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Preparation of 1,4-Bis(2-ethynyl-3-thienyl) benzene Derivatives Linked by Oligo(Ethyleneglycol) Chain

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ABSTRACT: *1-(2-Phenylethynyl-3-thienyl)-4-[2-(triisopropylsilyl)ethynyl-3-thienyl]benzene derivative, bearing both a polar oligo(ethyleneglycol) chain and hydrophobic alkyl chains, was prepared. The triisopropylsilyl group was then removed by tetrabutylammonium fluoride and the diphenylphosphinyl group was introduced by successive treatment with EtMgBr, chlorodiphenylphosphine, and aerial dioxygen.* © 2011 Wiley Periodicals, Inc. Heteroatom Chem 22:531–537, 2011; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.20718

INTRODUCTION

Artificially large and sophisticated molecular systems, such as artificial enzymes and artificial molecular architectures, are of current interest [1–4]. This category may also include the so-called biomimetic or bioinspired molecules [5–7], whose structures or functions are not always very similar to the biopolymers (such as peptides and proteins), but the design of which is inspired by them.

In both biological and artificially (biomimetic) large systems, heteroatoms play important and versatile roles in coordination, hydrogen bonding, and redox reaction. Moreover, heteroatoms (main group elements as well as transition metals) are very important in organic syntheses of large molecular systems at various synthetic stages such as protection, deprotection, and coupling reaction: cooperation of heteroatoms (boron, silicon, phosphorus, sulfur, halogens, palladium, and so on) will create a fascinating world of artificially large molecules.

By utilizing heteroatoms, we have developed peptide-inspired bis(ethynylthienyl)arene spacers (abbreviated as ETB or ETAr spacers, Fig. 1): we have prepared several ETB/ETAr-related derivatives such as **1–6** [8]. The spacers provide promising potential building blocks for the construction of larger systems such as linked ETB/ETAr system (Fig. 2).

Our linked ETB/ETAr system concept shown in the previous paper [8d,e] is very much bioinspired. Proteins, especially membrane binding proteins (transmembrane proteins and monotopic membrane proteins), normally contain both a hydrophobic and hydrophilic domain, and exhibit special functionality such as catalytic (or enzymatic) activity. Our synthetic strategy involves connecting the ETB or the related units to hydrophobic or hydrophilic chains to enable the preparation of large assembled molecules in water (in the presence or absence of surfactant or lipid bilayer). As a part of the fundamental research, we report here the preparation of novel ETB derivatives (structure **A** in Fig. 2)

Dedicated to Professor Kin-ya Akiba on the occasion of his 75th birthday.

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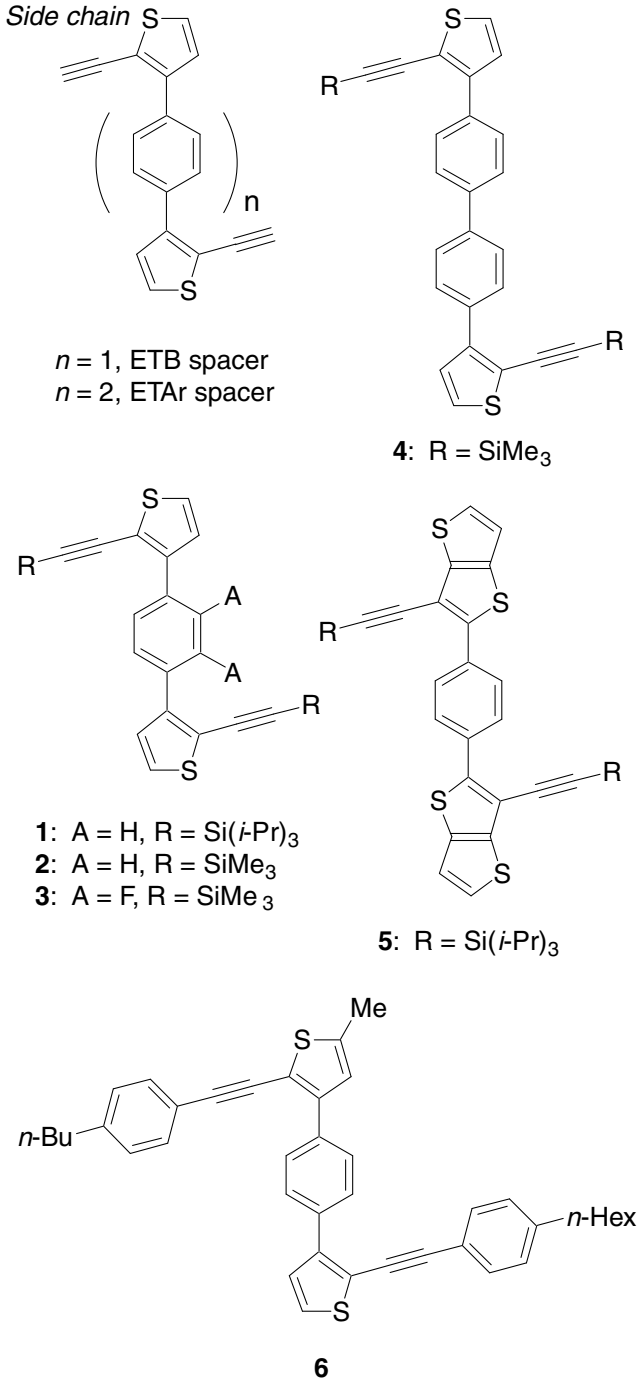


FIGURE 1 ETB spacer, ETAr spacer, and related compounds.

bearing a polar oligo(ethyleneglycol) chain and hydrophobic alkyl chains [9]. A very recent report of Kinbara et al. also shows a protein-mimicking concept similar to the linked ETB/ETAr system [10]. Compound **A** can be regarded as the simplest form of linked ETB system, containing both a polar domain and a hydrophobic domain.

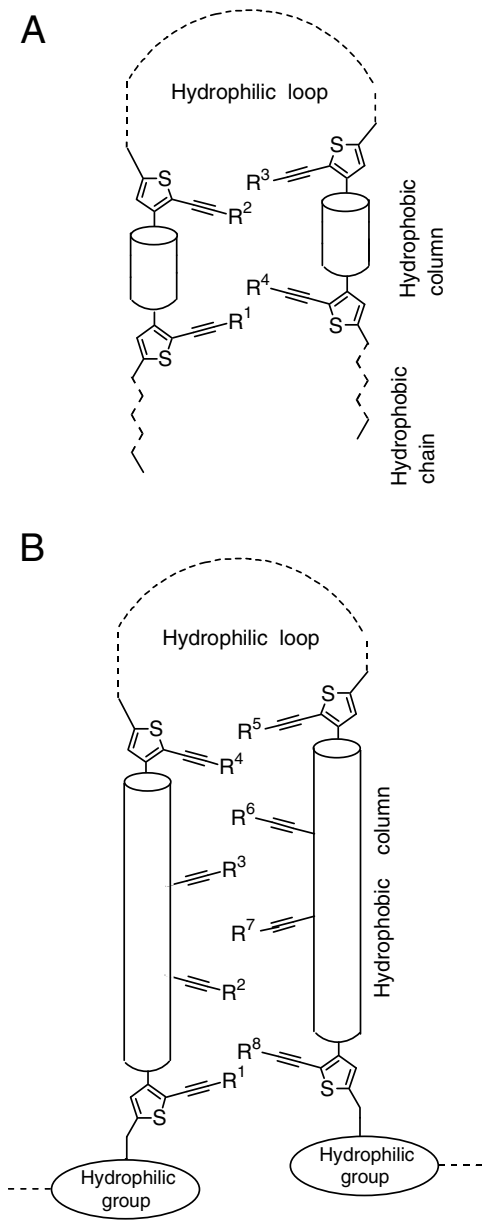
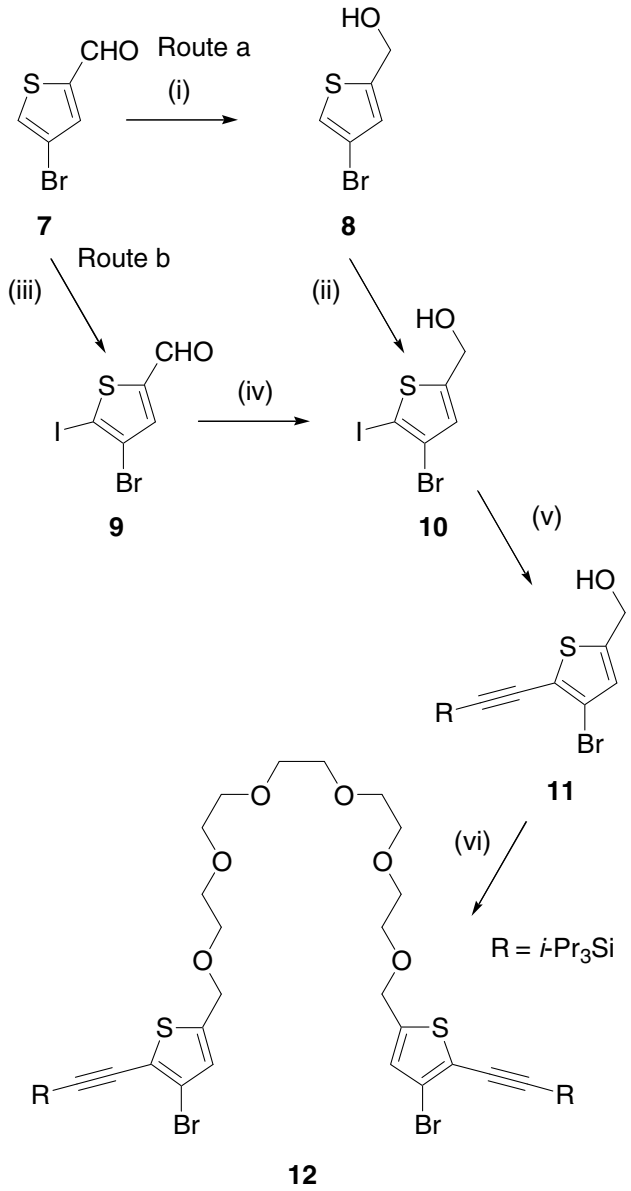


FIGURE 2 Concept of peptide-inspired "linked ETB/ETAr system." Above, monotopic membrane-peptide-inspired structure. Below, transmembrane-peptide-inspired structure.

RESULTS AND DISCUSSION

In the first place, we prepared the polar moiety of **A** (Fig. 2) as compound **12** in Scheme 1: commercially available 4-bromo-2-thiophenecarbaldehyde (**7**) was reduced by $NaBH_4$ to give **8** in 82% isolated yield (route a in the literature [11], 99% yield without purification). Iodination of **8** with *N*-iodosuccinimide (NIS) afforded **10** in 90% yield. Compound **10** was obtained via route b: 4-Bromo-5-iodothiophene-2-carbaldehyde (**9**) was prepared by reaction of **7** with NIS, in 77% yield. Reduction



SCHEME 1 Reagents and conditions: (i) $NaBH_4$, (82%); (ii) *N*-iodosuccinimide (NIS), acetic acid, THF, r.t., 5 h (90%); (iii) NIS, acetic acid, $CHCl_3$, r.t., 3 d (77%); (iv) $NaBH_4$, *i*-PrOH, r.t., 100 min (52%); (v) ethynyltriisopropylsilane, $PdCl_2(PPh_3)_2$, CuI, *i*-Pr_2NH, THF, 50°C, 17 h (76%); (vi) NaH, THF, then $TsO(CH_2CH_2O)_5Ts$, 60°C, 30 min (33%).

of **9** with $NaBH_4$ afforded the alcohol **10** in 52% yield. Probably, compound **9** is not so stable under the reduction conditions, resulting in the low yield of **10**. Thus, route a is superior to route b. Sonogashira coupling reaction of **10** with ethynyltriisopropylsilane afforded **11** in 76% yield, which was converted to **12** in 33% yield by successive treatment of **11** with NaH and penta(ethylene glycol)di-*p*-toluenesulfonate.

In the second place, preparation of model compound **14** (Scheme 2), whose triple bonds are protected by trialkylsilyl group, was studied. Synthetic procedure was based on the previously reported preparative method of unsymmetrical ETB derivatives [8c]: Suzuki-Miyaura cross coupling of the polar bromide **12** with borolane **13a** [9] afforded **14** in 36% yield.

We then planned to prepare analogous compounds bearing different side chains. Phenylethynyl side chain was chosen for a side chain of the hydrophobic domain and polar phosphynylethynyl group was chosen for the polar domain: Reaction of **12** and the phenylethynyl substituted (thienylphenyl)bolorane **13b** [9] gave compound **15** (49% yield). The silyl-protected ethynyl side chains of **15** are changeable to various side chains by deprotection and successive reactions such as metalation, cross coupling, or catalytic azide-alkyne cycloaddition. Actually, the silyl group was removed by addition of tetrabutylammonium fluoride to give **16** in 77% yield. Reaction of **16** with EtMgBr and chlorodiphenylphosphine, followed by oxidation by air, afforded **17**, bearing a hydrophobic group and a polar group, in 49% yield.

Figure 3 depicts ultraviolet–visible (UV–vis) spectra of **1** [8e], **14**, and **17** in CH_2Cl_2. Comparison of the UV spectra of **14** and **17** with that of **1** shows an apparent increase of the molar absorption coefficients, because compounds **14** and **17** have two ETB moieties in a molecule. The shape of the spectrum of **14** is not a simple multiplication of the spectrum of **1**; a significant change in shape was observed in 300–400 nm region. This fact suggests a change in

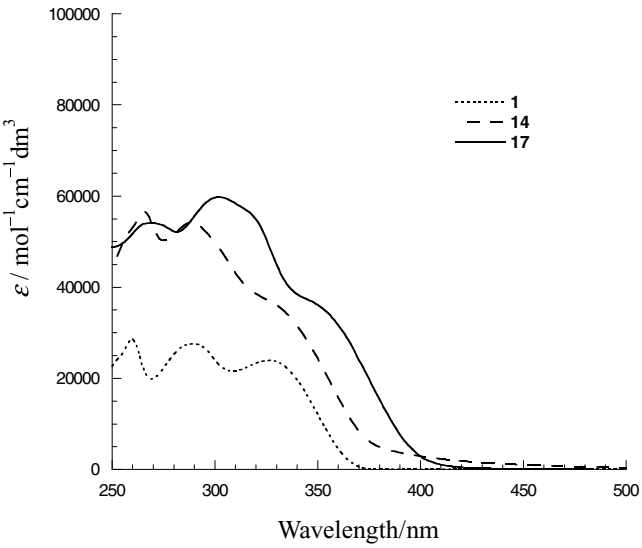
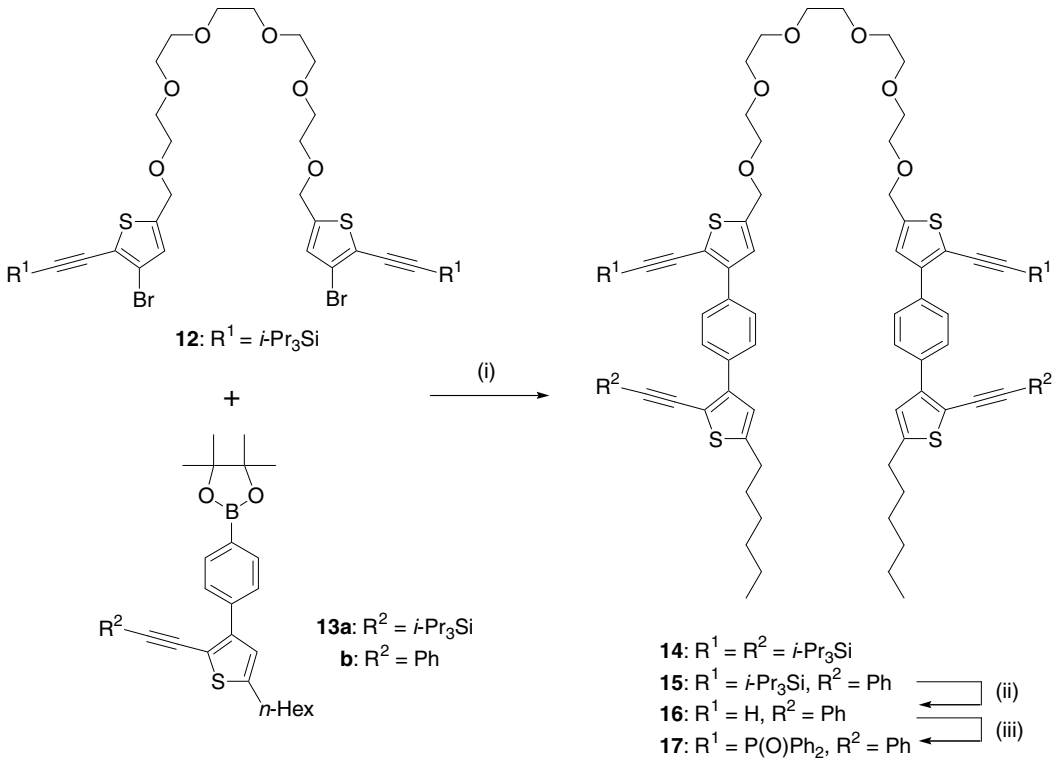


FIGURE 3 UV–vis spectra of **1, 14**, and **17** in CH_2Cl_2. Data for **1** was taken from [8d].



SCHEME 2 Reagents and conditions: (i) For **14**, $Pd(PPh_3)_4$, K_2CO_3, Toluene, THF, H_2O, 85°C, 17 h, 36%; for **15**, $Pd(PPh_3)_4$, K_2CO_3, 1,4-dioxane, H_2O, 80°C, 16 h, 49%; (ii) TBAF, THF, r.t., 1 h (77%); (iii) EtMgBr, THF, 0°C, 40 min, then Ph_2PCl, 0°C to r.t., 2 h, work up in the air (49%).

π conjugation in the linked compound **14** compared with **1**. One possible reason is a change in coplanarity of the dithienylbenzene moieties, caused by intramolecular interaction of the two ETB moieties, although a contribution of electronic effect of the alkyl chain and the ethyleneglycol chain cannot be neglected at all. On the other hand, little change was observed between the ^1H and ^{13}C nuclear magnetic resonance (NMR) chemical shifts of the central benzene rings of **1** and **14**, except for the fact that two different thienyl groups are substituted in the case of **14** and the benzene-ring signals become nonequivalent in **14**. Thus, intramolecular interactions between the ETB moieties, such as stacking of the aromatic rings, seem to be small.

Compounds **14–17** themselves are hardly soluble in water. However, investigation of behavior of **17** as a peptide-inspired compound was tried in aqueous media. Figure 4 shows the UV–vis spectrum of **17** in aqueous sodium dodecyl sulphate solution (ca. 0.01 mol/L). A significant change in the shape was observed in the 330–370 nm region. This may suggest conformational change of the dithienylbenzene moiety. As the concentration of **17** is low, due to poor solubility, ^{31}P NMR could not be measured.

In summary, we have prepared some 1,4-bis(2-ethynyl-3-thienyl)benzene derivatives, bearing both a polar oligo(ethyleneglycol) chain and hydrophobic alkyl chains. These derivatives may find practical application as functional units in future, particularly in the context of catalysis. Further studies on the application of the products and construction of linked ETAr systems with extended axis are in progress.

EXPERIMENTAL

Melting points were measured on a Yanagimoto MP-J3 micro melting point apparatus (Yanagimoto Seisakusyo Co., Ltd., Kyoto, Japan) and are uncorrected. NMR spectra were recorded on a Bruker Avance-400 or AM-600 spectrometer (Bruker Japan Co., Ltd., Tsukuba, Japan). UV–vis spectra were measured on a Hitachi U-3210 spectrometer (Hitachi, Ltd., Tokyo, Japan) whereas a Horiba FT-300 (Horiba, Ltd., Kyoto, Japan) or a Shimadzu FTIR-8100M spectrometer (Shimadzu Corporation, Kyoto, Japan) was used to obtain the infrared (IR) spectra. A Hitachi M-2500S spectrometer was used to obtain MS data. FT-ICR-MS spectra were measured on a Bruker APEX III spectrometer.

4-Bromo-5-iodothiophene-2-carbaldehyde **9**. A mixture of 4-bromothiophene-2-carbaldehyde (**7**,

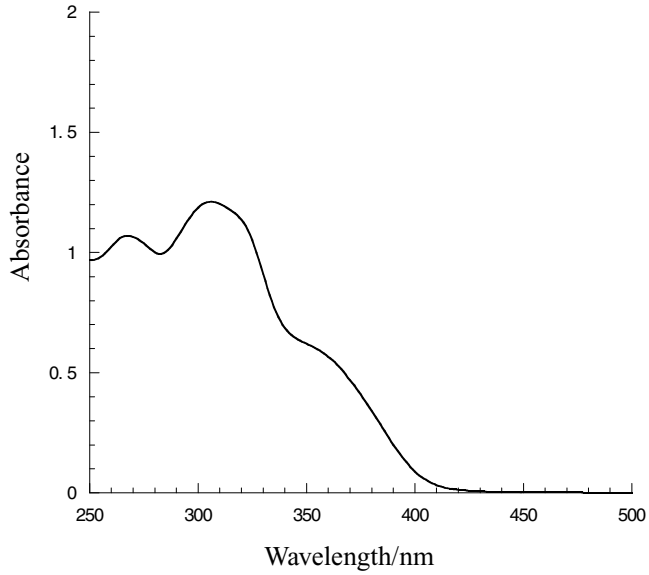


FIGURE 4 UV–vis spectrum of **17** (in ca. 0.01 mol/L aqueous sodium dodecyl sulfate solution). Concentration of **17** is ambiguous.

2.00 g, 10.5 mmol), NIS (2.82 g, 12.5 mmol), acetic acid (60 mL), and $CHCl_3$ (35 mL) was stirred at room temperature for 3 days. The reaction mixture was treated with saturated aqueous $NaHCO_3$ and then saturated aqueous $Na_2S_2O_3$ solution. The organic phase was separated, dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was treated with a silica-gel column (eluent = hexane-EtOAc 1:1) to give 2.55 g (8.05 mmol, 77% yield) of **9**: colorless solid, mp 96–97°C; $R_f = 0.12$ (SiO_2-CCl_4); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 7.50$ (1H, s, 3-thienyl) and 9.75 (1H, s, CHO); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) $\delta = 91.1$ (5-thienyl), 121.8 (4-thienyl), 137.3 (3-thienyl), 148.5 (2-thienyl), and 180.3 (CHO); IR (KBr) 3073, 2845, 1871, 1775, 1721, 1670 (C=O), 1507, 1397, 1358, 1298, 1218, 1167, 1117, 968, 839, 830, 712, 662, 583, 509, and 480 cm^{-1}; MS (70 eV) *m/z* (rel intensity) 318 ($M^+ + 2$; 100) and 316 (M^+; 98). Calcd for C_5H_2BrIOS: *m/z* 315.8054. Found: *m/z* 315.8052. Calcd for C_5H_2BrIOS: C, 18.95, H, 0.64%. Found: C, 19.20; H, 0.65%.

(3-Bromo-2-iodo-5-thienyl)methanol **10** *Route a.* 4-Bromo-2-hydroxymethylthiophene (**8**) was prepared according to the literature [10]. A mixture of **8** (5.00 g, 25.9 mmol), NIS (6.38 g, 28.3 mmol), acetic acid (30 mL), and tetrahydrofuran (THF, 40 mL) was stirred at room temperature for 5 h. $CHCl_3$ and water were added to the reaction mixture. The resulting mixture was treated with saturated aqueous $NaHCO_3$ and then saturated aqueous $Na_2S_2O_3$ solution. The organic phase was separated, dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was treated with an alumina column (eluent = $CHCl_3$) to give 7.44 g (23.3 mmol, 90% yield) of **10**.

Route b. A mixture of **9** (97.4 mg, 0.307 mmol) and $NaBH_4$ (19.0 mg, 0.502 mmol) in 2-propanol (5 mL) was stirred at room temperature for 100 min. Water and hexane were added to the reaction mixture, the organic phase was separated, washed with brine, dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was treated with a silica-gel column (eluent = $CHCl_3$) to give 51.0 mg (0.160 mmol, 52% yield) of **10**.

10: Colorless solid, mp 56–58°C; $R_f = 0.31$ (Al_2O_3-$CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 1.89$ (1H, t, $J = 6.0$ Hz, OH), 4.78 (2H, d, $J = 6.0$ Hz, CH_2), and 6.81 (1H, s, 3-thienyl); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) $\delta = 59.6$ (CH_2), 76.5 (5-thienyl), 119.6 (4-thienyl), 127.7 (3-thienyl), and 150.3 (2-thienyl); IR (KBr) 3350 (OH), 3081, 2928, 2869, 2637, 1725, 1671, 1530, 1455, 1422, 1401, 1369, 1302, 1238, 1165, 1121, 1000, 955, 837, 824, 681, 646, 581, 517, and 426 cm^{-1}; MS (70 eV) *m/z* (rel intensity) 320 ($M^+ + 2$; 100), 318 (M^+; 97), 303 ($M^+ - OH + 2$; 12), 301 ($M^+ - OH$; 12), 193 ($M^+ - I + 2$; 30), and 191 ($M^+ - I$; 29). Calcd for C_5H_4BrIOS: *m/z* 317.8211. Found: *m/z* 317.8208.

[3-Bromo-2-{2'-(triisopropylsilyl)ethynyl}-5-thieyl] methanol **11**. A mixture of **10** (7.44 g, 23.3 mmol), ethynyltriisopropylsilane (5.20 mL, 23.4 mmol), $PdCl_2(PPh_3)_2$ (325 mg, 0.463 mmol), CuI (87.2 mg, 0.458 mmol), and *N*,*N*-diisopropylamine (20 mL) in THF (100 mL) was stirred at 50°C for 17 h. After cooling to room temperature, $CHCl_3$ and water were added to the reaction mixture. The organic phase was separated, dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was treated with a silica-gel column (eluent = hexane-EtOAc 5:1) to give 6.62 g (17.7 mmol, 76% yield) of **11**: pale yellow oil; $R_f = 0.34$ (SiO_2-CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 1.09$–1.19 (21H, br s, isopropyl), 1.84 (1H, t, $J = 6.0$ Hz, OH), 4.76 (2H, d, $J = 6.0$ Hz, CH_2), and 6.85 (1H, s, 3-thienyl); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) $\delta = 11.2$ ($CHMe_2$), 18.6 (Me), 60.0 (CH_2), 97.3 (C≡C), 100.4 (C≡C), 116.1 (4-thienyl), 120.8 (5-thienyl), 127.4 (3-thienyl), and 145.1 (2-thienyl); IR (neat) 3350 (OH), 2945, 2867, 2147 (C≡C), 1526, 1464, 1383, 1366, 1235, 1107, 1073, 1017, 997, 920, 884, 833, 764, 677, 583, and 504 cm^{-1}; MS (70 eV) *m/z* (rel intensity) 374 ($M^+ + 2$; 25), 372 (M^+; 24), 331 ($M^+ - i$-Pr+2; 100), 329 ($M^+ - i$-Pr; 94), 303 ($M^+ - i$-Pr − Si + 2; 20), 301 ($M^+ - i$-Pr − Si; 19), 289 ($M^+ - 2i$-Pr + 3; 20),

287 ($M^+ - 2i$-Pr + 1; 19), 275 ($M^+ - i$-Pr − 2MeCH + 2; 18), 273 ($M^+ - i$-Pr − 2MeCH; 16), 261 ($M^+ - 2i$-Pr − Si + 3; 26), and 259 ($M^+ - 2i$-Pr − Si + 1; 25). Calcd for $C_{16}H_{25}BrOSSi$: M, 372.0579. Found: *m/z* 372.0574.

1,18-Bis[4-bromo-5-{2'-(triisopropylsilyl)ethynyl} thiophen-2-yl]-2,5,8,11,14,17-hexaoxaoctadecane **12**. Sodium hydride (dispersion in oil, 43.6 mg, ca. 1 mmol) was washed with dry hexane (8 mL) under nitrogen. To a mixture of the sodium hydride and **11** (191 mg, 0.510 mmol) in THF (10 mL), a THF (4 mL) solution of pentaethylene glycol di-*p*-toluenesulfonate (147 mg, 0.268 mmol) was added and the resulting mixture was stirred at 60°C for 30 min. The reaction mixture was cooled to room temperature and treated with 0.1 M hydrochloric acid. $CHCl_3$ and water were added to the mixture, the organic phase was separated, dried over $MgSO_4$, and the solvents were removed under reduced pressure. The crude products were treated with recycle gel permeation chromatography (eluent = CH_2Cl_2) to give 83.7 mg (0.0881 mmol, 33% yield) of **12**: yellow oil; $R_f = 0.69$ (SiO_2-EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 1.13$ (42H, br s, isopropyl), 3.63–3.65 (20H, m, CH_2), 4.63 (4H, s, CH_2), and 6.84 (2H, s, 3-thienyl); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta = 11.1$ (*C*HMe$_2$), 18.5 (Me), 67.4 (CH_2), 69.3 (CH_2), 70.4 (CH_2), 70.5 (CH_2), 70.6 (CH_2), 97.3 (C≡C), 100.2 (C≡C), 115.8 (4-thienyl), 120.8 (5-thienyl), 128.2 (3-thienyl), and 142.5 (2-thienyl); IR (neat) 2944, 2865, 2147 (C≡C), 1559, 1507, 1352, 1246, 1173, 1115, 997, 920, 884, 835, 764, 677, and 662 cm^{-1}. FT-ICR-MS Calcd for $C_{42}H_{68}Br_2NaO_6S_2Si_2$: $(M + Na)^+$, 969.2260. Found: *m/z* 969.2252.

Compound **14**. A mixture of **12** (30.6 mg, 0.0322 mmol), **13a** (105 mg, 0.190 mmol), $Pd(PPh_3)_4$ (13.2 mg, 0.0114 mmol), K_2CO_3 (124 mg, 0.894 mmol), THF (5 mL), toluene (3 mL), and water (2 mL) was heated at 85°C for 17 h. After cooling to room temperature, $CHCl_3$ and water were added to the reaction mixture. The organic phase was separated, washed with brine, dried over $MgSO_4$, and the solvent was removed under reduced pressure. Treatment of the residue with a silica-gel column chromatography (eluent = EtOAc) followed by gel-permeation column chromatography (eluent = CH_2Cl_2) afforded 19.0 mg of **14** (0.0116 mmol, 36% yield based on the starting **12**).

14: Yellow oil; $R_f = 0.37$ (SiO_2-hexane-EtOAc 1:1); ^{1}H NMR (600 MHz, $CDCl_3$) $\delta = 0.87$–1.71 (106H, m, Me$(CH_2)_4$ and isopropyl), 2.78 (4H, t, $^3J = 7.6$ Hz, CH_2), 3.64–3.67 (20H, m, CH_2CH_2O), 4.68 (4H, s, CH_2O), 6.89 (2H, s, thienyl), 7.09 (2H, s, thienyl), 7.81 (4H, d, $^3J = 8.8$ Hz, phenyl), and 7.84 (4H, d, $^3J = 8.8$ Hz, phenyl); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) $\delta = 11.3$ (*C*HMe$_2$), 11.4 (*C*HMe$_2$), 14.1 (*Me*CH$_2$), 18.7 (CH*Me*$_2$), 18.7 (CH*Me*$_2$), 22.5 (CH_2), 28.7 (CH_2), 30.3 (CH_2), 31.4 (CH_2), 31.5 (CH_2), 67.8 (CH_2O), 69.4 (CH_2O), 70.6 (CH_2O), 70.7 (CH_2O), 97.7 (C≡C), 98.8 (C≡C), 99.8 (C≡C), 100.2 (C≡C), 115.8 (thienyl), 118.4 (thienyl), 124.7 (thienyl), 126.5 (thienyl), 127.6 (phenyl), 127.7 (phenyl), 134.1 (phenyl), 134.7 (phenyl), 141.8 (thienyl), 144.0 (thienyl), 144.1 (thienyl), and 146.9 (thienyl); UV–vis (CH_2Cl_2) 266 (log ε, 4.75), 289 (4.73), and 335 nm (sh, 4.53); IR (neat) 2865, 2137 (C≡C), 1717, 1559, 1541, 1516, 1509, 1262, 1098, 1019, 997, 920, 884, 828, 803, 772, 677, and 459 cm^{-1}. FT-ICR-MS Calcd for $C_{96}H_{146}NaO_6S_4Si_4$: $(M + Na)^+$, 1657.8972. Found: *m/z* 1657.8961.

Compound **15**. A mixture of **12** (209 mg, 0.221 mmol), **13b** (203 mg, 0.432 mmol), $Pd(PPh_3)_4$ (9.8 mg, 0.084 mmol), K_2CO_3 (302 mg, 2.18 mmol), 1,4-dioxane (4 mL), and water (4 mL) was heated under nitrogen atmosphere at 80°C for 16 h. After cooling to room temperature, Et_2O and water were added to the reaction mixture. The organic phase was separated, washed with brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was treated with a silica-gel column chromatography (eluent = hexane-EtOAc, 1:1) to give 154.7 mg (0.105 mmol, 49% yield) of **15**: yellow oil; $R_f = 0.29$ (SiO_2-hexane-EtOAc 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 0.90$ (6H, m, Me), 1.13 (42H, br s, *i*-Pr), 1.32–1.40 (12H, m, CH_2), 1.67–1.75 (4H, m, CH_2), 2.82 (4H, t, $^3J = 7.6$ Hz, CH_2), 3.64–3.66 (20H, m, OCH_2CH_2O), 4.68 (4H, s, thienylCH_2O), 6.93 (2H, s, thienyl), 7.13 (2H, s, thienyl), 7.30–7.32 (6H, m, Ph), 7.44–7.47 (4H, m, Ph), 7.85 (4H, d, $^3J = 8.4$ Hz, phenyl), and 7.92 (4H, d, $^3J = 8.4$ Hz, phenyl); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta = 11.2$ (*C*HMe$_2$), 14.0 (*Me*CH$_2$), 18.6 (CH*Me*$_2$), 22.5 (CH_2), 28.7 (CH_2), 30.2 (CH_2), 31.3 (CH_2), 31.5 (CH_2), 67.7 (CH_2O), 69.2 (CH_2O), 70.5 (CH_2O), 70.5 (CH_2O), 70.6 (CH_2O), 83.7 (C≡C), 94.7 (C≡C), 99.0 (C≡C), 99.8 (C≡C), 115.3, 118.3, 123.2, 124.9, 126.3, 127.6, 127.6, 128.1, 128.2, 131.1, 134.0, 134.7, 141.8, 143.6, 143.8, and 147.1; IR (neat) 2940, 2865, 2137 (C≡C), 1597, 1516, 1458, 1381, 1348, 1291, 1244, 1096, 995, 918, 884, 830, 772, 754, 679, 592, and 525 cm^{-1}. FT-ICR-MS Calcd for $C_{90}H_{114}NaO_6S_4Si_2$: $(M + Na)^+$, 1497.6929. Found: 1497.6922. Calcd for $C_{90}H_{114}O_6S_4Si_2 \cdot (H_2O)_{1/2}$: C, 72.78; H, 7.80%. Found: C, 72.58; H, 7.75%.

Compound **16**. To a solution of **15** (93.4 mg, 0.0633 mmol) in THF (1.4 mL), 0.140 mmol of

tetrabutylammonium fluoride (1.0 M solution in THF, 0.140 mL) was added at room temperature and the resulting mixture was stirred for 1 h. Et_2O and water were added to the reaction mixture. The organic phase was separated, washed with brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was treated with a silica-gel column chromatography (eluent = hexane to EtOAc) to give 57.0 mg (0.0490 mmol, 77% yield) of **16**: yellow oil; $R_f = 0.13$ (SiO_2-hexane-EtOAc 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 0.90$ (6H, t, $^3J = 7.0$ Hz, Me), 1.32–1.40 (12H, m, CH_2), 1.67–1.75 (4H, m, CH_2), 2.81 (4H, t, $^3J = 7.6$ Hz, CH_2), 3.44 (2H, s, C≡CH), 3.65–3.67 (20H, m, OCH_2CH_2O), 4.69 (4H, s, thienylCH_2O), 6.94 (2H, s, thienyl), 7.11 (2H, s, thienyl), 7.30–7.32 (6H, m, Ph), 7.44–7.47 (4H, m, Ph), 7.79 (4H, d, $^3J = 8.6$ Hz, phenyl), and 7.88 (4H, d, $^3J = 8.6$ Hz, phenyl); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta = 14.0$ (*Me*CH_2), 22.5 (CH_2), 28.7 (CH_2), 30.2 (CH_2), 31.3 (CH_2), 31.5 (CH_2), 67.7 (CH_2O), 69.4 (CH_2O), 70.5 (CH_2O), 70.6 (CH_2O), 77.4 (C≡C), 83.8 (C≡C), 83.8 (C≡C), 94.7 (C≡C), 115.4, 116.6, 123.2, 124.9, 126.6, 127.7, 127.8, 128.1, 128.3, 131.1, 133.9, 135.0, 142.5, 144.0, 145.1, and 147.2. FT-ICR-MS Calcd for $C_{72}H_{74}NaO_6S_4$: $(M + Na)^+$, 1185.4280. Found: 1185.4253.

Compound **17**. To a solution of **16** (57.0 mg, 0.0490 mmol) in THF (2 mL), 0.11 mmol of Et-MgBr (0.98 M solution in Et_2O, 0.11 mL) was added at 0°C and the resulting mixture was stirred for 40 min. To the solution, chlorodiphenylphosphine (0.030 mL, 0.16 mmol) was added at 0°C. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. Et_2O and water were added to the resulting solution, the organic phase was separated, washed with brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was treated with an alumina column chromatography (eluent = EtOAc to EtOH). A crude product thus obtained was further purified by gel permeation chromatography to give 36.6 mg (0.0239 mmol, 49% yield) of **17**: yellow oil; $R_f = 0.27$ (Al_2O_3-EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 0.91$ (6H, t, $^3J = 6.8$ Hz, Me), 1.33–1.42 (12H, m,CH_2), 1.69–1.76 (4H, m, CH_2), 2.83 (4H, t, ^3J =7.5 Hz, thienyl-CH_2), 3.64–3.67 (20H, m, OCH_2CH_2O), 4.71 (4H, s, thienylCH_2O), 6.91 (2H, s, thienyl), 7.15 (2H, s, thienyl), 7.27–7.29 (6H, m, Ph), 7.39–7.44 (4H, m, Ph), and 7.68–7.82 (8H, m, phenyl); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta = 14.1$ (*Me*CH_2), 22.5 (CH_2), 28.7 (CH_2), 30.3 (CH_2), 31.3 (CH_2), 31.5 (CH_2), 67.7 (CH_2O), 69.8 (CH_2O), 70.5 (CH_2O), 70.6 (CH_2O), 83.6 (C≡C), 89.0 (d, $^1J_{PC} = 168.4$ Hz, C≡C), 95.0 (C≡C), 99.5 (d, $^2J_{PC} = 30.1$ Hz, C≡C), 114.0 (d, $^2J_{PC} = 4.4$ Hz, *o*-Ph), 115.7, 123–136 (m, arom), 143.4, 146.4, 147.4, and 148.8; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) $\delta = 9.5$; UV–vis (CH_2Cl_2) 268 (log ε, 4.73), 302 (4.78), and 353 nm (sh, 4.55); IR (neat) 2926, 2854, 2150 (C≡C), 1717, 1438, 1205, 1120, 831, 795, 754, 725, and 692 cm^{-1}. FT-ICR-MS Calcd for $C_{96}H_{92}NaO_8P_2S_4$: $(M + Na)^+$, 1585.5042. Found: 1585.5047.

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