

Supporting Information

Resonant Acoustic Mixing for Green Guanylation: Thiourea Trioxide as a Solid Cyanamide Surrogate toward Guanidine Carbonate Salts

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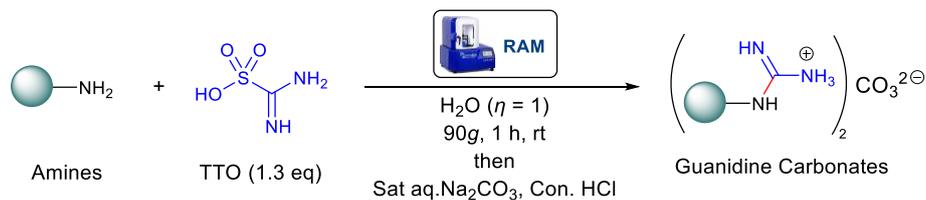
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General information

Commercially available reagents were purchased from Aldrich, Strem Chemicals, Alfa Aesar, Acros, and TCI Europe and used without further purification. All reactions were monitored by thin-layer chromatography (TLC) using an *n*-hexane-ethyl acetate mixture (composition depending on substrate polarity), and compound spots were visualised under UV light (254 nm) or with KMnO₄ stain and subsequent heating. The eluents were technical grade. Chemical reactions were carried out using a Resodyn Acoustic Mixer, LabRAM II, and Retsch Vibratory Mill (MM400 and MM 500 Control). The reagents were mixed using 1.5 mL glass vials sealed with a plastic stopper for the Resodyn Acoustic Mixer (LabRAM II) and a 4 × 10 mL stainless steel jar, containing a 10 mm stainless steel ball for ball milling experiments. These parameters were applied if not stated otherwise. ¹H and ¹³C liquid NMR spectra were recorded on a Varian 600 MHz and Bruker Avance III HD 600 MHz NMR spectrometer at 298 K. For high-temperature measurements, the specific temperature is indicated. Chemical shifts (δ) were calibrated using trimethylsilyl (TMS). Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referred to the residual hydrogen in the solvent (CDCl₃, δ 7.26 ppm, DMSO-*d*₆, δ 2.50 ppm and CD₃OD, δ 3.31 ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances, bs = broad singlet, and combination thereof), coupling constant (J) in Hertz (Hz) and integration. Carbon chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to the carbon resonances of the NMR solvent (CDCl₃, δ 77.16 ppm, δ DMSO-*d*₆, δ 39.52 ppm and CD₃OD, δ 49.00 ppm). Deuterated NMR solvents were obtained from Aldrich. All the experiments were carried out in duplicate to ensure reproducibility of the experimental data. Yields refer to pure, isolated materials.

Synthetic procedure

General Procedure A for the guanidine carbonates:

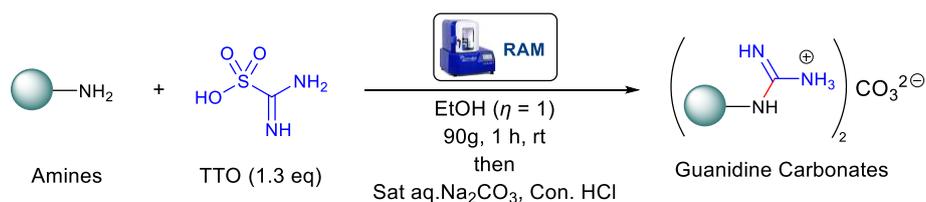


A 1.5 ml glass vial was filled with amine **1a-h/ 2a-i/3a-b** (0.5 mmol), thiourea trioxide (0.65 mmol), and distilled water (ratio of the water volume to the weight of reaction mixture $\eta = 1.00 \text{ mL mg}^{-1}$). The vial was closed, and the reaction was run for 1 hour at 90g using LabRAM II. At the end of the reaction, the mixture was transferred to a 10 mL vial, using a minimal amount of water (approximately 0.3-0.4 mL). Then, 1 mL of a saturated aqueous Na_2CO_3 solution, followed by 1 mmol of concentrated HCl in the sealed vial, was added to retain the generated carbon dioxide. The reaction mixture was then stirred for 4-5 hours. The resulting solid was filtered and washed with 3 mL of water, then rinsed with 0.5 mL of acetone and dried either overnight on filter paper or under an IR lamp, affording guanidine carbonates **6a-h, 7a-h, and 8a-b**.

*Note: I) In the case of 2-picolyamine guanidine carbonate **7i**, the salt preparation was carried out without the use of conc. HCl.*

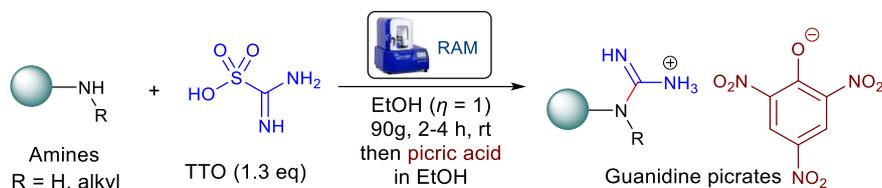
*II) The reaction for **6c, 7b** and **7e** was carried out using procedure B.*

General Procedure B for the guanidine carbonates:



A 1.5 mL glass vial was filled with amine **1c, 2b, 2c** and **3c-f** (0.5 mmol), thiourea trioxide (0.65 mmol), and EtOH (ratio of the EtOH volume to the weight of the reaction mixture, $\eta = 1.00 \text{ mL mg}^{-1}$). The vial was closed, and the reaction was run for 1-2 hours at 90 g using LabRAM II. At the end of the reaction, the mixture was transferred to a 10 mL vial, using a minimal amount of EtOH (approximately 0.3-0.4 mL). Then, 1 mL of a saturated aqueous Na_2CO_3 solution, followed by 1 mmol of concentrated HCl in the sealed vial, was added to retain the generated carbon dioxide. The reaction mixture was then stirred for 4-5 hours. The resulting solid was filtered and washed with 3 mL of water, then rinsed with 0.5 mL of acetone and dried either overnight on filter paper or under an IR lamp, affording guanidine carbonates **6c, 7b, 7e** and **8c-f**.

General Procedure C for the guanidine picrates:

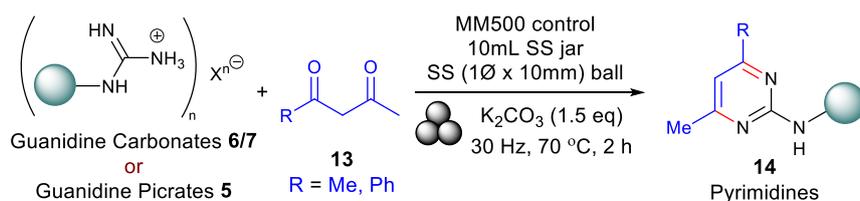


A 1.5 mL glass vial was filled with amine **1a**, **2b** and **2h/9a-c/10a** (0.5 mmol), thiourea trioxide (0.65 mmol), and EtOH (ratio of the EtOH volume to the weight of reaction mixture $\eta = 1.00$ mL mg⁻¹). The vial was closed, and the reaction was run for 1 and 2-4 hours at 90g using LabRAM II. At the end of the reaction, the mixture was transferred to a 10 mL vial, using a minimal amount of EtOH (approximately 0.3-0.4 mL) containing 2.5 mL of picric acid solution (1.5 eq. in EtOH) and stirred for 3 hours. The resulting solid was filtered and washed with 2-3 mL of EtOH, and dried either overnight on filter paper or under an IR lamp, affording guanidine picrates **5a** and **5h/11a-c/12a**.

Note: 1) The reaction for compound **1a** was carried out for 1 hour; those for **2b**, **2h**, and **9a** were conducted for 2 hours; and reactions for **9b-c** and **10a** were performed for 4 hours.

2) Reaction optimisation using RAM was initially performed on aniline **1a** at 60g, giving satisfactory results. However, substrate scope studies with guanidinium picrates and carbonates were conducted at 90g to account for variations in amine structure affecting the rheology and reaction outcome. Therefore, a constant 90g was used for all substrate scope experiments to ensure consistency.

General Procedure D for the 2-Aminopyrimidine:

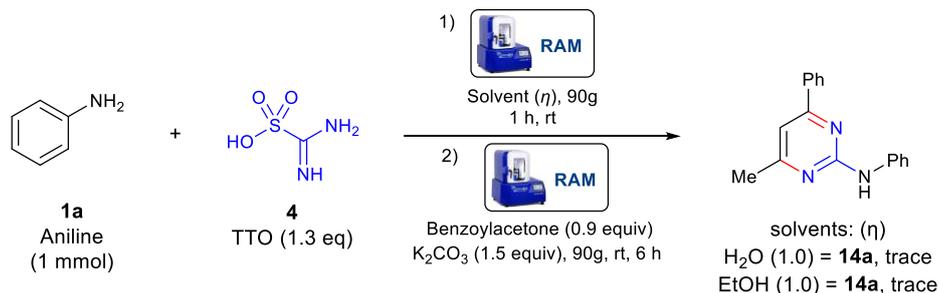


Guanidine carbonate/guanidine picrates **6/7** or **5** (0.5 mmol), 1,3-diketone **13** (0.45 mmol), potassium and potassium carbonate (1.5 equiv.) were loaded into a stainless-steel grinding jar (10 mL) equipped with 1 ball ($\phi = 10$ mm, $m = 2.87$ g) of the same material. The jar was sealed and milled at a frequency of 30 Hz in a Retsch shaker mill MM500 control at 70 °C for 2 hours. After completion of the reaction, the resulting reaction mixture was filtered through a small bed of celite using a sintered vacuum funnel with 20 mL of EtOAc. The filtrate was then evaporated under high vacuum, affording pyrimidine **14a-d**.

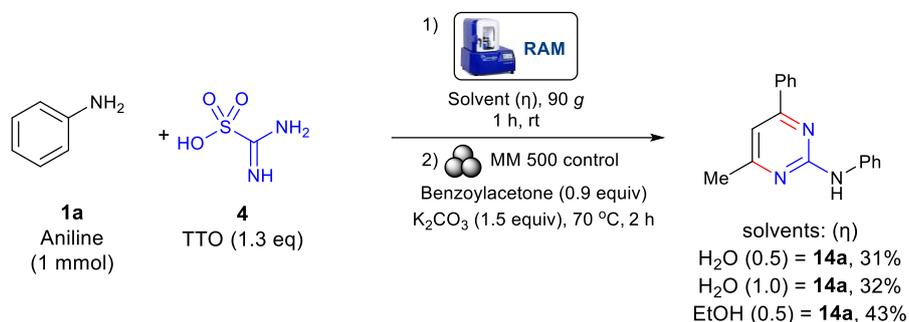
Note: Compounds **14c** and **14d** were further purified using a short pad of silica with heptane and ethyl acetate as eluents.

One-pot, two-step protocol for the synthesis of 2-aminopyrimidines **14a**:

A) One-pot, two-step protocol for the synthesis of aminopyrimidines (RAM)



B) One-pot, two-step protocol for the synthesis of aminopyrimidines (RAM) and complementary ball-milling (MM 500 control)



General procedure one-pot, two-step protocol for the synthesis of 2-aminopyrimidine **14a**: (RAM)

A 1.5 mL glass vial was filled with amine **1a**, (1 mmol), thiourea trioxide (1.3 mmol), and solvent (ratio of the solvent volume to the weight of the reaction mixture, $\eta = 1.00$ mL mg⁻¹). The vial was closed, and the reaction was run for 1 hours at 90g using LabRAM II. After completion of the first step, to the reaction mixture, benzoylacetone **13** (0.9 equiv) and K_2CO_3 (1.5 equiv) were added, and again run it at 90g for 6 h at room temperature. After completion of the reaction, the resulting reaction mixture was filtered through a small bed of celite using a sintered vacuum funnel with 20 mL of EtOAc. The filtrate was evaporated under high vacuum and dried.

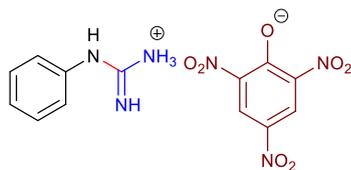
(Trace amount of product **14a** was observed based on the crude reaction mixture's ¹H NMR).

General procedure one-pot, two-step protocol for the synthesis of 2-aminopyrimidine **14a**: (RAM-Complementary ball milling MM 500 control)

A 1.5 mL glass vial was filled with amine **1a** (1 mmol), thiourea trioxide (1.3 mmol), and solvent (ratio of the solvent volume to the weight of the reaction mixture, $\eta = 0.5$ -1.00 mL mg⁻¹). The vial was closed, and the reaction was run for 1 hour at 90 g using LabRAM II. After completion of the first step, the reaction mixture was transferred to the 10 mL stainless-steel jar with one 10 mm stainless-steel ball and benzoylacetone **13** (0.9 equiv) and K_2CO_3 (1.5 equiv) were added, and then the reaction was run at 70 °C for 2 hours. After completion of the reaction, the resulting reaction

mixture was filtered through a small bed of celite using a sintered vacuum funnel with 20 mL of EtOAc. The product **14a** was isolated with a small pad of silica using heptane and ethyl acetate as eluents.

1-phenylguanidinium 2,4,6-trinitrophenolate 5a:



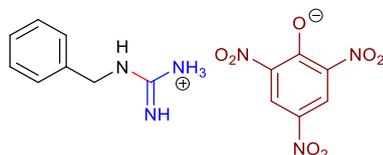
The title compound was synthesised according to General Procedure C stated above. Aniline (47 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 128 μ L of EtOH were mixed using a LabRAM II for 1 hour. The resulting crude mixture was then stirred with picric acid (172 mg, 0.75 mmol) in 2.5 mL of EtOH solvent to afford 1-phenylguanidinium 2,4,6-trinitrophenolate **5a** as a yellow solid (140 mg, 77%).

^1H NMR (600 MHz, DMSO- d_6): δ 8.60 (s, 2H), 7.44 (t, J = 7.7 Hz, 2H), 7.34 (s, 3H), 7.29 (t, J = 7.4 Hz, 1H), 7.23 (d, J = 7.8 Hz, 2H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 160.9, 155.7, 141.9, 135.3, 129.7, 126.6, 125.3, 124.6, 124.3.

HRMS: Calculated for $\text{C}_7\text{H}_{10}\text{N}_3$: 136.0868 $[\text{M}+\text{H}]^+$; found: 136.0865.

1-benzylguanidinium 2,4,6-trinitrophenolate 5bb:



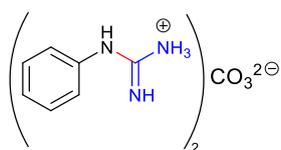
The title compound was synthesised according to General Procedure C stated above. Benzylamine (54 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 135 μ L of EtOH were mixed using LabRAM II for 1 hour. The resulting crude mixture was stirred with picric acid (172 mg, 0.75 mmol) in 2.5 mL of EtOH solvent to afford the 1-benzylguanidinium 2,4,6-trinitrophenolate **5bb** as a yellow solid (153 mg, 81%).

^1H NMR (600 MHz, DMSO- d_6): δ 8.60 (s, 2H), 7.88 (s, 1H), 7.38 (dd, J = 8.7, 6.7 Hz, 2H), 7.34 – 7.17 (m, 3H), 7.17 (d, J = 7.2 Hz, 3H), 4.37 (d, J = 5.7 Hz, 2H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 160.9, 156.8, 141.8, 137.1, 128.6, 127.6, 127.2, 125.3, 124.3, 44.1.

HRMS: Calculated for $\text{C}_8\text{H}_{12}\text{N}_3$: 150.1025 $[\text{M}+\text{H}]^+$; found: 150.1024.

Bis-phenylguanidinium carbonate 6a:



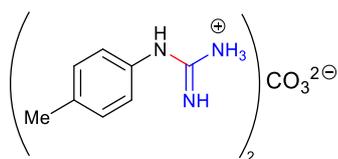
The title compound was synthesised according to General Procedure A stated above. Aniline (47 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 128 μL of H_2O were mixed using LabRAM II for 1 hour. The resulting crude mixture was then treated with Na_2CO_3 to afford the bis-phenylguanidinium carbonate **6a** as a white solid (68 mg, 81%).

$^1\text{H NMR}$ (600 MHz, $\text{DMSO-}d_6$): δ 7.28 (t, $J = 7.7$ Hz, 2H), 7.12 – 6.64 (m, 3H), 6.29 (bs, 3H).

$^{13}\text{C NMR}$ (151 MHz, $\text{DMSO-}d_6$): δ 160.9, 154.5, 142.7, 129.2, 128.7, 123.3.

The spectroscopic data closely match those previously reported in the literature.¹

Bis-1-(p-tolyl)guanidinium carbonate 6b:



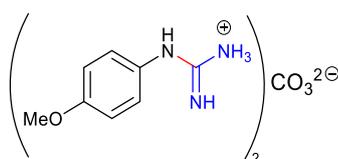
The title compound was synthesised according to General Procedure A stated above. *p*-Toluidine (54 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 135 μL of H_2O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-(*p*-tolyl)guanidinium carbonate **6b** as a white solid (61 mg, 68%).

$^1\text{H NMR}$ (600 MHz, $\text{DMSO-}d_6$): δ 7.13 (d, $J = 7.8$ Hz, 2H), 6.94 – 6.71 (m, 2H), 2.26 (s, 3H).

$^{13}\text{C NMR}$ (151 MHz, $\text{DMSO-}d_6$): δ 160.3, 155.2, 137.6, 133.3, 129.8, 123.6, 20.5.

The spectroscopic data closely match those previously reported in the literature.¹

Bis-1-(4-methoxyphenyl)guanidinium carbonate 6c:



The title compound was synthesised according to General Procedure B stated above. *p*-Anisidine (62 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 143 μL of EtOH were mixed using

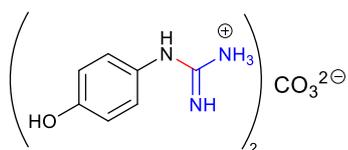
LabRAM II for 1 hour. The resulting crude mixture was treated with Na₂CO₃ to afford the bis-1-(4-methoxyphenyl)guanidinium carbonate **6c** as a white solid (65 mg, 66%).

¹H NMR (600 MHz, DMSO-*d*₆): δ 6.99 (bs, 2H), 6.90 (d, J = 8.2 Hz, 2H), 3.73 (s, 3H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 160.5, 156.6, 155.8, 131.9, 125.7, 114.6, 55.3.

The spectroscopic data closely match those previously reported in the literature.¹

Bis-1-(4-hydroxyphenyl)guanidinium carbonate 6d:



The title compound was synthesised according to General Procedure A stated above. 4-Aminophenol (55 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 136 μL of H₂O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na₂CO₃ to afford the bis-1-(4-hydroxyphenyl)guanidinium carbonate **6d** as a white solid (40 mg, 44%).

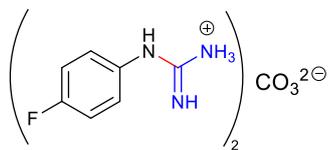
Note: Yield after crystallisation in a small amount of EtOH.

¹H NMR (600 MHz, DMSO-*d*₆): δ 6.88 (d, J = 8.2 Hz, 2H), 6.73 (d, J = 8.1 Hz, 2H), 5.85 (bs, 3H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 160.4, 156.3, 156.0, 128.0, 126.3, 116.1.

HRMS: Calculated for C₇H₁₀N₃O: 152.0818 [M+H]⁺; found: 152.0817.

Bis-1-(4-fluorophenyl)guanidinium carbonate 6e:



The title compound was synthesised according to General Procedure A stated above. 4-Fluoroaniline (56 mg, 0.5 mmol), thiourea trioxide (106 mg, 0.85mmol), and 162 μL of H₂O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na₂CO₃ to afford the bis-1-(4-fluorophenyl)guanidinium carbonate **6e** as a white solid (69 mg, 75%).

Note: TTO was used 1.7 equivalents.

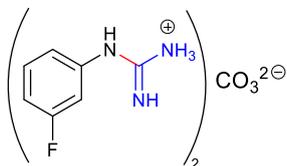
¹H NMR (600 MHz, DMSO-*d*₆): δ 7.02 (t, J = 8.6 Hz, 2H), 6.89 – 6.78 (m, 2H), 6.08 (bs, 3H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 158.2, 156.7, 153.4, 144.0, 124.5, 124.4, 115.4, 115.3.

¹⁹F NMR (DMSO-*d*₆): δ -123.03.

HRMS: Calculated for C₇H₉FN₃: 154.0774 [M+H]⁺; found: 154.0774.

Bis-1-(3-fluorophenyl)guanidinium carbonate 6f:



The title compound was synthesised according to General Procedure A stated above. 4-Fluoroaniline (56 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 137 μL of H₂O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na₂CO₃ to afford the Bis-1-(3-fluorophenyl)guanidinium carbonate **6f** as a white solid (30 mg, 32%).

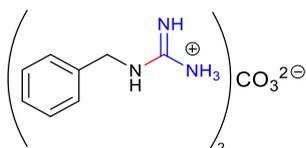
¹H NMR (600 MHz, DMSO-*d*₆): δ 7.25 – 7.20 (m, 1H), 6.70 – 6.65 (m, 3H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 163.6, 162.0, 148.5, 130.2, 130.1, 119.1, 109.6, 109.4.

¹⁹F NMR (DMSO-*d*₆): δ -113.5.

HRMS: Calculated for C₇H₉FN₃: 154.0774 [M+H]⁺; found: 154.0774.

Bis-1-benzylguanidinium carbonate 7a:



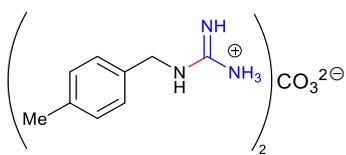
The title compound was synthesised according to General Procedure A stated above. Benzylamine (54 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 135 μL of H₂O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na₂CO₃ to afford the bis-1-benzylguanidinium carbonate **7a** as a white solid (66 mg, 74%).

¹H NMR (600 MHz, DMSO-*d*₆): δ 8.58 (bs, 3H), 7.35 (t, J = 7.5 Hz, 2H), 7.31 – 7.26 (m, 3H), 4.33 – 4.32 (m, 2H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 160.3, 157.5, 137.9, 128.5, 127.1, 43.6.

HRMS: Calculated for C₈H₁₂N₃: 150.1025 [M+H]⁺; found: 150.1024.

Bis-1-(4-methylbenzyl)guanidinium carbonate 7b:



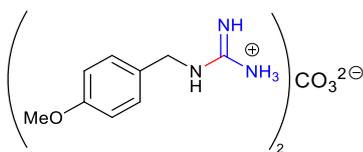
The title compound was synthesised according to General Procedure B stated above. 4-methylbenzylamine (61 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 147 μL of EtOH were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-(4-methylbenzyl)guanidinium carbonate **7b** as a white solid (66 mg, 68%).

^1H NMR (600 MHz, DMSO- d_6): δ 8.19 (bs, 3H), 7.19-7.15 (m, 4H), 4.30 (s, 2H), 2.28 (s, 3H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 160.1, 157.4, 136.4, 134.7, 129.0, 127.2, 43.4, 20.7.

HRMS: Calculated for $\text{C}_9\text{H}_{14}\text{N}_3$: 164.1181 $[\text{M}+\text{H}]^+$; found: 164.1182.

Bis-1-(4-methoxybenzyl)guanidinium carbonate 7c:



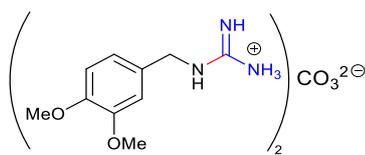
The title compound was synthesised according to General Procedure A stated above. 4-Methoxybenzylamine (69 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 150 μL of H_2O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-(4-methoxybenzyl)guanidinium carbonate **7c** as a white solid (83 mg, 74%).

^1H NMR (600 MHz, DMSO- d_6): δ 8.38 (bs, 3H), 7.23 (d, $J = 8.2$ Hz, 2H), 6.90 (d, $J = 8.2$ Hz, 2H), 4.23 (s, 2H), 3.73 (s, 3H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 160.3, 158.6, 157.3, 129.1, 128.7, 113.9, 55.1, 43.2.

HRMS: Calculated for $\text{C}_9\text{H}_{14}\text{N}_3\text{O}$: 180.1131 $[\text{M}+\text{H}]^+$; found: 180.1129.

Bis-1-(3,4-dimethoxybenzyl)guanidinium carbonate 7d:



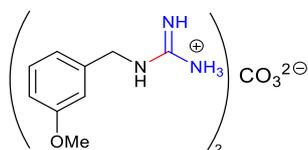
The title compound was synthesised according to General Procedure A stated above. 3, 4-Dimethoxybenzylamine (84 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 165 μ L of H₂O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na₂CO₃ to afford the bis-1-(3,4-dimethoxybenzyl)guanidinium carbonate **7d** as a white solid (94 mg, 78%).

¹H NMR (600 MHz, DMSO-*d*₆): δ 8.35 (bs, 3H), 6.95 (d, *J* = 2.0 Hz, 1H), 6.91 (d, *J* = 8.2 Hz, 1H), 6.84 – 6.83 (m, 1H), 4.22 (s, 2H), 3.73 (s, 3H), 3.72 (s, 3H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 159.6, 157.3, 148.7, 148.2, 130.0, 119.5, 111.8, 111.5, 55.6, 55.5, 43.6.

HRMS: Calculated for C₁₀H₁₆N₃O₂: 210.1236 [M+H]⁺; found: 210.1235.

Bis-1-(3-methoxybenzyl)guanidinium carbonate 7e:



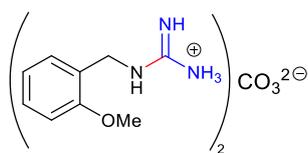
The title compound was synthesised according to General Procedure B stated above. 3-Methoxybenzylamine (69 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 150 μ L of EtOH were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na₂CO₃ to afford the bis-1-(3-methoxybenzyl)guanidinium carbonate **7e** as a white solid (77 mg, 73%).

¹H NMR (600 MHz, DMSO-*d*₆): δ 8.46 (bs, 3H), 7.26 (t, *J* = 7.8 Hz, 1H), 6.88 – 6.84 (m, 3H), 4.28 (s, 2H), 3.74 (s, 3H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 160.1, 159.8, 157.4, 139.4, 129.6, 119.2, 112.9, 112.6, 55.0, 43.6.

HRMS: Calculated for C₉H₁₄N₃O: 180.1131 [M+H]⁺; found: 180.1129.

Bis-1-(2-methoxybenzyl)guanidinium carbonate 7f:



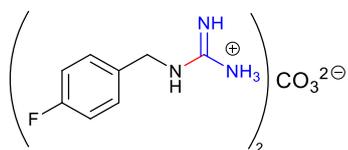
The title compound was synthesised according to General Procedure A stated above. 2-Methoxybenzylamine (69 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 150 μL of H_2O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-(2-methoxybenzyl)guanidinium carbonate **7f** as a white solid (84 mg, 80%).

^1H NMR (600 MHz, DMSO- d_6): δ 8.32 (bs, 3H), 7.30 (td, $J = 7.8, 1.7$ Hz, 1H), 7.23 (d, $J = 7.5$ Hz, 1H), 7.02 (d, $J = 8.2$ Hz, 1H), 6.94 (td, $J = 7.4, 1.1$ Hz, 1H), 4.30 (s, 2H), 3.81 (s, 3H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 159.8, 157.0, 156.8, 128.9, 128.1, 125.0, 120.3, 110.8, 55.4, 40.1.

HRMS: Calculated for $\text{C}_9\text{H}_{14}\text{N}_3\text{O}$: 180.1131 $[\text{M}+\text{H}]^+$; found: 180.1129.

Bis-1-(4-fluorobenzyl)guanidinium carbonate 7g:



The title compound was synthesised according to General Procedure A stated above. 4-Fluorobenzylamine (63 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 144 μL of H_2O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-(4-fluorobenzyl)guanidinium carbonate **7g** as a white solid (64 mg, 65%).

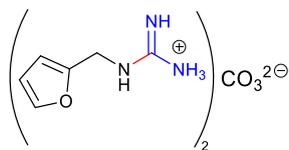
^1H NMR (600 MHz, DMSO- d_6): δ 8.50 (bs, 3H), 7.35 – 7.33 (m, 2H), 7.16 (t, $J = 8.8$ Hz, 2H), 4.30 (d, $J = 1.2$ Hz, 2H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 162.2, 160.6, 160.3, 157.4, 134.1, 129.2, 129.2, 115.3, 115.1, 42.9.

^{19}F NMR (DMSO- d_6): -115.53.

HRMS: Calculated for $\text{C}_8\text{H}_{11}\text{FN}_3$: 168.0931 $[\text{M}+\text{H}]^+$; found: 168.0929.

Bis-1-(furan-2-ylmethyl)guanidinium carbonate 7h:



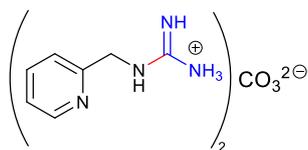
The title compound was synthesised according to General Procedure A stated above. Furfurylamine (49 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 130 μL of H_2O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-(furan-2-ylmethyl)guanidinium carbonate **7h** as a white solid (12 mg, 14%).

^1H NMR (600 MHz, DMSO- d_6): δ 8.43 (bs, 3H), 7.62 (s, 1H), 6.41 (t, $J = 2.4$ Hz, 1H), 6.35 (d, $J = 3.1$ Hz, 1H), 4.36 (s, 2H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 159.9, 157.1, 150.6, 142.8, 110.5, 107.6, 37.3.

HRMS: Calculated for $\text{C}_6\text{H}_{10}\text{N}_3\text{O}$: 140.0818 $[\text{M}+\text{H}]^+$; found: 140.0799.

Bis-1-(pyridin-2-ylmethyl)guanidinium carbonate 7i:



The title compound was synthesised according to General Procedure A stated above. 2-picolylamine (54 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 135 μL of H_2O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-(pyridin-2-ylmethyl)guanidinium carbonate **7i** as a white solid (40 mg, 44%).

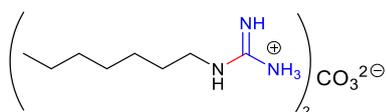
Note: Carbonate salt formation was carried out without the use of Conc. HCl.

^1H NMR (600 MHz, DMSO- d_6): δ 8.54 (d, $J = 4.7$ Hz, 1H), 8.20 (bs, 3H), 7.81 (td, $J = 7.7, 1.9$ Hz, 1H), 7.32 (dd, $J = 10.8, 6.6$ Hz, 2H), 4.44 (s, 2H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 159.6, 157.9, 156.8, 149.1, 137.2, 122.7, 121.3, 45.6.

HRMS: Calculated for $\text{C}_7\text{H}_{11}\text{N}_4$: 151.0977 $[\text{M}+\text{H}]^+$; found: 151.0978.

Bis-1-heptylguanidinium carbonate 8a:



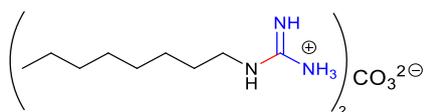
The title compound was synthesised according to General Procedure A stated above. Heptylamine (63 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 144 μL of H_2O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-heptylguanidinium carbonate **8a** as a white solid (63 mg, 67%).

^1H NMR (600 MHz, $\text{DMSO-}d_6$): δ 8.17 (bs, 3H), 3.02 (s, 2H), 1.44 (s, 2H), 1.29 – 1.25 (m, 8H), 0.87 – 0.84 (m, 3H).

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$): δ 159.9, 157.3, 40.6, 31.2, 28.5, 28.3, 26.1, 22.0, 13.9.

HRMS: Calculated for $\text{C}_8\text{H}_{20}\text{N}_3$: 158.1651 $[\text{M}+\text{H}]^+$; found: 158.1650.

Bis-1-octylguanidinium carbonate 8b:



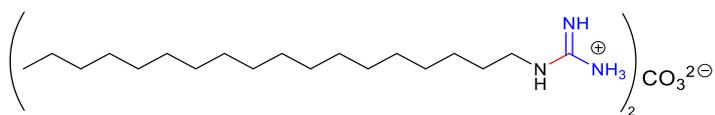
The title compound was synthesised according to General Procedure A stated above. Octylamine (65 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 146 μL of H_2O were mixed using LabRAM II for 1 hour. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-octylguanidinium carbonate **8b** as a white solid (83 mg, 82%).

^1H NMR (600 MHz, $\text{DMSO-}d_6$): δ 8.09 (bs, 3H), 3.03 (dt, $J = 14.8, 7.2$ Hz, 2H), 1.43 (q, $J = 7.0$ Hz, 2H), 1.26 (dd, $J = 11.8, 6.0$ Hz, 10H), 0.85 (t, $J = 6.8$ Hz, 3H).

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$): δ 159.8, 157.3, 40.6, 31.2, 28.7, 28.6, 28.5, 26.2, 22.1, 13.9.

HRMS: Calculated for $\text{C}_9\text{H}_{22}\text{N}_3$: 172.1807 $[\text{M}+\text{H}]^+$; found: 172.1806.

Bis-1-octadecylguanidinium carbonate 8c:



The title compound was synthesised according to General Procedure B stated above. Octadecylamine (135 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 216 μL of EtOH were mixed using LabRAM II for 2 hours. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-octadecylguanidinium carbonate **8c** as a white solid (155 mg, 90%).

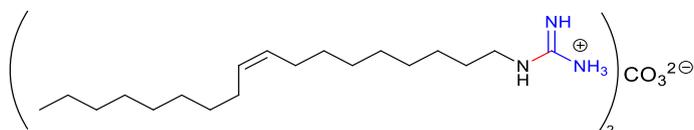
^1H NMR (600 MHz, DMSO- d_6): δ 3.10 (t, $J = 7.0$ Hz, 2H), 1.48 (q, $J = 7.2$ Hz, 2H), 1.30-1.26 (m, 30H), 0.87 (t, $J = 6.8$ Hz, 3H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 156.5, 40.3, 30.9, 28.6, 28.5, 28.2, 28.2, 25.7, 21.6, 13.4.

IR(Neat, KBr): 3492.45, 3339.41, 2915.84, 2848.35, 1696.09, 1631.48, 1465.63, 1397.17, 1192.76, 1158.04, 984.48, 831.16, 716.42, 666.28, 609.39.

HRMS: Calculated for $\text{C}_{19}\text{H}_{42}\text{N}_3$: 312.3372 $[\text{M}+\text{H}]^+$; found: 312.3378.

Bis-(Z)-1-(octadec-9-en-1-yl)guanidinium carbonate 8d:



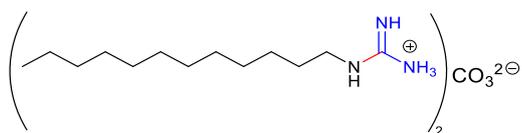
The title compound was synthesised according to General Procedure B stated above. Oleylamine (134 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 215 μL of EtOH were mixed using LabRAM II for 2 hours. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-(Z)-1-(octadec-9-en-1-yl)guanidinium carbonate **8d** as a white solid (68 mg, 40%).

^1H NMR (600 MHz, DMSO- d_6): δ 7.00 (bs, 3H), 5.34 (dt, $J = 21.2, 4.6$ Hz, 2H), 3.06 (t, $J = 7.1$ Hz, 2H), 1.96 (dd, $J = 16.6, 10.0$ Hz, 4H), 1.45-1.43 (m, 2H), 1.29-1.24 (m, 22H), 0.85 (t, $J = 6.8$ Hz, 3H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 156.8, 129.6, 129.6, 40.7, 31.3, 29.1, 29.1, 29.0, 28.9, 28.8, 28.7, 28.6, 28.5, 28.4, 26.6, 26.5, 26.1, 22.1, 13.9.

HRMS: Calculated for $\text{C}_{19}\text{H}_{40}\text{N}_3$: 310.3216 $[\text{M}+\text{H}]^+$; found: 310.3215.

Bis-1-dodecylguanidinium carbonate 8e: [Dodine (fungicide) carbonate derivative]



The title compound was synthesised according to General Procedure B stated above. Dodecylamine (93 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 174 μL of EtOH were mixed using LabRAM II for 2 hours. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-dodecylguanidinium carbonate **8e** as a white solid (116 mg, 90%).

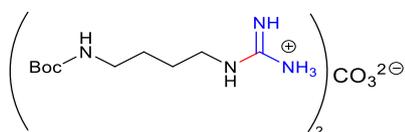
^1H NMR (600 MHz, DMSO- d_6): δ 3.09 (t, $J = 7.0$ Hz, 2H), 1.47 (q, $J = 7.0$ Hz, 2H), 1.30 – 1.27 (m, 20H), 0.87 (t, $J = 6.9$ Hz, 3H).

^{13}C NMR (151 MHz, DMSO- d_6): δ 156.4, 40.2, 30.9, 28.6, 28.6, 28.5, 28.3, 28.2, 25.8, 21.6, 13.4.

IR(Neat, KBr): 3336.25, 3064.33, 2919.70, 2849.31, 1694.16, 1635.34, 1465.63, 1397.17, 1192.76, 984.48, 831.16, 776.20, 709.67, 666.28, 607.46, 567.93.

HRMS: Calculated for $\text{C}_{13}\text{H}_{30}\text{N}_3$: 228.2433 $[\text{M}+\text{H}]^+$; found: 228.2433.

Bis-1-(4-((tert-butoxycarbonyl)amino)butyl)guanidinium carbonate 8f: [Agmatine carbonate]



The title compound was synthesised according to General Procedure B stated above. *tert*-Butyl (4-aminobutyl)carbamate (94 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 175 μL of EtOH were mixed using LabRAM II for 2 hours. The resulting crude mixture was treated with Na_2CO_3 to afford the bis-1-(4-((tert-butoxycarbonyl)amino)butyl)guanidinium carbonate **8f** as a white solid (60 mg, 46%).

^1H NMR (600 MHz, DMSO- d_6): δ 3.10 (t, $J = 6.7$ Hz, 2H), 2.95 (t, $J = 6.6$ Hz, 2H), 1.49 – 1.45 (m, 4H), 1.39 (s, 9H).

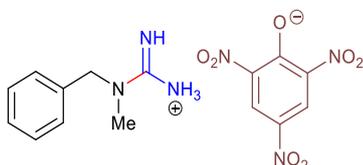
^{13}C NMR (151 MHz, DMSO- d_6): δ 156.8, 155.3, 77.2, 40.1, 40.0, 28.0, 26.4, 25.6.

IR(Neat, KBr): 3329.50, 2925.48, 2531.11, 1916.9, 1615.09, 1449.24, 1282.43, 1166.72, 988.33, 830.20, 692.32, 654.71.

HRMS: Calculated for $\text{C}_{10}\text{H}_{23}\text{N}_4\text{O}_2$: 231.1815 $[\text{M}+\text{H}]^+$; found: 231.1814.

Note: Due to the compound's limited solubility, one quaternary carbon signal did not appear in the NMR spectrum for compound **8c-f**, even after high-temperature measurements; however, the HRMS and IR spectra confirm the formation of the product.

1-benzyl-1-methylguanidinium 2,4,6-trinitrophenolate 11a:



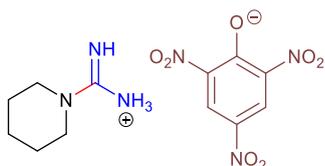
The title compound was synthesised according to General Procedure C stated above. *N*-Benzylmethylamine (61 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.65 mmol), and 142 μ L of EtOH were mixed using LabRAM II for 2 hours. The resulting crude mixture was treated with picric acid (1.5 eq.) in 2.5 mL of EtOH to afford the 1-benzyl-1-methylguanidinium 2,4,6-trinitrophenolate **11a** as a yellow solid (114 mg, 58%).

¹H NMR (600 MHz, DMSO-*d*₆): δ 8.59 (s, 2H), 7.42 – 7.39 (m, 2H), 7.34 – 7.33 (m, 4H), 7.32 – 7.21 (m, 2H), 4.59 (s, 2H), 2.93 (s, 3H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 160.8, 156.8, 141.8, 135.5, 128.8, 127.7, 126.9, 125.2, 52.7, 36.2.

HRMS: Calculated for C₉H₁₄N₃: 164.1181 [M+H]⁺; found: 164.1159.

1-carbamimidoylpiperidin-1-ium 2,4,6-trinitrophenolate 11b:



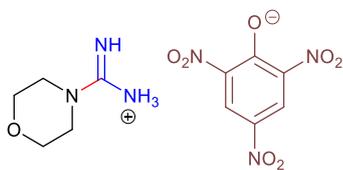
The title compound was synthesised according to General Procedure C stated above. Piperidine (43 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.5 mmol), and 124 μ L of EtOH were mixed using LabRAM II for 4 hours. The resulting crude mixture was treated with picric acid (1.5 eq.) in 2.5 mL of EtOH to afford the 1-carbamimidoylpiperidin-1-ium 2,4,6-trinitrophenolate **11b** as a yellow solid (102 mg, 57%).

¹H NMR (600 MHz, DMSO-*d*₆): δ 8.59 (s, 2H), 7.17 (d, *J* = 2.5 Hz, 3H), 3.38 – 3.36 (m, 4H), 1.59 (qd, *J* = 6.1, 4.0 Hz, 2H), 1.51 (td, *J* = 6.9, 4.3 Hz, 4H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 160.8, 155.4, 141.8, 125.2, 124.2, 46.2, 24.9, 23.1.

HRMS: Calculated for C₆H₁₄N₃: 128.1181 [M+H]⁺; found: 128.1160.

4-carbamimidoylmorpholin-4-ium 2,4,6-trinitrophenolate 11c:



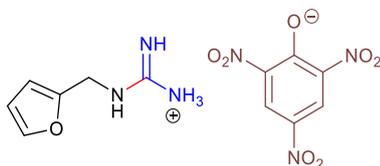
The title compound was synthesised according to General Procedure C stated above. Morpholine (44 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.5 mmol), and 125 μ L of EtOH were mixed using LabRAM II for 4 hours. The resulting crude mixture was treated with picric acid (1.5 eq.) in 2.5 mL of EtOH to afford the 4-carbamimidoylmorpholin-4-ium 2,4,6-trinitrophenolate **11c** as a yellow solid (111 mg, 62%).

¹H NMR (600 MHz, DMSO-*d*₆): δ 8.59 (s, 2H), 7.33 (s, 3H), 3.64 (t, J = 4.9 Hz, 4H), 3.40 (t, J = 4.9 Hz, 4H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 160.8, 156.2, 141.8, 125.1, 124.2, 65.2, 45.2.

HRMS: Calculated for C₅H₁₂N₃O: 130.0974 [M+H]⁺; found: 130.0952.

1-(furan-2-ylmethyl)guanidinium 2,4,6-trinitrophenolate 5h:



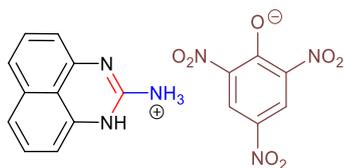
The title compound was synthesised according to General Procedure C stated above. Furfurylamine (49 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.5 mmol), and 130 μ L of EtOH were mixed using LabRAM II for 2 hours. The resulting crude mixture was treated with picric acid (1.5 eq.) in 2.5 mL of EtOH to afford the 1-(furan-2-ylmethyl)guanidinium 2,4,6-trinitrophenolate **5h** as a yellow solid (124 mg, 67%).

¹H NMR (600 MHz, DMSO-*d*₆): δ 8.59 (s, 2H), 7.83 (t, J = 6.1 Hz, 1H), 7.66 (dt, J = 1.9, 1.0 Hz, 1H), 7.14 (bs, 3H), 6.44 (dd, J = 3.3, 1.8 Hz, 1H), 6.38 (d, J = 3.2 Hz, 1H), 4.39 (d, J = 6.0 Hz, 2H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 160.8, 156.6, 150.0, 143.0, 141.8, 125.2, 124.3, 110.6, 108.0, 37.5.

HRMS: Calculated for C₆H₁₀N₃O: 140.0818 [M+H]⁺; found: 140.0799.

1H-perimidin-2-aminium 2,4,6-trinitrophenolate 12a:



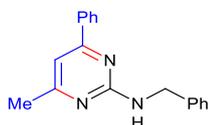
The title compound was synthesised according to General Procedure C stated above. 1,8-diaminonaphthalene (79 mg, 0.5 mmol), thiourea trioxide (80.6 mg, 0.5 mmol), and 160 μ L of EtOH were mixed using LabRAM II for 4 hours. The resulting crude mixture was treated with picric acid (1.5 eq.) in 2.5 mL of EtOH to afford the 1H-perimidin-2-aminium 2,4,6-trinitrophenolate **12a** as a brown solid (165 mg, 80%).

¹H NMR (600 MHz, DMSO-*d*₆): δ 11.25 (s, 2H), 8.57 (s, 2H), 7.85 (s, 2H), 7.32 – 7.31 (m, 4H), 6.78 (dt, *J* = 6.3, 3.1 Hz, 2H).

¹³C NMR (151 MHz, DMSO-*d*₆): δ 160.8, 149.9, 141.7, 133.7, 132.8, 128.2, 125.3, 124.4, 120.4, 115.2, 106.7.

HRMS: Calculated for C₁₁H₁₀N₃: 184.0868 [M+H]⁺; found: 184.0867.

***N*-benzyl-4-methyl-6-phenylpyrimidin-2-amine 14a:** (From guanidinium carbonate salt)



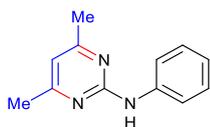
The title compound was synthesised according to General Procedure D stated above. Bis-1-benzylguanidinium carbonate **7a** (180 mg, 0.5 mmol), 1-phenylbutane-1,3-dione **13a** (68 μ L, 0.45 mmol), and K₂CO₃ (104 mg, 0.75 mmol) were milled using a Retsch MM500 Control at 30Hz at 70 °C for 2 h. The resulting reaction mixture was filtered through celite with 20 mL of EtOAc, and the filtrate was concentrated to afford *N*-benzyl-4-methyl-6-phenylpyrimidin-2-amine **14a** as a white solid (72 mg, 58%).

¹H NMR (600 MHz, CDCl₃): δ 8.02 – 8.01 (m, 2H), 7.46 – 7.44 (m, 3H), 7.41 (d, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.27 (d, *J* = 1.4 Hz, 1H), 6.90 (s, 1H), 4.75 (s, 2H), 2.41 (s, 3H).

¹³C NMR (151 MHz, CDCl₃): δ 168.6, 164.7, 162.7, 139.8, 137.8, 130.4, 128.7, 128.6, 127.7, 127.2, 127.1, 106.6, 45.6, 24.4.

The spectroscopic data closely match those previously reported in the literature.²

4,6-dimethyl-*N*-phenylpyrimidin-2-amine 14b: (From guanidinium carbonate salt)



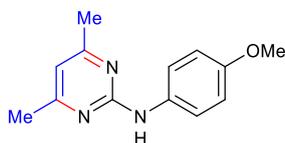
The title compound was synthesised according to General Procedure D stated above. Bis-phenylguanidinium carbonate **6a** (166 mg, 0.5 mmol), acetylacetone **13b** (46 μ L, 0.45 mmol), and K_2CO_3 (104 mg, 0.75 mmol) were milled using a Retsch MM500 Control at 30Hz at 70 $^{\circ}C$ for 2 h. The resulting reaction mixture was filtered through celite with 20 mL of EtOAc, and the filtrate was concentrated to afford 4,6-dimethyl-*N*-phenylpyrimidin-2-amine **14b** as a white solid (67 mg, 75%).

1H NMR (600 MHz, $CDCl_3$): δ 7.69 – 7.67 (m, 2H), 7.46 (bs, 1H), 7.33 – 7.30 (m, 2H), 7.00 (tt, $J = 7.3, 1.1$ Hz, 1H), 6.48 (s, 1H), 2.37 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 167.6, 159.9, 140.1, 128.9, 128.8, 122.0, 118.9, 111.6, 23.9.

The spectroscopic data closely match those previously reported in the literature.²

***N*-(4-methoxyphenyl)-4,6-dimethylpyrimidin-2-amine 14c:** (From guanidinium carbonate salt)



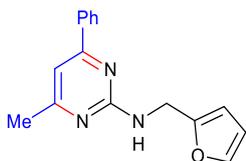
The title compound was synthesised according to General Procedure D stated above. Bis-1-(4-methoxyphenyl)guanidinium carbonate **6c** (196 mg, 0.5 mmol), acetylacetone **13b** (46 μ L, 0.45 mmol), and K_2CO_3 (104 mg, 0.75 mmol) were milled using a Retsch MM500 Control at 30Hz at 70 $^{\circ}C$ for 2 h. The resulting reaction mixture was filtered through celite with 20 mL of EtOAc, and the filtrate was concentrated to afford *N*-(4-methoxyphenyl)-4,6-dimethylpyrimidin-2-amine **14c** as a white solid (48 mg, 52%).

1H NMR (600 MHz, $CDCl_3$): δ 7.55 – 7.53 (m, 2H), 7.20 (bs, 1H), 6.87 – 6.86 (m, 2H), 6.43 (s, 1H), 3.78 (s, 3H), 2.33 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 167.6, 160.1, 155.2, 133.3, 121.0, 121.0, 114.2, 111.2, 55.6, 24.0.

The spectroscopic data closely match those previously reported in the literature.²

***N*-(furan-2-ylmethyl)-4-methyl-6-phenylpyrimidin-2-amine 14d:** (From guanidinium picrate salt)



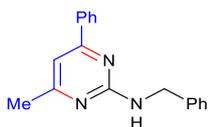
The title compound was synthesised according to General Procedure D stated above. 1-(furan-2-ylmethyl)guanidinium 2,4,6-trinitrophenolate **5h** (184 mg, 0.5 mmol), 1-phenylbutane-1,3-dione **13a** (68 μ L, 0.45 mmol), and K_2CO_3 (104 mg, 0.75 mmol) were milled using a Retsch MM500 Control at 30Hz at 70 $^{\circ}C$ for 2 h. The resulting reaction mixture was filtered through celite with 20 mL of EtOAc, and the filtrate was concentrated to afford *N*-(furan-2-ylmethyl)-4-methyl-6-phenylpyrimidin-2-amine **14d** as a brown sticky solid (95 mg, 79%).

1H NMR (600 MHz, $CDCl_3$): δ 8.04 (dd, $J = 6.7, 3.1$ Hz, 2H), 7.47 – 7.45 (m, 3H), 7.36 (dd, $J = 1.9, 0.8$ Hz, 1H), 6.92 (s, 1H), 6.31 (dd, $J = 3.2, 1.9$ Hz, 1H), 6.28 – 6.27 (m, 1H), 5.55 (s, 1H), 4.74 (d, $J = 5.8$ Hz, 2H), 2.42 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 168.3, 164.9, 162.1, 152.9, 142.0, 137.7, 130.5, 128.8, 127.2, 110.5, 106.9, 106.8, 38.8, 24.3.

The spectroscopic data closely match those previously reported in the literature.²

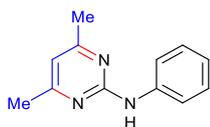
***N*-benzyl-4-methyl-6-phenylpyrimidin-2-amine 14a:** (From guanidinium picrate salt)



The title compound was synthesised according to General Procedure D stated above. 1-benzylguanidinium 2,4,6-trinitrophenolate **5bb** (185 mg, 0.5 mmol), 1-phenylbutane-1,3-dione **13a** (68 μ L, 0.45 mmol), and K_2CO_3 (104 mg, 0.75 mmol) were milled using a Retsch MM500 Control at 30Hz at 70 $^{\circ}C$ for 2 h. The resulting reaction mixture was filtered through celite with 20 mL of EtOAc, and the filtrate was concentrated to afford *N*-benzyl-4-methyl-6-phenylpyrimidin-2-amine **14a** as a white solid (91 mg, 73%).

Note: For data, please see above **14a**, which was prepared from a guanidinium carbonate salt.

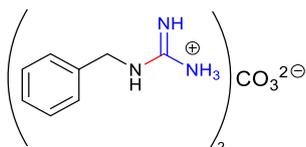
4,6-dimethyl-N-phenylpyrimidin-2-amine 14b: (From guanidinium picrate salt)



The title compound was synthesised according to General Procedure D stated above. 1-phenylguanidinium 2,4,6-trinitrophenolate **5a** (182 mg, 0.5 mmol), acetylacetone **13b** (46 μ L, 0.45 mmol), and K_2CO_3 (104 mg, 0.75 mmol) were milled using a Retsch MM500 Control at 30Hz at 70 $^\circ$ C for 2 h. The resulting reaction mixture was filtered through celite with 20 mL of EtOAc, and the filtrate was concentrated to afford N-benzyl-4-methyl-6-phenylpyrimidin-2-amine **14a** as a brown sticky solid (67 mg, 74%).

Note: For data, please see above **14b**, which was prepared from guanidinium carbonate salt.

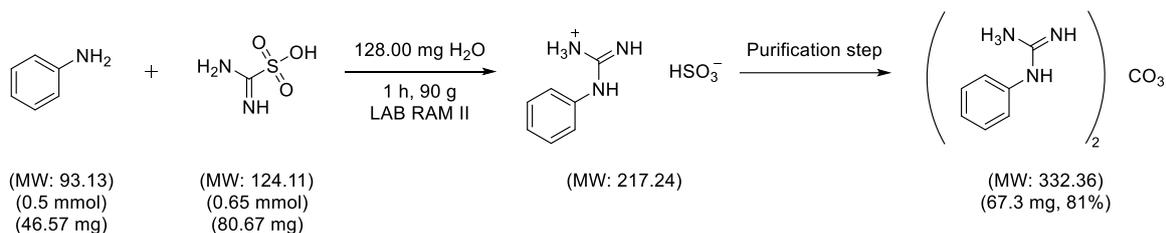
Gram Scale Synthesis: Bis-1-benzylguanidinium carbonate 7a



A 10 ml glass vial was filled with amine **2a** (10 mmol), thiourea trioxide (13 mmol), and 2.6 mL of distilled water. The vial was closed, and the reaction was run for 1 hour at 90 g using LabRAM II. At the end of the reaction, the mixture was transferred to a 30 mL vial, using a minimal amount of water (approximately 1-2 mL). Then, 20 mL of a saturated aqueous Na_2CO_3 solution followed by 1.6 mL of concentrated HCl (2 equiv.) in the sealed vial was added to retain the generated carbon dioxide. The reaction mixture was then stirred for 4-5 hours. The resulting solid was filtered and washed with 15-20 mL of water, then rinsed with 4-5 mL of acetone and dried on filter paper under an IR lamp, affording guanidine carbonates **7a** as a white solid (1.24g, 67%).

Green Chemistry Metrics Calculation

Calculation of the Green Chemistry Metrics for the Preparation of **6a** using RAM:



| | | | | | |
|--------------------------------|--------------------------------|--|-----------|--|-------------------------------|
| Excess Reagents Waste | TTO | | | | |
| | | 18.62 mg | | | |
| Reaction Waste | H ₂ SO ₃ | | | | |
| | | 40.99 mg | | | |
| Purification Step Waste | H ₂ O for recovery | Na ₂ CO ₃ sat. aq. | HCl conc. | H ₂ O for washing the solid | Acetone for washing the solid |
| | 400.00 mg | 1000.00 mg + 340.70 mg | 98.54 mg | 3000.00 mg | 392.25 mg |

Scheme S1. Preparation of **6a** under RAM conditions.

Calculation of Green Chemistry Metrics

Atom Economy (AE)

$$\frac{\text{Mass of desired useful product}}{\text{Total Mass of all reactants}} \times 100 = \frac{217.24}{93.13 + 124.11} \times 100 = 100\%$$

Process Mass Intensity (PMI)

$$\frac{\text{Mass of total waste}}{\text{Mass of desired product}} = \frac{18.62 + 40.99 + 128.00 + 400.00 + 1000.00 + 340.70 + 98.54 + 3000.00 + 392.25}{67.30} = 65.7$$

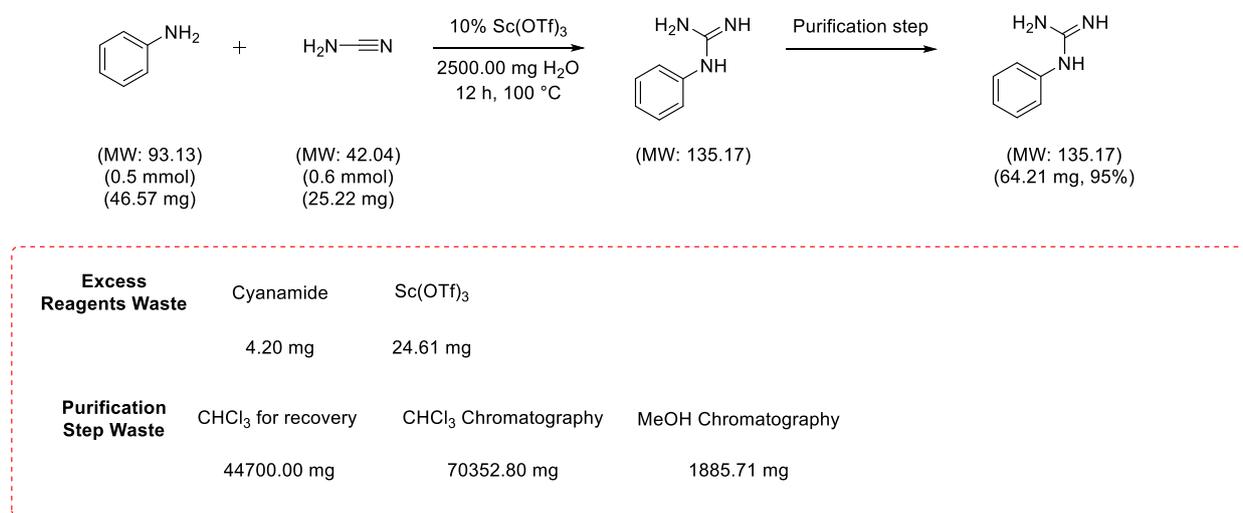
Environmental Factor (EF)

$$\frac{\text{Mass of total waste (no water considered)}}{\text{Mass of desired product}} = \frac{18.62 + 40.99 + 128.00 + 340.70 + 98.54 + 392.25}{67.30} = 15.1$$

Reaction Mass Efficiency (RME)

$$\frac{\text{Actual mass of desired product}}{\text{Mass of reactants}} \times 100 = \frac{67.30}{46.57 + 80.67 + 340.70 + 98.54} \times 100 = 12\%$$

Calculation of the Green Chemistry Metrics for the Preparation of **6a** using a solution approach reported in the literature:³



Scheme S2. Preparation of **6a** in solution.³ For the purification by silica pad, the eluent volume (Chloroform/Methanol 20:1) was not reported; therefore, a value of 50 mL was assumed for the calculations.

Calculation of Green Chemistry Metrics

Atom Economy (AE)

$$\frac{\text{Mass of desired useful product}}{\text{Total Mass of all reactants}} \times 100 = \frac{135.17}{93.13 + 42.04} \times 100 = 100\%$$

Process Mass Intensity (PMI)

$$\frac{\text{Mass of total waste}}{\text{Mass of desired product}} = \frac{4.20 + 24.61 + 2500.00 + 44700.00 + 70352.80 + 1885.71}{64.21} = 1860.6$$

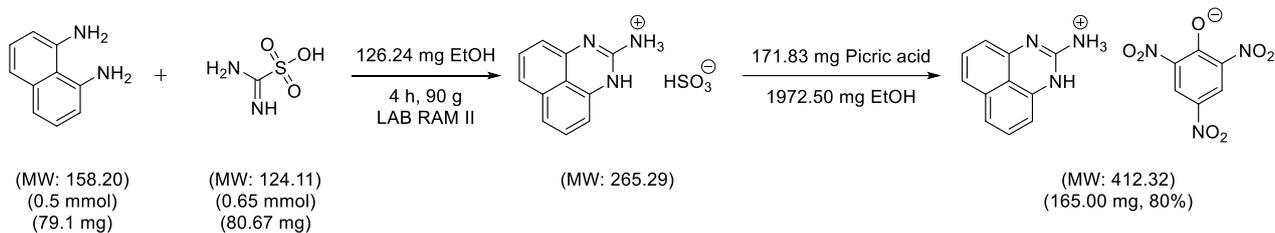
Environmental Factor (EF)

$$\frac{\text{Mass of total waste (no water considered)}}{\text{Mass of desired product}} = \frac{4.20 + 24.61 + 2500.00 + 44700.00 + 70352.80 + 1885.71}{64.21} = 1860.6$$

Reaction Mass Efficiency (RME)

$$\frac{\text{Actual mass of desired product}}{\text{Mass of reactants}} \times 100 = \frac{64.21}{46.57 + 25.22 + 24.61} \times 100 = 67\%$$

Calculation of the Green Chemistry Metrics for the Preparation of **12a** using RAM:



| | | | |
|--------------------------------|--------------------------------|-----------------|-------------------|
| Excess Reagents Waste | TTO | | |
| | 18.62 mg | | |
| Reaction Waste | H ₂ SO ₃ | NH ₃ | EtOH for reaction |
| | 40.99 mg | 8.52 mg | 126.24 mg |
| Purification Step Waste | EtOH for salt formation | | Picric acid |
| | 1972.50 mg | | 57.33 mg |

Scheme S3. Preparation of **12a** under RAM conditions.

Calculation of Green Chemistry Metrics

Atom Economy (AE)

$$\frac{\text{Mass of desired useful product}}{\text{Total Mass of all reactants}} \times 100 = \frac{265.29}{158.20 + 124.11} \times 100 = 94\%$$

Process Mass Intensity (PMI)

$$\frac{\text{Mass of total waste}}{\text{Mass of desired product}} = \frac{18.62 + 40.99 + 8.52 + 126.24 + 1972.50 + 57.33}{165.00} = 13.5$$

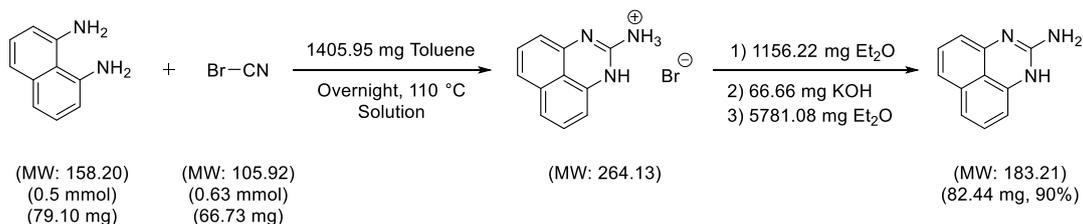
Environmental Factor (EF)

$$\frac{\text{Mass of total waste (no water considered)}}{\text{Mass of desired product}} = \frac{18.62 + 40.99 + 8.52 + 126.24 + 1972.50 + 57.33}{165.00} = 13.5$$

Reaction Mass Efficiency (RME)

$$\frac{\text{Actual mass of desired product}}{\text{Mass of reactants}} \times 100 = \frac{165.00}{79.1 + 80.67 + 171.63} \times 100 = 50\%$$

Calculation of the Green Chemistry Metrics for the Preparation of **12a** using a solution approach reported in the literature:⁴



| | | | | |
|--------------------------------|-------------------------------|----------|----------|-------------------------------|
| Excess Reagents Waste | BrCN | | | |
| | 13.77 mg | | | |
| Reaction Waste | Toluene for reaction | | | |
| | 1405.95 mg | | | |
| Purification Step Waste | Et ₂ O for washing | KBr | KOH | Et ₂ O for washing |
| | 1156.22 mg | 53.55 mg | 41.41 mg | 5781.08 mg |

Scheme S4. Preparation of **12a** in solution.⁴ The calculations were made by considering the process reported on a 0.5 mmol scale for a better comparison with the RAM protocol. The amount of water used for dissolving KOH and the quantity of Na₂SO₄ used for drying were not considered due to the absence of data.

Calculation of Green Chemistry Metrics

Atom Economy (AE)

$$\frac{\text{Mass of desired useful product}}{\text{Total Mass of all reactants}} \times 100 = \frac{264.13}{158.20 + 105.92} \times 100 = 100\%$$

Process Mass Intensity (PMI)

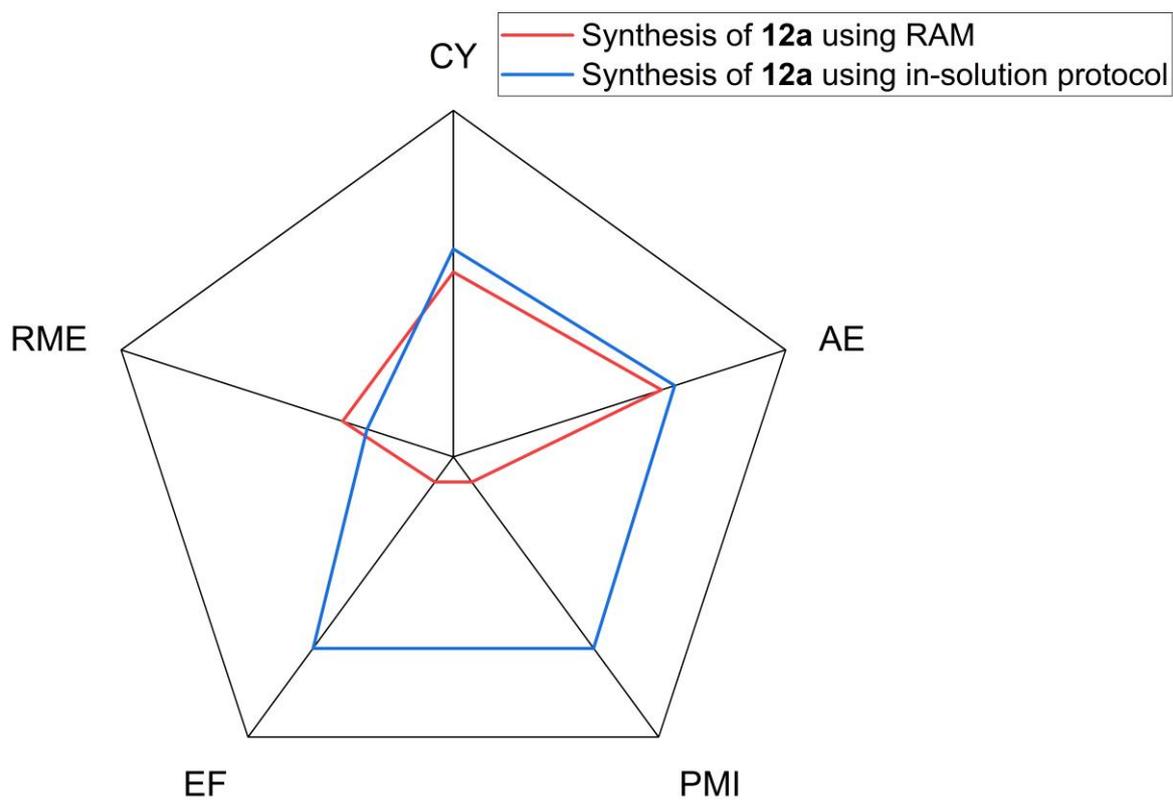
$$\frac{\text{Mass of total waste}}{\text{Mass of desired product}} = \frac{13.77 + 1405.95 + 1156.22 + 53.55 + 41.41 + 5781.08}{82.44} = 102.5$$

Process Mass Intensity (PMI)

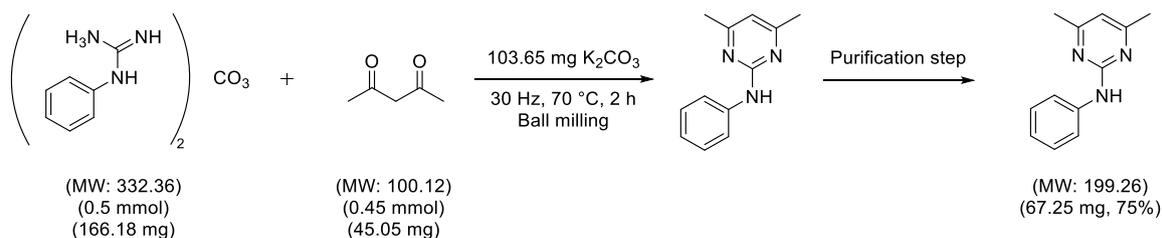
$$\frac{\text{Mass of total waste (no water considered)}}{\text{Mass of desired product}} = \frac{13.77 + 1405.95 + 1156.22 + 53.55 + 41.41 + 5781.08}{82.44} = 102.5$$

Reaction Mass Efficiency (RME)

$$\frac{\text{Actual mass of desired product}}{\text{Mass of reactants}} \times 100 = \frac{82.44}{79.10 + 66.73 + 66.66} \times 100 = 39\%$$



Calculation of the Green Chemistry Metrics for the Preparation of **14b** using ball-milling:



| | | | |
|--------------------------------|--|--------------------------------|--|
| Excess Reagents Waste | Bis-phenylguanidinium carbonate | | |
| | 91.40 mg | | |
| Reaction Waste | K ₂ CO ₃ unreacted | H ₂ CO ₃ | K ₂ CO ₃ generated |
| | 34.55 mg | 31.01 mg | 69.1 mg |
| Purification Step Waste | EtOAc for recovery | | |
| | 18040.00 mg | | |

Scheme S5. Preparation of **14b** under RAM conditions.

Calculation of Green Chemistry Metrics

Atom Economy (AE)

$$\frac{\text{Mass of desired useful product}}{\text{Total Mass of all reactants}} \times 100 = \frac{199.26}{332.36 + 100.12} \times 100 = 46\%$$

Process Mass Intensity (PMI)

$$\frac{\text{Mass of total waste}}{\text{Mass of desired product}} = \frac{91.40 + 34.55 + 31.01 + 69.10 + 18040.00}{67.25} = 271.6$$

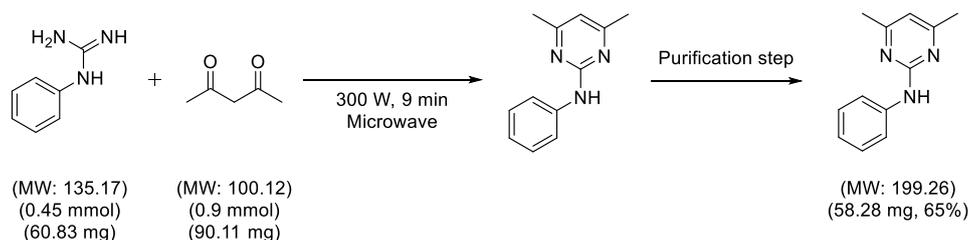
Environmental Factor (EF)

$$\frac{\text{Mass of total waste (no water considered)}}{\text{Mass of desired product}} = \frac{91.40 + 34.55 + 31.01 + 69.10 + 18040.00}{67.25} = 271.6$$

Reaction Mass Efficiency (RME)

$$\frac{\text{Actual mass of desired product}}{\text{Mass of reactants}} \times 100 = \frac{67.25}{166.18 + 45.05 + 103.65} \times 100 = 21\%$$

Calculation of the Green Chemistry Metrics for the Preparation of **14b** using a solution approach reported in the literature:²



| | | |
|--------------------------------|--------------------------|------------------------------------|
| Excess Reagents Waste | Acetylacetone | |
| | | 45.05 mg |
| Reaction Waste | Water | |
| | | 5.27 mg |
| Purification Step Waste | EtOAc for chromatography | Petroleum Ether for chromatography |
| | 4100.00 mg | 30045.45 mg |

Scheme S6. Preparation of **14b** in solution.² For the purification by chromatography, the eluent volume (Petroleum Ether/Ethyl acetate 10:1) was not reported; therefore, a value of 50 mL was assumed for the calculations. The amount of water and chloroform used for recovering and washing were not taken into account because no data were reported about the quantities used.

Calculation of Green Chemistry Metrics

Atom Economy (AE)

$$\frac{\text{Mass of desired useful product}}{\text{Total Mass of all reactants}} \times 100 = \frac{199.26}{135.17 + 100.12} \times 100 = 85\%$$

Process Mass Intensity (PMI)

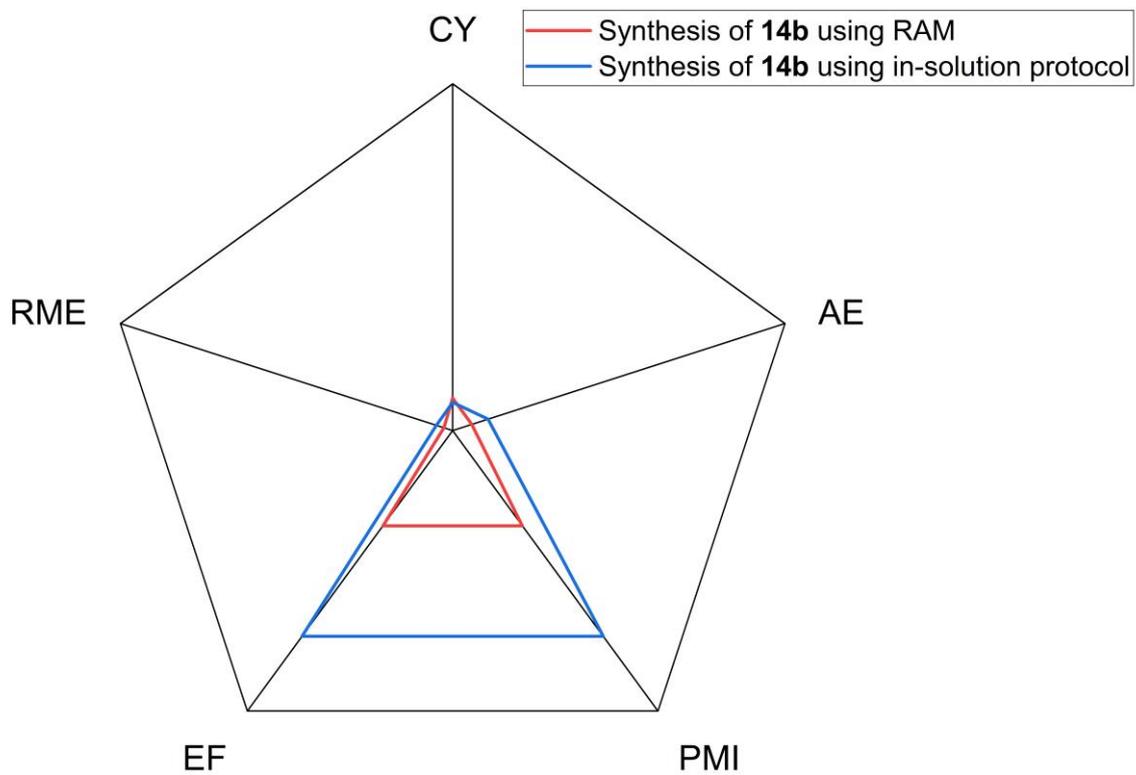
$$\frac{\text{Mass of total waste}}{\text{Mass of desired product}} = \frac{45.05 + 5.27 + 4100.00 + 30045.45}{58.28} = 586.8$$

Environmental Factor (EF)

$$\frac{\text{Mass of total waste (no water considered)}}{\text{Mass of desired product}} = \frac{45.05 + 4100.00 + 30045.45}{58.28} = 586.7$$

Reaction Mass Efficiency (RME)

$$\frac{\text{Actual mass of desired product}}{\text{Mass of reactants}} \times 100 = \frac{58.28}{60.83 + 90.11} \times 100 = 39\%$$



Calculation of energy consumed

The amount of energy consumed using RAM was calculated and compared with the in-solution procedures reported for the calculation of green metrics. The calculation have been made by checking the power input of LabRAM II and a generic Heidolph stirring plate.

Based on the power inputs reported in the manual, a LabRAM II requires around 1.9 kW if considering a typical European 230 V main. This value can then be multiplied for the amount of time required for preparing the products **6a** (1 hour) and **12a** (4 hours) resulting in a consumption of 1.9 kWh and 7.6 kWh, respectively. These amounts can finally be multiplied for the average price of electricity in Italy which is approximately 0,25 € per hour leading to a final price of 0,48€ for product **6a** and 1,90 € for **12a**.

Similar calculations can be done taking as a reference a generic Heidolph stirring plate which, instead, requires a power input of around 0.83 kW if considering a typical European 230 V main. Despite being lower than the one requested by RAM, it has to be multiplied for the amount of time required for preparing the products **6a** (12 hour) and **12a** (12 hours) in solution. This results g in a total consumption of 9.96 kWh in both cases. This amount is then multiplied for the average price of electricity in Italy which is approximately 0,25 € per hour leading to a final price of 2,49€ for both **6a** and **12a**.

NMR Spectra

¹H NMR (600 MHz, DMSO-*d*₆)

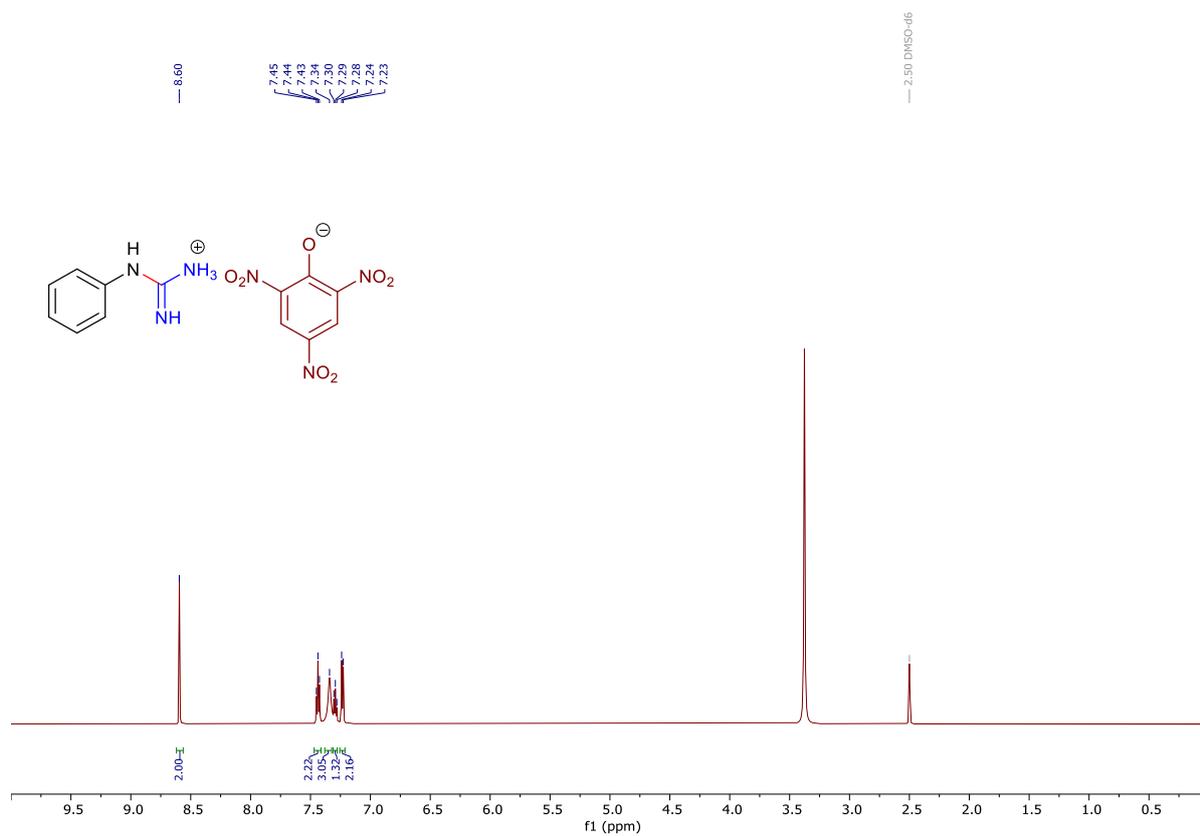


Figure 1a. ¹H NMR spectrum of 1-phenylguanidinium 2,4,6-trinitrophenolate (**5a**)

¹³C NMR (600 MHz, CDCl₃)

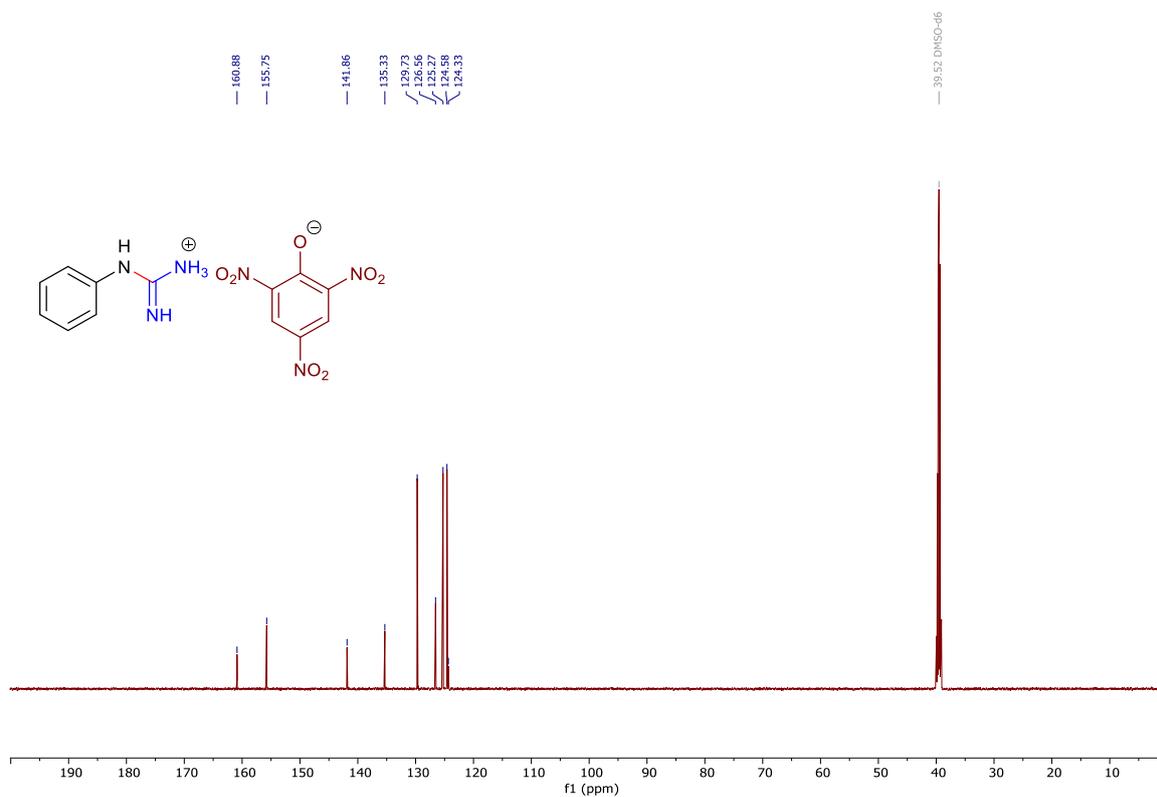


Figure 1b. ¹³C NMR spectrum of 1-phenylguanidinium 2,4,6-trinitrophenolate (**5a**)

¹H NMR (600 MHz, DMSO-*d*₆)

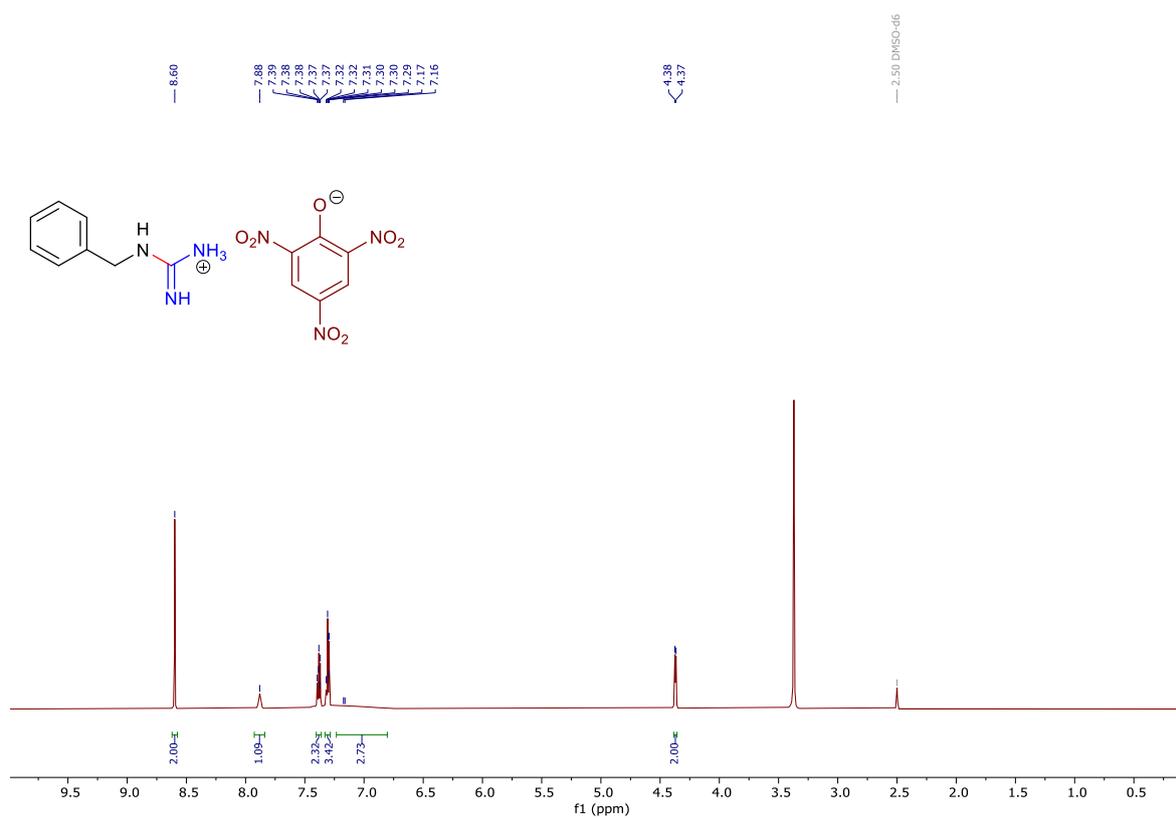


Figure 2a. ¹H NMR spectrum of 1-benzylguanidinium 2,4,6-trinitrophenolate (**5bb**)

¹³C NMR (151 MHz, DMSO-*d*₆)

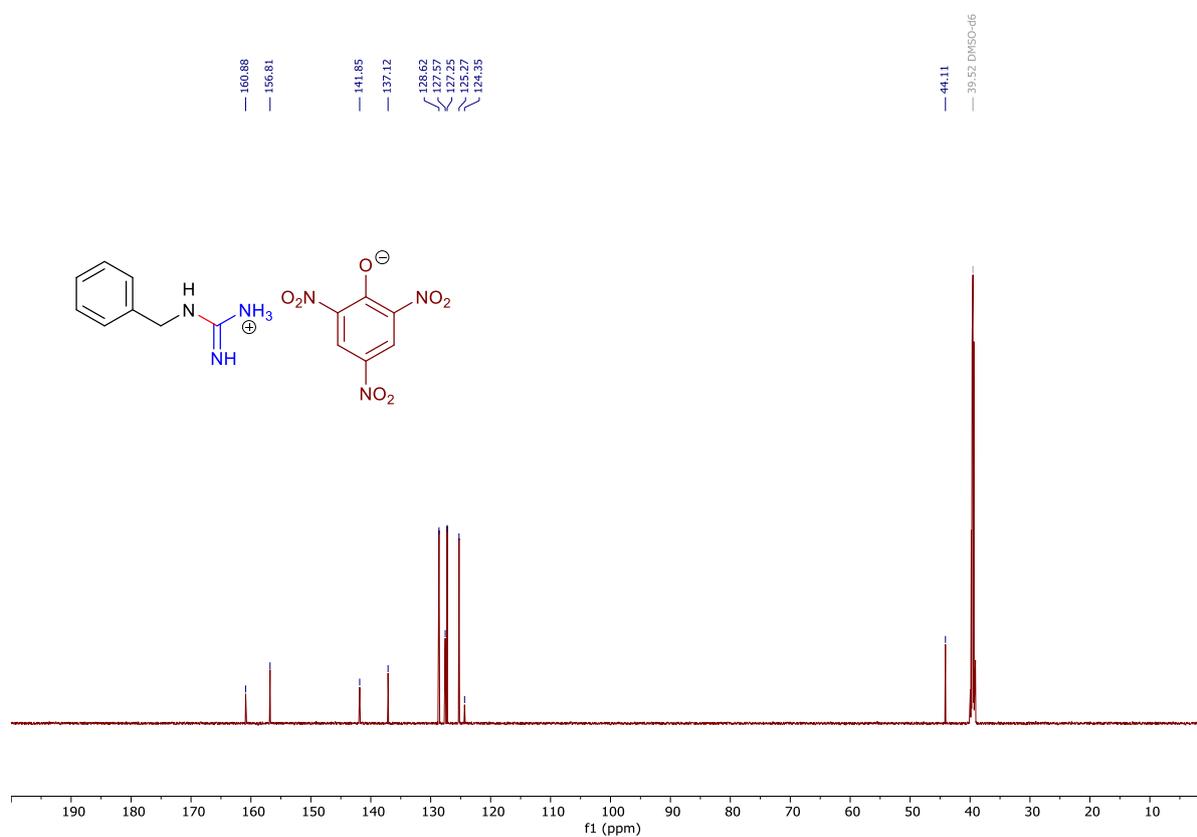


Figure 2b. ¹³C NMR spectrum of 1-benzylguanidinium 2,4,6-trinitrophenolate (**5bb**)

¹H NMR (600 MHz, DMSO-*d*₆)

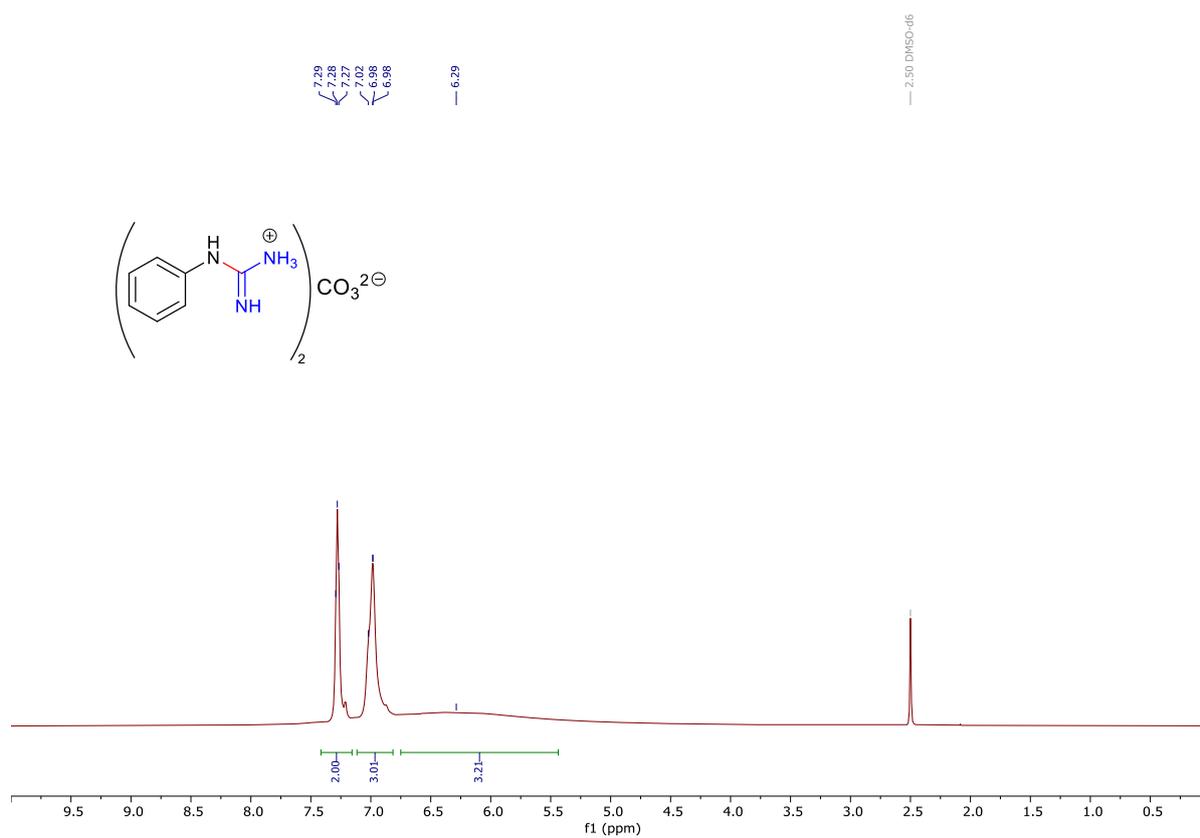


Figure 3a. ¹H NMR spectrum of bis-phenylguanidinium carbonate (**6a**)

¹³C NMR (151 MHz, DMSO-*d*₆)

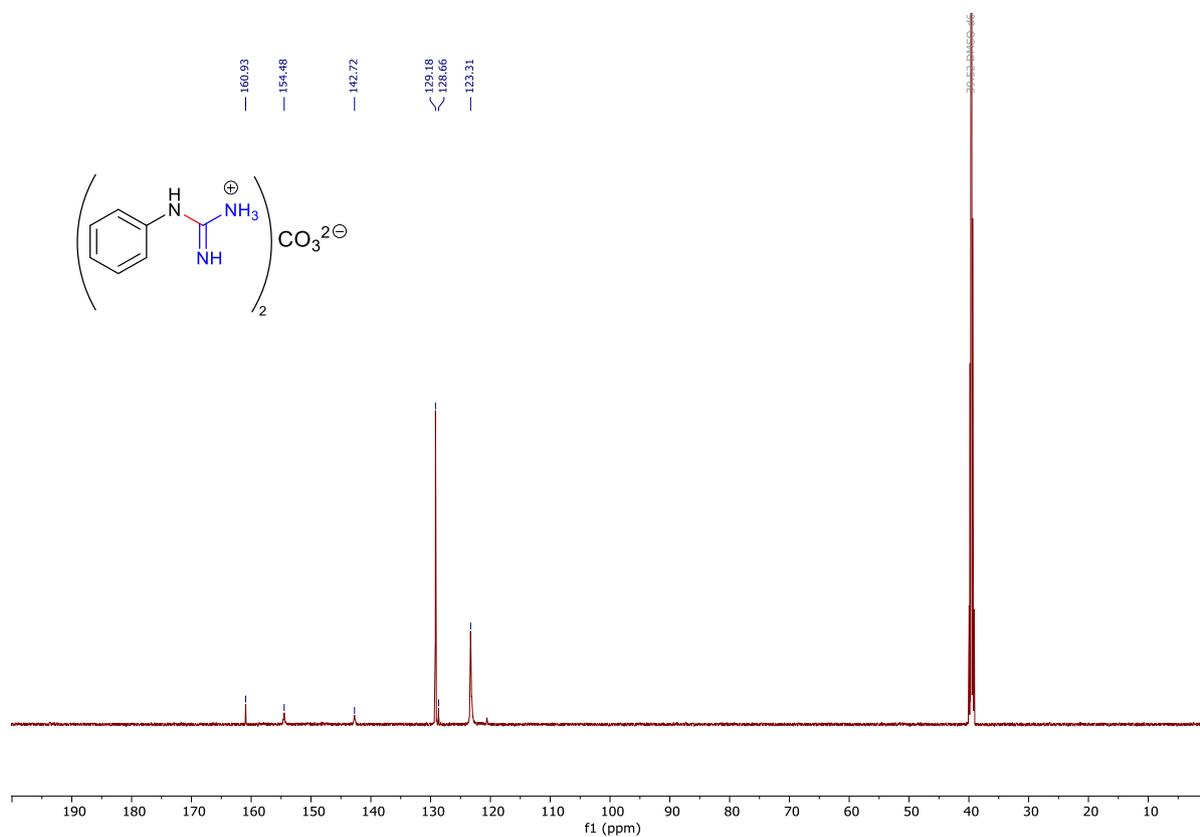


Figure 3b. ^{13}C NMR spectrum of bis-phenylguanidinium carbonate (**6a**)

^1H NMR (600 MHz, $\text{DMSO-}d_6$)

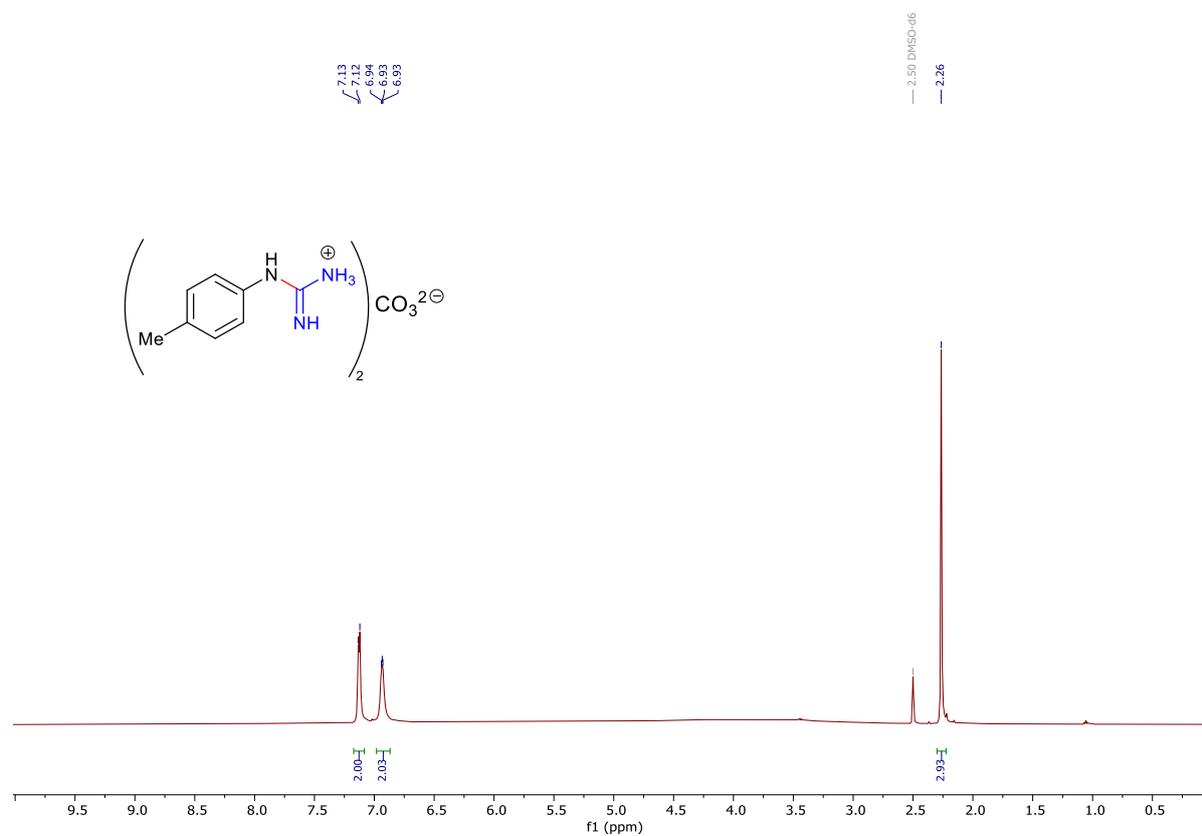


Figure 4a. ^1H NMR spectrum of bis-1-(p-tolyl)guanidinium carbonate (**6b**)

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$)

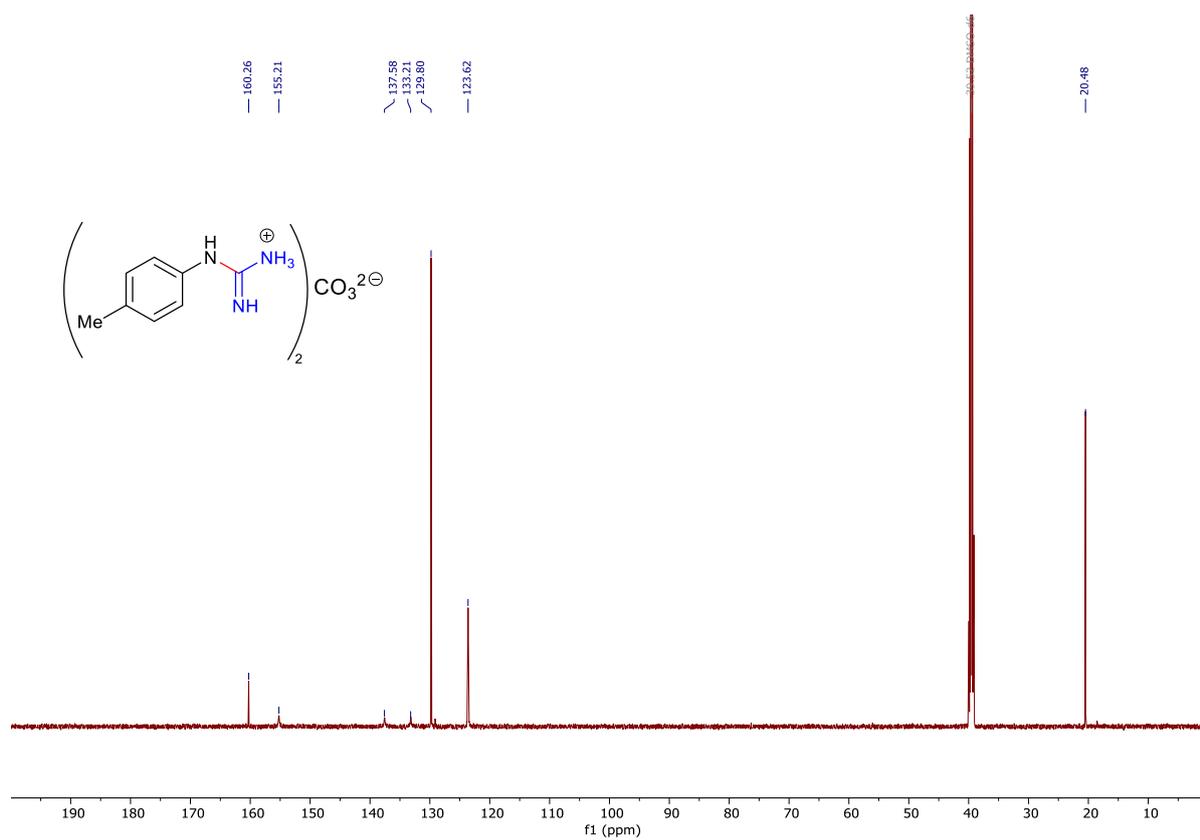


Figure 4b. ^{13}C NMR spectrum of bis-1-(p-tolyl)guanidinium carbonate (**6b**)

^1H NMR (600 MHz, $\text{DMSO-}d_6$)

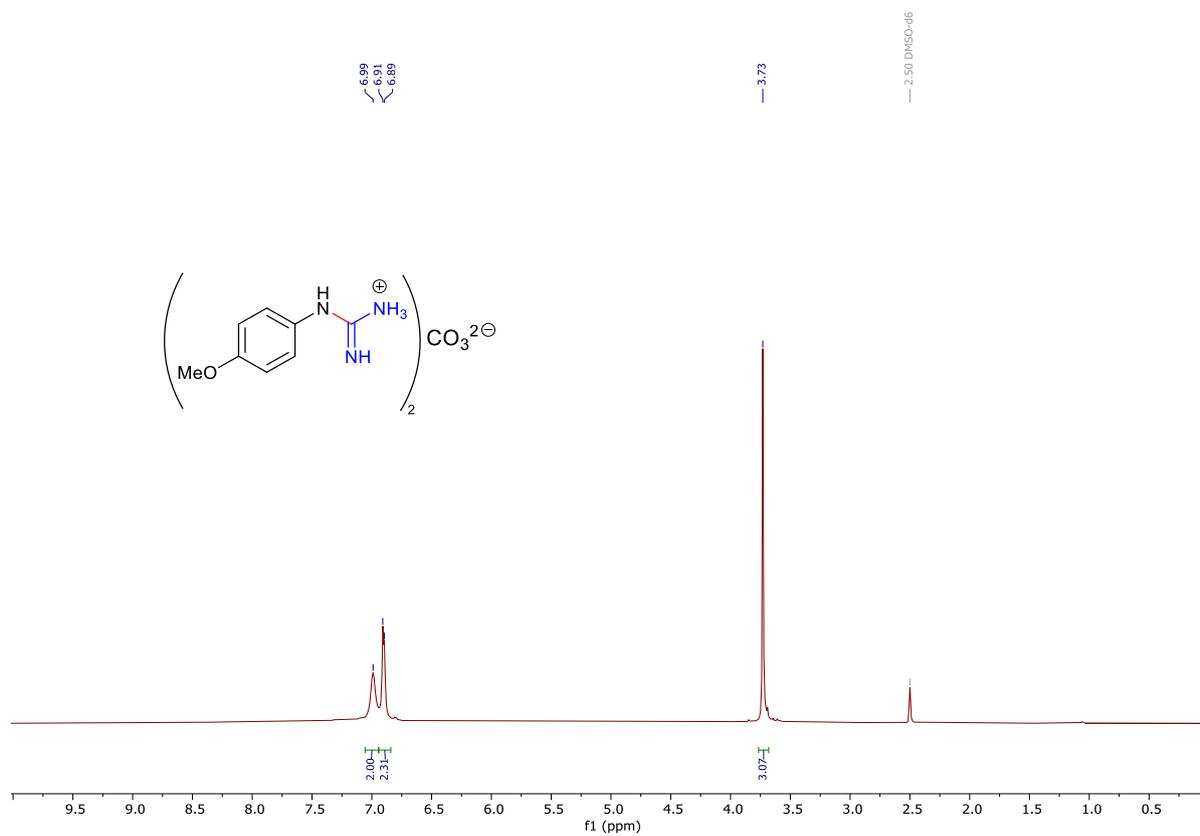


Figure 5a. ^1H NMR spectrum of bis-1-(4-methoxyphenyl)guanidinium carbonate (**6c**)

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$)

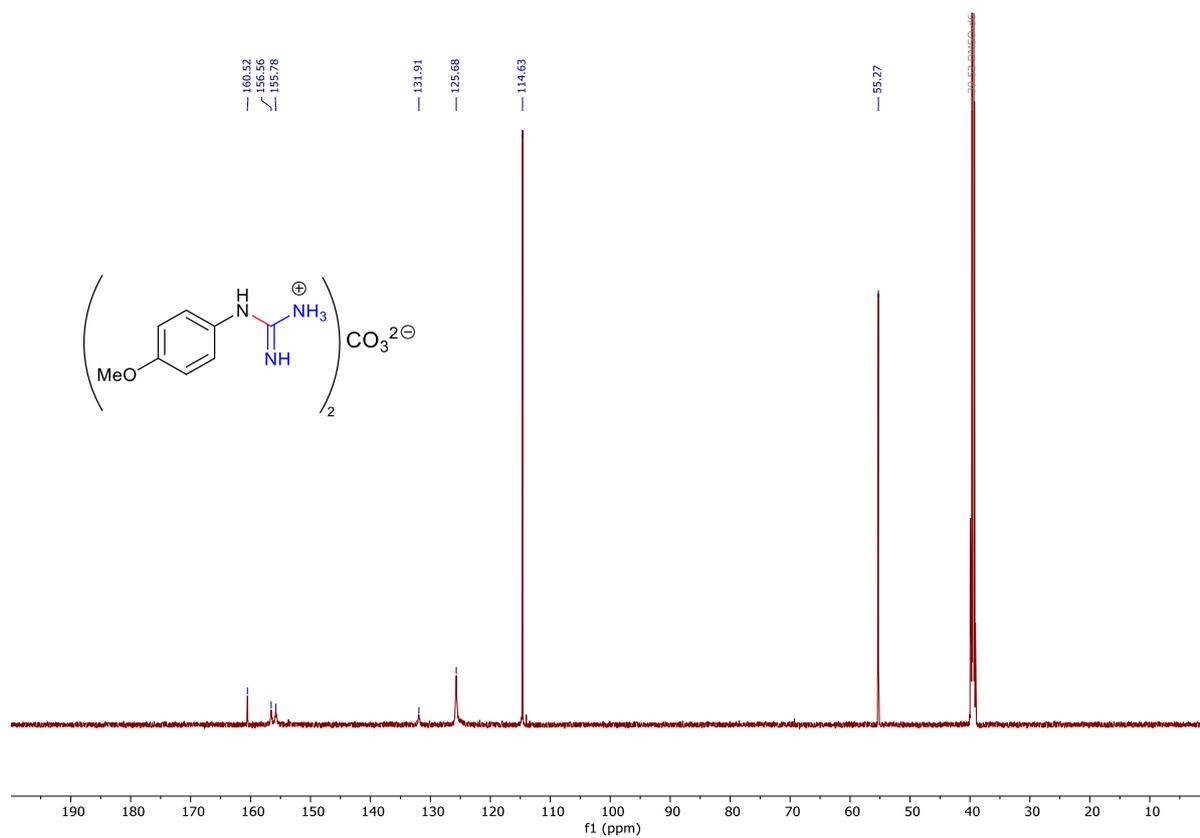


Figure 5b. ^{13}C NMR spectrum of bis-1-(4-methoxyphenyl)guanidinium carbonate (6c)

^1H NMR (600 MHz, $\text{DMSO-}d_6$)

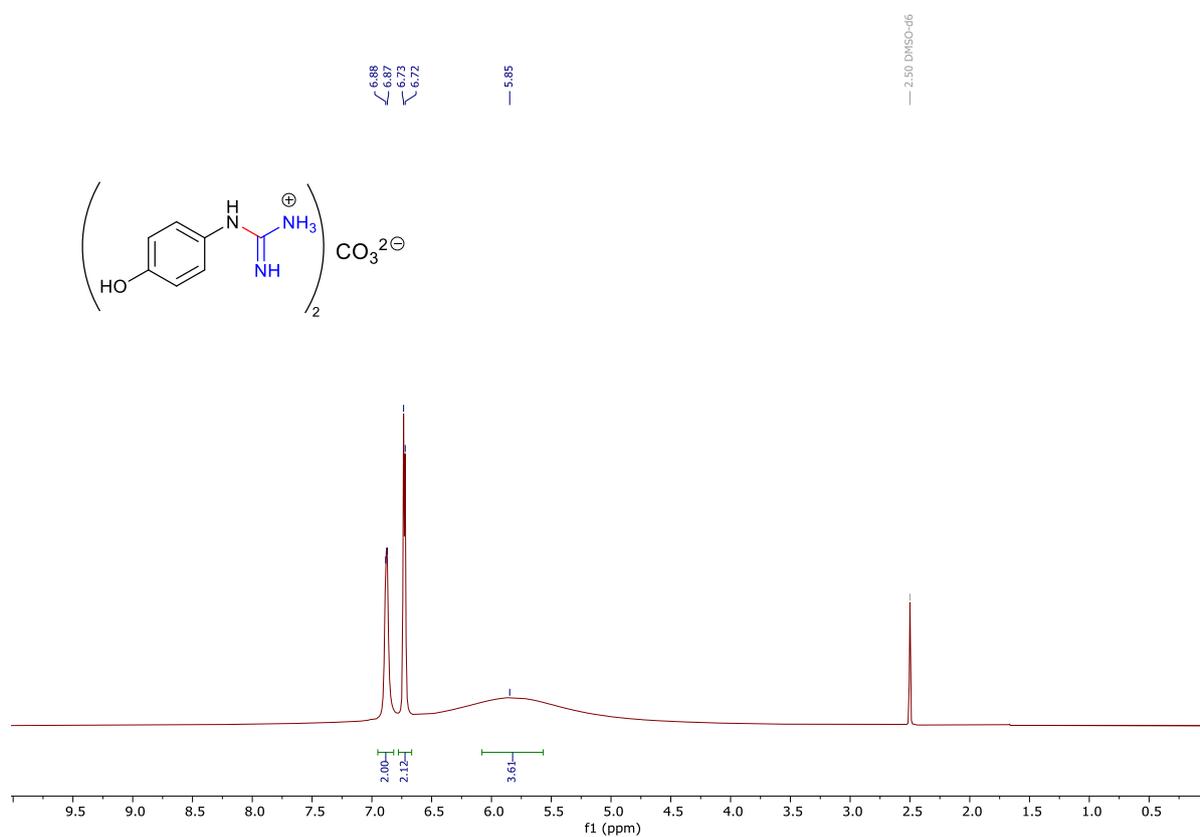


Figure 6a. ^1H NMR spectrum of bis-1-(4-hydroxyphenyl)guanidinium carbonate (**6d**)

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$)

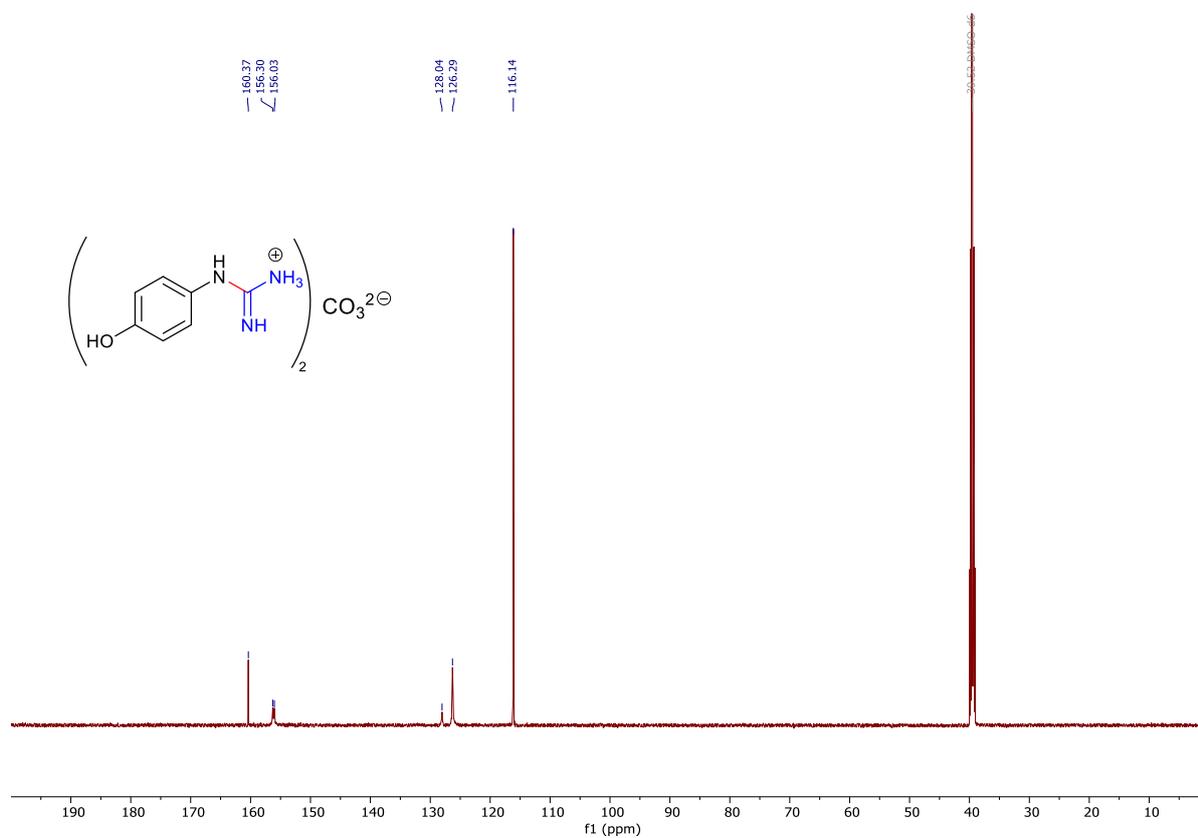


Figure 6b. ^{13}C NMR spectrum of bis-1-(4-hydroxyphenyl)guanidinium carbonate (**6d**)

^1H NMR (600 MHz, $\text{DMSO-}d_6$)

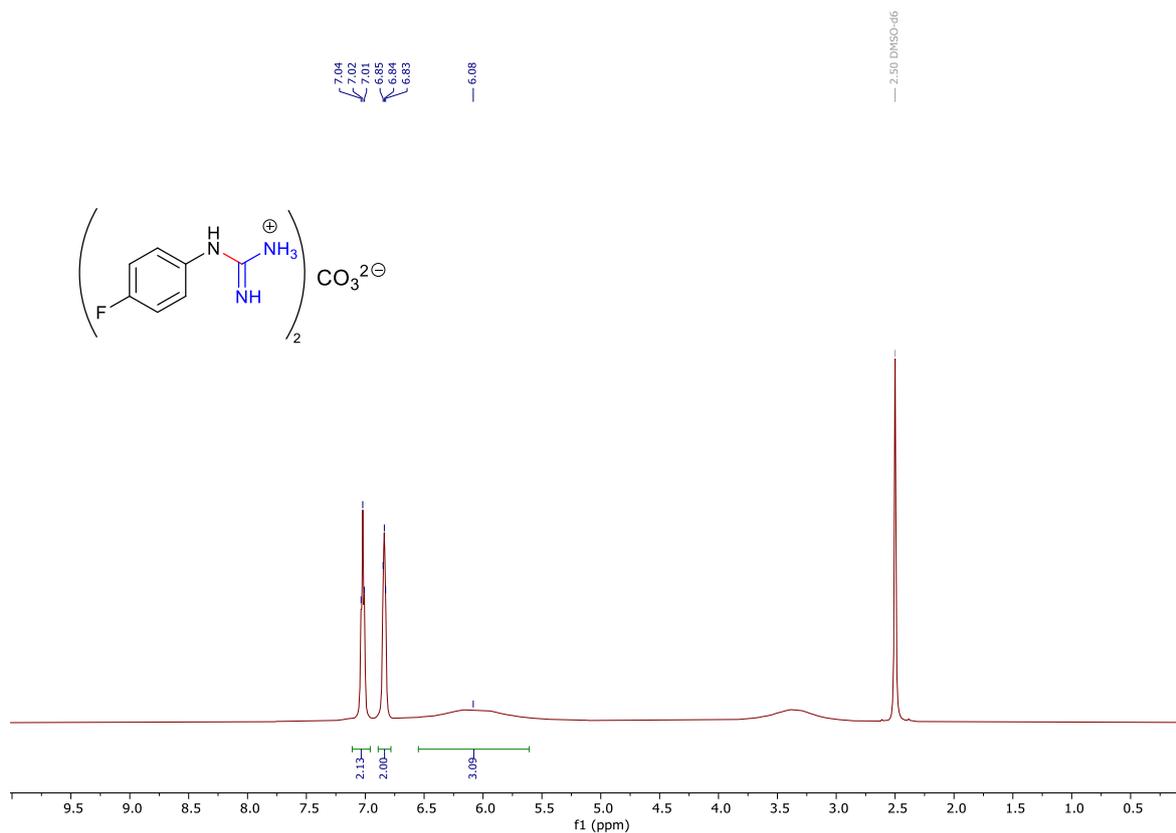


Figure 7a. ^1H NMR spectrum of bis-1-(4-fluorophenyl)guanidinium carbonate (6e)

^{13}C NMR (151 MHz, DMSO- d_6)

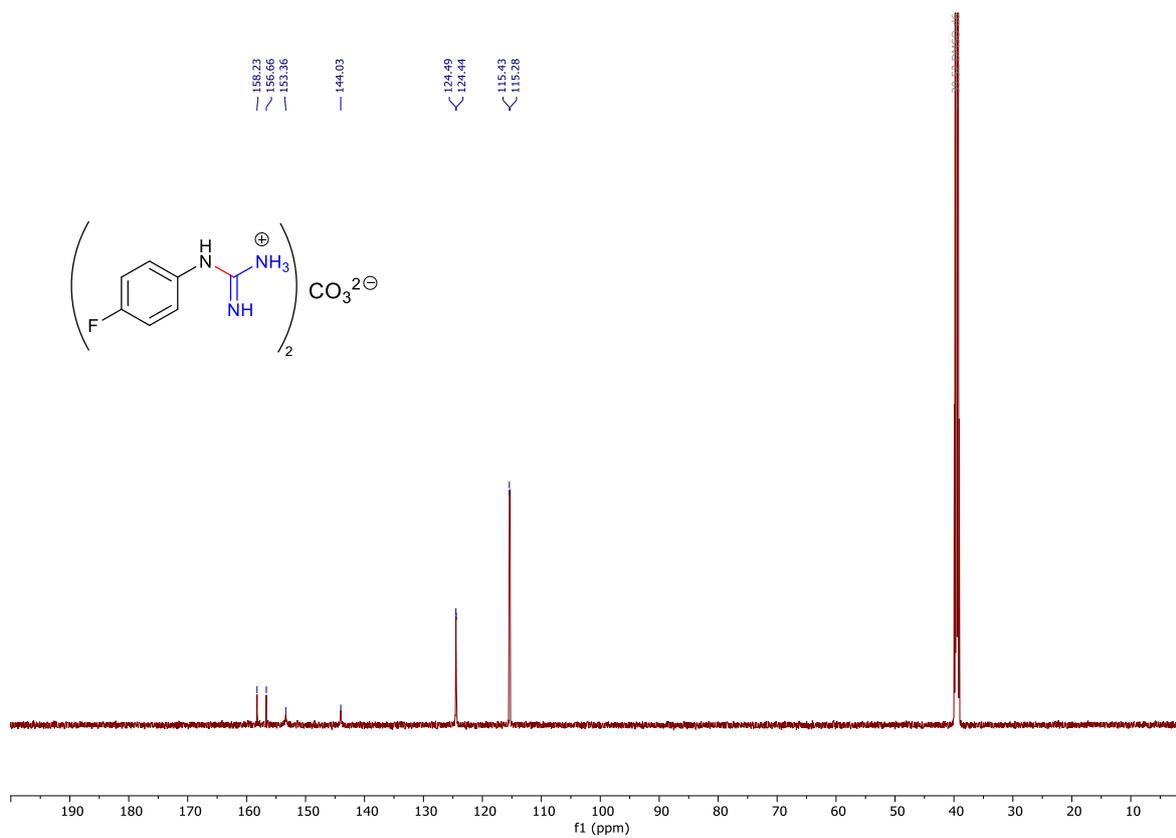


Figure 7b. ^{13}C NMR spectrum of bis-1-(4-fluorophenyl)guanidinium carbonate (6e)

^{19}F NMR (DMSO- d_6)

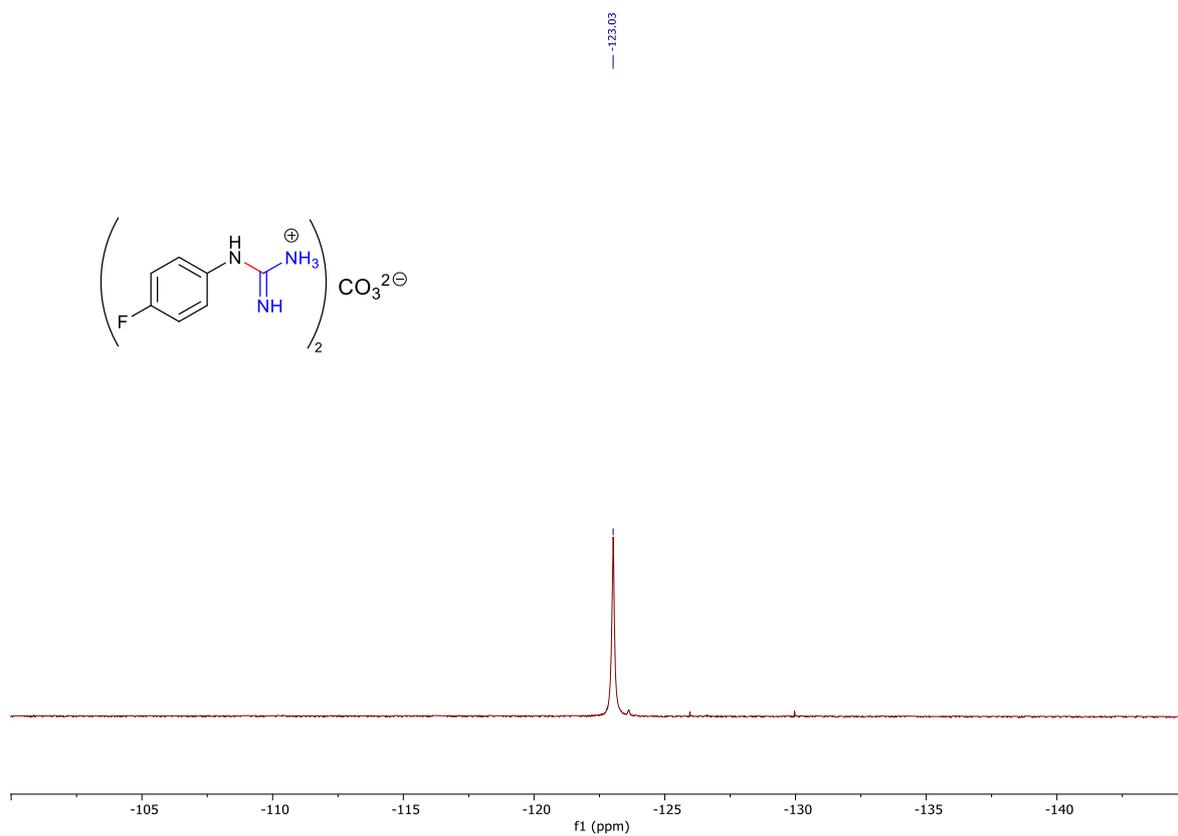


Figure 7c. ^{19}F NMR spectrum of bis-1-(4-fluorophenyl)guanidinium carbonate (**6e**)

¹H NMR (600 MHz, DMSO-*d*₆)

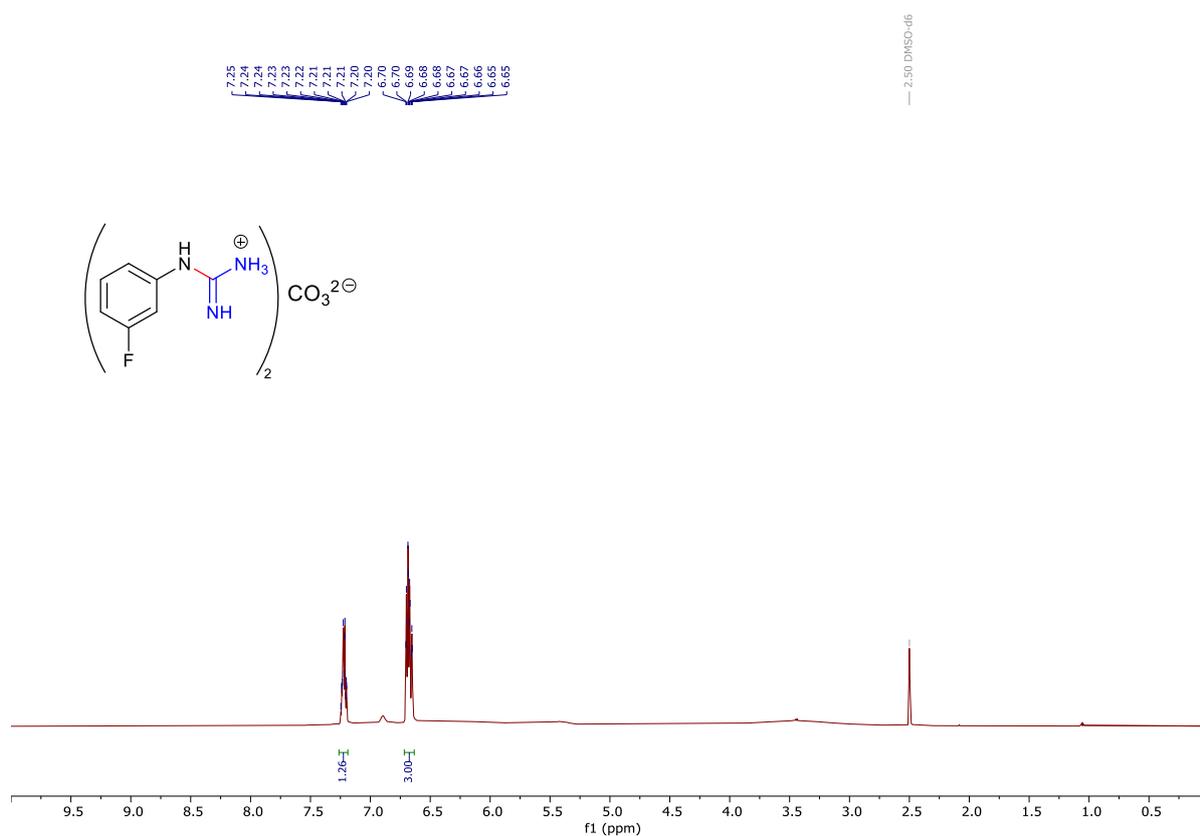


Figure 8a. ¹H NMR spectrum of bis-1-(3-fluorophenyl)guanidinium carbonate (**6f**)

¹³C NMR (151 MHz, DMSO-*d*₆)

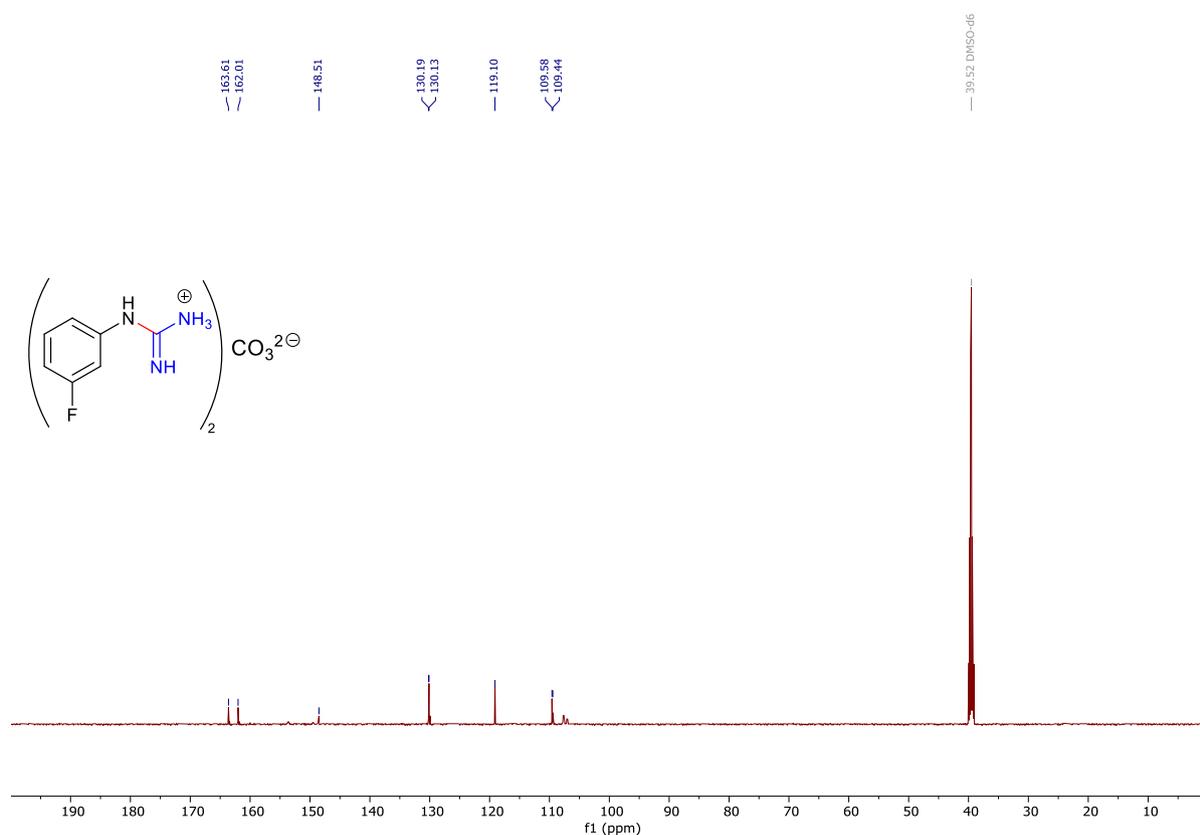


Figure 8b. ^{13}C NMR spectrum of bis-1-(3-fluorophenyl)guanidinium carbonate (**6f**)

^{19}F NMR (DMSO- d_6)

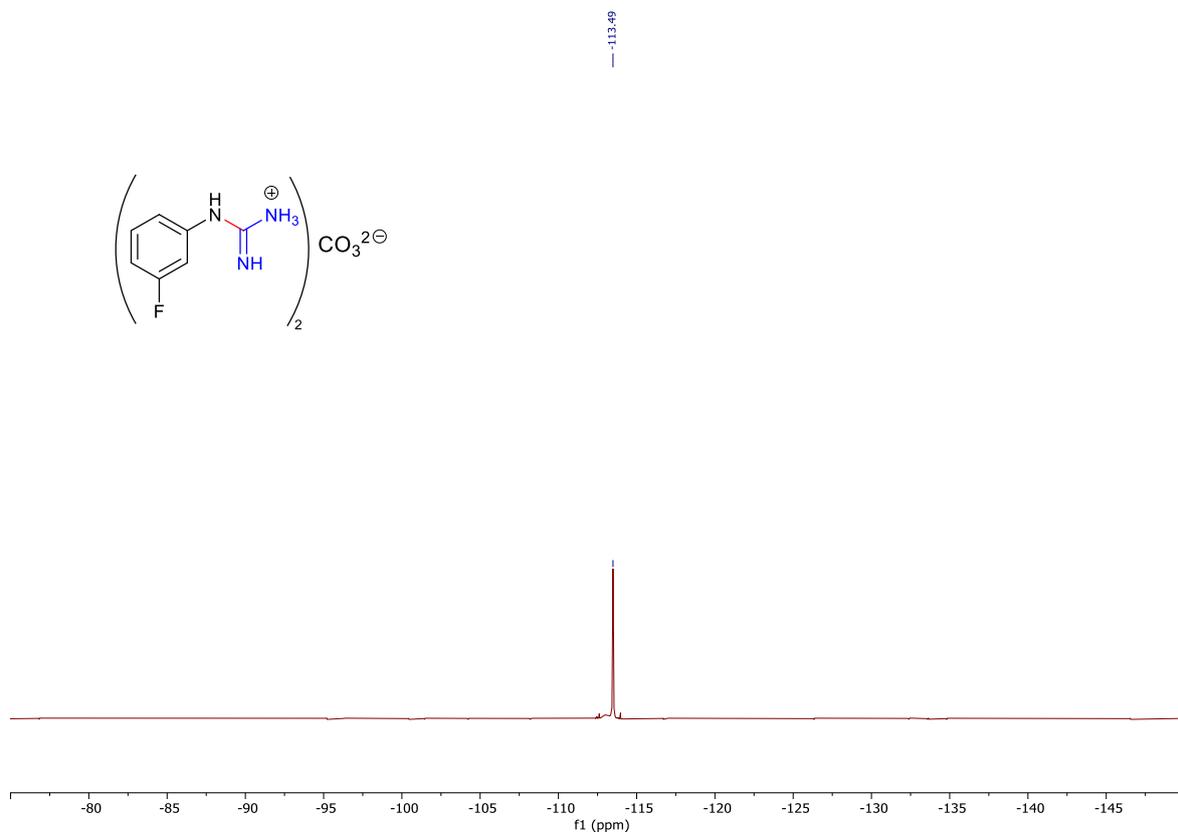


Figure 8c. ^{19}F NMR spectrum of bis-1-(3-fluorophenyl)guanidinium carbonate (**6f**)

¹H NMR (600 MHz, DMSO-*d*₆)

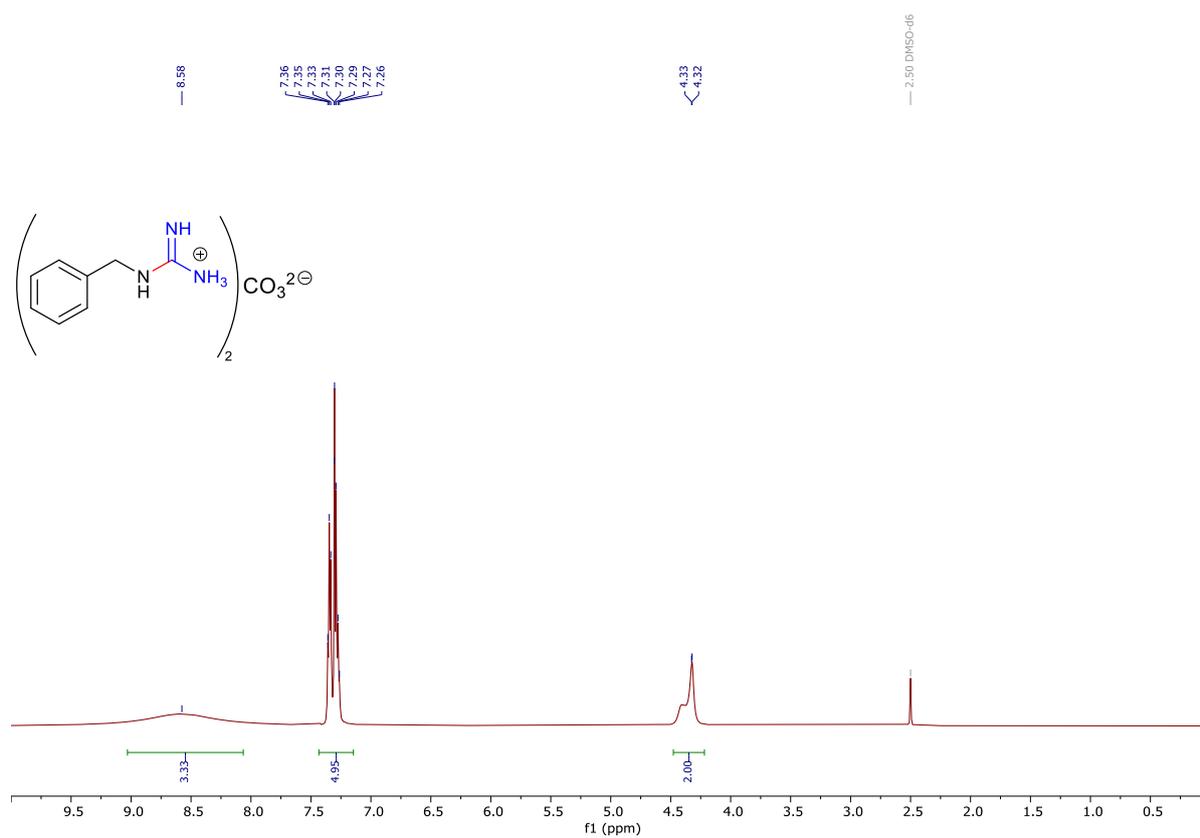


Figure 9a. ¹H NMR spectrum of bis-1-benzylguanidinium carbonate (**7a**)

¹³C NMR (151 MHz, DMSO-*d*₆)

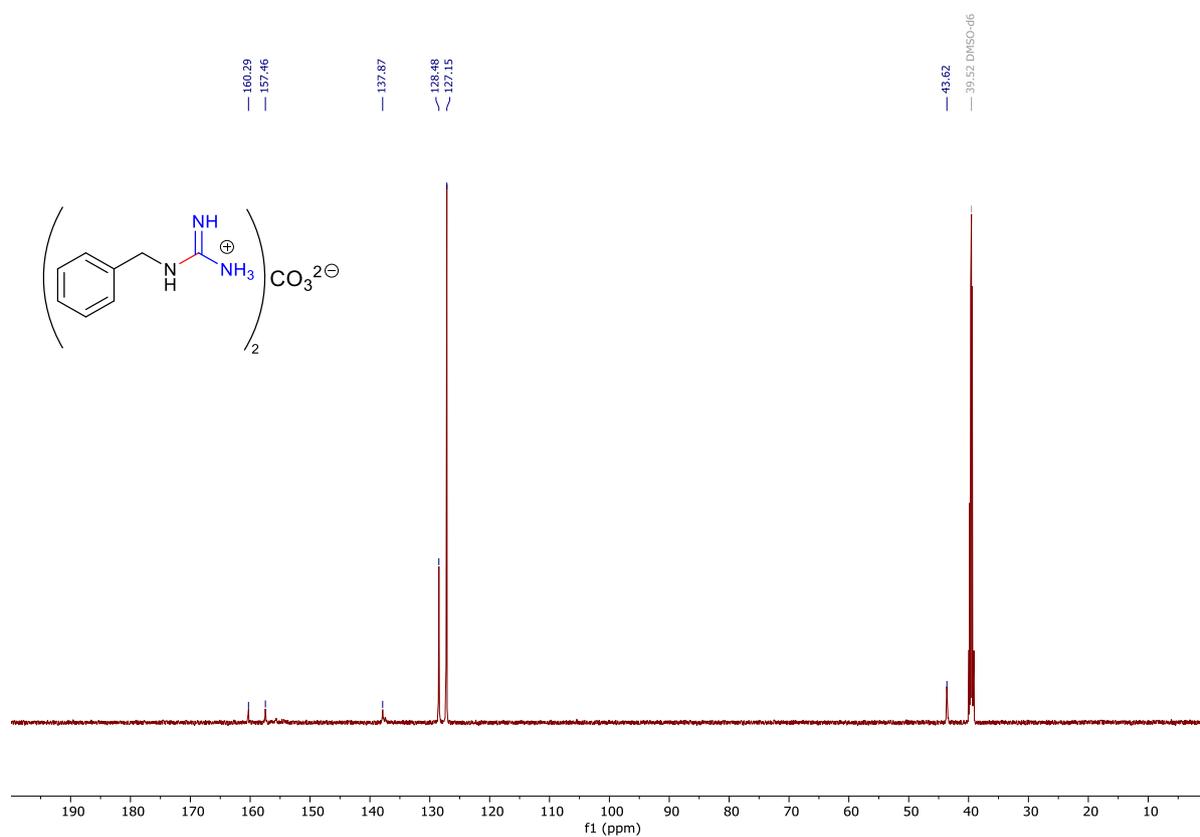


Figure 9b. ^{13}C NMR spectrum of bis-1-benzylguanidinium carbonate (**7a**)

^1H NMR (600 MHz, $\text{DMSO-}d_6$)

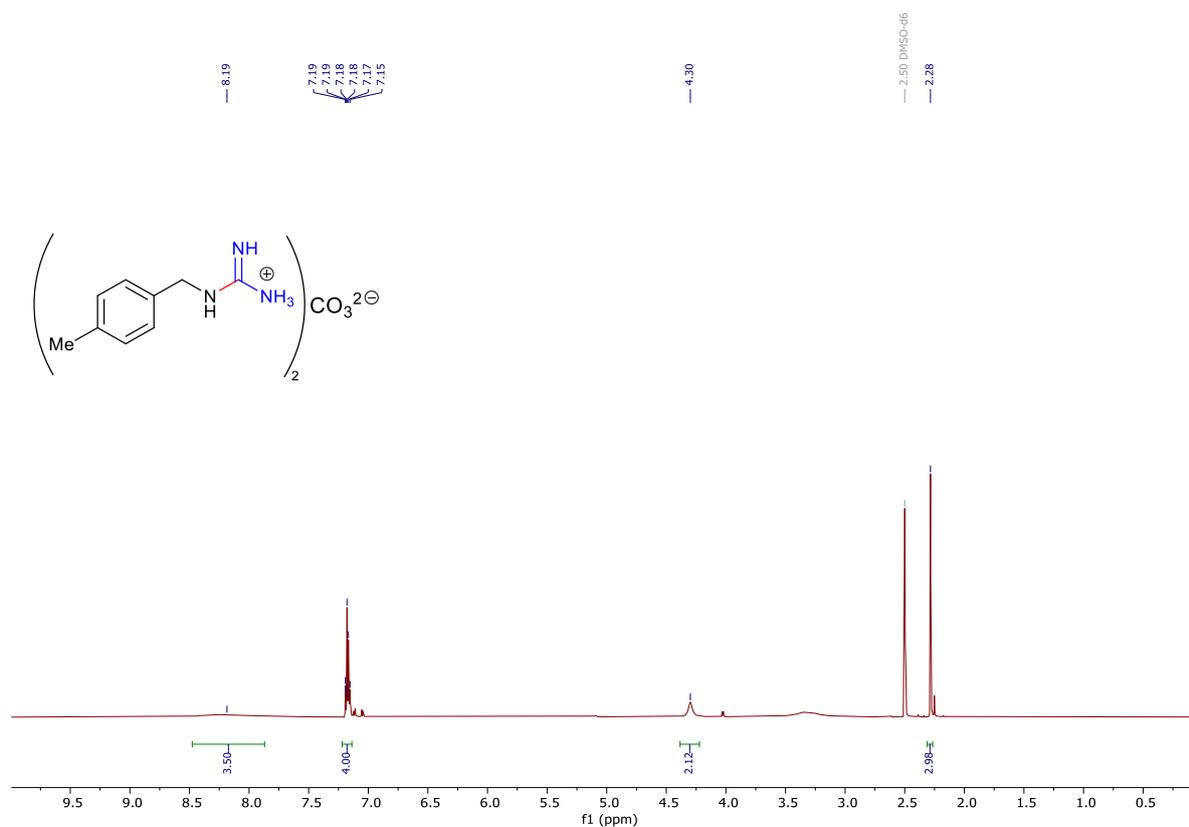


Figure 10a. ^1H NMR spectrum of bis-1-(4-methylbenzyl)guanidinium carbonate (**7b**)

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$)

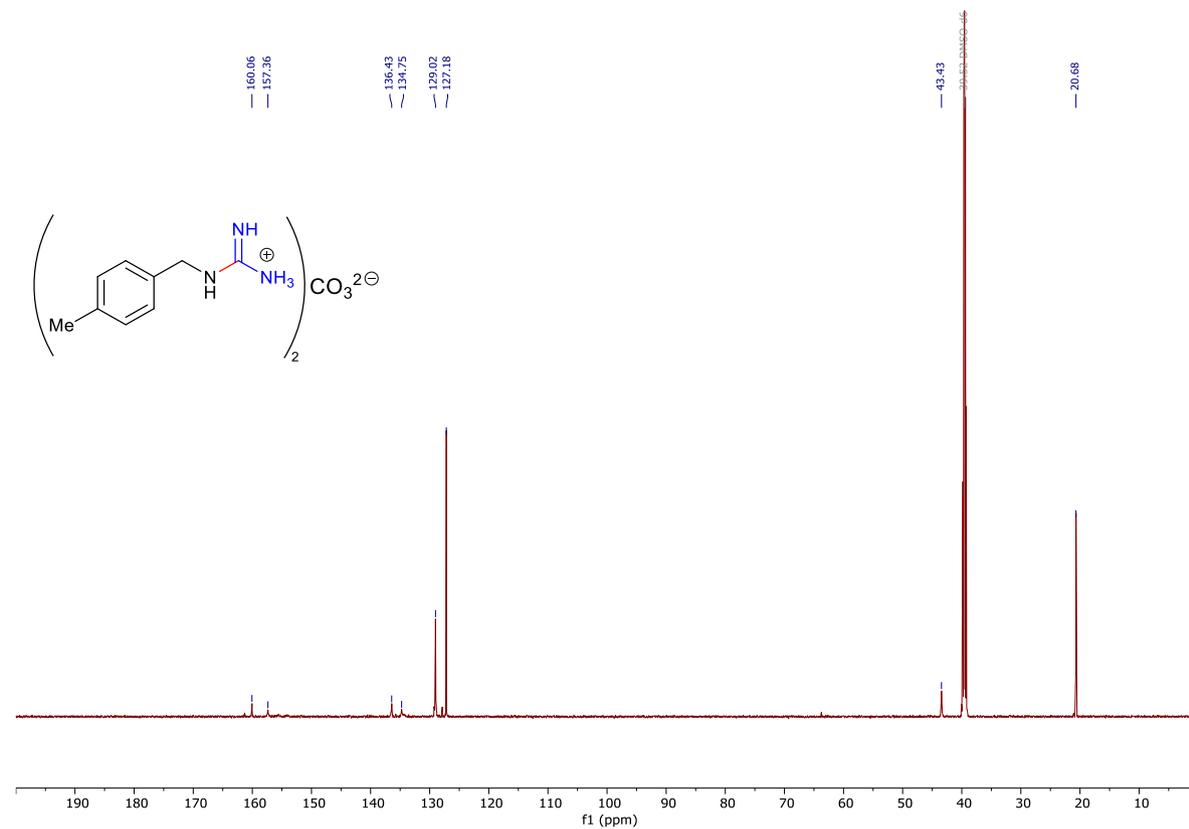


Figure 10b. ^{13}C NMR spectrum of bis-1-(4-methylbenzyl)guanidinium carbonate (**7b**)

^1H NMR (600 MHz, $\text{DMSO-}d_6$)

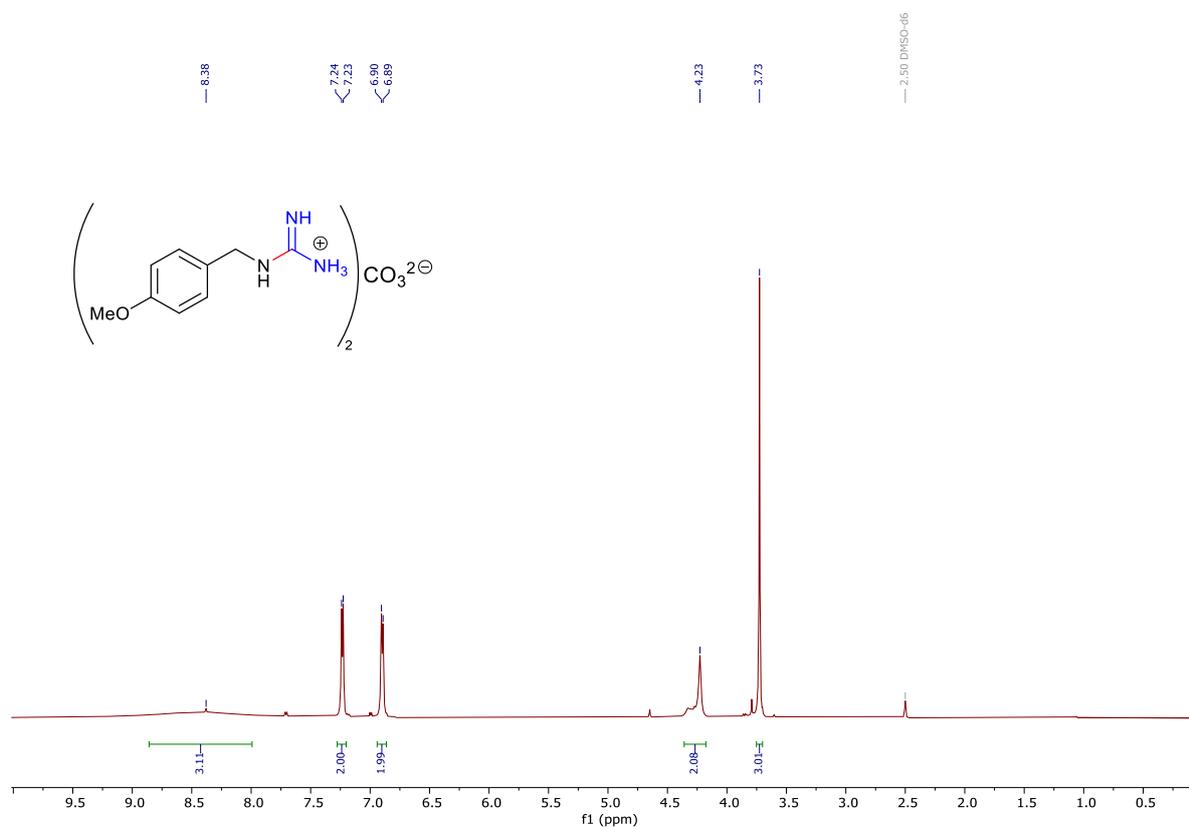


Figure 11a. ^1H NMR spectrum of bis-1-(4-methoxybenzyl)guanidinium carbonate (**7c**)

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$)

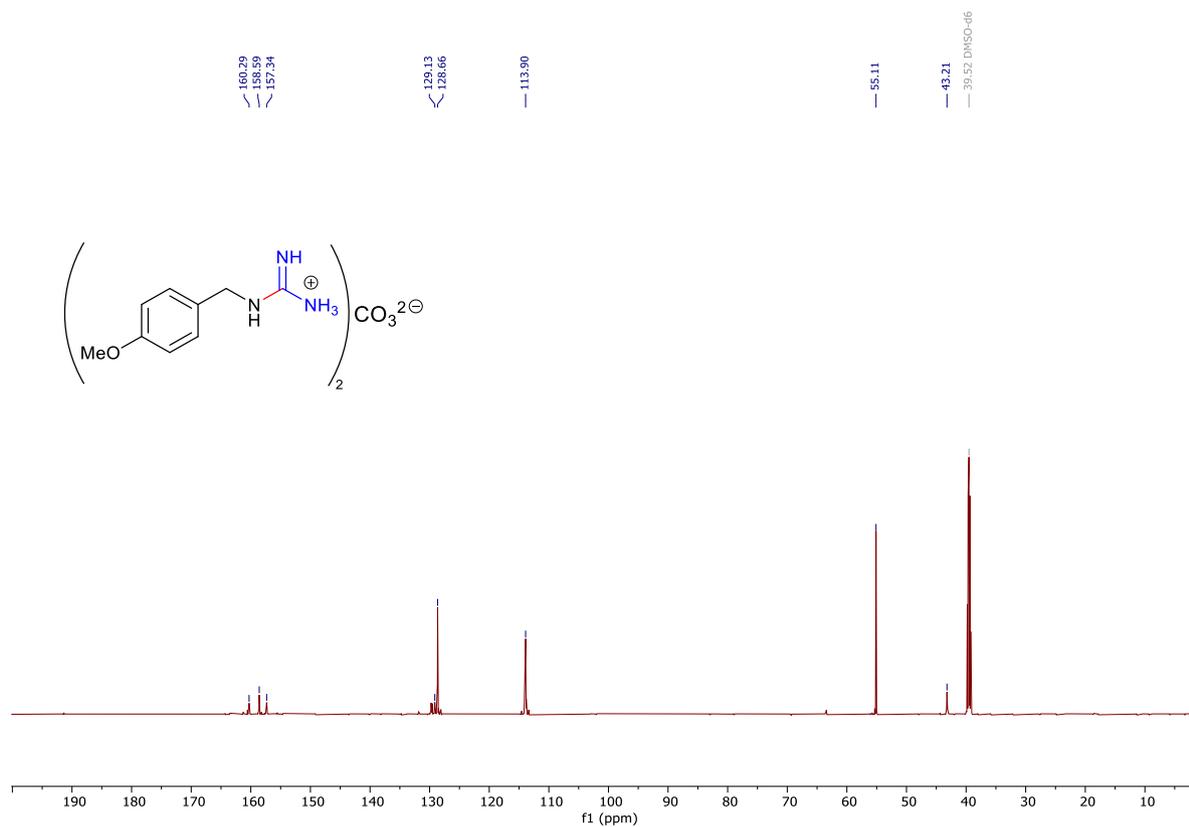


Figure 11b. ^{13}C NMR spectrum of bis-1-(4-methoxybenzyl)guanidinium carbonate (7c)

^1H NMR (600 MHz, $\text{DMSO-}d_6$)

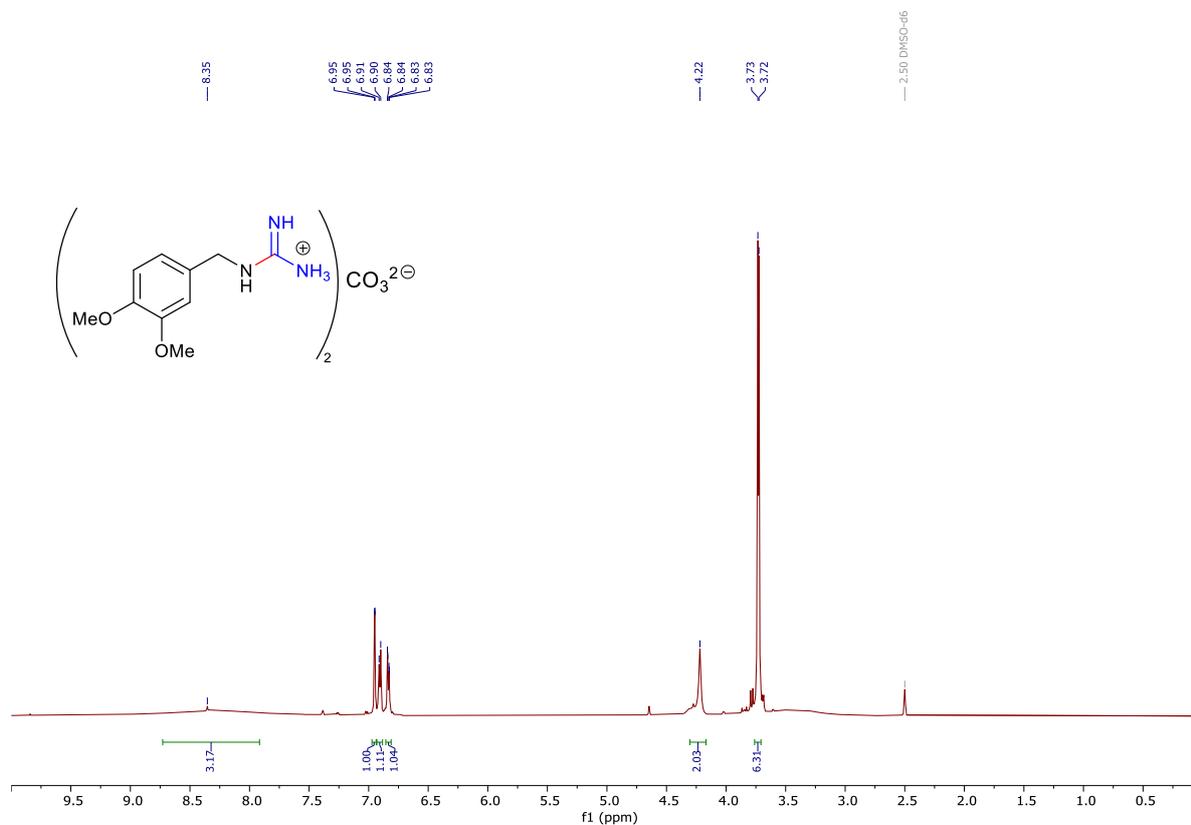


Figure 12a. ^1H NMR spectrum of bis-1-(3,4-dimethoxybenzyl)guanidinium carbonate (7d)

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$)

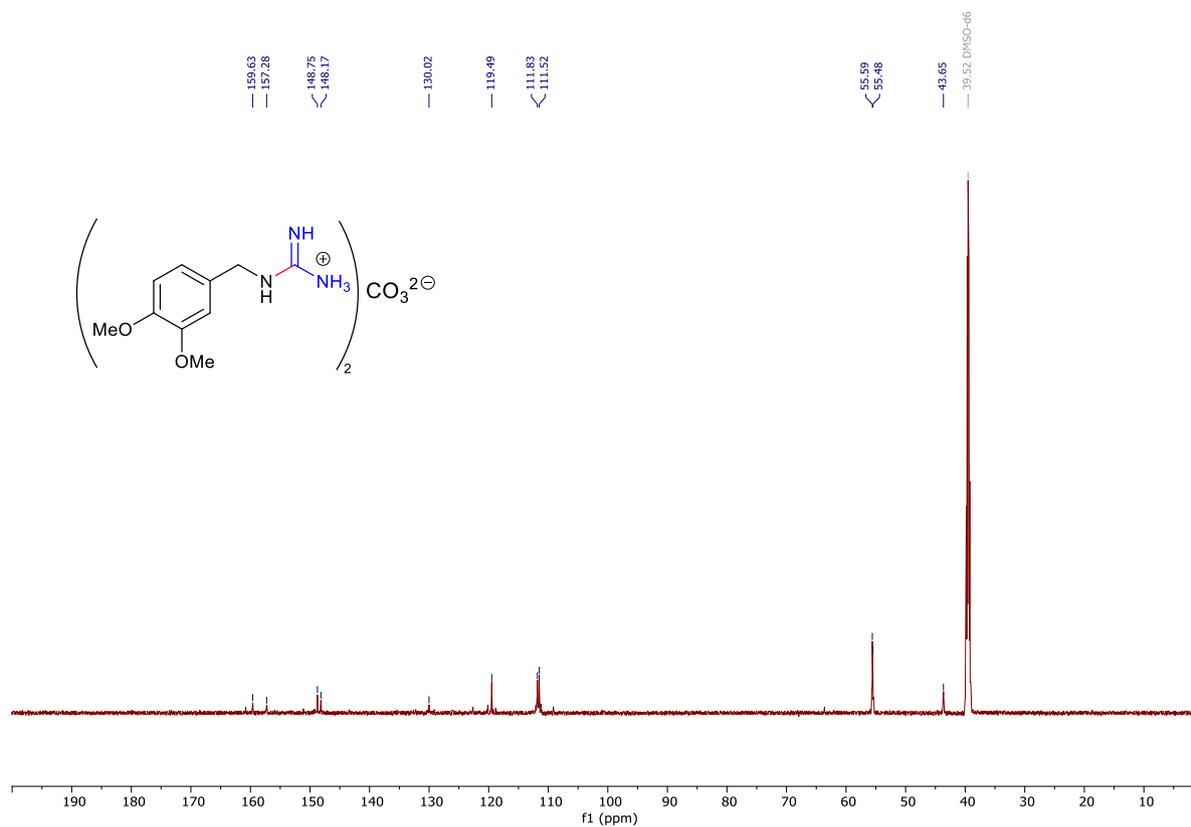


Figure 12b. ^{13}C NMR spectrum of bis-1-(3,4-dimethoxybenzyl)guanidinium carbonate (**7d**)

^1H NMR (600 MHz, $\text{DMSO-}d_6$)

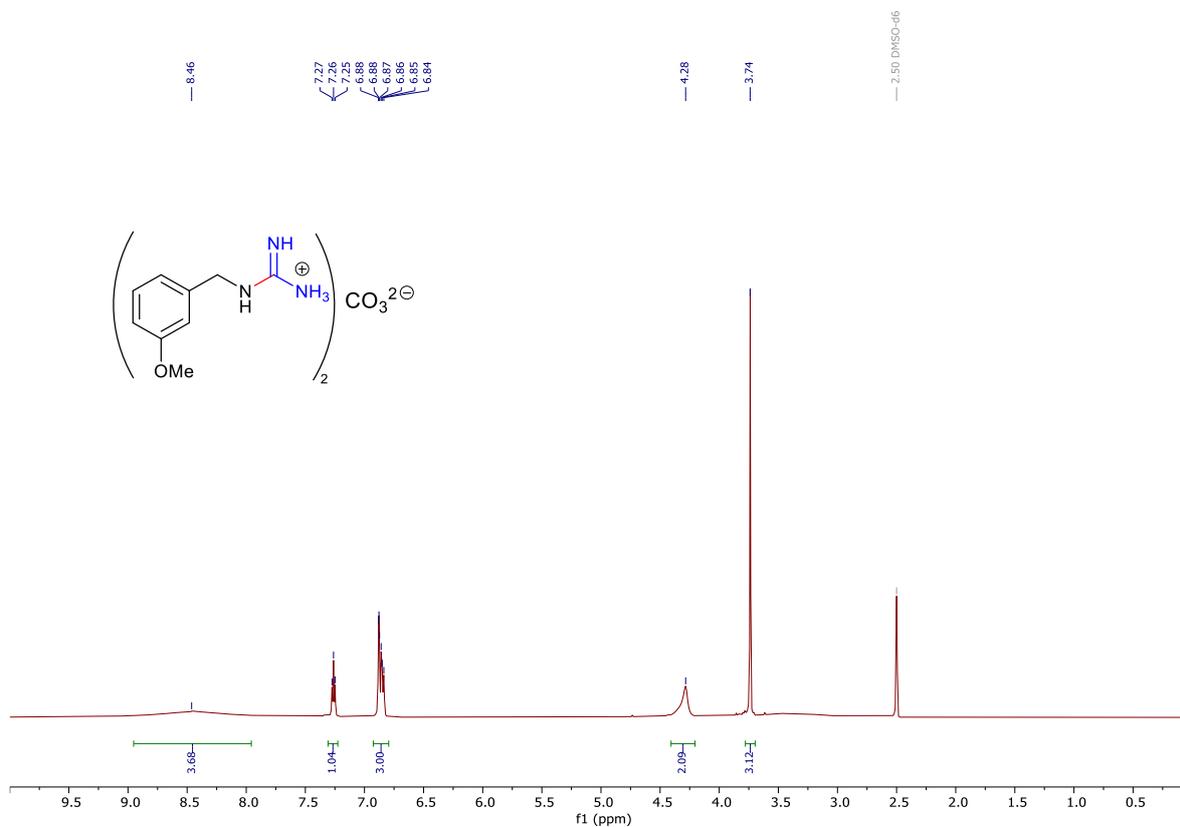


Figure 13a. ^1H NMR spectrum of bis-1-(3-methoxybenzyl)guanidinium carbonate (**7e**)

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$)

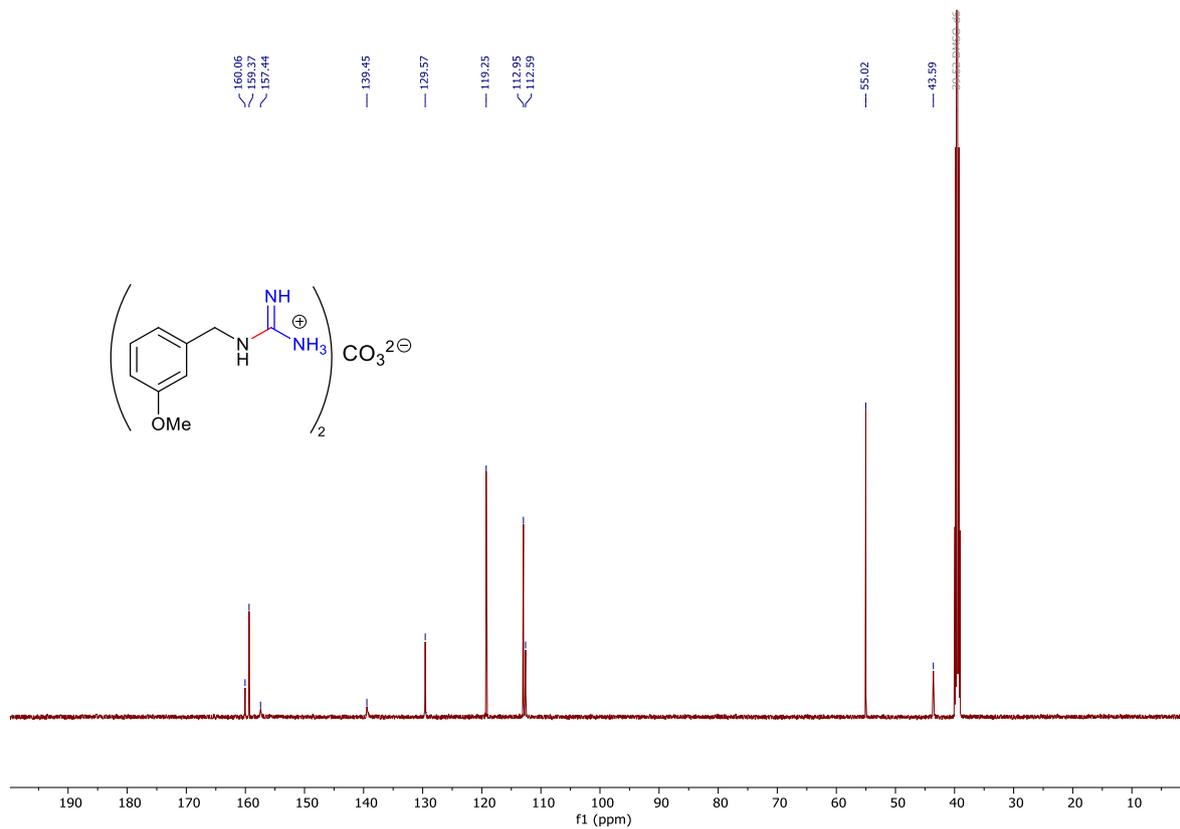


Figure 13b. ^1H NMR spectrum of bis-1-(3-methoxybenzyl)guanidinium carbonate (**7e**)

^1H NMR (600 MHz, $\text{DMSO-}d_6$)

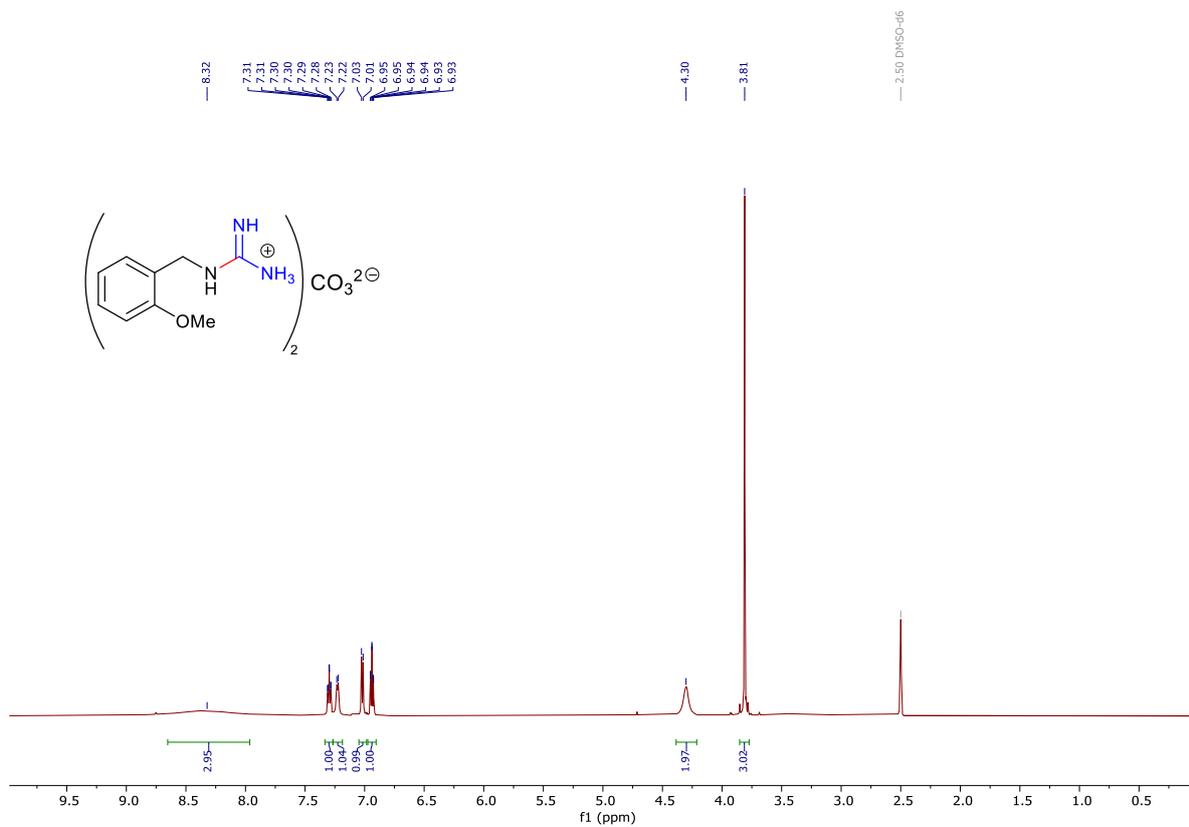


Figure 14a. ^1H NMR spectrum of bis-1-(2-methoxybenzyl)guanidinium carbonate (**7f**)

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$)

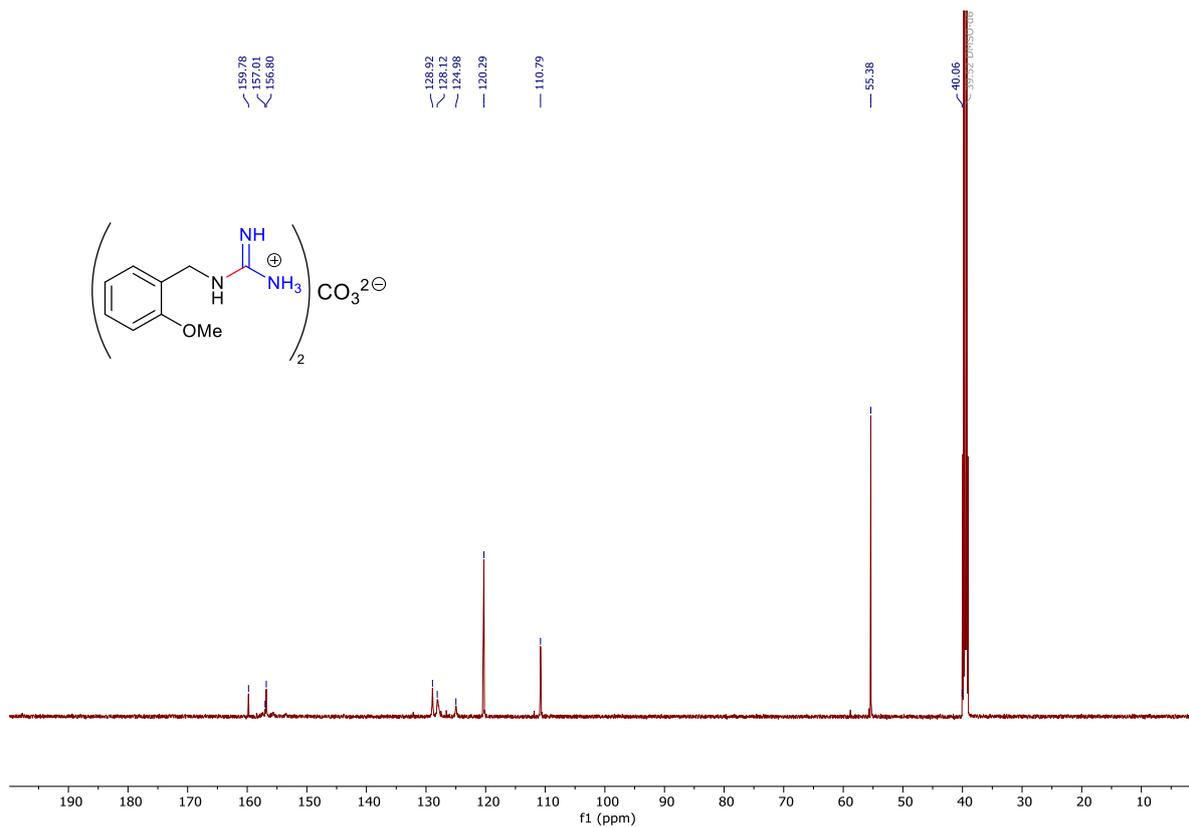


Figure 14b. ^{13}C NMR spectrum of bis-1-(2-methoxybenzyl)guanidinium carbonate (**7f**)

^1H NMR (600 MHz, $\text{DMSO-}d_6$)

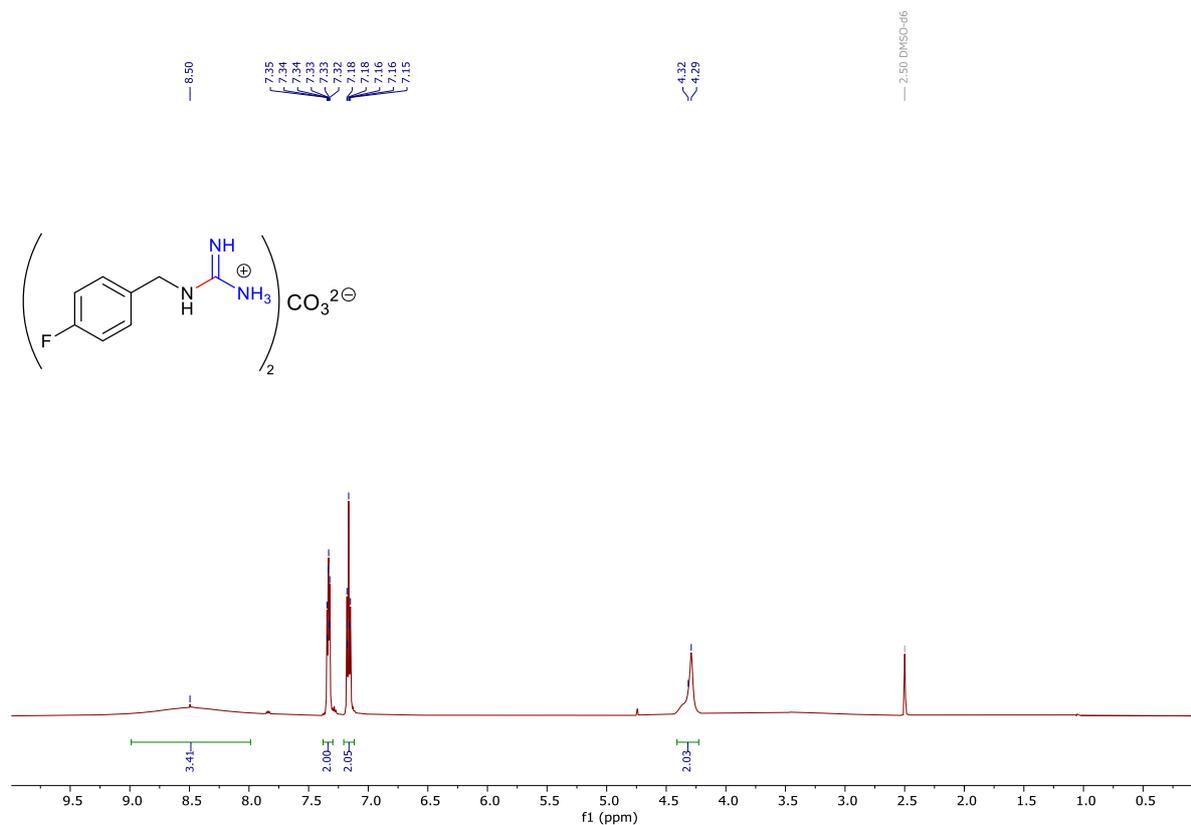


Figure 15a. ^1H NMR spectrum of bis-1-(4-fluorobenzyl)guanidinium carbonate (**7g**)

^{13}C NMR (151 MHz, $\text{DMSO-}d_6$)

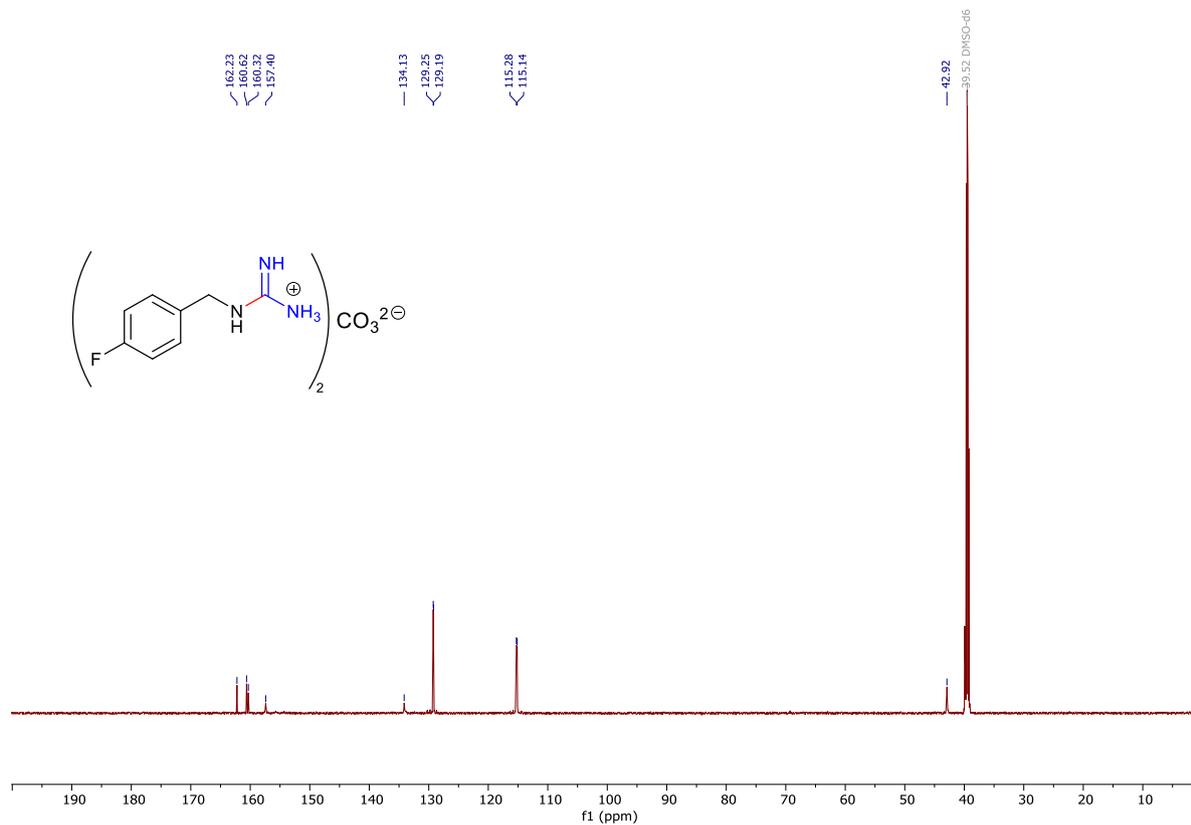


Figure 15b. ^{13}C NMR spectrum of bis-1-(4-fluorobenzyl)guanidinium carbonate (**7g**)

^{19}F NMR ($\text{DMSO-}d_6$)

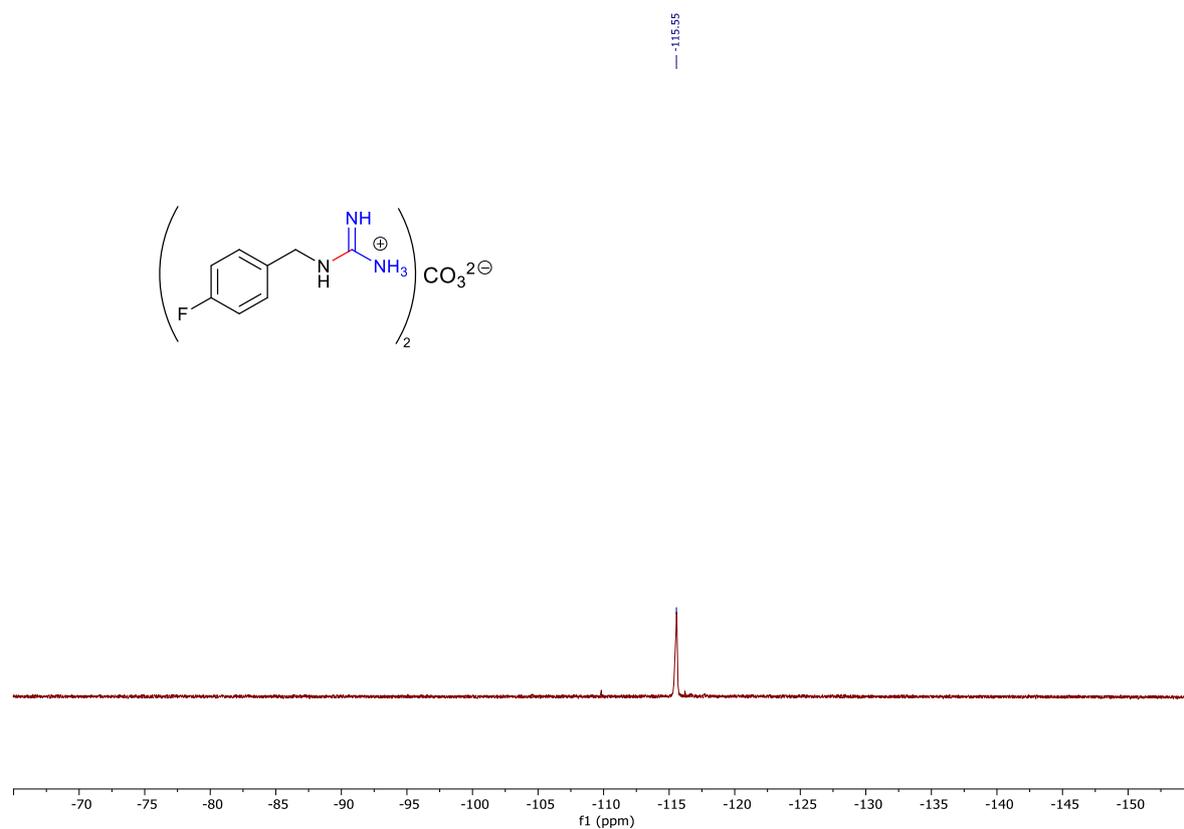


Figure 15c. ^{19}F NMR spectrum of bis-1-(4-fluorobenzyl)guanidinium carbonate (**7g**)

¹H NMR (600 MHz, DMSO-*d*₆)

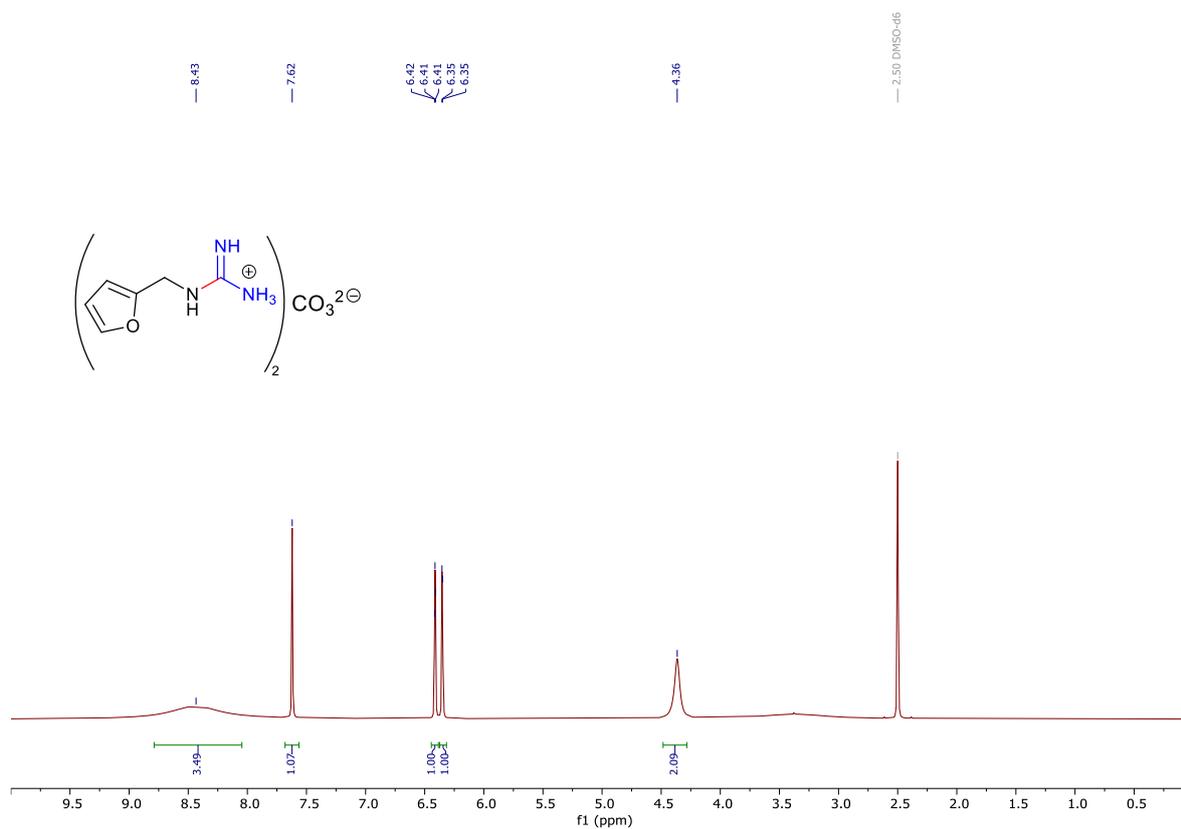


Figure 16a. ¹H NMR spectrum of bis-1-(furan-2-ylmethyl)guanidinium carbonate (**7h**)

¹³C NMR (151 MHz, DMSO-*d*₆)

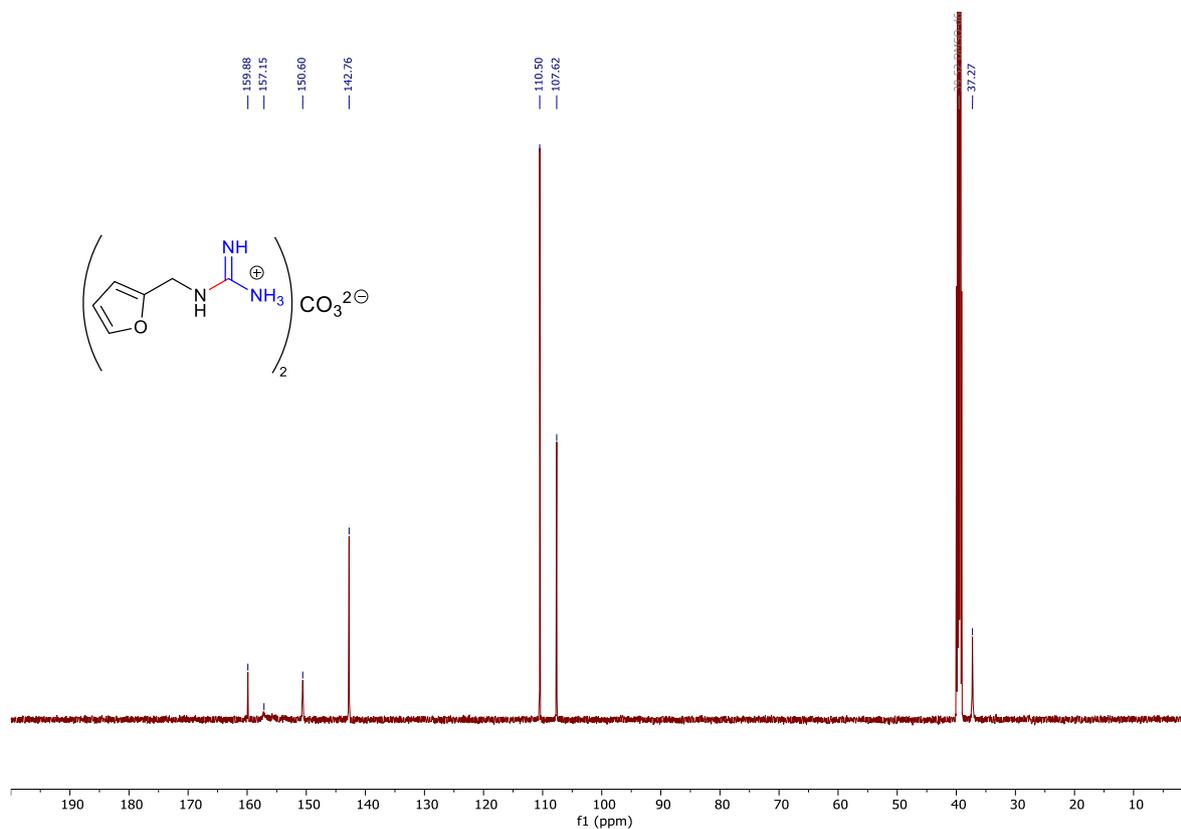


Figure 16b. ¹³C NMR spectrum of bis-1-(furan-2-ylmethyl)guanidinium carbonate (**7h**)

¹H NMR (600 MHz, DMSO-*d*₆)

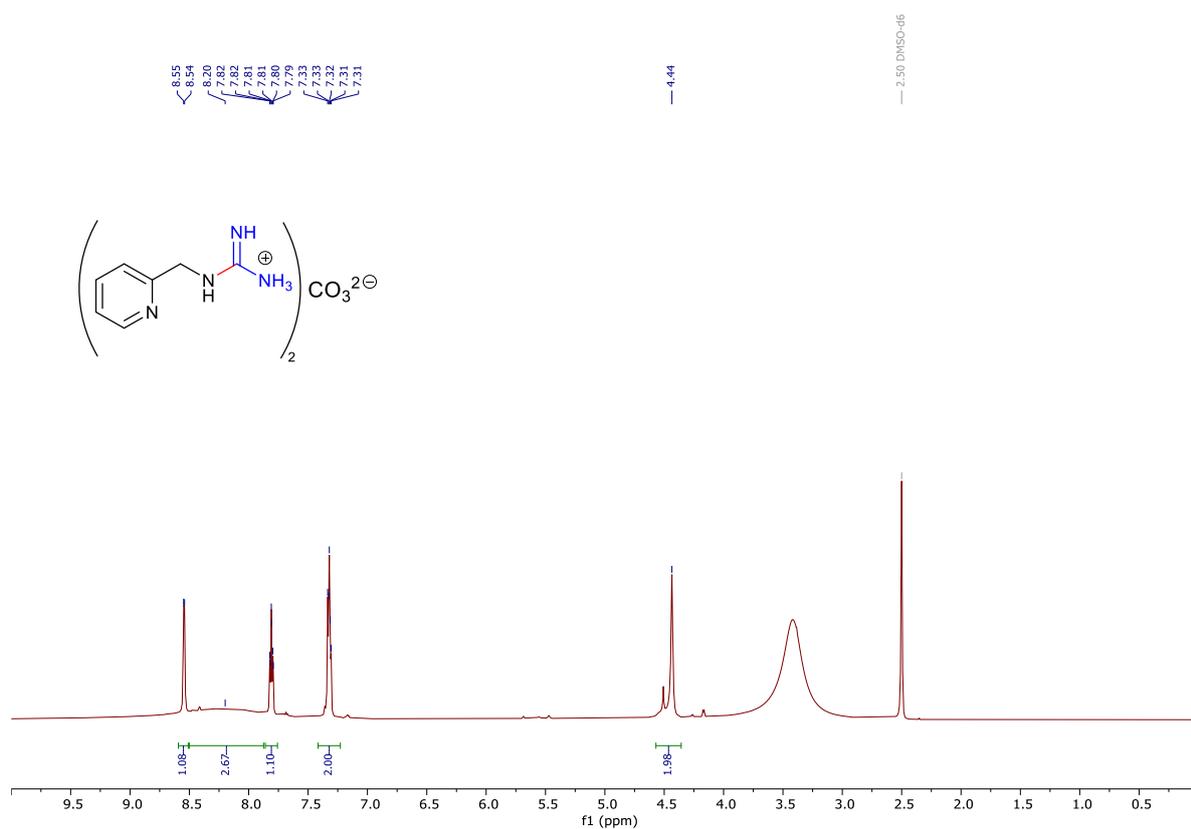


Figure 17a. ¹H NMR spectrum of bis-1-(pyridin-2-ylmethyl)guanidinium carbonate (**7i**)

¹³C NMR (151 MHz, DMSO-*d*₆)

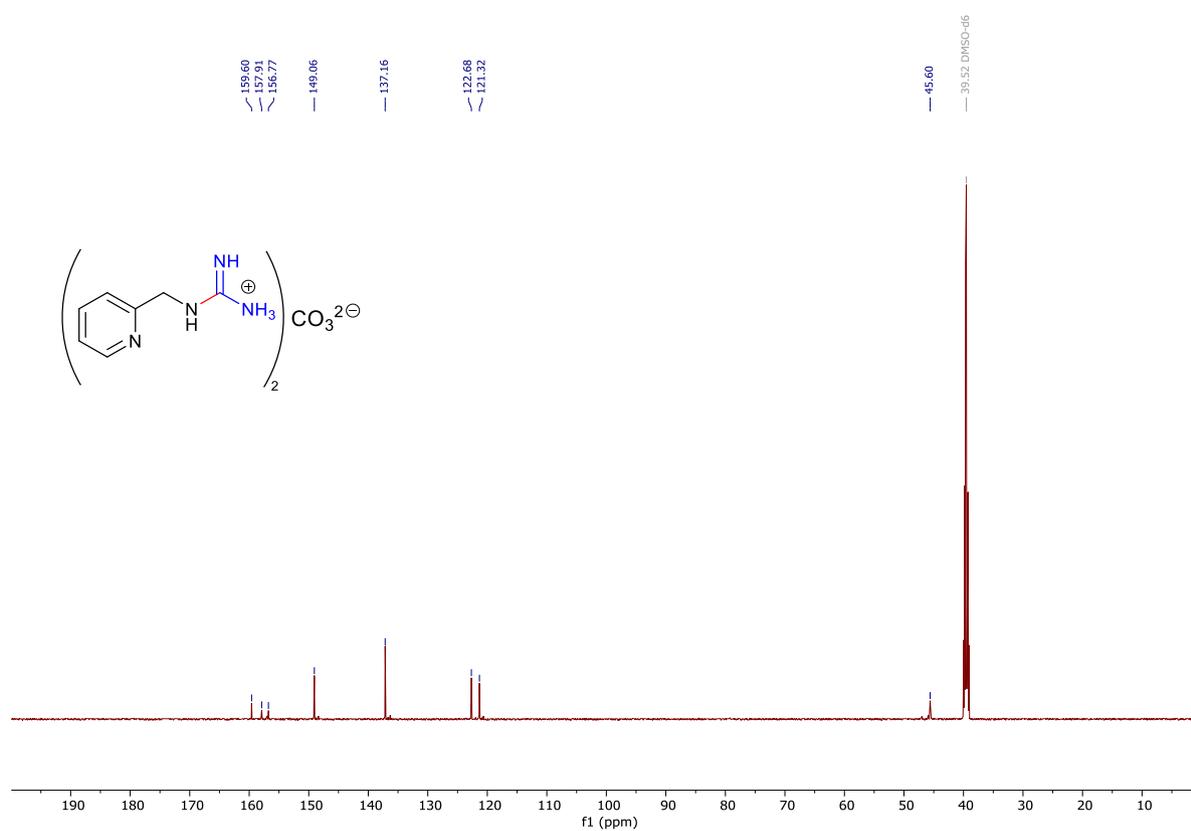


Figure 17b. ¹³C NMR spectrum of bis-1-(pyridin-2-ylmethyl)guanidinium carbonate (**7i**)

¹H NMR (600 MHz, DMSO-*d*₆)

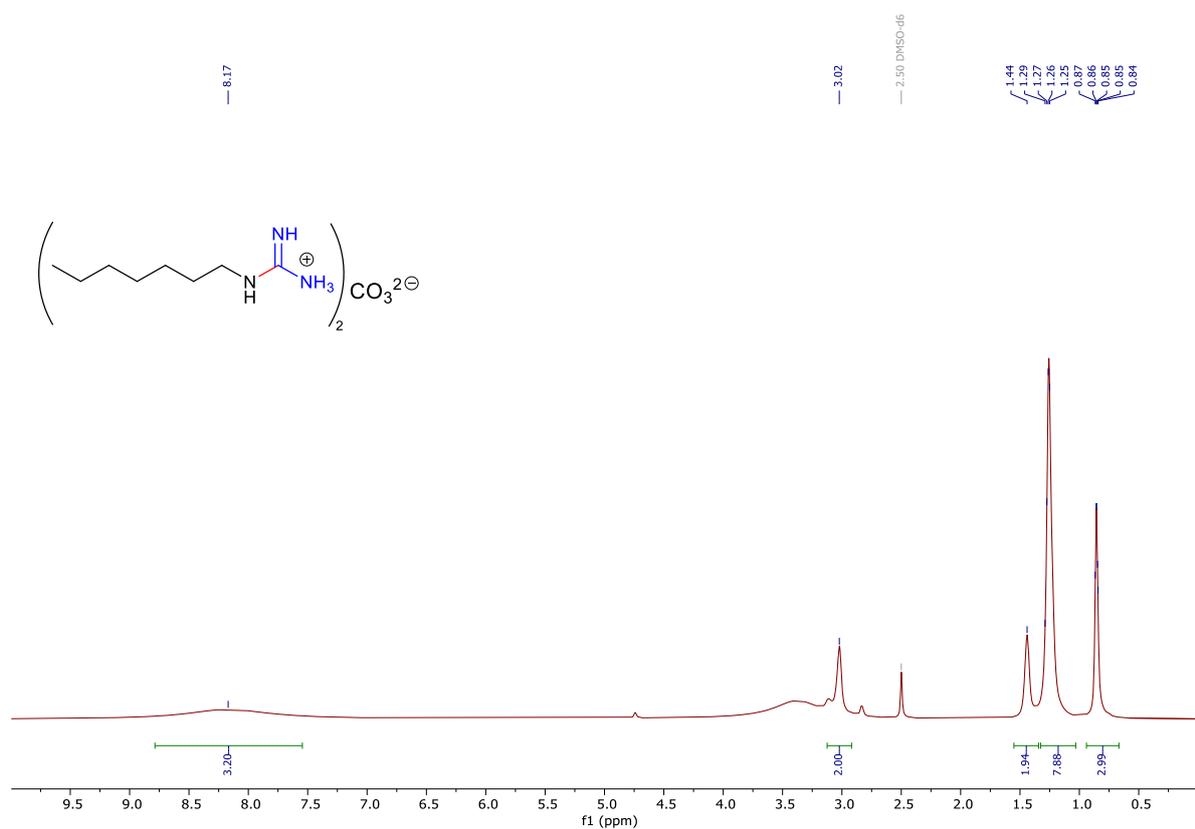


Figure 18a. ¹H NMR spectrum of bis-1-heptylguanidinium carbonate (**8a**)

¹³C NMR (151 MHz, DMSO-*d*₆)

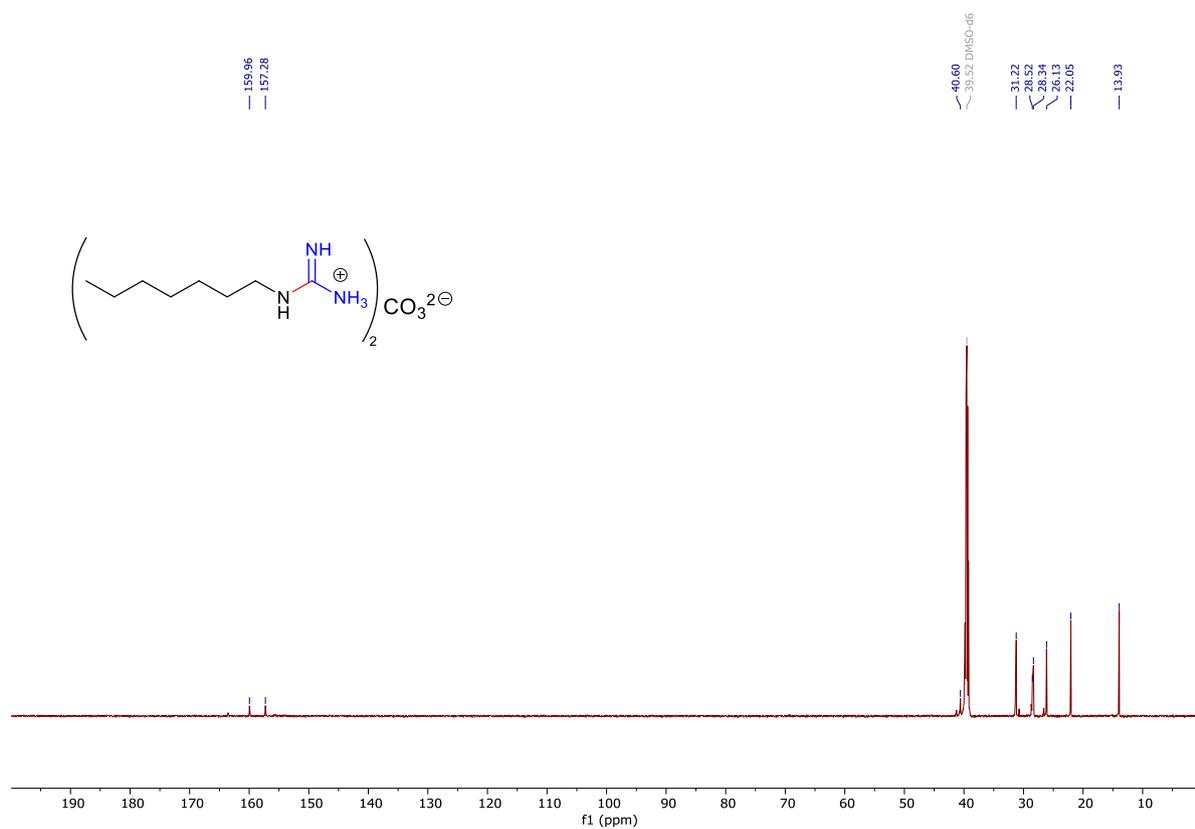


Figure 18b. ¹³C NMR spectrum of bis-1-heptylguanidinium carbonate (**8a**)

¹H NMR (600 MHz, DMSO-*d*₆)

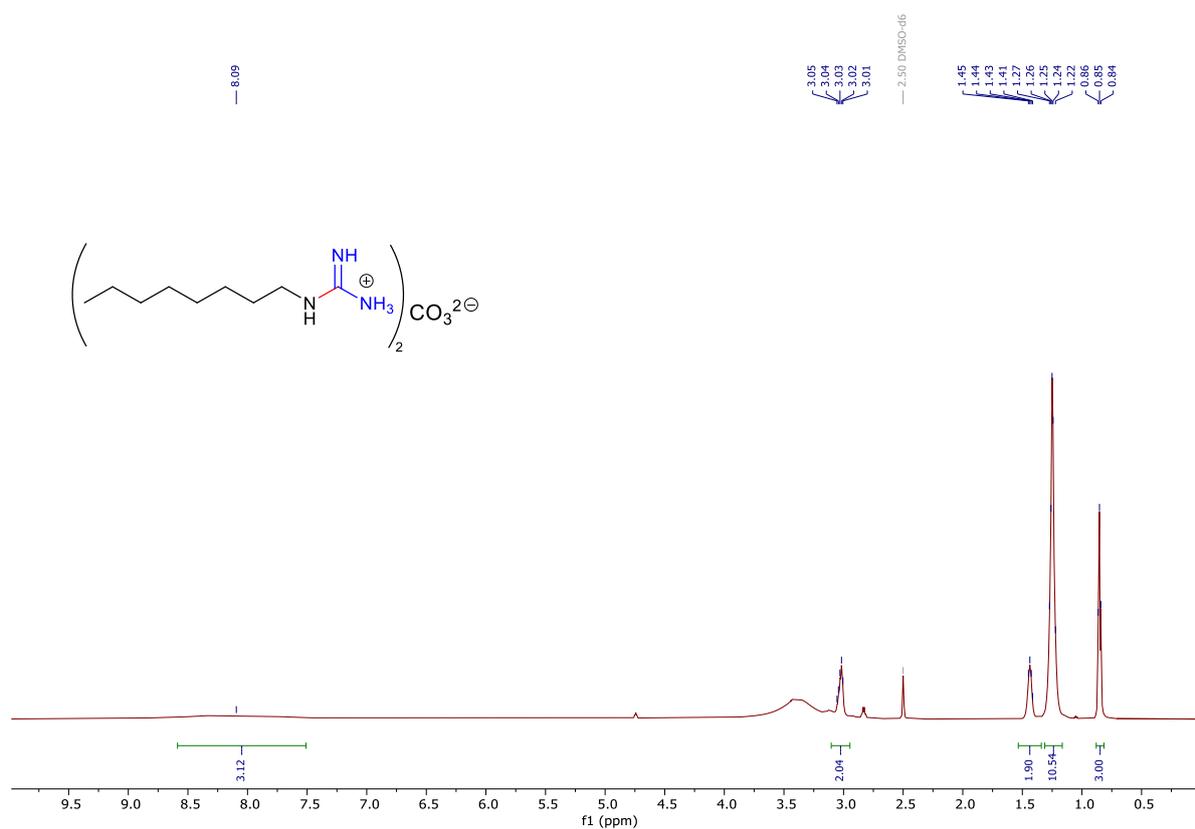


Figure 19a. ¹H NMR spectrum of bis-1-octylguanidinium carbonate (**8b**)

¹³C NMR (151 MHz, DMSO-*d*₆)

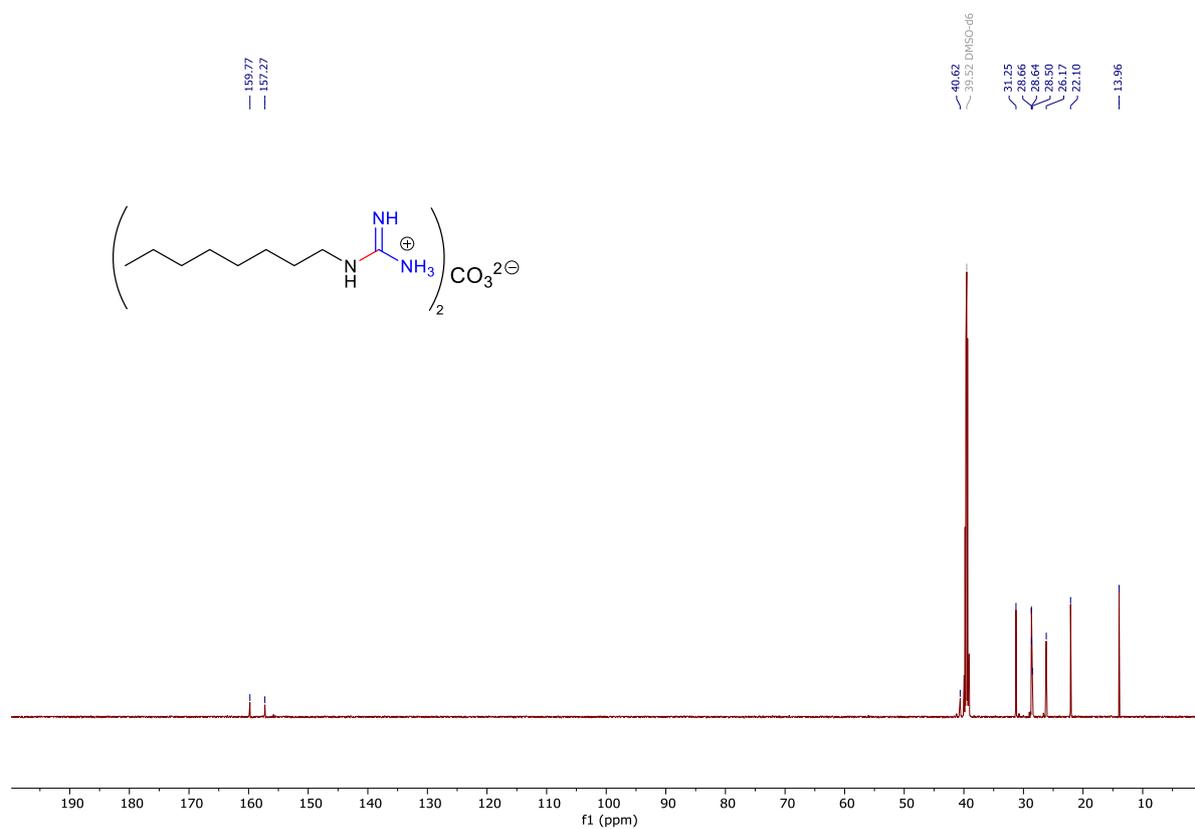


Figure 19b. ¹³C NMR spectrum of bis-1-octylguanidinium carbonate (**8b**)

¹H NMR (600 MHz, DMSO-*d*₆) (343k temperature)

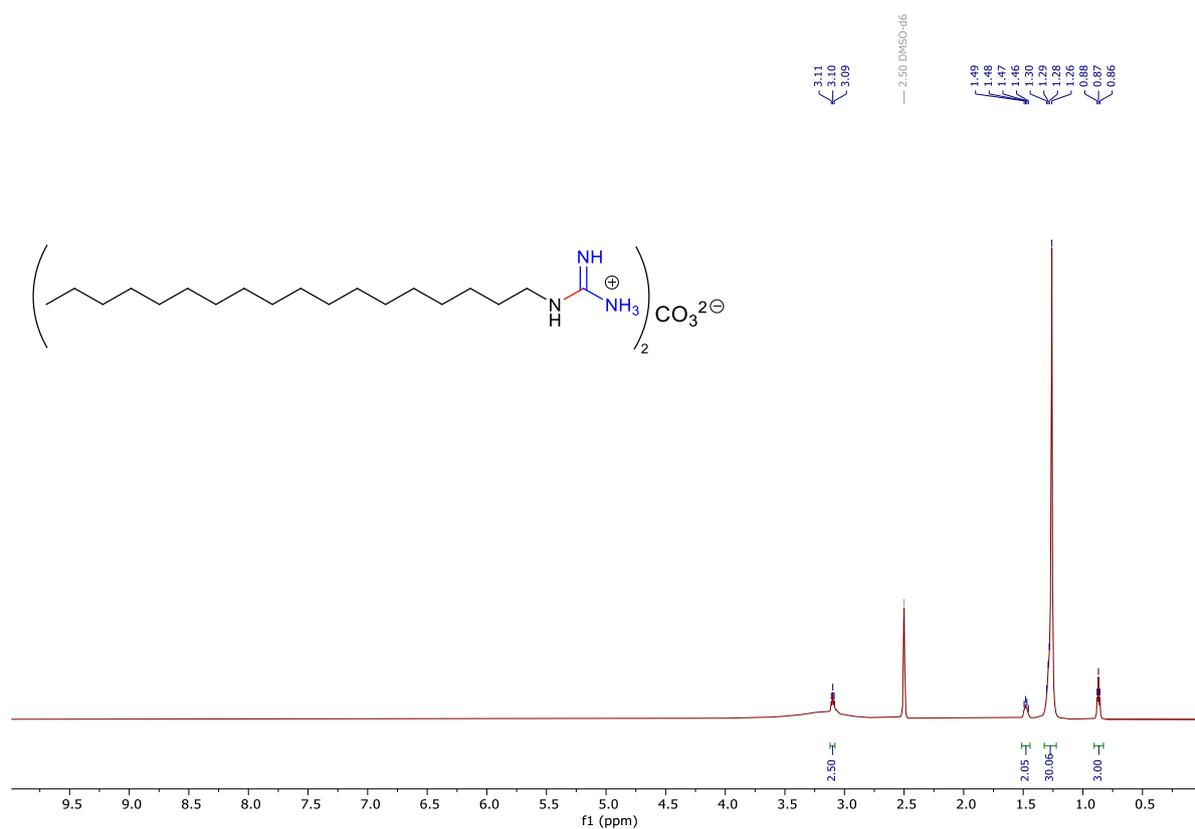


Figure 20a. ¹H NMR spectrum of bis-1-octadecylguanidinium carbonate (**8c**)

¹³C NMR (151 MHz, DMSO-*d*₆) (343k temperature)

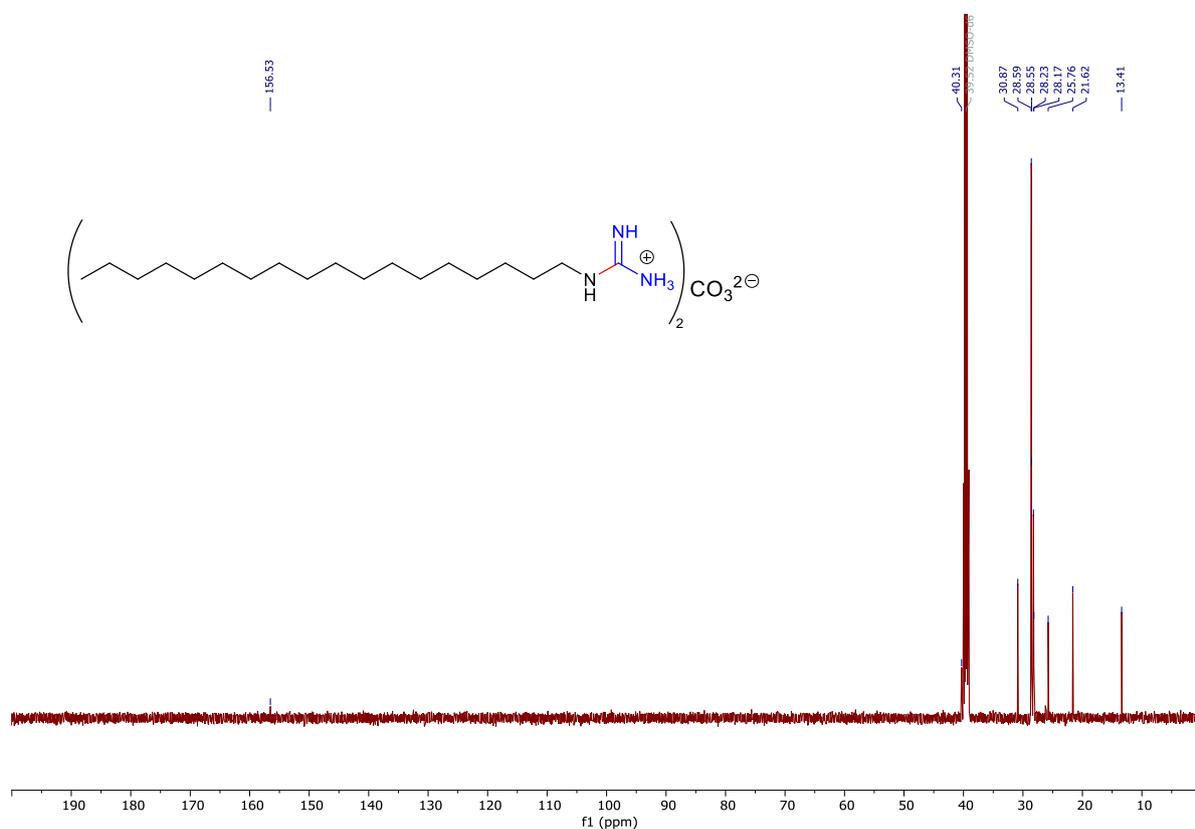


Figure 20b. ¹³C NMR spectrum of bis-1-octadecylguanidinium carbonate (**8c**)

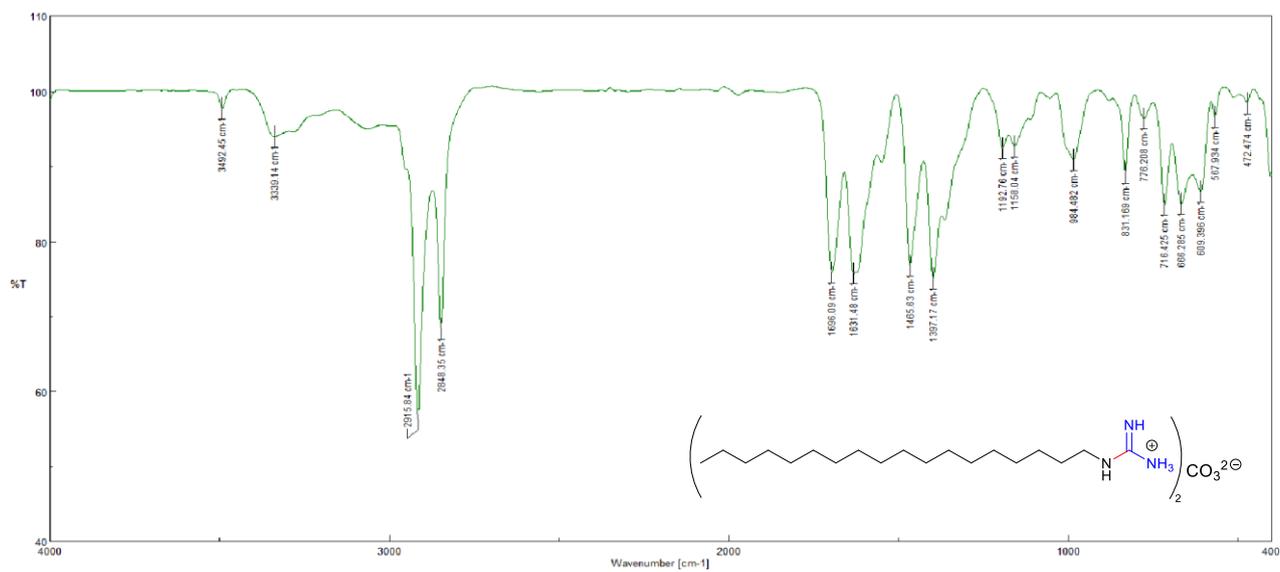


Figure 20c. IR spectrum of bis-1-octadecylguanidinium carbonate (**8c**)

¹H NMR (600 MHz, DMSO-*d*₆) (343k temperature)

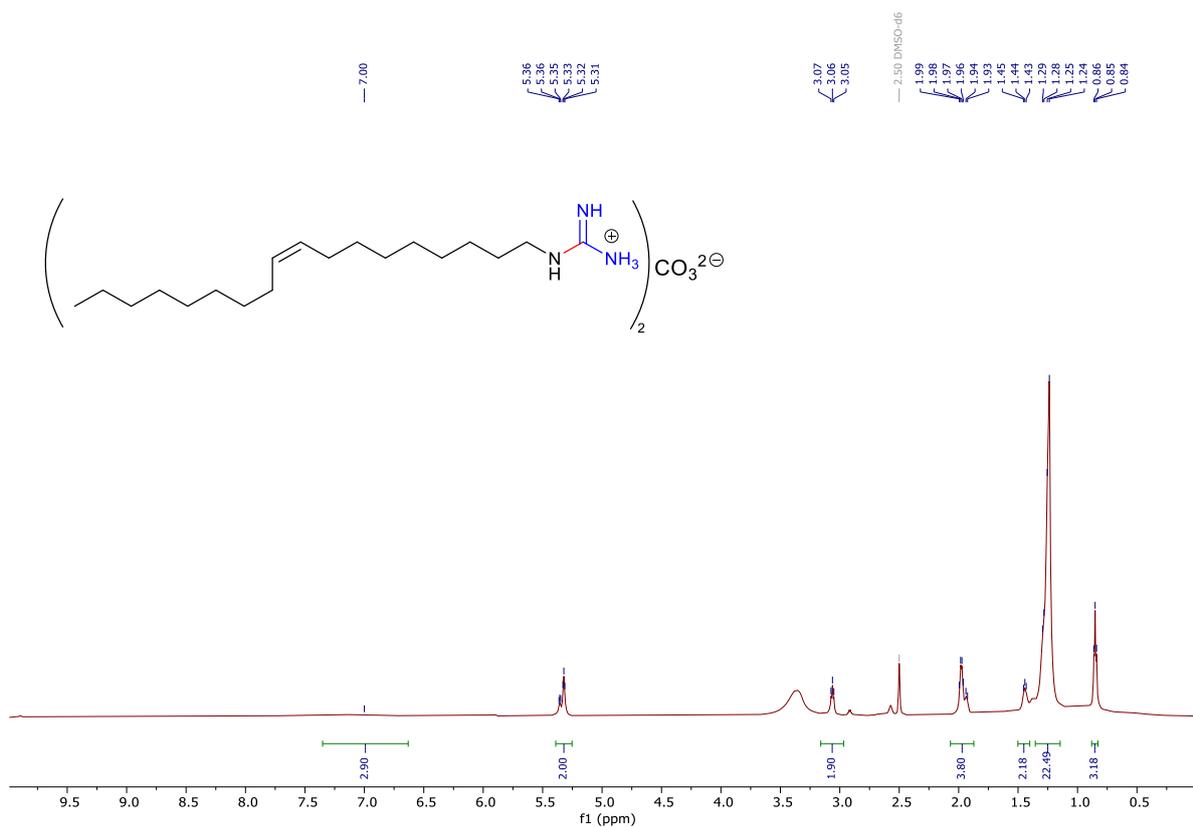


Figure 21a. ¹H NMR spectrum of bis-(Z)-1-(octadec-9-en-1-yl)guanidinium carbonate (**8d**)

¹³C NMR (151 MHz, DMSO-*d*₆) (343k temperature)

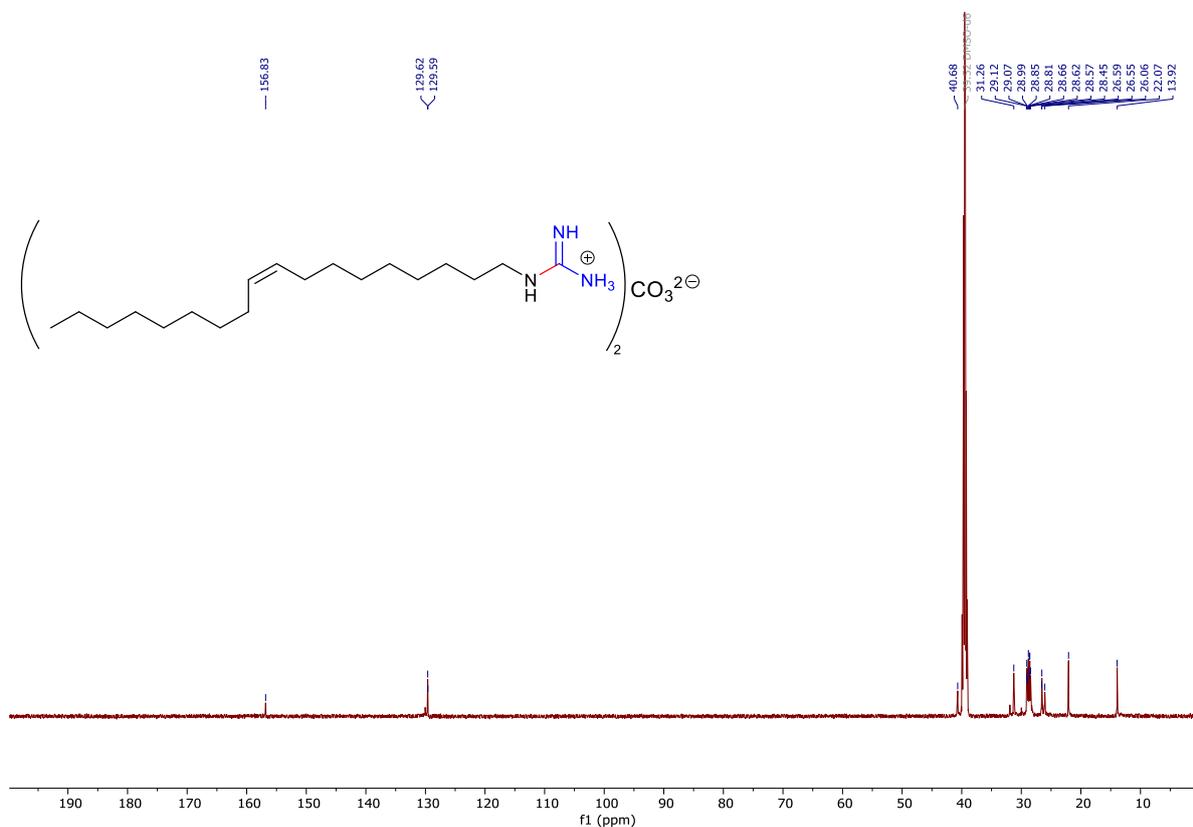


Figure 21b. ¹³C NMR spectrum of bis-(Z)-1-(octadec-9-en-1-yl)guanidinium carbonate (**8d**)

¹H NMR (600 MHz, DMSO-*d*₆) (343k temperature)

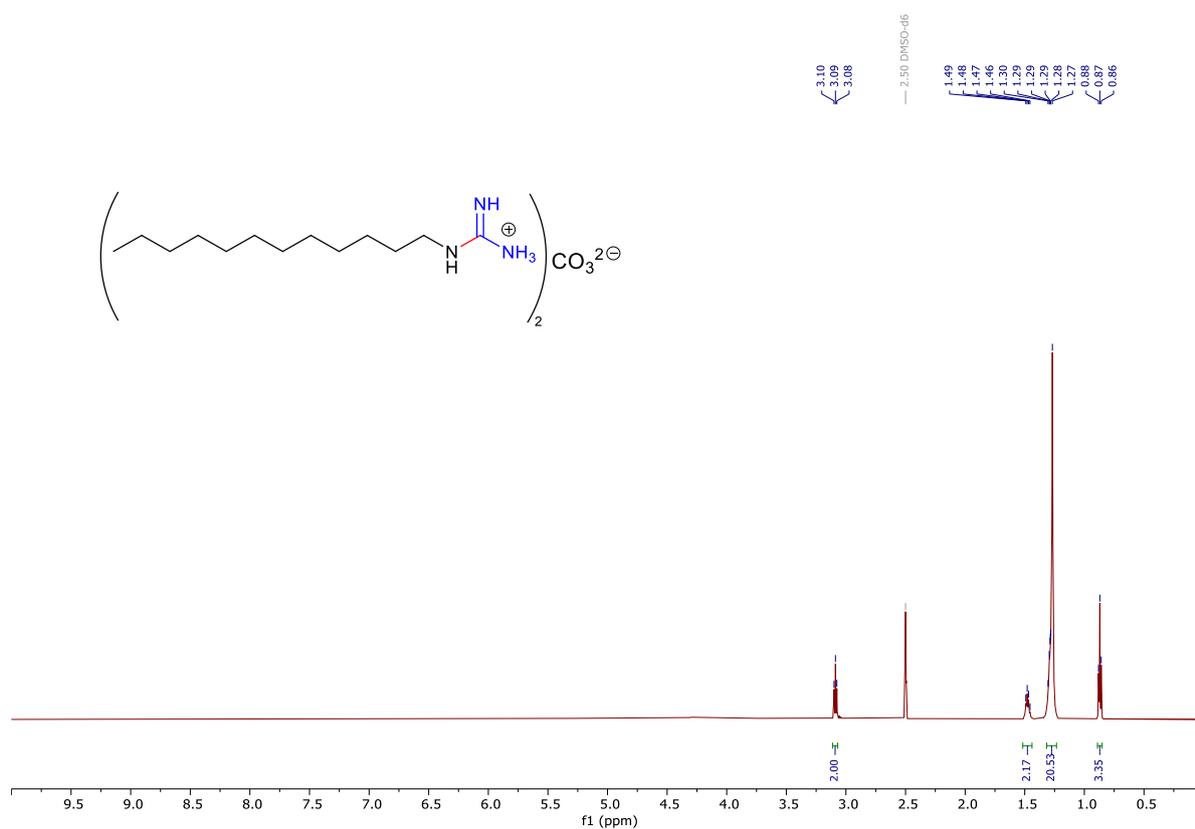


Figure 22a. ¹H NMR spectrum of bis-1-dodecylguanidinium carbonate (**8e**)

¹³C NMR (151 MHz, DMSO-*d*₆) (343k temperature)

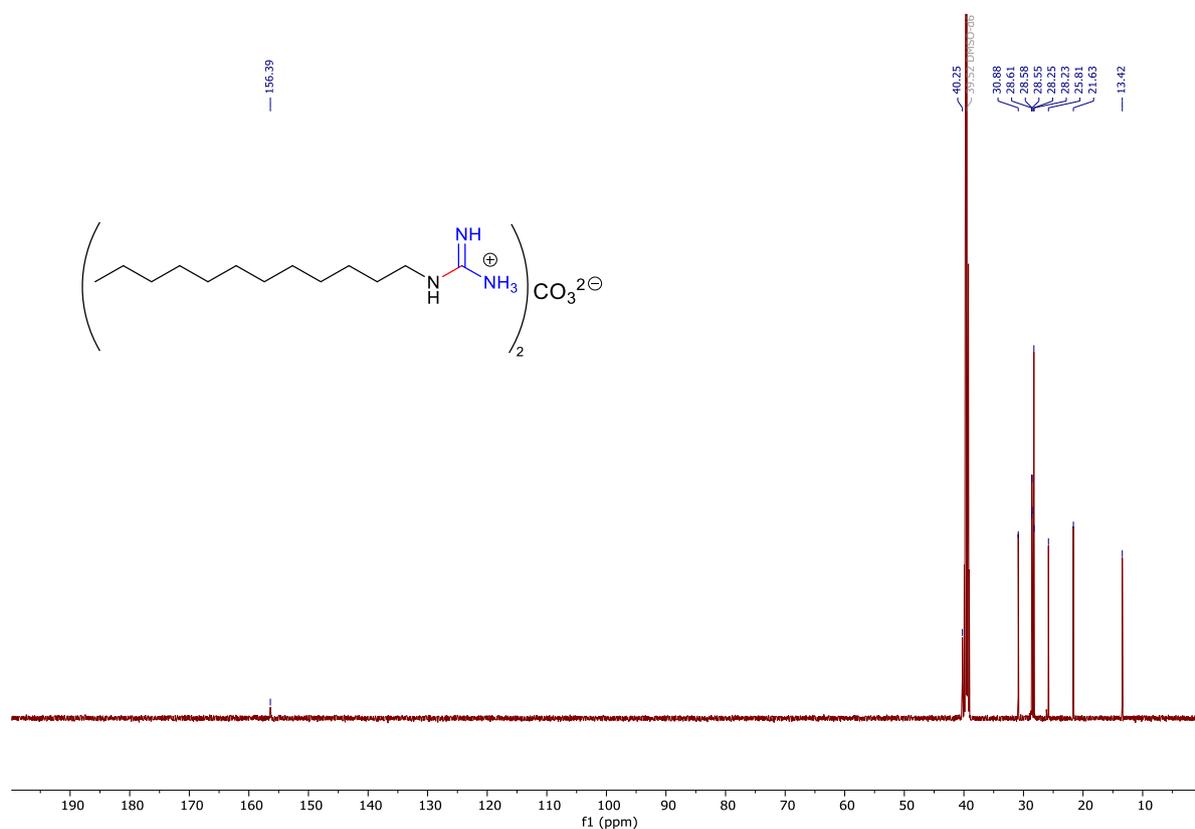


Figure 22b. ¹³C NMR spectrum of bis-1-dodecylguanidinium carbonate (**8e**)

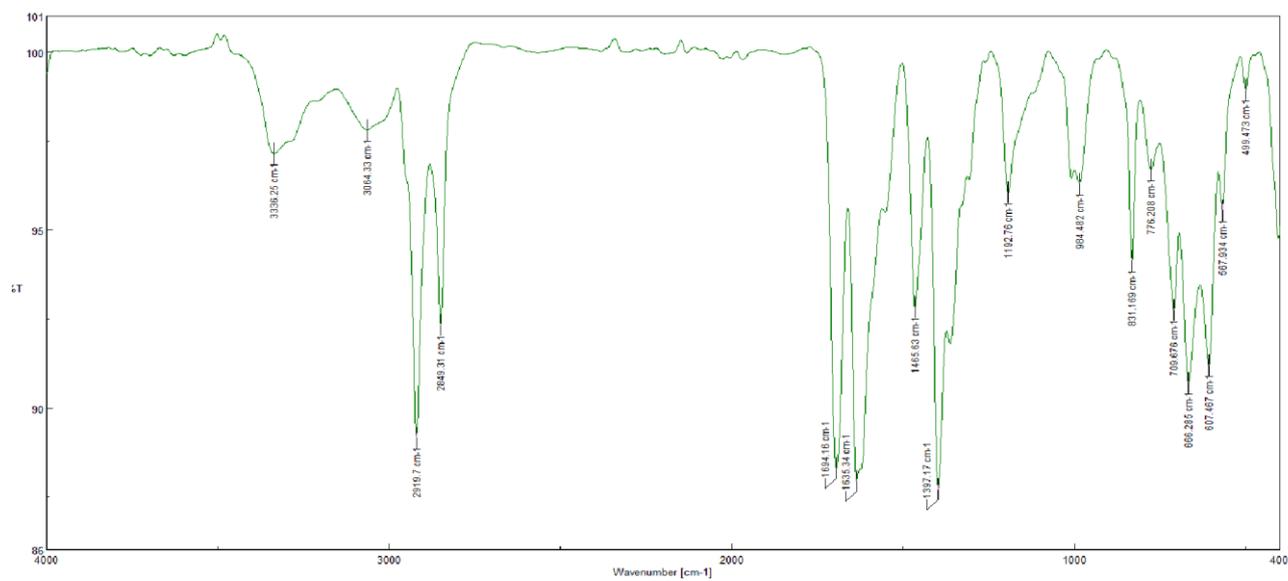


Figure 22c. IR spectrum of bis-1-dodecylguanidinium carbonate (**8e**)

¹H NMR (600 MHz, DMSO-*d*₆) (343k temperature)

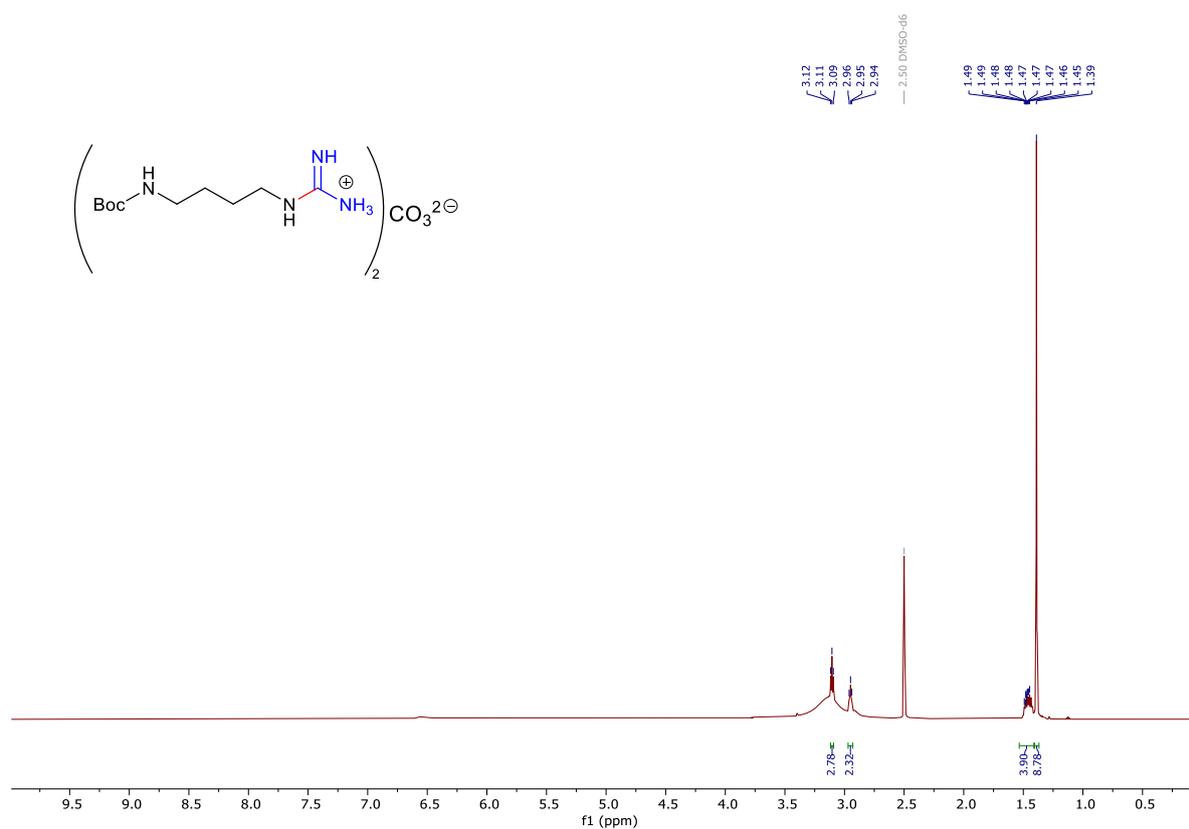


Figure 23a. ¹H NMR spectrum of bis-1-(4-((tert-butoxycarbonyl)amino)butyl)guanidinium carbonate (**8f**)

¹³C NMR (151 MHz, DMSO-*d*₆) (343k temperature)

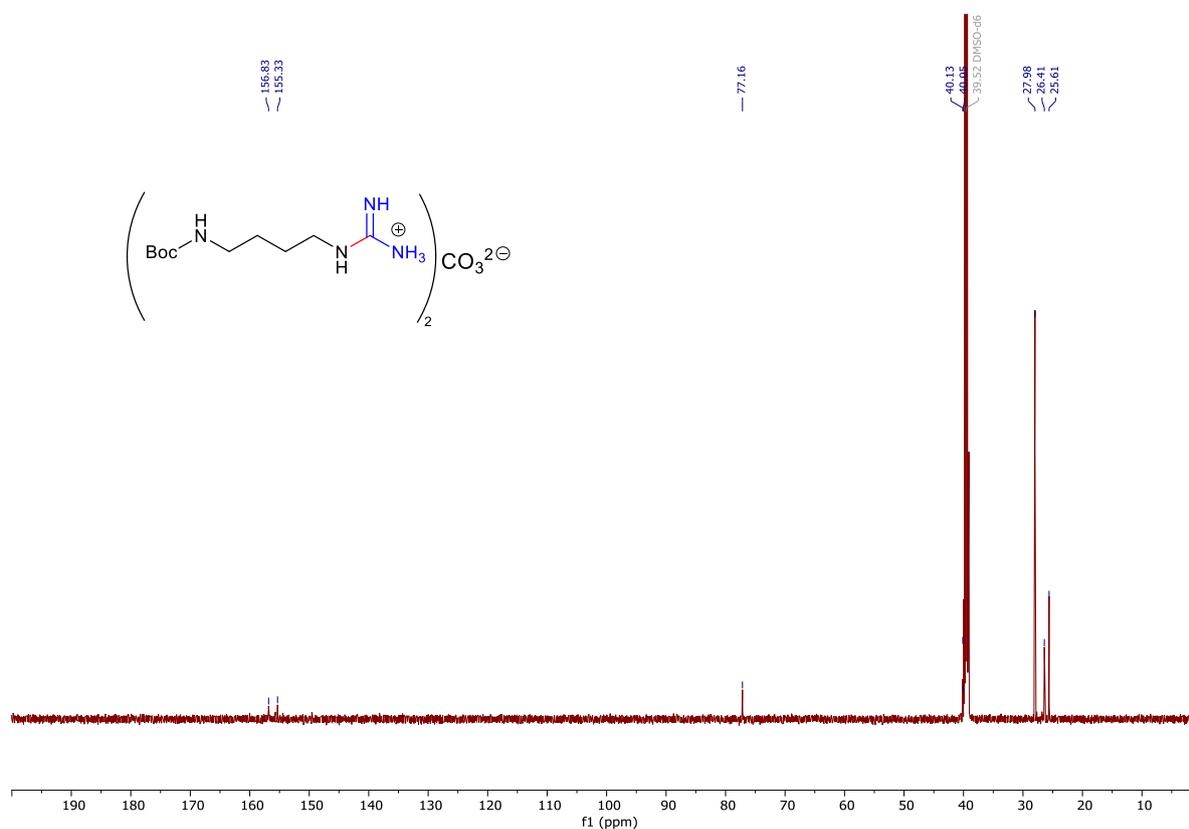


Figure 23b. ¹³C NMR spectrum of bis-1-(4-((tert-butoxycarbonyl)amino)butyl)guanidinium carbonate (**8f**)

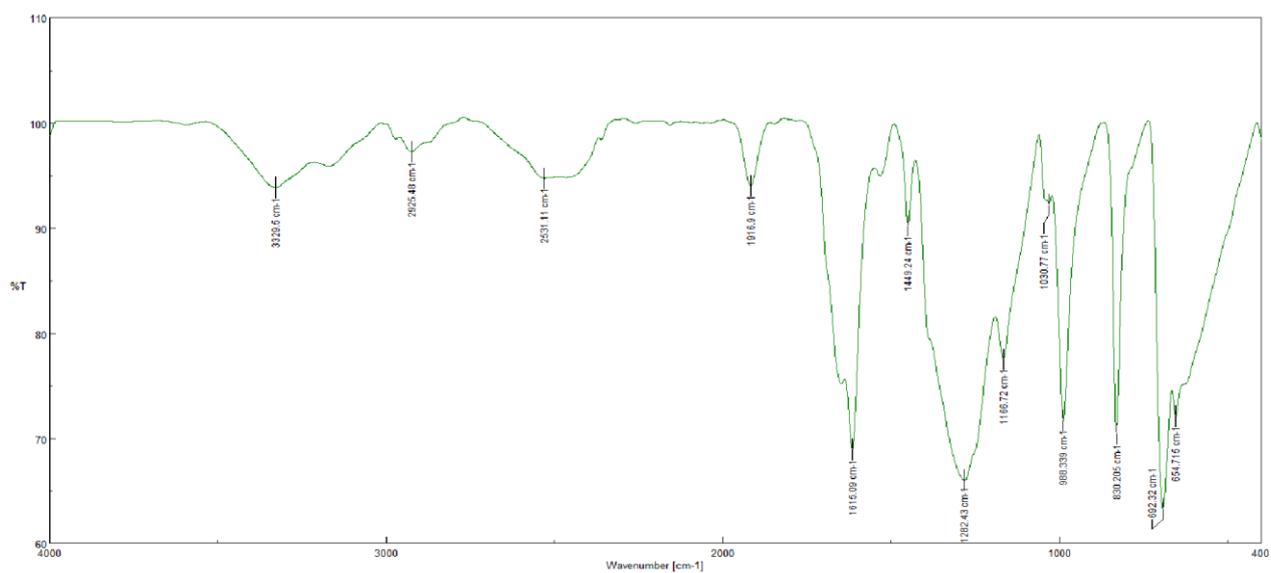


Figure 23c. IR NMR spectrum of bis-1-(4-((tert-butoxycarbonyl)amino)butyl)guanidinium carbonate (**8f**)

¹H NMR (600 MHz, DMSO-*d*₆)

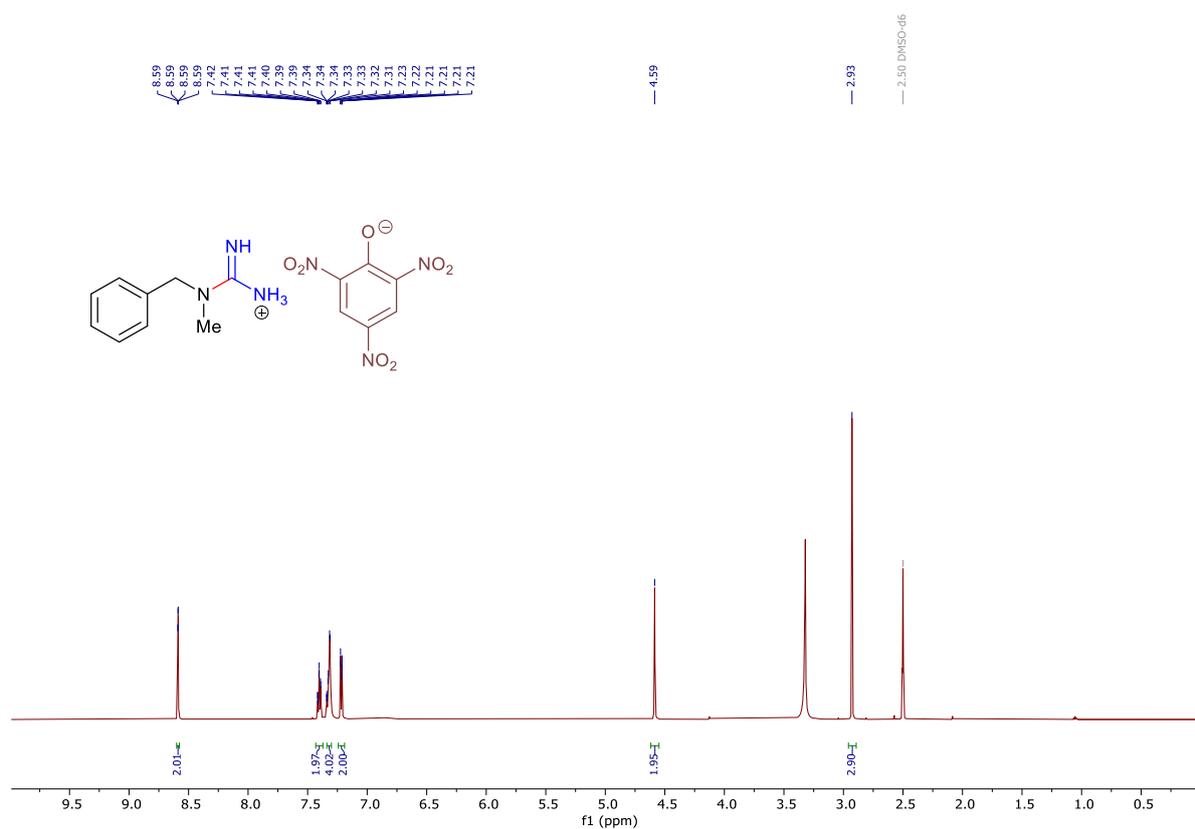


Figure 24a. ¹H NMR spectrum of 1-benzyl-1-methylguanidinium 2,4,6-trinitrophenolate (**11a**)

¹³C NMR (151 MHz, DMSO-*d*₆)

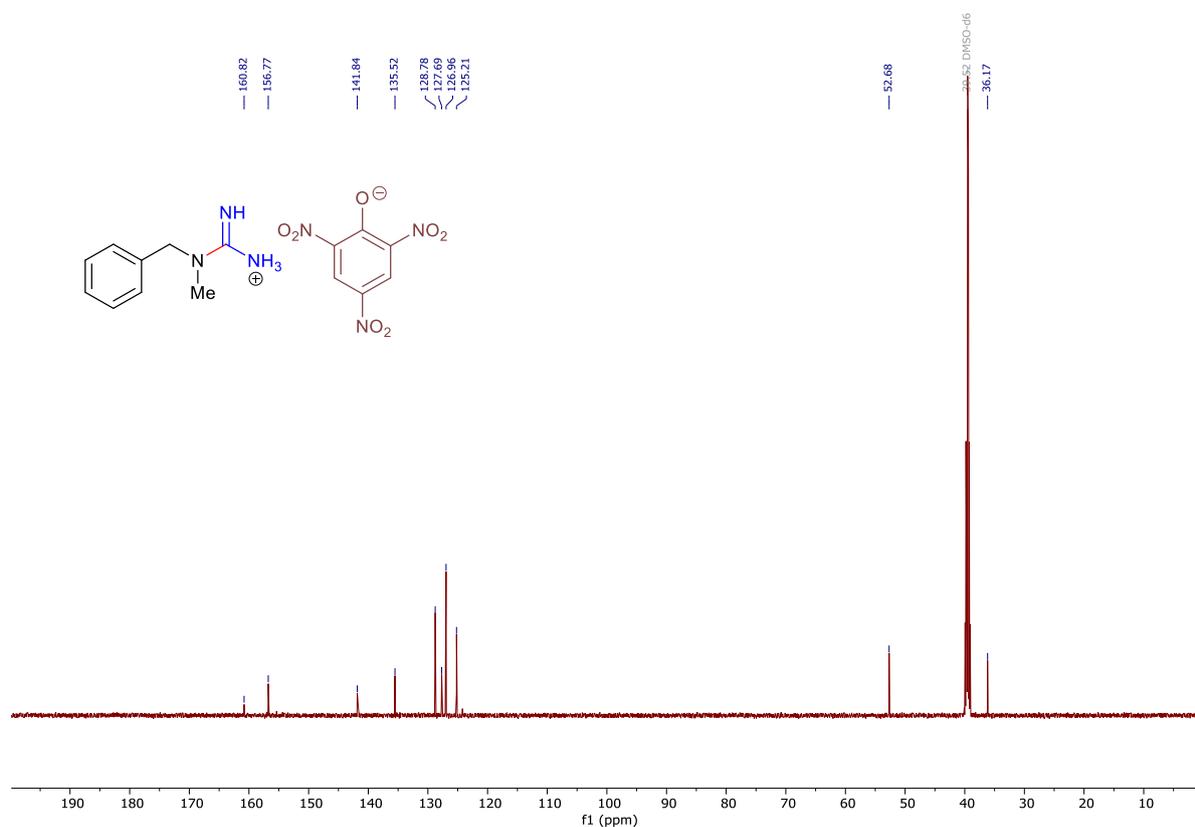


Figure 24b. ¹³C NMR spectrum of 1-benzyl-1-methylguanidinium 2,4,6-trinitrophenolate (**11a**)

¹H NMR (600 MHz, DMSO-*d*₆)

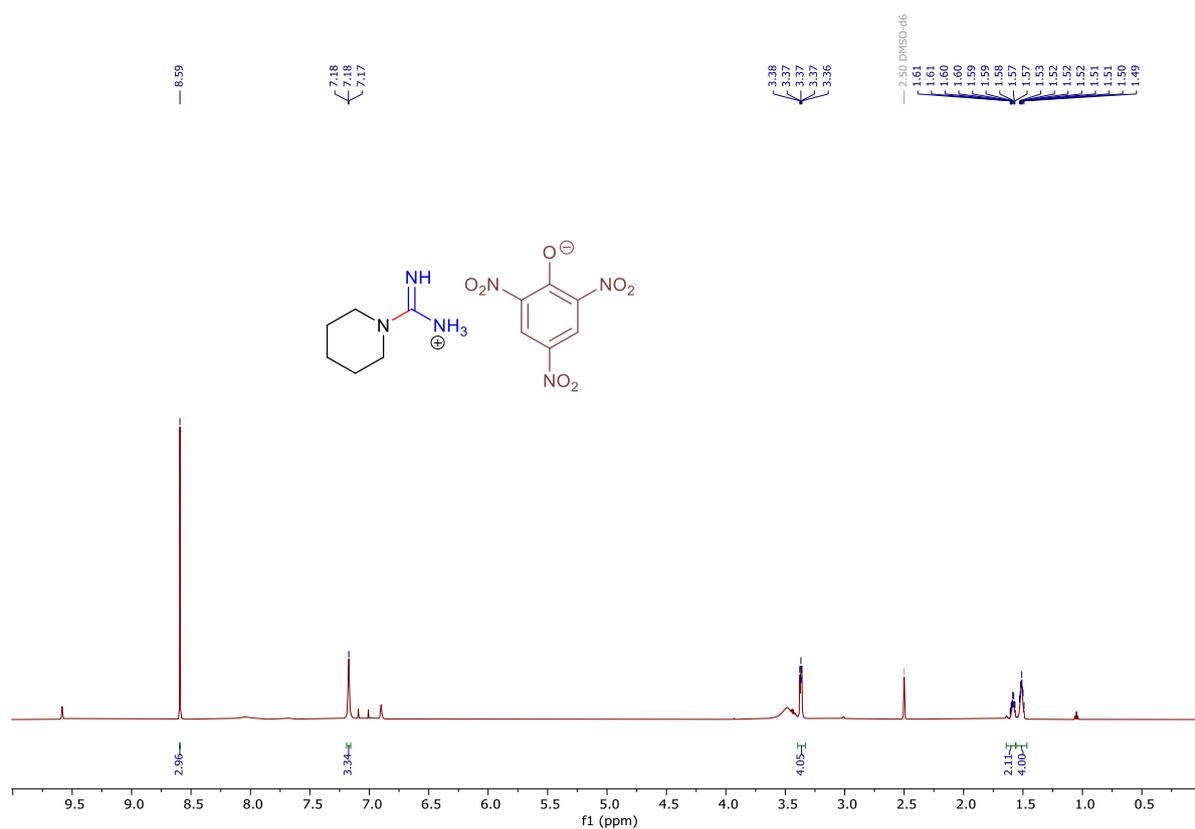


Figure 25a. ¹H NMR spectrum of 1-carbamimidoylpiperidin-1-ium 2,4,6-trinitrophenolate (**11b**)

¹³C NMR (151 MHz, DMSO-*d*₆)

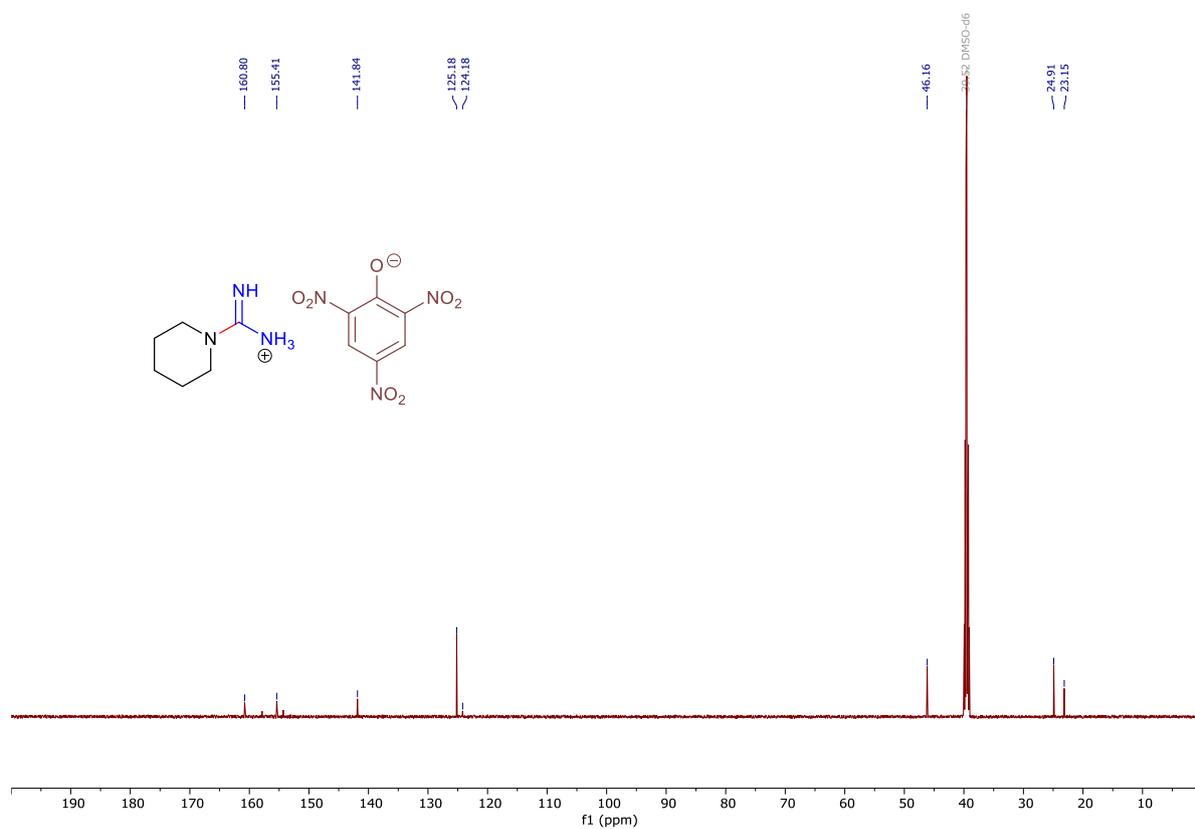


Figure 25b. ¹³C NMR spectrum of 1-carbamimidoylpiperidin-1-ium 2,4,6-trinitrophenolate (**11b**)

¹H NMR (600 MHz, DMSO-*d*₆)

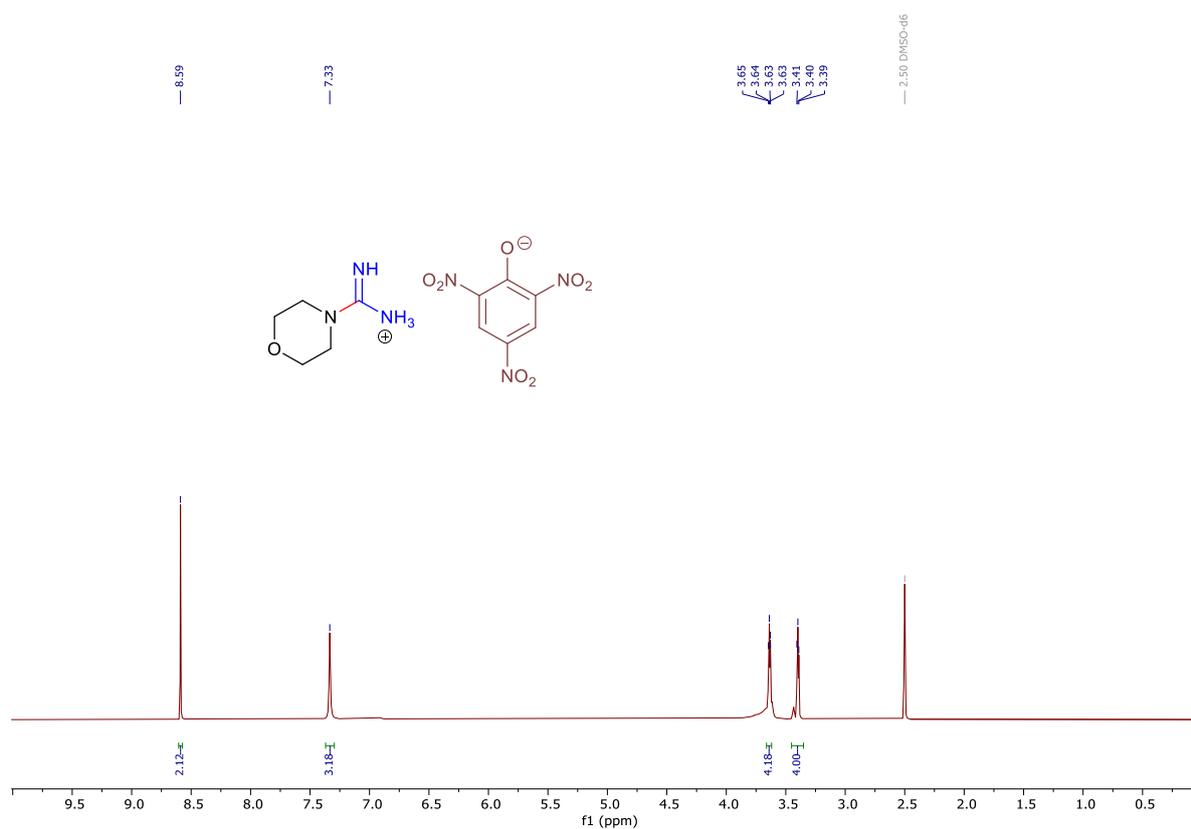


Figure 26a. ¹H NMR spectrum of 4-carbamimidoylmorpholin-4-ium 2,4,6-trinitrophenolate (**11c**)

¹³C NMR (151 MHz, DMSO-*d*₆)

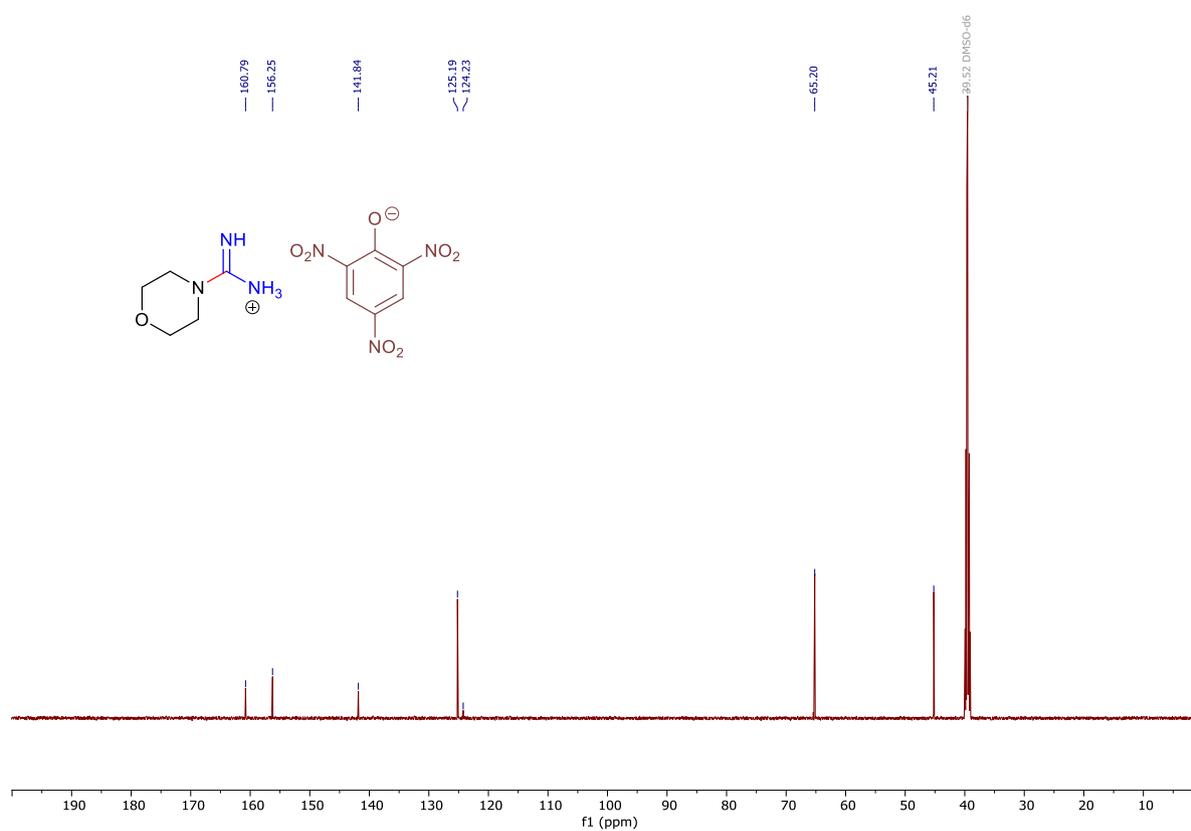


Figure 26b. ¹³C NMR spectrum of 4-carbamimidoylmorpholin-4-ium 2,4,6-trinitrophenolate (**11c**)

¹H NMR (600 MHz, DMSO-*d*₆)

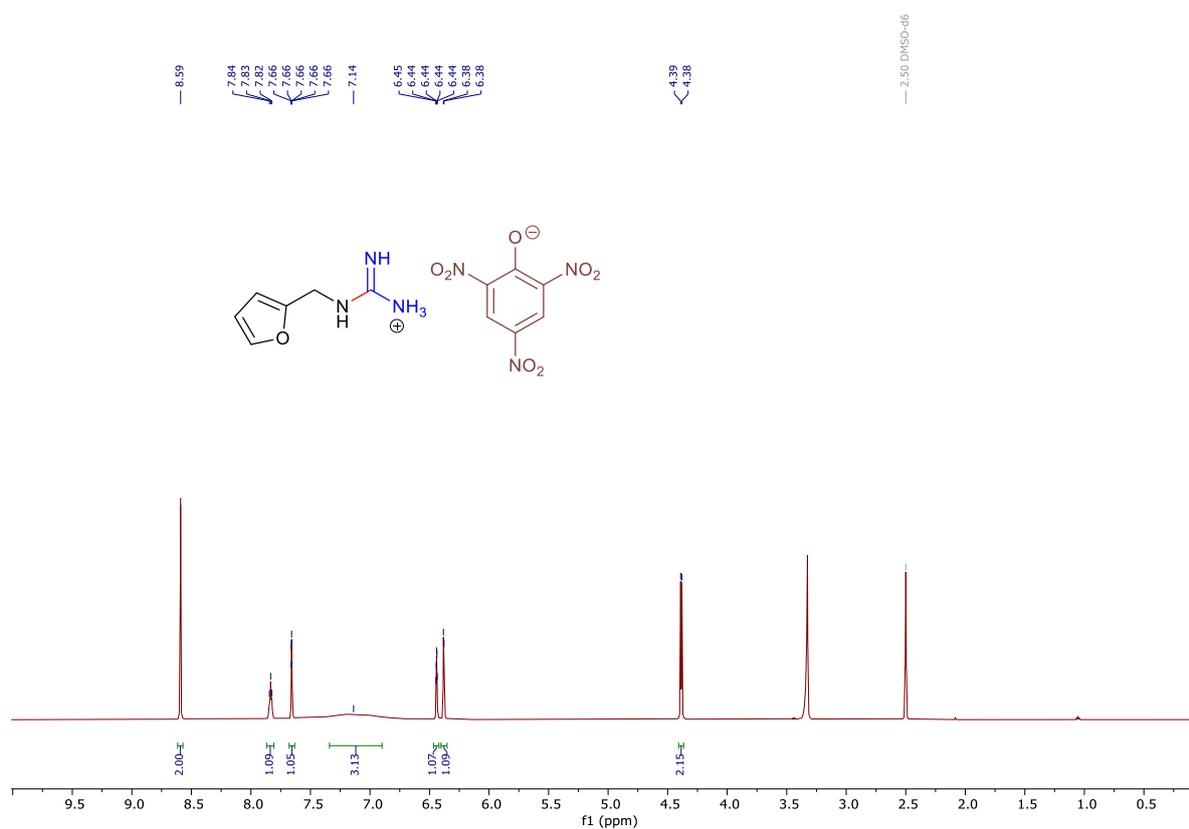


Figure 27a. ¹H NMR spectrum of 1-(furan-2-ylmethyl)guanidinium 2,4,6-trinitrophenolate (**5h**)

¹³C NMR (151 MHz, DMSO-*d*₆)

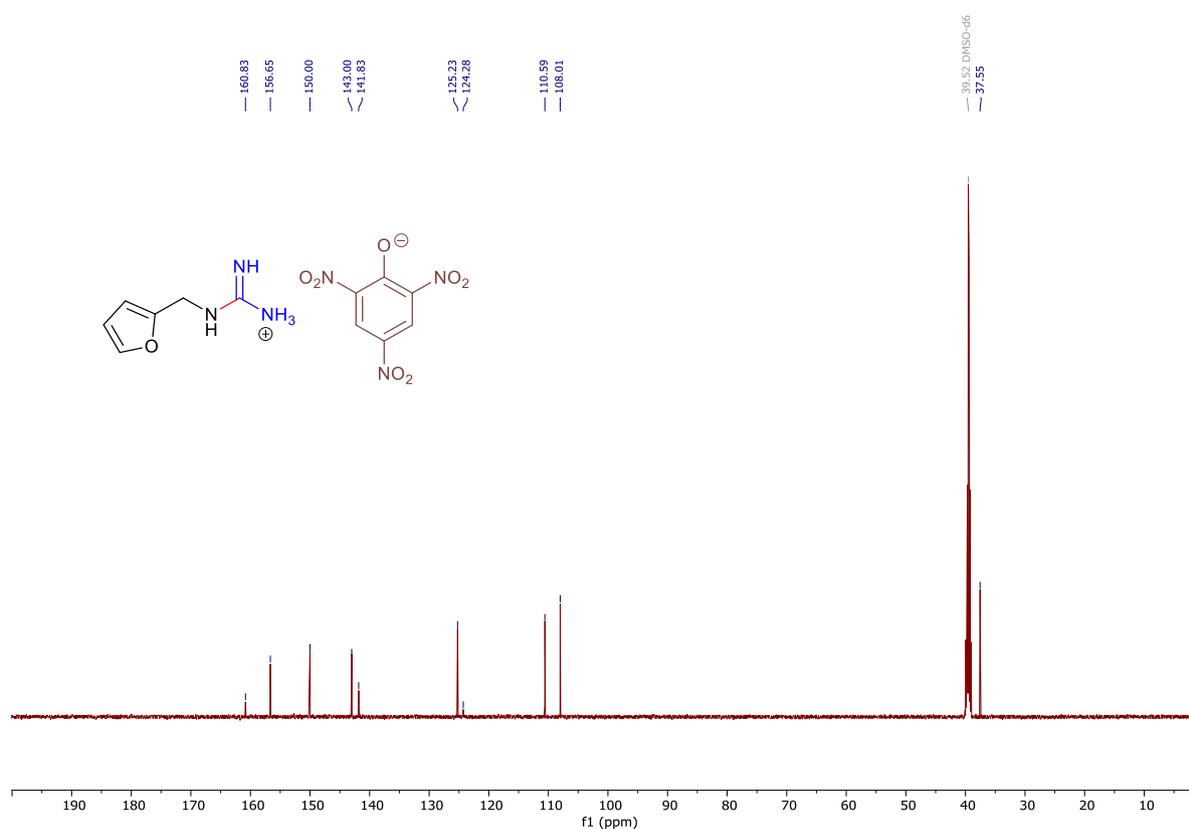


Figure 27b. ¹³C NMR spectrum of 1-(furan-2-ylmethyl)guanidinium 2,4,6-trinitrophenolate (**5h**)

¹H NMR (600 MHz, DMSO-*d*₆)

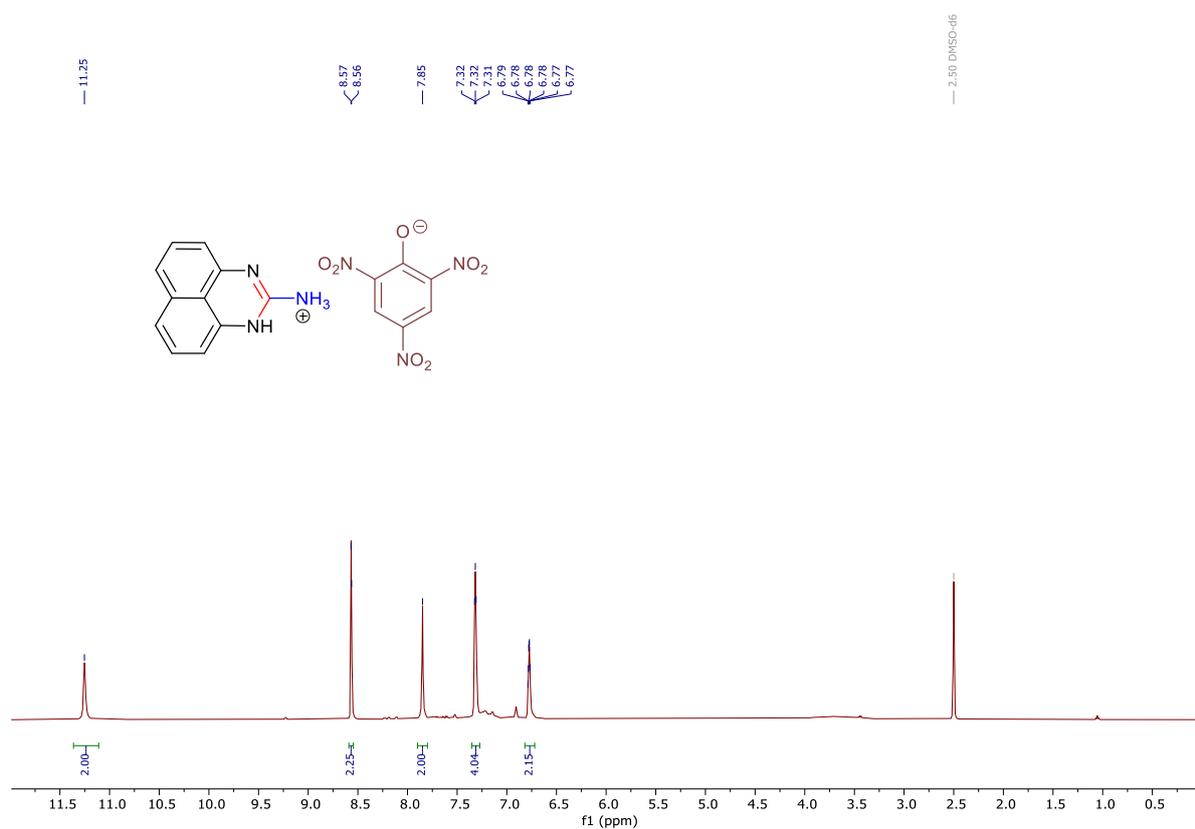


Figure 28a. ¹H NMR spectrum of 1H-perimidin-2-aminium 2,4,6-trinitrophenolate (**12a**)

¹³C NMR (151 MHz, DMSO-*d*₆)

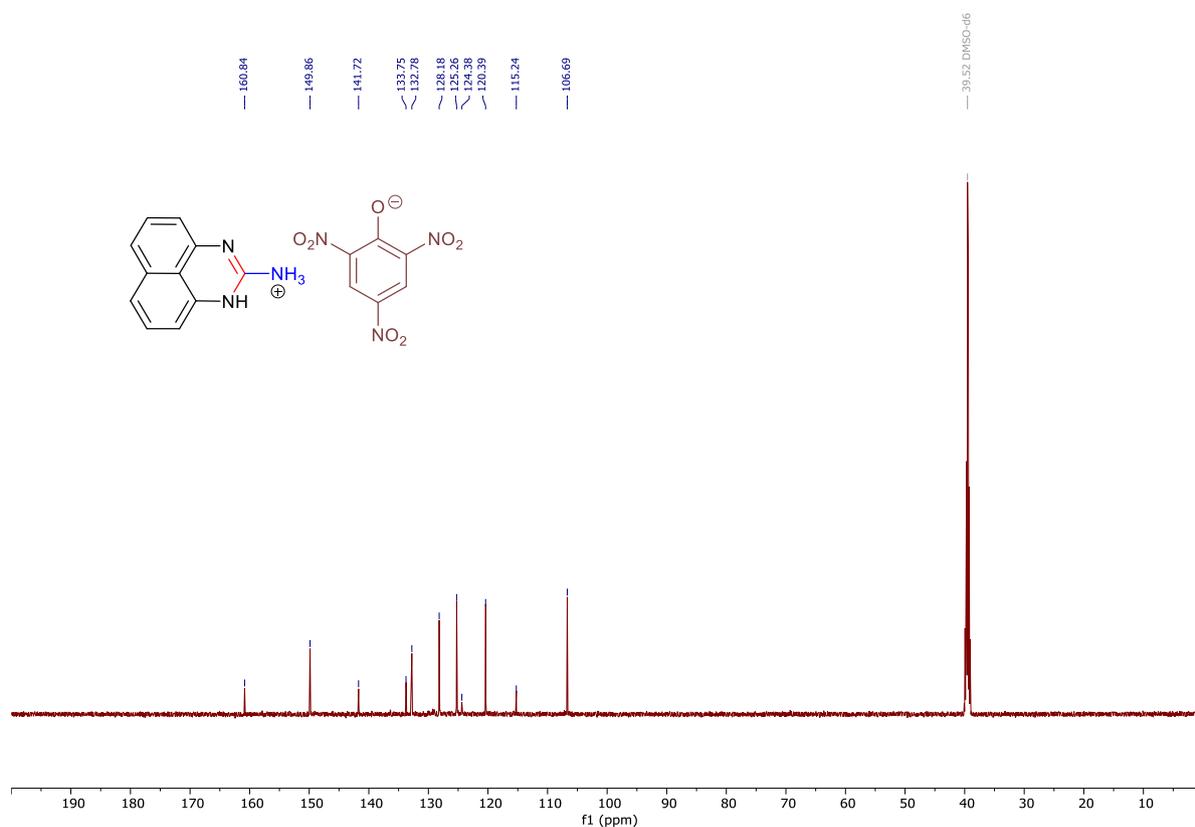


Figure 28b. ¹³C NMR spectrum of 1H-perimidin-2-aminium 2,4,6-trinitrophenolate (**12a**)

¹H NMR (600 MHz, CDCl₃)

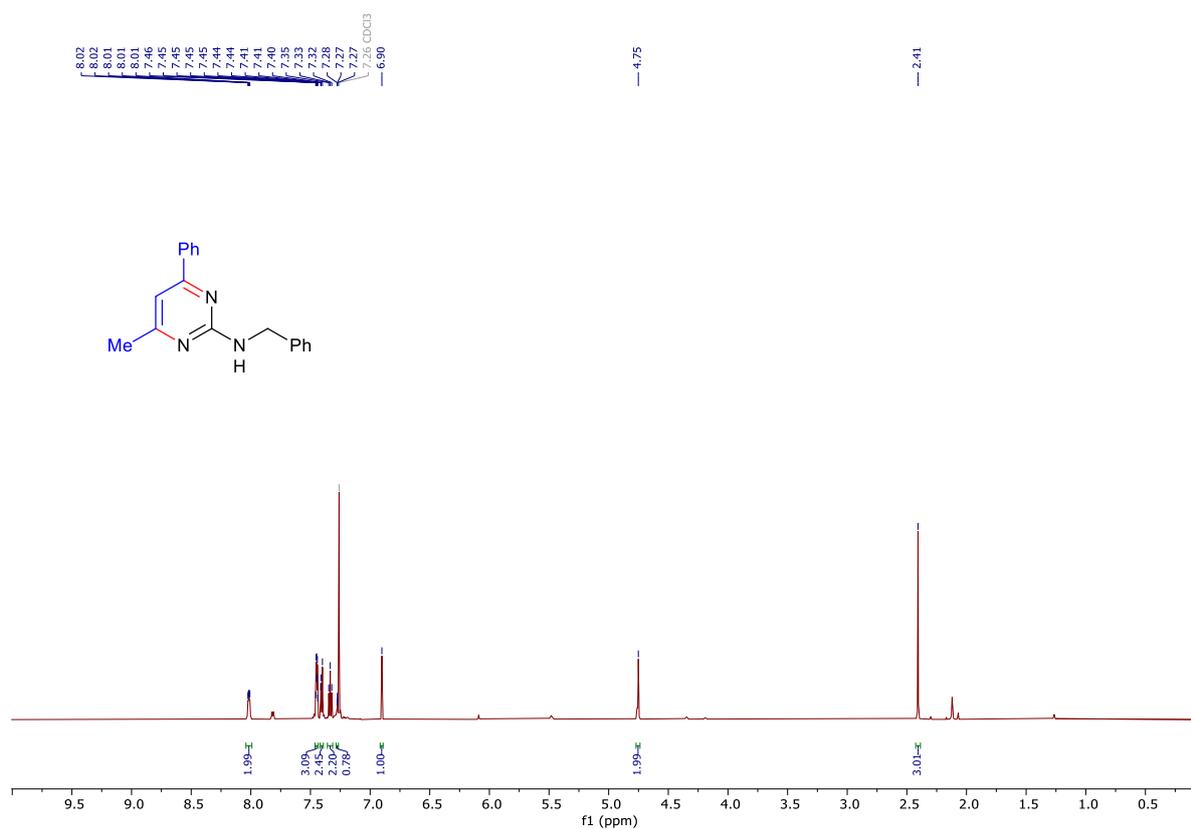


Figure 29a. ¹H NMR spectrum of *N*-benzyl-4-methyl-6-phenylpyrimidin-2-amine (**14a**)

¹³C NMR (151 MHz, CDCl₃)

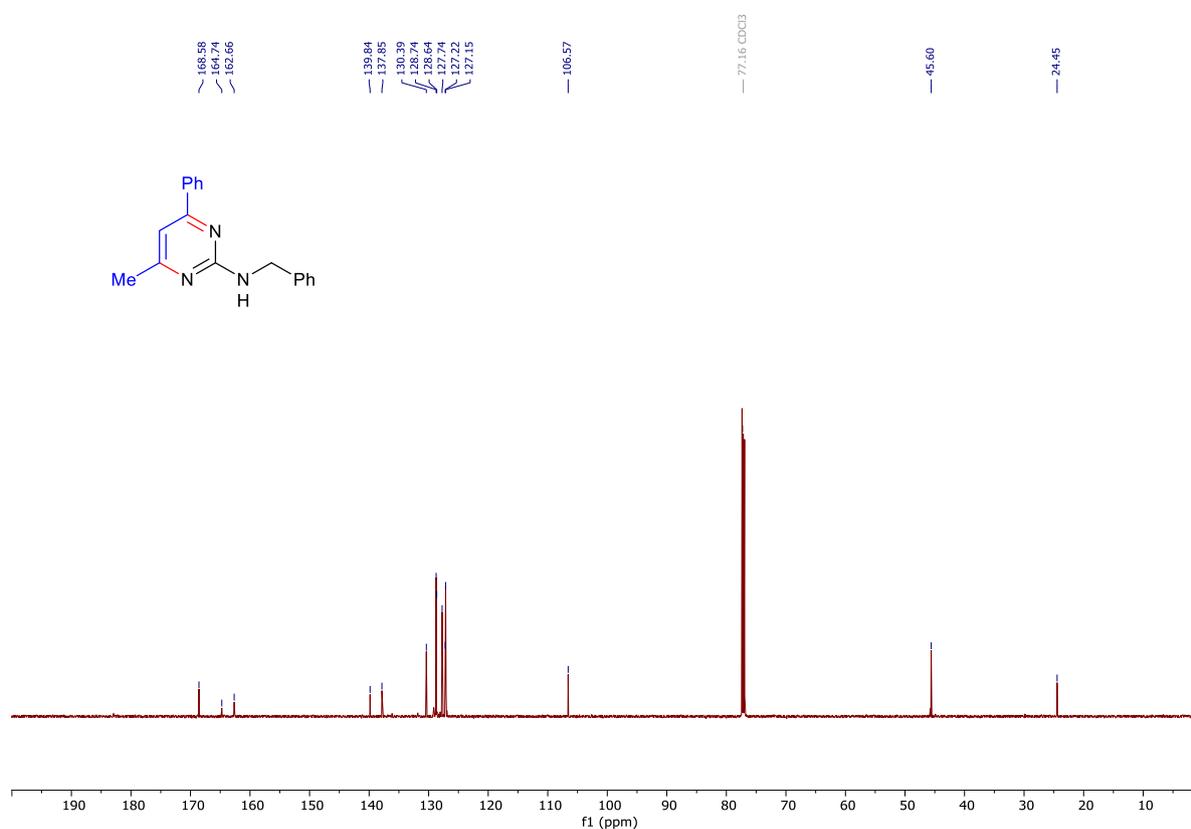


Figure 29b. ¹³C NMR spectrum of *N*-benzyl-4-methyl-6-phenylpyrimidin-2-amine (**14a**)

¹H NMR (600 MHz, CDCl₃)

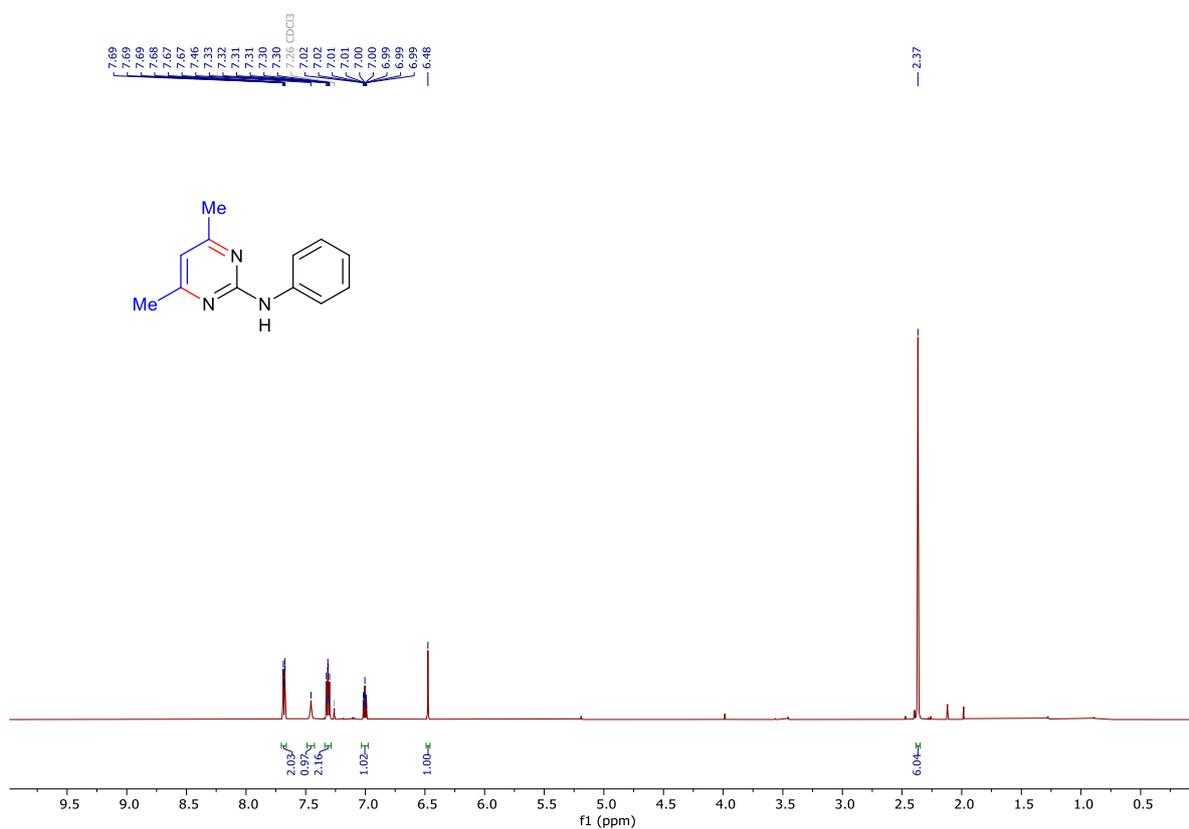


Figure 30a. ¹H NMR spectrum of 4,6-dimethyl-N-phenylpyrimidin-2-amine (14b)

¹³C NMR (151 MHz, CDCl₃)

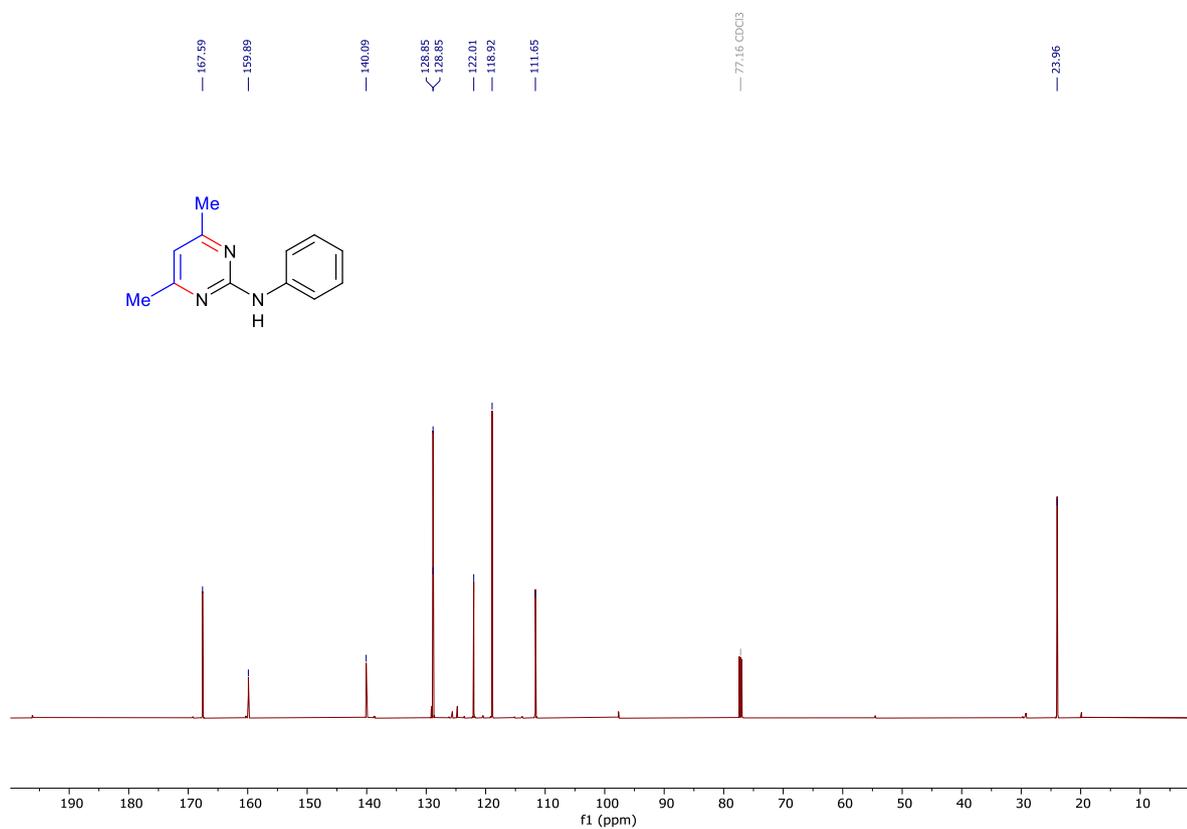


Figure 30b. ¹³C NMR spectrum of 4,6-dimethyl-N-phenylpyrimidin-2-amine (14b)

¹H NMR (600 MHz, CDCl₃)

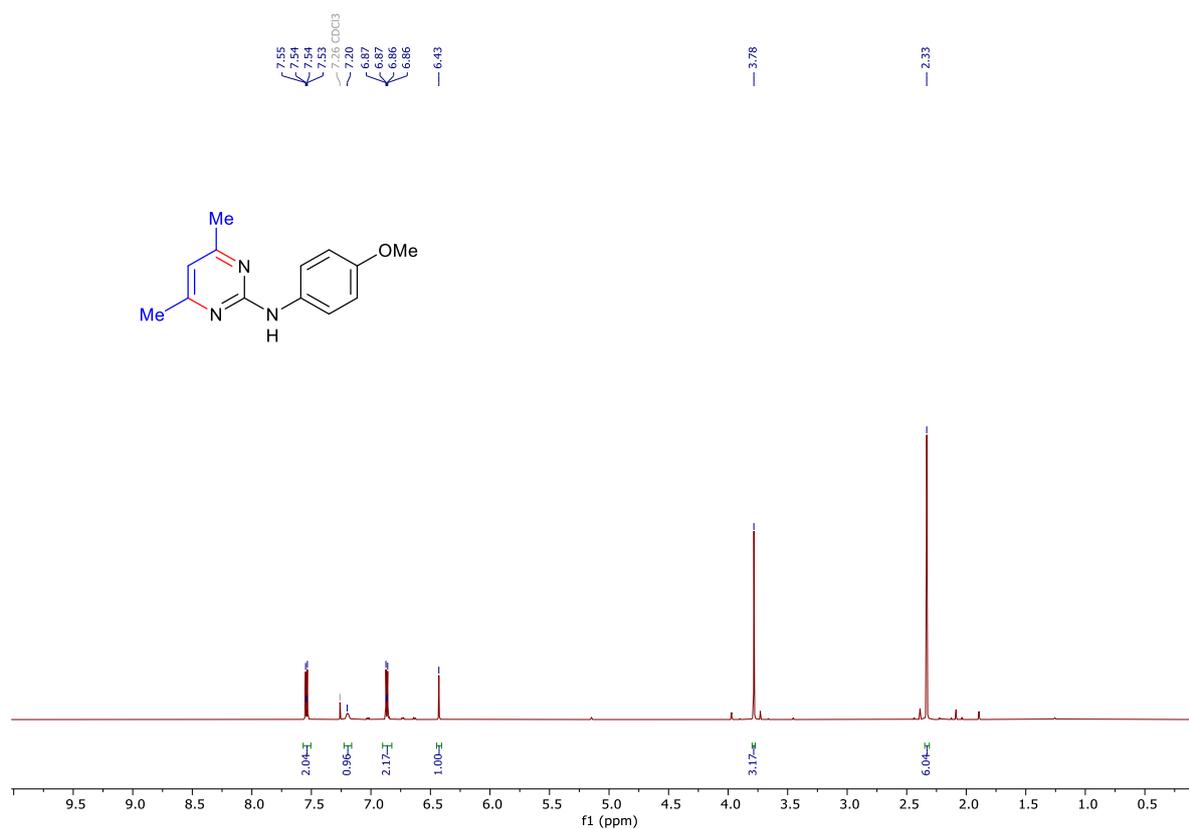


Figure 31a. ¹H NMR spectrum of *N*-(4-methoxyphenyl)-4,6-dimethylpyrimidin-2-amine (14c)

¹³C NMR (151 MHz, CDCl₃)

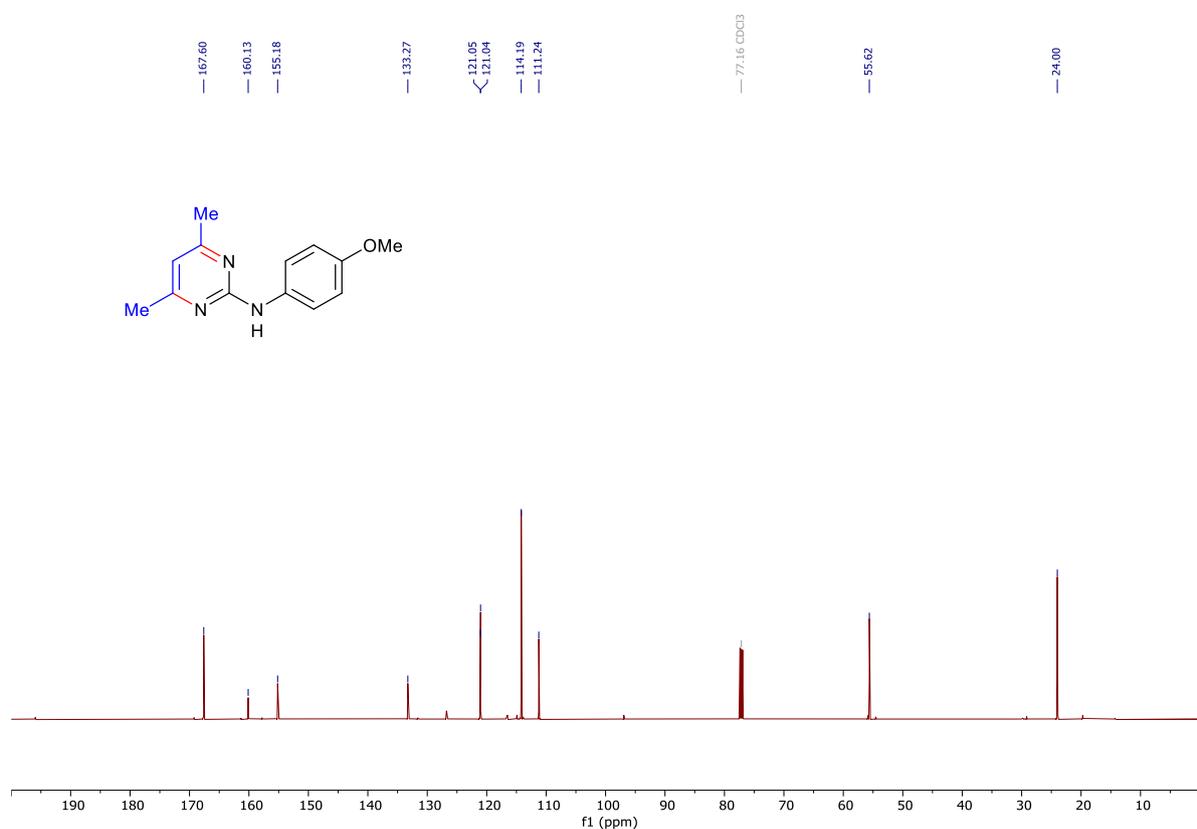


Figure 31b. ¹³C NMR spectrum of *N*-(4-methoxyphenyl)-4,6-dimethylpyrimidin-2-amine (14c)

1. T. An; Y. Lee *Org. Lett.* **2021**, *23*, 9163-9167.
2. S. Goswami; A. Hazra; S. Jana *Bull. Chem. Soc. Jpn.* **2009**, *82*, 1175-1181.
3. K. Tsubokura; T. Iwata; M. Taichi; A. Kurbangaliev; K. Fukase; Y. Nakao; K. Tanaka *Synlett* **2014**, *25*, 1302-1306.
4. S. Revathi; A. L. Shinde; M. K. Rajashekhar; D. Mandal; A. R. Maity; S. Garai; T. Ghatak *Chemical Communications* **2023**, *59*, 12699-12702.