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Stereospecific synthesis of *cis–trans*-dicyclohexano-18-crown-6 and K^+ complexation by the five dicyclohexano-18-crown-6 isomers

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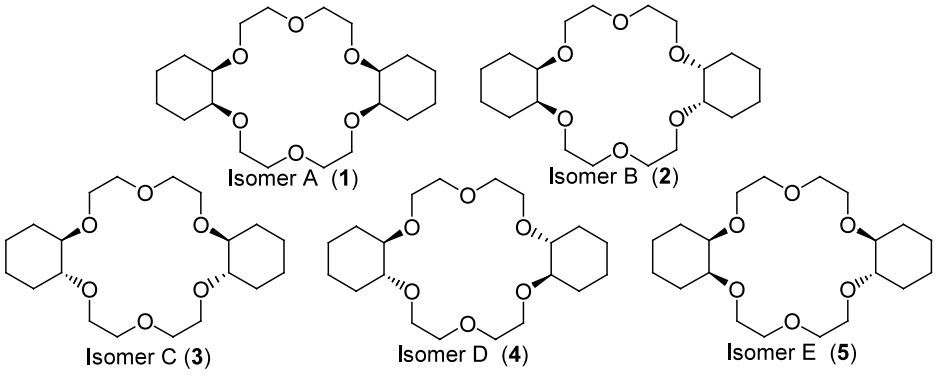
Abstract—Stereospecific syntheses of the *cis–trans*-isomer of dicyclohexano-18-crown-6 allows the K^+ complexation behavior of all five dicyclohexano-18-crown-6 isomers to be compared.

Crown ether compounds have been widely used for complexation and separation of metal ions and small molecules, supramolecular chemistry, host–guest chemistry and phase-transfer catalysis.[1,2] The complexation properties of crown ether compounds are controlled by several structural features, including the ring size, number of donor atoms and stereochemistry. Dicyclohexano-18-crown-6 (DC18C6) is a well-known crown ether that can exist as five stereoisomers based on the fusion of the cyclohexane ring (*cis* or *trans*) and the relationships of the two cyclohexane ring (*syn* or *anti*). Since *cis–syn–cis*- and *cis–anti–cis*-DC18C6 (Isomers A and B, respectively) are easily obtained by hydrogenation of dibenzo-18-crown-6 (DB18C6) and separation of the isomers and are commercially available,[2,3] their complexation and metal-ion separation behaviors are well established. However, systematic studies of all five isomers including *trans–syn–trans*-, *trans–anti–trans*- and *cis–trans*-DC18C6 (Isomers C, D and E) have been rarely reported.[4] In large part, this is due to the synthetic difficulties in preparing these three isomers. Several researchers have reported the syntheses of Isomers C and D.[5–8] However, Isomer E has been only isolated by HPLC[9] or selective precipitation[10] from the product mixture obtained by the catalytic hydrogenation of DB18C6. Herein, we report the first stereospecific synthesis of Isomer E.

Isomer E (**5**) was synthesized by two routes (Scheme 1). Reaction of 1 equiv. of cyclohexene oxide, 1 equiv. of di(ethylene glycol) monobenzyl ether (**7**) and 0.1 equiv. of NaH gave mono-alkylated *trans*-cyclohexane diol **11**



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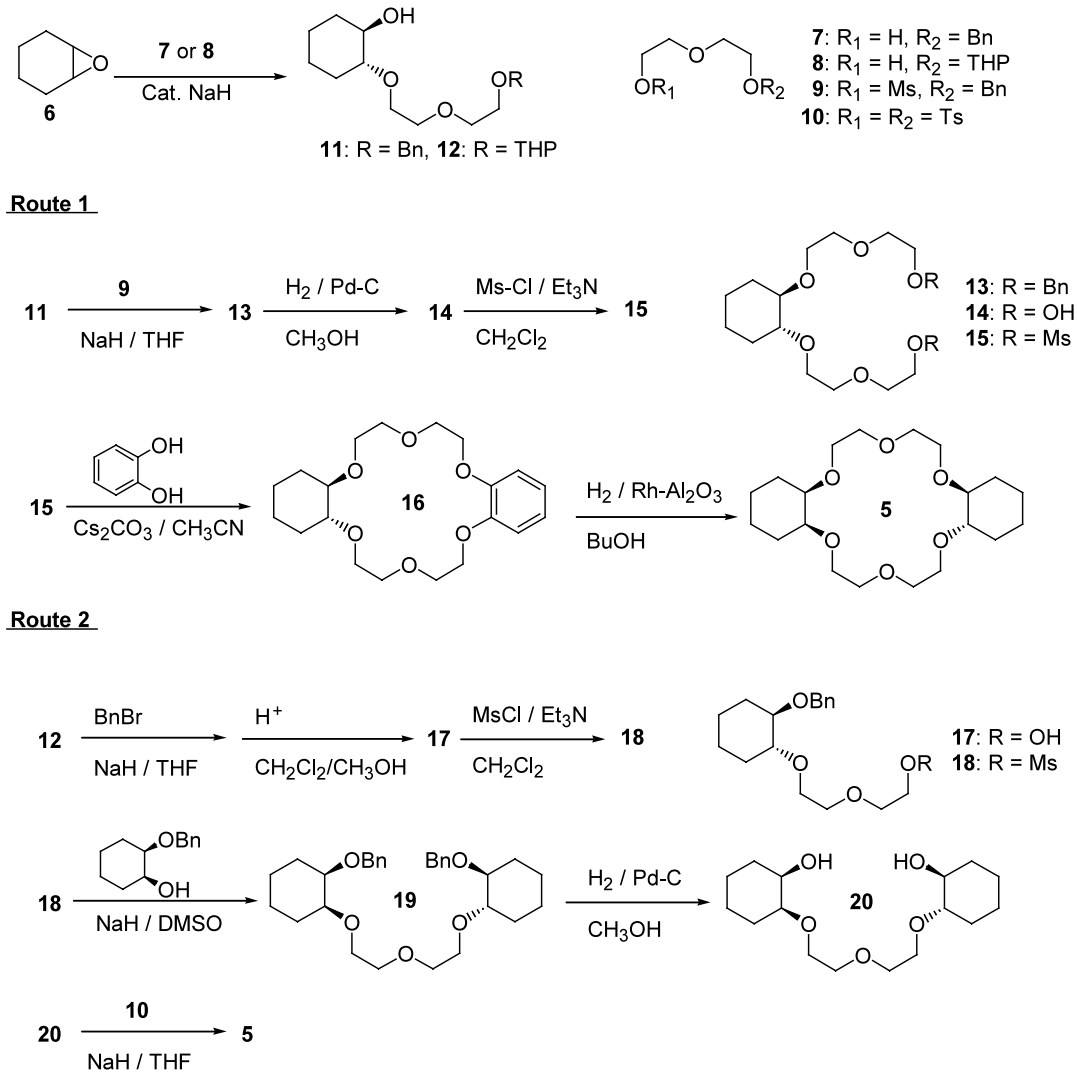

Scheme 1. Two synthetic routes to *cis–trans*-dicyclohexano-18-crown-6.

in 64% yield.[11] Subsequent alkylation of **11** with 2-[2-(benzyloxy)ethoxy]ethyl mesylate (**9**) and NaH in THF gave dibenzyl ether **13** (Route 1).[12] Catalytic hydrogenolysis of **13** produced diol **14**[13] that was converted into the corresponding dimesylate **15**.[14] Cyclization of **15** by reaction with catechol and Cs_2CO_3 gave benzo-*trans*-cyclohexano-18-crown-6 (*trans*-BC18C6, **16**) in 67% yield.[15] Hydrogenation of *trans*-BC18C6 with Rh on alumina catalyst gave Isomer E, which contained small amounts of isomers C and D as impurities. Flash column chromatography on aminopropyl silica gel gave pure Isomer E (**5**).[16]

Since catalytic hydrogenation of *trans*-BC18C6 gave isomers C and D as impurities, Isomer E was also synthesized by an alternate method (Route 2). In the first step, di(ethylene glycol) monotetrahydropyranyl ether (**8**) was used instead of the analogous monobenzyl ether to give **12**.[17] The secondary hydroxyl group was protected as a benzyl ether, followed by deprotection of the THP ether group to give primary alcohol **17**.[18] Reaction of **17** with methanesulfonyl chloride gave **18**[19] that was reacted with *cis*-2-benzyloxy-1-cyclohexanol to give *cis-trans*-dibenzyl ether **19** in 60% yield.[20] Catalytic hydrogenolysis of the dibenzyl ether gave *cis–trans* diol **20**,[21] followed by cyclization with di(ethylene glycol) ditosylate (**10**) provided pure Isomer E without contamination by Isomers C and D.[22]

Among the alkali metal cations, crown ethers with 18-crown-6 rings exhibit strongest binding of K^+.[1a] The availability of Isomer E allows the K^+ binding behavior for all five dicyclohexano-18-crown-6 isomers to be compared for the first time. Stability constants for K^+ complexation in methanol at 25°C were measured by isothermal titration calorimetry (isomer, log K_s): **1**, 5.88; **2**, 5.33; **3**, 4.08; **4**, 3.10; **5**, 4.53. Although Isomer E is the least symmetrical of the five dicyclohexano-18-crown-6 isomers, it binds K^+ more efficiently than do Isomers C and D. Thus, the number of *cis*-fused cyclohexane rings appears to be a controlling factor in the strength of K^+ complexation by the dicyclohexano-18-crown-6 isomers.

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References

1. For recent reviews on crown ether and related systems, see: (a) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1991**, *91*, 1721–2085; (b) Izatt, R. M.; Bradshaw, J. S.; Pawlak, K.; Bruening, R. L.; Tarbet, B. J. *Chem. Rev.* **1992**, *92*, 1261–1354; (c) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1995**, *95*, 2529–2586; (d) Gokel, G. W. *Crown Ethers and Cryptands*; Royal Society of Chemistry: Cambridge, 1991; (e) Zhang, X. X.; Bradshaw, J. S.; Izatt, R. M. *Chem. Rev.* **1997**, *97*, 3313–3361; (f) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3349–3391.
2. Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 2495–2496, 7017–7036.
3. Izatt, R. M.; Haymore, B. L.; Bradshaw, J. S. *Inorg. Chem.* **1975**, *14*, 3132–3133.
4. (a) Dietz, M. L.; Bond, A. H.; Hay, B. P.; Chiarizia, R.; Huber, V. J.; Herlinger, A. W. *Chem. Commun.* **1999**, 1177–1178; (b) Bond, A. H.; Chiarizia, R.; Huber, V. J.; Dietz, M. L.; Herlinger, A. W.; Hay, B. P. *Anal. Chem.* **1999**, *71*, 2757–2765.
5. (a) Stoddart, J. F.; Wheatley, C. M. *J. Chem. Soc., Chem. Commun.* **1974**, 390–391; (b) Burden, I. J.; Coxon, A. C.; Stoddart, J. F.; Wheatley, C. M. *J. Chem. Soc., Perkin Trans. 1* **1977**, 220–226.
6. Hayward, R. C.; Overton, C. H.; Whitham, G. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2413–2415.
7. Huber, V. J.; Dietz, M. L. *Tetrahedron Lett.* **2001**, *42*, 2945–2948.
8. (a) Yamato, K.; Bartsch, R. A.; Dietz, M. L.; Rogers, R. D. *Tetrahedron Lett.* **2002**, *43*, 2153–2156; (b) Yamato, K.; Bartsch, R. A.; Broker, G. A.; Rogers, R. D.; Dietz, M. L., in press.
9. (a) Laskorin, B. N.; Yakshin, V. V.; Fedorova, A. T. *Zh. Anal. Khim. (Russ.)* **1983**, *39*, 1115–1119; (b) Laskorin, B. N.; Yakshin, V. V.; Fedorova, A. T. *J. Anal. Chem. USSR* **1984**, *39*, 898–902.
10. (a) Yakshin, V. V.; Zhukova, N. G.; Tsarenko, N. A.; Fedorova, A. T.; Laskorin, B. N. *Dokl. Akad. Nauk SSSR (Russ.)* **1983**, *273*, 160–165; (b) Yakshin, V. V.; Zhukova, N. G.; Tsarenko, N. A.; Fedorova, A. T.; Laskorin, B. N. *Dokl. Phys. Chem.* **1984**, *273*, 160–165.
11. Compound **11** was synthesized by adaptation of a previously described procedure.[8a] Under nitrogen, 95% NaH (0.48 g, 20 mmol, 0.10 equiv.) was added to 2-[2-(benzyloxy)ethoxy]ethanol (39.5 g, 200 mmol) and the reaction temperature was increased at 80°C until a solution was obtained. The temperature was heated to 130°C and cyclohexene oxide (19.60 g, 200 mmol) was added dropwise. The solution was stirred for 3 h at 130°C and cooled to room temperature. After CH_2Cl_2 (100 mL) was added, the solution was washed with brine, dried over $MgSO_4$ and evaporated in vacuo. Vacuum distillation (170–180°C/0.4 Torr) of the residue gave the product in 64% yield. Anal found C, 69.50; H, 9.03. Calcd for $C_{17}H_{26}O_4$ C, 69.36; H, 8.90%. IR (neat) 3453 (OH), 1099 and 1044 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.16–1.27 (m, 4H), 1.67–1.72 (m, 2H), 1.98–2.04 (m, 2H), 3.04–3.08 (m, 1H), 3.41–3.45 (m, 1H), 3.49 (s, 1H), 3.59–3.70 (m, 7H), 3.86–3.89 (m, 1H), 4.57 (s, 2H), 7.27–7.29 (m,1H), 7.32–7.37 (m, 4H). ^{13}C NMR ($CDCl_3$; 127 Hz) δ 24.01, 24.43, 29.89, 32.15, 68.68, 69.37, 70.55, 70.87, 73.28, 73.96, 84.83, 127.58, 127.77, 128.34, 138.19.
12. Under nitrogen, **11** (17.50 g, 60 mmol) was added to a suspension of NaH (1.72 g, 68 mmol) in THF and the mixture was refluxed for 0.5 h. A THF solution of 2-[2-(benzyloxy)ethoxy]ethyl mesylate (18.10 g, 66 mmol) (**9**) was added dropwise and the reaction mixture was refluxed overnight. After the solution cooled to room temperature, water was added slowly and the mixture was extracted three times with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography on Al_2O_3:hexane:ethyl acetate = 20:1 to give **13** in 72% yield. Anal found C, 71.43; H, 8.74. Calcd for $C_{28}H_{40}O_6$ C, 71.16; H, 8.53%. IR (neat) 1101 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.15–1.29 (m, 4H), 1.62–1.66 (m, 2H), 1.95–1.97 (m, 2H), 3.17–3.22 (m, 2H), 3.59–3.64 (m, 8H), 3.65–3.72 (m, 4H), 3.73–3.77 (m, 4H), 4.56 (s, 4H), 7.25–7.29 (m, 2H), 7.31–7.35 (m, 8H). ^{13}C NMR ($CDCl_3$; 126 Hz) δ 23.61, 30.29, 69.40, 69.47, 70.59, 71.05, 73.21, 127.53, 127.71, 128.32.
13. To a solution of **13** (20.60 g, 43 mmol) in MeOH, 10% Pd–C (2.00 g) and a few drops of glacial acetic acid were added. The mixture was shaken for 12 h under H_2 (70 psi). The catalyst was removed by filtration through Celite and the filtrate was evaporated in vacuo to give diol **14** in 93% yield that was used without further purification. Anal found C, 57.34; H, 9.73. Calcd for $C_{19}H_{28}O_6$ C, 57.51; H, 9.65%. IR (neat) 3416 (OH), 1100 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.16–1.26 (m, 4H), 1.67–1.68 (m, 2H), 2.01–2.05 (m, 2H), 3.22–3.28 (m, 2H), 3.56 (br, 2H), 3.58–3.64 (m, 4H), 3.64–3.69 (m, 4H), 3.69–3.76 (s, 6H), 3.78–3.84 (m, 4H). ^{13}C NMR ($CDCl_3$; 127 Hz) δ 23.91, 30.53, 61.73, 69.05, 71.00, 72.70, 82.32.
14. To a CH_2Cl_2 solution of **14** (11.90 g, 41 mmol) and triethylamine (16.16 g, 160 mmol) under nitrogen, a CH_2Cl_2 solution of MsCl (11.02 g, 96 mmol) was added dropwise and the solution was stirred for 6 h. The mixture was washed with 1N HCl, saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. The solvent was evaporated in vacuo to give **15** in 91% yield that was used for the next reaction without further purification. Yield 91%. Anal found C, 43.13; H, 7.34. Calcd for $C_{16}H_{32}O_{10}S_2$ C, 42.84; H, 7.19%. IR (neat) 1352 and 1174 (S=O), 1103 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.18–1.26 (m, 4H), 1.65–1.66 (m, 2H), 1.96–1.98 (m, 2H), 3.08 (s, 6H), 3.16–3.18 (m, 2H), 3.61–3.68 (m, 4H), 3.71–3.76 (m, 4H), 3.7–3.81 (m, 4H), 4.37–4.39 (m, 4H).^{13}C NMR ($CDCl_3$; 127 Hz) δ 23.64, 30.32, 37.70, 68.94, 69.24, 69.35, 71.16, 82.15.

15. To an MeCN solution of catechol (3.90 g, 35 mmol), Cs_2CO_3 (23.0 g, 70 mmol) was added and the mixture was refluxed. A MeCN solution of **15** (15.8 g, 35 mmol) was added with a syringe pump over a 20 h period. After the addition was completed, the mixture was refluxed overnight and cooled to room temperature. Solid material was removed by filtration and the filtrate was evaporated in vacuo. The residue was dissolved in CH_2Cl_2, washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo. The crude product was purified by recrystallization from heptane to give **16** in 67% yield. Anal found C, 65.48; H, 8.39. Calcd for $C_{20}H_{30}O_6$ C, 65.55; H, 8.25%. Mp 83–85°C. IR (neat) 1257 and 1112 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.13–1.25 (m, 4H), 1.66–1.68 (m, 2H), 2.01–2.03 (m, 2H), 3.04–3.08 (m, 1H), 3.15–3.20 (m, 1H), 3.74–3.98 (m, 12H), 4.12–4.21 (m, 4H), 6.88–6.93 (m, 4H). ^{13}C NMR ($CDCl_3$; 126 Hz) δ 24.16, 30.90, 69.53, 69.67, 69.80, 71.28, 82.72, 114.52, 121.49, 149.09.
16. To a 1-butanol solution of **16** (4.70 g), glacial acetic acid (1.60 g) and 5% Rh on alumina catalyst (0.75 g) were added. The mixture was hydrogenated under H_2 (700 psi) at 110°C After 2 and 4 h, additional portions of catalyst (0.75 g) were added and the hydrogenation was continued for another 2 h. The catalyst was removed by filtration through Celite and the filtrate was evaporated in vacuo. The residue was purified by column chromatography (Al_2O_3:CH_2Cl_2) and further purified by flash column chromatography on aminopropyl silica gel (Bakerbond Amino (NH_2) 40 μm average particle diameter) with CH_3CN as eluent to give **5** in 30% yield. Anal found C, 64.53; H, 9.83. Calcd for $C_{20}H_{36}O_6$ C, 64.49; H, 9.74%. IR (neat) 1108 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.14–1.30 (m, 6H), 1.43–1.45 (m, 2H), 1.56–1.63 (m, 2H), 0.65–1.67 (m, 2H), 1.82–1.86 (m, 2H), 2.00–2.02 (m, 2H), 3.12–3.17 (m, 1H), 3.19–3.23 (m, 1H), 3.51–3.52 (m, 1H), 3.56–3.58 (m, 1H), 3.62–3.77 (m, 14H), 3.81–3.89 (m, 2H). ^{13}C NMR ($CDCl_3$; 126 Hz) δ 21.83, 23.87, 27.31, 27.44, 30.57, 30.60, 67.66, 68.08, 69.22, 69.43, 70.39, 70.58, 70.71, 82.22, 82.47.
17. Compound **12** was prepared in 59% yield by a method similar to that used for **11**. Yield anal found C, 62.56; H, 9.64. Calcd for $C_{15}H_{28}O_5$ C, 62.47; H, 9.79%. IR (neat) 1124 and 1077 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.14–1.31 (m, 4H), 1.67–1.73 (m, 2H), 1.98–2.04 (m, 2H), 3.04–3.09 (m, 1H), 3.39 (s, 1H), 3.40–3.46 (m, 1H), 3.49 (d, 1H, $J=1.2$ Hz), 3.54–3.57 (m, 2H), 3.58–3.63 (m, 1H), 3.65–3.70 (m, 4H), 3.85–3.89 (m, 1H). ^{13}C NMR ($CDCl_3$; 126 Hz) δ 19.39, 19.40, 24.00, 24.43, 25.40, 29.90, 29.91, 30.48, 30.49, 32.15, 62.16, 62.18, 66.61, 68.69, 68.75, 70.43, 70.48, 70.80, 84.78, 84.82, 98.97, 99.00.
18. Under nitrogen, **12** (28.84 g, 100 mmol) was added to a suspension of 95% NaH (2.90 g, 120 mmol) in THF and the mixture was refluxed for 0.5 h. Benzyl bromide (17.11 g, 100 mmol) was added dropwise, and the solution was refluxed ovenight and cooled to room temperature. Water was added and the mixture was extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$ and evaporated in vacuo. The residue was dissolved in a mixture of CH_2Cl_2 and methanol and a few drops of conc. HCl were added. The solution was stirred for 4 h and poured into saturated $NaHCO_3$. The organic layer was washed with brine, dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography (SiO_2:hexane:ethyl acetate = 10:1) to give **17** in 63% yield. Anal found C, 69.08; H, 8.64. Calcd for $C_{17}H_{26}O_4$ C, 69.36; H, 8.90%. IR (neat) 1099 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.18–1.34 (m, 4H), 1.64–1.68 (m, 2H), 2.01–2.05 (m, 2H), 2.65 (t, 1H), 3.29–3.36 (m, 2H), 3.59–3.61 (m, 2H), 3.65–3.70 (m, 4H), 3.74–3.80 (m, 2H), 4.61 (d, 1H, $J=15.4$ Hz), 4.84 (d, 1H, $J=15.4$ Hz), 7.25–7.28 (m, 1H), 7.32–7.38 (m, 1H). ^{13}C NMR ($CDCl_3$; 126 Hz) δ 23.90, 30.57, 62.09, 69.68, 71.26, 72.07, 72.64, 81.44, 82.52, 127.59, 127.81, 128.52, 139.46.
19. Mesylate **18** was synthesized in 95% yield by a method similar to that utilized for **15**. Anal found C, 57.85; H, 7.52. Calcd for $C_{18}H_{28}O_6S$ C, 58.04; H, 7.58%. IR (neat) 1354 and 1175 (S=O), 1101 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.18–1.33 (m, 4H), 1.65–1.68 (m, 2H), 1.98–2.04 (m, 2H), 3.01 (s, 3H), 3.24–3.28 (m, 1H), 3.30–3.34 (m, 1H), 3.62–3.68 (m, 2H), 3.73–3.77 (m, 4H), 4.32–4.33 (m, 2H), 4.65 (s, 2H), 7.25–7.28 (m, 1H), 7.32–7.37 (m, 1H). ^{13}C NMR ($CDCl_3$; 126 Hz) δ 23.58, 23.60, 30.19, 30.29, 37.63, 68.95, 69.31, 69.37, 71.14, 71.70, 81.13, 82.17, 127.34, 127.48, 128.27, 139.24.
20. Dibenzyl ether **19** was synthesized in 50% yield from **18** and *cis*-2-benzyloxy-1-cyclohexanol by a method similar to that described above for **13**. Anal found C, 74,45; H, 8.72. Calcd for $C_{30}H_{42}O_5$ C, 74.54; H, 8.77%. IR (neat) 1099 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.17–1.35 (m, 6H), 1.42–1.46 (m, 2H), 1.60–1.65 (m, 4H), 1.85–1.90 (m, 2H), 1.98–2.01 (m, 2H), 3.24–3.28 (m, 1H), 3.30–3.35 (m, 1H), 2.49–3.51 (m, 1H), 3.58–3.61 (m, 1H), 3.61–3.69 (m, 6H), 3.72–3.77 (m, 2H), 4.60 (s, 1H, $J=12.5$ Hz), 4.63 (s, 1H, $J=12.5$ Hz), 4.64 (s, 1H, $J=11.8$ Hz), 4.70 (s, 1H, $J=12.0$ Hz), 7.23–7.26 (m, 2H), 7.30–7.33 (m, 4H), 7.36 (d, 2H, $J=7.6$ Hz). ^{13}C NMR ($CDCl_3$; 126 Hz) δ 21.91, 22.29, 23.57, 23.62, 27.70, 27.79, 30.23, 30.34, 68.26, 69.42, 69.44, 70.43, 70.94, 71.10, 71.12, 71.95, 80.94, 82.23, 127.17, 127.23, 127.41, 127.53, 128.17, 128.23, 139.43.
21. Diol **20** was prepared in 90% yield from **19** by a method similar to that utilized for **14**. Anal found C, 63.95; H, 10.04. Calcd for $C_{16}H_{30}O_5$ C, 63.55; H, 10.00%. IR (neat) 3417 (OH), 1090 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$; 500 MHz) δ 1.14–1.31 (m, 6H), 1.48–1.52 (m, 2H), 1.57–1.71 (m, 4H), 1.77–1.83 (m, 2H), 1.99–2.02 (m, 2H), 3.03–3.10 (m, 2H), 3.32–3.48 (m, 4H), 3.57–3.76 (m, 6H), 3.82–3.88 (m, 2H). ^{13}C NMR ($CDCl_3$; 126 Hz) δ 23.96, 24.06, 24.37, 24.48, 29.89, 29.92, 32.17, 32.35, 61.77, 68.16, 68.55, 70.72, 70.74, 72.53, 73.65, 74.03, 84.83, 84.93.
22. Under nitrogen, **20** (4.24 g, 14 mmol) was added to a suspension of 95% NaH (0.96 g, 40 mmol) in THF and the mixture was refluxed for 0.5 h. A THF solution of di(ethylene glycol) ditosylate (**10**) (5.80 g 14 mmol) was added over 6 h period. The solution was refluxed ovenight and cooled to room temperature. Brine was added and the mixture was extracted with Et_2O. Organic layer was washed with brine, dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography (Al_2O_3:hexane:ethyl acetate = 10:1) to give a 21% yield of **5**. The yield of **5** was not significantly affected by replacing di(ethylene glycol) ditosylate with the corresponding dimesylate, performing the reaction at room temperature or changing the reaction solvent to DMSO.