JOURNAL OF THE CHEMICAL SOCIETY

Chemical Communications

Number 3
1984

Preparative Separation of the Enantiomers of *trans,trans*- and *cis,trans*-2,8-Dimethyl-1,7-dioxaspiro[5.5]undecane, Main Pheromone Components of *Adrena* Bees, by Liquid Chromatography on Triacetylcellulose

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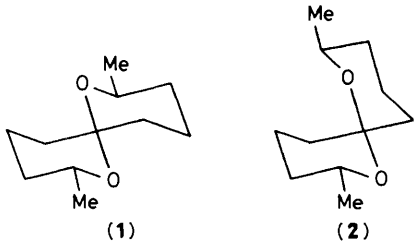
The title compounds were separated into their enantiomers with at least 98% optical purity using liquid chromatography on swollen, microcrystalline triacetylcellulose.

Many insect species use chiral compounds as pheromone components and it has generally been found that they respond to one enantiomer in preference to the other one.[1] In some case the 'wrong' enantiomer has been found to be inhibitory. Thus, it is of great importance in laboratory and field studies on insect communication to have access to pheromone components of high optical purity. Much work has been devoted to asymmetric synthesis of enantiomers of chiral pheromone components.[2] In general a large number of steps are required and high optical purity is often hard to achieve. In contrast, the corresponding racemic compounds may often be easily prepared in high yields. It would then be a significant achievement if the enantiomers could be obtained from racemic material by chromatographic techniques.

Chiral spiroacetals occur widely as insect pheromone components. This class of compounds has been identified from bark beetles as well as from wasps and bees.[3—5] Francke *et al.* identified *trans,trans*- and *cis,trans*-2,8-dimethyl-1,7-dioxaspiro[5.5]undecane, (**1**) and (**2**), respectively, in the mandibular gland secretion of *Adrena* bees.[3,4] Mori and Tanida have reported a synthesis of the enantiomers of (**1**) by a multistep procedure.[6] This, however, failed to produce the enantiomers of (**2**).[6] The racemic spiroacetals (**1**) and (**2**) are conveniently prepared as a 3:2 mixture according to the method described by Francke *et al.*[7] The diastereoisomers could easily be separated by preparative g.l.c. (column OV 351, 6 ft). We report here a preparative separation of (+)- and (−)-(**1**) and (**2**) by liquid chromatography on swollen, microcrystalline triacetylcellulose. This method has previously been successfully applied to chiral compounds with conjugated π-systems.[8—10] A glass column (60 × 2.5 cm) containing *ca.* 180 g of triacetylcellulose (particle size 30—45 μm) prepared according to the procedure of Hesse and Hagel[11] was used. Ethanol/water (96:4) was used as eluant with a flow rate of *ca.* 100 ml h^{-1} at 3.6 bar.



In a single run 140 mg of (**1**) afforded *ca.* 50 mg of each enantiomer after dilution of the ethanol solution with water (containing 2.5% $NaHCO_3$) and extraction with n-pentane. In the same way *ca.* 30 mg of each of the enantiomers of (**2**) were obtained from 80 mg of racemic material. The isolated enantiomers were free from impurities (g.l.c., OV 17 and OV 351). The ^1H n.m.r. spectra (360 MHz) were in agreement with literature data.[6,7] The specific rotations measured in freshly distilled n-pentane were: (+)-(**1**), $[\alpha]_D^{24}$ 44.6±0.7° (*c* 1.140); (−)-(**1**), $[\alpha]_D^{24}$ −44.3±0.7° (*c* 1.180); (+)-(**2**), $[\alpha]_D^{24}$ 44.0±1.3° (*c* 1.705); (−)-(**2**), $[\alpha]_D^{24}$ −44.6±1.3° (*c* 1.740). Chromatograms of the *cis,trans*-isomer (**2**) with continuous recording of the angle of rotation are shown in Figure 1. The corresponding chromatograms for (**1**) are very similar [retention volumes: (+)-(**1**), 228; (−)-(**1**), 280 ml]. Computer simulations of the chromatograms indicate that impurities comprising at least 2% of the enantiomer with the rotational angle of opposite sign should be clearly

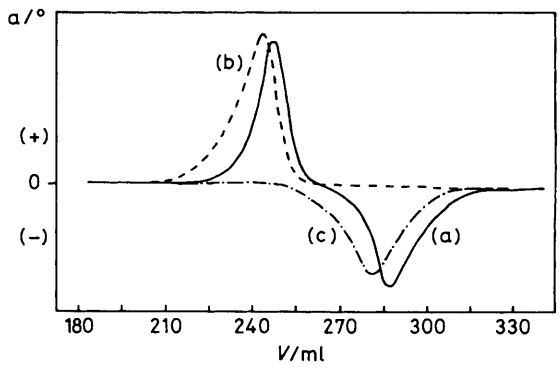


Figure 1. Chromatograms of (a): racemic (**2**), (b) and (c): (+)-(**2**) and (−)-(**2**), respectively, after separation. V = retention volume, α = angle of rotation (at 364 nm).

detectable (*cf.* Figure 1). We thus conclude that our isolated enantiomers are at least 98% optically pure. Mori and Tanida reported the specific rotations ($[\alpha]_D^{24}$) of (+)-(**1**) and (−)-(**1**) to be 51.6 and −51.7° in n-pentane, respectively, although their chiral starting material was of only 92% optical purity. Thus, there is a discrepancy between our values and those of Mori and Tanida. The reason for this is not clear to us.

The successful separation of the title compounds into their enantiomers using liquid chromatography on microcrystalline triacetylcellulose indicates the possibility that enantiomers of high optical purity of other spiroacetals of biological interest may be prepared.

We thank Dr. Francke, University of Hamburg for a gift of samples for preliminary investigations, Dr. Jan Tengö, Ecological Station of Uppsala University, for valuable discussions and Miss Kristina Stenvall for skilful technical assistance. This work was supported by the Swedish Natural Science Research Council and the Royal Physiographic Society of Lund.

Received, 2nd November 1983; Com.1434

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