Supporting Information

Electronic Activity Tuning of Acyclic Guanidines for Lactide Polymerization

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1. General Methods

Solvents and commercial starting materials were used as received. Solvents were dried before use by employing an Innovative Technologies solvent purification system. Reactions were monitored by thin layer chromatography (TLC) carried out on silica gel plates (Merck 60F-254) using UV light for visualization. Column chromatography was carried out with silica gel (Merck 60, particle size 0.040–0.063 mm) using eluents as specified. NMR spectra were recorded on a 500 MHz Bruker AV 500, a 400 MHz Bruker AV 400, or a 300 MHz Bruker DPX 300 spectrometer at 25 °C using residual protonated solvent signals as internal standards for ^{1}H and ^{13}C spectra (^{1}H: $\delta(CDCl_3)$ = 7.26 ppm, $\delta(CD_3OD)$ = 4.87 ppm, and $\delta(DMSO\text{-}d_6)$ = 2.50 ppm; ^{13}C: $\delta(CDCl_3)$ = 77.16 ppm, $\delta(CD_3OD)$ = 49.00 ppm, and $\delta(DMSO\text{-}d_6)$ = 39.5 ppm). The splitting patterns are abbreviated as follows: singlet (s), doublet (d), triplet (t), quadruplet (q), multiplet (m), and broad (br). UPLC/MS was performed with a Waters UPLC Acquity equipped with a Waters LCT Premier XE Mass Detector for UPLC-HR-MS, with Waters Alliance systems (consisting of a Waters Separations Module 2695, a Waters Diode Array Detector 996 and a Waters Mass Detector ZQ 2000). Masses were recorded with a Thermo scientific LTQ Orbitrap XL mass spectrometer. GPC measurements in THF as the mobile phase were performed with a WGE Dr. Bures system equipped with three 300x8 mm SDV columns (50 Å, 5 µm, 500 Å, 5 µm, 1000 Å, 5 µm) in a WGE Dr. Bures TAU 2010 column oven at 60 °C and at room temperature, using a WGE Dr. Bures Q-2010 GPC pump and a Knauer Smartline 3800 autosampler. Detection was achieved using a Knauer K2301 RI-detector and a Knauer Smartline 2500 UV-detector. Flow-rate was 1.0 mL/min. Columns were calibrated using a Polystyrene Calibration Kit S-L-10 LOT 79, using 2,4-di-tert-butyl-4-methoxy-phenol as internal standard. Thermal analysis was carried out using a PerkinElmer Differential Scanning Calorimeter DSC 8000.

2. ROP of L-lactide

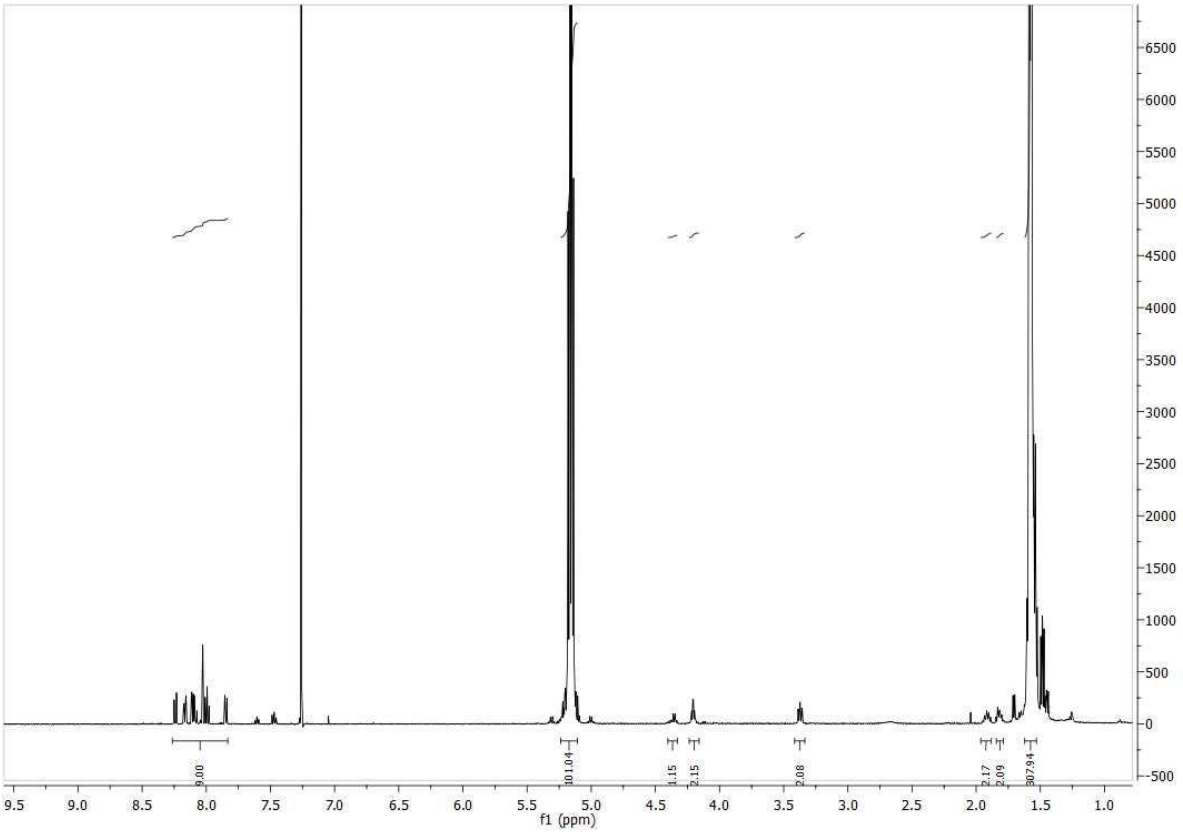
All polymerization experiments were conducted in flame-dried glassware under inert conditions, thereby using a MBraun Glovebox with a MB 20G LMF purification system. L-Lactide was recrystallized three times from toluene and dried in a vacuum prior to use. Pre-dried CH_2Cl_2 was received from drying columns using a setup from Innovative Systems, subsequently distilled over CaH_2, and stored over molecular sieves (4 Å) for no longer than two weeks. 1-Pyrenebutanol was dried by azeotropic distillation of toluene followed by lyophilization out of benzene. All catalysts were dried by lyophilization out of benzene. To investigate the course of the polymerization process aliquots were taken from the polymerization solution at different times, treated with excess of benzoic acid and analyzed by ^{1}H NMR spectroscopy. Conversion of the monomer was determined by comparison of the ^{1}H NMR signals caused by the methine groups of both polymer and residual monomer. In order to determine the molecular weight and PDI values PLA was precipitated from MeOH. The resulting white solid was dried *in vacuo* and examined by NMR spectroscopy and GPC.

2.1 Polymerization procedure

L-Lactide (288 mg, 2.00 mmol, 50 eq.), 1-pyrenebutanol (11 mg, 0.04 mmol, 1 eq.), and guanidine catalyst (0.04 mmol, 1 eq.) were added to a flame-dried flask, dissolved in 1.0 mL of CH_2Cl_2 and stirred at room temperature. After complete conversion of the monomer benzoic acid was added to quench the reaction and the mixture was added to an excess of MeOH (*ca.* 20 mL) to obtain polylactide as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ(ppm) = 8.26 - 7.83 (m, 9H, CH_{aryl}), 5.24-5.11 (m, 100 H, C*H*), 4.33 (m, 1H, C*H*), 4.21 (m, 2H, CH_2), 3.37 (m, 2H, CH_2), 1.92 (m, 2H, CH_2), 1.82 (m, 2H, CH_2), 1.61-1.41 (m, 300 H, CH_3). **^{13}C-NMR (125 MHz, $CDCl_3$):** δ(ppm) = 169.8, 69.2, 16.8.

(a)



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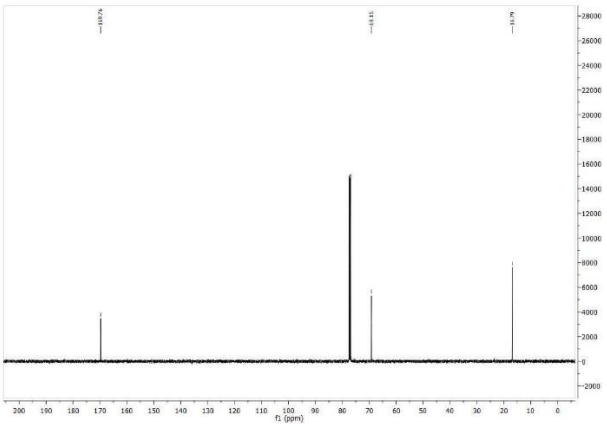

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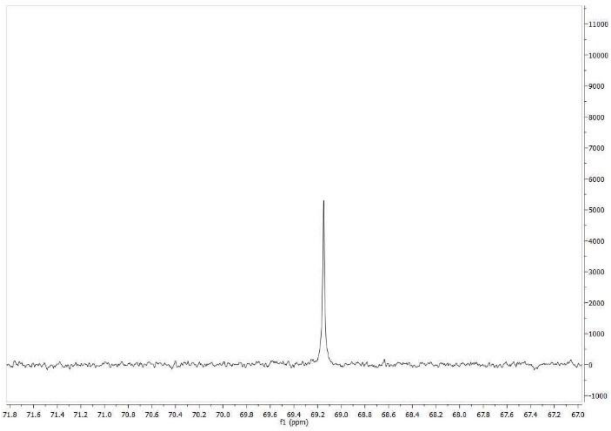
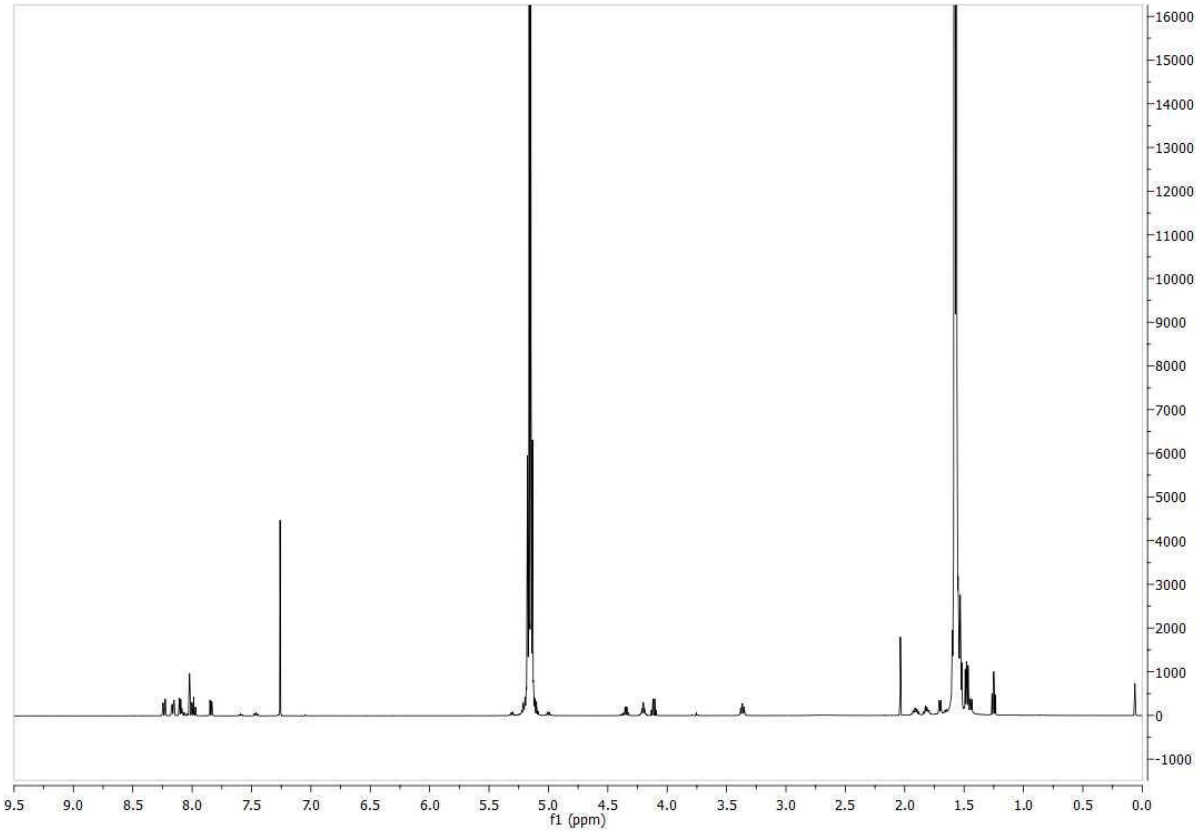


Figure S1 (a) ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of PLA (DP = 50) prepared using **1d**. Signals are classified as described in literature[1]; (b) ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of PLA; (c) ^{13}C signal of methine group at 69.2 ppm.

(a)



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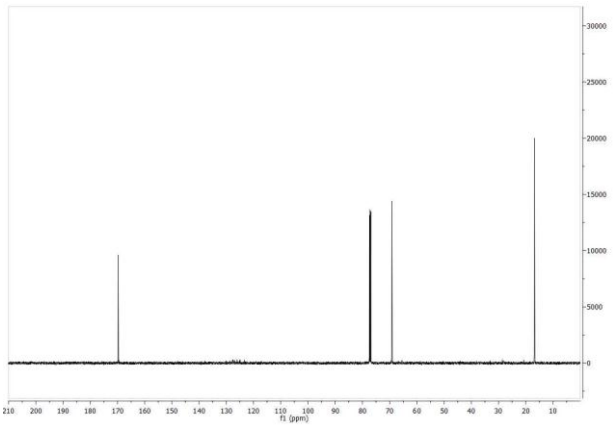

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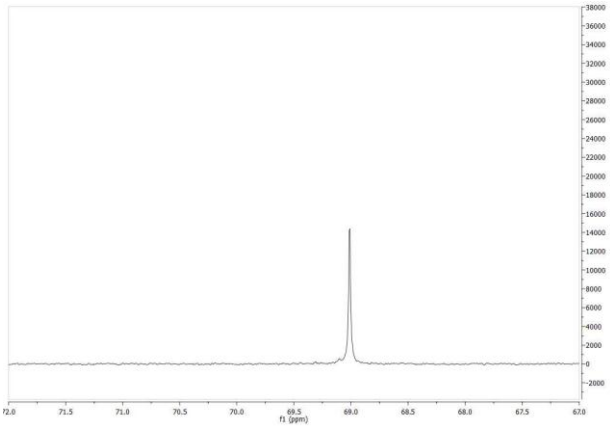
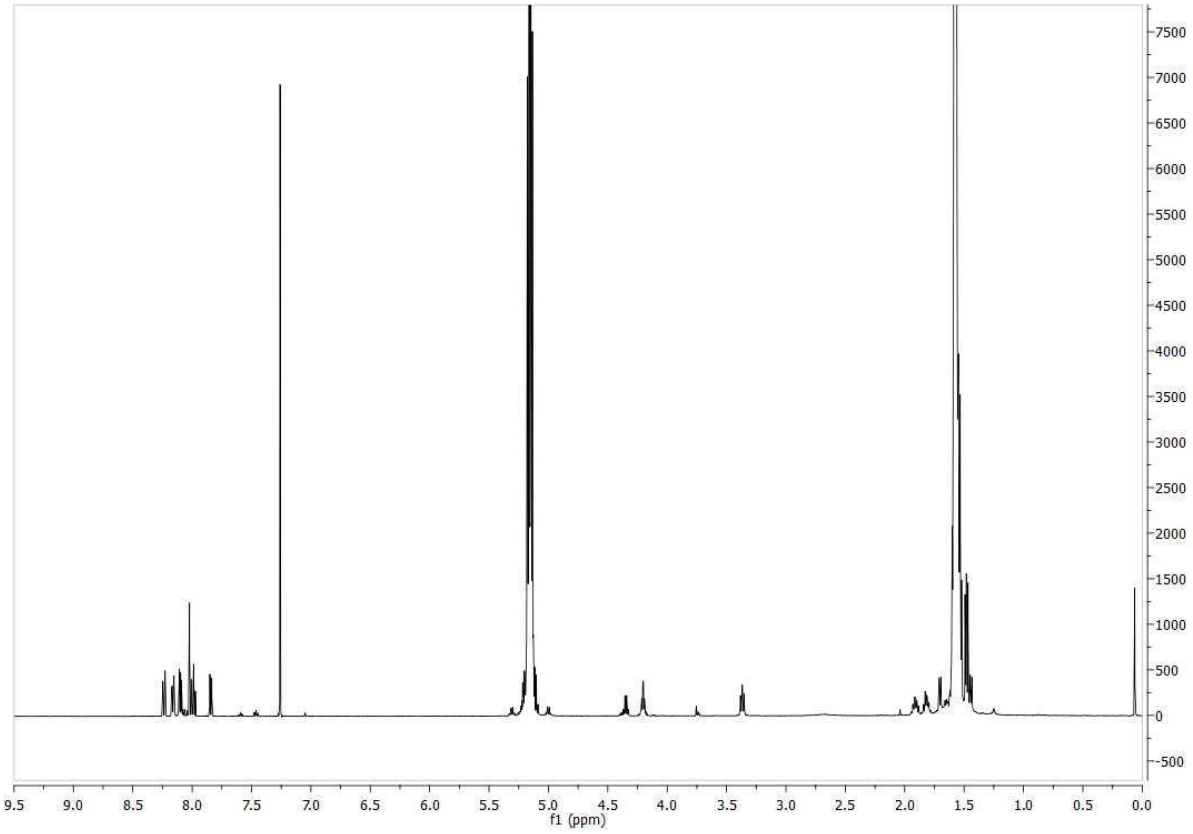


Figure S2 (a) ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of PLA (DP = 50) prepared using **1c**; (b) ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of PLA; (c) ^{13}C signal of methine group at 69.2 ppm.

(a)



(b) (c)

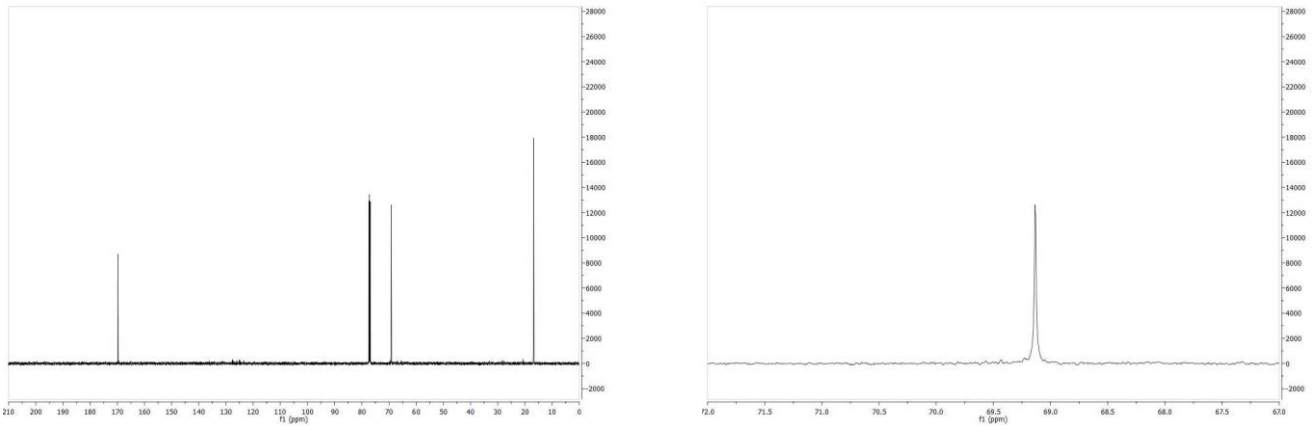
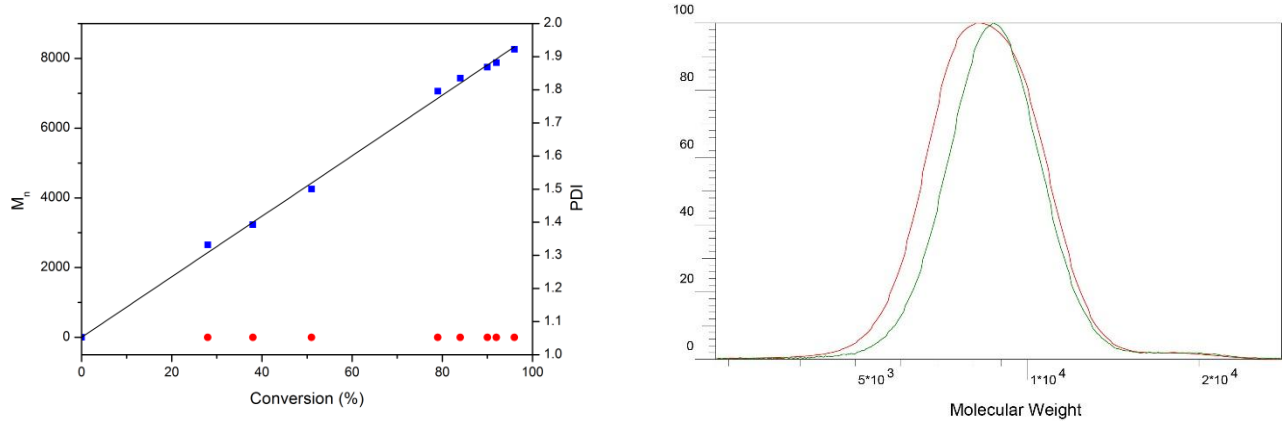


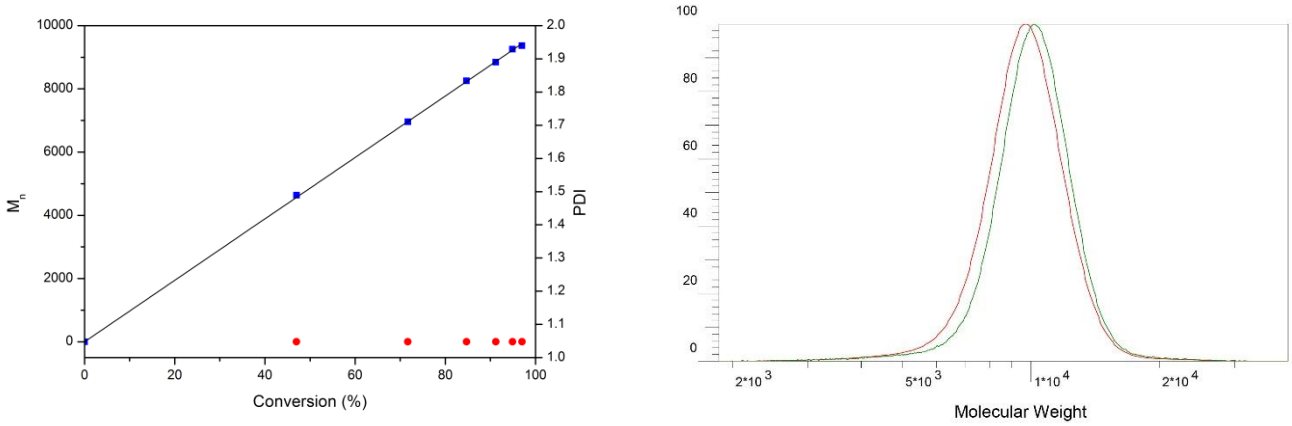
Figure S3 (a) ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of PLA (DP = 50) prepared using **1b**; (b) ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of PLA; (c) ^{13}C signal of methine group at 69.2 ppm.

2.2 GPC measurements

(a) (b)



(c) (d)



(e) (f)

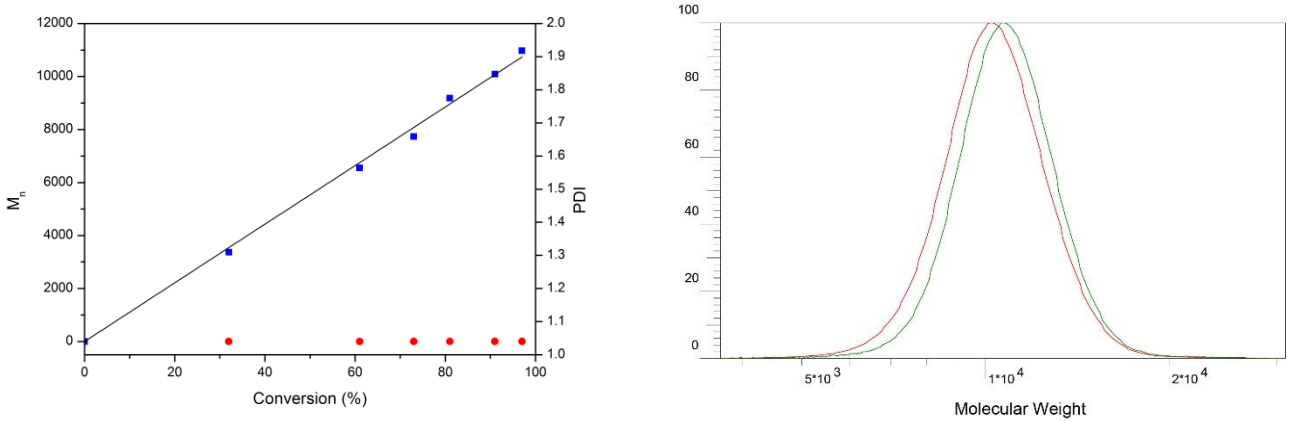


Figure S4 M_n and PDI *vs.* monomer conversion for catalyst (a) **1b,** (c) **1c,** (e) **1d** determined by GPC in THF; Overlap of UV signal (red line) and RI signal (green line) of GPC detectors for catalyst (b) **1b,** (d) **1c,** (f) **1d**.

2.3 DSC Measurement

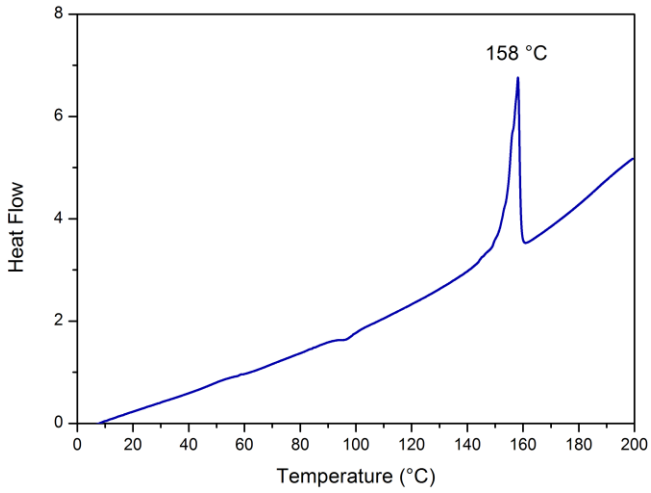


Figure S5 DSC measurement of PLA (DP = 100) prepared using catalyst **1d**.

2.4 Molecular Weights

Table S1 Comparison of differently determined molecular weights

Catalyst	*M/I/C*	M_n*(theo.)*	M_n*(NMR)*	M_n*(GPC)*	$M_n(GPC)_{corr}$
1a	50	7500	-	-	-
1b	50	7500	7500	8300	6300
1c	50	7500	7900	9400	7100
1d	50	7500	7500	9300	7000
1d	100	14700	12800	17400	13000
1d	150	21900	19100	22800	17000
1d	200	29100	26100	21300	15900

M_n(NMR) values were determined by end-group analysis *via* ^{1}H NMR spectroscopy. M_n(GPC) values were obtained using GPC calibrated with polystyrene standards in THF. The Kuhn-Mark-Houwink-Sakurada equation was applied to correct M_n(GPC), since the GPC was not calibrated with polylactide standards. The respective Mark-Houwink parameters for PLA and polystyrene were used as reported in the literature.[2]

Kuhn-Mark-Houwink-Sakurada equation: $$M2 = \left(\frac{K1M1^{a1+1}}{K2}\right)^{\frac{1}{a2+1}}$$

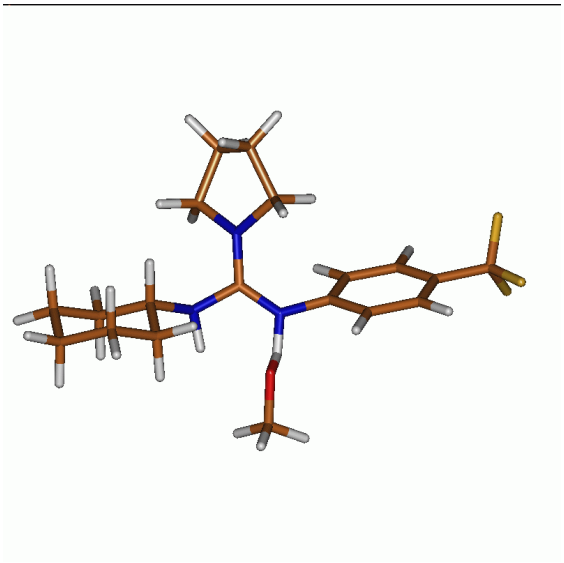
3. DFT calculations

All calculations were performed using the Turbomole 6.5 software package[3] and its implementation of the DFT functional B3LYP[4]. If not stated differently all structures were optimized employing the def2-TZVP basis set by Ahlrichs[5] for all atoms followed by the calculation of the vibrational spectrum within the harmonic approximation to check whether a minimum structure was actually found.

In the first attempt the molecules were looked at in the gas phase employing only a def2-SVP[6] basis set. Furthermore, the effects of the solvent on the investigated properties was studied with the polarizable continuum model (PCM) from the COSMO package[7] implemented in Turbomole. Here only default parameters were used for van der Waals-radii *etc.* The dielectric constant was set to 8.9 to simulate CH_2Cl_2.[8]

For the calculation of the gas-phase basicities, following a method given elsewhere[9], all involved structures were optimized using the double zeta basis set (B3LYP/def2-SVP). Analytical frequency analysis was performed on the same level to get the thermochemical data (ZPVE, partition functions). The electronical energy was then determined by a single point calculation using the triple zeta basis set on the before optimized structures (B3LYP/def2-TZYP//B3LYP/def2-SVP).

(a)



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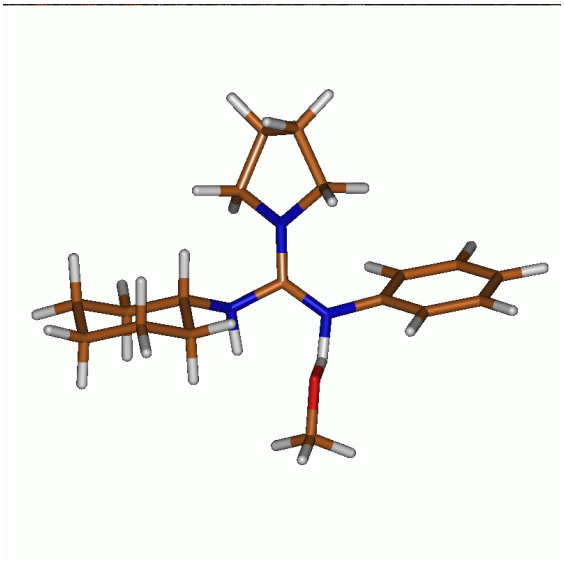

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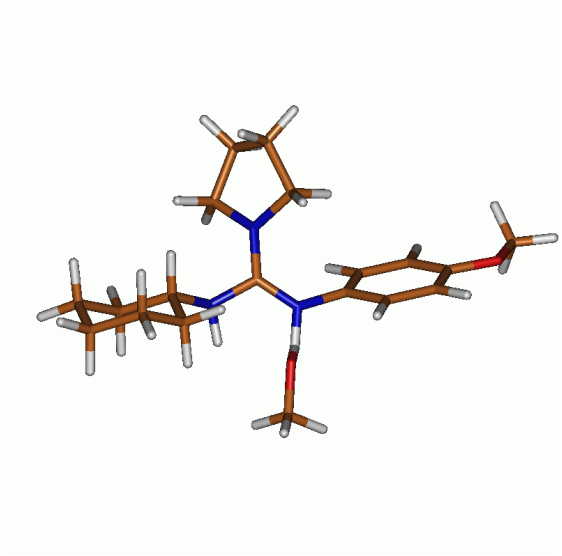

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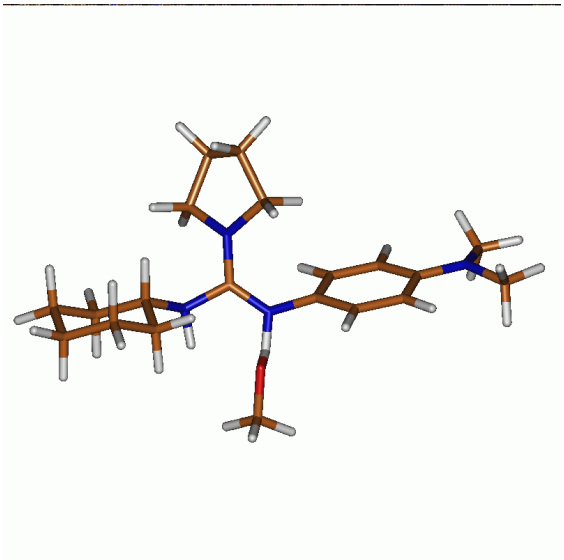
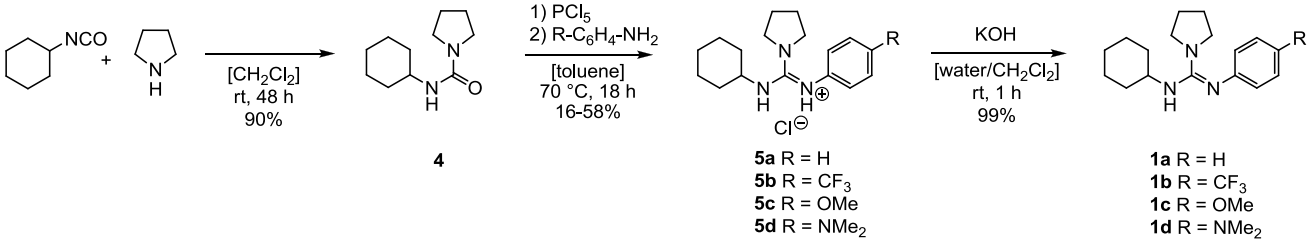


Figure S6 Geometry-optimized methanol-guanidine adducts: (a) **1a**, (b) **1b**, (c) **1c**, (d) **1d**.

4. Synthesis

4.1 Synthesis of 1



***N*-Cyclohexylpyrrolidine carboxamide 4**

A solution of cyclohexylisocyanate (6.26 g, 50.0 mmol, 1 eq.) in 250 mL of dry CH_2Cl_2 was cooled to 0 °C. Pyrrolidine (3.56 g, 50.0 mmol, 1 eq.) was added carefully over 20 min. Upon complete addition, the mixture was warmed to rt and stirred for 48 h. After the reaction was completed the solvent was removed *in vacuo*. The resulting solid was washed with petroleum ether and dried *in vacuo*. The product was recrystallized from MeOH/H_2O and isolated in 90% yield (8.84 g, 47.5 mmol) as a white solid.

^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ(ppm) = 5.63 (d, 1H, N*H*, ^{3}J = 7.9 Hz), 3.42 - 3.32 (m, 1H, C*H*), 3.17 (m, 4H, C*H*$_2$), 1.79-1.63 (m, 8H, C*H*$_2$), 1.59-1.52 (m, 1H, C*H*), 1.27-0.99 (m, 5H, C*H*$_2$).

^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ(ppm) = 155.8; 48.7; 45.2; 33.3; 25.4; 25.2; 25.0.

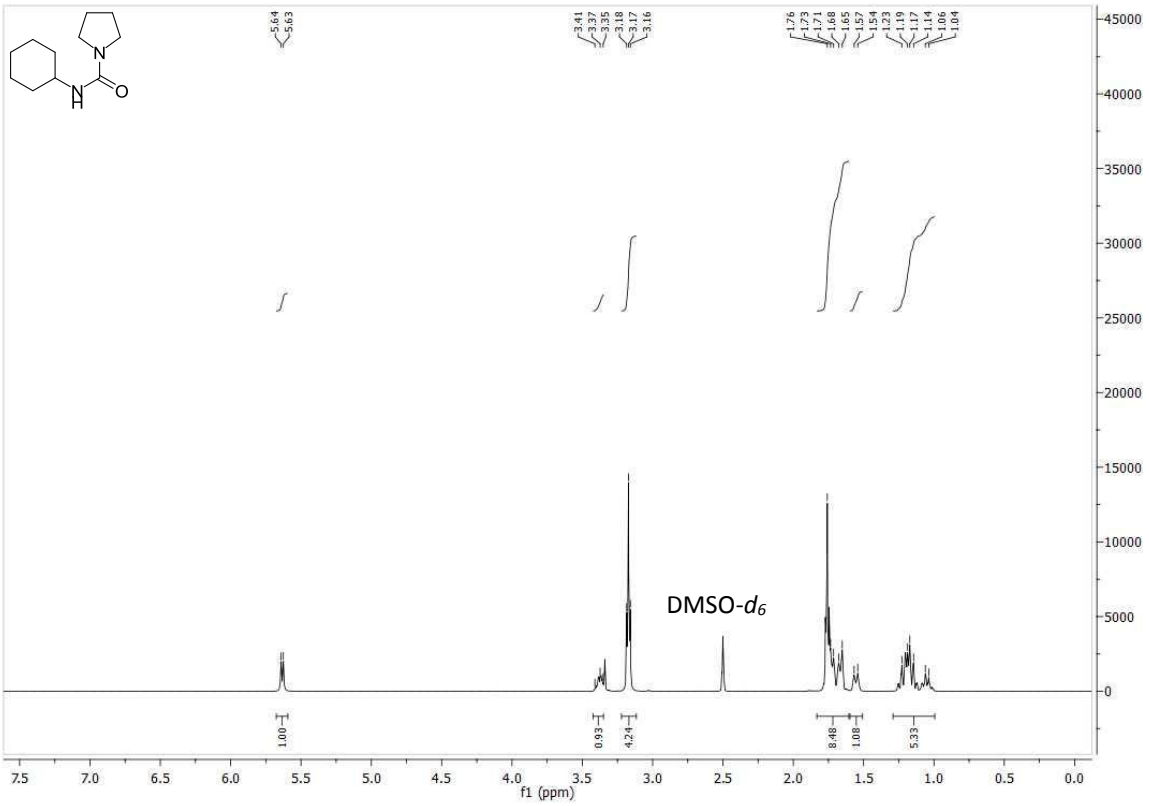


Figure S7 ^{1}H NMR spectrum (500 MHz, DMSO-d_6, 298 K) of compound **4**.

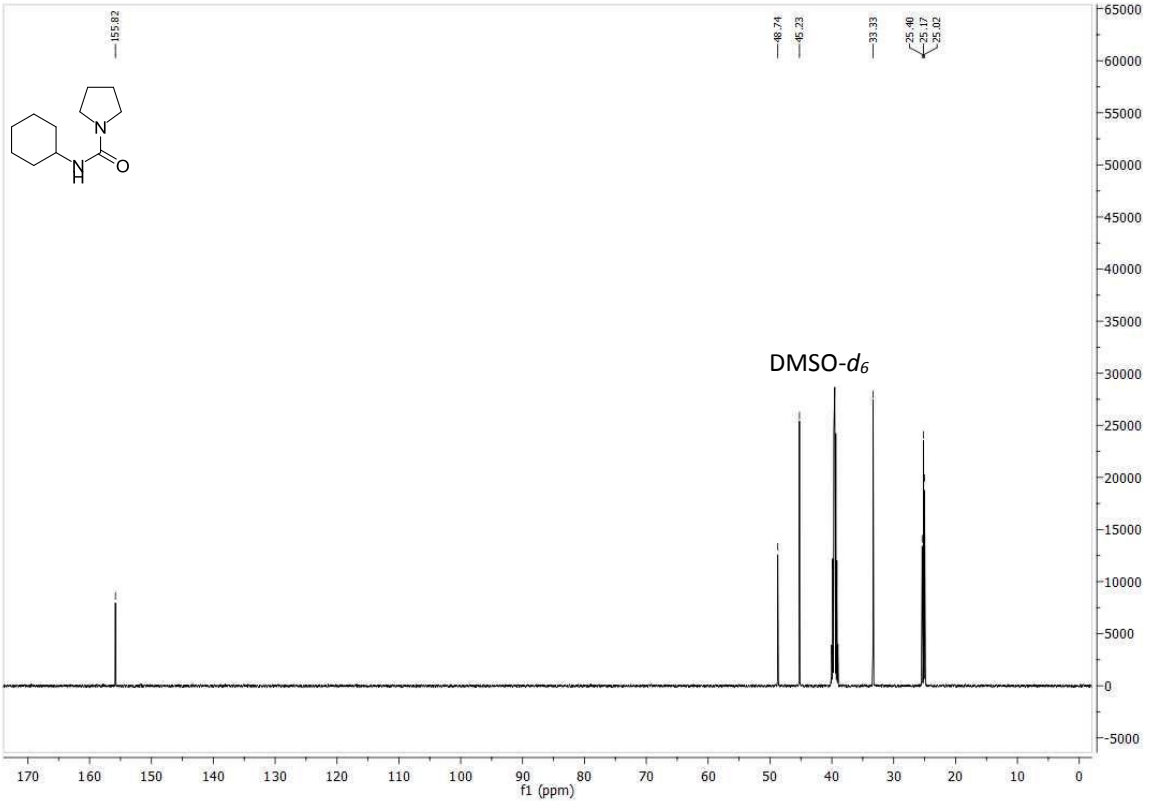


Figure S8 ^{13}C NMR spectrum (125 MHz, DMSO-d_6, 298 K) of compound **4**.

_N_-(4-Trifluoromethylphenyl)-_N'_-cyclohexylpyrrolidine guanidine hydrochloride 5a

A mixture of carboxamide **4** (0.98 g, 5.0 mmol, 1 eq.) and PCl_5 (1.04 g, 5.0 mmol, 1 eq.) in 25 mL of dry toluene was heated to 60 °C for 1 h until a white solid precipitated. After cooling to rt the solvent was removed *in vacuo*. The resulting white solid was used immediately without any further purification and dissolved in 100 mL of dry toluene. 4-Trifluoromethylaniline (0.63 mL, 5.0 mmol, 1 eq.) was added in one portion and the mixture was heated to 70 °C for 18 h. After cooling to rt the solvent was removed *in vacuo*. The resulting solid was washed with 30 mL of toluene (3x), 30 mL of a toluene/CH_2Cl_2 1:1 mixture (3x) and subsequently purified by column chromatography (CH_2Cl_2/MeOH = 95:5) to give the product (550 mg, 1.46 mmol) in 29% yield as a white solid.

^{1}H-NMR (500 MHz, CD_3OD): δ(ppm) = 7.71 (d, 2H, CH_{aryl}, ^{3}J = 7.7 Hz), 7.31 (d, 2H, CH_{aryl}, ^{3}J = 7.3 Hz), 3.56-3.37 (m, 5H), 2.05-1.95 (m, 4H), 1.95-1.88 (m, 2H), 1.81-1.72 (m, 2H), 1.65-1.57 (m, 1H), 1.51-1.39 (m, 2H), 1.27-1.11 (m, 3H).

^{13}C-NMR (125 MHz, CD_3OD): δ(ppm) = 153.5; 143.2; 128.1; 127.7: 127.4; 126.6; 124.4; 122.0; 55.7; 55.0; 34.2; 26.4.

^{19}F-NMR (470 MHz, CD_3OD): -64.8

MS (ESI$^+$) m/z calculated for $C_{18}H_{25}N_3F_3^+$ $[M\text{-}Cl]^+$ 340.1995, found 340.198.

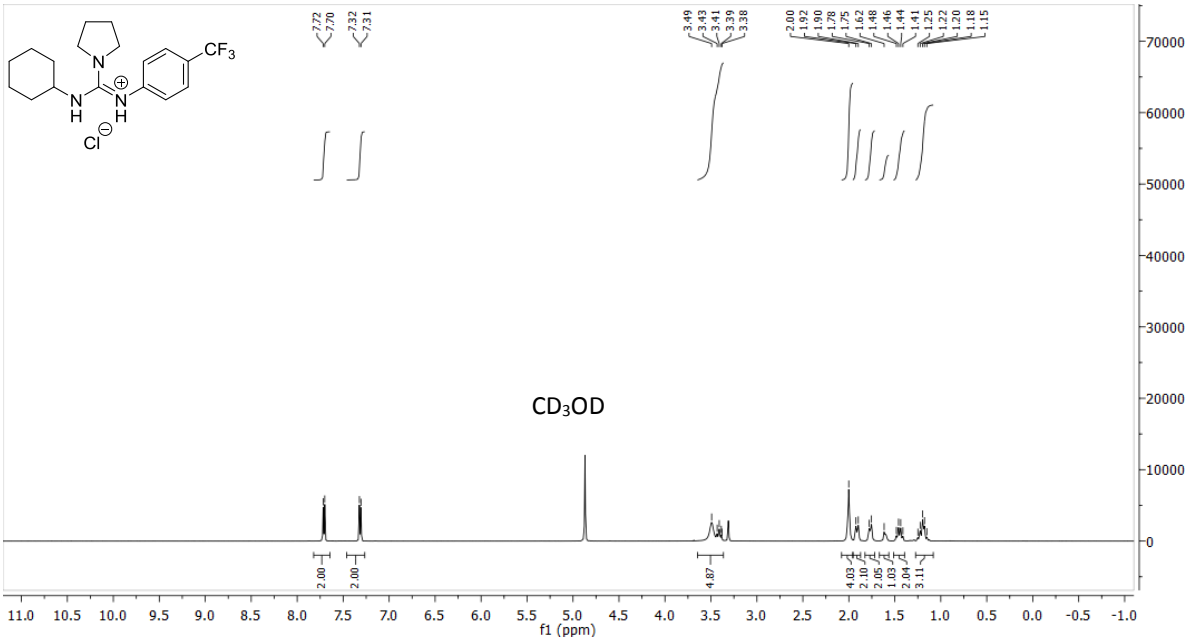


Figure S9 ^{1}H NMR spectrum (500 MHz, CD_3OD, 298 K) of compound **5a**.

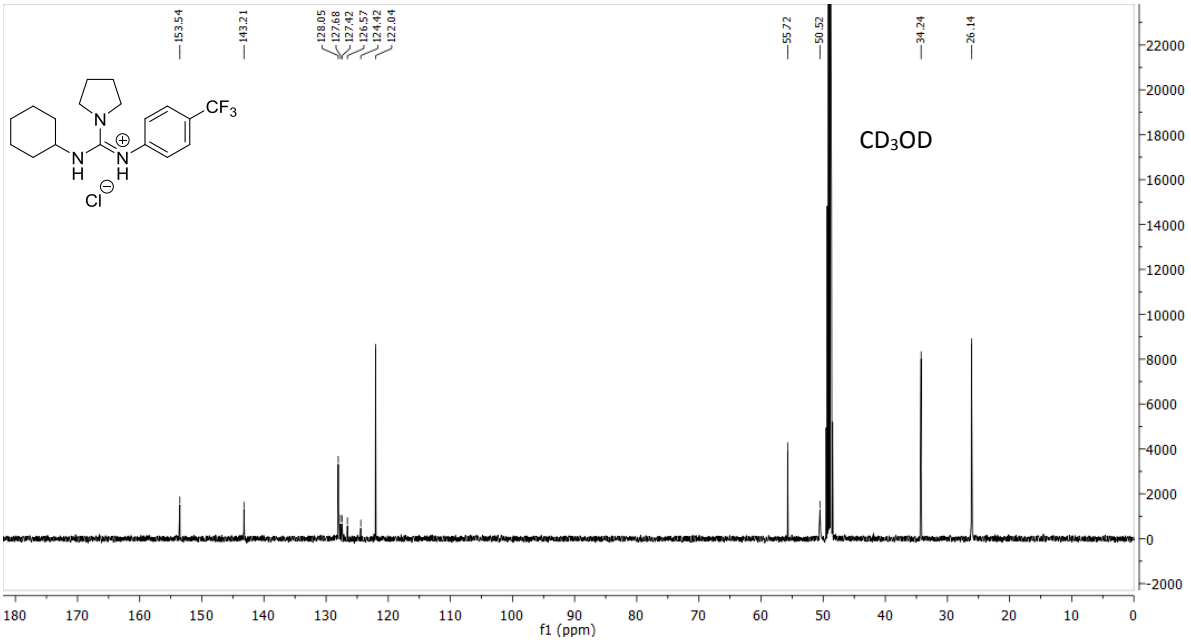


Figure S10 ^{13}C NMR spectrum (125 MHz, CD_3OD, 298 K) of compound **5a**.

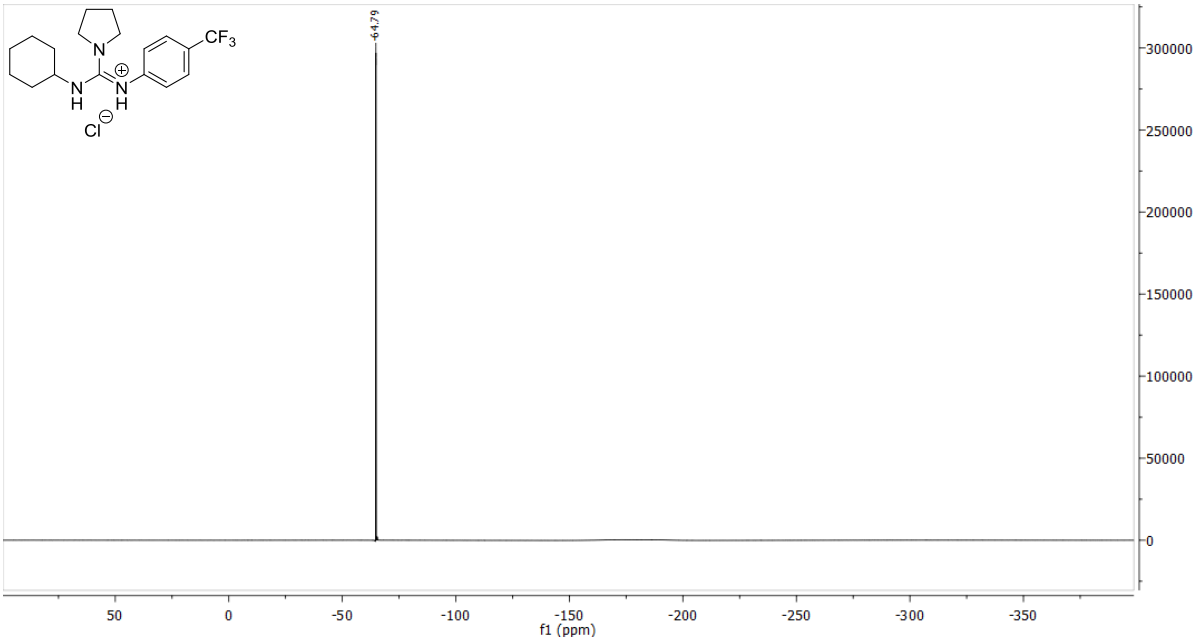


Figure S11 ^{19}F NMR spectrum (470 MHz, CD_3OD, 298 K) of compound **5a**.

***N*-Phenyl-*N'*-cyclohexylpyrrolidine guanidine hydrochloride 5b**

A mixture of carboxamide **4** (0.98 g, 5.0 mmol, 1 eq.) and PCl_5 (1.04 g, 5.0 mmol, 1 eq.) in 25 mL of dry toluene was heated to 60 °C for 1 h until a white solid precipitated. After cooling to rt, the solvent was removed *in vacuo*. The resulting white solid was used immediately without any further purification and dissolved in 100 mL of dry toluene. Aniline (0.47 g, 5.0 mmol, 1 eq.) was added in one portion and the mixture was heated to 70 °C for 18 h. After cooling to rt the solvent was removed *in vacuo*. The resulting solid was washed with 30 mL of toluene (3x), 30 mL of a toluene/CH_2Cl_2 1:1 mixture (3x) and subsequently purified by column chromatography (CH_2Cl_2/MeOH = 95:5) to give the product (430 mg, 1.27 mmol) in 25% yield as a white solid.

^{1}H-NMR (500 MHz, CD_3OD): δ(ppm) = 7.44-7.39 (m, 2H, CH_{aryl}), 7.24-7.20 (m, 1H, CH_{aryl}), 7.18-7.15 (m, 2H, CH_{aryl}), 3.53-3.40 (br, 4H), 3.40-3.33 (m, 1H), 2.01-1.93 (m, 4H), 1.91-1.84 (m, 2H), 1.79-1.69 (m, 2H), 1.62-1.54 (m, 1H), 1.46-1.35 (m, 2H), 1.22-1.11 (m, 3H).

^{13}C-NMR (125 MHz, CD_3OD): δ(ppm) = 154.0; 139.4; 131.3; 130.8; 126.6; 124.0; 123.2; 55.2; 50.2; 34.2; 26.1.

MS (ESI$^+$) m/z calculated for $C_{17}H_{26}N_3^+$ $[M\text{-}Cl]^+$ 272.2121, found 272.206.

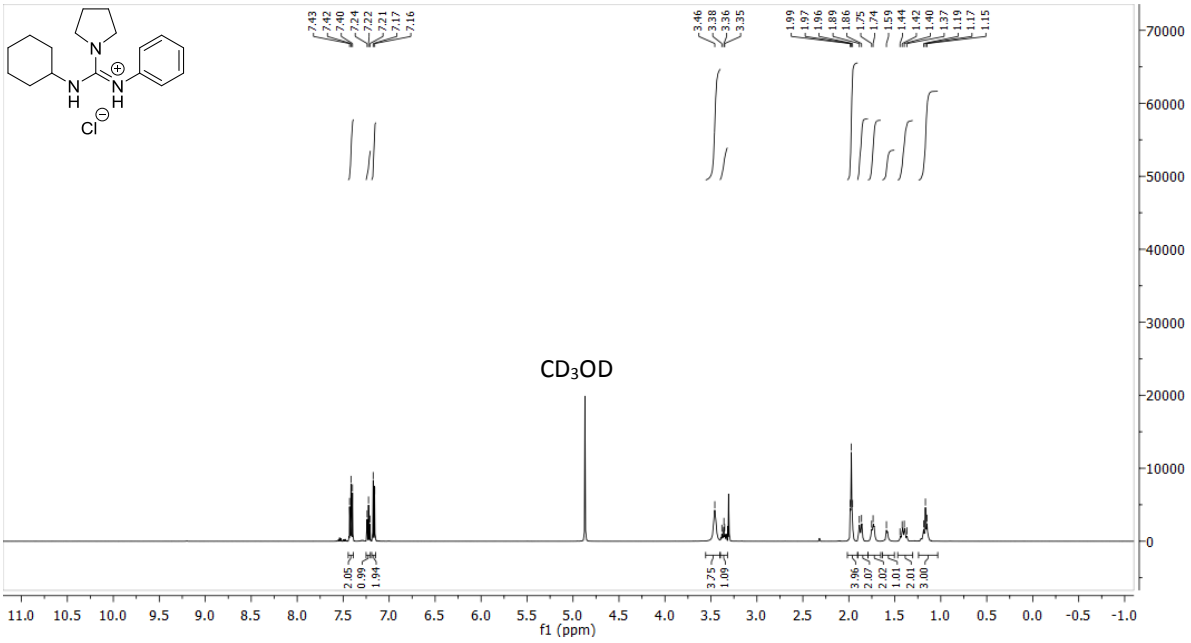


Figure S12 ^{1}H NMR spectrum (500 MHz, CD_3OD, 298 K) of compound **5b**.

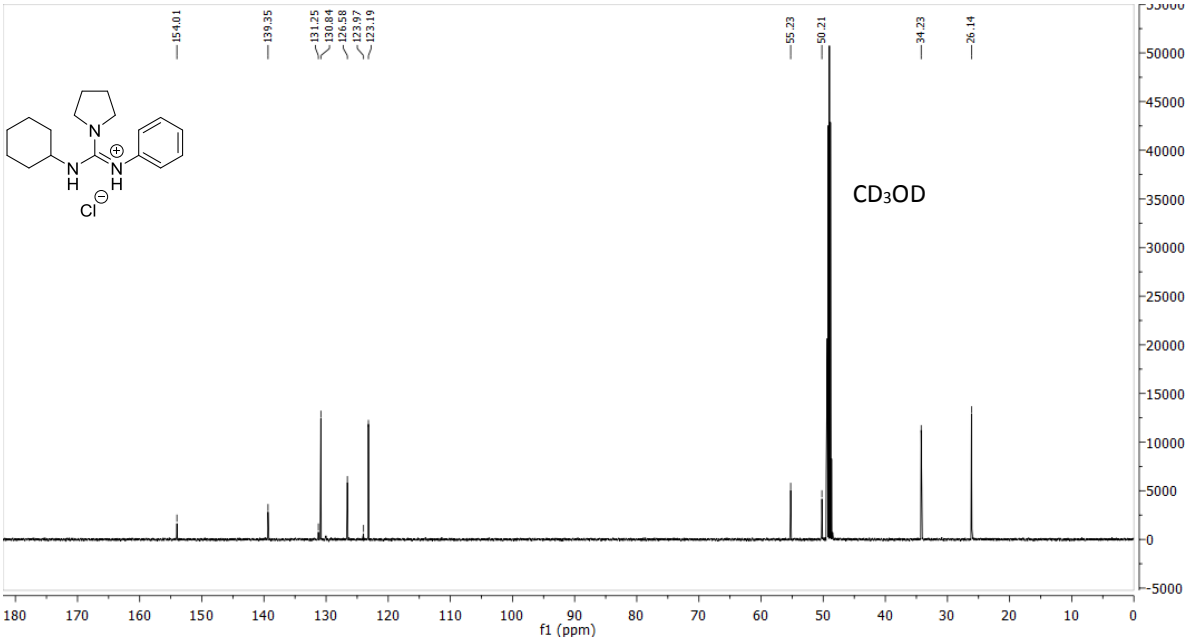


Figure S13 ^{13}C NMR spectrum (125 MHz, CD_3OD, 298 K) of compound **5b**.

_N_-(4-Methoxyphenyl)-_N'_-cyclohexylpyrrolidine guanidine hydrochloride 5c

A mixture of carboxamide **4** (0.98 g, 5.0 mmol, 1 eq.) and PCl_5 (1.04 g, 5.0 mmol, 1 eq.) in 25 mL of dry toluene was heated to 60 °C for 1 h until a white solid precipitated. After cooling to rt the solvent was removed *in vacuo*. The resulting white solid was used immediately without any further purification and dissolved in 100 mL of dry toluene. 4-Methoxyaniline (0.62 g, 5.0 mmol, 1 eq.) was added in one portion and the mixture was heated to 70 °C for 18 h. After cooling to rt the solvent was removed *in vacuo*. The resulting solid was washed with 30 mL of toluene (3x), 30 mL of a toluene/ CH_2Cl_2 1:1 mixture (3x) to give the product (980 mg, 2.90 mmol) in 58% yield as a white solid.

^{1}H-NMR (500 MHz, CD_3OD): δ(ppm) = 7.14-7.09 (m, 2H, CH_{aryl}), 7.00-6.95 (m, 2H, CH_{aryl}), 3.81 (s, 3H, CH_3), 3.47-3.40 (br, 4H), 3.40-3.33 (m, 1H), 3.38-3.32 (m, 1H), 1.99-1.92 (m, 4H), 1.89-1.82 (m, 2H), 1.78-1.69 (m, 2H), 1.62-1.54 (m, 1H), 1.43-1.32 (m, 2H), 1.24-1.10 (m, 3H).

^{13}C-NMR (125 MHz, CD_3OD): δ(ppm) = 159.3; 154.5; 154.5; 131.9; 131.8; 125.7; 116.0; 56.0; 55.0; 50.1; 34.3; 26.2.

MS (ESI$^+$) m/z calculated for $C_{18}H_{28}ON_3^+$ $[M\text{-}Cl]^+$ 302.2222, found 302.221.

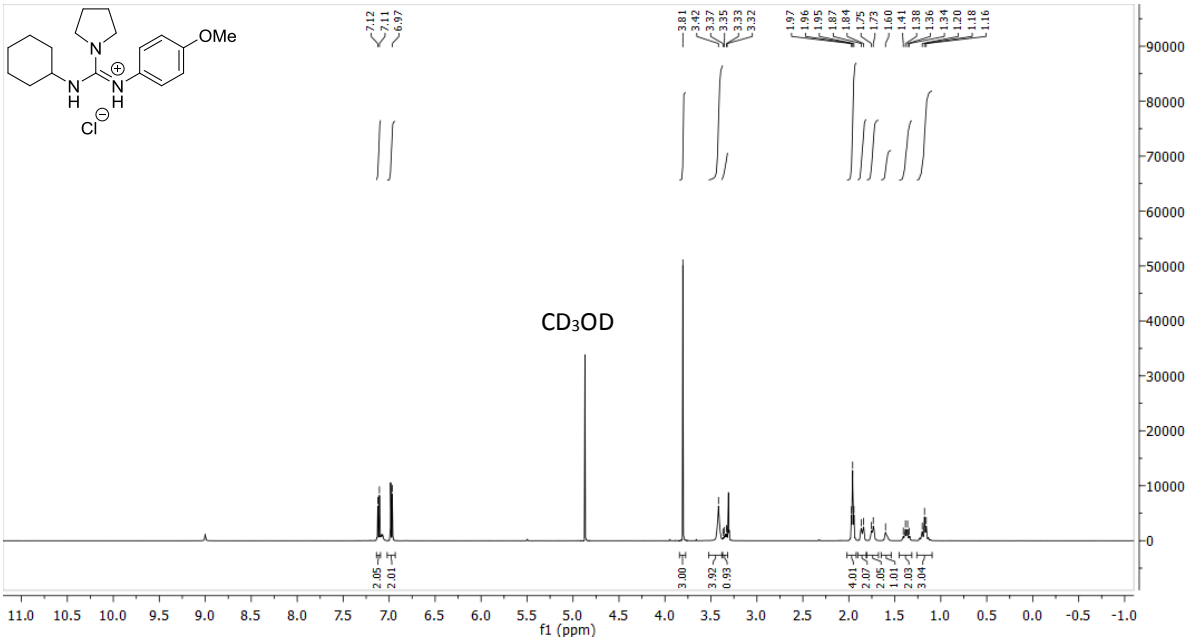


Figure S14 ^{1}H NMR spectrum (500 MHz, CD_3OD, 298 K) of compound **5c**.

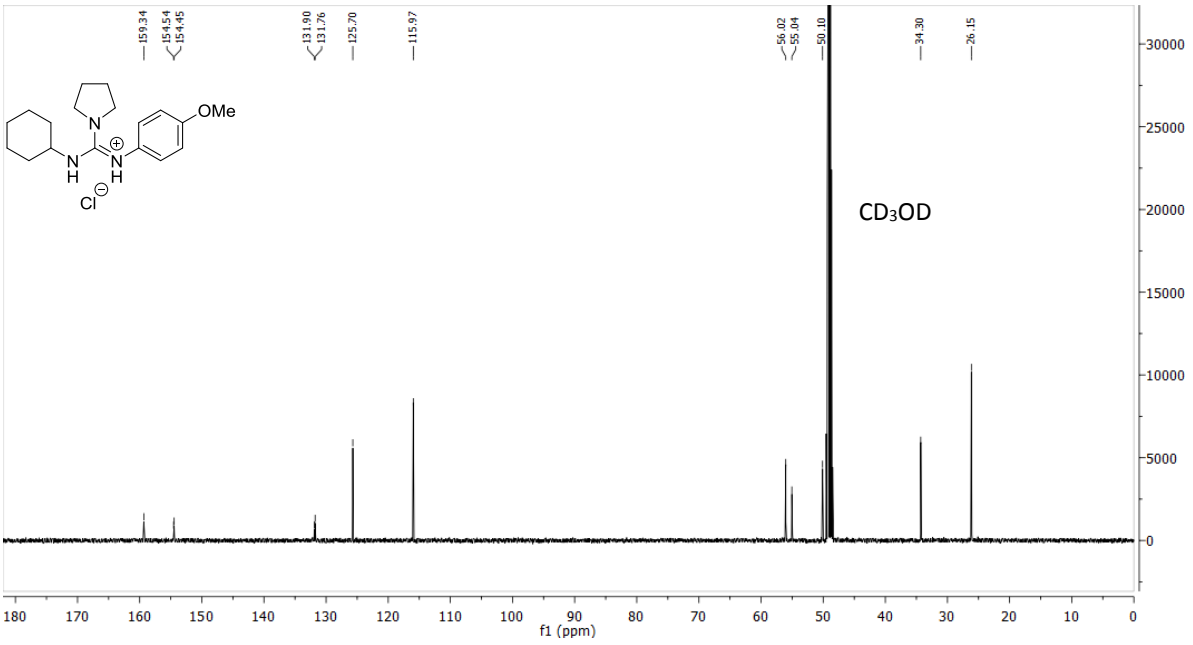


Figure S15 ^{13}C NMR spectrum (125 MHz, CD_3OD, 298 K) of compound **5c**.

_N_-(4-Dimethylaminophenyl)-_N'_-cyclohexylpyrrolidine guanidine hydrochloride 5d

A mixture of carboxamide **4** (1.08 g, 5.5 mmol, 1 eq.) and PCl_5 (1.15 g, 5.5 mmol, 1 eq.) in 25 mL of dry toluene was heated to 60 °C for 1 h until a white solid precipitated. After cooling to rt the solvent was removed *in vacuo*. The resulting white solid was used immediately wjithout any further purification and dissolved in 100 mL of dry toluene. *N*,*N*-dimethyl-1,4-phenylenediamine (0.75 g, 5.5 mmol, 1 eq.) was added in one portion and the mixture was heated to 70 °C for 18 h. After cooling to rt the solvent was removed *in vacuo*. The resulting solid was purified by column chromatography (CH_2Cl_2/MeOH = 95:5) to give the product (310 mg, 0.88 mmol) in 16% yield as an off-white solid.

^{1}H-NMR (500 MHz, CD_3OD): δ(ppm) = 7.08-7.00 (d, 2H, CH_{aryl}, ^{3}J = 7.0 Hz), 6.83-6.76 (d, 2H, CH_{aryl}, ^{3}J = 6.8 Hz), 3.50-3.29 (m, 5H), 2.95 (s, 6H, CH_3), 2.02-1.92 (m, 4H), 1.89-1.81 (m, 2H), 1.78-1.68 (m, 2H), 1.63-1.54 (m, 1H), 1.44-1.31 (m, 2H), 1.27-1.10 (m, 3H).

^{13}C-NMR (125 MHz, CD_3OD): δ(ppm) = 154.5; 150.6; 127.8; 125.7; 114.4; 54.7; 50.0; 40.9; 34.3; 26.2.

MS (ESI$^+$) m/z calculated for $C_{19}H_{31}N_4^+$ $[M\text{-}Cl]^+$ 315.2538, found 315.251.

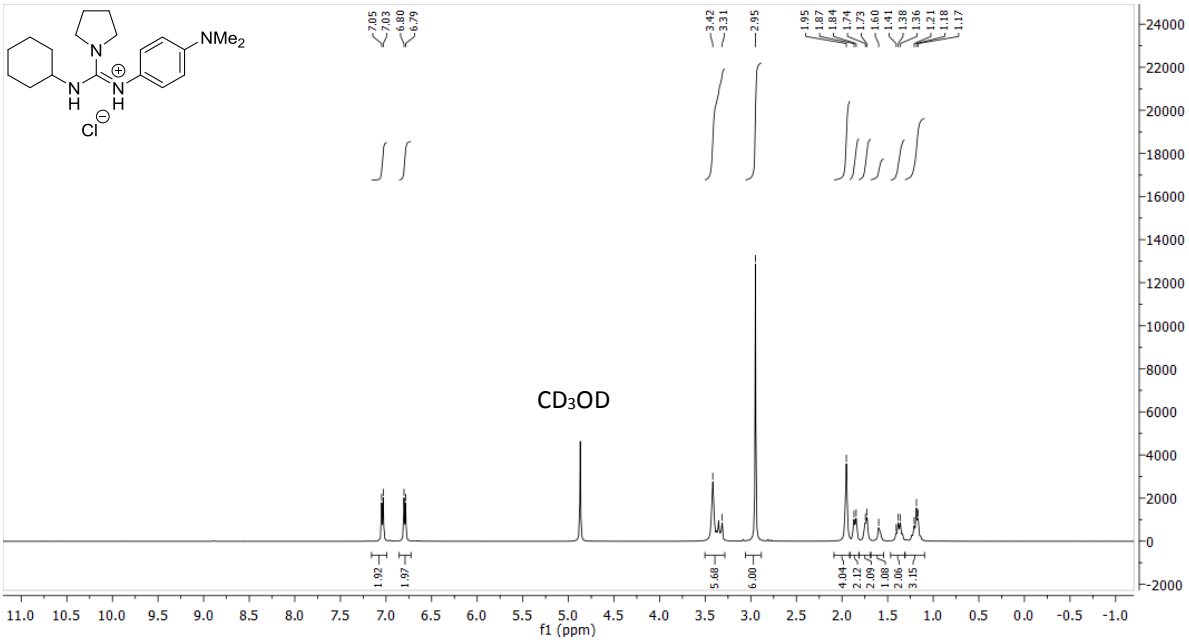


Figure S16 ^{1}H NMR spectrum (500 MHz, CD_3OD, 298 K) of compound **5d**.

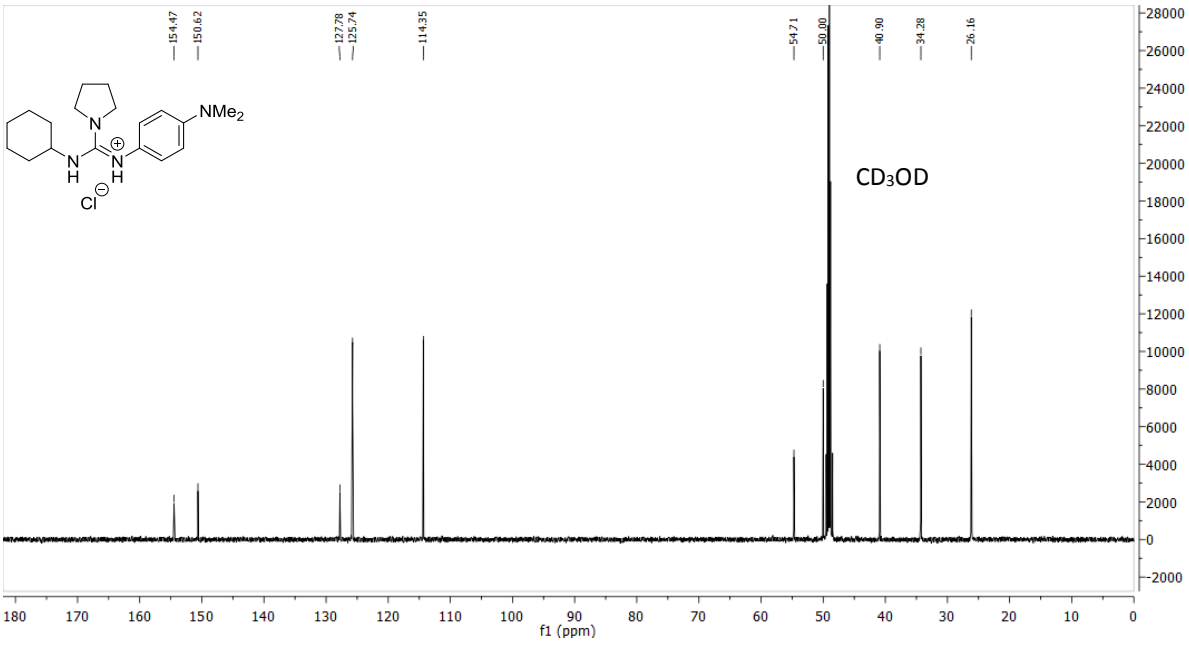


Figure S17 ^{13}C NMR spectrum (125 MHz, CD_3OD, 298 K) of compound **5d**.

***N*-(4-Trifluoromethylphenyl)-*N*'-cyclohexylpyrrolidine guanidine 1a**

The guanidine hydrochloride **5a** (251 mg, 0.67 mmol, 1 eq.) was dissolved in 80 mL of water. KOH (563 mg, 10.05 mmol, 15 eq.) was added and the resulting solution was stirred for 1 h at rt. The aqueous solution was extracted with 80 mL of CH_2Cl_2 (3x) and the combined organic phases were dried over $MgSO_4$. After removing the solvent *in vacuo* the resulting solid was dried by lyophilization out of benzene to yield the desired product (227 mg, 0.67 mmol) in quantitative yield as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ(ppm) = 7.39 (d, 2H, C*H*$_{aryl}$, ^{3}J = 8.5 Hz), 6.83 (d, 2H, C*H*$_{aryl}$, ^{3}J = 8.2 Hz), 3.74 (s, br, 1H, N*H*), 3.37-3.21 (m, 5H), 1.95-1.81 (m, 6H), 1.68-1.60 (m, 2H), 1.59-1.51 (m, 1H), 1.27-1.17 (m, 2H), 1.15-0.98 (m, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ(ppm) = 155.1; 152.7; 126.1; 124.2; 121.9; 121.1; 51.6; 48.3; 34.1; 25.7; 25.6; 25.0.

^{19}F-NMR (470 MHz, $CDCl_3$): δ(ppm) = -61.3.

MS (ESI$^+$) m/z calculated for $C_{18}H_{25}N_3F_3^+$ $[M+H]^+$ 340.1995, found 340.1989.

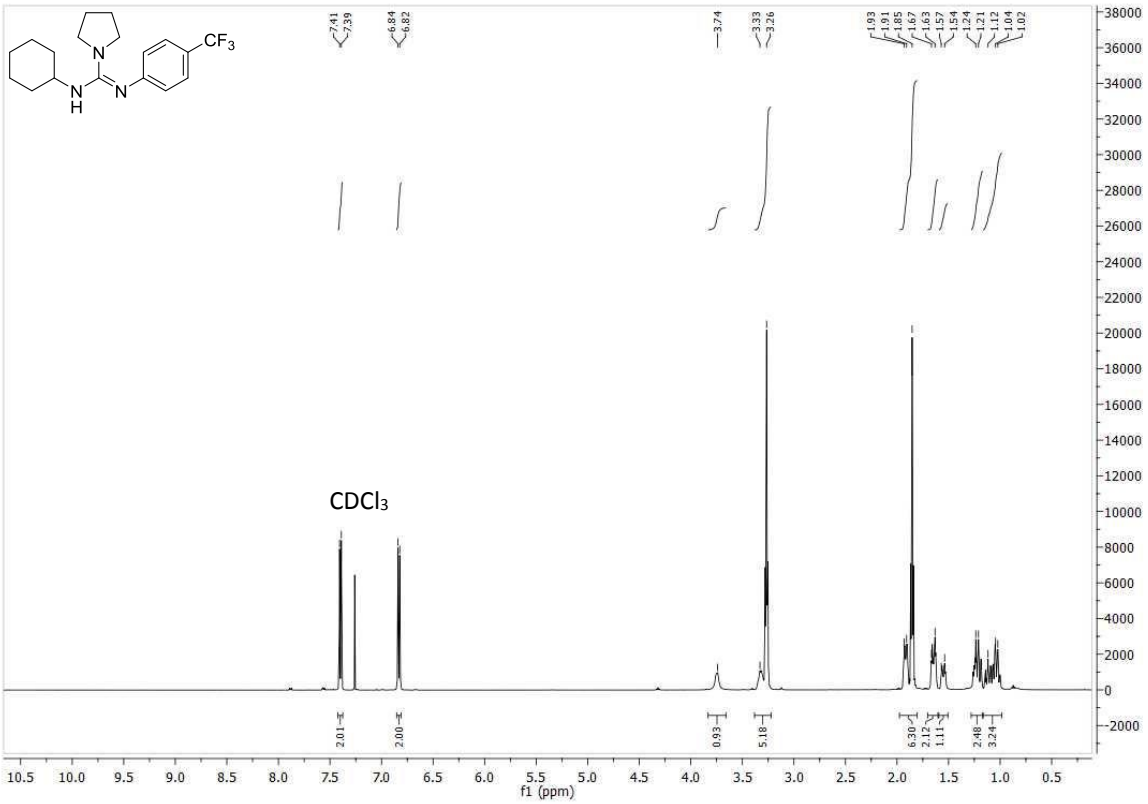


Figure S18 ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of compound **1a**.

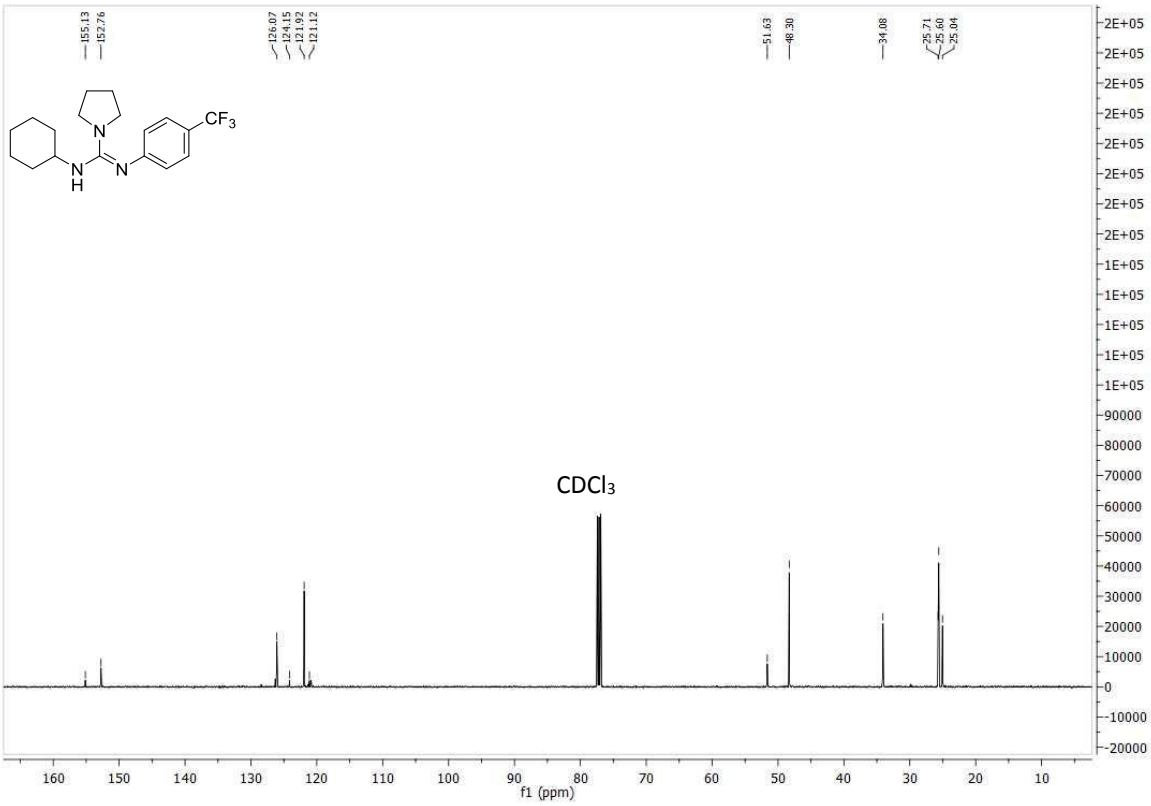


Figure S19 ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of compound **1a**.

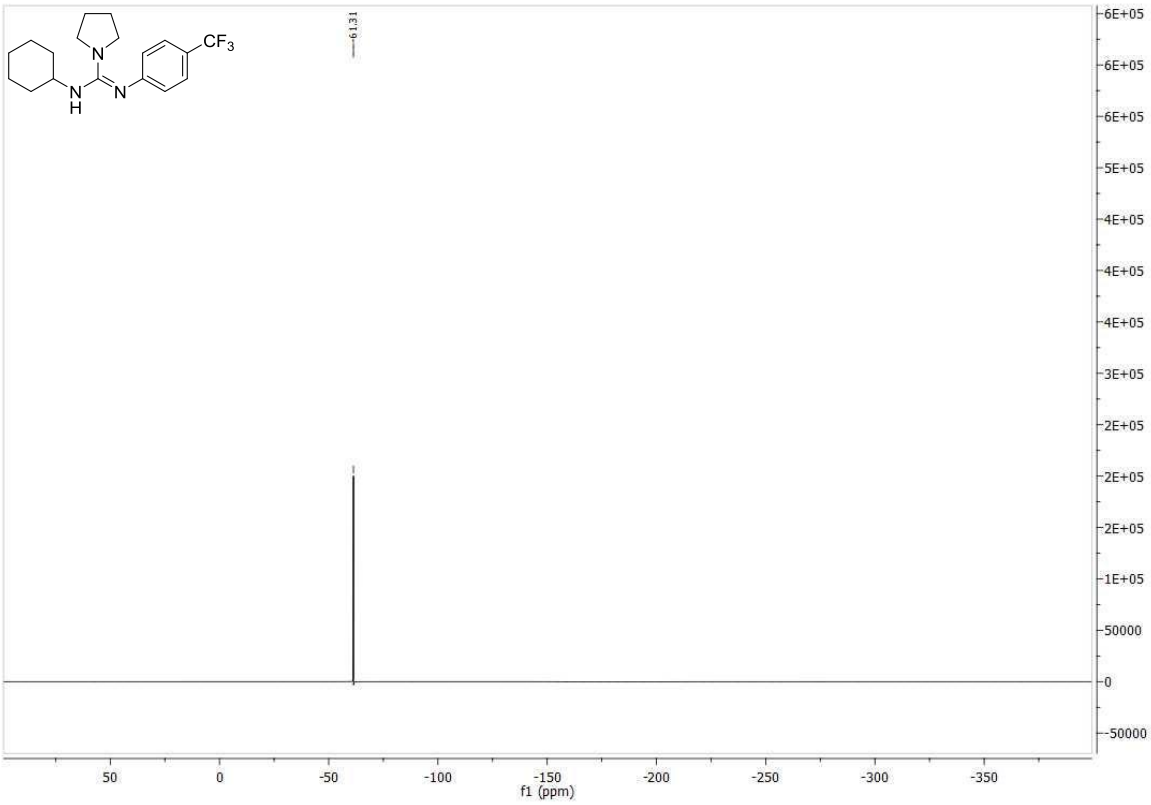


Figure S20 ^{19}F NMR spectrum (470 MHz, $CDCl_3$, 298 K) of compound **1a**.

_N_-Phenyl-_N'_-cyclohexylpyrrolidine guanidine 1b

The guanidine hydrochloride **5b** (280 mg, 0.91 mmol, 1 eq.) was dissolved in 80 mL of water. KOH (764 mg, 13.65 mmol, 15 eq.) was added and the resulting solution was stirred for 1 h at rt. The aqueous solution was extracted with 80 mL of CH_2Cl_2 (3x) and the combined organic phases were dried over $MgSO_4$. After removing the solvent *in vacuo* the resulting solid was dried by lyophilization out of benzene to yield the desired product (247 mg, 0.91 mmol) in quantitative yield as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ(ppm) = 7.23-7.18 (m, 2H, C*H*$_{aryl}$), 6.87 (m, 1H, C*H*$_{aryl}$), 6.82 (m, 2H, C*H*$_{aryl}$), 3.74 (s, br, 1H, N*H*), 3.37-3.31 (m, 4H), 3.24-3.15 (m, 1H), 1.93-1.83 (m, 6H), 1.67-1.59 (m, 2H), 1.57-1.49 (m, 1H), 1.26-1.15 (m, 2H), 1.12-0.93 (m, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ(ppm) = 153.2; 150.8; 129.0; 122.9; 120.8; 52.2; 48.4; 34.2; 25.7; 25.6; 25.1.

MS (ESI$^+$) m/z calculated for $C_{17}H_{26}N_3^+$ $[M+H]^+$ 272.2121, found 272.2117.

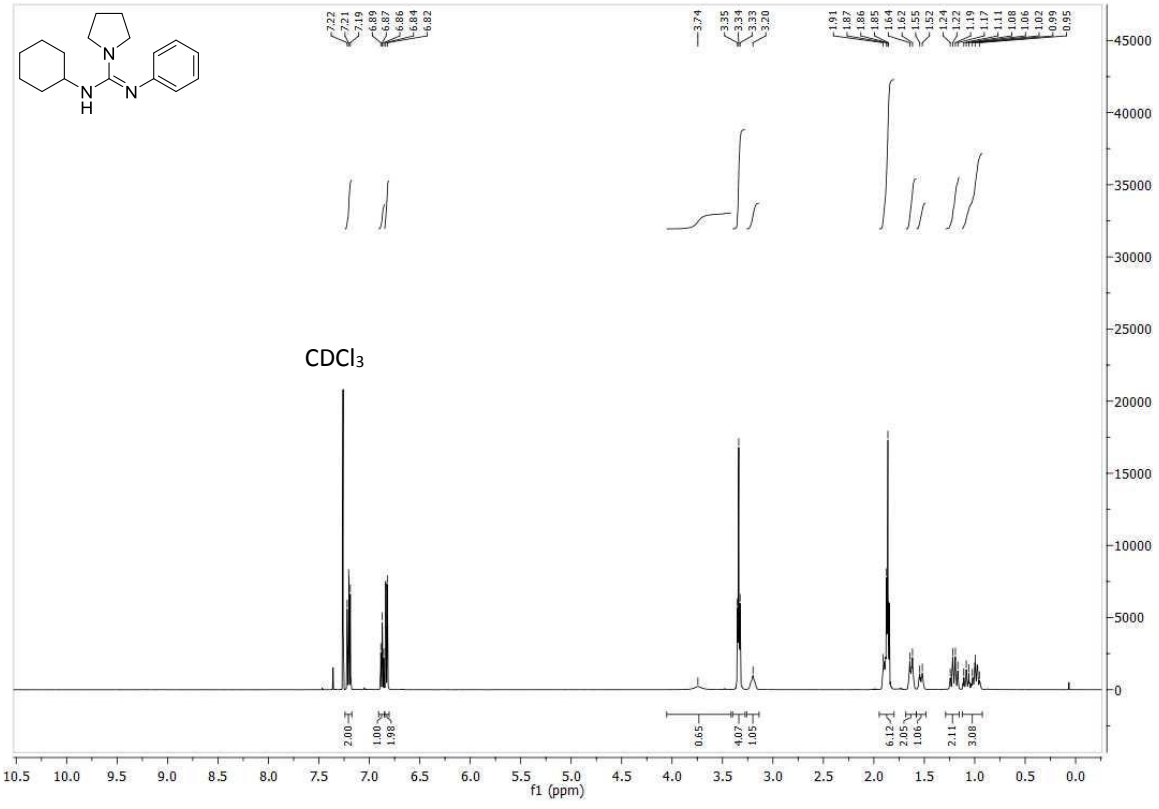


Figure S21 ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of compound **1b**.

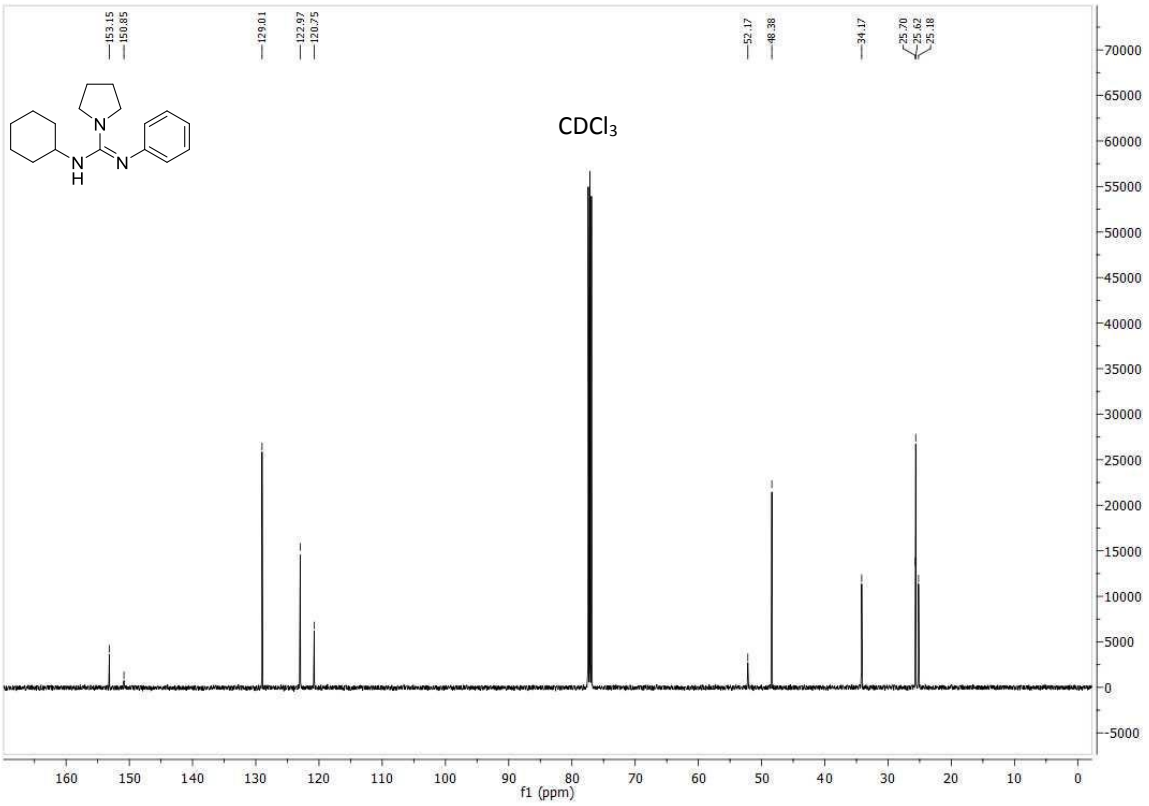


Figure S22 ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of compound **1b**.

***N*-(4-Methoxyphenyl)-*N*'-cyclohexylpyrrolidine guanidine 1c**

The guanidine hydrochloride **5c** (405 mg, 1.20 mmol, 1 eq.) was dissolved in 125 mL of water. KOH (806 mg, 14.4 mmol, 12 eq.) was added and the resulting solution was stirred for 1 h at rt. The aqueous solution was extracted with 125 mL of CH_2Cl_2 (3x) and the combined organic phases were dried over $MgSO_4$. After removing the solvent *in vacuo* the resulting solid was dried by lyophilization out of benzene to yield the desired product (362 mg, 1.20 mmol) in quantitative yield as a yellow oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ(ppm) = 6.77 (m, 2H, C*H*$_{aryl}$), 6.73 (m, 2H, C*H*$_{aryl}$), 3.75 (s, 1H, C*H*$_3$), 3.58 (s, br, 1H, N*H*), 3.33 (m, 4H), 3.15-3.06 (m, 1H), 1.89-1.80 (m, 6H), 1.65-1.58 (m, 2H), 1.55-1.48 (m, 1H), 1.25-1.13 (m, 2H), 1.09-1.00 (m, 1H), 0.98-0.88 (m, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ(ppm) = 154.3; 153.9; 144.3; 123.9; 114.4; 55.6; 52.3; 48.3; 34.2; 25.6; 25.6; 25.2.

MS (ESI$^+$) m/z calculated for $C_{18}H_{28}ON_3^+$ $[M+H]^+$ 302.2222, found 302.2227.

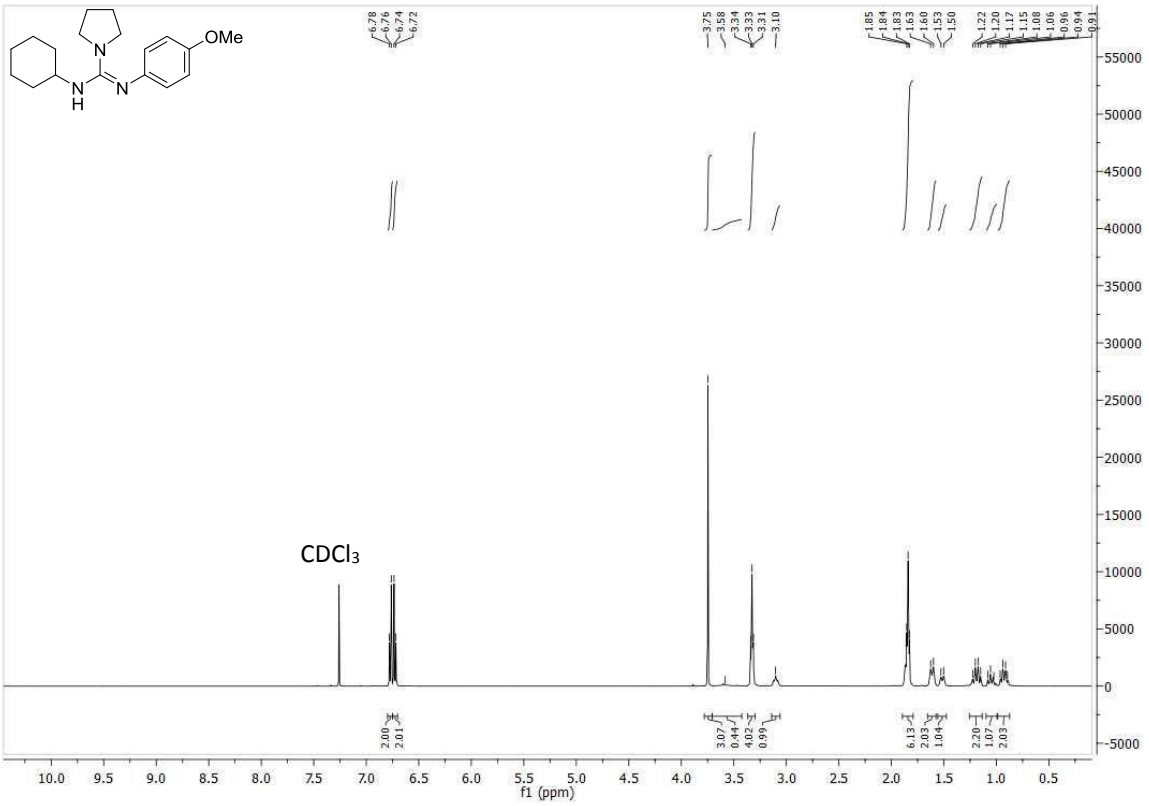


Figure S23 ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of compound **1c**.

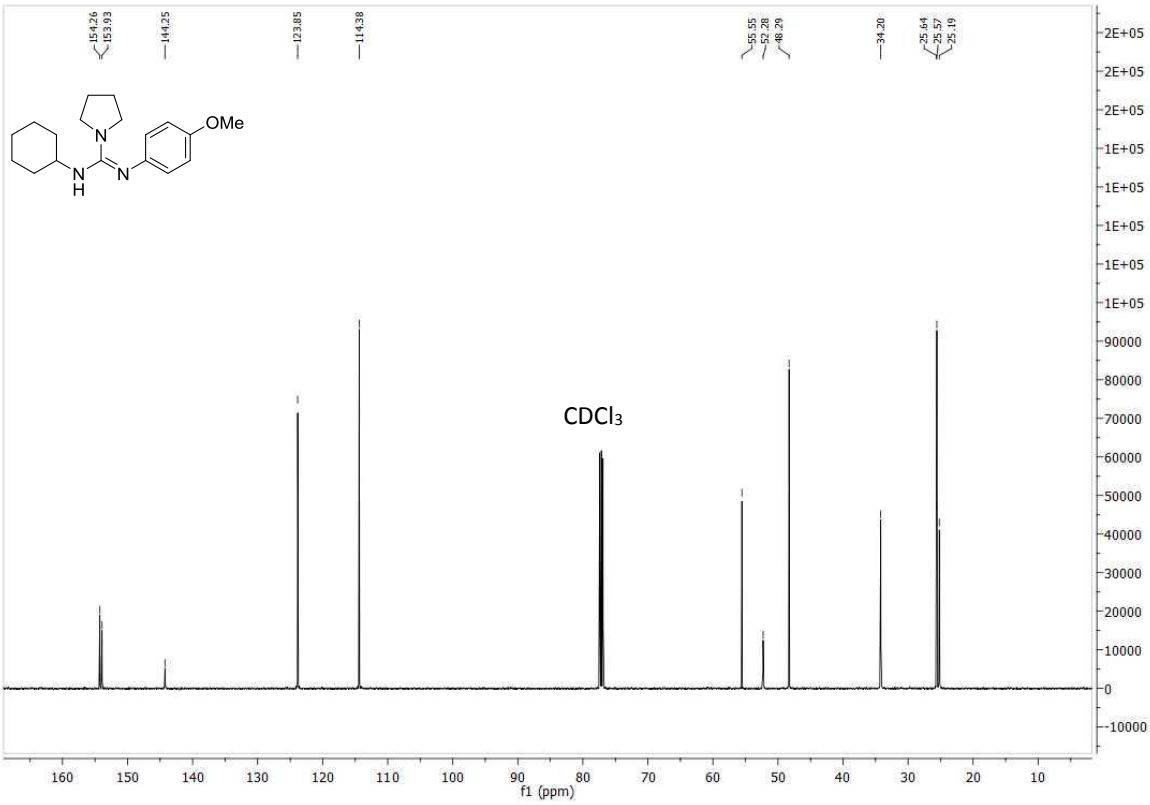


Figure S24 ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of compound **1c**.

_N_-(4-Dimethylaminophenyl)-_N'_-cyclohexylpyrrolidine guanidine 1d

The guanidine hydrochloride **5d** (140 mg, 0.40 mmol, 1 eq.) was dissolved in 40 mL of water. KOH (336 mg, 6.00 mmol, 15 eq.) was added and the resulting solution was stirred for 1 h at rt. The aqueous solution was extracted with 40 mL of CH_2Cl_2 (3x) and the combined organic phases were dried over $MgSO_4$. After removing the solvent *in vacuo* the resulting solid was dried by lyophilization out of benzene to yield the desired product (126 mg, 0.40 mmol) in quantitative yield as a brown oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ(ppm) = 6.74-6.67 (m, 4H, C*H*$_{aryl}$), 3.68 (s, br, 1H, N*H*), 3.38-3.30 (m, 4H), 3.15-3.05 (m, 1H), 2.85 (s, 6H, C*H*$_3$), 1.90-1.79 (m, 6H), 1.66-1.58 (m, 2H), 1.55-1.48 (m, 1H), 1.26-1.14 (m, 2H), 1.10-0.99 (m, 1H), 0.99-0.88 (m, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ(ppm) = 154.2; 146.0; 141.5; 123.7; 114.7; 55.5; 48.3; 41.7; 34.2; 25.7; 25.6; 25.3.

MS (ESI$^+$) m/z calculated for $C_{19}H_{31}N_4^+$ $[M+H]^+$ 315.2538, found 315.2543.

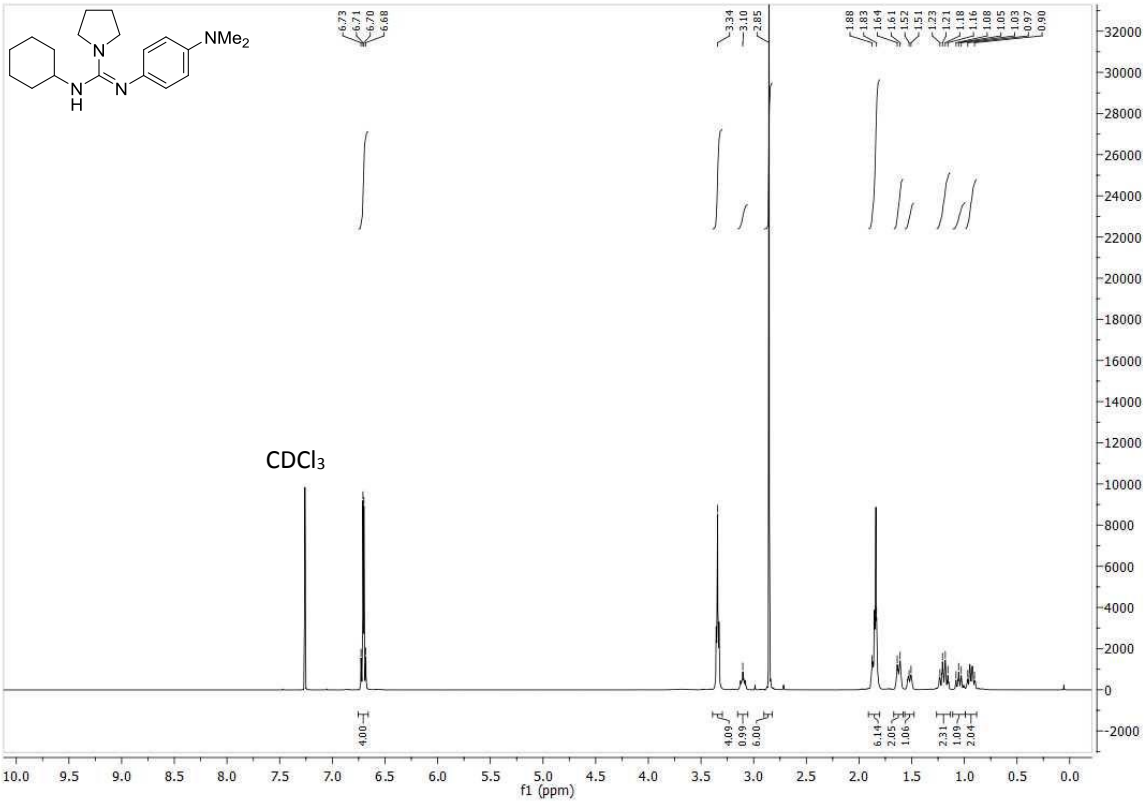


Figure S25 ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of compound **1d**.

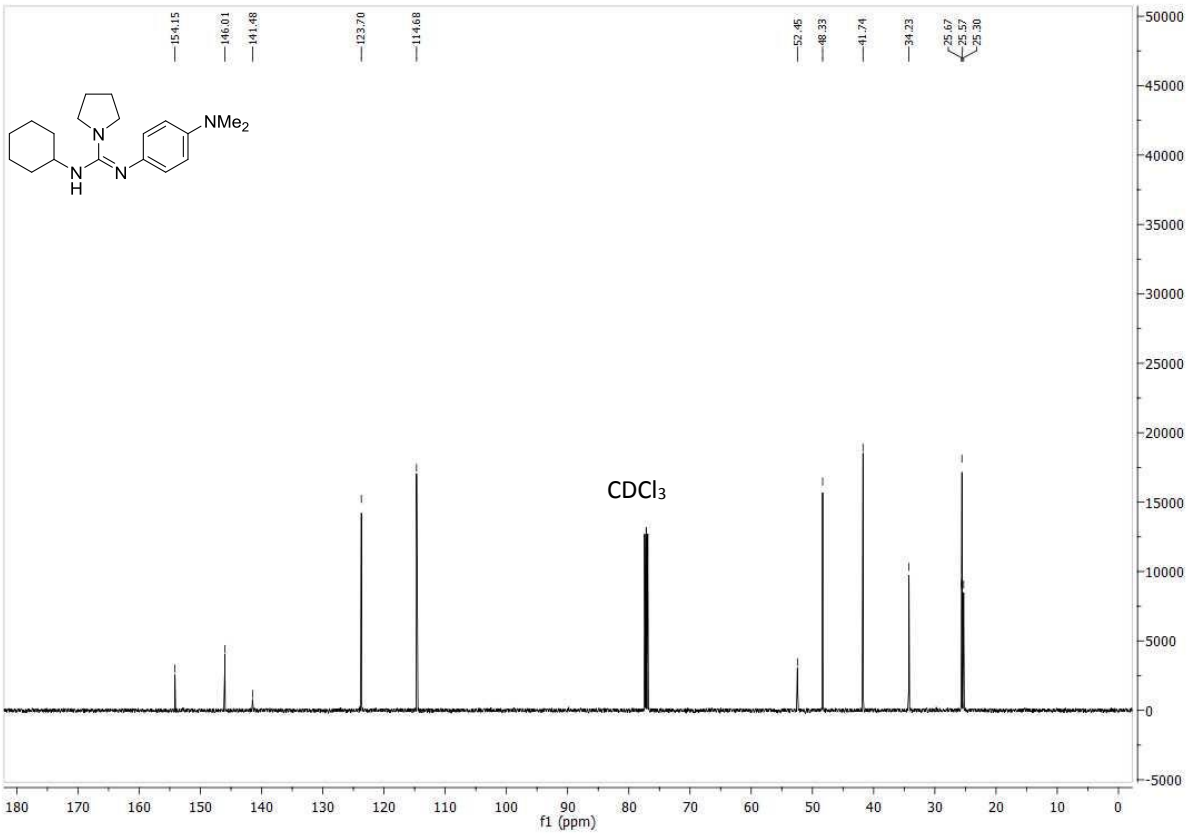
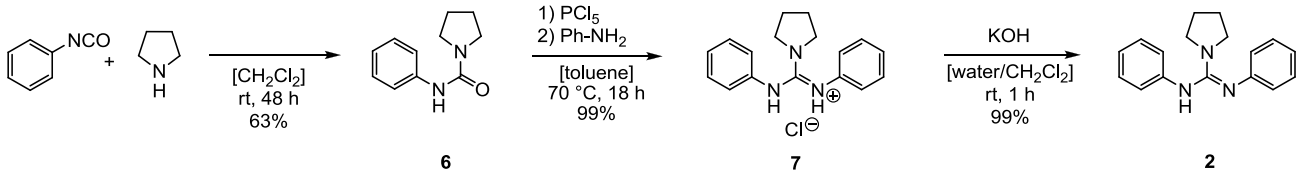


Figure S26 ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of compound **1d**.

4.2 Synthesis of 2



***N*-Phenylpyrrolidine carboxamide 6**

A solution of phenylisocyanate (2.98 g, 25.0 mmol, 1 eq.) in 300 mL dry CH_2Cl_2 was cooled to 0 °C. Pyrrolidine (1.78 g, 25.0 mmol, 1 eq.) was added carefully over 20 min. Upon complete addition, the mixture was warmed to rt and stirred for 48 h. After the reaction was completed the solvent was removed *in vacuo*. The resulting solid was washed with petroleum ether and dried *in vacuo*. The product was recrystallized from MeOH/H_2O and isolated in 63% yield (3.00 g, 16.0 mmol) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ(ppm) = 7.36-7.32 (m, 2H, C*H*$_{aryl}$), 7.21-7.15 (m, 2H, C*H*$_{aryl}$), 7.95-7.89 (m, 1H, C*H*$_{aryl}$), 6.26 (s, 1H, N*H*), 3.38-3.31 (m, 4H, C*H*$_2$), 1.88-1.81 (m, 4H, C*H*$_2$).

^{13}C-NMR (125 MHz, $CDCl_3$): δ(ppm) = 154.1, 139.4, 128.8, 122.7, 119.6, 45.8, 25.6

MS (ESI$^+$) m/z calculated for $C_{11}H_{15}N_2O^+$ $[M+H]^+$ 191.118, found 191.110.

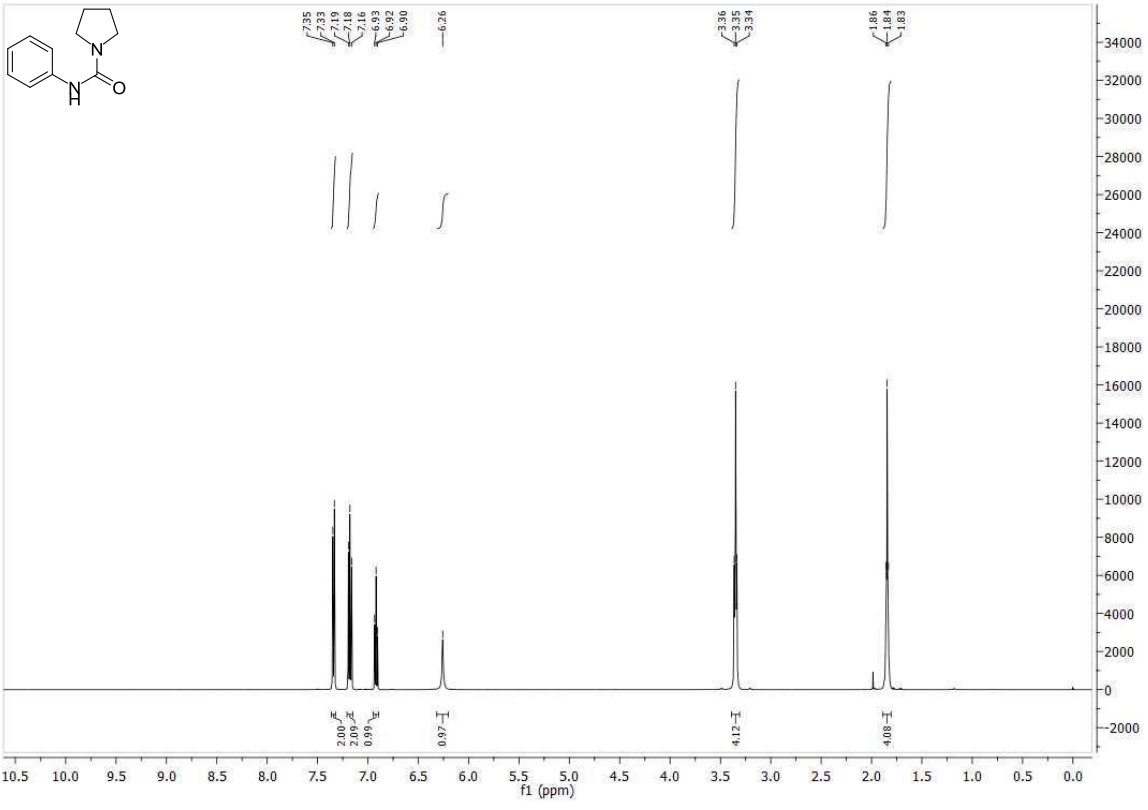


Figure S27 ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of compound **6**.

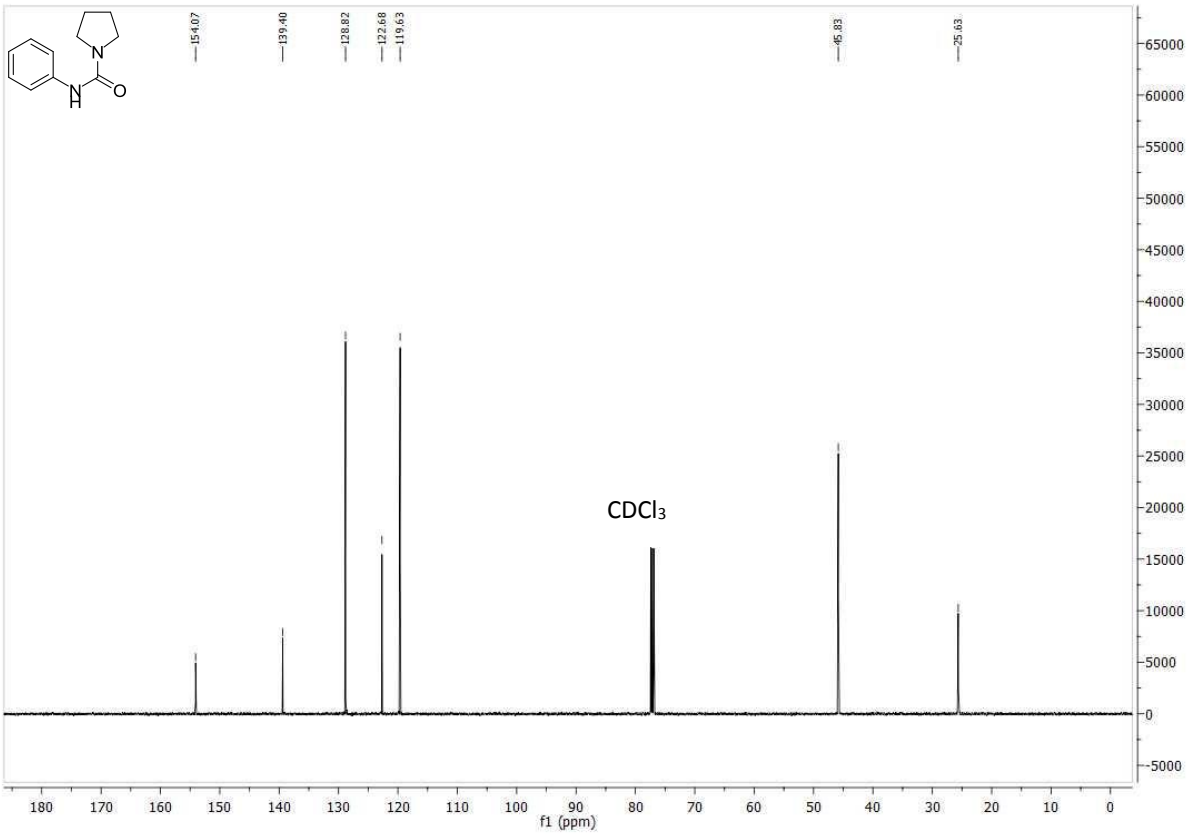


Figure S28 ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of compound **6**.

***N*,*N*'-Diphenylpyrrolidine guanidine hydrochloride 7**

A mixture of carboxamide **6** (0.951 g, 5.0 mmol, 1 eq.) and PCl_5 (1.04 g, 5.0 mmol, 1 eq.) in 25 mL of dry toluene was heated to 60 °C for 1 h until a white solid precipitated. After cooling to rt the solvent was removed *in vacuo*. The resulting white solid was used immediately without any further purification and dissolved in 100 mL of dry toluene. Aniline (0.47 mL, 5.0 mmol, 1 eq.) was added in one portion and the mixture was heated to 70 °C for 18 h. After cooling to rt the solvent was removed *in vacuo*. The resulting solid was washed with 30 mL of toluene (3x), 30 mL of a toluene/CH_2Cl_2 1:1 mixture (3x) to give the product (1.49 g, 4.9 mmol) in 99% yield as a white solid.

^{1}H-NMR (500 MHz, CD_3OD): δ(ppm) = 7.28-7.23 (m, 4H, CH_{aryl}), 7.17-7.13 (m, 4H, CH_{aryl}), 7.11-7.07 (m, 2H, CH_{aryl}), 3.71-3.66 (m, 4H), 2.12-2.06 (m, 4H).

^{13}C-NMR (125 MHz, CD_3OD): δ(ppm) = 152.8; 138.2; 130.3; 126.7; 123.7; 50.6; 26.2.

MS (ESI$^+$) m/z calculated for $C_{17}H_{20}N_3^+$ $[M+H-Cl]^+$ 266.1652, found 266.160.

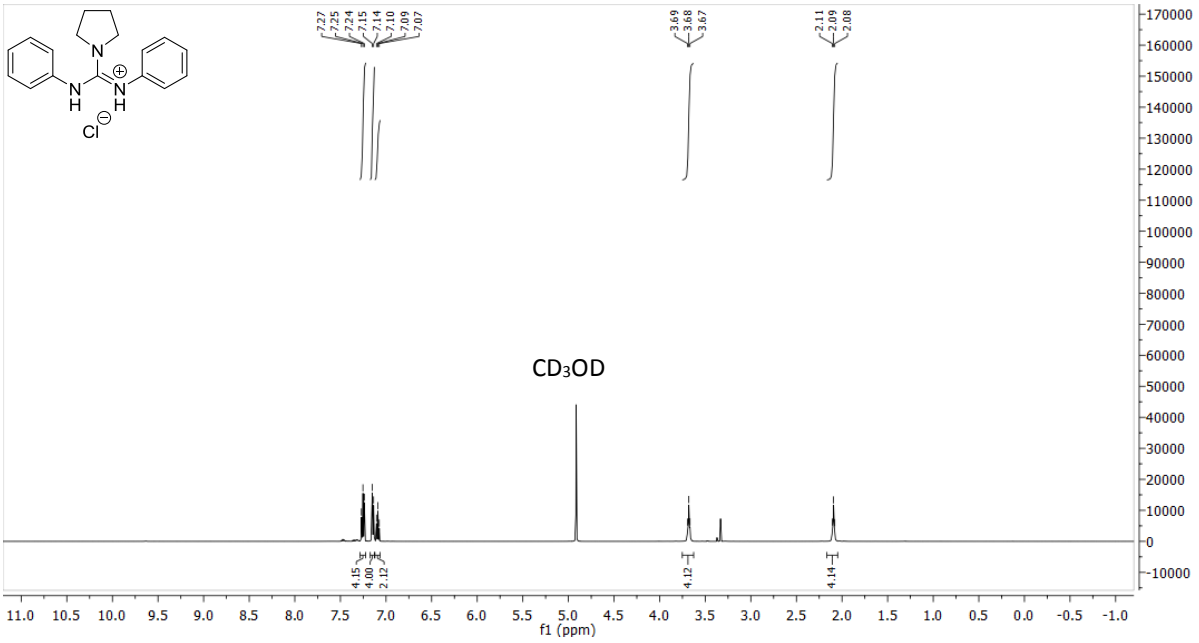


Figure S29 ^{1}H NMR spectrum (500 MHz, CD_3OD, 298 K) of compound **7**.

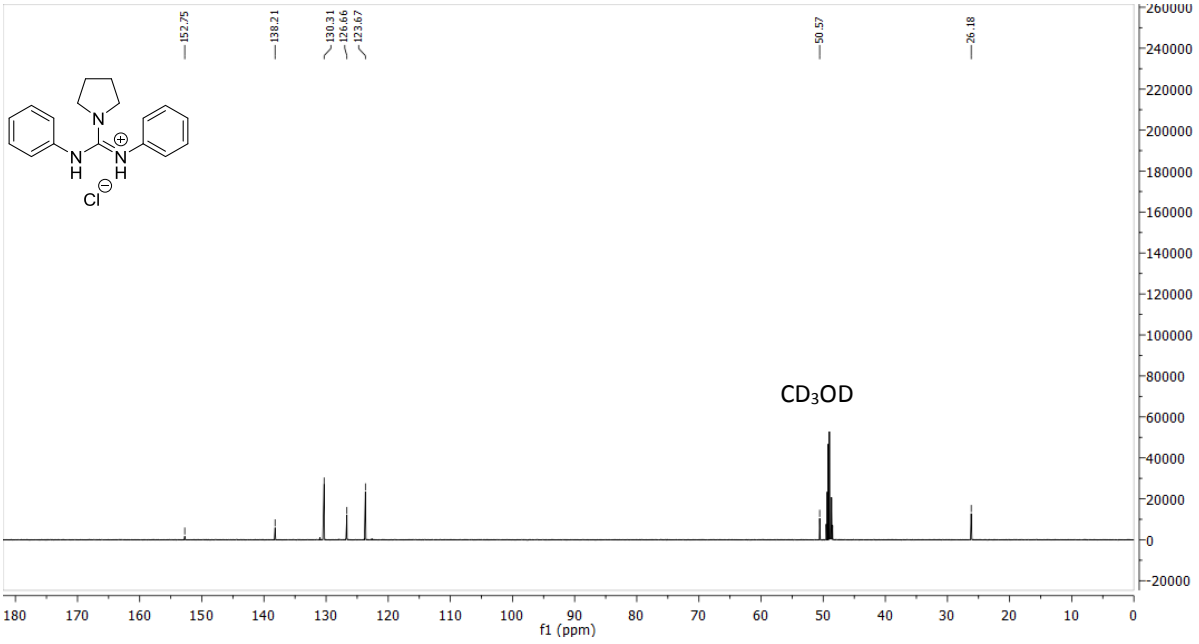


Figure S30 ^{13}C NMR spectrum (125 MHz, CD_3OD, 298 K) of compound **7**.

***N*,*N*′-Diphenylpyrrolidine guanidine 2**

The guanidine hydrochloride **7** (106 mg, 0.35 mmol, 1 eq.) was dissolved in 125 mL of water. KOH (294 mg, 5.25 mmol, 15 eq.) was added and the resulting solution was stirred for 1 h at rt. The aqueous solution was extracted with 70 mL of CH_2Cl_2 (3x) and the combined organic phases were dried over $MgSO_4$. After removing the solvent *in vacuo* the resulting solid was dried by lyophilization out of benzene to yield the desired product (93 mg, 0.35 mmol) in quantitative yield as a yellow solid.

^{1}H-NMR (500 MHz, DMSO-d_6): δ(ppm) = 7.87 (br, 1H, N*H*), 7.08 (t, 4H, CH_{aryl}, ^{3}J = 7.8 Hz), 7.09 (d, 4H, CH_{aryl}, ^{3}J = 7.6 Hz), 7.02 (t, 2H, CH_{aryl}, ^{3}J = 7.3 Hz), 3.32 (m, 4H), 1.80 (m, 4H).

^{13}C-NMR (125 MHz, DMSO-d_6): δ(ppm) = 147.9, 128.5, 119.9, 119.5, 47.2, 24.9.

MS (ESI$^+$) m/z calculated for $C_{17}H_{20}N_3^+$ $[M+H]^+$ 266.1652, found 266.1652.

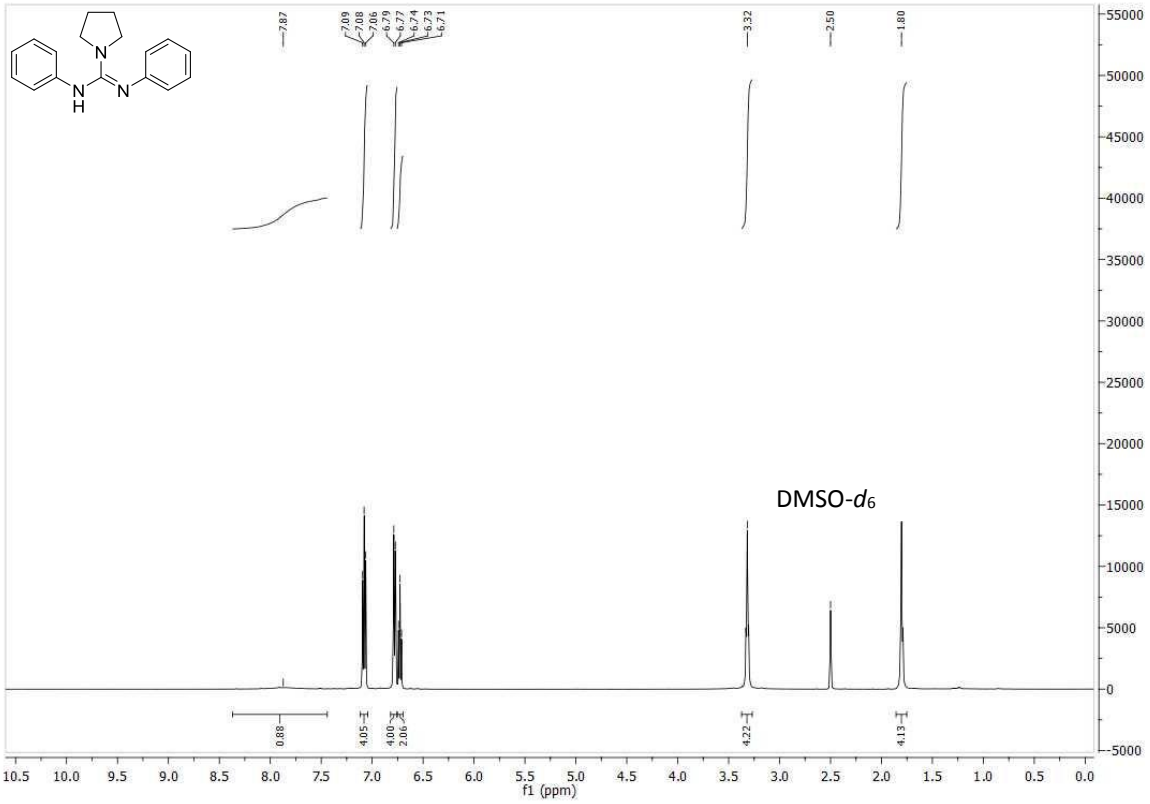


Figure S31 ^{1}H NMR spectrum (500 MHz, DMSO-d_6, 298 K) of compound **2**.

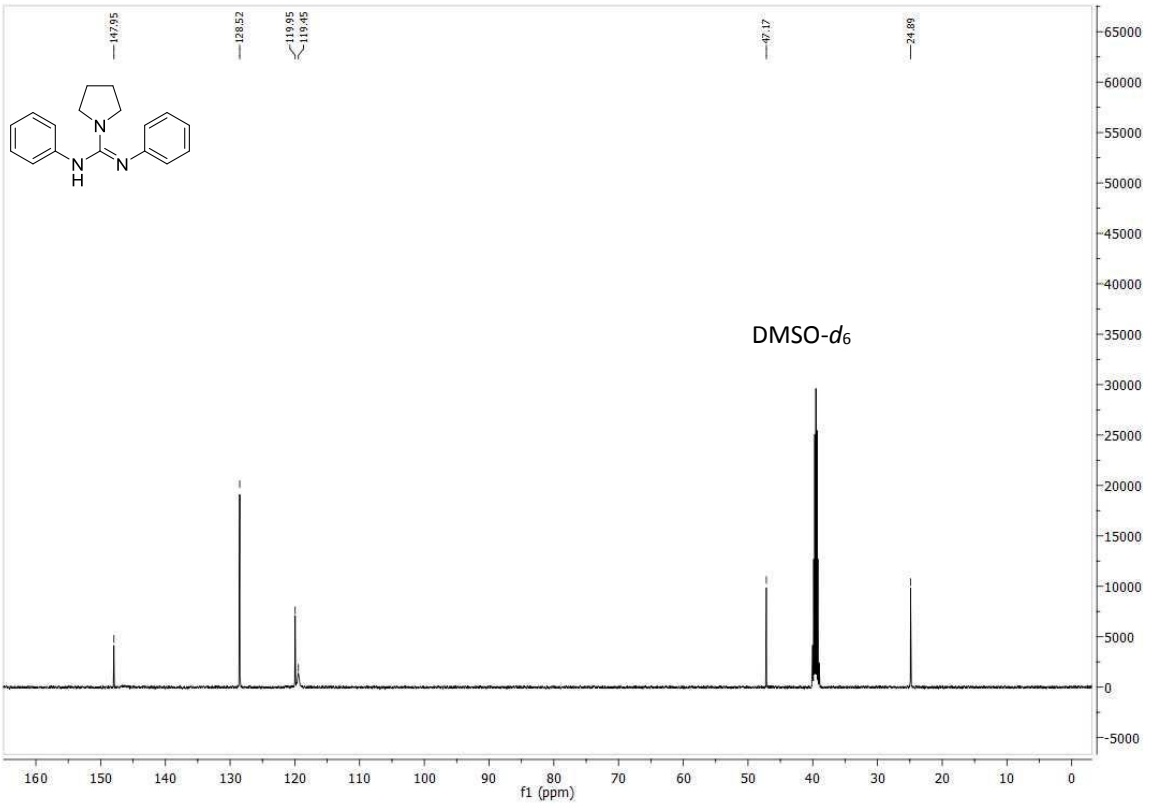
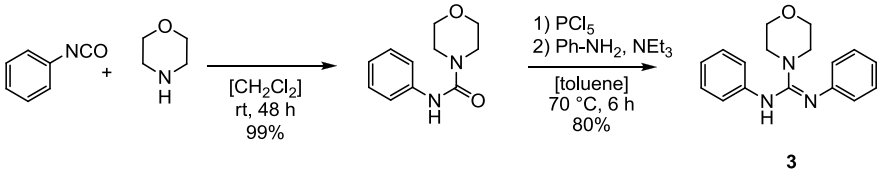


Figure S32 ^{13}C NMR spectrum (125 MHz, DMSO-d_6, 298 K) of compound **2**.

4.3 Synthesis of 3



The synthesis was carried out as described in literature.[10]

5. References

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