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Heteroatom Chemistry of Cyclic Benzopolychalcogenides: Synthesis and Characterization

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ABSTRACT: *Many benzopolychalcogenides, for example benzotrithioles, benzotetrathiins, and benzopentathiepins were synthesized from corresponding 1,2-benzenedichalcogenols as starting compounds. The stability of the pentathiepin ring toward functional groups was confirmed by use of amino and sulfide groups as substituents in the molecule of benzopentathiepin. Furthermore, the intramolecular interaction between two polysulfide rings was also studied by synthesis of bisbenzotrithiole, 7,7′-diethyl-4,4′-ethylenedioxybis(benzo[1,2-d][1,2,3]trithiole).* Heteroatom Chem 13:419–423, 2002; Published online in Wiley Interscience (www.interscience.wiley.com). DOI 10.1002/hc.10069

Cyclic benzopolychalcogenides such as benzopentathiepins [1–4], benzotetrathiins [5], and benzotrithioles [6–7] have been studied by many heteroatom chemists in fields of synthetic, structural, and biological chemistry [8–12] (Fig. 1). We also established a synthetic methodology for obtaining benzopenthiepins [13–16] and benzotrithioles [17,18] by the sulfurization–cyclization of the corresponding 1,2-benzenedithiols or their synthetic equivalents. For example, several benzopentathiepins having substituents on the benzene ring were synthesized in good yields by the treatment of 1,2-benzenedithiol or 1,3-benzenedithiol-1,2-thione with elemental sulfur in liquid ammonia [13–16] (Scheme 1). These reactions were explained in the light of sulfurization by a new species generated from elemental sulfur in liquid ammonia. Thus, formation of polysulfide linkages by sulfurization of the thiolate anion gives pentathiepin, which is the most thermodynamically stable compound in this reaction system.

Other ring systems such as benzopenthathiocin and benzotetrathiepin were also obtained by using elemental sulfur in liquid ammonia (Fig. 2). These products are stable thermodynamically and can easily be isolated; especially two compounds, 4,8-disubstituted benzo[1,2-d;4,5-d′]bis[1,2,3]trithiole (BBTT) and 6,10-disubstituted[1,2,3]tri-thiolo[5,4-h]-benzopentathiepin (TBPT), are characterized by having two polysulfide rings on one of the benzene ring [17–19].

Based on these successful results, we felt challenged to effect the synthesis of the benzopolychalcogenides such as benzotrithiole and benzotriselenole. These benzopolychalcogenoles are known to be labile and to require kinetic stabilization for their synthesis. We established the synthetic methodology of several benzotrithioles stabilized kinetically with bulky substituents at a neighboring position of the trithiole ring. Thus, many benzotrithioles were synthesized from the corresponding 1,4-disubstituted 2,3-benzenedithiols or the synthetic equivalents, 1,4-disubstituted 1,3,2-benzodithiastannoles, in

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This paper is dedicated to the late professor Shigeru Oae.

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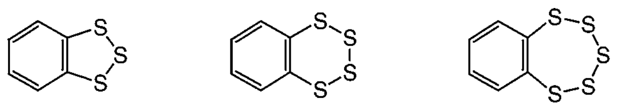
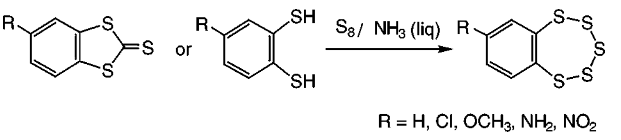

Benzotrithiole Benzotetrathiin Benzopentathiepin

FIGURE 1 Typical benzopolysulfides.

satisfactory yields [20,21] (Scheme 2). This result reveals that the introduction of two substituents into the 1- and 4-positions of the benzene ring stabilized the trithiole ring sufficiently. This methodology led us to success in syntheses of many benzopolychalcogenides containing sulfur and/or selenium atoms in the polychalcogenide ring [22–24] (Fig. 3). These benzopolychalcogenoles were found to give a new species, a benzotrichacogenolium radical cation, by oxidation with an one electron-oxidizing reagent such as $NOPF_6$.

On the other hand, the chemical properties of benzopentathiepin were studied in the area of the synthesis of heterocyclic compounds. Based on the reactivity of benzopentathiepin, many reactions were developed to give many kinds of heterocyclic compounds that included sulfur atoms on the benzene ring, as shown in Scheme 3 [25–33]. These successes in the synthesis of cyclic benzopolychalcogenides and related compounds have allowed us to study reactions between the polysulfide ring and a functional group, such as the amino and sulfide groups. It is well known that a polysulfide ring such as benzopentathiepin is sensitive to nucleophilic attack, for example by an amine and thiolate anion, to bring about cleavage of the sulfur–sulfur linkage as well as in a linear disulfide and the related polysulfides. Thus, there is a significant problem to be solved: how do the substituents affect the stability of polysulfide rings such as pentathiepin?

To clarify the effect of a functional group towards the pentathiepin ring, we synthesized several benzopentathiepins having nucleophilic substituent at a neighboring position of the pentathiepin ring. We were able to confirm that the benzopentathiepin is stable toward cyclic amines such as pyridine and pyrimidine and also toward the sulfide moiety contained in a thiophene ring [34,35] (Fig. 4). This result



SCHEME 1

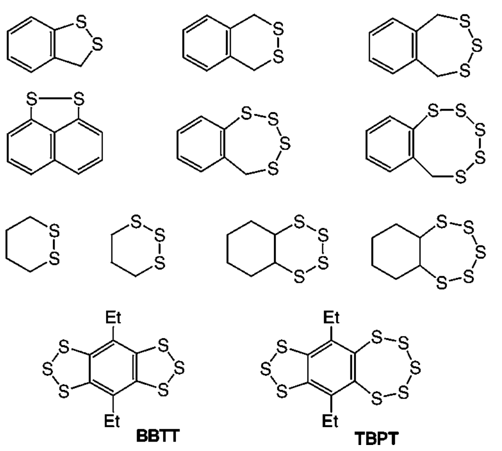
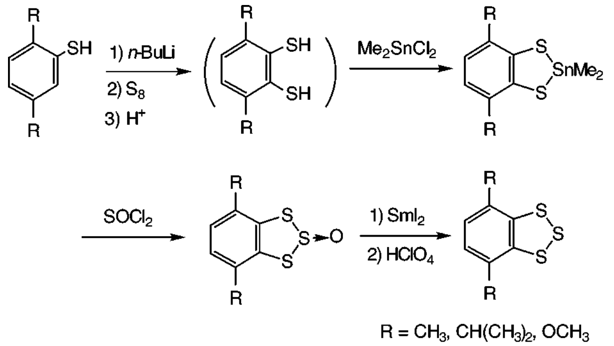
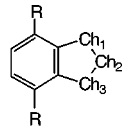


FIGURE 2 Cyclic polysulfides synthesized by using S_8/NH_3 (liq).



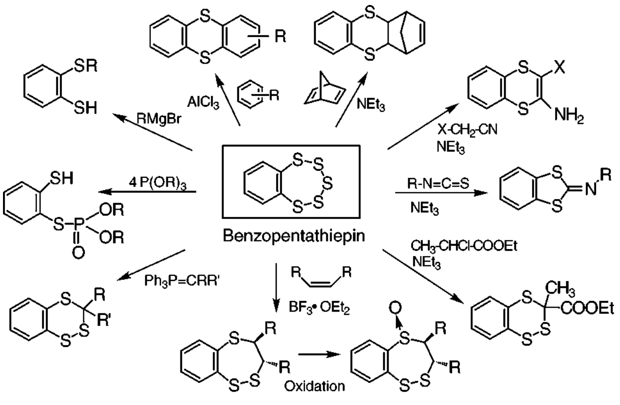
SCHEME 2



Ch_1 = S, S, S, S, Se, Se
Ch_2 = S, S, Se, Se, S, Se
Ch_3 = S, Se, S, Se, Se, Se

R = $CH(CH_3)_2$, OCH_3

FIGURE 3 Benzotrichalcogenoles containing sulfur and/or selenium.



SCHEME 3

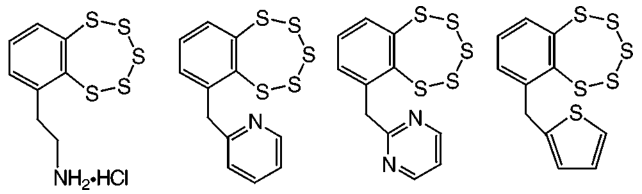
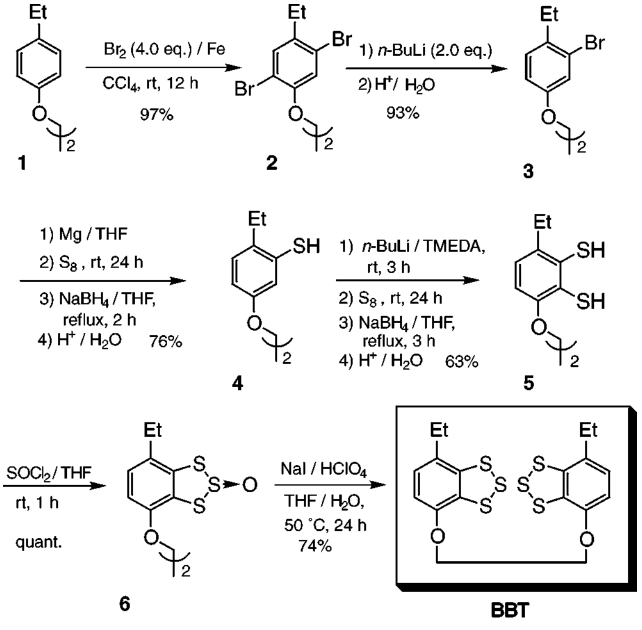


FIGURE 4 Benzopentathiepins having another functional group.

is noteworthy, because the natural product varacin has a benzopentathiepin ring in the molecule, together with an aminoethyl substituent and these substituents are found to play biologically important roles, respectively [36–38]. Thus, we were able to confirm the stability of the pentathiepin ring toward a nucleophilic functional group containing nitrogen or sulfur.

Our next interests focused on the intramolecular interaction of two polysulfide rings linked with a spacer such as an alkanediyl or an alkanedioxy group. We succeeded in the synthesis and the electrochemical characterization of 7,7′-diethyl-4,4′-ethylenedioxybis-(benzo[1,2-*d*][1,2,3]trithiole) (BBT), containing two benzotrithiole rings linked by an ethylenedioxy group [39] (Scheme 4).

The synthesis of BBT was established as follows. Tetrabromination of bis[1,2-(4-ethylphenoxy)] ethane (**1**) with bromine in CCl_4 and then debromination of the resulting **2** using *n*-BuLi afforded bis[1,2-(3-bromo-4-ethylphenoxy)]ethane (**3**) in high yield. A Grignard reagent obtained from **3** was treated with elemental sulfur and then reduced with $NaBH_4$ under reflux in THF, to give 1,2-bis(4-ethyl-3-mercaptophenoxy)-ethane (**4**). The dithiol **4** obtained was converted to 1,2-bis(4-ethyl-2,3-dimercaptophenoxy)-ethane (**5**) by ortho lithiation, sulfurization, and then reduction with $NaBH_4$. Treatment of **5** with thionyl chloride afforded trithiole-2-oxide (**6**) and reduction of **6** with sodium iodide in the presence of $HClO_4$ gave the target bisbenzotrithiole BBT in 32% overall yield.



SCHEME 4

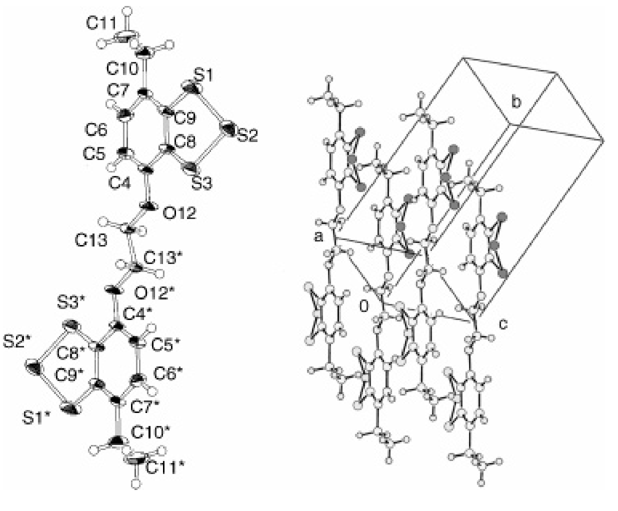


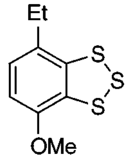
FIGURE 5 ORTEP drawing and crystal packing of BBT.

The structure of BBT was confirmed spectroscopically and finally determined by X-ray crystallography (Fig. 5). According to the result of X-ray crystallography, most bond lengths and angles and torsion angles of each trithiole ring were similar to the previous data for the benzotrithiole ring [20] (Table 1). It is very interesting that the whole structure of BBT is linear and that the two benzotrithiole rings are independent of each other. Based on the results of the crystal structure analysis,

TABLE 1 Selected Distances (Å) and Angles (°) of BBT

Bond lengths	
S(1)—C(9)	1.791 (6)
S(3)—C(8)	1.765 (6)
S(1)—S(2)	2.057 (3)
S(2)—S(3)	2.062 (2)
Bond angles	
S(3)—C(8)—C(9)	120.8 (4)
S(1)—C(9)—C(8)	114.3 (5)
S(2)—S(1)—C(9)	95.2 (2)
S(2)—S(3)—C(8)	93.1 (2)
S(1)—S(2)—S(3)	95.1 (1)
Torsion angles	
S(3)—S(2)—S(1)—C(9)	40.3 (2)
S(1)—S(2)—S(3)—C(8)	−39.7 (2)

TABLE 2 Redox Potential of BBT

	BBT	
Epa (V)	0.67	0.66
Epc (V)	0.57	0.57
E1/2 (V)	0.62	0.62

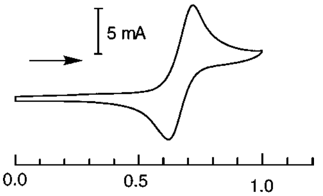
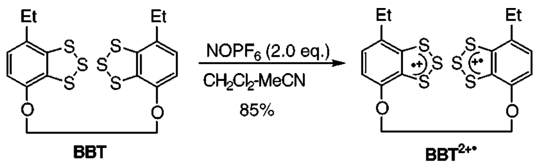


FIGURE 6 Cyclic voltammogram of BBT.



SCHEME 5

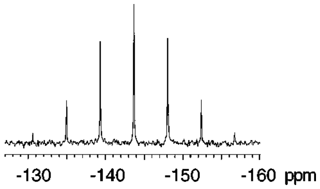


FIGURE 7 ^{31}P NMR spectrum of **BBT$^{2+\cdot}$**.

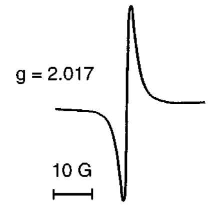


FIGURE 8 ESR spectrum of **BBT$^{2+\cdot}$**.

we were not able to observe any interaction between the two benzotrithiole rings in the crystal packing.

The cyclic voltammogram for BBT showed a clear reversible redox property based on one step oxidation–reduction as shown in Fig. 6. The $E_{1/2}$ value of 0.62 V obtained for BBT is close to that for 1-ethyl-4-methoxybenzotrithiole (Table 2). According to this result, we concluded that a radical cation species could be formed electrochemically by the oxidation of BBT and this could return to a neutral molecule by reduction and that each ring of the two trithioles was oxidized independently.

Based on the results of electrochemistry, the oxidation of bisbenzotrithiole BBT was studied using two equivalents of a one-electron oxidation reagent. Thus, the oxidation of BBT with $NOPF_6$ in a mixed solvent of CH_2Cl_2/MeCN yielded the bis-radical cation BBT$^{2+\cdot}$ as a dark blue powder, which decomposed at 109.2°C (Scheme 5). The formation of a bis-radical cation **BBT$^{2+\cdot}$** was confirmed by ^{31}P NMR spectroscopy, to show a typical septet peak at -143.7 ppm ($^1J_{P-F} = 707$ Hz) as shown in Fig. 7. ESR spectroscopy of the bis-radical cation **BBT$^{2+\cdot}$** showed a broad signal at $g = 2.017$ G as shown in Fig. 8, but the superfine structure could not be observed. These results suggest that both benzotrithiole rings were oxidized simultaneously by the one electron oxidant $NOPF_6$ to form two radical cation moieties in the molecule.

REFERENCES

[1] Fehér, F.; Langer, M. Tetrahedron Lett 1971, 2125.
[2] Chenard, B. L.; Miller, T. J. J Org Chem 1984, 49, 1221.
[3] Chenard, B. L.; Harlow, R. L.; Johnson, A. L.; Vladuchick, S. A. J Am Chem Soc 1985, 107, 3871.
[4] Nakayama, J.; Kashiwagi, M.; Yomoda, R.; Hoshino, M. Nippon Kagaku Kaishi 1987, 1424.
[5] Toste, F. D.; Still, W. J. J Am Chem Soc 1995, 117, 7261.
[6] Rasheed, K.; Warkentin, J. D. J Org Chem 1980, 45, 4806.
[7] Plater, M. J.; Rees, C. W. J Chem Soc, Perkin Trans 1 1991, 317.
[8] Davidson, B. S.; Molinski, T. F.; Barrows, L. R.; Ireland, C. M. J Am Chem Soc 1991, 113, 4709.
[9] Litaudon, M.; Guyot, M. Tetrahedron Lett 1991, 32, 911.
[10] Behar, V.; Danishefsky, S. J. J Am Chem Soc 1993, 115, 7018.
[11] Ford. P. W.; Davidson, B. S. J Org Chem 1993, 58, 4522.
[12] Ford, P. W.; Narbut, M. R.; Belli, J.; Davidson, B. S. J Org Chem 1994, 59, 5955.
[13] Sato, R.; Saito, S.; Chiba, H.; Goto, T.; Saito, M. Chem Lett 1986, 349.
[14] Sato, R.; Saito, S.; Chiba, H.; Goto, T.; Saito, M. Bull Chem Soc Jpn 1988, 61, 1647.
[15] Sato, R.; Kimura, T.; Goto, T.; Saito, M. Tetrahedron Lett 1988, 29, 6291.
[16] Sato, R.; Kimura, T.; Goto, T.; Saito, M.; Kabuto, C. Tetrahedron Lett 1989, 30, 3453.
[17] Kimura, T.; Hanzawa, M.; Horn, E.; Kawai, Y.; Ogawa, S.; Sato, R. Tetrahedron Lett 1997, 38, 1607.
[18] Kimura, T.; Kawai, Y.; Ogawa, S.; Sato, R. Chem Lett 1997, 1305.

[19] Kimura, T.; Tsujimura, K.; Mizusawa, S.; Ito, S.; Kawai, Y.; Ogawa, S.; Sato, R. Tetrahedron Lett 2000, 41, 1801.
[20] Ogawa, S.; Yomoji, N.; Chida, S.; Sato, R. Chem Lett 1994, 507.
[21] Ogawa, S.; Kikuchi, T.; Sasaki, A.; Chida, S.; Sato, R. Tetrahedron Lett 1994, 35, 5469.
[22] Ogawa, S.; Kikuchi, T.; Niizuma, S.; Sato, R. J Chem Soc, Chem Commun 1994, 1593.
[23] Ogawa, S.; Saito, S.; Kikuchi, T.; Kawai, Y.; Niizuma, S.; Sato, R. Chem Lett 1995, 321.
[24] Ogawa, S.; Ohmiya, T.; Kikuchi, T.; Kawai, Y.; Niizuma, S.; Sato, R. Heterocycles 1996, 43, 1843.
[25] Sato, R.; Akutsu, Y.; Goto, T.; Saito, M. Chem Lett 1987, 2161.
[26] Sato, R.; Onodera, A.; Goto, T.; Saito, M. Heterocycles 1988, 27, 2563.
[27] Sato, R.; Onodera, A.; Goto, T.; Saito, M. Chem Lett 1988, 2111.
[28] Sato, R.; Kanazawa,Y.; Akutsu, Y.; Saito, M. Heterocycles 1989, 29, 2097.
[29] Sato, R.; Chino, K.; Saito, M. Sulfur Lett 1990, 10, 233.
[30] Sato, R.; Ishigami, K.; Sato, M. Sulfur Lett 1990, 12, 61.
[31] Sato, R.; Yamaichi, S. Chem Lett 1991, 355.
[32] Sato, R.; Chino, K. Tetrahedron Lett 1991, 32, 6345.
[33] Sato, R.; Murata, T.; Chida, S.; Ogawa, S. Chem Lett 1993, 1325.
[34] Sato, R.; Ohyama, T.; Ogawa, S. Heterocycles 1995, 41, 893.
[35] Sato, R.; Ohyama, T.; Kawagoe, T.; Baba, M.; Nakajo, S.; Kimura, T.; Ogawa, S. Heterocycles 2001, 55, 145.
[36] Hertzberg, R. P.; Dervan, P. B. J Am Chem Soc 1982, 104, 313.
[37] Schneider, H.-J.; Blatter, T. Angew Chem Int Ed Engl 1992, 31, 1207.
[38] Singh, U. S.; Scannell, R. T.; Barbara, H. A.; Carter, B. J.; Hecht, S. M. J Am Chem Soc 1995, 117, 12691.
[39] Sato, R.; Utsumi, Y.; Nakajo, S.; Ogawa, S.; Kawai, Y. Heterocycles 2001, 55, 851.