

## Supplementary materials

### Preparation of benzo- and polybenzocrown ethers by macrocyclization reactions

Robert E. Hanes, Jr.,<sup>a\*</sup> Jong Chan Lee,<sup>b</sup> Sheryl N. Ivy,<sup>b</sup> Anna Palka, and  
Richard A. Bartsch<sup>b</sup>

<sup>a</sup>*Beacon Sciences, LLC, 11412 Bee Cave Rd. Austin, Texas 78738, USA*

<sup>b</sup>*Department of Chemistry and Biochemistry, Texas Tech University,  
Lubbock, Texas 79409-1061, USA*

*E-mail: [rhanes@beaconsciences.com](mailto:rhanes@beaconsciences.com)*

#### Table of contents

1. Benzo-12-crown-4	S2
2. 4- <i>t</i> -Butylbenzo-12-crown-4	S2
3. 3,5-Di- <i>t</i> -Butylbenzo-12-crown-4	S2
4. Benzo-15-crown-5	S2
5. 4- <i>t</i> -Butylbenzo-15-crown-5	S2
6. 3,5-Di- <i>t</i> -Butylbenzo-15-crown-5	S3
7. 4- <i>t</i> -Butylbenzo-18-crown-6	S3
8. 3,5-Di- <i>t</i> -Butylbenzo-18-crown-6	S3
9. 4- <i>t</i> -Butylbenzo-21-crown-7	S3
10. 3,5-Di- <i>t</i> -Butylbenzo-21-crown-7	S3

The following benzocrown and substituted benzocrown ethers were prepared using the general procedure for cesium-assisted cyclizations given in the Experimental Section of the paper.

**Benzo-12-crown-4 (1)** was obtained as a white solid with mp 44.5-45.5 °C (lit.<sup>1</sup> mp 44-45.5 °C) in 54% yield after recrystallization from hexanes. Mass spectroscopy revealed that the recrystallized product did not contain any [2+2] adduct. IR (deposit from a CDCl<sub>3</sub> solution onto a NaCl plate): 1260, 1142, 1124 and 1077 (C-O) cm<sup>-1</sup>. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ 3.74 (s, 4H); 3.78-3.96 (m, 4H); 4.10-4.16 (m, 4H); 6.86-6.99 (m, 4H).

**4-*t*-Butylbenzo-12-crown-4 (2)**, a white solid, was isolated in 70% yield and contained 10-20% of the [2+2] adduct as estimated by <sup>1</sup>H NMR and mass spectroscopy. A small sample was recrystallized from hexanes for elemental analysis and the [1+1] adduct was obtained with mp 47-49 °C. Reaction products from several runs (4.10 g) were combined and purified by Kugelrohr distillation (130 °C/0.8 Torr) and the [1+1] adduct (1.10 g, 29%) was obtained with a mp of 47-49 °C. IR (deposit from a CDCl<sub>3</sub> solution onto a NaCl plate): 1237, 1122 and 1049 (C-O) cm<sup>-1</sup>. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ 1.26 (s, 9H); 3.79 (s, 4H); 3.80-3.86 (m, 4H); 4.11-4.20 (m, 4H); 6.85-6.99 (m, 3H). Anal. calcd for C<sub>16</sub>H<sub>24</sub>O<sub>4</sub>: C, 68.55; H, 8.63. Found: C, 68.50; H, 8.59. MS (DIP-EI) *m/e* 280.30 (280.17 calculated for C<sub>16</sub>H<sub>24</sub>O<sub>4</sub>) and 560.45 (560.34 calculated for C<sub>32</sub>H<sub>48</sub>O<sub>8</sub>).

**3,5-Di-*t*-Butylbenzo-12-crown-4 (3)** was obtained as a white solid in 82% yield and contained ~50% of the [2+2] adduct as estimated from the <sup>1</sup>H NMR and mass spectra. Reaction products from several runs (2.02 g) were combined and purified by Kugelrohr distillation (140 °C/0.8 Torr) and the [1+1] adduct (1.10 g, 54%) was obtained with mp 147-149 °C. Although the product could be recrystallized from hexanes, Kugelrohr distillation was found to be the superior method of isolating the pure [1+1] adduct. IR (deposit from a CDCl<sub>3</sub> solution onto a NaCl plate): 1235, 1135 and 1069 (C-O) cm<sup>-1</sup>. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ 1.26 (s, 9H); 1.35 (s, 9H); 3.80 (d, 7.4 Hz, 4H); 3.83-3.93 (m, 4H); 4.10-4.14 (m, 2H); 4.24 (t, 5.4 Hz, 2H); 6.76 (d, 2.2 Hz, 1H); 6.90 (d, 2.2 Hz, 1H). Anal. calcd for C<sub>20</sub>H<sub>32</sub>O<sub>4</sub>: C, 71.39; H, 9.59. Found: C, 71.40; H, 9.54. MS (DIP-EI) *m/e* 336.40 (336.23 calculated for C<sub>20</sub>H<sub>32</sub>O<sub>4</sub>); [2+2] *m/e* exceeds the detection limit.

**Benzo-15-crown-5 (4)** was isolated as a white solid in 69% yield and contained 10-20% of the [2+2] adduct as estimated from the <sup>1</sup>H NMR and mass spectra. The reaction products from several runs (1.52 g) were combined and recrystallized from heptane. The [1+1] adduct was isolated (1.10 g, 72%) with mp 77.5-79 °C (lit.<sup>1</sup> mp 79-79.5 °C). IR (deposit from a CDCl<sub>3</sub> solution onto a NaCl plate): 1230, 1121 and 1075 (C-O) cm<sup>-1</sup>. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ 3.88 (s, 8H); 3.90-3.93 (m, 4H); 4.10-4.16 (m, 4H); 6.64-6.94 (m, 4H). *m/e* 268.20 (268.13 calculated for C<sub>14</sub>H<sub>20</sub>O<sub>5</sub>) and 536.40 (536.26 calculated for C<sub>32</sub>H<sub>48</sub>O<sub>8</sub>).

**4-*t*-Butylbenzo-15-crown-5 (5)** was obtained as a colorless oil (71%) after Kugelrohr distillation and identified by its <sup>1</sup>H NMR and mass spectra as the [1+1] product. After crystallization from diethyl ether at 0 °C, the [1+1] adduct had mp 42-44 °C (lit.<sup>1</sup> mp below 26 °C). IR (deposit from a CDCl<sub>3</sub> solution onto a NaCl plate): 1264 and 1141 (C-O) cm<sup>-1</sup>. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ

1.26 (s, 9H); 3.73 (s, 8H); 3.84-3.92 (m, 4H); 4.08-4.16 (m, 4H); 6.79-6.90 (m, 3H). MS (DIP-EI)  $m/e$  324.25 (324.19 calculated for  $C_{18}H_{28}O_5$ ) and 648.35 (648.38 calculated for  $C_{36}H_{56}O_8$ ).

**3,5-Di-*t*-Butylbenzo-15-crown-5 (6)** was a white crystalline solid formed in 87% yield and contained 10-20% of the [2+2] adduct as estimated by the  $^1H$  NMR and mass spectra. Reaction products from several runs were combined (3.02 g, 82%) and recrystallized from heptane and the [1+1] product was isolated with mp of 99.5-100.5 °C. IR (deposit from a  $CDCl_3$  solution onto a NaCl plate): 1234, 1133 and 1073 (C-O)  $cm^{-1}$ .  $^1H$  NMR (200 MHz,  $CDCl_3$ ):  $\delta$  1.26 (s, 9H); 1.35 (s, 9H); 3.72-3.80 (m, 8H); 3.87-3.91 (m, 2H); 4.02 (t, 4.0 Hz, 2H); 4.10-4.12 (m, 2H); 4.26 (t, 4.0 Hz, 2H); 6.76 (d, 2.2 Hz, 1H); 6.89 (d, 2.2 Hz, 1H). Anal. calcd for  $C_{22}H_{36}O_5$ : C, 69.44; H, 9.53. Found: C, 69.84; H, 9.70. MS (DIP-EI)  $m/e$  380.40 (380.26 calculated for  $C_{22}H_{36}O_5$ ) and 760.70 (760.52 calculated for  $C_{44}H_{72}O_{10}$ ).

**4-*t*-Butylbenzo-18-crown-6 (7)** was a yellow oil obtained in 72% yield and contained 10-20% of the [2+2] adduct as shown by the  $^1H$  NMR and mass spectra. Reaction products from several runs (4.55 g) were combined then purified by Kugelrohr distillation (180° C, 0.8 Torr) and the [1+1] adduct (4.31 g, 95%) was obtained. Upon standing over a period of several months, the yellow oil spontaneously crystallized resulting in a white solid identified as the [1+1] adduct with mp 34-36 °C (lit.<sup>1</sup> mp below 26 °C). IR (deposit from a  $CDCl_3$  solution onto a NaCl plate): 1266 and 1136 (C-O)  $cm^{-1}$ .  $^1H$  NMR (200 MHz,  $CDCl_3$ ):  $\delta$  1.26 (s, 9H); 3.64-3.77 (m, 12H); 3.86-3.93 (m, 4H); 4.09-4.16 (m, 4H); 6.76-6.92 (m, 3H). MS (DIP-EI)  $m/e$  368.30 (368.22 calculated for  $C_{20}H_{32}O_6$ ) and 736.40 (736.60 calculated for  $C_{16}H_{24}O_4$ ).

**3,5-Di-*t*-Butylbenzo-18-crown-6 (8)** was a yellow oil obtained in 82% yield and contained 10-20% of the [2+2] adduct as shown by the  $^1H$  NMR and mass spectra. Reaction products from several runs (6.43 g) were combined then purified by Kugelrohr distillation (190° C/0.8 Torr) and the [1+1] adduct (3.97 g, 62%) was obtained. IR (deposit from a  $CDCl_3$  solution onto a NaCl plate): 1234, 1129 and 1073 (C-O)  $cm^{-1}$ .  $^1H$  NMR (200 MHz,  $CDCl_3$ ):  $\delta$  1.26 (s, 9H); 1.35 (s, 9H); 3.66-3.76 (m, 12H); 3.89-3.96 (m, 4H) 3.89-3.96 (m, 4H); 4.11 (t, 5.4 Hz, 2H); 4.24 (t, 5.4 Hz, 2H); 6.78 (d, 2.2 Hz, 1H); 6.690 (d, 2.2 Hz, 1H). Anal. calcd for  $C_{24}H_{40}O_6$ : C, 67.89; H, 9.50. Found: C, 68.04; H, 9.36. MS (DIP-EI)  $m/e$  424.30 (424.28 calculated for  $C_{24}H_{40}O_6$ ); [2+2]  $m/e$  exceeds detection limit.

**4-*t*-Butylbenzo-21-crown-7(9)** was a yellow oil obtained in 78% yield and contained 10-20% of the [2+2] adduct as estimated by the  $^1H$  NMR and mass spectra. Reaction products from several runs (~ 23 g) were combined then purified by Kugelrohr distillation (190° C/0.8 Torr) and the [1+1] adduct was obtained. The product (13.11 g, 57%) combined after 3 Kugelrohr distillations was identified as the desired [1+1] adduct by the  $^1H$  NMR and mass spectra. IR (deposit from a  $CDCl_3$  solution onto a NaCl plate): 1266 and 1128 (C-O)  $cm^{-1}$ .  $^1H$  NMR (200 MHz,  $CDCl_3$ ):  $\delta$  1.26 (s, 9H); 3.62-3.78 (m, 16H); 3.85-3.92 (m, 4H); 4.09-4.17 (m, 4H); 6.79-6.90 (m, 3H). MS (DIP-EI)  $m/e$  412.30 (412.25 calculated for  $C_{22}H_{36}O_7$ ); [2+2]  $m/e$  exceeds detection limit.

**3,5-Di-*t*-Butylbenzo-21-crown-7 (10)** was a yellow oil obtained in 78% yield and contained 10-20% of the [2+2] adduct as estimated by the  $^1H$  NMR and mass spectra. Reaction products from several runs (6.21 g) were combined and purified by Kugelrohr distillation (190 °C/0.8 Torr) and

the [1+1] adduct (1.00 g, 16%) was obtained. IR (deposit from a  $\text{CDCl}_3$  solution onto a NaCl plate): 1234, 1126 and 1071 (C-O)  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.26 (s, 9H); 1.35 (s, 9H); 3.65-3.73 (m, 16H); 3.86-3.95 (m, 4H); 4.12 (t, 5.0 Hz, 2H); 4.24 (t, 5.0 Hz, 2H); 6.77 (d, 2.2 Hz, 1H); 6.90 (d, 2.2 Hz, 1H). Anal. calcd for  $\text{C}_{26}\text{H}_{44}\text{O}_7$ : C, 66.64; H, 9.46. Found: C, 66.91; H, 9.56. MS (DIP-EI)  $m/e$  424.25 (424.28 calculated for  $\text{C}_{26}\text{H}_{44}\text{O}_7$ ); [2+2]  $m/e$  exceeds detection limit.

## References

1. Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017.