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Synthesis and absolute stereochemistry of spiroacetals in rove beetles (*Coleoptera: Staphylinidae*)

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Abstract

The unusual branched-carbon chain spiroacetal, 2,2,8-trimethyl-1,7-dioxaspiro[5.5]undecane, has been synthesised as its racemate and (6*S*,8*R*)-isomer. The natural compound, identified in the rove beetle, *Ontholestes murinus* (L.) proved to be the (6*R*,8*S*)-isomer. (*E,E*)-2,8-Dimethyl-1,7-dioxaspiro[5.5]undecane, a major component of the volatiles from the same insect, is the (2*S*,6*R*,8*S*)-isomer, but is largely racemic in *Ontholestes tesselatus* (Geoffr. Fourcr.). © 1999 Elsevier Science Ltd. All rights reserved.

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The defensive strategy evolved by rove beetles (Coleoptera: Staphylinidae) involves abdominal elevation and the discharge of a secretion from a pair of everted glands, in the direction of the molestation. In 1986, Dettner and Schwinger[1] described the defensive secretion of *Ontholestes murinus* (L.), which contained (*E,E*)-2,8-dimethyl-1,7-dioxaspiro[5.5]undecane (M=184) (**1**) of undetermined stereochemistry. This spiroacetal was accompanied by another component with an apparent molecular mass of 198, and a spiroacetal-like mass spectral fragmentation pattern.[2] In a subsequent report,[3] this latter compound was described as a 2,2,8-trimethyl-1,7-dioxaspiro[5.5]undecane (**2**) without further data. In view of the fact that branched-carbon chain spiroacetals are rare in insects[4,5] (only two are now known),[6] we have undertaken syntheses which permit the determination of the absolute configuration of this unusual compound **2**, as well as that of **1**. The other insect-derived, branched-carbon chain spiroacetal is (2*S*,4*R*,6*R*,8*S*)-2,4,8-trimethyl-1,7-dioxaspiro[5.5] undecane (**3**), the major component of the abdominal gland secretion of the shield bug, *Cantao parentum* (White).[7,8]

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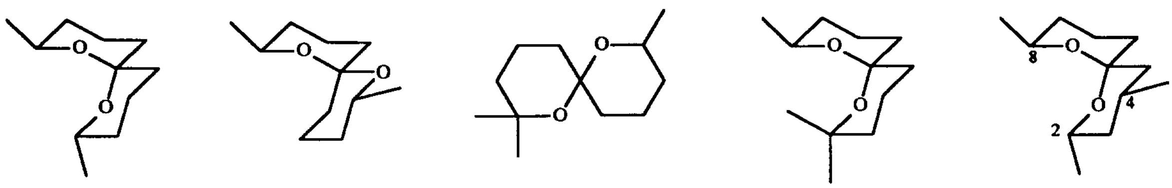
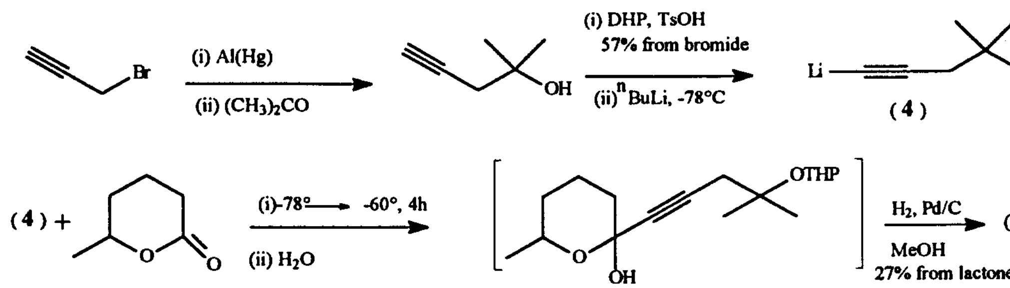


(*E,E*)-(**1**) (*E,Z*)-(**1**) (**2**) (6*R*,8*S*)-(**2**) (**3**)

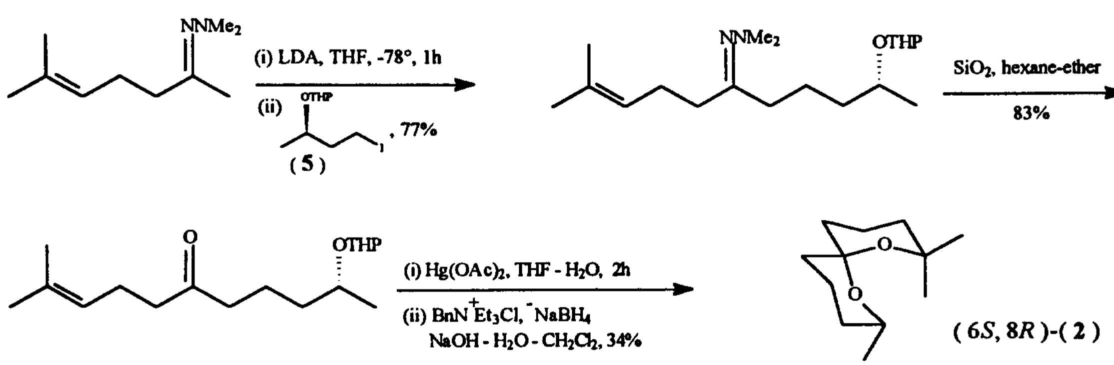
Racemic **2** was synthesised in a straightforward way by addition of the lithium salt of the protected ynol (**4**), to δ-caprolactone, followed by hydrogenation–deprotection and cyclisation[9] of the initial addition product, in 27% overall yield from the lactone (Scheme 1).



Scheme 1.

Final purification of **2**[10] was achieved by flash chromatography on silica gel (30:1, hexane:ether) followed by preparative gas chromatography. The enantiomers of **2** were very well separated on a J&W Cyclodex-B Column (conditions: splitless injection, 40°C for 2 min then 20°C/min to 120°C then 1°C/min).

Acquisition of the (6*S*,8*R*)-enantiomer of **2** was based on hydrazone alkylation with the (*R*)-iodide (**5**),[11] followed by an oxymercuration–deprotection–cyclisation sequence[12] as shown below (Scheme 2). The resulting (6*S*,8*R*)-enantiomer ($[\alpha]_D^{22}$ +46.2, *c* 7.09, $CHCl_3$),[13] thus produced, exhibited MS and NMR parameters identical with those of (racemic) **2**, and eluted earlier than its antipode. The EI mass spectrum of synthesised (6*S*,8*R*)-**2** is shown in Fig. 1.



Scheme 2.

Three gland reservoirs from *O. murinus* were crushed in hexane and examined by high quality GC–MS. A low level of 2,2,8-trimethyl-1,7-dioxaspiro[5.5]undecane (**2**) was identified, and comparisons with synthesised racemic **2** and (6*S*,8*R*)-**2** demonstrated that the natural **2** was the (6*R*,8*S*)-isomer of >95% ee. The accompanying (*E,E*)-**1** was the (2*S*,6*R*,8*S*)-enantiomer (as drawn above) of >98% ee.

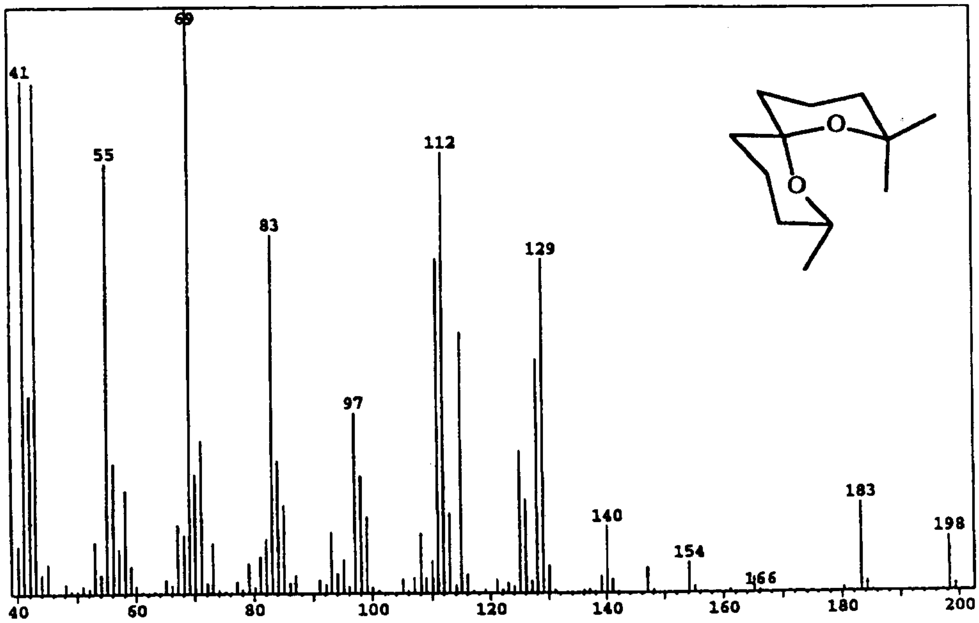


Figure 1. EI mass spectrum of 2,2,8-trimethyl-1,7-dioxaspiro[5.5]undecane (2)

Another rove beetle, *O. tesselatus*, also contains (*E,E*)-2,8-dimethyl-1,7-dioxaspiro[5.5]undecane (**1**), and GC–MS comparisons (J&W Cylodex-B, as before) with authentic samples revealed comparable levels of the widely occurring (2*S*,6*R*,8*S*)-isomer and its (2*R*,6*S*,8*R*) antipode, with the latter unreported from an insect source.[5,6] In some respects, the presence of the (2*R*,6*S*,8*R*)-isomer is not too surprising, as (*E,Z*)-**1**, which often accompanies[5,6] (*E,E*)-**1**, has opposite configurations at carbon atoms 2 and 8, confirming the possibility of both (*R*)- and (*S*)-hydroxylation modes. This outcome can be accommodated within the hypothesis recently proposed[14] for spiroacetal biosynthesis in fruit-fly species, if fundamentally similar processes are operating. The defensive secretions of rove beetles of the sub-tribe Staphylinina are dominated by biologically active iridoid compounds,[3] but the biological significance of the spiroacetals in these defensive glands or secretions is not known. They are inactive if applied topically but exhibit a drastic insecticidal fumigancy at very low vapour concentrations towards adults of *Drosophilia melanogester.*[15] It is remarkable how diverse are the components of these defensive secretions and also the structure and stereochemistry of the spiroacetals utilised. Spiroacetal (**2**) co-occurs in *O. murinus* with terpenoid components, and its structure in part may be isoprenoid derived, however, biosynthesis involving valine or leucine may also be possible.

References

1. Dettner, K.; Schwinger, G. *Z. Naturforsch* **1986**, *42c*, 366.
2. Francke, W.; Hindorf, G.; Reith, W. *Naturwissenschaften* **1979**, *66*, 618. Comparison with the mass spectra of known spiroacetals with M=198 showed no coincidence. A notable feature of the mass spectrum of the unknown compound was the relatively high abundance of the M-15 ion (*m/z* 183), when compared with the M-15 ion for **1**. This indicated an especially stabilised oxonium ion, possibly arising from methyl loss from a *gem*-dimethyl group adjacent to oxygen. For a plotted 70 ev mass spectrum of (*E,E*)-**1**, see: Francke, W.; Reith, W.; Bergström, G.; Tengö, J. *Naturwissenschaften* **1980**, *67*, 619.
3. Huth, A.; Dettner, K. *J. Chem. Ecol.* **1990**, *16*, 2691.
4. Francke, W. *Les Mediateurs Chimiques*; INRA: Versailles, 1982; p. 81.

5. Fletcher, M. T.; Kitching, W. *Chem. Rev.* **1995**, *95*, 789.
6. Francke, W.; Kitching, W. *Current Organic Chemistry* **1999**, in press. Thirty different spiroacetal structures, not including stereoisomers, are known from insects.
7. Moore, C. J.; Hubener, A.; Tu, Y. Q.; Kitching, W.; Aldrich, J. R.; Waite, G. K.; Schulz, S.; Francke, W. *J. Org. Chem.* **1994**, *59*, 6136.
8. Tu, Y. Q.; Moore, C. J.; Kitching, W. *Tetrahedron: Asymmetry* **1995**, *6*, 397.
9. Jacobson, R.; Taylor, R. J.; Williams, H. J.; Smith, L. R. *J. Org. Chem.* **1982**, *47*, 3140, and references cited therein.
10. Compound **2**: For EIMS, see Fig. 1. HRMS: $C_{12}H_{22}O_2$ requires: 198.1620. Measured: 198.1616. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.04 (d, *J*=6.3, 3H), 1.13 (s, 3H), 1.30 (s, 3H), 1.32–2.02 (m, 12H), 3.82–3.92 (m, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 15.8, 19.2, 21.5, 25.3, 32.8, 32.9, 36.4, 37.1, 37.2, 65.7, 72.0, 96.2.
11. (a) Mori, K.; Watanabe, H. *Tetrahedron* **1986**, *42*, 295. (b) Perkins, M. V.; Jacobs, M. F.; Kitching, W.; Cassidy, P. J.; Lewis, J. A.; Drew, R. A. I. *J. Org. Chem.* **1992**, *57*, 3365.
12. See, for example: Perkins, M. V.; Kitching, W.; König, W. A.; Drew, R. A. I. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2501.
13. Spiroacetals with *S* chirality at the spirocentre are dextrorotatory. See: Mori, K.; Ikunaka, M. *Liebigs Ann. Chem.* **1987**, 333.
14. Hungerford, N. L.; Mazomenos, B. E.; Konstantopoulou, M. A.; Krokos, F. D.; Haniotakis, G. E.; Hübener, A.; Fletcher, M. T.; Moore, C. J.; DeVoss, J. J.; Kitching, W. *Chem. Commun.* **1998**, 863.
15. Dettner, K.; Fettköther, R.; Ansteeg, O.; Demi, R.; Liepert, C.; Petersen, B.; Haslinger, E.; Francke, W. *J. Appl. Ent.* **1992**, *113*, 128.