

## Absolute Configuration and Odour Analysis of the Enantiomeric *tert.*-Butylbicyclo[4.4.0]decan-3-ols

Gerhard Buchbauer<sup>a,\*</sup>, Helmut Spreitzer<sup>a</sup>, Helene Swatonek<sup>a,1</sup>,  
and Peter Wolschann<sup>b</sup>

<sup>a</sup> Institute of Pharmaceutical Chemistry of the University,  
A-1090 Vienna, Währingerstraße 10, Austria

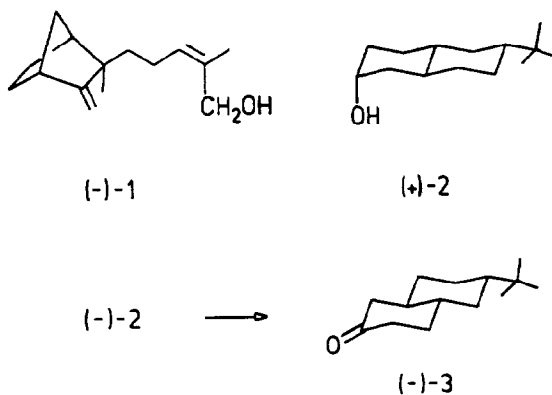
<sup>b</sup> Institute of Theoretical Chemistry and Radiation Chemistry  
of the University, A-1090 Vienna, Währingerstraße 38, Austria

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**Abstract:** Both enantiomers of *tert.*-butylbicyclo[4.4.0]decan-3-ol, a Sandalwood odorant, used as standard for molecular calculations on the group of Sandalwood fragrant molecules, were separated and analyzed in terms of their odour impression as well as their absolute configuration.

The importance of chirality in fragrance chemistry has become evident in the last years<sup>2</sup>. Recently Krotz and Helmchen<sup>3</sup> showed the stereoselectivity within the class of Sandalwood odorants. They succeeded in elucidating the influence of the chirality upon the odour of the enantiomers of  $\beta$ -Santalol, the most characteristic odour constituent of the East Indian Sandalwood oil: The naturally occurring (-)-1 shows the typical Sandalwood scent, whereas its synthetic enantiomer (+)-1 lacks it completely.

In continuation of our studies in structure-activity-relationships of Sandalwood fragrance with the help of computer aided fragrance design (CAFD)<sup>4</sup> it was necessary to perform a detailed odour analysis of the enantiomers of *tert.*-butylbicyclo[4.4.0]decan-3-ol (2)<sup>5</sup>, a compound with a typical Sandalwood fragrance, which is used as a standard for the molecular calculations and surface comparisons of Sandalwood odour molecules, due to its rigid structure<sup>6,7</sup>. Racemic 2 was prepared according to a procedure given in the literature<sup>5</sup>, and after its optical resolution the absolute chiralities of the antipodes have been determined. Finally a detailed analysis of the odour of the enantiomers was performed.



The optical resolution of **2** was done via the diastereomeric ephedrine salts of the phthalic acid half ester of **2**. Recrystallization of the less soluble salts was repeated until constant rotation of the compounds was observed ((-)-ephedrine salt:  $[\alpha]_D^{20} = -14.6$ ,  $c=1.47$ , ethanol; (+)-ephedrine salt:  $[\alpha]_D^{20} = +14.3$ ,  $c=1.19$ , ethanol). Subsequent saponification by LiOH/THF/H<sub>2</sub>O<sup>8</sup> afforded (-)-**2** from the (+)-ephedrine salt after purification preparative TLC (petroleum ether (b.p. 50-70°C) : ethyl acetate = 3 : 1) as white crystals with a yield of 71% ( $[\alpha]_D^{20} = -4.7$ ,  $c=1.16$ , ethanol). (+)-**2** was obtained similarly from the (-)-ephedrine salt ( $[\alpha]_D^{20} = +4.8$ ,  $c=1.25$ , ethanol).

By odour analysis the fragrance of (+)-**2** was described as strong, sandalwood like, warm, sweet and fatty, long persisting, whereas the scent of (-)-**2** appears as very weak, fatty, hardly perceptible, remote reminiscent to animal notes.

In order to establish the absolute configuration of **2** by means of the octant rule<sup>9</sup> (-)-**2** was oxidized to the ketone (-)-**3** using the Jones method ( $[\alpha]_D^{20} = -16.1$ ,  $c=1.13$ , ethanol). The electron absorption spectrum of **3** shows a maximum at 278nm ( $\epsilon=85$ ). A negative CD-band, indicating a negative Cotton-effect, was observed with a maximum at 289nm and a  $\Delta\epsilon$  value of -0.65 (ethanol). The absolute configuration could therefore be established 1R, 6S, 8S.

By odour analysis (-)-**3** was described to possess only a weak odour, at the beginning reminiscent to costus root, with animal and urinous notes and also long persisting.

From the results of Krotz and Helmchen<sup>3</sup> and from our findings it can be shown that the Sandalwood odour is highly sensitive to the chiroptical properties of the molecules. This result is rather noteworthy, in particular because the molecular shape, which should be responsible for an association of the molecules at a convenient receptor site, is not very different for the enantiomers of **2**.

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