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Mendeleev Commun., 2014, **24**, 32–34
Mendeleev Communications

Preparation of conjugated 6,6′-bibenzo[*b*]selenophenes

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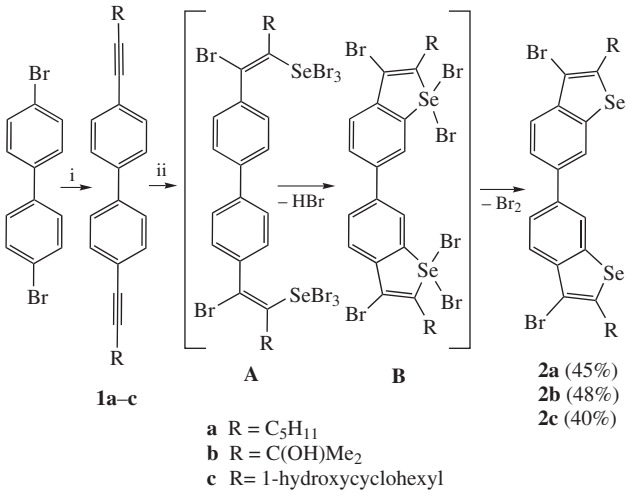
DOI: 10.1016/j.mencom.2013.12.010

6,6′-Bibenzo[*b*]selenophenes were prepared from 4,4′-dibromobiphenyl by the Sonogashira coupling with terminal alkynes followed by heterocyclization with $SeBr_4$.

Selenophenes represent an important class of heterocycles because of their excellent biological effects.[1] They are used as building blocks to create selenophene-containing oligomers and polymers. Many synthetic methods, including electrophilic and transition metal catalyzed intramolecular cyclization, have been successfully employed in the synthesis of selenophenes.[2] Electrophilic selenium reagents such as selenium(II) and (IV) halogenides play an important role in organic synthesis.[3] Amosova's group[4] reported addition of selenium(II) chloride and bromide at alkenes and alkynes. Recently, Braverman's group[5] published cycloaddition of phenylpropargylic alcohols with $SeCl_4$ and $SeBr_4$ in dry chloroform at 0 °C leading to benzo[*b*]selenophenes, albeit no pure hydroxymethyl derivatives have been isolated. Here we present a simple synthesis of conjugated 6,6′-bibenzo[*b*]selenophenes from 4,4′-dibromobiphenyl.

Substituted bibenzo[*b*]selenophenes **2a–c** were prepared in two steps from 4,4′-dibromobiphenyl (Scheme 1). Bromine atoms in the starting compound were replaced with alkynyl groups by the Sonogashira cross-coupling with terminal alkynes, affording products **1a**,**b** in almost quantitative yields (up to 96%). However, in the case of 1-ethynylcyclohexanol product **1c** was obtained in only 58% yield due to steric hindrance.† At the second step, bisalkynes **1a–c** were treated with the *in situ* prepared selenium(IV) (reaction between SeO_2 and HBr was used). According to the plausible mechanism, intermediate **A** forms upon $SeBr_4$ addition to C≡C triple bond with the following formation of intermediate **B** *via* electrophilic heterocyclization. After the bromine molecule elimination bibenzo[*b*]selenophenes **2a–c** were obtained in low yields (20–25%). Apparently, in the course of cyclization bromine molecule can add to triple bonds of the starting compound that would dramatically drop the yield. To overcome this, we used two equivalents of cyclohexene as the bromine scavenger, which provided the yield increase to 40–45%.‡



Scheme 1 *Reagents and conditions*: i, RC≡CH (2.5 equiv.), $PdCl_2$ (5%), Ph_3P (10%), CuI (10%), DMF/Pr^i_2NH, 100 °C, 12 h; ii, SeO_2 (3.0 equiv.), HBr, cyclohexene, dioxane.

† For synthesis and characteristics of compounds **1a–c**, see Online Supplementary Materials.

Molecular structures of **2a**,**b** were unambiguously confirmed by X-ray analysis[§,6] (Figure 1). In both crystals molecules lie in special positions (center of inversion). Therefore, bibenzoselenophene systems are planar and C(6)–C(6′) bonds are lengthened [1.505(4) and 1.504(9) Å for **2a** and **2b**, respectively] due to repulsion of hydrogen atoms [H(5)···H(5′) and H(7)···H(7′)]. The intermolecular hydrogen bonds of O–H···O type [with H-bond lengths 2.804(6) and 2.833(6) Å] are observed in the crystal structure of **2b**. All other intermolecular contacts correspond to sum of van der Waals radii.

Bibenzoselenophene derivative **2b** was converted into synthones which seem promising for the preparation of more complicated π-oligomers (Scheme 2).¶ 2-Hydroxyprop-2-yl substituents are acid-sensitive, therefore debromination of compound **2b** was performed by *tert*-octylamine in the presence of Cu^0, CuI and

‡ *Synthesis of 3,3′-dibromo-6,6′-bibenzo[*b*]selenophenes* **2a–c** *(general procedure).* 4,4′-Dialkynylbiphenyl **1a–c** and cyclohexene (3 equiv.) in dioxane were added to the solution of selenium dioxide (3 equiv.) in HBr (2.5 equiv.), and the mixture was stirred at room temperature for 48 h. After the consumption of substrate **1a–c** (TLC), water (50 ml) was added and the mixture was extracted with ethyl acetate (100 ml). The organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by flash chromatography on silica gel using light petroleum–ethyl acetate (**2a**) or CH_2Cl_2–ethyl acetate (**2b**,**c**) as eluent. For details, see Online Supplementary Materials.

For **2a**: yield 45%, yellow solid, mp 115–117 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.93 (t, 6H, Me, *J* 6.8 Hz), 1.35–1.48 (m, 8H, CH_2), 1.72–1.79 (m, 4H, CH_2), 3.01 (t, 4H, CH_2, *J* 7.6 Hz), 7.68 (dd, 2H, 5,5′-CH, *J* 1.5 Hz, *J* 8.4 Hz), 7.85 (d, 2H, 4,4′-CH, *J* 8.4 Hz), 8.05 (d, 2H, 7,7′-CH, *J* 1.5 Hz). ^{13}C NMR ($CDCl_3$, 100.3 MHz) δ: 13.6, 22.1, 30.5, 30.9, 31.9, 106.8, 123.5, 124.4, 124.8, 137.3, 138.1, 139.2, 144.5.

For **2b**: yield 48%, yellowish solid, mp 164–167 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.86 (s, 12H, Me), 2.62 (s, 2H, OH), 7.71 (dd, 2H, 5,5′-CH, *J* 1.5 Hz, *J* 8.4 Hz), 7.89 (d, 2H, 4,4′-CH, *J* 8.4 Hz), 8.10 (d, 2H, 7,7′-CH, *J* 1.5 Hz). ^{13}C NMR ($CDCl_3$, 100.3 MHz) δ: 29.2, 74.4, 101.4, 123.6, 124.7, 125.2, 137.7, 141.2, 154.0.

For **2c**: yield 40%, white solid, mp 168–170 °C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.27–1.33 (m, 2H, 2,5-$CH_{cyclohexanol}$), 1.58–1.71 (m, 14H, CH_2), 2.37–2.45 (m, 4H, CH_2), 6.26 (s, 2H, OH), 7.79 (d, 2H, 4,4′-CH, *J* 8.4 Hz), 7.83 (dd, 2H, 5,5′-CH, *J* 1.5 Hz, *J* 8.4 Hz), 8.44 (d, 2H, 7,7′-CH, *J* 1.5 Hz). ^{13}C NMR (DMSO-d_6, 100.3 MHz) δ: 21.1, 24.6, 34.2, 73.6, 98.8, 123.6, 124.0, 124.3, 136.1, 137.5, 141.1, 159.3.

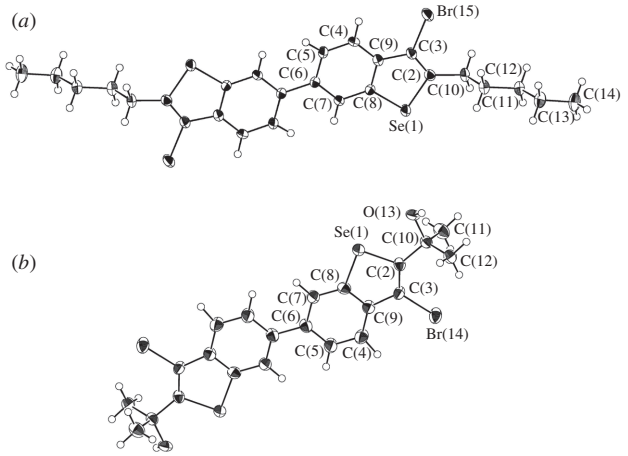
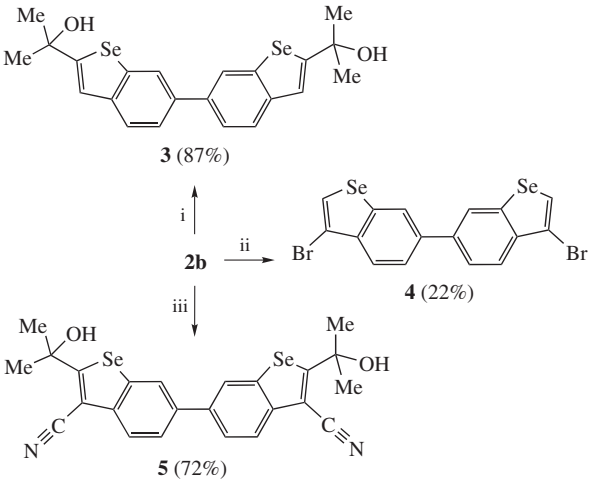
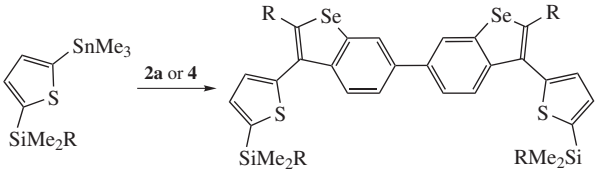


Figure 1 ORTEP molecular structures of (*a*) **2a** and (*b*) **2b**.



Scheme 2 *Reagents and conditions*: i, CuI, Cu^0, K_3PO_4, $Me_2NCH_2CH_2OH$, *tert*-octylamine, 100 °C, 72 h; ii, NaH/DMF, 120 °C; iii, $Zn(CN)_2$, $Pd(PPh_3)_4$, DMF, microwave irradiation, 140 °C, 3 min.

K_3PO_4 in *N*,*N*-dimethylaminoethanol medium (the yield of product **3** reached 87%). Note that the nature of amine has no effect on a yield. For deacetonation, compound **2b** was treated with NaH in dry DMF and 3,3′-dibromo-6,6′-bibenzo[*b*]selenophene **4** was isolated in 22% yield. Other deacetonation methods using NaH/THF, K_2CO_3/DMSO or Pr^iONa/Pr^iOH were even less successful. With the aim to raise the fugacity of 2-hydroxyprop-2-yl substituent we introduced electron-accepting cyano groups into 3 and 3′ positions. We found that microwave irradiation of **2b** in the presence of 2 equiv. of zinc cyanide and 10% $Pd(PPh_3)_4$ in DMF for only 3 min at 140 °C afforded dinitrile **5** in 72% yield.



6a R = $(CH_2)_3Cl$
6b R = $CH_2CH{=}CH_2$

7a R = $(CH_2)_3Cl$, R′ = C_5H_{11} (70%)
7b R = $CH_2CH{=}CH_2$, R′ = C_5H_{11} (68%)
7c R = $CH_2CH{=}CH_2$, R′ = H (40%)

Scheme 3 *Reagents and conditions*: $Pd(PPh_3)_4$, Ph_3As, xylene, 120 °C.

In past years the interest in selenophene containing oligomers rapidly increased compared to oligothiophenes since selenium exhibits better metallic properties than sulfur.[7] In order to prolong π-conjugation we decided to bind thiophene rings to bibenzo[*b*]-selenophene moiety. For this purpose we synthesized 5-silyl-2-trimethylstannylthiophenes **6a**,**b** with chloropropyl and allyldimethylsilyl substituents.¶ We expected that long chains would increase final oligomer solubility due to high lipophilicity and 3-chloropropyl and allyl groups may be involved in the formation of benzo[*b*]selenophene-containing π-polymers. Compounds **6a**,**b** were prepared in two stages from thiophene in good overall yields (60–65%). 2-[(3-Chloropropyl)dimethylsilyl]- and 2-(allyldimethylsilyl)thiophenes were obtained from 2-thienyllithium and the corresponding chlorosilane. Then these products were treated with BuLi (1.2 equiv.) in THF followed by quenching with chlorotrimethylstannane. Stannanes **6a**,**b** were coupled with dibromobibenzo[*b*]selenophenes **2a** and **4** according to the Stille protocol (Scheme 3). Typical heating (130 °C) of stannanes **6a**,**b** with **2a** or **4** in xylene in the presence of $Pd(PPh_3)_4$ led to the target compounds **7a**–**c** in low yields. To reduce the reaction time and activate the catalyst, a catalytic amount (7%) of triphenylarsine[8] was used. This afforded the products **7a**,**b** in reasonable (68–70%) yields.†† However, the yield of derivative **7c** was 40% only, probably, due to the lower solubility of reactant **4** in xylene. Our attempts to accomplish cross-coupling between **2b** and **6b** failed,

§ *Crystal data*. **2a**: monoclinic, space group $P2_1/a$, a = 12.7455(4), b = = 6.7102(2) and c = 14.5471(6) Å, β = 100.748(2)°, V = 1222.31(7) Å^3, Z = 2, d_{calc} = 1.789 g cm^{-3}, μ = 6.306 mm^{-1}. A total of 3638 independent reflection intensities were collected at –120 °C up to $2\theta_{max}$ = 61°; for structure refinement 2404 reflections with $I > 3\sigma(I)$ were used. The final R factor is 0.044.

2b: monoclinic, space group $C2/c$, a = 30.8260(9), b = 8.1667(3) and c = 8.8183(3) Å, β = 91.496(2)°, V = 2219.2(1) Å^3, Z = 4, d_{calc} = 1.898 g cm^{-3}, μ = 6.948 mm^{-1}. A total of 2551 independent reflection intensities were collected at –100 °C up to $2\theta_{max}$ = 55°; for structure refinement 1843 reflections with $I > 2\sigma(I)$ were used. The final R factor is 0.046.

Diffraction data for **2a**,**b** were collected on a Bruker-Nonius Kappa CCD diffractometer using graphite monochromated MoKα radiation (λ = 0.71073 Å). The crystal structures were solved by direct methods and refined by full-matrix least squares using programs.[6(a)–(c)]

CCDC 891124 and 891125 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2014.

¶ For synthesis and characteristics of compounds **3**–**6**, see Online Supplementary Materials.

†† *Synthesis of compounds* **7a**–**c** *(general procedure)*. A vial charged with **2a**, **2b** or **4** (0.30 mmol), **6a** or **6b** (1.20 mmol), $Pd(PPh_3)_4$ (75 mg, 0.06 mmol) and $AsPh_3$ (20 mg, 0.06 mmol) in xylene (5 ml) was flushed with Ar for 10 min. Then the mixture was heated at 120 °C for 24–48 h. After cooling, the mixture was poured into aqueous Na_2CO_3 (50 ml) and ethyl acetate (100 ml) and stirred for 15 min. The organic phase was washed with brine (2×50 ml), dried over anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by flash chromatography on silica gel using light petroleum–ethyl acetate as eluent.

For **7a**: yield 70%, yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.39 (s, 12H, MeSi), 0.85–0.96 (m, 10H, $MeCH_2$), 1.24–1.40 (m, 8H, CH_2), 1.68–1.92 (m, 8H, CH_2), 2.94 (t, 4H, CH_2Ar, J 7.2 Hz), 3.49–3.55 (m, 4H, CH_2), 7.13 (d, 2H, 3-C*H*-thiophene, J 3.3 Hz), 7.31 (d, 2H, 4-C*H*-thiophene, J 3.3 Hz), 7.57–7.62 (m, 4H, 4,4′-CH, 5,5′-CH), 8.10 (s, 2H, 7,7′-CH). ^{13}C NMR ($CDCl_3$, 100.3 MHz) δ: –2.2, 13.6, 14.0, 22.0, 27.2, 30.9, 32.0, 47.4, 123.3, 123.8, 124.6, 124.8, 128.3, 128.7, 134.2, 134.9, 136.9, 138.7, 139.2, 141.7, 142.1, 150.2. LC-MS, *m*/*z*: 934.0 [M$^+$], 978.0 [M + HCOO$^-$].

For **7b**: yield 68%, yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.38–0.42 (m, 12H, MeSi), 0.88 (t, 6H, CH_2Me, J 7.2 Hz), 1.19–1.39 (m, 8H, CH_2Me), 1.67–1.75 (m, 4H, CH_2), 1.83–1.89 (m, 4H, CH_2), 2.94 (t, 4H, CH_2, J 7.2 Hz), 4.90–4.96 (m, 4H, CH_2=CH), 5.80–6.26 (m, 2H, CH_2=C*H*), 7.12–7.13 (d, 2H, 3-C*H*-thiophene, J 3.3 Hz), 7.30–7.32 (m, 2H, 4-C*H*-thiophene, J 3.3 Hz), 7.57–7.61 (m, 4H, 4,4′-CH, 5,5′-CH), 8.10 (s, 2H, 7,7′-CH). ^{13}C NMR ($CDCl_3$, 100.3 MHz) δ: –2.2, –1.2, 13.9, 22.3, 24.5, 31.2, 32.3, 113.8, 123.6, 124.1, 124.9, 128.7, 128.9, 134.0, 134.5, 137.2, 139.0, 139.5, 142.0, 142.4, 144.5, 150.5. LC-MS, *m*/*z*: 862.0 [M + 1], 901.0 [M + HCOO$^-$].

apparently, owing to deactivation of bromine atoms in **2b** by 2-hydroxyprop-2-yl groups.

In summary, a new simple strategy for the preparation of a new type of conjugated bibenzo[*b*]selenophenes starting from 4,4′-dibromobiphenyl has been developed. Further studies will be connected with the synthesis and properties of conjugated bibenzo[*b*]selenophenes with more branched structures.

This work was supported by the Latvian Council of Science (447/2012).

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2013.12.010.

References

1 (*a*) M. Ninomiya, D. R. Garud and M. Koketsu, *Coord. Chem. Rev*., 2011, **255**, 2968; (*b*) P. Arsenyan, E. Paegle, S. Belyakov, I. Shestakova, E. Jaschenko, I. Domracheva and J. Popelis, *Eur. J. Med. Chem*., 2011, **46**, 3434; (*c*) H. S. Shiah, W. S. Lee, S. H. Juang, P. C. Hong, C. C. Lung, C. J. Chang, K. M. Chou and J. Y. Chang, *Biochem. Pharmacol.*, 2007, **73**, 610; (*d*) E. A. Wilhelm, C. R. Jesse, C. F. Bortoletto, C. W. Nogueira and L. Savegnago, *Brain Res. Bull*., 2009, **79**, 281.

For **7c**: yield 40%, yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.41–0.45 (m, 12 H, MeSi), 1.86–1.92 (m, 4 H, CH_2), 4.94–5.00 (m, 4 H, CH_2=CH), 5.83–5.94 (m, 2 H, CH_2=C*H*), 7.33 (d, 2 H, 3-C*H*-thiophene, *J* 3.3 Hz), 7.40 (d, 2 H, 4-C*H*-thiophene, *J* 3.3 Hz), 7.75 (dd, 2 H, 5,5′-CH, *J* 1.5 Hz, *J* 8.4 Hz), 8.06 (s, 2 H, 7,7′-CH), 8.18 (d, 2 H, 4,4′-CH, *J* 8.4 Hz), 8.24 (d, 2 H, 2,2′-CH, *J* 1.5 Hz). ^{13}C NMR ($CDCl_3$, 100.3 MHz) δ: –2.2, –1.3, 22.6, 24.4, 114.0, 124.4, 124.5, 126.7, 127.3, 133.6, 133.9, 134.9, 137.5, 138.1, 138.8, 142.6, 144.0. LC-MS, *m*/*z*: 722.0 [M + 1].

2 (*a*) C. R. B. Rhodena and G. Zeni, *Org. Biomol. Chem*., 2011, **9**, 1301; (*b*) E. T. Pelkey, in *Comprehensive Heterocyclic Chemistry III*, eds. A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. Taylor, Elsevier, Oxford, 2008, vol. 3, pp. 975–1006.

3 (*a*) N. Petragnani, H. A. Stefani and C. J. Valduga, *Tetrahedron*, 2001, **57**, 1411; (*b*) T. G. Back, in *Organoselenium Chemistry*, ed. D. Liotta, John Wiley, New York, 1987, p. 1.

4 (*a*) S. V. Amosova, M. V. Penzik, A. I. Albanov and V. A. Potapov, *Tetrahedron Lett*., 2009, **50**, 306; (*b*) S. V. Amosova, M. V. Penzik, A. I. Albanov and V. A. Potapov, *Russ. J. Gen. Chem*., 2009, **79**, 161 (*Zh. Obshch. Khim*., 2009, **79**, 164); (*c*) V. A. Potapov, E. O. Kurkutov, M. V. Musalov and S. V. Amosova, *Tetrahedron Lett*., 2010, **51**, 5258; (*d*) S. V. Amosova and A. V. Martynov, *Mini-Rev. Org. Chem*., 2010, **7**, 23.

5 S. Braverman, H. E. Pechenick-Azizi, T. Gottlieb, E. Hugo and M. Sprecher, *Synthesis*, 2011, **4**, 577.

6 (*a*) A. Altomare, M. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, A. Moliterni and R. Spagna, *J. Appl. Crystallogr*., 1999, **32**, 115; (*b*) S. Mackay, W. Dong, C. Edwards, A. Henderson, C. J. Gilmore, N. Stewart, K. Shankland and A. Donald, *maXus, Integrated Crystallography Software*, Bruker-Nonius and University of Glasgow, 2003; (*c*) G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 2008, **64**, 112.

7 (*a*) K. Takimiya and T. Otsubo, *Phosphorus Sulfur Silicon Relat. Elem*., 2005, **180**, 873; (*b*) A. V. Pivtsov, L. Y. Kulik, A. Y. Makarov and F. Blockhuys, *Phys. Chem. Chem. Phys*., 2011, **13**, 3873.

8 P. Arsenyan, M. Ikaunieks and S. Belyakov, *Tetrahedron Lett*., 2007, **48**, 961.

Received: 12th August 2013; Com. 13/4178