Tetrahedron: Asymmetry Vol. 4, No. 4, pp. 651-654, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00
© 1993 Pergamon Press Ltd

STEREOISOMERIC FLAVOUR COMPOUNDS LXII. STRUCTURE ELUCIDATION OF 8-MERCAPTO-P-MENTHAN-3-ONE ISOMERS

Armin Mosandl*[a], Thomas Köpke[a], and Wolfgang Bensch[b]

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

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

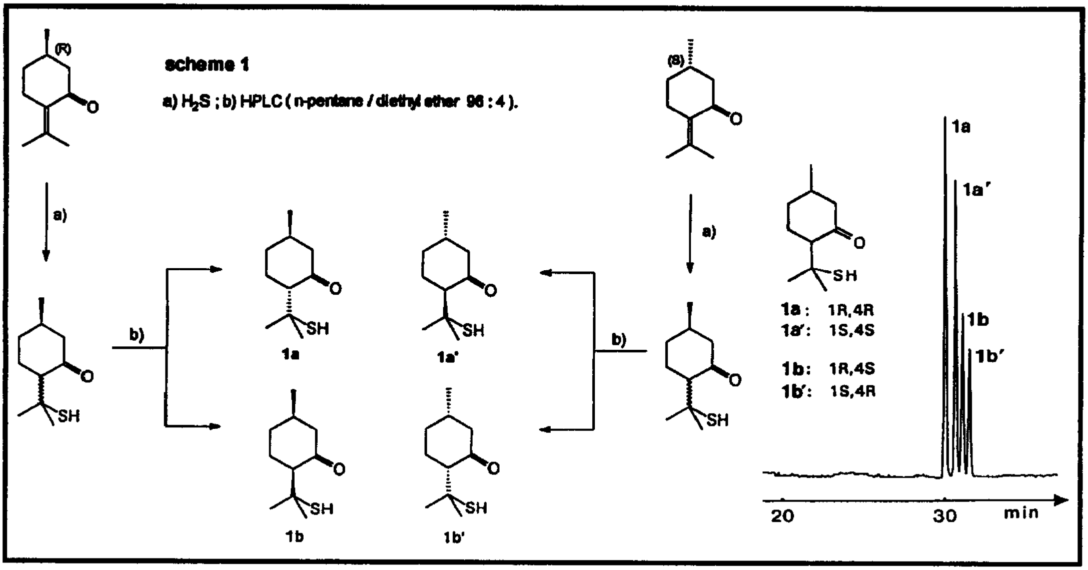
(*Received in UK* 25 *February* 1993)

Key Words: Buchu leaf oil; Cassis flavour, chiral flavour compounds

Abstract: The stereoisomers of 8-mercapto-p-menthan-3-one have been synthesized by addition of H_2S to (R)- and (S)-pulegone to yield enantiomerically pure cis/trans diastereomers by subsequent liquid chromatography (SiO_2; n-pentane/diethyl ether, 94:6). Their stereochemistry is concluded from X-ray structure analyses as well as ^{13}C-NMR-spectroscopy of the corresponding 3',5'-dinitrobenzoyl thiolates.

With respect to human nutrition the evaluation of the sensory properties of optical isomers and their stereoselective purity control from natural flavour sources is of fundamental interest. 8-mercapto-p-menthan-3-one (**1**) has been described as an impact flavour compound from buchu leaf oil [1, 2], the steam distilled oil of *Agathosma betulina* Barth. or *Agathosma crenulata* (L.) Hook, which is frequently used in "cassis"-type flavour and fragrance compositions.

The diastereomers of **1** have been synthesized by addition of H_2S to pulegone enantiomers to yield 22 % of enantiopure stereoisomers (trans: 58 %; cis: 42 %). Using heptakis (2,3-6-tri-O-methyl)-β-cyclodextrin as the chiral stationary phase (CGC-conditons: split/splitless injector; injector temperature: 210°C; injection mode: split 20 ml/min; detector: FID; detector temperature: 230°C; carrier gas: 150 kPa H_2; column temperature 130°C isotherm; column: 56m x 0,23mm i.D. Duran glass capillary, coated with a 0,3 µm film of 10% modified cyclodextrin in OV 1701vi) in enantioselective capillary gas chromatogaphy, all the four stereoisomers were chirospecifically analysed and their main sensory properties described, proving the (1S)-configured diastereomers of **1** to be exclusively peculiar to buchu leaf oil [3, 4]. Although reminiscent of the flavour of black currant, these extremely potent odorants have not yet been identified in these fruits.



scheme 1

a) H_2S ; b) HPLC (n-pentane / diethyl ether 96 : 4).

This communication deals with the structural assignment of all the stereoisomers of 1 concluded from ^{13}C-NMR measurements as well as X-ray structure analyses of the corresponding 3',5'-dinitrobenzoyl thiolates A, B [7,8].

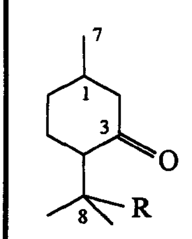
	relative configuration **trans**				relative configuration **cis**			
C_X	R=H	R=SH	R=SAc	R=SBz	R=H	R=SH	R=SAc	R=SBz
1	35,5	36,0	36,4	36,3	34,3	32,3	33,2	32,1
2	50,9	51,8	52,1	51,9	48,1	49,9	50,1	49,9
3	211,5	209,4	210,4	209,6	215,7	210,3	210,8	210,1
4	55,9	60,8	55,3	55,6	57,2	61,0	55,7	60,0
5	28,0	34,2	34,5	34,4	26,8	31,1	31,29	31,3
6	34,0	29,3	29,6	29,5	29,6	25,2	25,2	25,2
7	22,3	22,2	22,2	22,2	19,9	18,6	18,6	18,6

Table 1: ^{13}C-NMR-data of diastereomeric p-menthan-3-one derivatives [75Mhz; δ (ppm);
SAc : thiolacetate; SBz : (3',5'-dinitro) thiolbenzoate].

As recently reported for the thiols and the thiol acetates [3,4], the location of the ^{13}C - signals of the p-menthan-3-one ring atoms allows the assignment of the relative configuration. Compared with the well known ^{13}C-NMR data of nonsubstituted p-menthan-3-one diastereomers [5,6] all the *cis*-configurated compounds exhibit significant high field shifts for the signals of C_1, C_2, C_5, C_6 and C_7. On the other hand the signal at C_3 is shifted downfield in the case of the *cis*-compounds. This structural assignment is now ascertained by ^{13}C-NMR data and X-ray diffraction of the corresponding 3',5'-dinitrobenzoyl thiolates respectively.

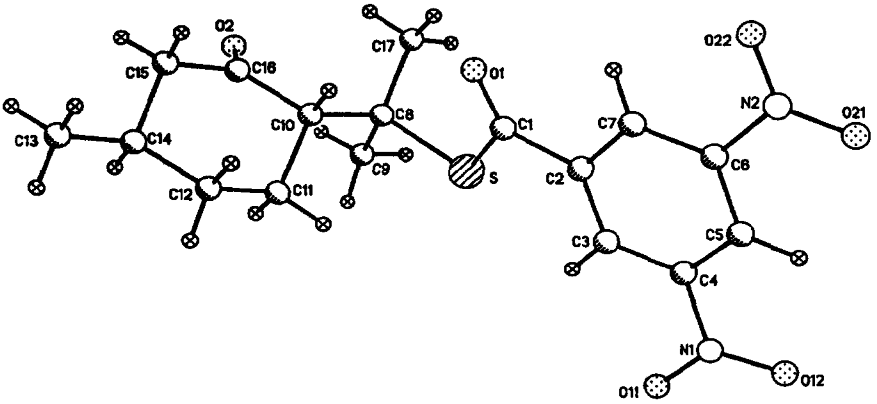


Figure 1: *trans*-(1R, 4R)-3-oxo-p-menthane-8-thiol (3`,5`-dinitro) benzoate (**A**); Molecular structure of A Selected bond distances (Å) and angles are:

C1-C2 1.516(5), C2-C3 1.382(5), C3-C4 1.384(5), C4-C5 1.376(5), C5-C6 1.382(6), C6-C7 1 379(5), C7-C2 1.389(5), C4-N1 1.491(5), N1-O11 1.212(5), N1-012 1.209(6), C6-N2 1.461(5), N2-021 1.219(5), N2-022 1.215(6), C1-01 1.206(5), C1-S1 1.756(4), S - C8 1.861(4), C8-C9 1.535(5), C8-C17 1.532(6), C8-C10 1.555(5), C10-C11 1.543(6), C11-C12 1.516(6), C12-C14 1.507(6), C14-C13 1.522(6), C14-C15 1.530(7), C15-C16 1.503(6), C16-C10 1.522(5), C16-02 1.211(5); 01-C1-S 125.4(3); 01-C1-C2 120.8(3); C1-S-C8 105.8(2); S-C8-C10 110.4(2); S-C8-C9 101.3(2); S-C8-C17 108.7(2); C10-C16-02 124.7(4); C6-N2-021 118.1(4); C6-N2-022 117.8(3); C5-C4-N1 118.4(3); C4-N1-O11 117.4(4); C4-N1-012 116.8(4)

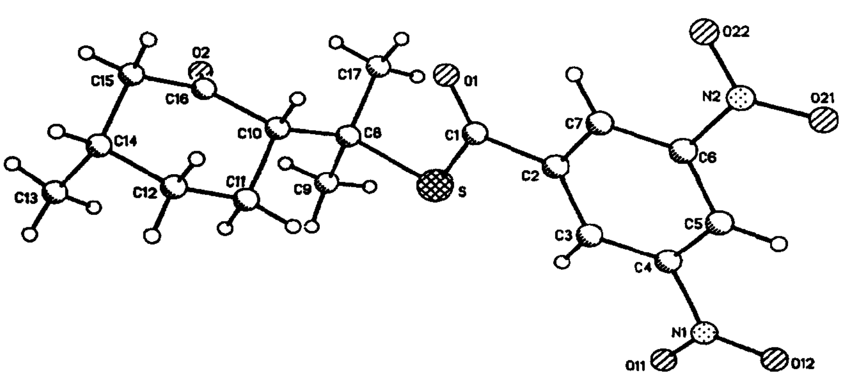


Figure 2: *cis*-(1S, 4R)-3-oxo-p-menthane-8-thiol (3`,5`-dinitro) benzoate (**B**); Molecular structure of **B**.

Selected bond distances (Å) and angles are:

C1-C2 1.505(4), C2-C3 1.392(5), C3-C4 1.374(4), C4-C5 1.378(4), C5-C6 1.382(6), C6-C7 1.375(4), C7-C2 1.388(4), C4-N1 1.485(4), N1-011 1.218(4), N1-012 1.223(4), C6-N2 1.472(4), N2-021 1.210(4), N2-022 1.216(4), C1-01 1.205(4), C1-S 1.751(3), S-C8 1.858(3), C8-C9 1.537(4), C8-C17 1.533(5), C8-C10 1.545(4), C10-C11 1.536(5), C11-C12 1.529(5), C12-C14 1.514(5), C14-C13 1.525(5), C14-C15 1.526(5), C15-C16 1.500(5), C16-C10 1.525(5), C16-02 1.206(5); 01-C1-S 125.7(3); 01-C1-C2 120.3(3); C1-S-C8 106.8(2); S-C8-C10 110.2(2); S-C8-C9 101.6(2); S-C8-C17 108.3(2); C10-C16-02 124.4(3); C6-N2-021 118.1(3); C6-N2-022 117.2(3); C5-C4-N1 117.6(3); C4-N1-011 117.6(3); C4-N1-012 117.5(3)

References and Notes

1) E. Sundt, B. Willhalm, R. Chappaz, G. Ohloff, Helv. Chim. Acta 54 (1971) 1801.
2) D. Lamparsky, P. Schudel, Tetrahedron Letters 36 (1971) 3323.
3) T. Köpke, A. Mosandl, Z. Lebensm. Unters. Forsch. 194 (1992) 372.
4) T. Köpke, H.-G. Schmarr, A. Mosandl, Flav. Fragr. J. 7 (1992) 205.
5) F. Bohlmann, R. Zeisberg, Org. Magn. Reson. 7 (1975) 462
6) F. Bohlmann, C. Zdero, H. Schwarz, Chem. Ber. 108 (1975) 1369
7) T. Köpke, doctoral thesis, Univ. Frankfurt, in preparation.
8) Crystal data: *trans-(1R, 4R)-3-oxo-p-menthane-8-thiol (3',5'-dinitro) benzoate (A)*, $SO_6N_2C_{17}H_{20}$; orthorhombic, space group $P2_12_12_1$, a = 6.287(2), b = 21.314(6), c = 14.032(9), V = 1880.3 Å^3, Z = 4 *cis-(1S, 4R)-3-oxo-p-menthane-8-thiol (3',5'-dinitro)-benzoate (B)*, $SO_6N_2C_{17}H_{20}$, orthorhombic, space group $P2_12_12_1$, a = 6.104(3), b= 9.334(4), c = 32.472(9), V = 1850.1 Å^3, Z = 4.

MoK$_\alpha$ radiation, λ = 0.717 Å, Graphite Monochromator, Ω-2Θ scan technique. Compound A: 1988 data with $I_{obs} > 2\sigma (I_{obs})$ (3004 unique data); final R- and Rw-values are 0.0396 and 0.0396, respectively. Compound **B**: 2094 data with $I_{obs} >$ (2525 unique data); final R- and Rw-values are 0.0376 and 0.0383, respectively. Complete data have been deposited at the Fachinformationszentrum Energie, Physik, Mathematik, D-7514 Eggenstein-Leopoldshafen 2, deposition No. CSD 56 906