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Comparative study of azobenzene and stilbene bridged crown ether *p-tert*-butylcalix[4]arene

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Abstract—Photo-switchable calixarenes consisting of a stilbene or azobenzene bridge, spanning the narrow rim as a switching unit, were synthesized through reductive coupling of *o*-, *m*- and *p*-bis-benzaldehyde and bis-nitrobenzene-substituted calix[4]arenes. Both *cis*- and *trans*-stilbenes were produced from the reductive coupling of the *o*- and *m*-bis-benzaldehyde with the *cis* isomer being predominant for both regioisomers, whilst the coupling of *p*-bis-benzaldehyde gave only *cis* product. On the other hand, the only isolable product obtained from the reductive coupling of bis-*o*- and bis-*m*-nitrobenzene was the corresponding *trans*-azobenzene and the coupling product from bis-*p*-nitrobenzene was not stable. Each of the synthesized compounds showed a photostationary state in their *cis–trans* isomerization. The complexation of alkali metal ions was observed for only the *o*-azobenzene derivative suggesting that the lone pair of N-atom in the azo bridge participates in this process.

1. Introduction

On a cell membrane, there are plenty of specific receptors that control the diffusion of molecules or ions in and out of the cell; these include the potassium channel,[1] maltoporin[2] and sucroporin,[3] which control the diffusion of potassium ion, maltose and sucrose respectively. To specifically complex each particular molecule or ion, the shape and size of the receptor must exclusively fit with the preferred guest. An extraordinary natural molecule that is always chosen as an example of a receptor because of its extremely high binding specificity, is valinomycin, which can specifically complex potassium ions.[4,5] This cyclic molecule is composed of numerous oxygen donor atoms forming a nice pocket that fits perfectly around a potassium ion guest.

Aspiring to mimic or at least understand such natural processes, chemists have tried to design and synthesize novel molecules having particularly desired functions. The crown ether family is an appealing class of structures, which has been developed to mimic valinomycin by entrapment of a desired cation using the electron-rich pocket of donor atoms.[6] Since their discovery crown ether based ion receptors have been exploited extensively. Synthetic cation channels containing crown ether rings, called hydraphiles, have been reported recently.[7] These hydraphile channels can kill *Escherichia coli* bacteria effectively via incorporation into the surface membrane, thus disturbing sodium ion transport rate across the bacteria cell membrane.

Beside the donor atoms themselves, the pre-organized structure of the binding pocket is also a vital factor of binding properties. Calix[4]arene has become one of the most interesting platforms on which to construct a selective receptor molecule because of its four pre-organized conformations; cone, partial-cone, 1,2 alternating-cone and 1,3 alternating-cone.[8] The very first application of this well-ordered molecule as a cation receptor was calix[4]-arene crown ether, which can be used to trap a cesium ion as a result of its optimal fit.[9] Many receptors developed nowadays are calixarene-based but there is a crucial drawback of such a perfect fit host-guest pairs. The stronger the binding, the more difficult it becomes to regenerate the receptor after use. A proper attachment of a molecular switching unit to the receptor molecule should overcome this problem. There are many switching systems available, but among them, the photo-switching mode is one of the

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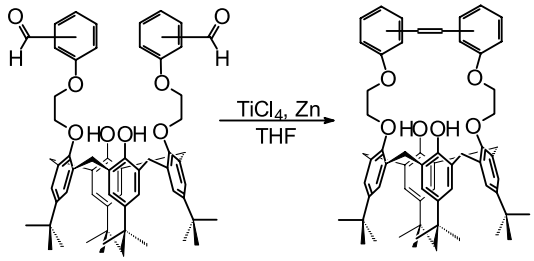
most easy-to-operate systems.[10] Azobenzene and stilbene are widely used because of their facile *cis–trans* photoisomerization.[11] Additionally, another appealing advantage potentially gained from switchable receptors is that amphiphilic-binding may be achieved.[12,13] During isomerization the binding cavity is altered and the binding property is then switched. This may be from binding to unbinding or from binding of one ion to another as a result of the change in the size and shape of the binding pocket before and after isomerization.

We report herein the synthesis of two series of photoswitchable calix[4]arene derivatives. One series incorporates a stilbene and the other an azobenzene switching unit as a bridge across the narrow rim of the calixarene platform. Photoisomerization and complexation properties of the synthesized compounds are also compared.

2. Results and discussion

2.1. Synthesis

Three positional isomers, *o*-, *m*- and *p*-stilbene crown ether *p-tert*-butylcalix[4]arenes (1) were synthesized from the corresponding bis-benzaldehydes by the McMurry coupling (Scheme 1).[14,15] The bis-benzaldehydes were prepared from the corresponding (2-bromoethoxy)benzaldehydes by nucleophilic substitution of *p-tert*-butylcalix[4]arene with the corresponding (2-bromoethoxy)benzaldehyde.



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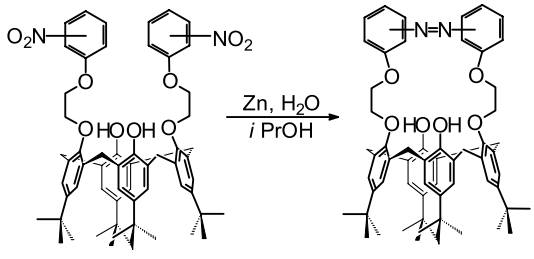
Scheme 1. Synthesis of stilbene crown ether calixarenes.

Analogously, all of the isomers of the azobenzene crown ether calixarenes (2) were synthesized by reductive coupling of the corresponding bis-nitrobenzenes (Scheme 2), these latter having been prepared by nucleophilic substitution of the corresponding (2-bromoethoxy)-nitrobenzene analogues.[12]



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Scheme 2. Synthesis of azobenzene crown ether calixarenes.

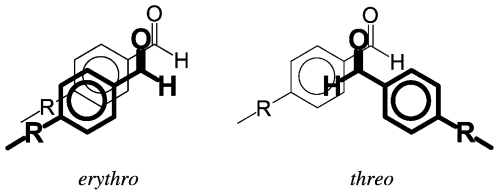
The *m*-stilbene derivatives were prepared under modified McMurry conditions to give both *cis*- and *trans*-stilbenes in 28% total yield (Table 1). This reaction also gave 20% of the corresponding pinacol byproduct. The coupling reaction of the *o*- and *p*-bisbenzaldehydes gave higher yields of the stilbenes *o*-**1** and *p*-**1** (67 and 51% respectively) without any observable pinacol product. Both *cis*- and *trans*-stilbenes were obtained from the coupling reactions involving the *o*- and *m*-bis-benzaldehydes but that for the *p*-isomer gave only *cis*-stilbene. It is important to note here that McMurry coupling proceeded successfully despite the presence of phenolic O H groups in the starting materials.

Table 1. Products from the synthesis of stilbene and azobenzene crown ether calixarenes

Products	% Yield	
	cis	*trans*
o-**1**	57	10
m-**1**	20	8
p-**1**	51	0
o-**2**	0	8
m-**2**	0	59[a]
p-**2**	0	0

[a] via high-pressure method.

The predominant preference for formation of *cis* over *trans* products in the McMurry coupling suggests that the preorganized structure of the starting bis-benzaldehyde *p-tert*-butylcalix[4]arene may play an important role in controlling the geometry of the products. The short ethylene glycol linkages attached to the small and rigid lower rim of the *p-tert*-butylcalix[4]arene are unlikely to allow formation of the *threo* orientation of the two benzaldehyde moieties (Fig. 1) resulting in no evidence for formation of the *trans*-product.



erythro *threo*

Figure 1. The proposed orientations, *erythro* and *threo*, of the two benzaldehyde groups that would lead to the formation of *cis* and *trans* products.

In the synthesis of the *o*-azobenzene crown ether calixarene at ambient pressure, only *trans* isomer was isolated in 8% yield. The *cis* isomer could not be obtained in a pure form because of its rapid thermal isomerization. In the case of the *m*-isomer a higher yield of the azobenzene product was observed compared to that obtained for the *o*-isomer because the high-pressure method was used (Table 1). The *p*-isomer however seemed to be unstable as the color of the solution at the end of the reaction changed rapidly from bright orange to dark brown upon exposure to air and moisture and none of the desired product could be isolated.

2.2. Characterization of products

Since all of the *cis*- and *trans*-stilbene derivatives possess a C_2 symmetry axis, the coupling between two vinylic protons

in ^{1}H NMR, which would normally be used for distinguishing between *cis* and *trans* isomers, does not exist. The assignment of *cis* and *trans* geometries was thus initially based on the chemical shift of vinylic protons and the UV–Vis absorption spectra using the parent *cis* and *trans* unsubstituted stilbenes as references. According to the chemical shifts observed for unsubstituted stilbenes, the *cis* geometry was assigned to the isomer possessing the vinylic protons with lower chemical shift values (Table 2). This assignment is consistent with the data from UV–Vis spectra that showed shorter λ_{max} and lower extinction coefficients for all *cis* isomers.

Table 2. ^{1}H NMR (in $CDCl_3$) and electronic absorption (in CH_2Cl_2) data of the synthesized stilbene-calix derivatives in comparison with stilbene

Compound	δ for vinylic proton (ppm)	λ_{max} (nm)	ε (cm^{-1} M^{-1})
cis-o-**1**	7.25	292	19,321
trans-o-**1**	7.74	291	30,106
		333	28,492
cis-m-**1**	6.71	286	20,955
		291	27,488
trans-m-**1**	7.24	308	24,866
		320	24,629
cis-p-**1**	6.68	283	16,632
cis-stilbene	6.57	223	20,600
		276	10,900
trans-stilbene	7.15	227	21,000
		294	33,200
		307	32,100

The structural assignments were confirmed by X-ray crystallography. The proposed *cis-o*-**1** was successfully isolated as a single crystal (Fig. 2). The X-ray data was in agreement with the proposed structure.

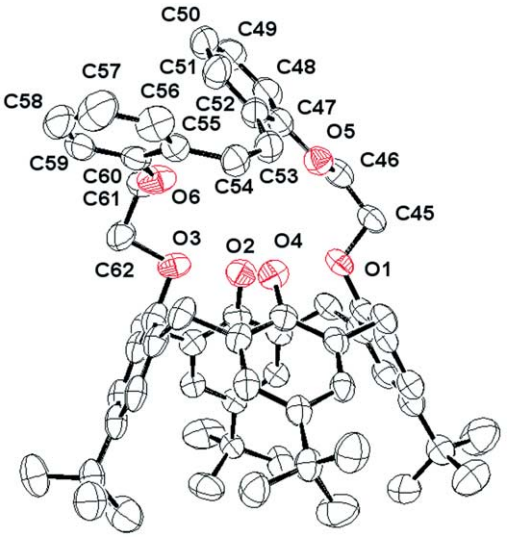


Figure 2. X-ray crystallographic structure of *cis-o*-**1**.

In the synthesis of azobenzene derivatives, only one product was isolated for each regioisomer, *o*-**2** and *m*-**2**. Since only one stereoisomer of each azobenzene derivative is available and, in the absence of protons on the nitrogen atoms providing an NMR probe, the assignment of *cis* and *trans* geometry was only possible through X-ray crystallography. Fortunately, both azobenzene derivatives (*o*-**2** and *m*-**2**) could be obtained as single crystals suitable for X-ray crystallography. The solid-state structures of these azobenzene derivatives revealed that both compounds were the *trans* isomers (Fig. 3).

2.3. Isomerization study

Whilst none of the stilbene crown ether *p-tert*-butylcalix[4]-arenes reported here isomerized in ambient light, they readily did so under UV irradiation (medium pressure mercury lamp). The *cis* and *trans* isomer-percentages for each derivative at the photostationary state were determined by ^{1}H NMR spectroscopy using the ratios of the peak areas of the best resolved resonances corresponding to each geometric isomer (Fig. 4).

The resonances of the corresponding protons in the *cis* and *trans* forms of each regioisomer (aromatic protons *ortho* to vinylic carbon for *o*-**1**, *t*-butyl protons for *m*-**1**, ethylene glycolic protons for *p*-**1**, methylene bridge protons in *o*-**2** and ethylene glycolic protons for *m*-**2**) were selected for the ratio calculation. The photo-stationary states were observed for all isomers and the percentages of *cis* and *trans* isomers were obtained from the ^{1}H NMR data (Table 3).

For stilbene derivatives, the same photostationary state was reached, no matter which geometrically pure isomer, *cis* or *trans*, was used as the starting material. However, in the case of the azobenzene analogues, the irradiation was performed on the only available, *trans* isomer.

Unlike the stilbene derivatives, the azobenzene calixarenes isomerized even in the absence of light because of the usual thermal isomerization of the diazo (N=N) unit.[16] While the photoisomerization of both stilbenes and azobenzenes under a medium pressure Hg lamp took minutes, the thermal isomerization of the azobenzenes was much slower, taking over a week to reach the equilibrium. Both thermal and photochemical isomerizations of the azobenzene derivatives produced the same final *cis*:*trans* product ratios implying that, under our experimental conditions, the product ratio from the photoizomerization directly correlates with the relative thermal stability of each isomer.

2.4. Complexation study

Picrate salt extraction was chosen for the complexation study. The complexation can be observed by several techniques: color change, ^{1}H NMR, and UV–Visible spectroscopy. To our surprise, (^{1}H NMR) complexation studies using each of the compounds synthesized revealed that only *o*-**2** showed any evidence for complexation with sodium and potassium picrate (Fig. 5).

The complexation results suggested that the lone pair electrons on nitrogen of the diazo group participated in the binding with the metal ions. Thus, only *o*-**2**, which possesses at least one nitrogen lone pair of electrons pointing into the crown ether biding cavity, can form a host-guest complex. It is also interesting to point out here that the complexation of *o*-**2** with Na^+ and K^+ ion shifted the thermal equilibrium between the *cis* and *trans* isomers in opposite directions.

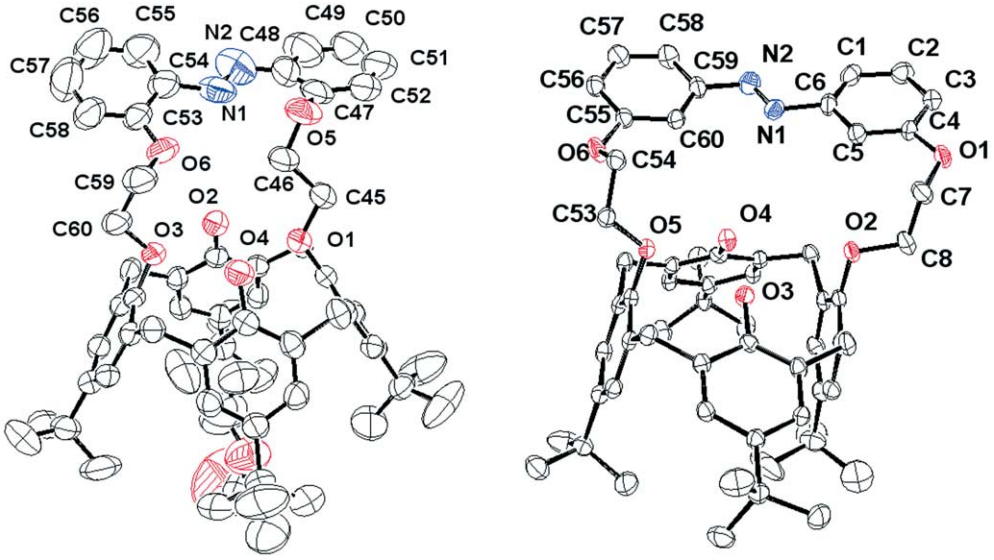


Figure 3. X-ray crystallographic structure of *trans-o*-**2**·$CH_3CO_2CH_2CH_3$ and *trans-m*-**2**.

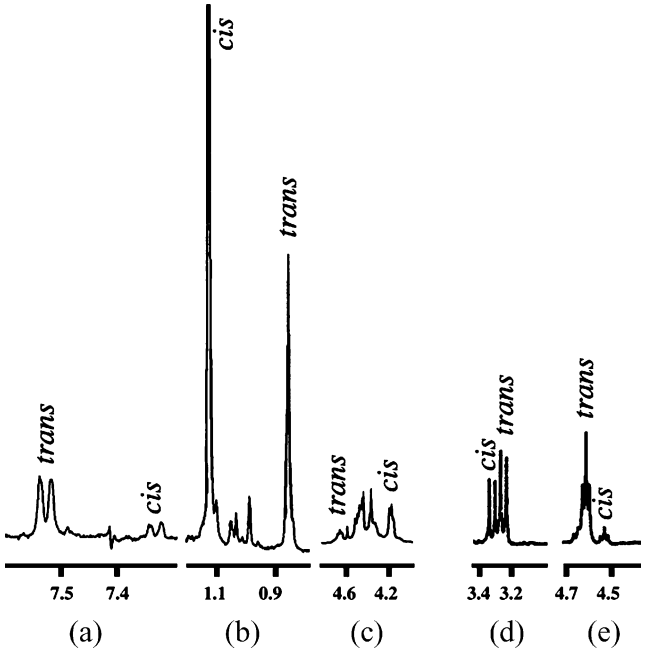


Figure 4. ^{1}H NMR signals used for calculation of *cis*/*trans* ratio at the photostationary state: (a) aromatic protons *ortho* to vinylic carbon in *o*-**1**; (b) *t*-butyl protons in *m*-**1**; (c) ethylene glycolic protons in *p*-**1**; (d) methylene bridge protons in *o*-**2**; and (e) ethylene glycolic protons in *m*-**2**.

Table 3. The percentages of *cis* and *trans* isomers at the photostationary states

Compound	% Isomer at photostationary state	
	cis	*trans*
o-**1**	15	85
m-**1**	70	30
p-**1**	75	25
o-**2**	36	64
m-**2**	13	87

The complexation with K^+ resulted in the equilibrium shift toward the *trans* isomer (compare Fig. 5c with b) while the complexation with Na^+ moved the equilibrium toward the *cis* isomer (compare Fig. 5d with b).

Unfortunately, we have not been able to crystallize the *o*-**2** metal complex as a single crystal to confirm our hypothesis about the participation of the nitrogen lone pair in the complexation. However, we have studied the complexation of the model compounds, calixarene derivatives **3** and **4** with sodium and potassium picrates. When solid sodium (or potassium) picrate was added to the colorless solution of **4** in CH_2Cl_2, the solution turned yellow and the UV–Visible spectrum showed a strong absorption band of the picrate ion

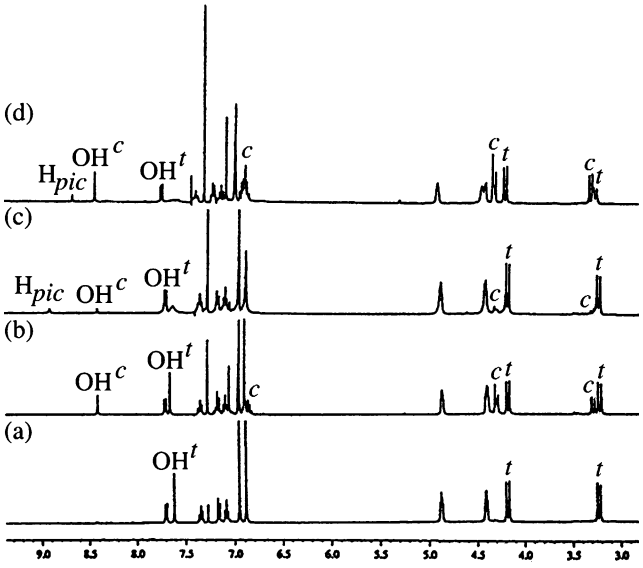


Figure 5. ^{1}H NMR spectra of: (a) *trans-o*-**2**; (b) *cis*- and *trans-o*-**2** at the photostationary state; (c) *o*-**2** with potassium picrate; and (d) *o*-**2** with sodium picrate. (*pic*=picrate, *c*=*cis*, *t*=*trans*).

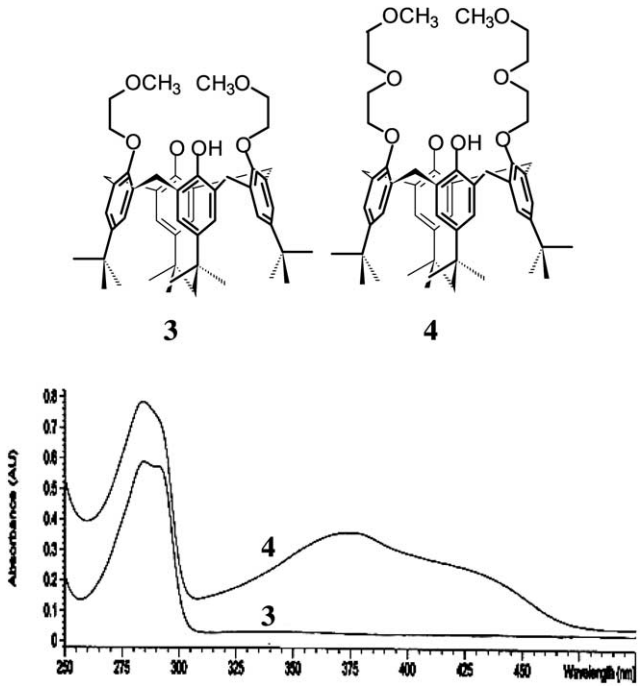


Figure 6. UV–Vis spectra of **3** and **4** in CH_2Cl_2 in the presence of sodium picrate salt added as a solid.

around 375 nm (Fig. 6), although there were minimal changes in the ^{1}H NMR spectrum upon complex formation. The mixture of **3** and sodium (or potassium) picrate in CH_2Cl_2, on the other hand, showed no absorption band corresponding with picrate anion. These results indicated that while compound **4** which contains eight oxygen donor atoms complexed with sodium and potassium ions, compound **3** which contains only six oxygen donor atoms complexed with neither ions. The results thus support our hypothesis that the presence of six ethereal oxygen donor atoms in this calixarene-based system is not sufficient for the binding of alkali metal cations.

3. Conclusion

We have successfully synthesized and fully characterized two series of photoswitchable calix[4]arenes incorporating different regioisomers of stilbene and azobenzene bridges. The *cis–trans* isomerization study indicates that the stilbene derivatives are isomerized only under UV irradiation while the azobenzene derivatives undergo either thermally or photochemically induced isomerization. Only the *o*-azobenzene derivative shows complexation with sodium and potassium ions presumably as a result of the participation of the nitrogen atom of the diazo group in coordination with these ions. The results represent a rare example of the coordination of the nonpolar diazo nitrogen to an alkali-metal cation. This complexation also induces a thermal equilibrium shift between *cis* and *trans* isomers of the azobenzenes. The present findings will lead to the design and synthesis of new, more effective, photoswitchable ionophores for sodium and potassium ions.

4. Experimental

4.1. Data for compounds

4.1.1. Synthesis of bis-benzaldehyde. In a 1 L, two-necked, round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser, *p-tert*-butyl-calix[4]arene (7.8 mmol, 5.00 g) and K_2CO_3 (57.9 mmol, 8.00 g) were dissolved in CH_3CN (300 mL). The mixture was stirred for 30 min at room temperature and (2-bromoethoxy)-benzaldehyde (17.5 mmol, 4.00 g) was then added dropwise. The mixture was refluxed for 60 h and then allowed to cool to room temperature. The mixture was filtered and washed with acetone and CH_2Cl_2. The filtrate was combined and the solvent was evaporated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (150 mL) and then extracted with aqueous HCl (2 M, 4×25 mL). The organic phase was separated and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The product was further purified by crystallization in CH_2Cl_2/CH_3OH yielding a white solid as the product.

o-isomer (5.5 mmol, 5.16 g, 70%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.00 (s, 18H), 1.24 (s, 18H), 3.29 (d, 4H, J= 13.0 Hz), 4.29 (d, 4H, J=13.0 Hz), 4.38–4.40 (m, 8H), 6.85 (s, 4H), 7.00 (s, 4H) 6.94–7.04 (m, 4H), 7.50 (s, 4H), 7.45–7.55 (m, 2H), 7.82 (dd, 2H, J=7.5, 2.0 Hz), 10.48 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 31.1, 31.7, 31.8, 33.8, 34.0, 67.5, 73.6, 112.4, 121.0, 125.2, 125.2, 125.8, 127.7, 128.2, 132.6, 135.8, 141.7, 147.3, 149.8, 150.3, 160.8, 190.2.

m-isomer (4.7 mmol, 4.42 g, 60%). Mp (decompose)= 184.8–185.3 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.00 (s, 18H), 1.27 (s, 18H), 3.32 (d, 4H, J=13.0 Hz), 4.30–4.40 (m, 12H), 6.85 (s, 4H), 7.04 (s, 4H) 7.20–7.45 (m, 8H), 9.93 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 31.1, 31.7, 31.7, 33.8, 34.0, 66.9, 73.7, 113.4, 122.4, 123.6, 125.2, 125.7, 127.8, 130.2, 132.8, 137.8, 141.5, 147.1, 149.7, 150.5, 159.2, 192.1; IR (neat) ν_{max} 3336 (phenolic O–H stretching), 3050, 2958, 2869 (aldehydic C–H stretching), 2731 (aldehydic C–H stretching), 1697 (aldehydic C=O stretching), 1597, 1485, 1450, 1265 cm^{-1}; Anal. Calcd for $C_{62}H_{72}O_8$: C, 78.78; H, 7.68; Found: C, 76.80; H, 7.95.

p-isomer (4.3 mmol, 4.05 g, 55%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.18 (s, 18H), 1.50 (s, 18H), 3.49 (d, 4H, J= 13.0 Hz), 4.80–4.52 (m, 8H), 4.54 (d, 4H, J=13.0 Hz), 7.02 (s, 4H), 7.19 (d, 4H, J=8.5 Hz), 7.24 (s, 4H), 7.42 (s, 2H), 10.06 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 31.0, 31.5, 31.7, 33.8, 34.0, 66.9, 73.5, 115.1, 125.2, 125.7, 127.8, 130.2, 131.9, 132.6, 141.6, 147.2, 149.6, 150.4, 163.5, 190.8.

4.1.2. Synthesis of bis-nitrobenzene. In a 500 mL, round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser, a mixture of potassium carbonate (0.43 mmol, 6.0 g), (2-bromoethoxy)nitrobenzene (40.64 mmol, 10.0 g)and *p-tert*-butyl calyx[4]arene (18.85 mmol, 8.0 g) were stirred in CH_3CN (200 mL). The mixture was kept stirring at reflux temperature overnight. The reaction mixture was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2

(150 mL) and then extracted with water for several times. The combined organic phase was separated and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum. The product was further purified crystallisation using CH_2Cl_2/MeOH solvent system. The purified product was obtained as a yellow crystal.

o-isomer (12.44 mmol, 12.2 g, 66%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.99 (s, 18H), 1.26 (s, 18H), 3.31 (d, 4H, J=13.0 Hz), 4.33 (s, 8H), 4.35 (d, 4H, J=13.0 Hz), 6.85 (s, 4H), 7.03 (s, 4H), 7.24 (ddd, 2H, J=8.0, 2.0, 1.0 Hz), 7.35 (s, 2H), 7.40 (t, 2H, J=8.0 Hz), 7.74 (t, 2H, J=2.0 Hz), 7.81 (ddd, 2H, 8.0, 2.0, J=1.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 31.1, 31.7, 31.7, 33.9, 34.0, 67.4, 73.4, 109.1, 116.2, 122.2, 125.2, 125.8, 127.8, 130.0, 132.8, 141.8, 147.5, 149.1, 149.5, 150.3, 159.1; Anal. Calcd for $C_{60}H_{70}N_2O_{10}$: C, 73.60; H, 7.21; N, 2.386; Found: C, 73.62; H, 7.27; N, 2.73: mp=205–207 °C.

m-isomer (13.28 mmol, 13.0 g, 70%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.99 (s, 18H), 1.26 (s, 18H), 3.31 (d, 4H, J=13.0 Hz), 4.33 (s, 8H), 4.35 (d, 4H, J=13.0 Hz), 6.85 (s, 4H), 7.03 (s, 4H), 7.24 (ddd, 2H, J=8.0, 2.0, 1.0 Hz), 7.35 (s, 2H), 7.40 (t, 2H, J=8.0 Hz), 7.74 (t, 2H, J=2.0 Hz), 7.81 (ddd, 2H, 8.0, 2.0, J=1.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 31.1, 31.7, 31.7, 33.9, 34.0, 67.4, 73.4, 109.1, 116.2, 122.2, 125.2, 125.8, 127.8, 130.0, 132.8, 141.8, 147.5, 149.1, 149.5, 150.3, 159.1.

p-isomer (15.1 mmol, 14.8 g, 80%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.96 (s, 18H), 1.27 (s, 18H), 3.30 (d, 4H, J=13.0 Hz), 4.31 (s, 8H), 4.35 (d, 4H, J=13.0 Hz), 6.80 (s, 4H), 6.98 (d, 4H, J=9.0 Hz), 7.05 (s, 4H), 7.07 (s, 2H), 8.18 (d, 4H, J=9.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 31.0, 31.5, 31.7, 33.9, 34.0, 67.4, 73.5, 114.8, 125.2, 125.7, 125.9, 127.7, 132.5, 141.8, 141.8, 147.3, 149.4, 150.4, 163.5.

4.1.3. Synthesis of 1. Typically, $TiCl_4$ (3.17 mmol, 0.60 g) was charged into a two-necked, round-bottomed flask under a N_2 atmosphere. Anhydrous THF (30 mL) was added dropwise and activated Zn powder (6.35 mmol, 0.41 g) was added cautiously. After 1 h reflux, the bisbenzaldehyde (1.06 mmol, 1.00 g) in THF (10 mL) was added dropwise. The mixture was refluxed for additional 15 h and it was allowed to cool to room temperature. A solution of K_2CO_3 (15% w/v) was added to quench the excess $TiCl_4$. The precipitate was filtered over celite and washed with acetone and CH_2Cl_2. The filtrate was evaporated to give the residue which was dissolved in CH_2Cl_2 (20 mL) and then extracted with water (3×25 mL). The organic phase was dried over anhydrous Na_2SO_4 and the solvent was removed to give the crude product. The *cis* and *trans* isomers was separated by column chromatography using 5% ethyl acetate in hexane as eluent (*cis* isomers have a higher R_f value).

cis-o-**1**. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.03 (s, 18 C(CH_3)$_3$), 1.22 (s, 18 C(CH_3)$_3$), 3.25 (d, 4 Ar$_2$CH_2, J=13.0 Hz), 4.16 (broad, 4 OCH_2), 4.26 (broad, 4 OCH_2), 4.35 (d, 4 Ar$_2$CH_2, J=13.0 Hz), 6.83 (t, 2 stilbene-ArH, J=7.5 Hz), 6.88 (d, 2 stilbene-ArH, J=7.5 Hz), 6.90 (s, 4 calix-ArH), 6.97 (s, 4 calix-ArH), 7.17 (t, 2 stilbene-ArH, J=7.5 Hz), 7.25 (s, 2 CH=CH), 7.29 (d, 2 stilbene-ArH, J=7.5 Hz), 7.70 (s, 2 OH); ^{13}C NMR (200 MHz, $CDCl_3$) δ 31.1 (6 C(*C*H$_3$)$_3$), 31.7 (6 C(*C*H$_3$)$_3$), 31.9 (4 Ar$_2$*C*H$_2$), 33.8 (2 *C*(CH$_3$)$_3$), 34.0 (2 *C*(CH3)3), 67.8 (2 O*C*H$_2$), 74.1 (2 O*C*H$_2$), 113.4 (2 stilbene-Ar*C*), 120.8 (2 stilbene-Ar*C*), 125.1 (4 calix-Ar*C*), 125.4 (2 *C*H=*C*H), 125.7 (4 calix-Ar*C*), 127.7 (4 calix-Ar*C*), 127.9 (2 stilbene-Ar*C*), 129.0 (2 stilbene-Ar*C*), 129.5 (2 stilbene-Ar*C*), 133.3 (4 stilbene-Ar*C*), 141.0 (2 calix-Ar*C*), 147.0 (2 calix-Ar*C*), 149.6 (2 calix-Ar*C*), 150.8 (2 calix-Ar*C*), 155.7 (2 stilbene-Ar*C*); Anal. Calcd for $C_{62}H_{72}O_6\cdot CH_2Cl_2$: C, 75.88; H, 7.38; Found: C, 76.12; H, 7.25: mp=292–294 °C (decomposed).

trans-o-**1**. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.06 (s, 18 C(CH_3)$_3$), 1.18 (s, 18 C(CH_3)$_3$), 3.21 (d, 4 Ar$_2$CH_2, J=12.5 Hz), 4.23 (d, 4 Ar$_2$CH_2, J=12.5 Hz), 4.51 (broad, 4 OCH_2), 4.68 (broad, 4 OCH_2), 6.82 (d, 2 stilbene-ArH, J=8.0 Hz), 6.93 (m, 4 calix-ArH and 2 stilbene-ArH), 6.97 (s, 4 calix-ArH), 7.15 (t, 2 stilbene-ArH, J=8.0 Hz), 7.50 (d, 2 stilbene-ArH, J=8.0 Hz), 7.74 (s, 2 CH=CH), 8.43 (s, 2 OH); ^{13}C NMR (200 MHz, $CDCl_3$) δ 31.2 (6 C(*C*H$_3$)$_3$), 31.6 (6 C(*C*H$_3$)$_3$), 32.1 (4 Ar$_2$*C*H$_2$), 33.8 (2 *C*(CH$_3$)$_3$), 34.1 (2 *C*(CH3)3), 66.6 (2 O*C*H$_2$), 73.6 (2 O*C*H$_2$), 111.1 (2 stilbene-Ar*C*), 120.8 (2 stilbene-Ar*C*), 125.0 (4 calix-Ar*C*), 125.9 (4 calix-Ar*C*), 127.5 (4 calix-Ar*C*), 127.5 (2 *C*H=*C*H), 127.7 (2 stilbene-Ar*C*), 128.0 (2 stilbene-Ar*C*), 129.6 (2 stilbene-Ar*C*), 133.7 (4 calix-Ar*C*), 141.2 (2 calix-Ar*C*), 147.4 (2 calix-Ar*C*), 149.3 (2 calix-Ar*C*), 150.7 (2 calix-Ar*C*), 155.9 (2 stilbene-Ar*C*); Anal. Calcd for $C_{62}H_{72}O_6$: C, 81.54; H, 7.95; Found: C, 81.41; H, 7.94: mp=278–280 °C (decomposed).

cis-m-**1**. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.09 (s, 18 C(CH_3)$_3$), 1.25 (s, 18 C(CH_3)$_3$), 3.32 (d, 4 Ar$_2$CH_2, J=12.5 Hz), 3.94 (broad, 4 OCH_2), 4.12 (broad, 4 OCH_2), 4.38 (d, 4 Ar$_2$CH_2, J=12.5 Hz), 6.69 (broad, 2 stilbene-ArH), 6.71 (s, 2 CH=CH), 6.89 (m, 4 stilbene-ArH), 6.97 (s, 4 calix-ArH), 7.02 (s, 4 calix-ArH), 7.24 (t, 2 stilbene-ArH, J=8.5 Hz), 8.08 (s, 2 OH); ^{13}C NMR (200 MHz, $CDCl_3$) δ 31.2 (6 C(*C*H$_3$)$_3$), 31.7 (6 C(*C*H$_3$)$_3$), 31.7 (4 Ar$_2$*C*H$_2$), 33.8 (2 *C*(CH$_3$)$_3$), 34.1 (2 *C*(CH$_3$)$_3$), 66.2 (2 O*C*H$_2$), 73.7 (2 O*C*H$_2$), 111.8 (2 stilbene-Ar*C*), 117.0 (2 stilbene-Ar*C*), 121.5 (2 stilbene-Ar*C*), 125.0 (4 calix-Ar*C*), 125.7 (4 calix-Ar*C*), 127.3 (4 calix-Ar*C*), 129.6 (2 *C*H=*C*H), 130.9 (2 stilbene-Ar*C*), 133.5 (4 calix-Ar*C*), 138.3 (2 stilbene-Ar*C*), 140.9 (2 calix-Ar*C*), 147.2 (2 calix-Ar*C*), 149.2 (2 calix-Ar*C*), 151.1 (2 calix-Ar*C*), 158.2 (2 stilbene-Ar*C*); Anal. Calcd for $C_{62}H_{72}O_6$: C, 81.54; H, 7.95; Found: C, 81.48; H, 7.92: mp=264–265 °C.

trans-m-**1**. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.83 (s, 18 C(CH_3)$_3$), 1.31 (s, 18 C(CH_3)$_3$), 3.29 (d, 4 Ar$_2$CH_2, J=13.5 Hz), 4.25 (t, 4 OCH_2, J=5.0 Hz), 4.41 (d, 4 Ar$_2$CH_2, J=13.5 Hz), 4.57 (t, 4 OCH_2, J=5.0 Hz), 5.84 (s, 2 OH), 6.60 (s, 4 calix-ArH), 6.87 (t, 2 stilbene-ArH, J=8.5 Hz), 7.06 (s, 4 calix-ArH), 7.14 (d, 2 stilbene-ArH, J=7.5 Hz), 7.24 (s, 2 CH=CH), 7.25 (t, 2 stilbene-ArH, J=7.5 Hz), 7.74 (s, 2 stilbene-ArH); ^{13}C NMR (200 MHz, $CDCl_3$) δ 30.8 (6 C(*C*H$_3$)$_3$), 31.2 (4 Ar$_2$*C*H$_2$), 31.7 (6 C(*C*H$_3$)$_3$), 33.8 (2 *C*(CH$_3$)$_3$), 33.9 (2 *C*(CH3)3), 69.3 (2 O*C*H$_2$), 75.0 (2 O*C*H$_2$), 114.3 (2 stilbene-Ar*C*), 118.0 (2 stilbene-Ar*C*), 119.9 (2 stilbene-Ar*C*), 125.3 (4 calix-Ar*C*), 125.4 (4 calix-Ar*C*), 128.5 (4 calix-Ar*C*), 128.9 (2 *C*H=*C*H), 129.8 (2 stilbene-Ar*C*), 131.6 (4 calix-Ar*C*), 139.1 (2 stilbene-Ar*C*), 141.8 (2 calix-Ar*C*), 146.7 (2 calix-Ar*C*), 150.3 (2 calix-Ar*C*), 150.8 (2 calix-Ar*C*), 158.8 (2 stilbene-Ar*C*);

Anal. Calcd for $C_{62}H_{72}O_6$: C, 81.54; H, 7.95; Found: C, 81.59; H, 8.00: mp=281–283 °C (decomposed).

cis-p-**1**. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.85 (s, 18 C(CH_3)$_3$), 1.31 (s, 18 C(CH_3)$_3$), 3.28 (d, 4 Ar_2CH_2, J=13.5 Hz), 4.17 (t, 4 OCH_2, J=4.0 Hz), 4.38 (d, 4 Ar_2CH_2, J=13.5 Hz), 4.45 (t, 4 OCH_2, J=4.0 Hz), 6.29 (s, 2 O*H*), 6.66 (s, 4 calix-Ar*H*), 6.68 (s, 2 C*H*=C*H*), 6.85 (d, 4 stilbene-Ar*H*, J=9.0 Hz), 6.93 (d, 4 stilbene-Ar*H*, J=9.0 Hz), 7.06 (s, 4 calix-Ar*H*); ^{13}C NMR (200 MHz, $CDCl_3$) δ 31.0 (6 C(*C*H$_3$)$_3$), 31.1 (4 Ar_2CH_2), 31.8 (6 C(*C*H$_3$)$_3$), 33.8 (2 *C*(CH$_3$)$_3$), 33.8 (2 *C*(CH3)3), 68.4 (2 O*C*H$_2$), 74.8 (2 O*C*H$_2$), 115.8 (4 stilbene-Ar*C*), 125.2 (4 calix-Ar*C*), 125.4 (4 calix-Ar*C*), 128.1 (4 calix-Ar*C*), 130.4 (4 stilbene-Ar*C*), 130.8 (2 *C*H=*C*H), 131.3 (2 stilbene-Ar*C*), 132.0 (4 calix-Ar*C*), 141.4 (2 calix-Ar*C*), 146.8 (2 calix-Ar*C*), 149.9 (2 calix-Ar*C*), 150.5 (2 calix-Ar*C*), 157.7 (2 stilbene-Ar*C*); Anal. Calcd for $C_{62}H_{72}O_6$: C, 81.54; H, 7.95; Found: C, 81.57; H, 8.14: mp=290–291 °C (decomposed).

4.1.4. Synthesis of 2. *Ambient pressure method*. In a 50 mL round-bottomed flask equipped with a magnetic bar and a reflux condenser, a mixture of 25,27-bis-2-(2-nitrophenol)-ethoxy-*p*-*tert*-butylcalix[4]arene, (0.71 mmol, 0.70 g) in isopropanol (8 mL), sodium hydroxide (7.0 mmol, 0.28 g) in water (4 mL) and zinc (3.06 mmol, 0.20 g) was stirred. The mixture was refluxed under nitrogen atmosphere for 48 h and it was then allowed to cool to room temperature. The mixture was filtered off and washed with CH_2Cl_2. The filtrate was evaporated and the residue was dissolved in CH_2Cl_2 and then extracted with 2 M HCl (2×20 mL). The organic phase was dried over anhydrous Na_2SO_4 and the solvent was removed to give the crude product, which was purified by column chromatography using 15% ethyl acetate in hexane as eluent. The *trans* isomers was collected and crystallized in CH_2Cl_2/CH_3OH mixture to give orange crystals.

High pressure method. In a 100 mL high-pressure glass tube equipped with pressure gauge and a magnetic bar, a mixture of 25,27-bis-2-(2-nitrophenol)ethoxy-*p*-*tert*-butylcalix[4]-arene, (0.71 mmol, 0.70 g) in isopropanol (8 mL), sodium hydroxide (7.0 mmol, 0.28 g) in water (4 mL) and zinc (3.06 mmol, 0.20 g) was added and stirred. The reaction was operated under 3 atm nitrogen atmosphere for overnight at 130 °C and it was then allowed to cool to room temperature. The mixture was filtered off and washed with CH_2Cl_2. The filtrate was evaporated to give the residue which was dissolved in CH_2Cl_2 and then extracted with 2 M HCl (2× 20 mL). The organic phase was dried over anhydrous Na_2SO_4 and the solvent was removed to give the crude product, which was purified by column chromatography using 5% ethyl acetate in hexane as eluent. The *trans* isomers was separated and crystallized in CH_2Cl_2/CH_3OH mixture to give orange crystals.

trans-o-**2**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 18 C(CH_3)$_3$), 1.20 (s, 18 C(CH_3)$_3$), 3.20 (d, 4 Ar_2CH_2, J=13.0 Hz), 4.15 (d, 4Ar_2CH_2, J=13.0 Hz), 4.38 (br t, 4 OCH_2), 4.84 (br t, 4 OCH_2), 6.86 (s, 4 calix-Ar*H*), 6.92 (s, 4 calix-Ar*H*), 7.08 (d, 2 azobenzene-Ar*H*, J=6.0 Hz), 7.16 (d, 2 azobenzene-Ar*H*, J=8.0 Hz), 7.34 (t, 2 azobenzene-Ar*H*, J=6.0 Hz), 7.61 (s, 2 O*H*), 7.70 (d, 2 azobenzene-Ar*H*, J=8.0 Hz); Anal. Calcd for $C_{60}H_{70}N_2O_6$: C, 78.74; H, 7.71; N, 3.06; Found: C, 77.21; H, 7.51, N 2.72 mp: 195–197 °C (decomposed).

trans-m-**2**. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.83 (s, 18 C(CH_3)$_3$), 1.28 (s, 18 C(CH_3)$_3$), 3.26 (d, 4 Ar_2CH_2, J=13.0 Hz), 4.38 (t, 4 OCH_2, J=5.0 Hz), 4.34 (d, 4 Ar_2CH_2, J=13.0 Hz), 4.66 (t, 4 OCH_2, J=5.0 Hz), 6.07 (s, 2 O*H*), 6.61 (s, 4 calix-Ar*H*), 7.03 (s, 4 calix-Ar*H*), 7.08 (d, 2 azobenzene-Ar*H*, J=8.0 Hz), 7.39 (t, 2 azobenzene-Ar*H*, J=8.0 Hz), 7.60 (d, 2 azobenzene-Ar*H*, J=8.0 Hz), 8.19 (s, 2 azobenzene-Ar*H*); ^{13}C NMR (200 MHz, $CDCl_3$) δ 30.9 (6 C(*C*H$_3$)$_3$), 31.2 (4 Ar_2CH_2), 31.7 (6 C(*C*H$_3$)$_3$), 33.8 (2 *C*(CH$_3$)$_3$), 33.8 (2 *C*(CH3)3), 69.1 (2 O*C*H$_2$), 74.4 (2 O*C*H$_2$), 110.9 (2 azobnzene-Ar*C*), 116.2 (2 azobnzene-Ar*C*), 121.4 (2 azobnzene-Ar*C*), 125.2 (4 calix-Ar*C*), 125.5 (4 calix-Ar*C*), 128.2 (4 calix-Ar*C*), 129.8 (2 azobnzene-Ar*C*), 131.7 (4 calix-Ar*C*), 141.6 (2 calix-Ar*C*), 146.7 (2 calix-Ar*C*), 150.4 (2 calix-Ar*C*), 150.7 (2 calix-Ar*C*), 153.7 (2 azobnzene-Ar*C*), 159.4 (2 stilbene-Ar*C*); Anal. Calcd for $C_{60}H_{70}N_2O_6$: C, 78.74; H, 7.71; N, 3.06; Found: C, 78.41; H, 7.78, N 3.01 mp: 351–352 °C.

4.2. Complexation study

For the ^{1}H NMR study, the studied calixarene derivative (10 mg) was dissolved in $CDCl_3$ (0.7 mL) in an NMR tube and the ^{1}H NMR spectrum was collected. Sodium or potassium picrate (20 mg) was added as a solid into the solution. The mixture was sonicated for 1 h before the spectrum was collected again. The color would turn to deep yellow and a singlet signal of the aromatic picrate proton could be observed around 9.0 ppm if complexation had taken place. If the signal was not observed by ^{1}H NMR, the results was confirmed by UV–Vis which was the cases for compounds **4** that the complexation was clearly observed in UV–Vis spectra but barely seen from the ^{1}H NMR spectra.

4.3. Isomerization study

The studied compound was dissolved in $CDCl_3$ at 0.0060 mol and into an NMR tube. Using a Hanovia 450 W medium pressure murcury lamp equipped with a cooling Jacket, the sample was irradiated at 30 cm away from the lamp for a specific period of time. The ^{1}H NMR was checked. Once the NMR spectra were unchanged, the *cis*:*trans* ratio of that specific analogue was determined by NMR integration of a selected signal.

4.4. Crystallographic data

4.4.1. *cis-o*-1. $C_{63}H_{74}Cl_2O_6$, monoclinic, space group $P2_1/c$, a=20.7486(5) Å, b=12.3713(4) Å, c=22.6335(5) Å, β=109.373(2)°, U=5480.8(3) Å^3, D_c=1.210 Mg m^{-3}, Z=4, T=120(2) K, colourless block, 0.24×0.18×0.12 mm^3. Data collection was carried out using a Bruker–Nonius KappaCCD area detector and SHELXS-97 and SHELXL-97 programs were used for structure solution and refinement. 32,983 reflections collected, 12,074 independent [R(int)=0.0700], giving R_1=0.0931 for observed unique reflections [$F^2>2\sigma(F^2)$] and wR_2=0.3186 for all data. The max. and min. residual electron densities on the final difference Fourier map were 0.975 and −0.588e Å^{-3}, respectively. The asymmetric unit contains a disordered molecule of

dichloromethane and exhibits conformational disorder in one of the lower rim cage arms and rotational disorder in one of the tertiary butyl groups. Supplementary data have been deposited with the CCDC in CIF format with the deposition number CCDC249144.

4.4.2. *trans-o*-2. $C_{64}H_{78}N_2O_8$, Monoclinic, space group *Cc*, $a=15.1260(3)$ Å, $b=31.1347(3)$ Å, $c=12.6692(3)$ Å, $\beta=98.4970(10)°$, $U=5900.99(19)$ Å^3, $D_c=1.129$ Mg m^{-3}, $Z=4$, $T=293(2)$ K, dark-orange block, $0.60\times0.30\times0.30$ mm^3. Data collection was carried out using a Bruker SmartCCD detector and SHELXS-97 and SHELXL-97 programs were used for structure solution and refinement. 21,046 reflections collected, 14,604 independent [R(int)=0.0190], giving $R_1=0.0731$ for observed unique reflections [$F^2>2\sigma(F^2)$] and $wR_2=0.1982$ for all data. The max. and min. residual electron densities on the final difference Fourier map were 0.225 and -0.211e Å^{-3}, respectively. Supplementary data have been deposited with the CCDC in CIF format with the deposition number CCDC137509.

4.4.3. *trans-m*-2. $C_{60}H_{70}N_2O_6$, Triclinic, space group *P*-1, $a=11.8283(3)$ Å, $b=12.7292(4)$ Å, $c=19.5738(8)$ Å, $\alpha=82.2330(10)°$, $\beta=74.9430(10)°$, $\gamma=66.7110(10)°$, $U=2612.32(15)$ Å^3, $D_c=1.163$ Mg m^{-3}, $Z=2$, $T=120(2)$ K, dark-orange block, $0.40\times0.20\times0.15$ mm^3. Data collection was carried out using a Bruker–Nonius KappaCCD area detector and SHELXS-97 and SHELXL-97 programs were used for structure solution and refinement. 39,735 reflections collected, 11,605 independent [R(int)=0.1407], giving $R_1=0.0777$ for observed unique reflections [$F^2>2\sigma(F^2)$] and $wR_2=0.2157$ for all data. The max. and min. residual electron densities on the final difference Fourier map were 0.801 and -0.556e Å^{-3}, respectively. Supplementary data have been deposited with the CCDC in CIF format with the deposition number CCDC249145.

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