Stereoisomeric Flavor Compounds. 20.[1] Structure and Properties of γ-Lactone Enantiomers

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Racemic 4-hydroxyalkanoic acid isopropyl esters were transferred to diastereomeric (4*R*,4*S*)-[(*R*)-(2-phenylpropionyl)oxy]alkanoic acid isopropyl esters (**11**,**11′**–**20**,**20′**) and to diastereomeric (4*R*,4*S*)-[(1*S*,4*R*)-camphanoyloxy]alkanoic acid isopropyl esters (**21**,**21′**–**30**,**30′**), respectively, which were separated by liquid chromatography. The absolute configurations were derived from ^{1}H NMR data of **11**–**20** and **11′**–**20′** and optical activity could be estimated after hydrolysis and recyclization to optically active lactones **1**–**10** and **1′**–**10′**. From **21**–**30** and **21′**–**30′** optically pure stereoisomers of **1**–**10** and **1′**–**10′** have been obtained on a preparative scale. Sensoric characteristics of the optically pure γ-lactones are given.

It is well established that chiral discrimination is an important principle of odor perception (Ohloff, 1986; Russell and Hills, 1971; Friedman and Miller, 1971). Therefore, the evaluation of structure–function relationships of naturally occurring chiral flavor compounds is of fundamental interest.

The present study is devoted to the description of enantiomeric (diastereomeric) γ-lactones, which are pleasant, widespread aroma components of fruits. In spite of the importance of γ-lactones as natural flavor constituents, the chiroptical and sensory properties of their enantiomers are rather unknown (Masuda and Nishimura, 1981; Mosandl et al., 1986; Günther and Mosandl, 1986; Günther and Mosandl, 1987).

EXPERIMENTAL SECTION

Materials. Optically pure (*R*)-(−)-2-phenylpropionic acid (I) and (1*S*,4*R*)-camphanoic acid (II) were synthesized, according to the literature [Helmchen and Schmierer (1976) and Gerlach (1968, 1978), respectively]. Racemic, aroma-relevant γ-lactones were purchased or synthesized (Günther, 1988).

Gas–Liquid Chromatography. A Hewlett-Packard 5830 and a DANI 6500 gas chromatograph with FID, equipped with fused silica columns DB 210-30W (30 m) and SE 54 (25 m), 0.32-mm i.d., were used; for conditions, see Synthesis and Separation of Compounds.

Gas–Liquid Chromatography—Mass Spectrometry. A Carlo-Erba HRGC 5160 coupled to a Finnigan MAT ion trap detector 700 was available. The apparatus was equipped with fused silica columns DB 210-30W (30 m) or SE 54 (25 m), 0.32-mm i.d. Conditions: ion source temperature, 230 °C; electron energy, 70 eV.

NMR Spectral Analyses. NMR spectra were recorded on Bruker AC 200 (200 MHz), WM 300 (300 MHz), and WM 400 (400 MHz) instruments. Samples were run in C_6D_6 ($CDCl_3$) with Me_4Si as internal standard.

IR Spectral Analyses. The IR spectra were measured as a smear on sodium chloride plates with a Beckman IR 4240 spectrophotometer or by FT/IR with a Nicolet 20 SXB instrument.

Liquid Chromatography. Analytical method: Gilson, Model 303 with Gilson Holochrome UV/vis detector (190–600 nm); syringe loading sample injector, Model 7125 (Rheodyne). Preparative method: LEWA pump with maximum pump capacity 3.3 L/h; maximum pressure 160 bar, equipped with pulsation compensator and KNAUER filterphotometer, λ = 220 nm (254 nm).

Optical Rotation. Conditions: Zeiss Präzisionspolarimeter, ±0.005° accuracy; cells, 5 cm or 1 cm; solvent, CH_3OH (Uvasol, Merck); optical purity control, by HRGC (HPLC) methods (cf. Separation Conditions).

Synthesis and Separation of Compounds (Günther, 1988). (*1*) *Hydroxyalkanoic Acid Isopropyl Ester. General Procedure.* A sample of chemically pure, racemic γ-lactone is hydrolyzed by 1.1 mmol equiv of KOH (5% in methanol) at 20 °C overnight. The solvent is removed in vacuo, and the last traces of solvent are distilled with diethyl ether. The potassium salt of 4-hydroxyalkanoic acid is suspended in anhydrous dimethylformamide, 1.5 mol equiv of 2-brompropane is added, and the mixture is stirred at 20 °C. After 24 h, a second portion of 1.5 mol equiv of the reagent is added and stirring continued, until reaction is complete (HRGC control) (Table I).

Workup Conditions. If reaction control indicates complete reaction, water is added and the 4-hydroxyalkanoic acid isopropyl ester extracted by diethyl ether. The organic layer is dried with Na_2SO_4 and the solvent removed. Without further purification, the residue is converted to diastereomeric esters **2** and **3**.

(*2*) *Diastereomeric (4R,4S)-[(R)-(2-Phenylpropionyl)-oxy]alkanoic Acid Isopropyl Esters (11,11′-20,20′). General Procedure.* Optically pure (*R*)-(−)-2-phenylpropionic acid, $[\alpha]^{20}_D$ −80.8° (*c* 1.36, EtOH) and an excess of oxalyl chloride (1 mL of oxalyl chloride for 1 mmol of (*R*)-2-phenylpropionic acid) are stirred at 20 °C for 15 min (Helmchen and Schmierer, 1976). The excess oxalyl chloride is distilled in vacuo; last traces of the reagent are removed by distillation with anhydrous benzene. The freshly prepared (*R*)-2-phenylpropionic acid chloride is diluted with CCl_4 and at once reacted with 1 mol equiv of 4-hydroxyalkanoic acid isopropyl ester and 1 mol equiv of 4-(dimethylamino)pyridine (DMAP) as a catalyst in CCl_4 solution under N_2 atmosphere (20 °C, 3 h).

Workup Conditions. Water is added and the solution quantitatively extracted with diethyl ether. The organic layer is dried with Na_2SO_4 and solvent removed in vacuo and purified by LC on silica (63–200 μm); eluent petroleum ether/diethyl ether (95:5) (Table II).

(*3*) *Diastereomeric (4R,4S)-[(1S,4R)-Camphanoyloxy]-alkanoic Acid Isopropyl Esters (21,21′-30,30′). General Procedure.* A 7-mmol (1.39-g) portion of (1*S*,4*R*)-camphanoic acid is stirred with 20 mL of $SOCl_2$, freshly distilled, at 82 °C for 2 h. Excess thionyl chloride is removed by distillation with dry benzene. The residue of camphanoyl chloride is dissolved in 20 mL of CCl_4, and equimolar amounts of DMAP are added. 4-Hydroxyalkanoic acid

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[1] Part 19: Gessner et al. (1987). Dedicated to Professor Dr. C. H. Brieskorn, Würzburg, FRG, on the occasion of his 75th birthday.

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Table I[a]

lactone racemates	t_R, min: lactone	t_R, min: 4-hydroxyalkanoic acid isopropyl ester	HRGC condition
γ-pentalactone (1,1′)	1.91	3.27	A
γ-hexalactone (2,2′)	2.12	3.31	B
γ-heptalactone (3,3′)	2.83	4.33	B
γ-octalactone (4,4′)	4.08	5.55	B
γ-nonalactone (5,5′)	7.43	10.51	A
γ-decalactone (6,6′)	6.37	7.89	B
γ-undecalactone (7,7′)	12.03	14.91	A
γ-dodecalactone (8,8′)	8.79	10.11	B
β-methyl-γ-pentalactone, cis (9,9′)	2.55	3.99	A
β-methyl-γ-pentalactone, trans (10,10′)	2.25	3.85	A

[a] HRGC conditions: A, SE 54, 90°, rate 5°/min; B, SE 54, 90°, rate 10°/min. t_R = retention time. FID detector.

Table II. Analytical Purity Control

(a) HRGC (11,11′–14,14′, 19,19′, 20,20′)[a]

I (4R)	t_R, min	II (4S)	t_R, min
SE 54, 90 °C, rate 10 °C/min			
11	10.84	11′	11.04
12	11.31	12′	11.51
13	11.98	13′	12.05
14	13.07	14′	13.15
15	13.87	15′	13.87
16	14.71	16′	14.71
17	15.78	17′	15.78
18	16.46	18′	16.46
19	11.16	19′	11.33
20	11.21	20′	11.32
no resolution: 15,15′–18,18′			
DB 210-30W, 140 °C, 2 min isothermal, rate 2 °C/min to 245 °C maximum			
11	17.72	11′	18.57
12	19.90	12′	20.47
13	21.86	13′	22.30
14	24.84	14′	25.09
15	27.86	15′	27.97
16	30.97	16′	30.97
17	34.05	17′	34.05
18	36.96	18′	37.10
19	19.29	19′	20.12
20	19.76	20′	20.44
no resolution: 16,16′–18,18′			

(b) HPLC (15,15′–18,18′)[b]

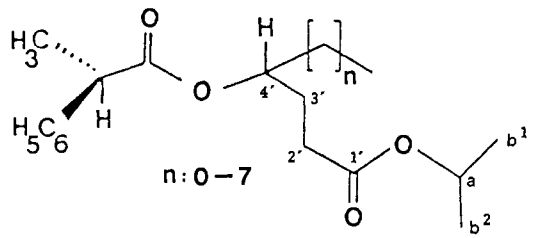
I (4R)	t_R, min	II (4S)	t_R, min	R_s
11	18.7	11′	19.8	0.3
12	13.2	12′	14.0	0.7
13	11.0	13′	12.1	1.1
14	9.8	14′	10.5	1.1
15	10.1	15′	11.2	1.2
16	9.0	16′	10.0	1.2
17	8.4	17′	9.5	1.3
18	8.1	18′	9.3	1.3
19	15.6	19′	16.5	
20	12.8	20′	13.4	

[a] Order of elution on SE 54, DB 210–30W, SiO_2 phases if (R)-2-phenylpropionic acid as a chiral auxiliary is used: 11–18, first peak (4R); 11′–18′, second peak (4S). 19 (cis), first peak (3R,4R); 19′ (cis), second peak (3S,4S). 20 (trans), first peak (3S,4R); 20′ (trans), second peak (3R,4S). Separation conditions (11,11′–20,20′): preparative LC on SiO_2 (15–25 μm), eluent petroleum ether/diethyl ether (96:4); p = 6.5 bar, flow 46 mL/min; detection, λ = 254 nm. [b] Conditions: SiO_2 7 μm, eluent petroleum ether/diethyl ether (96:4); flow 2.5 mL/min, p = 30 bar; detection, λ = 220 nm; R_s = resolution. Base-line resolution ($R_s \geq 1.5$) is not achieved by this HPLC method.

isopropyl ester (5.5 mol) dissolved in CCl_4 is added dropwise, and the mixture is stirred for 2 h (20 °C).

Workup Conditions. Water (20 mL) is added and the solution quantitatively extracted by 4 × 50 mL portions of diethyl ether. The organic layer is washed with water and dried with Na_2SO_4 and the solvent removed in vacuo (Table III).

Chart I. Trans Conformation of Diastereomeric (R)-2-Phenylpropionic Acid Esters



(4) Hydrolysis of Diastereomers and Recyclization. General Procedure. After preparative LC and analytical purity control (cf. methods 2–4), the chromatographically pure diastereomers 11–20, 11′–20′, 21–30, and 21′–30′ were hydrolyzed and recyclized to optically pure γ-lactone stereoisomers in the following manner: Hydrolysis of the diastereomer by addition of 2 mol equiv of KOH in methanol and stirring (20 °C, 24 h). The solvent is thoroughly removed by vacuo and the residue treated with HCl (5 mL of 3 N HCl for 1 mmol of stereoisomer) at 50 °C for 24 h.

Workup Conditions. The solution is saturated with $(NH_4)_2SO_4$ and extracted quantitatively with diethyl ether. Organic layers are washed with water and dried by Na_2SO_4 and solvent is removed by vacuo. Purification: LC on silica (63–200 μm), eluent petroleum ether/diethyl ether (95:5, 90:10, 85:15).

(5) Chiral Identity. Absolute configurations of the chiral γ-lactones were elucidated by ^1H NMR behavior of their (R)-2-phenylpropionic acid diastereomers 11–20 and 11′–20′, referring to Helmchen (1976). This method is well established and based on chemical shift differences for protons with equivalent constitution. The shift differences result from the upfield shift by the phenyl ring of the acid moiety, because trans conformation is preferred by the diastereomers in the NMR solution (Chart I).

This method proves the (4R)-(+) and (4S)-(−) configurations of the investigated chiral γ-lactones (Table IV). Specific rotation values of the optically active lactones were not taken from these products, because a partial racemization (up to 5%) of the chiral reagent (R)-2-phenylpropionic acid chloride, influenced by the basic catalyst DMAP during esterification, cf. method 2, cannot be excluded. But the estimation of specific optical rotation of the γ-lactones from the diastereomers 21–30 and 21′–30′ yields reliable values for optically pure lactones (cf. Tables V and VI).

Absolute configurations of the diastereomers 21–30 and 21′–30′ were concluded from the optical activity of their

Table III. Analytical Purity Control

(a) HRGC (21,21′–30,30′)[a]

t_R, min		t_R, min	
SE 54, 90 °C, rate 10 °C/min			
21	13.26	**21′**	13.31
22	13.98	**22′**	13.98
23	14.60	**23′**	14.60
24	15.32	**24′**	15.32
25	16.09	**25′**	16.09
26	16.83	**26′**	16.83
27	17.78	**27′**	17.78
28	18.31	**28′**	18.31
29	14.29	**29′**	14.39
30	14.09	**30′**	14.23
no resolution: **22,22′–28,28′**			
DB 210–30W, 140 °C, 2 min isothermal, rate 2 °C/min to 180 °C; rate 1 °C/min to 245 °C maximum			
21	45.53	**21′**	46.50
22	48.71	**22′**	48.92
23	51.91	**23′**	52.17
24	56.13	**24′**	56.52
25	60.75	**25′**	61.13
26	65.44	**26′**	65.87
27	70.25	**27′**	70.66
28	75.13	**28′**	75.51
29	52.77	**29′**	54.24
30	53.45	**30′**	55.51

(b) HPLC (21,21′–30,30′)

	t_R, min		t_R, min	R_s
		SiO_2 Phase[b]		
21	15.6	**21′**	15.9	
22′	11.8	**22**	12.6	0.5
23′	10.1	**23**	11.1	0.8
24′	9.1	**24**	10.0	0.9
25′	9.0	**25**	10.0	1.0
26′	8.4	**26**	9.2	1.0
27′	8.2	**27**	9.1	1.0
28′	8.0	**28**	8.9	1.1
		CN Phase[c]		
21	12.2	**21′**	14.7	1.5
22	10.8	**22′**	12.1	1.1
23	9.8	**23′**	10.8	1.1
24	9.4	**24′**	10.6	1.3
25	9.2	**25′**	10.4	1.3
26	8.7	**26′**	9.9	1.3
27	8.6	**27′**	9.8	1.3
28	8.4	**28′**	9.5	1.3
29	11.8	**29′**	14.7	1.6
30	12.8	**30′**	17.4	1.7

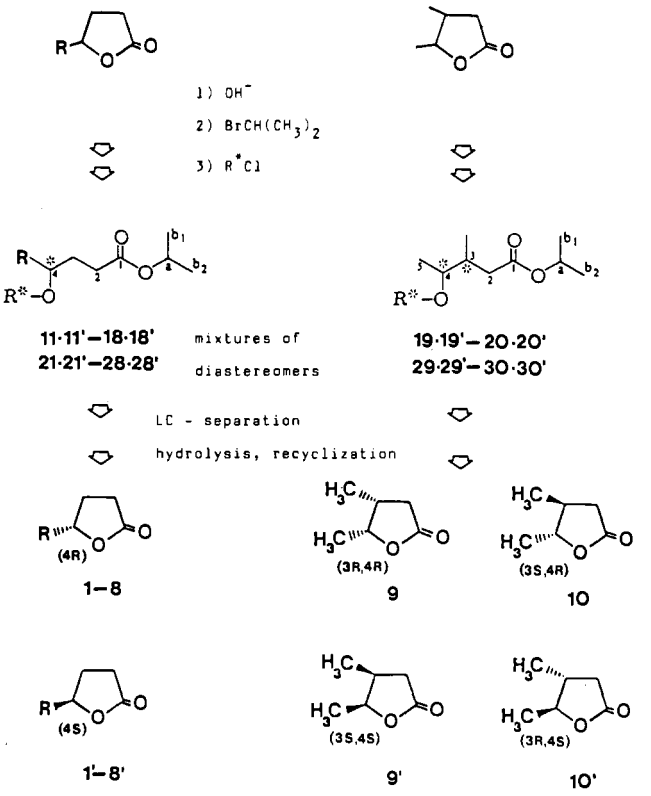
[a] Order of elution on SE 54, DB 210-30-W, CN phases, if (1*S*,4*R*)-camphanoic acid as a chiral auxiliary is used: **21–28**, first peak (4*S*); **21′–28′**, second peak (4*R*). **29**, first peak (3*S*,4*S*); **29′**, second peak (3*R*,4*R*). **30**, first peak (3*R*,4*S*); **30′**, second peak (3*S*,4*R*). Note: The order of elution is inverted in the cases of **22,22′–28,28′**, if the SiO_2 phase is used: first peak (4*R*), second peak (4*S*). The alternative application of CN or SiO_2 phases is a suitable method to check the purity of the higher homologues of diastereomers. Separation conditions (**21,21′–30,30′**): preparative LC on Lobar–B (Merck); 310 × 25 mm (three columns, close to one another, loaded with LiChroprep CN, 40–60 μm), eluent petroleum ether/diethyl ether (80:20); p = 7.5 bar, flow 48 mL/min; detection, λ = 220 nm. [b] Conditions: SiO_2 7 μm; eluent petroleum ether/diethyl ether (85:15), flow 2.5 mL/min, p = 30 bar; detection, λ = 220 nm; R_s = resolution. [c] Conditions: CN phase 5 μm; eluent petroleum ether/diethyl ether (85:15), flow 2.6 mL/min, p = 40 bar; detection, λ = 220 nm.

corresponding γ-lactones, according to method 5.

(6) *Optical Purity Control.* (*i*) *Hydrolysis and recyclization*, method 5, occurs without any racemization (Günther and Mosandl, 1986).

(*ii*) *Reductive cleavage of γ-lactones* with $LiAlH_4$ yields chiral 1,4-diols. Their stereodifferentiation via diastereomeric diesters with (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid by HPLC (Gessner et al., 1987) and via (*S*)-*O*-acyllactic acid esters (Deger et al., 1988) are well documented. The γ-lactones **1–10** and **1′–10′** are proved to be optically pure by these methods (ee ≥ 99.8%).

Scheme I. Procedure to Optically Pure γ-Lactones



(7) *Sensory Description.* It was carried out by a panel of experts. For evaluation of sensory characteristics we are indebted to Messrs. Dragoco, Gerberding & Co., GmbH, 3450 Holzminden, FRG, who smelled and tasted solutions of γ-lactone enantiomers (cf. Tables V and VI).

RESULTS AND DISCUSSION

Spectral data of the investigated compounds are given in this paper only in extracts. Comprehensive documentation of all spectral data (IR, $^1H/^{13}C$ NMR, MS) are published elsewhere (Günther, 1988).

^1H NMR chemical shifts of diastereomeric (*R*)-2-phenylpropionic acid esters **11–20** and **11′–20′**, which are decisive for structure elucidation, are outlined in Table IV.

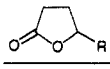
In a previous paper it was demonstrated the method to transfer 3-methyl-4-octanolide (Quercus or Whiskylactone) into diastereomeric esters of 4-hydroxy-3-methyloctanoic acid isopropyl ester, which were separated by liquid chromatography. Subsequent hydrolysis and relactonization were proved to be without any racemization (Günther and Mosandl, 1986). In this paper the procedure is extended to all aroma-relevant γ-lactones (Scheme I). Starting from racemic γ-lactones, 4-hydroxyalkanoic acid isopropyl esters were synthesized by ring opening of the lactone with KOH in methanolic solution and alkylating the corresponding carboxylates with 2-bromopropane in dimethylformamide. With suitable chiral acid chlorides (I, II) diastereomeric esters were synthesized, which were separated by LC to yield pure diastereomeric esters. Absolute configurations were elucidated from ^1H NMR data of the stereochemically pure (4*R*)- and (4*S*)-[(*R*)-(2-phenylpropionyl)oxy]alkanoic acid isopropyl esters **11–20** and **11′–20′**, respectively. The pure stereoisomers, obtained by liquid chromatography, were hydrolyzed by KOH in

Table IV. Significant ^1H NMR Chemical Shifts of Diastereomeric (*R*)-2-Phenylpropionic Acid Esters 11–20 and 11′–20′ (400 MHz, C_6D_6, Me_4Si Internal Standard)

	a-H (sept, 1 H)	2-H (t, J = 7.5 Hz, 2 H)	3-H (m, 2 H)	b_1/b_2-H (2 d, J = 6 Hz, 6 H)	H_3C terminal (t (d), J = 7 Hz, 3 H)
11	4.93	1.89	1.69–1.52	1.03, 1.01	0.98
11′	5.01	2.12	1.76–1.62	1.05, 1.04	0.84
12	4.96	1.93	1.74–1.60	1.05, 1.02	0.71
12′	5.02	2.16	1.78–1.71	1.08, 1.06	0.52
13	4.98	1.94	1.76–1.61	1.06, 1.02	0.76
13′	5.03	2.18	1.82–1.75	1.08, 1.06	0.64
14	4.98	1.96	1.78–1.62	1.06, 1.03	0.79
14′	5.03	2.20	1.82–1.74	1.09, 1.07	0.69
15	4.98	1.97	1.80–1.64	1.05, 1.02	0.83
15′	5.04	2.21	1.84–1.78	1.08, 1.06	0.78
16	4.97	1.96	1.79–1.63	1.06, 1.03	0.87
16′	5.03	2.20	1.84–1.75	1.09, 1.07	0.85
17	4.99	1.97	1.81–1.65	1.06, 1.02	0.90
17′	5.05	2.22	1.85–1.77	1.09, 1.06	0.90
18	4.97	1.96	1.80–1.63	1.06, 1.06	0.91
18′	5.03	2.20	1.84–1.76	1.09, 1.09	0.91

	a-H (sept, 1 H)	2-H (dd, 1 H)	2-H (dd, 1 H)	3-H (m, 1 H)	b_1/b_2-H (2 d, J = 6 Hz, 6 H)	5-H (d, J = 6.5 Hz, 3 H)
19	4.98	2.03 (15, 5.5 Hz)	1.77 (15, 8.5 Hz)	2.08	1.04, 1.01	0.96
19′	5.02	2.25 (15, 5.5 Hz)	1.95 (15, 8.5 Hz)	2.16	1.05, 1.04	0.83
20	4.97	2.14 (15, 4.5 Hz)	1.82 (15, 9 Hz)	2.09	1.03, 1.01	0.98
20′	5.02	2.28 (15, 4.5 Hz)	1.97 (15, 9 Hz)	2.16	1.06, 1.04	0.83

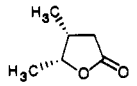
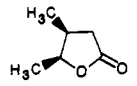
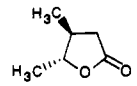
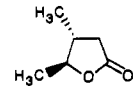
Table V. Structure and Properties of 4-Alkyl-Substituted γ-Lactones

 R		config	$[\alpha]^{20}_D$ (*c* 1.5–2.5, CH_3OH)	sensory characteristics: odor: soln (1%, propylene glycol), tested by smelling strips	sensory characteristics: taste: solns in invert sugar (10%) + 0.015% citric acid[a]
1	C_1	4*R*	+37.6	faint, sweet	(A) (B) sweet, caramel (C) sweet, spicy
1′		4*S*	−38.0	nearly odorless	(A) (B) sweet, caramel (C) sweet, spicy
2	C_2	4*R*	+56.3	faint, sweet coconut with a fatty-herbaceous hay note	(A) (B) herbaceous
2′		4*S*	−56.5	sweet, creamy coconut, with some woody aspects	(A) (B) herbaceous
3	C_3	4*R*	+59.4	sweet, spicy, herbaceous hay note, reminiscent of coumarin	(A) (B) coconut, faint sweet, nutty
3′		4*S*	−59.1	fatty, coconut note, with fruity-sweet aspects, less intens than 3	(B) coconut, faint sweet, nutty
4	C_4	4*R*	+56.2	spicy-green, coconut note, with almond notes	(A) coconut (B) coconut, extremely sweet
4′		4*S*	−56.6	fatty, coconut note less intense than 4	(A) coconut (B) coconut, extremely sweet more intense than 4
5	C_5	4*R*	+51.8	strong, sweet, soft coconut with fatty-milky aspects	(A) coconut (B) coconut
5′		4*S*	−51.6	fatty, moldy, weak coconut note less intense than 5	(A) coconut, more intense than 5 (B) coconut, less intense than 5
6	C_6	4*R*	+48.5	strong, fatty-sweet fruity note, some reminiscence to coconut, caramel	(A) (B) creamy, peach note
6′		4*S*	−48.1	soft, sweet coconut note with fruity-fatty aspects	(A) (B) creamy, peach note
7	C_7	4*R*	+45.3	strong, fatty-sweet, reminiscent of peach, with some bloomy aspects	(A) sweet, caramel (B) sweet, lactone character
7′		4*S*	−45.8	fatty-sweet aldehyde note less intens than 7	(A) sweet, caramel (B) sweet, lactone character
8	C_8	4*R*	+42.2	strong, fruity-sweet, bloomy note with aldehyde and woody aspects	(A) fruity-sweet, peach, apricot lactone character (B) sweet peach note
8′		4*S*	−42.6	fatty-fruity, milky note less intense than 8	(A) fruity-sweet lactone (B) less intense than 8

[a] Key (ppm): A, 1; B, 10; C, 20.

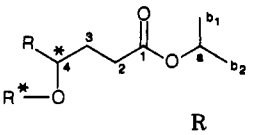
methanol and recyclized to optically active γ-lactones. This method proves the (4*R*)-(+), (4*S*)-(−) configuration of the investigated γ-lactone antipodes (Table VII). The diastereomers (4*R*)- and (4*S*)-[(1*S*,4*R*)-camphanoyloxy]-alkanoic acid isopropyl esters have been synthesized and separated by liquid chromatography on a preparative scale

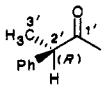
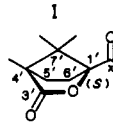
Table VI. Structure and Properties of 3,4-Dimethyl γ-Lactone Isomers

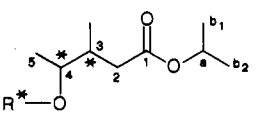
	confign	$[\alpha]^{20}_D$ (c 1.5–2.5, CH_3OH)	odor: soln (1% propylene glycol), tested by smelling strips	taste: solns in invert sugar (10% + 0.015% citric acid[a]
 9	3R,4R	+59.8	faint, sweet hay note	(A) (B) herbaceous, raw potatoes
 9′	3S,4S	−60.2	faint, fatty-nutty moldy note	(A) (B) similar to 9, less intense
 10	3S,4R	+69.1	faint, fatty-spicy note	(A) (B) paint sweet, caramel
 10′	3R,4S	−68.7	faint spicy, fatty-fruity note	(A) (B) similar to 10

[a] Key (ppm): A, 1; B, 10; C, 20.

Table VII. Diastereomeric Esters of 4-Hydroxyalkanoic Acid Isopropyl Esters with (R)-2-Phenylpropionic Acid (I) and (1S)-Camphanoic Acid (II) (Cf. Separation Conditions, Experimental Section)



R*	R: C_1		C_2		C_3		C_4		C_5		C_6		C_7		C_8	
 I	11 (4R)	11′ (4S)	12 (4R)	12′ (4S)	13 (4R)	13′ (4S)	14 (4R)	14′ (4S)	15 (4R)	15′ (4S)	16 (4R)	16′ (4S)	17 (4R)	17′ (4S)	18 (4R)	18′ (4S)
 II	21 (4S)	21′ (4R)	22 (4S)	22′ (4R)	23 (4S)	23′ (4R)	24 (4S)	24′ (4R)	25 (4S)	25′ (4R)	26 (4S)	26′ (4R)	27 (4S)	27′ (4R)	28 (4S)	28′ (4R)



I	19 (3R,4R)	19′ (3S,4S)	20 (3S,4R)	20′ (3R,4S)
II	29 (3S,4S)	29′ (3R,4R)	30 (3R,4S)	30′ (3S,4R)

on silica and CN phases (21–30, 21′–30′). The stereochemical purity of the separated diastereomers was proved by HRGC (HPLC) methods, and optically pure γ-lactones have been obtained on a preparative scale.

Sensory Evaluation of Optically Pure γ-Lactones (1–10, 1′–10′). Stereoisomeric flavor compounds not only differ in their odor quality but also often exhibit tremendous differences in their odor thresholds (Acree et al., 1985). In this respect, optical isomers of highest enantiomeric purity (ee ≥ 99.5 %) have to be assumed for the description of their structure–function relationships.

At present, the described derivatization of alkyl-substituted γ-lactones to diastereomers of 4-hydroxyalkanoic acid isopropyl esters with subsequent separation by liquid chromatography and relactonization is the most reliable method to generate optically pure γ-lactones, as they are needed for sensory evaluation. Nevertheless, the description of sensory experiences remains incomplete in principle. Attempts to characterize sensory properties of the synthesized γ-lactone enantiomers are outlined in Tables V and VI. These results are evaluated qualitatively by standard test methods:

4-Alkyl-substituted γ-lactone enantiomers exhibit characteristic differences in odor quality as well as odor intensity. The (4R)-configurated antipodes are responsible for the pleasant, natural fruity, aroma note. Their tastes are mainly characterized by differences in intensity (Tables V and VI). Besides the chirality of the γ-lactone, the size of the alkyl side chain in the 4-position plays a key role in sensory activity. The series of (4R)-configurated γ-octa-, γ-nona-, and (4R)-γ-dodecalactones exhibit the highest sensory activity, whereas (4R)-γ-pentalactone is less intense (odor threshold ≈20 ppm). Asymmetric reduction of 4-oxoalkanoic acids by baker's yeast predominantly yields (4R)-configurated γ-lactones with increasing size of the alkyl side chain. Within the series γ-hexalactone to

γ-dodecalactone, the yeast reduction product is nearly optically pure and (4*R*)-configurated (Gessner et al., 1987). For the case of 3,4-dimethyl γ-lactone the odor activity depends on geometric as well as optical isomerism (Table VI). The (4*S*)-configurated isomer is much more intense as the (4*R*)-isomer in both the cis and trans series. This means that chirality is of special importance for odor intensity. On the other hand, odor quality seems to be mainly influenced by geometric isomerism. While the odor quality of 3,4-dimethyl γ-lactone stereoisomers is different between the cis and trans series, the intensities of taste within cis and trans series, respectively, are comparable.

Research on chirality evaluation of natural occurring γ-lactones in fruits is still under investigation.

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Registry No. 1, 58917-25-2; 1′, 19041-15-7; 2, 63357-95-9; 2′, 41035-07-8; 3, 88270-38-6; 3′, 31323-51-0; 4, 107797-24-0; 4′, 107797-25-1; 5, 63357-96-0; 5′, 63357-97-1; 6, 107797-26-2; 6′, 107797-27-3; 7, 74568-06-2; 7′, 74568-05-1; 8, 69830-91-7; 8′, 69830-92-8; 9, 90026-55-4; 9′, 80009-59-2; 10, 90026-46-3; 10′, 110171-22-7; 11, 118437-75-5; 11′, 118437-76-6; 12, 118437-77-7; 12′, 118437-78-8; 13, 118437-79-9; 13′, 118437-80-2; 14, 118437-81-3; 14′, 118437-82-4; 15, 118437-83-5; 15′, 118437-84-6; 16, 118437-85-7; 16′, 118437-86-8; 17, 118437-87-9; 17′, 118437-88-0; 18, 118437-89-1; 18′, 118437-90-4; 19, 118437-91-5; 19′, 118492-34-5; 20, 118492-35-6; 20′, 118492-36-7; 21, 118437-92-6; 21′, 118492-37-8; 22, 118437-93-7; 22′, 118492-38-9; 23, 118437-94-8; 23′, 118492-39-0; 24, 118437-95-9; 24′, 118492-40-3; 25, 118437-96-0; 25′, 118492-41-4; 26, 118437-97-1; 26′, 118492-42-5; 27, 118437-98-2; 27′, 118492-43-6; 28, 118437-99-3; 28′, 118492-44-7; 29, 118438-00-9; 29′, 118492-45-8; 30, 118492-46-9; 30′, 118492-47-0; I, 7782-26-5; II, 13429-83-9; II (acid chloride), 39637-74-6; isopropyl (±)-4-hydroxypentanoate, 118438-01-0; isopropyl (±)-4-hydroxyhexanoate, 118438-02-1; isopropyl (±)-4-hydroxyheptanoate, 118438-03-2; isopropyl (±)-4-hydroxyoctanoate, 118438-04-3; isopropyl (±)-4-hydroxynonanoate, 118438-05-4; isopropyl (±)-4-hydroxydecanoate, 118438-06-5; isopropyl (±)-4-hydroxyundecanoate, 118438-07-6; isopropyl (±)-4-hydroxydodecanoate, 118438-08-7; 2-bromopropane, 75-26-3; (*R*)-2-phenylpropionic acid chloride, 36240-11-6.

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Volatile Components of Bittermelon

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Volatile components of bittermelon (*Momordica charantia* L.) fruit and bittermelon vines were identified by gas chromatography–mass spectrometry. Major constituents were myrtenol, *cis*-hex-3-enol, benzyl alcohol, pent-1-en-3-ol, *cis*-pent-2-enol, and *trans*-hex-2-enal. *cis*-Sabinol was identified as a naturally occurring compound. Bittermelon volatiles are attractive to the melon fly, *Dacus cucurbitae*.

Bittermelon, *Momordica charantia* L., is a major host for the melon fly, *Dacus cucurbitae* Coquillett (Diptera: Tephridae). In Hawaii, bittermelon was more frequently infested by this fly than watermelon, squash, tomato, and cucumber, other major hosts (Harris et al., 1986). In Taiwan, the population density of melon flies in a bittermelon field was greater than in litchi, pear, loquat, and grape fields (Fang and Chang, 1984), and the population buildup of the melon fly in Punjab was bolstered by bittermelon (Bains and Sidhu, 1984).

Our study of bittermelon volatile compounds was undertaken because we seek to identify compounds attractive to the melon fly for use in population monitoring and control programs.

There is no previous study of bittermelon volatiles, but

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