Electronic Supplementary Information

Guanidinium salts as catalysers for ε-caprolactam production

V. Fernández-Stefanuto,[a] P. Verdía[a] and E. Tojo[a*]

[a]Department of Organic Chemistry, Faculty of Chemistry, University of Vigo, 36210 Vigo, Spain

*etojo@uvigo.es

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Experimental

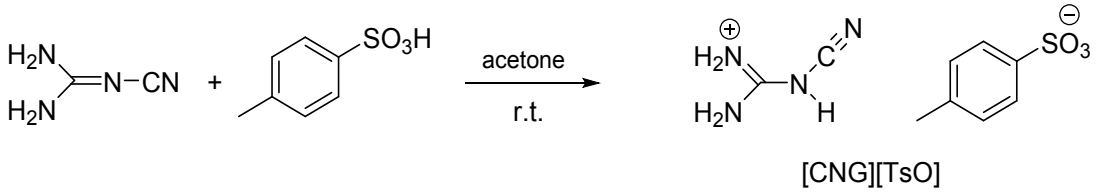
Materials and methods

The following reagents and solvents were purchased from commercial suppliers and employed without further purification: N-cyanoguanidine (Acros Organics, 99.5 %), *p*-toluensulfonic acid monohydrate (Sigma Aldrich ACS reagent, 98.5 %), acetone (Sigma Aldrich ACS reagent, 99.5 %), nitric acid (Acros Organics, 65 %), cyclohexanone oxime (Acros Organics, 97 %).

The glass material employed in the synthetic reactions was dried in an oven at 60 ºC during 24 h before its use. The evolution of the reactions was monitored by thin layer chromatography (t.l.c.) employing silica-gel sheets (Merck, TLC Silica gel 60 F_{254}). For the synthesis of the salts, a mixture of MeOH:CH_2Cl_2 = 1:9 was employed as eluent; for the synthesis of ε-caprolactam a mixture of AcOEt:Hex = 2:1 was employed as eluent; t.l.c. plates were visualized by exposure to U.V. (254 nm) and revealed by exposure to iodide (I_2) or, in the case of ε-caprolactam, by treatment with a solution of a revealing agent (*p*-anisaldehyde) and subsequent heating.

Spectroscopic data were provided by the Center of Scientific-Technological Support to Research (CACTI) of the University of Vigo. ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER ARX 4CO spectrometer at 400.1621 (^{1}H) and 100.6314 (^{13}C) MHz, respectively. $CDCl_3$ (ACROS Organics, 99.6+ atom % D) and DMSO-d_6 (ACROS Organics, 99.5+ atom % D) were employed as deuterated solvents as received from the supplier. Chemical shifts are quoted in parts per million (ppm) relative to the signals corresponding to the residual non-deuterated solvents ($CDCl_3$: δH =7.26 ppm, δC = 77.16 ppm; DMSO-d_6: δH = 2.50 ppm, δC = 39.52 ppm). Coupling constants are given in hertz (Hz). Mass spectra were recorded on a BRUKER FTMS APEXIII mass spectrometer. Elemental analysis were recorded on a Fisons Carlo Erba EA1108 elemental analyzer. The resolution of the structure of N-carbamoylguanidinium tosylate [NH_2COG][TsO] by X-Ray diffraction, was achieved on a BRUKER APEXII CCD and a BRUKER SMART 6000 CD diffractometers. Melting points of the solids were recorded on a STUART CIENTIFIC MELTING POINT APPARATUS SMP3. The pH values of the salts in solution were recorded at 70 ºC with a Crison PH-25 Crison Instruments pH meter employing standard solutions of known pH values of 4.01 (potassium hydrogen phthalate), 7.00 (Potassium dihydrogen phosphate/ di-sodium hydrogen phosphate) and 9.21 (sodium tetraborate) for the calibration of the apparatus.

Synthesis of 1-cyanoguanidinium *p*-toluensulfonate [CNG][TsO]



P-Toluensulfonic acid monohydrated (1.00 g, 5.20 mmol) was dissolved in acetone (5 mL) and added over a suspension of N-cyanoguanidine (0.45 g, 5.2 mmol) in acetone (2 mL). The mixture was allowed to stir at r.t. during 4 h until the end of reaction, as indicated by t.l.c. (silica gel, MeOH:CH_2Cl_2 = 1:9). The solid obtained was filtered, washed with acetone and dried under high vacuum (2 x 10^{-1} Pa) to give [CNG][TsO] (1.30 g, 96%) as a white solid; mp 230-231 ºC (from acetone); pH (70 ºC): 1.86; ^{1}H RMN (400 MHz, DMSO-d_6, referenced to DMSO-d_6) δ: 7.5 (2 H, d, *J* 7.7 Hz, Ar(2)H, Ar(6)H), 7.1 (2 H, d, *J* 7.7 Hz, Ar(3)H, Ar(5)H), 6.6 (4 H, br s, NH_2), 2.3 (3 H, s, CH_3); ^{13}C RMN (100 MHz, DMSO-d_6, referenced to DMSO-d_6) δ: 163.2, 145.2, 138.6, 128.7, 125.9, 118.7, 21.2; MS-ESI *m/z* (%): 341 ($[(C_2H_5N_4)_2(C_7H_7SO_3)]^+$, 100%) ($[A_2B]^+$), 597 ($[(C_2H_5N_4)_3(C_7H_7SO_3)_2]^+$, 73) ($[A_3B_2]^+$) , 853 ($[(C_2H_5N_4)_5(C_7H_7SO_3)_3]^+$, 12) ($[A_4B_3]^+$); Elemental Analysis (Found: C, 41.9; H, 5.0; N, 21.7; S, 12.4. $C_9H_{12}N_4O_3S$ requires C, 42.2; H, 4.7; N, 21.9; S, 12.5%).

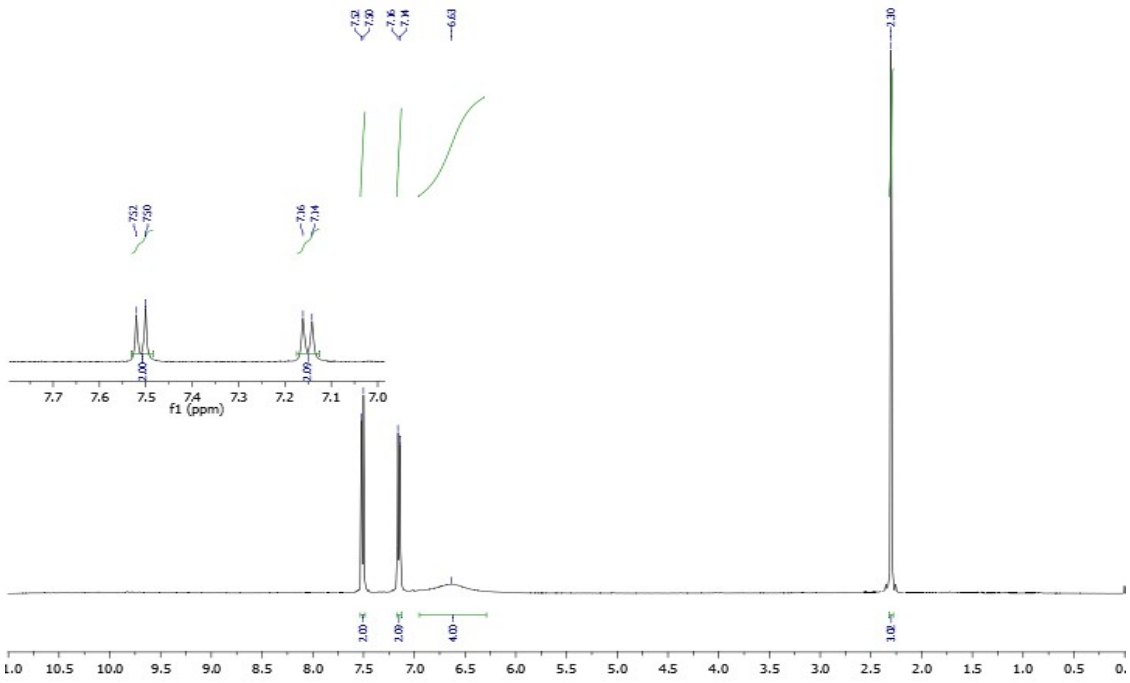


Fig S1.^{1}H RMN spectrum of [CNG][TsO].

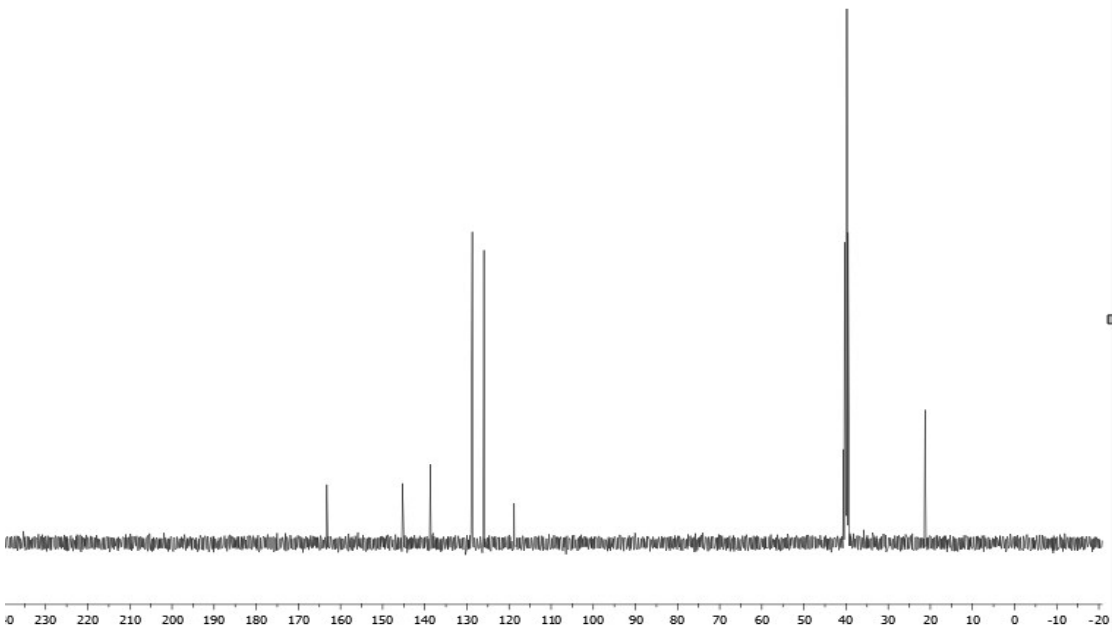


Fig S2. ^{13}C RMN spectrum of [CNG][TsO].

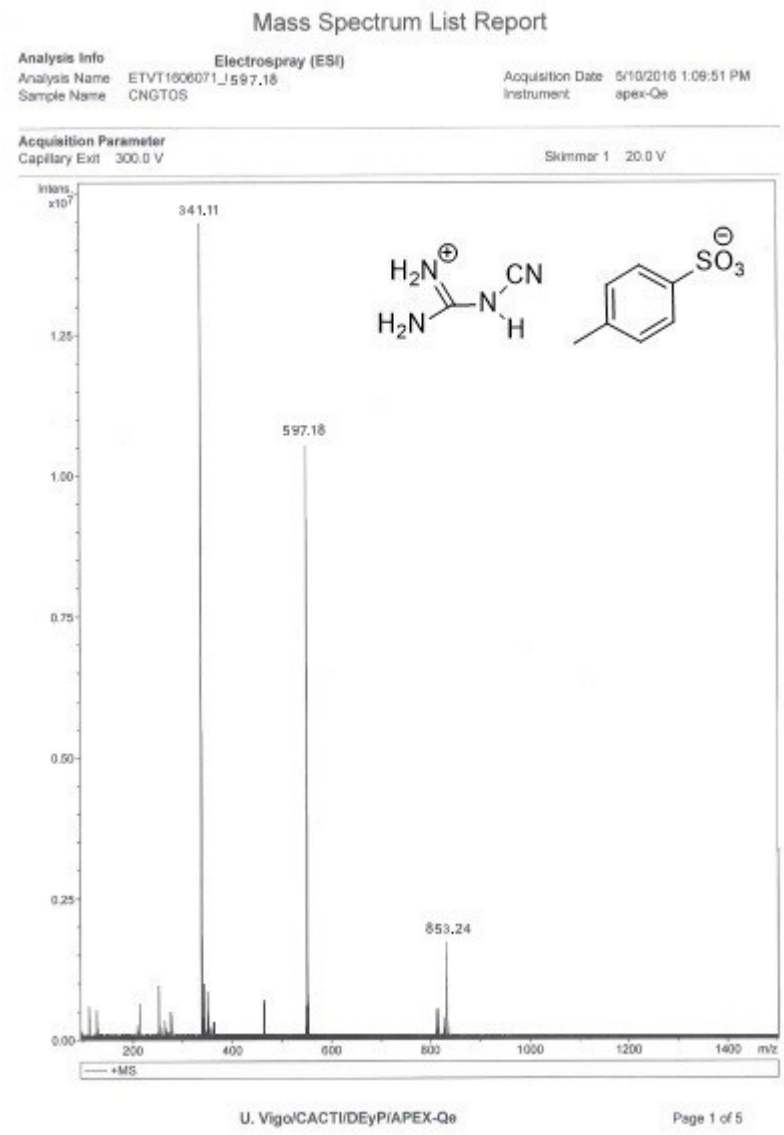
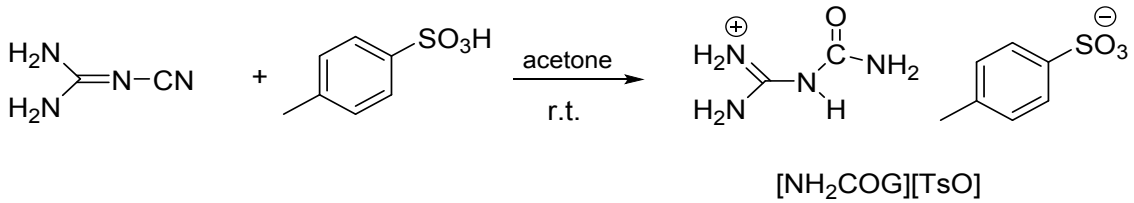


Fig S3. Mass spectrum of [CNG][TsO].

Synthesis of 1-carbamoylguanidinium*p*-toluensulfonate [NH_2COG][TsO]



[NH_2COG][TsO]

P-Toluensulfonic acid monohydrated (1.00 g, 5.20 mmol) was dissolved in acetone (5 mL) and added over a suspension of N-cyanoguanidine (0.45 g, 5.2 mmol) in acetone (2 mL). The mixture was allowed to stir at r.t. during 12 h until the end of reaction, as indicated by t.l.c. (silica gel, MeOH:CH_2Cl_2 = 1:9). The solid obtained was filtered, recrystallized in H_2O and dried under high vacuum (2 x 10^{-1} Pa) to give [NH_2COG][TsO] (1.25 g, 93%) as colourless crystals; mp178-80 ºC (from H_2O); ^{1}H RMN (400 MHz, DMSO-d_6, referenced to DMSO-d_6) δ: 9.7 (1 H, s, NH), 8.0 (4 H, br s, C(NH_2)$_2$), 7.2 (2 H, s,NH_2C=O), 7.5 (2 H, d, *J* 7.7 Hz,Ar(2)H, Ar(6)H), 7.1 (2 H, d, *J* 7.7 Hz, Ar(3)H, Ar(5)H), 2.3 (3 H, s, CH_3); ^{13}C RMN (100 MHz, DMSO-d_6, referenced to DMSO-d_6) δ: 155.8, 154.8, 144.7, 139.0, 128.8, 125.9, 21.2; MS-ESI *m/z* (%): 377 ([$(C_2H_7N_4O)_2(C_7H_7SO_3)$]$^+$, 100%) ([$A_2B$]$^+$), 651([$(C_2H_7N_4O)_3(C_7H_7SO_3)_2$]$^+$, 62) ([$A_3B_2$]$^+$), 925 ([$(C_2H_7N_4O)_5(C_7H_7SO_3)_3$]$^+$, 32) ([$A_4B_3$]$^+$); Elemental Analysis (Found: C, 40.8; H, 5.1; N, 20.2; S, 10.95. $C_9H_{14}N_4O_4S$ requires C, 40.9; H, 5.1; N, 20.1; S, 10.85%).

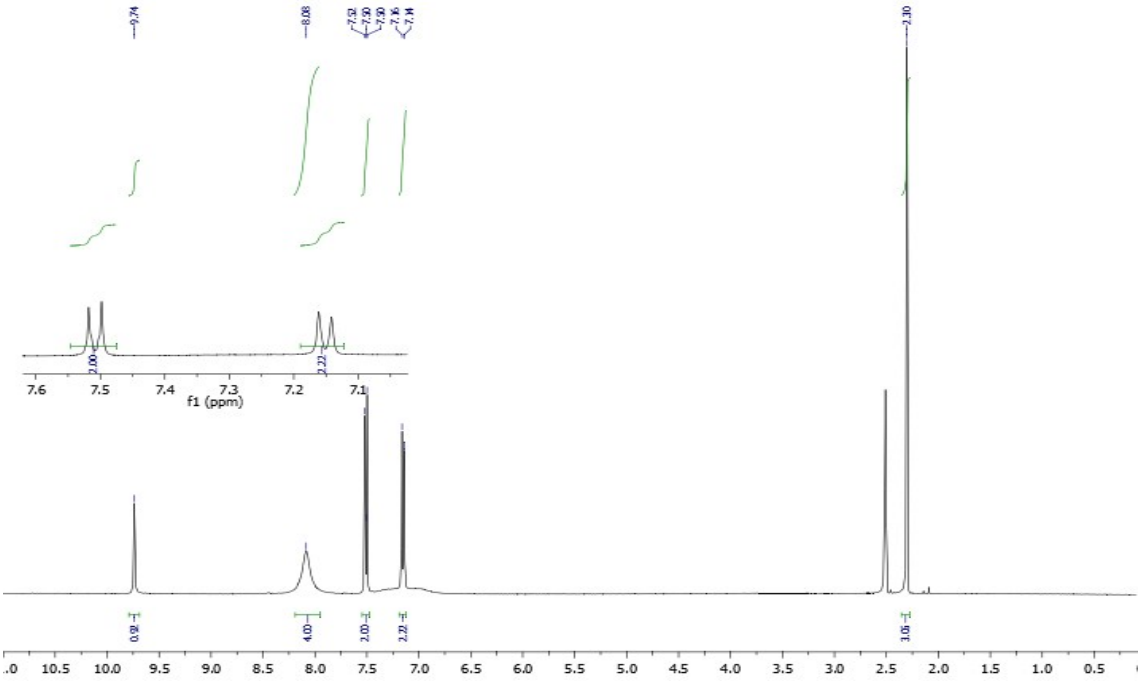


Fig S4. ^{1}H RMN spectrum of [NH_2COG][TsO].

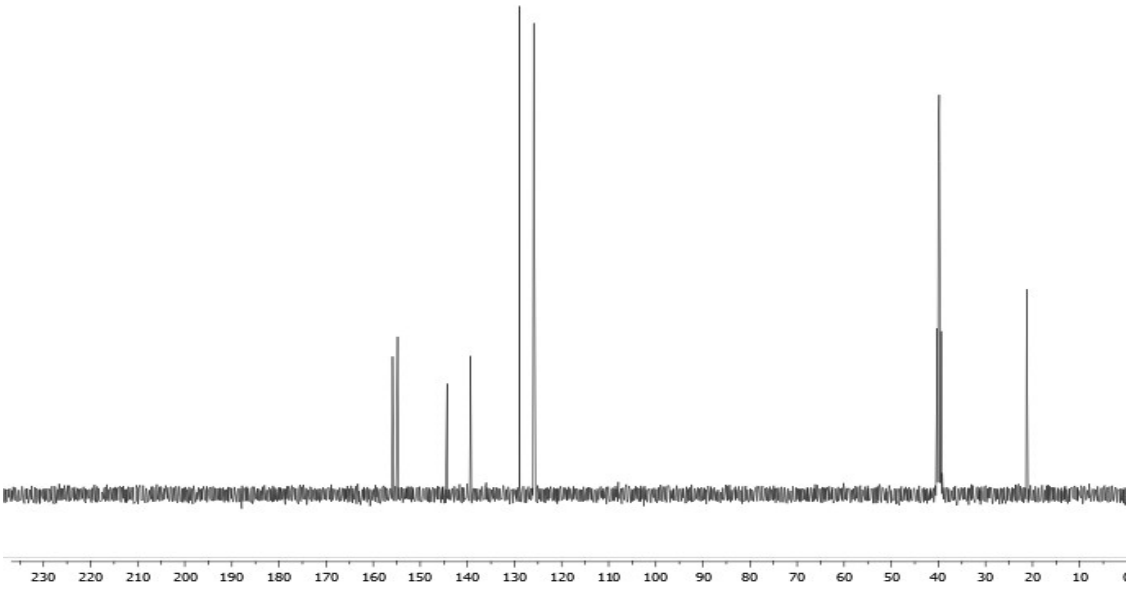


Fig S5. ^{13}C RMN spectrum of $[NH_2COG][TsO]$.

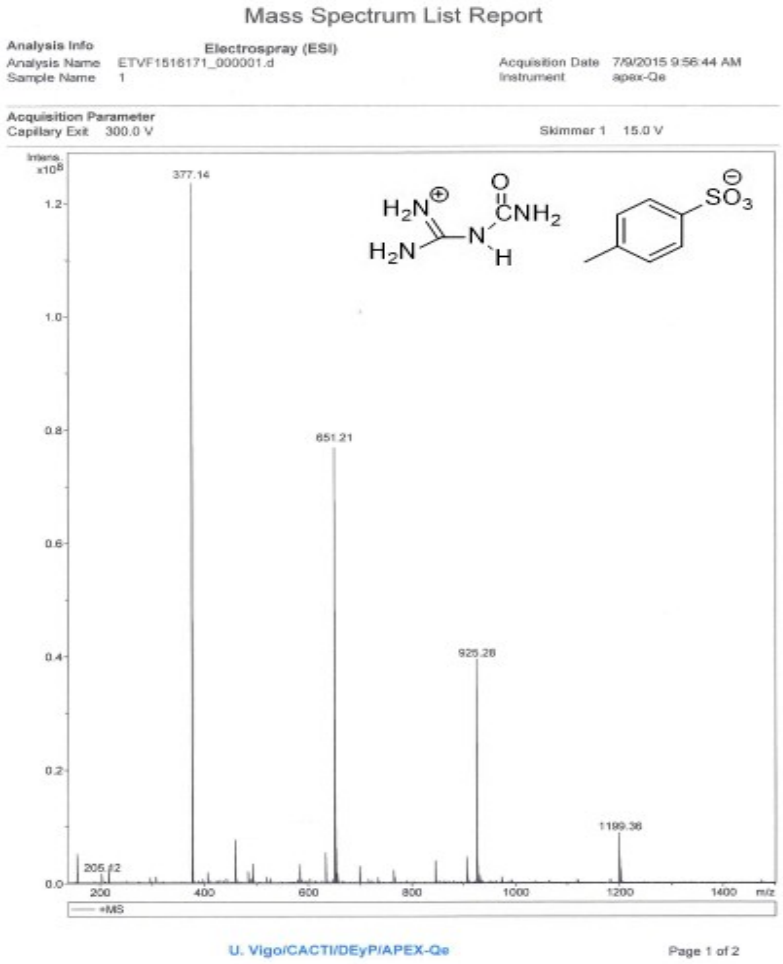
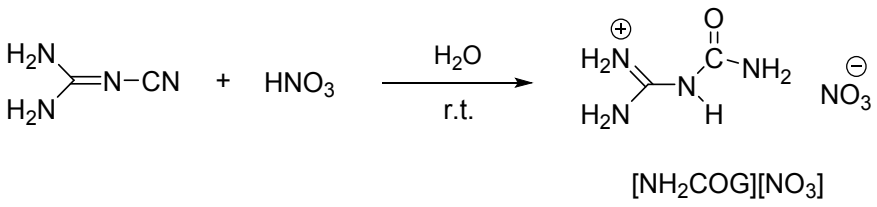


Fig S6. Mass spectrum of $[NH_2COG][TsO]$.

Synthesis of 1-carbamoylguanidinium nitrate [NH_2COG][NO_3]



[NH_2COG][NO_3]

Nitric acid (65%, 0.50 mL) was added dropwise over a solution of N-cyanoguanidine (0.50 g, 5.90 mmol) in H_2O (5 mL). The mixture was allowed to stir at r.t. for 15 min, and then it was boiled at 100 ºC during 3 min. It was allowed to cool down to r.t. and a white precipitate was obtained; it was filtered, washed with H_2O and dried under high vacuum (2 x 10^{-1} Pa) giving [NH_2COG][NO_3] (1.00 g, 94%) as a white solid ; mp 202-203 ºC (from H_2O) (lit.,[1] 200 ºC); ^{1}H RMN (400 MHz, DMSO-d_6, referenced to DMSO-d_6) δ: 9.7 (1 H, s, NH), 8.0 (4 H, s, $C(NH_2)_2$), 7.1 (2 H, s, NH_2C=O); ^{13}C RMN (100 MHz, DMSO-d_6, referenced to DMSO-d_6) δ: 155.8, 154.8.

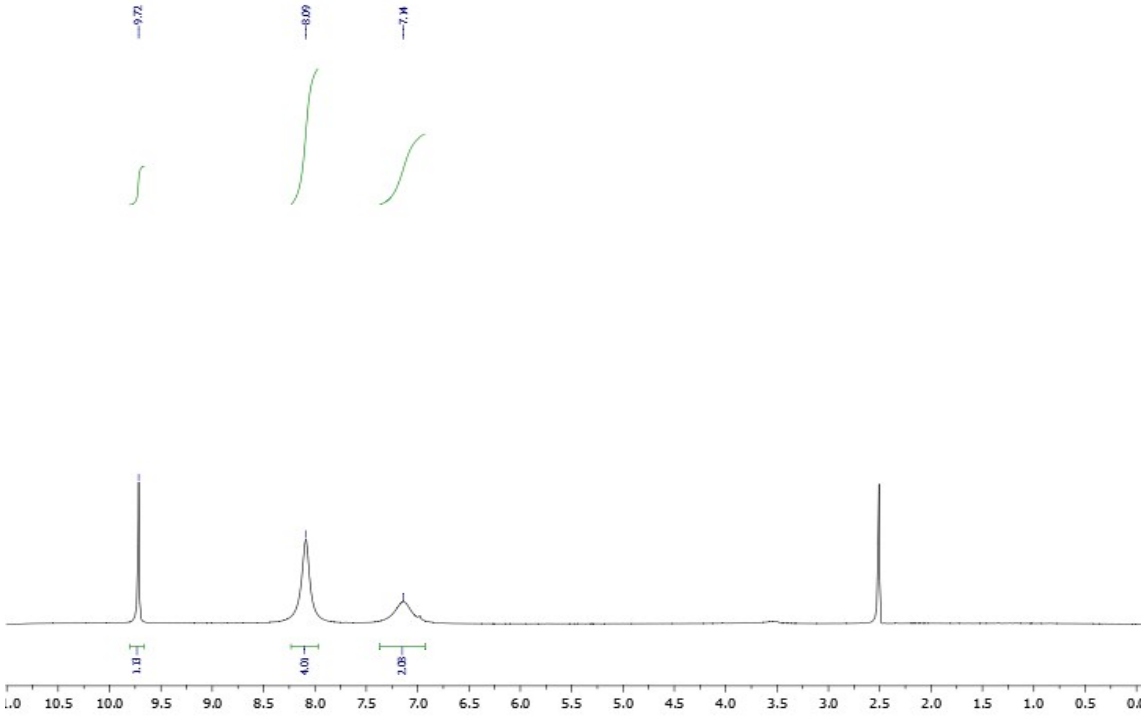


Fig S7. ^{1}H RMN spectrum of [NH_2COG][NO_3].

[1]T.M. Klapötke, C. Miró Sabaté, *Heteroatom Chem.*, **2008**, *19*, 301-306.

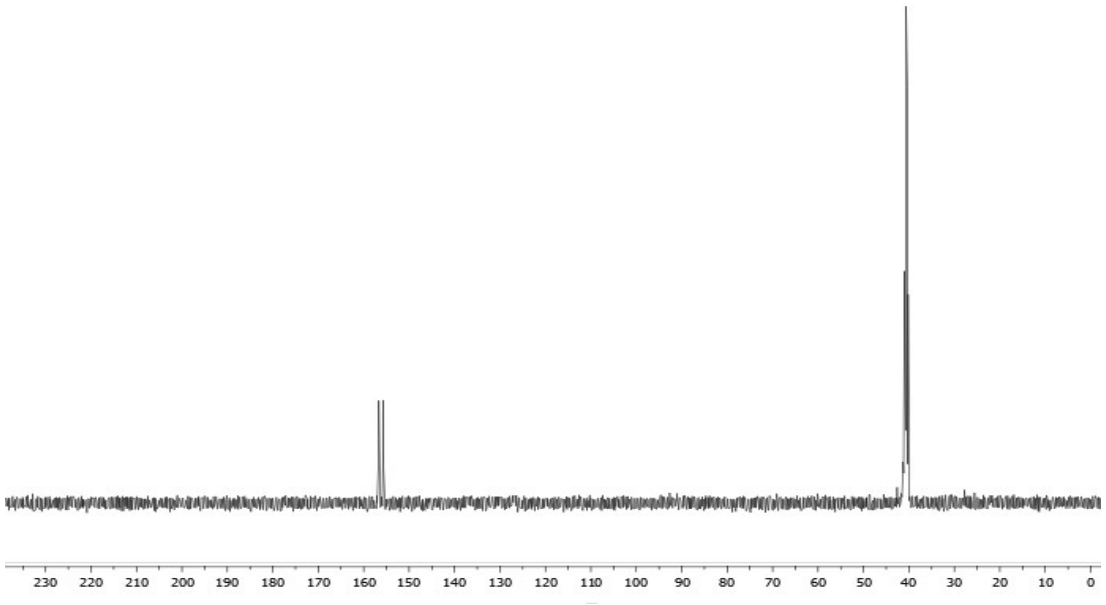
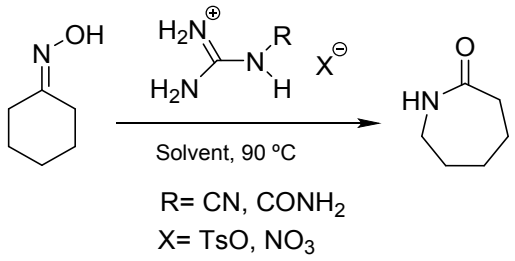


Fig S8. ^{13}C RMN spectrum of $[NH_2COG][NO_3]$.

Synthesis of ε-caprolactam



A solution of the cyclohexanone oxime (1.00 g, 8.80 mmol) in 25 mL of the selected solvent (H_2O, MeOH or DMF) was added over a suspension of the corresponding guanidinium salt (1-2 eq.) in 20 mL of the same solvent (Table 1). The mixture was heated at a temperature ranging from 60 ºC to 90 ºC and allowed to stir until the end of reaction, as indicated by t.l.c. (silica gel, AcOEt:Hex = 2:1). The solvent was then removed by heating under reduced pressure and the resulting crude reaction product was worked up by one of the following methods:

a) CH_2Cl_2 (20 mL) was added to the crude reaction product and the mixture was kept at -20 ºC during 10 h. A precipitate was formed and separated by filtration under vacuum. The solvent was removed by heating under reduced pressure. H_2O (25 mL) was added and ε-caprolactam was extracted with CH_2Cl_2 (4 x 20 mL). CH_2Cl_2 was removed by heating under reduced pressure and ε-caprolactam (0.597 g, 60 %) was isolated with high purity (99%).

b) As an alternative method, ε-caprolactam was isolated by sublimation from the mixture with the guanidinium salt. The mixture of ε-caprolactam and guanidinium salt was heated at 120 ºC under reduced pressure (2 x 10^{-1} Pa), employing a cold finger kept cool with a stream of water at 20 ºC to allow the deposition of the sublimate. Crystals of pure ε-caprolactam (0.984 g, 99 %) were collected.

Data: mp 69.5-71 ºC (from hexane) (lit.,[2] 72 ºC); ^{1}H RMN (400 MHz, DMSO-d_6, referenced to DMSO-d_6) δ: 6.0 (1 H, s, NH), 3.2 (2 H, dd, J_1 5.7 Hz, J_2 9.6 Hz, C(3)H), 2.4 (2 H, m,C(7)H), 1.77* (2 H, m, C(6)H), 1.72* (2 H, m, C(4)H), 1.68 (2 H, m, C(5)H); ^{13}C RMN (100 MHz, DMSO-d_6, referenced to DMSO-d_6) δ: 179.3, 42.8, 36.7, 30.6, 29.7, 23.2.

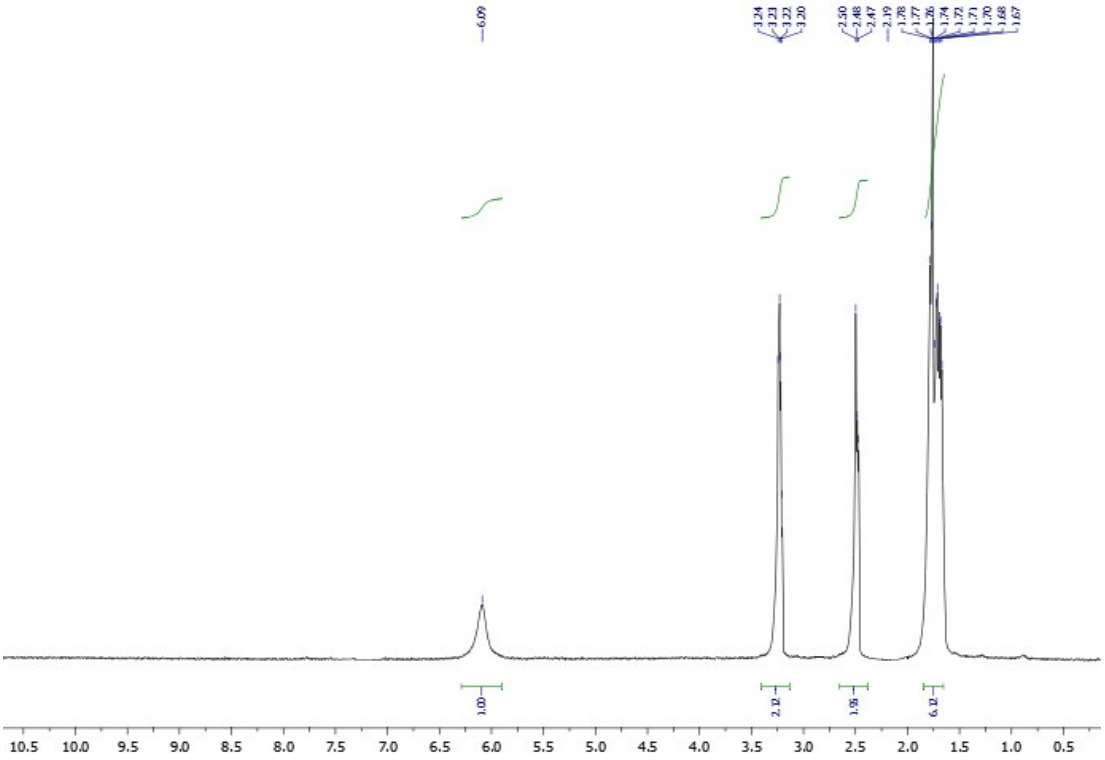


Fig S9. ^{1}H RMN spectrum of ε-caprolactam.

[2]Y. Izumi, S. Sato, K. Urabe, *Chem. Lett*., **1983**, 1649-1652.

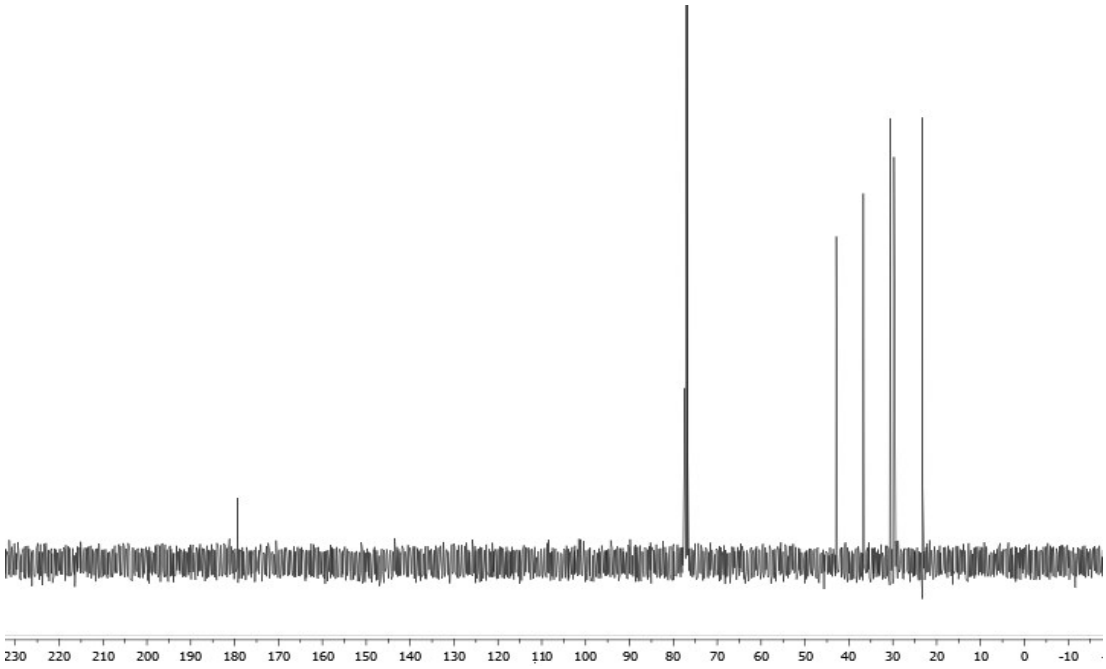


Fig S10. ^{13}C RMN spectrum of ε-caprolactam.

X-Ray data of 1-carbamoylguanidinium *p*-toluensulfonate ([NH_2COG][TsO])

Table S1. Crystal data and structure refinement for 1-carbamoylguanidinium *p*-toluensulfonate [NH_2COG][TsO]

Empirical formula	$C_9 H_{14} N_4 O_4 S$	
Formula weight	274.30	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 6.6195(13) Å	α= 96.15(3)°.
	b = 8.2505(19) Å	β= 99.794(18)°.
	c = 12.924(5) Å	γ = 97.771(14)°.
Volume	683.0(3) $Å^3$	
Z	2	
Density (calculated)	1.334 Mg/m^3	
Absorption coefficient	2.254 mm^{-1}	
F(000)	288	
Crystal size	0.124 x 0.109 x 0.031 mm^3	
Theta range for data collection	3.502 to 68.189°.	
Index ranges	-7<=h<=7, -9<=k<=9, -15<=l<=15	
Reflections collected	14099	
Independent reflections	2439 [R(int) = 0.0578]	

Completeness to theta = 67.679°	98.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7530 and 0.5733
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2439 / 7 / 179
Goodness-of-fit on F^2	1.069
Final R indices [I>2sigma(I)]	R1 = 0.0573, wR2 = 0.1658
R indices (alldata)	R1 = 0.0680, wR2 = 0.1763
Extinction coefficient	n/a
Largest diff. peak and hole	0.388 and -0.170 e.Å^{-3}

Table S2. Bond lengths [Å] and angles [°] for 1-carbamoylguanidinium *p*-toluensulfonate ([NH_2COG][TsO]).

C(1)-O(1)		1.216(3)
C(1)-N(1)		1.322(4)
C(1)-N(2)		1.396(3)
C(2)-N(3)		1.304(3)
C(2)-N(4)		1.315(4)
C(2)-N(2)		1.347(3)
S(1)-O(4)		1.426(2)
S(1)-O(3)		1.443(2)
S(1)-O(2)		1.452(2)
S(1)-C(3)		1.749(3)
C(4)-C(3)	1.3900	
C(4)-C(5)		1.3900
C(3)-C(4')		1.3900
C(4')-C(5')		1.3900
C(5')-C(6)		1.3900
C(6)-C(5)		1.3900
C(6)-C(7)		1.533(8)
O(1)-C(1)-N(1)	124.4(3)	
O(1)-C(1)-N(2)	121.7(2)	
N(1)-C(1)-N(2)	113.9(2)	
N(3)-C(2)-N(4)	120.9(2)	
N(3)-C(2)-N(2)	121.6(2)	
N(4)-C(2)-N(2)	117.5(2)	

C(2)-N(2)-C(1)	125.4(2)
O(4)-S(1)-O(3)	112.31(15)
O(4)-S(1)-O(2)	113.64(15)
O(3)-S(1)-O(2)	111.23(14)
O(4)-S(1)-C(3)	106.22(15)
O(3)-S(1)-C(3)	107.06(18)
O(2)-S(1)-C(3)	105.80(14)
C(3)-C(4)-C(5)	120.0
C(4)-C(3)-C(4')	120.0
C(4)-C(3)-S(1)	120.0(2)
C(4')-C(3)-S(1)	119.9(2)
C(5')-C(4')-C(3)	120.0
C(6)-C(5')-C(4')	120.0
C(5)-C(6)-C(5')	120.0
C(5)-C(6)-C(7)	118.4(8)
C(5')-C(6)-C(7)	121.6(8)
C(6)-C(5)-C(4)	120.0

Table S3. Hydrogen bonds for 1-carbamoylguanidinium *p*-toluensulfonate ([NH_2COG][TsO]) [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(3)-H(3A)...O(3)#1	0.865(19)	2.09(2)	2.912(3)	157(3)
N(1)-H(1A)...O(2)#2	0.840(18)	2.18(2)	3.005(4)	165(3)
N(2)-H(2)...O(2)	0.862(18)	2.008(18)	2.867(3)	173(3)
N(1)-H(1B)...O(3)	0.855(19)	2.04(2)	2.875(4)	165(3)
N(3)-H(3B)...O(1)	0.855(18)	2.00(3)	2.638(3)	131(3)
N(3)-H(3B)...O(4)#3	0.855(18)	2.47(3)	3.072(3)	128(3)
N(4)-H(4A)...O(4)#1	0.849(18)	2.30(2)	3.104(4)	159(3)
N(4)-H(4A)...O(3)#1	0.849(18)	2.62(3)	3.263(4)	134(3)
N(4)-H(4B)...O(1)#4	0.860(18)	2.10(3)	2.735(3)	130(3)

Symmetry transformations used to generate equivalent atoms:

#1 x,y+1,z #2 x+1,y,z #3 x+1,y+1,z #4 x-1,y,z