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Synthesis of upper rim *N*-formamido and isocyanocalix[4]arenes: adaptation of Ugi-4-CR on calix[4]arenes towards peptide-like architectures

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ABSTRACT

Methods are described for the selective diametrical functionalization of calix[4]arenes at the upper rim by formamide and isocyanide functional groups. The adaptation of Ugi-4-CR to calix[4]arenes leading to α-acylaminocarboxamide derivatives is also discussed.

1. Introduction

Calixarenes, which are probably the world's most readily available synthetic molecular baskets enjoy considerable reputation of being applied in diverse areas.[1] The incredible development of calix[4]arenes as molecular receptors is related to many possible structural and functional modifications of their core molecular architecture,[2] which constitutes a hollow cavity flanked by a hydrophobic upper rim and a hydrophilic lower rim. Introduction of multifunctional groups at the upper rim of calix[4]arenes reflects a current trend, aiming towards 'smart' materials, informationally rich molecular devices, and nanofabrication.[3] Regioselective modification of the upper rim can be achieved through partial or total de-*tert*-butylation of *p*-*tert*-butylcalix[4]arenes followed by the appropriate derivatization.[4] To date, various approaches towards the construction of multivalent calixarenes,[4a] such as peptidocalixarenes[5,13] and glycocalixarenes[6] have been reported in literatute.[7] The use of peptidocalixarenes as hosts is attractive because of the chirality and range of functional groups provided by them.[5,13] The syntheses of such calixarenes involve selective protection of the lower rim and then multi steps including established techniques for the formation of peptide and glycoside bonds. Rapid and direct access to calix[4]arenes with peptide-like linkage on the upper rim, which is particularly attractive and effective, are not reported. Herein we report a facile and efficient route to libraries of such multifunctionalized calix[4]arenes involving Ugi-4-component reaction. We also describe a firsthand report of a facile methodology for the synthesis of upper rim disubstituted *N*-formamide and isocyanide derivatives of calix[4]arene.

Multicomponent reactions[8] (MCRs) have become an important component of the combinatorial chemistry, as a great number of compounds can be produced in a rapid parallel synthetic program. The high atom economy, convergent character, operational simplicity, structural diversity and complexity of molecules are the major advantages associated with the MCRs. Multicomponent reactions are also emerging as a powerful tool in the synthesis of biologically active compounds, which have recently attracted the attention of several academic and industrial researchers, since accessing diversity is of paramount importance in search of new biologically active candidates. Large portion of MCR chemistry has developed from isocyanides. Isocyanide based multicomponent reactions (IMCRs) are of great importance among MCRs.[8a] IMCRs allow for the synthesis of the largest number of different scaffolds. The outstanding position of IMCRs can be traced back to the exceptional reactivity of the isocyanide functional group. The introduction of isocyanide group on to the calixarene scaffold makes it highly functionalizable, which ensures construction of libraries of multi-functionalised derivatives using IMCR. A large number of multicomponent reactions are possible on these newly introduced isocyanide group, which ensures the construction of libraries of highly functionalized calixarene derivatives. Among the isocyanide based multicomponent reactions, Ugi-4-component reaction[9] occupies a leading position since it represents a valuable method to access peptide-like moiety, such as α-acylaminocarboxamide in a straight forward manner by coupling isocyanides with carbonyl

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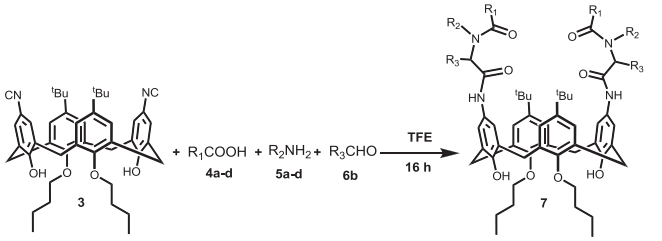
compounds, primary amines and carboxylic acids. Calixarene chemistry has been relatively untouched by the concept of multicomponent reactions. Our interest in this area stemmed from a need to synthesize multiply functionalized calix[4]arenes from isocyanide derivatized calix[4]arene.

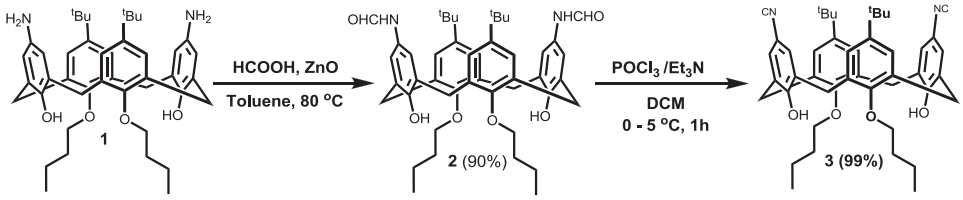
2. Results and discussion

The basic precursor of our investigation, diaminocalix[4]arene **1** was prepared in good yield using previously reported synthetic procedures.[10] Preliminary endeavours towards transformation of diaminocalix[4]arene **1** to its *N*-formamide counterpart focused on optimizing the utility of various formylating agents available. In an original work, Shargi and co-workers employed formic acid supported on non-toxic, inexpensive and bio-compatible ZnO as the formylating agent.[11] When we applied this procedure to **1**, the reaction furnished *N*-formamide derivatized calix[4]arene **2** as a 1:1 mixture of *cis*/*trans* isomer in 90% yield (Scheme 1) (See SI).

Table 1
Ugi-4-CR of diisocyanocalix[4]arene **3**



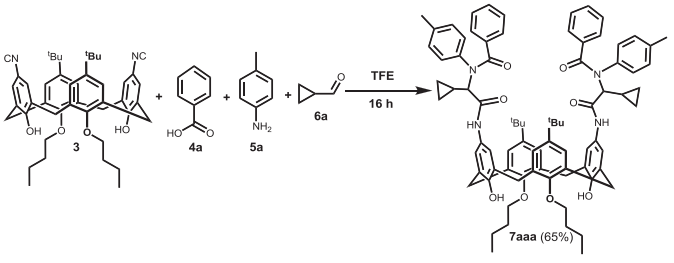
Entry	R_1	R_2	R_3	Yield of **7** (%)
1	**4a**, C_6H_5–	**5a**, $(4\text{-}CH_3)C_6H_5$–	**6b**, $(4\text{-}OCH_3)C_6H_5$–	**7aab**, 65
2	**4a**, C_6H_5–	**5b**, $C_6H_5CH_2$–	**6b**, $(4\text{-}OCH_3)C_6H_5$–	**7abb**, 61
3	**4a**, C_6H_5–	**5c**, $(4\text{-}OCH_3)C_6H_5$–	**6b**, $(4\text{-}OCH_3)C_6H_5$–	**7acb**, 60
4	**4a**, C_6H_5–	**5d**, (6-CH3)Py–	**6b**, $(4\text{-}OCH_3)C_6H_5$–	**7adb**, 63
5	**4b**, $(3\text{-Cl})C_6H_5$–	**5a**, $(4\text{-}CH_3)C_6H_5$–	**6b**, $(4\text{-}OCH_3)C_6H_5$–	**7bab**, 60
6	**4c**, $(4\text{-}NO_2)C_6H_5$–	**5a**, $(4\text{-}CH_3)C_6H_5$–	**6b**, $(4\text{-}OCH_3)C_6H_5$–	**7cab**, 61
7	**4d**, CH_3–	**5a**, $(4\text{-}CH_3)C_6H_5$–	**6b**, $(4\text{-}OCH_3)C_6H_5$–	**7dab**, 62



Scheme 1. Synthesis of *N*-formamide **2** and isocyanide **3**.

The *N*-formamide **2** was effortlessly converted into the required isocyanide **3** in quantitative yield by its reaction with $POCl_3$ and Et_3N in 1 h (Scheme 1). In contrast to the obnoxious odour, which is characteristic of isocyanides, the diisocyanocalix[4]arene **3** was odourless.

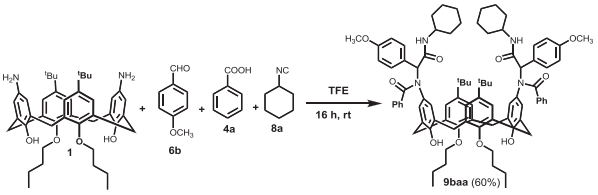
The unique properties of the isocyano group, which may function as both electrophile and nucleophile, have turned these compounds into indispensable reagents for organic synthesis.[12] Taking into account this fact and our interest in the adaptation of multicomponent reactions to calixarene scaffolds, we attempted an Ugi-4-component reaction with the hope of preparing highly functionalized calixarene based macrocycles. Thus when we reacted the diisocyanide **3** with benzoic acid **4a**, toluidine **5a** and cyclopropane carboxaldehyde **6a** in 2,2,2-trifluoroethanol (TFE) at room temperature (Scheme 2) and stirring was continued until the consumption of the starting material as indicated by TLC. After 16 h, removal of the solvent followed by column chromatography of the residue on alumina afforded the highly functionalized α-acylaminocarboxamide derivative **7aaa** in 65% yield.



Scheme 2. Ugi reaction of diisocyanocalix[4]arene **3**.

To further demonstrate the efficiency of the Ugi reaction based on calix[4]arenes, the scope of the reaction with various aromatic and aliphatic acids, amines and aldehydes were explored and the results obtained are summarized in Table 1.

To expand the scope of scaffold diversity generated by this versatile reaction, amino derivatives of calix[4]arene was subjected to Ugi reaction. The diaminocalix[4]arene **1** was reacted with anisaldehyde **6b**, benzoic acid **4a** and cyclohexyl isocyanide **8a** in TFE for 16 h at room temperature to afford the corresponding carboxamide derivative **9baa** in 60% yield (Scheme 3).

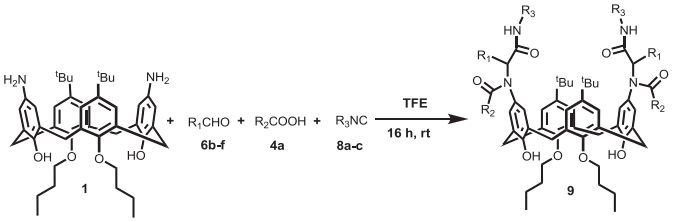


Scheme 3. Ugi reaction of diaminocalix[4]arene **1**.

The reaction of diaminocalix[4]arene **1** with various aldehydes, acids and isocyanides provided the multifunctionalized peptide-like calix[4]arenes in good yields as outlined in Table 2.

The ^1H NMR spectra of products obtained from diaminocalix[4]arene provide evidence for asymmetric structural features. All of them presented two pairs of doublets around δ 3.00 and 4.10 ppm (see SI) that have arisen due to the non-equivalency of protons of the methylene bridges (Ar–CH_2–Ar). Some of the ^1H NMR spectra showed even finer splitting in the case of these signals. As previously reported in the literature,[13] this can be explained by the presence of chiral substituents at the upper rim. Unlike α-acylaminocarboxamide derivatives obtained from amines, the ^1H NMR spectra for compounds derived from the diisocyanocalix[4]arene showed only a pair of doublets, eventhough they contained a stereocenter. This might probably be due to the fact that the stereocenter in the latter is one carbon away from the calixarene core than that in the amine derived carboxamides. Chiral resolution of

Table 2
Ugi-4-CR of diaminocalix[4]arene **1**



Entry	R_1	R_2	R_3	Yield of **9** (%)
1	**6c**, (2,4-diMe)C_6H_5-	**4a**, C_6H_5-	**8a**, Cy	**9caa**, 65
2	**6d**, (2-Me)C_6H_5-	**4a**, C_6H_5-	**8a**, Cy	**9daa**, 63
3	**6e**, (4-Me)C_6H_5-	**4a**, C_6H_5-	**8a**, Cy	**9eaa**, 62
4	**6f**, (4-OMe)C_6H_5Py-	**4a**, C_6H_5-	**8a**, Cy	**9faa**, 70
5	**6b**, (4-OMe)C_6H_5-	**4b**, (3-Cl)C_6H_5-	**8a**, Cy	**9bba**, 62
6	**6b**, (4-OMe)C_6H_5-	**4a**, C_6H_5-	**8b**, (4-OMe)C_6H_5-	**9bab**, 60
7	**6b**, (4-OMe)C_6H_5-	**4a**, C_6H_5-	**8c**, β-Np	**9bac**, 61

these compounds may provide new series of calixarene derivatives, which are capable of stereo recognition in addition to the ionic and molecular recognition.

The presence of two pairs of NH donor sites and carbonyl groups at the upper rim of the newly synthesized receptors prompted us to investigate their molecular/ion recognition properties. However, preliminary binding studies using UV–vis and ^{1}H NMR spectroscopy towards anions (fluoride, chloride, bromide, iodide, benzoate, acetate, perchlorate and bisulphate), cations as metal perchlorates (Cr^{3+}, Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Hg^{2+}, Ag^{+}, Pb^{2+}, Cd^{2+}, Na^{+}, K^{+}, Ca^{2+}, Al^{3+}) and neutral molecules (acetone, methanol) indicated no significant activity. This could be probably due to the overcrowding around the binding sites by *t*-butyl as well as bulky substituent at the upper rim. Fig. 1.

3. Conclusion

In conclusion, we have documented a multicomponent approach to access large diversities of multifunctionalized calix[4]arenes via Ugi reaction of aminocalix[4]arenes and novel isocyanocalix[4]arenes. The reaction allows us to make a variety of α-acylaminocarboxamide derivatives of calix[4]arene with considerable generality and simplicity. This methodology enabled the synthesis of multifunctionalized calixarenes bearing heteroaromatic rings and also chromophoric groups like naphthyl moeity in the peptoid chain. In contrast to many other peptidocalixarenes reported, the compounds obtained using the current methodology has excellent solubility in non-polar solvents. During the course of the present study, we have successfully optimized the conditions for attaining *N*-formamido and diisocyanocalix[4]arenes, which are of great synthetic use. Recognition studies using neutral heterocycles and organic cations are being currently undertaken in our laboratory and will be duly reported.

4. Experimental section

4.1. General

All reactions were conducted in oven dried glassware. Solvents used for the experiments were distilled or dried as specified. Analytical thin layer chromatography was performed on glass plates coated with silica gel (E-Merck) containing 13% $CaSO_4$ as binder. Column chromatography was done using 100–200 mesh silica gel and appropriate mixture of petroleum ether and ethyl acetate for elution. The solvents were removed using Buchi E.L. rotary evaporator.

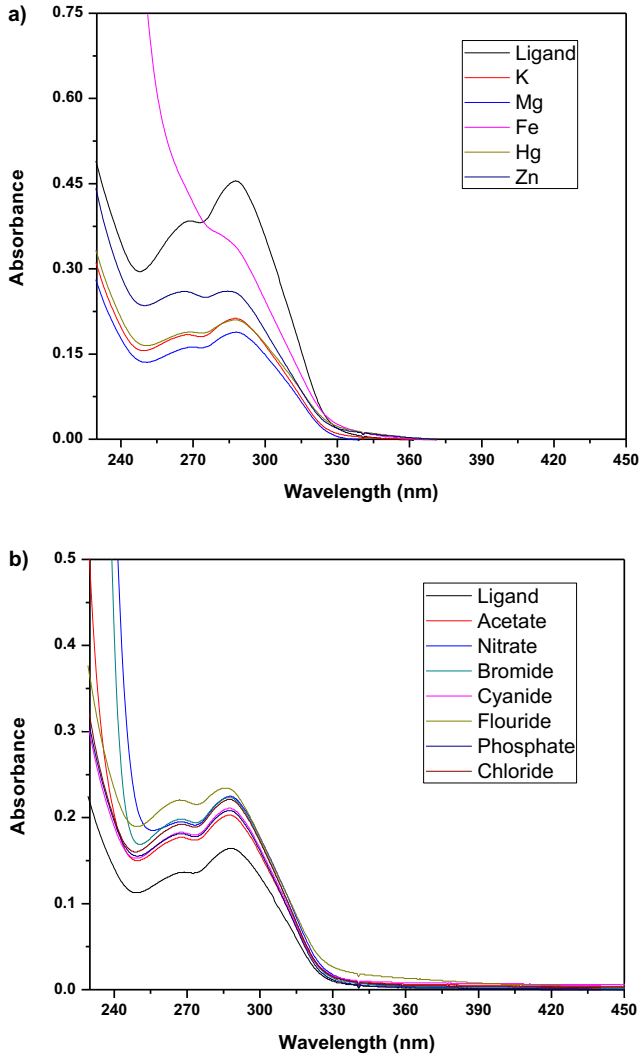


Fig. 1. (a) UV–vis spectra of **9faa** upon addition of some of the metal ions used in the binding studies; (b) anions.

HPLC analyses were conducted with a LC9101 Recycling Preparative chromatograph. The IR spectra were taken on Nicolet impact 400d FTIR spectrophotometer. NMR spectra were recorded at 300 and 500 (^{1}H) and 75 and 125 (^{13}C) MHz, respectively, on a Bruker DPX-300 and 500 MHz FT-NMR spectrophotometer. NMR spectra were obtained using $CDCl_3$+CCl_4 as the solvent. Chemical shifts are given in δ scale with TMS as internal standard. Abbreviations used in ^{1}H NMR are s: singlet, bs: broad singlet, d: doublet, t: triplet, m: multiplet. Mass spectra were recorded by MALDI technique using Shimadzu MALDI-TOF mass spectrophotometer. Elemental analysis was done using Perkin-Elmer-2400 CHNS analyser.

4.2. Procedure for the synthesis of upper rim formamidocalix[4]arene (2)

To a mixture of HCO_2H (0.22 mL, 6 mmol) and ZnO (160.0 mg, 2 mmol) in toluene (2 mL) was added the diaminocalix[4]arene **1** (100.0 mg, 0.15 mmol) and the reaction mixture was heated in an oil bath at 75 °C. The progress of the reaction was monitored by TLC. After the reaction was complete, dichloromethane was added to the reaction mixture and ZnO was filtered off. The organic solvent was washed with H_2O (2×20 mL) and saturated solution of $NaHCO_3$. After the removal of the solvent, the pure product was obtained as a mixture of *cis* and *trans* isomers.

*4.2.1. Formamidocalix[4]arene (**2**).* Yield: 90% as white solid. R_f: 0.09 (15:85 EtOAc/Hexane). Mp:> 250 °C. IR (KBr) υ_{max}: 3279, 3011, 2961, 1688, 1483, 1252, 1215, 1101, 756, 665 cm^{-1} ^1H NMR: δ 8.56 (s, CHO, 2H), 8.40 (s, NH, 2H), 8.36 (dd, J=3.5 Hz, J=11.5 Hz, CHO, 2H), 8.25 (d, J=1.5 Hz, NH, 2H), 7.56 (broad s, OH, 4H), 7.21 (s, ArH, 2H), 7.00 (d, J=2.0 Hz, ArH, 2H), 6.98 (s, ArH, 2H), 6.97 (s, ArH, 2H), 6.95 (d, J=2.0 Hz, ArH, 4H), 6.77 (d, J=2.5 Hz, ArH, 4H), 4.32 (m, $ArCH_2Ar$, 8H), 3.99 (m, $-OCH_2$, 8H), 3.33 (m, $ArCH_2Ar$, 8H), 2.08 (m, $-CH_2$, 8H), 1.71 (m, $-CH_2$, 8H), 1.13 (s, *t*-Bu, 36H), 1.09 (m, $-CH_3$, 12H). ^{13}C NMR: δ 168.2 (−CHO), 158.5 (−CHO), 151.4, 150.2, 147.7, 133.3, 132.8, 132.6, 130.0, 129.8, 129.1, 128.5, 127.7, 126.0, 125.7, 121.1, 120.5, 76.3 ($-OCH_2$), 32.1, 31.9, 31.7, 31.3, 29.7, 29.4, 19.3, 14.1, (*t*-Bu, Ar−CH_2−Ar, $-CH_2$, $-CH_3$). Anal. Calcd for $C_{46}H_{58}N_2O_6$: C, 75.17; H, 7.95; N, 3.81. Found: C, 75.23; H, 7.89; N, 3.76.

4.3. Procedure for the synthesis of calix[4]arene isocyanide (3)

To a solution of formamidocalix[4]arene **2** (136.0 mg, 0.19 mmol) in dichloromethane (5 mL), was added triethyl amine (11 equiv) and $POCl_3$ (5.5 equiv) at 0 °C under nitrogen. After being stirred for 1 h, the reaction mixture was poured into 10% aqueous Na_2CO_3 solution. The reaction mixture was worked up with dichloromethane-water mixture. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (hexanes−ethyl acetate in 95:5).

*4.3.1. calix[4]arene isocyanide (**3**).* Yield: 99% as white solid. R_f : 0.65 (15:85 EtOAc/Hexane). Mp: 53−55 °C. IR (KBr) υ_{max}: 3277, 2961, 2932, 2119, 1476, 1362, 1196, 995 cm^{-1} ^1H NMR: δ 8.73 (s, OH, 2H), 7.09 (s, ArH, 4H), 6.91 (s, ArH, 4H), 4.24 (d, J=13.0 Hz, $ArCH_2Ar$, 4H), 3.98 (t, J=5.0 Hz, $-OCH_2$, 4H), 3.33 (d, J=13.5 Hz, $ArCH_2Ar$, 4H), 2.03 (m, $-CH_2$, 4H), 1.72 (m, $-CH_2$, 4H), 1.09 (s, *t*-Bu, 18H), 0.87 (m, $-CH_3$, 6H). ^{13}C NMR: δ 161.1, (NC) 154.2, 149.9, 148.2, 131.7, 130.8, 129.3, 128.8, 126.2, 117.8, 115.9 (Ar−C), 64.9 ($-OCH_2$), 34.2, 32.2, 31.9, 31.6, 29.7, 22.7, 19.4 (*t*-Bu, Ar−CH_2−Ar, CH_2, CH_3). MS (MALDI-TOF): Calcd for $C_{46}H_{54}N_2O_4$, $[M+Na]^+$: 721.4084; Found: 721.4254.

4.4. General procedure for the synthesis of α-acylaminocarboxamidocalix[4]arene (7) by the U-4CR

Amine **5a** (0.0534 mmol) and aldehyde **6a** (0.0534 mmol) were stirred in 0.5 mL TFE for 2 h. Then, carboxylic acid **4a** (0.1335 mmol) and diisocyanocalix[4]arene **3** (20 mg, 0.0267 mmol) were added and the reaction mixture was stirred for 16 h at room temperature. The solvent was removed in vacuo. Product was purified by column chromatography on neutral alumina (Hexane/EtOAc).

*4.4.1. Compound **7aaa**.* Yield: 65% as white solid. R_f : 0.50 (35:75 EtOAc/Hexane). Mp: 123−126 °C. IR (KBr) ν_{max}: 3327, 2957, 2927, 2870, 1692, 1628, 1511, 1249 cm^{-1} ^1H NMR (500 MHz, $CDCl_3$): δ 8.56 (s, NH, 2H), 8.39 (s, OH, 2H), 7.43 (s, ArH, 2H), 7.24 (m, ArH, 4H), 7.20 (m, ArH, 4H), 7.11 (m, ArH, 4H), 7,04 (m, ArH, 2H), 7.00 (m, ArH, 6H), 6.94 (m, ArH, 4H), 4.44 (d, J=10.5 Hz, CH, 2H), 4.32 (d, J=12.5 Hz, $ArCH_2Ar$, 4H), 3.99 (t, J_1=7 Hz, J_2=6.5 Hz, OCH_2, 4H), 3.34 (d, J=13.0 Hz, $ArCH_2Ar$, 4H), 2.23 (s, $ArCH_3$, 6H), 2.08 (m, CH_2, 4H), 1.71 (m, CH_2, 4H), 1.11 (m, *t*-Bu, CH_3, 24H), 0.87 (m, CH_2, 4H), 0.78 (m, CH_2, 2H), 0.52 (m, CH_2, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.1 (C=O), 167.8 (C=O), 150.3, 149.6, 147.4, 137.5, 135.7, 133.04, 129.98, 129.56, 129.1, 128.4, 127.6, 125.9, 119.95, 119.86, (Ar−C), 76.56 (OCH_2), 66.63, 34.2, 31.4, 29.7, 22.7, 21.0, 19.3, 14.1, 10.4, 5.9, 4.2 ($ArCH_2Ar$,, *t*-Bu, CH, $ArCH_3$, CH_2). MS (MALDI-TOF): Calcd for $C_{82}H_{92}N_4O_8$, $[M+Na]^+$: 1283.6915; Found: 1283.6469.

*4.4.2. Compound **7aab**.* Yield: 65% as white solid. R_f: 0.25 (35:75 EtOAc/Hexane). Mp: 118−120 °C. IR (KBr) ν_{max}: 3318, 2957, 2931, 2871,2931, 1693, 1632, 1511, 1483, 1250 cm^{-1} ^1H NMR (500 MHz, $CDCl_3$): δ 8.29 (s, OH, 2H), 7.83 (s, NH, 2H), 7.31 (d, J=7 Hz, ArH, 4H), 7.19 (m, ArH, 10H), 7.12 (m, ArH, 4H), 6.97 (d, J=4.5 Hz, ArH, 4H), 6.82 (s, ArH, 8H), 6.76 (d, J=8.5 Hz, ArH, 4H), 6.29 (s, CH, 2H), 4.30 (m, $ArCH_2Ar$, 4H), 3.98 (t, J_1=6.5 Hz, J_2=7 Hz, OCH_2, 4H), 3.75 (s, OCH_3, 6H), 3.32 (m, $ArCH_2Ar$, 4H), 2.17 (s, $ArCH_3$, 6H), 2.06 (m, CH_2, 4H), 1.68 (m, CH_2, 4H), 1.12 (m, *t*-Bu, 18H), 1.07 (t, J_1=7.5 Hz, J_2=7.5 Hz, CH_3, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.54 (C=O), 167.42 (C=O), 159.57, 159.3, 149.83, 138.5, 137.07, 136.05, 132.98, 131.4, 129.9, 129.5, 129.2, 128.06, 127.6, 126.6, 125.8, 120.4, 113.81 (Ar−C), 76.56 (−OCH_2) 66.6, 55.2, 34.2, 32.1, 31.1, 29.7, 20.1, 19.3, 14.1 ($ArCH_2Ar$, *t*-Bu, $ArCH_3$, CH_3, CH_2, OCH_3). Anal. Calcd for $C_{90}H_{96}N_4O_{10}$: C, 77.56; H, 6.94; N, 4.02. Found: C, 77.43; H, 7.01; N, 4.13.

*4.4.3. Compound **7abb**.* Yield: 61% as a white solid. R_f: 0.33 (45:55 EtOAc/Hexane). Mp: 100−102 °C. IR (KBr) ν_{max}: 3308, 2958, 2930, 2871, 1687, 1613, 1512, 1251 cm^{-1} ^1H NMR (500 MHz, $CDCl_3$): δ 7.46 (m, ArH, 4H), 7.31 (m, ArH, OH, NH, 10H), 7.16 (m, ArH, 8H), 7.08 (m, ArH, 6H), 6.96 (d, J=9 Hz, ArH, 6H), 6.79 (d, 6H. J=8.5 Hz, ArH, 6H), 5.67 (s, CH, 2H), 4.73 (d, J=16.5 Hz, $ArCH_2$, 2H), 4.49 (m, $ArCH_2$, 2H), 4.29 (d, J=12.5 Hz, $ArCH_2Ar$, 4H), 3.97 (m, OCH_2, 4H), 3.76 (s, OCH_3, 6H), 3.29 (d, J=13 Hz, $ArCH_2Ar$, 4H), 2.06 (m, CH_2, 4H), 1.68 (m, CH_2, 4H), 1.12 (s, *t*-Bu, 18H), 1.07 (t, J_1=J_2=7.5 Hz, CH_3, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.4 (C=O), 167.2 (C=O), 160.9, 159.8, 150.3, 149.9, 147.4, 136.2, 133.0, 130.9, 129.9, 128.8, 128.75, 128.4, 127.8, 126.97, 126.8, 126.7, 125.8, 120.4, 114.25 (Ar−C), 76.59 (OCH_2), 55.3 (OCH_3), 34.2, 32.1, 31.9, 31.7, 31.3, 29.7, 29.4, 22.7, 19.3, 14.1 (CH_2, CH_3, *t*-Bu, $ArCH_2Ar$). Anal. Calcd for $C_{90}H_{96}N_4O_{10}$: C, 77.56; H, 6.94; N, 4.02. Found: C, 77.62; H, 7.02; N, 4.17.

*4.4.4. Compound **7acb**.* Yield: 60% as a white solid. R_f: 0.23 (45:55 EtOAc/Hexane). Mp: 120−124 °C. IR (KBr) ν_{max}: 3304, 2957, 2924, 2854, 1681, 1632, 1513, 1253 cm^{-1} ^1H NMR (500 MHz, $CDCl_3$): δ 8.28 (s, OH, 2H), 7.70 (s, NH, 2H), 7.30 (d, J=7 Hz, ArH, 4H), 7.18 (m, ArH, 10H), 7.12 (m, ArH, 4H), 6.97 (d, J=9 Hz, ArH, 4H), 6.84 (bs, ArH, 4H), 6.76 (d, J=9 Hz, ArH, 4H), 6.52 (d, J=9 Hz, ArH, 4H), 6.36 (s, CH, 2H), 4.30 (m, $ArCH_2Ar$, 4H), 3.98 (t, J_1=6.5 Hz, J_2=7 Hz, OCH_2, 4H), 3.76 (s, OCH_3, 6H), 3.65 (s, OCH_3, 6H), 3.32 (m, $ArCH_2Ar$, 4H), 2.06 (m, CH_2, 4H), 1.68 (m, CH_2, 4H), 1.11 (d, J=3.5 Hz, *t*-Bu, 18H), 1.09 (t, J_1=7.5 Hz, J_2=7 Hz, CH_3, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.66 (C=O), 167.5 (C=O), 159.6, 158.4, 150.3, 149.8, 136.1, 132.97, 131.7, 131.6, 129.3, 128.5, 127.6, 126.4, 125.8, 120.4, 113.8, 113.5 (Ar−C), 76.56 (OCH_2), 55.21 (OCH_3), 55. 19 (OCH_3), 34.2, 32.1, 31.3, 29.7, 19.3, 14.1 ($ArCH_2Ar$, *t*-Bu, CH_2, CH_3). Anal. Calcd for $C_{90}H_{96}N_4O_{12}$: C, 75.82; H, 6.79; N, 3.93. Found: C, 75.69; H, 6.83; N, 4.03.

*4.4.5. Compound **7adb**.* Yield: 62% as a white solid. R_f: 0.13 (60:40 EtOAc/Hexane). Mp: 115−119 °C. IR (KBr) ν_{max}: 3340, 2924, 2854, 1659, 1642 cm^{-1} ^1H NMR (500 MHz, $CDCl_3$): δ 8.29 (d, J=2.5 Hz, OH, 2H), 7.79 (s, NH, 2H), 7.43 (m, ArH, 2H), 7.29 (m, ArH, 6H), 7.20 (m, ArH, 2H), 7.15 (m, ArH, 10H), 6.95 (m, ArH, 4H), 6.84 (d, J=5 Hz, ArH, 2H), 6.75 (d, J=8.5 Hz, ArH, 4H), 6.44 (s, CH, 2H), 4.30 (m, $ArCH_2Ar$, 4H), 3.98 (t, J_1=7 Hz, J_2=6.5 Hz, OCH_2, 6H), 3.75 (s, OCH_3, 6H), 3.32 (m, $ArCH_2Ar$, 4H), 2.36 (s, $ArCH_3$, 6H), 2.06 (m, CH_2, 4H), 1.69 (m, CH_2, 4H), 1.11 (d, J=2.5 Hz, *t*-Bu, 18H), 1.08 (t, J_1=7 Hz, J_2=7.5 Hz, CH_3, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.5 (C=O), 167.3 (C=O), 159.9, 150.3, 150.0, 147.4, 135.5, 133.0, 132.9, 132.8, 131.7, 129.7, 129.3, 129.2, 129.1, 120.5, 128.5, 127.9, 125.85, 125.76, 122.75, 120.6, 114.2 (Ar−C), 76.58 (OCH_2), 55.2, 34.2, 32.1, 31.76, 31.57, 31.3, 29.7, 19.3, 14.1 ($ArCH_2Ar$, CH_2, CH_3, OCH_3). Anal. Calcd for $C_{88}H_{94}N_6O_{10}$: C, 75.73; H, 6.79; N, 6.02. Found: C, 75.78; H, 6.88; N, 6.16.

*4.4.6. Compound **7bab**.* Yield: 65% as a white solid. R_f: 0.36 (45:55 EtOAc/Hexane). Mp: 117−121 °C. IR (KBr) ν_{max}: 3305, 2923, 2853, 1680, 1632, 1511, 1252 cm^{-1} ^1H NMR (500 MHz, $CDCl_3$): δ 8.30 (d, J=1.5 Hz, OH, 2H), 7.55 (s, NH, 2H), 7.35 (s, ArH, 2H), 7.16 (m, ArH, 12H), 7.03 (m, ArH, 2H), 6.97 (m, ArH, 4H), 6.83 (s, ArH, 8H), 6.76 (d, J=8.5 Hz, ArH, 4H),

6.28 (s, CH, 2H), 4.30 (m, $ArCH_2Ar$, 4H), 3.98 (t, J_1=7 Hz, J_2=6.5 Hz, OCH_2, 4H), 3.75 (s, OCH_3, 6H), 3.32 (m, $ArCH_2Ar$, 4H), 2.18 (s, CH_3, 6H), 2.06 (m, CH_2, 4H), 1.68 (m, CH_2, 4H), 1.12 (s, *t*-Bu, 18H), 1.07 (t, J_1=J_2=7.5 Hz, CH_3, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.95 (C=O), 167.20 (C=O), 159.7, 150.3, 149.9, 147.4, 137.8, 137.4, 133.7, 133.0, 131.6, 130.0, 129.5, 129.3, 128.8, 128.7, 126.6, 126.2, 125.8, 120.4, 113.9 (Ar–C),76.57 (OCH_2), 66.4, 55.2, 34.2, 32.1, 31.6, 31.3, 20.99, 19.3, 14.1 ($ArCH_2Ar$, *t*-Bu, CH_2, $ArCH_3$, CH_3, OCH_3). Anal. Calcd for $C_{90}H_{94}Cl_2N_4O_{10}$: C, 73.91; H, 6.48; N, 3.83. Found: C, 73.81; H, 6.59; N, 3.75.

4.4.7. Compound ***7cab***. Yield: 60% as a light yellow solid. R_f: 0.35 (45:55 EtOAc/Hexane). Mp: 122–124 °C. IR (KBr) ν_{max}: 3312, 2958, 2931, 2871, 1690, 1634, 1512, 1483, 1252 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.33 (d, J=3.5 Hz, OH, 2H), 7.98 (d, J=9 Hz, ArH, 4H), 7.46 (d, J=8.5 Hz, ArH, 4H), 7.28 (s, NH, 2H), 7.15 (m, ArH, 8H), 6.97 (m, ArH, 4H), 6.78 (m, ArH, 12H), 6.33 (s, CH, 2H), 4.29 (m, $ArCH_2Ar$, 4H), 3.98 (t, J_1=7 Hz, J_2=6.5 Hz, OCH_2, 4H), 3.76 (s, OCH_3, 6H), 3.22 (m, $ArCH_2Ar$, 4H), 2.17 (s, $ArCH_3$, 6H), 2.07 (m, CH_2, 4H), 1.68 (m, CH_2, 4H), 1.12 (d, J=4 Hz, *t*-Bu, 18H), 1.07 (t, J_1=7 Hz, J_2=7.5 Hz, CH_3, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.3 (C=O), 166.9 (C=O), 159.9, 150.3, 149.48, 147.7, 142,56, 137.9, 133.06, 133.00, 131.81, 113.3, 129.4, 129.2, 129.1, 125.9, 125.8, 122.9, 120.5, 114.0 (Ar–C), 76.60 (OCH_2), 65.91, 55.2, 34.2, 32.1, 31.3, 21.0, 19.3, 14.1 ($ArCH_2Ar$, $ArCH_3$, CH_2, CH_3, OCH_3). Anal. Calcd for $C_{90}H_{94}N_6O_{14}$: C, 72.85; H, 6.39; N, 5.66. Found: C, 72.94; H, 6.48; N, 5.73.

4.4.8. Compound ***7dab***. Yield: 60% as a white solid. R_f: 0.23 (35:75 EtOAc/Hexane). Mp: 106–108 °C. IR (KBr) ν_{max}: 3309, 2958, 2933, 2871, 1689, 1640, 1512, 1483, 1251 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (s, OH, 2H), 7.56 (d, J=3.5 Hz, NH, 2H), 7.17 (m, ArH, 4H), 7.06 (d, 4H, J=8.56 Hz, 4H), 6.99 (d, J=6.5 Hz, ArH, 4H), 6.93 (m, ArH, 6H), 6.69 (m, ArH, 6H), 6.23 (s, CH, 2H), 4.23 (m, $ArCH_2Ar$, 2H), 3.96 (t, J_1=6.5 Hz, J_2=7 Hz, OCH_2, 4H), 3.73 (s, OCH_3, 6H), 3.30 (m, $ArCH_2Ar$, 4H), 2.23 (s, $ArCH_3$, 6H), 2.04 (m, CH_2, 4H), 1.86 (s, O=C–CH_3, 6H), 1.68 (m, CH_2, 4H), 1.098 (m, *t*-Bu, 18H), 1.08 (t, J_1=J_2=8 Hz, CH_3, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.66 (C=O), 167.52 (C=O), 159.52, 150.25, 149.8, 147.3, 138.0, 137.8, 132.8, 131.85, 129.91, 129.6, 129.4, 129.0, 126.3, 125.8, 120.2, 113.6 (Ar–C), 76.5 (OCH_2), 64.4, 55.16, 34.22, 32.13, 23.2, 21.1, 19.3, 14.07 ($ArCH_2Ar$, O=C–CH3, *t*-Bu, $ArCH_3$, CH_3, CH_2, OCH_3). Anal. Calcd for $C_{80}H_{92}N_4O_{10}$: C, 75.68; H, 7.30; N, 4.41. Found: C, 75.63; H, 7.46; N, 4.29.

4.5. General procedure for the synthesis of α-acylaminocarboxamidocalix[4]arene (9) by the U-4CR

Diaminocalix[4]arene **1** (30.0 mg, 0.044 mmol) and aldehyde **6b** (0.088 mmol) were stirred in 1 mL TFE for 2 h. Then, carboxylic acid **4a** (0.176 mmol) and isocyanide **8a** (0.132 mmol) were added and the reaction mixture was stirred for 16 h at room temperature. The solvent was removed in vacuo. Product was purified by column chromatography on neutral alumina (Hexane/EtOAc).

4.5.1. Compound ***9baa***. Yield: 60% as a white solid. R_f: 0.43 (45:55 EtOAc/Hexane). Mp: 110–112 °C. IR (KBr) ν_{max}:3332, 2929, 2855, 1665, 1637, 1512, 1479, 1251 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, J=5 Hz, OH, 2H), 7.39 (d, J=7 Hz, ArH, 4H), 7.31 (d, J=8 Hz, ArH, 4H), 7.13 (m, ArH, 2H), 7.07 (m, ArH, 6H), 6.84 (d, J=8.5 Hz, ArH, 4H), 6.59 (s, ArH, 2H), 6.54 (m, ArH, 2H), 6.43 (m, ArH, 2H), 5.79 (d, J=8 Hz, CH, 2H), 5.59 (bs, NH, 2H), 4.09 (dd, J_1=4 Hz, J_2=13.5 Hz, $ArCH_2Ar$, 2H), 3.99 (dd, J_1=2.5 Hz, J_2=13.5 Hz, $ArCH_2Ar$, 2H), 3.86 (m, CH, OCH_2, 6H), 3.80 (s, OCH_3, 6H), 3.18 (dd, J_1=6 Hz, J_2=13 Hz, $ArCH_2Ar$, 2H), 2.99 (dd, J_1=4 Hz, J_2=13 Hz, $ArCH_2Ar$, 2H), 1.91 (m, CH_2, 8H), 1.62 (m, CH_2, 8H), 1.36 (m, CH_2, 4H), 1.13 (m, CH_2, 8H), 1.02 (m, CH_3, 6H), 0.83 (m, *t*-Bu, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): 170.6 (C=O), 168.7 (C=O), 159.5, 152.6, 149.9, 147.2, 147.1, 136.1, 131.6, 131.0, 129.6, 128.8, 128.3, 127.5, 125.4, 125.2, 113.9 (Ar–C), 76.36 (OCH_2), 55.2, 48.6, 33.8, 32.9, 32.8, 32.2, 31.2, 25.6, 24.8, 24.7, 19.3, 14.07 ($ArCH_2Ar$, CH_2, CH_3, *t*-Bu, OCH_3). MS (MALDI-TOF): Calcd for $C_{88}H_{104}N_4O_{10}$ [M+Na]+: 1399.7752; Found: 1399.7487.

4.5.2. Compound ***9caa***. Yield: 65% as a white solid. R_f: 0.54 (45:55 EtOAc/Hexane). Mp: 97–101 °C. IR (KBr) ν_{max}: 3318, 2953, 2930, 2856, 1680, 1636, 1515, 1251 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (s, OH, 2H), 7.38 (m, ArH, 4H), 7.29 (bs, ArH, 2H), 7.16 (m, ArH, 2H), 7.05 (m, ArH, 6H), 6.96 (s, ArH, 4H), 5.96 (bs, CH, 2H), 5.50 (m, NH, 2H), 3.99 (m, $ArCH_2Ar$, 4H), 3.82 (m, OCH_2, CH, 6H), 3.19 (d, J=13.5 Hz, $ArCH_2Ar$, 2H), 2.89 (m, $ArCH_2Ar$, 2H), 2.29 (s, CH_3, 6H), 2.23 (s, CH_3, 6H), 1.90 (m, CH_2, 8H), 1.56 (m, CH, OCH_2, 4H), 1.33 (m, CH_2, 6H), 1.09 (m, CH_2, 6H), 1.00 (m, CH_3, 6H), 0.792 (m, *t*-Bu, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8 (C=O), 168.6 (C=O), 152.5, 150.5, 146.9, 137.97, 137.2, 136.2, 131.7, 131.5, 130.4, 129.5, 129.1, 128.7, 128.2, 127.5, 127.1, 125.2, 125.11 (Ar–C), 76.5 (OCH_2), 48.7, 33.8, 32.8, 32.1, 31.5, 31.2, 25.1, 24.9, 21.06, 19.5, 19.3, 14.0 ($ArCH_2Ar$, *t*-Bu, CH_2, CH_3). MS (MALDI-TOF): Calcd for $C_{90}H_{108}N_4O_{10}$, [M+Na]+: 1395.8167; Found: 1395.9396.

4.5.3. Compound ***9daa***. Yield: 63% as a white solid. R_f: 0.57 (45:55 EtOAc/Hexane). Mp: 98–100 °C. IR (KBr) ν_{max}: 3341, 2928, 2855, 1691, 1642, 1534, 1275 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47 (s, OH, 2H), 7.39 (m, ArH, 6H), 7.10 (m, ArH, 14H), 6.42 (m, ArH, 6H), 6.09 (bs, CH_2, 2H), 5.50 (m, NH, 2H), 3.89 (m, OCH_2, $ArCH_2Ar$, CH, 10H), 3.15 (d, J=13.5 Hz, $ArCH_2Ar$, 2H), 2.89 (d, J=13.5 Hz, $ArCH_2Ar$, 2H), 2.32 (s, $ArCH_3$, 6H), 1.95 (m, CH_2, 4H), 1.87 (m, CH_2, 4H), 1.66 (m, CH_2, 4H), 1.56 (m, CH_2, 6H), 1.35 (m, CH_2, 4H), 1.10 (m, CH_2, 6H), 0.99 (m, CH_3, 6H), 0.81 (m, *t*-Bu, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9 (C=O), 168.6 (C=O), 152.6, 150.06, 146.9, 137.5, 136.19, 133.46, 131.8, 131.46, 129.8, 129.5, 129.3, 128.7, 128.4, 128.0, 127.5, 126.3, 125.4 (Ar–C), 76.3 (OCH_2), 48.8, 33.8, 32.8, 32.1, 31.6, 31.3, 31.0, 25.5, 24.8, 19.6, 19.25, 14.0 ($ArCH_2Ar$, CH_2, CH_3, *t*-Bu). MS (MALDI-TOF): Calcd for $C_{88}H_{104}N_4O_{10}$, $[M+Na]^+$: 1367.7854; Found: 1367.7379.

4.5.4. Compound ***9eaa***. Yield: 62% as white solid. R_f: 0.57 (45:55 EtOAc/Hexane). Mp: 100–102 °C. IR (KBr) ν_{max}: 3319, 2954, 2929, 2855, 1679, 1634, 1479, 1250 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, J=5 Hz, OH, 2H), 7.40 (d, J=7.5 Hz, ArH, 4H), 7.29 (d, J=7.5 Hz, ArH, 4H), 7.14 (m, ArH, 6H), 7.07 (m, ArH, 6H), 6.62 (s, ArH, 2H), 6.55 (m, ArH, 2H), 6.41 (m, ArH, 2H), 5.84 (d, J=8 Hz, NH, 2H), 5.53 (s, CH, 2H), 4.09 (dd, J_1=3 Hz, J_2=13 Hz, $ArCH_2Ar$, 2H), 3.98 (m, $ArCH_2Ar$, 2H), 3.85 (m, OCH_2, CH, 6H), 3.18 (dd, J_1=6.5 Hz, J_2=13.5 Hz, $ArCH_2Ar$, 2H), 2.99 (m, $ArCH_2Ar$, 2H), 2.34 (s, $ArCH_3$, 6H),1.91 (m, CH_2, 8H), 1.63 (m, CH_2, 8H), 1.35 (m, CH_2, 6H), 1.12 (m, CH_2, 6H), 1.02 (m, CH_3, 6H), 0.83 (m, *t*-Bu, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6 (C=O), 168.6 (C=O), 152.6, 149.96, 147.1, 137.99, 136.1, 13.5, 131.66, 131.60, 129.64, 129.39, 128.80, 128.42, 127.53, 125.42, 125.19 (Ar–C), 76.30 (OCH_2), 48.64, 33.88, 32.86, 32.80, 32.17, 31.18, 26.9, 25.56, 24.76, 21.20, 19.3, 14.07 ($ArCH_2Ar$, CH_2, $ArCH_3$, CH_3, *t*-Bu). Anal. Calcd for $C_{88}H_{104}N_4O_8$: C, 78.54; H, 7.79; N, 4.16. Found: C, 78.69; H, 7.92; N, 4.21.

4.5.5. Compound ***9faa***. Yield: 70% as a light yellow solid. R_f: 0.29 (45:55 EtOAc/Hexane). Mp: 118–120 °C. IR (KBr) ν_{max}: 3289, 2929, 2854, 1669, 1651, 1515, 1479, 1452, 1251 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (d, J=7.5 Hz, OH, 2H), 7.89 (m, NH, ArH, 6H), 7.74 (m, ArH, 2H), 7.59 (d, J=8 Hz, ArH, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.46 (d, J=7.5 Hz, ArH, 4H), 7.24 (s, ArH, 2H), 7.12 (m, ArH, 2H), 7.06 (m, ArH, 4H), 6.99 (d, J=8.5 Hz, ArH, 4H), 6.84 (m, ArH, 2H), 6.66 (d, J=14 Hz, ArH, 2H), 6.45 (d, J=14 Hz, ArH, 2H), 5.59 (s, CH, 2H), 4.14 (d, J=13 Hz, $ArCH_2Ar$, 2H), 4.05 (d, J=13 Hz, $ArCH_2Ar$, 2H), 3.87 (m, OCH_2, OCH_3, CH, 12H), 3.25 (m, $ArCH_2Ar$, 2H), 3.07 (m, $ArCH_2Ar$, 2H), 1.92 (m, CH_2, 6H), 1.81 (m, CH_2, 2H), 1.66 (m, CH_2, 6H), 1.52 (m, CH_2, 4H), 1.21 (m, CH_2, 10H), 1.04 (m, CH_3, 6H), 0.81 (m, *t*-Bu, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3 (C=O), 166.6 (C=O), 156.12, 155.5, 152.6, 149.9, 147.2,

137.99, 135.8, 131.7, 131.4, 129.8, 128.9, 128.6, 128.3, 128.0, 127.5, 125.5, 125.3, 118.1, 114.1 (Ar–C), 76.3 (OCH_2), 55.4, 48.3, 33.9, 33.0, 32.8, 32.2, 31.2, 29.7, 25.6, 25.4, 24.6, 19.4, 14.06 ($ArCH_2Ar$, CH_2, CH_3, *t*-Bu, OCH_3). Anal. Calcd for $C_{98}H_{110}N_6O_{10}$: C, 76.83; H, 7.24; N, 5.49. Found: C, 76.97; H, 7.41; N, 5.62.

4.5.6. Compound ***9bba****.* Yield: 62% as a white solid. R_f: 0.48 (45:55 EtOAc/Hexane). Mp: 112–114 °C. IR (KBr) ν_{max}: 3315, 2925, 2856, 1660, 1642, 1513, 1479, 1252 cm^{-1} ^1H NMR (500 MHz, $CDCl_3$): δ 8.059 (bs, OH, 2H), 7.30 (m, ArH, 4H), 7.187 (m, ArH, 4H), 6.19 (m, ArH, 4H), 6.83 (d, J=10 Hz, ArH, 6H), 6.65 (bs, ArH, 2H), 6.56 (bs, ArH, 2H), 6.501 (bs, ArH, 2H), 5.66 (m, CH, 2H), 5.53 (bs, NH, 2H), 4.14 (dd, J_1=5 Hz, J_2=13 Hz, $ArCH_2Ar$, 2H), 4.02 (dd, J_1=5 Hz, J_2=13 Hz, $ArCH_2Ar$, 2H), 3.87 (m, CH, OCH_2, 6H), 3.80 (s, OCH_3, 6H), 3.23 (m, $ArCH_2Ar$, 2H), 3.03 (m, $ArCH_2Ar$, 2H), 1.94 (m, CH_2, 8H), 1.65 (m, CH_2, 8H), 1.35 (m, CH_2, 6H), 1.11 (m, CH_2, 6H), 1.04 (m, CH_3, 6H), 0.828 (m, *t*-Bu, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.7(C=O), 168.4 (C=O), 159.56, 152.8, 149.8, 147.3, 137.65, 133.76, 131.8, 131.14, 131.01, 129.69, 129.27, 128.94, 128.59, 127.29, 126.89, 125.62, 125.2, 114.06 (Ar–C), 76.47 (OCH_2), 55.21, 48.7, 33.8, 32.86, 31.38, 31.29, 31.11, 25.55, 24.77, 19.3, 14.09 ($ArCH_2Ar$, CH_2, CH_3, *t*-Bu, OCH_3). Anal. Calcd for $C_{88}H_{102}C_{12}N_4O_{10}$: C, 73.06; H, 7.11; N, 3.87. Found: C, 73.14; H, 7.30; N, 3.74.

4.5.7. Compound ***9bab****.* Yield: 60% as a red solid. R_f: 0.22 (45:55 EtOAc/Hexane). Mp: 118–120 °C. IR (KBr) ν_{max}: 3313, 2956, 1928, 2871, 1680, 1620, 1247 cm^{-1} ^1H NMR (500 MHz, $CDCl_3$): δ 7.87 (s, OH, 2H), 7.70 (s, NH, 2H), 7.41 (m, ArH, 12H), 7.17 (m, ArH, 2H), 7.08 (m, ArH, 6H), 6.88 (d, J=8.5 Hz, ArH, 4H), 6.83 (d, J=9 Hz, ArH, 4H), 6.64 (s, ArH, 2H), 6.55 (m, ArH, 2H), 6.46 (m, ArH, 2H), 5.73 (bs, CH, 2H), 4.09 (m, $ArCH_2Ar$, 2H), 4.01 (m, $ArCH_2Ar$, 2H), 3.87 (m, OCH_2, 4H), 3.82 (s, OCH_3, 6H), 3.78 (s, OCH_3, 6H), 3.19 (m, $ArCH_2Ar$, 2H), 3.02 (m, $ArCH_2Ar$, 2H), 1.91 (m, CH_2, 4H), 1.63 (m, CH_2, 4H), 1.04 (m, CH_3, 6H), 0.83 (m, *t*-Bu, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.82 (C=O), 167.8 (C=O), 159.7, 156.5, 152.86, 146.97, 147.2, 135.7, 131.6, 131.56, 131.01, 130.9, 129.9, 128.9, 128.6, 127.6, 127.1, 125.4, 125.1, 121.9, 114.2 (Ar–C), 76.33, 55.5, 55.3, 33.9, 32.2, 31.4, 31.2, 29.7, 19.4, 14.1 ($ArCH_2Ar$, OCH_2, OCH_3, CH_2, CH_3). MS (MALDI-TOF): Calcd for $C_{90}H_{96}N_4O_{12}$, $[M+Na]^+$: 1447.7025; Found: 1447.7314.

4.5.8. Compound ***9bac****.* Yield: 61% as light red solid. R_f: 0.46 (45:55 EtOAc/Hexane). Mp: 120–123 °C. IR (KBr) ν_{max}: 3284, 2823, 2852, 1661, 1643, 1589, 1120 cm^{-1} ^1H NMR (500 MHz, $CDCl_3$): δ 8.27 (s, ArH, 2H), 8.24 (s, OH, 2H), 7.75 (m, ArH, 8H), 7.42 (m, ArH, 14H), 1.17 (m, ArH, 2H), 7.10 (m, ArH, 6H), 6.91 (d, J=9 Hz, ArH, 4H), 6.67 (s, ArH, 2H), 6.57 (bs, NH, 2H), 6.46 (m, ArH, 2H), 5.81 (bs, CH, 2H), 4.10 (m, $ArCH_2Ar$, 2H), 4.03 (m, $ArCH_2Ar$, 2H), 3.86 (m, OCH_2, OCH_3, 10H), 3.20 (m, $ArCH_2Ar$, 2H), 3.02 (d, J=13 Hz, $ArCH_2Ar$, 2H), 1.90 (m, CH_2, 4H), 1.63 (m, CH_2, 4H), 1.03 (t, J_1=7 Hz, J_2=7.5 Hz, CH_3, 6H), 0.84 (m, *t*-Bu, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9 (C=O), 168.1 (C=O), 159.8, 152.9, 144.97, 147.2, 136.6, 135.3, 133.88, 131.5, 130.0, 129.0, 128.6, 127.6, 126.9, 126.4, 125.4, 125.3, 124.09, 120.1, 116.7, 114.28 (Ar–C), 76.35 (OCH_2), 55.28 (OCH_3), 33.88, 32.2, 31.27, 29.69, 19.36, 14.06 ($ArCH_2Ar$, CH_2, CH_3, *t*-Bu). MS (MALDI-TOF): Calcd for $C_{96}H_{96}N_4O_{10}$, $[M+Na]^+$: 1487.7126; Found: 1487.8248.

Titration with Analytes: Because of the poor solubility of metal perchlorates in chloroform, all the UV-visible experiments reported in this work were carried out in acetonitrile. The UV-visible spectra of the receptors in the presence of analytes were recorded as increasing amounts of analytes were added to the acetonitrile. Titration plots were generated by using Origin 6.0 (Microcal software).

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Supplementary data

Supplementary data associated with this article: characterization datas of the prepared compounds and the UV–vis spectra of the compound **9faa.** Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2012.05.023. These data include MOL files and InChIKeys of the most important compounds described in this article.

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