to a total of 1 H (diastereomeric C_2 H's, which are clearly distinguishable so that ≤5% of either diastereomer can be deleted), 5.05 (m, 1 H, apparent double heptuplet), 11.13 (s, 1 H, CO_2H).

When the reaction was carried out by adding only 1 equiv of LiI portionwise, a single diastereomer (2*S*,3*S*) of **9** was obtained as an oil in 85% yield: IR (neat) 1705–1745 cm^{-1} (br); ^1H NMR (90 MHz) δ 1.28 (d, 6 H), 1.33 (d, 3 H), 3.18 (m, 1 H), 4.51 (d, 1 H, J = 10.5 Hz), 5.08 (m, 1 H), 11.13 (s, 1 H, CO_2H).

Isopropyl 2(*S*)-Chloro-3(*S*)-methylsuccinate (12). A solution of the β-lactone **8** (500 mg, 2.91 mmol) and LiCl (366 mg, 8.72 mmol) in 15 mL of dry THF was stirred under N_2 at room temperature for 24 h. The reaction was worked up in the same manner as the corresponding iodide **9** to give 430 mg (71%) of **12** as an oil: IR (neat) 1705–1745 cm^{-1} (br); ^1H NMR (90 MHz) δ 1.30 (d, 6 H), 1.32 (d, 3 H), 3.20 (m, 1 H), 4.52 (d, 1 H, J = 7.5 Hz) 5.10 (m, 1 H), 11.5 (s, 1 H, CO_2H); mass spectrum, m/e 208 (^{35}Cl), 210 (^{37}Cl).

2(*R*)-Methyl-4-isopropylsuccinic Acid Monoester 10. To a solution of the cis β-lactone **8** (0.5 g, 2.91 mmol) and NaI (1.3 g, 8.72 mmol) in 30 mL of acetonitrile at room temperature was added 1.10 mL (8.72 mmol) of $(CH_3)_3SiCl$ with continuous stirring under N_2. The reaction mixture was then heated to reflux and maintained at reflux for 24 h. It was then cooled to room temperature, poured into a separatory funnel containing ethyl acetate, and extracted with two 25-mL portions of 10% $NaHCO_3$. The combined aqueous layers were acidified to pH 2 with 6 N HCl and then extracted with several portions of ethyl acetate. The ethyl acetate layers were combined, washed with brine, dried over $MgSO_4$, filtered, and evaporated to give 304 mg (60%) of pure **10** as an oil. Before measuring the optical rotation a sample was chromatographed on silica gel with ethyl acetate-hexanes (3:7). $[\alpha]^{20}_D$ +4.50 (*c* 2.5, CH_3OH); IR (neat) 1700–1730 cm^{-1} (br); ^1H NMR (90 MHz) δ 1.23 (d, 6 H), 1.24 (d, 3 H), 2.23–3.17 (m, 3 H for 1 C_2 H and 2 C_3 H's), 5.03 (m, 1 H), 11.67 (s, 1 H, CO_2H); mass spectrum (CI with CH_4), m/e 175 (M + 1).

Similar treatment of α-iodo ester **9** gave **10** in 74% yield. The spectroscopic data of this sample were identical with those obtained above.

Reduction of Dimethyl 2-Bromosuccinate (15a). A 50-mL flask was charged with NaI (933 mg, 6.67 mmol), dimethyl bromosuccinate **15a** (0.50 g, 2.22 mmol), and CH_3CN (25 mL). The suspension was stirred under N_2, and $(CH_3)_3SiCl$ (0.85 mL, 6.67 mmol) was added. The reaction mixture was heated at reflux for 16 h and then worked up in the same manner as for **10** above (except that a 10% sodium thiosulfate wash was added during the extraction). The dimethyl succinate obtained (74% yield) was identical in all respects with an authentic sample.

2(*R*)-Methylsuccinic Acid (11). To a solution of the monoisopropyl ester **10** (0.7 g, 4.02 mmol) in 5 mL of dioxane was added 2.9 mL of a 20% KOH solution (aqueous). Dioxane–water (1:1) was added portionwise until the reaction mixture became homogeneous. The mixture was then heated at reflux for 12 h. After cooling to room temperature the solution was passed through an ion-exchange resin (Dowex, SO_3H) by eluting with water. The eluant was evaporated under reduced pressure to give a white solid which was recrystallized from ethyl acetate–hexanes to yield 465 mg (88%) of **11** as white crystals: mp 111–112 °C (lit.[12] mp 115 °C); $[\alpha]^{22}_D$ +16.2° (*c* 2.14, absolute ethanol) [lit.[12] $[\alpha]^{20}_D$ +16.59° (*c* 4.136, absolute ethanol); ^1H NMR (Me_2SO-d_6, 300 MHz) δ 1.11 (d, 3 H, J = 7.2 Hz), 2.25–2.33 (m, apparent q, 1 H), 2.47–2.55 (m, apparent q, 1 H), 2.61–2.71 (m, 1 H), 12.25 (s, 2 H, CO_2H's).

***N*-Benzyloxy *O*-isopropyl 2(*S*)-methyl-3(*S*)-chlorosuccinamate (13)** was prepared by the previously reported procedure.[9] Thus, 414 mg (1.986 mmol) of **12** was dissolved along with 380 mg (2.4 mmol) of OBHA·HCl in 20 mL of THF–H_2O (1:1) at an apparent pH of 4.5. A solution of 760 mg (3.97 mmol) of water-soluble carbodimide [*N*-ethyl-*N*^{1}-[3-(dimethylamino)-propyl]carbodiimide] was added and the pH maintained at 4.5 by addition of either 1.0 N NaOH or 1.0 N HCl as required. After 30 min, the solution was extracted with three 25-mL portions of ethyl acetate. The combined ethyl acetate was washed with two 20-mL portions of 1 M citric acid, 20 mL of H_2O, and 20 mL of brine, dried over $MgSO_4$, filtered, and evaporated to give a solid. Recrystallization from ether–hexanes gave 436 mg (70%) of **13** as white crystals: mp 131–131.5 °C; $[\alpha]^{23}_D$ +6.3° (*c* 2.96, CH_3OH); IR ($CHCl_3$) 3410, 1730, 1690 cm^{-1}; ^1H NMR (90 MHz) δ 1.17 (d, 3 H, J = 7.5), 1.28 (d, 6 H), 2.67 (m, 1 H), 4.40 (d, 1 H, J = 10.5 Hz), 4.95 (s, 2 H), 5.07 (m, 1 H), 7.45 (s, 5 H), 8.78 (s, NH); mass spectrum, m/e 255 [M − 58 (OC_3H_7)]. Anal. Calcd for $C_{15}H_{20}NO_4Cl$: C, 57.42; H, 6.38; N, 4.47; Cl, 11.32. Found: C, 57.29; H, 6.16; N, 4.53; Cl, 11.36.

1-(Benzyloxy)-3(*R*)-methyl-4(*R*)-(isopropoxycarbonyl)-2-azetidinone (14). A solution of 100 mg (0.319 mmol) of the hydroxamate **13** in 8 mL of DMF–CH_2Cl_2 (3:5) was added to 15 mg of a 50% mineral oil suspension of NaH under N_2 at room temperature and stirred for 1.5 h. Ether (100 mL) was added, and the resulting solution was washed with water and brine. The ether was then dried ($MgSO_4$), filtered, and evaporated to give 96 mg of an oil. The crude product was purified by chromatography on silica gel by eluting with 20% ethyl acetate in hexanes to provide 86 mg (98%) of pure **14** as an oil: $[\alpha]^{23}_D$ +27.7 ± 1.5 (*c* 1.77, CH_3OH); IR (neat) 1780, 1730 cm^{-1}; ^1H NMR (300 MHz) δ 1.19 (d, 3 H, J = 7.5 Hz), 1.295 (2 overlapping d, 6 H), 3.23 (m, 1 H), 4.24 (d, 1 H, J = 6.3 Hz), 5.09–5.19 (m, 1 H), 5.13 (d, 2 H, diastereotopic protons of OCH_2Ph), 7.35–7.43 (m, 5 H); mass spectrum m/e 277. The ^1H NMR (300 MHz) was also run in the presence of a chiral shift reagent (0.25 M solution of **14** in $CDCl_3$ which was also 0.125 M in tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III). As described earlier,[5] these conditions clearly distinguish the diastereotopic benzylic protons of *N*-(benzyloxy)-2-azetidinones.

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Efficient Synthesis of C-Pivot Lariat Ethers. 2-(Alkoxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecanes[1]

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Catalysis of ester aminolysis by cyclic and acyclic polyethers reported from this laboratory[2] has served as an encouragement to examine polyether catalysis in other reactions of amines as well as to develop new polyethers. Recently, syntheses of crown ethers with functionalized side chains (lariat ethers[3]) have been reported.[3-7] In particular, alkoxymethyl-substituted crown ethers have attracted considerable attention as synthons for more complex macrocycles and polymer-supported crowns.[4,7-11]

(1) Supported by a grant from the Dow Chemical Company.
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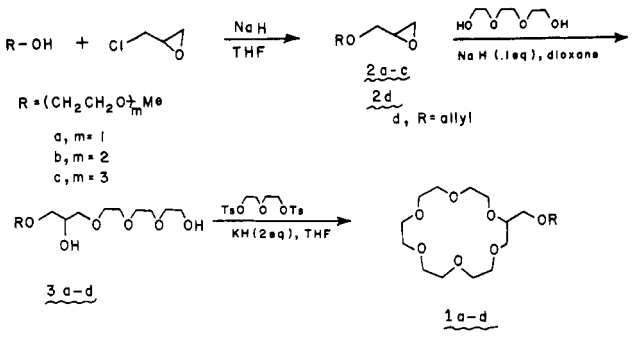
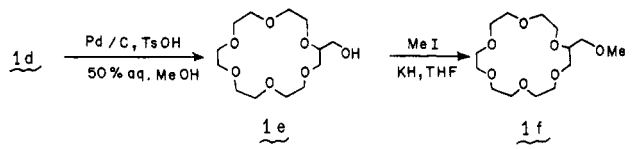
Scheme I



Scheme II



The more tedious problems in syntheses of these lariat ethers are preparation and isolation of the diol precursors. These difficulties have been resolved by methods reported below.

This report describes a simple, high-yield procedure for syntheses of 2-(alkoxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecanes [(alkoxymethyl)-18-crown-6, **1**], which utilized inexpensive and readily available starting materials (Scheme I).

Reaction of an alcohol with excess (chloromethyl)oxirane (epichlorohydrin) produces the desired (alkoxymethyl)-oxirane (**2**) in excellent yield (Table I). Treatment of **2** with excess 3,7-dioxaoctane-1,8-diol (triethylene glycol) in the presence of catalytic amounts of NaH affords the 1-(alkoxymethyl)-3,6,9-trioxaundecane-1,11-diol (**3**) in surprisingly high yields. It has been found that **3** can be easily isolated from triethylene glycol by continuous extracton with 15% 2,2,4-trimethylpentane in benzene. This method has proven quite efficacious for the preparation and isolation of a variety of analogues of **3** (Table II).

The yields of purified product depend on the polarity of the material. Thus, the less polar allyloxymethyl analogue (**3d**) is obtained in better yields than those with polyether side chains (**3a–c**). Furthermore, with longer polyether side chains, the amount of the isolated material declines. This lower yield is due to their reduced solubility in the hydrocarbon solvent, because the polarity of these larger molecules increases with longer polyether side chains.

Cyclization of **3** with 3-oxapentamethylene ditosylate in the presence of KH affords the corresponding lariat ethers, **1** (Table III). (Hydroxymethyl)-18-crown-6 (**1e**) can be easily prepared by removal of the allyl group of **1d**. Methylation of this crown produces **1f** (Scheme II).

The yields of the crown ethers are consistently less than ideal even though NMR spectra of the crude products indicate that only the desired crowns are present (yields 80–90% of theoretical). The substantial losses are attributed to the purification process.

Experimental Section

All ^1H NMR spectra were recorded on a Varian A-60-A spectrophotometer with tetramethylsilane as an internal reference standard. Infrared spectra were recorded on a Perkin-Elmer 621 spectrophotometer by using a thin film of the sample on NaCl plates. Mass spectra were obtained by solid inlet on a Hewlett-Packard 5985 mass spectrometer. Solvents were purified by the standard methods. All reactions were performed under ni-

Table I. Pertinent Data for (Alkoxymethyl)oxiranes (**2**)

compd	R	yield, %	bp, °C (mmHg)	NMR (CCl_4), δ	MS, *m/e*	IR, cm^{-1}
2a	$CH_3OCH_2CH_2$	96.7	64–69 (5) [lit.[14] 80–81 (13)]	3.4–3.6 (m, 6 H), 3.3 (s, 3 H, CH_3), 2.8–3.1 (m, 1 H), 2.4–2.8 (m, 2 H)	132 (0.1, M^+), 100 (17.9, $M^+ - CH_3OH$), 87 (21.0, $CH_2CH_2OCH_2CHO^+$), 73 (23.2, $CH_3OCH_2CHO^+$), 59 (69.2, OCH_2CHO^+), 45 (100, $(CH_2CH_2O)H^+$)	2900 (s), 1450 (m), 1110 (s), 760 (m)
2b	$CH_3(OCH_2CH_2)_2$	93.2	116 (5) [lit.[15] 95–97 (4)]	3.4–3.6 (m, 10 H), 3.3 (s, 3 H, CH_3), 2.8–3.1 (m, 1 H), 2.3–2.8 (m, 2 H)	176 (0.2, M^+), 100 (21.9, $M^+ - CH_3OCH_2CH_2OH$), 89 (27.3, $(CH_2CH_2O)_2H^+$), 59 (100), 45 (47.3)	2900 (s), 1460 (m), 1110 (s), 850 (m), 750 (m)
2c	$CH_3(OCH_2CH_2)_3$	86.6	140–145 (5)	3.4–3.7 (m, 14 H), 3.3 (s, 3 H, CH_3), 2.8–3.2 (m, 1 H), 2.4–2.8 (m, 2 H)	221 (0.1, $M^+ + 1$), 103 (17.1, $CH_3(OCH_2CH_2)_2^+$), 100 (17.5, $M^+ - CH_3(OCH_2CH_2)_2OH$), 89 (20.1), 87 (21.5), 73 (15.9), 59 (100), 45 (46.9)	2900 (s), 1460 (m), 1120 (s), 860 (m), 770 (m)

Table II. Pertinent Data for 1-(Alkoxymethyl)-3,6,9-oxaundecane-1,11-diols (3)

compd	R	yield, %	bp, °C (mmHg)	NMR (CCl_4), δ	MS, *m/e*	IR, cm^{-1}
3a	$CH_3OCH_2CH_2$	74.5	210–215 (1.0)	3.4–3.7 (m, 21 H), 3.3 (s, 3 H, CH_3), 3.2 (br s, 2 H, OH)	252 (0.4, $M^+ - CH_2O$), 175 (34.2, $CH_3OCH_2CH(OH)CH_2(OCH_2CH_2)_2^+$), 89 (57.3, $(OCH_2CH_2)_2^+$), 87 (53.0, $CH_2CH_2OCH_2CHO^+$), 59 (78.2, $CH_3OCH_2CH_2^+$), 45 (100, $HOCH_2CH_2^+$)	3600 (s), 2890 (s), 1645 (w), 1450 (m), 1110 (s)
3b	$CH_3(OCH_2CH_2)_2$	66.0	175–180 (0.3)	3.4–3.8 (m, 25 H), 3.3 (s, 3 H, CH_3), 2.9 (br s, 2 H, OH)	327 (0.2, $M^+ + 1$), 239 (1.0, $M^+ - CH_2CH_2OCH_2CHO$), 193 (17.1, $M^+ - CH_3(OCH_2CH_2)_2$), 175 (100), 163 (58.2), 133 (16.2), 103 (43.4), 89 (56.9), 87 (58.8), 59 (54.5), 45 (58.8)	3400 (s), 2900 (s), 1655 (w), 1460 (m), 1110 (s)
3c	$CH_3(OCH_2CH_2)_3$	61.6	240–245 (1.0)	3.4–3.8 (m, 31 H), 3.3 (s, 3 H, CH_3)	340 (0.2, $M^+ - CH_2O$), 207 (3.85, $M^+ - CH_3(OCH_2CH_2)_3O$), 175 (52.8), 103 (46.9, $OCHCH_2OCH_2CH_2O^+$), 89 (60.8), 87 (60.1), 59 (100), 45 (100)	3600 (s), 2900 (s), 1650 (m), 1455 (m), 1100 (s)
3d	allyl	87.3	195–200 (0.8)	5.0–6.2 (m, ABX, 3 H, vinyl), 3.9–4.1 (octet, 2 H, vinyl), 3.3–4.7 (m, 19 H)	265 (0.1, $M^+ + 1$), 193 (3.4, $M^+ - CH_2OCH_2CHCH_2$), 175 (47.4), 89 (66.3), 45 (48.4)	3600 (s), 2900 (s), 2860 (s), 1645 (m), 1455 (m), 1100 (s), 925 (m)

trogen. Elemental analyses of the lariat ethers were found to be within acceptable limits (±0.4%). Distillations were performed on an Aldrich Kugelrohr apparatus.

(Alkoxymethyl)oxirane (2). An oil slurry of NaH (5 g of a 50% suspension; Alfa) was rinsed with toluene and added to THF (100 mL). The alcohol (100 mmol) was then added and stirred for 2 h. (Chloromethyl)oxirane (40 mL) was added, and the solution was stirred for 16 h at room temperature, followed by 4 h at reflux. After the excess base was neutralized with 30% methanolic H_2SO_4, the solution was filtered, concentrated under reduced pressure and distilled under vacuum (Table I).

1-(Alkoxymethyl)-3,6,9-undecane-1,11-diols (3). To dioxane (300 mL) were added NaH suspended in oil (1 g) and triethyleneglycol (40 mL), and the reaction mixture was stirred until all the NaH was consumed. After the solution had been heated to reflux, the (alkoxymethyl)oxirane (100 mmol) in dioxane (125 mL) was added over 2.5 h. The reflux was continued for another 24 h. After the reaction mixture had been cooled to room temperature, enough H_2SO_4 was added to neutralize the base. The solution was decolorized, filtered, and concentrated under reduced pressure, leaving an oil.

The oil was exhaustively triturated with cyclohexane and then dissolved in water (250 mL). The aqueous solution was continuously extracted with 15% 2,2,4-trimethylpentane in benzene for 2 weeks. Although this was quite a long time, the extraction could be left unattended. Analytical samples were prepared by distillation (Table II), but the purity of the extracted material was sufficient for subsequent reactions.

2-(Alkoxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecanes [2-(Alkoxymethyl)-18-crown-6's, 1a-d]. An oil slurry (25%) of KH (6.4 g; Alfa) was washed with hexane and suspended in THF (100 mL). Diol **3** (20 mmol) was added, and the solution was stirred for 3 h.

A three-necked round-bottomed flask was fitted with two dropping funnels equipped with equilibration arms and with a reflux condenser. The alkoxide solution was poured into one addition funnel, and a THF solution of 3-oxapentamethylene ditosylate[12] (8.28 g, 20 mmol, in 100 mL of solvent) was poured into the second funnel. Both solutions were added simultaneously to a small amount of THF residing in the reaction vessel (50 mL). The solution was stirred for 15 h at room temperature and 24 h at reflux.

The cooled reaction mixture was filtered through Celite and concentrated under vacuum. The residue, dissolved in approximately 5 mL of CH_2Cl_2, was layered onto a 3 × 11 cm column of activated alumina (80–325 mesh; MCB) and flushed with hexane (200 mL). The crown ether was removed by elution with CH_2Cl_2 (200 mL; followed by *i*-PrOH, 200 mL). These fractions were combined and the solvents stripped off. The lariat ethers **1a–d** were distilled (Table III). The crown **1d** was used without further purification.

2-(Hydroxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecane [(Hydroxymethyl)-18-crown-6), 1e].[13] The crude **1d** was mixed with Pd/C (5%, Engelhard, 1.3 g) and TsOH (1.3 g) in 50% aqueous methanol (200 mL). The black suspension was refluxed for 24 h, cooled, and filtered, and the solution was concentrated under reduced pressure. The acid was neutralized with 5% NaOH, and the water was then removed under vacuum.

The thick syrup, dissolved in CH_2Cl_2 (about 10 mL), was chromatographed on a 3 × 11 cm column of alumina with CH_2Cl_2 (700 mL), THF (500 mL), and *i*-PrOH (100 mL) as the eluting solvents in sequence. The combined fractions were concentrated to yield a pale yellow oil. Distillation at 0.13 mm yielded **1e**.

2-(Methoxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecane [2-(Methoxymethyl)-18-crown-6, 1f]. An oil slurry of KH (1 g) was washed with toluene and suspended in THF (50 mL). To this suspension was added **1e** (1.42 g, 5mmol), and the mixture was stirred for 2 h. Methyl iodide (5 mL) was added, and the

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Table III. Pertinent Data for Lariat Ethers 1

compd	R	yield, %	bp, °C (mm)	NMR, δ	MS, *m/e*	IR, cm^{-1}
1a	$CH_3OCH_2CH_2$	34.1	155 (0.13)	3.4–3.7 (s over m, 29 H), 3.3 (s, 3 H, CH_3)	352 (0.1, M^+), 263 (1.6, $(CH_2CH_2O)_5CH_2CHO^+$), 133 (28.2, $(CH_2CH_2O)_2CH_2CHO^+$), 89 (100), 73 (42.5), 59 (42.5), 45 (62.1)	3400 (s, H_2O), 3870 (s), 1690 (w), 1455 (m), 1355 (m), 1110 (s)
1b	$CH_3(OCH_2CH_2)_2$	20.0	160 (0.13)	3.4–3.7 (s over m, 33 H), 3.3 (s, 3 H, CH_3)	396 (0.4, M^+), 293 (1.7, $M^+ - CH_3OCH_2CH_2)_2$), 263 (6.3), 175 (15.8), 149 (18.7, $H(OCH_2CH_2)_3O^+$), 133 (25.0), 103 (44.4, $CH_3(OCH_2CH_2)_2^+$), 89 (49.5), 87 (100), 73 (39.0), 59 (55.1), 45 (50.5)	3470 (s, H_2O), 2880 (s), 1650 (w), 1465 (m), 1370 (m), 1120 (s)
1c	$CH_3(OCH_2CH_2)_3$	20.7	165 (0.13)	3.5–3.7 (s over m, 37 H), 3.3 (s, 3 H, CH_3)	440 (3.1, M^+), 293 (13.9, $M^+ - CH_3(OCH_2CH_2)_3$), 263 (22.4), 175 (40.7), 147 (37.3, $(CH_3(OCH_2CH_2)_3^+$), 133 (64.8), 103 (58.2), 89 (70.6), 87 (90.7), 59 (79.6), 45 (100)	3500 (s, H_2O), 2970 (s), 1650 (w), 1360 (m), 1115 (s)
1d	allyl	*c*	162	5.0–6.2 (m, ABX, 3 H, vinyl), 3.9–4.1 (m, 2 H, allyl), 3.3–3.8 (m, 25 H)	293 (1.1, M^+ – allyl), 275 (1.2, $M^+ - H_2O$), 263 (1.2, $M^+ - CH_2CHCH_2OCH_2$), 175 (19.9), 133 (12.6), 89 (65.5), 82 (100), 73 (35.4), 45 (100), 43 (31.0, CH_2CHO^+), 41 (45.3, allyl$^+$)	3400 (s, H_2O), 2900 (s), 1650 (w), 1465 (m), 1360 (m), 1255 (w), 1115 (s), 945 (m)
1e[a]	H	48.1	208	3.5–3.7 (s over m)	294 (0.1, M^+), 263 (1.0), 221 (2.2, $M^+ - CH_2OCH_2CHO^+$), 175 (11.2), 133 (25.0), 89 (76.3), 87 (94.7), 73 (33.8), 59 (31.7), 45 (100)	3350 (s, H_2O), 2900 (s), 1650 (w), 1470 (m), 1300 (m), 1260 (m), 1120 (s)
1f[b]	CH_3	39.0	132	3.3–3.7 (s over m, 25 H), 3.3 (s, 3 H, CH_3)	308 (0.4, M^+), 263 (7.2), 175 (15.2), 133 (16.2), 131 (15.0, $OHCCH_2O(CH_2CH_2O)_2^+$), 103 (14.5), 89 (39.0), 87 (100), 73 (31.4), 59 (39.4), 45 (60.1)	2870 (s), 1640 (w), 1460 (m), 1300 (m), 1110 (s)

[a] Prepared by deallylation of 1d (see Experimental Section). [b] Prepared by methylation of 1e. [c] Not determined.

mixture was stirred for 20 h and then refluxed for 4 h.

The cooled solution was concentrated by flash evaporation and chromatographed on a 3 × 11 cm column of alumina with the following solvents: hexane (200 mL), CH_2Cl_2 (200 mL), *i*-PrOH (200 mL). The last 400 mL of solvents were combined and concentrated. Distillation of this residue afforded 600 mg of the desired crown (39.0% yield).

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Registry No. **1a**, 84812-01-1; **1b**, 84812-02-2; **1c**, 84812-03-3; **1d**, 84812-04-4; **1e**, 70069-04-4; **1f**, 84812-05-5; **2a**, 13483-49-3; **2b**, 71712-93-1; **2c**, 73692-54-3; **2d**, 106-92-3; **3a**, 84812-06-6; **3b**, 84812-07-7; **3c**, 84812-08-8; **3d**, 84812-09-9; $HOCH_2CH_2OMe$, 109-86-4; $HO(CH_2CH_2O)_2Me$, 111-77-3; $HO(CH_2CH_2O)_3Me$, 112-35-6; (chloromethyl)oxirane, 106-89-8; triethylene glycol, 112-27-6; 3-oxapentamethylene ditosylate, 7460-82-4.

Base-Induced Fragmentation of Ethanediyl *S,S*-Acetals Bearing Two Aromatic Substituents at C-2

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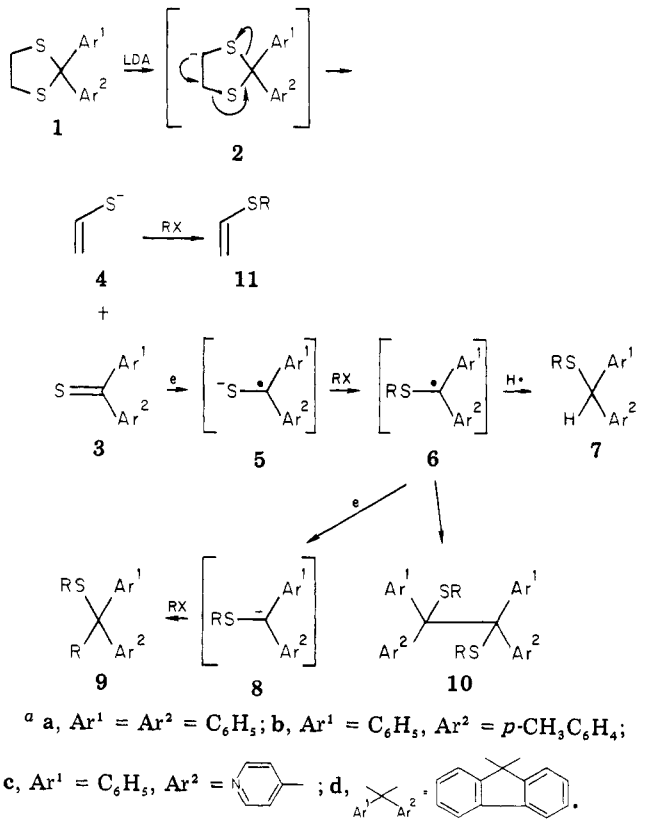
Several papers have appeared[1-6] in the literature which have dealt with the reaction involving cleavage of ethanediyl *S,S*-acetals to ethylene and dithiocarbonate. Recently, Wilson and co-workers have observed[7,8] the metalation of several ethanediyl *S,S*-acetals with *n*-butyllithium, which resulted in fragmentation to the corresponding thiocarbonyl compound and vinyl thiolate anion. The former has been further converted to thiols or sulfides via a process involving reduction, S-addition, C-addition, or double addition with excess *n*-butyllithium. We now report the fragmentation of ethanediyl *S,S*-acetals bearing two aromatic substituents at C-2 and the behavior of the resulting fragments, using the less nucleophilic lithium diisopropylamide (LDA),[9] which avoids nucleophilic butylation of the intermediate thiocarbonyl compound by *n*-butyllithium.

The reaction of the ethanediyl *S,S*-acetal of benzophenone or *p*-methylbenzophenone (**1a** or **1b**) with LDA in tetrahydrofuran proceeds via proton abstraction at C-4 followed by cycloelimination to afford the corresponding thioketone (**3a** or **3b**) and vinyl thiolate anion (**4**; Scheme I). The isolation of **3a** or **3b** was impossible, presumably because they are immediately converted to radical anions (**5**) by one-electron transfer[10] from LDA.

Scheme I[a]



[a] a, $Ar^1 = Ar^2 = C_6H_5$; b, $Ar^1 = C_6H_5$, $Ar^2 = p\text{-}CH_3C_6H_4$; c, $Ar^1 = C_6H_5$, Ar^2 = ; d, .

However, when the ethanediyl *S,S*-acetal of acetophenone[11] was submitted to similar fragmentation by LDA and subsequent protonation, the formation of thioacetophenone was evident from its characteristic color.

When the appropriate alkyl halide was added to the above reaction mixture containing **4** and **5**, the former was easily converted to the corresponding alkyl vinyl sulfide (**11**) and the latter to alkyl diarylmethyl sulfide (**7**). Though the exact mechanism is still in doubt, the radical anion **5** is thought to be alkylated with the alkyl halide to afford a radical species (**6**), which can produce the final product (**7**) by abstraction of a hydrogen radical from tetrahydrofuran.

Wilson and co-workers previously proposed[7,8] a very similar sequence for the reaction of the ethanediyl *S,S*-acetals of aliphatic ketones with *n*-butyllithium.

In this way a series of alkyl benzhydryl sulfides (**7a**) and their methylated compounds (**7b**) were produced in fairly good yields along with compounds **11** as byproducts (Table I).

When the same fragmentation–alkylation sequence was applied to the ethanediyl *S,S*-acetal of 4-benzoylpyridine (**1c**), a sulfide (**9c**) bearing a tertiary alkyl group was obtained in moderately good yields.

The sulfide **9c** may be produced in a process involving one-electron transfer[10] between **6c** similarly formed and LDA to afford an anion (**8c**), which on subsequent trapping by the remaining alkyl halide leads to **9c**.

An electron-withdrawing effect of the pyridyl group in **6c** would account for such the behavior of **6c**. In the case

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