PREPARATION OF 1,4-BIS(3-ETHYNYLTHIENO[3,2-b]THIOPHEN-2-YL)BENZENE DERIVATIVES AS PEPTIDE-INSPIRED MOLECULES

Kozo Toyota,* Hiroshi Katsuta, Yasutomo Tsuji, Takeaki Iwamoto, and Noboru Morita

Department of Chemistry, Graduate School of Science, Tohoku University, Sendai 980-8578, Japan; E-mail toyota@mail.tains.tohoku.ac.jp

Abstract – 1,4-Bis(3-ethynylthieno[3,2-b]thiophen-2-yl)benzene derivatives, as well as 1-(3-ethynylthieno[3,2-b]thiophen-2-yl)-4-(2-ethynyl-3-thienyl)benzene derivative and 2,5-bis(2-ethynyl-3-thienyl)thieno[3,2-b]thiophene derivative, containing thieno[3,2-b]thiophene moieties with pseudoaxis, was prepared and their UV-vis spectra were studied. Extension of π-system through the central aromatic ring was suggested by the UV-vis spectra.

INTRODUCTION

Bio-inspired or biomimetic artificial large molecular systems, including artificial molecular architecture, are of current interest. On the other hand, heteroarene-based large molecular systems, such as oligothiophenes and polythiophenes, have attracted much interest in the fields of physical organic chemistry, materials science, and synthetic organic chemistry. We previously reported the development of peptide-inspired spacers such as a 1,4-bis(2-ethynyl-3-thienyl)benzene spacer (Chart 1, abbreviated to the ETB spacer) and a 4,4'-bis(2-ethynyl-3-thienyl)biphenyl spacer (ETAr spacer). We have reported the related compounds such as 1a–d, an unsymmetrical compound 2, and a linked system 3. The ETB spacer is a promising and easily tunable spacer of three-ring system, which has a six-membered ring (1,4-phenylene moiety) and a pair of five-membered rings (3-thienyl moieties) at the both ends of the 1,4-phenylene axis. Rebek, Jr. and co-workers have independently reported an α-helix mimicking three-ring system 4. Hamilton and co-workers recently reported compound 5 and mentioned about the effectiveness of such 5-6-5 three-ring scaffold for α-helix mimetics. Although polarity of the molecules and the directions of the side chains are different in these systems, our system, by tuning the side chains, may lead to the peptide-inspired large molecular systems.
In order to progress the investigation of our ETB/ETAr spacer-linked systems (Chart 1), preparations of various molecular components including auxiliary spacers are desirable. Thieno[3,2-\(b\)]thiophen-2,5-diyl is one of versatile \(\pi\)-spacers\(^{12}\) in materials science and it is often used with other spacers such as 1,4-phenylene, 2,5-thienylene, vinylene, and ethynylene. For our purpose, utilization of 3-ethynylthieno[3,2-\(b\)]thiophen-2,5-diyl (A in Chart 2) is desirable, because it has an ethynyl side chain
and a pseudoaxis through the 2,5-positions and it will work as an alternative spacer for the 2-ethynylthiophene moiety of the ETB/ETAr system. However, studies on 3-ethynylthieno[3,2-b]thiophenes or 1,4-bis(thieno[3,2-b]thiophene-2-yl)benzenes are limited. We now report development of 3-ethynylthieno[3,2-b]thiophene derivatives B and C (Chart 2), containing the auxiliary π-spacers for our ETB/ETAr spacer-linked systems. In addition, we describe here preparations of related compounds containing the structures D or E.

**RESULTS AND DISCUSSION**

3-[2-(Triisopropylsilyl)ethynyl]thieno[3,2-b]thiophene (7a) and 3-[2-(4-hexylphenyl)ethynyl]thieno[3,2-b]thiophene (7b) were prepared by the Sonogashira cross coupling reaction of 3-bromothieno[3,2-b]thiophene (6) with the corresponding alkynes in 97% and 87% yield, respectively (Scheme 1). Similarly, 3-[2-(trimethylsilyl)ethynyl]thieno[3,2-b]thiophene (7c) was prepared in 90% yield. Structures of the compounds 7a, b can be regarded as alternatives for the 2-ethynl-3-thiophene structures in the ETB systems.

Utilization of compounds 7a, b was performed as follows: Reaction of 7a with butyllithium followed by treatment with 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane afforded 8a as a major product, along with some by-products such as 12 (see below). Suzuki-Miyaura cross coupling reaction of the crude 8a with 1,4-diiodobenzene afforded a symmetrically substituted compound 9 in 13% yield (based on the starting 7a). On the other hand, reaction of crude 8a with 1-bromo-4-iodobenzene gave 10 (21% yield based on the starting 7a), which was converted to an unsymmetrical derivative 11, by a cross coupling reaction of 10 with 8b (prepared from 7b), in 62% yield (based on 10).
Reagents and conditions: i, PdCl₂(PPh₃)₂, CuI, i-Pr₂NH, 1,4-dioxane or THF; ii, n-BuLi (ca. 1 equiv.), THF, then 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (ca. 1 equiv.); iii, n-BuLi (2 equiv.), THF, then 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.4 equiv.); iv, 1,4-diiodobenzene, Pd(PPh₃)₄, K₂CO₃, THF, toluene, H₂O; v, 1-bromo-4-iodobenzene, Pd(PPh₃)₄, K₂CO₃, THF, toluene, H₂O; vi, 8b, Pd(PPh₃)₄, K₂CO₃, THF, toluene, H₂O.
As for the preparation of compounds with structure C in Chart 2, 1-bromo-4-[2-(triisopropylsilylethynyl)-3-thienyl]benzene (14) was prepared from 1-bromo-4-(2-iodo-3-thienyl)benzene (13)\(^2\) (Scheme 2). Suzuki-Miyaura cross coupling reaction of 14 with crude 8a afforded (thieno[3,2-b]thiophen-2-yl)(3-thienyl)benzene derivative 15 in 21% yield (based on the starting 7a, Scheme 1). In this reaction, compound 16 was also obtained (8% yield based on 7a), because the crude starting material of 8a contained 12 as mentioned above. When butyllithium (2 equiv.) was reacted with 7a and the reaction mixture was treated with 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2 equiv.), compound 12 was formed as a major product (Scheme 1). A cross coupling reaction of 12 (containing a trace amount of 8a) with 14 afforded 16 in 58% yield based on 7a. It should be mentioned that compound 16 can be regarded as a kind of extended ETAr derivatives (Chart 1), in which the auxiliary ethynylthieno[3,2-b]thiophene spacer is inserted between the benzene rings.

Reagents and conditions:  i, ethynyltriisopropylsilane, CuI, PdCl\(_2\)(PPh\(_3\))\(_2\), i-Pr\(_2\)NH, THF; ii, 8a, Pd(PPh\(_3\))\(_4\), K\(_2\)CO\(_3\), THF, toluene, H\(_2\)O; iii, 12, Pd(PPh\(_3\))\(_4\), K\(_2\)CO\(_3\), THF, toluene, H\(_2\)O.

Scheme 2

A related compound 20, containing thienothiophene moiety between the thiophene rings, was also prepared (Scheme 3): Suzuki-Miyaura cross coupling reaction of 3-thiopheneboronic acid with 2,5-dibromothieno[3,2-b]thiophene (17)\(^2\)\(^1\) afforded 18. Compound 18 was almost insoluble in common solvent, however, a suspension of 18 and N-iodosuccinimide (NIS) in AcOH-CHCl\(_3\) under thermal conditions gave diiodo derivative 19 as a crude product. It should be mentioned that reaction of 18 with 1 equiv. (2 molar amounts) of NIS may lead to an over-iodinated product and recovery of unreacted 18, because 19 is more soluble (in AcOH-CHCl\(_3\)) than 18. In order to avoid the over reaction, 0.5 equiv. (1 molar amount) of NIS was used in the reaction described above (85% yield based on NIS used).
Sonogashira reaction of 19 with ethynyltriisopropylsilane afforded the desired 20 in 37% yield after purification.

\[
\begin{array}{c}
\text{Br} & \text{Br} \\
\text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S}
\end{array}
\]

\[
\begin{array}{c}
\text{Br} & \text{Br} \\
\text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S}
\end{array}
\]

\[
\begin{array}{c}
\text{Br} & \text{Br} \\
\text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S}
\end{array}
\]

\[
\begin{array}{c}
\text{Si-Pr}_3 \\
\text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S} & \text{S}
\end{array}
\]

**Reagents and conditions:** i, 3-thiopheneboronic acid, Pd(PPh₃)₄, K₂CO₃, 1,4-dioxane, H₂O; ii, N-iodosuccinimide, AcOH, CHCl₃, AIBN; iii, ethynyltriisopropylsilane, PdCl₂(PPh₃)₂, CuI, i-Pr₂NH, THF.

**Scheme 3**

Figure 1 shows UV-visible spectra of the ETB derivative 1a, ethynlthienothiophene derivative 7a, symmetrically substituted derivative 9, and 1-(thieno[3,2-b]thiophen-2-yl)-4-(3-thienyl)benzene derivatives 15 and 16 in CH₂Cl₂. When the thiophene ring of 1a is replaced to thienothiophene ring, the spectra shifted to the longer wavelength: A bathochromic shift is observed in the order 1a<15<9. When the [(triisopropylsilyl)thienyl]phenyl groups are substituted to the ethynlthienothiophene 7a, large bathochromic shift is observed in the order 7a<15<16, indicating efficient \(\pi\) conjugation of the [(triisopropylsilyl)thienyl]phenyl moiety with the central thienothiophene moiety.

Figure 2 exhibits UV-visible spectra of the triisopropylsilyl derivatives 1a and 9, hexylphenyl derivative 1b (data taken from ref. 22), unsymmetrically substituted derivative 11, and 2,5-dithienyl-thieno[3,2-b]thiophene derivative 20 in CH₂Cl₂. As expected from the difference between the spectra of 1a and 1b, compound 11 showed a red shift, compared to 9. Central thienothiophene moiety causes large bathochromic shift, compared to the central benzene ring. This is shown by comparison of the spectra of compounds 1a and 20. It should be mentioned that the large red shift of 20 is in contrast with the case of ETAr spacer (Chart 1) containing a biphenyl moiety. Effect of central biphenyl moiety in the ETAr spacer has turned out to be not so large: A spectrum of 4,4’-bis[2-(trimethylsilyl-ethynyl)-3-thienyl]biphenyl \([\lambda_{\text{max}}/\text{nm} 271 (\log \varepsilon 4.51), 293 (4.52), 302 (4.52), 329 (4.56)]\) is similar to that of 1c \([\lambda_{\text{max}}/\text{nm} 259 (\log \varepsilon 4.46), 289 (4.45), 327 (4.38)]\), from viewpoint of \(\lambda_{\text{max}}\) value of the absorption band with the longest wavelength. The absorption band with the longest wavelength. The different electronic and structural character of the central moieties (i.e., thienothiophene moiety) may work in the tuning of the ETB/ETAr system.
In summary, we have prepared various compounds containing thieno[3,2-b]thiophene moieties. They have trialkylsilylethynyl branches on the 3-position of the thienothiophene moieties and/or 2-position of the thiophene moieties. Some of them have pseudoaxes through the 2- and 5-positions of the thienothiophene moieties. Extension of $\pi$-system through the central benzene ring (or thienothiophene ring) was suggested by UV-vis spectra. These ETB-related units will help construction of larger systems, by linking the units, like the case of compound 3.

**EXPERIMENTAL**

Melting points were measured on a Yanagimoto MP-J3 micro melting points apparatus and were uncorrected. NMR spectra were recorded on a Bruker Avance-400 or a JEOL ECA-600 spectrometer. UV-vis spectra were measured on a Hitachi U-3210 spectrometer. IR spectra were obtained on a Shimadzu FTIR-8100M spectrometer. MS spectra were taken on a Hitachi M-2500S spectrometer. FT-ICR-MS spectra were measured on a Bruker APEX III spectrometer.

3-[2-(Triisopropylsilyl)ethynyl]thieno[3,2-b]thiophene (7a). A mixture of 3-bromothieno-[3,2-b]thiophene (6) (1.27 g, 5.80 mmol), ethynyltriisopropylsilane (1.93 mL, 8.69 mmol), dichlorobis(triphenylphosphine)palladium(II) (94.4 mg, 0.134 mmol), copper(I) iodide (25.8 mg, 0.136 mmol), and diisopropylamine (10 mL) in 1,4-dioxane (50 mL) was refluxed under nitrogen atmosphere for 43 h. After cooling to room temperature, CHCl$_3$ and water were added to the filtrate. The organic phase was separated and dried over MgSO$_4$. The solvent was removed under reduced pressure and the residue was treated with a silica-gel column chromatography (hexane) to give 1.80 g (5.62 mmol, 97% yield) of 7a: Colorless oil; $R_f = 0.33$ (SiO$_2$-hexane); $^1$H NMR (400 MHz, CDCl$_3$) $\delta = 1.15$ (21H, s, i-Pr),
7.28 (1H, d, \( ^3J = 5.2 \) Hz), 7.41 (1H, dd, \( ^3J = 5.2 \) Hz and \( ^5J = 1.6 \) Hz), and 7.51 (1H, d, \( ^5J = 1.6 \) Hz); \( ^{13}\)C\{\( ^1\)H\} NMR (100 MHz, CDCl\(_3\)) \( \delta = 11.2 \) (CHMe\(_2\)), 18.7 (Me), 93.6 (C=C), 99.6 (C=C), 115.6, 119.7, 128.0, 130.6, 138.0 and 141.7; UV (CH\(_2\)Cl\(_2\)) 248 (log \( \varepsilon \) 4.28), 278 (4.10), 286 (4.19), and 296 nm (4.16); IR (neat) 3104, 2944, 2892, 2865, 2145 (C≡C), 1495, 1461, 1383, 1366, 1347, 1244, 1192, 1167, 1092, 1076, 1017, 995, 909, 884, 847, 797, 752, 716, 677, 650, 559, 505, 471, and 455 cm\(^{-1}\); MS (70 eV) \( m/z \) (rel intensity) 320 (M\(^+\); 58), 277 (M\(^+\)–i-Pr; 100), 249 (M\(^+\)–i-Pr–2Me+2; 26), 235 (M\(^+\)–2i-Pr+1; 35), 221 (M\(^+\)–2i-Pr–Me+2; 27), and 207 (M\(^+\)–i-Pr\(_2\)Si+1; 41). Calcd for C\(_{17}\)H\(_{24}\)S\(_2\): M, 320.1089. Found: \( m/z \) 320.1084.

3-[2-(4-Hexylphenyl)ethynyl]thieno[3,2-b]thiophene (7b). A mixture of 6 (142.0 mg, 0.648 mmol), 1-ethynyl-4-hexylbenzene (199.9 mg, 1.073 mmol), dichlorobis(triphenylphosphine)palladium(II) (22.0 mg, 0.0313 mmol), copper(I) iodide (3.1 mg, 0.016 mmol), and diisopropylamine (2 mL) in 1,4-dioxane (10 mL) was stirred at 80 °C for 2 d. After cooling to room temperature, CHCl\(_3\) (ca. 100 mL) and water (ca. 100 mL) were added. 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 (hexane) to give 182.0 mg (0.5608 mmol, 87 % yield) of 7b: Colorless oil; \( R_f = 0.30 \) (SiO\(_2\)-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta = 0.88 \) (3H, t, \( ^3J = 6.8 \) Hz, Me), 1.2–1.3 (6H, m, CH\(_2\)), 1.61 (2H, quin, \( ^3J = 7.6 \) Hz, CH\(_2\)), 2.61 (2H, t, \( ^3J = 7.6 \) Hz, CH\(_2\)), 7.17 (2H, \( ^3J = 8.1 \) Hz, phenyl), 7.24 (1H, d, \( ^3J = 5.2 \) Hz), 7.43 (1H, dd, \( ^3J = 5.2 \) Hz and \( ^5J = 1.5 \) Hz), 7.47 (2H, d, \( ^3J = 8.1 \) Hz, phenyl), and 7.54 (1H, d, \( ^5J = 1.5 \) Hz); \( ^{13}\)C\{\( ^1\)H\} NMR (100 MHz, CDCl\(_3\)) \( \delta = 14.1 \) (Me), 22.6 (CH\(_2\)), 28.9 (CH\(_2\)), 31.2 (CH\(_2\)), 31.6 (CH\(_2\)), 35.9 (CH\(_2\)), 81.9 (C=C), 91.8 (C=C), 115.3, 119.7, 119.9, 127.9, 128.5, 130.0, 131.5, 138.2, 141.0, and 143.7; UV (CH\(_2\)Cl\(_2\)) 262 (sh, log \( \varepsilon \) 4.37), 270 (4.46), 287 (sh, 4.34), 296 (4.42), 304 (4.39), and 315 nm (4.37); IR (neat) 3102, 2955, 2928, 2865, 2217 (C≡C, weak), 1520, 1466, 1350, 1088, 1051, 1019, 909, 853, 835, 818, 797, 714, 650, 563, and 529 cm\(^{-1}\); MS (70 eV) \( m/z \) (rel intensity) 324 (M\(^+\); 83), and 253 (M\(^+\)–C\(_5\)H\(_{11}\); 100). Calcd for C\(_{20}\)H\(_{20}\)S\(_2\): M, 324.1006. Found: \( m/z \) 323.9369.

3-[2-(Trimethylsilyl)ethynyl]thieno[3,2-b]thiophene (7c). A mixture of 6 (184.5 mg, 0.843 mmol), ethynyltrimethylsilane (99.5 mg, 1.073 mmol), dichlorobis(triphenylphosphine)palladium(II) (32.8 mg, 0.0468 mmol), copper(I) iodide (10.3 mg, 0.0541 mmol), and diisopropylamine (2 mL) in THF (10 mL) was stirred under nitrogen atmosphere at 70 °C for 28 h. After cooling to room temperature, CHCl\(_3\) (ca. 100 mL) and water (ca. 100 mL) were added to the filtrate. 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 (CHCl\(_3\)) to give a mixture of 3-[2-(trimethylsilyl)ethynyl]thieno[3,2-b]thiophene and the starting 6. To this mixture, were added ethynyltrimethylsilane (54.5 mg, 0.555 mmol), dichlorobis(triphenylphosphine)palladium(II) (11.9 mg, 0.017 mmol), copper(I) iodide (5.7 mg, 0.030 mmol), diisopropylamine (1 mL), and 1,4-dioxane (5 mL). The resulting mixture was stirred
under nitrogen atmosphere at 101 °C for 20 h. After cooling to room temperature, CHCl₃ and water were added to the filtrate. The organic phase was separated and dried over MgSO₄. The solvent was removed under reduced pressure and the residue was treated with a silica-gel column chromatography (hexane) to give 179.2 mg (0.758 mmol, 90% yield) of 7c: Colorless oil; \( R_f = 0.26 \) (SiO₂-hexane); \(^1\)H NMR (400 MHz, CDCl₃) \( \delta = 0.28 \) (9H, s, Me), 7.23 (1H, d, \(^3 J = 5.2 \) Hz), 7.42 (1H, dd, \(^3 J = 5.2 \) Hz and \(^5 J = 1.6 \) Hz), and 7.53 (1H, d, \(^5 J = 1.6 \) Hz); \(^13\)C\{\(^1\)H\} NMR (150 MHz, CDCl₃) \( \delta = \) –0.5 (Me), 97.1 (C≡C), 97.8 (C≡C), 115.2, 119.7, 128.1, 131.3, 138.1, and 141.2; IR (neat) 3104, 2959, 2899, 2161, 2147 (C≡C), 2068, 1491, 1468, 1347, 1250, 1192, 1167, 1090, 1078, 909, 858, 843, 797, 776, 714, 650, 558, and 471 cm\(^{-1}\); MS (70 eV) \( m/z \) (rel intensity) 236 (M\(^+\); 63) and 221 (M\(^+\)–Me; 100). Calcd for C\(_{11}\)H\(_{12}\)S\(_2\): M, 236.0150. Found: \( m/z \) 236.0145.

1,4-Bis[3-{2-(triisopropylsilyl)ethynyl]thieno[3,2-b]thiophen-2-yl]benzene (9). To a solution of 7a (90.6 mg, 0.283 mmol) in THF (5 mL) was added 0.43 mmol of butyllithium (1.65 M solution in hexane, 0.26 mL) at –78 °C and the resulting mixture was stirred for 40 mim. To the solution was added 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.090 mL, 0.441 mmol) at 0 °C, and the reaction mixture was stirred for 45 min. To the resulting mixture were added water (ca. 100 mL) and EtOAc (ca. 100 mL), the organic phase was separated and dried over MgSO₄. The solvent was removed under reduced pressure to give crude 8a. This crude product was used in the following reaction without further purification. 8a: \(^1\)H NMR (400 MHz, CDCl₃) \( \delta = 1.18 \) (21H, s, i-Pr), 1.25 (12H, s, CMe₂), 7.22 (1H, d, \(^3 J = 5.2 \) Hz), and 7.47 (1H, d, \(^3 J = 5.2 \) Hz). A mixture of crude 8a (ca. 0.27 mmol), 1,4-diiodobenzene (43.9 mg, 0.133 mmol), tetrakis(triphenylphosphine)palladium (14.5 mg, 0.0125 mmol), K₂CO₃ (180.3 mg), THF (2.5 mL), toluene (2.5 mL), and water (1 mL) was heated at 85 °C for 20 h. After cooling to rt, CHCl₃ (ca. 100 mL) and water (ca. 100 mL) were added to the reaction mixture. The organic phase was separated, washed with brine, and dried over MgSO₄. The solvent was removed under reduced pressure and the residue was treated with a silica-gel column chromatography (hexane-EtOAc: 10:1 to 0:1) to give 12.8 mg of 9 (0.0179 mmol, 13% yield based on the starting 7a). 9: Pale yellow solid, mp 162–165 °C; \( R_f = 0.26 \) (SiO₂-hexane); \(^1\)H NMR (400 MHz, CDCl₃) \( \delta = 1.17 \) (42H, s, i-Pr), 7.23 (2H, d, \(^3 J = 5.2 \) Hz), 7.41 (2H, d, \(^3 J = 5.2 \) Hz), and 8.04 (4H, s, phenyl); \(^13\)C\{\(^1\)H\} NMR (100 MHz, CDCl₃) \( \delta = 11.2 \) (CHMe₂), 18.7 (Me), 98.0 (C=C), 100.4 (C=C), 111.3, 119.7, 127.5, 134.0, 135.5, 143.8, and 146.9; UV-vis (CH₂Cl₂) 250 (log \( \varepsilon \) 4.45), 320 (4.21), and 380 nm (4.57); IR (KBr) 2940, 2863, 1468, 1347, 1250, 1192, 1167, 1090, 1078, 909, 858, 843, 797, 776, 714, 650, 558, and 471 cm\(^{-1}\); MS (70 eV) \( m/z \) (rel intensity) 714 (M\(^+\); 100), 157 (i-Pr₂Si\(^+\); 18), and 115 (i-Pr₂Si\(^+\)+1; 13). Calcd for C\(_{40}\)H\(_{50}\)S\(_4\)Si\(_2\): M, 714.2334. Found: \( m/z \) 714.2331.

1-Bromo-4-[3-{2-(triisopropylsilyl)ethynyl]thieno[3,2-b]thiophen-2-yl]benzene (10). A mixture of 1-bromo-4-iodobenzene (783.7 mg, 2.77 mmol), crude 8a [prepared from 517.2 mg (1.613 mmol) of 7a
by the method described above], tetrakis(triphenylphosphine)palladium (44.8 mg, 0.0388 mmol), K₂CO₃ (1.12 g), THF (15 mL), toluene (15 mL), and water (8 mL) was heated at 70 °C for 13 h. After cooling to room temperature, CHCl₃ (ca. 200 mL) and water (ca. 100 mL) were added to the reaction mixture. The organic phase was separated and dried over MgSO₄. The solvent was removed under reduced pressure. To the residue was added hexane and an insoluble material was removed by filtration. The filtrate was concentrated under reduced pressure and the residue was treated with a silica-gel column chromatography (hexane-CHCl₃, 1:0 to 0:1) to give 160.6 mg (0.3377 mmol, 21 % yield based on the starting 7a) of 10: Pale yellow solid, mp 70–72 °C; Rᶠ = 0.35 (SiO₂-hexane); ¹H NMR (400 MHz, CDCl₃) δ = 1.16 (21H, s, i-Pr), 7.22 (1H, d, ³J = 5.2 Hz), 7.41 (1H, d, ³J = 5.2 Hz), 7.52 (2H, d, ³J = 8.4 Hz, phenyl), and 7.88 (2H, d, ³J = 8.4 Hz, phenyl); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 11.3 (C≡CHMe₂), 18.7 (Me), 98.1 (C≡C), 100.1 (C≡C), 111.4, 119.6, 122.2, 127.6, 128.8, 131.6, 133.1, 135.4, 143.6, and 146.0; IR (KBr) 2957, 2888, 2861, 2149 (C≡C), 1505, 1483, 1464, 1397, 1356, 1190, 1059, 955, 912, 884, 820, 777, 712, 561, 504, and 426 cm⁻¹; MS (70 eV) m/z (rel intensity) 476 (M+2; 100), 474 (M⁺; 85), 433 (M⁺–i-Pr+2; 76), 431 (M⁺–i-Pr₂; 35), 361 (M⁺–i-Pr₂+1; 34), 309 (M⁺–Br–i-Pr₂; 59), and 188 (M⁺–Br–i-Pr₂SiC₂–S–1; 36); Found: m/z 474.0505. Calcd for C₂₃H₂₇BrS₂Si: M, 474.0507. Anal. Calcd for C₂₃H₂₇BrS₂Si: C, 58.09; H, 5.72%. Found: C, 58.47; H, 5.85%.

1-[3-{2-(4-Hexylphenyl)ethynyl]thieno[3,2-b]thiophen-2-yl]-4-[3-{2-(triisopropylsilyl)ethynyl]thieno[3,2-b]thiophen-2-yl]benzene (11). To a solution of 7b (82.8 mg, 0.255 mmol) in THF (4.5 mL) was added 0.25 mmol of butyllithium (1.65 M solution in hexane, 0.15 mL) at −78 °C and the resulting mixture was allowed to warm to 0 °C and stirred for 20 min. To the solution was added 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.05 mL, 0.25 mmol) and the reaction mixture was allowed to warm to room temperature. To the resulting mixture were added water (ca. 100 mL) and EtOAc (ca. 100 mL), the organic phase was separated and dried over MgSO₄. The solvent was removed under reduced pressure to give crude 8b. 8b: ¹H NMR (400 MHz, CDCl₃) δ = 0.89 (3H, t, ³J = 6.8 Hz, Me), 1.32 (6H, m, CH₂), 1.40 (12H, s, CMe₂), 1.61–1.64 (2H, m, CH₂), 2.63 (2H, t, ³J = 7.8 Hz, CH₂), 7.18 (2H, d, ³J = 8.0 Hz, phenyl), 7.25 (1H, d, ³J = 5.2 Hz), 7.51 (1H, d, ³J = 5.2 Hz), and 7.52 (2H, d, ³J = 8.0 Hz, phenyl). A mixture of the crude 8b, 10 (106.4 mg, 0.224 mmol), tetrakis(triphenylphosphine)palladium (6.9 mg, 0.0060 mmol), K₂CO₃ (177 mg), THF (5 mL), toluene (5 mL), and water (2 mL) was heated at 85 °C for 17 h. After cooling to room temperature, CHCl₃ (ca. 100 mL) and water (ca. 100 mL) were added to the reaction mixture. The organic phase was separated, washed with brine, and dried over MgSO₄. The solvent was removed under reduced pressure and the residue was treated with a silica-gel column chromatography (hexane-CHCl₃, 1:0 to 0:1) to give 99.4 mg (0.138 mmol, 62% yield based on 10) of 11. 11: Yellow oil; Rᶠ = 0.14 (SiO₂-hexane); ¹H NMR (400 MHz, CDCl₃) δ = 0.89 (3H, t, ³J = 6.8 Hz, Me), 1.15 (21H, s, i-Pr), 1.31 (6H, m, CH₂), 1.62 (2H, m, CH₂),
2.63 (2H, t, \( ^3J = 7.6\) Hz, CH\(_2\)), 7.19 (2H, d, \( ^3J = 8.4\) Hz, phenyl), 7.24 (1H, d, \( ^3J = 5.2\) Hz), 7.26 (1H, d, \( ^3J = 5.2\) Hz), 7.41 (1H, d, \( ^3J = 5.2\) Hz), 7.43 (1H, d, \( ^3J = 5.2\) Hz), 7.49 (2H, d, \( ^3J = 8.4\) Hz, phenyl), 8.04 (2H, d, \( ^2J = 8.4\) Hz, phenyl), and 8.13 (2H, d, \( ^3J = 8.4\) Hz, phenyl); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\)) \(\delta = 11.3\) (CHMe\(_2\)), 14.1 (CH\(_2\)Me), 18.7 (CHMe\(_2\)), 22.6 (CH\(_3\)), 28.9 (CH\(_2\)), 31.2 (CH\(_2\)), 31.7 (CH\(_2\)), 35.9 (CH\(_2\)), 82.8 (C=\(\equiv\)), 95.3 (C=\(\equiv\)), 98.2 (C=\(\equiv\)), 100.5 (C=\(\equiv\)), 111.1, 111.2, 119.7, 120.0, 127.3, 127.4, 127.5, 128.5, 131.6, 133.9, 134.2, 135.4, 135.6, 143.0, 143.8, 143.8, 146.1, and 146.9; UV-vis (CH\(_2\)Cl\(_2\)) 248 (log \(\varepsilon\) 4.48), 253 (sh, 4.47), 287 (4.41), 316 (4.41), and 386 nm (4.56); IR (KBr) 2926, 2862, 2147 (C=\(\equiv\)), 1516, 1464, 1358, 1339, 1067, 995, 943, 910, 833, 710, 665, 635, and 529 cm\(^{-1}\). Calcd for C\(_{43}\)H\(_{46}\)NaS\(_4\)Si: (M+Na\(^+\), 741.2144. Found: m/z 741.2143.

1-Bromo-4-[2-(triisopropylsilyl)ethylthienyl]-3-thienyl|benzene (14). 1-Bromo-4-(2-iodo-3-thienyl)-benzene (13) was prepared according to the previously reported method\(^9\) \([\text{\(^1\)H NMR (CDCl\(_3\)) \(\delta = 6.94\) (1H, d), 7.38 (2H, AA'BB''), 7.50 (1H, d), and 7.57 (2H, AA'BB'')]\). A mixture of 13 (1.047 g, 2.87 mmol), ethynyltriisopropylsilane (0.65 mL, 2.9 mmol), dichlorobis(triphenylphosphine)palladium(II) (105.2 mg, 0.15 mmol), copper(I) iodide (41 mg, 0.22 mmol), and diisopropylamine (40 mL) in THF (40 mL) was stirred at 50 °C for 116 h. After cooling to room temperature, CHCl\(_3\) (ca. 200 mL) and water (ca. 100 mL) 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 (hexane) to give 1.035 g (2.47 mmol, 86% yield) of 14: Colorless oil; \(R_f = 0.47\) (SiO\(_2\)-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 1.10\) (21H, br s, i-Pr), 7.15 (1H, d, \( ^3J = 5.5\) Hz, thienyl), 7.24 (1H, d, \( ^3J = 5.5\) Hz, thienyl), 7.50 (2H, d, \( ^3J = 8.5\) Hz, phenyl), and 7.72 (2H, d, \( ^3J = 8.5\) Hz, phenyl); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\)) \(\delta = 11.3\) (CHMe\(_2\)), 18.6 (Me), 99.0 (C=\(\equiv\)), 99.3 (C=\(\equiv\)), 118.9 (2-thienyl), 121.5 (1-Ph), 126.4 (4-thienyl), 127.2 (5-thienyl), 129.5 (3- and 5-Ph), 131.4 (2- and 6-Ph), 134.0 (4-Ph), and 143.4 (3-thienyl); IR (neat) 2938, 2865, 2141 (C=\(\equiv\)), 1592, 1524, 1487, 1464, 1368, 1277, 1067, 1011, 997, 888, 824, 762, 733, 677, and 663 cm\(^{-1}\); MS (70 eV) \(m/z\) (rel intensity) 420 (M\(^+\)+2; 48), 418 (M\(^+\)); 45), 377 (M\(^+\)–i-Pr+2; 100), 375 (M\(^+\)–i-Pr; 95), 307 (M\(^+\)–2i-Pr–Si+3; 30), 305 (M\(^+\)–2i-Pr–Si+1; 27), and 253 (M\(^+\)–2i-Pr–Br; 35). Calcd for C\(_{43}\)H\(_{27}\)BrSSi: M, 418.0786. Found: \(m/z\) 418.0787.

1-[3-[2-(Triisopropylsilyl)ethylthieno[3,2-b]thiophen-2-yl]-4-[2-(triisopropylsilyl)ethylthienyl]-3-thienyl|benzene (15). A mixture of 14 (732.0 mg, 1.75 mmol), crude 8a [prepared from 500.7 mg (1.56 mmol) of 7a by the method described above], tetrakis(triphenylphosphine)palladium (38.8 mg, 0.0336 mmol), K\(_2\)CO\(_3\) (1.08 g), THF (15 mL), toluene (15 mL), and water (8 mL) was heated at 85 °C for 17 h. After cooling to room temperature, CHCl\(_3\) (ca. 200 mL) and water (ca. 100 mL) were added to the reaction mixture. The organic phase was separated and dried over MgSO\(_4\). The solvent was removed under reduced pressure and the residue was treated with a silica-gel column chromatography.
(hexane-CHCl₃, 1:0 to 0:1) to give 363.9 mg of crude 15 and 227.7 mg of crude 16. The crude 15 was recrystallized from hexane to give 213.0 mg (0.323 mmol, 21% yield based on the starting 7a) of 15. The crude 16 was recrystallized from CHCl₃ to give 122.7 mg (0.123 mmol, 8% yield based on the starting 7a) of 16. 15: Pale yellow solid, mp 130–134 °C (decomp); R_f = 0.22 (SiO₂-hexane); ¹H NMR (400 MHz, CDCl₃) δ = 1.11 (21H, s, i-Pr), 1.17 (21H, s, i-Pr), 7.22 (1H, d, 3_J = 5.2 Hz), 7.23 (1H, d, 3_J = 5.2 Hz), 7.26 (1H, d, 3_J = 5.2 Hz), 7.40 (1H, d, 3_J = 5.2 Hz), 7.87 (2H, d, 3_J = 8.4 Hz, phenyl), and 8.03 (2H, d, 3_J = 8.4 Hz, phenyl); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 11.3 (C_HMe₂), 18.7 (Me), 97.7 (C≡C), 98.9 (C≡C), 99.7 (C≡C), 100.5 (C≡C), 111.2, 115.5, 118.7, 119.7, 126.3, 127.2, 127.3, 127.6, 128.1, 133.2, 133.6, 135.1, 135.3, 138.3, 143.8, and 147.4; UV-vis (CH₂Cl₂) 248 (log ε 4.38), 303 (4.33), and 356 nm (4.49); IR (KBr) 2942, 2865, 2137 (C≡C), 1554, 1462, 1381, 1356, 1094, 1017, 995, 957, 882, 839, 776, 762, 743, 712, 677, 623, 538, 507, and 467 cm⁻¹; MS (70 eV) m/z (rel intensity) 658 (M⁺; 100), 157 (i-Pr₃Si⁺; 43), and 115 (i-Pr₂Si⁺+1; 20); Found: m/z 658.2614. Calcd for C₃₈H₅₀S₃Si₂: M, 658.2613. Anal. Calcd for C₃₈H₅₀S₃Si₂: C, 69.24; H, 7.65%. Found: C, 69.41; H, 7.72%.

Preparation of compound 16. To a solution of 7a (45.1 mg, 0.141 mmol) in THF (3 mL) was added 0.30 mmol of butyllithium (1.65 M solution in hexane, 0.18 mL) at –78 °C, the resulting mixture was allowed to warm to 0 °C, and stirred for 30 min. To the solution was added 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.070 mL, 0.34 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 30 min. To the resulting mixture were added water (ca. 100 mL) and EtOAc (ca. 100 mL), the organic phase was separated and dried over MgSO₄. The solvent was removed under reduced pressure to give crude 12. 12: ¹H NMR (400 MHz, CDCl₃) δ = 1.17–1.18 (21H, br s, i-Pr), 1.34 (12H, s, OCMe₂), 1.36 (12H, s, OCMe₂), and 7.71 (1H, s, thienothiophene). A mixture of 14 (122.1 mg, 0.2911 mmol), the crude 12, tetrakis(triphenylphosphine)palladium (7.4 mg, 0.0064 mmol), K₂CO₃ (256 mg), THF (5 mL), toluene (5 mL), and water (3 mL) was heated at 85 °C for 16 h. After cooling to room temperature, CHCl₃ (ca. 100 mL) and water (ca. 100 mL) were added to the reaction mixture. The organic phase was separated and dried over MgSO₄. The solvent was removed under reduced pressure and the residue was treated with a silica-gel column chromatography (hexane - CHCl₃, 1:0 to 5:1) to give 81.4 mg (0.0816 mmol, 58% yield based on 7a) of 16: Yellow solid, mp 184–189 °C (decomp); R_f = 0.05 (SiO₂-hexane); ¹H NMR (600 MHz, CDCl₃) δ = 1.12-1.16 (42H, i-Pr), 1.20-1.22 (21H, i-Pr), 7.19 (1H, d, 3_J = 5.3 Hz), 7.20 (1H, d, 3_J = 5.3 Hz), 7.24 (1H, d, 3_J = 5.3 Hz), 7.24 (1H, d, 3_J = 5.3 Hz), 7.43 (1H, s), 7.64 (2H, d, 3_J = 8.6 Hz, phenyl), 7.87 (2H, d, 3_J = 8.8 Hz, phenyl), 7.89 (2H, d, 3_J = 8.6 Hz, phenyl), and 8.04 (2H, d, 3_J = 8.8 Hz, phenyl); ¹³C{¹H} NMR (150 MHz, CDCl₃) δ = 11.4 (CHMe₂ x 3), 18.7 (Me x 3), 97.9 (C≡C), 98.9 (C≡C), 98.9 (C≡C), 99.6 (C≡C), 99.7 (C≡C), 100.4 (C≡C), 111.2, 115.5, 118.7, 118.8, 125.7, 126.3, 126.4, 127.2, 127.4, 127.6, 128.1, 128.5, 133.2, 133.6, 134.8, 135.1, 136.2, 143.1, 144.1, 146.1, and 146.8;
UV-vis (CH₂Cl₂) 253 (log ε 4.56), 274 (sh, 4.40), 301 (4.42), and 389 nm (4.78); IR (KBr) 2942, 2890, 2865, 2136 (C≡C), 1534, 1505, 1462, 1383, 1366, 1092, 1061, 1017, 995, 882, 841, 814, 762, 743, 712, 677, 57, and 465 cm⁻¹; Found: m/z 1019.4029. Calcd for C₅₉H₇₆NaS₄Si₃: (M+Na)⁺, 1019.4030. Anal. Calcd for C₅₉H₇₆NaS₄Si₃·H₂O: C, 69.76; H, 7.74%. Found: C, 70.16; H, 7.68%.

2,5-Di(3-thienyl)thieno[3,2-b]thiophene (18). A mixture of 2,5-dibromothieno[3,2-b]thiophene (17) (510.2 mg, 1.71 mmol), 3-thiopheneboronic acid (472 mg, 3.69 mmol), tetrakis(triphenylphosphine)-palladium (22.6 mg, 0.020 mmol), K₂CO₃ (1.15 g), 1,4-dioxane (50 mL), and water (30 mL) was heated under nitrogen at 100 °C for 1.5 h. Insoluble material was collected by filtration and washed with CHCl₃ (ca. 50 mL) to give 18 (462.7 mg, 1.52 mmol) in 89% yield. This compound was almost insoluble in common solvents and used in the succeeding reaction without recrystallization. 18: Pale yellow solid, mp > 300 °C; IR (KBr) 3096, 3083, 1638, 1543, 1470, 1404, 1375, 1248, 1213, 1194, 1179, 1088, 1013, 1005, 947, 911, 872, 855, 841, 818, 662, 633, 536, and 453 cm⁻¹; MS (70 eV) m/z (rel intensity) 304 (M⁺ 100), 259 (M⁺−S−CH; 6), and 152 (M⁺/2; 7). Calcd for C₁₄H₈S₄: M⁺, 303.9509. Found: m/z 303.9505.

2,5-Bis(2-iodo3-thienyl)thieno[3,2-b]thiophene (19). A suspension of 18 (119.8 mg, 0.393 mmol), N-iodosuccinimide (NIS, 88.9 mg, 0.395 mmol, 1.01 molar ratio based on 18), and acetic acid (5 mL) in CHCl₃ (10 mL) was stirred at 60 °C for 3 h. The insoluble starting material 18 (25.3 mg) was recovered by filtration in 21% recovery. CHCl₃ (ca. 20 mL) and water (ca. 20 mL) were added to the filtrate and the organic phase was separated, washed with saturated aqueous NaHCO₃ solution, and then washed with saturated aqueous NaHSO₃ solution. The organic phase was dried over MgSO₄, and the solvent was removed under reduced pressure. The residue was treated with a silica-gel column chromatography (CCl₄) to give 93.0 mg (0.167 mmol, 85% yield based on NIS) of 19: Yellow solid, mp 176–178 °C; Rf = 0.55 (SiO₂-CCl₄); ¹H NMR (600 MHz, CDCl₃) δ = 7.07 (2H, d, 3J = 5.5 Hz, 4-thienyl), 7.50 (2H, d, 3J = 5.5 Hz, 5-thienyl), and 7.61 (2H, s); ¹³C{¹H} NMR (150 MHz, CDCl₃) δ = 73.0 (2-thienyl), 118.5, 128.9 (4-thienyl), 131.6 (5-thienyl), 139.0, and 139.7 (thienothiophene and 3-thienyl); IR (KBr) 3094, 1487, 1387, 1320, 1240, 1053, 955, 805, 826, 723, 716, 669, 627, and 544 cm⁻¹; MS (70 eV) m/z (rel intensity) 556 (M⁺; 100), 430 (M⁺−I+1; 10), and 302 (M⁺−2I; 18). Calcd for C₁₄H₈I₂S₄: M⁺, 555.7442. Found: m/z 555.7443.

2,5-Bis[2-{2-(triisopropylsilyl)ethyl}yl]-3-thienyl]thieno[3,2-b]thiophene (20). A mixture of 19 (72.8 mg, 0.131 mmol), ethynyltriisopropylsilane (0.123 mL, 0.672 mmol), dichlorobis(triphenylphosphine)-palladium(II) (21.7 mg, 0.031 mmol), copper(I) iodide (6.7 mg, 0.035 mmol), and diisopropylamine (10 mL) in THF (15 mL) was stirred under nitrogen atmosphere at 60 °C for 40 h. CHCl₃ (ca. 20 mL) and water (ca. 20 mL) were added to the reaction mixture. The organic phase was separated and dried over MgSO₄. The solvent was removed under reduced pressure, the residue was treated with a silica-gel
column chromatography (CCl₄) to give a crude product (77.7 mg, ca. 90% yield), which was purified by additional silica-gel column (CCl₄) to give 32.2 mg (0.048 mmol, 37% yield) of 20: Yellow solid, m.p 148–149 °C; Rᵢ = 0.60 (SiO₂-CCl₄); ¹H NMR (400 MHz, CDCl₃) δ = 1.18 (s, 42H, s, i-Pr), 7.21 (s, 4H, 4- and 5-thienyl), and 7.94, (s, 2H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 11.3 (CHMe₂), 18.6 (Me), 99.5 (C≡C), 101.6 (C≡C), 117.0, 117.6, 126.3, 126.6, 137.9, 138.9, and 139.7; UV-vis (CH₂Cl₂) 283 (log ε 4.45), 308 (4.38), 370 (sh, 4.43), 387 (4.52), and 406 (sh, 4.40); IR (KBr) 2942, 2865, 2137 (C≡C), 1462, 1092, 1051, 1017, 882, 847, 826, 812, 758, 727, 644, 613, and 534 cm⁻¹; MS (70 eV) m/z (rel intensity) 664 (M⁺; 100), 579 (M⁺–2i-Pr+1; 8), and 537 (M⁺–3i-Pr+2; 4); Found: m/z 664.2175. Calcd for C₃₆H₄₈S₄Si₂: M, 664.2177. Anal. Calcd for C₃₆H₄₈S₄Si₂: C, 65.00; H, 7.27%. Found: C, 65.02; H, 7.26%.

ACKNOWLEDGEMENTS

This work was supported in part by the Grants-in-Aid for Scientific Research (No. 20550030) from the Ministry of Education, Culture, Sports, Science and Technology.

REFERENCES AND NOTES

1. Chemistry of bis(2-ethynyl-3-thienyl)arene and related systems, Part 7. For Part 6, see Ref. 8.