A New Route to 1,3-Disubstituted Benzo[c]thiophenes

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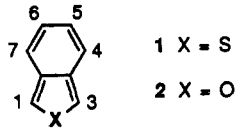
A facile synthesis of 1,3-dichlorobenzo[c]thiophene **3** is described. Lithium–chlorine exchange of **3**, followed by reaction with various electrophiles, provides a route to 1-acyl-3-chlorobenzo[c]thiophenes, as well as to the very stable 1,3-bis(*tert*-butyldimethylsilyl)benzo[c]thiophene (**9**). Compound **9** undergoes silyl replacement reactions with acylating agents, as well as an unusual oxidative desilylation by I_2 or $TiCl_4$, to give the capped disilylated dimer, trimer, and tetramer (**16**, **17**, and **18**) of benzo[c]thiophene.

Benzo[c]thiophene(isothianaphthene, ITN, **1**) and benzo[c]furan (isobenzofuran, IBF, **2**) form a pair of closely related and highly reactive *o*-quinonoid heterocycles. In contrast to the chemistry of isobenzofuran, which has been extensively explored in recent years, that of isothianaphthene has been only sparsely investigated. A modest number of stable ITN derivatives substituted at the 1- and 3-positions by aryl, alkyl, or carboxyl groups are known; all of these result from direct ring syntheses rather than by electrophilic substitution reactions.[1] The parent ITN **1** was unknown until 1962;[2] an improved synthesis using a Pummerer-type dehydration was reported in 1966.[3] The only known reactions of ITN itself are Diels–Alder additions across the 1- and 3-positions[2,3] and its ready oxidative polymerization to give an interesting conducting polymer having an unusually small band gap.[4]



1 X = S

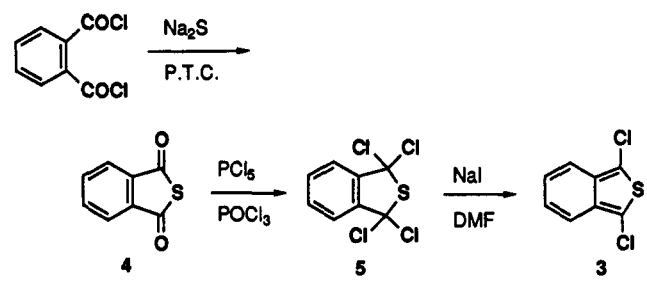
2 X = O

Although no α-halo derivatives of ITN have been described, such compounds could provide a valuable entry to a variety of new ITN derivatives. We now report a facile synthesis of the previously unknown 1,3-dichloro-ITN **3**, as well as the use of this compound to achieve a number of synthetic transformations in the ITN series.

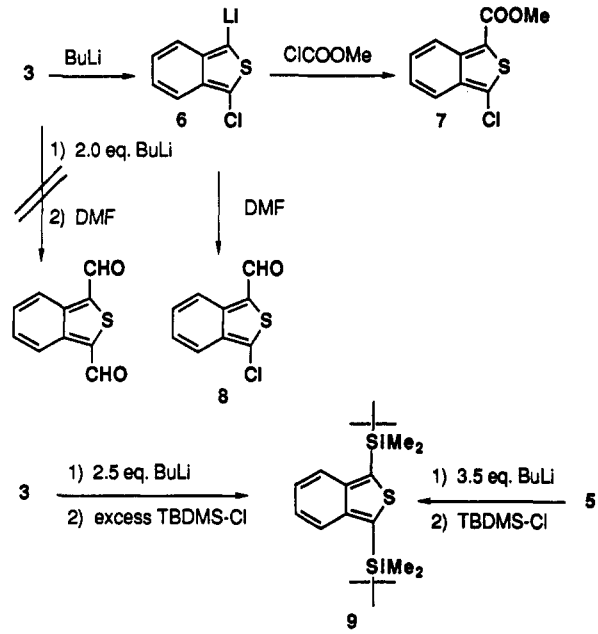
Dichloride **3** was easily prepared in several steps from commercial *o*-phthaloyl chloride. Thus, reaction of *o*-phthaloyl chloride with sodium sulfide under phase-transfer conditions gave thiophthalic anhydride **4**[5] which, in turn, was heated with phosphorus pentachloride and phosphorus oxychloride to give the known 1,1,3,3-tetrachloro compound **5**.[6] The latter tetrachloride reacted readily with sodium iodide in cold dimethylformamide to give dichloride **3** as pale yellow crystals, mp 57–58 °C (Scheme I). The dichloride was quite stable to storage under nitrogen in the refrigerator, although it darkens somewhat on keeping.

Dichloride **3** reacts readily with *n*-butyllithium to afford solutions of the monochloro monolithio derivative **6**. Reaction of this intermediate with either methyl chloroformate or with DMF yielded, respectively, the chloro ester **7** or the chloro aldehyde **8** in good yield. Treatment of dichloride **3** with 2 equiv of *n*-butyllithium followed by excess DMF did not yield a dialdehyde, indicating that 1,3-dilithio-ITN was not produced. On the other hand, when dichloride **3** was reacted with 2.5 equiv of *n*-butyllithium at −78 °C, followed by excess *tert*-butyldimethylsilyl chloride (TBDMS-Cl) and the reaction mixture was then warmed to room temperature, 1,3-bis(*tert*-butyldimethylsilyl)benzo[c]thiophene (**9**) was formed in good yield (Scheme II). In this case, the 1-chloro-3-lithio intermediate **6** undergoes successive silylation, lithium–halogen exchange, and further silylation more rapidly than the reaction of *n*-butyllithium with the TBDMS-Cl reagent. Remarkably, the same product **9** can be prepared in 85% yield by direct treatment of tetrachloride **5** with 3.5 equiv of *n*-butyllithium followed by TBDMS-Cl. In this reaction, dichloride **3** is apparently generated in situ by

Scheme I



Scheme II



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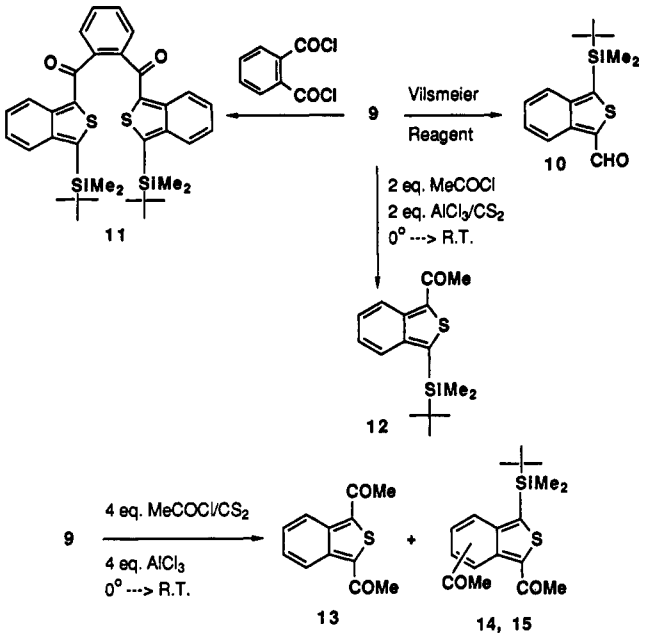
Scheme III



the first equivalent of lithium reagent.

Disilyl compound **9** forms pale yellow crystals which can be stored indefinitely in the presence of air at room temperature. Since it is well established that silyl groups in arylsilanes are readily displaced by electrophiles,[7] disilyl compound **9** seemed to be an ideal stable substitute for the exceedingly reactive parent ITN in an electrophilic substitution study.

Replacement of one of the two silyl groups of **9** took place readily using Vilsmeier reagent, as well as *o*-phthaloyl chloride or acetyl chloride under Friedel–Crafts conditions to give the monocarboxaldehyde **10**, the phthaloyl derivative **11**, or the monoacetyl compound **12**, respectively. Replacement of both the silyl groups of **9** by the Vilsmeier reagent failed, but 1,3-diacetyl-ITN **13** was formed in reasonable yield from acetyl chloride under forcing conditions along with smaller amounts of two diacetyl derivatives which still contained a silyl substituent; these were assigned the tentative structures **14** and **15** based upon NMR data (Scheme III).

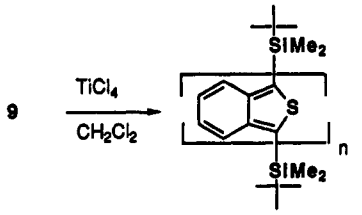
Attempts to synthesize 1,3-diiodo-ITN by treatment of disilyl compound **9** with iodine failed. The reaction afforded instead, a black polymer as well as nonpolar yellow, red, and violet products. The same three products were formed in better yield by reaction of **9** with titanium tetrachloride. These stable products, of which the yellow was the major constituent, proved to be the capped disilylated dimer, trimer, and tetramer of ITN (**16**, **17**, and **18**), respectively. Oligomers of this type are quite novel and are particularly interesting in view of the current interest in the conducting polymer derived from ITN (Scheme IV).

The formation of dimer **16** probably proceeds via a radical mechanism as illustrated below (Scheme V) for the case of titanium tetrachloride. It should be mentioned that nonreducible Lewis acids (i.e., $AlCl_3$ or BF_3) did not react with **9** to give the oligomer series.

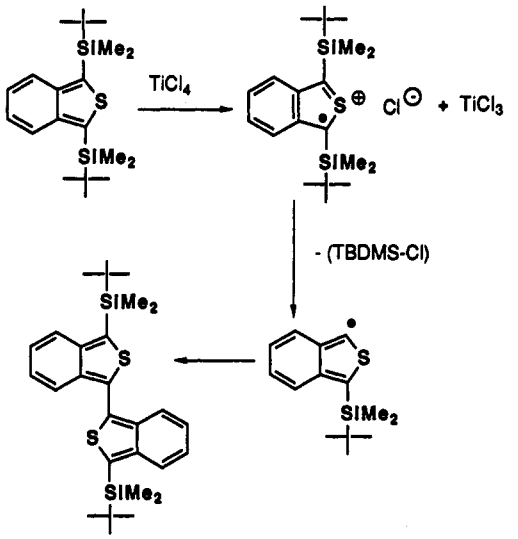
Experimental Section

General. All extracts were washed with water to neutrality and dried over anhydrous Na_2SO_4. All NMR spectra were determined in $CDCl_3$ solution and are described in ppm downfield from TMS.

Scheme IV



Scheme V



1,1,3,3-Tetrachlorothiophthalan (5). An intimate mixture of thioanhydride **4** (24.6 g, 0.15 mol),[5] phosphorus pentachloride (78.0 g, 0.37 mol), and phosphorus oxychloride (2.0 mL) was heated in an oil bath (160 °C) for 15 h. Phosphorus oxychloride was removed under reduced pressure. Toluene was added to the residue and removed by distillation (2x). The residue was dissolved in chloroform, which was washed with a 1 M sodium bicarbonate solution several times and with water twice. The organic extract was evaporated, and the residue was crystallized from *n*-hexane with decolorizing carbon to give 34.2 g (yield 83.2%) of the product **5** as white crystals: mp 111–112 °C (lit.[6] 112–113 °C); ^1H NMR δ 7.62 (2 H, dd, J = 5.8, 3.2 Hz, Ar-H), 7.78 (2 H, dd, J = 6.0, 3.2 Hz, Ar-H).

1,3-Dichloroisothianaphthene (3). To a stirred solution of (2.74 g, 10 mmol) of tetrachloride **5** in dimethylformamide (10 mL) was added sodium iodide (3.0 g, 20 mmol) at 0 °C under nitrogen. After being stirred overnight at room temperature, the reaction mixture was poured into a mixture of ice and 1 M sodium thiosulfate (100 mL) and was extracted with *n*-hexane. The dried organic extract was treated with decolorizing carbon, filtrated through neutral alumina, and concentrated under reduced pressure at room temperature to give the pure product **3** (1.23 g, 60.1%) as a pale yellow crystalline solid: mp 57–58 °C; ^1H NMR δ 7.08 (2 H, dd, J = 7.2, 3.2 Hz, Ar-H), 7.45 (2 H, dd, J = 6.8, 3.2 Hz, Ar-H); MS m/e 202 (M^+, 100), 167 (M^+ – Cl, 50), 132 (M^+ – 2Cl, 28), 123 (34). Anal. Calcd for $C_8H_4Cl_2S$: C, 47.31; H, 1.99; S, 15.79. Found: C, 47.39; H, 2.01; S, 15.87.

1-Chloro-3-(methoxycarbonyl)isothianaphthene (7). *n*-Butyllithium (2.5 M, 0.22 mL, 0.55 mmol) was added to a stirred solution of dichloride **3** (0.1 g, 0.5 mmol) in THF (2 mL) under nitrogen at –78 °C, followed by a solution of methyl chloroformate (0.052 g, 0.55 mmol) in THF (0.5 mL). The mixture was stirred overnight at room temperature and poured into ice–water. The product was extracted into ether. Removal of ether and chromatography of the residue (silica/*n*-hexane) yielded ester **7** (85 mg, 75.1% yield) as a yellow crystalline solid. Recrystallization

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from acetonitrile yielded pure **7**: mp 50–51 °C; ^{1}H NMR δ 7.38 (2 H, m, Ar-H), 7.61 (1 H, dd, J = 8.6, 1.0 Hz, Ar-H), 8.38 (1 H, dd, J = 8.6, 0.6 Hz, Ar-H); MS m/e 226 (M^+, 24), 195 (100), 183 (6), 167 (60), 132 (52); IR (KBr) 1710, 1520, 1450, 1400, 1340, 1270, 1210 cm^{-1}; UV (CH_2Cl_2) λ_{max} (log ϵ) 375 (4.05), 321 (3.55), 245 (3.80), 231 (3.91), 214 (3.06) nm. Anal. Calcd for $C_{10}H_7ClO_2S$: C, 52.99; H, 3.11; S, 14.12. Found: C, 53.22; H, 3.17; S, 14.02.

1-Chloro-3-formylisothianaphthene (8). n-Butyllithium (2.5 M, 0.5 mL, 1.25 mmol) was added to a stirred solution of dichloride **3** (0.1 g, 0.5 mmol) in THF (2 mL) under nitrogen at −78 °C. The mixture was warmed to 0 °C, treated with DMF (0.1 g, 1.5 mmol), stirred for 10 min more, and then poured into ice–hydrochloric acid. The product was extracted into ether. The dried extract was filtered, decolorized with charcoal, and evaporated. The residue was subjected to column chromatography (silica, n-hexane/benzene = 1/1) to give 85.7 mg (87.2%) of the crude product **8** as a greenish yellow crystalline solid. Recrystallization from n-hexane gave an analytically pure sample as yellow crystals (71.1 mg, 72.5%): mp 86–87 °C; ^{1}H NMR δ 7.29–7.47 (2 H, m, Ar-H), 7.66 (1 H, d, J = 8.6 Hz, Ar-H), 8.21 (1 H, d, J = 9.2 Hz, Ar-H), 10.22 (1 H, s, CHO); MS m/e 196 (M^+, 100), 168 (37), 132 (30); UV (CH_2Cl_2) λ_{max} (log ϵ) 392 (3.92), 3.27 (3.36), 233 (3.53) nm. Anal. Calcd for C_9H_5ClOS: C, 54.97; H, 2.56; S, 16.30. Found: C, 55.21; H, 2.58; S, 16.17.

1,3-Bis(*tert*-butyldimethylsilyl)isothianaphthene (9). Method A. A solution of dichloride **3** (0.1 g, 0.5 mmol) in THF (2 mL) was treated with n-butyllithium (2.5 M, 0.5 mL, 1.25 mmol) at −78 °C followed by the addition of TBDMS-Cl (0.23 g, 1.5 mmol) in THF (0.5 mL). The mixture was warmed to room temperature and stirred for 30 min more. It was poured into ice–water, and the product was extracted into n-hexane. The residue was subjected to flash column chromatography (neutral alumina, n-hexane) to give a quantitative yield of the crude product **9** as a yellow crystalline solid. Recrystallization from acetonitrile gave 140 mg (77%) of pure **9** as pale yellow crystals: mp 78 °C; ^{1}H NMR δ 0.50 (12 H, s, CH_3), 0.94 (18 H, s, CH_3), 7.08 (2 H, dd, J = 6.6, 2.8 Hz, Ar-H), 7.79 (2 H, dd, J = 7.0, 2.8 Hz, Ar-H); MS m/e 362 (53.6), 305 (100), 249 (24.42), 233 (12.8), 191 (27.2), 159 (11.12), 145 (21.01); UV (CH_2Cl_2) λ_{max} (log ϵ) 262 (3.86), 348 (3.95), 235 (4.10) nm. Anal. Calcd for $C_{20}H_{34}SSi_2$: C, 66.23; H, 9.45; S, 8.84. Found: C, 66.33; H, 9.47; S, 8.92.

Method B. To a stirred solution of tetrachloride **5** (1.37 g, 5 mmol) in THF (20 mL) was added n-butyllithium (2.5 M, 7.0 mL, 17.5 mmol) dropwise at −78 °C followed by the addition of a THF solution (2 mL) of TBDMS-Cl (1.9 g, 12.5 mmol). The reaction mixture was allowed to warm to room temperature and was stirred for an additional 30 min. The resulting dark green reaction mixture was worked up as described in method A to give **9** (1.53 g; yield 84.8%).

1-(*tert*-Butyldimethylsilyl)-3-formylisothianaphthene (10). To a stirred solution of Vilsmeier reagent which was prepared from phosphorus oxychloride (320 mg, 2.1 mmol) and DMF (150 mg, 2.1 mmol) in dichloromethane (2 mL) was added a solution of disilyl compound **9** (360 mg, 1 mmol) in dichloromethane (1 mL) dropwise at room temperature. After stirring for 15 h, the reaction mixture was poured into a 0.5 M sodium carbonate solution (25 mL) with vigorous stirring. The product was extracted with ether. The residue was subjected to column chromatography (silica, n-hexane/benzene = 1/1) to give **10** (261 gm, 94%). Recrystallization from acetonitrile gave yellow crystals: mp 90–92 °C; ^{1}H NMR δ 0.55 (6 H, s, CH_3), 0.96 (9 H, s, CH_3), 7.25–7.45 (2 H, m, Ar-H), 7.81 (1 H, d, J = 8.7 Hz, Ar-H), 8.40 (1 H, d, J = 8.7 Hz, Ar-H), 10.29 (1 H, s, CHO); MS m/e 276 (M^+, 42), 219 (100), 189 (14), 147 (17), 115 (32); UV (CH_2Cl_2 λ_{max} (log ϵ) 387 (4.02), 327 (3.60), 229 (3.35) nm. Anal. Calcd for $C_{15}H_{20}OSSi$: C, 65.17; H, 7.29; S, 11.60. Found: C, 65.25; H, 7.34; S, 11.52.

Diketone 11. To a stirred solution of disilylisothianaphthene **9** (540 mg, 1.5 mmol) and phthaloyl chloride (100 mg, 0.5 mmol) in dichloromethane (5 mL) was added aluminum chloride (200 mg, 1.5 mmol) at room temperature. After being stirred for 6 h, the reaction mixture was poured into ice–water and was extracted with ether. The residue from the ether extract was subjected to column chromatography (silica, n-hexane/benzene = 1/1) to give **11** (230 mg, 73%, based on phthaloyl chloride). Recrystallization from n-hexane/benzene gave white crystals: mp 213 °C; ^{1}H NMR δ 0.51 (12 H, s, CH_3), 0.97 (18 H, s, CH_3), 6.84–8.06 (12 H, m, Ar-H); MS m/e 626 (M+, 100). Anal. Calcd for $C_{36}H_{42}O_2S_2Si_2$: C, 68.96; H, 6.75; S, 10.23. Found: C, 69.06; H, 6.79; S, 10.28.

1-(*tert*-Butyldimethylsilyl)-3-acetylisothianaphthene (12). To a stirred mixture of disilyl compound **9** (360 mg, 1.0 mmol) and aluminum chloride (260 mg, 2.0 mmol) in carbon disulfide (2 mL) was added acetyl chloride (0.14 mL, 2.0 mmol) at 0 °C. The reaction mixture was stirred at this temperature for 30 min and then at room temperature over night. The resulting red reaction mixture was poured into ice–water and was extracted with ether. The residue from the ether extract was subjected to column chromatography (silica, hexane/benzene = 1/1) to give **12** (233 mg, 80%). Recrystallization from hexane gave pale yellow crystals of **12**: mp 80–81 °C; ^{1}H NMR 0.55 (6 H, s, CH_3), 0.97 (9 H, s, CH_3), 2.73 (3 H, s, CH_3), 7.19–7.43 (2 H, m, Ar-H), 7.78 (1 H, d, J = 8.7 Hz, Ar-H), 8.68 (1 H, d, J = 8.7 Hz, Ar-H); MS m/e 290 (M^+, 24), 233 (100), 190 (64), 175 (6), 161 (29), 147 (5), 133 (25), 115 (18); UV (CH_2Cl_2) λ_{max} (log ϵ) 378 (4.09), 326 (3.68), 246 (3.81), 236 (3.82), 216 (3.50) nm. Anal. Calcd for $C_{16}H_{22}OSSi$: C, 66.15; H, 7.63; S, 11.04. Found: C, 66.24; H, 7.67; S, 10.98.

Reaction of 9 with Excess Acetyl Chloride. To a stirred mixture of disilyl compound **9** (360 mg, 1.0 mmol) and aluminum chloride (520 mg, 4.0 mmol) in carbon disulfide (2 mL) was added acetyl chloride (0.28 mL, 4.0 mmol) at 0 °C. The reaction mixture was stirred at this temperature for 30 min, at room temperature overnight, and then refluxed for an additional 3 h. After being cooled to room temperature, the resulting red reaction mixture was poured into ice–water and was extracted with ether. The residue from the ether extract was subjected to column chromatography (silica, n-hexane/benzene = 1/1) to give **13** (100 mg, 46%) as well as **14** and **15** [31 mg (9%) and 82 mg (24%), respectively]. Ketone **13** was crystallized from n-hexane/benzene to give light brown crystals: mp 123–124 °C; ^{1}H NMR δ 2.76 (6 H, s, CH_3), 7.44 (2 H, dd, J = 6.7, 3.2 Hz, Ar-H), 8.56 (2 H, dd, J = 6.7, 3.2 Hz, Ar-H); MS m/e 218 (M^+, 82), 203 (100), 161 (73), 147 (14), 133 (31); UV (CH_2Cl_2) λ_{max} (log ϵ) 400 (4.03), 347 (3.65), 267 (3.91), 229 (3.36) nm.

Diketones 14 and 15. 14: crystals from benzene-hexane, mp 169 °C; ^{1}H NMR δ 0.60 (6 H, s, CH_3), 0.99 (9 H, s, CH_3), 2.67 (3 H, s, CH_3), 2.74 (3 H, s, CH_3), 7.97 (1 H, d, J = 9.2 Hz, Ar-H), 8.44 (1 H, s, Ar-H), 8.68 (1 H, d, J = 9 Hz, Ar-H). **15**: red oil; ^{1}H NMR δ 0.56 (6 H, s, CH_3), 0.97 (9 H, s, CH_3), 2.66 (3 H, s, CH_3), 2.70 (3 H, s, CH_3), 7.22–7.37 (2 H, m, Ar-H), 7.44 (1 H, d, J = 6.8 Hz, Ar-H), 7.87 (1 H, d, J = 9.0 Hz, Ar-H).

Oligomerization of Disilylisothianaphthene 9 to 16–18. Method A. To a solution of disilylisothianaphthene **9** (360 mg, 1.0 mmol) in dichloromethane (2.0 mL), titanium tetrachloride (1.0 M in dichloromethane 2.0 mL, 2.0 mmol) was added all at once at room temperature. After being stirred for 10 h, the reaction mixture was poured into ice–water and was extracted with ether. The residue from the ether was subjected to column chromatography (silica, n-hexane) to give dimer **16** (110 mg, 44%) and a small amount of oligomers **17** and **18**. Recrystallization of dimer **16** from acetonitrile gave light yellow crystals: mp 145–147 °C; ^{1}H NMR δ 0.56 (12 H, s, CH_3), 1.02 (18 H, s, CH_3), 7.11–7.16 and 7.74–7.90 (8 H, m, Ar-H); MS m/e 494 (M^+, 58), 437 (100), 275 (54), 215 (40); UV (CH_2Cl_2) λ_{max} (log ϵ) 406 (4.06), 329 (3.45), 238 (4.27) nm. Anal. Calcd for $C_{28}H_{38}S_2Si_2$: C, 67.95; H, 7.74; S, 12.93. Found: C, 68.01; H, 7.74; S, 12.86. Trimer **17**: orange oil; ^{1}H NMR δ 0.55 (12 H, s, CH_3), 1.02 (18 H, s, CH_3), 7.13–7.19 and 7.74–7.98 (12 H, m, Ar-H); MS m/e 626 (M^+, 100), 569 (79); UV (CH_2Cl_2) λ_{max} (log ϵ) 478 (4.50), 391 (4.10), 329 (3.88), 232 (4.46) nm. Tetramer **18**: dark violet solid; ^{1}H NMR δ 0.54 (12 H, s, CH_3), 1.02 (18 H, s, CH_3), 7.14–7.23 and 7.75–8.00 (16 H, br, Ar-H); MS m/e 758 (M^+, 100), 701 (36); UV (CH_2Cl_2) λ_{max} (log ϵ) 517 (4.62), 377 (4.07), 332 (3.94), 232 (4.59) nm. Anal. Calcd for $C_{44}H_{46}S_4Si_2$: C, 69.60; H, 6.11; S, 16.89. Found: C, 69.70; H, 6.19; S, 16.75.

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