

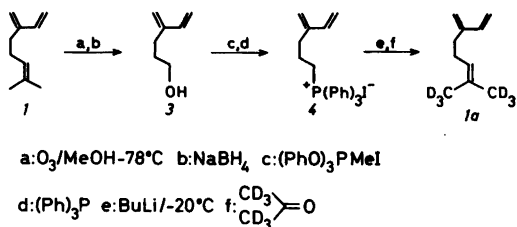
## Facile Syntheses of Specifically Deuterated $\beta$ -Myrcene and $\alpha$ -Pinene

YNGVE STENSTRØM and LARS SKATTEBØL

Kjemisk Institutt, Universitetet i Oslo, Oslo 3, Norway

Recent work expresses a growing interest in the biosynthetic origin of insect pheromones. There are some indications that *Dendroctonus* and *Ips* species of bark beetles use terpenes present in the host plant, as starting material for syntheses of pheromone components.<sup>1-5</sup> Because of our interest in the biosynthesis of the *Ips typographus* pheromone<sup>6</sup> we needed specifically deuterium-labelled  $\beta$ -myrcene (**1**) and  $\alpha$ -pinene (**2**), and the present report describes convenient syntheses of these compounds.

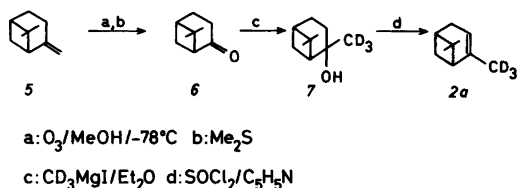
In Scheme 1 the route to the hexadeuterated  $\beta$ -myrcene **1a** is shown. Ozonolysis of **1** followed by



Scheme 1.

reduction gave a 63% yield of the unstable alcohol **3**<sup>7</sup> which was subsequently converted *via* the iodide to the phosphonium salt **4**. A Wittig reaction on **4** using butyllithium as base and hexadeuterioacetone afforded **1a** in 60% yield, and with an overall yield of 18% based on **1**. The structure of **1a** was determined spectroscopically. The C–D stretching vibrations appeared as expected at 2240–2080  $cm^{-1}$ . The methyl resonances at  $\delta$  1.60 and 1.68 present in the  $^1H$  NMR spectrum of compound **1** are absent in that of **1a**. Due to deuterium carbon coupling the three carbon resonances of the isopropylidene group are not strong enough to be observed in the  $^{13}C$  NMR spectrum. Apart from the expected molecular ion at  $m/e$  142 in the mass spectrum, it is worth remarking that fragment  $m/e$  41 derives exclusively from the isopropylidene part of the molecule in contrast to a previous suggestion.<sup>8</sup>

In Scheme 2 the route to trideuterated  $\alpha$ -pinene **2a** is depicted. Ozonolysis of  $\beta$ -pinene **5** with an excess of ozone gave the ketone **6**<sup>9</sup> in 78% yield. The reaction of **6** with methylmagnesium halide



Scheme 2.

had previously been carried out using an excess Grignard reagent,<sup>10-12</sup> which in our case contained the deuterium label. By varying the amount of ketone relative to trideuteriomethylmagnesium iodide was obtained a maximum yield of 71% of the alcohol **7** with a molar ratio of 1.23. Dehydration of the alcohol was a sensitive step because of its propensity to carbenium ion rearrangements.<sup>13,14</sup> The presence of acid must be avoided; even the use of catalytic amounts of anilinium hydrobromide resulted in a complex mixture, which also was the result after treatment with phosphorus oxychloride in pyridine.<sup>15</sup> However, the use of thoroughly purified thionyl chloride in pyridine<sup>16</sup> gave the desired product in 75% yield and the overall yield of trideuterio- $\alpha$ -pinene **2a** was 42% based on **2**.

In the  $^1H$  NMR spectrum of **2a** the quadruplet at  $\delta$  1.65 due to the vinylic methyl group is absent and the  $^{13}C$  NMR spectrum is also practically identical with that of **2** except for the absence of the resonance at  $\delta$  20.7. The mass spectrum is in agreement with structure **2a** exhibiting a molecular ion at  $m/e$  139.

**Experimental. General.** Most of the instruments employed have been described elsewhere.<sup>17</sup> The  $^{13}C$  NMR spectra were recorded on a Jeol, JNM-FX60 Fourier transform spectrometer. The MS spectra are recorded for peaks,  $m/e \geq 39$ , with relative intensities of more than 10% except for the molecular ion.

**Starting material.** Commercially available  $\beta$ -myrcene was distilled prior to use on an efficient column to give at least 99% pure (GLC)  $\beta$ -myrcene. Commercially available  $\beta$ -pinene was also distilled prior to use on the same column to give at least 98% pure (GLC)  $\beta$ -isomer.

**4-Methylene-5-hexen-1-ol 3.** Freshly distilled  $\beta$ -myrcene **1** (10.00 g, 73.4 mmol) was dissolved in 100 ml of dry methanol and cooled to  $-78^\circ C$ . Ozone (59.0 mmol) was bubbled through the solution and after flushing with  $N_2$ , 1.6 g (42.3 mmol) of  $NaBH_4$  in 40 ml methanol–water (1:1) was added at  $0^\circ C$ . After 2 h at room temperature most of the solvent was removed and the residue extracted with ether. The ether was washed three times with brine, dried and evaporated. The

residue was short path distilled (82 °C/20 mmHg) to give 5.22 g (63 %) of 3,  $n_D^{23}$  1.4784 (lit.<sup>7</sup>  $n_D^{20}$  1.4790). The IR- and <sup>1</sup>H NMR-spectra were consistent with published data.<sup>7</sup>

**4-Methylene-5-hexenyl triphenylphosphonium iodide 4.** 6-Iodo-3-methylene-1-hexene<sup>7</sup> was prepared in 63 % yield from 3 and converted immediately with triphenylphosphine to 4, m.p. 144–145 °C (Lit.<sup>7</sup> 146 °C) in 77 % yield.

**Hexadeuterated  $\beta$ -myrcene 1b.** Finely powdered 5 (9.01 g, 18.6 mmol) was suspended in dry THF at –20 °C and 12.0 ml (1.63 N, 19.6 mmol) of BuLi in hexane was added. After 45 min the temperature was lowered to –60 °C and 1.19 g (18.6 mmol) of hexadeuterioacetone was added. After 4 h at room temperature the solution was diluted with light petroleum (b.p. 40–60 °C) and a mixture of ice and water was added. The organic layer was separated, dried and most of the solvent was removed. Precipitated Ph<sub>3</sub>PO was filtered off and the residue was chromatographed on 120 g alumina (basic, activity II) with light petroleum (b.p. 40–60 °C). After removal of the solvent pure (GLC) 1b remained. Yield 1.65 g (62 %),  $n_D^{21}$  1.4732. <sup>1</sup>H NMR (CCl<sub>4</sub>):  $\delta$  2.00–2.18 (4H,m), 4.78–5.28 (5H,m), 5.98–6.52 (1H,q). <sup>13</sup>C NMR (CCl<sub>4</sub>):  $\delta$  26.5 (t), 31.3 (t), 112.6 (t), 115.5 (t), 124.4 (d), 138.9 (d), 145.7 (s). IR (film): 2250–2080 (C–D), 1605 (C=C), 1060, 1005, 905 cm<sup>-1</sup>. MS [70 eV, *m/e* (% rel.int.)]: 142 (M<sup>+</sup>, 7), 93 (100), 92 (10), 80 (11), 75 (81), 45 (32), 44 (44), 43 (21), 41 (12).

**6,6-Dimethylbicyclo[3.1.1]heptan-2-one, (6)** was synthesized using a slight modification of a published procedure.<sup>9</sup> Freshly distilled  $\beta$ -pinene (30.2 g, 221 mmol) in 125 ml dry methanol was treated with 270 mmol ozone at –78 °C. The solution was flushed with N<sub>2</sub> and allowed to attain 0 °C. Dimethylsulfide (24.0 ml, 330 mmol) was added and the solution was left at room temperature overnight. Water was added and the solution was extracted with light petroleum (b.p. 40–60 °C). The organic phase was dried (MgSO<sub>4</sub>) and evaporated. The residue was distilled to give 23.0 g (78 %) of 6, b.p. 50–52 °C (2 mm Hg),  $n_D^{20}$  1.4828 (lit.<sup>9</sup> 50–51 °C (2 mm Hg),  $n_D^{20}$  1.4802). Spectral data were consistent with those in the literature.<sup>8</sup>

**$\alpha$ -Pinene-10d<sub>3</sub> (2b).** Magnesium (0.17 g, 7.0 mmol) in 10 ml of dry ether together with 1.01 g (6.9 mmol) CD<sub>3</sub>I was refluxed for 1.5 h and stirred for another 23 h. The ketone 6 (1.2 g, 8.7 mmol) in 5 ml of dry ether was added at 0–5 °C and the solution was stirred for another 3 h. After the usual workup a residue of 1.3 g consisting of 59 % of the alcohol and 41 % of the ketone (GLC)<sup>1</sup>H NMR remained. Without further purification the mixture was dissolved in 8.0 ml of dry pyridine, cooled to 0 °C and 1.34 ml (2.22 g, 18.6 mmol) of pure SOCl<sub>2</sub> was added. After 45 min of stirring small

pieces of ice were added to destroy excess SOCl<sub>2</sub>. Water was added and the mixture extracted with ether. The ether solution was washed three times with 0.1 N HCl, 10 % Na<sub>2</sub>CO<sub>3</sub> and water and dried (MgSO<sub>4</sub>). Evaporation of the ether gave a residue which was distilled to give 0.45 g 2b (48 % from CD<sub>3</sub>I) of 2b. Two impurities were observed (GLC) of which 2 % was  $\beta$ -pinene and 2 % was an unidentified compound. <sup>1</sup>H NMR (CCl<sub>4</sub>):  $\delta$  0.83 (3H,s), 1.08 (1H,d,J 8 Hz), 1.27 (3H,s), 1.77–2.53 (5H,m), 5.17 (1H,m). <sup>13</sup>C NMR (CCl<sub>4</sub>):  $\delta$  20.7 (q), 26.3 (q), 31.0 (t), 31.2 (t), 37.8 (s), 40.5 (d), 46.8 (d), 115.9 (d), 143.7 (s). MS [70 eV (% rel.int.)]: 139 (M<sup>+</sup>, 12), 124 (13), 96 (100), 95 (44), 94 (14), 93 (19), 79 (15), 77 (14), 43 (10), 41 (15), 39 (11).

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