Large-Ring, Chromogenic Benzocrown Compounds

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Eight novel, large-ring chromogenic benzocrown compounds have been synthesized. Two incorporate 19-and 20-membered crown units with six ring oxygens. Six others contain large rings ranging from 21-crown-7 to 30-crown-10. For all six benzocrown compounds, the 4′-(2″,4″-dinitro-6″-trifluoromethylphenyl)amino group was employed as the chromogenic unit. In addition, 4′-picrylamino and 4′-(2″,6″-dinitro-4″-trifluoromethylphenyl)amino groups were also attached to benzo-21-crown-7.

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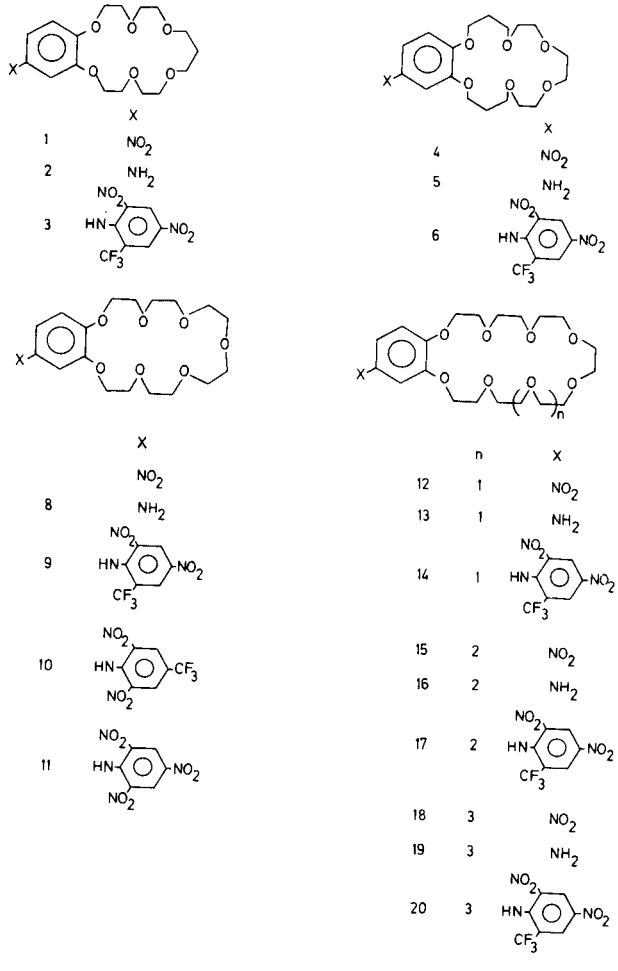
In 1971, Takagi, Nakamura and Ueno introduced crown ether-based chromogenic compounds for colorimetric determination of alkali metal cations [1]. The Japanese group demonstrated that 4′-picrylamino-15-crown-5 functioned as a selective chromogenic reagent for the determination of potassium cations. Subsequently, more than a dozen chromogenic benzocrown compounds, including benzo-12-crown-4 [2], benzo-14-crown-4 [3], benzo-15-crown-5 [4-6], and benzo-18-crown-6 [7] bearing various chromogenic substituents have been prepared and investigated.

We now report the synthesis of chromogenic crown ether compounds based upon benzocrown ethers with ring sizes ranging from 19-crown-6 to 30-crown-10.

Results and Discussion.

Benzocrown ethers available from other work [8] were nitrated at the 4′-position with concentrated nitric acid in a glacial acetic acid-chloroform mixture [9] to give nitro derivatives **1**, **4**, **7**, **12**, **15**, and **18** in yields of 88, 76, 85, 93, 94, and 85%, respectively. Reduction of the nitro groups with hydrogen at 40 psi pressure, over a 10% Pd/C catalyst in DMF [2] produced aminobenzocrowns **2**, **5**, **8**, **13**, **16**, and **19** in high yields of 93, 92, 94, 92, 96, and 94%, respectively. A series of six, large-ring benzocrown ethers with 4′-(2″,4″-dinitro-6″-trifluoromethylphenyl)-amino groups, **3**, **6**, **9**, **14**, **17** and **20**, were realized in yields of 85, 87, 88, 91, 96 and 92%, respectively, from reactions of the corresponding 4′-aminobenzocrown compounds with 1-chloro-2,4-dinitro-6-trifluoromethylbenzene [6] in methanol in the presence of sodium bicarbonate. For 4′-aminobenzo-21-crown-7, two additional chromogenic crown compounds were prepared by changing the activated aryl chloride component to 1-chloro-2,6-dinitro-4-trifluoromethylbenzene [6] and picryl chloride which produced **10** and **11** in yields of 94 and 90%, respectively. Physical and spectral data and elemental analysis results for eight new large-ring chromogenic crown ethers and their precursors are recorded in Table 1.



Analytical evaluation of these novel chromogenic ionophores has been partially reported elsewhere [10].

EXPERIMENTAL

Melting points were taken with either a Mel-Temp or Fisher Johns melting point apparatus and are uncorrected. The ir spectra were obtained with a Nicolet MX-S spectrometer and are reported in reciprocal centimeters. The pmr spectra were recorded with Varian EM360 or

Table 1

Yields, Physical Properties, Spectral Data, and Elemental Analysis Data for Chromogenic Crown Ethers and Intermediates **1-20**

Compound No.	Yield, %	mp, °C	^{1}H NMR spectra (60 MHz), ppm	IR spectra, cm^{-1}		Elemental Analysis Theory	Found
1	88	95-96	1.6-2.2 (pentet, 2H) 3.35-4.5 (m, 20H), 6.8-7.1 (m, 1H), 7.65-8.1 (m, 2H)	1514, 1342 (NO_2), [a] 1111 (C-O)	C H	54.98 6.78	55.24 6.70
2	93	oil	1.6-2.2 (m, 2H) 3.25-4.35 (m, 20H), 6.1-6.9 (m, 3H)	3431, 3354, 3232 (NH_2), [b] 1120 (C-O)	C H	59.81 7.97	59.63 8.02
3	85	161-164 orange crystals	1.4-2.15 (m, 2H), 3.45-4.45 (m, 20H) 6.45-7.1 (m, 3H), 7.70 (s, 1H), 8.55-9.0 (m, 2H)	3412, 3298 (N-H), [a] 1547 (NO_2), 1134 (C-O)	C H	50.09 4.90	50.33 4.91
4	76	oil	1.85-2.4 (m, 4H), 3.45-4.4 (m, 20H), 6.85-7.1 (m, 1H), 7.65-8.1 (m, 2H)	1516, 1340 (NO_2), [b] 1126 (C-O)	C H	56.09 7.06	55.88 7.24
5	92	oil	1.8-2.4 (m, 4H), 3.35-4.3 (m, 22H) 6.15-6.75 (m, 3H)	3437, 3358, 3232 (NH_2) [b] 1113 (C-O)	C H	60.83 8.22	60.60 8.38
6	87	118-120, red crystals	1.9-2.4 (m, 4H), 3.35-4.4 (m, 20H), 6.45-7.2 (m, 3H) 7.85 (br s, 1H), 8.55-9.0 (m, 2H)	3410, 3313 (N-H), [a] 1545 (NO_2), 1128 (C-O) 1128 (C-O)	C H	50.93 5.13	50.75 5.02
7	85	67-68	3.5-4.4 (m, 24H), 6.75-7.95 (m, 3H)	1518, 1342 (NO_2), [a] 1099 (C-O)	C H	53.86 6.78	53.74 6.56
8	94	oil	3.45-4.25 (m, 26H), 6.0-6.95 (m, 3H)	3445, 3356, 3234 (NH_2), [b] 1105 (C-O)	C [c] H	56.82 7.95	56.49 7.92
9	88	113-114, red crystals	3.6-4.3 (m, 24H), 6.5-6.9 (m, 3H), 7.55-7.8 (s, 1H), 8.75 (dd, 2H)	3420, 3304 (N-H), [a] 1545 (NO_2), 1134 (C-O)	C H	49.59 4.99	49.43 5.16
10	94	110-111 red crystals	3.5-4.3 (m, 24H), 6.4-6.9 (m, 3H), 8.38 (s, 2H), 9.85 (s, 1H)	3420, 3319 (N-H), [a] 1543 (NO_2) 1134 (C-O)	C H	49.59 4.99	49.37 5.12
11	90	red oil	3.55-4.25 (m, 24H), 6.45-6.85 (m, 3H), 9.05 (s, 2H) 10.25 (s, 1H)	3298 (N-H), [b] 1537 (NO_2), 1132 (C-O)	C H	49.48 5.19	49.30 5.24
12	93	oil	3.3-4.5 (m, 28H), 6.85-7.1 (m, 1H), 7.7-8.1 (m, 2H)	1516, 1338 (NO_2), [b] 1134 (C-O)	C H	53.93 7.01	53.97 7.10
13	92	oil	3.15-4.35 (m, 30H), 6.15-6.95 (m, 3H)	3431, 3356, 3227 (NH_2), [b] 1126 (C-O)	C H	57.82 8.01	57.84 8.11
14	91	93-95, red crystals	3.25-4.3 (m, 28H), 6.3-6.95 (m, 3H), 7.65 (br s, 1H) 8.5-8.95 (m, 2H)	3300 (N-H), [a] 1545 (NO_2), 1132 (C-O)	C H	49.92 5.28	49.93 5.07
15	94	oil	3.25-4.4 (m, 32H) 6.8-7.15 (m, 1H) 7.6-8.1 (m, 2H)	1516, 1338 (NO_2), [b] 1136 (C-O)	C H	53.98 7.21	53.89 7.29

Table 1 (continued)

Compound No.	Yield, %	mp, °C	^{1}H NMR spectra (60 MHz), ppm	IR spectra, cm^{-1}		Elemental Analysis Theory	Found
16	96	oil	3.3-4.45 (m, 34H), 6.1-6.45 (m, 2H) 6.65-6.9 (m, 1H)	3433, 3356, 3238 (NH_2), [b] 1113 (C-O)	C H	57.50 8.12	57.23 8.26
17	96	red oil	3.35-4.33 (m, 32H), 6.4-7.0 (m, 3H), 7.80 (br s, 1H), 8.5-8.9 (m, 2H)	3306 (N-H), [b] 1545 (NO_2), 1128 (C-O)	C H	50.22 5.52	49.97 5.51
18	85	oil	3.25-4.3 (m, 36H), 6.7-8.0 (m, 3H)	1518, 1338 (NO_2), [b] 1126 (C-O)	C H	54.03 7.37	54.06 7.59
19	94	oil	3.1-4.25 (m, 38H), 6.0-6.85 (m, 3H)	3433, 3356, 3232 (NH_2), [b] 1122 (C-O)	C H	57.24 8.21	57.02 8.58
20	92	red oil	3.3-4.4 (m, 36H), 6.4-6.95 (m, 3H), 7.73 (s, 1H) 8.5-8.95 (m, 2H)	3306 (N-H), [b] 1545 (NO_2), 1132 (C-O)	C H	50.48 5.74	50.40 5.92

[a] Deposit on a sodium chloride plate. [b] Neat. [c] Analyzed as a 0.5 hydrate.

EM360A spectrometers in deuteriochloroform and chemical shifts are reported in parts per million (δ) downfield from TMS. Elemental analysis was performed by Galbraith Laboratories, Inc. (Knoxville, Tennessee).

Unless specified otherwise, reagent grade reactants and solvents were used as received. DMF was purified by distillation from calcium hydride. Absolute methanol was obtained by refluxing with magnesium turnings and distillation. Benzo-21-crown-7 was prepared by a known method [11]. Benzo-19-crown-6, benzo-20-crown-6, benzo-24-crown-8, benzo-27-crown-9, and benzo-30-crown-10 were available from earlier work [8]. Syntheses of nitrobenzocrowns **1**, **4**, **7**, **12**, **15**, and **18**, and aminobenzocrowns **2**, **5**, **8**, **13**, **16**, and **19** were carried out according to published methods [2,9].

Preparation of Chromogenic Crown Ethers.

A published procedure [4] for the synthesis of similar compounds was adapted and modified. The 4'-aminobenzocrown compound (0.89 mmole), the appropriate activated aryl chloride (0.92 mmole), and sodium bicarbonate (0.10 g) in 10 ml of absolute methanol were stirred and refluxed overnight. The solvent was removed *in vacuo* and the residue was chromatographed on an alumina column with ethyl acetate as eluent to give the pure chromogenic crown ether.

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