Enantiomeric Odor Differences and Gas Chromatographic Properties of Flavors and Fragrances.

A Selected Review

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Flavors and fragrances are complex mixtures of volatile compounds and generally consist of hundreds of substances with different functionalities. Whereas the first era of flavor research was directed to the gas chromatographic analysis (GC, GC-MS) and stock-taking of all volatile constituents of complex flavor and fragrance extracts, the main efforts during the last decade have been focused on constitutional and stereochemical features, chemoreception and sensory relevance as well as biogenesis and biotechnological synthesis of sensory active compounds.[1-4]

The enantioselectivity of flavor compounds was still questioned as recently as 1982.[5] Meanwhile, chiral discrimination has been recognized as one of the most important principles in biological activity as well as odor perception.[6-8] As early as 1945, Prelog et al.[9] described the differences in the odor of the enantiomers (mirror image isomers) of androsta-4,16-dien-3-one; while the (+)-enantiomer, functioning as a sexual hormone of the boar, shows a strong sweaty, urine-like smell, the (–)-enantiomer is odorless to humans. Another classical example is the odor difference of the enantiomers of carvone, independently reported by two groups in 1970;[10,11] the (R)-(–)- and the (S)-(+)-enantiomer have the odor of caraway and spearmint, respectively. These odor differences were ignored or attributed to impurities, until Friedman and Miller showed in an elegant experimental scheme that synthetic (R)-(+)- and (S)-(–)-limonene could be interconverted, and still adhere to the characteristic pattern (Figure 1).[11] Since then, these studies have been extended to a large collection of enantiomeric pairs of volatile compounds.[2,12]

Although there is a variety of methods available for chirospecific analysis, gas chromatography (GC) is the preferred method for analysis of flavor compounds. The high

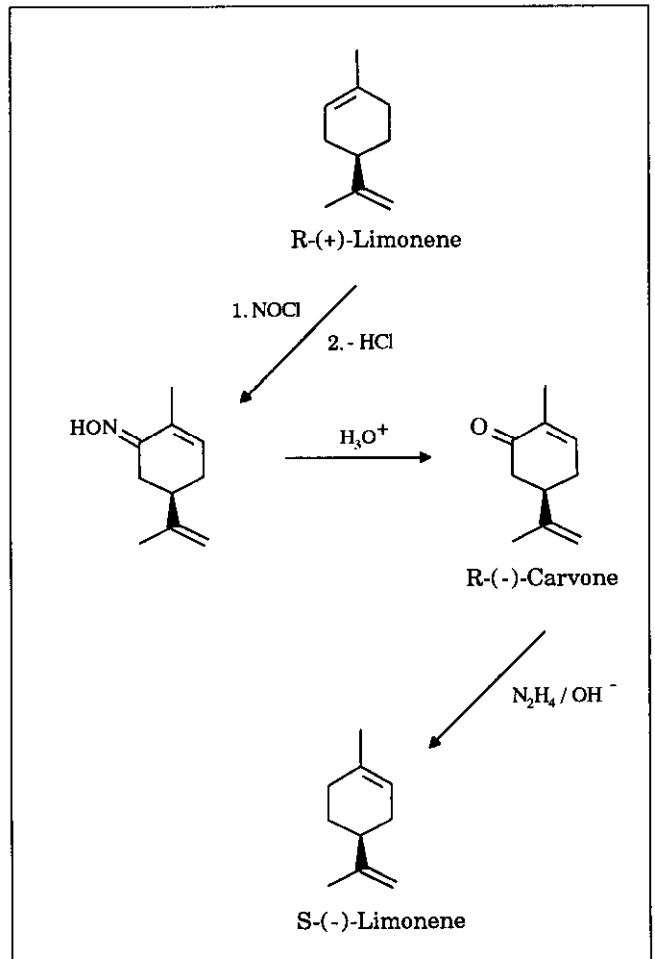

Figure 1. Conversion of (R)-(+)- into (S)-(–)-limonene (and *vice versa*) demonstrates that differences in odor are not to be traced back to impurities.

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resolution power of GC is particularly necessary to determine the enantiomeric composition in complex mixtures and to determine trace compounds with a very low odor threshold.[12]

There are two ways to analyze chiral flavor compounds by means of gas chromatography.[13]

- ***Indirect method:*** Derivatization of enantiomers using chiral derivatization agents (CDA). The diastereomeric derivatives formed can be separated on achiral stationary phases.
- ***Direct method:*** Gas chromatographic separation of the enantiomers on chiral stationary phases (CSP), which are of high, but not necessarily total, enantiomeric purity.

The indirect method has drawbacks, such as insufficient enantiomeric purity of the CDA, incomplete reaction of the CDA with the enantiomers, and racemization during the derivatization reaction. Therefore, the direct method has become the method of choice.

As early as 1966, Gil-Av, Freibush and Charles-Siegler demonstrated the success of this method with CSPs based on amino acid derivatives (amides) capable of hydrogen bonding.[14] This attracted great attention and several research groups optimized the enantiomeric separation on amide CSPs.[15-17] A restricted number of lactones[18,19] and terpenes[17] can be resolved on the polymeric amino acid phases L-Chirasil-Val[15] and D-Chirasil-Val.[20] In 1971, the introduction of metal coordination complexes as CSPs[21-23] extended the scope of enantiomer separation to many classes of compounds. The full potential of the methodology was reached in the 1980s. Shortly after the first reports on cyclodextrin CSPs had appeared,[24-26] several groups started to exploit this new type of "shape-recognition," for example, to separate the enantiomers of hydrocarbons and other simple molecules.[27-29]

According to our most recent investigation,[30] more than 230 different CSPs for GC were described in the literature, and more than 40 of them have been commercialized.

CHIRBASE

With the present state of knowledge, the mechanisms of enantiomer separation are seemingly unpredictable; one occasionally observes unusual chromatographic behavior, such as the inversion of the elution order, for instance, in a homologue series of flavor compounds[31] and for a given compound at different temperatures.[32] Thus, the separation factor α for a particular enantiomeric pair of analytes on a given CSP as well as the order of elution must be determined case by case, unless this information can be retrieved from more than a thousand articles published on this topic.

To cope with this challenge, the graphic molecular database CHIRBASE was created to store and retrieve chiral separation data. CHIRBASE is based on two software packages—ChemBase*[33-35] and the more recent ISIS/Base*[30]—which allow storage and retrieval of molecular structures and reactions on a personal computer. CHIRBASE attempts to cover all information published on the separation of enantiomers by gas chromatography (GC), supercritical fluid chromatography (SFC), and liquid chromatography (LC, HPLC). Additional sections on thin layer chromatography (TLC) and capillary electrophoresis (CE) are in progress.

Each database record has 32 fields of three types:

- ***Graphic fields*** for the molecular structures of both analyte and CSP.
- ***Numeric fields*** for separation data, e.g. the separation factor α, peak resolution R, and net retention times ($t'_{R(S)}$ and $t'_{R(R)}$).
- ***Text fields*** containing bibliographic data, compound names, commercial suppliers of CSPs, stereochemical descriptors, separation conditions and standard comments.

Each field may be retrieved and sorted by the built-in capabilities of ChemBase and ISIS/Base.

In practice, a substantial saving of experimental cost, for both working time and chromatographic equipment, may be expected from this approach. The structure and substructure querying functions, in particular, allow the plan-

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ning of the most promising separation experiments for a given pair of enantiomers. In many relevant examples, the target structure or at least an analogous structure may be retrieved in either one of the different sections of the database. In any case, CHIRBASE supports the selection of optimum chromatographic operation conditions, such as chromatographic method, stationary phase, column dimension, mobile phase, temperature, pressure, and, if necessary, allows the planning of suitable derivatization reactions.

In order to demonstrate the utility of the gas chromatography section of CHIRBASE for the enantioseparation of flavors and fragrances, we have chosen 17 important compounds out of four main classes of flavors and fragrances. These classes and compounds are listed in Table I along with the highest separation factor α reported.

The different odor characteristics of the single enantiomers of the selected compounds are compiled in Table II.[36-44] The benefit of CHIRBASE/GC in the selection of the most convenient chiral stationary phase is obvious.

For the selected 17 flavors and fragrances reviewed in this study, 478 separations using 71 different CSPs are reported in the database. Since this flood of information is beyond the scope of this article, we can only describe the gas chromatographic separation of limonene and γ-decalactone in detail; that data is shown in Tables III and IV.

Table I. Flavors and fragrances: Selected entries in CHIRBASE/GC with Maximum Resolution Factors (a)

Analyte	α	Entry No.
Acyclic carboxylic acid and alcohol derivatives		
2-Methylbutanoic acid	1.073	4203
Ethyl 2-methylbutanoate	1.027	4210
2-Ethylhexanoic acid	1.054	6059
1-Octen-3-ol	1.080	6564
Acyclic terpene derivatives		
Linalool	1.080	7848
(E)-Nerolidol	1.043	8265
(Z)-Nerolidol	1.005	3808
Cyclic terpene derivatives		
Limonene	1.261	3503
α-Terpineol	1.052	8440
Carvone	1.090	1743
α-Phellandrene	1.248	3502
Menthol	1.060	5527
(E)-a-Ionone	2.020	8169
Oxygen- and oxygen, sulphur-containing heterocyclic compounds		
γ-Decalactone	1.163	6963
(E)-Whiskey lactone	1.060	1824
(Z)-Whiskey lactone	1.021	1823
δ-Decalactone	1.040	1741
(E)-Theaspirane	1.065	3923
(Z)-Theaspirane	1.039	3924
(E)-2-Methyl-4-propyl-1,3-oxathiane	not published	3475
(Z)-2-Methyl-4-propyl-1,3-oxathiane	not published	3474

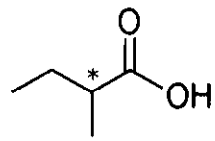
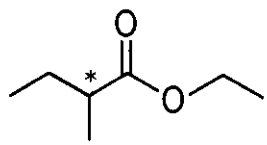
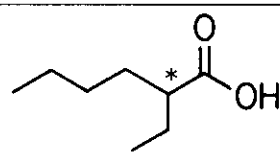
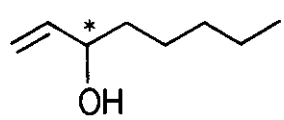
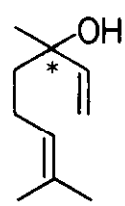
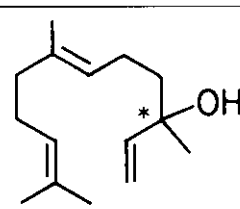
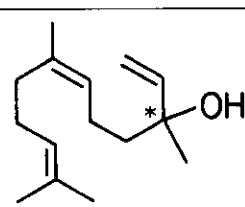
a : separation factor ($\alpha = k'_2/k'_1$)

Limonene

This colorless liquid belongs to the monoterpene hydrocarbons accounting for up to 90% of the plant volatiles. (R)-(+)-limonene is found with a concentration of over 90% in citrus peel oils. It is a by-product in the production of orange juice. A low concentration of (S)-(–)-limonene is found in oils from the *Mentha* species and conifers. Racemic limonene ("dipentene") possesses a lemon-like odor and is commercially used as fragrance material for perfuming household products.

Table III shows the different cyclodextrins used for the separation of limonene. König and co-workers investigated monoterpene hydrocarbons of spice oils using capillary columns coated with 6-O-methyl-2,3-di-O-pentyl-β-cyclodextrin and 6-O-methyl-2,3-di-O-pentyl-γ-cyclodextrin, both diluted in the polysiloxane OV-1701. The latter CSP showed a substantially higher separation factor α. The columns proved complementary properties. Peak identification was facilitated by the fact that the enantiomers eluted in reverse order from the two columns.[45] Monoterpene hydrocarbons of spruce phloem were examined by Roeraade and co-workers by fractionating the mixture for individual GC separation on α-cyclodextrin at 25°C.[46] Molecular modelling experiments on the chiral recognition in the selector-selectand system were performed by Kobor et al. for 2,3-di-O-methyl-6-O-tert.butyldimethylsilyl-β-cyclodextrin and permethylated-β-cyclodextrin, respectively. They concluded that the less flexible 2,3-di-O-methyl-6-O-tert.butyldimethylsilyl-β-cyclodextrin seems to possess advantages for certain separations of enantiomers, especially of the non-polar type.[47] In addition to investigations by Venema et al. on the effect of size and position of alkylated substituents on the separation ability of modified β-cyclodextrins,[48] König and co-workers compared the selectivity of a complete set of regio-selectively methylated and pentylated β- and γ-cyclodextrins.[49] Bicchi and co-workers compared the separation abilities of 2,6-di-O-methyl-3-O-pentyl-β-cyclodextrin and permethylated β-cyclodextrin, and described the influence of factors like the structure of the cyclodextrin derivatives, the polysiloxane ratio, and the minimum operating temperature on the reproducibility and life-time of the columns.[50] Likewise, the same authors evaluated the influence of column length and film thickness

Table II. Odor characteristics of separate enantiomers of 17 selected flavors and fragrances from four classes

Class	Structure	Odor description	Ref.
1	 **2-Methylbutanoic acid**	R-(–) penetrating, reminiscent of cheese and sweat S-(+) pleasant, sweet, elegant, fruity note	36
1	 **Ethyl 2-methylbutanoate**	R-(–) first medical, phenolic note, later sweet, fruity S-(+) ether-like, sweet, after dilution pleasant apple note	36
1	 **2-Ethylhexanoic acid**	R-(–) herbaceous, earthy S-(+) sweet, herbaceous, faint musty	37
1	 **1-Octen-3-ol**	R-(–) intensive mushroom note, fruity, soft S-(+) herbaceous, green, musty	36
2	 **Linalool**	R-(–) flowery-fresh, reminiscent of lily of the valley S-(+) differs slightly in odor	36
2	 **(E)-Nerolidol**	R-(–) pleasant, woody, warm, musty S-(+) slightly sweet, mild, soft, flowery different to (Z), less intensive	39
2	 **(Z)-Nerolidol**	R-(–) intensive, flowery, sweet, fresh S-(+) woody, green-like, fresh bark	39

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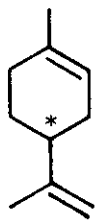
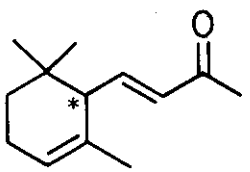
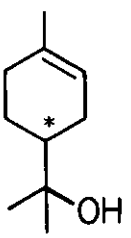
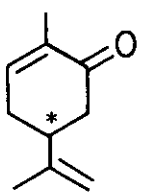
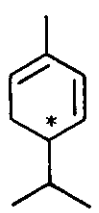
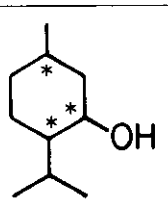
3	 **Limonene**	R-(+) fresh, pleasant, orange-like S-(–) faint mint note, turpentine note	36,37
3	 **α-Ionone**	R-(+) fine violet-like, fruity, flowery, raspberry-like S-(–) strong woody aspects, raspberry-like	5,38
3	 **α-Terpineol**	R-(+) strong, flowery sweet, lilac S-(–) tarry, reminiscent of cold pipe	36,37
3	 **Carvone**	R-(–) herbaceous odor, reminiscent of dill seeds S-(+) herbaceous odor, reminiscent of spearmint	36,40
3	 **α-Phellandrene**	R-(–) citrus odor, slight peppery note S-(+) weed-like, dill-like	36,40
3	 **Menthol**	R,R,S-(–) refreshing, mint note, cool S,S,R-(+) mint, phenolic note, medical note camphor, not refreshing	38

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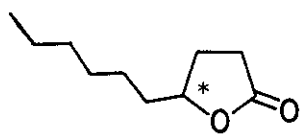
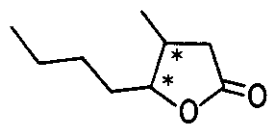
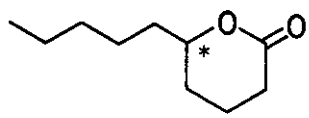
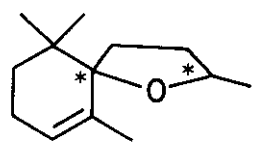
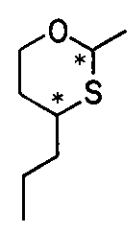
4	 γ-Decalactone	R strong fatty-sweet fruity note, some reminiscence to coconut, caramel S soft, sweet coconut note with fruity-fatty aspects	36
4	 Whiskey Lactone	3R,4S-(–) strong coconut note, reminiscent of celery 3S,4R-(+) piquant celery note, faint coconut note, green walnut note 3R,4R-(+) sweet woody, bright fresh coconut note 3S,4S-(–) faint coconut note, faint musty, earthy, remeniscent of hay	41
4	 δ-Decalactone	R-(+) sweet, fruity, milk note S-(–) sweet, fruity, peach note, fatty, butter-like	38
4	 Theaspirane	2R,5S-(–) highly attractive intense fresh-fruity 2S,5R-(+) naphthalene-like 2R,5R-(+) weak camphoraceous note 2S,5S-(–) fresh camphoraceous note	42,44
4	 2-Methyl-4-propyl-1,3-oxathiane	2R,4S-(–) sulfurous, herbaceous-green, roasty, linseed oil-like, onion 2S,4R-(+) sulfurous, fatty, fruity-green, tropical fruits, grapefruits 2R,4R-(–) green grass root, earthy, red radish note 2S,4S-(+) sulfurous, slight bloomy-sweet	41

on the separation using columns coated with 2,6-di-O-methyl-3-O-TFA derivatives of α-, β-, and γ-cyclodextrin, respectively, diluted in polysiloxanes.[44] Interestingly, although not unusual, a reversal of the elution order was observed with 6-O-methyl-2,3-di-O-pentyl-β-cyclodextrin instead of 6-O-methyl-2,3-di-O-pentyl-γ-cyclodextrin,[45] and also when α-cyclodextrin phases[46] were used instead of β- or γ-cyclodextrin phases.[53]

γ-Decalactone

In nature, γ- and δ-lactones are ubiquitous and have been isolated from all major food systems. Due to their mostly low odor thresholds averaging about 0.1 ppm, lactones often have a high flavor value. Whereas γ-lactones preferentially occur in plants, δ-lactones are mainly found in animal products. Usually, lactones are derived from straight-chain hydroxy fatty acids of varying chain length and only a few of them are branched.

γ-Decalactone (also called 4-decanolide) is present in a wide variety of foods. It is described as intensely fruity, reminiscent of peaches. In perfumery, γ-decalactone is used for heavy, fruity flower odors and in aroma composition in particular peach flavors.

The resolution of enantiomers of γ-lactones has been

Table III. Selected data from CHIRBASE/GC for limonene

Chiral Stationary Phase	Res	k'_1	α	First eluted	T (°C)	Carrier Gas	Ref.
6-O-Methyl-2,3-di-O-pentyl-γ-cyclodextrin	1.00	a	1.261	R	35	H_2	45
α-Cyclodextrin	0.85	3.68	1.123	S	25	He	46
2,3-Di-O-methyl-6-tert.butyldimethylsilyl-β-cyclodextrin	1.50	7.80	1.078	S	80	H_2	47
2,6-Di-O-methyl-3-O-pentyl-γ-cyclodextrin	a	a	1.046	a	70	a	49
3,6-Di-O-pentyl-2-O-methyl-β-cyclodextrin	a	a	1.043	a	40	a	49
2,3,6-Tri-O-methyl-β-cyclodextrin	2.01	a	1.037	S	70	H_2	64
2,3-Di-O-methyl-6-O-pentyl-β-cyclodextrin	a	a	1.032	a	50	a	49
2,3,6-Tri-O-methyl-β-cyclodextrin-5-oct-1-enyl-siloxane*	1.50	9.10	1.030	a	70	H_2	52
Permethyl-(S)-hydroxypropyl-β-cyclodextrin*	a	a	1.030	a	100	N_2	54
Permethyl-(S)-hydroxypropyl-α-cyclodextrin*	a	a	1.030	a	70	N_2	54
3,6-Di-O-methyl-2-O-pentyl-γ-cyclodextrin	a	a	1.027	a	50	a	49
6-O-Methyl-2,3-di-O-pentyl-β-cyclodextrin	a	a	1.026	S	35	H_2	45
2,6-Di-O-pentyl-3-O-methyl-β-cyclodextrin	1.00	a	1.019	S	60	H_2	55
2,3,6-Tri-O-pentyl-β-cyclodextrin*	a	a	1.018	S	70	H_2	56
2,3-Di-O-methyl-6-O-pentyl-γ-cyclodextrin	a	a	1.009	a	50	a	49
2,6-Di-O-methyl-3-O-pentyl-β-cyclodextrin	2.20	a	a	a	TP	a	50
β-Cyclodextrin	a	a	a	R	60	He	53
γ-Cyclodextrin	a	a	a	R	60	He	53
2,3,6-Tri-O-methyl-γ-cyclodextrin	a	a	a	a	TP	H_2	57
2,3,6-Tri-O-methyl-α-cyclodextrin	a	a	a	a	TP	H_2	57
2,6-Di-O-pentyl-3-O-methyl-γ-cyclodextrin	1.00	a	a	S	60	H_2	58
2,6-Di-O-methyl-3-O-TFA-α-cyclodextrin	a	a	a	a	a	a	51
2,6-Di-O-methyl-3-O-TFA-β-cyclodextrin	a	a	a	a	a	a	51
2,6-Di-O-methyl-3-O-TFA-γ-cyclodextrin	a	a	a	a	a	a	51
3,6-Di-O-methyl-2-O-pentyl-β-cyclodextrin	-	a	1.000	-	70	a	49
3,6-Di-O-pentyl-2-O-methyl-γ-cyclodextrin	-	a	1.000	-	70	a	49
2,3,6-Tri-O-n-butylcarbamate amylose	-	a	1.000	-	a	H_2	59

TP : temperature programming
* : commercial phase
a : not published
k'_1 : net retention time
α : separation factor ($\alpha = k'_2/k'_1$)
Res : resolution, set to unity for baseline resolution

widely investigated. Out of these, we selected γ-decalactone, in order to demonstrate the abundance of enantioselective GC analysis published in this area (Table IV). Several modified β-cyclodextrins were found to be suited for the separation of γ-lactones.[60-64] The best separation factor α was produced by the polysiloxane-anchored 2,6-di-O-methyl-3-O-TFA-β-cyclodextrin phase reported by Schurig et al.[60] The performance of this CSP was superior to solutions of 2,6-di-O-methyl-3-O-TFA-β-cyclodextrin diluted in OV-1701.[60] Almost comparably high α-values were achieved with permethylated β-cyclodextrin.[61] Bicchi and co-workers investigated 2,6-di-O-methyl-3-O-TFA-γ-cyclodextrin for the separation of γ-lactones.[68] They found a remarkable behavior in the elution order of the homologues (γ-C5 - γ-C12). Until C7 γ-lactone, the S-enantiomer eluted first, while from C8 to C12 γ-lactones the R-enantiomer was first.[68] Similar results were published by Schreier and co-workers for δ-lactones.[75] Bicchi tried to give a tentative explanation of this phenomenon proposing that the size of the side chain in these lactones had an influence on the effectiveness of their interaction with the cyclodextrin.[68] Fellous et al. reported on a mixture of maltosyl α-, β-, and γ-cyclodextrins (6/3/1) as CSP for a series of homologous 4-alkyl-γ-lactones (methyl to octyl) with the R-enantiomer eluting prior to S.[69] A more mechanistic view on the separation behavior of different cyclodextrin derivatives for γ-

Table IV. Selected Data from CHIRBASE/GC for γ-Decalactone

Chiral Stationary Phase	Res	k'_1	α	First eluted	T (°C)	Carrier Gas	Ref.
2,6-Di-O-methyl-3-O-trifluoroacetyl-β-cyclodextrin-monokis-6-O-(oct-7-enyl)-polysiloxane	1.00	10.49	1.163	a	170	H_2	60
2,6-Di-O-pentyl-3-O-trifluoroacetyl-γ-cyclodextrin*	1.00	7.10	1.060	a	140	N_2	65
2,6-Di-O-pentyl-3-O-acetyl-β-cyclodextrin*	1.00	a	1.052	R	150	He	62
2,6-Di-O-methyl-3-O-trifluoroacetyl-β-cyclodextrin	1.54	9.88	1.050	a	170	N_2	63
2,6-Di-O-pentyl-3-O-acetyl-α-cyclodextrin*	a	a	1.035	R	170	H_2	66
2,6-Di-O-methyl-3-O-acetyl-β-cyclodextrin*	1.69	a	1.035	a	170	H_2	64
2,6-Di-O-pentyl-3-O-phenylcarbamate-β-CD	0.18	10.10	1.020	a	170	N_2	70
Polysiloxane funct. with L-valine tert.butyl-amide*	0.14	6.48	1.010	a	150	N_2	70
2,3,6-Tri-O-methyl-β-cyclodextrin*	1.00	20.25	a	a	TP	H_2	61
2,6-Di-O-pentyl-3-O-butyryl-γ-cyclodextrin*	1.00	10.00	a	a	TP	H_2	61
2,6-Di-O-methyl-3-O-trifluoroacetyl-γ-cyclodextrin	4.42	26.00	a	R	TP	H_2	68
Permethyl-(α/β/γ)-cyclodextrin (6/3/1)	1.00	8.37	a	R	TP	H_2	69
2,3-Di-O-acetyl-6-O-tert.butyldimethylsilyl-α-cyclodextrin	9.00	a	a	R	TP	H_2	71
2,6+1-Di-O-pentyl-3-O-acetyl-α-cyclodextrin	4.80	a	a	a	TP	H_2	72
2,6-Di-O-methyl-3-O-pentyl-β-cyclodextrin	1.70	a	a	a	TP	a	67
2,6-Di-O-methyl-3-O-trifluoroacetyl-α-cyclodextrin	1.30	a	a	a	TP	a	51
2,6-Di-O-pentyl-3-O-butyryl-α-cyclodextrin	1.00	a	a	R	TP	H_2	58
2,3-Di-O-acetyl-6-O-tert.butyldimethylsilyl-γ-cyclodextrin	0.85	a	a	a	TP	H_2	71
2,3-Di-O-pentyl-6-O-acetyl-α-cyclodextrin	a	a	a	a	TP	H_2	71
2,3,6-Tri-O-methyl-α-cyclodextrin	a	a	a	a	TP	H_2	57
2,3,6-Tri-O-methyl-γ-cyclodextrin	a	a	a	a	TP	H_2	57
2,3-Di-O-acetyl-6-O-tert.butyldimethylsilyl-β-cyclodextrin	a	a	a	R	TP	H_2	73
2,6-Di-O-methyl-3-O-pentyl-β-cyclodextrin (OV-225)	-	a	1.000	-	TP	a	67
2,3,6-Tri-O-pentyl-β-cyclodextrin*	-	a	1.000	-	TP	He	74
2,6-Di-O-pentyl-3-O-methyl-β-cyclodextrin	-	a	1.000	-	a	a	50
2,6-Di-O-pentyl-3-O-isopropylcarbamate-β-cyclodextrin	-	13.60	1.000	-	170	N_2	70
2,6-Di-O-pentyl-3-O-propylcarbamate-β-cyclodextrin	-	12.20	1.000	-	170	N_2	70

TP : temperature programming
* : commercial phase
a : not published
k'_1 : net retention time
α : separation factor ($\alpha = k'_2/k'_1$)
Res : resolution, set to unity for baseline resolution

and δ-lactones was reported by Mosandl and co-workers. They examined inversion-modified cyclodextrins,[71] arguing that a polar group in the 2- and/or 3-position was crucial for the enantioselectivity of the cyclodextrins for γ/δ-lactones, while the size of the cavity was also considered an important factor. Other modified cyclodextrins were examined by Mosandl et al.[71,73] and Bicchi et al.[51] The last-named reported a decrease in the resolution power of a column coated with 2,6-di-O-methyl-3-O-TFA-α-cyclodextrin dissolved in OV-1701-OH after one month. Takeichi et al. reported a relatively poor resolution from columns coated with carbamate derivatives of β-cyclodextrin.[70]

Summary

Enantiomers of flavors and fragrances show characteristic differences in odor and taste; thus, the enantiomer composition is an important property that should be determined by analytical resolution on a chiral stationary phase in gas chromatography. The graphical database CHIRBASE provides a fast and direct access to the molecular structures of both analytes and stationary phases, and all information required to immediately reproduce separation experiments.

With two examples we have demonstrated the mounting number of papers on the subject of enantiomer separation. The crucial information on this subject is increasingly spread

into many journals, and often incomplete. In order to keep track of all separations published, CHIRBASE is being maintained by a number of scientists committed to this task. The user can find all relevant information within a few seconds. We illustrated this with a table (Table I, created with the Tablemaker of ChemBase) which summarizes some typical flavor and fragrance compounds, along with the highest separation factors α reported. It shows that in recent years, at least one satisfactory solution has been found for most of the relevant separation tasks in this field.

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