Electrochemical NaI-mediated one-pot synthesis of guanidines from isothiocyanates *via* tandem addition-guanylation

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Electronic Supplementary Information

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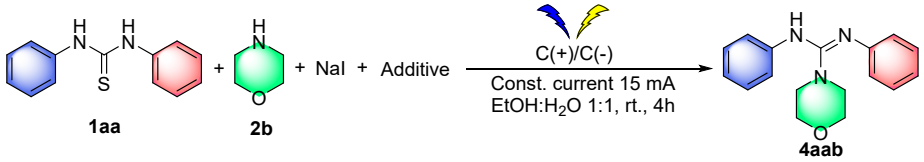
Table S1. Additive screening



Entry	Additive	Yield(%)[b]
1	NaCl	40
2	$LiClO_4$	58
3	$TBABF_4$	29
4	NaOH	63
5	K_2CO_3	62
6	Cs_2CO_3	42
7	Et_3N	50
8	DBU	61
9	**DIPEA**	**69**

Reaction conditions: **1aa** (0.5 mmol, 1.0 eq.), **2b** (0.75 mmol, 1.5 eq.), NaI (0.5 mmol, 1.0 eq.), additive (0.5 mmol, 1.0 eq.), graphite rod (ϕ 5 mm, 20 mm immersion depth) as both cathode and anode, constant current 15 mA (4.5 F/mol), EtOH 2.5 mL, water 2.5 mL, room temperature, 4 hrs., undivided cell.

Faradaic efficiency calculation for the model substrate **4aab**:

$$Faradaic\ efficiency = \frac{Q_{experimental}}{Q_{theoretical}} \times 100$$

$$Faradaic\ efficiency = \frac{z \times n \times F}{Q_{theoretical}} \times 100$$

With z = number of electron that the reaction used = 2

n = mol of product that obtained = 0.5 x 80% = 0.4 mmol

F = Faradaic constant (96485 C/mol)

$Q_{theoretical}$ can be calculated from I (current, Ampere) x t (reaction time, second)

$$Faradaic\ efficiency = \frac{2 \times 0.4 \times 10^{-3} \times 96485}{0.015 \times 7200} \times 100$$

$$Faradaic\ efficiency = 72\ \%$$

Experimental Section

Materials and methods

All chemicals and solvents were obtained from commercially available suppliers such as Sigma-Aldrich and TCI (Japan) and were used without further purification, unless otherwise stated. Pyrex reactor (ϕ = 2.0 cm, Height = 6.2 cm) was used for electrochemical reaction. Power supply (KORAD, KA3005D) was purchased from Shenzhen Korad Technology CO., LTD. All electrodes such as graphite rod (ϕ = 5 mm) and platinum plate (5x5x0.1 mm) were purchased from Minihua Store, China. Electrochemical reaction setup was depicted in Figures S1-S3. Analytical thin layer chromatography (TLC) was performed with precoated Merck silica gel 60 F254 plates (0.25 mm for thick layer) and visualized at 254 nm using an ultraviolet lamp. Column chromatography was performed with Silicycle silica gel 60-200 μm (70-230 mesh). ^{1}H-NMR, ^{13}C-NMR spectra were obtained with JEOL JNM-ECZ500R/S1 NMR spectrometers operating at 500 MHz for ^{1}H or 125 MHz for ^{13}C nuclei or 470 MHZ for ^{19}F nuclei. Melting points are measured with Barnstead international mel-temp meliting point apparatus model 1201D. High-resolution mass spectra (HRMS) were recorded using electron spray ionization (ESI) with a MicroTOF Bruker mass spectrometer.

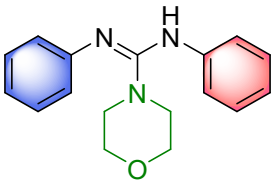
General procedure for synthesis of guanidine from thiourea (General Procedure A)

A mixture of thiourea **1** (1.0 eq., 0.5 mmol), amines **2** (3.0 eq., 1.5 mmol), sodium iodide (1.0 eq., 0.5 mmol), and DIPEA (1.0 eq., 0.5 mmol) were dissolved in mixed 2.5 mL of water with 2.5 mL of ethanol in a Pyrex reactor (ϕ = 2.0 cm, height = 6.2 cm). The reaction mixture was electrolysed at a constant current of 15 mA (4.5 F/mol), graphite rods as both cathode and anode (ϕ = 20 mm, about 20 mm immersion depth in solution) at room temperature for 4 hours. After the reaction, the crude mixture was extracted with water and ethyl acetate. The organic layer was evaporated under reduced pressure to give the crude product, which was further

purified by column chromatography (eluted with ethyl acetate/hexane) to afford the desired compound.

General procedure for synthesis of guanidine from amines and isothiocyanate (General Procedure B)

A mixture of amines **2** (1.0 eq., 0.5 mmol), isothiocyanates **3** (1.0 eq., 0.5 mmol), were dissolved in 2.5 mL of ethanol in a Pyrex reactor (ϕ = 2.0 cm, height = 6.2 cm) and was allowed to stir without electricity for 1 hours at room temperature. After that, sodium iodide (1.0 eq., 0.5 mmol) in 2.5 mL of water, DIPEA (1.0 eq., 0.5 mmol), and amines **2** (3.0 eq., 1.5 mmol) were added to the solution. The reaction mixture was electrolysed at a constant current of 15 mA (4.5 F/mol), graphite rods as both cathode and anode (ϕ = 20 mm, about 20 mm immersion depth in solution) at room temperature for 4 hours. After the reaction, the crude mixture was extracted with water and ethyl acetate. The organic layer was evaporated under reduced pressure to give the crude product, which was further purified by column chromatography (eluted with ethyl acetate/hexane) to afford the desired compound.

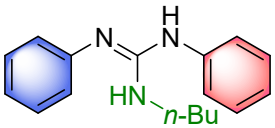


4aab

N,*N*′-diphenylmorpholine-4-carboximidamide (**4aab**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aab** (108.1 mg, 0.385 mmol, 77%) as a yellow solid; Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aab** (112.2 mg, 0.4 mmol, 80%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$)

δ ppm 7.25 (t, J = 7.8 Hz, 4H), 7.0-6.94 (m, 6H), 3.68 (t, J = 4.8 Hz, 4H), 3.34 (t, J = 4.8 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 151.0, 129.5, 122.7, 66.5, 47.1. Melting point: 133-134^{o}C. Data is consistent with reported literatures.[1-3]

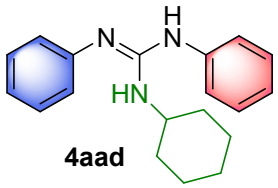
For gram-scale synthesis: A mixture of aniline **2a** (1.0 eq., 466.0 mg, 5.0 mmol), phenyl isothiocyanate **3a** (1.0 eq., 675 mg, 5.0 mmol), was dissolved in 25 mL of ethanol and stir at room temperature for 2 hours in a 100 mL three-necked round bottom flask. After that, sodium iodide (1.0 eq., 749.5 mg, 5.0 mmol) in 25 mL of water, DIPEA (1.0 eq., 646.0 mg, 5.0 mmol), and morpholine **2b** (3.0 eq., 1.307 g, 15 mmol) were added in the flask. The reaction mixture was then electrolysed at a constant current of 30 mA (4.5 F/mol), graphite rods as both cathode and anode at room temperature for 20 hours. The reaction was extracted with water and ethyl acetate. The organic layer was evaporated under reduced pressure to give the crude product, which was further purified by column chromatography in ethyl acetate/hexane to afford the desired compound (1.0011 g, 3.55 mmol, 71%).



4aac

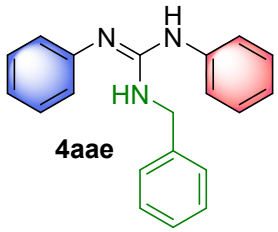
1-butyl-2,3-diphenylguanidine (**4aac**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), *n*-butylamine **2c** (109.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aac** (65.2 mg, 0.245 mmol, 49%) as a brown solid; Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), *n*-butylamine **2c** (109.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aac** (71.9 mg, 0.27 mmol, 54%) as a light brown solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.31-7.28 (m, 4H), 7.05-7.02 (m, 6H), 3.31 (t, J = 7.3 Hz, 2H), 1.57-1.51 (m, 2H), 1.4-1.32 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 148.6, 138.3, 129.5,

123.2, 123.1, 41.7, 31.8, 20.3, 14.0. Melting point: 68-69°C. Data is consistent with reported literatures.[1-3]



4aad

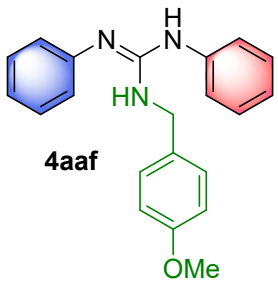
1-cyclohexyl-2,3-diphenylguanidine (**4aad**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), cyclohexylamine **2d** (144.8 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aad** (92.1 mg, 0.315 mmol, 63%) as a yellow solid; Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), cyclohexylamine **2d** (144.8 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aad** (127.5 mg, 0.435 mmol, 87%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.29 (t, J = 7.9 Hz, 4H), 7.03 (d, J = 7.9 Hz, 2H), 3.76 (b, 1H), 2.09 (d, J = 9.5 Hz, 2H), 1.71-1.67 (m, 2H), 1.62-1.58 (m, 1H), 1.43-1.34 (m, 2H), 1.2-1.09 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 147.5, 129.5, 129.2, 123.0, 49.9, 33.5, 25.8, 25.0. Melting point: 141-142°C. Data is consistent with reported literatures.[1-3]



4aae

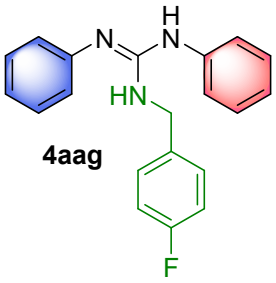
1-benzyl-2,3-diphenylguanidine (**4aae**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), benzylamine **2e** (160.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aae** (90.1 mg, 0.3 mmol, 60%) as a yellow solid;

Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), benzylamine **2e** (160.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aae** (132.5 mg, 0.44 mmol, 88%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.39-7.36 (m, 4H), 7.33-7.3 (m, 5H), 7.09-7.04 (m, 6H), 4.56 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 148.3, 139.1 129.6, 128.7, 127.8, 127.4, 123.2, 45.9. Melting point: 98-99^{o}C. Data is consistent with reported literatures.[1,2]



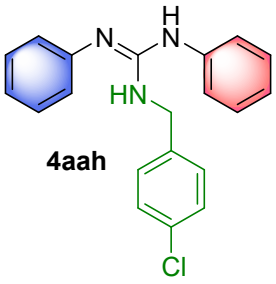
4aaf

1-(4-methoxybenzyl)-2,3-diphenylguanidine (**4aaf**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), 4-methoxybenzylamine **2f** (205.8 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aaf** (88.4 mg, 0.265 mmol, 53%) as a yellow solid; Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), 4-methoxybenzylamine **2f** (205.8 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aaf** (160.3 mg, 0.485 mmol, 97%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.31-7.28 (m, 6H), 7.06-7.02 (m, 6H), 6.89-6.87 (m, 2H), 4.47 (s, 2H), 3.81 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 159.0, 148.3, 131.2, 129.6, 129.2, 123.2, 114.1, 55.4, 45.5. Melting point: 115-116^{o}C. Data is consistent with reported literatures.[2]



4aag

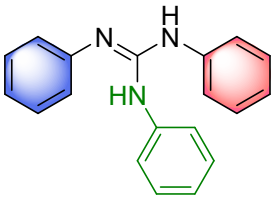
1-(4-fluorobenzyl)-2,3-diphenylguanidine (**4aag**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), 4-fluorobenzylamine **2g** (188.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aag** (110.9 mg, 0.35 mmol, 70%) as a yellow solid; Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), 4-fluorobenzylamine **2g** (188.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aag** (132.8 mg, 0.415 mmol, 83%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.37-7.31 (m, 6H), 7.09-7.03 (m, 8H), 4.53 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 163.2, 161.2, 154.0, 148.2, 135.1, 129.7, 129.5 (d, J = 7.5 Hz), 116.3, 115.5, 45.2. ESI-MS: m/z: 320.15706 $[M+H]^+$ (calcd for $[C_{20}H_{19}FN_3]^+$ 320.15630).



4aah

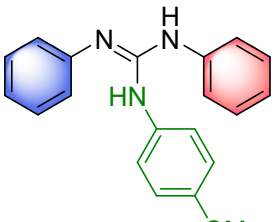
1-(4-chlorobenzyl)-2,3-diphenylguanidine (**4aah**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), 4-chlorobenzylamine **2h** (212.4 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aah** (107.1 mg, 0.32 mmol, 64%) as a white solid; Synthesized according to the General procedure B using aniline

2a (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), 4-chlorobenzylamine **2h** (212.4 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aah** (154.2 mg, 0.46 mmol, 92%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.31 (t, J = 7.8 Hz, 8H), 7.08-7.04 (m, 6H), 4.51 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 148.1, 137.9, 133.0, 129.6, 129.1, 128.8, 123.3, 45.1. Melting point: 117-118°C. Data is consistent with reported literatures.[2]



4aaa

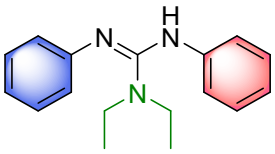
1,2,3-triphenylguanidine (**4aaa**) Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), aniline **2a** (139.8 mg, 1.5 mmol), sodium iodide (149.9 mg, 1.0 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aaa** (88.5 mg, 0.31 mmol, 62%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.33 (t, J = 7.9 Hz, 6H), 7.23 (b, 6H), 7.07 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 145.0, 129.5, 123.3, 121.7; ^{13}C NMR (125 MHz, CD_3OD + 0.1% TFA): δ ppm 151.0, 142.6, 130.1, 124.5, 122.5. Melting point: 145-146°C. ESI-MS: m/z: 288.15092 $[M+H]^+$ (calcd for $[C_{19}H_{18}N_3]^+$ 288.15007). Data is consistent with reported literatures.[3]



4aai

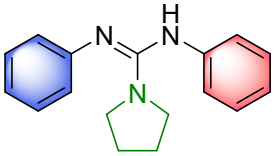
1-(4-methoxyphenyl)-2,3-diphenylguanidine (**4aai**) Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg,

0.5 mmol), *p*-anisidine **2i** (184.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aai** (90.1 mg, 0.285 mmol, 57%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.32-7.28 (m, 4H), 7.22 (b, 4H), 7.14 (d, *J* = 8.7 Hz, 2H), 7.04 (t, *J* = 7.3 Hz, 2H), 6.88-6.86 (m, 2H), 3.79 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 145.8, 129.4, 123.1, 121.6, 114.8, 55.6. Data is consistent with reported literatures.[2,3]



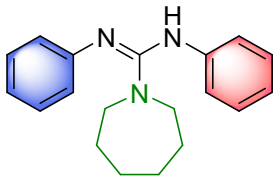
4aal

1,1-diethyl-2,3-diphenylguanidine (**4aal**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), diethylamine **2l** (109.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aal** (83.6 mg, 0.315 mmol, 63%) as a yellow solid; Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), diethylamine **2l** (109.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aal** (136.4 mg, 0.44 mmol, 88%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.22 (t, *J* = 7.7 Hz, 4H), 6.95 (t, *J* = 7.3 Hz, 2H), 6.88 (d, *J* = 7.5 Hz, 4H), 3.34 (q, *J* = 7.1 Hz, 4H), 1.17 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 150.3, 129.3, 122.0, 42.1, 13.0. Melting point: 94-95°C. Data is consistent with reported literatures.[1,2]



4aam

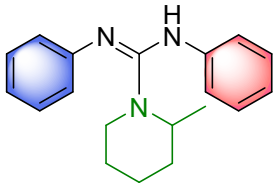
N,*N*′-diphenylpyrrolidine-1-carboximidamide (**4aam**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), pyrrolidine **2m** (106.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aam** (74.1 mg, 0.28 mmol, 56%) as a yellow solid; Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), pyrrolidine **2m** (106.7 mg, 1.5 mmol), sodium iodide (149.9 mg, 1.0 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aam** (88.2 mg, 0.335 mmol, 67%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.22-7.18 (m, 4H), 7.0-6.96 (m, 6H), 3.30 (t, *J* = 6.4 Hz, 4H), 1.82-1.80 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 150.7, 141.3, 129.4, 123.9, 121.5, 48.7, 25.2. Data is consistent with reported literatures.[1-3]



4aan

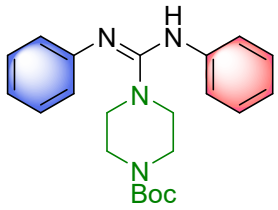
N,*N*′-diphenylazepane-1-carboximidamide (**4aan**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), azepane **2n** (148.8 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aan** (111.6 mg, 0.38 mmol, 76%) as a yellow solid; Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), azepane **2n** (148.8 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aan** (127.2 mg, 0.435 mmol, 87%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.23 (t, *J* = 7.8 Hz, 4H), 6.97 (t, *J* = 7.4 Hz, 2H), 6.96-6.86 (m, 4H), 3.48 (t, *J* =

5.8 Hz, 4H), 1.78-1.77 (m, 4H), 1.65-1.63 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 150.9, 129.3, 121.9, 48.8, 28.3, 27.9. Data is consistent with reported literatures.[1,2]



4aao

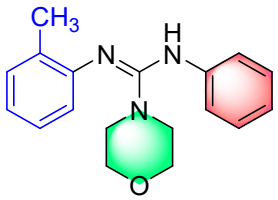
2-Methyl-*N*,*N*′-diphenylpiperidine-1-carboximidamide (**4aao**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), 2-methylpiperidine **2o** (148.8 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aao** (102.3 mg, 0.35 mmol, 70%) as a yellow solid; Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), 2-methylpiperidine **2o** (148.8 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aao** (122.6 mg, 0.42 mmol, 84%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.23 (t, J = 7.8 Hz, 4H), 6.95-6.91 (m, 6H), 4.14-4.12 (m, 1H), 3.71-3.68 (m, 1H), 3.05-2.99 (m, 1H), 1.75-1.69 (m, 1H), 1.66-1.60 (m, 3H), 1.56-1.50 (m, 1H), 1.45-1.42 (m, 1H), 1.21 (d, J = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 150.8, 129.3, 122.0, 48.8, 41.4, 29.9, 25.6, 19.1, 14.6. Data is consistent with reported literatures.[1,2]



4aap

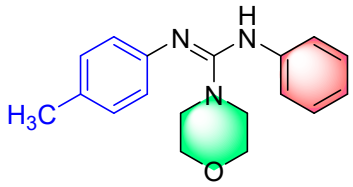
tert-Butyl-4-(N,*N*′-diphenylcarbamimidoyl)piperazine-1-carboxylate (**4aap**)

Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), *tert*-butyl piperazine-1-carboxylate **2p** (279.4 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4aap** (74.2 mg, 0.195 mmol, 39%) as a yellow solid; Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), *tert*-butyl piperazine-1-carboxylate **2p** (279.4 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aap** (139.4 mg, 0.365 mmol, 73%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.25 (t, *J* = 7.6 Hz, 4H), 6.99-6.92 (m, 6H), 3.42-3.40 (m, 4H), 3.32-3.30 (m, 4H), 1.46 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 154.9, 151.0, 129.5, 122.7, 121.6, 80.1, 46.5, 28.5. Melting point: 125-126°C. Data is consistent with reported literatures.[1,2]



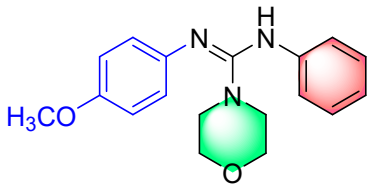
4qab

N-phenyl-*N*′-(*o*-tolyl)morpholine-4-carboximidamide (**4qab**) Synthesized according to the General procedure B using *o*-toluidine **2q** (53.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4qab** (127.8 mg, 0.435 mmol, 87%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.28-7.24 (m, 2H), 7.16 (d, *J* = 7.1 Hz, 2H), 7.0-6.95 (m, 4H), 3.70 (b, 4H), 3.35 (t, *J* = 4.3 Hz, 4H), 2.14 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 130.8, 129.4, 126.9, 122.9, 122.5, 121.0, 118.8, 66.5, 47.2, 18.0. Data is consistent with reported literatures.[1-3]



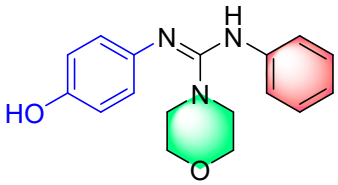
4rab

N-phenyl-*N*′-(*p*-tolyl)morpholine-4-carboximidamide (**4rab**) Synthesized according to the General procedure B using *p*-toluidine **2r** (53.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4rab** (125.0 mg, 0.425 mmol, 85%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.25 (t, *J* = 7.7 Hz, 2H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.99-6.96 (m, 5H), 3.67 (t, *J* = 4.8 Hz, 4H), 3.32 (t, *J* = 4.8 Hz, 4H), 2.29 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 151.2, 132.1, 130.0, 129.4, 122.5, 118.7, 66.5, 47.0, 20.8. Data is consistent with reported literatures.[1-3]



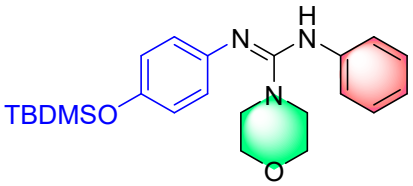
4iab

N′-(4-methoxyphenyl)-*N*-phenylmorpholine-4-carboximidamide (**4iab**) Synthesized according to the General procedure B using *p*-anisidine **2i** (61.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4iab** (143.3 mg, 0.46 mmol, 92%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.26 (t, *J* = 7.9 Hz, 2H), 6.99-6.85 (m, 5H), 6.8 (d, *J* = 8.7 Hz, 2H), 3.76 (s, 3H), 3.65 (t, *J* = 4.4 Hz, 4H), 3.31 (t, *J* = 4.7 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 155.6, 129.5, 122.5, 114.7, 66.5, 55.6, 47.1. Data is consistent with reported literatures.[1-3]



4sab

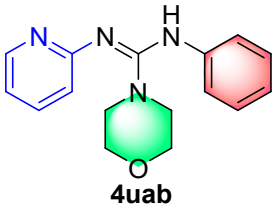
N′-(4-hydroxyphenyl)-*N*-diphenylmorpholine-4-carboximidamide (**4sab**) Synthesized according to the General procedure B using 4-aminophenol **2s** (54.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (149.9 mg, 1.0 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4sab** (80.1 mg, 0.27 mmol, 54%) as a brown powder: ^{1}H NMR (500 MHz, $(CD_3)_2SO$) δ ppm 7.11 (t, *J* = 7.8 Hz, 2H), 6.82-6.74 (m, 5H), 6.54 (d, J = 8.3 Hz, 2H), 3.56 (t, *J* = 4.3 Hz, 4H), 3.20 (t, *J* = 4.2 Hz, 4H). ^{13}C NMR (125 MHz, $(CD_3)_2SO$): δ ppm 151.8, 128.7, 120.2, 115.3, 65.8, 46.8; ^{13}C NMR (125 MHz, $(CD_3)_2SO$ + 0.1% TFA): δ ppm 152.8, 151.2, 128.9, 122.0, 121.6, 119.9, 115.5 65.7, 47.2. Melting point: 192-194°C. ESI-MS: m/z: 298.15555 $[M+H]^+$ (calcd for $[C_{17}H_{20}N_3O_2]^+$ 298.15620).



4tab

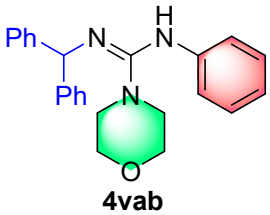
N′-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-*N*-phenylmorpholine-4-carboximidamide (**4tab**) Synthesized according to the General procedure B using 4-((*tert*-butyldimethylsillyl)oxy)aniline **2t** (111.7 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4tab** (123.9 mg, 0.3 mmol, 60%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.25 (t, *J* = 7.9 Hz, 2H), 6.99-6.82 (m, 5H), 6.74 (d, *J* = 8.6 Hz, 2H), 3.64 (b, 4H), 3.30 (t, *J* = 4.5 Hz, 4H), 0.96 (s, 9H),

0.16 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 151.5, 129.5, 122.6, 120.9, 66.5, 47.2, 25.8, 18.3, -4.3. ESI-MS: m/z: 412.24336 $[M+H]^+$ (calcd for $[C_{23}H_{34}N_3O_2Si]^+$ 412.24203).



4uab

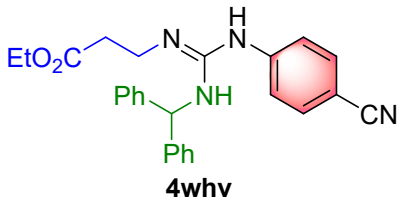
N-phenyl-*N*′-(pyridin-2-yl)morpholine-4-carboximidamide (**4uab**) Synthesized according to the General procedure A using 1-phenyl-3-(pyridin-2-yl)thioureas **1ua** (114.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **4uab** (71.0 mg, 0.25 mmol, 50%) as a white solid; Synthesized according to the General procedure B using 2-aminopyridine **2u** (47.0 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (149.9 mg, 1.0 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4uab** (11.4 mg, 0.04 mmol, 8%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.22-8.21 (m, 1H), 7.56-7.53 (m, 1H), 7.28 (t, J = 8.0 Hz, 2H), 7.16 (d, J = 6.6 Hz, 2H), 7.01-6.98 (m, 2H), 6.82-6.80 (m, 1H), 3.68 (t, J = 4.6 Hz, 4H), 3.44 (t, J = 4.8 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 161.7, 154.0, 146.1, 141.1, 137.7, 129.4, 122.9, 121.0, 120.2, 116.8, 66.6, 47.4. Melting point: 86-88^{o}C. Data is consistent with reported literatures.[1,2]



4vab

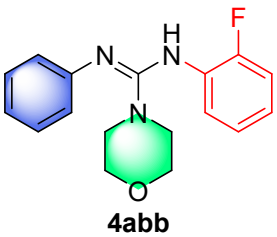
N′-benzhydryl-*N*-phenylmorpholine-4-carboximidamide (**4vab**) Synthesized according to the General procedure B using benzhydrylamine **2v** (91.6 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide

(149.9 mg, 1.0 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4vab** (88.9 mg, 0.24 mmol, 48%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.32-7.27 (m, 8H), 7.16 (b, 4H), 7.07-7.04 (m, 2H), 6.89-6.86 (m, 1H), 5.63 (s, 1H), 3.74 (t, J = 4.6 Hz, 4H), 3.24 (t, J = 4.7 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 129.2, 128.8, 127.5, 127.3, 122.3, 66.9, 62.8, 48.5. Melting point: 142-143°C. ESI-MS: m/z: 372.20858 $[M+H]^+$ (calcd for $[C_{24}H_{26}N_3O]^+$ 372.20759).



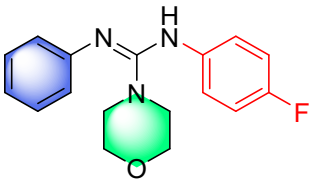
4whv

Ethyl-3-(((benzhydrylamino)((4-cyanophenyl)amino)methylene)amino)propanoate (**4whv**) Synthesized according to the General procedure B using *β*-alanine ethyl ester hydrochloride **2a** (76.8 mg, 0.5 mmol), phenyl isothiocyanate **3a** (67.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (added twice into the reaction: 1st step: 193.8 mg, 1.5 mmol; 2nd step: 64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4whv** (144.2 mg, 0.34 mmol, 68%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.48-7.46 (m, 2H), 7.35-7.32 (m, 4H), 7.30-7.26 (m, 2H), 7.24-7.23 (m, 4H), 6.92-6.89 (m, 2H), 5.70 (s, 1H), 4.05 (q, J = 7.1 Hz, 2H), 3.49 (t, J = 5.6 Hz, 2H), 2.50 (t, J = 5.9 Hz, 2H), 1.20 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 172.7, 150.4, 141.4, 133.7, 129.1, 128.1, 127.2, 123.9, 120.1, 103.9, 69.1, 60.8, 60.5, 37.3, 34.3, 14.3. ESI-MS: m/z: 427.21480 $[M+H]^+$ (calcd for $[C_{20}H_{27}N_4O_2]^+$ 427.21340).



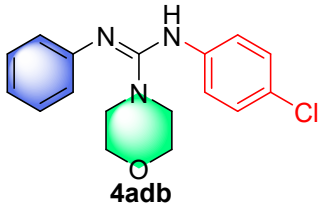
4abb

N-(2-fluorophenyl)-*N*′-phenylmorpholine-4-carboximidamide (**4abb**) Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), 2-fluorophenyl isothiocyanate **3b** (76.6 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4abb** (116.2 mg, 0.39 mmol, 78%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.26 (m, 2H), 7.01-6.84 (m, 7H), 3.67 (t, *J* = 4.8 Hz, 4H), 3.36 (t, *J* = 4.8 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 129.4, 124.7 (d, *J* = 3.8 Hz), 123.2, 122.8, 119.2, 118.9, 116.2 (d, *J* = 21.3 Hz), 66.5, 47.2; ^{13}C NMR (125 MHz, CD_3OD + 0.1% TFA): δ ppm 155.8, 141.5, 130.1, 126.5, 125.7, 124.6, 121.8, 116.9 (d, *J* = 20.0 Hz), 67.3, 48.9. ESI-MS: m/z: 300.15160 $[M+H]^+$ (calcd for $[C_{17}H_{19}FN_3O]^+$ 300.15122).



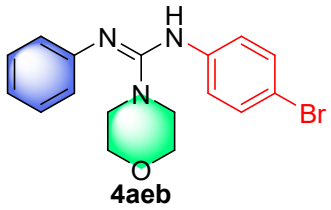
4acb

N-(4-fluorophenyl)-*N*′-phenylmorpholine-4-carboximidamide (**4acb**) Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), 4-fluorophenyl isothiocyanate **3c** (76.6 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (149.9 mg, 1.0 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4acb** (70.2 mg, 0.235 mmol, 47%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.28 (m, 2H), 7.01-6.84 (m, 7H), 3.67 (t, *J* = 4.7 Hz, 4H), 3.32 (t, *J* = 4.7 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 151.3, 129.6, 122.7, 116.2 (d, *J* = 22.5 Hz), 66.5, 47.1; ^{13}C NMR (125 MHz, CD_3OD + 0.1% TFA): δ ppm 155.5, 144.2, 138.3, 130.7, 127.2, 125.6, 125.5, 123.4, 117.3 (d, *J* = 23.8 Hz), 66.9, 49.7. ESI-MS: m/z: 300.15216 $[M+H]^+$ (calcd for $[C_{17}H_{19}FN_3O]^+$ 300.15122).



4adb

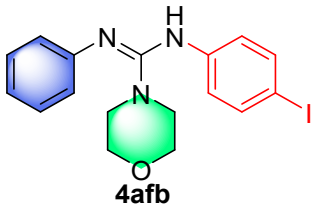
N-(4-chlorophenyl)-*N*′-phenylmorpholine-4-carboximidamide (**4adb**) Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), 4-chlorophenyl isothiocyanate **3d** (84.8 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4adb** (97.8 mg, 0.31 mmol, 62%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.27 (t, *J* = 7.9 Hz, 2H), 7.19 (d, *J* = 8.6 Hz, 2H), 7.01-6.84 (m, 5H), 3.67 (t, *J* = 4.8 Hz, 4H), 3.32 (t, *J* = 4.8 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 151.1, 129.6, 129.5, 127.7, 122.8, 66.4, 47.1; ^{13}C NMR (125 MHz, CD_3OD + 0.1% TFA): δ ppm 154.5, 146.5, 145.2, 130.1, 129.8, 128.0, 123.5, 123.3, 121.2, 67.4, 48.4. ESI-MS: m/z: 316.12268 $[M+H]^+$ (calcd for $[C_{17}H_{19}ClN_3O]^+$ 316.12166). Data is consistent with reported literatures[3].



4aeb

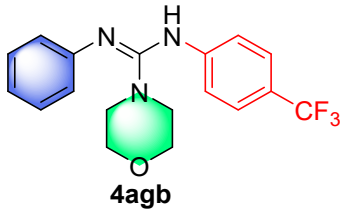
N-(4-bromophenyl)-*N*′-phenylmorpholine-4-carboximidamide (**4aeb**) Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), 4-bromophenyl isothiocyanate **3e** (107.0 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (149.9 mg, 1.0 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aeb** (116.8 mg, 0.325 mmol, 65%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.32 (d, *J* = 8.7 Hz, 2H), 7.26 (t, *J* = 7.9 Hz, 2H), 7.0-6.77 (m, 5H), 3.65 (t, *J* = 4.8 Hz, 4H), 3.31 (t, *J* = 4.8 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 150.9, 137.9, 132.3, 129.5,

122.7, 115.1, 66.3, 47.0. Melting point: 129-130°C. Data is consistent with reported literatures.[1-3]



4afb

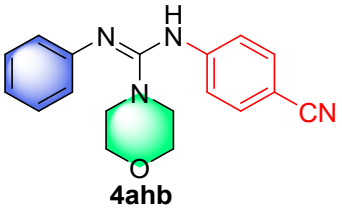
N-(4-iodophenyl)-*N*′-phenylmorpholine-4-carboximidamide (**4afb**) Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), 4-iodophenyl isothiocyanate **3f** (130.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4afb** (118.2 mg, 0.29 mmol, 58%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.51 (d, J = 8.4 Hz, 2H), 7.27-7.24 (m, 2H), 7.0-6.94 (m, 3H), 6.66 (b, 2H), 3.66 (t, J = 4.7 Hz, 4H), 3.31 (t, J = 4.8 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 151.0, 138.3, 129.4, 124.9, 122.7, 118.4, 85.5, 66.4, 47.0. Melting point: 148-150°C. Data is consistent with reported literatures.[1,2]



4agb

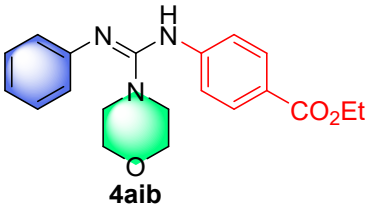
N′-phenyl-*N*-(4-(trifluoromethyl)phenyl)morpholine-4-carboximidamide (**4agb**) Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), 4-(trifluoromethyl)phenyl isothiocyanate **3g** (101.6 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (149.9 mg, 1.0 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4agb** (125.6 mg, 0.36 mmol, 72%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.48 (d, J = 8.2 Hz, 2H), 7.29-7.26 (overlap with solvent, 2H), 7.02- 6.96 (m, 5H), 3.70 (b, 4H), 3.36 (t, J = 4.8 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm

151.2, 143.0, 129.6, 127.8, 126.7 (d, J = 3.4 Hz), 125.6, 124.4 (q, J = 32.2 Hz, C-F coupling), 123.5, 123.3, 120.0, 66.2, 47.2. ^{19}F NMR (470 MHz, $CDCl_3$): δ ppm -61.6 ($-CF_3$). Melting point: 108-109°C. Data is consistent with reported literatures.[1,2]



4ahb

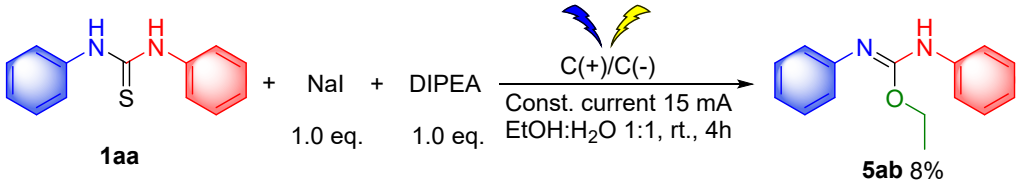
N-(4-cyanophenyl)-*N*′-phenylmorpholine-4-carboximidamide (**4ahb**) Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), 4-cyanophenyl isothiocyanate **3h** (80.1 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4ahb** (125.1 mg, 0.41 mmol, 82%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.47 (d, J = 8.5 Hz, 2H), 7.27 (t, J = 7.9 Hz, 2H), 7.01 (t, J = 7.4 Hz, 1H), 6.93 (d, J = 7.5 Hz, 4H), 3.69 (t, J = 4.7 Hz, 4H), 3.36 (t, J = 4.8 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 133.6, 129.7, 123.2, 104.8, 66.4, 47.1; ^{13}C NMR (125 MHz, CD_3OD + 0.1% TFA): δ ppm 154.4, 142.0, 134.3, 130.3, 124.9, 122.6, 122.0, 120.1, 106.1, 67.2, 48.9. ESI-MS: m/z: 307.15531 $[M+H]^+$ (calcd for $[C_{18}H_{19}N_4O]^+$ 307.15589).



4aib

Ethyl-4-(*N*′-phenylmorpholine-4-carboximidamido)benzoate (**4aib**) Synthesized according to the General procedure B using aniline **2a** (46.6 mg, 0.5 mmol), 4-ethylbenzoate isothiocyanate **3i** (103.5 mg, 0.5 mmol), morpholine **2b** (130.7 mg, 1.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL), to afford **4aib** (134.1 mg, 0.38 mmol, 76%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm

7.92 (d, J = 8.5 Hz, 2H), 7.26 (t, J = 7.8 Hz, 2H), 7.01-6.92 (m, 5H), 4.32 (q, J = 7.2 Hz, 2H), 3.69 (t, J = 4.7 Hz, 4H), 3.35 (t, J = 4.8 Hz, 4H), 1.36 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 166.6, 131.3, 129.6, 124.2, 123.0, 113.9, 66.4, 60.8, 47.1, 14.5. Melting point: 89-90°C. ESI-MS: m/z: 354.18279 $[M+H]^+$ (calcd for $[C_{20}H_{24}N_3O_3]^+$ 354.18177). Data is consistent with reported literatures.[3]



Ethyl-*N*,*N*′-diphenylcarbamimidate (**5ab**) Synthesized according to the General procedure A using 1,3-diphenylthioureas **1aa** (114.0 mg, 0.5 mmol), sodium iodide (74.9 mg, 0.5 mmol), DIPEA (64.6 mg, 0.5 mmol) in ethanol (2.5 mL) and water (2.5 mL) to afford **5ab** (10.4 mg, 0.04 mmol, 8%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.35-7.31 (m, 2H), 7.26 (m, overlap with solvent, 2H), 7.06-6.98 (m, 5H), 4.42 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 150.2, 129.8, 129.2, 129.0, 123.1, 122.9, 120.4, 62.9, 14.4, 14.5. ESI-MS: m/z: 241.13421 $[M+H]^+$ (calcd for $[C_{15}H_{17}N_2O]^+$ 241.13409).

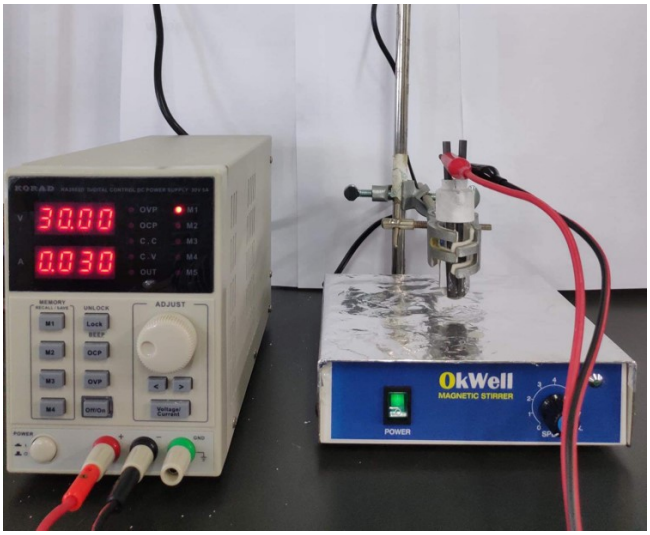


Figure S1. Reactors set up.

a) b)

Figure S2. Electrodes a) Carbon and b) Platinum.

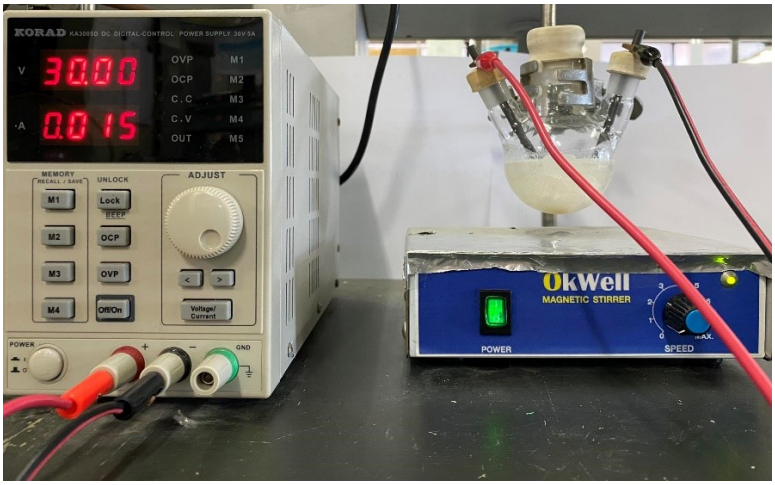


Figure S3. Gram scale set up.

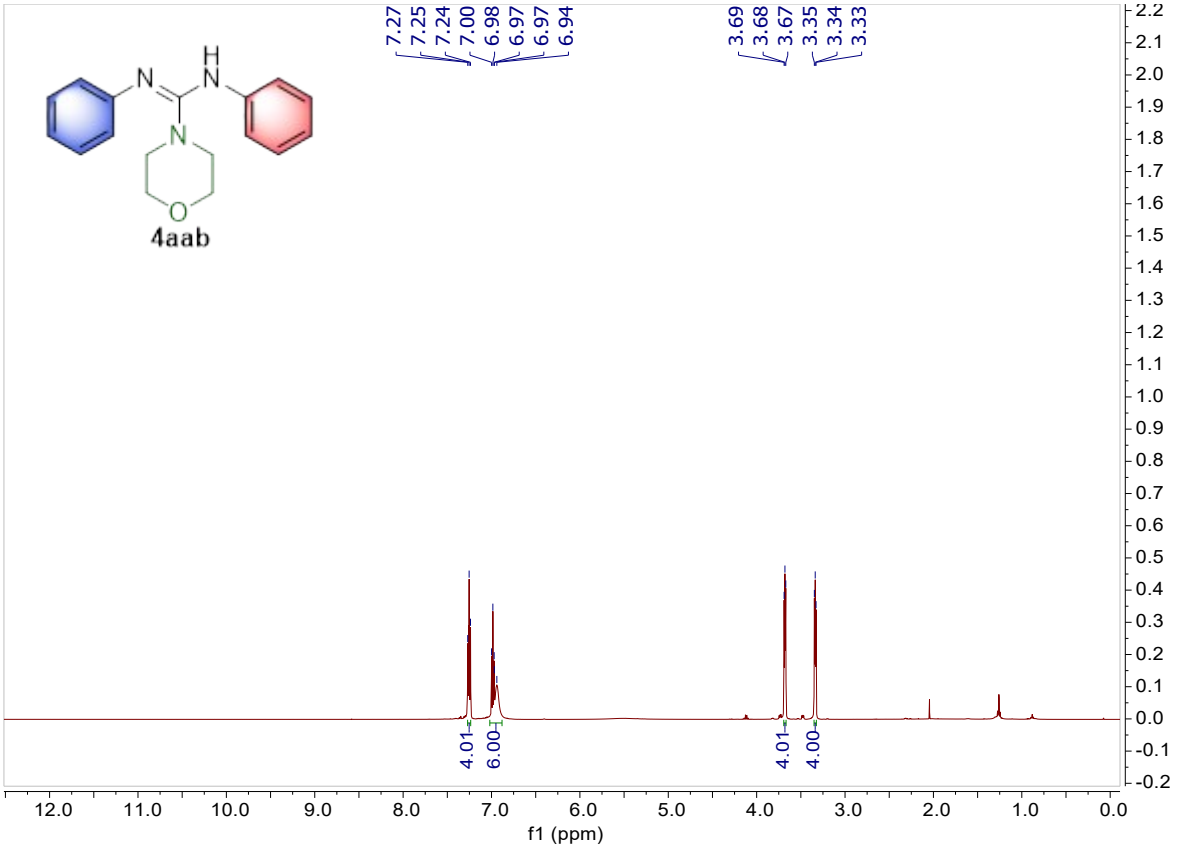


Figure S4 ^{1}H NMR spectra of **4aab** ($CDCl_3$).

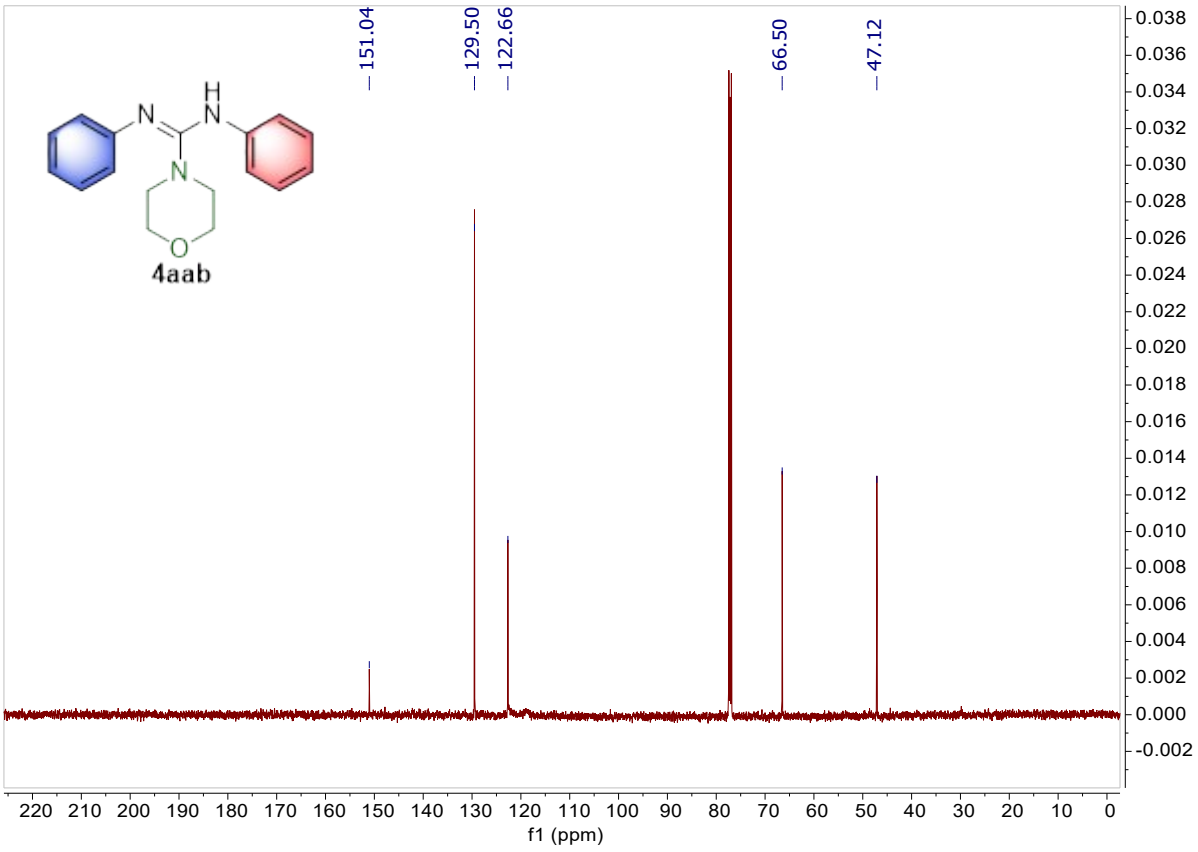


Figure S5 ^{13}C NMR spectra of **4aab** ($CDCl_3$).

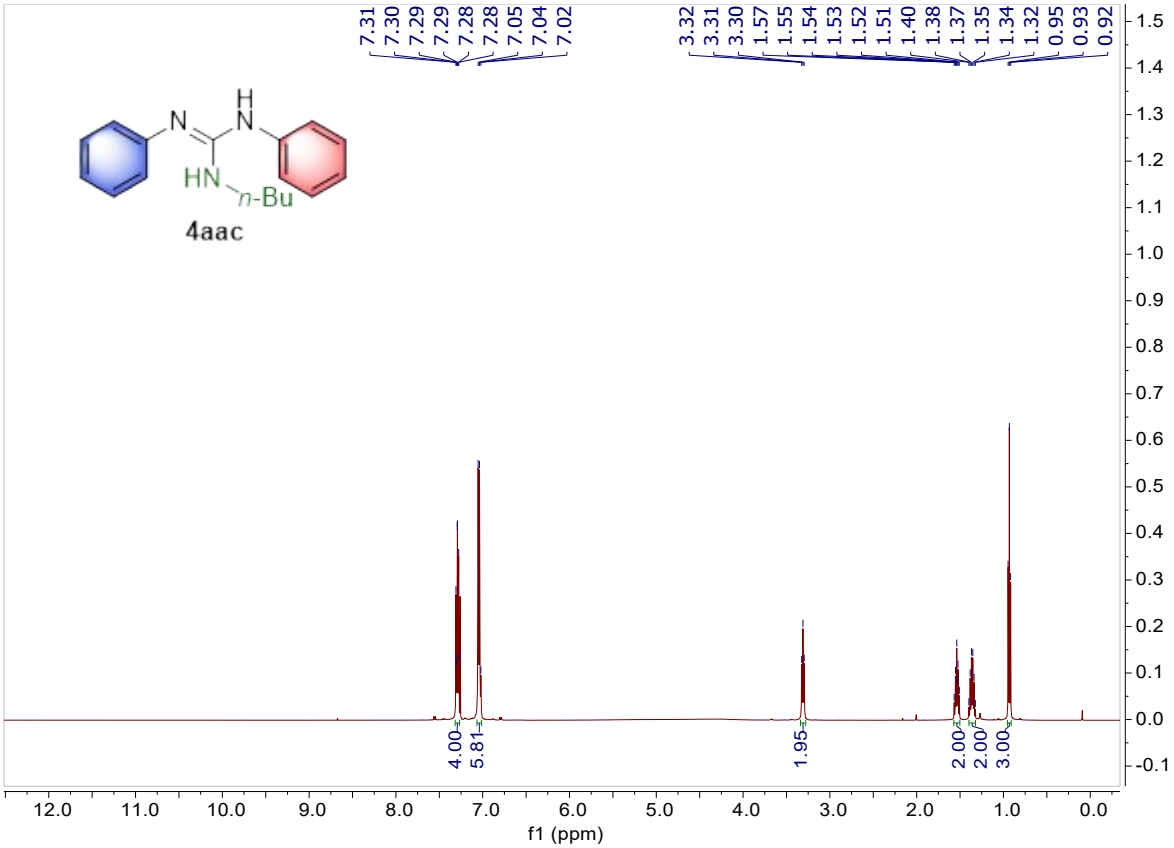


Figure S6 ^{1}H NMR spectra of **4aac** ($CDCl_3$).

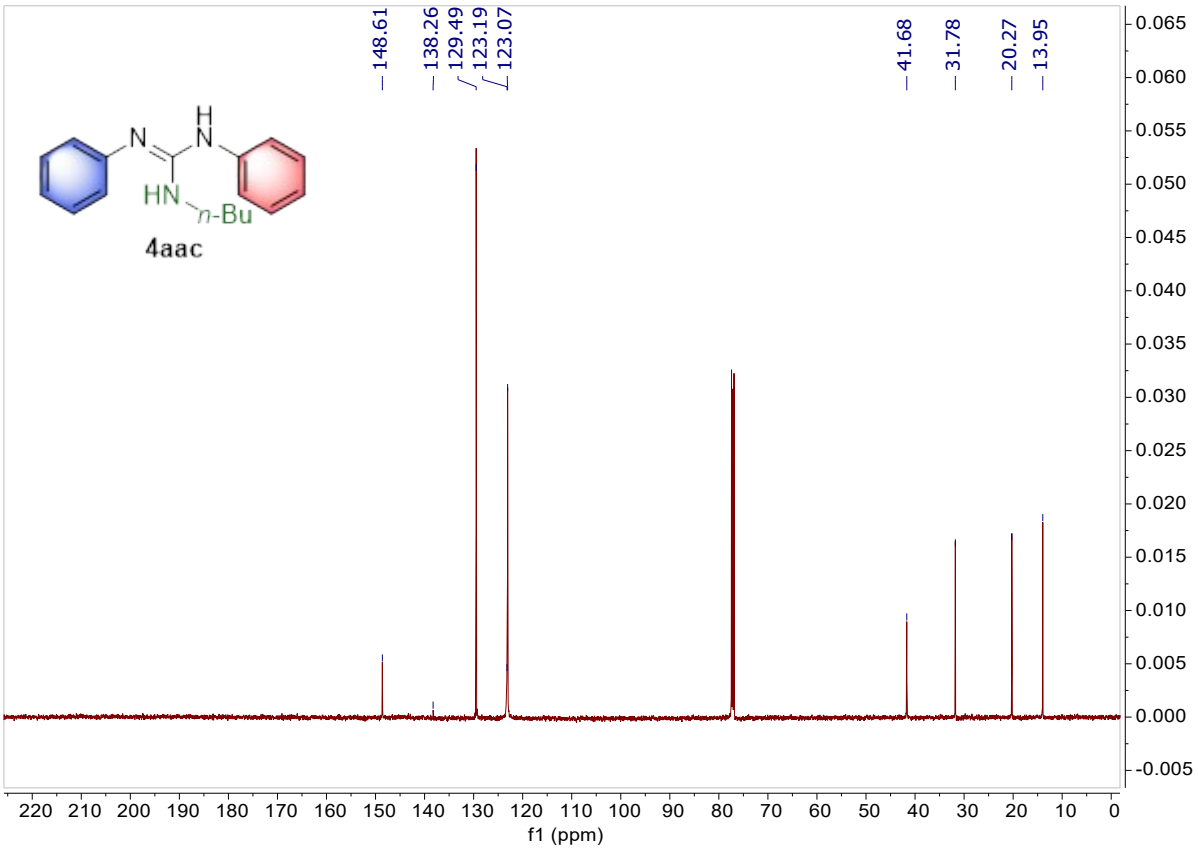


Figure S7 ^{13}C NMR spectra of **4aac** ($CDCl_3$).

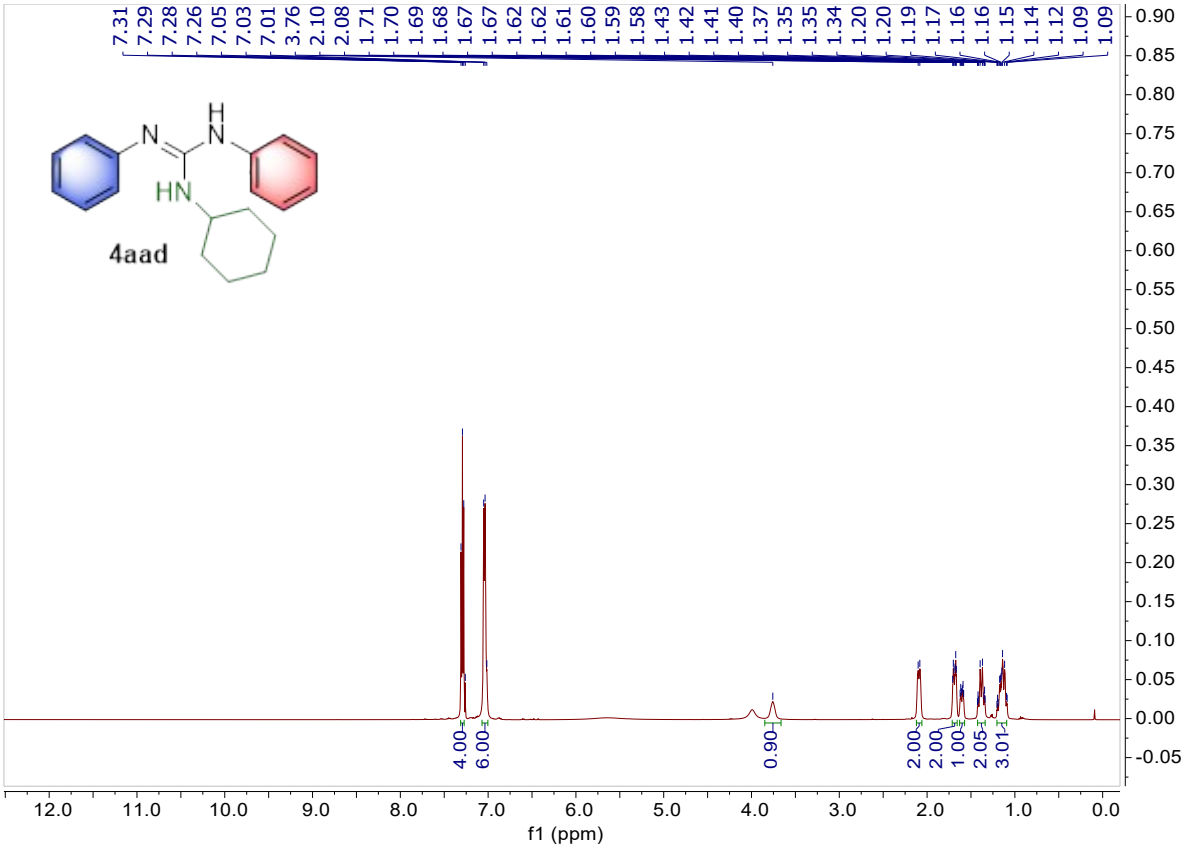


Figure S8 ^{1}H NMR spectra of **4aad** ($CDCl_3$).

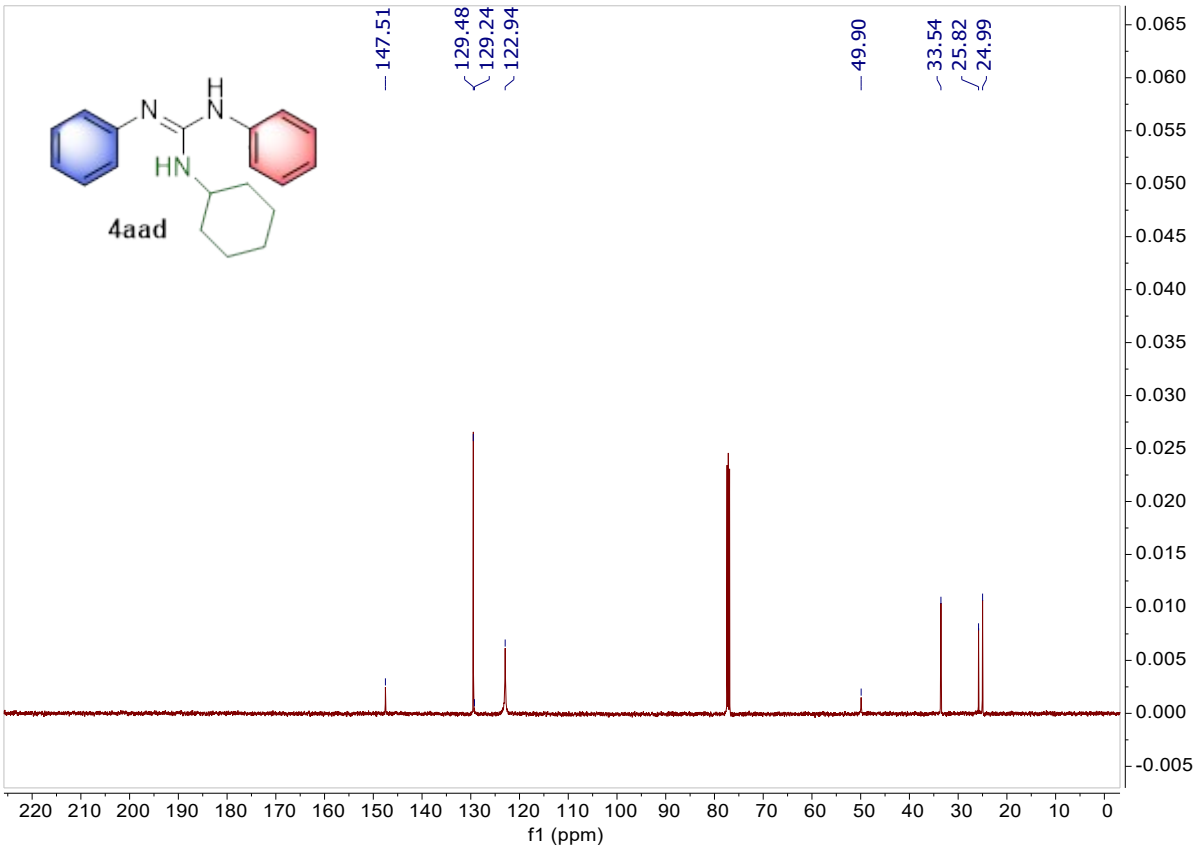


Figure S9 ^{13}C NMR spectra of **4aad** ($CDCl_3$).

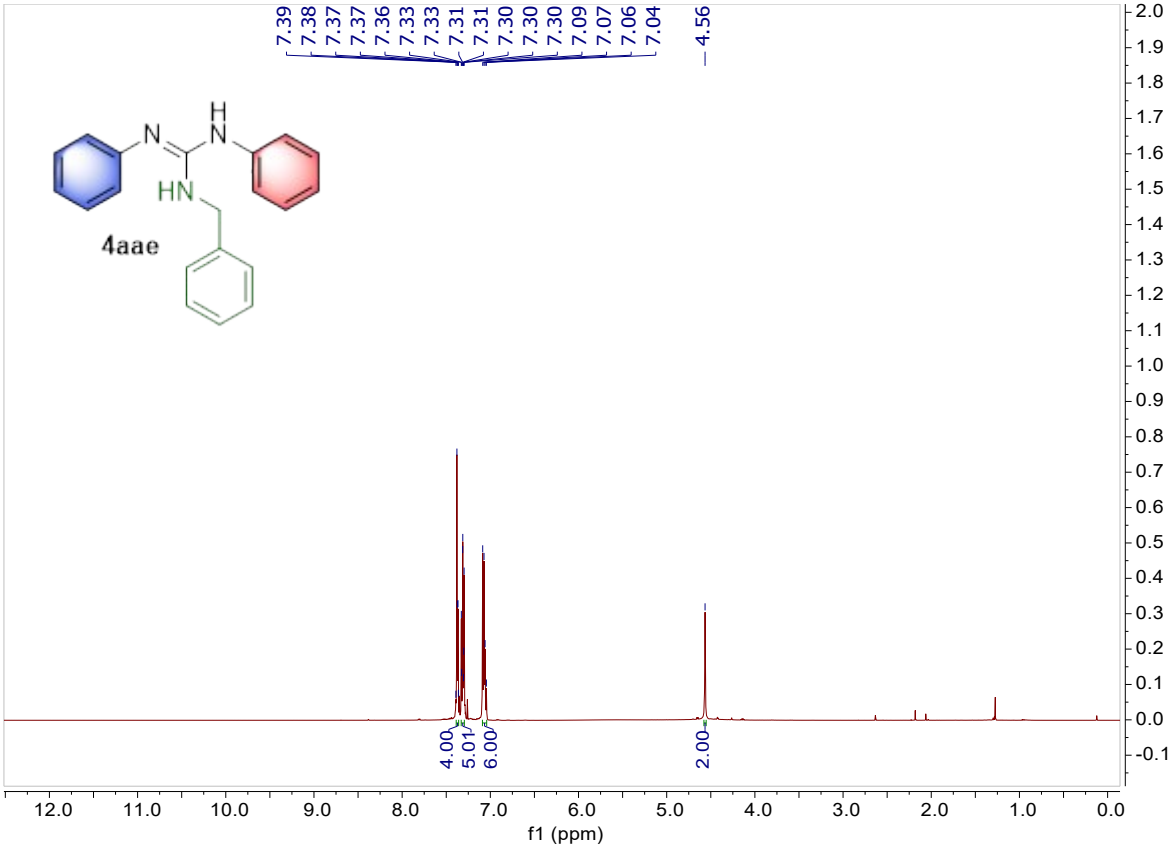


Figure S10 ^{1}H NMR spectra of **4aae** ($CDCl_3$).

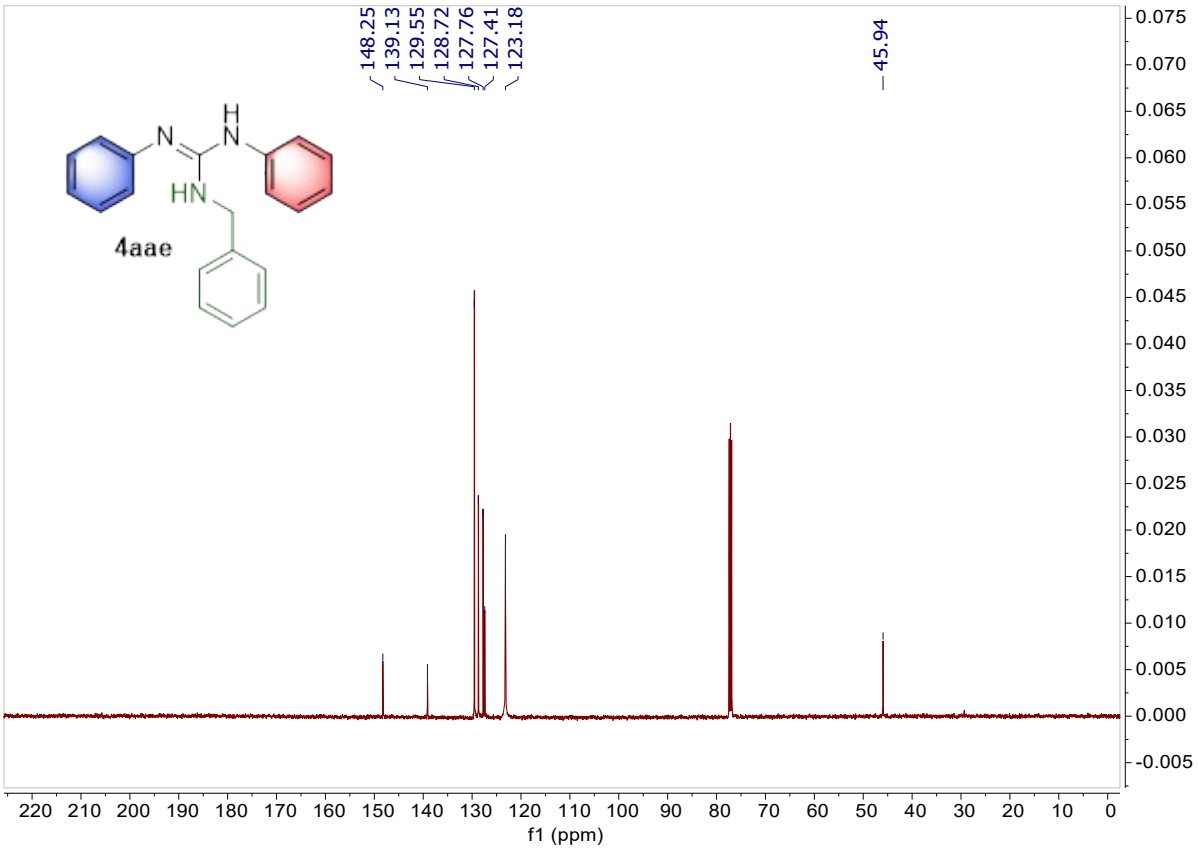


Figure S11 ^{13}C NMR spectra of **4aae** ($CDCl_3$).

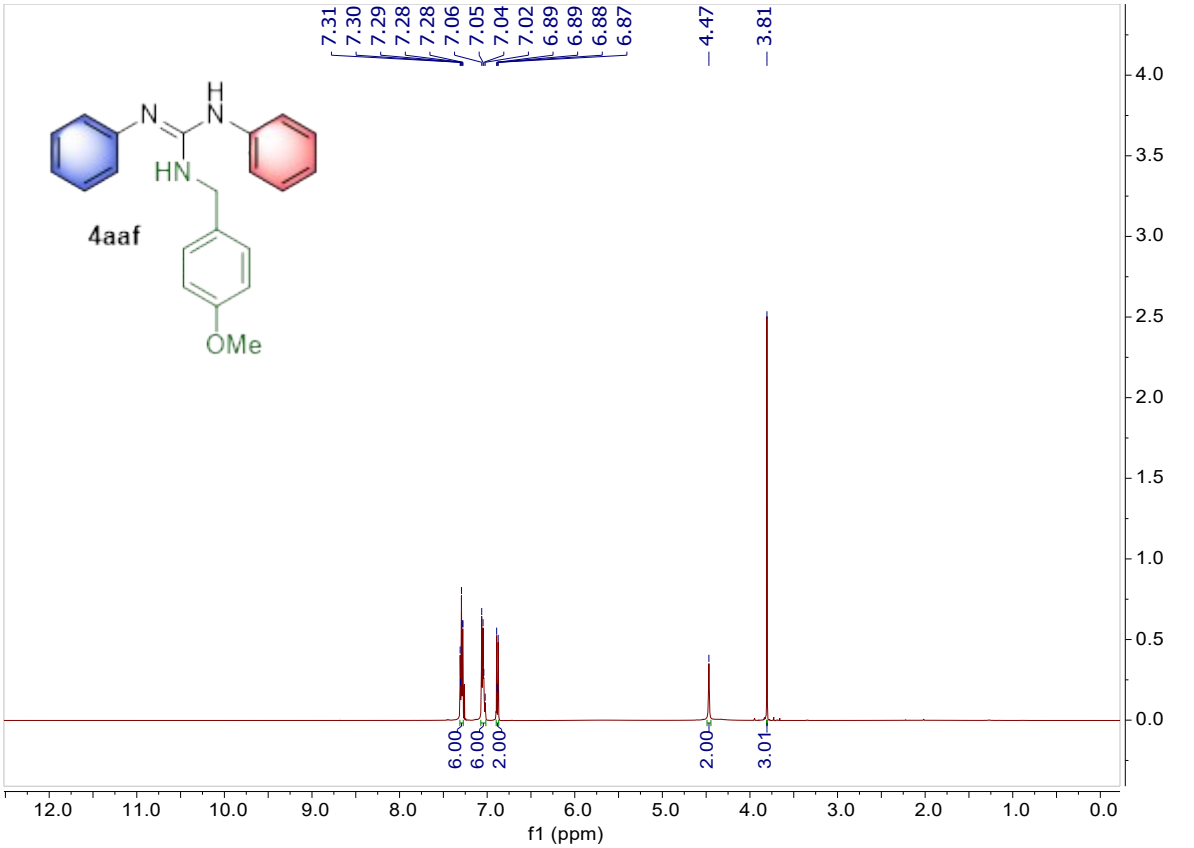


Figure S12 ^{1}H NMR spectra of **4aaf** ($CDCl_3$).

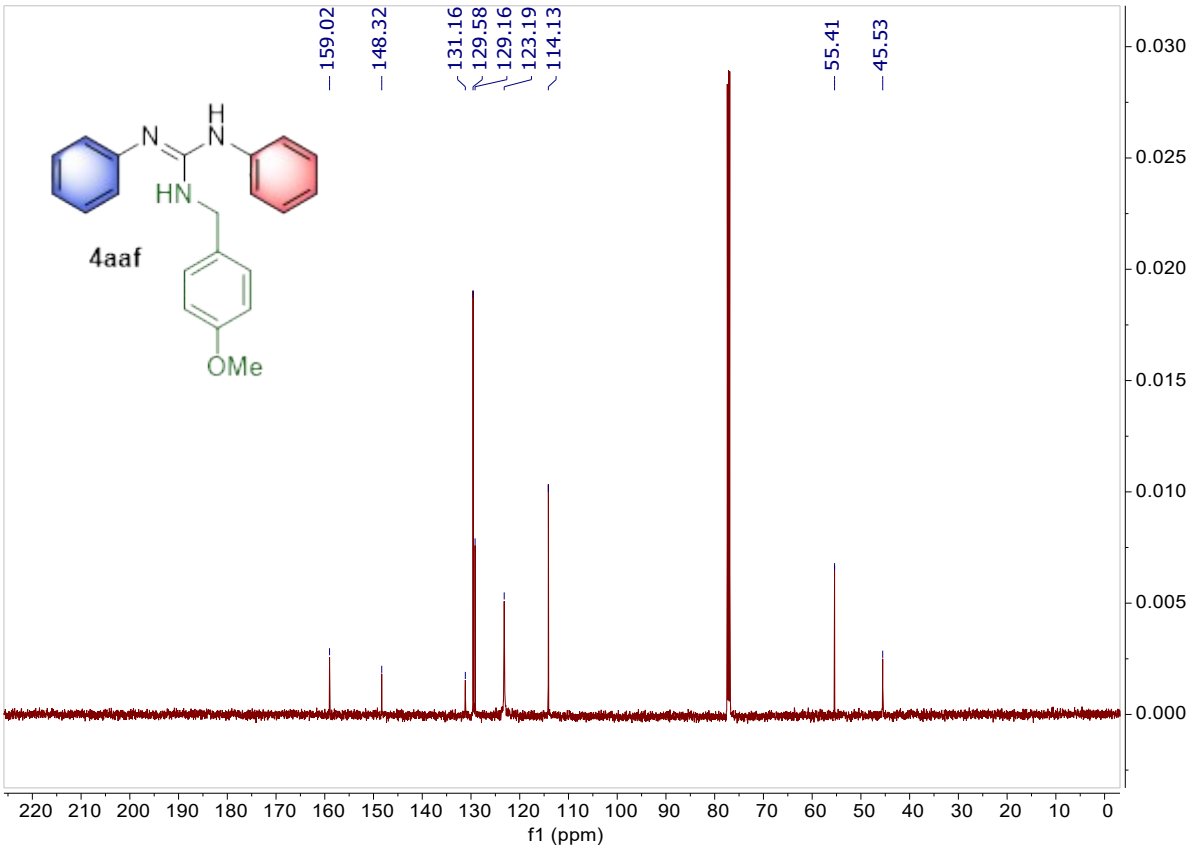


Figure S13 ^{13}C NMR spectra of **4aaf** ($CDCl_3$).

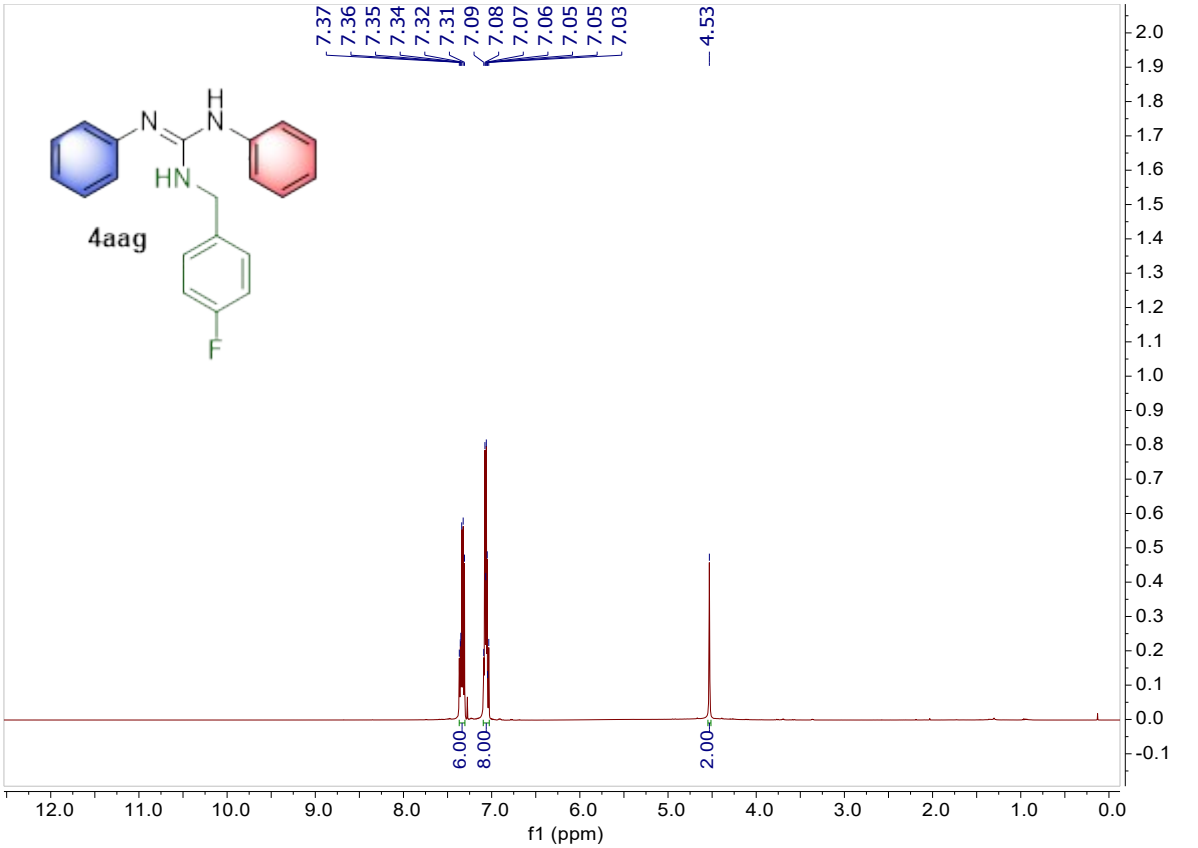


Figure S14 ^{1}H NMR spectra of **4aag** ($CDCl_3$).

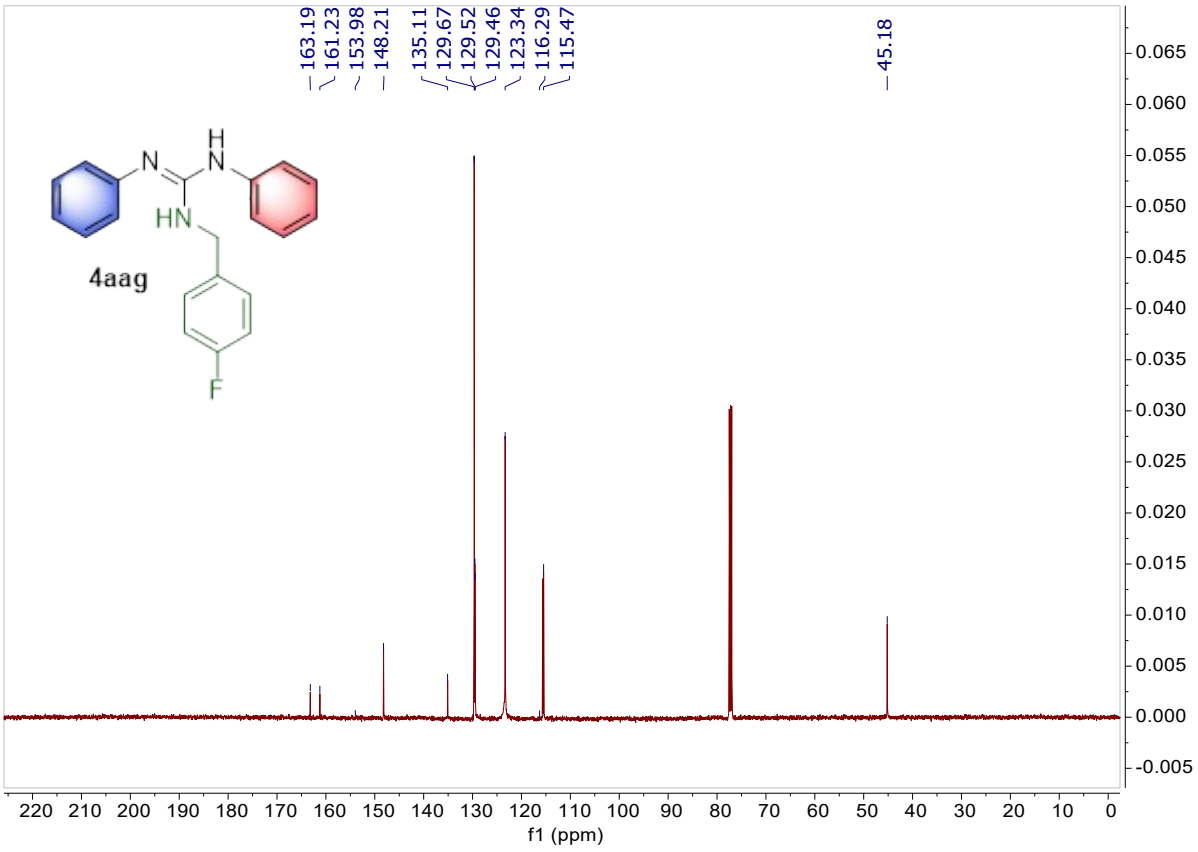


Figure S15 ^{13}C NMR spectra of **4aag** ($CDCl_3$).

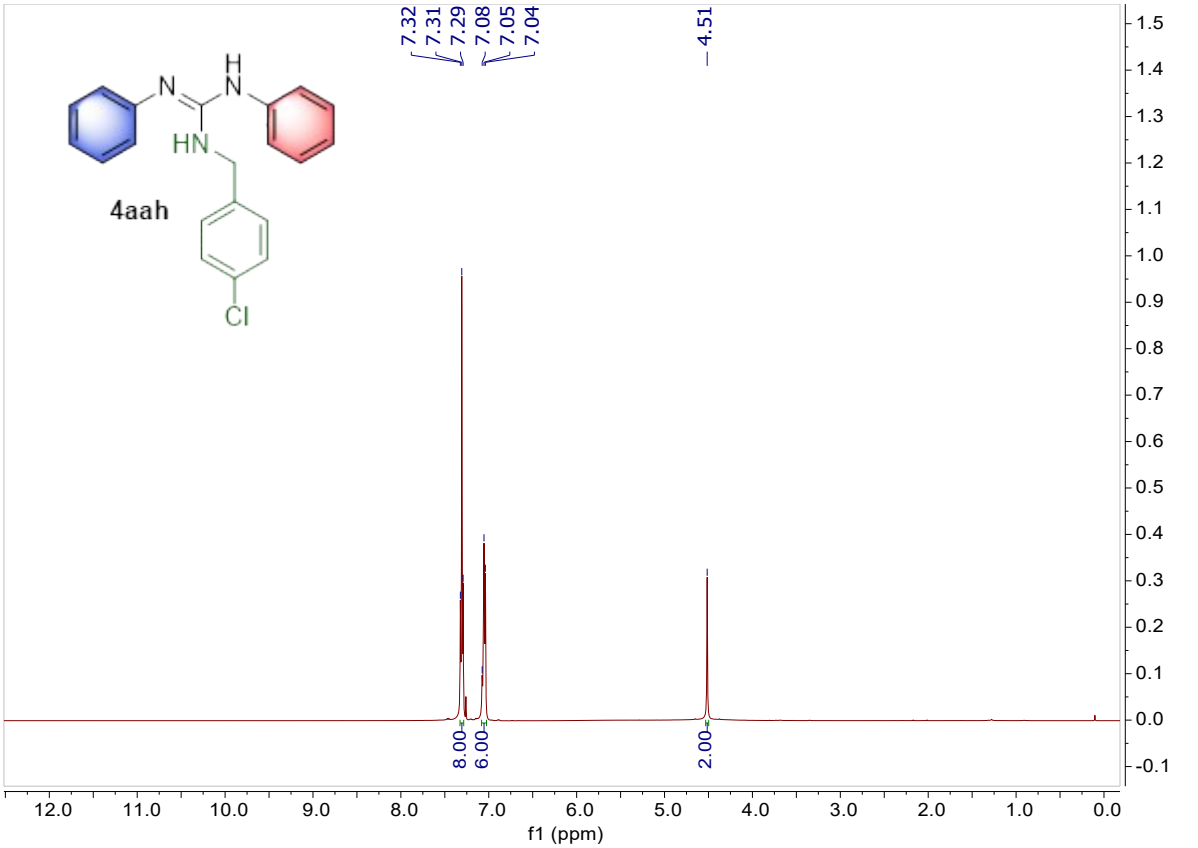


Figure S16 ^{1}H NMR spectra of **4aah** ($CDCl_3$).

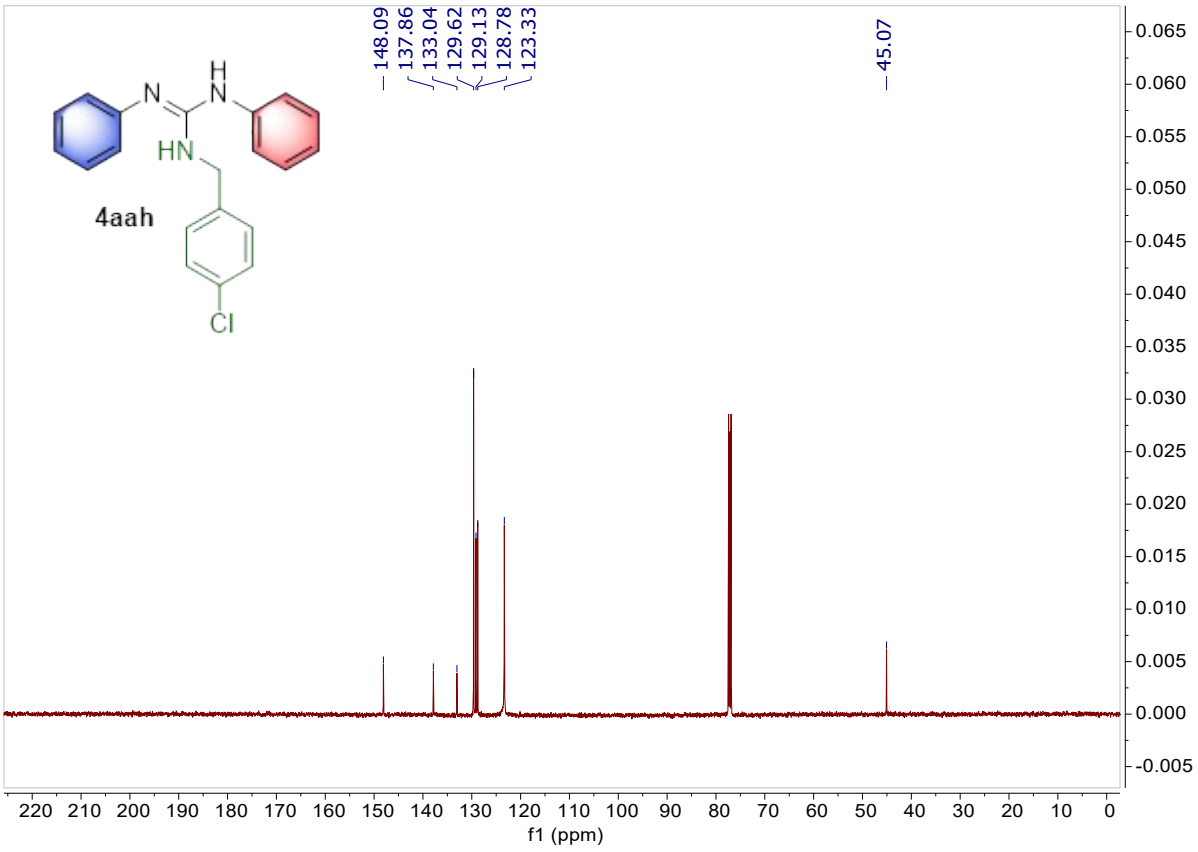


Figure S17 ^{13}C NMR spectra of **4aah** ($CDCl_3$).

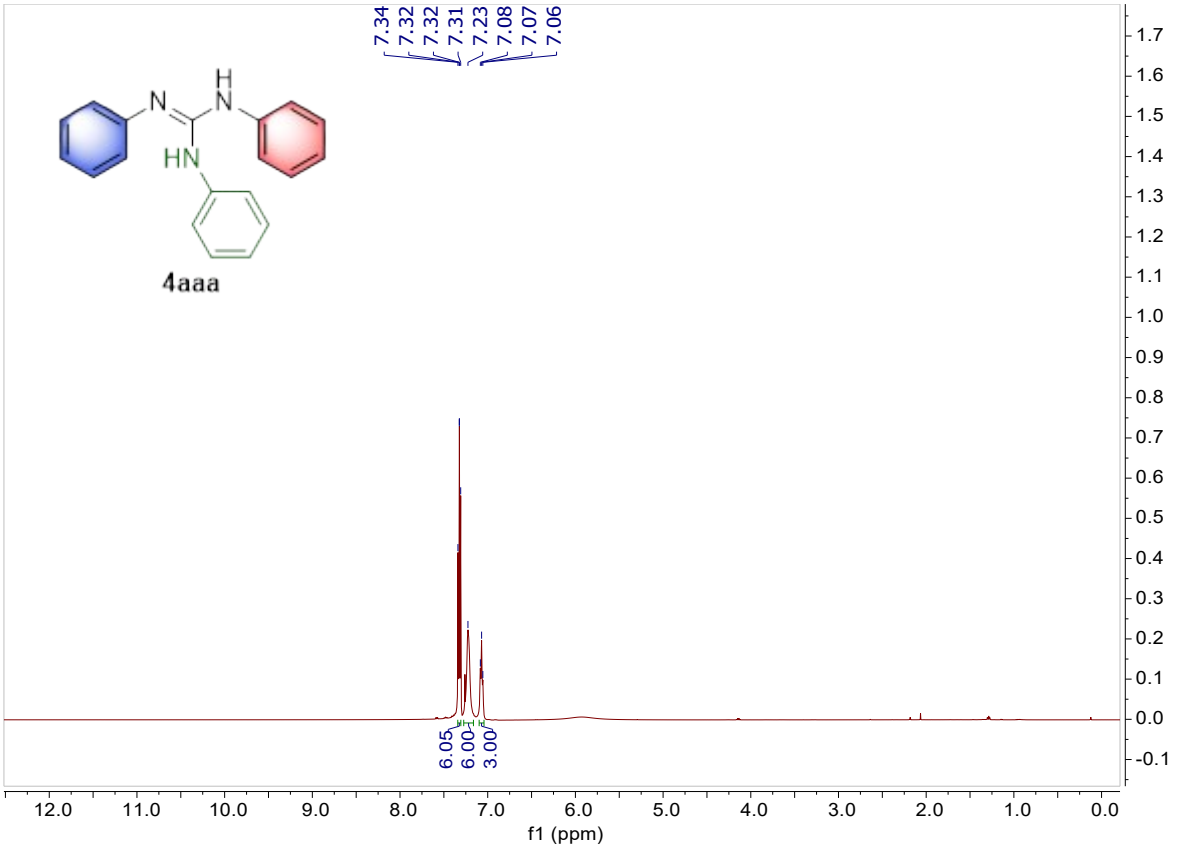


Figure S18 ^{1}H NMR spectra of **4aaa** ($CDCl_3$).

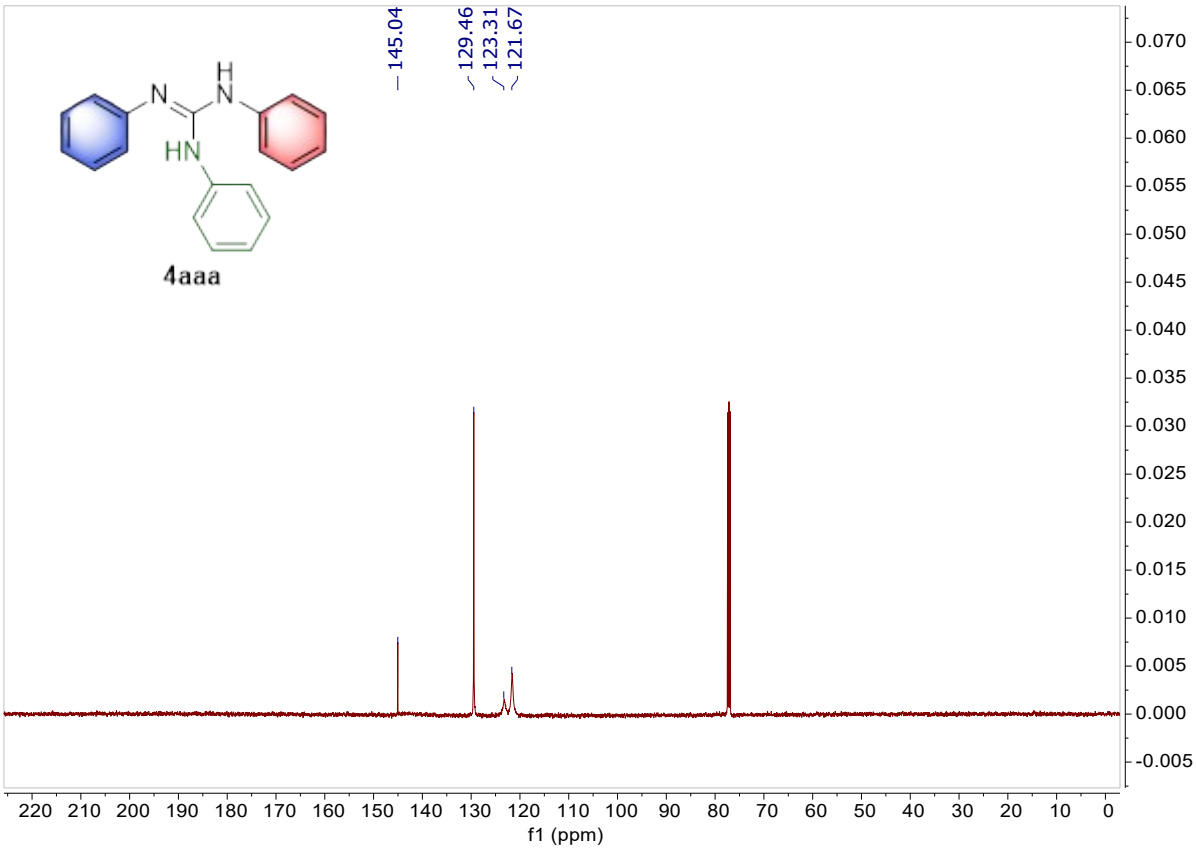


Figure S19 ^{13}C NMR spectra of **4aaa** ($CDCl_3$).

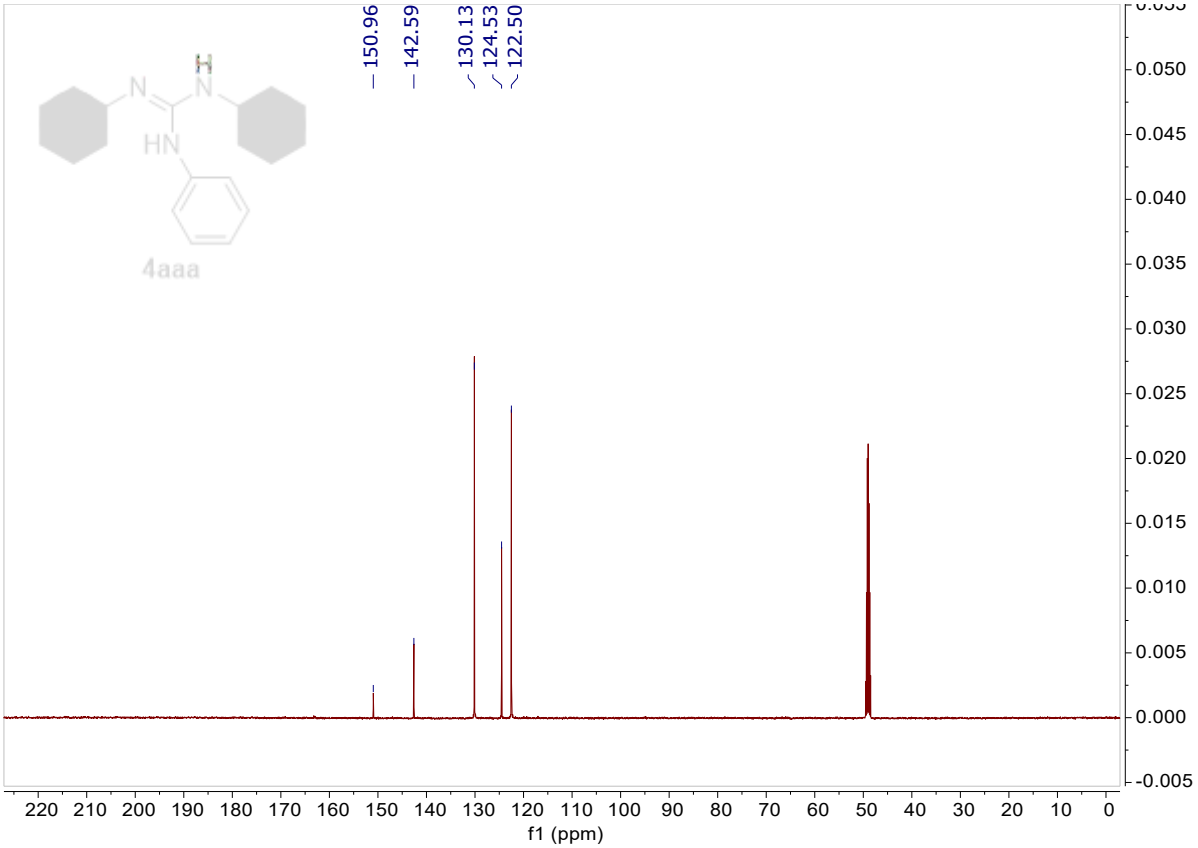


Figure S20 ^{13}C NMR spectra of **4aaa** (CD_3OD + 0.1% TFA).

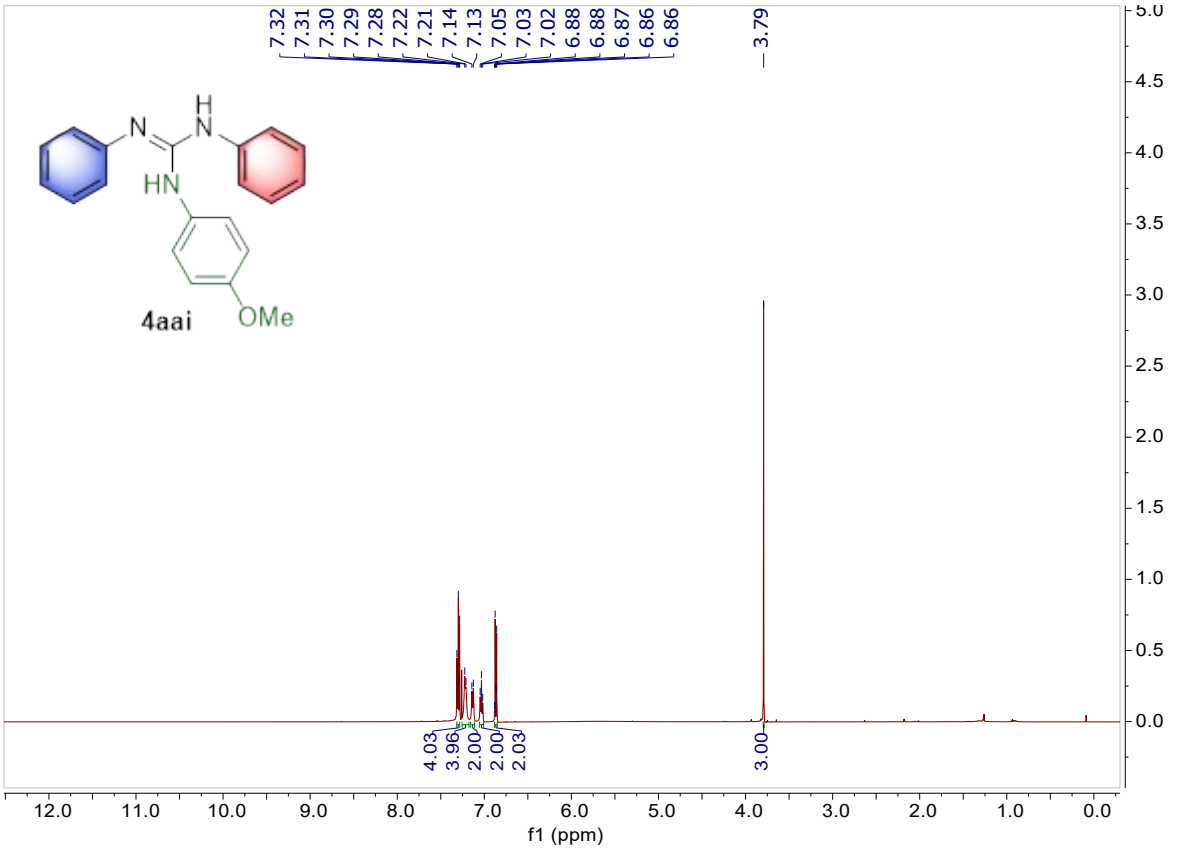


Figure S21 ^{1}H NMR spectra of **4aai** ($CDCl_3$).

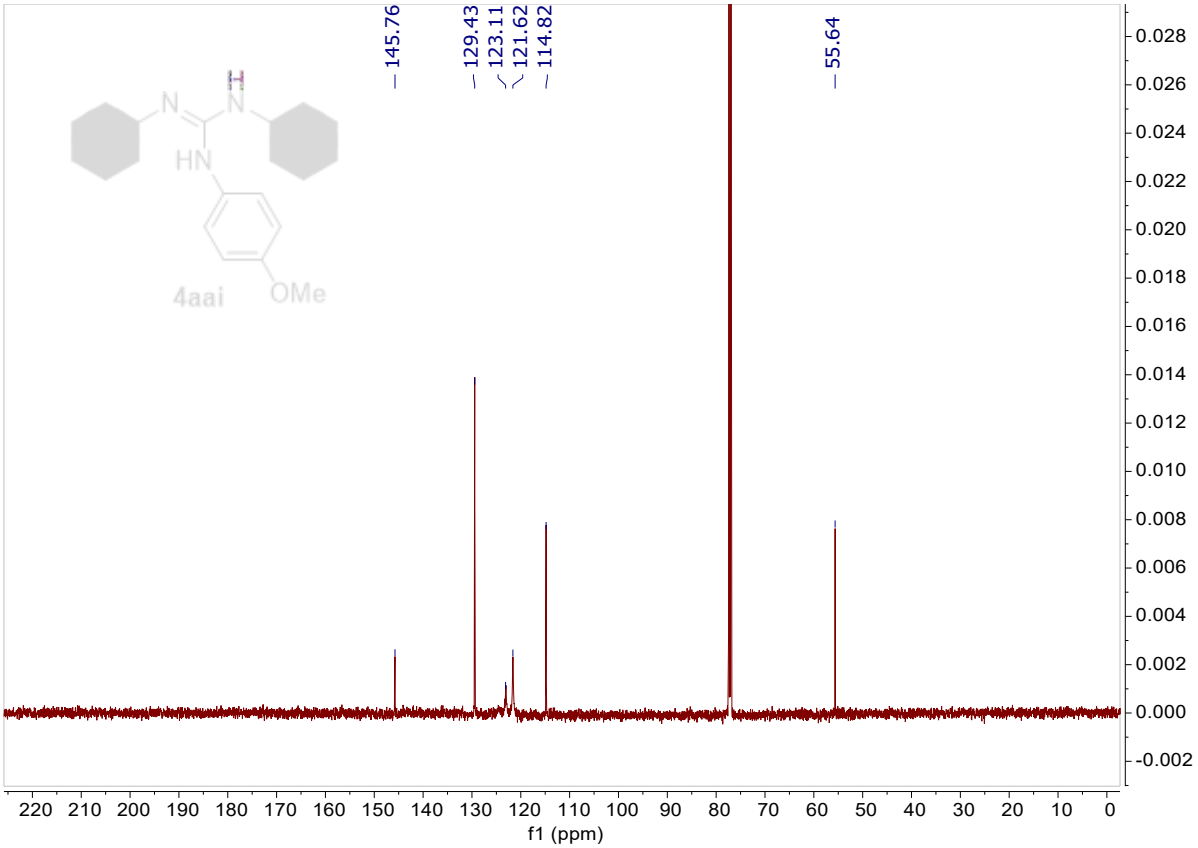


Figure S22 ^{13}C NMR spectra of **4aai** ($CDCl_3$).

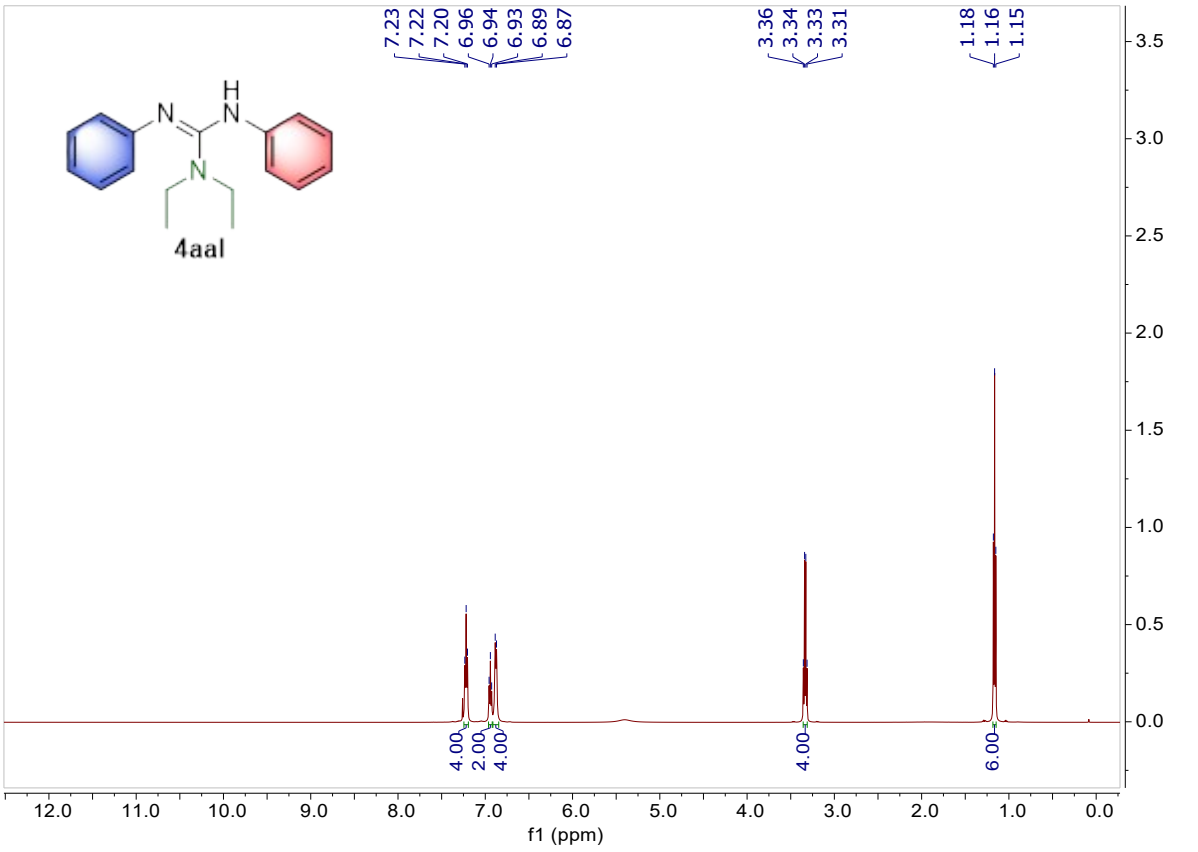


Figure S23 ^{1}H NMR spectra of **4aal** ($CDCl_3$).

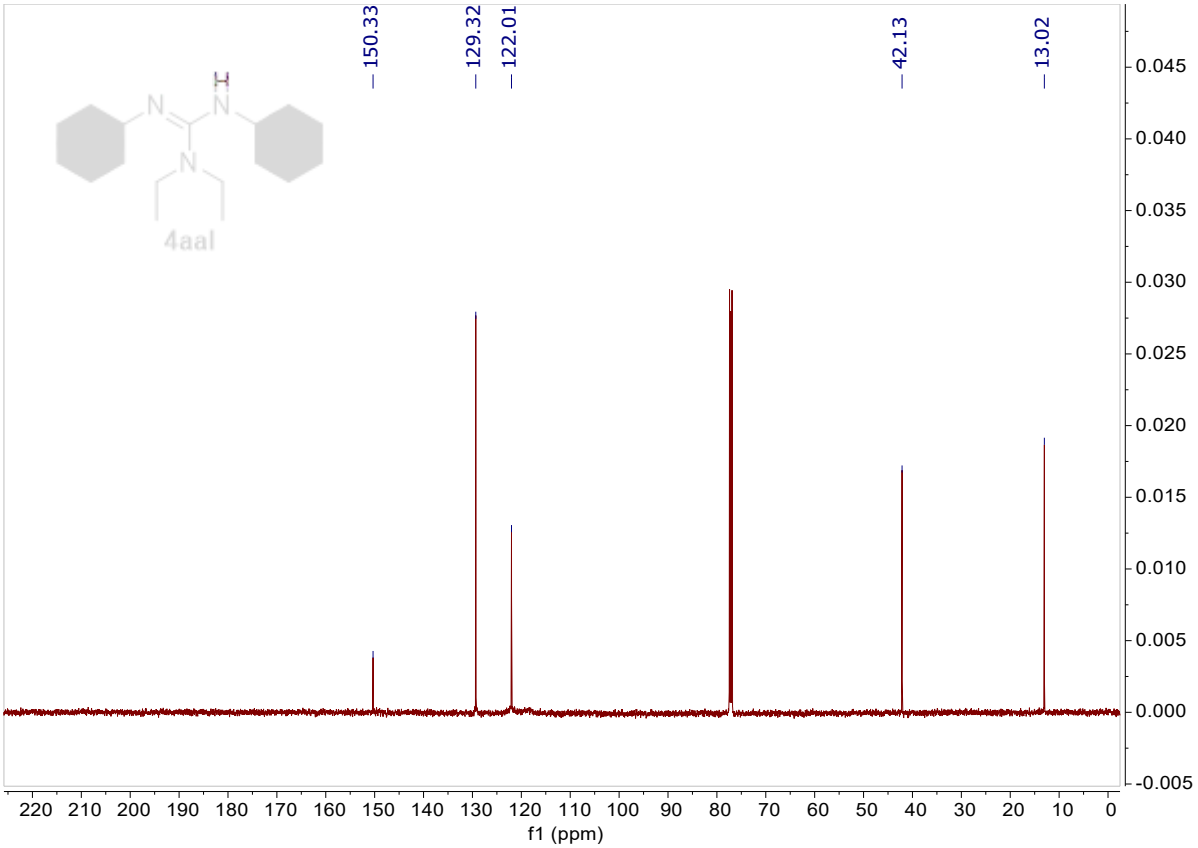


Figure S24 ^{13}C NMR spectra of **4aal** ($CDCl_3$).

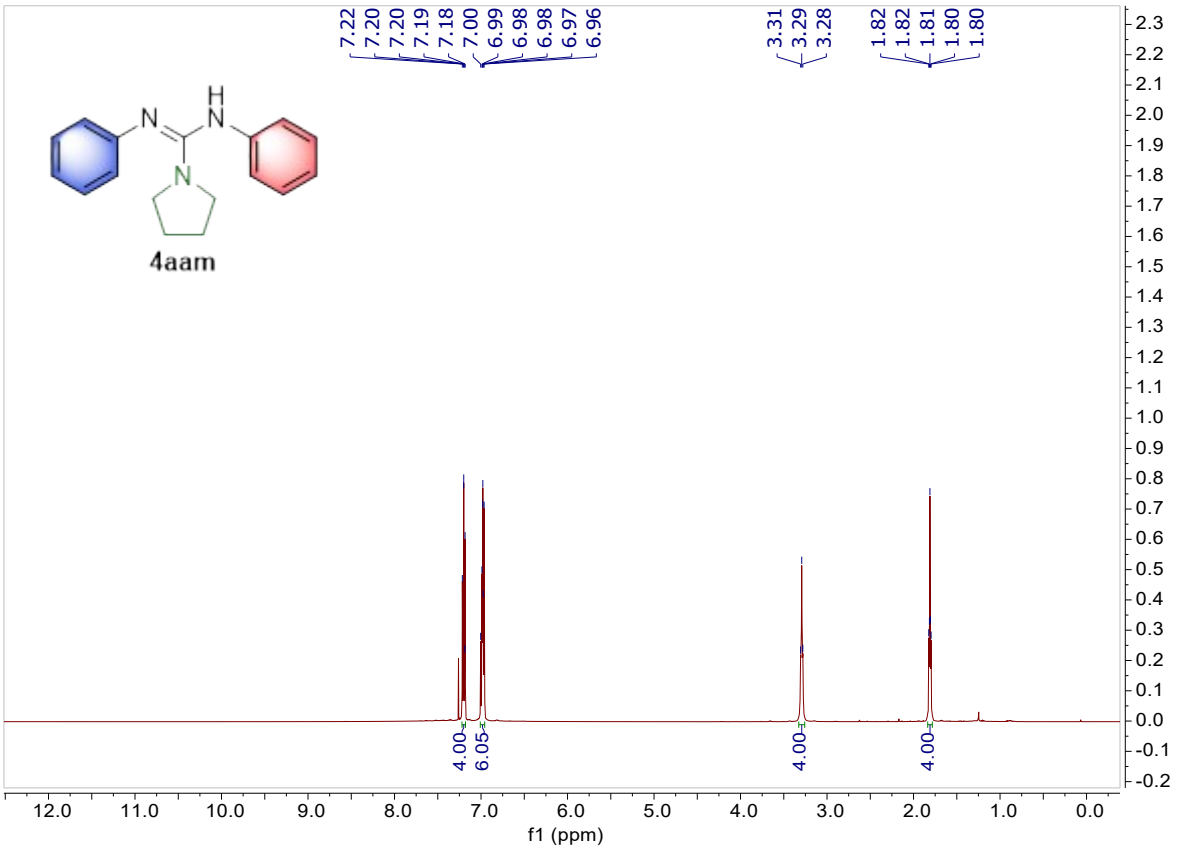


Figure S25 ^{1}H NMR spectra of **4aam** ($CDCl_3$).

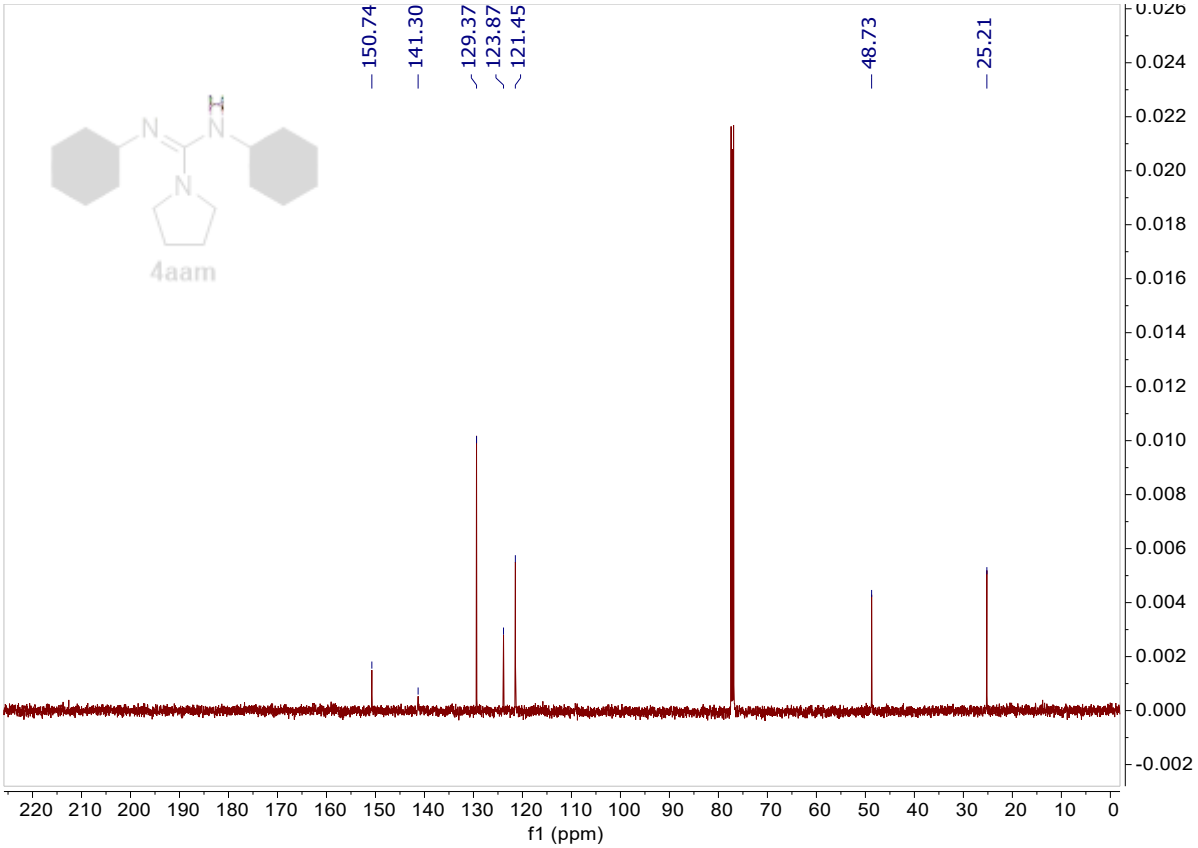


Figure S26 ^{13}C NMR spectra of **4aam** ($CDCl_3$).

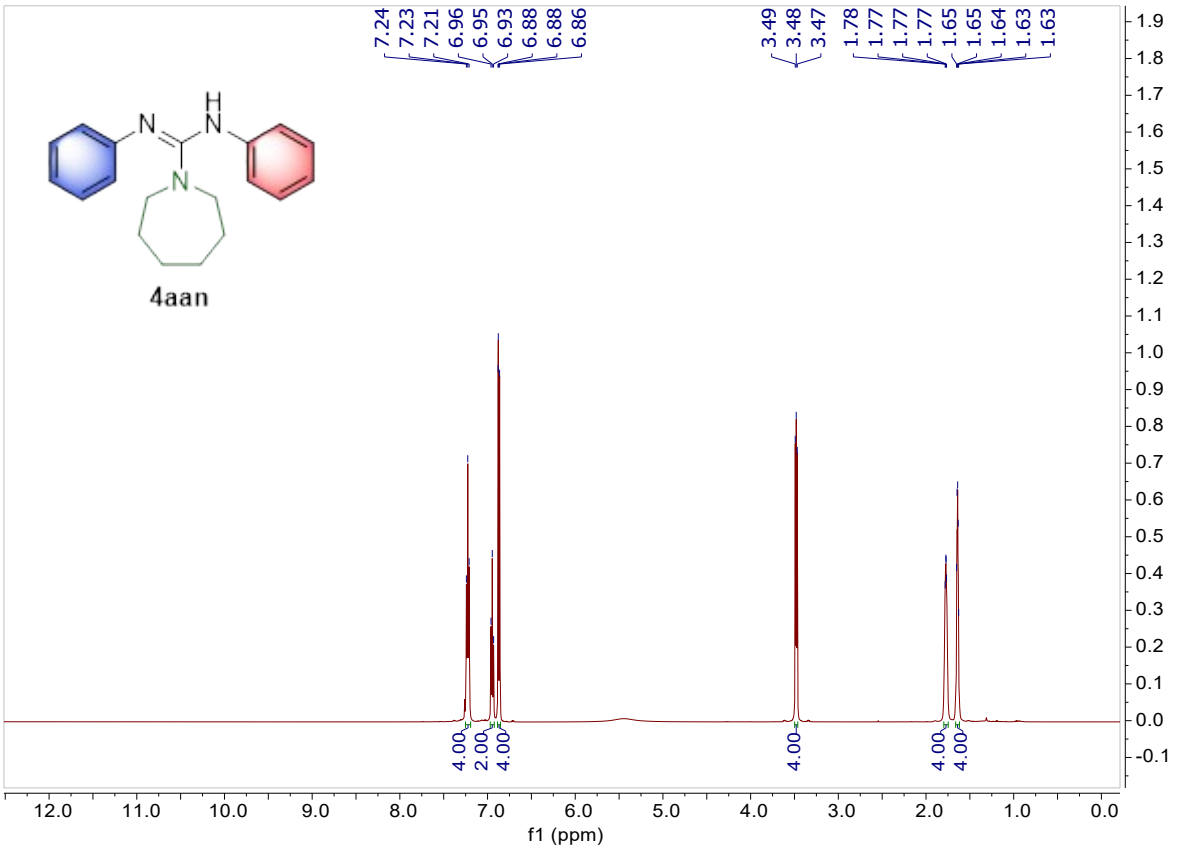


Figure S27 ^{1}H NMR spectra of **4aan** ($CDCl_3$)..

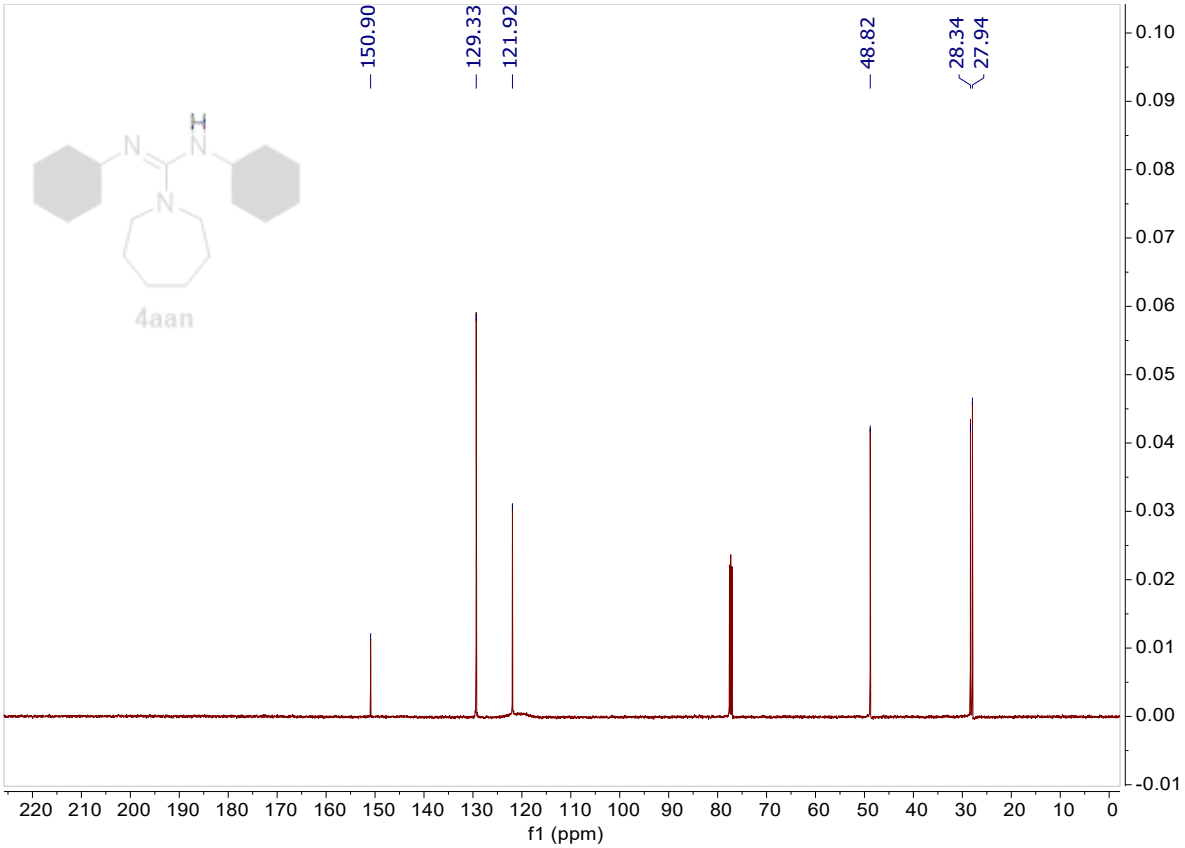


Figure S28 ^{13}C NMR spectra of **4aan** ($CDCl_3$)

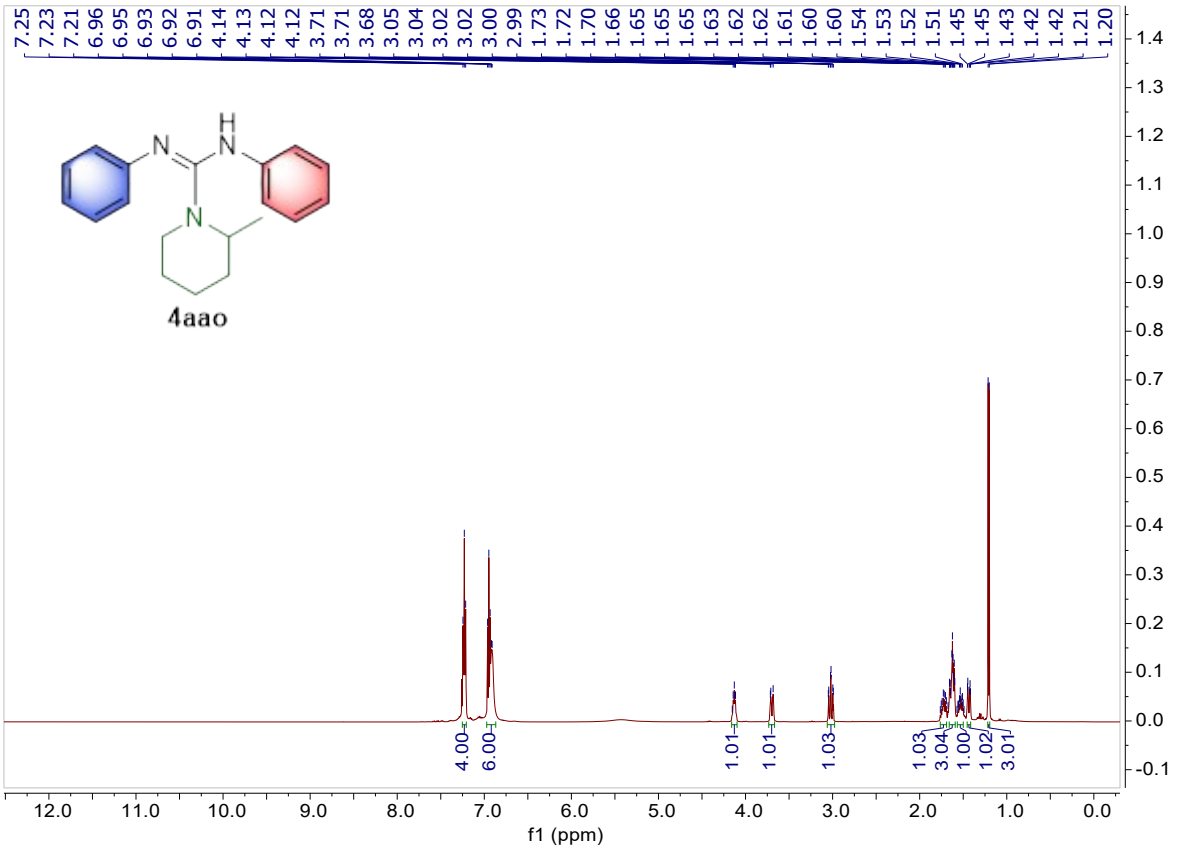


Figure S29 ^{1}H NMR spectra of **4aao** ($CDCl_3$).

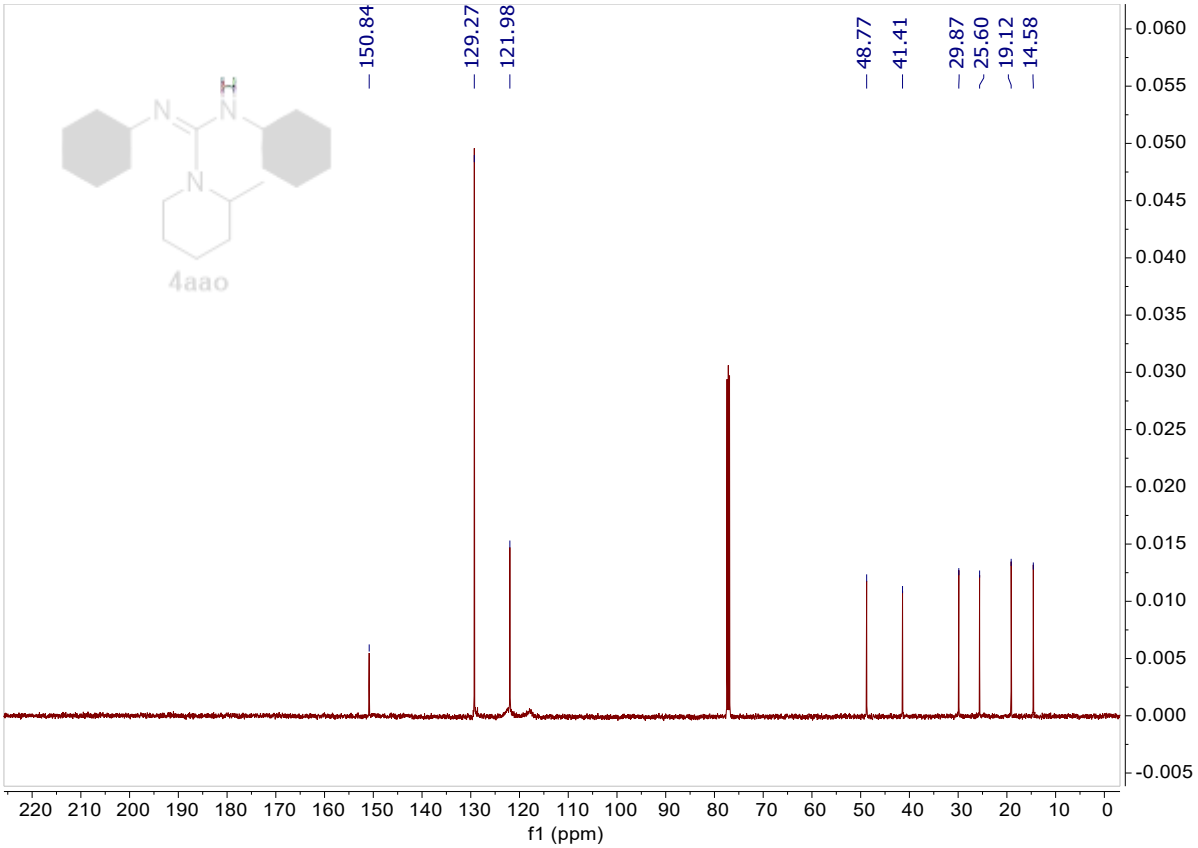


Figure S30 ^{13}C NMR spectra of **4aao** ($CDCl_3$).

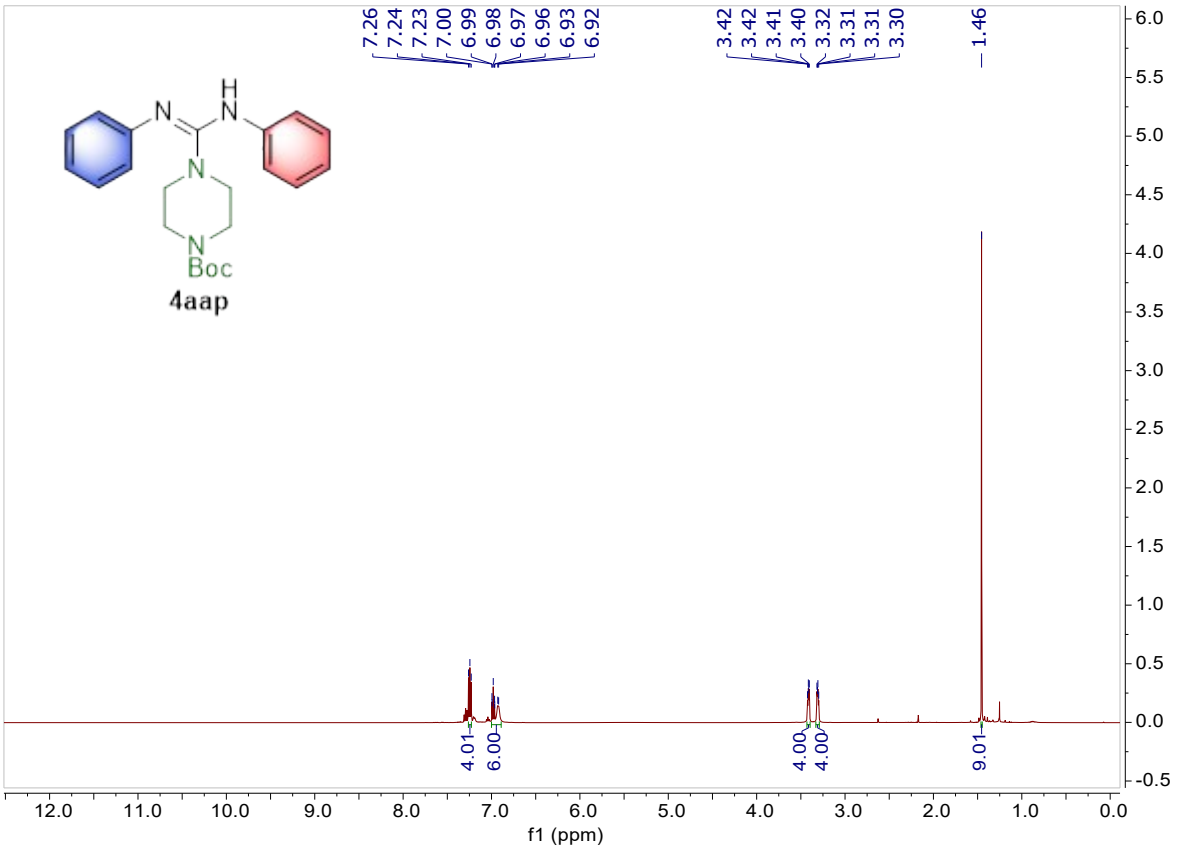


Figure S31 ^{1}H NMR spectra of **4aap** ($CDCl_3$).

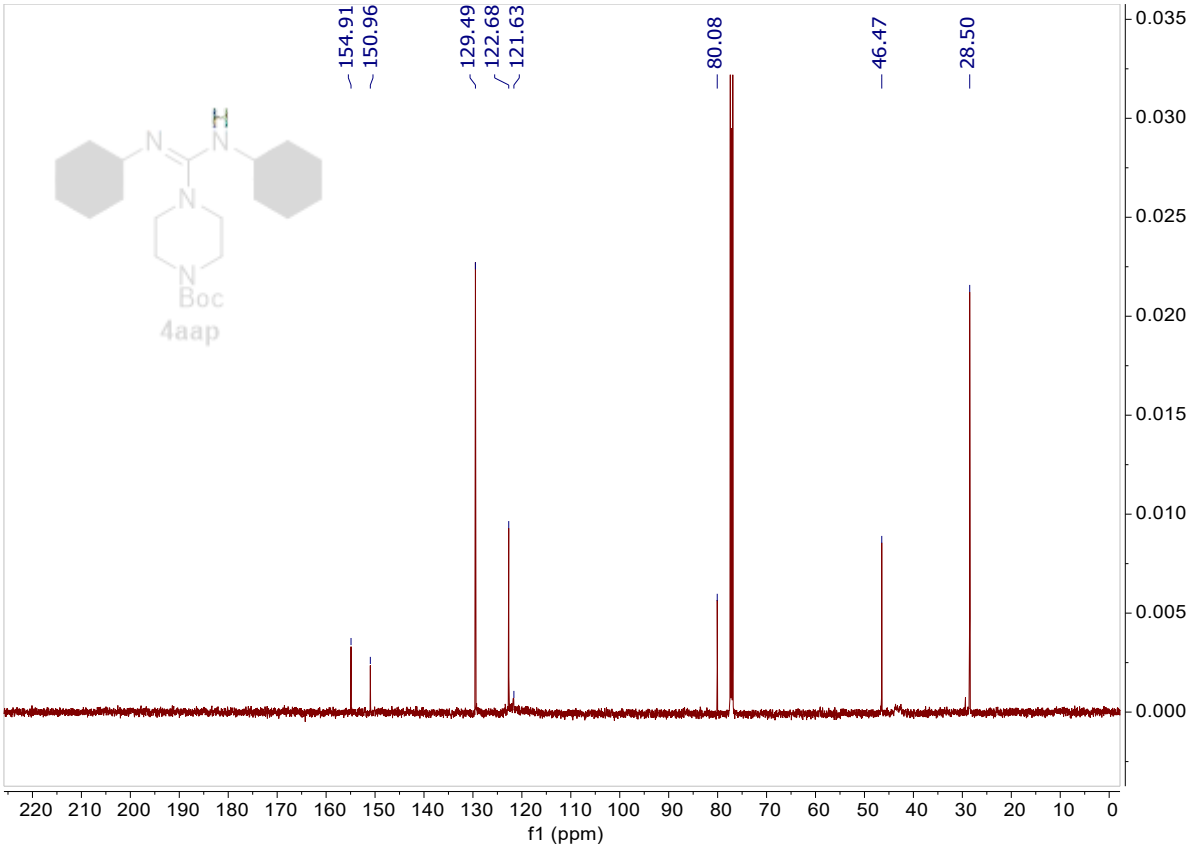


Figure S32 ^{13}C NMR spectra of **4aap** ($CDCl_3$).

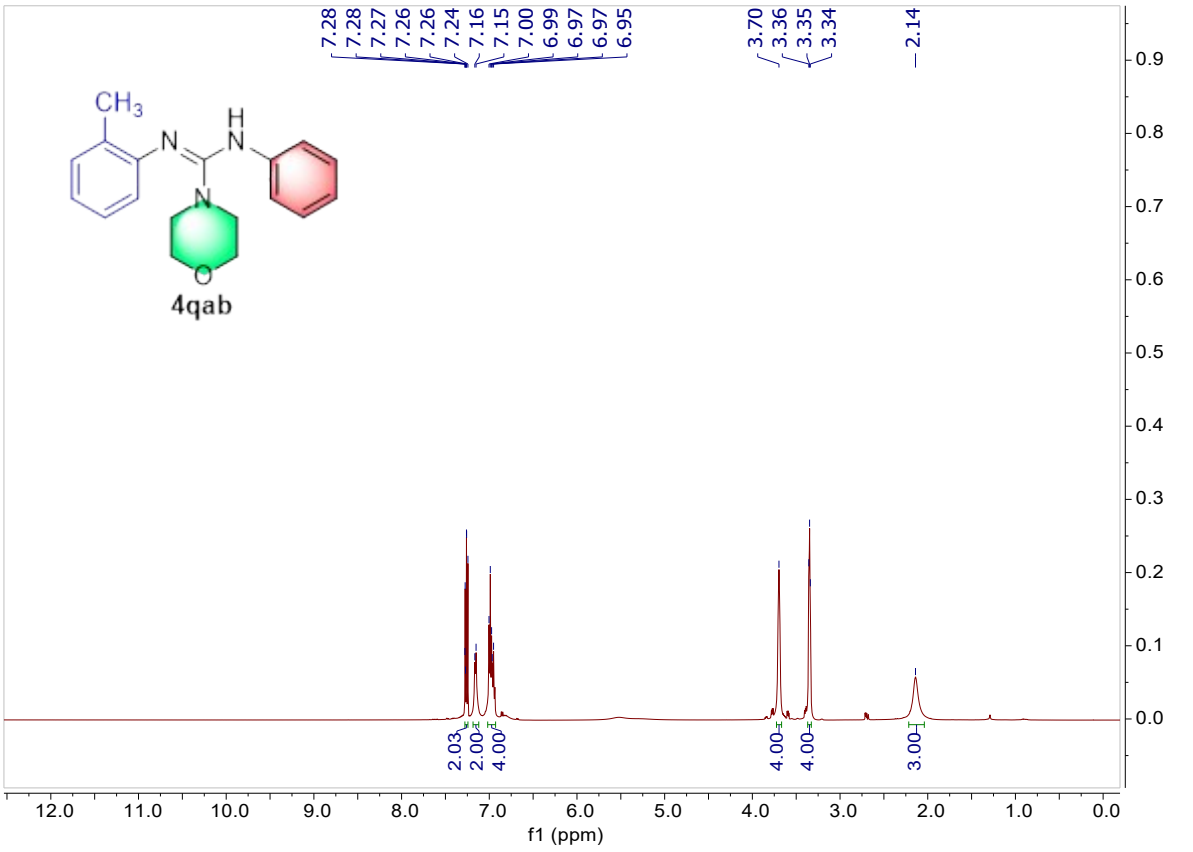


Figure S33 ^{1}H NMR spectra of **4qab** ($CDCl_3$).

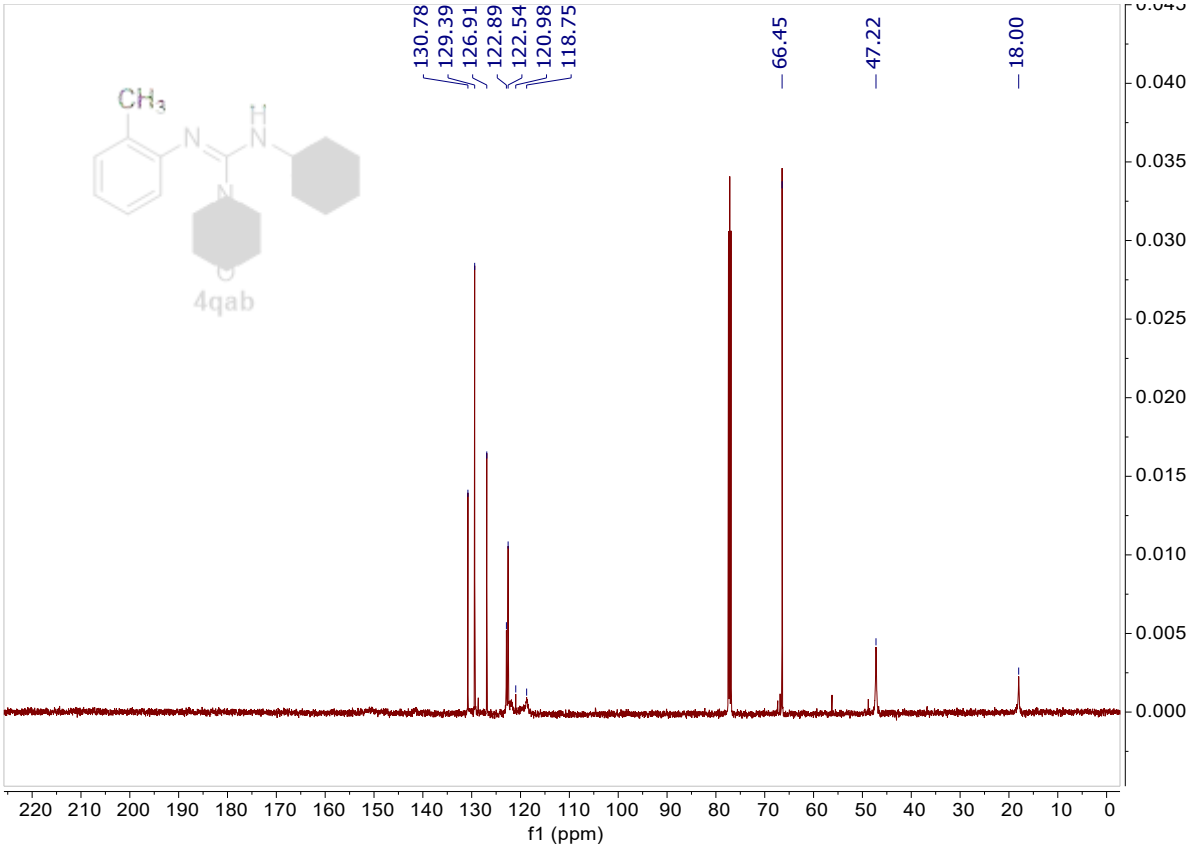


Figure S34 ^{13}C NMR spectra of **4qab** ($CDCl_3$).

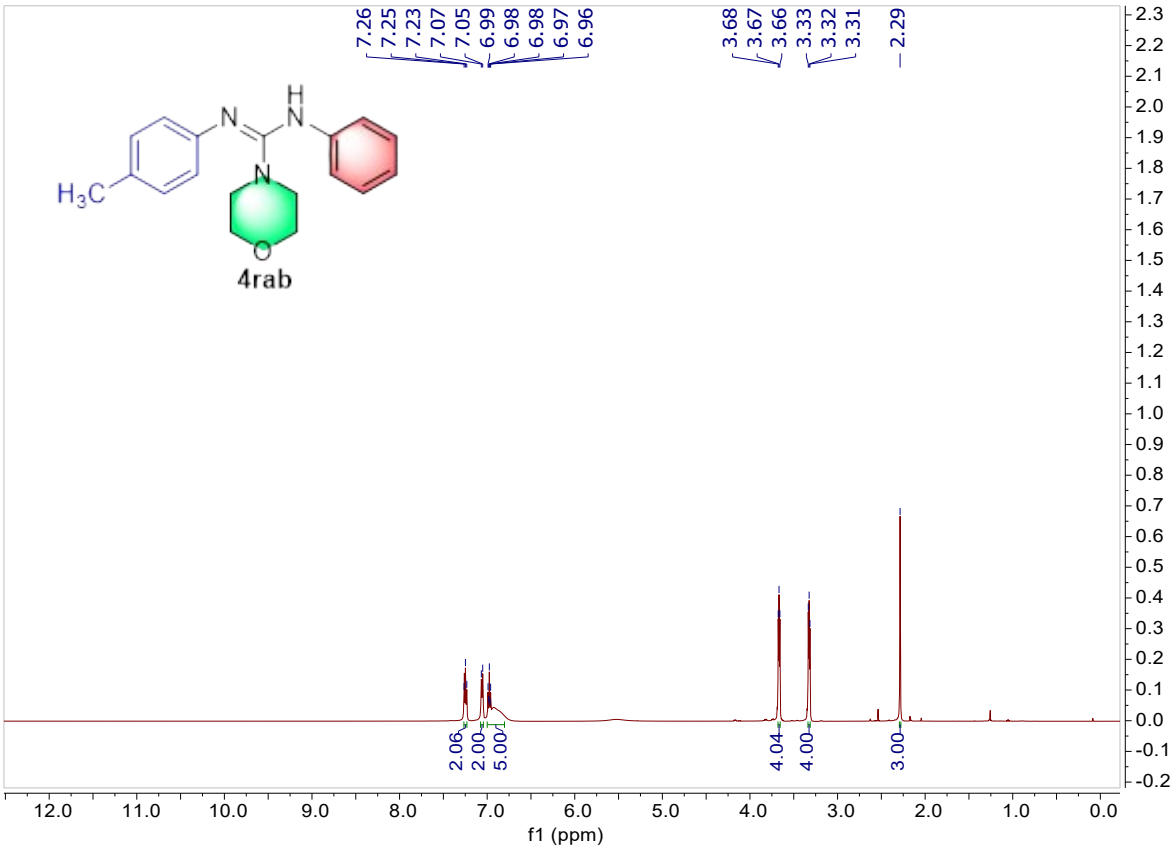


Figure S35 ^{1}H NMR spectra of **4rab** ($CDCl_3$).

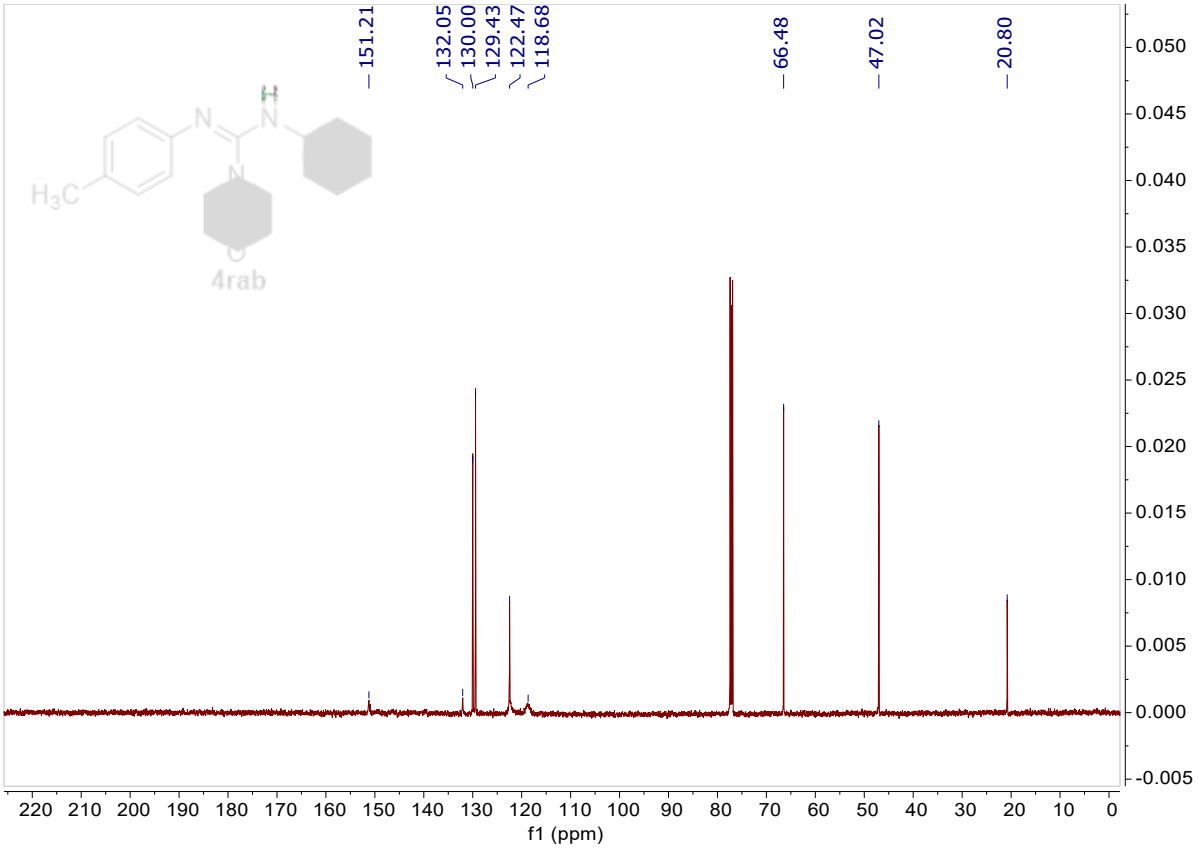


Figure S36 ^{13}C NMR spectra of **4rab** ($CDCl_3$).

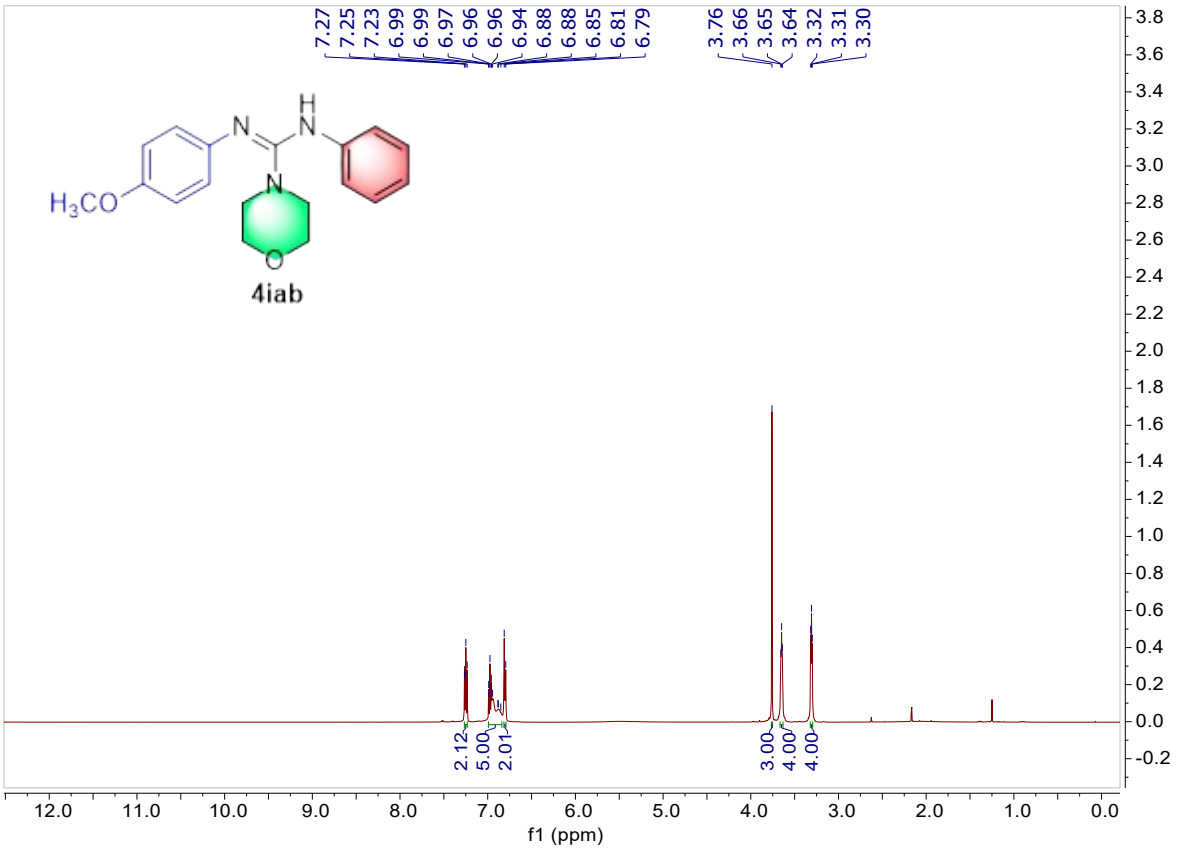


Figure S37 ^{1}H NMR spectra of **4iab** ($CDCl_3$).

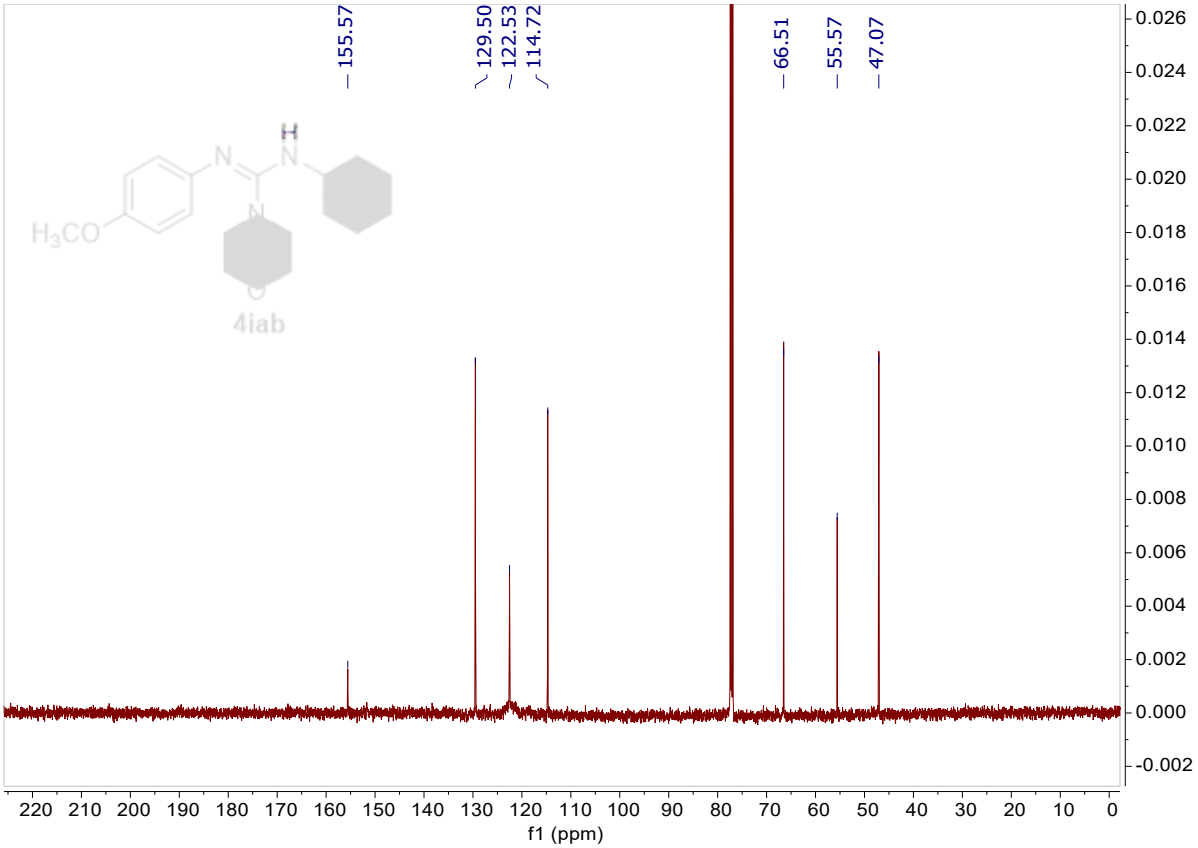


Figure S38 ^{13}C NMR spectra of **4iab** ($CDCl_3$).

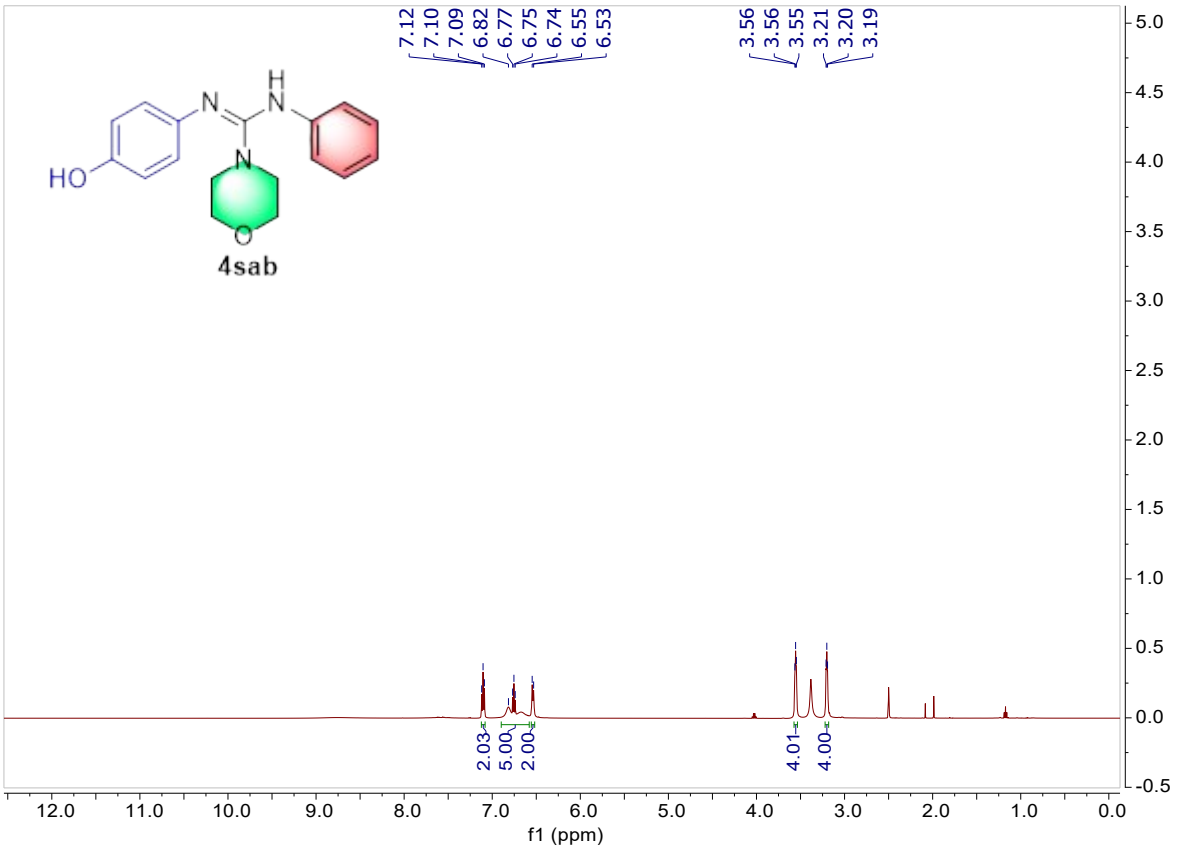


Figure S39 ^{1}H NMR spectra of **4sab** ($(CD_3)_2SO$).

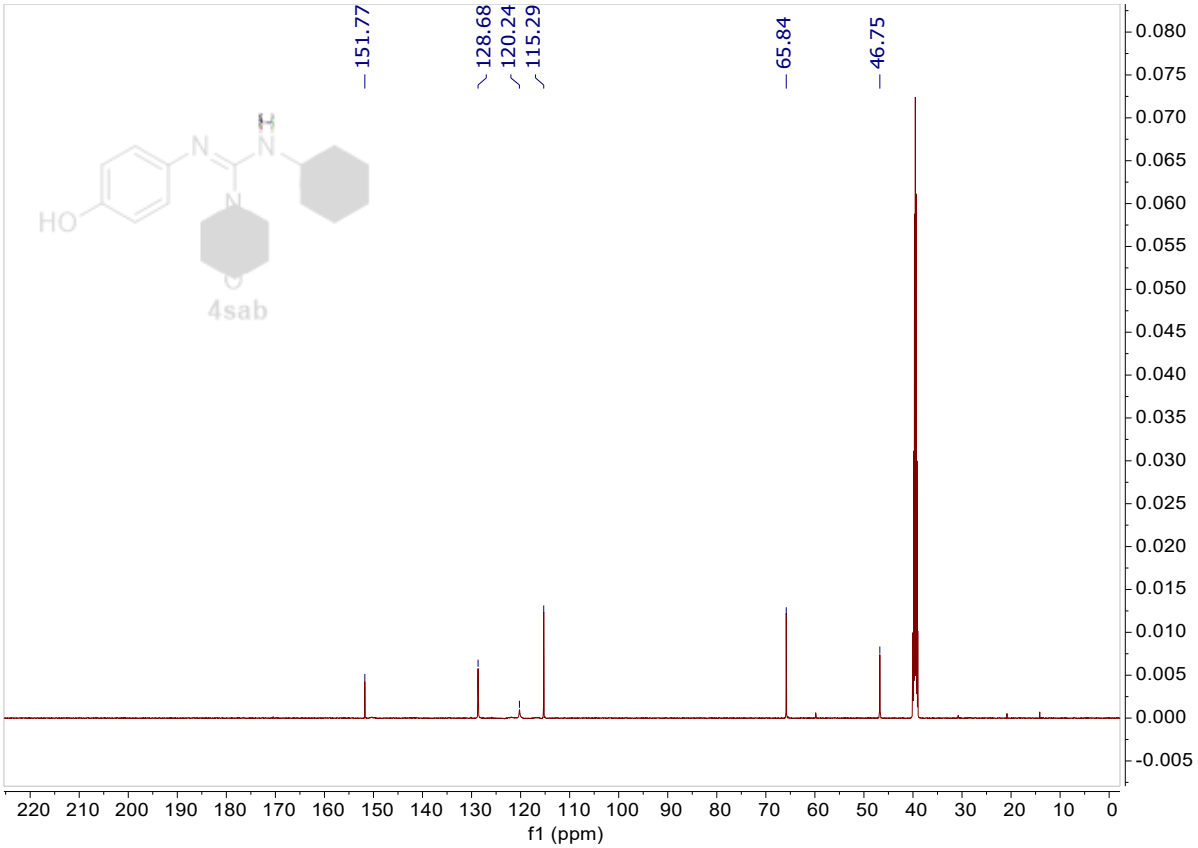


Figure S40 ^{13}C NMR spectra of **4sab** ($(CD_3)_2SO$).

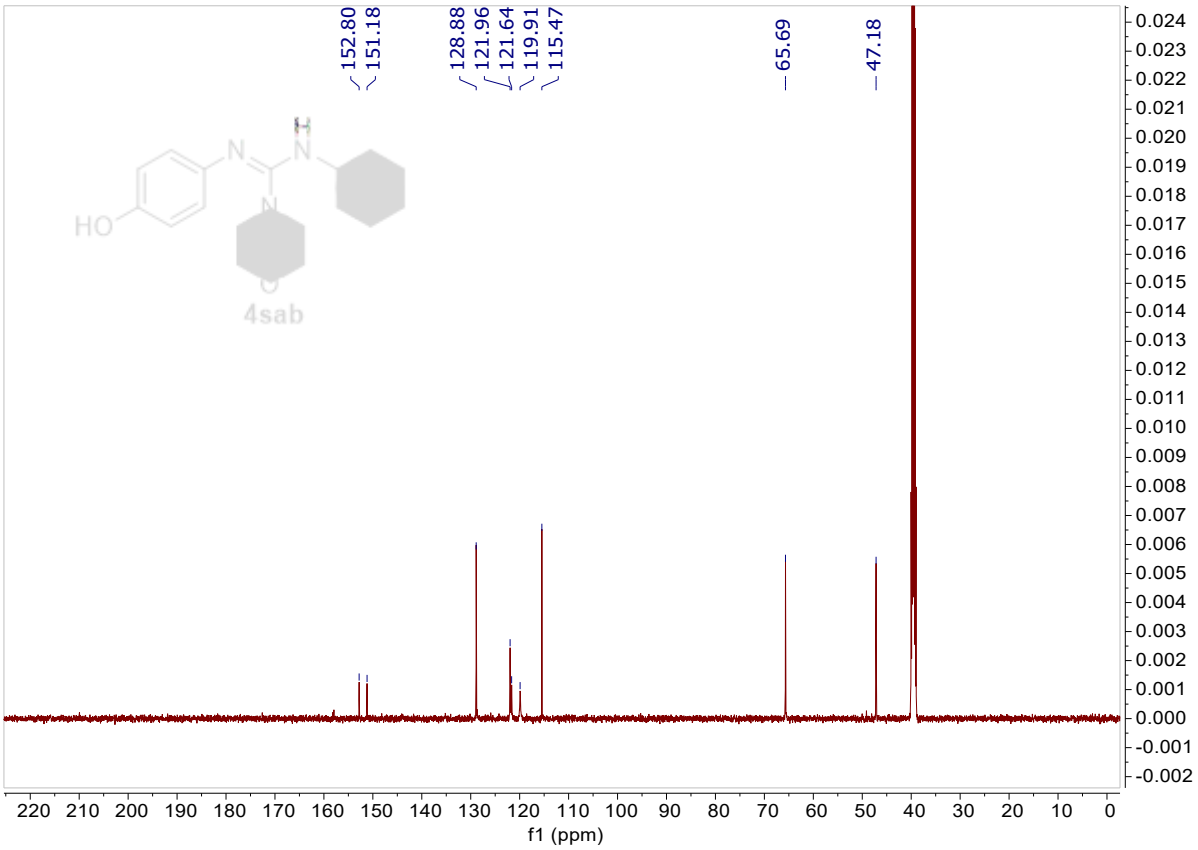


Figure S41 ^{13}C NMR spectra of **4sab** ($(CD_3)_2SO$ + 0.1% TFA).

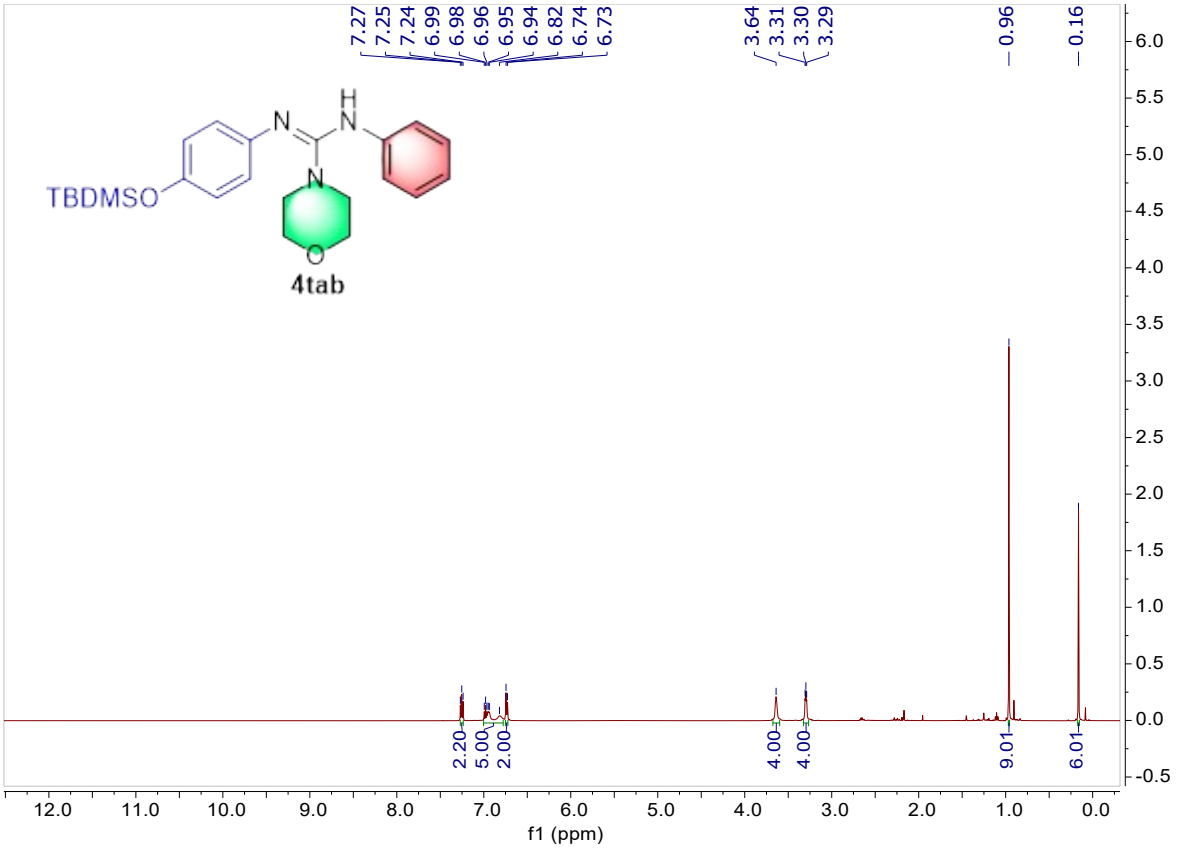


Figure S42 ^{1}H NMR spectra of **4tab** ($CDCl_3$).

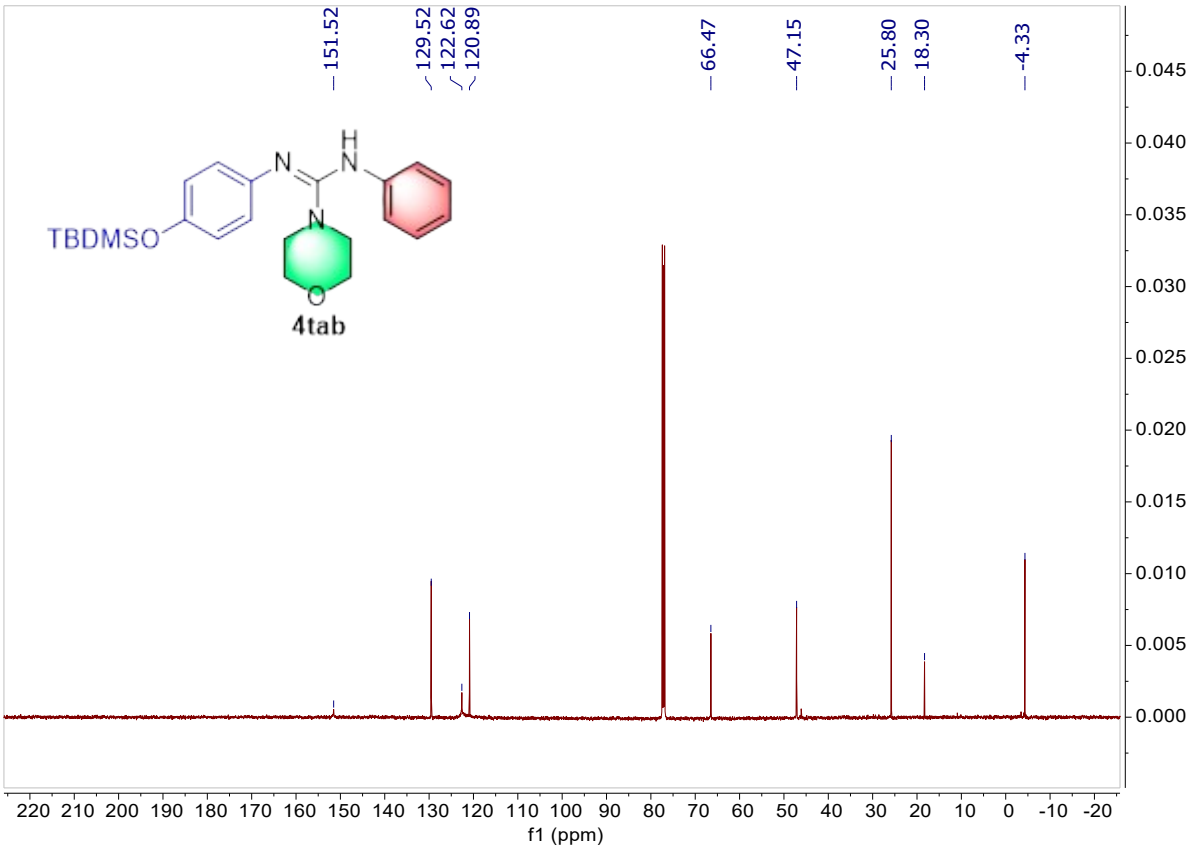


Figure S43 ^{13}C NMR spectra of **4tab** ($CDCl_3$).

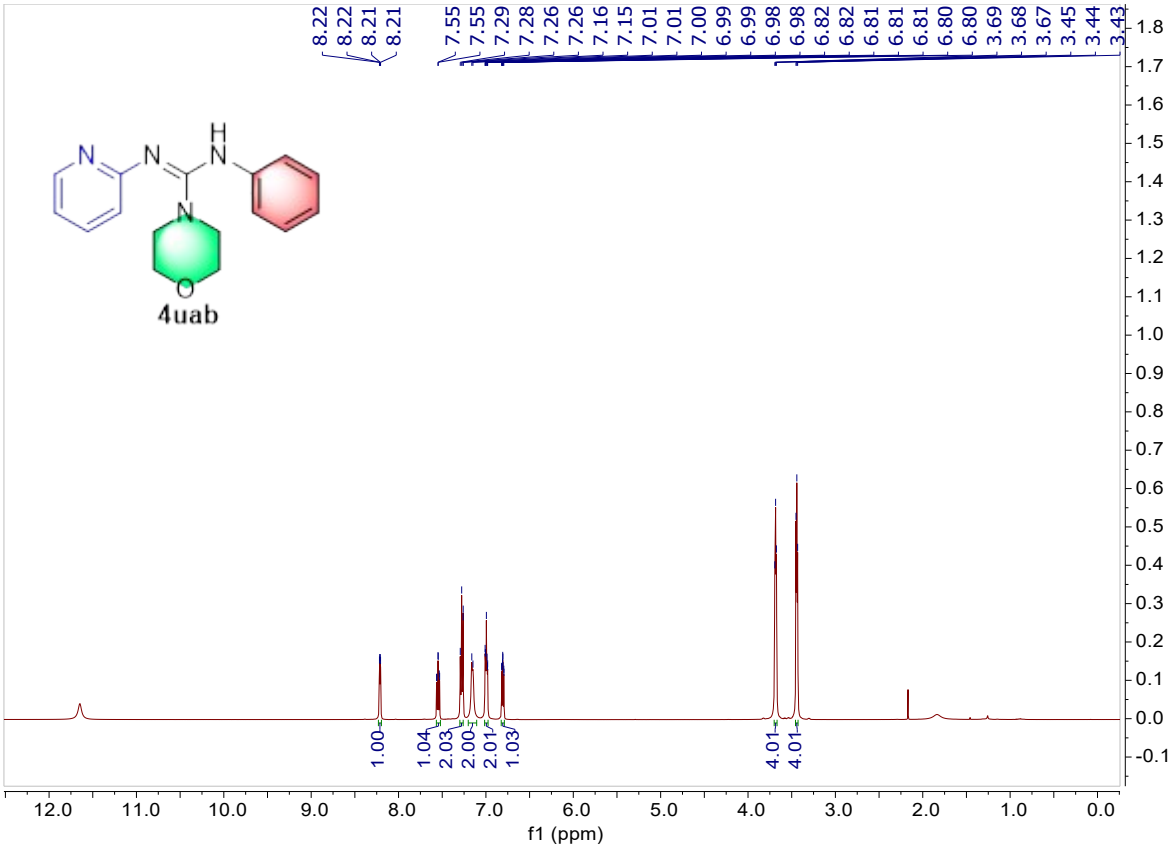


Figure S44 ^{1}H NMR spectra of **4uab** ($CDCl_3$).

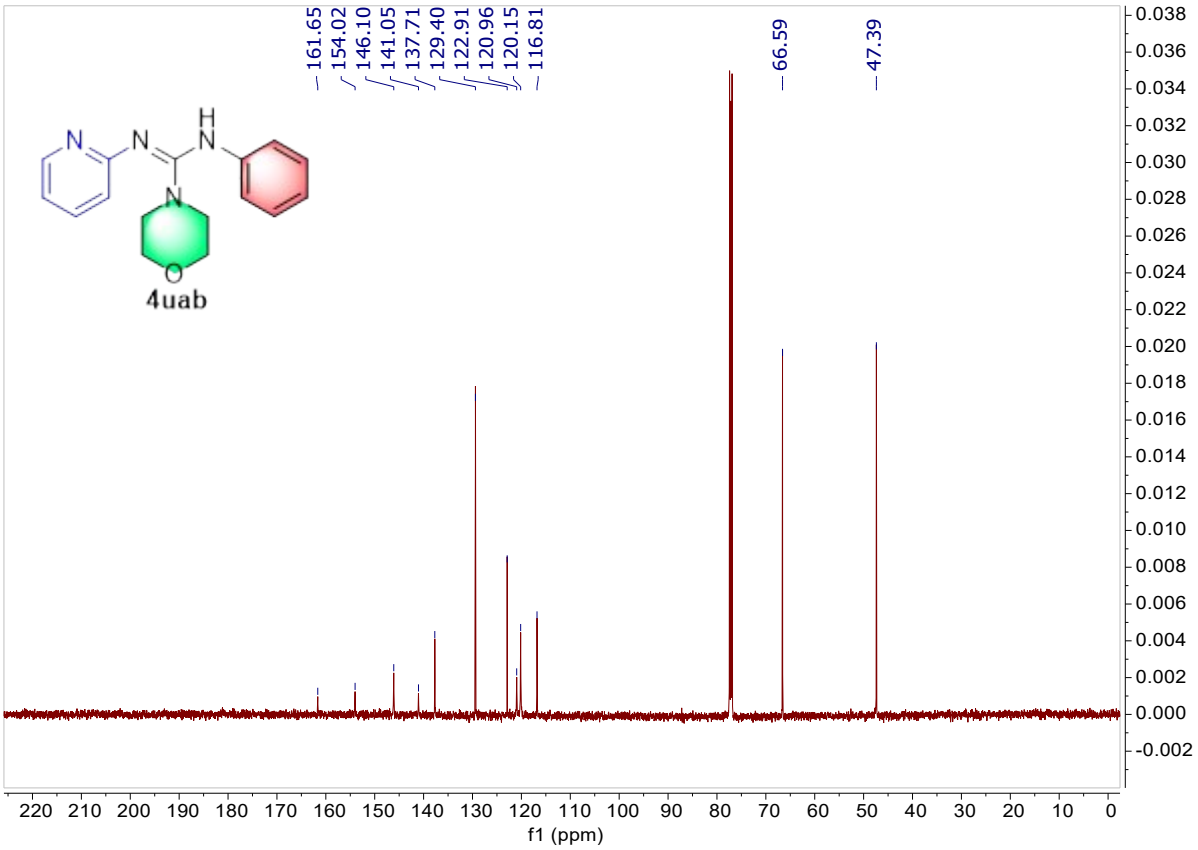


Figure S45 ^{13}C NMR spectra of **4uab** ($CDCl_3$).

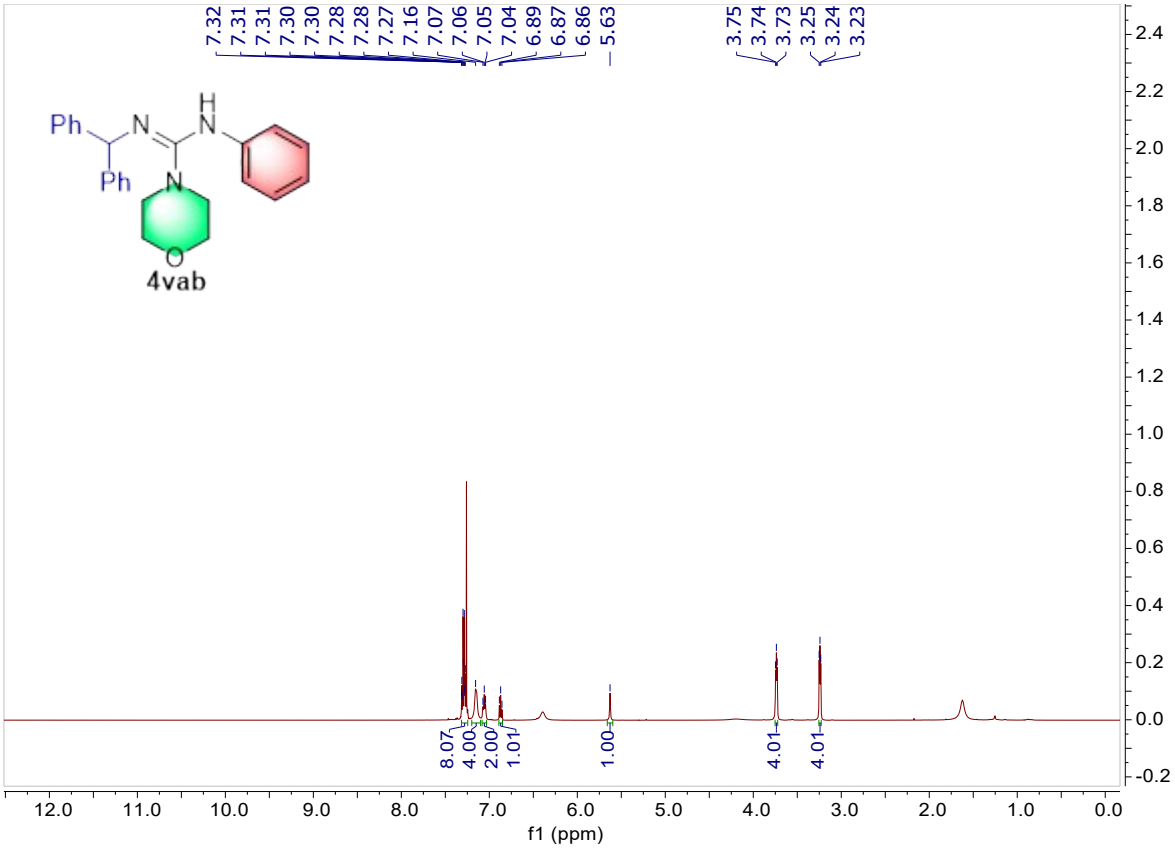


Figure S46 ^{1}H NMR spectra of **4vab** ($CDCl_3$).

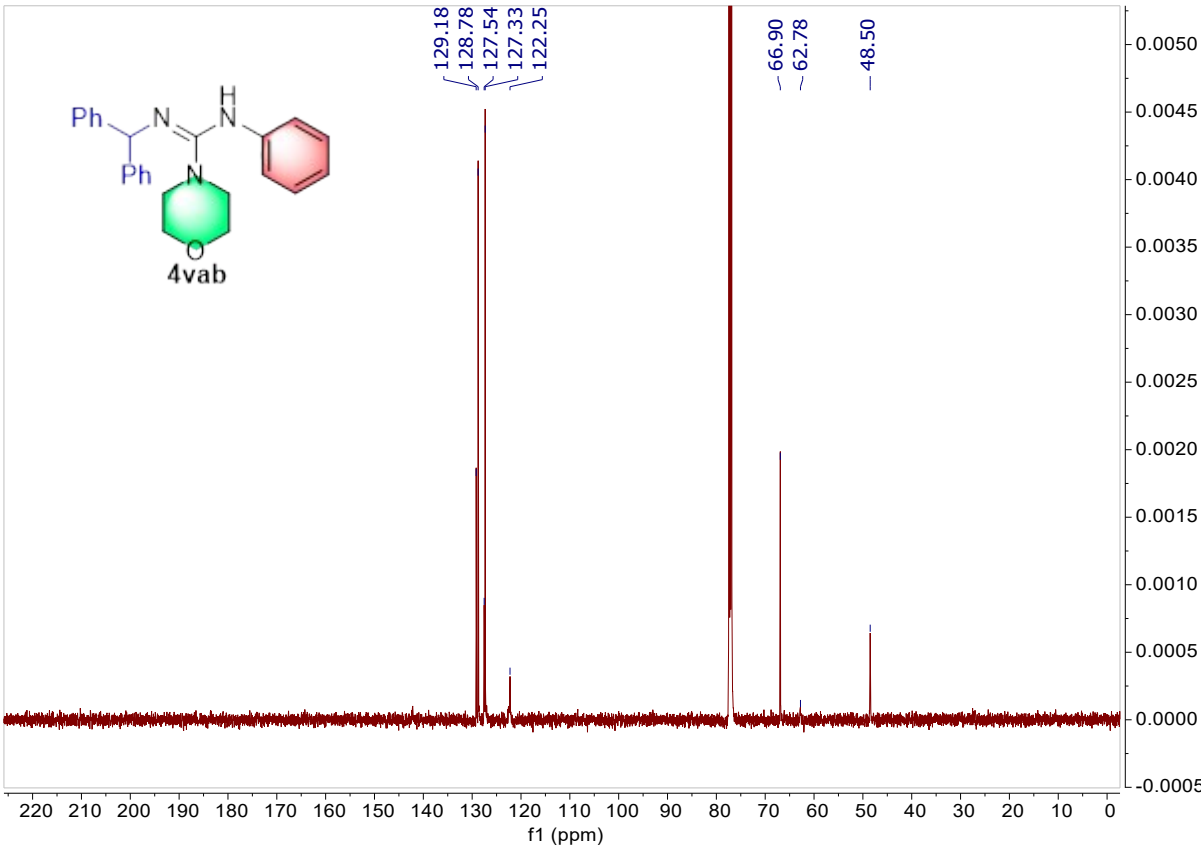


Figure S47 ^{13}C NMR spectra of **4vab** ($CDCl_3$).

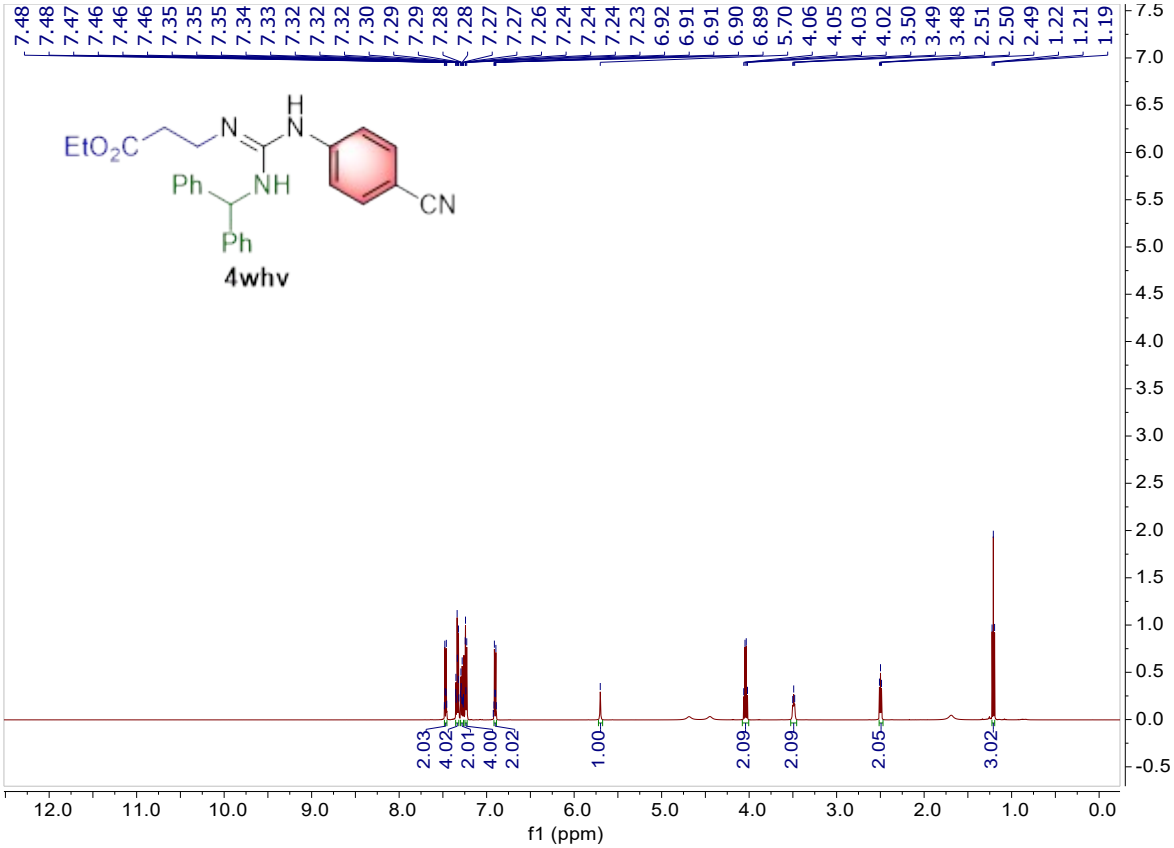


Figure S48 ^{1}H NMR spectra of **4whv** ($CDCl_3$).

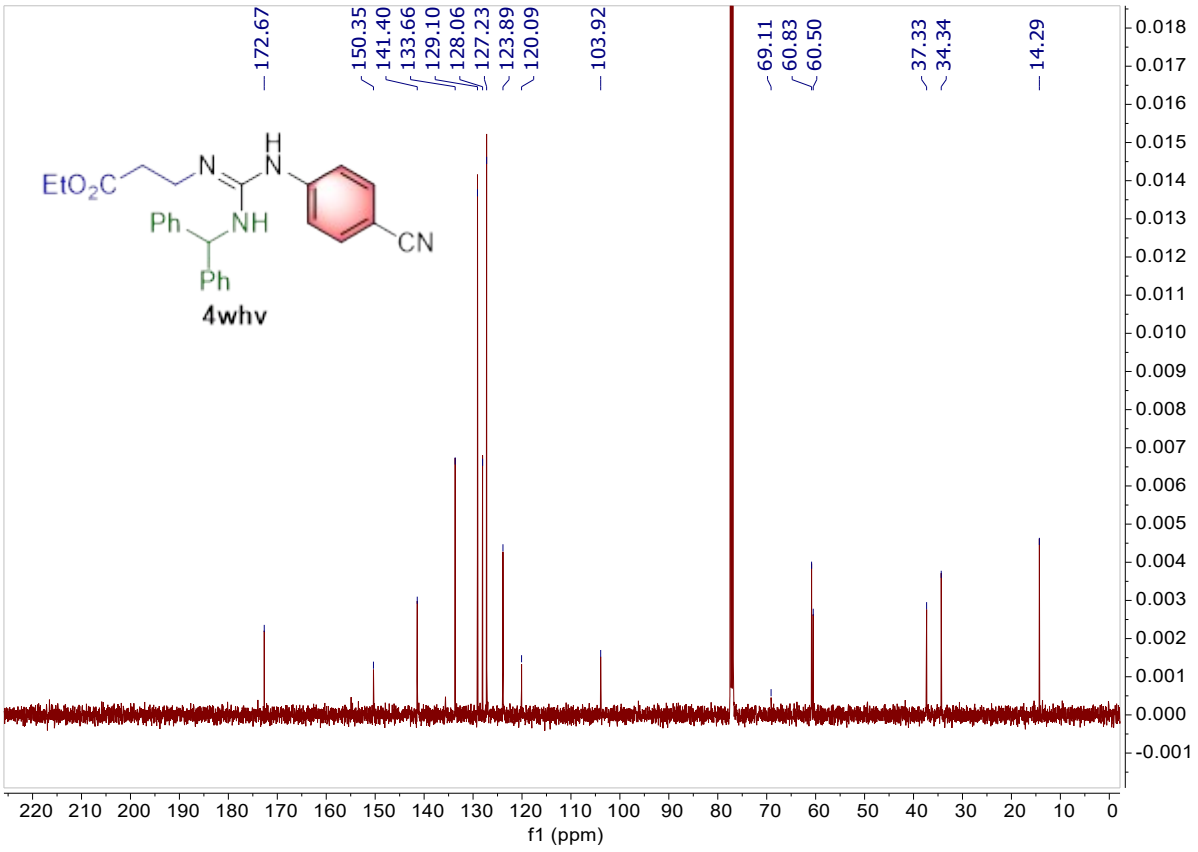


Figure S49 ^{13}C NMR spectra of **4whv** ($CDCl_3$).

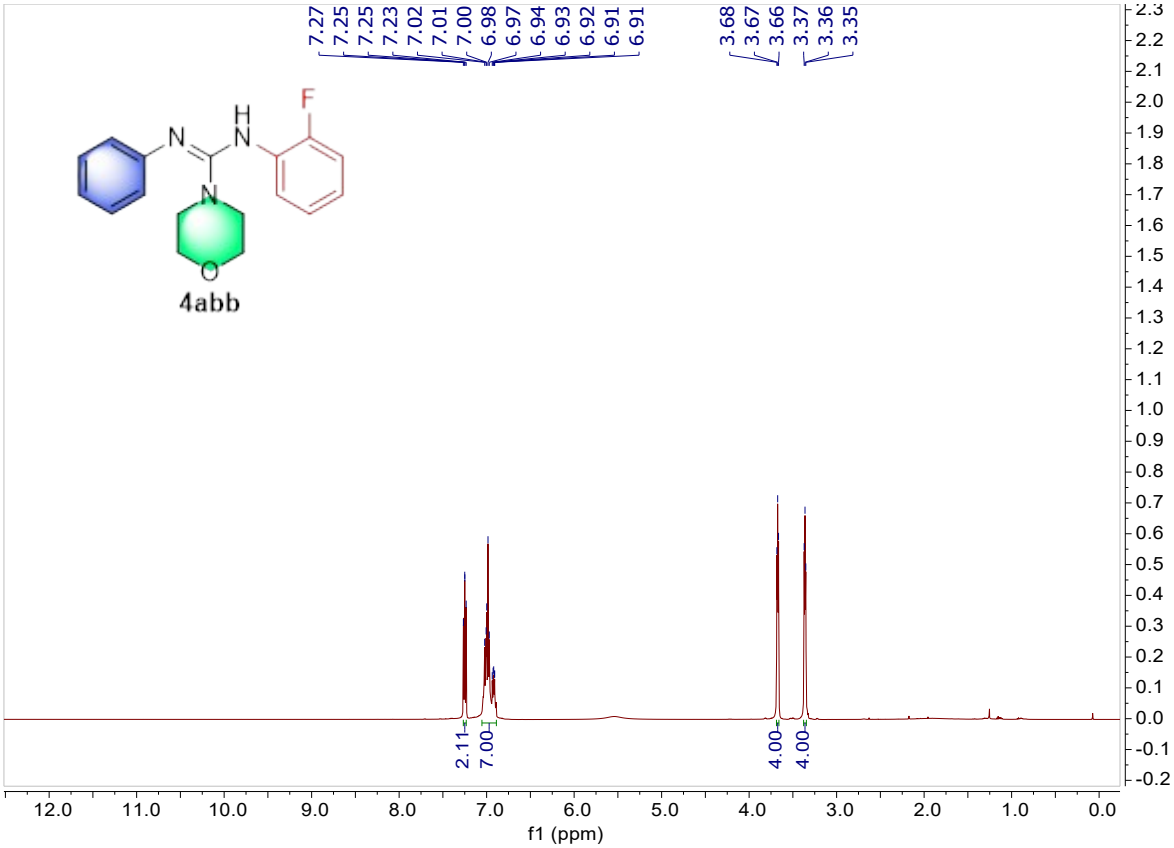


Figure S50 ^{1}H NMR spectra of **4abb** ($CDCl_3$).

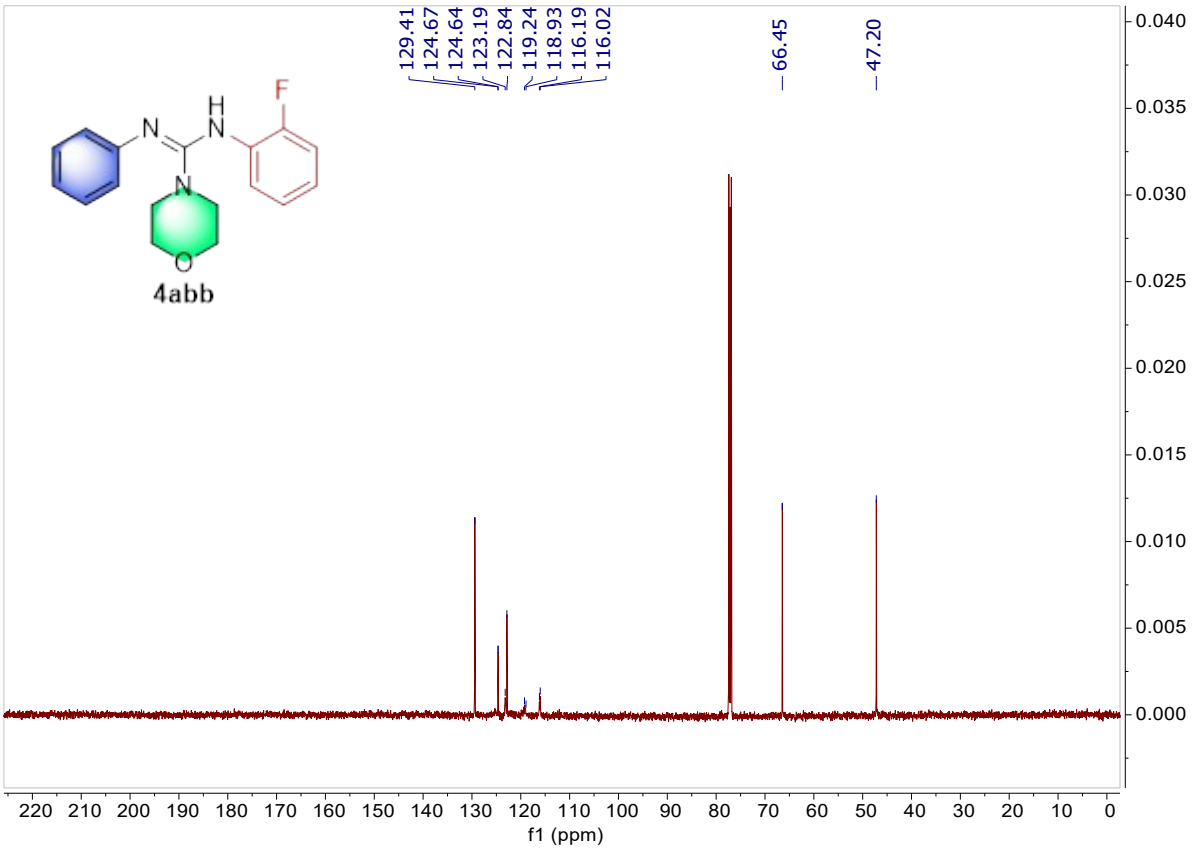


Figure S51 ^{13}C NMR spectra of **4abb** ($CDCl_3$).

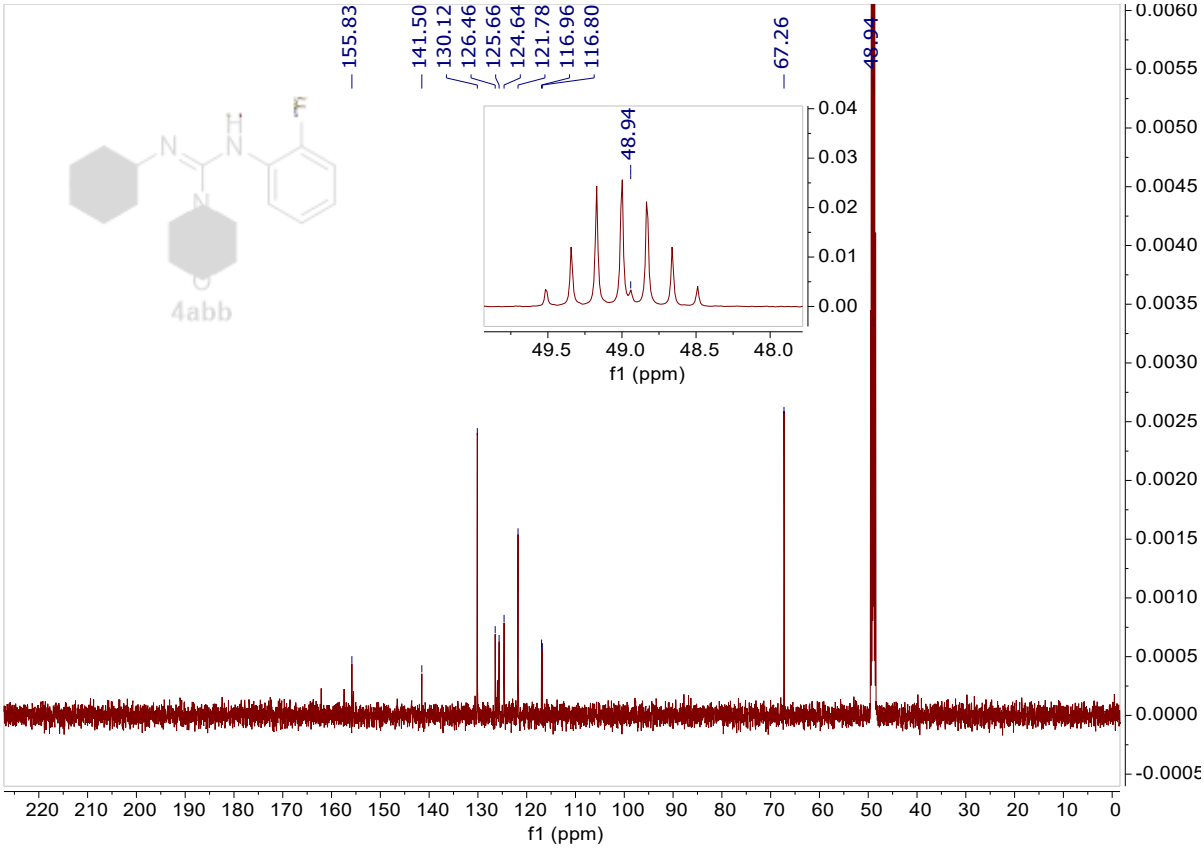


Figure S52 ^{13}C NMR spectra of **4abb** (CD_3OD + 0.1% TFA).

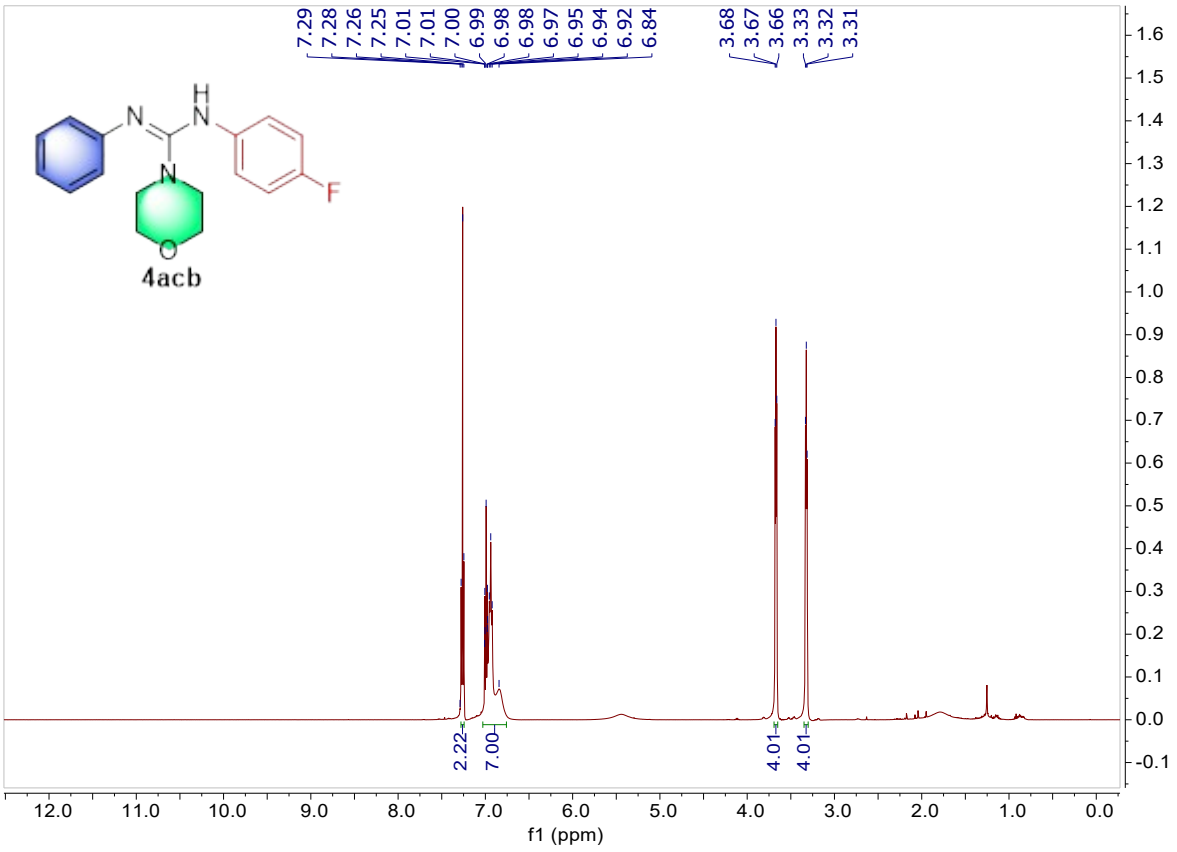


Figure S53 ^{1}H NMR spectra of **4acb** ($CDCl_3$).

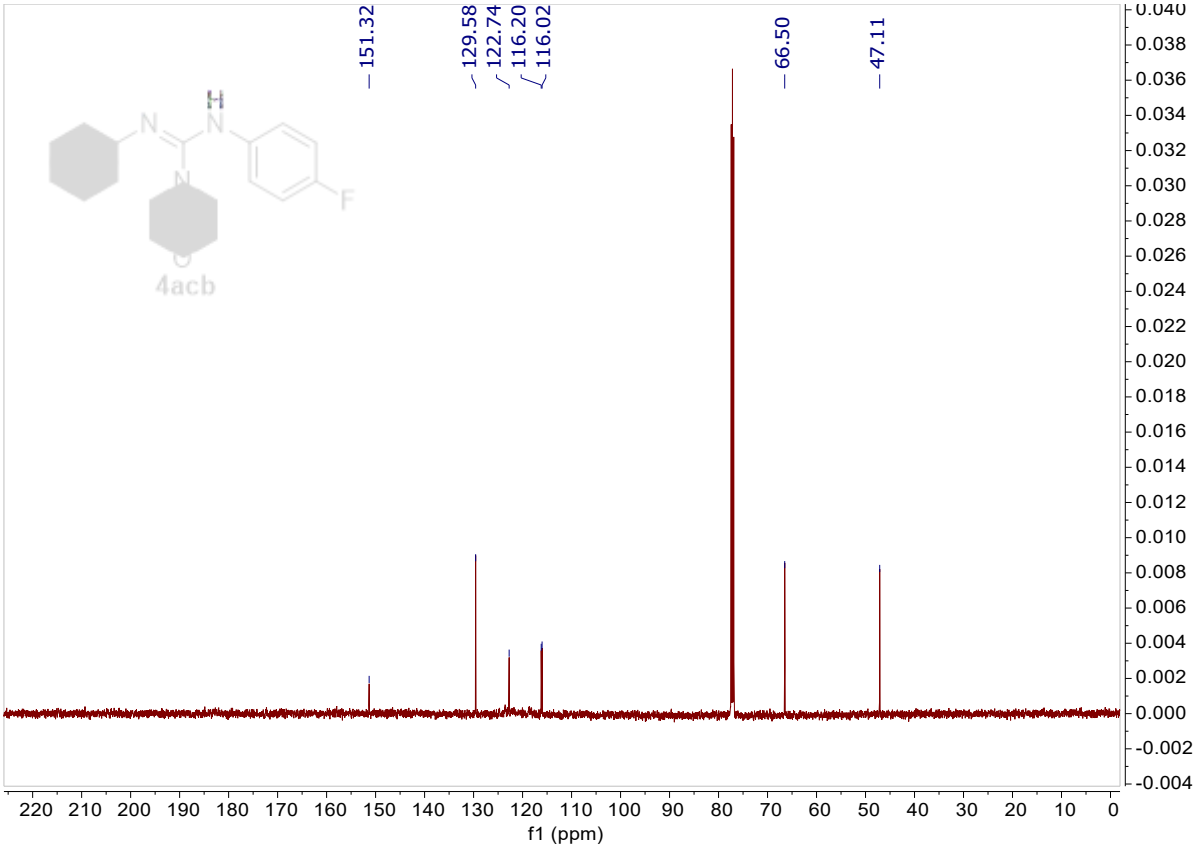


Figure S54 ^{13}C NMR spectra of **4acb** ($CDCl_3$).

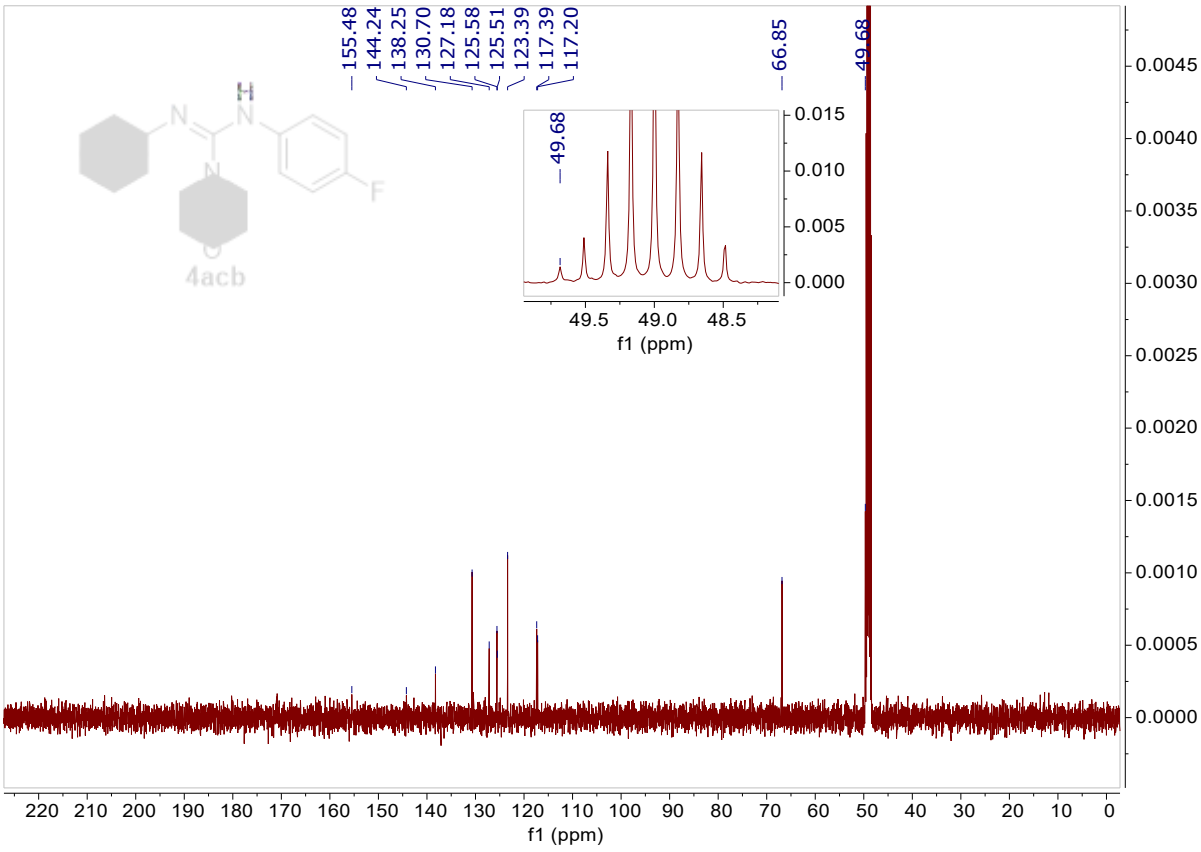


Figure S55 ^{13}C NMR spectra of **4acb** (CD_3OD + 0.1% TFA).

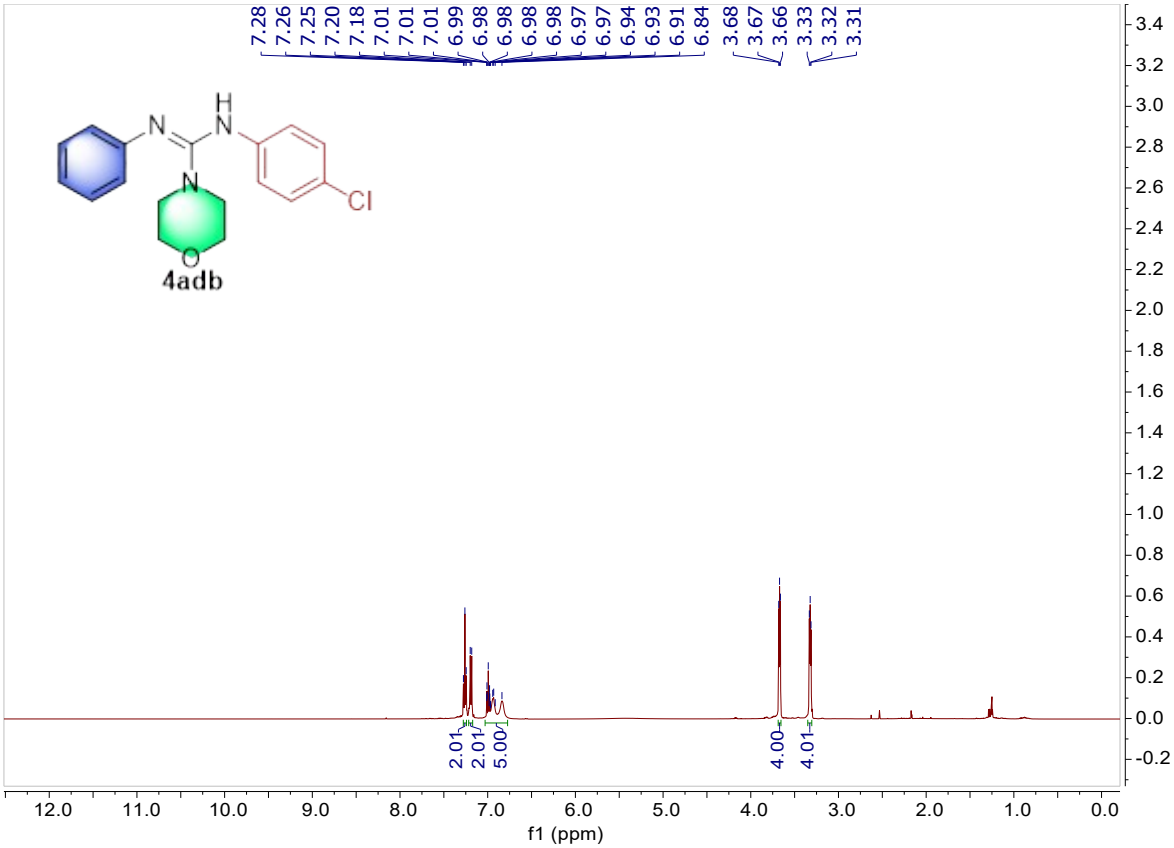


Figure S56 ^{1}H NMR spectra of **4adb** ($CDCl_3$).

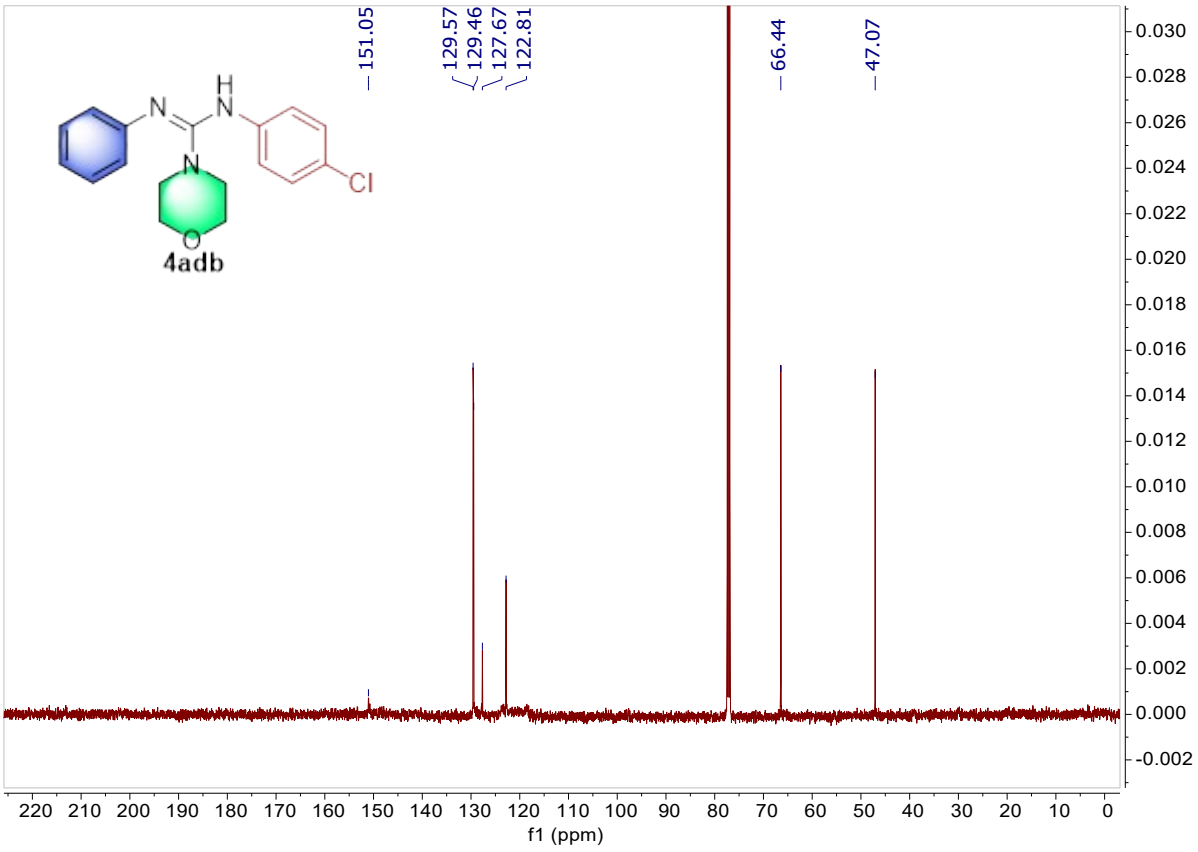


Figure S57 ^{13}C NMR spectra of **4adb** ($CDCl_3$).

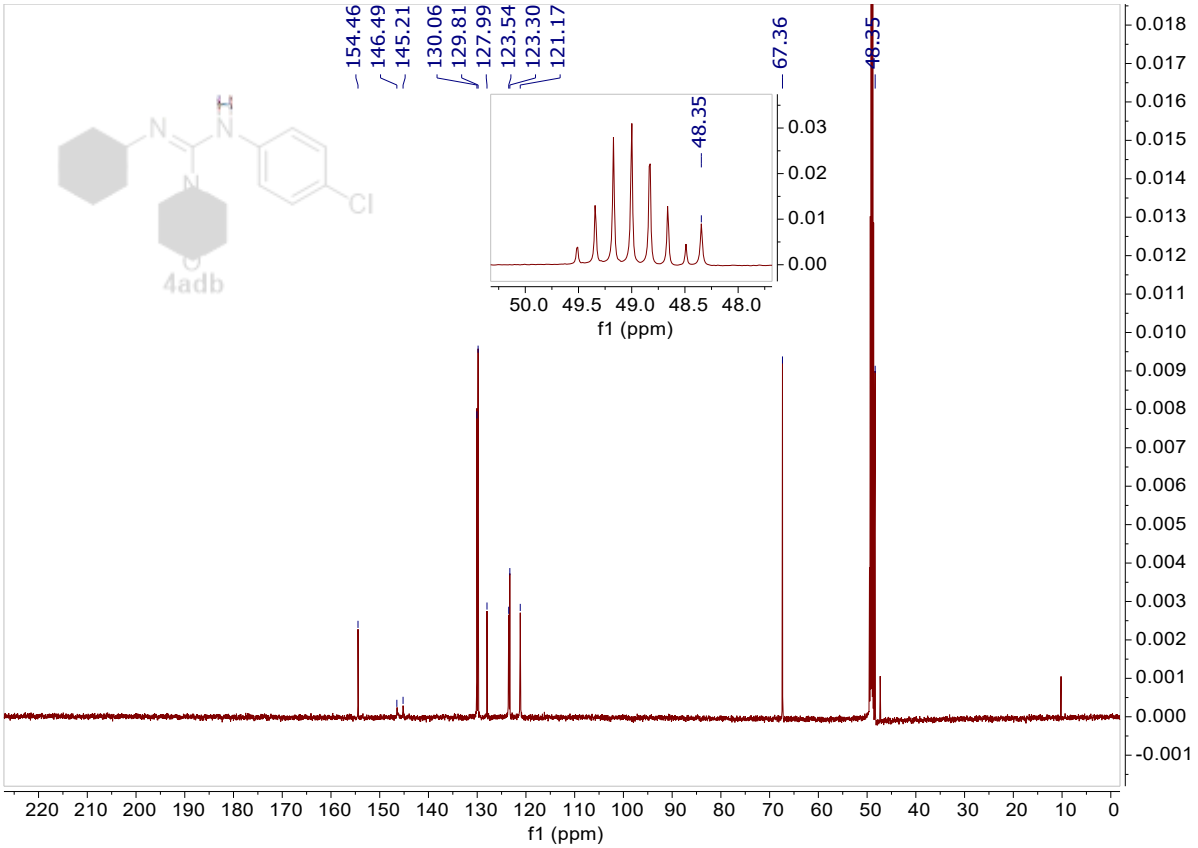


Figure S58 ^{13}C NMR spectra of **4aag** (CD_3OD + 0.1% TFA).

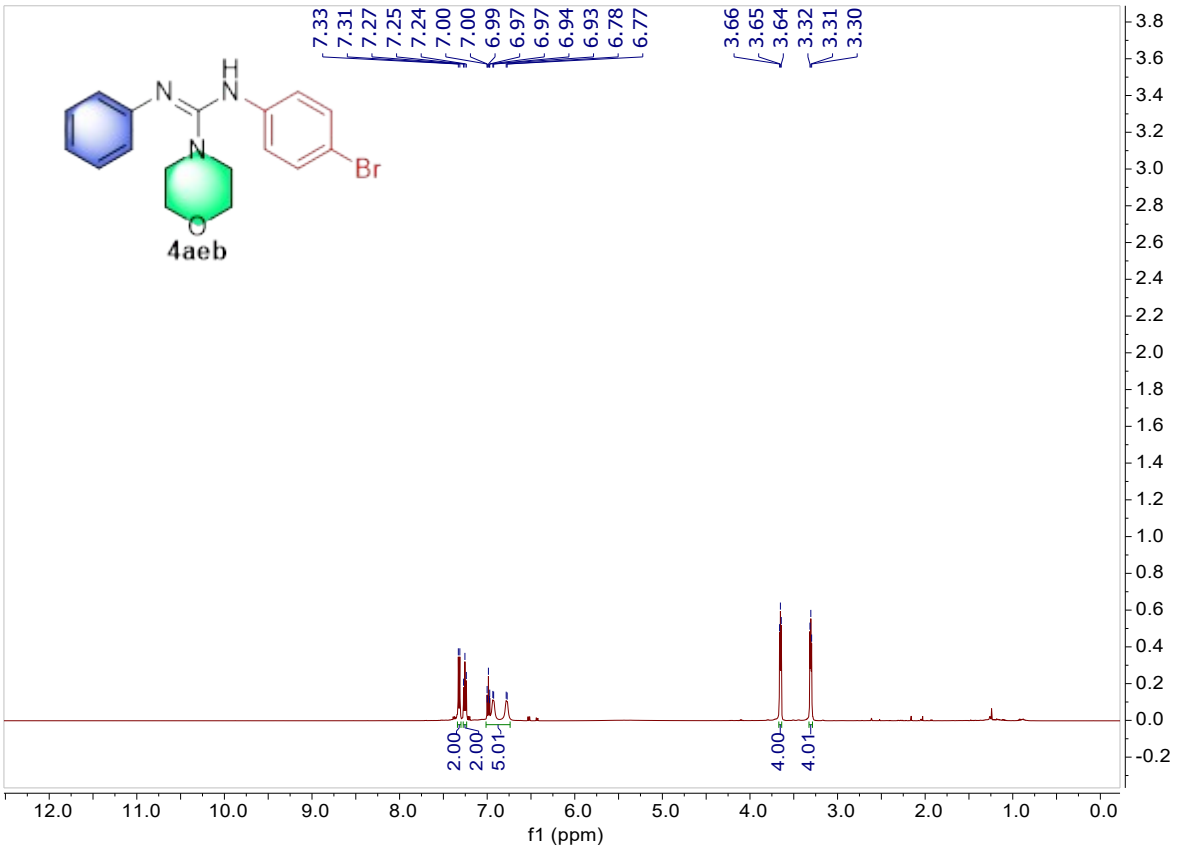


Figure S59 ^{1}H NMR spectra of **4aeb** ($CDCl_3$).

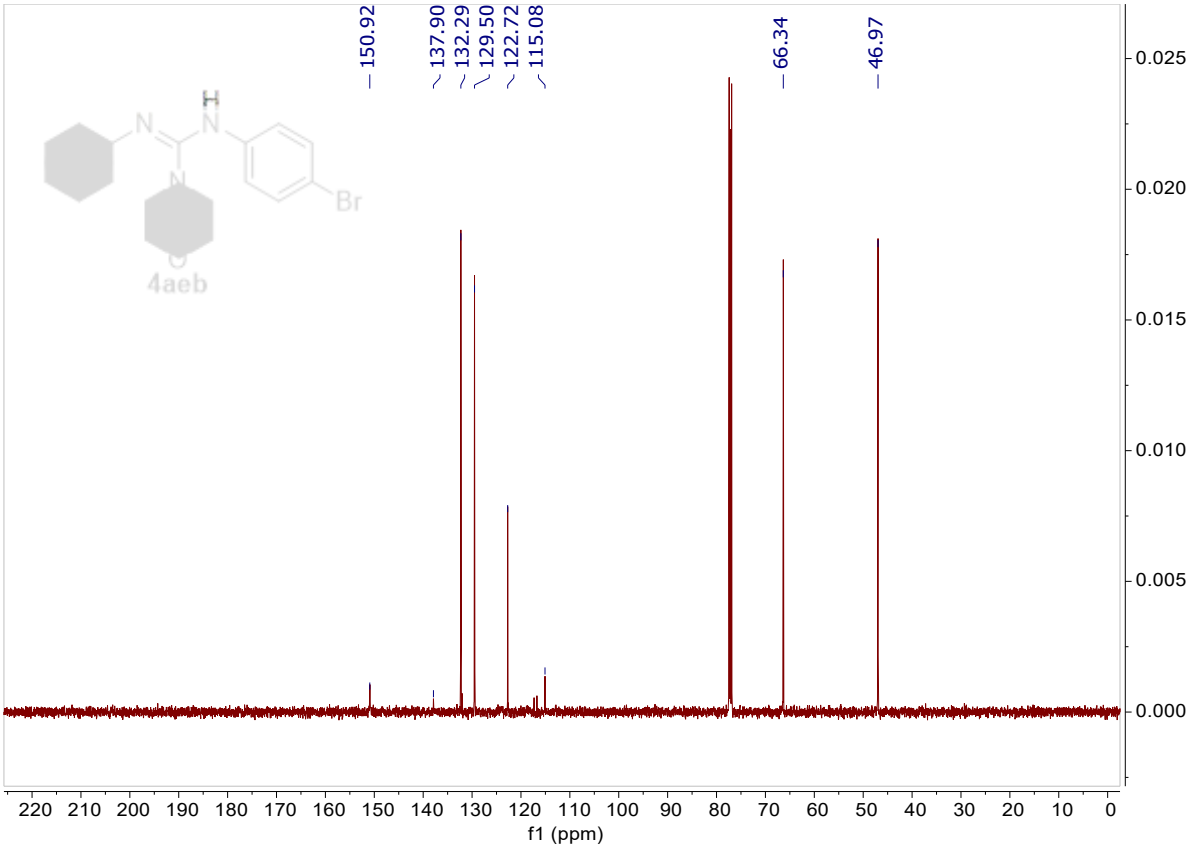


Figure S60 ^{13}C NMR spectra of **4aeb** ($CDCl_3$).

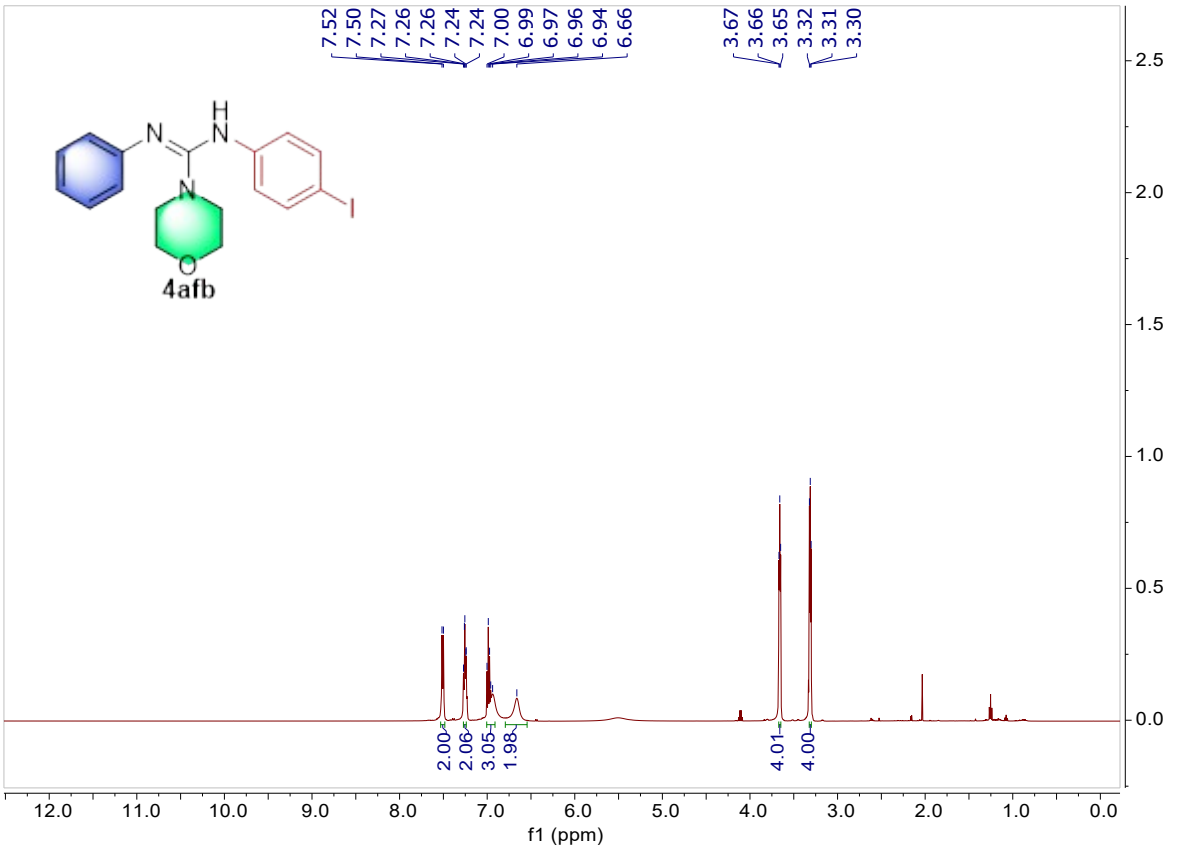


Figure S61 ^{1}H NMR spectra of **4afb** ($CDCl_3$).

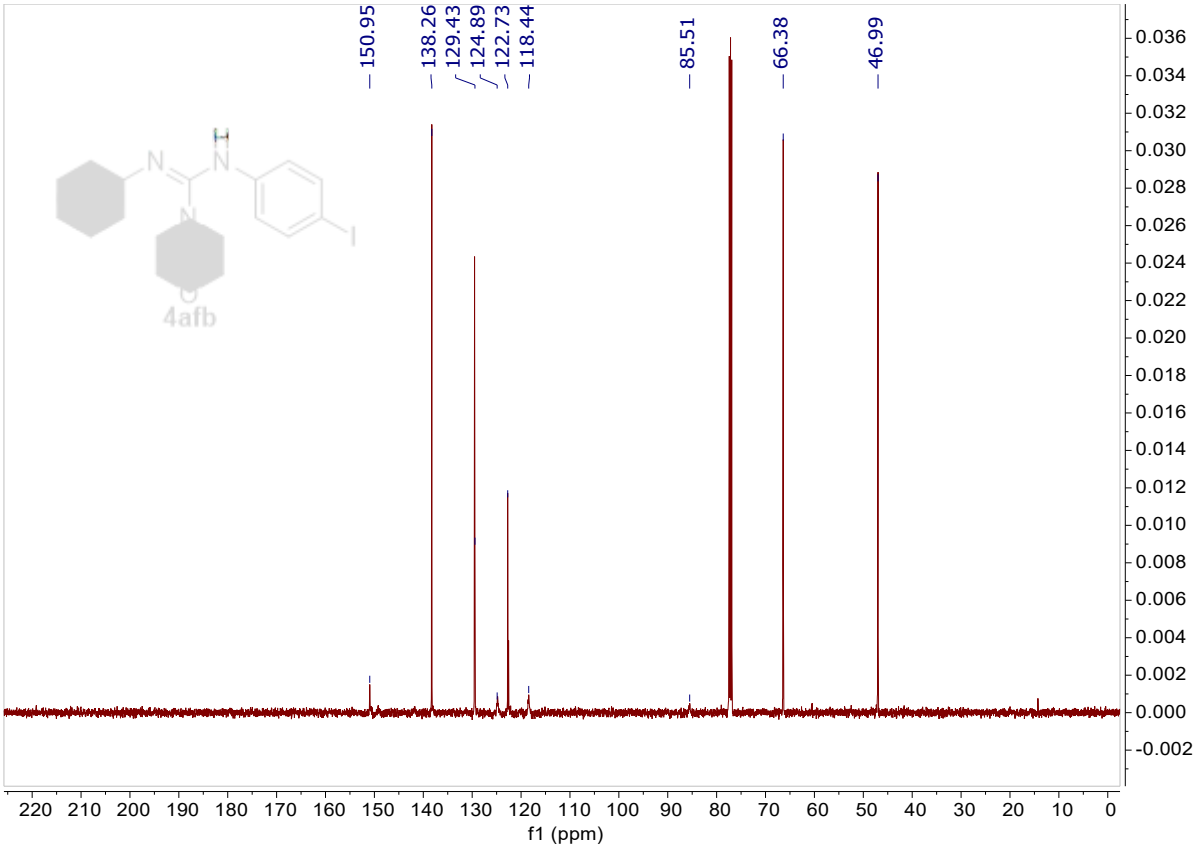


Figure S62 ^{13}C NMR spectra of **4afb** ($CDCl_3$).

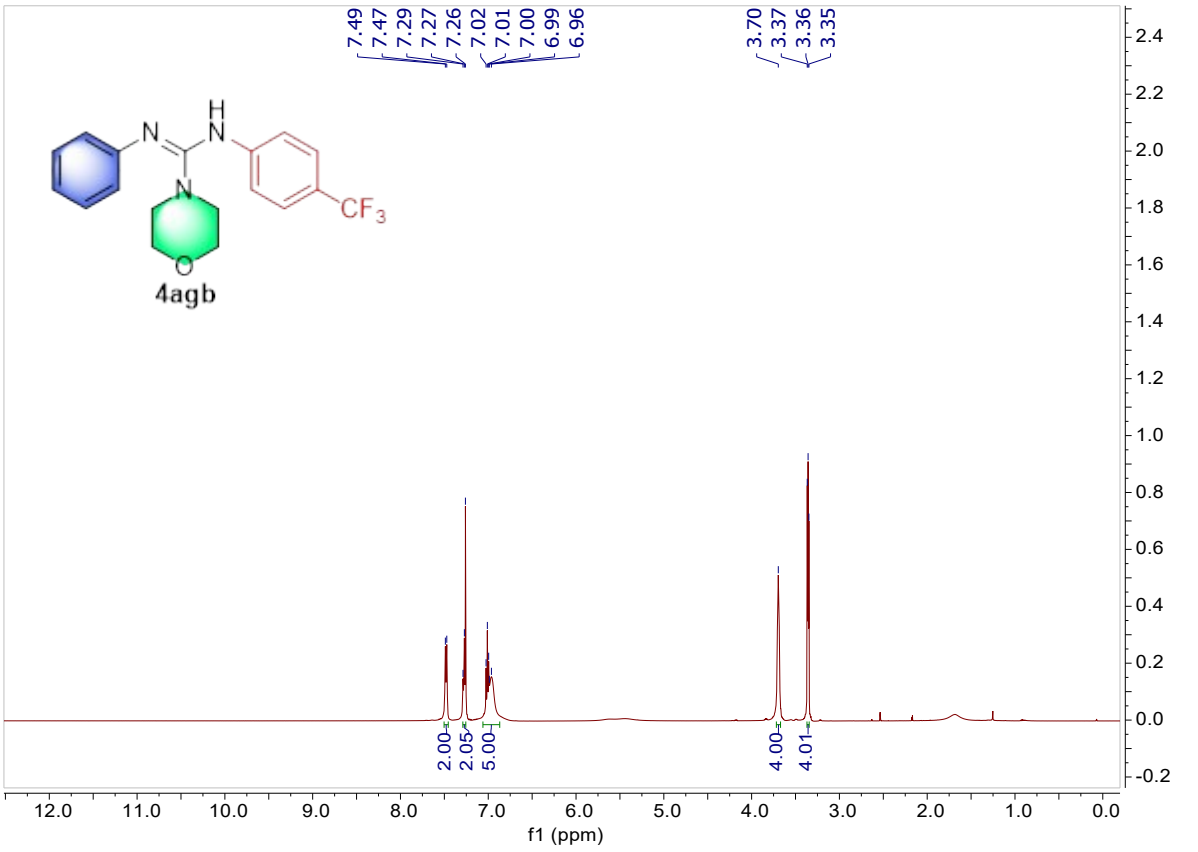


Figure S63 ^{1}H NMR spectra of **4agb** ($CDCl_3$).

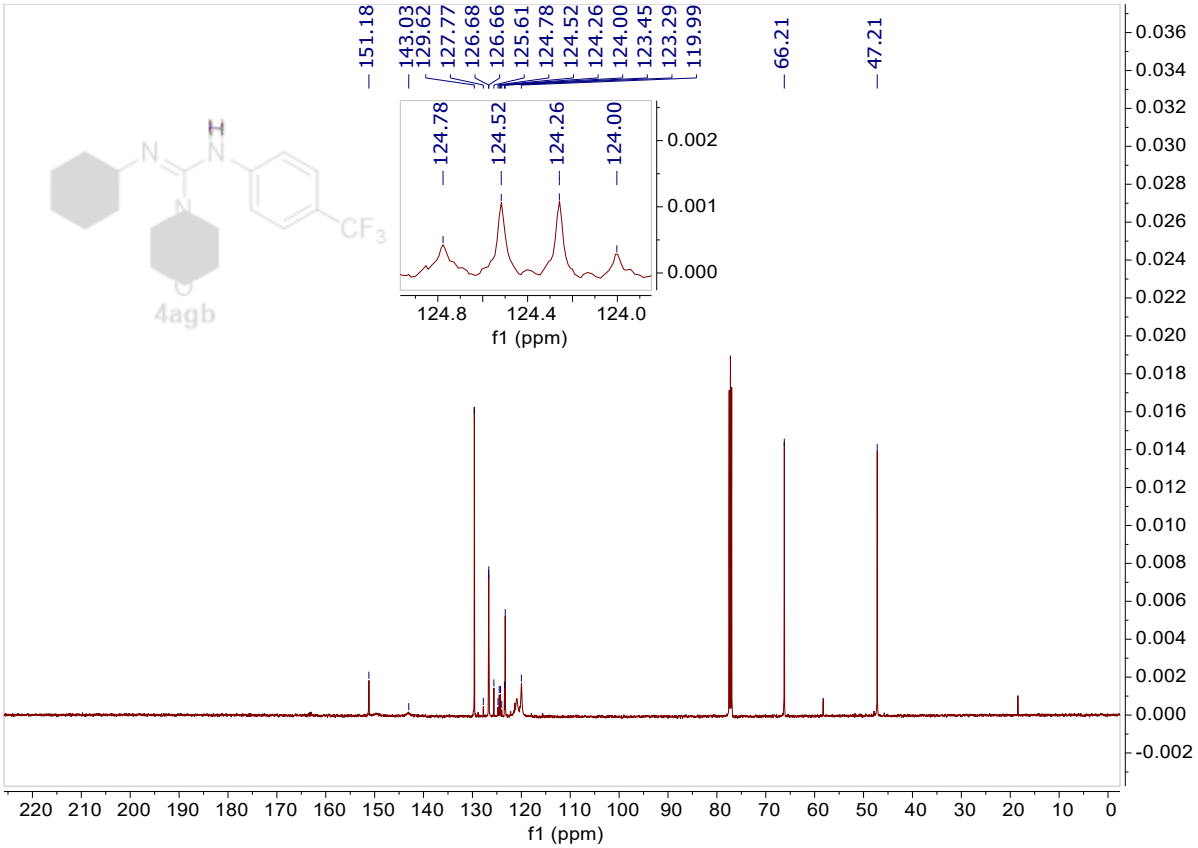


Figure S64 ^{13}C NMR spectra of **4agb** ($CDCl_3$).

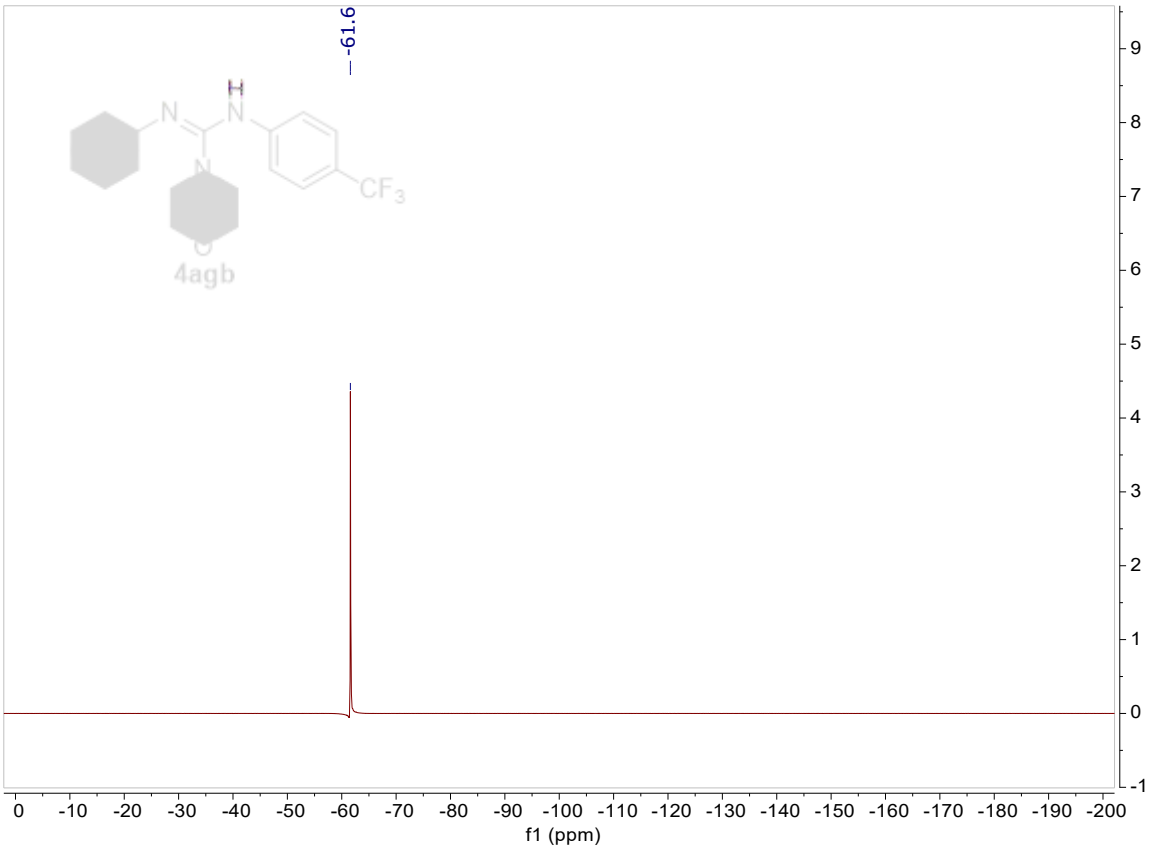


Figure S65 ^{19}F NMR spectra of **4agb** ($CDCl_3$).

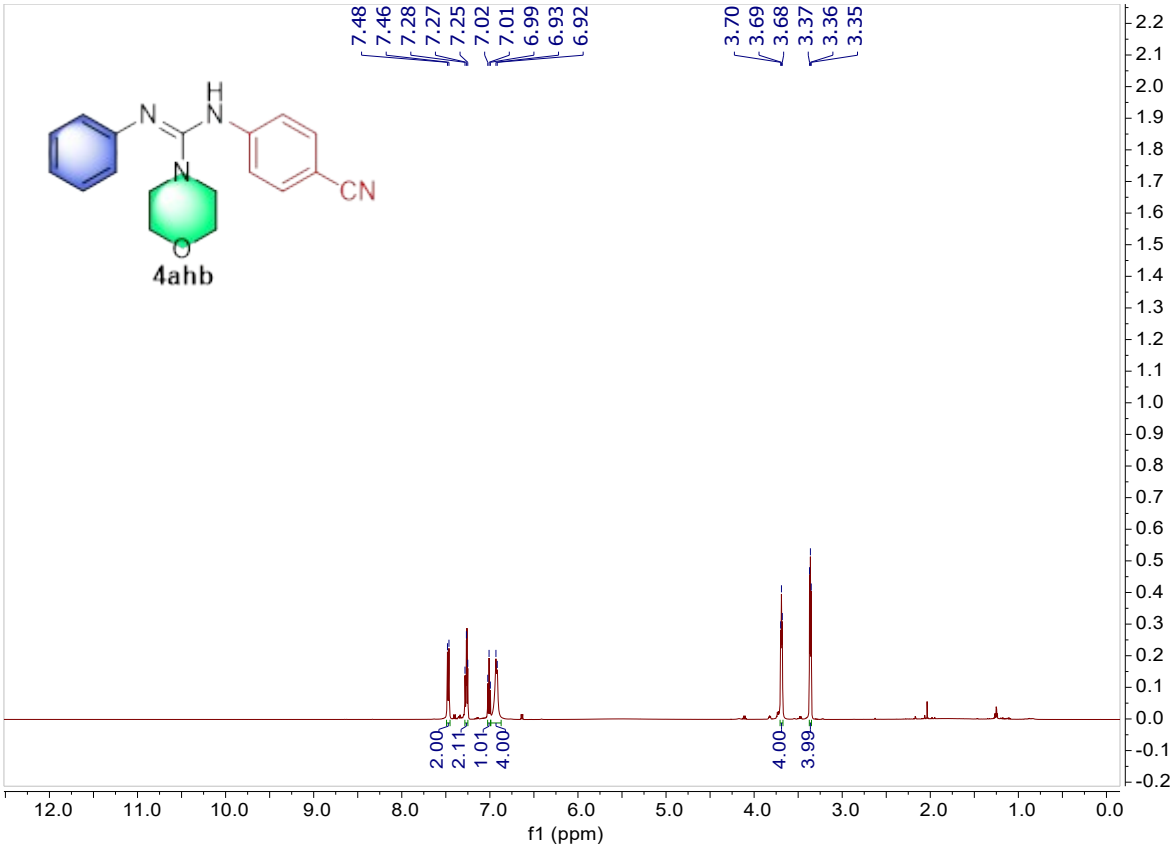


Figure S66 ^{1}H NMR spectra of **4ahb** ($CDCl_3$).

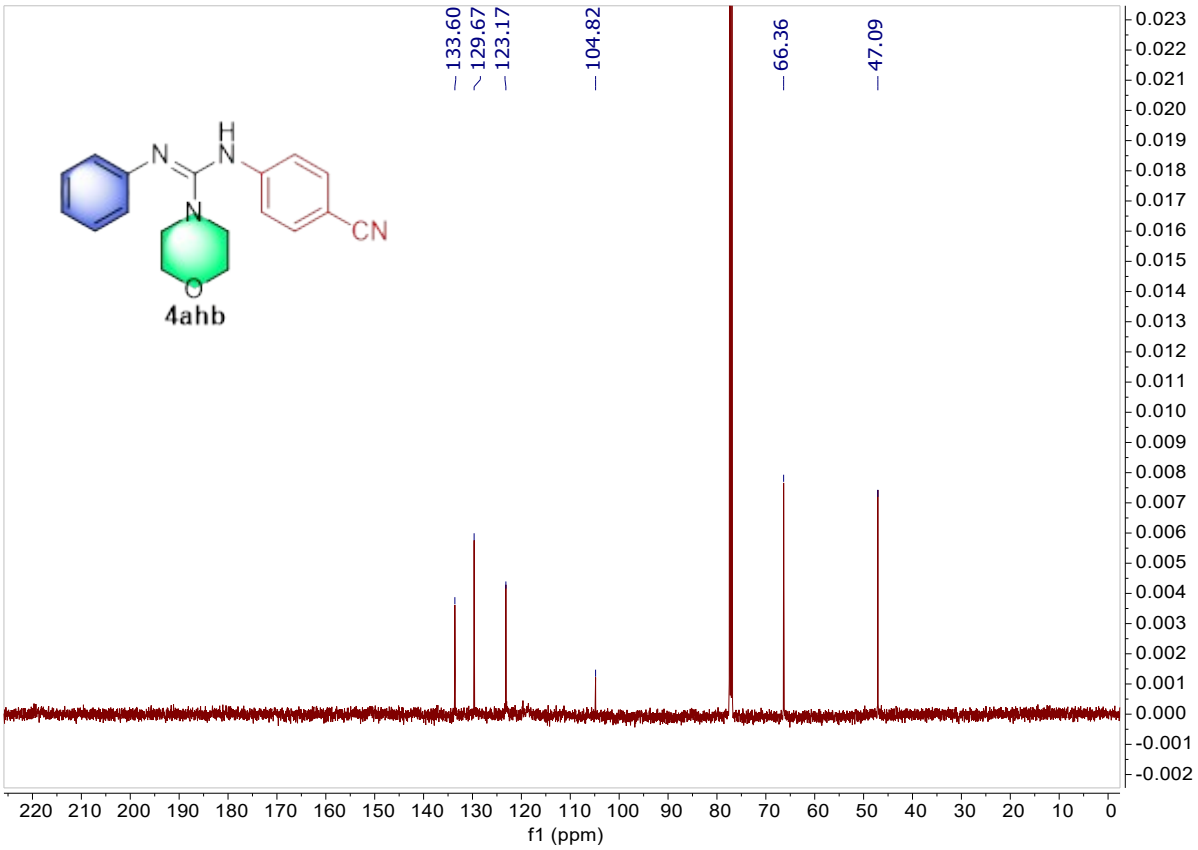


Figure S67 ^{13}C NMR spectra of **4ahb** ($CDCl_3$).

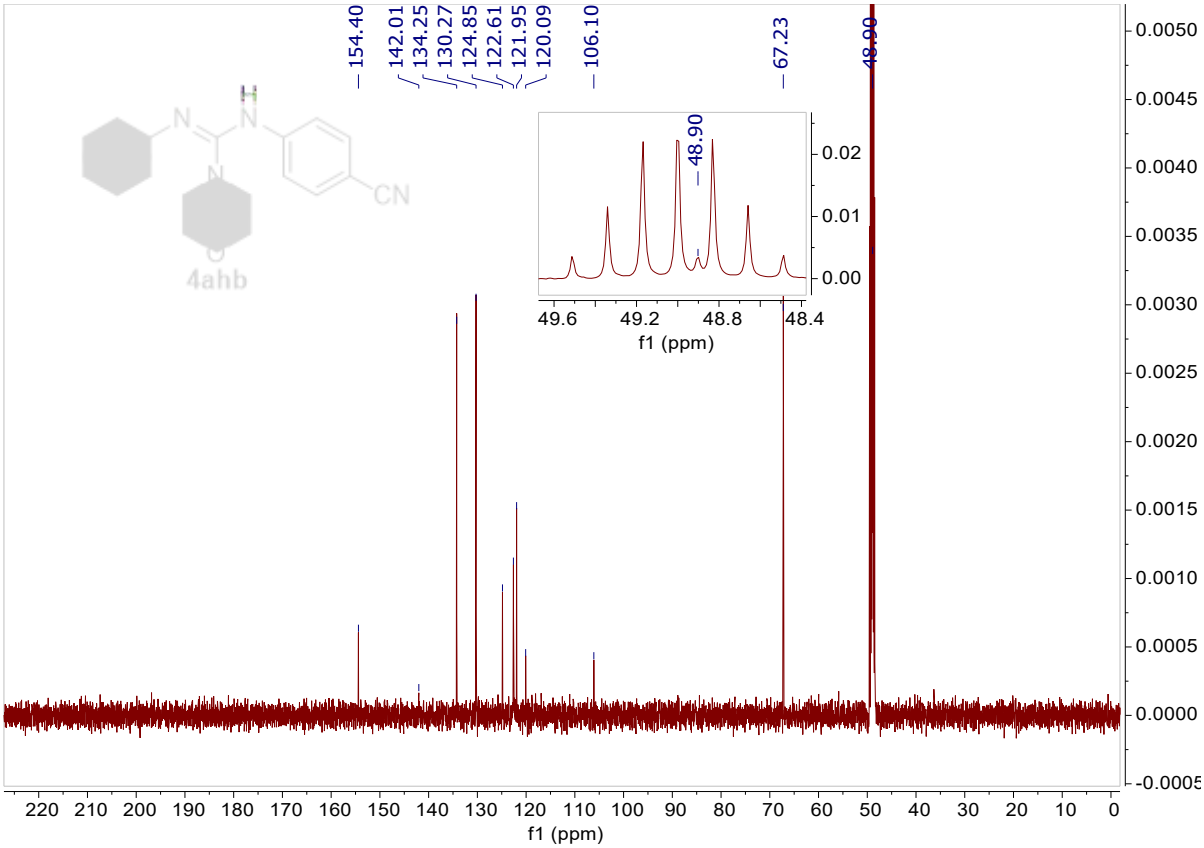


Figure S68 ^{13}C NMR spectra of **4ahb** (CD_3OD + 0.1% TFA).

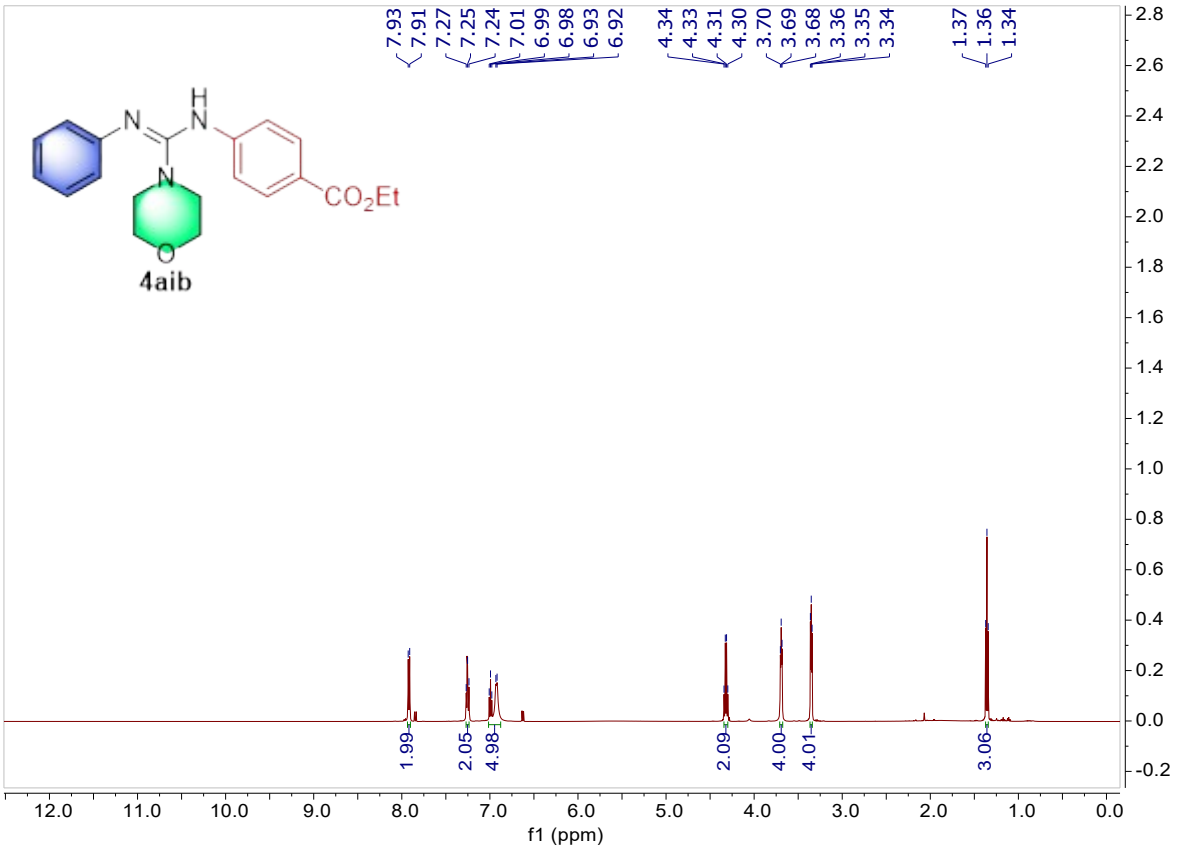


Figure S69 ^{1}H NMR spectra of **4aib** ($CDCl_3$).

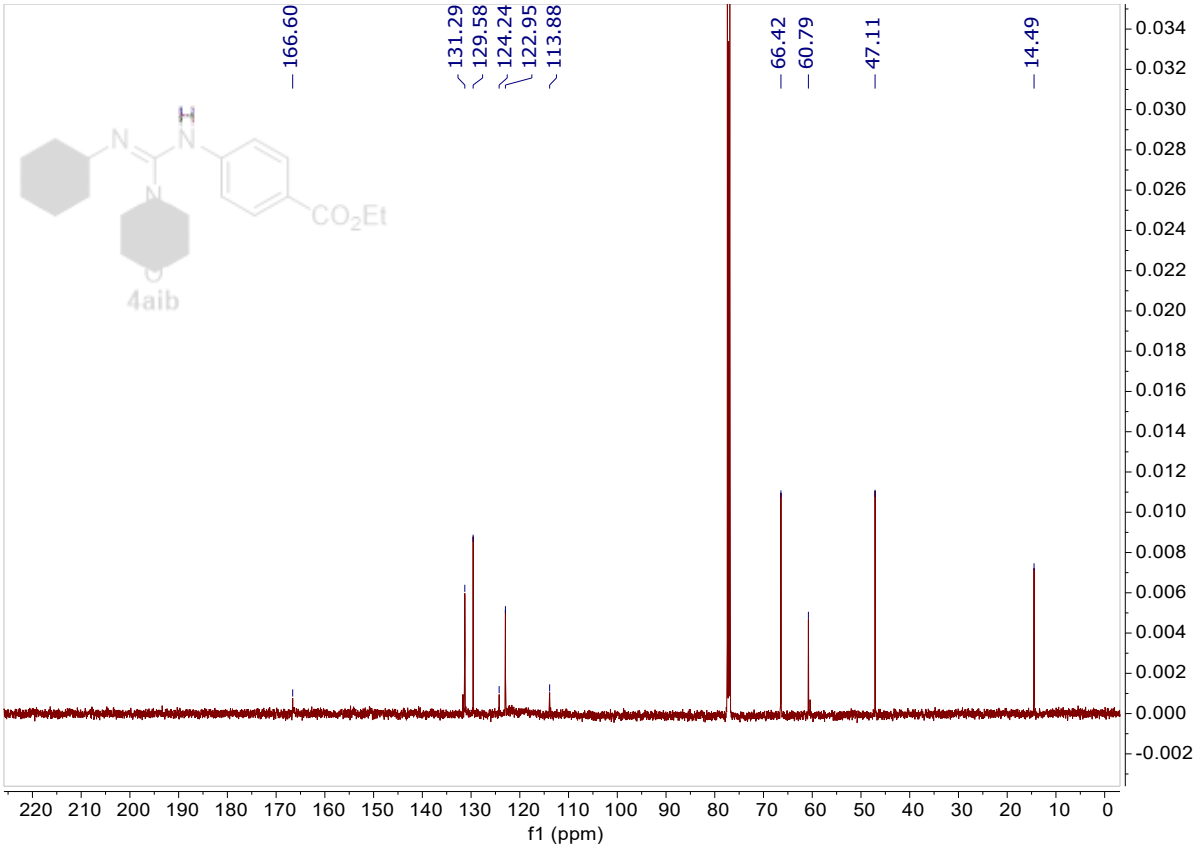


Figure S70 ^{13}C NMR spectra of **4aib** ($CDCl_3$).

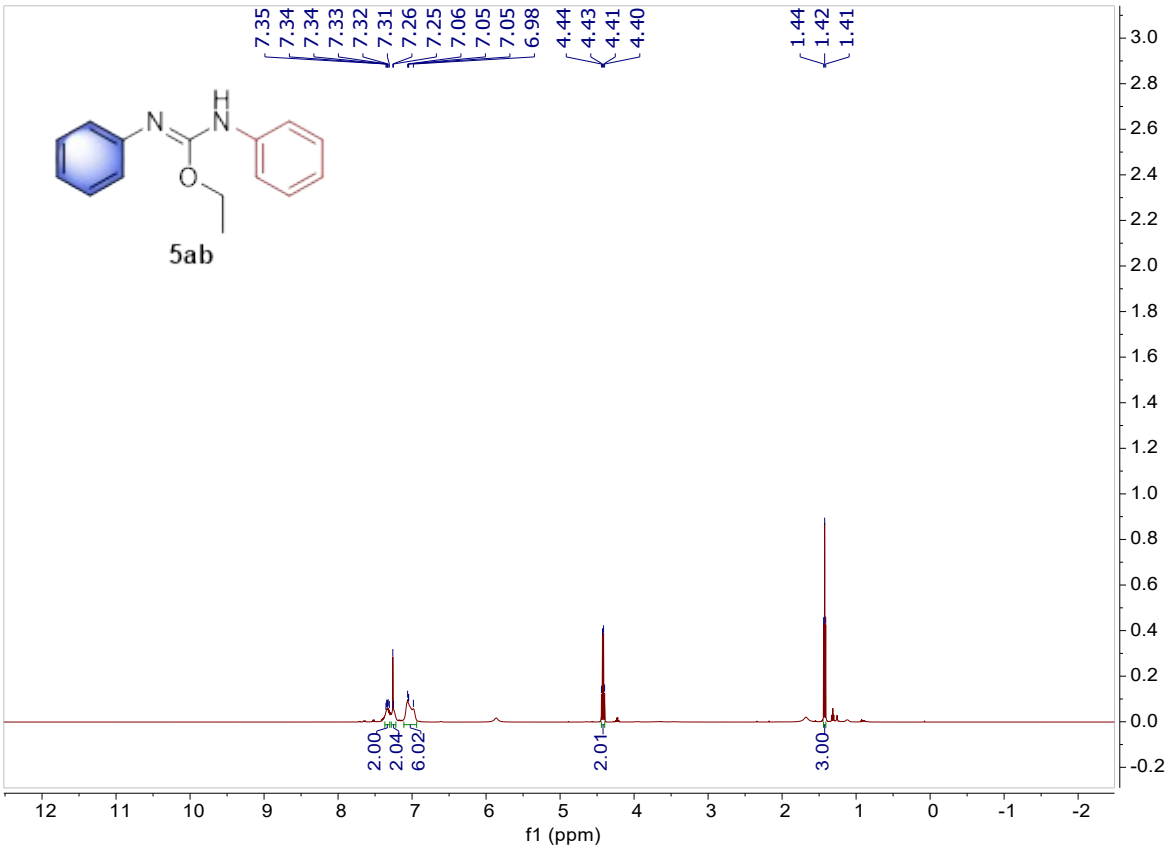


Figure S71 ^{1}H NMR spectra of **5ab** ($CDCl_3$).

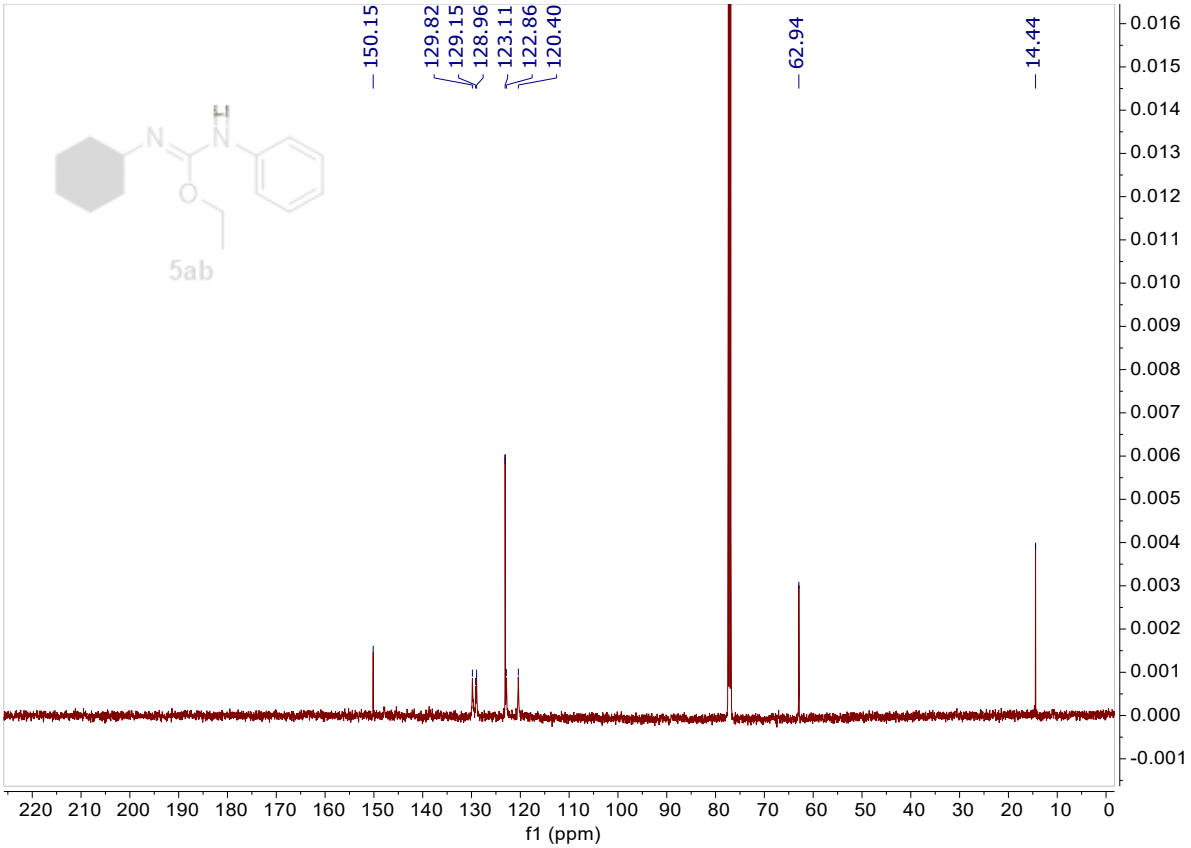


Figure S72 ^{13}C NMR spectra of **5ab** ($CDCl_3$).

Generic Display Report

Analysis Info

Analysis Name	D:\Data\Data Service\230515\TM_FBnNH2 Guanidine_RA8_01_7106.d	Acquisition Date	5/15/2023 1:44:15 PM
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Sample Name	TM_FBnNH2 Guanidine	Instrument	micrOTOF-Q
Comment			

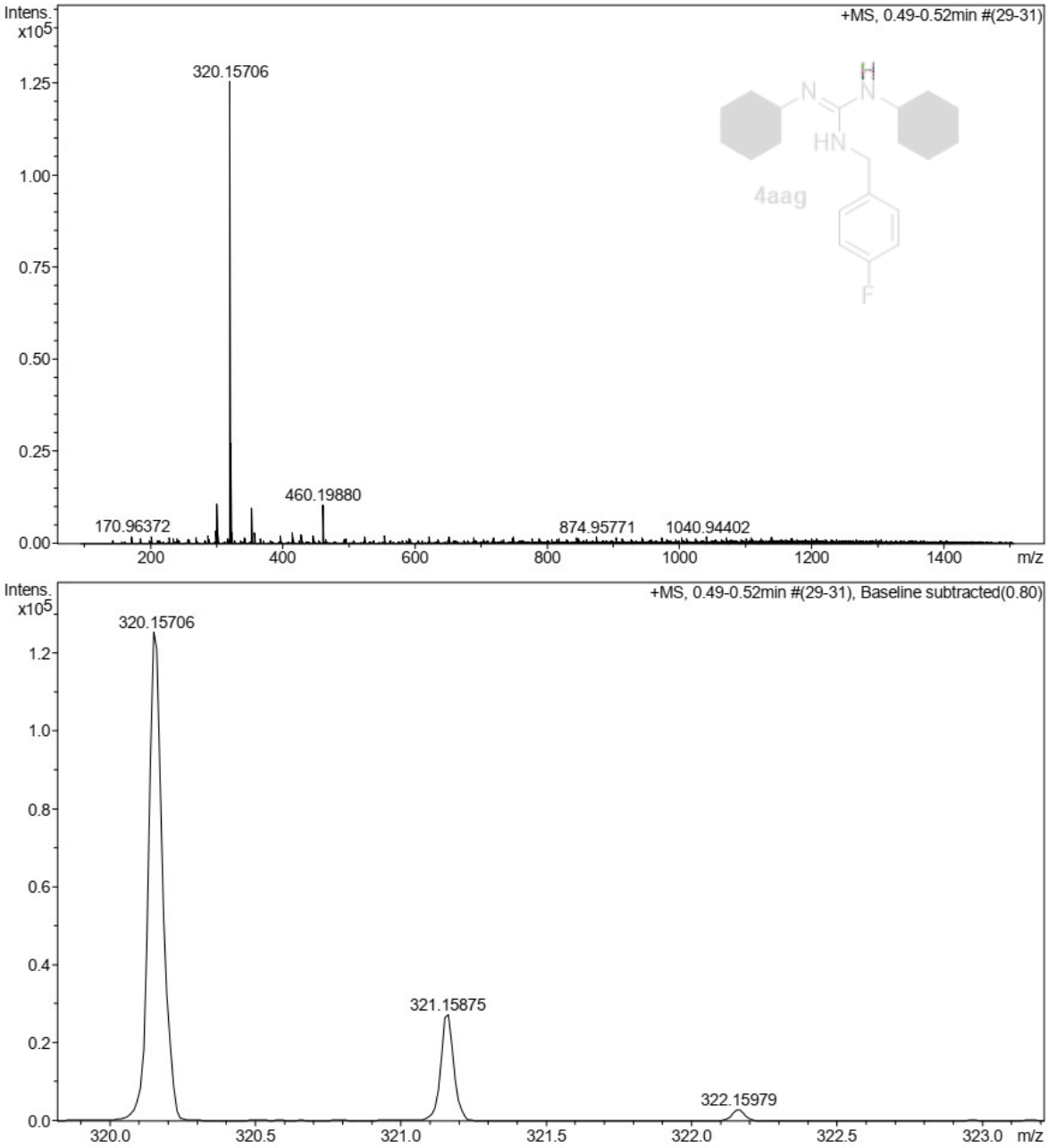

Figure S73 Mass spectrum of **4aag**.

Generic Display Report

Analysis Info

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Sample Name	TM_PhNH2 Model Guanidine	Instrument	micrOTOF-Q
Comment			

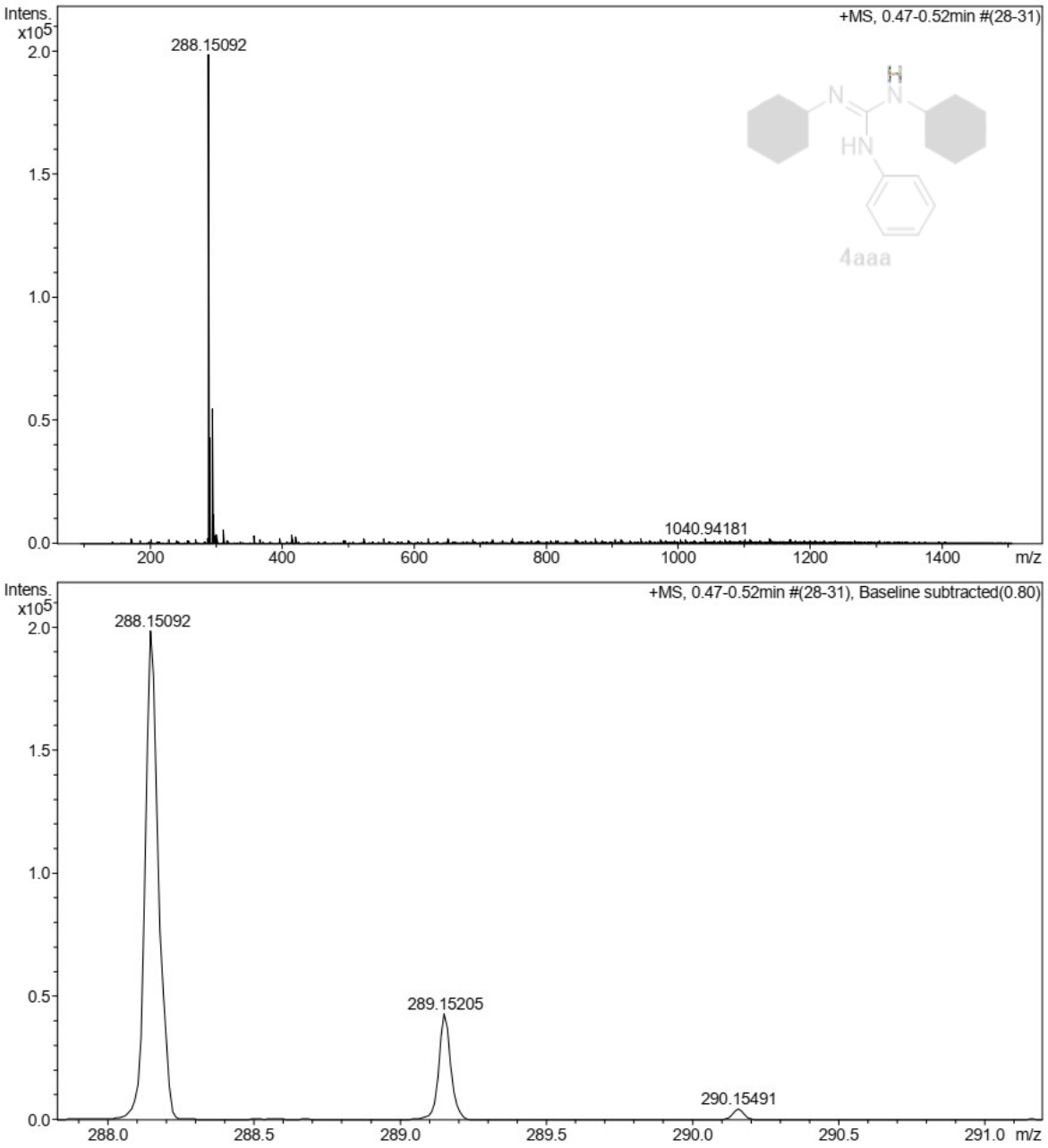

Figure S74 Mass spectrum of **4aaa**.

Generic Display Report

Analysis Info

Analysis Name	D:\Data\Data Service\230612\TM_4-OH Guanidine_RA6_01_7179.d	Acquisition Date	6/12/2023 3:25:24 PM
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Comment			

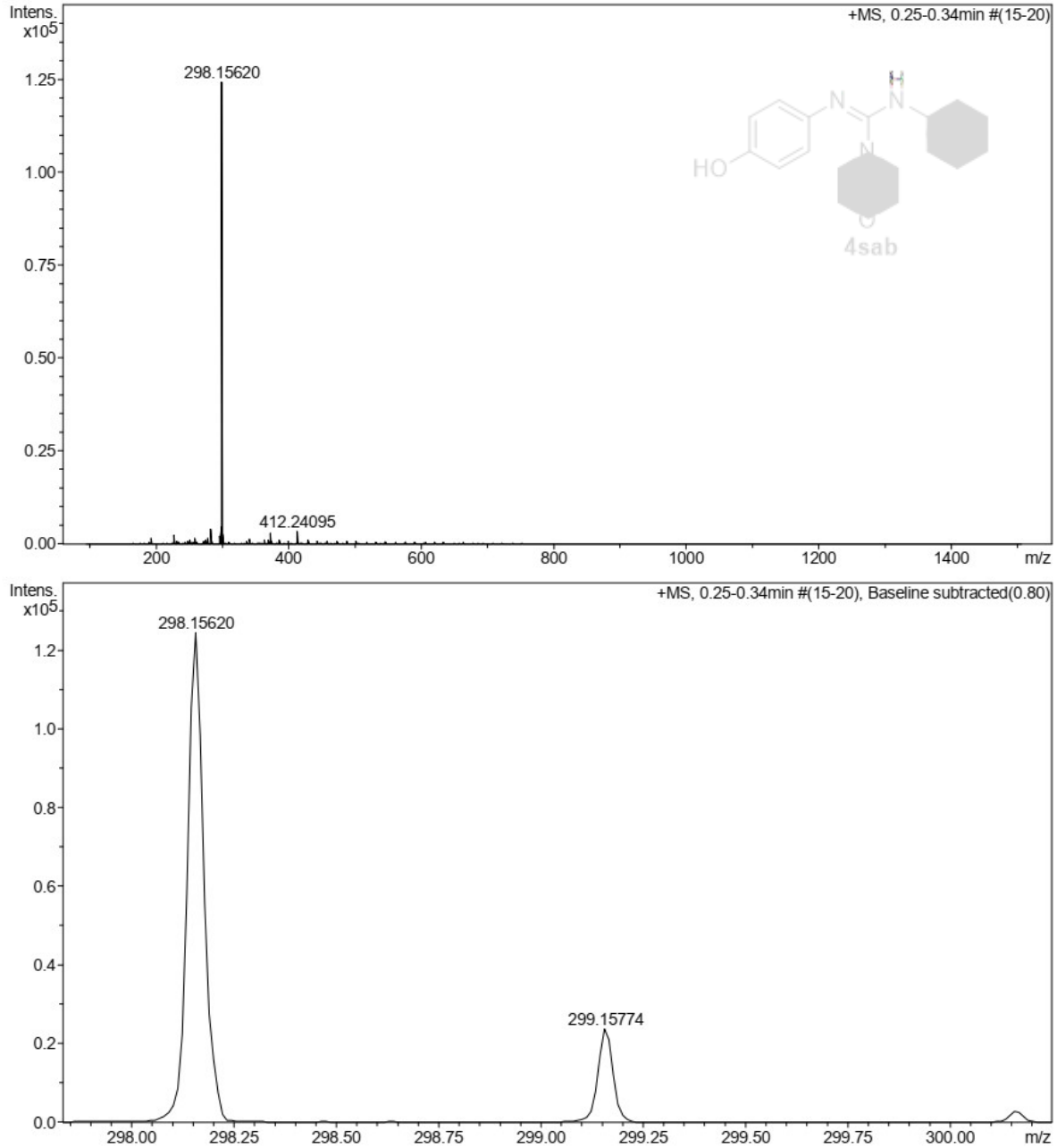

Figure S75 Mass spectrum of **4sab**.

Generic Display Report

Analysis Info

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Comment			

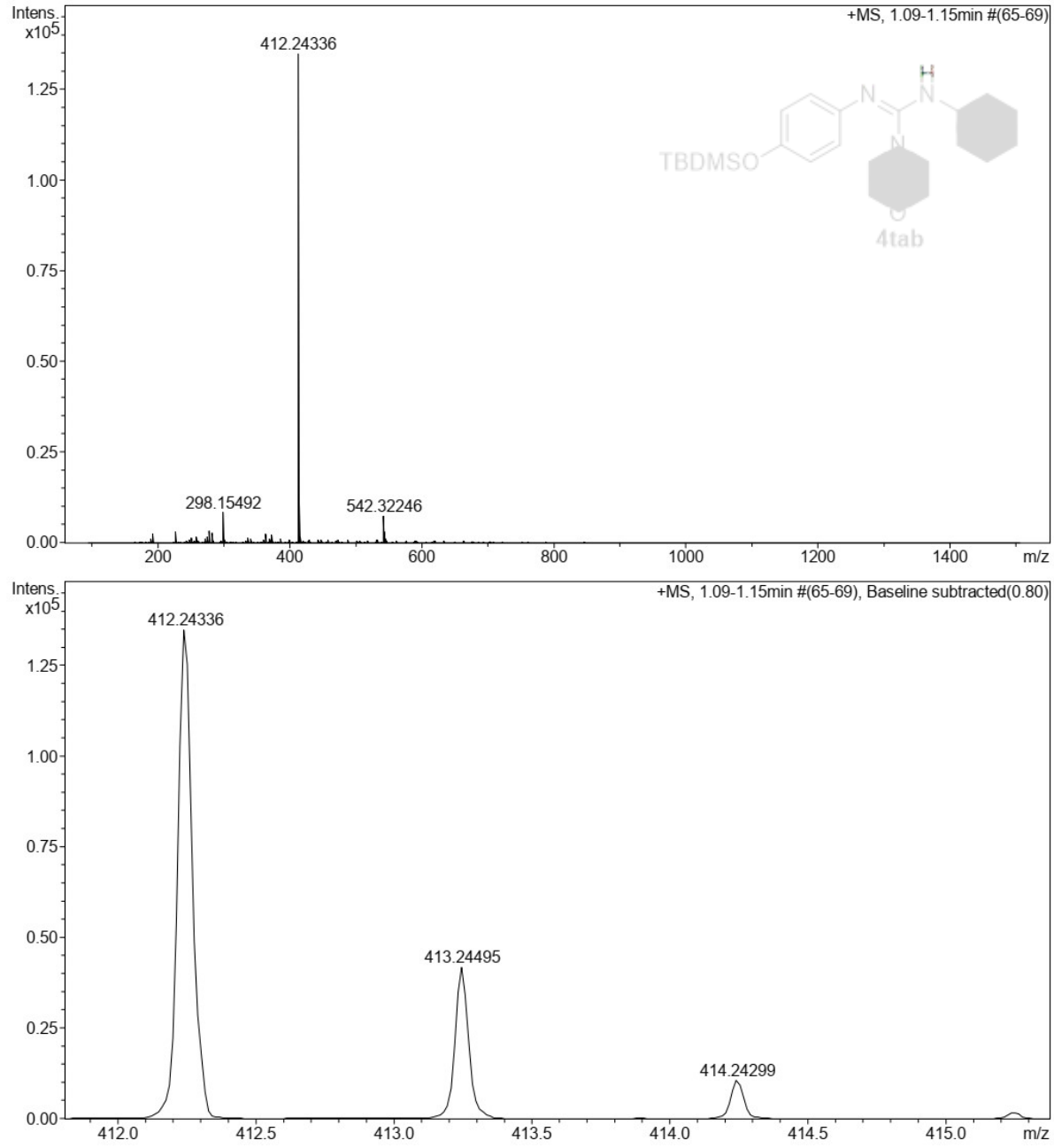

Figure S76 Mass spectrum of **4tab**.

Generic Display Report

Analysis Info

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Comment			

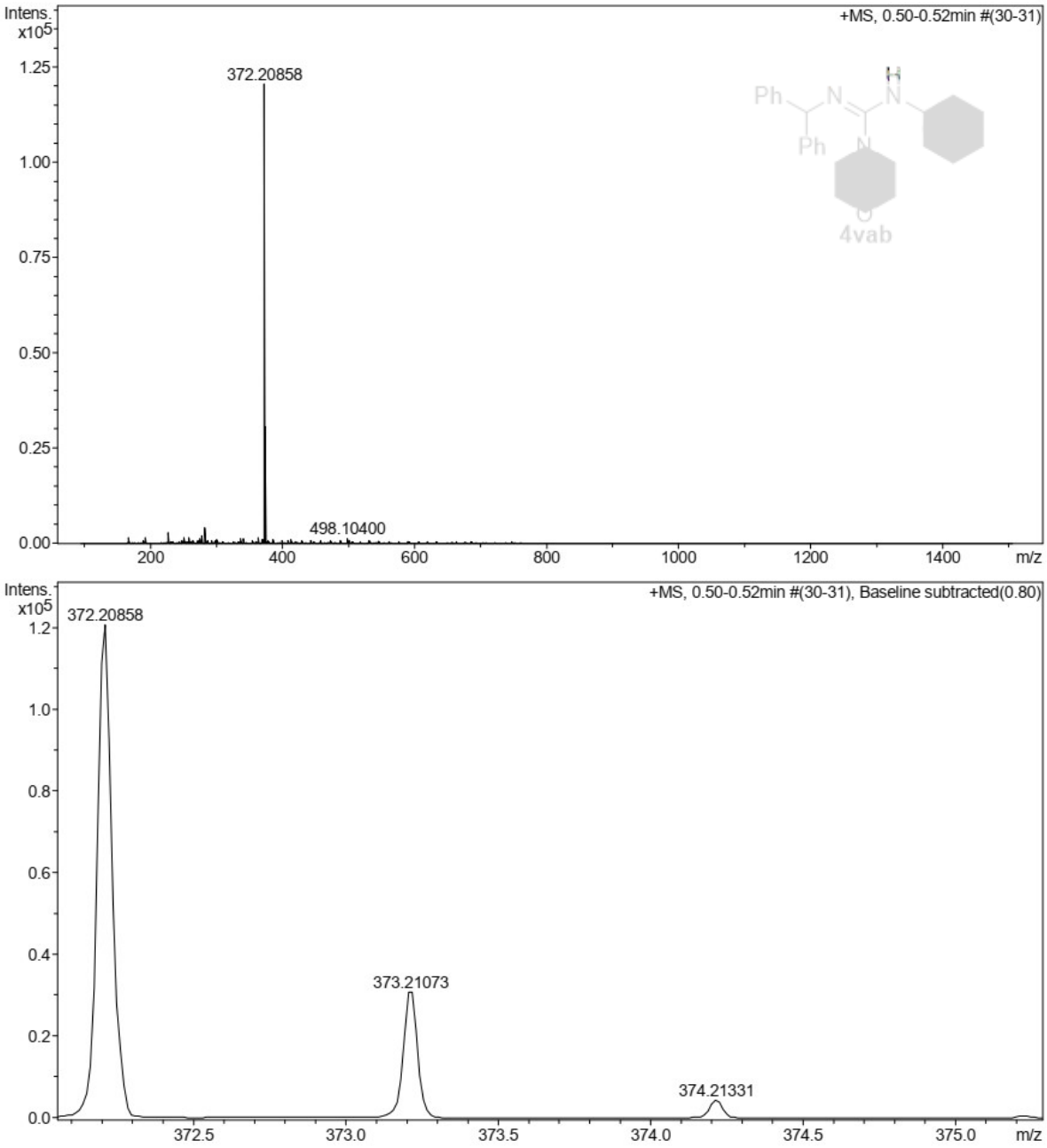

Figure S77 Mass spectrum of **4vab**.

Generic Display Report

Analysis Info

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Sample Name	TM_SW Guanidine	Instrument	micrOTOF-Q
Comment			

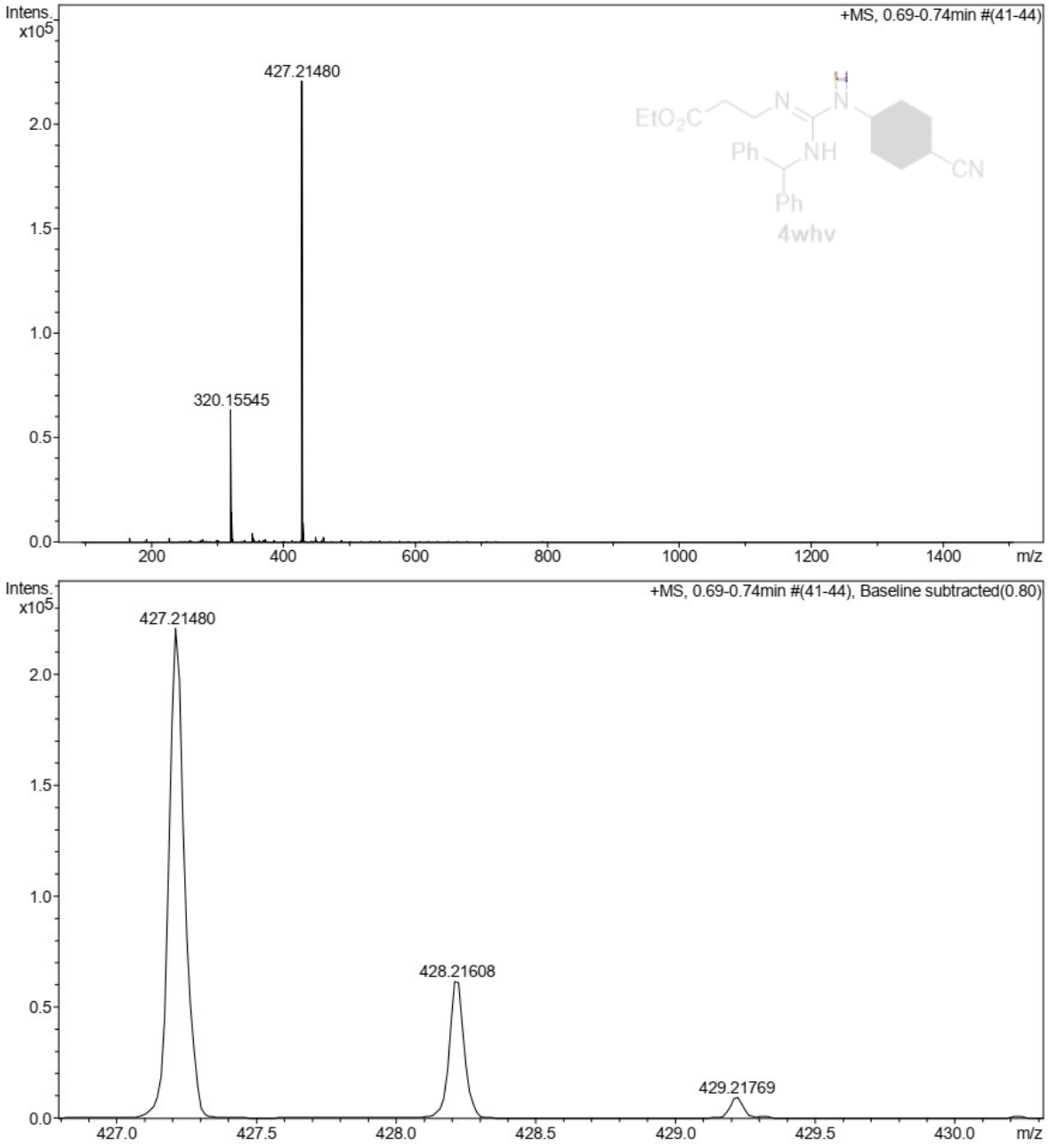

Figure S78 Mass spectrum of **4whv**.

Generic Display Report

Analysis Info

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Sample Name	TM_2-FGuanidine	Instrument	micrOTOF-Q
Comment			

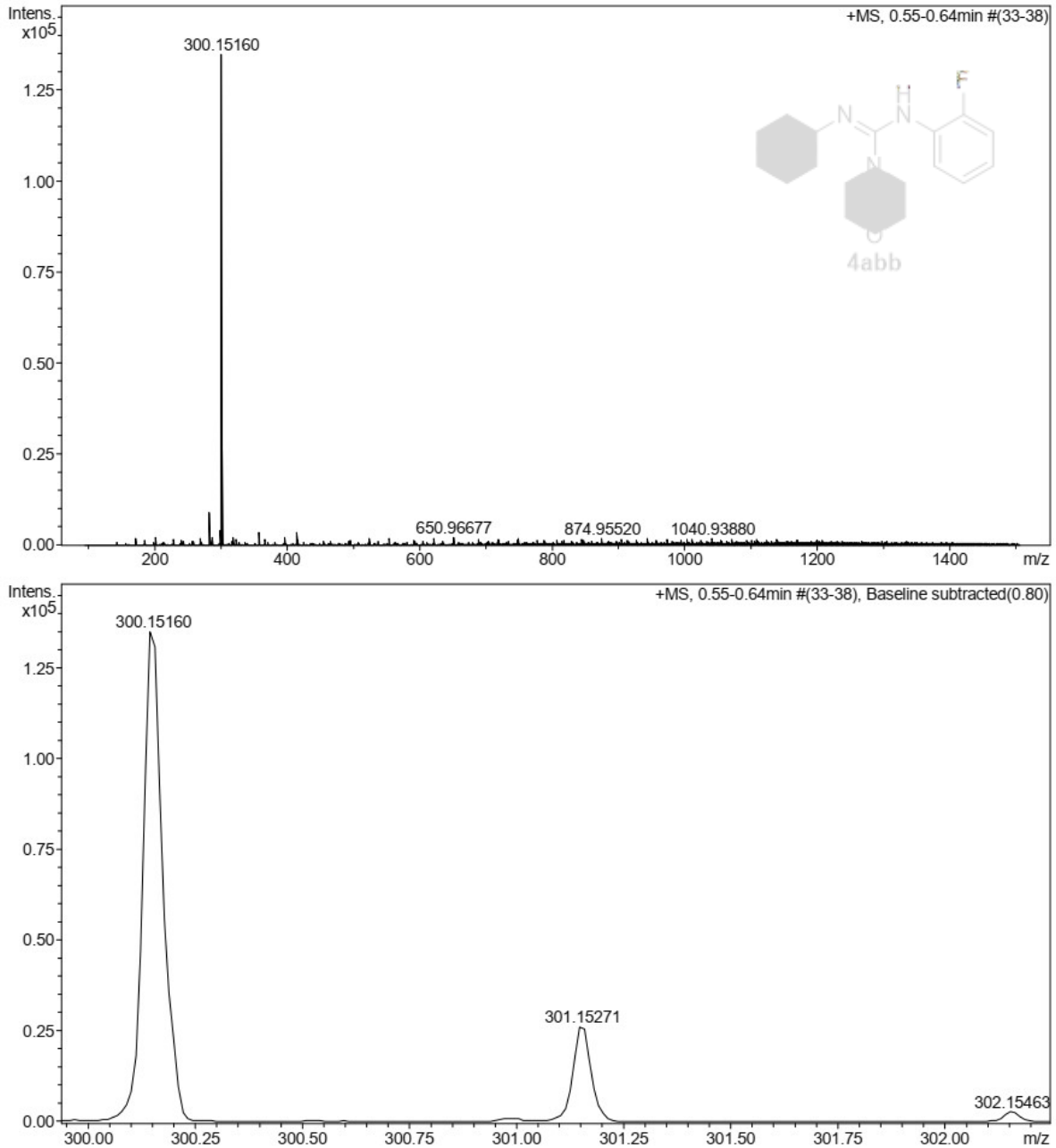

Figure S79 Mass spectrum of **4abb**.

Generic Display Report

Analysis Info

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Sample Name	TM_4-FGuanidine	Instrument	micrOTOF-Q
Comment			

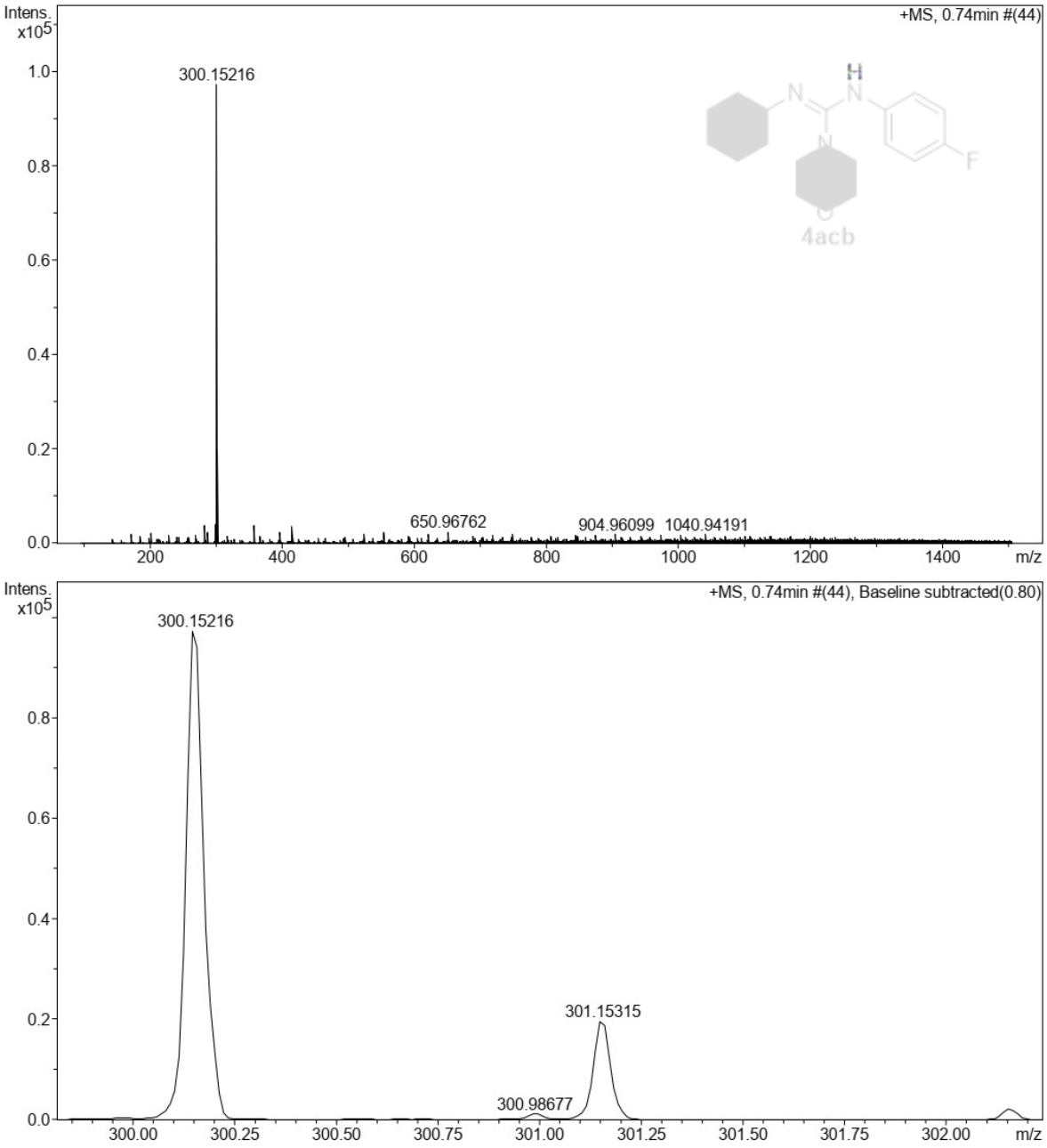
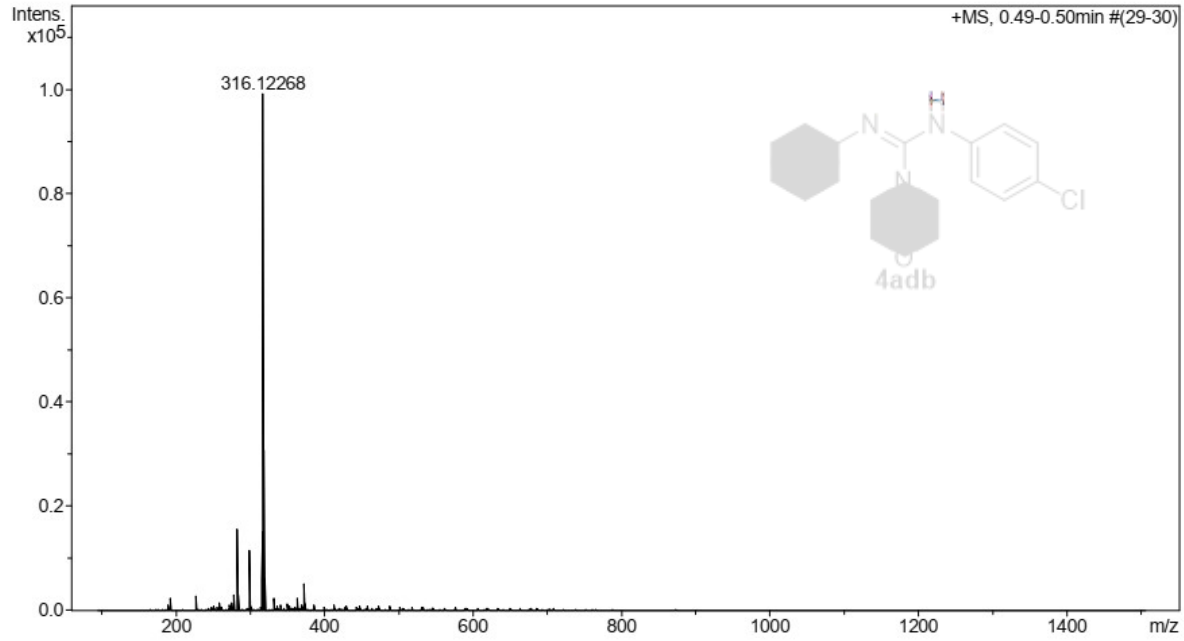


Figure S80 Mass spectrum of **4acb**.

Generic Display Report

Analysis Info

Acquisition Date	6/12/2023 2:28:25 PM		
Analysis Name	D:\Data\Data Service\230612\TM_4-Cl Guanidine_RA7_01_7170.d		
Method	nv_pos_5min_profile_190214.m	Operator	CU.
Sample Name	TM_4-Cl Guanidine	Instrument	micrOTOF-Q
Comment			



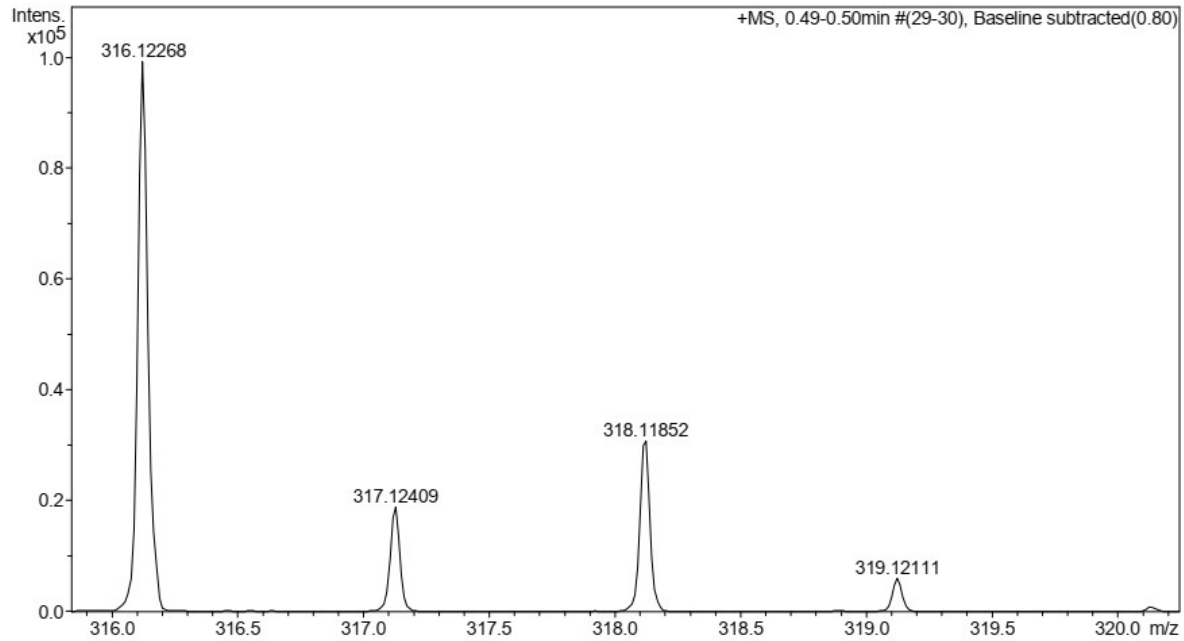


Figure S81 Mass spectrum of **4adb**.

Generic Display Report

Analysis Info

Acquisition Date	5/15/2023 1:24:54 PM		
Analysis Name	D:\Data\Data Service\230515\TM_4-CNGuanidine_RA5_01_7103.d		
Method	nv_pos_5min_profile_190214.m	Operator	CU.
Sample Name	TM_4-CNGuanidine	Instrument	micrOTOF-Q
Comment			

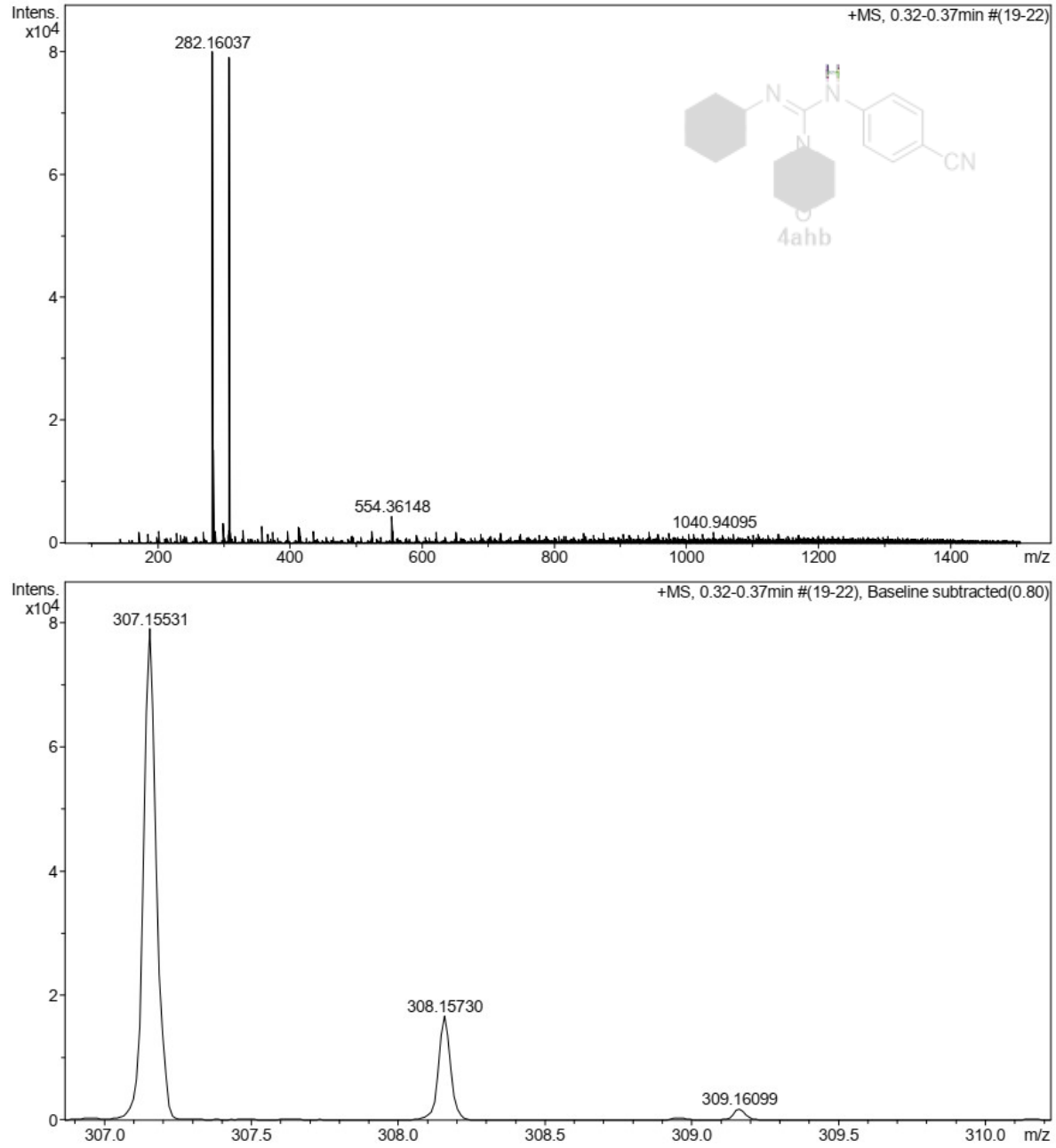


Figure S82 Mass spectrum of **4ahb**.

Generic Display Report

Analysis Info

Acquisition Date	6/12/2023 2:34:42 PM		
Analysis Name	D:\Data\Data Service\230612\TM_4-CO2Et Guanidine_RA8_01_7171.d		
Method	nv_pos_5min_profile_190214.m	Operator	CU.
Sample Name	TM_4-CO2Et Guanidine	Instrument	micrOTOF-Q
Comment			

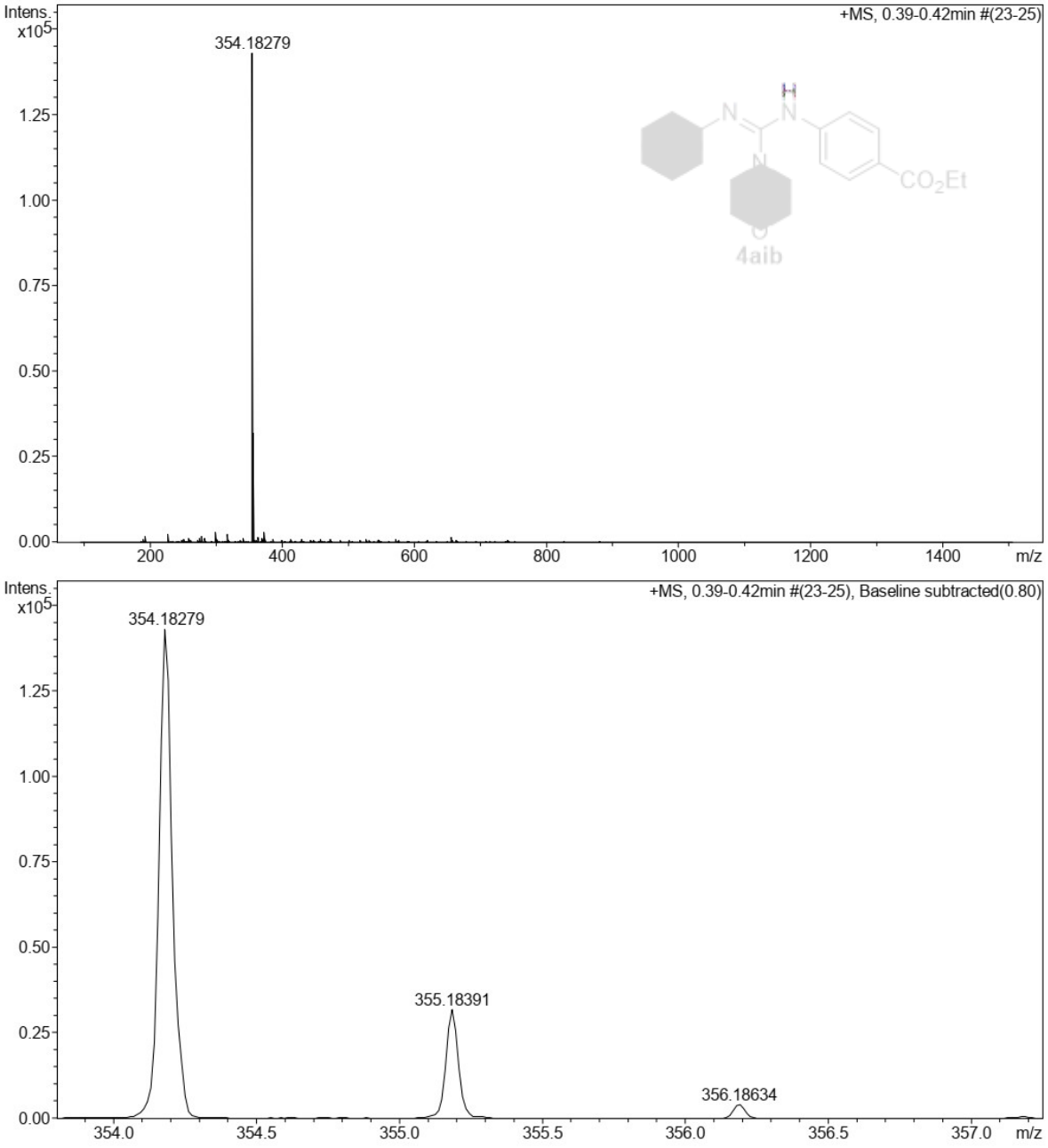
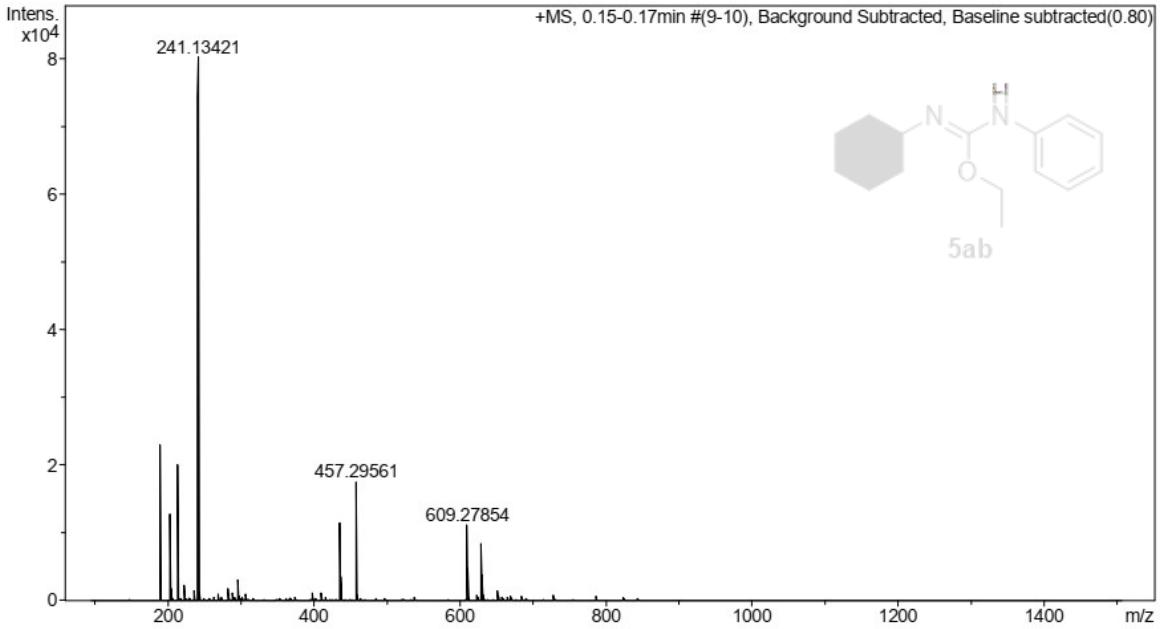


Figure S83 Mass spectrum of **4aib**.

Generic Display Report

Analysis Info

Acquisition Date	8/7/2023 4:48:26 PM		
Analysis Name	D:\Data\Data Service\230807\TM_EtOH Guanidine_RC6_01_7439.d		
Method	nv_pos_5min_profile_190214.m	Operator	CU.
Sample Name	TM_EtOH Guanidine	Instrument	micrOTOF-Q
Comment			



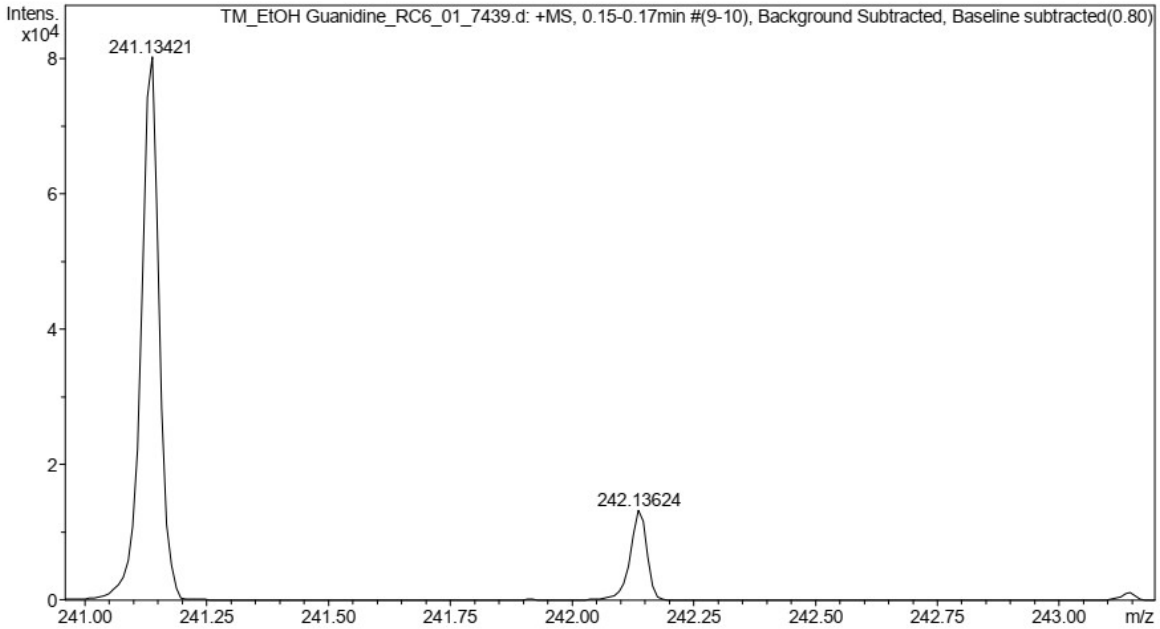


Figure S84 Mass spectrum of **5ab**.

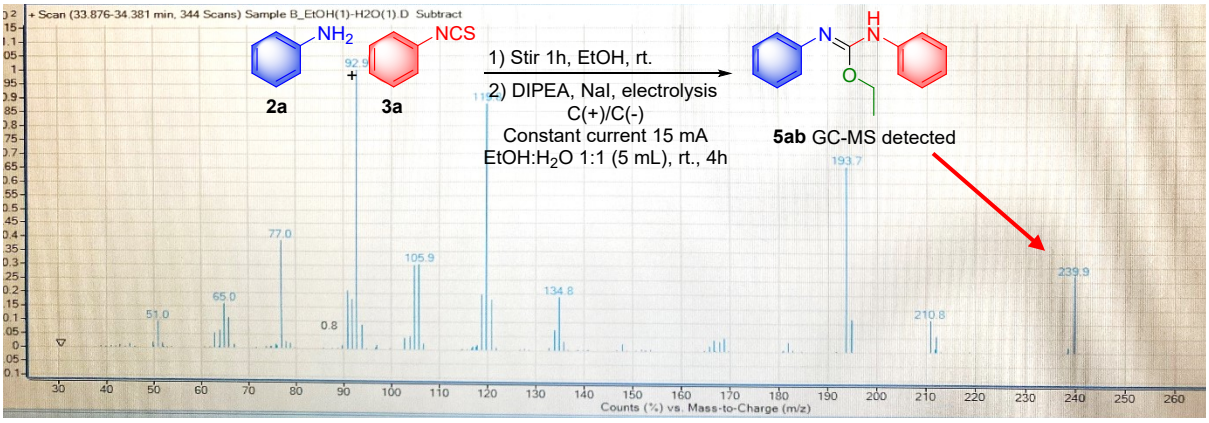
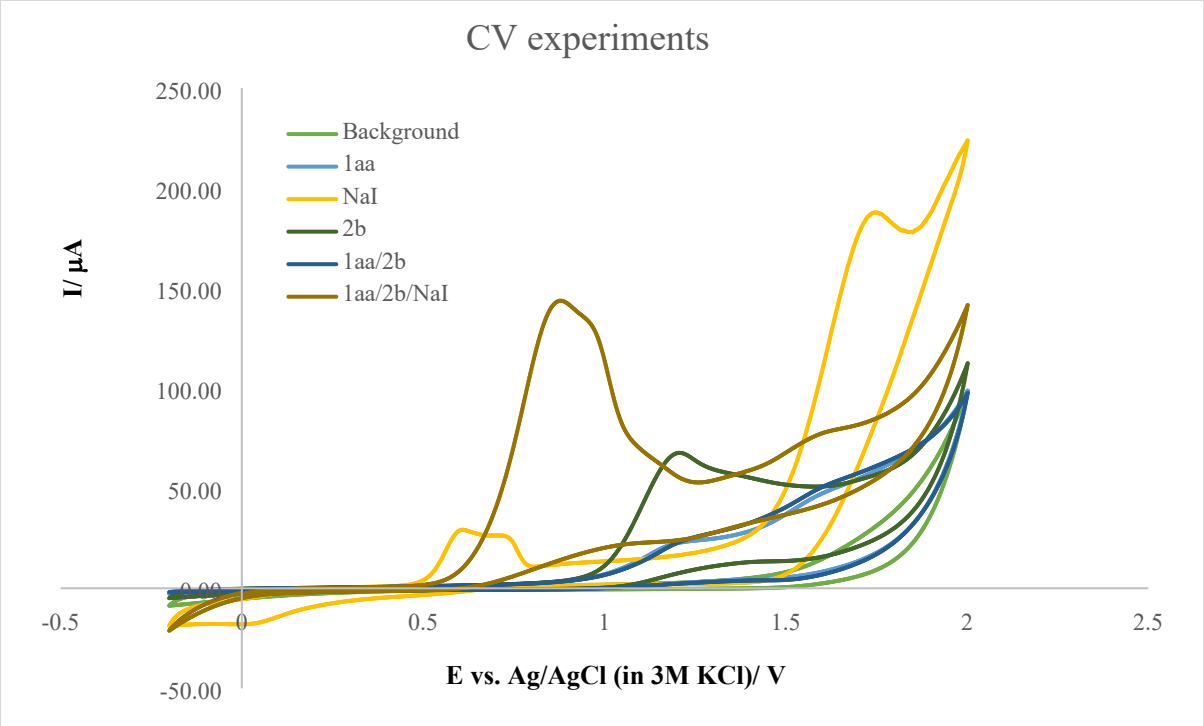


Figure S85 Mass spectrum of compound **5ab** from GC-MS.



Scheme S2. Cyclic voltammogram of **1aa**, **2b** and **NaI** in 0.1 M $TBABF_4$/EtOH:H_2O (1:1) using glassy carbon electrode (A = 0.71 cm^2) as working electrode, Pt wire and Ag/AgCl (3M KCl) as counter and reference electrodes at scan rate 0.1 V/s. In case of **1aa**, **2b**, NaI, **1aa**/**2b**, and **1aa**/**2b**/NaI experiments,10 mM solution of compounds were prepared.

References

1. Saetan, T.; Sukwattanasinitt, M.; Wacharasindhu, S., A mild photocatalytic synthesis of guanidine from thiourea under visible light. *Org. Lett.* **2020,** *22*, 7864-7869.

2. Annuur, R. M.; Saetan, T.; Sukwattanasinitt, M.; Wacharasindhu, S., Metal-free synthesis of guanidines from thioureas in water reactions mediated by visible light. *Synthesis* **2023**.

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