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Absolute Configuration of Secondary Alcohols Determined by Gas Chromatography

Short Communication

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The absolute configuration of secondary alcohols is determined by the characteristic GC-peaks pattern of their acetals obtained from their reaction with racemic or optically pure *MBF*-OH and *MBP*-OH due to the enantiomeric selectivity in acetalisation.

(Keywords: Enantiomeric selectivity; Acetalisation)

Bestimmung der Absolutkonfiguration sekundärer Alkohole mittels Gaschromatographie

Die absolute Konfiguration sekundärer Alkohole wurde aus den charakteristischen GC-Peaks der entsprechenden Acetale bestimmt. Grundlage dafür ist die enantiomere Selektivität der Acetalbildung mittels racemischem oder optisch reinem *MBF*-OH und *MBP*-OH.

The use of lactoles derived from camphor 2*S*-(2α,3aα,4α,7α)-2,3,3a,4,5,6,7,7a-Octahydro-7,8,8-trimethyl-4,7-methanobenzofuran-2-ol [(+)-*MBF*-OH] and 2*S*-(2α,4aα,5α,8α,8aα)-3,4,4a,5,6,7,8,8a-Octahydro-8,9,9-trimethyl-5,8-methano-2*H*-1-benzopyran-2-ol [(+)-*MBP*-OH] for separating enantiomers and in asymmetric synthesis has already been described[1].

Now dimeric (+) and (—)-*MBF*-OH are commercially available. Fig. 1 shows the two diastereomers obtained by the acetalisation of a secondary alcohol, where "b" stands for a bulky group, such as an alkyl,

Table 1

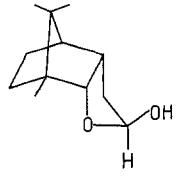
	Alcohol	Corr. rel. retention	GC-integration ratio A/B	Elution order	Condition of GC
1	$C_6H_5CH(OH)CH_3$	1.07	2.9	B, A	a
2	$C_6H_5CH(OH)C_2H_5$	1.07	2.7	B, A	a
3	$C_6H_5CH(OH)(CH_2)_2CH_3$	1.07	2.8	B, A	b
4	$C_6H_5CH(OH)CH(CH_3)_2$	1.07	3.8	B, A	a
5	$C_6H_5CH(OH)C(CH_3)_3$	1.10	4.1	B, A	b
6	$C_6H_5CH(OH)CHCl_2$	1.10	1.6	B, A	d
7	$C_6H_5CH(OH)CCl_3$	1.09	3.7	B, A	d
8	(α-Naphthyl)$CH(OH)CF_3$	1.23	1.44	B, A	d
9	$C_6H_5CH(OH)C{\equiv}CH$	1.02	2.1	A, B	e
10	$CH_3CH(OH)C{\equiv}CH$	1.03	3.1	A, B	e
11	$C_2H_5CH(OH)C{\equiv}N$	1.04	1.4	A, B	c
12	$C_6H_5CH_2OCH_2CH(OH)C{\equiv}N$	1.05	1.6	A, B	f

GC-Conditions

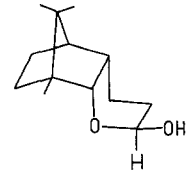
	Temp. of Injection	Initial temp.	For min	Time (min) for reaching	Final temp.
a	285 °C	150 °C	4	10	230 °C
b	300 °C	180 °C	4	10	230 °C
c	285 °C	150 °C	5	5	330 °C
d	365 °C	200 °C	4	10	240 °C
e	285 °C	150 °C	4	10	200 °C
f	300 °C	200 °C	4	10	250 °C

and "pl" for a planar one, such as phenyl or naphthyl or a linear group such as alkinyl or nitrile.

The configurational assignment as depicted in Fig. 1 has been proved by X-ray and NMR-spectroscopy[1]. Due to enantiomeric selectivity the A-diastereomer is formed preferentially. The acetals are suitable for GC and base line resolution was found in every case. Another method based on differential formation of diastereomeric esters has been described by *Horeau*[2].



(+)-MBF-OH



(+)-MBP-OH

Our method is extremly simple: 0.04 mmol (15 mg) of dimeric (+)-*MBF*-OH and 0.24 mmol of a secondary racemic alcohol are dissolved in 100 µl CH_2Cl_2, approximately 15 mg molecular sieve (0.4 nm, Merck 5708) and approximately 15 mg ion exchange resin (Amberlyst 15, strongly acid) are added. After standing for at least 15 min at room temperature the sample is ready for gas chromatography (Shimadzu GC-9A, 20 meter long FS-OV-101 capillary, N_2-flow: 50 ml/min, split ratio 100 : 1). In all

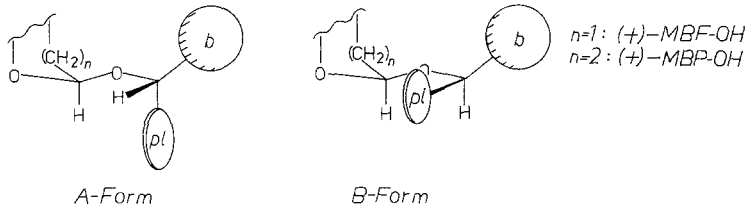


Fig. 1

cases of this preliminary investigation the A-form is formed predominantly from the racemate (Tab. 1).

Integration ratios of all the alcohols with a plain group exceeded 1.5 with the only exception of **8**. Electronegative substituents (**6**, **7**, and **8**) did not reverse the effect of building the A-diastereomer preferentially. Acetalisation with (+)-*MPB*-OH gave similar results.

For the configurational assignment of a single enantiomer another method is used if there is no racemate available. 1-Phenylethanol of unknown configuration and high optical purity was used to illustrate this method: 0.08 mmol of dimeric racemic *MBF*-OH and 0.08 mmol of 1-phenylethanol are dissolved in 100 µl CH_2Cl_2 and treated with molecular sieve and ion exchange resin as described above. The GC-peak with higher intensity and retention time belongs to one of the two possible enantiomers of the A-form [that is the acetal formed by (*S*)-phenylethanol and (—)-*MBF*-OH or the acetal formed by (*R*)-phenylethanol and (+)-*MBF*-OH]. As next step the same 1-phenylethanol is reacted with (+)-*MBF*-OH and if the product shows the same retention in GC as the higher peak, the *R*-configuration of the sample is proved. In a similar way, of course, (—)-*MBF*-OH can be used in this step.

Acetalisation is also useful for the determination of the enantiomeric excess. In this case the reaction is performed with an excess of alcohol as described above. Due to the enantiomeric selectivity no direct assay is possible but a calibration graph is required. If the decadic logarithm of the

ratio of the integrated GC-areas is plotted against the percentage of one enantiomer a straight line results between 10 and 90% in the case of 1-phenylethanol (Fig. 2).

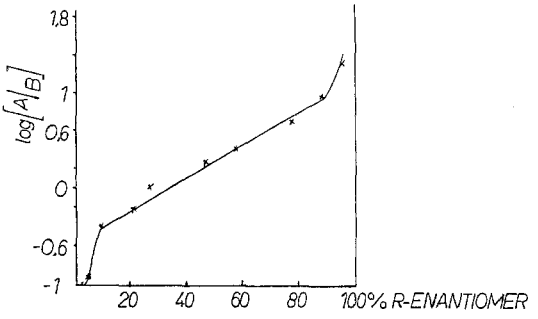


Fig. 2

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