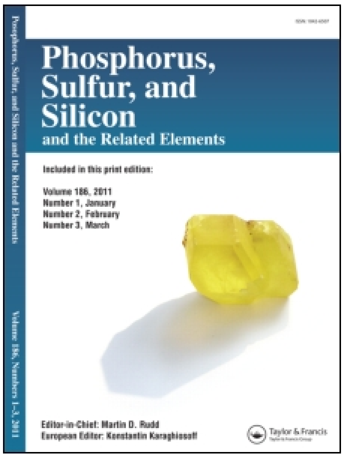

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Interesting Transformations of Thiocamphor

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Interesting Transformations of Thiocamphor

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Thiocamphor has been found to furnish bornane, camphor, isoborneol, isobornylthiol, bornylthiol, tetrahydro-bis-(1,7,7-trimethylbicyclo[2.2.1]heptyl)-3,3′-disulfide, and three isomeric bis-(1,7,7-trimethylbicyclo[2.2.1]heptyl)-3,3′-dithiols when treated with $NaBH_4$ *either in dry THF or dry diethylene glycol diethyl ether. The origins of the above interesting compounds and their mass spectral characterization are presented in this article.*

Keywords GC-MS; mass spectrometry; pathway; radicals

INTRODUCTION

Thiocamphor (**1**) exhibits unusual properties unlike aromatic thioketones. Thus when reacted with aminosulfuric acid, it yields camphor oxime and bis-(1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl) disulfide.[1] Thiocamphor (**1**) upon treatment with benzeneselenic anhydride has been reported to yield camphor, camphoquinone, and 3-endo-phenylselenium camphor.[2] A variety of reagents have been described to transform **1** into camphor.[3] When **1** was reacted with diaryl tellurium oxide, it gave a number of products, of which two were identified as bis-(1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl) disulfide (**2**) and {3, 3′- bis-(1,7,7-trimethylbicyclo[2.2.1]heptane)}-2, 2′-dithione (dithione, **3**) (Figure 1).[3b]b Even under mild conditions, **1** undergoes phase-catalyzed transformation to carbonyl compounds.[4] Oxidation of **1** with either NBS or chloramine T has been reported to give bis-bornenedisulfide or bis-(1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl)-disulfide (**2**) via the enethithiyl radical (**1A**).[5] The suggested mechanism for this transformation is the dimerization of the thiyl radical (**1B**) formed from **1** via

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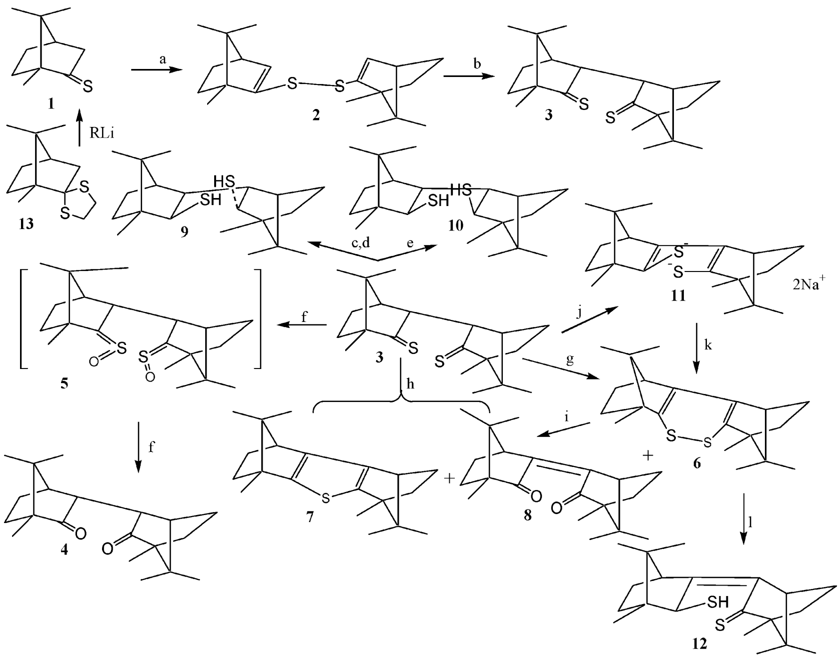

[(a) oxidation; (b) heat; (c) Al-Hg reduction; (d) BH_3-DMS; toluene, 100°(e) B_2H_6-DMS, toluene, 100°; (f) mcpb-oxidation; (g) $Hg(OAc)_2$, Toluene, AcOH , r. t. to 60° C; (h) $Hg(OAc)_2$, Toluene, AcOH, 100° C; reverse addition; (i) $Hg(OAc)_2$; (j) NaH-DMF; (k) $K_3[Fe(CN)_6]$; (l) $NaBH_4$-C_6H_6, 20° C ; C_6H_5SH, NEt_3, DMF, 20° C.]

FIGURE 1 Transformations of thiocamphor.

pathway A (Figure 2). Since thiocamphor has been stated to exist as a tautomer,[2,3b] it seems that the alternate pathway B appears be more appropriate. This observation derives support from the suggestion of Barton and co-workers that the enolizable CH_2 group makes the thiocarbonyl group of thiocamphor more reactive and that it reacts as a tautomeric mixture.[1,2,3b] The dimerized disulfide was obtained when **1** was exposed to UV light in the presence of I_2.[5] The iodine-catalyzed oxidation of **1** had been previously reported to furnish the bicyclic disulfide, which was subsequently converted into dithiones and reduced to dithiols respectively.[6]

Disulfide **2** upon prolonged standing or on heating was transformed into {3,3′-bis-(1,7,7-trimethyl-bicyclo[2.2.1]heptano)}-2,2′-dithione (**3**) via the 3, 3-sigmatropic hetero–Cope rearrangement. Even though the presence of stereomeric dithiones has been mentioned, so far only one isomer has been isolated, and its mass spectral breakdown has been described[7] and its X-ray structure has been published.[8] Oxidation of

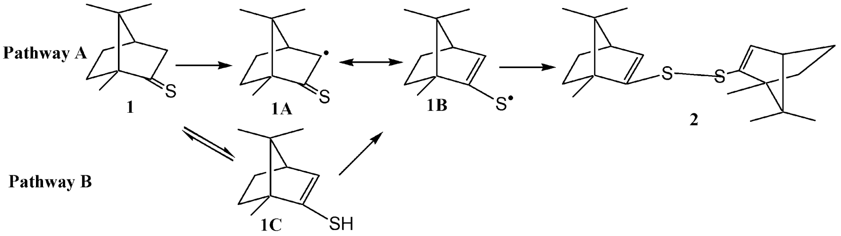

FIGURE 2 Alternate pathways for the formation of the 1,2-disulfide (**2**).

the dithione (**3**) with m-chloroperbenzoic acid yields bis-camphor (**4**) via the disulfine intermediate (**5**).

However, the oxidation of the dithione with mercuric acetate has been described to give the dithiine (**6**), thiophene (**7**), and *α*,*β*-unsaturated ketone (**8**) (Figure 1) depending upon the experimental conditions. Thiophene (**7**) and *α*,*β*-unsaturated ketone (**8**) are also obtained when dithiine (**6**) is oxidized with mercuric acetate. The reduction of di-thiocaphor (**3**) with Al-Hg amalgam has been reported to give dithiols.[6] However, the borane-dimethyl sulfide complex yields isomeric bis-camphorthiols (exo-exo, **9** or exo-endo, **10**) depending upon the stoichiometry of the reducing agent.[7] It is interesting to note that the reaction of camphor thioketal (**13**) with alkali metal reagents gives thiocamphor (**1**), isobornylthiol (**15**), and bornylthiol (**16**).[9] It was stated that the isomeric camphorthiols (**9** and **10**) could not be separated either by TLC and GC, and that a long special GC column was required to finally separate the isomers.

According to a published report,[7] it is observed that the exo-isomer (**15**) has a longer retention time than the endo-isomer (**16**). Treatment of **3** with NaH in DMF, followed by the oxidation of the dithio-disodium salt with $K_3[Fe(CN)_6]$, also furnishes the dithiine (**6**), which upon reduction with $NaBH_4$ yields a unique compound, namely a conjugated monothiol mono-thione (**12**). This compound contains a bridgehead carbon–carbon double bond just like the diketone, **8**. It was recently reported that the reduction of thiocamphor (**1**) with $NaBH_4$ in ethyl ether of ethylene glycol gives 92% of a single camphorthiol (isobornylthiol, **15**).[10] When we explored this approach, a complex mixture of nine compounds excluding the substrate was obtained. The formation and the GC-MS identification of these compounds are described in this article.

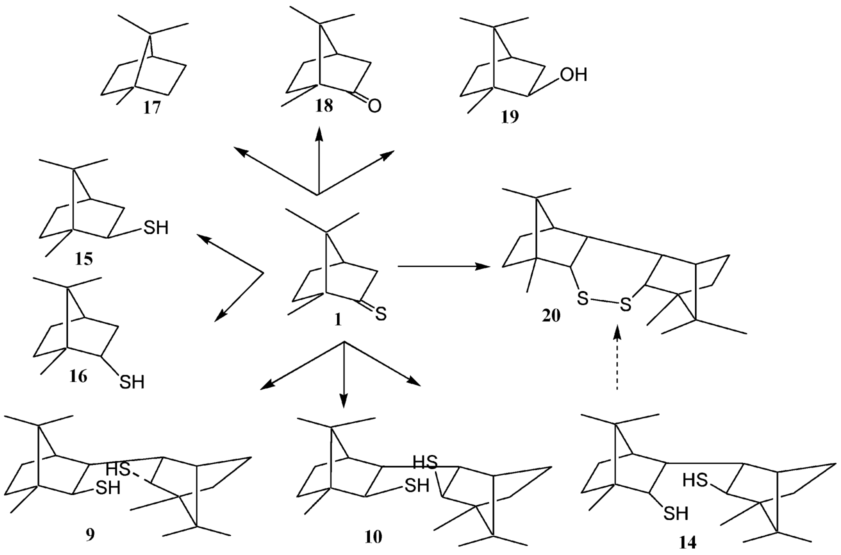

FIGURE 3 Reaction of thiocamphor with $NaBH_4$.

RESULTS AND DISCUSSION

The reaction of thiocamphor (**1**) with $NaBH_4$ both in dry THF and diethylene glycol diethyl ether gave a complex mixture of compounds contrary to a recent report.[10] The GC analysis of the reaction mixture showed it to consist of at least 10 components. GC-MS examination of the above reaction product showed it to consist of the following compounds (Figure 3): (i) 1,7,7-trimethylbicyclo[2.2.21]heptane (bornane, **17**); (ii) camphor (**18**); (iii) isoborneol (**19**); (iv) isobornylthiol (**15**); (v) bornylthiol (**16**); (vi) di-(1,7,7-trimethylbicyclo[2.2.1]heptyl)-3,3′dithiol (exo-exo, **9**); (vii) di-(1,7,7-trimethylbicyclo[2.2.1]heptyl)-3,3′dithiol (exo-endo, bis-bornyldithiol, **10**); (viii) di-(1, 7,7-trimethylbicyclo-[2.2.1]heptyl)-3, 3′-dithiol (endo-endo, or bis-bornyl dimercaptan, **14**), and (ix) bis-bornyl tetrahydro-1,2-dithiine (**20**). Also identified was the substrate of the reaction, (**1**). The formation of the above unexpected compounds can be attributed to the labile nature of sulfur present as a thiocarbonyl moiety of the substrate. The results appear to reflect the observation that the presence of the enolizable methylene moiety next to the thicarbonyl group gives rise to the formation of a more complex product.[2a]

It is known that **1** gives rise to **18** under a variety of experimental coniditions.[3] It is also known that the reduction of **18** with various reducing agents usually yields a mixture of exo- and endo-isomeric alcohols.[11] In view of the above cited generality, the formation of the endo- and exo-thiols (**15** and **16**) is not surprising. What is interesting to note is the formation of tetrahydrodithiine (**20**) and bis-bornyl dimercaptans, **9**, **10**, and **14**. The origin of **20** can be ascribed to the formation of the intramolecular disulfide bond from the corresponding dithiols either during the course of the reaction or during the workup of the reaction product. Compounds **9** and **10** had been previously reported,[8] while **14** has not been observed when bis-camphor dithione **3** was reduced by borane-dimethyl sulfide complex.[8] The three dithiols, namely **9**, **10**, and **14**, have been characterized by their mass spectral fragmentation patterns, which are similar in many respects.

The mass spectral breakdown of thiocamphor (**1**),[12] camphor (**18**),[13] and borneol (**19**)[13] has been previously discussed, and the occurrence of the skeletal rearrangement during the mass spectral fragmentation has been described.[11–13] The mass spectral fission of organic sulfur-containing compounds is further complicated by α- and β-cleavages, McLafferty rearrangement, double McLafferty rearrangement, the cleavage of the remote carbon–carbon bond, the elimination of HS and HS_2 radical-fragments, hydrogen transfer from remote sites to sulfur, retro Diels–Alder reaction, etc.[15] The mass spectra of bis-bornyl-1,2-disulfide (**2**) and bis-camphor dithione (**3**) have been previously described.[7] The X-ray crystallographic structure determination of bis-camphor 1,4-dithione (**3**) and 1,2-dithiine (**6**) has been published.[8] The major cleavage seems to cause the fission of the 3, 3′-carbon–carbon bond between the bicyclic moieties or of the bond between sulfur and sulfur. The former fission is then followed by the extrusion of sulfur to furnish the m/e = 137 ($C_{10}H_{17}$) peak, which happens to be the most intensive ion in the mass spectra of two stereomeric dithiols and a major ion peak (70%) in the third isomer. The remainder of the peaks are similar to the ones that are usually seen during the mass spectral breakdown of the bicyclo[2.2.1]heptanes. A detailed mass spectral breakdown of the compounds cited in the narrative is given in Table I.

EXPERIMENTAL

EI mass spectra were obtained using a model 5973i GC/MSD (Agilent Technologies, Wilmington, DE) equipped with a 30 m × 0.25 mm HP-5ms capillary column (0.25 μm film). The carrier gas was helium at 1.1 mL/min (constant flow), the injection temperature was 250°C, transfer line temperature was 280°C, electron energy was 70 eV, and the oven was programmed from 60°C to 280°C at 15°C/min with a 10 min hold at 280°C. The mass range was scanned from 45–500 Daltons at

TABLE I Mass Spectral Fragmentation of Compounds Listed in the Narrative

(1) Bornane (**14**): $M^+ = 138$, (r.t. = 3.01 min, 1.1%). 123 (M—CH_3); 107 (123—CH_4); 96 (M—C_3H_6, 100%); 93 (107—CH_2). 86 (C_6H_{14}); 67 (C_5H_7) and 41 (C_3H_5).

(2) Thiocamphor (**1**): $M^+ = 168$, (r.t. = 6.04 min, 0.5%) [cf. A. Daniel and A. A. Pavia, Org. Mass. Spectrom.; 5, 1237 (1971).]

(3) Camphor (**15**): $M^+ = 152$, (r.t. = 5.00 min, 2.9%). [cf. D. C. Dimmel and J. Wolinsky, J. Org. Chem, 32, 410 (1967) and refs. cited there in.]

(4) Isoborneol (**16**): $M^+ = 154$, (r.t. = 5.15 min, 1.3%). [cf. D. C. Dimmel and J. Wohnsky, J. Org. Chem., 32, 410 (1967) and refs. cited there in.]

(5) Bornyl mercaptan (**18**): $M^+ = 170$, (r.t. = 5.84 min, 16.4%); 155 (M—CH_3); 137 (M—HS); 136 (M—H_2S); 127 (M—C_3H_7); 121 (155—H_2S); 110 (M—C_2H_4S or C_8H_{14}); 108 (C_8H_{12}); 100 (C_5H_8S); 95 (C_7H_{11}, 100%); 93 (C_7H_9); 91 (C_7H_7); 87 (C_4H_7S); 81 (C_6H_9); 67 (C_5H_7); 53 (C_4H_5); 47 (SCH_3) and 41 (C_3H_5).

(6) Isobornyl mercaptan (**17**): $M^+ = 170$, (r.t. = 5.97 min, 63.0%);155 (M—CH_3); 137 (M—HS); 136 (M -H_2S); 110 (M—C_2H_4S or C_8H_{14}); 108 (C_8H_{12}); 100 (C_5H_8S); 95 (C_7H_{11}, 100%); 93 (C_7H_9); 91 (C_7H_7); 87 (C_4H_7S); 81 (C_6H_9); 67 (C_5H_7); 59 (C_2H_3S); 53 (C_4H_5); 47 (SCH_3) and 41 (C_3H_5).

(7) Bis-bornyl disulfide (**19**): $M^+ = 336$, (r.t. = 13.83 min, 0.30%); 321 (M—CH_3); 303 (M -HS); 293 (M -C_3H_7); 283 (M—C_4H_5); 267 (283—CH_4); 213 (267—C_4H_6); 201 ($C_{10}Hl_7S_2$); 168 ($C_{10}H_{14}S$); 153 (C_9H1_3S): 135($C_{10}H_{15}$); 125 ($C_7H_{10}S$); 113 (C_6H_9S or C_8H_{17}); 95 (C_7H_{11}); 85 (C_6H_{13} or C_4H_5S); 67 (C_5H_7); 55 (C_4H_7) and41(C_3H_5, 100%).

(8) Bis-camphordithiol (exo-exo) (**9**): $M^+ = 338$, (r.t. = 14.13 min, 0.30%); 281 (M—C_4H_9); 267 (281—CH_2); 249 (281—S); 207 (249—C_3H_6); 193 (207—CH_2); 177 (207—C_2H_6); 147 (193—C_3H_8); 137 ($C_{10}H_{17}$, 70%); 121 (C_9H_{13}); 95 (C_4H_5S or C_7H_{11}); 81 (C_6H_9, 100%); 69 (C_5H_9); 53 (C_4H_5) and 41 (C_3H_5).

(9) Bis-camphordithiol (exo-endo) (**10**): M^+ 338 (r.t. = 14.20 min, 6.40%); 281 (M—C_4H_9); 267 (281—CH_2): 253 (281- C_2H_4); 207 (253—C_3H_8); 153 ($C_9H_{13}S$); 137 ($C_{10}H_{17}$, 97%); 121 (C_9H_{13}); 107 (C_8H_n); 95 (C_4H_5S or C_7H_{11}); 81 (C_6H_9, 100%); 69 (C_5H_9); 53 (C_4H_5); 43 (C_3H_7) and 41 (C_3H_5).

(10) Bis-camphordithiol (endo-endo) (**13**): $M^+ = 338$, (r.t. = 14.28 min, 7.50%); 285 (M—C_4H_5); 267 (281 -CH_2); 249 (281—S); 207 (253—C_3H_8); 168 ($C_{10}H_{16}S$); 137 ($C_{10}H_{17}$, 100%); 121 (C_9H_{13}); 107 (C_8H_{11}); 95 (C_4H_5S or C_7H_{11}); 81 (C_6H_9, 99%); 67 (C_5H_7); 55 (C_4H_7) and 41 (C_3H_5).

1.66 scans/sec. Injection was in the split (50:1) mode. CI mass spectra were obtained using a model TSQ-7000 GC/MS/MS (ThermoFisher, San Jose, CA) equipped with a 30 m × 0.25 mm HP-5ms capillary column (0.25 μm film). The carrier gas was helium at 1 mL/min, injection temperature was 250°C, transfer line temperature was 250°C, electron energy was 200 eV, and the oven was programmed from 60°C to 270°C at 15°C/min with a 14 min hold at 270°C. Methane (UHP grade) was used as the CI reagent gas at 3500 mT. The mass range was scanned from 60–500 Daltons at 0.7 sec/scan. Injection was in the split (50:1) mode.

Reaction of Thiocamphor (1) with $NaBH_4$

To a solution of thiocamphor (0.60 g, 3.57 mmol) in dry THF (10 mL), stoichiometric amounts of $NaBH_4$ were added in small portions under nitrogen at 0°C with stirring during 30 min, and the reaction mixture was allowed to come to ambient temperature and was stirred overnight. The excess of the reducing agent was destroyed and the reaction mixture was extracted with dichloromethane. Then the organic extract was washed with water and a saturated solution of sodium chloride, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was analyzed first by TLC and GC. A similar reaction was also carried out in diethylene glycol diethyl ether. Both reactions were repeated, and the results were found to be consistent. The GC-MS analysis of the reaction product permitted the identification of compounds described in Table I.

REFERENCES

[1] M. M. Campbell and D. M. Evgenios, *J. Chem. Soc., Perkin Trans.*, **1,** 2862 (1973).

[2] D. H. R. Barton, J. Cussans, and S. V. Ley, *J. Chem. Soc., Chem. Comm.*, 393 (1978).

[3] (a) cf. Ref. 8, S. V. Ley, C. A. Meerhalz, and D. H. R. Barton, *Tetrahedron*, **37,** Suppl. 1, 213 (1981); (b) T. Ravidran, S. P. Chavan, M. M. Awachat, and S. V. Kelkar, *Tetrahedron Lett.*, **36,** 2277 (1995) and refs. cited therein.

[4] H. Alper, C. Kwiatkowska, J.-F. Petrignani, and F. Sibtain, *Tetrahedron Lett.*, **27,** 5449 (1986).

[5] M. M. Campbell and D. M. Evgenios, *J. Chem. Soc., Perkin Trans.*, **1,** 2866 (1973).

[6] P. C. Ray, *Nature*, **138,** 548 (1936).

[7] M. Bonnat, J.-O. Dur, and M. Le Corre, *Tetrahedron: Asymmetry*, **7,** 559 (1996).

[8] W. Schroth, E. Hintzsche, R. Spitzner, H. Imgartinger, and V. Siemund, *Tetrahedron Lett.*, **35,** 1973 (1994).

[9] S. R. Wilson, P. Caldera, and M. A. Jester, *J. Org. Chem.*, **47,** 3319 (1982).

[10] J. H. Zaidi, F. Naeem, K. M. Khan, R. Iqbal, and Zia-Ullah, *Synth. Commun.*, **34,** 2642 (2004).

[11] (a) S. Beckman, *Bull. Soc. Chim. (France)*, 1319 (1960) (b) G. Ourisson and A. Rassaat, *Tetrahedron Lett.*, 16 (1960).

[12] (a) A. Daniel and A. A. Pavia, *Org. Mass. Spectrom.*, **5,** 1237 (1971) (b) M. M. Campbell, G. M. Anthony, and C. J. W. Brooks, *Org. Mass Spectrom.*, **5,** 297 (1971).

[13] D. C. Dimmel and J. Wolinsky, *J. Org. Chem.*, **32,** 410 (1967) and refs. cited therein.

[14] J. W. Bowie, B. K. Simmons, and S. O. Lawesson, *Rev. Pure Appl. Chem.*, **19,** 61 (1969).

[15] C. C. van de Sande, In *The Chemistry of the Ethers, Crown-Ethers, Hydroxy Groups and Their Sulfur Analogs, Chapter 7, Part 2, Supplement* (Wiley and Sons, New York, 1980), pp. 299–325.