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FACILE SYNTHESIS OF OPTICALLY ACTIVE 2-ETHYL-1,6-DIOXASPIRO[4.4]NONANE, COMPONENT OF THE AGGREGATION PHEROMONE OF THE BEETLE PITYOGENES CHALCOGRAPHUS (L.)

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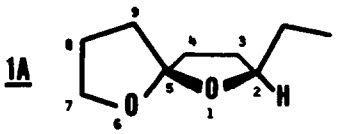
Francke et al. recently reported[1] that the interesting spirocyclic compound, 2-ethyl-1,6-dioxaspiro[4.4]nonane (1), serves as the principal component of the aggregation pheromone of the beetle Pityogenes chalcographus (L.), a pest of Norway spruce. This compound exists as a mixture of diastereomers, 1A and 1B, both of which



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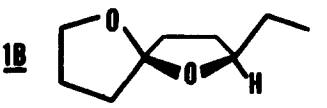
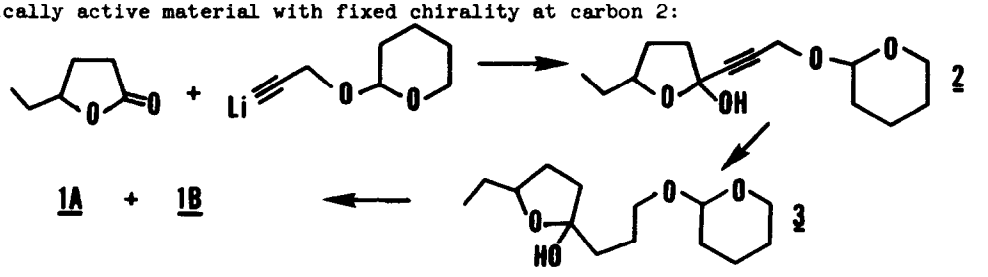


(and enantiomer)

were natural pheromone components separable for GC/MS analysis on a capillary GC column. The structure was confirmed by high resolution MS and proton NMR of the combined isomers. A synthesis from 3-(2-furyl)-propionaldehyde was also reported. This synthesis did not fix the stereochemistry at carbon 2 and therefore cannot be used to determine which of the 4 stereoisomers, ± 1A and ± 1B, are biologically active.

The ready availability of γ-caprolactone in high optical purity, from our recent synthesis[2], prompted us to devise the following route to 1, adaptable to preparation of optically active material with fixed chirality at carbon 2:



Propargyl alcohol tetrahydropyranyl ether[3] (3.5 g, 25 mmol) in 50 ml of anhydrous ether was treated with 12.5 ml of 2M MeLi in ether. The resulting soln. was syringed into a stirred soln. of γ-caprolactone (3.0 g, 26 mmol) in 50 ml of ether. After 1.5 hr, the stirred soln. was treated with 20 ml of 20% aq. NH_4Cl soln. After 10 min, the organic layer was separated, dried (K_2CO_3), and evaporated to an oil. The oil, whose IR and NMR spectra were consistent with structure 2, was dissolved in 100 ml anhydrous MeOH and hydrogenated to 3 at 1 atm over 0.5 g of 5% Rh/alumina. The filtered soln. was treated with 2 ml conc. aq. HCl and held at room temp. for 24 hr. Dist. at 1 atm gave 1.5 g (37% from γ-caprolactone) of 1, bp 190-195°, whose spectral properties agreed with those reported in ref. 1.

Optically active 1 (R at C-2), prepared on a smaller scale from (R)-(+)-γ-caprolactone, was isolated by preparative GC (6% OV-101 col., 2.5 m x 9 mm O.D., 100°). The 2-R-1 was a mixture of C-5 epimers, inseparable on a variety of GC columns. However, a sufficient separation was achieved on a 6 m x 6 mm 5% FFAP column at 55°, with a helium flow of 180 ml/min (ret. time ca. 55 min.). The minor (shorter ret. time) and major isomers were initially present in about a 1:2 ratio. Collection allowed purification of the major isomer to 90%, of the minor isomer to 79%.[4] Using optically active material, and correcting for the presence of diastereomer, we obtained $[\alpha]_D^{25}$ values (C_6D_6) of +62° and -76° for the major and minor isomers respectively. Use of EuFOD shift reagent, to alter the ^{13}C-NMR spectrum of 1A and 1B, resulted in distinctly larger shifts for the major isomer (esp. for signals assigned to C-2, C-5, and C-7). This, and the major isomer's longer GC retention time, indicate that it has structure 1A, in which the ketal linkage is unhindered by the ethyl group at C-2.

Use of the available (S)-(-)-γ-caprolactone[2] will permit access to the other two enantiomers of 1. Availability of the synthetic enantiomers may allow the determination of the enantiomer composition of the natural pheromone component.

References and Notes

1. W. Francke, V. Heeman, B. Gerken, J. A. A. Renwick, and J. P. Vité, Naturwissenschaften, 64, 590 (1977).
2. (a) U. Ravid and R. M. Silverstein, Tetrahedron Lett., 423 (1977);
   (b) U. Ravid, R. M. Silverstein, and L. R. Smith, Tetrahedron, in press.
3. P. P. Montijn, L. Brandsma, and J. F. Aren, Rec. Trav. Chim. Pays-Bas, 86, 129 (1967); also Chem. Abstr., 66, 85383n (1967).
4. Significant epimerization at C-5 took place when a soln. of the purified material (C_6D_6) stood for one week in a base-washed tube.

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