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hydroxy-2,5,5-trimethyldecalin (Table I), ^{1}H NMR chemical shifts and coupling constants (Table II), a drawing illustrating the shielding of the axial methyl group in **5b** (Figure 1), and the 360-MHz ^{1}H NMR spectrum of **2c** with various amounts of shift reagent added (Figure 2) (4 pages). Ordering information is given on any current masthead page.

Poly(ethylene glycols) as Soluble, Recoverable, Phase-Transfer Catalysts

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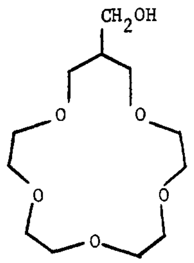
Poly(ethylene glycols) (PEG's) of molecular weights from 1500 to 6800 g/mol can be quantitatively precipitated from benzene, acetone, acetonitrile, methanol, or methylene chloride by addition of ethyl ether. This property offers the possibility of designing various soluble but recoverable materials such as catalysts and synthetic intermediates. Other work has shown that glymes and PEG's can act as phase-transfer catalysts (PTC's),[1-7] presumably operating by the same mechanism as crown ethers. However, the potential recoverability of these catalysts has not been described. A soluble, recoverable PTC provides an interesting alternative to the popular practice[8-12] of immobilizing PTC's on insoluble polymer backbones. In the present paper we describe the attachment of crown ethers to PEG's and examine the utility of PEG and PEG crown as soluble, recoverable PTC's.

The crown ethers (hydroxymethyl)-16-crown-5 (**1**), (hydroxymethyl)-19-crown-6 (**2**), and diaza-18-crown-6 (**3**) were attached to a PEG of molecular weight 3400 or 6800 g/mol as shown in eq 2 and 3. To indicate the molecular weight of the polymer backbones, we will use notation of the type **5**-3400, where the number after the hyphen denotes the PEG molecular weight.



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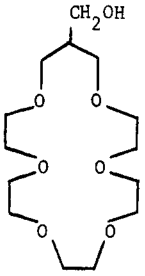

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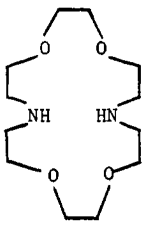

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Table I. Partitioning of Polyethers between Equal Volumes of Water and Methylene Chloride and between Water and Benzene at 25 °C

ether	% in organic phase CH_2Cl_2 [a]	C_6H_6 [b]
15-crown-5	68	
18-crown-6	75	
PEG-1000	80	
PEG-6800	75 (99)[b]	0.1

[a] Measured by HPLC beginning with a 5% (w/w) solution in water. Results are accurate within 3%. [b] Measured by using ^{14}C-labeled PEG and scintillation counting, starting with 0.25 mM PEG in water.

Table II. Phase Transfer of Metal Picrates from Water into Methylene Chloride[a]

	[PTA]		% in CH_2Cl_2 [b]	
PTA	g/100 mL of soln	M × 10^3	Na picrate	K picrate
none			0.7	0.7
15-crown-5	0.013	0.58	1.5	1.7
18-crown-6	0.015	0.56	2.4	17.3
PEG-1000	0.047	0.47	2.0	8.2
	0.181	1.81	3.9	14.5
PEG-6800	0.242	0.36	4.7	20.8
	0.181	0.27	3.6	19.2
5-3400	0.181	0.50		18.8
6-3400	0.181	0.49		18.1

[a] Aqueous potassium picrate and sodium picrate were 0.0954 and 0.085 mM, respectively. [b] Error limits ±0.1% for sodium picrate and ±0.5% for potassium picrate.

$$\text{PEG–CH}_2\text{OH} + \text{TsCl} \xrightarrow[\text{NaH}]{\text{CH}_2\text{Cl}_2} \text{PEG–CH}_2\text{OTs} \qquad (1)$$

$$\underset{\mathbf{1,\,2}}{\text{ROH}} + \text{PEG–CH}_2\text{OTs} \xrightarrow[\text{C}_6\text{H}_6]{\text{NaH}} \underset{\substack{\mathbf{5},\ \text{R} = \mathbf{1}\\ \mathbf{6},\ \text{R} = \mathbf{2}}}{\text{PEG–CH}_2\text{OR}} \qquad (2)$$

$$\underset{\mathbf{3}}{\text{R}_2\text{NH}} + \text{PEG–CHO} \xrightarrow[\text{CH}_3\text{OH}]{\text{NaCNBH}_3} \underset{\mathbf{7}}{\text{PEG–CH}_2\text{NR}_2} \qquad (3)$$

Preparation of the PEG tosylate has been reported by Mutter.[13] However, upon repeating this procedure, we found by HPLC analysis that extensive chain cleavage and molecular weight reduction had occurred. The NaH–TsCl method (eq 1) gave product with no chain cleavage. The crown alcohols **1** and **2** were prepared by the method of Tomoi et al.[14] We found it was critical in following this method that (a) the reaction of glycol and 3-chloro-2-(chloromethyl)-1-propene be conducted by very slow (24–48 h) addition of reagents, (b) potassium hydride rather than sodium hydride be used in the preparation of methyl-19-crown-6, and (c) the water solubility of the alcohols be considered in the hydroboration of the methylene crowns.

Compounds **5**–**7** are readily soluble in benzene, acetonitrile, methylene chloride, and acetone, so phase-transfer

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Table III. Pseudo-First-Order Rate Constants for Reaction of Benzyl Bromide with Potassium Acetate (Solid) and PTC in Acetonitrile[a]

	[PTC]			
PTC	M	g/10 mL of soln	10^3k, min^{-1}	k/k_0
none			0.048 ± 0.05	1
18-crown-6	0.076	0.2	70 ± 1	150
PEG-6800	0.0029	0.2	9.1 ± 0.3	19
	0.0058	0.4	16 ± 1	33
7-6800	0.0028	0.2	13 ± 1	26
PEG-3400	0.0059	0.2	6.6 ± 0.2	14
5-3400	0.0055	0.2	9.5 ± 0.1	20
6-3400	0.0055	0.2	6.5 ± 0.4	14

[a] Benzyl bromide, 1.7 M; potassium acetate, 3.4 M; and temperature = 25–28 °C.

of solid salts into these organic liquids should be possible if **5**–**7** are effective phase-transfer agents (PTA's). We have examined the partitioning of PEG-6800 between water and several organic liquids (Table I) by scintillation counting of carbon-14-labeled PEG and by liquid chromatographic analysis. Methylene chloride is the only solvent of the ones examined which is favored by PEG in partitioning relative to water. Consequently, it appears that phase-transfer experiments with aqueous salts and PEG's as PTC's would best be conducted with methylene chloride as the organic phase.

In order to assess the ability of the crown polymers to act as PTA's, we have determined the extent of transfer of sodium and potassium picrate from water into methylene chloride in the presence of crown ethers, PEG's, and polymer-attached crowns **5** and **6** (Table II). As can be seen, PEG and PEG crown ethers are effective as PTA's and show pronounced selectivity for potassium over sodium; this selectivity on the part of PEG itself is especially intriguing and must result from a steric preference for coils of a size more compatible with potassium than with sodium.[4] It is also interesting and puzzling that PEG-6800 is a more effective PTA than PEG-1000, even when the two are compared on an equal-mass basis. Comparison of the monomeric crowns with PEG-6800 and the polymer-bound crowns shows comparable PTA activity among the agents. A more precise comparison is hindered by the much greater molecular weight of the polymeric materials. A final point of interest is that the bound form of the smaller crown **1** (**5**-3400) is more effective than that of the larger crown **2** (**6**-3400) at transferring the potassium salt into methylene chloride.

The ability of the PEG's, PEG-bound crowns, and 18-crown-6 to catalyze the reaction of potassium acetate with benzyl bromide (eq 4) was determined (Table III). All

$$C_6H_5CH_2Br + CH_3COOK \xrightarrow[PTC]{CH_3CN} C_6H_5CH_2O_2CCH_3 + KBr \quad (4)$$

of the materials examined are effective catalysts, although not to the extent of 18-crown-6. Several results are noteworthy. First, PEG-6800 is a more effective catalyst that PEG-3400 when the two compounds are compared on an equal-mass basis. This result relates to that mentioned earlier for the metal–picrate partitioning by PEG-6800 and PEG-1000. Again the difference must be due to the preference for a specific type of coiling in the PEG's. It is also interesting that **5**-3400 is a more effective catalyst than **6**-3400; this result is in agreement with the earlier observation that the smaller crown is more effective in transferring potassium picrate into methylene chloride.

As a final point regarding the utility of the PEG materials as recoverable PTC's it remains to demonstrate their recoverability. We have carefully measured the extent of recovery of the PEG's and derivatives **5**–**7** from methylene chloride and acetonitrile by ether precipitation. In every case recovery was essentially quantitative, with only minor loss of material on glassware surfaces.

Experimental Section

Infrared spectra were recorded on a Beckman Acculab 1, ultraviolet–visible spectra on a Perkin-Elmer Hitachi 200 spectrometer, and proton NMR spectra on a Bruker HFX 90/2 spectrometer. Gas chromatographic analyses of the mixture of benzyl bromide and benzyl acetate (for the kinetics of Table III) were performed on a Varian 4600 gas chromatograph with a flame-ionization detector and a 9 ft × 0.125 in. column of SE-30 (5%) of 60/80 Chromosorb. HPLC analyses were performed on a Perkin-Elmer Series 2 chromatograph, with a UV-visible detector, an LDC 1107 RI detector, and a 30-cm Varian TSK 2000 SW column. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. Benzene was dried by being stirred over 4A molecular sieves for 48 h and distilled from sodium.

PEG-3400 Ditosylate. PEG-3400 (Union Carbide; 3.4 g) was dissolved in 15 mL of dry benzene, added dropwise to a suspension of 0.08 g of sodium hydride in 15 mL of benzene, and stirred for 1 h under nitrogen. The mixture was filtered and cooled to 15 °C. Tosyl chloride (5 g) dissolved in benzene (10 mL) was added dropwise. The solution was stirred for 18 h at room temperature and filtered. The crude product was precipitated by dropwise addition to 400 mL of ethyl ether. This precipitation process was repeated twice. The molecular weight of the ditosylate was determined by size-exclusion chromatography (SEC) on a calibrated column (2900 ± 100 g/mol) and by hydrolysis followed by titration of the released acid (3100 ± 20 g/mol). The starting PEG was also examined by SEC and found to have a molecular weight of 3300 ± 100 g/mol. The rate of hydrolysis was determined by conductimetric monitoring to be 5.18×10^{-4} s^{-1} at 100 °C. UV analysis of the ditosylate showed strong absorption peaks at 265, 255, 235, and 200 nm. Log ϵ at 265 nm is calculated to be 2.42 by assuming a molecular weight of 3100 g/mol; this value compares favorably to that of other tosylates (e.g., α-cyclodextrin tosylate[15]).

PEG-3400–16-Crown-5 (5). (Hydroxymethyl)-16-crown-5 (**1**, 0.21 g) dissolved in 10 mL of dry benzene was added dropwise under nitrogen to 0.026 g of sodium hydride suspended in 20 mL of dry benzene and stirred for 20 min; the solution turned pale brown. PEG-3400 ditosylate dissolved in 50 mL of dry benzene was added over a 30-min period. The reaction mixture was stirred for 12 h at room temperature and for 20 h at 50 °C. The reaction mixture was concentrated to half its original volume by rotary evaporation and added dropwise to 300 mL of diethyl ether to precipitate the product. The solid product was dissolved in 10 mL of methylene chloride and chromatographed on a small (4.5 in. × 1 in.) alumina column (70/30 methanol/methylene chloride eluent) to remove sodium tosylate. SEC confirmed an increase in molecular weight of 240 ± 100 g/mol; the expected increase was 168 g/mol. UV analysis revealed no absorption at >200 nm. The yield was 0.94 g (64%).

PEG-3400–19-Crown-6 (6). This compound was prepared as described for **5**.

PEG-6800 Dialdehyde. Pyridinium chlorochromate (1.5 mmol) was suspended in methylene chloride (ca. 2 mL), and the PEG (1 mmol in 10 mL of CH_2Cl_2) was added rapidly at room temperature. After 2 h the polymer was precipitated by being dropped into ethyl ether, and then purified by chromatography on neutral alumina with acetone as the eluent. The product gave a positive Tollen's test and was revealed by SEC to be unchanged in molecular weight (yield 94%). We have had difficulty reproducing this oxidation procedure and are in the process of developing more efficient methods for preparation of this aldehyde.

PEG-6800–Diaza-18-crown-6 (7). The general reductive-amination procedure of Borch[16] was used with 5 g of PEG-6800

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dialdehyde and 0.55 g of diaza-18-crown-6 (Parish Chemical Co.). The product gave a negative Tollen's test, revealed no chain cleavage on SEC, and gave a nitrogen analysis of 1.02% (theoretical 0.8%). The yield was 96%.

Kinetic Measurements. Acetonitrile was dried by being stirred with calcium hydride until gas evolution ceased, fractionally distilled from diphosphorus pentoxide (5 g/L) in an all-glass apparatus, refluxed over calcium hydride (5 g/L) for at least 1 h, and slowly distilled (81.6 °C) from calcium hydride. The first 5% and the last 10% of the final distillate were discarded. Potassium acetate was dried at 90–100 °C for at least 2 days.

Dry acetonitrile (6 mL) was added to the PTA (0.2 or 0.4 g) and dry potassium acetate (6.67 g, 3.4 M) in a septum-topped Erlenmeyer flask. The heterogeneous system was stirred for 30 min before benzyl bromide (4 mL, 1.7 M) was added. Aliquots (0.2 mL) were withdrawn, diluted in acetonitrile (2 mL), and injected into the gas chromatograph. For PTA's of limited availability, a 5 mL total volume reaction was run (everything used in half the above amounts).

Results of the pseudo-first-order reaction were analyzed by plotting ln $(A_0/A_0 - x)$ vs. time (minutes) where A_0 is the initial reactant concentration (benzyl bromide) and $A_0 - x$ is the reactant concentration at time t. Duplicate reactions were normally followed through 3 half-lives and gave correlation coefficients better than 0.999.

Extraction Studies. The aqueous metal picrate solutions (0.0954 mM in potassium picrate or 0.085 mM in sodium picrate) were extracted with an equal volume of methylene chloride containing the PTA. The solutions were then analyzed by spectrophotometric analysis of the picrate absorptions at 357 nm in water ($\epsilon = 1.5 \times 10^4\ M^{-1}\ cm^{-1}$) and at 374 nm in CH_2Cl_2 ($\epsilon = 1.8 \times 10^4\ M^{-1}\ cm^{-1}$).

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Registry No. 1, 69496-25-9; 2, 83314-02-7; 3, 23978-55-4; poly(ethylene glycol), 25322-68-3; potassium picrate, 573-83-1; sodium picrate, 3324-58-1; PEG-3400 ditosylate, 35164-96-6; PEG-6800 dialdehyde, 83314-03-8; 18-crown-6, 17455-13-9; 15-crown-5, 33100-27-5; CH_3COOK, 127-08-2; $C_6H_5CH_2B$, 100-39-0.

An Annulative Route to Enediones

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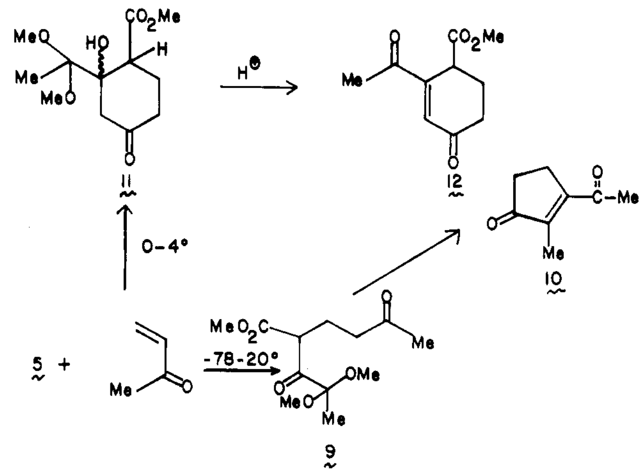
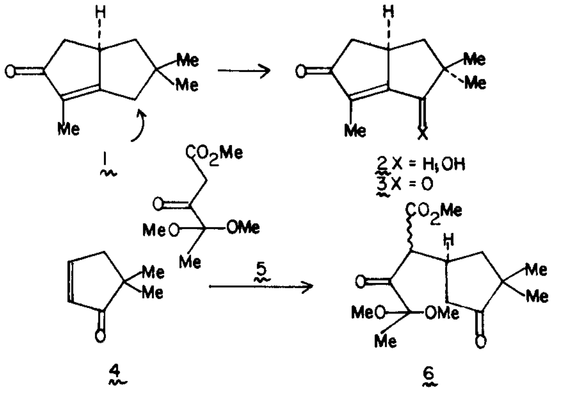
A central intermediate in our recent total synthesis of coriolin was the enedione **3**.[1,2] As a result of investigations which were directed toward the total synthesis and through follow-up studies,[3,4] we have developed the capability to introduce carbon functionality at either ethylenic carbon of enedione **1**.

Our initial approaches to **3** involved a variety of attempts to achieve, in essence, oxidation at the γ-carbon of enone **1**. A series of initiatives in this connection (attempted extended enol acetylation, attempted formation of the extended dienamine, attempted reaction with a Bredereck reagent at the γ-carbon) were unsuccessful, possibly as a consequence of steric resistance to attack at the neopentyl center. Unacceptably low yields (5–10%) of **2** and **3** were obtained by direct oxidation of **1** with selenium dioxide.[5]

Scheme I





Accordingly, a new annulation was developed to provide a route from **4** to **3**. The experimental details of the particular synthesis of compound **3** were published elsewhere.[2] Herein, we report our results on the scope and limitations of this type of annulation.[6]

The required β-keto ester **5**[2] was prepared by the carbomethoxylation of the readily available 3,3-dimethoxy-2-butanone.[7] Michael additions of **5** to cyclopentenone, cyclohexenone, and cycloheptenone were achieved. The reactions were carried out by using sodium methoxide (0.25 equiv) in methanol at room temperature. No attempt was made to separate the mixture of diastereomeric Michael products.

Cyclization to enediones **8**, as well as decarbomethoxylation could be achieved in one step by heating the adducts with *p*-TsOH in toluene or xylene for short periods of time. Serious difficulties were encountered only in the case of unsubstituted cyclopentenone (case **8c**). Here the yield of the Michael step was only 47%. Moreover, the quality of the decarbomethoxylation–cyclization step was undermined by difficulties in achieving complete cleavage of the ester. This was eventually accomplished through the action of HCl in aqueous dioxane though in poor yield.

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