Macrocycles

Straightforward Synthesis, Electrochemical Properties, and Gel Formation of Thiacalix[n]thiophenes

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Abstract: A facile synthetic approach toward thiacalix[n]-thiophene homologues (n = 4–6) is presented herein. Pd-catalyzed coupling of 2,5-dibromothiophene derivatives with stannyl sulfide gave various thiacalix[n]thiophenes in good yields. The optical and electrochemical properties of the produced cavitands were investigated. Furthermore, gelation was observed in some solvents.

Thiacalix[*n*]thiophenes are cyclic oligomers comprising sulfurbridged thiophenes; they are analogues of thiacalix[*n*]arenes, which are employed as host molecules in supramolecular chemistry (Figure 1).^[1–3] The presence of thiophene moieties



Figure 1. Structures of thiacalix[n]thiophenes (1 a-c).

endows these cavitands with potentially interesting properties derived from their electron-donating ability. While a rich set of examples of thiacalix[n]arenes have been reported, thiacalix[n]-thiophenes have not been extensively explored thus far due to synthetic difficulties. In 1997, two groups independently reported the synthesis of **1a** via a difficult approach based on a multistep structural elongation or a simple approach from a thiophene framework in extremely low yield.^[4,5] Therefore, details such as the electrochemical and supramolecular properties of thiacalix[n]thiophenes are still unknown. To develop thiacalix[n]thiophenes for intriguing applications, it is necessary to improve their accessibility and structural diversity.

Recently, we established a simple protocol for the synthesis of sulfur-bridged dithienothiophene macrocycles using Pd-cat-

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alyzed coupling between a 2,5-dibromodithienothiophene (dibromo-DTT) derivative and (*n*Bu₃Sn)₂S as the sulfur source.^[6] Typically, this type of coupling reaction is employed for the preparation of symmetrical thioethers.^[7] However, in our case, the coupling reaction resulted in cyclic homologues of 4–9mers in high yields, together with only small amounts of acyclic products. This result strongly encouraged us to employ the developed method for the synthesis of a series of thiacalix[*n*]thiophenes that are inaccessible by conventional cyclization methods. Here, we report an efficient approach toward a series of novel thiacalix[*n*]thiophenes with various substituents (Scheme 1). The electronic structure and redox properties of the produced compounds are also presented. Moreover, we found that some thiacalix[*n*]thiophenes exhibited gelation in



Scheme 1. Synthesis of thiacalix[n]thiophenes 1–7 and 8.

certain solvents.

The results of the cyclization reactions are listed in Table 1. 2,5-dibromo-3,4-disubstituted-thiophenes Treatment of (0.5 mmol) with (nBu₃Sn)₂S (0.5 mmol) in the presence of $[Pd(PPh_3)_4]$ (0.06 mmol, 12 mol%) in DMF at 110 °C provided the corresponding thiacalix[n]thiophenes (n = 4-6). Initially, we employed 2,5-dibromothiophene as a pristine thiophene resource for the reaction (entry 1). However, only acyclic oligothiophenes linked with sulfur atoms were obtained. On the other hand, a small amount of 4-mer 2a and 5-mer 2b together with acyclic molecules as the main products were formed when 2,5-dibromo-3,4-dimethylthiophene was employed (entry 2). Although the coupling reaction proceeded smoothly, the cyclization to thiacalix[n]thiophene was disfavored under the reaction conditions. Improved yields were observed when

Table 1. tives. ^[a]	Palladium-catalyzed cycl	ization of 2,5-dil	promothiophen	e deriva-
Entry	R	Yield [%] ^[b] n=4	n=5	n=6
1	Н	-	-	-
2	CH₃	2 a, 7	2 b , 3	-
3 ^[c]	<i>n</i> Bu	3 a , 27	3 b , 11	3 c , 5
4	<i>t</i> Bu	4a, trace	-	-
5		5 a , 8	5 b , trace	-
6		6 a , 27	6 b , 6	6c , 5
7		7 a , 26	7 b , 8	7 c , 2
[a] Reaction conditions: [thiophene]/[S(nBu_3Sn_2]/[Pd(PPh ₃) ₄] = 0.5:0.5:0.06 (mmol for entries 1, 3–7), 0.5:0.5:0.09 (mmol for entry 2), in 25 mL DMF at				

(mmol for entries 1, 3–7), 0.5:0.5:0.09 (mmol for entry 2), in 25 mL DMF at 110°C under Ar. [b] Isolated yield. [c] Trace amount of 7-mer **3 d** was obtained.

*n*Bu was employed as the substituent (entry 3). Cyclic 4-mer (**3**a), 5-mer (**3**b), 6-mer (**3**c), and 7-mer (**3**d) were obtained after GPC separation. In contrast, in the reaction with *t*Bu, only a trace amount of **4**a was observed in the mass spectrum, together with the recovered starting dibromothiophene and its dehalogenated counterparts (entry 4). These results imply that the bulkiness of the substituents in the 3,4-position affects the cyclization.

These results encouraged us to explore other thiacalix[*n*]thiophenes with moderately bulky substituents. Indeed, 3,4bis(4-alkylphenyl)thiophenes readily underwent cyclization (Table 1; entries 5–7). When the reaction was performed with 2,5-dibromo-4,5-bis(*p*-tolyl)thiophene as the starting compound, **5a** was obtained in 8% yield together with a trace amount of **5b**. However, compound **5a** was not very soluble in common organic solvents. Higher yields of the cyclic 4-mer were obtained in the reactions carried out with 4-(*n*-butyl)phenyl (entry 6) and 4-*tert*-butylphenyl (entry 7) substituents. In these cases, larger cyclic oligomers were also obtained, together with small amounts of the acyclic products. Thus, the solubility of the product would be critical to the reaction yield.

Although we did not obtain a single crystal suitable for Xray analysis, we carried out DFT calculations of the model compound 2a-c and 5a to obtain structural information of the macrocyclic compounds. Thus, DFT calculations of 2a, performed at the B3LYP/6-31G(d,p) level of theory, revealed that the 1,3-alternate geometry with S_4 symmetry was the most stable conformer (Figure 2a), with a considerably energy difference from the others.^[8] The 1,3-alternate conformer of 2a possesses a square cavity with a diagonal distance of ca. 8.4 Å. The four sulfur atoms at the corners are almost coplanar. In sharp contrast, the optimized 1,3-alternate geometry of 5 a exhibits a puckered quadrilateral conformation, while its diagonal distance is similar to that of 2a (Figure 2b). This distortion of the four sulfur atoms arises from the steric repulsion of the ptolyl groups on the adjacent thiophene rings. On the contrary, DFT calculation suggests a folding pentagonal conformation in



Figure 2. DFT-optimized structures (alternate conformations) of (a) **2a**, (b) **5a**, (c) **2b**, and (d) **2c** in ball-and-stick views. The methyl and *p*-tolyl group substituents are represented in a wire-frame view for clarity.

2b as an energy minimum structure (Figure 2 c). The diagonal distance S···S in the pentagonal shape is calculated to be about 9.5 Å. As for the calculation of **2 c**, a higher symmetrical structure having a larger cavity (ca. 11.8 Å of the diagonal distance) was obtained as a minimum (Figure 2 d).

To investigate the electronic structure of the produced compounds, their absorption spectra were measured in CH₂Cl₂. Similar spectra were observed for **3a**-**c** in CH₂Cl₂ (Figure S19, Supporting Information). The longest absorption maxima were in the range of 290–300 nm, suggesting little extension of the π -conjugation through the S atoms at the corners of the compounds.

The electrochemical properties of homologues 3a-c, together with 3,4-dibutyl-2,5-bis(phenylthio)thiophene 8 (Scheme 1), were investigated using cyclic voltammetry (CV) and differential pulse voltammetry (DPV) in 1,2-dichloroethane (Figure 3); the results are summarized in Table 2. Compound 3a showed two well-dissolved reversible redox waves in CV, while compound 8 showed two irreversible redox waves. In DPV measurements, compound 3a exhibited redox peaks at 0.50 and 0.78 (vs. Fc/Fc⁺), while compound 8 showed redox peaks at 0.62 and 1.13 V. Considering the number of observed redox waves in 8, the redox process of these systems is associated with the sulfide linkage atoms. This result is consistent with the redox processes of the DTT ring system found in a previous study.^[6] In addition, the E¹ value of **3a** was much lower than that of 8. The lowering of the first redox of 3a relative to 8 suggests the formation of 3a⁺⁺, and its charge/electron can be delocalized over the sulfide linkers.^[9] In fact, electronic spectra in oxidation state of 3a⁺⁺ by applying the constant voltage beyond the E^1 value gave a very broad absorption band in the NIR region (λ_{max} : 1240 nm) owing to the charge resonance among the thiophene moieties (Figure S20).



Figure 3. (a) Cyclic and (b) differential pulse voltammograms of 3 a (0.63 mm), 3 b (0.38 mm), and 3 c (0.34 mm) in 1,2-dichloroethane.

Table 2. Redox potentials of 3 a-c and 8. ^[a]							
Compd.	E_1^{ox} [V]	E_2^{ox} [V]	E_3^{ox} [V]	<i>Е</i> _{НОМО} [eV] ^[b]	Calc. <i>E</i> _{HOMO} [eV] ^[c]		
3 a 3 b 3 c 8	0.50 0.57 0.53 0.62	0.78 0.80 0.85 1.13	- 0.97 1.02 -	5.28 5.37 5.33 5.42	5.46 5.92 6.22 		
[a] All potentials were obtained from DPV measurements in 1,2-dichloro- ethane containing 0.1 μ <i>n</i> Bu ₄ NPF ₆ at 25 °C with a Pt working electrode. Potentials were measured against Ag/AgCl/KCl in a Luggin capillary and were converted to the values vs. Fc/Fc ⁺ . [b] Estimated from $E_{HOMO} =$ $-(4.80 + E_1^{1/2} \text{ (vs. Fc/Fc^+)})$. [c] Using HOMO energy levels of 2 a–c in DFT calculations.							

As for **3b**, three redox waves were found, and their potentials were at 0.57, 0.80, and 0.97 V. The E^1 value of **3b** was slightly higher than that of **3a**, presumably due to the less conjugated structure of **3b** arising from the folded molecular structure revealed in DFT calculations (Figure 2c). Finally, compound **3c** exhibited a complex redox behavior. Three redox peaks at 0.53, 0.85, and 1.02 V were observed owing to the sequential redox process. From the comparison of the first redox potentials, the HOMO levels of these homologues are in the order of **3a** > **3c** > **3b**, although the calculated HOMO levels of the model compounds are **2a** > **2b** > **2c**. These inconsistencies are presumably attributed to the conformational fluctuation in the larger cyclic oligomers in solution.

Interestingly, compound **7a** formed an opaque gel in toluene and PhCl (CGC: critical gel concentration = 6.6 wt% and 4.4 wt%, respectively) after a heating-cooling procedure (Figure 4a). SEM observation of the resulting xerogel air-dried on a Si-wafer revealed that the gel had retiform structures composed of entangled nanoscale fibrous rods. In other solvents, a precipitate or rod-shaped small crystals were formed. Although compound **5a** exhibited very poor solubility in a wide variety of solvents, a jelly-like precipitate was formed in CHCl₃ at low concentrations. Furthermore, compounds **2a**, **3a**, and





Figure 4. (a) Photograph of the gel of **7 a** (toluene), (b, c) SEM images obtained from the air-dried gel, and (d) UV/Vis spectra of **7 a** in the gel state from toluene (air-dried gel on a quartz plate), in CH_2Cl_2 (7.9×10⁻⁵ M), and in toluene at lower concentration (6.6×10⁻⁵ M).

6a formed no gel precipitates due to high solubility in various solvents.

To investigate the driving force for the gelation behavior, UV/Vis absorption and VT-NMR spectroscopic data of 7a were measured. The absorption of the gel was slightly red-shifted compared with the solution spectra, implying intermolecular interactions in the π -frameworks of thiacalix[4]thiophene. Although compound 7 a did not exhibit a remarkable concentration-dependence in the ¹H NMR spectra at room temperature, a temperature dependence of the chemical shift was observed in [D₈]toluene solution (Figure 5). When the temperature was decreased from 85° C to -10° C, the signals assigned to the aromatic proton H_a on the benzene ring and the methyl proton of tBu group shifted upfield from $\delta = 7.14$ and 1.15 ppm to 7.07 and 1.07 ppm, respectively, while the signals assigned to $H_{\rm b}$ shifted downfield from $\delta = 7.09$ to 7.21. Finally, a broadening of the signals was observed after turning off the spinning in the NMR spectrometer due to the formation of a gel in the tube. The spectrum of the gel is quite similar to that of the solution at lower temperature. Thus, the observed upfield shifts of H_a and tBu protons might be attributed to the shielding effect of neighboring aromatic rings derived from the molecular association in [D₈]toluene solution. In sharp contrast, the signals of all protons slightly shifted downfield in a uniform way upon cooling in CDCl₃, and no gelation occurred under the conditions.

In general, calix[*n*]arenes bearing hydrogen-bonding (Hbonding) units often form supramolecular gels through self-assembly.^[10,11] These gel materials lead to cavity-assembled porous solids (CAPs), which can provide excellent molecular recognition abilities. However, in the present system, there is no H-bonding site to facilitate supramolecular assemblies. In addition, only thiacalix[*n*]thiophene having *tert*-butylphenyl groups exhibits the gelation properties. Thus, a subtle balance between the π -framework and alkyl groups on the thiophene as well as the solubility is an important factor for the gelation.

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Figure 5. VT ¹H NMR spectra of 7 a in [D₈]toluene (40 mm) and its gel.

Recently, the gelation behavior of π -conjugated molecules having bulky *tert*-butyl groups has been reported, and the *tert*-butyl unit acts a key role for the formation of organogels.^[12] Hence, in the present gel materials, the cavity of thiacalix[4]-thiophene may confine proximal alkyl chains via van der Waals forces,^[13] and elongation can occur in the direction perpendicular to the sulfide square plane. Indeed, X-ray diffraction (XRD) profiles of the air-dried xerogel from toluene exhibited two broad reflections (d = ca. 16.7 and 5.3 Å), and the former value is roughly consistent with the molecular size of **7 a**.

In summary, the palladium-catalyzed coupling of various dibromothiophenes with stannyl sulfide facilitated the formation of thiacalix[*n*]thiophenes bearing alkylphenyl groups. In this reaction, the bulkiness of the substituents and the solubility were critical for effective cyclization. CV and DPV measurements revealed the simple oxidation of the thiacalix[*n*]thiophenes (n = 4, 5, 6). Despite the lack of H-bonding units, thiacalix[4]thiophenes with phenyl groups formed gels through molecular association. To the best of our knowledge, there have not been any previous examples of organic gelators based on calix[4]arene without H-bonding units. Further investigation is currently in progress on functionalized CAPs based on these appealing frameworks.

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