Synthesis of Dibenzocrown Ethers with Pendent Amide Groups

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Synthetic routes to twenty six crown ether compounds with pendent amide, *N*-alkylamide, or *N,N*-dialkylamide groups are reported. The new crown ether compounds are based on *sym*-dibenzo-16-crown-5-oxyacetamide and *sym*-(propyl)-dibenzo-16-crown-5-oxyacetamide and are obtained in high yields.

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Introduction.

To complement studies of metal ion separations by crown ethers which possess pendent proton-ionizable groups [1-3], investigations of metal ion complexation with analogous macrocyclic polyethers which contain potential neutral chelating functions in the side arms are being undertaken. The coordinating properties of amide groups are well known [4] and other researchers have prepared crown ether and diazacrown ether compounds with pendent amide and *N,N*-dialkylamide functionality [5-9].

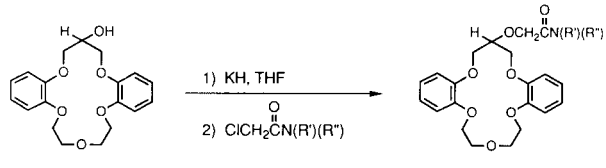
For the solvent extraction and liquid membrane transport of alkali metal cations by *sym*-(R)dibenzo-16-crown-5-oxyacetic acids **1**, selectivity for sodium complexation is observed as would be expected for a 16-crown-5 ring [10]. However the sodium selectivity is considerably higher when R = alkyl rather than R = H. It has been proposed that when the hydrophobic alkyl group extends away from the polar polyether portion of the molecule then the carboxylic acid-containing side arm is positioned over the crown ether cavity which preorganizes the metal ion binding site and enhances selectivity [2,3]. Replacement of the carboxylic acid group in **1** with a carboxamide function gives *sym*-(R)dibenzo-16-crown-5-oxyacetamides **2**. In **2** alkyl groups may be attached to the crown ether ring (R) or the nitrogen of the amide group (R′ or R′ and R″). We now report preparative routes to twenty six new crown ether amides, *N*-alkylamides, and *N,N*-dialkylamides based upon *sym*-dibenzo-16-crown-5-oxyacetamide (R, R′, R″ = H) and *sym*-(propyl)-dibenzo-16-crown-5-oxyacetamide (R = C_3H_7; R′, R″ = H).

Results and Discussion.

Using the reported procedure [11], 2-chloroacetamide was prepared from ethyl 2-chloroacetate and ammonium hydroxide. *N*-Propyl [12], *N*-pentyl [13], *N*-piperidino, *N*-morpholino, *N,N*-dimethyl, *N,N*-diethyl [14,15], *N,N*-dipropyl [13], *N,N*-dibutyl [13], *N,N*-dipentyl [13], *N,N*-dihexyl [13], *N,N*-di(3-oxabutyl) and *N,N*-di(3,6-dioxaheptyl)-2-chloroacetamides were prepared in high yields (>90% except for *N,N*-dimethyl-2-chloroacetamide) by reaction of the appropriate primary or secondary amine with chloroacetyl chloride in diethyl ether at -10° [12-15].

Reaction of *sym*-hydroxydibenzo-16-crown-5 [16] with potassium hydride in tetrahydrofuran followed by addition of the crude 2-chloroacetamide, *N*-alkyl 2-chloroacetamide or *N,N*-dialkyl-2-chloroacetamide gave *syn*-dibenzo-16-crown-5-oxyacetamides **3-15** in high yields (89% or greater for all compounds, except for **4** which was realized in 68% yield) (Scheme 1). For this series of compounds, the pendent oxyacetamide group is changed from unsubstituted with **3** to *N*-substituted with a propyl or pentyl group for **6** and **9**, respectively, to *N,N*-disubstituted with methyl, ethyl, propyl, butyl, pentyl or hexyl groups in **4**, **5**, **7**, **8**, **10** and **11**, respectively. For the latter grouping, the side arm lipophilicity is systematically enhanced by increasing the chain length of the alkyl group. The *N*-piperidino derivative **14** has a cyclic structure for the tertiary amide. Finally compounds **12**, **13** and **15** have one or more ether oxygens in the tertiary amide group. Such ether oxygens provide additional potential metal ion coordinating sites in the side arm. Yields, spectral data and combustion analysis data for the *sym*-dibenzo-16-crown-5-oxyacetamides **3-15** are presented in Table I.

Scheme 1



Reactions of *sym*-(hydroxy)(propyl)dibenzo-16-crown-5 [17] with potassium hydride in tetrahydrofuran then with *N,N*-dimethyl, *N,N*-diethyl, *N,N*-dipropyl, *N,N*-dibutyl, *N,N*-dipentyl, *N,N*-dihexyl, *N,N*-di(3-oxabutyl), *N,N*-di(3,6-dioxaheptyl), *N*-piperidino or *N*-morpholino 2-chloroacetamide gave *sym*-(propyl)dibenzo-16-crown-5-oxyacetamide derivatives **17**, **18**, **20**, **21**, **23-28**, respectively. Except for **17** and **26** the yields were 93% or greater. Attempts to couple 2-chloroacetamide or its *N*-propyl or *N*-pentyl derivatives with the crown ether alkoxide under the same conditions were unsuccessful. To prepare the unsubstituted oxyacetamide, *sym*-(propyl)dibenzo-18-crown-6-oxyacetic acid

Table I

Yields, Spectral Data and Combustion Analysis Data for Crown Ether Amides **3-28** [a]

Compound	Yield %	^{1}H NMR Spectra (200 MHz), ppm [b]	IR Spectrum cm^{-1} [c]	Molecular Formula	Combustion Analysis Theory/Found C	H
3	93	3.91-4.34 (m, 15H), 5.65 (s, 1H), 6.64-7.00 (m, 8H), 7.65 (s, 1H)	3450, 3346 (N-H), 1686 (C=O), 1258, 1124 (C-O)	$C_{21}H_{25}NO_7$• $0.1CH_2Cl_2$	61.52 61.65	6.17 5.94
4	68	2.93 + 2.97 + 3.07 + 3.08 (s, 6H) 3.92-4.37 (m, 13H), 4.57 + 4.72 (s, 2H), 6.82-7.01 (m, 8H)	1654 (C=O), 1257, 1112 (C-O)	$C_{23}H_{29}NO_7$• $0.3CH_2Cl_2$	61.24 61.26	6.53 6.61
5	96	1.08-1.24 (m, 6H), 3.34-3.42 (m, 4H), 3.91-4.41 (m, 13H), 4.60 + 4.71 (s, 2H), 6.82-7.02 (m, 8H)	1643 (C=O), 1256, 1124 (C-O)	$C_{25}H_{33}NO_7$	65.34 64.97	7.24 7.38
6	89	0.88 (t, 3H), 1.45-1.56 (m, 2H), 3.26 (q, 2H), 3.93-4.35 (m+s, 15 H), 6.84-7.04 (m, 8H), 7.65 (br s, 1H)	3353 (N-H), 1673 (C=O), 1258, 1122 (C-O)	$C_{24}H_{31}NO_7$• $0.1C_6H_6$	65.18 65.26	7.03 6.93
7	92	0.86-0.94 (m, 6H), 1.45-1.65 (m, 4H), 3.19-3.34 (m, 4H), 3.91-4.45 (m, 13H), 4.61 + 4.73 (s, 2H), 6.82-7.01 (m, 8H)	1645 (C=O), 1257, 1124 (C-O)	$C_{27}H_{37}NO_7$	66.50 66.69	7.65 7.86
8	98	0.85-0.96 (m, 6H), 1.25-1.36 (m, 4H), 1.45-1.60 (m, 4H), 3.24-3.37 (m, 4H), 3.90-4.39 (m, 13H), 4.61 + 4.72 (s, 2H), 6.82-7.06 (m, 8H)	1643 (C=O), 1253, 1130 (C-O)	$C_{29}H_{41}NO_7$	67.55 67.24	8.01 8.08
9	97	0.77-0.84 (m, 3H), 1.21-1.30 (m, 4H), 1.40-1.60 (m, 2H), 3.23-3.33 (m, 2H), 3.92-4.33 (m, 15H), 6.83-7.04 (m, 8H), 7.70 (br s, 1H)	3339 (N-H), 1673 (C=O), 1259, 1123 (C-O)	$C_{26}H_{35}NO_7$	65.94 66.34	7.45 7.54
10	96	0.83-0.93 (m, 6H), 1.22-1.31 (m, 8H), 1.45-1.60 (m, 4H), 3.20-3.36 (m, 4H), 3.89-4.41 (m, 13H), 4.60 + 4.75 (s, 2H), 6.82-7.01 (m, 8H)	1645 (C=O), 1258, 1124 (C-O)	$C_{31}H_{45}NO_7$	68.48 68.78	8.34 8.14
11	96	0.80-0.95 (m, 6H), 1.15-1.40 (m, 12H), 1.45-1.65 (m, 4H), 3.20-3.35 (m, 4H), 3.85-4.50 (m, 13H), 4.60 + 4.71 (s, 2H), 6.82-7.01 (m, 8H)	1648 (C=O), 1256, 1124 (C-O)	$C_{33}H_{49}NO_7$• $0.15CH_2Cl_2$	68.12 68.25	8.50 8.54
12	100	3.30 + 3.32 (s, 6H), 3.48-3.62 (m, 8H), 3.87-4.40 (m, 13H), 4.69 + 4.85 (s, 2H), 6.82-7.03 (m, 8H)	1654 (C=O), 1257, 1115 (C-O)	$C_{27}H_{37}NO_9$	62.41 62.43	7.18 7.38
13	91	3.33 + 3.36 (s, 6H), 3.47-3.64 (m, 16H), 3.90-4.45 (m, 13H), 4.69 + 4.90 (s, 2H), 6.82-7.02 (m, 8H)	1653 (C=O), 1257, 1113 (C-O)	$C_{31}H_{45}NO_{11}$	61.27 61.59	7.46 7.48
14	100	1.45-1.65 (m, 6H), 3.48-3.59 (m, 4H), 3.90-4.39 (m, 13H), 4.56 + 4.71 (s, 2H), 6.82-7.01 (m, 8H)	1644 (C=O), 1257, 1124 (C-O)	$C_{26}H_{33}NO_7$• $0.8CH_2Cl_2$	59.66 59.40	6.40 6.14
15	100	3.55-3.70 (m, 8H), 3.91-4.34 (m, 13H), 4.54 (s, 2H), 6.82-6.99 (m, 8H)	1648 (C=O), 1259, 1114 (C-O)	$C_{25}H_{31}NO_8$	63.41 63.66	6.60 6.62
16	95	1.03 (t, 3H), 1.43-1.55 (m, 2H), 1.86-1.94 (m, 2H), 3.81-4.53 (m, 12H) (including ABq at 4.00, 4.05, 4.48, 4.58 (s, 2H), 6.77-6.98 (m, 8H)	3466, 3209 (N-H), 1683 (C=O), 1256, 1120 (C-O)	$C_{24}H_{31}NO_7$• $0.1CH_2Cl_2$	63.75 63.74	6.93 6.87
17	66	1.00 (t, 3H), 1.45-1.55 (m, 2H), 1.92-2.00 (m, 2H), 2.89 (s, 3H), 3.10 (s, 3H), 3.88-4.41 (m, 12H) (including ABq at 4.15, 4.20, 4.36, 4.41), 4.58 (s, 2H), 6.81-6.98 (m, 8H)	1654 (C=O), 1257, 1122 (C-O)	$C_{26}H_{35}NO_7$• $0.55CH_2Cl_2$	61.29 61.14	6.99 7.04
18	100	0.96-1.19 (m, 9H), 1.43-1.58 (m, 2H), 1.93-2.02 (m, 2H), 3.29-3.44 (m, 4H), 3.89-4.40 (m, 12H), (including ABq at 4.17, 4.22, 4.35, 4.40), 4.57 (s, 2H), 6.80-6.98 (m, 8H)	1639 (C=O), 1257, 1122 (C-O)	$C_{28}H_{39}NO_7$	67.04 66.71	7.84 8.01
19	97	0.86 (t, 3H), 1.03 (t, 3H), 1.41-1.57 (m, 4H), 1.87-1.96 (m, 2H), 3.20 (q, 2H), 3.84-4.51 (m, 12H) (including part of an ABq at 4.46, 4.51), 4.55 (s, 2H), 6.79-6.99 (m, 8H), 7.65 (br s, 1H)	3416 (N-H), 1671 (C=O), 1257, 1122 (C-O)	$C_{27}H_{37}NO_7$	66.51 66.19	7.65 7.86

Table I (continued)

Compound	Yield %	^{1}H NMR Spectra (200 MHz), ppm [b]	IR Spectrum cm^{-1} [c]	Molecular Formula	Combustion Analysis Theory/Found C	H
20	100	0.80-0.89 (m, 6H), 0.99 (t, 3H), 1.48-1.65 (m, 6H), 1.93-2.02 (m, 2H), 3.20-3.33 (m, 4H), 3.87-4.40 (m, 12H), (including ABq at 4.16, 4.21, 4.35, 4.40), 4.58 (s, 2H), 6.79-6.95 (m, 8H)	1643 (C=O), 1257, 1122 (C-O)	$C_{30}H_{43}NO_7$	68.02 67.77	8.18 8.15
21	100	0.82-0.92 (m, 6H), 0.99 (t, 3H), 1.15-1.40 (m, 4H), 1.40-1.60 (m, 6H), 1.94-2.02 (m, 2H), 3.23-3.35 (m, 4H), 3.87-4.40 (m, 12H) (including ABq at 4.16, 4.21, 4.35, 4.40), 4.59 (s, 2H), 6.79-6.97 (m, 8H)	1642 (C=O), 1257, 1122 (C-O)	$C_{32}H_{47}NO_7$	68.91 68.56	8.49 8.28
22	97	0.77-0.84 (m, 3H), 1.03 (t, 3H), 1.18-1.27 (m, 4H), 1.39-1.53 (m, 4H), 1.88-1.96 (m, 2H), 3.18-3.28 (m, 2H), 3.85-4.52 (m, 12H) (including ABq at 4.01, 4.06, 4.47, 4.52), 4.55 (s, 2H), 6.79-6.99 (m, 8H), 6.90 (br s, 1H)	3416 (N-H), 1672 (C=O), 1257, 1122 (C-O)	$C_{29}H_{41}NO_7 \cdot 0.2CH_2Cl_2$	65.84 65.78	7.83 7.48
23	98	0.78-0.91 (m, 6H), 1.00 (t, 3H), 1.19-1.32 (m, 8H), 1.42-1.60 (m, 6H), 1.93-2.02 (m, 2H), 3.23-3.35 (q, 4H), 3.89-4.41 (m, 12H) (including ABq at 4.16, 4.21, 4.35, 4.40), 4.59 (s, 2H), 6.79-6.96 (m, 8H)	1642 (C=O), 1256, 1122 (C-O)	$C_{34}H_{51}NO_7$	69.71 69.35	8.78 8.54
24	100	0.80-0.95 (m, 6H), 1.00 (t, 3H), 1.15-1.35 (m, 12H), 1.35-1.65 (m, 6H), 1.85-2.05 (m, 2H), 3.23-3.40 (m, 4H), 3.75-4.41 (m, 12H) (including ABq at 4.16, 4.21, 4.36, 4.41), 4.60 (s, 2H), 6.80-6.94 (m, 8H)	1643 (C=O), 1257, 1122 (C-O)	$C_{36}H_{55}NO_7 \cdot 0.1CH_2Cl_2$	69.67 69.71	8.94 8.89
25	97	1.00 (t, 3H), 1.46-1.58 (m, 2H), 1.93-2.01 (m, 2H), 3.25 + 3.28 (s, 6H), 3.47-3.69 (m, 8H), 3.90-4.39 (m, 12H) (including ABq at 4.17, 4.22, 4.34, 4.39), 4.63 (s, 2H), 6.80-6.98 (m, 8H)	1645 (C=O), 1257, 1120 (C-O)	$C_{30}H_{43}NO_9$	64.15 64.32	7.72 7.95
26	63 [d]	1.00 (t, 3H), 1.45-1.55 (m, 2H), 1.92-2.00 (m, 2H), 3.31 + 3.36 (s, 6H), 3.40-3.67 (m, 16H), 3.90-4.39 (m, 12H) (including part of an ABq at 4.34, 4.39), 4.63 (s, 2H), 6.80-6.98 (s, 8H)	1648 (C=O), 1257, 1122 (C-O)	$C_{34}H_{51}NO_{11} \cdot 0.1CH_2Cl_2$	62.22 62.06	7.84 7.87
27	93	0.99 (t, 3H), 1.45-1.65 (m, 8H), 1.91-1.99 (m, 2H), 3.51-3.50 (m, 4H), 3.51-4.40 (m, 12H) (including ABq at 4.15, 4.20, 4.35, 4.40), 4.56 (s, 2H), 6.80-6.99 (m, 8H)	1641 (C=O), 1256, 1122 (C-O)	$C_{29}H_{39}NO_7 \cdot 0.5CH_2Cl_2$	63.71 63.79	7.25 7.46
28	95	1.00 (t, 3H), 1.43-1.55 (m, 2H), 1.81-1.95 (m, 2H), 3.55-3.75 (m, 8H), 3.86-4.43 (m, 12H) (including part of an ABq at 4.38, 4.43), 4.58 (s, 2H), 6.81-6.98 (m, 8H)	1648 (C=O), 1257, 1115 (C-O)	$C_{28}H_{37}NO_8$	65.22 65.62	7.23 7.27

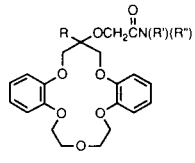
[a] All compounds were isolated as oils. In some cases the oil crystallized after long standing. [b] In deuteriochloroform. [c] Deposited from deuteriochloroform onto a sodium chloride plate. [d] Purified by column chromatography on alumina with chloroform- ethyl acetate (1:1) as eluent.

(**1** with R = C_3H_7) [17] was reacted with oxalyl chloride in benzene to give the corresponding acid chloride. Bubbling ammonia gas through a benzene solution of the acid chloride produced **16** in 95% yield. When solutions of the acid chloride in benzene were treated with propylamine and pentylamine, *N*-propyl and *N*-pentyl *sym*-(propyl)dibenzo-16-crown-5-oxyacetamides (**19** and **22**, respectively) were isolated in yields exceeding 95%. Yields, spectral data and combustion analysis data for the *syn*-(propyl)dibenzo-16-crown-5-oxyacetamides **16-28** are collected in Table I.

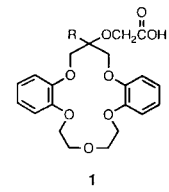
Relative to the series of compounds **3-15**, it is anticipated that the presence of a propyl group on the center carbon of the three-carbon bridge will help position the amide group-containing side arm over the crown ether cavity and thereby enhance metal ion recognition by preorganization of the binding site. Evidence for greater con-

formational flexibility of the oxyamide side arms for most of the tertiary amide derivatives of *sym*-dibenzo-16-crown-5-oxyacetamide is provided by their ^{1}H nmr spectra. For compounds **4**, **5**, **7**, **8**, **10-14**, the methylene group of the oxyacetamide linkage appears as two singlets separated by 0.11-0.21 ppm. If the carbons of the three-carbon bridge and the two attached ether oxygens are envisioned in a half-chair conformation, the oxyacetamide side arm may occupy either a pseudo-equitorial or a pseudo-axial position. In the former, the side arm would extend away from the crown ether ring. In the latter, the side arm could be positioned over the crown ether cavity. The magnetic environments of the oxyacetamide methylene hydrogens in the two conformations would by somewhat different due to the benzene ring currents. Thus the ^{1}H nmr spectral observations for compounds **4**, **5**, **7**, **8**, **10-14** are consistent with the presence of these two conformations and their slow interconversion on the nmr time scale.

In the ^{1}H nmr spectra for the corresponding tertiary amides derived from *sym*-(propyl)dibenzo-16-crown-5-oxyacetamide, only one singlet is observed for the oxyacetamide methylene hydrogens. The chemical shift for this absorption is very nearly the same as that for the higher field singlet noted with the corresponding *sym*-dibenzo-16-crown-5-oxyacetamide compound. Thus attachment of a propyl group to the central carbon of the three-carbon bridge is found to appreciably reduce the conformational mobility of the geminal oxyacetamide function. In the X-ray crystal structure of *sym*-(decyl)dibenzo-16-crown-5-oxyacetic acid (**1** with R = decyl), the decyl group is pseudo-equitorial with a pseudo-axial oxyacetic acid function which is located over the crown ether ring [23]. In view of the ^{1}H nmr results described above and by anology with this X-ray crystal structure, the oxyacetamide groups in compounds **16-28** are expected to be pseudo-axial and positioned over the crown ether cavity.



When R = H	R'	R''	When R = C_3H_7
3	-H	-H	16
4	$-CH_3$	$-CH_3$	17
5	$-C_2H_5$	$-C_2H_5$	18
6	-H	$-C_3H_7$	19
7	$-C_3H_7$	$-C_3H_7$	20
8	$-C_4H_9$	$-C_4H_9$	21
9	-H	$-C_5H_{11}$	22
10	$-C_5H_{11}$	$-C_5H_{11}$	23
11	$-C_6H_{13}$	$-C_6H_{13}$	24
12	$-CH_2CH_2OCH_3$	$-CH_2CH_2OCH_3$	25
13	$-CH_2CH_2OCH_2CH_2OCH_3$	$-CH_2CH_2OCH_2CH_2OCH_3$	26
14	$-CH_2CH_2CH_2CH_2CH_2-$		27
15	$-CH_2CH_2OCH_2CH_2-$		28



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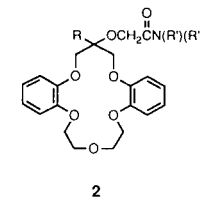

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EXPERIMENTAL

The ir spectra were obtained with a Perkin Elmer Model 1600 spectrophotometer and are reported in reciprocal centimeters. The ^{1}H nmr spectra were recorded with an IBM AF-200 spectrometer in deuteriochloroform and chemical shifts are reported in parts per million downfield (δ) from TMS. Combustion analysis was performed by Desert Analytics (Tucson, Arizona).

Unless specified otherwise, reagent grade reactants and solvents were used as received from commercial suppliers. Tetrahydrofuran was purified by distillation from benzophenone ketyl. *sym*-Hydroxydibenzo-16-crown-5, *sym*-(hydroxy)(propyl)dibenzo-16-crown-5 and *sym*-(propyl)dibenzo-16-crown-5-oxyacetic acid were prepared by reported procedures [16,17]. 2-Chloroacetamide was synthesized by the published method [11]. The requisite 1,11-dimethoxy-3,9-dioxa-6-azaundecane was prepared from 3,9-dioxa-6-(*N*-tosylaza)undecane-1,11-diol [18] by reaction with sodium hydride then excess iodomethane in tetrahydrofuran. The resulting tosylamide was reduced to the requisite amine with sodium amalgam [19].

Preparation of *N,N*-Dibutyl-2-chloroacetamide.

The following procedure is representative of that by which the *N*-alkyl and *N,N*-dialkyl-2-chloroacetamides, except for *N,N*-dimethyl-2-chloroacetamide, were prepared [12-15].

A solution of chloroacetyl chloride (11.3 g, 0.10 mole) in 250 ml of anhydrous diethyl ether was cooled to -15° in an ice-salt bath. A solution of dibutylamine (25.9 g, 0.20 mole) in 50 ml of anhydrous diethyl ether was added at such a rate that the temperature of the reaction mixture was kept below -10°. After the addition was completed, a small amount of water was added to dissolve the precipitated amine hydrochloride [20]. The organic layer was separated, washed successively with 5% hydrochloric acid, 5% sodium bicarbonate, and water and dried over magnesium sulfate. The solution was evaporated *in vacuo* with a rotary evaporator and then subjected to oil pump vacuum at 40° for one hour to yield 19.7 g (97%) of the desired product as an oil.

Preparation of *N,N*-Dimethyl-2-chloroacetamide.

To a vigorously stirred mixture of 50% aqueous sodium hydroxide (100 ml) and diethyl ether (50 ml) was added portion-wise 16.31 g (0.20 mole) of diethylamine hydrochloride. The generated dimethylamine gas was passed *via* a glass tube into a solution of chloroacetyl chloride (5.65 g, 0.050 mole) in diethyl ether which was cooled to -10° in an ice-salt bath. After two hours, a very small amount of water was added to dissolve the precipitated amine hydrochloride. The organic phase was separated, washed successively with small amounts of 5% hydrochloride acid, 5% sodium bicarbonate and water and dried over magnesium sulfate. The solution was evaporated *in vacuo* leaving 1.10 g (18%) of an oily product. Presumably the low yield was due to the high water solubility of the product.

Preparation of *N,N*-Diethyl-*sym*-(propyl)dibenzo-16-crown-5-oxyacetamide (**18**).

The following procedure is representative of that by which crown ether amides **3-15**, **17**, **18**, **20-28** were prepared.

The protecting mineral oil was removed from 1.32 g (0.011 mole) of potassium hydride (35% in mineral oil) by washing with dry pentane under nitrogen. Dry tetrahydrofuran (250 ml) then 3.88 g (0.010 mole) of *sym*-(hydroxy)(propyl)dibenzo-16-crown-5 [17][21] were added and the mixture was stirred at room temperature for one hour. A solution of *N,N*-diethyl 2-chloroacetamide (1.50 g, 0.010 mole) in 50 ml of dry tetrahydrofuran was added dropwise during a two-hour period. After stirring for an additional 15 minutes, the solvent was evaporated *in vacuo*. The residue was dissolved in dichloromethane and the solution was washed with water. The organic layer was dried over magnesium sulfate and the solvent was evaporated *in vacuo* to give 5.02 g (100%) of **18** as an oil. See Table I for spectral and combustion analysis data for **18**.

Preparation of *sym*-(Propyl)dibenzo-16-crown-5-oxyacetyl Chloride.

A mixture of *sym*-(propyl)dibenzo-16-crown-oxyacetic acid (6.06 g, 15.0 mmoles) and 5.0 ml of oxalyl chloride in 100 ml of dry benzene was stirred at room temperature under nitrogen for 20 hours. (A homogeneous solution was obtained after three hours). The solvent and excess oxalyl chloride were evaporated *in vacuo*. The crude solid acid chloride was obtained in quantitative yield and used without further purification.

Preparation of *sym*-(Propyl)dibenzo-16-crown-5-oxyacetamide (**16**).

Ammonia gas was bubbled into a stirred solution of 2.32 g (5.0 mmoles) of *sym*-(propyl)dibenzo-16-crown-5-oxyacetyl chloride in 50 ml of dry benzene for 15 minutes at room temperature. The reaction mixture was stirred for an additional 3 hours then water was added. The organic layer was separated, washed with 10% hydrochloric acid and then with water, and dried over calcium chloride. The solvent was evaporated *in vacuo* to provide 2.14 g (96%) of **16** as an oil. Spectral and combustion analysis data for **16** are given in Table I.

Preparation of *N*-Pentyl *sym*-(Propyl)dibenzo-16-crown-5-oxyacetamide (**22**) [22].

To a stirred solution of 5.58 g (12.0 mmoles) of *sym*-(propyl)-dibenzo-16-crown-5-oxyacetyl chloride in 25 ml of dry benzene at room temperature under nitrogen was added dropwise a solution of 2.09 g (24.0 mmoles) of pentylamine in 50 ml of dry benzene. After the addition was completed, the reaction mixture was stirred for two hours, then washed successively with water, 10% hydrochloric acid and water and dried over calcium chloride. Evaporation of the benzene *in vacuo* gave 6.02 g (97%) of **22** as an oil.

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[20] In the synthesis of *N,N*-dihexyl-2-chloroacetamide, the amine hydrochloride did not dissolve in water so it was removed by filtration.

[21] For the preparation of crown ether amides **3-15**, *sym*-hydroxydibenzo-16-crown-5 [16] was utilized.

[22] With replacement of pentylamine by propylamine, this procedure was used to prepare *N*-propyl *sym*-(propyl)dibenzo-16-crown-5-oxyacetamide (**19**).

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