stable [(diethoxyphosphinyl)difluoromethyl]zinc bromide (IV) which is acylated with acyl chlorides to yield (2-oxo-1,1-difluoroalkyl)phosphonates.[12] However, acylation of IV with ethyl chloroformate gave little or no II. However, catalysis with cuprous bromide gave a smooth reaction of IV and ethyl chloroformate to provide a good yield of II. Similar catalysis permitted the acylation of IV with diethylcarbamoyl chloride to give the corresponding amide derivative.[13]

Conversion of II to I was accomplished via selective silylation[14,15] of II at the phosphonic ester site to give V.[16] Further silylation of V with the more reactive iodotrimethylsilane gave the trisilylated ester VI.[17] Dissolution of VI in water immediately gave I in quantitative yield. I is extremely hygroscopic but may be isolated as a white crystalline monoamine salt[18] (VII) or as a stable monohydrate of the disodium salt[19] (VIII) of I.

Aqueous titration[20] of I gave two breaks with a stoichiometry of 1.993 (± 0.013) to 1 indicative of three acidic protons. Ionization constants of I were determined from titration of multiple independent titrations. The ionization constants were calculated by fitting the titration data to a titration function via a nonlinear least-squares program.[21] Table I summarizes the ionization constants of I relative to phosphonoacetic acid[22] and the analogous (difluoromethylene)bis[phosphonic acid].[23]

A typical preparation of II is described with operational details. To a 2-L flask equipped with a reflux condenser and cooled in an ice bath was added 267.0 g (1.0 mol) of III and 500 mL of dry monoglyme. Then 65.4 g (1.0 mol) of acid-washed zinc powder was added in one portion. The temperature was allowed to slowly rise until a vigorous exothermic reaction was initiated. After 4 days at room temperature, the solution was filtered in a Schlenk funnel (medium frit) and diluted with 250 mL of dry CH_3CN. Then 2.0 g (0.014 mol) of Cu^IBr were added followed by 115 mL (1.2 mol) of ethyl chloroformate. The reaction mixture was stirred overnight and the volume was reduced by rotary evaporation and then diluted with 500 mL of water. The insoluble inorganic salts were separated by suction filtration and washed with 100 mL of CH_2Cl_2. The aqueous portion was twice extracted with 200 mL of CH_2Cl_2. The organic fractions were combined, dried over Na_2SO_4, rotary evaporated, and flash distilled. Redistillation gave 131 g (50%) of II: bp 74–77 °C (0.2 mmHg); ^{19}F NMR ϕ^* −116.3 (d) $J_{P,F} = 96$ Hz; ^{31}P NMR δ 2.91 (t); ^{13}C NMR δ 111.2 (td) (CF_2) $J_{C,F} = 272$ Hz, $J_{C,P} = 204$ Hz; ^{1}H NMR δ 1.38 (t) $J_{H,H} = 7.1$ Hz, 1.40 (t) 7.0 Hz, 4.34 (dq) $J_{H,H} = 7.3$ Hz, 4.40 (q) $J_{H,H} = 7.3$ Hz; IR (neat) 1770 cm^{-1} (CO), 1290 (PO). Anal. Calcd for $C_8H_{15}F_2O_5P$: C, 36.93; H, 5.81. Found: C, 36.94; H, 5.69.

The described work now makes available a convenient source of difluorophosphonoacetic acid and its derivatives for detailed biological and chemical investigation. Future reports will detail additional studies in our laboratories in these directions.

Acknowledgment. The work of D.J.B. was supported by NSF and AFOSR. The work of D.J.P. was supported by NIH (Grant AM 28077).

Registry No. I, 91410-83-2; II, 17843-01-5; III, 65094-22-6; V, 91410-84-3; VI, 91410-85-4; VII, 91410-86-5; VIII, 91410-87-6; CuBr, 7787-70-4; Zn, 7440-66-6; ClC(O)OEt, 541-41-3.

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[12] Burton, D. J.; Ishihara, T.; Maruta, M. *Chem. Lett.* **1982**, 755.

[13] bp 105 °C (0.2 mmHg); ^{19}F NMR ϕ^* −108.8 (d) $J_{P,F} = 100$ Hz; ^{31}P NMR 3.92 (t); IR 1660 cm^{-1} (CO), 1280 (PO).

[14] Morita, T.; Okamato, Y.; Sakura, H. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2169.

[15] Sekine, M.; Futsuaki, T.; Yamada, Z.; Hata, T. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2509.

[16] bp 75–80 °C (0.1 mmHg); ^{19}F NMR ϕ^* −118.2 (d) $J_{P,F} = 100$ Hz; ^{31}P NMR δ −15.7 (t); ^{1}H NMR δ 0.35 (s), 1.37 (t) $J_{H,H} = 7.2$ Hz, 4.37 (q) $J_{H,H} = 7.0$ Hz.

[17] bp 88–92 °C (0.3 mmHg); ^{19}F NMR ϕ^* −118.0 (d) $J_{P,F} = 102$ Hz; ^{31}P NMR δ −16.3 (t); ^{1}H NMR δ 0.35 (s) $P(OSiMe_3)_2$, (s) CO_2SiMe_3.

[18] mp 210–212 °C dec; ^{19}F NMR (H_2O) ϕ^* −112.5 (d) $J_{P,F} = 89$ Hz; ^{31}P NMR δ 0.8 (t). Anal. Calcd for $C_{14}H_{26}F_2NO_5$: C, 47.06; H, 7.33; N, 3.92. Found: C, 47.17; H, 7.07; N, 3.76.

[19] Titration of VIII gave a M_r of 237.5; calcd M_r 238.0; mp (VIII) 271–275 °C dec.

[20] M_r of I from titration was found to be 176.5 (calcd 176.8). The anhydrous acid does not appear thermally stable above 100 °C and shows some decomposition at room temperature after several weeks.

[21] Cf. ref 3 and 4 for details of the titration procedure and calculation of K_a's.

[22] Heubel, P. C.; Popov, A. I. *J. Solution Chem.* **1979**, *8*, 615.

[23] Cf. ref 4—data corrected for Na^+ ion effects.

Organotin Chemistry. Preparation of 2,3-Disubstituted 1,3-Butadienes Using 2,3-Bis(trimethylstannyl)-1,3-butadiene and 1,4-Bis(trimethylstannyl)-2-butyne

Summary: 2,3-Bis(trimethylstannyl)-1,3-butadiene is a versatile synthon for the 2,3-dianion of 1,3-butadiene; mono and bis derivatizations with electrophiles such as halosilanes, disulfides, selenium, alkyl halides, aldehydes, and ketones have been carried out.

Sir: We report here procedures for the preparation of a wide variety of 2,3-disubstituted 1,3-butadienes using two new synthetic equivalents of the 2,3-dianion of 1,3-butadiene.[1] Treatment of either 2,3-dichloro-1,3-butadiene[2] or 1,4-dichloro-2-butyne[3] with 2 equiv of (trimethylstannyl)lithium gave the somewhat air-sensitive bis(trimethylstannyl)acetylene **1** (Scheme I). This compound was isomerized to the more stable butadiene **2**,[4] an air-stable distillable liquid which can be stored in the freezer

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[1] Other butadiene anions have been prepared. (a) Monoanions: Wender, P. A.; Sieburth, S. M.; Petraitis, J. J.; Singh, S. K. *Tetrahedron* **1981**, *37*, 3967. Brown, P. A.; Jenkins, P. R. *Tetrahedron Lett.* **1982**, *23*, 3733. (b) Cuprate: Nunomato, S.; Kawakami, Y.; Yamashita, Y. *J. Org. Chem.* **1983**, *48*, 1912. (c) Substituted 1,4-dilithio-1,3-butadienes: Reich, H. J.; Reich, I. L. *J. Org. Chem.* **1975**, *40*, 2248. Atwell, W. H.; Weyenberg, D. R.; Gilman, H. *J. Org. Chem.* **1967**, *32*, 885. Smith, L. I.; Hoehn, H. H. *J. Am. Chem. Soc.* **1941**, *63*, 1184. Braye, E. H.; Hübel, W.; Caplier, I. *J. Am. Chem. Soc.* **1961**, *83*, 4406.

[2] Gibbs, H. N.; Day, R. W. *Brit. Pat.* 1 084 742; *Chem. Abstr.* **1967**, *67*, P108184*k*. The reaction of 2,3-dichlorobutadiene with lithium diphenylphosphide gives 1,4-bis(diphenylphosphino)-2-butyne: Arthurs, M.; Nelson, S. M.; Walker, B. J. *Tetrahedron Lett.* **1978**, 1153.

[3] This compound as well as 1,4-dihydroxy-2-butyne has been frequently used as a precursor for 2- and 2,3-substituted butadienes: Bridges, A. J.; Fischer, J. W. *Tetrahedron Lett.* **1983**, *24*, 445. Jeganathan, S.; Okamura, W. H. *Tetrahedron Lett.* **1982**, *21*, 4763. Batt, D. G.; Ganem, B. *Tetrahedron Lett.* **1978**, 3323. Ishino, Y.; Nishiguchi, I.; Kim, M.; Hirashima, T. *Synthesis* **1982**, 740.

[4] Compound **1** can be reliably isomerized to **2** by treatment with a catalytic amount of $(CH_3)_3SnLi$ or CH_3Li in THF/HMPA (2 equiv) at 25 °C for 30 min. The minimum conditions needed for the isomerization vary with the batch of $(CH_3)_3SnLi$. One-pot conversion of 1,4-dichloro-2-butyne to **2** can be accomplished in 70% yield. To reproducibly obtain **1** free of **2**, the original reaction mixture must be quenched with H_2O at −78 °C (84% yield). Trimethyltinlithium was prepared from $(CH_3)_3SnBr$ by the procedure of Tamborski, C.; Ford, F. E.; Soloski, E. J. *J. Org. Chem.* **1963**, *28*, 237. We found it necessary to employ lithium wire containing 1% sodium.

0022-3263/84/1949-3438$01.50/0

Scheme I

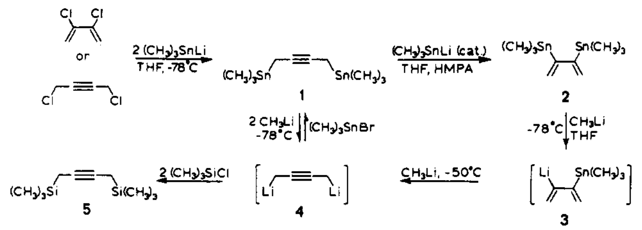
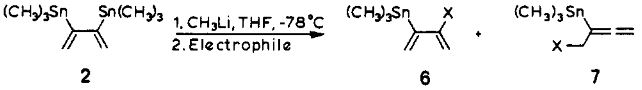


Table I. Preparation of 2-X-3-(Trimethylstannyl)-1,3-butadienes from Compound 2



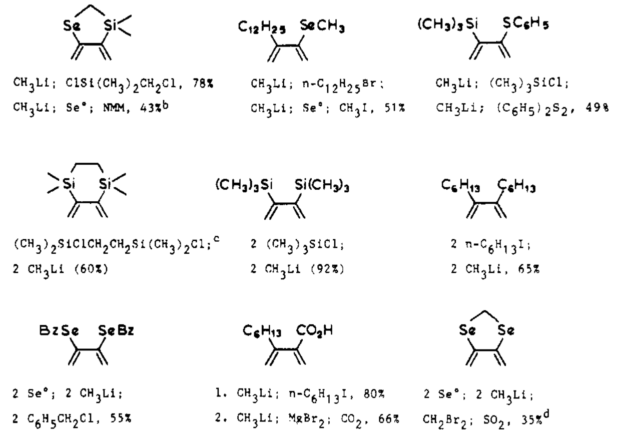
entry no.	electrophile[a]	X	yield,[b] % 6	yield,[b] % 7
1	$(CH_3)_3SiCl$	$Si(CH_3)_3$	78 (91)[c]	
2	$(CH_3)_2SiCl(CH_2Cl)$	$Si(CH_3)_2CH_2Cl$	78	
3	1. $MgBr_2$ 2. $C_6H_5SSC_6H_5$	SC_6H_5	74	
4	1. $MgBr_2$ 2. $C_6H_5SO_2Cl$	Cl	60 (83)[c]	
5	n-$C_6H_{13}I$	n-C_6H_{13}	80	
6	$ClCH_2Si(CH_3)_3$	$CH_2Si(CH_3)_3$	(64)[c]	
7	$(n$-$C_3H_7)_2CO$	$C(OH)(C_3H_7)_2$	61 (63)[c]	
8	$C_6H_5CH_2CH_2CHO$	$CH(OH)CH_2$-$CH_2C_6H_5$	42	
9	1. $MgBr_2$ 2. $C_6H_5(CH_2)_2CHO$	$CH(OH)CH_2$-$CH_2C_6H_5$	(14)[c]	(80)[d]
10	1. $CuBr{\cdot}SMe_2$ 2. $C_6H_5CH{=}CH$-$C(O)C_6H_5$	$CH(C_6H_5)CH_2$-$C(O)C_6H_5$	52 (55)[c]	

[a] In a typical experimental procedure, a solution of 3 was prepared by adding CH_3Li/ether (~1 M, 1.0 equiv) to a solution of 2 in THF (0.25 M). This solution was then transferred by using a cooled (−78 °C), jacketed syringe or cannula to a solution of the electrophile in ether, THF or pentane at −78 °C. The reaction mixture was quenched either at −78 °C or 25 °C, depending on the reactivity of the electrophile. All new compounds were characterized spectroscopically and elemental composition was determined by C and H analyses or mass spectrometry. [b] Yields are for material purified by distillation or chromatography. [c] Yields in parentheses were determined by NMR integration of crude products. [d] A pure sample of the allene was not obtained because of decomposition during purification.

(−20 °C) as a low-melting solid for at least 1 year.

Treatment of 2 with methyllithium in THF at −78 °C led within minutes to Li/Sn exchange to give a monolithiobutadiene 3[5,6] as shown by silylation and other derivatization reactions (Table I). When excess methyllithium was present a slower second Li/Sn exchange occurred at −50 °C to give dianion 4,[5,7] silylation or stannylation of which led almost exclusively to the disubstituted butynes 5 or 1 (Scheme I). If a solution of 3 is warmed to 0 °C it disproportionates to 4 and 2. This is, therefore, one of those unusual cases where a dianion is more stable than a related monoanion.[8]

Scheme II. 2,3-Disubstituted Butadienes Prepared from 2[a]



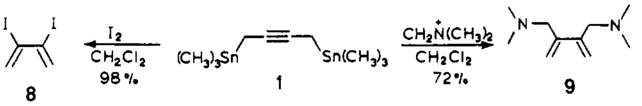
[a] See footnote a in Table I. Yields are for isolated materials, except when enclosed in parentheses, where yields were determined by NMR integration. [b] Isolated and purified as N-methylmaleimide (NMM) adduct. [c] Carried out at higher dilution (0.02 M). [d] Isolated and purified as SO_2 adduct.

We have explored the utility of 3 as a precursor to 2-X-3-(trimethylstannyl)-1,3-butadienes and found that silylation, alkylation (1° iodides and bromides), sulfenylation, selenenylation, and hydroxyalkylation could be carried out in generally good yields (Table I). The amounts of allenic products formed were small or undetectable in most cases. However, when 3 was converted to the Grignard reagent by reaction with $MgBr_2$ in ether/benzene, formation of allene was observed on reaction with aldehydes and ketones (Table I, entry 9). Lithium reagent 3 was also converted to a cuprate, and this used for conjugate addition reactions (Table I, entry 10). No allene was seen in this reaction.

If the groups introduced during the above reactions are stable toward strong bases, a second Li/Sn exchange–derivatization can be performed. Several butadienes prepared in this way together with reagents and yields are shown in Scheme II.

The Li/Sn exchange of 2 and the monoderivatized butadienes 6 appears to be more rapid than the reaction of methyllithium with many electrophiles, so that double derivatizations can be carried out in situ by simply adding 2–3 equiv of MeLi to a solution of 2 and 2 equiv of the electrophile in THF at −78 °C. Scheme II also gives several examples of this technique.

Propargylstannanes and silanes generally undergo electrophilic substitution with the formation of allenes.[9] Two sequential reactions of the bis(stannyl)acetylene 1 should thus lead to butadienes. Two successful examples of this process are the reaction with iodine to give the easily polymerizable 2,3-diiodobutadiene (8) and with Eschenmoser's salt to give the bis(dimethylamino)methyl diene 9.[10] Several others we have tried (Lewis acid catalyzed



8 9

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(5) Structures 3 and 4 are represented as shown since most of the derivatizations proceed to give diene and acetylene products, respectively. We have not characterized these lithium reagents spectroscopically.

(6) Other bis-tin compounds of actual or potential use for the preparation of dianions have been prepared: Seyferth, D.; Vick, S. C. *J. Organomet. Chem.* **1978**, *144*, 1. Jutzi, P.; Baumgärtner, J. *J. Organomet. Chem.* **1978**, *148*, 257. Seitz, D. E.; Lee, S.-H.; Hanson, R. N.; Bottaro, J. C. *Synth. Commun.* **1983**, *13*, 121. Chandrasekhar, S.; Latour, S.; Wuest, J. D.; Zacharie, B. *J. Org. Chem.* **1983**, *48*, 3810.

(7) This dianion is not formed by metalation of 2-butyne: Klein, J.; Becker, J. Y. *Tetrahedron* **1972**, *28*, 5385. Priester, W.; West, R.; Chwang, T. L. *J. Am. Chem. Soc.* **1976**, *98*, 8413. For calculations on 4, see: Radom, L.; Stiles, P. J.; Vincent, M. A. *J. Mol. Struct.* **1978**, *48*, 259.

(8) Several examples of preferential dimetalation are known: Costa, A. M. B. S. R. C. S.; Dean, F. M.; Jones, M. A.; Smith, D. A. *J. Chem. Soc. Chem. Commun.* **1983**, *1098*. Barfield, M.; Bates, R. B.; Beavers, W. A.; Blacksberg, I. R.; Brenner, S.; Mayall, B. I.; McCulloch, C. S. *J. Am. Chem. Soc.* **1975**, *97*, 900. Kloosterziel, H.; Zwanenburg, E. *Recl. Trav. Chim. Pays-Bas* **1969**, *88*, 1373.

(9) (a) Kitching, W.; Fong, C. W.; Smith, A. J. *J. Am. Chem. Soc.* **1969**, *91*, 767. (b) 1,4-Bis(trimethylsilyl)-2-butyne has been mono- and bisalkoxyalkylated: Pornet, J.; Kolani, N. *Tetrahedron Lett.* **1981**, *22*, 3609.

bis-acylations and hydroxyalkylations[9b]) have not been successful.

In summary, the ready availability of the two bis-stannylated compounds 1 and 2 has opened short pathways to a wide variety of both symmetric and unsymmetric 2,3-disubstituted 1,3-butadienes, many of which would be difficult or impossible to prepare by current methodologies.[11]

Acknowledgment. We thank the donors of the Petroleum Research Foundation, administered by the American Chemical Society, the National Institutes of Health, and the National Science Foundation for support of this work. H. E. Zimmerman and L. W. Linder[13] first prepared compounds 1 and 2 and converted 1 to the mono and disilyl (5) derivatives by treatment with *n*-butyllithium and trimethylsilyl chloride. We thank them for providing details of their work.

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(10) Allylstannanes react with Mannich reagents to give aminomethylated products: Reich, H. J.; Schroeder, M. C.; Reich, I. L. *Isr. J. Chem.* **1984**, *24*, 157.

(11) Of all of the 2,3-disubstituted butadienes reported here, only three have been previously prepared: the 2,3-bis(trimethylsilyl)-,[12a] the 2,3-diiodo-,[12b] and the 2,3-di-*n*-hexyl-1,3-butadienes.[12c]

(12) (a) Bock, H.; Seidle, H. *J. Am. Chem. Soc.* **1968**, *90*, 5694. (b) Wille, F.; Dirr, K.; Kerber, H. *Liebigs Ann. Chem.* **1955**, *591*, 177. (c) Hhota, S.; Tosaka, T.; Sonoda, N.; Shimotsuma, W. *Eur. Pat. Appl.* EP61 264; *Chem. Abstr.* **1983**, *98*, p99701*n*.

(13) L. W. Linder, Ph.D. Thesis, University of Wisconsin, Madison, 1984.

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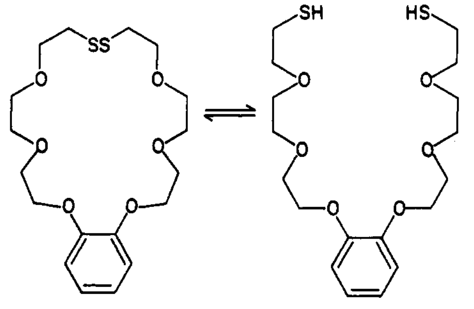
Redox-Switched Crown Ethers. Cyclic–Acyclic Interconversion Coupled with Redox between Dithiol and Disulfide

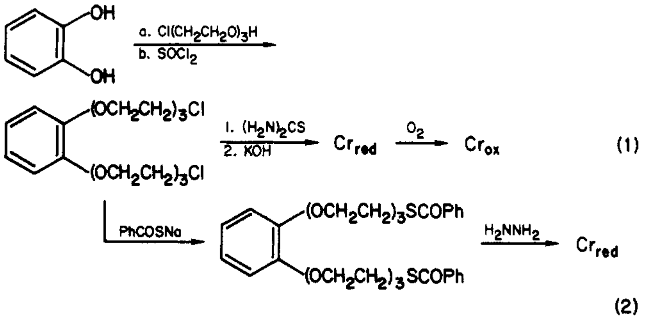
Summary: Synthesis, ion affinity, and redox properties of a pair of "redox-switched" crown analogues with a dithiol group at α,ω-positions (Cr_{red}) and a disulfide bond in the ring (Cr_{ox}) are described.

Sir: Macrocyclic polyethers contain intramolecular cavities delineated by molecular segments and are capable of specific chelation with alkali and alkaline earth metal cations. It is now established that the specificity stems from a host–guest relationship.[1-3] As the ion selectivity is largely governed by the size of the intramolecular cavities, one may expect that if the topological ring shape can be reversibly changed, it would lead to the control of ion-binding ability and ion selectivity. The photo- and pH-responsive crown ethers are typical examples.[4-10] It occurred to us that the most direct change in the cavity shape would be attained by reversible bond formation and bond scission leading to cyclic–acyclic interconversion and the redox reaction of a thiol–disulfide couple would be the most suitable candidate for this.[11,12] We here report a pair of new "redox-switched" crown ether analogues bearing a disulfide bond in the ring and a dithiol group at its α,ω-positions. The oxidized form (Cr_{ox}; 2,3-benzo-1,4,7,10,17,20-hexaoxa-13,14-dithiacyclodocos-2-ene) is a coronand analogue and expected to bind metal ions in the cavity. The reduced form (Cr_{red}: 10,11-benzo-3,6,9,12,15,18-hexaoxaeicos-10-ene-1,20-dithiol) is a podand analogue and expected to show poor ion affinity.



Cr_{ox} Cr_{red}

Cr_{ox} and Cr_{red} were synthesized according to the following reaction sequence and identified by IR, NMR, mass spectrum and elemental analysis.[13] Cr_{ox} was synthesized by route 1 and finally isolated by a TLC method. On the other hand, purification of Cr_{red} was very difficult because of ready oxidation either to Cr_{ox} or to oligomeric materials. We thus developed route 2 in which the final step (H_2NNH_2 treatment) proceeded under reductive atomosphere. As the product was protected from air oxidation, Cr_{red} could be easily isolated.



The ion-binding ability of Cr_{red} and Cr_{ox} was estimated by anaerobic solvent extraction of alkali metal salts of 8-anilinonaphthalene-1-sulfonate (ANS)[14] from water to chloroform and was compared with that of monobenzo-

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(1) Cram, D. J.; Cram, J. M. *Acc. Chem. Res.* **1978**, *11*, 8.

(2) Lehn, J.-M. *Acc. Chem. Res.* **1978**, *11*, 49.

(3) Gokel, G. W.; Korzeniowski, S. H. In "Macrocyclic Polyether Syntheses"; Springer-Verlag: Berlin, 1982.

(4) Yamashita, I.; Fujii, M.; Kaneda, T.; Misumia, S.; Otsubo, T. *Tetrahedron Lett.* **1980**, *21*, 541.

(5) Shiga, M.; Takagi, M.; Ueno, K. *Chem. Lett.* **1980**, 1021.

(6) Shinkai, S.; Nakaji, T.; Nishida, Y.; Ogawa, T.; Manabe, O. *J. Am. Chem. Soc.* **1980**, *102*, 5860.

(7) Nakatsuji, Y.; Kobayashi, H.; Okahara, M. *J. Chem. Soc., Chem. Commun.* **1983**, 800.

(8) Wirenga, W.; Evans, B. R.; Woltersom, J. A. *J. Am. Chem. Soc.* **1979**, *101*, 1334.

(9) (a) Frederick, L. A.; Fyles, T. M.; Malik-Diemer, V. A.; Whitfield, D. M. *J. Chem. Soc., Chem. Commun.* **1980**, 1211. (b) Yamazaki, N.; Nakahama, S.; Hirao, A.; Negi, S. *Tetrahedron Lett.* **1978**, 2429.

(10) (a) Hiratani, K.; Aiba, S.; Nakagawa, O. *Chem. Lett.* **1980**, 477. (b) Charewicz, W. A.; Bartsch, R. A. *J. Membr. Sci.* **1983**, *12*, 323.

(11) (a) Minami, T.; Shinkai, S.; Manabe, O. *Tetrahedron Lett.* **1982**, *23*, 5167. (b) Shinkai, S.; Inuzuka, K.; Manabe, O. *Chem. Lett.* **1983**, 747.

(12) A similar idea has recently been offered by M. Rabin et al. (private communication).

(13) Cr_{red}: oil; IR (neat) ν_{SH} 2560 cm^{-1}, ν_{C-O-C} 1130, and 1260 cm^{-1}; NMR ($CDCl_3$) δ 1.58 (2 H, t, SH), 2.68 (4 H, h, SCH_2), 3.74 (16 H, m, $CH_2OCH_2CH_2OCH_2$), 4.18 (4 H, t, $ArOCH_2$), 6.92 (4 H, s, Ar protons). Found: C, 52.06; H, 7.47; S, 15.57. Calcd for $C_{18}H_{30}O_6S_2$: C, 53.18; H, 7.44; S, 15.77. Cr_{ox}: mp 46–49 °C; IR (neat) ν_{C-O-C} 1120 and 1260 cm^{-1}; MS, M^+ (*m/e*) 404; NMR ($CDCl_3$) δ 2.92 (4 H, t, SCH_2), 3.76 (16 H, m, $CH_2OCH_2CH_2OCH_2$), 4.16 (4 H, t, $ArOCH_2$), 6.87 (4 H, s, Ar protons).

(14) Picrate ion, usually employed for solvent extraction, was not used in the present "redox" system because of its oxidative properties.

0022-3263/84/1949-3440$01.50/0