

**A genomic DNA reporter screen identifies squalene synthase inhibitors which act cooperatively with statins to upregulate the low-density lipoprotein receptor**

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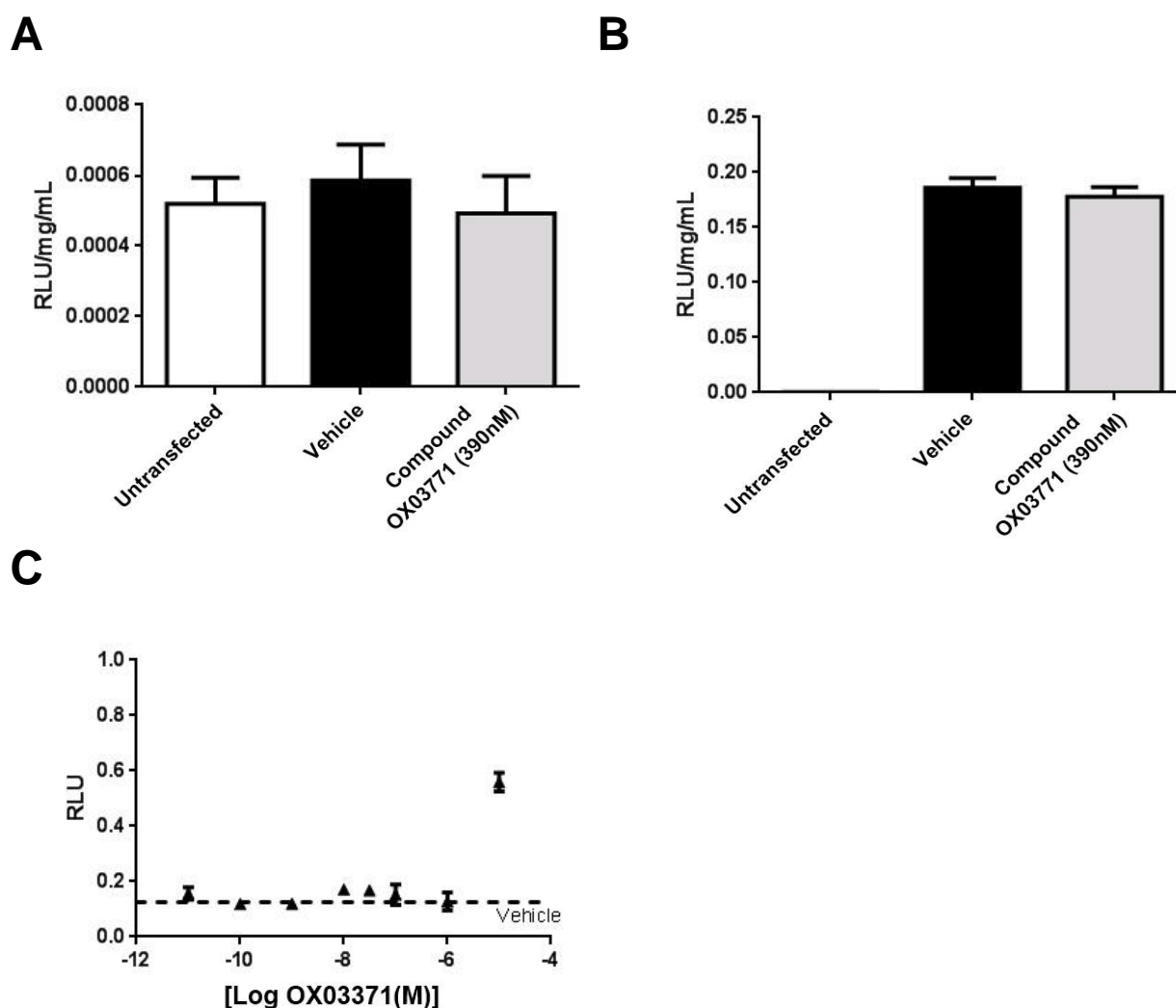
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## **Supplementary Information**

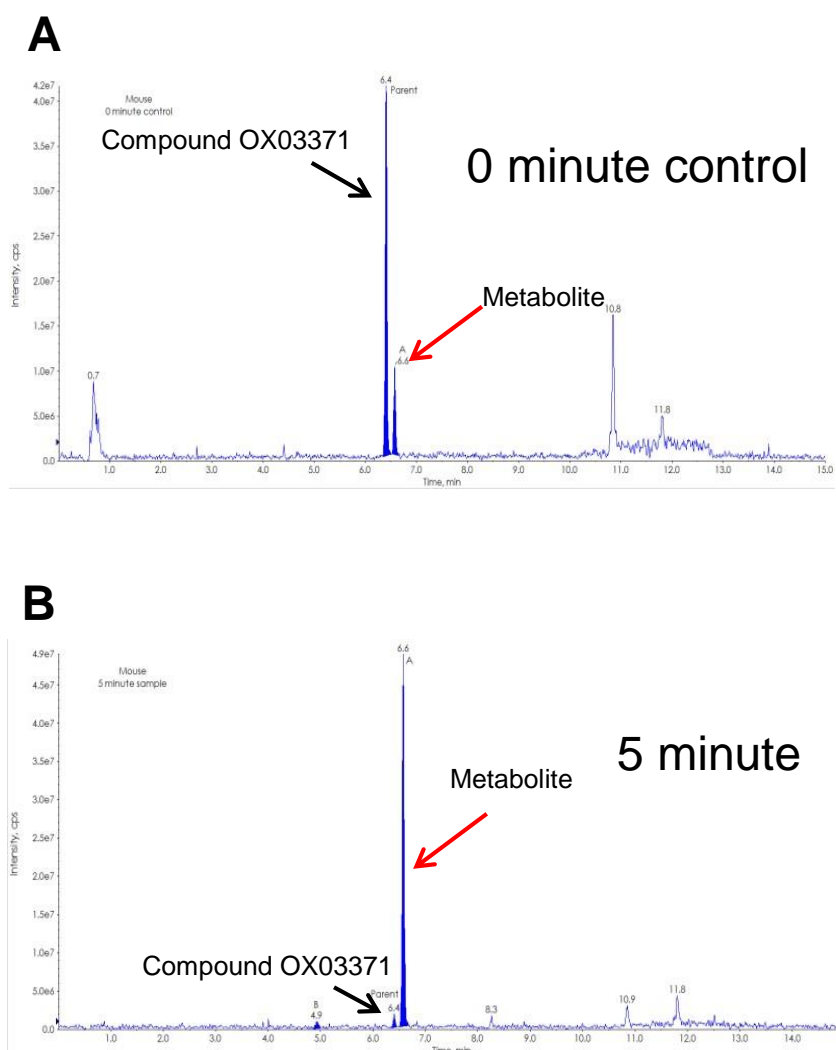


**Supplementary Figure 1. Compounds OX03371 does not stabilise or interact with  $\beta$ -Luciferin or luciferase nor fluoresce itself and demonstrates a favourable toxicity profile.**

(A) Hep3B cells were transfected with a pCMV-Luc plasmid 24 hours prior to compound treatment of OX03371 or vehicle control. An untransfected well was left to control for transfection. 48 hours after compound treatment luciferase expression was analysed with no differences detected between vehicle and compound treated cells. (B)

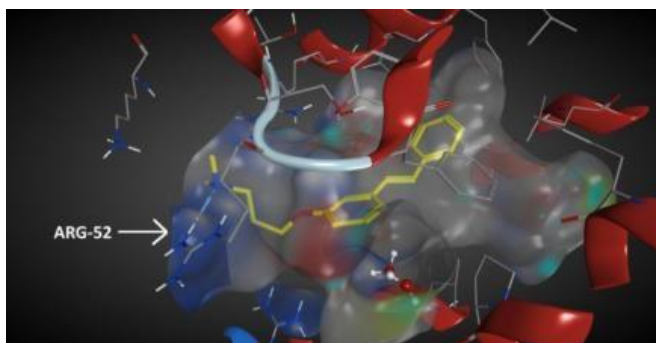
Untransfected Hep3B cells were treated with either compound OX03371 or vehicle control. 48 hours after compound treatment no significant differences could be detected

between any group. Luciferase expression was normalised to total protein. n=2. Error bars denote SD. (C) CHO-pLDLR-Luc cells were treated with compound OX03371 for 48 hours before Adenylate kinase release into the media was measured to quantify the cytotoxicity profile. n=4. Error bars denote standard deviation (SD).



**Supplementary Figure 2. Compound OX03371 has a half-life of under five minutes when spiked into mouse liver microsomes.**

Representative LC/MS trace of compound OX03371 (black arrow) and the detection of a potential metabolite (red arrow), (A) 0 and (B) 5 minutes after being spiked into mouse liver microsomes.



**Supplementary Figure 3. OX03394 a compound with no activity is predicted to sit in a different conformation in the active site of squalene synthase compared with compounds which are shown to inhibit this enzyme.**

In silico modelling of OX03394 using MOE software.

### General procedures:

All reactions involving organometallic or other moisture-sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was oven dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs *et al.*<sup>1</sup> Water was purified by an Elix® UV-10 system. All other reagents were used as supplied (analytical or HPLC grade) without prior purification. Thin layer chromatography was performed on aluminium plates coated with 60 F<sub>254</sub> silica. Plates were visualised using UV light (254 nm), or 1% aq KMnO<sub>4</sub>. Flash column chromatography was performed on Kieselgel 60 silica. Melting points were recorded on a Gallenkamp Hot Stage apparatus and are uncorrected. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer with a diamond ATR module. Selected characteristic peaks are reported in cm<sup>-1</sup>. NMR spectra were recorded on Bruker Avance spectrometers at rt in a solution of deuterated acetone unless stated otherwise. The field was locked by external referencing to the relevant deuterium resonance. Chemical shifts (δ) are reported in ppm and coupling constants *J* in Hz. Low resolution mass spectra were recorded on either a VG MassLab 20-250 or a Micromass Platform 1 spectrometer. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyalanine, or a Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m × 0.25 mm) using amyl acetate as a lock mass.

*General Procedure 1 – Preparation of Stilbenes by Horner-Wadsworth-Emmons (HWE) Reaction*

*n*-BuLi (2.5M in hexanes, 1.5 eq.) was added to a solution of diethyl benzylphosphonate (1.5 eq.) in toluene (2 mL) at 0 °C, and stirred for 30 min. A solution of the requisite aldehyde (1 eq.) in toluene (1 mL) was then added dropwise to the reaction, which was then stirred for 16 h. The reaction mixture was quenched with NH<sub>4</sub>Cl (sat. aq., 20 mL) and extracted with EtOAc (3 x 30 mL). The organic phase was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to yield the crude product. Purification by column chromatography on silica gel afforded the desired product.

*General Procedure 2 – Alkylation of Hydroxides*

K<sub>2</sub>CO<sub>3</sub> (3 eq.) was added to a solution of the requisite alcohol (1 eq.) in DMF (1 mL) in a microwave vial. The resulting suspension was heated at 90 °C for 30 min before addition of a solution of the alkyl chloride (1.1 eq.) in DMF (1 mL). The microwave vial was sealed and heated at 90 °C for 16 h. After cooling, the reaction mixture was quenched with H<sub>2</sub>O (10 mL), extracted with EtOAc (3 x 15mL), the organic layer washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to yield the crude product.

Purification by column chromatography afforded the desired product.

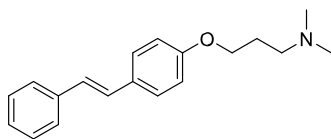
*General Procedure 3 – Preparation of Stilbenes by Heck Coupling using Pd(OAc)<sub>2</sub>*

Iodoarene (1 eq.), requisite styrene (1.2 eq.), Et<sub>3</sub>N (2.5 eq.), Pd(OAc)<sub>2</sub> (0.03 eq.) and PPh<sub>3</sub> (0.06 eq.) were dissolved in degassed 1,4-dioxane (2 mL) in a sealed microwave vial, and heated to 100 °C for 16 h. The reaction mixture was allowed to cool, then quenched 1M HCl<sub>(aq)</sub> (100 mL) and extracted with EtOAc (3 x 30 mL); the organic phase was washed with water, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to yield the crude product.

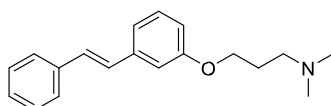
Purification by column chromatography afforded the desired product.

*General Procedure 4 – Preparation of Stilbenes by Heck Coupling using Pd(NH<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>*

Haloarene (1 eq.), requisite styrene (1.5 eq.), *n*-Bu<sub>3</sub>N (2 eq.), Pd(NH<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (0.015 eq.) and tetrabutylammonium bromide (1 eq.) were dissolved in H<sub>2</sub>O (6 mL) in a sealed microwave vial, and heated to 140 °C for 24 h. After cooling, the reaction mixture was extracted with EtOAc (3 x 15 mL), the organic phase dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to yield the crude product. Purification by column chromatography afforded the desired product.

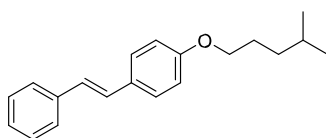
**Experimental data:****(*E*)-*N,N*-Dimethyl-3-(4-styrylphenoxy)propan-1-amine OX03371**

*n*-BuLi (2.5M in hexanes, 0.57 mL, 1.42 mmol) was added to a stirred solution of diethyl benzylphosphonate (0.3 mL, 1.42 mmol) in THF (2 mL) at 0 °C, and stirred for 30 min. A solution of the aldehyde **17a** (0.24 mL, 1.21 mmol) in THF was then added dropwise to the reaction, which was then stirred for 16 h. The reaction mixture was quenched with NH<sub>4</sub>Cl (sat. aq. sol. 20 mL) and extracted with EtOAc (3 x 30 mL). The organic phase was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to yield the crude product. Purification by recrystallisation in Pet Ether (40-60 °C) afforded the title compound as a white solid (22 mg, 7%). mp 75-77 °C;  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 2940, 2774, 1687, 1602, 1510, 1246, 1178, 1055;  $\delta_{\text{H}}$  (400 MHz, acetone-*d*<sub>6</sub>) 7.56 (2H, m), 7.53 (2H, apparent ddd *J* 8.7, 2.9, 2.1) 7.36 (2H, m), 7.23 (1H, m), 7.18 (1H, d, *J* 16.3), 7.08 (1H, d, *J* 16.3), 6.94 (2H, apparent ddd *J* 8.7, 2.9, 2.1), 4.05 (2H, t *J* 6.5), 2.40 (2H, t, *J* 7.0), 2.18 (6H, s), 1.90 (2H, m);  $\delta_{\text{C}}$  (100 MHz, acetone-*d*<sub>6</sub>) 160.0, 138.8, 130.9, 129.5, 129.2, 128.7, 128.0, 127.1, 126.1, 115.6, 66.9, 56.9, 45.8, 28.3; *m/z* (ESI<sup>+</sup>) 282 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>19</sub>H<sub>24</sub>NO ([M+H]<sup>+</sup>) requires 282.1852, found 282.1855.

**(*E*)-*N,N*-Dimethyl-3-(3-styrylphenoxy)propan-1-amine OX03372**

Following *general procedure 1*, the requisite aldehyde (197 mg, 0.948 mmol) gave the title compound as a viscous oil. (51 mg, 19%).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3376, 2945, 1599, 1579, 1449, 1272, 1157;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 7.52 (2H, d *J* 7.9), 7.37 (2H, m), 7.27 (2H, m), 7.09

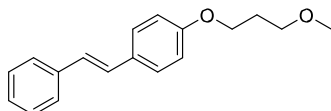
(4H, m), 6.82 (1H, dd, *J* 8.1, 2.5), 4.08 (2H, t, *J* 6.3), 2.58 (2H, t, *J* 7.5), 2.35 (6H, s), 2.05 (2H, m);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 159.2, 138.7, 137.2, 129.6, 128.9, 128.7, 128.5, 127.6, 126.5, 119.3, 113.8, 112.2, 66.0, 56.4, 45.2, 27.2; *m/z* (ESI<sup>+</sup>) 282 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>19</sub>H<sub>24</sub>NO ([M+H]<sup>+</sup>) requires 282.1852, found 282.1860.

**(*E*)-1-((4-Methylpentyl)oxy)-4-styrylbenzene OX03373**

Alcohol **OX03395** (100 mg, 0.510 mmol, 1 eq.) was dissolved in DMF (1 mL) in a microwave vial with K<sub>2</sub>CO<sub>3</sub> (211 mg, 1.53 mmol, 3 eq.) and stirred at 90 °C for 30 min. The tosylate (144 mg, 0.561 mmol, 1.1 eq.) was added, and the reaction was stirred at 90 °C for a further 16 h. After cooling, the reaction mixture was diluted with H<sub>2</sub>O (10 mL) and extracted with EtOAc. The combined organics were dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to yield the crude product. Purification by column chromatography (0.3% - 4% EtOAc in Pet Ether) yielded the title compound as a white solid (114 mg, 80%). mp 97-98 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 2955, 1603, 1510, 1241, 1175, 967;  $\delta_{\text{H}}$  (600 MHz) 7.98

(2H, d, *J* 8.0) 7.96 (2H, d, *J* 7.6), 7.78 (3H, dd, *J* 7.4, 6.9), 7.66 (1H, dd, *J* 8.0, 6.9), 7.62 (1H, d, *J* 16.4), 7.54 (1H, d, *J* 16.4) 7.37 (2H, d, *J* 7.4), 4.43 (2H, t *J* 6.6), 2.48 (1H, br s), 2.21 (2H, m) 1.79 (2H, m), 1.36 (6H, d, *J* 6.3);  $\delta_{\text{C}}$  (125 MHz) 160.0, 138.8, 130.9, 129.6, 129.2, 128.7, 128.0, 127.1, 127.1, 115.6, 69.0, 36.0, 28.6, 28.0, 23.0; HRMS (FI) C<sub>20</sub>H<sub>24</sub>O (M) requires 280.1827, found 280.1829.

**(*E*)-1-(3-Methoxypropoxy)-4-styrylbenzene OX3374**

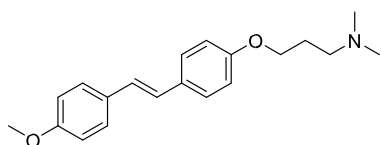


Alcohol **OX03395** (44 mg, 0.173 mmol, 1 eq.) in THF (0.5 mL) was added to a solution of NaH (140 mg, 3.46 mmol, 60% w/w in mineral oil, 20 eq.) in THF (0.5 mL), and stirred for 1 h at RT. Iodomethane (0.05 mL, 0.865 mmol, 5 eq.) was added, and the reaction was allowed to continue stirring for a further 16 h. The reaction mixture was then concentrated *in vacuo* to give the crude product; purification by flash chromatography yielded the title compound as a white solid (22 mg, 45%). mp 77.8-81.0 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 2861, 1604, 1510, 1123;  $\delta_{\text{H}}$  (400 MHz) 7.56 (2H, d *J* 7.9, H<sub>4</sub>, H<sub>5</sub>), 7.53 (2H, apparent ddd *J* 8.7, 2.9, 2.1), 7.35 (2H, apparent dd *J* 7.8, 7.5), 7.22 (2H, m), 7.09 (1H, d *J* 16.5),

6.94 (2H, apparent ddd *J* 8.7, 2.9, 2.1), 4.08 (2H, t *J* 6.3), 3.53 (2H, t *J* 6.3), 3.29 (3H, s),

2.00 (2H, observed quintet, *J* 6.3);  $\delta_{\text{C}}$  (100 MHz) 159.9, 138.8, 131.0, 129.6, 129.1, 128.7, 128.0, 127.2, 127.1, 115.6, 69.9, 65.7, 58.7, 30.4; HRMS (FI) C<sub>18</sub>H<sub>20</sub>O<sub>2</sub> (M) requires 268.1463, found 268.1460.

**(*E*)-3-(4-(4-Methoxystyryl)phenoxy)-*N,N*-dimethylpropan-1-amine OX03375**

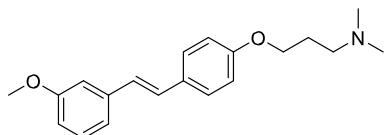


Following *general procedure 2*, the requisite stilbene (50 mg, 0.221 mmol) and 3dimethylamino-1-propylchloride hydrochloride (38 mg, 0.243 mmol) gave the title

compound as a white solid (24 mg, 35%). mp 138-140 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 2954, 1605, 1512, 1247, 1176, 1030;  $\delta_{\text{H}}$  (400 MHz) 7.49 (4H, m), 7.04 (2H, s), 6.92 (4H, m), 4.05 (2H, t  $J$

6.4), 3.81 (3H, s), 2.40 (2H, t  $J$  7.0), 2.18 (6H, s), 1.91 (2H, m);  $\delta_{\text{C}}$  (100 MHz) 160.2, 159.7, 131.5, 131.4, 128.4, 128.4, 127.0, 126.9, 115.6, 115.0, 66.9, 56.9, 55.6, 45.8, 28.4;  $m/z$  (ESI<sup>+</sup>) 312 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>26</sub>NO<sub>2</sub> ([M+H]<sup>+</sup>) requires 312.1958, found 312.1965.

**(*E*)-3-(4-(3-Methoxystyryl)phenoxy)-*N,N*-dimethylpropan-1-amine OX03376**

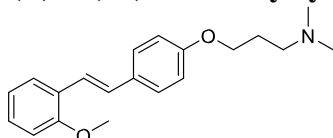


Following *general procedure 2*, the requisite alcohol (100 mg, 0.441 mmol) and 3dimethylamino-1-propylchloride hydrochloride (76 mg, 0.485 mmol) gave the title compound as a brown solid (71 mg, 52%). mp 28-32 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 2944, 2762, 1598, 1510, 1254, 1154, 1042;  $\delta_{\text{H}}$  (400 MHz) 7.51 (2H, apparent ddd  $J$  8.8, 2.8, 1.9), 7.26 (1H, m), 7.20 (1H, d  $J$  16.3), 7.14 (2H, m), 7.06 (1H, d  $J$  16.3), 6.93 (2H, apparent ddd  $J$  8.8,

2.8, 1.9), 6.82 (1H, m), 4.04 (2H, t  $J$  6.4), 3.82 (3H, s), 2.39 (2H, t  $J$  7.0), 2.17 (6H, s), 1.90 (2H, m);  $\delta_{\text{C}}$  (100 MHz) 161.1, 160.0, 140.2, 130.8, 130.5, 129.4, 128.7, 127.1, 119.7,

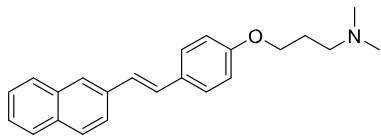
115.6, 113.8, 112.3, 66.9, 56.8, 55.5, 45.8, 28.3;  $m/z$  (ESI<sup>+</sup>) 312 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>26</sub>NO<sub>2</sub> ([M+H]<sup>+</sup>) requires 312.1958, found 312.1957.

**(*E*)-3-(4-(2-Methoxystyryl)phenoxy)-*N,N*-dimethylpropan-1-amine OX03377**

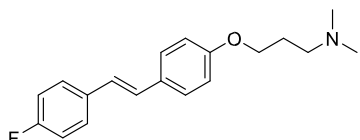


Following *general procedure 2*, the requisite alcohol (71 mg, 0.313 mmol) and 3dimethylamino-1-propylchloride hydrochloride (54 mg, 0.344 mmol) gave the title compound as a white solid (52 mg, 53%). mp 177.6-180.9 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 2418 (w), 1604 (w), 1509 (m), 1240 (s), 1173 (s);  $\delta_{\text{H}}$  (400 MHz) 7.63 (1H, dd  $J$  7.7, 1.6), 7.51 (2H, apparent ddd  $J$  8.8, 2.8, 2.0), 7.37 (1H, d  $J$  16.6), 7.23 (1H, m), 7.17 (1H, d  $J$  16.6), 6.97 (4H, m), 4.18 (2H, t  $J$  6.1), 3.89 (3H, s), 3.27 (2H, m), 2.80 (6H, s), 2.36 (2H, m);  $\delta_{\text{C}}$  (125 MHz) 159.4, 157.9, 130.0, 129.3, 129.3, 128.6, 127.4, 126.9, 122.2, 121.6, 115.7, 112.1, 66.3, 56.0, 55.4, 42.7, 25.3;  $m/z$  (ESI<sup>+</sup>) 312 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>26</sub>NO<sub>2</sub> ([M+H]<sup>+</sup>) requires 312.1958, found 312.1959;

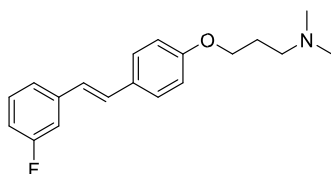


**(E)-N,N-Dimethyl-3-(4-(2-(naphthalen-2-yl)vinyl)phenoxy)propan-1-amine OX03378**

Following *general procedure 2*, the requisite alcohol (200 mg, 0.812 mmol) and 3dimethylamino-1-propylchloride hydrochloride (141 mg, 0.893 mmol) gave the title compound as a beige solid (209 mg, 78%). mp 138.3-139.7 °C;  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 2937, 2774, 1600, 1509, 1250;  $\delta_{\text{H}}$  (500 MHz, DMSO- $d_6$ ) 7.95 (1H, s, H10), 7.86 (4H, m), 7.58 (2H, apparent ddd  $J$  8.7, 3.0, 2.0), 7.48 (2H, m), 7.35 (1H, d  $J$  16.4), 7.25 (1H, d  $J$  16.4), 6.96 (2H, apparent ddd  $J$  8.7, 3.0, 2.0), 4.01 (2H, t  $J$  6.4), 2.35 (2H, t  $J$  7.0), 2.14 (6H, s), 1.85 (2H, m);  $\delta_{\text{C}}$  (125 MHz, DMSO- $d_6$ ) 158.5, 135.0, 133.4, 132.4, 129.6, 128.7, 128.1, 127.9, 127.7, 127.6, 126.4, 126.0, 125.8, 125.8, 123.5, 114.7, 65.8, 55.7, 45.2, 26.9;  $m/z$  (ESI<sup>+</sup>) 332 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>23</sub>H<sub>26</sub>NO ([M+H]<sup>+</sup>) requires 332.20089, found 332.19998.

**(E)-3-(4-(4-Fluorostyryl)phenoxy)-N,N-dimethylpropan-1-amine OX03379**

Following *general procedure 2*, the requisite alcohol (199 mg, 0.929 mmol) and 3dimethylamino-1-propylchloride hydrochloride (161 mg, 1.02 mmol) gave the title compound as a white solid (232 mg, 83%); mp 128.8-129.9 °C;  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 2951, 2767, 1510, 1247, 831;  $\delta_{\text{H}}$  (400 MHz, DMSO- $d_6$ ) 7.60 (2H, m), 7.51 (2H, d  $J$  8.6), 7.17 (3H, m, H8), 7.08 (1H, d  $J$  16.5), 6.93 (2H, d  $J$  8.6), 4.00 (2H, t  $J$  6.4), 2.43 (2H, t  $J$  7.2), 2.20 (6H, s), 1.87 (2H, m);  $\delta_{\text{C}}$  (125 MHz, DMSO- $d_6$ ) 161.4 (d  $J$  244.0), 158.3, 134.0 (d  $J$  2.8), 129.5, 128.0, 127.9, 127.7, 124.9, 115.5 (d  $J$  21.3), 114.7, 65.7, 55.5, 44.9, 26.6;  $m/z$  (ESI<sup>+</sup>) 300 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>19</sub>H<sub>23</sub>FNO ([M+H]<sup>+</sup>) requires 300.1758, found 300.1750;

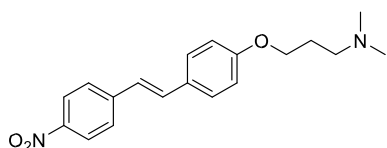
**(E)-3-(4-(3-Fluorostyryl)phenoxy)-N,N-dimethylpropan-1-amine OX03380**

$\text{Pd}(\text{OAc})_2$  (4 mg, 0.017 mmol, 0.05 eq.) and  $\text{PPh}_3$  (13 mg, 0.051 mmol, 0.15 eq.) were added to a sealed microwave vial in DMF (1 mL), and the resulting solution was flushed with nitrogen. The resulting orange solution was then heated with stirring at 110 °C for 10 min. A solution of the requisite styrene (55 mg, 0.434 mmol, 1.3 eq.), 4-iodophenol (73 mg, 0.334 mmol, 1 eq.) and  $\text{K}_2\text{CO}_3$  (185 mg, 1.34 mmol, 4 eq.) in DMF (0.5 mL) was then added, and the reaction mixture heated at 110 °C for a further 2 h. The reaction mixture was allowed to cool, then extracted with EtOAc. The combined organic layers were washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ), filtered and reduced *in vacuo* to give a solid (49 mg). This was redissolved in DMF (1 mL), treated with  $\text{K}_2\text{CO}_3$  (94 mg, 0.681 mmol, 3 eq.) and heated at 90 °C for 30 min before addition of a solution of 3-dimethylamino-1-propylchloride hydrochloride (40 mg, 0.250 mmol, 1.1 eq.) neutralised previously with  $\text{K}_2\text{CO}_3$  in DMF (0.5 mL). The microwave vial was sealed and heated at 90 °C for 16 h.

After cooling, the reaction mixture was quenched with  $\text{H}_2\text{O}$  (10 mL), extracted with EtOAc (3 x 15 mL), the organic layer washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo* to yield the crude product. Purification by column chromatography (16% MeOH in  $\text{CH}_2\text{Cl}_2$ ) afforded the desired product as a white solid (68 mg, 68%). mp 56.2-58.6 °C;  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 2813, 1600, 1510, 1253, 1177;  $\delta_{\text{H}}$  (400 MHz) 7.55 (2H, apparent ddd  $J$  8.7, 2.9, 2.0), 7.36 (3H, m), 7.27 (1H, d  $J$  16.5), 7.11 (1H, d  $J$  16.5), 6.98 (3H, m), 4.08 (2H, t  $J$  6.4), 2.52 (2H, t  $J$  7.2), 2.25 (6H, s), 1.98 (2H, m);  $\delta_{\text{C}}$  (100 MHz) 164.2 (d  $J$  243.0), 160.3, 141.6 (d  $J$  7.3), 131.3 (d  $J$  8.8), 130.8, 130.6, 129.0, 125.9 (d  $J$

2.9), 123.4 (d  $J$  2.9), 115.6, 114.5 (d  $J$  21.3), 113.1 (d,  $J$  22.0), 66.8, 56.7, 45.4, 28.9;  $m/z$  ( $\text{ESI}^+$ ) 300 ( $[\text{M}+\text{H}]^+$ ); HRMS ( $\text{ESI}^+$ )  $\text{C}_{19}\text{H}_{23}\text{NOF}$  ( $[\text{M}+\text{H}]^+$ ) requires 300.1758, found 300.1754.

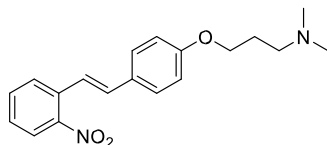
**(*E*)-*N,N*-Dimethyl-3-(4-(4-nitrostyryl)phenoxy)propan-1-amine OX03381**



Following *general procedure 2*, the alcohol (92 mg, 0.381 mmol) and 3-dimethylamino-1-propylchloride hydrochloride (66 mg, 0.419 mmol) gave the title compound as an orange solid (93 mg, 75%). mp 85.2-85.9 °C;  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 2937, 1589, 1502, 1332, 1174;  $\delta_{\text{H}}$  (400 MHz) 8.21 (2H, d  $J$  8.7), 7.81 (2H, d  $J$  8.7), 7.61 (2H, d  $J$  8.6), 7.46 (1H, d  $J$  16.4), 7.24 (1H, d  $J$  16.4), 6.97 (2H, apparent ddd  $J$  8.6, 3.1, 2.3), 4.08 (2H, t  $J$  6.4), 2.46

(2H, t  $J$  7.1), 2.22 (6H, s), 1.94 (2H, m);  $\delta_{\text{C}}$  (100 MHz) 160.8, 147.3, 145.7, 134.0, 130.1,

129.5, 127.7, 124.9, 124.9, 115.7, 66.9, 56.7, 45.6, 28.1;  $m/z$  ( $\text{ESI}^+$ ) 327 ( $[\text{M}+\text{H}]^+$ ); HRMS ( $\text{ESI}^+$ )  $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_3$  ( $[\text{M}+\text{H}]^+$ ) requires 327.17032, found 327.16962.

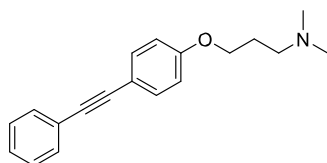
**(E)-N,N-Dimethyl-3-(4-(2-nitrostyryl)phenoxy)propan-1-amine OX03397**

Following *general procedure 2*, the requisite alcohol (81 mg) and 3-dimethylamino-1-propylchloride hydrochloride (58 mg) gave the title compound as an orange solid (48 mg, 44%). mp 51.9-57.1 °C;  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 2942, 1599, 1512, 1342, 1250;  $\delta_{\text{H}}$  (400 MHz) 7.94

(2H, m), 7.69 (1H, apparent dd  $J$  8.0, 7.3), 7.56 (2H, apparent ddd  $J$  8.8, 2.9, 2.0), 7.49 (1H, m), 7.41 (1H, d  $J$  16.2), 7.27 (1H, d  $J$  16.2), 6.97 (2H, apparent ddd  $J$  8.8, 2.9, 2.0),

4.08 (2H, t  $J$  6.4), 2.51 (2H, t  $J$  7.1), 2.25 (6H, s), 1.96 (2H, m);  $\delta_{\text{C}}$  (100 MHz) 160.7, 149.2, 134.3, 134.0, 133.5, 130.2, 129.4, 128.8, 128.6, 125.4, 121.3, 115.7, 66.9, 56.6,

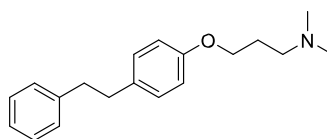
45.4, 27.9;  $m/z$  (ESI<sup>+</sup>) 327 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>19</sub>H<sub>23</sub>N<sub>2</sub>O<sub>3</sub> ([M+H]<sup>+</sup>) requires 327.17032, found 327.16966.

**N,N-Dimethyl-3-(4-(phenylethynyl)phenoxy)propan-1-amine OX03383**

Following *general procedure 2*, the requisite alcohol (100 mg, 0.515 mmol) and 3dimethylamino-1-propylchloride hydrochloride (89 mg, 0.561 mmol) gave the title compound as a beige solid (104 mg, 73%). mp 51-52 °C  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 2938, 2214, 1510, 1249;  $\delta_{\text{H}}$  (400 MHz, CD<sub>3</sub>OD) 7.47 (2H, m), 7.42 (2H, apparent ddd  $J$  8.8, 2.8, 2.0), 7.33 (3H, m), 6.90 (2H, apparent ddd  $J$  8.8, 2.8, 2.0), 3.99 (2H, t  $J$  6.2), 2.60 (2H, t  $J$  7.9), 2.34

(6H, s), 1.97 (2H, m);  $\delta_{\text{C}}$  (100 MHz, CD<sub>3</sub>OD) 160.6, 134.2, 132.5, 129.7, 129.2, 125.1,

116.8, 115.8, 90.4, 89.0, 67.1, 57.3, 45.3, 27.9;  $m/z$  (ESI<sup>+</sup>) 280 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>19</sub>H<sub>22</sub>NO ([M+H]<sup>+</sup>) requires 280.1694, found 280.1696.

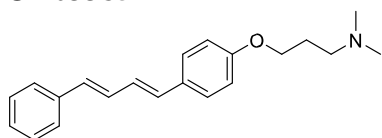
**N,N-Dimethyl-3-(4-phenethylphenoxy)propan-1-amine OX03384**

Stilbene **OX03371** (50 mg, 0.178 mmol) was suspended in MeOH (4 mL) with 10% Pd/C (10 mg) and stirred under 1 atm hydrogen for 3 h. Upon completion, the suspension was filtered over a celite pad, and the filtrate concentrated *in vacuo* to give the desired product as a clear oil (28 mg, 56%).  $\nu_{\max}$  (cm<sup>-1</sup>) 2939, 2361, 1511, 1242, 1156;  $\delta_{\text{H}}$  (400 MHz) 7.26 (2H, m), 7.21 (2H, m), 7.17 (1H, m), 7.11 (2H, apparent ddd  $J$  8.6, 3.0, 2.1), 6.82

(2H, apparent ddd  $J$  8.6, 3.0, 2.1), 3.99 (2H, t  $J$  6.4), 2.86 (4H, m), 2.39 (2H, t  $J$  7.0), 2.16

(6H, s), 1.88 (2H, m);  $\delta_{\text{C}}$  (100 MHz) 158.5, 142.9, 134.5, 130.2, 129.4, 129.1, 126.7, 115.2, 66.7, 56.9, 45.8, 39.0, 37.8, 28.4; (ESI<sup>+</sup>) 284 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>19</sub>H<sub>26</sub>NO ([M+H]<sup>+</sup>) requires 284.2009 found 284.2017.

***N,N*-Ddimethyl-3-(4-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)phenoxy)propan-1-amine**  
**OX03385**



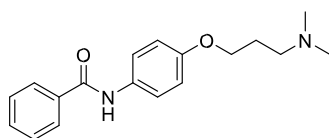
Following *general procedure 2*, the requisite alcohol (67 mg, 0.301 mmol) and 3dimethylamino-1-propylchloride hydrochloride (52 mg, 0.331 mmol) gave the title compound as a white solid (51 mg, 55%). mp not obtained due to decomposition at 250 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 3015 (w), 1943 (w), 1600 (m), 1509 (m), 1241 (s);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>)

7.44 (2H, d  $J$  7.8), 7.38 (2H, d  $J$  8.8), 7.34 (2H, m), 7.23 (1H, m), 6.95 (1H, dd  $J$  15.1,

10.6), 6.86 (3H, m), 6.63 (2H, d  $J$  15.1) 4.04 (2H, t  $J$  6.4), 2.50 (2H, t  $J$  7.3), 2.29 (6H, s),

1.99 (2H, m);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 158.7, 137.5, 132.5, 131.6, 130.1, 129.5, 128.6, 127.6, 127.3, 127.1, 126.2, 114.7, 66.2, 56.3, 45.4, 27.4;  $m/z$  (ESI<sup>+</sup>) 308 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>21</sub>H<sub>26</sub>NO ([M+H]<sup>+</sup>) requires 308.2009, found 308.2004.

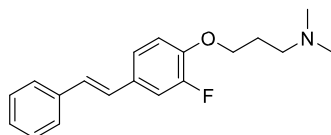
***N*-(4-(3-(Dimethylamino)propoxy)phenyl)benzamide** **OX03386**



Following *general procedure 2*, the requisite alcohol (56 mg) and 3-dimethylamino-1propylchloride hydrochloride (46 mg) gave the title compound as a beige solid (26 mg, 33%). mp 145.5-146.8 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 3274, 2765, 1642, 1509, 1232;  $\delta_{\text{H}}$  (400 MHz) 9.42 (1H, br. s), 7.99 (2H, m), 7.74 (2H, apparent ddd  $J$  9.1, 3.4, 2.3), 7.56 (1H, m), 7.49 (2H, m), 6.92 (2H, apparent ddd  $J$  9.1, 3.4, 2.3), 4.04 (2H, t  $J$  6.4), 2.43 (2H, t  $J$  7.1), 2.20 (6H,

s), 1.91 (2H, m);  $\delta_c$  (100 MHz) 165.9, 156.6, 136.5, 133.5, 132.2, 129.3, 128.3, 122.6, 115.3, 67.0, 56.9, 45.7, 28.3;  $m/z$  (ESI<sup>+</sup>) 299 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>18</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub> ([M+H]<sup>+</sup>) requires 299.17540, found 299.17514.

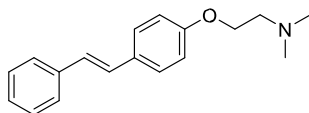
**(E)-3-(2-Fluoro-4-styrylphenoxy)-N,N-dimethylpropan-1-amine OX03387**



Following *general procedure 2*, the requisite alcohol (53 mg, 0.247 mmol) and 3dimethylamino-1-propylchloride hydrochloride (43 mg, 0.272 mmol) gave the title compound as a cream solid (31 mg, 42%). mp 68.2-72.6 °C;  $u_{max}$  (cm<sup>-1</sup>) 2940 (w), 2816 (m), 2766 (m), 1513 (s), 1273 (s), 1017 (s);  $\delta_H$  (400 MHz) 7.57 (2H, d  $J$  7.9) 7.44 (1H, dd  $J$  12.9, 2.1), 7.36 (2H, apparent dd  $J$  7.9, 7.5), 7.31 (1H, d  $J$  8.5), 7.23 (1H, m), 7.15 (3H, m), 4.14 (2H, t  $J$  6.4), 2.41 (2H, t  $J$  6.9), 2.17 (6H, s), 1.93 (2H, m);  $\delta_c$  (125 MHz) 153.6 (d  $J$  244.0), 147.7 (d  $J$  11.1), 138.4, 131.9 (d  $J$  6.5), 129.6, 128.7, 128.4, 128.2 (d  $J$  2.8),

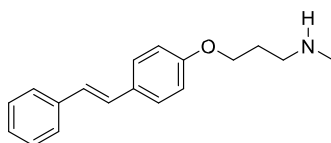
127.3, 124.2 (d,  $J$  2.8), 115.8, 114.1 (d  $J$  19.4), 68.2, 56.7, 45.8, 28.3;  $m/z$  (ESI<sup>+</sup>) 300 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>19</sub>H<sub>23</sub>NOF ([M+H]<sup>+</sup>) requires 300.1758, found 300.1753.

**(E)-N,N-Dimethyl-2-(4-styrylphenoxy)ethanamine OX03388**



Following *general procedure 2*, alcohol **OX03395** (200 mg, 1.02 mmol) and 2-chloroN,N-dimethylethanamine (162 mg, 1.12 mmol) gave the title compound as a white solid (61 mg, 22%). mp 102-106 °C;  $u_{max}$  (cm<sup>-1</sup>) 2938, 2759, 1603, 1509, 1251, 1032;  $\delta_H$  (400 MHz) 7.55 (4H, m), 7.35 (2H, apparent dd  $J$  7.8, 7.5), 7.21 (2H, m), 7.10 (1H, d  $J$  16.3), 6.95 (2H, apparent ddd  $J$  8.8, 2.9, 2.0), 4.10 (2H, t  $J$  5.9), 2.68 (2H, t  $J$  6.0), 2.27 (6H, s);  $\delta_c$  (100 MHz) 159.8, 138.8, 131.1, 129.6, 129.1, 128.7, 128.0, 127.2, 127.1, 115.6, 67.3, 59.0, 46.2;  $m/z$  (ESI<sup>+</sup>) 268 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>18</sub>H<sub>22</sub>NO ([M+H]<sup>+</sup>) requires 268.1696, found 268.1701.

**(E)-N-Methyl-3-(4-styrylphenoxy)propan-1-amine OX03389**



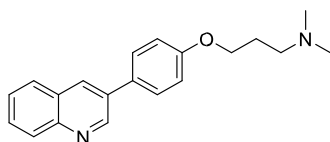
Stilbene **OX03371** (40 mg, 0.142 mmol, 1 eq) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (0.7 mL) to give a 0.2 M solution, and was added to 1-chloroethyl chloroformate (0.05 mL,

0.426 mmol, 3 eq) in a sealed microwave vial, to be heated to reflux for 16 h. After cooling, the reaction mixture was concentrated *in vacuo*. The residue was then redissolved in MeOH (1.5 mL), transferred to a sealed microwave vial, and refluxed for a further 2 h. The reaction mixture was left to cool, and concentrated *in vacuo* to yield the crude product. Purification by column chromatography (18% MeOH, 0.5% TEA in CH<sub>2</sub>Cl<sub>2</sub>) afforded the title compound as a cream solid (20 mg, 52 %). mp 84.2-87.7 °C;  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 2925, 1623, 1510, 1384, 1305;  $\delta_{\text{H}}$  (400 MHz, CD<sub>3</sub>OD) 7.48 (4H, m), 7.32 (2H, apparent dd *J* 7.8, 7.5),

7.21 (1H, m), 7.10 (1H, d *J* 16.5), 7.00 (1H, d *J* 16.5), 6.91 (2H, apparent ddd *J* 8.8, 2.9, 1.9), 4.04 (2H, t *J* 6.2), 2.78 (2H, t *J* 7.2), 2.42 (3H, s), 1.99 (2H, m), 1.27 (1H, broad s);  $\delta_{\text{C}}$  (100 MHz, CD<sub>3</sub>OD) 160.2, 131.8, 129.8, 129.8, 129.4, 128.9, 128.3, 127.7, 127.4, 115.9, 67.3, 49.7, 36.0, 29.9; *m/z* (ESI<sup>+</sup>) 268 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>18</sub>H<sub>22</sub>NO

([M+H]<sup>+</sup>) requires 268.1696, found 268.1693

### ***N,N*-Dimethyl-3-(4-(quinolin-3-yl)phenoxy)propan-1-amine OX03390**



Following *general procedure 2*, the requisite alcohol (74 mg, 0.334 mmol) and 3dimethylamino-1-propylchloride hydrochloride (58 mg, 0.367 mmol) gave the title compound as a white solid (47 mg, 46%). mp 54.6-57.2 °C;  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 2926, 2763, 1606, 1516, 1252, 1181;  $\delta_{\text{H}}$  (500 MHz) 9.20 (1H, d *J* 2.2), 8.46 (1H, d *J* 2.2), 8.06 (1H, d *J* 8.5),

8.00 (1H, d *J* 8.1), 7.79 (2H, apparent ddd *J* 8.7, 3.0, 2.2), 7.73 (1H apparent ddd *J* 8.5,

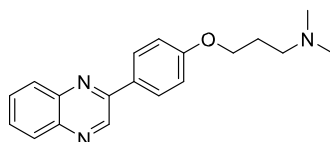
6.9, 1.5), 7.61 (1H, ddd 8.1, 6.9, 1.2), 7.11 (2H, apparent ddd *J* 8.7, 3.0, 2.2), 4.13 (2H, t *J*

6.5), 2.44 (2H, t *J* 7.1), 2.20 (6H, s), 1.95 (2H, m);  $\delta_{\text{C}}$  (125 MHz) 160.5, 150.5, 148.2,

134.3, 132.7, 130.9, 130.1, 129.8, 129.4, 129.2, 129.1, 127.8, 116.2, 67.0, 56.9, 45.8, 28.3

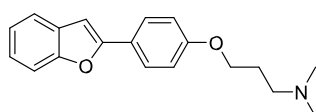
; *m/z* (ESI<sup>+</sup>) 307 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>23</sub>N<sub>2</sub>O ([M+H]<sup>+</sup>) requires 307.1805, found 307.1797.

### ***N,N*-Dimethyl-3-(4-(quinoxalin-2-yl)phenoxy)propan-1-amine OX03391**



Following *general procedure 2*, the requisite alcohol (58 mg, 0.261 mmol) and 3dimethylamino-1-propylchloride hydrochloride (45 mg, 0.287 mmol) gave the title compound as a white solid (68 mg, 84%). mp > 300 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 2475, 1506, 1270, 810;  $\delta_{\text{H}}$  (500 MHz, CDCl<sub>3</sub>) 9.26 (1H, s), 8.14 (2H, apparent ddd  $J$  8.9, 2.9, 2.0), 8.08 (2H, m), 7.73 (1H, m), 7.68 (1H, m), 7.05 (2H, apparent ddd  $J$  8.9, 2.9, 2.0), 4.09 (2H, t  $J$  6.3), 2.55 (2H, t  $J$  7.3), 2.32 (6H, s), 2.04 (2H, m);  $\delta_{\text{C}}$  (125 MHz, CDCl<sub>3</sub>) 160.7, 151.3, 143.0, 142.2, 141.1, 130.1, 129.3, 129.1, 129.0, 128.9, 128.8, 115.0, 66.1, 56.2, 45.2, 27.1; m/z (ESI<sup>+</sup>) 308 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>19</sub>H<sub>22</sub>N<sub>3</sub>O ([M+H]<sup>+</sup>) requires 308.1757, found 308.1756.

### 3-(4-(Benzofuran-2-yl)phenoxy)-*N,N*-dimethylpropan-1-amine OX03392

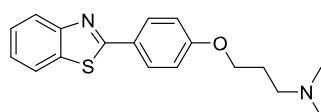


Following *general procedure 2*, the requisite alcohol (34 mg, 0.163 mmol) and 3dimethylamino-1-propylchloride hydrochloride (28 mg, 0.179 mmol) gave the title compound as a cream solid (29 mg, 60%). mp 203-206 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 2473, 1505, 1250, 797;  $\delta_{\text{H}}$  (400 MHz) 7.86 (2H, apparent ddd  $J$  8.9, 2.9, 2.1), 7.60 (1H, apparent dd  $J$  7.4,

1.3), 7.53 (1H, d  $J$  8.0), 7.28 (1H, apparent ddd  $J$  7.8, 7.4, 1.4), 7.22 (1H, m), 7.13 (1H, s), 7.05 (2H, apparent ddd  $J$  8.9, 2.9, 2.1), 4.11 (2H, t  $J$  6.4), 2.42 (2H, t  $J$  7.0), 2.19 (6H,

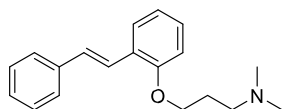
s), 1.94 (2H, m);  $\delta_{\text{C}}$  (100 MHz) 160.8, 157.0, 155.6, 130.6, 127.3, 124.8, 123.9, 123.8, 121.6, 115.8, 111.7, 100.7, 67.0, 56.8, 45.8, 28.3; HRMS (FI) C<sub>19</sub>H<sub>21</sub>NO<sub>2</sub> (M) requires 295.1572, found 295.1586.

### 3-(4-(Benzo[d]thiazol-2-yl)phenoxy)-*N,N*-dimethylpropan-1-amine OX03393



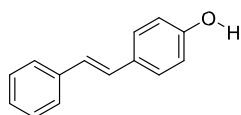
Following *general procedure 2*, the requisite alcohol (33 mg, 0.142 mmol) and 3dimethylamino-1-propylchloride hydrochloride (25 mg, 0.157 mmol) gave the title compound as a beige solid (24 mg, 54%). mp 206-209 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 2926, 2760, 1604, 1519, 1255, 1174;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 8.02 (3H, m), 7.88 (1H, d  $J$  7.9), 7.47 (1H, apparent dd  $J$  7.7, 7.5), 7.36 (1H, apparent dd  $J$  7.7, 7.5), 6.99 (2H, d  $J$  8.6), 4.11 (2H, t  $J$  6.0), 2.69 (2H, t  $J$  7.1), 2.43 (6H, s), 2.11 (2H, m);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 167.8, 161.1,

154.1, 134.8, 129.1, 126.4, 126.2, 124.8, 122.8, 121.5, 114.8, 65.9, 56.1, 44.8, 26.6; HRMS (ESI<sup>+</sup>) C<sub>18</sub>H<sub>21</sub>N<sub>2</sub>OS ([M+H]<sup>+</sup>) requires 313.1369, found 313.1370. (**E**)-*N,N*-Dimethyl-3-(2-styrylphenoxy)propan-1-amine OX03394<sup>2</sup>



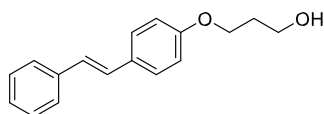
Following *general procedure 1*, the requisite aldehyde (124 mg, 0.596 mmol) gave the title compound as a viscous oil (67 mg, 40%). The analytical data were in accordance with those reported in the literature.<sup>2</sup>  $\nu_{\max}$  (cm<sup>-1</sup>) 3329, 2945, 1596, 1453, 1240, 1053;  $\delta_{\text{H}}$  (400 MHz) 7.65 (1H, dd  $J$  7.7, 1.6), 7.56 (3H, m), 7.36 (2H, m), 7.24 (3H, m), 7.00 (1H, d  $J$  8.2), 6.95 (1H, apparent dd  $J$  7.6, 7.5), 4.11 (2H, t  $J$  6.3), 2.53 (2H, t  $J$  7.1), 2.23 (6H, s), 2.02 (2H, m);  $\delta_{\text{C}}$  (100 MHz) 157.5, 139.0, 129.7, 129.7, 129.6, 128.3, 127.4, 127.3, 127.1, 124.5, 121.5, 113.2, 67.3, 57.0, 45.7, 28.2;  $m/z$  (ESI<sup>+</sup>) 282 ([M+H]<sup>+</sup>); HRMS (ESI<sup>+</sup>) C<sub>19</sub>H<sub>24</sub>NO ([M+H]<sup>+</sup>) requires 282.1852, found 282.1855.

### (*E*)-4-Styrylphenol OX03395<sup>3</sup>



Following *general procedure 3*, 4-iodophenol (561 mg, 2.55 mmol) and styrene (0.35 mL, 3.06 mmol) gave the title compound as a white solid (122 mg, 24%). The analytical data were in accordance with those reported in the literature.<sup>3</sup> mp 180-182 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 3409, 1591, 1508, 1450, 1369, 1245, 960;  $\delta_{\text{H}}$  (400 MHz) 8.49 (1H, s), 7.54 (2H, d  $J$  8.0), 7.46 (2H, apparent ddd  $J$  8.7, 2.9, 2.1), 7.34 (2H, m), 7.20 (2H, m), 7.05 (1H, d  $J$  16.5), 6.86 (2H, apparent ddd  $J$  8.7, 2.9, 2.1);  $\delta_{\text{C}}$  (100 MHz) 158.3, 138.9, 130.0, 129.5, 129.4, 128.8, 127.9, 127.0, 126.5, 116.5;  $m/z$  (ESI<sup>-</sup>) 195 ([M-H]<sup>-</sup>).

### (*E*)-3-(4-Styrylphenoxy)propan-1-ol OX3050<sup>4</sup>



Following *general procedure 2*, alcohol **OX03395** (100 mg, 0.51 mmol) and 3-chloro-1propanol (0.05 mL, 0.56 mmol) gave the title compound as a white fluffy solid (92 mg, 71%). The analytical data were in accordance with those reported in the literature.<sup>4</sup> mp 166-167 °C;  $\nu_{\max}$  (cm<sup>-1</sup>) 3275, 1601, 1507, 1235, 1043;  $\delta_{\text{H}}$  (400 MHz) 7.56 (2H, d  $J$  7.7),

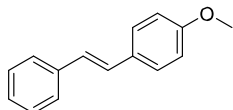
7.54 (2H, apparent ddd  $J$  8.7, 2.9, 2.0), 7.35 (2H, m), 7.21 (2H, m), 7.09 (1H, d  $J$  16.4),

6.95 (2H, apparent ddd  $J$  8.7, 2.9, 2.0), 4.13 (2H, t  $J$  6.3), 3.74 (2H, m), 3.69 (1H, t  $J$  5.2), 1.97 (2H, m);  $\delta_{\text{C}}$  (100 MHz) 160.0, 138.8, 131.0, 129.6, 129.2, 128.7, 128.0,



127.1, 127.1, 115.6, 65.7, 59.1, 33.4;  $m/z$  (ESI<sup>-</sup>) 254 ([M-H]<sup>-</sup>); HRMS (FI) C<sub>17</sub>H<sub>18</sub>O<sub>2</sub> (M) requires 254.1307, found 254.1317.

**(*E*)-1-Methoxy-4-styrylbenzene OX03396<sup>5</sup>**

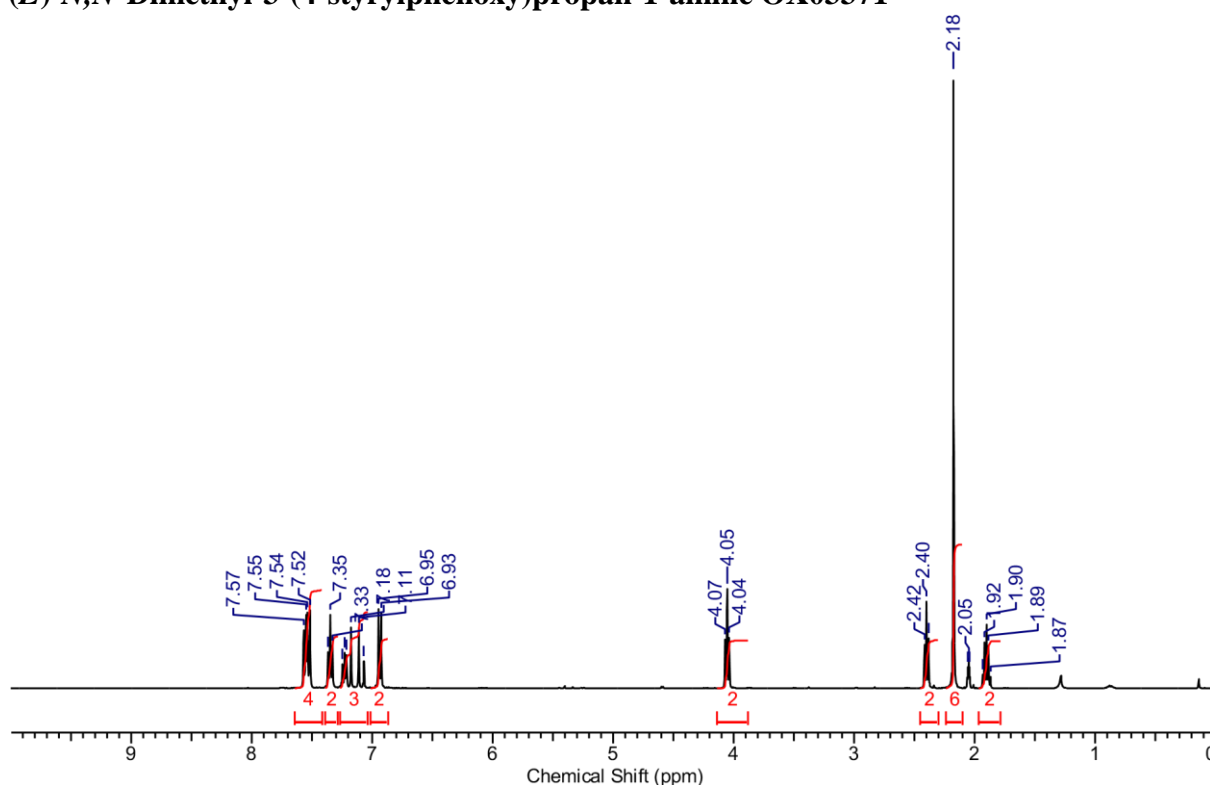


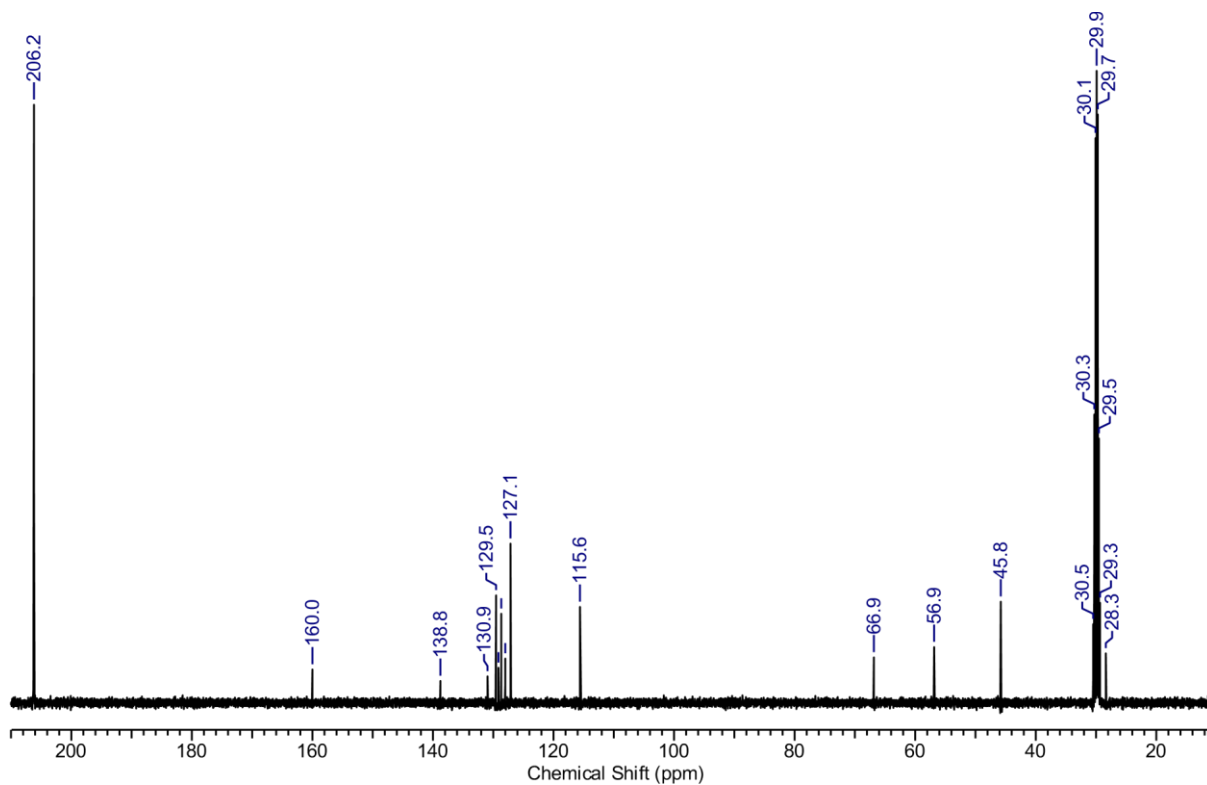
Following *general procedure 4*, 4-iodoanisole (557 mg, 2.38 mmol) and styrene (0.33 mL, 2.85 mmol) gave the title compound as a white solid (236 mg, 47%). The analytical data were in accordance with those reported in the literature.<sup>5</sup> mp 129-132 °C;  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3003, 1600, 1508, 1244, 1177;  $\delta_{\text{H}}$  (400 MHz) 7.55 (4H, m), 7.35 (2H, m), 7.22 (2H, m),

7.10 (1H, d  $J$  16.5), 6.94 (2H, apparent ddd  $J$  8.8, 3.0, 2.1), 3.81 (3H, s);  $\delta_{\text{C}}$  (100 MHz) 160.5, 138.8, 131.1, 129.6, 129.1, 128.7, 128.1, 127.2, 127.1, 115.0, 55.7; HRMS (FI) C<sub>15</sub>H<sub>14</sub>O (M) requires 210.1045, found 210.1052.

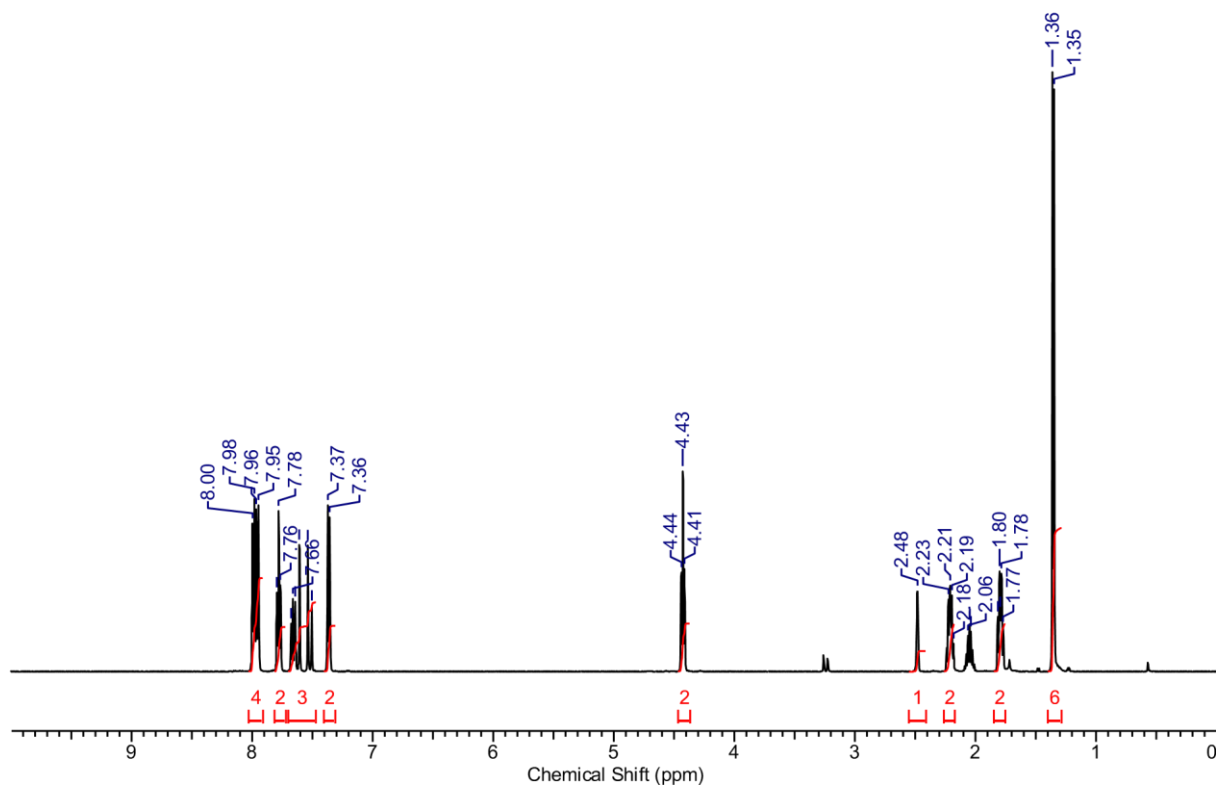
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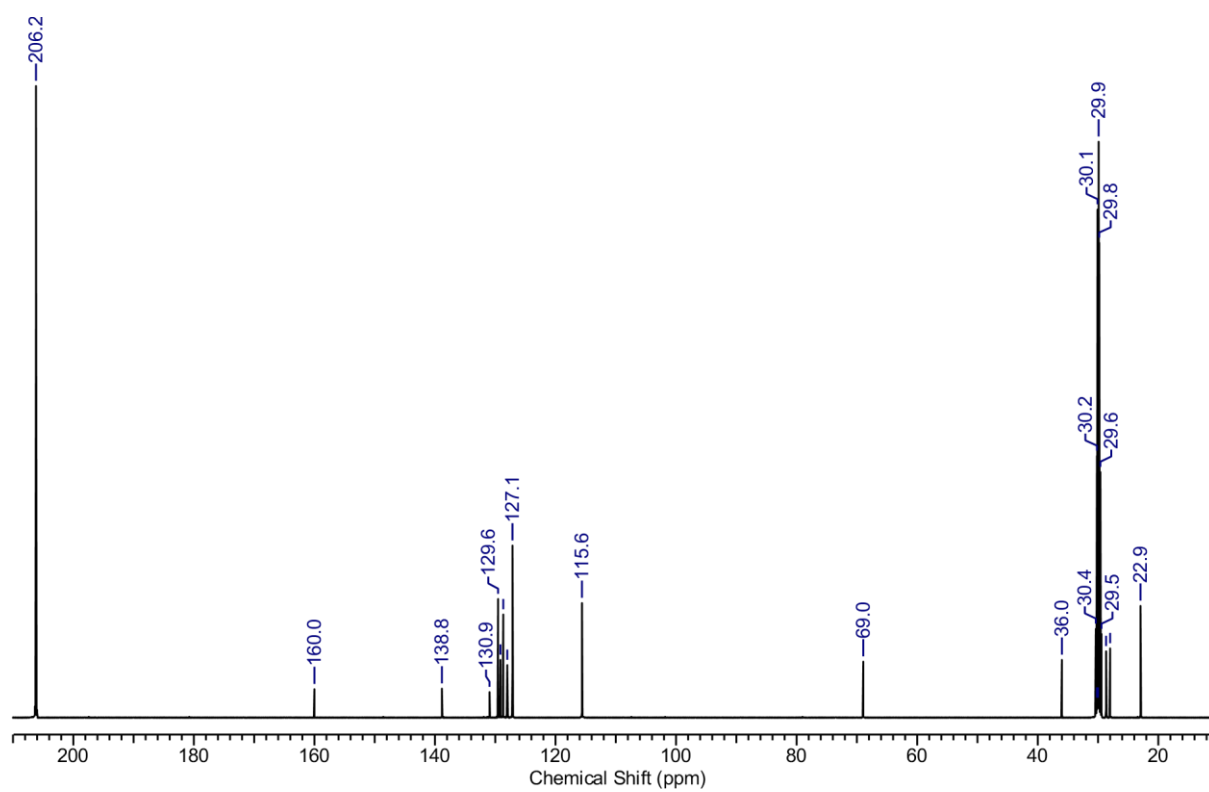
**(*E*)-*N,N*-Dimethyl-3-(4-styrylphenoxy)propan-1-amine OX03371**

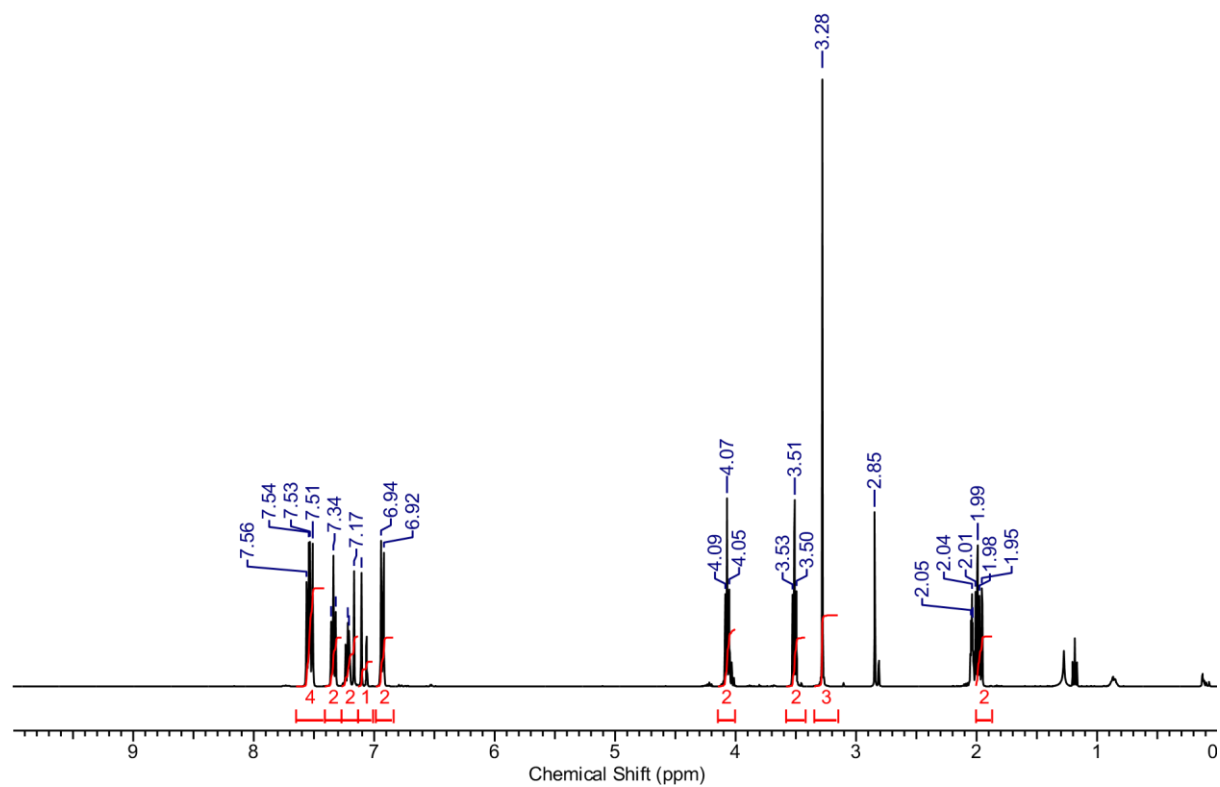


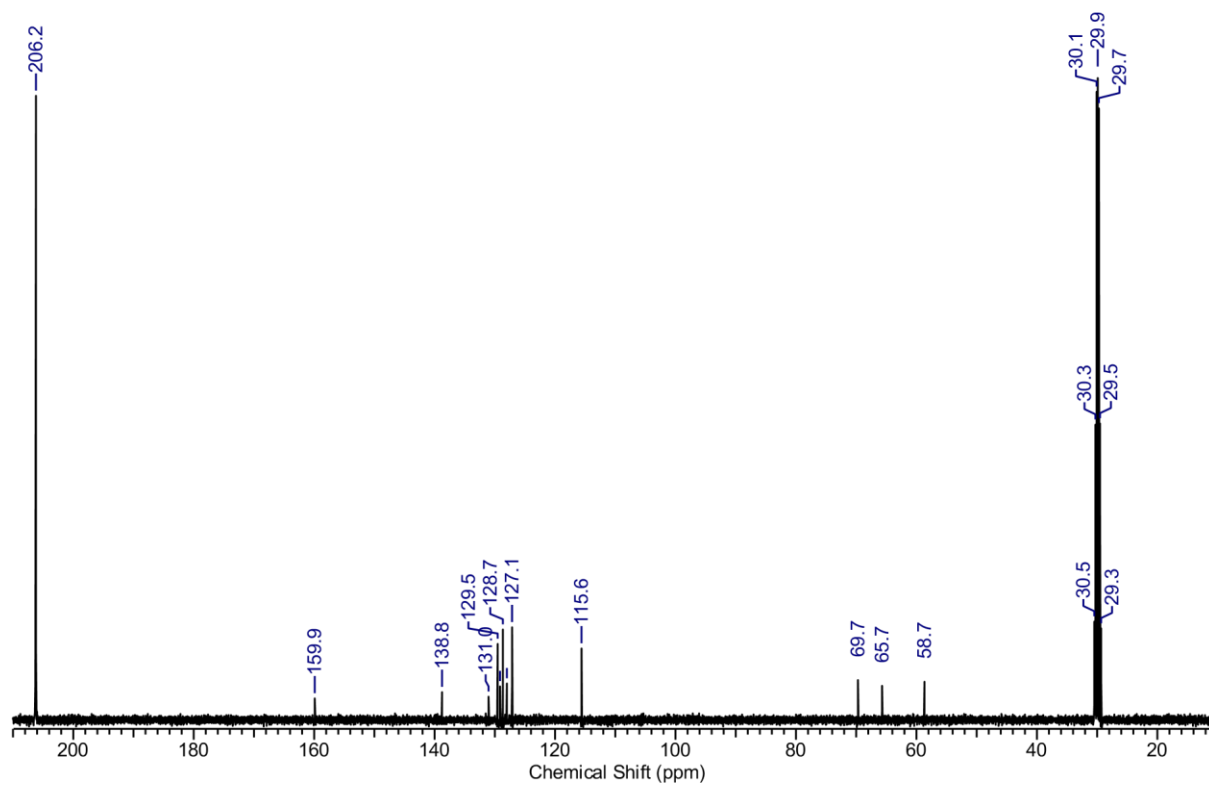


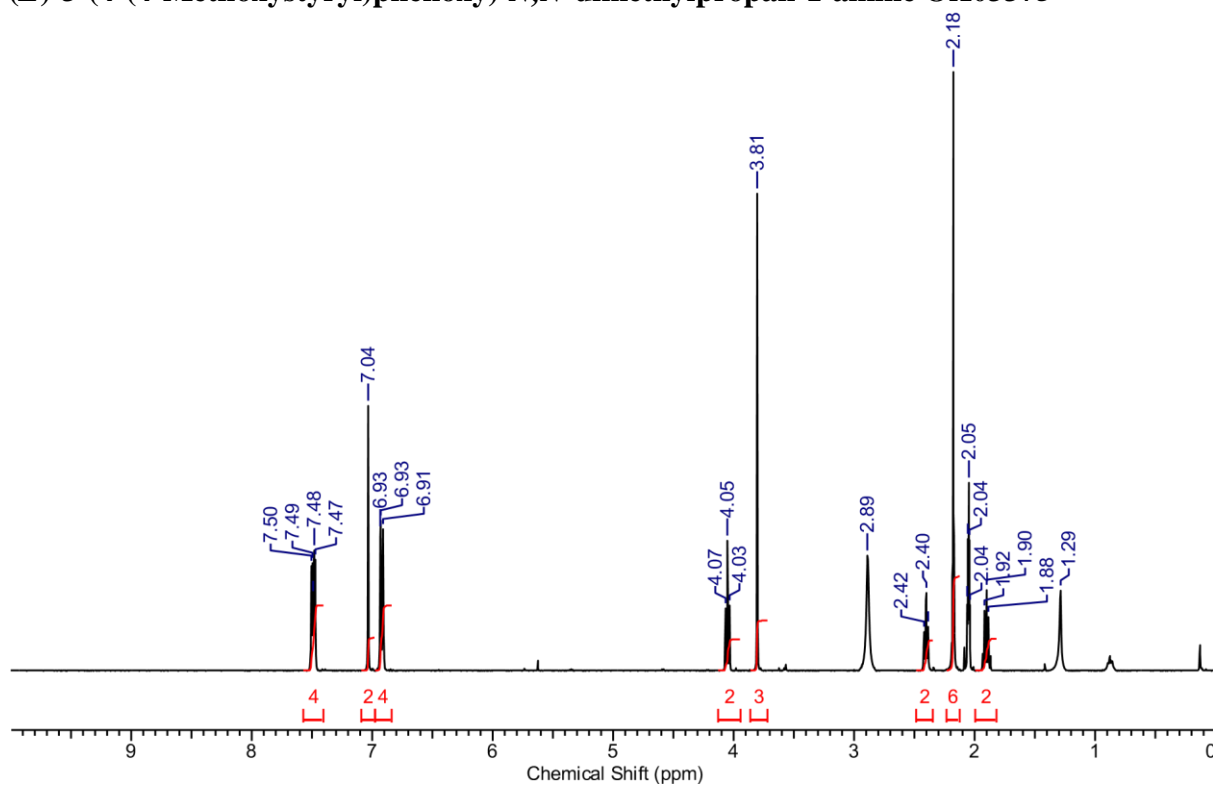
**(*E*)-1-((4-Methylpentyl)oxy)-4-styrylbenzene OX03373**

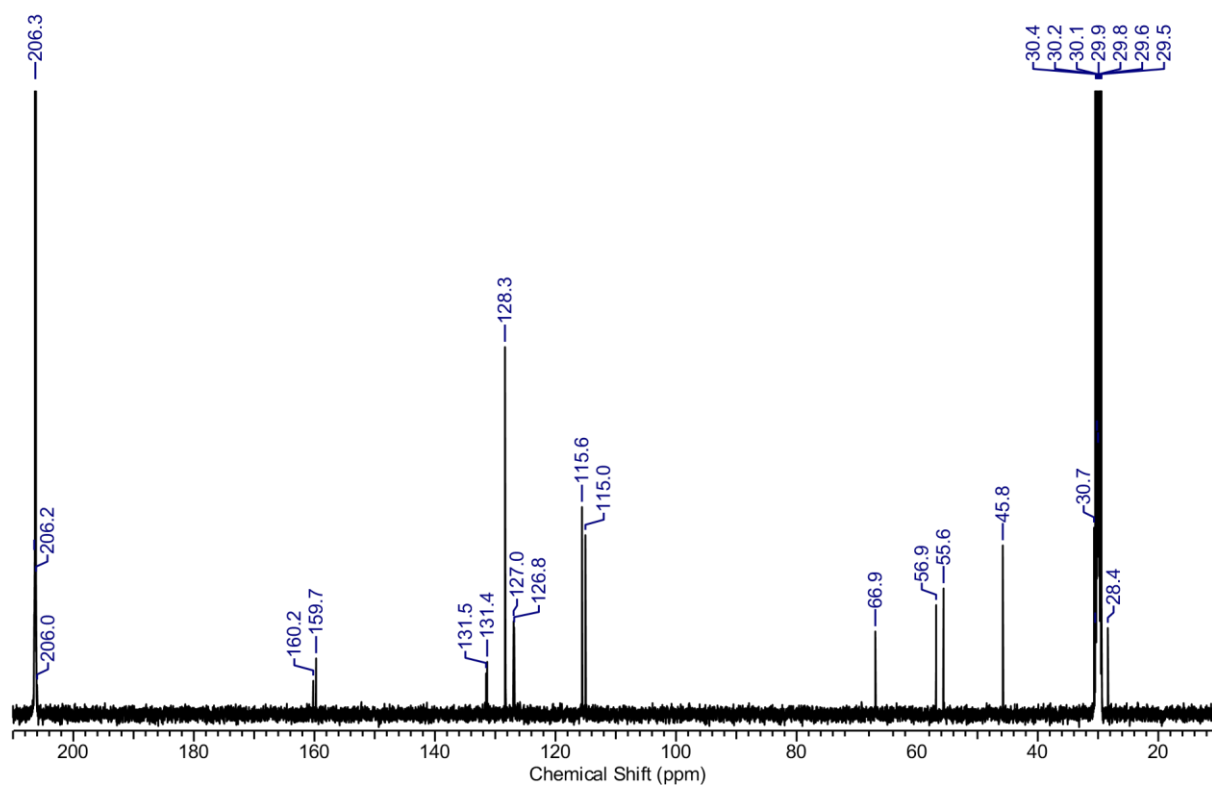




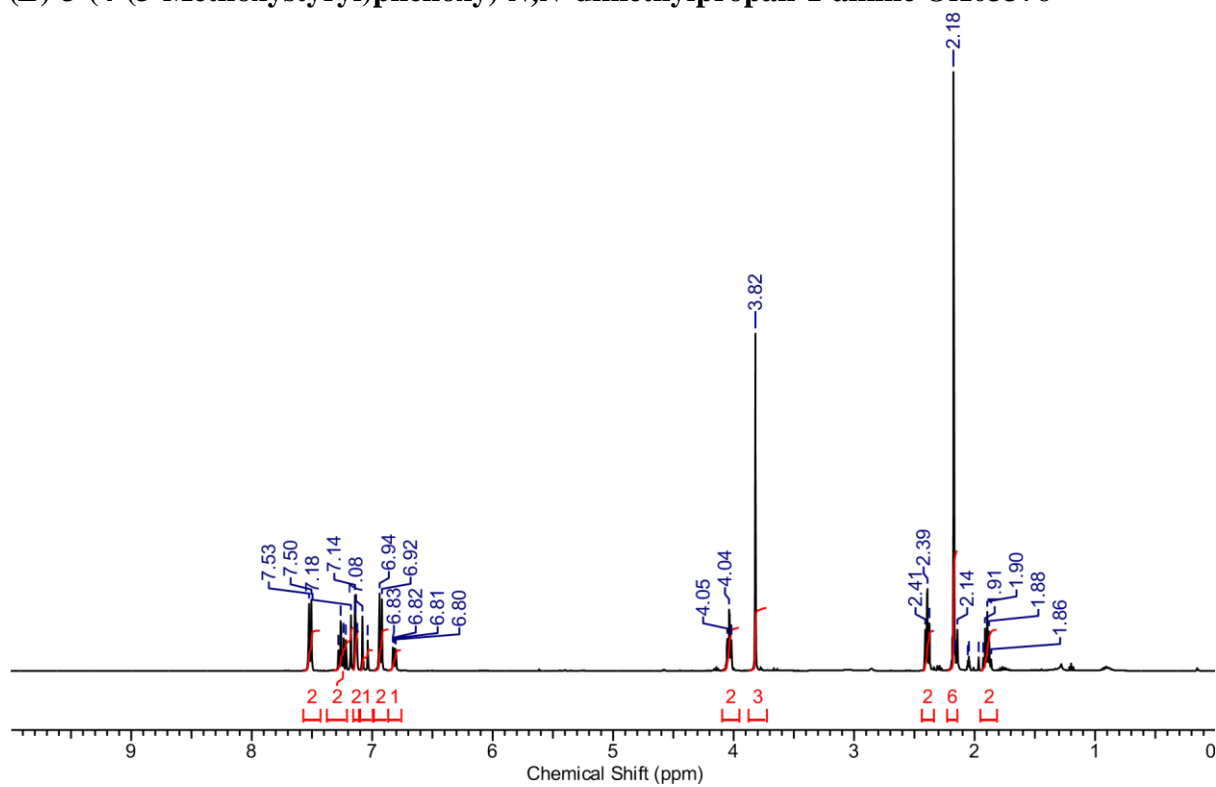
**(E)-1-(3-Methoxypropoxy)-4-styrylbenzene OX03374**



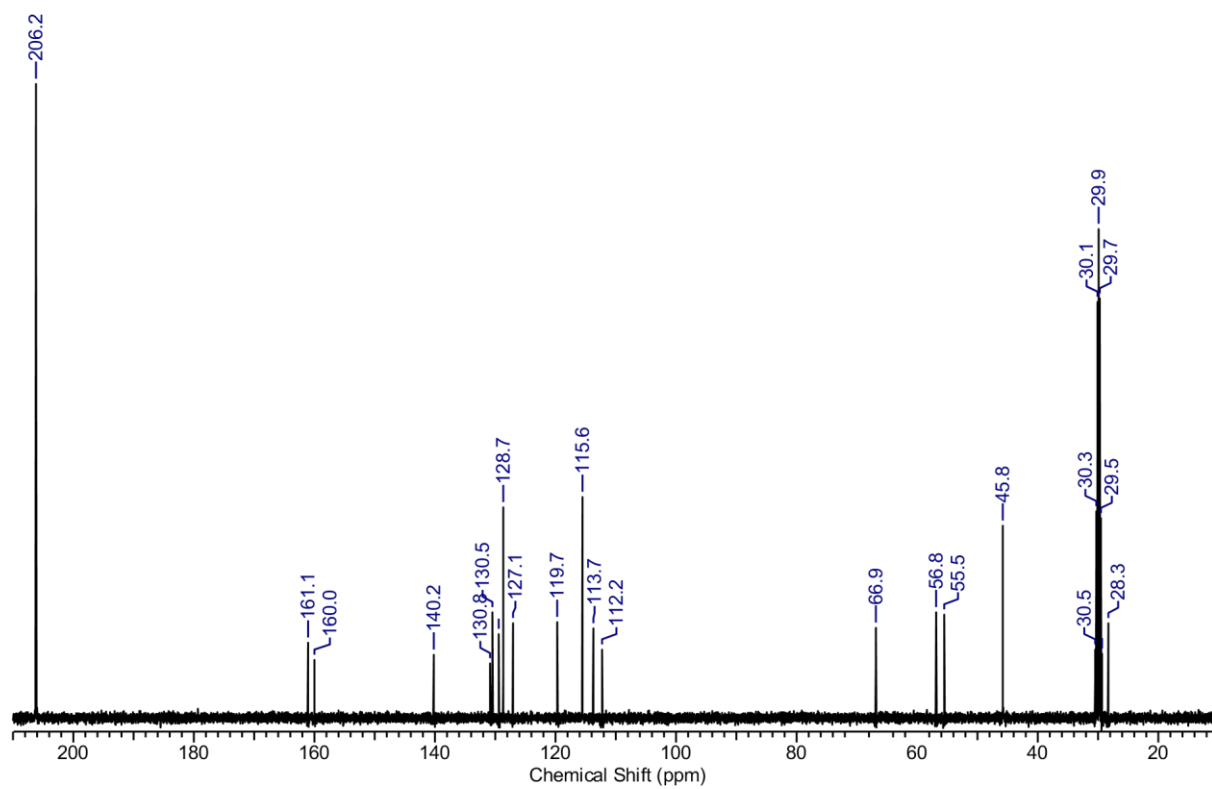
**(E)-3-(4-(4-Methoxystyryl)phenoxy)-N,N-dimethylpropan-1-amine OX03375**



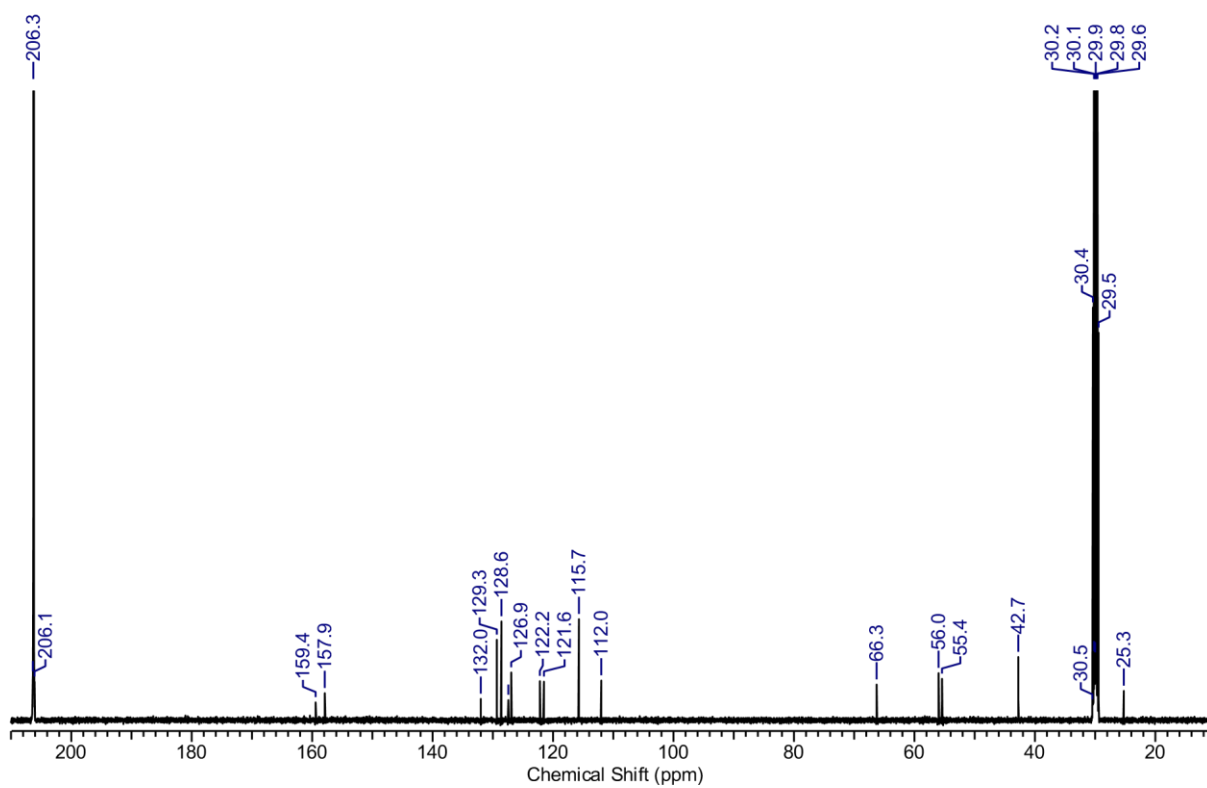
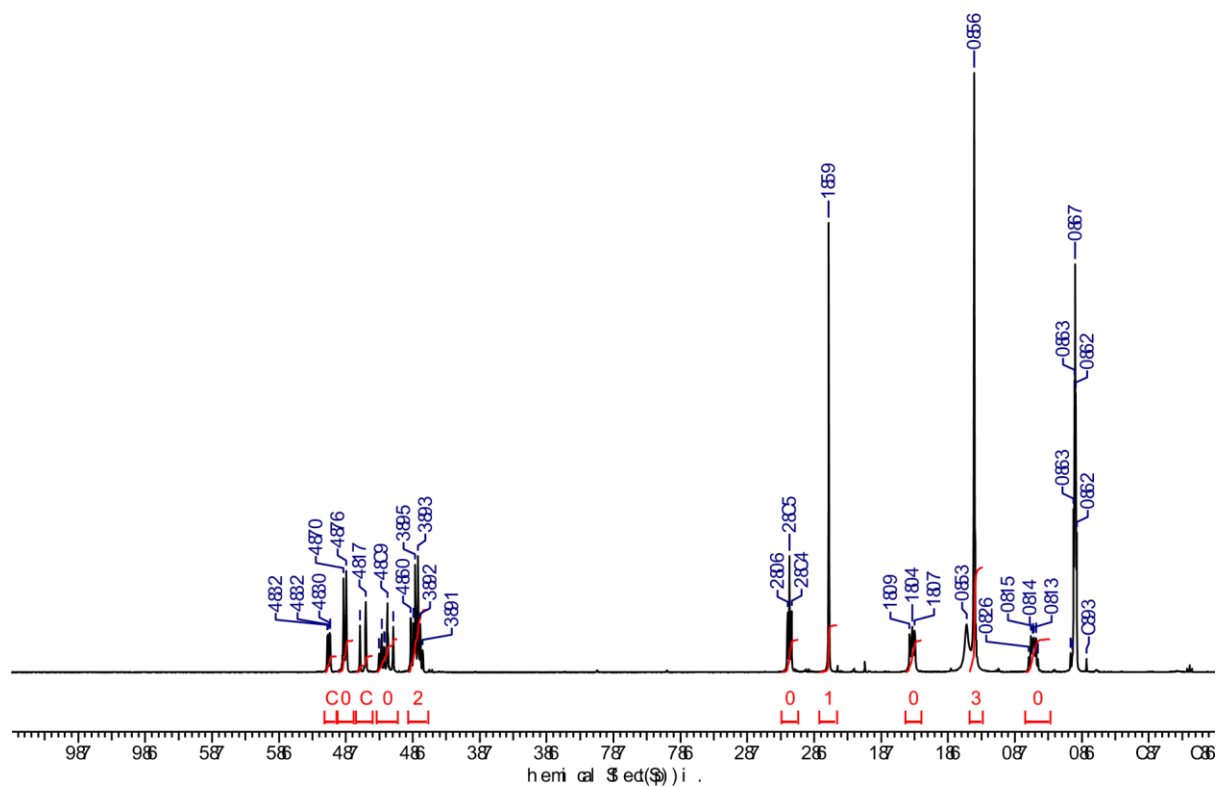
**(*E*)-3-(4-(3-Methoxystyryl)phenoxy)-*N,N*-dimethylpropan-1-amine OX03376**



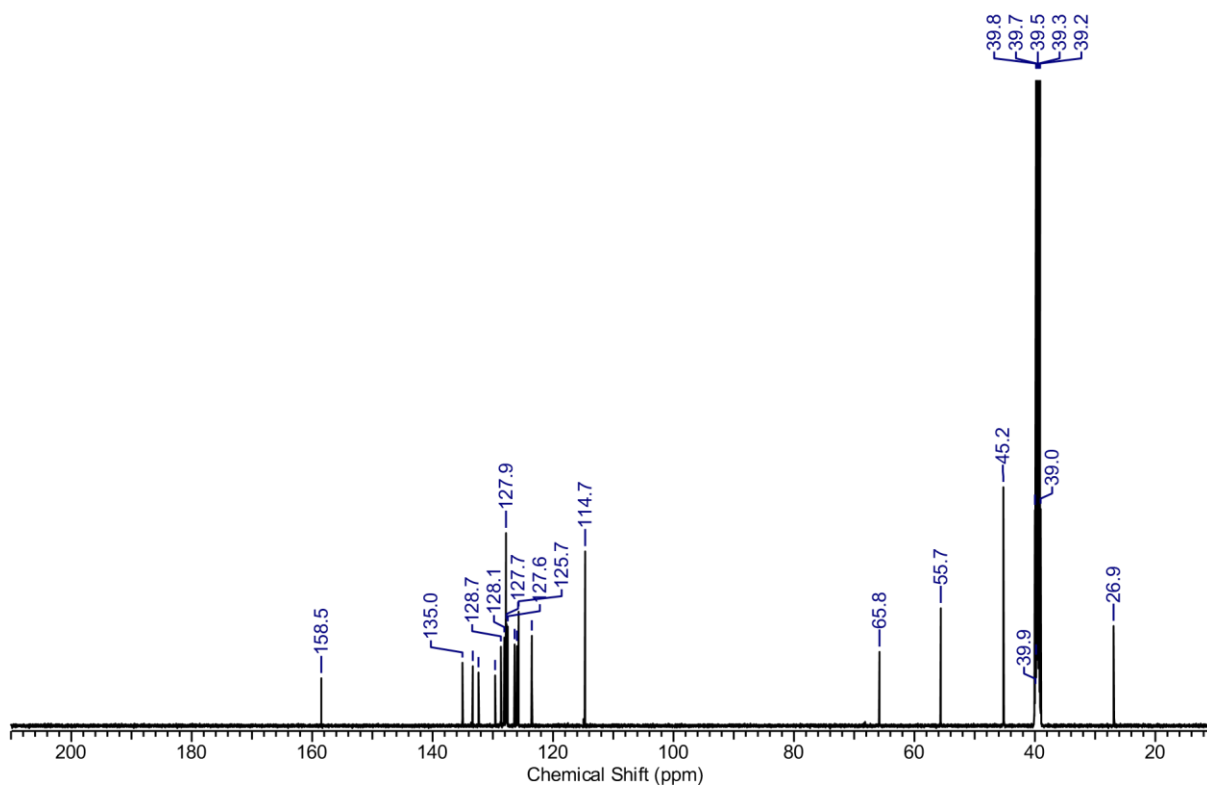
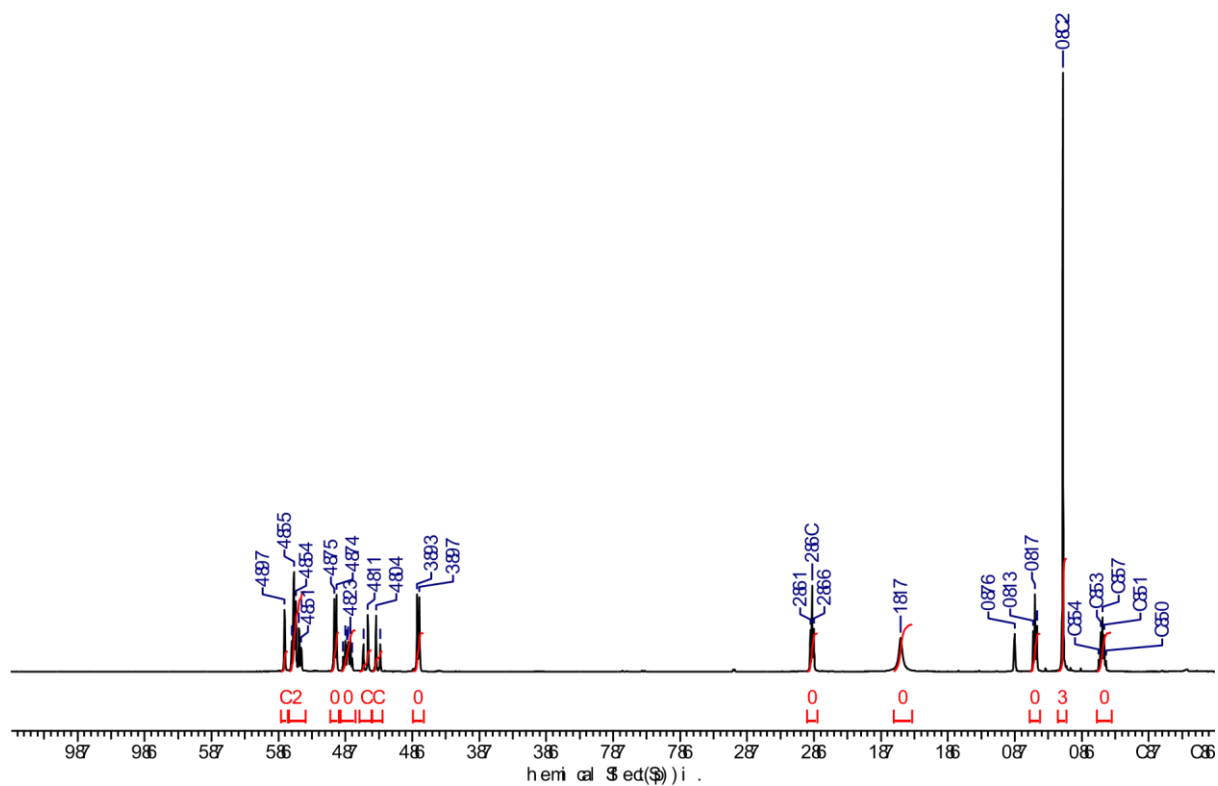




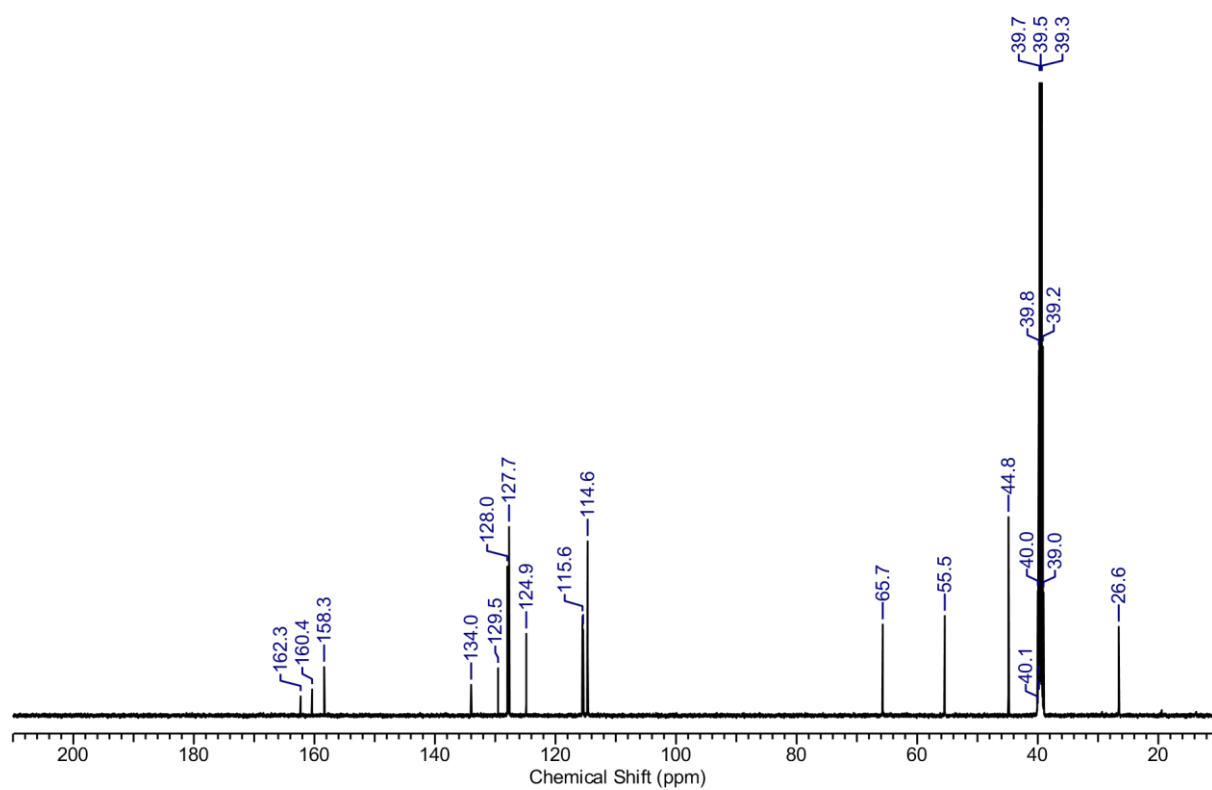
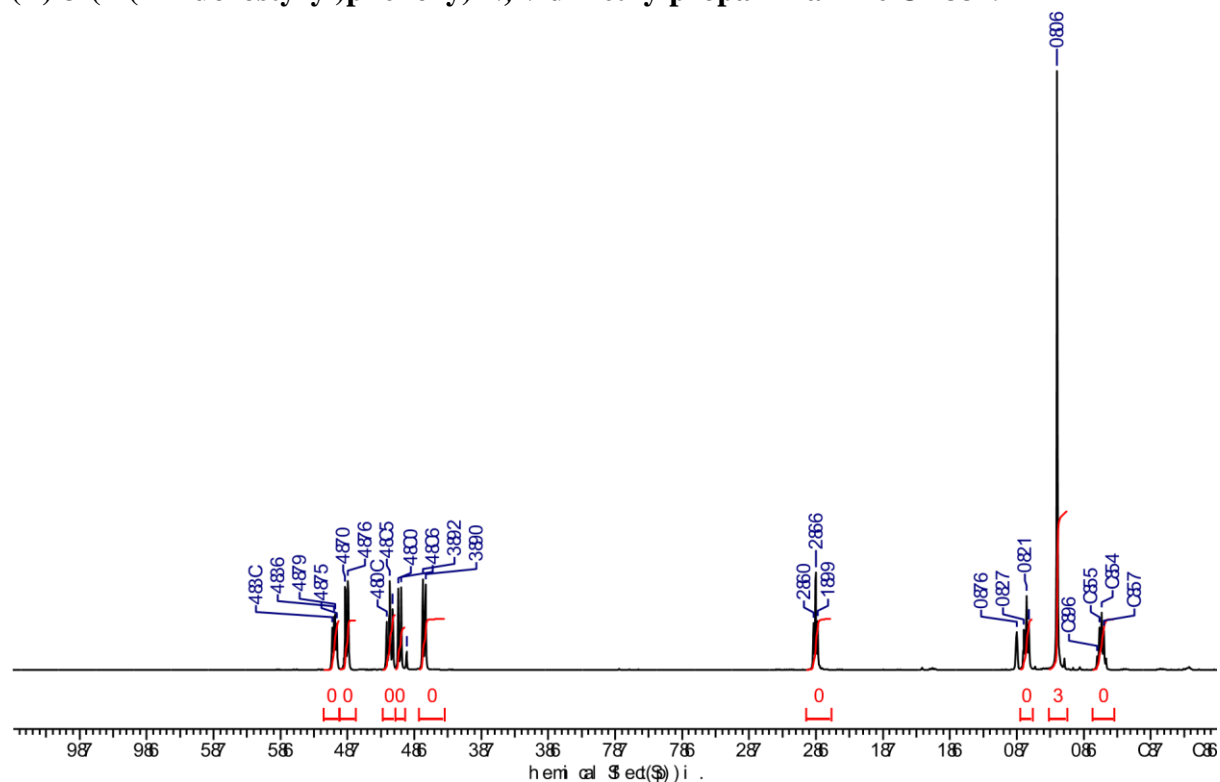
**(E)-3-(4-(2-Methoxystyryl)phenoxy)-N,N-dimethylpropan-1-amine OX03377**



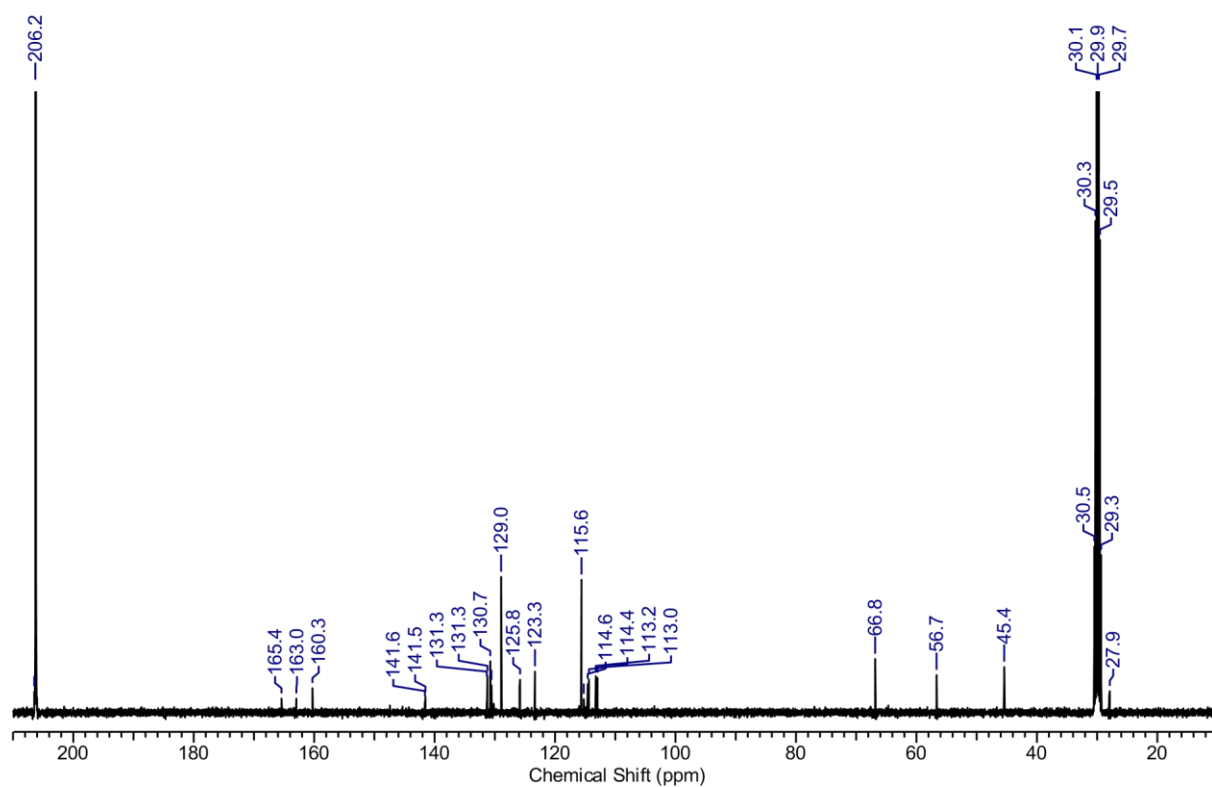
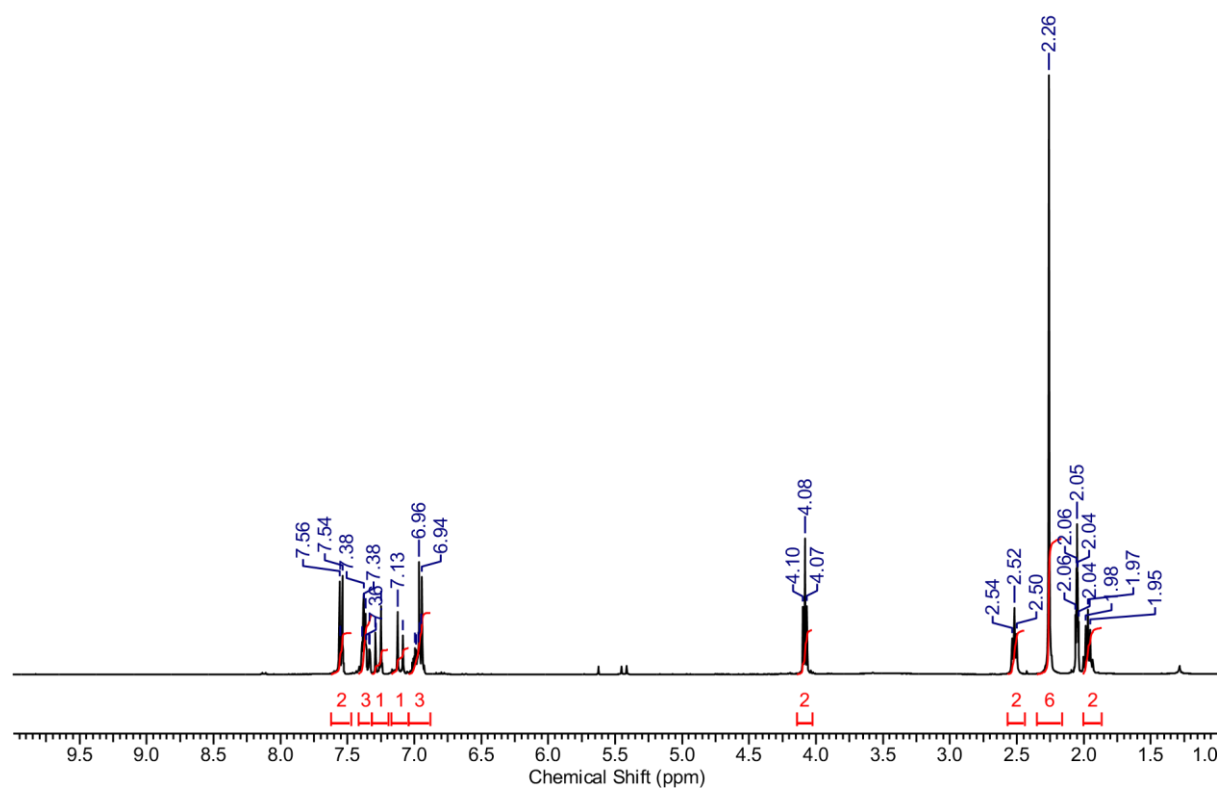
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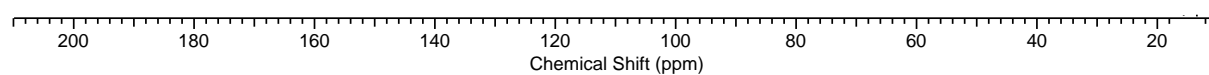
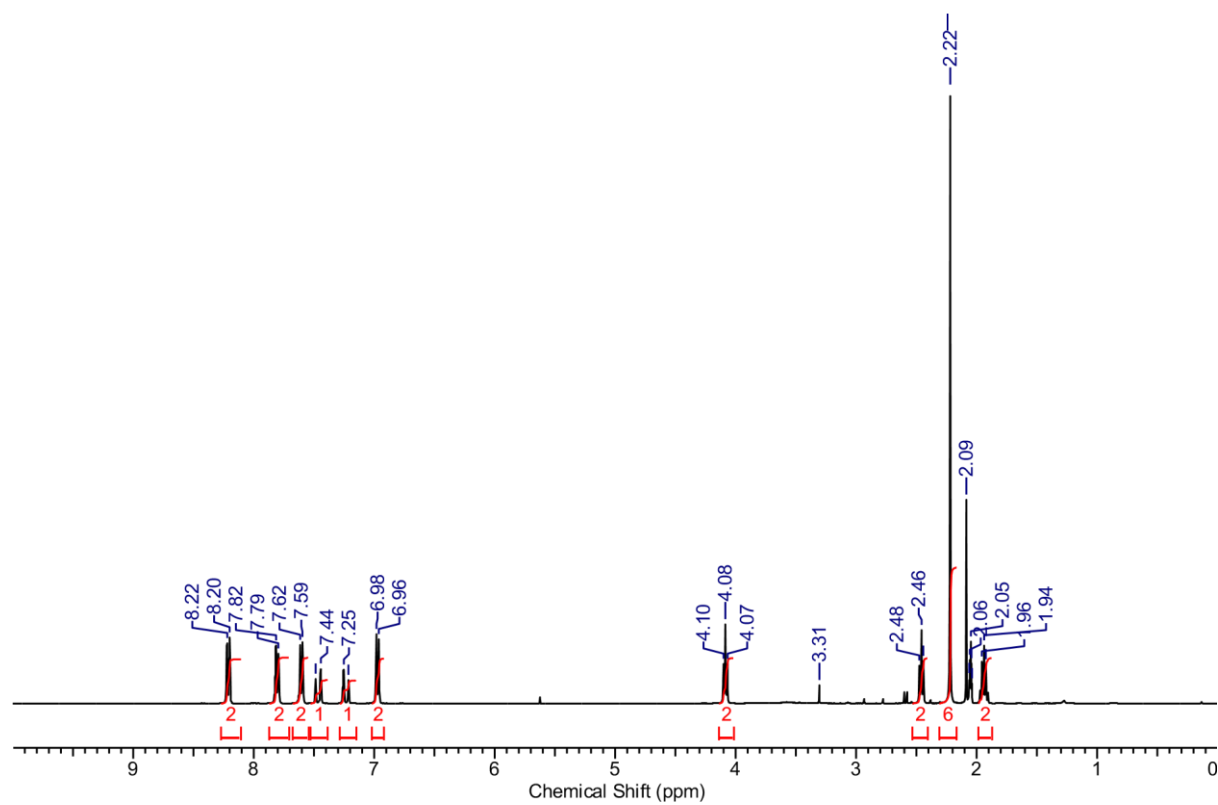
**(*E*)-3-(4-(4-Fluorostyryl)phenoxy)-*N,N*-dimethylpropan-1-amine OX3379**

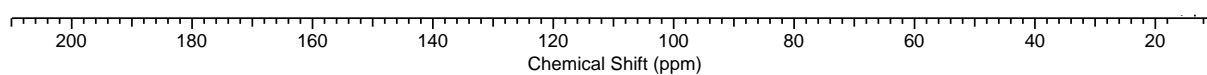


**(*E*)-3-(4-(3-Fluorostyryl)phenoxy)-*N,N*-dimethylpropan-1-amine OX03380**



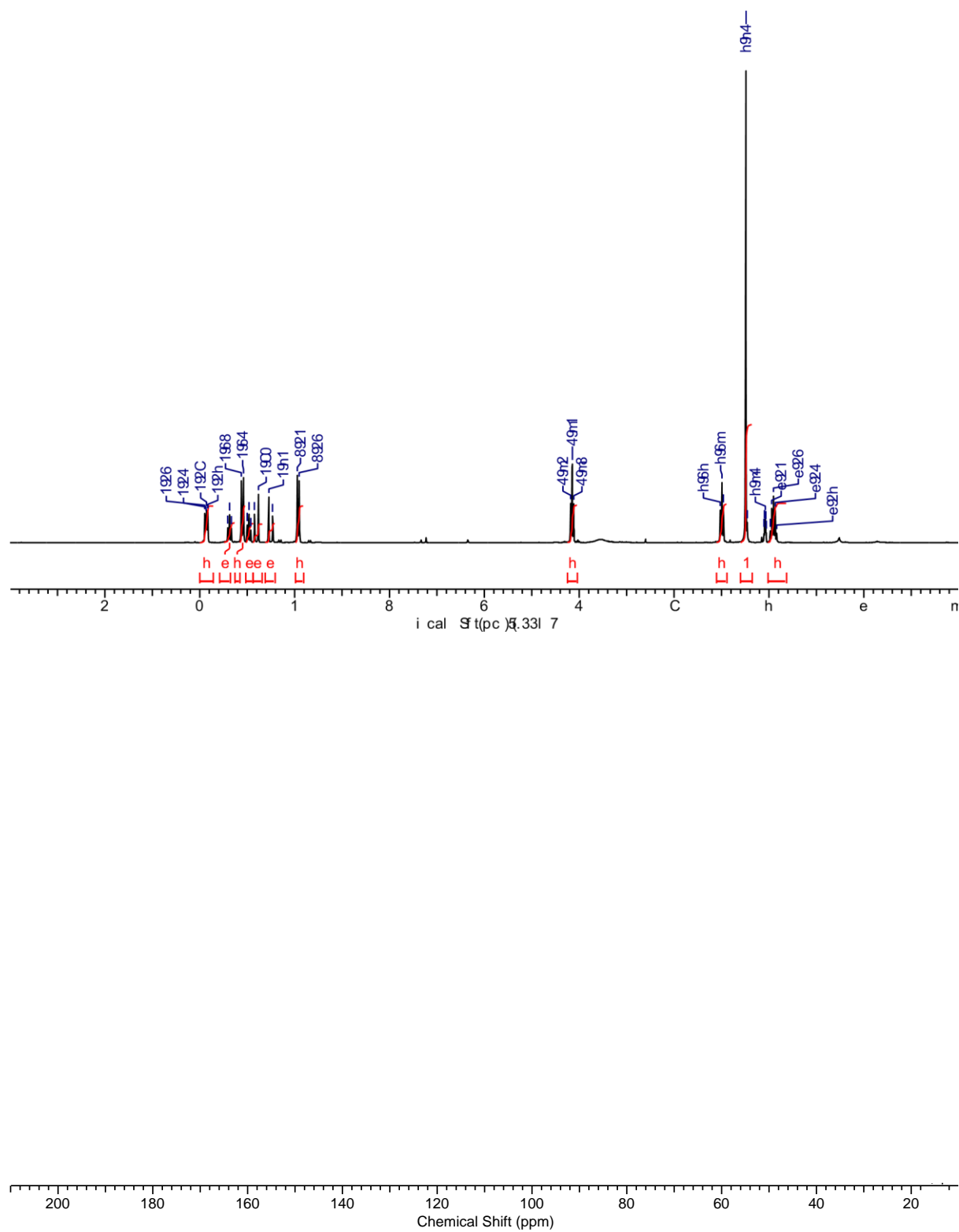


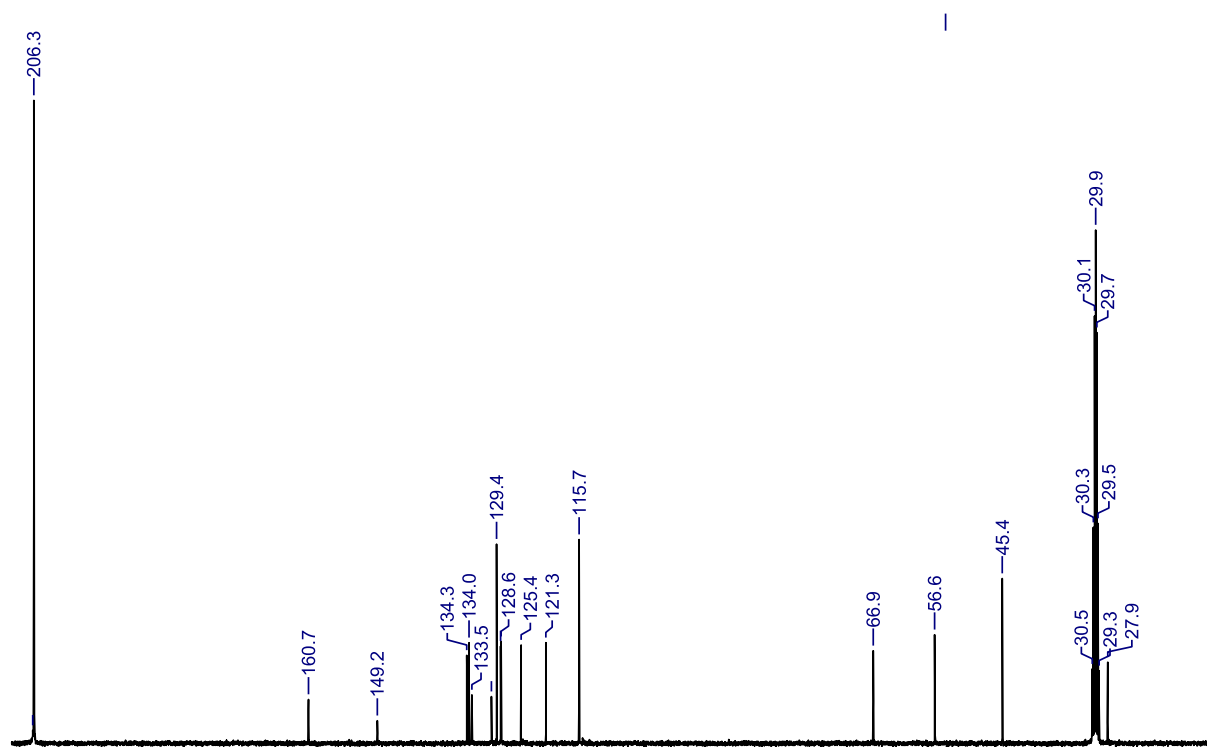
**(E)-N,N-Dimethyl-3-(4-(4-nitrostyryl)phenoxy)propan-1-amine OX03381**



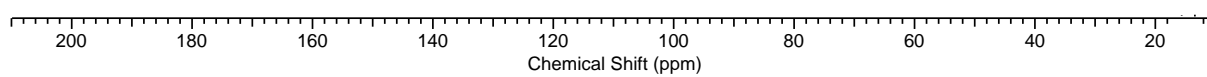


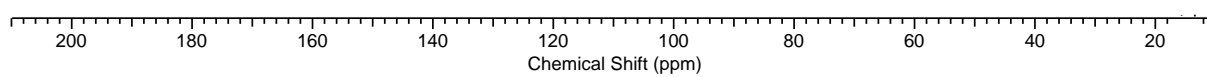
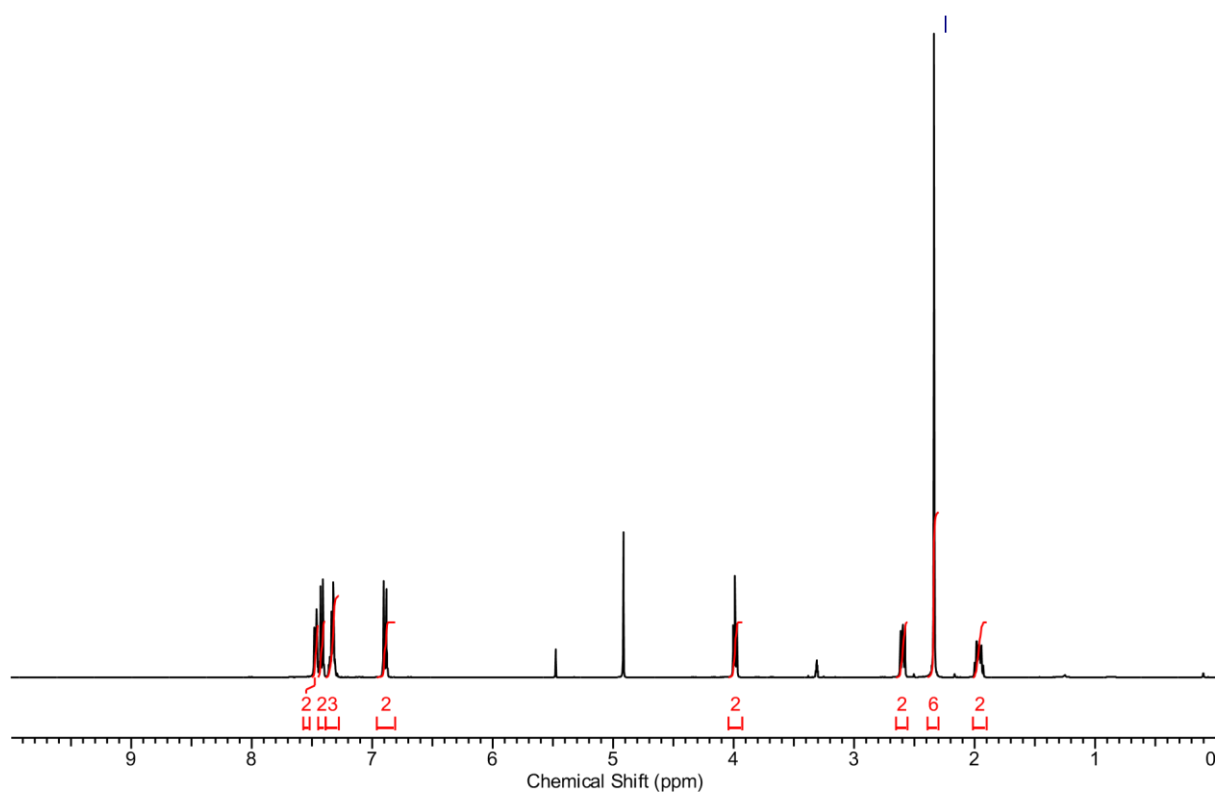
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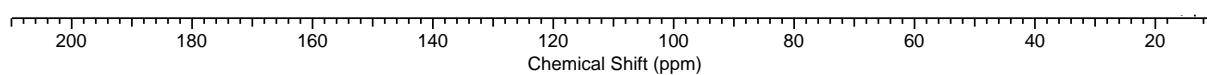
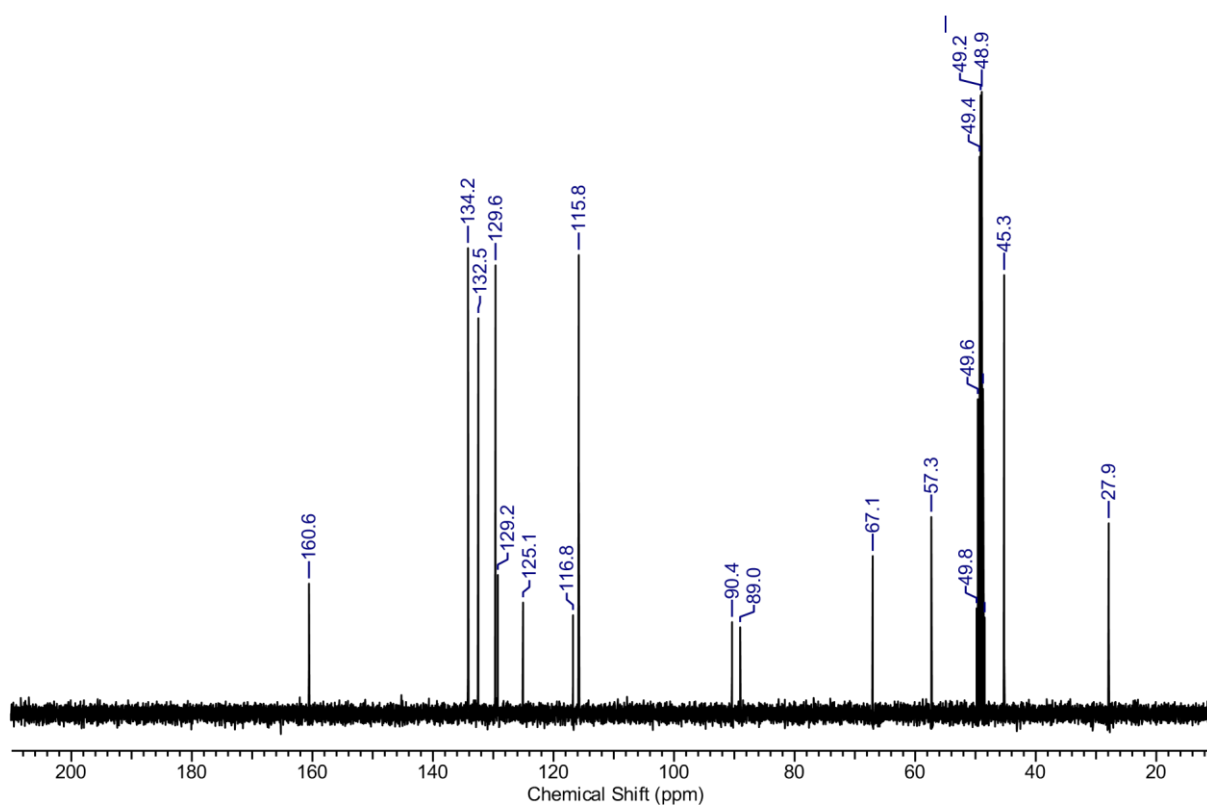


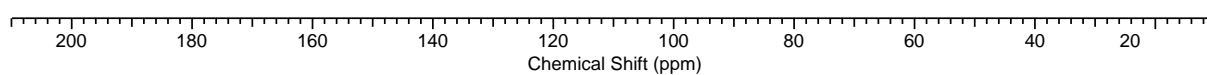
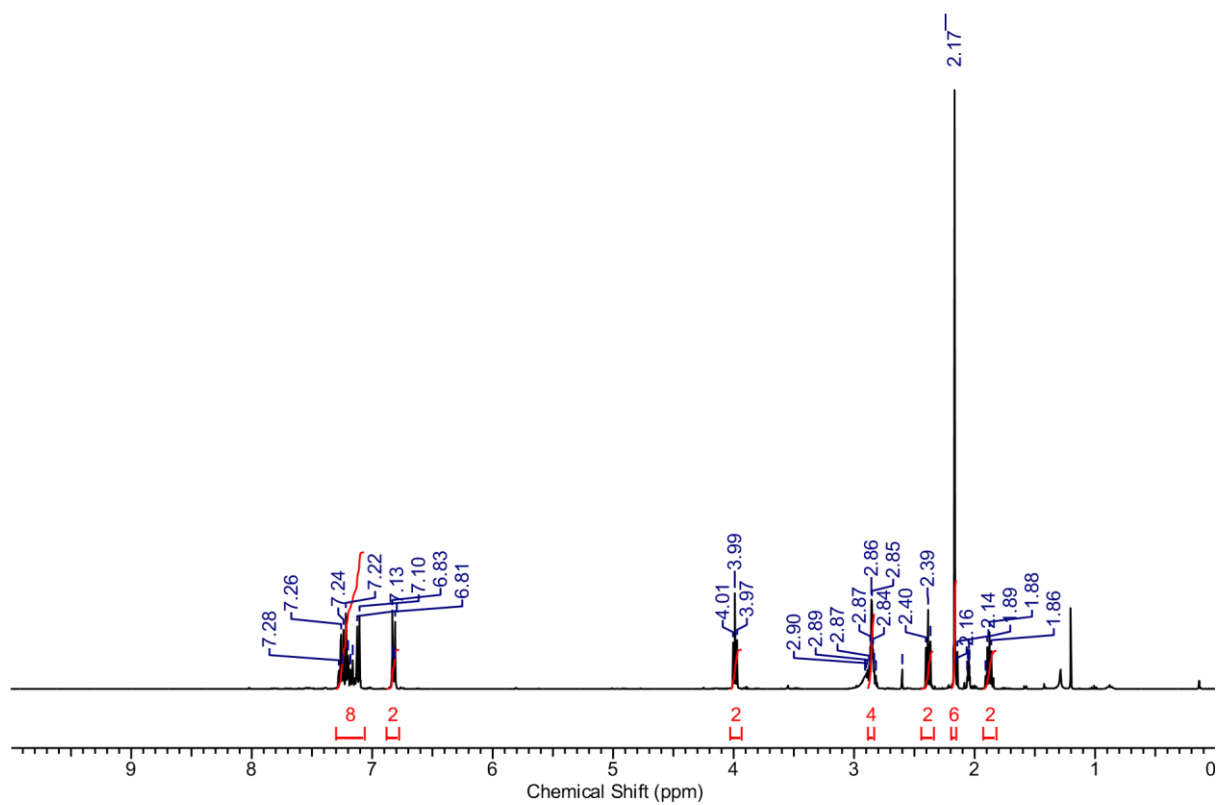


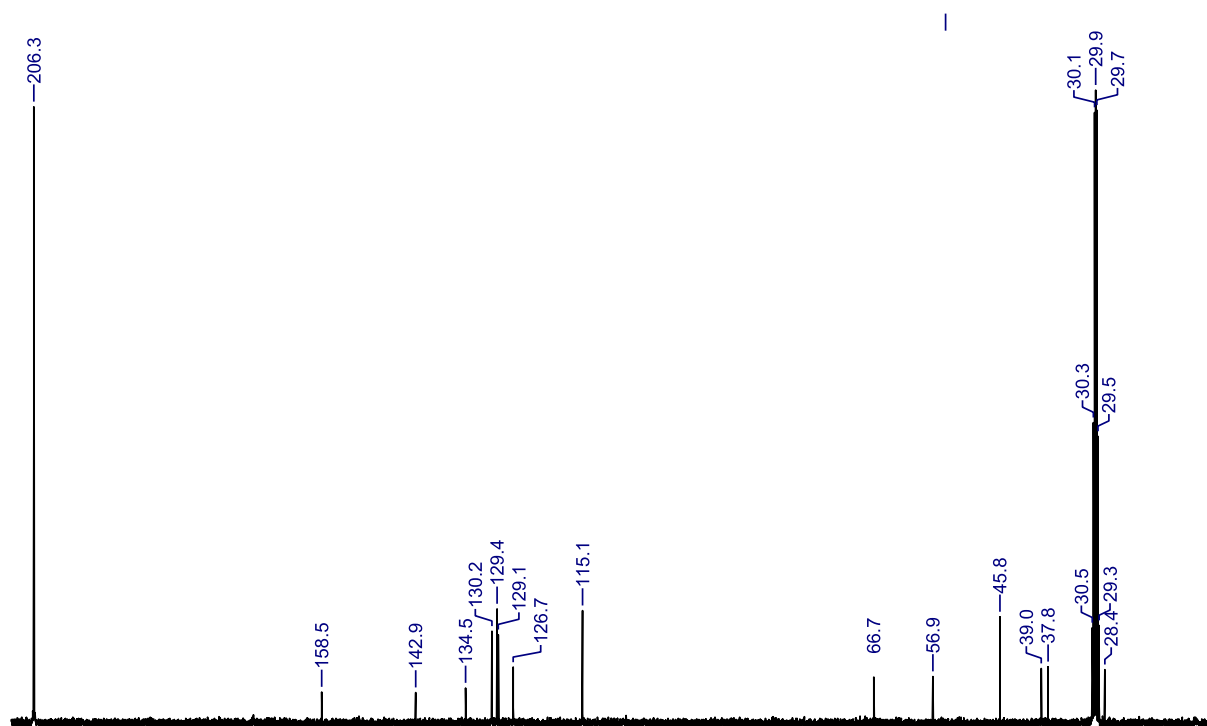
***N,N*-Dimethyl-3-(4-(phenylethynyl)phenoxy)propan-1-amine OX03383**



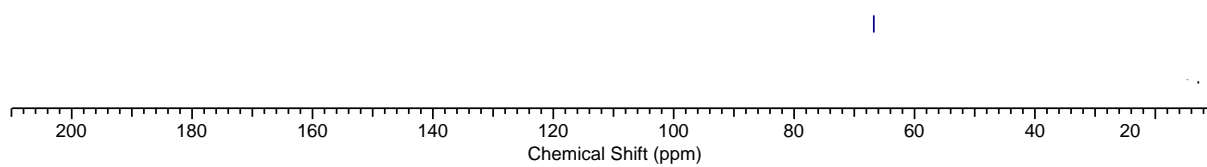


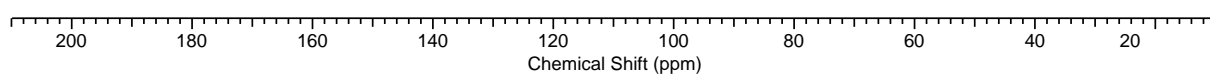
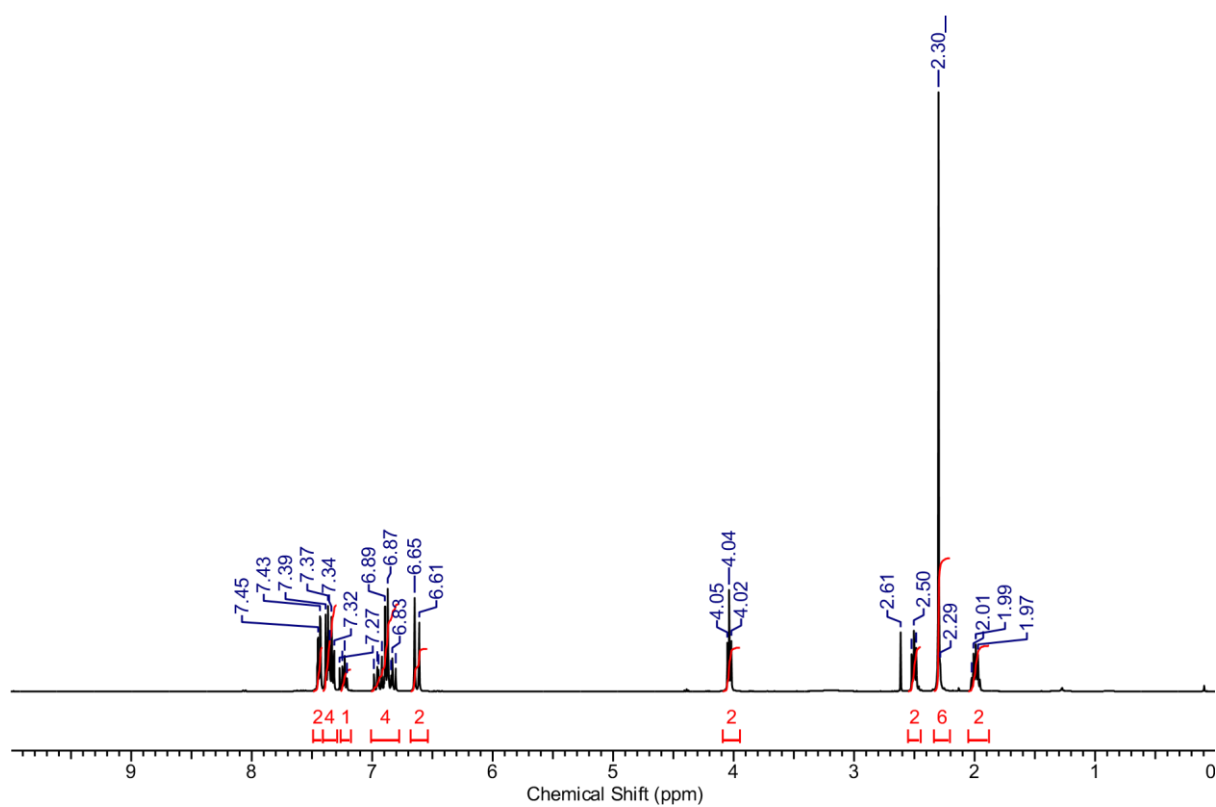


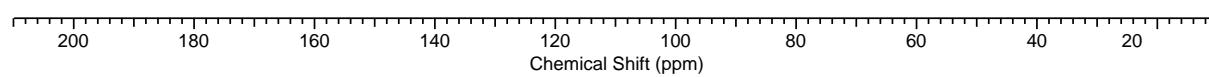
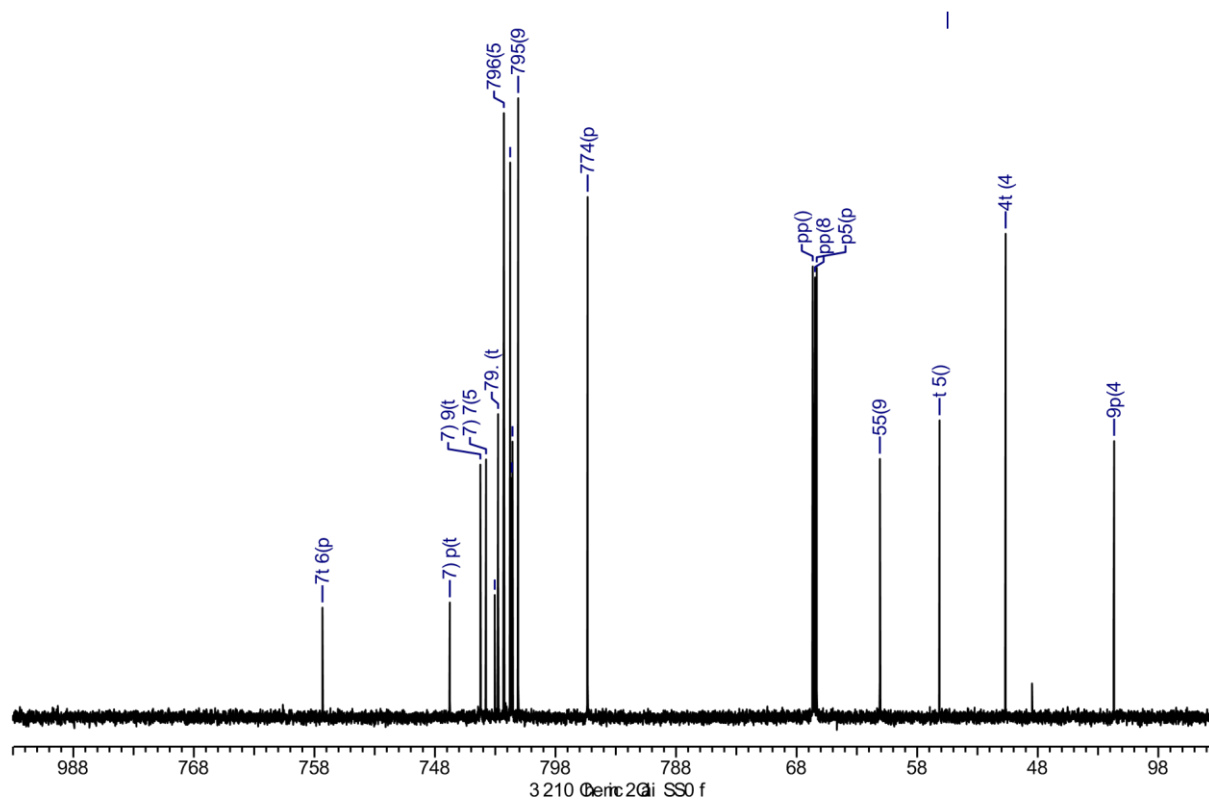
***N,N*-Dimethyl-3-(4-phenethylphenoxy)propan-1-amine OX03384**



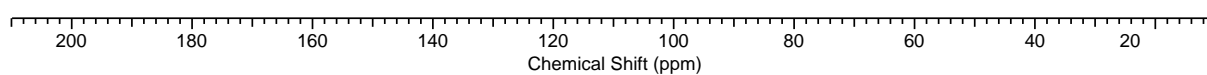
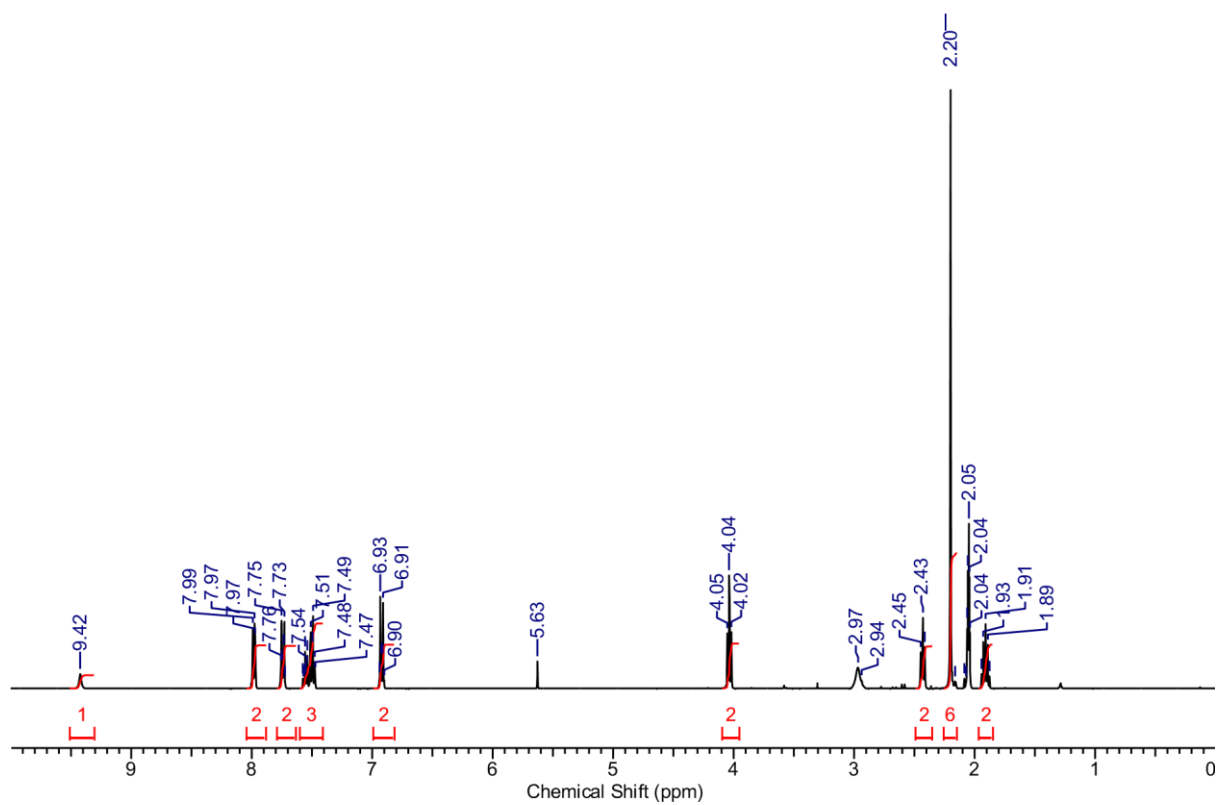
***N,N*-Ddimethyl-3-(4-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)phenoxy)propan-1-amine  
OX03385**

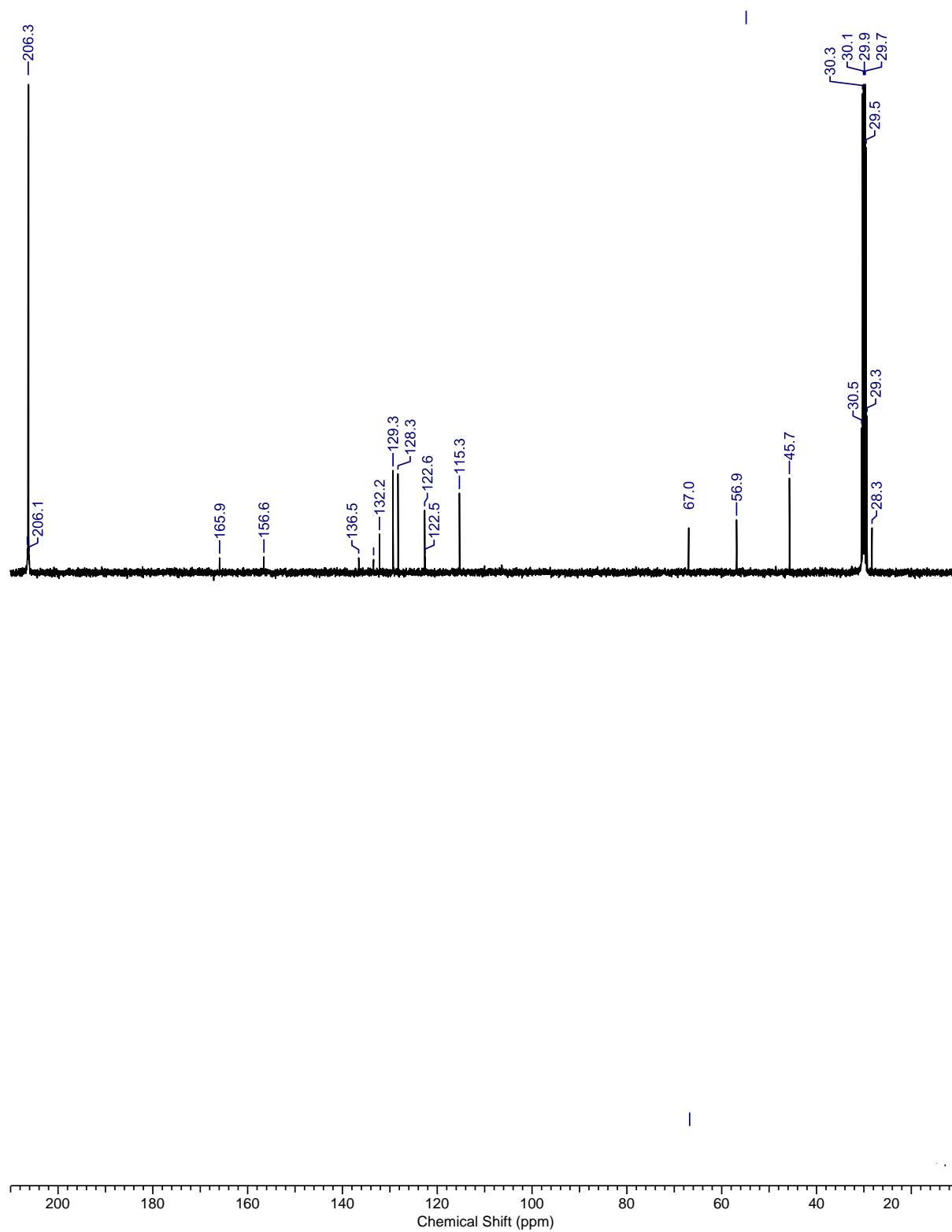


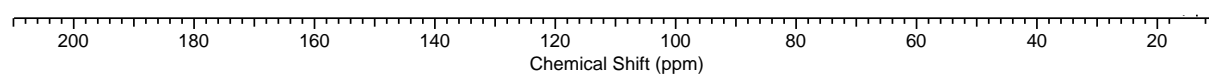
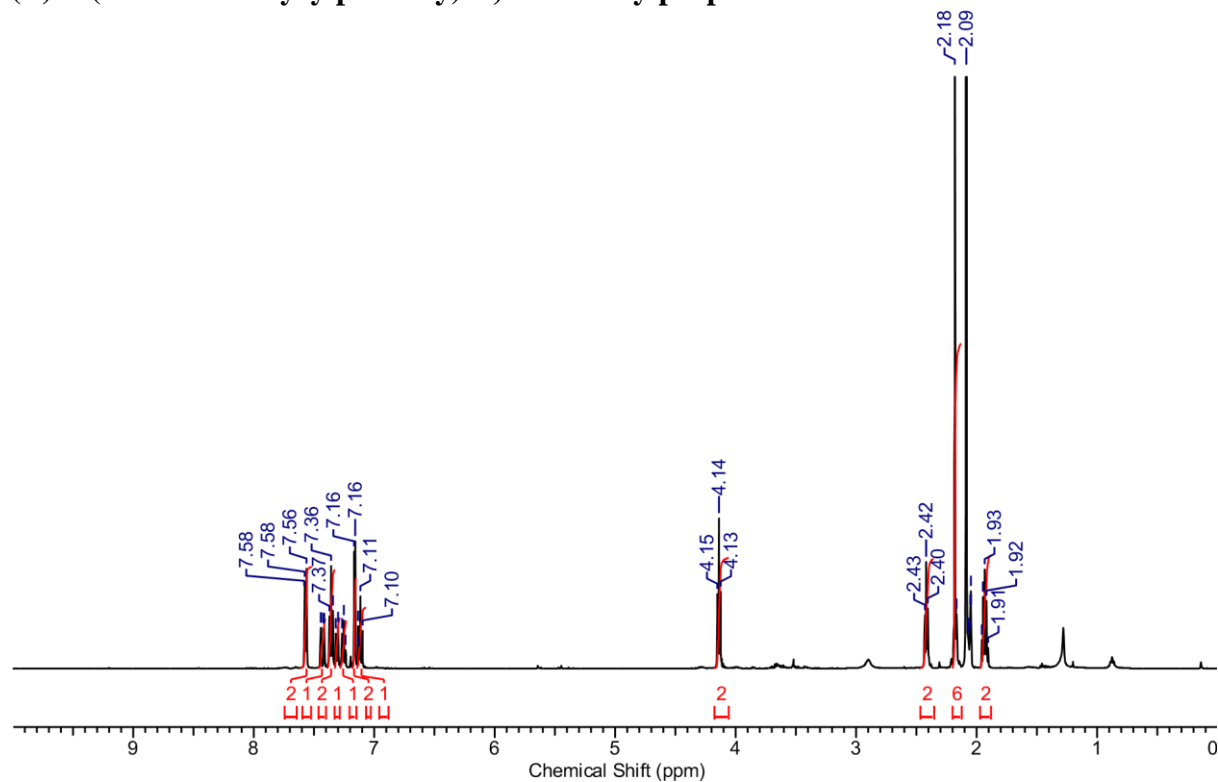


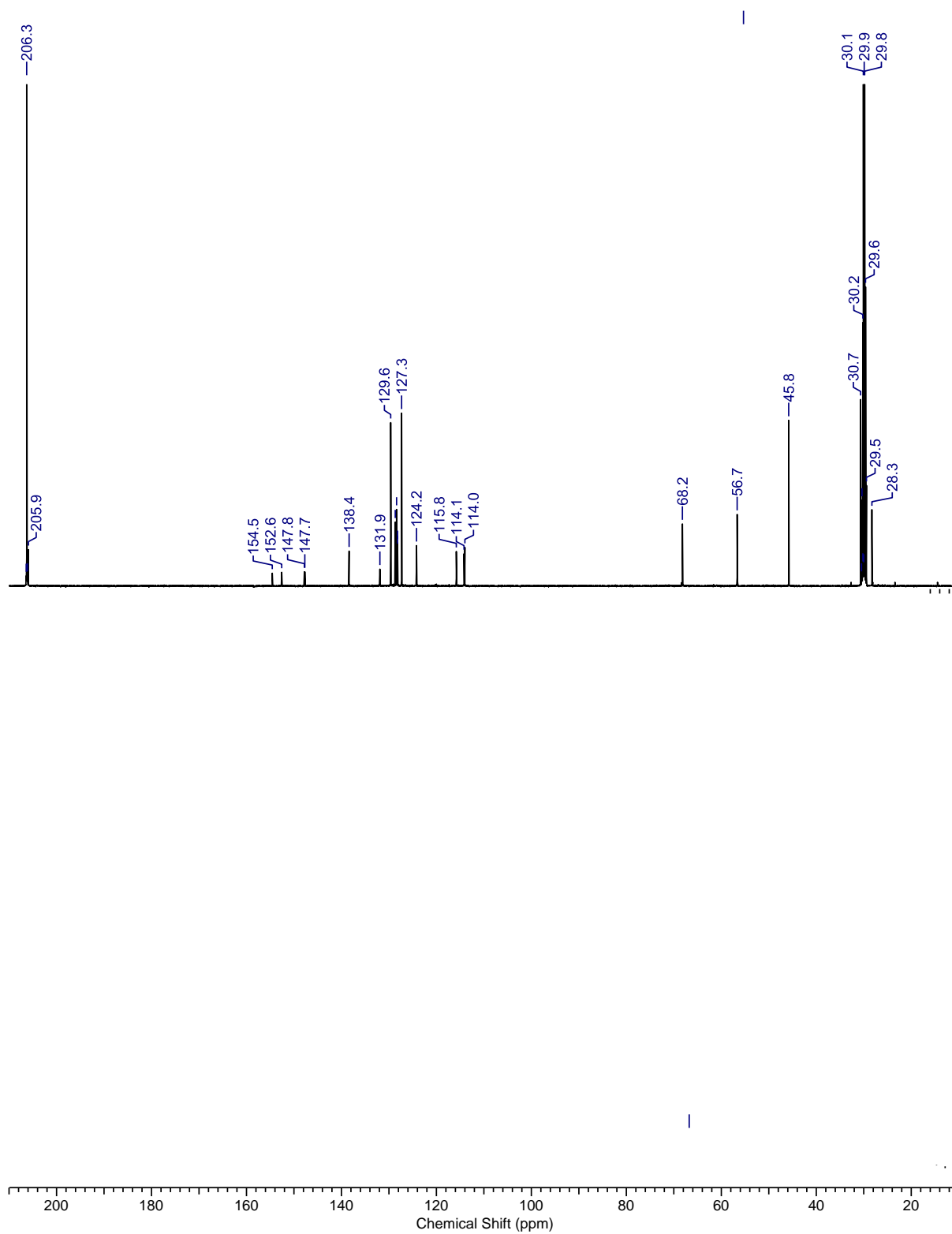


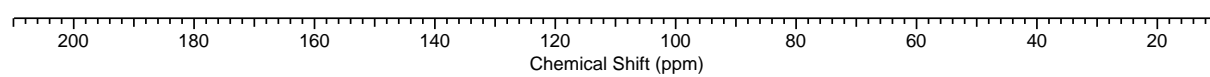
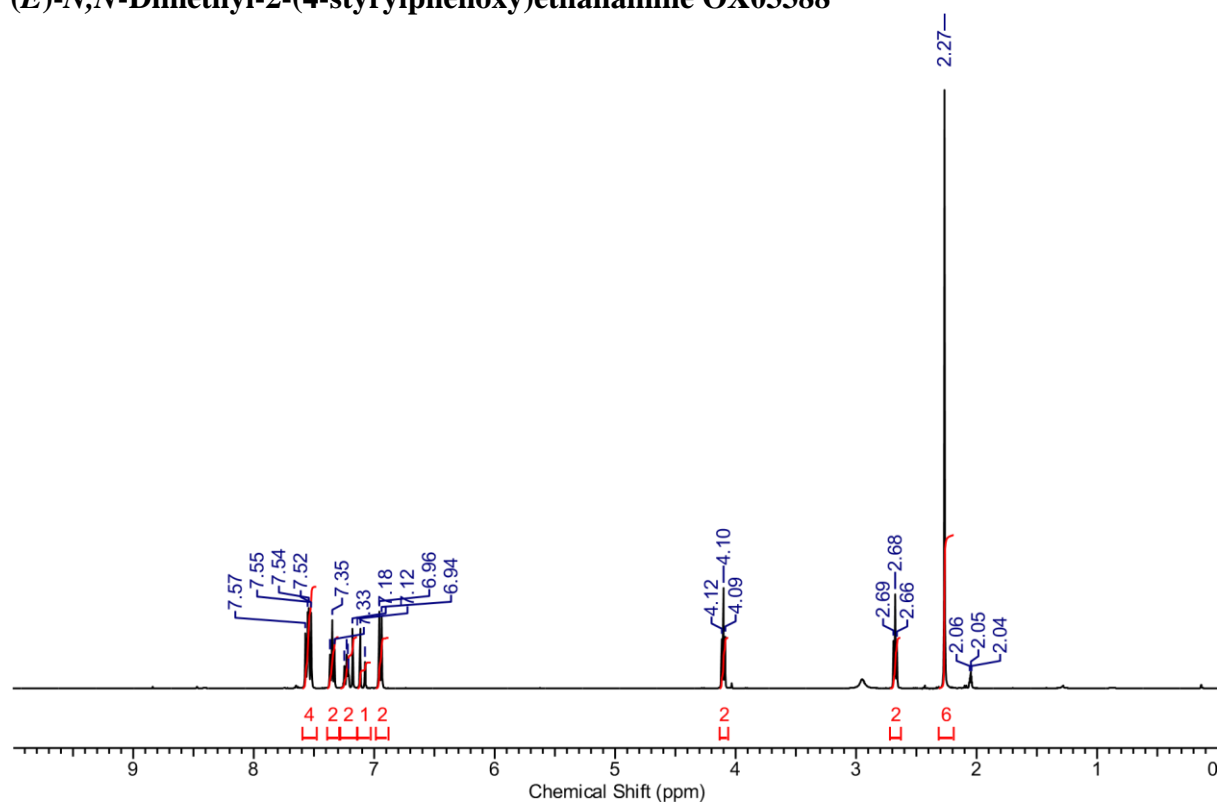


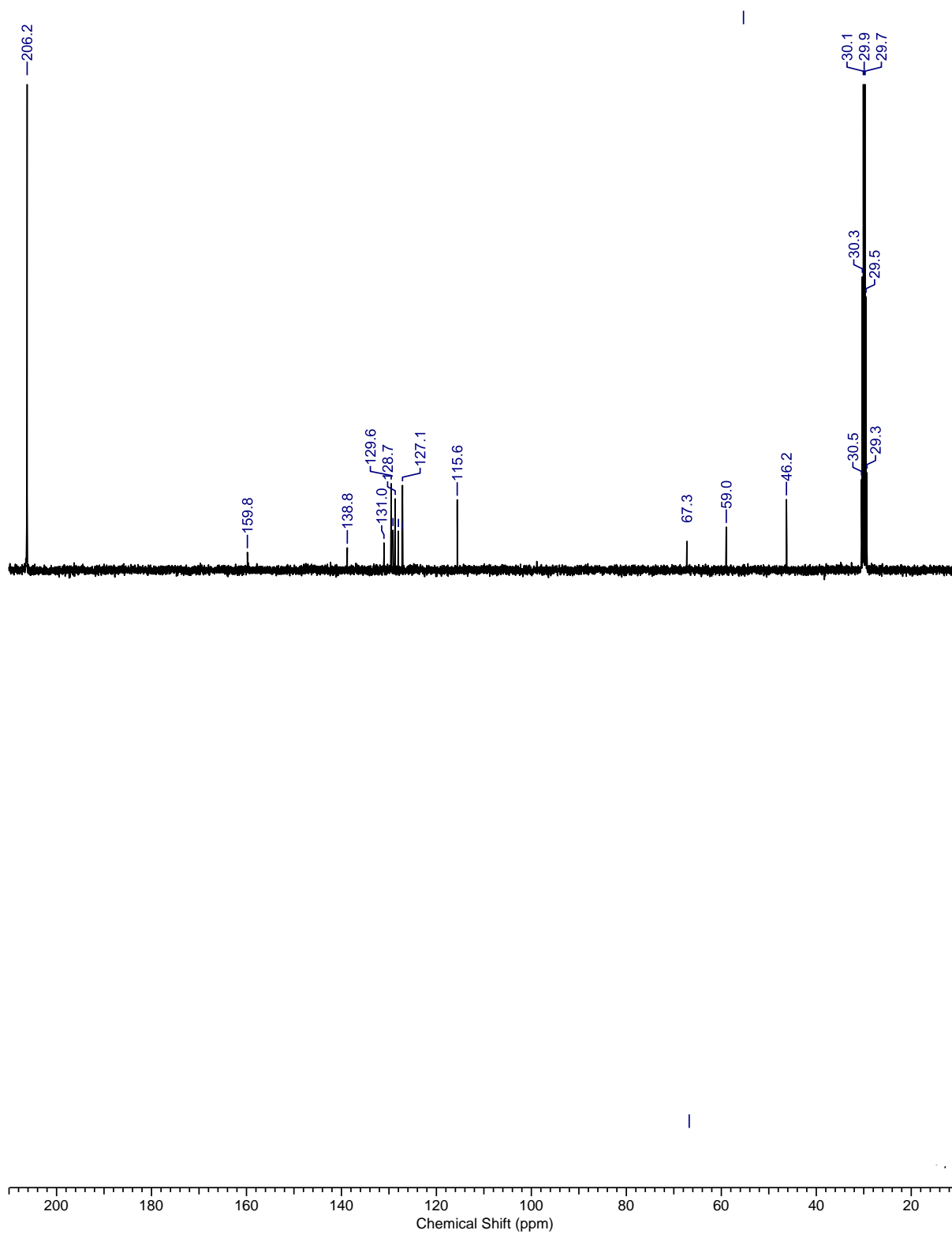
***N*-(4-(3-(Dimethylamino)propoxy)phenyl)benzamide OX03386**

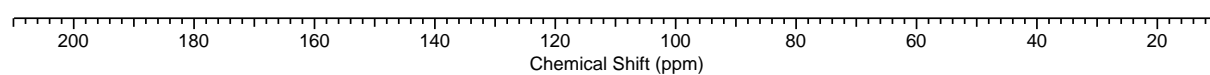
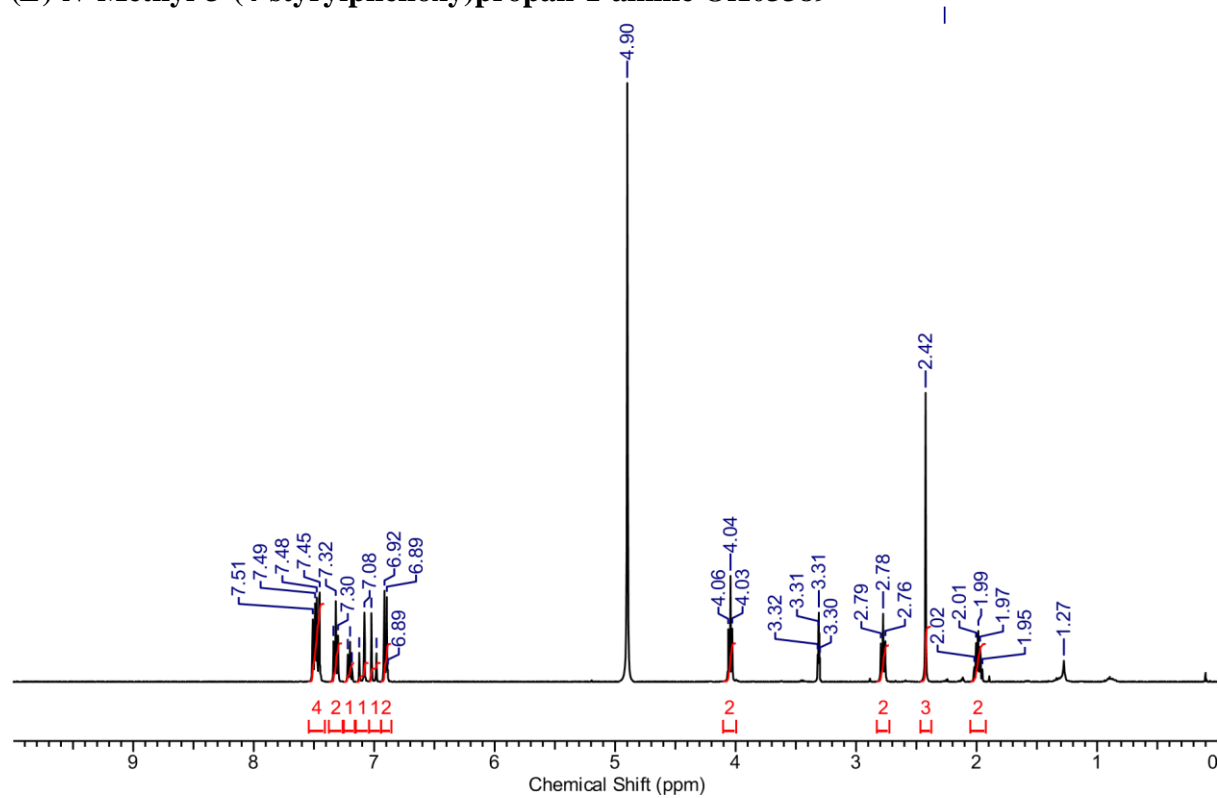


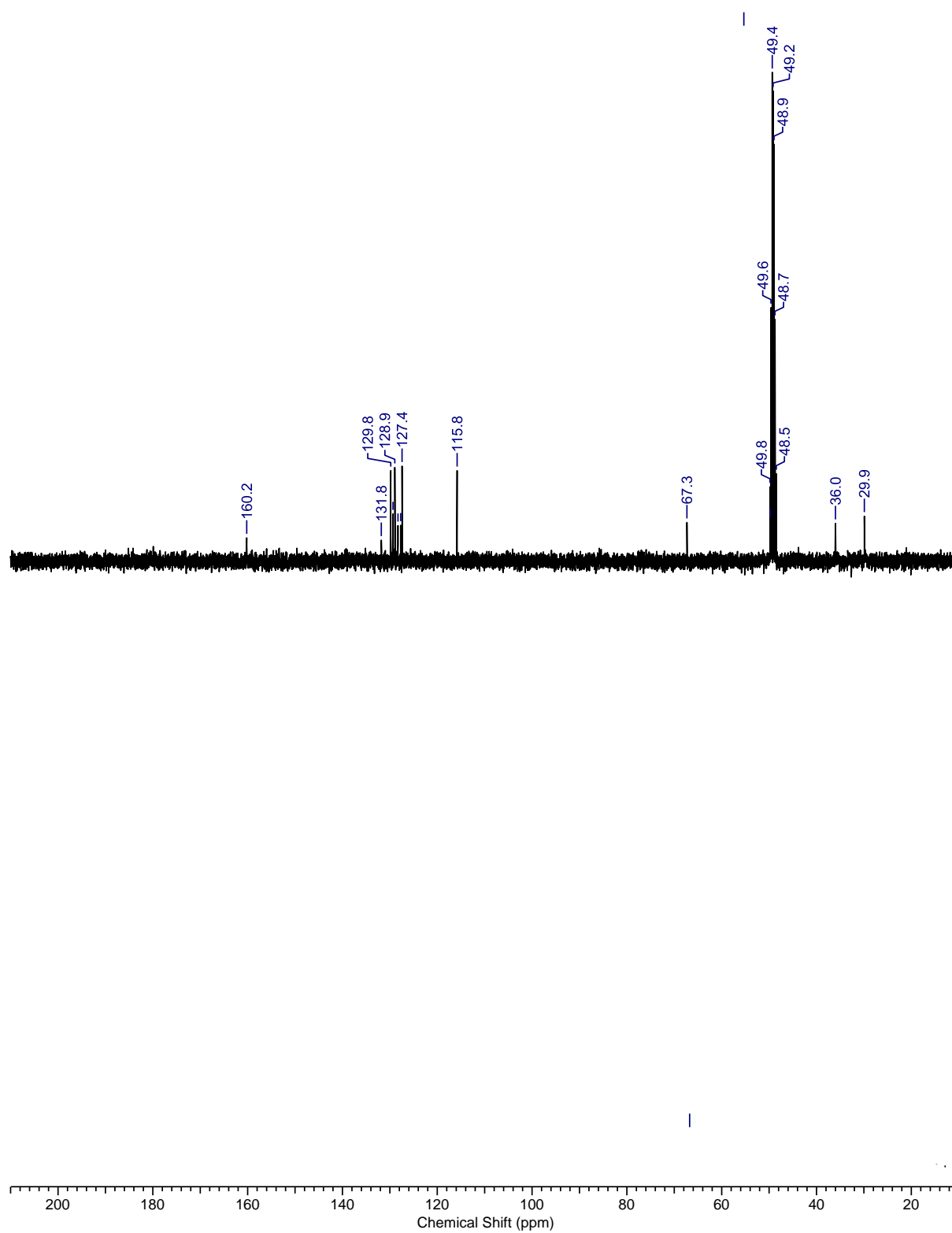
**(E)-3-(2-Fluoro-4-styrylphenoxy)-N,N-dimethylpropan-1-amine OX03387**



**(E)-N,N-Dimethyl-2-(4-styrylphenoxy)ethanamine OX03388**

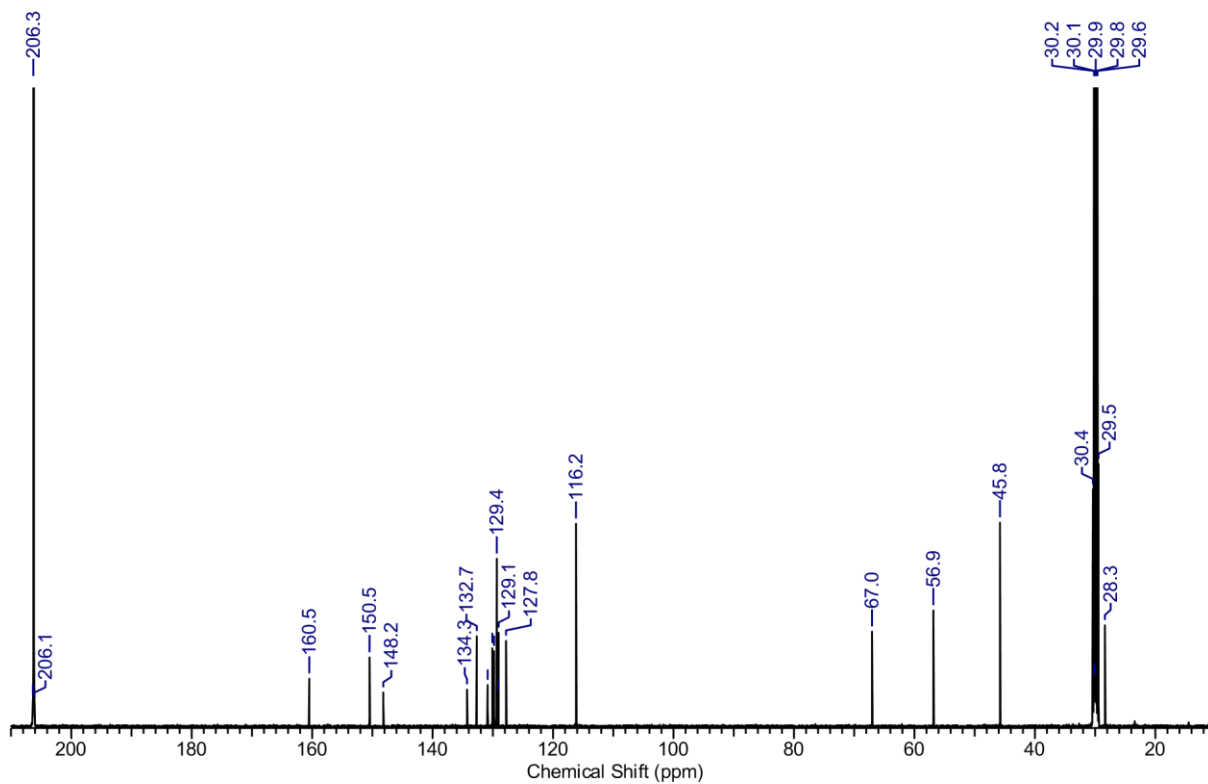
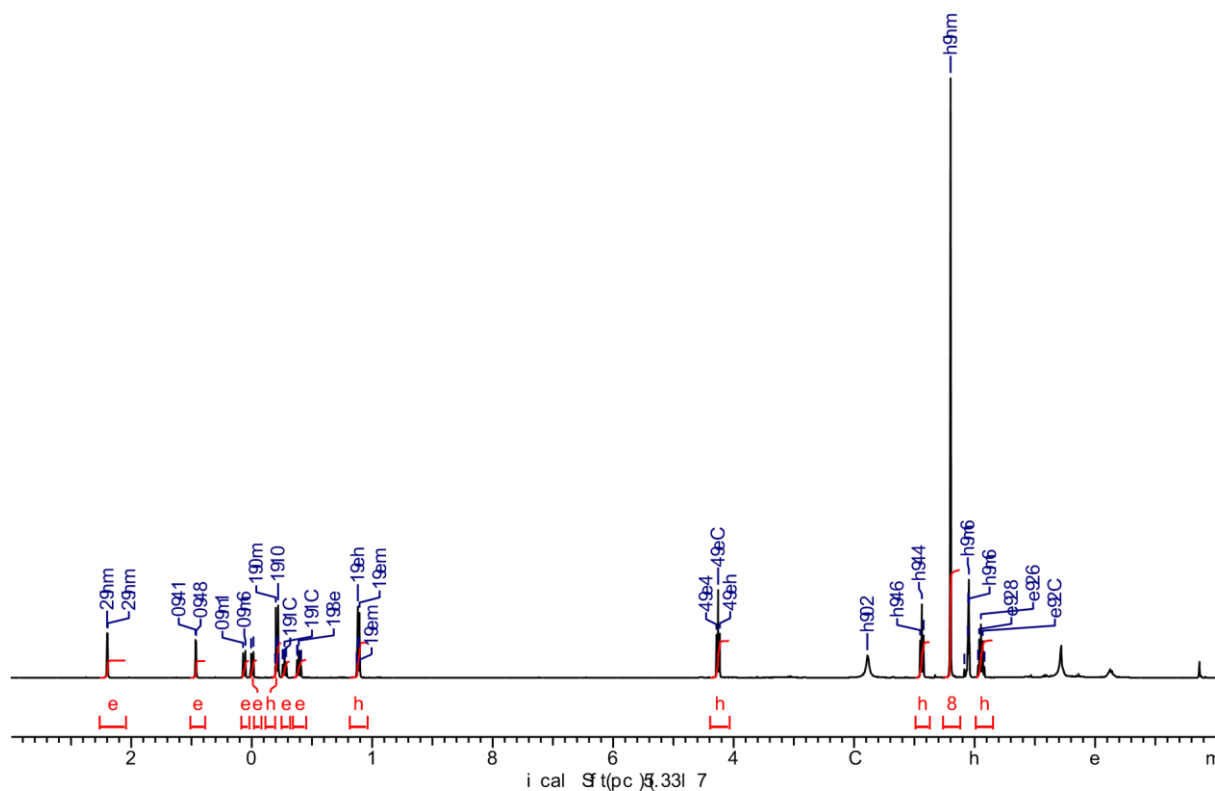


**(*E*)-*N*-Methyl-3-(4-styrylphenoxy)propan-1-amine OX03389**

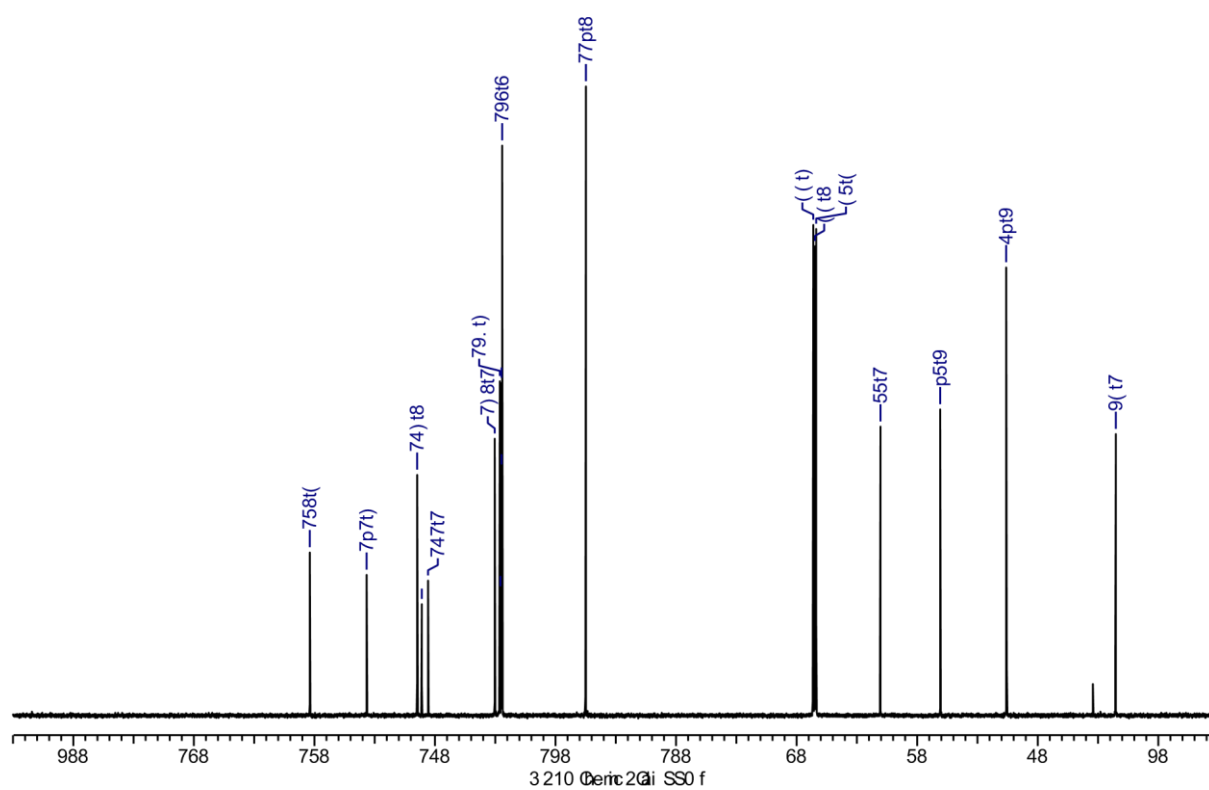


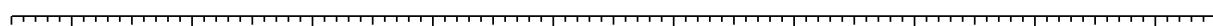
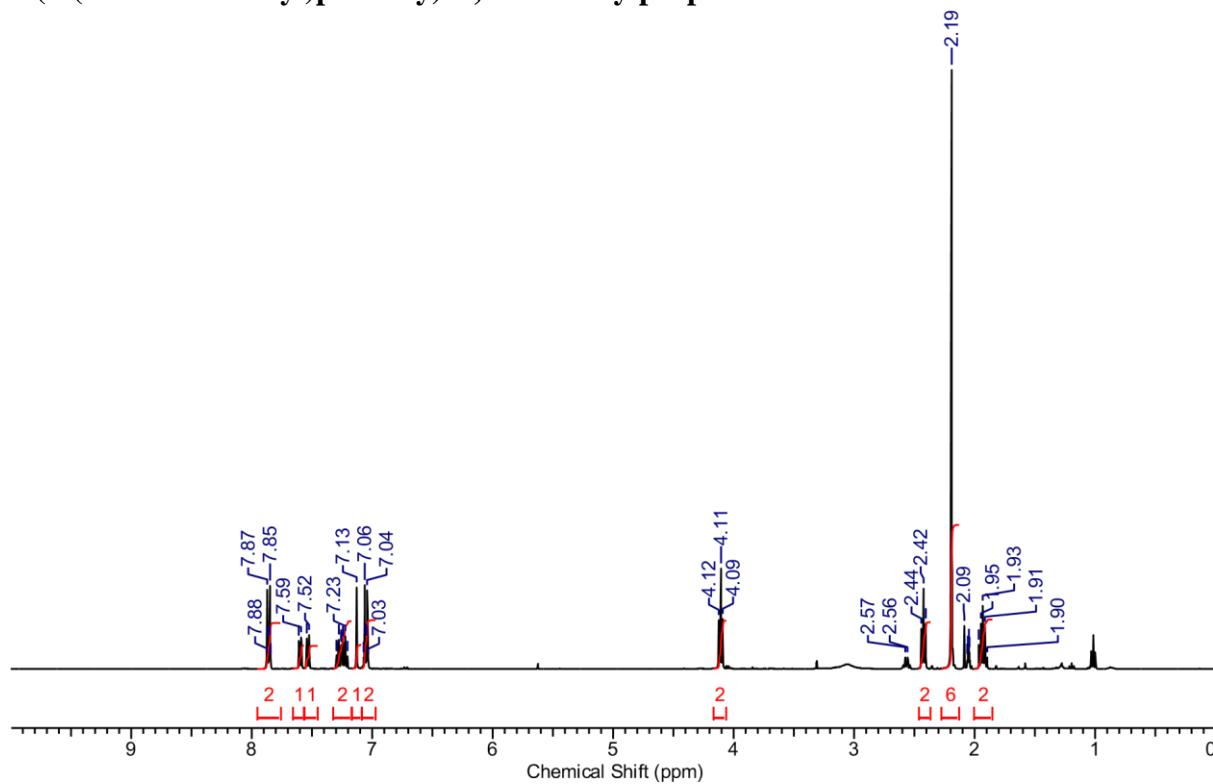


***N,N*-Dimethyl-3-(4-(quinolin-3-yl)phenoxy)propan-1-amine OX03390**

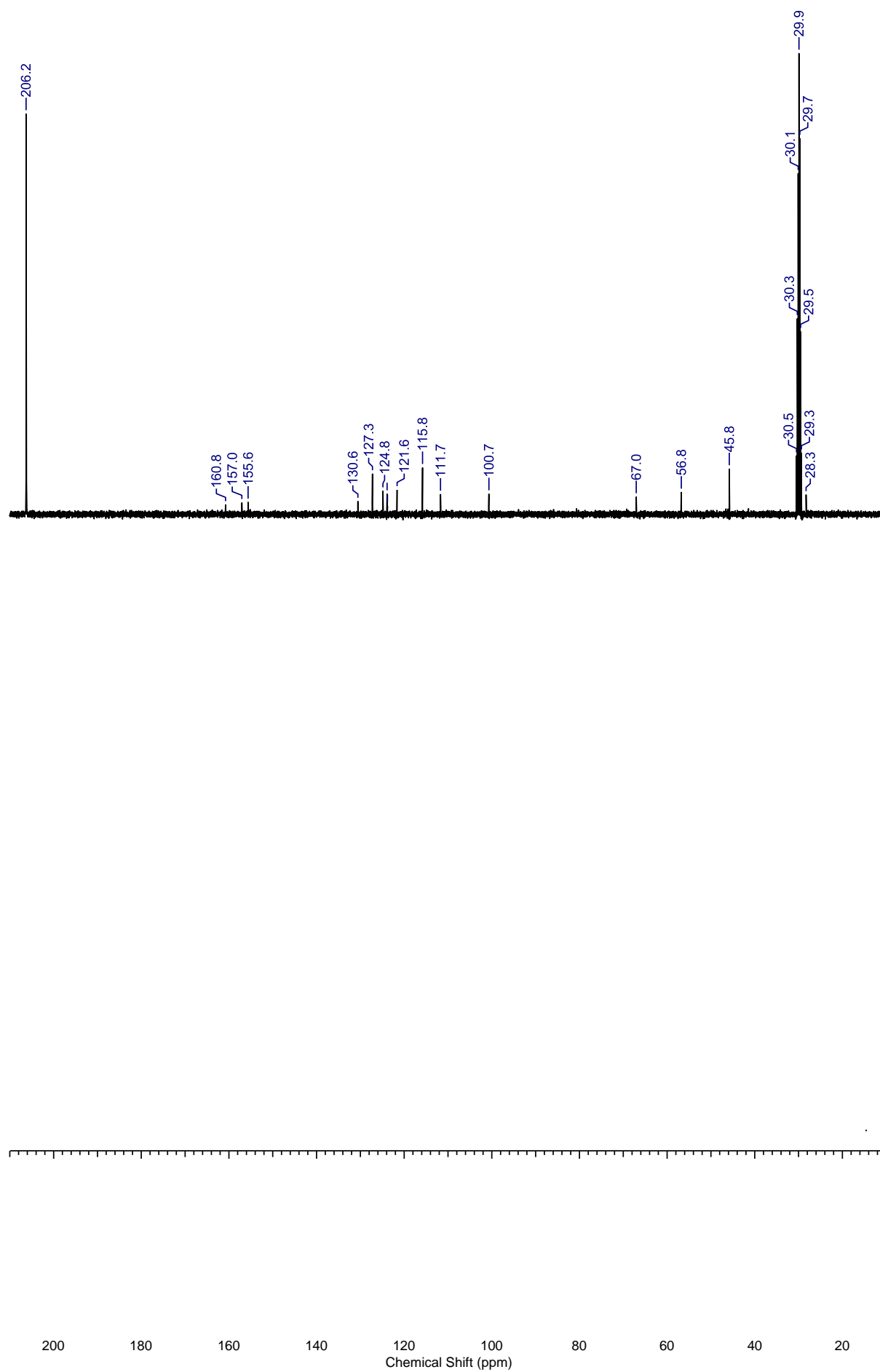


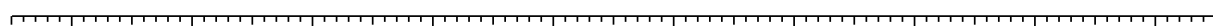
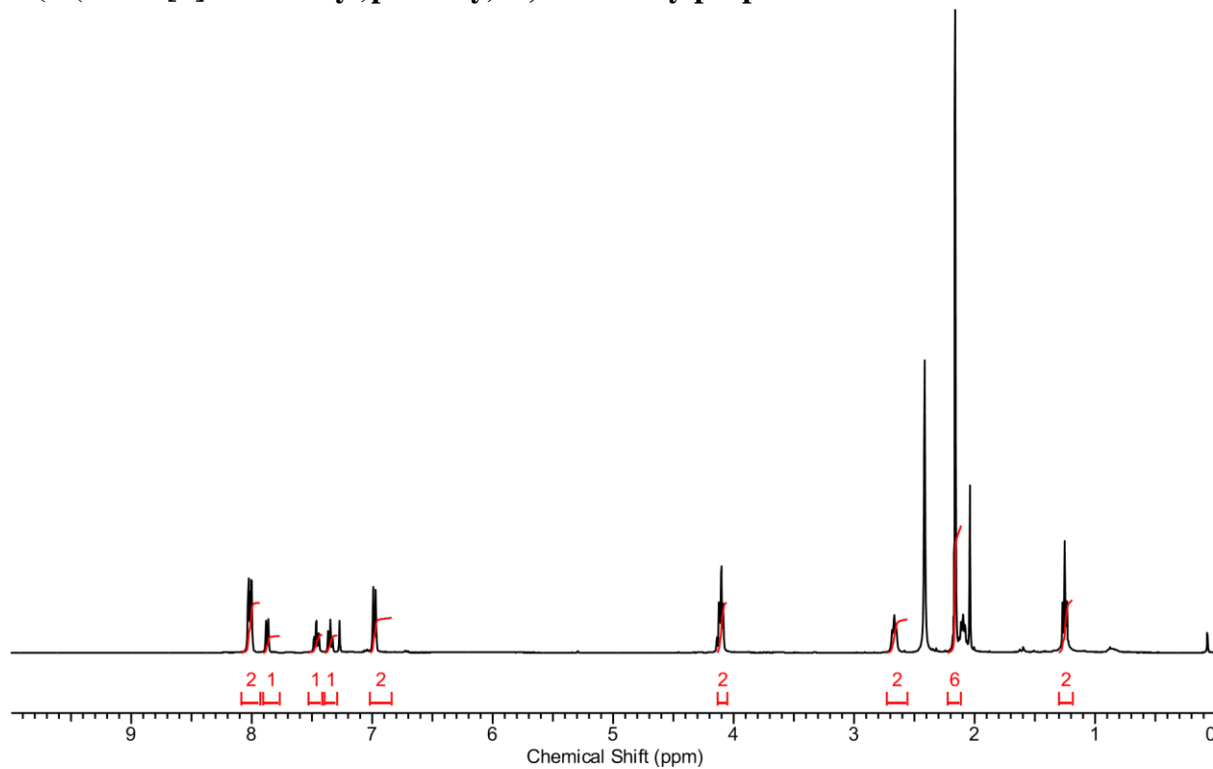




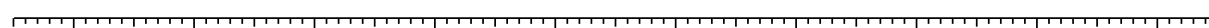
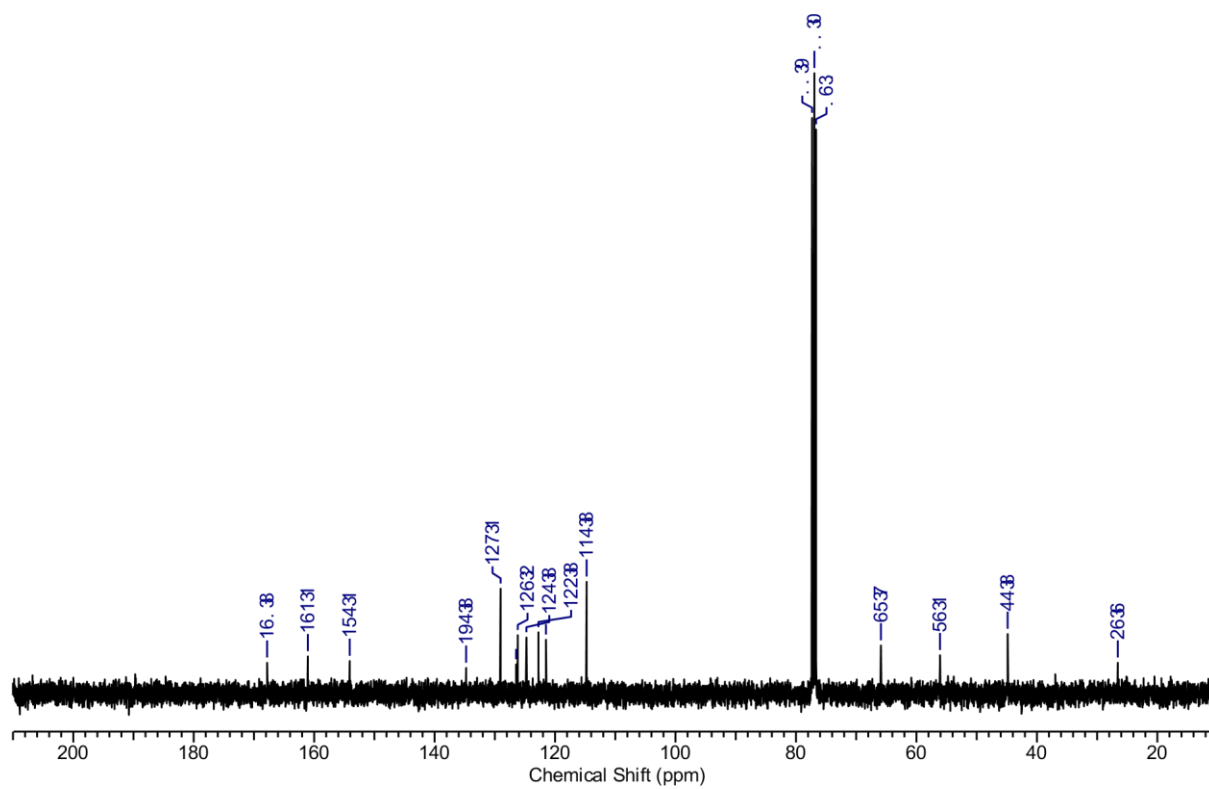
**3-(4-(Benzofuran-2-yl)phenoxy)-*N,N*-dimethylpropan-1-amine OX03392**

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Chemical Shift (ppm)

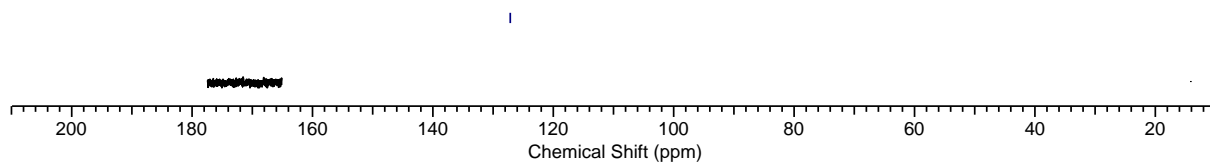
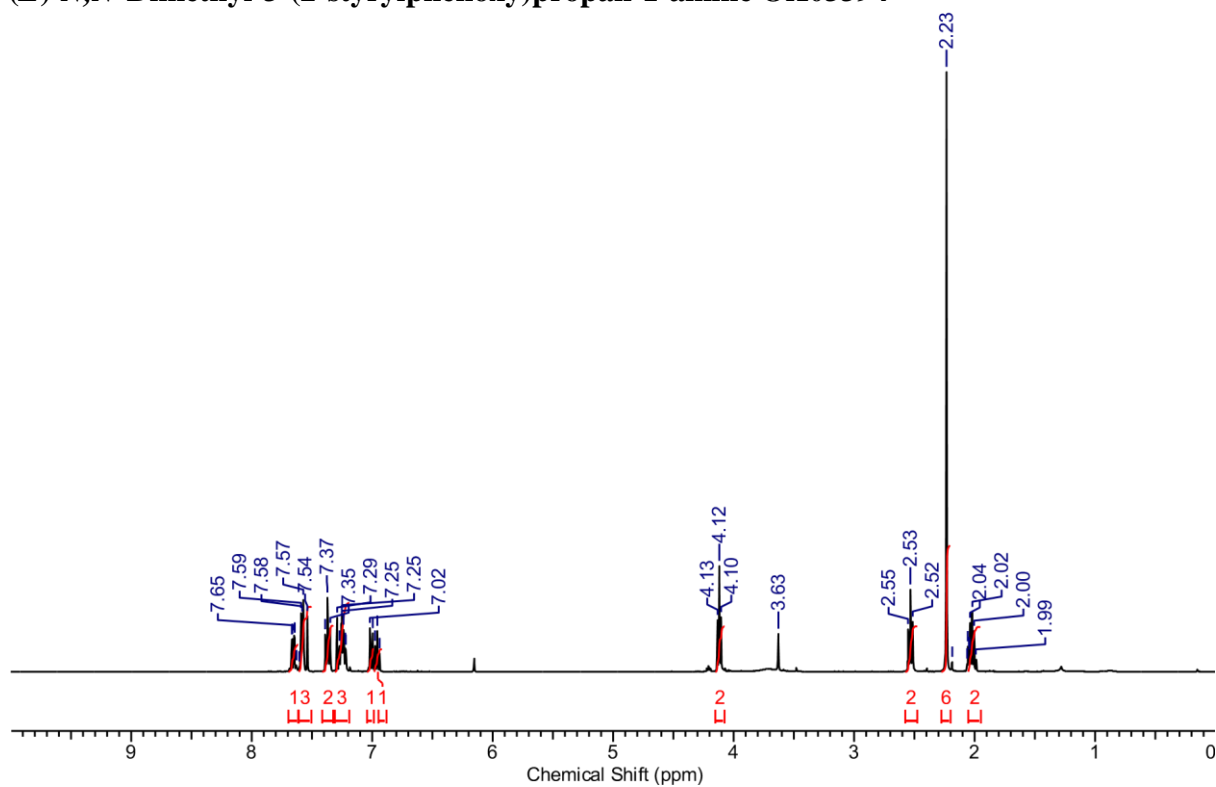


**3-(4-(Benzo[d]thiazol-2-yl)phenoxy)-*N,N*-dimethylpropan-1-amine OX03393**

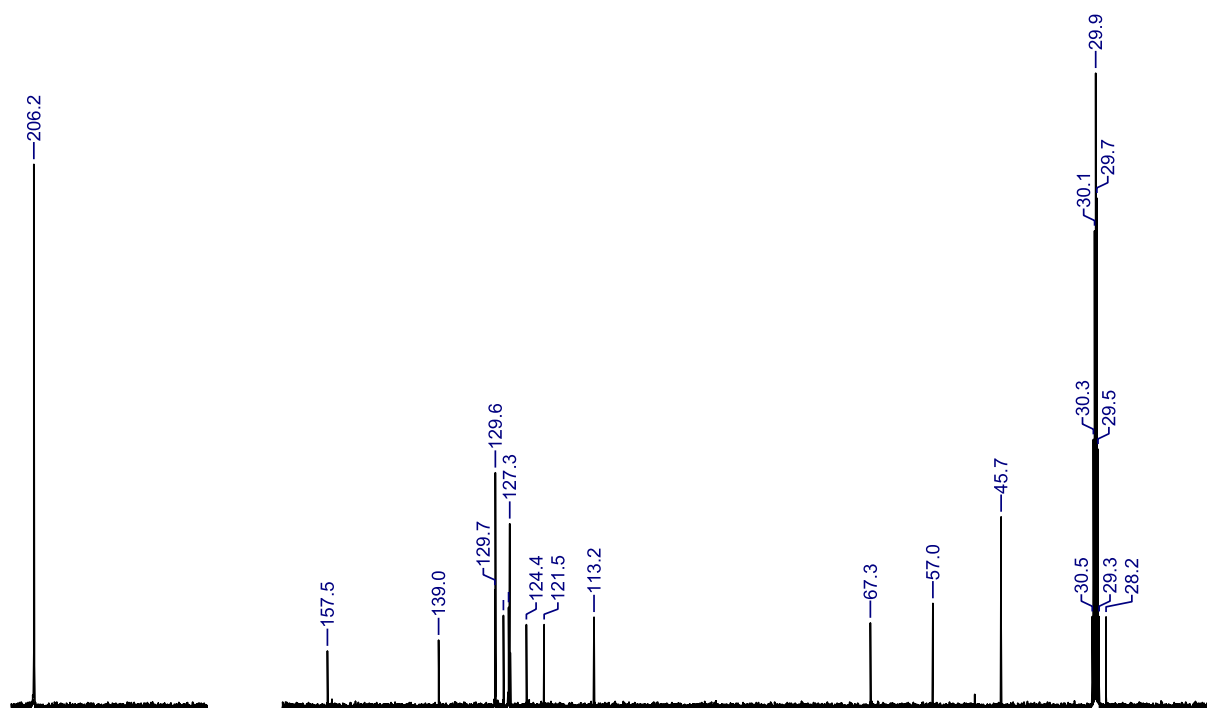
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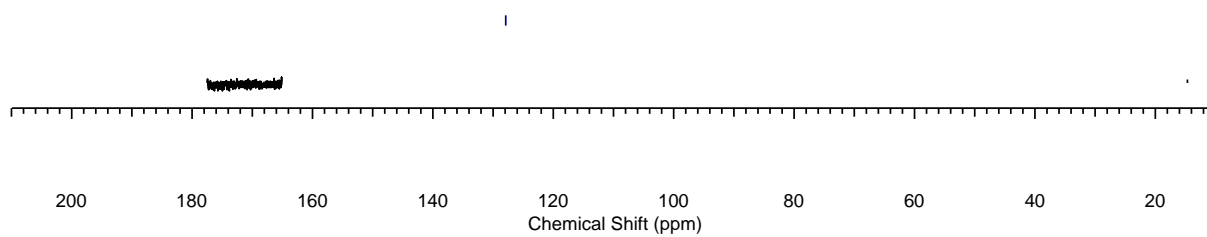
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Chemical Shift (ppm)

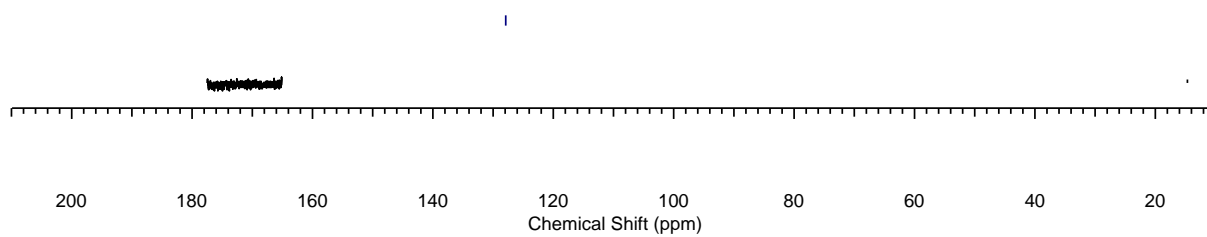
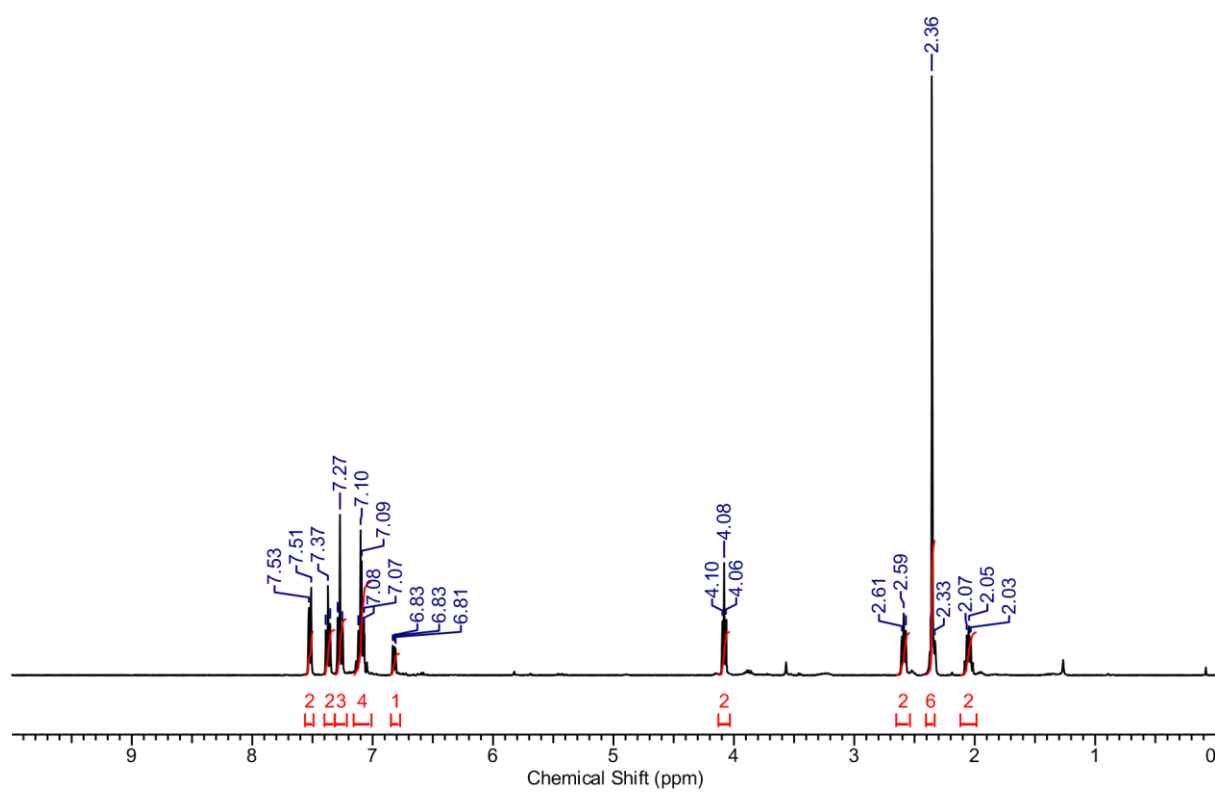
**(E)-N,N-Dimethyl-3-(2-styrylphenoxy)propan-1-amine OX03394<sup>55</sup>**

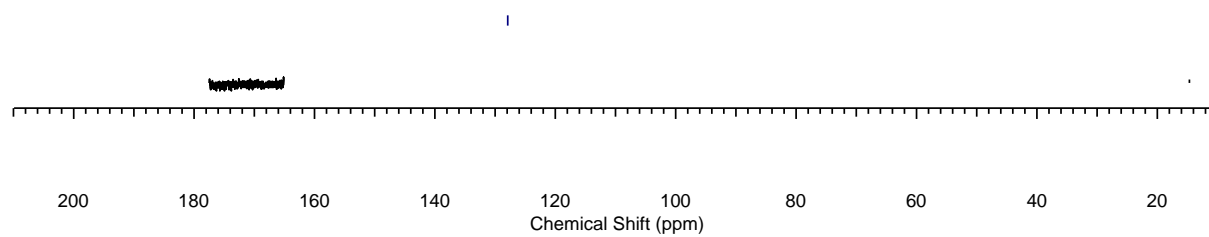
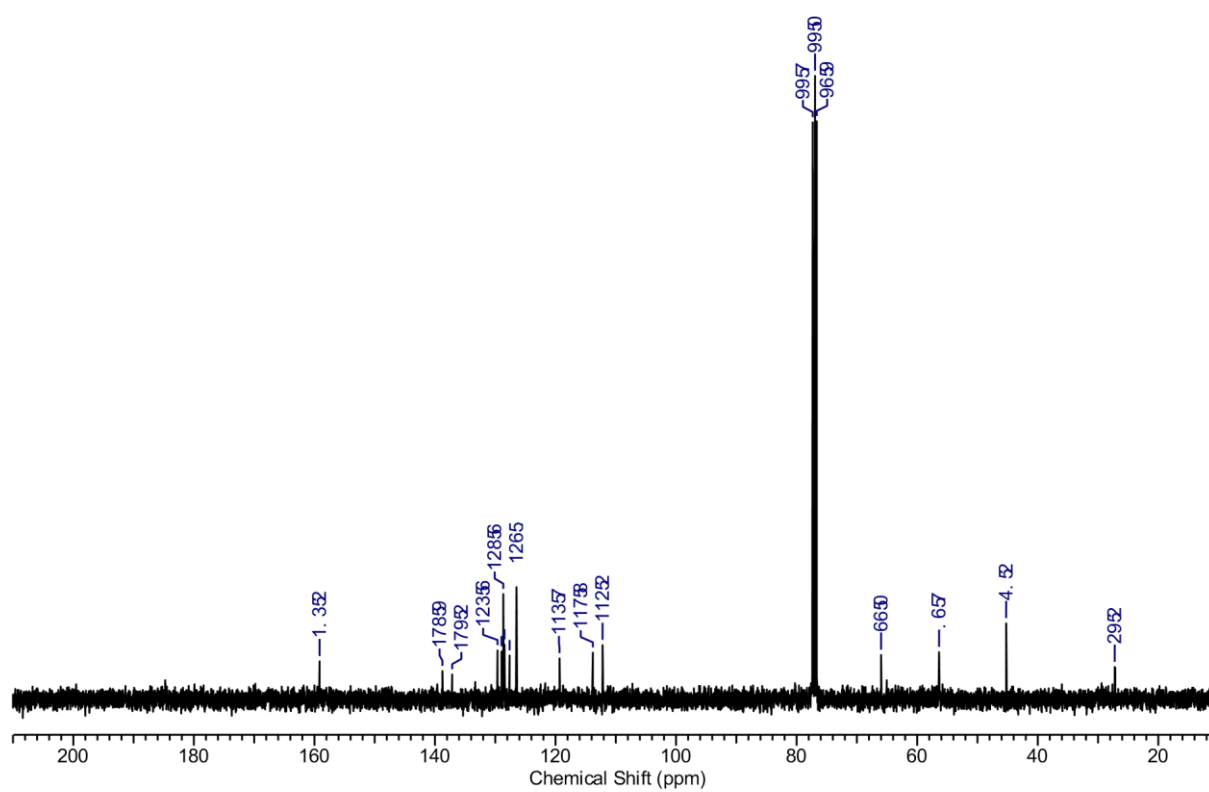


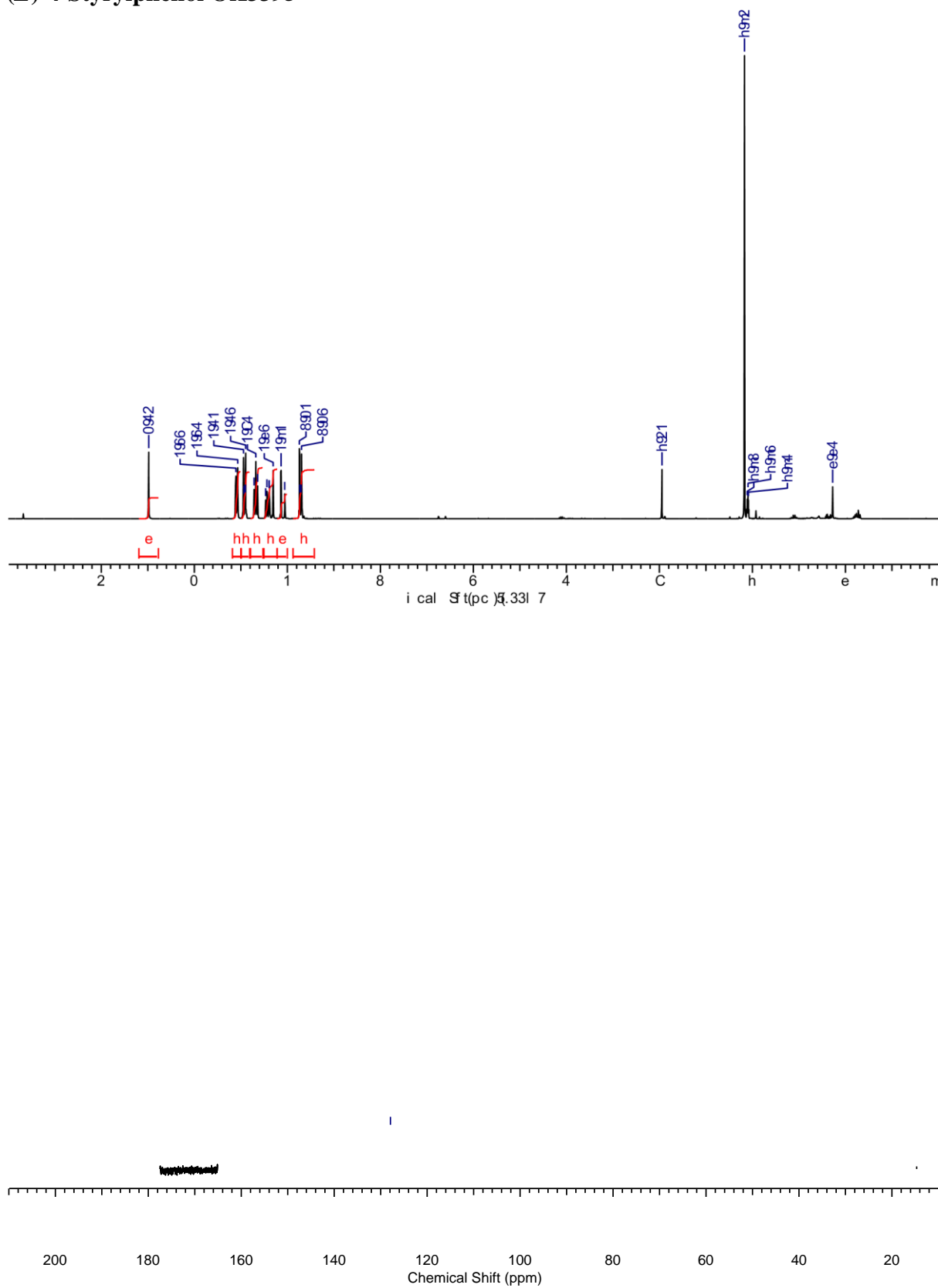


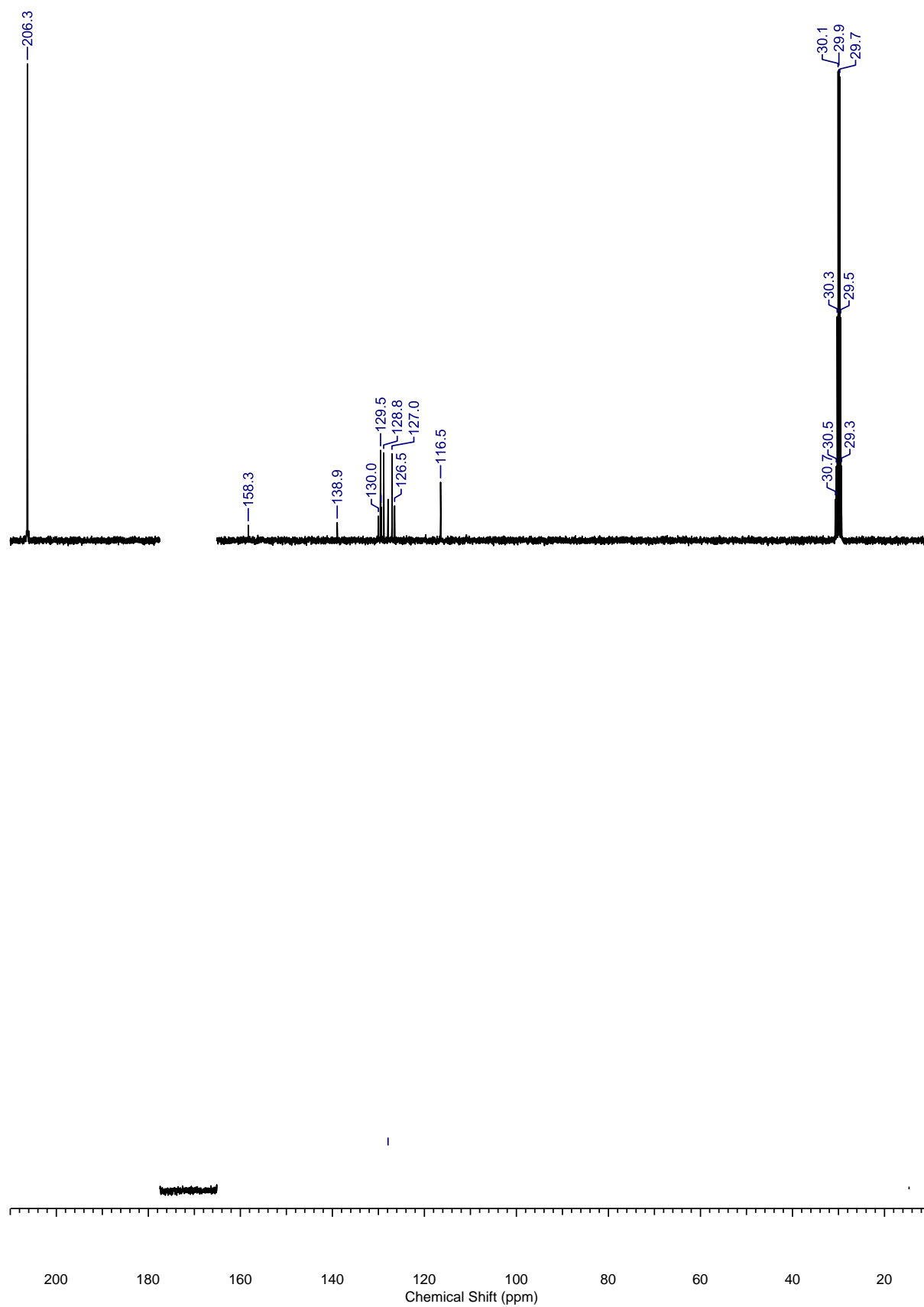
**(E)-N,N-Dimethyl-3-(3-styrylphenoxy)propan-1-amine OX03372**

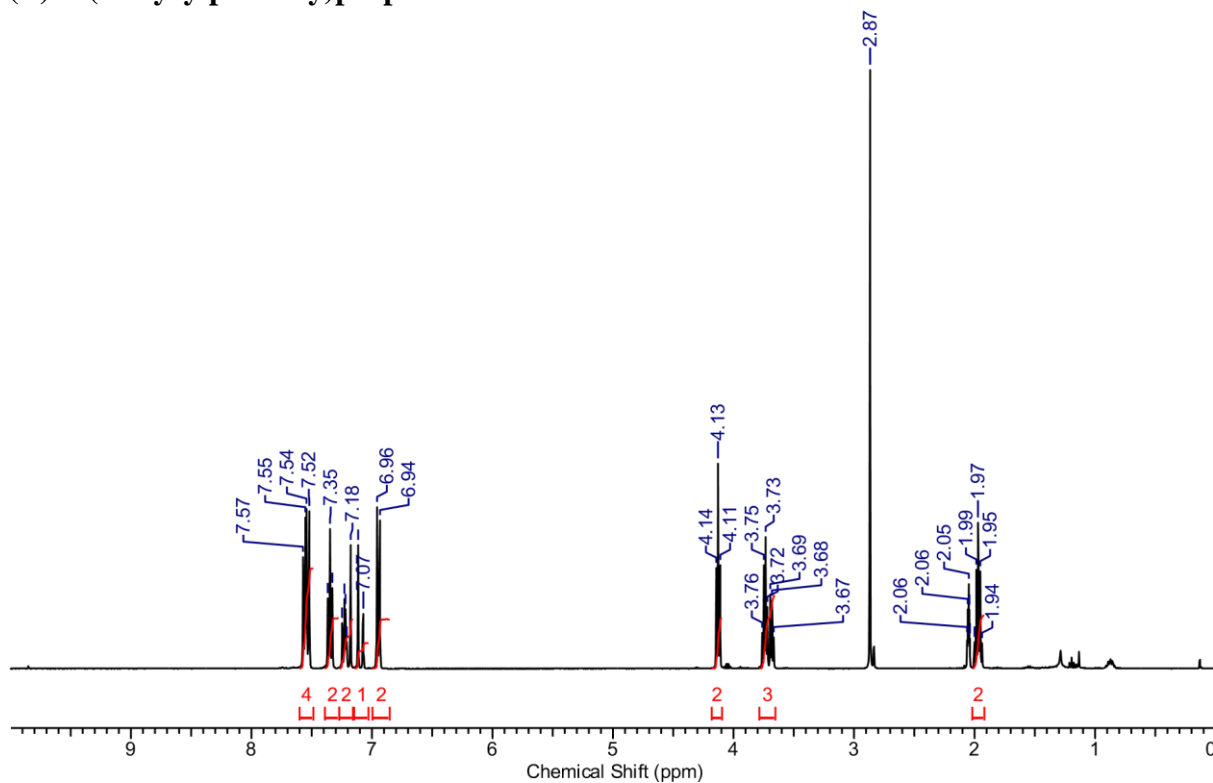






**(E)-4-Styrylphenol OX3395<sup>56</sup>**



**(E)-3-(4-Styrylphenoxy)propan-1-ol OX03050<sup>57</sup>**

200

180

160

140

120

100

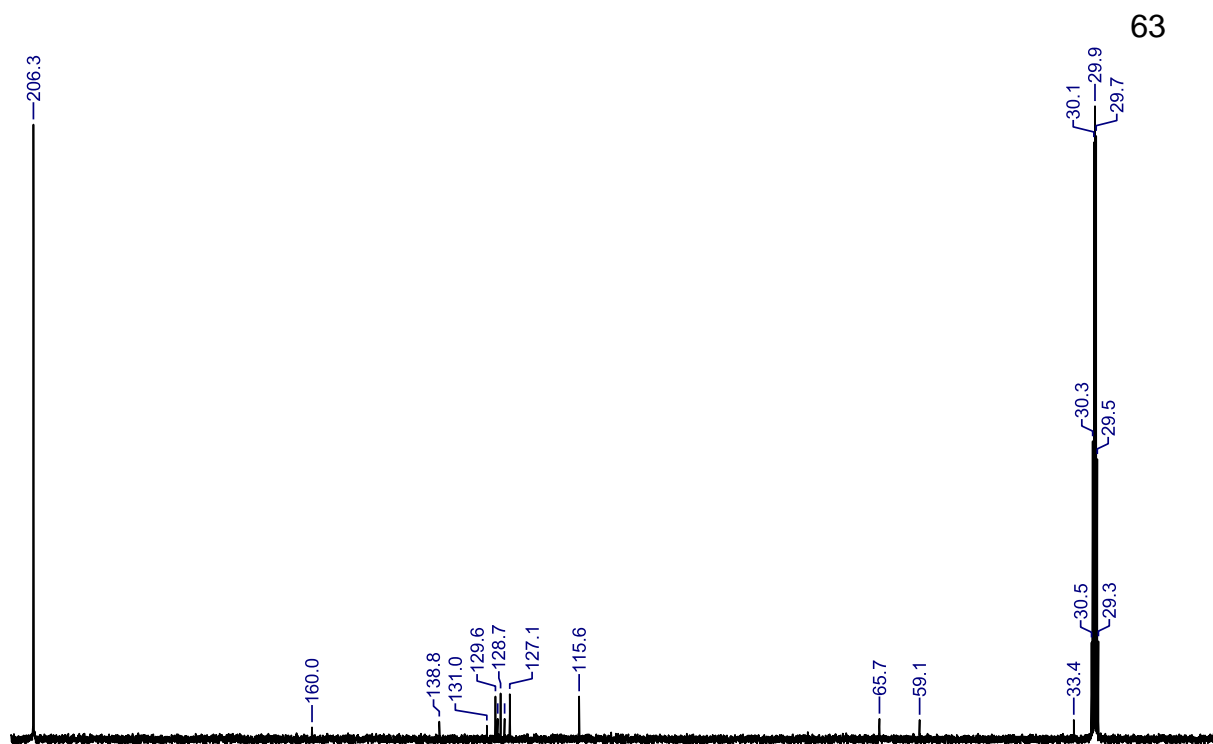
Chemical Shift (ppm)

80

60

40

20



63

200

180

160

140

120

100

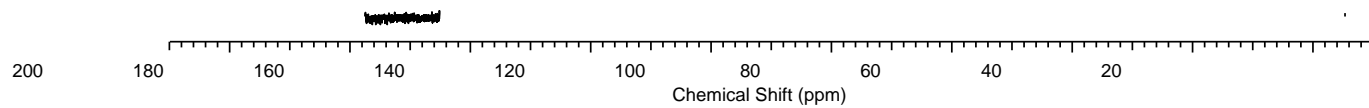
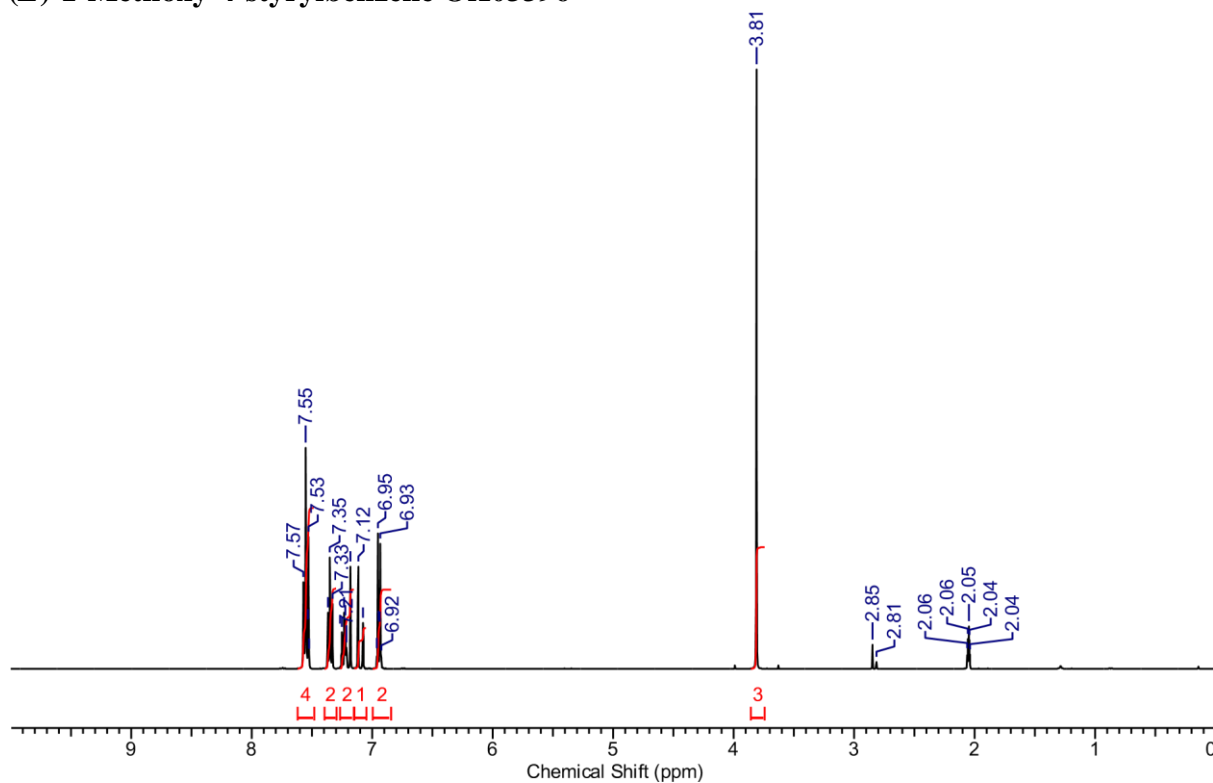
80

60

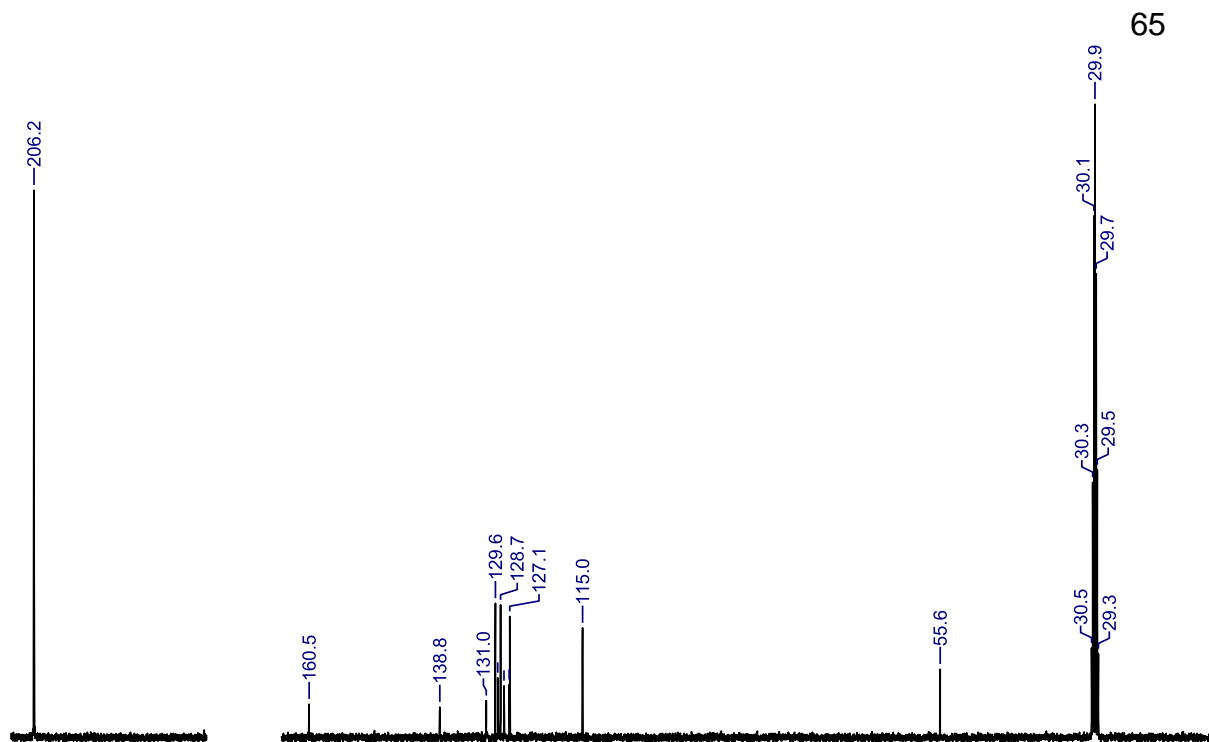
40

20

Chemical Shift (ppm)

**(E)-1-Methoxy-4-styrylbenzene OX03396**<sup>58</sup>





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