

Specific features of the chemical behavior of acetylenic derivatives of benzocrown ethers

S. V. Klyatskaya, E. V. Tretyakov, and S. F. Vasilevsky*

*Institute of Chemical Kinetics and Combustion, Siberian Branch of the Russian Academy of Sciences,
3 ul. Institutskaya, 630090 Novosibirsk, Russian Federation.
Fax: +7 (383 2) 34 2350. E-mail: vasilev@ns.kinetics.nsc.ru*

4'-Ethynylbenzo-12-crown-4 (**8**), 4'-ethynylbenzo-15-crown-5 (**9**), and 4'-ethynylbenzo-18-crown-6 (**10**) were synthesized by cross-coupling of the corresponding aryl iodides **1–3** with 2-methylbut-3-yn-2-ol (**4a**) followed by the retro-Favorsky cleavage of the resulting carbinols. Unlike the corresponding benzo-12-crown-4 derivative (**5a**), the cleavage of tertiary acetylenic alcohols of benzo-15-crown-5 (**6a**) and benzo-18-crown-6 (**7a**) requires more than one molar equivalent of KOH. Aminoalkylation of crown ether **8** gives Mannich bases, independently of the reaction conditions and the nature of amine. The aminomethylation of acetylenic crown ethers **9** and **10** with paraform—piperidine (morpholine) in the presence of CuCl yields 1,4-disubstituted buta-1,3-diynes (**19**, **20**) rather than Mannich bases.

Key words: benzocrown ethers, alkynes, the retro-Favorsky reaction, the Mannich reaction, Frank—Meister—Hay modification, crown effect.

The discovery of crown compounds capable of binding certain ions with high selectivity has exerted a great effect on organic chemistry and on the development of new technological processes.¹ This can be illustrated with the comparatively recent data on the use of unsaturated benzocrown ethers in modern technology (components of liquid-crystal formulations, nonlinear optics, catalysts, *etc.*).^{2–5}

From this point of view, introduction of an acetylenic fragment into the crown ether molecule can give rise to a new promising intermediate product. The mutual influence of the crown ether ring and the acetylenic substituents in its molecule makes it possible to use this compound for preparative and applied purposes. Thus, even in the first study concerning acetylenic derivatives of crown ethers, they were used to obtain long-chain crown ethers and other unique compounds.⁶

Nevertheless, the chemistry of acetylenic derivatives of crown ethers remains poorly investigated so far. Only a few published papers are devoted to the synthesis of alkynylbenzocrown ethers by cross-coupling of aryl iodides with terminal acetylene derivatives,^{7,8} whereas the preparation of ethynylbenzocrown ethers are not described at all.

It is known that crown ethers can form 1 : 1 or "sandwich" complexes with metal cations of different sizes, which makes it difficult to predict *a priori* the behavior of their ethynyl derivatives in reactions in the presence of Cu^I salts (the Mannich, Cadot—Chodkiewicz, and Hay reactions) or inorganic bases (the retro-Favorsky reaction, *i.e.*, cleavage of tertiary acetylenic alcohols).

The goal of the present work is to synthesize ethynylcrown ethers and study their chemical transformations.^{9,10}

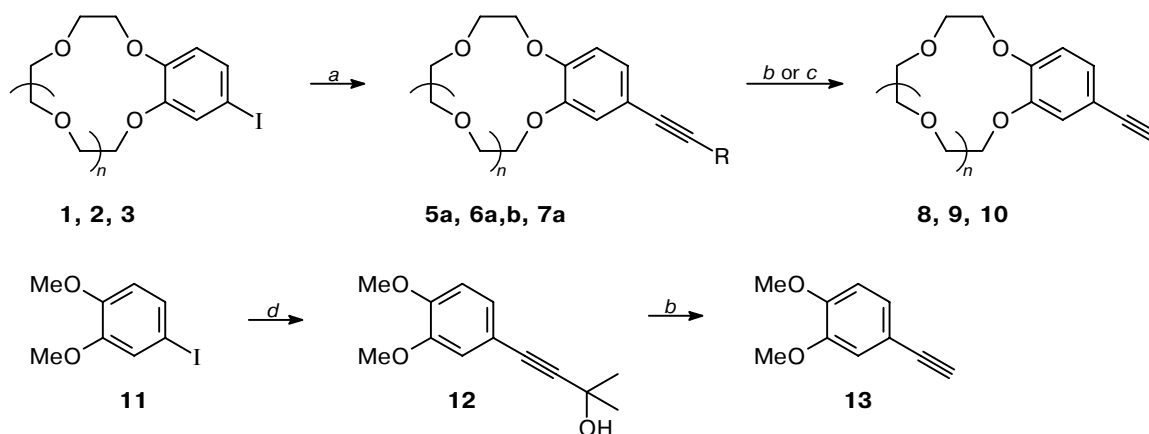
Results and Discussion

Synthesis of 4-(RC≡C)-benzocrown ethers. Terminal arylacetylene derivatives can be obtained by alkaline cleavage of tertiary arylacetylenic alcohols according to the retro-Favorsky reaction (Scheme 1),¹¹ which is usually carried out in anhydrous benzene at 75–80 °C and catalyzed by calcined KOH.

Tertiary acetylenic alcohols **6a** and **7a** are cleaved neither under the above conditions used earlier in the synthesis of some aryl- and hetarylacetylenes¹² nor in boiling toluene. This transformation was successful only in the presence of more than one molar equivalent of alkali, suggesting that the potassium cation plays an important part in the cleavage of tertiary arylacetylenic alcohol.

According to the literature data,^{11,13} the cleavage of carbinolates includes proton transfer from the alkyl group of the dialkylcarbinol fragment. On the other hand, when acetylenic alcohols are cleaved with KOH, the reaction mixture contains water, which suggests another mechanism. The authors of the paper¹⁴ actually led to the same conclusion, showing that the cleavage of tertiary diacetylenic alcohols in the presence of proton donors prevents isomerization of the resulting terminal diynes and increases the reaction rate. We believe that both a proton donor (*e.g.*, water or alcohol) and tertiary acetylenic alcoholate are involved in the elementary reaction event.

Scheme 1



4a,b = HC≡CR

R = C(OH)Me₂ (**a**); SiMe₃ (**b**). *n* = 1 (**1**, **5a**, **8**); 2 (**2**, **6a,b**, **9**); 3 (**3**, **7a**, **10**)

Reagents and conditions: *a.* **4a,b**, NEt₃, PdCl₂(PPh₃)₂, CuI; *b.* KOH, PhH; *c.* KOH, MeOH; *d.* **4a**, NEt₃, PdCl₂(PPh₃)₂, CuI.

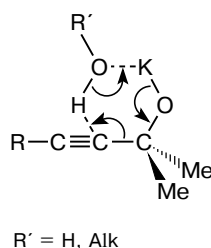
Based on this assumption, one can explain why the retro-Favorsky reaction is impossible for compounds **6a** and **7a**, which contain a polyether fragment capable of forming complexes with the potassium cation. Although the formation of alcoholate is favored by complexation here, its cleavage seems to be prevented within the framework of the discussed process.

It follows from the above reasoning that compounds containing substituents with analogous electron-donating properties but exhibiting no complexation effect can be involved in the retro-Favorsky reaction in the presence of catalytic amounts of KOH. Indeed, derivatives of veratrole **12** and benzo-12-crown-4 (**5a**) are cleaved in boiling benzene in the presence of 5–10 mol % KOH (see Scheme 1).

The starting alcohols **5a**, **6a**, **7a**, and **12** were prepared by cross-coupling of aryl iodides **1**, **3**, and **11** with 2-methylbut-3-yn-2-ol (**4a**) in 70–90% yields.

Ethynylbenzocrown ethers can also be obtained in a different way. For example, the reaction of iodobenzocrown ether **2** with trimethylsilylacetylene **4b** in the presence of NEt₃, PdCl₂(PPh₃)₂, and CuI gives a trimethylsilylethynyl derivative of benzocrown ether **6b**. When treated with 20% methanolic KOH at 25 °C, compound **6b** affords ethynylbenzocrown ether **9** (its total yield is 84%) (see Scheme 1).

Aminomethylation of 4-ethynylbenzocrown ethers. Aminomethylation of ethynylbenzocrown ethers is not reported in the literature, though terminal acetylene groups have long been involved in the Mannich reac-



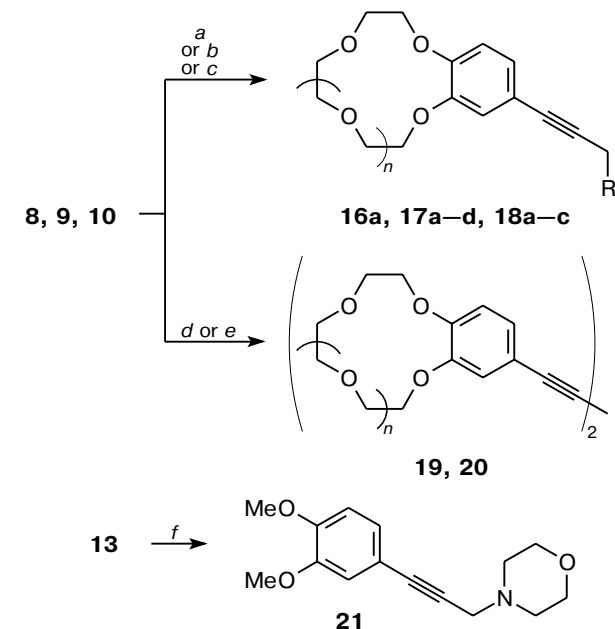
tion.¹⁵ Aminomethylation of alk-1-ynes accelerates significantly in the presence of copper salts.¹⁶ Further study of the Mannich reaction gave rise to its several versions. Propargylamines are most often synthesized by aminomethylating alkynes with a mixture of paraform with secondary amines in dioxane in the presence of CuCl; with a mixture of paraform with secondary amines in the presence of Cu(OAc)₂ and sulfuric acid; or with diaminomethanes in the presence of CuCl.^{12b} For this reason, the Mannich reaction is discussed below only under these conditions.

The aminomethylation of ethynylbenzocrown ethers **9** and **10** with a mixture of paraform with acyclic secondary amines **14c,d** in dioxane in the presence of 12 mol % CuCl in an atmosphere of argon gave the corresponding Mannich bases **17c,d** and **18c,d**. However, the reactions with cyclic amines **14a,b** under analogous conditions unexpectedly resulted, upon treating the reaction mixtures in the air, in disubstituted butadiynes **19** and **20** in 80–86% yields rather than aminomethylation products (Scheme 2).



The structures of diynes **19** and **20** were confirmed by spectral data; in addition, they were synthesized independently by oxidative dimerization of compounds **9** and **10** according to the Hay method¹⁷ (see Scheme 2). Alkynes **9** and **10** are oxidized by atmospheric oxygen in pyridine at 35–40 °C within 1–1.5 h. Under these conditions, dehydrodimerization gives the corresponding butadiyne (**19** or **20**) as the sole product.

Previously, various acetylene derivatives have been aminomethylated, never yielding products of oxidative dimerization.¹² To reveal the factors influencing such a reaction outcome, we carried out a series of experiments and found the following:

Scheme 2



14a–d = HR; **15a,b** = CH₂R₂

R =  (a);  (b); NEt₂ (c); NBu₂ (d)

n = 1 (**16a**), 2 (**17a–d**), 3 (**18a–c**, **20**)

Reagents and conditions: a. **14c,d**, (CH₂O)_x, CuCl, dioxane; b. **14a,b**, Cu(OAc)₂, 30% H₂SO₄, dioxane; c. **15a,b**, CuCl, dioxane; d. **14a,b**, (CH₂O)_x, CuCl, dioxane; e. **14a,b**, O₂, CuCl, Py; f. **14a**, (CH₂O)_x, CuCl, dioxane.

1) the Mannich reactions with preliminarily prepared bis-aminomethanes **15a,b** give only the Mannich bases **17a,b** and **18a,b**;

2) the Mannich reaction of 4-ethynylveratrole (**13**) or crown ether **8** with morpholine **14a** gives only the Mannich bases **21** and **16a**; and

3) the acid-catalyzed Mannich reactions of ethynylbenzocrown ethers **9** and **10** with amines **14a,b** (in the presence of H₂SO₄) give only the Mannich bases **17a,b** and **18a,b**.

Thus, base-catalyzed homolytic linking of alkynes rather than the Mannich reaction occurs in the presence of CuCl only when cyclic amines **14a,b** and ethynyl derivatives of benzo-15-crown-5 (**9**) and benzo-18-crown-6 (**10**) are used. These data suggest a specific crown effect, but the mechanism of the formation of dimeric products still remains unclear.

Experimental

¹H NMR spectra were recorded on a Bruker AM-300 spectrometer. IR spectra were recorded on a Bruker IFS-66 spectrometer (KBr). Mass spectra were recorded on a Finnigan

SSQ-710 instrument (direct inlet, EI, 70 eV, ionization chamber temperature 220–270 °C). Column chromatography was carried out on KSK silica gel (60–200 μm). Preparative TLC used a mixture of Al₂O₃ (high-purity grade) with a K-35 luminophore. The course of the reactions was monitored and the purity of the reaction products was checked by TLC on Silufol UV-254 plates. 2-Methylbut-3-yn-2-ol (**4a**) (Aldrich), trimethylsilylacetylene (**4b**) (Fluka), PdCl₂(PPh₃)₂ (Lancaster) were not purified additionally before use. The known procedures were used to prepare 12-iodo-2,3,5,6,8,9-hexahydro-1,4,7,10-tetraoxabenzocyclododecene (**1**),¹⁸ 15-iodo-2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecene (**2**), 18-iodo-2,3,5,6,8,9,11,12,14,15-decahydro-1,4,7,10,13,16-hexaoxabenzocyclooctadecene (**3**),¹⁹ 4-iodo-1,2-dimethoxybenzene (**11**),²⁰ 4-(morpholinomethyl)morpholine (**15a**),²¹ and 1-(piperidinomethyl)piperidine (**15b**).²² The other reagents and solvents were prepared according to the standard procedures.²³

2-Methyl-4-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecen-15-yl)but-3-yn-2-ol (6a). A mixture of iodide **2** (0.8 g, 2 mmol), alkyne **4a** (0.24 mL, 3.3 mmol), PdCl₂(PPh₃)₂ (30 mg, 0.043 mmol), and CuI (15 mg, 0.15 mmol) in 2 mL of Et₃N and 8 mL of PhH was stirred in an atmosphere of argon at 70–75 °C for 1 h. When the reaction was completed, the reaction mixture was cooled and filtered through a SiO₂ layer (2.5×2 cm). The solvent was removed *in vacuo*, and the residue was recrystallized from hexane. The yield of **6a** was 0.6 g (86%), m.p. 64–66 °C. ¹H NMR (CDCl₃), δ: 1.45 (s, 6 H, CMe₂); 2.02 (s, 1 H, OH); 3.72–3.81 (m, 8 H, 4 OCH₂); 3.87–3.95 (m, 4 H, Ar(OCH₂CH₂)₂); 4.10–4.17 (m, 4 H, Ar(OCH₂)₂); 6.41 (d, 1 H, H(6), *J* = 8.3 Hz); 6.98 (s, 1 H, H(3)); 7.12 (d, 1 H, H(5), *J* = 8.3 Hz). IR, ν/cm^{−1}: 2221 (C≡C); 3326 (br, OH). Mass spectrum, *m/z* (*I*_{rel} (%)): 350.1 [M]⁺ (21), 262.1 (11), 204.0 (15), 203.0 (100), 175.0 (13), 161.1 (12), 94.1 (10). Found: *m/z* 350.1734 [M]⁺. C₁₉H₂₆O₆. Calculated: *M* = 350.17292.

2-Methyl-4-(2,3,5,6,8,9-hexahydro-1,4,7,10-tetraoxabenzocyclododecen-12-yl)but-3-yn-2-ol (5a) was obtained as described for **6a**, yield 91%, m.p. 63–65 °C (benzene–hexane). ¹H NMR (CD₂Cl₂), δ: 1.59 (s, 6 H, CMe₂); 2.05 (s, 1 H, OH); 3.67–3.75 (m, 4 H, 2 OCH₂); 3.76–3.85 (m, 4 H, Ar(OCH₂CH₂)₂); 4.10–4.20 (m, 4 H, Ar(OCH₂)₂); 6.91 (d, 1 H, H(6), *J* = 7.5 Hz); 7.00–7.12 (m, 2 H, H(3), H(5)). IR, ν/cm^{−1}: 2145 (C≡C); 3216 (br, OH). Found (%): C, 66.72; H, 7.19. C₁₇H₂₂O₅. Calculated (%): C, 66.63; H, 7.23.

2-Methyl-4-(2,3,5,6,8,9,11,12,14,15-decahydro-1,4,7,10,13,16-hexaoxabenzocyclooctadecen-18-yl)but-3-yn-2-ol (7a) was obtained as described for **6a**, yield 69%, m.p. 58–60 °C (hexane). ¹H NMR (CDCl₃), δ: 1.54 (s, 6 H, CMe₂); 2.04 (s, 1 H, OH); 3.69–3.82 (m, 12 H, 6 OCH₂); 3.90–3.99 (m, 4 H, Ar(OCH₂CH₂)₂); 4.12–4.20 (m, 4 H, Ar(OCH₂)₂); 6.79 (d, 1 H, H(6), *J* = 8.2 Hz); 6.93 (s, 1 H, H(3)); 7.01 (d, 1 H, H(5), *J* = 8.2 Hz). IR, ν/cm^{−1}: 2200 (C≡C); 3357 (br, OH). MS, *m/z* (*I*_{rel} (%)): 394.2 [M]⁺ (60), 217.9 (10), 202.8 (100), 186.9 (11), 174.9 (14), 160.8 (11), 145.1 (53), 93.8 (13), 88.9 (19), 72.9 (13). Found: *m/z* 394.1919 [M]⁺. C₂₁H₃₀O₇. Calculated: *M* = 394.19914.

2-Methyl-4-(3,4-dimethoxyphenyl)but-3-yn-2-ol (12) was obtained as described for **6a**, yield 91%, m.p. 52–54 °C (hexane). ¹H NMR (CDCl₃), δ: 1.66 (s, 6 H, CMe₂); 2.02 (s, 1 H, OH); 3.89 (s, 6 H, 2 OMe); 6.79 (d, 1 H, H(6), *J* = 7.7 Hz); 6.93 (s, 1 H, H(3)); 7.03 (d, 1 H, H(5), *J* = 7.7 Hz). IR, ν/cm^{−1}: 2235 (C≡C); 3574 (OH). Found (%): C, 70.79; H, 7.62. C₁₃H₁₆O₃. Calculated (%): C, 70.89; H, 7.32.

Trimethyl-[2-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecen-15-yl)ethynyl]silane (6b). A mixture of iodide **2** (1.8 g, 4.6 mmol), alkyne **4b** (1.1 g, 11.5 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (80 mg, 0.11 mmol), and CuI (40 mg, 0.4 mmol) in 3 mL of Et_3N and 15 mL of PhH was stirred in an atmosphere of argon at 40–45 °C for 2.5 h. When the reaction was completed, the reaction mixture was cooled and filtered through a SiO_2 layer (2.5×2 cm). The solvent was removed *in vacuo*, and the residue was recrystallized from PhH–hexane. The yield of **6b** was 1.5 g (87%), m.p. 48–49.5 °C. ^1H NMR (CDCl_3), δ : 0.24 (s, 9 H, SiMe_3); 3.72–3.81 (m, 8 H, 4 OCH_2); 3.87–3.95 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.10–4.17 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.77 (d, 1 H, H(6), $J = 7.9$ Hz); 6.97 (s, 1 H, H(3)); 7.06 (d, 1 H, H(5), $J = 7.9$ Hz). IR, ν/cm^{-1} : 2146 ($\text{C}\equiv\text{C}$). MS, m/z (I_{rel} (%)): 364.2 [$\text{M}]^+$ (34), 232.2 (17), 217.2 (100), 101.1 (16). Found: m/z 364.169 [$\text{M}]^+$. $\text{C}_{19}\text{H}_{28}\text{O}_5\text{Si}$. Calculated: $M = 364.17059$.

15-Ethynyl-2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecene (9). A. A mixture of alkyne **6a** (1.4 g, 4 mmol) and calcined KOH (0.34 g, 6 mmol) in 30 mL of PhH was refluxed for 2.5–3 h. Then the reaction mixture was cooled and filtered through a SiO_2 layer (2.5×2 cm), and the solvent was removed *in vacuo*. The residue was recrystallized from PhH–hexane. The yield of compound **9** was 0.73 g (63%).

B. A mixture of alkyne **6b** (0.79 g, 2.2 mmol) and 20 mL of 10% methanolic KOH was stirred at ~20 °C for 2–2.5 h. Then the reaction mixture was filtered through a SiO_2 layer (2.5×2 cm). The solvent was removed, and the residue was recrystallized from PhH–hexane. The yield of compound **9** was 0.62 g (97%), m.p. 60–61 °C. ^1H NMR (CDCl_3), δ : 2.75 (s, 1 H, $\text{C}\equiv\text{CH}$); 3.70–3.80 (m, 8 H, 4 OCH_2); 3.85–3.95 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.12–4.17 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.51 (d, 1 H, H(6), $J = 8.3$ Hz); 6.91 (s, 1 H, H(3)); 7.15 (d, 1 H, H(5), $J = 8.3$ Hz). IR, ν/cm^{-1} : 2221 ($\text{C}\equiv\text{C}$); 3281 ($\text{C}\equiv\text{CH}$). MS, m/z (I_{rel} (%)): 292.3 [$\text{M}]^+$ (21), 204.1 (11), 161.1 (11), 160.1 (100.00), 145.1 (52), 134.1 (12), 131.1 (6), 105.1 (14), 104.1 (70), 89.1 (15). Found: m/z 292.13090 [$\text{M}]^+$. $\text{C}_{16}\text{H}_{20}\text{O}_5$. Calculated: $M = 292.13106$.

18-Ethynyl-2,3,5,6,8,9,11,12,14,15-decahydro-1,4,7,10,13,16-hexaoxabenzocyclooctadecene (10) was obtained as described for **9** from compound **7a** in 69% yield, m.p. 95–96 °C (PhH–hexane). ^1H NMR (CDCl_3), δ : 3.00 (s, 1 H, $\text{C}\equiv\text{CH}$); 3.75–3.82 (m, 12 H, 6 OCH_2); 3.90–3.98 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.12–4.17 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.81 (d, 1 H, H(6), $J = 8.1$ Hz); 7.01 (s, 1 H, H(3)); 7.09 (d, 1 H, H(5), $J = 8.1$ Hz). IR, ν/cm^{-1} : 2225 ($\text{C}\equiv\text{C}$); 3229 ($\text{C}\equiv\text{CH}$). MS, m/z (I_{rel} (%)): 336.1 [$\text{M}]^+$ (46), 176.1 (9), 175.1 (8), 190.1 (100), 161.1 (15), 145.0 (49), 134.1 (11), 105.1 (9), 104.0 (50), 89.0 (16). Found: m/z 336.15280 [$\text{M}]^+$. $\text{C}_{18}\text{H}_{24}\text{O}_6$. Calculated: $M = 336.15728$.

4-Ethynyl-1,2-dimethoxybenzene (13) was obtained as described for **9** from alcohol **12** (2.3 g, 10.5 mmol) in the presence of KOH (0.06 g, 1.1 mmol). The yield of **13** was 1.5 g (88%), m.p. 51–52 °C (hexane). ^1H NMR (C_6D_6), δ : 2.82 (s, 1 H, $\text{C}\equiv\text{CH}$); 3.24 (s, 3 H, $\text{OMe}(2)$); 3.28 (s, 3 H, $\text{OMe}(1)$); 6.37 (d, 1 H, H(6), $J = 7.5$ Hz); 6.98 (s, 1 H, H(3)); 7.15 (d, 1 H, H(5), $J = 7.5$ Hz). IR, ν/cm^{-1} : 2230 ($\text{C}\equiv\text{C}$); 3244 ($\text{C}\equiv\text{CH}$). Found (%): C, 73.77; H, 6.03. $\text{C}_{10}\text{H}_{10}\text{O}_2$. Calculated (%): C, 74.06; H, 6.21.

12-Ethynyl-2,3,5,6,8,9-hexahydro-1,4,7,10-tetraoxabenzocyclododecene (5a) was obtained as described for compound **13** from alcohol **8a** in 50% yield, m.p. 57–59 °C (PhH–hexane). ^1H NMR (CD_2Cl_2), δ : 3.07 (s, 1 H, $\text{C}\equiv\text{CH}$); 3.71–3.76 (m, 4 H, 2 OCH_2); 3.76–3.85 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.08–4.15

(m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.91 (d, 1 H, H(6), $J = 7.5$ Hz); 7.11 (s, 1 H, H(3), $J = 7.5$ Hz); 7.15 (d, 1 H, H(5), $J = 7.5$ Hz). IR, ν/cm^{-1} : 2101 ($\text{C}\equiv\text{C}$); 3228 ($\text{C}\equiv\text{CH}$). Found (%): C, 67.53; H, 6.39. $\text{C}_{14}\text{H}_{16}\text{O}_4$. Calculated (%): C, 67.73; H, 6.50.

***N,N*-Diethyl-*N*-[3-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecen-15-yl)prop-2-ynyl]amine (17c).** A mixture of Et_2NH (**14c**) (0.21 mL, 2 mmol), paraform (0.06 g, 2 mmol), and 3 mL of dioxane was heated in an atmosphere of argon at 45 °C for 30 min. CuCl (25 mg, 0.25 mmol) was added, and the reaction mixture was stirred until a blue color appeared. Then compound **9** (0.52 g, 1.8 mmol) was added, and heating was continued at 80 °C for 2.5–3 h. When the reaction was completed, the reaction mixture was filtered through an Al_2O_3 layer (2.5×2 cm), and the solvent was removed *in vacuo*. The residue was recrystallized from PhH–hexane to give compound **17c** (0.49 g, 72%), m.p. 51–52 °C. ^1H NMR (CDCl_3), δ : 1.15 (t, 6 H, Me, $J = 7.5$ Hz); 2.60–2.71 (m, 4 H, $\text{N}(\text{CH}_2)_2$); 3.62 (s, 2 H, CH_2N); 3.74–3.81 (m, 8 H, 4 OCH_2); 3.89–3.95 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.11–4.18 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.79 (d, 1 H, H(6), $J = 7.5$ Hz); 6.94 (s, 1 H, H(3)); 7.02 (d, 1 H, H(5), $J = 7.5$ Hz). IR, ν/cm^{-1} : 2220 ($\text{C}\equiv\text{C}$). MS, m/z (I_{rel} (%)): 377.3 [$\text{M}]^+$ (42), 376.3 (18), 363.4 (14), 362.3 (59), 305.3 (51), 217.2 (16), 174.2 (20), 173.2 (100), 147.1 (13), 115.1 (33), 107.6 (15.68). Found: m/z 377.22120 [$\text{M}]^+$. $\text{C}_{21}\text{H}_{31}\text{NO}_5$. Calculated: $M = 377.22021$.

4-[3-(2,3,5,6,8,9-Hexahydro-1,4,7,10-tetraoxabenzocyclododecen-12-yl)prop-2-ynyl]morpholine (16a) was obtained from compound **8** and morpholine **14a** by analogy with **17c** (oil, yield 65%). ^1H NMR (CDCl_3), δ : 2.59 (t, 4 H, $\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$, $J = 4.4$ Hz); 3.47 (s, 2 H, NCH_2); 3.68–3.75 (m, 8 H, 2 OCH_2 , $\text{O}(\text{CH}_2\text{CH}_2)_2\text{N}$); 3.77–3.83 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.11–4.18 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.9 (d, 1 H, H(6), $J = 8.4$ Hz); 7.01–7.08 (m, 2 H, H(3), H(5)). IR, ν/cm^{-1} : 2251 ($\text{C}\equiv\text{C}$). Amine **16a**, picrate, yield 58%, m.p. 165–166.5 °C (from PhH). Found (%): C, 54.61; H, 5.03; N, 9.11. $\text{C}_{25}\text{H}_{28}\text{N}_4\text{O}_{12} \cdot 0.5\text{PhH}$. Calculated (%): C, 54.63; H, 5.08; N, 9.10.

***N,N*-Dibutyl-*N*-[3-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecen-15-yl)prop-2-ynyl]amine (17d)** was obtained from compound **9** and dibutylamine **14d** as described for **17c**. Yield 62%, m.p. 98–100 °C (PhH–hexane). ^1H NMR (CDCl_3), δ : 0.94 (t, 6 H, 2 Me, $J = 4.5$ Hz); 1.28–1.35 (m, 4 H, 2 CH_2Me); 1.53–1.64 (m, 4 H, 2 $\text{CH}_2\text{CH}_2\text{Me}$); 2.54–2.60 (m, 4 H, $\text{N}(\text{CH}_2\text{CH}_2)_2\text{Me}$); 3.63 (s, 2 H, CH_2N); 3.69–3.85 (m, 8 H, 4 OCH_2); 3.86–3.99 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.06–4.24 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.82 (d, 1 H, H(6), $J = 8.2$ Hz); 6.92 (s, 1 H, H(3)); 7.0 (d, 1 H, H(5), $J = 8.2$ Hz). IR, ν/cm^{-1} : 2230 ($\text{C}\equiv\text{C}$). MS, m/z (I_{rel} (%)): 433.1 [$\text{M}]^+$ (32), 347.1 (20), 310.1 (22), 287.0 (21), 270.0 (20), 258.0 (42), 261.0 (100), 243.0 (20), 242.0 (83), 241.0 (36), 215.0 (29), 91.0 (41.61). Found: m/z 433.5868 [$\text{M}]^+$. $\text{C}_{25}\text{H}_{39}\text{NO}_5$. Calculated: $M = 433.5884$.

***N*-[3-(2,3,5,6,8,9,11,12,14,15-Decahydro-1,4,7,10,13,16-hexaoxabenzocyclooctadecen-18-yl)prop-2-ynyl]-*N,N*-diethylamine (18c)** was obtained from compound **10** by analogy with **17c** (oil, yield 76%). ^1H NMR (CDCl_3), δ : 1.11 (t, 6 H, 2 Me, $J = 4.7$ Hz); 2.62–2.68 (m, 4 H, $\text{N}(\text{CH}_2\text{Me})_2$); 3.62 (s, 2 H, CH_2N); 3.67–3.86 (m, 12 H, 6 OCH_2); 3.88–4.00 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.10–4.21 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.79 (d, 1 H, H(6), $J = 8.8$ Hz); 6.94 (s, 1 H, H(3)); 7.02 (d, 1 H, H(5), $J = 8.8$ Hz). IR, ν/cm^{-1} : 2220 ($\text{C}\equiv\text{C}$). Amine **18c**, picrate, yield 85%, m.p. 63–65 °C (from hexane). Found (%): C, 53.58; H, 6.09; N, 8.80. $\text{C}_{29}\text{H}_{38}\text{N}_4\text{O}_{13}$. Calculated (%): C, 53.48; H, 5.88; N, 8.60.

4-[3-(3,4-Dimethoxyphenyl)prop-2-ynyl]morpholine (21) was obtained from compound **13** and morpholine **14a** by analogy with **17c** (oil, yield 60%). ^1H NMR (CDCl_3), δ : 2.77 (t, 4 H, $\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$, $J = 4.2$ Hz); 3.56 (s, 2 H, CH_2N); 3.78 (s, 6 H, 2 OMe); 3.84 (t, 4 H, $\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$, $J = 4.2$ Hz); 6.91–7.03 (m, 3 H, arom.). IR, ν/cm^{-1} : 2006 ($\text{C}\equiv\text{C}$). **Amine 21, picrate**, yield 69%, m.p. 111–113 °C (from PhH). Found (%): C, 51.41; H, 4.62; N, 11.52. $\text{C}_{21}\text{H}_{22}\text{N}_4\text{O}_{10}$. Calculated (%): C, 51.43; H, 4.52; N, 11.42.

4-[3-(2,3,5,6,8,9,11,12-Octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecen-15-yl)prop-2-ynyl]morpholine (17a). **A.** A mixture of morpholine **14a** (0.17 mL, 2 mmol) and paraform (0.06 g, 2 mmol) in 3 mL of dioxane was heated in an atmosphere of argon at 45 °C for 30 min. $\text{Cu}(\text{OAc})_2$ (25 mg, 0.17 mmol) and 1 mL of 30% H_2SO_4 were added, and the reaction mixture was stirred until a blue color appeared. Then compound **9** (0.52 g, 1.8 mmol) was added, and heating was continued at 80 °C for 2.5–3 h. When the reaction was completed, the reaction mixture was filtered through an Al_2O_3 layer (2.5×2 cm), and the solvent was removed *in vacuo*. The residue was purified by preparative TLC on Al_2O_3 with CHCl_3 – AcOEt (5 : 3) as the eluent to give compound **17a** as an oil (0.45 g, 87%).

B. A mixture of bis-amine **15a** (0.32 g, 1.7 mmol), compound **9** (1 g, 3.4 mmol), CuCl (50 mg, 0.5 mmol), and 3 mL of dioxane was heated in a flow of argon at 80 °C for 2–2.5 h. The product was isolated in the form of an oil as described in procedure **A**. The yield of **17a** was 0.94 g (71%). ^1H NMR (CDCl_3), δ : 2.59 (t, 4 H, $\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$, $J = 4.8$ Hz); 3.46 (s, 2 H, CH_2N); 3.65–3.75 (m, 12 H, 4 OCH_2 , $\text{O}(\text{CH}_2\text{CH}_2)_2\text{N}$); 3.83–3.90 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.06–4.12 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.77 (d, 1 H, $\text{H}(6)$, $J = 8.2$ Hz); 6.94 (s, 1 H, $\text{H}(3)$); 7.02 (d, 1 H, $\text{H}(5)$, $J = 8.2$ Hz). IR, ν/cm^{-1} : 2141 ($\text{C}\equiv\text{C}$).

Picrate (general procedure). A hot solution of picric acid (0.25 g, 1.1 mmol) in 5 mL of 95% EtOH was added to a hot solution of amine **17a** (0.5 g, 1.3 mmol) in 3 mL of 95% EtOH. The precipitate that formed was filtered off and recrystallized from PhH. **Amine 17a, picrate**, yield 0.69 g (86%), m.p. 171–172 °C. ^1H NMR ($\text{DMSO}-d_6$), δ : 3.71–3.78 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.06–4.14 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.99 (d, 1 H, $\text{H}(6)$, $J = 8.3$ Hz); 7.06 (s, 1 H, $\text{H}(3)$); 7.11 (d, 1 H, $\text{H}(5)$, $J = 8.2$ Hz); 8.62 (s, 2 H, Ar), the other signals overlap the solvent signals. IR, ν/cm^{-1} : 1334, 1516 (NO_2); 2246 ($\text{C}\equiv\text{C}$), 3611 (NH). Found (%): C, 56.70; H, 5.78; N, 8.15. $\text{C}_{27}\text{H}_{32}\text{N}_4\text{O}_{13} \cdot \text{PhH}$. Calculated (%): C, 56.73; H, 5.48; N, 8.01.

1-[3-(2,3,5,6,8,9,11,12-Octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecen-15-yl)prop-2-ynyl]piperidine (17b) was obtained as described for **17a** from piperidine **14b** and compound **9** (procedure **A**) in 64% yield or from bis-amine **15b** and compound **9** (procedure **B**) in 60% yield, m.p. 70–72 °C (PhH–hexane). ^1H NMR (CD_2Cl_2), δ : 1.59–1.63 (m, 6 H, $(\text{CH}_2)_3$); 2.53 (t, 4 H, $(\text{CH}_2)_2\text{N}$, $J = 3.1$ Hz); 3.41 (s, 2 H, CH_2N); 3.69–3.80 (m, 8 H, 4 OCH_2); 3.85–3.93 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.01–4.09 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.79 (d, 1 H, $\text{H}(6)$, $J = 8.3$ Hz); 6.93 (s, 1 H, $\text{H}(3)$); 7.00 (d, 1 H, $\text{H}(5)$, $J = 8.3$ Hz). IR, ν/cm^{-1} : 2200 ($\text{C}\equiv\text{C}$). Found (%): C, 67.92; H, 8.15; N, 3.45. $\text{C}_{22}\text{H}_{31}\text{NO}_5$. Calculated (%): C, 67.84; H, 8.02; N, 3.59.

4-[3-(2,3,5,6,8,9,11,12,14,15-Decahydro-1,4,7,10,13,16-hexaoxabenzocyclooctadecen-18-yl)prop-2-ynyl]morpholine (18a) was obtained in the form of an oil by analogy with **17a** from compound **10** in 75% (procedure **A**) and 76% yield (procedure **B**). ^1H NMR (CDCl_3), δ : 2.68–2.59 (m, 4 H, $\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$); 3.48 (s, 2 H, CH_2N); 3.65–3.83 (m, 16 H, 6 OCH_2 , $\text{O}(\text{CH}_2\text{CH}_2)_2\text{N}$); 3.88–3.98 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.11–4.20 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.79 (d,

1 H, $\text{H}(6)$, $J = 7.5$ Hz); 6.94 (s, 1 H, $\text{H}(3)$); 6.78 (d, 1 H, $\text{H}(5)$, $J = 7.5$ Hz). IR, ν/cm^{-1} : 2140 ($\text{C}\equiv\text{C}$). **Amine 18a, picrate**, yield 71%, m.p. 79–81 °C (from PhH). Found (%): C, 56.81; H, 5.89; N, 7.76. $\text{C}_{29}\text{H}_{36}\text{N}_4\text{O}_{14} \cdot \text{PhH}$. Calculated (%): C, 56.60; H, 5.66; N, 7.54.

1-[3-(2,3,5,6,8,9,11,12,14,15-Decahydro-1,4,7,10,13,16-hexaoxabenzocyclooctadecen-18-yl)prop-2-ynyl]piperidine (18b) was obtained in the form of an oil by analogy with **17a** from piperidine **14b** and compound **10** in 67% yield (procedure **A**) or from bis-amine **15b** and compound **10** in 72% yield (procedure **B**). ^1H NMR (CDCl_3), δ : 1.62–1.66 (m, 6 H, $-(\text{CH}_2)_3-$); 2.63 (t, 4 H, $(\text{CH}_2)_2\text{N}$, $J = 3.3$ Hz); 3.40 (s, 2 H, CH_2N); 3.69–3.82 (m, 12 H, 6 OCH_2); 3.90–3.98 (m, 4 H, $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.12–4.16 (m, 4 H, $\text{Ar}(\text{OCH}_2)_2$); 6.72 (d, 1 H, $\text{H}(6)$, $J = 7.8$ Hz); 6.89 (s, 1 H, $\text{H}(3)$); 7.05 (d, 1 H, $\text{H}(5)$, $J = 7.8$ Hz). IR, ν/cm^{-1} : 2140 ($\text{C}\equiv\text{C}$). **Amine 18b, picrate**, yield 71%, m.p. 96–98 °C (from AcOEt). Found (%): C, 54.44; H, 5.53; N, 8.34. $\text{C}_{30}\text{H}_{38}\text{N}_4\text{O}_{13}$. Calculated (%): C, 54.38; H, 5.78; N, 8.46.

1,4-Bis(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecen-15-yl)buta-1,3-diyne (19). **A.** Air was bubbled through a mixture of compound **9** (0.58 g, 2 mmol) and CuCl (50 mg, 0.5 mmol) in 20 mL of Py at 35–40 °C for 1–1.5 h. The reaction mixture was poured into 25 mL of water, and the products were extracted with CHCl_3 (3×15 mL). The extract was washed with 20% HCl (3×20 mL) and water (50 mL), dried over Na_2SO_4 , and filtered through an Al_2O_3 layer (2.5×2 cm). The solvent was removed, and the residue was crystallized from PhH–hexane to give compound **19** (0.35 g, 60%), m.p. 144–144.5 °C.

B. A mixture of amine **14a** (0.1 g, 1.2 mmol) or compound **14b** (0.1 g, 1.2 mmol) and paraform (0.04 g, 1.2 mmol) in 3 mL of dioxane was heated in an atmosphere of argon at 45 °C for 30 min. CuCl (25 mg, 0.25 mmol) was added, and the reaction mixture was stirred until a blue color appeared. Then compound **9** (0.29 g, 1 mmol) was added, and heating was continued at 80 °C for 2.5–3 h. When the reaction was completed, the reaction mixture was filtered through an Al_2O_3 layer (2.5×2 cm), and the solvent was removed *in vacuo*. The residue was crystallized from PhH–hexane to give compound **19** (0.21 g, 72.4%). ^1H NMR (CDCl_3), δ : 3.69–3.85 (m, 16 H, 8 OCH_2); 3.88–4.04 (m, 8 H, 2 $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.16–4.28 (m, 8 H, 2 $\text{Ar}(\text{OCH}_2)_2$); 6.21 (d, 2 H, 2 $\text{H}(6)$, $J = 8.7$ Hz); 6.83 (s, 2 H, 2 $\text{H}(3)$); 7.02 (d, 2 H, 2 $\text{H}(5)$, $J = 8.7$ Hz). IR, ν/cm^{-1} : 2141, 2200 ($\text{C}\equiv\text{C}-\text{C}\equiv\text{C}$). Found (%): C, 66.32; H, 6.75. $\text{C}_{32}\text{H}_{38}\text{O}_{10}$. Calculated (%): C, 65.96; H, 6.57.

1,4-Bis(2,3,5,6,8,9,11,12,14,15-decahydro-1,4,7,10,13,16-hexaoxabenzocyclooctadecen-18-yl)buta-1,3-diyne (20) was obtained as described for **19** according to procedures **A** in 68% yield or **B** in 86% yield, m.p. 120–122 °C (PhH–hexane). ^1H NMR (CDCl_3), δ : 3.69–3.86 (m, 24 H, 12 OCH_2); 3.88–4.06 (m, 8 H, 2 $\text{Ar}(\text{OCH}_2\text{CH}_2)_2$); 4.18–4.25 (m, 8 H, 2 $\text{Ar}(\text{OCH}_2)_2$); 6.81 (d, 2 H, $\text{H}(6)$, $J = 8.9$ Hz); 7.02 (s, 2 H, $\text{H}(3)$); 7.12 (d, 2 H, $\text{H}(5)$, $J = 8.9$ Hz). IR, ν/cm^{-1} : 2140, 2210 ($\text{C}\equiv\text{C}-\text{C}\equiv\text{C}$). Found (%): C, 64.85; H, 7.19. $\text{C}_{36}\text{H}_{46}\text{O}_{12}$. Calculated (%): C, 64.85; H, 6.96.

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