

SUPPLEMENTARY MATERIAL TO

**Design, synthesis and biological evaluation of new substituted benzofuran-based derivatives via C–H bond activation**

BEHJAT POURAMIRI<sup>1\*</sup>, MAHBOOBEB ZAHEDIFAR<sup>2</sup>, ADILEH AYATI<sup>3</sup>,  
FARAH POURAMIRI<sup>4</sup> and MAHDIYEH AHMADI<sup>1</sup>

<sup>1</sup>Student Research Committee, Jiroft University of Medical Sciences, 76179, Jiroft, Iran,

<sup>2</sup>Department of Chemistry, Faculty of Science, University of Jiroft, 7867161167, Jiroft, Iran,

<sup>3</sup>Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran and <sup>4</sup>Department of Internal Medicine, Afzalipour Hospital, Kerman University of Medical Sciences, Kerman, Iran

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*1-(4-(3-Phenylbenzofuran-2-yl)benzyl)piperidine (3a)*. Yellowish powder, yield: 88 %; m.p. 115–117 °C. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3132, 3052, 1506, 1481, 1109, 1084, 971, 816, 739, 682. <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 7.87–7.82 (*m*, 1H), 7.66–7.60 (*m*, 4H), 7.54–7.45 (*m*, 3H), 7.42–7.27 (*m*, 5H), 3.57 (*s*, 2H), 2.51–2.44 (*m*, 2H), 2.44–2.37 (*m*, 2H), 1.57–1.49 (*m*, 4H), 1.47–1.39 (*m*, 2H). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 155.65, 154.46, 138.84, 131.19, 129.92, 128.91, 128.85, 128.26, 128.05, 127.63, 126.54, 123.67, 123.61, 120.67, 118.63, 110.81, 61.23, 54.21, 25.44, 23.97. MS (ESI): *m/z* (%): 367 [M<sup>+</sup>, 19]; Anal. Calcd. for C<sub>26</sub>H<sub>25</sub>NO: C, 84.98; H, 6.86; N, 3.81; Found C, 84.66; H, 6.49; N, 4.06 %.

*4-(4-(3-Phenylbenzofuran-2-yl)benzyl)morpholine (3b)*. White solid; yield: 67%; m.p. 136–137 °C. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3030, 2964, 1450, 750. <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 7.84 (*d*, *J* = 7.8 Hz, 1H), 7.66–7.60 (*m*, 5H), 7.54–7.45 (*m*, 3H), 7.40–7.27 (*m*, 6H), 3.62 (*t*, *J* = 6.0 Hz, 5H), 3.57 (*s*, 2H), 2.49 (*d*, *J* = 7.3 Hz, 5H). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 155.65, 154.46, 138.82, 131.19, 129.92, 128.90, 128.84, 128.26, 128.05, 127.63, 126.54, 123.67, 123.62, 120.67, 118.63, 110.81, 66.55, 61.09, 53.95. MS (ESI): *m/z* (%): 369 [M<sup>+</sup>, 10]; Anal. Calcd. for C<sub>25</sub>H<sub>23</sub>NO<sub>2</sub>: C, 81.27; H, 6.27; N, 3.79. Found: C, 81.50; H, 6.26; N, 3.45 %.

*4-(4-(3-Phenylbenzofuran-2-yl)benzyl)thiomorpholine (3c)*. Yellow solid; yield: 78 %; m.p. 185–187 °C. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3022, 2985, 1458, 753. <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 7.84 (*d*, *J* = 8.1 Hz, 1H), 7.66–7.60

\*Corresponding author. E-mail: [etavakoly@yahoo.com](mailto:etavakoly@yahoo.com)

(*m*, 5H), 7.54–7.45 (*m*, 4H), 7.40–7.27 (*m*, 6H), 3.66 (*s*, 2H), 2.81–2.83 (*m*, 5H), 2.73 (*m*, 5H). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 155.64, 154.38, 138.83, 131.19, 129.92, 128.90, 128.87, 128.29, 128.01, 127.63, 126.58, 123.67, 123.62, 120.67, 118.78, 110.76, 61.22, 51.63, 28.16. MS (ESI): *m/z* (%): 385 [M<sup>+</sup>, 8]; Anal. Calcd. for C<sub>25</sub>H<sub>23</sub>NOS: C, 77.89; H, 6.01; N, 3.63. Found: C, 77.46; H, 5.92; N, 3.96 %.

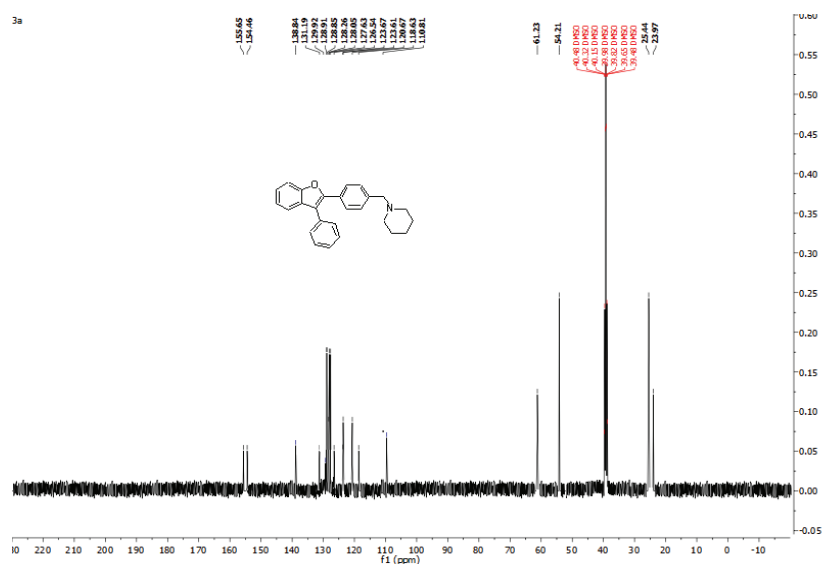
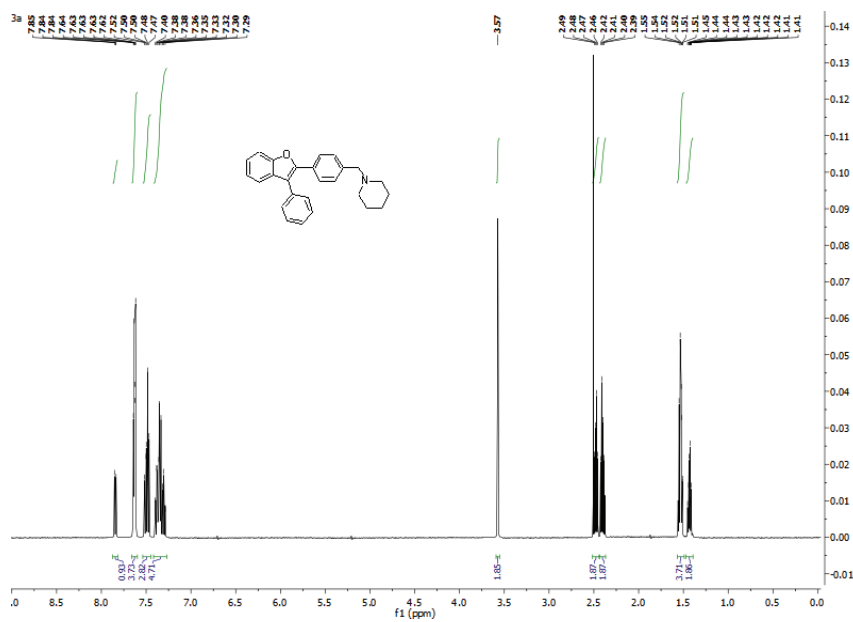
*1-(4-(3-Phenylbenzofuran-2-yl)benzyl)piperazine (3d)*. Cream solid; yield: 70 %; m.p. 198–201 °C. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3036, 2977, 1458, 786. <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 7.84 (*d*, *J* = 8.9 Hz, 1H), 7.66–7.60 (*m*, 4H), 7.52–7.45 (*m*, 3H), 7.42–7.26 (*m*, 5H), 3.67 (*t*, *J* = 1.0 Hz, 2H), 2.75–2.65 (*m*, 5H), 2.65–2.58 (*m*, 2H), 2.52–2.43 (*m*, 2H). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 155.65, 154.46, 138.79, 131.19, 129.92, 128.90, 128.87, 128.26, 128.05, 127.63, 126.54, 123.67, 123.62, 120.67, 118.63, 110.81, 61.75, 52.94, 45.82. MS (ESI): *m/z* (%): 368 [M<sup>+</sup>, 15]; Anal. Calcd. for C<sub>25</sub>H<sub>24</sub>N<sub>2</sub>O: C, 81.49; H, 6.57; N, 7.60. Found: C, 81.68; H, 6.17; N, 7.82 %.

*1-(4-(3-(4-Nitrophenyl)benzofuran-2-yl)benzyl)piperidine (3e)*. Cream solid; yield: 70 %; m.p. 175–178 °C. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3030, 2985, 1460, 786. <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 8.19 (*d*, *J* = 8.5 Hz, 2H), 7.88 – 7.81 (*m*, 3H), 7.61 (*d*, *J* = 8.4 Hz, 2H), 7.51 (*d*, *J* = 7.7 Hz, 1H), 7.39–7.30 (*m*, 4H), 3.57 (*s*, 2H), 2.48 (*m*, 2H), 2.43–2.37 (*m*, 2H), 1.59–1.50 (*m*, 4H), 1.47–1.38 (*m*, 2H). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 155.85, 154.31, 147.45, 139.20, 136.73, 136.13, 134.20, 132.95, 131.72, 129.56, 129.37, 128.66, 127.82, 119.82, 110.39, 60.14, 55.26, 23.17, 20.89. MS (ESI): *m/z* (%): 412.48 [M<sup>+</sup>, 12]; Anal. Calcd. for C<sub>26</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub>: C, 75.71; H, 5.86; N, 6.79. Found: C, 75.70; H, 5.84; N, 6.80 %.

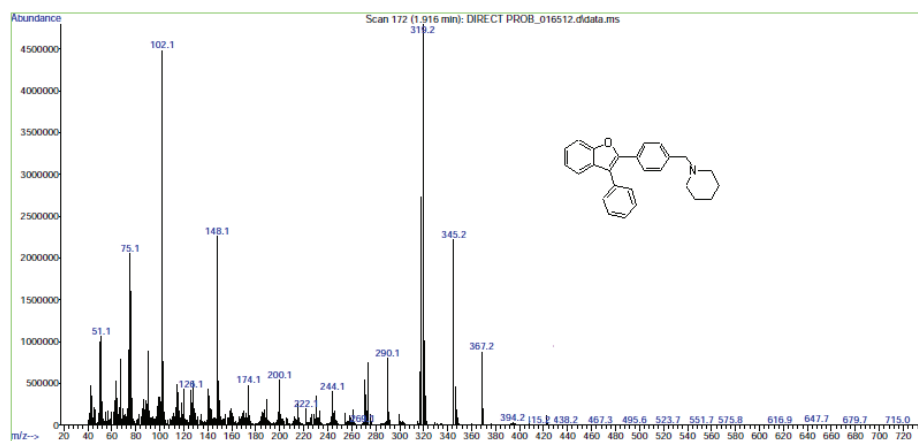
*4-(4-(3-(3-Nitrophenyl)benzofuran-2-yl)benzyl)morpholine (3f)*. Yellow solid; yield: 68 %; m.p. 183–185 °C. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3022, 2982, 1472, 777. <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 8.39 (*s*, 1H), 8.25 (*d*, *J* = 8.0 Hz, 1H), 7.97 – 7.91 (*m*, 1H), 7.84 (*d*, *J* = 8.0 Hz, 1H), 7.65 (*t*, *J* = 7.8 Hz, 1H), 7.61–7.56 (*m*, 2H), 7.50 (*d*, *J* = 7.7 Hz, 1H), 7.42–7.31 (*m*, 3H), 7.30 (*d*, *J* = 8.9 Hz, 1H), 3.66 (*m*, 4H), 3.56 (*s*, 2H), 2.49–2.53 (*m*, 4H). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 155.41, 153.71, 145.59, 136.78, 133.57, 132.23, 131.04, 130.21, 129.63, 128.27, 127.19, 126.02, 124.53, 123.73, 122.64, 120.13, 117.94, 111.94, 66.73, 60.02, 53.23. MS (ESI): *m/z* (%): 414.16 [M<sup>+</sup>, 8]; Anal. Calcd. for C<sub>25</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub>: C, 72.45; H, 5.35; N, 6.76. Found: C, 72.43; H, 5.33; N, 6.77 %.

*1-(4-(3-(*p*-Tolyl)benzofuran-2-yl)benzyl)piperidine (3g)*. Yellow solid; yield: 65 %; m.p. 169–171 °C. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3012, 2982, 1512, 780. <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 7.84 (*d*, *J* = 7.1 Hz, 1H), 7.59 (*d*, *J* = 7.2 Hz, 2H), 7.51 (*d*, *J* = 8.7 Hz, 1H), 7.50–7.40 (*m*, 4H), 7.40–7.28 (*m*, 4H), 3.57 (*s*, 2H), 2.51–2.39 (*m*, 4H), 2.37 (*s*, 3H), 1.53 (*m*, 4H), 1.46–1.39 (*m*, 2H). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  / ppm: 155.25, 151.64, 140.28, 134.53,

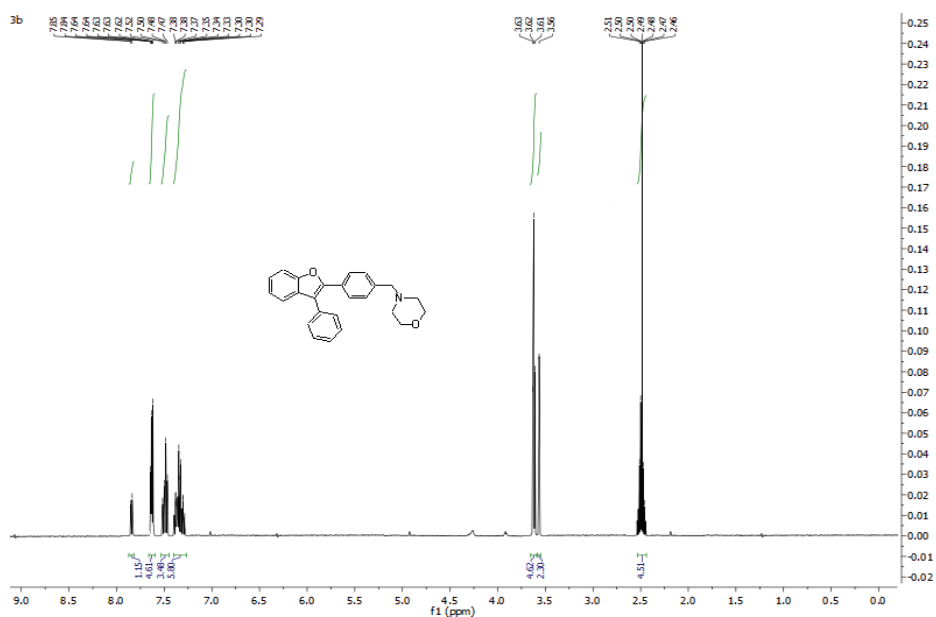
132.98, 130.44, 129.29, 128.18, 127.79, 127.13, 126.60, 118.48, 114.80, 12.27, 64.75, 55.99, 26.29, 24.05, 21.24. MS (ESI):  $m/z$  (%): 381.5 [M<sup>+</sup>, 10]; Anal. Calcd. for C<sub>27</sub>H<sub>27</sub>NO: C, 85.00; H, 7.13; N, 3.67. Found: C, 85.01; H, 7.15; N, 3.69 %.



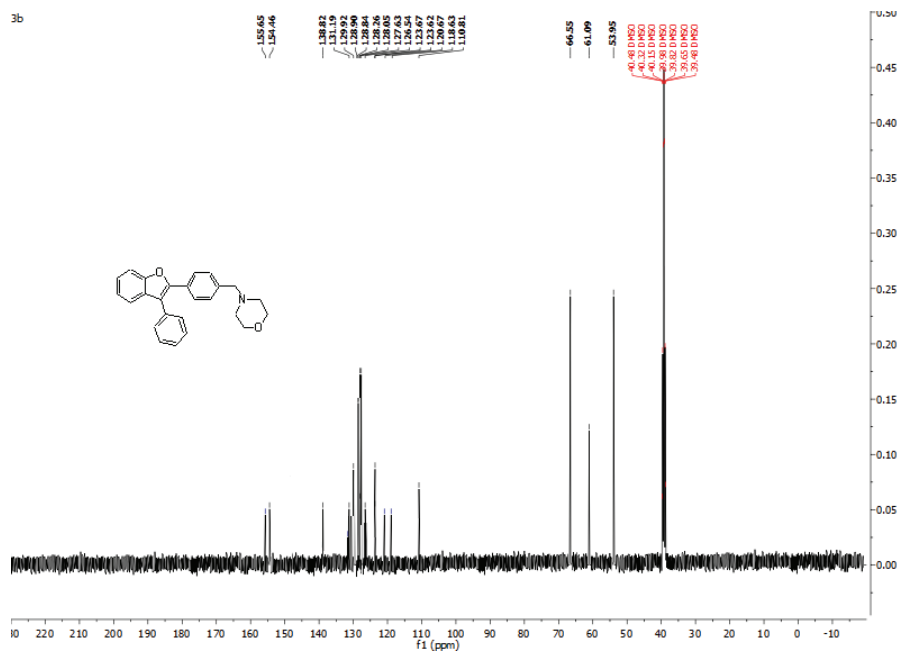
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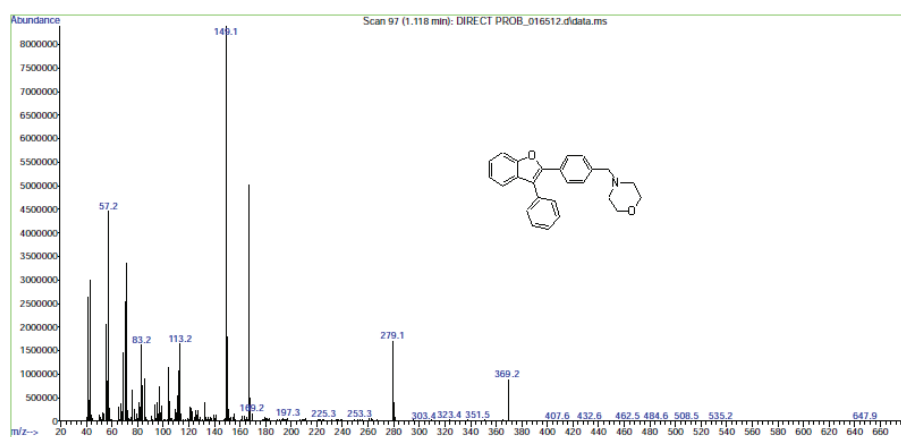
Mass of compound 3a



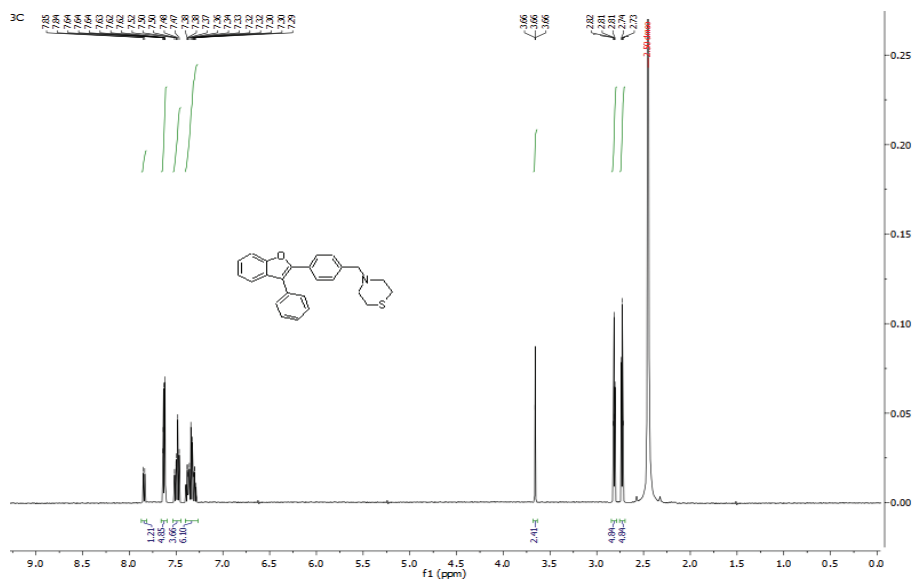
<sup>1</sup>H-NMR of compound 3b

 $^{13}\text{C}$ -NMR of compound 3b

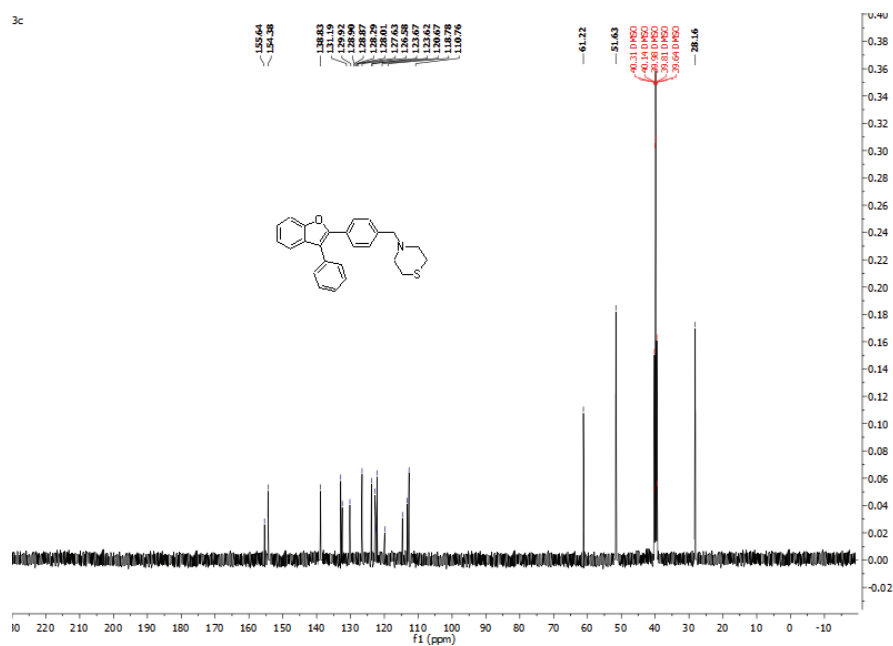
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Mass of compound 3b

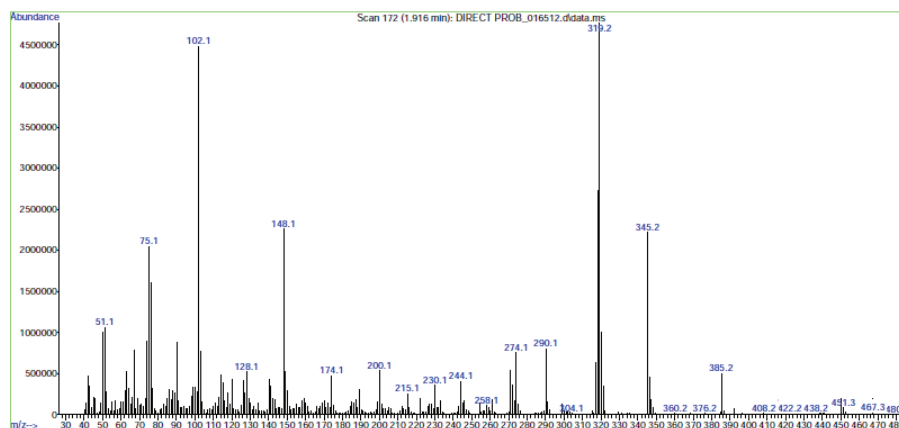


<sup>1</sup>H-NMR of compound 3c

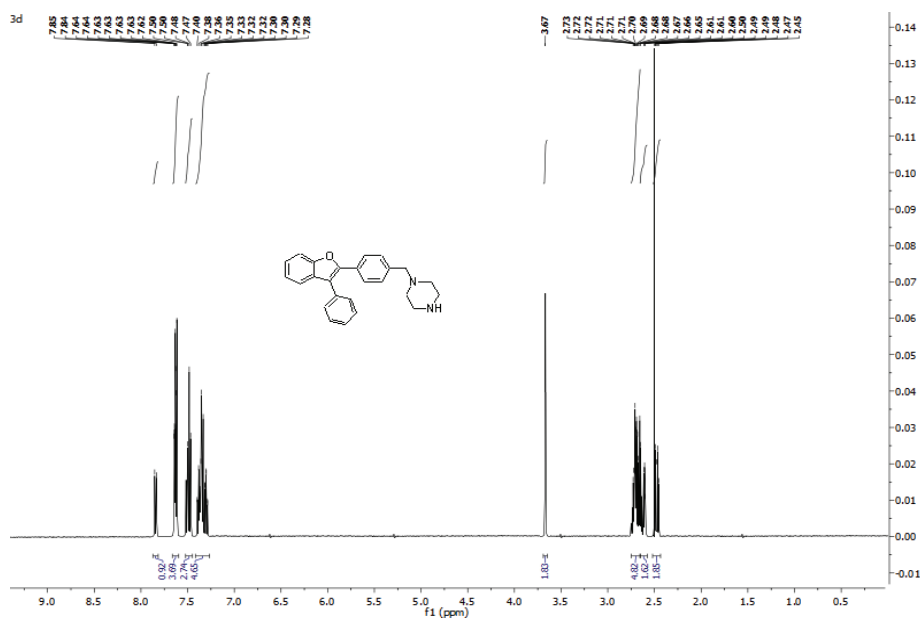


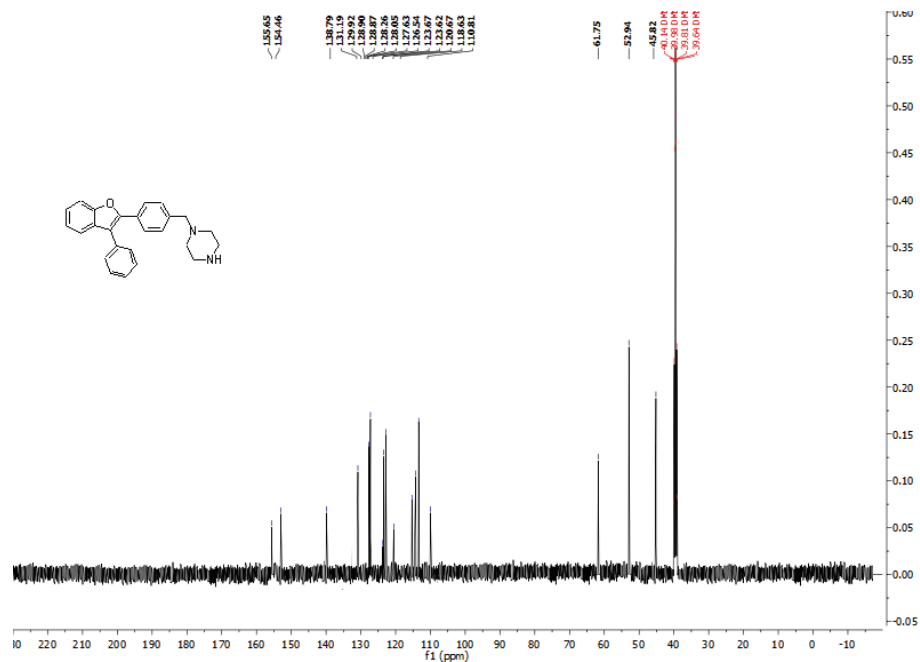
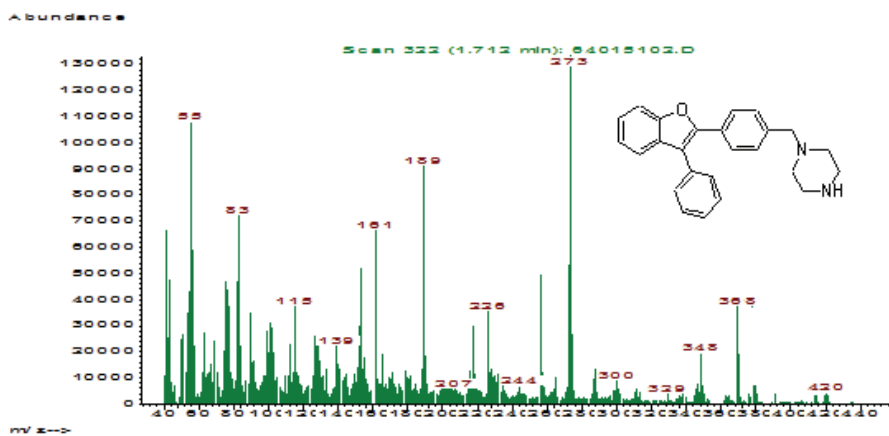
<sup>13</sup>C-NMR of compound 3c

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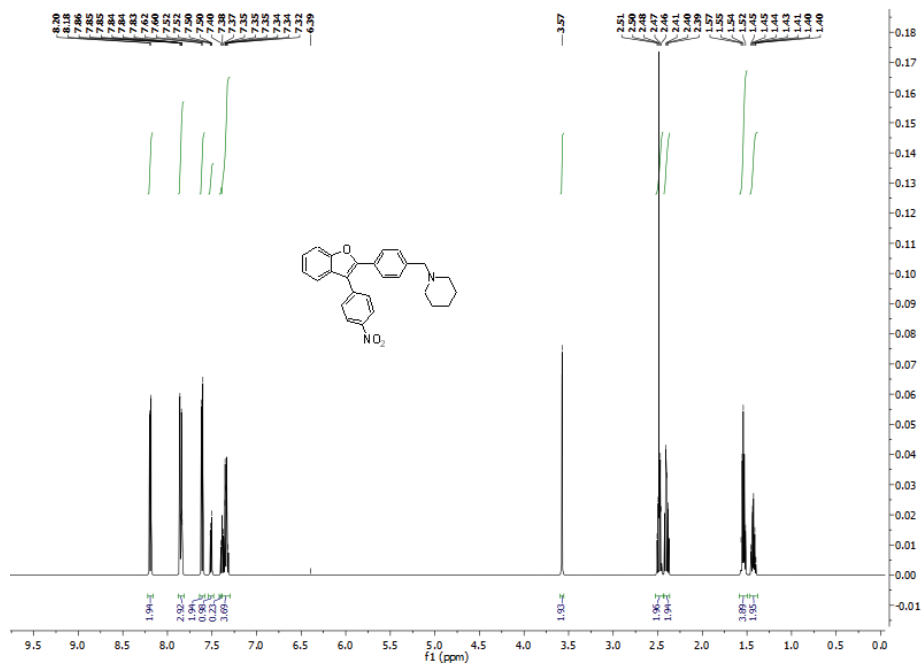
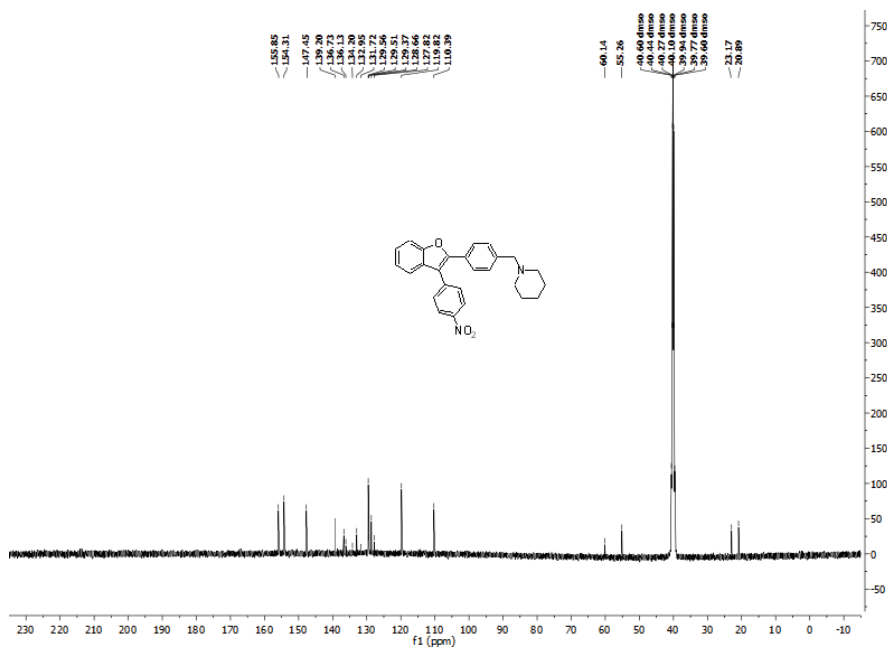
Mass of compound 3c

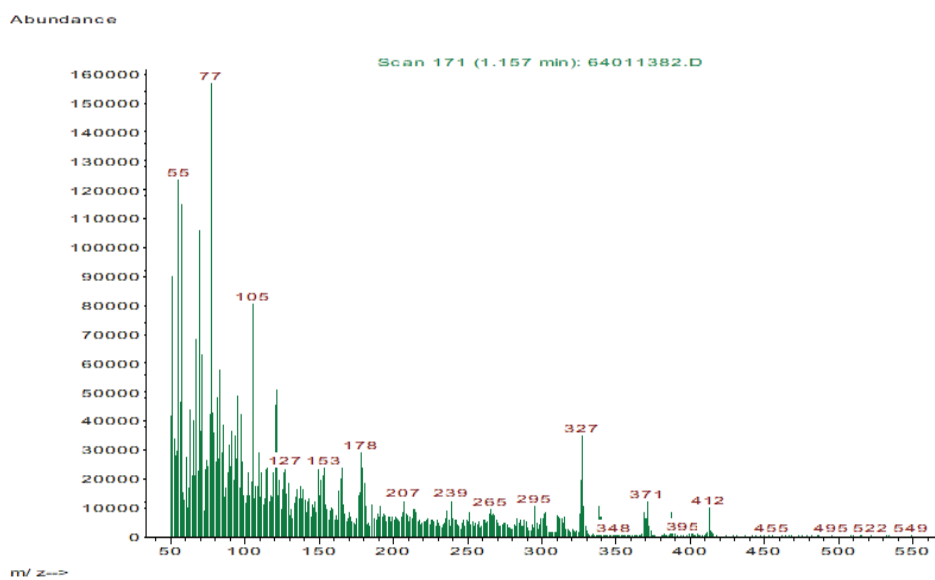
<sup>1</sup>H-NMR of compound 3d

<sup>13</sup>C-NMR of compound 3d

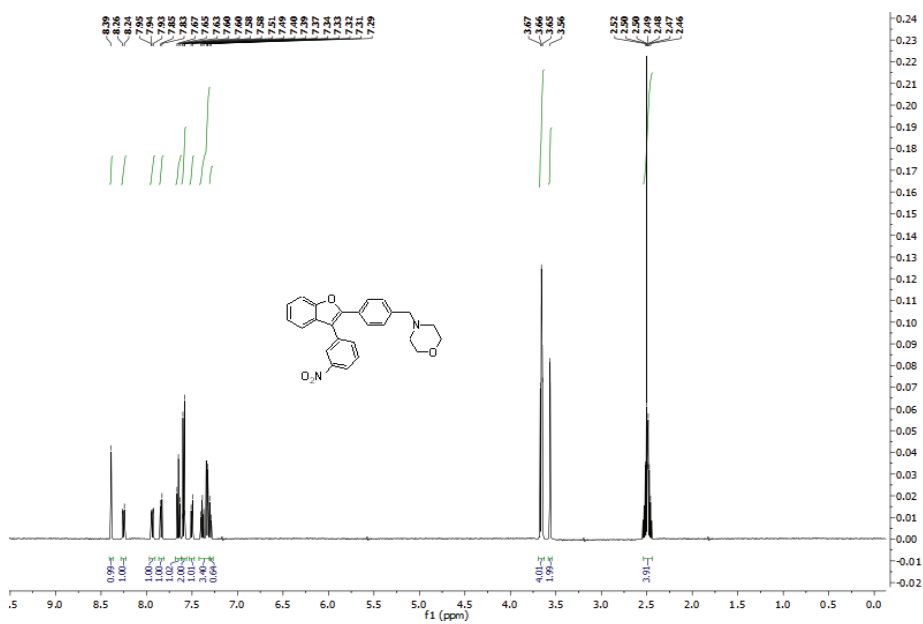
Mass of compound 3d



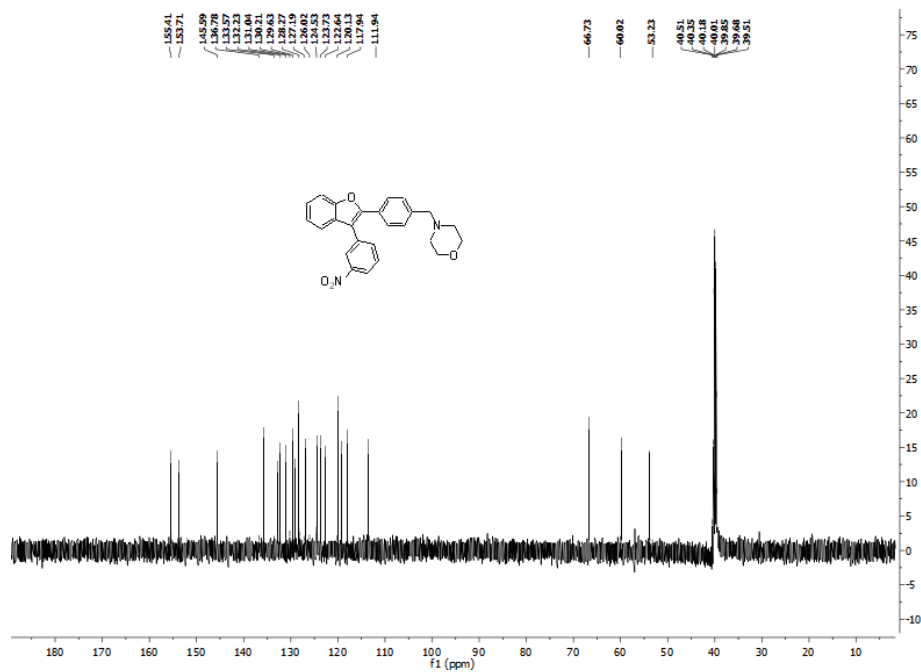
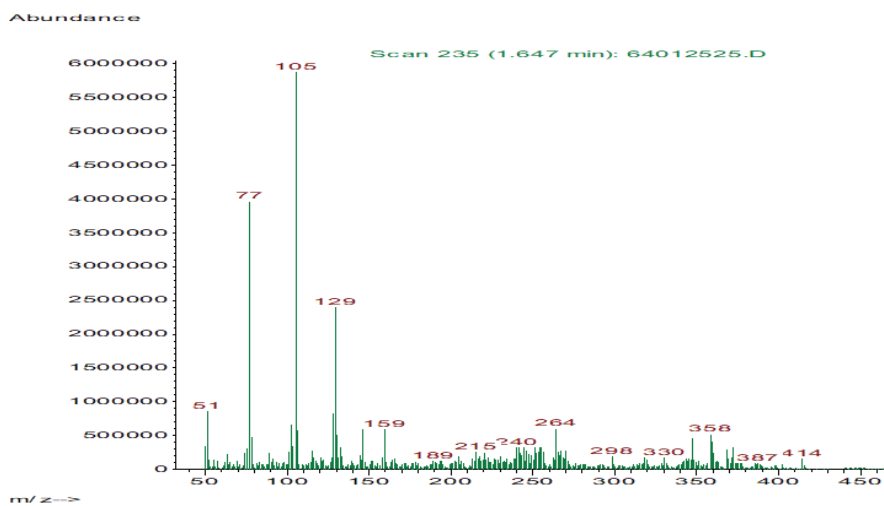
<sup>1</sup>H-NMR of compound 3e<sup>13</sup>C-NMR of compound 3e



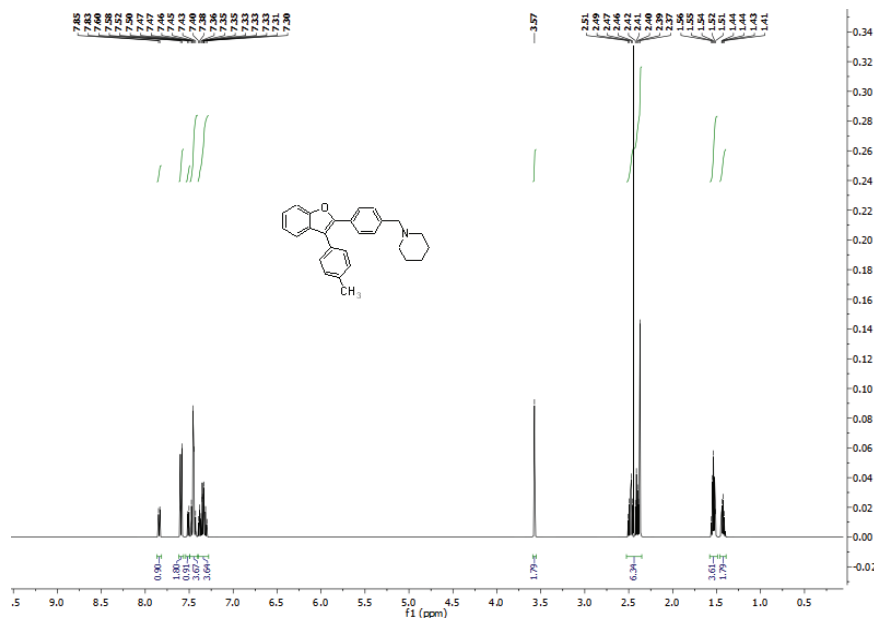
Mass of compound 3e



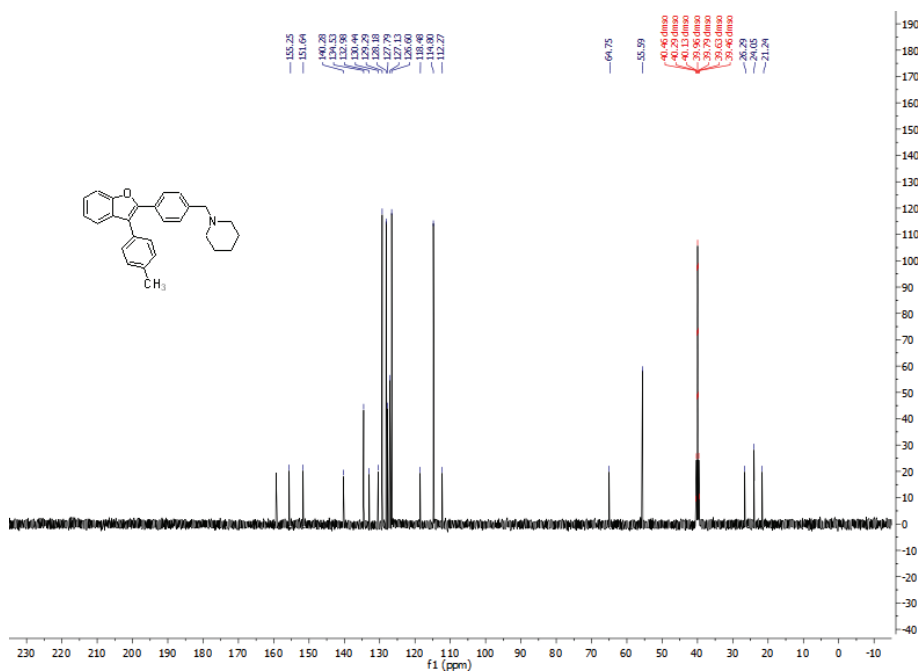
<sup>1</sup>H-NMR of compound 3f

 $^{13}\text{C}$ -NMR of compound 3f

Mass of compound 3f



<sup>1</sup>H-NMR of compound 3g



<sup>13</sup>C-NMR of compound 3g

