Tetrahedron: Asymmetry Vol. 4, No. 4, pp. 655-656, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00

STEREOISOMERIC FLAVOUR COMPOUNDS. LXIII. 4-HYDROXYPENTAN-2-ONE ENANTIOMERS - STRUCTURE AND PROPERTIES

Wolfgang Bensch[a], Armin Mosandl*[b], and Katja Fischer[b]

Institut für Anorganische Chemie der Universität Frankfurt, Niederurseler Hang, D-6000 Frankfurt/Main, Germany[a]

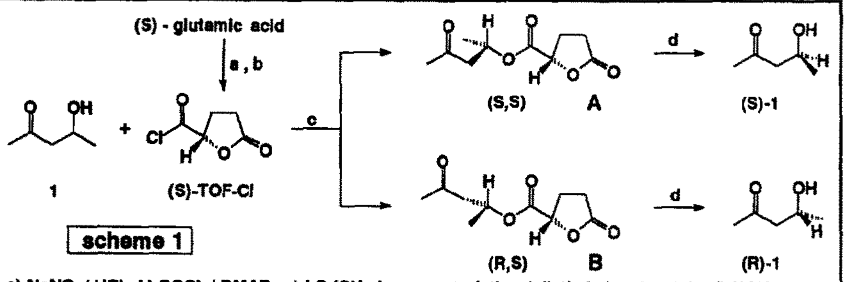
Institut für Lebensmittelchemie der Universität Frankfurt, Robert-Mayer-Straße 7-9, D-6000 Frankfurt/Main, Germany[b]

(*Received in UK* 18 *February* 1993)

Key words: Chiral 1,3-ketols; flavour compounds; chirality and odour

Abstract: From racemic 4-hydroxypentan-2-one and (S)-tetrahydro-5-oxo-2-furancarboxylic acid chloride the corresponding diastereomeric esters were generated, subsequently separated by liquid chromatography and hydrolyzed to yield pure enantiomers of 4-hydroxypentan-2-one. The X-ray crystal structures of the diastereomeric esters as well as the odour impression of the pure 1,3-ketol enantiomers are reported.

Among the neutral volatile components of Swiss Gruyère cheese and other fermented food and beverages a lot of chiral alkan-2-ols and 1,2 (1,3)-ketoalcohols were identified by GC/MS, indicating an intense microbiological activity during maturation [1], but without knowledge of the stereochemical composition and sensory quality of their enantiomers until recently [2-5]. This paper reports on stucture elucidation and sensory properties of the enantiomers of 4-hydroxypentan-2-one (**1**). (S)-Tetrahydro-5-oxo-2-furancarboxylic acid [(S)-TOF] has been introduced as an efficient chiral auxiliary reagent in the chromatographic separation of chiral alcohols by Doolittle et al [6].



scheme 1

a) $NaNO_2$/ HCl ; b) $SOCl_2$/ DMAP ; c) LC (CN-phases, petrolether / diethylether 40 : 60) ; d) KOH.

By use of (S)-TOF chloride [in dichloromethane/dimethylamino pyridine (DMAP)] racemic 4-hydroxy-pentan-2-one (**1**) was transferred to its corresponding diastereomeric (S)-TOF esters, which were successfully separated by liquid chromatography on cyanophases with petrolether/diethylether (40:60) as the eluent, yielding colourless needles, overall yield 80 % (**A**) and 74 % (**B**). The stereochemistry of 4-hydroxypentan-2-one (**1**) enantiomers was concluded from the relative configurations of the 4-hydroxypentan-2-one moiety of the investigated (S)-TOF diastereomers **A** (**B**) by X-ray structural analyses [5, 7].

The esters **A** (**B**) were subsequently hydrolyzed to the pure enantiomers of 4-hydroxypentane-2-one (S)-**1**, (R)-**1** in 90% yield, each. In order to avoid the elimination of water during the liberation of the pure 1,3-ketol enantiomers, the (S)-TOF esters **A** (**B**) must by hydrolyzed carefully. Only less than equimolar amounts of alkali should be added. By use of heptakis (2,3,6-tri-O-methyl)-β-cyclodextrin as the chiral stationary phase the direct enantioselective analysis of (S)-**1** and (R)-**1** was achieved, proving the existence of pure enantiomers from (S)-TOF ester hydrolysis. While the (S)-**1** enantiomer emits a fresh herbaceous, grassy note, the (R)-configured isomer exhibits a rather musty odour, but with some reminiscence of the (S)-**1** [5].

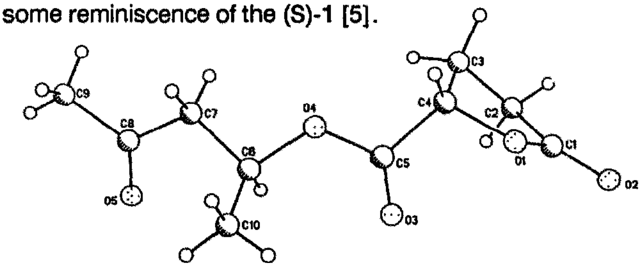


Figure 1 (S)-TOF ester of (S)-4-hydroxypentan-2-one (**A**)
Selected bond distances (Å) and angles are: C1-C2 1.483(4), C2-C3 1.512(4), C3-C4 1.519(4), C4-01 1.439(3), C1-01 1.351 (3), C1-02 1.203 (3), C4-C5 1.508 (3), C5-03 1.199(3), C5-04 1.333(3), C6-04 1.465(3), C6-C7 1.499(4), C6-C10 1.493 (4), C7-C8 1.495 (4), C8-05 1.213(3), C8-C9 1.489(4), C1-01-C4 109.7 (2); 01-C1-02 119.7(2); 01-C1-C2 110.7(2); 02-C1-C2 129.6(2); C1-C2-C3 103.2(2); C2-C3-C4 102.4(2); 01-C4-C3 104.9(2); 01-C4-C5 108.8(2); 03-C5-C4 124.3(2); 04-C5-C4 110.2(2); C5-04-C6 117.8(2); 04-C6-C7 104.9(2); 04-C6-C10 109.6(2); C6-C7-C8 114.8(2); C7-C8-C9 116.8(2); C7-C6-C10 113.7(2); 05-C8-C7 121.5(2); 05-C8-C9 121.6(3);

References and Notes

1) J. O. Bosset, R. Liardon, Lebensm. Wiss. Technol. 17 (1984) 359.

2) A. Mosandl, K. Rettinger, K. Fischer, V. Schubert, H.-G. Schmarr, B. Maas, J. High Resolut. Chromatogr. 13 (1990) 382.

3) K. Fischer, A. Mosandl, Z. Lebensm. Unters. Forsch. 192 (1991) 30.

4) A. Mosandl, K. Fischer, U. Hener, P. Kreis, K. Rettinger, V. Schubert, H.-G. Schmarr, J. Agric. Food Chem. 39 (1991) 1131.

5) K. Fischer, Struktur und Analyse chiraler 1,2- und 1,3-Ketole, doctoral thesis Univ. Frankfurt (1990).

6) R. E. Doolittle, R. R. Heath, J. Org. Chem. 49 (1984) 5041.

7) Crystal data: $C_{10}O_5H_{14}$, orthorhombic, space group $P2_12_12_1$, a = 5.9765 (7), b= 9.781 (2), c = 19.141 (4), V = 1118.9 $Å^3$, Z = 4, Mo K_α radiation, λ = 0.7107 Å, Graphite Monochromator, Ω- 2Θ scan technique. Out of 1878 unique data 1583 were considered observed ($I_{obs} > 1.5r$ (I_{obs}). The structure was solved with Direct Methods (SHELXTL plus). Least squares (full matrix) refinement yielded R- and Rw-values of 0.0381 and 0.0406, respectively. Complete data have been deposited at the Fachinformationszentrum Energie, Physik, Mathematik, D- 7514 Eggenstein-Leopoldshafen 2, deposition No. CSD 56 907.