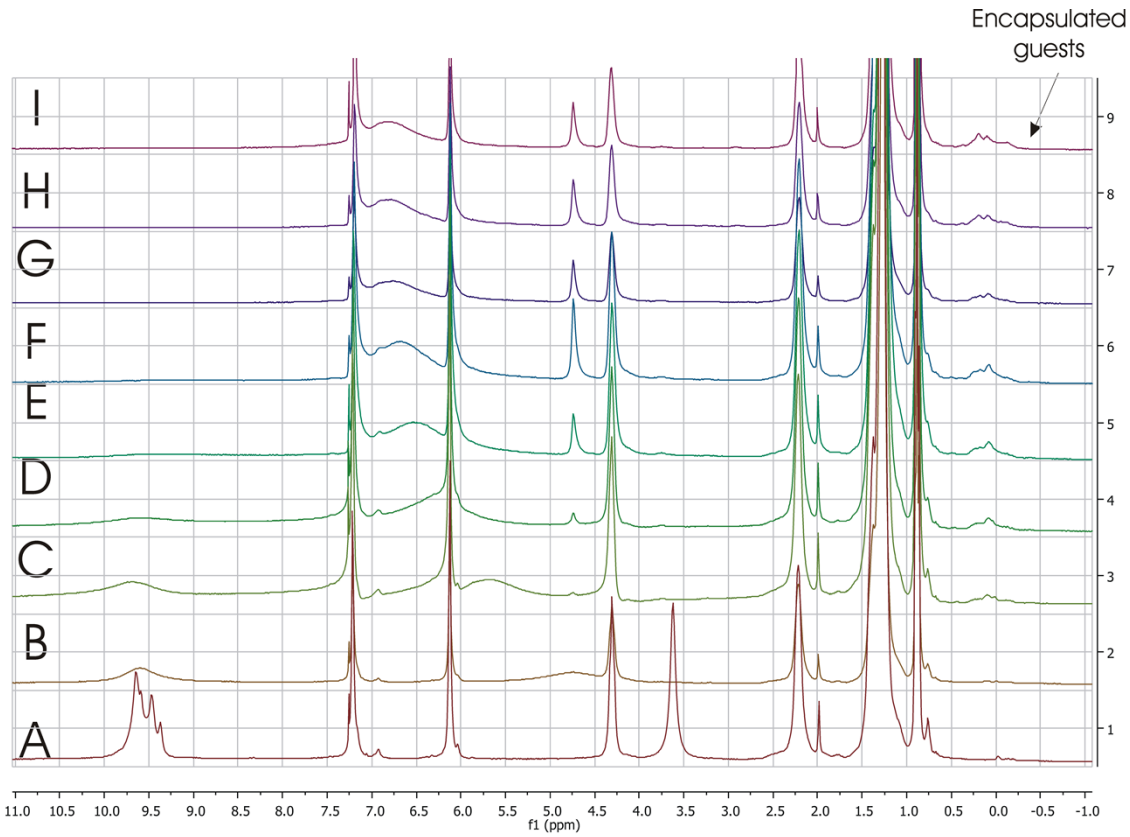


Figure S4. ^{1}H NMR spectra in water saturated chloroform-d: A) Hexameric capsule **1**$_6$·8H_2O (13.5 mM); B) Hexameric capsule **1**$_6$·8H_2O (13.5 mM) and 0.2 eq. of butylamine; C) Hexameric capsule **1**$_6$·8H_2O (13.5 mM) and 0.4 eq. of butylamine; D) Hexameric capsule **1**$_6$·8H_2O (13.5 mM) and 0.6 eq. of butylamine; E) Hexameric capsule **1**$_6$·8H_2O (13.5 mM) and 0.8 eq. of butylamine; F) Hexameric capsule **1**$_6$·8H_2O (13.5 mM) and 1.0 eq. of butylamine; G) Hexameric capsule **1**$_6$·8H_2O (13.5 mM) and 1.2 eq. of butylamine; H) Hexameric capsule **1**$_6$·8H_2O (13.5 mM) and 1.6 eq. of butylamine; I) Hexameric capsule **1**$_6$·8H_2O (13.5 mM) and 2.0 eq. of butylamine. ↓ encapsulated n-butylammonium cation.

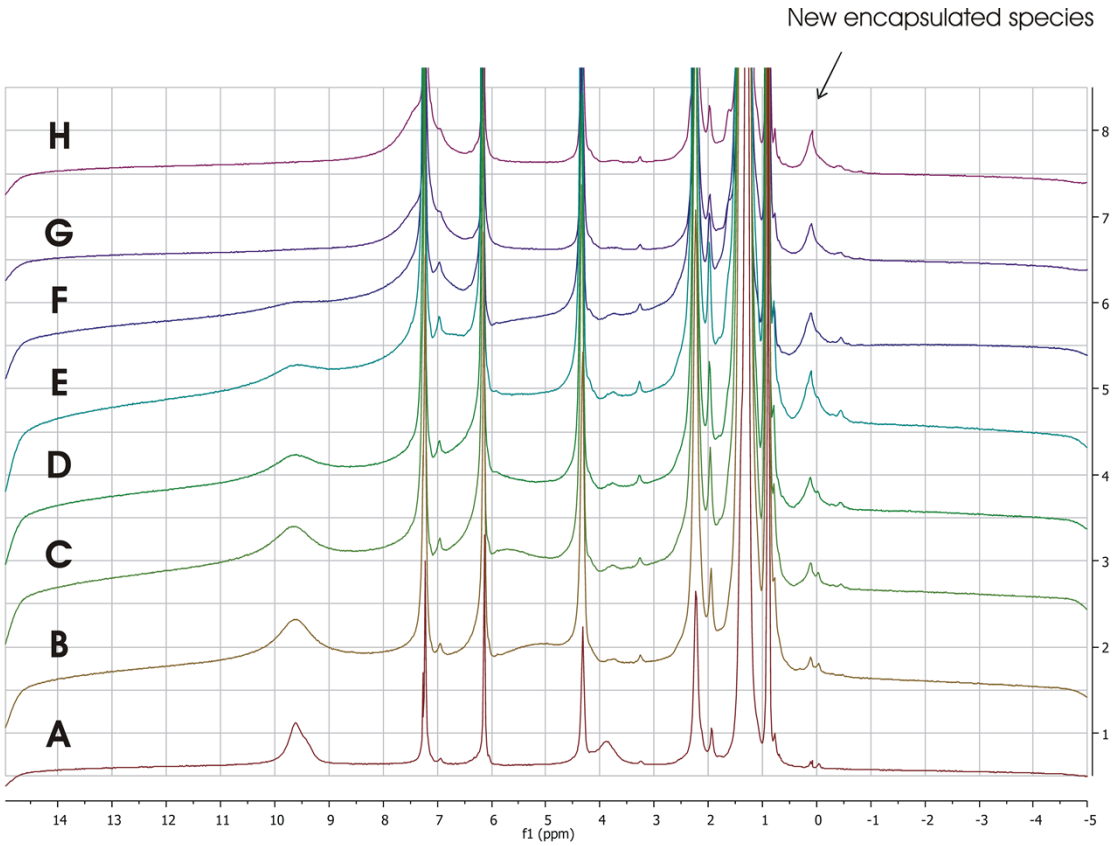


Figure S6. ^{1}H NMR spectra in water saturated chloroform-d: A) Hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) and 0.1 eq. of butylamine and 0.1 eq. of hexanoic acid; B) Hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) and 0.2 eq. of butylamine and 0.2 eq. of hexanoic acid; C) Hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) and 0.4 eq. of butylamine and 0.4 eq. of hexanoic acid; D) Hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) and 0.6 eq. of butylamine and 0.6 eq. of hexanoic acid; E) Hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) and 0.8 eq. of butylamine and 0.8 eq. of hexanoic acid; F) Hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) and 1.0 eq. of butylamine and 1.0 eq. of hexanoic acid; G) Hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) and 1.5 eq. of butylamine and 1.5 eq. of hexanoic acid; H) Hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) and 2.0 eq. of butylamine and 2.0 eq. of hexanoic acid. ⬇ encapsulated new species.

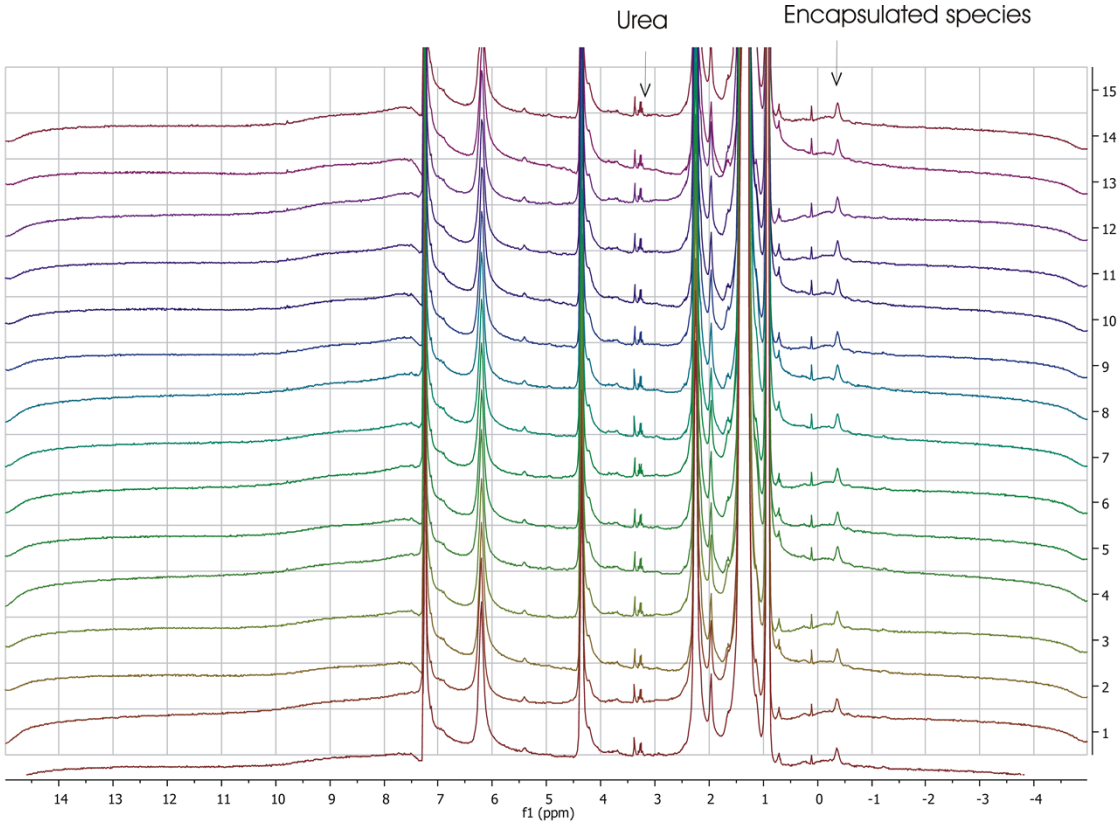
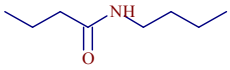
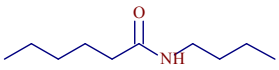
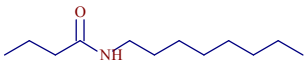
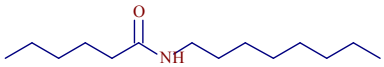
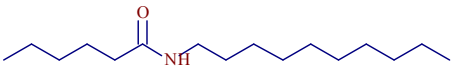
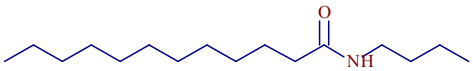
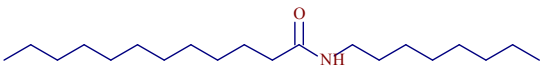
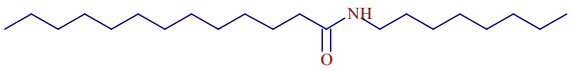
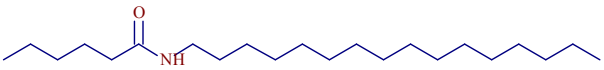
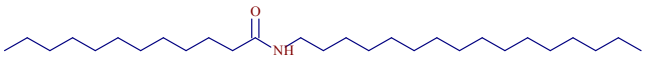


Figure S7. ^{1}H NMR spectra in water saturated chloroform-d for the reaction at 50°C monitored every 1h (from bottom to top) for the hexameric capsule $\mathbf{1}_6 \cdot 8H_2O$ (13.5 mM) octylamine (6.7 mM) hexanoic acid (6.7 mM) and **2** (13.2 mM).

GC-MS spectra of amide products

Reagents	RT	Product	PM	Internal Standard
C3COOH + C4NH2	9.57		143	Octane
C5COOH + C4NH2	10.63		171	Decane
C3COOH + C8NH2	11.51		199	Dodecane
C5COOH + C8NH2	12.27		227	Tetradecane
C5COOH + C10NH2	12.97		255	Tetradecane
C11COOH + C4NH2	12.99		255	Octane
C11COOH + C8NH2	14.31		311	Docosane
C12COOH + C8NH2	14.72		325	Docosane
C5COOH + C16NH2	15.21		339	Docosane
C11COOH + C16NH2	20.66		423	Tetradecane

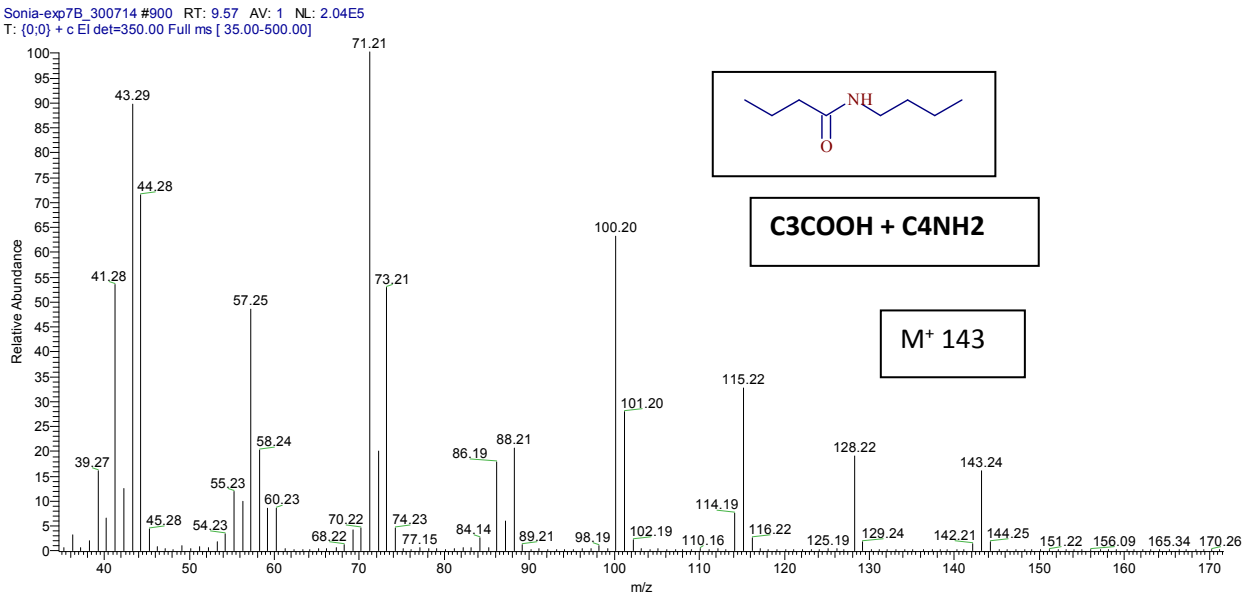


Figure S1. GC-MS of 5aa.

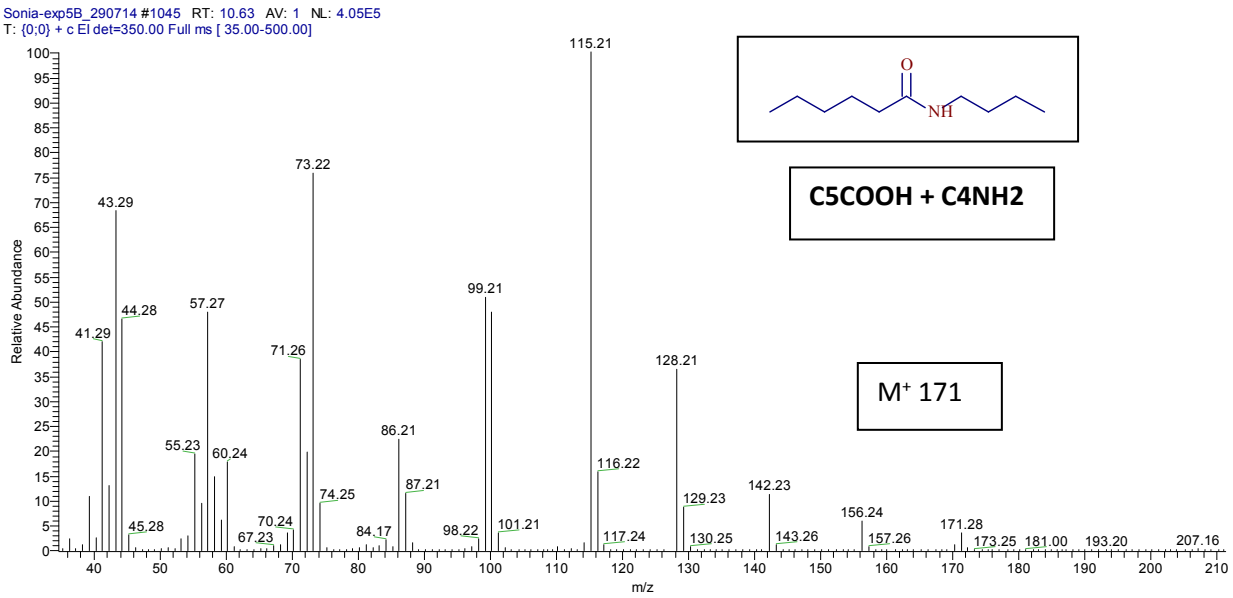


Figure S2. GC-MS of 5ba.

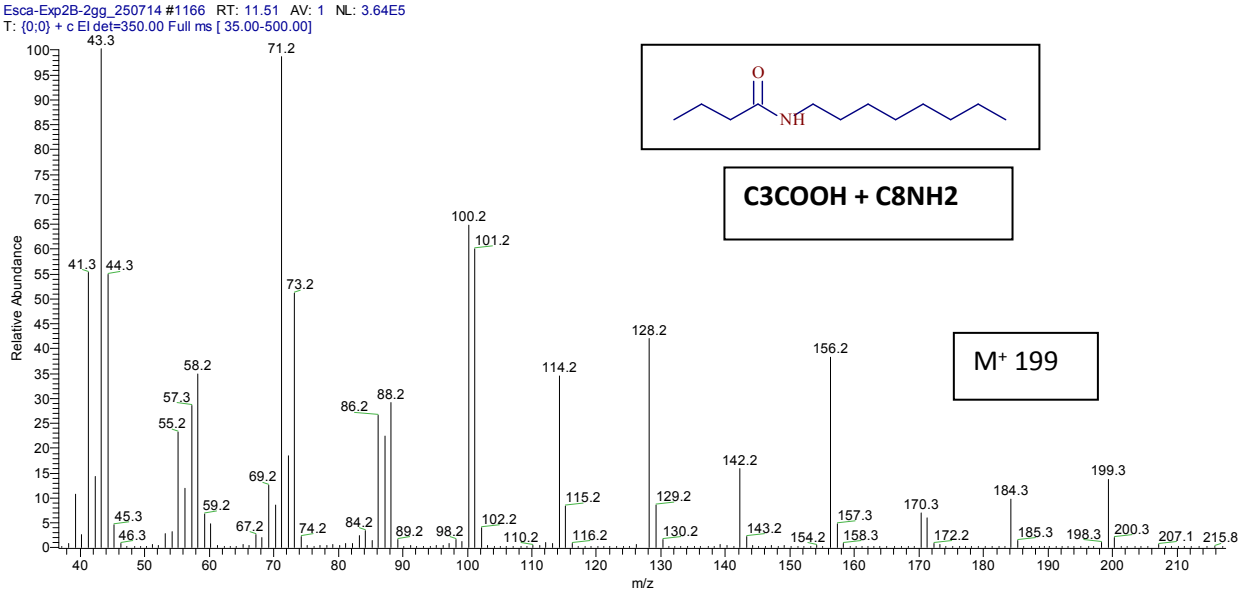


Figure S3. GC-MS of 5ab.

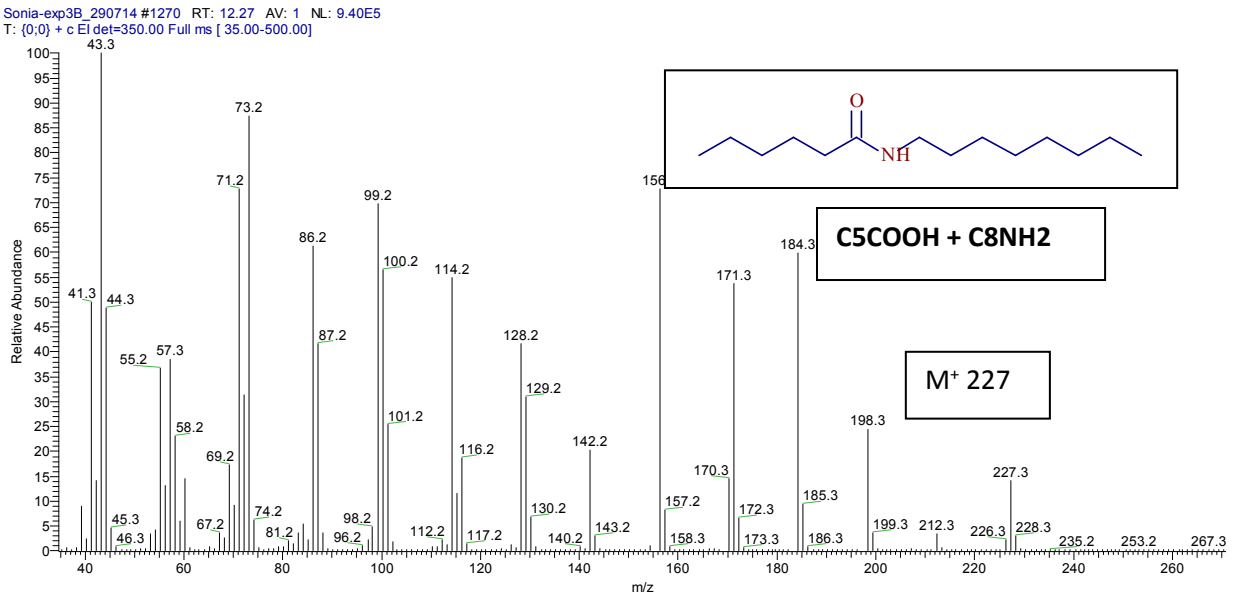


Figure S4. GC-MS of 5bb.

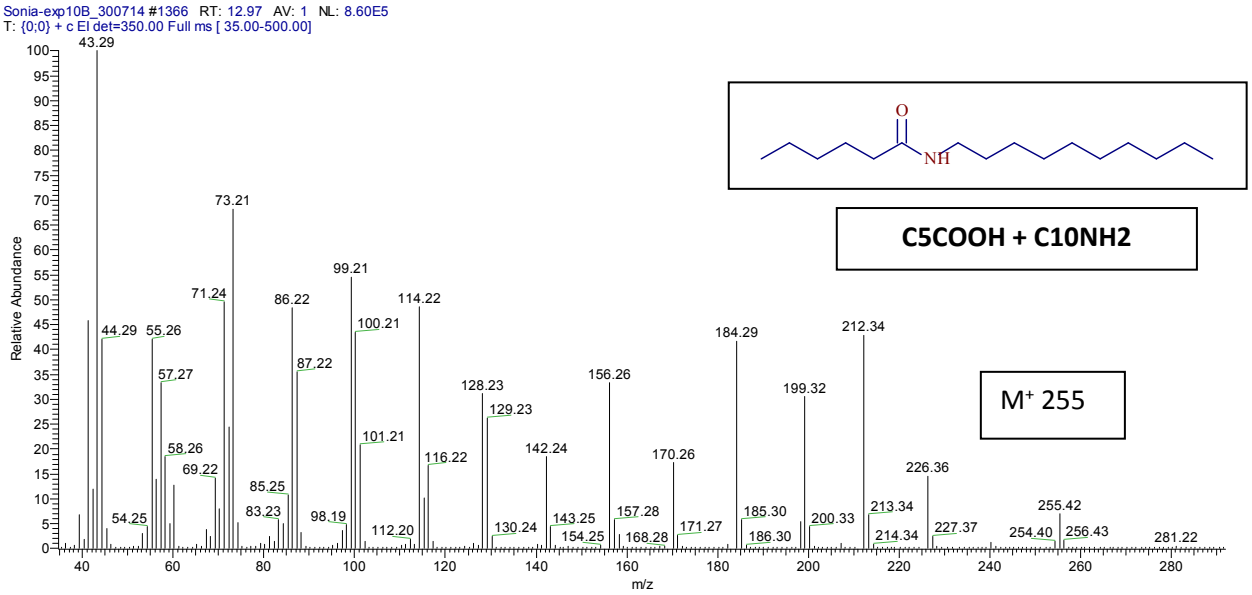


Figure S5. GC-MS of 5bc.

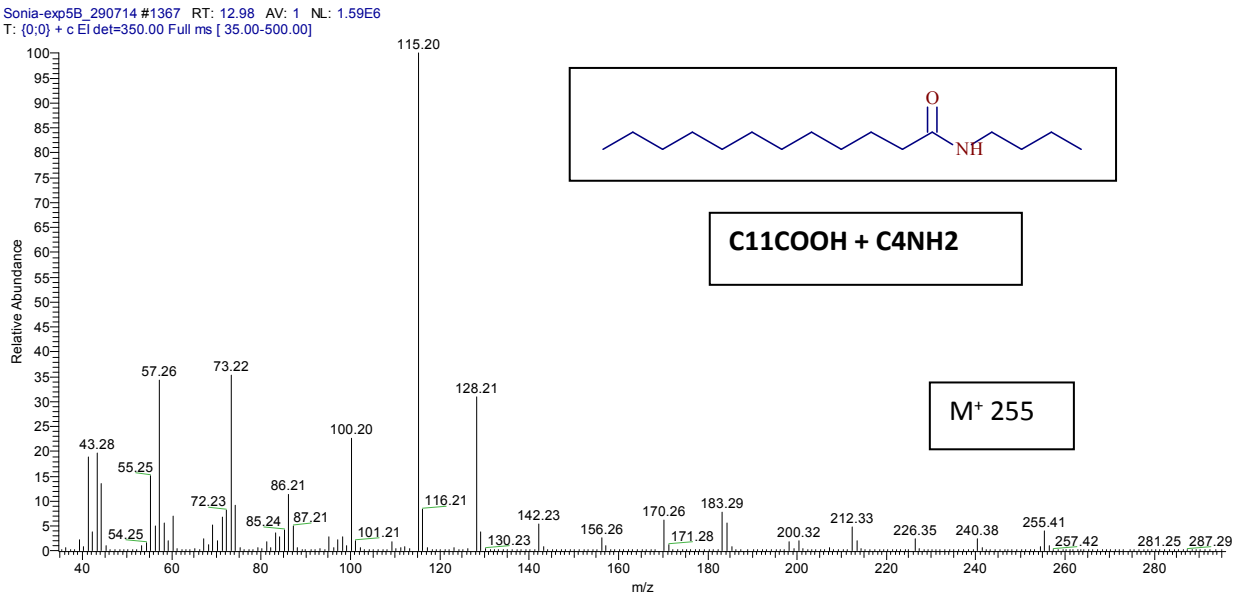


Figure S6. GC-MS of 5ca.

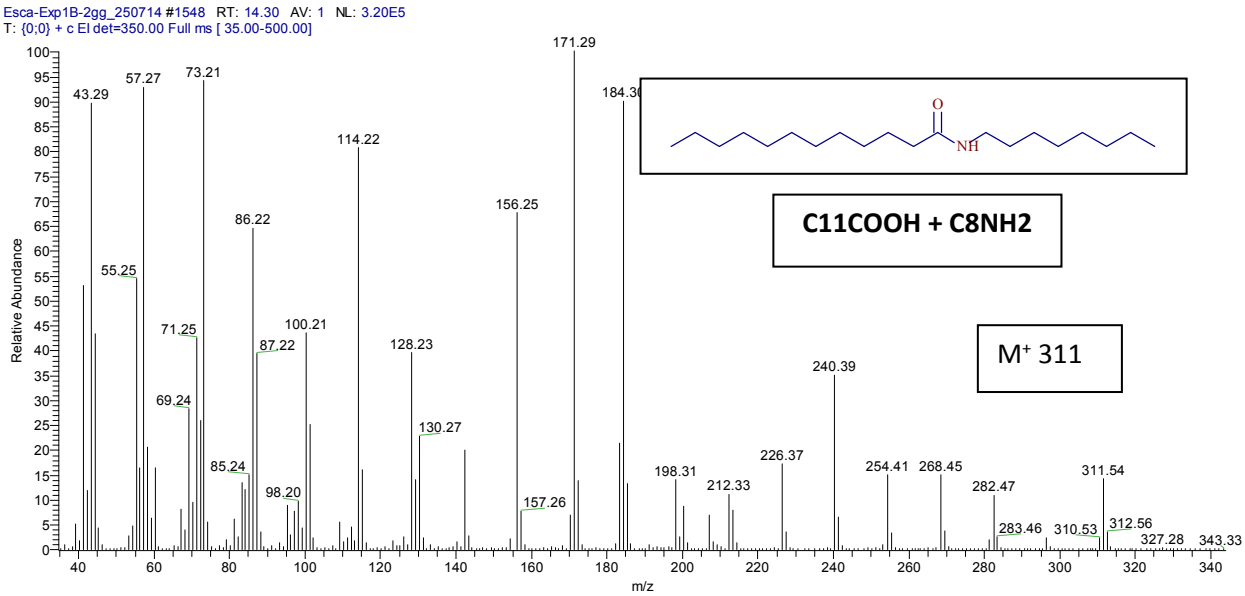


Figure S7. GC-MS of 5cb.

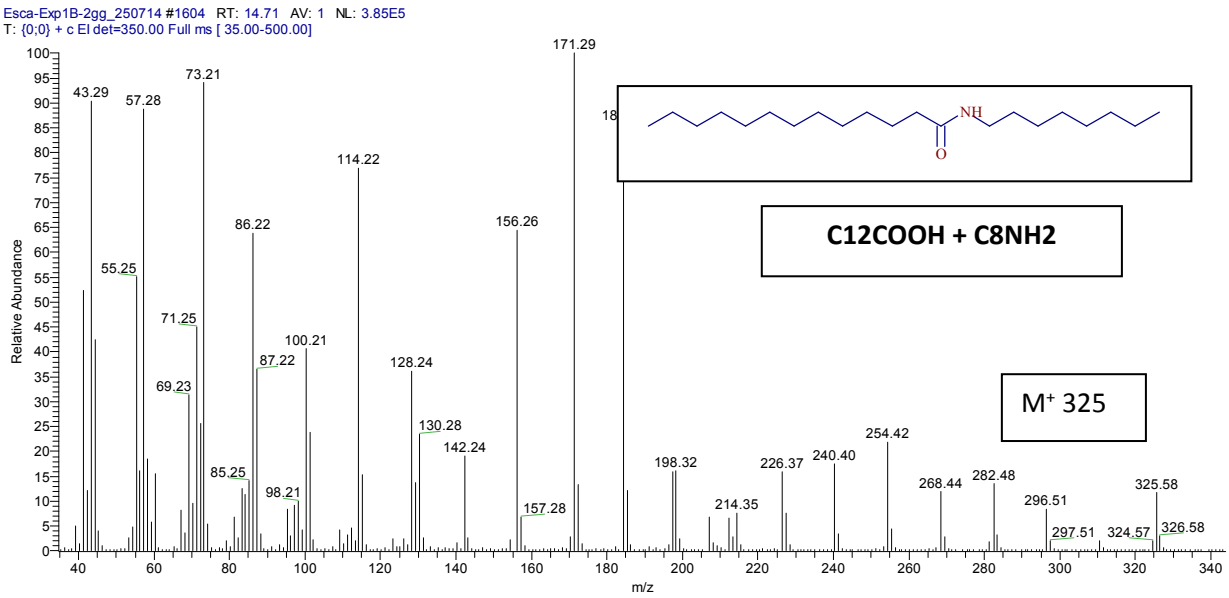


Figure S8. GC-MS of 5db.

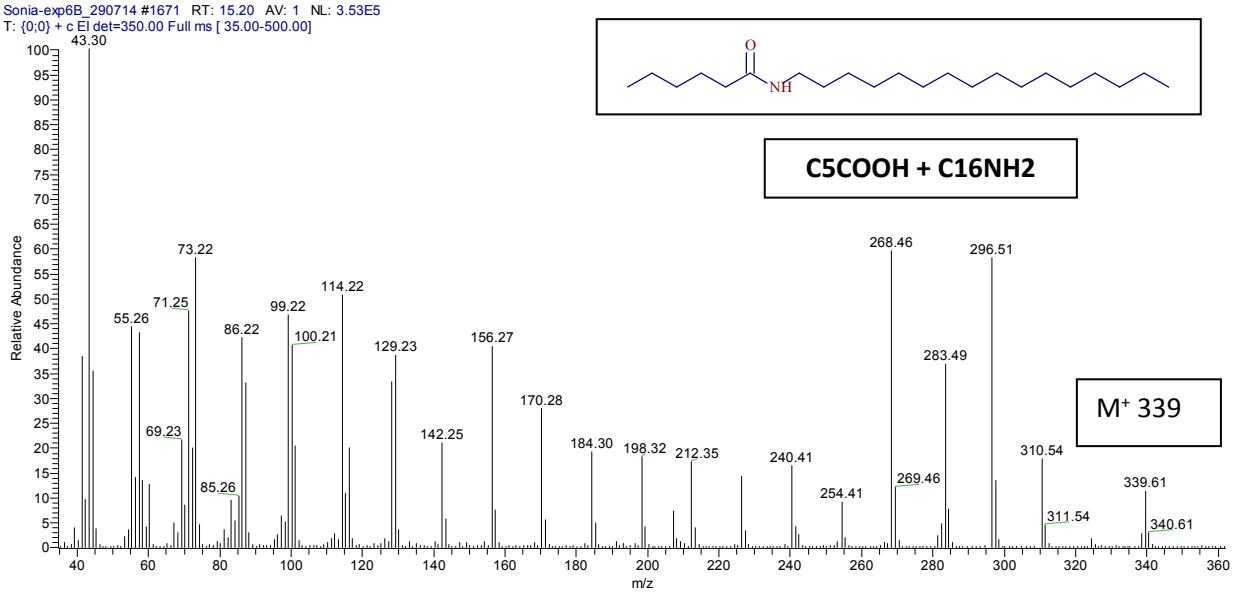


Figure S9. GC-MS of 5bc.

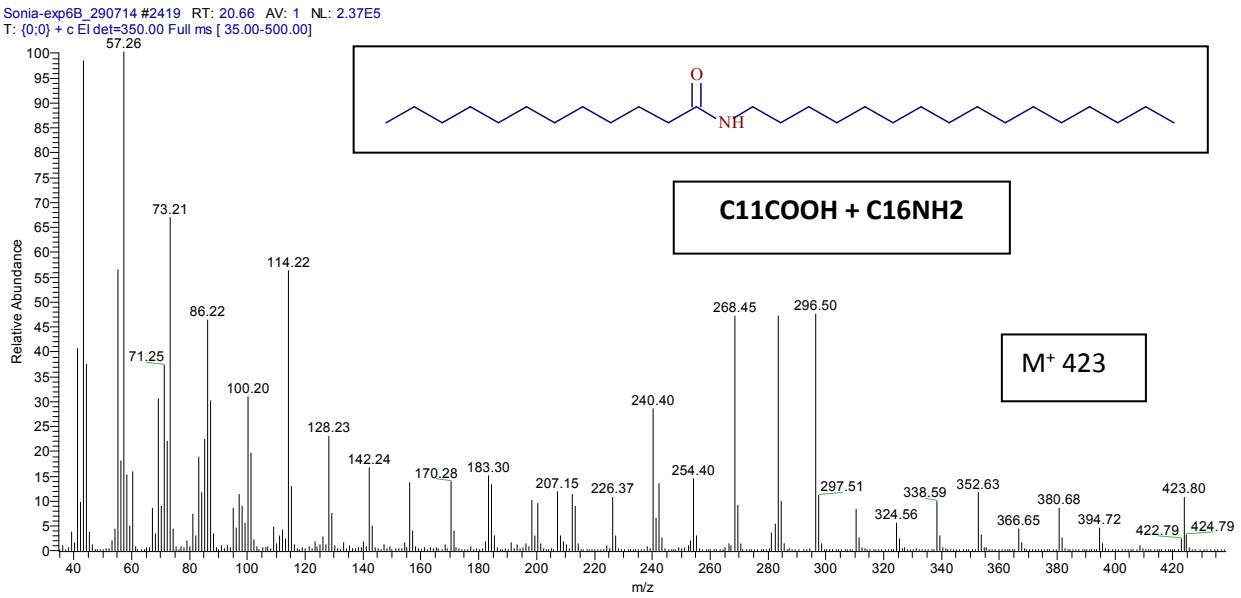


Figure S10. GC-MS of 5cc.

1 D.D. Perrin, W.L.F. Armarego, Purification of laboratory chemicals, 3rd edition, , Pergamon Press, 1993.
2 W. C. Still, M. Khan, A. Mitra *J. Org. Chem.* 1978, **43**, 2923.
3 Y. Aoyama, Y. Tanaka, S. Sugahara, *J. Am. Chem. Soc.,* **1989**, *111*, 5397-5404.