

# Supplementary Information

## **From wood to tetrahydro-2-benzazepines in three waste-free steps: modular synthesis of biologically active lignin-derived scaffolds**

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## Table of Contents

<b>1. General information.....</b>	<b>4</b>
<b>1.1 Preparation of Cu<sub>2</sub>O-PMO catalyst .....</b>	<b>7</b>
<b>1.2 Synthesis of dihydroconiferyl alcohol (1G) and dihydrosinapyl alcohol (1S).....</b>	<b>7</b>
<b>1.2.1 Synthesis of dihydroconiferyl alcohol (1G).....</b>	<b>7</b>
<b>1.2.2 Synthesis of dihydrosinapyl alcohol (1S) .....</b>	<b>8</b>
<b>1.3 General experimental procedures .....</b>	<b>9</b>
<b>1.3.1 General procedure (A) for reductive catalytic fractionation (RCF) of lignocellulose.....</b>	<b>9</b>
<b>1.3.2 General procedure (B) for Ru-catalyzed amination of 1G and 1S.....</b>	<b>9</b>
<b>1.3.3 General procedure (C) for the synthesis of tetrahydro-2-benzazepines in deep eutectic solvents (DES) .....</b>	<b>10</b>
<b>2. Comparison of the synthesis of tetrahydro-2-benzazepine from fossil fuels and lignocellulose .....</b>	<b>11</b>
<b>2.1 Analysis of a multi-step reaction pathway for the synthesis of 7-methoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol from petrochemical sources .....</b>	<b>11</b>
<b>2.2 Green route to the synthesis of 2-(4-chlorophenyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol directly from raw lignocellulose in three steps.....</b>	<b>12</b>
<b>2.3 Multi-step syntheses of tetrahydro-2-benzazepines: detailed description of reaction steps.....</b>	<b>14</b>
<b>3. Establishing the selective catalytic amination of dihydroconiferyl alcohol (1G) with aniline .....</b>	<b>16</b>
<b>4. Development of efficient reactive separation of dihydroconiferyl alcohol (1G) from lignocellulose depolymerization mixtures .....</b>	<b>17</b>
<b>4.1 Reductive catalytic fractionation (RCF) of pine lignocellulose and separation of dihydroconiferyl alcohol (1G).....</b>	<b>17</b>
<b>4.2 Highly selective catalytic amination of dihydroconiferyl alcohol (1G) in the presence of 4-propylguaiaicol (3G) .....</b>	<b>18</b>
<b>4.3 Reactive separation of 1G from reaction mixtures obtained by RCF of pine lignocellulose by catalytic amination-separation of lignin-derived secondary amine 5Gb and other products .....</b>	<b>22</b>
<b>4.3.1 Fractionation, reactive separation and analysis of the crude mixture obtained from RCF of pine lignocellulose .....</b>	<b>22</b>
<b>4.3.2 Direct reactive separation of 1G from crude product mixture upon RCF of pine lignocellulose .....</b>	<b>28</b>
<b>4.4 Reductive catalytic fractionation (RCF) of poplar lignocellulose and separation of dihydroconiferyl alcohol (1G) and dihydrosinapyl alcohol (1S) .....</b>	<b>30</b>

<b>4.5 Reactive separation of 1G and 1S from reaction mixtures obtained by RCF of poplar lignocellulose by catalytic amination-separation of lignin-derived secondary amine 5Gb and 5Sb and other products .....</b>	<b>32</b>
<b>4.5.1 Fractionation, reactive separation and analysis of the crude mixture obtained from RCF of poplar lignocellulose .....</b>	<b>32</b>
<b>4.5.2 Direct reactive separation of 1G and 1S from crude product mixture upon RCF of poplar lignocellulose.....</b>	<b>37</b>
<b>4.6 Supplementary Note 1 .....</b>	<b>40</b>
<b>4.6.1 Control experiments to elucidate catalyst compatibility with various components of the crude and fractionated depolymerization mixture .....</b>	<b>40</b>
<b>5. Diverse alkylaminophenols by Ru-catalysed amination of dihydroconiferyl alcohol (1G) and dihydrosinapyl alcohol (1S) with various amines.....</b>	<b>42</b>
<b>5.1 Highly selective Ru-catalyzed amination of dihydroconiferyl alcohol (1G) with various amines.....</b>	<b>42</b>
<b>5.2 Highly selective Ru-catalyzed amination of dihydrosinapyl alcohol (1S) with various amines.....</b>	<b>45</b>
<b>5.3 Synthesis of 4-(3-aminopropyl)-2-methoxyphenol (5Gw) by selective amination of dihydroconiferyl alcohol (1G) with ammonia .....</b>	<b>47</b>
<b>6. Development of a novel highly efficient method for the construction of tetrahydro-2-benzazepines in deep eutectic solvents .....</b>	<b>49</b>
<b>6.1 Attempts for the formation of tetrahydro-2-benzazepines in classical organic solvents using Brønsted and Lewis acids .....</b>	<b>49</b>
<b>6.2 Construction of tetrahydro-2-benzazepines using deep eutectic solvents (DES)....</b>	<b>53</b>
<b>6.3 Synthesis of a library of tetrahydro-2-benzazepine derivatives in a specific DES .</b>	<b>56</b>
<b>7. Testing of biological activities of the obtained lignin-derived amine libraries.....</b>	<b>58</b>
<b>8. Characterization data of isolated compounds .....</b>	<b>59</b>
<b>9. References .....</b>	<b>82</b>
<b>10. <sup>1</sup>H and <sup>13</sup>C NMR spectra of the isolated compounds .....</b>	<b>84</b>

## 1. General information

**Safety statement:** No unexpected or unusually high safety hazards were encountered

**Column chromatography** was performed using Merck silica gel type 9385 230-400 mesh and typically pentane and ethyl acetate as eluent.

**Thin layer chromatography (TLC):** Merck silica gel 60, 0.25 mm. The components were visualized by UV or  $\text{KMnO}_4$  staining.

**Gas Chromatography (GC)** was used for product identification as well as determination of conversion and selectivity values. Product identification was performed by GC-MS (Shimadzu QP2010 Ultra) with an HP-1MS column, and helium as carrier gas. GC-MS method: The temperature program started at 50 °C for 5 min, heated by 30 °C/minute to 250 °C and held for 15 min. Conversions and product selectivity were determined by GC-FID (Agilent Technologies 6890) with an HP-5MS column using nitrogen as carrier gas. GC-FID analysis method: The temperature program started at 50 °C for 5 min, heated by 30 °C/min to 320 °C and held for 15 min.

**Mass spectrometry:** Mass spectra were recorded on an AEI-MS-902 mass spectrometer ( $\text{EI}^+$ ) or an LTQ Orbitrap XL ( $\text{ESI}^+$ ).

**Gel Permeation Chromatography (GPC):** GPC was performed on a Hewlett Packard 1100 system equipped with three PL-gel 3  $\mu\text{m}$  MIXED-E columns in series. The columns were operated at 40 °C with a flow rate of 1 mL/min of THF. Detection was accomplished at 40 °C using a GBC LC 1240 RI detector. The molecular weight estimations were performed using polystyrene standards of known molecular weight distribution.

**NMR spectroscopy:**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Varian Mercury Plus 400, Agilent MR 400 (400 and 101 MHz, respectively), Varian Inova 500 (500 and 126 MHz, respectively) and Bruker Avance NEO 600 (600 and 151 MHz, respectively) using  $\text{CDCl}_3$ ,  $\text{CD}_3\text{OD}$  and  $\text{DMSO-d}_6$  as a solvent.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded at room temperature. Chemical shift values are reported in ppm with the solvent resonance as the internal standard ( $\text{CDCl}_3$ : 7.26 for  $^1\text{H}$ , 77.00 for  $^{13}\text{C}$ ;  $\text{CD}_3\text{OD}$ : 3.31 for  $^1\text{H}$ , 49.00 for  $^{13}\text{C}$ ;  $\text{DMSO-d}_6$ : 2.50 for  $^1\text{H}$ , 39.52 for  $^{13}\text{C}$ ). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br. = broad, m = multiplet), coupling constants (Hz), and integration.

**Standard techniques under inert atmosphere:** Amination of alcohols was carried out under an argon atmosphere using oven (120 °C) dried glassware and standard Schlenk techniques as follows. The solid materials were weighed into a Schlenk tube under air and the Schlenk tube

was subsequently connected to an argon line and vacuum-argon exchange was performed three times. Liquid starting materials and the solvent were charged under an argon stream. The Schlenk tube was capped and the mixture was rapidly stirred at room temperature for 1 min, then it was placed into a pre-heated oil bath to carry out the reaction at the indicated temperature for an indicated time.

**Reagents and solvents:** 1-Hydroxytetraphenylcyclopentadienyl-(tetraphenyl-2,4-cyclopentadien-1-one)- $\mu$  hydrotetracarbonyl diruthenium(II) (Shvo's catalyst) was purchased from Strem chemicals, Cyclopentyl methyl ether (CPME, 99.9%, anhydrous) was purchased from Sigma-Aldrich without further purification. All other reagents were purchased from Sigma-Aldrich, Acros and TCI in reagent or higher grade and were used as received without further purification. Deep Eutectic Solvents (DES) were prepared by the reported procedures.<sup>1,2</sup> Pine lignocellulose was purchased from Bemap Houtmeel B.V., and poplar lignocellulose was purchased from Morrow Oregon.

**Evaluation of antibacterial effects:** Antibacterial activities of compounds were determined in *E. coli* K12 (DSM 18039), *E. coli* TolC and *Staphylococcus aureus subsp. aureus* (Newman strain). As a bacteria start OD<sub>600</sub>, we used 0.03 (optical density of the bacteria at 600 nm) in a total volume of 200  $\mu$ L in lysogeny broth (LB) medium containing the compounds predissolved in DMSO (maximal DMSO concentration: 1%). Final compound concentrations prepared from serial dilutions ranged from 0.02 to 50 or 100  $\mu$ M, depending on their solubility. The ODs at 600 nm were determined directly after addition of the compounds and again after incubation at 37 °C for 16 hours and 50 rpm in 96 well plates (Sarstedt, Nümbrecht, Germany) using a FLUOstar Omega microplate reader (BMG labtech). Percent inhibition values at defined compound concentrations could be determined by relating the ODs hereof to those of DMSO controls. Given minimal inhibitory concentrations (MIC) values are means of at least two independent determinations and are defined as the lowest concentration of compounds that reduced OD<sub>600</sub> by  $\geq 95\%$ .

**Cytotoxicity assay:** Hep G2 (hepatocellular carcinoma) cells ( $2 \times 10^5$  cells per well) were seeded in 24-well, flat-bottomed plates. Culturing of cells, incubations and OD measurements were performed as described previously<sup>3</sup> with small modifications. Twenty-four hours after seeding the cells, the incubation was started by the addition of compounds in a final DMSO concentration of 1%. The living cell mass was determined after 48 hours in a PHERAstar microplate reader (BMG labtech, Ortenberg, Germany). At least two independent measurements were performed for each compound. The calculation of IC<sub>50</sub> values was

performed by plotting the percent inhibition vs the concentration of inhibitor on a semi-log plot. From this, the molar concentration causing 50% inhibition was calculated.

## 1.1 Preparation of Cu20-PMO catalyst

The hydrotalcite (HTC) catalyst precursors and Cu20-PMO were prepared according to our previously reported procedure.<sup>4</sup> In a typical procedure, a solution containing  $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$  (12.07 g, 0.05 mol),  $\text{Cu}(\text{NO}_3)_2 \cdot 2.5\text{H}_2\text{O}$  (6.98 g, 0.03 mol) and  $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$  (24.40 g, 0.12 mol) in deionized water (0.2 L) was added to a solution containing  $\text{Na}_2\text{CO}_3$  (5.30 g, 0.05 mol) in water (0.3 L) at 60 °C under vigorous stirring. The pH was kept between 9 and 10 by addition of small portions of a 1 M solution of NaOH. The mixture was vigorously stirred at 60 °C for 72 h. After cooling to room temperature, the light blue solid was filtered and resuspended in a 2 M solution of  $\text{Na}_2\text{CO}_3$  (0.3 L) and stirred overnight at 40 °C. The catalyst precursor was filtered and washed with deionized water until chloride free. After drying the solid for 6 h at 100 °C, 15.07 g of the HTC was obtained. Before use, 4 g of HTC was calcined at 460 °C for 24 h in air and 2.5 g of Cu20-PMO can be obtained.

## 1.2 Synthesis of dihydroconiferyl alcohol (1G) and dihydrosinapyl alcohol (1S)

### 1.2.1 Synthesis of dihydroconiferyl alcohol (1G)

**1G** was synthesized by slight modification of the literature procedure.<sup>5</sup> A mixture of (*E*)-3-(4-hydroxy-3-methoxyphenyl)acrylic acid (10 g, 51.54 mmol) and 5% Pd/C (0.2 g) in methanol/EtOAc (50 mL, 1:1) were placed in a high pressure Parr autoclave. The reactor was sealed, purged 3 times with  $\text{H}_2$  and then pressurized with  $\text{H}_2$  (40 bar) and stirred at room temperature for 18 h. After filtering through a Celite plug, the solvent was evaporated under reduced pressure to provide 10 g of 3-(4-hydroxy-3-methoxyphenyl)propanoic acid (51.04 mmol, 99% yield), which was used without further purification. To a rapidly stirred suspension of  $\text{LiAlH}_4$  (1.45 g, 38.26 mmol) in 50 mL of THF was added over 50 min a solution of 3-(4-hydroxy-3-methoxyphenyl)propanoic acid (5 g, 25.51 mmol) in 20 mL of THF at 0 °C. After the addition was complete, the reaction mixture was allowed to room temperature and refluxed for 60 min, and then the mixture was cooled again to room temperature, poured into ice water which was then poured into a solution of 5% HCl over ice, and extracted once with diethyl ether (100 mL) and twice with ethyl acetate (50 mL). The combined organic extract was washed with a saturated solution of  $\text{NaHCO}_3$  (50 mL) and brine (100 mL), dried over anhydrous  $\text{MgSO}_4$  and the solvent was evaporated under reduced pressure to provide 3.7 g of dihydroconiferyl alcohol (80% yield).

### 1.2.2 Synthesis of dihydrosinapyl alcohol (1S)

**1S** was synthesized by slight modification of the literature procedure.<sup>5</sup> A mixture of (*E*)-3-(4-hydroxy-3,5-dimethoxyphenyl)acrylic acid (5 g, 22.32 mmol) and 5% Pd/C (0.1 g) in THF (80 mL) were placed in a high pressure Parr autoclave. The reactor was sealed, purged 3 times with H<sub>2</sub> and then pressurized with H<sub>2</sub> (40 bar) and stirred at room temperature for 18 h. After filtering through a Celite plug, the solvent was evaporated under reduced pressure to provide 5 g of 3-(4-hydroxy-3,5-dimethoxyphenyl)propanoic acid (22.12 mmol, 99% yield), which was used without further purification. To a rapidly stirred suspension of LiAlH<sub>4</sub> (1.26 g, 33.18 mmol) in 50 mL of THF was added over 50 min a solution of 3-(4-hydroxy-3,5-dimethoxyphenyl)propanoic acid (5 g, 22.12 mmol) in 20 mL of THF at 0 °C. After the addition was complete, the reaction mixture was refluxed for 60 min, and then the mixture was cooled again to room temperature, poured into ice water, which was then poured into a solution of 5% HCl over ice, and extracted once with diethyl ether (100 mL) and twice with 50 mL portions of EtOAc. The combined organic extract was washed with a saturated solution of NaHCO<sub>3</sub> (50 mL) and brine (100 mL), dried over anhydrous MgSO<sub>4</sub> and the solvent was evaporated under reduced pressure to provide 3.8 g of dihydrosinapyl alcohol (81% yield).

## 1.3 General experimental procedures

### 1.3.1 General procedure (A) for reductive catalytic fractionation (RCF) of lignocellulose

Reductive catalytic fractionation (RCF) of lignocellulose was carried out according to our previously reported procedure.<sup>6</sup> Reductive catalytic fractionation (RCF) of pine or poplar lignocellulose was carried out in a 100 mL high pressure Parr autoclave with an overhead stirrer. Typically, the autoclave was charged with Cu<sub>2</sub>O-PMO catalyst (0.4 g), pine or poplar lignocellulose (2 g), and methanol (20 mL). Once the reactor was sealed, purged 3 times with hydrogen and then pressurized with hydrogen (40 bar) at room temperature. The reactor was heated to 180 °C and stirred at 400 rpm for 18 h. After reaction, the reactor was cooled to room temperature. Then 0.1 mL solution was collected through a syringe and injected to GC-MS or GC-FID after filtration through a PTFE filter (0.45 μm). After that the solution and solids were transferred into a 50 mL centrifuge tube. The solid was separated from the reaction solution by centrifugation and subsequent decantation, and additionally washed with methanol (2×20 mL). All solutions were combined in a round bottom flask and the solvent was removed *in vacuo*. The crude product (195 mg for pine and 223 mg for poplar) was dried in a desiccator *in vacuo* for overnight and was further used as specified below (See **Supplementary Section 4.3** for pine and **Supplementary Section 4.5** for poplar)

### 1.3.2 General procedure (B) for Ru-catalyzed amination of 1G and 1S

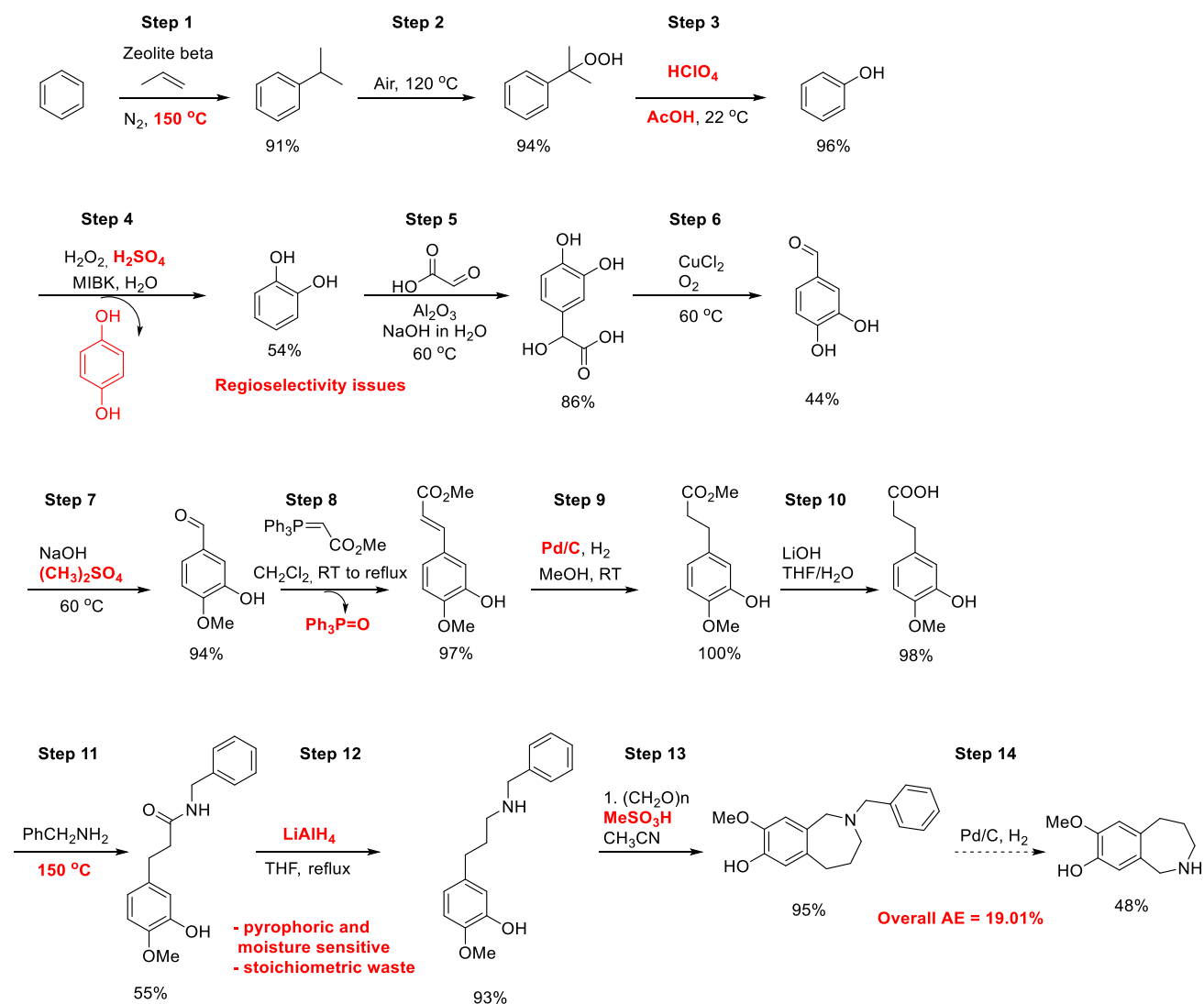
An oven-dried 20 mL Schlenk tube, equipped with a stirring bar, was charged with amine **4a-4w** (0.4 mmol, 1 equiv.), **1G** or **1S** (0.48 mmol, 1.2 equiv.), Shvo's catalyst (**C1**, 0.004 mmol, 1 mol%) and cyclopentyl methyl ether (CPME, 2 mL). The solid materials were weighed into the Schlenk tube under air and the Schlenk tube was subsequently connected to an argon line and vacuum-argon exchange was performed three times. Liquid starting materials and the solvent were charged under an argon stream. The Schlenk tube was capped and the mixture was rapidly stirred at room temperature for 1 min, then it was placed into a pre-heated oil bath at 130 °C and stirred for 20 h. The reaction mixture was cooled down to room temperature and the crude mixture was filtered through silica gel, eluted with ethyl acetate (10 mL), and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography (typically with ethyl acetate and pentane) to provide the pure amine product.

### 1.3.3 General procedure (C) for the synthesis of tetrahydro-2-benzazepines in deep eutectic solvents (DES)

An oven-dried vial equipped with a stirring bar, was charged with aminoalkylphenol or **5Ga-5Gp** and **6Ga-6Sp** (0.150-0.366 mmol), paraformaldehyde (0.150-0.366 mmol) and ChCl/Oxalic acid (1:1 molar ratio, 1g) under air. Then the vial was capped and the mixture was rapidly stirred at room temperature for 1 min, then it was heated to 70-80 °C and stirred for 20-48 h. The reaction mixture was cooled down to room temperature, water (2 mL) and saturated solution of NaHCO<sub>3</sub> (2 mL) was added and then the reaction mixture was stirred for one hour at room temperature. The crude mixture was extracted with ethyl acetate (3 × 10 mL) and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography (typically with pentane and ethyl acetate).

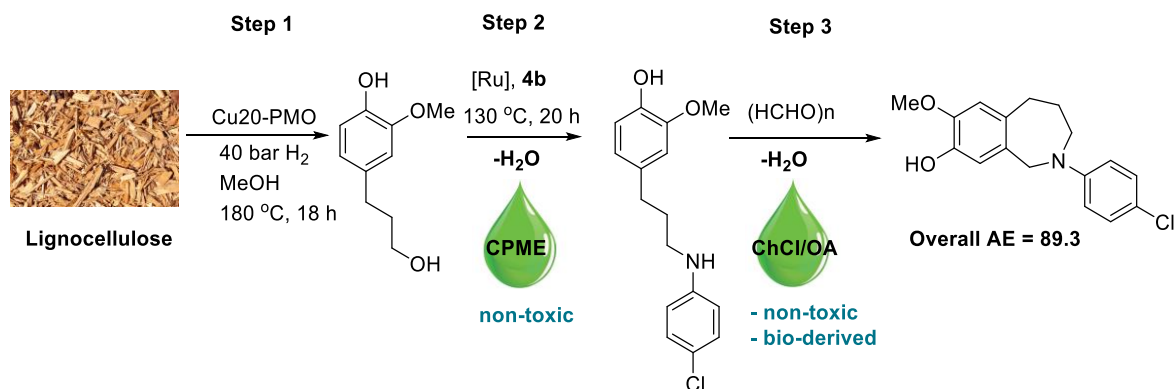
## 2. Comparison of the synthesis of tetrahydro-2-benzazepine from fossil fuels and lignocellulose

### 2.1 Analysis of a multi-step reaction pathway for the synthesis of 7-methoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol from petrochemical sources



**Supplementary Figure 1.** Analysis of reaction steps for the synthesis of 7-methoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol starting from benzene. Selection of pathways are based on the available literature.<sup>7,8,9,10</sup>

## 2.2 Green route to the synthesis of 2-(4-chlorophenyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol directly from raw lignocellulose in three steps



**Supplementary Figure 2.** Three-step synthesis of 2-(4-chlorophenyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol from lignocellulose.

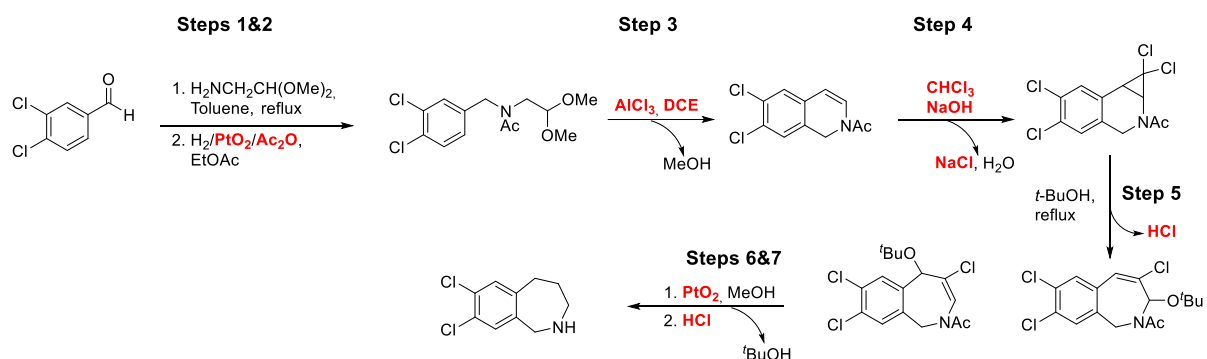
**Supplementary table 1.** Synthesis of tetrahydro-2-benzazepine: Classical synthesis vs this work

**Classical synthesis (13 steps)**

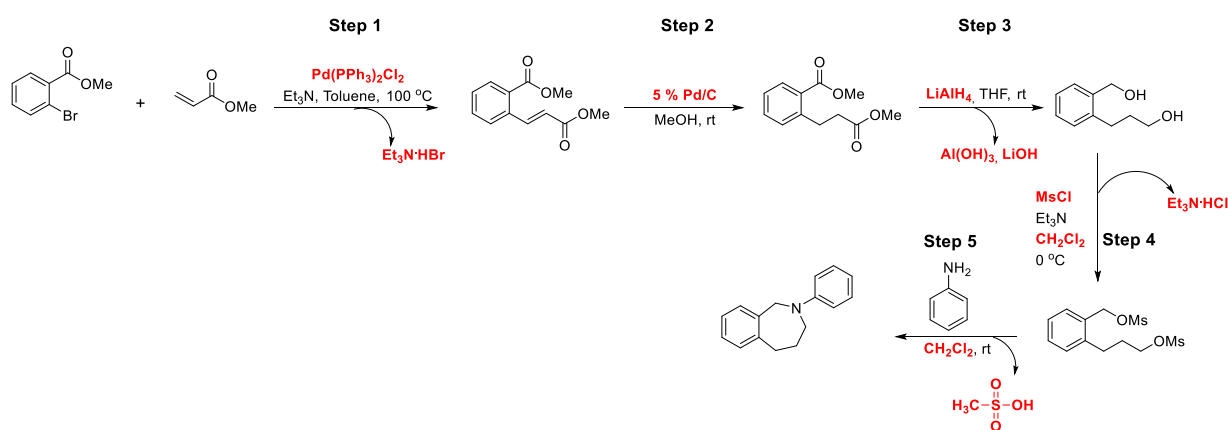
Step	Solvents	Temp (°C)	Reagents or Catalysts used (mol%)	Waste/By-product	AE (%)
1	No solvent	<b>150</b>	-	-	100
2	No solvent	120	-	-	100
3	<b>AcOH</b>	<22	<b>HClO<sub>4</sub></b> (7)	Acetone	62
4	H <sub>2</sub> O	50	<b>H<sub>2</sub>SO<sub>4</sub></b> (0.1) MIBK (5.0)	4-Hydroxyphenol	85
5	H <sub>2</sub> O	60	Al <sub>2</sub> O <sub>3</sub> (44) NaOH ( <b>170</b> )	-	100
6	EtOAc, H <sub>2</sub> O	60	CuCl <sub>2</sub> (0.6)	HCOOH	75
7	<b>CH<sub>2</sub>Cl<sub>2</sub></b> , H <sub>2</sub> O	60	NaOH ( <b>80</b> )	Na <sub>2</sub> SO <sub>4</sub>	57
8	<b>CH<sub>2</sub>Cl<sub>2</sub></b>	r.t to reflux	<b>Ph<sub>3</sub>P=CH<sub>2</sub>COOMe</b> ( <b>100</b> )	Ph <sub>3</sub> P=O	43
9	MeOH	r.t	<b>Pd/C</b> (0.4)	-	100
10	THF	r.t	LiOH (100)	MeOH	93
11	No solvent	<b>150</b>	PhCH <sub>2</sub> NH <sub>2</sub> ( <b>600</b> )	H <sub>2</sub> O	34
12	THF	reflux	<b>LiAlH<sub>4</sub></b> ( <b>200</b> )	Al(OH) <sub>3</sub> , LiOH	75
13	CH <sub>3</sub> CN	reflux	<b>MeSO<sub>3</sub>H</b> ( <b>110</b> )	H <sub>2</sub> O	94
<b>This work</b>					
15	MeOH	180	Cu20-PMO (0.4 g)	-	-
16	CPME	130	Ru (1 mol%)	H <sub>2</sub> O	94
17	ChCl/OA	70	ChCl/OA (1g)	H <sub>2</sub> O	94

## 2.3 Multi-step syntheses of tetrahydro-2-benzazepines: detailed description of reaction steps

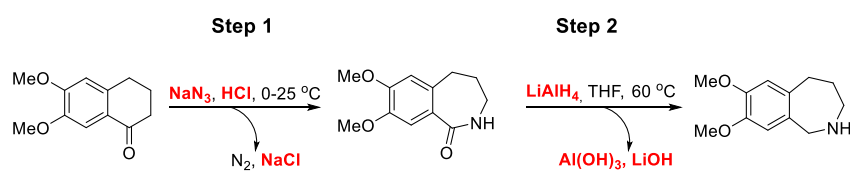
### Route 1. From dichlorobenzaldehyde<sup>11</sup>



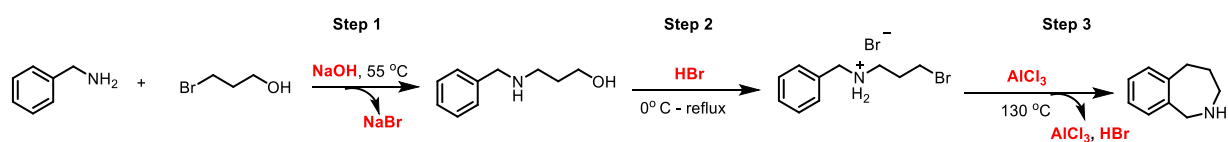
### Route 2. From methyl 2-bromobenzoate<sup>12</sup>



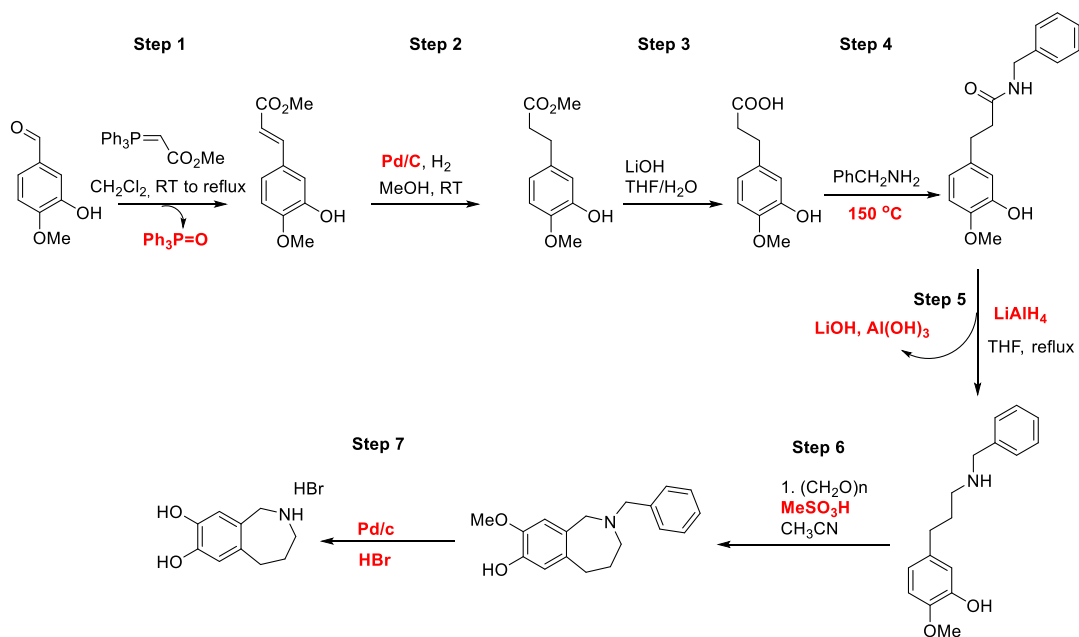
### Route 3. From tetralone<sup>13</sup>



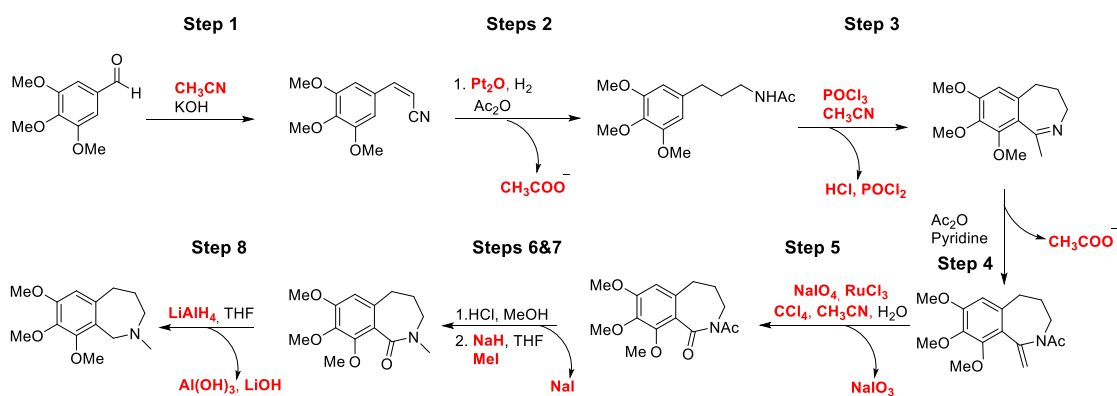
### Route 4. From benzylamine<sup>14</sup>



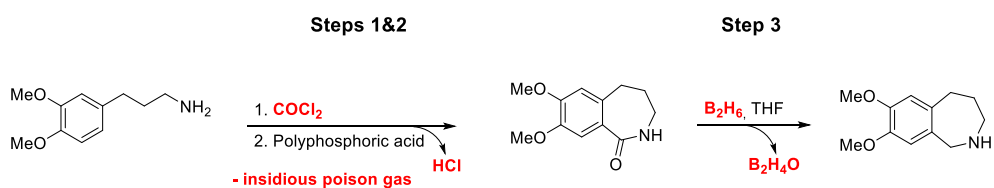
## Route 5. From Isovaniline<sup>8</sup>



## Route 6. From syringaldehyde<sup>15</sup>



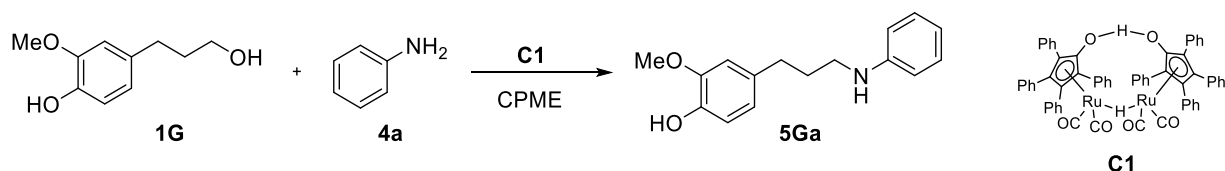
## Route 7. From 3-(3,4-dimethoxyphenyl)propan-1-amine<sup>16</sup>



### 3. Establishing the selective catalytic amination of dihydroconiferyl alcohol (**1G**) with aniline

An oven-dried 20 mL Schlenk tube, equipped with a stirring bar, was charged with **4a** (0.25 mmol, 1 equiv.), **1G** (0.3 mmol, 1.2 equiv.), **C1** (0.5-1 mol%) and cyclopentyl methyl ether (CPME, 1 mL). The reaction was set up according to standard Schlenk techniques (see **Supplementary Section 1**). The reaction was performed at 100-130 °C and stirred for 8-20 h. The reaction mixture was cooled down to room temperature and the crude mixture was filtered through silica gel, eluted with ethyl acetate (10 mL), and concentrated *in vacuo*. The crude mixture was analyzed by GC-FID and GC-MS.

**Supplementary Table 2.** Establishing the selective catalytic amination of dihydroconiferyl alcohol (**1G**) with **4a** using Ru-based catalyst (**C1**)



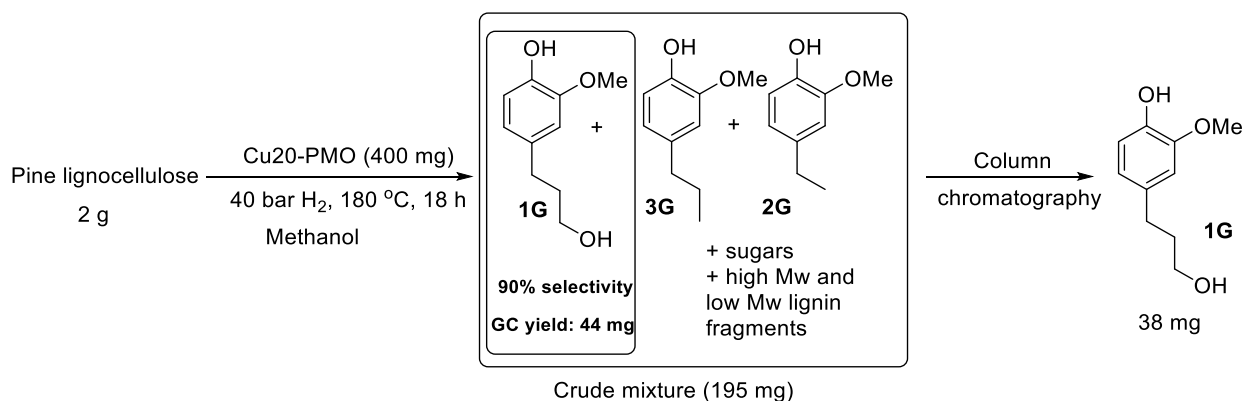
Entry <sup>a</sup>	<b>C1</b> (mol%)	<b>1G</b> (equiv.)	Amine	Temp (°C)	Time (h)	Yield <b>5Ga</b> (%) <sup>b</sup>
1	<b>C1</b> (1)	1.2	<b>4a</b>	130	20	>99 (75)
2	<b>C1</b> (0.5)	1.2	<b>4a</b>	130	20	33
3	<b>C1</b> (1)	1.2	<b>4a</b>	100	20	42
4	<b>C1</b> (1)	1	<b>4a</b>	130	20	93
5	<b>C1</b> (1)	1.2	<b>4a</b>	130	8	52
6 <sup>c</sup>	<b>C1</b> (1)	1.2	<b>4a</b>	130	20	98
7	-	1.2	<b>4a</b>	130	20	-
8 <sup>d</sup>	<b>C1</b> (1)	1.2	<b>4b</b>	130	20	>99 (94)

**Reaction conditions:** <sup>a</sup>**4a** (0.25 mmol), **1G** (0.3 mmol), **C1** (0.5-1 mol%), CPME (1 mL), 100-130 °C, 8-20 h. <sup>b</sup> Conversions and yields were determined by GC-FID (Isolated yield). <sup>c</sup> 10 equiv. of Hg used. <sup>d</sup> 4-chloroaniline **4b** (5.95 mmol), **1G** (7.14 mmol), CPME (20 mL), 130 °C, 20 h.

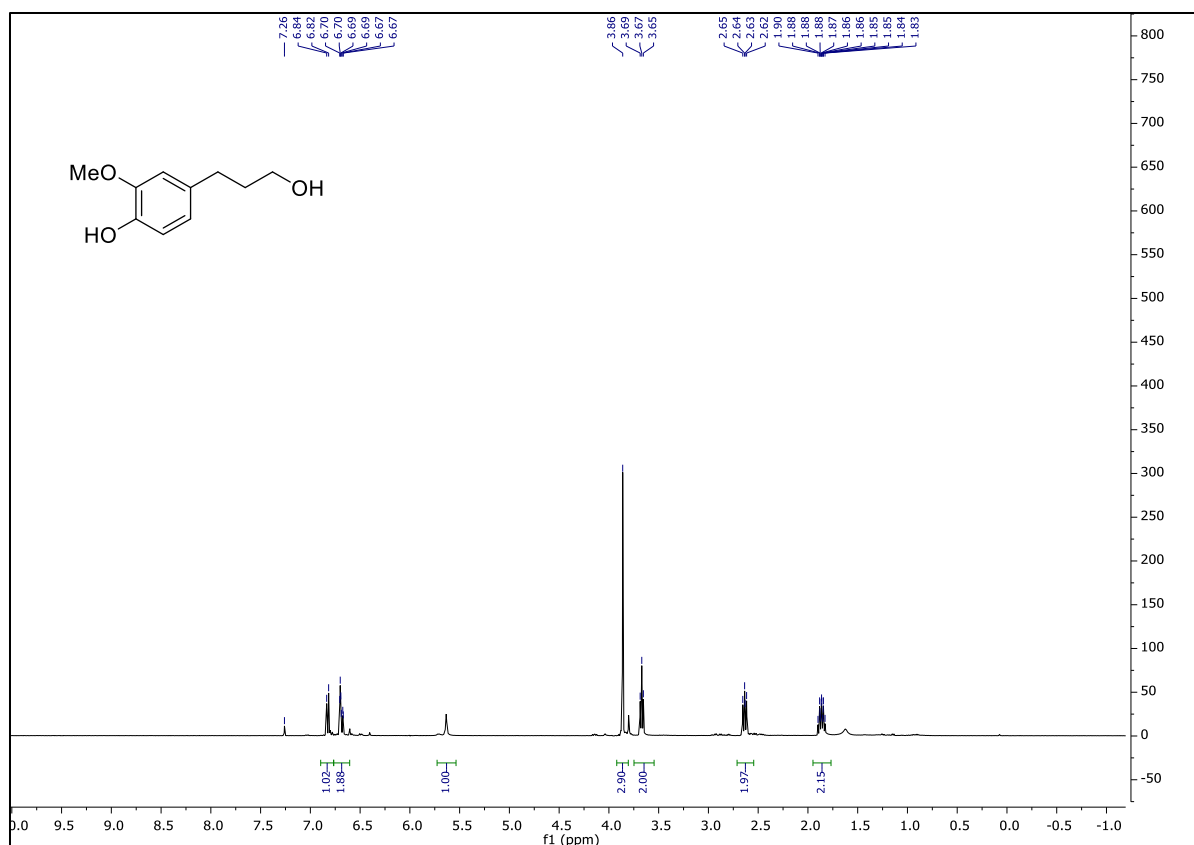
## 4. Development of efficient reactive separation of dihydroconiferyl alcohol (1G) from lignocellulose depolymerization mixtures

### 4.1 Reductive catalytic fractionation (RCF) of pine lignocellulose and separation of dihydroconiferyl alcohol (1G)

Reductive catalytic fractionation (RCF) of pine lignocellulose was carried out in a 100 mL high pressure Parr reactor with an overhead stirrer. Typically, the autoclave was charged with Cu20-PMO catalyst (0.4 g), pine lignocellulose (2 g), and methanol (20 mL). Once the reactor was sealed, purged 3 times with hydrogen and then pressurized with hydrogen (40 bar) at room temperature. The reactor was heated to 180 °C and stirred at 400 rpm for 18 h. After reaction, the reactor was cooled to room temperature and then the solution and solids were transferred into a 50 mL centrifuge tube. The solids were separated from the reaction solution by centrifugation and subsequent decantation, and additionally washed with methanol (2 × 20 mL). All solutions were combined in a round bottom flask and the solvent was removed *in vacuo*. The crude product was purified by column chromatography using pentane/ethyl acetate (60:40) affording **1G** (0.208 mmol, 38 mg) as a pure product in accordance with previously observed **1G** amounts.<sup>6</sup> This quantity was used to calculate the amount of amine added during reactive separation in **Supplementary Section 4.3**.



**Supplementary Figure 3.** Reductive catalytic fractionation of pine lignocellulose over Cu20-PMO and separation of dihydroconiferyl alcohol **1G**. Selectivity of **1G** (90%) is based on GC-FID analysis.



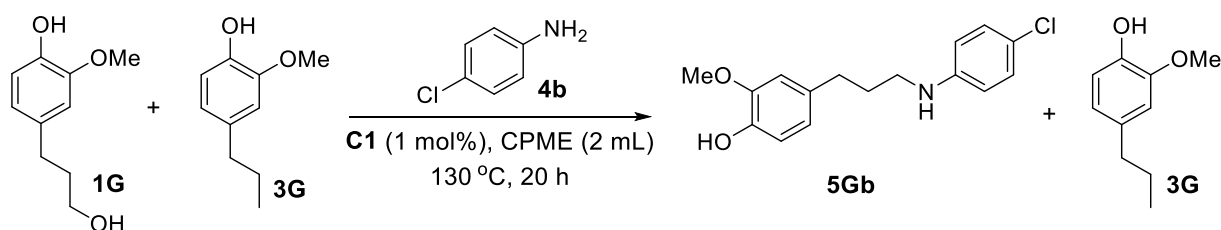
**Supplementary Figure 4.**  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of **1G** isolated by column chromatography from the crude product mixture obtained upon RCF of pine lignocellulose.

## 4.2 Highly selective catalytic amination of dihydroconiferyl alcohol (**1G**) in the presence of 4-propylguaiacol (**3G**)

Reductive catalytic fractionation (RCF) of pine lignocellulose in the presence of Cu20-PMO (LignoFlex) delivers **1G** in high selectivity (up to 90%) under optimized reaction conditions. However, beside **1G** other monomers (**3G**, **2G**) also presence in the crude product mixture which may influence further reactivity of the crude mixture. Therefore, before exploring the actual reactive separation of crude depolymerization mixtures that also contain other components, we have first performed catalytic amination of **1G** using 4-chloroaniline **4b** as substrate in simple model mixtures also containing **3G** in different ratio, in order to verify possible influence of **3G** on the catalytic amination method. **General procedure (B)** was used. Gratifyingly, **3G** showed no detrimental effect on the amination method and **5Gb** could be obtained in 85% (1:1) and 87% (3:1) yield upon column chromatography, with full substrate conversion seen in both cases. Furthermore, the unreacted **3G** was also isolated in 90% (1:1) and 94% (3:1) yield (For results see **Supplementary Table 3**). Separation of **5Gb** and **3G** by column chromatography was carried out using ethyl acetate and pentane (30:70) as

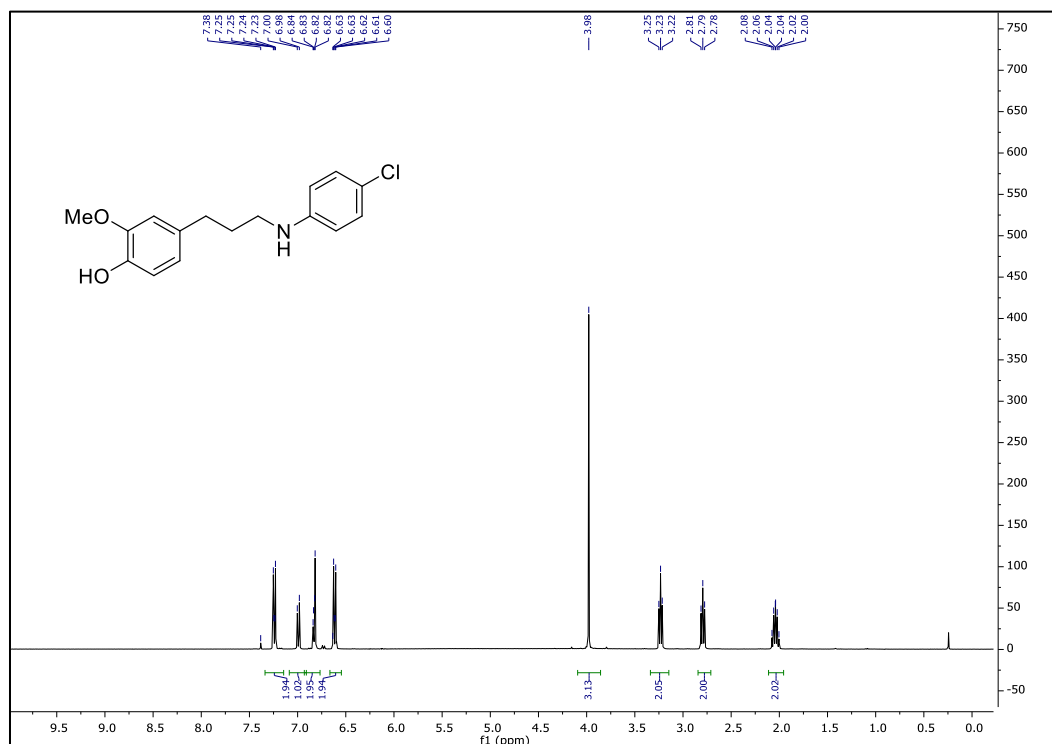
eluent. **3G** was isolated at 10% ethyl acetate in pentane and **5Gb** was isolated at 30% ethyl acetate in pentane.

**Supplementary Table 3.** Catalytic amination of dihydroconiferyl alcohol (**1G**) in the presence of 4-propylguaiacol (**3G**)

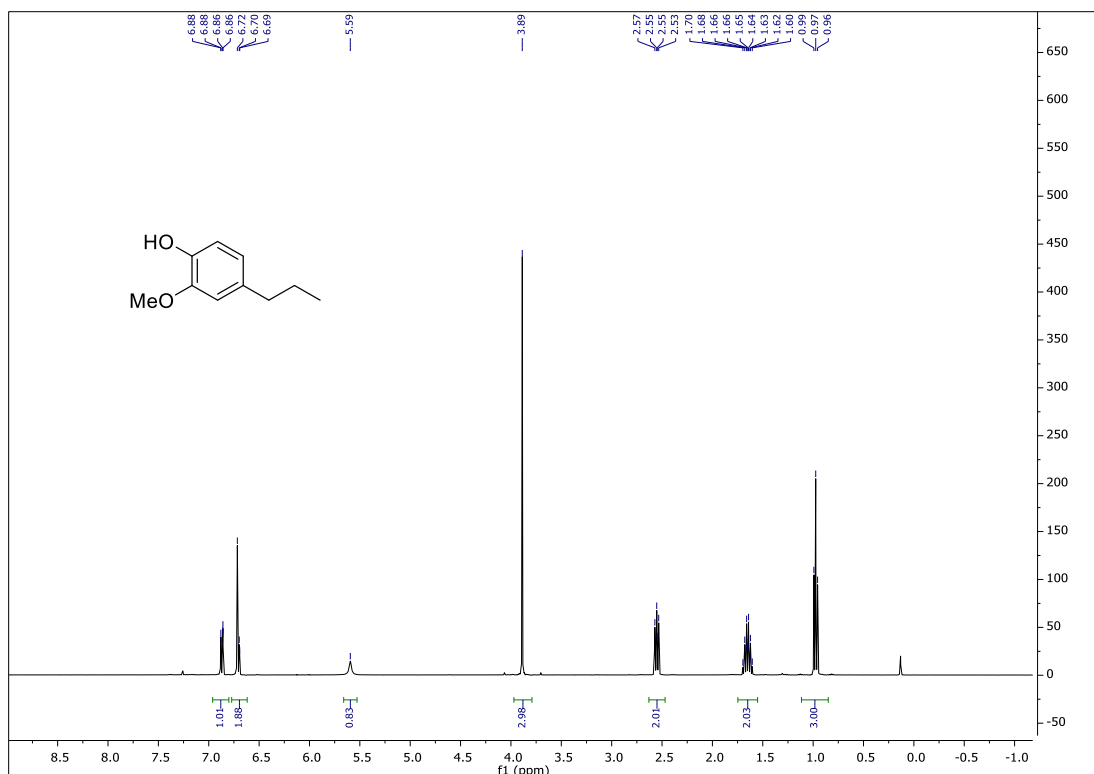


Entry <sup>a</sup>	<b>1G</b> (mmol)	<b>3G</b> (mmol)	<b>4b</b> (mmol)	<b>C1</b> (mmol)	Yield <b>5Gb</b> (%) <sup>b</sup>	Yield <b>3G</b> (%) <sup>b</sup>
1	0.6	0.6	0.5	0.005	85	90
2	0.6	1.8	0.5	0.005	87	94

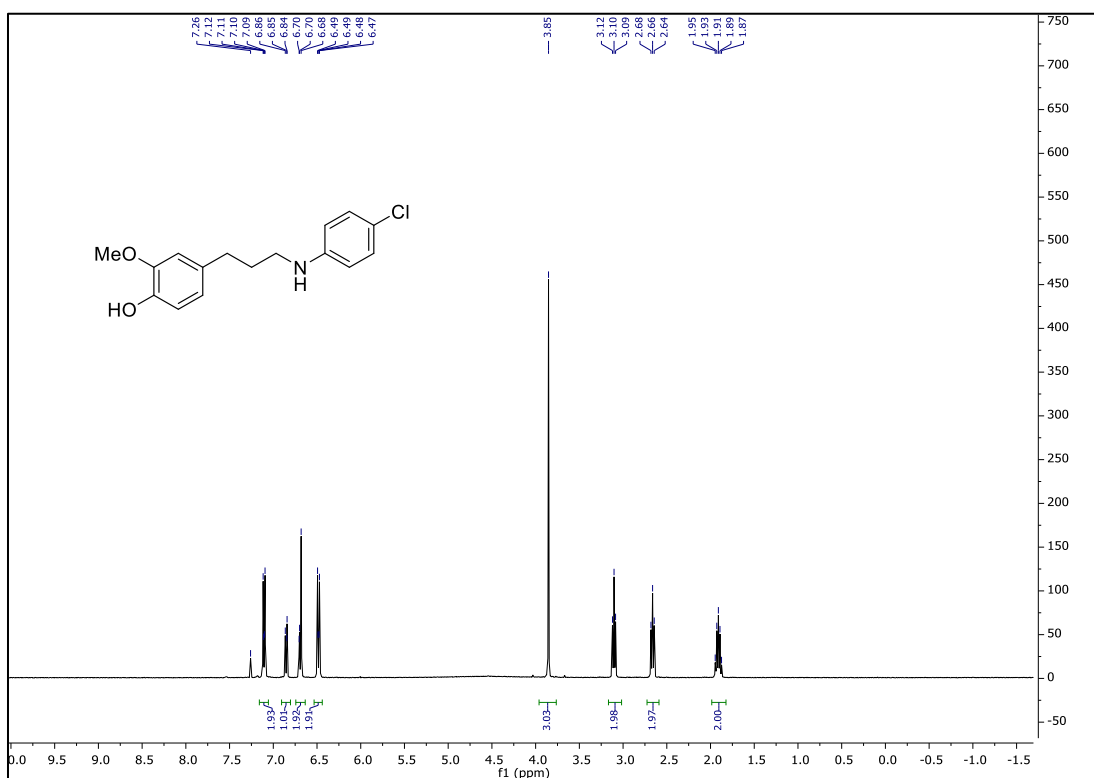
<sup>a</sup>Reaction conditions: 130 °C, 20 h, CPME (2 mL). <sup>b</sup>Isolated yield.



**Supplementary Figure 5.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of **5Gb** isolated from the catalytic amination reaction using a 1:1 mixture of **3G** and **1G** and 4-chloroaniline **4b**.



**Supplementary Figure 6.**  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of **3G** isolated from the catalytic amination reaction using a 1:1 mixture of **3G** and **1G** and 4-chloroaniline **4b**.



**Supplementary Figure 7.**  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of **5Gb** isolated from the catalytic amination reaction using a 3:1 mixture of **3G** and **1G** and 4-chloroaniline **4b**.



**Supplementary Figure 8.**  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of **3G** isolated from the catalytic amination reaction using a 3:1 mixture of **3G** and **1G** and 4-chloroaniline **4b**.

### 4.3 Reactive separation of 1G from reaction mixtures obtained by RCF of pine lignocellulose by catalytic amination-separation of lignin-derived secondary amine 5Gb and other products

#### 4.3.1 Fractionation, reactive separation and analysis of the crude mixture obtained from RCF of pine lignocellulose

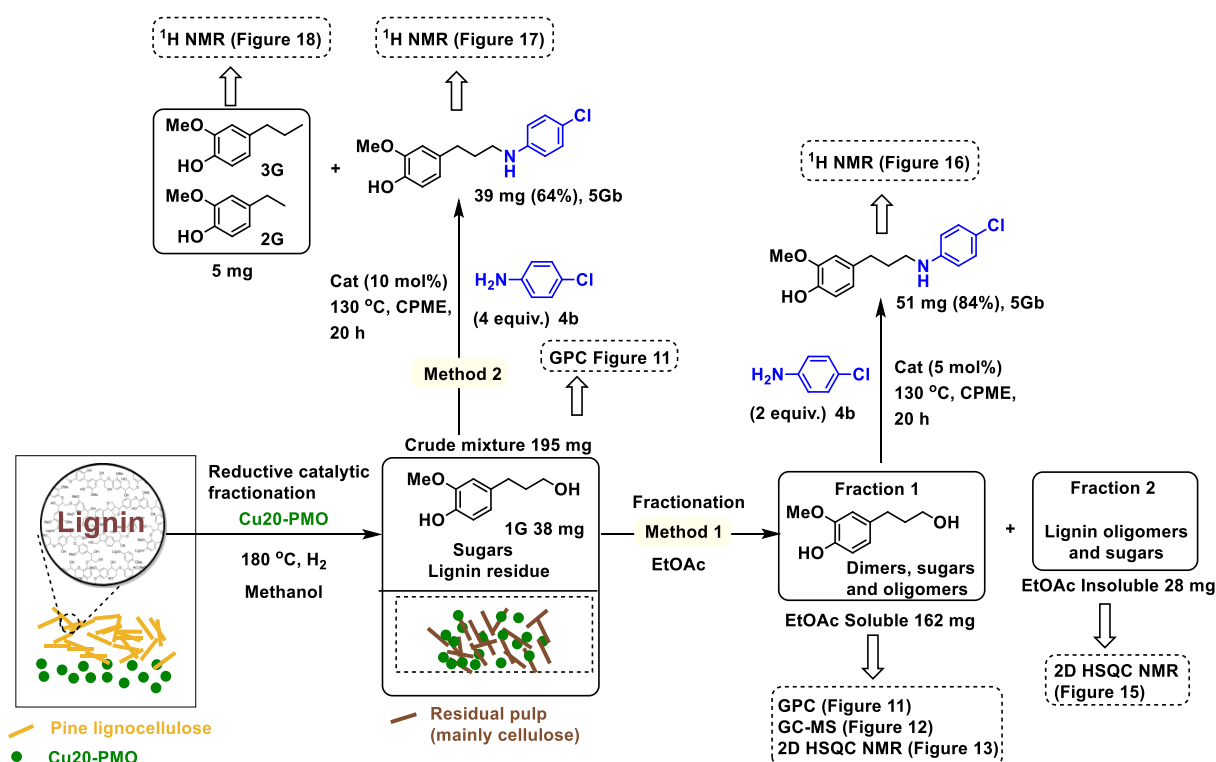
Reductive catalytic fractionation (RCF) of pine lignocellulose was carried out using Cu<sub>2</sub>O-PMO according to the procedure indicated above in **General procedure (A)**. The so obtained crude product mixture (195 mg) was subjected to a fractionation procedure followed by the desired reactive separation. These processing steps allowed for analysis of the non-monomeric side-products. First, we aimed to find a convenient step to separate possible oligomeric lignin residues. Therefore, the fractionation of the crude depolymerization oil was attempted with ethyl acetate being most efficient solvent for this purpose.

**Fractionation of the crude mixture:** To the crude mixture (195 mg), ethyl acetate was added (10 mL) and it was stirred for overnight at room temperature, which resulted in precipitation of brownish colored solid. The suspension was transferred into a 20 mL centrifuge tube. The solid was separated by centrifugation and subsequent decantation and additionally washed with ethyl acetate (2×10 mL). All liquids were combined in a round bottom flask and the solvent was removed *in vacuo*. The soluble and insoluble fractions were additionally dried *in vacuo* under constant weight. The ethyl acetate insoluble fraction (**Fraction 2**) was characterized by 2D-HSQC, which confirmed the presence of lignin oligomers. Small amount of sugars were also detected (**Supplementary Fig. 15**). To conclude, ethyl acetate is a suitable solvent for easily separating lignin oligomers that may interfere with the reactive separation step (**Supplementary Fig. 9**). The ethyl acetate soluble fraction (**Fraction 1**, see **Supplementary Fig. 10c**) was further characterized by GPC (**Supplementary Fig. 11**), GC-MS and NMR spectroscopic measurements (**Supplementary Figs. 12 & 13**). When comparing the GPC traces of the crude depolymerization mixture vs **Fraction 1**, the disappearance of the higher Mw (> ~1000g/mol) lignin fragments that are present in the crude, can be confirmed, while in **Fraction 1** this region is much less pronounced and mainly shows side-products in the oligomeric Mw range (<1000 g/mol). The GC-MS trace of **Fraction 1** displayed 1G as dominant monomer in **Fraction 1** (**Supplementary Fig. 12**) and small amount of dimers were also seen. This was further confirmed by 2D-HSQC analysis (**Supplementary Fig. 13**) that showed mainly the corresponding signals of monomer 1G.

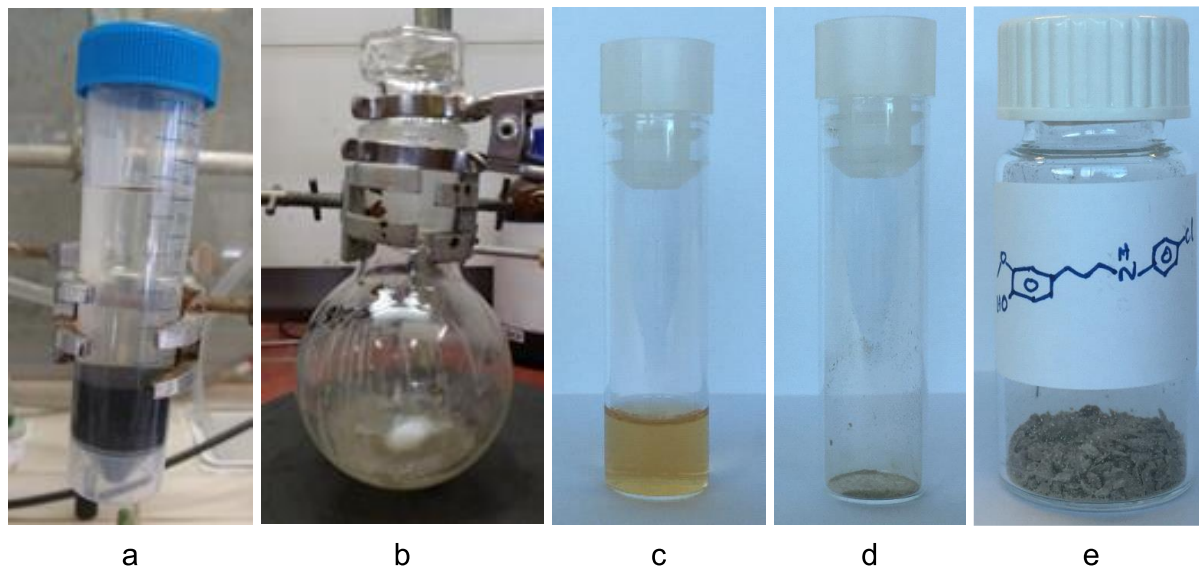
Taking into account the weight of **Fraction 1** (162 mg) vs mass of **1G** (assumed 38 mg), we attempted further analysis by treatment with water. Indeed, 58 mg of water-soluble material was obtained and characterized as sugars by 2D-HSQC (**Supplementary Fig. 14**). We assume the rest of **Fraction 1** to be unreacted lignin oligomers.

**Catalytic amination using Fraction 1:** **Fraction 1** (162 mg) was subjected to the previously developed Ru-catalyzed amination protocol in order to assess whether reactive separation of **1G** is possible. The reaction was conducted according to **General procedure (B)** using previously under optimized conditions (130 °C, 20 h) with **4b** (0.417 mmol, 2 equiv.), **C1** (0.011 mmol, 5 mol%) (with respect to the yield of **1G**) and CPME (2 mL). The reaction mixture was completely soluble in the reaction solvent CPME. After reaction, the solvent was evaporated and the product **5Gb** was isolated (51 mg, 84%) by column chromatography using pentane/ethyl acetate (60:40).

A specific scheme summarizing the fractionation as well as reactive separation procedure is shown below on **Supplementary Fig. 9**, and images of products obtained in each step are shown in **Supplementary Fig. 10**. The analytical details related to **Fraction 1** and **Fraction 2** are displayed below.

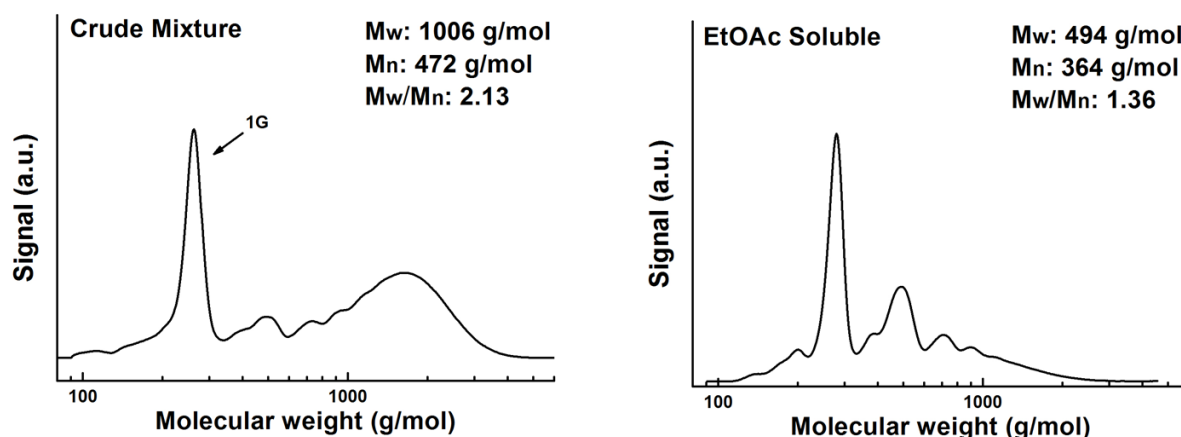


**Supplementary Figure 9.** Reactive separation of **1G** to yield lignin derived amine **5Gb** from pine lignocellulose through RCF, selective amination and separation of other monomers, oligomers and sugar derivatives.

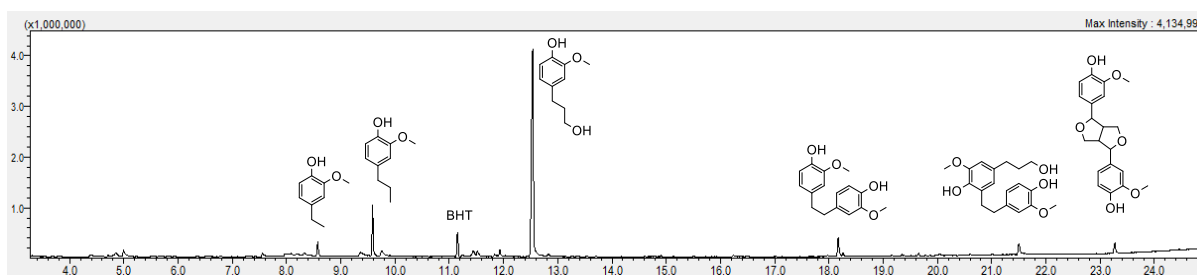


**Supplementary Figure 10.** Images of reaction mixtures or products obtained in the different steps displayed on **Supplementary Fig. 9**. (a) Crude depolymerization mixture obtained upon RCF of pine lignocellulose. (b) Crude mixture suspended and partially dissolved in ethyl acetate. (c) Ethyl acetate soluble fraction (**Fraction 1**) after separation from the crude mixture, containing mainly **1G** and sugars. (d) Ethyl acetate insoluble fraction (**Fraction 2**) showing brown residue containing predominantly higher Mw lignin. (e) Isolated **5Gb** after reactive separation from **Fraction 1**.

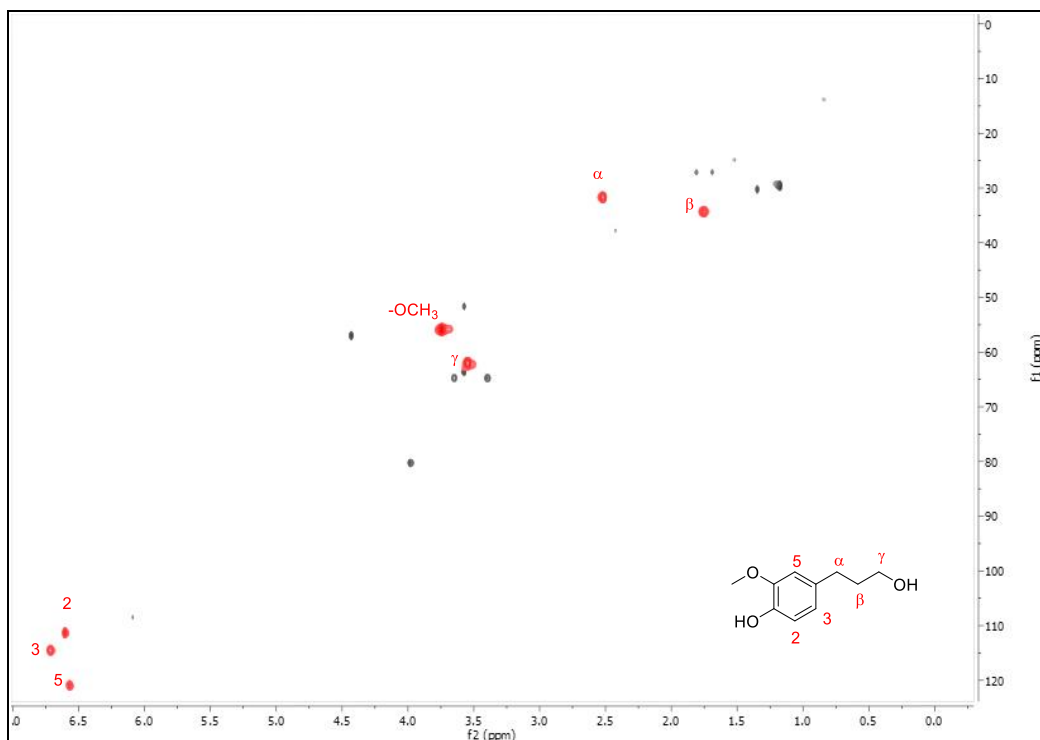
## Analytical data belonging to Fraction 1 and Fraction 2



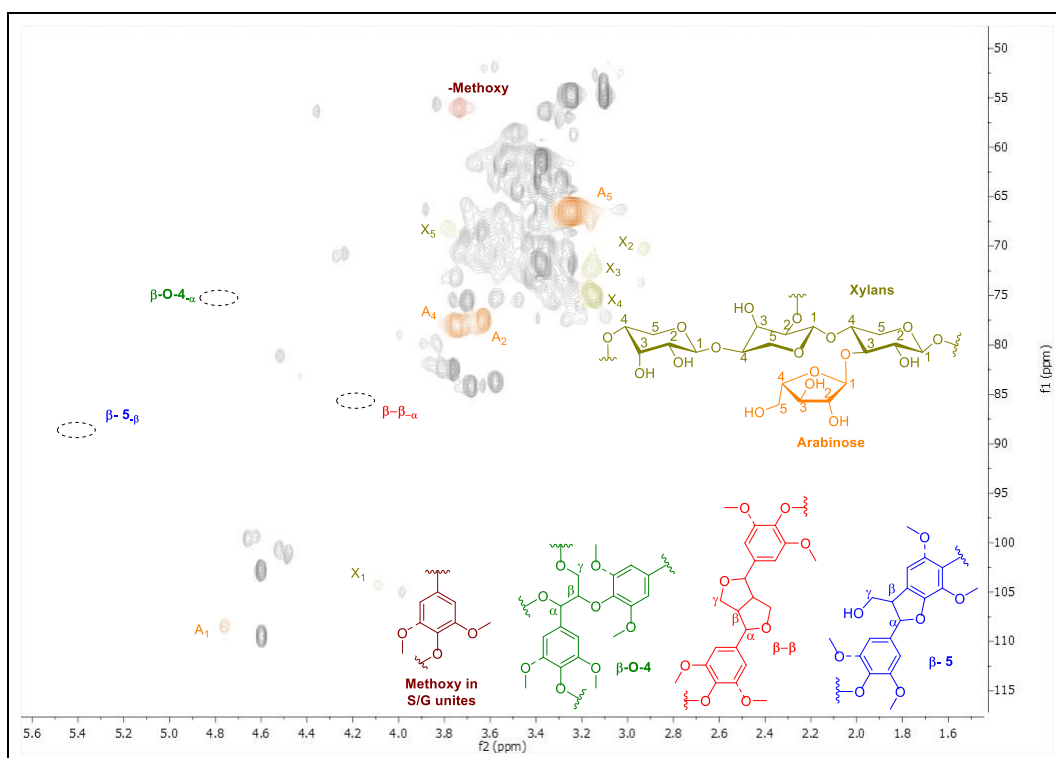
**Supplementary Figure 11.** GPC trace of the crude pine RCF mixture (left) and GPC trace of **Fraction 1**, obtained upon fractionation (right) showing loss of higher Mw lignin oligomers. (Note: **Fraction 2** displayed very low solubility in THF therefore GPC cannot be provided.)



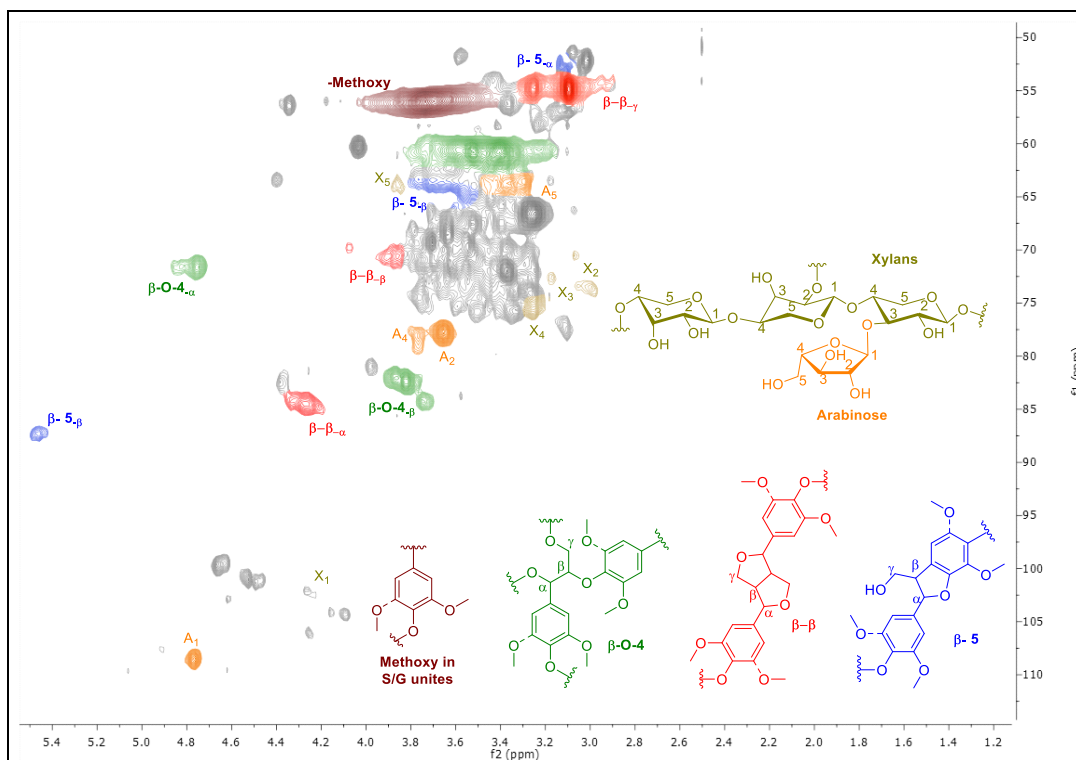
**Supplementary Figure 12.** GC-MS chromatogram of the ethyl acetate soluble fraction (**Fraction 1**) obtained upon fractionation of crude RCF product mixture from pine lignocellulose.



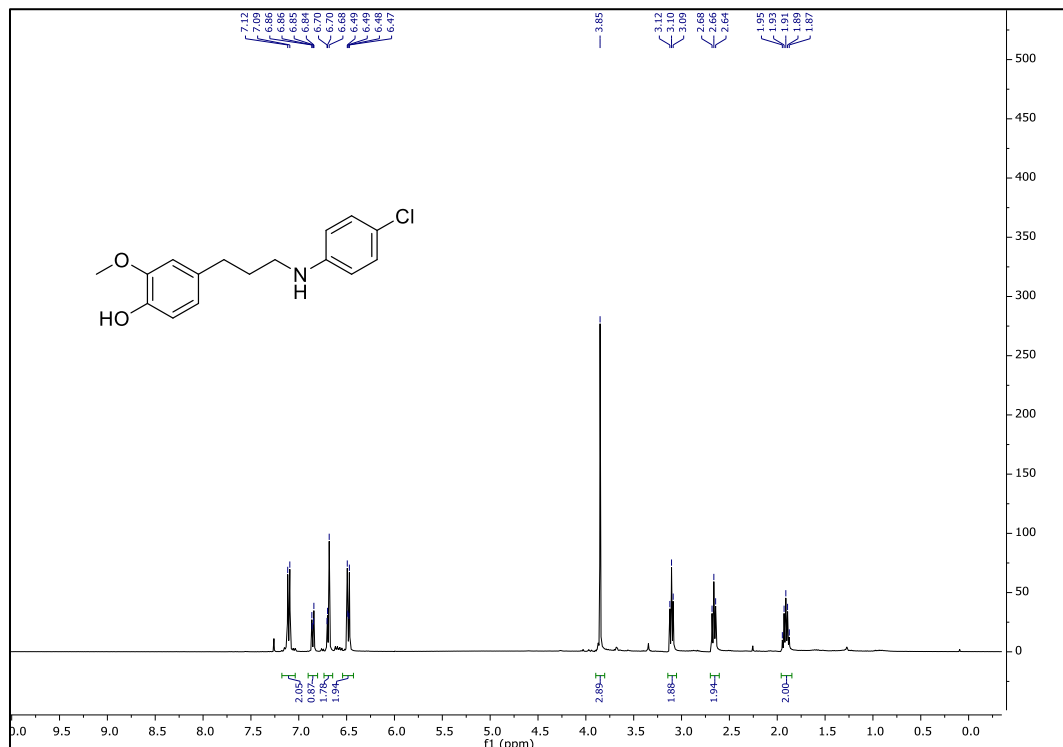
**Supplementary Figure 13.** 2D-HSQC NMR spectrum (600 MHz,  $\text{CDCl}_3$ ) of the ethyl acetate soluble fraction (**Fraction 1**) obtained upon fractionation of crude RCF product mixture from pine lignocellulose.



**Supplementary Figure 14.** 2D-HSQC NMR spectrum (600 MHz,  $\text{DMSO-d}_6$ ) of the sample obtained upon treatment of **Fraction 1** with water. Water-soluble fraction, showing the presence of sugars.



**Supplementary Figure 15.** 2D-HSQC NMR spectrum (600 MHz, DMSO-d<sub>6</sub>) of the ethyl acetate insoluble fraction (**Fraction 2**) obtained upon fractionation of crude RCF product mixture from pine lignocellulose. Showing typical moieties expected in residual lignin.<sup>17</sup>



**Supplementary Figure 16.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of **5Gb** isolated by reactive separation of **1G** from **Fraction 1**.

### 4.3.2 Direct reactive separation of 1G from crude product mixture upon RCF of pine lignocellulose

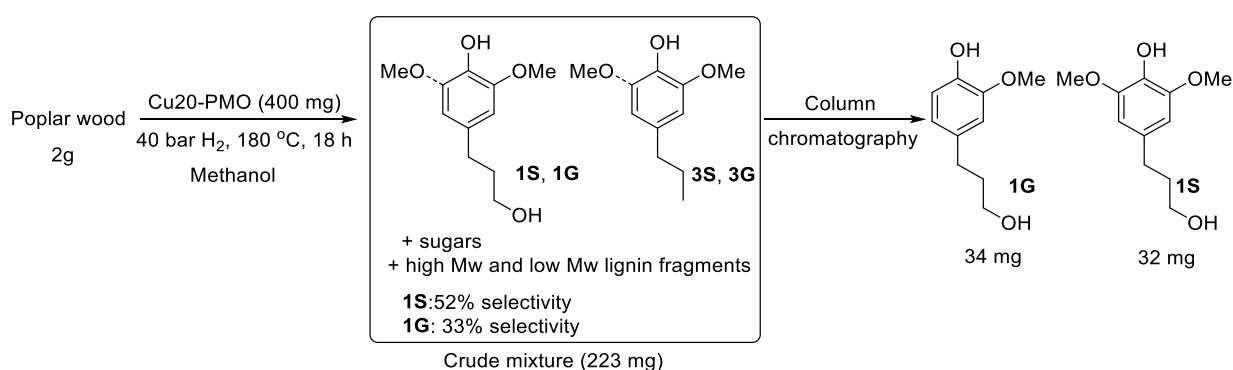
Reductive catalytic fractionation (RCF) of pine lignocellulose using Cu<sub>2</sub>O-PMO catalyst was carried out according to the **General procedure (A)** indicated above in **Supplementary Section 1.3.1**. The so obtained crude product mixture (195 mg) was taken directly to the next step for reactive separation *via* the Ru-catalyzed amination, using specific **C1** and amine **4b** amount according to the **General procedure (B)**. The reaction was first conducted under the reaction conditions also used previously with **Fraction 1** at 130 °C for 20 h using **4b** (2 equiv.), **C1** (5 mol%) in CPME (2 mL). It was assumed that the amount of **1G** in the crude is (0.208 mmol and 38 mg) as previously determined by isolation of **1G** from a separate crude RCF mixture (See **Supplementary Section 4.1**). The reaction mixture was not completely soluble in the reaction solvent even at 130 °C, as expected. After the reaction, the solvent was evaporated and the product was isolated by column chromatography using pentane/ethyl acetate as eluent furnishing 30% yield of **5Gb** lower than that seen with **Fraction1**. This can be attributed to the non-homogeneous nature of the reaction due to the presence of insoluble high Mw lignin residue present in the crude. In order to improve the yield, we further increased the catalyst loading (**C1**, 10 mol%) and amine equivalent (**4b**, 4 equiv.) in which case a 64% (39 mg) isolated yield of **5Gb** could be obtained (**Supplementary Fig. 17**). In addition, the aliphatic alkyl-guaiacol derivatives **3G** and **2G** also present in the crude, were isolated (5 mg) as mixture of pure compounds (**Supplementary Fig. 18**). All the compounds were isolated by column chromatography using pentane/ethyl acetate as eluent. **3G** and **2G** was isolated in 10% ethyl acetate in pentane and **5Gb** was isolated in 30% ethyl acetate in pentane.



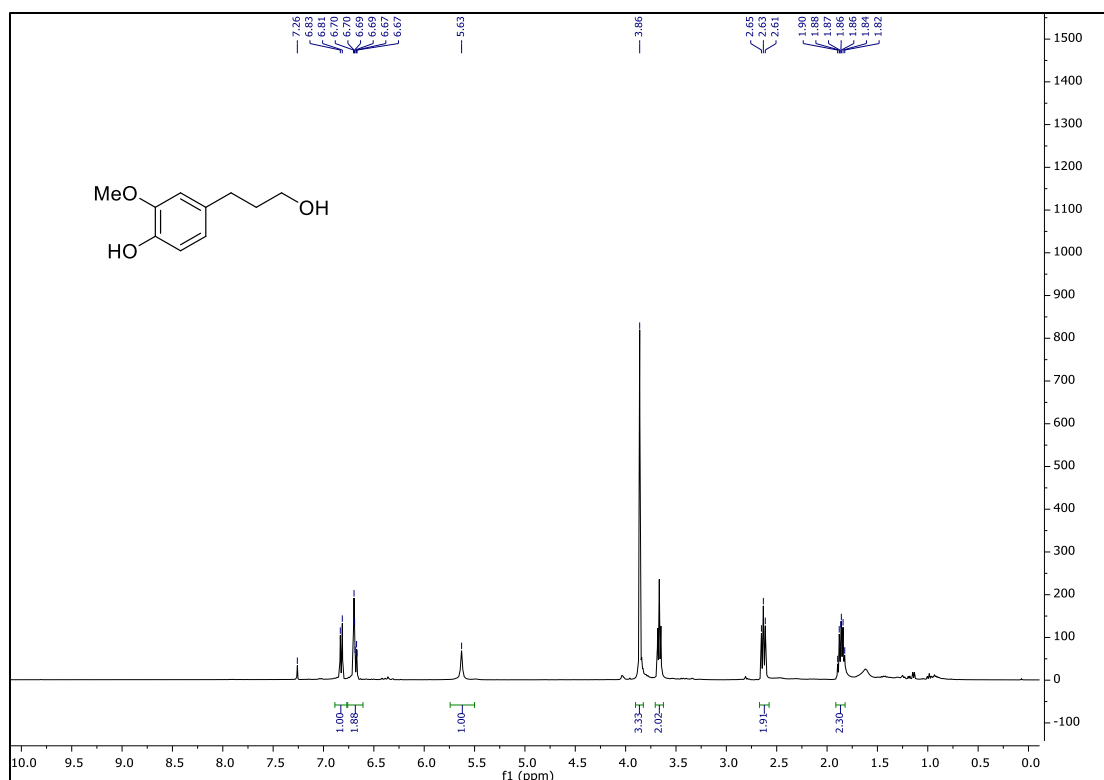
In conclusion, applying the developed Ru-catalyzed amination procedure on the crude product mixture obtained upon RCF of pine lignocellulose without any further treatment, resulted in a good, 64% yield of the lignin-derived secondary amine **5Gb**. Applying a simple fractionation procedure using ethyl acetate in order to first eliminate any high Mw lignin residues, resulted in **Fraction 1**. Catalytic amination of **Fraction 1** resulted in **5Gb** in a high 84% isolated yield even in the presence of other monomers and oligomeric side products.

#### 4.4 Reductive catalytic fractionation (RCF) of poplar lignocellulose and separation of dihydroconiferyl alcohol (**1G**) and dihydrosinapyl alcohol (**1S**)

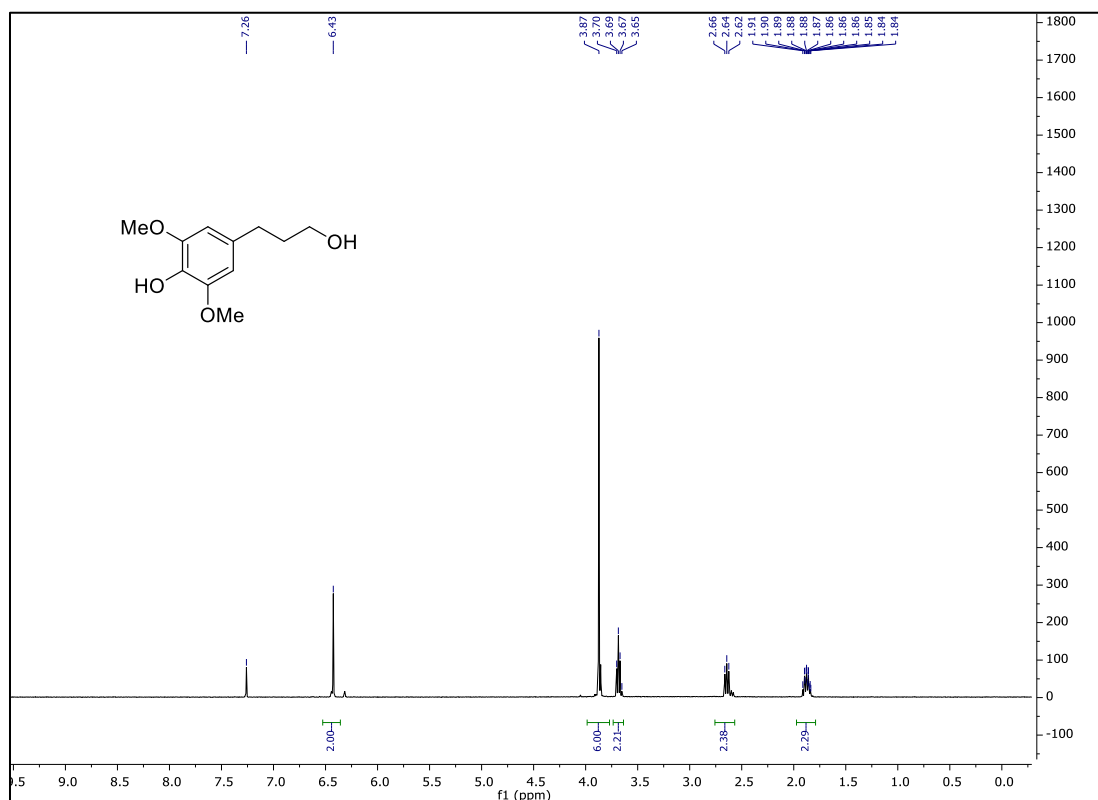
Reductive catalytic fractionation (RCF) of poplar lignocellulose was carried out in a 100 mL high pressure Parr reactor with an overhead stirrer. Typically, the autoclave was charged with Cu20-PMO catalyst (0.4 g), poplar lignocellulose (2 g), and methanol (20 mL). Once the reactor was sealed, purged 3 times with hydrogen and then pressurized with hydrogen (40 bar) at room temperature. The reactor was heated to 180 °C and stirred at 400 rpm for 18 h. After reaction, the reactor was cooled to room temperature. After that the solution and solids were transferred into a 50 mL centrifuge tube. The solids were separated from the reaction solution by centrifugation and subsequent decantation, and additionally washed with methanol (2 × 20 mL). All solutions were combined in a round bottom flask and the solvent was removed *in vacuo*. The crude product was purified by column chromatography using pentane/ethyl acetate (60:40) affording **1G** (0.187 mmol, 34 mg) and **1S** (0.151 mmol, 32 mg) as a pure product (See **Supplementary Figs. 20 & 21**). This quantity was used to calculate the amount of amine added during reactive separation. **1G** was isolated at 40% ethyl acetate in pentane and **1S** was isolated at 50% ethyl acetate in pentane.



**Supplementary Figure 19.** Reductive catalytic fractionation of poplar lignocellulose over Cu20-PMO and separation of dihydroconiferyl alcohol (**1G**) and dihydrosinapyl alcohol (**1S**). Selectivity of **1G** (33%) and **1S** (52%) is based on GC-FID analysis.



**Supplementary Figure 20.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of **1G** isolated from the crude product mixture obtained upon RCF of poplar lignocellulose.



**Supplementary Figure 21.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of **1S** isolated from the crude product mixture obtained upon RCF of poplar lignocellulose.

## 4.5 Reactive separation of 1G and 1S from reaction mixtures obtained by RCF of poplar lignocellulose by catalytic amination-separation of lignin-derived secondary amine 5Gb and 5Sb and other products

### 4.5.1 Fractionation, reactive separation and analysis of the crude mixture obtained from RCF of poplar lignocellulose

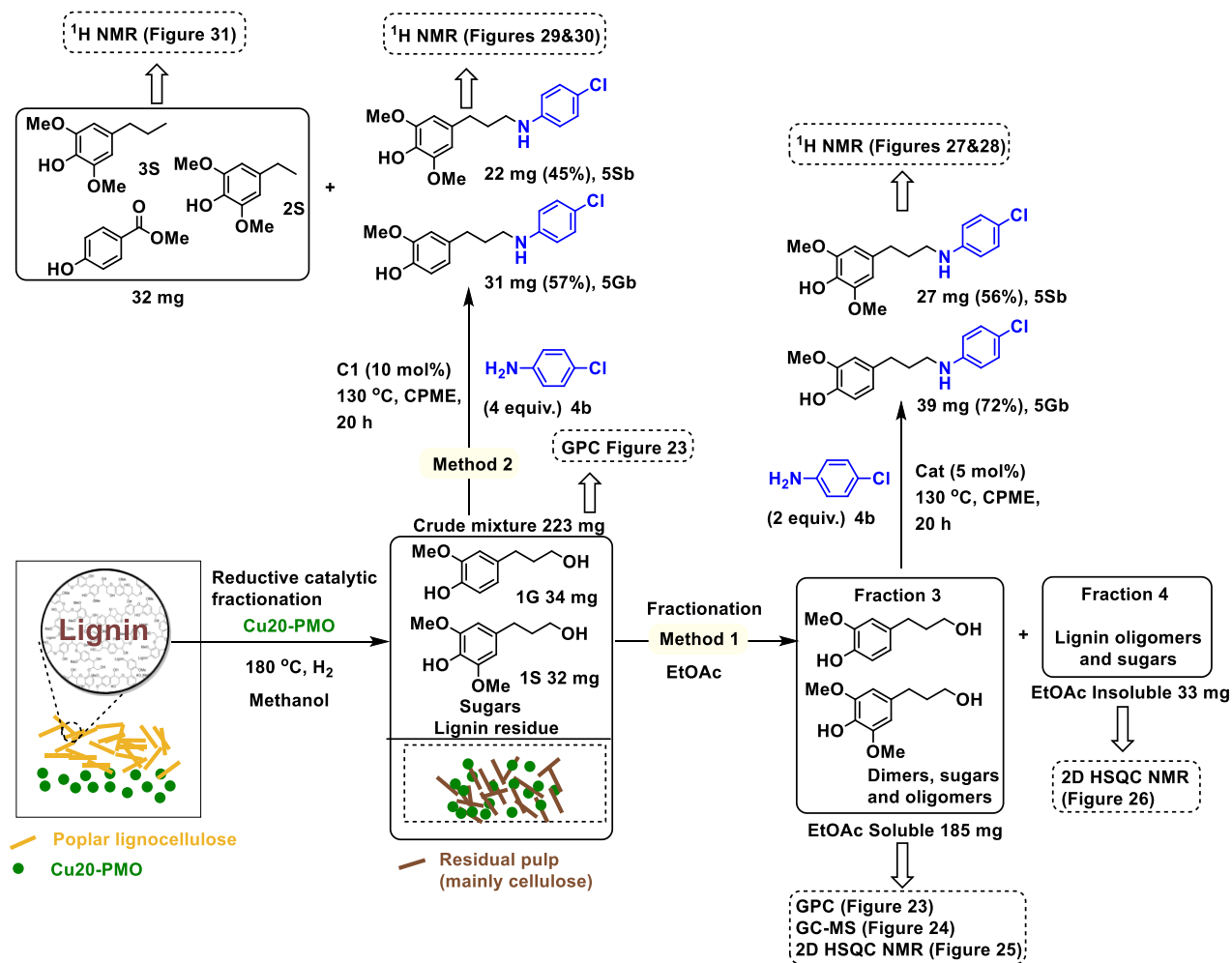
Reductive catalytic fractionation (RCF) of poplar lignocellulose was carried out using Cu<sub>2</sub>O-PMO according to the **General procedure (A)** indicated above in the **Supplementary Section 1.3.1**. The so obtained crude product mixture (223 mg) was subjected to a fractionation procedure followed by the desired reactive separation as mentioned previously for pine lignocellulose (**Supplementary Section 4.3.1**).

**Fractionation of the crude mixture:** To the crude mixture (223 mg) ethyl acetate was added (10 mL) and it was stirred for overnight at room temperature, which resulted in precipitation of brownish colored solid. The suspension was transferred into a 20 mL centrifuge tube. The solid was separated by centrifugation and subsequent decantation and additionally washed with ethyl acetate (2×10 mL). All liquids were combined in a round bottom flask and the solvent was removed *in vacuo*. The soluble and insoluble fractions were additionally dried *in vacuo* under constant weight. The ethyl acetate insoluble fraction (**Fraction 4**) was characterized by 2D-HSQC, which confirmed the presence of lignin oligomers. (**Supplementary Fig. 26**).

The ethyl acetate soluble fraction (**Fraction 3**) was further characterized by GPC (**Supplementary Fig. 23**), GC-MS and NMR spectroscopic measurements (**Supplementary Fig. 24 & 25**). The GPC traces of the crude depolymerization mixture and **Fraction 3**, shows the major signals of the monomers. The GC-MS trace of **Fraction 3** displayed **1G** and **1S** are dominant monomers in **Fraction 3** (**Supplementary Fig. 24**). This was further confirmed by 2D-HSQC analysis (**Supplementary Fig. 25**) that showed mainly the corresponding signals of monomers **1G** and **1S**.

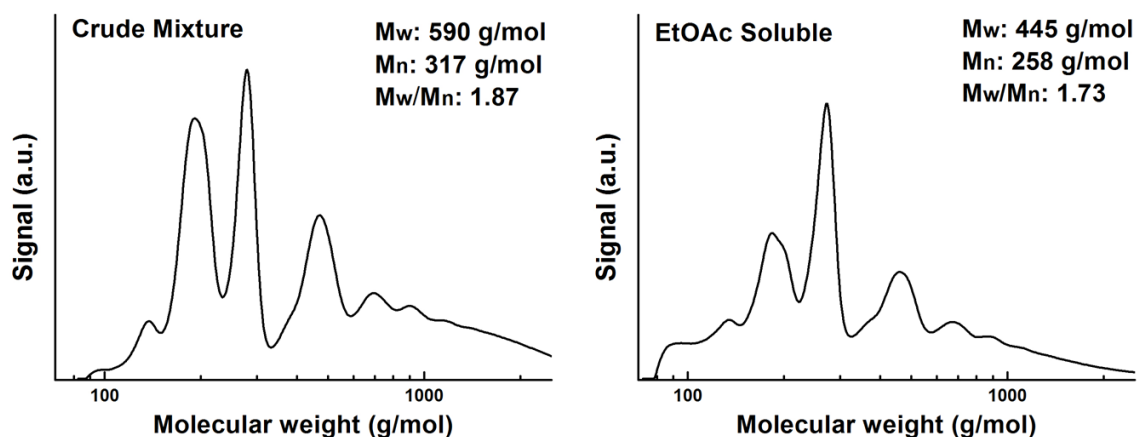
**Catalytic amination using Fraction 3:** **Fraction 3** (223 mg) was subjected to the previously developed Ru-catalysed amination protocol in order to assess whether reactive separation of **1G** and **1S** are possible. The reaction was conducted according to **General procedure (B)** using previously optimized conditions (130 °C, 20 h) with **4b** (2 equiv.), **C1** (5 mol%) (with respect to the yield of **1G** and **1S**) and CPME (2 mL). After reaction, the solvent was removed and the product **5Gb** (39 mg, 72%) and **5Sb** (27 mg, 56%) was isolated by column chromatography using pentane/ethyl acetate (60:40).

A specific scheme summarizing the fractionation as well as reactive separation procedure is shown below on **Supplementary Fig. 22**. The analytical details related to **Fraction 3** and **Fraction 4** are displayed below.

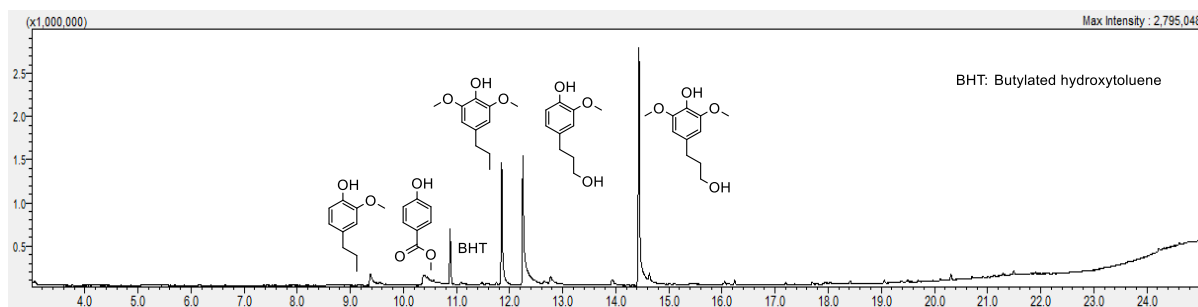


**Supplementary Figure 22.** Reactive separation of **1G** and **1S** to yield lignin derived amine **5Gb** and **5Sb** from poplar lignocellulose through RCF, selective amination and separation of other monomers, oligomers and sugar derivatives.

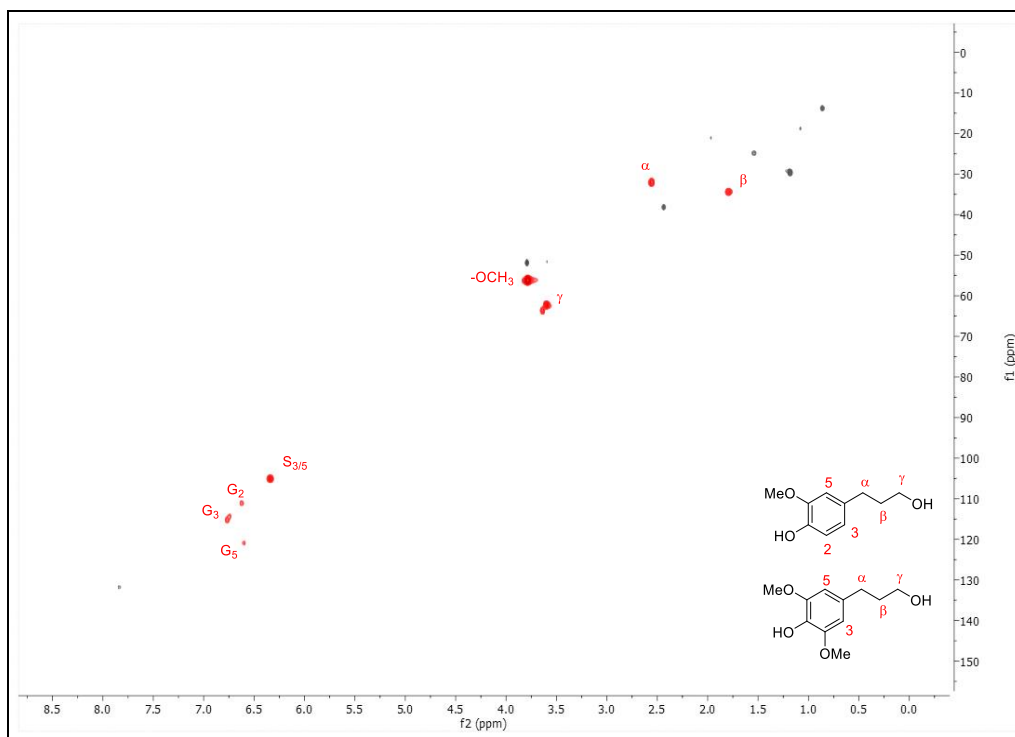
### Analytical data belonging to Fraction 3 and Fraction 4



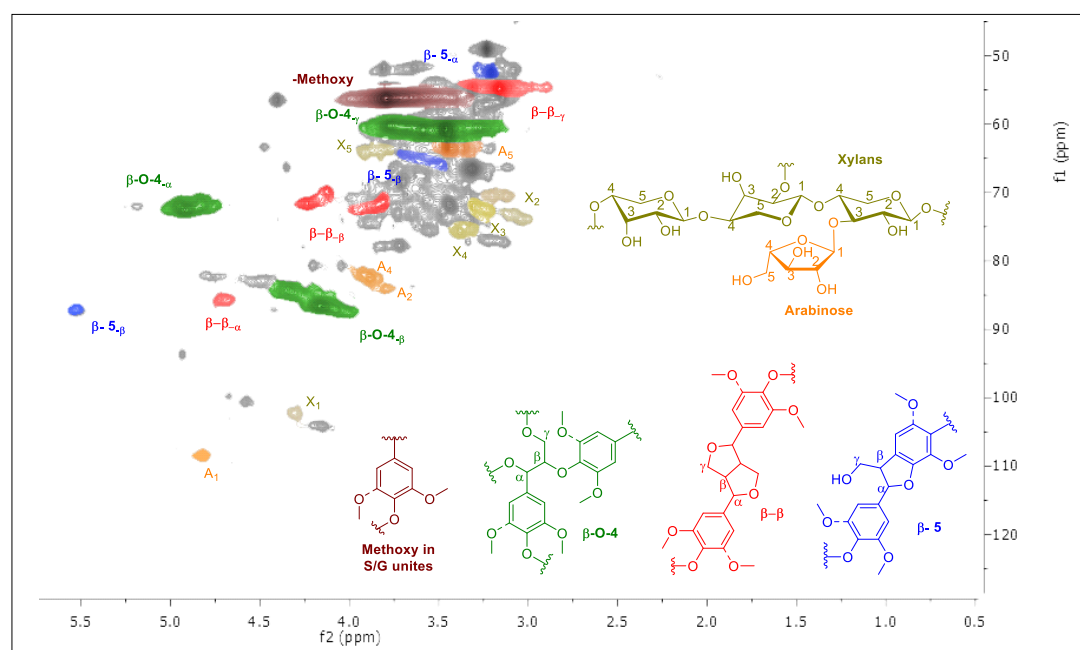
**Supplementary Figure 23.** GPC trace of the crude poplar RCF mixture (left) and GPC trace of **Fraction 3**, obtained upon fractionation (right).



**Supplementary Figure 24.** GC-MS chromatogram of the ethyl acetate soluble fraction (**Fraction 3**) obtained upon fractionation of crude RCF product mixture from poplar lignocellulose.

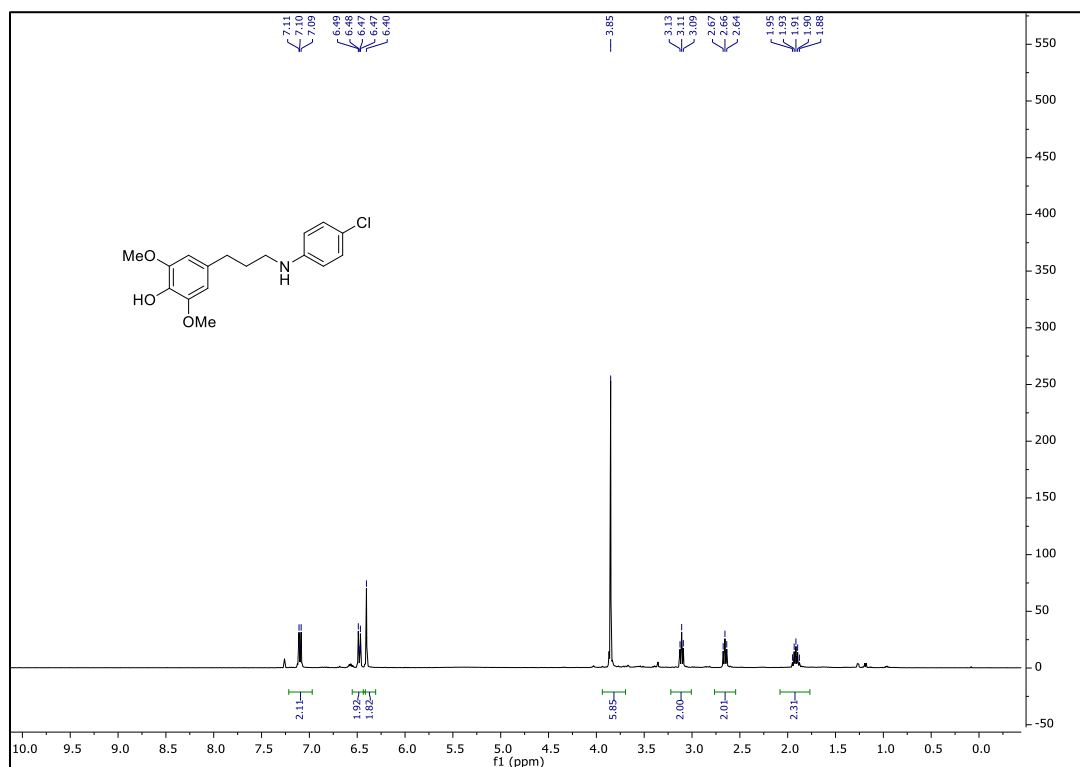


**Supplementary Figure 25.** 2D-HSQC NMR spectrum (600 MHz,  $\text{CDCl}_3$ ) of the ethyl acetate soluble fraction (**Fraction 3**) obtained upon fractionation of crude RCF product mixture from poplar lignocellulose.

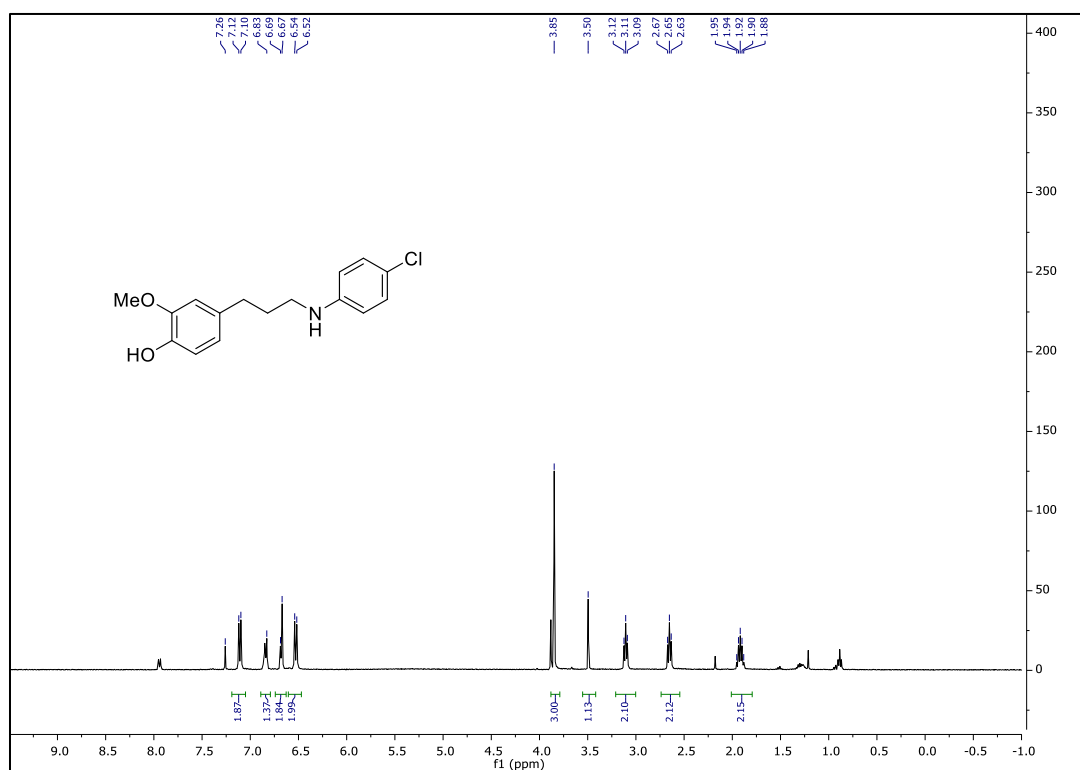


**Supplementary Figure 26.** 2D-HSQC NMR spectrum (600 MHz,  $\text{DMSO-d}_6$ ) of the ethyl acetate insoluble fraction (**Fraction 4**) obtained upon fractionation of crude RCF product mixture from poplar lignocellulose. Showing typical moieties expected in residual lignin.<sup>17</sup>

## Analytical data of products obtained upon reactive separation



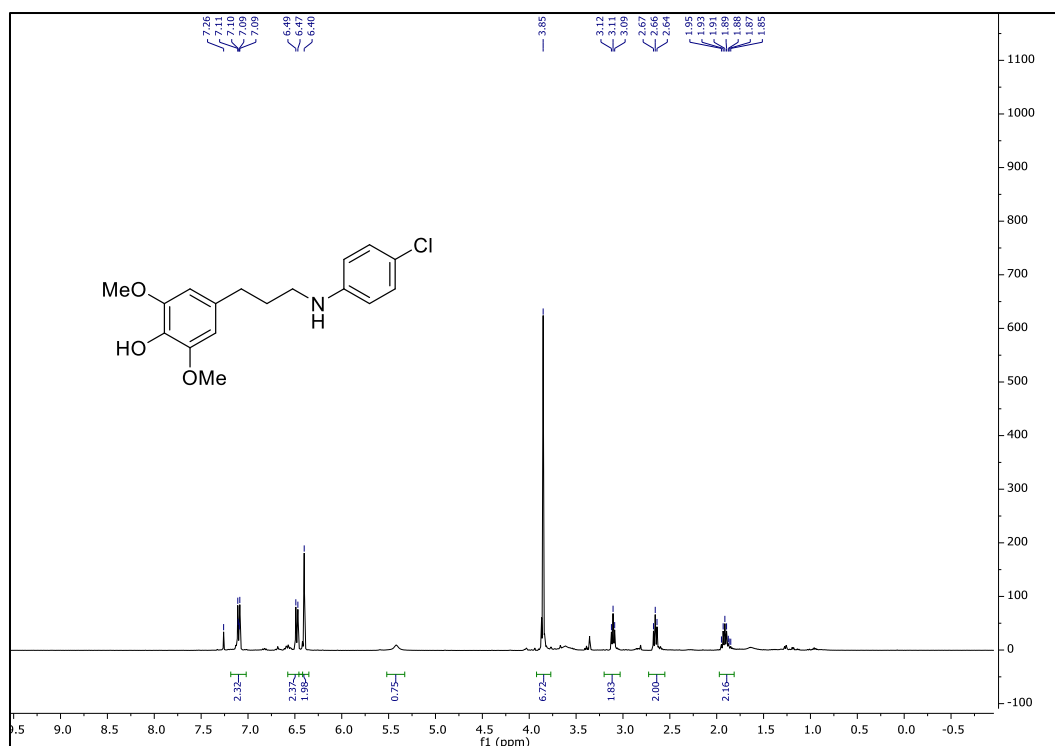
**Supplementary Figure 27.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of **5Sb** isolated by reactive separation of **1S** and **1G** from **Fraction 3**.



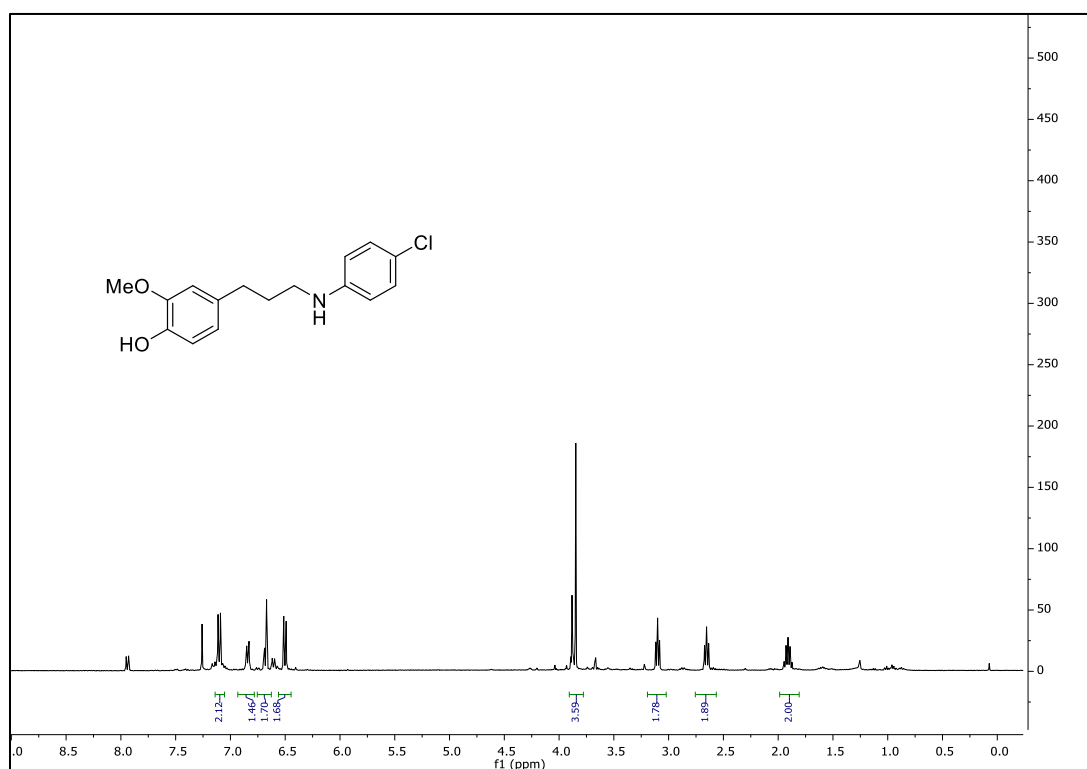
**Supplementary Figure 28.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of **5Gb** isolated by reactive separation of **1G** and **1S** from **Fraction 3**.

#### **4.5.2 Direct reactive separation of 1G and 1S from crude product mixture upon RCF of poplar lignocellulose**

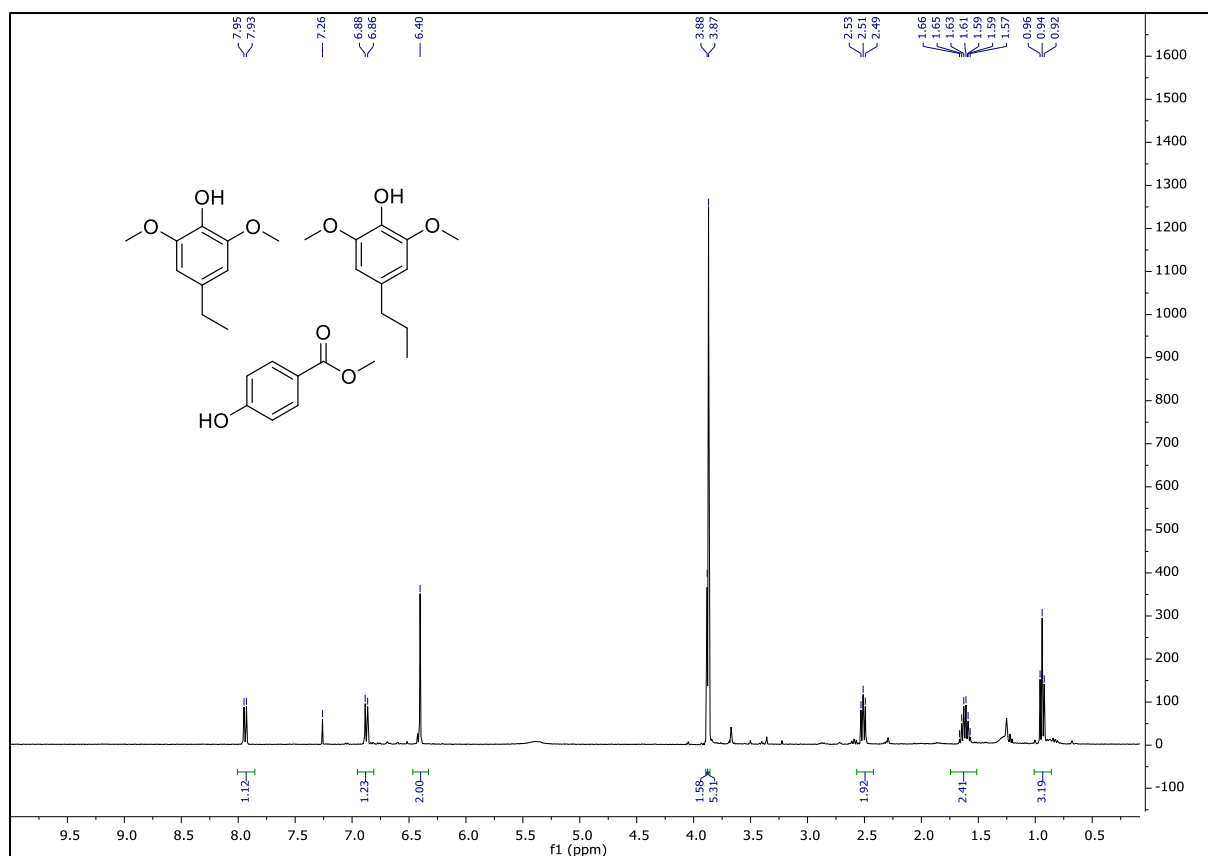
Reductive catalytic fractionation (RCF) of poplar lignocellulose using Cu<sub>2</sub>O-PMO catalyst was carried out according to the **General procedure (A)** indicated above in the **Supplementary Section 1.3.1**. The so obtained crude product mixture (223 mg) was taken directly to the next step for reactive separation *via* the Ru-catalyzed amination, using specific **C1** and amine **4b** amount according to the **General procedure (B)**. The reaction was conducted under previously optimized reaction conditions (**Supplementary Section 4.3.2**) at 130 °C for 20 h using **4b** (4 equiv.), **C1** (10 mol%) in CPME (2 mL). It was assumed that the amount of **1G** in the crude is (0.187 mmol and 34 mg) and **1S** in the crude is (0.151 mmol and 32 mg) as previously determined by isolation of **1G** and **1S** from a separate crude RCF mixture (**Supplementary Section 4.4**). The direct amination of crude mixture delivered two secondary amines **5Gb** and **5Sb** with isolated yield of 57% (31 mg) and 45% (22 mg) respectively. All the compounds were isolated by column chromatography using pentane/ethyl acetate as eluent. In addition **3S**, **2S** and methyl-4-hydroxy benzoate was isolated (32 mg) as a mixture in 15% ethyl acetate in pentane. **5Gb** was isolated at 30% ethyl acetate in pentane and **5Sb** was isolated at 50% ethyl acetate in pentane.



**Supplementary Figure 29.**  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of **5Sb** obtained upon reactive separation of **1G** and **1S** directly from the crude depolymerization mixture obtained upon RCF of poplar lignocellulose



**Supplementary Figure 30.**  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of **5Gb** obtained upon reactive separation of **1G** and **1S** directly from the crude depolymerization mixture obtained upon RCF of poplar lignocellulose.



**Supplementary Figure 31.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of **3S**, **2S** and methyl-4-hydroxy benzoate isolated upon reactive separation procedure from the crude depolymerization mixture obtained upon RCF of pine lignocellulose.

**Supplementary Table 4.** Fractionation of products from pine and poplar lignocellulose after reactive separation and the corresponding weights

Entry	Lignocellulose (mg)	Methanol soluble (mg)			Methanol insoluble (mg)
		Before Ethyl acetate treatment	Ethyl acetate soluble	Ethyl acetate insoluble	
1	Pine (2000 mg)	195	162	28	1800
2	Poplar (2000 mg)	223	185	33	1700

## 4.6 Supplementary Note 1

### 4.6.1 Control experiments to elucidate catalyst compatibility with various components of the crude and fractionated depolymerization mixture

When catalytic amination of **1G** (or **1S**) in the crude lignocellulose depolymerization mixtures according to *Method 2* was carried out, the catalyst loading was increased to 10 mol% and 4 equivalents of amine **4b** was used. When the catalytic amination of **1G** (or **1S**) in *Fraction 1* was carried out according to *Method 1*, 5mol% catalyst loading and 2 equivalents of amine **4b** were used. (see also **Supplementary Figure 9** and **Supplementary Figure 22**) We attribute the increased need for catalyst and amine loading compared to the scope experiments (1 mol % catalyst, 1:1.2 amine: **1G**) to the complexity of the crude depolymerization mixture.

Direct reactive separation in crude depolymerization mixture: Initial attempts to use 1 mol% of Ru-catalyst (**C1**) and 1 equivalent of amine (**4b**) for the N-alkylation of **1G** in the crude depolymerization mixture of pine lignocellulose resulted in low product (**5Gb**) yield (>5% and 30% respectively). We attribute this partially to the presence of sugar oligomers as well as the inhomogeneity of the mixture caused primarily by the high Mw lignin present in the crude. As evidence, after fractionation of the crude with ethyl-acetate, and removal of these components as EtOAc insolubles (*Fraction 2*, see also **Supplementary Figure 15**), the remaining *Fraction 1* could be successfully aminated with 5 mol% **C1**.

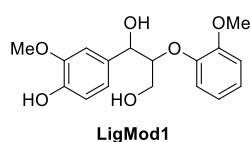
Reactive separation using *Fraction 1*: After removal of *Fraction 2* from the crude, *Fraction 1* was successfully aminated using 5 mol % **C1** and 2 equivalents of **4b**. Besides **1G**, *Fraction 1* may contain lignin dimers and oligomers, as well as sugar monomers or oligomers. In order to gain insight into the role of these components on reactivity, a series of systematic experiments with various additives were performed. Reactions carried out with glucose:**1G** (1:1 ratio) showed a 90% **1G** conversion and 85% **5Gb** selectivity when 1 mol% **C1** and 1 equivalents of **4b** were used and full **1G** conversion and 92% **5Gb** selectivity, when 5 mol% **C1** and 2 equivalents of **4b** were used, indicating that glucose slightly affected the reaction at low catalyst loadings (Entry 1 vs Entry 2). Similarly, when the complex  $\beta$ -O-4 model compound (**LigMod1**), as model for lignin dimers and oligomers was used, the reaction was clearly affected at 1 mol% **C1** loading and 1 equivalents of **4b** as evidenced by the formation of several smaller side products and incomplete conversion of **1G**. While at 5 mol% **C1** loading and 2 equivalents of **4b**, full conversion of **1G** and a good **5Gb** selectivity could be obtained (Entry 3 vs Entry 4). The full conversion of **1G** by 2 equivalents of amine used signifies that

all of **1G** has been converted to the desired **5Gb**, while the smaller side products originate from **LigMod1**. The types of side products (see below) clearly showed participation of the primary alcohol functionality of **LigMod1** in catalytic N-alkylation as well as the involvement of the primary and secondary alcohol moieties of the  $\beta$ -O-4 linkage in dehydrogenation. Besides catalytic amination, **LigMod1** also participated in a hydrogen neutral C-O bond cleavage, as expected. In a similar manner, the participation of other dimers or oligomers involving linkage types such as the  $\beta$ -5 or a combination of a  $\beta$ -5 and  $\beta$ -O-4 is expected. Furthermore, interestingly experiments performed with smaller Mw lignin oligomers obtained upon acidolysis (thus with low  $\beta$ -O-4 linkage content) have shown no change in the catalytic N-alkylation of **1G** either at 1 mol% or 5 mol% **C1** loading (Entry 5 and 6), showing that free phenolic end groups do not influence reactivity.

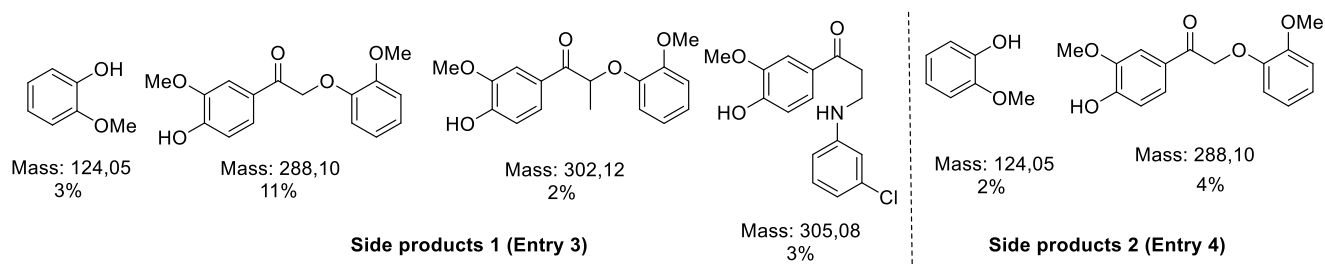
Entry	1G (equiv.)	4b (equiv.)	C1 (mol%)	Additive (equiv.)	Results		
					1G (Conv. %) <sup>a</sup>	5Gb (Sel. %) <sup>b</sup>	Observations
1	1	1	1	Glucose (1)	90	85	-
2	1	2	5	Glucose (1)	>99	92	-
3	1	1	1	LigMod1 (1)	78	61	Side products 1 <sup>c</sup>
4	1	2	5	LigMod1 (1)	>99	73	Side products 2 <sup>c</sup>
5	1	1	1	Lignin1 (1)	>99	91	-
6	1	2	5	Lignin1 (1)	>99	87	-

Reaction conditions: 1G (typically 0.2 mmol), 130 °C, CPME, 20 h, <sup>a</sup>conversion and <sup>b</sup>selectivity were determined by GC-FID. <sup>c</sup> Compounds were identified by GC-MS by exact mass and library match;

**Lignin 1:** [Mw:639 g/mol; PD: 1.35, purity 90%]



### Side products:

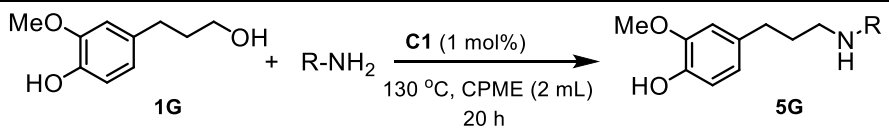
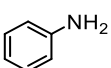
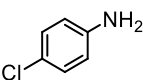
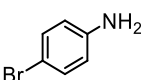
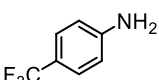


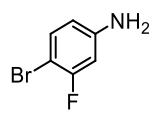
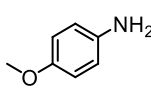
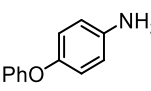
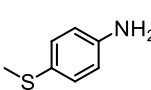
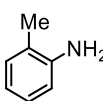
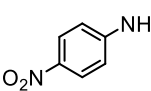
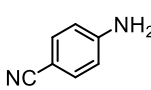
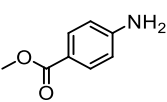
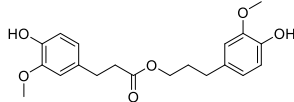
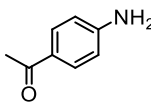
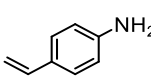
## 5. Diverse alkylaminophenols by Ru-catalysed amination of dihydroconiferyl alcohol (**1G**) and dihydrosinapyl alcohol (**1S**) with various amines

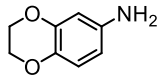
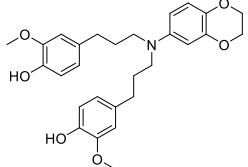
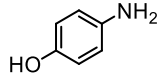
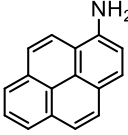
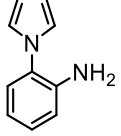
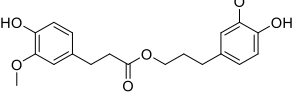
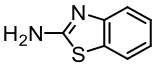
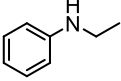
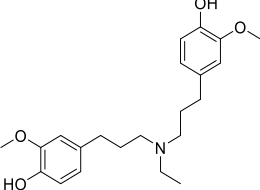
### 5.1 Highly selective Ru-catalyzed amination of dihydroconiferyl alcohol (**1G**) with various amines

For the Ru-catalyzed amination **General procedure (B)** was followed. Catalytic aminations were carried out with various amines in order to establish the scope of the reaction. In most cases the reactions proceeded smoothly with high selectivity. In selected specific cases, the formation of a tertiary amine was formed due to over-alkylation or **1G** underwent self-coupling to form the corresponding ester (**Supplementary Table 5**, entry 12 & 18).

**Supplementary Table 5.** Amination of dihydroconiferyl alcohol (**1G**) with various aromatic and aliphatic amines

						
Entry	Substrate		Conv. (%) <sup>a</sup>	Product	Yield (%) <sup>b</sup>	Side products <sup>a</sup>
1		<b>4a</b>	>99	<b>5Ga</b>	75	-
2		<b>4b</b>	>99	<b>5Gb</b>	97	-
3		<b>4c</b>	>99	<b>5Gc</b>	96	-
4		<b>4d</b>	>99	<b>5Gd</b>	87	-

5		<b>4e</b>	>99	<b>5Ge</b>	95	-	
6		<b>4f</b>	>99	<b>5Gf</b>	81	-	
7		<b>4g</b>	97	<b>5Gg</b>	91	-	
8		<b>4h</b>	98	<b>5Gh</b>	83	-	
9		<b>4i</b>	97	<b>5Gi</b>	89	-	
10		<b>4j</b>	>99	<b>5Gj</b>	93	-	
11		<b>4k</b>	94	<b>5Gk</b>	88	-	
12		<b>4l</b>	90	<b>5Gl</b>	60		<b>6%</b>
13		<b>4m</b>	98	<b>5Gm</b>	82	-	
14		<b>4n</b>	98	<b>5Gn</b>	43	-	

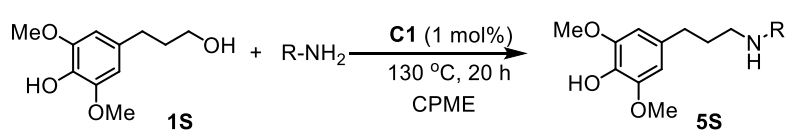
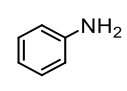
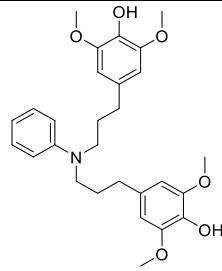
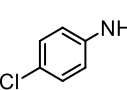
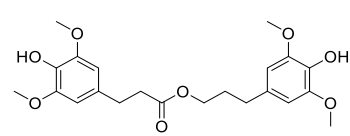
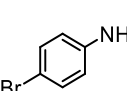
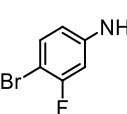
15		<b>4o</b>	>99	<b>5Go</b>	61		24% <sup>b</sup>
16		<b>4p</b>	85	<b>5Gp</b>	81	-	
17		<b>4q</b>	95	<b>5Gq</b>	81	-	
18		<b>4r</b>	87	<b>5Gr</b>	53		6%
19		<b>4s</b>	56	<b>5Gs</b>	55	-	
20		<b>4t</b>	95	<b>5Gt</b>	85	-	
21	Me <sub>2</sub> NH	<b>4u</b>	81	<b>5Gu</b>	53 <sup>c</sup>	-	
22	Et <sub>2</sub> NH	<b>4v</b>	99	<b>5Gv</b>	56 <sup>c,d</sup>		13% <sup>b</sup>

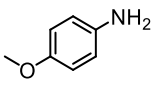
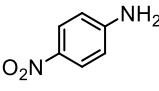
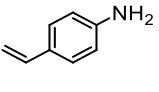
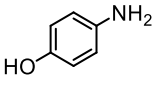
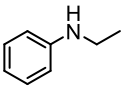
**General reaction conditions:** amine (0.4 mmol), **1G** (0.48 mmol), **C1** (1 mol%), CPME (2 mL), 130 °C, 20 h. <sup>a</sup> Conversion and yield of the side product was determined by GC-MS analysis. <sup>b</sup> Isolated yields. <sup>c</sup> **1G** (0.5 mmol), 3 equiv. of amine was used and the yield based on **1G**. <sup>d</sup> 3 mol% **C1**

## 5.2 Highly selective Ru-catalyzed amination of dihydrosinapyl alcohol (**1S**) with various amines

**General procedure (B)** was followed for the Ru-catalyzed amination. Catalytic aminations of **1S** were carried out with various amines in order to establish the scope of the reaction. In most cases, similar to **1G** the reactions proceeded smoothly with high selectivity. In selected specific cases, the formation of a tertiary amine was formed due to over-alkylation or **1S** underwent self-coupling to form the corresponding ester.

**Supplementary Table 6.** Amination of dihydrosinapyl alcohol (**1S**) with various aromatic amines

					
Entry	Substrate	Conv. (%) <sup>a</sup>	Product	Yield (%) <sup>b</sup>	Side products <sup>a</sup>
1		97	<b>5Sa</b>	62	 4%
2		96	<b>5Sb</b>	61	 7%
3		96	<b>5Sc</b>	63	-
4		>99	<b>5Se</b>	70	-

5		<b>4f</b>	69	<b>5Sf</b>	60	-
6		<b>4j</b>	>99	<b>5Sj</b>	98	-
7		<b>4n</b>	>99	<b>5Sn</b>	64	-
8		<b>4p</b>	>99	<b>5Sp</b>	50	-
9		<b>4t</b>	93	<b>5St</b>	88	-

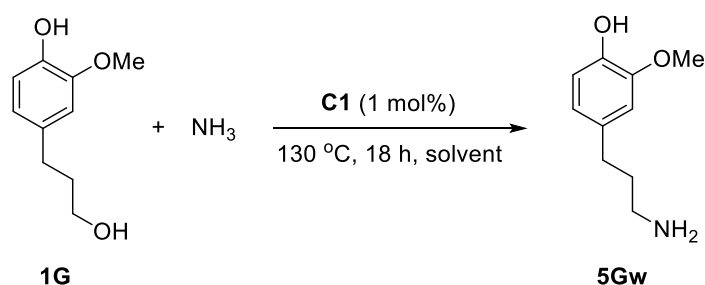
**General reaction conditions:** amine (0.4 mmol), **1S** (0.48 mmol), **C1** (1 mol%), CPME (2 mL), 130 °C, 20 h. <sup>a</sup> Conversion and yield of the side product was determined by GC-MS analysis. <sup>b</sup> Isolated yields.

### 5.3 Synthesis of 4-(3-aminopropyl)-2-methoxyphenol (5Gw) by selective amination of dihydroconiferyl alcohol (1G) with ammonia

#### Attempt for Ru-catalyzed amination of dihydroconiferyl alcohol (1G) with ammonia using C1

The selective amination of dihydroconiferyl alcohol (**1G**) (0.25 mmol) was attempted with **C1** (1 mol%) by following slight modification of the **General procedure (B)**. Instead of aromatic or aliphatic amines, an appropriate ammonia source was used either in the form of an ammonium salt (1 mmol) or gaseous ammonia in organic solvent (2 mL).

**Supplementary Table 7.** Amination of dihydroconiferyl alcohol (**1G**) with ammonia: optimization of the reaction conditions

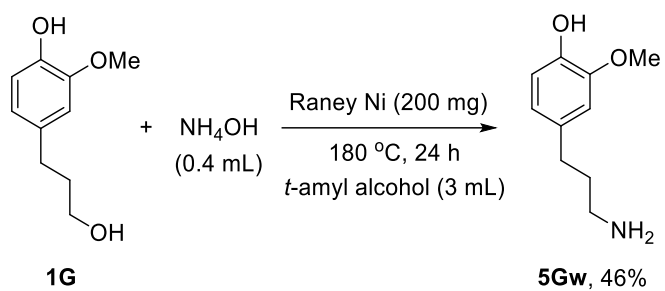


Entry	$\text{NH}_3$ source	Solvent/mL	<b>5Gw</b> Yield (%)
1	0.5M $\text{NH}_3$ in THF	THF/2	0
2	0.5M $\text{NH}_3$ in dioxane	Dioxane/2	0
3	$(\text{NH}_4)_2\text{CO}_3$ (1 mmol)	Toluene/2	0
4	$\text{NH}_4\text{Cl}$ (1 mmol)	Toluene/2	0
5	$\text{NH}_4\text{OAc}$ (1 mmol)	Toluene/2	0

#### Selective catalytic amination of dihydroconiferyl alcohol (1G) with ammonia using Raney Ni<sup>18</sup>

A 10 mL Swagelok stainless steel micro reactor, equipped with a stirring bar was charged with substrate **1G** (0.50 mmol), 200 mg Raney Ni, 0.4 mL aqueous ammonia (25%) and 3 mL *t*-amyl alcohol. The reactor was sealed and placed in a pre-heated aluminum heating block at 180 °C. After 24 h, the micro reactor was cooled down to room temperature using ice-water bath. The crude mixture was separated from catalyst by filtration, concentrated *in vacuo* and then diethyl ether (20 mL) and 0.5 mL of 1M HCl in diethyl ether was added. A precipitate was formed immediately, the HCl salt of the desired primary amine was isolated by filtration

and washed with diethyl ether (2×10 mL) furnishing the pure amine product **5Gw** (0.23 mmol, 46%) as HCl salt.



**Supplementary Figure 32.** Selective nickel catalyzed amination of **1G** with aqueous ammonia.

## 6. Development of a novel highly efficient method for the construction of tetrahydro-2-benzazepines in deep eutectic solvents

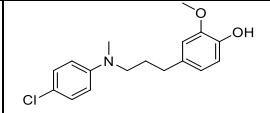
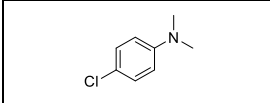
### 6.1 Attempts for the formation of tetrahydro-2-benzazepines in classical organic solvents using Brønsted and Lewis acids

Pictet–Spengler cyclization is a powerful method for construction of 7-member *N*-heterocycles. Such reaction is usually carried out in an aprotic solvent in the presence of stoichiometric amount of strong acid catalyst under reflux condition.<sup>8</sup> In the beginning, we tested several Brønsted and Lewis acids for intramolecular cyclisation reactions using **5Gb** as a model substrate and paraformaldehyde as a carbon source. Although cyclization to the desired product proceeded effectively, reductive methylation on the nitrogen of the starting material **5Gb** was observed as a side reaction. Another interesting side reaction was the formation of an 9 membered *N*-heterocycle, **7Gb**, which was isolated and characterized by NMR spectroscopy.

**Experimental procedure:** An oven-dried 20 mL Schlenk tube, equipped with a stirring bar, was charged with **5Gb** (0.086 mmol, 1 equiv.), paraformaldehyde (0.086-0.129 mmol, 1-1.5 equiv.), Brønsted/Lewis acid (0.086-0.129 mmol, 1-1.5 equiv.) and solvent (1 mL) under argon. Then the Schlenk tube was capped and the mixture was rapidly stirred at room temperature for 1 min, then was heated to 80-100 °C and stirred for 20 h. The reaction mixture was cooled down to room temperature and subsequently water (2 mL) and a saturated aqueous solution of NaHCO<sub>3</sub> (2 mL) was added. The crude mixture was extracted with ethyl acetate (15 mL) and the solvent was removed *in vacuo*, then it was analyzed by GC-FID and GC-MS

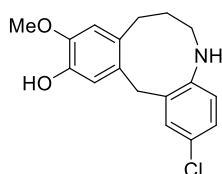
**Supplementary Table 8.** Attempts for constructing tetrahydro-2-benzazepines starting from **5Gb** in organic solvents, applying various Lewis/ Brønsted acids

Entry	Acid (equiv.)	(HCHO) <sub>n</sub> (equiv.)	Temp (°C)	Solvent (1 mL)	Conv. (%)	Yield <sup>a</sup> 6Gb (%)	Side products <sup>a</sup>	
1	MeSO <sub>3</sub> H (1.1)	1.5	100	CH <sub>3</sub> CN	>99	57		7%
								6%
							<b>7Gb<sup>b</sup></b>	21%
2	MeSO <sub>3</sub> H (1.1)	1.2	80	CH <sub>3</sub> CN	>99	45		13%
								3%
3	PTSA (1.1)	1.2	100	CH <sub>3</sub> CN	>99	-		17%
4	AlCl <sub>3</sub> (1.1)	1.2	100	CH <sub>3</sub> CN	>99	43		25%
5	Diphenyl phosphate (1.1)	1.2	100	CH <sub>3</sub> CN	>99	53		34%
								9%
6	MeSO <sub>3</sub> H (1.1)	1.2	100	CPME	84	19		54%
7	Amberlite IR 120 (20 mg)	1	90	CH <sub>3</sub> CN	70	26		44%

8	Diphenyl phosphate (1.1)	1 <sup>c</sup>	90	CH <sub>3</sub> CN	>99	46		51%
								3%

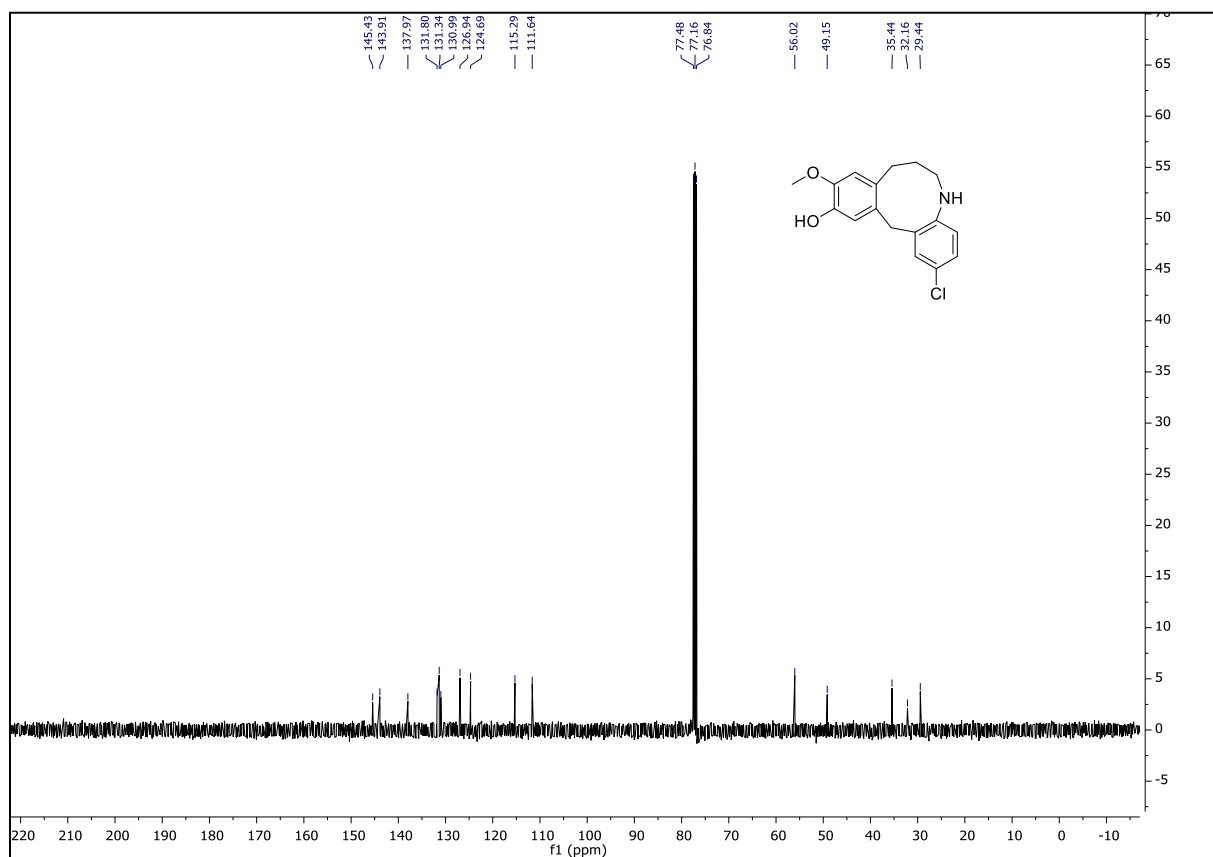
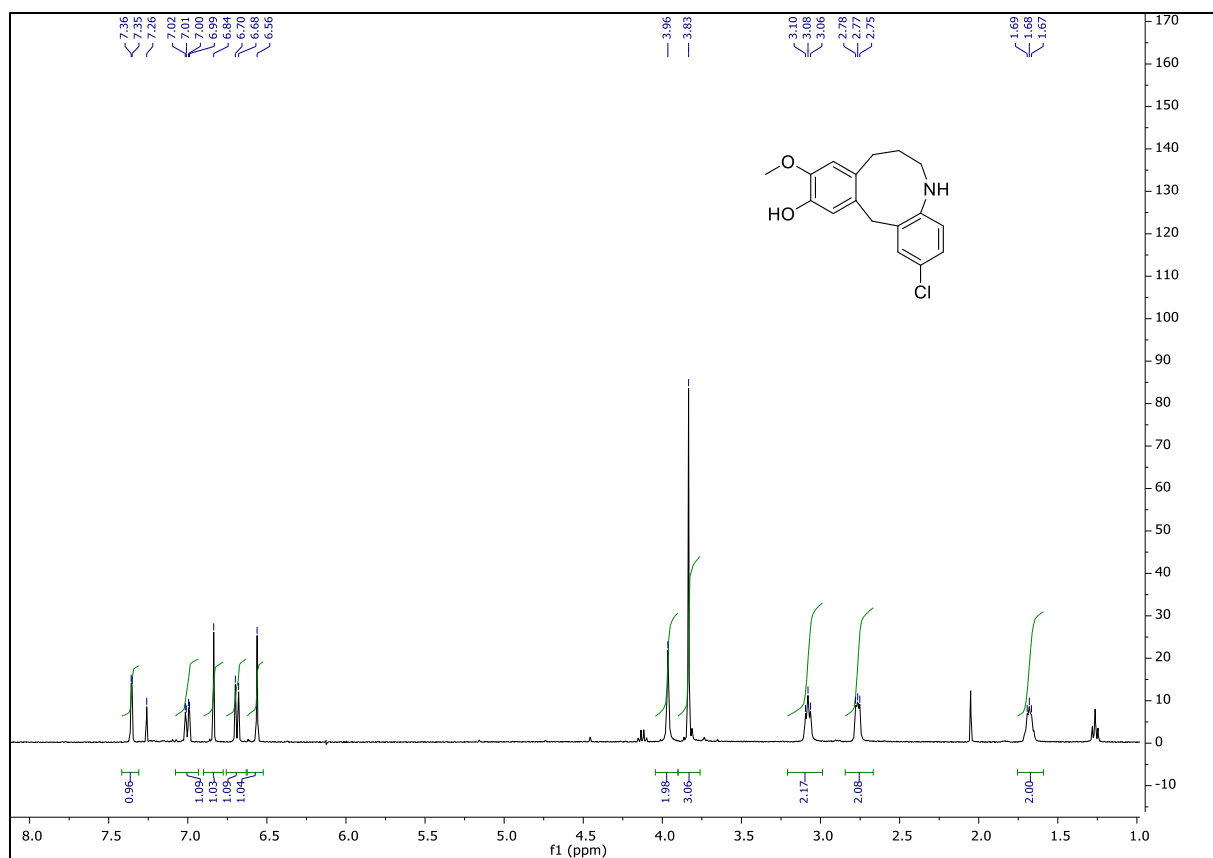
**General reaction conditions:** **5Gb** (0.086 mmol), paraformaldehyde (1-1.5 equiv.), acid (1-1.5 equiv.), 80-100 °C, 20 h. <sup>a</sup> Yields were determined by GC-MS analysis. <sup>b</sup> Isolated by column chromatography and characterized by NMR. Details are given below. <sup>c</sup> 37 wt. % Formaldehyde solution

### Characterization of 7Gb



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.35 (d, *J* = 2.5 Hz, 1H), 7.00 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.84 (s, 1H), 6.69 (d, *J* = 8.3 Hz, 1H), 6.56 (s, 1H), 3.96 (s, 2H), 3.83 (s, 3H), 3.08 (t, *J* = 6.4 Hz, 2H), 2.84 – 2.67 (m, 2H), 1.68 (t, *J* = 5.5 Hz, 2H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 145.43, 143.91, 137.97, 131.80, 131.34, 130.99, 126.94, 124.69, 115.29, 111.64, 56.02, 49.15, 35.44, 32.16, 29.44.



Supplementary Figure 33. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 7Gb.

## 6.2 Construction of tetrahydro-2-benzazepines using deep eutectic solvents (DES)

DESs were prepared by stirring hydrogen bond acceptor (ChCl) and hydrogen bond donors (organic acids) with appropriate molar ratio at 80 °C until a homogeneous colorless liquid was formed as previously reported.<sup>2</sup> Typically, ChCl/OA DES was prepared by mixing ChCl (4.2 g, 0.03 mol) and oxalic acid dihydrate (3.78 g, 0.03 mol), at 80 °C and stirred for 1 h. The colorless liquid was used without further purification.

**Experimental procedure:** An oven-dried vial equipped with a stirring bar, was charged with **5Gb** (0.086 mmol, 1 equiv.), paraformaldehyde (0.086 mmol, 1 equiv.) and DES (1:1 molar ratio, 1 g) under air. Then the vial was capped and the mixture was rapidly stirred at room temperature for 1 min, then was heated to 50-80 °C and stirred for 8-20 h. The reaction mixture was then cooled to room temperature, diluted with water (2 mL) and saturated NaHCO<sub>3</sub> (2 mL) was added and then the reaction mixture was stirred for one hour at room temperature. The crude mixture was extracted with ethyl acetate (3×10 mL) and the solvent was evaporated *in vacuo*. The residue was purified by flash column chromatography using pentane and ethyl acetate as eluent.

**Supplementary Table 9.** Establishing reaction methodology for the construction of tetrahydro-2-benzazepines using model compound **5Gb** in various deep eutectic solvents (DES) and Lewis acid additives

Entry	DES	Temp (°C)	Additive (5 mol%)	Conv. (%)	Yield 6Gb (%) <sup>a</sup>	Side products <sup>a</sup>	
1	ChCl/Oxalic acid	90	-	>99	99	-	
2	ChCl/TSA	90	-	>99	99	-	
3	ChCl/Lactic acid	90	-	77	29		36%
5	ChCl/Levulinic acid	90	-	84	5		45%
6	ChCl/Citric acid	90	-	>99	15		7%
							44%
7	<b>ChCl/Oxalic acid</b>	<b>70</b>	-	<b>&gt;99</b>	<b>95 (87)</b>	-	
8	ChCl/TSA	70	-	>99	93	-	
9	ChCl/Urea	70	-	0	-	-	
10	ChCl/Oxalic acid	70	Fe(OTf) <sub>3</sub>	>99	92 (65)	<b>7Gb</b>	4%
11	ChCl/Oxalic acid	70	Al(OTf) <sub>3</sub>	>99	97	<b>7Gb</b>	3%
12	ChCl/Oxalic acid	70	Yb(OTf) <sub>3</sub>	>99	75	<b>7Gb</b>	14%
13	ChCl/Oxalic acid	70	Eu(OTf) <sub>3</sub>	>99	67	<b>7Gb</b>	19%
14	ChCl/Oxalic acid	70	Hf(OTf) <sub>4</sub>	>99	75	<b>7Gb</b>	12%
15	ChCl/Oxalic acid	70	La(OTf) <sub>3</sub>	>99	61	<b>7Gb</b>	23%
16	ChCl/Oxalic acid	70	Bi(OTf) <sub>3</sub>	>99	65	<b>7Gb</b>	17%
17	ChCl/Oxalic	70	Fe(OAc) <sub>2</sub>	>99	96 (83)	<b>7Gb</b>	2%

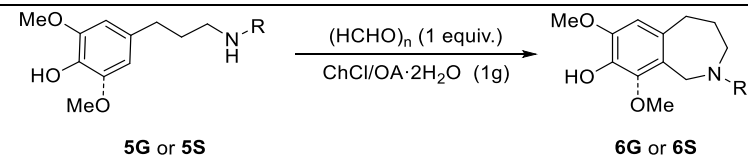
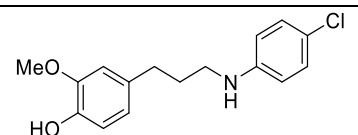
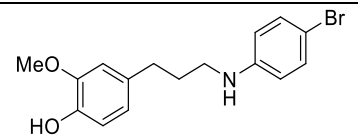
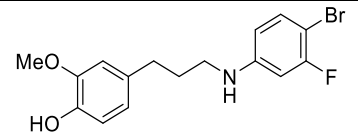
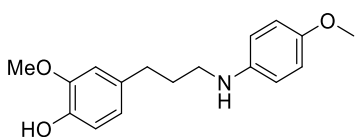
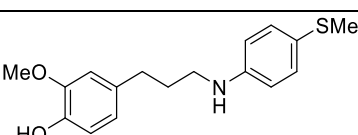
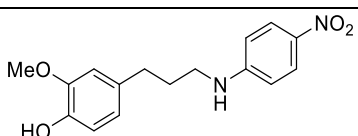
	acid					
18	ChCl/Oxalic acid	50	-	77	76	-
19 <sup>b</sup>	ChCl/Oxalic acid	70	-	66	66	-
20 <sup>c</sup>	ChCl/Oxalic acid	70	-	82	82	-

**General reaction conditions:** **5Gb** (0.086 mmol), paraformaldehyde (0.086 mmol), DES (1:1 molar ratio, 1 g), 50-90 °C. Oxalic acid dihydrate (C<sub>2</sub>H<sub>2</sub>O<sub>4</sub>·2H<sub>2</sub>O) was used to prepare ChCl/Oxalic acid DES. ChCl/Urea (1:2 molar ratio) used. <sup>a</sup> Yields were determined by GC-MS analysis; isolated yield in parentheses. <sup>b</sup> 8 h. <sup>c</sup> 0.5 g ChCl/Oxalic acid·2H<sub>2</sub>O.

### 6.3 Synthesis of a library of tetrahydro-2-benzazepine derivatives in a specific DES

As can be seen in **Supplementary Table 10**, the outcome of the reaction was influenced by the type of DES used with highest yield and product selectivity obtained with ChCl/OA. Interestingly, the presence of Lewis acid additives resulted in changes of the outcome of the reaction, but did not lead to significant improvement. Therefore, we selected the ChCl/OA system as a suitable reaction medium for establishing the scope of the reaction methodology.

**Supplementary Table 10.** Synthesis of tetrahydro-2-benzazepine derivatives in ChCl/OA DES

							
Entry	Substrate	Amount (mmol)	Temp (°C)	Time (h)	Yield (%)		
1		<b>5Gb</b>	0.343	70	20	87	<b>6Gb</b>
2		<b>5Gc</b>	0.297	70	20	82	<b>6Gc</b>
3		<b>5Ge</b>	0.241	70	48	63	<b>6Ge</b>
4		<b>5Gf</b>	0.250	80	48	51	<b>6Gf</b>
5		<b>5Gh</b>	0.330	80	48	59	<b>6Gh</b>
6		<b>5Gj</b>	0.165	70	20	91	<b>6Gj</b>

7		<b>5Gp</b>	0.260	80	48	61	<b>6Gp</b>
8		<b>5Sa</b>	0.173	70	48	70	<b>6Sa</b>
9		<b>5Sb</b>	0.299	70	20	71	<b>6Sb</b>
10		<b>5Sc</b>	0.314	70	20	83	<b>6Sc</b>
11		<b>5Sf</b>	0.157	70	48	66	<b>6Sf</b>
12		<b>5Sj</b>	0.150	70	20	95	<b>6Sj</b>
13		<b>5Sp</b>	0.366	80	48	41	<b>6Sp</b>

**General reaction conditions:** **5G** or **5S** (0.150-0.366 mmol), paraformaldehyde (1 equiv.)  
 ChCl/OA·2H<sub>2</sub>O (1 g), 70-80 °C, 20-48 h. Isolated yields are presented.

## 7. Testing of biological activities of the obtained lignin-derived amine libraries

**Supplementary Table 11.** Activity of selected lignin-derived inhibitors and the reference compound Erythromycin toward *S. aureus*. Values are means of at least two independent determinations. MIC: minimal inhibitory concentration.

Compound	MIC values in <i>S. aureus</i> ( $\mu\text{M}$ )
<b>6Gc</b>	$53 \pm 9$
<b>6Ge</b>	$37 \pm 18$
<b>6Sb</b>	$51 \pm 5$
<b>6Sc</b>	$50 \pm 4$
<b>erythromycin</b>	$3.8 \pm 1.5$

**Supplementary Table 12.** Activity of selected lignin-derived inhibitors and the reference compound Chloramphenicol toward *E. coli* K12 and *E. coli* TolC. Values are means of at least two independent determinations. MIC: minimal inhibitory concentration. n.d.: not determined.

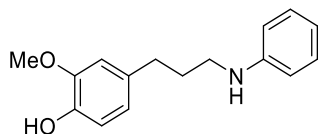
Compound	<i>E. coli</i> K12		<i>E. coli</i> TolC	
	% growth inhibition at 50 $\mu\text{M}$	MIC value ( $\mu\text{M}$ )	% growth inhibition at 50 $\mu\text{M}$	MIC value ( $\mu\text{M}$ )
<b>5Gg</b>	$9 \pm 1$	> 50	$88 \pm 2$	> 50
<b>5Gr</b>	$7 \pm 1$	> 50	$92 \pm 9$	$52 \pm 5$
<b>6Ge</b>	$13 \pm 4$	> 50	$102 \pm 0$	$23 \pm 5$
<b>6Sb</b>	$14 \pm 5$	> 50	$97 \pm 1$	$49 \pm 2$
<b>chloramphenicol</b>	n.d.	$26 \pm 6$	n.d.	$4.2 \pm 1.7$

**Supplementary Table 13.** Activity of selected lignin-derived inhibitors and the reference compound Doxorubicin toward HepG2 cells. Values are means of at least two independent determinations.

Compound	Inhibition of HepG2 viability ( $\text{IC}_{50}$ values)
<b>5Gd</b>	$33.0 \pm 3.9 \mu\text{M}$
<b>5Gt</b>	$30.4 \pm 0.4 \mu\text{M}$
<b>5Sb</b>	$53.2 \pm 13.7 \mu\text{M}$
<b>5St</b>	$39.9 \pm 1.8 \mu\text{M}$
<b>6Gc</b>	$48.1 \pm 5.0 \mu\text{M}$
<b>6Ge</b>	$31.6 \pm 10.8 \mu\text{M}$
<b>6Sb</b>	$40.1 \pm 5.2 \mu\text{M}$
<b>doxorubicin</b>	$0.69 \pm 0.39 \mu\text{M}$

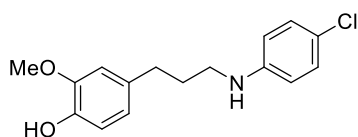
## 8. Characterization data of isolated compounds

### 2-methoxy-4-(3-(phenylamino)propyl)phenol (**5Ga**)



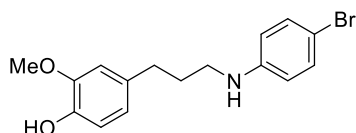
The compound was synthesized according to the **General procedure (B)**. Aniline (37.2 mg, 0.4 mmol) affords **5Ga** (77 mg, 75% yield). Pale yellow solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.19 (t, *J* = 7.2 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 1H), 6.74-6.71 (m, 3H), 6.61 (d, *J* = 8.4 Hz, 2H), 3.86 (s, 3H), 3.16 (t, *J* = 6.8 Hz, 2H), 2.69 (t, *J* = 7.6 Hz, 2H), 1.94 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 151.02, 149.06, 146.44, 136.22, 131.88, 123.59, 119.87, 116.90, 115.41, 113.59, 58.51, 46.01, 35.72, 33.95. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>16</sub>H<sub>20</sub>NO<sub>2</sub>[M+H]<sup>+</sup>: 258.1489; found: 258.1488.

### 4-(3-((4-chlorophenyl)amino)propyl)-2-methoxyphenol (**5Gb**)



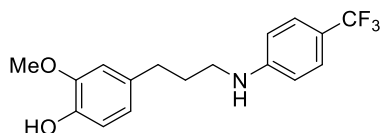
The compound was synthesized according to the **General procedure (B)**. 4-Chloroaniline (50.8 mg, 0.4 mmol) affords **5Gb** (113 mg, 97% yield). Brown solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.11 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.71-6.69 (m, 2H), 6.49 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 3.11 (t, *J* = 6.8 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.91 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 149.55, 149.13, 146.50, 136.06, 131.67, 124.35, 123.57, 116.98, 116.48, 113.60, 58.52, 46.13, 35.68, 33.74. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>16</sub>H<sub>19</sub>ClNO<sub>2</sub> [M+H]<sup>+</sup>: 292.1099; found: 292.1099.

#### 4-(3-((4-bromophenyl)amino)propyl)-2-methoxyphenol (5Gc)



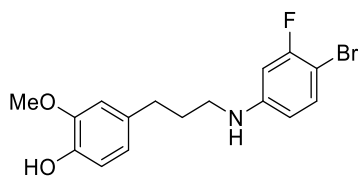
The compound was synthesized according to the **General procedure (B)**. 4-Bromoaniline (69 mg, 0.4 mmol) affords **5Gc** (129 mg, 96% yield). Off-white solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.25 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 1H), 6.71-6.70 (m, 2H), 6.45 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 3.10 (t, *J* = 6.8 Hz, 2H), 2.67 (t, *J* = 7.2 Hz, 2H), 1.92 (p, *J* = 7.2 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 149.98, 149.15, 146.50, 136.09, 134.54, 123.59, 117.03, 113.64, 111.34, 104.99, 58.55, 46.04, 35.68, 33.71. HRMS (APCI<sup>+</sup>, *m/z*) calculated for C<sub>16</sub>H<sub>19</sub>BrNO<sub>2</sub> [M+H]<sup>+</sup>: 336.0594; found: 336.0594.

#### 2-methoxy-4-(3-((4-(trifluoromethyl)phenyl)amino)propyl)phenol (5Gd)



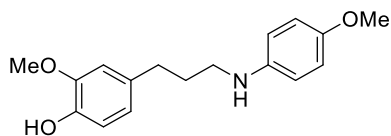
The compound was synthesized according to the **General procedure (B)**. 4-(Trifluoromethyl)aniline (64 mg, 0.4 mmol) affords **5Gd** (113 mg, 87% yield). Yellow oil was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 80:20). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.39 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.71-6.68 (m, 2H), 6.55 (d, *J* = 8.4 Hz, 2H), 5.51 (s, 1H), 3.85 (s, 3H), 3.17 (t, *J* = 6.8 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.94 (p, *J* = 7.6 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 153.36, 149.13, 146.54, 135.86, 129.21 (q, *J*<sub>C-F</sub> = 3.8 Hz), 127.67 (q, *J*<sub>C-F</sub> = 271.5 Hz), 123.55, 121.19 (q, *J*<sub>C-F</sub> = 32.7 Hz), 116.97, 114.37, 113.54, 58.49, 45.49, 35.61, 33.58. HRMS (APCI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>19</sub>F<sub>3</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 326.13624; found: 326.13679.

#### 4-(3-((4-bromo-3-fluorophenyl)amino)propyl)-2-methoxyphenol (5Ge)



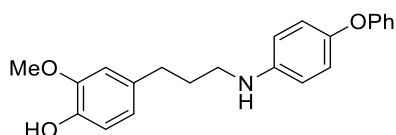
The compound was synthesized according to the **General procedure (B)**. 4-Bromo-3-fluoroaniline (76 mg, 0.4 mmol) affords **5Ge** (135 mg, 95% yield). Off-white solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.23 (t, *J* = 8.4 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.70-6.68 (m, 2H), 6.32 (dd, *J* = 11.2 Hz, *J* = 2.4 Hz, 1H), 6.23 (dd, *J* = 8.8 Hz, *J* = 2.4 Hz, 1H), 3.86 (s, 3H), 3.08 (t, *J* = 7.2 Hz, 2H), 2.66 (t, *J* = 7.2 Hz, 2H), 1.91 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 162.48 (d, *J*<sub>C-F</sub> = 244.6 Hz), 151.92 (d, *J*<sub>C-F</sub> = 10.1 Hz), 149.18, 146.53, 135.91, 123.57, 117.01, 113.60, 112.76 (d, *J*<sub>C-F</sub> = 2.5 Hz), 102.97 (d, *J*<sub>C-F</sub> = 26.1 Hz), 96.96 (d, *J*<sub>C-F</sub> = 21.5 Hz), 58.54, 45.95, 35.60, 33.49. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>16</sub>H<sub>18</sub>BrFNO<sub>2</sub> [M+H]<sup>+</sup>: 354.0499; found: 354.0500.

#### 2-methoxy-4-(3-((4-methoxyphenyl)amino)propyl)phenol (5Gf)



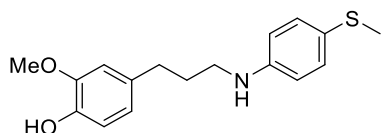
The compound was synthesized according to the **General procedure (B)**. 4-Methoxyaniline (49.2 mg, 0.4 mmol) affords **5Gf** (93 mg, 81% yield). Pale brown solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 6.84 (d, *J* = 8.4 Hz, 1H), 6.78 (d, *J* = 8.8 Hz, 2H), 6.70-6.69 (m, 2H), 6.57 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 3.75 (s, 3H), 3.10 (t, *J* = 6.8 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.91 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 154.79, 149.09, 146.44, 145.18, 136.27, 123.57, 117.56, 116.94, 116.91, 113.62, 58.50, 58.49, 47.16, 35.75, 34.02. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>22</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 288.1594; found: 288.1593.

### 2-methoxy-4-(3-((4-phenoxyphenyl)amino)propyl)phenol (**5Gg**)



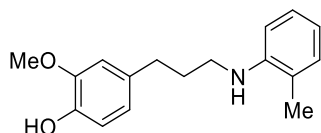
The compound was synthesized according to the **General procedure (B)**. 4-Phenoxyaniline (74 mg, 0.4 mmol) affords **5Gg** (127 mg, 91% yield). Pale brown solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.31 (t, *J* = 7.6 Hz, 2H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.98-6.88 (m, 5H), 6.74-6.73 (m, 2H), 6.60 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H), 3.16 (t, *J* = 6.8 Hz, 2H), 2.71 (t, *J* = 7.2 Hz, 2H), 1.96 (p, *J* = 7.2 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 161.81, 150.23, 149.17, 147.69, 146.52, 136.22, 132.19, 124.61, 123.93, 123.62, 119.75, 117.03, 116.51, 113.68, 58.54, 46.68, 35.76, 33.97. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>22</sub>H<sub>24</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 350.17507; found: 350.17501.

### 2-methoxy-4-(3-((4-(methylthio)phenyl)amino)propyl)phenol (**5Gh**)



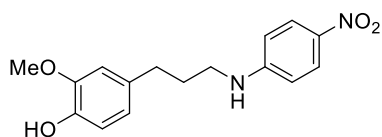
The compound was synthesized according to the **General procedure (B)**. 4-(Methylthio)aniline (56 mg, 0.4 mmol) affords **5Gh** (101 mg, 83% yield). Light yellow solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 80:20). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.21 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.70-6.68 (m, 2H), 6.52 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 3.12 (t, *J* = 6.8 Hz, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 2.40 (s, 3H), 1.91 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 149.79, 149.06, 146.46, 136.06, 134.24, 126.74, 123.56, 116.91, 116.04, 113.55, 58.51, 46.05, 35.67, 33.79, 21.91. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>22</sub>NO<sub>2</sub>S [M+H]<sup>+</sup>: 304.13658; found: 304.13703.

### 2-methoxy-4-(3-(*o*-tolylamino)propyl)phenol (**5Gi**)



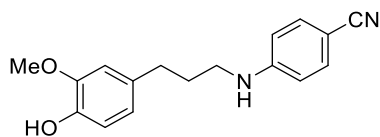
The compound was synthesized according to the **General procedure (B)**. *o*-Toluidine (42.8 mg, 0.4 mmol) affords **5Gi** (96 mg, 89% yield). White semi-solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.18 (t, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.78-6.76 (m, 2H), 6.71 (t, *J* = 7.2 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 3.88 (s, 3H), 3.25 (t, *J* = 7.2 Hz, 2H), 2.75 (t, *J* = 7.6 Hz, 2H), 2.16 (s, 3H), 2.04 (p, *J* = 7.2 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 149.18, 148.91, 146.54, 136.28, 132.75, 129.83, 124.52, 123.65, 119.49, 117.04, 113.67, 112.39, 58.55, 46.10, 35.90, 33.92, 20.11. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>22</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 272.16451; found: 272.16459.

### 2-methoxy-4-(3-((4-nitrophenyl)amino)propyl)phenol (**5Gj**)



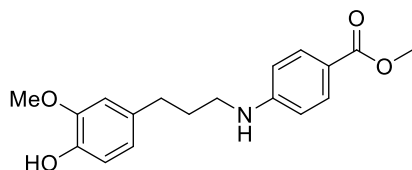
The compound was synthesized according to the **General procedure (B)**. 4-Nitroaniline (55.2 mg, 0.4 mmol) affords **5Gj** (112 mg, 93% yield). Yellow solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 8.06 (d, *J* = 9.2 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 1H), 6.69-6.67 (m, 2H), 6.47 (d, *J* = 9.2 Hz, 2H), 5.52 (*br s*, 1H), 3.85 (s, 3H), 3.22 (t, *J* = 6.8 Hz, 2H), 2.68 (t, *J* = 7.2 Hz, 2H), 1.96 (p, *J* = 7.2 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 155.95, 149.20, 146.65, 140.51, 135.47, 129.07, 123.53, 117.04, 113.65, 113.51, 58.53, 45.44, 35.53, 33.33. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>16</sub>H<sub>19</sub>N<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 303.13393; found: 303.13409.

#### 4-((3-(4-hydroxy-3-methoxyphenyl)propyl)amino)benzonitrile (5Gk)



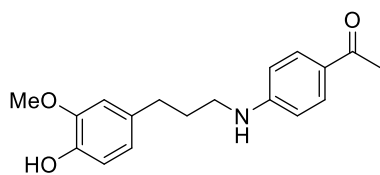
The compound was synthesized according to the **General procedure (B)**. 4-Aminobenzonitrile (47.2 mg, 0.4 mmol) affords **5Gk** (99 mg, 88% yield). Pale yellow solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.38 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.68-6.67 (m, 2H), 6.49 (d, *J* = 8.8 Hz, 2H), 5.57 (*br s*, 1H), 4.24 (*br s*, 1H), 3.84 (s, 3H), 3.16 (t, *J* = 7.2 Hz, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.93 (p, *J* = 7.2 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 154.03, 149.18, 146.59, 136.32, 135.67, 123.53, 123.23, 117.02, 114.75, 113.57, 100.95, 58.53, 45.20, 35.55, 33.39. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 283.14410; found: 283.14410.

#### Methyl 4-((3-(4-hydroxy-3-methoxyphenyl)propyl)amino)benzoate (5GI)



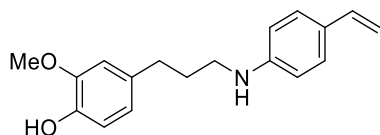
The compound was synthesized according to the **General procedure (B)**. Methyl 4-aminobenzoate (60.5 mg, 0.4 mmol) affords **5GI** (76 mg, 60% yield). Light yellow solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.85 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 1H), 6.69-6.62 (m, 2H), 6.51 (d, *J* = 8.8 Hz, *J* = 2.0 Hz, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 3.18 (t, *J* = 6.8 Hz, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.93 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 169.99, 154.54, 149.15, 146.55, 135.80, 134.19, 123.54, 120.89, 116.99, 116.46, 114.14, 113.57, 58.51, 54.19, 45.44, 35.58, 33.56. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>18</sub>H<sub>22</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 316.15488; found: 316.15492.

### 1-(4-((3-(4-hydroxy-3-methoxyphenyl)propyl)amino)phenyl)ethan-1-one (5Gm)



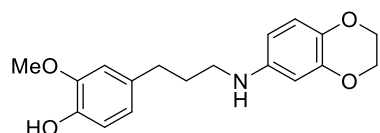
The compound was synthesized according to the **General procedure (B)**. 1-(4-Aminophenyl)ethan-1-one (54 mg, 0.4 mmol) affords **5Gm** (98 mg, 82% yield). White solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 80:20). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.81 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.70-6.63 (m, 2H), 6.51 (d, *J* = 8.8 Hz, 2H), 5.56 (s, 1H), 4.20 (s, 1H), 3.84 (s, 3H), 3.22-3.18 (m, 2H), 2.67 (t, *J* = 7.2 Hz, 2H), 2.49 (s, 3H), 1.94 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 198.96, 154.84, 149.15, 146.58, 135.74, 133.45, 129.22, 123.54, 117.00, 113.95, 113.55, 58.51, 45.31, 35.58, 33.58, 28.63. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>18</sub>H<sub>22</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 300.15942; found: 300.15993.

### 2-methoxy-4-(3-((4-vinylphenyl)amino)propyl)phenol (5Gn)



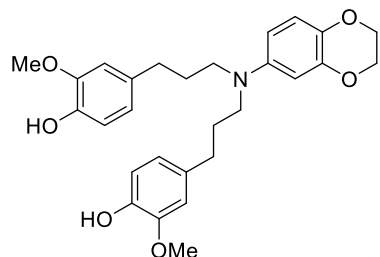
The compound was synthesized according to the **General procedure (B)**. 4-Vinylaniline (48 mg, 0.4 mmol) affords **5Gn** (49 mg, 43% yield). Light yellow oil was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 80:20). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.26 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.72-6.70 (m, 2H), 6.63 (dd, *J* = 17.6 Hz, *J* = 11.2 Hz, 1H), 6.54 (d, *J* = 8.4 Hz, 2H), 5.54 (d, *J* = 17.6 Hz, 1H), 5.03 (d, *J* = 10.8 Hz, 1H), 3.86 (s, 3H), 3.16 (t, *J* = 7.2 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 1.93 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 150.79, 149.11, 146.47, 139.32, 136.16, 130.01, 129.70, 123.59, 116.95, 115.27, 113.61, 111.93, 58.52, 45.95, 35.70, 33.88. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>18</sub>H<sub>22</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 284.16451; found: 284.18041.

#### 4-(3-((2,3-dihydrobenzo[b][1,4]dioxin-6-yl)amino)propyl)-2-methoxyphenol (5Go)



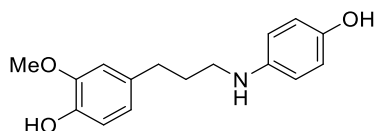
The compound was synthesized according to the **General procedure (B)**. 2,3-dihydrobenzo[b][1,4]dioxin-6-amine **5Go** (60.5 mg, 0.4 mmol) affords (76 mg, 61% yield). Light yellow oil was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 6.85-6.83 (m, 1H), 6.71-6.68 (m, 3H), 6.17-6.12 (m, 2H), 4.24-4.22 (m, 2H), 4.19-4.17 (m, 2H), 3.85 (s, 3H), 3.07 (t, *J* = 6.8 Hz, 2H), 2.65 (t, *J* = 7.6 Hz, 2H), 1.89 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 149.11, 146.68, 146.44, 146.09, 138.21, 136.27, 123.58, 120.26, 116.96, 113.63, 109.52, 104.20, 67.43, 66.86, 58.51, 46.90, 35.74, 33.97. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>18</sub>H<sub>22</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 316.15488; found: 316.15484.

#### 4,4'-(((2,3-dihydrobenzo[b][1,4]dioxin-6-yl)azanediyl)bis(propane-3,1-diyl))bis(2-methoxyphenol) (5GoS1)



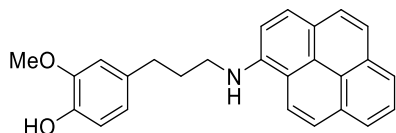
The compound was synthesized according to the **General procedure (B)**. 2,3-dihydrobenzo[b][1,4]dioxin-6-amine (60.5 mg, 0.4 mmol) affords **5GoS1** (46 mg, 24% yield). Light yellow oil was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 6.85-6.82 (m, 2H), 6.73 (d, *J* = 8.8 Hz, 1H), 6.67-6.66 (m, 4H), 6.22-6.16 (m, 2H), 5.53 (*br s*, 2H), 4.25-4.23 (m, 2H), 4.20-4.18 (m, 2H), 3.85 (s, 6H), 3.18 (t, *J* = 7.6 Hz, 4H), 2.56 (t, *J* = 7.6 Hz, 4H), 1.84 (p, *J* = 7.6 Hz, 4H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 149.06, 146.56, 146.44, 146.35, 137.51, 136.38, 123.53, 120.09, 116.87, 113.51, 109.63, 104.86, 67.45, 66.92, 58.51, 53.77, 35.63, 31.56. **HRMS** (APCI<sup>+</sup>, *m/z*) calculated for C<sub>28</sub>H<sub>34</sub>NO<sub>6</sub> [M+H]<sup>+</sup>: 480.23861; found: 480.23861.

#### 4-(3-((4-hydroxyphenyl)amino)propyl)-2-methoxyphenol (**5Gp**)



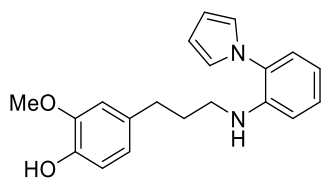
The compound was synthesized according to the **General procedure (B)**. 4-Aminophenol (43.6 mg, 0.4 mmol) affords **5Gp** (88 mg, 81% yield). Pale brown solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 8.62 (*br s*, 1H), 8.34 (*br s*, 1H), 6.74-6.73 (m, 1H), 6.67-6.65 (m, 1H), 6.58-6.51 (m, 3H), 6.42-6.38 (m, 2H), 4.78 (*br s*, 1H), 3.71 (s, 3H), 2.88 (t, *J* = 6.8 Hz, 2H), 2.54 (t, *J* = 7.6 Hz, 2H), 1.76 (p, *J* = 7.6 Hz, 2H). <sup>13</sup>C NMR (101 MHz, DMSO-d<sub>6</sub>): δ 151.22, 150.47, 147.51, 145.13, 135.90, 123.44, 118.76, 118.38, 116.40, 115.59, 58.61, 46.61, 35.50, 34.09. HRMS (APCI<sup>+</sup>, *m/z*) calculated for C<sub>16</sub>H<sub>20</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 274.14377; found: 274.14376.

#### 2-methoxy-4-(3-(pyren-1-ylamino)propyl)phenol (**5Gq**)



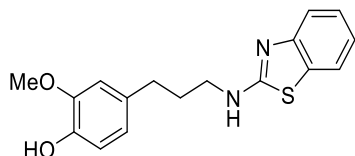
The compound was synthesized according to the **General procedure (B)**. Pyrene-1-amine (87 mg, 0.4 mmol) affords **5Gq** (123 mg, 81% yield). Yellow solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 90:10). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ 8.02-8.01 (m, 3H), 7.96 (d, *J* = 9.0 Hz, 1H), 7.91-7.83 (m, 3H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.33 (*br s*, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.72 (d, *J* = 1.8 Hz, 1H), 5.48 (*br s*, 1H), 3.77 (s, 3H), 3.50 (t, *J* = 6.6 Hz, 2H), 2.80 (t, *J* = 7.2 Hz, 2H), 2.18 (p, *J* = 7.2 Hz, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>): δ 146.53, 143.98, 133.33, 132.34, 131.62, 127.67, 126.26, 125.94, 125.61, 123.89, 123.30, 120.99, 119.31, 114.38, 110.98, 55.83, 44.15, 33.32, 30.93. HRMS (APCI<sup>+</sup>, *m/z*) calculated for C<sub>26</sub>H<sub>24</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 382.18016; found: 382.18056.

#### 4-(3-((2-(1H-pyrrol-1-yl)phenyl)amino)propyl)-2-methoxyphenol (5Gr)



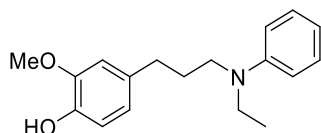
The compound was synthesized according to the **General procedure (B)**. 2-(1H-pyrrol-1-yl)aniline (63 mg, 0.4 mmol) affords **5Gr** (69 mg, 53% yield). Light yellow oil was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.27 (td, *J* = 8.4 Hz, *J* = 1.6 Hz, 1H), 7.17 (dd, *J* = 7.2 Hz, *J* = 1.2 Hz, 1H), 6.86-6.83 (m, 3H), 6.76-6.71 (m, 2H), 6.67-6.65 (m, 2H), 6.39-6.38 (m, 2H), 5.54 (s, 1H), 3.87 (s, 3H), 3.82 (br s, 1H), 3.14-3.11 (m, 2H), 2.60 (t, *J* = 7.2 Hz, 2H), 1.87 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 149.10, 146.54, 146.48, 135.93, 131.60, 129.86, 129.76, 124.58, 123.60, 118.92, 116.99, 113.76, 113.58, 112.09, 58.54, 45.27, 35.41, 33.58. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>20</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub>[M+H]<sup>+</sup>: 323.17540; found: 323.17588.

#### 4-(3-(benzo[d]thiazol-2-ylamino)propyl)-2-methoxyphenol (5Gs)



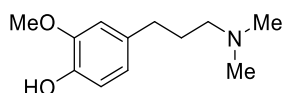
The compound was synthesized according to the **General procedure (B)**. Benzo[d]thiazol-2-amine (60 mg, 0.4 mmol) affords **5Gs** (69 mg, 55% yield). White solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, DMSO-d<sub>6</sub>): δ 8.64 (s, 1H), 8.01 (t, *J* = 5.2 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.18 (td, *J* = 7.2 Hz, *J* = 1.2 Hz, 1H), 6.98 (td, *J* = 6.8 Hz, *J* = 1.2 Hz, 1H), 6.76 (d, *J* = 1.6 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 6.58 (dd, *J* = 8.0 Hz, *J* = 2.0 Hz, 1H), 3.71 (s, 3H), 3.35-3.29 (m, 2H), 2.55 (t, *J* = 7.2 Hz, 2H), 1.83 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, DMSO-d<sub>6</sub>): δ 192.81, 169.20, 155.78, 150.49, 147.61, 135.40, 133.30, 128.59, 123.96, 123.47, 121.00, 118.41, 115.64, 58.62, 46.57, 35.13, 33.82. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub>S [M+H]<sup>+</sup>: 315.11616; found: 315.11688.

#### 4-(3-(ethyl(phenyl)amino)propyl)-2-methoxyphenol (**5Gt**)



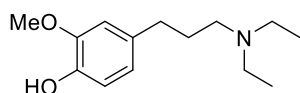
The compound was synthesized according to the **General procedure (B)**. *N*-ethylaniline (48 mg, 0.4 mmol) affords **5Gt** (97 mg, 85% yield). Light yellow oil was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 90:10). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.21 (d, *J* = 7.6 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.73-6.71 (m, 2H), 6.67-6.64(m, 3H), 5.50 (s, 1H), 3.88 (s, 3H), 3.37 (q, *J* = 7.2 Hz, 2H), 3.29 (t, *J* = 7.6 Hz, 2H), 2.62 (t, *J* = 7.6 Hz, 2H), 1.92 (p, *J* = 7.2 Hz, 2H), 1.15 (t, *J* = 6.8 Hz, 3H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 150.61, 149.05, 146.38, 136.38, 131.88, 123.57, 118.12, 116.87, 114.63, 113.52, 58.54, 52.41, 47.60, 35.68, 31.82, 14.97. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>18</sub>H<sub>24</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 286.18016; found: 286.18062.

#### 4-(3-(dimethylamino)propyl)-2-methoxyphenol (**5Gu**)



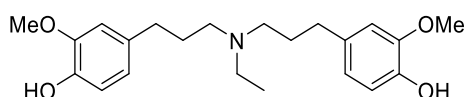
The compound was synthesized according to the **General procedure (B)**. 4-(3-Hydroxypropyl)-2-methoxyphenol (91 mg, 0.5 mmol) affords **5Gu** (55 mg, 53% yield). White semi-solid was obtained after column chromatography (SiO<sub>2</sub>, MeOH/EtOAc 50:50 to 100:0). **<sup>1</sup>H NMR** (400 MHz, CD<sub>3</sub>OD): δ 7.76 (d, *J* = 1.6 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.61 (dd, *J* = 8.0 Hz, *J* = 2.0 Hz, 1H), 3.82 (s, 3H), 2.53 (t, *J* = 7.6 Hz, 2H), 2.35-2.31 (m, 2H), 2.23 (s, 6H), 1.77 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CD<sub>3</sub>OD): δ 150.12, 146.89, 135.88, 122.99, 117.33, 114.30, 61.34, 57.59, 46.61, 35.40, 31.52. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>12</sub>H<sub>20</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 210.14886; found: 210.14863.

#### 4-(3-(diethylamino)propyl)-2-methoxyphenol (**5Gv**)



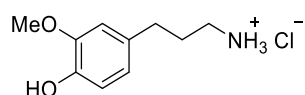
The compound was synthesized according to the **General procedure (B)**. 4-(3-Hydroxypropyl)-2-methoxyphenol (91 mg, 0.5 mmol) affords **5Gv** (66mg, 56% yield). White semi-solid was obtained after column chromatography (SiO<sub>2</sub>, MeOH/EtOAc 50:50 to 100:0). **<sup>1</sup>H NMR** (400 MHz, CD<sub>3</sub>OD): δ 6.75 (d, *J* = 1.6 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.61 (dd, *J* = 8.0 Hz, *J* = 2.0 Hz, 1H), 3.82 (s, 3H), 2.56-2.44 (m, 8H), 1.75 (p, *J* = 7.6 Hz, 2H), 1.01 (t, *J* = 7.2 Hz, 6H). **<sup>13</sup>C NMR** (101 MHz, CD<sub>3</sub>OD): δ 150.16, 147.01, 135.88, 123.02, 117.38, 114.31, 57.60, 54.24, 48.92, 35.59, 30.20, 12.44. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>14</sub>H<sub>24</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 238.18016; found: 238.18004.

#### 4,4'-((ethylazanediyl)bis(propane-3,1-diyl))bis(2-methoxyphenol) (**5GvS1**)



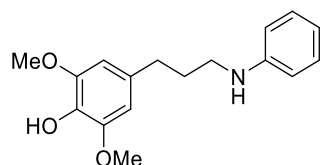
The compound was synthesized according to the **General procedure (B)**. 4-(3-Hydroxypropyl)-2-methoxyphenol (91 mg, 0.5 mmol) affords **5GvS1** (25 mg, 13% yield). Colourless oil was obtained after column chromatography (SiO<sub>2</sub>, MeOH/EtOAc 50:50). **<sup>1</sup>H NMR** (400 MHz, CD<sub>3</sub>OD): δ 6.73 (d, *J* = 1.6 Hz, 2H), 6.69 (d, *J* = 8.0 Hz, 2H), 6.59 (dd, *J* = 8.0 Hz, *J* = 2.0 Hz, 2H), 3.80 (s, 6H), 2.59 (q, *J* = 7.2 Hz, 2H), 2.50 (t, *J* = 8.0 Hz, 8H), 1.73 (p, *J* = 7.6 Hz, 4H), 1.00 (t, *J* = 7.2 Hz, 3H). **<sup>13</sup>C NMR** (101 MHz, CD<sub>3</sub>OD): δ 150.11, 146.89, 135.82, 123.03, 117.35, 114.29, 57.61, 54.73, 35.38, 30.03, 12.40. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>22</sub>H<sub>32</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 374.23258; found: 374.23283.

### 3-(4-hydroxy-3-methoxyphenyl)propan-1-aminium chloride<sup>19</sup> (5Gw)



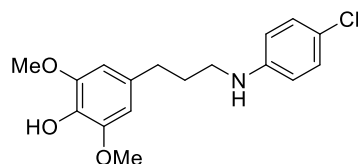
The compound was synthesized according to the **General procedure (B)**. 4-(3-hydroxypropyl)-2-methoxyphenol (91 mg, 0.5 mmol) affords **5Gw** (50 mg, 46% yield). White solid. **<sup>1</sup>H NMR** (400 MHz, D<sub>2</sub>O): δ 6.84 (s, 1H), 6.79-6.77 (m, 1H), 6.70-6.67 (m, 1H), 3.76 (s, 3H), 2.90 (t, *J* = 7.9 Hz, 2H), 2.58-2.53 (m, 2H), 1.88 – 1.84 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, D<sub>2</sub>O): δ 149.98, 145.67, 136.21, 123.64, 118.12, 115.42, 58.57, 41.60, 33.95, 31.20. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>10</sub>H<sub>16</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 182.11756; found: 182.11745.

### 2,6-dimethoxy-4-(3-(phenylamino)propyl)phenol (5Sa)



The compound was synthesized according to the **General procedure (B)**. Aniline (37 mg, 0.4 mmol) affords **5Sa** (71 mg, 62% yield). White solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.18 (t, *J* = 7.6 Hz, 2H), 6.71 (t, *J* = 7.2 Hz, 1H), 6.59 (d, *J* = 8.0 Hz, 2H), 6.43 (s, 2H), 3.86 (s, 6H), 3.16 (t, *J* = 6.8 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 1.94 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 151.03, 149.65, 135.57, 135.40, 131.89, 119.91, 115.45, 107.65, 58.92, 46.01, 36.23, 33.91. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>22</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 288.15942; found: 288.15991.

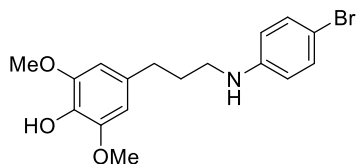
### 4-(3-((4-chlorophenyl)amino)propyl)-2,6-dimethoxyphenol (5Sb)



The compound was synthesized according to the **General procedure (B)**. 4-Chloroaniline (64 mg, 0.5 mmol) affords **5Sb** (98 mg, 61% yield). White solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 80:20). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.10 (d, *J* = 8.8 Hz, 2H), 6.48 (d, *J* = 8.8 Hz, 2H), 6.40 (s, 2H), 5.39 (*br s*, 1H), 3.85 (s, 6H), 3.60 (*br s*, 1H), 3.11 (t, *J* = 6.8 Hz, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.91 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 149.63, 149.51, 135.59, 135.17, 131.66, 124.39, 116.40, 107.57, 58.90,

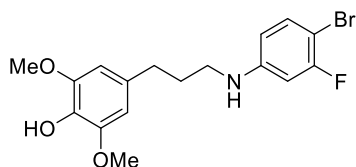
46.07, 36.18, 33.71. **HRMS** (APCI<sup>+</sup>, m/z) calculated for C<sub>17</sub>H<sub>21</sub>ClNO<sub>3</sub> [M+H]<sup>+</sup>: 322.12045; found: 322.12001.

#### 4-(3-((4-bromophenyl)amino)propyl)-2,6-dimethoxyphenol (**5Sc**)



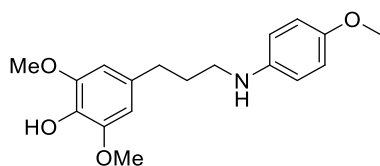
The compound was synthesized according to the **General procedure (B)**. 4-Bromoaniline (86 mg, 0.5 mmol) affords **5Sc** (115 mg, 63% yield). White solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 80:20). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.23 (d, *J* = 8.8 Hz, 2H), 6.43 (d, *J* = 8.8 Hz, 2H), 6.40 (s, 2H), 5.38 (*br s*, 1H), 3.85 (s, 6H), 3.62 (*br s*, 1H), 3.11 (t, *J* = 6.8 Hz, 2H), 2.65 (t, *J* = 7.6 Hz, 2H), 1.91 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 149.92, 149.63, 135.59, 135.16, 134.53, 116.90, 111.36, 107.57, 58.91, 45.97, 36.17, 33.68. **HRMS** (APCI<sup>+</sup>, m/z) calculated for C<sub>17</sub>H<sub>21</sub>BrNO<sub>3</sub> [M+H]<sup>+</sup>: 366.06993; found: 366.07050.

#### 4-(3-((4-bromo-3-fluorophenyl)amino)propyl)-2,6-dimethoxyphenol (**5Se**)



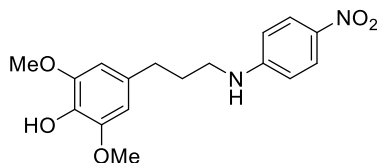
The compound was synthesized according to the **General procedure (B)**. 4-Bromo-3-fluoroaniline (76 mg, 0.4 mmol) affords **5Se** (108 mg, 70% yield). White solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.21 (t, *J* = 8.0 Hz, 1H), 6.40 (s, 2H), 6.30 (dd, *J* = 11.2 Hz, *J* = 2.4 Hz, 1H), 6.22 (dd, *J* = 8.8 Hz, *J* = 2.0 Hz, 1H), 5.41 (s, 1H), 3.85 (s, 6H), 3.08 (t, *J* = 6.8 Hz, 2H), 2.65 (t, *J* = 7.2 Hz, 2H), 1.91 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 162.48 (d, *J*<sub>C-F</sub> = 244.8 Hz), 151.96 (d, *J*<sub>C-F</sub> = 10.1 Hz), 149.67, 135.89 (d, *J*<sub>C-F</sub> = 2.4 Hz), 135.65, 135.03, 112.64, 107.59, 102.87 (d, *J*<sub>C-F</sub> = 26.2 Hz), 96.91 (d, *J*<sub>C-F</sub> = 21.6 Hz), 58.92, 45.87, 36.11, 33.49. **HRMS** (APCI<sup>+</sup>, m/z) calculated for C<sub>17</sub>H<sub>20</sub>BrFNO<sub>3</sub> [M+H]<sup>+</sup>: 384.06051; found: 384.05365.

### 2,6-dimethoxy-4-(3-((4-methoxyphenyl)amino)propyl)phenol (**5Sf**)



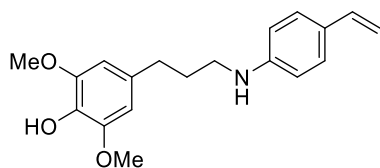
The compound was synthesized according to the **General procedure (B)**. 4-Methoxyaniline (49 mg, 0.4 mmol) affords **5Sf** (77 mg, 60% yield). Light yellow solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 6.78 (d, *J* = 9.2 Hz, 2H), 6.56 (d, *J* = 8.8 Hz, 2H), 6.42 (s, 2H), 3.85 (s, 6H), 3.74 (s, 3H), 3.10 (t, *J* = 6.8 Hz, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.91 (p, *J* = 7.2 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 154.72, 149.64, 145.31, 135.55, 135.46, 117.56, 116.80, 107.63, 58.90, 58.49, 47.07, 36.27, 34.03. HRMS (ESI<sup>+</sup>, *m/z*) calculated for C<sub>18</sub>H<sub>24</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 318.16998; found: 318.17046.

### 2,6-dimethoxy-4-(3-((4-nitrophenyl)amino)propyl)phenol (**5Sj**)



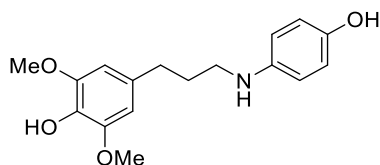
The compound was synthesized according to the **General procedure (B)**. 4-Nitroaniline (55 mg, 0.4 mmol) affords **5Sj** (130 mg, 98% yield). Yellow solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.03 (d, *J* = 9.2 Hz, 2H), 6.46 (d, *J* = 9.2 Hz, 2H), 6.40 (s, 2H), 5.43 (s, 1H), 4.65-4.63 (*br m*, 1H), 3.84 (s, 6H), 3.22 (q, *J* = 6.0 Hz, 2H), 2.66 (t, *J* = 7.2 Hz, 2H), 1.96 (p, *J* = 7.6 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 156.09, 149.70, 140.36, 135.72, 134.75, 129.06, 113.59, 107.61, 58.94, 45.40, 36.02, 33.34. HRMS (ESI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>21</sub>N<sub>2</sub>O<sub>5</sub> [M+H]<sup>+</sup>: 333.14450; found: 333.14488.

### 2,6-dimethoxy-4-(3-((4-vinylphenyl)amino)propyl)phenol (**5Sn**)



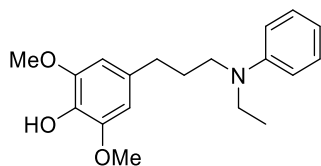
The compound was synthesized according to the **General procedure (B)**. 4-Vinylaniline (48 mg, 0.4 mmol) affords **5Sn** (80 mg, 64% yield). Yellow oil was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.26-7.23 (m, 2H), 6.61 (dd, *J* = 17.2 Hz, *J* = 10.8 Hz, 1H), 5.52 (d, *J* = 8.8 Hz, 2H), 6.41 (s, 2H), 5.52 (d, *J* = 17.6 Hz, 1H), 5.01 (d, *J* = 11.2 Hz, 1H), 3.85 (s, 6H), 3.16 (t, *J* = 6.8 Hz, 2H), 2.67 (t, *J* = 7.2 Hz, 2H), 1.93 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 150.75, 149.63, 139.27, 135.56, 135.29, 129.99, 129.73, 115.24, 111.96, 107.61, 58.91, 45.92, 36.20, 33.85. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>19</sub>H<sub>24</sub>NO<sub>3</sub>[M+H]<sup>+</sup>: 314.17507; found: 314.17556.

### 4-(3-((4-hydroxyphenyl)amino)propyl)-2,6-dimethoxyphenol (**5Sp**)



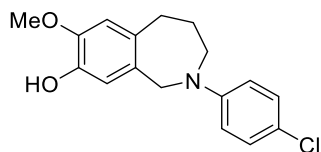
The compound was synthesized according to the **General procedure (B)**. 4-Aminophenol (44 mg, 0.4 mmol) affords **5Sp** (61 mg, 50% yield). Light yellow solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 20:80). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 6.69 (d, *J* = 8.8 Hz, 2H), 6.50 (d, *J* = 8.8 Hz, 2H), 6.41 (s, 2H), 5.37 (*br s*, 1H), 3.86 (s, 6H), 3.09 (t, *J* = 7.2 Hz, 2H), 2.66 (t, *J* = 7.2 Hz, 2H), 1.91 (p, *J* = 7.6 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 150.19, 149.59, 145.30, 135.51, 135.43, 118.79, 116.88, 107.59, 58.91, 47.07, 36.27, 34.01. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>22</sub>NO<sub>4</sub>[M+H]<sup>+</sup>: 304.15433; found: 304.15478.

#### 4-(3-(ethyl(phenyl)amino)propyl)-2,6-dimethoxyphenol (**5St**)



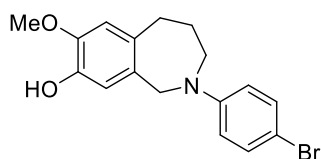
The compound was synthesized according to the **General procedure (B)**. *N*-ethylaniline (48 mg, 0.4 mmol) affords **5St** (111 mg, 88% yield). Colourless oil was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.20 (t, *J* = 7.6 Hz, 2H), 6.66-6.63 (m, 3H), 6.42 (s, 2H), 5.38 (s, 1H), 3.87 (s, 6H), 3.37 (q, *J* = 7.2 Hz, 2H), 3.28 (t, *J* = 7.6 Hz, 2H), 2.61 (t, *J* = 7.6 Hz, 2H), 1.92 (p, *J* = 7.2 Hz, 2H), 1.15 (t, *J* = 7.2 Hz, 3H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 150.60, 149.59, 135.52, 135.48, 131.88, 118.16, 114.63, 107.55, 58.92, 52.32, 47.58, 36.14, 31.70, 14.95. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>19</sub>H<sub>26</sub>NO<sub>3</sub>[M+H]<sup>+</sup>: 316.19072; found: 316.19117.

#### 2-(4-chlorophenyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (**6Gb**)



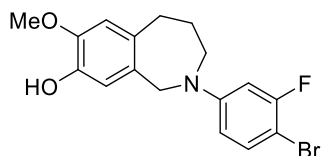
The compound was synthesized according to the **General procedure (C)**. **5Gb** (100 mg, 0.343 mmol) affords **6Gb** (91 mg, 87% yield). Pale brown solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 60:40). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.17 – 7.03 (m, 2H), 6.87 (s, 1H), 6.69 (d, *J* = 9.0 Hz, 2H), 6.63 (s, 1H), 5.45 (s, 1H), 4.46 (s, 2H), 3.81 (s, 3H), 3.78 – 3.70 (m, 2H), 2.98 – 2.80 (m, 2H), 1.93 – 1.76 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 146.29, 145.06, 143.15, 133.36, 131.25, 129.09, 120.95, 116.34, 114.05, 113.09, 56.08, 54.69, 52.74, 35.70, 25.95. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>19</sub>ClNO<sub>2</sub> [M+H]<sup>+</sup>: 304.10988; found: 304.08550.

### 2-(4-bromophenyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Gc)



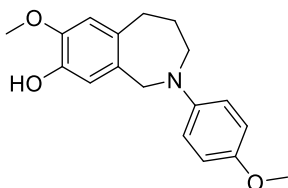
The compound was synthesized according to the **General procedure (C)**. **5Gc** (100 mg, 0.297 mmol) affords **6Gc** (85 mg, 82% yield). Brown solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 60:40). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.23 – 7.21 (m, 2H), 6.86 (s, 1H), 6.66 – 6.62 (m, 3H), 4.45 (s, 2H), 3.81 (s, 3H), 3.74 – 3.71 (m, 2H), 2.91 – 2.88 (m, 2H), 1.86 – 1.81 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 146.67, 145.06, 143.13, 133.32, 131.95, 131.16, 116.34, 114.56, 113.10, 108.04, 56.08, 54.60, 52.66, 35.68, 25.93. **HRMS** (APCI<sup>+</sup>, m/z) calculated for C<sub>17</sub>H<sub>18</sub>BrNO<sub>2</sub> [M+H]<sup>+</sup>: 348.05937; found: 348.05878.

### 2-(4-bromo-3-fluorophenyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Ge)



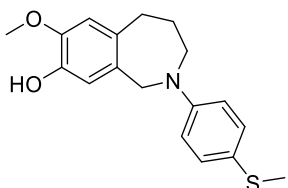
The compound was synthesized according to the **General procedure (C)**. **5Ge** (85 mg, 0.241 mmol) affords **6Ge** (55 mg, 63% yield). White solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.29 – 7.16 (m, 1H), 6.86 (s, 1H), 6.63 (s, 1H), 6.50 (dd, *J* = 12.6, 2.9 Hz, 1H), 6.45–6.42 (m, 1H), 4.43 (s, 2H), 3.82 (s, 3H), 3.77 – 3.66 (m, 2H), 2.96 – 2.82 (m, 2H), 1.92 – 1.75 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 159.96 (d, *J*<sub>C-F</sub> = 243.4 Hz), 148.67 (d, *J*<sub>C-F</sub> = 10.1 Hz), 145.20, 143.24, 133.29 (d, *J*<sub>C-F</sub> = 3.0 Hz), 133.17, 130.63, 116.27, 113.16, 109.97 (d, *J*<sub>C-F</sub> = 3.0 Hz), 100.93 (d, *J*<sub>C-F</sub> = 26.3 Hz), 93.68 (d, *J*<sub>C-F</sub> = 21.2 Hz), 56.09, 54.62, 52.74, 35.54, 25.96. **HRMS** (ESI<sup>+</sup>, m/z) calculated for C<sub>17</sub>H<sub>17</sub>BrFNO<sub>2</sub> [M+H]<sup>+</sup>: 366.04995; found: 366.03433.

**7-methoxy-2-(4-methoxyphenyl)-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Gf)**



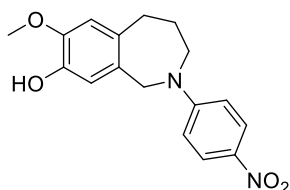
The compound was synthesized according to the **General procedure (C)**. **5Gf** (72 mg, 0.25 mmol) affords **6Gf** (38 mg, 51% yield). Pale brown solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 60:40). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 6.87 (s, 1H), 6.78 – 6.61 (m, 4H), 6.61 (s, 1H), 4.45 (s, 2H), 3.81 (s, 3H), 3.75 – 3.71 (m, 2H), 3.71 (s, 3H), 2.91 – 2.88 (m, 2H), 1.87 – 1.82 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 151.24, 144.93, 143.10, 142.51, 133.68, 132.16, 116.44, 114.94, 114.51, 112.94, 56.09, 55.81, 55.47, 53.50, 35.92, 26.18. **HRMS** (ESI<sup>+</sup>, m/z) calculated for C<sub>18</sub>H<sub>21</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 300.15942; found: 300.15950.

**7-methoxy-2-(4-(methylthio)phenyl)-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Gh)**



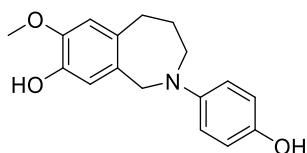
The compound was synthesized according to the **General procedure (C)**. **5Gh** (100 mg, 0.33 mmol) affords **6Gh** (61 mg, 59% yield). Pale brown solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 60:40). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.20 – 7.18 (m, 2H), 6.88 (s, 1H), 6.73 (d, *J* = 8.9 Hz, 2H), 6.62 (s, 1H), 5.46 (s, 1H), 4.47 (s, 2H), 3.81 (s, 3H), 3.76-3.73 (m, 2H), 2.95 – 2.82 (m, 2H), 2.37 (s, 3H), 1.87-1.83 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 146.57, 145.04, 143.14, 133.39, 131.56, 116.37, 113.50, 113.07, 56.09, 54.58, 52.59, 35.70, 26.15, 19.15. **HRMS** (ESI<sup>+</sup>, m/z) calculated for C<sub>18</sub>H<sub>22</sub>NO<sub>2</sub>S [M+H]<sup>+</sup>: 316.13658; found: 316.13615.

### 7-methoxy-2-(4-nitrophenyl)-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Gj)



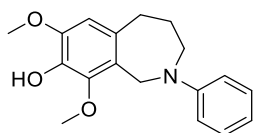
The compound was synthesized according to the **General procedure (C)**. **5Gj** (50 mg, 0.165 mmol) affords **6Gj** (47 mg, 91% yield). Bright yellow solid was obtained after workup. **<sup>1</sup>H NMR** (400 MHz, DMSO-*d*<sub>6</sub>): δ 8.68 (s, 1H), 7.95 (d, *J* = 9.4 Hz, 2H), 7.01 – 6.81 (m, 3H), 6.73 (s, 1H), 4.60 (s, 2H), 3.96 – 3.81 (m, 2H), 3.69 (s, 3H), 2.99 – 2.79 (m, 2H), 1.84 – 1.62 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, DMSO-*d*<sub>6</sub>): δ 152.50, 146.01, 143.61, 135.52, 132.20, 129.69, 125.78, 117.71, 114.51, 111.51, 55.63, 53.31, 52.69, 34.33, 26.06. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 315.13393; found: 315.12835.

### 2-(4-hydroxyphenyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Gp)



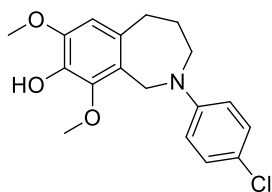
The compound was synthesized according to the **General procedure (C)**. **5Gp** (71 mg, 0.260 mmol) affords **6Gp** (45 mg, 61% yield). White solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 50:50). **<sup>1</sup>H NMR** (400 MHz, CD<sub>3</sub>OD): δ 6.77 (s, 1H), 6.76 (d, *J* = 8.7 Hz, 2H), 6.70 (s, 1H), 6.64 (d, *J* = 9.0 Hz, 2H), 4.40 (s, 2H), 3.79 (s, 3H), 3.69 – 3.66 (m, 2H), 2.92 – 2.89 (m, 2H), 1.84 – 1.82 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CD<sub>3</sub>OD): δ 150.03, 147.32, 144.76, 143.39, 134.93, 133.05, 118.61, 117.13, 116.76, 114.76, 57.23, 56.53, 55.68, 36.46, 27.35. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>17</sub>H<sub>19</sub>NO<sub>3</sub> [M-H]<sup>+</sup>: 284.12867; found: 284.12963.

### 7,9-dimethoxy-2-phenyl-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Sa)



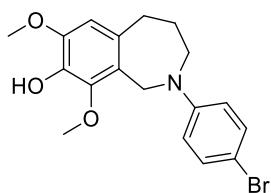
The compound was synthesized according to the **General procedure (C)**. **5Sa** (50 mg, 0.173 mmol) affords **6Sa** (36 mg, 70% yield). Off-white solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.25 – 7.06 (m, 2H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.44 (s, 1H), 5.38 (s, 1H), 4.64 (s, 2H), 3.92 (s, 3H), 3.81 (s, 3H), 3.77 (t, *J* = 5.3 Hz, 2H), 3.00 – 2.81 (m, 2H), 1.98 – 1.76 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 147.70, 145.77, 145.52, 136.27, 133.45, 129.34, 125.01, 116.19, 112.66, 108.84, 61.92, 56.25, 52.72, 46.78, 36.60, 26.07. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>18</sub>H<sub>22</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 300.15942; found: 315.15931.

### 2-(4-chlorophenyl)-7,9-dimethoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Sb)



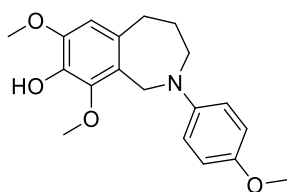
The compound was synthesized according to the **General procedure (C)**. **5Sb** (95 mg, 0.299 mmol) affords **6Sb** (71 mg, 71% yield). Off-white solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.11 – 7.07 (m, 2H), 6.82 – 6.79 (m, 2H), 6.45 (s, 1H), 5.45 (s, 1H), 4.61 (s, 2H), 3.92 (s, 3H), 3.80 (s, 3H), 3.77 – 3.73 (m, 2H), 2.93 – 2.90 (m, 2H), 1.86 - 1.80 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 146.15, 145.84, 145.44, 136.21, 133.35, 129.03, 124.51, 120.85, 113.84, 108.83, 61.88, 56.16, 53.12, 46.83, 36.60, 25.71. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>18</sub>H<sub>20</sub>ClNO<sub>3</sub> [M+H-Cl]<sup>+</sup>: 298.14377; found: 298.14392.

### 2-(4-bromophenyl)-7,9-dimethoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Sc)



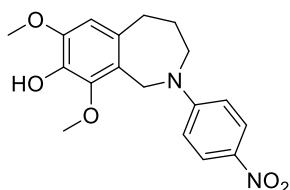
The compound was synthesized according to the **General procedure (C)**. **5Sc** (100 mg, 0.314 mmol) affords **6Sc** (85 mg, 83% yield). Off-white solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.23 – 7.19 (m, 2H), 6.78 – 6.73 (m, 2H), 6.44 (s, 1H), 5.43 (s, 1H), 4.60 (s, 2H), 3.92 (s, 3H), 3.80 (s, 3H), 3.75-3.72 (m, 2H), 2.92 – 2.89 (m, 2H), 1.85-1.81 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 146.53, 145.84, 145.42, 136.21, 133.32, 131.91, 124.45, 114.37, 108.83, 108.01, 61.88, 56.17, 53.06, 46.77, 36.60, 25.69. **HRMS** (ESI<sup>+</sup>, m/z) calculated for C<sub>18</sub>H<sub>20</sub>BrNO<sub>3</sub> [M+H]<sup>+</sup>: 378.06993; found: 378.06997.

### 7,9-dimethoxy-2-(4-methoxyphenyl)-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Sf)



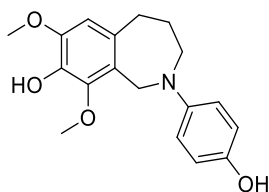
The compound was synthesized according to the **General procedure (C)**. **5Sf** (50 mg, 0.157 mmol) affords **6Sf** (34 mg, 66% yield). Light brown solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 70:30). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 6.86 – 6.82 (m, 2H), 6.78 – 6.75 (m, 2H), 6.44 (s, 1H), 5.39 (s, 1H), 4.59 (s, 2H), 3.90 (s, 3H), 3.81 (s, 3H), 3.72 – 3.70 (m, 2H), 3.70 (s, 3H), 2.92 – 2.89 (m, 2H), 1.87-1.82 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 151.29, 145.73, 145.55, 142.48, 136.26, 133.67, 125.29, 114.92, 114.27, 108.75, 61.89, 56.21, 55.78, 53.76, 47.51, 36.70, 25.98. **HRMS** (ESI<sup>+</sup>, m/z) calculated for C<sub>19</sub>H<sub>23</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 330.16998; found: 330.16924.

### 7,9-dimethoxy-2-(4-nitrophenyl)-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Sj)



The compound was synthesized according to the **General procedure (C)**. **5Sj** (50 mg, 0.150 mmol) affords **6Sj** (49 mg, 95% yield). Yellow solid was obtained after workup. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 8.03 (d, *J* = 9.5 Hz, 2H), 6.82 (d, *J* = 9.5 Hz, 2H), 6.46 (s, 1H), 5.46 (s, 1H), 4.69 (s, 2H), 3.96 (s, 3H), 3.85 (t, *J* = 4.0 Hz, 2H), 3.81 (s, 3H), 3.06 – 2.82 (m, 2H), 1.86 (t, *J* = 5.3 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 154.92, 148.81, 147.68, 139.59, 138.91, 135.43, 128.95, 125.68, 113.60, 111.44, 64.48, 58.77, 55.91, 49.72, 38.75, 28.94. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>18</sub>H<sub>20</sub>N<sub>2</sub>O<sub>5</sub> [M+H]<sup>+</sup>: 345.14450; found: 345.13826.

### 2-(4-hydroxyphenyl)-7,9-dimethoxy-2,3,4,5-tetrahydro-1H-benzo[c]azepin-8-ol (6Sp)



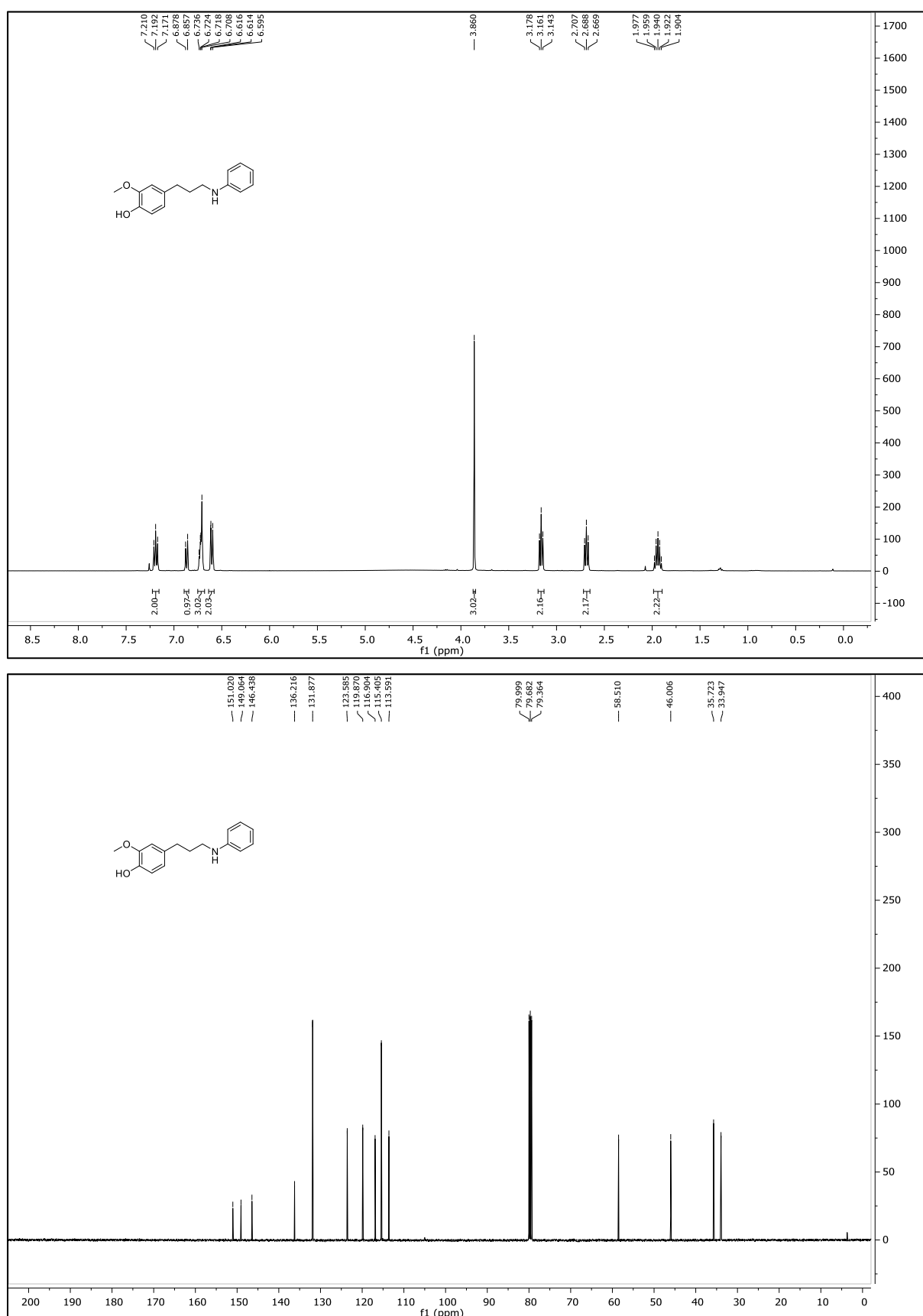
The compound was synthesized according to the **General procedure (C)**. **5Sp** (100 mg, 0.366 mmol) affords **6Sp** (47 mg, 41% yield). Brown solid was obtained after column chromatography (SiO<sub>2</sub>, Pentane/EtOAc 50:50). **<sup>1</sup>H NMR** (400 MHz, CD<sub>3</sub>OD): δ 6.83 – 6.81 (m, 2H), 6.62 – 6.60 (m, 2H), 6.52 (s, 1H), 4.52 (s, 2H), 3.80 (s, 3H), 3.77 (s, 3H), 3.66-3.63 (m, 2H), 2.91 – 2.88 (m, 2H), 1.82 – 1.80 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CD<sub>3</sub>OD): δ 150.31, 148.23, 147.60, 143.44, 138.06, 134.84, 125.82, 117.07, 116.77, 110.16, 61.88, 56.62, 56.06, 37.10, 27.26. **HRMS** (ESI<sup>+</sup>, *m/z*) calculated for C<sub>18</sub>H<sub>22</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 316.15433; found: 316.15.

## 9. References

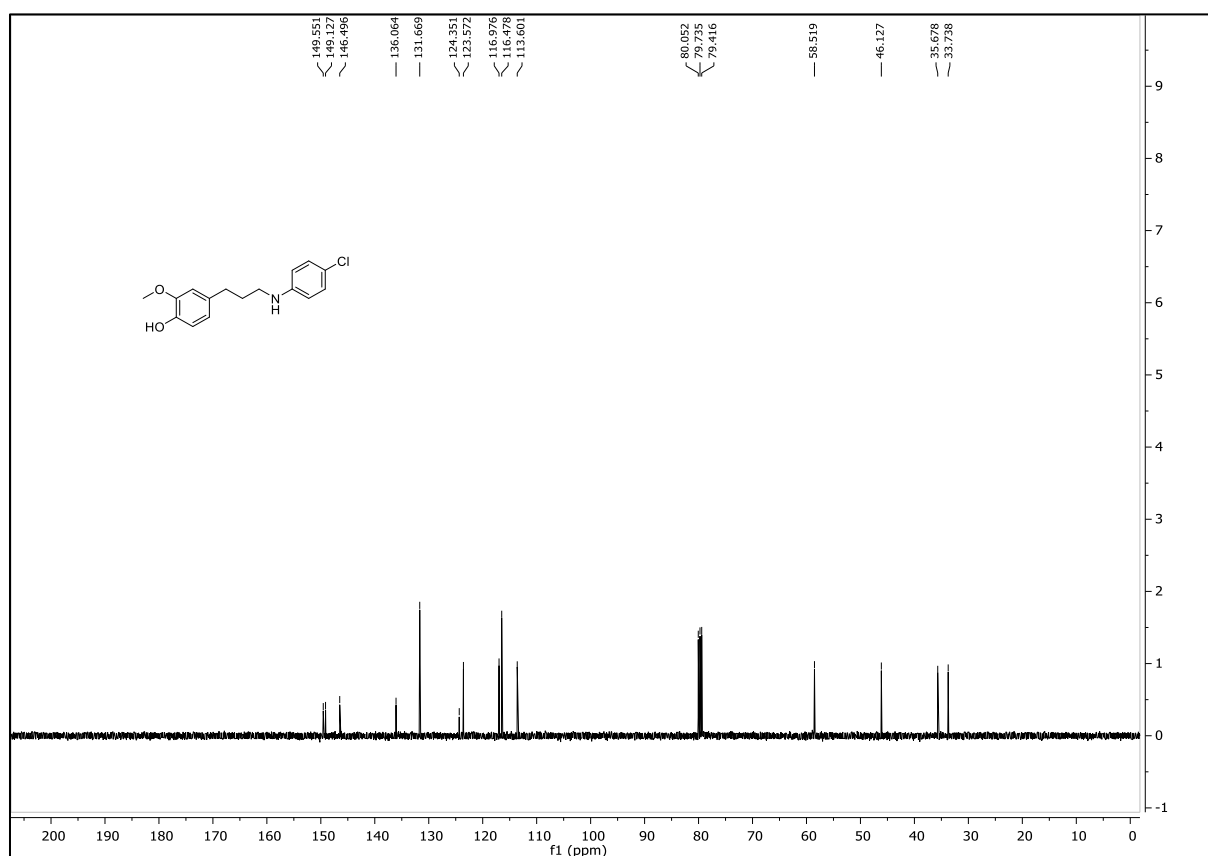
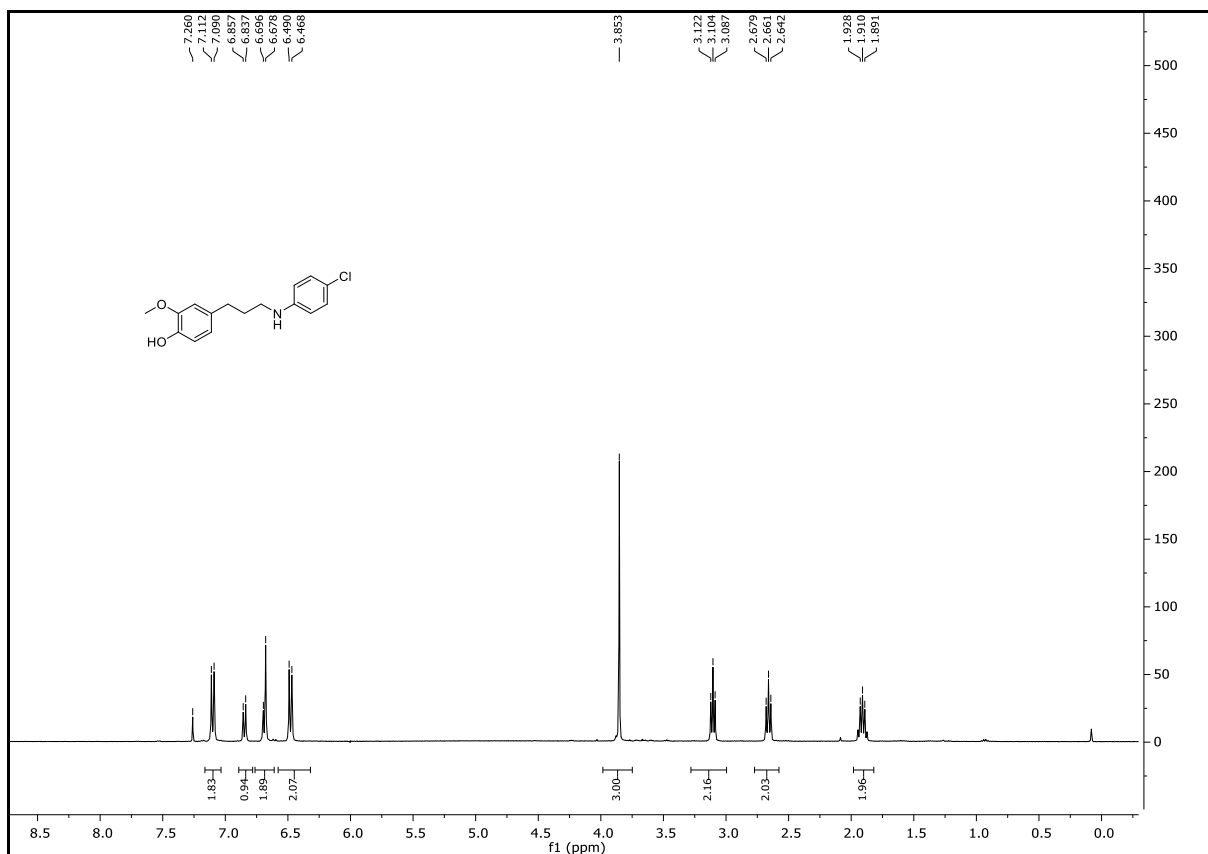
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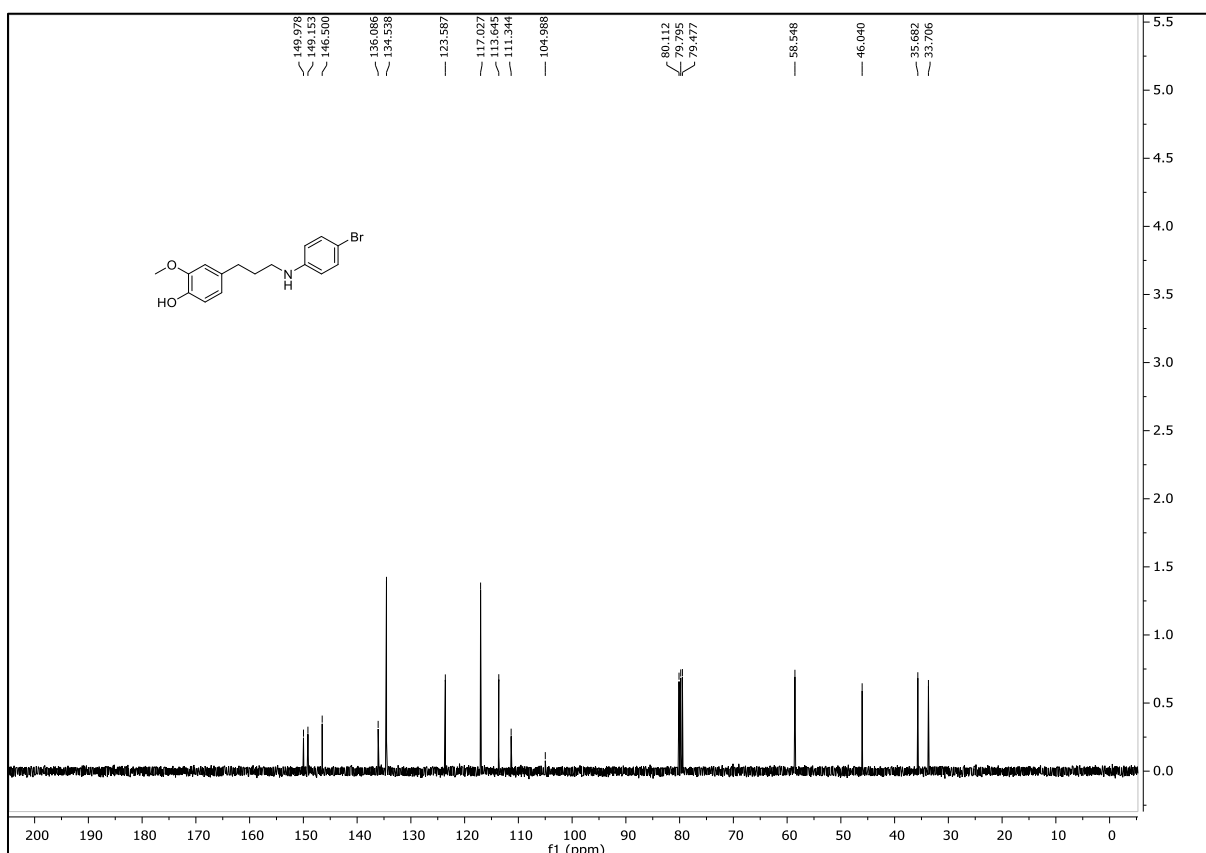
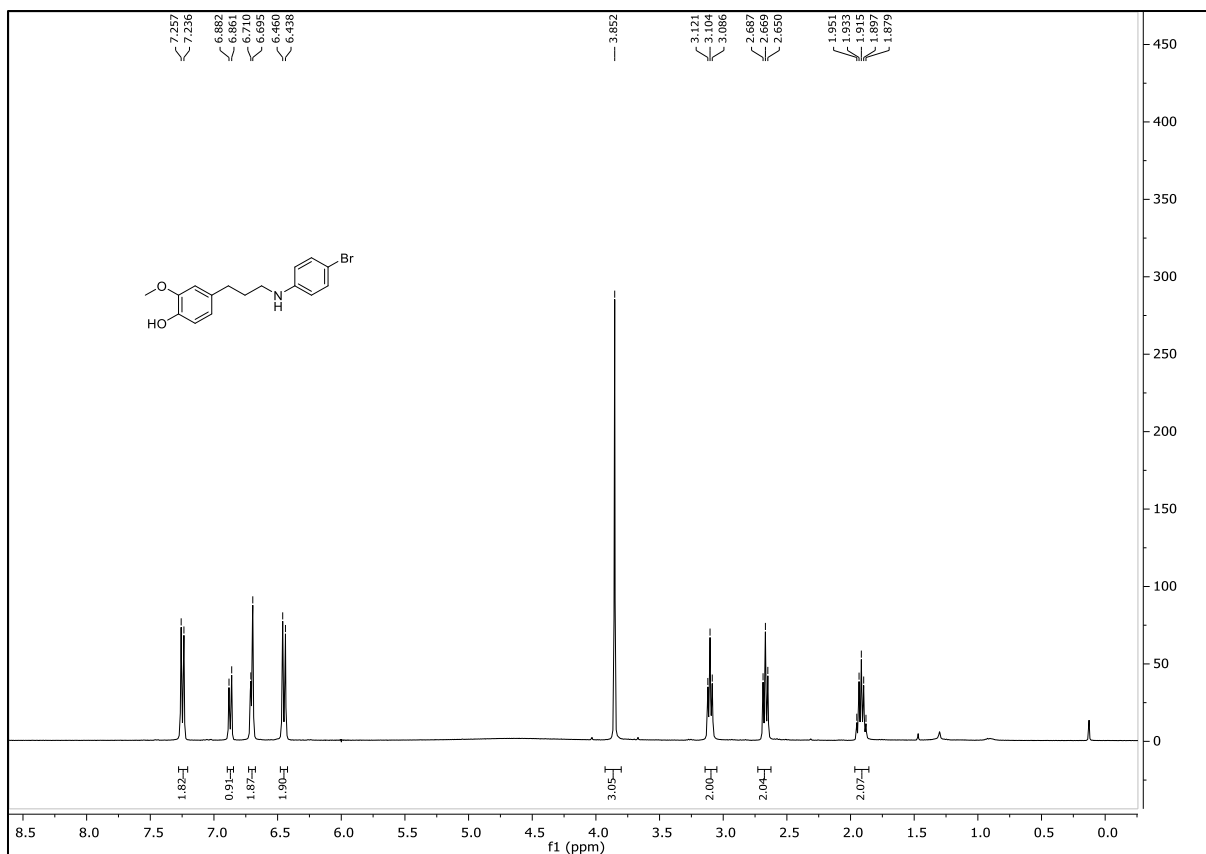
## 10. $^1\text{H}$ and $^{13}\text{C}$ NMR spectra of the isolated compounds



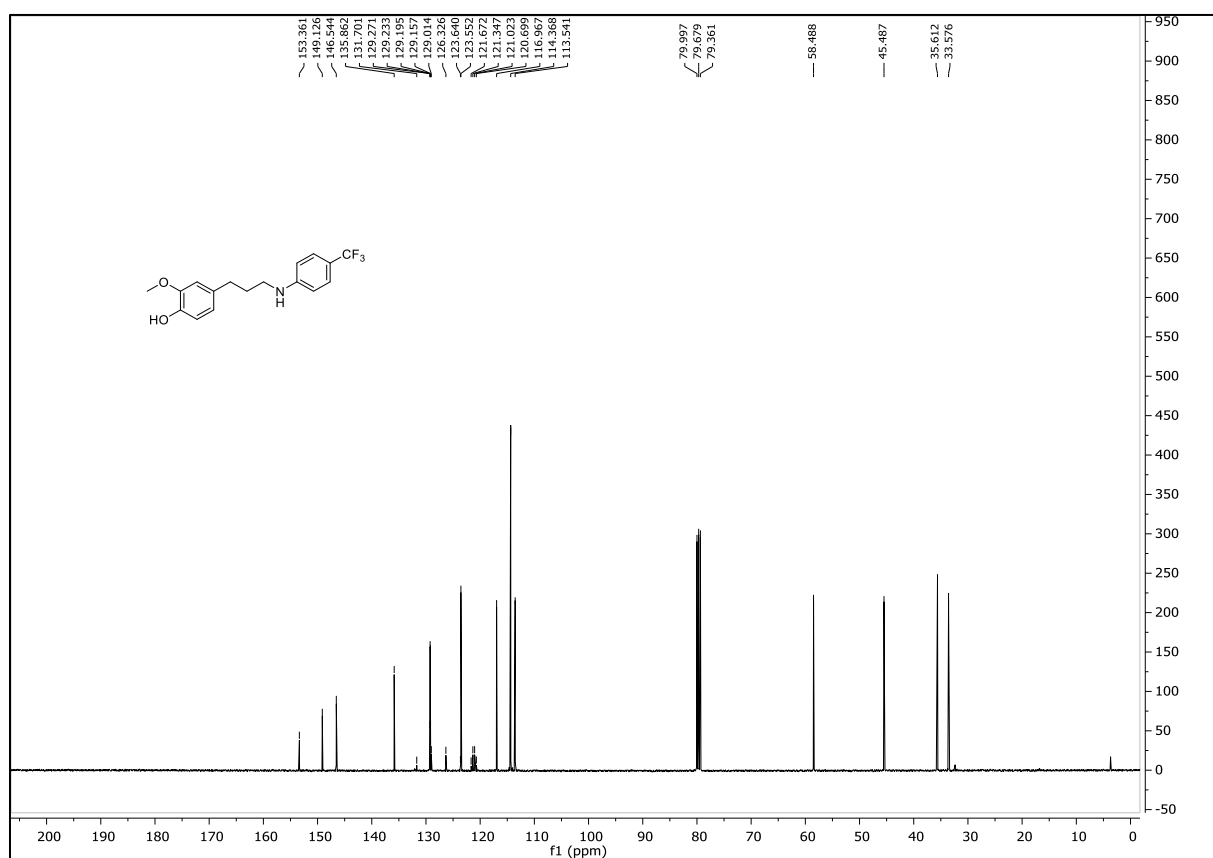
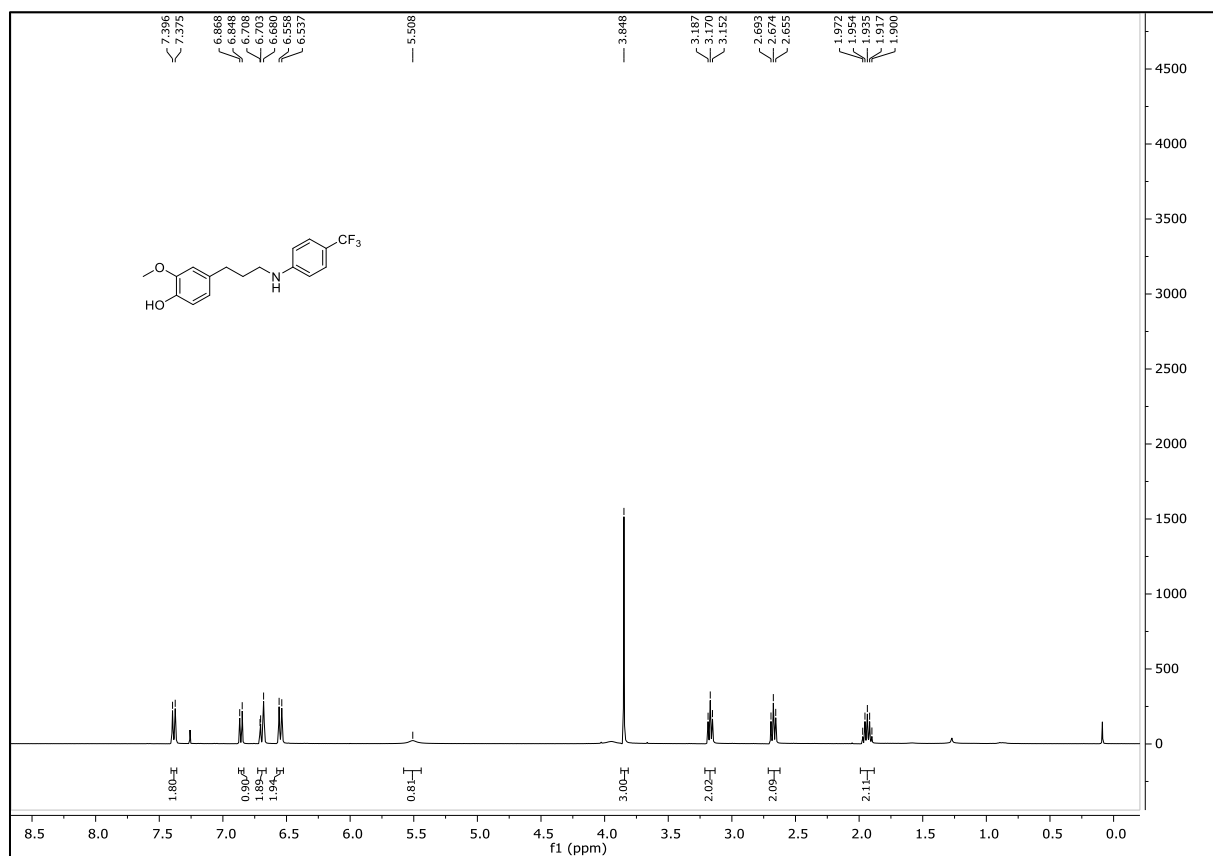
Supplementary Figure 34.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5Ga.



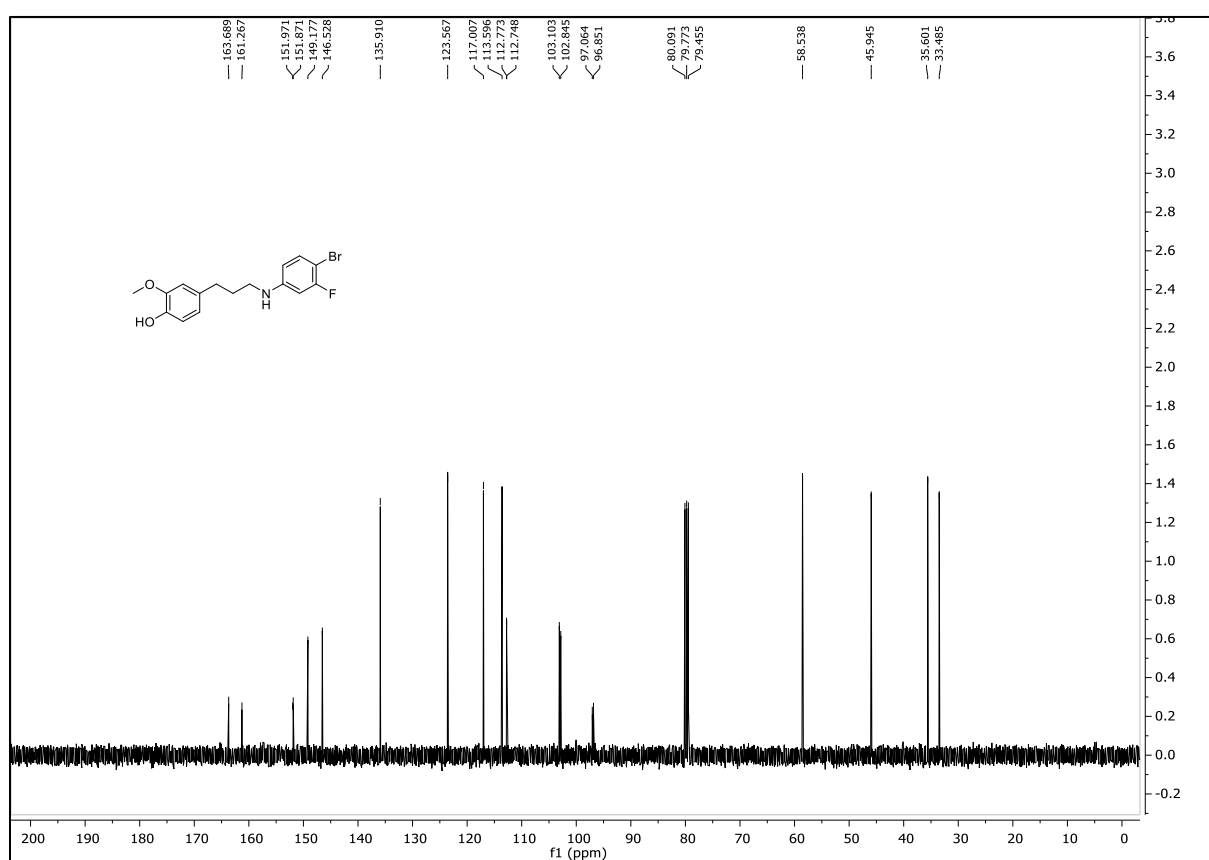
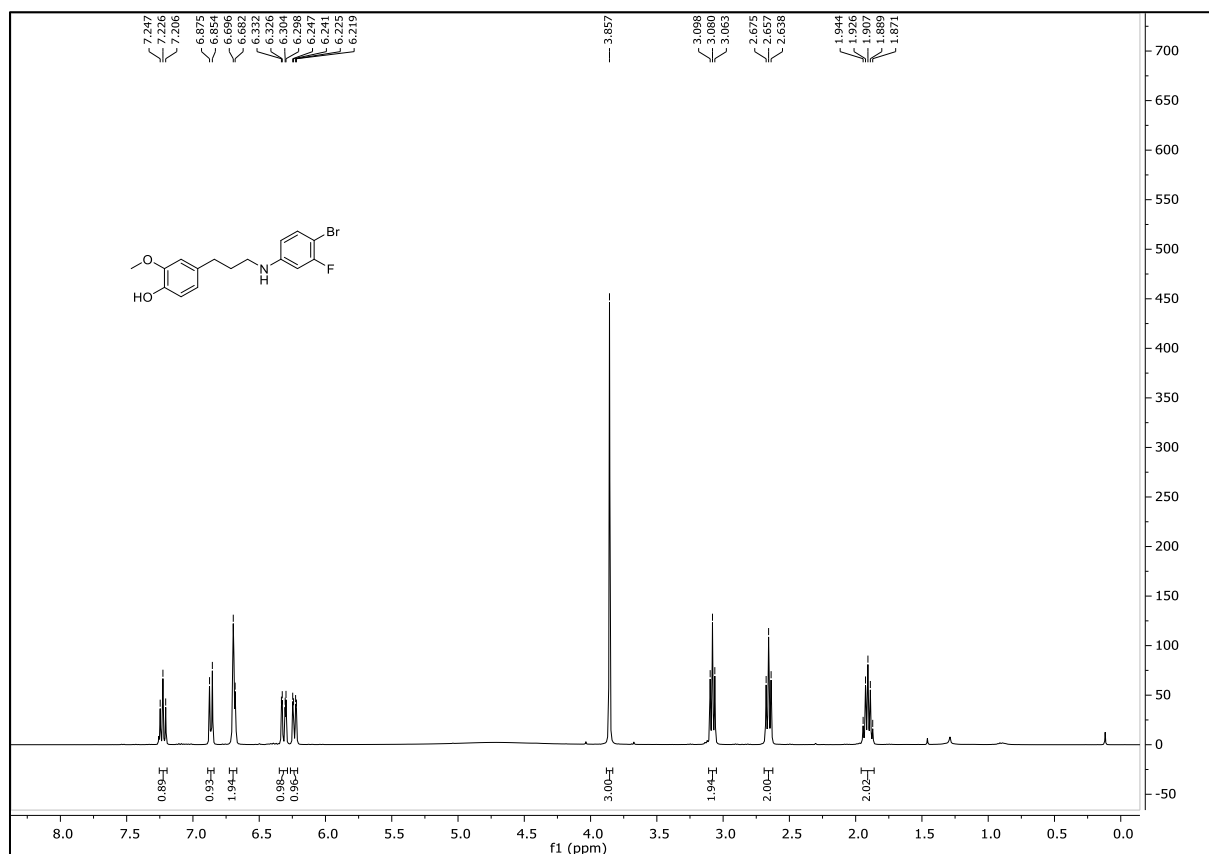
Supplementary Figure 35. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gb.



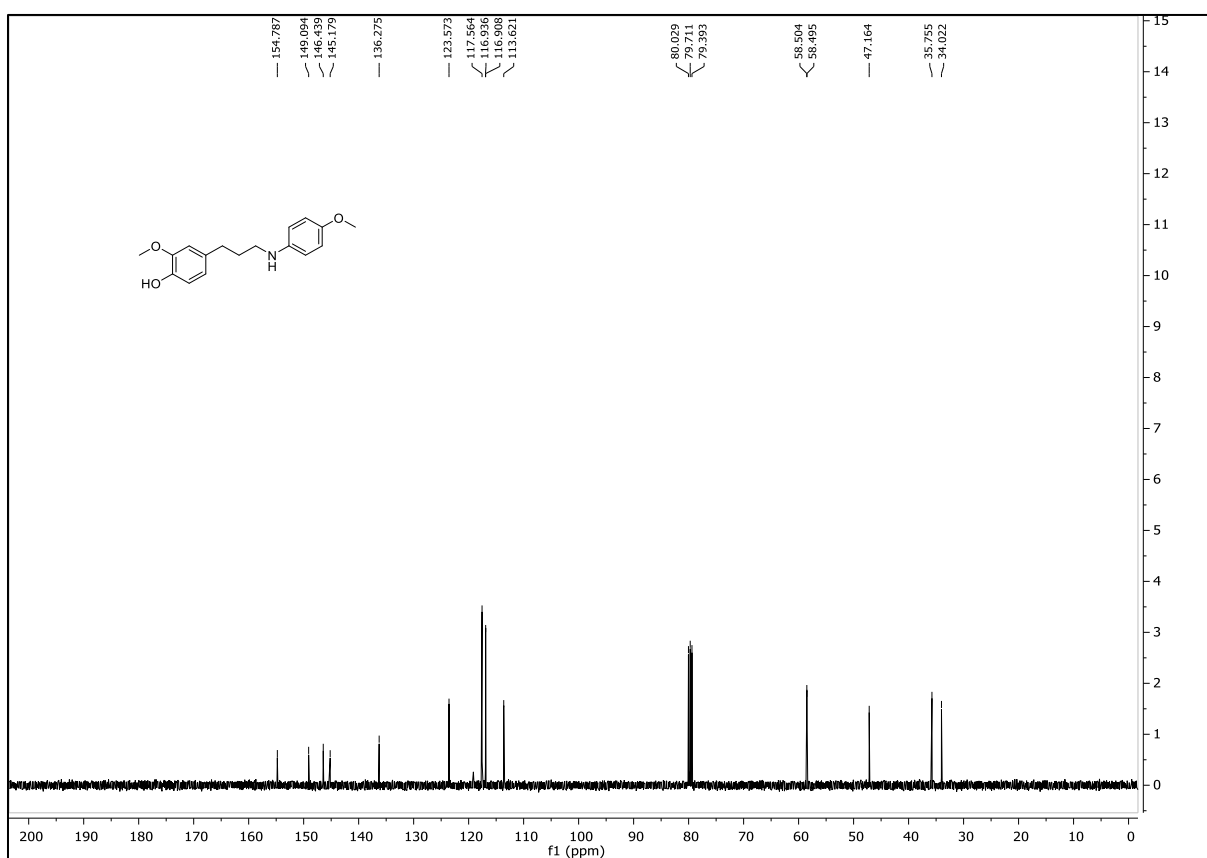
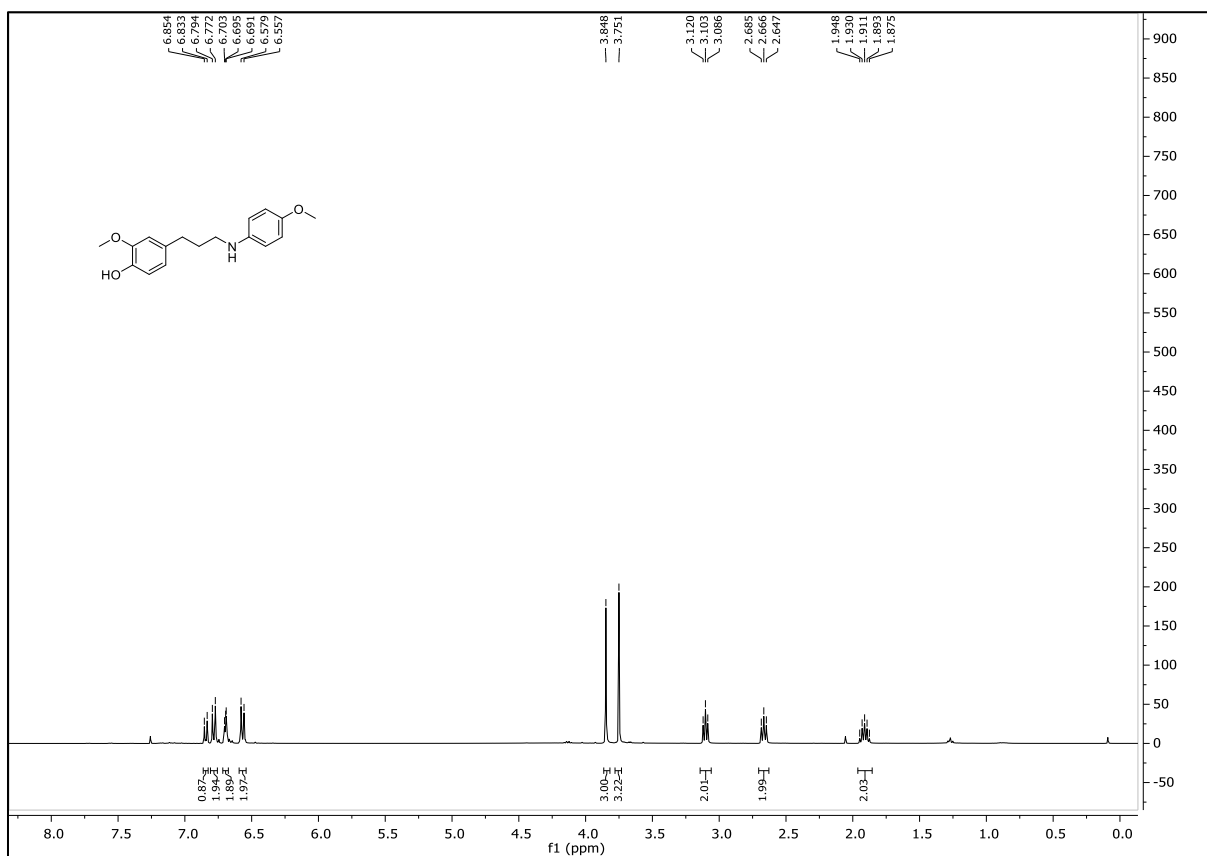
Supplementary Figure 36.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5Gc.



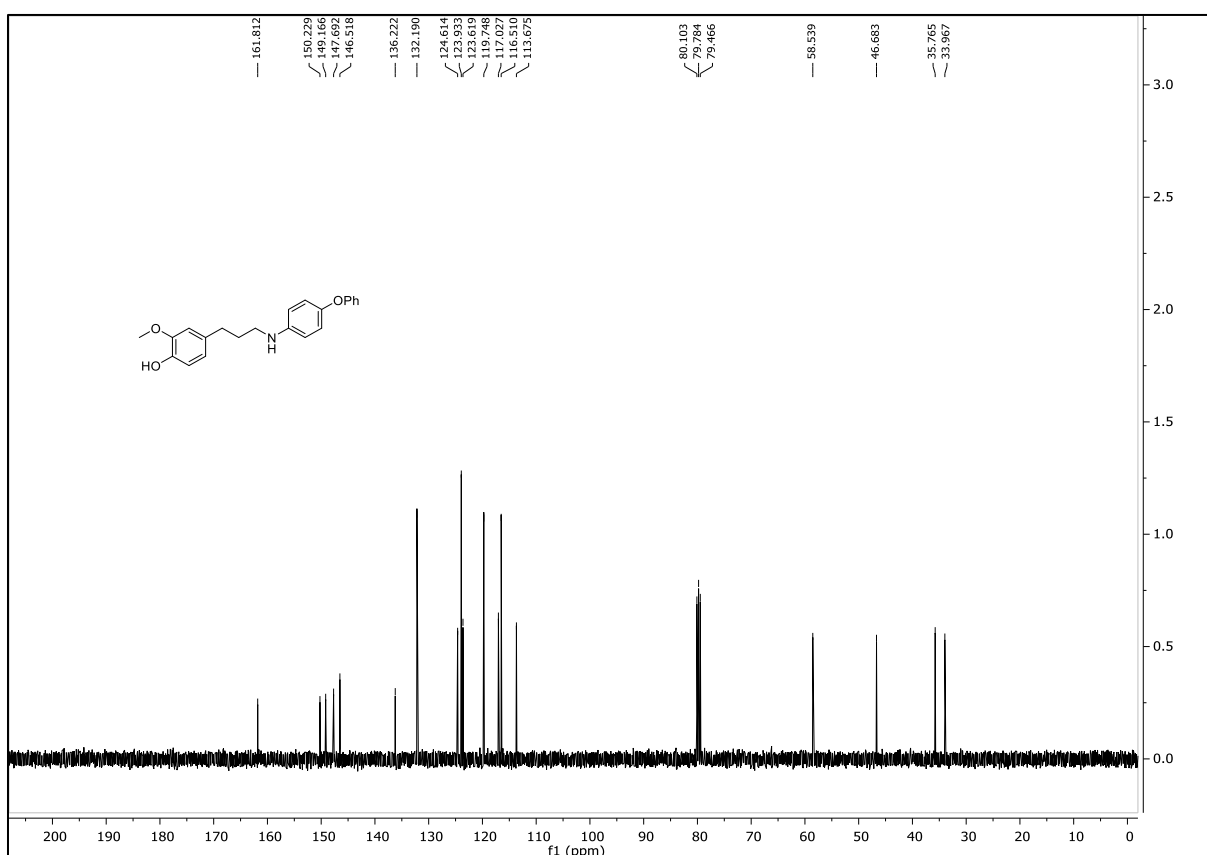
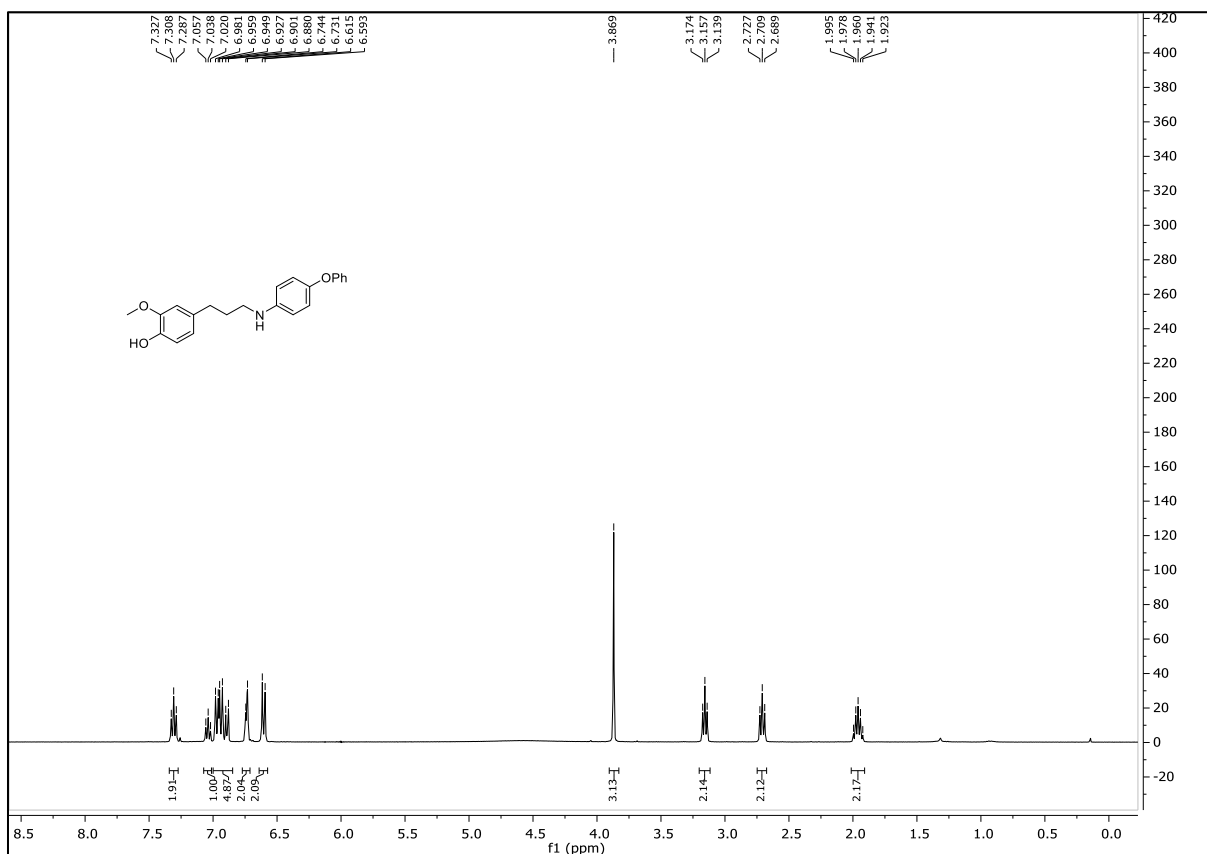
Supplementary Figure 37. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gd.



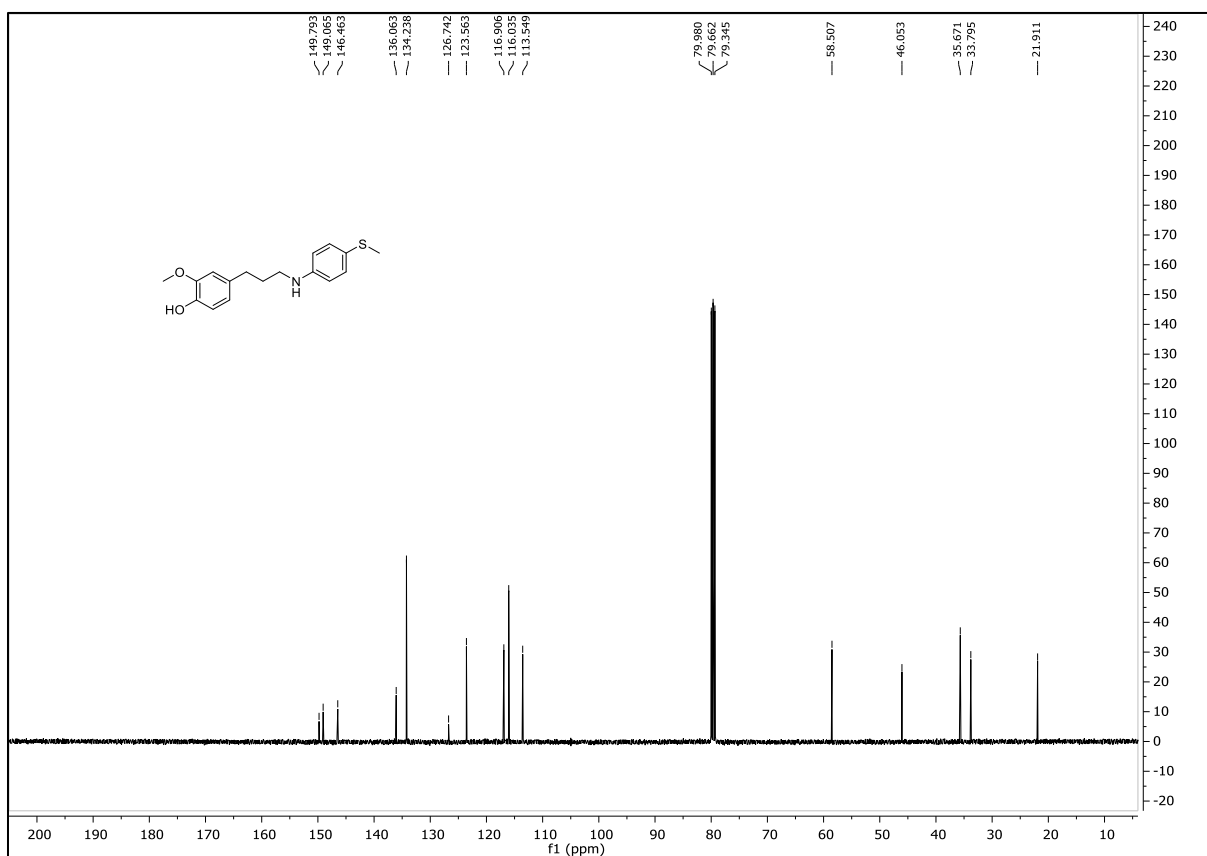
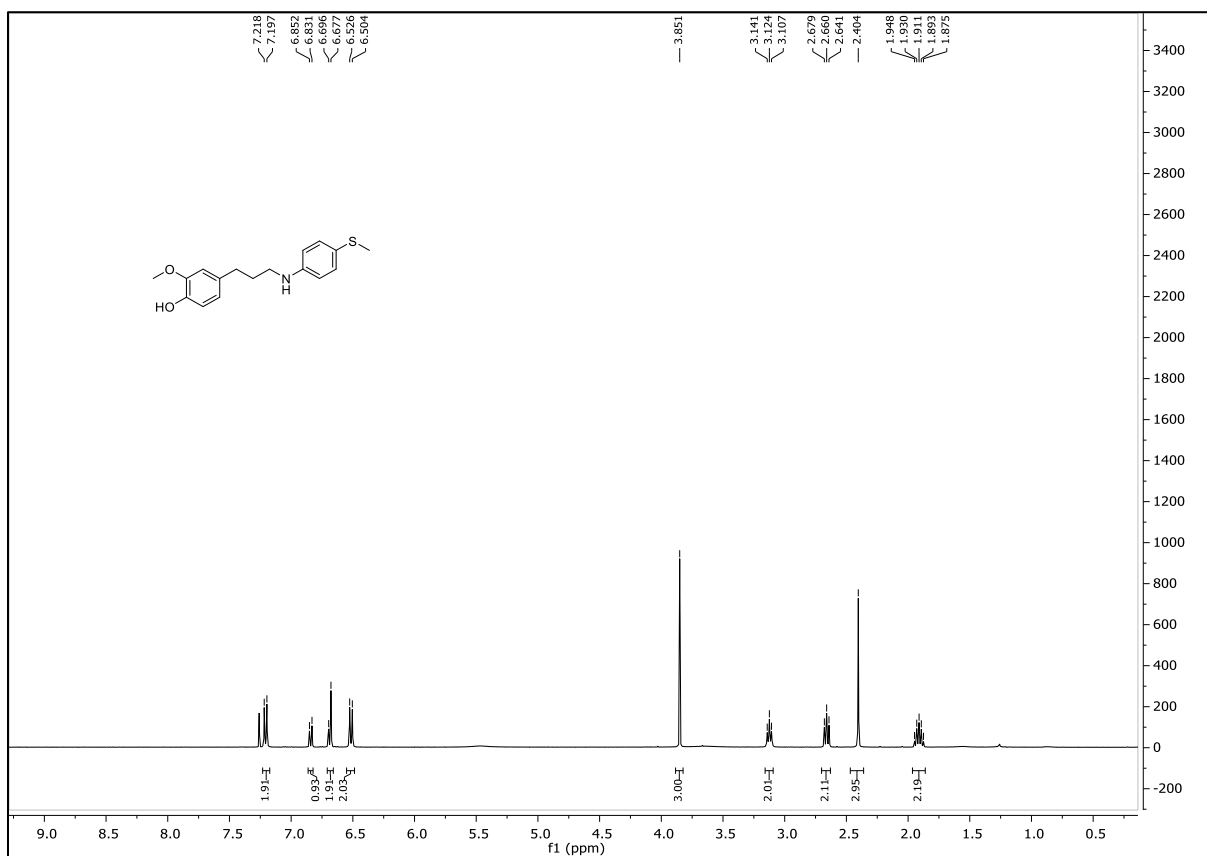
Supplementary Figure 38.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5Ge.



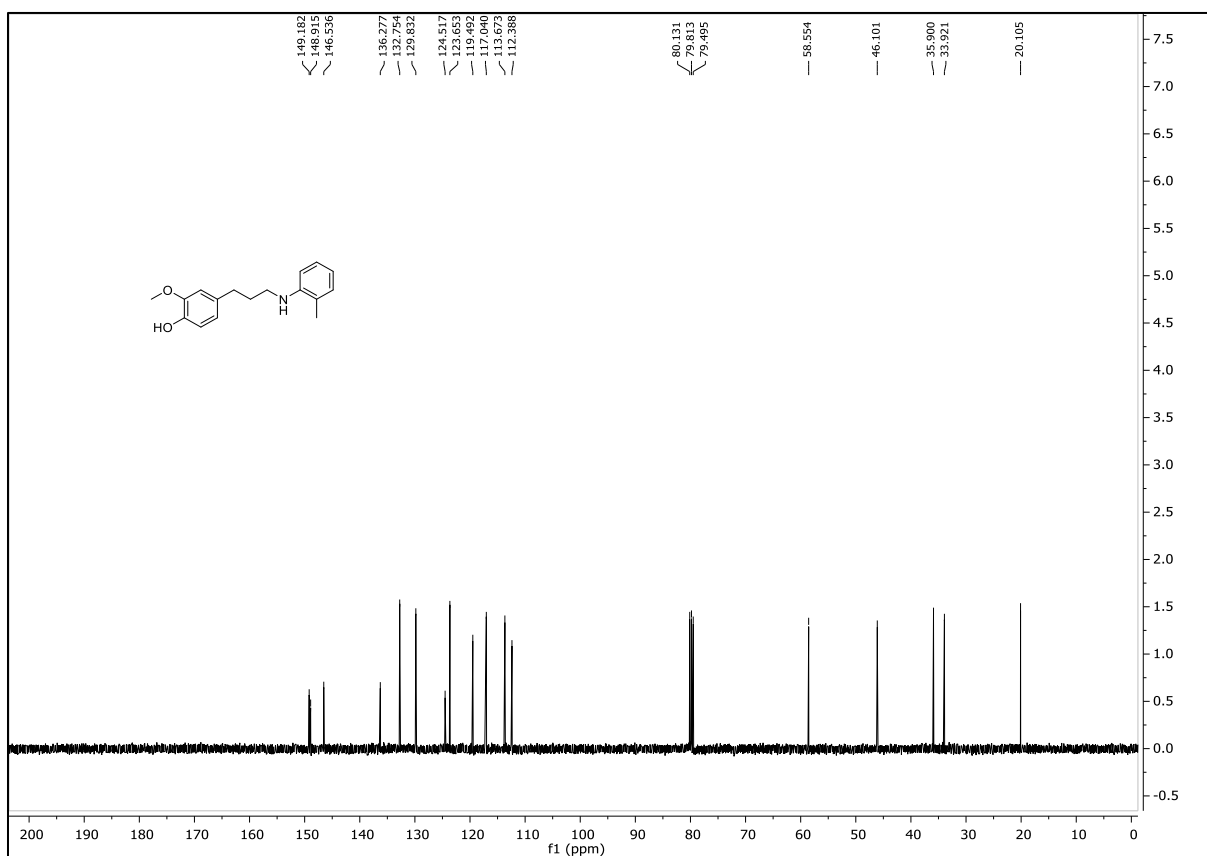
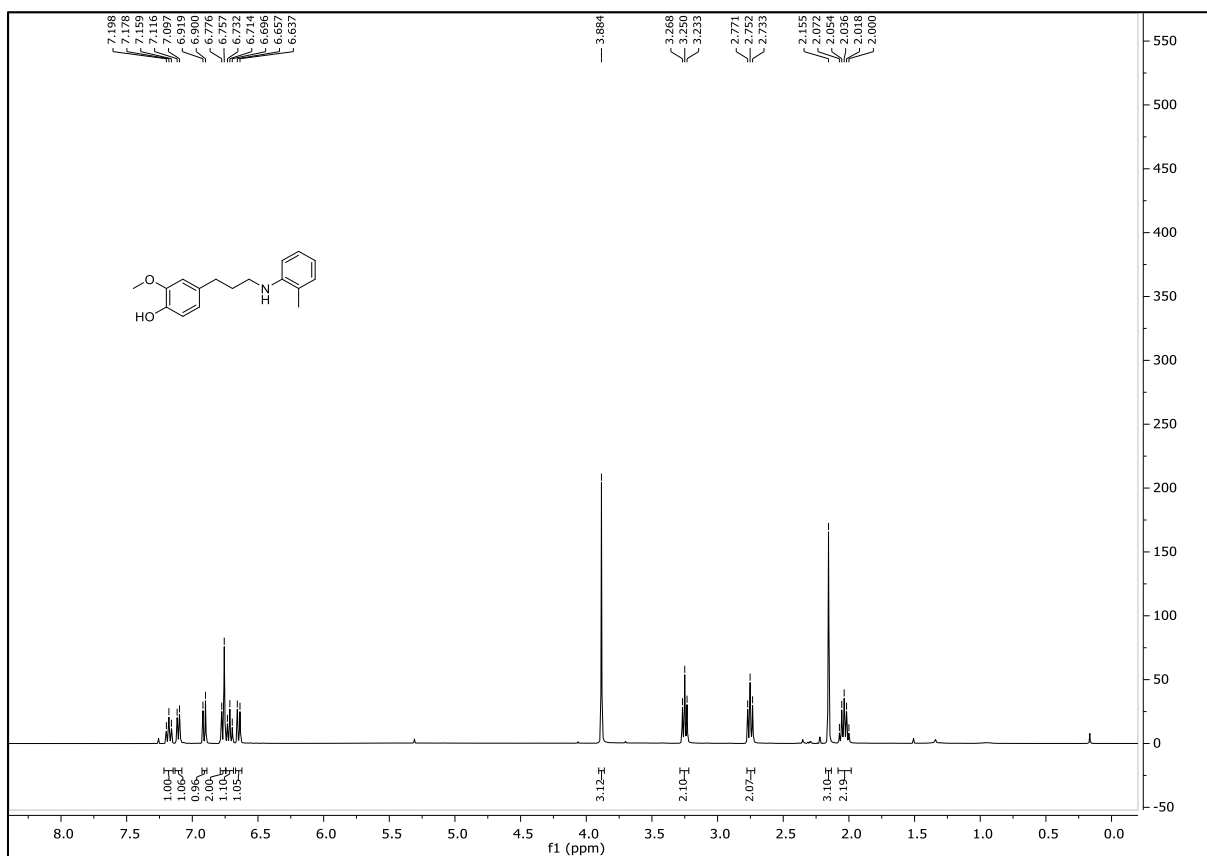
Supplementary Figure 39. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gf.



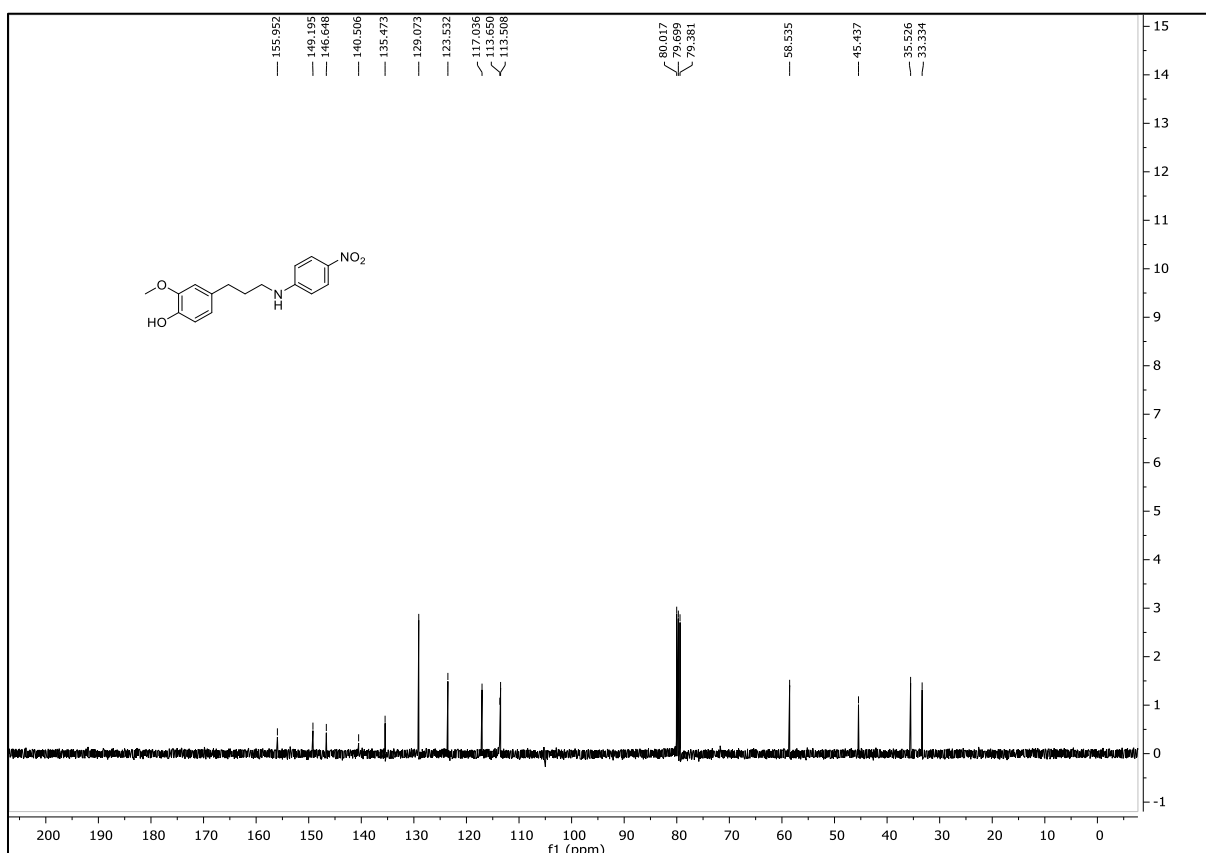
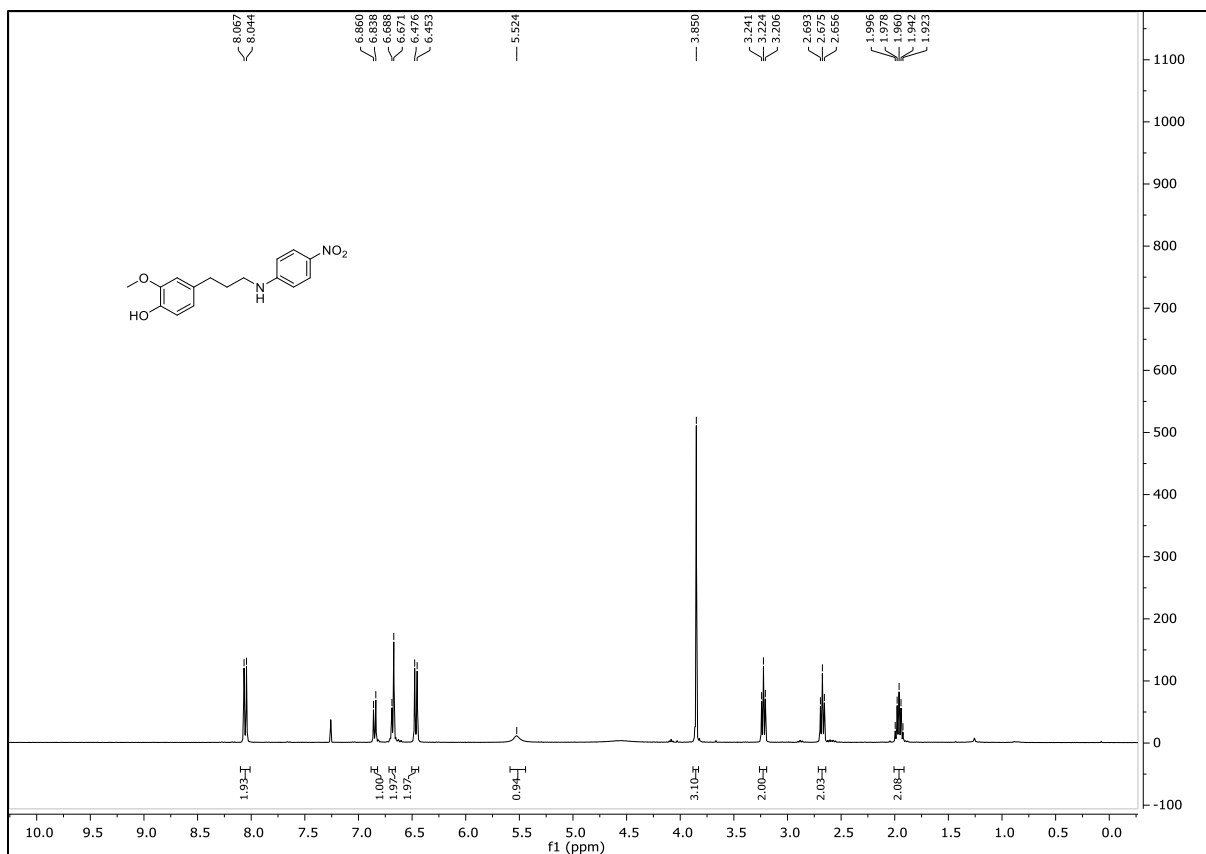
Supplementary Figure 40. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gg.



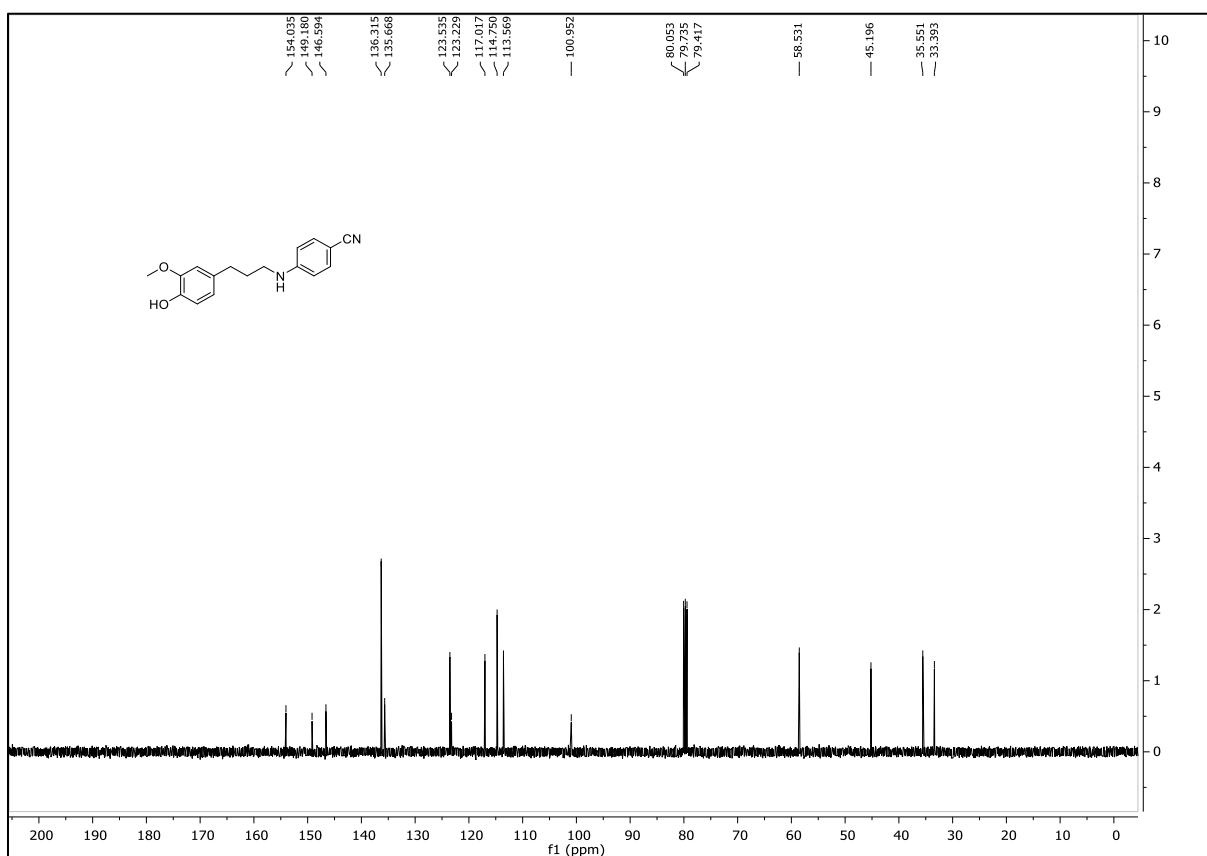
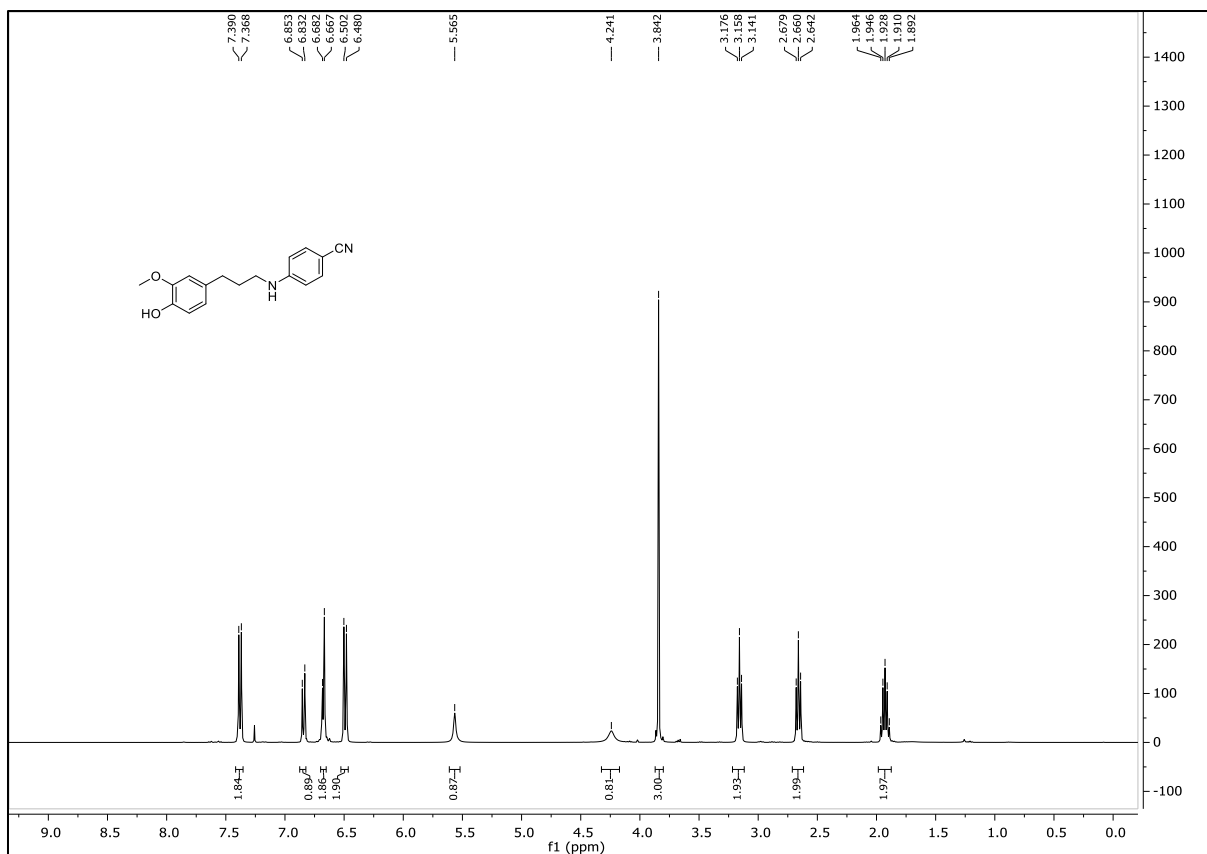
Supplementary Figure 41. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gh.



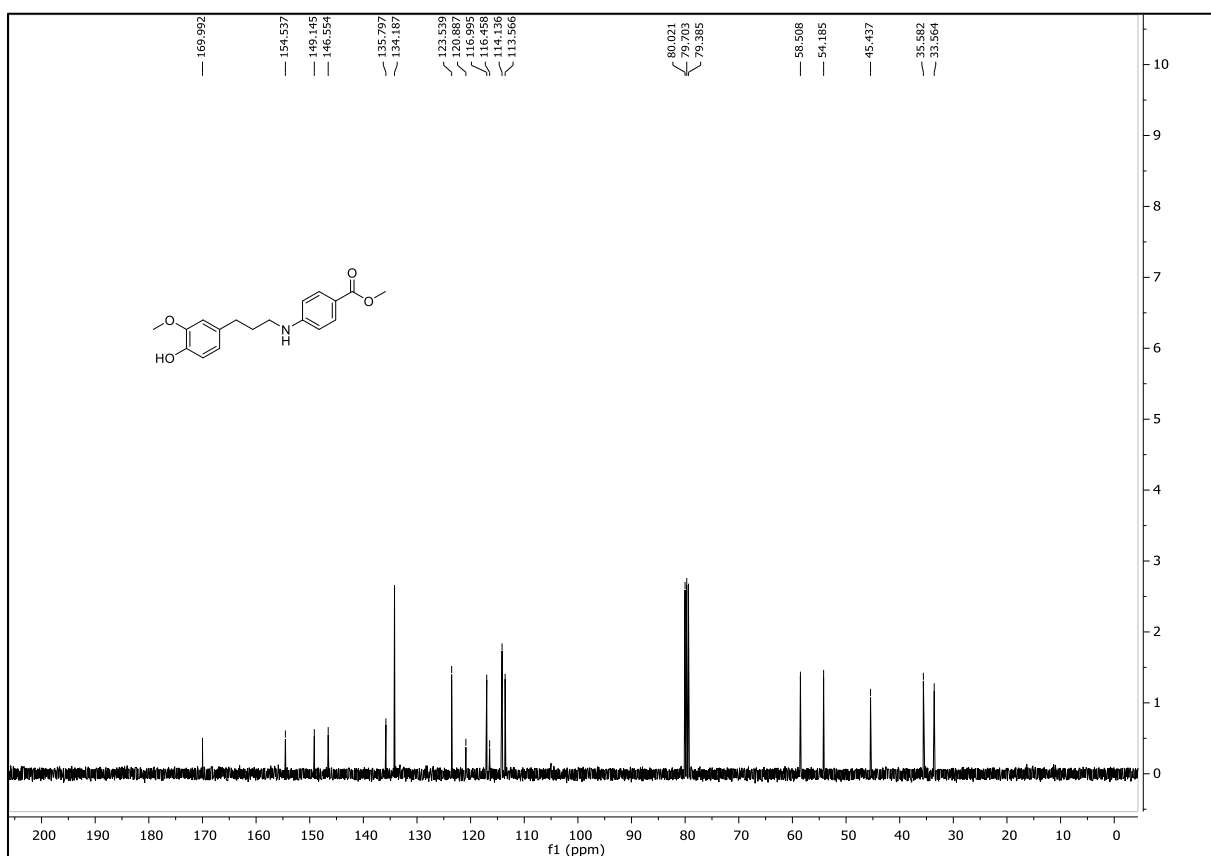
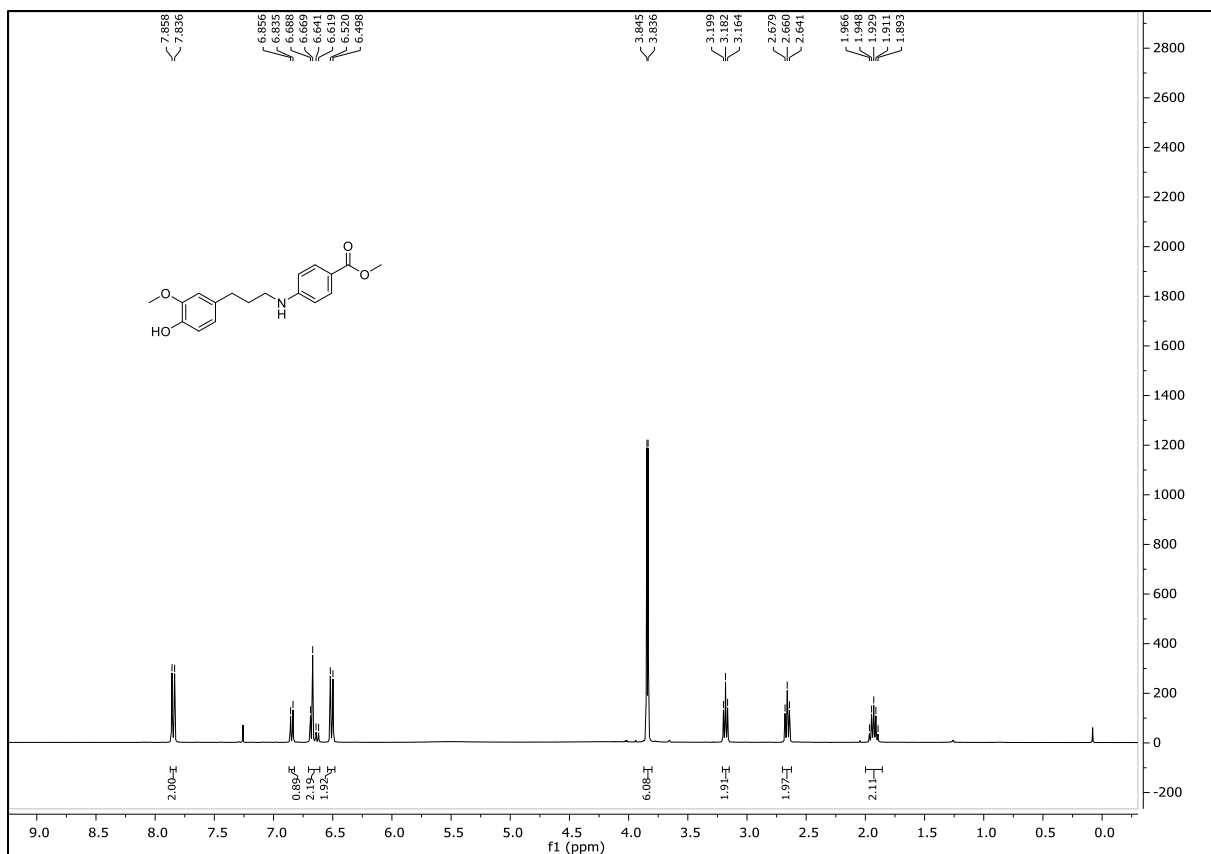
Supplementary Figure 42. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gi.



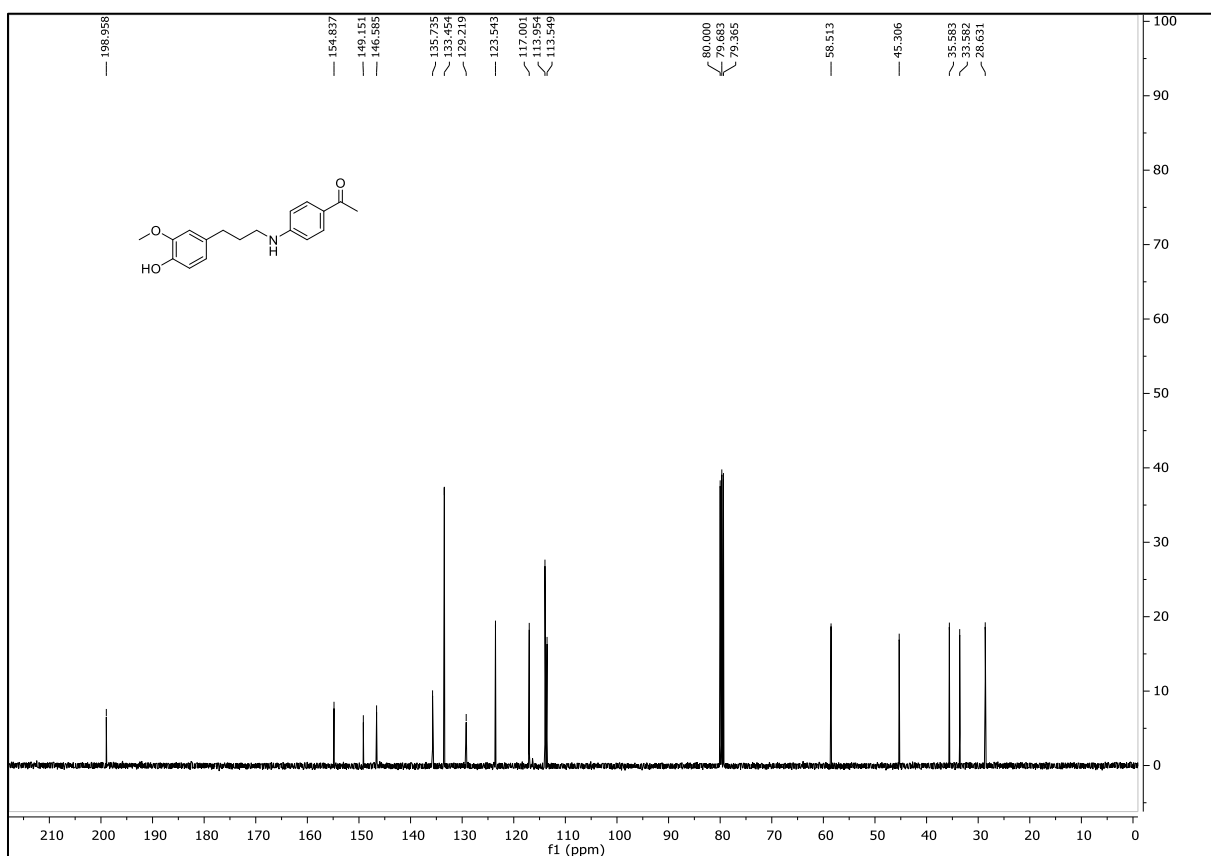
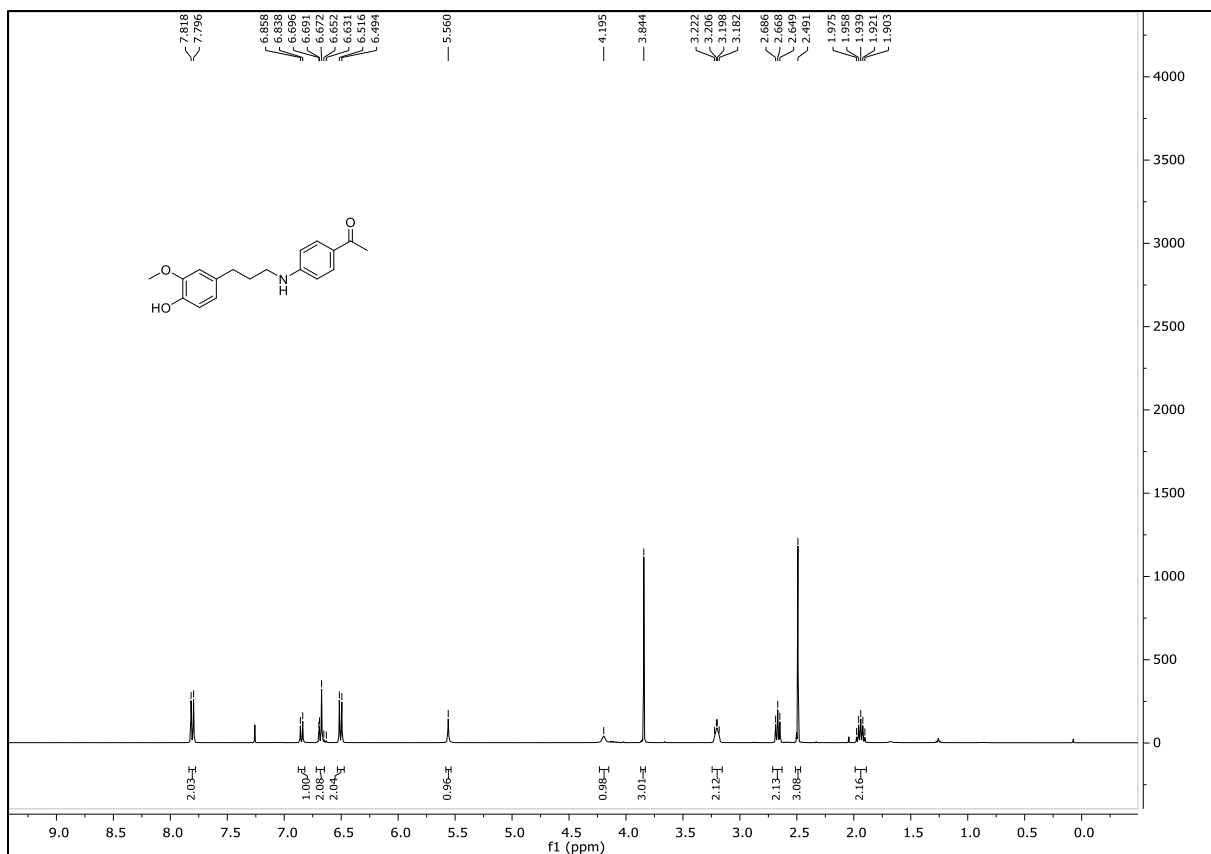
Supplementary Figure 43. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gj.



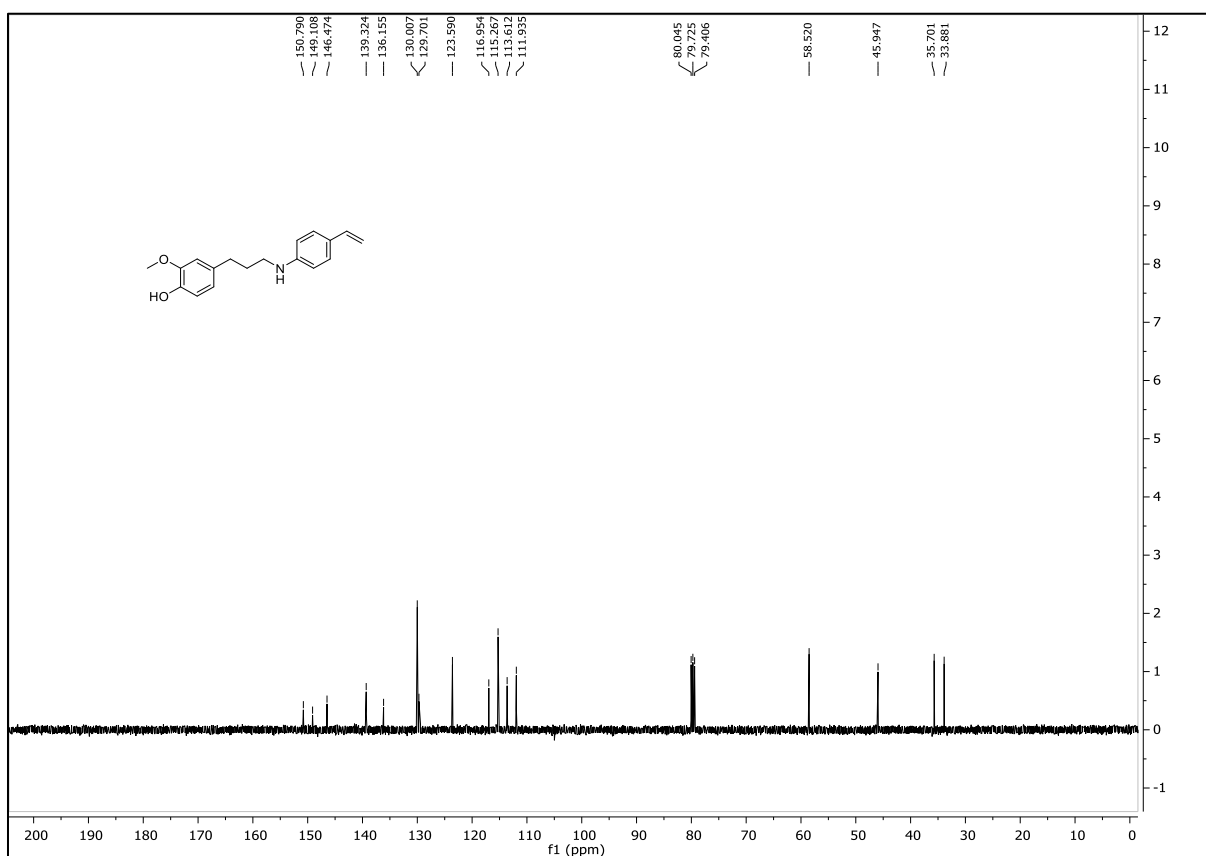
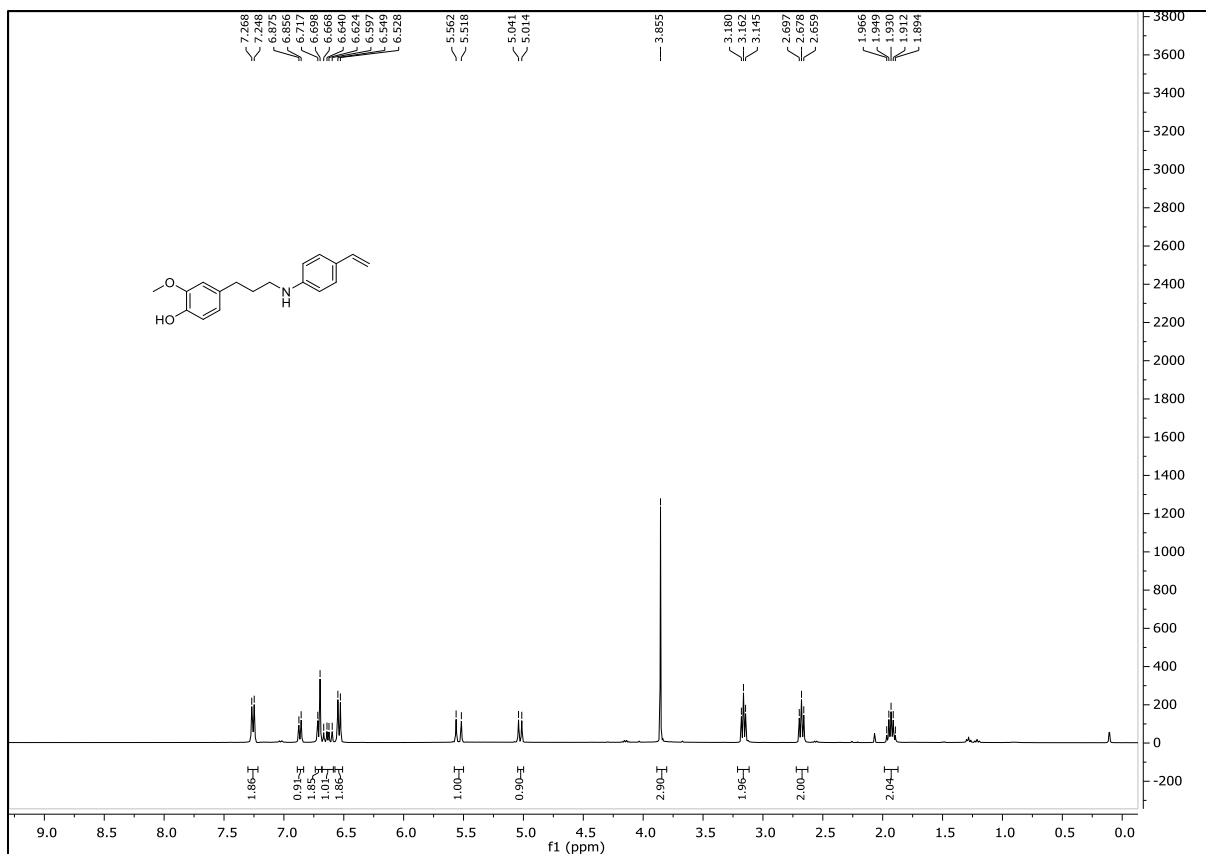
Supplementary Figure 44. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gk.



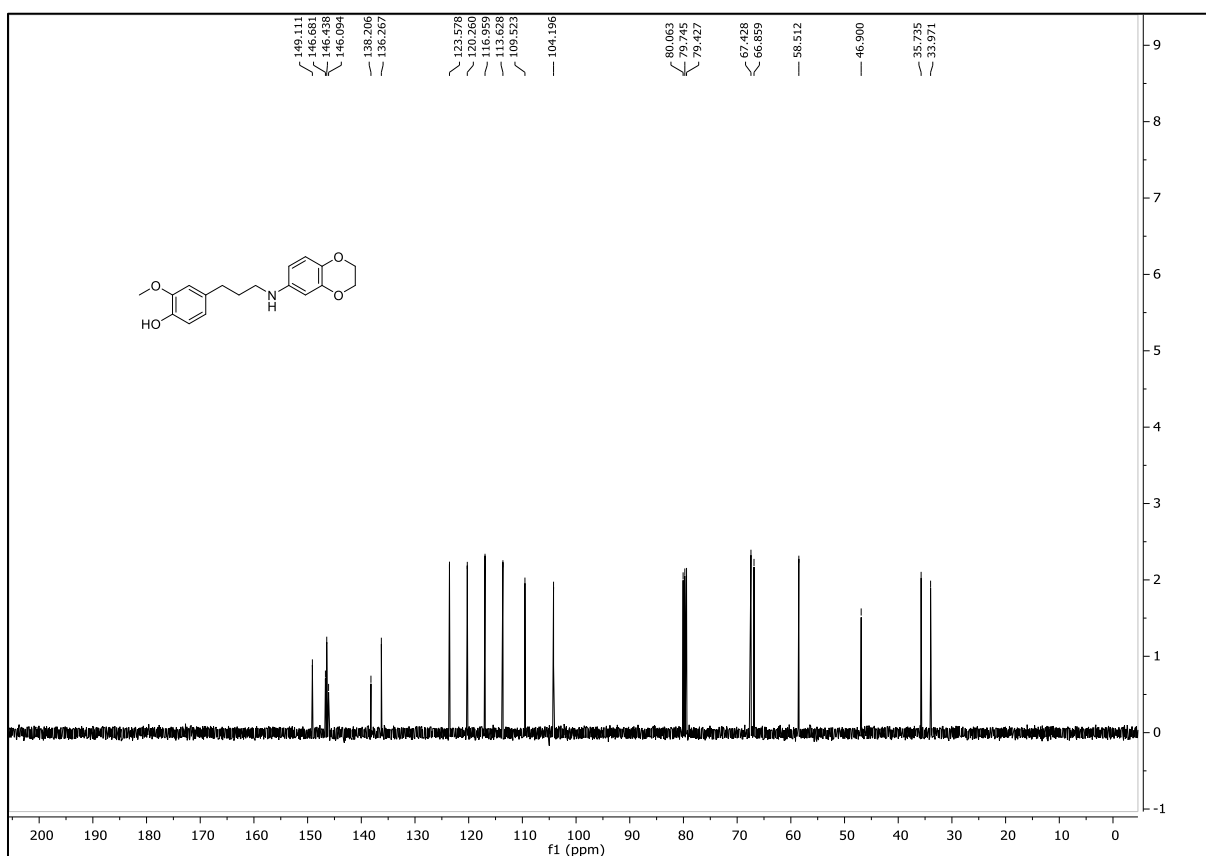
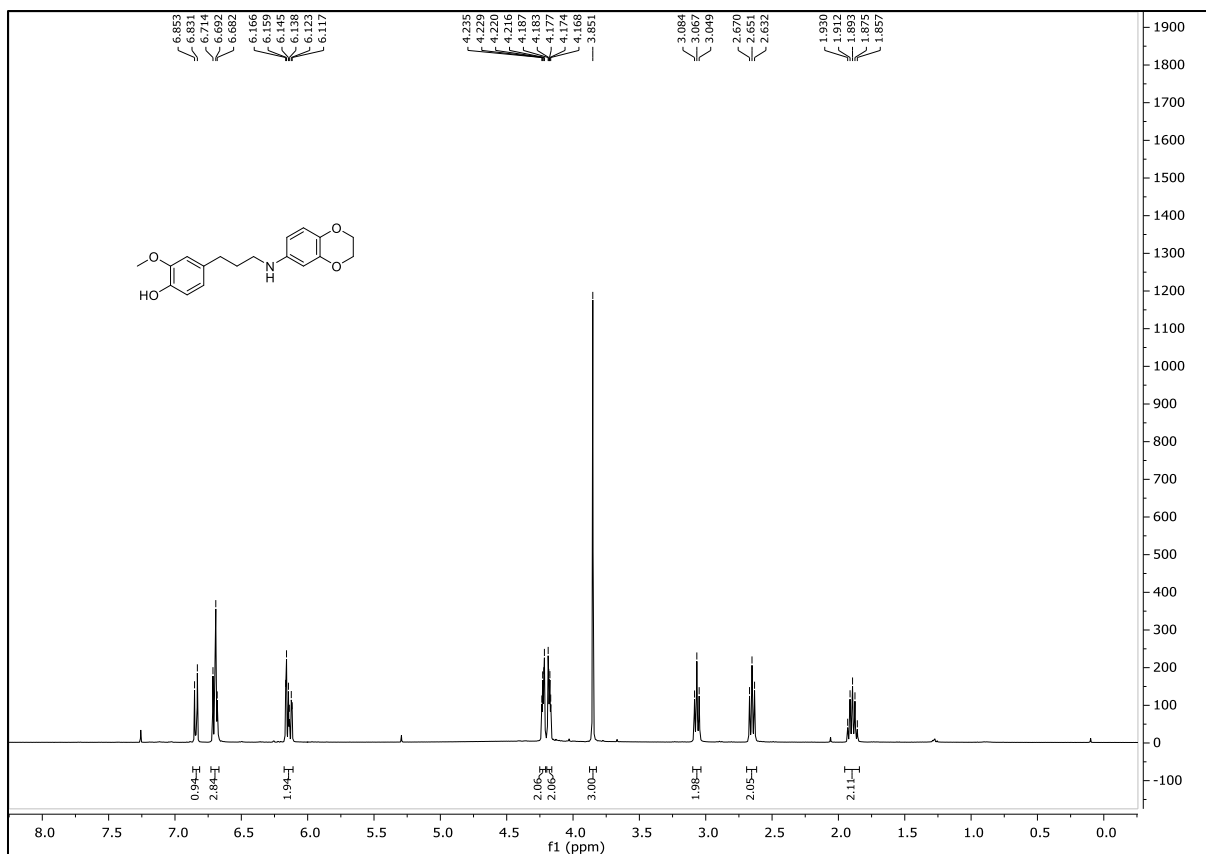
Supplementary Figure 45.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5GI.



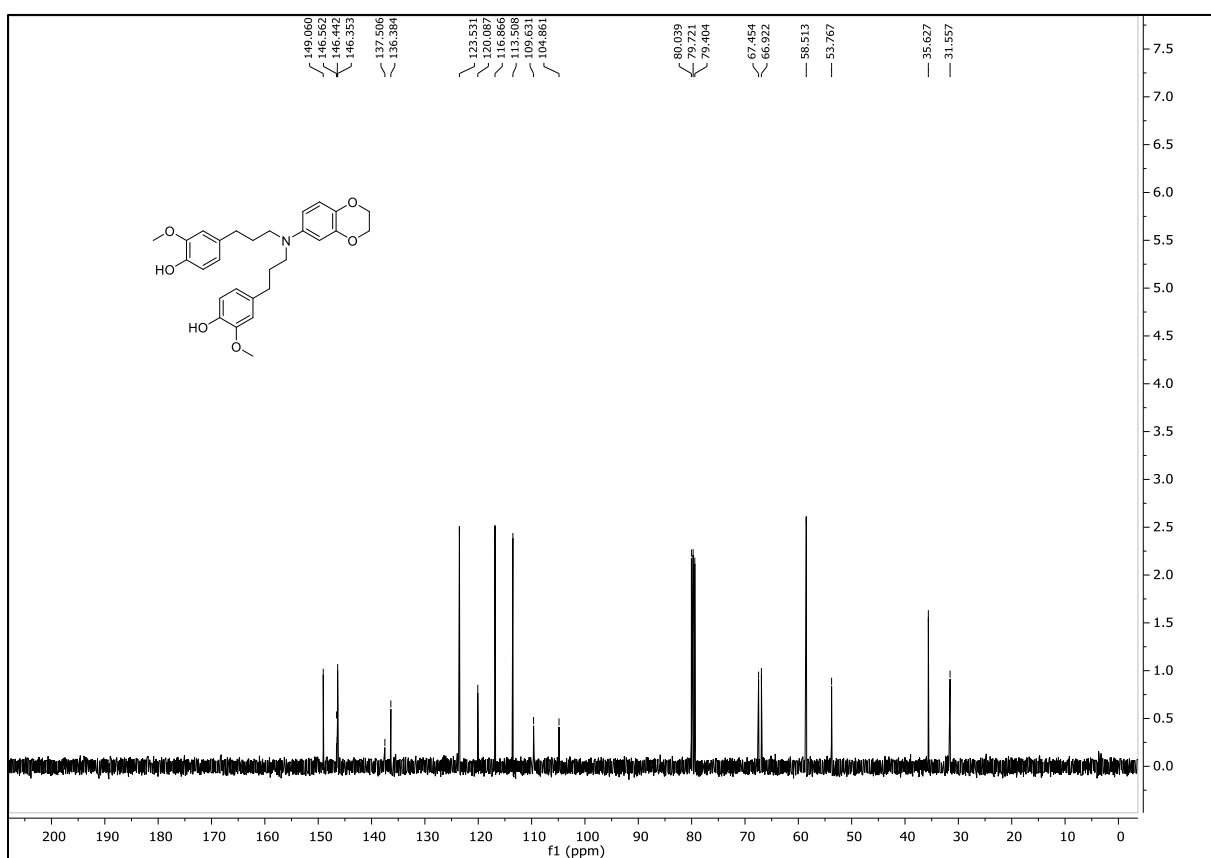
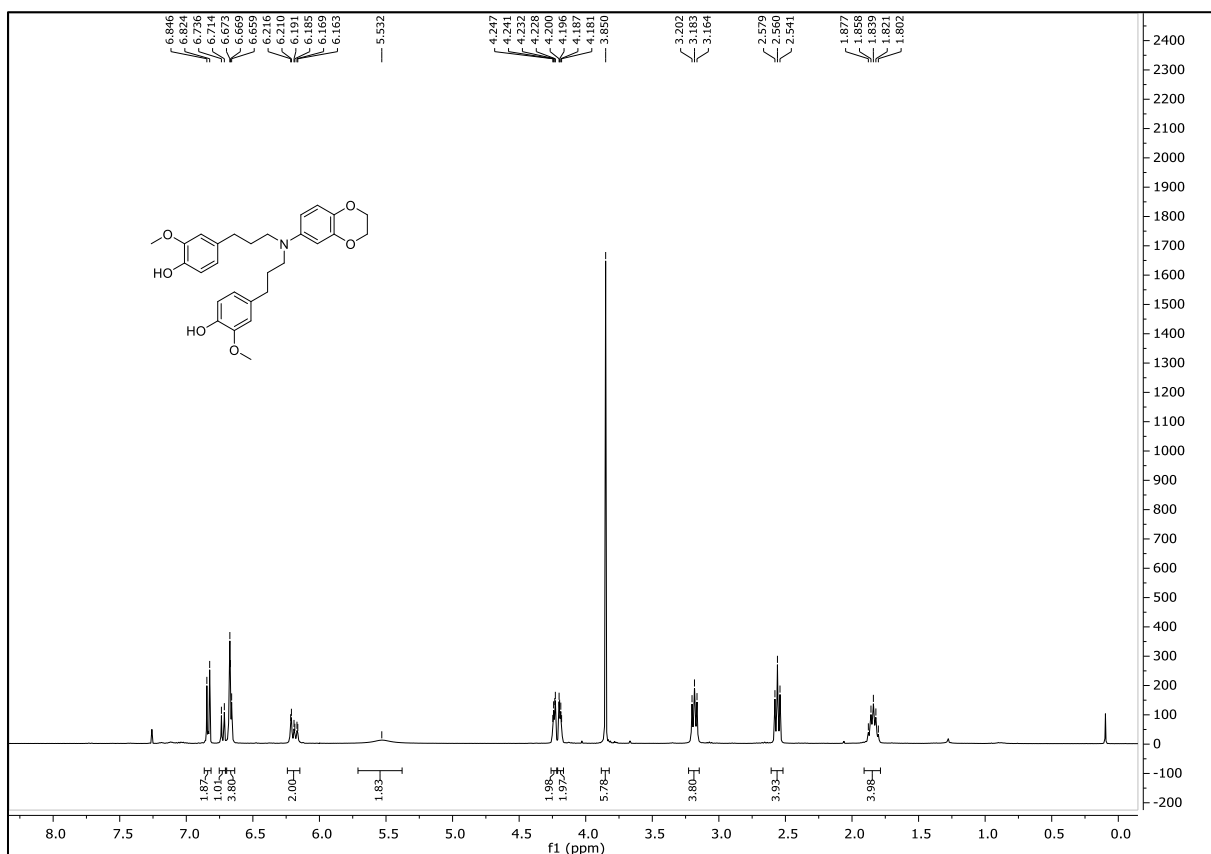
Supplementary Figure 46.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5Gm.



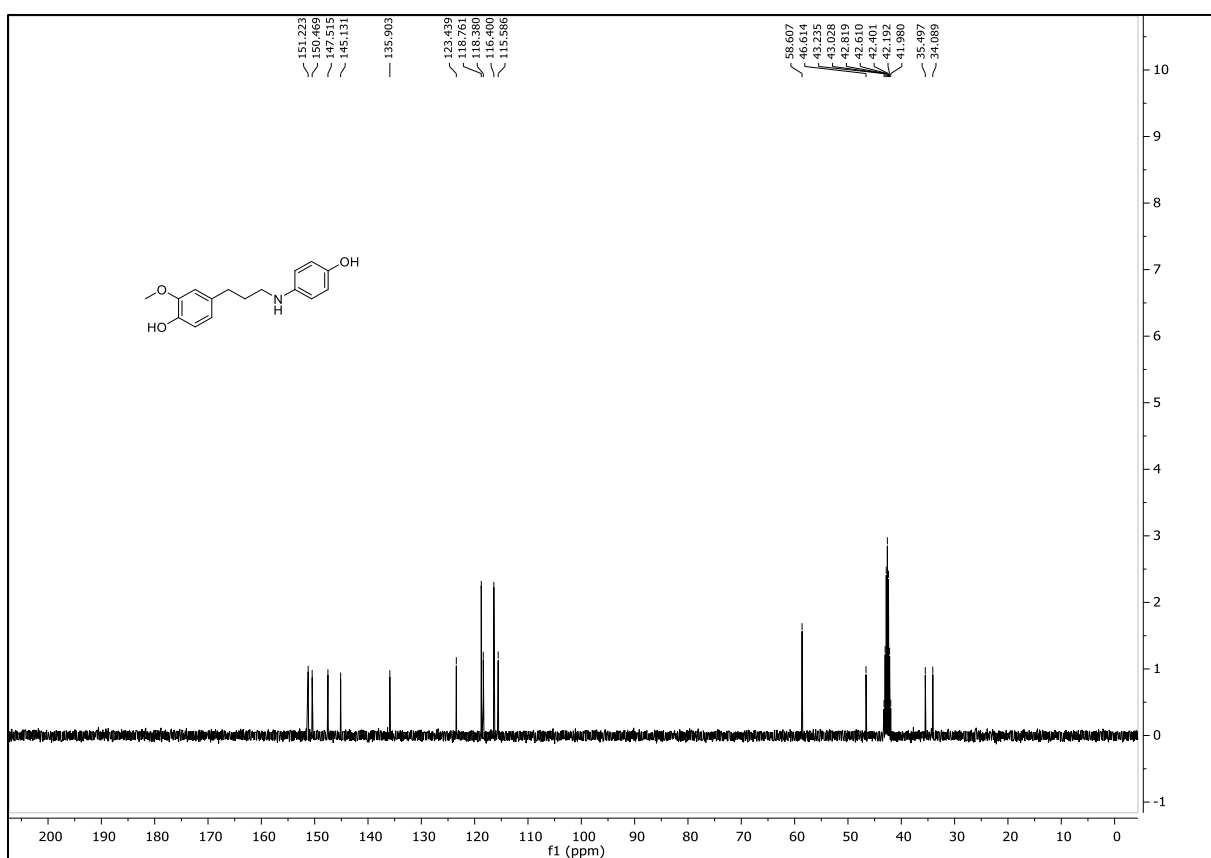
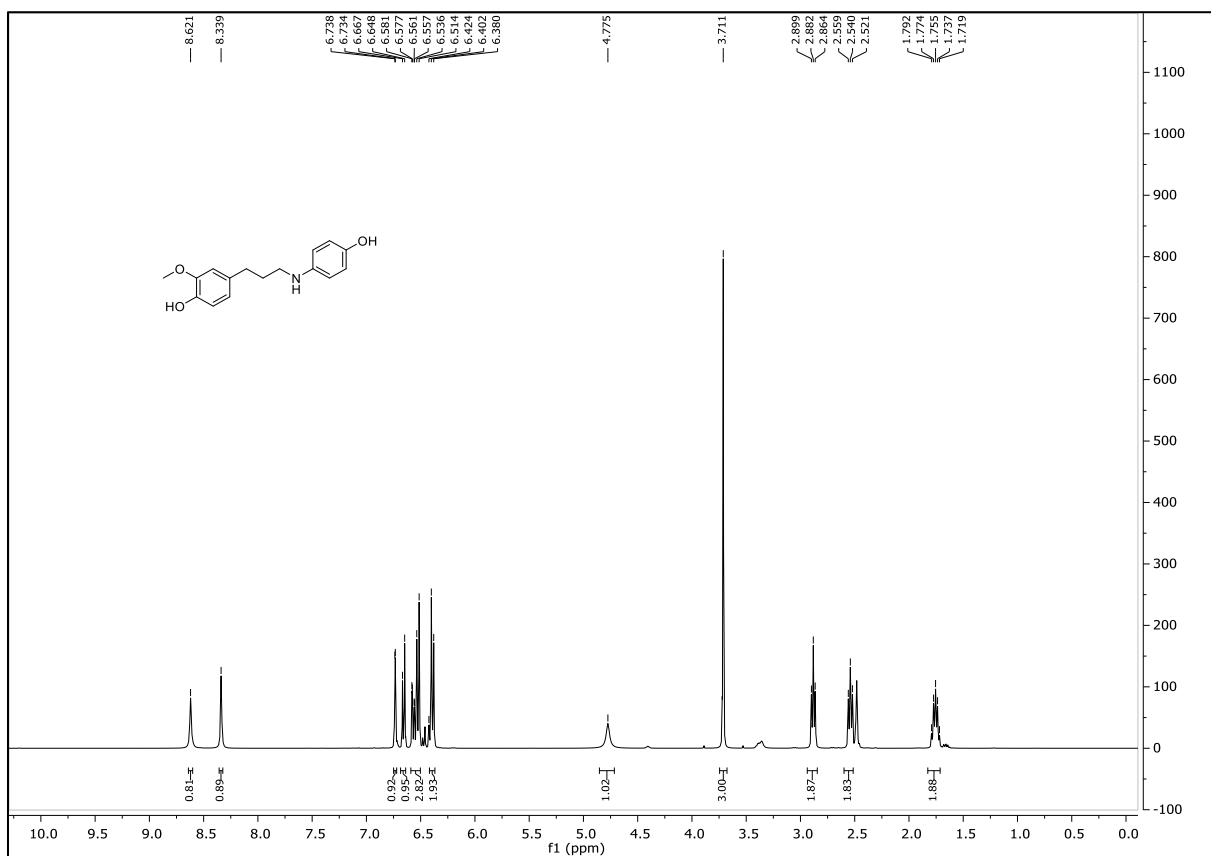
Supplementary Figure 47.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5Gn.



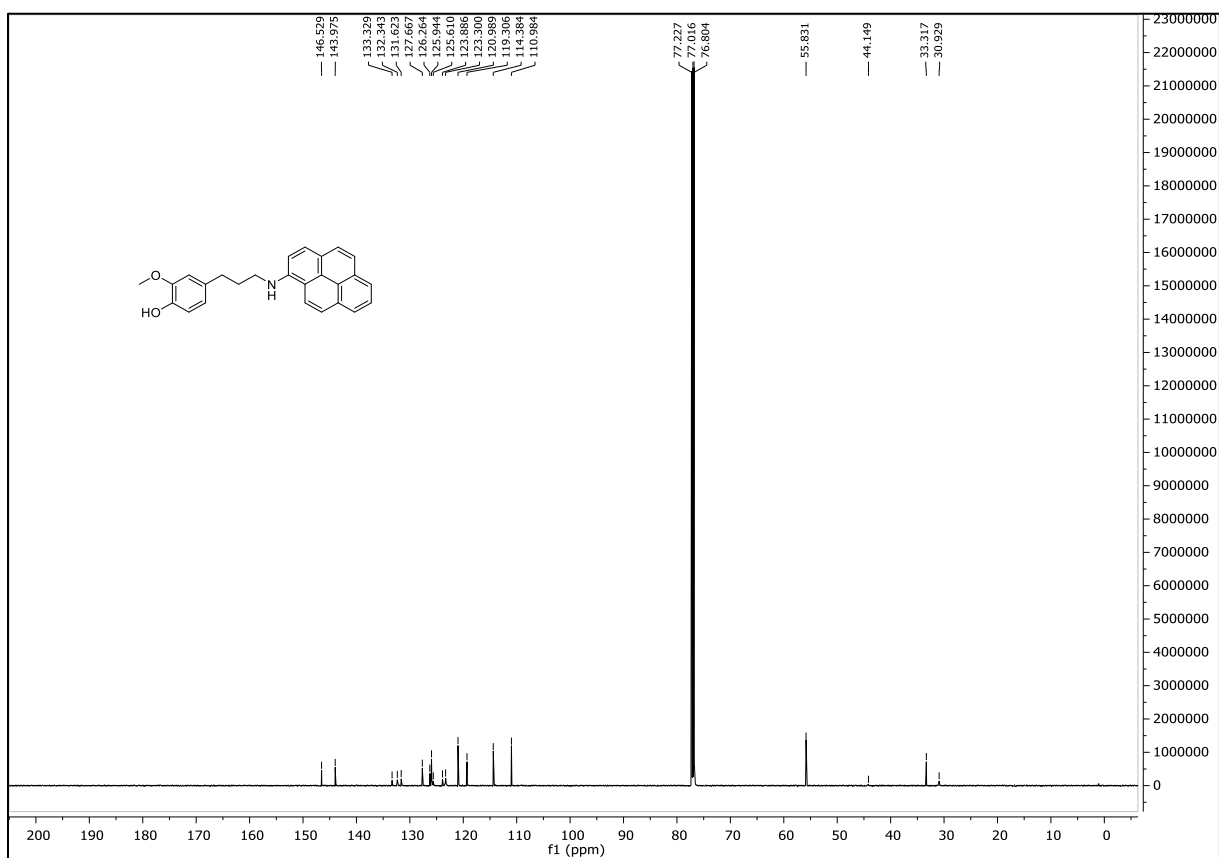
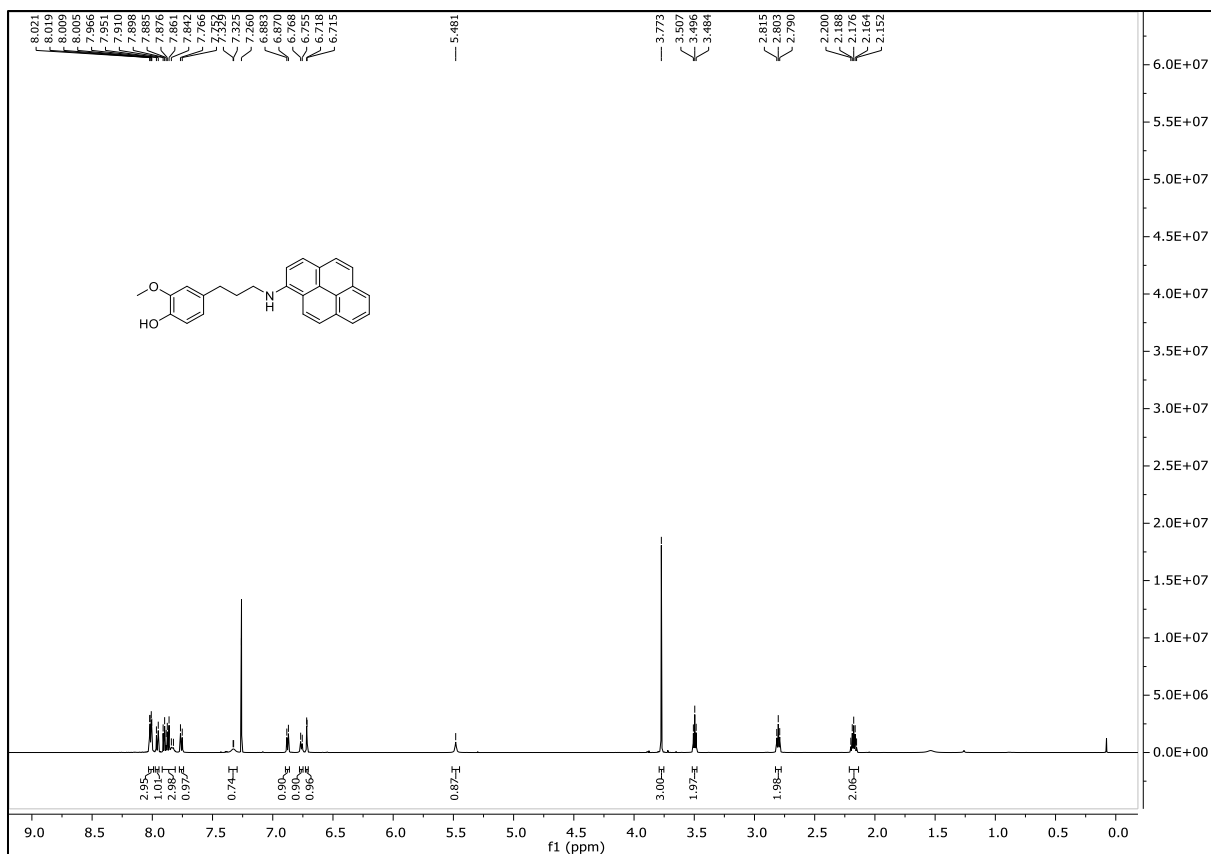
Supplementary Figure 48. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Go.



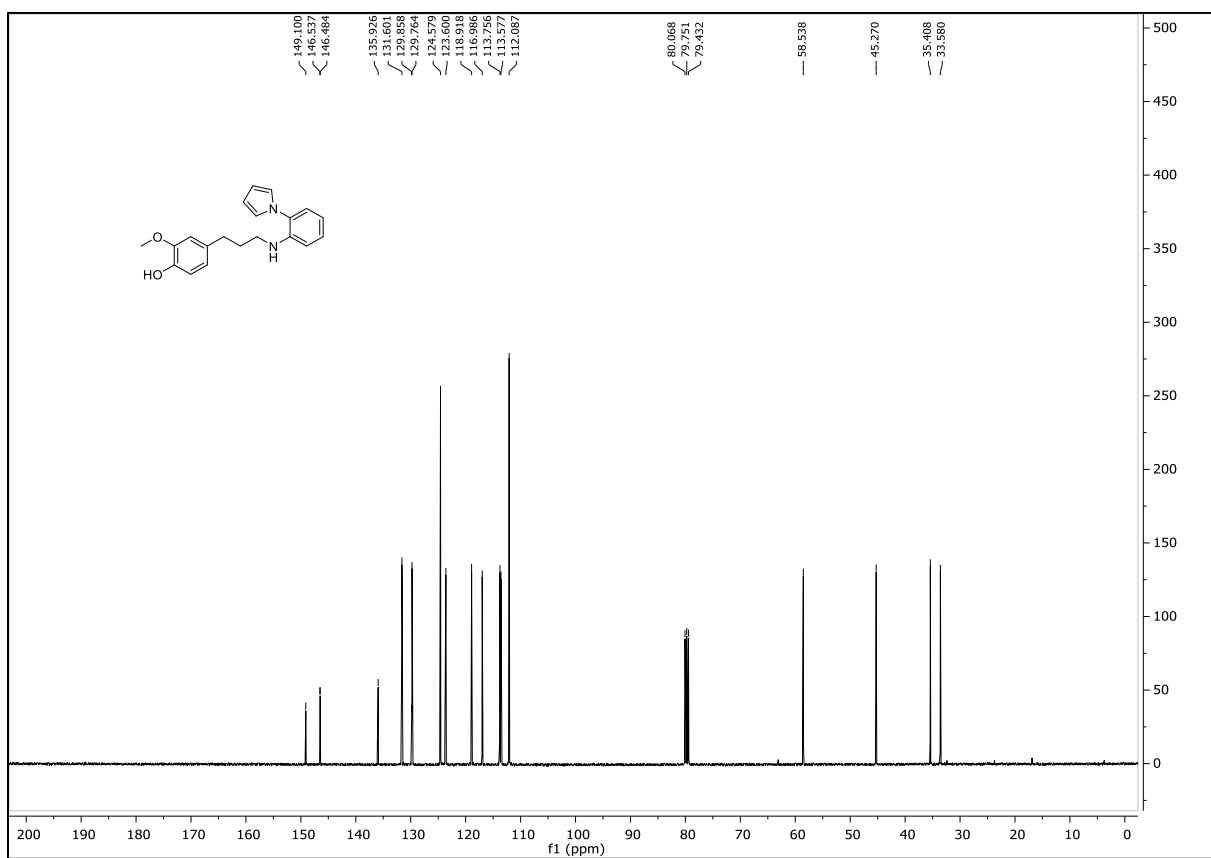
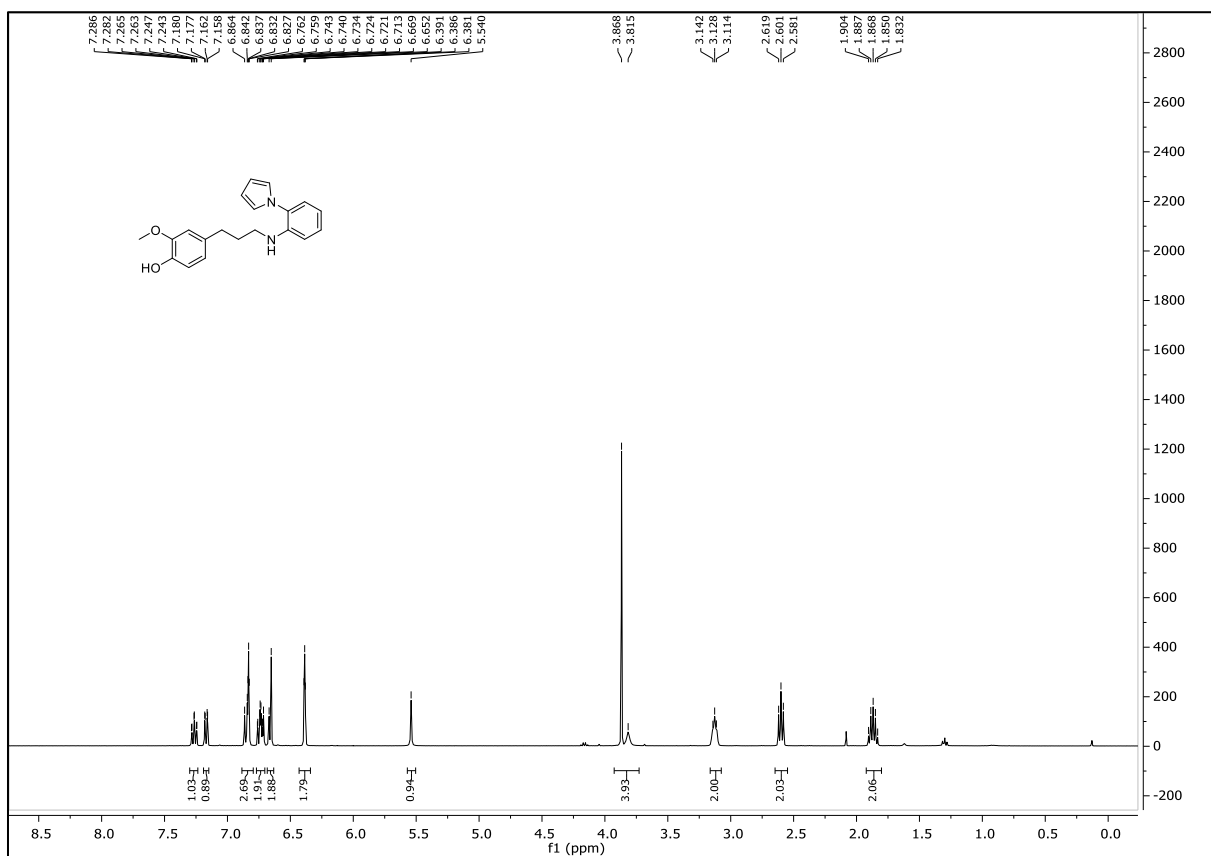
Supplementary Figure 49.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5GoS1.



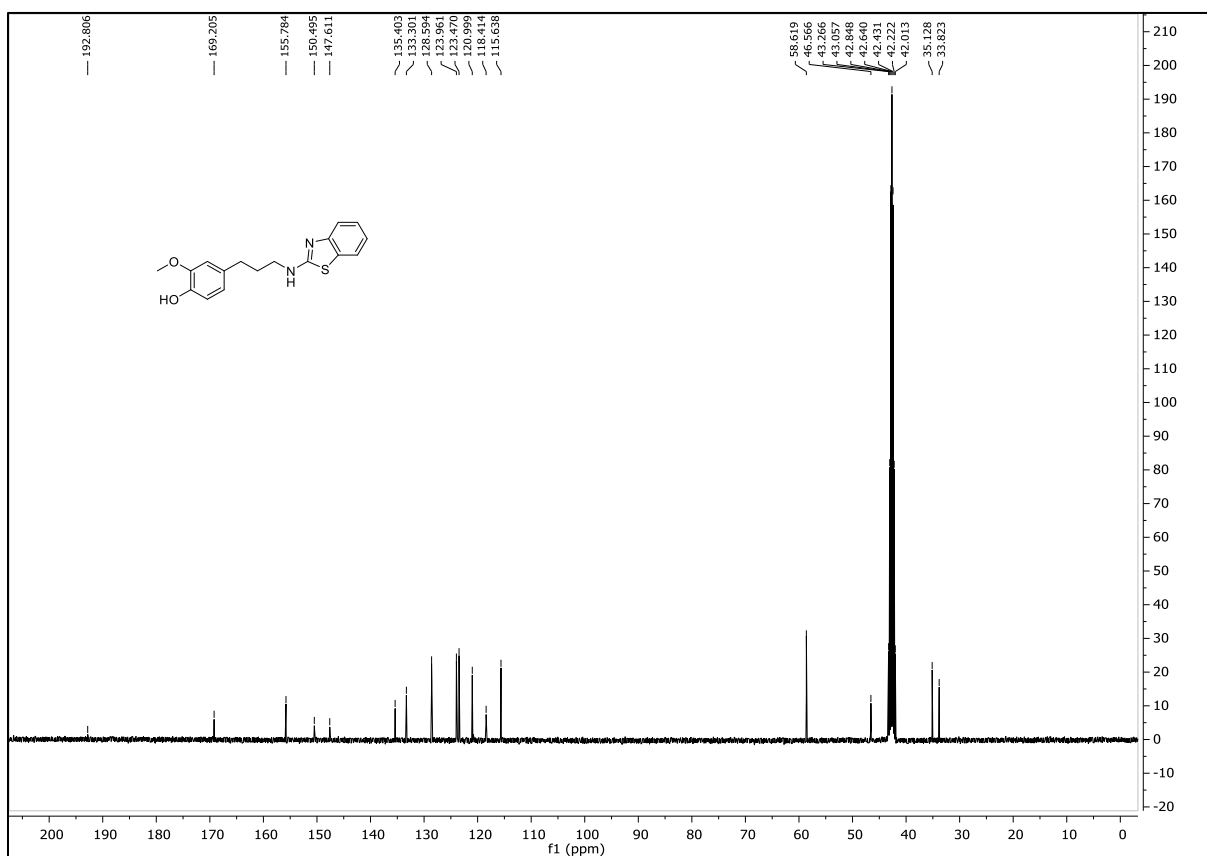
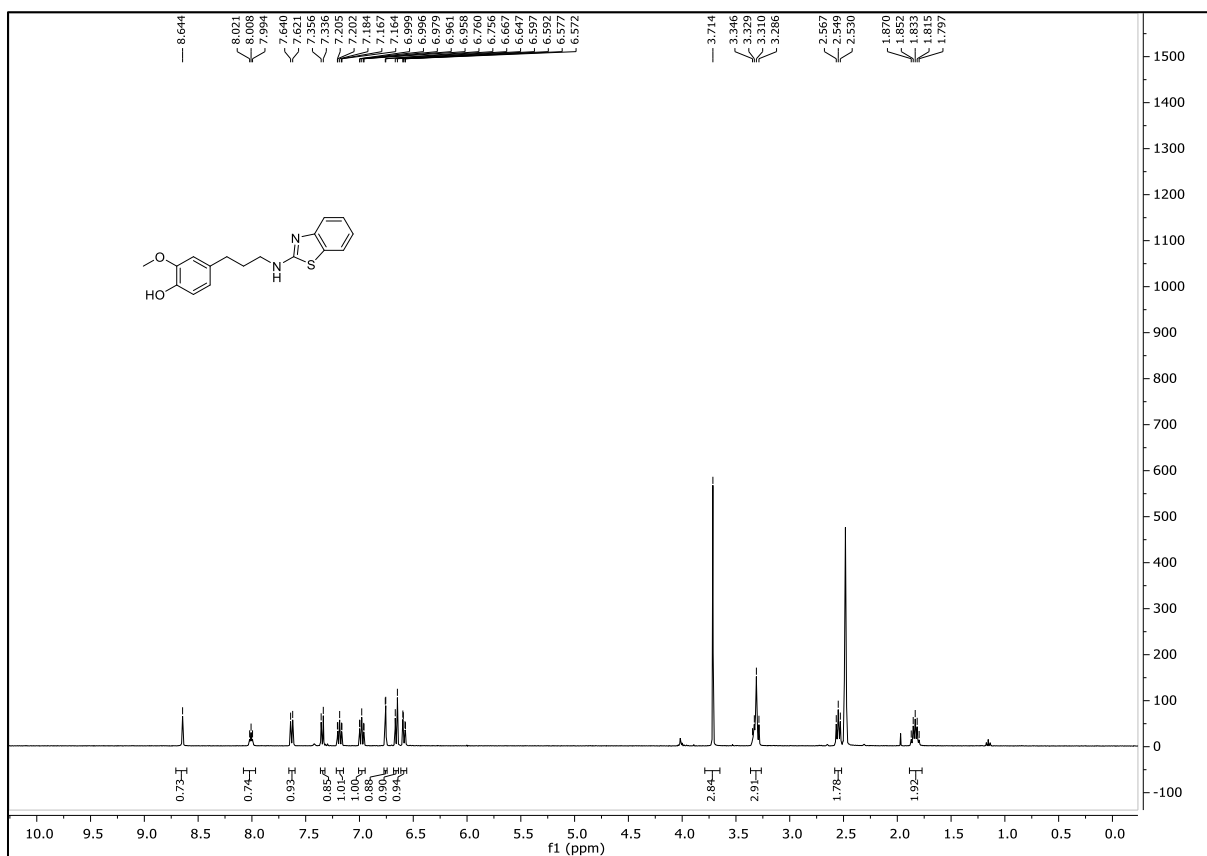
Supplementary Figure 50. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gp.



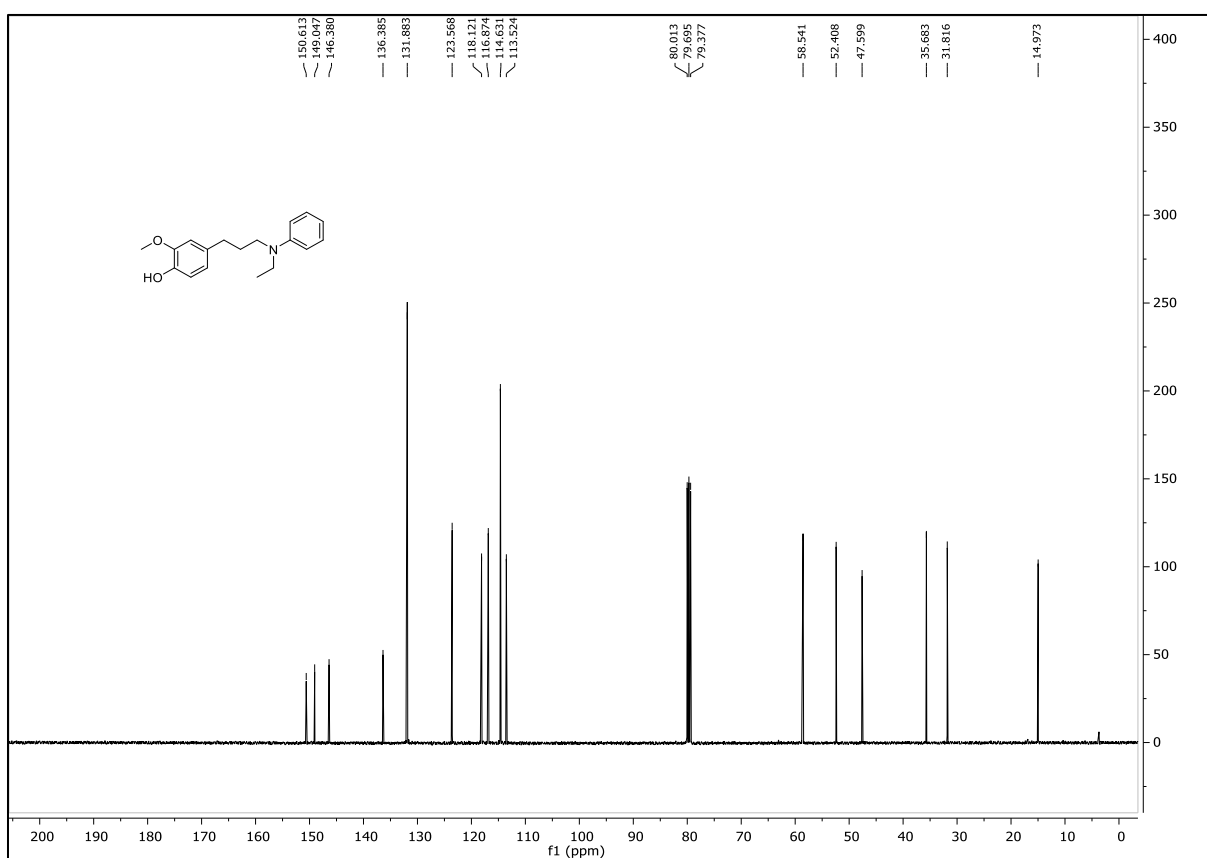
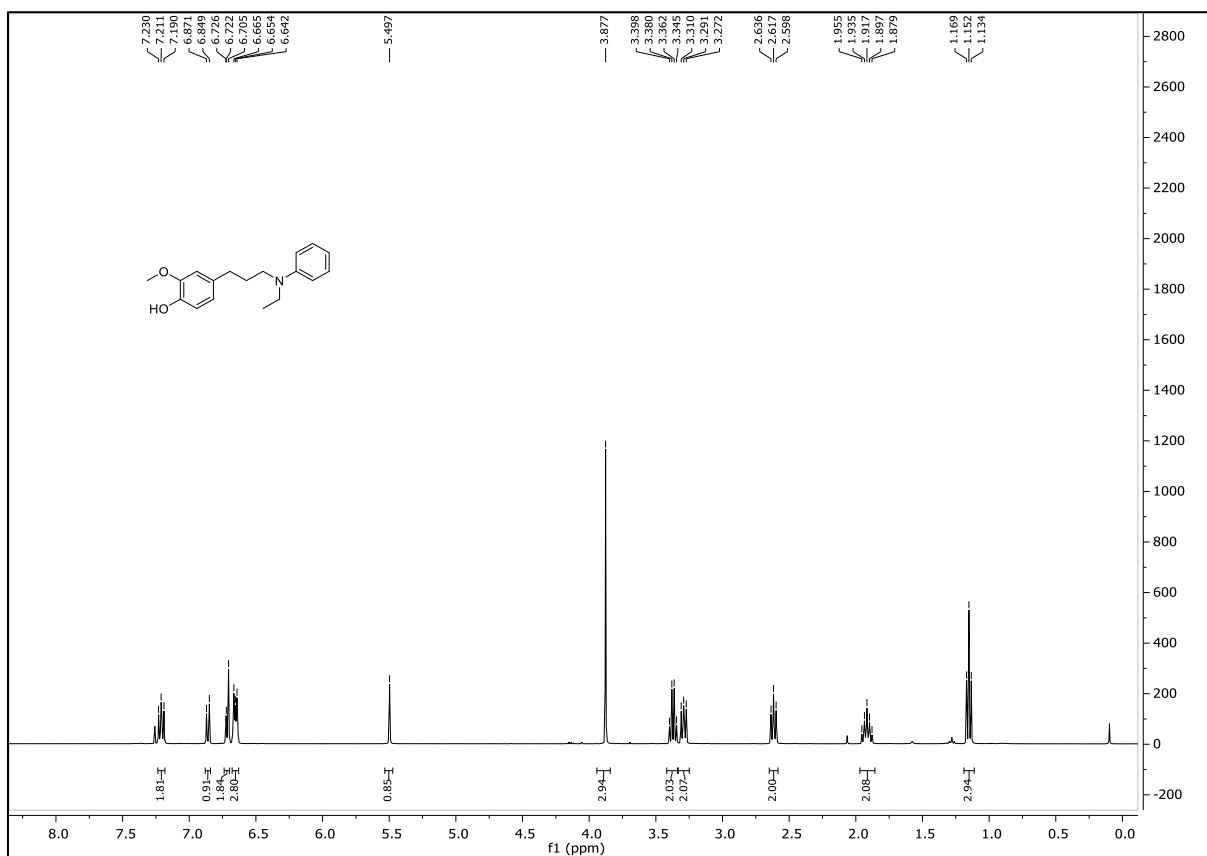
Supplementary Figure 51. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gq.



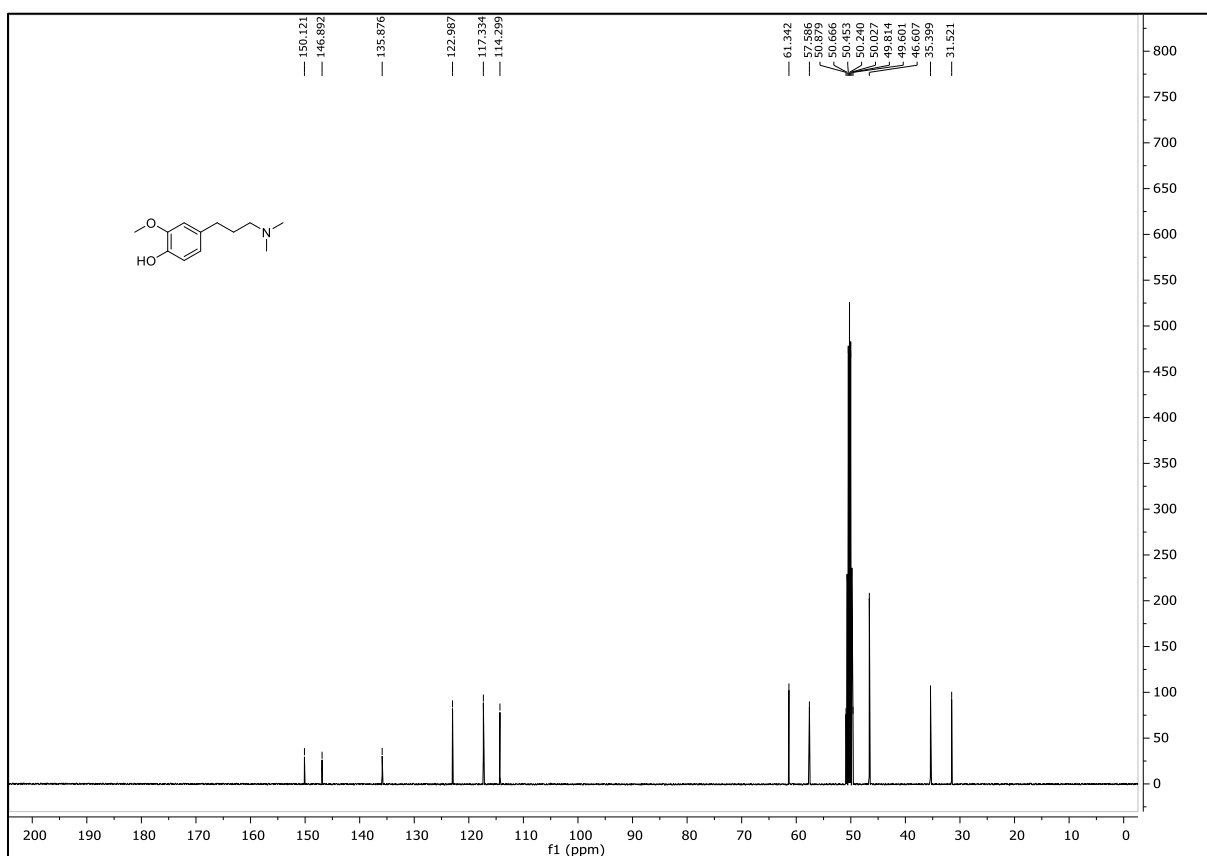
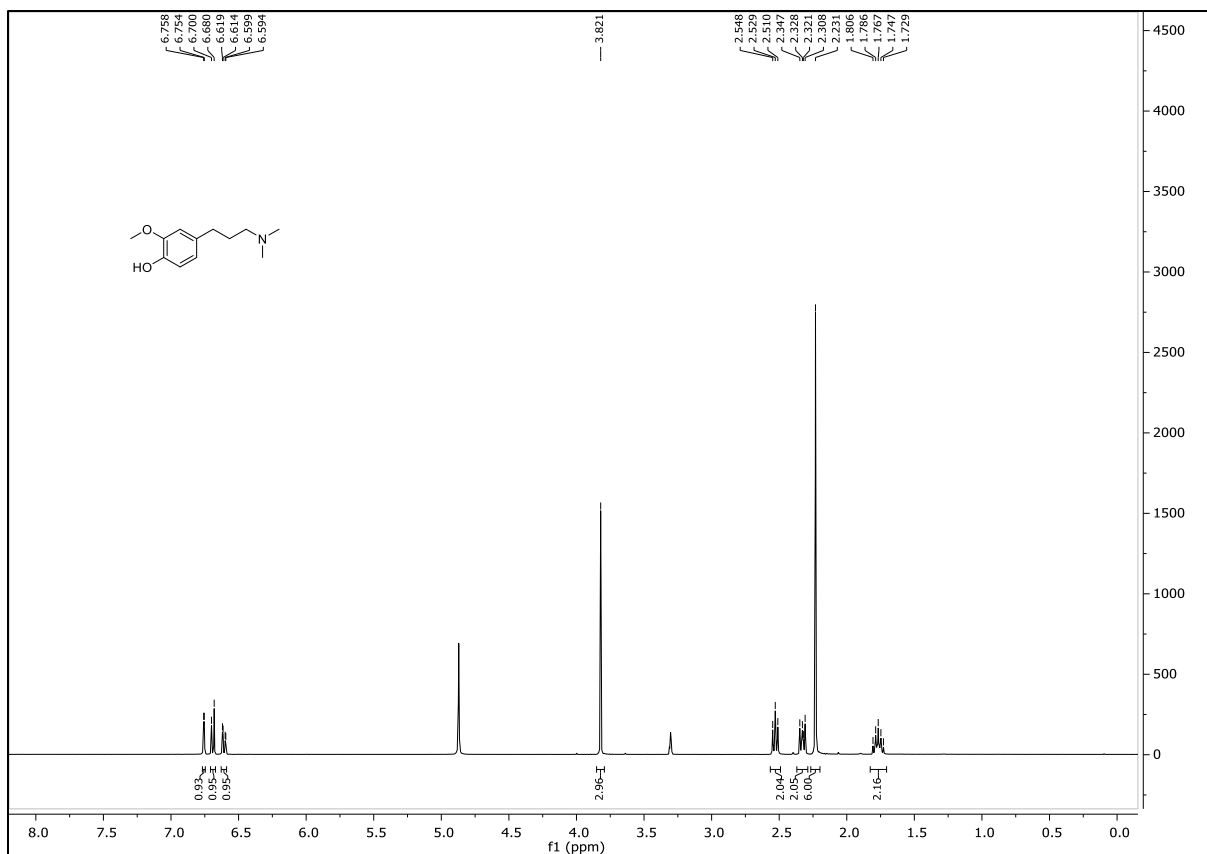
Supplementary Figure 52.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5Gr.



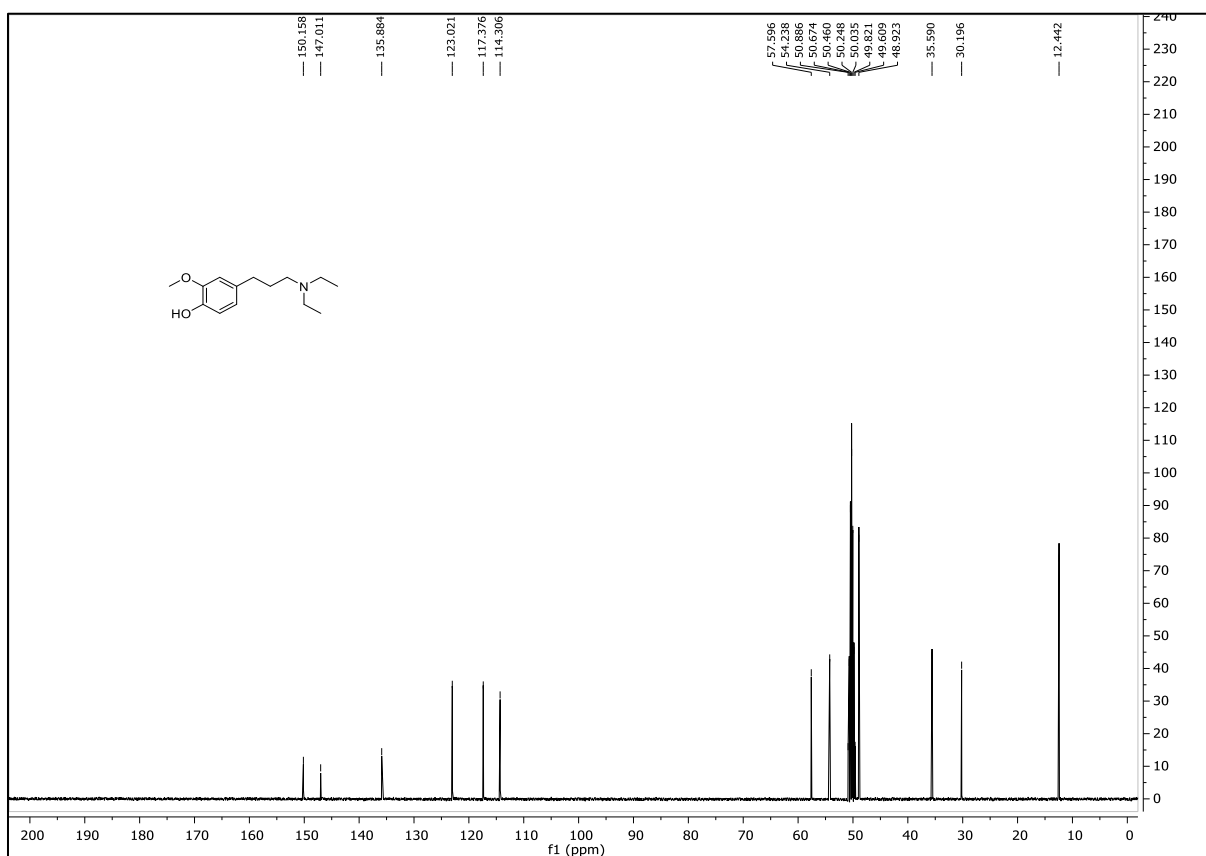
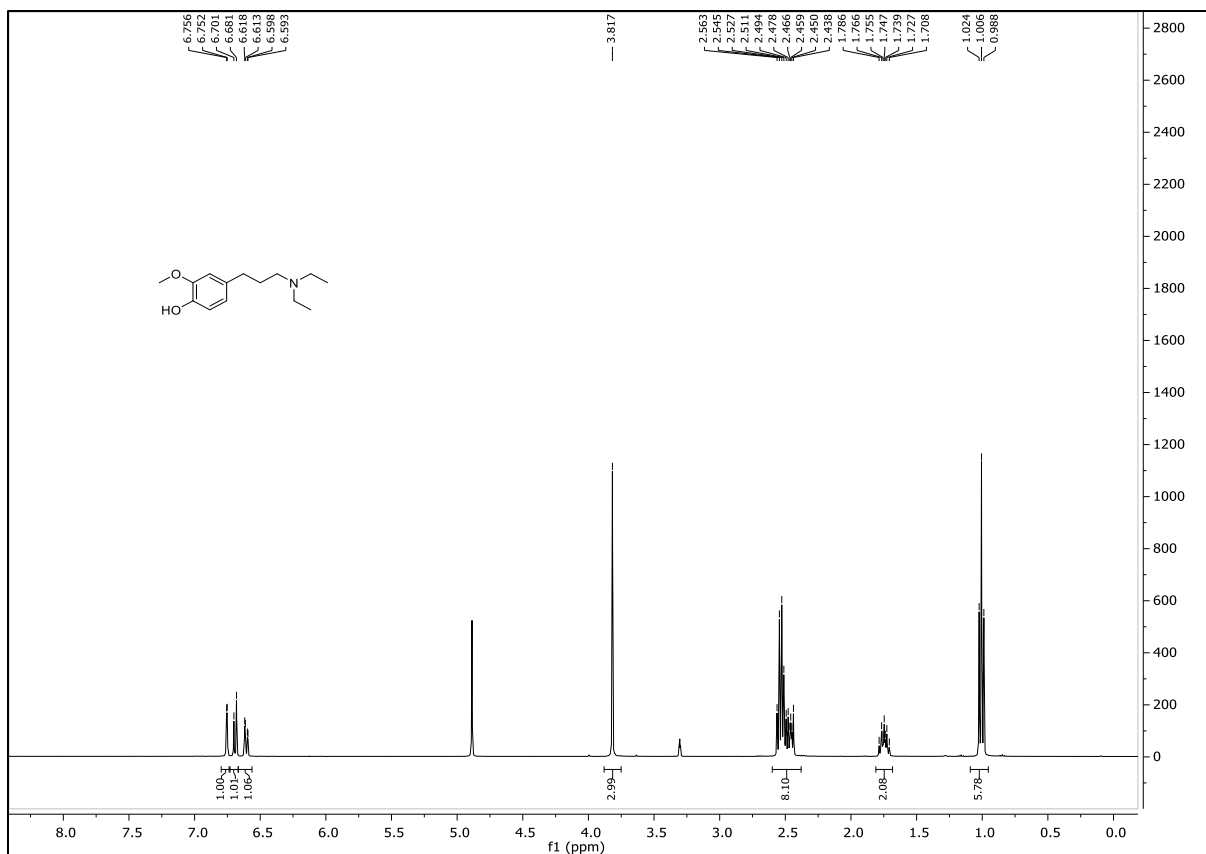
Supplementary Figure 53. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gs.



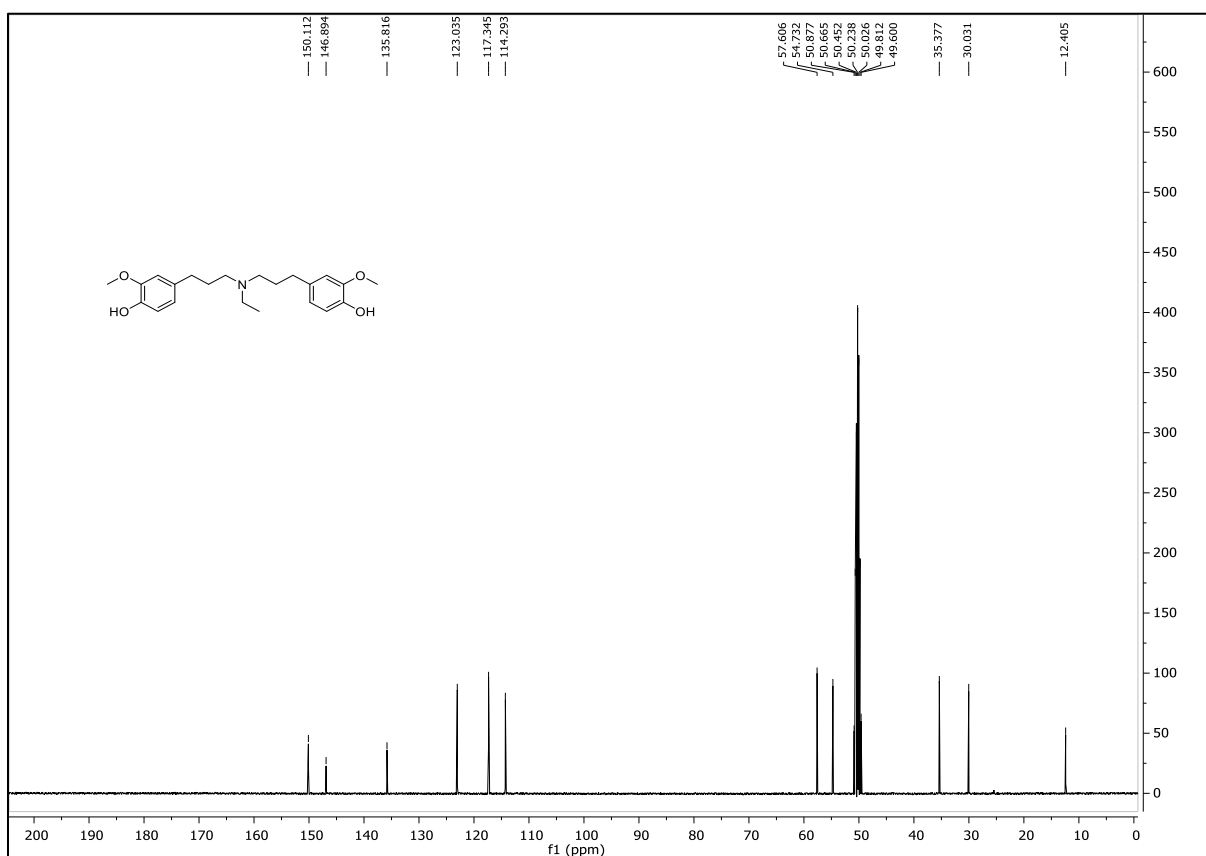
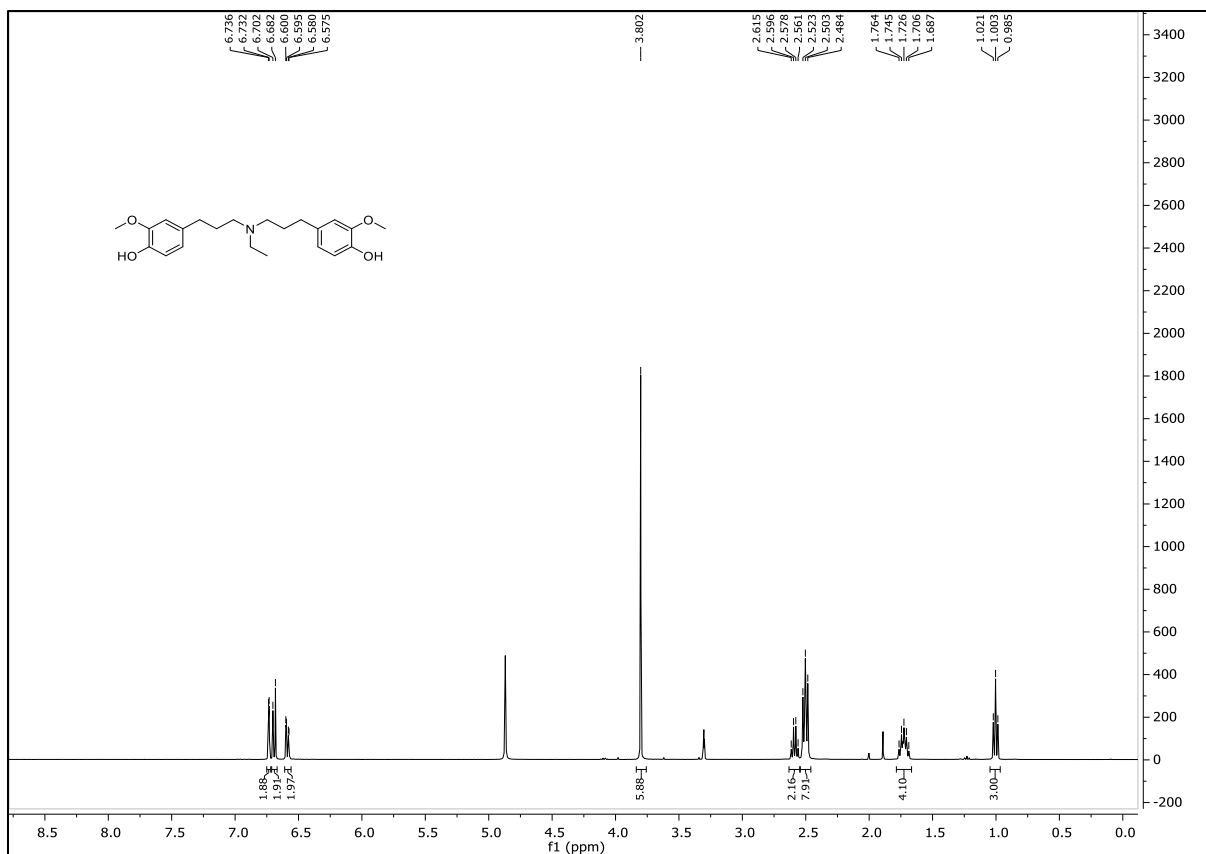
Supplementary Figure 54. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gt.



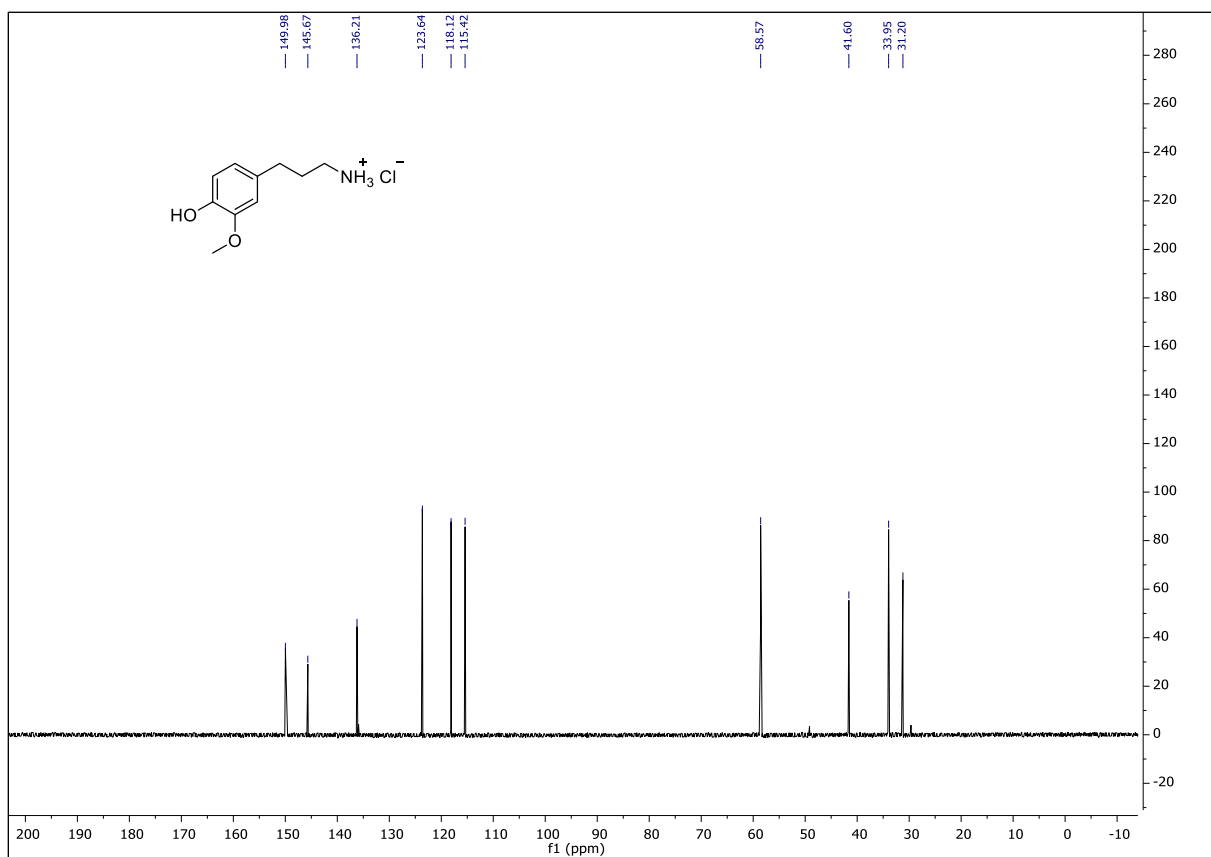
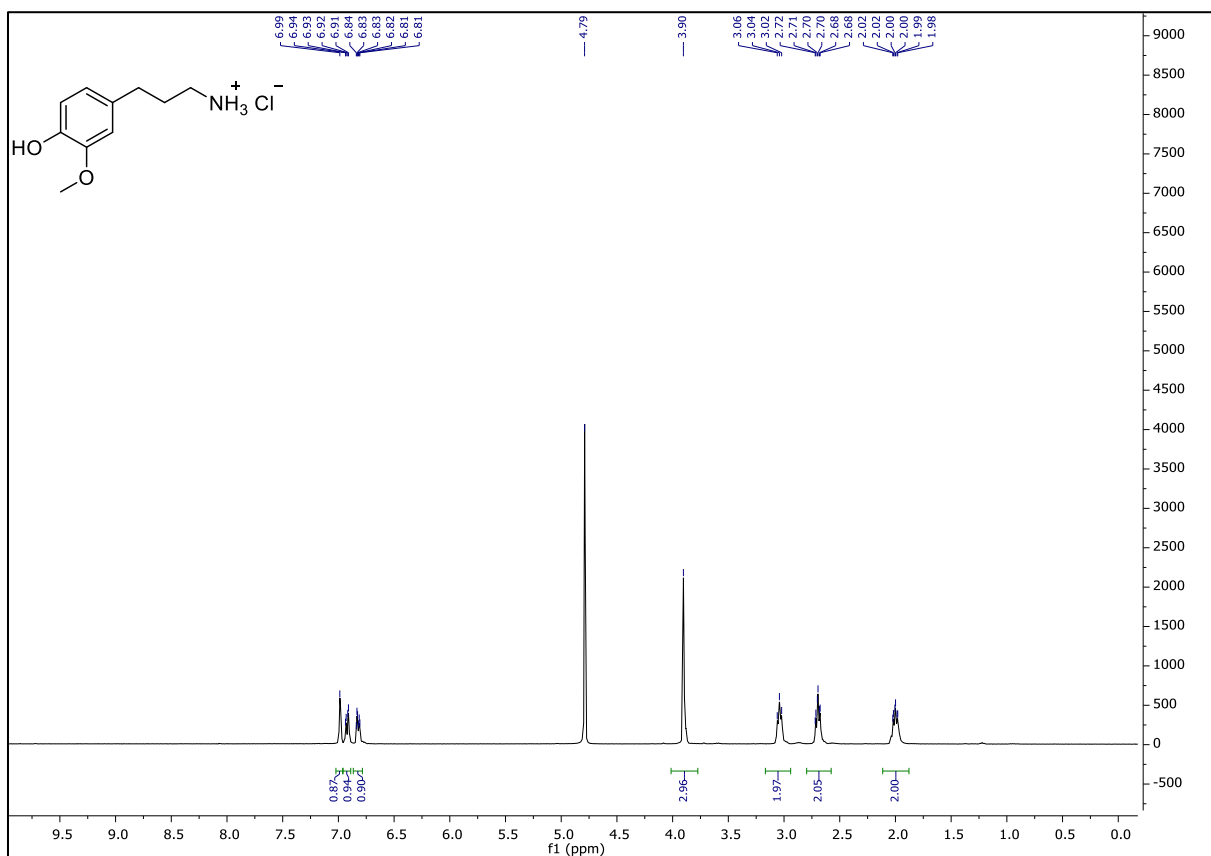
Supplementary Figure 55. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gu.



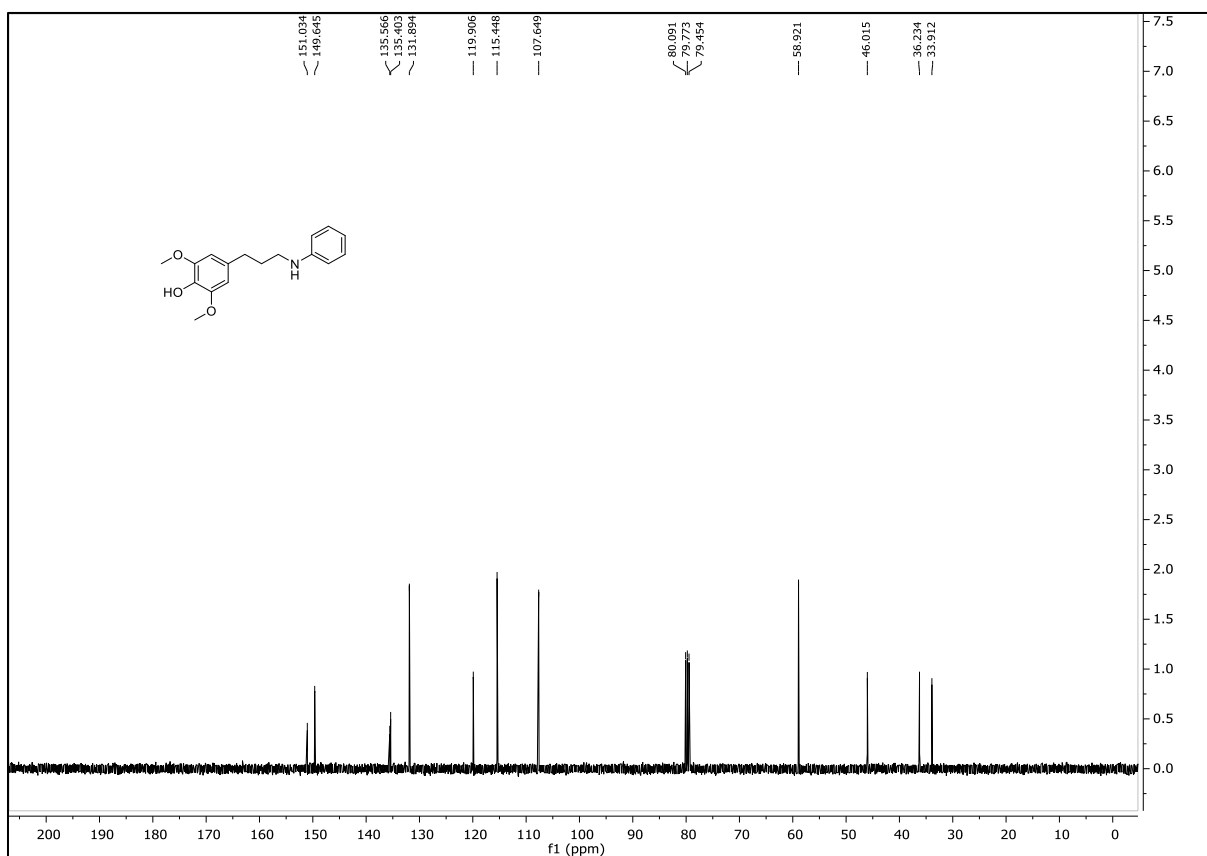
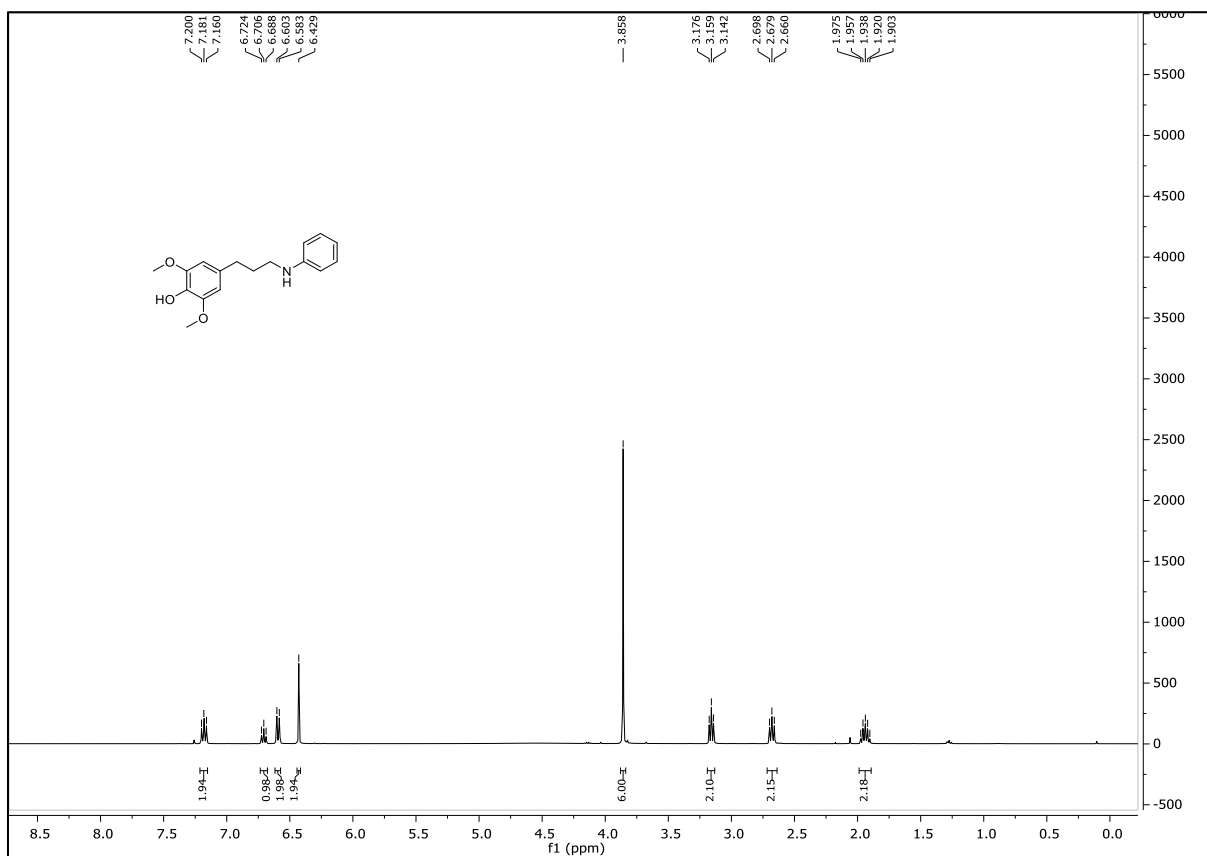
Supplementary Figure S6. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gv.



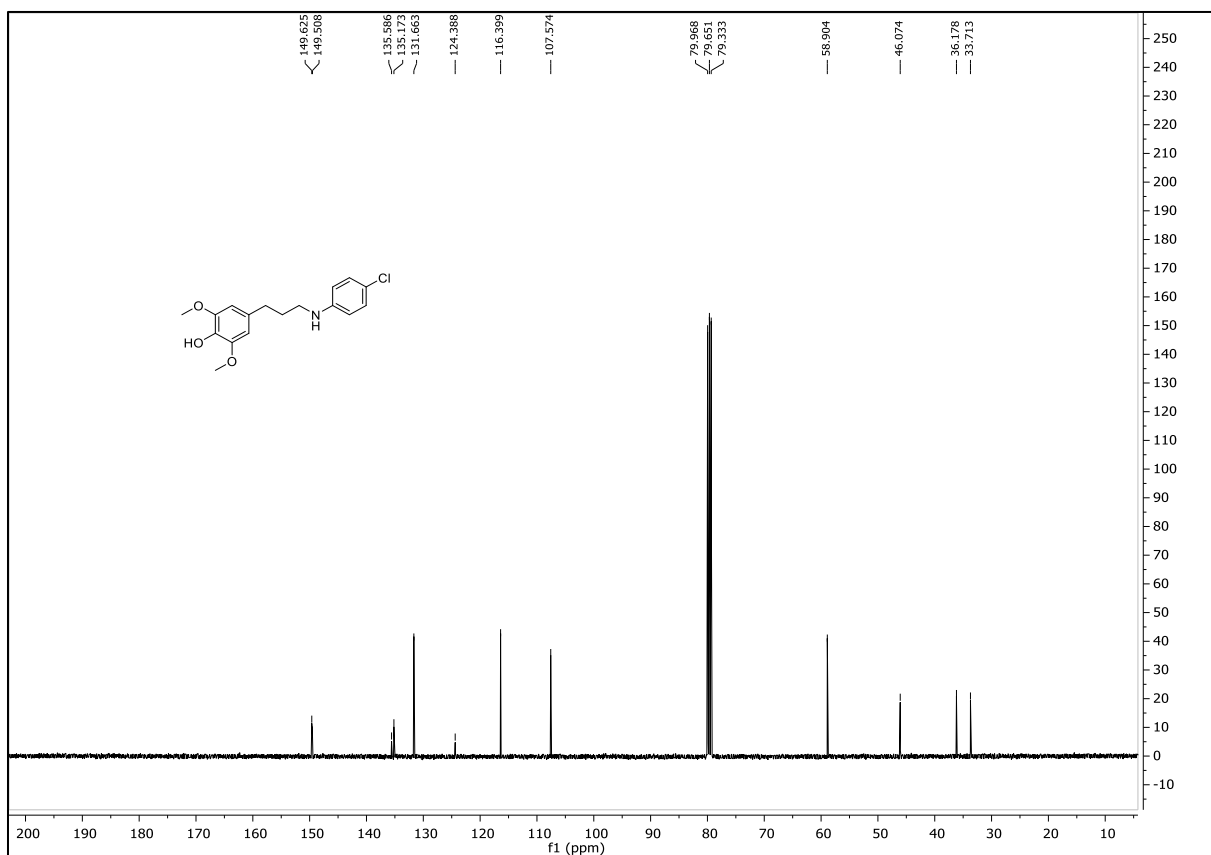
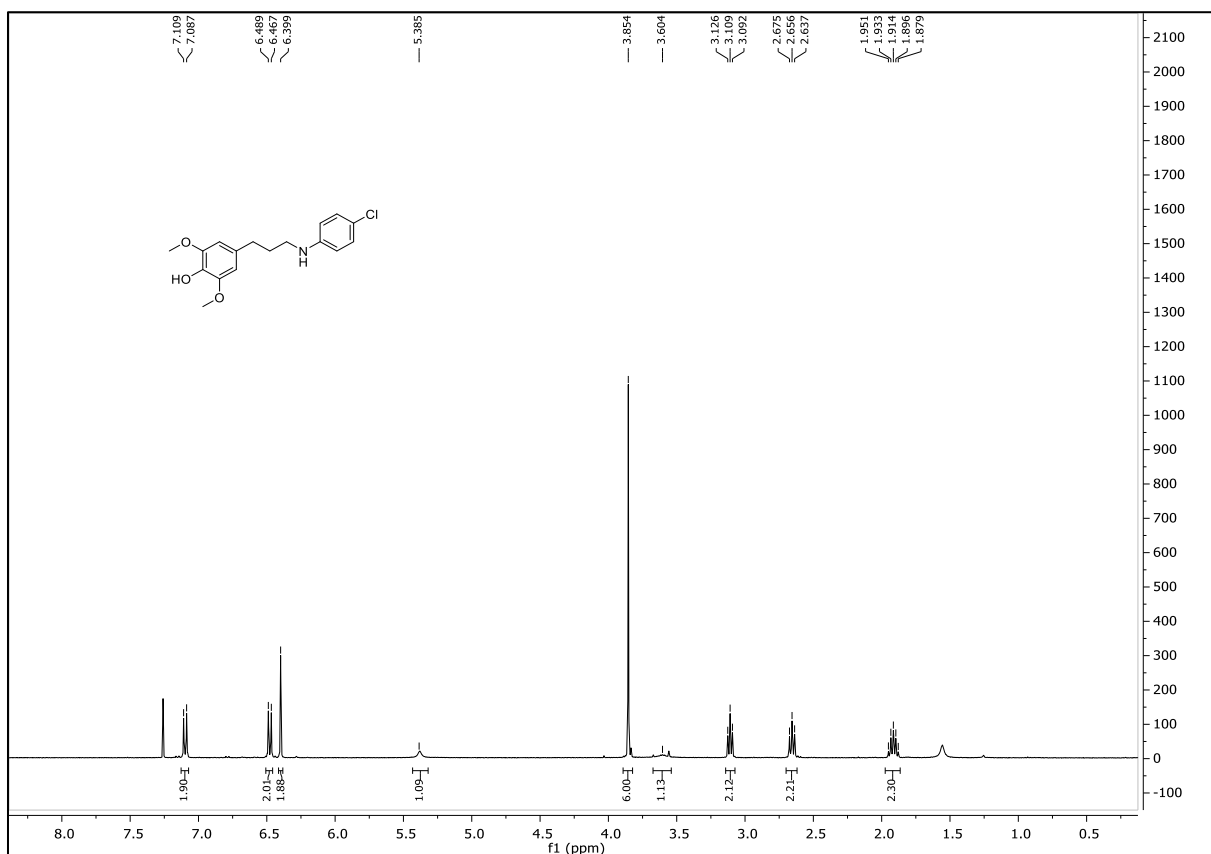
Supplementary Figure 57.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5GvS1.



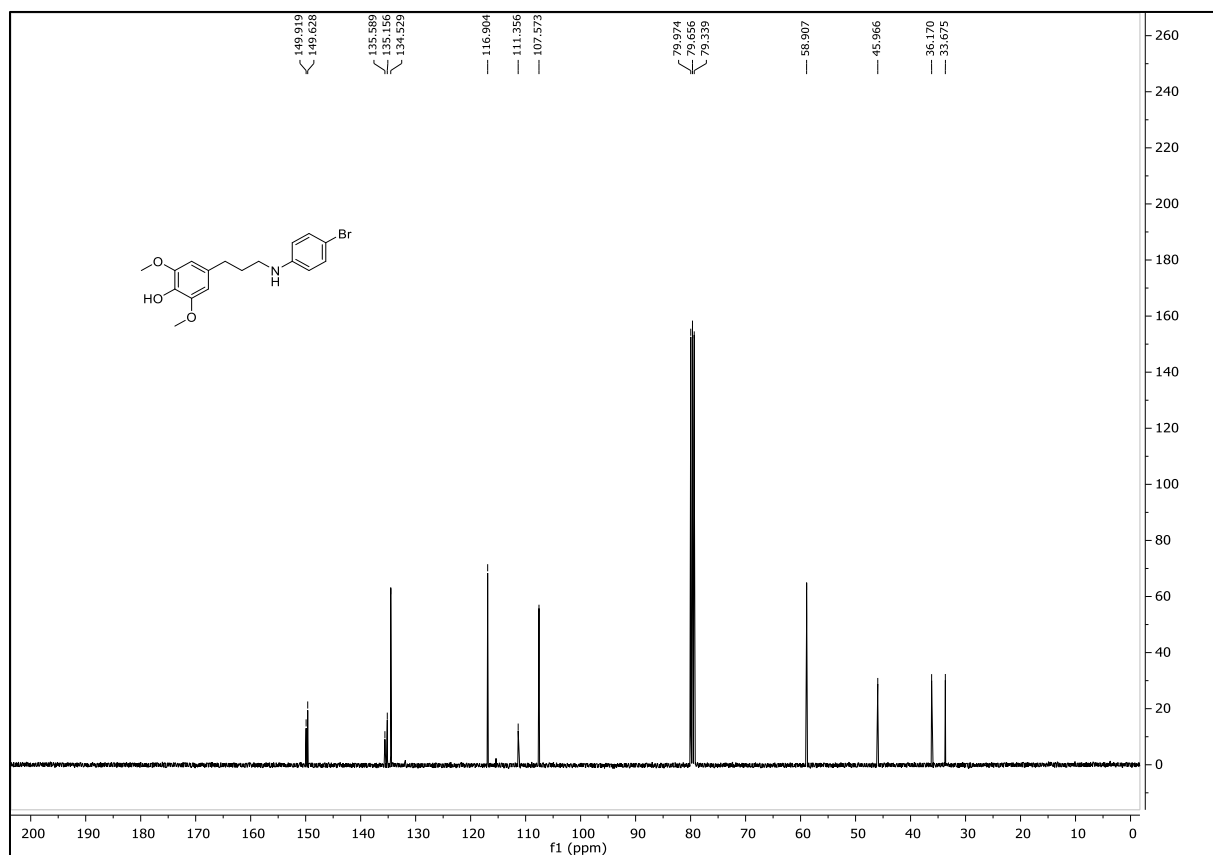
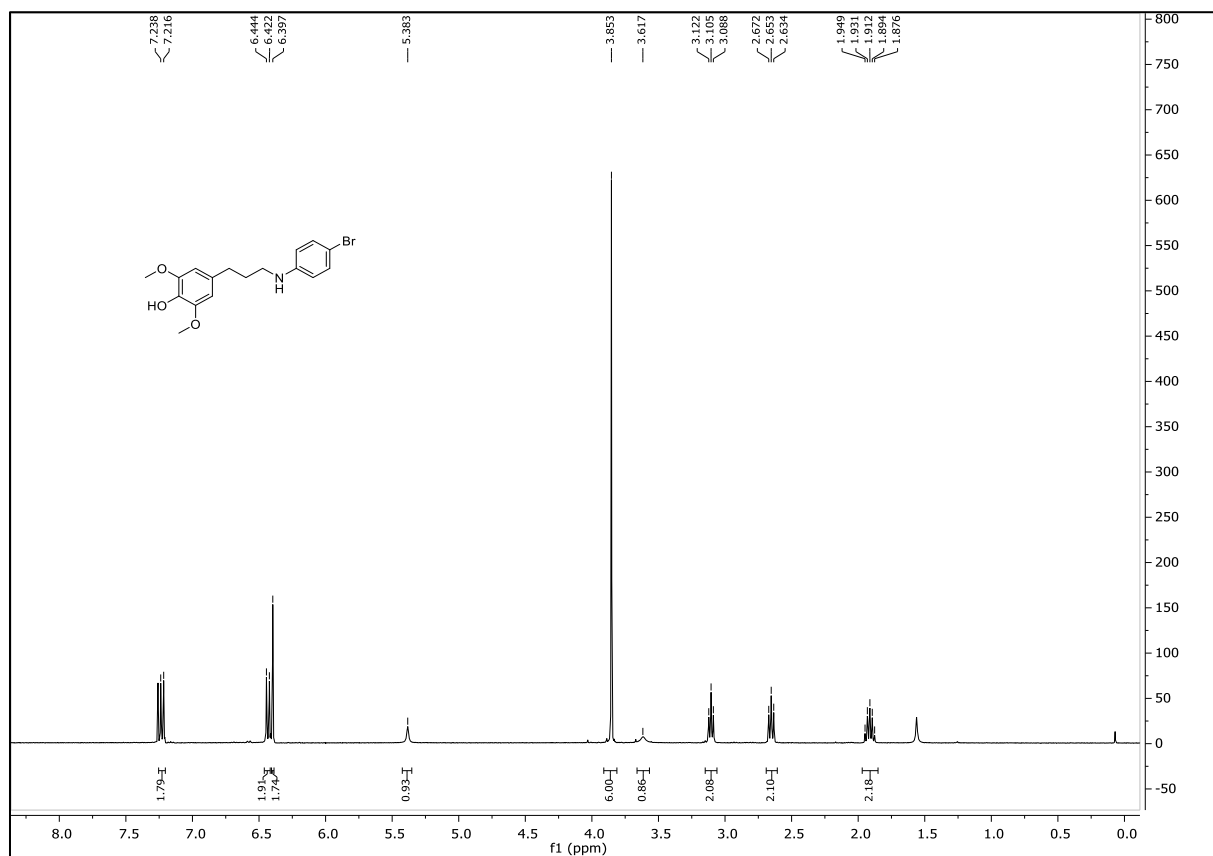
**Supplementary Figure 58.** <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Gw.



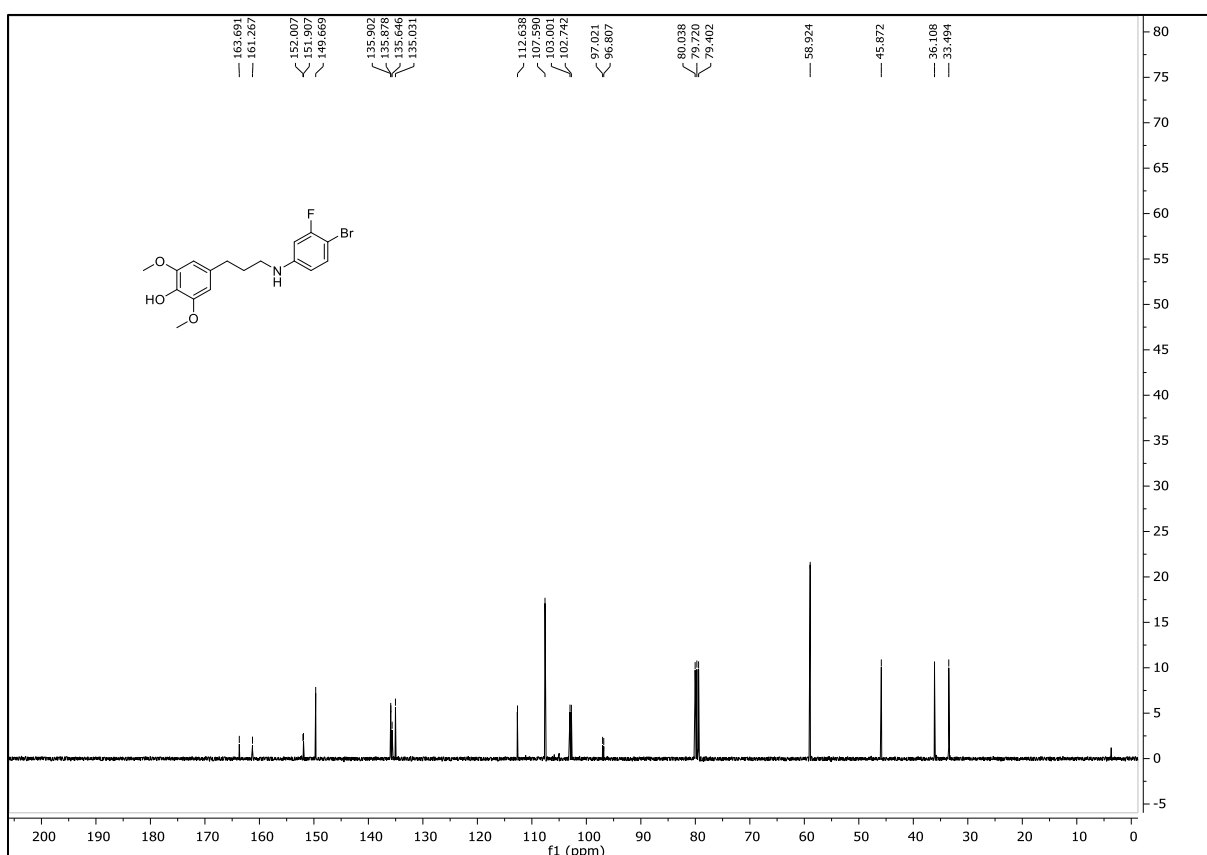
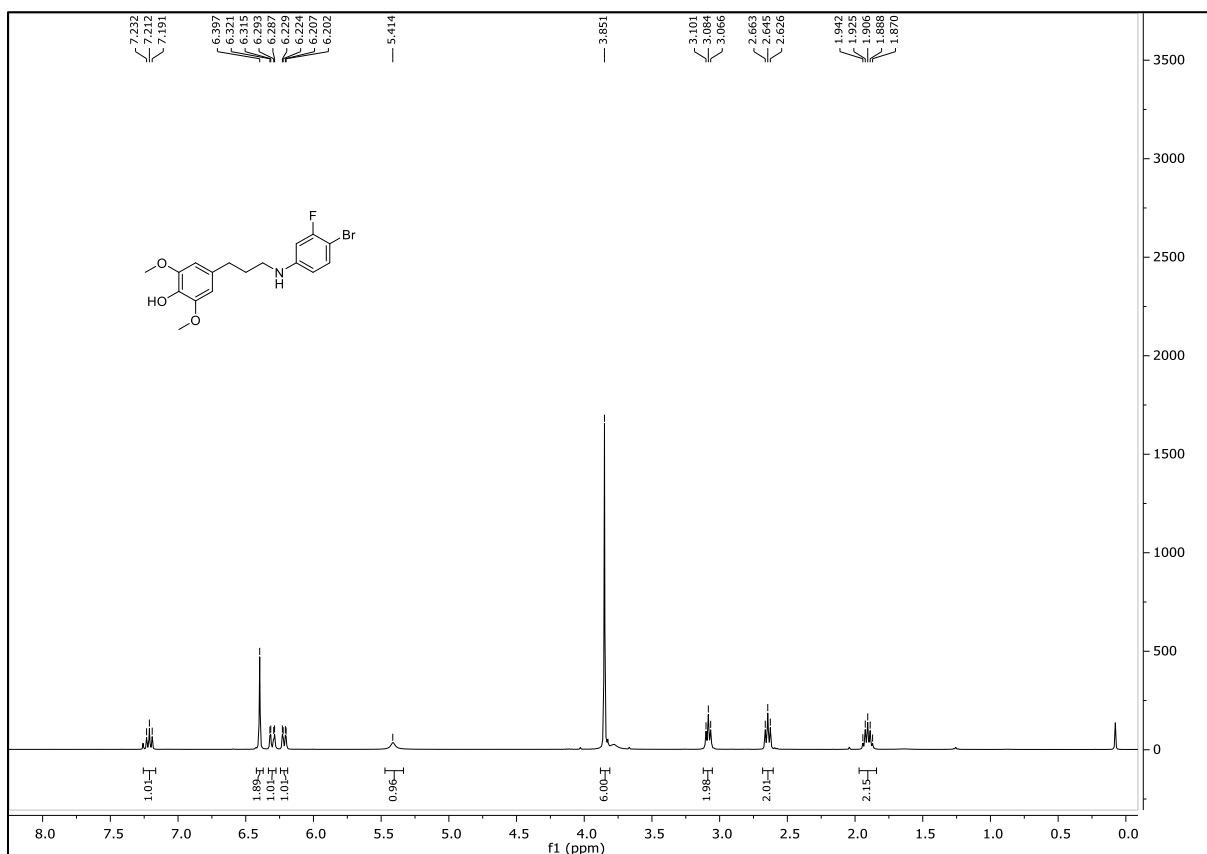
Supplementary Figure 59.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5Sa.



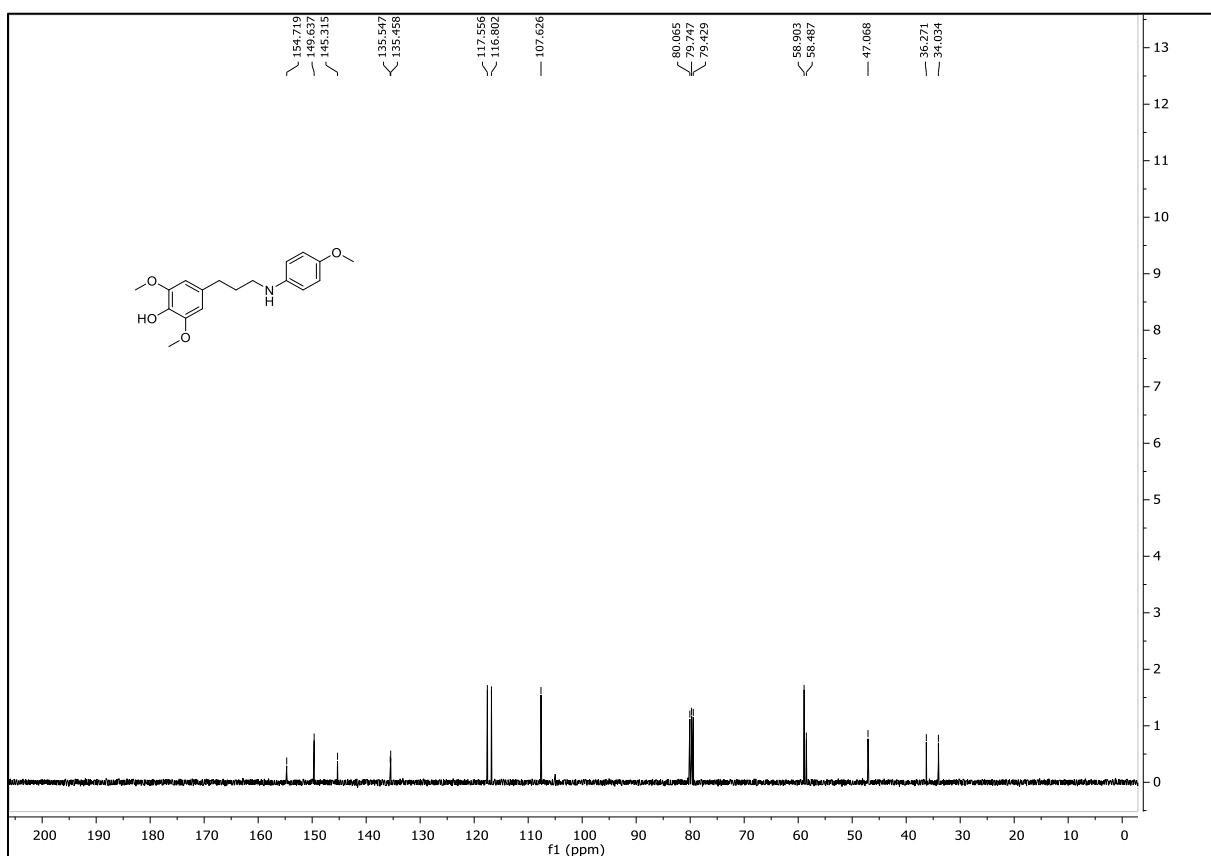
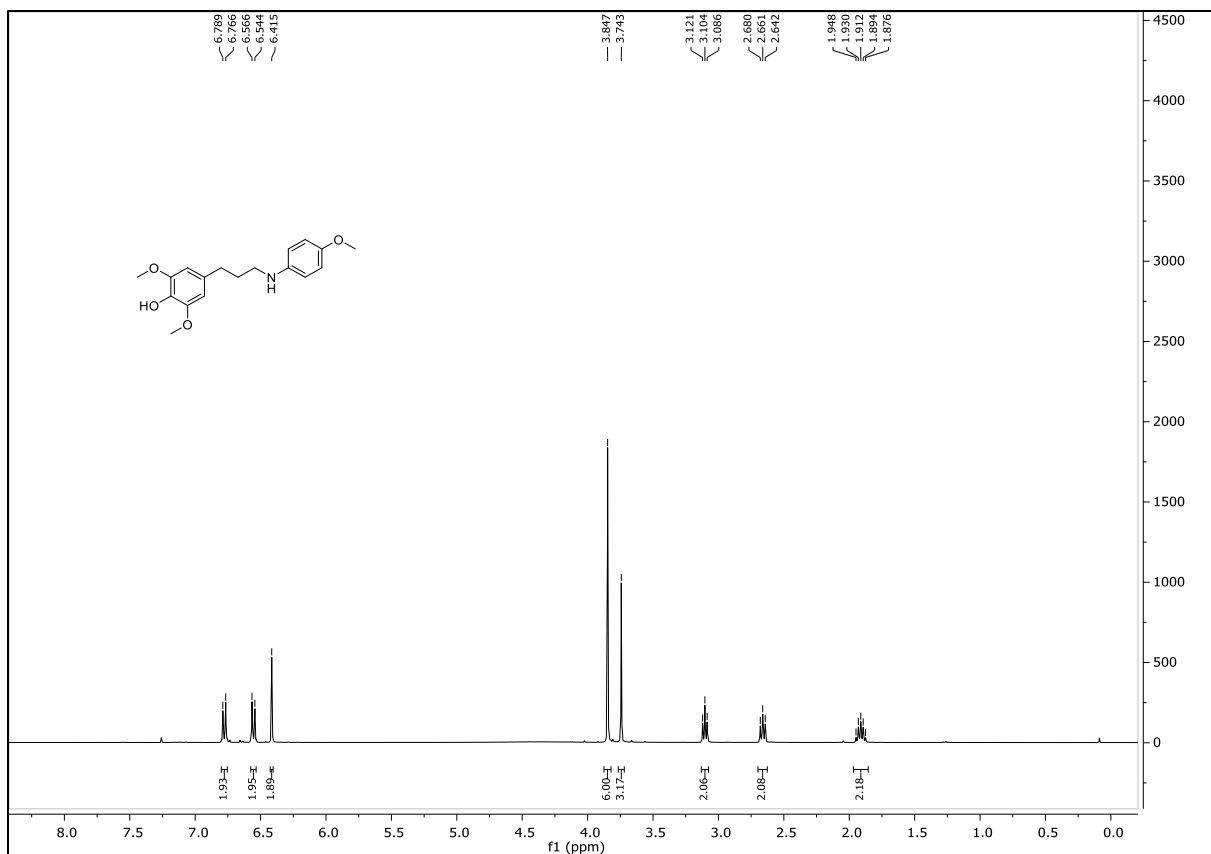
**Supplementary Figure 60.** <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Sb.



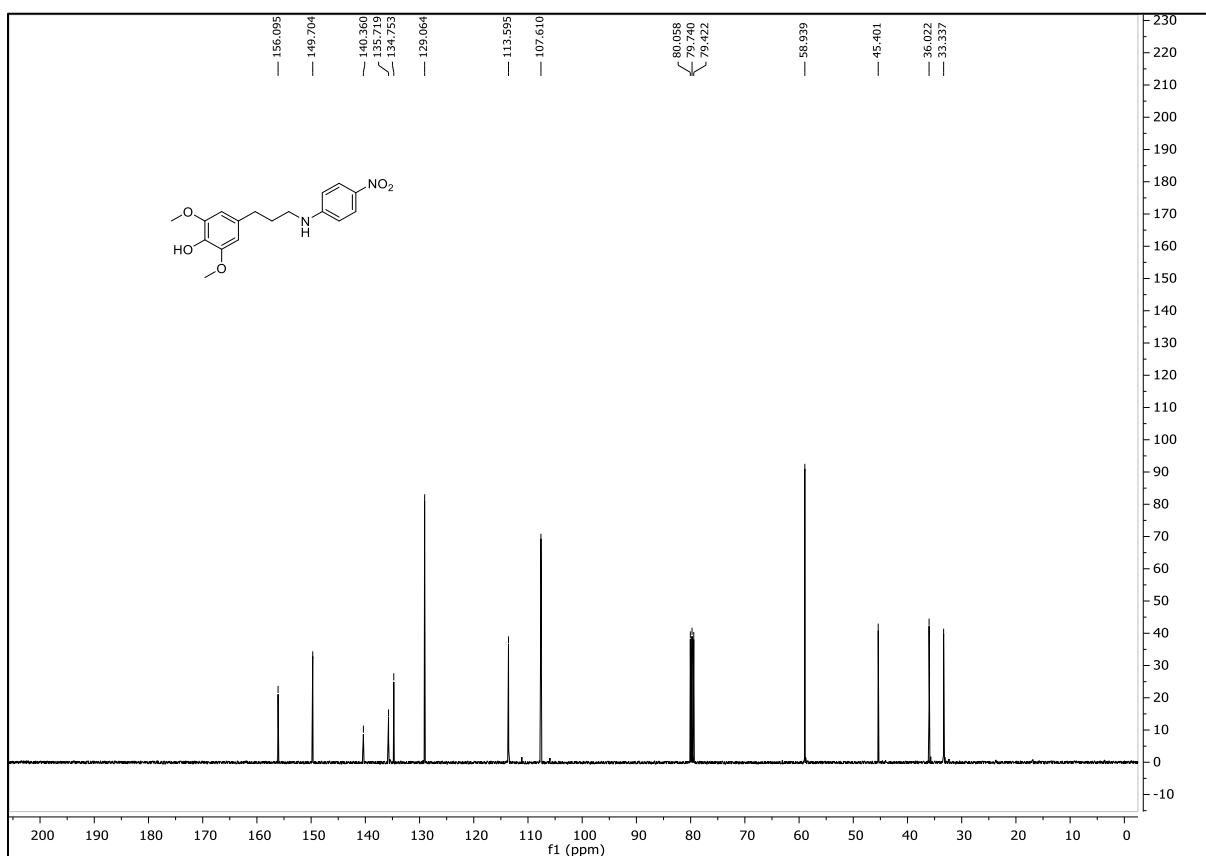
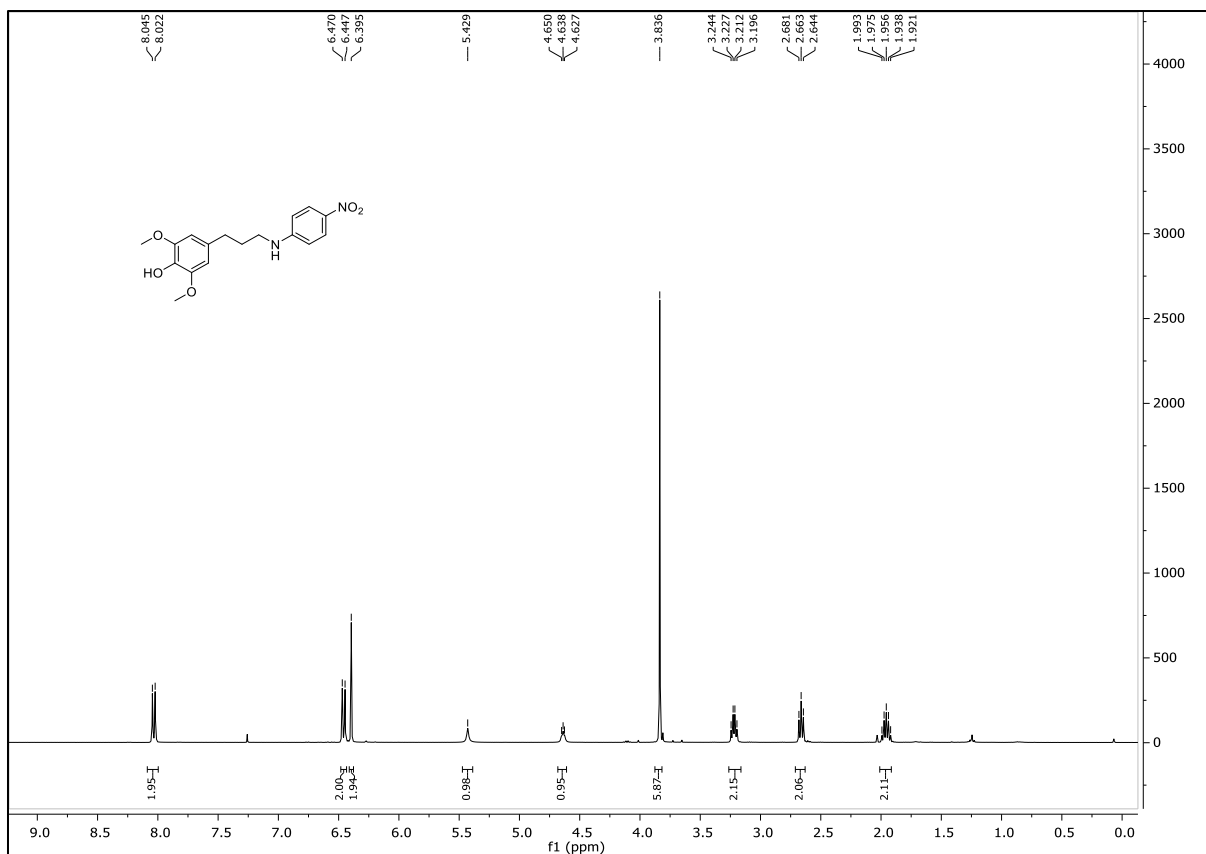
Supplementary Figure 61.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5Sc.



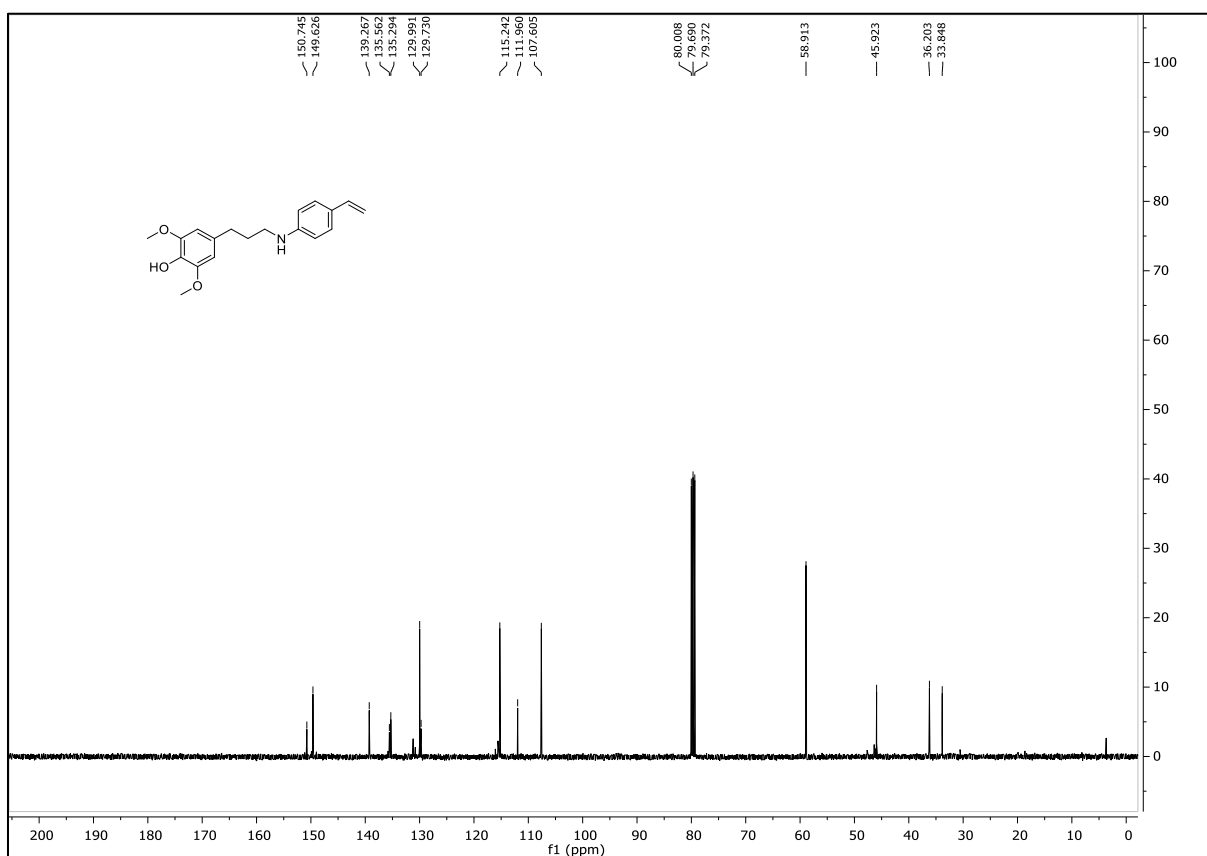
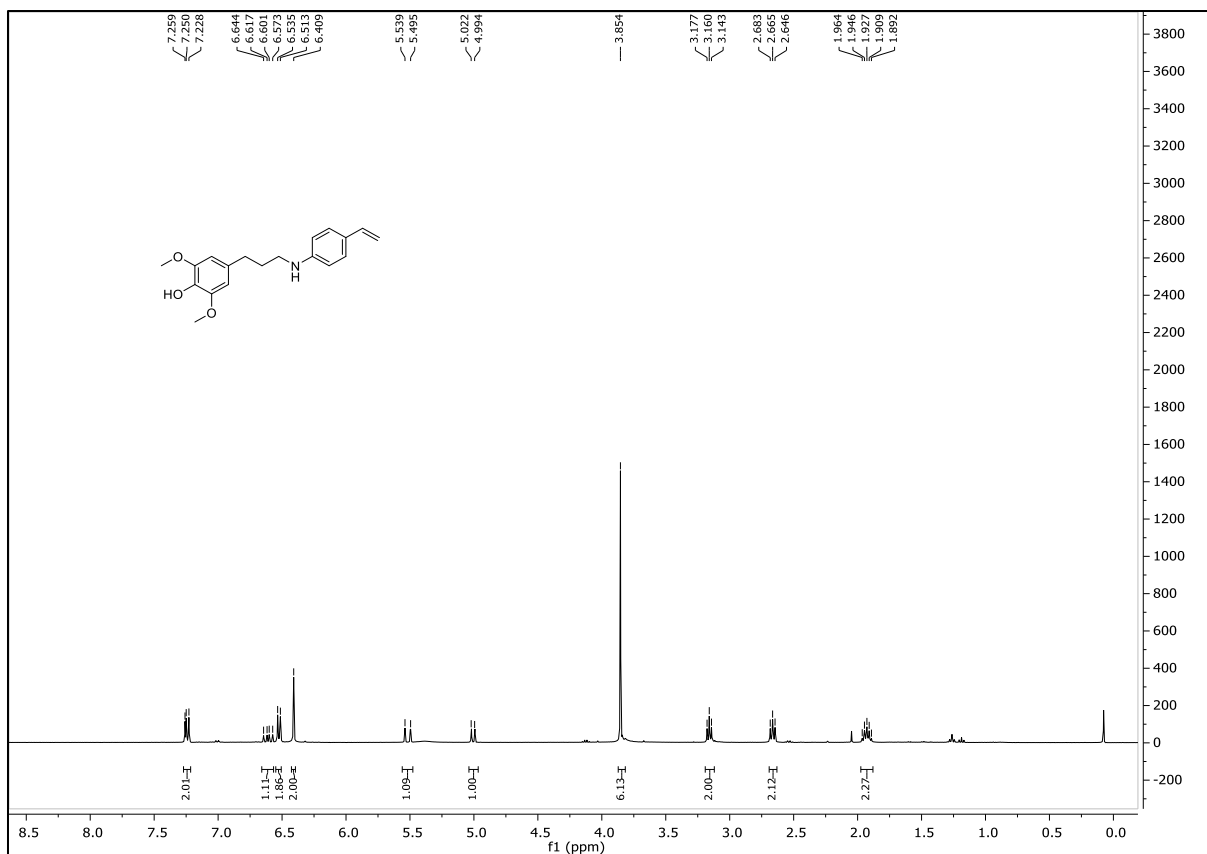
Supplementary Figure 62. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Se.



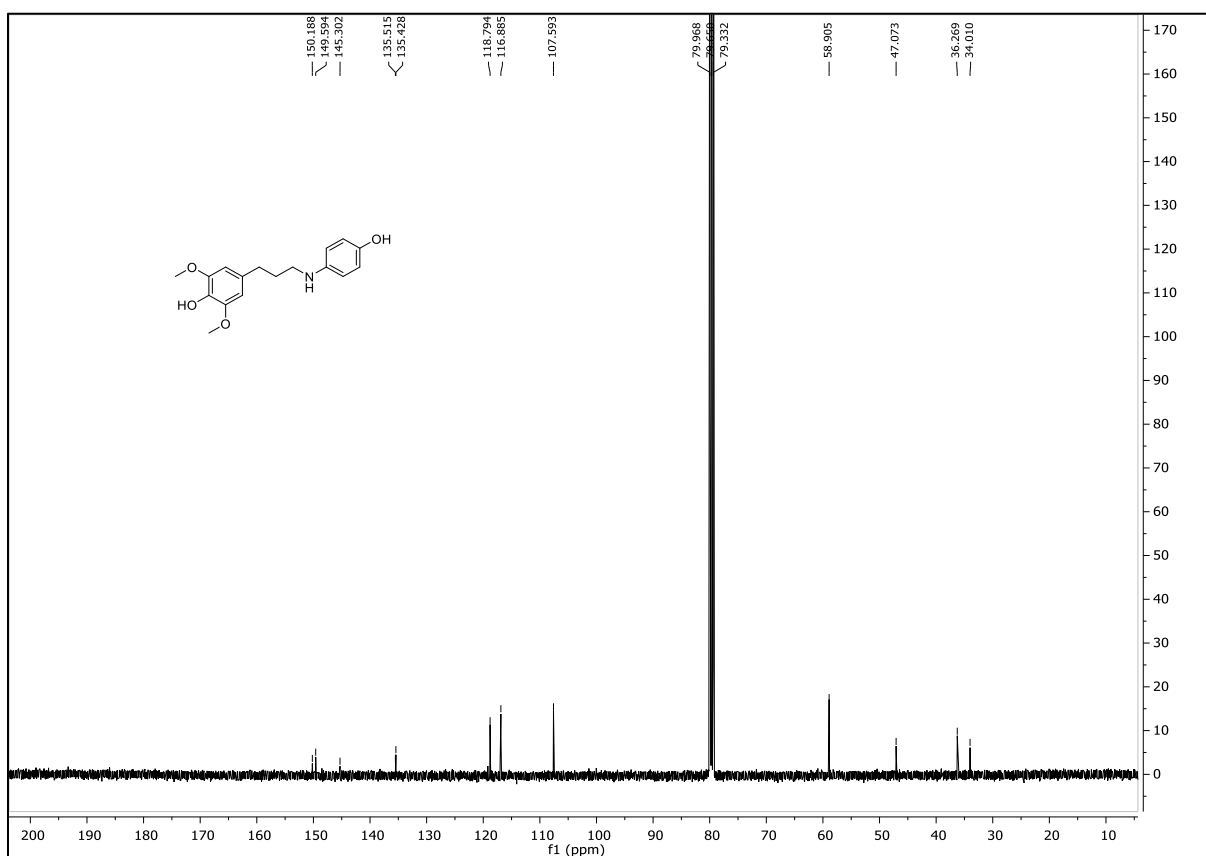
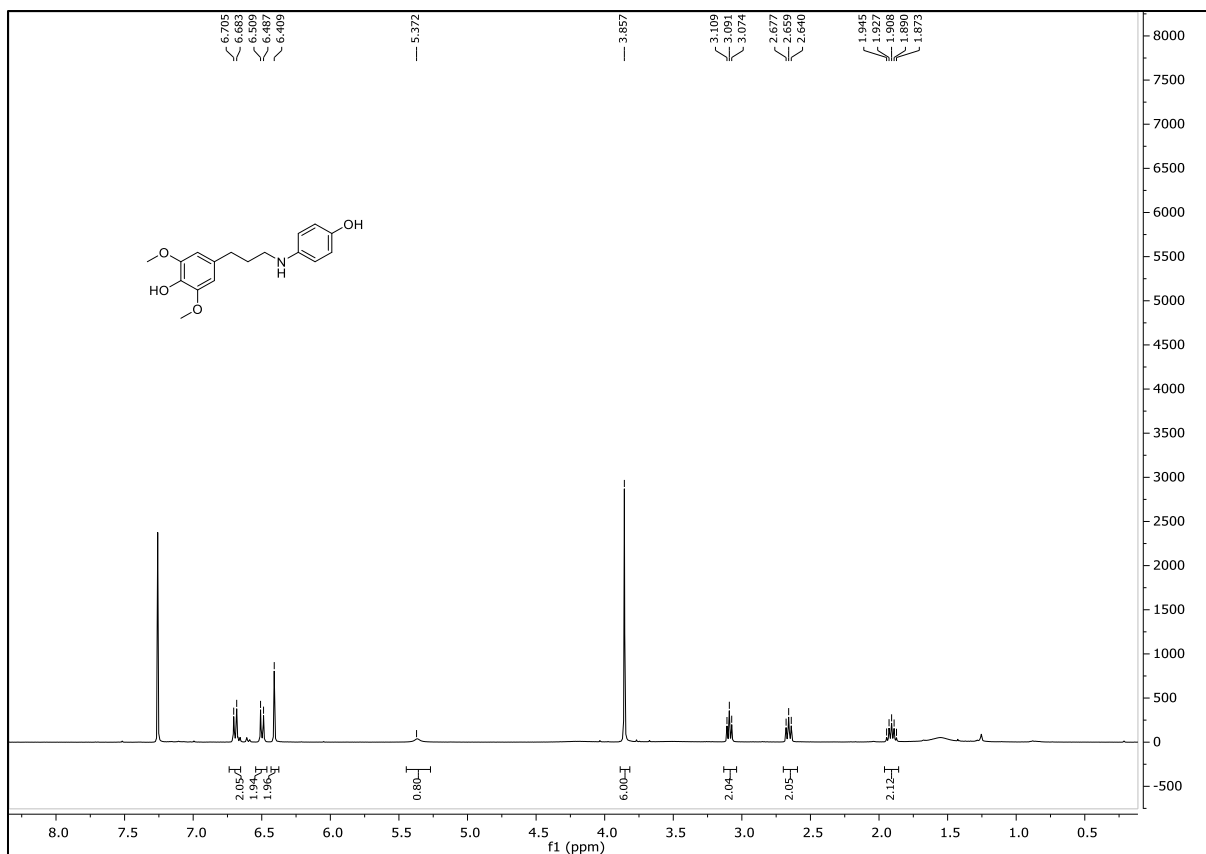
Supplementary Figure 63.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5Sf.



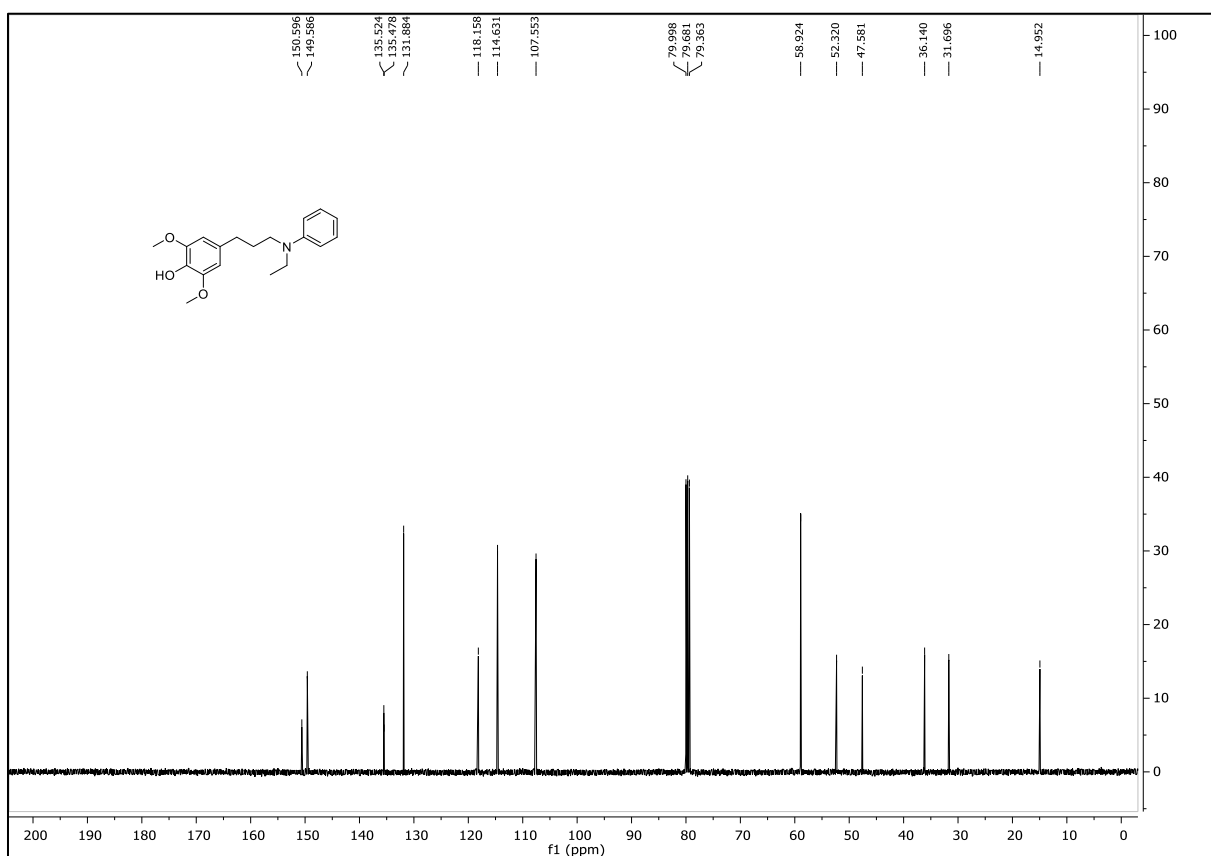
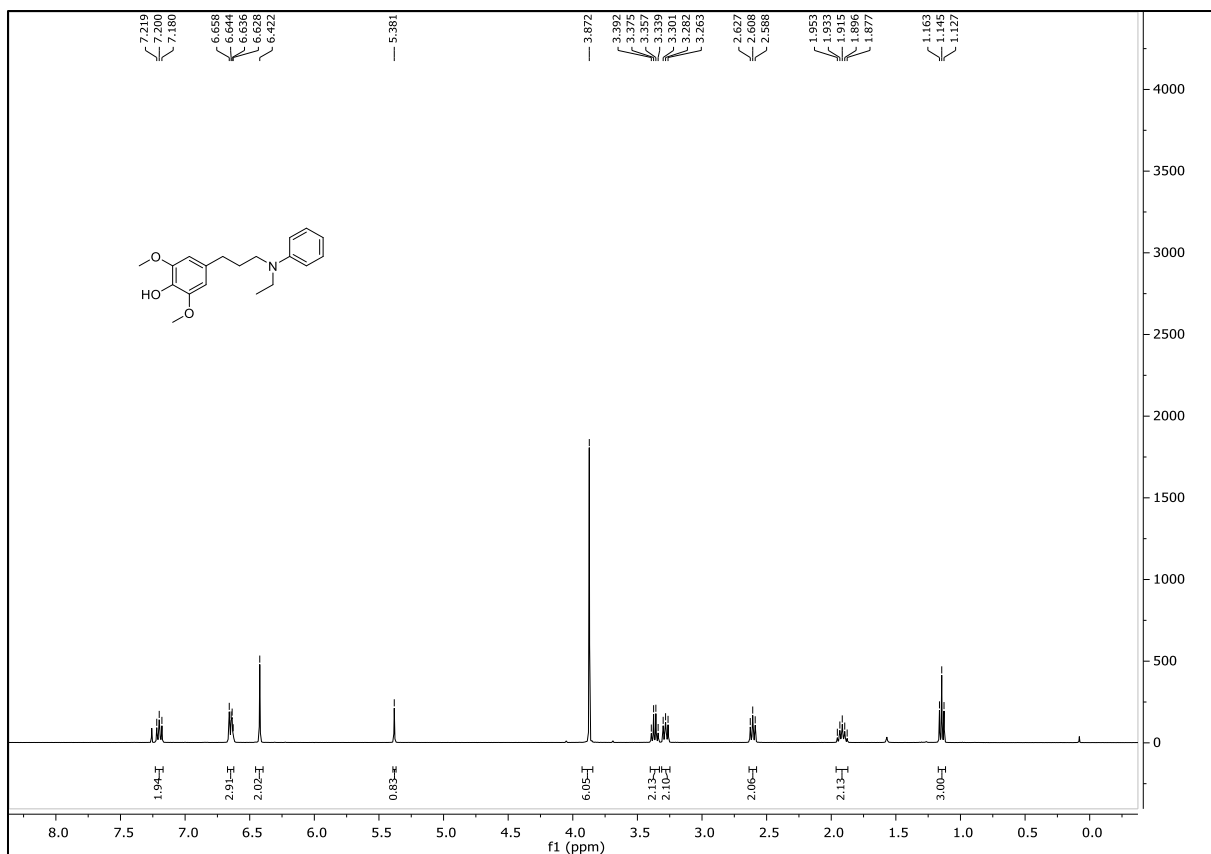
Supplementary Figure 64. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Sj.



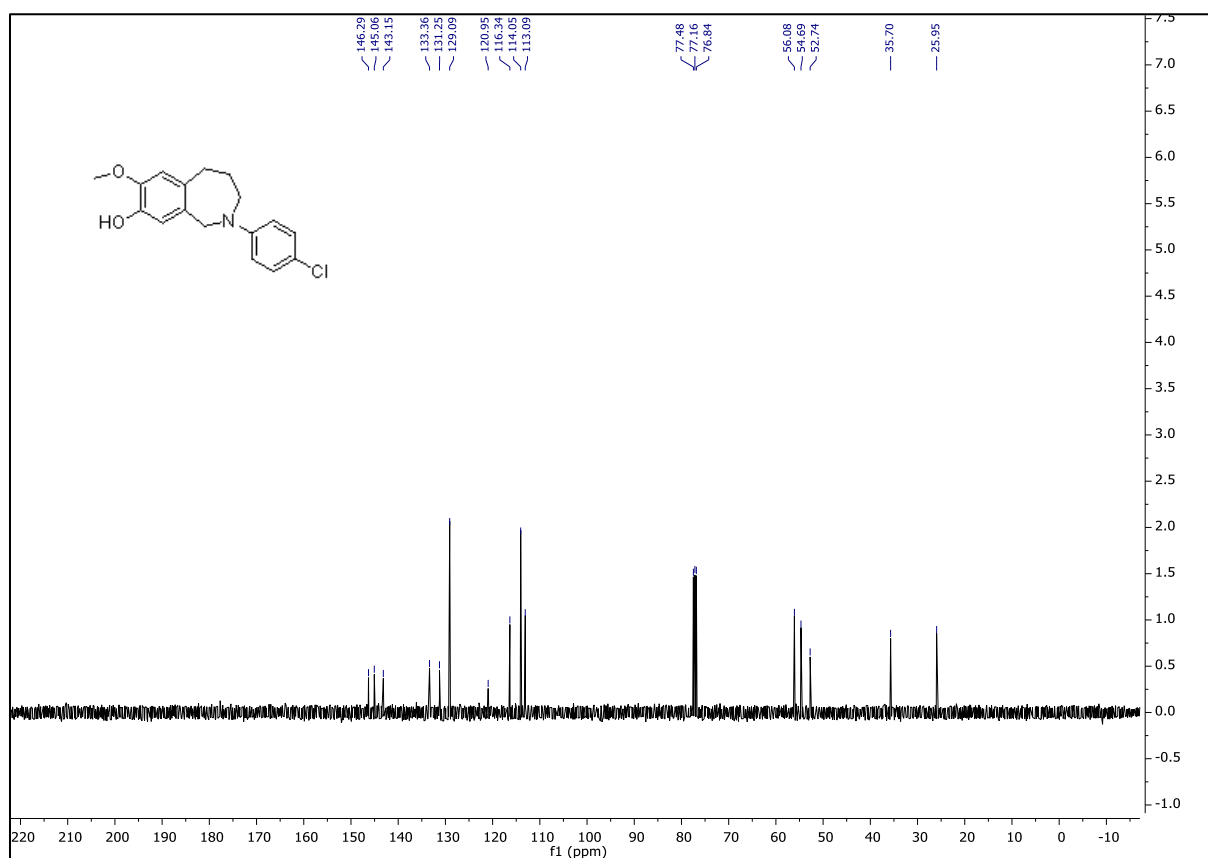
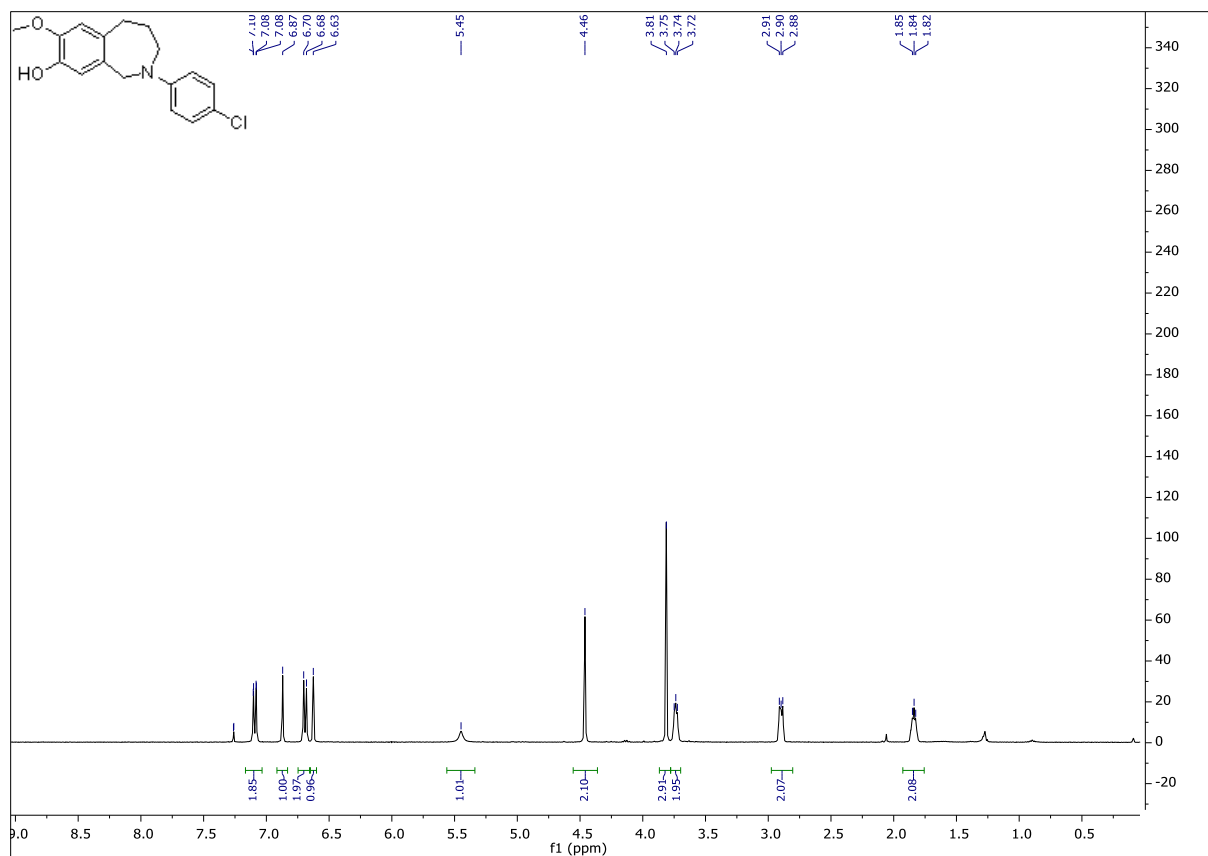
Supplementary Figure 65.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5Sn.



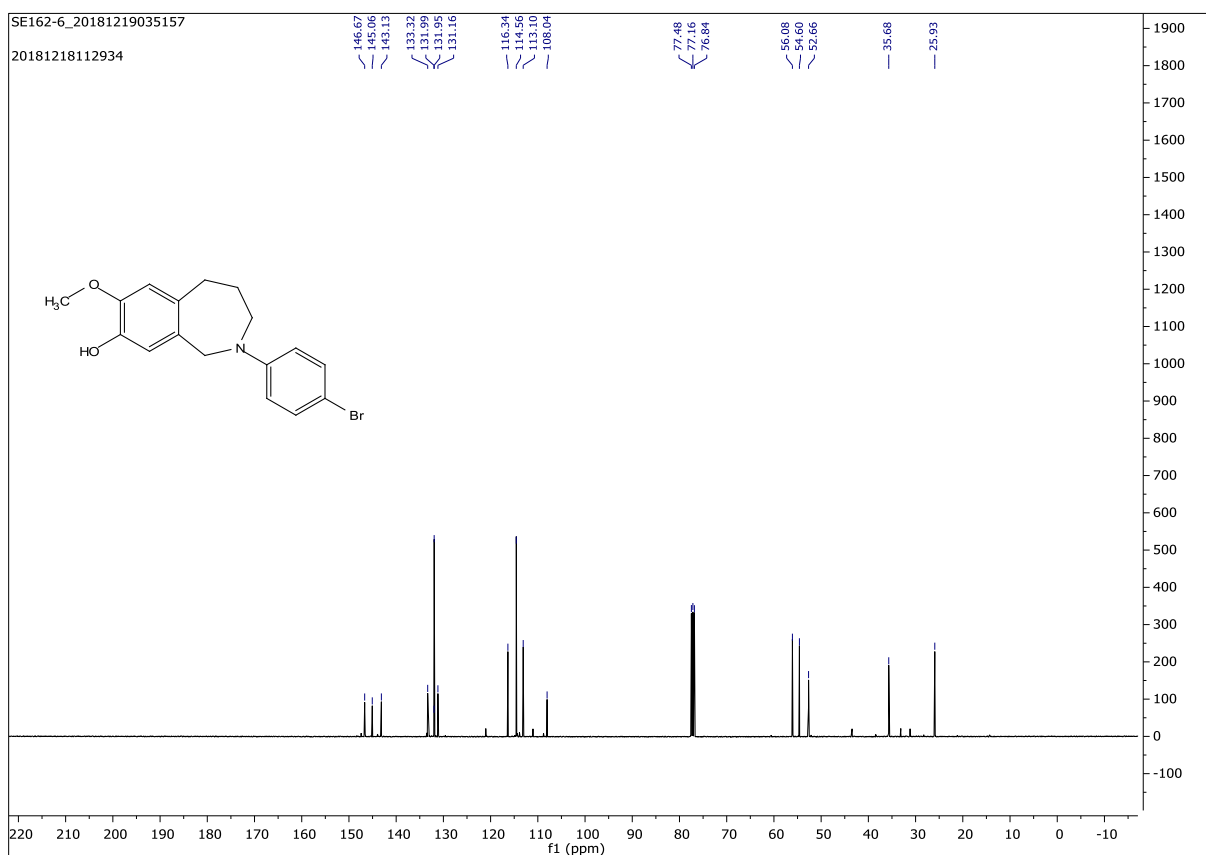
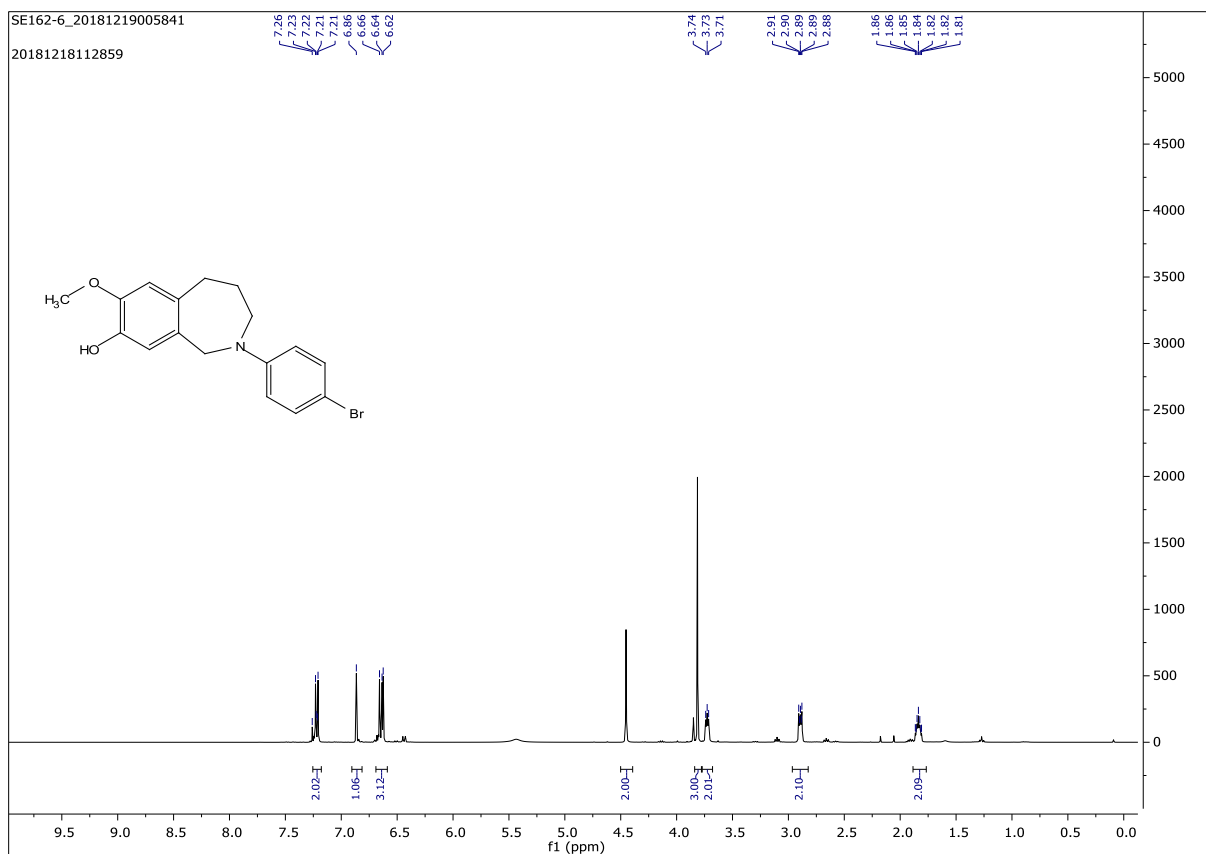
Supplementary Figure 66. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 5Sp.



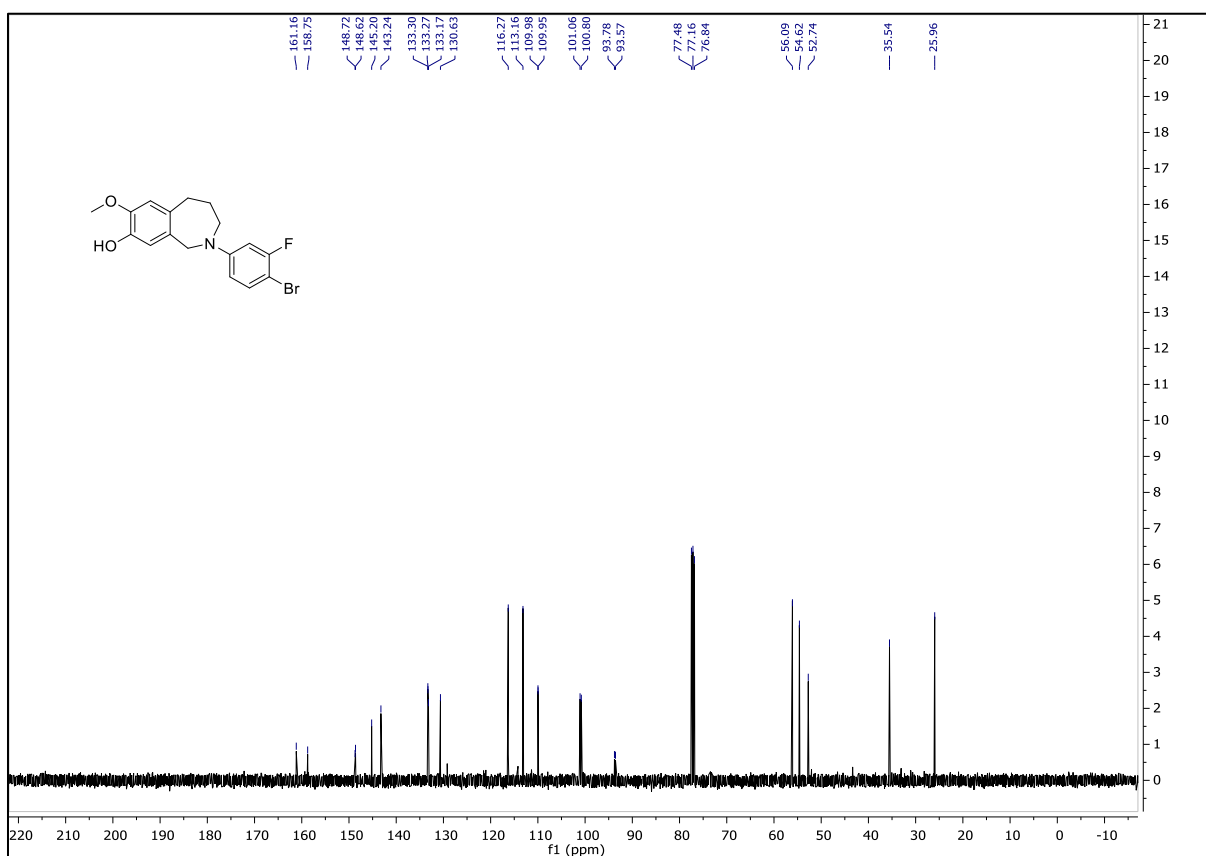
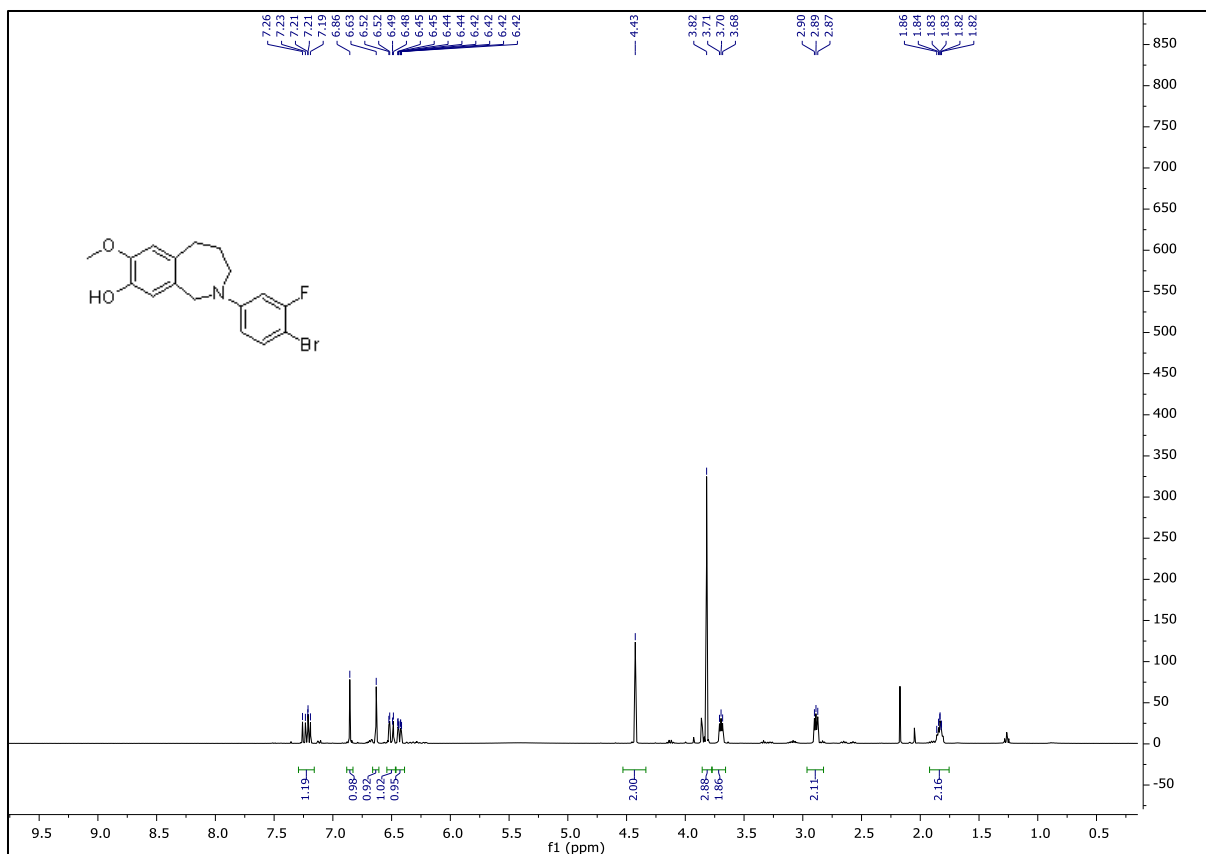
Supplementary Figure 67.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 5St.



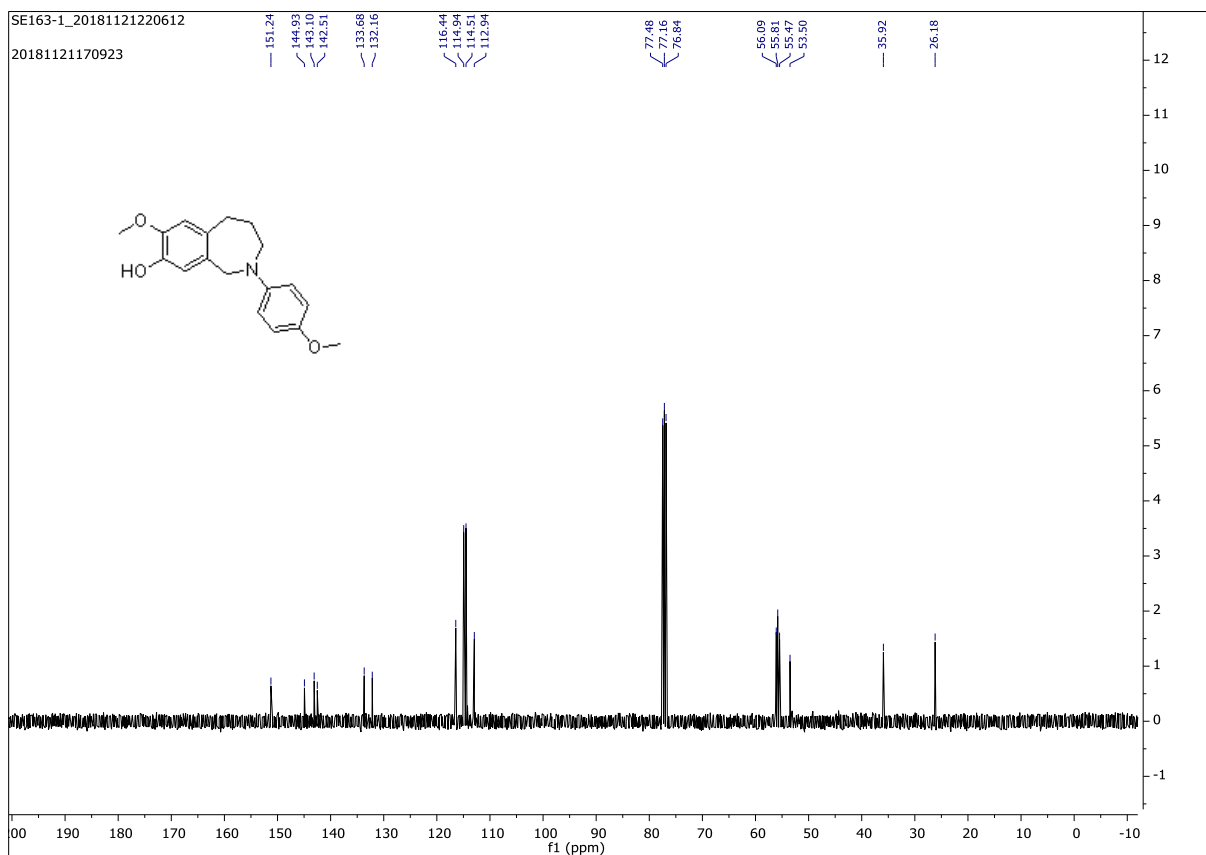
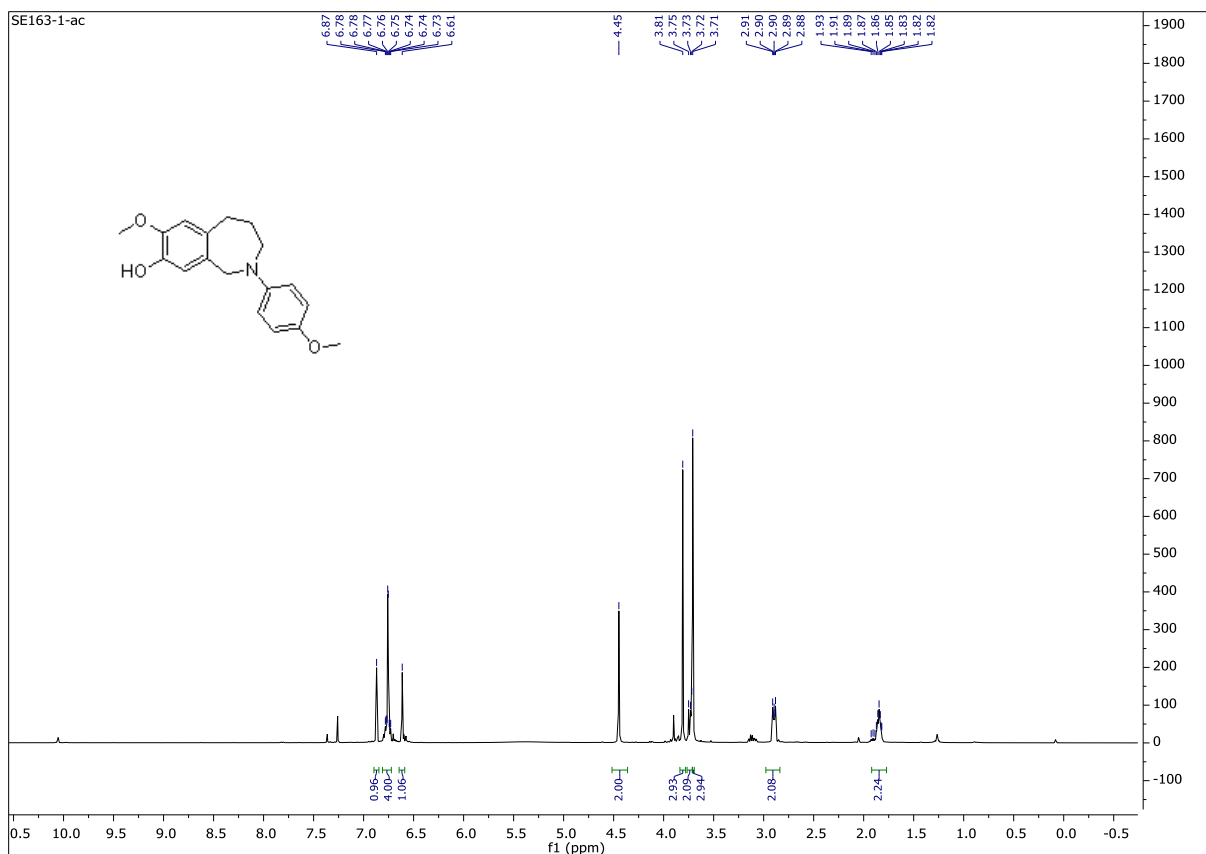
Supplementary Figure 68. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 6Gb.



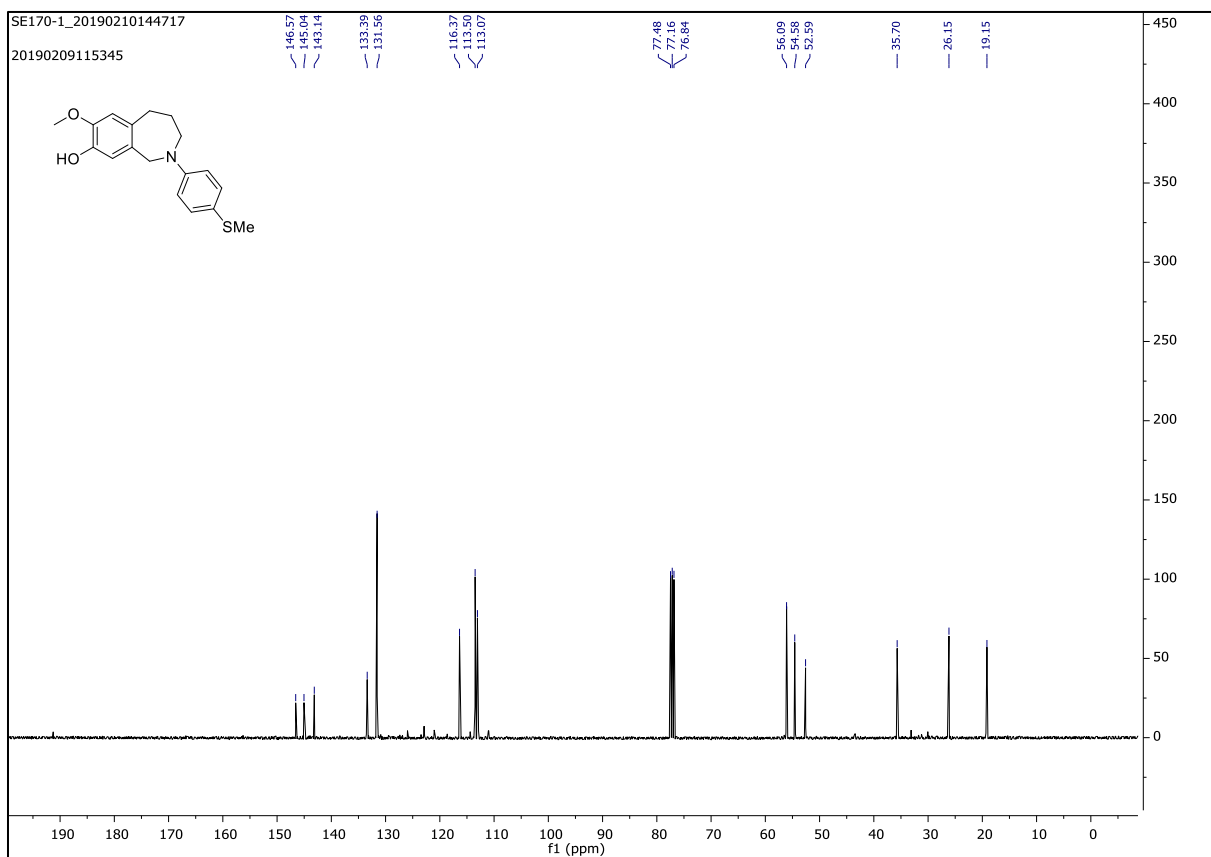
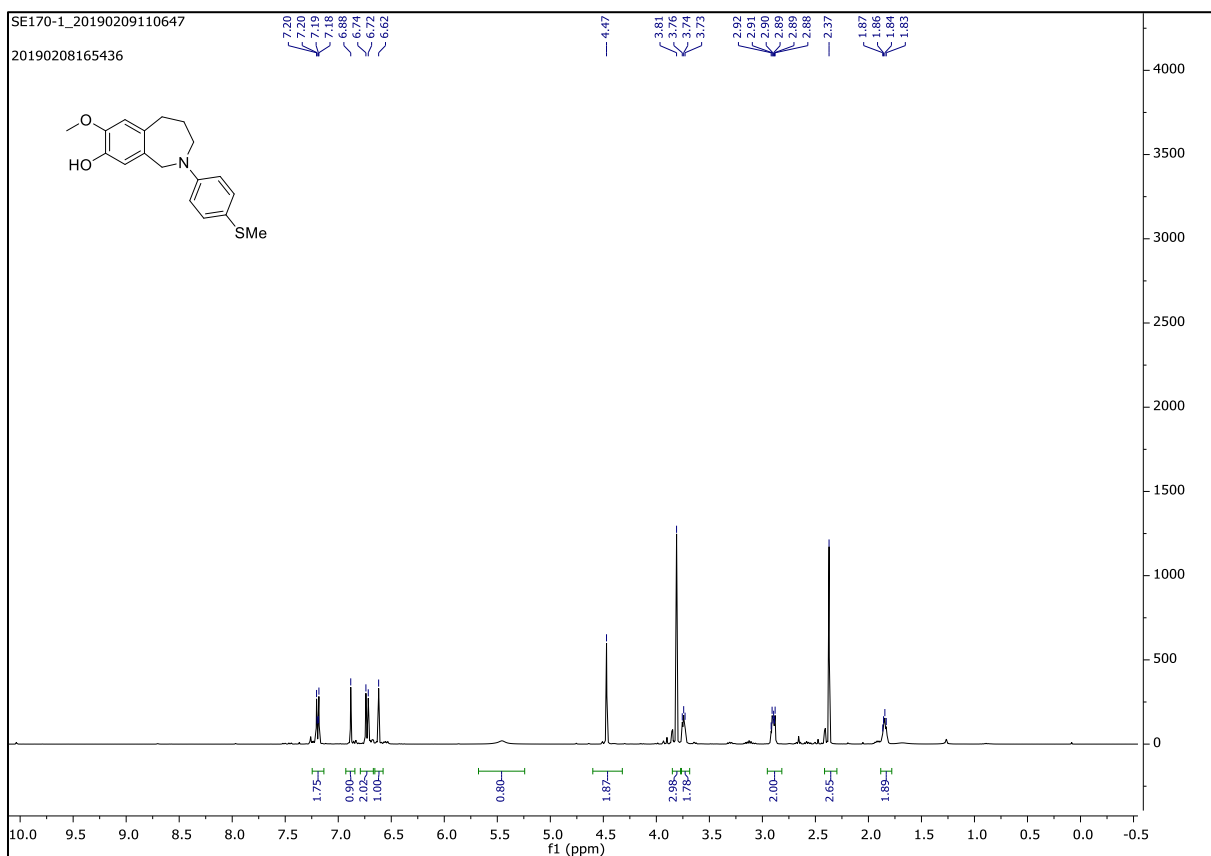
Supplementary Figure 69.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 6Gc.



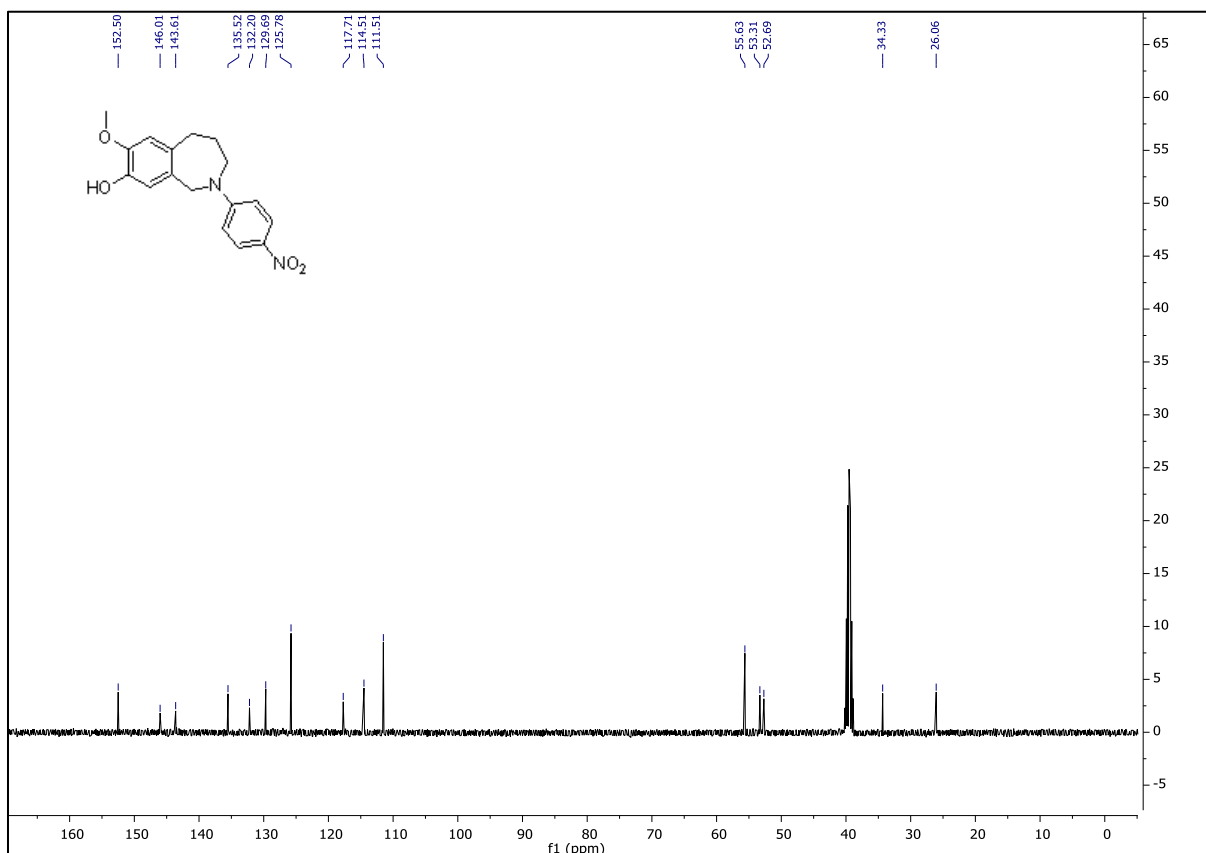
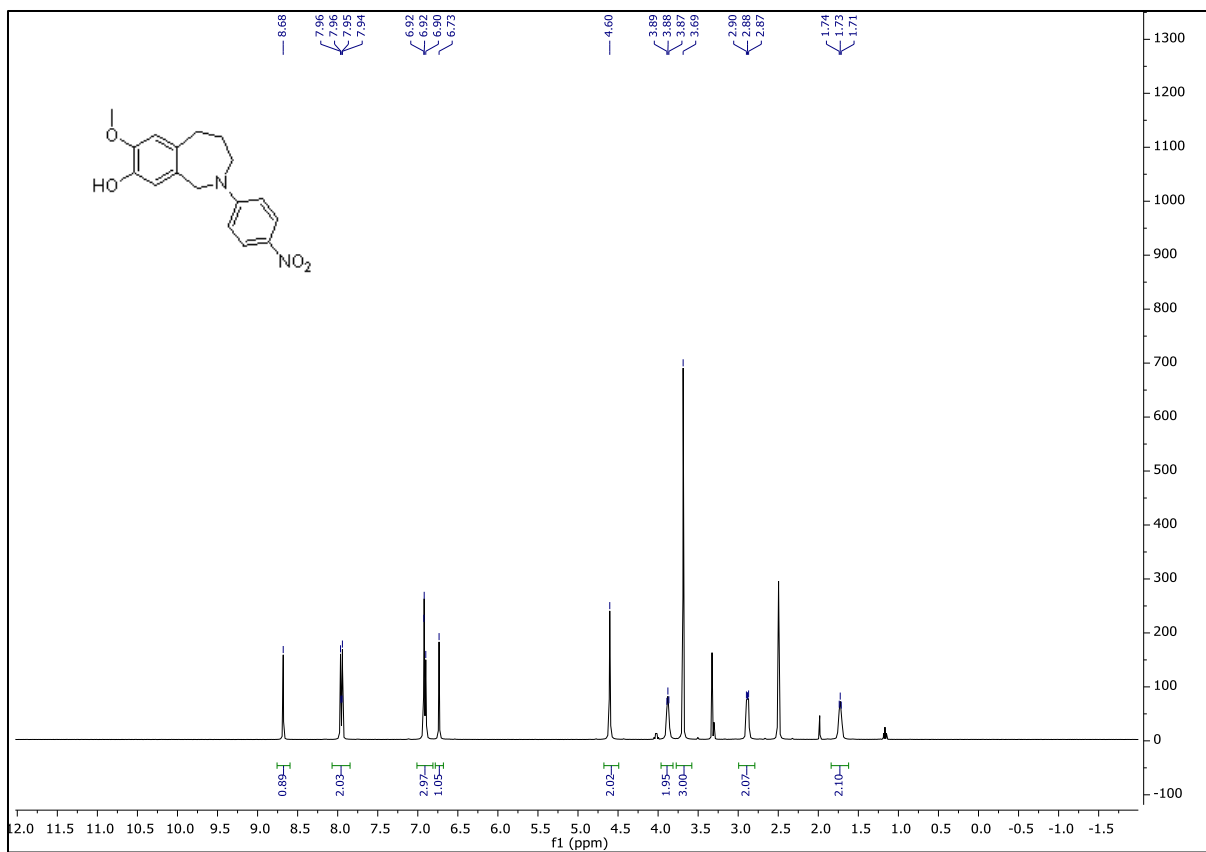
Supplementary Figure 70. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 6Ge.



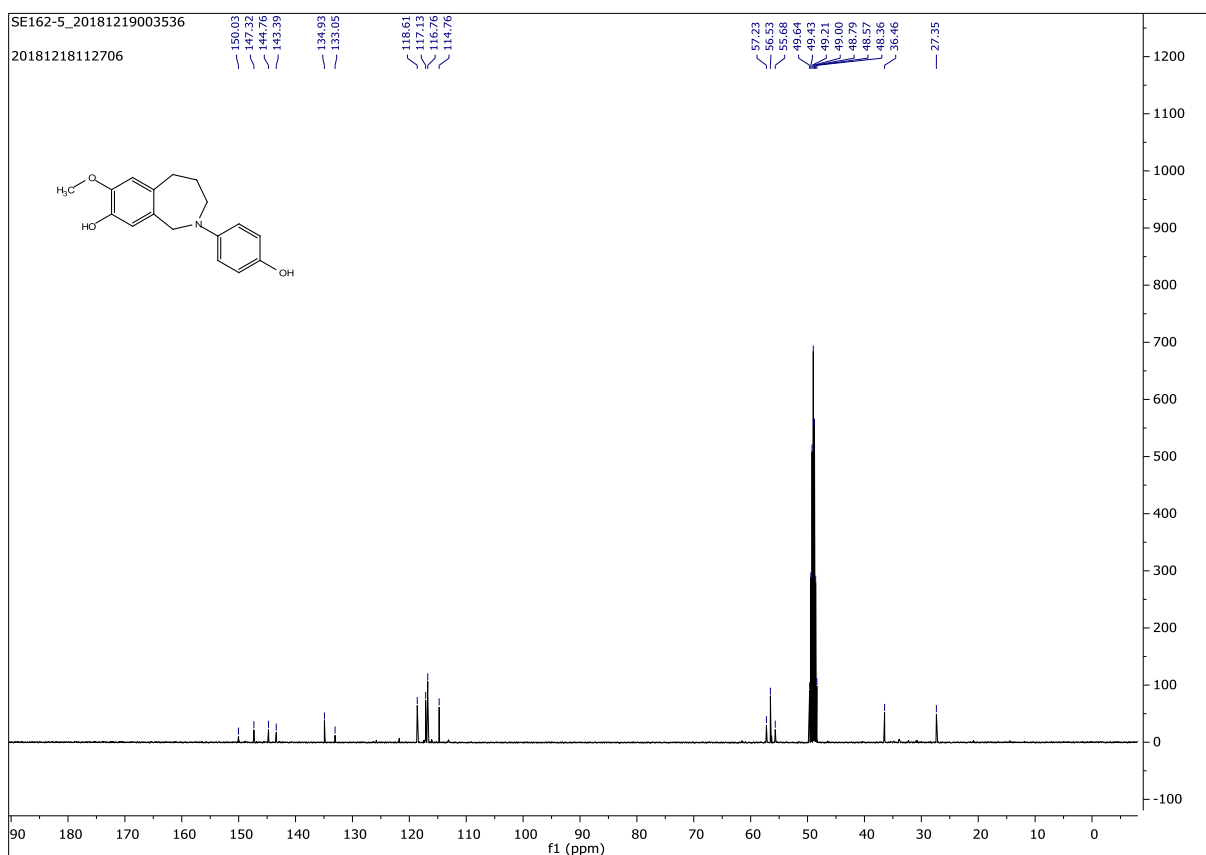
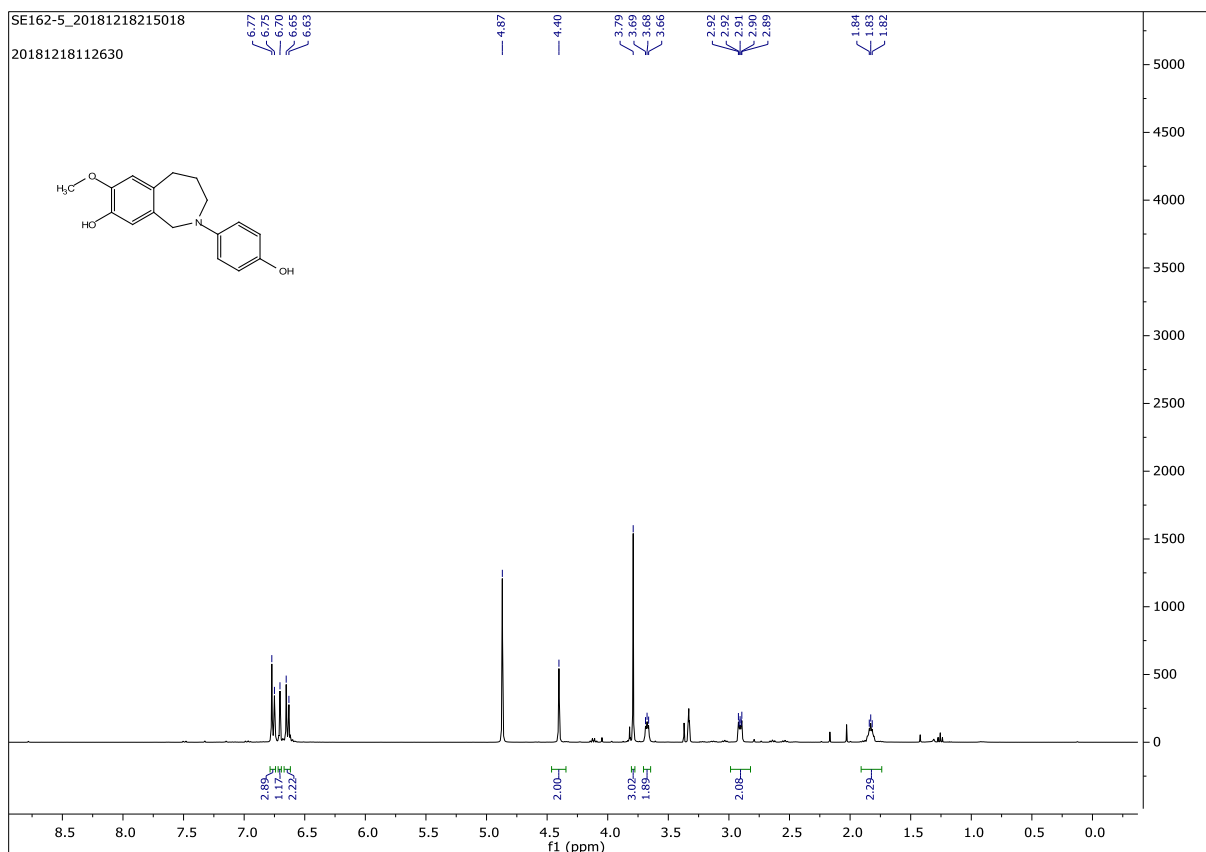
Supplementary Figure 71.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 6Gf.



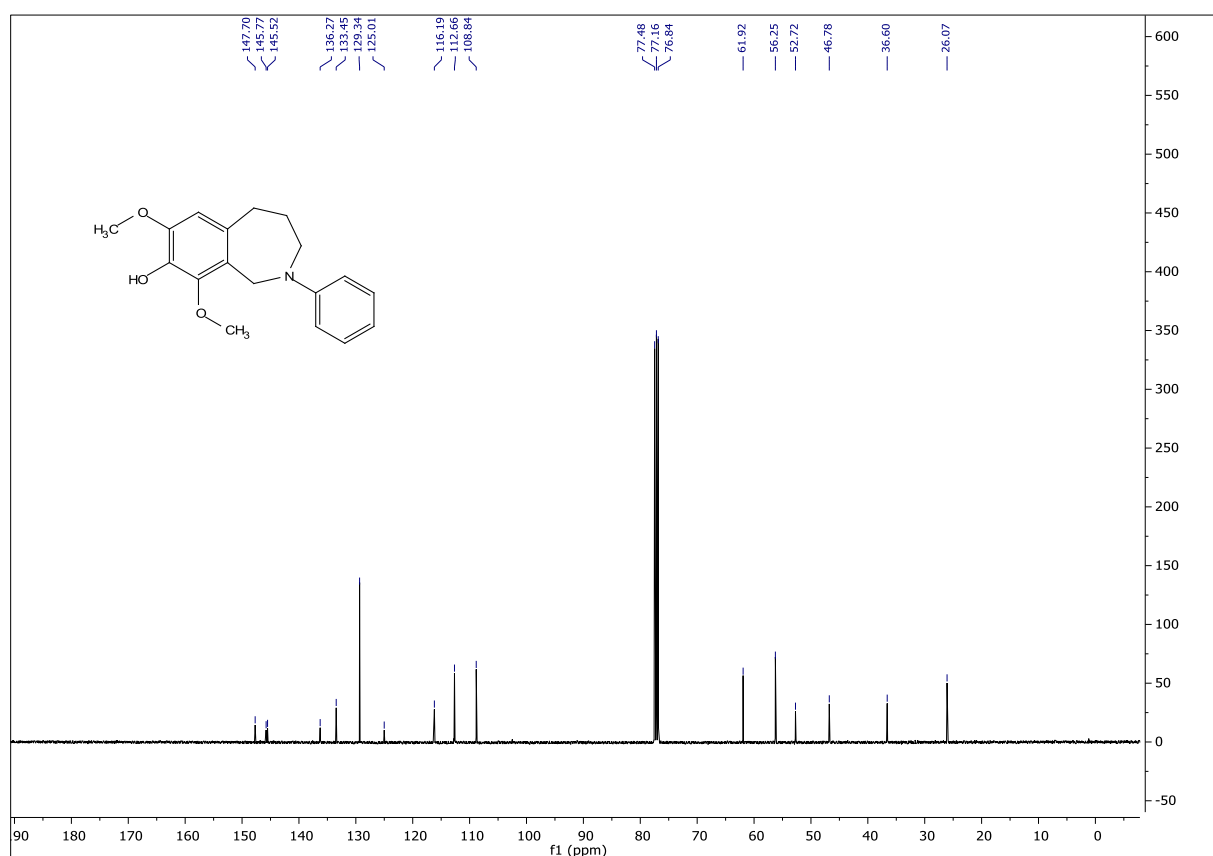
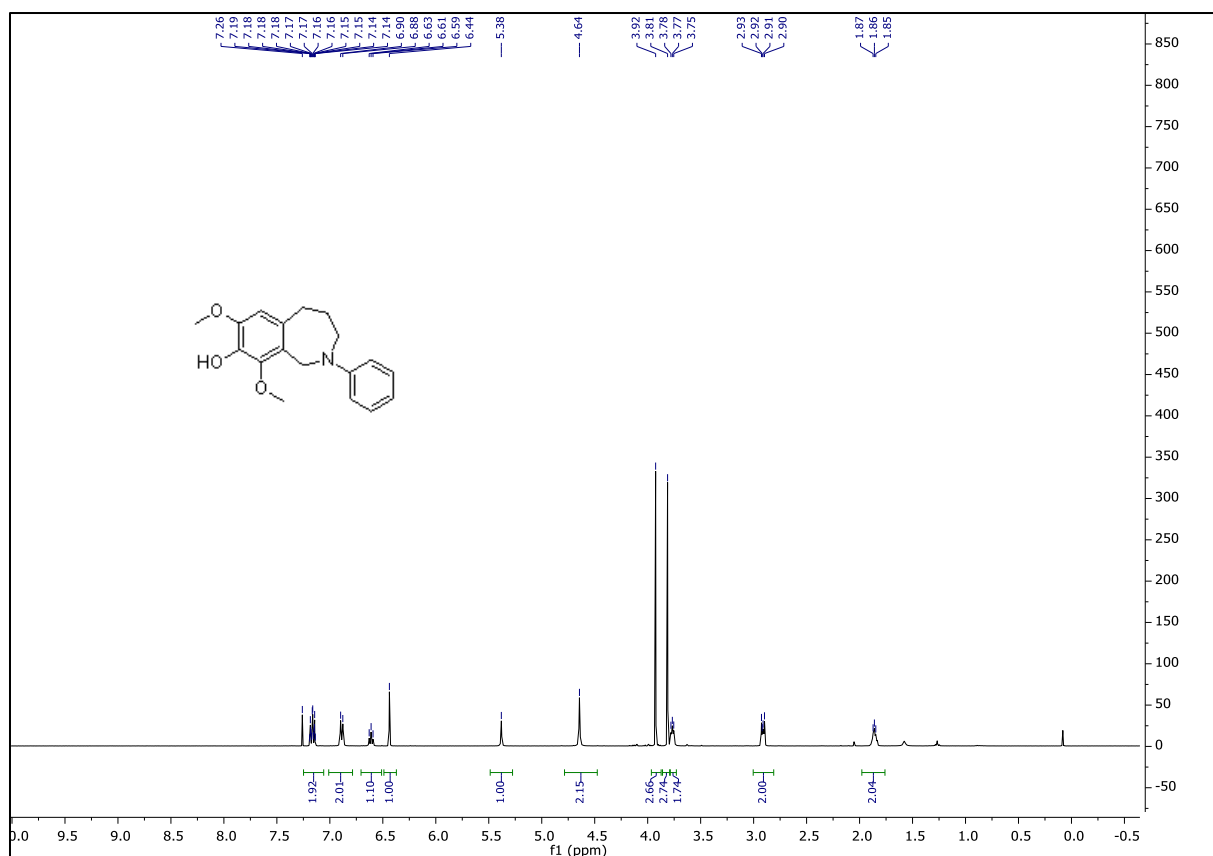
Supplementary Figure 72.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 6Gh.



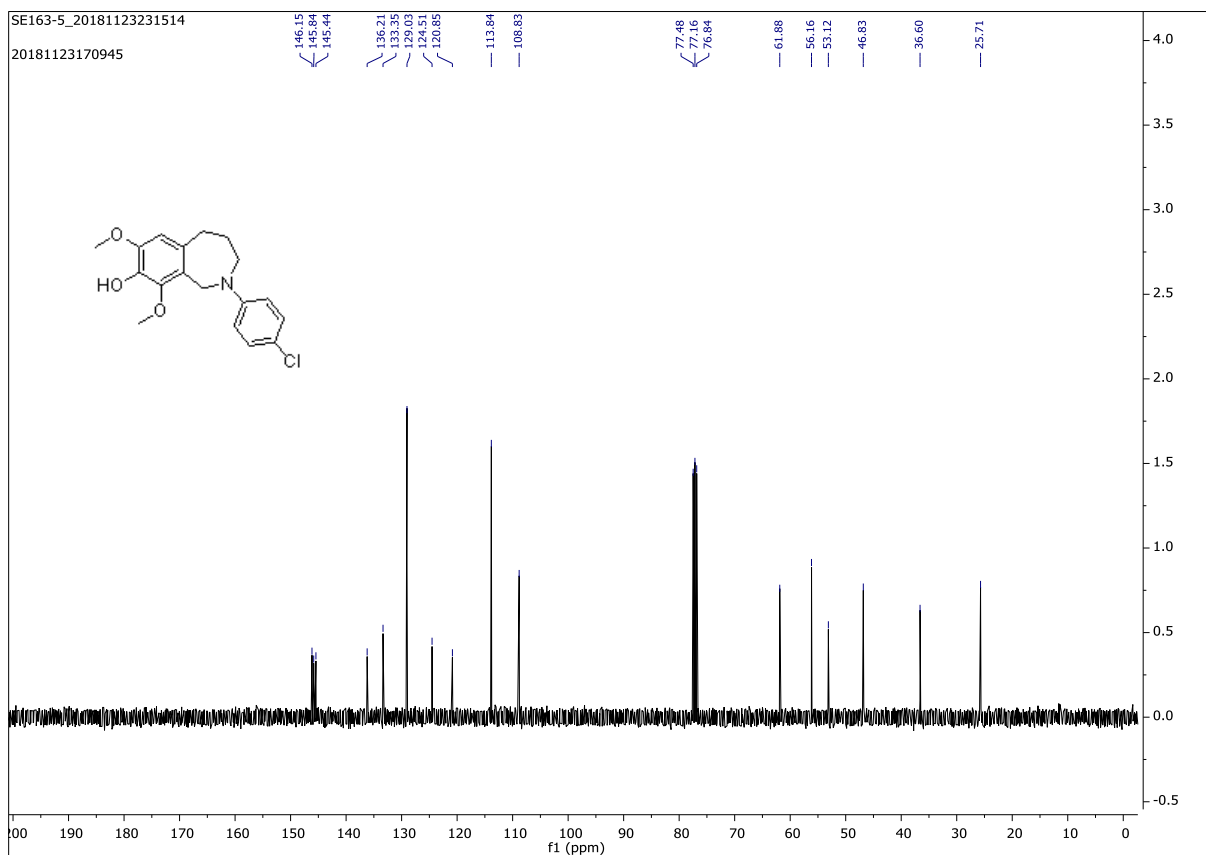
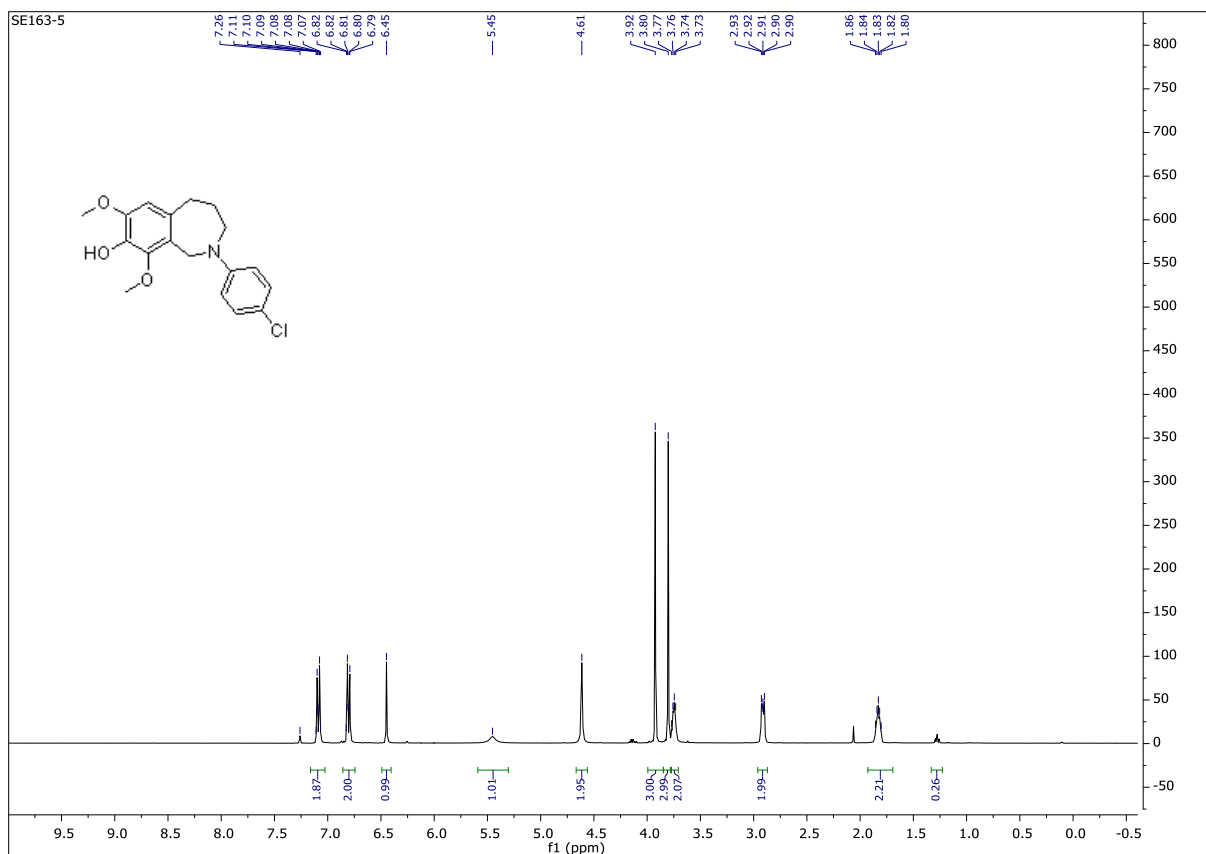
Supplementary Figure 73.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 6Gj.



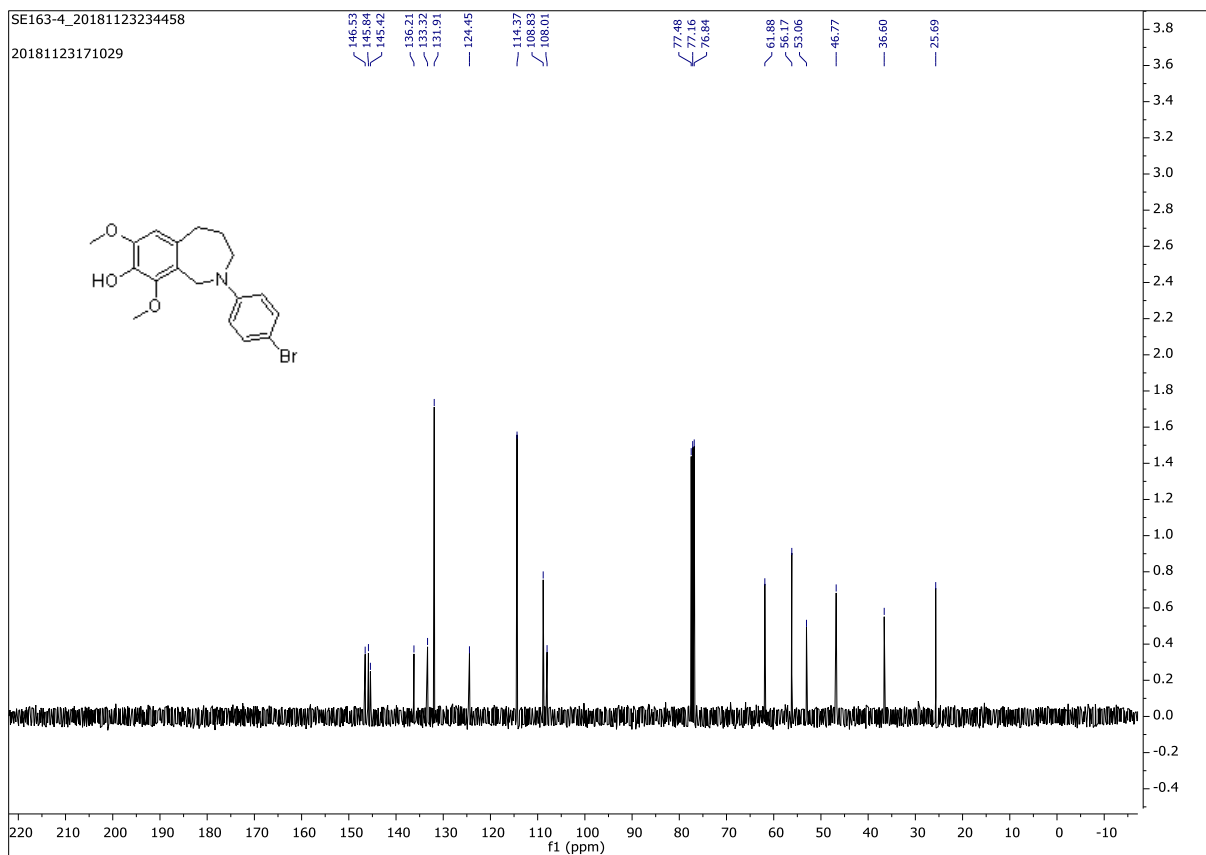
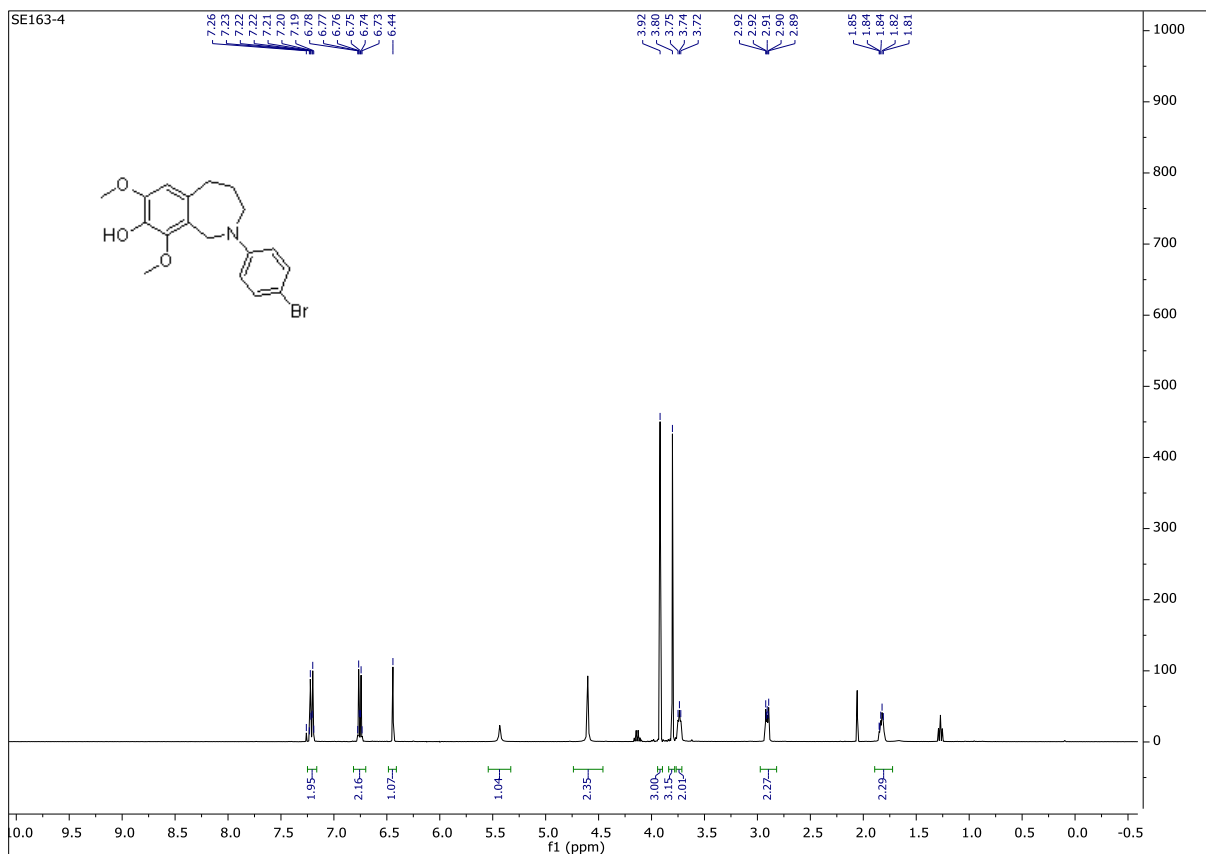
Supplementary Figure 74.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 6Gp.



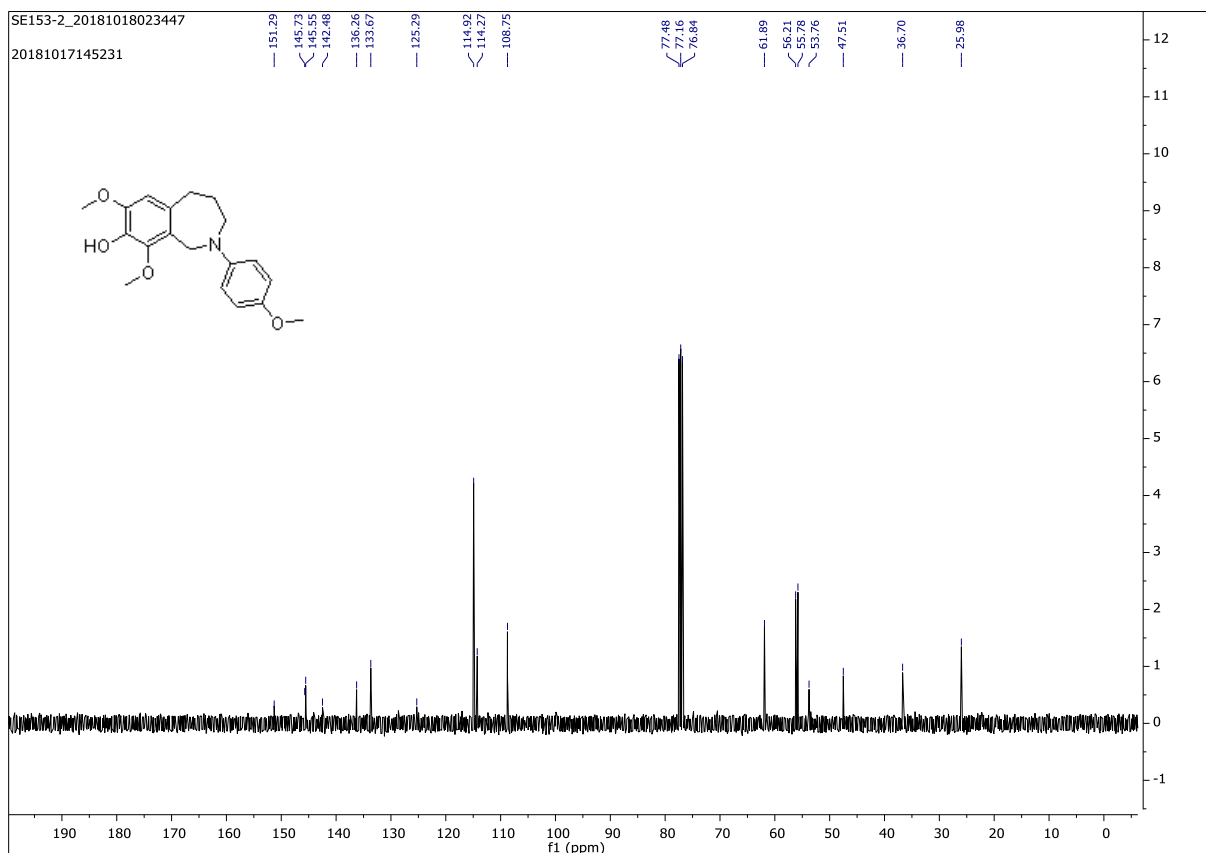
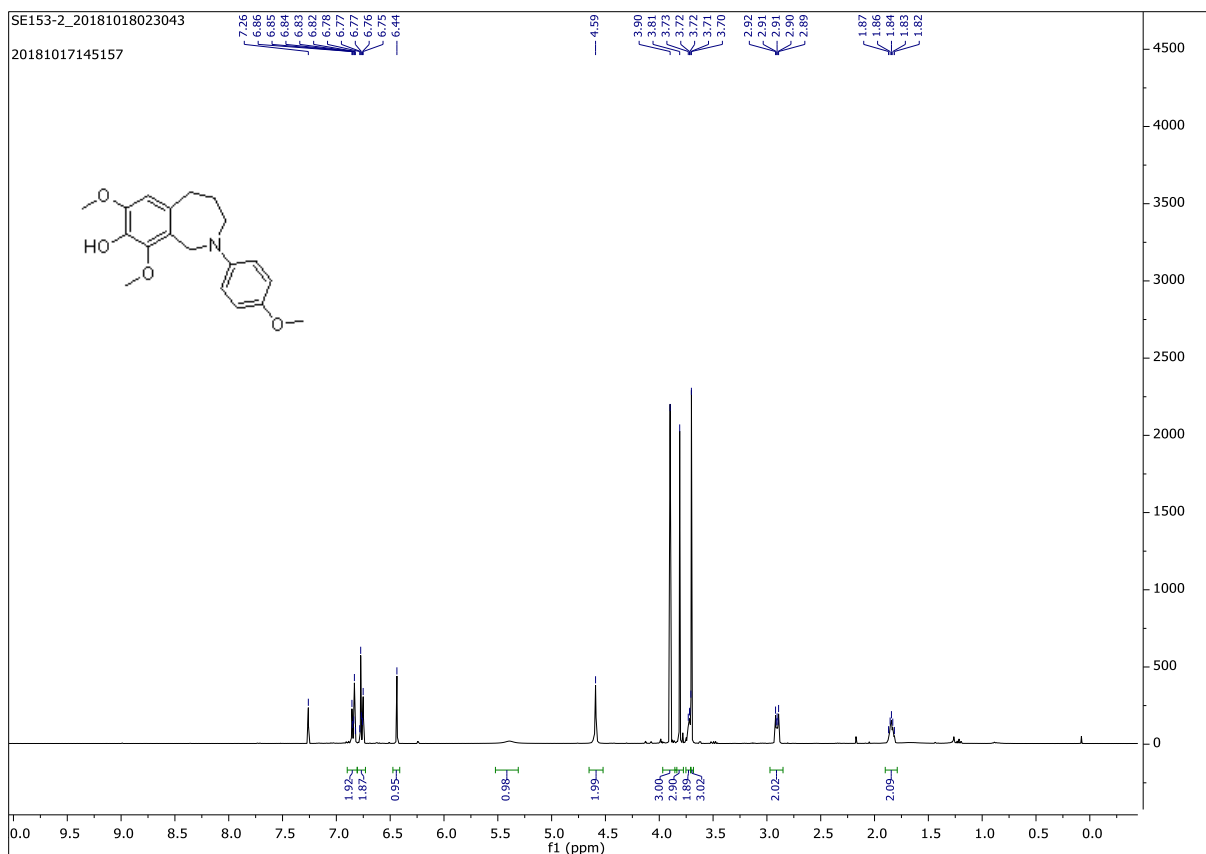
Supplementary Figure 75. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 6Sa.



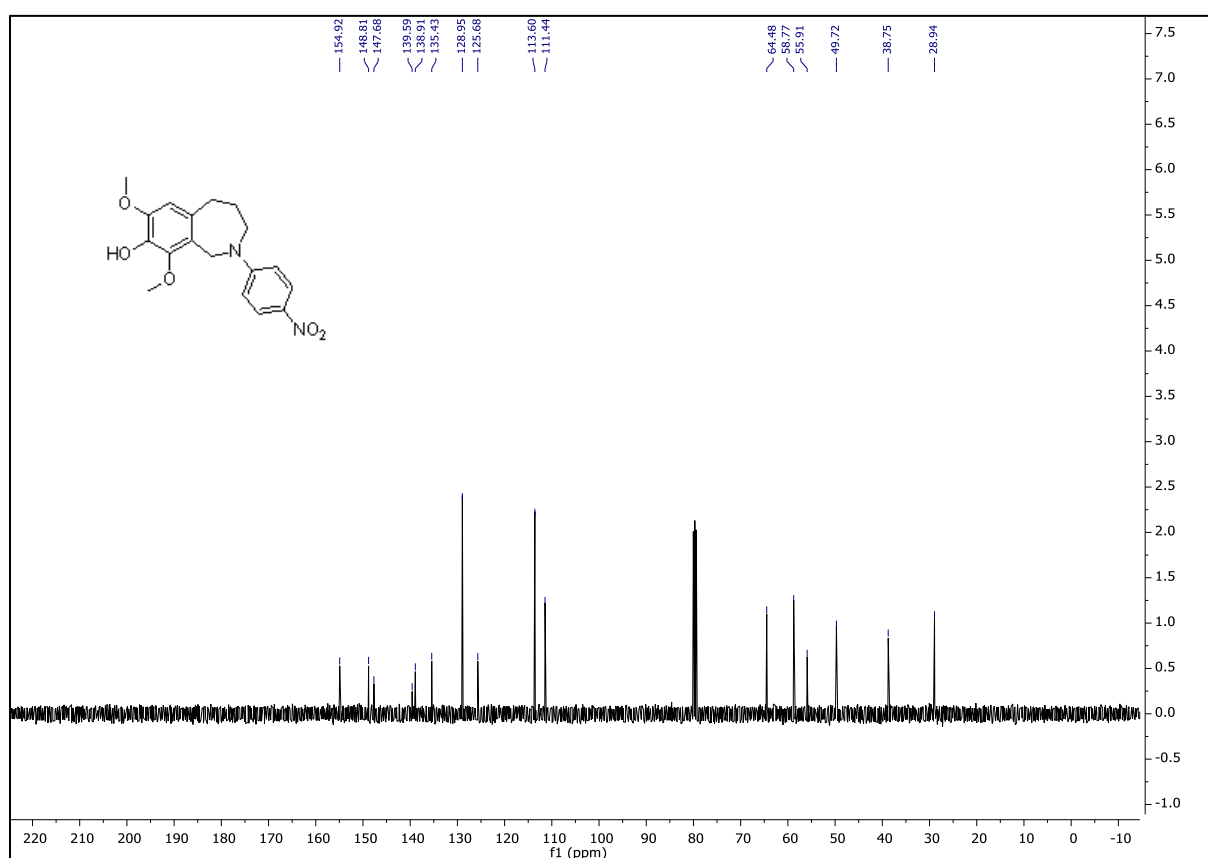
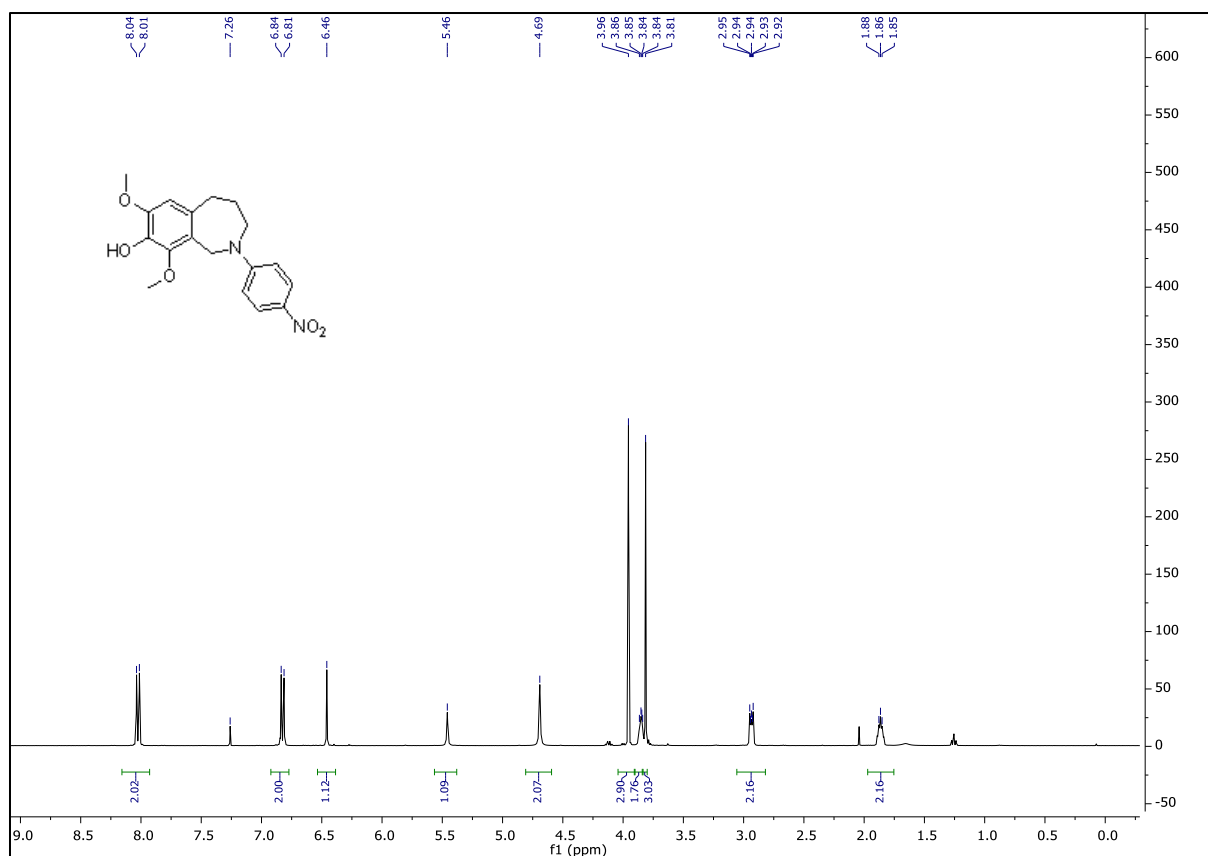
Supplementary Figure 76.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 6Sb.



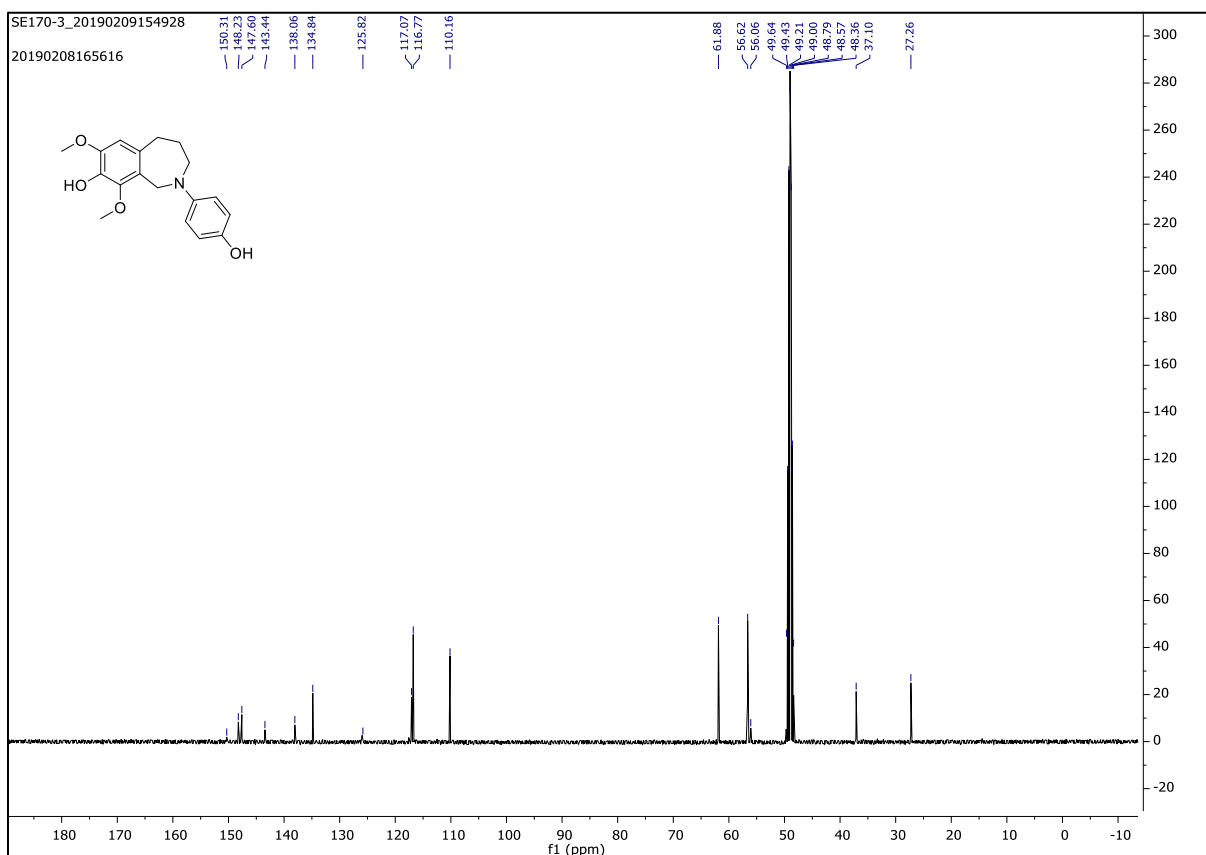
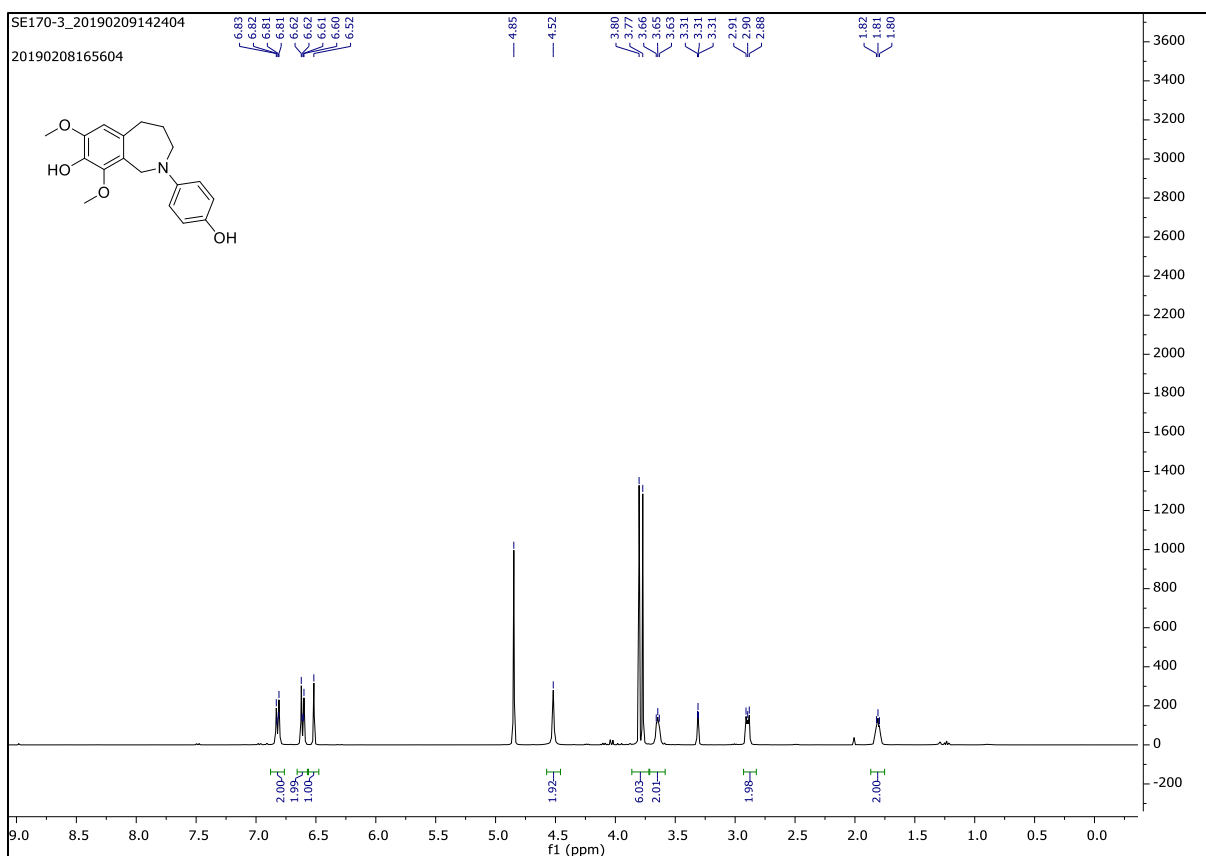
Supplementary Figure 77.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 6Sc.



Supplementary Figure 78.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 6Sf.



Supplementary Figure 79. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound 6Sj.



Supplementary Figure 80.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound 6Sp.

### **Author contributions**

S. E. designed and performed experiments in all stages of the work except biological studies, collected and analysed data, wrote the first manuscript draft and was further engaged in writing the manuscript. A. A. performed experiments related to Ru catalysis and cyclization, collected and analysed data and contributed to preparing the supporting information. Z. S. provided input into experiments related to lignocellulose, analysed and displayed 2D-HSQC NMR and GPC data. Z. S. and Y. L. provided input for Figure 1 and 2. Y. L. developed the Ni catalysed amination with ammonia, conceived the idea of the DES experiments and prepared the DES. J. H coordinated the biological testing, analysed the data, prepared Figure 3 and wrote the corresponding manuscript chapter. A. K. H. H wrote the manuscript chapter on biological studies and supervised all studies related to biological testing. K. B. contributed to data analysis and experiment design, conceived and supervised the research, and wrote the manuscript. All authors commented on the manuscript.