

Synthesis of Azobenzenes Tethered with Polyether Unit at the *meta*-Positions

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Azobenzenes tethered with crown ether display photo-responsive complexation with alkali and alkali earth metal ions, and have potential applications in ion-selective membranes, chemically-modified field effect transistors, and photo-switchable receptors.^{1,2} Figure 1 shows a few selected early examples of azobenzocrown ethers; azobenzene **1** bearing two crown ether units,³ azobenzocrown ether **2** with the direct connection to the azobenzene unit (at the *para*-positions) within the macrocycle,⁴ and one linked to the

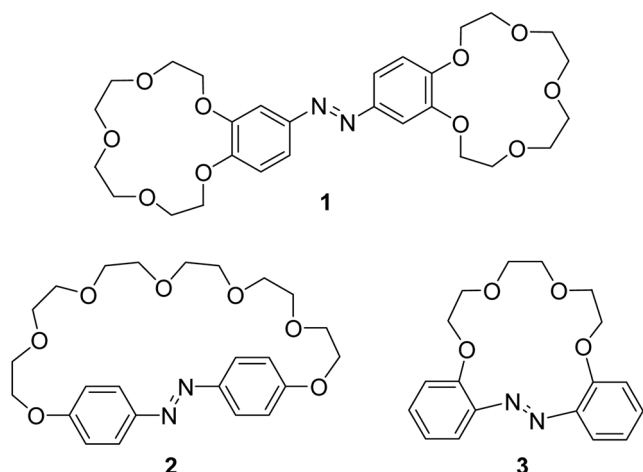


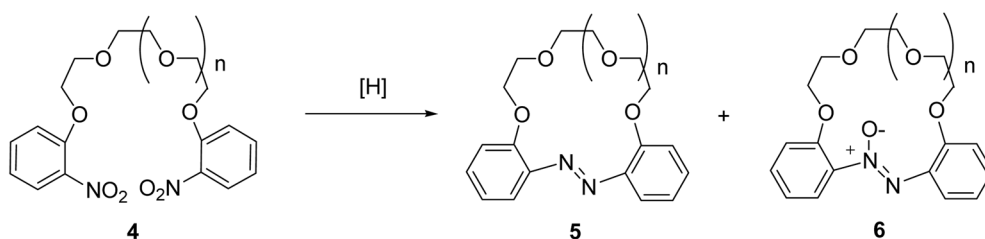
Figure 1. Selected examples of azobenzocrown ethers.

ortho-positions of azobenzene **3**.⁵

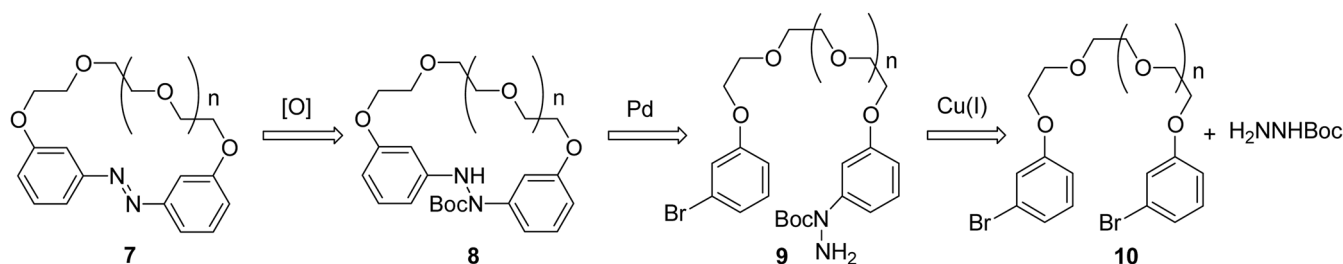
Despite the advances in the applications, there are only limited synthetic methods available for the preparation of azobenzocrown ethers. Most of the methods currently used rely on reductive macrocyclization of the corresponding nitroarenes, which often provides the desired azobenzocrown ether **5** in low yield with a substantial amount of the undesired azoxycrown ethers **6** as a byproduct (Scheme 1).^{2c} As a result, their structural variation is mostly confined to the modification of substituents on the aromatic ring of azobenzene **3**. In addition, the azobenzenes incorporating crown ether unit at the *meta*-positions have not been reported despite the potential interest.

A few years ago, we reported a new synthetic approach to azobenzene, starting from aryl halides and *N*-aryl hydrazides, via the Pd-catalyzed coupling followed by direct oxidation of the resultant *N,N'*-diaryl hydrazides.⁶ We anticipated that our methodology would translate well for the synthesis of azobenzocrown ethers.⁷ Herein we wish to present our investigation on the synthesis of azobenzocrown ethers **7** tethered with a polyether unit at the *meta*-positions (Scheme 2).

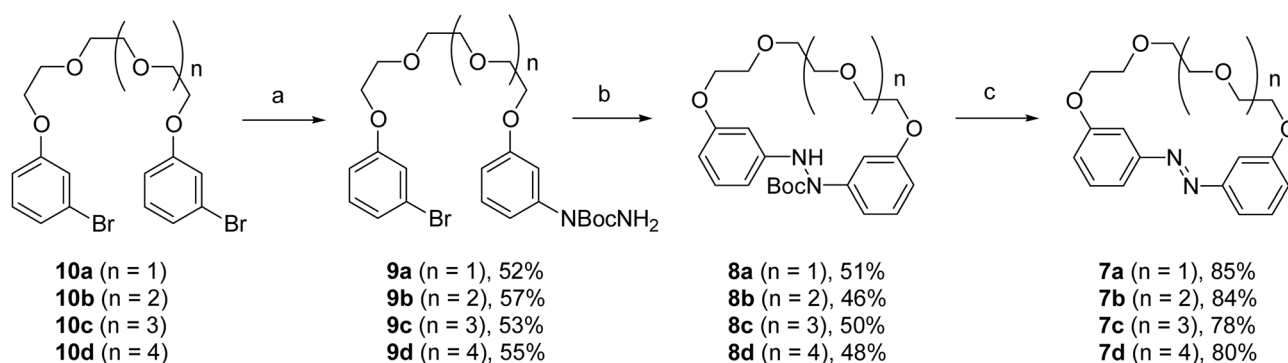
The synthesis began with the preparation of bis(*m*-bromophenyl) ethers **10a-10d**, readily accessed from *m*-bromophenol and polyether bis-tosylates. Cu(I)-catalyzed coupling reactions of **10a-10d** with *N*-Boc hydrazine provided the



Scheme 1. Reductive macrocyclization of **4**.



Scheme 2. Retrosynthesis of azobenzocrown ethers **7**.



Scheme 3. Synthesis of azobenzocrown ethers **7a-7d**. (a) BocNHNH₂, CuI, Cs₂CO₃, 1,10-phenanthroline, DMF, 80 °C; (b) Pd(OAc)₂, P(*t*Bu)₃, toluene, 110 °C; (c) CuI, Cs₂CO₃, DMF, 130 °C.

corresponding hydrazides **9a-9d**, which were subjected to the intramolecular Pd-catalyzed coupling reactions under high dilution conditions to afford polyether tethered *N,N'*-diaryl hydrazides **8a-8d**.⁸ The Cu(I)-mediated oxidations of the resultant cyclic hydrazides furnished azobenzocrown ethers **7a-7d** in good isolation yields (78-85%) after flash column chromatography (Scheme 3).⁷

In summary, we have prepared azobenzenes tethered with a polyether unit at the *meta*-positions in good overall yields. Our method would allow a systematic design and synthesis of structurally and functionally diverse azobenzocrown ethers. Photo-responsive metal ion complexation behavior of our new azobenzocrown ethers will be explored and published in due course.

Experimental Section

General Experimental Methods. Reactions were carried out in oven or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents used were dried and purified before use in a Grubbs column. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.25 mm E. Merck pre-coated silica gel plates. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Proton and carbon-13 NMR spectra were recorded on a Varian 400 MHz spectrometer. Chemical shifts are reported relative to chloroform ($\delta = 7.26$) or TMS ($\delta = 0.00$) for ¹H NMR and chloroform ($\delta = 77.0$) for ¹³C NMR. High resolution mass spectra were measured by using FAB method at the Korean Basic Research Center, Seoul, Korea.

Preparation of 7a as Representative Procedure for 7a-7d: **7a.** To a round bottomed flask were charged 115 mg (0.27 mmol) of **8a**, 316 mg (3 equiv) of Cs₂CO₃, 185 mg (3 equiv) of CuI, and DMF (7 mL) under Ar atmosphere. After 8 h at 130 °C, the reaction mixture was quenched with H₂O and extracted with diethyl ether. The combined organic solution was dried over anhydrous MgSO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography to give 74 mg of **7a** (85% yield); ¹H NMR (400 MHz, CDCl₃) δ 8.17 (t, *J* = 2.2 Hz, 2H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.38 (t, *J* = 8.1 Hz, 2H), 7.01 (dd, *J* =

8.1, 2.6 Hz, 2H), 4.84 (t, *J* = 4.8 Hz, 4H), 3.81 (t, *J* = 4.8 Hz, 4H), 3.69 (s, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 160.0, 154.5, 130.4, 120.5, 114.8, 111.1, 71.6, 69.5; FT-IR (CH₂Cl₂) 3065, 2895, 1594, 1483, 1324, 1227, 1136, 1102, 1068, 1049 cm⁻¹; HRMS calcd for C₁₈H₂₀N₂NaO₄ (M + Na)⁺: 351.1321, found 351.1324.

7b. 84% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.98 (t, *J* = 2.2 Hz, 2H), 7.56 (d, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 8.1 Hz, 2H), 7.04 (dd, *J* = 8.1, 2.6 Hz, 2H), 4.42 (t, *J* = 4.4 Hz, 4H), 3.82 (t, *J* = 4.8 Hz, 4H), 3.68 (s, 8H); ¹³C NMR (100 MHz, CDCl₃) δ 160.3, 153.6, 129.4, 120.7, 115.9, 109.1, 71.3, 71.2, 71.1, 68.8; FT-IR (CH₂Cl₂) 3076, 2875, 1590, 1484, 1315, 1230, 1119, 1077, 1045 cm⁻¹; HRMS calcd for C₂₀H₂₅N₂O₅ (M + 1)⁺: 373.1763, found 373.1769.

7c. 78% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.70 (t, *J* = 1.8 Hz, 2H), 7.55 (d, *J* = 7.7 Hz, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.04 (dd, *J* = 8.1, 1.8 Hz, 2H), 4.34 (t, *J* = 4.8 Hz, 4H), 3.86 (t, *J* = 5.1 Hz, 4H), 3.67 – 3.73 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 160.5, 154.4, 130.4, 119.9, 116.7, 109.6, 72.01, 71.61, 71.4, 70.6, 68.8; FT-IR (CH₂Cl₂) 3068, 2913, 1603, 1480, 1362, 1330, 1265, 1126 cm⁻¹; HRMS calcd for C₂₂H₂₈N₂NaO₆ (M + Na)⁺: 439.1845, found 439.1843.

7d. 80% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.60 (s, 2H), 7.55 (d, *J* = 7.7 Hz, 2H), 7.41 (t, *J* = 8.1 Hz, 2H), 7.04 (dd, *J* = 8.1, 1.5 Hz, 2H), 4.30 (t, *J* = 5.13 Hz, 4H), 3.88 (t, *J* = 5.14 Hz, 4H), 3.72-3.90 (m, 4H), 3.64-3.67 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 160.3, 154.4, 130.4, 119.4, 116.9, 109.0, 71.8, 71.5, 71.4, 71.3, 70.4, 68.5; FT-IR (CH₂Cl₂) 3064, 2892, 1736, 1596, 1463, 1348, 1323, 1272, 1094 cm⁻¹; HRMS calcd for C₂₂H₂₈N₂NaO₆ (M + Na)⁺: 439.1845, found 439.1843.

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