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Synthesis of indenothiophenone derivatives by cycloaromatization of non-conjugated thienyl tetraynes

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Abstract—Non-conjugated thienyl tetrayne derivatives **1**–**3** are prepared as novel building block for the construction of indenothiophenone derivatives. Oxidation of **1**–**3**, followed by cycloaromatization of the corresponding ketone derivatives **13**–**15** proceeds smoothly to afford indenothiophenone derivatives **16**–**21** in good yields.

Indenothiophene derivatives have received considerable attention in the field of organometallic chemistry because their transition metal complexes have been found to be promising catalysts for olefin polymerization.[1,2] The synthesis of indenothiophene derivatives are achieved in good yields by Wolff–Kishner reduction of indenothiophenone derivatives. Therefore, development of new synthetic methods for the preparation of indenothiophenone derivatives would lead us to novel indenothiophene and its transition metal complexes. However, far less attention has been devoted to their synthesis in the literature to date.[3–7] Recently, we reported that aromatic acyclic polyyne derivatives underwent cycloaromatization under mild conditions to afford polycyclic aromatic compounds such as fluorenol and semibullvalene skeletons.[8–11] In this study, new non-conjugated thienyl tetrayne derivatives **1**–**3** were designed. These compounds would be expected to the formation of indenothiophenone skeletons by their oxidation and the following cycloaromatization. We herein describe the synthesis of **1**–**3** and their cycloaromatization to indenothiophenone skeletons (Fig. 1).

Stille coupling reaction was selected as a key step for the synthesis of **1**–**3**.[12,13] Scheme 1 shows an outline for preparation of **1**–**3**. Trimethylsilyl-monoprotected butadiynylstannane (TRIBS) was prepared in situ by lithiation of bis(trimethylsilyl)butadiyne (BTB),[14] followed by stannylation of the resulting monolithio derivative. Butadiynylthiophene derivative **4** was prepared in 89% yield by the Stille coupling reaction of TRIBS with commercially available 3-bromothiophene in the presence of

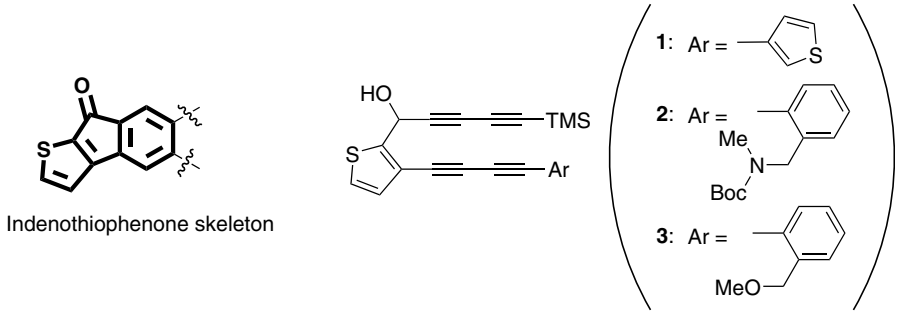

Figure 1.

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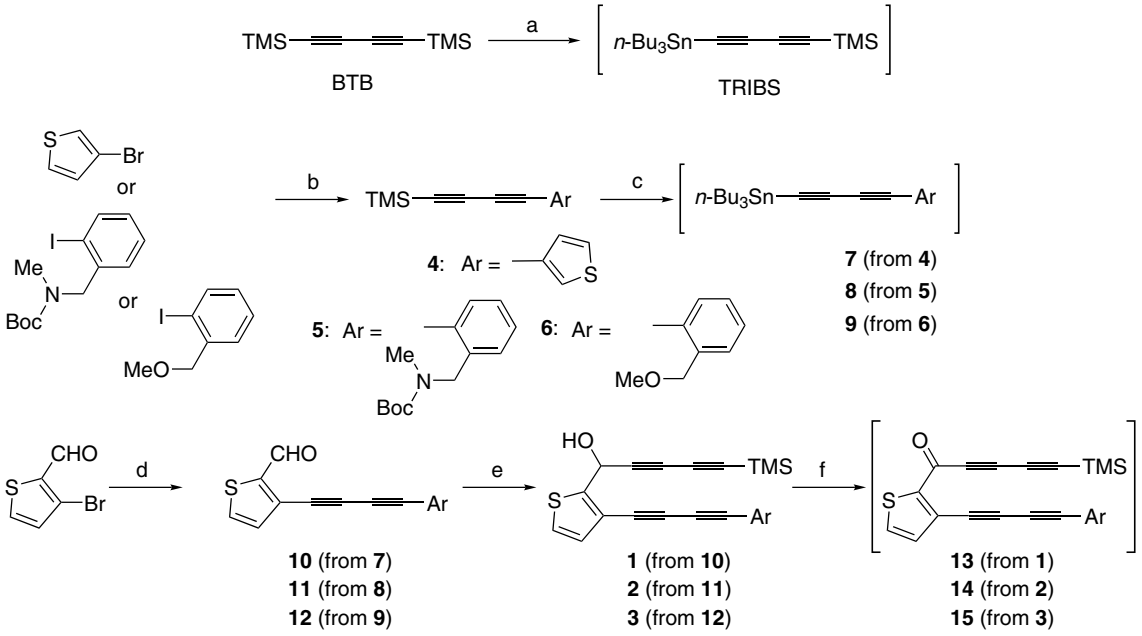


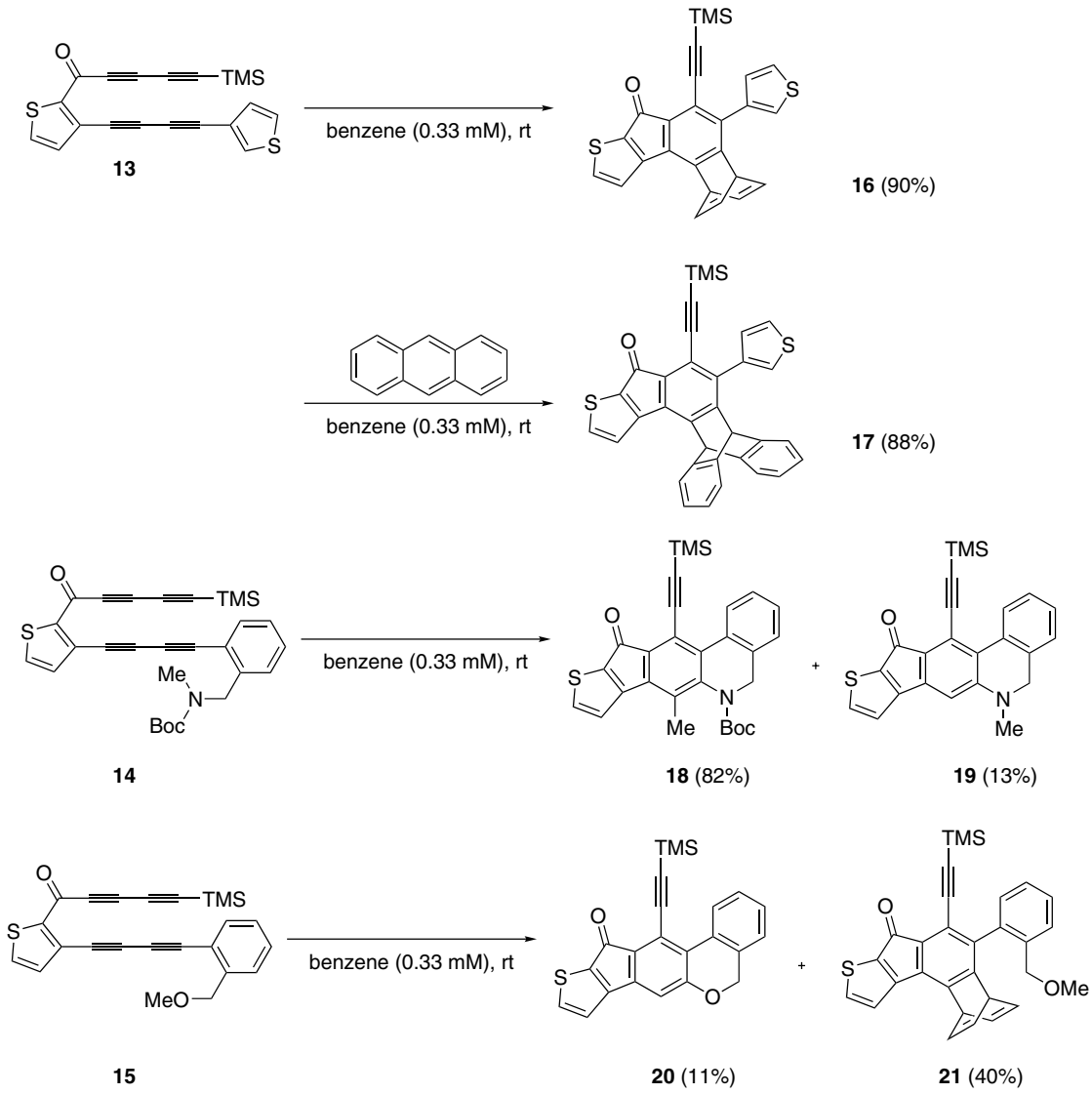
Scheme 1. Preparation of compounds **1**–**3**. Reagents and conditions: (a) (1) MeLi–LiBr, ether, rt; (2) *n*-Bu_3SnCl, rt; (b) 3-bromothiophene (for **4**) or 2-(*N*-*tert*-butoxycarbonyl-*N*-methyl)aminomethyl)-1-iodobenzene (for **5**) or 2-(methoxymethyl)-1-iodobenzene (for **6**), TRIBS, $PdCl_2(PPh_3)_2$, toluene, 110 °C; (c) (1) K_2CO_3, MeOH, 0 °C, (2) *n*-Bu_3SnCl, diisopropylamine, rt; (d) stannanes **7**–**9**, $PdCl_2(PPh_3)_2$, toluene, 80 °C; (e) MeLi–LiBr, BTB, ether, −78 °C; (f) Dess–Martin periodinane, CH_2Cl_2, 0 °C.

dichlorobis(triphenylphosphine)palladium(II), [$PdCl_2(PPh_3)_2$], in toluene at 110 °C. Similarly, butadiynylbenzene derivatives **5** and **6** were prepared in 97% and 99% yields, respectively, by the Stille coupling reaction of TRIBS with the corresponding iodobenzene derivatives, which was prepared according to the literature procedure,[15] under the same condition. Cleavage of the silyl group of **4**–**6** with potassium carbonate in methanol at 0 °C, followed by stannylation by tri-*n*-butyltin chloride in diisopropylamine at room temperature gave stannanes **7**–**9**, which were used for the next step without purification because of their instability. The reaction of stannanes **7**–**9** with 3-bromothiophene-2-carbaldehyde in the presence of $PdCl_2(PPh_3)_2$ in toluene at 80 °C gave coupling products **10**–**12** in 84%, 93% and 77% yields, respectively. The resulting coupling products **10**–**12** were allowed to react with monolithio derivative of BTB in ether at −78 °C to afford desired products **1**–**3** in 90%, 91% and 83% yields, respectively.[16] Dess–Martin oxidation of **1**–**3** in dichloromethane at 0 °C gave the corresponding ketone derivatives **13**–**15** in quantitative yields. These compounds were also used for the next step without further purification due to their instability.

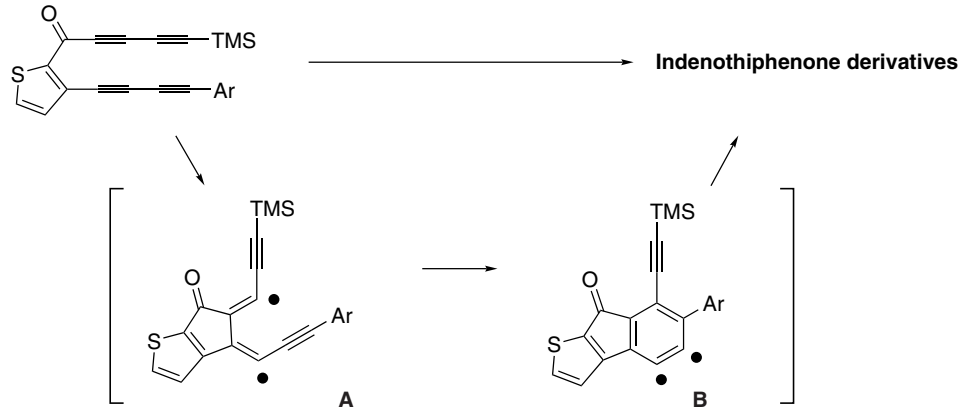
When a solution of **13** in dry benzene was vigorously stirred at room temperature under argon atmosphere, its cycloaromatization proceeded smoothly, after purification by silica gel column chromatography (eluent: hexane–ethyl acetate), to afford indenothiophenone derivative **16** in 90% yield (Scheme 2). In the presence of anthracene (20 equiv), the cycloaromatization of **13** led to a Diels–Alder adduct **17** in 88% yield. On the other hand, cycloaromatization of **14** in dry benzene at room temperature under argon atmosphere gave isoquinoline ring-fused indenothiophenone derivatives **18** and **19** in 82% and 13% yields, respectively. According to their ^1H NMR spectra, compound **18** has been found to possess two substituents of a methyl group at the 7-position and a Boc group at the 6-position. On the other hand, compound **19** has been found to possess a methyl group at the 6-position. Cycloaromatization of **15** under the same condition afforded desired products **20** and **21** in 11% and 40% yields, respectively. In contrast to the cycloaromatization of ketone derivatives **13**–**15**, it is noteworthy that no desired products were obtained when a solution of the corresponding alcohol derivatives **1**–**3** in dry benzene under the same conditions, and that cycloaromatization of compounds **1**–**3** at 80 °C gave the corresponding cyclic alcohol derivatives in 8%, 9% and 6% yields, respectively. The reason why the reactivity of alcohol derivatives **1**–**3** were low compared to ketone derivatives might be that ketone derivatives have conjugated ene–yne skeleton, though alcohol derivatives have non-conjugated one, and then facile overlapping of orbitals in the triple bonds of different substituents easily makes possible cycloaromatization of ketone derivatives.

Although we do not have sufficient evidence to discuss this reaction mechanism in this study, a proposed mechanism for the formation of indenothiophenone derivatives in this study is illustrated in Scheme 3.[17–22]

At the first step, ketone derivative gives outer-ring diradical **A**, which is generated by intramolecular annulation between two butadiynyl functions of ketone derivatives. The diradical **A** undergoes further cyclization to afford an indenothiophenone diradical intermediate **B**. In the case of the cycloaromatization of compound **13**, reaction of **B** with benzene, which is the



Scheme 2. Cycloaromatization to indenothiophenone derivatives.



Scheme 3. A proposed mechanism for the construction of indenothiophenone derivatives.

solvent in this reaction, gives product **16**. In the presence of diradical trapping reagent such as anthracene, intermediate **B** reacts with the reagent to yield desired product **17**. In the case of the cycloaromatization of compound **14**, intermediate **B** reacts with nitrogen atom in substituent of benzene ring to yield multicyclic ring product **18** associated with migration of methyl group, along with **19**, which is associated with liberation of a

Boc group as carbon dioxide and isobutene. In the case of compound **15**, low yield of compounds **20** and **21** might be due to fast decomposition of intermediate **B**. Further studies on the effect of the aromatic moiety and substituents on the reactivity of the tetraynes will be reported in detail elsewhere.

In conclusion, we have demonstrated a novel synthetic method for the preparation of indenothiophenone derivatives by cycloaromatization of non-conjugated thienyl tetraynes. Further studies on the mechanism of the reaction in this study, and application to other hetero ring-fused indene derivatives are now in progress.

Acknowledgments

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16. All new products obtained in this study were characterized by spectroscopy (NMR, IR and FABMS) and elemental analysis. Selected physical data are as follows. Compound **1**: brown oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, 1H, J = 2.9 Hz), 7.30 (dd, 1H, J = 2.9, 5.1 Hz), 7.25 (d, 1H, J = 5.1 Hz), 7.18 (d, 1H, J = 5.1 Hz), 7.06 (d, 1H, J = 5.1 Hz), 5.98 (d, 1H, J = 5.4 Hz), 2.52 (d, 1H, J = 5.4 Hz), 0.20 (s, 9H) ppm. IR (neat) ν 3400, 2140, 2100 cm^{-1}. Anal. Calcd for $C_{20}H_{16}OS_2Si$: C, 65.89; H, 4.42; S, 17.59. Found: C, 65.99; H, 4.64; S, 17.66. FABMS (NBA) *m/z* 387 $[M+Na]^+$. Compound **2**: brown powder, mp 56.7–58.5 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, 1H, J = 7.6 Hz), 7.37 (t, 1H, J = 7.6 Hz), 7.32–7.20 (m, 3H), 7.07 (d, 1H, J = 5.4 Hz), 6.00 (d, 1H, J = 5.4 Hz), 4.64 (s, 2H) 2.91–2.84 (m, 3H), 2.72 (s, 1H), 1.50–1.44 (m, 9H), 0.20 (s, 9H) ppm. IR (neat) ν 3340, 2220, 2100, 1660 cm^{-1}. Anal. Calcd for $C_{29}H_{31}NO_3SSi$: C, 69.42; H, 6.22; N, 2.79; S, 6.39. Found: C, 69.15; H, 6.01; N, 2.65; S, 6.56. FABMS (NBA) *m/z* 524 $[M+Na]^+$. Compound **3**: pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, 1H, J = 7.6 Hz), 7.49 (d, 1H, J = 7.6 Hz), 7.40 (t, 1H, J = 7.6 Hz), 7.27 (t, 1H, J = 7.6 Hz), 7.26 (d, 1H, J = 5.1 Hz), 7.08 (d, 1H, J = 5.1 Hz), 6.00 (d, 1H, J = 5.4 Hz), 4.66 (s, 2H), 3.49 (s, 3H), 2.53 (d, 1H, J = 5.4 Hz), 0.20 (s, 9H); IR (neat): 3340, 2350, 2100 cm^{-1}; Anal. Calcd for $C_{24}H_{22}O_2SSi$: C, 71.60; H, 5.51; S, 7.96. Found: C, 71.40; H, 5.39; S, 7.78. FABMS (NBA) *m/z* 402 $[(M+H)]^+$. Calcd for Compound **16**: yellow powder, mp 206.0–207.0 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, 1H, J = 4.6 Hz), 7.41 (d, 1H, J = 4.6 Hz), 7.40 (d, 1H, J = 4.9 Hz), 7.25 (s, 1H), 7.11 (d, 1H, J = 4.9 Hz), 6.89–6.86 (m, 2H), 6.77–6.74 (m, 2H), 5.27 (t, 1H, J = 5.9 Hz), 4.94 (t, 1H, J = 5.9 Hz), 0.12 (s, 9H) ppm. IR (neat) ν 2150, 1700 cm^{-1}. Anal. Calcd for $C_{26}H_{20}OS_2Si$: C, 70.87; H, 4.57; S, 14.45. Found: C, 70.62; H, 4.49; S, 14.82. FABMS (NBA) *m/z* 441 $[M+H]^+$. Compound **18**: red powder, mp 194.5–195.0 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, 1H, J = 7.3 Hz), 7.67 (d, 1H, J = 4.9 Hz), 7.35–7.30 (m, 2H), 7.20 (d, 1H, J = 7.3 Hz), 7.14 (d, 1H, J = 4.9 Hz), 4.07 (s, 2H) 2.73 (s, 3H), 1.66 (s, 9H), 0.31 (s, 9H) ppm. IR (neat) ν 2160, 1720, 1710 cm^{-1}. Anal. Calcd for $C_{29}H_{29}NO_3SSi$: C, 69.70; H, 5.85; N, 2.80; S, 6.42. Found: C, 69.93; H, 5.89; N, 2.66; S, 6.46. FABMS (NBA) *m/z* 500 $[M+H]^+$. Compound **20**: yellow plates; mp 129.4–129.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, 1H, J = 7.6 Hz), 7.71 (d, 1H, J = 4.6 Hz), 7.40–7.30 (m, 2H), 7.20 (d, 1H, J = 7.6 Hz), 7.10 (d, 1H, J = 4.6 Hz), 6.86 (s, 1H), 5.05 (s, 2H), 0.34 (s, 9H); IR (KBr): 2150, 1700 cm^{-1}; Anal. Calcd for $C_{23}H_{18}O_2SSi$: C, 71.47; H, 4.69; S, 8.30. Found: C, 71.20; H, 4.65; S, 8.47. FABMS (NBA) *m/z* 387 $[(M+H)]^+$.
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