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Indium Triflate-Catalysed Addition of Thio Compounds to Camphene: A Novel Route to 2,3,3-Trimethyl-2-thiobicyclo[2.2.1]heptane Derivatives

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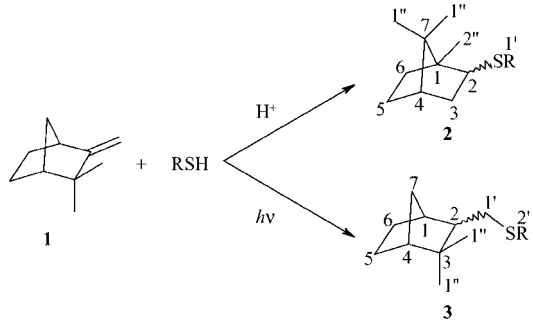
In^{III} triflate-catalysed addition of thiols and thiocarboxylic acids to camphene under mild conditions has allowed the functionalisation of the alkene for the first time, with suppression of the classical rearrangement of the camphene terpene skeleton to isobornane structures.

Introduction

The addition of thiols and thioacids to nonactivated olefins constitutes a powerful method for the synthesis of sulfides, thioesters and thiols.[1] Generally, this reaction proceeds through a radical-type mechanism with initiators, such as peroxides, AIBN or photochemistry, resulting in the addition of thio derivatives to the double bond with anti-Markovnikov regioselectivity.[2,3] Electrophilic-type additions with strong protic[4–6] or Lewis[7,8] acids in over-stoichiometric amounts result in the formation of Markovnikov-type adducts with some olefin polymerisation. We recently reported on the catalytic and efficient use of "super" Lewis acids derived from triflates for the selective functionalisation of nonactivated olefins in hydroalkoxylation cycloisomerisations and hydrothiolations.[9]

We have also been working on the catalytic functionalisation of camphene by sulfur derivatives; the synthesis of novel sulfur-containing terpenoid compounds is of interest in the field of flavour and fragrance chemistry, because of the high organoleptic impact of this class of compounds.[10] Several sulfur-derived terpenoid derivatives such as 1-*p*-menthene-8-thiol have been found in trace amounts in natural compounds[11] and contribute to a great extent to their olfactory and flavour properties.[12]

Classically, electrophilic addition to camphene-type structures involves a Wagner–Meerwein rearrangement.[13] Electrophilic additions of thiols to camphene **1** in the presence of stoichiometric amounts of $EtAlCl_2$ as the Lewis acid have been reported to afford thioisobornane derivatives of type **2**, in a process involving the rearrangement of the camphene skeleton to the isobornane structure **2** (Scheme 1).[14] It has been proposed that this rearrangement proceeds via a nonclassical carbocation, resulting from a σ-delocalised bond.[15] In the case of BuSH addition to **1**, rearranged **2** (R = Bu) was obtained in 52% yield, while the addition of H_2S to **1** in the presence of stoichiometric amounts of $AlBr_3$ resulted in rearrangement and dimerisation to diisobornyl sulfide.[16] Isobornyl structures have also been obtained in addition reactions of camphene and sulfides in the presence of stoichiometric amounts of triflic acid.[17] To the best of our knowledge, electrophilic functionalisation of camphene without isomerisation of the bicyclo[2.2.1]heptane structure has not been reported.



Scheme 1. Protic and radical-type addition of sulfur derivatives to camphene.

The radical-type addition of thioacetic acid to **1**, affording the expected anti-Markovnikov compounds **3** (Scheme 1), has also been reported.[16] The use of AcSH under UV irradiation conditions thus afforded the corresponding thioacyl derivative **3** in 64% yield with no stereochemical assignment.

We report here the results of a novel *rac*-camphene functionalisation that does not involve the classical isomerisation of the bicyclic structure under catalytic Lewis acid conditions.

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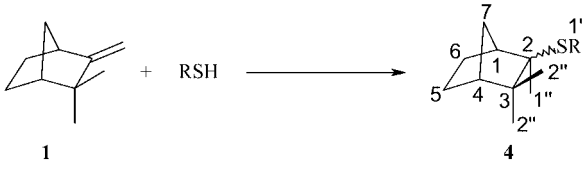
Results and Discussion

The capability to add nucleophiles such as sulfur derivatives (thiols or thioacids) to the internal disubstituted position of the double bond of **1** without skeletal rearrangement should enable the synthesis of novel and interesting terpene derivatives of type **4** (Scheme 2). No example of a method that affords such sulfur derivatives **4** without skeletal rearrangement to isobornyl structures has yet been reported.



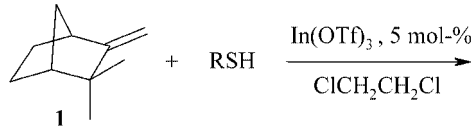
Scheme 2. Camphene functionalisation by sulfur nucleophiles without skeletal rearrangement.

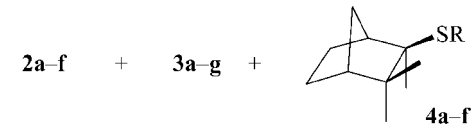
Preliminary tests on the functionalisation of the double bond of **1** in the presence of thioacids, with the goal of limiting its rearrangement, were carried out with several protic and Lewis acids as the catalysts. The results are summarised in Table 1.

The addition of thioacetic and thiobenzoic acids to **1** in the absence of catalyst (Entries 1, 2) through a light-induced radical-type reaction resulted in the selective formation of **3a** and **3b** with 88 and 100% selectivities, respectively (see Scheme 1 and Scheme 3).

The reaction between **1** and AcSH carried out in the presence of *p*-toluenesulfonic acid (5 mol-%) gave very low conversion (only 15% after 5 h at room temp., Entry 3) and no formation of the expected thioacetate **4a** was observed, with only the anti-Markovnikov-type adduct **3a** being obtained. The reaction run with a catalytic amount of triflic acid (CF_3SO_3H, Entry 4) produced total conversion of **1** in 20 min, but only compounds **2a** and **3a** were formed, in a 75:25 ratio.

When $InCl_3$ was used as the catalyst (5 mol-%) the reaction selectivity was strongly dependent on the reaction temperature. Thus, at reflux in dichloroethane (Entry 5) the main compound was the rearranged isobornane derivative **2a**, obtained with 77% selectivity after complete conversion of **1** in 0.5 h. At room temperature, the reaction took 5 h to go to completion and a mixture of **2a**, **3a** and **4a** was





a: R = COMe
b: R = COPh
c: R = n-C_8H_{17}
d: R = CH_2Ph
e: R = $CH_2C_6H_2$-2,4,6-Me_3
f: R = Ph
g: R = Et

Scheme 3. $In(OTf)_3$-catalysed addition of S-nucleophiles to camphene.

formed unselectively, though with the main compound being the desired **4a**, obtained with 56% selectivity (Entry 6). Lowering the reaction temperature to –10 °C did not result in an increase of selectivity towards **4a** (Entry 7). Similar trends were obtained with thiobenzoic acid (Entry 8).

Interestingly, however, when thioacetic acid was added to **1** in an $In(OTf)_3$-catalysed process (5 mol-%) a rapid reaction occurred at room temperature, with the formation of **4a** with 64% selectivity (Entry 9), while the reaction run at 0 °C afforded the desired thioacetate **4a** with 81% selectivity after 5 h (Entry 10). This last process constitutes the first example of a selective camphene functionalisation in an electrophilic medium without the classical camphene–isobornane rearrangement.

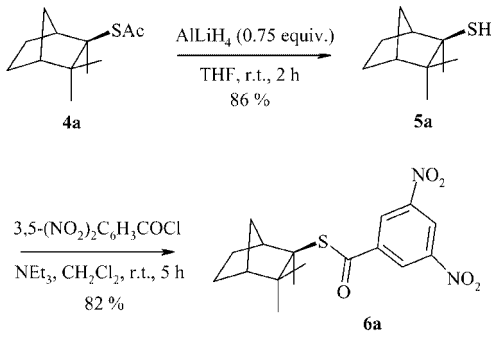
The relative configurations of thioacetates **2a** and **3a** were determined by ^1H NMR NOESY experiments and they were shown to be the *exo* stereoisomers in both cases. However, the NOESY experiments did not allow the relative configuration of **4a** to be determined, so this stereochemistry was determined by X-ray crystallography of the corresponding 3,5-dinitrothiobenzoate derivative. Thioacetate **4a** was reduced to the corresponding thiol **5a** in the presence of lithium aluminium hydride and was further

Table 1. Addition of thioacids to *rac*-**1** in the presence of several catalytic systems in 1,2-dichloroethane.

Entry	Sulfur nucleophile	Catalyst (5 mol-%)	Temperature reaction time	Yield of **2**+**3**+**4**	Selectivity[a] **2**:**3**:**4**
1	AcSH	–	20 °C, 12 h	88%	00:88:12
2	PhCOSH	–	20 °C, 4 h	90%	00:100:00
3	AcSH	*p*-$TolSO_3H$	20 °C, 5 h	15%	00:100:00
4	AcSH	TfOH	40 °C, 0.3 h	100%	75:25:00
5	AcSH	$InCl_3$	84 °C, 0.5 h	91%	77:21:2
6	AcSH	$InCl_3$	20 °C, 5 h	88%	23:21:56
7	AcSH	$InCl_3$	–10 °C, 12 h	90%	23:18:56
8	PhCOSH	$InCl_3$	20 °C, 4 h	84%	38:15:47
9	AcSH	$In(OTf)_3$	20 °C, 0.25 h	91%	30:6:64
10	AcSH	$In(OTf)_3$	0 °C, 5 h	90%	00:18:82

[a] The selectivity was calculated by GC.

thioesterified with 3,5-dinitrobenzoyl chloride to afford the 3,5-dinitrothiobenzoate **6a** in 82% yield (Scheme 4). After recrystallisation from ethanol, X-ray analysis confirmed the absence of rearrangement of the camphene structure and indicated the *exo* configuration for the sulfur substituent (Figure 1).



Scheme 4. Preparation of camphene derivative **6a** for crystallographic analysis.

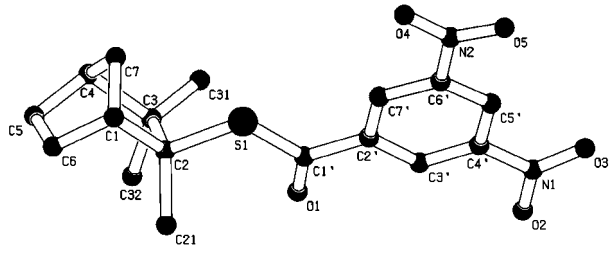


Figure 1. X-ray structure of **6a**.

The novel thio-functionalisation of **1** to afford the thio derivatives **4**, with suppression of the camphene–isobornane rearrangement (Scheme 3) through the use of In^{III} triflate as the catalyst (5 mol-%) in dichloroethane, generally at 0 °C, was extended to several thiols and thioacids. The results are summarised in Table 2.

Table 2. $In(OTf)_3$-catalysed (5 mol-%) *S*-functionalisation of camphene **1** in dichloroethane at 0 °C.[a]

Entry	RSH	Reaction time (h)	Yield of **2**+**3**+**4** (%)	% Selectivity for **4**[a]
1	CH_3COSH	5 h	90	**4a** 81
2	PhCOSH	6 h	90	**4b** 65
3	n-$C_8H_{17}SH$	9 h	81	**4c** 85
4	$PhCH_2SH$	9 h	83	**4d** 87
5	2,4,6-$(CH_3)_3C_6H_2CH_2SH$	9 h	40	**4e** 76
6	C_6H_5SH	9 h	79	**4f** 86
7	EtSH[b]	7 h	71	**4g** 91

[a] The selectivity for compounds **4** is given in % for a mixture of isomers **2** and **3** and was calculated by GC. [b] The reaction was run at –8 °C.

Addition of thiobenzoate to **1** at room temperature resulted in **4b** with a selectivity of 55%; at 0 °C the selectivity towards **4b** was raised to 65% (Entry 2).

The addition of *n*-octanethiol to **1** at 84 °C (1,2-dichloroethane at reflux) resulted in the formation of sulfide **2c** with 85% selectivity involving the camphene–isobornane isomerisation. This result may be compared with the reversed selectivity of 85% towards unrearranged **4c** obtained at 0 °C (Entry 3).

With phenylmethanethiol the $In(OTf)_3$-catalysed reaction run in at reflux in dichloroethane afforded isomerised **2d** with 92% selectivity. At 0 °C, in contrast, the desired unrearranged **4d** was formed with 87% selectivity (Entry 4). At room temperature the **2**/**3**/**4** isomer ratio was 31:3:66. An analogous highly substituted benzyl sulfide addition to **1** occurred with 76% selectivity when run at 0 °C (Entry 5).

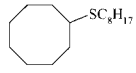
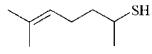
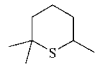
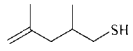
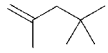
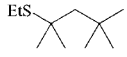
The adduct with benzenethiol afforded the expected unrearranged sulfide **4f** with a selectivity of 86% (Entry 6).

In the EtSH additions to **1** run at room temperature or at 40 °C, the selectivities towards **2f** were 87% and 95%, respectively. However, a reversed selectivity of 91% towards **4f** was attained in the reaction run at –8 °C (Entry 7).

In the examples of thiol additions to **1**, the desired unrearranged sulfides **4** were obtained in all cases, with good selectivities of 85–91%, in reactions run from 0 °C to –8 °C for 5 to 9 h. The rearranged isobornane sulfides **2** were obtained in less than 10% yields. For the addition of thioacids, the selectivities were in the range of 65 to 81%.

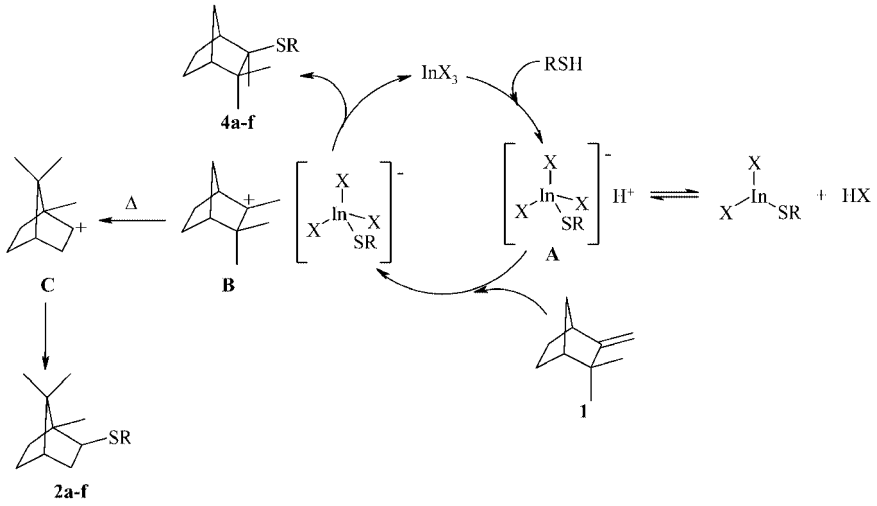
Besides the addition to camphene, $In(OTf)_3$ was also an efficient catalyst for the addition of sulfur nucleophiles to olefins.[9b] Internal di- and trisubstituted olefins afford good yields of hydrothiolation products, as summarised in Table 3 (Entries 1, 2) both in intra- and in intermolecular reactions. Terminally disubstituted olefins were also efficient, as shown in Entries 3 and 4.

Table 3. $In(OTf)_3$-catalysed (5 mol-%) *S*-functionalisation of olefins.

Entry	Olefin	RSH	Reaction conditions	Product (% yield)
1	cyclooctene	n-$C_8H_{17}SH$	20 h, reflux $MeNO_2$	 (81)
2			16 h, reflux CH_2Cl_2	 (83)
3			1.5 h, reflux CH_2Cl_2	 (91)
4		EtSH	3 h, reflux CH_2Cl_2	 (87)

Proposed Mechanism

From a mechanistic point of view, our results suggest that In^{III} triflate is an efficient catalyst for the activation of thiols and thioacids through the formation of indium thiolate derivatives of type **A** (Scheme 5). The released proton may undergo an electrophilic attack on the camphene double bond in a Markovnikov-type process, to afford **B**. Thanks to the mild conditions under which the reaction is run, the carbocation intermediate species **B** is not re-



Scheme 5. Proposed catalytic cycle.

arranged (or is only partially rearranged) to carbocation intermediate **C**. This allows the reaction with the indium thiolate derivative to form structures **4** selectively. At higher reaction temperatures, carbocation **B** undergoes a rearrangement to the isobornane intermediate **C** with further S-functionalisation to give **2**. Derivatives **2** are obtained under classical electrophilic conditions, normally in the presence of an excess of protic or Lewis acid at room temperature or higher. In agreement with literature data, we were also able to observe that in reactions catalysed by In^{III} run at or above 40 °C, the sulfide addition to **1** was directed towards the formation of **2** with high selectivities.

Potential applications of new compounds **4** lie in the field of flavour and fragrance chemistry.[10–12,18] The strong impact of volatile sulfur compounds is due to the generally very low threshold levels of these derivatives, in particular of thiols and sulfides.[10] Preliminary olfactory tests carried out with new compound **4a** indicated that it presented a camphor-like persistent odour.[19]

Conclusions

In conclusion, In^{III} triflate has been shown to be an active and efficient catalyst for the regio- and stereoselective addition of thioacids and thiols to camphene with selectivities of 65–91%, with suppression of the classical camphene–isobornane rearrangement. The *exo*-Markovnikov-type products **4** were obtained for the first time with good yields and selectivities, in reactions run at 0 °C or above. At higher temperatures, high regioselectivities towards the isomerised isobornyl thio-functionalised structures **2** were obtained. The access to new compounds, the use of a catalytic amount of $In(OTf)_3$ under mild conditions, without the need for an additional ligand, and the potential to recover and recycle the catalyst[20] constitute further advantages of this new catalytic reaction.

Experimental Section

General Remarks: All chemicals were purchased from Aldrich or Acros and were used without further purification. Solvents were dried and distilled by classical procedures and stored on molecular sieves (4 Å). X-ray analyses were performed on a Bruker Smart-Apex diffractometer (detector CCD) at the University of Aix-Marseille, France.

General Procedure: The thioacid or the thiol (5 mmol) was added to a mixture of camphene **1** (5 mmol), and $In(OTf)_3$ (0.25 mmol) in dichloroethane (5 mL) and the mixture was stirred at the desired temperature. The progress of the reaction was monitored by GC analysis. On completion of the reaction, the mixture was quenched with HCl (0.1 M) and extracted with Et_2O. The organic layer was washed with saturated aqueous $NaHCO_3$ and dried with $MgSO_4$, the solvent was evaporated, and the products were purified by flash chromatography on silica gel with pentane/Et_2O as the eluents (95:5 to 90:10 for thioacetates and 100:0 to 95:5 for sulfides) and analysed by ^1H and ^{13}C NMR and mass spectrometry. NMR spectra were recorded in $CDCl_3$ at room temperature.

See Scheme 1 for numbering of compounds of type **2** and **3** for NMR assignments and Scheme 2 for numbering of compounds **4**.

1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl *exo*-Thioacetate (2a): Colourless liquid, 815 mg, 77%. ^1H NMR: δ = 3.6 (dd, J = 9.5, 5.6 Hz, H^2), 2.3 (s, 3 $H^{2'}$), 1.9 (dd, J = 12.7, 9.5 Hz, 1 H^3), 1.8–1.6 (m, 1 H^6, 1 H^5, 1 H^4 and 1 H^3), 1.5–1.4 (m, 1 H^6), 1.3–1.2 (m, 1 H^5), 0.85 and 0.83 (s, 6 $H^{1''}$ and 3 $H^{2''}$) ppm. ^{13}C NMR: δ = 195.9 ($C^{1'}$), 49.5 (C^2), 48.9 (C^1), 47.4 (C^7), 45.7 (C^4), 38.9 (C^3), 37.8 (C^5), 30.3 ($C^{2'}$), 27.2 (C^6), 20.0–19.8–13.2 (2 $C^{1''}$ and C^2) ppm. GC-MS (EI): m/z (%) = 212(3) $[M]^{+\cdot}$, 169 (39), 136 (6), 110 (15), 95 (100), 81 (26), 55 (25).

(3,3-Dimethylbicyclo[2.2.1]hept-2-yl)methyl *exo*-Thioacetate (3a): Colourless liquid, 932 mg, 88%. ^1H NMR: δ = 2.9 (dd, J = 5.3, 2.7 Hz, 1 H^1), 2.8 (dd, J = 5.3, 4.0 Hz, 1 H^1), 2.3 (s, 3 $H^{3'}$), 2.2 (s, H^4), 1.7 (s, H^1), 1.6–1.5 (m, H^2, 1 H^5 and 1 H^7), 1.4–1.2 (m, 2 H^6 and 1 H^7), 1.1 ("d", 1 H^5), 1.0 (s, 3 $H^{1''}$), 0.9 (s, 3 H^1) ppm. ^{13}C NMR: δ = 195.9 ($C^{2'}$), 49.7 (C^2), 49.2 (C^4), 41.7 (C^1), 37.6 (C^3), 36.8 (C^5), 32.1 (1 $C^{1''}$), 30.6 ($C^{3'}$), 27.5 ($C^{1'}$), 24.5 (C^7), 21.1 (1 $C^{1''}$), 20.0 (C^6) ppm. GC-MS (EI): m/z (%) = 212 (7) $[M]^{+\cdot}$, 169 (8), 137 (55), 121 (29), 107 (15), 93 (54), 81 (100), 67 (80), 55 (54).

2,3,3-Trimethylbicyclo[2.2.1]hept-2-yl *exo*-Thioacetate (4a): Colourless liquid, 773 mg, 73%. ^{1}H NMR: δ = 2.4 ("s", H^4), 2.2 (s, 3 H$^{2'}$), 2.1–2.0 (m, 1 H^7), 1.8 ("s", H^1), 1.7–1.6 (m, 1 H^7), 1.6 (s, 3 H$^{1''}$), 1.5–1.1 (m, 2 H^5 and 2 H^6), 1.1 (s, 3 H$^{2''}$), 1.0 (s, 3 H$^{2''}$) ppm. ^{13}C NMR: δ = 197.2 (C$^{1'}$), 64.5 (C^2), 50.9 (C^1), 49.4 (C^4), 44.5 (C^3), 35.8 (C^7), 31.2 (C$^{2'}$), 28.9 (1 C$^{2''}$), 23.4–23.3 (C^5 and C^6), 22.8 (1 C$^{2''}$), 20.1 (C$^{1''}$) ppm. GC-MS (EI): *m*/*z* (%) = 212 (15) [M]$^{+\cdot}$, 169 (100), 137 (29), 109 (28), 93 (53), 81 (66), 67 (58), 59 (35). $C_{12}H_{20}OS$ (212.35): calcd. C 67.87, H 9.49, S 15.10; found C 66.56, H 9.23, S 15.02.

2,3,3-Trimethylbicyclo[2.2.1]hept-2-yl *exo*-3,5-Dinitrothiobenzoate (6a): Compound **4a** (3.63 mmol, 770 mg) was dissolved in anhydrous THF (10 mL) and treated with $LiAlH_4$ (0.75 equiv.) at room temperature for 2 h. After classical workup, the obtained white solid was dissolved in dichloromethane. Triethylamine was added (1.3 equiv.), followed by 3,5-dinitrobenzoyl chloride (1.2 equiv.), and the mixture was stirred at room temperature for 5 h. The crude mixture was dissolved in dichloromethane and successively washed with aqueous HCl (1 M) and saturated aqueous $NaHCO_3$. The organic phase was dried with $MgSO_4$ and concentrated under reduced pressure to give a white solid. Recrystallization from ethanol afforded white crystals (1.083 g, 82%). ^{1}H NMR: δ = 9.2–9.1 (m, H$^{5'}$), 9.0–8.9 (m, 2 H$^{3'}$), 2.5 (s, H^4), 2.1–2.0 (m, 1 H^7), 1.8 (s, H^1), 1.8 (s, 3 H$^{1''}$), 1.7–1.6 (m, 1 H^7), 1.5–1.1 (m, 2 H^5 and 2 H^6), 1.2 (s, 3 H$^{2''}$), 1.1 (s, 3 H$^{2''}$) ppm. ^{13}C NMR: δ = 189.3 (C$^{1'}$), 149.0 (2 C$^{4'}$), 141.7 (C$^{2'}$), 127.2 (2 C$^{3'}$), 122.0 (C$^{5'}$), 68.1 (C^2), 51.5 (C^1), 50.3 (C^4), 45.6 (C^3), 36.4 (C^7), 29.7 (1 C$^{2''}$), 24.0–23.6 (C^5 and C^6), 23.2 (1 C$^{2''}$), 20.5 (C$^{1''}$) ppm. The X-ray structure is shown in Figure 1. CCDC-636096 contains the supplementary crystallographic data for **6a**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl *exo*-Thiobenzoate (2b): Colourless liquid, 1.109 g, 81%. ^{1}H NMR: δ = 8.0–7.9 (m, 2 H$^{3'}$), 7.6–7.3 (m, 2 H$^{4'}$ and H$^{5'}$), 3.9 (dd, *J* = 9.2, 5.9 Hz, H^2), 2.6–2.5 (m, 1 H^4), 1.9–1.6 (m, 1 H^6, 1 H^5 and 2 H^3), 1.5–1.2 (m, 1 H^6 and 1 H^5), 0.95 (s, 3 H$^{1''}$), 0.93 (s, 3 H$^{1''}$), 0.86 (s, 3 H$^{2''}$) ppm. ^{13}C NMR: δ = 192.6 (C$^{1'}$), 133.1 (C$^{5'}$), 128.9 (2 C$^{4'}$), 128.5 (C$^{2'}$), 127.6 (2 C$^{3'}$), 50.0 (C^2), 49.7 (C^1), 48.0 (C^7), 46.3 (C^4), 39.5 (C^3), 38.4 (C^5), 27.7 (C^6), 20.6–20.3–13.7 (2 C$^{1''}$ and C$^{2''}$) ppm. GC-MS (EI): *m*/*z* (%) = 274 (2) [M]$^{+\cdot}$, 169 (25), 105 (100), 95 (32), 81 (20), 77 (44), 55 (9).

(3,3-Dimethylbicyclo[2.2.1]hept-2-yl)methyl *exo*-Thiobenzoate (3b): Colourless liquid, 151 mg, 11%. ^{1}H NMR: δ = 8.0–7.9 (m, 2 H$^{4'}$), 7.6–7.3 (m, 2 H$^{5'}$ and H$^{6'}$), 3.1 (dd, *J* = 5.2, 2.7 Hz, 1 H$^{1'}$), 3.0 (dd, *J* = 5.2, 4.0 Hz, 1 H$^{1'}$), 2.3 (s, H^4), 1.8 (s, H^1), 1.7–1.6 (m, H^2, 1 H^5 and 1 H^7), 1.4–1.1 (m, 2 H^6, 1 H^5 and 1 H^7), 1.0 (s, 3 H$^{1''}$), 0.9 (s, 3 H$^{1''}$) ppm. ^{13}C NMR: δ = 192.6 (C$^{2'}$), 133.1 (C$^{6'}$), 128.9 (2 C$^{5'}$), 128.5 (C$^{3'}$), 127.6 (2 C$^{4'}$), 50.2 (C^2), 49.7 (C^4), 42.3 (C^1), 37.9 (C^3), 37.3 (C^5), 32.6 (1 C$^{1''}$), 28.0 (C$^{1'}$), 25.0 (C^7), 21.6 (1 C$^{1''}$), 20.5 (C^6) ppm. GC-MS (EI): *m*/*z* (%) = 274 (0.2) [M]$^{+\cdot}$, 137 (58), 105 (100), 93 (21), 81 (30), 77 (75), 69 (12), 55 (14).

2,3,3-Trimethylbicyclo[2.2.1]hept-2-yl *exo*-Thiobenzoate (4b): Colourless liquid, 808 mg, 59%. ^{1}H NMR: δ = 8.0–7.9 (m, 2 H$^{3'}$), 7.6–7.3 (m, 2 H$^{4'}$ and H$^{5'}$), 2.3 ("s", H^4), 2.1–2.0 (m, 1 H^7), 1.8 ("s", H^1), 1.7 (s, 3 H$^{1''}$), 1.7–1.6 (m, 1 H^7), 1.5–1.1 (m, 2 H^5 and 2 H^6), 1.2 (s, 3 H$^{2''}$), 1.1 (s, 3 H$^{2''}$) ppm. ^{13}C NMR: δ = 194.0 (C$^{1'}$), 133.1 (C$^{5'}$), 129.4 (C$^{2'}$), 128.9 (2 C$^{4'}$), 127.6 (2 C$^{3'}$), 65.1 (C^2), 51.5 (C^1), 50.3 (C^4), 45.4 (C^3), 36.2 (C^7), 29.6 (1 C$^{2''}$), 24.0–23.6 (C^5 and C^6), 23.2 (1 C$^{2''}$), 20.7 (C$^{1''}$) ppm. GC-MS (EI): *m*/*z* (%) = 274 (0.5) [M]$^{+\cdot}$, 169 (46), 137 (41), 109 (17), 105 (100), 93 (29), 81 (39), 77 (55), 67 (20), 55 (11).

Octyl (1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl) *exo*-Sulfide (2c): Colourless liquid, 1.198 g, 85%. ^{1}H NMR: δ = 2.6 (dd, *J* = 8.2, 6.7 Hz, H^2), 2.5–2.4 (m, 2 H$^{1'}$), 1.8–1.1 (m, 7 H$^{3–6}$ and 12 H$^{2'–7'}$), 0.92 (s, 3 H$^{1''}$), 0.89 (s, 3 H$^{1''}$), 0.8 (t, *J* = 6.8 Hz, 3 H$^{8'}$), 0.7 (s, 3 H$^{2''}$) ppm. ^{13}C NMR: δ = 55.1 (C^4), 49.7 (C^1), 47.7 (C^7), 46.3 (C^2), 41.4 (C^6), 38.9 (C^3), 35.3–32.2–30.4–29.6–29.5–23.0 (7C$^{1'–7'}$), 27.8 (C^5), 20.8–20.6 (2 C$^{1''}$), 14.5 (C$^{2''}$), 14.3 (C$^{8'}$) ppm. GC-MS (EI): *m*/*z* (%) = 282 (0.4) [M]$^{+\cdot}$, 111 (100), 105 (94), 95 (11), 81 (8), 77 (55), 69 (77), 55 (38).

Octyl (2,3,3-Trimethylbicyclo[2.2.1]hept-2-yl) *exo*-Sulfide (4c): Colourless liquid, 973 mg, 69%. ^{1}H NMR: δ = 2.6–2.4 (m, 2 H$^{1'}$), 2.4–2.2 (m, 1 H^7), 2.2 ("s", H^4), 1.8–1.5 (m, H^1, 1 H^5, 1 H^6, and 1 H^7), 1.5–1.0 (m, 1 H^5, 1 H^6 and 12 H$^{2'–7'}$), 1.4 (s, 3 H$^{1''}$), 1.2 (s, 3 H$^{2''}$), 1.0 (s, 3 H$^{2''}$), 0.9 (t, *J* = 6.8 Hz, 3 H$^{8'}$) ppm. ^{13}C NMR: δ = 58.3 (C^2), 51.7 (C^1), 49.9 (C^4), 41.4 (C^3), 36.2 (C^7), 32.2–30.6–30.2–29.8–29.7–29.6–29.4 (7C$^{1'–7'}$), 28.6 (1 C$^{2''}$), 24.5–24.0 (C^5 and C^6), 23.8 (1 C$^{2''}$), 22.4 (C$^{1''}$), 14.5 (C$^{8'}$) ppm. GC-MS (EI): *m*/*z* (%) = 282 (0.2) [M]$^{+\cdot}$, 213 (12), 153 (24), 111 (100), 83 (13), 81 (26), 77 (5), 69 (9), 55 (12).

Benzyl (1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl) *exo*-Sulfide (2d): Colourless liquid, 1.196 g, 92%. ^{1}H NMR: δ = 7.3–7.1 (m, 5 H$^{3'–5'}$), 3.5 (s, 2 H$^{1'}$), 2.5 (dd, *J* = 7.7, 7.4 Hz, H^2), 1.7–1.5 (m, 2 H^3, H^4, 1 H^5 and 1 H^6), 1.1–0.9 (m, 1 H^5 and 1 H^6), 0.9 (s, 6 H$^{1''}$), 0.7 (s, 3 H$^{2''}$) ppm. ^{13}C NMR: δ = 139.3 (C$^{2'}$), 129.4 (2 C$^{3'}$), 128.8 (2 C$^{4'}$), 127.2 (C$^{5'}$), 53.8 (C^4), 49.8 (C^1), 47.8 (C^7), 46.3 (C^2), 41.0–39.2–38.8 (C$^{1'}$, C^3 and C^6), 27.7 (C^5), 20.9–20.6 (2 C$^{1''}$), 14.3 (C$^{2''}$) ppm. GC-MS (EI): *m*/*z* (%) = 260 (12) [M]$^{+\cdot}$, 169 (55), 135 (15), 109 (16), 95 (24), 91 (100), 81 (32), 77 (10), 67 (15), 55 (12).

Benzyl (2,3,3-Trimethylbicyclo[2.2.1]hept-2-yl) *exo*-Sulfide (4d): Colourless liquid, 936 mg, 72%. ^{1}H NMR: δ = 7.4–7.1 (m, 5 H$^{3'–5'}$), 3.6 (s, 2 H$^{1'}$), 2.4–2.2 (m, H^4 and 1 H^7), 1.7–1.4 (m, H^1, 1 H^5, and 1 H^7), 1.4 (s, 3 H$^{1''}$), 1.4–1.0 (m, 2 H^6 and 1 H^5), 1.1 (s, 3 H$^{2''}$), 0.9 (s, 3 H$^{2''}$) ppm. ^{13}C NMR: δ = 138.9 (C$^{2'}$), 129.5 (2 C$^{3'}$), 128.9 (2 C$^{4'}$), 127.2 (C$^{5'}$), 59.4 (C^2), 51.7 (C^1), 49.9 (C^4), 44.5 (C^3), 38.9 (C$^{1'}$), 36.3 (C^7), 28.4 (1 C$^{2''}$), 24.5–24.1 (C^5 and C^6), 22.6 (1 C$^{2''}$), 22.6 (C$^{1''}$) ppm. GC-MS (EI): *m*/*z* (%) = 260 (1) [M]$^{+\cdot}$, 207 (2), 169 (100), 137 (13), 109 (28), 93 (45), 81 (41), 77 (13), 67 (23), 55 (13).

2,4,6-Trimethylbenzyl (2,3,3-Trimethylbicyclo[2.2.1]hept-2-yl) *exo*-Sulfide (4e): Colourless liquid, 453 mg, 30%. ^{1}H NMR: δ = 6.8 (s, 2 H$^{4'}$), 3.6 (s, 2 H$^{1'}$), 2.4 (s, 6 H$^{3''}$), 2.2 (s, 3 H$^{5''}$), 2.4–2.2 (m, H^4 and 1 H^7), 1.7–1.4 (m, H^1, 1 H^5, and 1 H^7), 1.5 (s, 3 H$^{1''}$), 1.4–1.0 (m, 2 H^6 and 1 H^5), 1.2 (s, 3 H$^{2''}$), 1.0 (s, 3 H$^{2''}$) ppm. ^{13}C NMR: δ = 136.1 (C$^{2'}$), 135.3 (2 C$^{3'}$), 129.9 (C$^{5'}$), 128.1 (2 C$^{4'}$), 57.3 (C^2), 50.3 (C^1), 48.2 (C^4), 43.0 (C^3), 35.0 (C$^{1'}$), 28.2 (C^7), 26.9 (1 C$^{2''}$), 23.2–23.0 (C^5 and C^6), 22.6 (1 C$^{2''}$), 20.7 (C$^{1''}$), 20.0 (C$^{5''}$), 18.5 (2 C$^{3''}$) ppm. GC-MS (EI): *m*/*z* (%) = 302 (0.4) [M]$^{+\cdot}$, 170 (10), 169 (90), 133 (100), 121 (8), 117 (10), 109 (14), 95 (8), 81 (22), 67 (10), 41 (11).

Phenyl (2,3,3-Trimethylbicyclo[2.2.1]hept-2-yl) *exo*-Sulfide (4f): Colourless liquid, 836 mg, 68%. ^{1}H NMR: δ = 7.4 (m, 2 H$^{3'}$), 7.3–7.1 (m, 3 H$^{2'–4'}$), 2.5 (m, H^4), 2.2 (m, 1 H^7), 1.7–1.4 (m, H^1, 1 H^5, and 1 H^7), 1.2 (s, 3 H$^{1''}$), 1.4–1.0 (m, 2 H^6 and 1 H^5), 1.1 (s, 3 H$^{2''}$), 0.9 (s, 3 H$^{2''}$) ppm. ^{13}C NMR: δ = 158.6 (C$^{1'}$), 138.3 (2 C$^{2'}$), 128.8 (C$^{4'}$), 128.5 (2 C$^{3'}$), 62.5 (C^2), 52.1 (C^1), 49.7 (C^4), 44.4 (C^3), 36.0 (C^7), 28.4 (1 C$^{2''}$), 25.9 (C^5 and C^6), 25.8 (1 C$^{2''}$), 22.9 (C$^{1''}$) ppm. GC-MS (EI): *m*/*z* (%) = 246 (3) [M]$^{+\cdot}$, 137 (10), 109 (15), 95 (20), 81 (100), 77 (18), 69 (21), 67 (26), 55 (12).

Ethyl (1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl) *exo*-Sulfide (2g): Colourless liquid, 900 mg, 91%. ^{1}H NMR: δ = 2.6 (dd, *J* = 8.3, 6.7 Hz, H^2), 2.5 (q, *J* = 7.5 Hz, 2 H$^{1'}$), 1.9–1.7 (m, 2 H^3), 1.7–1.5

(m, 1 H^6 and 1 H^5), 1.2 (t, J = 7.5 Hz, 3 $H^{2'}$), 1.1–1.0 (m, 1 H^6 and 1 H^5), 0.92 (s, 3 $H^{1''}$), 0.89 (s, 3 $H^{1''}$), 0.7 (s, 3 $H^{2''}$) ppm. ^{13}C NMR: δ = 54.7 (C^4), 49.7 (C^1), 47.7 (C^7), 46.3 (C^2), 41.4 (C^6), 38.9 (C^3), 29.0 ($C^{1'}$), 27.8 (C^5), 20.8–20.6 (2 $C^{1''}$), 15.4 ($C^{2''}$), 14.3 ($C^{2'}$) ppm. GC-MS (EI): *m*/*z* (%) = 198 (32) $[M]^{+\cdot}$, 169 (34), 136 (23), 108 (21), 95 (87), 91 (19), 88 (100), 81 (55), 77 (17), 67 (26), 55 (23).

Ethyl (2,3,3-Trimethylbicyclo[2.2.1]hept-2-yl) *exo*-Sulfide (4g): Colourless liquid, 643 mg, 65%. ^1H NMR: δ = 2.6–2.4 (q, J = 6.8 Hz, 2 $H^{1'}$), 2.4–2.2 (m, 1 H^7), 2.3 ("s", H^4), 1.9–1.5 (m, H^1, 1 H^5, 1 H^6, and 1 H^7), 1.5–1.0 (m, 1 H^5, 1 H^6), 1.4 (s, 3 $H^{1''}$), 1.2 (s, 3 $H^{2''}$), 1.1 (s, 3 $H^{2''}$), 0.9 (t, J = 6.8 Hz, 3 $H^{2'}$) ppm. ^{13}C NMR: δ = 58.1 (C^2), 51.3 (C^1), 48.9 (C^4), 41.1 (C^3), 36.2 (C^7), 29.8 ($C^{1'}$), 28.1 (1 $C^{2''}$), 24.6–23.1 (C^5 and C^6), 23.8 (1 $C^{2''}$), 22.4 ($C^{1''}$), 15.1 ($C^{2'}$) ppm. GC-MS (EI): *m*/*z* (%) = 198 (8) $[M]^{+\cdot}$, 169 (100), 137 (46), 109 (31), 93 (55), 81 (95), 77 (19), 67 (42), 55 (27).

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