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A series of novel 1,3-alternate calix[4]arene azacrowns having mono and bis crown ethers on the lower rim of the calix[4]arene framework were synthesized. Solid-state structures confirmed the three dimensional conformation of compounds **1**-**3**.

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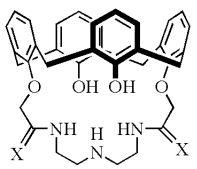
Introduction.

Calix[4]arenes have been used for useful 3-D molecular building blocks for the synthesis of receptors with specific properties [1]. They can exist in four different conformations: cone, partial cone, 1,2-alternate, and 1,3-alternate [2,3]. Recently, calix[4]crown ethers in which conventional crown ethers are incorporated into a rigid calix[4]arene in the 1,3-alternate type have attracted intense interest as cesium-selective extractants [4-8]. Macrocyclic compounds containing nitrogen atom, called as azacrown ethers, have been of particular interest because the cation-ligating side arms such as carboxylic acid [9-12], chromogenic [9], and fluorogenic groups [12] on the nitrogen atom have capabilities to form strong and selective interactions with various charged and neutral guest molecules by three-dimensional encapsulation. So, over the past few decades, a considerable number of *N*-pivot azacrown ethers have been investigated [12].

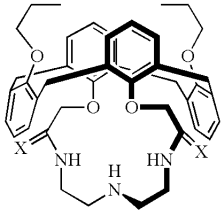
Previously we also reported that calix[4]azacrown having *N*-nitrophenol as a proton-ionizable side arm showed an exceptional potassium selectivity over other alkali metal ions in two phase extraction and membrane transport experiments [8]. Queslati *et al.* [13] also reported the synthesis of a series of *tert*-butyl-calix[4](aza)crowns and their complexing properties towards Co^{2+}, Ni^{2+}, and Cu^{2+} ions. Abidi *et al.* [14] reported the synthes Pis of *tert*-butylcalix[4](aza)crowns capped by one 'tren' or doubly capped by two azacrowns. Bitter *et al.* [15] reported a synthetic strategy for a series of calix[4](aza)crowns having amide groups and their NMR properties and crystal structures.

With the aim of developing new types of calix[4]azacrown receptors based on the previous investigations above, we report herein a more complete study on these families of ligands **1**-**7** and newly determined crystalline structures of **1**-**3**.



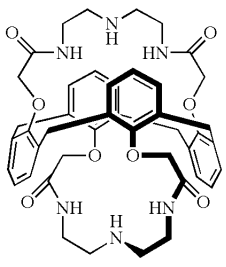
X

O **1**
H **2**



X

O **3**
H **4**



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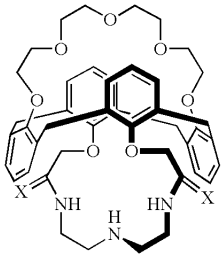


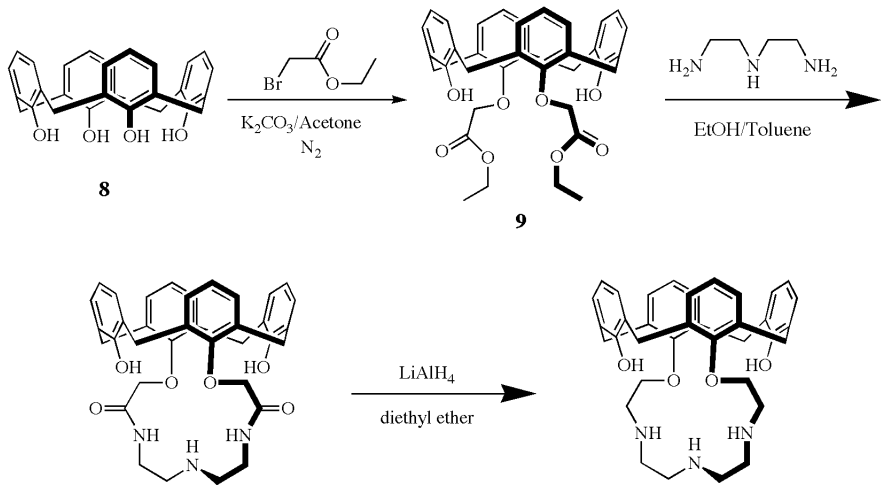
X

O **6**
H **7**

Results and Discussion.

As shown in Scheme 1, for compounds **1** and **2**, synthesis began with calix[4]arene **8** which reacted with ethyl bromoacetate in the presence of K_2CO_3 in acetone to give calix[4]arene diethyl ester **9** in the cone conformation. Amino-cyclization using 2-aminodiethylamine provided compound **1** in moderate yield which can be converted into compound **2** using conventional reducing agent, LAH in diethylether. The simple reduction process gave a modest yield in this case but poor or nothing in the formation of compounds **4** and **7**. Each structural conformation was confirmed by ^{1}H NMR spectroscopy. For instance, in the ^{1}H NMR spectrum of **1**, two doublets at 4.24 and 3.45 ppm with an intensity of 8 methylene hydrogen atoms (Ar-CH_2-Ar) connected to benzene rings and one signal at 31.13 ppm for bridging four methylene carbons (Ar-CH$_2$-Ar) in the ^{13}C NMR spectrum indicates the characteristic cone conformation. No other isomers were indicated by this NMR measurement. This cone conformation was also clearly proved by the X-ray crystal structures as shown in Figure 1 for which more detail explanation is below. For

Scheme 1



Synthetic route for compounds **1** and **2**.

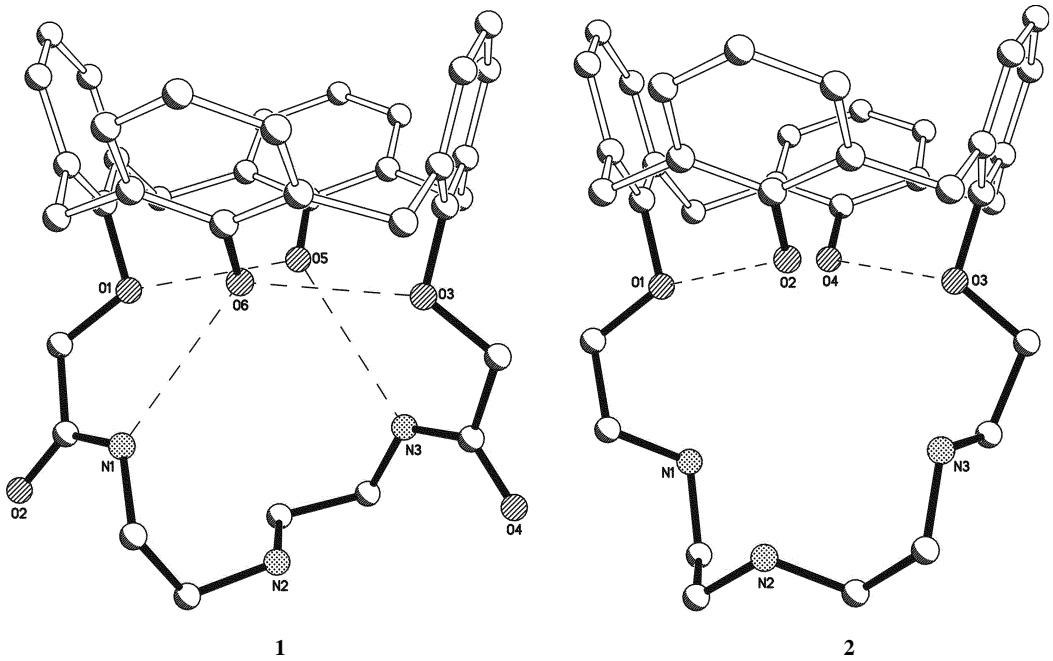


Figure 1. X-ray crystal structures of **1** and **2**.

reduced compound **2**, its conformation was also proven by ^{1}H and ^{13}C NMR spectra and X-ray crystal structures (Figure 1).

Synthesis of monocyclic calix[4]azacrown was also carried out as shown in Scheme 2. Synthesis of target **4** was initially designed through **10** → **11** → **3** → **4**. However, we encountered a problem in the reduction step from **3** to **4**. Unlike from cone **1** to cone **2**, the 1,3-alternate conformation system of **3** did not provide the reduction product with a number of various reaction conditions. Alternatively, the product **4** could be obtained through **10** → **12** → **4** pathway. The conformations of each compound indicated in Scheme 2 were confirmed by ^{1}H and ^{13}C NMR spectra as well.

Calix[4]bis-amidocrown **5** was prepared from calix[4]-arene **8** by way of compound **13** as shown in Scheme 3. Cyclization of calix[4]arene tetraester **13** with diethylenetriamine in EtOH/toluene gave crystalline product **5** in 74 % yield. Reduction of **5** to give calix[4]bis-triazacrown-5 was not successful in spite of a number of trials.

Scheme 4 indicates a synthetic pathway for calix[4]-crown-5-triazacrown-5. Since we had a problem in

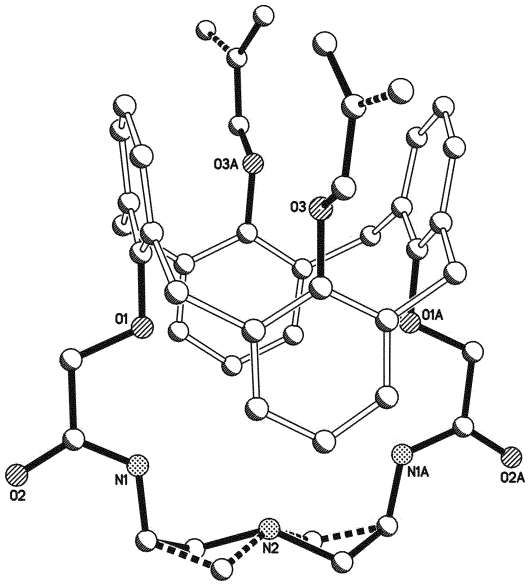


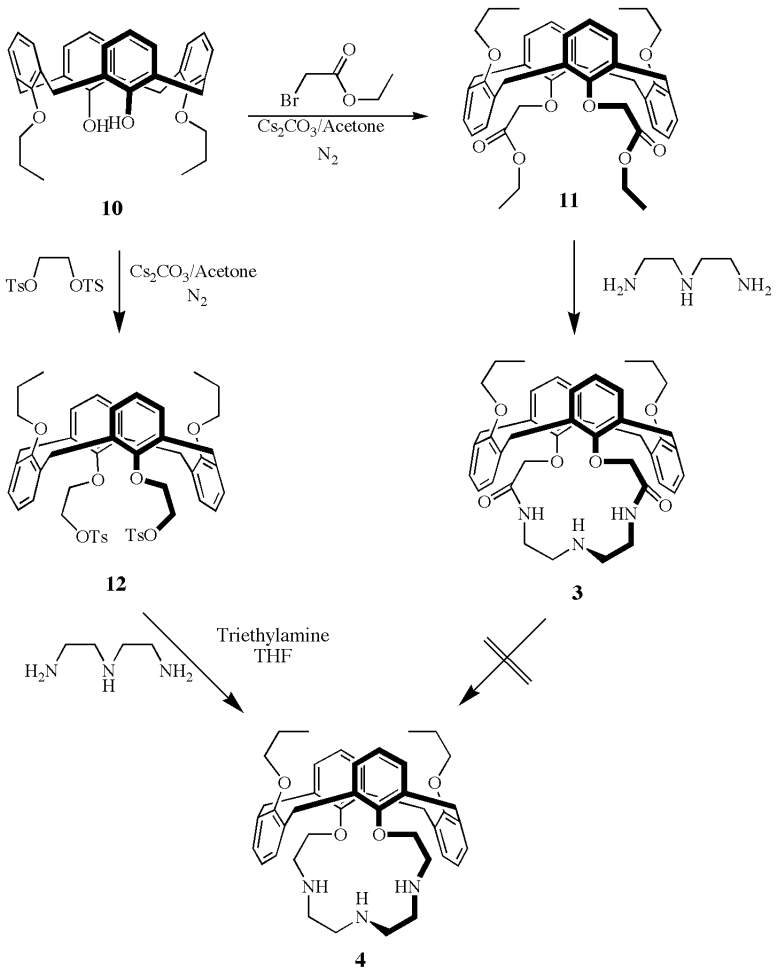
Figure 2. X-ray crystal structure of **3**.

reduction from compound **6** to **7**, we were forced to carry out two different synthetic pathways. For calixcrown-diamide **6**, the synthetic pathway followed **14** → **16** → **6** and gave 25 % yield for **6**. For calixcrown-triazacrown **7**, however, the reaction scheme took **14** → **15** → **7** because the reduction was unsuccessful like that in previous steps. Only in the case of **1**, the reduction of the amide carbonyl with LAH could be successfully achieved.

Attachment of fluorescent arms such as pyrene and anthracene molecules on the each nitrogen atoms of the calix[4]triazacrown compounds are now in progress and their complexation behavior with alkali and alkaline earth metal ions will be reported elsewhere.

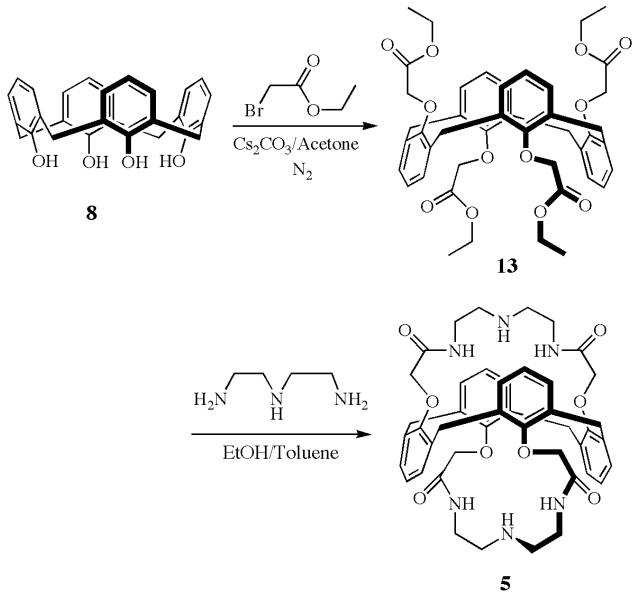
Single crystals of **1**, **2** and **3** suitable for X-ray crystallography were prepared by slow evaporation of methanol solutions. Crystallographic data and structure refinement parameters for the compounds are listed in Table 1. The torsion angles and the distances between donor atoms in the azacrown moieties are compiled in Table 2. In Figure 1, the crystal structures obviously show that **1** and **2** have

Scheme 2



Synthesis of compounds **3** and **4**

Scheme 3



Synthesis of compound **5**.

Table 2

Torsion Angles [°] and Inter-atomic Distances [Å] for **1**, **2** and **3**

	1	**2**	**3**
Torsion angles			
O1-C-C-N1	14.1(2)	-60.0(3)	-1.1(4)
N1-C-C-N2	60.2(2)	-55.9(3)	63.4(8)
N1-C-C'-N2			-57(1)
N2-C-C-N3	-69.3(2)	-67.5(3)	
N3-C-C-O3	20.6(2)	-68.5(2)	
Interatomic distances			
O1…N2	4.814(2)	4.769(3)	4.758(4)
O1…N3	4.845(2)	5.410(3)	
O1…O3	4.702(2)	4.614(2)	
N1…N3	4.624(2)	4.719(3)	
N1…O3	5.066(2)	5.155(3)	
N2…O3	4.652(2)	5.134(3)	
O1…N1A [a]			5.832(3)
O1…O1A [a]			5.195(3)
N1…N1A [a]			5.224(6)
N1…O1A [a]			5.832(3)
O3…O3A [a]			5.267(4)

[a] Symmetry code: A) *y*, *x*, *-z*.

the highly distorted cone conformations. The distortions from the regular cones are reflected by the considerable tilting of the phenyl rings. In **1**, for example, the two phenyl rings linked by the rim are considerably tilted from the perpendicular plane of the α-C_4 core plane (defined with a square plane from four methylene carbon atoms) [72.07(4)° and 76.10(4)°, respectively], whereas the other two phenol rings are tilted away from that plane as much

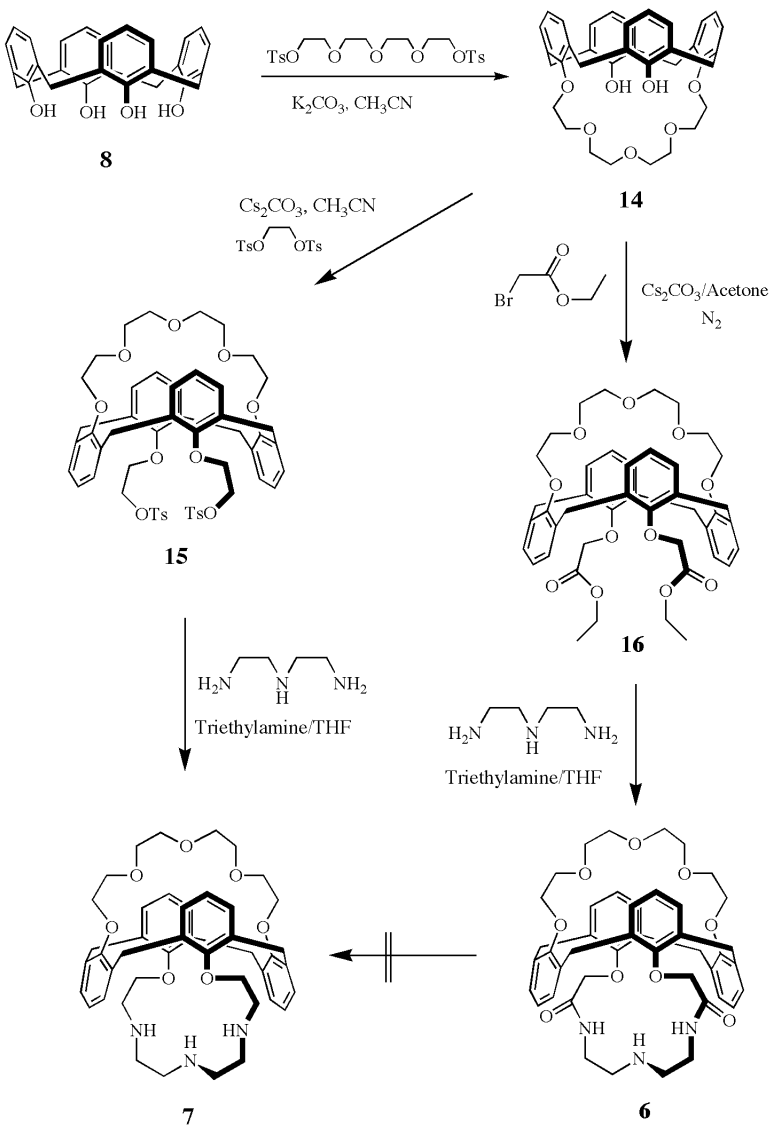
Table 1

Crystallographic Data and Structure Refinement Parameters for **1**, **2** and **3**

Compound	**1** $C_{36}H_{37}N_3O_6$•CH_3OH	**2** $C_{36}H_{41}N_3O_4$•$2CH_3OH$	**3** $C_{42}H_{49}N_3O_6$
Empirical formula	$C_{37}H_{41}N_3O_7$	$C_{38}H_{49}N_3O_6$	$C_{42}H_{49}N_3O_6$
Formula weight	639.73	643.80	691.84
Temperature (K)	173(2)	173(2)	298(2)
Crystal system	Triclinic	Triclinic	Trigonal
Space group	P-1	P-1	$P3_221$
a (Å)	10.4342(18)	10.063(2)	11.8723(7)
b (Å)	11.608(2)	11.467(2)	11.8723(7)
c (Å)	15.156(3)	15.846(3)	23.5356(19)
α (°)	75.571(3)	110.842(3)	90
β (°)	77.305(3)	94.589(4)	90
γ (°)	70.390(3)	94.456(4)	90
V (Å^3)	1655.9(5)	1692.3(6)	2872.9(3)
Z	2	2	3
D_{calc} (g cm^{-3})	1.283	1.263	1.200
Absorption coefficient (mm^{-1})	0.089	0.085	0.080
F(000)	680	692	1110
Crystal size (mm)	0.2 ¥ 0.3 ¥ 0.4	0.4 ¥ 0.4 ¥ 0.6	0.20 ¥ 0.20 ¥ 0.30
θ Range (°)	1.40 to 28.28	1.38 to 28.38	1.98 to 28.28
Reflections collected	10624	10501	18570
Independent reflections	7432 [R_{int} = 0.0477]	7376 [R_{int} = 0.0382]	4607 [R_{int} = 0.0870]
Data / restraints / parameters	7432 / 0 / 424	7376 / 0 / 427	4607 / 0 / 251
Goodness-of-fit on F^2	1.023	1.074	0.890
Final *R* indices [$I>2\sigma(I)$]	R_1 = 0.0473 [a], wR_2 = 0.1217 [b]	R_1 = 0.0662 [a], wR_2 = 0.2009 [b]	R_1 = 0.0535 [a], wR_2 = 0.1003 [b]
R indices (all data)	R_1 = 0.0683 [a], wR_2 = 0.1389 [b]	R_1 = .0795 [a], wR_2 = 0.2154 [b]	R_1 = 0.1610 [a], wR_2 = 0.1290 [b]

[a] $R_1 = \Sigma| |F_o|-|F_c| |/\Sigma|F_o|$; [b]$wR_2 = [\Sigma [w(F_o^2-F_c^2)^2]/ \Sigma w(F_o^2)^2]^{1/2}$.

Scheme 4



Synthetic route for compound **6** and **7**.

as 37.54(5)° and 41.46(5)°, respectively. In **2**, the orientations of the phenyl rings are quite similar to those of **1** regardless of the elimination of two oxygen atoms of the amido groups. A detailed inspection of the crystal structures of **1** and **2** reveals that the cone conformations and each rim are stabilized by intramolecular hydrogen bonds (dashed lines in Figure 1) between phenolic hydroxy groups and O/N donors (for **1**) or O donor (for **2**). The hydrogen bonding parameters are listed in Table 3. The torsion angles between donor atoms in N_3O_2 rims for **1** and **2**, which have the values 1-69º, are in the *gauche* arrangements. It is known that 1,4-interactions between heteroatoms (E=O, N or S) in the -E-CH_2-CH_2-E- bond depend on whether E is a first or second-row element [16-18]. For example, O and N heteroatoms stabilize the *gauche* conformation because of the dispersion forces between the hetero E atoms. In contrast, for E=S, the larger size of atoms causes greater repulsion between electrons, which disfavors *gauche* conformations. The present rules readily apply to the structure of **1** and **2** shown in Figure 1.

Its crystal structure shows that **3** has a typical saddle-shaped 1,3-alternate conformation: the aromatic rings are tilted up and down alternately related to the α-C_4 core (Figure 2). In the structure, a two-fold symmetry axis passes along the vector linked N2 and the center of calixarene circle. The crystal structure also indicates that it exists in a non-folded configuration. Two types of aromatic rings are slightly tilted from the perpendicular plane

Table 3

Hydrogen-bonding Geometry in **1** and **2** (Å, °)

D-H…A	D-H	H…A	D…A	D-H…A
Compound **1**				
N1-H1…O6	0.95	2.24	3.184 (2)	174.34
N3-H3…O5	0.97	2.24	3.185 (2)	169.09
O5-H5…O1	0.84	2.01	2.838 (2)	169.75
O6-H6…O3	0.84	2.22	2.910 (2)	139.59
O7-H7…N2	0.84	2.01	2.844 (2)	171.65
N2-H2…O4^{i}	0.94	2.12	3.009 (2)	158.79
Compound **2**				
O2-H2A…O1	0.84	2.05	2.859(2)	160.66
O4-H4…O3	0.84	1.97	2.775(2)	160.56
O5-H5A…N1	0.84	2.15	2.777(3)	130.98

Symmetry code: (i) 1-*x*, 1-*y*, 1-*z*.

of the α-C_4 core plane: 86.52(6)° for the ring with propyloxy substituent and 81.29(5)° for the ring with amidocrown rim, respectively. The dihedral angles between opposite aromatic systems are 7.0(1)° (for azacrown attached rings) and 17.4(2)° (for propanoxy pendant attached rings), respectively. The torsion angles between donor atoms in the N_3O_2 rim are in the *gauche* arrangements as expected. The azacrown segment near N2 atom and methyl carbon of propanoxy terminal group are partially disordered, occupying two positions.

EXPERIMENTAL

Synthesis.

Compounds **8** [1], **9** [19], **10** [2] and **14** [20] were prepared from the adaptation of the reported procedures.

Calix[4]amidocrown-5, Cone (**1**).

To a solution of **9** (1.00 g, 1.68 mmol) in absolute ethanol (60 mL) and toluene (60 mL) was added 6 mL of diethylenetriamine under an Ar atmosphere. The mixture was refluxed for 48 hr. Solvent was removed *in vacuo* and the residue triturated with MeOH overnight. The precipitated solid was collected, washed with methanol and then dried to afford 509 mg (50.0 %) of the desired product as crystalline solid. Mp 250 °C (dec.); IR (KBr): 3329, 1683 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 8.26 (br. t, 3 H, N*H*, *J* = 5.9 & 5.4 Hz), 7.72 (br. s, 2 H, O*H*), 7.15 (d, 4 H, Ar*H*, *J* = 7.3 Hz), 6.98 (d, 4 H, Ar*H*, *J* = 7.3 Hz), 6.76 (t, 2 H, Ar*H*, *J* = 7.6 Hz), 6.63 (t, 2 H, Ar*H*, *J* = 7.6 Hz), 4.45 (s, 4 H, OCH_2CO), 4.24 (d, 4 H, ArCH_2Ar, *J* = 13.2 Hz), 3.45 (d, 4 H, ArCH_2Ar, *J* = 13.2 Hz), 3.39 (br. q, 4 H, NCH_2, *J* = 5.9 & 5.4 Hz), 2.82 (br. t, 4 H, NCH_2, *J* = 5.4 Hz). ^{13}C NMR ($CDCl_3$): δ 168.53 (*C*=O), 152.88, 152.85, 133.94, 129.80, 129.48, 128.40, 126.17, 120.25 (Ar), 75.32 (OCH_2CO), 49.08, 40.41 (NCH_2), 31.13 ppm (ArCH_2Ar).

Anal. Calcd. for $C_{36}H_{37}O_6N_3$: C, 71.15; H, 6.14. Found: C, 71.21; H, 6.08.

Calix[4]triazacrown-5, Cone (**2**).

To the suspension of $LiAlH_4$ (1.56 g, 41.2 mmol) in absolute ethyl ether (15 mL) was added the solution of **1** (1.50 g, 0.82 mmol) in ether (30 mL), and the reaction mixture was then refluxed for 24 hr. After cooling to 0 °C, a small amount of water was added to quench the reaction, which was extracted with methylene chloride (30 mL) twice. The organic layer was collected, washed with water, and dried over anhydrous $MgSO_4$, and the solvent was evaporated to yield a slightly colored solid. Pure product was isolated by the flash chromatographic separation (eluent was a 1:20 mixture of methanol and methylene chloride) to give 252 mg (53.6 %) of the product **2** as a crystalline solid. mp 240 °C; IR (KBr) 3372, 3198 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.05 (d, 4 H, Ar*H*, *J* = 7.4 Hz), 6.85 (d, 4 H, Ar*H*, *J* = 7.6 Hz), 6.70 (t, 2 H, Ar*H*, *J* = 7.6 Hz), 6.65 (t, 2 H, Ar*H*, *J* = 7.4 Hz), 4.36 (d, 4 H, ArCH_2Ar, *J* = 13.1 Hz), 4.11 (t, 4 H, CH_2, *J* = 4.6 Hz), 3.36 (d, 4 H, ArCH_2Ar, *J* = 13.1 Hz), 3.16 (t, 4 H, CH_2, *J* = 4.6 Hz), 2.86 (m, 8 H, CH_2), 2.00 (br, 5 H, O*H* & N*H*). ^{13}C NMR ($CDCl_3$): δ 153.42, 152.10, 133.28, 129.22, 128.70, 128.35, 125.60, 119.33 (Ar), 77.23 (OCH_2), 50.64, 49.79, 49.63 (NCH_2), 31.48 ppm (ArCH_2Ar).

Anal. Calcd. for $C_{36}H_{41}O_4N_3$: C, 74.58; H, 7.13. Found: C, 74.31; H, 7.08.

Calix[4]amidocrown Dipropyl Ether, 1,3-Alternate (**3**).

To a solution of **11** (900 mg, 1.32 mmol) in absolute ethanol (50 mL) and toluene (50 mL) was added 3.8 mL of diethylenetriamine under an Ar atmosphere. The mixture was refluxed for 24 hr. Solvent was removed *in vacuo* and the resulting material was recrystallized from methylene chloride and methanol to afford 595 mg (65%) of **3** as crystalline solid. Mp 198 °C. IR (KBr): 3399, 1671 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.03 (d, 4 H, Ar*H*, *J* = 7.6 Hz), 6.90 (d. 4 H, Ar*H*, *J* = 7.6 Hz), 6.77 (t, 2 H, Ar*H*, *J* = 7.6 Hz), 6.61 (br, 5 H, Ar*H* & N*H*), 4.24 (s, 4 H, OCH_2CO), 3.65 (d, 4 H, ArCH_2Ar, *J* = 14.4 Hz), 3.62 (m, 8 H, OCH_2 & NH_2), 3.47 (d, 4 H, ArCH_2Ar, *J* = 14.4 Hz), 2.91 (br. t, 4 H, NCH_2, *J* = 4.6 Hz), 1.77 (sextet, 4 H, CH_2, *J* = 7.4 Hz), 0.94 (t, 6 H, CH_3, *J* = 7.6 Hz). ^{13}C NMR ($CDCl_3$): δ 168.64 (*C*=O), 157.23, 154.00, 134.38, 133.30, 131.48, 130.47, 122.89, 121.14 (Ar), 73.73 (OCH_2CO), 69.75 (OCH_2), 49.69, 39.55 (NCH_2), 36.91 (ArCH_2Ar), 23.90 (OCH_2CH_3), 0.94 (CH_2) ppm.

Anal. Calcd. for $C_{42}H_{49}O_6N_3$: C, 72.91; H, 7.14. Found: C, 72.79; H, 6.98.

Calix[4]triazacrown Dipropyl Ether, 1,3-Alternate (**4**).

To a solution of compound **12** (500 mg, 0.593 mmol) and pyridine (0.15 mL) in 40 mL of acetonitrile, diethylenetriamine (2.5 mL, 23 mmol) was added and the mixture was refluxed for 24 hr. Solvent was removed *in vacuo* and then a small amount of water was added to precipitate the product **4** (250 mg, 68.2%) as crystalline solid. Mp 180 - 182 °C; IR (KBr) 3435 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.18 (d, 4 H, Ar*H*, *J* = 7.4 Hz), 7.03 (d, 4 H, Ar*H*, *J* = 7.4 Hz), 6.75 (t, 4 H, Ar*H*, *J* = 7.4 Hz), 3.92 (br. t, 4 H, OCH_2CH_2N, *J* = 4.7Hz), 3.67 (s, 8 H, $ArCH_2Ar$), 3.52 (t, 4 H, $OCH_2CH_2CH_3$, *J* = 7.5 Hz), 2.97 (br, 4 H, OCH_2CH_2N), 2.88 (br, 4 H, NCH_2CH_2N), 2.82 (br, 4 H, NCH_2CH_2N), 1.71 (br, 3 H, N*H*), 1.66 (sextet, 4 H, $OCH_2CH_2CH_3$, *J* = 7.5 Hz), 0.89 (t, 6 H, $OCH_2CH_2CH_3$, *J* = 7.5 Hz). ^{13}C NMR ($CDCl_3$): δ 157.01, 156.89, 134.08, 134.02, 130.98, 130.85, 122.08, 121.44 (Ar), 73.16, 70.28 (CH_2), 51.42, 51.10, 50.01 (NCH_2), 37.57 ($ArCH_2Ar$), 23.53 (CH_2), 10.36 ppm (CH_3).

Anal. Calcd. for $C_{42}H_{53}O_4N_3$: C, 75.98; H, 8.05. Found: C, 76.14; H, 7.99.

Calix[4]bis-amidocrown, 1,3-Alternate (**5**).

To a solution of **13** (1.00 g, 1.68 mmol) in absolute ethanol (80 mL) and toluene (80 mL) was added 12 mL of diethylenetriamine under an Ar atmosphere. The mixture was refluxed for 48 hr. Solvent was removed *in vacuo* and the residue triturated with MeOH overnight. The precipitated solid was collected, washed with methanol and then recrystallized from methylene chloride and methanol to afford 382 mg (74.2 %) of the desired product **5** as crystalline solid. Mp 220 °C. IR (KBr): 3398, 1671 cm^{-1}. ^1H NMR (DMSO-d_6): δ 6.87 (d, 8 H, Ar*H*, *J* = 7.3 Hz), 6.79 (t, 4 H, Ar*H*, *J* = 7.3 Hz), 6.40 (t, 6 H, N*H*, *J* = 4.5 Hz), 4.13 (s, 4 H, OCH_2CO), 3.54 (s, 8 H, $ArCH_2Ar$), 3.43 (br, 8 H, NCH_2), 2.71 (br, 8 H, CH_2N). ^{13}C NMR (DMSO-d_6): δ 167.73 (*C*=O), 154.32, 134.21, 131.09, 123.30 (Ar), 70.04 (OCH_2CO), 50.01, 39.29 (NCH_2), 35.94 ppm ($ArCH_2Ar$).

Anal. Calcd. for $C_{44}H_{50}O_8N_6$: C, 66.82; H, 6.37. Found: C, 66.74; H, 6.28.

Calix[4]crown-5-diamidocrown-5 (**6**).

Under nitrogen, to a three-neck round-bottom flask were added **16** (1.00 g, 1.32 mmol), diethylenetriamine (0.27 g, 2.6 mmol) and ethanol (50ml)/toluene (50ml), and the mixture was refluxed for 24 hr. Reaction solvents were completely removed *in vacuo*, and 100 mL of 10 % aqueous $NaHCO_3$ solution and 100 mL of CH_2Cl_2 were added. The organic layer was separated and washed three times with 50 mL of water, dried over $MgSO_4$, and then filtered. Evaporation of CH_2Cl_2 *in vacuo* gave a white solid, which was purified by recrystallization from methanol to provide 0.3 (30 % yield) of **6** a white solid. Mp 223-235 °C. IR (neat, cm^{-1}): 3426, 2919, 1652, 1472, 1051, 1005, 927. ^1H NMR (400 MHz, $CDCl_3$): δ 7.21-7.19 (d, 4 H, Ar-H_m, *J* = 7.49 Hz), 6.99-6.95 (d, 4 H, Ar-H_m, *J* = 7.44 Hz), 6.95-6.91 (t, 2 H, Ar-H_p, *J* = 7.51 Hz), 6.72-6.68 (t, 2 H, Ar-H_p, *J* = 7.51 Hz), 6.49 (s, 2 H, -CON*H*CH_2-), 4.19 (s, 4 H, $ArOCH_2$ CO), 3.76-3.49 (m, 8 H, Ar-CH_2 –Ar; 20 H, -OCH_2CH_2O-; 1 H, -N*H*), 2.88 (broad t, 4 H, -CH_2NHCH_2-), ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 161.2, 158.3, 129.2, 129.1, 126.9, 126.5, 121.8, 121.1, 76.9, 73.6, 70.4, 50.3, 45.2, 22.1 ppm. FAB MS *m*/*z* (M^+) calcd 765.8, found 765.6.

Anal. Calcd. for $C_{44}H_{51}N_3O_9$: C, 68.94; H, 6.66. Found: C, 68.91; H, 6.64.

Calix[4]crown-5-triazacrown-5 (**7**).

Under nitrogen, to a three-neck round-bottom flask were added **15** (1.00 g, 1.02 mmol), diethylentriamine (0.32 g, 3.1 mmol) and dry THF and the mixture was refluxed for 24 hr. Reaction solvents were completely removed *in vacuo*, and 100 mL of 10 % aqueous $NaHCO_3$ solution and 100 mL of CH_2Cl_2 were added. The organic layer was separated and washed three times with 50 mL of water, dried over $MgSO_4$, and then filtered. Evaporation of CH_2Cl_2 *in vacuo* gave a white solid, which was purified by recrystalization from methanol to provide 0.11 (15 % yield) of **8** a white solid. Mp 249-253 °C. IR (KBr pellet, cm^{-1}): 3413, 2927, 1460, 1097, 1047, 784). ^1H NMR (400 MHz, $CDCl_3$): δ 7.13-7.03 (broad m, 8 H, Ar-H_m), 7.13-7.04 (broad m, 4 H, Ar-H_p), 3.96-3.53 (m, 20 H, -OCH_2CH_2O-; 8 H, Ar-CH_2 –Ar), 3.22-2.62 (m, 12 H, -CH_2NHCH_2-; 3 H, -N*H*), ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 129.2, 126.5, 121.1, 74.3, 73.6, 70.9, 70.5, 51.4, 51.1, 49.5, 22.1 ppm. FAB MS *m*/*z* (M^+) calcd 737.9, found 738.2.

Anal. Calcd. for $C_{44}H_{54}N_3O_7$: C, 71.55; H, 7.32. Found: C, 71.53; H, 7.30.

25,27-Bis(ethyl acetoethoxy)-26,28-dipropyloxycalix[4]arene, 1,3-Alternate (**11**).

Compound **10** (1.50 g, 2.95 mmol), cesium carbonate (4.50 g, 13.8 mmol) and acetonitrile (60 mL) were stirred magnetically for 20 min in 100 mL round bottomed reaction flask. Ethyl bromoacetate (4.5 mL, 40.4 mmol) was added then the reaction mixture was refluxed for 2 days. Solvent was removed *in vacuo* and then the organic material was extracted with methylene chloride. The organic layer was washed with water, dried and evaporated to afford slightly colored residue, which was recrystallized from methylene chloride and methanol to produce 1.24 g (62%) of the product **11** as crystalline solid. Mp 142 °C; IR (KBr) 1759 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.09 (d, 4 H, Ar*H*, *J* = 7.6 Hz), 7.00 (d, 4 H, Ar*H*, *J* = 7.6 Hz), 6.72 (t, 2 H, Ar*H*, *J* = 7.6 Hz), 6.71 (t, 2 H, Ar*H*, *J* = 7.6 Hz), 4.12 (q, 4 H, OCH_2, *J* = 7.1Hz), 3.89 (d, 4 H, $ArCH_2Ar$, *J* = 14.8Hz), 3.68 (d, 4 H, $ArCH_2Ar$, *J* = 14.8Hz), 3.57 (s, 4 H, OCH_2CO), 3.51 (t, 4 H, O CH_2, *J* = 7.4 Hz), 1.45 (sextet, 4 H, CH_2, *J* = 7.4 Hz), 1.23 (t, 6 H, CH_3, *J* = 7.1 Hz), 0.84 (t, 6 H, CH_3, *J* = 7.4 Hz). ^{13}C NMR ($CDCl_3$): δ 170.29 (*C*=O), 157.18, 155.40, 134.56, 133.84, 130.44, 130.27, 122.70, 122.54 (Ar), 73.66, 69.10, 60.64 (OCH_2), 23.14 (CH_2), 14.35, 10.44 (CH_3) ppm.

Anal. Calcd. for $C_{42}H_{46}O_8$: C, 74.09; H, 7.11. Found: C, 74.17; H, 7.04.

25,26-Bis(tosyloxyethyl)oxy-26,28-dipropyloxycalix[4]arene, 1,3-Alternate (**12**).

Compound **10** (500 mg, 0.983 mmol), cesium carbonate (961 mg, 2.95 mmol) and acetonitrile (40 mL) were stirred magnetically for 20 min. Ethylene glycol ditosylate (1.09 g, 2.95 mmol) was added and the mixture was refluxed for 24 hr. After cooling to room temperature, solvent was removed *in vacuo* and then the organic material was extracted with methylene chloride. The organic layer was washed with water, dried and evaporated to afford slightly colored residue, which was separated with flash chromatography (eluent was 9:1 mixture of hexane and acetone) to afford the product **12** (450 mg, 54.3%) as crystalline solid. Mp 139-140 °C; IR (KBr) 1360, 1189 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.81 (d, 4 H, Ar*H*, *J* = 7.4 Hz), 7.37 (d, 4 H, Ar*H*, *J* = 7.4 Hz), 6.95 (d, 4 H, Ar*H*, *J* = 7.4 Hz), 6.86 (d, 4 H, Ar*H*, *J* = 7.4 Hz), 6.72 (t, 2 H, Ar*H*, *J* = 7.4 Hz), 6.50 (t, 2 H, Ar*H*, *J* = 7.4 Hz), 3.71 (t, 4 H, OCH_2, *J* = 6.0Hz), 3.66 (d, 4 H, $ArCH_2Ar$, *J* = 14.8Hz),

3.58 (d, 4 H, ArCH_2Ar, J = 14.8Hz), 3.47 (t, 4 H, CH_2, J = 6.0Hz), 3.39 (t, 4 H, CH_2, J = 7.4Hz), 2.45 (s, 6 H, CH_3), 1.36 (sextet, 4 H, CH_2, J = 7.4Hz), 0.72 (t, 6 H, CH_3, J = 7.4Hz). ^{13}C NMR ($CDCl_3$): δ 157.01, 155.31, 145.17, 134.05, 133.80, 130.17, 130.06, 129.58, 129.32, 128.22, 122.75, 122.40 (Ar), 72.94, 68.21, 67.83 (*C*H_2), 37.25 (Ar*C*H_2Ar), 23.21 (*C*H_2), 21.90 (Ar*C*H_3), 10.45 ppm (*C*H_3).

Anal. Calcd. for $C_{52}H_{56}O_{10}S_2$: C, 69.00; H, 6.24. Found: C, 69.24; H, 6.16.

25,26,27,28-Tetra(ethyl acetoethoxy)calix[4]arene, 1,3-Alternate (**13**).

To a refluxing suspension of calix[4]arene (2.00 g, 4.53 mmol) and Cs_2CO_3 (8.87 g, 27.0 mmol) in dry acetone (150 mL) was added dropwise a solution of ethyl 2-bromoacetate (6.05 g, 36.2 mmol) in dry acetone (50 mL) over 3 h under nitrogen atmosphere. The reaction mixture was refluxed for an additional 24 hr. After cooling to room temperature, the salt was filtered and the solvent (acetone) was removed *in vacuo*. The reaction mixture was extracted with CH_2Cl_2 (3x50 mL), washed twice with water, dried over anhydrous $MgSO_4$, and the solvent was removed *in vacuo*. The crude product was chromatographed on silica gel using ethyl acetate and *n*-hexane (1:5) as eluent. Recrystallization from CH_2Cl_2/*n*-hexane (1:30, *v*/*v*) gave a white crystalline solid **6** in 29% yield (1.02 g). Mp 118~119 °C (lit. [9] 111~112 °C). IR (KBr pellet): 2921, 1771, 1439, 1181, 1092, 1048, 760 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.16 (d, 8 H, Ar-*H*), 6.71 (t, 4 H, Ar-*H*), 4.23 (q, 8 H, OCH_2CH$_3$), 4.04 (s, 8 H, ArCH_2Ar), 3.78 (s, 8 H, ArOCH_2), 1.33 (t, 12 H, OCH$_2$CH_3). ^{13}C NMR ($CDCl_3$): δ 169.5, 155.4, 133.4, 130.3, 122.8, 69.6, 60.7, 35.5, 14.1 ppm.

Anal. Calcd. for $C_{44}H_{44}O_{12}$: C, 69.10; H, 5.76. Found: C, 69.27; H, 5.75.

25,27-Bis(tosyloxyethoxy)-26,28-calix[4]crown-5, 1,3-Alternate (**15**).

Under nitrogen, a solution of calix[4]arene monocrown-5 **14** (3.00 g, 5.15 mmol), ethylene glycol ditosylate (4.00 g, 10.8 mmol) and Cs_2CO_3 (5.03 g, 15.4 mmol) in 100 mL of acetonitrile was heated to reflux temperature. After refluxing for 24 hr, acetonitrile was removed *in vacuo*. To the resulting brownish solid, 100 mL of 5 % aqueous HCl solution and 50 mL of CH_2Cl_2 were added and the organic layer was separated and washed three times with 50 mL of water. The organic layer was dried over anhydrous $MgSO_4$ and the solvent was evaporated *in vacuo* to give a brownish oil. Recrystalization from methylene chloride/diethyl ether (1:5) gave 2.82 g (56 % yield) of **19** as white solid. Mp: 181-182 °C. IR (KBr pellet, cm^{-1}): 3035, 2911, 1460, 1359, 1182, 1097, 996, 934, 826, 772, 664, 556. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.38 (dd, 8 H, tosyl Ar-*H*), 7.08-6.91 (dd, 8H, Ar-H_m), 6.91-6.59 (tt, 4 H, Ar-H_p), 3.85-3.09 (m, 24 H, -OCH_2CH_2O-), 2.47 (s, 3 H, tosyl Ar-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.5, 145.1, 131.9, 130.3, 129.2, 127.6, 126.5, 121.1, 73.6, 72.2, 70.4, 70.2, 61.7, 22.1, 20.9 ppm. FAB MS *m*/*z* (M^+) calcd 979.1, found 978.7.

Anal. Calcd. for $C_{54}H_{58}O_{13}S_2$: C, 66.20; H, 5.92. Found: C, 66.24; H, 5.90.

25,27- Bis(ethyl acetoethoxy)-26,28-calix[4]crown-5, 1,3-Alternate (**16**).

Under nitrogen, a solution of calix[4]arene monocrown-5 (**14**) (5.00 g, 8.58 mmol), ethyl bromoacetate (4.30 g, 25.7 mmol) and Cs_2CO_3 (8.39 g, 25.7 mmol) in 100 mL of acetonitrile was heated to reflux temperature. After refluxing for 24 hr, acetonitrile was removed *in vacuo*. To the resulting white solid, 100 mL of 5 % aqueous HCl solution and 50 mL of CH_2Cl_2 were added and the organic layer was separated and washed three times with 50 mL of water. The organic layer was dried over anhydrous $MgSO_4$ and the solvent was evaporated *in vacuo* to give a white solid. Column chromatography on silica gel using ethyl acetate/hexane (1:3) as eluents gave 5.34 g (82 % yield) of **20** as a white solid. Mp: 170 °C. IR (KBr pellet, cm^{-1}): 2919, 1669, 1460, 1251, 1205, 1128, 1097, 1042, 927, 760. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15-7.11 (dd, 8 H, Ar-H_m, J = 8.21 Hz), 6.92-6.88 (t, 2 H, Ar-H_p, J = 7.47 Hz), 6.86-6.82 (t, 2 H, Ar-H_p), 4.16-4.12 (d, 4 H, Ar-CH_2 –Ar, J = 16.14 Hz), 4.05-4.00 (q, 4 H, -COOCH_2CH$_3$), 3.87-3.83 (d, 4 H, Ar-CH_2 –Ar, J = 16.11 Hz), 3.66-3.56 (m, 12 H, -OCH_2CH_2O-), 3.36 (s, 4 H, Ar-OCH_2 CO), 3.17-3.14 (t, 4 H, -OCH_2CH$_2$O-, J = 6.76), 1.19-1.15 (t, 6H, -COOCH$_2$CH_3, J = 7.12). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 161.8, 158.2, 129.1, 126.9, 126.5, 121.8, 121.1, 76.2, 73.6, 70.9, 70.5, 59.2, 22.1, 13.6 ppm. FAB MS *m*/*z* (M^+) calcd 754.8, found 755.5.

Anal. Calcd. for $C_{44}H_{50}O_{11}$: C, 70.03; H, 6.63. Found: C, 70.05; H, 6.64.

X-ray Crystal Structures.

Data were collected on a Bruker SMART diffractometer equipped with graphite monochromated Mo Kα (λ = 0.71073 Å) radiation source and CCD detector; 45 frames of two-dimensional diffraction images were collected and processed to obtain the cell parameters and orientation matrix [21]. The data for **1** and **2** were collected at -100 °C, while the data for **3** were collected at ambient temperature. The raw data were processed to give structure factors using the SAINT program [21]. The structure was solved by direct method and refined by full matrix least squares against F^2 for all data using SHELXTL software [22]. All non-hydrogen atoms were anisotropically refined. In compounds **1** and **2**, all hydrogens except those of secondary amine were included in the calculated position and refined using a riding model. The initial positions of the hydrogen atoms attached to nitrogen atoms were obtained from difference electron density maps. Their positional parameters were then fixed and refined isotropically. Although the lengths of the N-H vectors are almost certainly slightly underestimated, their directional components can be considered to be quite reliable. In compound **3**, all hydrogen atoms were placed in the calculated positions and refined using a riding model. Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Centre, CCDC No. 217675 for **1**, No. 217676 for **2** and No. 217677 for **3**. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk)

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