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A Suite of Odd and Even Carbon-Numbered Spiroacetals in *Bactrocera latifrons*. Synthesis and Stereochemistry.

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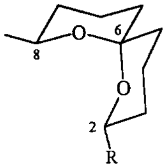
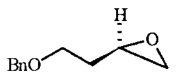
Abstract: Female abdominal tips from the pestiferous fruit-fly species, *Bactrocera latifrons* (Hendel) provide a suite of odd and even 2-alkyl-8-methyl-1,7-dioxaspiro[5.5] undecanes (alkyl = methyl, ethyl, ⁿpropyl, ⁿbutyl) which are shown by synthesis and enantioselective gas chromatography to possess the (2*S*, 6*R*, 8*S*) stereochemistry. © 1997 Elsevier Science Ltd.

Alkyl- and hydroxy-substituted spiroacetals have been identified from Tephritid fruit-fly species, particularly those from the genus *Bactrocera.*[1] With a few exceptions, alkyl spiroacetals contain nine, eleven or thirteen carbons in an unbranched arrangement, and any accompanying even carbon-numbered spiroacetal is of much lower relative abundance. Only in the case of 2-ethyl-8-methyl-1,7-dioxaspiro[5.5] undecane **2**, from *B.nigrotibialus* (Perkins), has the sense of chirality been determined. The absolute stereochemistry of **2** was (2*S*, 6*R*, 8*S*) the same as for the major accompanying 2,8-dimethyl-1,7-dioxaspiro[5.5]undecane **1**.[2] In view of our interest in insect-derived oxygen heterocycles and the necessity to furnish structural and stereochemical data for biosynthetic proposals, we now wish to report that females of the pest species *B.latifrons* (Hendel) provide a suite of four homologous 2-alkyl-8-methyl-1,7-dioxaspiro[5.5]undecanes, whose structures and absolute stereochemisty have been established by synthesis and enantioselective gas chromatography as (2*S*,6*R*,8*S*)-**1**, **2**, **3** and **4** in accord with our previous prediction.[2]



1 R = CH_3
2 R = C_2H_5
3 R = $^nC_3H_7$
4 R = $^nC_4H_9$



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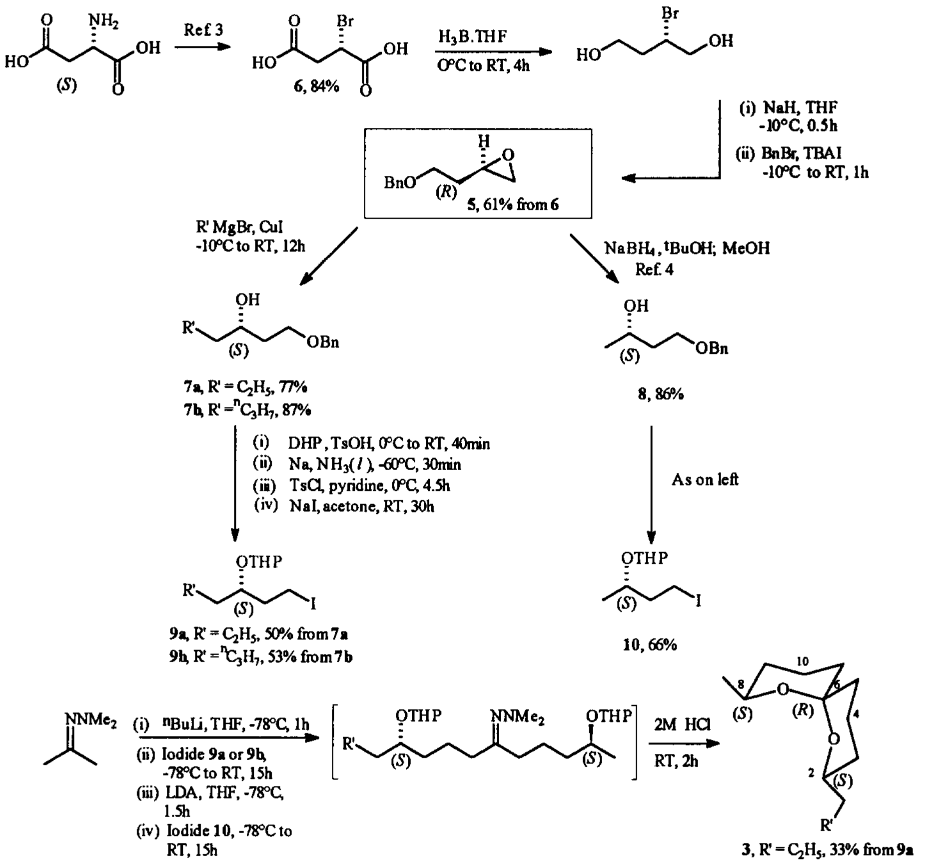
A general synthetic approach to enantiomers of **3** - **4** utilises (*R*) - (2-benzyloxyethyl)oxirane **5**, now readily available from (*S*)-aspartic acid.[3] (Both (*S*) and (*R*)-aspartic acids are commercially available). This procedure, in which **5** is the convenient precursor of both required alkylating agents **7** and **8**, would also furnish enantiomers **1** and **2**, but we had already synthesised these by other means.[2] The steps are outlined in Scheme 1, and we found that reduction of the bromo-succinic acid **6** was better behaved with freshly prepared H_3B.THF. Reductive opening of the oxirane **5** with $NaBH_4$ in ᵗBuOH-MeOH proceeds without removal of the benzyl group.[4] Spiroacetals **3** and **4**[5] acquired in this way possessed (2*S*, 6*R*, 8*S*) stereochemistry with >99.5%ee, based on enantioselective gas chromatography. Optical rotations for **3** and **4** were consistent with those previously reported for **1** and **2.**[6]

Racemic **3** and **4** resulted from use of racemic (2-benzyloxethyl)oxirane, formed by epoxidation of but-3-en-1-ol. (Racemic **1** and **2** were already available).[2] Examination of a hexane abdominal tip extract of female *B.latifrons* showed the four spiroacetals **1** - **4** were the (*E,E*) diastereomers with (2*S*,6*R*,8*S*) stereochemistry, and ee >95% for **1**, **2**, and **4** and ee 91% for **3**. It is of interest to note that one alkyl group is unchanging, with variation in the other from methyl to ⁿbutyl.



Scheme 1

Although the spiroacetals **1** - **4** are present in comparable amounts, overall they are minor components of the abdominal tip extracts. A detailed analysis of female and male rectal components from *B. latifrons* has recently been reported.[7] Isomers **2** and **4** were previously reported[8] as very low level components from the rectal gland of **male** *B. latifrons* and it is very likely the (2*S*,6*R*,8*S*) stereochemistry applies also. The biological role of these components is currently being assessed.

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5. All new compounds exhibited satisfactory HRMS for M^+ and concordant ^1H and ^{13}C nmr spectra. **^{13}C nmr ($CDCl_3$, 125 MHz) 3**: 96.0, 68.7, 65.1, 38.7, 35.5, 35.3, 32.9, 31.4, 21.8, 19.1, 19.0, 18.9, 14.2. **4**: 96.0, 68.9, 65.0, 36.2, 35.5, 35.3, 32.9, 31.4, 28.1, 22.9, 21.8, 19.0, 18.9, 14.1. Optical rotations: **3**, $[\alpha]_D^{23}$ -40.5° (c, 1.08, pentane) and **4**, $[\alpha]_D^{23}$ -53.0° (c, 0.67, pentane).
6. Optical rotations: **1**, $[\alpha]_D^{23}$ -58.7° (c, 1.6 in pentane) and **2**, $[\alpha]_D^{23}$ -72.9° (c, 0.38 in pentane). See also (a) Mori, K.; Watanabe, H. *Tetrahedron*, **1986**, *42*, 295 and ref. 2 and (b) Mori, K.; Ikunaka, M. *Liebigs Ann. Chem.*, **1987**, 333.
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