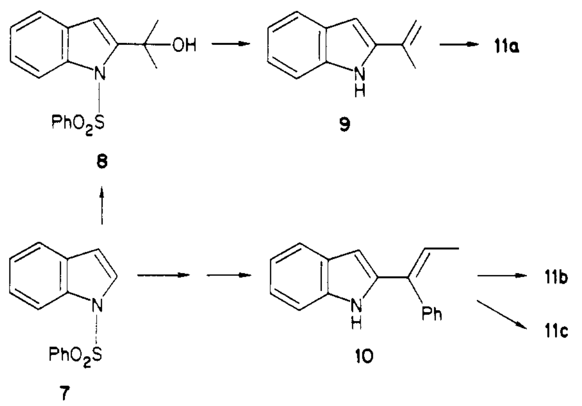
Scheme II



reduced pressure, and the residue was distilled under reduced pressure (Table I).

α-[1-(Phenylsulfonyl)-2-indolyl]-α,α-dimethylmethanol (8). To a stirred solution of lithium diisopropylamide [prepared from 1.5 M *n*-hexane solution of *n*-BuLi (57.3 mL, 0.086 mol) and diisopropylamine (12.6 mL, 0.09 mol) in anhydrous THF (60 mL)] was added a solution of *N*-(phenylsulfonyl)indole (7) (20 g, 0.078 mol). After 0.5 h a solution of acetone (6.7 mL, excess) in anhydrous THF was added at −78 °C. The mixture was gradually warmed to room temperature and kept there for 4 h with stirring. It was poured into aqueous NH_4Cl solution and extracted with EtOAc. The extract was dried over anhydrous Na_2SO_4 and evaporated. The residue was purified by column chromatography (silica gel, 300 g) using 1% EtOAc/*n*-hexane to give 8 (7.5 g, 30.5%) and recovered starting material (10.5 g). 8: mp 71–73 °C; mass spectrum, *m/e* 315 (M^+), 300 ($M^+ - 15$), 258 (base); ^1H NMR δ 1.82 (6 H, s, CH_3).

2-Isopropenylindole (9). A stirred mixture of 8 (23.2 g, 0.074 mol), 10% NaOH solution (100 mL), and ethanol (200 mL) was refluxed for 2 h. The solvent was evaporated, and the residue was extracted with benzene, which was washed with brine and evaporated. Purification by column chromatography (silica gel, 300 g) using 0.5% EtOAc/*n*-hexane gave 9 (8.7 g, 75%): mp 116–118 °C; mass spectrum, *m/e* 157 (M^+); ^1H NMR δ 2.16 (3 H, bs, CH_3), 5.03 (1 H, bs, vinyl H), 5.25 (1 H, s, vinyl H); HRMS, calcd for $C_{11}H_{11}N$, 157.0890, found 157.0860.

Methyl 2-[2-(1-Methylvinyl)-3-indolyl]-2-oxoacetate (11a) and Methyl 2-[2-(1-Phenyl-1-propenyl)-3-indolyl]-2-oxoacetate (11b). 9 or 10 (0.025–0.03 mol) was treated with 1.5 equiv of oxalyl chloride and 2.2 equiv of triethylamine at 0 °C for 2 h with stirring. Excess methanol was added, and the mixture was stirred at room temperature overnight.

11a: The mixture was diluted with EtOAc, and the organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography (silica gel, 100 g) (Table II).

11b: The precipitate was collected, washed with ether, and recrystallized from benzene (see Table II).

1-(Methoxycarbonyl)-3-methyl-4-phenyl-5*H*-pyrido[4,3-*b*]indole (13b) and 1-(Methoxycarbonyl)-4-methyl-5*H*-pyrido[4,3-*b*]indole (13a). Keto ester 11a or 11b was treated with 1.5–2.0 equiv each of $NH_2OH{\cdot}HCl$ and NaOAc in MeOH under reflux overnight. The MeOH was replaced by toluene, and the mixture was refluxed for 6–14 h. Column chromatography over silica gel and elution with benzene/$CHCl_3$ gave recovered starting keto ester. The second eluate with 1% MeOH/$CHCl_3$ gave the pyridoindole (Table II).

3-Methyl-4-phenyl-5*H*-pyrido[4,3-*b*]indole (13c). Oxime **12c** was refluxed in toluene for 6 h. The toluene was evaporated and the residue was crystallized from ethanol to give **13c**.

Registry No. 1, 13250-82-3; **2**, 13250-83-4; **3**, 92642-98-3; **4a**, 41057-09-4; **4b**, 92642-99-4; **4c**, 92643-00-0; **5a**, 41056-88-6; **5b**, 92643-01-1; **5c**, 92643-02-2; **6a**, 272-14-0; **6b**, 39677-82-2; **6c**, 92643-03-3; **7**, 40899-71-6; **8**, 92643-04-4; **9**, 78133-83-2; **10**, 78329-46-1; **11a**, 92643-05-5; **11b**, 92643-06-6; **11c**, 77092-51-4; **12a**, 92643-07-7; **12b**, 92643-08-8; **12c**, 92669-35-7; **13a**, 92643-09-9; **13b**, 92643-10-2; **13c**, 92643-11-3; 2-(2-hydroxy-2-propanyl)-3-(1,3-dioxolan-2-yl)thiophene, 92643-12-4; 2-(1-hydroxy-1-phenylethyl)-3-(1,3-dioxolan-2-yl)thiophene, 92643-13-5; 2-(1-hydroxyphenylpropyl)-1-(phenylsulfonyl)indole, 77092-50-3; 3-(1,2-dioxo-2-chloroethyl)-2-isopropenylindole, 92643-14-6; 3-(1,2-dioxo-2-chloroethyl)-2-(1-phenyl-1-propenyl)indole, 92643-15-7.

Electrochemical Behavior of Nitroaromatic Podands: Contrast between Lariat Ethers and Their Open-Chained Analogues

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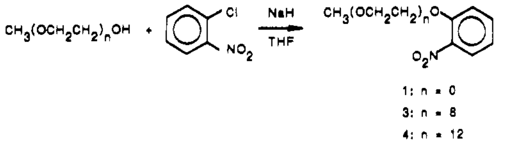
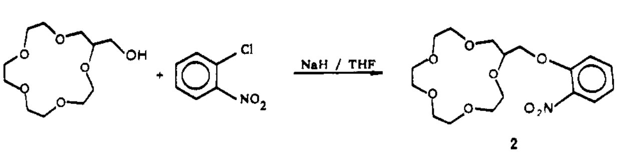
During recent years, there has been substantial interest in polyethylene glycols (PEGs) and polyethylene glycol ethers as complexing ligands for a variety of cations.[1] Podands[2] are more economically attractive than crown[3] or lariat ethers[4] in those cases where the podand is functionally equivalent to the cyclic material (the coronand).[2] Indeed, numerous examples of this functional equivalence have been noted,[5] and in recent work of our own, we have studied binding profiles for several PEGs and assessed their efficacy in phase-transfer reactions.[1] We now report that in contrast to many recent examples of podand–coronand equivalence, the electrochemical behavior of nitroarene-substituted PEGs is similar to that of 2-nitroanisole (1) but not to 2-[(2-nitrophenoxy)methyl]-15-crown-5 (2).[6]

Results and Discussion

Nitroarene-substituted podands 3 and 4 were prepared by treatment of 2-chloronitrobenzene in THF with the anion (NaH) of $CH_3(OCH_2CH_2)_nOH$ where *n* is 8 or 12.[6] The compounds were obtained in analogy to the previously reported[6] crown 2 in 68% and 61% yields, respectively, as shown in eq 1. Both compounds were obtained as yellow oils and each was pure after chromatography over alumina.





2

The cyclic voltammograms of 2-nitroanisole, 2-(1,4,7,10,13,16,19,22,25-nonaoxahexaeicosyl)nitrobenzene (also called 2-[methoxyocta(ethoxy)]nitrobenzene, **3**), and 2-[methoxydodeca(ethoxy)]nitrobenzene (**4**) as well as the corresponding crown **2** were determined as previously described[6,7] (see Experimental Section), and scans for **3**

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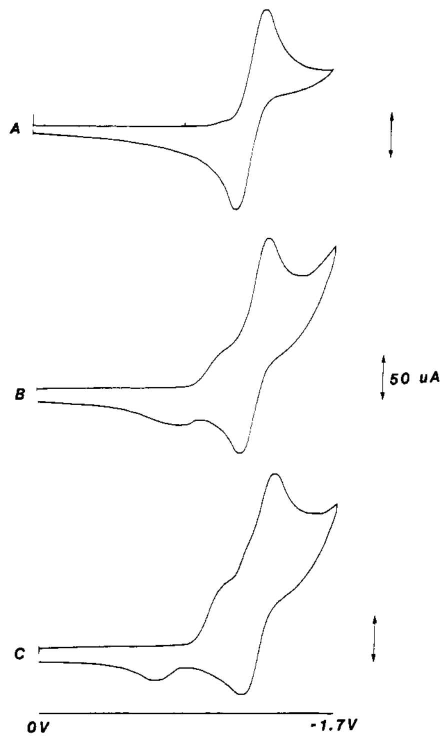


Figure 1. Cyclic voltammograms for **3**: A, in the absence of any cation; B, in the presence of 0.5 equiv of $NaClO_4$; and C, in the presence of 1.0 equiv of $NaClO_4$. The cyclic voltammograms for **4** are identical with these.

Table I. Cyclic Voltammetry Data for Compounds 1–4

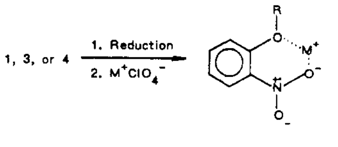
no.	cation added	equiv	E_p(c)	E_p(a)	$E°'$
1	none		−1.36	−1.22	−1.29
	Na^+	0.5	−1.37	−1.21	−1.29
			−1.20	−0.87	
		1.0	−1.37	−1.21	−1.29
			−1.20	−0.78	−0.99
	K^{+a}	0.5	−1.36	−1.22	−1.29
		1.0	−1.36	−1.22	−1.29
2	none		−1.36	−1.21	−1.28
	Na^+	0.5	−1.38	−1.18	−1.28
			−1.17	−1.04	−1.11
		1.0			
			−1.22	−1.00	−1.11
	K^+	0.5	−1.37	−1.20	−1.28
		1.0	−1.37	−1.20	−1.28
3	none		−1.26	−1.13	−1.20
	Na^+	0.5	−1.28	−1.12	−1.20
			−1.01[b]	−0.78	
		1.0	−1.29	−1.12	−1.20
			−1.02[b]	−0.62	
	K^{+a}	0.5	−1.28	−1.13	−1.20
		1.0	−1.24	−1.12	−1.18
4	none		−1.27	−1.13	−1.20
	Na^+	0.5	−1.28	−1.13	−1.20
			−1.02	−0.79	
		1.0	−1.28	−1.13	−1.20
			−1.02	−0.63	
	K^+	0.5	−1.28	−1.13	−1.20
		1.0	−1.26	−1.11	−1.18

[a] $KClO_4$ is insoluble in MeCN and dissolves only when the ligand assists it. As a result, the solubility of K^+ cation is these cases is marginal. [b] This peak is a shoulder on the first reduction peak.

and **4** are shown in Figure 1. A quasi-reversible redox couple characteristic of the 2-alkoxynitrobenzene residue is observed for **1**,[6] **2**,[6] **3**, or **4** in the absence of cations (see scan A in the Figure). When 0.5 equiv of $NaClO_4$ is added to **2**, a new redox couple appears at more positive potential.[6] Similar behavior is observed for compounds **1**, **3**, and **4** (see figure). When a full equivalent of $NaClO_4$ is added, the original quasi-reversible redox couple of **2** disappears and only the new, more positive redox couple is observed.[6] In contrast to this previously reported work, when a full equivalent of $NaClO_4$ is added to a solution of either **1**, **3**, or **4**, the new redox couple becomes more irreversible and intensifies slightly. The original redox couple is never dissipated.

Similar behavior is observed with Li^+ and K^+ although the latter results are somewhat tenuous. $KClO_4$ is nearly insoluble in anhydrous MeCN and the salt is not solubilized to a great enough extent to affect the voltammogram. In the Na^+ cation case, the combination of coordination and inherent solubility permit a direct comparison. These results are summarized in Table I.

The results presented here, while to some extent negative, are important because they show a contrast in coronand–podand behavior and because they show that arenes having a nitro group *ortho* to a methoxy (or perhaps other Lewis basic donor) group can interact strongly with cations in a bidentate fashion. The interaction we envision between acyclic compounds **1**, **3**, or **4** and an alkali metal cation is illustrated in eq 2. Although this effect might have been intensified by the presence of a polyethyleneoxy chain, it is not.



When the nitroarene undergoes reduction, the two negatively charged nitro group oxygen atoms become strong donor groups. Although the unpaired electron is largely localized on nitrogen, the functional group is con-

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jugated to and coplanar with the benzene ring. For bidentate coordination to occur, the oxygen lone pair(s) must be turned inward and the alkyl or alkoxyalkyl side chain must be turned away. The geometry will vary slightly depending on the extent to which the aryl oxygen is sp^2 hybridized but the side chain will be remote and unable to fully coordinate to the cation as the corresponding lariat ethers do.[6-8]

It appears that when an integral crown ring is present, it binds the cation and the nitro group serves as an additional donor. In contrast, the acyclic compound is a poorer cation binder, increasing the importance of the *ortho* oxygen atom. Once bidentate complexation occurs, the polyethyleneoxy chain cannot fully wrap about the cation so even its weak binding potential cannot be fully realized. It should be noted that the possibility exists that nitroarene-substituted podands having different geometrical arrangements might function as the lariat ethers do. Even so, this is an unusual instance in which acyclic podands fail to afford similar properties to those of the crown ethers.

Experimental Section

Reagents and Solvents. Acetonitrile (MCB, distilled in glass) was stored over Linde 4-A molecular sieves and flask-to-flask distilled from CaH_2 in a vacuum line immediately before use. All solutions were prepared under an inert atmosphere of dry N_2 gas. Tetrabutylammonium perchlorate ($Bu_4N^+ClO_4^-$, TBAP, from MCB) was recrystallized twice from EtOAc and stored in a desiccator. Alkali metal perchlorate salts were recrystallized from deionized water and dried in a vacuum oven at 110 °C for 24 h.

Apparatus. A standard, three-compartment cell, glassy carbon (0.35 cm^2 surface), and Pt wire electrodes were used. $E°'$ values are reported vs. a saturated aqueous calomel electrode (SCE). The measurements were done on a Bioanalytical Systems (Model CV-1B) apparatus (which does not provide for IR drop compensation) and recorded on a Hewlett-Packard Moseley 7035-B x–y recorder. A 100 mv/s sweep rate was used for all cyclic voltammetry experiments. All transfers were effected by syringe. The electroactive species were present in millimolar concentrations.

Substrates. 2-Nitroanisole (**1**) was obtained from Aldrich Chemical Co. and distilled prior to use. 2-[(2-Nitrophenoxy)methyl]-15-crown-5 (**2**) was prepared as previously described[6] from 1-chloro-2-nitrobenzene. 2-(1,4,7,10,13,16,19,22,25-Nonaoxahexaeicosyl)nitrobenzene, also called 2-[methoxyocta(ethoxy)]nitrobenzene (**3**), was obtained in 68% yield as a faintly yellow oil by treating $CH_3(OCH_2CH_2)_8OH$ (PEG monomethyl ether, MW 350) with NaH and 1-chloro-2-nitrobenzene in THF solution. Attempted distillation of **3** (or **4**, see below) led to decomposition. Osmometric molecular weight determination (494 ± 15 daltons) showed that an average of 7.8 ethyleneoxy units were present in the side chain. A previous, independent molecular weight determination[4d] on the starting ether gave a molecular weight of 400, suggesting approximately 8 ethyleneoxy units. The analysis below is calculated for $n = 8$. Anal. Calcd for $C_{23}H_{39}NO_{11}$: C, 54.65; H, 7.72; N, 2.77. Found: C, 54.45; H, 7.66; N, 3.23. Note that the nitrogen value is high (+0.46) as suggested by the integral and molecular weight data. ^1H NMR ($CDCl_3$), best fit of integral is for $n = 7$: 8.0–6.8 (m, 4 H), 4.4–3.5 (m, 28 H), 3.35 (s, 3 H). IR (neat, strong bands) 2900, 1600, 1525, 1350, 1280, 1120 cm^{-1}. Compound **4** was obtained similarly in 61% yield as a faintly yellow oil. Its ^1H NMR and IR spectral properties were essentially identical with those of **3**. Anal. Calcd for $C_{31}H_{55}NO_{15}$: C, 54.63; H, 8.08; N, 2.06. Found: C, 54.36; H, 8.30; N, 2.40.

Registry No. **1**, 91-23-6; **2**, 87453-20-1; **3**, 92670-57-0; **4**, 92670-58-1; $CH_3(OCH_2CH_2)_8OH$, 25990-96-9; 1-chloro-2-nitrobenzene, 88-73-3.

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Stereospecific Cobalt-Mediated Enediyne Cyclization Involving a Tetrasubstituted Double Bond: One-Step Construction of the Hydrophenanthrene Nucleus Incorporating Two Adjacent Quaternary Centers

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We have recently reported that intramolecular enediyne [2 + 2 + 2] cycloadditions are effected by (η^5-cyclopentadienyl)cobalt dicarbonyl [$CpCo(CO)_2$] with pronounced chemo-, regio-, and stereoselectivity, giving rise to complex polycycles from acyclic starting materials, including steroids.[1] The range of double bonds employed in these transformations encompassed 1-mono-,[1b] 1,1-[1c] or 1,2-di-,[1d] and 1,1,2-trisubstituted[1d] patterns. We report in this note that *tetrasubstituted* double bonds appear to be equally capable of entering the cyclization manifold, showing no sign of steric hindrance, unlike other cycloaddition reactions, such as the Diels–Alder, [3 + 2], and other cyclization strategies. The reaction proceeds with complete stereospecificity with respect to the original alkene moiety and also the complexed cobalt center and allows the one-step construction of a tricyclic diene containing two adjacent quaternary carbons starting from acyclic material.

Scheme I outlines an efficient stereospecific approach to the synthesis of starting enediyne **7**, employing five metals (Li, Al, Zr, Mg, Pd) other than cobalt in various steps, a powerful demonstration of the utility of both main group and transition metals in organic synthesis.

The sequence chosen en route to starting material begins with the protected 5-hexyn-1-ol **1**[2,3] which is alkylated with 4-bromobutanol tetrahydropyranyl ether[3] to give **2**. Attempted carboalumination[4] of this compound was unsuccessful, only starting material being recovered. The protecting groups were therefore removed to furnish diol **3** which was added to a solution of 1 equiv of Cp_2ZrCl_2 and 7 equiv of trimethylaluminum in dichloroethane. The resulting lemon yellow solution was heated at 50 °C for 48 h. At this point the product could be trapped at −30 °C with 3 equiv of iodine in THF to give **4**, in addition to a small amount of a product assumed to be derived from hydrolysis of the vinylaluminum intermediate. The second methyl group was introduced by initially protecting **4** and subsequently exposing it to palladium-catalyzed (10%) Grignard coupling conditions[5] to furnish **5**. Deprotection was followed by an unsuccessful attempt to turn the resulting enediol into the corresponding diiodide directly.[6] Similarly, ditosylate formation from the diol was sluggish and gave low yields. Finally, dimesylate formation oc-

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