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Oxa-bridged cyclophanes featuring thieno[2,3-*b*]thiophene and C_2-symmetric binol or bis-naphthol rings: synthesis, structures, and conformational studies

Sabir H. Mashraqui [a,*], Yogesh S. Sangvikar [a], Shailesh G. Ghadigaonkar [a], Mohamed Ashraf [a], M. Meetsma [b]

[a] Department of Chemistry, University of Mumbai, Vidyanagari, Santacruz-E, Mumbai 400 098, India
[b] Department of Chemistry, State University of Groningen, Nijenborg 9747 AG, Groningen, The Netherlands

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ABSTRACT

Oxa-bridged cyclophanes **4**/**6** and **8**/**10** featuring thieno[2,3-*b*]thiophene ring and binol or bis-naphthol have been synthesized. The structures are assigned by 2D NMR data and the identity of **4** is also independently established by a single X-ray crystallography. From dynamic NMR analysis, the Arrhenius energy of activation $\Delta G^{\#}$ for bridge inversions in **4** and **6** was calculated to be 15.3 and 12.9 kcal/mol, respectively. A higher $\Delta G^{\#}$ for **4**, relative to the ester free **6** is attributable to the steric compression stemming from C2/C5 ester substituents to the bridge inversion processes. While the methylene bridges undergo inversion in **4** and **6**, the naphthyl–naphthyl pseudo-rotation appears to be restricted even at higher temperatures. This is supported by retention of the optical purity of the chiral (−) **4** under thermal condition. For the case of bis-naphthol cyclophane **8**, we observed the flipping of both the $-OCH_2-$ and the naphthyl–CH_2–naphthyl bridges with $\Delta G^{\#}$ of ca. 11.4 kcal/mol. However, the ester free cyclophane **10** remained conformationally mobile even at −55 °C and its $\Delta G^{\#}$ was assumed to be <11.4 kcal/mol. The presence of an extra $-CH_2-$ linker in bis-naphthol cyclophanes **8**/**10** renders them relatively more conformationally mobile compared to binol cyclophanes **4**/**6**, possessing a rigid naphthyl–naphthyl geometry.

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1. Introduction

Understanding and controlling the conformational and chiroptic properties of constrained systems are fundamental to designing chiral receptors and asymmetric catalysts.[1] Constrained cyclophanes are recognized as one of the important classes of supramolecular motifs with relevance in many areas of chemistry including the chiral chemistry.[2] New structural variants of cyclophanes are continued to be designed in search of unraveling novel stereochemical and spectral aspects associated with such molecules.[3] Dynamic NMR technique has been widely used to study the solution conformations of cyclophanes.[4] These studies have revealed that the energy barriers to conformational inversions in cyclophanes markedly depend up on three factors: (a) the size of the *phane* cavity, (b) nature of ring(s)/bridges, and (c) the steric bulk of the substituent(s) involved in the inversion processes.[3a,5] An impressive range of heterophanes incorporating simple heterorings, viz. furan, thiophene, pyrrole, and pyridine are known.[6] However, examples of heterophanes encompassing bi-fused heterocycles are indeed sparse.[7] Consequently, little information is currently available concerning their structures or conformational properties.

Macrocycles derived from C_2-symmetric 1,1′-binaphthol have been widely exploited by Cram and others for their applications in stereo-differentiating reactions and molecular recognition.[8] A few examples of macrocycles derived from bis-naphthol have also been described in the literature.[9] On the other hand, the chemistry of the 10π rich thieno[2,3-*b*]thiophene,[10] a bi-fused heterocycle is of current interest in the development of axially chiral systems,[11] liquid crystals,[12] and nonlinear optics materials.[13] In the context to our interest in heterophanes, we recently reported synthesis and nonlinear optic property of a novel dithia-bridged thieno[2,3-*b*]thiophenophane.[14] We now report the synthesis of oxa-bridged cyclophane diesters **4** and **8** and their corresponding ester free analogs, **6** and **10** by bridging together an appropriately functionalized thieno[2,3-*b*]thiophene with binol and bis-naphthol, respectively. Presently, our main objective in the synthesis of these cyclophanes was to examine how conformational dynamics might be affected by placing torsionally constrained binol and torsionally flexible bis-naphthol within the cyclophane frameworks.

* Corresponding author. Tel./fax: +91 22 26528547.
E-mail address: sh_mashraqui@yahoo.com (S.H. Mashraqui).

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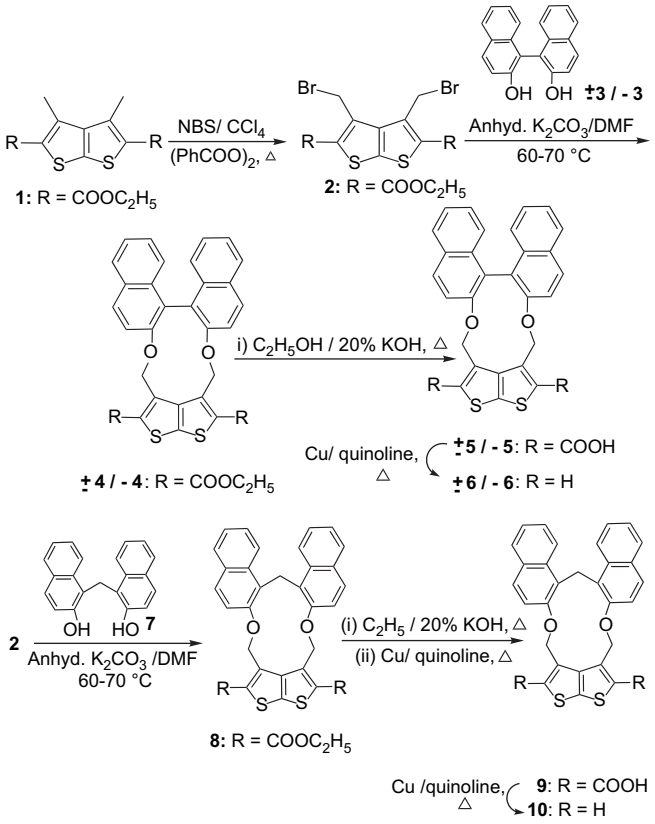

Scheme 1. Synthesis of oxa-bridged cyclophanes **4**, **6**, **8**, and **10**.

The synthetic route implemented for oxa-bridged cyclophanes is depicted in Scheme 1. Readily available thienothiophene diester **1**[15] was subjected to twofold bromination using a slightly more than 2 equiv of *N*-bromosuccinimide in refluxing CCl_4 containing a catalytic amount of dibenzoyl peroxide. Crude product obtained on work-up was crystallized from alcohol affording pure dibromide **2** in 70% yield. Coupling reaction of **2** with racemic binol ±**3** was carried out in dry DMF using K_2CO_3 under high dilution conditions. Following the extractive work-up and purification by SiO_2 column chromatography, we isolated ±**4** as a colorless crystalline solid in 52% yield. Base hydrolysis of ±**4** (20% KOH in DMSO, 100 °C, 6 h), followed by acidification gave diacid ±**5** in high yield. Decarboxylation of ±**5** was affected in refluxing quinoline–Cu system affording the target cyclophane ±**6** as a colorless solid in 81% yield. In like fashion, use of (−) binol allowed access to chiral diester (−) **4** and, the ester free analogs (−) **6** with [α] −186.89 (*c* 1 in $CHCl_3$) and [α] −8.88 (*c* 1 in $CHCl_3$), respectively. Condensation of dibromide **2** with bis-naphthol **7** under the conditions described for ±**4** afforded diester cyclophane **8** as a colorless solid in 21% yield. Base catalyzed hydrolysis of **8** furnished diacid **9**, which upon decarboxylation (Cu–quinoline) followed by SiO_2 column purification afforded cyclophane **10** as a colorless crystalline solid. The structures of cyclophanes **4**, **6**, **8**, and **10** follow from their elemental composition and spectral data.

2. Structural assignments of oxa-bridged cyclophanes ±4, ±6, 8, and 10 by 2D NMR

The ^{1}H NMR assignments for ±**4**, ±**6**, **8**, and **10** were made from the corresponding 2D NMR data and the complete ^{1}H NMR assignments are collected in Table 1. ^{1}H NMR spectrum of binol cyclophane diester ±**4** and its ester free analog ±**6** revealed a broad signal each centered at δ 5.91 and 5.42 (2H each), respectively, for their bridging $-OCH_2-$ groups. The appearance of broad peaks, instead of a sharp singlet for the $-OCH_2-$ protons is consistent with the slow bridge inversion in these molecules with respect to the NMR time scale. In contrast, bis-naphthol cyclophanes revealed for their $-OCH_2-$ and naphthyl–CH_2–naphthyl protons sharp singlets at δ 5.94 and 4.64, respectively, for **8** and δ 5.42 and 4.76, respectively, for **10**. This observation implies that the bridge inversions in **8** and **10** are relatively fast on the NMR time scale.

3. Conformational analysis of binol cyclophanes ±4 and ±6

As already pointed out, the appearance of a broad signal for the $-OCH_2-$ protons in ±**4** implies that the bridge inversion is restricted with respect to the NMR time scale at ambient temperature. As shown in Figure 1a, raising the temperature to around 60 °C resulted in the conversion of the broad peak into a sharp singlet with the coalescence occurring around 40 °C. This observation indicates that at or above 40 °C, ±**4** is undergoing unhindered bridge flipping, leading to the equivalence of the bridged $-CH_2-$ protons. On the other hand, cooling the sample to −10 °C resulted in the development of a clear AB system out of the $-CH_2-$ protons. Apparently, at this temperature, the $-CH_2-$ protons become diastereotropic as a result of the frozen conformation. The rate of bridge inversion (K) and Arrhenius energy of activation ($\Delta G^{\#}$) were calculated by using the literature protocol.[16] From the $\Delta\nu$ of 89 Hz and the coalescence temperature T_c of 313 K, we calculated K and $\Delta G^{\#}$ to be 133 s^{-1} and 15.3 kcal/mol, respectively.

However, no changes were noticeable in the naphthalene spectral region (δ 7.10–7.90) when the NMR spectra were scanned from −50 to +130 °C. This observation, in principle is compatible with either a free pseudo-rotation around bi-naphthyl bond or a rigid bi-naphthyl conformation. Lai et al. have studied conformational analysis of a series of dithia[3.3]/[4.4]biphenylenocyclophanes and demonstrated that only the thia-methylene bridges are conformationally flexible, while the rotation around the phenyl–phenyl bond is restricted (estimated $\Delta G^{\#}>18$ kcal/mol) even at elevated temperatures.[17] Moreover, several known macrocycles

Table 1
^{1}H NMR assignments of cyclophanes **4**, **6**, **8**, and **10** (300 MHz, $CDCl_3$)

H type	Diester naphthol	Plain naphthol	Diester bisnaphthol	Plain bisnaphthol
H3/H3′	7.64 (d), J=7.1 Hz	7.60 (d), J=7.2 Hz	7.56 (d), J=7.2 Hz	7.72 (d), J=7.2 Hz
H4/H4′	7.87 (d), J=7.1 Hz	7.95 (d),[a] J=7.3 Hz	7.69 (d), J=7.2 Hz	7.76 (d), J=7.0 Hz
H5/H5′	7.80 (d), J=8.5 Hz	7.95 (d),[a] J=8.5 Hz	8.09 (d), J=7.9 Hz	8.06 (d), J=7.9 Hz
H6H6′	7.27 (t), J=8.5 Hz	7.22 (t), J=8.5 Hz	7.33 (t), J=7.9 Hz	7.35 (t), J=7.8 Hz
H7/H7′	7.14 (t), J=8.7 Hz	7.38 (t), J=8.8 Hz	7.27 (t), J=8.0 Hz	7.38 (t), J=8.0 Hz
H8/H8′	7.11 (d), J=9.1 Hz	7.16 (d), J=8.9 Hz	7.75 (d), J=8.1 Hz	7.83 (d), J=8.2 Hz
Th–H[b]	—	7.48 (s)	—	7.42 (s)
$-CH_2-O$	5.91 (br s)	5.42 (br s)	5.94 (s)	5.42 (s)
Naph–CH_2–naph	—	—	4.64 (s)	4.76 (s)

[a] Overlapping resonances.
[b] Th–H denoted thienothiophene ring protons.

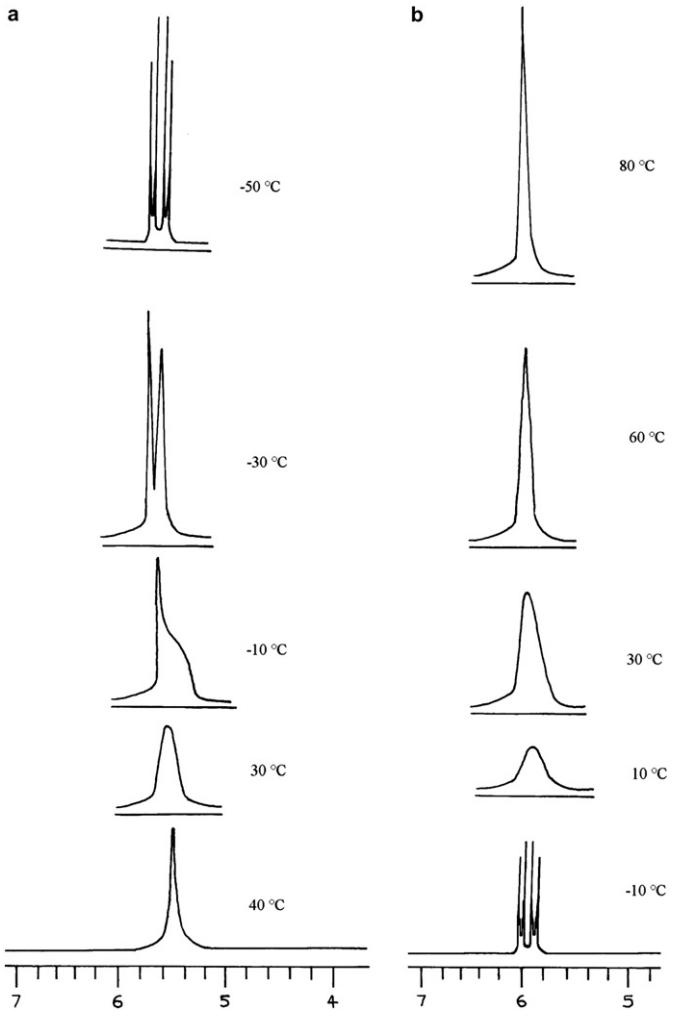

Figure 1. Compound **1a**: dynamic ^{1}H NMR of ±**4** (−10 to 80 °C) showing changes in the δ 5.91 resonance. Compound **1b**: dynamic ^{1}H NMR of ±**6** from −50 to +40 °C for the resonance at δ 5.42.

and crown ethers derived from the chiral binol are reported to be conformationally robust, surviving racemization even at high temperatures.[8]

As proposed in Figure 2, rotamer A to rotamer B interconversions for ±**4** necessitate the conversion of a twisted naphthyl–naphthyl geometry into a coplanar transition state (T.S.). The latter entails a destabilizing non-bonded interaction between H8 and H8′, rendering the T.S. energetically unaccessible. Consequently, it is reasonable to assume that only –OCH_2– bridges are subject to temperature dependent conformational variations and that the pseudo-rotation around naphthyl–naphthyl bond in ±**4** ought to be restricted even at high temperatures. High degree of torsion involving the naphthyl–naphthyl bond (see discussion

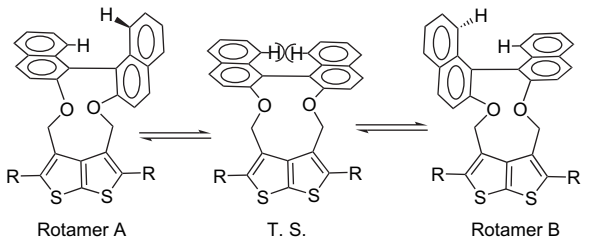

Figure 2. Proposed transition state (T.S.) for rotamers interconversion in **4**.

on X-ray) also underscores this point. In order to substantiate the restricted rotation of the naphthyl–naphthyl bond, we heated chiral diester cyclophane (−) **4** in dry DMSO at 120 °C for 1 h. The optical activity [α] −186.69 (*c* 1 in $CHCl_3$) of the recovered sample was found to be virtually the same as that of the pre-heated sample [α] −186.89 (*c* 1 in $CHCl_3$). This experiment confirms the absence of naphthyl–naphthyl bond rotation at least up to 120 °C. Furthermore, this observation suggests that cyclophane ±**4** should exists as a potentially resolvable axially chiral molecule. Indeed, this was found to be the case by successful resolution of racemic cyclophane ±**4** on chiral HPLC. Cyclophane ±**4** could be separated into two epimers with the intensity ratio of ca. 47.5:52.5, corresponding to the retention times of 7.77 and 10.31 min, respectively. Under the same condition, (−) **4** eluted essentially as a single peak (ca. 98.7% purity) with a retention time of 7.66 min.

In contrast to ±**4**, the ambient temperature NMR of the ester free cyclophane ±**6** revealed a sharp singlet for the –CH_2– protons thereby indicating unhindered bridge inversion. ^{1}H NMR spectra were therefore, recorded at lower temperatures to see if the bridge flipping could be arrested. In the event, lowering the temperatures led to the broadening of the singlet and eventually a well resolved double doublets (AB type system) appeared around −35 °C (Fig. 1b). From $\Delta\nu$ of 51 Hz, and the coalescening temperature of −10 °C, we calculated *K* of 113 s^{-1} and $\Delta G^{\#}$ of 12.86 kcal/mol. No changes, however were noticed in the spectral region of the naphthyl protons (δ 7.0–8.3) in the temperature range −50 to +130 °C. This observation coupled with the preservation of the optically active (−) **6** on heating at 120 °C for 1 h in DMSO confirmed the absence of naphthyl–naphthyl bond rotation in this molecule as well even at high temperatures. A higher activation energy of the bridge inversion in ±**4** (15.3 kcal/mol) relative to ±**6** (12.9 kcal/mol) is presumably due to the steric encumbrance imposed on the bridge flipping by the C2/C5 ester substituents. Similar observation was recently made by us in 3,4-dipyridyl thienothiophene wherein compared to the ester free system, the ester substituted analog showed higher energy of activation by ca. 0.9 kcal/mol.[12c] Interestingly, the eleven membered phane cavity in the cyclophanes **4** and **6** appears to be large enough to not only accommodate the orthogonal naphthalene planes, but also allows for the bridge inversions at moderate temperatures.

4. Conformational analysis of bis-naphthol cyclophanes 8 and 10

^{1}H NMR of diester **8** and its ester free **10** both at room temperature exhibited sharp singlets for their bridged –OCH_2– and Ar–CH_2–Ar protons. This observation implies the occurrence of facile bridge inversions of both the bridges at ambient temperatures. For the case of **8**, as the temperature was lowered, these singlets began to split and around −45 °C, a well resolved pair of double doublets exhibiting nearly identical $\Delta\nu$ of 128 Hz appeared for these protons. The coalescences of these multiplets were noted at around −30 °C. From the T_c=243 K, the rate of inversion, *K* and Arrhenius energy of activation, $\Delta G^{\#}$ were calculated to be 128 s^{-1} and 11.4 kcal/mol, respectively, for the flippings of both –OCH_2– and Ar–CH_2–Ar. For ester free **10**, the singlets for the –OCH_2– and Ar–CH_2–Ar retained their singlet character even at −55 °C, with only a slight broadening being observed around −60 °C. From these observations, we can conclude that the bridge pseudo-rotation is not inhibited at least up to −55 °C. Since, we failed to detect a clear coalescence, the $\Delta G^{\#}$ for bridge inversions in **10** could not be calculated. However, in analogy to the lower energy barrier observed for ±**6** relative to ±**4**, we can assume that $\Delta G^{\#}$ for the bridge flipping in ester free cyclophane **10**, in comparison to **8** should be <11.4 kcal/mol.

Table 2
Summary of crystallographic data and refinement details

Empirical formula	$C_{25}H_{18}O_2S_2 \cdot 0.5(CHCl_3)$
Formula mass	510.27
Crystal color and habit	Colorless, platelet
Crystal size (nm^3)	0.31×0.23×0.08
Crystal system	Monoclinic
a (Å)	15.780(2)
b (Å)	7.437(1)
c (Å)	19.355(3)
β (°)	97.185(2)
V ($Å^3$)	2253.6(5)
Z	4.0
ρ_{calcd} (g/cm^3)	1.504
F (000)	1052
μ (cm^{-1})	4.41 (Mo Kα)
No. of reflections	5144
R_{int}	0.0508
No. of parameters	397
R	0.0521
R_W	0.1351
GOF	1.040

5. Single X-ray crystal structure of ±6

Crystals of ±**6** suitable for X-ray structure were obtained by slow evaporation from the $CHCl_3$. Colorless crystal having dimension of 0.52×0.48×0.36 mm was used for characterization and data collection. The unit cell of ±**6** was identified as monoclinic and the structure was resolved by Patterson methods using DIRDIF program.[18] Crystal data and numerical details from the data collection[19] and refinements[20] are given in Table 2. A perspective ORTEP drawing of structure ±**6** is shown in Figure 3.

The data obtained from X-ray analysis revealed that the oxamethylene bridges are anti-oriented. The bridging angles O1–C5–C4 (119.29°) and O2–C26–C27 (115°) are unequal, presumly to accommodate the high degree of torsion around the naphthyl–naphthyl bond. To relieve the macro-ring strain, the inner bond angle involving O1–C6–C15 (117.54°) is slightly compressed compared to the outer bond angle encompassing O1–C6–C7 (120.73°). The angle C14–C15–C16 (122.1°) is larger than C6–C15–C16 (119.7°) presumably to minimize the non-bonded interaction between the H13 and H18. However, the angles C13–C14–C15 and C16–C17–C18 (122.5°) are identical and the bond length C15–C16 between the two naphthalene rings at 1.490(3) Å is quite normal. The torsion angles in thienothiophene ring involving atoms [C4, C1, C2, and S2] and atoms [C3, S1, C2, and C1] are found to be −178.58(16)° and 0.65(19)°, respectively. This observation suggests that thienothiophene ring is almost planar. The inter-planner dihedral angle [C14, C15, C16, and C17] is found to be 70.3°, which is comparable to the torsional angle of 77° reported for binol.[21] Clearly, the 11-membered phane cavity in ±**6** is large enough to accommodate the twisted binol without causing appreciable deviation in the torsion angle.

6. Conclusions

Oxa-bridged cyclophanes **4**, **6**, **8**, and **10**, derived from a bi-fused thienothiophene ring and either binol or bisphenol have been synthesized and their structures established by 2D NMR spectral analysis. The molecular structure of **6** is also confirmed by a single X-ray crystallography. All the cyclophanes exhibited temperature dependent conformational behaviors. The $\Delta G^{\#}$ of 15.3 kcal/mol for bridge inversion in **4** is 2.4 kcal/mol higher compared to its ester free analog **6**. Though not a part of the *phane cavity*, the C2/C5 ester substituents make sizeable contribution to $\Delta G^{\#}$ in **4** by exerting a marked degree of steric impediment to bridge inversion. We also find that only the $-OCH_2-$ bridges undergo inversion in cyclophanes **4** and **6** with the pseudo-rotation around the naphthyl–naphthyl bond being restricted even at higher temperatures. For bis-naphthol cyclophane **8**, both the $-OCH_2-$ and the naphthyl–CH_2–naphthyl bridges undergo inversions at nearly the same rate with $\Delta G^{\#}$ of ca. 11.4 kcal/mol. However, for ester free cyclophane **10**, the bridge inversions are facile even up to −55 °C and its $\Delta G^{\#}$ can be assumed to be <11.4 kcal/mol. Evidently, the presence of an extra $-CH_2-$ spacer renders cyclophanes **8**/**10** conformationally more flexible compared to **4**/**6**, possessing a rigid naphthyl–naphthyl geometry. Our findings demonstrate that subtle structural variations could have small but significant influences on the conformational dynamics of short-bridged cyclophanes.

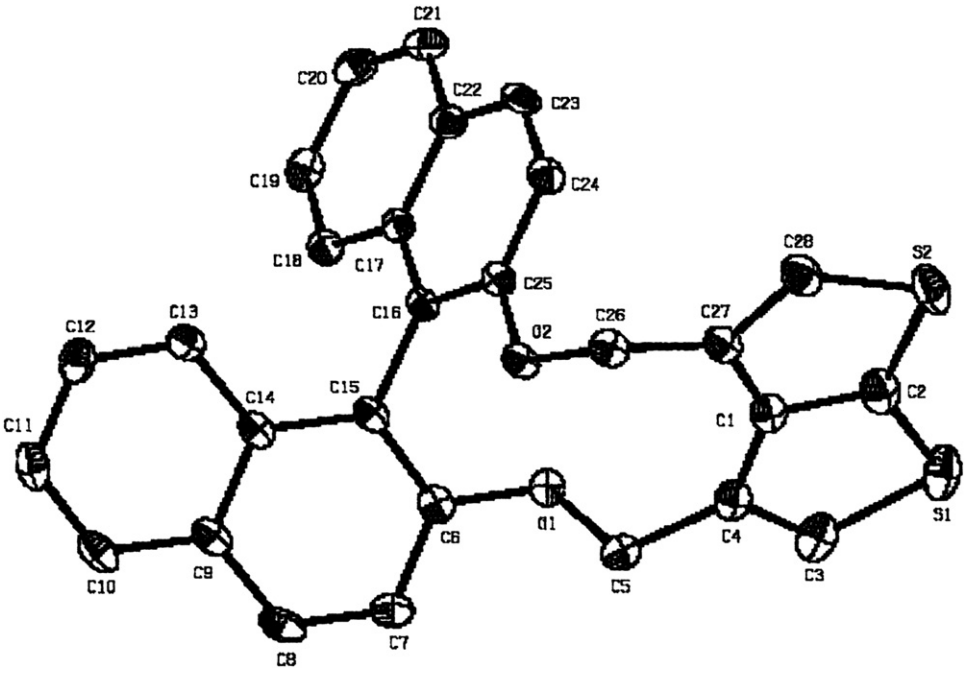

Figure 3. ORTEP plot of ±**6**.

7. Experimental

7.1. General

The chemicals and spectral grade solvents were purchased from S/D Fine Chemicals (India) and Aldrich and used as received. IR spectra were recorded on a Shimadzu FTIR-420 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were scanned in $CDCl_3$ using Bruker 300 MHz spectrometer with TMS as an internal standard. Elemental analyses were done in the Department of Chemistry, University of Mumbai on Carlo Enra instrument EA-1108 Elemental analyzer.

*7.1.1. Preparation of dibromo thienothiophene diester **2***

Diester thienothiophene **1**[15] (3.12 g, 10 mmol) and NBS (3.90 g, 21.5 mmol) were dissolved in 150 mL dried CCl_4. A catalytic amount of dibenzoyl peroxide (100 mg) was added and the reaction refluxed for 4 h on water bath. After cooling the reaction mixture to room temperature, insoluble succinimide was removed by filtration. The filtrate was distilled-off and the crude solid was repeatedly crystallized from ethanol–chloroform (3:1) to afford colorless crystals of dibromide **2** (3.71 g, 79%). Mp 130–133 °C. IR (KBr, ν, cm^{-1}): 3100, 2950, 1720, 1700, 1490, 1460, 1380, 1310, 1280, 1240, 1100, 1020, and 740. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.3 (4H, s, $-CH_2Br$), 4.5 (4H, q, $-CH_2CH_3$), 1.4 (6H, t, $-CH_2CH_3$). Anal. Calcd for $C_{14}H_{14}O_4S_2Br_2$: C, 35.75; H, 2.98; S, 34.04; Br, 13.62. Found: C, 35.64; H, 2.95; S, 34.24; Br, 13.79%.

*7.1.2. Preparation of oxa-bridged binol-thienothiophene cyclophane diester ±**4***

A solution of **2** (4.70 g, 10 mmol) and ±1,1′-bi-2-naphthol **3** (2.86 g, 10 mmol) in dry DMF (150 mL) was added dropwise to a suspension of K_2CO_3 (3.46 g, 25 mmol) in dry DMF (100 mL) at 70–75 °C during 10 h. After the addition, the reaction was continued to be stirred at this temperature for an additional 16 h. After cooling to room temperature, the reaction mixture was filtered through a pad of Celite. The filtrate was concentrated under vacuum to give a dark brown semi-solid residue. The residual solid was extracted in chloroform (3×100 mL), and the extract repeatedly washed with water, dried over anhyd Na_2SO_4, and the solvent stripped-off. The crude was purified on SiO_2 column chromatography (R_f=0.3) (pet. ether–chloroform; 60:40 as eluant) to afford ±**4** as colorless solid (3.08 g, 52%). Mp 276–278 °C. IR (KBr, ν, cm^{-1}): 3059, 2974, 2902, 1712, 1621, 1589, 1499, 1471, 1443, 1431, 1365, 1280, 1204, 1137, 1104, 1071, 1004, 921, 807, and 744. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.87 (2H, d, Ar–H), 7.80 (2H, d, Ar–H), 7.64 (2H, d, Ar–H), 7.27 (2H, t, Ar–H), 7.14 (2H, t, Ar–H), 7.11 (2H, d, Ar–H), 5.91 (4H, s, $-OCH_2-$), 4.43 (4H, q, $-CH_2CH_3$), 1.38 (6H, t, $-CH_2CH_3$). ^{13}C NMR (300 MHz, $CDCl_3$): 161.9, 154.1, 146.4, 146.1, 138.4, 134.4, 133.7, 129.7, 129.4, 127.9, 126.3, 126.2, 123.7, 63.2, 61.9, 14.3. Anal. Calcd for $C_{34}H_{26}O_6S_2$: C, 68.69; H, 4.38; S, 10.77. Found: C, 68.77; H, 4.49; S, 10.91%.

*7.1.3. Preparation of cyclophane diacid ±**5***

Dioxa cyclophane ±**4** (1.19 g, 2.0 mmol) was dissolved in alcohol (30 mL) containing 10 mL 20% KOH. The reaction was stirred and refluxed for 10 h. It was diluted with water (100 mL) and alcohol was boiled-off. After cooling, the reaction was acidified with concd HCl to precipitate the diacid cyclophane ±**5** as a colorless solid (1.02 g, 95%). Mp >300 °C (decomp.). IR (KBr, ν, cm^{-1}): 3460–2590, 2850, 1682, 1621, 1591, 1489, 1428, 1357, 1307,1270, 1223, 1088, 996, 920, 811, and 741. Anal. Calcd for $C_{30}H_{18}O_6S_2$: C, 66.91; H, 3.35; S, 11.90. Found: C, 70.03; H, 3.39; S, 11.86%.

*7.1.4. Preparation of oxa-bridged binol-thienothiophene cyclophane ±**6***

The diacid cyclophane ±**5** (0.54 g, 1 mmol) was dissolved in quinoline (10 mL). After adding Cu powder (25 mg), the reaction mixture stirred and heated up to 200 °C under N_2 atmosphere for 20 min till the evolution of CO_2 ceased. The reaction mixture was cooled to room temperature and filtered to remove Cu powder. The reaction was poured into 25% HCl (200 mL) and extracted with ether (3×50 mL). The organic extract was washed with 10% HCl to remove traces of quinoline, then with brine and dried over anhyd Na_2SO_4. The extract was concentrated and the residual solid was purified by SiO_2 column chromatography (R_f=0.39) (pet. ether–chloroform; 1:1 as eluant) to afford ±**6** as colorless solid (0.37 g, 82%). Mp 197–200 °C. IR (KBr, ν, cm^{-1}): 3052, 2924, 2873, 1620, 1590, 1507, 1471, 1430, 1353, 1325, 1271, 1230, 1082, 1002, 917, 832, 803, and 741. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (2H, d, Ar–H), 7.95 (2H, d, Ar–H), 7.60 (2H, d, Ar–H), 7.48 (2H, s, thienothiophene proton), 7.38 (2H, t, Ar–H), 7.22 (2H, t, Ar–H), 7.16 (2H, d, Ar–H), 5.42 (4H, s, $-OCH_2-$). ^{13}C NMR (300 MHz, $CDCl_3$): 153.9, 143.7, 140.2, 133.6, 130.4, 129.4, 129.1, 128.9, 127.9, 126.1, 126.0, 123.6, 119.7, 115.9, 66.5. Mass: m/z 450. Anal. Calcd for $C_{28}H_{18}O_2S_2$: C, 74.67; H, 4.00; S, 14.22. Found: C, 74.52; H, 3.87; S, 14.39%.

*7.1.5. Preparation of oxa-bridged binol-thienothiophene cyclophane (−) **6***

(−) Naphthol (286 mg, 1 mmol) was condensed with **2** (470 mg, 1 mmol) under the conditions described for ±**4**. After work-up, the crude was purified by SiO_2 column chromatography (R_f=0.39) (pet. ether–chloroform; 60:40 as eluant) to afford (−) **4** as colorless solid in (270 mg, 42% yield), $[\alpha]_D$ −186.89 (*c* 1 in $CHCl_3$). Mp and spectral data are identical naphthol with that of ±**4**. Cyclophane (−) **4** was subjected to base catalyzed hydrolysis to obtain diacid (−) **5**, which was used directly for decarboxylation and the crude product thus obtained purified by SiO_2 column chromatography as described for ±**6** to furnish (−) **6** in 83% yield, $[\alpha]_D$ −8.88 (*c* 1 in $CHCl_3$). Mp and spectral data are identical with that of ±**6**.

*7.1.6. Preparation of oxa-bridged bis-naphtho-thienothiophene diester cyclophane **8***

Dibromide **2** (2.35 g, 5 mmol) and 2,2′-dihydroxy-1,1′-diphathylmethane (1.50 g, 5 mmol) were condensed under the conditions described for ±**4**. The crude was purified by SiO_2 column chromatography (R_f=0.33) (pet. ether–chloroform; 1:1 as eluant) affording **8** as a colorless solid (638 mg, 21%). Mp 250–252 °C. IR (KBr, ν, cm^{-1}): 3052, 2980, 2935, 1718, 1707, 1623, 1594, 1506, 1406, 1431, 1365, 1305, 1275, 1135, 1103, 1063, 1101, 953, 804, and 745. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.09 (2H, d, Ar–H), 7.75 (2H, d, Ar–H), 7.69 (2H, d, Ar–H), 7.56 (2H, d, Ar–H), 7.33 (2H, t, Ar–H), 7.27 (2H, t, Ar–H), 5.94 (4H, s, $-OCH_2-$), 4.64 (2H, s, Ar–CH_2–Ar), 4.42 (4H, q, $-CH_2CH_3$), 1.36 (6H, t, $-CH_2CH_3$). ^{13}C NMR (300 MHz, $CDCl_3$): 162.0, 151.6, 146.5, 142.7, 136.5, 133.5, 129.7, 128.9, 128.9, 126.8, 123.3, 123.1, 118.1, 117.2, 61.9, 61.5, 27.3, 14.3. Anal. Calcd for $C_{35}H_{28}O_6S_2$: C, 69.08; H, 4.61; S, 10.53. Found: C, 69.19; H, 4.83; S, 10.67%.

*7.1.7. Preparation of cyclophane diacid **9***

Diester cyclophane **8** (152 mg, 0.25 mmol) was hydrolyzed as described for ±**5** to afford **9** as a colorless solid (92 mg, 66%). Mp >290 °C (decomp.). IR (KBr, ν, cm^{-1}): 3550, 2965, 1690, 1607, 1567, 1436, 1383, 1361, 1241, 1100, 1022, 828, and 750. Anal. Calcd for $C_{31}H_{20}O_6S_2$: C, 67.39; H, 3.62; S, 11.59. Found: C, 67.43; H, 3.82; S, 11.70%.

*7.1.8. Preparation of oxa-bridged bis-naphtho-thienothiophene cyclophane **10***

The diacid **9** (82 mg, 0.15 mmol) was decarboxylated as described for ±**6**. The crude was purified by SiO_2 column chromatography (R_f=0.55) (pet. ether–chloroform; 1:1 as eluant) to afford **10** as a colorless solid (26 mg, 40%). Mp 263–264 °C. IR (KBr, ν, cm^{-1}): 3053, 2925, 2877, 1620, 1590, 1507, 1469, 1434, 1353, 1325, 1271, 1230, 1082, 1004, 915, 833, 801, and 741. ^{1}H NMR (300 MHz,

$CDCl_3$): δ 8.06 (2H, d, Ar–H), 7.83 (2H, d, Ar–H), 7.76 (2H, d, Ar–H), 7.72 (2H, d, Ar–H), 7.42 (2H, s, thienothiophene proton), 7.35 (2H, t, Ar–H), 7.38 (2H, t, Ar–H), 5.42 (4H, s, $-OCH_2-$), 4.67 (2H, s, Ar–CH_2–Ar). ^{13}C NMR (300 MHz, $CDCl_3$): 151.5, 143.4, 139.8, 133.7, 131.5, 130.0, 129.8, 128.8, 128.3, 126.7, 122.7, 122.6, 117.1, 116.9, 64.9, 27.6. Mass: m/z 464. Anal. Calcd for $C_{29}H_{20}O_2S_2$: C, 75.0; H, 4.31; S, 13.79. Found: C, 74.92.10; H, 4.25; S, 13.91%.

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