Synthesis and NMR Conformational Studies of *p-tert*-Butyldihomooxacalix[4]arene Derivatives Bearing Pyridyl Pendant Groups at the Lower Rim

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Direct *O*-alkylation of *p-tert*-butyldihomooxacalix[4]arene (**1**) with 2-(chloromethyl)pyridine hydrochloride and NaH in DMF provided six of the nine possible (2-pyridylmethoxy)dihomooxacalix[4]arene conformers in the cone conformation. Mono- and tetrasubstituted derivatives were obtained, as well as all four (1,2-, 1,3-, 1,4- and 2,3-) types of disubstituted compounds. The conformations and the substitution patterns were established by NMR spectroscopy (^{1}H, ^{13}C, COSY, NOESY and TOCSY 1D). From the same reaction, another tetrasubstituted derivative (**6**) in a 1,2-alternate A conformation was also isolated and characterised.

Introduction

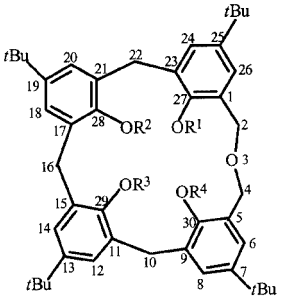
Recent research in the host-guest chemistry of calixarenes[1−4] has shown the vast ability of these compounds as selective binders and carriers, and also as building blocks for the construction of highly complex host molecules.

Many studies have focussed on the binding ability towards metal ions, predominantly alkali and alkaline earth cations, of calixarene derivatives with carbonyl groups at their lower rims.[4a] These studies have been extended to calixarenes with donor atoms other than oxygen, such as nitrogen, in order to favour complexation of transition and heavy metals. Among these compounds, some calix[*n*]arenes with pyridyl pendant groups at the lower rim have been synthesised. This synthesis has largely been done by direct *O*-alkylation with 2-(chloromethyl)pyridine hydrochloride in the presence of a base,[5] to afford *p-tert*-butylcalix-[4]-,[6−9] -[5]-,[10] -[6]-[11−13] and -[8]arene[11] derivatives. Other kinds of calixarenes bearing pyridyl groups, such as calixcrowns[14−18] and homocalix[4]-[19] and -[3]arenes,[20] have also been reported.

For a few years we have been synthesising dihomooxacalix[4]arene derivatives with carbonyl group containing substituents on the lower rim.[21−23] The binding properties of such compounds bearing ketone[22,24] and ester[23,24] groups towards alkali, alkaline earth and some transition and heavy metal cations have recently been reported by us.

Dihomooxacalix[4]arenes, with a larger cavity than the calix[4]arenes but still possessing a true cone conformation, are potential host molecules for larger cations.

With the aim of extending this study towards transition and heavy cations, we began the synthesis of dihomooxa derivatives bearing softer donor atoms at the lower rim. We report here the synthesis and conformational analysis of six of the nine possible (2-pyridylmethoxy)dihomooxacalix[4]-arenes in the cone conformation (**2a**, **3a**, **3b**, **3c**, **3d** and **5**) and of another tetrasubstituted derivative in a 1,2-alternate A conformation (**6**),[25] all obtained by direct substitution onto *p-tert*-butyldihomooxacalix[4]arene (**1**) (Scheme 1).



	R^1	R^2	R^3	R^4
1	H	H	H	H
2a	H	CH_2Py	H	H
2b	CH_2Py	H	H	H
3a	H	CH_2Py	H	CH_2Py
3b	CH_2Py	CH_2Py	H	H
3c	H	CH_2Py	CH_2Py	H
3d	CH_2Py	H	H	CH_2Py
4a	H	CH_2Py	CH_2Py	CH_2Py
4b	CH_2Py	H	CH_2Py	CH_2Py
5	CH_2Py	CH_2Py	CH_2Py	CH_2Py

Scheme 1

Results and Discussion

Synthesis

Treatment of the parent *p-tert*-butyldihomooxacalix[4]-arene (**1**) with an excess of 2-(chloromethyl)pyridine hydro-

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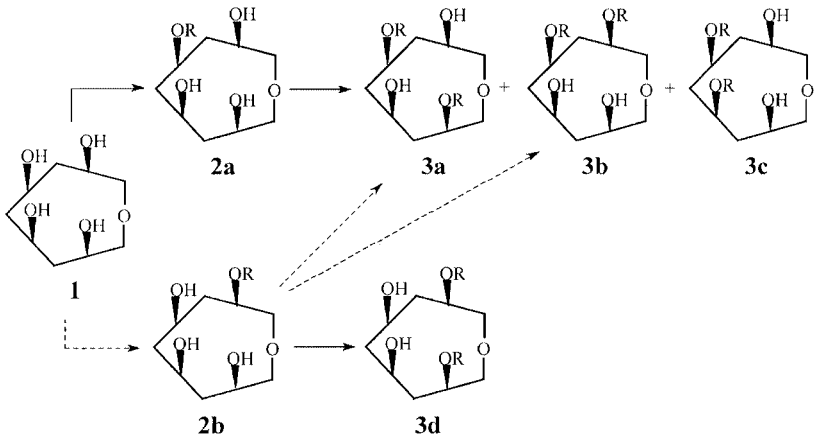


Figure 1. Possible reaction pathways for the formation of disubstituted derivatives; dashed arrows indicate less probable reaction courses

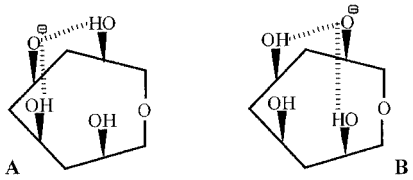
chloride and NaH (80% oil dispersion) in dry DMF at 60 °C for 24 h afforded a mixture composed mainly of monopyridyl derivative **2a** and unreacted **1**. When the reaction was conducted for 48 h, mono- and dipyridyl derivatives **2a** and **3a**, respectively, were isolated as the main compounds, along with minute amounts of dipyridyl derivatives **3b**, **3c**, and **3d**.

On replacement of NaH with K_2CO_3, but under otherwise similar conditions, a mixture of products was also obtained, dipyridyl derivative **3a** being produced as the major component.

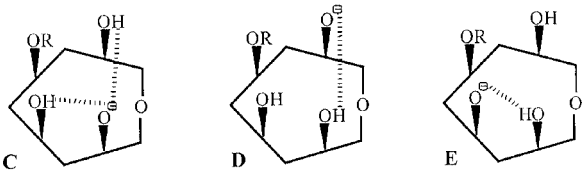
The use of 95% NaH, according to ref.[7], and a longer reaction time (nearly 3 d) gave a product mainly consisting of tetrapyridyl derivative **5**, accompanied by minor amounts of tetrapyridyl derivative **6**.

Separation of the reaction products into the pure components was achieved by column and preparative chromatography.

Two main reaction pathways for the formation of disubstituted derivatives can be envisaged (Figure 1). On the assumption that the reaction proceeds through stepwise substitution of the OH groups, the first step is the alkylation of parent **1** to **2a** and **2b**. Preferential formation of **2a** occurs because the negative charge on the phenoxide anion formed is here more strongly stabilized by the hydrogen bonds than in **2b**, possibly due to the smaller distance between the phenoxide anion and the OH groups in **2a** (Scheme 2). Further alkylation of **2a** preferentially gives derivative **3a**, in which the phenoxide anion (**C**) is stabilized by two hydrogen bonds, as opposed to just one in intermediates **D** and



Scheme 2



Scheme 3

E (Scheme 3). In addition, steric effects can also play an important role in further alkylation of the monosubstituted species, taking place at the less crowded site. Derivatives **3b** and **3c** arise from intermediates **D** and **E**, respectively, and were only obtained in minute amounts. Compound **2b** afforded derivative **3d**, also obtained in very small amounts.

NMR Conformational Analysis

The conformations of the pyridyl derivatives and the position of the substituent groups in the partially alkylated compounds were established by proton, carbon-13, COSY, NOESY and TOCSY 1D NMR spectroscopy in chloroform at room temperature.

All derivatives exist in fixed conformations, indicating that the introduction of just one picolyl group is sufficient to reduce the conformational mobility drastically.

Derivatives **2a**, **3a**, **3b**, **3c**, **3d** and **5** were found to be in cone conformations, while derivative **6** exhibits a 1,2-alternate A conformation[25] (elsewhere designated as 1,2-alternate[4b]).

Dihomooxacalix[4]arene derivatives in the cone conformation with only two different substituents at the lower rim are inherently chiral. Hence, monopyridyl derivative **2a** and dipyridyl derivatives **3a** and **3b** are inherently chiral and their chirality was demonstrated by the addition of an excess of Pirkle's reagent, (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol, to $CDCl_3$ solutions of each calixarene, causing

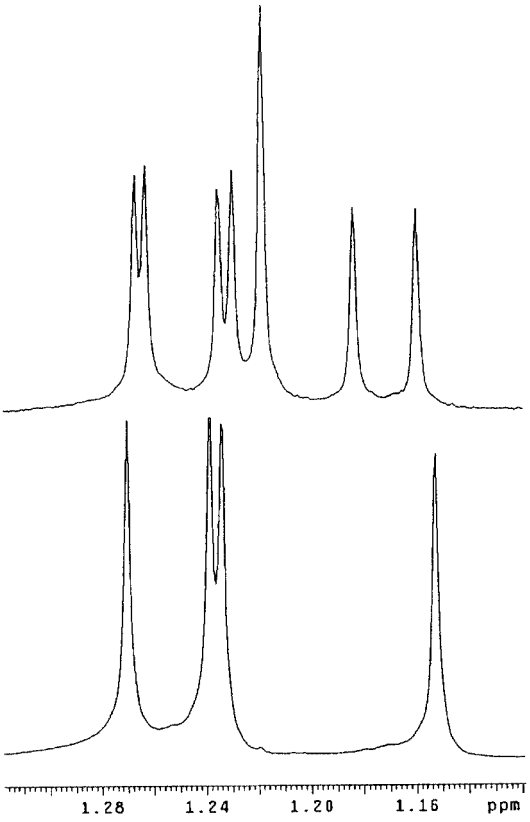


Figure 2. Partial 300 MHz ^{1}H NMR spectra for compound **2a** in $CDCl_3$ at 22 °C in the absence (bottom) or in the presence (top) of Pirkle's reagent

duplication of proton signals. The split pattern for the *tert*-butyl protons of compound **2a** is shown in Figure 2.

Monopyridyl Derivative 2a

The complete absence of symmetry in derivative **2a** is reflected by its proton and carbon-13 NMR spectra.

The ^{1}H NMR spectrum displays four singlets for the *tert*-butyl groups, five AB quadruplets for the CH_2 bridge protons, one AB quadruplet for the OCH_2Py group, four pairs of doublets for the aromatic protons, three singlets for the OH groups and four distinct multiplets for the heteroaromatic protons. The AB systems were corroborated by cross-peak correlations in a COSY spectrum (Figure 3).

Because of overlapping of signals in the ^{13}C NMR spectrum, fewer lines than expected were obtained. Thus, this spectrum shows a pattern containing 27 of the 29 expected downfield resonances arising from the aromatic carbon atoms, three midfield resonances arising from the methylene carbon atoms of the OCH_2Py and CH_2OCH_2 groups, and nine of the expected eleven upfield resonances arising from the quaternary carbon atoms $C(CH_3)$ (two lines in a 1:3 ratio), the methyl carbon atoms of the *tert*-butyl groups $C(CH_3)$ (four lines), and the methylene carbon atoms $ArCH_2Ar$ (three lines). All resonances were assigned by DEPT experiments. The three $ArCH_2Ar$ resonances appear in the $\delta = 31.1-32.5$ ppm range (see Table 1), indicating a cone conformation[26] for compound **2a**.

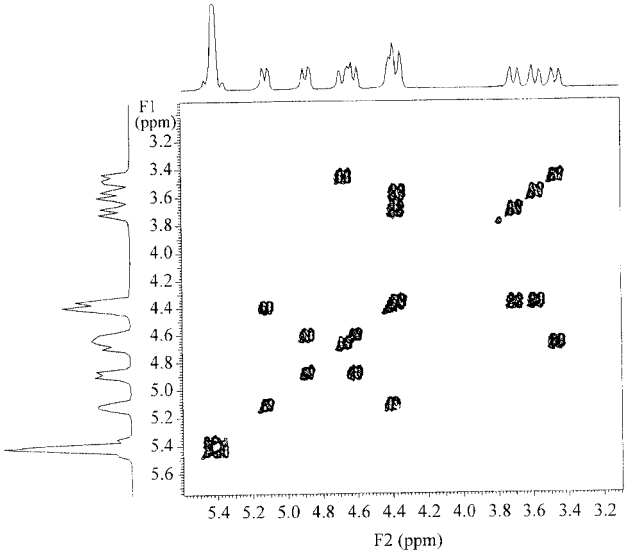


Figure 3. Methylene region of the COSY spectrum of **2a** in $CDCl_3$ at 22 °C and 300 MHz

Table 1. Relevant ^{13}C NMR data (75 MHz, $CDCl_3$, 22 °C) and conformations of pyridyldihomooxa derivatives

Compd.	$ArCH_2Ar$[a]	OCH_2Py[a]	Conformation
2a	31.1, 31.3, 32.5	78.3	cone
3a	30.3, 30.4, 32.3	78.1, 78.3	cone
3b	29.7, 30.1, 31.8	77.2, 77.8	cone
3c	30.7, 31.4 (2 C)	77.5	cone
3d	29.7, 32.0 (2 C)	77.0	cone
5	30.0 (2 C), 30.2	76.6, 77.0	cone
6	27.5, 38.9 (2 C)	74.3, 75.1	1,2-alternate A

[a] Chemical shift δ [ppm].

The cone conformation and the position of the pyridyl group were further confirmed by proton-proton correlations observed in the NOESY spectrum of **2a**. The NOEs observed between the oxymethylene protons (OCH_2Py) and the two axial methylene protons at positions 16 and 22, and also those observed between the OH proton at $\delta = 7.82$ ppm (position 27) and the two axial methylene protons at positions 2 and 22 (see Scheme 1), are conclusive for the location of the substituent group.

Dipyridyl Derivative 3a

The ^{1}H NMR spectrum of derivative **3a** [Figure 4 (a)], also asymmetric, shows the same number and type of signals as derivative **2a** for *tert*-butyl, CH_2 bridge and aromatic protons. Besides these peaks, **3a** also displays two AB quadruplets for the OCH_2Py groups, two singlets (one of them very broad) for the OH groups, and a set of seven multiplets for the heteroaromatic protons. Because of overlapping of the signals of two PyH protons from different rings, the spectrum shows only seven of the expected eight lines.

The ^{13}C NMR spectrum shows 34 downfield, four midfield and eight of the expected eleven upfield resonances. The presence of the three $ArCH_2Ar$ methylene resonances

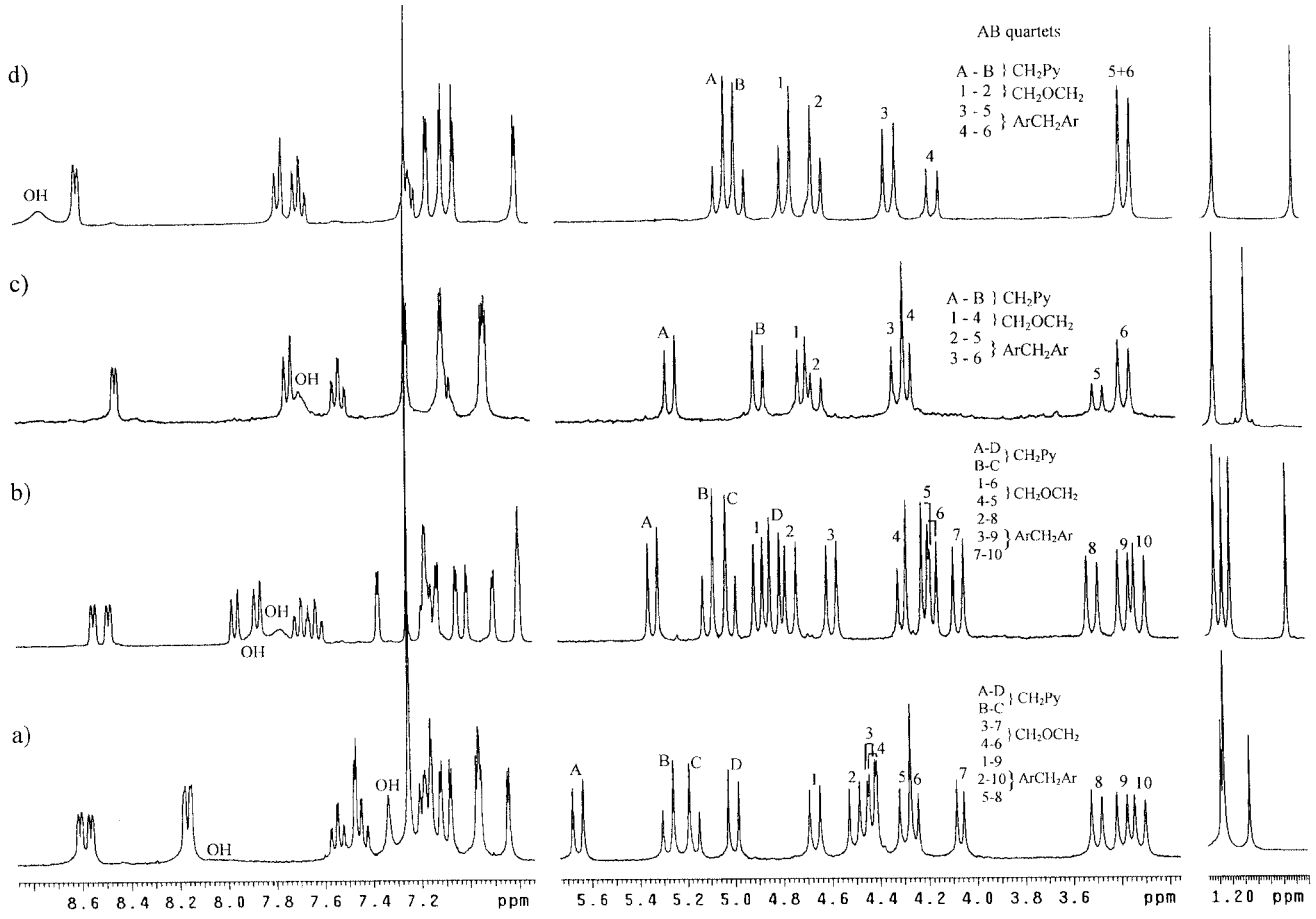


Figure 4. 300 MHz ^{1}H NMR spectra ($CDCl_3$, 22 °C) of compounds: (a) **3a**, (b) **3b**, (c) **3c** and (d) **3d**

in the δ = 30.3−32.3 ppm range (Table 1) also indicates a cone conformation for dipyridyl derivative **3a**. Further confirmation of the cone conformation was provided by a NOESY spectrum. The more relevant NOE enhancements are shown in Figure 5.

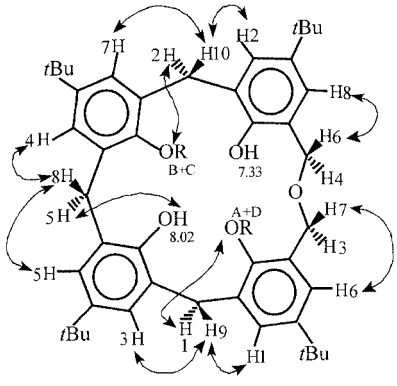


Figure 5. Relevant NOE enhancements used to confirm the cone conformation and the positions of pyridyl groups in **3a**

The 1,3-type of substitution could not be confirmed by NOE data alone. Two simultaneous NOE effects between the oxymethylene protons B + C and the two axial methylene protons 2 and 5 were expected, as well as for the oxymethylene protons A + D and the two axial methylene protons 1 and 3. In fact, though, only one NOE was observed in each case (see Figure 5). If both OCH_2Py groups were on the same side of the oxygen bridge (1,2-substitution), it would be difficult to observe, for example, NOEs between the A + D protons and the axial methylene proton 1. However, the 1,3-substitution was easily confirmed by 1D TOCSY experiments. Selective irradiation of the OH protons at δ = 7.33 and 8.02 ppm gives responses in the aromatic protons of the attached phenyl rings, protons 2−8 and 3−5, respectively, as shown in Figure 6.

Dipyridyl Derivative 3b

Unlike the homologous 1,2- and 1,3-disubstituted derivatives of *p-tert*-butylcalix[4]arene,[7] compounds **3a** and **3b** cannot be distinguished by their proton and carbon-13 NMR spectra alone. As illustrated in Figure 4 (b), derivative **3b** also shows an asymmetric proton spectrum similar to that of **3a**. The main difference is observed in the OH group signals: for **3b** both singlets are very broad and they have closer chemical shifts at a slightly lower field (on average) than those in **3a**. The ^{13}C NMR spectra are also similar for both isomers, **3b** exhibiting a cone conformation with the three Ar***C***H_2Ar resonances around δ = 30 ppm (Table 1).

The positions of the pyridyl groups were confirmed by a NOESY spectrum, and also by the fact that there are only

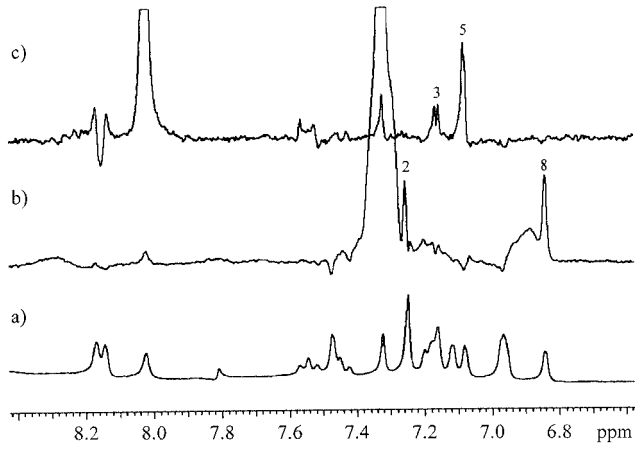


Figure 6. Partial 300 MHz ^{1}H NMR spectra ($CDCl_3$, 27 °C) of **3a**: (a) normal spectrum, (b) and (c) 1D TOCSY spectra obtained by selective irradiation of OH protons at δ = 7.33 and 8.02 ppm, respectively

two possible disubstituted asymmetric dihomooxacalix[4]-arene conformers in the cone conformation.

Dipyridyl Derivatives 3c and 3d

Compounds **3c** and **3d** both exhibit symmetric proton and carbon-13 NMR spectra, compatible with disubstituted symmetric derivatives in cone conformations. The proton spectra [Figure 4 (c) and (d)] each display two singlets for the *tert*-butyl groups, three AB quadruplets in a 2:2:1 ratio for the CH_2 bridge protons, one AB quadruplet for the OCH_2Py groups, two pairs of doublets for the aromatic protons and four multiplets for the heteroaromatic protons. The signal for the OH groups allow some differentiation between isomers. While **3d** shows a broad downfield singlet (δ = 8.76 ppm), **3c** displays a sharper one at a higher field (δ = 7.69 ppm) than for **3d**. This is in agreement with the hypothesis that in **3d** the OH groups can be closer to each other than in **3c** and, consequently, that they can form a stronger hydrogen bond. The ^{13}C NMR spectra indicate cone conformations for both derivatives. Their $ArCH_2Ar$ resonances appear at δ = 30.7 (one carbon atom) and 31.4 ppm (two carbon atoms) for **3c**, and at δ = 29.7 (one carbon atom) and 32.0 ppm (two carbon atoms) for **3d**.

The positions of the pyridyl groups were further confirmed by NOESY spectra. The more relevant NOEs for compound **3d** are those observed between the oxymethylene protons (OCH_2Py) and the two axial methylene protons at positions 2 and 22, and also those observed between the OH proton (position 28) and the two axial methylene protons at positions 16 and 22 (see Scheme 1).

Tetrapyridyl Derivative 5

Proton and carbon-13 NMR spectra of derivative **5** show spectral patterns fully compatible with a conformation containing a symmetry plane.

The ^{1}H NMR spectrum [Figure 7 (a)] displays two singlets for the *tert*-butyl groups, three AB quadruplets in a 2:2:1 ratio for the CH_2 bridge protons, two AB quadruplets for the OCH_2Py groups, two pairs of doublets for the aromatic protons, and seven of the eight expected multiplets for the heteroaromatic protons.

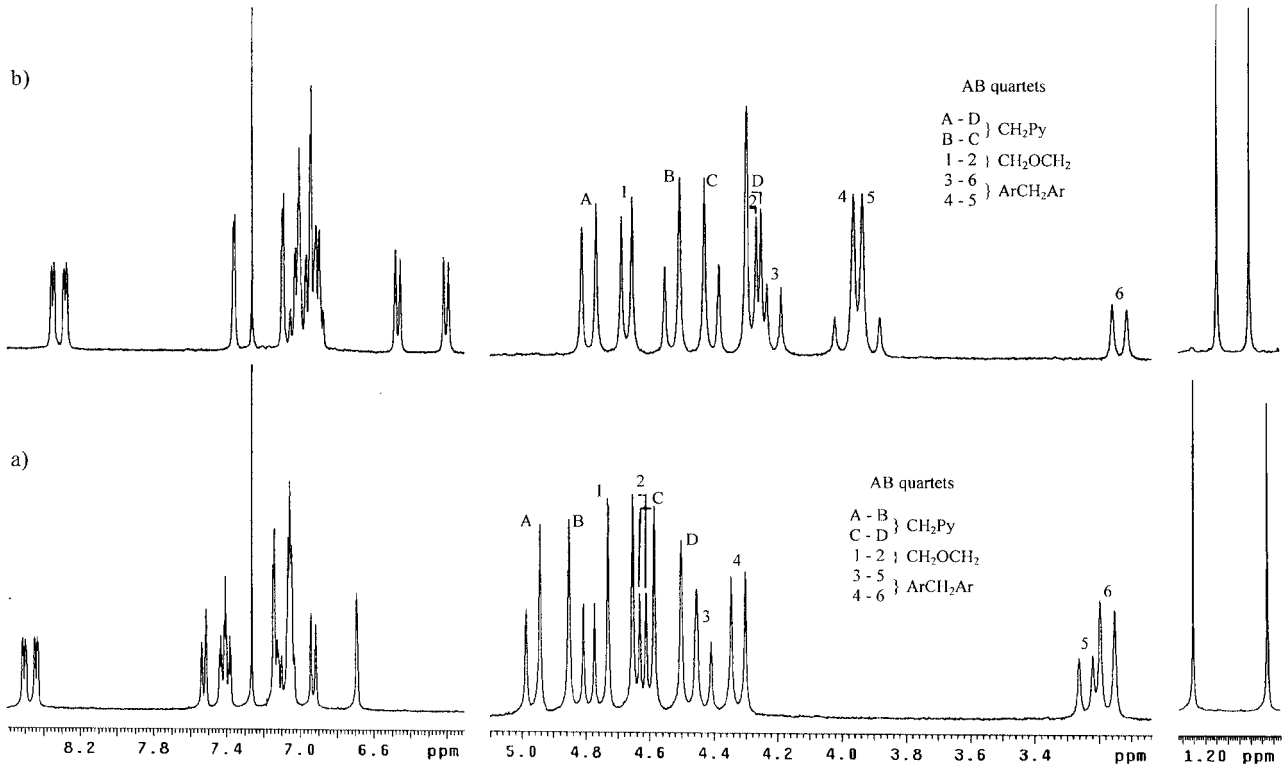


Figure 7. 300 MHz ^{1}H NMR spectra ($CDCl_3$, 22 °C) of compounds: (a) **5**, (b) **6**

The ^{13}C NMR spectrum exhibits 22 downfield resonances arising from the aromatic carbon atoms (twelve from the calixarene skeleton and ten from the pyridine rings), three midfield resonances arising from the methylene carbon atoms (two from OCH_2Py and one from CH_2OCH_2 groups), and six upfield resonances arising from the quaternary carbon atoms $C(CH_3)$ (2 lines), the Me carbon atoms of the *t*Bu groups (2 lines) and the methylene carbon atoms $ArCH_2Ar$ (2 lines).

This spectrum indicates the cone conformation for derivative **5**, showing one $ArCH_2Ar$ resonance at $\delta = 30.2$ ppm corresponding to one carbon atom, and another at $\delta = 30.0$ ppm corresponding to two carbon atoms. The cone conformation was also confirmed by a NOESY spectrum.

Preliminary extraction studies (metal picrates, water/CH_2Cl_2) towards alkali, alkaline earth, and some transition and heavy metal cations were performed with **5**. As expected, **5** shows little affinity for hard alkali and alkaline earth cations, but presents very high extraction levels for the softer Ag^+, Hg^{2+} and Pb^{2+} cations (90, 70 and 40% extraction, respectively).

Tetrapyridyl Derivative 6

Similarly to derivative **5**, tetrapyridyl derivative **6** also exhibits proton and carbon-13 NMR spectra compatible with a symmetry plane conformation. Its ^1H NMR spectrum [Figure 7 (b)] is similar to that of **5**, the major difference being the resonance of the $ArCH_2Ar$ bridge connecting two adjacent phenyl rings in a *anti* orientation. In this case, the axial and equatorial protons have closer chemical shifts than in **5**, giving an AB system with a larger coupling constant.

The ^{13}C NMR spectrum also shows the same line pattern as derivative **5**. However, the $ArCH_2Ar$ resonances allow distinctions to be made between conformers with a symmetry plane. Thus, the spectrum of **6** shows one CH_2 bridge resonance at $\delta = 27.5$ ppm corresponding to one carbon atom and another at $\delta = 38.9$ ppm corresponding to two carbon atoms. This agrees with a 1,2-alternate A conformation.[25]

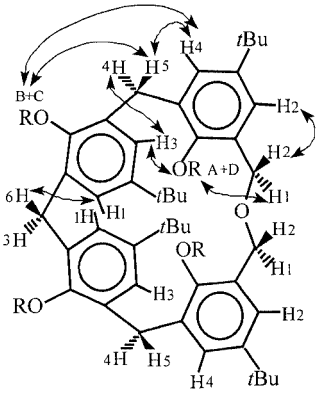


Figure 8. Relevant NOEs used to confirm the 1,2-alternate A conformation

A set of NOE 1D experiments (Figure 8) further corroborates this conformation assignment.

Conclusions

The alkylation of *p-tert*-butyldihomooxacalix[4]arene (**1**) with 2-(chloromethyl)pyridine hydrochloride and NaH in DMF resulted in the synthesis, isolation and identification of six pyridyldihomooxacalix[4]arenes, including mono-, di- and tetrasubstituted derivatives, in cone conformations. All have $ArCH_2Ar$ resonances at $\delta = 30-33$ ppm, and those of the OCH_2Py groups appear at $\delta \approx 77.5$ ppm (Table 1), as observed for pyridylcalix[4]arene derivatives[7] in a cone conformation. Another tetrasubstituted derivative (**6**) in a 1,2-alternate A conformation was also obtained.

Extraction experiments with metal picrates from aqueous solutions into dichloromethane were performed with tetrapyridyl derivative **5**. Preliminary results show a very high extraction percentage for Ag^+ (90% *E*) and also good levels for Hg^{2+} and Pb^{2+} cations.

Experimental Section

General: All chemicals were reagent grade and were used without further purification. Melting points were measured with a Stuart Scientific apparatus and are uncorrected. The ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ with a Varian Unity 300 spectrometer with TMS as internal reference. The NOE 1D difference spectra were acquired with a saturation delay of 5 s and 256 transients. The conventional COSY 45 and the phase-sensitive NOESY experiments were collected as 256×2 K complex points. A selective pulse of 180 ms, a mixing time of 0.2 s and 256 transients were used to obtain the TOCSY 1D spectra. Elemental analyses were determined with a Fisons EA 1108 microanalyser.

Procedure for the Synthesis of 2a, 3a, 3b, 3c and 3d: A mixture of *p-tert*-butyldihomooxacalix[4]arene (1 g, 1.48 mmol) and NaH (80% oil dispersion, 2.22 g, 74 mmol) in dry DMF (30 mL) was stirred and gently warmed under N_2 for 30 min. After the solution had cooled, 2-(chloromethyl)pyridine hydrochloride (4.92 g, 30 mmol) was added and the reaction mixture was then heated at 60 °C with stirring under N_2 for 48 h. Addition of MeOH (3 mL) and water (150 mL) to the cooled reaction mixture gave a light brown precipitate, which was filtered. The solid residue was subjected to flash chromatography (SiO_2, eluent increasing gradient of EtOAc in *n*-heptane), followed in the cases of **3b**, **3c** and **3d** by preparative chromatography, to give the following products.

7,13,19,25-Tetra-*tert*-butyl-27,29,30-trihydroxy-28-[(2-pyridyl)-methoxy]-2,3-dihomo-3-oxacalix[4]arene (2a): This compound was obtained in 22% yield (0.25 g). M.p. 259−261 °C. ^1H NMR ($CDCl_3$): $\delta = 1.15, 1.23, 1.24, 1.27$ [4 s, 36 H, $C(CH_3)_3$], 3.32, 4.53 (ABq, $J = 12.9$ Hz, 2 H, $ArCH_2Ar$), 3.44, 4.23 (ABq, $J = 13.7$ Hz, 2 H, $ArCH_2Ar$), 3.56, 4.23 (ABq, $J = 13.7$ Hz, 2 H, $ArCH_2Ar$), 4.26, 4.98 (ABq, $J = 9.3$ Hz, 2 H, CH_2OCH_2), 4.47, 4.75 (ABq, $J = 10.0$ Hz, 2 H, CH_2OCH_2), 5.27 (ABq, $J = 13.0$ Hz, 2 H, OCH_2Py), 6.90, 6.98, 7.06 (3 d, 3 H, ArH), 7.12 (3 d, 3 H, ArH), 7.29 (2 d, 2 H, ArH), 7.32 (m, 1 H, 5-PyH), 7.82, 8.53, 9.17 (3 s, 3 H, OH), 7.93 (td, $J = 7.7, 1.7$ Hz, 1 H, 4-PyH), 8.15 (d, $J = 8.0$ Hz, 1 H, 3-PyH), 8.64 (ddd, $J = 4.9, 1.8, 0.9$ Hz, 1 H, 6-PyH) ppm. ^{13}C NMR ($CDCl_3$): $\delta = 30.1, 31.3, 32.5$ ($ArCH_2Ar$), 31.2, 31.4, 31.5, 31.6 [$C(CH_3)_3$], 33.9, 34.2 [$C(CH_3)_3$], 71.7, 72.2 (CH_2OCH_2), 78.3 (OCH_2Py), 121.8, 123.1, 123.7, 125.3, 125.6, 125.75, 125.83, 126.8, 127.5, 128.2, 137.6, 149.2 (ArH), 122.6, 122.7, 126.5, 127.5,

128.4, 131.5, 132.7, 141.6, 142.5, 143.5, 147.7, 147.9, 149.5, 151.2, 152.8, 156.4 (Ar) ppm. $C_{51}H_{63}NO_5$ (770.06): calcd. C 79.55, H 8.25, N 1.82; found C 79.81, H 8.34, N 1.74.

7,13,19,25-Tetra-*tert*-butyl-27,29-dihydroxy-28,30-bis[(2-pyridyl)-methoxy]-2,3-dihomo-3-oxacalix[4]arene (3a): This compound was obtained in 26% yield (0.33 g). M.p. 200−202 °C. ^{1}H NMR ($CDCl_3$): δ = 1.14, 1.25 [2 s, 18 H, $C(CH_3)_3$], 1.24 [1 s, 18 H, $C(CH_3)_3$], 3.33, 4.51 (ABq, J = 13.0 Hz, 2 H, $ArCH_2Ar$), 3.40, 4.68 (ABq, J = 13.1 Hz, 2 H, $ArCH_2Ar$), 3.51, 4.30 (ABq, J = 13.6 Hz, 2 H, $ArCH_2Ar$), 4.07, 4.44 (ABq, J = 9.4 Hz, 2 H, CH_2OCH_2), 4.26, 4.43 (ABq, J = 9.4 Hz, 2 H, CH_2OCH_2), 5.01, 5.67 (ABq, J = 13.0 Hz, 2 H, OCH_2Py), 5.17, 5.29 (ABq, J = 13.3 Hz, 2 H, OCH_2Py), 6.85, 6.97, 6.98, 7.08, 7.13, 7.17, 7.26, 7.48 (8 d, 8 H, ArH), 7.19 (m, 2 H, 5-PyH and 5-Py′H), 7.33 (1 s, 1 H, OH), 7.45 (td, J = 7.7, 1.9 Hz, 1 H, 4-Py′H), 7.55 (td, J = 7.7, 1.9 Hz, 1 H, 4-PyH), 8.02 (1 bs, 1 H, OH), 8.16 (d, J = 4.4 Hz, 1 H, 3-Py′H), 8.19 (d, J = 4.4 Hz, 1 H, 3-PyH), 8.57 (ddd, J = 4.9, 1.9, 0.9 Hz, 1 H, 6-Py′H), 8.61 (ddd, J = 4.9, 1.9, 0.9 Hz, 1 H, 6-PyH) ppm. ^{13}C NMR ($CDCl_3$): δ = 30.3, 30.4, 32.3 ($ArCH_2Ar$), 31.2, 31.4, 31.6 [$C(CH_3)_3$], 33.8, 34.2 [$C(CH_3)_3$], 71.4, 72.2 (CH_2OCH_2), 78.1, 78.3 (OCH_2Py), 121.8, 122.8, 122.9, 123.0, 124.0, 125.1, 125.4, 125.5, 125.9, 126.1, 127.6, 129.7, 137.1, 137.2, 148.8, 149.2 (ArH), 122.3, 127.3, 127.6, 128.4, 129.2, 132.3, 132.6, 134.5, 141.4, 142.1, 146.7, 147.4, 149.7, 149.9, 152.8, 154.3, 156.9, 157.9 (Ar) ppm. $C_{57}H_{68}N_2O_5$ (861.17): calcd. C 79.50, H 7.96, N 3.25; found C 79.53, H 8.09, N 3.16.

7,13,19,25-Tetra-*tert*-butyl-29,30-dihydroxy-27,28-bis[(2-pyridyl)-methoxy]-2,3-dihomo-3-oxacalix[4]arene (3b): This compound was obtained in ca. 2% yield (22 mg). M.p. 127−129 °C. ^{1}H NMR ($CDCl_3$): δ = 0.98, 1.20, 1.23, 1.26 [4 s, 36 H, $C(CH_3)_3$], 3.32, 4.07 (ABq, J = 13.5 Hz, 2 H, $ArCH_2Ar$), 3.38, 4.59 (ABq, J = 13.0 Hz, 2 H, $ArCH_2Ar$), 3.51, 4.76 (ABq, J = 13.6 Hz, 2 H, $ArCH_2Ar$), 4.18, 4.90 (ABq, J = 10.5 Hz, 2 H, CH_2OCH_2), 4.20, 4.30 (ABq, J = 10.5 Hz, 2 H, CH_2OCH_2), 4.83, 5.34 (ABq, J = 12.2 Hz, 2 H, OCH_2Py), 5.01, 5.11(ABq, J = 12.8 Hz, 2 H, OCH_2Py), 6.80 (2 d, 2 H, ArH), 6.90, 7.01, 7.05, 7.13, 7.18, 7.38 (6 d, 6 H, ArH), 7.16 (m, 2 H, 5-PyH and 5-Py′H), 7.63 (td, J = 7.5, 1.8 Hz, 1 H, 4-Py′H), 7.69 (td, J = 7.5, 1.8 Hz, 1 H, 4-PyH), 7.78, 7.87 (2 bs, 2 H, OH), 7.87 (d, J = 7.8 Hz, 1 H, 3-Py′H), 7.97 (d, J = 7.8 Hz, 1 H, 3-PyH), 8.49 (m, 1 H, 6-Py′H), 8.55 (m, 1 H, 6-PyH) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.7, 30.1, 31.8 ($ArCH_2Ar$), 31.1, 31.5, 31.6 [$C(CH_3)_3$], 33.9, 34.0, 34.2 [$C(CH_3)_3$], 70.7, 71.3 (CH_2OCH_2), 77.2, 77.8 (OCH_2Py), 122.4, 122.7, 122.8, 123.5, 123.7, 124.8, 125.0, 125.3, 126.1, 126.5, 127.5, 129.7, 136.8, 137.1, 148.5, 149.0 (ArH), 122.1, 127.3, 128.4, 129.5, 130.2, 131.9, 133.4, 134.8, 142.5, 146.1, 146.7, 149.5, 150.4, 151.8, 154.2, 157.0, 157.5 (Ar) ppm. $C_{57}H_{68}N_2O_5$ (861.17): calcd. C 79.50, H 7.96, N 3.25; found C 79.27, H 8.16, N 3.16.

7,13,19,25-Tetra-*tert*-butyl-27,30-dihydroxy-28,29-bis[(2-pyridyl)-methoxy]-2,3-dihomo-3-oxacalix[4]arene (3c): This compound was obtained in low yield (10 mg). ^{1}H NMR ($CDCl_3$): δ = 1.13, 1.26 [2 s, 36 H, $C(CH_3)_3$], 3.37, 4.31 (ABq, 4 H, J = 13.7 Hz, $ArCH_2Ar$), 3.48, 4.65 (ABq, J = 13.0 Hz, 2 H, $ArCH_2Ar$), 4.27, 4.71 (ABq, 4 H, J = 9.8 Hz, CH_2OCH_2), 4.89, 5.26 (ABq, 4 H, J = 12.6 Hz, OCH_2Py), 6.92, 6.94, 7.11, 7.25 (4 d, 8 H, ArH), 7.09 (m, 2 H, 5-PyH), 7.53 (td, J = 7.7, 1.7 Hz, 2 H, 4-PyH), 7.69 (1 bs, 2 H, OH), 7.74 (d, J = 8.0 Hz, 2 H, 3-PyH), 8.45 (m, 2 H, 6-PyH) ppm. ^{13}C NMR ($CDCl_3$): δ = 30.7, 31.4 ($ArCH_2Ar$), 31.2, 31.5 [$C(CH_3)_3$], 33.8, 34.1 [$C(CH_3)_3$], 71.8 (CH_2OCH_2), 77.5 (OCH_2Py), 122.5, 122.7, 122.9, 124.7, 125.4, 126.0, 136.7, 148.5 (ArH), 128.06, 128.10, 132.5, 133.5, 141.8, 146.8, 151.3, 152.2, 156.9 (Ar).

7,13,19,25-Tetra-*tert*-butyl-28,29-dihydroxy-27,30-bis[(2-pyridyl)-methoxy]-2,3-dihomo-3-oxacalix[4]arene (3d): This compound was obtained in low yield (8 mg). ^{1}H NMR ($CDCl_3$): δ = 0.94, 1.25 [2 s, 36 H, $C(CH_3)_3$], 3.36, 4.16 (ABq, J = 13.9 Hz, 2 H, $ArCH_2Ar$), 3.36, 4.34 (ABq, 4 H, J = 13.9 Hz, $ArCH_2Ar$), 4.64, 4.77 (ABq, 4 H, J = 13.3 Hz, CH_2OCH_2), 4.96, 5.05 (ABq, 4 H, J = 13.3 Hz, OCH_2Py), 6.80, 7.05, 7.10, 7.16 (4 d, 8 H, ArH), 7.23 (m, 2 H, 5-PyH), 7.68 (td, J = 7.6, 1.7 Hz, 2 H, 4-PyH), 7.77 (d, J = 7.6 Hz, 2 H, 3-PyH), 8.60 (ddd, J = 4.7, 1.4, 0.8 Hz, 2 H, 6-PyH), 8.76 (1 bs, 2 H, OH) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.7, 32.0 ($ArCH_2Ar$), 31.1, 31.6 [$C(CH_3)_3$], 33.9, 34.1 [$C(CH_3)_3$], 66.7 (CH_2OCH_2), 77.0 (OCH_2Py), 121.8, 122.8, 124.6, 125.7, 126.0, 126.2, 137.2, 149.1 (ArH), 127.1, 127.4, 130.7, 132.7, 142.5, 147.0, 148.8, 151.0, 156.8 (Ar) ppm.

Procedure for the Synthesis of 5 and 6: A mixture of **1** (1 g, 1.48 mmol) and NaH (95%, 1.87 g, 74 mmol) in dry DMF (30 mL) was stirred and gently warmed under N_2 for 30 min. After the solution had cooled, 2-(chloromethyl)pyridine hydrochloride (4.92 g, 30 mmol) was added and the reaction mixture was then heated at 60 °C with stirring under N_2 for 3 d. By the same workup as above, it was obtained as a light yellow solid, which was chromatographed (the same conditions as above). Compounds **5** and **6** were recrystallised from aqueous MeOH and from *n*-heptane, respectively, furnishing white crystals.

7,13,19,25-Tetra-*tert*-butyl-27,28,29,30-tetrakis[(2-pyridyl)methoxy]-2,3-dihomo-3-oxacalix[4]arene (5): This compound was obtained in 36% yield (0.56 g). M.p. 213−214 °C. ^{1}H NMR ($CDCl_3$): δ = 0.93, 1.25 [2 s, 36 H, $C(CH_3)_3$], 3.17, 4.32 (ABq, 4 H, J = 13.4 Hz, $ArCH_2Ar$), 3.24, 4.43 (ABq, J = 13.0 Hz, 2 H, $ArCH_2Ar$), 4.48, 4.61 (ABq, 4 H, J = 13.8 Hz, OCH_2Py), 4.63, 4.75 (ABq, 4 H, J = 12.7 Hz, CH_2OCH_2), 4.83, 4.97 (ABq, 4 H, J = 13.4 Hz, OCH_2Py), 6.69, 7.05, 7.06, 7.14 (4 d, 8 H, ArH), 6.93 (d, J = 7.8 Hz, 2 H, 3-Py′H), 7.05 (m, 2 H, 5-Py′H), 7.12 (m, 2 H, 5-PyH), 7.40 (m, 4 H, 4-PyH and 4-Py′H), 7.52 (d, J = 7.8 Hz, 2 H, 3-PyH), 8.44 (ddd, J = 4.9, 1.7, 0.9 Hz, 2 H, 6-Py′H), 8.50 (ddd, J = 4.9, 1.7, 0.9 Hz, 2 H, 6-PyH) ppm. ^{13}C NMR ($CDCl_3$): δ = 30.0, 30.2 ($ArCH_2Ar$), 31.45, 31.50 [$C(CH_3)_3$], 34.08, 34.13 [$C(CH_3)_3$], 68.4 (CH_2OCH_2), 76.6, 77.0 (OCH_2Py), 122.1, 122.3, 122.8, 123.5, 125.95, 126.04, 126.2, 136.4, 136.8, 148.2, 148.9 (ArH), 131.2, 133.0, 133.4, 134.2, 145.6, 145.7, 151.3, 152.4, 157.5, 158.1 (Ar) ppm. $C_{69}H_{78}N_4O_5$ (1043.40): calcd. C 79.43, H 7.53, N 5.37; found C 79.35, H 7.69, N 5.24.

7,13,19,25-Tetra-*tert*-butyl-27,28,29,30-tetrakis[(2-pyridyl)methoxy]-2,3-dihomo-3-oxacalix[4]arene, 1,2-Alternate A Conformer (6): This compound was obtained in 4% yield (63 mg). M.p. 235−237 °C. ^{1}H NMR ($CDCl_3$): δ = 1.01, 1.15 [2 s, 36 H, $C(CH_3)_3$], 3.14, 4.21 (ABq, J = 13.5 Hz, 2 H, $ArCH_2Ar$), 3.91, 4.00 (ABq, 4 H, J = 16.7 Hz, $ArCH_2Ar$), 4.28, 4.79 (ABq, 4 H, J = 13.3 Hz, OCH_2Py), 4.29, 4.67 (ABq, 4 H, J = 9.9 Hz, CH_2OCH_2), 4.41, 4.53 (ABq, 4 H, J = 13.5 Hz, OCH_2Py), 6.21 (d, J = 7.7 Hz, 2 H, 3-Py′H), 6.47 (d, J = 7.7 Hz, 2 H, 3-PyH), 6.91 (m, 4 H, 5-PyH and 5-Py′H), 6.94, 7.01, 7.09, 7.36 (4 d, 8 H, ArH), 6.97 (td, J = 7.6, 1.9 Hz, 2 H, 4-Py′H), 7.03 (td, J = 7.6, 1.9 Hz, 2 H, 4-PyH), 8.28 (ddd, J = 4.8, 1.6, 0.9 Hz, 2 H, 6-Py′H), 8.35 (ddd, J = 4.8, 1.6, 0.9 Hz, 2 H, 6-PyH) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.5, 38.9 ($ArCH_2Ar$), 31.3, 31.5 [$C(CH_3)_3$], 33.9, 34.1 [$C(CH_3)_3$], 68.3 (CH_2OCH_2), 74.3, 75.1 (OCH_2Py), 121.4, 121.6, 121.67, 121.71, 126.1, 126.4, 126.5, 127.8, 136.3, 136.9, 147.6, 148.3 (ArH), 130.5, 132.3, 132.5, 133.6, 145.3, 145.4, 153.0, 154.4, 157.4, 158.1 (Ar) ppm. $C_{69}H_{78}N_4O_5$ (1043.40): calcd. C 79.43, H 7.53, N 5.37; found C 79.22, H 7.69, N 5.36.

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