

## Electronic Supplementary Information (ESI)

### Design, synthesis and antitumor activity of novel 8-substituted 2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b'*]difuran imidazolium salt derivatives

Cheng-Jun Sun <sup>a</sup>, Wen Chen <sup>a</sup>, Yan Li <sup>b</sup>, Lan-Xiang Liu <sup>a</sup>, Xue-Quan  
Wang <sup>a</sup>, Li-Juan Li <sup>a</sup>, Hong-Bin Zhang <sup>a, \*</sup>, Xiao-Dong Yang <sup>a, \*</sup>

<sup>a</sup>Key Laboratory of Medicinal Chemistry for Natural Resource (Yunnan University), Ministry of Education, School of Chemical Science and Technology, Yunnan University, Kunming, 650091, P. R. China. Tel.: +86-871-5031119; Fax.: +86-871-5035538. E-mail: xdyang@ynu.edu.cn, zhanghbyd@gmail.com

<sup>b</sup>State Key Laboratory for Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Science, Kunming, 650204, P. R. China

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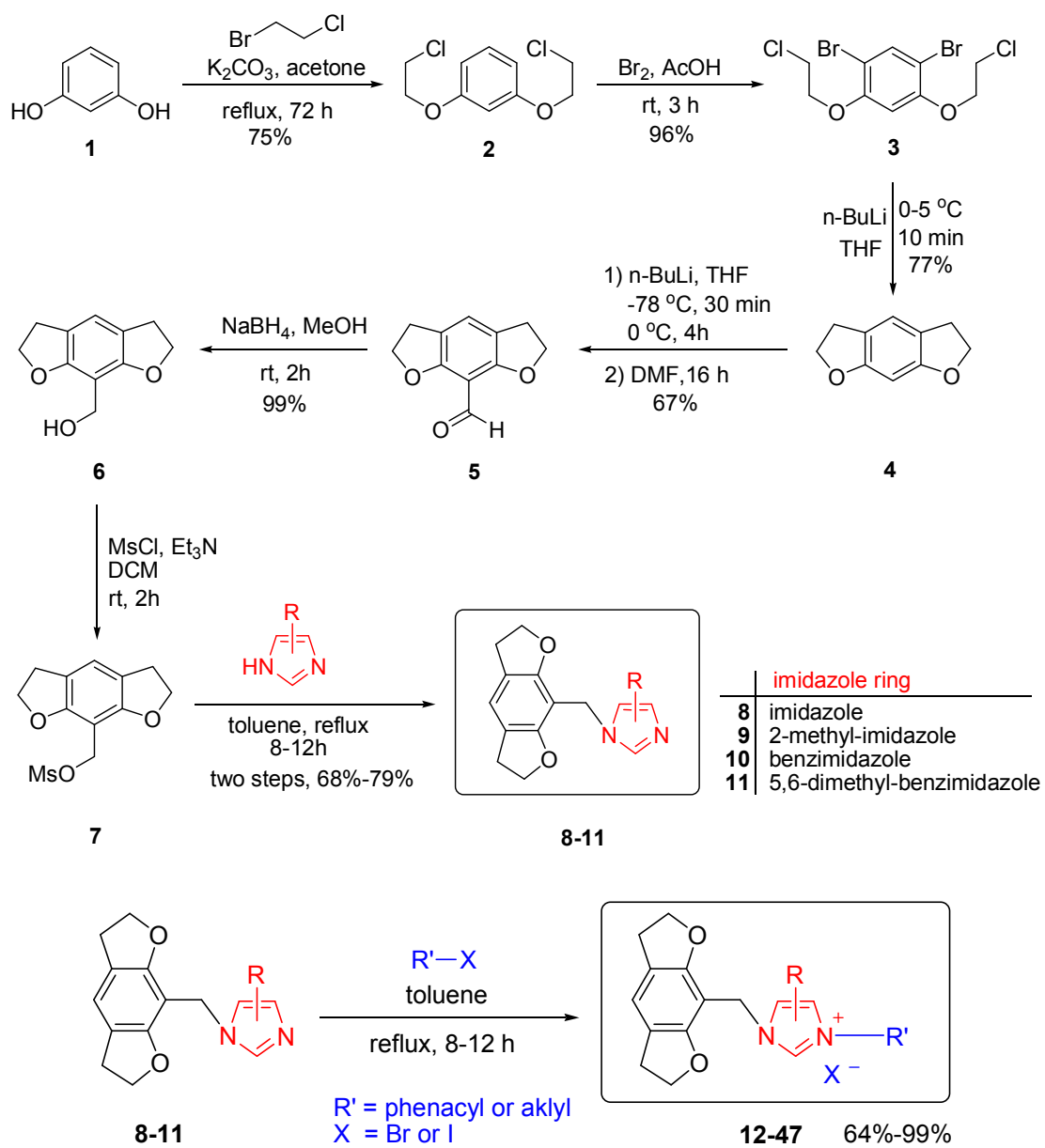
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## 1. General Experimental

Melting points were obtained on a XT-4 melting-point apparatus and were uncorrected. Proton nuclear magnetic resonance ( $^1\text{H-NMR}$ ) spectra were recorded on a Bruker Avance 300 spectrometer at 300 MHz. Carbon-13 nuclear magnetic resonance ( $^{13}\text{C-NMR}$ ) was recorded on Bruker Avance 300 spectrometer at 75 MHz. Chemical shifts are reported as  $\delta$  values in parts per million (ppm) relative to tetramethylsilane (TMS) for all recorded NMR spectra. Low-resolution Mass spectra were recorded on a VG Auto Spec-3000 magnetic sector MS spectrometer. High Resolution Mass spectra were taken on AB QSTAR Pulsar mass spectrometer.

Silica gel (200–300 mesh) for column chromatography and silica GF<sub>254</sub> for TLC were produced by Qingdao Marine Chemical Company (China). All air- or moisture-sensitive reactions were conducted under an argon atmosphere. Starting materials and reagents used in reactions were obtained commercially from Acros, Aldrich, Fluka and were used without purification, unless otherwise indicated.

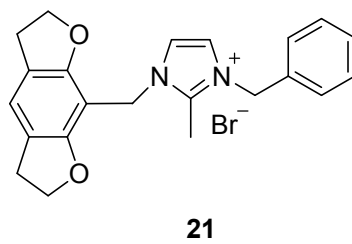
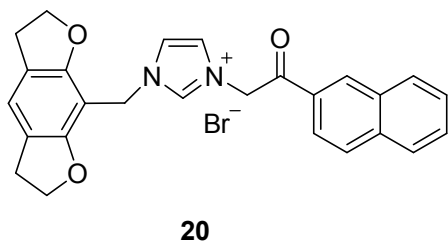
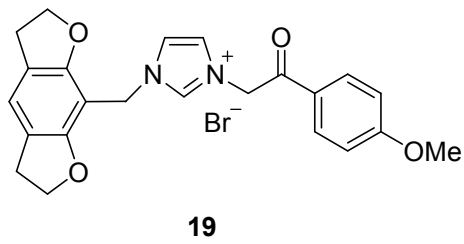
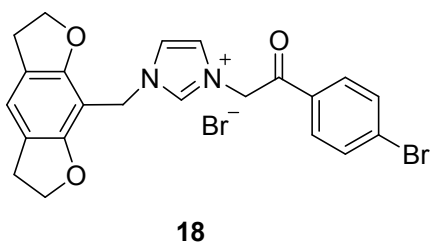
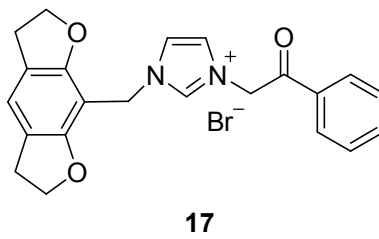
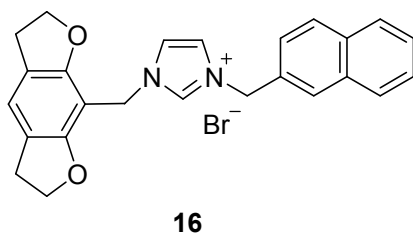
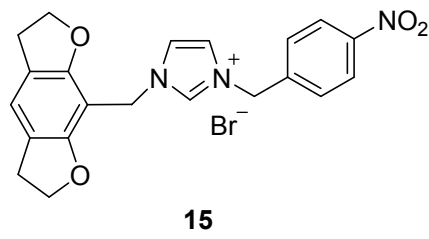
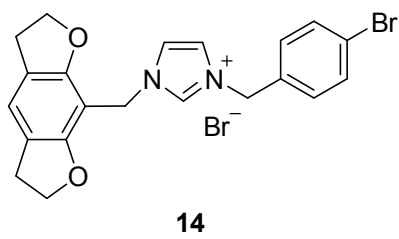
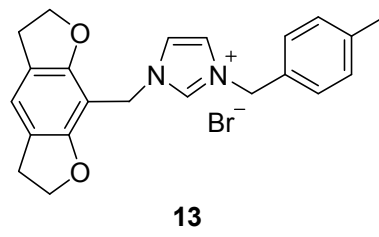
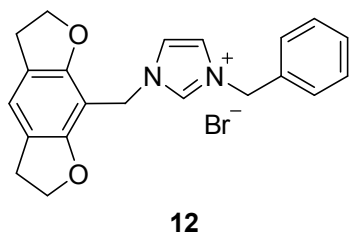
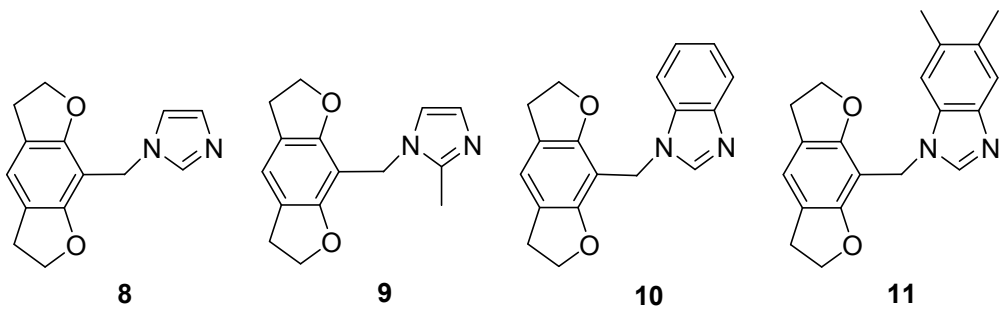
## 2. Experimental Procedures and Analytical Data

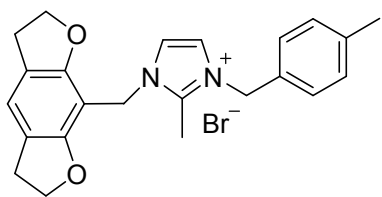


Synthesis of compounds **8–47**.

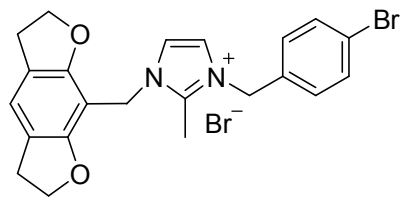
Structures and yields of compounds **8–47**

Entry	Compound no.	imidazole ring	R'	X	Yields (%)
1	<b>8</b>	imidazole	–	–	73
2	<b>9</b>	2-methyl-imidazole	–	–	68
3	<b>10</b>	benzimidazole	–	–	79
4	<b>11</b>	5,6-dimethyl-benzimidazole	–	–	68
5	<b>12</b>	imidazole	benzyl	Br	92
6	<b>13</b>	imidazole	4-methylbenzyl	Br	83
7	<b>14</b>	imidazole	4-bromobenzyl	Br	88
8	<b>15</b>	imidazole	4-nitrobenzyl	Br	95
9	<b>16</b>	imidazole	2-naphthylmethyl	Br	90
10	<b>17</b>	imidazole	phenacyl	Br	91
11	<b>18</b>	imidazole	4-bromophenacyl	Br	95
12	<b>19</b>	imidazole	4-methoxyphenacyl	Br	95
13	<b>20</b>	imidazole	naphthylacyl	Br	90
14	<b>21</b>	2-methyl-imidazole	benzyl	Br	84
15	<b>22</b>	2-methyl-imidazole	4-methylbenzyl	Br	97
16	<b>23</b>	2-methyl-imidazole	4-bromobenzyl	Br	79
17	<b>24</b>	2-methyl-imidazole	4-nitrobenzyl	Br	97
18	<b>25</b>	2-methyl-imidazole	2-naphthylmethyl	Br	91
19	<b>26</b>	2-methyl-imidazole	phenacyl	Br	98
20	<b>27</b>	2-methyl-imidazole	4-bromophenacyl	Br	79
21	<b>28</b>	2-methyl-imidazole	4-methoxyphenacyl	Br	86
22	<b>29</b>	2-methyl-imidazole	naphthylacyl	Br	93
23	<b>30</b>	benzimidazole	butyl	I	77
24	<b>31</b>	benzimidazole	benzyl	Br	85
25	<b>32</b>	benzimidazole	4-methylbenzyl	Br	77
26	<b>33</b>	benzimidazole	4-bromobenzyl	Br	70
27	<b>34</b>	benzimidazole	2-naphthylmethyl	Br	64
28	<b>35</b>	benzimidazole	phenacyl	Br	95
29	<b>36</b>	benzimidazole	4-bromophenacyl	Br	88
30	<b>37</b>	benzimidazole	4-methoxyphenacyl	Br	96
31	<b>38</b>	benzimidazole	naphthylacyl	Br	86
32	<b>39</b>	5,6-dimethyl-benzimidazole	butyl	I	75
33	<b>40</b>	5,6-dimethyl-benzimidazole	benzyl	Br	96
34	<b>41</b>	5,6-dimethyl-benzimidazole	4-methylbenzyl	Br	83
35	<b>42</b>	5,6-dimethyl-benzimidazole	4-bromobenzyl	Br	93
36	<b>43</b>	5,6-dimethyl-benzimidazole	2-naphthylmethyl	Br	70
37	<b>44</b>	5,6-dimethyl-benzimidazole	phenacyl	Br	99
38	<b>45</b>	5,6-dimethyl-benzimidazole	4-bromophenacyl	Br	93
39	<b>46</b>	5,6-dimethyl-benzimidazole	4-methoxyphenacyl	Br	98
40	<b>47</b>	5,6-dimethyl-benzimidazole	naphthylacyl	Br	89

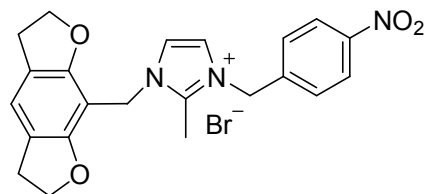




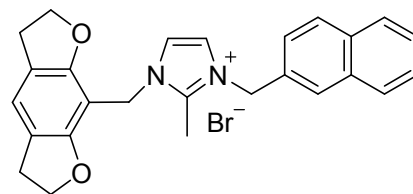
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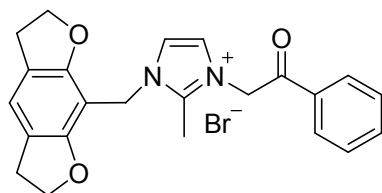
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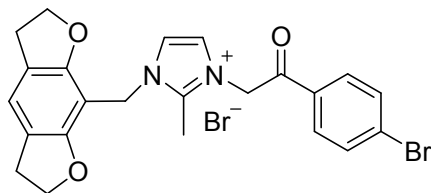
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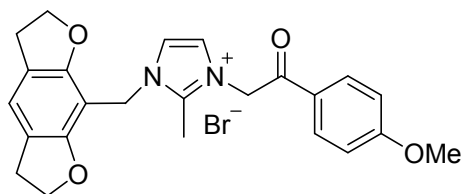
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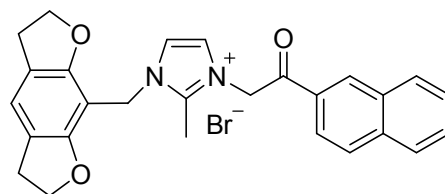
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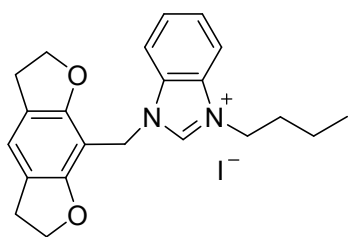
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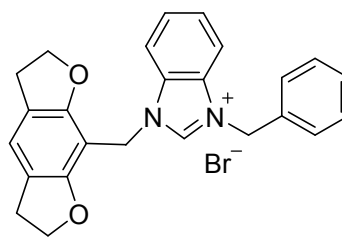
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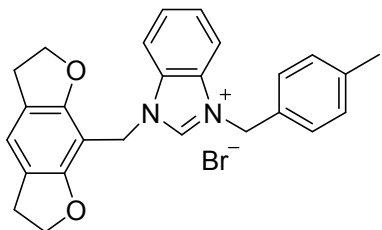
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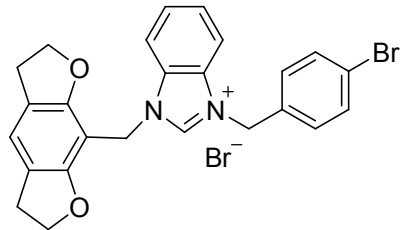
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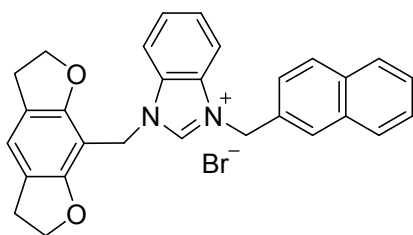
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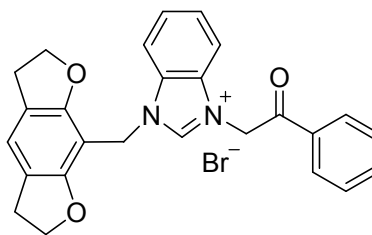
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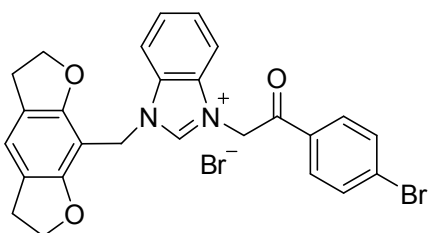
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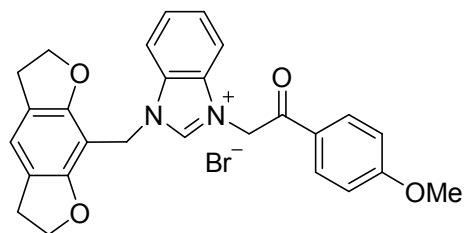
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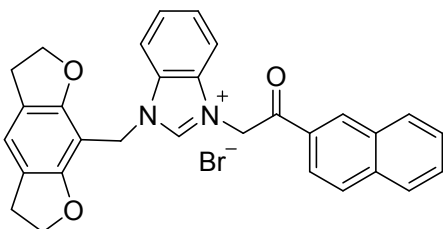
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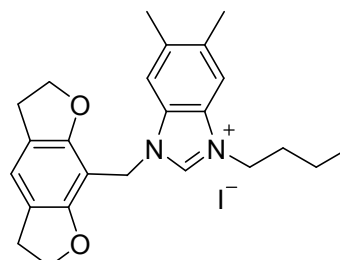
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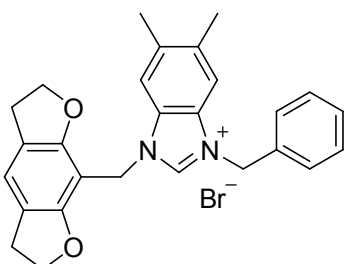
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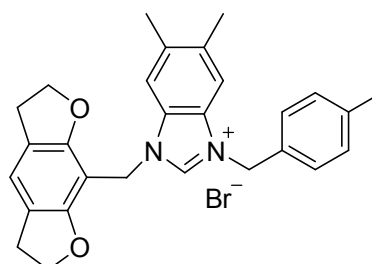
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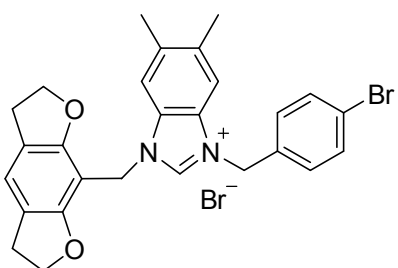
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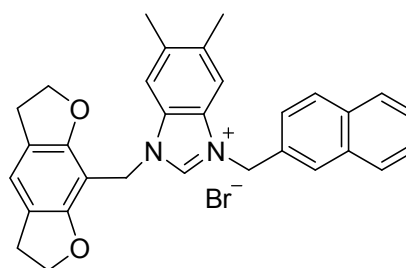
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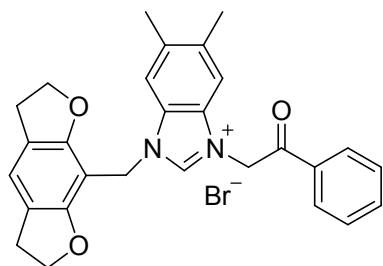
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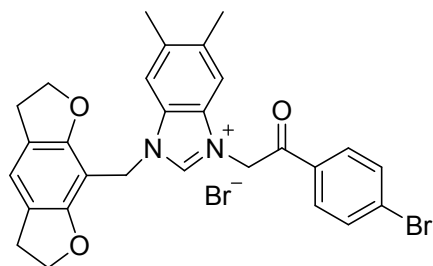
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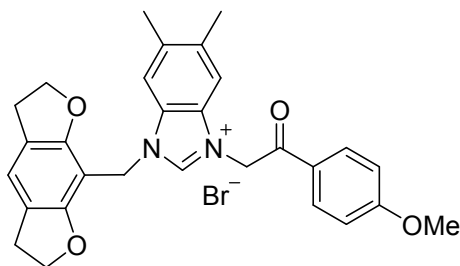
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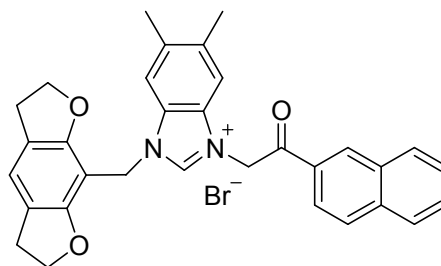
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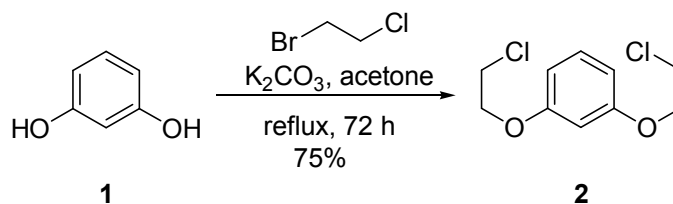


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**47**

## 2.1 Synthesis of compound 2

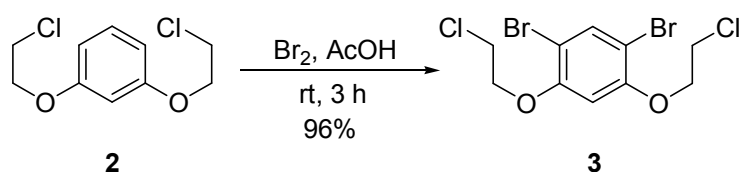


A mixture of resorcinol **1** (5.0 g, 45.4 mmol), 1-bromo-2-chloroethane (30 mL, 363 mmol), finely powdered  $K_2CO_3$  (19.0 g, 137 mmol) and acetone (30 mL) was stirred and heated at reflux under argon for 72 h. The reaction was cooled to room temperature and filtered through a short pad of Celite. The Celite was washed with  $CH_2Cl_2$ , and the filtrate and washes were combined and evaporated to dryness by rotatory evaporation. The residue was partitioned between AcOEt (20 mL) and  $H_2O$  (20 mL). The organic phase was washed with 2 M NaOH (2×30 mL), then  $H_2O$  (2×30 mL) and brine (30 mL), dried over  $Na_2SO_4$  and evaporated under reduced pressure to yield the products **2** (8.0 g, 75%) as white powder.



Yield 75%, White powder, mp 75-77 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ: 7.19 (1H, t, *J* = 8.1 Hz), 6.56-6.50 (3H, m), 4.20 (4H, t, *J* = 6.0 Hz), 3.79 (4H, t, *J* = 6.0 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ: 159.47, 130.16, 107.58, 102.18, 68.07, 41.87.

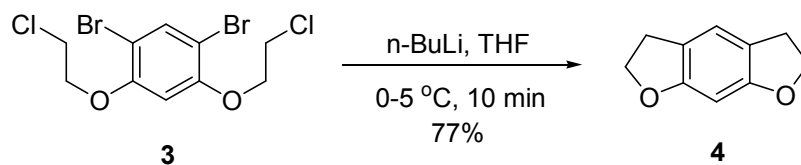
## 2.2 Synthesis of compound 3



The ether **2** (8.0 g, 34.0 mmol) was suspended in glacial acetic acid (25 mL) and a solution of Br<sub>2</sub> (4.4 mL) in glacial acetic acid (10 mL) was added dropwise at 0–5 °C. The reaction mixture was allowed to reach room temperature and stirred for 3 h. The mixture was poured into ice/water (50 mL) and stirred for 15 min. The precipitate was filtered off and the solid was washed with cold 1:1 AcOH/H<sub>2</sub>O (5×30 mL), then with cold H<sub>2</sub>O until neutral pH (5×50 mL) and dried under reduced pressure until constant weight to yield the products **3** (12.8 g, 96%) as pale yellow powder.

Yield 96%, Yellow powder, mp 104-106 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ: 7.70 (1H, s), 6.54 (1H, s), 4.26 (4H, t, *J* = 6.0 Hz), 3.85 (4H, t, *J* = 6.0 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ: 154.92, 136.42, 105.07, 102.21, 70.07, 41.43.

## 2.3 Synthesis of compound 4

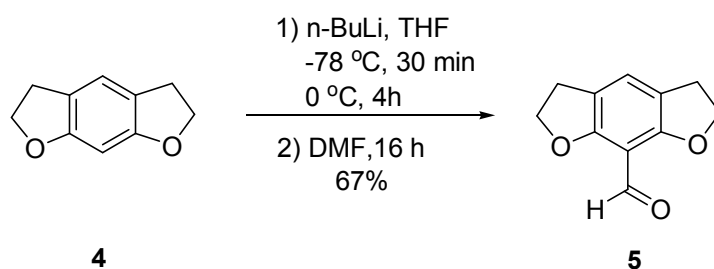


A solution of the dibromo compound **3** (8.00 g, 20.4 mmol) in 250 mL of anhydrous THF was placed in a N<sub>2</sub> atmosphere and cooled to 0 °C. A solution of

*n*-butyllithium (21.4 mL, 2.5 M in hexanes, 2.1 equiv) was added very quickly (addition time: 7 s) to the rapidly stirred solution using a syringe with a large gauge needle. The reaction mixture was stirred for 10 min, and solvent was removed. The residue was partitioned between AcOEt and H<sub>2</sub>O, and the organic phase was dried with Ma<sub>2</sub>SO<sub>4</sub> and evaporated to furnish the crude product, which was chromatographed on silica gel (petroleum ether 60-90 °C : ethyl acetate = 20:1) to afford the products **4** (2.53 g, 77%) as white crystals.

Yield 67%, White crystals, mp 61- 63 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ: 6.84 (1H, s), 6.18 (1H, s), 4.44 (4H, t, *J* = 9.0 Hz), 2.98 (4H, t, *J* = 9.0 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ: 160.33, 120.37, 118.21, 92.54, 72.14, 29.30.

## 2.4 Synthesis of compound 5

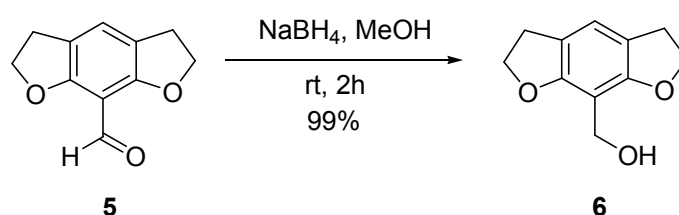


To a solution of the tetrahydrobenzo[1,2-*b*;4,5-*b'*]difuran **4** (2.53 g, 15.6 mmol) in anhydrous THF (150 mL) was added *n*-butyllithium (10.0 mL, 2.5 M in hexanes, 1.6 equiv) by syringe at -78 °C in a N<sub>2</sub> atmosphere. The mixture was stirred for 30 min. The external cool bath was replaced by an ice/water bath and the reaction mixture was stirred at 0–5 °C. Upon completion of the reaction (4 h), DMF (3.6 mL, 46.8 mmol) was added and the mixture was stirred for a further 16 h while the temperature was allowed to increase slowly to room temperature. Then 0.5 M HCl (125 mL) was added at 0 °C to quench the reaction and the mixture was stirred 15 min. The resulting mixture was extracted with AcOEt (3×100 mL), the organic phases were combined and washed with H<sub>2</sub>O (3×50 mL) until neutral pH and finally with brine (2×50 mL). The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated under reduced pressure to yield crude product, which was chromatographed on silica gel (petroleum ether 60-90

°C : ethyl acetate = 3:1) to afford the products **5** (1.98 g, 67%) as yellow powder.

Yield 67%, Yellow powder, mp 133-134 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ: 10.10 (1H, s), 7.08 (1H, s), 4.63 (4H, t, *J* = 8.7 Hz), 3.02 (4H, t, *J* = 8.7 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ: 186.94, 160.93, 126.84, 119.38, 106.71, 73.66, 28.28.

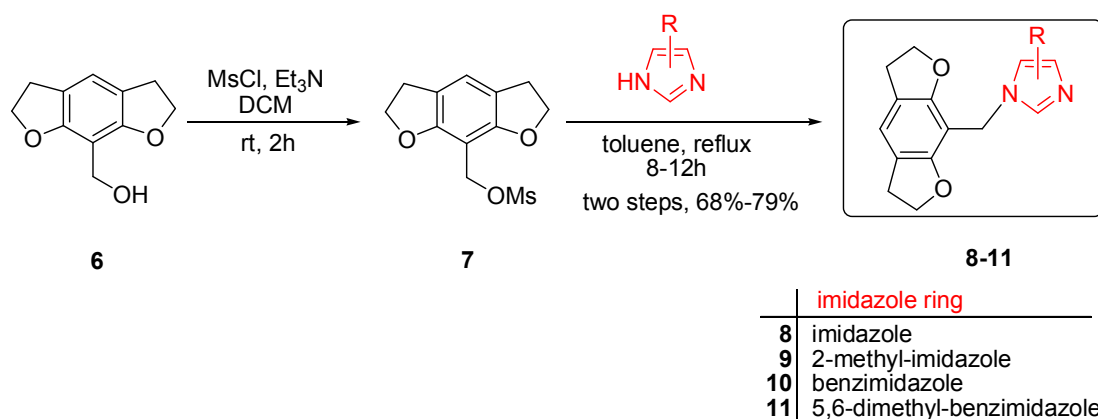
## 2.5 Synthesis of compound **6**



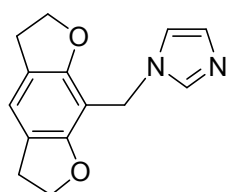
To a stirred solution of tetrahydrobenzo[1,2-*b*;4,5-*b'*]difuran-8-carboxaldehyde **5** (1.98 g, 10.4 mmol) in MeOH (50 mL) at 0 °C was added NaBH<sub>4</sub> (0.40 g, 10.4 mmol) in small portions over a period of 20 minutes, and then at ambient temperature for 2 h. Reaction progress was monitored by TLC. A small amount of water was added and the mixture was stirred for 15 min before rotary evaporation. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel (petroleum ether 60-90 °C : ethyl acetate = 1:1) to afford the products **6** (1.99 g, 99%) as white powder.

Yield 99%, White powder, mp 149-151 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ: 6.81 (1H, s), 4.58 (2H, s), 4.50 (4H, t, *J* = 8.7 Hz), 3.01 (4H, t, *J* = 8.7 Hz), 2.38 (1H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ: 157.95, 119.67, 118.30, 106.45, 72.39, 55.77, 29.39.

## 2.6 Synthesis of compounds 8-11



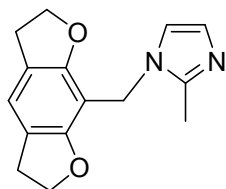
To a solution of tetrahydrobenzo[1,2-*b*;4,5-*b'*]difuran-8-methanol **6** (192 mg, 1 mmol) in dichloromethane (30 mL) was added methanesulfonyl chloride (1.5 mmol) and triethylamine (2 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 2 h. After quenching the reaction with water (30 mL), the layers were separated. The organic phase was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated, and used for the next synthetic step. A mixture of the previous methanesulfonate and imidazole or substituted imidazole (3 mmol) was stirred in toluene (15 mL) at reflux for 8–12 h (monitored by TLC). After cooling to room temperature, the solvent was concentrated, and the residue was diluted with EtOAc (20 mL). The organic layer was washed with water (20 mL) and brine (20 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by column chromatography (silica gel, petroleum ether 60–90 °C : ethyl acetate = 3:1→1:1) to afford **8–11** in 68–79% yield (two steps) as yellow or white powder.



**8**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b'*]difuran-8-yl)methyl)-1*H*-imidazole**

Yield 73%. Yellow powder, mp 116-118 °C. IR  $\nu_{\text{max}}$  (cm<sup>-1</sup>): 3434, 3108, 2972, 2925, 2852, 1616, 1499, 1454, 1323, 1235, 1061, 936, 819, 742, 646. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.60 (1H, s), 7.03 (1H, s), 6.70 (1H, s), 6.91 (1H, s), 4.98 (2H, s), 4.59 (4H,

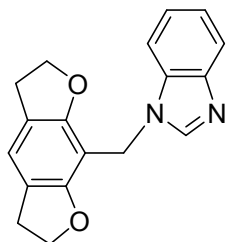
t,  $J = 8.7$  Hz), 3.10 (4H, t,  $J = 8.7$  Hz).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 158.40, 137.54, 128.79, 120.59, 119.42, 118.30, 102.18, 72.52, 39.84, 29.53. HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}_2$   $[\text{M}+1]^+$  243.1128, found 243.1127.



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1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b'*]difuran-8-yl)methyl)-2-methyl-1*H*-imidazole

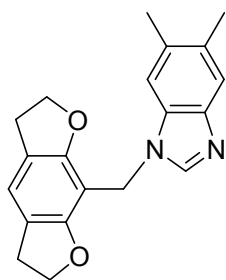
Yield 68%. White powder, mp 133-134 °C. IR  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ): 3421, 2961, 2911, 2852, 1617, 1464, 1432, 1369, 1328, 1265, 1131, 1059, 974, 931, 757, 637.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.00 (1H, d,  $J = 1.2$  Hz), 6.91 (1H, s), 6.81 (1H, d,  $J = 1.2$  Hz), 4.88 (2H, s), 4.58 (4H, t,  $J = 8.7$  Hz), 3.10 (4H, t,  $J = 8.7$  Hz), 2.48 (3H, s).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 158.39, 144.73, 126.51, 120.46, 119.92, 118.31, 102.30, 72.42, 39.13, 29.53, 12.95. HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_2$   $[\text{M}+1]^+$  257.1284, found 257.1280.



10

1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b'*]difuran-8-yl)methyl)-1*H*-benzo[*d*]imidazole

Yield 79%. Yellow powder, mp 179-181 °C. IR  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ): 3432, 3052, 2962, 2908, 1616, 1474, 1368, 1245, 1193, 1057, 1009, 936, 761.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.10 (1H, s), 7.74 (1H, dd,  $J = 7.2, 1.8$  Hz), 7.70 (1H, dd,  $J = 7.2, 1.8$  Hz), 7.28-7.19 (2H, m), 6.87 (1H, s), 5.21 (2H, s), 4.60 (4H, t,  $J = 8.7$  Hz), 3.07 (4H, t,  $J = 8.7$  Hz).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 158.49, 144.17, 143.61, 133.91, 122.50, 121.67, 120.61, 119.87, 118.37, 110.37, 101.58, 72.59, 38.10, 29.48. HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{18}\text{H}_{17}\text{N}_2\text{O}_2$   $[\text{M}+1]^+$  293.1284, found 293.1279.

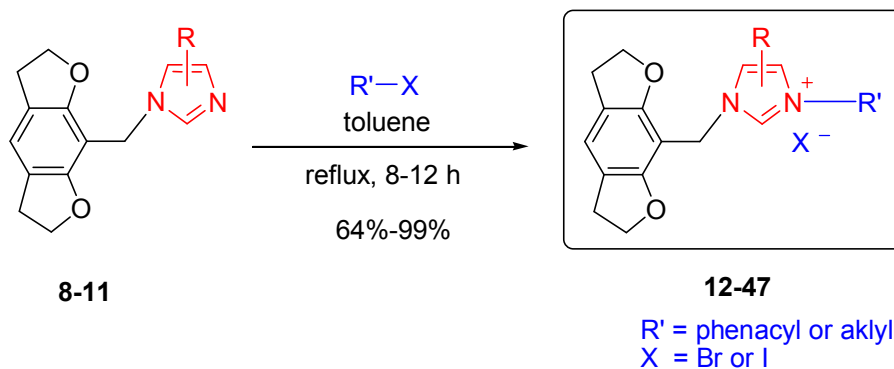


11

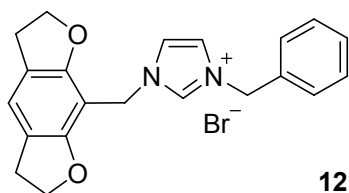
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b'*]difuran-8-yl)methyl)-5,6-dimethyl-1*H*-benzo[*d*]imidazole**

Yield 68%. Yellow powder, mp 184-185 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3430, 3023, 2960, 1619, 1457, 1359, 1223, 1125, 1054, 937, 854, 763. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.98 (1H, s), 7.49 (1H, s), 7.45 (1H, s), 6.87 (1H, s), 5.15 (2H, s), 4.60 (4H, t, *J* = 8.7 Hz), 3.07 (4H, t, *J* = 8.7 Hz), 2.38 (3H, s), 2.34 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.49, 143.43, 142.24, 132.42, 131.41, 130.41, 120.52, 119.86, 118.33, 110.62, 101.77, 72.52, 38.02, 29.53, 20.72, 20.21. HRMS (ESI-TOF) *m/z* Calcd for C<sub>20</sub>H<sub>21</sub>N<sub>2</sub>O<sub>2</sub> [M+1]<sup>+</sup> 321.1597, found 321.1596.

## 2.7 Synthesis of compounds 12-47



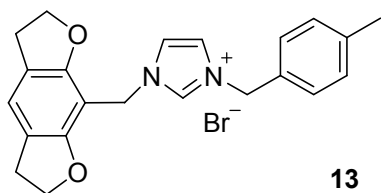
A mixture of tetrahydrobenzo[1,2-*b*;4,5-*b'*]difuran–imidazole hybrids **8–11** (0.2 mmol) and phenacyl bromides or alkyl bromides (0.24 mmol) was stirred in toluene (5 ml) at reflux for 8-12 h. An insoluble substance was formed. After completion of the reaction as indicated by TLC, the precipitate was filtered through a small pad of Celite, and washed with toluene (3 × 10 ml), then dried to afford imidazolium salts **12-47** in 64–99% yields.



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**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*:4,5-*b'*]  
difuran-8-yl)methyl)-3-  
benzyl-1*H*-imidazol-3-ium bromide**

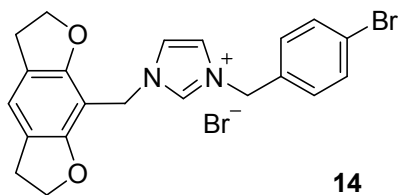
Yield 92%. Brown oil, IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3420, 3047, 2972, 2852, 1619, 1556, 1457, 1326, 1239, 1147, 1066, 933, 765, 718, 645. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.09 (1H, s), 7.55-7.51 (2H, m), 7.48 (1H, s), 7.36-7.34 (3H, m), 7.21 (1H, s), 6.97 (1H, s), 5.72 (2H, s), 5.24 (2H, s), 4.60 (4H, t,  $J = 8.7$  Hz), 3.11 (4H, t,  $J = 8.7$  Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.37, 136.36, 133.43, 129.24, 129.19, 122.24, 122.14, 121.19, 118.74, 98.28, 73.05, 53.24, 43.48, 29.36. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>21</sub>H<sub>21</sub>N<sub>2</sub>O<sub>2</sub> [M-Br]<sup>+</sup> 333.1597, found 333.1596.



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**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*:4,5-*b'*]  
difuran-8-yl)methyl)-3-  
(4-methylbenzyl)-1*H*-imidazol-3-ium  
bromide**

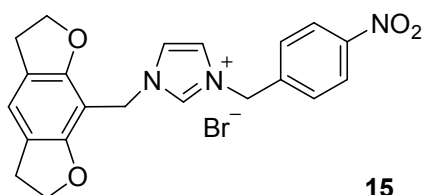
Yield 83%. Brown oil, IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3420, 3044, 2969, 2852, 1619, 1556, 1457, 1325, 1238, 1145, 1065, 934, 758, 642. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.09 (1H, s), 7.45 (2H, d,  $J = 1.6$  Hz), 7.41 (2H, d,  $J = 8.1$  Hz), 7.20 (1H, t,  $J = 1.6$  Hz), 7.15 (2H, d,  $J = 8.1$  Hz), 6.97 (1H, s), 5.66 (2H, s), 5.23 (2H, s), 4.60 (4H, t,  $J = 8.7$  Hz), 3.11 (4H, t,  $J = 8.7$  Hz), 2.32 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.38, 139.23, 136.50, 130.37, 129.88, 129.17, 122.12, 121.86, 118.71, 98.28, 73.03, 53.06, 43.43, 29.36, 21.17. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>22</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub> [M-Br]<sup>+</sup> 347.1751, found 347.1754.



14

**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(4-bromobenzyl)-1*H*-imidazol-3-ium bromide**

Yield 88%. Brown powder, mp 105-107 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3434, 3371, 3067, 2971, 2848, 1618, 1555, 1462, 1325, 1242, 1145, 1064, 1014, 755, 654. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.12 (1H, s), 7.65-7.62 (1H, m), 7.54 (2H, d,  $J$  = 8.3 Hz), 7.47-7.44 (2H, m), 7.20 (1H, s), 6.97 (1H, s), 5.77 (2H, s), 5.21 (2H, s), 4.60 (4H, t,  $J$  = 8.1 Hz), 3.11 (4H, t,  $J$  = 8.1 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.34, 136.50, 132.76, 132.32, 131.08, 123.47, 122.50, 122.20, 121.94, 118.74, 98.15, 73.07, 52.18, 43.39, 29.36. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>21</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>Br [M-Br]<sup>+</sup> 411.0702, found 411.0708.

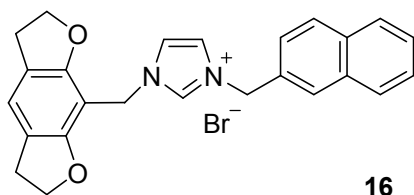


15

**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(4-nitrobenzyl)-1*H*-imidazol-3-ium bromide**

Yield 95%. Yellow powder, mp 280-282 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3417, 3084, 3023, 2967, 2860, 1610, 1522, 1466, 1342, 1239, 1149, 1066, 937, 871, 725, 642. <sup>1</sup>H-NMR (300 MHz, DMSO)  $\delta$ : 9.41 (1H, s), 8.29 (2H, d,  $J$  = 8.7 Hz), 7.88 (1H, s), 7.70 (1H, s), 7.68 (2H, d,  $J$  = 8.7 Hz), 7.11 (1H, s), 5.66 (2H, s), 5.27 (2H, s), 4.59 (4H, t,  $J$  = 8.7 Hz), 3.11 (4H, t,  $J$  = 8.7 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 157.83, 147.55, 142.23, 136.63, 129.34, 123.97, 123.12, 122.83, 121.84, 118.67, 98.69, 72.66, 50.90, 42.92, 28.80. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>21</sub>H<sub>20</sub>N<sub>3</sub>O<sub>4</sub> [M-Br]<sup>+</sup> 378.1448, found 378.1448.

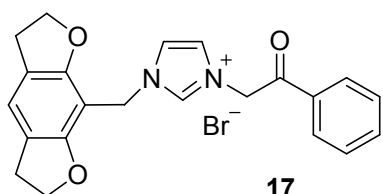




16

1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-naphthylmethyl)-1*H*-imidazol-3-ium bromide

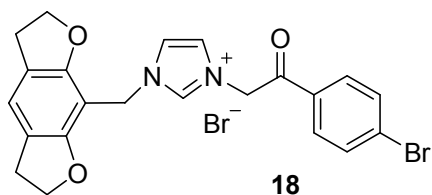
Yield 90%. Brown powder, mp 159-161 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3415, 3052, 2975, 2852, 1618, 1556, 1459, 1325, 1237, 1147, 1065, 924, 766, 731, 650. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.12 (1H, s), 8.02 (1H, s), 7.85-7.78 (3H, m), 7.59 (1H, d, *J* = 8.3 Hz), 7.52-7.47 (3H, m), 7.17 (1H, s), 6.94 (1H, s), 5.88 (2H, s), 5.57 (2H, s), 4.56 (4H, t, *J* = 8.7 Hz), 3.07 (4H, t, *J* = 8.7 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.34, 136.60, 133.29, 133.12, 130.79, 129.26, 128.86, 128.16, 127.69, 126.89, 126.67, 126.04, 122.37, 122.12, 121.91, 118.71, 98.26, 73.02, 53.38, 43.46, 29.33. HRMS (ESI-TOF) *m/z* Calcd for C<sub>25</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub> [M-Br]<sup>+</sup> 383.1754, found 383.1756.



17

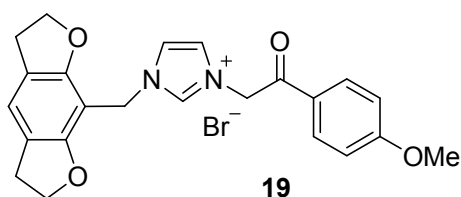
1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-oxo-2-phenylethyl)-1*H*-imidazol-3-ium bromide

Yield 91%. White powder, mp 247-248 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3418, 3037, 2966, 2844, 1696, 1614, 1557, 1461, 1338, 1231, 1155, 1064, 991, 931, 764, 660. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 9.78 (1H, s), 8.15 (2H, d, *J* = 7.5 Hz), 7.63-7.61 (1H, m), 7.56-7.49 (3H, m), 7.31 (1H, s), 7.00 (1H, s), 6.57 (2H, s), 5.24 (2H, s), 4.68 (4H, t, *J* = 8.7 Hz), 3.15 (4H, t, *J* = 8.7 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 190.95, 158.41, 137.46, 134.70, 133.53, 129.16, 128.78, 124.24, 122.35, 121.20, 118.83, 98.11, 73.19, 56.09, 43.58, 29.41. HRMS (ESI-TOF) *m/z* Calcd for C<sub>22</sub>H<sub>21</sub>N<sub>2</sub>O<sub>3</sub> [M-Br]<sup>+</sup> 361.1546, found 361.1545.



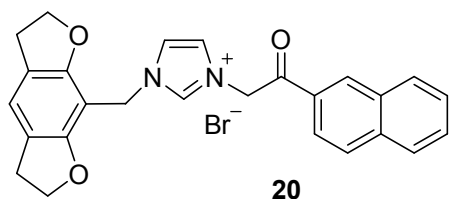
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(4-bromophenyl)-2-oxoethyl)-1H-imidazol-3-ium bromide**

Yield 95%. White powder, mp 232-233 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3414, 3072, 2964, 2905, 2852, 1700, 1583, 1463, 1397, 1334, 1232, 1158, 1066, 990, 825, 766, 627. <sup>1</sup>H-NMR (300 MHz, MeOD)  $\delta$ : 9.01 (1H, s), 7.99 (2H, d,  $J = 8.7$  Hz), 7.78 (2H, d,  $J = 8.7$  Hz), 7.65 (1H, d,  $J = 1.5$  Hz), 7.59 (1H, d,  $J = 1.5$  Hz), 7.09 (1H, s), 5.98 (2H, s), 5.37 (2H, s), 4.67 (4H, t,  $J = 8.7$  Hz), 3.17 (4H, t,  $J = 8.7$  Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 191.21, 159.72, 138.89, 134.12, 133.51, 131.05, 130.60, 125.45, 123.41, 123.33, 120.39, 100.06, 74.23, 56.50, 44.37, 30.33. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>22</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>Br [M-Br]<sup>+</sup> 439.0651, found 439.0651.



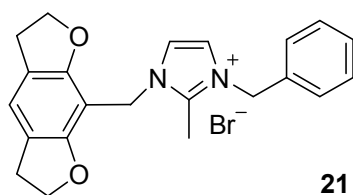
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(4-methoxyphenyl)-2-oxoethyl)-1H-imidazol-3-ium bromide**

Yield 95%. Yellow powder, mp 163-165 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3426, 3075, 2965, 2848, 1687, 1604, 1510, 1461, 1323, 1244, 1163, 1065, 1022, 933, 834, 773, 633. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 9.65 (1H, s), 8.12 (2H, d,  $J = 8.7$  Hz), 7.61 (1H, s), 7.30 (1H, d,  $J = 3.9$  Hz), 6.98 (2H, d,  $J = 5.4$  Hz), 6.95 (1H, s), 6.45 (2H, s), 5.23 (2H, s), 4.67 (4H, t,  $J = 8.7$  Hz), 3.86 (3H, s), 3.14 (4H, t,  $J = 8.7$  Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 189.13, 164.73, 158.38, 137.25, 131.25, 126.49, 124.38, 122.29, 121.15, 118.80, 114.37, 98.17, 73.15, 55.62, 43.49, 29.39. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>23</sub>H<sub>23</sub>N<sub>2</sub>O<sub>4</sub> [M-Br]<sup>+</sup> 391.1652, found 391.1655.



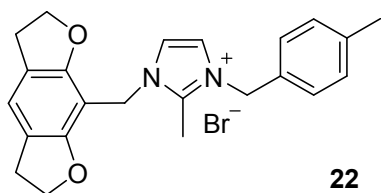
**20**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(naphthalen-2-yl)-2-oxoethyl)-1*H*-imidazol-3-ium bromide**

Yield 90%. White powder, mp 222-223 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3410, 3036, 2970, 2902, 1694, 1621, 1562, 1464, 1331, 1231, 1159, 1067, 934, 819, 755, 631. <sup>1</sup>H-NMR (300 MHz, MeOD)  $\delta$ : 9.07 (1H, s), 8.74 (1H, s), 8.12 (1H, d,  $J = 7.8$  Hz), 8.07-7.96 (3H, m), 7.72-7.61 (4H, m), 7.08 (1H, s), 6.15 (2H, s), 5.36 (2H, s), 4.67 (4H, t,  $J = 8.7$  Hz), 3.16 (4H, t,  $J = 8.7$  Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 191.89, 159.72, 138.94, 137.62, 133.93, 132.43, 131.77, 130.90, 130.46, 130.02, 128.98, 128.38, 125.54, 124.26, 123.33, 120.39, 100.08, 74.25, 56.66, 44.38, 30.34. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>26</sub>H<sub>23</sub>N<sub>2</sub>O<sub>3</sub> [M-Br]<sup>+</sup> 411.1703, found 411.1705.



**21**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-benzyl-2-methyl-1*H*-imidazol-3-ium bromide**

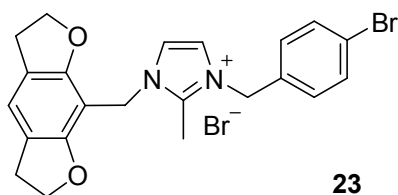
Yield 84%. Yellow powder, mp 199-201 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3417, 3074, 2968, 2905, 1614, 1527, 1453, 1330, 1250, 1182, 1059, 1011, 942, 727, 641. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.82 (1H, d,  $J = 1.8$  Hz), 7.42 (1H, d,  $J = 1.8$  Hz), 7.40 (1H, d,  $J = 1.2$  Hz), 7.38-7.32 (4H, m), 6.98 (1H, s), 5.67 (2H, s), 5.09 (2H, s), 4.60 (4H, t,  $J = 8.7$  Hz), 3.12 (4H, t,  $J = 8.7$  Hz), 2.88 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.09, 143.92, 133.27, 129.20, 128.86, 128.46, 122.45, 122.03, 121.61, 118.77, 98.62, 73.01, 52.40, 42.33, 29.35, 10.92. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>22</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub> [M-Br]<sup>+</sup> 347.1754, found 347.1753.



**22**

**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(4-methylbenzyl)-2-methyl-1*H*-imidazol-3-ium bromide**

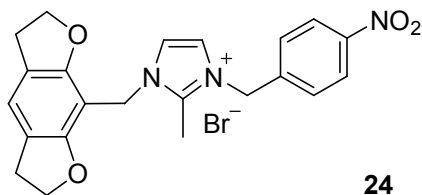
Yield 97%. Yellow powder, mp 207-209 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3416, 3048, 2961, 1619, 1522, 1457, 1361, 1255, 1177, 1060, 976, 931, 759, 672. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.69 (1H, s), 7.30-7.26 (3H, m), 7.15 (2H, d,  $J$  = 7.8 Hz), 6.98 (1H, s), 5.58 (2H, s), 5.09 (2H, s), 4.61 (4H, t,  $J$  = 8.7 Hz), 3.13 (4H, t,  $J$  = 8.7 Hz), 2.32 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.13, 143.85, 138.90, 130.15, 129.89, 128.47, 122.23, 122.03, 121.57, 118.79, 98.69, 73.02, 52.34, 42.28, 29.37, 21.15, 10.91. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>23</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub> [M-Br]<sup>+</sup> 361.1910, found 361.1915.



**23**

**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(4-bromobenzyl)-2-methyl-1*H*-imidazol-3-ium bromide**

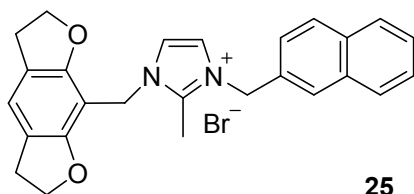
Yield 79%. Yellow powder, mp 117-118 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3453, 3023, 2971, 2893, 1619, 1516, 1454, 1342, 1250, 1174, 1060, 1010, 934, 753, 674. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.91 (1H, d,  $J$  = 1.8 Hz), 7.46 (2H, d,  $J$  = 8.4 Hz), 7.39 (2H, d,  $J$  = 8.4 Hz), 7.29 (1H, d,  $J$  = 1.8 Hz), 6.98 (1H, s), 5.73 (2H, s), 5.08 (2H, s), 4.60 (4H, t,  $J$  = 8.7 Hz), 3.13 (4H, t,  $J$  = 8.7 Hz), 2.88 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.10, 143.99, 132.48, 132.28, 130.47, 123.04, 122.44, 122.07, 121.65, 118.80, 98.57, 73.04, 51.55, 42.35, 29.37, 10.94. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>22</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>Br [M-Br]<sup>+</sup> 425.0859, found 425.0852.



24

**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(4-nitrobenzyl)-2-methyl-1*H*-imidazol-3-ium bromide**

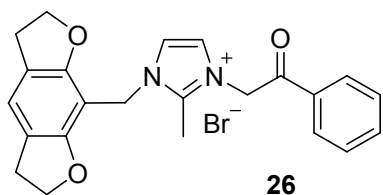
Yield 97%. Yellow powder, mp 199-201 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3424, 3050, 2959, 2913, 1611, 1520, 1458, 1345, 1254, 1181, 1061, 932, 857, 771, 734. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.13 (2H, d,  $J$  = 8.7 Hz), 8.12 (1H, s), 7.75 (2H, d,  $J$  = 8.7 Hz), 7.34 (1H, d,  $J$  = 1.8 Hz), 6.99 (1H, s), 6.06 (2H, s), 5.09 (2H, s), 4.60 (4H, t,  $J$  = 8.7 Hz), 3.13 (4H, t,  $J$  = 8.7 Hz), 2.90 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.09, 147.90, 144.30, 140.76, 129.60, 124.15, 122.79, 122.16, 121.91, 118.84, 98.43, 73.08, 51.13, 42.49, 29.36, 10.95. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>22</sub>H<sub>22</sub>N<sub>3</sub>O<sub>4</sub> [M-Br]<sup>+</sup> 392.1604, found 392.1604.



25

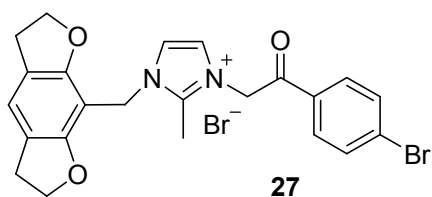
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-naphthylmethyl)-2-methyl-1*H*-imidazol-3-ium bromide**

Yield 91%. Yellow powder, mp 115-117 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3425, 3048, 2961, 1618, 1522, 1456, 1330, 1252, 1181, 1060, 976, 931, 765, 661. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.90 (1H, s), 7.85-7.77 (4H, m), 7.50-7.46 (3H, m), 7.29 (1H, s), 6.96 (1H, s), 5.82 (2H, s), 5.06 (2H, s), 4.58 (4H, t,  $J$  = 8.7 Hz), 3.10 (4H, t,  $J$  = 8.7 Hz), 2.88 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.12, 144.06, 133.12, 130.63, 129.22, 128.13, 127.98, 127.67, 126.79, 126.69, 125.56, 122.44, 122.01, 121.62, 118.77, 98.67, 73.00, 52.65, 42.30, 29.36, 10.94. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>26</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub> [M-Br]<sup>+</sup> 397.1910, found 397.1909.



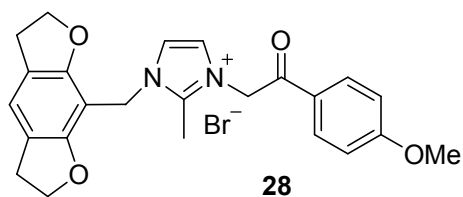
**26**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-oxo-2-phenylethyl)-2-methyl-1H-imidazol-3-ium bromide**

Yield 98%. White powder, mp 232-234 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3427, 3060, 2902, 1696, 1615, 1530, 1454, 1333, 1234, 1185, 1060, 996, 936, 761, 687. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.22 (2H, d,  $J$  = 8.4 Hz) 7.79 (1H, s), 7.62-7.60 (1H, m), 7.53-7.48 (2H, m), 7.35 (1H, s), 7.01 (1H, s), 6.55 (2H, s), 5.12 (2H, s), 4.65 (4H, t,  $J$  = 8.7 Hz), 3.16 (4H, t,  $J$  = 8.7 Hz), 2.78 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 191.03, 158.15, 145.35, 134.67, 133.45, 129.10, 128.99, 123.44, 122.21, 121.19, 118.86, 98.44, 73.08, 56.48, 42.29, 29.40, 10.57. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>23</sub>H<sub>23</sub>N<sub>2</sub>O<sub>3</sub> [M-Br]<sup>+</sup> 375.1703, found 375.1705.



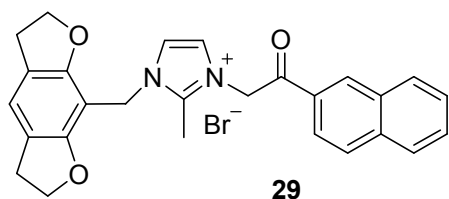
**27**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-oxo-2-(4-bromophenyl)-2-methyl-1H-imidazol-3-ium bromide**

Yield 79%. Yellow powder, mp 227-229 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3441, 3070, 2962, 2905, 1696, 1622, 1584, 1528, 1461, 1396, 1332, 1233, 1180, 1064, 993, 933, 826, 763. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.14 (2H, d,  $J$  = 8.4 Hz), 7.82 (1H, d,  $J$  = 1.5 Hz), 7.63 (2H, d,  $J$  = 8.4 Hz), 7.34 (1H, d,  $J$  = 1.5 Hz), 7.01 (1H, s), 6.62 (2H, s), 5.12 (2H, s), 4.65 (4H, t,  $J$  = 8.7 Hz), 3.16 (4H, t,  $J$  = 8.7 Hz), 2.79 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 190.45, 158.15, 145.41, 132.39, 132.26, 130.60, 130.07, 123.40, 122.23, 121.21, 118.86, 98.40, 73.10, 56.45, 42.32, 29.40, 10.60. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>23</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>Br [M-Br]<sup>+</sup> 453.0808, found 453.0811.



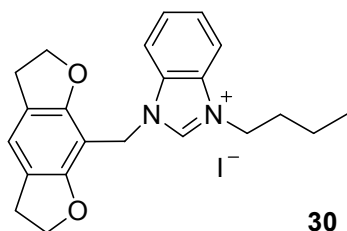
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(4-methoxyphenyl)-2-oxoethyl)-2-methyl-1*H*-imidazol-3-ium bromide**

Yield 86%. White powder, mp 209-210 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3437, 3039, 2950, 2908, 1679, 1602, 1514, 1455, 1326, 1242, 1178, 1063, 1011, 935, 756. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.23 (2H, d,  $J$  = 8.7 Hz), 7.70 (1H, d,  $J$  = 1.8 Hz), 7.34 (1H, d,  $J$  = 1.8 Hz), 7.30 (1H, s), 7.00 (1H, s), 6.98 (2H, d,  $J$  = 8.7 Hz), 6.44 (2H, s), 5.10 (2H, s), 4.65 (4H, t,  $J$  = 8.7 Hz), 3.87 (3H, s), 3.16 (4H, t,  $J$  = 8.7 Hz), 2.78 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 189.19, 164.79, 158.14, 145.31, 131.53, 126.40, 123.38, 122.20, 121.13, 118.85, 114.38, 98.45, 73.07, 56.07, 55.62, 42.25, 29.39, 10.52. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>24</sub>H<sub>25</sub>N<sub>2</sub>O<sub>4</sub> [M-Br]<sup>+</sup> 405.1808, found 405.1812.



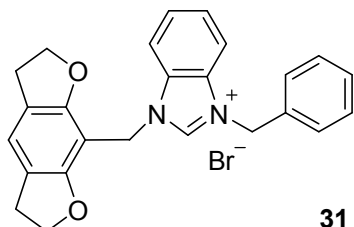
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(naphthalen-2-yl)-2-oxoethyl)-2-methyl-1*H*-imidazol-3-ium bromide**

Yield 93%. Yellow powder, mp 146-148 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3399, 3054, 2954, 2910, 1689, 1621, 1526, 1460, 1366, 1262, 1182, 1061, 933, 822, 750. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 9.08 (1H, s), 8.13 (1H, d,  $J$  = 6.6 Hz), 8.02 (1H, d,  $J$  = 7.8 Hz), 7.83-7.77 (3H, m), 7.57-7.55 (1H, m), 7.50-7.48 (1H, m), 7.32 (1H, s), 6.99 (1H, s), 6.60 (2H, s), 5.08 (2H, s), 4.63 (4H, t,  $J$  = 8.1 Hz), 3.13 (4H, t,  $J$  = 8.1 Hz), 2.78 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 191.02, 158.13, 145.30, 136.08, 132.47, 132.17, 130.65, 129.21, 128.74, 127.51, 126.89, 123.42, 123.31, 122.15, 121.20, 118.82, 98.45, 73.06, 56.25, 42.26, 29.37, 10.55. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>27</sub>H<sub>25</sub>N<sub>2</sub>O<sub>3</sub> [M-Br]<sup>+</sup> 425.1859, found 425.1868.



**30**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-butyl-1*H*-benzo[*d*]imidazol-3-ium iodide**

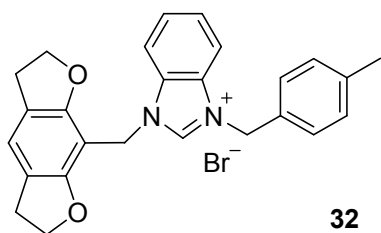
Yield 77%. White powder, mp 215-217 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3434, 3055, 2947, 1621, 1560, 1459, 1330, 1239, 1191, 1066, 936, 766. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.54 (1H, s), 7.90-7.86 (1H, m), 7.75-7.71 (1H, m), 7.65-7.58 (2H, m), 6.96 (1H, s), 5.60 (2H, s), 4.75 (2H, t, *J* = 7.5 Hz), 4.68 (4H, t, *J* = 8.7 Hz), 3.12 (4H, t, *J* = 8.7 Hz), 2.07-1.97 (2H, m), 1.50-1.40 (2H, m), 0.99 (3H, t, *J* = 7.5 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.29, 142.19, 131.20, 130.96, 127.21, 127.08, 121.95, 118.79, 113.55, 113.03, 98.06, 73.24, 47.48, 41.47, 31.26, 29.32, 19.55, 13.55. HRMS (ESI-TOF) *m/z* Calcd for C<sub>22</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub> [M-I]<sup>+</sup> 349.1910, found 349.1910.



**31**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-benzyl-1*H*-benzo[*d*]imidazol-3-ium bromide**

Yield 85%. White powder, mp 234-236 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3453, 3108, 2965, 1616, 1555, 1463, 1371, 1330, 1234, 1197, 1130, 1065, 1014, 935, 756, 704. <sup>1</sup>H-NMR (300 MHz, MeOD)  $\delta$ : 9.79 (1H, s), 7.95 (1H, dd, *J* = 1.5, 2.1 Hz), 7.88 (1H, dd, *J* = 2.1, 1.8 Hz), 7.67-7.58 (2H, m), 7.50-7.40 (5H, m), 7.03 (1H, s), 5.81 (2H, s), 5.62 (2H, s), 4.64 (4H, t, *J* = 8.7 Hz), 3.11 (4H, t, *J* = 8.7 Hz). <sup>13</sup>C-NMR (75 MHz, MeOD)  $\delta$ : 159.50, 143.75, 134.93, 132.75, 132.64, 130.45, 130.29, 129.30, 128.34, 128.27, 123.13, 120.50, 114.92, 114.69, 99.72, 74.37, 51.78, 42.41, 30.21. HRMS (ESI-TOF) *m/z* Calcd for C<sub>25</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub> [M-Br]<sup>+</sup> 383.1754, found 383.1753.

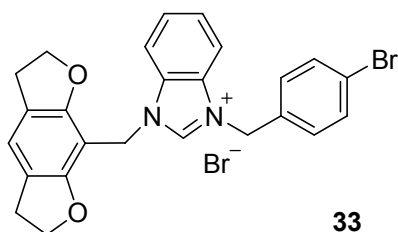




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**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(4-methylbenzyl)-1*H*-benzo[*d*]imidazol-3-ium bromide**

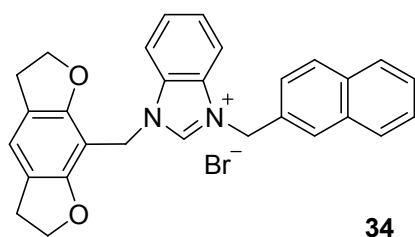
Yield 77%. Yellow powder, mp 119-122 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3403, 3112, 3015, 2967, 1615, 1555, 1460, 1367, 1329, 1230, 1192, 1126, 1063, 1013, 932, 763. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.85 (1H, s), 7.74 (1H, d,  $J$  = 7.2 Hz), 7.58 (1H, dd,  $J$  = 8.4, 1.5 Hz), 7.50-7.42 (2H, m), 7.34 (2H, d,  $J$  = 7.5 Hz), 7.08 (2H, d,  $J$  = 7.5 Hz), 6.88 (1H, s), 5.90 (2H, s), 5.52 (2H, s), 4.58 (4H, t,  $J$  = 8.7 Hz), 3.03 (4H, t,  $J$  = 8.7 Hz), 2.23 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.27, 143.05, 138.93, 131.12, 130.20, 129.79, 128.29, 126.99, 126.89, 121.85, 118.77, 113.60, 113.40, 98.17, 73.17, 50.97, 41.47, 29.29, 21.13. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>26</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub> [M-Br]<sup>+</sup> 397.1910, found 397.1912.



33

**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(4-bromobenzyl)-1*H*-benzo[*d*]imidazol-3-ium bromide**

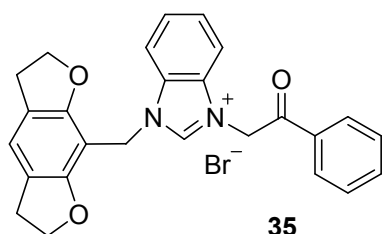
Yield 70%. Yellow powder, mp 138-141 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3414, 3019, 2927, 1617, 1557, 1449, 1371, 1333, 1234, 1190, 1126, 1065, 1012, 930, 756. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.99 (1H, s), 7.77 (1H, dd,  $J$  = 8.4, 1.5 Hz), 7.68 (1H, dd,  $J$  = 8.4, 1.5 Hz), 7.57-7.45 (4H, m), 7.37 (2H, d,  $J$  = 8.1 Hz), 6.90 (1H, s), 6.06 (2H, s), 5.51 (2H, s), 4.60 (4H, t,  $J$  = 8.7 Hz), 3.05 (4H, t,  $J$  = 8.7 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.27, 143.02, 132.50, 132.21, 131.03, 130.26, 127.08, 123.10, 121.94, 118.80, 113.67, 113.46, 98.01, 73.22, 50.25, 41.51, 29.30. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>25</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>Br [M-Br]<sup>+</sup> 461.0859, found 461.0858.



**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-naphthylmethyl)-1*H*-benzo[*d*]imidazol-3-ium bromide**

**34**

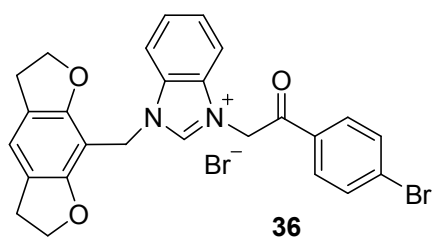
Yield 64%. White powder, mp 145-147 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3408, 3111, 2963, 1617, 1558, 1462, 1371, 1332, 1236, 1192, 1131, 1013, 930, 756. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 11.03 (1H, s), 7.99 (1H, s), 7.77-7.65 (5H, m), 7.55 (1H, d,  $J = 8.1$  Hz), 7.43-7.40 (4H, m), 6.86 (1H, s), 6.17 (2H, s), 5.50 (2H, s), 4.55 (4H, t,  $J = 8.1$  Hz), 3.01 (4H, t,  $J = 8.1$  Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.27, 143.22, 133.15, 133.06, 131.17, 131.02, 130.71, 129.14, 128.03, 127.95, 127.67, 126.94, 126.75, 126.64, 125.37, 121.86, 118.74, 113.72, 113.33, 98.05, 73.16, 51.25, 41.48, 29.28. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>29</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub> [M-Br]<sup>+</sup> 433.1910, found 433.1910.



**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-oxo-2-phenylethyl)-1*H*-benzo[*d*]imidazol-3-ium bromide**

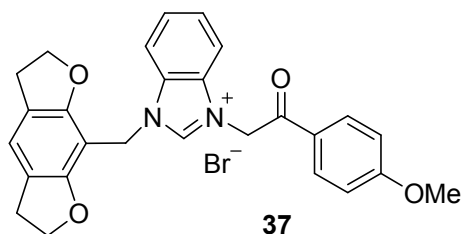
**35**

Yield 95%. Yellow powder, mp 193-195 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3400, 3019, 2948, 1695, 1615, 1561, 1448, 1350, 1232, 1066, 980, 935, 757, 689. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.48 (1H, s), 8.21 (1H, s), 8.19 (1H, s), 7.94 (1H, d,  $J = 7.5$  Hz), 7.67-7.51 (6H, m), 6.97 (1H, s), 6.86 (2H, s), 5.52 (2H, s), 4.72 (4H, t,  $J = 8.7$  Hz), 3.13 (4H, t,  $J = 8.7$  Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 190.54, 143.57, 134.67, 133.66, 132.21, 130.78, 129.15, 128.81, 127.06, 126.99, 122.17, 118.85, 113.36, 113.20, 97.69, 73.34, 54.12, 41.38, 29.35. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>26</sub>H<sub>23</sub>N<sub>2</sub>O<sub>3</sub> [M-Br]<sup>+</sup> 411.1703, found 411.1707.



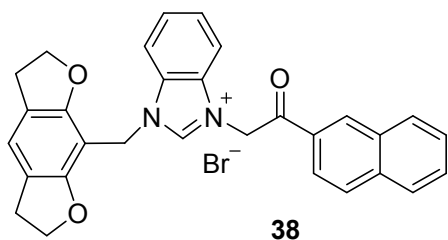
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(4-bromophenyl)-2-oxoethyl)-1H-benzo[*d*]imidazol-3-ium bromide**

Yield 88%. White powder, mp 227-229 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3419, 3015, 2959, 1698, 1626, 1567, 1463, 1353, 1229, 1067, 984, 758. <sup>1</sup>H-NMR (300 MHz, DMSO)  $\delta$ : 9.72 (1H, s), 8.11-8.00 (4H, m), 7.90 (2H, d,  $J$  = 8.7 Hz), 7.75-7.64 (2H, m), 7.10 (1H, s), 6.47 (2H, s), 5.65 (2H, s), 4.64 (4H, t,  $J$  = 8.7 Hz), 3.10 (4H, t,  $J$  = 8.7 Hz). <sup>13</sup>C-NMR (75 MHz, DMSO)  $\delta$ : 190.65, 157.94, 143.47, 132.82, 132.10, 131.93, 130.34, 128.63, 126.77, 121.96, 118.74, 114.09, 113.32, 98.12, 72.86, 53.33, 40.88, 28.77. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>26</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>Br [M-Br]<sup>+</sup> 489.0808, found 489.0805.



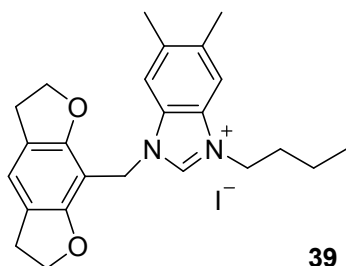
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(4-methoxyphenyl)-2-oxoethyl)-1H-benzo[*d*]imidazol-3-ium bromide**

Yield 96%. White powder, mp 232-233 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3417, 3015, 2958, 1687, 1603, 1563, 1461, 1350, 1240, 1177, 1066, 1018, 980, 834, 760. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.40 (1H, s), 8.22 (2H, d,  $J$  = 8.7 Hz), 7.93 (1H, dd,  $J$  = 6.6, 2.2 Hz), 7.61-7.56 (3H, m), 7.01 (2H, d,  $J$  = 8.7 Hz), 6.97 (1H, s), 6.77 (2H, s), 5.51 (2H, s), 4.72 (4H, t,  $J$  = 8.7 Hz), 3.89 (3H, s), 3.13 (4H, t,  $J$  = 8.7 Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 188.74, 164.78, 158.43, 143.47, 132.32, 131.32, 130.79, 127.00, 126.92, 126.64, 122.15, 118.84, 114.41, 113.37, 113.29, 97.72, 73.33, 55.65, 53.75, 41.33, 29.35. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>27</sub>H<sub>25</sub>N<sub>2</sub>O<sub>4</sub> [M-Br]<sup>+</sup> 441.1808, found 441.1808.



**38**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(naphthalen-2-yl)-2-oxoethyl)-1H-benzo[*d*]imidazol-3-ium bromide**

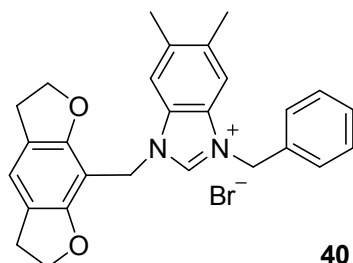
Yield 86%. Yellow powder, mp 188-190 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3415, 3036, 2962, 2893, 1690, 1620, 1559, 1463, 1362, 1231, 1188, 1059, 939, 820, 759. <sup>1</sup>H-NMR (300 MHz, DMSO)  $\delta$ : 9.81 (1H, s), 8.97 (1H, s), 8.23 (1H, d,  $J = 7.5$  Hz), 8.15-8.01 (5H, m), 7.77-7.64 (4H, m), 7.09 (1H, s), 6.65 (2H, s), 5.66 (2H, s), 4.65 (4H, t,  $J = 8.4$  Hz), 3.10 (4H, t,  $J = 8.4$  Hz). <sup>13</sup>C-NMR (75 MHz, DMSO)  $\delta$ : 191.14, 157.95, 143.57, 135.53, 132.01, 131.04, 130.91, 130.38, 129.66, 129.30, 128.64, 127.84, 127.34, 126.78, 123.31, 121.94, 118.74, 114.10, 113.31, 98.13, 72.87, 53.43, 40.91, 28.79. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>30</sub>H<sub>25</sub>N<sub>2</sub>O<sub>3</sub> [M-Br]<sup>+</sup> 461.1859, found 461.1860.



**39**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-butyl-5,6-dimethyl-1H-benzo[*d*]imidazol-3-ium iodide**

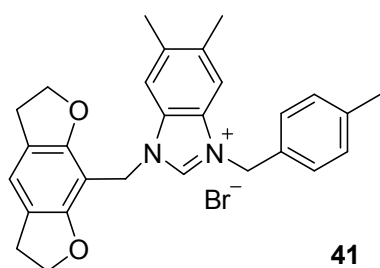
Yield 75%. Yellow powder, mp 206-207 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3428, 3116, 2956, 1619, 1558, 1462, 1341, 1240, 1135, 1065, 1015, 939, 865, 765. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.23 (1H, s), 7.57 (1H, s), 7.41 (1H, s), 6.91(1H, s), 5.46 (2H, s), 4.62 (4H, t,  $J = 8.7$  Hz), 3.07 (4H, t,  $J = 8.7$  Hz), 2.38 (3H, s), 2.37 (3H, s) 1.98-1.89 (2H, m), 1.45-1.33 (2H,m), 0.93 (3H, t,  $J = 7.2$  Hz). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 18.32, 140.99, 137.09, 129.76, 129.53, 121.88, 118.77, 113.32, 112.58, 98.27, 73.17, 47.31,

41.21, 31.29, 29.36, 20.87, 20.66, 19.54, 13.58. HRMS (ESI-TOF)  $m/z$  Calcd for  $C_{24}H_{29}N_2O_2$   $[M-I]^+$  377.2223, found 377.2221.



**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-benzyl-5,6-dimethyl-1*H*-benzo[*d*]imidazol-3-ium bromide**

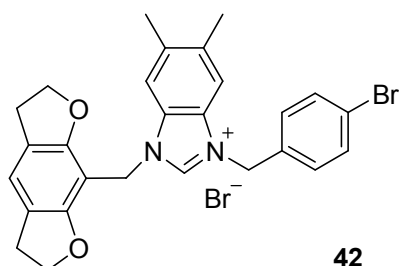
Yield 96%. White powder, mp 229-230 °C. IR  $\nu_{\max}$  ( $\text{cm}^{-1}$ ): 3411, 3113, 2959, 1619, 1557, 1455, 1344, 1235, 1130, 1064, 936, 859, 710.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 10.85 (1H, s), 7.55 (1H, s), 7.49-7.47 (2H, d,  $J = 6.0$  Hz), 7.35-7.32 (4H, m), 6.94 (1H, s), 5.97 (2H, s), 5.51 (2H, s), 4.63 (4H, t,  $J = 8.7$  Hz), 3.10 (4H, t,  $J = 8.7$  Hz), 2.36 (3H, s), 2.34 (3H, s).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 158.27, 142.06, 136.96, 133.59, 129.70, 129.55, 129.08, 128.80, 128.13, 121.80, 118.73, 113.19, 113.03, 98.27, 73.09, 50.75, 41.24, 29.31, 20.81, 20.62. HRMS (ESI-TOF)  $m/z$  Calcd for  $C_{27}H_{27}N_2O_2$   $[M-\text{Br}]^+$  411.2067, found 411.2068.



**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(4-methylbenzyl)-5,6-dimethyl-1*H*-benzo[*d*]imidazol-3-ium bromide**

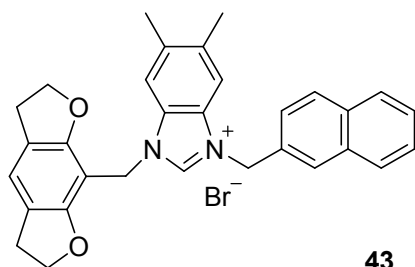
Yield 83%. Yellow powder, mp 232-234 °C. IR  $\nu_{\max}$  ( $\text{cm}^{-1}$ ): 3403, 3105, 2965, 1619, 1554, 1460, 1344, 1238, 1195, 1128, 1064, 939, 863, 763.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 10.76 (1H, s), 7.48 (1H, s), 7.32-7.29 (3H, m), 7.07 (2H, d,  $J = 7.8$  Hz), 6.88 (1H, s), 5.84 (2H, s), 5.45 (2H, s), 4.58 (4H, t,  $J = 8.7$  Hz), 3.04 (4H, t,  $J = 8.7$

Hz), 2.30 (3H, s), 2.28 (3H, s), 2.23 (3H, s).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 158.28, 141.99, 138.72, 136.92, 130.53, 129.71, 129.60, 128.10, 121.77, 118.72, 113.16, 113.07, 98.31, 73.08, 50.63, 41.21, 29.31, 21.13, 20.80, 20.62. HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{28}\text{H}_{29}\text{N}_2\text{O}_2$   $[\text{M-Br}]^+$  425.2223, found 425.2223.



**42**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(4-bromobenzyl)-5,6-dimethyl-1H-benzo[*d*]imidazol-3-ium bromide**

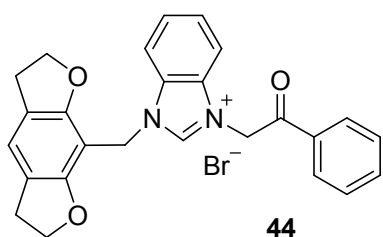
Yield 93%. White powder, mp 230-231 °C. IR  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ): 3403, 3105, 2964, 1619, 1554, 1460, 1346, 1237, 1193, 1128, 1064, 1014, 938, 854, 730.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 10.81 (1H, s), 7.50 (1H, s), 7.43-7.35 (5H, m), 6.89 (1H, s), 5.98 (2H, s), 5.43 (2H, s), 4.59 (4H, t,  $J = 8.7$  Hz), 3.05 (4H, t,  $J = 8.7$  Hz), 2.31 (3H, s), 2.30 (3H, s).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 158.28, 141.86, 137.21, 137.11, 132.80, 132.13, 130.09, 129.58, 129.51, 122.92, 121.88, 118.76, 113.20, 113.12, 98.12, 73.14, 49.94, 41.27, 29.32, 20.81, 20.62. HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{27}\text{H}_{26}\text{N}_2\text{O}_2\text{Br}$   $[\text{M-Br}]^+$  489.1172, found 489.1174.



**43**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-naphthylmethyl)-5,6-dimethyl-1H-benzo[*d*]imidazol-3-ium bromide**

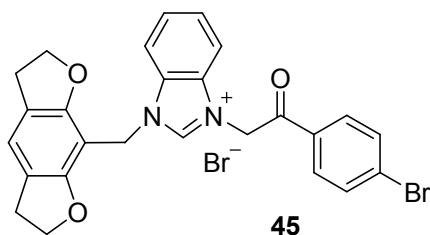
Yield 70%. White powder, mp 161-163 °C. IR  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ): 3399, 3116, 2960, 1618, 1557, 1455, 1343, 1237, 1130, 1064, 1017, 934, 858, 762.  $^1\text{H-NMR}$  (300 MHz,

CDCl<sub>3</sub>)  $\delta$ : 10.84 (1H, s), 7.92 (1H, s), 7.79-7.72 (3H, m), 7.52-7.48 (2H, m), 7.44-7.41 (2H, m), 7.34 (1H, s), 6.89 (1H, s), 6.11 (2H, s), 5.47 (2H, s), 4.57 (4H, t,  $J = 8.7$  Hz), 3.04 (4H, t,  $J = 8.7$  Hz), 2.29 (3H, s), 2.26 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 158.34, 142.15, 137.05, 136.97, 133.15, 131.07, 129.80, 129.62, 129.12, 128.04, 127.72, 127.60, 126.69, 126.63, 125.26, 121.84, 118.78, 113.17, 98.34, 73.14, 51.05, 41.31, 29.36, 20.82, 20.63. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>31</sub>H<sub>29</sub>N<sub>2</sub>O<sub>2</sub> [M-Br]<sup>+</sup> 461.2223, found 461.2220.



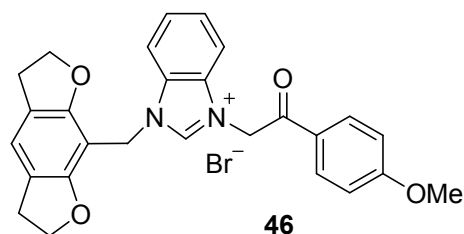
**44**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-oxo-2-phenylethyl)-5,6-dimethyl-1H-benzo[*d*]imidazol-3-ium bromide**

Yield 99%. Yellow powder, mp 209-211 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3368, 3105, 2968, 1690, 1611, 1558, 1457, 1335, 1238, 1132, 1067, 1007, 933, 868, 730, 634. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.24 (1H, s), 8.16 (2H, d,  $J = 7.2$  Hz), 7.63 (1H, s), 7.60-7.57 (1H, m), 7.51-7.46 (2H, m), 7.20 (1H, s), 6.92 (1H, s), 6.75 (2H, s), 5.38 (2H, s), 4.67 (4H, t,  $J = 8.7$  Hz), 3.08 (4H, t,  $J = 8.7$  Hz), 2.37 (3H, s), 2.31 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 190.68, 158.41, 142.18, 137.24, 136.99, 134.57, 133.74, 130.73, 129.28, 129.11, 128.81, 122.10, 118.82, 113.14, 112.76, 97.86, 73.27, 54.00, 41.14, 29.37, 20.83, 20.60. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>28</sub>H<sub>27</sub>N<sub>2</sub>O<sub>3</sub> [M-Br]<sup>+</sup> 439.2016, found 439.2016.



**45**  
**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(4-bromophenyl)-2-oxoethyl)-5,6-dimethyl-1H-benzo[*d*]imidazol-3-ium bromide**

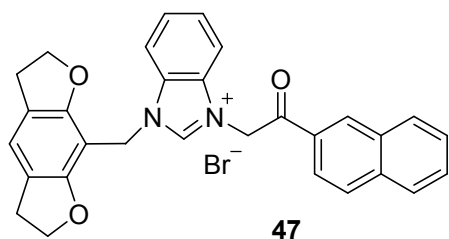
Yield 93%. Yellow powder, mp 242-244 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3389, 3117, 2964, 1698, 1626, 1564, 1461, 1393, 1344, 1231, 1133, 1065, 1007, 950, 824, 767. <sup>1</sup>H-NMR (300 MHz, DMSO)  $\delta$ : 9.55 (1H, s), 8.05 (2H, d,  $J$  = 8.4 Hz), 7.89 (2H, d,  $J$  = 8.4 Hz), 7.88 (1H, s), 7.78 (1H, s), 7.10 (1H, s), 6.39 (2H, s), 5.56 (2H, s), 4.64 (4H, t,  $J$  = 8.7 Hz), 3.11 (4H, t,  $J$  = 8.7 Hz), 2.41 (3H, s), 2.35 (3H, s). <sup>13</sup>C-NMR (75 MHz, DMSO)  $\delta$ : 190.64, 157.92, 142.16, 136.52, 136.30, 132.82, 132.08, 130.44, 130.31, 128.84, 128.60, 121.94, 118.75, 113.54, 112.85, 98.21, 72.83, 53.20, 40.68, 28.79, 20.62, 19.91. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>28</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub>Br [M-Br]<sup>+</sup> 517.1121, found 517.1125.



**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(4-methoxyphenyl)-2-oxoethyl)-5,6-dimethyl-1*H*-benzo[*d*]imidazol-3-ium bromide**

Yield 98%. White powder, mp 242-243 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3397, 3113, 2962, 1687, 1602, 1560, 1459, 1347, 1241, 1178, 1065, 1017, 951, 835, 771. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.13 (1H, s), 8.14 (2H, d,  $J$  = 8.7 Hz), 7.60 (1H, s), 7.24 (1H, s), 6.93 (2H, d,  $J$  = 8.4 Hz), 6.91 (1H, s), 6.64 (2H, s), 5.36 (2H, s), 4.65 (4H, t,  $J$  = 8.7 Hz), 3.81 (3H, s), 3.06 (4H, t,  $J$  = 8.7 Hz), 2.35 (3H, s), 2.29 (3H, s). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 188.88, 164.63, 158.36, 142.03, 137.14, 136.88, 131.27, 130.77, 129.21, 126.69, 122.03, 118.77, 114.30, 113.00, 97.88, 73.21, 55.61, 53.60, 41.05, 29.33, 20.79, 20.51. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>29</sub>H<sub>29</sub>N<sub>2</sub>O<sub>4</sub> [M-Br]<sup>+</sup> 469.2121, found 469.2122.

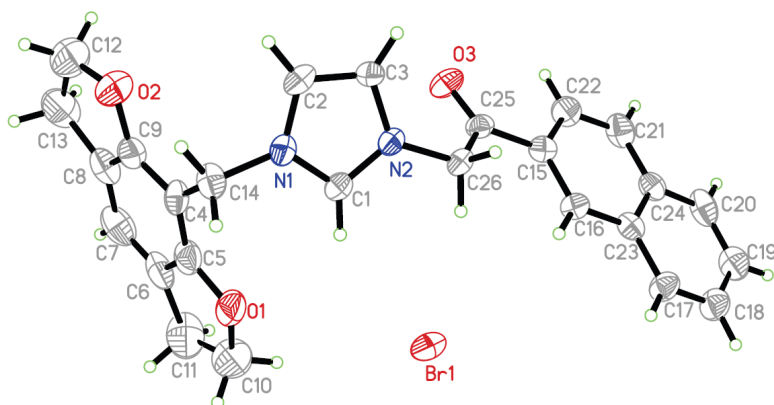




**1-((2,3,5,6-tetrahydrobenzo[1,2-*b*;4,5-*b*]difuran-8-yl)methyl)-3-(2-(naphthalen-2-yl)-2-oxoethyl)-5,6-dimethyl-1*H*-benzo[*d*]imidazol-3-ium bromide**

Yield 89%. Yellow powder, mp 169-171 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3385, 3117, 2965, 1686, 1623, 1558, 1463, 1357, 1235, 1189, 1128, 1063, 1019, 935, 824, 760. <sup>1</sup>H-NMR (300 MHz, DMSO)  $\delta$ : 9.63 (1H, s), 8.95 (1H, s), 8.23 (1H, d,  $J = 7.5$  Hz), 8.14 (1H, d,  $J = 8.7$  Hz), 8.07 (2H, d,  $J = 6.3$  Hz), 7.92 (1H, s), 7.78-7.68 (3H, m), 7.10 (1H, s), 6.56 (2H, s), 5.58 (2H, s), 4.66 (4H, t,  $J = 8.7$  Hz), 3.11 (4H, t,  $J = 8.7$  Hz), 2.41 (3H, s), 2.34 (3H, s). <sup>13</sup>C-NMR (75 MHz, DMSO)  $\delta$ : 191.67, 158.44, 142.76, 137.05, 136.80, 136.02, 132.52, 131.54, 131.35, 131.01, 130.16, 129.81, 129.37, 129.14, 128.34, 127.85, 123.81, 122.45, 119.26, 114.05, 113.36, 98.74, 73.34, 53.78, 41.20, 29.30, 20.77, 20.40. HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>32</sub>H<sub>29</sub>N<sub>2</sub>O<sub>3</sub> [M-Br]<sup>+</sup> 489.2172, found 489.2170.

### 3. X-ray crystal structure of compound 20



**Fig. 1** X-ray crystal structure of compound 20.

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loop\_

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'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

'H' 'H' 0.0000 0.0000

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'N' 'N' 0.0061 0.0033

'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

'O' 'O' 0.0106 0.0060

'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

'Br' 'Br' -0.2901 2.4595

'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

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loop\_

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'x, y, z'	
'-x, -y, -z'	
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_cell_length_b	10.2016(16)
_cell_length_c	12.6394(19)
_cell_angle_alpha	78.083(2)
_cell_angle_beta	70.581(2)
_cell_angle_gamma	70.890(2)
_cell_volume	1122.7(3)
_cell_formula_units_Z	2
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_cell_measurement_reflns_used	1486
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_exptl_absorpt_correction_T_min	0.2769
_exptl_absorpt_correction_T_max	1.0000
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_exptl_special_details	?
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_computing_data_reduction	'Bruker SAINT'
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_computing_publication_material	'Bruker SHELXTL'
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Refinement of  $F^2$  against ALL reflections. The weighted R-factor wR and goodness of fit S are based on  $F^2$ , conventional R-factors R are based on F, with F set to zero for negative  $F^2$ . The threshold expression of  $F^2 > 2\sigma(F^2)$  is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on  $F^2$  are statistically about twice as large as those based on F, and R-

factors based on ALL data will be even larger.

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_atom_sites_solution_secondary    difmap
_atom_sites_solution_hydrogens    geom
_refine_ls_hydrogen_treatment     mixed
_refine_ls_extinction_method      SHELXL
_refine_ls_extinction_coef        0.000(3)
_refine_ls_extinction_expression
'Fc*^=kFc[1+0.001xFc^2^l^3^/sin(2\q)]^-1/4^'
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_refine_ls_number_parameters       290
_refine_ls_number_restraints       0
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\_atom\_site\_type\_symbol

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\_atom\_site\_adp\_type

\_atom\_site\_occupancy

\_atom\_site\_symmetry\_multiplicity

\_atom\_site\_calc\_flag

\_atom\_site\_refinement\_flags

\_atom\_site\_disorder\_assembly

\_atom\_site\_disorder\_group

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N2 N 0.0393(5) 0.7234(4) 0.9539(4) 0.0483(12) Uani 1 1 d . . .

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O2 O -0.0500(7) 1.1993(5) 0.6655(5) 0.0927(17) Uani 1 1 d . . .

O3 O 0.2365(5) 0.7403(4) 1.0574(4) 0.0707(13) Uani 1 1 d . . .  
Br1 Br 0.24258(7) 0.38483(5) 0.78174(6) 0.0678(4) Uani 1 1 d . . .  
C1 C 0.0369(6) 0.7353(5) 0.8472(6) 0.0500(14) Uani 1 1 d . . .  
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C2 C -0.1056(7) 0.9311(5) 0.9170(6) 0.0603(17) Uani 1 1 d . . .  
H2 H -0.1680 1.0220 0.9220 0.072 Uiso 1 1 calc R . .  
C3 C -0.0508(7) 0.8442(5) 1.0016(5) 0.0557(15) Uani 1 1 d . . .  
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C4 C 0.0439(7) 0.9566(6) 0.6303(6) 0.0592(16) Uani 1 1 d . . .  
C5 C 0.1640(8) 0.8644(7) 0.5655(6) 0.0686(19) Uani 1 1 d . . .  
C6 C 0.2882(9) 0.8990(10) 0.4866(7) 0.083(2) Uani 1 1 d . . .  
C7 C 0.2942(10) 1.0352(11) 0.4691(7) 0.091(3) Uani 1 1 d . . .  
H7 H 0.3748 1.0614 0.4156 0.109 Uiso 1 1 calc R . .  
C8 C 0.1771(10) 1.1323(9) 0.5330(7) 0.078(2) Uani 1 1 d . . .  
C9 C 0.0583(8) 1.0930(7) 0.6079(6) 0.0653(17) Uani 1 1 d . . .  
C10 C 0.3113(12) 0.6581(11) 0.5001(10) 0.124(4) Uani 1 1 d . . .  
H10A H 0.2933 0.6142 0.4468 0.148 Uiso 1 1 calc R . .  
H10B H 0.3722 0.5866 0.5423 0.148 Uiso 1 1 calc R . .  
C11 C 0.3921(12) 0.7683(12) 0.4376(10) 0.135(5) Uani 1 1 d . . .  
H11A H 0.4891 0.7461 0.4512 0.162 Uiso 1 1 calc R . .  
H11B H 0.4065 0.7767 0.3570 0.162 Uiso 1 1 calc R . .  
C12 C -0.0006(14) 1.3244(9) 0.6241(10) 0.115(3) Uani 1 1 d . . .



H12A H 0.0132 1.3584 0.6850 0.137 Uiso 1 1 calc R . .  
H12B H -0.0754 1.3969 0.5944 0.137 Uiso 1 1 calc R . .  
C13 C 0.1445(14) 1.2892(10) 0.5333(9) 0.114(3) Uani 1 1 d . . .  
H13A H 0.2232 1.3106 0.5508 0.137 Uiso 1 1 calc R . .  
H13B H 0.1341 1.3392 0.4610 0.137 Uiso 1 1 calc R . .  
C14 C -0.0845(7) 0.9144(7) 0.7158(6) 0.0614(17) Uani 1 1 d . . .  
H14A H -0.1730 0.9941 0.7260 0.074 Uiso 1 1 calc R . .  
H14B H -0.1058 0.8429 0.6888 0.074 Uiso 1 1 calc R . .  
C15 C 0.3258(6) 0.4972(6) 1.1094(5) 0.0524(15) Uani 1 1 d . . .  
C16 C 0.3409(6) 0.3645(5) 1.0924(5) 0.0499(14) Uani 1 1 d . . .  
H16 H 0.2860 0.3510 1.0502 0.060 Uiso 1 1 calc R . .  
C17 C 0.4582(7) 0.1087(6) 1.1184(6) 0.0634(18) Uani 1 1 d . . .  
H17 H 0.4034 0.0938 1.0767 0.076 Uiso 1 1 calc R . .  
C18 C 0.5547(8) -0.0019(7) 1.1592(7) 0.072(2) Uani 1 1 d . . .  
H18 H 0.5673 -0.0913 1.1442 0.087 Uiso 1 1 calc R . .  
C19 C 0.6354(8) 0.0182(8) 1.2237(7) 0.078(2) Uani 1 1 d . . .  
H19 H 0.6999 -0.0582 1.2534 0.093 Uiso 1 1 calc R . .  
C20 C 0.6200(7) 0.1495(8) 1.2435(6) 0.073(2) Uani 1 1 d . . .  
H20 H 0.6764 0.1613 1.2852 0.088 Uiso 1 1 calc R . .  
C21 C 0.5032(8) 0.4031(7) 1.2196(6) 0.0717(19) Uani 1 1 d . . .  
H21 H 0.5551 0.4173 1.2639 0.086 Uiso 1 1 calc R . .  
C22 C 0.4106(8) 0.5176(7) 1.1730(6) 0.0681(18) Uani 1 1 d . . .

H22 H 0.4040 0.6074 1.1832 0.082 Uiso 1 1 calc R . .  
 C23 C 0.4380(6) 0.2472(6) 1.1374(5) 0.0495(14) Uani 1 1 d . . .  
 C24 C 0.5208(6) 0.2679(6) 1.2022(5) 0.0558(15) Uani 1 1 d . . .  
 C25 C 0.2279(6) 0.6242(5) 1.0591(5) 0.0506(14) Uani 1 1 d . . .  
 C26 C 0.1191(6) 0.5975(5) 1.0116(5) 0.0503(14) Uani 1 1 d . . .  
 H26A H 0.1735 0.5281 0.9589 0.060 Uiso 1 1 calc R . .  
 H26B H 0.0466 0.5598 1.0724 0.060 Uiso 1 1 calc R . .  
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   \_atom\_site\_aniso\_label  
   \_atom\_site\_aniso\_U\_11  
   \_atom\_site\_aniso\_U\_22  
   \_atom\_site\_aniso\_U\_33  
   \_atom\_site\_aniso\_U\_23  
   \_atom\_site\_aniso\_U\_13  
   \_atom\_site\_aniso\_U\_12  
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 N2 0.051(3) 0.038(2) 0.054(4) -0.003(2) -0.014(2) -0.0114(18)  
 O1 0.094(4) 0.068(3) 0.078(4) -0.002(2) -0.028(3) 0.010(2)  
 O2 0.107(4) 0.065(3) 0.105(5) -0.013(3) -0.032(4) -0.019(3)  
 O3 0.080(3) 0.044(2) 0.097(4) -0.014(2) -0.027(3) -0.0241(19)  
 Br1 0.0664(5) 0.0498(4) 0.0834(7) -0.0204(3) -0.0104(4) -0.0145(3)  
 C1 0.046(3) 0.042(3) 0.059(4) -0.006(3) -0.017(3) -0.007(2)

C2 0.055(4) 0.039(3) 0.081(5) -0.008(3) -0.017(4) -0.006(2)  
C3 0.066(4) 0.045(3) 0.045(4) -0.011(3) -0.006(3) -0.008(2)  
C4 0.054(4) 0.060(3) 0.061(5) 0.010(3) -0.029(3) -0.010(3)  
C5 0.062(4) 0.075(4) 0.063(5) 0.001(3) -0.030(4) -0.005(3)  
C6 0.072(5) 0.116(6) 0.045(5) 0.003(4) -0.020(4) -0.008(4)  
C7 0.073(5) 0.143(8) 0.059(6) -0.001(5) -0.013(4) -0.045(5)  
C8 0.088(6) 0.103(5) 0.052(5) 0.007(4) -0.024(5) -0.043(4)  
C9 0.070(4) 0.069(4) 0.059(5) -0.006(3) -0.030(4) -0.013(3)  
C10 0.099(7) 0.114(7) 0.118(10) -0.037(7) -0.034(7) 0.039(6)  
C11 0.094(7) 0.144(9) 0.088(8) -0.008(7) 0.013(6) 0.026(7)  
C12 0.148(9) 0.083(6) 0.123(10) -0.004(6) -0.045(8) -0.043(6)  
C13 0.179(11) 0.110(7) 0.084(8) 0.004(6) -0.039(8) -0.087(7)  
C14 0.045(3) 0.074(4) 0.056(5) 0.003(3) -0.013(3) -0.012(3)  
C15 0.050(3) 0.054(3) 0.054(4) -0.010(3) -0.012(3) -0.016(2)  
C16 0.043(3) 0.051(3) 0.060(4) -0.011(3) -0.018(3) -0.012(2)  
C17 0.061(4) 0.051(3) 0.080(5) -0.008(3) -0.031(4) -0.006(3)  
C18 0.064(4) 0.060(4) 0.078(6) -0.005(3) -0.020(4) 0.000(3)  
C19 0.057(4) 0.081(5) 0.072(6) -0.005(4) -0.021(4) 0.010(3)  
C20 0.049(4) 0.108(6) 0.060(5) 0.011(4) -0.025(3) -0.020(3)  
C21 0.074(5) 0.092(5) 0.067(5) 0.004(4) -0.036(4) -0.038(4)  
C22 0.080(5) 0.071(4) 0.068(5) -0.006(3) -0.021(4) -0.041(3)  
C23 0.036(3) 0.066(3) 0.045(4) -0.008(3) -0.009(3) -0.012(2)

C24 0.048(3) 0.072(4) 0.047(4) -0.005(3) -0.010(3) -0.021(3)

C25 0.049(3) 0.045(3) 0.051(4) -0.013(2) -0.005(3) -0.010(2)

C26 0.054(3) 0.035(2) 0.058(4) -0.003(2) -0.017(3) -0.009(2)

\_geom\_special\_details

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

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## 4. Biological Assay Procedures and Results

### 4.1 Cytotoxicity assay

The assay was in five kinds of cell lines (HL-60, SMMC-7721, A549, MCF-7 and SW480). Cells were cultured at 37 °C under a humidified atmosphere of 5% CO<sub>2</sub> in RPMI 1640 medium supplemented with 10% fetal serum and dispersed in replicate 96-well plates. Compounds were then added. After 48 h exposure to the compounds, cells viability were determined by the [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide] (MTT) cytotoxicity assay by measuring the absorbance at 570 nm with a microplate spectrophotometer. Each test was performed in triplicate.

### 4.2 Cytotoxic Activities of Compounds 7–42 *in vitro*<sup>b</sup> (IC<sub>50</sub>, μM<sup>a</sup>)

Entry	Compound no.	HL-60	MCF-7	SW480	A549	SMMC-7721
1	<b>8</b>	>40	>40	>40	>40	>40
2	<b>9</b>	>40	>40	>40	>40	>40
3	<b>10</b>	>40	>40	>40	>40	>40
4	<b>11</b>	>40	>40	>40	>40	>40
5	<b>12</b>	12.27	16.70	25.07	32.92	>40
6	<b>13</b>	1.84	3.49	4.72	6.64	10.28
7	<b>14</b>	2.22	12.16	15.67	34.29	28.60
8	<b>15</b>	>40	>40	>40	>40	>40
9	<b>16</b>	1.13	2.90	3.62	7.22	10.49
10	<b>17</b>	>40	>40	>40	>40	>40
11	<b>18</b>	3.66	14.65	17.46	39.93	>40
12	<b>19</b>	>40	>40	>40	>40	>40
13	<b>20</b>	1.09	3.43	4.63	9.08	9.02
14	<b>21</b>	3.96	15.79	9.65	11.48	17.17
15	<b>22</b>	0.63	6.98	3.50	3.39	2.59
16	<b>23</b>	0.77	3.46	10.08	7.81	13.08
17	<b>24</b>	>40	>40	>40	>40	>40
18	<b>25</b>	0.51	0.65	3.89	1.86	3.36
19	<b>26</b>	3.61	18.80	32.26	32.80	>40
20	<b>27</b>	1.99	4.26	13.85	10.22	15.03
21	<b>28</b>	0.82	4.66	15.11	5.82	6.45
22	<b>29</b>	1.04	1.21	4.61	3.61	7.64

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23	<b>30</b>	1.65	1.58	4.06	9.60	8.56
24	<b>31</b>	1.21	0.80	2.45	3.83	5.48
25	<b>32</b>	0.42	0.27	0.92	0.96	2.13
26	<b>33</b>	0.58	2.36	1.84	3.58	7.45
27	<b>34</b>	0.31	1.13	0.57	0.55	1.35
28	<b>35</b>	2.03	5.16	3.77	3.16	8.22
29	<b>36</b>	1.17	1.60	3.20	5.44	6.41
30	<b>37</b>	0.87	2.96	2.75	5.63	5.13
31	<b>38</b>	0.83	1.19	2.93	3.30	5.17
32	<b>39</b>	0.57	0.94	0.89	1.48	1.25
33	<b>40</b>	0.50	0.69	1.01	1.62	0.73
34	<b>41</b>	0.40	0.65	0.64	1.06	2.21
35	<b>42</b>	0.79	0.97	0.96	1.45	1.81
36	<b>43</b>	0.26	0.20	0.26	0.83	1.81
37	<b>44</b>	1.23	1.04	1.21	4.39	3.97
38	<b>45</b>	1.18	1.02	1.63	4.13	3.07
39	<b>46</b>	0.95	0.61	1.41	2.55	4.89
40	<b>47</b>	0.98	0.83	1.36	3.28	3.92
41	DDP	5.52	12.99	12.61	16.51	18.77

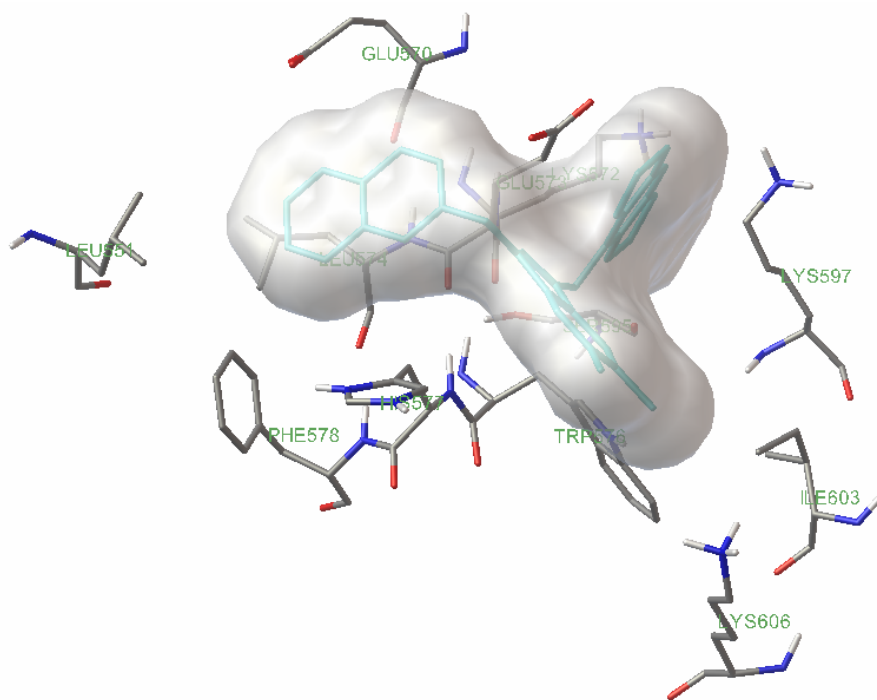
<sup>a</sup> Cytotoxicity as IC<sub>50</sub> for each cell line, is the concentration of compound which reduced by 50% the optical density of treated cells with respect to untreated cells using the MTT assay.

<sup>b</sup> Data represent the mean values of three independent determinations.

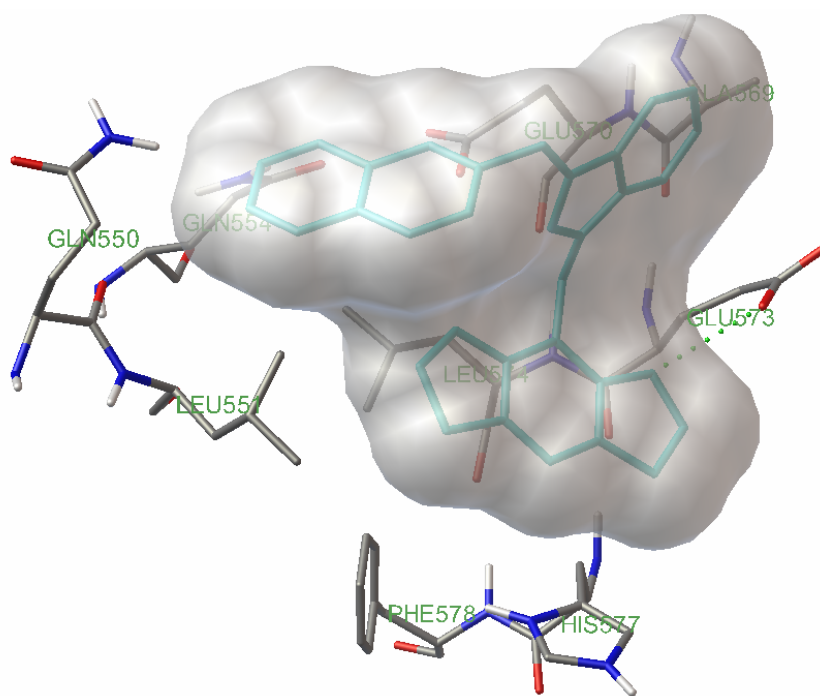
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## 5. Docking Calculations

Compounds **43** and **34** were docked into PI3K $\gamma$  [from the complex between PI3K and 4-amino-2-methyl-N-(1*H*-pyrazol-3-yl)quinazoline-8-carboxamide, PDB code 3PRZ] using AutoDock (Version 4.0). A grid of 118, 126, and 126 points in the x, y, and z directions was constructed centered on 8.0, -7.0, and 8.0. We used a grid spacing of 0.375 Å and a distance-dependent function of the dielectric constant for the energetic map calculations. Docking simulations of the compounds were carried out using the Lamarckian genetic algorithm and through a protocol with an initial population of 150 randomly placed individuals, a maximum number of 250 million energy evaluations, a mutation rate of 0.02, a crossover rate of 0.8, and an elitism value of 1. Fifty independent docking runs were carried out for each compound, and the resulting conformations that differed by 1.0 Å in positional root-mean-square deviation (rmsd) were clustered together. Cluster analysis was performed by selecting the most populated cluster, which in all cases coincided with the one endowed with the best energy.



**Fig.2** Model of hybrid compound **43** docked into PI3K $\gamma$

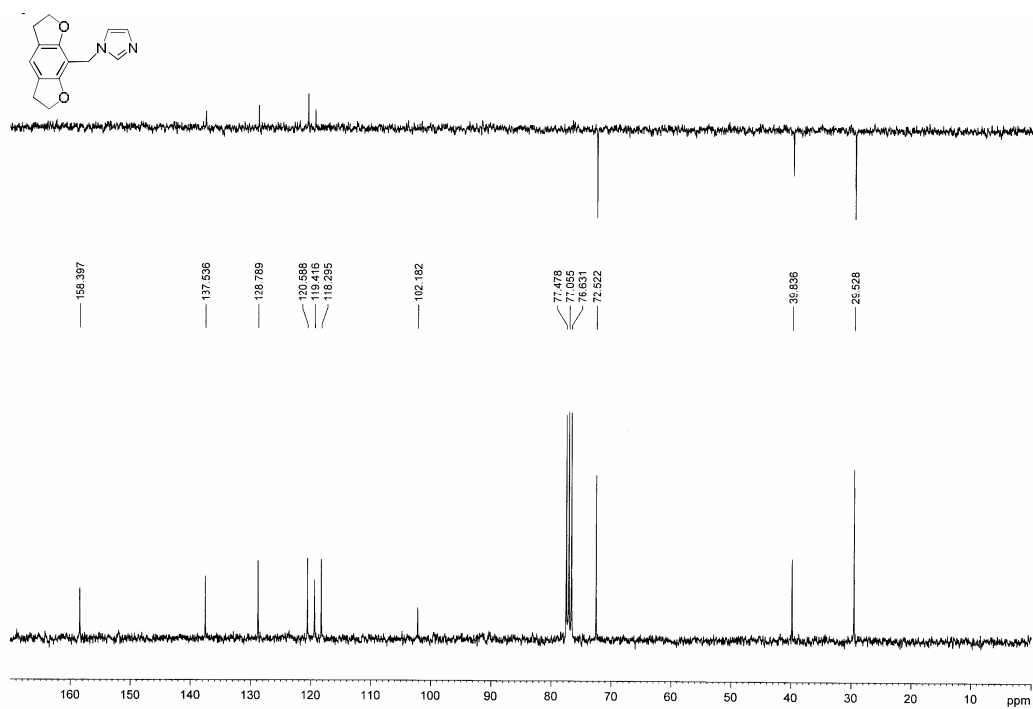
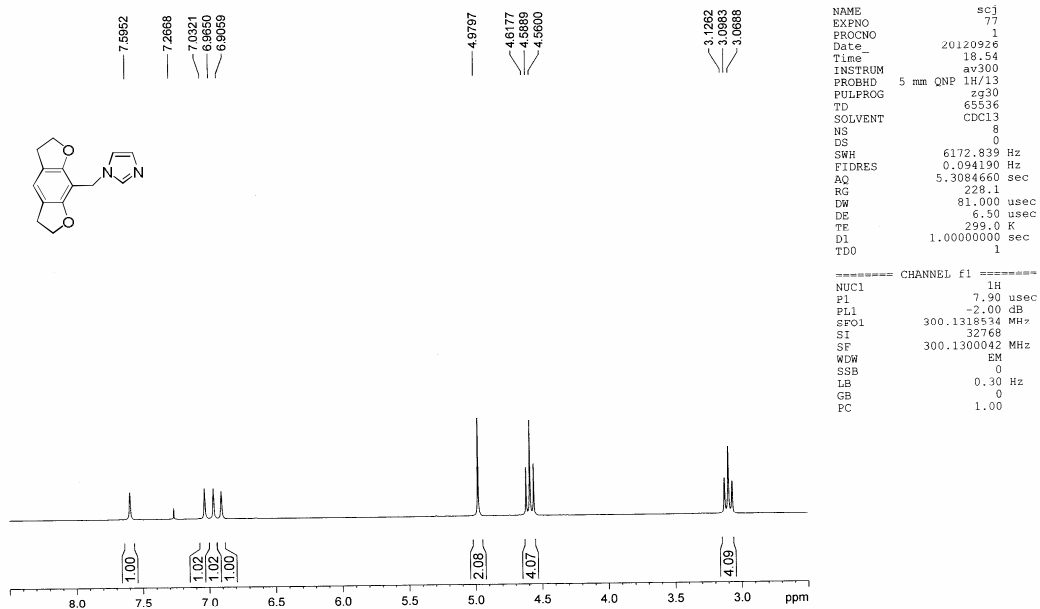


**Fig.3** Model of hybrid compound **34** docked into PI3K $\gamma$

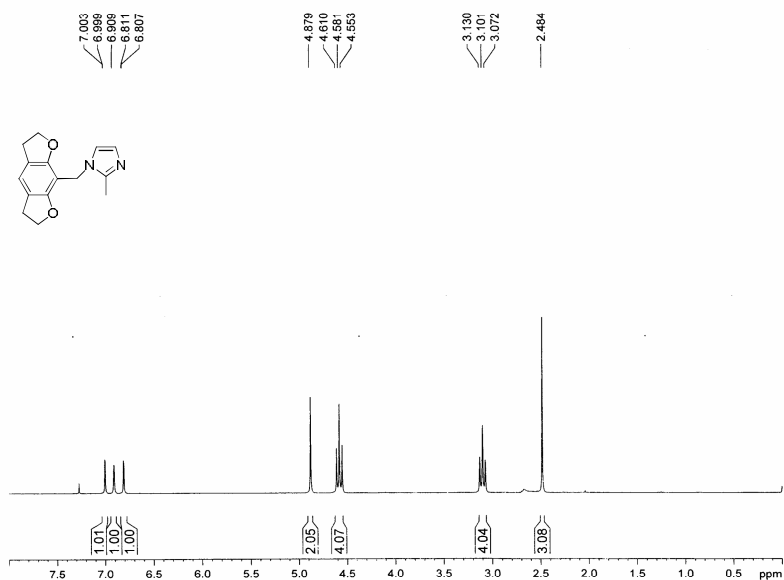


# 6. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR Spectral of New Compounds 8-47

## Compound 8



# Compound 9

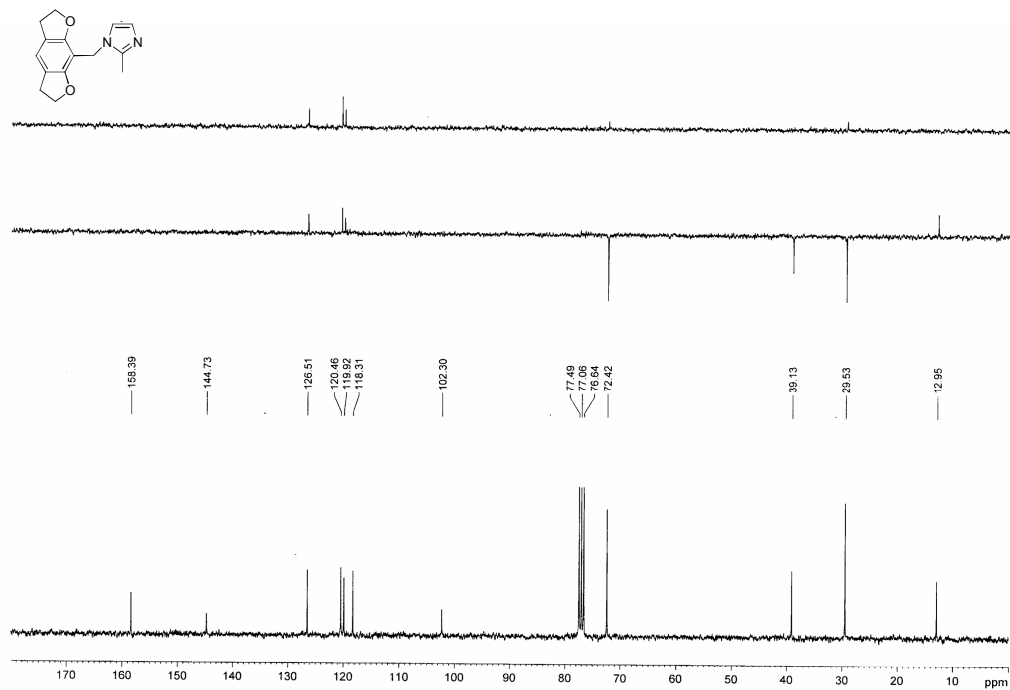


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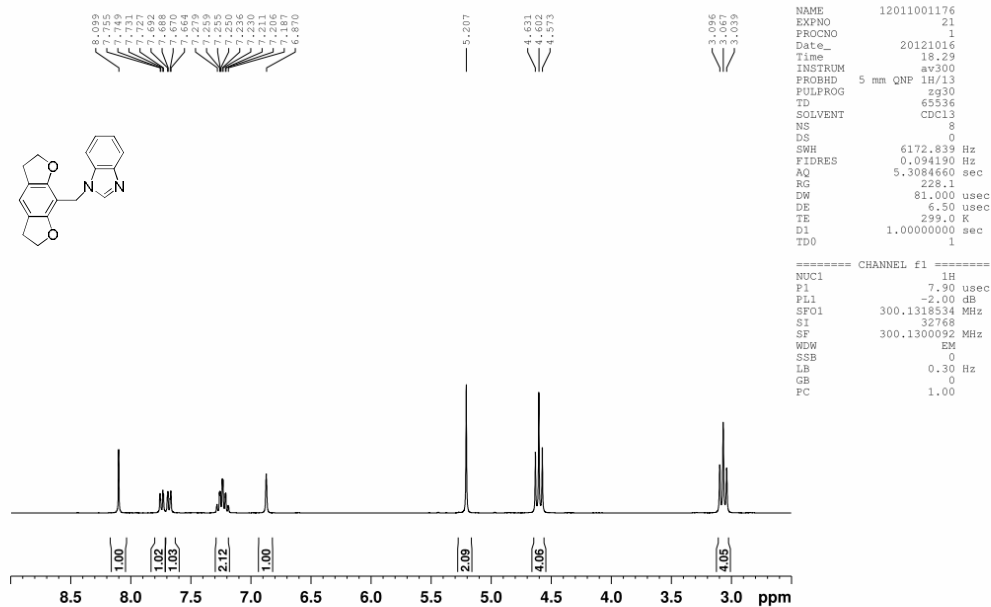
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EXPNO         91
PROCNO        1
Date_         20120927
Time          16.34
INSTRUM       av300
PROBHD        5 mm QNP 1H/13
PULPROG       zg30
TD            65536
SOLVENT       CDCl3
NS            8
DS            0
SWH           6172.839 Hz
FIDRES        0.094190 Hz
AQ            5.3084660 sec
RG            181
DW            81.000 usec
DE            6.50 usec
TE            297.5 K
D1            1.00000000 sec
TDO           1
  
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P1            7.90 usec
PL1           -2.00 dB
SFO1         300.1318534 MHz
SI            32768
SF           300.1360033 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
FC            1.00
  
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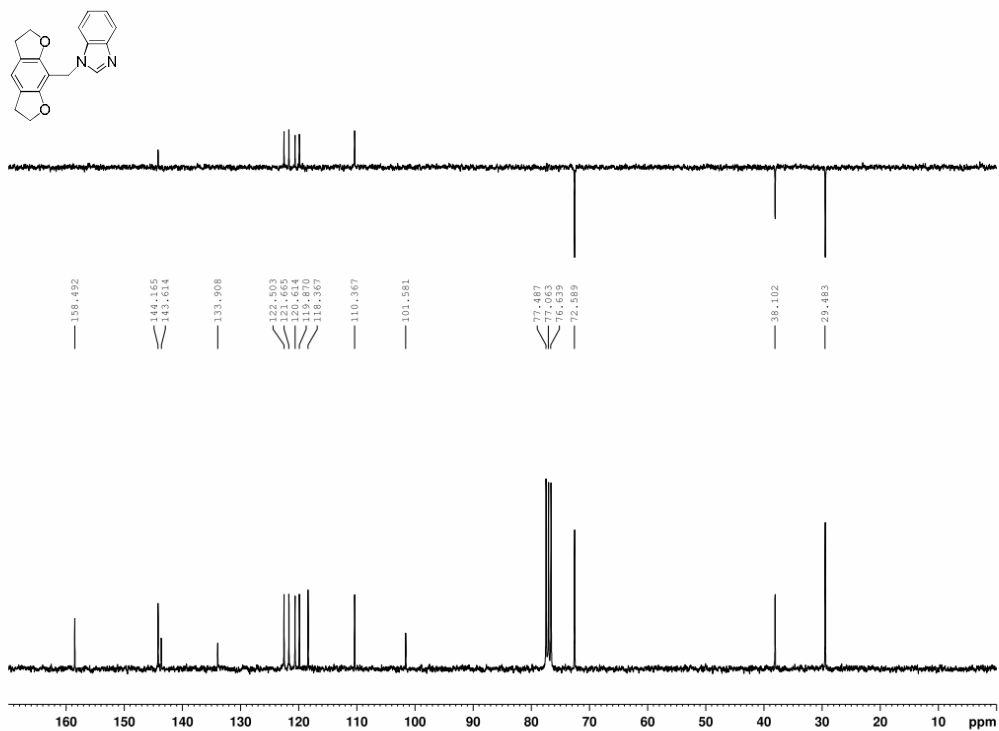
# Compound 10



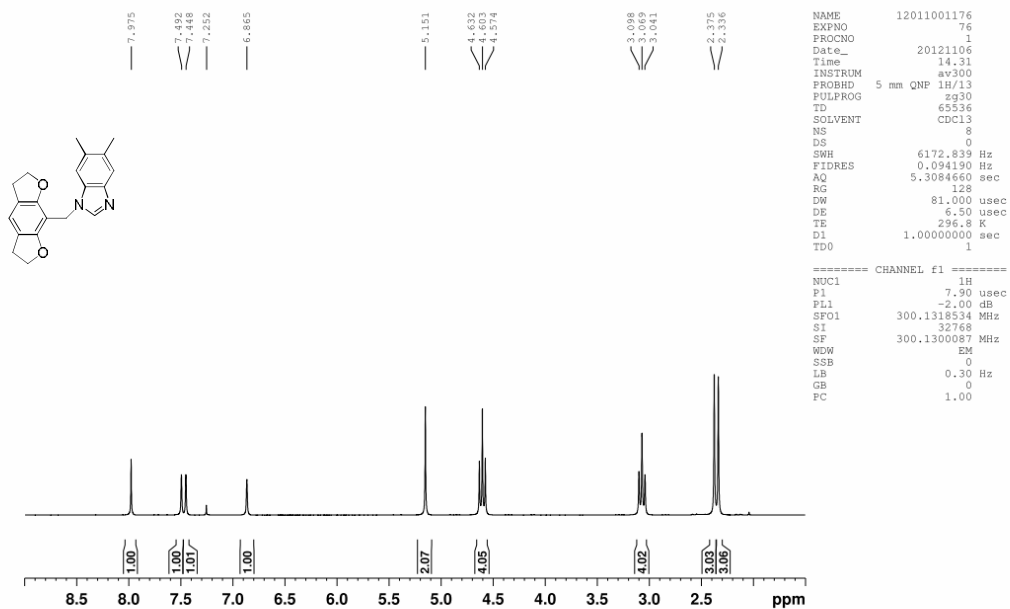
```

NAME      12011001176
EXPNO    21
PROCNO   1
Date_    20121016
Time     18.29
INSTRUM  av300
PROBHD   5 mm QNP 1H/13
PULPROG  zg30
TD       65536
SOLVENT  cdcl3
NS       8
DS       0
SWH      6172.839 Hz
FIDRES   0.094190 Hz
AQ       5.3084660 sec
RG       228.1
DW       81.000 usec
DE       6.50 usec
TE       299.0 K
D1       1.00000000 sec
TD0      1

===== CHANNEL f1 =====
NUC1     1H
P1       7.90 usec
PL1     -2.00 dB
SFO1    300.1318534 MHz
SI       32768
SF       300.1300092 MHz
WDW      EM
SSB      0
LB       0.30 Hz
GB       0
PC       1.00
  
```



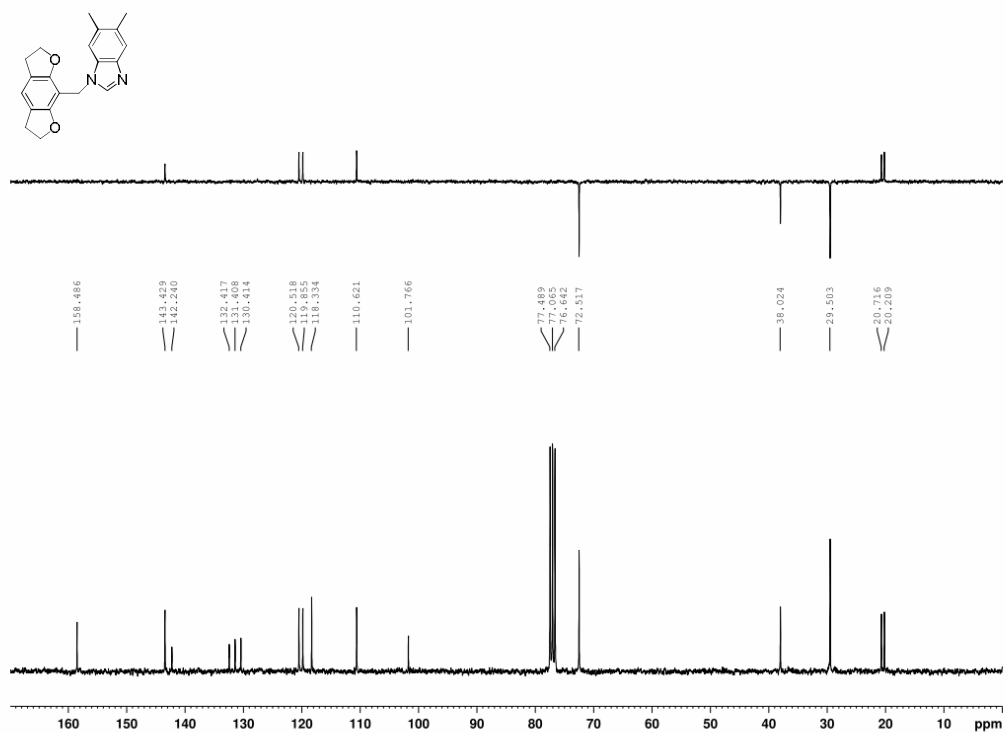
# Compound 11



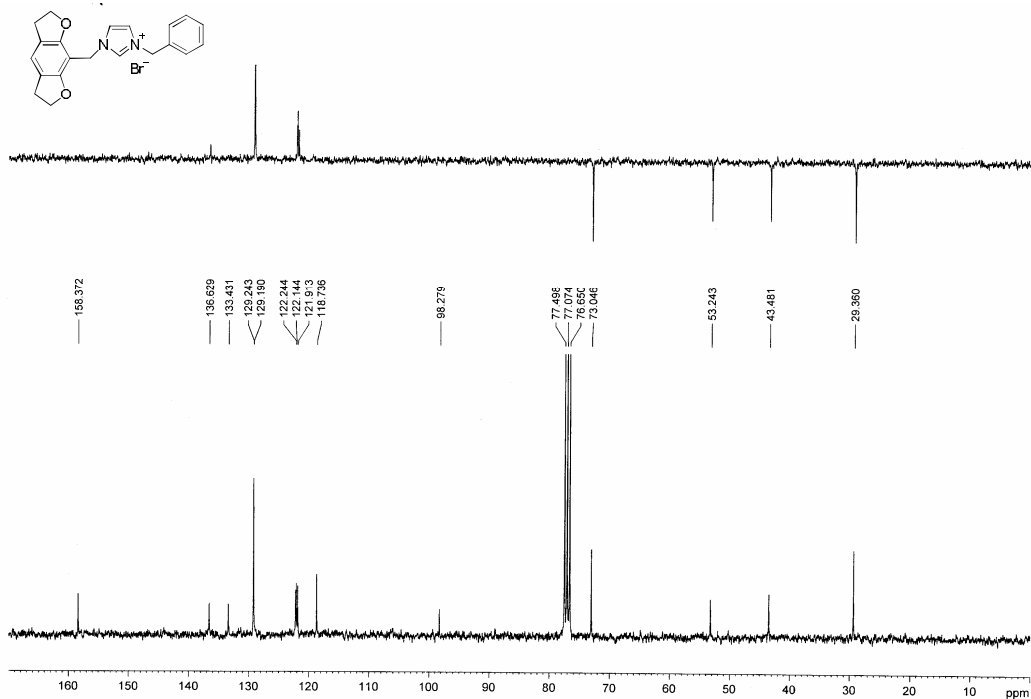
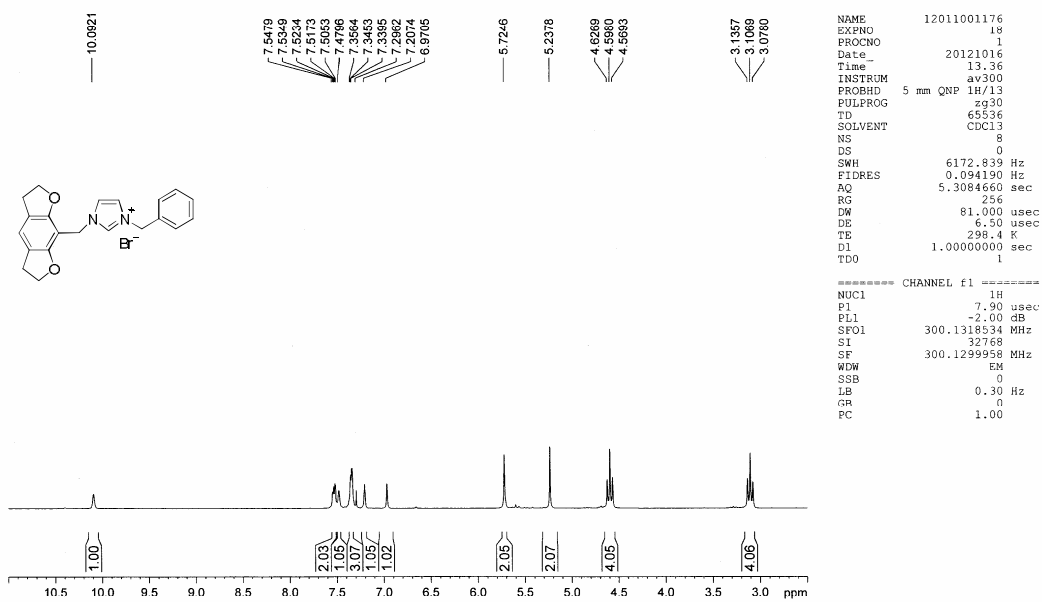
```

NAME      12011001176
EXPNO     76
PROCNO    1
Date_     20121106
Time      14.31
INSTRUM   av300
PROBHD    5 mm QNP 1H/13
PULPROG   zg30
TD         65536
SOLVENT   CDCl3
NS         8
DS         0
SWH        6172.839 Hz
FIDRES     0.094190 Hz
AQ         5.3084660 sec
RG         128
DW         81.000 usec
DE         6.50 usec
TE         296.8 K
D1         1.00000000 sec
TD0        1

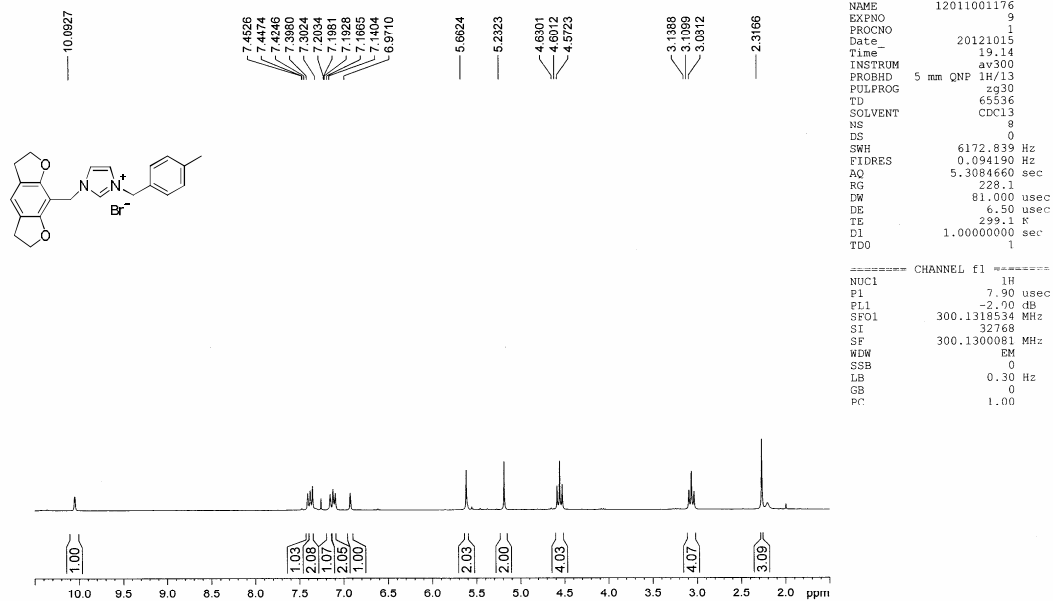
===== CHANNEL f1 =====
NUC1       1H
P1         7.90 usec
PL1        -2.00 dB
SFO1       300.1318534 MHz
SI         32768
SF         300.1300087 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```



# Compound 12

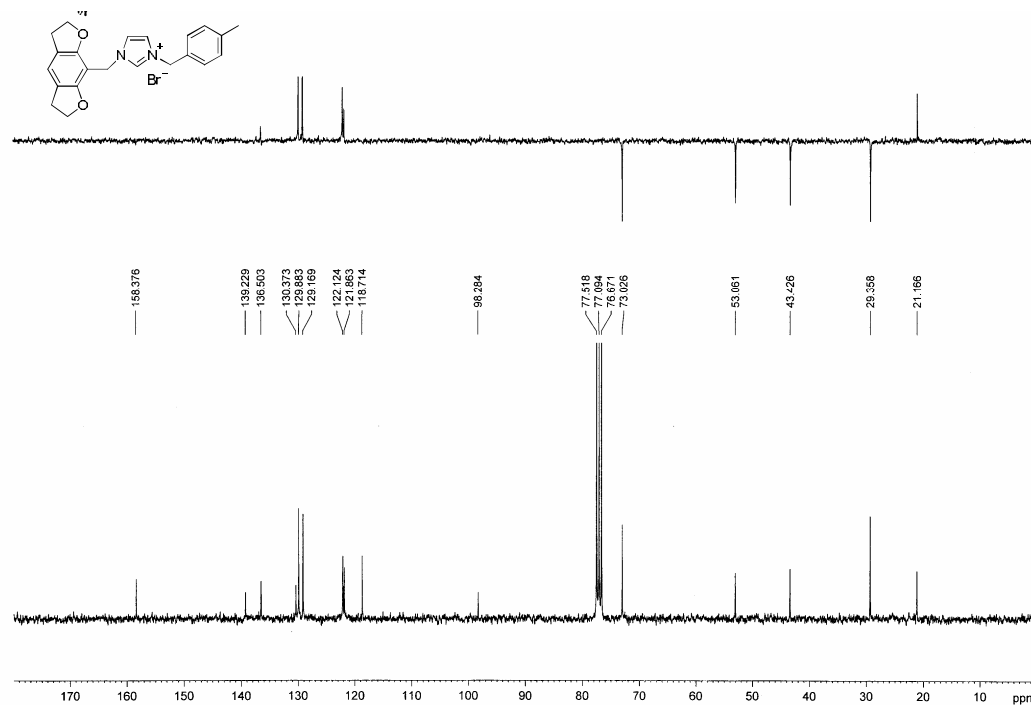


# Compound 13

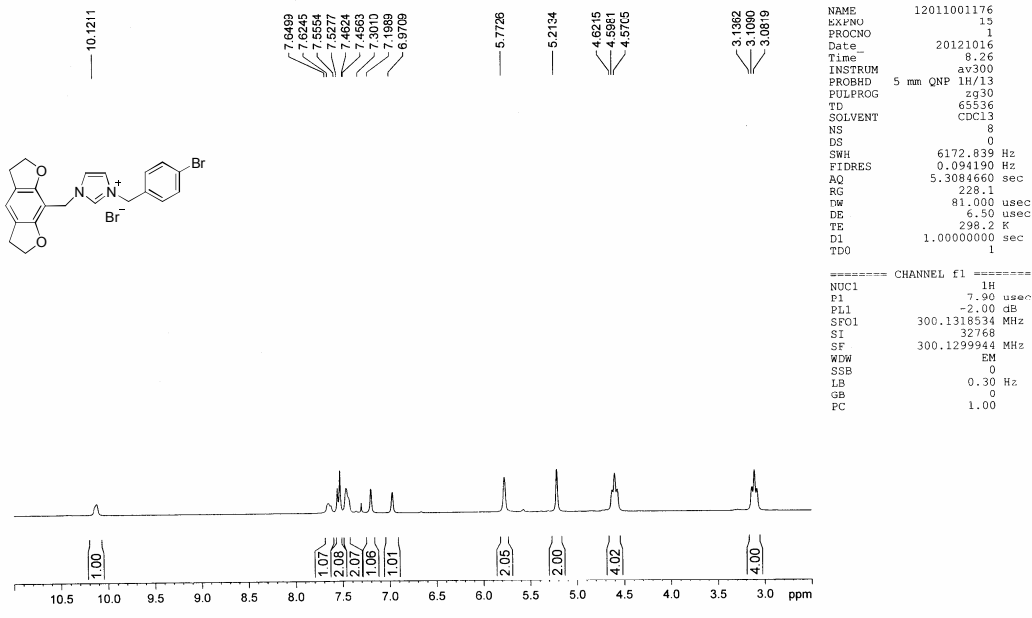


```

NAME 12011001176
EXPNO 9
PROCNO 1
Date_ 20121015
Time 19.14
INSTRUM av300
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 6172.839 Hz
FIDRES 0.094190 Hz
AQ 5.3084660 sec
RG 228.1
DW 81.000 usec
DE 6.50 usec
TE 299.1 K
D1 1.00000000 sec
TDO 1
===== CHANNEL f1 =====
NUC1 1H
P1 7.90 usec
PL1 -2.00 dB
SFO1 300.1318534 MHz
SI 32768
SF 300.1300081 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
  
```

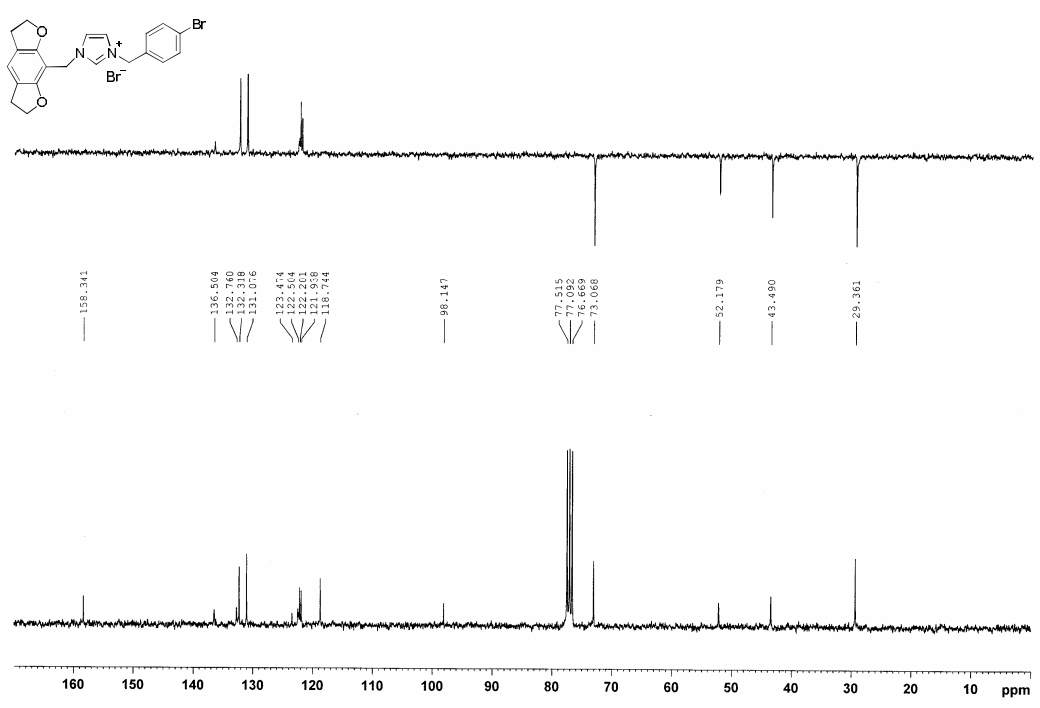


# Compound 14

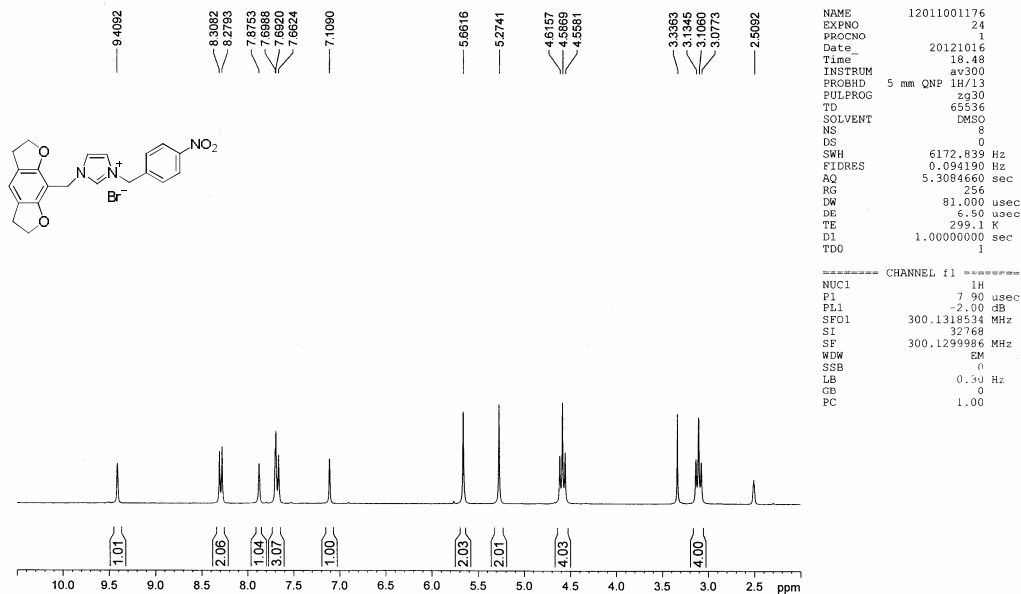


```

NAME      12011001176
EXPNO    15
PROCNO    1
Date_    20121016
Time     8.26
INSTRUM  av300
PROBHD   5 mm QNP 1H/13
PULPROG  zg30
TD       65536
SOLVENT  CDCl3
NS       8
DS       0
SWH     6172.839 Hz
FIDRES  0.094190 Hz
AQ     5.3084660 sec
RG      228.1
DW     81.000 usec
DE     6.50 usec
TE     298.2 K
D1     1.0000000 sec
TDO
===== CHANNEL f1 =====
NUC1      1H
P1       7.90 usec
PL1     -2.00 dB
SFO1    300.1318534 MHz
SI      32768
SF     300.1299944 MHz
WDW     EM
SSB     0
LB     0.30 Hz
GB     0
PC     1.00
    
```



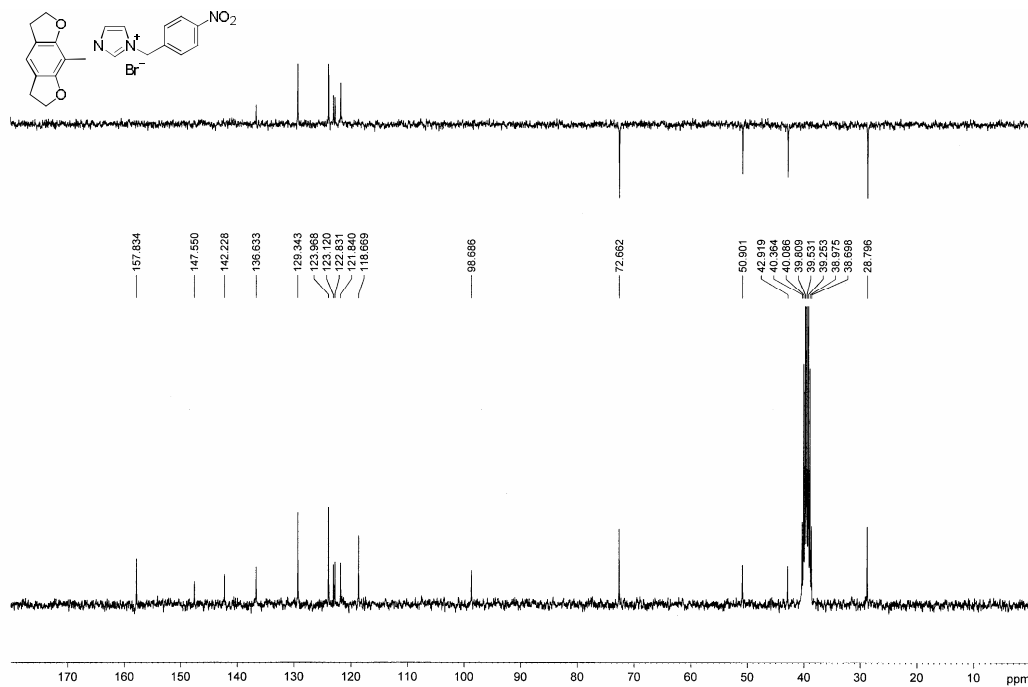
# Compound 15



```

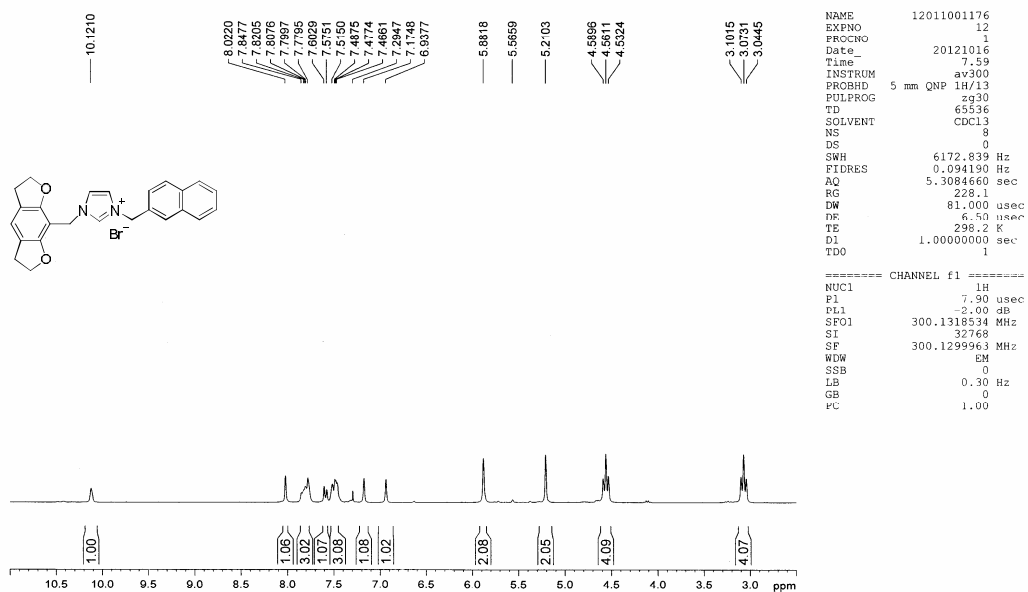
NAME      12011001176
EXPNO    24
PROCNO    1
Date_     20121016
Time      18:48
INSTRUM   av300
PROBHD    5 mm QNP 1H/13
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        6172.839 Hz
FIDRES     0.094130 Hz
AQ         5.3084660 sec
RG         256
DW         81.000 usec
DE         6.50 usec
TE         299.1 K
D1         1.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         7.90 usec
PL1        -2.00 dB
SFO1       300.1318534 MHz
SI         32768
SF         300.1299996 MHz
WDW        EM
SSB        0
LB         0.50 Hz
GB         0
PC         1.00
  
```





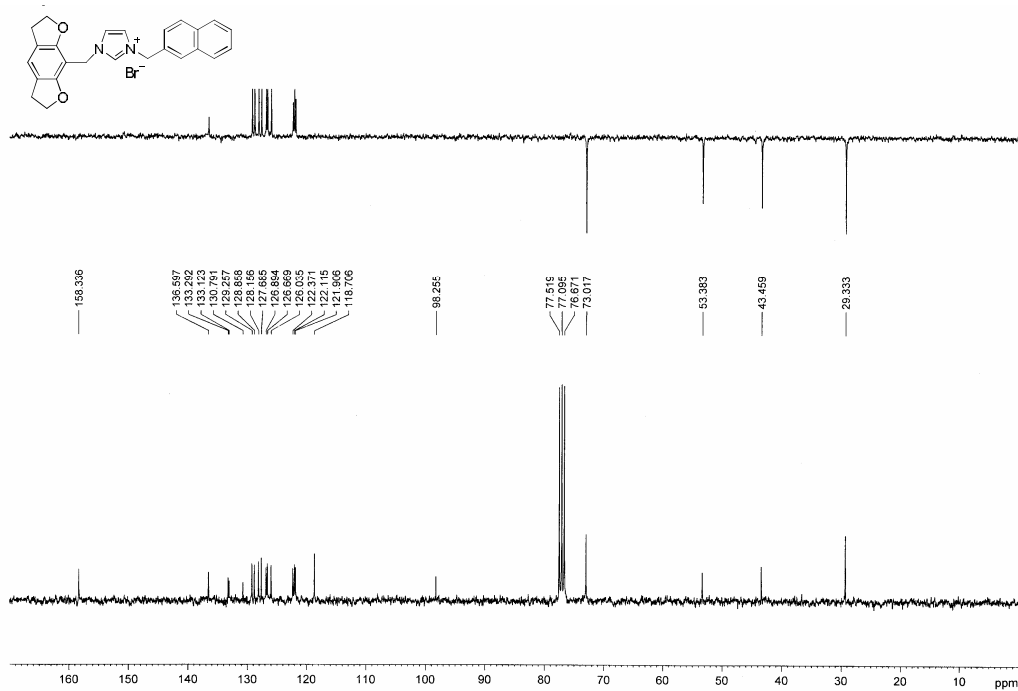
# Compound 16



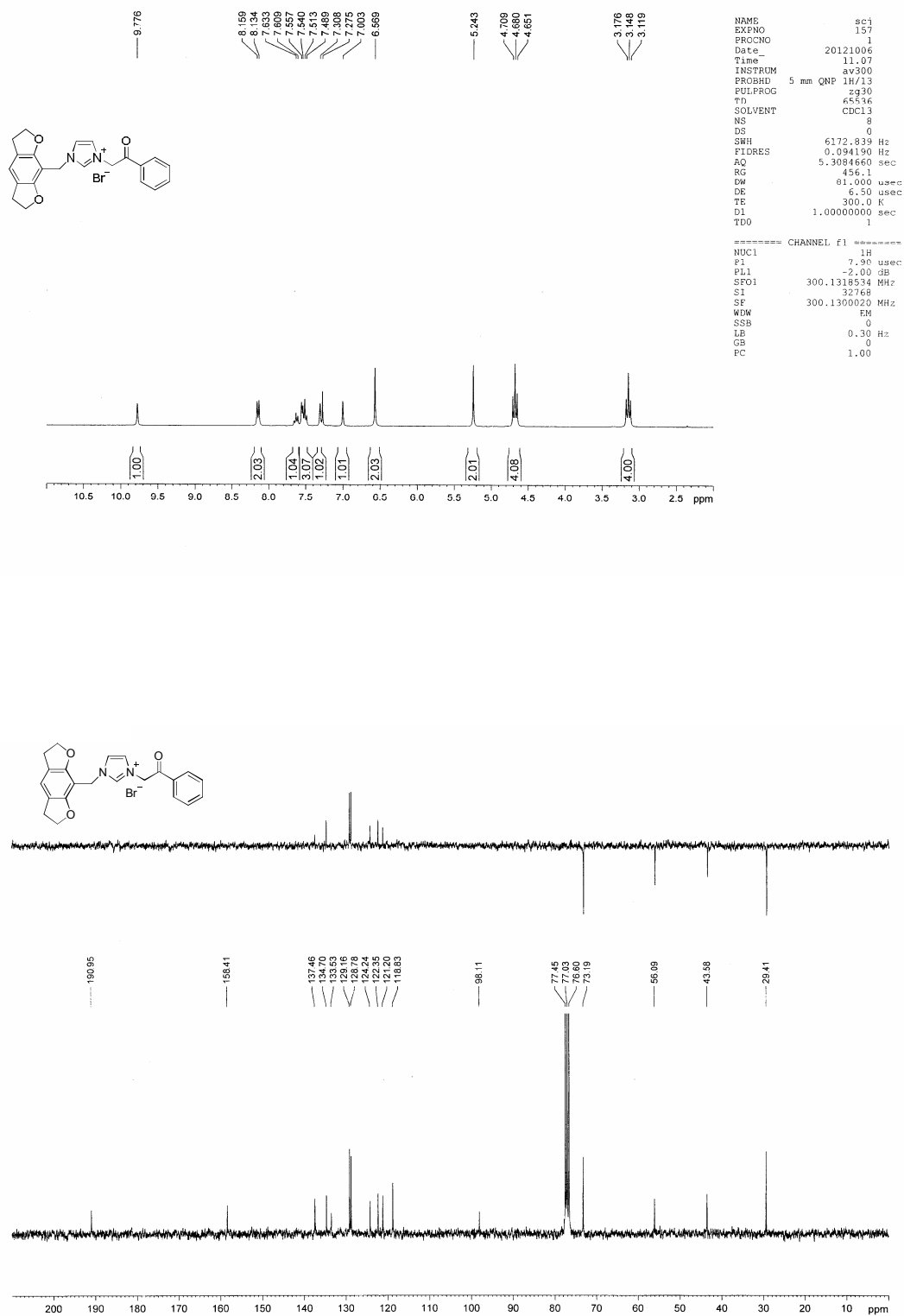
```

NAME      12011001176
EXPNO    12
PROCNO   1
Date_    20121016
Time     7.59
INSTRUM  av300
PROBHD   5 mm QNP 1H/13
PULPROG  zg30
TD        65536
SOLVENT  CDCl3
NS        8
DS        0
SWH       6172.839 Hz
FIDRES   0.094190 Hz
AQ        5.3084660 sec
RG        228.1
DW        81.000 usec
DE        6.50 usec
TE        298.2 K
D1        1.00000000 sec
TDO       1

===== CHANNEL f1 =====
NUC1      1H
P1        7.90 usec
PL1       -2.00 dB
SFO1      300.1318534 MHz
SI        32768
SF        300.1299963 MHz
WDW       EM
SSB       0
LB        0.30 Hz
GB        0
PC        1.00
    
```



# Compound 17

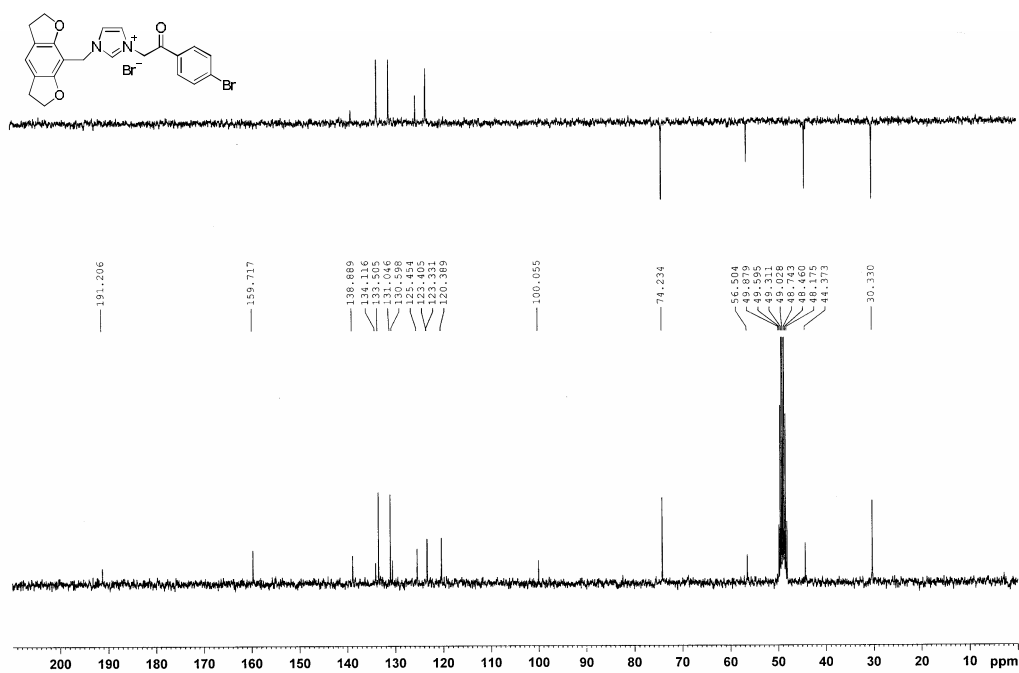


# Compound 18

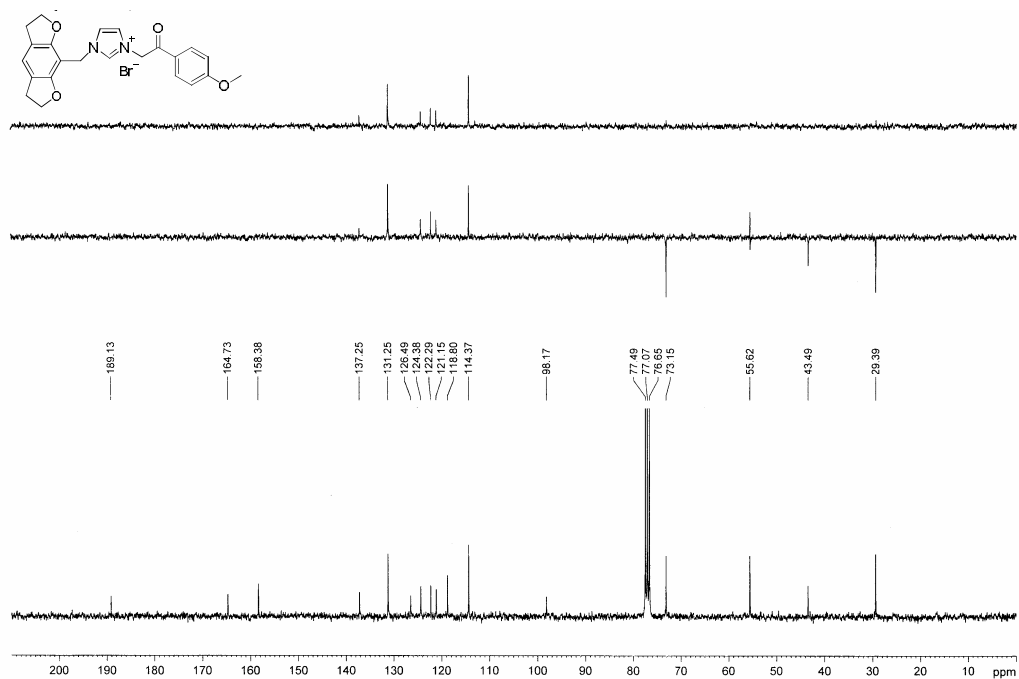
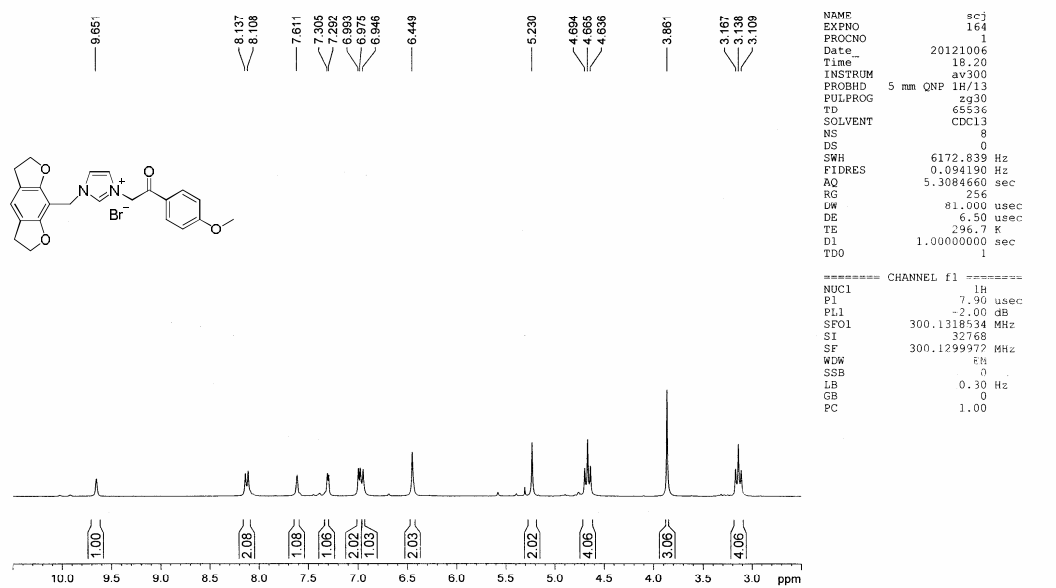


```

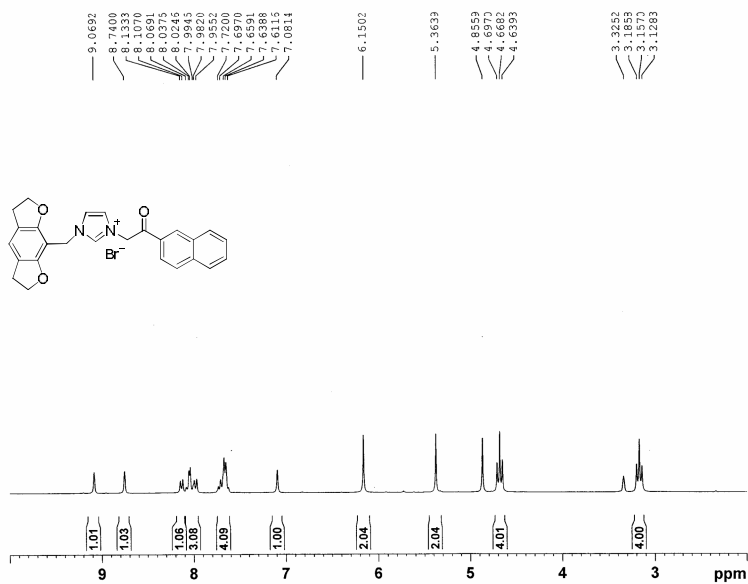
NAME      12011001176
EXPNO     1
PROCNO    1
Date_     20121013
Time      14.28
INSTRUM   av300
PROBHD    5 mm QNP 1H/13
PULPROG   zg30
TD         65536
SOLVENT   MeOD
NS         8
DS         0
SWH        6172.839 Hz
FIDRES     0.094190 Hz
AQ         5.3084660 sec
RG         256
EW         81.000 usec
DE         6.50 usec
TE         297.3 K
D1         1.00000000 sec
TDO        1
===== CHANNEL f1 =====
NUC1      1H
P1         7.90 usec
PL1        -2.00 dB
SFO1      300.1318534 MHz
SI         32768
SF         300.1300056 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



# Compound 19



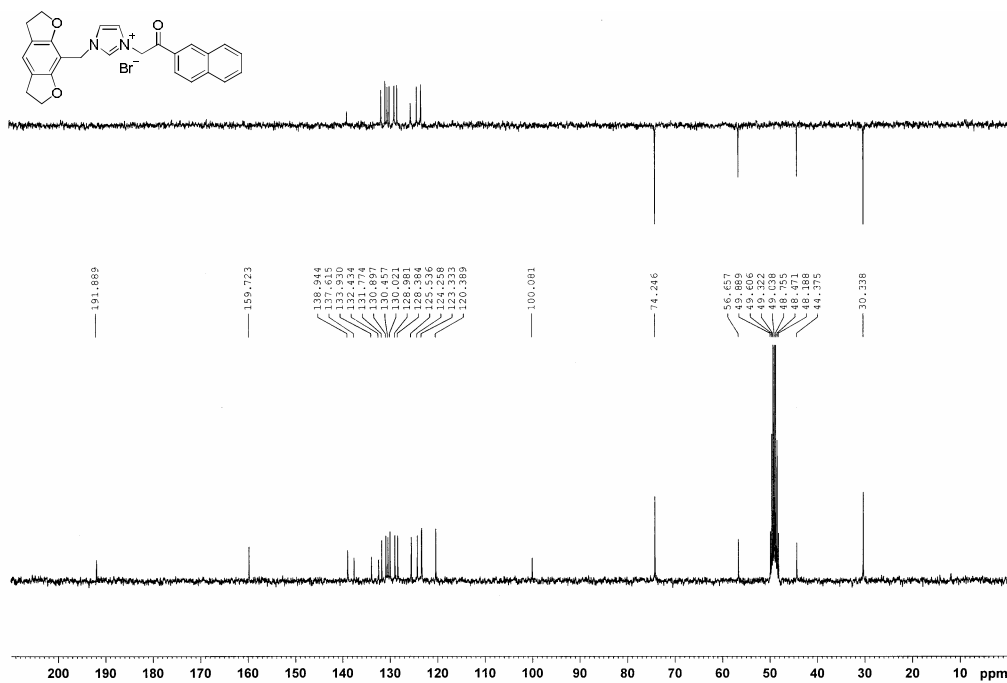
# Compound 20



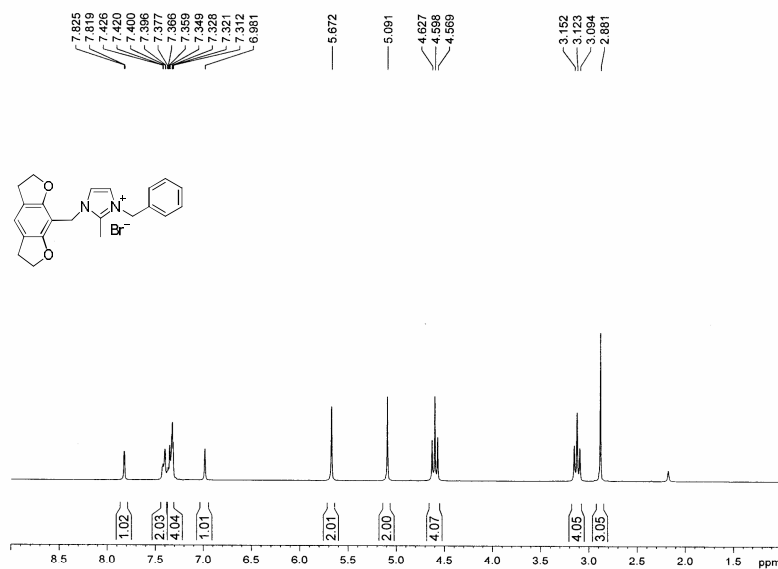
```

NAME      12011001176
EXPNO    6
PROCNO   1
Date_    20121015
Time     10.33
INSTRUM  av300
PROBHD   5 mm QNP 1H/13
PULPROG  zg30
TD        65536
SOLVENT  MeOD
NS        8
DS        0
SWH       6172.839 Hz
FIDRES    0.094190 Hz
AQ        5.3084660 sec
RG        181
DW        81.000 usec
DE        6.50 usec
TE        297.9 K
D1        1.00000000 sec
TD0       1

===== CHANNEL f1 =====
NUC1      1H
P1        7.90 usec
PL1       -2.00 dB
SFO1      300.1318534 MHz
SI        32768
SF        300.1299961 MHz
WVW       EM
SSB       0
LB        0.30 Hz
GB        0
PC        1.00
    
```



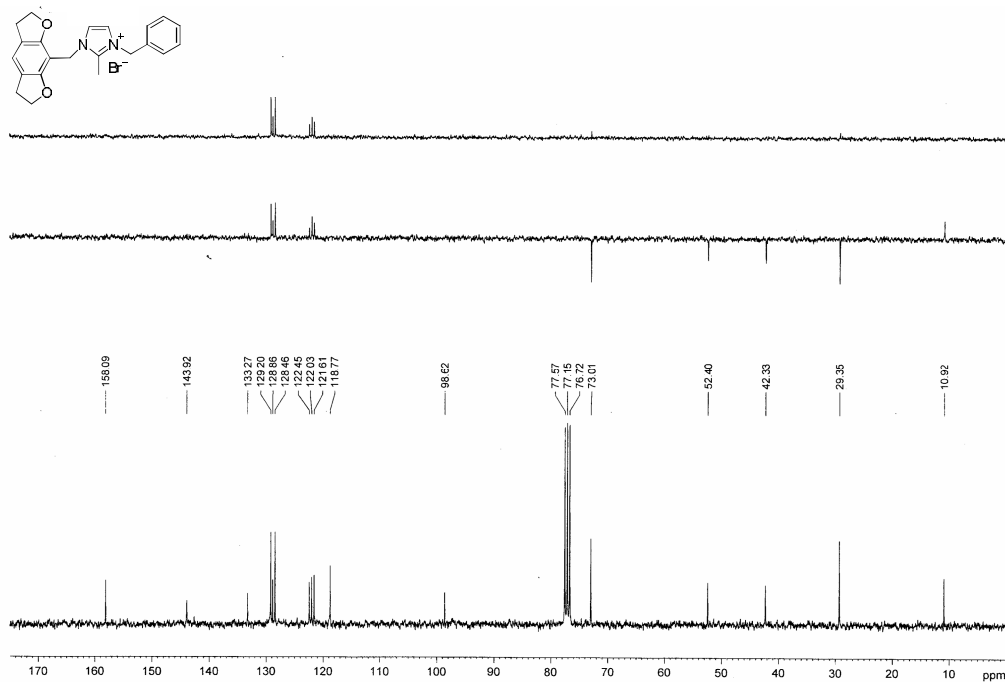
# Compound 21



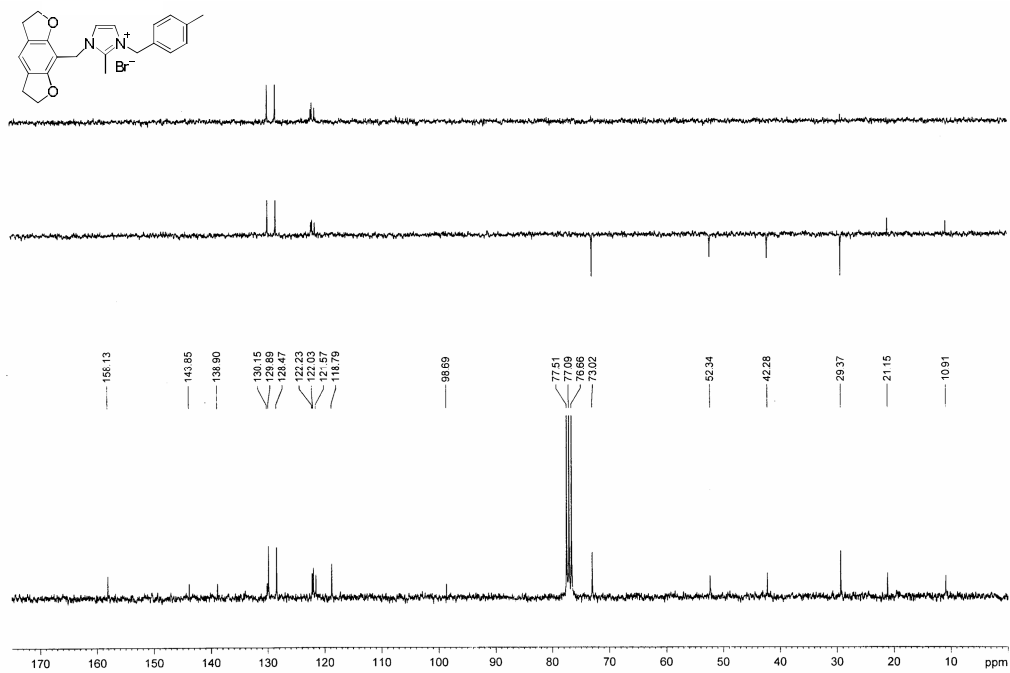
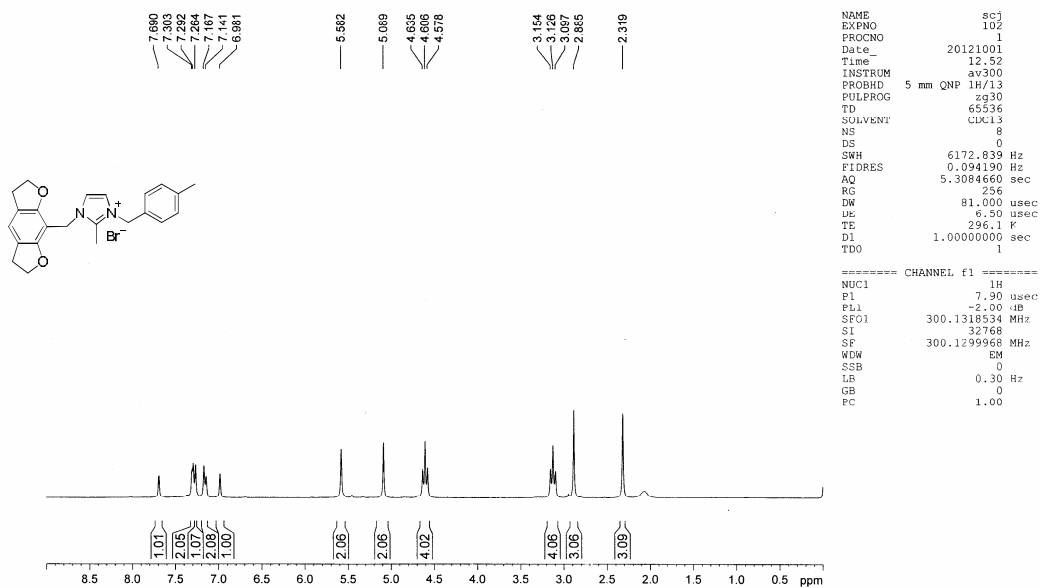
```

NAME          scj
EXPNO         122
PROCNO        1
Date_         20121001
Time          16.38
INSTRUM       av300
PROBHD        5 mm QNP 1H/13
PULPROG       zg30
TD            65536
SOLVENT       CDCl3
NS            8
DS            0
SWH           6172.839 Hz
FIDRES        0.094190 Hz
AQ            5.3084660 sec
RG            181
DW            81.000 usec
DE            6.50 usec
TE            296.2 K
D1            1.00000000 sec
TDO           1

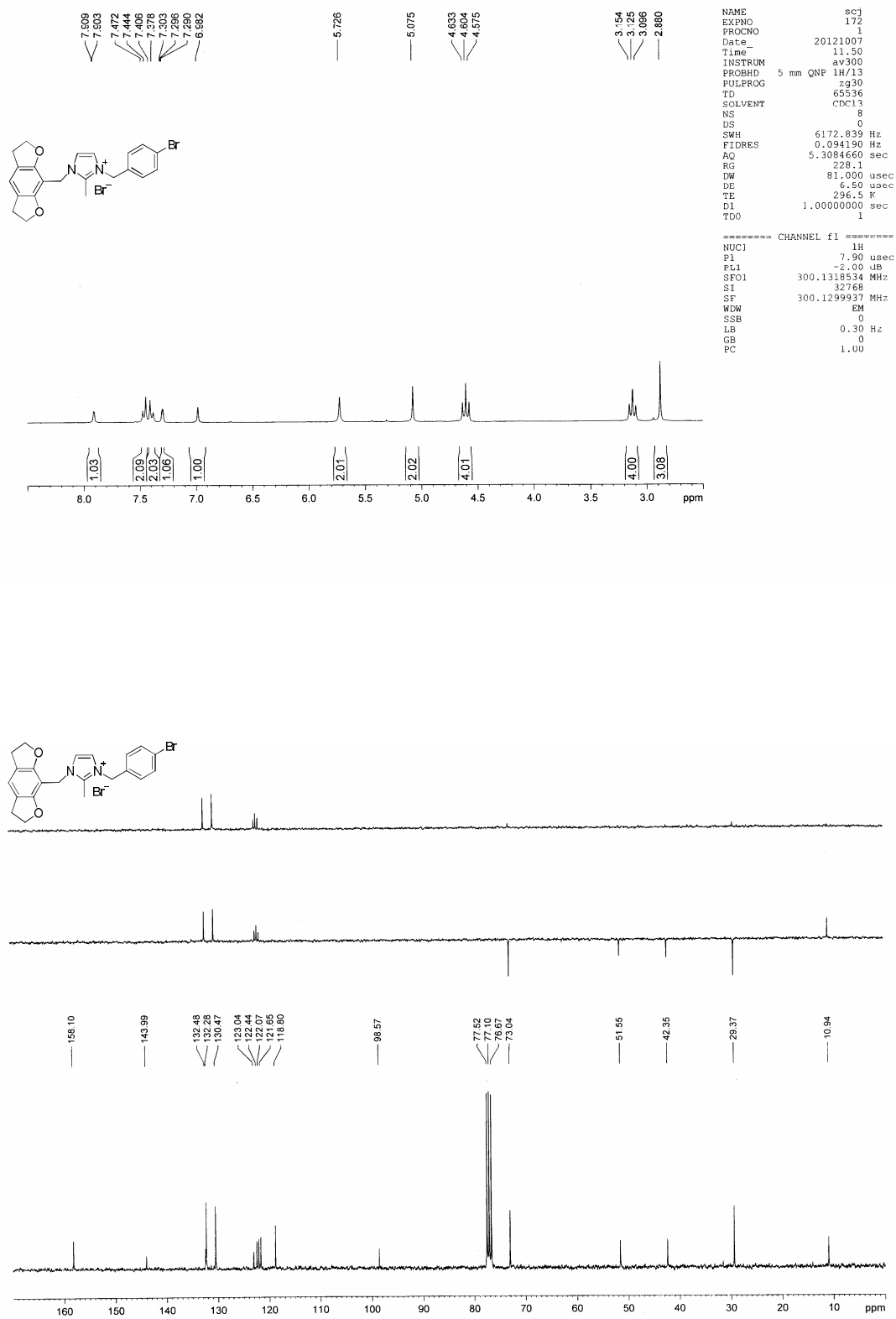
===== CHANNEL f1 =====
NUC1          1H
P1            7.90 usec
PL1          -2.00 dB
SFO1         300.1315534 MHz
SI           32768
SF           300.1299888 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



# Compound 22

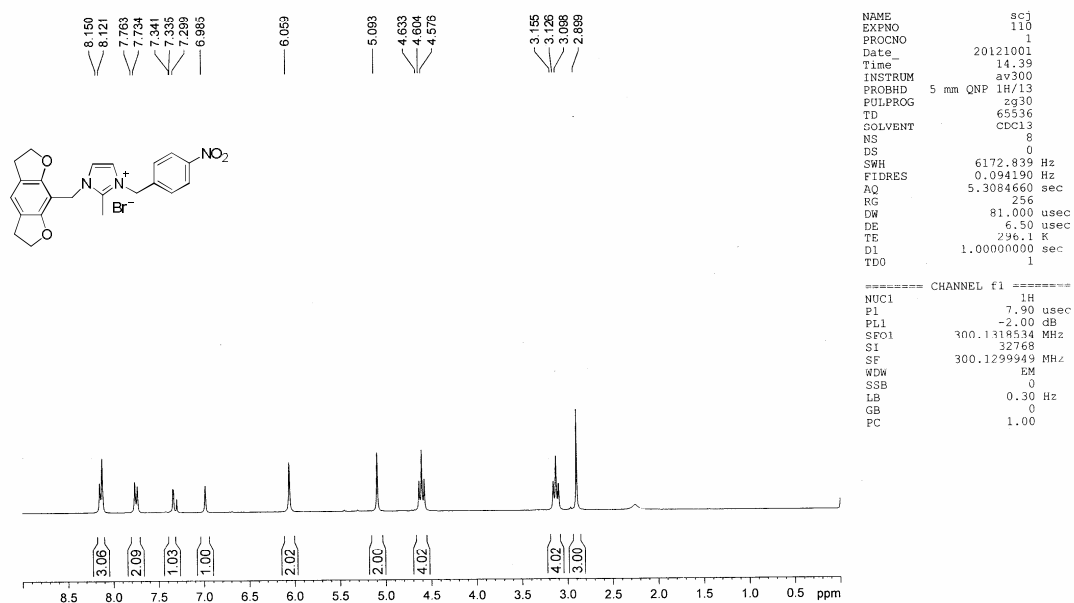


# Compound 23





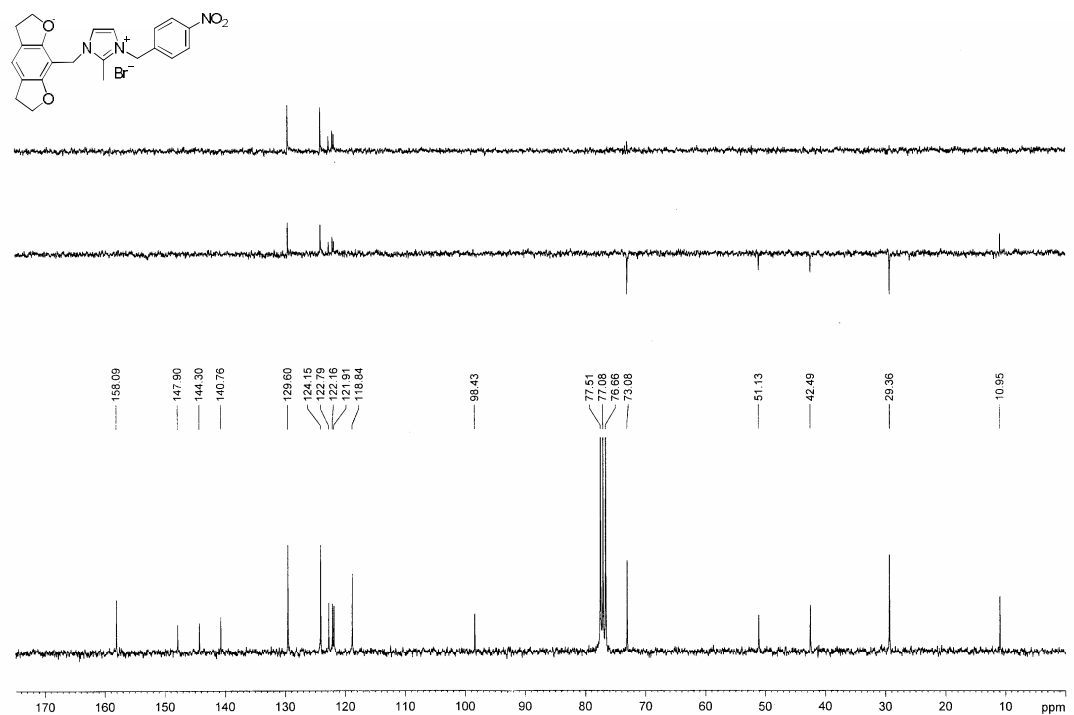
# Compound 24



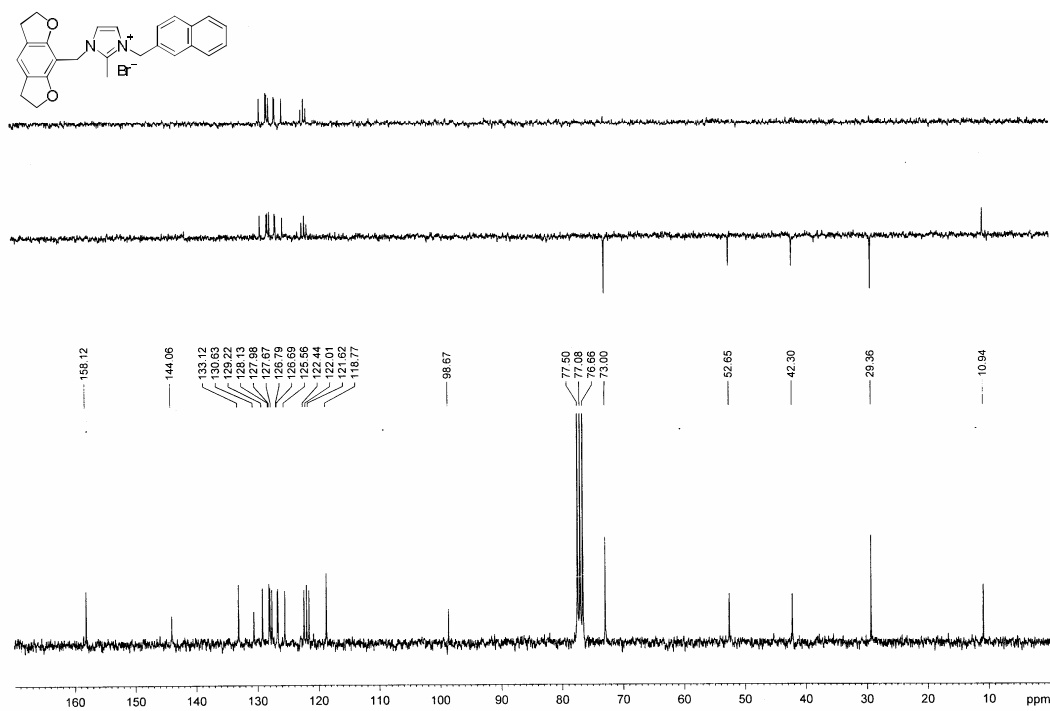
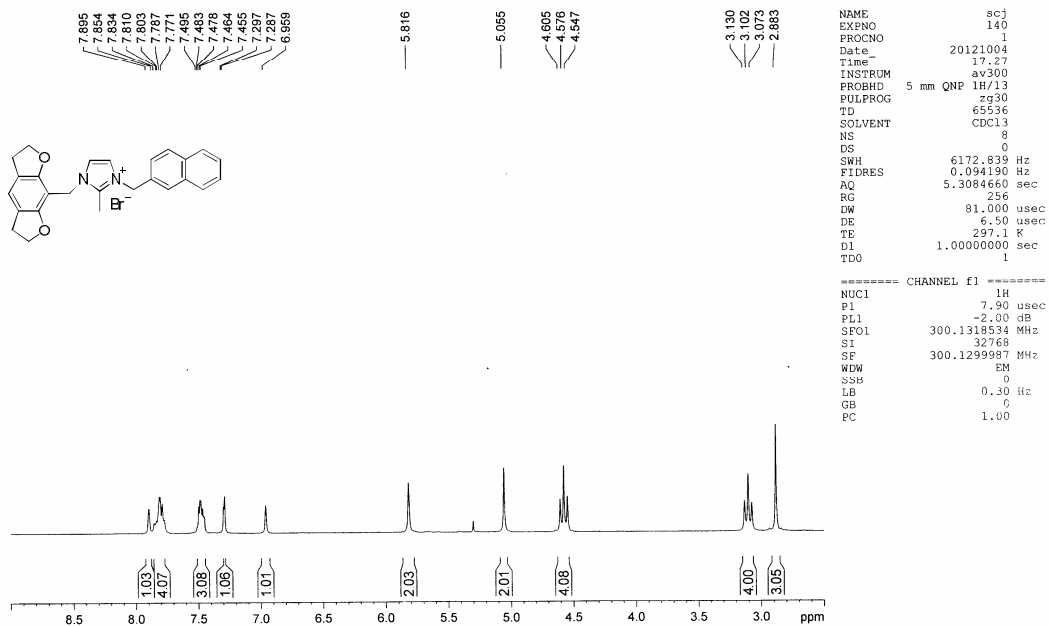
```

NAME          scj
EXPNO         110
PROCNO        1
Date_         20121001
Time          14.39
INSTRUM       av300
PROBHD        5 mm QNP 1H/13
PULPROG       zg30
TD            65536
SOLVENT       CDCl3
NS            8
DS            0
SWH           6172.839 Hz
FIDRES        0.094190 Hz
AQ            5.3084660 sec
RG            256
DW            81.000 usec
DE            6.50 usec
TE            296.1 K
D1            1.00000000 sec
TD0           1

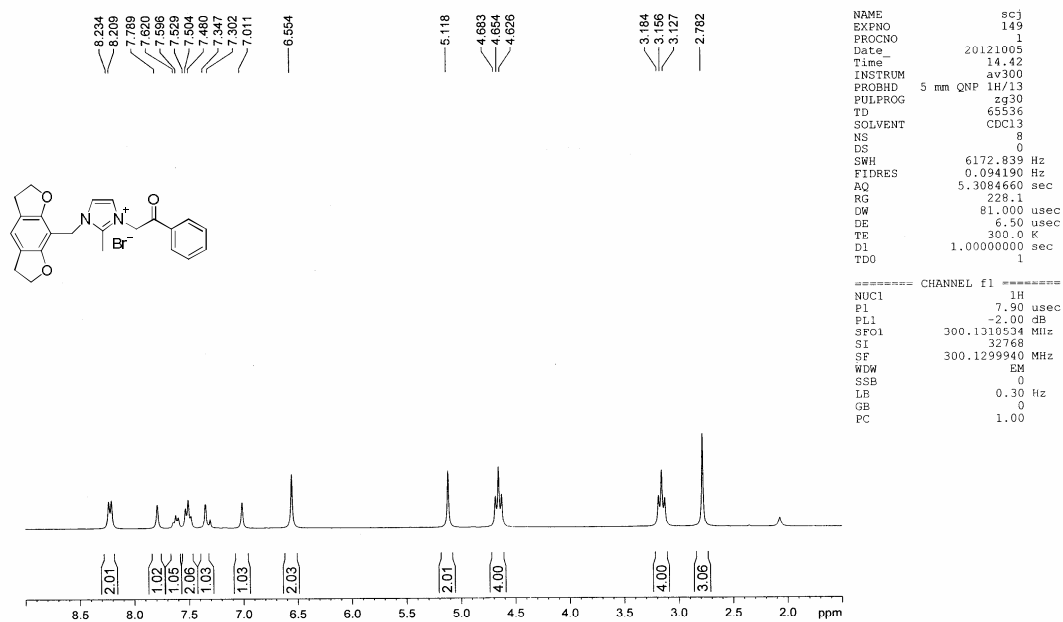
===== CHANNEL f1 =====
NUC1          1H
P1            7.90 usec
PL1           -2.00 dB
SFO1         300.1318534 MHz
SI            32768
SF           300.1299949 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
    
```



# Compound 25



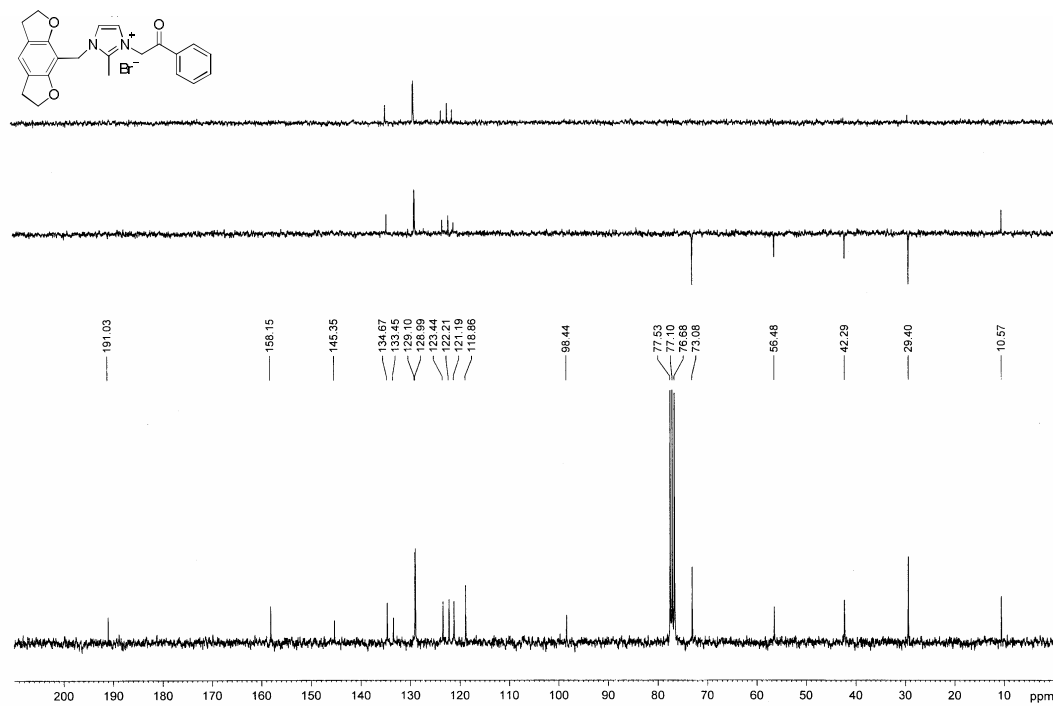
# Compound 26



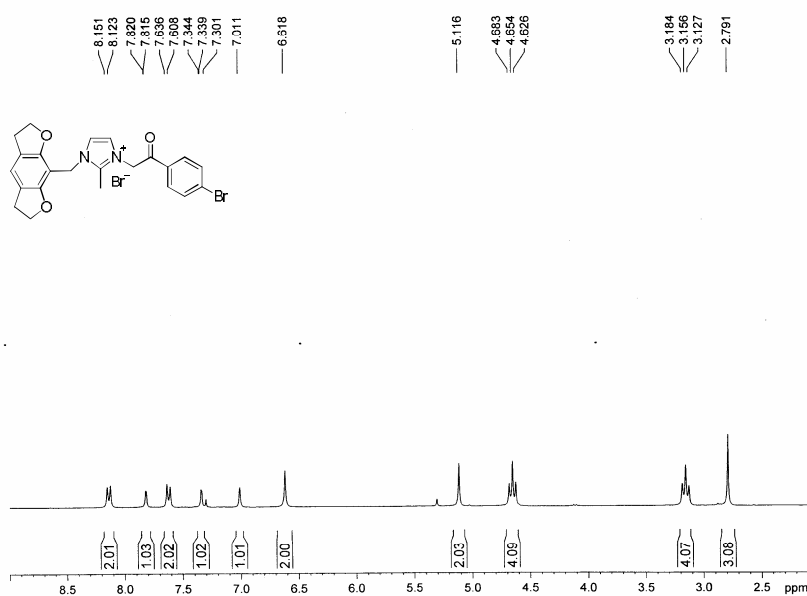
```

NAME          scj
EXPNO         149
PROCNO        1
Date_         20121005
Time          14.42
INSTRUM       av300
PROBHD        5 mm QNP 1H/13
PULPROG       zg30
TD            65536
SOLVENT       CDCl3
NS            8
DS            0
SWH           6172.839 Hz
FIDRES        0.094190 Hz
AQ            5.3084660 sec
RG            228.1
DW            81.000 usec
DE            6.50 usec
TE            300.0 K
D1            1.00000000 sec
TDO           1

===== CHANNEL f1 =====
NUC1          1H
P1            7.90 usec
PL1           +2.00 dB
SFO1         300.1310534 MHz
SI            32768
SF           300.1299940 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



# Compound 27

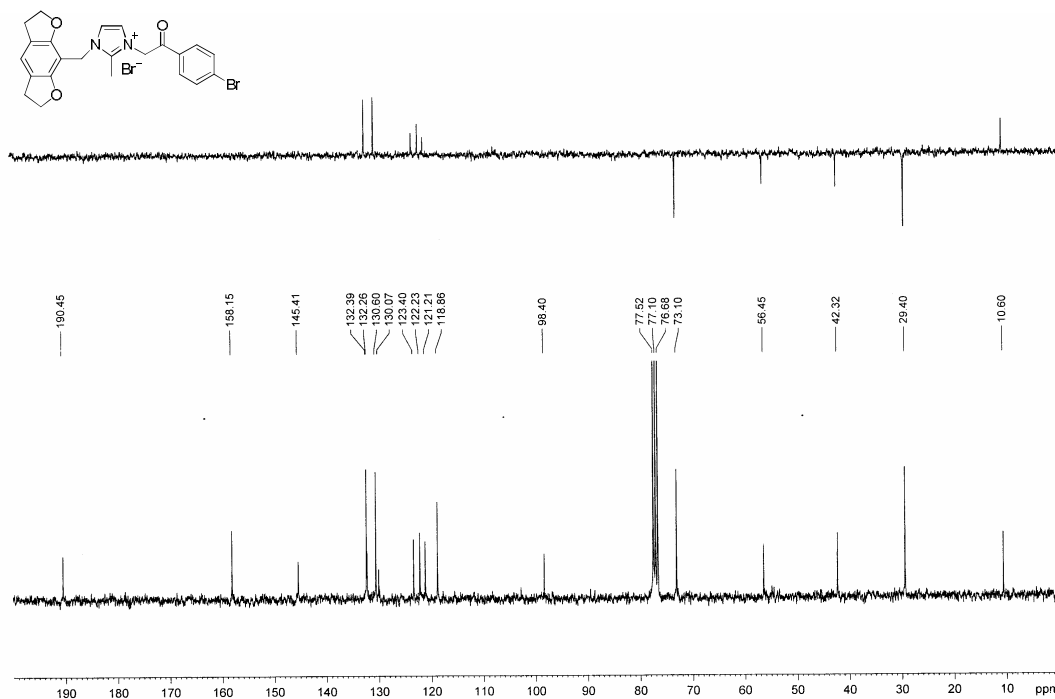


```

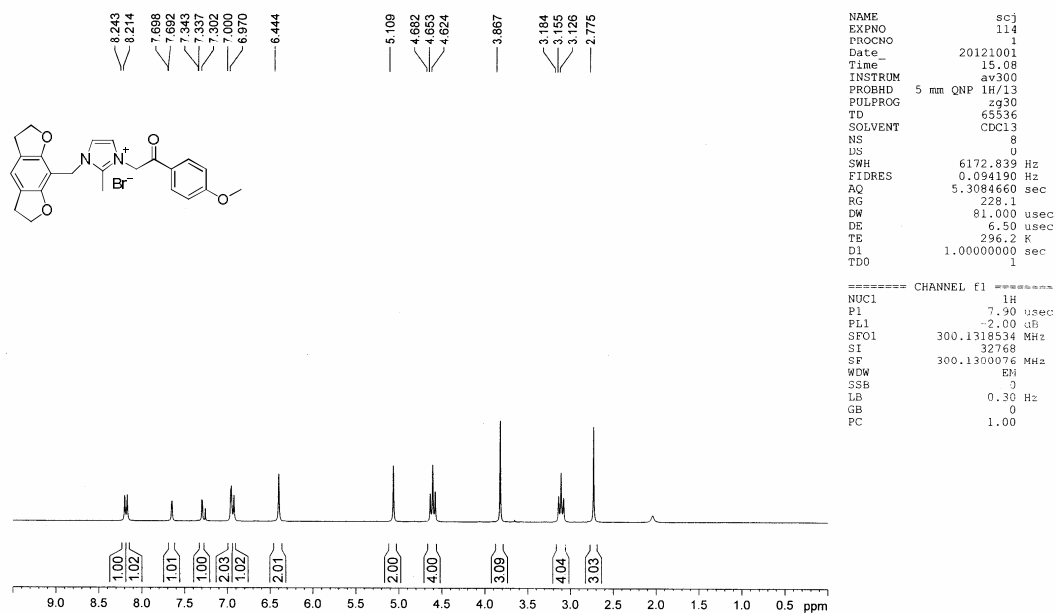
NAME          scj
EXPNO         135
PROCNO        1
Date_         20121004
Time_         12.59
INSTRUM       av300
PROBHD        5 mm QNP
PULPROG       zg30
TD            65536
SOLVENT       CDCl3
NS            8
DS            0
SWH           6172.839 Hz
FIDRES        0.094190 Hz
AQ            5.3084660 sec
RG            228.1
DW            81.000 usec
DE            6.50 usec
TE            296.3 K
D1            1.00000000 sec
TDO           1
  
```

```

----- CHANNEL f1 -----
NUC1          1H
P1            7.90 usec
PL1           2.00 dB
SFO1         300.1318534 MHz
SI            32768
SF           300.1299943 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



# Compound 28

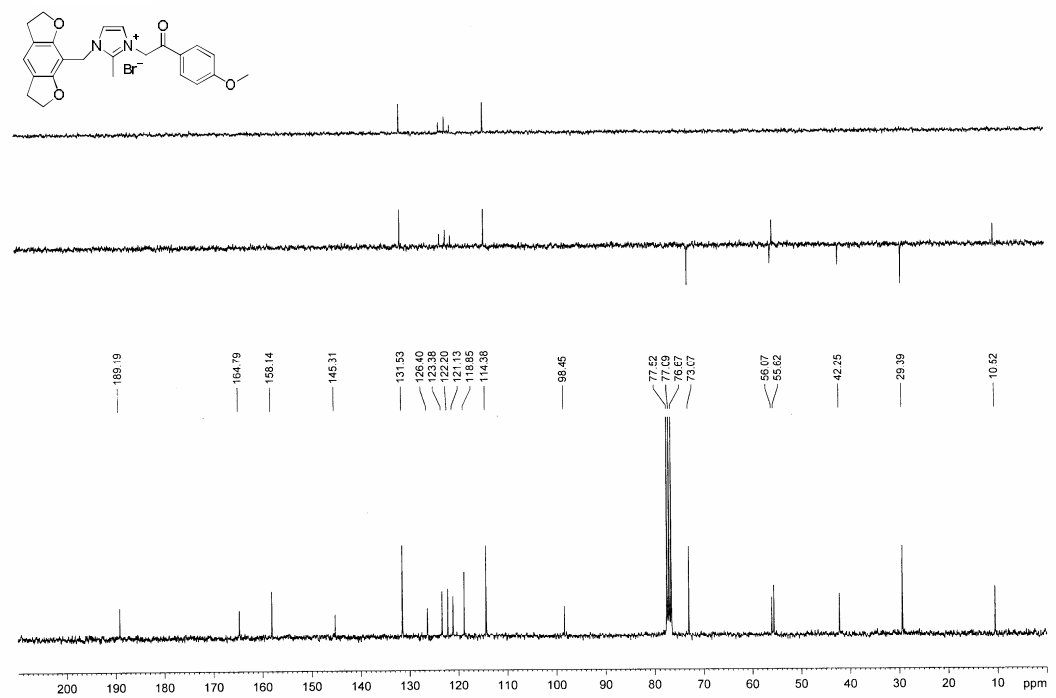


```

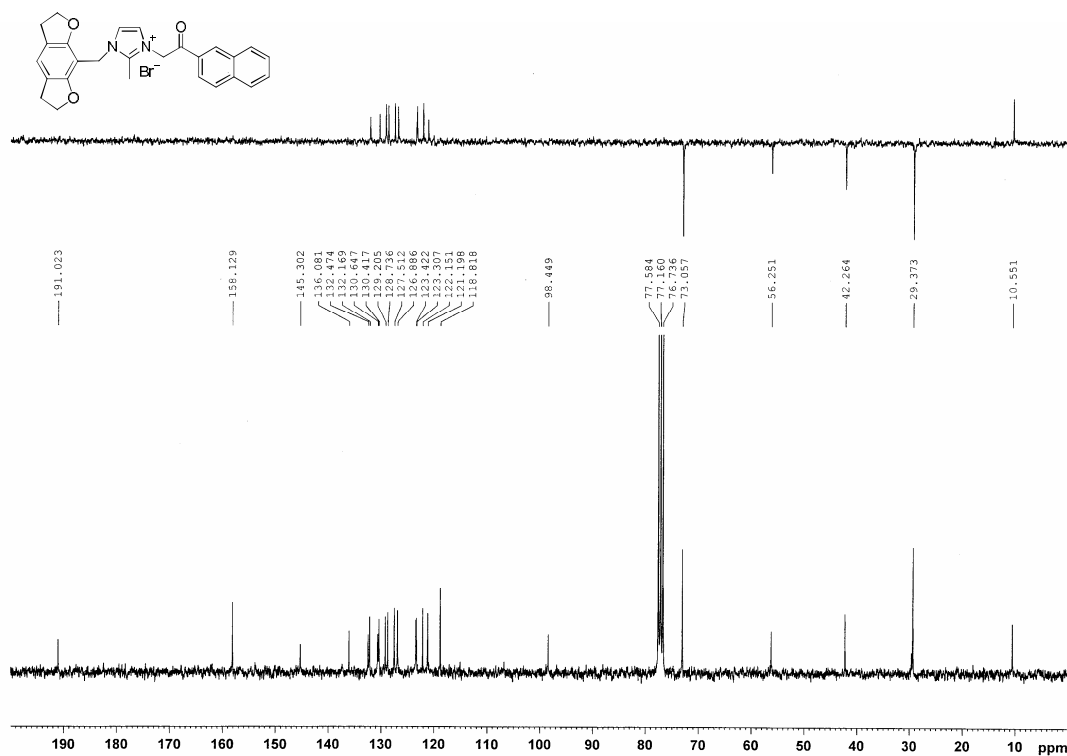
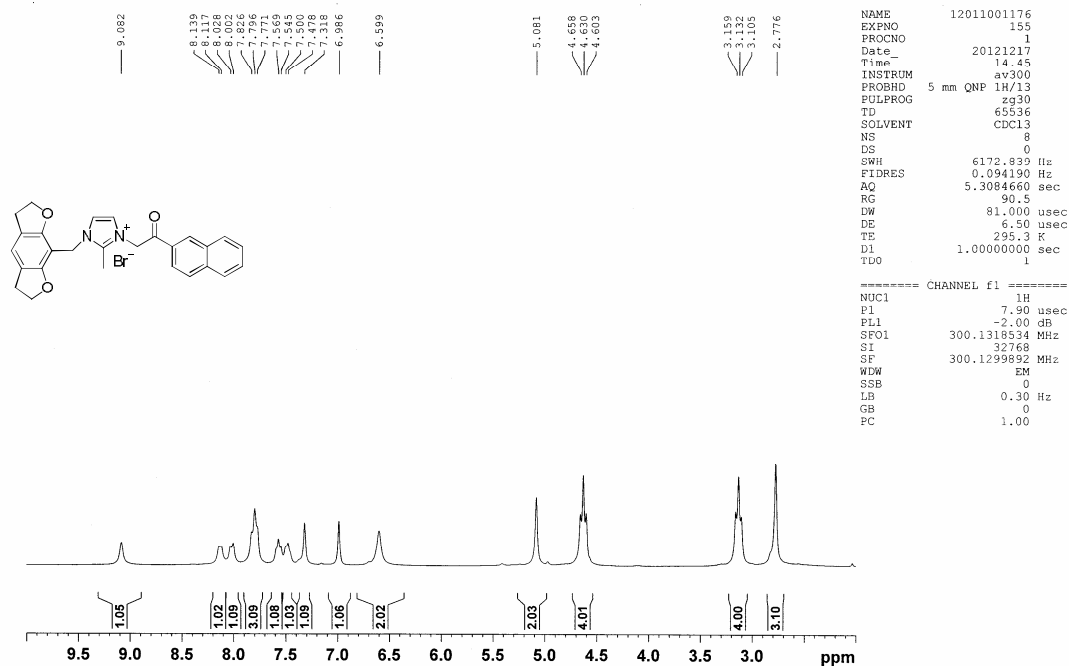
NAME          scj
EXPNO         114
PROCNO        1
Date_         20121001
Time          15.08
INSTRUM       av300
PROBHD        5 mm QNP 1H/13
PULPROG       zg30
TD            65536
SOLVENT       CDCl3
NS            8
DS            0
SWH           6172.839 Hz
FIDRES        0.094190 Hz
AQ            5.3084660 sec
RG            228.1
DW            81.000 usec
DE            6.50 usec
TE            296.2 K
D1            1.00000000 sec
D11           3
TDO
  
```

```

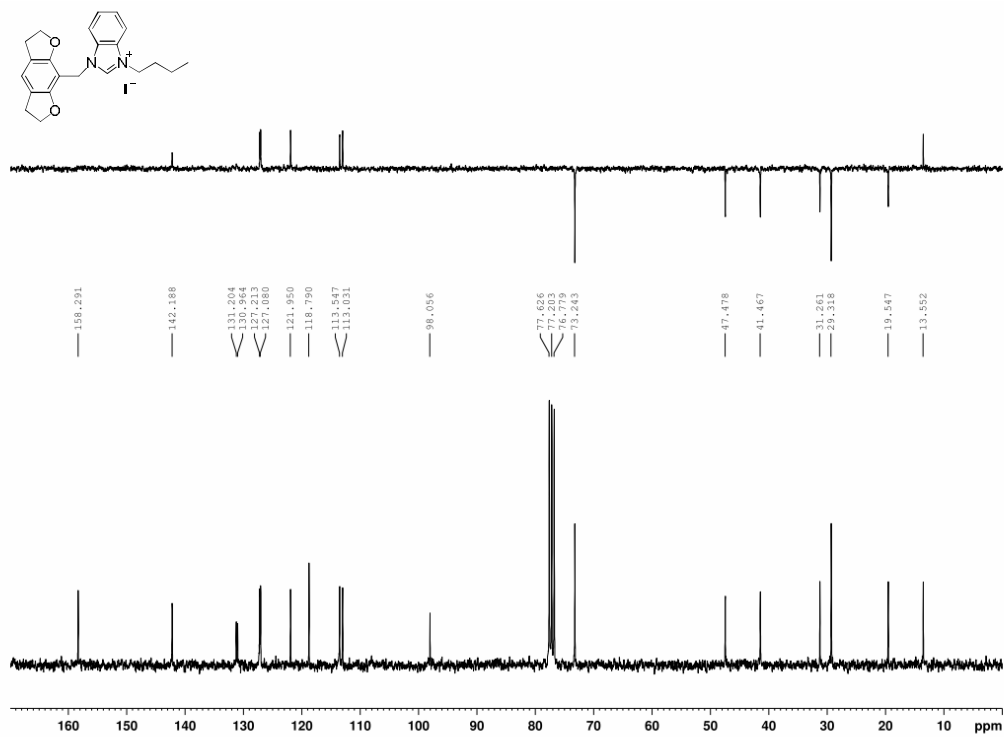
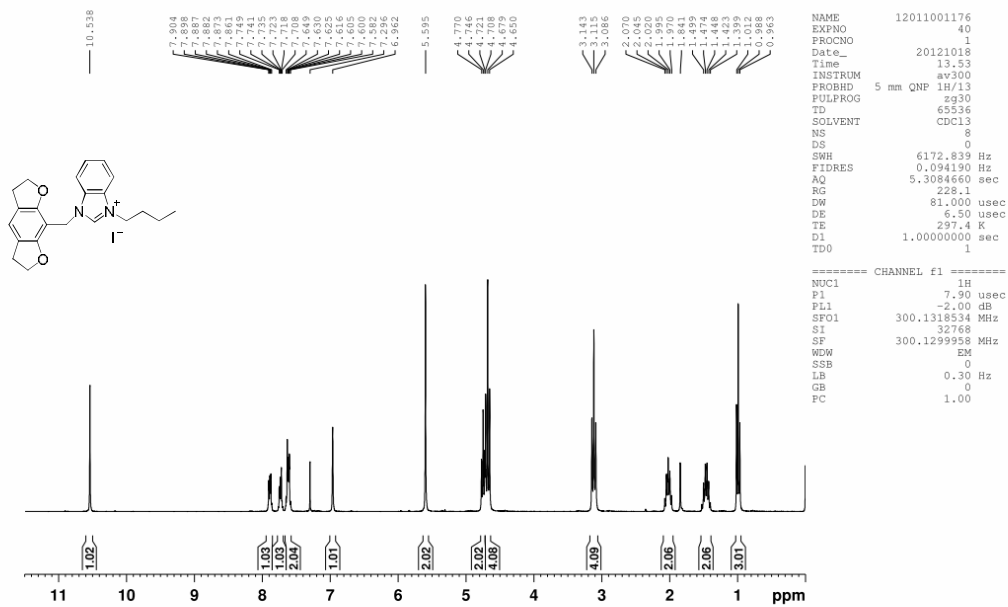
===== CHANNEL f1 =====
NUC1          1H
P1            7.90 usec
PL1           -2.00 dB
SFO1         300.1318534 MHz
SI            32768
SF           300.1300076 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



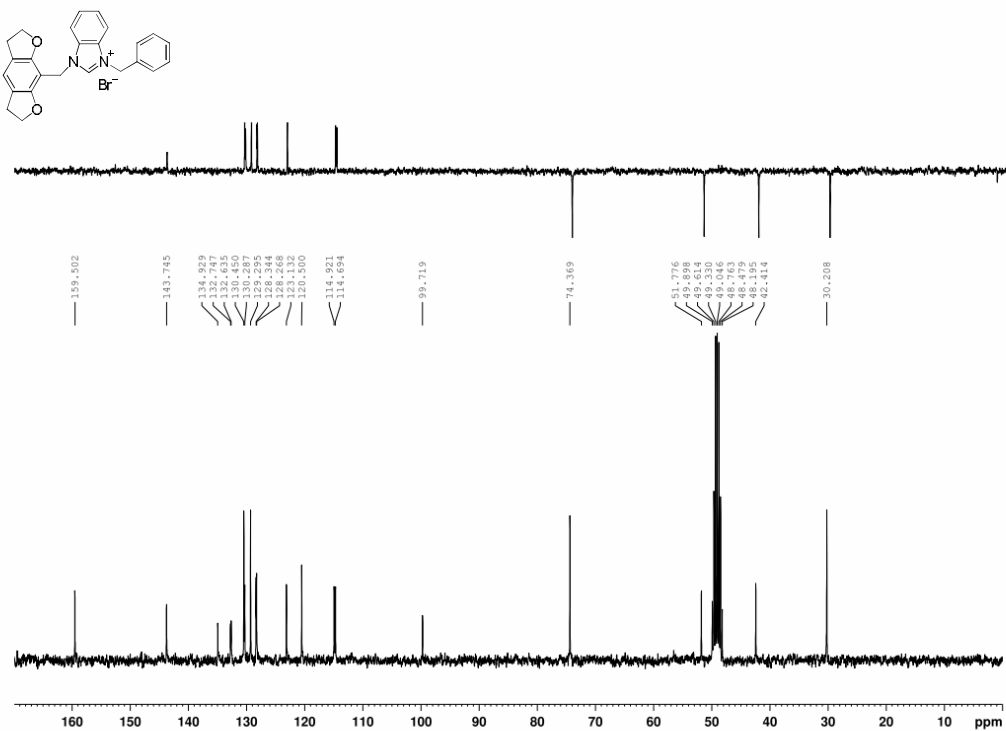
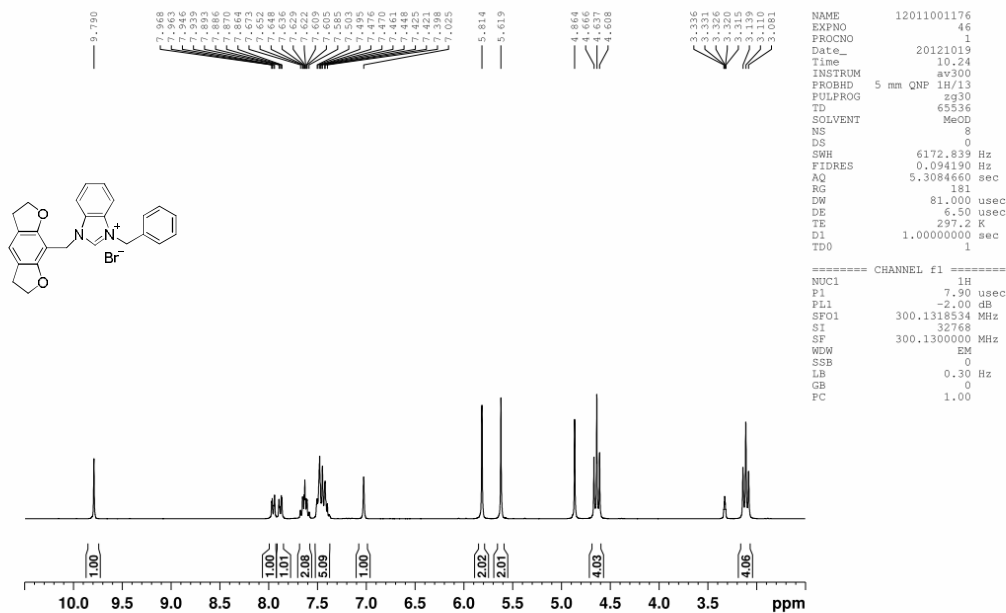
# Compound 29



# Compound 30

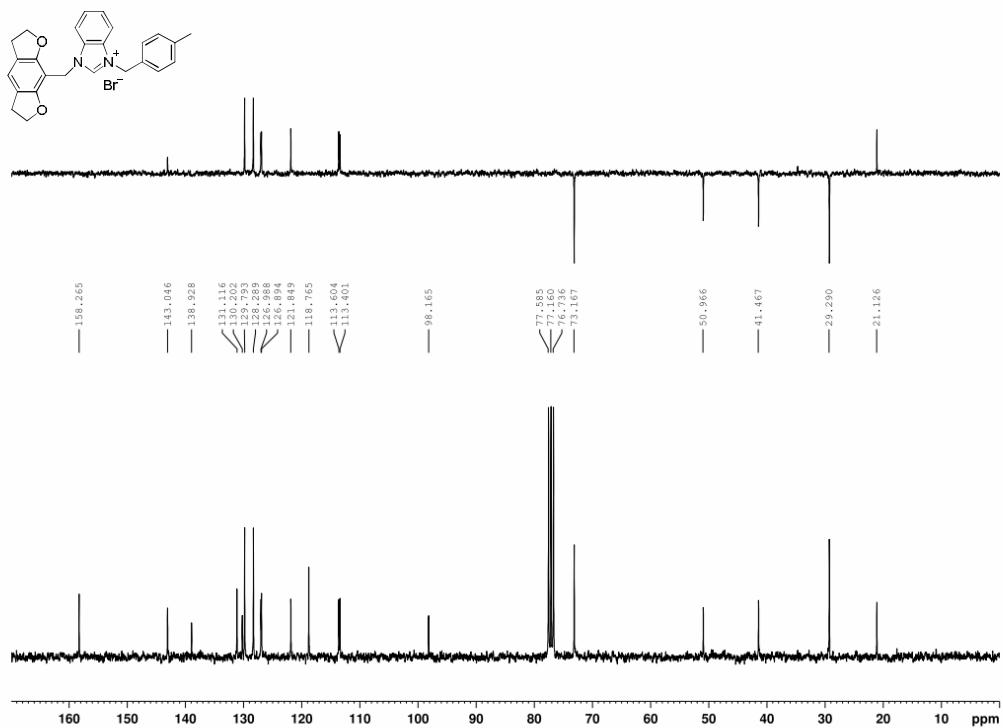
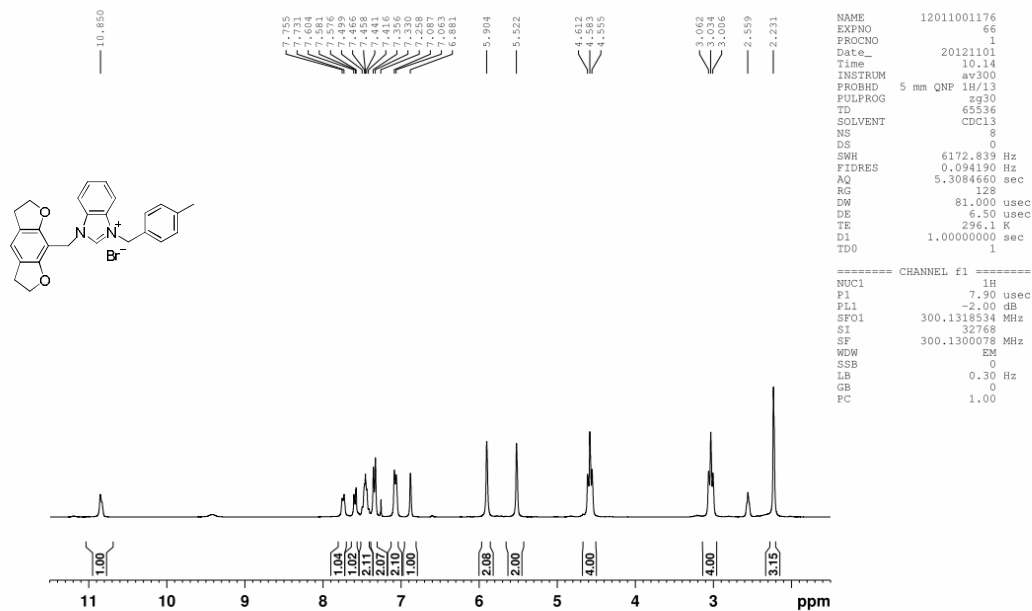


# Compound 31

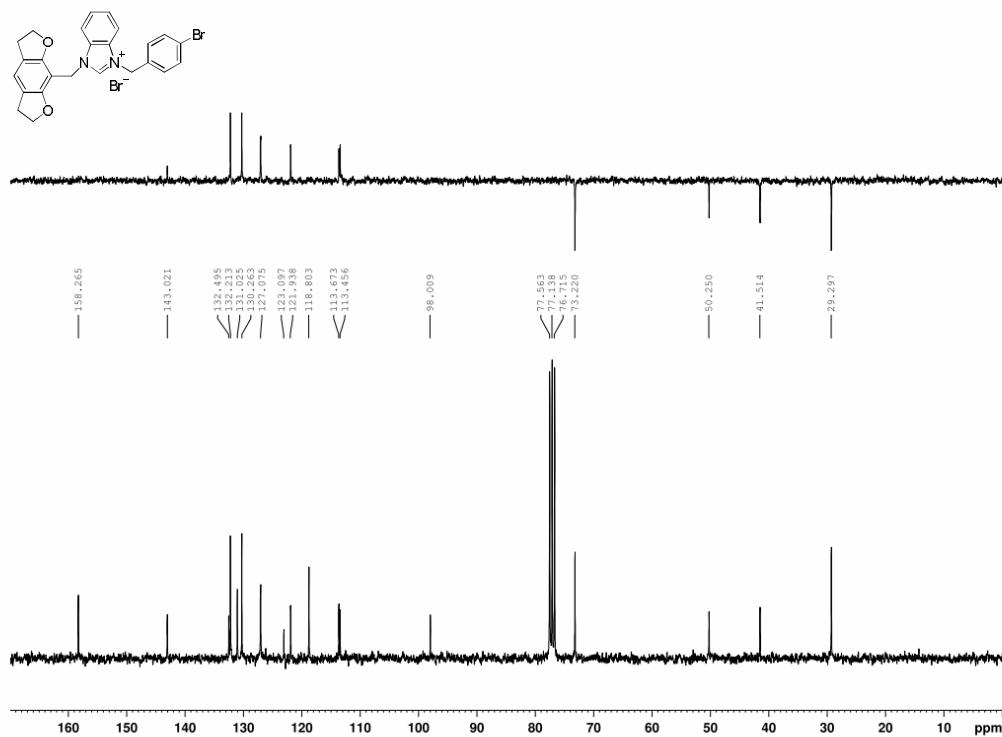
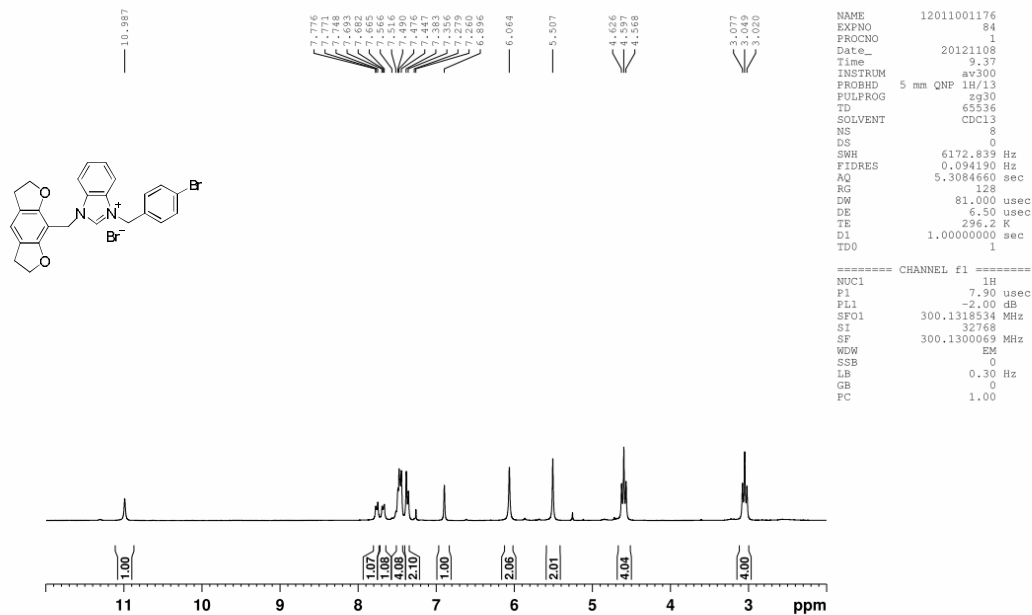




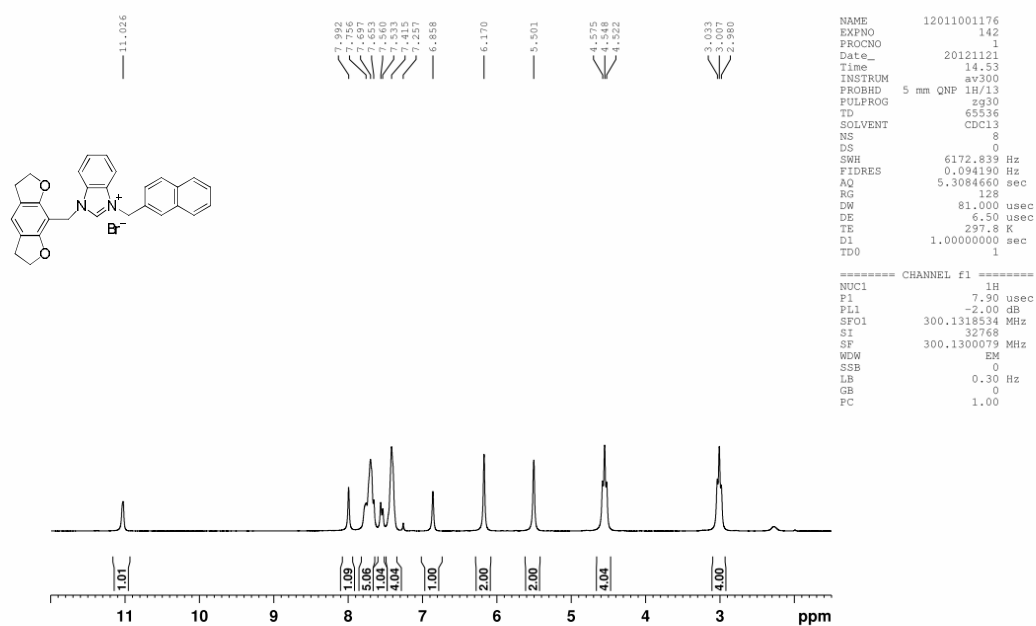
# Compound 32



# Compound 33



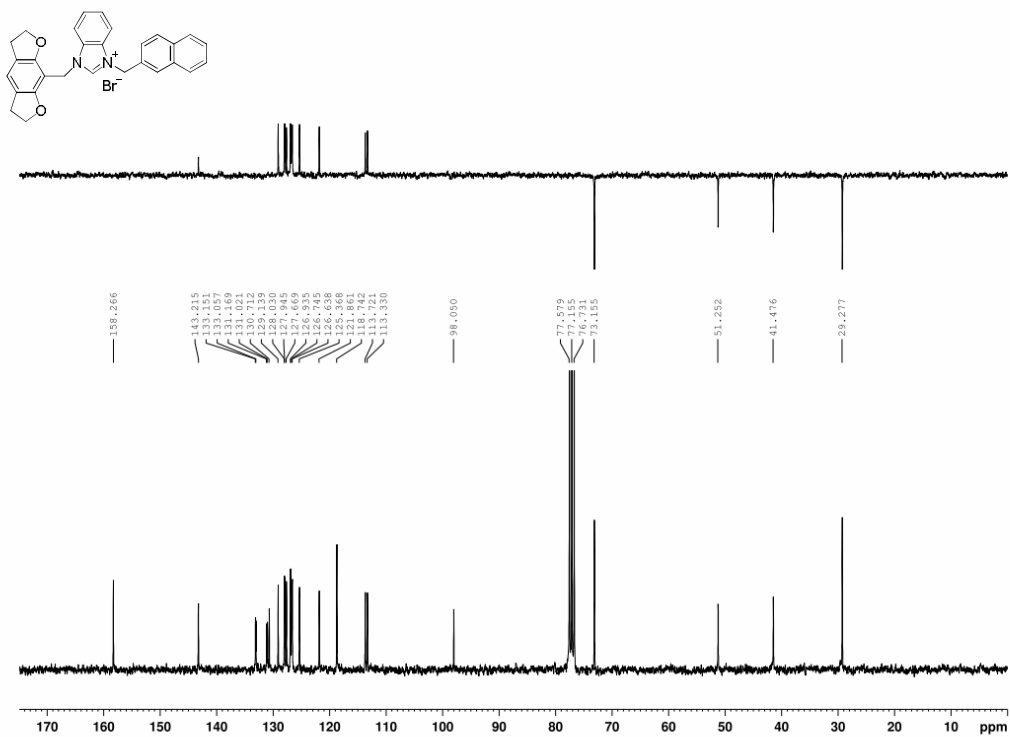
# Compound 34



```

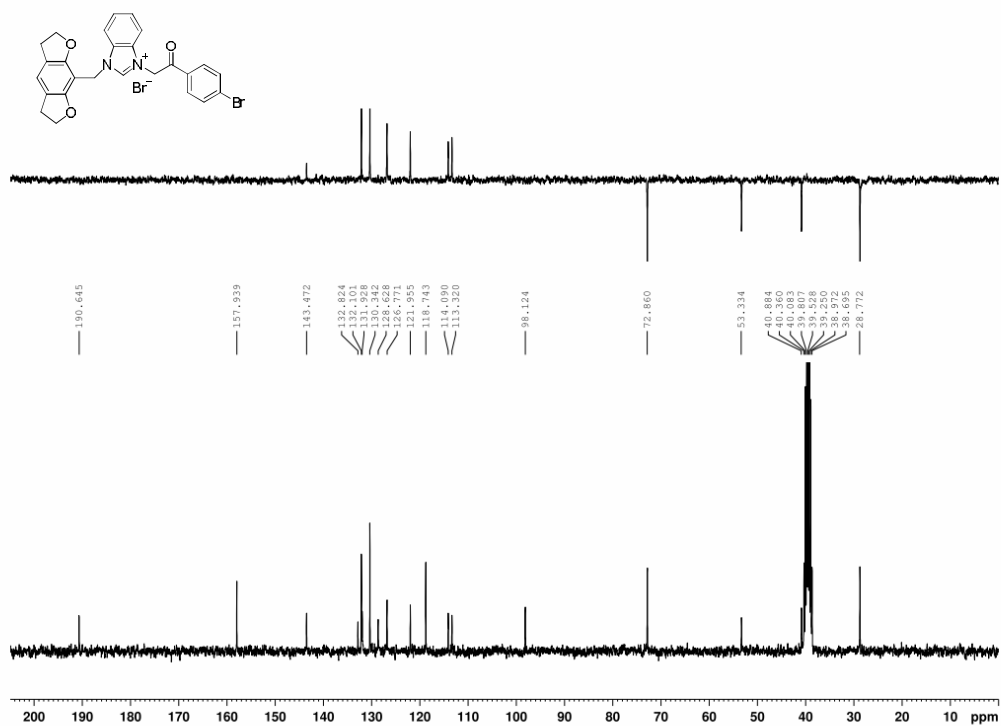
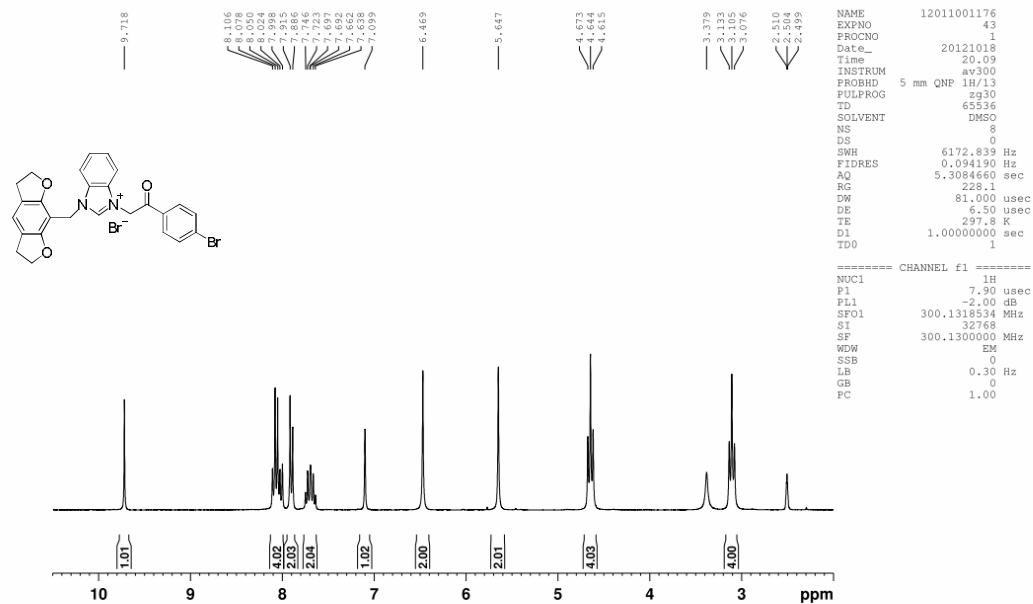
NAME      12011001176
EXPNO     142
PROCNO    1
Date_     20121121
Time      14.53
INSTRUM   av300
PROBHD    5 mm QNP 1H/13
PULPROG   zg30
TD         65536
SOLVENT   CDCl3
NS         8
DS         0
SWH        6172.839 Hz
FIDRES     0.094190 Hz
AQ         5.3084660 sec
RG         128
DW         81.000 usec
DE         6.50 usec
TE         297.8 K
D1         1.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         7.90 usec
PL1        -2.00 dB
SFO1       300.1318534 MHz
SI         32768
SF         300.1300079 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```

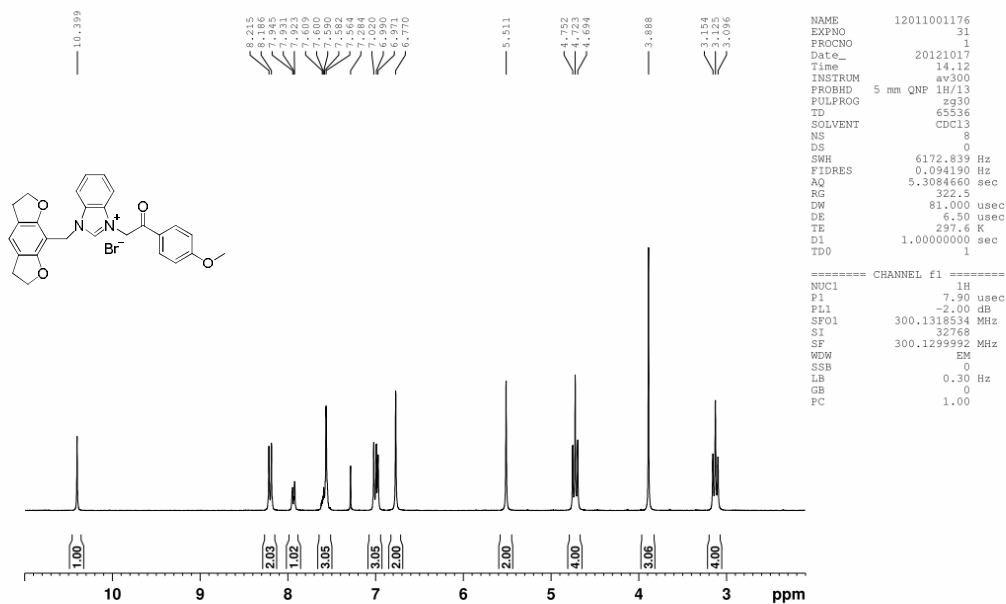




# Compound 36



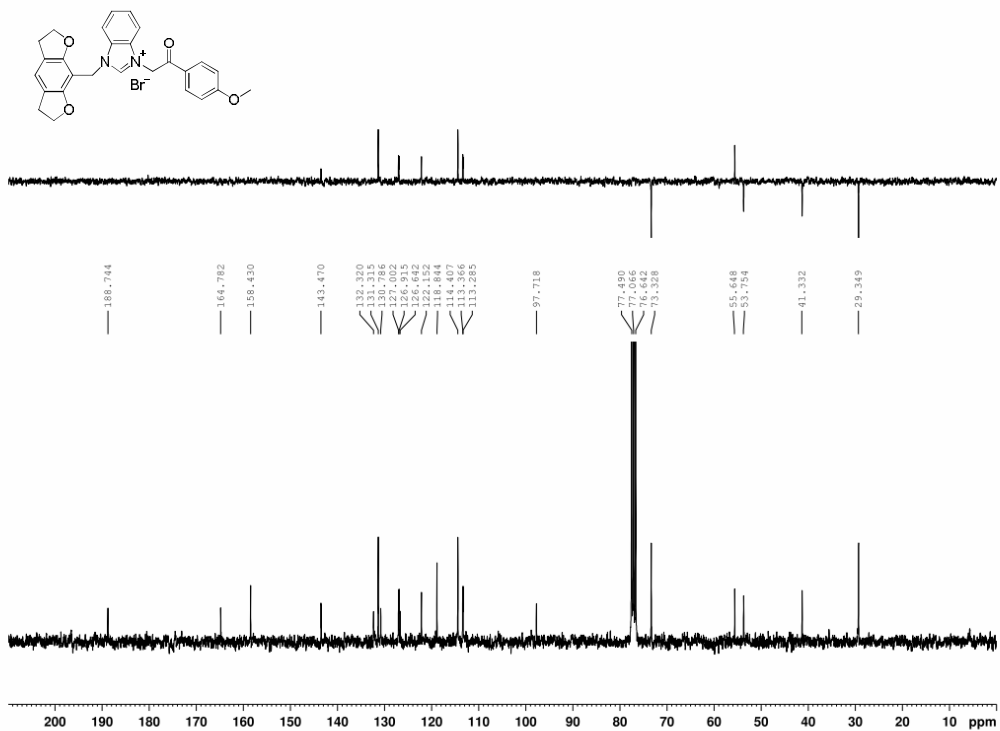
# Compound 37



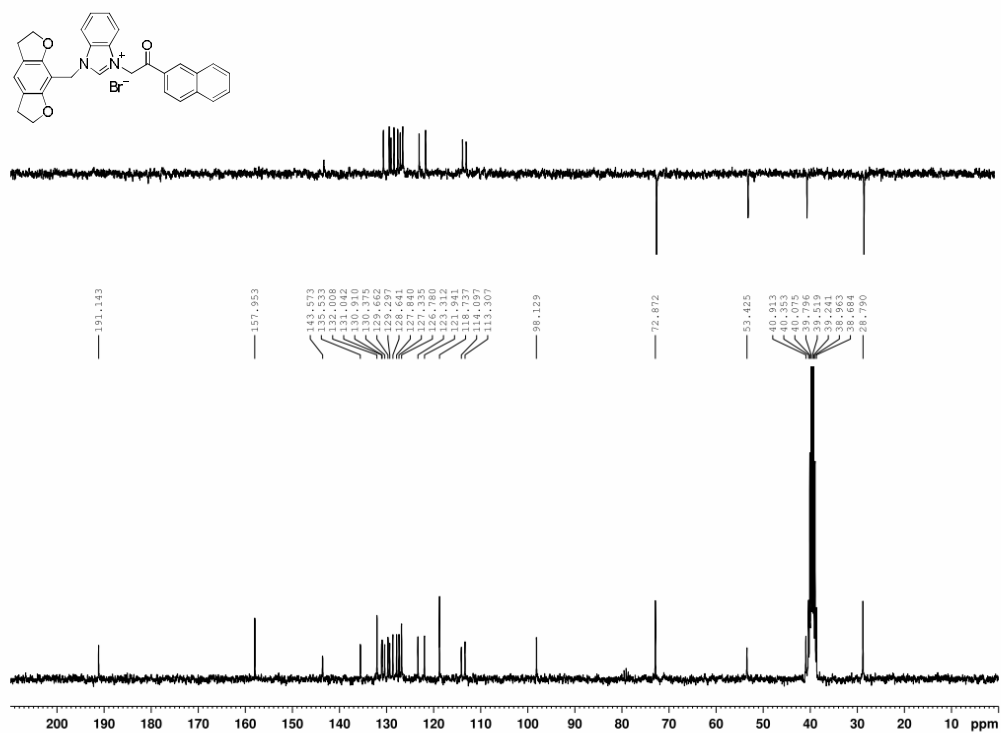
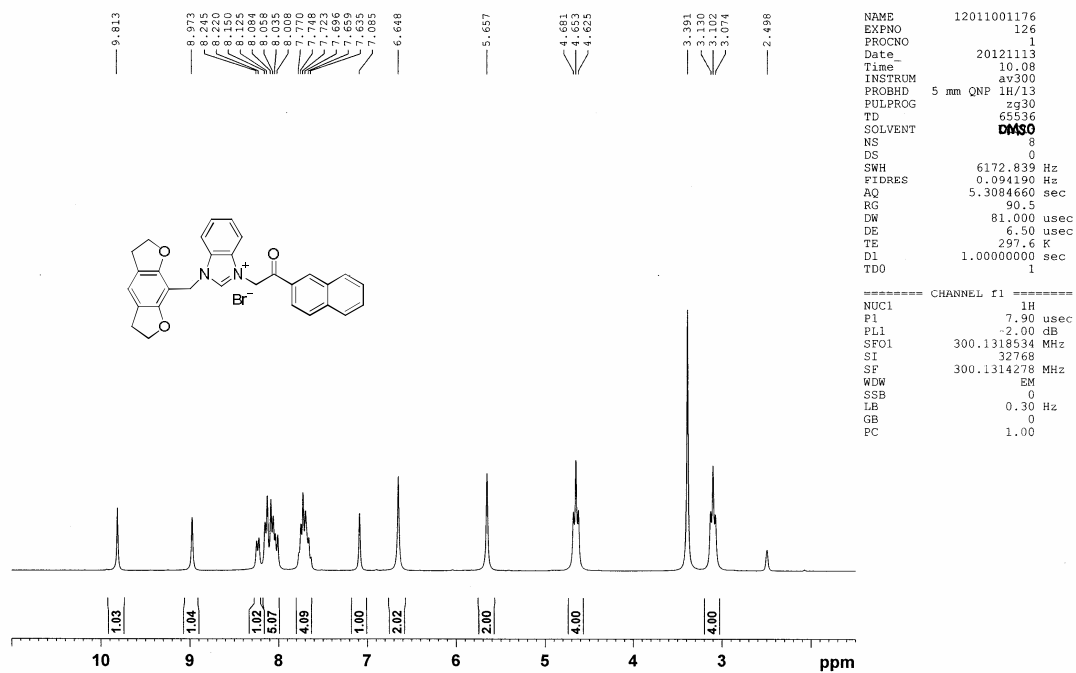
```

NAME      12011001176
EXPNO     31
PROCNO    1
Date_     20121017
Time      14.12
INSTRUM   av300
PROBHD    5 mm QNP 1H/13
PULPROG   zg30
TD         65536
SOLVENT   CDCl3
NS         8
DS         0
SWH        6172.839 Hz
FIDRES     0.094190 Hz
AQ         5.3084660 sec
RG         322.5
DW         81.000 usec
DE         6.50 usec
TE         297.6 K
D1         1.00000000 sec
TD0        1

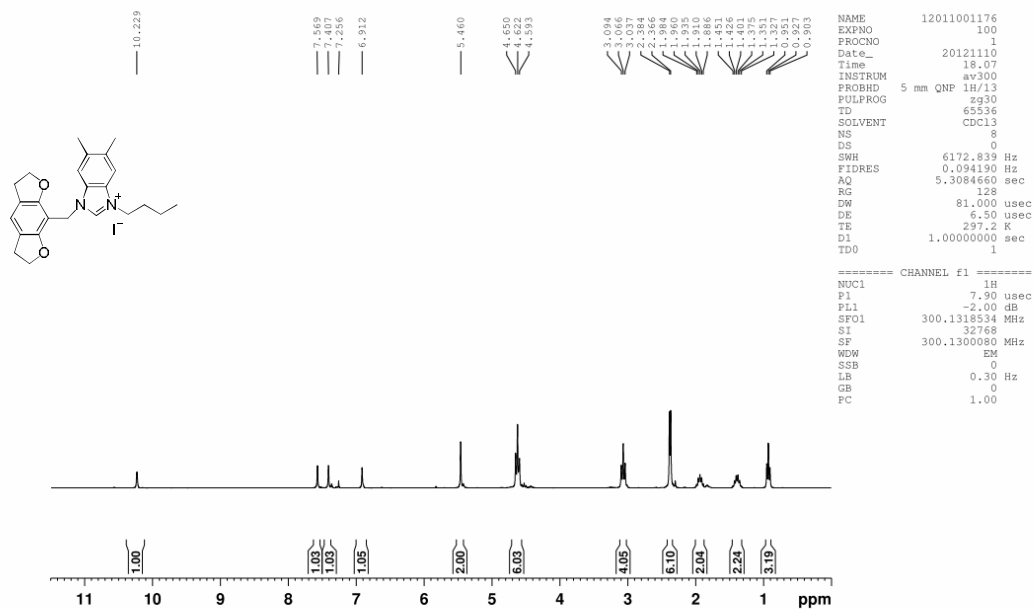
===== CHANNEL f1 =====
NUC1       1H
P1         7.90 usec
PL1        -2.00 dB
SFO1       300.1318534 MHz
SI         32768
SF         300.1299992 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```



# Compound 38



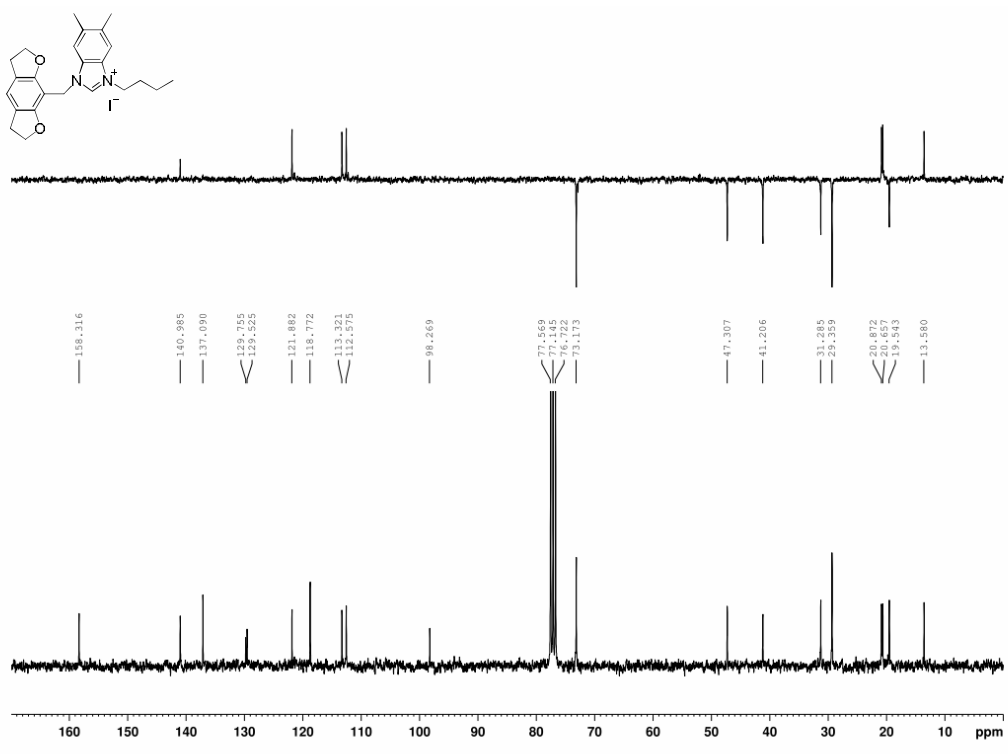
# Compound 39



```

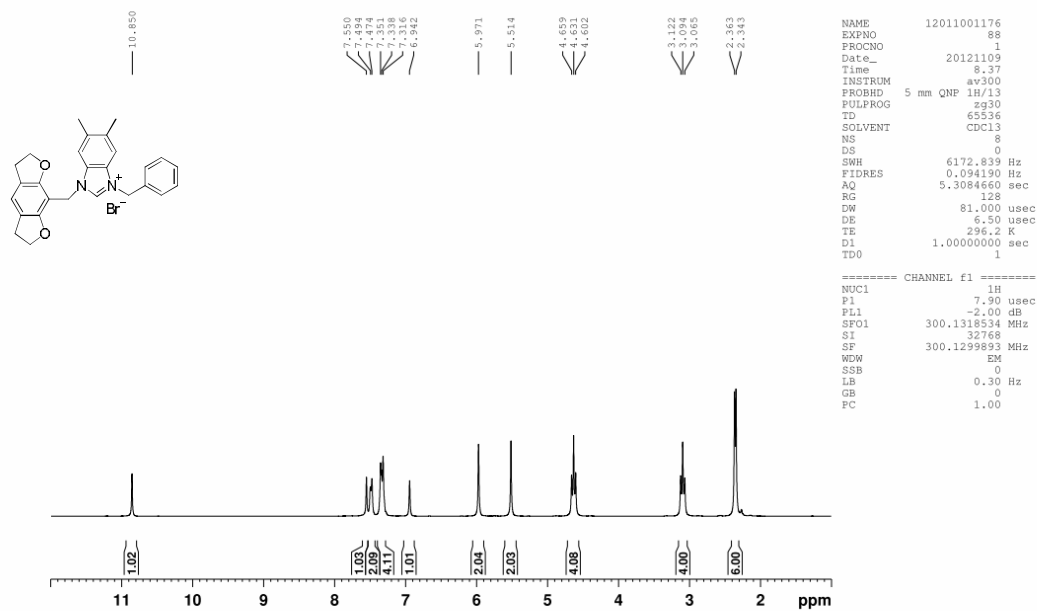
NAME      12011001176
EXPNO     100
PROCNO    1
Date_     20121110
Time      18.07
INSTRUM   av300
PROBHD    5 mm QNP 1H/13
PULPROG   zg30
TD         65536
SOLVENT   CDCl3
NS         8
DS         0
SWH        6172.839 Hz
FIDRES     0.094190 Hz
AQ         5.3084660 sec
RG         128
DW         81.000 usec
DE         5.50 usec
TE         297.2 K
D1         1.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1      1H
P1        7.90 usec
PL1       -2.00 dB
SFO1      300.1318534 MHz
SI        32768
SF        300.1300000 MHz
WDW       EM
SSB       0
LB        0.30 Hz
GB        0
PC        1.00
    
```



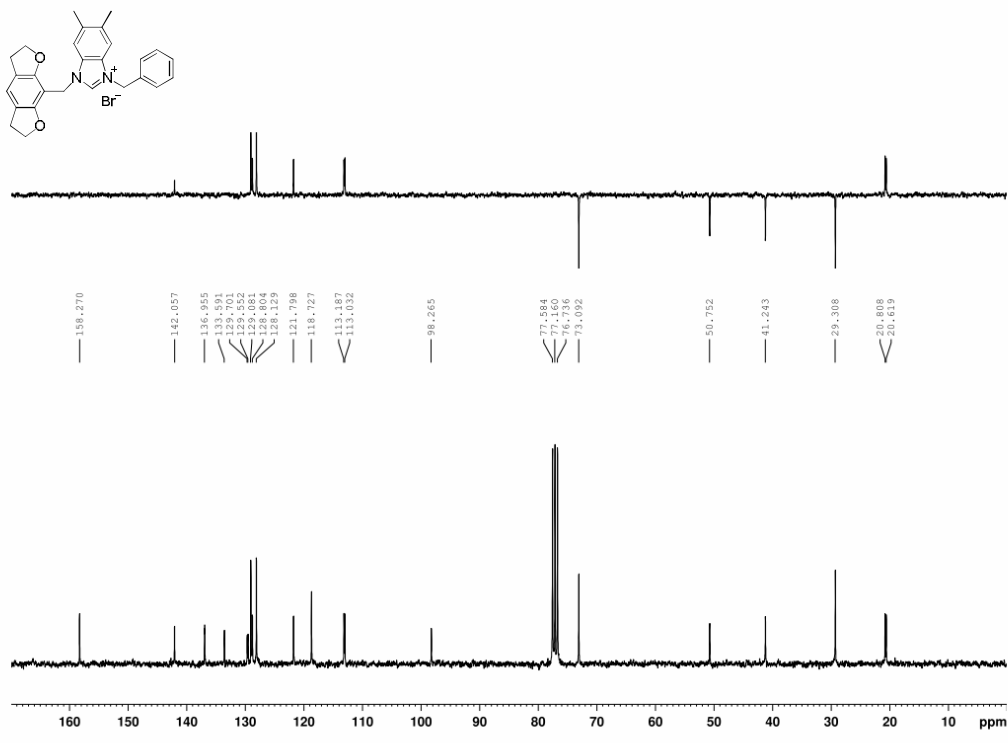


# Compound 40

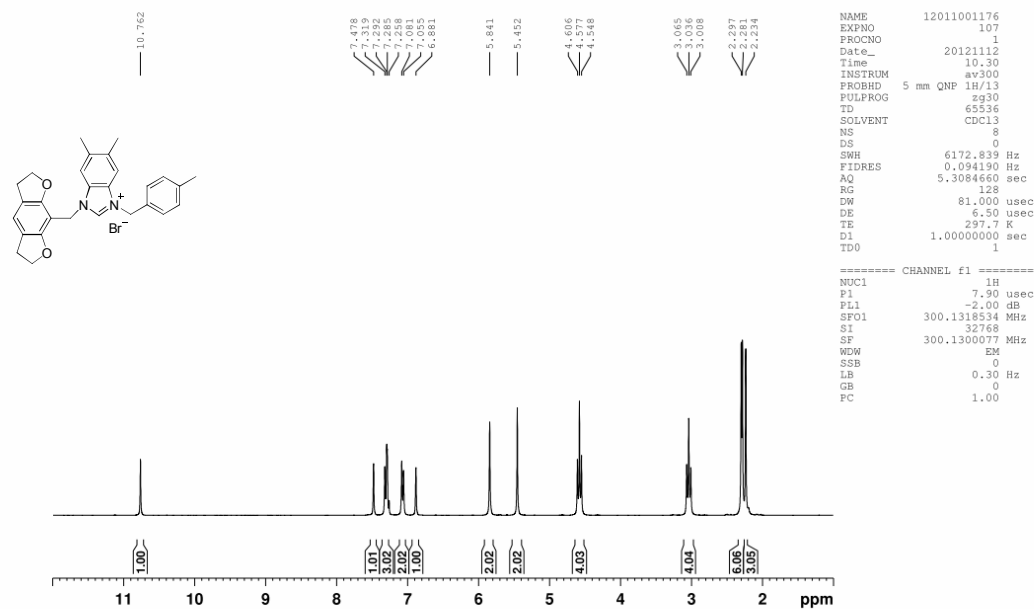


```

NAME      12011001176
EXPNO     88
PROCNO    1
Date_     20121103
Time      8.37
INSTRUM   av300
PROBHD    5 mm QNP 1H/13
PULPROG   zg30
TD         65536
SOLVENT   CDCl3
NS         8
DS         0
SWH        6172.839 Hz
FIDRES     0.094190 Hz
AQ         5.3084560 sec
RG         128
DW         81.000 usec
DE         6.50 usec
TE         296.2 K
D1         1.00000000 sec
TD0        1
===== CHANNEL f1 =====
NUC1       1H
P1         7.90 usec
PL1        -2.00 dB
SFO1       300.1318534 MHz
SI         32768
SF         300.1299893 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```



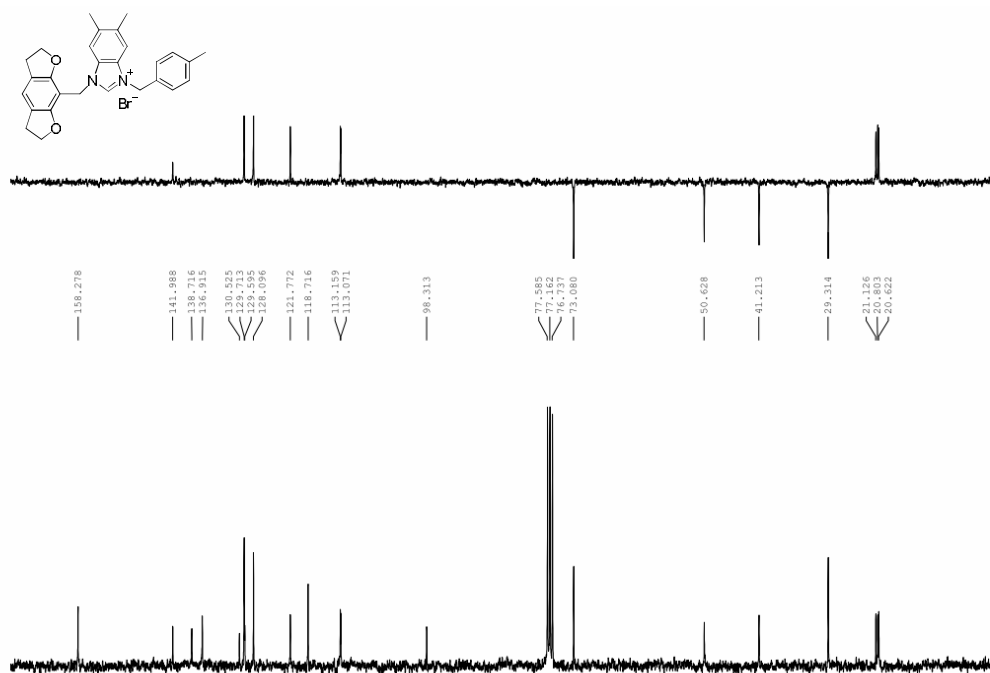
# Compound 41



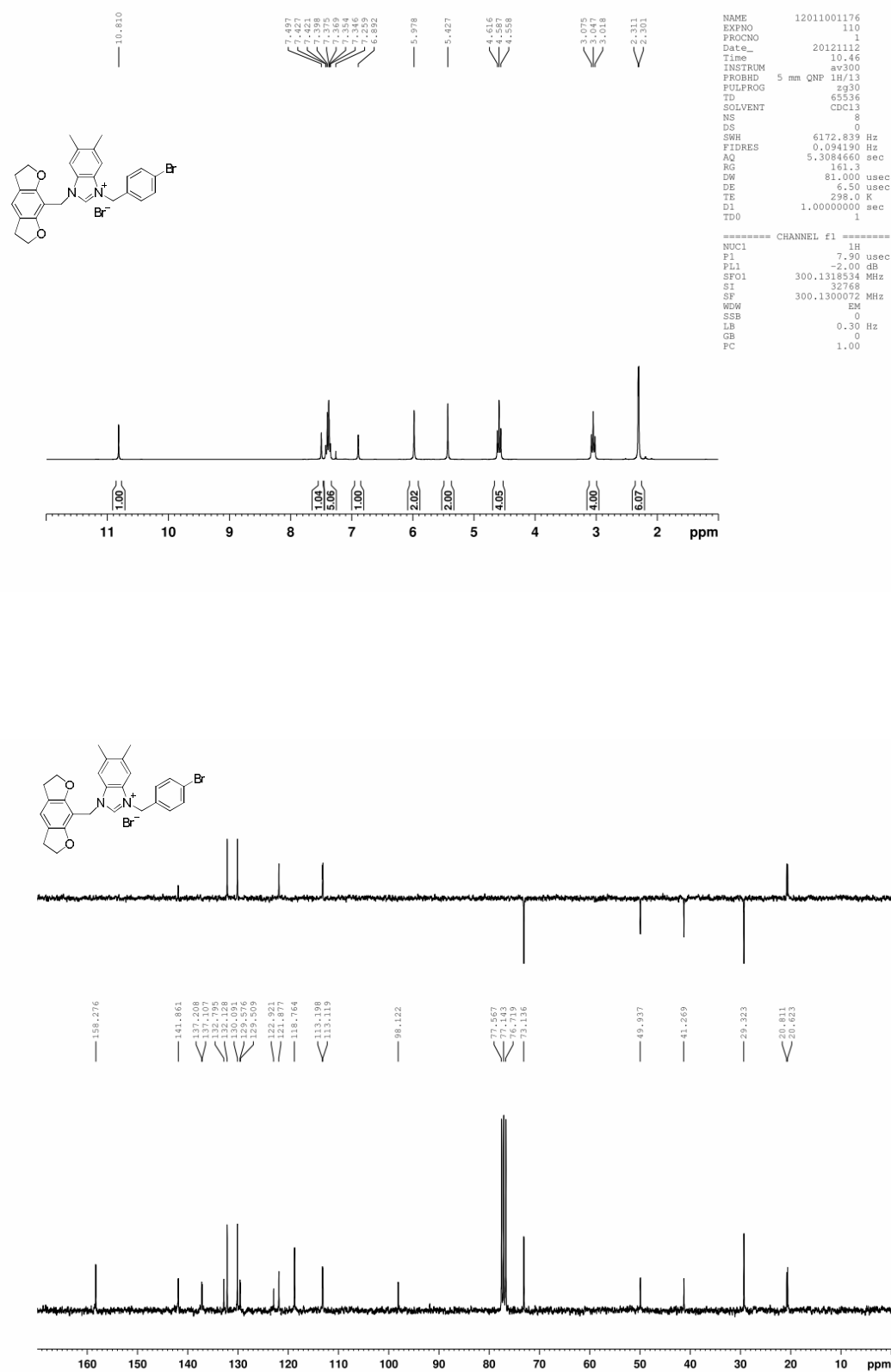
```

NAME      12011001176
EXPNO    107
PROCNO   1
Date_    20121112
Time     10.30
INSTRUM  av300
PROBHD   5 mm QNP 1H/13
PULPROG  zg30
TD        65536
SOLVENT  CDCl3
NS        8
DS        0
SWH       6172.839 Hz
FIDRES    0.094190 Hz
AQ         5.3084660 sec
RG         128
EW         81.000 usec
DE         6.50 usec
TE         297.7 K
D1         1.00000000 sec
TD0        1

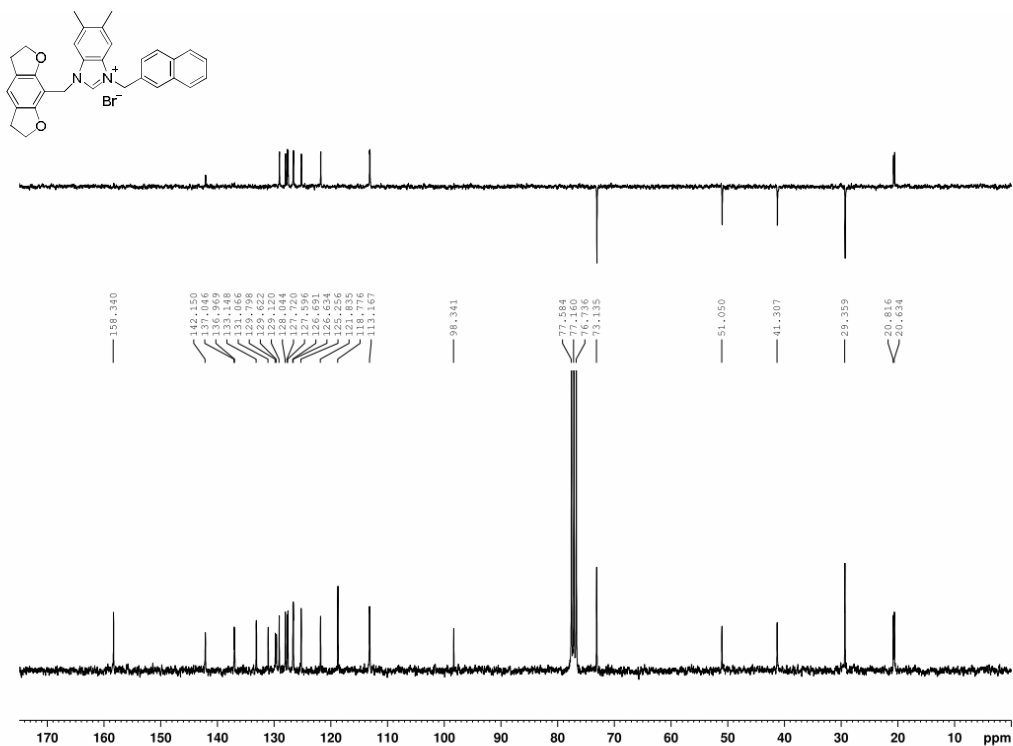
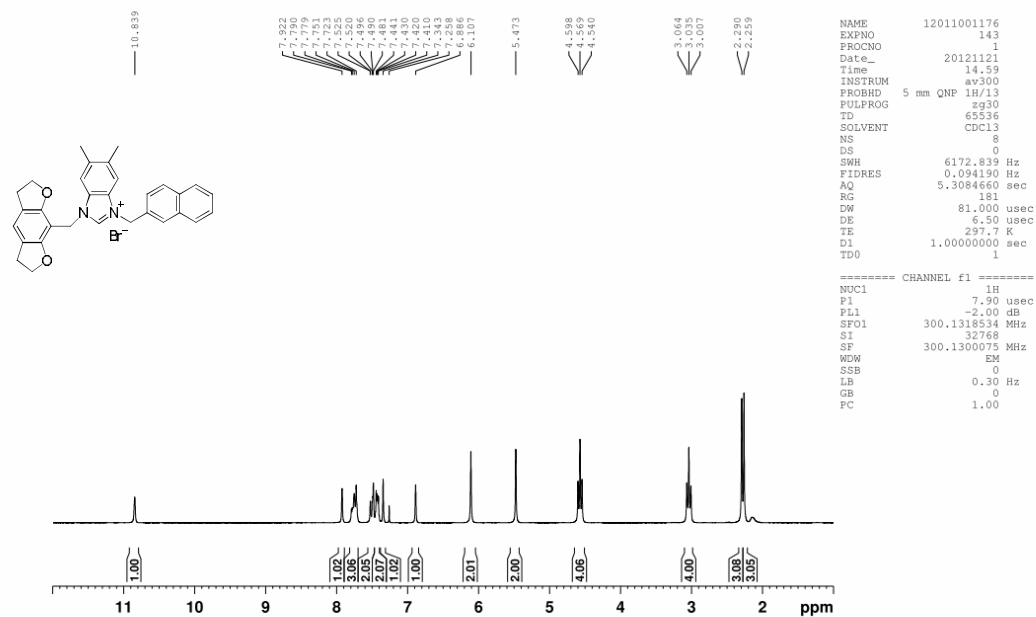
===== CHANNEL f1 =====
NUC1      1H
P1         7.90 usec
PL1        -2.00 dB
SFO1      300.1318534 MHz
SI         32768
SF         300.1300077 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



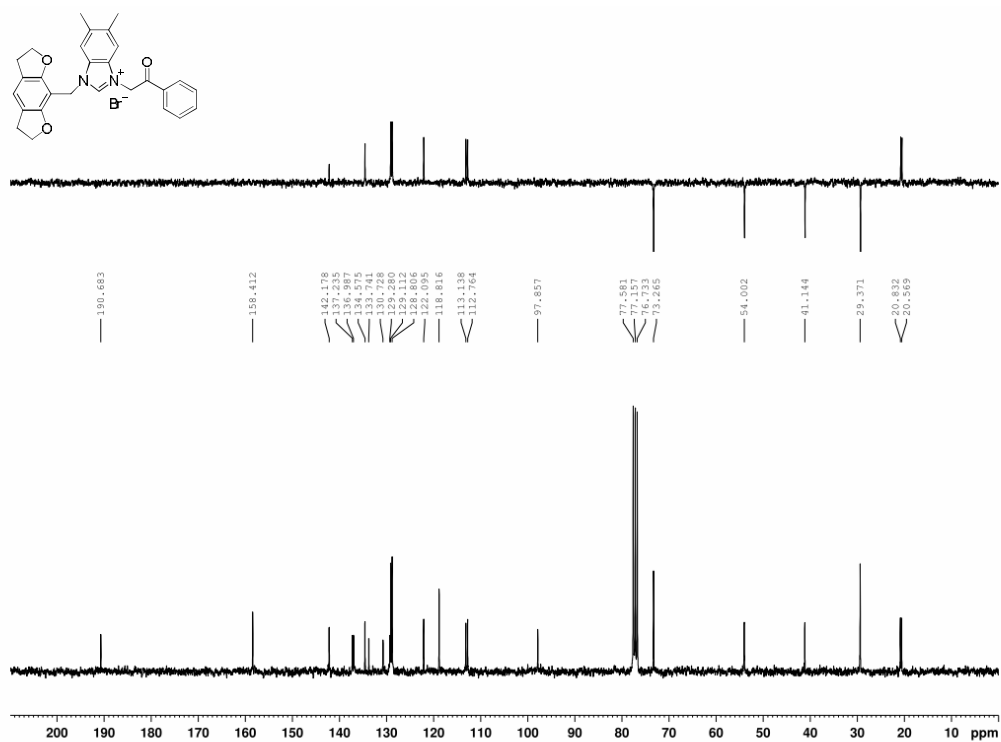
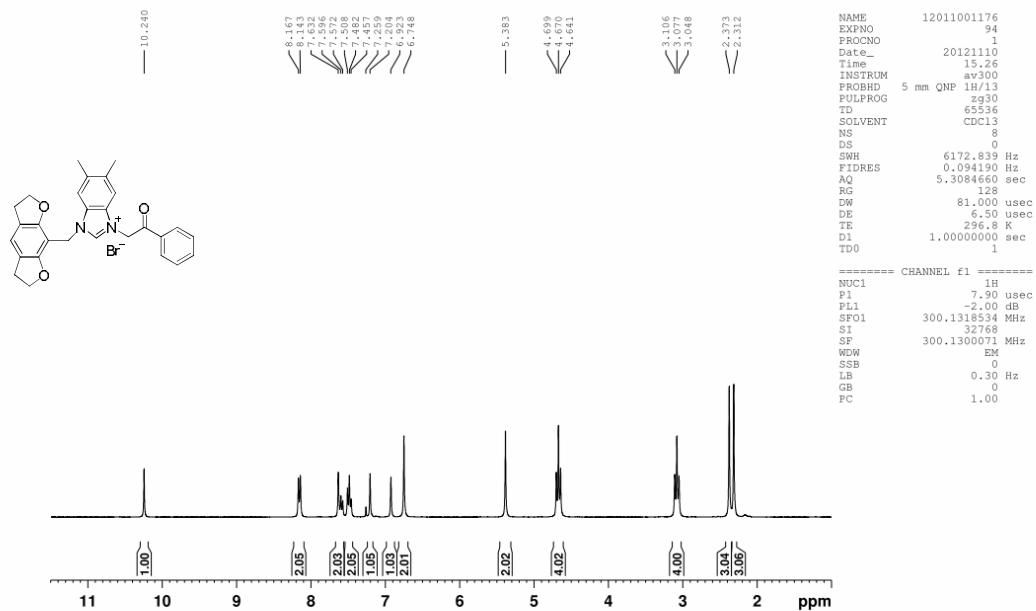
# Compound 42



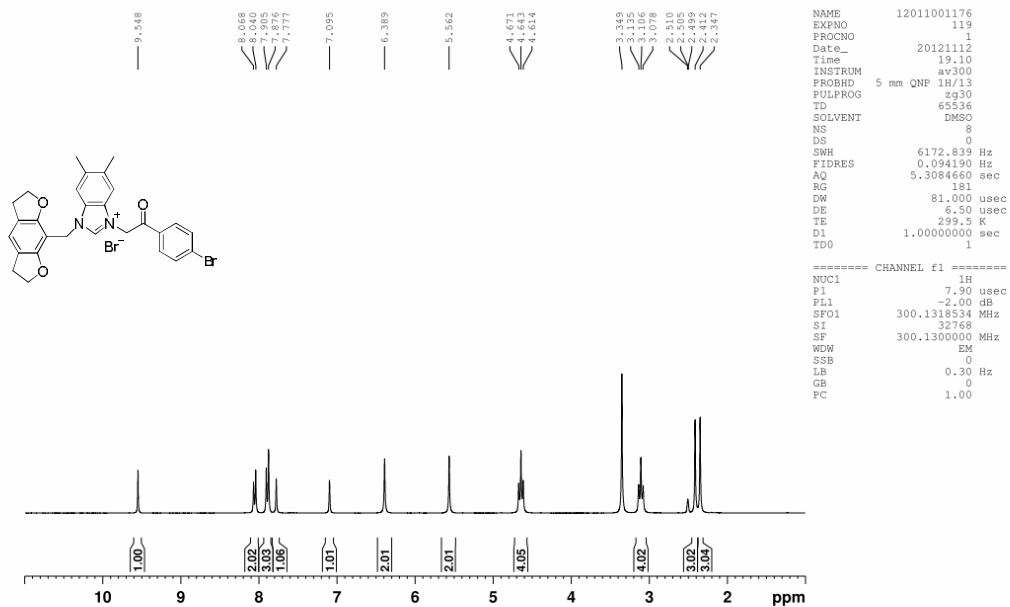
# Compound 43



# Compound 44



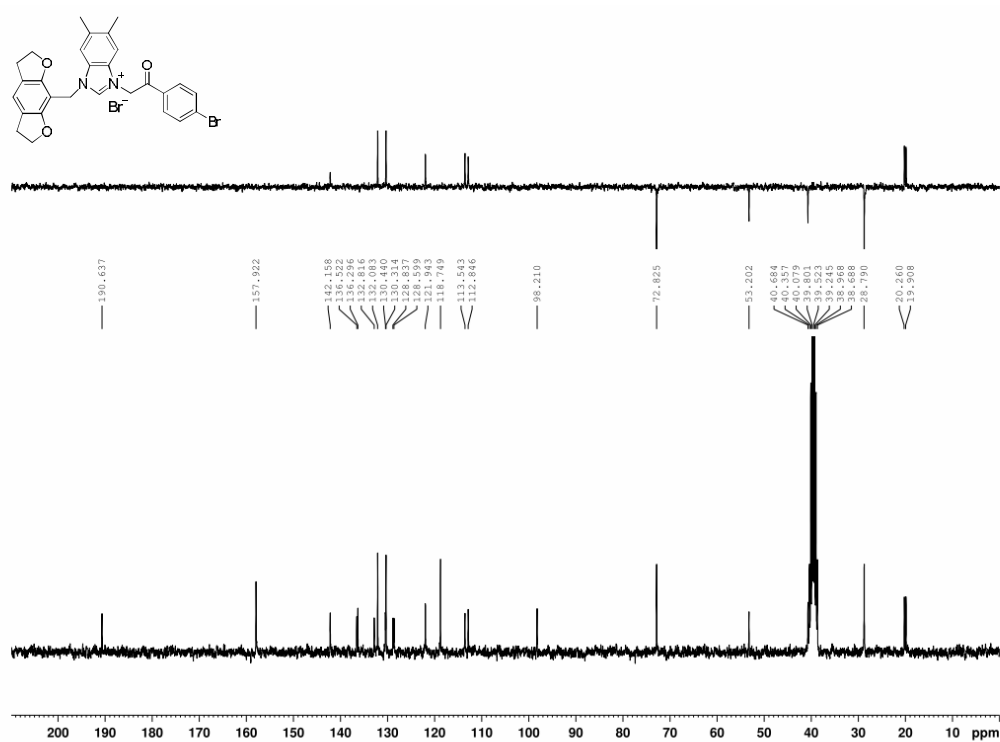
# Compound 45



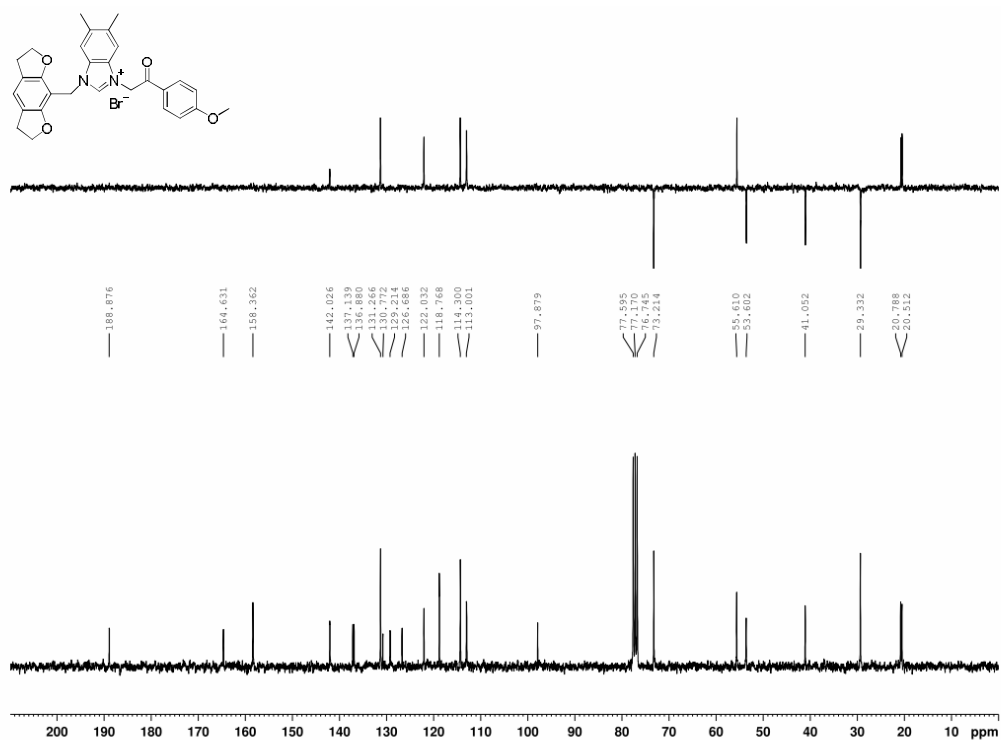
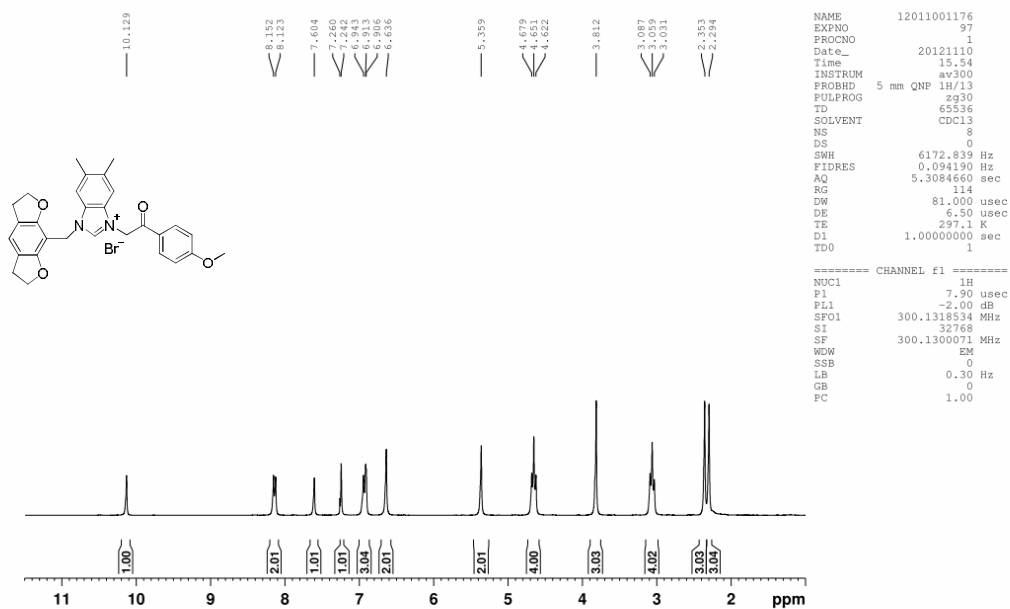
```

NAME      12011001176
EXPNO     119
PROCNO    1
Date_     20121112
Time      19.10
INSTRUM   av300
PROBHD    5 mm QNP 1H/13
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        6172.839 Hz
FIDRES     0.094190 Hz
AQ         5.3084660 sec
RG         181
DW         81.000 usec
DE         6.50 usec
TE         299.5 K
D1         1.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         7.90 usec
PL1        -2.00 dB
SFO1       300.1318534 MHz
SI         32768
SF         300.1300000 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```



# Compound 46



# Compound 47

