

Hong-Seok Kim*, Young Kook Koh, and Jun-Hyeak Choi

Department of Industrial Chemistry, Kyungpook National University,
Taegu 702-701, Korea

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A series of benzo-crown ethers containing the thiazole subcyclic moiety have been synthesized. Reaction of 1,2-bis(thioamidomethoxy)benzene **2** with ethyl bromopyruvate in ethanol provided 1,2-bis(thiazolyl)benzene **4** (80%) along with thiazole **5** (14%). Reduction of **4** with lithium aluminum hydride followed by mesylation-bromination gave **7**. Similar treatment of **5** with lithium aluminum hydride followed by bromination resulted in **12**. Benzo-crown ethers **8**, **9**, **10**, and **13** were prepared from the reactions of 4-bromomethylthiazole derivatives **7** and **12** with catechol and resorcinol derivatives in the presence of potassium hydride.

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In the last decade, macrocyclic compounds containing heterocycles have been prepared and employed in alkali, alkaline earth and transition metal cation determinations and separations due to their superior binding ability for these metal ions [1]. Although many macrocyclic compounds containing heterocycles, such as pyridine, bipyridine, triazole, pyrazole, and thiophene have been synthesized and studied [2]. The thiazole ring as a sub-unit of a macrocyclic compound has been reported in only a few cases [3,4]. We now report the synthesis of benzo-crown ethers which contain thiazoles.

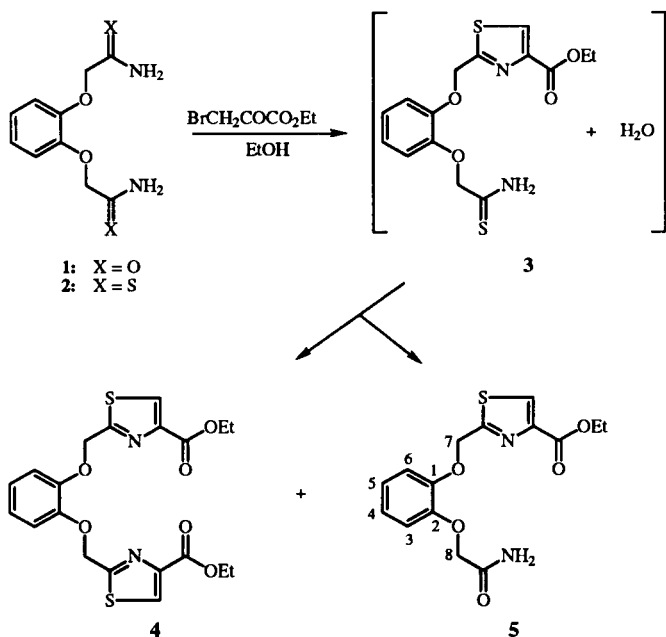
The requisite starting material for the synthesis of the thiazole-containing benzo-crown ethers **8**, **9**, and **10** was 1,2-bis[2'(4'-carboxy)thiazolyl]methoxybenzene **4**. The preparation of **4** is shown in Scheme 1. Thioamide **2** was synthesized in a 70% yield by treatment of amide **1** with Lawesson's reagent. Amide **1** was prepared in 76% yield by allowing catechol to react with iodoacetamide in the presence of potassium carbonate. Cyclocondensation of

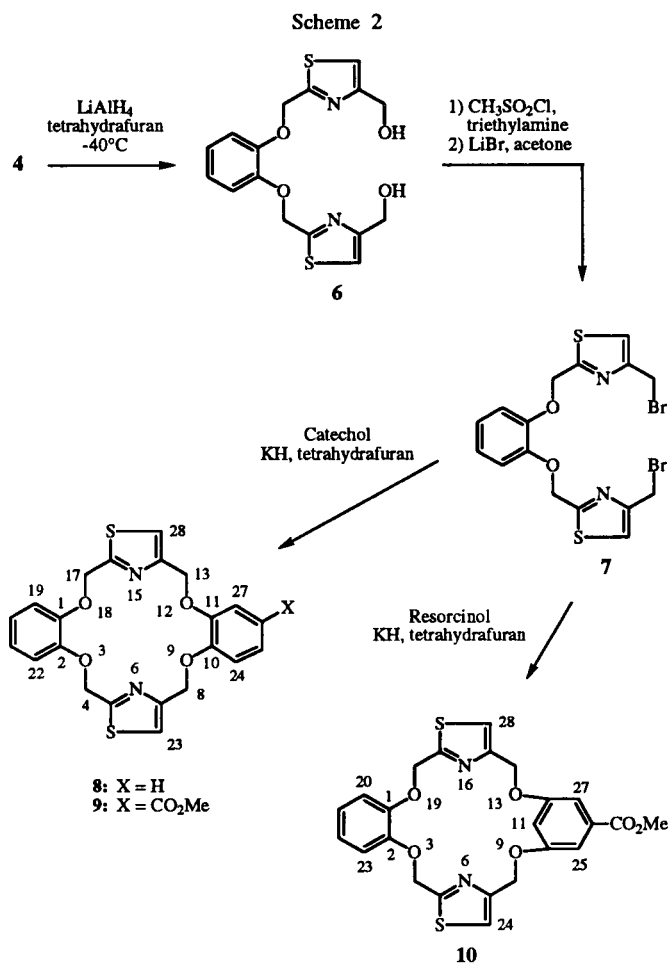
thioamide **2** with ethyl bromopyruvate in ethanol resulted in 1,2-bis(thiazolyl)benzene **4** (80%) along with thiazole **5** (14%). We have found that using dry conditions in this reaction is quite essential to improve the yield of **4**. Thus when the reaction was carried out in 99.5% ethanol, **4** (50%) and **5** (34%) were obtained, while when absolute ethanol was used as a solvent, **4** was the predominant product. Other methods which have been used successfully for cyclocondensation of similar compounds, namely treatment of a thioamide with ethyl diazopyruvate in the presence of a Lewis acid [5,6], was not satisfactory in this case. Treatment of thioamide **2** with ethyl diazopyruvate in the presence of boron trifluoride gave a poor conversion (20%). The formation of **5** may be explained by hydrolysis of reaction intermediate **3** by water that was generated from the cyclocondensation of the thioamide with ethyl bromopyruvate.

The structures of compound **4** and **5** were confirmed by spectroscopic and analytical data. For instance, the ¹H nmr spectrum of **4** showed one thiazole proton at δ 8.34 (s) and methylene protons at δ 5.45 (s). The three thiazole carbons of **4** appeared at δ 160.7, 147.5 and 128.5 and the methylene carbons at δ 68.2 in the ¹³C nmr spectrum. The mass spectrum of **4** showed the molecular ion at 448 (7% relative abundance). The most characteristic features of **5** involve the appearance of two infrared stretching bands at 1751 and 1717 cm⁻¹ for the two ester carbonyl groups in addition to the ¹H nmr signals at δ 5.46 (s) and 4.70 (s) assignable to the H-7 and H-8 protons, and the ¹³C nmr spectral peaks at δ 68.9 and 66.5 for the C-7 and C-8 carbons. The molecular ion peak of **5** appeared at 365 (2% relative abundance) and its fragmentation is in accordance with the assigned structure.

The synthesis of 1,2-bis[2'(4'-bromomethyl)thiazolyl]-methoxybenzene (**7**) was carried out by the reaction sequences shown in Scheme 2. 1,2-Bis[2'(4'-hydroxymethyl)thiazolyl]methoxybenzene (**6**) was prepared in a 98% yield from reduction of **4** with lithium aluminum hydride at -40°. Mesylation of **6** with methanesulfonyl chloride in dichloromethane at 0° for 30 minutes followed by bromine exchange of the non-isolated mesylated intermediate with lithium bromide gave **7** in an 89% yield. Treatment of catechol with potassium hydride in tetrahydrofuran then

Scheme 1

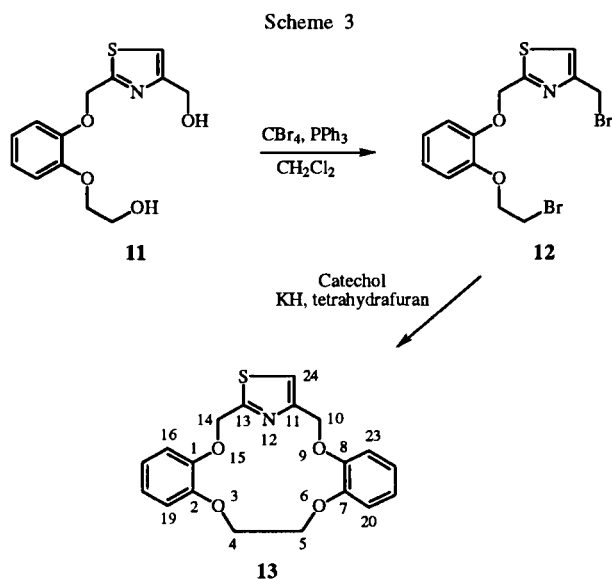




subsequently with **7** provided bis(5,16-thiazolyl-1,2,10,11-benzene) coronand **18-C-6 (8)** in a 66% yield. Compound **8** exhibited, in its ¹H nmr spectrum, signals of one thiazole proton at δ 7.20 (s, H-23, H-28) and two methylene protons at δ 5.08 (s, H-8, H-13) and 5.23 (s, H-4, H-17). Its ¹³C nmr spectrum showed three thiazole carbons at δ 166.3 (C-5, C-16), 153.4 (C-7, C-14), 117.9 (C-23, C-28), and two methylene carbons at δ 69.3 (C-8, C-13) and 70.1 (C-4, C-17). Similarly reaction of **7** with methyl 3,4-dihydroxybenzoate and methyl 3,5-dihydroxybenzoate produced the corresponding benzo-crown ethers **18-C-6 (9)** and **19-C-6 (10)** in 40 and 72% yields. Compound **9** showed an ester carbonyl absorption in the ir spectrum at 1715 cm⁻¹. Due to the dissymmetry of the molecule, the ¹H nmr spectrum of **9** exhibited a pair of signals for the thiazole protons at δ 7.22 (s, H-23) and 7.23 (s, H-28) and two pairs of two methylene protons at δ 5.12 (s, H-8) and 5.13 (s, H-13) and at 5.22 (s, H-4) and 5.24 (s, H-17) and one carbomethoxy proton at δ 3.91 (s). The mass spectrum of **9** displayed the molecular ion at 496 (49% relative abundance). Compound **10** showed an ester carbonyl absorption in the ir spectrum at 1723 cm⁻¹. In the ¹H nmr spectrum, **10** showed the thiazole protons at δ 6.88

(s, H-24, H-28) and two methylene protons at δ 5.22 (s, H-8, H-14) and 5.25 (s, H-4, H-18) and one carbomethoxy proton at δ 3.92 (s). The ¹³C nmr spectrum of **10** revealed three thiazole carbons at δ 166.7 152.0, 117.9 and two methylene carbons at δ 66.8 and 69.6, and ester carbonyl carbon at δ 166.5. The structure of **10** was also confirmed by a mass spectrum and elemental analysis.

Compound **13** was prepared by an analogous sequence of steps (Scheme 3) starting with **5**. Reduction of **5** with lithium aluminum hydride at -40° gave **11** in a 68% yield. Subsequent bromination of **11** with carbon tetrabromide and triphenyl phosphine resulted in a 57% yield of **12**. Cyclization of dibromide **12** with catechol in tetrahydrofuran provided 13-thiazolyl-1,2,7,8-dibenzene coronand **15-C-5 (13)** in a 20% yield. The structure of **13** was confirmed from its mass spectrum and the ¹H and ¹³C nmr spectra. The mass spectrum of **13** showed the molecular ion at 355 (36% relative abundance) and high resolution mass spectrum indicated the M⁺ to be C₁₉H₁₇NO₄S. In the ¹H nmr spectrum, **13** exhibited signals for two methylene protons at δ 5.13 (s, H-14) and 5.30 (s, H-10) and two clearly discernable AB patterns at δ 4.08 (2H, dd, J = 13.0, 4.2 Hz), 4.16 (2H, dd, J = 13.0, 4.2 Hz) were evident for the diastereotopic methylene protons H-4 and H-5, and one thiazole proton at δ 6.77 (s, H-24). The ¹³C nmr spectrum showed three signals for the thiazole carbons at δ 168.8 (C-13), 151.8 (C-11), 118.7 (C-24) and four methylene carbons at δ 72.6, 71.6, 67.0, 66.8.



Thus, the present procedure provides a series of benzo-crown ethers, which contain the thiazole subcyclic group. Our future publications will describe utilization of some of these benzo-crown ethers in supramolecular chemistry.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. The ir spectra were measured with a Galaxy FT-IR 7000 spectrophotometer and are reported in reciprocal centimeters. The nmr spectra were obtained on a Varian Unity Plus 300 spectrometer. The chemical shifts in the ^1H nmr spectra (300.1 MHz) are reported in ppm (δ) relative to tetramethylsilane as the internal standard and ^{13}C nmr (75.5 MHz) are referenced to deuteriochloroform at 77.0 ppm. Mass spectra were recorded on a Shimadzu QP-100 spectrometer with an electron energy of 20 or 70 eV. Elemental analyses were performed on a Calro Erba 1106 instrument. Analyses (tlc) were performed on precoated 0.2 mm Merck Kieselgel 60F₂₅₄ plates, visualizing with a 254-nm uv lamp. Column chromatography was performed using Merck silica gel 70-230 mesh. All reactions were carried out under an atmosphere of argon. Solvents were dried and purified by known methods [7].

1,2-Bis(amidomethoxy)benzene (1).

A mixture of catechol (1.27 g, 11.5 mmoles), iodoacetamide (4.27 g, 23.1 mmoles) and potassium carbonate (3.18 g, 23.1 mmoles) in 150 ml of acetone was heated under reflux for 5 hours. After the reaction was completed, 150 ml of water was added to the resulting mixture. The precipitate was filtered, allowed to air-dry and then recrystallized from dichloromethane and hexane to give a white solid (1.95 g, 76% yield), mp 204-206°; ir (potassium bromide): 3381, 3194, 1655, 1501, 1414, 1192, 1128, 1045, 746, 709 cm^{-1} ; ms: m/z 224 (M^+ , 23), 180 ($\text{M}-\text{CONH}_2$, 29), 163 (20), 150 (24), 135 (23), 122 (48), 59 (100).

Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_4$: C, 53.55, H, 5.40, N, 12.50. Found: C, 53.79; H, 5.10; N, 12.33.

1,2-Bis(thioamidomethoxy)benzene (2).

To a suspension of 1 (14.14 g, 63 mmoles) in 400 ml of dry tetrahydrofuran was added Lawesson's reagent (50.96 g, 126 mmoles), and the mixture was refluxed until it became a homogeneous solution. After removal of the solvent, the residue was dissolved in dichloromethane and allowed to solidify during a period of 4 hours. The precipitate was filtered, allowed to air-dry and then recrystallized from dichloromethane and hexane to give a white solid (11.42 g, 70% yield), mp 154-155°; ir (potassium bromide): 3374, 3266, 3158, 1621, 1506, 1459, 1251, 1205, 1120, 1035, 965, 741, 625 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 9.95 (s, 2H, NH), 9.12 (s, 2H, NH), 6.88-6.96 (m, 4H, Ph), 4.79 (s, 4H, $\text{OCH}_2\text{CSNH}_2$); ^{13}C nmr (deuteriochloroform): δ 198.8 (CSNH_2), 145.5 (C-1 of Ph), 120.6 (C-4, 5 of Ph), 112.7 (C-3, 6 of Ph), 72.6 ($\text{OCH}_2\text{CSNH}_2$); ms: m/z 265 (M^+ , 2), 222 (3), 196 (2), 109 (15), 74 (CH_2SNH_2 100); R_f 0.40 (ethyl acetate-hexane, 1:1).

Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_2\text{S}_2$: C, 46.86; H, 4.72; N, 10.93; S, 25.01. Found: C, 46.78; H, 5.03; N, 10.79; S, 25.49.

1,2-Bis[2'(4'-carboxy)thiazolyl]methoxybenzene (4) and 1-[2'(4'-Carboxy)thiazolyl]methoxy-2-carboxymethyl-oxybenzene (5).

A mixture of 2 (12.4 g, 48.4 mmoles) and ethyl bromopyruvate (20.8 g, 106 mmoles) in 200 ml of dry ethanol was heated under reflux for 7 hours. Analysis by tlc (silica gel, 50% ethyl acetate in hexane) indicated two components with R_f 's of 0.30 and 0.57. These were separated by flash chromatography (silica gel, ethyl

acetate-hexane, 2:1) to give 4 (10.19 g, 80% yield) and 5 (1.46 g, 14% yield), respectively.

Compound 4 was obtained as a white solid, which was recrystallized from dichloromethane and hexane, mp 132-133°; ir (potassium bromide): 3089, 1722, 1498, 1328, 1228, 1112, 1027, 749 cm^{-1} ; ^1H nmr (deuteriochloroform + deuteriodimethyl sulfoxide): δ 8.34 (s, 2H, H of thiazole), 6.98-7.10 (m, 4H, Ph), 5.45 (s, 4H, OCH_2 -thiazole), 4.38 (q, $J = 6.9$ Hz, 4H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 1.40 (t, $J = 6.9$ Hz, 6H, $\text{CO}_2\text{CH}_2\text{CH}_3$); ^{13}C nmr (deuteriochloroform + deuteriodimethyl sulfoxide): δ 167.8 (CO_2), 160.7, 147.5, 146.4, 128.5, 122.7, 115.2, 68.2 (OCH_2 -thiazole), 61.0 ($\text{CO}_2\text{CH}_2\text{CH}_3$), 14.1 ($\text{CO}_2\text{CH}_2\text{CH}_3$); ms: m/z 448 (M^+ , 7), 403 (5), 340 (27), 278 (30), 170 (100), 142 (23), 121 (42); R_f 0.30 (ethyl acetate-hexane, 1:1).

Anal. Calcd. for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_6\text{S}_2$: C, 53.56; H, 4.49; N, 6.25; S, 14.30. Found: C, 53.69; H, 4.79; N, 6.04; S, 14.74.

Compound 5 was obtained as a white solid, which was recrystallized from dichloromethane and hexane, mp 80°; ir (potassium bromide): 3086, 1751, 1717, 1505, 1456, 1331, 1229, 1192, 1130, 1024, 743 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 8.20 (s, 1H, H of thiazole), 6.96-6.98 (m, 4H, Ph), 5.46 (s, 2H, OCH_2 -thiazole), 4.70 (s, 2H, $\text{OCH}_2\text{CO}_2\text{CH}_2\text{CH}_3$), 4.34 (q, $J = 7.1$ Hz, 2H, thiazole- $\text{CO}_2\text{CH}_2\text{CH}_3$), 4.26 (q, $J = 7.1$ Hz, 2H, $\text{OCH}_2\text{CO}_2\text{CH}_2\text{CH}_3$), 1.42 (t, $J = 7.1$ Hz, 3H, thiazole- $\text{CO}_2\text{CH}_2\text{CH}_3$), 1.26 (q, $J = 7.1$ Hz, 3H, $\text{OCH}_2\text{CO}_2\text{CH}_2\text{CH}_3$); ^{13}C nmr (deuteriochloroform): δ 168.7 ($\text{CO}_2\text{CH}_2\text{CH}_3$), 161.2, 148.1, 147.7, 147.0, 128.1, 122.8, 122.6, 115.7, 115.0, 68.9 (OCH_2 -thiazole), 66.5 ($\text{OCH}_2\text{CO}_2\text{CH}_2\text{CH}_3$), 61.5 (thiazole- $\text{CO}_2\text{CH}_2\text{CH}_3$), 61.3 ($\text{OCH}_2\text{CO}_2\text{CH}_2\text{CH}_3$), 14.3 (thiazole- $\text{CO}_2\text{CH}_2\text{CH}_3$), 14.1 ($\text{OCH}_2\text{CO}_2\text{CH}_2\text{CH}_3$); ms: m/z 365 (M^+ , 2), 336 (2), 292 (33), 278 (5), 245 (11), 195 (14), 170 (100), 142 (37), 121 (42); R_f 0.57 (ethyl acetate-hexane, 1:1)

Anal. Calcd. for $\text{C}_{17}\text{H}_{19}\text{NO}_6\text{S}$: C, 55.88, H, 5.24, N, 3.83, S, 8.77. Found: C, 55.62; H, 5.24; N, 3.56; S, 8.72.

1,2-Bis[2'(4'-hydroxymethyl)thiazolyl]methoxybenzene (6).

To a suspension of lithium aluminum hydride (21 mg, 0.55 mmole) in tetrahydrofuran (15 ml) was added 110 mg of 4 (0.25 mmole) at -78°. After the mixture was stirred for 2 hours, the mixture was warmed to the room temperature and ethyl acetate and water were added to the mixture. The mixture was washed with 5% hydrochloric acid solution and then extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous sodium sulfate and evaporated. The residue was purified by flash chromatography (silica gel, ethyl acetate) to give 6 (88 mg, 98% yield), which was recrystallized from dichloromethane and hexane, mp 112-113°; ir (potassium bromide): 3418, 2922, 2857, 1636, 1508, 1360, 1263, 1211, 1130, 1045, 743 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 7.27 (s, 2H, H of thiazole), 6.95-7.06 (m, 4H, Ph), 5.39 (s, 4H, OCH_2 -thiazole), 4.75 (s, 4H, thiazole- CH_2OH), 4.74 (bs, 2H, thiazole- CH_2OH); ^{13}C nmr (deuteriochloroform): δ 166.5, 156.8, 147.6, 122.2, 115.2, 114.6, 68.2 (OCH_2 -thiazole), 60.1 (thiazole- CH_2OH); ms: m/z 364 (M^+ , 4), 256 (14), 236 (8), 220 (2), 144 (1), 128 (100); R_f 0.16 (ethyl acetate).

Anal. Calcd. for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_4\text{S}_2$: C, 52.73; H, 4.43; N, 7.69; S, 17.59. Found: C, 52.61; H, 4.32; N, 7.56; S, 17.69.

1,2-Bis[2'(4'-bromomethyl)thiazolyl]methoxybenzene (7).

To a solution of 6 (178 mg, 0.49 mmole) and triethylamine (0.68 ml, 0.49 mmole) in dry dichloromethane (50 ml) was added methanesulfonyl chloride (0.083 ml, 1.07 mmoles). The mixture

was stirred for 30 minutes in an ice bath. To this solution was added lithium bromide (357 mg, 4.11 mmoles) in acetone (10 ml), and the resulting mixture was stirred at room temperature for 1 hour. After the reaction was completed, the solution was passed through a celite pad and the filtrate was concentrated. The residue was purified by flash chromatography (silica gel, ethyl acetate-hexane, 1:4) to give **7** (213 mg, 89% yield) which was recrystallized from dichloromethane and hexane, mp 115-116°; ir (potassium bromide): 3106, 2909, 1510, 1361, 1267, 1227, 1130, 1043, 743 cm^{-1} ; ^1H nmr (500 MHz, deuteriochloroform): δ 7.58 (s, 2H, H of thiazole), 7.18 (dd, $J = 5.99, 3.58$ Hz, 2H), 7.07 (dd, $J = 5.99, 3.58$ Hz, 2H), 5.42 (s, 4H, OCH_2 -thiazole), 4.71 (s, 4H, thiazole- CH_2Br); ^{13}C nmr (deuteriochloroform): δ 167.6, 152.3, 148.1, 122.7, 119.4, 115.8, 68.4 (OCH_2 -thiazole), 27.4 (thiazole- CH_2Br); ms: m/z 492 ($\text{M}^+ + 2, 5$), 490 ($\text{M}^+, 9$), 488 ($\text{M}^+ - 2, 3$), 411 (8), 409 (7), 382 (14), 303 (12), 301 (14), 300 (18), 298 (16), 192 (69), 190 (63), 112 (100); R_f 0.57 (ethyl acetate-hexane, 1:1).

Anal. Calcd. for $\text{C}_{16}\text{H}_{14}\text{Br}_2\text{N}_2\text{O}_2\text{S}_2$: C, 39.20; H, 2.88; N, 5.71; S, 13.08. Found: C, 39.69; H, 2.85; N, 5.62; S, 12.84.

Bis(5,16-thiazolyl-1,2,10,11-benzene) coronand 18-C-6 (**8**).

A mixture of catechol (20 mg, 0.18 mmole) and potassium hydride (16 mg, 0.40 mmole) in tetrahydrofuran (230 ml) was heated under reflux for 1 hour. A solution of **7** (86 mg, 0.18 mmole) in tetrahydrofuran (10 ml) was added to the resulting mixture via a syringe pump for 3 hours. After removal of the solvent at reduced pressure, the residue was extracted with ethyl acetate. The organic layer was washed with a 10% hydrochloric acid solution and brine, dried over anhydrous sodium sulfate and evaporated. The residue was purified by flash chromatography (silica gel, ethyl acetate-hexane, 1:4) to give **8** (53 mg, 66% yield), which was recrystallized from dichloromethane and hexane, mp 172-174°; ir (potassium bromide): 3109, 3061, 2922, 2861, 1591, 1501, 1454, 1246, 1209, 1119, 1011, 737 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 7.20 (s, 2H, H-23, H-28), 6.95-7.10 (m, 8H, Ph), 5.23 (s, 4H, H-4, H-17), 5.08 (s, 4H, H-8, H-13); ^{13}C nmr (deuteriochloroform): δ 166.3 (C-5, C-16), 153.4 (C-7, C-14), 150.5 (C-1), 149.9 (C-2), 124.1, 123.4, 118.7, 118.2, 118.0, 70.1 (C-4, C-17), 69.3 (C-8, C-13); ms: m/z 438 ($\text{M}^+, 30$), 330 (35, M-catechol), 313 (11), 222 (30), 197 (20), 189 (46), 121 (23), 112 (100); R_f 0.22 (ethyl acetate-hexane, 1:1).

Anal. Calcd for $\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_4\text{S}_2$: C, 60.26; H, 4.14; N, 6.39; S, 14.62. Found: C, 59.98; H, 3.89; N, 5.98; S, 14.47.

1,2-Benzene-5,16-dithiazolyl-10,11-(4'-carbomethoxy)benzene coronand 18-C-6 (**9**).

The procedure to prepare **9** was the same as for the preparation of **8** starting with 105 mg of **7** (0.21 mmole), 36 mg of methyl 3,4-dihydroxybenzoate (0.21 mmole) and 19 mg of potassium hydride (0.47 mmole) in tetrahydrofuran (230 ml). Compound **9** was obtained as a colorless solid (dichloromethane-hexane) in a 40% yield, mp 142-144°; ir (potassium bromide): 3115, 2947, 2868, 1715, 1595, 1505, 1439, 1271, 1246, 1211, 1119, 1012, 760 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 7.73-7.75 (m, 2H, H-25, H-27), 7.23 (s, 1H, H-28), 7.22 (s, 1H, H-24), 7.02-7.12 (m, 5H, H-19, H-20, H-21, H-22, H-24), 5.24 (s, 2H, H-17), 5.22 (s, 2H, H-4), 5.13 (s, 2H, H-13), 5.12 (s, 2H, H-8), 3.91 (s, 3H, CO_2CH_3); ^{13}C nmr (deuteriochloroform): δ 166.6, 165.8, 165.2, 153.7, 152.3, 151.7, 149.1, 148.9, 148.8, 125.0, 123.9, 123.3, 123.1, 118.4, 118.0, 117.7, 117.1, 114.7, 69.1, 68.7, 68.6, 67.5, 52.0; ms: m/z 496 ($\text{M}^+, 49$), 470 (10), 388 (17), 330 (24), 221

(32), 189 (52), 121 (24), 111 (100); R_f 0.15 (ethyl acetate-hexane, 1:1).

Anal. Calcd. for $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}_6\text{S}_2$: C, 58.05; H, 4.06; N, 5.64; S, 12.91. Found: C, 57.86; H, 4.40; N, 5.34; S, 13.00.

1,2-Benzene-5,17-dithiazolyl-10,12-(5'-carbomethoxy)benzene coronand 19-C-6 (**10**).

The procedure to prepare **10** was the same as for the preparation of **8** starting with 140 mg of **7** (0.28 mmole), 47 mg of methyl 3,5-dihydroxybenzoate (0.28 mmole) and 25 mg of potassium hydride (0.62 mmole) in tetrahydrofuran (230 ml). Compound **10** was obtained as a colorless solid (dichloromethane-hexane) in a 72% yield, mp 185°; ir (potassium bromide): 3121, 2951, 2872, 1723, 1589, 1499, 1456, 1326, 1268, 1233, 1159, 1069, 1028, 770 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 7.33 (d, $J = 2.4$ Hz, 2H, H-25, H-27), 7.05-7.14 (m, 4H, H-20, H-21, H-22, H-23), 6.88 (s, 2H, H-24, H-28), 6.36 (dd, $J = 2.6, 2.6$ Hz, 1H, H-11), 5.25 (s, 4H, H-4, H-18), 5.22 (s, 4H, H-8, H-14), 3.92 (s, 3H, CO_2CH_3); ^{13}C nmr (deuteriochloroform): δ 166.7 (C-5, C-17), 166.5 (CO_2CH_3), 158.9 (C-10, C-12), 152.0 (C-7, C-15), 149.2 (C-1, C-2), 132.2 (C-26), 123.6 (C-21, C-22), 117.9 (C-24, C-28), 115.9 (C-20, C-23), 111.6 (C-25, C-27), 104.3 (C-11), 69.6 (C-4, C-18), 66.8 (C-8, C-14), 52.3 (CO_2CH_3); ms: m/z 496 ($\text{M}^+, 98$), 388 (26), 329 (10), 276 (49), 121 (23), 111 (100); R_f 0.38 (ethyl acetate-hexane, 1:1).

Anal. Calcd. for $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}_6\text{S}_2$: C, 58.05; H, 4.06; N, 5.64; S, 12.91. Found: C, 57.97; H, 4.26; N, 5.54; S, 12.80.

1-[2'(4'-Hydroxymethyl)thiazolyl]methoxy-2-hydroxyethyl-oxybenzene (**11**).

The procedure to prepare **11** was the same as for the preparation of **6** by lithium aluminum hydride reduction starting with 115 mg (0.21 mmole) of **5** and 26 mg (0.69 mmole) of lithium aluminum hydride. Compound **11** was obtained as a colorless oil in a 68% yield; ir (neat): 3303, 2940, 2872, 1504, 1455, 1033, 915, 795 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 7.19 (s, 1H, H of thiazole), 6.86-7.01 (m, 4H, Ph), 5.28 (s, 2H, OCH_2 -thiazole), 4.70 (s, 2H, thiazole- CH_2OH), 4.45 (bs, 2H, CH_2OH), 4.09 (t, $J = 4.2$ Hz, 2H, $\text{OCH}_2\text{CH}_2\text{OH}$), 3.92 (t, $J = 4.2$ Hz, 2H, $\text{OCH}_2\text{CH}_2\text{OH}$); ^{13}C nmr (deuteriochloroform): δ 167.2, 156.4, 149.4, 147.6, 123.4, 121.5, 117.3, 116.1, 114.4, 70.7 (OCH_2 -thiazole), 68.8 ($\text{OCH}_2\text{CH}_2\text{OH}$), 60.8 (thiazole- CH_2OH), 60.2 ($\text{OCH}_2\text{CH}_2\text{OH}$); ms: m/z 281 ($\text{M}^+, 5$), 251 (8), 198 (8), 172 (6), 154 (12), 128 (100), 110 (63); R_f 0.56 (methanol-ethyl acetate, 1:9); hrms: Calcd. for $\text{C}_{13}\text{H}_{15}\text{NO}_4\text{S}$: 281.0722. Found: 281.0708.

1-[2'(4'-Bromomethyl)thiazolyl]methoxy-2-bromoethoxybenzene (**12**).

To a solution of **11** (544 mg, 1.93 mmoles) in dry dichloromethane (10 ml) was added carbon tetrabromide (3.85 g, 11.60 mmoles), triphenyl phosphine (3.04 g, 11.60 mmoles) and the mixture was stirred at room temperature for 5 hours. After removal of the solvent, the residue was purified by flash chromatography (silica gel, ethyl acetate-hexane, 1:4) to give **12** (448 mg, 57% yield), which was recrystallized from dichloromethane and hexane, mp 79-80°; ir (potassium bromide): 3084, 2974, 2932, 2863, 1510, 1260, 1221, 1128, 733 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 7.32 (s, 1H, H of thiazole), 6.94-7.03 (m, 4H, Ph), 5.38 (s, 2H, OCH_2 -thiazole), 4.58 (s, 2H, thiazole- CH_2Br), 4.35 (t, $J = 6.9$ Hz, 2H, $\text{OCH}_2\text{CH}_2\text{Br}$), 3.66 (t, $J = 6.9$ Hz, 2H, $\text{OCH}_2\text{CH}_2\text{Br}$); ^{13}C nmr (deuteriochloroform): δ 168.4, 151.9,

148.4, 148.1, 123.0, 122.4, 118.4, 116.2, 115.5, 69.3 (OCH₂-thiazole), 69.1 (OCH₂CH₂Br), 29.2 (thiazole-CH₂Br), 26.9 (OCH₂CH₂Br); ms: m/z 409 (M⁺+2, 4), 407 (M⁺, 8), 405 (M⁺-2, 4), 328 (51), 326 (50), 192 (99), 190 (100), 121 (25), 111 (73); R_f 0.26 (ethyl acetate-hexane, 1:4).

Anal. Calcd. for C₁₃H₁₃Br₂NO₂S: C, 38.35; H, 3.22; N, 3.44; S, 7.87. Found: C, 38.32; H, 3.26; N, 3.47; S, 7.84.

13-Thiazolyl-1,2,7,8-dibenzene coronand 15-C-5 (13).

The procedure to prepare **13** was the same as for the preparation of **8** starting with 169 mg of **12** (0.41 mmole), 45 mg of catechol (0.41 mmole) and 36 mg of potassium hydride (0.90 mmole) in tetrahydrofuran (230 ml). Compound **13** was obtained as a colorless solid (dichloromethane-hexane) in a 20% yield, mp 105-107°; ir (potassium bromide): 3071, 2935, 1591, 1500, 1452, 1260, 1207, 1121, 988, 749 cm⁻¹; ¹H nmr (deuteriochloroform): δ 6.80-7.26 (m, 8H, Ph), 6.77 (s, 1H, H-24), 5.30 (s, 2H, H-14), 5.13 (s, 2H, H-10), 4.16 (dd, J = 13.0, 4.2 Hz, 2H, OCH₂CH₂O), 4.08 (dd, J = 13.0, 4.2 Hz, 2H, OCH₂CH₂O); ¹³C nmr (deuteriochloroform): δ 166.8 (C-13), 151.8 (C-H), 157.1, 151.1, 148.5, 147.9, 124.6, 124.2, 122.1, 121.7, 118.7 (C-24), 113.4, 113.3, 72.6 (OCH₂CH₂O), 71.6 (OCH₂CH₂O), 67.0 (C-14), 66.8 (C-10); ms: m/z 355 (M⁺, 36), 247 (24), 219 (16), 163 (8), 138 (38), 121 (35), 111 (100); R_f 0.37 (ethyl acetate-hexane, 1:1); hrms: Calcd. for C₁₉H₁₇NO₄S: 355.0878. Found: 355.0897.

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REFERENCES AND NOTES

* To whom correspondence should be addressed.
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