

Available online at www.sciencedirect.com



Tetrahedron Letters

Tetrahedron Letters 46 (2005) 7077-7079

## Conversion of norbornene derivatives into vicinal-dithioethers via $S_8$ activation

Sophie Poulain,<sup>a,\*</sup> Sandy Julien<sup>a</sup> and Elisabet Duñach<sup>a,b</sup>

<sup>a</sup>Laboratoire Arômes, Synthèses et Interactions, Faculté des Sciences de Nice-Sophia Antipolis, Parc Valrose, 06108 Nice cedex 2, France

<sup>b</sup>Laboratoire de Chimie Bioorganique, CNRS, UMR 6001, Faculté des Sciences de Nice-Sophia Antipolis, Parc Valrose, 06108 Nice cedex 2. France

Received 23 May 2005; revised 28 July 2005; accepted 29 July 2005

Abstract—Norbornene reacts with elemental sulfur to give a mixture of trithiolane and pentathiepane. Sulfuration of norbornene derivatives was achieved with elemental sulfur, by using a catalytic amount of a nickel complex, to afford selectively the corresponding trithiolanes. The most effective catalytic system was Ni(NH<sub>3</sub>)<sub>6</sub>Cl<sub>2</sub> in dimethylformamide. The trithiolanes were reduced with super-hydride into 1,2-dithiolate salts, and quenched in situ to form vicinal-dithioethers. © 2005 Elsevier Ltd. All rights reserved.

The direct functionalisation of non-activated alkenes in the presence of thiol derivatives (RSH or  $H_2S$ ) has been reported to afford the corresponding thioethers via radical reactions<sup>1</sup> with an *anti* Markovnikov-type selectivity. In the context of 1,2-functionalisation of alkenes by sulfur derivatives, Kondo et al.<sup>2</sup> have described the Ru-catalysed addition of organic disulfides with alkenes, for the synthesis of vicinal-dithioethers. A mild method for addition of alkyl disulfides to alkenes and conjugated polyenes promoted by ZnCl<sub>2</sub>/montmorillonite clays has also been reported.<sup>3</sup> We have been interested in the transformation of C–C double bonds into 1,2dithioether derivatives and here we describe the two-step synthesis of some 1,2-disulfides derived from norbornene. The synthesis involves the initial double bond selective sulfurisation by  $S_8$ , and the further reduction and alkylation of the isolated trithiolanes to the desired 1,2-dithioethers (Scheme 1).

Particularly strained olefins have been reported to react with elemental sulfur (S<sub>8</sub>) to afford mixtures of cyclic polysulfides, such as trithiolanes and pentathiepanes.<sup>4–8</sup> The chemistry of sulfur allotropes has also been investigated: cyclodecasulfur (S<sub>10</sub>) reacted with norbornene to furnish the trisulfide in good yield and selectivity.<sup>9</sup> With S<sub>8</sub> as sulfur source, the corresponding thiiranes could be





Keywords: Norbornene; Elemental sulfur; Trithiolane; Nickel catalysis; Dithioethers.

\* Corresponding author. Tel.: +33 (0) 4 92 07 65 77; fax: +33 (0) 4 92 07 61 25; e-mail: poulain@unice.fr

<sup>0040-4039/\$ -</sup> see front matter @ 2005 Elsevier Ltd. All rights reserved. doi:10.1016/j.tetlet.2005.07.161

obtained only in a few cases.<sup>5,10,11</sup> Synthesis of thiiranes by direct sulfur transfer has been recently reviewed by Adam and Bargon.<sup>12</sup>

Upon studying alkene functionalisation by  $S_8$ , we found that Ni(II) complexes were able to catalyse the sulfurisation of norbornene derivatives to give selectively the corresponding 1,2,3-trithiolane heterocycles, **2**. Thus, the reaction of norbornene **1a** with elemental sulfur in the presence of [Ni(NH<sub>3</sub>)<sub>6</sub>]Cl<sub>2</sub> as the catalyst (2 mol %), in DMF at 120 °C, afforded a 75% isolated yield of *exo*-1,2,3-trithiolane **2a** with 97% selectivity (Table 1, entry 1).

The *exo*-selectivity of **2a** was determined by <sup>1</sup>H NMR analysis by the W-coupling of  ${}^{4}J = 1.8$  Hz between the *endo* proton at C-1 (carbon bearing the sulfur atom) and the *anti* proton at the bridge C-3. The W-coupling is absent in the *endo* isomer.

In the absence of Ni(II) catalyst, **1a** reacted with elemental sulfur in DMF to give a 3.5:1 mixture of trisulfide **2a** and pentasulfide (pentathiepane, entry 2), in agreement with previous results.<sup>4</sup> The reaction selectivity was dependent on the amount of  $S_8$  and was optimised for an alkene:  $S_8$  ratio of 1:3/8. Higher  $S_8$  ratios led to the formation of pentathiepane in up to 26% selectivity (entry 3).

The effect of the nickel catalyst was examined and the results on the use of different catalysts are presented in Table 1 (entries 4–6). Raney-Ni was very selective towards 2a though the reaction occurred at a very slow

rate. Replacing the NH<sub>3</sub> ligand on Ni(II) by the cyclic tetraamine cyclam (1,4,7,11-tetraazacyclotetradecane) afforded **2a** in 47% yield and 95% selectivity. The use of nickel acetate as the catalyst did not improve the results with respect to the use of  $[Ni(NH_3)_6]Cl_2$ . With  $[Ni(NH_3)_6]Cl_2$ , the sulfuration of 5-vinyl-2-norbornene, **1b** and of 2-acetyl-5-norbornene, **1c** afforded the corresponding trithiolane derivatives **2b** (entry 7) and **2c** (entry 8) in 95% and 96% selectivities and 82% and 77% yields, respectively.<sup>14</sup> Less strained alkenes such as cyclohexene were not reactive under the reaction conditions used.

The reduction of trithiolanes 2 to the corresponding 1,2disulfides 3 (Scheme 1) was attempted using different reducing metals (Ni<sup>0</sup>, Na<sup>0</sup> and Zn/AcOH) or hydrides (NaH and LiAlH<sub>4</sub>). All these reducing systems led to the recovery of the starting material 2 or to decomposition. The formation of vicinal-disulfides 3 from trithiolanes 2a-c could be efficiently carried out by reduction with LiEt<sub>3</sub>BH in refluxing THF, followed by the addition of methyl iodide or benzyl bromide as the electrophiles. The results, summarised in Table 2, indicated that 3-4 equiv of the hydride were necessary to efficiently transform the trithiolanes into the corresponding 1,2-dithiolate salts before electrophilic quenching. Yields of **3a** and **b** from 71% to 91% were obtained; for 3c the yields were lower, due to the partial reduction of the acetyl group.

The reduction of trithiolane structures 2a and b was also studied by using an electrochemical methodology. No electrochemical trithiolane reduction has been yet

Table 1. Sulfuration of norbornene derivatives (alkene 5.3 mmol, S<sub>8</sub> 3/8 equiv, catalyst 0.02 equiv, 15 ml DMF)<sup>13</sup>

Table 1. Subtration of horsonnene derivatives (alkene 5.5 minor, 58 5/6 equiv, eatalyst 0.02 equiv, 15 min Divity)					
Entry	Substrate	Catalyst, reaction time (h)	Selectivity of $2$ , $\%^a$ (% of isolated yield of $2$ )		
1	1a	[Ni(NH <sub>3</sub> ) <sub>6</sub> ]Cl <sub>2</sub> , 11	97 (75)		
2	1a	— , 11	76 (48)		
3	1a	$[Ni(NH_3)_6]Cl_2, 1^b$	74 (54)		
4	1a	Ni(OAc) <sub>2</sub> ·4H <sub>2</sub> O, 39	90 (48)		
5	1a	Raney-Ni, 65	100 (26)		
6	1a	$Ni(cyclam)(BF_4)_2, 50$	95 (47)		
7	1b	$[Ni(NH_3)_6]Cl_2, 7$	95 (82)		
8	1c	$[Ni(NH_3)_6]Cl_2, 11$	96 (77)		

<sup>a</sup> Selectivity calculated according to <sup>1</sup>H NMR spectra of the crude reaction mixture.

<sup>b</sup> 5/4 equiv of elemental sulfur were employed.

**Table 2.** Reduction of trithiolane derivatives  $2\mathbf{a}-\mathbf{c}^{15}$ 

Entry	Substrate	Reagent (nb equiv), time (h)	Electrophile	Yield of <b>3</b> (%)
1	2a	LiEt <sub>3</sub> BH (2), 4	b	19
2	2a	LiEt <sub>3</sub> BH (3), 2	b	90
3	2a	LiEt <sub>3</sub> BH (4), 1	CH <sub>3</sub> I	91
4	2a	LiEt <sub>3</sub> BH (4), 1.5	PhCH <sub>2</sub> Br	98
5	2b	LiEt <sub>3</sub> BH (4), 1	CH <sub>3</sub> I	71
6	2c	LiEt <sub>3</sub> BH (4), 1	CH <sub>3</sub> I	21
8	2a	Electrolysis, <sup>a</sup> 7	CH <sub>3</sub> I	84
9	2b	Electrolysis, <sup>a</sup> 7	CH <sub>3</sub> I	50

<sup>a</sup> The reaction was carried out at constant current intensity, at room temperature, in DMF containing LiClO<sub>4</sub> as supporting electrolyte. The reaction, followed by GC, consumed 8 F/mol of substrate for a complete conversion.

<sup>b</sup> The reaction was quenched with H<sub>2</sub>O and the vicinal-dithiol was isolated.

reported. Efficient reactions were obtained in a singlecompartment cell, with a consumable magnesium anode.<sup>16</sup> In DMF, at room temperature, and after quenching with MeI, the 1,2-dimethylthio derivatives **3a** and **b** were obtained in 84% and 50% yields, respectively (Table 2, entries 8 and 9).

In conclusion, a Ni(II)-catalysed selective functionalisation of norbornene derivatives to trithiolanes was developed by using elemental sulfur as the sulfurating reagent. The further transformation of the trithiolanes to the corresponding 1,2-disulfides was achieved by a chemical reduction with LiEt<sub>3</sub>BH or by an electrochemical reduction procedure.

## **References and notes**

- 1. Griesbaum, K. Angew. Chem., Int. Ed. Engl. 1970, 9, 273–287.
- Kondo, T.; Uenoyama, S.; Fujita, K.; Mitsudo, T. J. Am. Chem. Soc. 1999, 121, 482–483.
- Clark, P.; Mesher, S.; Parvez, M. Catal. Lett. 1997, 47, 73– 75.
- Bartlett, P. D.; Ghosh, T. J. Org. Chem. 1987, 52, 4937– 4943.
- 5. Nakayama, J.; Ito, Y.; Mizumura, A. Sulfur Lett. 1992, 14, 247–250.
- Sugihara, Y.; Takeda, H.; Nakayama, J. *Tetrahedron Lett.* 1998, 39, 2605–2608.
- 7. Weller, K.; Hwang, L. U.S. Patent 6211345, 2001, 7 pp.
- Emsley, J.; Griffiths, D.; Jayne, G. J. Chem. Soc. Perkin Trans. 1 1979, 228–232.
- 9. Lesté-Lasserre, P.; Harpp, D. Tetrahedron Lett. 1999, 40, 7961–7964.
- Ashitani, T.; Nagahama, S. Nat. Prod. Lett. 1999, 13, 163– 167.
- 11. Sugihara, Y.; Noda, K.; Nakayama, J. *Tetrahedron Lett.* **2000**, *41*, 8913–8916.
- 12. Adam, W.; Bargon, R. Chem. Rev. 2004, 104, 251-261.
- 13. Elemental sulfur  $S_8$  (510 mg, 2 mmol) and the catalyst [Ni(NH<sub>3</sub>)<sub>6</sub>]Cl<sub>2</sub> (25 mg, 0.1 mmol) were added to a solution of alkene 1 (500 mg, 5.3 mmol) in 15 ml of DMF, at room temperature. The reaction mixture was stirred at 120 °C during 11 h. The reaction was followed by GC. After cooling down to room temperature, the mixture was filtered on silica gel and eluted with petroleum ether. The filtrate was washed with water (3 × 10 ml). The organic layer was concentrated under reduced pressure to afford the norbornane trithiolane 2 as a colourless oil. The trisulfides 2a–c were obtained following the same procedure.
- For example, spectral data for compound, 5-acetylhexahydro-4,7-methanobenzotrithiole 2c: colourless oil, yield = 77%. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 3.69 and 3.67 (2H,

d × 2, CHS × 2,  ${}^{4}J = 1.8$  Hz), 2.63 (1H, m, CH), 2.46 (2H, m, CHCO and CH), 2.16 (3H, s, CH<sub>3</sub>), 2.05 (1H, m, CHH<sub>a</sub>CHCO), 1.82 (1H, dt, CHHanti,  ${}^{2}J = 10.9$  Hz,  ${}^{4}J = 1.7$  Hz), 1.44 (1H, ddd, CHH<sub>b</sub>CHCO,  ${}^{2}J = 11.8$  Hz,  ${}^{3}J = 8.9$  Hz,  ${}^{3}J = 2.4$  Hz), 1.06 (1H, dt, CHHsyn,  ${}^{2}J = 10.9$  Hz,  ${}^{4}J = 1.7$  Hz).  ${}^{13}C$  NMR (CDCl<sub>3</sub>)  $\delta$ : 207.3 (CO), 70.1 and 70.0 (CHS × 2), 53.5 (CHCO), 44.1 and 41.1 (CH × 2), 31.1 (CH<sub>2</sub>CHCO), 30.8 (CH<sub>2</sub>), 29.5 (CH<sub>3</sub>). MS (EI, 70 eV): m/z (%) 232 (M<sup>+</sup>, 38.9), 198 (5.2), 168 (19.5), 125 (26.9), 98 (53.3), 91 (30.9), 71 (37.2), 66 (54.7), 43 (100), 39 (26.6).

15. To a stirred solution of trithiolane 2 (200 mg, 1.05 mmol) in THF (2 ml) was added LiEt<sub>3</sub>BH (1 M in THF, 4.2 ml, 4.2 mmol) dropwise, at room temperature. The mixture was heated to 65 °C. After 1 h, the reaction mixture was quenched with CH<sub>3</sub>I (0.65 ml, 10.5 mmol). The mixture was cooled and poured into 10 ml of H<sub>2</sub>O. It was extracted with Et<sub>2</sub>O ( $3 \times 10$  ml) and washed with 10 ml of H<sub>2</sub>O. The organic layer was dried over MgSO<sub>4</sub> and concentrated under reduced pressure. The resulting oil was purified by column chromatography (eluant: petroleum ether) to give the dithioether **3** as a colourless oil. Following the same procedure, the reduction of **2a–c** gave the corresponding vicinal-dithioethers **3a–c**, as colourless oils.

For example, spectral data for compounds **3b** and **c**. 5-Ethenyl-2,3-bis(methylthio)bicyclo[2.2.1]heptane **3b**: colourless oil, yield = 71%. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 5.77 (1H, ddd, CH=CH<sub>2</sub>, <sup>3</sup>J<sub>trans</sub> = 16.9 Hz, <sup>3</sup>J<sub>cis</sub> = 10.8 Hz, <sup>3</sup>J = 5.5 Hz), 5.03 (1H, ddd, CH=CHH<sub>a</sub>, <sup>3</sup>J<sub>cis</sub> = 10.8 Hz, <sup>2</sup>J = 1.6 Hz, <sup>4</sup>J = 1.6 Hz), 4.99 (1H, ddd, CH=CHH<sub>b</sub>, <sup>3</sup>J<sub>trans</sub> = 16.9 Hz, <sup>2</sup>J = 1.6 Hz, <sup>4</sup>J = 1.6 Hz), 3.12 (1H, dd, CHS, <sup>3</sup>J = 7.8 Hz, <sup>4</sup>J = 1.8 Hz), 2.81 (1H, dd, CHS, <sup>3</sup>J = 7.8 Hz, <sup>4</sup>J = 1.8 Hz), 2.81 (1H, dd, CHS, <sup>3</sup>J = 6.8 Hz, <sup>3</sup>J = 5.5 Hz, <sup>4</sup>J = 1.8 Hz, 2.2 (2H, m, CH×2), 2.1 (6H, s, CH<sub>3</sub>×2), 1.82 (2H, m, CHH×pn), 1.02 (1H, ddd, CHHarti), 1.28 (1H, m, CHHsyn), 1.02 (1H, ddd, CHH<sub>b</sub>CHCH=CH<sub>2</sub>, <sup>2</sup>J = 11.0 Hz, <sup>3</sup>J = 6.8 Hz, <sup>3</sup>J = 2.2 Hz). <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$ : 140.1 (CH=CH<sub>2</sub>), 115.8 (CH=CH<sub>2</sub>), 57.4 (CHS), 50.4 (CHS), 49.3 (CHCH=CH<sub>2</sub>), 44.8 and 43.5 (CH × 2), 35.9 and 34.0 (CH<sub>2</sub>×2), 17.9 and 18.0 (CH<sub>3</sub>×2). MS (EI, 70 eV): *m*/*z* (%) 214 (M<sup>+</sup>, 100), 167 (45.7), 113 (97.1), 91 (64.5), 66 (63.6).

5-Acetyl-2,3-bis(methylthio)bicyclo[2.2.1]- heptane **3c**: colourless oil, yield = 21%. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 2.68 and 2.62 (2H, d×2, CHS×2, <sup>4</sup>J = 2.0 Hz), 2.38 (1H, m, CHCO), 2.23 (2H, m, CH×2), 2.17 (3H, s, CH<sub>3</sub>CO), 2.04 (6H, s, CH<sub>3</sub>S×2), 1.55 (1H, m, CH*Hanti*), 1.25–1.08 (3H, m, CH<sub>2</sub> and CH*Hsyn*). <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$ : 64.9 (CHCO), 48.3 (CHS×2), 44.6 and 42.9 (CH×2), 38.6 and 35.6 (CH<sub>2</sub>×2), 22.4 (CH<sub>3</sub>CO), 19.0 (CH<sub>3</sub>S×2). MS (EI, 70 eV): m/z (%) 230 (M<sup>+</sup>, 44.1), 215 (20.6), 167 (47.1), 135 (11.8), 127 (15.7), 107 (54.9), 91 (57.4), 75 (47.1), 55 (37.3), 45 (100).

 Chaussard, J.; Folest, J. C.; Nedelec, J. Y.; Perichon, J.; Sibille, S.; Troupel, M. Synthesis 1990, 5, 369–381.