

## Supplementary Material

### **Flexible Analogues of Azaindole DYRK1A Inhibitors Elicit Cytotoxicity in Glioblastoma Cells**

*Qingqing Zhou,<sup>A</sup> Tristan A. Reekie,<sup>A</sup> Ramzi H. Abbassi,<sup>B</sup> Dinesh Indurthi Venkata,<sup>B</sup> Josep S. Font,<sup>C</sup> Renae M. Ryan,<sup>C</sup> Louis M. Rendina,<sup>A</sup> Lenka Munoz,<sup>B</sup> and Michael Kassiou<sup>A,D</sup>*

<sup>A</sup>School of Chemistry, The University of Sydney, Sydney, NSW 2006, Australia.

<sup>B</sup>School of Medical Sciences, Discipline of Pathology and Charles Perkins Centre, The University of Sydney, Sydney, NSW 2006, Australia.

<sup>C</sup>School of Medical Sciences, Discipline of Pharmacology, The University of Sydney, Sydney, NSW 2006, Australia.

<sup>D</sup>Corresponding author. Email: michael.kassiou@sydney.edu.au

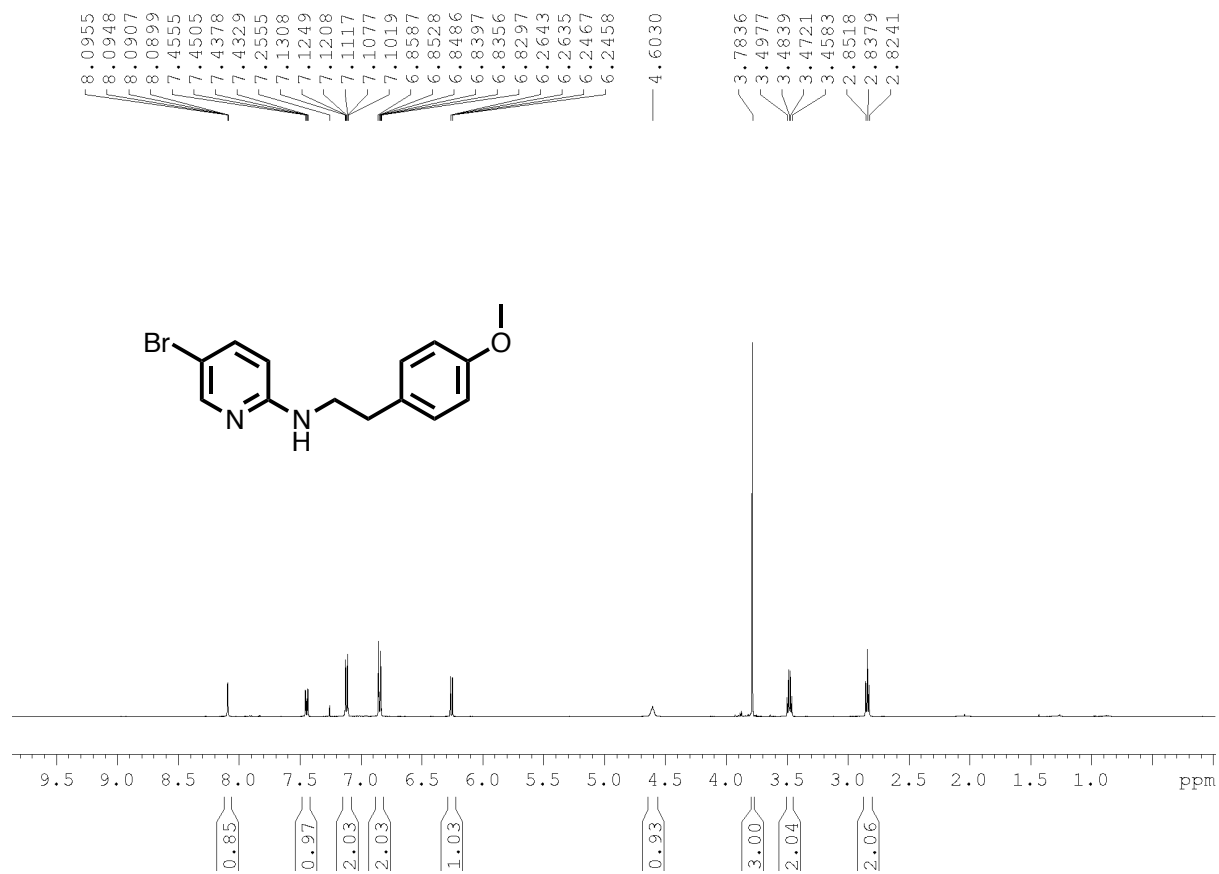


Figure S1 <sup>1</sup>H NMR spectrum of compound 6 in CDCl<sub>3</sub> (500 MHz).

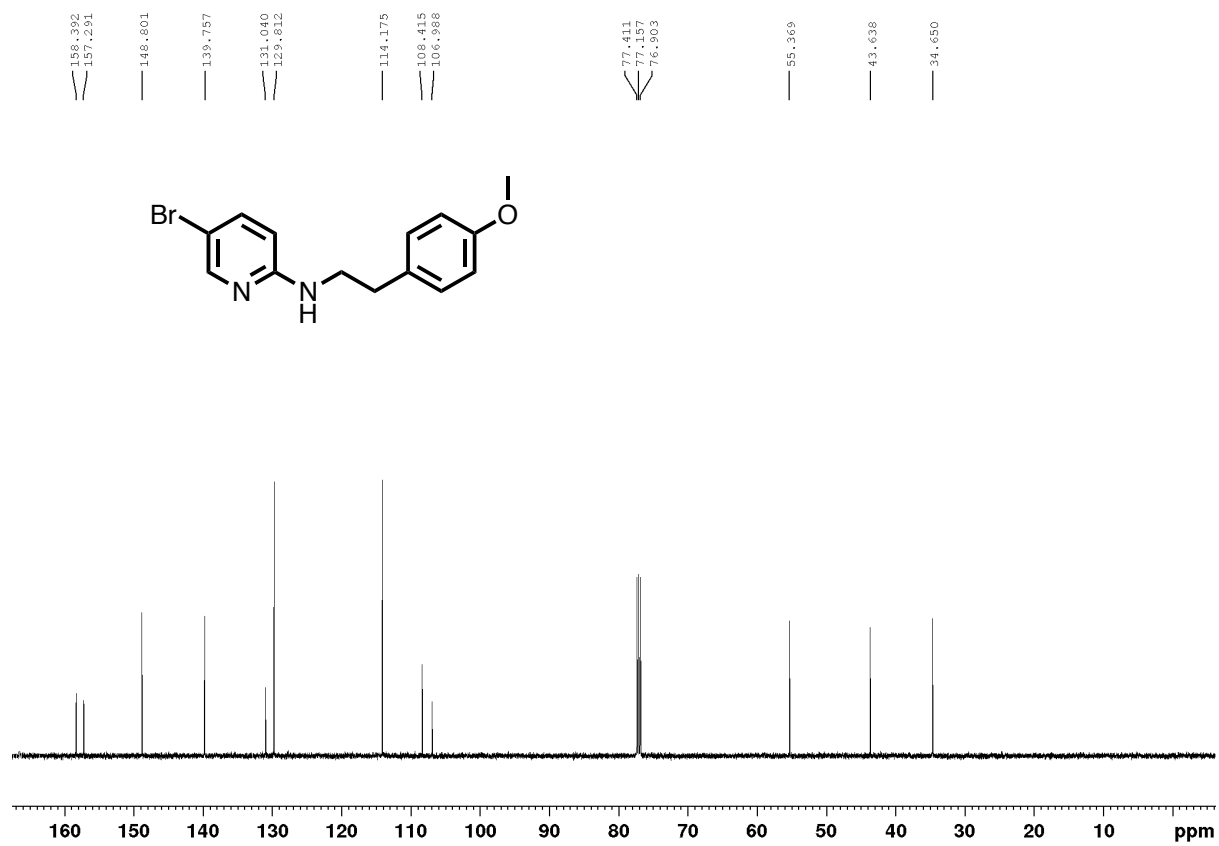


Figure S2 <sup>13</sup>C NMR spectrum of compound 6 in CDCl<sub>3</sub> (125 MHz).



Figure S3 <sup>1</sup>H NMR spectrum of compound 7 in CDCl<sub>3</sub> (400 MHz).

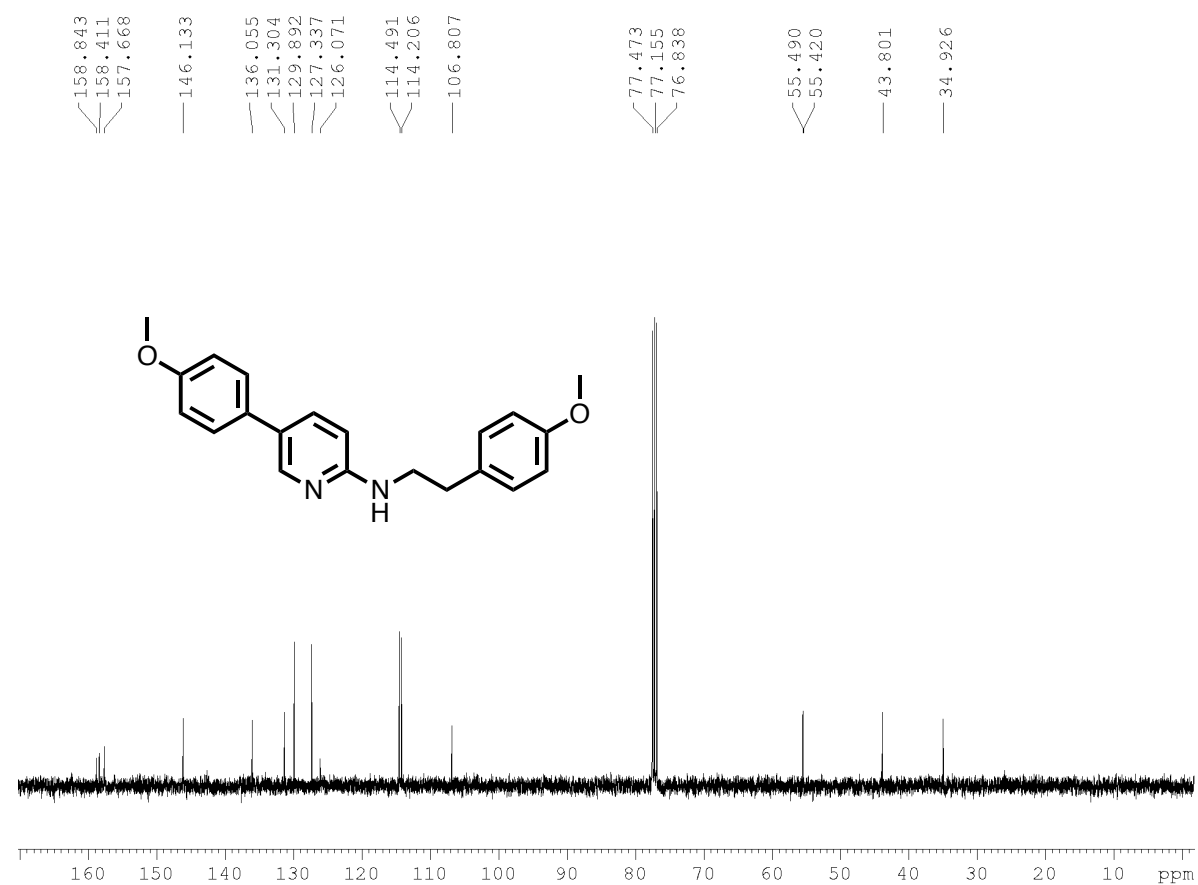


Figure S4 <sup>13</sup>C NMR spectrum of compound 7 in CDCl<sub>3</sub> (100 MHz).

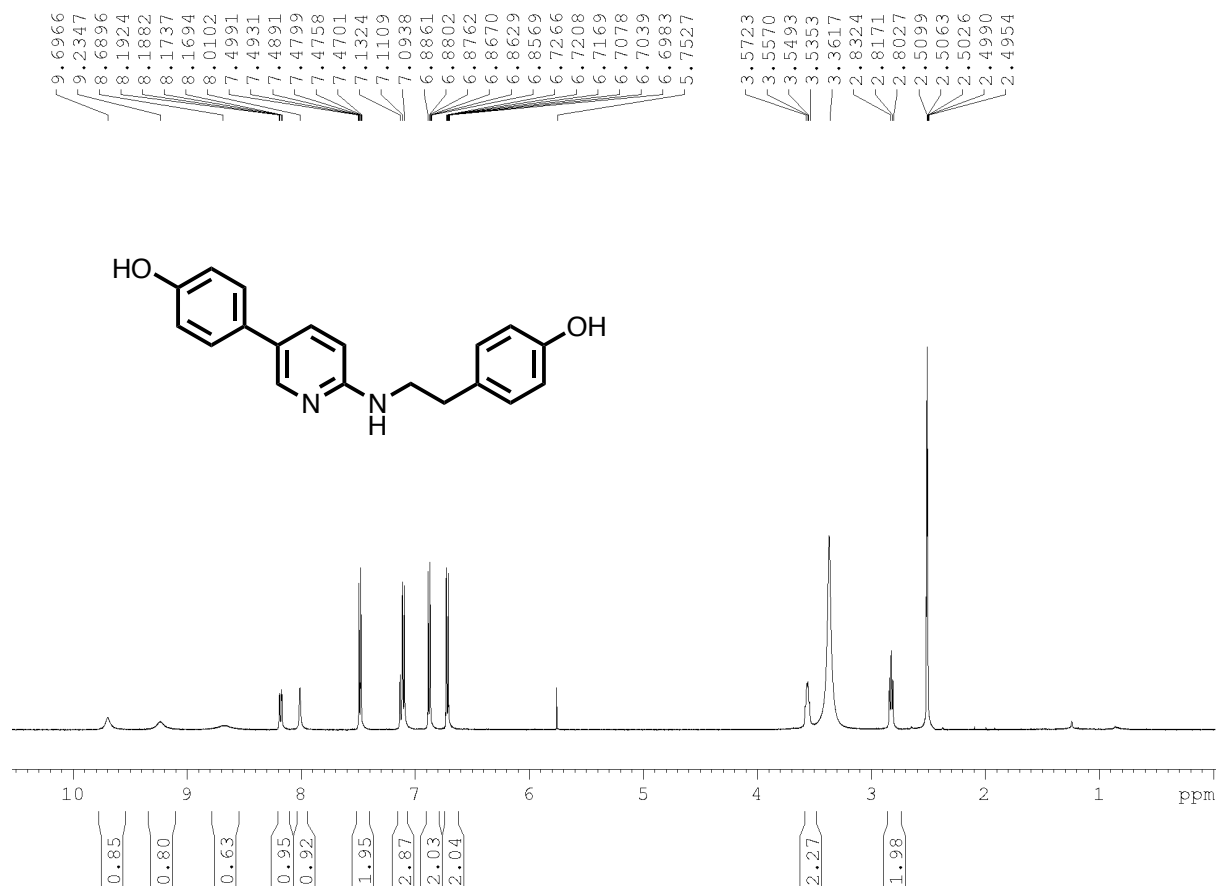


Figure S5 <sup>1</sup>H NMR spectrum of compound 2c in d-DMSO (500 MHz).

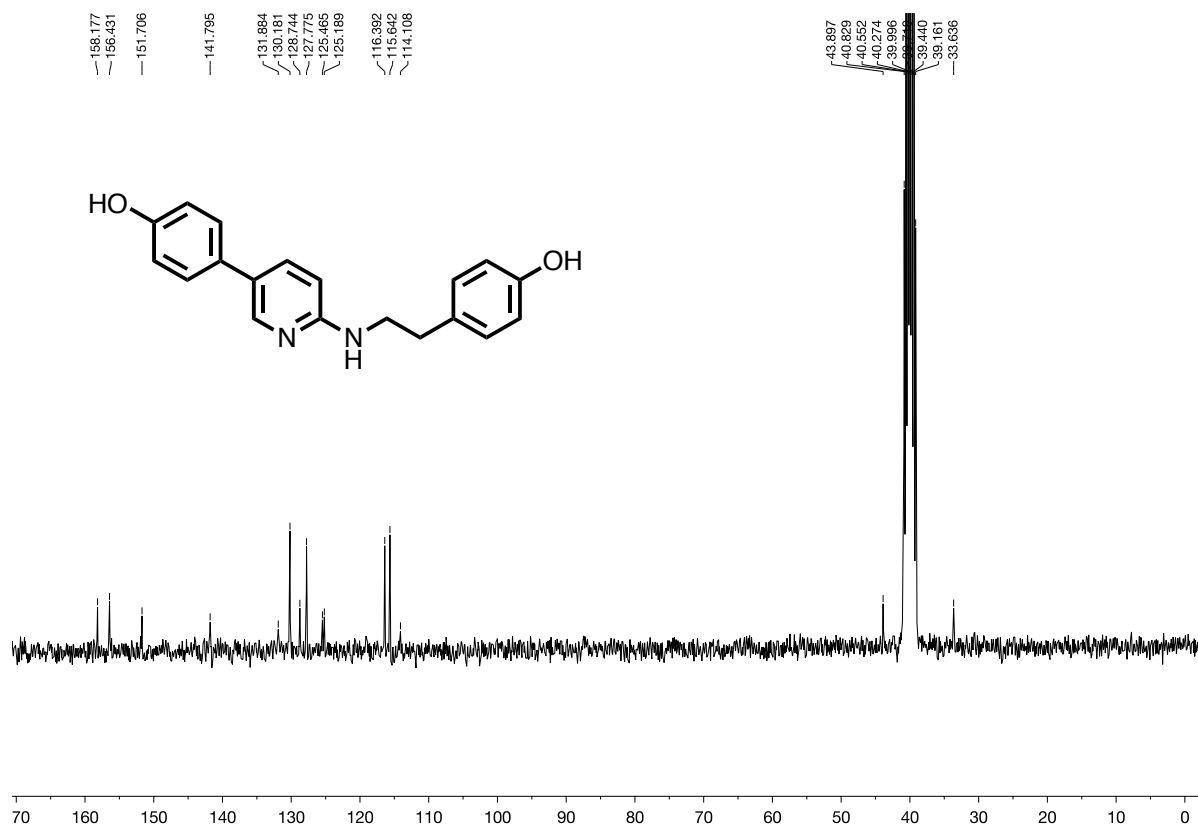
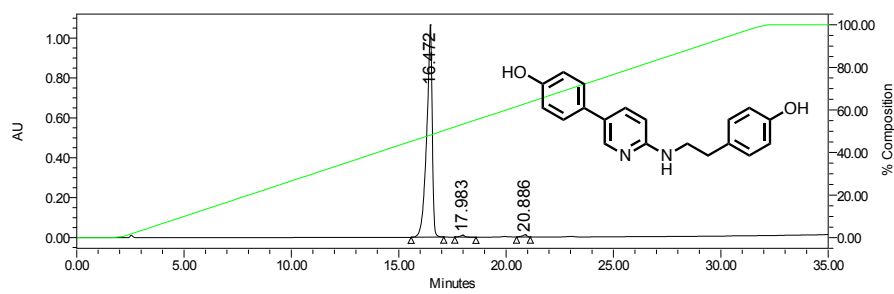


Figure S6 <sup>13</sup>C NMR spectrum of compound 2c in d-DMSO (75 MHz).



Peak information

	RT	Area	% Area
1	16.472	18809791	98.35
2	17.983	144280	0.75
3	20.886	170729	0.89

Figure S6\* HPLC chromatogram of compound 2c.

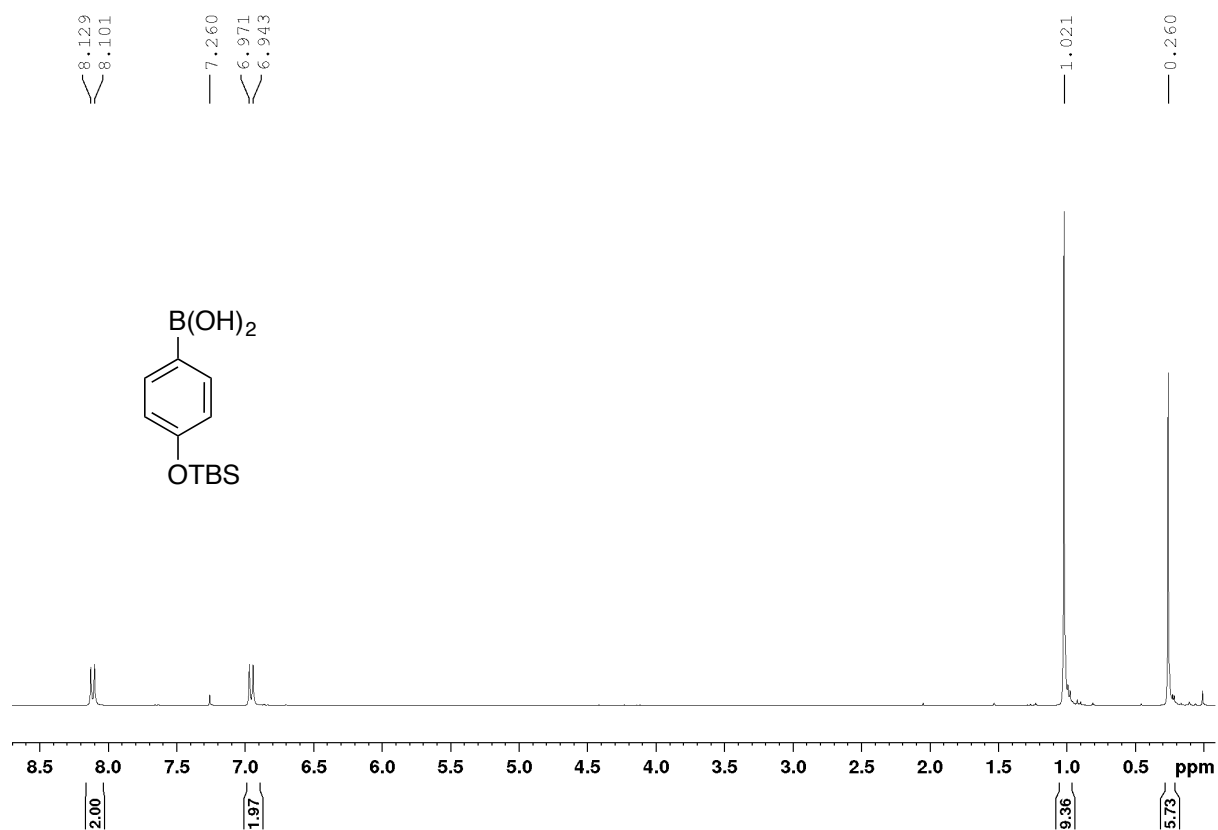


Figure S7 <sup>1</sup>H NMR spectrum of compound 9 in CDCl<sub>3</sub> (300 MHz).

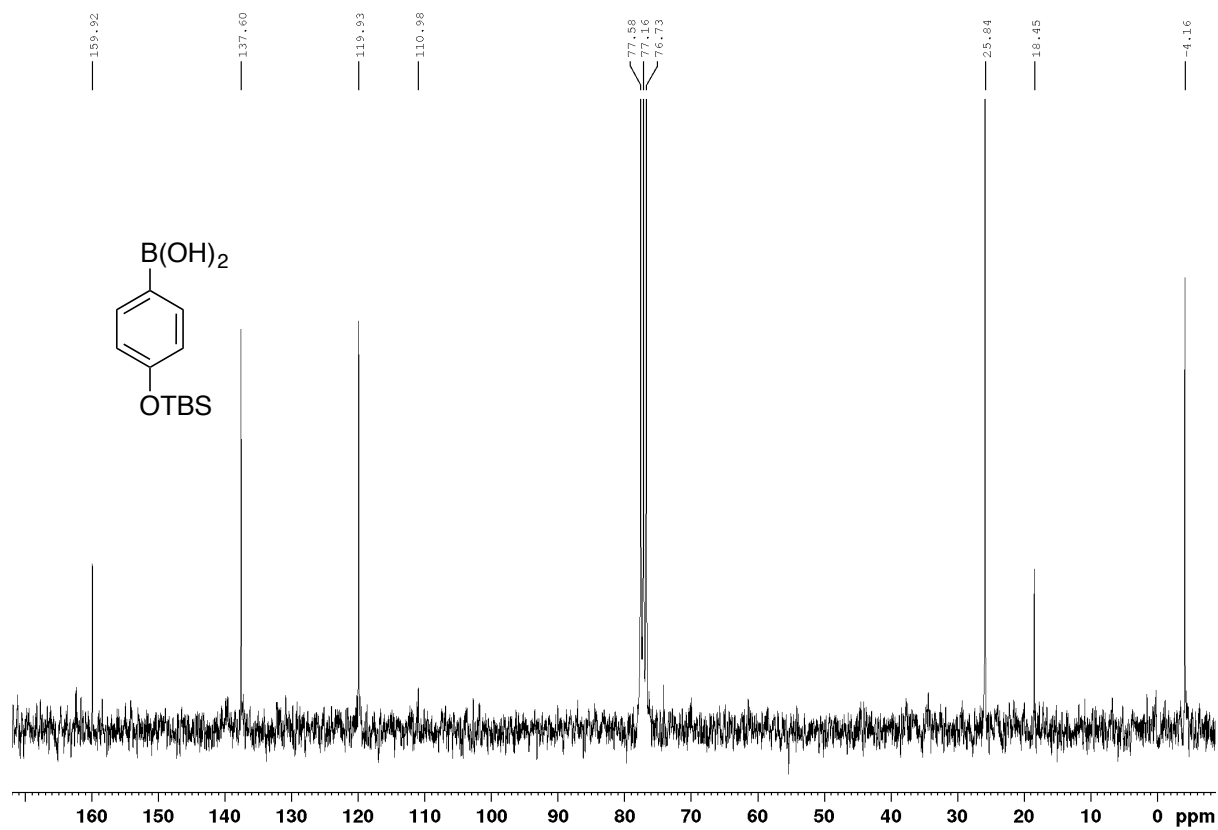


Figure S8 <sup>13</sup>C NMR spectrum of compound **9** in CDCl<sub>3</sub> (75 MHz).

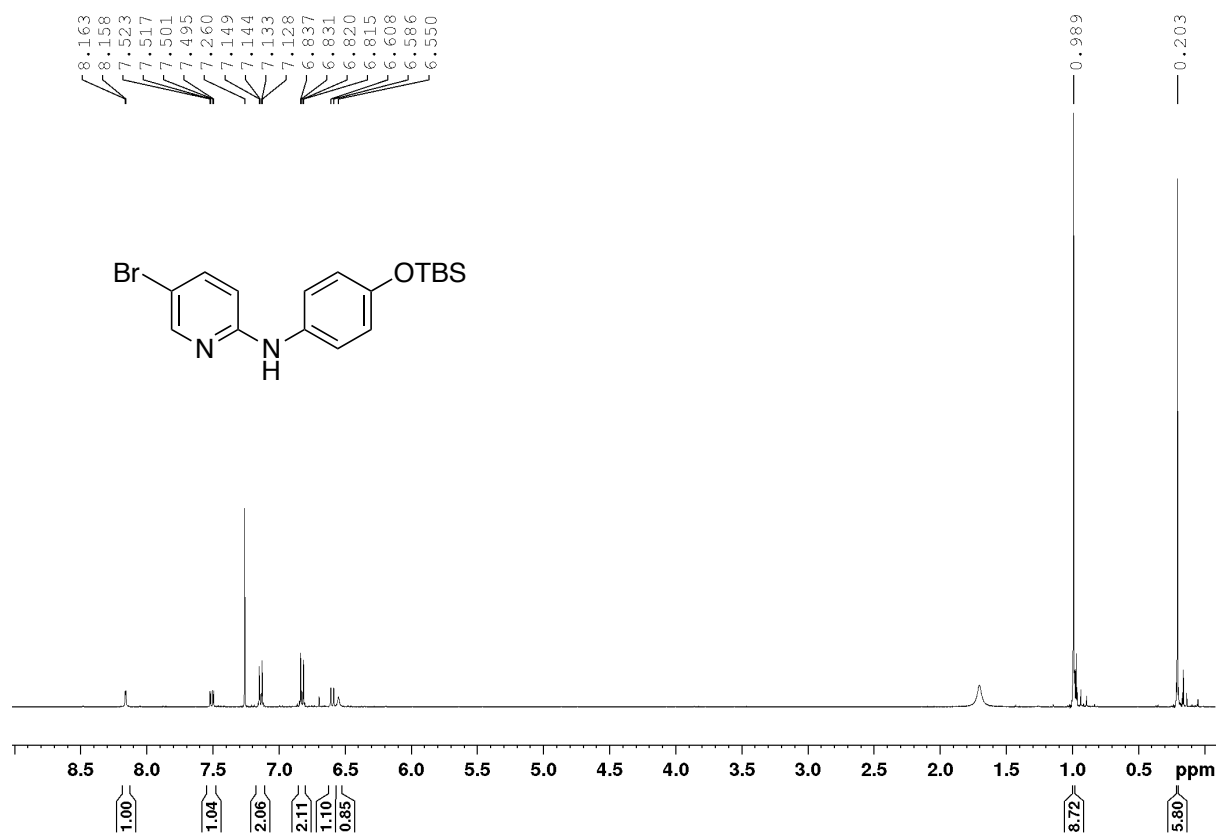


Figure S9 <sup>1</sup>H NMR spectrum of compound **10** in CDCl<sub>3</sub> (400 MHz).

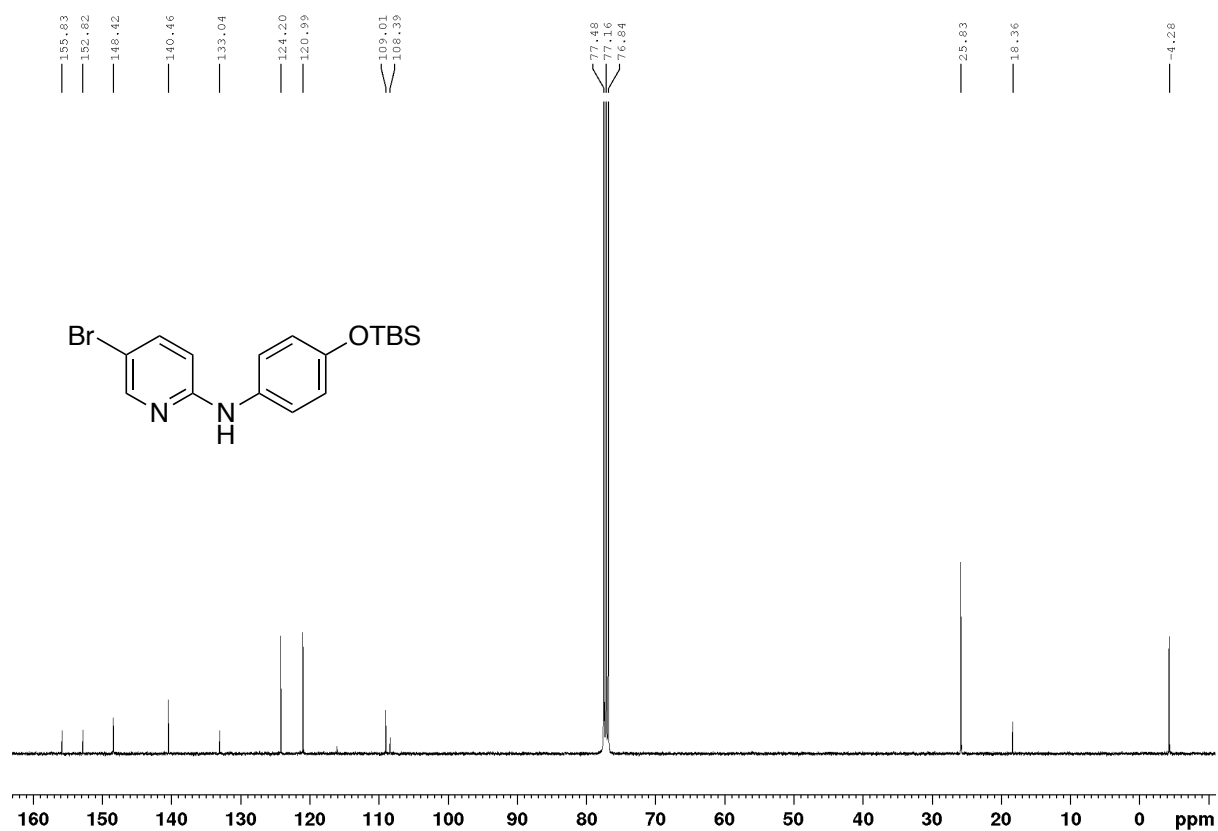


Figure S10  $^{13}\text{C}$  NMR spectrum of compound **10** in  $\text{CDCl}_3$  (100 MHz).

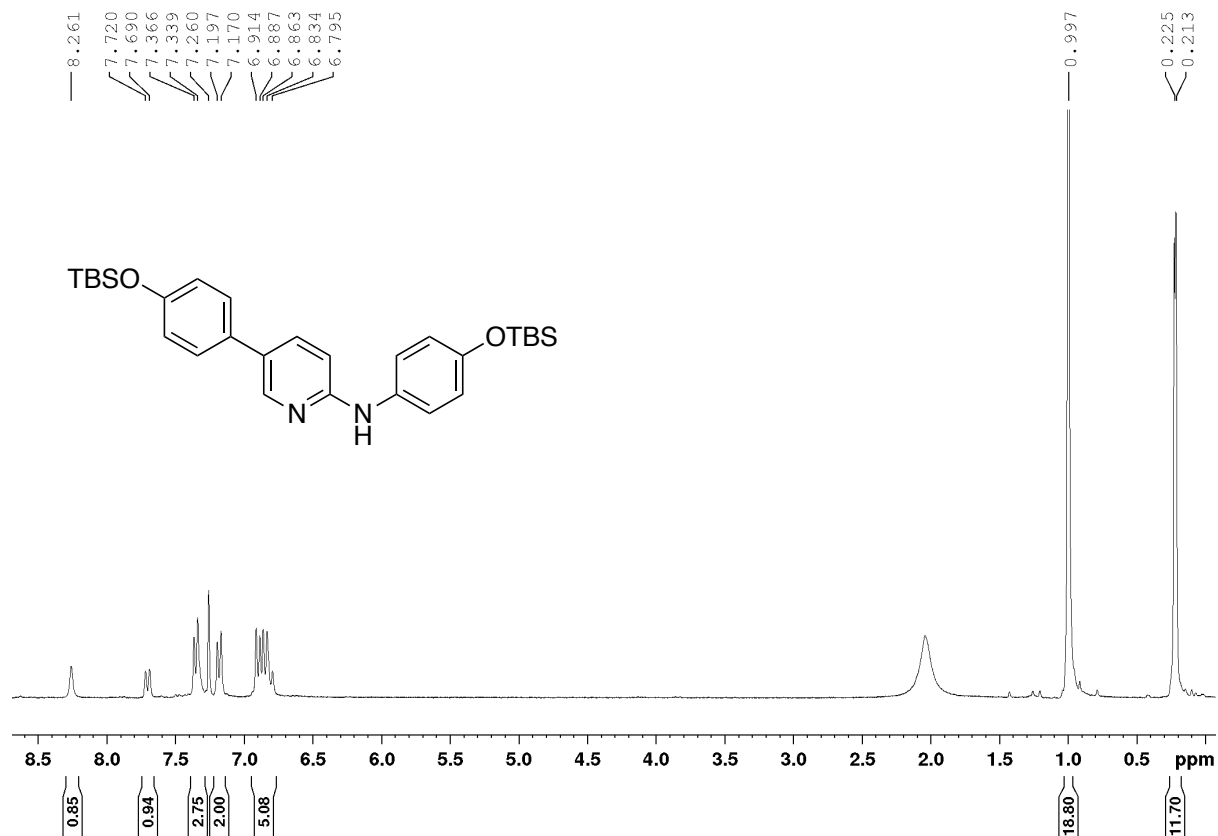


Figure S11  $^1\text{H}$  NMR spectrum of compound **11** in  $\text{CDCl}_3$  (300 MHz).

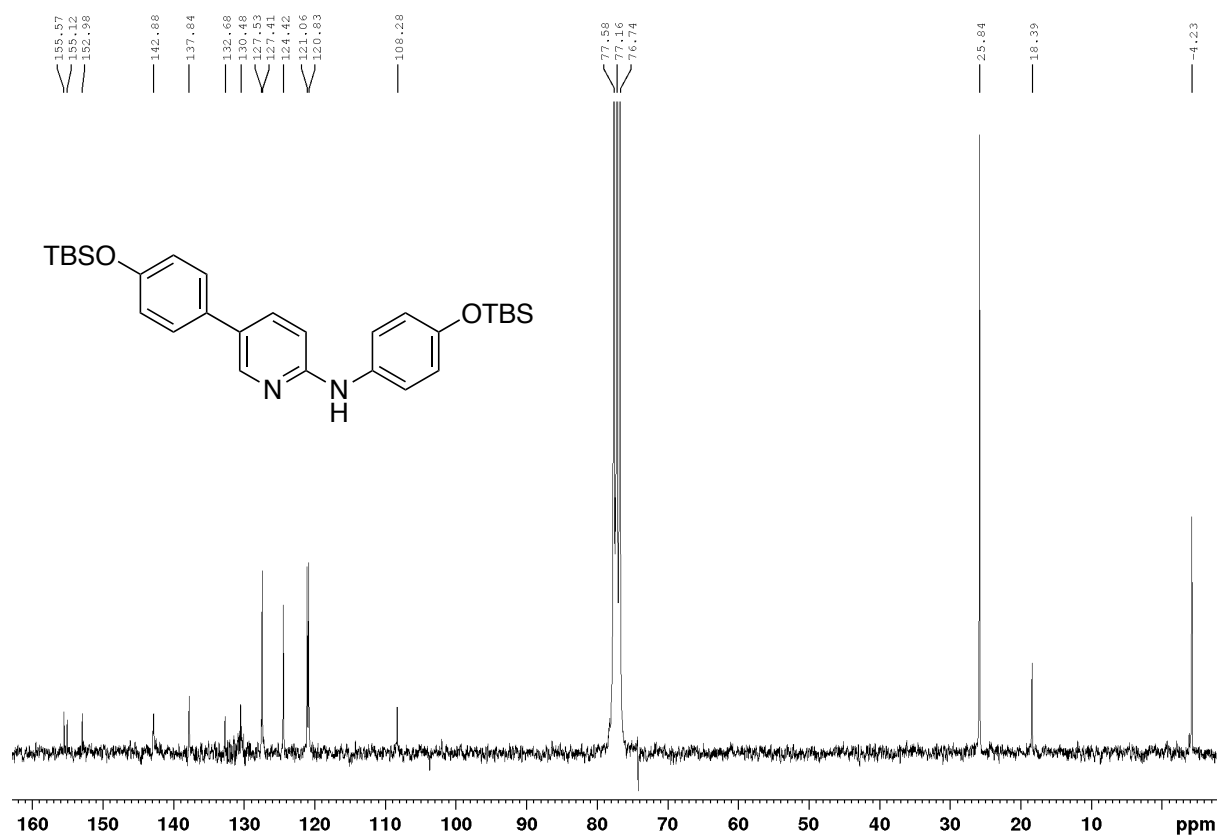


Figure S12 <sup>13</sup>C NMR spectrum of compound **11** in CDCl<sub>3</sub> (75 MHz).

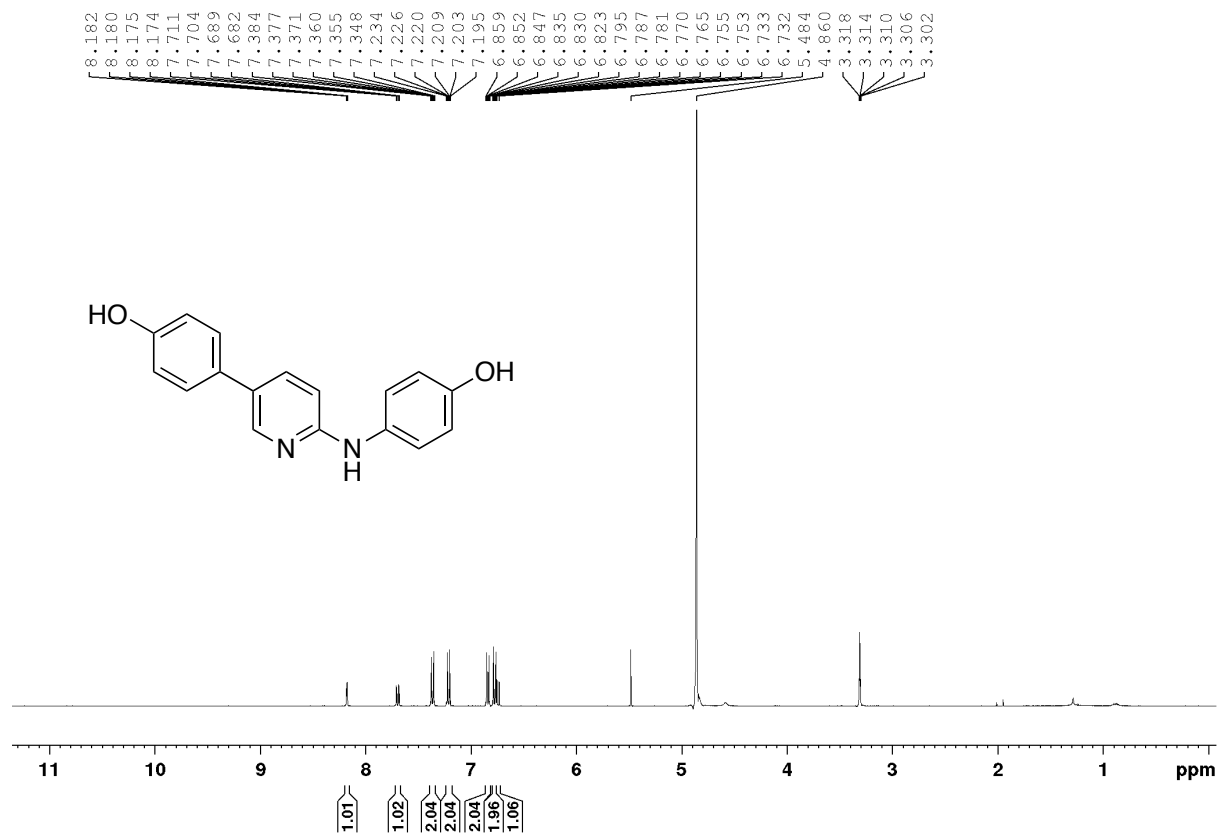


Figure S13 <sup>1</sup>H NMR spectrum of compound **2a** in d-MeOD (400 MHz).



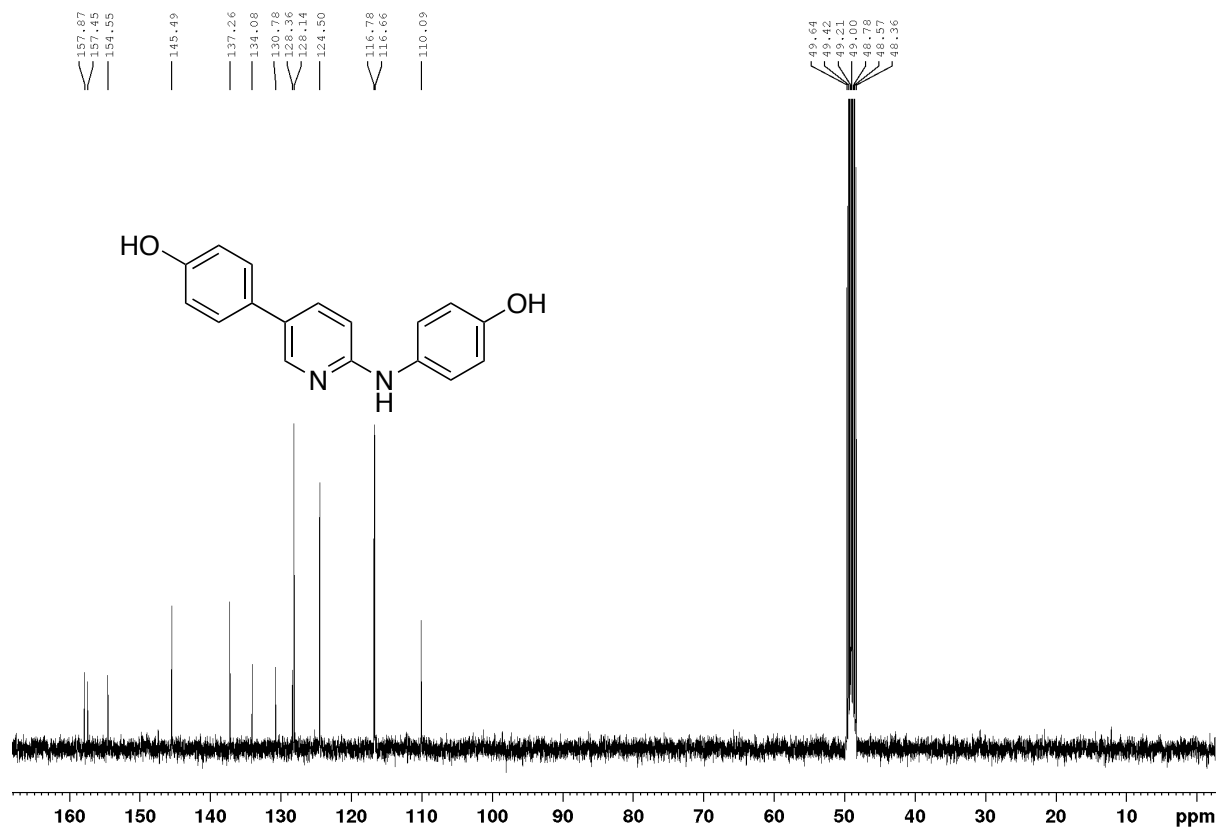
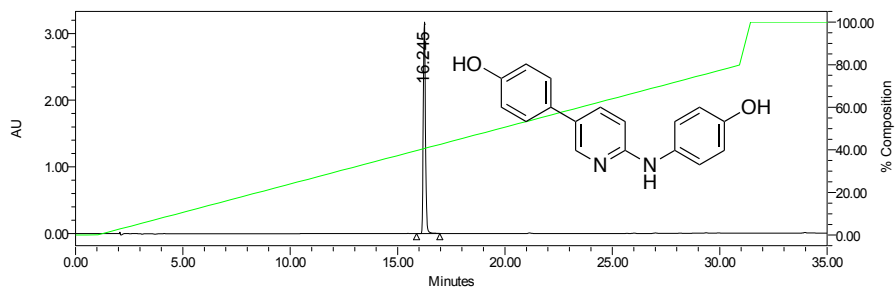


Figure S14 <sup>13</sup>C NMR spectrum of compound **2a** in *d*-MeOD (100 MHz).



	RT	Area	% Area
1	16.245	22795731	100.00

Figure S14\* HPLC chromatogram of compound **2a**.

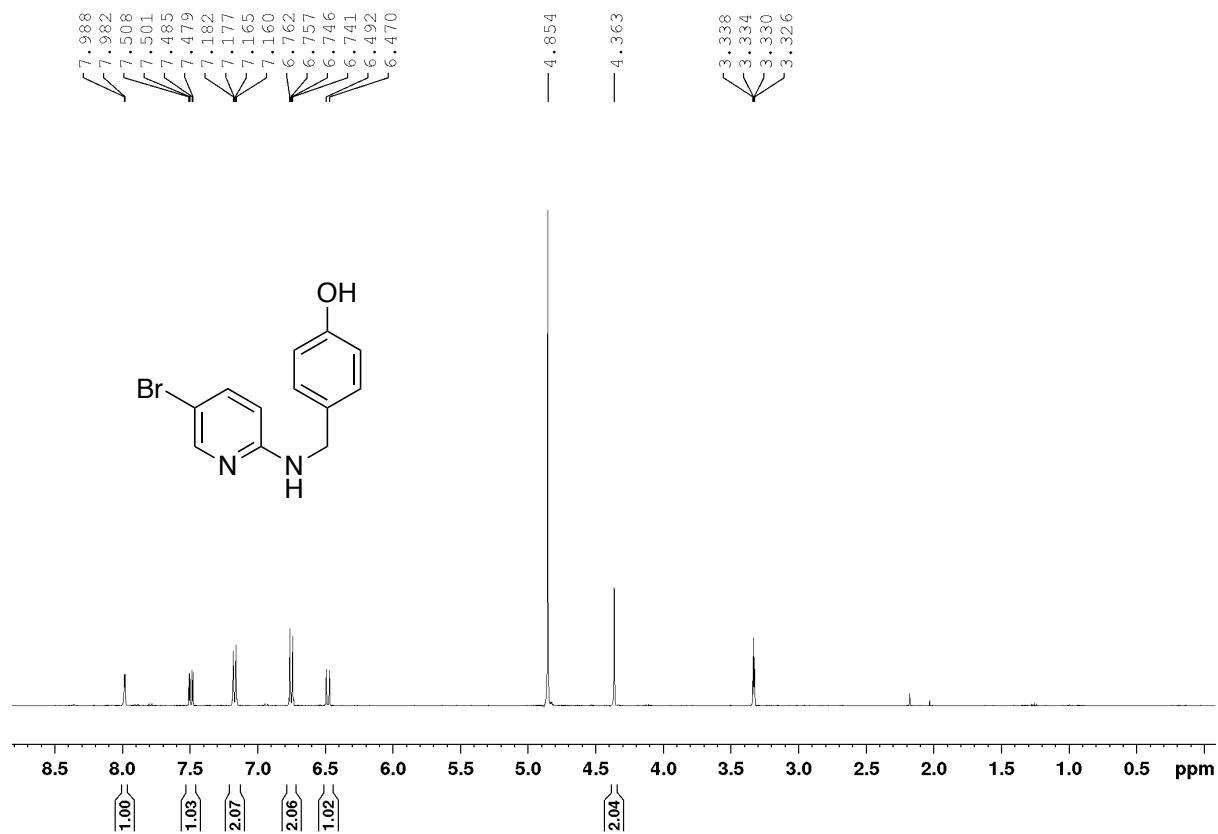


Figure S15 <sup>1</sup>H NMR spectrum of compound 12 in d-MeOD (400 MHz).

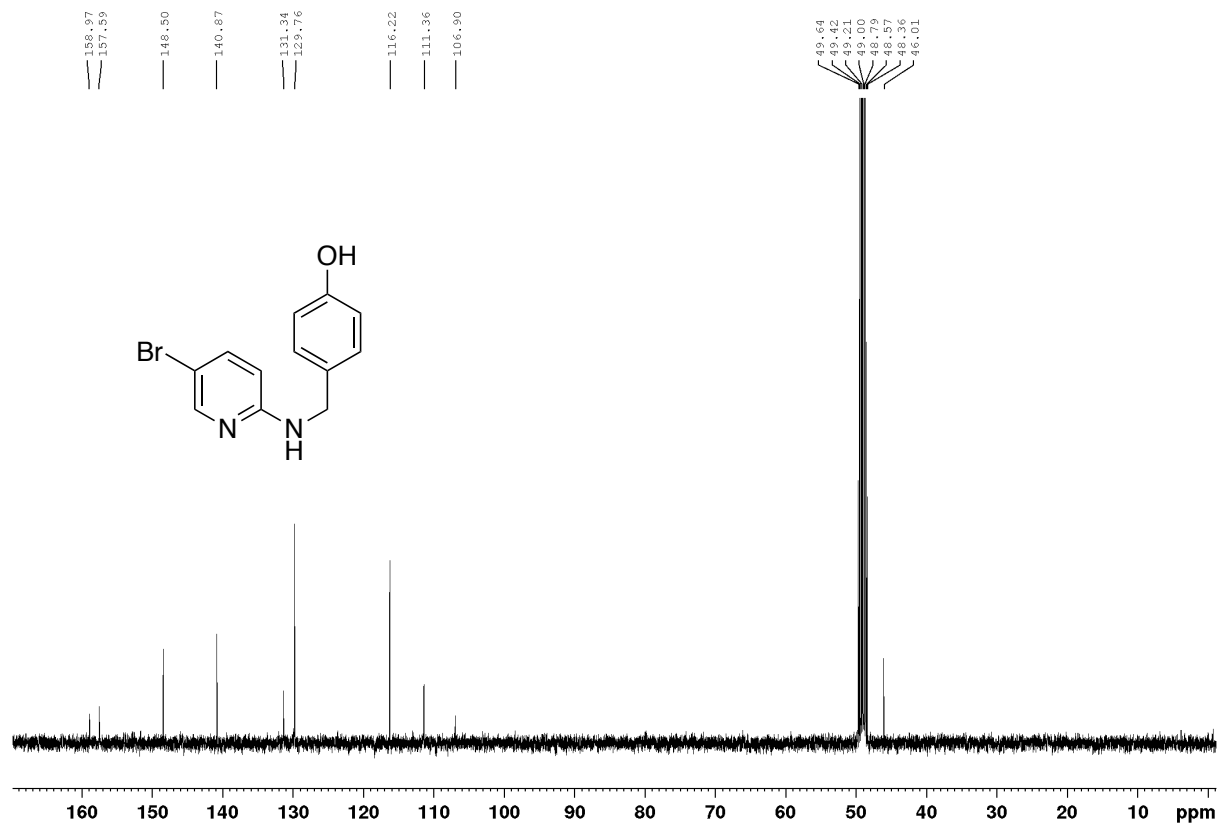


Figure S16 <sup>13</sup>C NMR spectrum of compound 12 in d-MeOD (100 MHz).

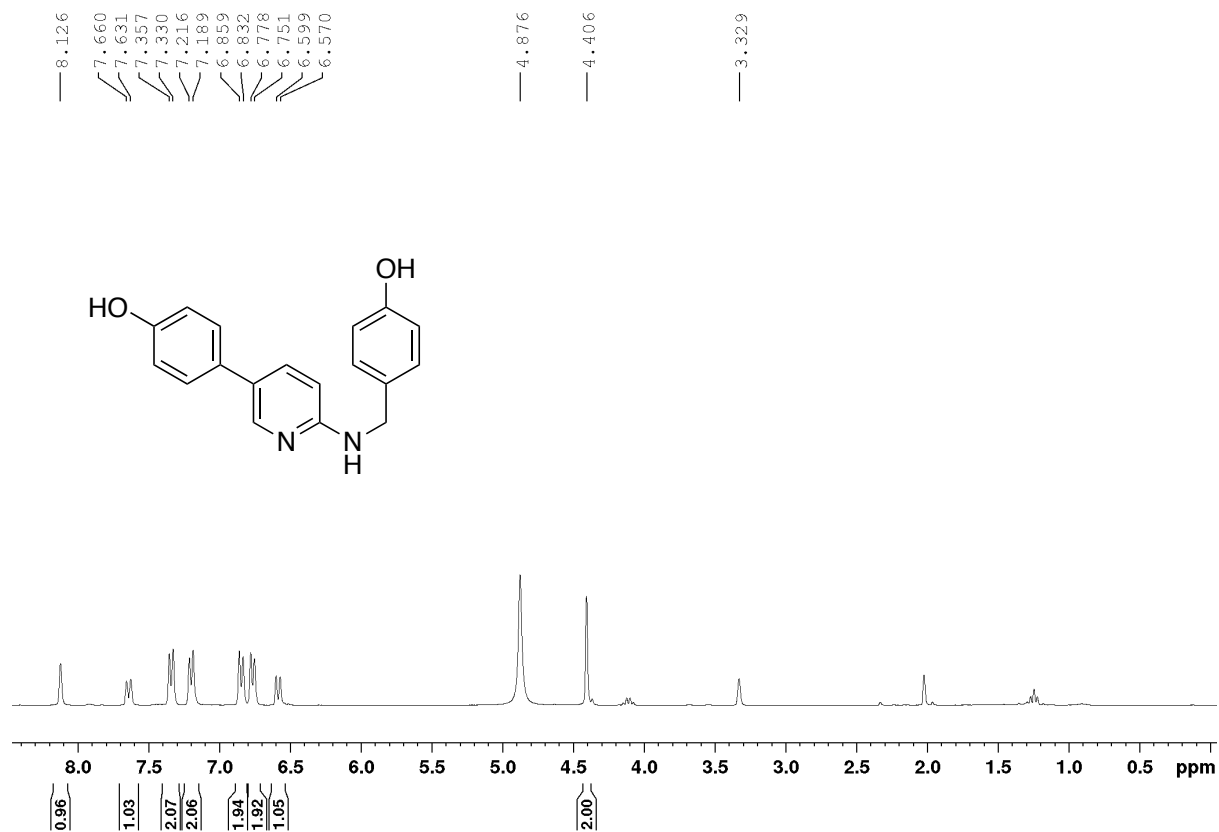


Figure S17 <sup>1</sup>H NMR spectrum of compound **2b** in d-MeOD (300 MHz).

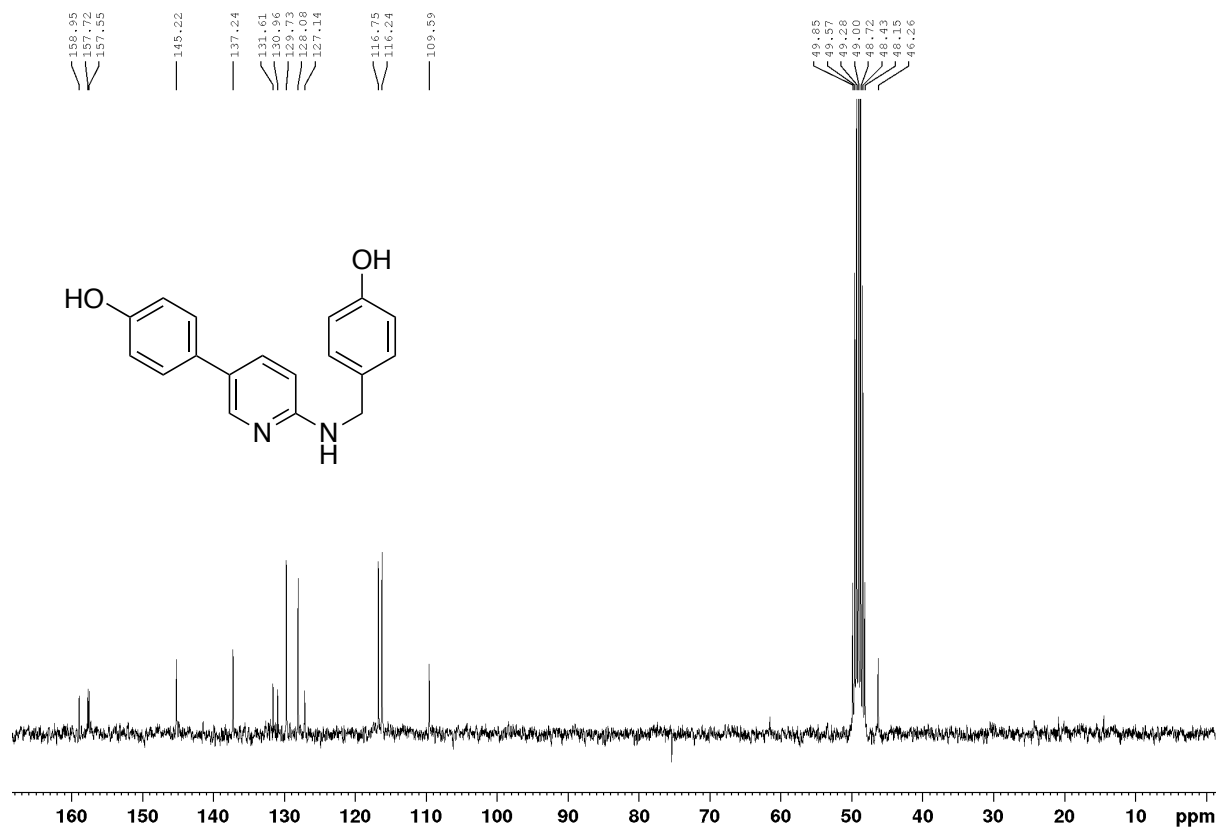
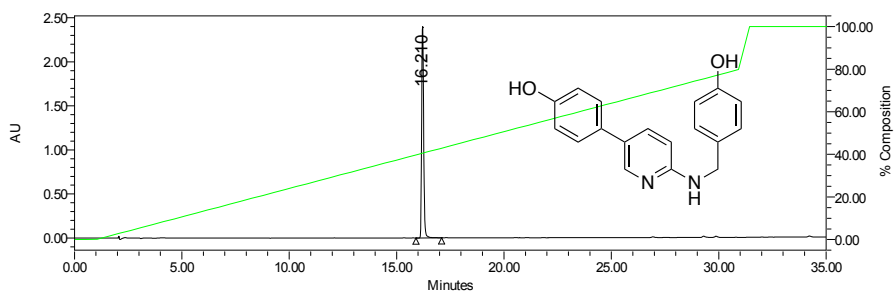


Figure S18 <sup>13</sup>C NMR spectrum of compound **2b** in d-MeOD (75 MHz).



	RT	Area	% Area
1	16.210	15564916	100.00

Figure S18\* HPLC chromatogram of compound **2b**.

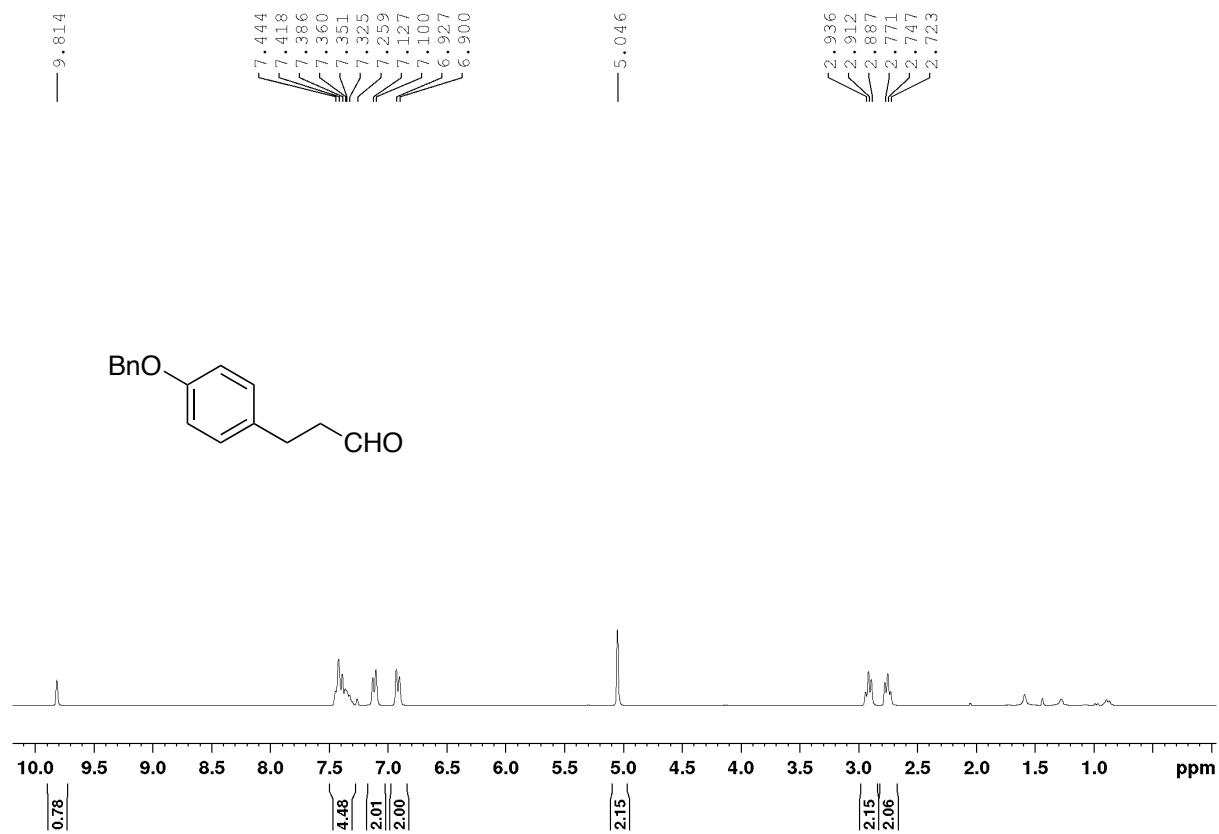


Figure S19  $^1\text{H}$  NMR spectrum of compound **13** in  $\text{CDCl}_3$  (300 MHz).

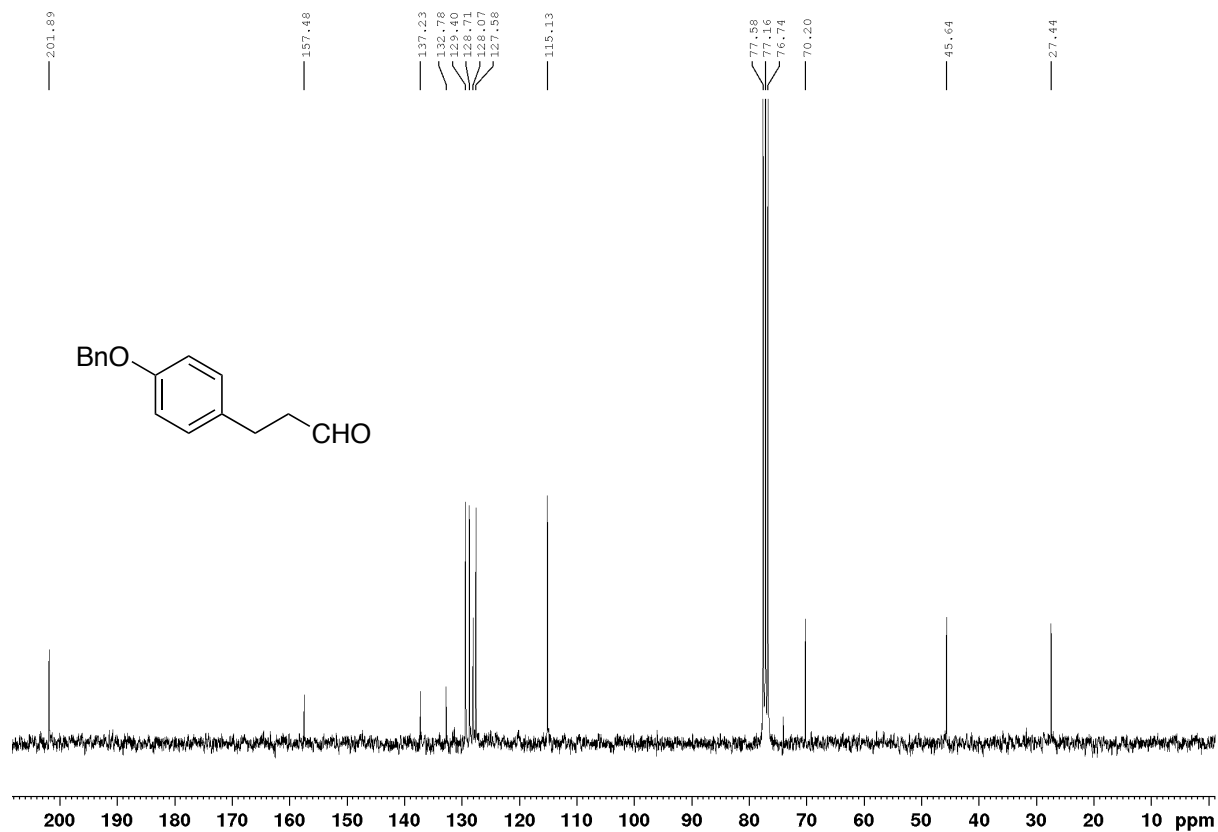


Figure S20  $^{13}\text{C}$  NMR spectrum of compound 13 in  $\text{CDCl}_3$  (75 MHz).

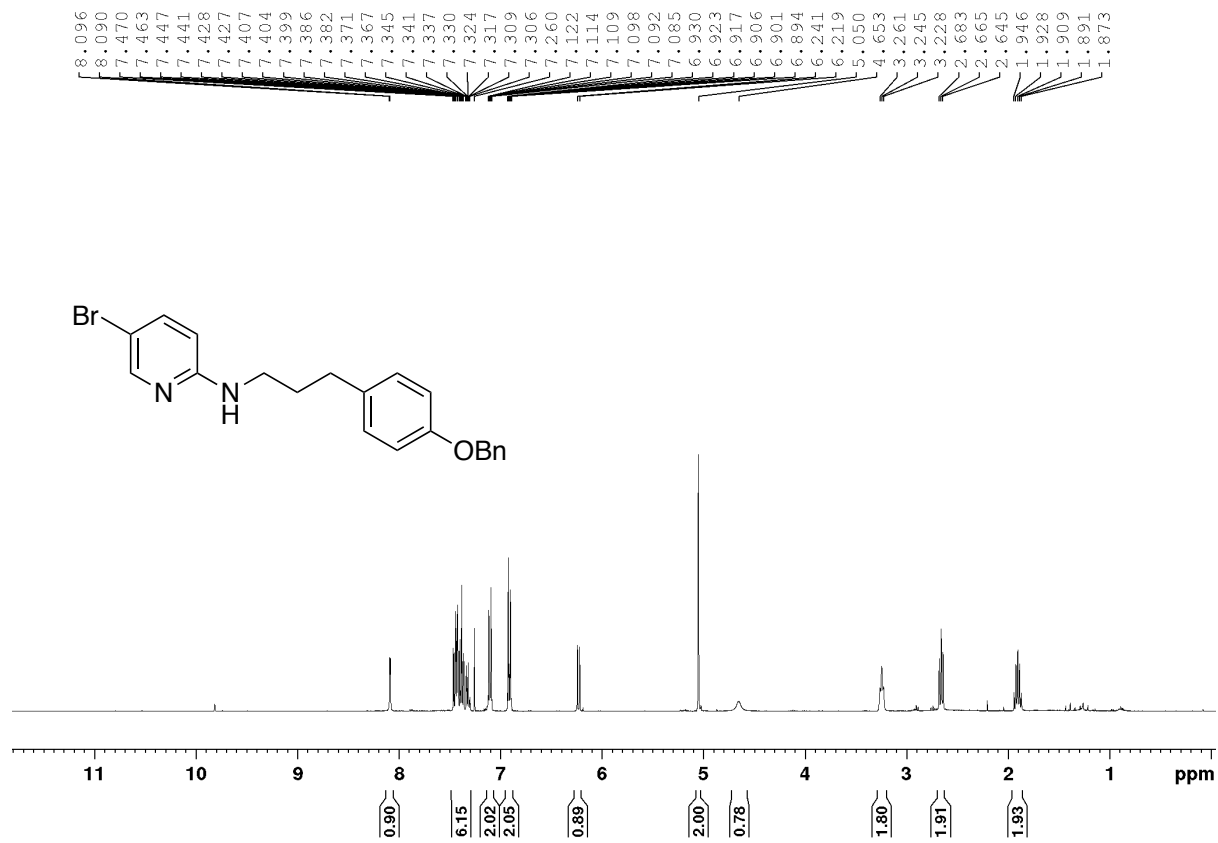


Figure S21  $^1\text{H}$  NMR spectrum of compound 14 in  $\text{CDCl}_3$  (400 MHz).

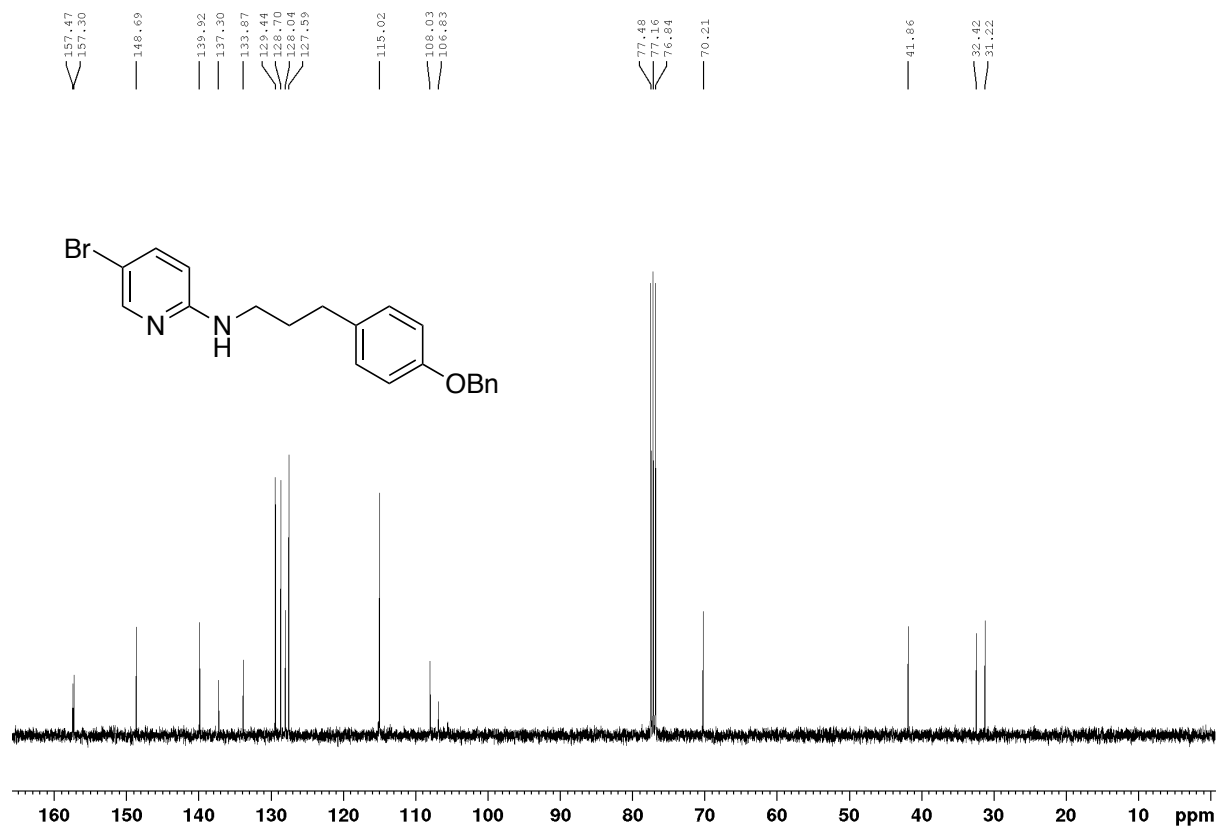


Figure S22 <sup>13</sup>C NMR spectrum of compound **14** in CDCl<sub>3</sub> (100 MHz).

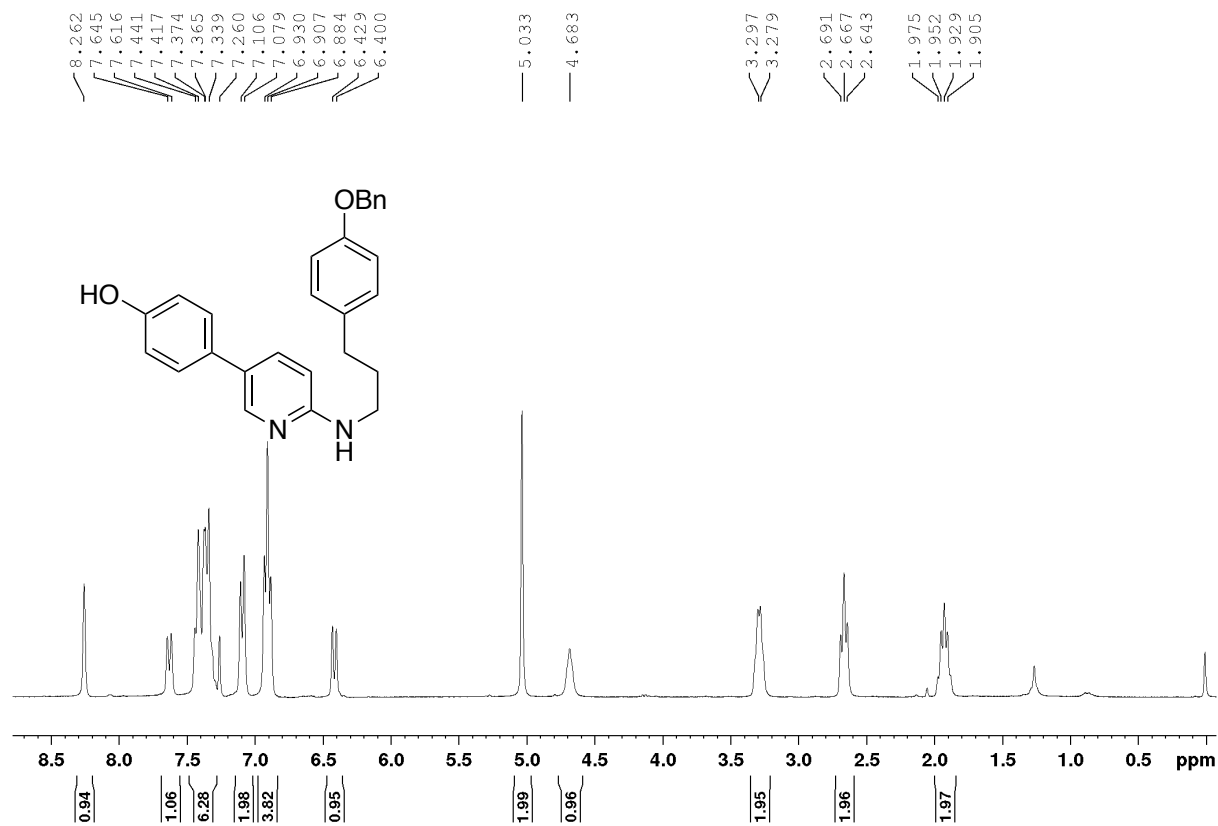


Figure S23 <sup>1</sup>H NMR spectrum of compound **15** in CDCl<sub>3</sub> (300 MHz).

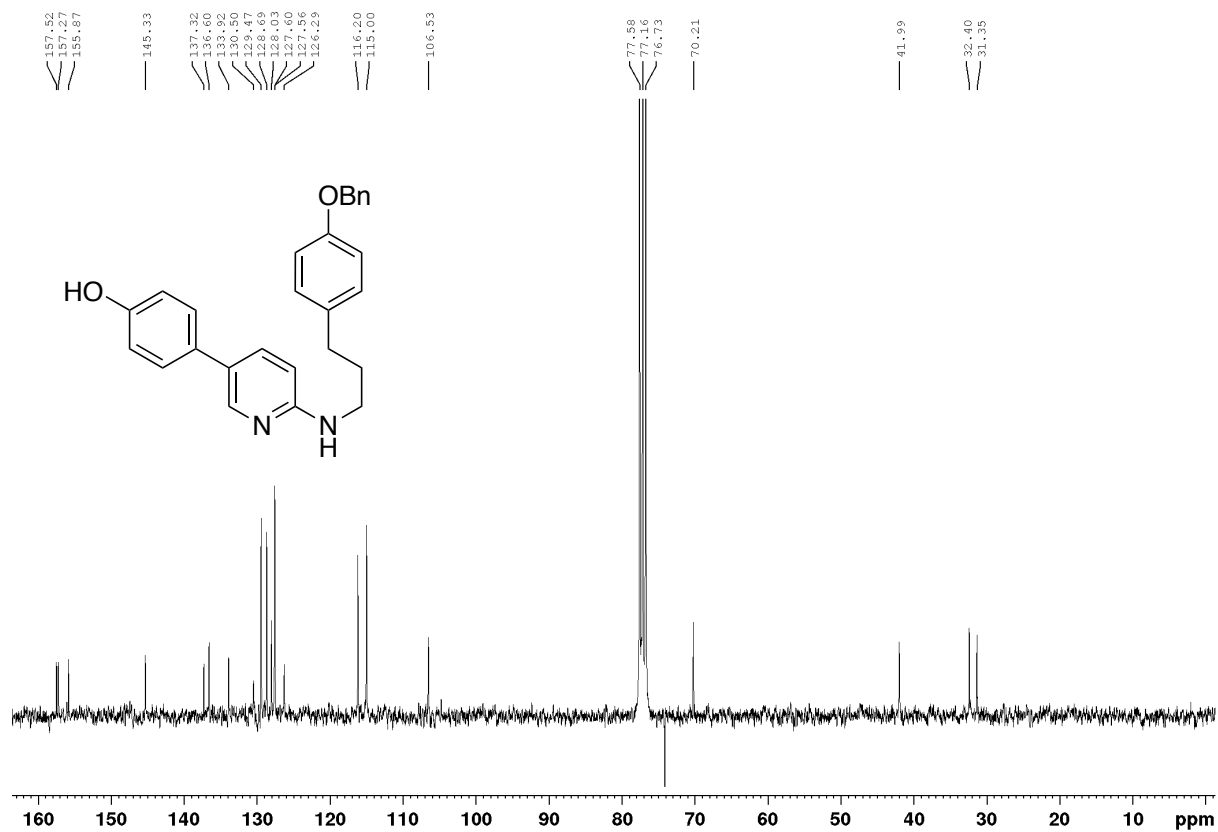


Figure S24 <sup>13</sup>C NMR spectrum of compound **15** in CDCl<sub>3</sub> (75 MHz).

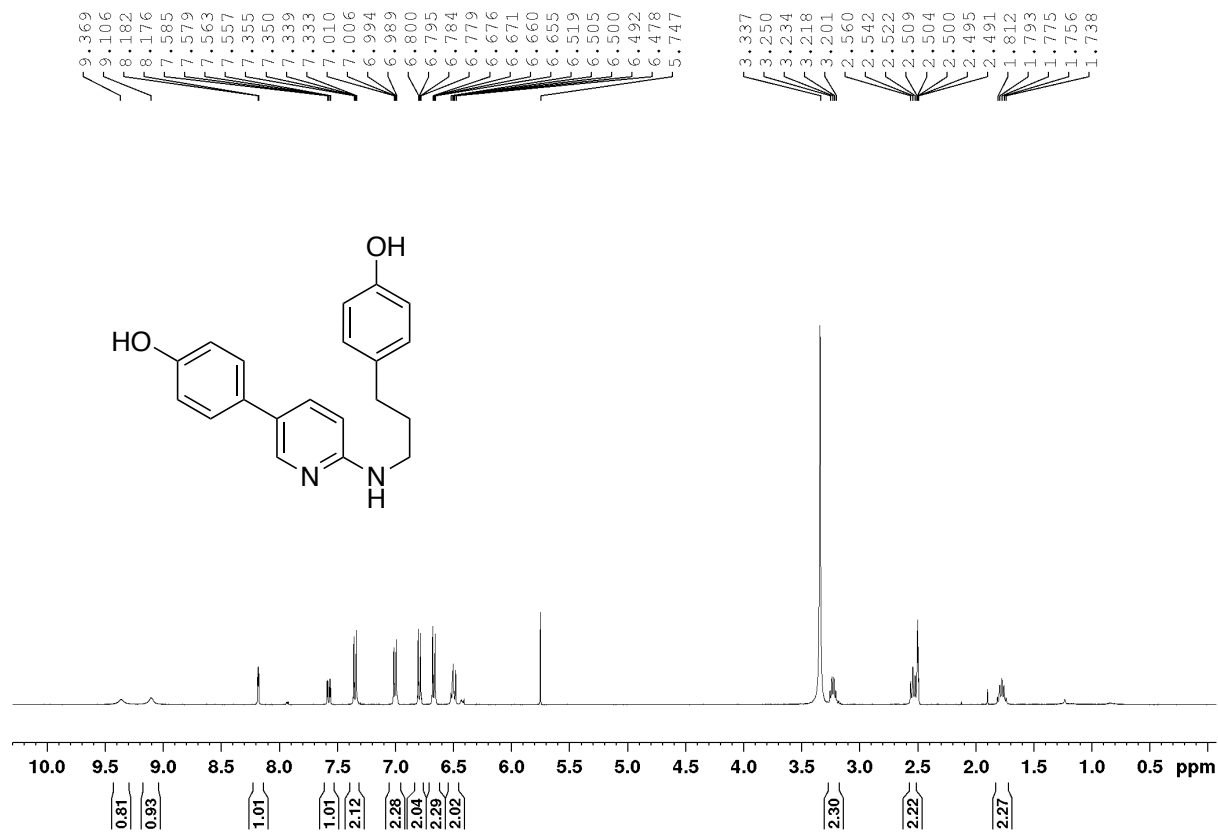


Figure S25 <sup>1</sup>H NMR spectrum of compound **2d** in d-DMSO (400 MHz).

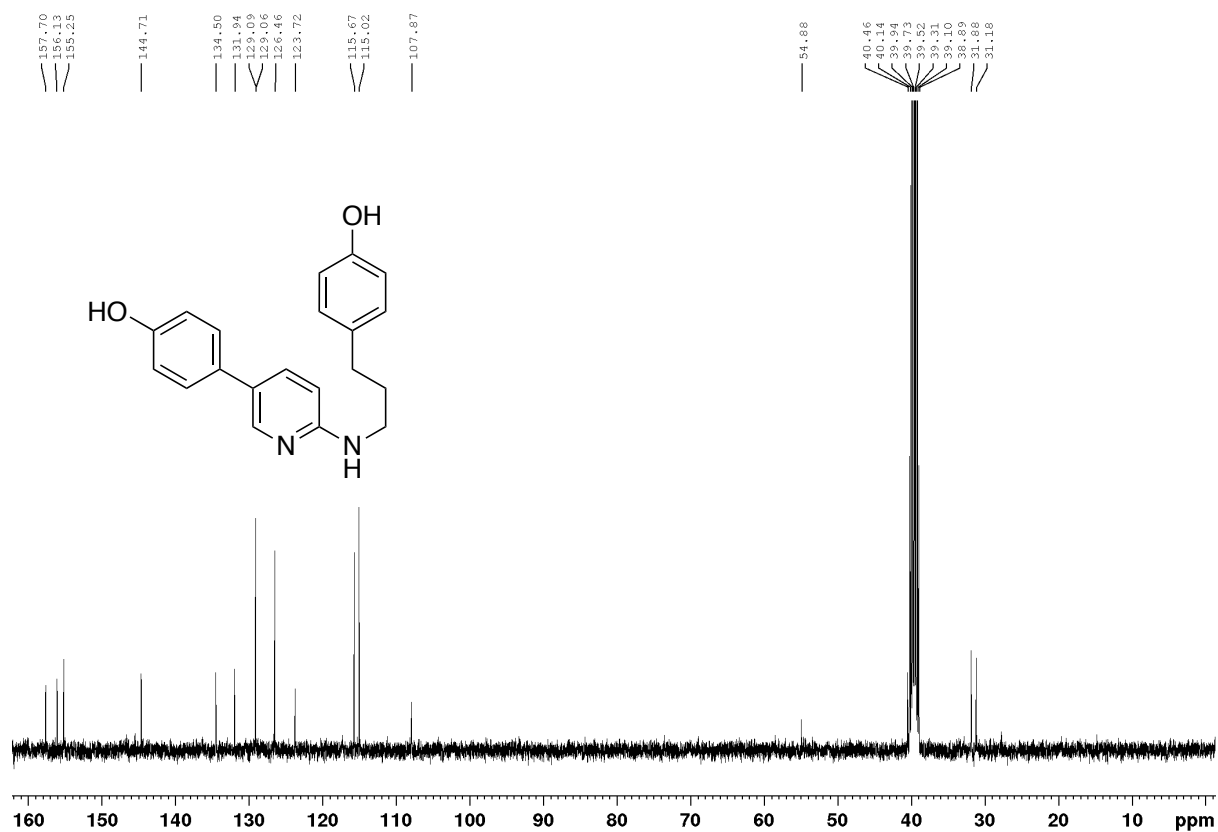
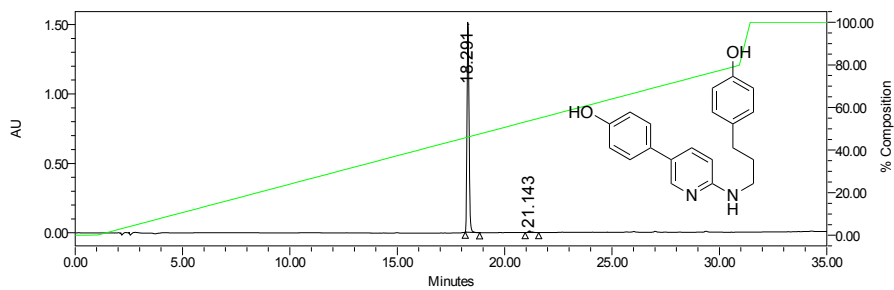


Figure S26  $^{13}\text{C}$  NMR spectrum of compound **2d** in *d*-DMSO (100 MHz).



	RT	Area	% Area
1	18.291	9871019	98.99
2	21.143	100604	1.01

Figure S26\* HPLC chromatogram of compound **2d**.



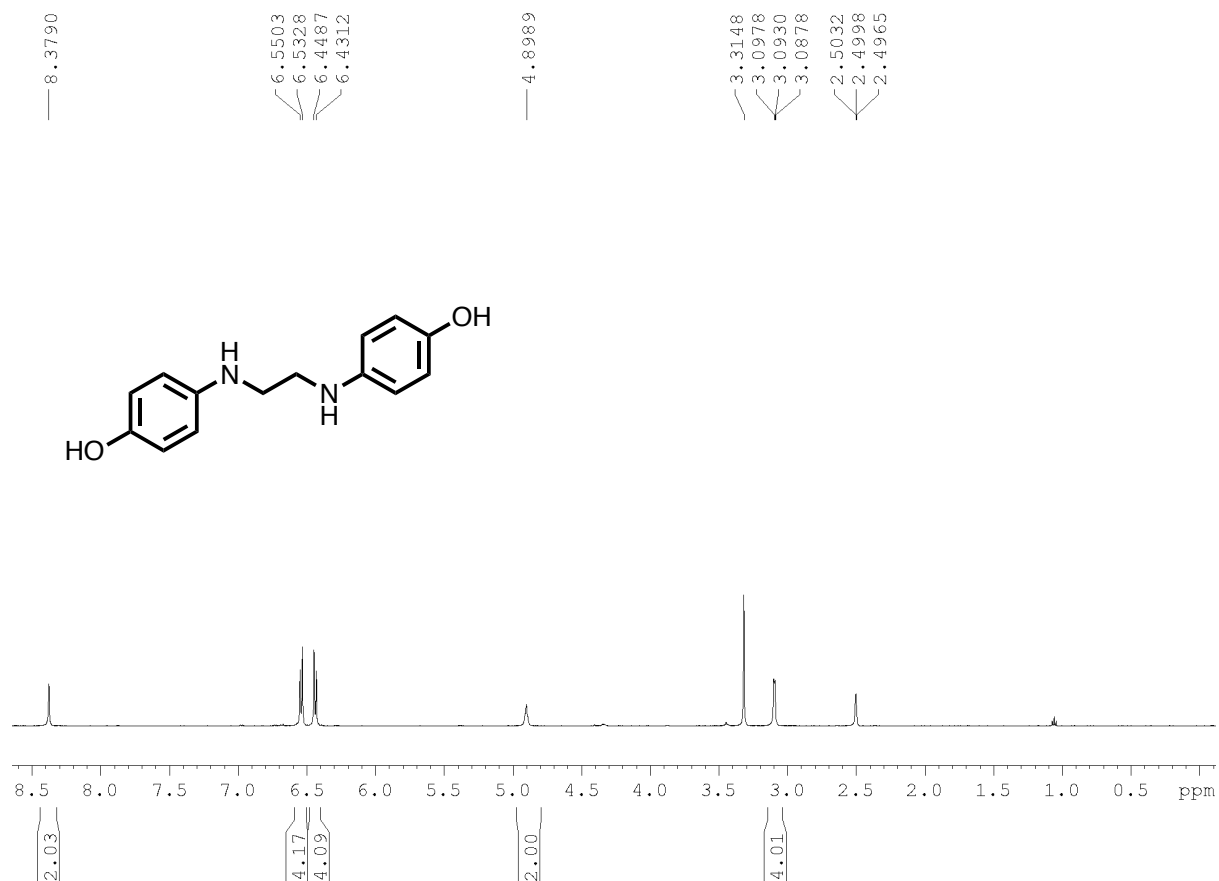


Figure S27 <sup>1</sup>H NMR spectrum of compound **3a** in d-DMSO (500 MHz).

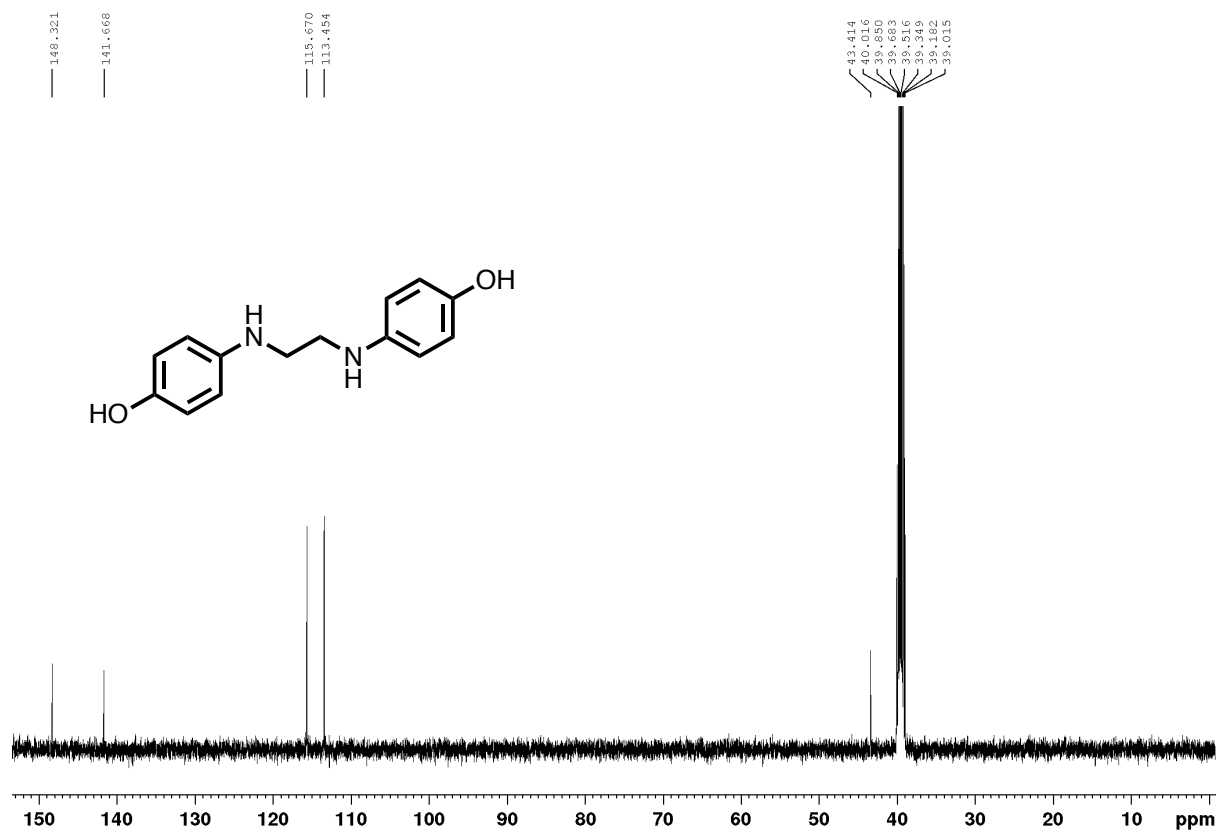
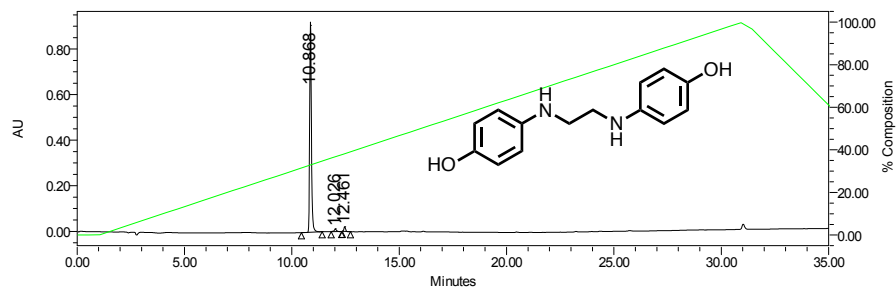


Figure S28 <sup>13</sup>C NMR spectrum of compound **3a** in d-DMSO (125 MHz).



Peak information

	RT	Area	% Area
1	10.868	5313505	96.47
2	12.026	82062	1.49
3	12.461	112191	2.04

Figure S28\* HPLC chromatogram of compound 3a.

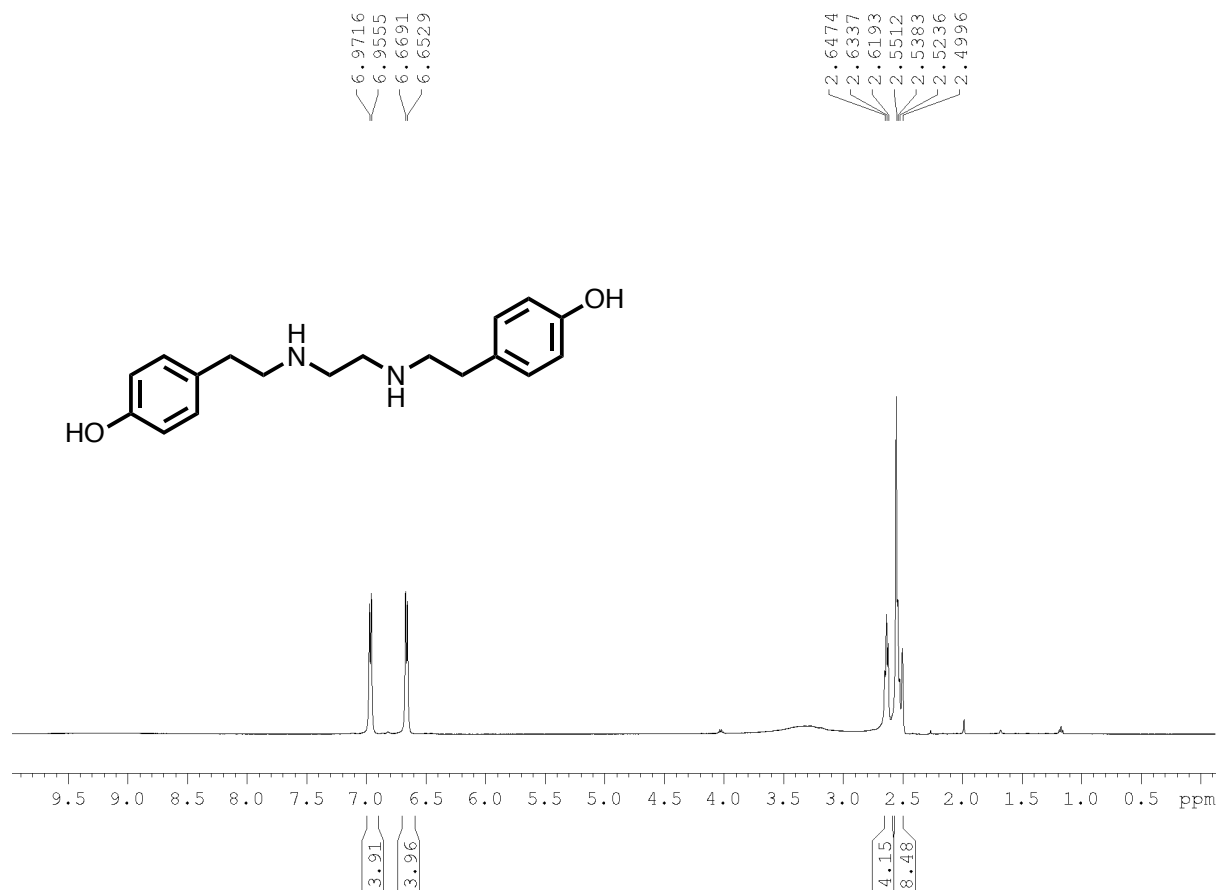


Figure S29 <sup>1</sup>H NMR spectrum of compound 3c in d-DMSO (500 MHz).

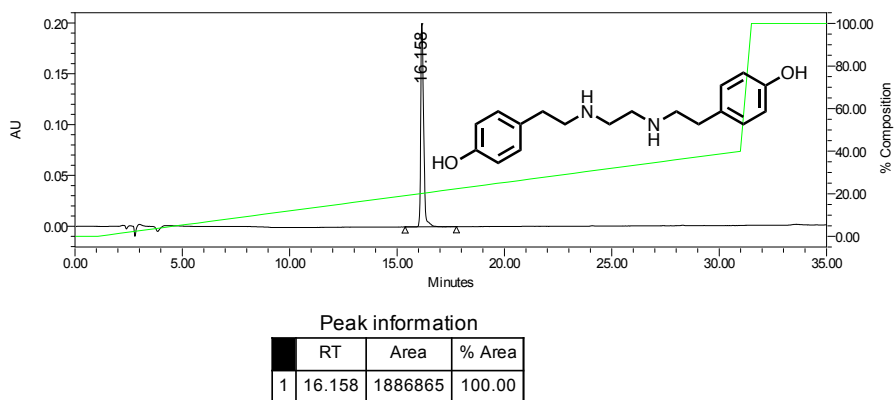
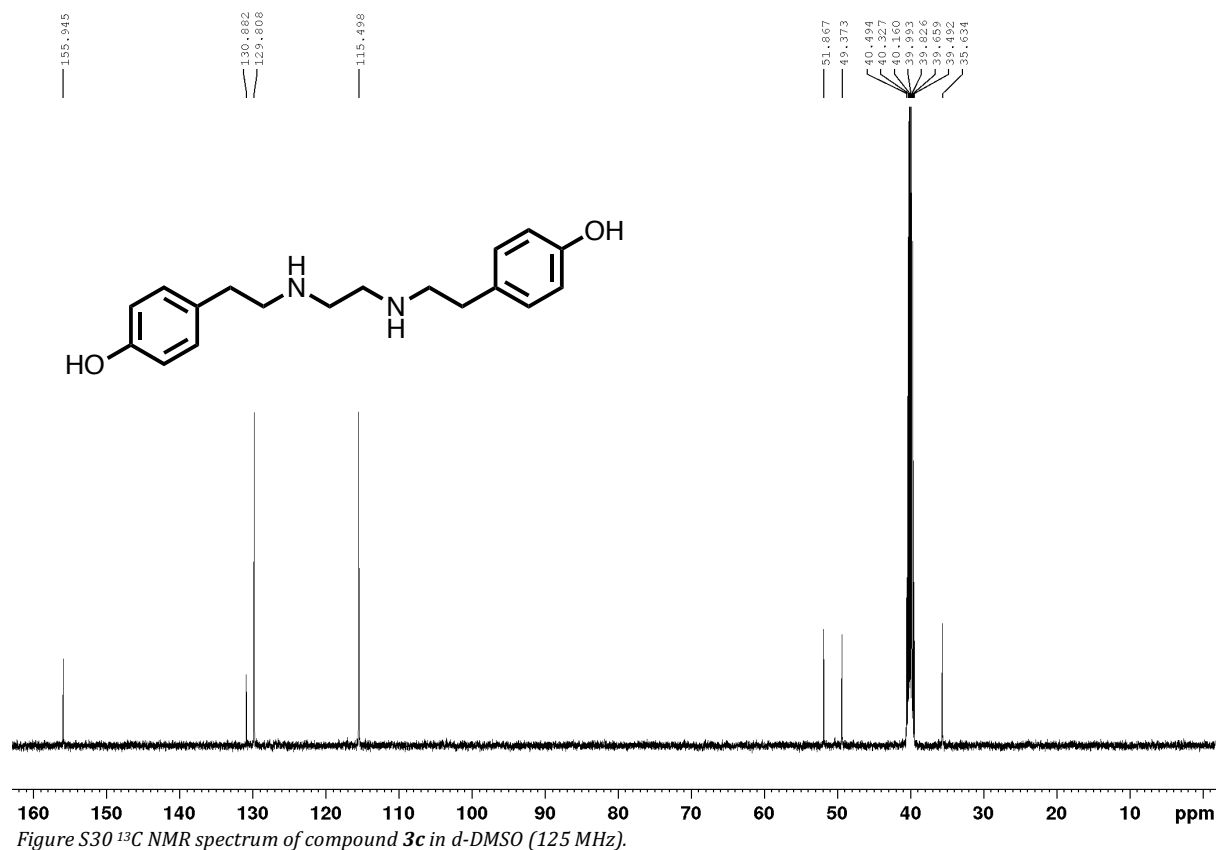


Figure S30\* HPLC chromatogram of compound **3c**.

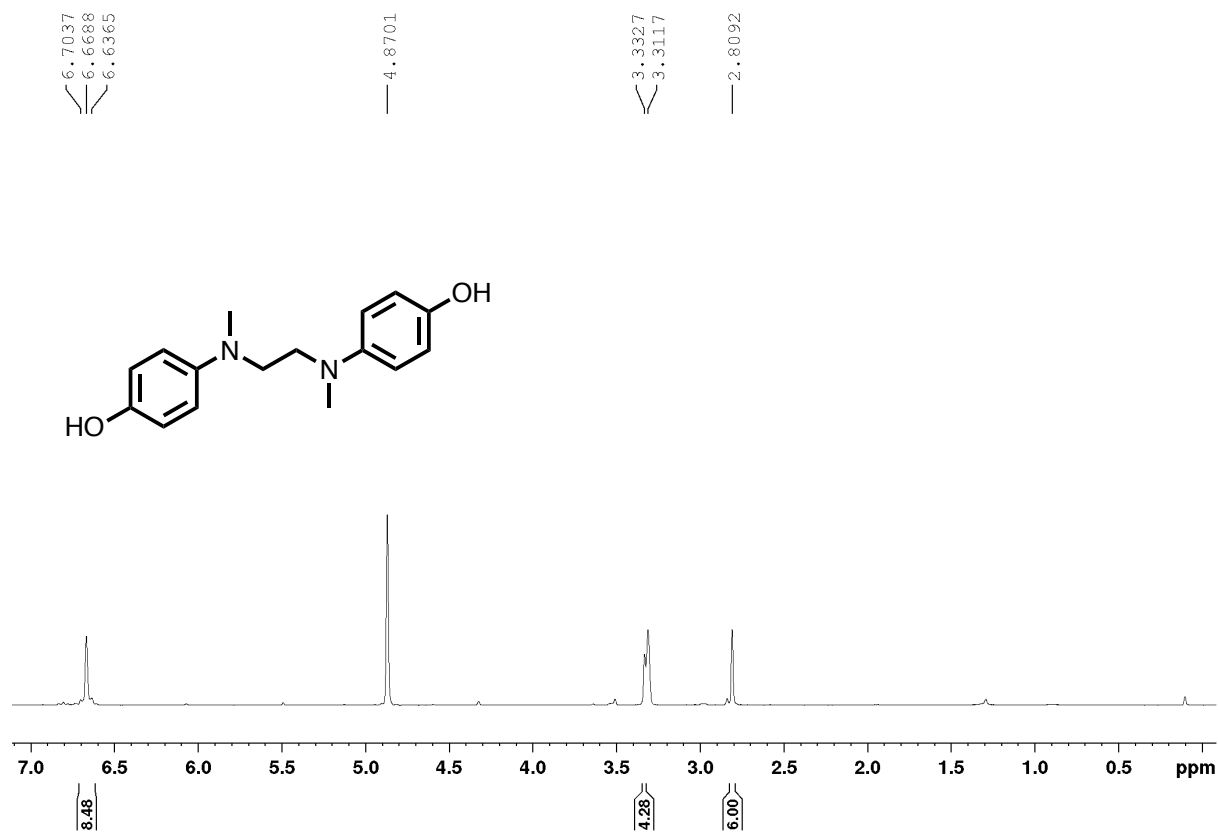


Figure S31  $^1\text{H}$  NMR spectrum of compound **4a** in *d*-MeOD (400 MHz).

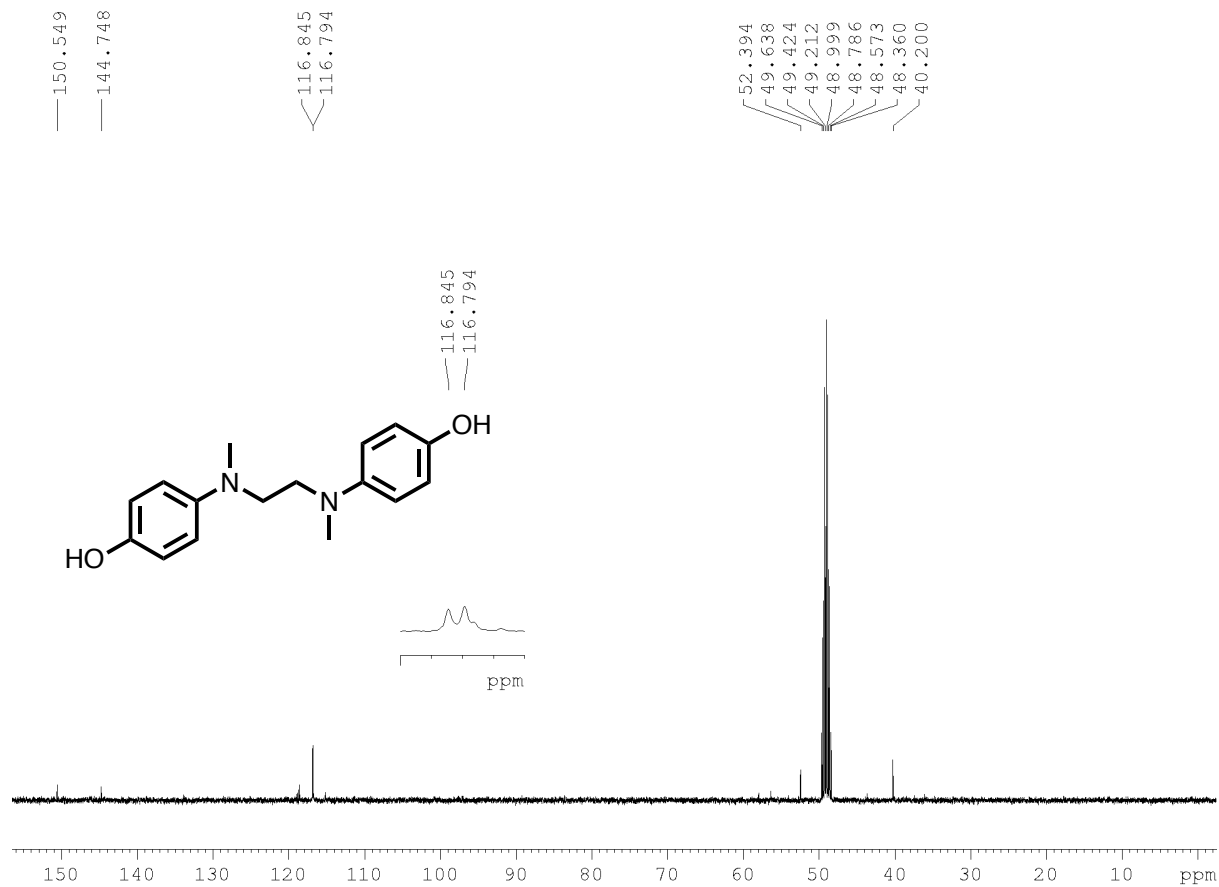
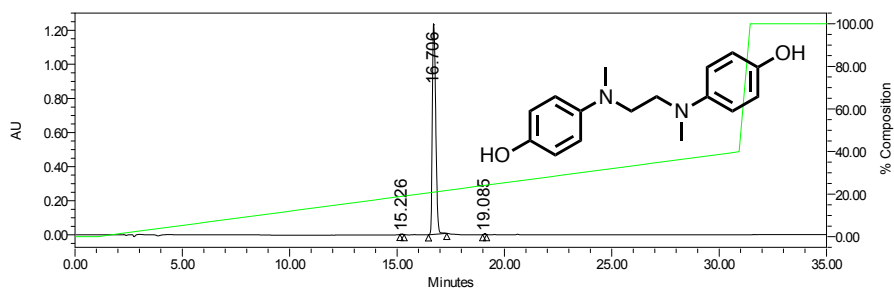


Figure S32  $^{13}\text{C}$  NMR spectrum of compound **4a** in *d*-MeOD (100 MHz).



Peak information

	RT	Area	% Area
1	15.226	13360	0.10
2	16.706	13590867	99.67
3	19.085	31497	0.23

Figure S32\* HPLC chromatogram of compound 4a.

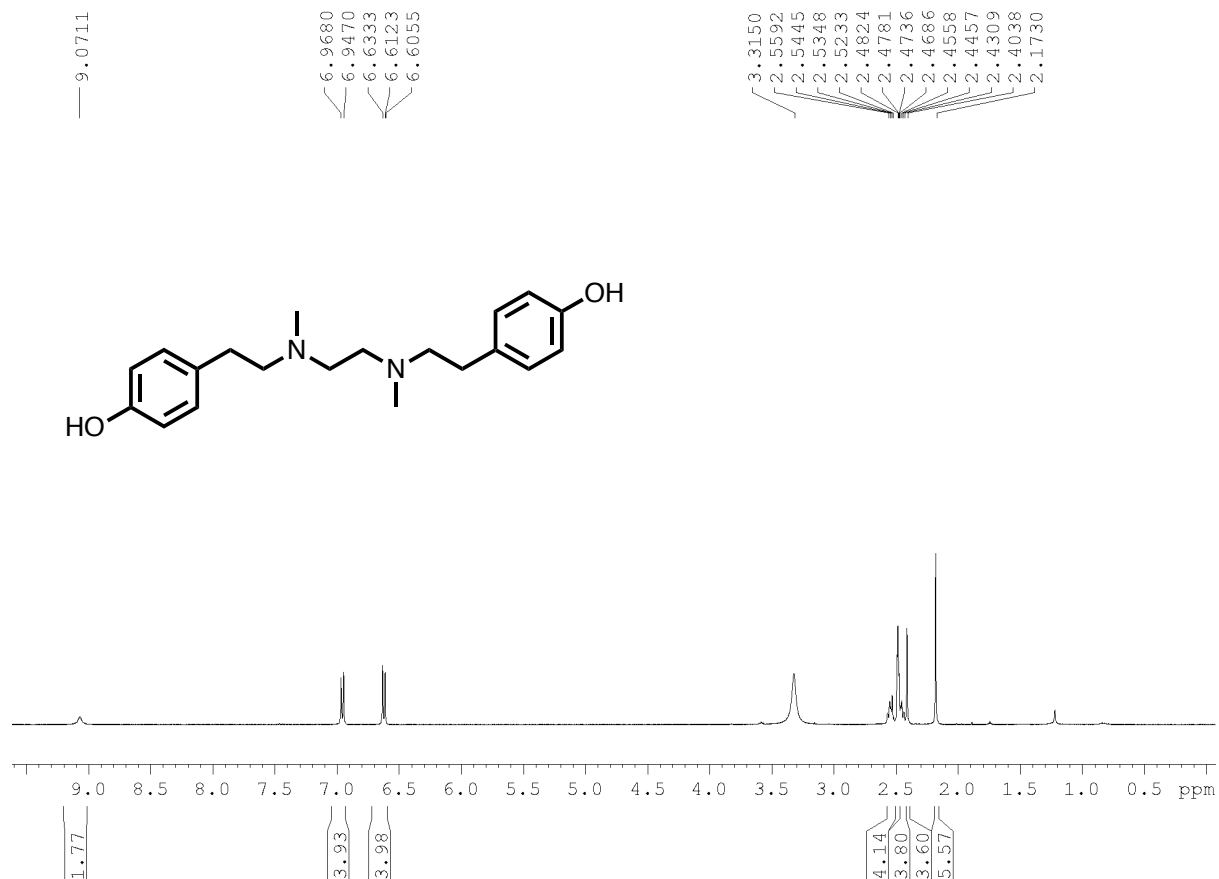


Figure S33 <sup>1</sup>H NMR spectrum of compound 4c in d-DMSO (400 MHz).

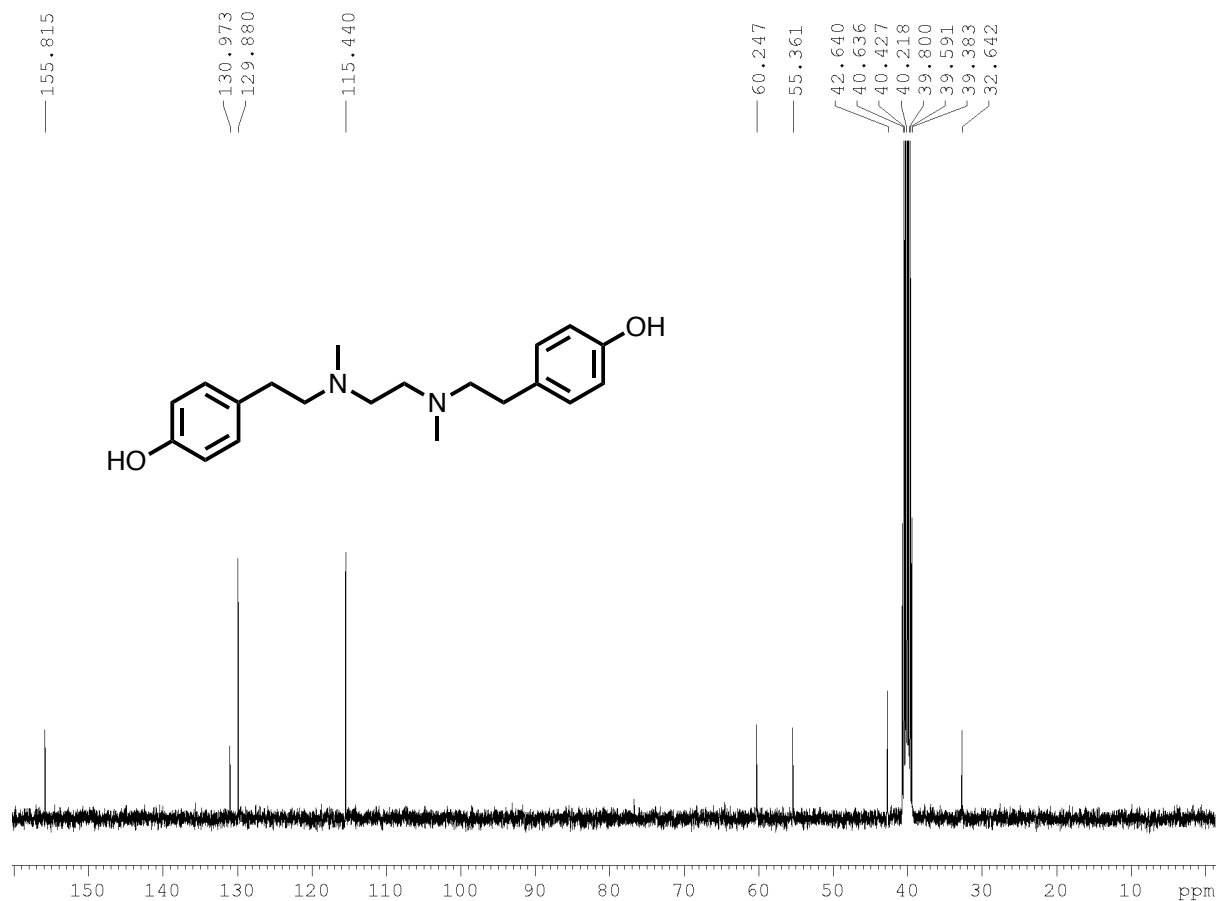
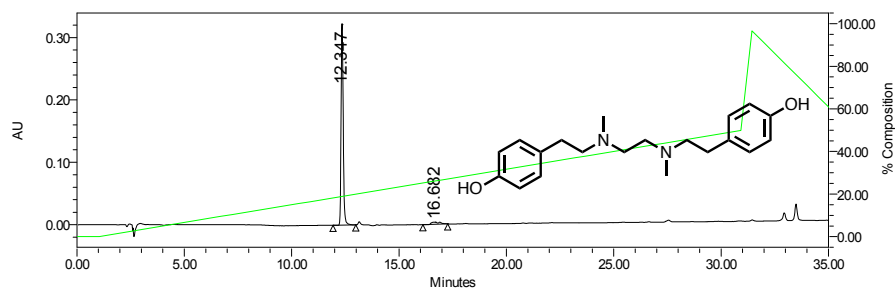


Figure S34 <sup>13</sup>C NMR spectrum of compound 4c in d-DMSO (100 MHz).



Peak information

	RT	Area	% Area
1	12.347	2252913	95.69
2	16.682	101566	4.31

Figure S34\* HPLC chromatogram of compound 4c.

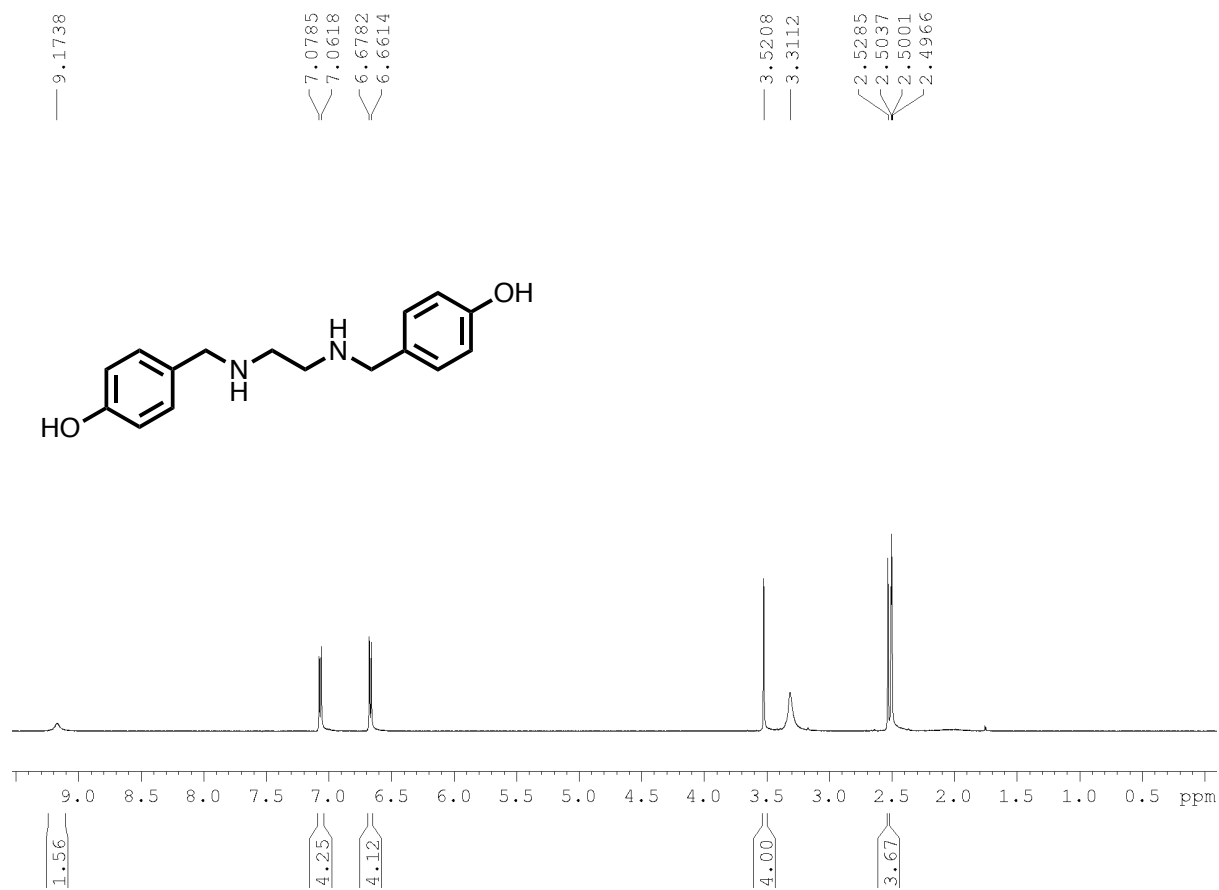


Figure S35 <sup>1</sup>H NMR spectrum of compound **3b** in d-DMSO (500 MHz).

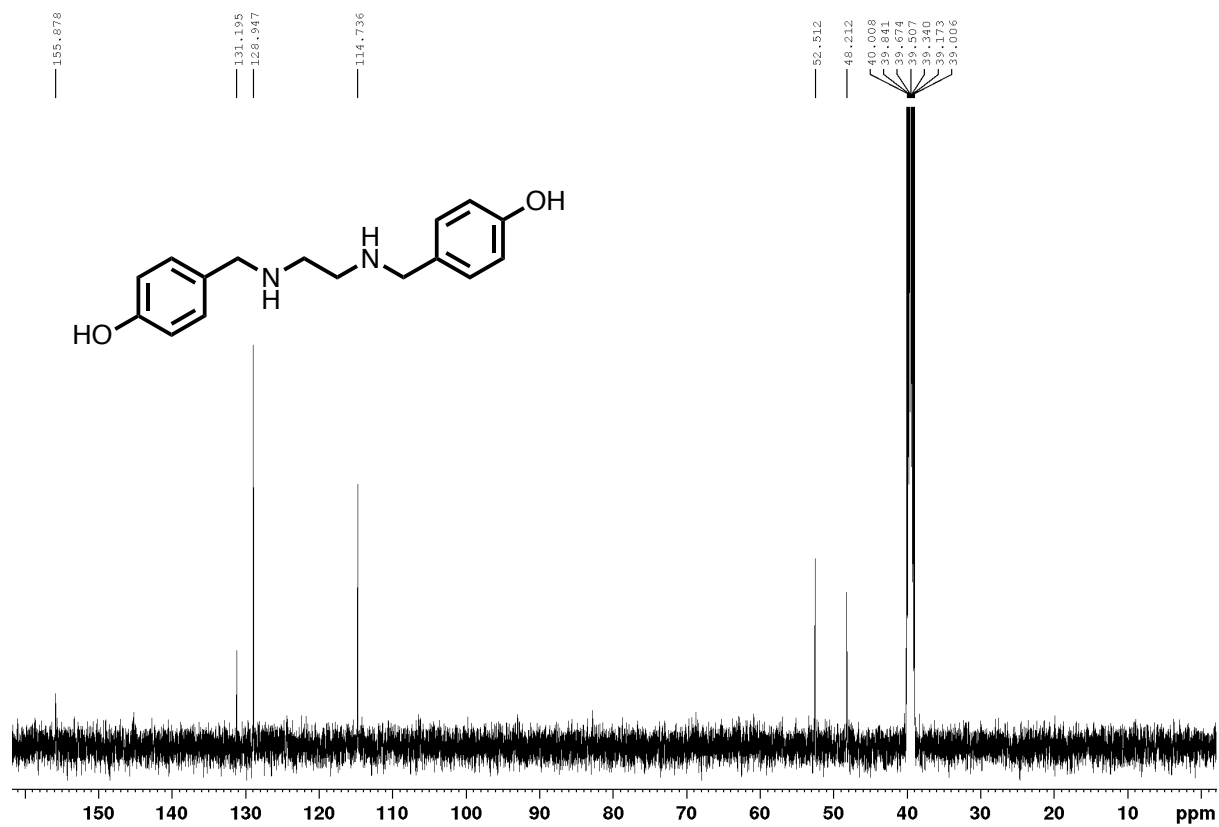


Figure S36 <sup>13</sup>C NMR spectrum of compound **3b** in d-DMSO (125 MHz).

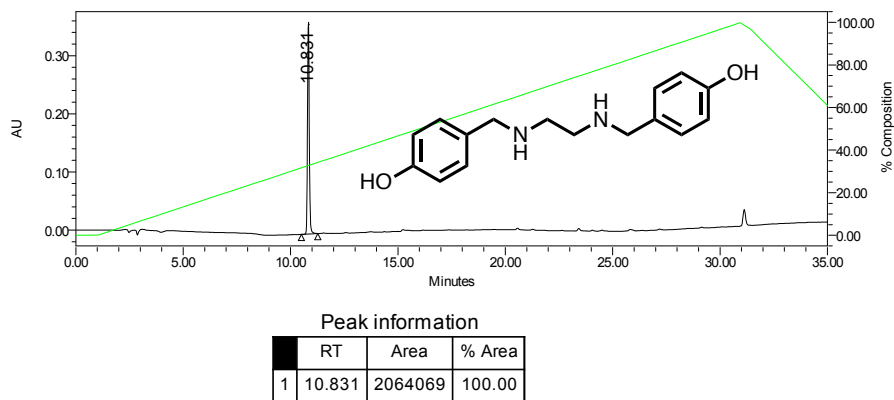
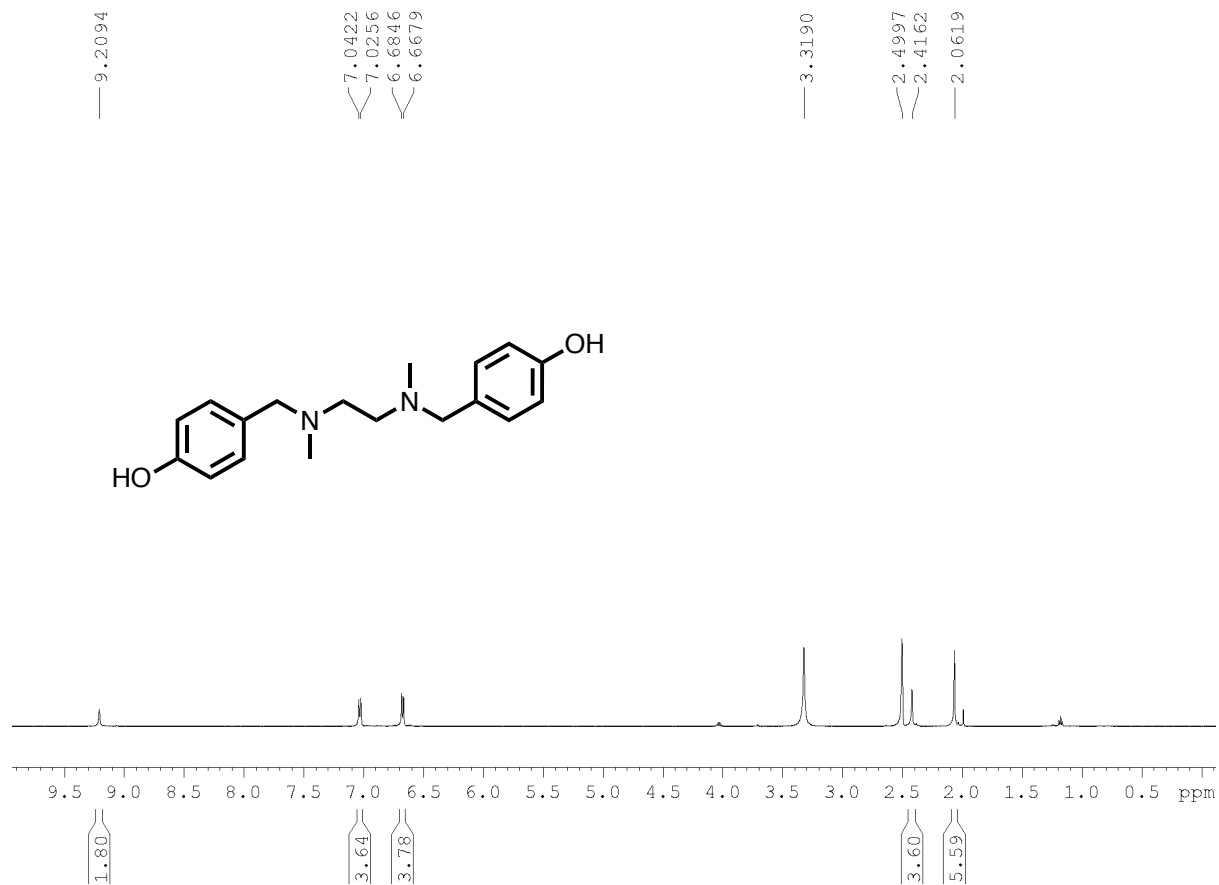


Figure S36\* HPLC chromatogram of compound **3b**.





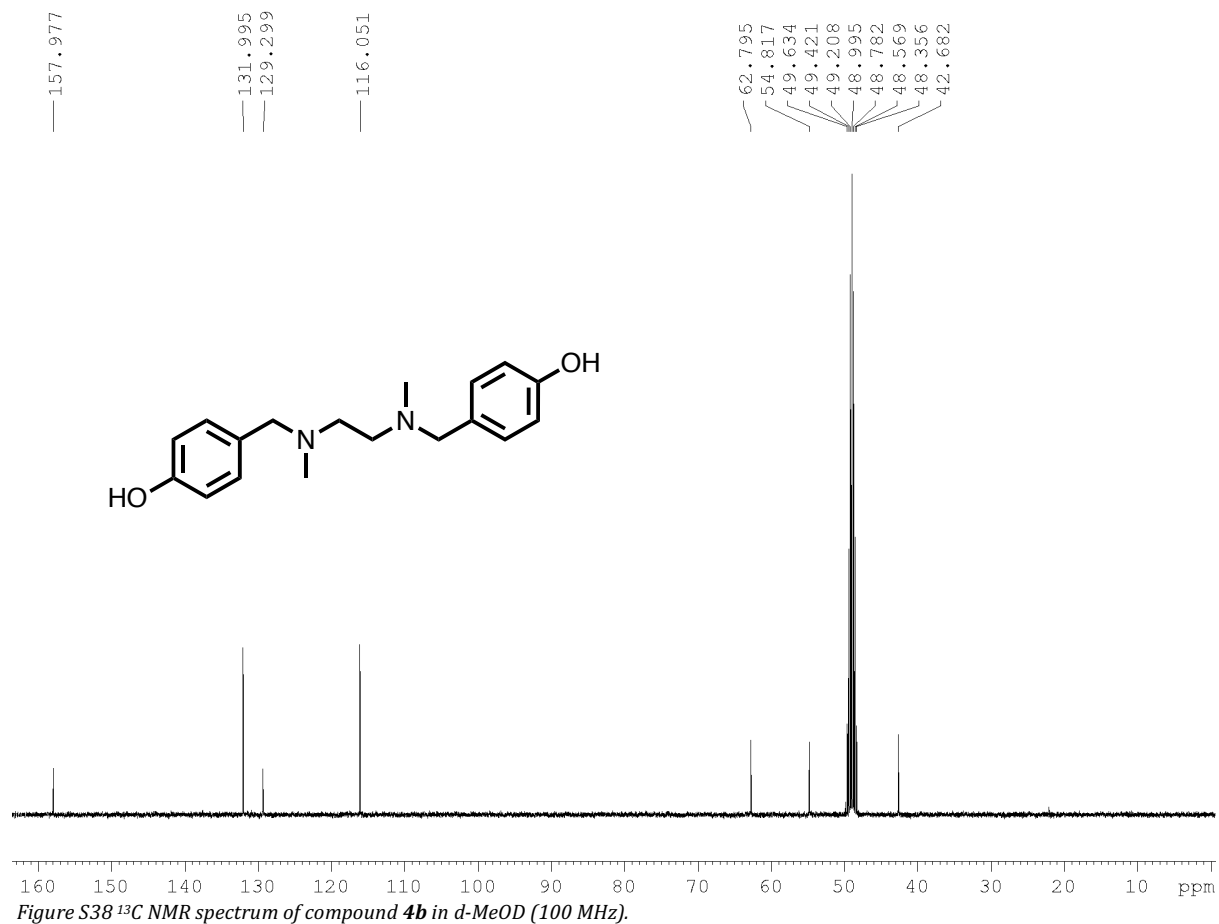


Figure S38 <sup>13</sup>C NMR spectrum of compound **4b** in d-MeOD (100 MHz).

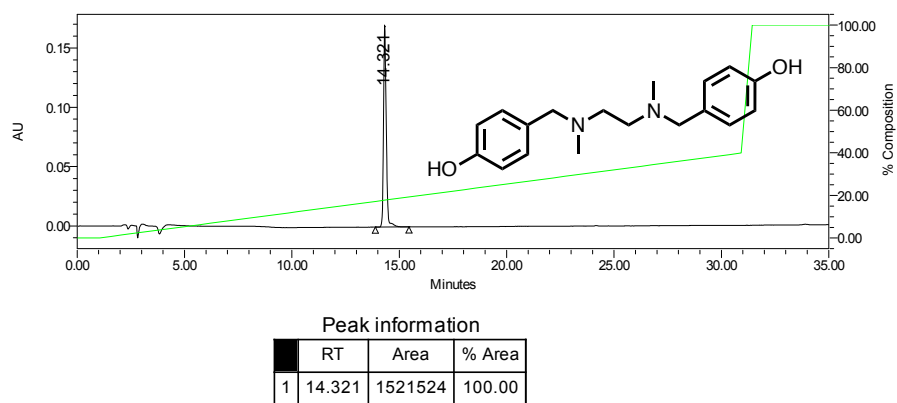


Figure S38\* HPLC chromatogram of compound **4b**.