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Synthesis of stilbene crown ether *p-tert*-butylcalix[4]arenes

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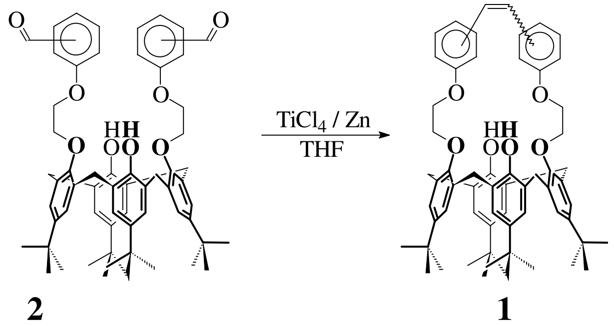
Abstract—Photo-switchable calixarene crown ether derivatives were synthesized in order to control the ring sizes and shapes of ionophores by isomerization between two different geometrical isomers. Five stilbene crown ether calix[4]arenes were prepared via McMurry coupling of the corresponding bisbenzaldehyde–calix[4]arene derivatives. The coupling reactions yielded both *cis*- and *trans*-stilbenes from *o*- and *m*-bisbenzaldehydes while only the *cis*-isomer was obtained from the reaction of the *p*-isomer. Unlike diazobenzene analogues, the stilbene crown ether calix[4]arene derivatives did not undergo thermal isomerization. Nevertheless, the isomerization of all synthesized stilbene crown ether calix[4]arenes can be photochemically induced. © 2001 Elsevier Science Ltd. All rights reserved.

Recently, supramolecular chemistry has become one of the most dynamic fields in chemistry. The molecular architecture required for selective recognition of molecules or ions by shape and size is one of the key points of interest in this subject.[1] The crown ether family is well known as ionophores.[2] In 1980, Shinkai and his colleagues synthesized an azobenzene containing crown ether to be used as a switchable alkali ion receptor.[3] The azobenzene moiety isomerized from the *trans*- to the *cis*-isomer upon irradiation, while the more sterically hindered *cis*-isomer converted back to the *trans*-isomer in the dark. The *cis*-isomer suitably bound K^+, Rb^+, and Cs^+ but the *trans*-isomer preferred to bind Li^+ and Na^+. An azobenzene-containing cryptand was also later synthesized by this group.[4] The switching of this cryptand from the *trans*- to the *cis*-isomer resulted in ring expansion that altered its binding preference from Na^+ to K^+.

Owing to its pre-organized structure, calix[4]arene is currently a popular molecular platform for designing highly selective receptors.[5] Several isomerizable azobenzene crown ether calix[4]arenes have been prepared and studied.[6–8] Although the *cis*- and *trans*-isomers of these azobenzene derivatives display different selectivity in binding alkali metal ions, their thermal isomerization has prevented them from being good candidates for controllable molecular photo-switches. Unlike azobenzenes, the stilbene analogues have been found not to undergo thermal isomerization[9] and thus are more promising as switching units for molecular photo-switches.

The *p-tert*-butylcalix[4]arene derivatives containing multiple benzaldehyde groups have been demonstrated



Scheme 1.

Table 1. Yields and *cis*:*trans* ratios of the products from the coupling reactions

Compound	Yield (%)		*cis*:*trans* ratio
	cis	*trans*	
o-**1**	57	10	85:15
m-**1**	20	8	73:27
p-**1**	51	0	100:0

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to be useful for syntheses of several selective host molecules.[10,11] We report herein syntheses of stilbene crown ether *p*-*tert*-butylcalix[4]arenes from *p*-*tert*-butylcalix[4]arene derivatives containing two benzaldehyde groups.

Three regioisomers, *o*-, *m*- and *p*-stilbene crown ether *p*-*tert*-butylcalix[4]arenes (**1**) were synthesized from McMurry coupling[12,13] of the corresponding bisbenzaldehydes (**2**) (Scheme 1). The bisbenzaldehydes were prepared by nucleophilic substitution reactions between *p*-*tert*-butylcalix[4]arene and the corresponding (2-bromoethoxy)benzaldehydes.[10,11]

The *m*-stilbene derivatives were prepared under modified McMurry conditions.[12,13] The *m*-bisbenzaldehyde reaction yielded 28% of the stilbene (*m*-**1**) and 20% of the corresponding pinacol by-product. The reaction of the *o*- and *p*-bisbenzaldehydes gave higher yields of stilbenes (*o*-**1** and *p*-**1**), 67% and 51%, respectively, and no pinacol by-product. Both *cis*- and *trans*-stilbenes were obtained from the coupling reaction of *o*- and *m*-bisbenzaldehydes but only the *cis*-stilbene was obtained from the *p*-isomer (Table 1). The assignment of *cis*- and *trans*-geometries was based on ^{1}H NMR and UV–vis spectra. The *cis*-geometry was assigned to the isomer possessing lower chemical shift values for the vinylic protons relative to the chemical shifts observed for unsubstituted stilbene (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 3).

Table 2. Chemical shifts of the vinylic protons of the stilbene products and stilbene in ($CDCl_3$)

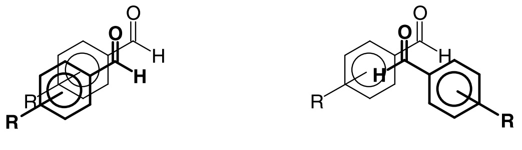
Compound	^{1}H NMR (ppm)	
	cis-isomer	*trans*-isomer
o-**1**	7.25	7.74
m-**1**	6.71	7.24
p-**1**	6.68	–
Stilbene[a]	6.57	7.15

[a] Measured in methanol.

Table 3. λ_{max} and extinction coefficient (ε) of the stilbene products and stilbene (in CH_2Cl_2)

Compound	*cis*-isomer		*trans*-isomer	
	λ_{max} (nm)	ε (cm^{-1} M^{-1})	λ_{max} (nm)	ε (cm^{-1} M^{-1})
o-**1**	292	19321	291	30106
			333	28492
m-**1**	286	20955	291	27488
			308	24866
			320	24629
p-**1**	283	16632	n.a.	n.a.
Stilbene[a]	223	20600	227	21000
	276	10900	294	33200
			307	32100

[a] Measured in methanol.



erythro *threo*

Figure 1. Proposed orientations of the two benzaldehyde groups that would lead to the formation of *cis*- and *trans*-products.

The predominant formation of the *cis*- over *trans*-products in this coupling reaction suggests that the pre-organized structure of the starting bisbenzaldehyde *p*-*tert*-butylcalix[4]arene may play an important role in controlling the geometry of the product. The shorter ethylene glycol linkages over the small and rigid lower rim of the *p*-*tert*-butylcalix[4]arene are less likely to allow the *threo* orientation of the two benzaldehyde moieties (Fig. 1) resulting in less *trans*-product. The situation becomes more obvious for the coupling of the *p*-bisbenzaldehyde in which the *threo*-like orientation would be most difficult to form and no *trans*-isomer was observed.

As predicted, all the stilbene crown ether *p*-*tert*-butylcalix[4]arenes synthesized did not isomerize under room light but readily isomerized under UV light. The photostationary states were observed for all isomers. We are currently studying the photo-switchable properties of these stilbene crown ether *p*-*tert*-butylcalix[4]arenes and their metal ions binding properties and will report the results in due course.

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13. $TiCl_4$ (3.17 mmol, 0.60 g) was charged into a two-necked, round-bottomed flask under a nitrogen 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 an additional 15 h and was then 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 off over Celite and washed with acetone and CH_2Cl_2. The filtrate was evaporated and the residue was dissolved in CH_2Cl_2 and then extracted with water. 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 *cis*- and *trans*-isomers can be separated (*cis*-isomers have a higher R_f value).

cis-*o*-**1**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.03 (s, 18 $C(C\underline{H}_3)_3$), 1.22 (s, 18 $C(C\underline{H}_3)_3$), 3.25 (d, 4 $Ar_2C\underline{H}_2$, $J=13.0$), 4.16 (broad, 4 $OC\underline{H}_2$), 4.26 (broad, 4 $OC\underline{H}_2$), 4.35 (d, 4 $Ar_2C\underline{H}_2$, $J=13.0$), 6.83 (t, 2 stilbene-Ar$\underline{H}$, $J=7.5$), 6.88 (d, 2 stilbene-Ar$\underline{H}$, $J=7.5$), 6.90 (s, 4 calix-Ar$\underline{H}$), 6.97 (s, 4 calix-Ar$\underline{H}$), 7.17 (t, 2 stilbene-Ar$\underline{H}$, $J=7.5$), 7.25 (s, 2 $C\underline{H}{=}C\underline{H}$), 7.29 (d, 2 stilbene-Ar$\underline{H}$, $J=7.5$), 7.70 (s, 2 $O\underline{H}$). 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.

trans-*o*-**1**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.06 (s, 18 $C(C\underline{H}_3)_3$), 1.18 (s, 18 $C(C\underline{H}_3)_3$), 3.21 (d, 4 $Ar_2C\underline{H}_2$, $J=12.5$), 4.23 (d, 4 $Ar_2C\underline{H}_2$, $J=12.5$), 4.51 (broad, 4 $OC\underline{H}_2$), 4.68 (broad, 4 $OC\underline{H}_2$), 6.82 (d, 2 stilbene-Ar$\underline{H}$, $J=8.0$), 6.93 (m, 4 calix-Ar$\underline{H}$ and 2 stilbene-Ar$\underline{H}$), 6.97 (s, 4 calix-Ar$\underline{H}$), 7.15 (t, 2 stilbene-Ar$\underline{H}$, $J=8.0$), 7.50 (d, 2 stilbene-Ar$\underline{H}$, $J=8.0$), 7.74 (s, 2 $C\underline{H}{=}C\underline{H}$), 8.43 (s, 2 $O\underline{H}$). Anal. calcd for $C_{62}H_{72}O_6$: C, 81.54; H, 7.95. Found: C, 81.41; H, 7.94.

cis-*m*-**1**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.09 (s, 18 $C(C\underline{H}_3)_3$), 1.25 (s, 18 $C(C\underline{H}_3)_3$), 3.32 (d, 4 $Ar_2C\underline{H}_2$, $J=12.5$), 3.94 (broad, 4 $OC\underline{H}_2$), 4.12 (broad, 4 $OC\underline{H}_2$), 4.38 (d, 4 $Ar_2C\underline{H}_2$, $J=12.5$), 6.69 (broad, 2 stilbene-Ar$\underline{H}$), 6.71 (s, 2 $C\underline{H}{=}C\underline{H}$), 6.89 (m, 4 stilbene-Ar$\underline{H}$), 6.97 (s, 4 calix-Ar$\underline{H}$), 7.02 (s, 4 calix-Ar$\underline{H}$), 7.24 (t, 2 stilbene-Ar$\underline{H}$, $J=8.5$), 8.08 (s, 2 $O\underline{H}$). Anal. calcd for $C_{62}H_{72}O_6$: C, 81.54; H, 7.95. Found: C, 81.48; H, 7.92.

trans-*m*-**1**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.83 (s, 18 $C(C\underline{H}_3)_3$), 1.31 (s, 18 $C(C\underline{H}_3)_3$), 3.29 (d, 4 $Ar_2C\underline{H}_2$, $J=13.5$), 4.25 (t, 4 $OC\underline{H}_2$, $J=5.0$), 4.41 (d, 4 $Ar_2C\underline{H}_2$, $J=13.5$), 4.57 (t, 4 $OC\underline{H}_2$, $J=5.0$), 5.84 (s, 2 $O\underline{H}$), 6.60 (s, 4 calix-Ar$\underline{H}$), 6.87 (t, 2 stilbene-Ar$\underline{H}$, $J=8.5$), 7.06 (s, 4 calix-Ar$\underline{H}$), 7.14 (d, 2 stilbene-Ar$\underline{H}$, $J=7.5$), 7.24 (s, 2 $C\underline{H}{=}C\underline{H}$), 7.25 (t, 2 stilbene-Ar$\underline{H}$, $J=7.5$), 7.74 (s, 2 stilbene-Ar$\underline{H}$). Anal. calcd for $C_{62}H_{72}O_6$: C, 81.54; H, 7.95. Found: C, 81.59; H, 8.00.

cis-*p*-**1**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.85 (s, 18 $C(C\underline{H}_3)_3$), 1.31 (s, 18 $C(C\underline{H}_3)_3$), 3.28 (d, 4 $Ar_2C\underline{H}_2$, $J=13.5$), 4.17 (t, 4 $OC\underline{H}_2$, $J=4.0$), 4.38 (d, 4 $Ar_2C\underline{H}_2$, $J=13.5$), 4.45 (t, 4 $OC\underline{H}_2$, $J=4.0$), 6.29 (s, 2 $O\underline{H}$), 6.66 (s, 4 calix-Ar$\underline{H}$), 6.68 (s, 2 $C\underline{H}{=}C\underline{H}$), 6.85 (d, 4 stilbene-Ar$\underline{H}$, $J=9.0$ Hz), 6.93 (d, 4 stilbene-Ar$\underline{H}$, $J=9.0$), 7.06 (s, 4 calix-Ar$\underline{H}$). Anal. calcd for $C_{62}H_{72}O_6$: C, 81.54; H, 7.95. Found: C, 81.57; H, 8.14.