Abstract: The macrocyclic tetraamides 8a–e were obtained in good yields by bis-alkylation of the potassium salts of the appropriate bis-phenols 7a–c with the dihalo compounds 2a,b. Similarly, macrocyclic tetraamides with pendant hydroxy groups 5a,b were prepared by the nucleophilic reaction of the potassium salts of 7a,b with the dihalo compound 10. Acylation of 18a,b with chloroacetyl chloride gave the corresponding ester 19a,b. Compounds 19a,b reacted with different secondary amines to afford the corresponding lariat macrocycles 20a–d and novel bis-macrocycle 21 in 50–65% yield.

Key words: macrocyclic tetraamides, acyclic diamides, lariat macrocycles, bis-macrocyclic tetraamides

Much attention has been paid to the development of functional groups in the ring of crown ethers in an attempt to enhance the selectivity and the stability of complexes of these ligands.1–4 For example, incorporation of an amide linkage in a polyether macrocyclic has been reported to modify the binding properties of the crown ether compounds to favor alkali and alkaline earth cations.5–12 Also, it was reported that, macrocyclic ligands with amide functional groups as binding sites show strong and selective affinities for lithium over sodium and other alkali metal ions.22–24 Furthermore, there is an intensive development of the lariat crown ethers concept25 which led to the synthesis of large numbers of side-armed crown compounds, designed for uses ranging from routine (polymer-supported PTC catalysts, separation/extraction reagents, etc.) to sophisticated (application as redox switches for membrane transport, synthetic cation-conducting channels, etc.).26 Lariat crown compounds can mimic the cation binding behavior of naturally occurring ionophores such as valinomycin,27 where the side arm can effectively participate in the coordination and lead to higher cation-binding affinities for the new compounds compared with the parent macrocycle containing no extra donor sites.28,29

Keeping the above facts in mind, and in continuation of my interest in the synthesis of macrocyclic ligands with amide functional groups30–33 and bis-macrocycles,34 I am now engaged in a project directed towards the synthesis of 27–29-membered macrocyclic tetraamides, acyclic diamides and their lariat derivatives with strong donor heteroatoms in the side arm as well as the bis-macrocyclic tetraamides aiming at the increase of their cation binding affinities. In this project a new methodology for the synthesis of the target macrocycles from activated bis(chloroacetamidophenoxy)alkanes and bis-phenolic compounds was used which are easily prepared from commercially available starting materials. Thus, reaction of 1, o-bis(2-aminophenoxo)alkane hydrochlorides 1a,b with chloroacetyl chloride in DMF at 100 °C afforded exclusively the corresponding 1, o-bis(2-chloroacetamidophenoxy)alkanes 2a,b in 70–76% yields. The latter compounds exhibit high reactivity towards different nucleophiles as shown in Scheme 1. Reaction of 2a,b with the potassium salts of 3a,b [obtained upon treatment of salicylaldehyde (3a) and o-nitrophenol (3b) with methanolic potassium hydroxide solution] in boiling DMF gave the corresponding bis-[2-[2-formyl or (2-nitrophenoxy)acetamidophenoxy]]alkanes 4a,b, respectively, in moderate yields (50–60%). Moreover, compounds 2a,b reacted with different secondary amines (namely, piperidine, morpholine, and N,N-diethylamine) to furnish the corresponding 27-membered compounds 5a–c and 6a,b, respectively, in 59–70% yields. The structures of compounds 4a,b, 5a–c and 6a,b were inferred from the different spectroscopic and analytical data. These results prompted a study of the reactivity of 2a,b towards bis-phenolic compounds aiming at preparing novel macrocycles tetraamides. Thus, treatment of 2a with the potassium salt of bis-phenol 7a (obtained upon treatment of 7a with methanolic potassium hydroxide solution) under the same reaction conditions used for preparing 4a,b afforded the corresponding 27-membered macrocyclic tetraamide 8a in 30% yield. Similarly, the 27–29-membered macroyclic 8b–d were easily obtained in 26–35% yield by reacting the potassium salts of the appropriate bis-phenols 7a–c with 2a,b in refluxing DMF.

Next, the study was extended to include the synthesis of some new acyclic diamides, lariat macrocyclic tetraamides as well as bis-macrocyclic tetraamide as outlined in Schemes 2 and 3. For this purpose, our strategy was based on using 2-hydroxy-1,3-bis(2-aminophenoxy)propane hydrochloride (9) as a starting material to synthesize the...
key intermediate compound 10. Thus, reaction of two equivalents of chloroacetyl chloride with one equivalent of 9 in DMF at 100 °C afforded the trichloroacyl product 11 in 40% yield and not the desired dichloroacyl product 10 (<2%) as expected with recovery of about 30% of starting material (TLC and 1H NMR spectrum). As a result of the low yield of the target dichloroacyl product 10, the reaction was repeated using different reaction conditions and solvents. Surprisingly, compound 10 could be obtained as the major product (70% yield) by reacting one equivalent of 9 with two equivalents of chloroacetyl chloride in DMF at –5 °C with the formation of traces of 11 (<2%). It is noteworthy that compound 11 could be obtained in 90% yield by reaction of 9 with three equivalents of chloroacetyl chloride in DMF at 100 °C.

The reactivities of 10 and 11 towards different nucleophiles were investigated aimed at the preparation of new acyclic diamides, their lariat analogues and bis-acyclic diamides. Thus, compound 11 reacts exclusively with piperidine and morpholine to give the corresponding triamino derivatives 12a,b in 70% and 75% yields, respectively. Similarly, reaction of 10 as a representative example with morpholine gave the corresponding 2-hydroxy-1,3-bis(2-N-morpholinoacetamidophenoxy)propane (13) in 65% yield. Moreover, compound 10 reacted with the potassium salt of salicyaldehyde and o-nitrophenol in boiling DMF to afford the corresponding 2-formylphenoxy or 2-nitrophenoxy derivatives 14a,b in 55% and 60% yields, respectively. Consequently, 14b reacted with chloroacetyl chloride in DMF to afford the corresponding O-acyl product 15 which reacted with morpholine and piperazine in
acetone to furnish the corresponding 2-(N-morpholinoacetoxy) 16 and 1,4-bispiperazino derivative 17 in 70% and 60% yields, respectively as depicted in Scheme 2. The structure of the novel bis-product 17 was confirmed by IR, 1H NMR, 13C NMR, and elemental analyses data.

In continuation of the study and due to the success in the synthesis of the novel acyclic diamide 16 and bis-piperazino derivative 17, the strategy was extended to the synthesis of the target lariat and bis-macrocycles containing four amide groups. For this purpose, compound 10 was chosen as a key intermediate for preparing the macrocycles with a pendant hydroxy group 18a,b, as precursors for synthesis of lariat and bis-macrocycles as outlined in Scheme 3. Thus, reaction of 10 with the bis-potassium salt of 7a,b gave 15-hydroxy macrocyclic tetraamides 18a,b as expected in 40–45% yields. The latter compounds reacted with chloroacetyl chloride in DMF to furnish 15-(chloroacetoxy) macrocycles 19a,b in 70–85% yields. Treatment of esters 19a,b with N,N-diethylamine, morpholine, and piperazine afforded the corresponding 15-(N,N-diethylaminoacetoxy), 15-(N-morpholinoacetoxy) and 1,4-bis-macrocycles 20a–d and 21 in 50–65% yields, respectively. The structures of the compounds were confirmed by IR, 1H NMR, 13C NMR spectra and elemental analyses data.
From the $^1$H NMR and $^{13}$C NMR data of the new macrocyclic tetraamides $8a$–$e$, $18a$, $19a,b$ and $20a$–$d$, the following conclusions were obtained:

a) The magnetic equivalence of the OCH$_2$ and NCH$_2$ protons in $8a$–$e$ indicates rapid change in all macrocycles.

b) Contrary to compounds $8a$–$e$, the 15-substituted macrocycles $18a$, $b$, $19a$, $b$ and $20a$–$d$ show in their $^1$H NMR a geminal coupling and nonequivalence in all OCH$_2$ and NCH$_2$ protons. This indicates that the 15-substituted macrocycles are evidently present in one stable conformer or as slow (on the time scale of NMR) interconverting conformers. Evidence for the existence of the lariat derivatives entirely as one stable nonconvertible conformer comes from $^{13}$C NMR data (cf. experimental). Similar results were reported by Ibrahim et al. for some $N$-alkyl derivatives $A$ ($R = $ Me, Et, PhCH$_2$, and PhCO (Figure 1).

c) The $^1$H NMR of all macrocyclic tetraamides in CDCl$_3$ or DMSO-$d_6$ showed a triplet or a broad singlet for NH in NHCH$_2$ group indicating a reduced rate of exchange in these compounds. This behavior may be attributed to the intermolecular hydrogen bonded structure $B$ (Figure 1).
In conclusion, a new series of acyclic diamides and 27–29-membered tetrabenzo-substituted macrocyclic tetraamides and their 15-hydroxy derivatives have been synthesized as precursors for the synthesis of novel lariat macrocycles containing strong donor group as supporting ligand at the end of the side arm. The development of the present reactions will provide a new way for the synthesis of a new and wide variety of useful lariat macrocycles having a variety of donor/acceptor end groups with side arms of different lengths. In addition this project succeeded in synthesizing as precursors for the synthesis of novel lariat macrocycles having two crown units connected by flexible bridge (having two crown moieties per cation). A study of the completion and crystallized from the appropriate solvent to afford compounds 1a,b, 10 and 11. The reaction mixture was stirred at 100 °C [(for compounds 2a,b, and 11) and at –5 °C (for compound 10)] for 2 h. The mixture was then poured onto crushed ice. The solid obtained was collected by filtration and crystallized from the appropriate solvent to afford 2a,b, 10 and 11.

1,3-Bis-[2-chloroacetamido]phenoxy]propane (2a)

With the use of the general procedure, 1a gave crude 2a which was crystallized from toluene to give colorless crystals (70%); mp 182–184 °C.

IR (KBr): 3382 (NH), 1760, 1682 cm –1 (C=O).

For compounds 2a,b, and 10 or 1.69 g (15 mmol) for the preparation of 11. The reaction mixture was stirred at 100 °C [(for compounds 2a,b, and 11) and at –5 °C (for compound 10)] for 2 h. The mixture was then poured onto crushed ice. The solid obtained was collected by filtration and crystallized from the appropriate solvent to afford 2a,b, 10 and 11.

1,4-Bis-[2-chloroacetamido]phenoxylbutane (2b)

By the general procedure, 1b gave crude 2b which was crystallized from benzene to give colorless crystals (76%); mp 152–154 °C. IR (KBr): 3396 (NH), 4.85; N, 6.85; Cl, 17.12.

Potassium Salts of Compounds 3a,b and 7a-c; General Procedure

To a solution of KOH (1.14 g, 10 mmol) in MeOH (10 mL) was added salicyldehyde (3a), o-nitrophenol (3b) (10 mmol), or bisphenol 7a-c (5 mmol). The mixture was stirred at r.t. for 10 min. The solvent was then removed in vacuo. The remaining solid was triturated with anhyd Et2O, collected, dried, and used in the next step without further purification.

Compounds 4a,b, 14a,b and Macrocyclic Tetraamides 8a–e and 18a,b; General Procedure

A solution of the appropriate potassium salt of 3a,b (20 mmol), or 7a-c (10 mmol) and the appropriate dichloro compound 2a,b, or 10 (10 mmol) in DMF (20 mL) was heated under reflux for 10 min during which time KCl precipitated. The solvent was then removed in vacuo and the remaining material was washed with H2O (50 mL) and crystallized from the appropriate solvent to give compounds 4a,b, 14a,b, 8a–e and 18a,b.
H NMR (DMSO-\textsubscript{d}6): \(\delta = 2.2\) (quintet, \(J = 5.6\) Hz, 2 H, OCH\textsubscript{2}CH\textsubscript{3}), 4.17 (t, \(J = 5.4\) Hz, 4 H, OCH\textsubscript{2}), 4.89 (s, 4 H, COCH\textsubscript{3}), 6.85–8.01 (m, 16 H, ArH), 9.23 (s, 2 H, NH), 10.48 (s, 2 H, CHO).

Anal. Calcd for C\textsubscript{19}H\textsubscript{18}N\textsubscript{2}O\textsubscript{8} (582.61): C, 68.03; H, 5.19; N, 4.81.  
Found: C, 68.20; H, 5.25; N, 4.71.

1,4-Bis(2-(2-nitrophenoxy)acetamidophenoxy)butane (4b)

By the general procedure, the potassium salt of 3b and 2b gave crude 4b which was crystallized from AcOH to give colorless crystals (60%); mp 204–205 °C.

IR (KBr): 3372 (NH), 1673 (C=O), 1526, 1346 cm\(^{-1}\) (NO\textsubscript{2}).

\(^{1}H\) NMR (DMSO-\textsubscript{d}6): \(\delta = 1.89\) (brs, 4 H, OCH\textsubscript{2}CH\textsubscript{3}), 4.09 (br s, 4 H, OCH\textsubscript{2}), 4.88 (s, 4 H, COCH\textsubscript{3}), 8.87–8.15 (m, 16 H, ArH), 9.04 (s, 2 H, NH).

Anal. Calcd for C\textsubscript{31}H\textsubscript{26}N\textsubscript{2}O\textsubscript{11} (630.61): C, 60.95; H, 4.79; N, 8.88.  
Found: C, 61.06; H, 4.85; N, 8.78.

2-Hydroxy-1,3-bis(2-(2-formylaminophenoxy)propane (1a)

By the general procedure, the potassium salt of 3a and 10 gave crude 1a which was crystallized from dioxane–EtOH to give pale yellow crystals (55%); mp 190–192 °C.

IR (KBr): 3396 (NH), 1647 cm\(^{-1}\) (C=O).

\(^{1}H\) NMR (CDCl\textsubscript{3}): \(\delta = 4.21\) (d, \(J = 4.1\) Hz, 4 H, OCH\textsubscript{2}), 4.45 (br s, 1 H, CH\textsubscript{2}OH), 4.72 (s, 4 H, COCH\textsubscript{3}), 5.10 (d, \(J = 5.7\) Hz, 1 H, OH), 6.86–8.36 (m, 16 H, ArH), 9.34 (s, 2 H, NH), 10.22 (s, 2 H, CHO).

Found: C, 66.34; H, 4.99; N, 4.52.

2-Hydroxy-1,3-bis(2-(2-nitrophenoxy)acetamidophenoxy)propane (1b)

By the general procedure, the potassium salt of 3a and 10 gave crude 1b which was crystallized from dioxane to give pale yellow crystals (60%); mp 209–211 °C.

IR (KBr): 3359 (NH), 3340 (OH), 1691 (C=O), 1520, 1342 cm\(^{-1}\) (NO\textsubscript{2}).

\(^{1}H\) NMR (DMSO-\textsubscript{d}6): \(\delta = 4.18\) (m, 4 H, OCH\textsubscript{2}), 4.37 (br s, 1 H, CH\textsubscript{2}OH), 4.95 (s, 4 H, COCH\textsubscript{3}), 5.42 (d, \(J = 5.6\) Hz, 1 H, OH), 6.91–8.09 (m, 16 H, ArH), 9.23 (s, 2 H, NH).

Anal. Calcd for C\textsubscript{31}H\textsubscript{26}N\textsubscript{2}O\textsubscript{11} (632.58): C, 58.86; H, 4.46; N, 8.86.  
Found: C, 58.99; H, 4.31; N, 8.99.

15-Hydroxy-6,14,15,24,32,33-hexahydro-16\-H4\-tetrahydro\-1\,6-bis\-[2-\{(2-nitrophenoxy)acetylamidophenol\}-7b,21,22,31,34f\]-tetraone (18a)

By the general procedure, the potassium salt of 18a was purified by column chromatography using EtOAc–petroleum ether (bp 40–60 °C) as an eluent, to give colorless crystals (40%); mp 94–96 °C.

1H NMR (CDCl3): \( \delta = 3.70 \) (s, 2 H, CH3O), 3.76–3.92 (m, 4 H, CH2Cl, CH2N), 3.90–4.0 (m, 4 H, CH2O), 5.43 (quintet, \( J = 5.5 \) Hz, 2 H, upfield of COCH2O), 8.73 (t, \( J = 5.5 \) Hz, 2 H, CH2NCO2H).

MS: \( m / \zeta = 745 \) (M + , 12), 581 (11), 488 (11.5), 314 (85), 224 (23), 177 (100), 120 (52).

Anal. Calcd for \( C_{38}H_{37}ClN_4O_{10} \) (745.18): C, 61.25; H, 5.00; N, 7.52; Cl, 4.93.

15-Chloroacetoxy-6,14,15,24,32,33-hexahydro-16\-H4\-tetrahydro\-1\,6-bis\-[2-\{(2-nitrophenoxy)acetamidophenol\}-7b,21,22,31,34f\]-tetraone (19b)

By the general procedure, 18b gave crude 19b, which was purified from AcOH–EtOH, to give colorless crystals (70%); mp 244–246 °C.

IR (KBr): 3348, 3248 (NH), 1759, 1682, 1643 cm\(^{-1}\) (C=O).

1H NMR (CDCl3): \( \delta = 1.84 \) (m, 2 H, OCH2), 3.22–3.29 (m, 4 H, NCH2CO), 3.80–4.0 (m, 4 H, OCH2), 4.63 (d, \( J = 15.3 \) Hz, 2 H, downfield of COCH2O), 4.95 (d, \( J = 15.5 \) Hz, 2 H, upfield of COCH2O), 5.43 (quintet, \( J = 5.7 \) Hz, 2 H, upfield of COCH2O), 8.73 (t, \( J = 5.5 \) Hz, 2 H, CH2NCO2H).

MS: \( m / \zeta = 745 \) (M + , 12), 581 (11), 488 (11.5), 314 (85), 224 (23), 177 (100), 120 (52).

Anal. Calcd for \( C_{38}H_{37}ClN_4O_{10} \) (745.18): C, 61.25; H, 5.00; N, 7.52; Cl, 4.93.

1,3-Bis[2-(N-piperidino)acetamidophenol]propane (5a)

By the general procedure, 2a and piperidine gave crude 5a, which was crystallized from EtOH to give colorless crystals (65%); mp 150–152 °C.

1H NMR (CDCl3): \( \delta = 3.18 \) (quintet, \( J = 5.4 \) Hz, 4 H, CH2CH2CH2N), 1.55 (quintet, \( J = 5.1 \) Hz, 8 H, CH2CH2CH2N), 2.41–2.52 (m, 10 H, CH2N, CH2CH2CH2O), 3.08 (s, 4 H, OCH2), 4.31 (t, \( J = 6.3 \) Hz, 4 H, OCH2), 6.80–8.46 (m, 8 H, ArH), 9.81 (s, 2 H, NH).

Anal. Calcd for \( C_{32}H_{45}N_4O_2 \) (508.66): C, 68.48; H, 7.93; N, 11.01. Found: C, 68.40; H, 7.91; N, 11.21.
1.3-Bis[2-(N-morpholino)acetoxy]propane (5b)
By the general procedure, 2a and morpholine gave crude 5b, which was crystallized from EtOH to give colorless crystals (70%); mp 176–178 °C.
IR (KBr): 3321 (NH), 1682 cm⁻¹ (C=O).

mp 160–162 °C.
which was crystallized from EtOH to give colorless crystals (59%); mp 140–142 °C.
IR (KBr): 3231 (NH), 1685 cm⁻¹ (C=O).

IR (KBr): 3305 (NH), 1685 cm⁻¹ (C=O).

IR (KBr): 3305 (NH), 1685 cm⁻¹ (C=O).

IR (KBr): 3364 (NH), 1745, 1688 (C=O), 1528, 1348 cm⁻¹ (NO₂).

IR (KBr): 3308 (NH), 3300 (OH), 1684 cm⁻¹ (C=O).

By the general procedure, 11 and morpholine gave crude 12b, which was purified using short column of silica gel using EtOAc–n-hexane as an eluent to give an oil (70%).

1H NMR (CDCl₃): δ = 2.65 (s, 4 H, NCH₂CO), 3.22 (s, 2 H, OCOCH₂), 4.43 (d, J = 4.5 Hz, 4 H, OCH₂), 5.71 (quintet, J = 4.9 Hz, 1 H, OCH), 6.84–8.43 (m, 8 H, ArH), 9.48 (s, 2 H, NH).
Anal. Calcd for C₂₇H₂₅N₂O₁₀ (655.75): C, 60.44; H, 6.92; N, 10.68.
Found: C, 60.39; H, 6.86; N, 10.59.

2-Hydroxy-1,3-bis[2-(N-morpholino)acetoxy]propane (13)
By the general procedure, 10 and morpholine gave crude 15, which was crystallized from benzene to give colorless crystals (65%); mp 172–174 °C.

Anal. Calcd for C₂₃H₂₃N₂O₈ (526.80): C, 61.35; H, 6.86; N, 10.60.
Found: C, 61.46; H, 6.91; N, 10.71.

2-(N-Morpholinoacetoxy)-1,3-bis[2-(N-morpholinoacetamido)phenoxy]propane (16)
By the general procedure 15 and morpholine gave crude 16, which was crystallized from EtOH to give pale yellow crystals (70%); mp 146–148 °C.

IR (KBr): 3364 (NH), 1745, 1688 (C=O), 1528, 1348 cm⁻¹ (NO₂).

1H NMR (CDCl₃): δ = 2.46 (m, 4 H, NCH₂CH₂O), 3.16 (s, 2 H, COCH₂N), 3.63 (m, 4 H, OCH₂CH₂), 4.46 (m, 4 H, OCH₂), 4.68 (s, 4 H, OCH₂CO), 5.74 (quintet, J = 5.1 Hz, 1 H, OCH), 6.85–8.29 (m, 16 H, ArH), 9.01 (s, 2 H, NH).
Anal. Calcd for C₃₃H₄₅N₅O₉ (655.75): C, 60.44; H, 6.92; N, 10.68.
Found: C, 60.39; H, 6.86; N, 10.59.

1,4-Bis[1,3-bis[2-(2-nitrophenoxycetamido)phenoxy]propane-2-oxoethyl]carboxymethyl]piperazine (17)
By the general procedure 15 and piperazine gave crude 17, which was crystallized from dioxane–EtOH to give pale yellow crystals (65%); mp 194–196 °C.

IR (KBr): 3381 (NH), 1743, 1692 (C=O), 1526, 1346 cm⁻¹ (NO₂).

1H NMR (CDCl₃): δ = 2.43 (s, 8 H, CH₂N), 3.12 (s, 4 H, COCH₂N), 4.43 (m, 8 H, OCH₂), 4.69 (s, 4 H, OCH₂CO), 5.74 (quintet, J = 5.1 Hz, 2 H, OCH), 6.82–8.29 (m, 32 H, ArH), 9.09 (s, 4 H, NH).
1C NMR (APT pulse sequence, CDCl₃): δ = 51.41, 57.83, 66.19, 66.62, 67.84, 126.35, 138.73, 147.77, 150.18, 164.85 (C and CH₂), 69.82, 71.55, 112.19, 115.52, 120.76, 121.33, 124.54, 125.23, 134.62 (CH).
Found: C, 66.45; H, 6.87; N, 11.53.

15-[(N,N-Diethyldimethylamino)acetoxy]-6,14,15,24,33,33-Hexahydro-16I-tetrabenzo[b,h,p,r][1,7,18,24,4,11,14,21]tetroxatoalexeroaicycloheptacosen-7,33,30,35,39(S),22H,21I,31H,34I,tetraen(20a)
By the general procedure, 19a and N,N-diethyldimethylamine gave crude 20a, which was crystallized from CHCl₃–petroleum ether (bp 40–60 °C) to give colorless crystals (60%); mp 182–84 °C.
IR (KBr): 3391, 3350 (NH), 1743, 1688, 1644 cm⁻¹ (C=O).

1H NMR (CDCl3); δ = 0.89 (t, J = 6.9 Hz, 6 H, CH3), 2.42 (q, J = 7 Hz, 4 H, CH2CH3), 2.97 (s, 2 H, CH2CO), 3.75 (m, 4 H, CH2NH), 3.96 (d, J = 5.8 Hz, 4 H, OCH2), 4.78 (d, J = 15.3 Hz, 2 H, upfield of OCH2CO), 4.94 (d, J = 15.3 Hz, 2 H, downfield of OCH2CO), 5.45 (quintet, J = 5.5 Hz, 1 H, CHO), 6.62–8.89 (m, 20 H, ArH + NH).

MS: m/z (%) = 768 (M + 1, 0.5), 665 (0.5), 521 (1), 413 (2.1), 326 (2), 300 (140), 132 (85).


15-Morpholinooacte-6,14,15,24,32,33-hexahydro-16H-tetra-
benzo[b,h,p,v]$\text{[1,7,18,24,4,11,14,22]$\text{tetraoxatetraazacycloheptacosin}$-7,23,30,35-(8H,22H,31,34H)tetraene (20b)

By the general procedure 19b and morpholine gave crude 20b, which was crystallized from dioxane to give pale yellow crystals (50%); mp 248–250 °C.

IR (KBr): 3392, 3325 (NH), 1760, 1693, 1635 cm$^{-1}$ (C=O).

MS: m/z (%) = 795 (M$^+$, 11), 777 (23), 584 (17), 337 (25), 186 (100), 113 (88).

Anal. Calcd for C42H45N5O11 (795.85): C, 63.39; H, 5.70; N, 8.80. Found: C, 63.45; H, 5.55; N, 8.70.

1,4-Bis(6,14,15,24,32,33-hexahydro-16H-tetra-
benzo[b,h,p,v]$\text{[1,7,18,24,4,11,14,22]$\text{tetraoxatetraazacycloheptacosin}$-7,23,30,35-(8H,22H,31,34H)tetraene-15-xyloxybenzyl$\text{piperazine}$ (21)

By the general procedure 19a and piperazine gave crude 21, which was crystallized from dioxane to give pale yellow crystals (50%); mp 248–250 °C.

IR (KBr): 3392, 3325 (NH), 1760, 1693, 1636 cm$^{-1}$ (C=O).

MS: m/z (%) = 780 (M – 1, 7.1), 715 (7), 604 (13), 552 (17.2), 423 (25), 337 (25), 186 (100), 113 (88).


References