Tetrahedron 68 (2012) 6211–6217

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis and reaction of tricyclic tetrathiins and pentathiepins: novel formation of α-disulfines

Kentaro Okuma [a,*], Kazunori Munakata [a], Toshiaki Tsubota [a], Masayuki Kanto [a], Noriyoshi Nagahora [a], Kosei Shioji [a], Yoshinobu Yokomori [b]

[a] Department of Chemistry, Fukuoka University, Jonan-ku, Fukuoka 814-0180, Japan
[b] Department of Applied Chemistry, National Defense Academy, Hashirimizu, Yokosuka 239-8686, Japan

ARTICLE INFO

Article history:
Received 14 March 2012
Received in revised form 15 May 2012
Accepted 18 May 2012
Available online 26 May 2012

ABSTRACT

Cyclic polysulfanes containing a norbornane skeleton (tetrathiins and pentathiepins) were synthesized by two methods. One is the sulfurization of camphor hydrazone with disulfur dichloride, and the other is the reaction of thiocamphor with disulfur dichloride. The reduction of tetrathiin with $LiEt_3BH$ gave the corresponding dithiol that further reacted with methyl iodide to afford the corresponding methyl sulfide. Reaction of tetrathiin with $(Ph_3P)_2PdCl_2$ or $NiBr_2$ resulted in the formation of the corresponding dithiolene metal complexes. Tetrathiins were stereoselectively oxidized by *m*-CPBA to afford the corresponding α-disulfines.

1. Introduction

The only possible six- and seven-membered ring compounds containing a carbon-carbon double bond and sulfur atoms are 1,2,3,4-tetrathiins (**2**) and 1,2,3,4,5-pentathiepins (**3**). Pentathiepins, which are seven-membered cyclic polysulfanes, are very important compounds because of their pharmacological activity. They are synthesized by reacting benzodithiols with elemental sulfur in liquid ammonia,[1] by thermolysis of 1,2,3-thia- or selenadiazoles with elemental sulfur,[2] or dioxime with S_2Cl_2,[3] or by reacting benzyne with elemental sulfur.[4] Tetrathiins are novel six-membered cyclic tetrasulfanes that are synthesized by reacting sterically hindered alkynes with elemental sulfur,[5] alkenes with S_2Cl_2,[6] or titanocene dithiolene complexes with SO_2Cl_2.[7] Our unwavering interest in cyclic polysulfanes has led to the synthesis of sulfur-containing heterocycles, such as benzothietes,[8] α-dithiolactones,[9] 1,2-dithietan-3-ones,[10] and 1,2-dithiolane-3-thiones.[11] However, relatively little attention has been paid to the synthesis of sulfur-containing heterocycles by the reaction of bicyclic thiones, such as thiocamphor (**1**). The only reported examples are the synthesis of norbornanethiazolines and 6*H*-[1,3]oxathiin-6-ones from thiofenchone.[12] and the reaction of alkane sulfanyl chlorides with thiocamphor, which resulted in symmetrical and unsymmetrical disulfanes.[13] We have reported the synthesis and reaction of tetrathiin (**2**) by reacting thiocamphor **1** with sulfur monochloride.[14] In this paper, we show the full details of the chemistry of tricyclic tetrathiins.

2. Results and discussion

2.1. Synthesis of tricyclic polysulfanes

We first investigated the reaction of thiocamphor **1a** with S_2Cl_2 under several conditions to determine whether the corresponding cyclic polysulfanes would be formed. The results are shown in Table 1. When a solution of **1a** and triethylamine (1 equiv) in dichloromethane was added to a solution of S_2Cl_2 (1 equiv) in dichloromethane at 0 °C, 1,11,11-trimethyl-3,4,5,6-tetrathia-tricyclo[6.2.1.0^{2,7}]undeca-2(7)-ene (**2a**) and 1,12,12-trimethyl-3,4,5,6,7-pentathiatricyclo[7.2.1.0^{2,8}]dodeca-2(8)-ene (**3a**) were obtained in 15% and 12% yields, respectively (entry 1). The yields of **2a** and **3a** were improved in the absence of triethylamine (entry 2). The best yields of **2a** (69%) and **3a** (12%) were obtained by using 1.5 equiv of S_2Cl_2 at rt (entry 3). In contrast to the result of Mloston et al.,[13] no Wagner–Meerwein rearranged product was obtained, suggesting that the α-proton abstraction proceeds much faster than the rearrangement (Scheme 1). When the reaction conditions (temperature, amount of S_2Cl_2, and time) were varied, no dithiete was formed. The reactions of norbornene with active sulfur to afford cyclic polysulfanes are well known.[15] However, there is no report of the synthesis of tricyclic polysulfanes from thiocamphor **1a**.

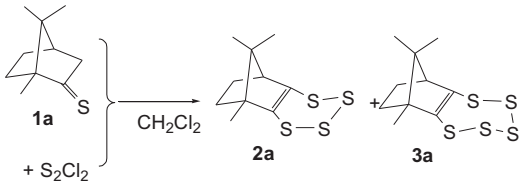
The present work is the first to provide a method for the synthesis of cyclic polysulfanes with a norbornene skeleton. The reaction might proceed as follows. Abstraction of a proton from

* Corresponding author. Tel.: +81 92 871 6631; fax: +81 92 865 6030; e-mail address: kokuma@fukuoka-u.ac.jp (K. Okuma).

0040-4020/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2012.05.069

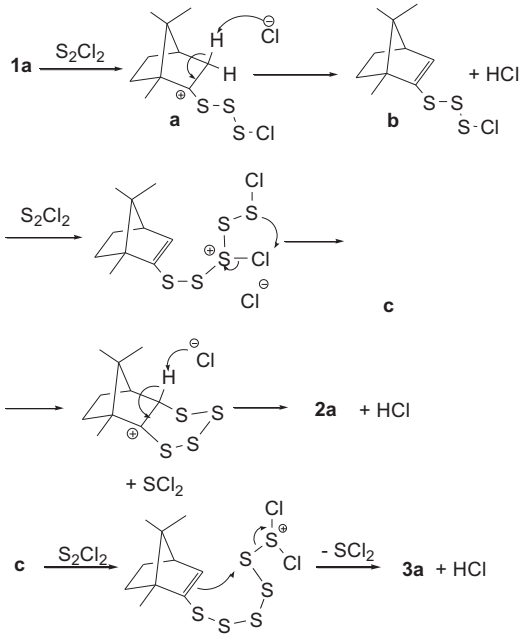
Table 1
Reaction of **1a** with S_2Cl_2

Entry	S_2Cl_2 (equiv)	Et_3N (equiv)	Temp(°C)	Product **2a**	(Yield/%) **3a**
1	1.0	1.0	0	15	12
2	1.0	0	0	36	15
3	1.5	0	rt	69	12
4	1.5	0	Reflux	35	11
5	2.0	0	rt	32	16



Scheme 1.

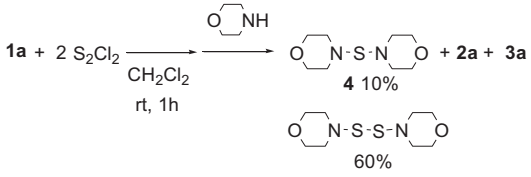
initially formed carbocation intermediate **a** dehydrochlorinated to give alkenyl trisulfanyl chloride **b**, which further reacted with S_2Cl_2 to give alkenyl pentasulfonium chloride **c**. Intramolecular cyclization of this chloride followed by proton abstraction afforded tetrathiin **2a** and SCl_2. Intermediate **c** was further reacted with S_2Cl_2 followed by the intramolecular cyclization to afford **3a** (Scheme 2).



Scheme 2.

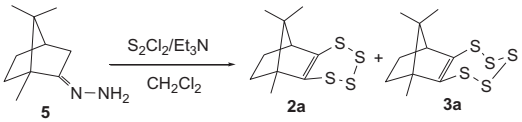
The formation of SCl_2 was easily observed from the emergence of an orange red color from the original pale yellow solution within a few minutes. Finally, the reaction of this solution with morpholine resulted in the formation of thiobismorpholine (**4**) in 10% yield along with dithiobismorpholine (60%) (Scheme 3).

As the reaction of ketone hydrazones with S_2Cl_2 gave thioketones via thiosulfine intermediates,[16] there would be a possibility to synthesize tricyclic polysulfanes such as **2a** and **3a**. We then performed the reaction of camphor hydrazone (**5**) with S_2Cl_2 in the presence of triethylamine to determine whether cyclic polysulfanes



Scheme 3.

2a and **3a** or thiocamphor **1a** would be formed. Treatment of camphor hydrazone **5** and triethylamine in dichloromethane with S_2Cl_2 in dichloromethane at 0 °C resulted in the formation of pentathiepin **3a** and tetrathiin **2a** in 40% and 19% yields, respectively (Scheme 4). In the present case, pentathiepin **3a** is the major product, which is different from that of the reaction of thiocamphor **1a** with S_2Cl_2. Thus, we changed S_2Cl_2 equivalent under several conditions. The results are shown in Table 2.

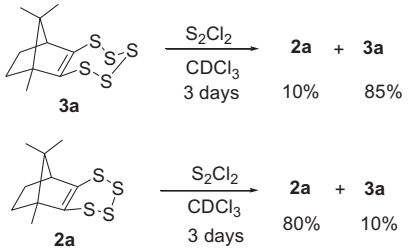


Scheme 4.

Table 2
Reaction of camphor hydrazone **5** with S_2Cl_2

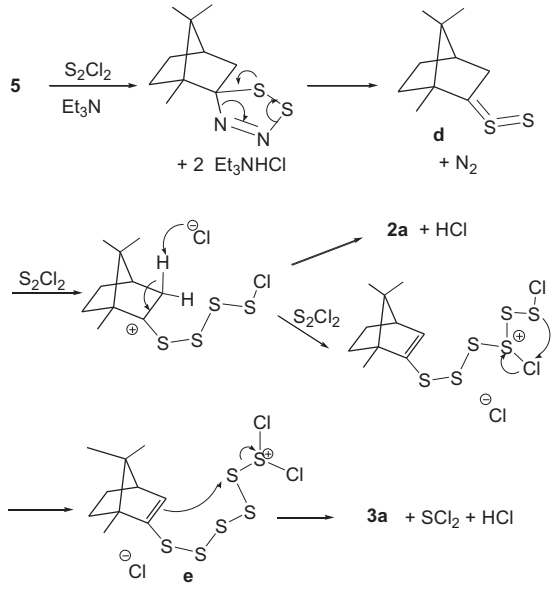
Entry	S_2Cl_2 (equiv)	Et_3N (equiv)	Temp (°C)	Products **2a**	(Yields/%) **3a**
1	0.8	1.6	0	0	8
2	1.2	2.4	0	19	40
3	2.4	4.8	0	16	11
4	1.5	2.0	rt	20	11
5	2.0	2.0	0	15	16

When 0.8 equiv of S_2Cl_2 was used, the yield of **3a** was only 8% along with starting hydrazone (25%), whereas 2 equiv of S_2Cl_2 resulted in the formation of **3a** in 16% yield (entries 1 and 5). When 1.2 equiv of S_2Cl_2 was used, **2a** and **3a** were obtained in 19 and 40% yields, respectively (entry 2). Thus, this method is adequate for the synthesis of pentathiepin **3a**. While we did not clearly understand why pentathiepin is the major product in the present case, we first thought that S_2Cl_2 plays a vital role in the selective synthesis of tetrathiin **2a**. When pentathiepin **3a** and S_2Cl_2 in $CDCl_3$ were left to stand at rt for 3 days, tetrathiin **2a** was formed in approximately 10% yield. In contrast, when tetrathiin **2a** and S_2Cl_2 in $CDCl_3$ were left to stand at rt for 3 days, pentathiepin **3a** was formed in 10% yield (Scheme 5).



Scheme 5.

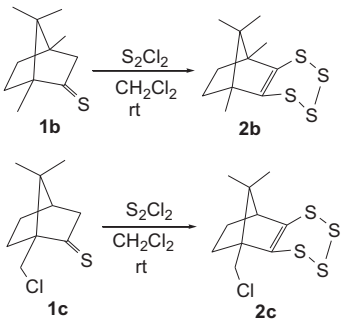
Although these results partly indicate the interconversion of tetrathiin **2a** and pentathiepin **3a** by the use of S_2Cl_2, they are not sufficient to explain the mechanism. Okazaki et al. have explained the formation of thiosulfine intermediate in the reaction of ketone hydrazone with S_2Cl_2.[16] Thus, the reaction might proceed as follows: initially afforded thiosulfine or dithiirane intermediate (**d**) reacted with S_2Cl_2, and this was followed by proton abstraction to afford sulfanyl chloride, intramolecular cyclization of which gave **2a** and HCl. Further addition of sulfur chloride gave sulfonium intermediate (**e**). Intramolecular addition followed by proton abstraction gave pentathiepin **3a** (Scheme 6). The formation of SCl_2 was also confirmed by the reaction with morpholine, which resulted in the formation of thiobismorpholine.



Scheme 6.

As the best result was obtained by reacting thiocamphor **1a** with S_2Cl_2, we tried to perform the synthesis of other tetrathiins **2** by using substituted camphor.

As shown in Scheme 7, corresponding tetrathiins **2b** and **2c** were obtained in 55% and 37% yields, respectively.

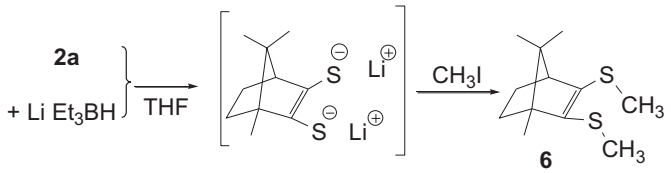


Scheme 7.

Thus, we have found two different methods for the general synthesis of tricyclic polysulfanes **2** and **3**.

2.2. Reduction of tetrathiin 2a

We then tried to reduce tetrathiin **2a** to investigate the chemical properties of tricyclic polysulfanes. The reaction of tetrathiin **2a** with lithium triethylborohydride resulted in the formation of a dithiolate anion. This was further reacted with methyl iodide to afford 2,3-bis(methylthio)-1,7,7-trimethylbicyclo[2.2.1]hept-2-ene (**6**) in 84% yield (Scheme 8).



Scheme 8.

2.3. Synthesis of Bornylenedithiolene Pd and Ni complexes

Since tetrathiin **2a** was obtained, we then tried the reaction with $(Ph_3P)_2PdCl_2$ in the hope of thiolate Pd complex. Treatment of tetrathiin **2a** with $(Ph_3P)_2PdCl_2$ followed by the addition of triphenylphosphine in dichloromethane resulted in the formation of a mixture of dithiolate–Pd complex (nearly 10:9 ratio) in 57% yield. The structure was confirmed by its ^1H NMR and ^{13}C NMR analysis. Although the reaction of **2a** with $(Ph_3P)_2PdCl_2$ took place to afford isomeric mixture of deep purple crystals, single crystals of major isomer were obtained, which was subjected to X-ray crystallographic analysis. ORTEP drawing of **7** was shown in Fig. 1. Similarly, treatment of tetrathiin **2a** with triphenylphosphine and $NiBr_2$ in acetonitrile/$CHCl_3$ (1:1) for 1 h resulted in the formation of **8** in 46% yield (Scheme 9). Perochon et al. have reported that the reaction of camphorquinone with P_4S_{10}, followed by the addition of $NiCl_2/6H_2O$, afforded bornylenedithiolene Ni complex (**7**) in its neutral form.[17] Although the intermediate of the reaction seemed to be α-dithione or tetrathiin, they were not able to isolate those intermediates. The present reaction offers an alternative route for the synthesis of Ni complex **8** from tetrathiine. The spectral data was identical with the reported one.[17] Thus, the present reaction provides another synthetic method for the bornylenedithiolene metal complexes.

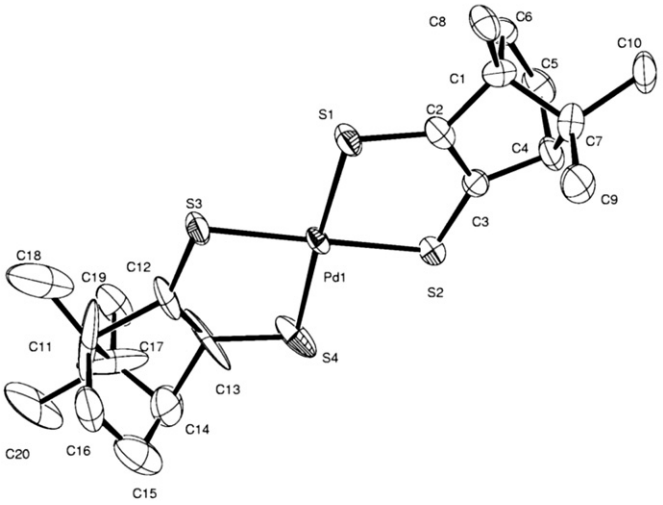
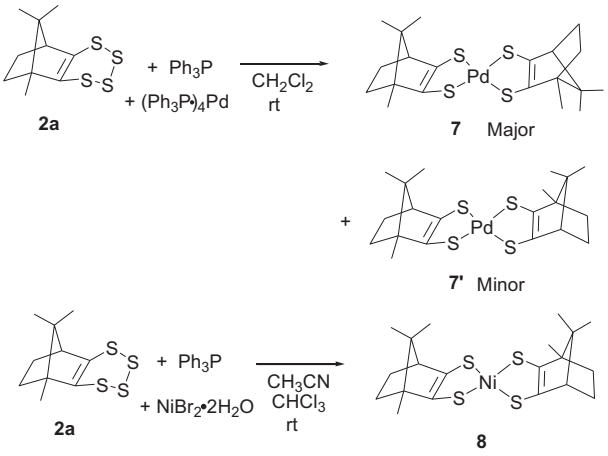


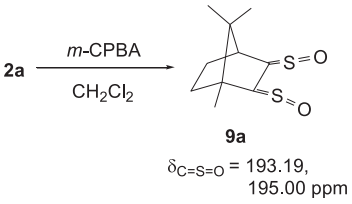
Fig. 1. ORTEP drawing of compound **7** (major).



Scheme 9.

2.4. Oxidation of tetrathiin 2: synthesis of α-disulfine

As the reduction of **2a** was carried out successfully, we tried to perform the oxidation of tetrathiin **2a** to investigate whether the corresponding sulfoxide or α-disulfine would be formed. Treatment of **2a** with *m*-CPBA (2 equiv) at rt resulted in the formation of 1,7,7-trimethylbicyclo[2.2.1]heptane-2,3-dithione *S*,*S*′-dioxide (**9a**) (α-disulfine) as the only isomer in 95% yield, suggesting that the reaction proceeded stereoselectively (Scheme 10). The structure of dioxide **9a** was confirmed by ^{1}H and ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis. The IR spectrum of **9a** showed peaks at 1044 (st), 1058, 1108, and 1124 cm^{-1} for C═S═O stretching.



Scheme 10.

To investigate the stereochemistry, we compared the ^{13}C NMR data of **9a** with those of bis(*tert*-butyl)sulfine (**9**), an aliphatic α-disulfine. Nakayama et al. reported the synthesis of a mixture of (*E*,*E*)-, (*E*,*Z*)-, and (*Z*,*Z*)-bis(*tert*-butyl)sulfines **10** by the oxidation of 1,2-dithietes and 1,2-dithiones (Fig. 2).[18] The ^{13}C NMR spectrum of compound **9a** shows peaks at 193.20 and 195.00 ppm for the C═S═O carbon. The ^{13}C NMR signal of the C═S═O carbon of disulfines **10** appears at 192.56 ppm for the *E*,*E*-configuration, 197.80 and 198.52 ppm for the *E*,*Z*-configuration, and 199.69 ppm for the *Z*,*Z*-configuration (in $CDCl_3$).

We initially thought that these data seem to indicate that sulfine **9a** has the *E*,*E*-configuration. However, we noted some ambiguity because the signal at 195.00 ppm of α-disulfine **9a** is relatively close to the reported signals of the *E*,*Z*-form of **10** (197.80 and 198.52 ppm). Fortunately, as we had 4-methyl derivative **2b** in hand, we tried to oxidize this compound with *m*-CPBA. Treatment of tetrathiin **2b** with *m*-CPBA in dichloromethane at 0 °C resulted in the formation of α-disulfine (**9b**) in 55% yield (Scheme 11). The structure of this compound was

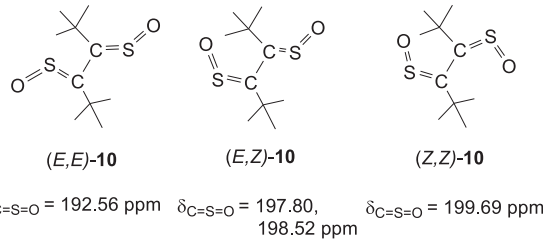
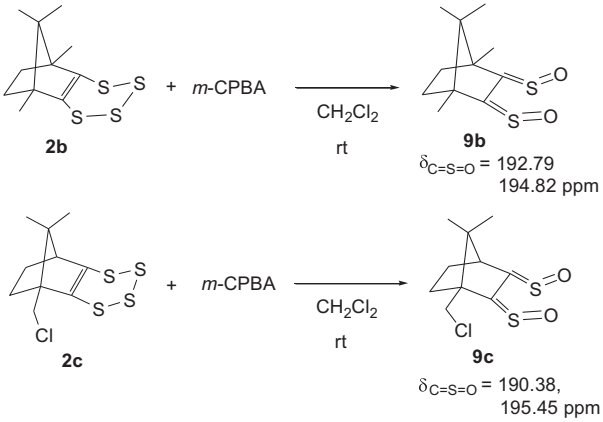


Fig. 2. ^{13}C NMR data for compound **10**.

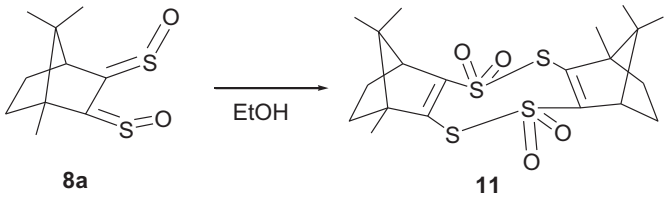
confirmed from spectroscopic data and elemental analysis data. Surprisingly, the ^{13}C NMR spectrum of compound **9b** shows two peaks at 192.8 and 194.8 ppm, which clearly indicates that compound **9b** has not the *E*,*E*- or *Z*,*Z*-form but the *E*,*Z*-form. Thus the structure of **9a** has the *E*,*Z*-form. Similarly, tetrathiin **2c** reacted with *m*-CPBA at rt to afford the *E*,*Z*-form of α-disulfine (**9c**).



Scheme 11.

The *E*,*Z*-structure would be also supported by the following result. When α-disulfine **9a** was left to stand in EtOH overnight, pale yellow crystals (**11**) were precipitated (Scheme 12). The ^{1}H NMR spectrum ($CDCl_3$) of compound **11** shows signals attributable to the norbornane structure (three methyl signals, two methylene signals, and one methine signal). In addition, one of the three methyl signals and one of the two methylene signals in the ^{1}H NMR spectrum ($CDCl_3$) show broadening, which suggested that the product would be an equilibrium mixture of conformational isomers. Its ESI mass spectrum shows a peak at 483 (*m*/*z*), which suggested a dimerized structure (460+Na^{+}). In addition, the IR spectrum of this compound shows strong absorptions at 1332 and 1130 cm^{-1}, which are evidence of the existence of an SO_2 component. Thus, the structure of **11** has a thiosulfonate component. As very fine single crystals of this compound were obtained, X-ray crystallographic analysis was performed. Although the R-value was not sufficient for the elucidation of the precise structure of this compound, it can be surmised that product **11** has an eight-membered cyclic thiosulfonate structure (Fig. 3). An oxygen group was positioned at the less bulky side of the norbornane skeleton.

Thus, the present oxidation would proceed through the following pathway: the oxidation of **2** gave the corresponding dioxide, stereoselectively. Then, the dioxide cycloreversed to give (*E*,*Z*)-α-disulfine exclusively (Scheme 13). The stereoselective synthesis of α-disulfine **9** from tetrasulfane **2** was achieved.



Scheme 12.

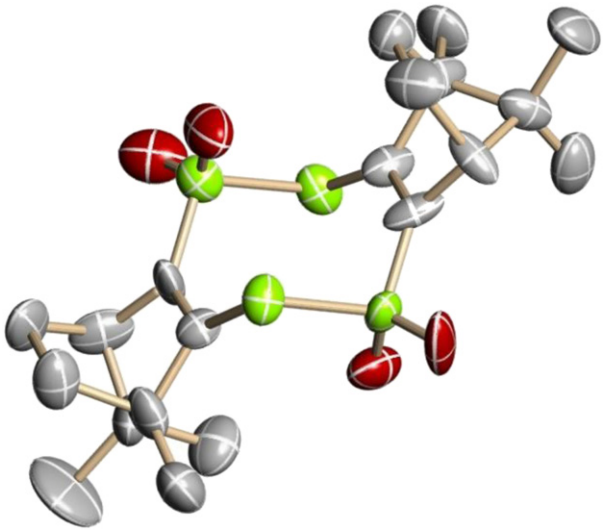
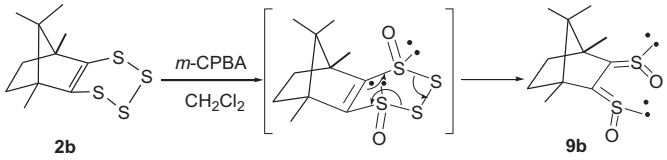


Fig. 3. ORTEP drawing of compound **11**.



Scheme 13.

3. Conclusion

We have synthesized tricyclic polysulfanes **2** and **3** by reacting thiocamphor **1** or camphor hydrazone **5** with S_2Cl_2. Reaction of tetrathiin **2a** with lithium triethylborohydride gave the corresponding dithiolate, and this was further reacted with methyl iodide to give dimethyl derivative. Reaction of **2a** with $PdCl_2$ or $NiBr_2$ in the presence of triphenylphosphine gave the corresponding dithiolene metal complexes **7** and **8**. Oxidation of **2a** with *m*-CPBA proceeded stereoselectively to give (*E*,*Z*)-α-disulfines **9a** in nearly quantitative yield. This method affords the first example of tricyclic polysulfanes.

CCDC 870747 and CCDC 866061 contain the supplementary crystallographic data for compound **7** and **11**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4. Experimental

4.1. General

All solvents were distilled prior to use. Analytical TLC was carried out on precoated plates (Merck silica gel 60, F_{254}) and flash column chromatography was performed with silica (Merck, 70–230 mesh). NMR spectra (^1H at 400 MHz; ^{13}C at 100 MHz) were recorded in $CDCl_3$ and chemical shifts are expressed in parts per million relative to internal TMS (δ=0.00) and $CDCl_3$ (δ=77.00) for ^1H and ^{13}C NMR. As compounds other than **9** and **11** did not show characteristic frequencies, their IR spectra were omitted. Melting points were uncorrected.

4.2. Materials

All chemicals were obtained from commercial suppliers and were used without further purification. Thiocamphor[19] and camphor hydrazone were synthesized by a reported method.[20]

4.3. Synthesis of 10-chlorothiocamphor 1c

To a solution of 10-chlorocamphor (5.10 g, 27.1 mmol) in toluene (100 mL) were added P_4S_{10} (2.80 g, 12.5 mmol) and hexamethyldisiloxane (5.10 g, 31 mmol) in one portion. After refluxing for 12 h, the reaction mixture was evaporated and chromatographed over silica gel by with hexane as eluent to give 10-chlorothiocamphor **1c** (2.30 g, 11.4 mmol). Pale yellow oil. ^1H NMR ($CDCl_3$) δ=0.94 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.37 (dt, 1H, *J*=6.4, 1.6 Hz, C*H*H), 1.45 (dt, 1H, *J*=2.8, 6.4 Hz, CH*H*), 2.02–2.34 (m, 3H, CH_2, and CH), 2.41 (d, 1H, *J*=20 Hz, C*H*H), 2.79 (br d, 1H, *J*=20 Hz, CH*H*), 3.76 (d, 1H, *J*=12 Hz, C*H*H), 4.06 (d, 1H, *J*=12 Hz, CH*H*). ^{13}C NMR ($CDCl_3$) δ=20.74 (CH_3), 21.17 (CH_3), 27.13 (CH_2), 30.49 (CH_2), 44.08 (CH), 46.36 (CH_2), 50.21 (q-C), 55.64 (CH_2), 71.36 (q-C), 266.26 (C=S). HRMS (GCEI) (*m*/*z*): calcd for $C_{10}H_{15}ClS$ 202.0583. Found 202.0589 (M^+).

4-Methylthiocamphor **1b**: pale yellow oil. ^1H NMR ($CDCl_3$) δ=0.66 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.25–1.31 (m, 1H, C*H*H), 1.40–1.45 (m, 1H, CH*H*), 1.65–1.76 (m, 2H, CH_2), 2.43 (d, 1H, *J*=18 Hz, C*H*H), 2.50 (br d, 1H, *J*=18 Hz, CH*H*). ^{13}C NMR ($CDCl_3$) δ=13.91 (CH_3), 14.97 (CH_3), 17.00 (CH_3), 17.20 (CH_3), 33.36 (CH_2), 34.26 (CH_2), 47.17 (q-C), 50.01 (q-C), 61.30 (CH_2), 70.89 (q-C), 271.10 (C=S). HRMS (GCEI) (*m*/*z*): calcd for $C_{11}H_{18}S$ 182.1129. Found 182.1122 (M^+).

4.4. Reaction of thiocamphor 1a with S_2Cl_2

To a solution of thiocamphor (0.337 g, 2.05 mmol) in dichloromethane (30 mL) was added a solution of S_2Cl_2 (0.405 g, 3.00 mmol) in dichloromethane (10 mL) at rt. After stirring for 1 h, the reaction mixture was washed with water, dried over Na_2SO_4, and filtered. The resulting solution was evaporated to yield a yellow oil, which was chromatographed over silica gel with hexane as eluent to give a mixture of tetrathiin **2a** and pentathiepin **3a**. The mixture was subjected to gel permiation chromatography to furnish **2a** (0.364 g, 1.37 mmol) and **3a** (0.071 g, 0.23 mmol). Tetrathiin **2a**: yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ=0.87 (s, 3H, CH_3), 0.91 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 1.28–1.36 (m, 2H, CH_2), 1.64–1.70 (m, 1H, CH_2), 1.89–1.95 (m, 1H, CH_2), 2.56 (d, *J*=3.0 Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=10.53, 18.71, 18.93, 26.30, 33.24, 53.04, 69.71, 60.02, 129.98, 131.62. MS (EI) *m*/*z*: found 262.00 (M^+). Calcd for $C_{10}H_{14}S_4$: 261.99. Anal. Calcd for $C_{10}H_{14}S_4$: C, 45.76; H, 5.38. Found: C, 45.36; H, 5.22. Pentathiepin **3a**: yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ=0.74 (s, 3H, CH_3), 0.79 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 1.49–1.57 (m, 2H, CH_2), 1.76–1.82 (m, 1H, CH_2), 2.06–2.12 (m, 1H, CH_2), 2.64 (d, *J*=3.9 Hz, 1H, CH); ^{13}C NMR (101 MHz, $CDCl_3$) δ=11.95, 18.63, 18.78, 24.99, 31.82, 56.53, 61.54, 61.63, 152.08, 155.86. MS (EI) *m*/*z*: found 294.00 (M^+). Calcd for $C_{10}H_{14}S_5$: 264.02. Anal. Calcd for $C_{10}H_{14}S_5$: C, 40.78; H, 4.79. Found: C, 40.70; H, 4.94.

Other reactions were carried out in a similar manner.

Tetrathiin **2b**: yellow oil, ^1H NMR ($CDCl_3$) δ=0.74 (3H, s, CH_3), 0.76 (3H, s, CH_3), 1.14 (6H, s, CH_3), 1.27–1.31 (2H, m), 1.60–1.64

(2H, m). ^{13}C NMR ($CDCl_3$) δ=11.56 (CH_3 ×2), 16.29 (CH_3), 17.18 (CH_3), 33.76 (CH_2 ×2), 55.49 (C), 61.22 (C ×2), 132.315 (C–S ×2). HRMS (*m*/*z*): calcd for $C_{11}H_{16}S_4$: 276.0135. Found: (M^+) 276.0135.

Tetrathiin **2c**: pale yellow oil, ^{1}H NMR ($CDCl_3$) δ=0.98 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.36 (dt, 1H, *J*=10.4 and 3.2 Hz, CH*H*), 1.54 (dt, 1H, *J*=10.4 and 3.2 Hz, C*H*H), 1.80–2.02 (m, 2H, CH_2), 2.55 (d, 1H, *J*=3.6 Hz, CH), 3.75 (d, 1H, *J*=12.0 Hz, C*H*H), 3.83 (d, 1H, *J*=12.0 Hz, CH*H*). ^{13}C NMR ($CDCl_3$) δ=19.94 (CH_3), 20.02 (CH_3), 26.23 (CH_2), 31.21 (CH), 42.87 (CH_2), 54.80 (q-C), 60.91 (CH_2Cl), 64.74 (q-C), 128.75 (=C), 132.58 (=C). HRMS (EI) *m*/*z*: found 295.9589 (M^+). Calcd for $C_{10}H_{13}ClS_4$: 295.9583.

4.5. Reaction of thiocamphor 1a with S_2Cl_2 followed by addition of morpholine

To a solution of thiocamphor (0.168 g, 1.05 mmol) in dichloromethane (30 mL) was added a solution of S_2Cl_2 (0.270 g, 2.0 mmol) in dichloromethane (10 mL) at rt. After stirring for 10 min, morpholine (0.350 g, 4.0 mmol) was added and stirring was commenced for an additional 1 h. The reaction mixture was washed with water, dried over Na_2SO_4, and filtered. The resulting solution was evaporated to give a yellow oil, the ^{1}H NMR spectrum of which was compared with those of authentic thiobismorpholine and dithiobismorpholine. Approximately 10% of thiobismorpholine **4** and 60% of dithiobismorpholine were detected (by NMR).[21] Compounds **2a** and **3a** were also formed.

4.6. Reaction of camphor hydrazone 5 with S_2Cl_2

To a solution of S_2Cl_2 (275 mg, 2.0 mmol) in dichloromethane (3 mL) was added a solution of camphor hydrazone **5** (175 mg, 1.07 mmol) and triethylamine (207 mg, 2.0 mmol) at 0 °C. After stirring for 1 h, water (10 mL) was added and extraction was carried out with dichloromethane (5 mL×3). The combined extract was dried over magnesium sulfate, filtered, and evaporated to give a pale yellow oil, which was chromatographed over silica gel with hexane as eluent to afford a yellow oil. Gel permiation chromatography of the oil gave tetrathiin **2a** (54 mg, 0.21 mmol) and pentathiepin **3a** (104 mg, 0.35 mmol).

4.7. Reaction of tetrathiin 2a with lithium triethylborohydride followed by addition of methyl iodide

To a solution of tetrathiin **2a** (50 mg, 0.19 mmol) in THF (1 mL) was added a solution of lithium triethylborohydride (1 Mol solution in THF, 0.8 mL) at 0 °C. After refluxing for 1 h, methyl iodide (167 mg, 1.19 mmol) was added. The reaction mixture was washed with water (10 mL) and extracted with ethyl acetate (3×5 mL). The combined extract was dried over magnesium sulfate, filtered, and evaporated to give a brown oil, which was chromatographed over silica gel with dichloromethane/hexane as eluent to afford 2,3-bis(methylthio)-1,7,7-trimethylbicyclo[2.2.1]hept-2-ene **6** (37 mg, 0.16 mmol).

Compound **6**: colorless oil: ^{1}H NMR ($CDCl_3$) δ=0.82 (s, 3H, CH_3), 0.84 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 1.06–1.18 (m, 2H, CH_2), 1.60–1.62 (m, 1H, C*H*H), 1.81–1.88 (m, 1H, CH*H*), 2.23 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.58 (d, 1H, *J*=4.0 Hz, CH). ^{13}C NMR ($CDCl_3$) δ=12.47 (CH_3), 14.84 (CH_3), 17.31 (CH_3), 19.10 (CH_3), 25.53 (CH_2), 43.21 (CH), 53.43 (q-C), 55.49 (CH), 59.92 (q-C), 136.00 (=C), 146.04 (=C). HRMS (GCEI) (*m*/*z*): calcd for $C_{12}H_{20}S_2$: 228.1006. Found: (M^+) 228.1006.

4.8. Synthesis of bornylidene dithiolate complexes

To a solution of tetrathiin **2a** (131 mg, 0.5 mmol) and $(Ph_3P)_2PdCl_2$ (210 mg, 0.3 mmol) in dichloromethane (20 mL) was added a solution of triphenylphosphine (262 mg, 1.0 mmol) in dichloromethane (5 mL) at rt. After being stirred for 1 h, the reaction mixture was evaporated to give a purple solid, which was chromatographed over silica gel with hexane: dichloromethane (2:1) as eluent to give deep reddish purple crystals (74 mg, 0.14 mmol). Recrystallization from methanol/dichloromethane (1:1) afforded an isomeric mixture of complex **7**. Pd complex **7**: isomeric mixture; deep red needles; mp 280 °C (dec). ^{1}H NMR ($CDCl_3$) δ=0.76 (s, 6H, CH_3), 0.79 (s, 6H, CH_3), 0.96 (s, 6H, CH_3), 1.32 (s, 6H, CH_3), 1.30–1.43 (m, 8H, CH_2), 1.33 (s, 6H, CH_3), 1.85–1.91 (m, 4H, CH_2), 2.09–2.16 (m, 4H, CH_2), 2.98–2.99 (m, 4H, *J*=3.6 Hz, CH). ^{13}C NMR ($CDCl_3$) δ=11.13 (CH_3), 11.15 (CH_3), 20.26 (CH_3), 20.28 (CH_3), 20.38 (CH_3), 20.40 (CH_3), 26.57 (CH_2), 26.61 (CH_2), 33.52 (CH_2), 33.54 (CH_2), 60.45 (CH), 60.46 (CH), 61.18 (q-C), 61.35 (q-C), 62.50 (q-C), 62.53 (q-C), 195.63 (C=S), 195.90 (C=S), 200.28 (C=S), 200.43 (C=S). Anal. Calcd for $C_{20}H_{28}S_4Pd$: C, 47.75; H, 5.61. Found C, 47.53; H, 5.83. Crystal data for compound **7**: MoKα; monoclinic, *M*=503.08, *a*=6.9456(7) Å, *b*=11.902(1) Å, *c*=13.284(1) Å, *V*=1090.0(2) Å^3, monoclinic, space group=$P2_1$, *Z*=2. Final *R* and *wR* were 0.0607 and 0.1308, respectively.

To a solution of tetrathiin **2a** (393 mg, 1.52 mmol) and $NiBr_2$ (645 mg, 3.0 mmol) in dichloromethane/CH_3CN (1:1; 10 mL) was added a solution of triphenylphosphine (1048 mg, 4.0 mmol) in dichloromethane (10 mL) at rt. After stirring this solution for 1 h, water (10 mL) was added. The organic layer was dried over magnesium sulfate, filtered, and evaporated to give a purple solid, the chromatography of which over silica gel with dichloromethane/hexane (1:1) as eluent gave purple crystals (159 mg, 0.36 mmol). Recrystallization from methanol/dichloromethane (1:1) afforded a pure complex of **8**. Purple needles: mp 276–278 °C (lit.[17] mp 278 °C). ^{1}H NMR ($CDCl_3$) δ=0.67 (s, 6H, CH_3), 0.97 (s, 6H, CH_3), 1.20–1.31 (m, 4H, CH_2), 1.42 (s, 6H, CH_3), 1.80–1.86 (m, 1H, C*H*H), 2.03–2.14 (m, 1H, CH*H*), 3.09 (d, 2H, *J*=3.6 Hz, CH). ^{13}C NMR ($CDCl_3$) δ=11.48 (CH_3), 20.22 (CH_3), 20.25 (CH_3), 25.93 (CH_2), 32.98 (CH_2), 59.68 (CH), 61.41 (q-C), 61.97 (q-C), 193.73 (C=S), 198.51 (C=S).

4.9. Oxidation of tetrathiin 2a

To a solution of tetrathiin **2a** (185 mg, 0.70 mmol) in CH_2Cl_2 (20 mL) was added a solution of *m*-CPBA (261 mg, 1.47 mmol) in dichloromethane (10 mL) at rt. After stirring for 1 h, the reaction mixture was filtered, washed with satd aq sodium carbonate (10 mL×3), filtered, dried over magnesium sulfate, and evaporated to give a yellow solid, the chromatography of which over silica gel with dichloromethane as eluent furnished yellow leaflets of α-disulfine **9a** (218 mg, 0.66 mmol). α-disulfine **9a**: pale yellow crystals, mp 72 °C (dec) ^{1}H NMR ($CDCl_3$) δ=0.85 (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.45 (m, 1H, C*H*H), 1.53 (m, 1H, C*H*H), 1.95 (m, 1H, C*H*H), 2.07 (m, 1H, C*H*H), 3.89 (d, 1H, *J*=4.0 Hz, CH). ^{13}C NMR ($CDCl_3$) δ=12.50 (Me), 18.18 (Me), 20.12 (Me), 25.89 (CH_2), 34.82 (CH_2), 51.99 (CH), 53.65 (q-C), 57.44 (q-C), 193.20 (C=S=O), 195.30 (C=S=O). IR ($\nu_{C=S=O}$)/cm^{-1}=1044 (st), 1058, 1108, and 1124. Anal. Calcd for $C_{10}H_{14}O_2S_2$: C, 52.14; H, 6.13. Found: C, 52.01; H, 6.12%.

The oxidation of **2b** was carried out in a similar manner by using **2b** (83 mg, 0.30 mmol) and *m*-CPBA (131 g, 0.74 mmol). Compound **9b** (40 mg): pale yellow crystals, mp 74 °C (dec). ^{1}H NMR ($CDCl_3$) δ=0.81 (s, 3H, CH_3), 0.83 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 2.13–2.23 (m, 2H), 3.73 (m, 2H). ^{13}C NMR ($CDCl_3$) δ=12.87 (CH_3), 13.90 (CH_3), 15.54 (CH_3), 18.29 (CH_3), 33.61 (CH_2), 34.86 (CH_2), 43.21 (C), 55.66 (C), 56.46 (C), 63.19 (C), 192.79 (C=S=O), 194.82 (C=S=O). IR ($\nu_{C=S=O}$)/cm^{-1}=1056 (st), 1085, 1130, and 1143. Anal. Calcd for $C_{11}H_{16}O_2S_2$: C, 54.06; H, 6.60. Found: C, 54.12; H, 6.97%.

Compound **9c**: pale yellow crystals, mp 78 °C (dec). ^{1}H NMR ($CDCl_3$) δ=1.01 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 1.54–1.59 (m, 1H, C*H*H), 1.90–1.96 (m, 1H, CH*H*), 2.13–2.23 (m, 2H, CH_2), 3.73 (d, 1H, *J*=12.0 Hz, C*H*HCl), 3.89 (d, 1H, CH*H*Cl), 4.02 (d, 1H, *J*=2.7 Hz, CH).

^{13}C NMR ($CDCl_3$) δ=19.04 (CH_3), 20.70 (CH_3), 25.50 (CH_2), 32.13 (CH_2), 43.21 (CH), 52.69 (CH_2Cl), 54.92 (q-C), 63.11 (q-C), 190.38 (C=S=O), 195.45 (C=S=O). IR ($\nu_{C=S=O}$)/cm^{-1}=1043 (st), 1065, 1098, and 1112. Anal. Calcd for $C_{10}H_{13}ClO_2S_2$: C, 45.36; H, 4.95. Found: C, 45.24; H, 4.94.

4.10. Synthesis of thiosulfonate 11

A solution of α-disulfine **9a** (45 mg, 0.19 mmol) in ethanol (10 mL) was left to stand overnight. A colorless solid precipitated was formed, which was filtered to give colorless fine plates (**11**). Mp 275 °C (dec). ^{1}H NMR ($CDCl_3$) δ=0.90 (s, 3H, CH_3), 0.96 (br s, 3H), 1.16 (br s, 3H, CH_3), 1.40–1.52 (m, 1H, C*H*H), 1.52–1.60 (m, 1H, CH*H*), 1.60–1.83 (C*H*H), 2.12–2.19 (m, 1H, CH*H*), 3.20 (d, 1H, *J*=4.0 Hz, CH). ^{13}C NMR ($CDCl_3$) δ=11.90 (CH_3), 18.62 (CH_3), 19.73 (CH_3), 25.81 (CH_2), 30.40 (CH_2), 56.82 (CH), 58.75 (q-C), 62.03 (q-C), 140.25 (=C), 158.04 (=C). MS (ESI) (*m*/*z*): calcd for $C_{20}H_{28}O_4S_2$+Na: 483. Found: (M+Na$^+$) 483. IR (ν)/cm^{-1}: 1130 and 1332 (SO_2). Anal. Calcd for $C_{20}H_{28}O_4S_2$: C, 52.14; H, 6.13. Found: C, 51.86; H, 6.11. Crystal data for compound **11**: *M*=460.66, *a*=7.422(8) Å, *b*=12.400(13) Å, *c*=11.759(12) Å, *V*=1082(2) Å^3, *T*=173(2) K, monoclinic, space group=*P*2(1), *Z*=2. The final *R* and *wR* were 0.1117 and 0.3099, respectively, using 12,434 reflections.

Acknowledgements

We thank Mr. Taisuke Matsumoto (Analytical Center, Institute for Materials Chemistry and Engineering, Kyushu University) for the X-ray diffraction analysis.

Supplementary data

^{1}H NMR, ^{13}C NMR of compounds **2a**, **2b**, **7**, **9a**, **9b**, and X-ray crystallographic data of compound **7** and **11**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2012.05.069.

References and notes

1. Sato, R.; Saito, S.; Chiba, H.; Goto, T.; Saito, M. *Chem. Lett.* **1986**, 349–352; (a) Ogawa, S.; Yomoji, N.; Sato, S.-i.; Sato, R. *Chem. Lett.* **1994**, 507–510.
2. Chenard, B. L.; Miller, T. J. *J. Org. Chem.* **1984**, *49*, 1221–1224; (a) Ando, W.; Tokitoh, N.; Kabe, Y. *Phosphorus, Sulfur Silicon Relat. Elem.* **1991**, *58*, 179–205.
3. Macho, S.; Rees, C. W.; Rodríguez, T.; Torroba, T. *Chem. Commun.* **2001**, 403–404.
4. Brzostowska, E. M.; Greeer, A. *J. Org. Chem.* **2004**, *69*, 5483–5485.
5. Krespan, C. G. *J. Am. Chem. Soc.* **1961**, *83*, 3432–3433; (a) Nakayama, J.; Choi, K. S.; Akiyama, I.; Hoshino, M. *Tetrahedron Lett.* **1993**, *34*, 115–118; (b) Choi, K. S.; Akiyama, I.; Hoshino, M.; Nakayama, J. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 623–629.
6. Buddensiek, D.; Dirk, K.; Brigitte, V. J. *Chem. Ber.* **1987**, *120*, 575–581.
7. Shimizu, T.; Murakami, M.; Kobayashi, Y.; Iwata, K.; Kamigata, N. *J. Org. Chem.* **1998**, *63*, 8192–8199.
8. Okuma, K.; Shiki, K.; Shioji, K. *Chem. Lett.* **1998**, *27*, 79–80; (a) Okuma, K.; Shibata, S.; Shioji, K.; Yokomori, Y. *Chem. Commun.* **2000**, 1535–1536; (b) Okuma, K.; Shigetomi, T.; Shibata, S.; Shioji, K. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 187–188.
9. Okuma, K.; Shigetomi, T.; Nibu, Y.; Shioji, K.; Yoshida, M.; Yokomori, Y. *J. Am. Chem. Soc.* **2004**, *126*, 9508–9509; (a) Shigetomi, T.; Soejima, H.; Nibu, Y.; Shioji, K.; Okuma, K.; Yokomori, Y. *Chem.—Eur. J.* **2006**, *12*, 7742–7748.
10. Shigetomi, T.; Okuma, K.; Yokomori, Y. *Tetrahedron Lett.* **2008**, *49*, 36–38.
11. Okuma, K.; Nojima, A.; Shigetomi, T.; Yokomori, Y. *Tetrahedron* **2007**, *63*, 11748–11753.
12. Martinez, A. G.; Vilar, E. T.; Moreno, F.; Garcia, A. M. A. *Tetrahedron: Asymmetry* **2006**, *17*, 2970–2975; (a) Okuma, K.; Mori, Y.; Tabuchi, M.; Shigetomi, T.; Shioji, K. *Tetrahedron Lett.* **2007**, *48*, 8311–8313.
13. Majchrzak, A.; Mloston, G.; Linded, A.; Heimgartner, H. *Helv. Chim. Acta* **2004**, 790–799.
14. Okuma, K.; Tsubota, T.; Tabuchi, M.; Kanto, M.; Nagahora, N.; Shioji, K.; Yokomori, Y. *Chem. Lett.* **2010**, *39*, 648–649; (a) Okuma, K.; Munakata, K. *Phosphorus, Sulfur Silicon Relat. Elem.* **2011**, *186*, 1196–1200.
15. Bartlett, P. D.; Ghosh, T. *J. Org. Chem.* **1987**, *52*, 4937–4943; (a) Williams, C. R.; Harpp, D. N. *Tetrahedron Lett.* **1991**, *32*, 7651–7654.
16. Okazaki, R.; Ishii, A.; Fukuda, N.; Oyama, H.; Inamoto, N. *J. Chem. Soc., Chem. Commun.* **1982**, 1187–1188; (a) Ishii, A.; Okazaki, R.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 861–867; (b) Jin, Y.-N.; Ishii, A.; Sugihara, Y.; Nakayama, J. *Heterocycles* **1997**, *44*, 255–262.
17. Perochon, R.; Poriel, C.; Jeannin, O.; Sady, L. P.; Fourigue, M. *Eur. J. Inorg. Chem.* **2009**, 5413–5421.
18. Ono, Y.; Sugihara, Y.; Ishii, A.; Nakayama, J. *J. Am. Chem. Soc.* **2003**, *125*, 12114–12115; (a) Nakayama, J.; Mizumura, A.; Yokomori, Y.; Krebs, A.; Shütz, K. *Tetrahedron Lett.* **1995**, *36*, 8583–8586.
19. Scheeren, J. W.; Ooms, P. H. J.; Nivard, R. J. F. *Synthesis* **1973**, 149–151.
20. Okazaki, R.; Inoue, K.; Inamoto, N. *Tetrahedron Lett.* **1979**, *20*, 3673–3676; (a) Okazaki, R. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3541–3545.
21. Kutateladze, T. G.; Kice, J. L.; Kutatedze, A. G.; Zefirov, N. S.; Zyk, N. V. *J. Org. Chem.* **1991**, *56*, 5235–5236.