Controlled-potential electrolysis was commenced at -0.8 V vs. SCE and continued until the current decayed to background level. Solution agitation was provided by magnetic stirring. Electrolysis duration was typically 2-3 h. After an electrolysis the anolyte and catholyte solutions were transferred to separate 5.0-mL volumetric flasks for analysis.

To carry out the series of chemical reactions, we dissolved SBr (0.178 g, 0.001 mol) and the desired amount of alkylating agent in 4.0 mL of AN in a 50-mL round-bottomed flask. The reaction was initiated when 5.0 mL (0.001 mol) of the appropriate tetraalkylammonium succinimide salt was added. Reactions were allowed to proceed for at least 24 h before analysis.

Identification and Determination of Products. The procedure employed to identify and determine succinimide and alkylated succinimides from VPC traces has been described.[14] Tri-*n*-butylamine and *n*-butyl bromide, which derived from the reaction of bromide ion with TBAF in the injection port, were also present in the VPC traces, but these decomposition products were not determined. Analysis of anolyte and catholyte solutions demonstrated that 2-3% of the total product yield was found in the anolyte. One particular SBr electrolysis mixture (Table I, expt 5) was analyzed by HPLC and linear-sweep voltammetry in addition to gas chromatography. The Corasil column used for HPLC was activated prior to use by heating overnight at 110 °C with a N_2 purge. The mobile phase was 99% CH_2Cl_2-1% CH_3CN for determination of *N*-*n*-butylsuccinimide and 97% CH_2Cl_2-3% CH_3CN for succinimide. The mobile phase flow rate was 1.0 mL/min for all runs. Component peaks were detected by UV absorbance at 254 nm; quantitative analyses were achieved by comparison of sample peak areas with those of authentic standards. Succinimide in the catholyte was determined by HPLC, VPC, and voltammetry; agreement among these three analytical methods was within 10%. *N*-*n*-Butylsuccinimide was determined by both HPLC and VPC, and the values obtained differed by less than 8%. A linear sweep voltammetric method for determination of bromide ion, utilizing the oxidation peak at +0.65 V vs. SCE, showed that the yield of bromide ion was 90%; this yield was based upon the initial SBr present plus the amount of *N*-*n*-butylsuccinimide formed during the electrolysis. With a separate electrolysis mixture (Table I, expt 12), the Volhard titration method was employed to determine that, based upon the number of moles of SBr, the bromide yield was 88%.

Analysis of the chemical reaction mixtures (Table II) required that SBr be determined as well as succinimide and *N*-alkylsuccinimides. The analytical scheme included determination of succinimide by standard additions by using the IR absorbance at 3280 cm^{-1} (N-H stretch). Spectra of reaction mixtures were obtained differentially in 0.2-mm cells with AN as a reference. Gas chromatography was used to determine *N*-alkylsuccinimides and the total of SBr and succinimide in chemical reactions. SBr decomposed to succinimide in the injection port, and thus a single peak was present for SBr and succinimide. However, since succinimide had been determined independently by IR, SBr could be estimated by difference. Uncertainty in the data for SBr, determined in this fashion, is probably ±10%. Bromide ion concentration following reaction of SBr with TBAS (Table II, expt 1) was determined by the Volhard titration method, and the yield was 97% based upon the number of moles of SBr.

Registry No. *N*-Bromosuccinimide, 128-08-5; succinimide, 123-56-8; *N*-butylsuccinimide, 3470-96-0; *N*-methylsuccinimide, 1121-07-9; *N*-benzylsuccinimide, 2142-06-5; 1-bromobutane, 109-65-9; butyl tosylate, 778-28-9; 1-chlorobutane, 109-69-3; methyl tosylate, 80-48-8; α-bromotoluene, 100-39-0; tetrabutylammonium succinimide, 74830-30-1; tetraethylammonium succinimide, 74830-35-6; succinimide anion, 28627-67-0; succinimidyl radical, 24344-83-0.

Hydroxymethyl Derivatives of 18-Crown-6 and [2.2.2]Cryptand: Versatile Intermediates for the Synthesis of Lipophilic and Polymer-Bonded Macrocyclic Ligands

Fernando Montanari*

Centro CNR and Istituto di Chimica Industriale dell'Università, Milano, Italy

Pietro Tundo*

Istituto di Chimica Organica dell'Università, Torino, Italy

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The synthesis of (hydroxymethyl)-18-crown-6 and of (hydroxymethyl)[2.2.2]cryptand is described. These systems allow facile binding of lipophilic chains and/or of polymeric matrices. In this way efficient chemically stable phase-transfer catalysts are obtained. Polymer-bound systems are easily recyclable without loss of catalytic activity. Use of these systems for the removal of lanthanide shift reagents from organic solutions is reported.

Use of multidentate macrocyclic and macrobicyclic polyethers is often limited by the difficulties of recovery at the end of reaction and, for cryptands, by the relatively complex multistep syntheses. The introduction of long alkyl chains, to make the polyether insoluble in water and soluble in nonpolar organic media, partially alleviates these problems.[1,2] An increased possibility of recycling is obtained by anchoring the polyether to a polymer support.[3]

An important use of polyether ligands is anion activation in nucleophilic reactions, particularly significant in the case of cryptates. It occurs both in nonpolar, homogeneous

(1) (a) Landini, D.; Montanari, F.; Pirisi, F. M. *J. Chem. Soc., Chem. Commun.* **1974**, 879-880. (b) Landini, D.; Maia, A.; Montanari, F.; Pirisi, F. M. *Gazz. Chim. Ital.* **1975**, *105*, 863-874. (c) Cinquini, M.; Tundo, P. *Synthesis* **1976**, 516-519. (d) Landini, D.; Maia, A.; Montanari, F.; Pirisi, F. M. *J. Chem. Soc., Perkin Trans. 2* **1980**, 46-51. (e) Makosza, M.; Ludwikow, M. *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 665-666. (f) Stott, P. E.; Bradshaw, J. S.; Parish, W. W. *J. Am. Chem. Soc.* **1980**, *102*, 4810-4815. (g) Mizuno, T.; Nakatsuji, Y.; Yanagida, S.; Okahara, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 481-484.

(2) (a) Cinquini, M.; Montanari, F.; Tundo, P. *J. Chem. Soc., Chem. Commun.* **1975**, 393-394. (b) Cinquini, M.; Montanari, F.; Tundo, P. *Gazz. Chim. Ital.* **1977**, *107*, 11-14. (c) Landini, D.; Maia, A.; Montanari, F.; Tundo, P. *J. Am. Chem. Soc.* **1979**, *101*, 2526-2530. (d) Landini, D.; Maia, A.; Montanari, F.; Rolla, F. *J. Chem. Soc., Perkin Trans. 2* **1981**, 821-824. (e) Clement, D.; Damm, F.; Lehn, J. M. *Heterocycles* **1976**, *5*, 477-484.

(3) (a) Cinquini, M.; Colonna, S.; Molinari, H.; Montanari, F.; Tundo, P. *J. Chem. Soc., Chem. Commun.* **1976**, 394-396. (b) Molinari, H.; Montanari, F.; Tundo, P. *Ibid.* **1977**, 639-641. (c) Montanari, F.; Tundo, P. *J. Org. Chem.* **1981**, *46*, 2125-2130. (d) Fukunishi, K.; Czech, B.; Regen, S. L. *Ibid.* **1981**, *46*, 1218-1221.

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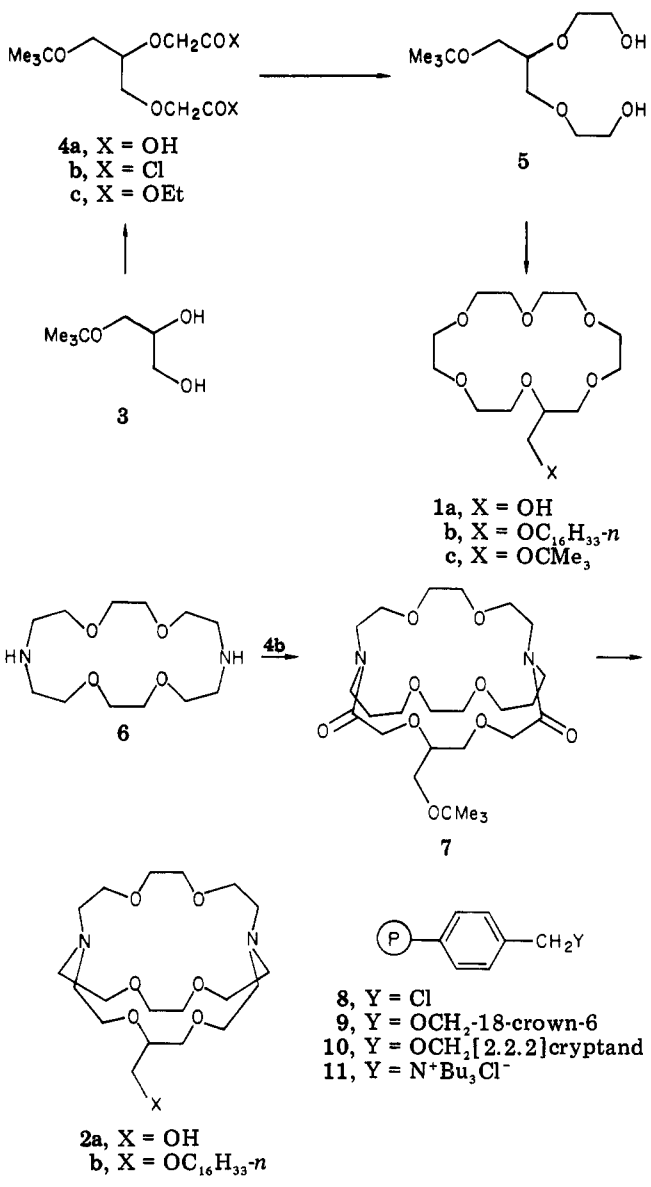
Scheme I



solutions and under phase-transfer conditions.[1-4] Polymer-linked systems are particularly attractive in the latter case, since the catalyst may be filtered at the end of the reaction and recycled indefinitely, provided that it is chemically stable in the reaction medium.

Lipophilic quaternary onium salts can easily be anchored to polymer supports, and they have been widely used as phase-transfer catalysts.[5] However, the relative instability of onium salts under severe conditions, due to Hofmann elimination and retro-Menschutkin reactions,[6] makes the use of polymer-supported crown ethers and cryptands preferable, in spite of their more complex synthesis. Only a few of these systems have been previously reported by us[3a-c] as well as by others.[3d,7] In this paper we describe the synthesis of (hydroxymethyl)-18-crown-6(1) and (hydroxymethyl) [2.2.2]cryptand (2), in which the presence of the hydroxymethyl group affords a very simple way to attach the two polyethers to any functionalized molecule.[8]

A variety of lipophilic and polymer-supported macrocyclic polyethers is thus available. They are efficient, stable, and easily recyclable phase-transfer catalysts. These same systems can be also used for selective complexation of cations both from aqueous and nonpolar organic solutions.

Table I. Observed Pseudo-First-Order Kinetic Constants for the Alkylation of Benzyl Methyl Ketone with 1-Bromobutane and Aqueous Sodium Hydroxide in the Presence of Polymer-Supported Phase-Transfer Catalysts

catalyst[a]	$10^5 k_{obsd}$,[b] s^{-1}	catalyst[a]	$10^5 k_{obsd}$,[b] s^{-1}
9	5.4, 5.3[c]	11	12.7, 3.9[c]
10	11.0, 10.5[c]		

[a] 0.01 molar equiv. [b] At 25 °C. [c] After two recycles of the catalyst.

Results and Discussion

3-*tert*-Butoxy-1,2-propanediol (3) was obtained from *tert*-butyl glycidyl ether[10] by treatment with formic acid followed by 50% aqueous sodium hydroxide. Condensation with chloroacetic acid afforded dicarboxylic acid **4a**, which was converted to diethyl ether **4c** and then reduced to diol **5** with $LiAlH_4$ (Scheme I). Reaction of **5** with triethyleneglycol ditosylate and KOH gave crown ether **1c**, which was converted with HBF_4 into (hydroxymethyl)-18-crown-6 (**1a**), isolated as its KBF_4 complex.

Condensation of acid dichloride **4b** with 1,10-diaza-18-coronand-6 (**6**)[11] under high-dilution conditions, subsequent reduction of the bicyclic diamide **7** with B_2H_6 in THF, and hydrolysis with 6 N HCl afforded hydroxymethyl derivative **2a**, isolated as its $NaBF_4$ cryptate.

By reaction with *n*-hexadecyl bromide in potassium *tert*-butoxide–*tert*-butyl alcohol, hydroxymethyl derivatives **1a** and **2a** gave *n*-hexadecyl ethers **1b** and **2b**, respectively. Condensation of **1a** and **2a** with (chloromethyl)polystyrene (**8**, 1% cross-linking with *p*-divinylbenzene) in the presence of potassium *tert*-butoxide in diglyme or DMF gave polymer-supported crown ether **9** and cryptand **10**, respectively.

Ethers **1b** and **2b** are practically insoluble in water but are soluble in nonpolar organic media: therefore, they show the best characteristics for use as phase-transfer catalysts.[12] Indeed, in addition to the analogous polymer-bonded systems **9** and **10**, they have been already tested as phase-transfer catalysts in some reactions,[8] such as Br–I and Br–CN exchanges in 1-bromooctane.

(4) (a) De Jong, F.; Reinhoudt, D. N. *Adv. Phys. Org. Chem.* **1980**, *17*, 279–433. (b) Lehn, J. M. *Pure Appl. Chem.* **1980**, *52*, 2303–2319.

(5) (a) Regen, S. L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 421–429. (b) Molinari, H.; Montanari, F.; Quici, S.; Tundo, P. *J. Am. Chem. Soc.* **1979**, *101*, 3920–3927. (c) Tomoi, M.; Ford, W. T. *J. Am. Chem. Soc.* **1981**, *103*, 3821–3832.

(6) (a) Dehmlow, E. V.; Dehmlow, S. S. "Phase Transfer Catalysis"; Verlag Chemie: Weinheim Bergstr. Germany, 1980; pp 53–54. (b) Dou, J. M.; Gallo, R.; Hassanaly, P.; Metzger, J. *J. Org. Chem.* **1977**, *42*, 4275–4276.

(7) (a) Smid, J. *Pure Appl. Chem.* **1976**, *48*, 343–353. (b) Bradshaw, J. D.; Stott, P. E. *Tetrahedron* **1980**, *36*, 461–510. (c) Mathias, L. J.; Al-Jumah, K. *Polym. News* **1979**, *6*, 9–18. (d) Tomoi, M.; Kihara, K.; Kakiuchi, H. *Tetrahedron Lett.* **1979**, 3485–3486. (e) Bogatskii, A. V.; Luk'yanenko, N. G.; Pastushok, V. N. *Dokl. Akad. Nauk SSSR* **1979**, *247*, 1153–1154.

(8) (a) Preliminary report: Montanari, F.; Tundo, P. *Tetrahedron Lett.* **1979**, 5055–5058. (b) Alternative syntheses of hydroxylmethyl-substituted crown ethers have been recently reported.[1c,3d,9]

(9) Czech, B. *Tetrahedron Lett.* **1980**, 4197–4198. (b) Ikeda, I.; Yamamura, S.; Nakatsuji, Y.; Okahara, M. *J. Org. Chem.* **1980**, *45*, 5355–5358.

(10) Ulbrich, V.; Makes, J.; Jurecek, M. *Collect. Czech. Chem. Commun.* **1964**, *29*, 1466–1475.

(11) Dietrich, B.; Lehn, J. M.; Sauvage, J. P.; Blanzat, *J. Tetrahedron* **1973**, *29*, 1629–1645.

(12) (a) Landini, D.; Maia, A.; Montanari, F. *J. Chem. Soc., Chem. Commun.* **1977**, 112–113. (b) Landini, D.; Maia, A.; Montanari, F. *J. Am. Chem. Soc. 1978*, *100*, 2796–2801.

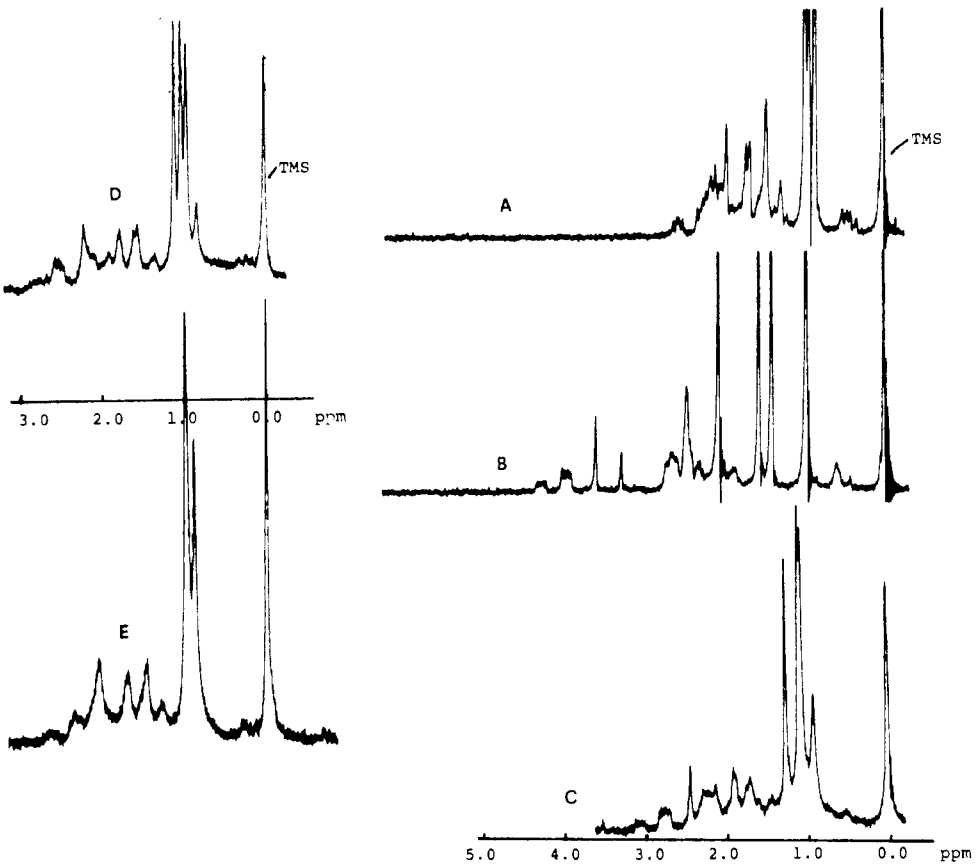


Figure 1. ^{1}H NMR spectrum (60 M Hz) of camphor: A, 0.2 M $CDCl_3$ solution; B, 0.25 molar equiv of $Eu(fod)_3$ added to C, 0.25 molar equiv of resin **10** added to B; D and E, 0.25 and 0.38 molar equiv of resin **9** added to B, respectively.

As stated above, a fundamental condition for the use of polymer bonded phase-transfer catalysts is their stability in the reaction conditions. An indication of the relative stabilities of polymer-supported ammonium salts **11**, crown ethers **9**, and cryptands **10** when used as catalysts under drastic phase-transfer conditions is reported in Table I. In the alkylation of benzyl methyl ketone with 1-bromobutane in the presence of 50% aqueous NaOH at 25 °C, tributyl ammonium salt **11** lost about two-thirds of its initial activity after two recycles (20 h total). Under the same conditions, crown ether **9** and cryptand **10** showed no relevant activity change.

The capability of polymer-bonded crown ethers and cryptands to efficiently extract cations from aqueous solutions is an important property, especially in the case of dangerous or expensive materials.[13] Suitable cations can be extracted from dilute aqueous solutions with a small excess of resin **9** or **10** swelled in toluene or methylene chloride and then recovered by washing the resin with acetone–water.[8a] This property has been used to return to the normal ^{1}H NMR spectrum of an organic compound after measurements in the presence of lanthanide shift reagents. Examples are reported in Figures 1 and 2. In Figure 1, absorptions of camphor, shifted downfield by addition of $Eu(fod)_3$, are reestablished as in the original spectrum upon progressive addition of polymer-bonded crown ether **9** or cryptand **10**. Similar behavior is observed in the spectrum of benzyl alcohols (Figure 2). In this case also, high-field absorptions due to the addition of $Pr(fod)_3$ are shifted downfield back to the original spectrum by addition of resin **9**. The complete disappearance from the spectrum of "fod" absorptions indicates that the latter too is absorbed into the solid phase, as the counterion of the lanthanide complexed by the macrocyclic polyether.

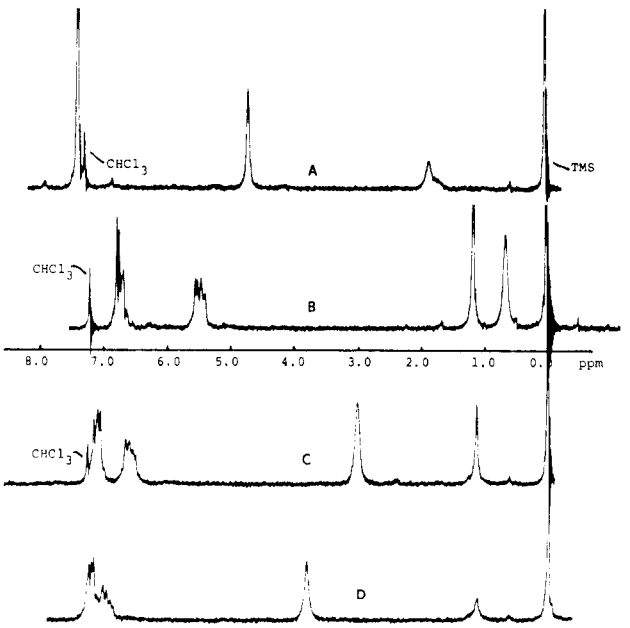


Figure 2. ^{1}H NMR spectrum (60 MHz) of benzyl alcohol: A, 0.2 M $CDCl_3$ solution; B, 0.25 molar equiv of $Pr(fod)_3$ added to A; C and D, 0.25 and 0.50 molar equiv of resin **9** added to B, respectively.

Experimental Section

General Methods. ^{1}H NMR spectra were recorded on a Hitachi Perkin-Elmer R-24B 60-MHz ^{1}H NMR spectrometer with Me_4Si as an internal standard. IR spectra were recorded on a Beckman IR-18A infrared spectrometer. GLC analyses were accomplished on a Varian 1400 instrument by using columns of 5% SE-30 on Chromosorb supports at 180–235 °C. Organic and

(13) Lehn, J. M. *Acc. Chem. Res.* **1978**, *11*, 49–57.

inorganic reagents were ACS reagent grade. (Chloromethyl)-polystyrene was purcahsed from Fluka AG.

3-*tert*-Butoxy-1,2-propanediol (3). *tert*-Butyl glycidyl ether [10] (141 mL, 1 mol) was added dropwise to 83 mL (2.2 mol) of 99% formic acid, keeping the temperature ≤30 °C. The mixture was left at room temperature for 12 h, and then a solution of sodium hydroxide (100 g, 2.5 mol) in 100 mL of water was added, keeping the temperature ≤40 °C. The organic phase was separated, and the aqueous phase was extracted several times with methylene chloride. The combined organic solutions were dried and evaporated, and the residue was distilled under vacuum to give 77.0 g (52%) of **3**: colorless oil; bp 114 °C (14 torr); IR (CCl_4) 3400 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.25–4.0 (m, 7 H), 1.20 (s, 9 H). Anal. Calcd for $C_7H_{16}O_3$: C, 56.73; H, 10.88. Found: C, 57.01; H, 10.64.

Diethyl 3,6-Dioxa-4-(*tert*-butoxymethyl)-1,8-octanedicarboxylate (4c). A solution of 23.6 g (0.25 mol) of chloroacetic acid in 80 mL of *tert*-butyl alcohol was added slowly to a refluxing mixture of 14.8 g (0.1 mol) of **3** and 56.1 g (0.5 mol) of potassium *tert*-butoxide in 400 mL of *tert*-butyl alcohol. Reflux and stirring were continued for 2 h. *tert*-Butyl alcohol was evaporated under vacuum; 100 mL of water was added to the residue. The aqueous phase was extracted with ethyl ether, acidified with hydrochloric acid, and repeatedly extracted with methylene chloride. The combined methylene chloride solutions were dried and evaporated under vacuum, affording acid **4a** as a noncrystallizable oil. Crude **4a** was dissolved in 400 mL of a 1:2 (v/v) mixture of absolute ethanol and benzene, 2.0 g of *p*-toluenesulfonic acid was added, and the mixture was heated to reflux for 4 h, with continuous circulation of condensed vapors through anhydrous sodium sulfate. The solvent was removed, the ethereal solution of the residue washed with aqueous sodium hydrogen carbonate, and the product distilled under vacuum to give 19.2 g (60%) of **4**: colorless oil; bp 135 °C (0.3 torr); ^1H NMR ($CDCl_3$) δ 4.32 (s, 2 H), 4.12 (s, 2 H), 4.18 (q, 4 H), 3.30–3.90 (m, 5 H), 1.28 (t, 6 H), 1.18 (s, 9 H). Anal. Calcd for $C_{15}H_{28}O_7$: C, 56.23; H, 8.81. Found: C, 56.19; H, 8.77.

3,6-Dioxa-4-(*tert*-butoxymethyl)-1,8-octanediol (5). Ester **4c** (23.6 g, 0.1 mol) was reduced with 10.0 g (0.26 mol) of lithium aluminum hydride in 300 mL of boiling tetrahydrofuran (THF). After the mixture was brought to room temperature, a mixture of 10 mL of water and 50 mL of THF, 10 mL of 15% aqueous sodium hydroxide, and a mixture of 50 mL of water and 50 mL of THF were added consecutively. The powdered inorganic material was filtered and washed several times with THF. The combined organic solutions were evaporated, and the residue was distilled to give 21.1 g (90%) of **5**: colorless oil; bp 127–130 °C (0.3 torr); ^1H NMR ($CDCl_3$) δ 3.20–4.20 (m, 15 H), 1.20 (s, 9 H). Anal. Calcd for $C_{11}H_{24}O_5$: C, 55.91; H, 10.24. Found: C, 55.76; H, 10.44.

2-(*tert*-Butoxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecane (1c). To a refluxing mixture of 23.6 g (0.1 mol) of **5** and 14.0 g of potassium hydroxide in 100 mL of THF and 10 mL of water was added with stirring 45.8 g (0.1 mol) of triethylene glycol ditosylate. Reflux and stirring were continued for 3 h. The solvent was removed, and the residue was diluted with 100 mL of water and continuously extracted for several days with ethyl ether. Ethyl ether was evaporated, the small amount of water was azeotropically removed with benzene, and the residue was stirred for 10 h with excess solid KBF_4 in methylene chloride. Noncomplexed salt was filtered, and the solvent was evaporated. Addition of diethyl ether afforded **1c** as a KBF_4 complex: 18.1 g (38%); mp 125–126 °C (from methylene chloride–ethyl ether); ^1H NMR ($CDCl_3$) δ 3.50–3.95 (m, 25 H), 1.20 (s, 9 H). Anal. Calcd for $C_{17}H_{34}O_7 \cdot KBF_4$: C, 42.87; H, 7.20. Found: C, 42.63; H, 7.26. A mixture of the KBF_4 complex of **1c** (5 g) and 25 mL of water was continuously extracted with ethyl ether for 15 h. Ethyl ether was removed, and the residue was azeotropically dried with benzene. The fraction of crown ether extracted as the KBF_4 complex was eliminated by addition of ethyl ether and subsequent filtration. Vacuum distillation of the residue gave **1c**: 3.1 g (85%); colorless oil; bp 166–167 °C (0.3 torr); n^{25}_D 1.4620; ^1H NMR ($CDCl_3$) δ 3.35–3.95 (m, 25 H), 1.18 (s, 9 H). Anal. Calcd for $C_{17}H_{34}O_7$: C, 58.26; H, 9.78. Found: C, 58.13; H, 9.43.

2-(Hydroxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecane (1a). KBF_4 Complex. To a solution of 10.0 g (0.02 mol) of **1c**, as the KBF_4 complex, in 30 mL of methylene chloride was added 4.0 mL of 54% tetrafluoroboric acid–ethyl ether complex, and the mixture was left at room temperature for 20 min. The acid was neutralized with solid potassium carbonate, inorganic salts were filtered, the solvent was evaporated, and compound **1a** was precipitated as the KBF_4 complex by addition of ethyl ether: 7.1 g (80%); mp 144–145 °C (from methylene chloride–ethyl ether); ^1H NMR ($CDCl_3$) δ 3.70 (s); mass spectrum, *m/e* 294 (M^+). Anal. Calcd for $C_{13}H_{26}O_7 \cdot KBF_4$: C, 37.16; H, 6.24. Found: C, 37.17; H, 6.03.

2-[(*n*-Hexadecyloxy)methyl]-1,4,7,10,13,16-hexaoxacyclooctadecane (1b). Sodium hydride (0.56 g, 24 mmol) was added to a mixture of 2.0 g (4.8 mmol) of **1a** (KBF_4 complex) and 30 mL of anhydrous THF. The mixture was heated to reflux, and a solution of 1.7 g (5.6 mmol) of 1-bromohexadecane in 20 mL of THF was added dropwise with stirring. Heating and stirring were continued for 30 min. The solvent was removed, a little water was added to the residue in order to dissolve the inorganic salts, and the organic material was extracted with ethyl ether. The solvent was dried and evaporated to afford **1b**: 2.2 g (89%); mp 38–39 °C (from pentane); ^1H NMR ($CDCl_3$) δ 3.25–4.05 (m, 27 H), 1.0–1.8 (br s, 28 H), 0.90 (t, 3 H); mass spectrum, *m/e* 518 (M^+); mass spectrum with ammonia as a reagent *m/e* 536 ($M + NH_4^+$). Anal. Calcd for $C_{29}H_{58}O_7$: C, 67.14; H, 11.27. Found: C, 66.97; H, 11.08.

4,7,13,16,21,24-Hexaoxa-2,9-dioxo-5-(*tert*-butoxymethyl)-1,10-diazabicyclo[8.8.8]hexacosane (7). A 50% aqueous solution (5 mL) of sodium hydroxide was added dropwise to a stirred solution of 4.8 g (0.015 mol) of diester **4c** in 5 mL of methanol, keeping the temperature ≤40 °C. The mixture was left at room temperature for 3 h, extracted with 70 mL of ethyl ether, and acidified with hydrochloric acid. Repeated extractions with methylene chloride, drying of the organic solution, and evaporation afforded 3.85 g (97%) of acid **4a**: noncrystallyzable oil; ^1H NMR ($CDCl_3$) δ 9.80 (br s, 2 H), 4.32 (s, 2 H), 4.18 (s, 2 H), 3.30–3.95 (m, 5 H), 1.20 (s, 9 H). A mixture of 3.97 g (0.015 mol) of **4a**, 12 mL of oxalyl chloride, and 2 drops of pyridine in 30 mL of anhydrous benzene was left at room temperature for 10 h. Excess oxalyl chloride was removed under vacuum, and anhydrous benzene was added twice and then removed to give the dichloride **4b**: nondistillable oil; ^1H NMR ($CDCl_3$) δ 4.68 (s, 2 H), 4.50 (s, 2 H), 4.35–4.28 (m, 5 H), 1.22 (s, 9 H).

A solution of **4b** in 500 mL of anhydrous benzene and a solution of 3.93 g (0.015 mol) of 1,10-diaza-18-coronand-6 (**6**)[11] and 3.34 g (0.033 mol) of triethylamine in 500 mL of anhydrous benzene were simultaneously dropped into 500 mL of the same solvent over an 8-h period, with vigorous stirring. Triethylamine hydrochloride was filtered, the solvent, was removed, and the crude reaction mixture was purified by chromatography on a short column of alumina (chloroform) to give **7**: 4.85 g (66%); nondistillable oil; ^1H NMR ($CDCl_3$) δ 3.20–4.90 (m, 37 H), 1.18 (s, 9 H). Anal. Calcd for $C_{23}H_{42}N_2O_9$: C, 56.31; H, 8.63; N, 5.71. Found: C, 55.99; H, 8.42; N, 5.59.

4,7,13,16,21,24-Hexaoxa-5-(hydroxymethyl)-1,10-diazabicyclo[8.8.8]hexacosane (2a). $NaBF_4$ Complex. A diborane solution (excess) was prepared from 15.6 mL of boron trifluoride–ethyl ether complex and 3.42 g of sodium borohydride in 80 mL of THF and kept at 0 °C. A solution of 4.85 g (0.01 mol) of **7** in 100 mL of anhydrous THF was added dropwise at 0 °C over a 0.5-h period, and the mixture was kept at room temperature for 0.5 h and then refluxed for 2 h. Excess diborane was destroyed with a few milliliters of water and the solvent evaporated. The borane complex obtained was heated to reflux for 3 h with 80 mL of 6 N HCl. The solvent was removed under vacuum and the residue neutralized with 15% aqueous sodium hydroxide. Repeated extraction with methylene chloride, drying, evaporation of the solvent, and final addition of ethyl ether afforded **2a** as $NaBF_4$ complex: 3.53 g (70%); mp 250 °C; ^1H NMR ($CDCl_3$) δ 3.35–4.05 (m, 26 H), 2.65 (br t, 12 H); mass spectrum, *m/e* 406 (M^+). Anal. Calcd for $C_{19}H_{38}N_2O_7NaBF_4$: C, 44.19; H, 7.42; N, 5.42. Found: C, 44.43; H, 7.57; N, 5.55.

4,7,13,16,21,24-Hexaoxa-5-[(hexadecyloxy)methyl]-1,10-diazabicyclo[8.8.8]hexacosane (2b). A mixture of 2.0 g (3.9 mmol) of **2a**, as a $NaBF_4$ complex, sodium *tert*-butoxide (prepared from 0.13 g, 5.7 mmol, of Na), and 1.73 g (5.7 mmol) of 1-bromohexadecane in 50 mL of *tert*-butyl alcohol was refluxed for

1 h. After removal of the solvent, the reaction mixture was acidified with aqueous HBF_4, and the ethyl ether soluble products were removed. Addition of aqueous sodium hydroxide, extraction with methylene chloride, drying, and removal of the solvent yielded 2.15 g (75%) of **2b** as the $NaBF_4$ complex, after crystallization from benzene–ethyl ether: mp 84–85 °C; ^1H NMR ($CDCl_3$) δ 3.2–4.0 (m, 27 H), 2.45–2.85 (br t, 12 H), 1.05–1.70 (br s, 28 H), 0.90 (s, 3 H); mass spectrum, m/e 630 (M^+). Anal. Calcd for $C_{35}H_{70}N_2O_7NaBF_4$: C, 56.75; H, 9.53; N, 3.78. Found: C, 56.67; H, 9.34; N, 3.81.

Polymer-Supported 18-Crown-6 (9). (Chloromethyl)polystyrene (8), 1% cross-linked with *p*-divinylbenzene (1.04 mequiv of Cl/g; 3.0 g, 3.12 mmol, of organic chlorine) was added to a stirred solution of 1.96 g (4.7 mmol) of **1a**, as a KBF_4 complex, and 0.70 g (6.3 mmol) of potassium *tert*-butoxide in 40 mL of diglyme at 80 °C. The temperature and stirring were maintained for 6 h. The mixture was acidified with hydrochloric acid, filtered, and successively washed with water, methanol, methylene chloride, and ethyl ether to give 3.70 g of functionalized resin **9**. Spectrophotometric titration with excess potassium picrate[3c] gave a crown ether content of 0.73 mequiv/g, in agreement with the observed weight increase and corresponding to 88% functionalization.

Polymer-Supported [2.2.2]Cryptand (10). One percent cross-linked (chloromethyl)polystyrene (8; 1.04 mequiv of Cl/g; 3.0 g, 3.12 mmol, of organic chlorine) was condensed with **2a**, as a $NaBF_4$ complex (2.41 g, 4.7 mmol), under conditions similar to those described for resin **9** but with *N,N*-dimethylformamide (DMF, 40 mL) instead of diglyme. After repeated washing as described above as well as with aqueous lithium hydroxide, 4.15 g of functionalized resin **10** was obtained. Spectrophotometric titration with excess potassium picrate[3c] gave a cryptand content of 0.75 mequiv/g in agreement with the observed weight increase and corresponding to 100% functionalization.

Polymer-Supported Tributylammonium Salt 11. The tributylammonium salt was prepared by reaction of 1% cross-linked (chloromethyl)polystyrene (1.04 mequiv of Cl/g) with excess tributylamine as previously described.[5b] It had a Cl^- content of 0.56 mequiv/g (64% of the expected value). When the catalyst was recovered from the reaction mixture (see below) the halide ion content ($Cl^- + Br^-$) progressively decreased in agreement with the observed rate constants.

Kinetic Measurements. Kinetics were run, as previously described,[5b] in a flask thermostated at 25 ± 0.02 °C, with a mixture of benzyl methyl ketone (2.0 mmol), 1-bromobutane (2.4 mmol), and 50% aqueous NaOH (2.0 mL) and 0.02 mmol of catalyst (stirring speed 1300 ± 50 rpm; conditioning time 3 h at 25 °C without 1-bromobutane). The reactions were followed by GLC analysis (5% SE-30 on Varaport), and results were corrected by calibration with standard mixtures. The pseudo-first-order rate constants (k_{obsd}) were obtained by plotting ln [substrate] vs. time and determining the slope of the straight lines by the least-square method ($r \geq 0.995$). When catalysts were recovered for reuse or for halide ion content determination, higher amounts of resin were used, all other conditions remaining the same. Ethyl ether and water were added, and the catalyst was filtered and washed with ethyl ether, methanol, aqueous hydrochloric acid, and water until the disappearance of acidity and then with methanol and ethyl ether.

Complexation of Eu^{3+} and Pr^{3+} by 9 and 10. To a 0.2 M $CDCl_3$ solution of camphor or benzyl alcohol was added a 0.05 M $CDCl_3$ solution of $Eu(fod)_3$ or $Pr(fod)_3$ (0.25 molar equiv). ^1H NMR spectra, before and after the addition of the shift reagents, are reported in Figures 1 and 2 (spectra A and B). Further addition of 0.25–0.50 molar equiv of polymer-bound crown ether or cryptand afforded within a few seconds spectra C–E and spectra C and D of Figures 1 and 2, respectively. The poor resolution of these spectra was due to the presence of the insoluble resins in the analyzed mixtures. The resolution improved with time as a consequence of the separation of the resin; after filtration, the resolution of the spectra was identical with that of the starting compounds. A cholesterol solution was treated in the same way, giving similar NMR results. After addition of 4 molar equiv of polymer-supported crown ether **9** with respect to $Eu(fod)_3$, the resin was filtered and washed with methylene chloride. The collected organic solutions were evaporated to give the recovered cholesterol, mp 146 °C (original, mp 147 °C).

Registry No. **1a**·KBF_4, 80540-30-3; **1b**, 74339-04-1; **1c**, 74339-05-2; **1c**·KBF_4, 80533-25-1; **2a**·$NaBF_4$, 80540-32-5; **2b**·$NaBF_4$, 80533-27-3; **3**, 74338-98-0; **4a**, 74338-99-1; **4b**, 74339-01-8; **4c**, 80515-71-5; **5**, 74339-00-7; **6**, 23978-55-4; **7**, 74339-02-9; *tert*-butyl glycidyl ether, 7665-72-7; benzyl methyl ketone, 103-79-7; 1-bromobutane, 109-65-9; camphor, 76-22-2; benzyl alcohol, 100-51-6; cholesterol, 57-88-5.

Alkaloid Synthesis via Intramolecular Ene Reaction. 2. Application to *dl*-Mesembrine and *dl*-Dihydromaritidine

Gary E. Keck*† and Robert R. Webb II

Department of Chemistry, The University of Utah, Salt Lake City, Utah 84112

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The total syntheses of mesembrine (**2**) and dihydromaritidine (**3**), alkaloids of the genera *Sceletium* and *Amaryllis* (respectively), are described. The key strategy in each case involves the intramolecular ene cyclization of an appropriately constructed acylnitroso olefin, giving cyclic hydroxamic acid ("ene product") **12**. Reduction of the hydroxamic acid to the lactam **4** is followed by N-methylation and hydroxylation at position C-6 via bromohydrin **15**, introducing the oxygen functionality present in **2**. Removal of bromine, oxidation of the alcohol to the keto lactam **13**, and reductive removal of the lactam carbonyl gave racemic mesembrine. Removal of bromine from bromohydrin **20**, obtained from lactam **4**, followed by reduction with lithium aluminum hydride and Pictet–Spengler cyclization gave dihydromaritidine (**3**).

Introduction

Previous investigations of electrocyclic reactions in which the acylnitroso moiety (RCONO) functions as a dienophile or an enophile have indicated the utility of such processes in the synthesis of a variety of nitrogen-containing materials. Intramolecular [4 + 2] cycloaddition utilizing an acylnitroso group as dienophile has been employed in construction of the pyrrolizidine alkaloids retronecine and heliotridine.[1] The perhydroindole skeletons characteristic of the *Amaryllis* and *Sceletium* alkaloids are easily con-

† Alfred P. Sloan Foundation Fellow, 1981–1983.

(1) Keck, G. E.; Nickell, D. G. *J. Am. Chem. Soc.* **1980**, *102*, 3632.

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