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111. The Absolute Configuration of Naturally Occurring (*cis*-6-Methyltetrahydropyran-2-yl)acetic Acid, a Constituent of Civet *(Viverra civetta)*[1]

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Summary

The absolute configuration of the title compound, a minor constituent of civet, is shown to be *S,S*.

We recently reported the isolation of a new compound, (*cis*-6-methyltetrahydropyran-2-yl)acetic acid (**1a**), from civet *(Viverra civetta)* [1]. Although the constitution

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[1] Supplement to [1].

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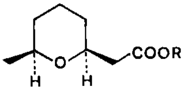
and the *cis*-configuration were established on spectral grounds and by synthesis of the racemic form, the amount of isolated material was too small (*ca.* 2 mg from 1 kg of civet) for the optical rotation to be measured.



1a R=H
b $R=CH_3$

The cumbersome isolation of more material in order to determine its $[\alpha]_D$ value and absolute configuration was circumvented by using NMR. spectroscopy in the presence of a chiral shift reagent [2]. This method requires much less substance and permits direct determination of the enantiomeric purity, but a reference sample of the optically active compound with known absolute configuration is needed. ***Seebach & Pohmakotr*** recently reported the synthesis of the dextrorotatory acid (+)-(*S,S*)-**1a** and the corresponding methyl ester (+)-(*S,S*)-**1b** [3]. These reference compounds, kindly provided by Professor *D. Seebach*²), enabled us to assign the *S,S*-configuration to the natural product **1a** from civet.

The 360-MHz-^{1}H-NMR. spectrum³) of a $CDCl_3$ solution of the racemic methyl ester (±)-**1b** containing the chiral shift reagent $Eu(HFC)_3$⁴) (molar shift reagent/substrate ratio *ca.* 0.2) shows the expected splitting of the signals; this splitting is best seen for the ester methyl signal (two *s* of equal intensity separated by *ca.* 6 Hz) and the secondary methyl signal (two *d* of equal intensity separated by *ca.* 3 Hz). Addition of a small amount of synthetic (+)-(*S,S*)-**1b**²) increases the intensity of the *d* at *lower* field and the *s* at *higher* field.

The ^{1}H-NMR. spectrum of the natural compound in the form of its methyl ester **1b** (1 mg) in the presence of $Eu(HFC)_3$ (4.3 mg) (molar shift reagent/substrate ratio 0.6) shows just one set of signals. This indicates an enantiomeric purity of >95%. Addition of a small amount of (±)-**1b** gives a spectrum which corresponds to that of the mixture of (±)- and (+)-(*S,S*)-**1b**. The absolute configuration of the acid **1a** from civet is therefore *S,S*; its specific rotation ($[\alpha]_D^{22} = +32.86°$ ($c = 1.05$, benzene)) is known from *Seebach*'s work.

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²) We are indebted to Prof. *D. Seebach* and his coworkers for communicating their results prior to publication and providing samples of enantiomerically pure (+)-(*S,S*)-**1a** and (+)-(*S,S*)-**1b**.

³) Recorded on a *Bruker* WH 360 instrument.

⁴) $Eu(HFC)_3$ = tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]Eu(III) was purchased from *Stohler* Isotope Chemicals, Rutherford, N.J. 07070.