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Novel supramolecular liquid crystals: synthesis and mesomorphic properties of calix[4]arene-cholesterol derivatives

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ABSTRACT

The first calix[4]arene-cholesterol liquid crystals were designed and synthesized in yields of 50–80%. Structural and conformational characterization of these new compounds had been achieved by NMR, MS, and elemental analysis. Their liquid crystalline behaviors were studied by polarizing optical microscopy, differential scanning calorimetry, and X-ray diffraction. All calix[4]arene derivatives with two or four cholesterol units show excellent mesomorphic properties of the columnar molecular arrangement of the calixarenes bowlic columns with cholesterol units as ancillary lateral columns. The long spacer and more cholesterol units were favorable for excellent mesophase.

Since Reinitzer reported his famous article on cholesteric liquid crystal (LC) in 1888,[1] all kinds of LC materials were studied and exhibited diverse physical properties of broad interest for both basic research and applied sciences, such as organic light-emitting diodes, organic field-effect transistors, organic photovoltaic cells, and gas sensors.[2–6] From then on, the design and synthesis of various liquid crystalline materials are interesting and challenging works for the chemists. Recently, much research attention was paid to the macrocycle-based liquid crystals. The mesomorphic properties of this kind of molecules could be tuned by the complexation behaviors of macrocycle units. For examples, Cammidge reported the triphenylene dimers containing a shape-persistent conjugated macrocycle or crown ether macrocycle with interesting mesomorphic properties.[7,8] Peng and Laschat, respectively, also studied the syntheses and properties of similar triphenylene dimers containing conjugated macrocycle or crown ether macrocycle.[9,10] Our group also described an interesting example of cyclodextrin-triphenylene liquid crystal lately.[11]

Calixarenes, possessing tunable 3D-shaped cavities, are the important supramolecular platforms after crown ether and cyclodextrin.[12] Various calixarene derivatives with special properties were designed and synthesized up to now.[13–17] Calixarene-based liquid crystals were also studied by introducing the long alkyl chains on calixarene skeleton.[18–23] Recently, our group presented series of triphenylene-based calixarene liquid crystals with different structures and interesting mesomorphic properties.[24–27] These researches suggested that the mesomorphic properties of calixarene LCs were mainly controlled by the structures of liquid crystal units. The spacers also made a difference on the molecular stacking behaviors of mesophase. On the other hand, it was well-known that cholesteric LCs have attracted considerable attention owing to their unique properties, such as selective reflection of circularly polarized light, high optical rotator power, circular dichroism and electrooptic effect.[28–31] Cholesterol was used as an excellent structural unit to construct all kinds of liquid crystalline materials with interesting mesomorphic properties.[6,32–34] Lately, two new cholesteryl derivatives of calix[4]arene were described as a mechano-responsive molecular gels, but no liquid crystalline property was investigated.[35] In the present study, we wish to report the design, syntheses, and mesomorphic properties of the first examples of cholesterol-based calixarene liquid crystals.

The synthetic routes for calix[4]arene-cholesterol liquid crystals **3a**, **3b**, **4a,** and **4b** are illustrated in Scheme 1. Due to the substituted patterns of calix[4]arene and the length of spacers making great influences on mesomorphic properties,[24–27] 1,3-bis-substituted and tetra-substituted calix[4]arenes with different alkyl bridging chains were designed as target molecules. By reacting cholesterol with 2-chloroacetic acid or 4-chlorobutanoic acid in CH_2Cl_2 using *N*,*N*′-dicyclohexylcarbodiimide (DCC) as coupling reagent and 4-dimethylaminopyridine (DMAP) as catalyst, the cholesterol chlorinated derivatives **2a** and **2b** were obtained in yields of 90% and 88%, respectively. Subsequently, the novel cholesterol-1,3-bis-substituted calix[4]arene derivatives **3a** and **3b** were

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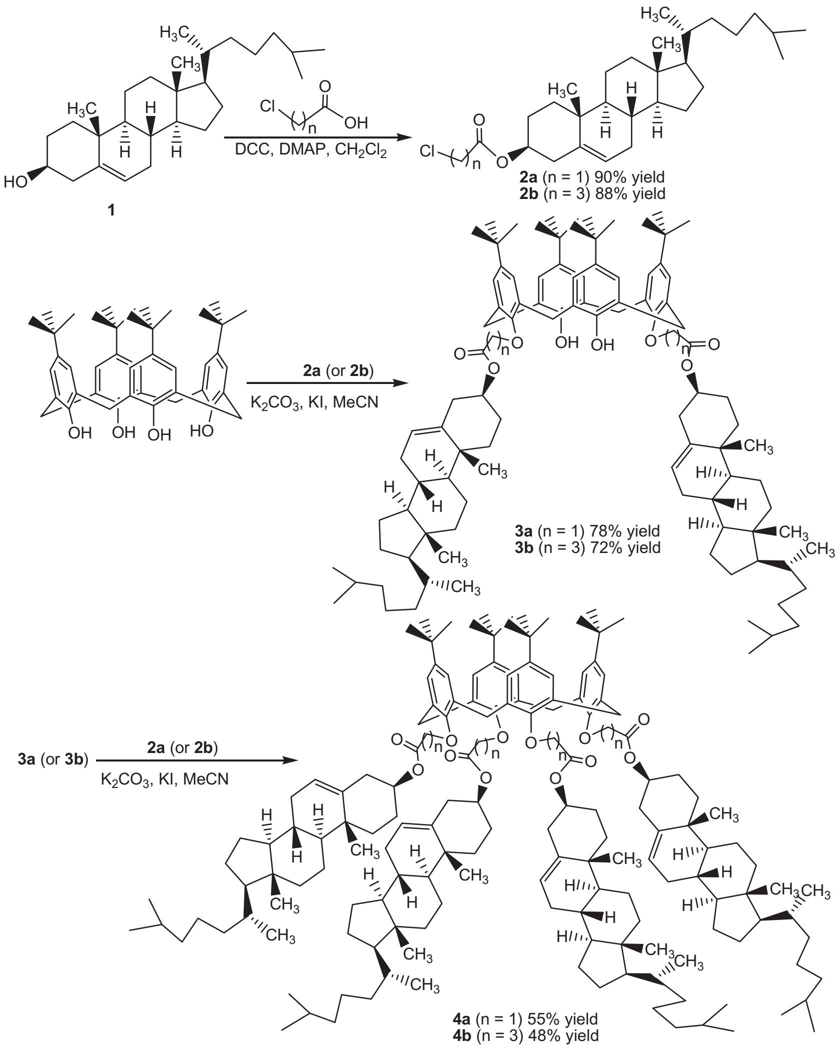

Scheme 1. Synthetic routes of compounds **3a**, **3b**, **4a,** and **4b**.

prepared by reacting calix[4]arene with compound **2a** or **2b** (2 equiv) in K_2CO_3/MeCN system using KI as catalyst. The yields were as high as 78% and 72% after column chromatography, respectively. Furthermore, by treating compound **3a** or **3b** with excess amount of compound **2a** or **2b** in K_2CO_3/MeCN system, the novel cholesterol-tetra-substituted calix[4]arene **4a** and **4b** were given in yields of 55% and 48% after column chromatography, respectively. In this reaction, no matter how changing the ratios of materials or prolonging the reaction times, the yields were stable with 50% approximately. These phenomena might be explained by that the steric hindrance of bulky cholesterol units made unfavorable effects on tetra-substituted calix[4]arene. On the other hand, we had also tried to obtain compounds **4a** and **4b** by reacting calix[4]arene with excess amount (more than 4 equiv) of compound **2a** or **2b** directly in same reaction condition. But the results showed that compounds **3a** and **3b** were always the main products. The yields of compounds **4a** and **4b** were lower than 25% and the separation was difficult due to some uncertain products appearing in these reactions.

The structures of new cholesterol-substituted calix[4]arene derivatives **3a**, **3b**, **4a,** and **4b** were confirmed by element analyses, ESI-MS, and NMR spectra. In their ESI-MS spectra, corresponding molecular ion peaks at 1501.26, 1557.39, 2354.64, and 2466.82 were observed, which suggested these novel compounds possessed the corresponding bis-substituted and tetra-substituted structures as expected. In the ^{1}H NMR spectra of compounds **3a** and **3b**, two singlets (1:1) for the *tert*-butyl groups, one pair of doublets (1:1) for the methylene bridges and two singlets (1:1) for ArH certainly indicated the cone conformation for calix[4]arene units. As to compounds **4a** and **4b**, their ^{1}H NMR spectra showed a singlet for the *tert*-butyl groups, one pair of doublets (1:1) for the methylene bridges, and a singlet for ArH, suggesting the cone conformation for calix[4]arene units. Moreover, their ^{13}C NMR spectra also exhibited corresponding peaks, for examples, the peaks for C=O, OCH, and OCH_2 at approximately 170, 75, and 74 ppm, respectively. These ^{13}C NMR data supported again the structures and conformations of compounds **3a**, **3b**, **4a,** and **4b**.

The mesomorphic behaviors of compounds **3a**, **3b**, **4a,** and **4b** were preliminarily investigated by differential scanning calorimetry (DSC). The results are shown in Figure 1 and Table 1. It could be seen that all new compounds possessed two thermic peaks on both second heating and cooling, respectively. Compound **3a** exhibited two endothermic peaks at 63.7 °C and 131.6 °C on heating, and two exothermic peaks at 56.9 °C and 124.1 °C on cooling. As to compound **3b**, the corresponding endothermic (or exothermic) peaks were at 43.9 (or 47.1) °C and 143.2 (or 131.9) °C upon heating (or cooling), respectively. Moreover, after calculation, the scope of mesomorphic temperature of compound **3b** was as wide as 99.3 °C, which was bigger than that of compound **3a** (67.9 °C). Compound **4a** had two endothermic peaks at 53.5 °C and 154.8 °C on

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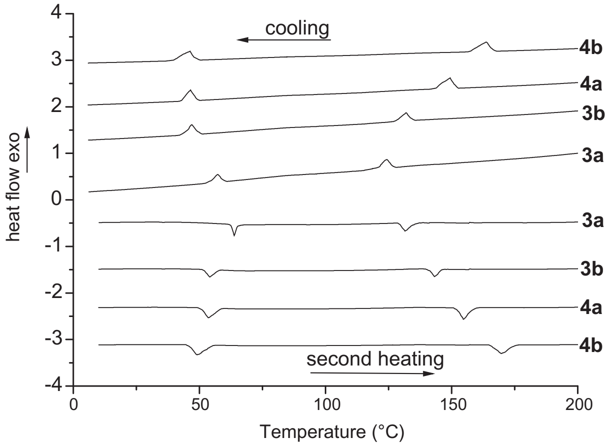

Figure 1. The DSC traces of compounds **3a**, **3b**, **4a**, and **4b** on second heating and cooling (scan rate 10 °C min^{-1}).

Table 1
Transition temperatures (°C) and enthalpies (kJ mol^{-1}) of compounds **3a**, **3b**, **4a**, and **4b**

Compd	Phase transition[a]	$T(\Delta H)$ heating scan	$T(\Delta H)$ cooling scan
3a	Cr-Col(Col-Cr)	63.7(4.01)	56.9(4.81)
	Col-Iso(Iso-Col)	131.6(5.27)	124.1(5.32)
3b	Cr-Col(Col-Cr)	43.9(3.66)	47.1(3.96)
	Col-Iso(Iso-Col)	143.2(4.92)	131.9(4.87)
4a	Cr-Col(Col-Cr)	53.5(5.41)	46.7(4.61)
	Col-Iso(Iso-Col)	154.8(6.53)	149.3(6.82)
4b	Cr-Col(Col-Cr)	49.5(4.31)	46.4(4.77)
	Col-Iso(Iso-Col)	170.1(5.84)	163.6(6.68)

[a] Cr = crystalline, Col = columnar phase, Iso = isotropic.

heating, and two exothermic peaks at 46.7 °C and 149.3 °C on cooling, while compound **4b** showed the corresponding temperatures at 49.5 (or 46.4) °C and 170.1 (or 163.6) °C for the endothermic (or exothermic) peaks. The scope of mesomorphic temperature of compound **4b** (121.4 °C) was also bigger than that of compound **4a** (101.3 °C). Judging from the heats of fusion and hysteresis between corresponding crystallization and melting peaks, two phase transitions of solid state-mesophase and mesophase-isotropic phase on cooling and heating existed for compounds **3a**, **3b**, **4a,** and **4b**, which were also confirmed by polarizing optical microscopy (POM). Compound **3b** (or **4b**) presented a wider scope of mesophase than compound **3a** (or **4a**), suggesting that the spacers between cholesterol unit and calixarene unit influenced on the mesomorphic properties greatly. The long spacer was more favorable for each part of the structure to find its own counterpart in the resulting mesophase. Moreover, it could be seen that the scope of mesomorphic temperature of compounds **4a** and **4b** with four cholesterol units were bigger than that of compounds **3a** and **3b** with two cholesterol units. These results might imply that the amounts of cholesterol units also played the important roles on mesomorphic properties. The more cholesterol units the compound had, the wider temperature scope of mesophase it possessed.

Furthermore, based on the DSC results, the mesophase textures of compounds **3a**, **3b**, **4a**, and **4b** were studied by POM. For all of them, two phase transitions of solid state-mesophase and mesophase-isotropic phase was clearly observed on heating and cooling. The phase transform temperatures were approximately in accord with the endothermic (or exothermic) peaks of DSC on heating and cooling. Figure 2 shows the liquid crystalline textures of compounds **3a**, **3b**, **4a,** and **4b** at corresponding temperatures under POM. One could see that the clear special textures on cooling for compounds **3a**, **3b**, **4a,** and **4b** were observed, respectively. These textures were similar to the typical focal-conic columnar liquid

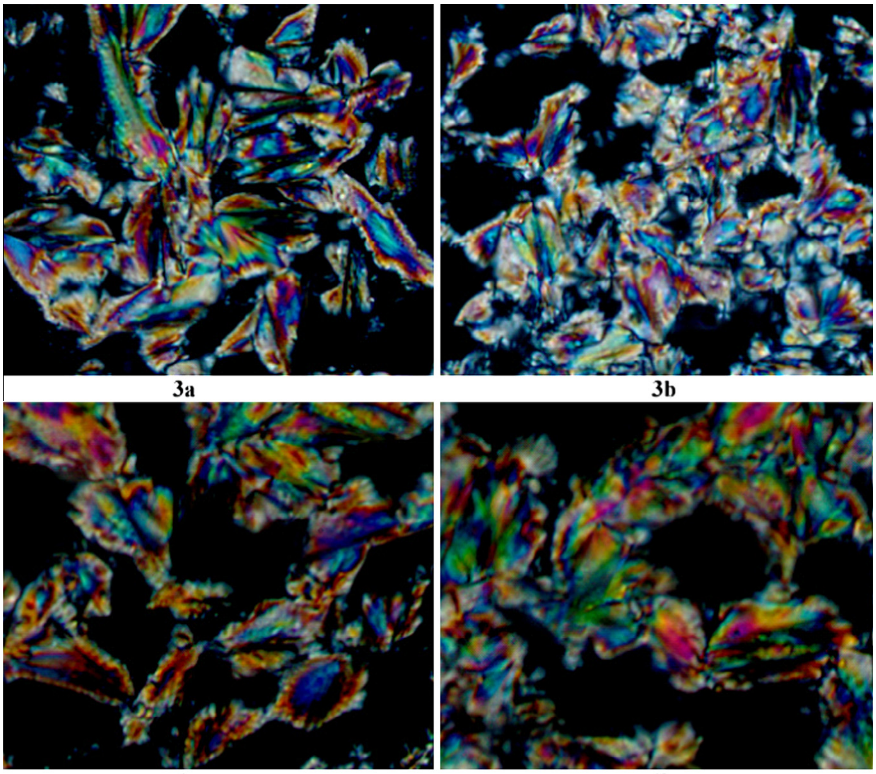
3a **3b** **4a** **4b**

Figure 2. Mesomorphic textures of compounds **3a**, **3b**, **4a,** and **4b** obtained under POM on cooling at 80 °C (×400).

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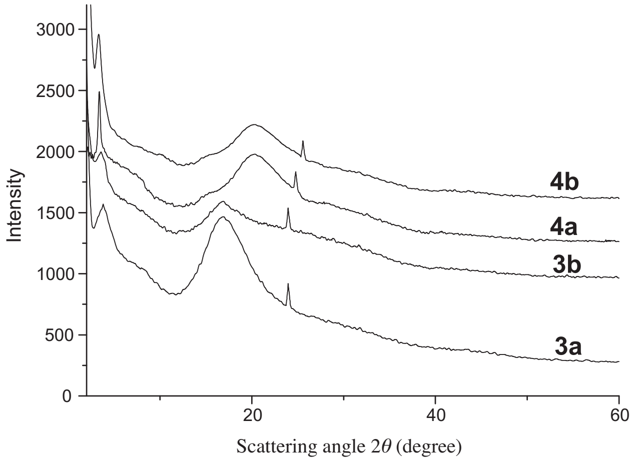

Figure 3. XRD traces of compounds **3a**, **3b**, **4a**, and **4b** measured at 80 °C

crystals, which were supported further by X-ray diffraction (XRD) analysis.

Compounds **3a**, **3b**, **4a,** and **4b** were also studied by XRD at the corresponding temperatures of mesomorphic states. The results are shown in Figure 3. As can be seen all of them exhibited a long range orientation ($2\theta = 3.3$–$3.8°$, sharp) and two short disordered orientations ($2\theta = 13$–$26°$, broad and $2\theta = 24°$, sharp). These results suggested that they might adopt bowlic columnar phase for liquid crystalline behaviors. The CPK molecular model indicated that the diameters of compounds **3a**, **3b**, **4a,** and **4b** including the cholesterol units were 26–28 Å approximately. Thus, the peaks at $2\theta = 3.3°$–$3.8°$ suggested the distances of 23.3–26.7 Å, which agreed approximately with the diameters of compounds **3a**, **3b**, **4a,** and **4b**, indicating the lattice constant arising from the columnar structures. Also, the reflections of 13–26° (3.5–6.8 Å broad halo) and 24° (3.7 Å) were assigned to the average distances of columnar structures of the molten cholesterol units and the intracolumnar order of calixarene units, respectively. The broad halo reflections of 13–26° might be attributed to the cooperating influences of the bridging alkyl spacers and the long alkyl groups on cholesterol units. These results suggested compounds **3a**, **3b**, **4a,** and **4b** adopted columnar phases for liquid crystalline behaviors. A survey of the literatures also indicated that the similar XRD traces were reported for calix[4]arene bowlic columnar liquid crystals with aliphatic chains.[24–27,36–40] Thus, it could be deduced that compounds **3a**, **3b**, **4a,** and **4b** possessed the columnar molecular arrangement of the calixarenes bowlic column with cholesterol units as ancillary lateral columns as shown in Figure 4. Moreover, the different lengths of spacers and the different amounts of cholesterol units on calixarene skeleton influenced on the column molecular stacking in a degree. The broad peaks for the molten cholesterol units of compounds **3a** and **3b** with two cholesterol units concentrated on 14–20° approximately, but the corresponding peaks for compounds **4a** and **4b** with four cholesterol units centered on 17–23° approximately. The shifts to wider angles from compounds **3a** and **3b** to compounds **4a** and **4b** might be ascribed to that the more cholesterol units in compounds **4a** and **4b** produced the more crowded stacking, resulting in the closer distances of the molten cholesterol units than compounds **3a** and **3b**.

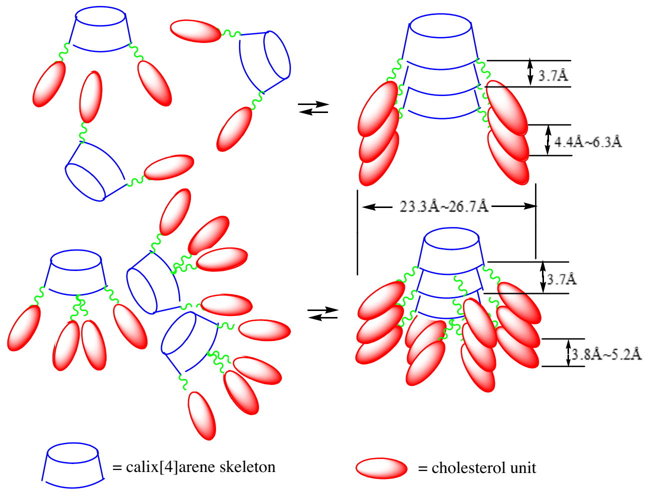

Figure 4. Schematic representations of the columnar molecular arrangements.

In conclusion, the design, synthesis, and mesomorphic properties of the first calix[4]arene-cholesterol liquid crystals were reported for the first time. By reacting cholesterol chlorinated derivatives with calix[4]arene, the bis-substituted and tetra-substituted calix[4]arene cholesterol derivatives were obtained in yields of 50–80%. Their structures and conformations were confirmed by NMR, MS, and elemental analysis. Their mesomorphic behaviors were studied by DSC, POM, and XRD. All of them showed excellent mesomorphic properties of the columnar molecular arrangement of the calixarenes bowlic column with cholesterol units as ancillary lateral columns. The scope of mesomorphic temperature of compounds **4a** and **4b** with four cholesterol units were as wide as 101.3 °C and 121.4 °C, respectively. The long spacers and more cholesterol units are favorable for producing excellent mesomorphic properties. The studies on the characteristic optical properties, complexation properties, and their influences on mesomorphic properties will be investigated in the following work.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.12.137.

References and notes

1. Reinitzer, F. *Monatsh. Chem.* **1888**, *9*, 421–441.
2. Sergeyev, S.; Pisula, W.; Geerts, Y. H. *Chem. Soc. Rev.* **2007**, *36*, 1902–1929.
3. Laschat, S.; Baro, A.; Steinke, N.; Giesselmann, F.; Hagele, C.; Scalia, G.; Judele, R.; Kapatsina, E.; Sauer, S.; Schreivogel, A.; Tosoni, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 4832–4887.
4. Kato, T.; Mizoshita, N.; Kishimoto, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 38–68.
5. Kumar, S. *Chem. Soc. Rev.* **2006**, *35*, 83–109.
6. Yelamaggad, C. V.; Shanker, G.; Hiremath, U. S.; Prasad, S. K. *J. Mater. Chem.* **2008**, *18*, 2927–2949.
7. Li, J.; He, Z.; Gopee, H.; Cammidge, A. N. *Org. Lett.* **2010**, *12*, 472–475.
8. Zhang, L.; Gopee, H.; Hughes, D.; Cammidge, A. N. *Chem. Commun.* **2010**, 4255–4257.
9. Wang, D.; Hsu, J. F.; Bagui, M.; Dusevich, V.; Wang, Y.; Liu, Y.; Holder, A.; Peng, Z. *Tetrahedron Lett.* **2009**, *50*, 2147–2149.
10. Kaller, M.; Deck, C.; Meister, A.; Hause, G.; Baro, A.; Laschat, S. *Chem. Eur. J.* **2010**, *16*, 6326–6337.
11. Yang, F. F.; Zhang, Y. M.; Guo, H. Y.; Bai, X. Y. *New J. Chem.* **2013**, *37*, 2275–2279.
12. For books on calixarenes, see: (a) Asfari, Z.; Böhmer, V.; Harrowfield, J.; Vicens, J. *Calixarenes*; Kluwer Academic Publishers: Dordrecht, 2001; (b) Mandolini, L.; Ungaro, R. *Calixarenes in Action*; Imperial College Press: London, 2000.
13. Casnati, A.; Sansone, F.; Ungaro, R. Calixarene Receptors in Ion Recognition and Sensing. In *Advances in Supramolecular Chemistry*; Cerberus Press: South Miami, FL, 2004.

14. Lhoták, P. Anion Receptors Based on Calixarenes. In *Anion Sensing in Topics in Current Chemistry*; Springer: Berlin, 2005.
15. Yakovenko, A. V.; Boyko, V. I.; Kalchenko, V. I.; Baldini, L.; Casnati, A.; Sansone, F.; Ungaro, R. *J. Org. Chem.* **2007**, *72*, 3223–3231.
16. Schazmann, B.; Diamond, D. *New J. Chem.* **2007**, *31*, 587–592.
17. Yang, F. F.; Guo, H. Y.; Vicens, J. *J. Incl. Phenom. Macrocycl. Chem.* **2014**, *80*, 177–186.
18. Kohmoto, S.; Someya, Y.; Masu, H.; Yamaguchi, K.; Kishikawa, K. *J. Org. Chem.* **2006**, *71*, 4509–4515.
19. Cometti, G.; Dalcanale, E.; Vosel, A. D.; Levelut, A. M. *J. Chem. Soc., Chem. Commun.* **1990**, *2*, 163–165.
20. Bonsignore, S.; Cometti, G.; Dalcanale, E.; Vosel, A. D. *Liq. Cryst.* **1990**, *8*, 639–649.
21. Lo, P. K.; Chen, D.; Meng, Q.; Wong, M. S. *Chem. Mater.* **2006**, *18*, 3924–3930.
22. Budig, H.; Diele, S.; Paschke, R.; Ströhl, D.; Tschierske, C. *J. Chem. Soc., Perkin Trans. 2* **1996**(9), 1901–1906.
23. Koh, K. N.; Araki, K.; Komori, T.; Shinkai, S. *Tetrahedron Lett.* **1995**, *36*, 5191–5194.
24. Yang, F. F.; Guo, H. Y.; Xie, J. W.; Lin, J. R. *Eur. J. Org. Chem.* **2011**, *26*, 5141–5145.
25. Yang, F. F.; Xu, B. T.; Guo, H. Y.; Xie, J. W. *Tetrahedron Lett.* **2012**, *53*, 1598–1602.
26. Yang, F. F.; Bai, X. Y.; Guo, H. Y.; Li, C. C. *Tetrahedron Lett.* **2013**, *54*, 409–413.
27. Hong, B. Q.; Yang, F. F.; Guo, H. Y.; Jiao, Z. Y. *Tetrahedron Lett.* **2014**, *55*, 252–255.
28. Bobrovsky, A. Y.; Boiko, N. I.; Shibaev, V. P. *Polym Sci.* **1998**, *40*, 232–242.
29. Kurihara, S.; Nomiyma, S.; Nonska, T. *Chem. Mater.* **2001**, *13*, 1992–1998.
30. Tamaoki, N.; Aoki, Y.; Moriyama, M. *Chem. Mater.* **2003**, *15*, 719–724.
31. Lee, J. W.; Park, Y.; Jin, J. *J. Mater. Chem.* **2003**, *13*, 1367–1375.
32. Kim, Y.; Wada, M.; Tamaoki, N. *J. Mater. Chem. C* **2014**, *2*, 1921–1926.
33. Achalkumar, A. S.; Hiremath, U. S.; Shankar, D. S.; Yelamaggad, C. V. *Liq. Cryst.* **2011**, *38*, 1563–1589.
34. Tandel, R. C.; Patel, N. K. *Liq. Cryst.* **2014**, *41*, 514–521.
35. Cai, X.; Wu, Y.; Wang, L.; Yan, N.; Liu, J.; Fang, X.; Fang, Y. *Soft Matter* **2013**, *9*, 5807–5812.
36. Yonetake, K.; Nakayama, T.; Ueda, M. *J. Mater. Chem.* **2001**, *11*, 761–767.
37. Komori, T.; Shinkai, S. *Chem. Lett.* **1993**, *8*, 1455–1458.
38. Xu, B.; Swager, T. M. *J. Am. Chem. Soc.* **1993**, *115*, 1159–1160.
39. Xu, B.; Swager, T. M. *J. Am. Chem. Soc.* **1995**, *117*, 5011–5012.
40. Patel, R. V.; Panchal, J. G.; Rana, V. A.; Menon, S. K. *J. Incl. Phenom. Macrocycl. Chem.* **2010**, *66*, 285–295.

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