126. Conformational Analysis of Open-Chain 1,2:3,4-Diepoxides: Comparison of Crystal Structures, NMR Data, and Molecular-Orbital Calculations

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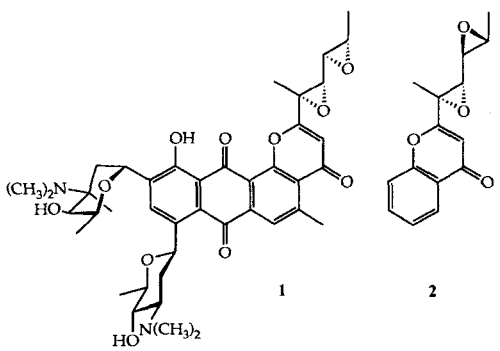
Dedicated to Professor Dr. *Christoph Tamm* on the occasion of his 70th birthday

(18.V.93)

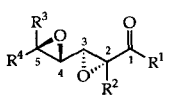
Several pairs of diastereoisomeric open-chain 1,2:3,4-diepoxides with different substitution patterns were prepared (see **3**–**9**). As far as possible, crystal structures were determined to corroborate the relative configurations and to give insight into the solid-state conformations of these compounds. The comparison with our earlier molecular-orbital calculations and with ^{1}H-NMR measurements shows that the solid-state conformations of eight out of the nine open-chain 1,2:3,4-diepoxides, whose crystal structures had been determined, correspond to minima on the calculated energy profiles for these compounds or for closely related derivatives. In solution, highly substituted diepoxides of the *erythro*-series (*e*-**6**, *e*-**7**, *e*-**9**) seem to prefer the same conformation as in the crystal. The solution conformations of all other diepoxides differ from the arrangement in the solid state.

Introduction. – Hedamycin (**1**) is an antitumor-active antibiotic of the pluramycin type [3] and contains the rare 1,2:3,4-diepoxy-1-methylpentyl side chain. It was first isolated by *Schmitz et al.* from *Streptomyces griseoruber* [4]. The constitution and configuration of **1** were determined in our laboratory by chemical and spectroscopic means [5] [6] and were eventually confirmed by an X-ray crystallographic analysis [7], which also supplied conformational information about **1**.



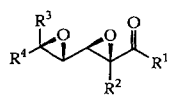
1

2



erythro-series

	R^1	R^2	R^3	R^4
e-**3**	MeO	H	H	Me
e-**4**	NH_2	H	H	Me
e-**5**	MeO	Me	H	Me
e-**6**	MeO	Me	Me	Me
e-**7**	NH_2	Me	Me	Me
e-**8**	MeO	Et	*t*-Bu	H
e-**9**	NH_2	Et	*t*-Bu	H



threo-series

	R^1	R^2	R^3	R^4
t-**3**	MeO	H	H	Me
t-**4**	NH_2	H	H	Me
t-**5**	MeO	Me	H	Me
t-**6**	MeO	Me	Me	Me
t-**7**	NH_2	Me	Me	Me
t-**8**	MeO	Et	*t*-Bu	H
t-**9**	NH_2	Et	*t*-Bu	H

[1]) From the Ph. D. thesis of *D. B.* [1].

[2]) From the Ph. D. thesis of *M. N.* [2].

In the course of our investigation of the photochemical behavior of **1** [8], the 2-substituted 4*H*-chromen-4-one **2** was synthesized as a model compound [9]. Whereas the constitution of the side chains in **1** and **2** were the same, they differed in their relative configurations. An X-ray structure analysis of **2** revealed that in **1** and **2** the side chains showed virtually the same conformations in terms of C–C–C–C torsion angles, apparently irrespective of the different relative configurations [10]. The torsion angles along the inter-epoxide bond in the solid-state conformations were −108° in **1** and −89° in **2**[3]). The question arose whether all similarly substituted open-chain 1,2:3,4-diepoxides[4]) adopt more or less the same conformation independent of their relative configurations. Recent molecular-orbital calculation for the gas phase [11] indicated that this is not necessarily the case. For *threo*-compounds[5]), two stable conformations with dihedral C–C–C–C angles of *ca.* 90 and *ca.* 270° were predicted from these calculations, whereas for *erythro*-compounds, three stable conformations with corresponding angles of *ca.* 90, *ca.* 180, and *ca.* 270° were found (more highly substituted compounds show only two stable conformations). To get additional insight into the conformational behavior of 1,2:3,4-diepoxides and for comparison with the results of the MO calculations, we synthesized suitable pairs of diastereoisomeric model compounds with different substitution patterns.

Selection and Synthesis of the Model Compounds. – The polycyclic nuclei of **1** and **2** were replaced in our model compounds by the simpler methyl carboxylate or amide functions. Seven pairs of diastereoisomeric diepoxides, *e*/*t*-**3**–**9**, were prepared. Thus, methyl sorbate (= methyl hexa-2,4-dienoate) was epoxidized with 3-chloroperbenzoic acid (3-$ClC_6H_4CO_3H$) to give in a rather low yield a mixture of *e*- and *t*-**3**, which could be separated by chromatography (*Florisil*). Ammonolysis of these two esters with 6M NH_3/MeOH gave the crystalline amides *e*- and *t*-**4**. Similarly, the two esters *e*- and *t*-**5** were obtained from the corresponding methyl dienoate [5]. *Reformatsky* condensation [12] of 3-methylbut-2-en-1-al (**10**) and methyl 2-bromopropionate (**11**) yielded a 1:1 mixture of the diastereoisomeric esters **12a**/**b** (*Scheme 1*), which was then dehydrated with P_2O_5 to a mixture of the hexadienoates **13** and **14**. The latter was refluxed in CH_2Cl_2 with 3-$ClC_6H_4CO_3H$ for 5 days [13]; a 3:2 mixture of the desired diepoxy esters *e*- and *t*-**6** was formed in 90% yield. When the epoxidation was carried out at room temperature [14], only the 4,5-double bond was oxidized, the product being the monoepoxy ester **15**. Ammonolysis of *e*- and *t*-**6** gave the amides *e*- and *t*-**7**, respectively. For the synthesis of the diepoxides *e*/*t*-**8** and *e*/*t*-**9** (*Scheme 2*), a dienoate with a (*Z*) double bond, **16**, was needed. It was obtained – together with **17** – from the corresponding ester **18** with the triple bond by hydrogenation over *Lindlar* catalyst [15]. Epoxidation of **16** gave the esters *e*- and *t*-**8**, which were again converted to the corresponding amides *e*- and *t*-**9** by ammonolysis.

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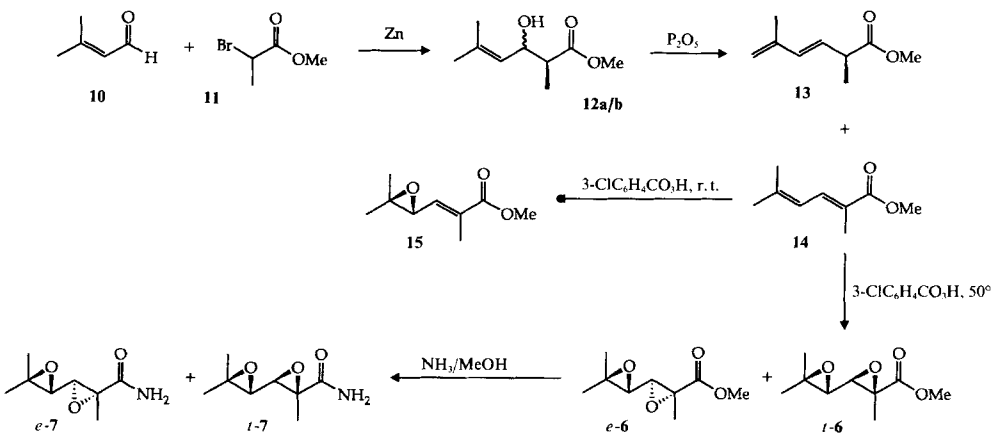
[3]) The signs of the dihedral angles (torsion angles) are given in accordance with IUPAC recommendations (*i.e.* positive for clockwise rotation, see rule E-5.4).

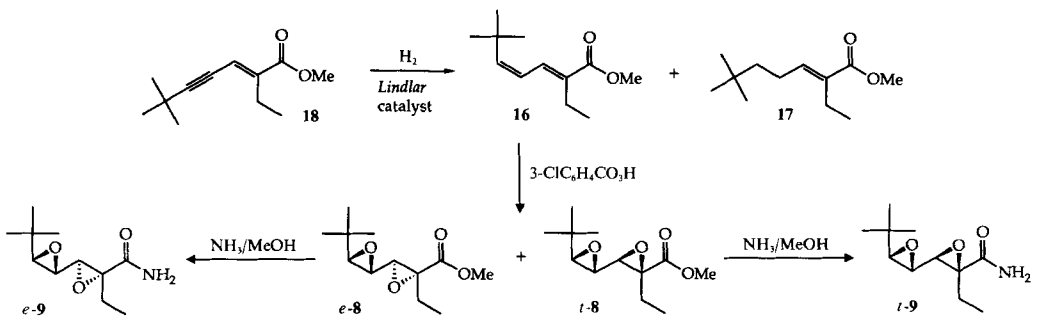
[4]) We call diepoxides 'open-chain' diepoxides, if they are not part of a larger ring system.

[5]) The terms *'erythro'* and *'threo'* (and the prefixes *'e'* and *'t'* of key numbers) are used depending on whether the C-atoms involved in the inter-epoxide bond have the same relative configurations as C(2) and C(3) in erythrose or threose, respectively.

Scheme 1



Scheme 2



The unselective epoxidation of the dienoates with 3-ClC$_6$H$_4$CO$_3$H always led to mixtures, which in general proved to be rather difficult to separate. Due to the very similar chromatographic behavior of the diastereoisomers, only small amounts of pure compounds could be obtained; quite a large portion of mixed fractions remained. The advantage of this procedure was, however, that both diastereoisomeric diepoxides were readily available, which was of importance for our conformational studies.

Conformational Analysis and Discussion. – Since the solid-state conformations of **1** and **2** as revealed in their crystal structures were the starting point of this investigation of the conformational behavior of 1,2:3,4-diepoxides, we tried to get information about the *solid-state conformation* of as many of the model compounds synthesized as possible. Crystals suitable for X-ray structure determinations were obtained from *e*- and *t*-**4**, *e*-**6**, *e*- and *t*-**7**, and *e*- and *t*-**9** (see *Figs. 1–7* and *Exper. Part*).

Fig. 1. *Crystal structure of* e-**4** (stereoview)

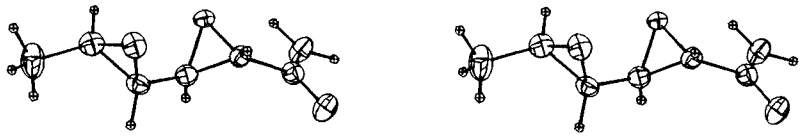


Fig. 2. *Crystal structure of* t-**4** (stereoview)

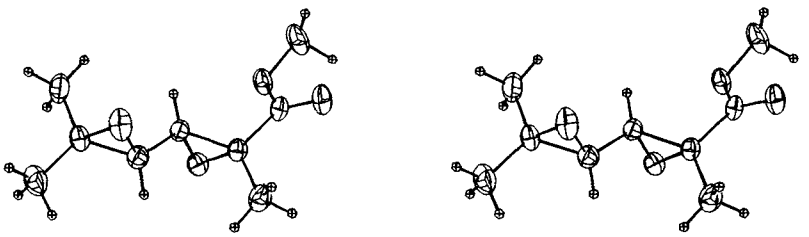


Fig. 3. *Crystal structure of* e-**6** (stereoview)

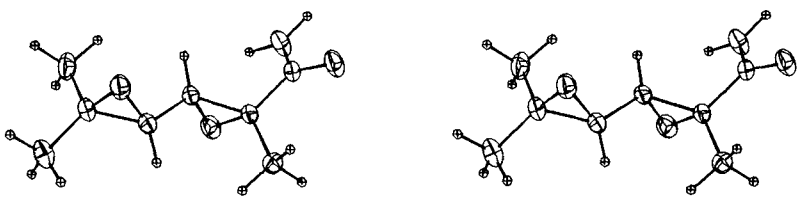


Fig. 4. *Crystal structure of* e-**7** (stereoview)

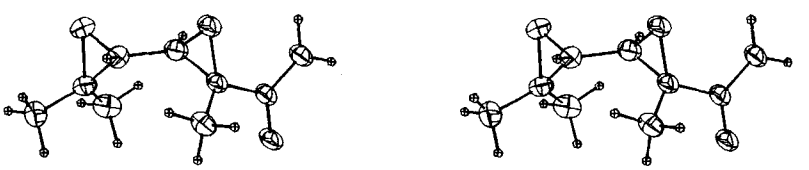


Fig. 5. *Crystal structure of* t-**7** (stereoview)

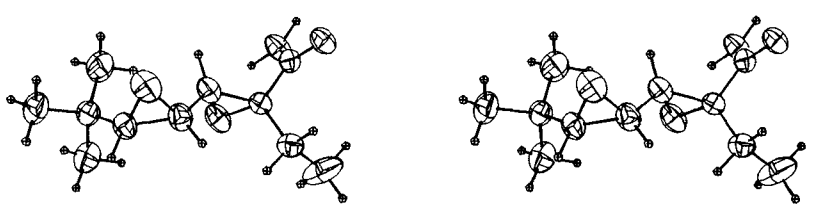


Fig. 6. *Crystal structure of* e-**9** (stereoview)

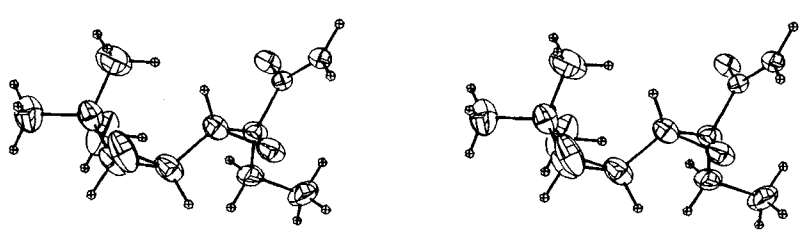


Fig. 7. *Crystal structure of* t-**9** (stereoview)

All six structures with amide groups have the characteristic H-bonding scheme shown in *Fig. 8*. In addition, short contacts between neighboring amide protons and epoxide or carbonyl O-atoms can be observed in various combinations. Two of the structures involve disordered solvent molecules. Thus, the crystals of *e*-**9** contain one molecule of cyclohexane per asymmetric unit with conformational disorder (interchanging boat and chair). The crystals of *t*-**7** contain one molecule of acetone which is located in a channel formed by H-bonded amide groups. There is no indication of a H-bonding which would have helped to stabilize the thermal disorder of the solvent molecule. Restraints for bond lengths and angles were used to define the geometries of the solvent molecules.

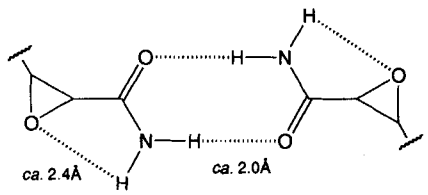
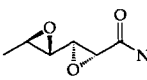
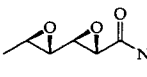
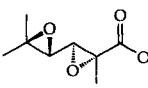
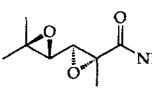
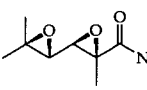
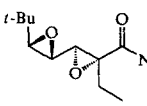
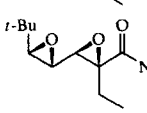


Fig. 8. *Schematic representation of the hydrogen bonding observed in the crystals of* e/t-**4**, e/t-**7**, *and* e/t-**9**

Besides giving insight into the conformations of the respective compounds, the crystal structures also allowed an unambiguous assignment of the relative configurations within pairs of diastereoisomers, a task which is otherwise very difficult to accomplish (*cf. e.g.* [5]). The C–C–C–C torsion angles along the inter-epoxide bond are compiled in *Table 1*. In no one of the three pairs of diastereoisomers were these torsion angles the same in both isomers, which again suggested that the very similar arrangement found in **1** and **2** was a coincidence. The C(2)–C(3)–C(4)–C(5) torsion angles measured for compounds *e*- and *t*-**4**, *e*-**6**, *t*-**7**, and *e*- and *t*-**9** as well as for **1** and **2** correspond quite well to energy minima obtained from the molecular-orbital calculations for each of these compounds or corresponding models [11]. This correspondence astonishingly fails completely for *e*-**7**. With *e*-**4**, *t*-**7**, and *e*- and *t*-**9** the crystal conformation even corresponds to the absolute minimum on the respective energy profile. It is further noteworthy that the solid-state conformation of the methyl ester *e*-**6** is virtually the same as that of the corresponding amide *e*-**7**.

The *conformation in solution* can be assessed through measurement of the NMR coupling constants between the protons attached to the two C-atoms involved in the inter-epoxide bond (*i.e.* H–C(3) and H–C(4)). This vicinal ^{1}H,^{1}H-coupling constant is correlated to the corresponding H–C–C–H torsion angle through the *Karplus*-like equation $^3J(H,H) = 2.99 - 2.11\cos\phi + 3.05\cos 2\phi$ that was recently derived for 1,2:3,4-diepoxides [16]. The comparison of the coupling constants obtained from the dihedral angles observed in the crystal conformations by applying this equation with those actually observed in the ^{1}H-NMR spectra (see *Table 1*) shows that the agreement is satisfactory for compounds *e*-**6** and *e*-**9**, somewhat less for *e*-**7**, but quite poor for *e*- and *t*-**4**, *t*-**7**, and *t*-**9**. This is an indication that at room temperature, these latter compounds adopt conformations in solution that differ from those in the crystal. Most probably, several favorable conformations are in a rapid equilibrium by rotation around the inter-epoxide bond; in the ^{1}H-NMR spectrum, an averaged coupling constant is then observed.

Table 1. *Dihedral Angles Obtained from X-Ray Structure Analyses and H,H-Coupling Constants*

Compound	Dihedral angles [°]		^3J(H–C(3),H–C(4)) [Hz]	
	C(2)–C(3)–C(4)–C(5)	H–C(3)–C(4)–H	calc.[a])	found[b])
 *e*-**4**	–178 (182)	–179	8.1	3.6
 *t*-**4**	104	52	1.0	5.0
 *e*-**6**	178	177	8.1	7.3
 *e*-**7**	–171 –163	–173 –163	8.0 7.5	6.7
 *t*-**7**	–103 (257)	–159	7.2	4.7
 *e*-**9**	–145 (215)	–150	6.3	5.6
 *t*-**9**	–94 (266)	–153	6.6	4.9

[a]) Calculated from the dihedral angle using the *Karplus*-like equation according to [16] (see text).
[b]) Measured at *ca.* 25° in $CDCl_3$; estimated error: ± 0.3 Hz.

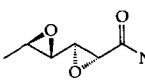
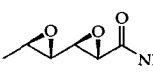
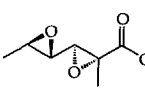
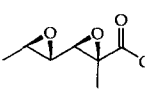
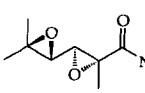
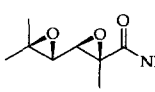
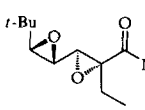
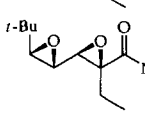
With compounds *e*- and *t*-**6**, and *e*- and *t*-**8**, ^{1}H-NMR measurements were carried out at various temperatures covering the range between –60 and +50°. No appreciable change of the pertinent coupling constant with the temperature could be observed, except for *e*-**6**, where it increased from 7.3 Hz at room temperature to 8.2 Hz at –60° [1]. At this temperature, the *transoid*-conformation found in the crystal seems also to be the predominant form in solution.

To check whether the results of the molecular-orbital calculations carried out for the gas phase [11] could also be used to predict to a certain extent the behavior of diepoxides in solution, the following procedure was applied: for each stable gas-phase conformation, the vicinal H,H-coupling constant was calculated using the *Karplus*-like equation (see above). These values were then weighted with the corresponding mole fractions obtained from the relative energies using the *Boltzmann* distribution and assuming that only the most stable conformations were present in solution to an appreciable amount. The 'averaged' coupling constants estimated in this way are compiled in *Table 2* together with the actually measured values. The estimated coupling constants agree remarkably well with the experimental values for all compounds of the *threo*-series as well as for the

less substituted members of the *erythro*-series (*e*-**4**, *e*-**5**). These facts, however, do not allow the conclusion that our molecular-orbital calculations carried out for the gas phase also represent the situation in solution. Due to the mirror symmetry of the *Karplus*-like equation (see above) with respect to $\phi = 180°$, the involvement of additional rotamers quite different from those predicted by the calculations can lead to the same experimental coupling constants.

Conclusion. – The comparison presented here shows that the molecular-orbital calculations [11] allow, indeed, a good prediction of the solid-state conformations of open-chain 1,2:3,4-diepoxides, since eight out of the nine crystal structures determined cor-

Table 2. *Comparison of H,H-Coupling Constants Obtained from Molecular-Orbital Calculations with Experimental Values*

Compound	Dihedral angles [°][a]		Relative energies[a] [kJ/mol]	^3J(H–C(3),H–C(4)) [Hz]	
	C(2)–C(3)–C(4)–C(5)	H–C(3)–C(4)–H		calc.[b]	found[c]
 *e*-**4**	70	69	1.8		
	186	185	0.0	4.5	3.6
	284	286	2.8		
 *t*-**4**	86	35	1.8		
	257	206	0.0	5.3	5.0
 *e*-**5**	179	180	0.0		
	275	278	4.3	6.9	6.5
 *t*-**5**	99	44	5.6		
	267	217	0.0	5.1	5.3
 *e*-**7**	92	86	1.5		
	254	258	0.0	0.4	6.7
 *t*-**7**	115	58	5.5		
	272	225	0.0	4.1	4.7
 *e*-**9**	110	107	0.1		
	230	236	0.0	2.1	5.6
 *t*-**9**	150	98	22.9		
	270	225	0.0	4.5	4.9

[a]) Computational methods: 6-31G*//3-21G for *e*/*t*-**4**, *e*/*t*-**5**, and *e*/*t*-**7**; 3-21G//AM1 for *e*/*t*-**9** (see [11]).
[b]) Calculated for 298 K; see text for mode of calculation.
[c]) Measured at *ca.* 298 K in $CDCl_3$; estimated error: ± 0.3 Hz.

respond to minima on the calculated energy profiles for these compounds or for closely related derivatives. Furthermore, we can conclude that highly substituted diepoxides of the *erythro*-series (*e*-**6**, *e*-**7**, *e*-**9**) seem to prefer the same *transoid*-conformation in solution as in the crystal. The solution conformations of all other diepoxides differ from the arrangement in the solid state.

We thank the *Swiss National Science Foundation* (grant No. 20-29817.90) and the *Ciba-Geigy-Jubiläums-Stiftung* for financial support.

Experimental Part

General. All solvents were distilled and dried. The reagents were of reagent grade and used without further purification. NH_3/MeOH (*ca.* 6M by titration) was obtained by dissolving gaseous NH_3 in MeOH. Org. extracts were dried (Na_2SO_4) and evaporated below 50°. TLC: silica gel *60* F_{254} (*Merck*). Column chromatography (CC): silica gel (35–70 μm, *Chemische Fabrik Uetikon*) or *Florisil* (*Fluka Chemie*); FC = flash chromatography. M.p.: *Kofler* hot stage; corrected. UV: λ_{max} (ε) in nm. IR: *Perkin-Elmer-781* or *Perkin-Elmer-1310* IR spectrometer; in cm^{-1}. NMR (*K. Aegerter, K. Ulrich*): *Bruker WH-90* (^1H, 90 MHz; ^{13}C, 22.63 MHz), *Bruker WP 200-SY* (^1H, 200 MHz), *Varian-Gemini-300* (^1H, 300 MHz; ^{13}C, 75 MHz), and *Varian VXR-400* (^1H, 400 MHz; ^{13}C, 101 MHz); ^{13}C: multiplicities, where listed, were determined by gated decoupling or off-resonance decoupling, otherwise APT experiments were performed; chemical shifts δ in ppm rel. to internal TMS (= 0 ppm), *J* in Hz; where necessary, assignments were corroborated by $^1H,^{13}C$-COSY. MS (Dr. *H. Nadig*, Dr. *J.-P. Stadelmann*): *VG-70-250* or *AEI-MS-9* spectrometer. GC/MS: *Hewlett Packard 5790A/5970A*.

*Methyl (2*RS,*3*SR,*4*SR,*5*RS*)- and (2*RS,*3*SR,*4*RS,*5*SR*)-2,3:4,5-Diepoxyhexanoate* (*e*- and *t*-**3**, resp). Methyl sorbate (25 ml, 0.20 mol; obtained from refluxing sorbic acid and MeOH in CCl_4 with a small amount of conc. H_2SO_4 for 10 h) and 55% 3-$ClC_6H_4CO_3H$ (186.5 g, 0.59 mol) were refluxed in 2 l of CH_2Cl_2 for 13 d at a bath temp. of 50°. After cooling to r.t., the 3-$ClC_6H_4CO_2H$ was removed by filtration and the soln. washed successively with 10% Na_2SO_3 soln. and 5% Na_2CO_3 soln., dried, and evaporated. The crude product (GC: methyl (2*E*,4*RS*,5*SR*)-4,5-epoxyhex-2-enoate (76%), *e*-**3** (12%), and *t*-**3** (12%) was submitted 3 times to FC (*Florisil*, cyclohexane/acetone 95:5): 90 mg of *e*-**3** as colorless platelets. Further successive FC's (*Florisil*, cyclohexane/acetone 95:5→90:10, CH_2Cl_2, or Et_2O (total of 9 columns)) finally gave 110 mg of *t*-**3** as a colorless oil.

Data of e-**3**: M.p. 47–48°. IR (KBr): 3000, 2950, 1740 (C=O), 1445, 1380, 1350, 1285, 1235, 1205, 1175, 1115, 990, 885, 830, 760, 740, 720. ^1H-NMR (400 MHz, $CDCl_3$): 3.78 (*s*, MeO); 3.44 (*d*, *J* = 1.8, H–C(2)); 3.18 (*dd*, *J* = 4.9, 1.8, H–C(3)); 3.02 (*qd*, *J* = 5.2, 2.1, H–C(5)); 2.70 (*dd*, *J* = 4.9, 2.1, H–C(4)); 1.35 (*d*, *J* = 5.2, Me(6)). ^{13}C-NMR (101 MHz, $CDCl_3$): 168.6 (C(1)); 56.8 (C(3)); 56.1 (C(4)); 53.4 (C(5)); 52.6 (MeO); 51.0 (C(2)); 17.0 (C(6)). EI-MS: 99 (43), 85 (7), 83 (10), 73 (6), 71 (73), 69 (38), 59 (37), 55 (19), 54 (6), 53 (6), 45 (100), 44 (9), 43 (74), 42 (18), 41 (27), 39 (17). CI-MS (NH_3): 177 (8, $[M + 19]^+$), 176 (100, $[M + 18]^+$), 159 (9, $[M + 1]^+$), 143 (7), 141 (17), 128 (5), 127 (35), 115 (8), 113 (6), 111 (20), 100 (9), 99 (39), 98 (5), 83 (10), 82 (6), 81 (7), 71 (6), 69 (20), 59 (14), 55 (13), 39 (6). Anal. calc. for $C_7H_{10}O_4$ (158.15): C 53.16, H 6.37; found: C 53.52, H 6.32.

Data of t-**3**: IR (film): 3000, 2960, 2930, 1750 (br., C=O), 1440, 1375, 1335, 1290, 1235, 1205, 1120, 1010, 990, 950, 895, 860, 755, 715, 650. ^1H-NMR (400 MHz, $CDCl_3$): 3.79 (*s*, MeO); 3.46 (*d*, *J* = 1.9, H–C(2)); 3.26 (*dd*, *J* = 4.0, 1.9, H–C(3)); 3.03 (*qd*, *J* = 5.2, 2.1, H–C(5)); 2.78 (*dd*, *J* = 4.0, 2.1, H–C(4)); 1.35 (*d*, *J* = 5.2, Me(6)). ^{13}C-NMR (101 MHz, $CDCl_3$): 168.7 (C(1)); 56.0 (C(3)); 55.9 (C(4)); 52.6 (MeO); 52.3 (C(5)); 50.4 (C(2)); 17.1 (C(6)). GC-MS: 127 (2), 115 (4), 101 (4), 99 (49), 85 (9), 83 (11), 82 (6), 73 (6), 71 (76), 70 (5), 69 (38), 68 (6), 59 (36), 57 (5), 55 (19), 54 (6), 53 (8), 45 (100), 44 (12), 43 (91), 42 (21), 41 (33). Anal. calc. for $C_7H_{10}O_4$ (158.15): C 53.16, H 6.37; found: C 53.22, H 6.48.

*(2*RS,*3*SR,*4*SR,*5*RS*)-2,3:4,5-Diepoxyhexanamide* (*e*-**4**). For 1 d, *e*-**3** (50 mg, 0.31 mmol) was left in 4 ml of *ca.* 6M NH_3/MeOH at r.t. After evaporation, the crude product was subjected to FC (*Florisil*, Et_2O/acetone gradient): 35 mg (77%) of *e*-**4** (95.5% pure according to GC). White solid. M.p. 123–127.5°. IR (KBr): 3375, 3190, 3010, 2970, 2930, 1670 (C=O), 1620, 1445, 1405, 1370, 1330, 1275, 1130, 1010, 950, 880, 850, 825, 760, 670, 620. ^1H-NMR ($CDCl_3$, 300 MHz): 6.10 (br. *s*, NH_2); 3.38 (*d*, *J* = 1.9, H–C(2)); 3.18 (*dd*, *J* = 3.6, 2.1, H–C(3)); 3.01 (*qd*, *J* = 5.2, 2.1, H–C(5)); 2.83 (*dd*, *J* = 3.6, 2.0, H–C(4)); 1.35 (*d*, *J* = 5.2, Me(6)). ^{13}C-NMR ($CDCl_3$, 75 MHz): 171.0 (C(1)); 57.6 (C(3)); 56.1 (C(4)); 53.2 (C(5)); 52.8 (C(2)); 17.1 (C(6)). EI-MS: 100 (4), 99 (48), 86 (20), 73 (11), 71 (67), 69 (13), 57 (5), 56 (14), 55 (35), 45 (92), 44 (100), 43 (69), 42 (11), 41 (18), 39 (13). CI-MS (NH_3): 162 (7,

$[M + 1 + NH_4]^+$), 161 (100, $[M + NH_4]^+$), 144 (15, $[M + 1]^+$), 128 (4), 126 (8), 112 (7), 100 (11), 44 (7). Anal. calc. for $C_6H_9NO_3$ (143.14): C 50.35, H 6.34, N 9.79, O 33.52; found: C 50.62, H 6.42, N 9.85, O 33.20.

*(2*RS*,3*SR*,4*RS*,5*SR*)-2,3:4,5-Diepoxyhexanamide* (*t*-**4**). For 5 h, *t*-**3** (50 mg, 0.31 mmol) was left in 2 ml of *ca.* 6M NH_3/MeOH at r.t. After evaporation, the crude product was submitted to FC (*Florisil*, Et_2O/acetone gradient). Recrystallization from CH_2Cl_2/Et_2O gave 35 mg (77%) of *t*-**4** (97.5% pure according to GC). White solid. M.p. 113.5–116.5°. IR (KBr): 3380, 3200, 3000, 2970, 2925, 1715, 1655, 1465, 1435, 1375, 1325, 1295, 1240, 1150, 1115, 1095, 1050, 1020, 950, 900, 850, 810, 740, 630. ^{1}H-NMR ($CDCl_3$, 400 MHz): 6.13 (*s*, 1 H, NH_2); 6.04 (*s*, 1 H, NH_2); 3.44 (*d*, *J* = 2.0, H–C(2)); 3.04 (*qd*, *J* = 5.2, 2.1, H–C(5)); 3.04 (*dd*, *J* = 5.0, 2.1, H–C(3)); 2.70 (*dd*, *J* = 4.9, 2.1, H–C(4)); 1.36 (*d*, *J* = 5.3, Me–C(5)). ^{13}C-NMR ($CDCl_3$, 101 MHz): 170.4 (*s*, C(1)); 57.4 (*d*, ^1J(H,C) = 186.0, C(3)); 56.6 (*d*, ^1J(H,C) = 176.9, C(4)); 52.4 (*d*, ^1J(H,C) = 179.2, C(2)); 52.3 (*d*, ^1J(H,C) = 174.1, C(5)); 17.0 (*q*, ^1J(H,C) = 127.3, C(6)). EI-MS: 149 (4), 100 (4), 99 (56), 73 (10), 71 (64), 69 (13), 57 (7), 56 (12), 55 (31), 45 (100), 44 (99), 43 (80), 42 (10), 41 (23), 39 (15). CI-MS (NH_3): 162 (7, $[M + 1 + NH_4]^+$), 161 (100, $[M + NH_4]^+$), 144 (6, $[M + 1]^+$), 100 (6), 44 (6).

*Methyl (2*RS*,3*SR*)- and (2*RS*,3*RS*)-3-Hydroxy-2,5-dimethylhex-4-enoates* (**12a**/**b**). Zn (29.4 g, 0.45 mol) was activated for 2 min with 2N HCl and then washed successively with H_2O, acetone, and benzene. It was suspended in dry benzene (300 ml), and then half of a mixture of 3-methylbut-2-en-1-al (**10** (*Fluka*); 35.5 g, 0.42 mol) and methyl 2-bromopropionate (**11**; 66.8 g, 0.40 mol) was added. After heating to reflux, the reaction started. Reflux was maintained by regulating the addition rate. When the addition was complete, the mixture was refluxed for additional 40 min. After cooling, 2N H_2SO_4 (300 ml) was added and the org. phase washed successively with 2N H_2SO_4, $NaHCO_3$ soln., and H_2O, dried, and evaporated: 48 g (70%) of crude **12a**/**12b** (5:4 according to GC; the configurations were not assigned). Separation of a sample was achieved by CC (silica gel, CH_2Cl_2/acetone 99:1).

Data of **12a**: Slightly yellowish oil. B.p. 115°/20 mbar. IR (film): 3450, 2980, 2940, 1745, 1680, 1455, 1445, 1380, 1350, 1260, 1205, 1165, 1015, 900, 860, 760. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.23 (*dquint.*, *J* = 8.5, 1.5, H–C(4)); 4.58 (*dd*, *J* = 8.5, 5, H–C(3)); 3.68 (*s*, MeO); 2.62 (*qd*, *J* = 7, 5, H–C(2)); 2.52 (br. *s*, OH); 1.74, 1.69 (2*d*, *J* = 1.5, 2 Me–C(5)); 1.08 (*d*, *J* = 7, Me–C(2)). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 175.6 (*s*, C(1)); 136.3 (*s*, C(5)); 124.9 (*d*, C(4)); 69.6 (*d*, C(3)); 51.6 (*q*, MeO); 45.8 (*d*, C(2)); 25.8 (*q*, *Me*–C(5), *trans* to C(3)); 18.3 (*q*, *Me*–C(5), *cis* to C(3)); 12.1 (*q*, *Me*–C(2)). CI-MS (NH_3): 190 (8, $[M + NH_4]^+$), 172 (26, M^+), 156 (10), 155 ($[M - OH]^+$), 139 (2), 123 (2), 99 (2), 95 (6), 85 (2).

Data of **12b**: B.p. 115°/20 mbar. IR (film): 3430 (br. OH), 2980, 2940, 1740, 1725, 1680, 1460, 1435, 1380, 1255, 1205, 1170, 1125, 1100, 1055, 1030, 895, 845. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.14 (br. *d*, *J* = 8.5, H–C(4)); 4.48 (*t*, *J* = 8.5, H–C(3)); 3.71 (*s*, MeO); 2.52 (*dq*, *J* = 8.5, 7, H–C(2)); 2.38 (br. *s*, OH); 1.76, 1.72 (2*d*, *J* = 1.5, 2 Me–C(5)); 1.11 (*d*, *J* = 7, Me–C(2)). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 176.2 (*s*, C(1)); 136.9 (*s*, C(5)); 125.4 (*d*, C(4)); 70.4 (*d*, C(3)); 51.6 (*q*, MeO); 46.5 (*d*, C(2)); 25.8 (*q*, C(6)); 18.5 (*q*, *Me*–C(5)); 13.7 (*q*, *Me*–C(2)). CI-MS (NH_3): 190 (8, $[M + NH_4]^+$), 189 (8), 173 (4), 172 (37, M^+), 155 (100, $[M - OH]^+$), 139 (1), 123 (1), 99 (2), 95 (2), 73 (2).

*Methyl (2*E*)-2,5-Dimethylhexa-2,4-dienoate* (**14**). A crude mixture of **12a** and **12b** (3.0 g, 17.4 mmol) was refluxed in toluene (30 ml) for 30 min with 3.75 g of *Sicapent* (P_2O_5 drying agent on an inert support; *Merck* No. 543). The mixture was filtered and the filtrate washed with H_2O, dried, and evaporated. Vacuum distillation (partial polymerization could not be avoided even when a radical scavenger, *Santonox R*, was added) gave 1.08 g (41%) of **14** [17]. Colorless oil. B.p. 96–97°/20 mbar. UV (EtOH, $c = 9.7 \cdot 10^{-5}$ mol/l): 276 (16700). IR (film): 2980, 2950, 2860, 1705, 1635, 1600, 1430, 1380, 1325, 1255, 1200, 1115, 1045, 940, 855, 755. ^{1}H-NMR (90 MHz, $CDCl_3$): 7.45 (*d*, *J* = 12.8, H–C(3)); 6.12 (*dq*, *J* = 12.8, 1.2, H–C(4)); 3.75 (*s*, MeO); 1.91 (br. *s*, Me–C(2), 2 Me–C(5)). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 169.4 (*s*, C(1)); 144.2 (*s*, C(5)); 134.7 (*d*, C(3)); 124.3 (*s*, C(2)); 121.3 (*d*, C(4)); 51.6 (*q*, MeO); 26.8 (*q*, *Me*–C(5), *trans* to C(3)); 18.8 (*q*, *Me*–C(5), *cis* to C(3)); 12.4 (*q*, *Me*–C(2)). EI-MS: 155 (5), 154 (50, M^+), 140 (9), 139 (100, $[M - Me]^+$), 123 (25, $[M - MeO]^+$), 107 (16), 95 (58, $[M - CO_2Me]^+$), 79 (46), 77 (21), 67 (33), 55 (24).

When the dehydration was carried out with P_2O_5 (*Fluka* No. 79610), a mixture of two substances in the ratio of 7:3 resulted. The minor product was the desired ester **14**, the major product *methyl (3*E*)-2,5-dimethylhexa-3,5-dienoate* (**13**): Colorless oil. UV (EtOH, $c = 3.57 \cdot 10^{-5}$ mol/l): 226 (21500). IR (film): 3090, 2980, 2960, 1740, 1645, 1610, 1455, 1440, 1375, 1250, 1200, 1170, 1050, 970, 890, 830, 770, 740. ^{1}H-NMR (90 MHz, $CDCl_3$): 6.23 (*d*, *J* = 15.5, H–C(4)); 5.69 (*dd*, *J* = 15.5, 7.8, H–C(3)); 4.94 (br. *s*, CH_2(6)); 3.67 (*s*, MeO); 3.21 (*dq*, *J* = 7.8, 7.0, H–C(2)); 1.84 (*t*, *J* = 1.1, Me–C(5)); 1.28 (*d*, *J* = 7, Me–C(2)). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 175.0 (*s*, C(1)); 141.7 (*s*, C(5)); 134.2, 128.8 (2*d*, C(3), C(4)), 116.2 (*t*, C(6)); 51.8 (*q*, MeO); 43.0 (*d*, C(2)); 18.5, 17.5 (2*q*, *Me*–C(5), *Me*–C(2)). CI-MS (NH_3): 174 (11), 172 (17, $[M + NH_4]^+$), 156 (10), 155 (100, $[M + 1]^+$), 139 (3, $[M - Me]^+$), 125 (14), 123 (2, $[M - MeO]^+$), 95 (8, $[M - CO_2Me]^+$).

*Methyl (2*RS*,3*SR*,4*RS*)- and (2*RS*,3*SR*,4*SR*)-2,3:4,5-Diepoxy-2,5-dimethylhexanoate* (*e*- and *t*-**6**, resp.). To a soln. of 6.67 g (39 mmol) of 3-$ClC_6H_4CO_3H$ (85%) in 70 ml of CH_2Cl_2 were added 1.94 g (12.6 mmol) of **14**.

The mixture was refluxed for 5 d. After cooling, the soln. was filtered to remove the precipitated 3-$ClC_6H_4CO_2H$. The filtrate was washed with 10% Na_2SO_3 soln. (2 × 50 ml) and 10% $NaHCO_3$ soln. (2 × 50 ml), dried, and evaporated: 2.85 g of crude *e*-**6**/*t*-**6** 3:2. Separation and purification by CC (*Florisil* (100 g), petroleum ether/0–3% acetone) of 1 g gave 100 mg of pure *e*-**6**, 30 mg of pure *t*-**6**, and 440 mg of mixed fractions.

Data of e-**6**: M.p. 44–46° (recryst. from hexane). IR (KBr): 3000, 2960, 2930, 1740, 1455, 1440, 1390, 1380, 1295, 1280, 1200, 1165, 1120, 1070, 910, 870, 815, 780, 760, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): 3.76 (*s*, MeO); 3.12 (*d*, *J* = 7.3, H–C(3)); 2.65 (*d*, *J* = 7.3, H–C(4)); 1.66 (*s*, Me–C(2)); 1.44 (*s*, Me–C(5)); 1.37 (*s*, Me(6)). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 170.7 (*s*, C(1)); 59.0 (*d*, C(4)); 58.7 (*d*, C(3)); 58.7 (*s*, C(5)); 57.3 (*s*, C(2)); 52.7 (*q*, MeO); 24.2 (*q*, *Me*–C(5), *trans* to C(3)); 19.5 (*q*, *Me*–C(5), *cis* to C(3)); 14.0 (*q*, *Me*–C(2)). EI-MS: 186 (M^+), 171 ([M – Me]$^+$), 153, 143, 127 ([M – CO_2Me]$^+$), 113, 101, 98, 97, 87, 85, 84, 83, 73, 71, 69, 59. Anal. calc. for $C_9H_{14}O_4$ (186.21): C 58.05, H 7.58; found: C 57.84, H 7.68.

Data of t-**6**: Colorless oil. IR (film): 2960, 1740, 1450, 1440, 1380, 1320, 1295, 1250, 1200, 1170, 1110, 905, 870, 815, 780, 755. ^{1}H-NMR (90 MHz, $CDCl_3$): 3.76 (*s*, MeO); 3.24 (*d*, *J* = 4, H–C(3)); 2.77 (*d*, *J* = 4, H–C(4)); 1.61 (*s*, Me–C(2)); 1.36 (*s*, 2 Me–C(5)). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 170.6 (*s*, C(1)); 59.9 (*d*, C(4)); 59.5 (*d*, C(3)); 57.8 (*s*, C(5)); 56.6 (*s*, C(2)); 52.7 (*q*, MeO); 24.3 (*q*, C(6)); 19.5 (*q*, Me–C(5)); 14.1 (*q*, Me–C(2)). CI-MS (NH_3): 204 (100, [M + NH_4]$^+$), 187 (27, [M + 1]$^+$), 169 (13, [M – 17]$^+$), 129 (5), 127 (13, [M – CO_2Me]$^+$), 114 (5), 84 (3), 71 (4). Anal. calc. for $C_9H_{14}O_4$ (186.21): C 58.05, H 7.58; found: C 57.68, H 7.58.

Methyl (2E,4RS)-4,5-Epoxy-2,5-dimethylhex-2-enoate (**15**). To a soln. of 0.62 g (3.3 mmol) of 85% 3-$ClC_6H_4CO_3H$ in 20 ml of dry CH_2Cl_2 were added 0.5 g (3.3 mmol) of **14**. The soln. was stirred at 25° for 90 min and then washed with 50 ml each of 10% Na_2SO_3 soln., 10% $NaHCO_3$ soln., and 0.2 N NaOH, dried, and evaporated: 0.5 g of a colorless oil. Purification by CC (silica gel, CH_2Cl_2) gave 0.35 g of pure **15**. B.p. 96°/23 mbar. IR (film): 2955, 1715, 1650, 1435, 1380, 1340, 1305, 1250, 1190, 1150, 1125, 1110, 1030, 940, 905, 810, 750. ^{1}H-NMR (90 MHz, $CDCl_3$): 6.52 (*dq*, *J* = 7.7, 1.3, H–C(3)); 3.75 (*s*, MeO); 3.42 (*d*, *J* = 7.7, H–C(4)); 1.99 (*d*, *J* = 1.3, Me–C(2)); 1.41, 1.32 (2*s*, 2 Me–C(5)). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 167.5 (*s*, C(1)); 136.6 (*d*, C(3)); 132.5 (*s*, C(2)); 60.7 (*s*, C(5)); 60.2 (*d*, C(4)); 51.9 (*q*, MeO); 24.7 (*q*, C(6)); 19.6 (*q*, *Me*–C(5)); 13.0 (*q*, *Me*–C(2)). EI-MS: 170 ([M + 1]$^+$), 154, 139 ([M – OMe]$^+$), 127, 113, 112, 111, 81, 73, 69, 59, 53, 43, 41.

(2RS,3SR,4RS)- and (2RS,3SR,4SR)-2,3:4,5-Diepoxy-2,5-dimethylhexanamide (*e*- and *t*-**7**, resp.). For 5 d, *e*-**6**/*t*-**6** 1:4 (0.42 g, 2.3 mmol) was left in 5.5 ml of *ca.* 4M NH_3/MeOH at r.t. After evaporation, the crude product was subjected to FC (silica gel, acetone/petroleum ether 2:3): 0.34 g (86%) of *e*-**7**/*t*-**7** 1:4. Fractional crystallization from heptane/Et_2O/acetone gave pure *t*-**7**.

Data of e-**7**: ^{1}H-NMR ($CDCl_3$, 400 MHz)[6]: 6.49 (br. *s*, NH); 6.28 (br. *s*, NH); 2.94 (*d*, *J* = 6.7, H–C(3)); 2.70 (*d*, *J* = 6.6, H–C(4)); 1.65 (*s*, Me–C(2)); 1.43 (*s*, Me–C(5)); 1.37 (*s*, Me–C(5)). ^{13}C-NMR ($CDCl_3$, 101 MHz)[6]): 173.5 (*s*, C(1)); 59.8 (*d*, ^1J(H,C) = 179.8, C(3)); 59.5 (*s*, C(2)); 58.7 (*d*, ^1J(H,C) = 173.5, C(4)); 58.7 (*s*, C(5)); 24.2 (*q*, ^1J(H,C) = 126.8, C(6)); 19.4 (*q*, ^1J(H,C) = 126.8, *Me*–C(5)); 13.4 (*q*, ^1J(H,C) = 129.1, *Me*–C(2)). GC-MS: 127 (18), 87 (6), 85 (12), 59 (7), 55 (4), 44 (17), 43 (100), 42 (6), 41 (12).

Data of t-**7**: M.p. 116–116.5°. IR (KBr): 3420, 3180, 2980, 2940, 1690, 1660, 1460, 1415, 1380, 1310, 1250, 1205, 1120, 1070, 1035, 990, 900, 865, 845, 805, 740, 685, 620. ^{1}H-NMR ($CDCl_3$, 400 MHz)[6]): 6.40 (br. *s*, NH); 6.35 (br. *s*, NH); 3.00 (*d*, *J* = 4.7, H–C(3)); 2.74 (*d*, *J* = 4.6, H–C(4)); 1.60 (*s*, Me–C(2)); 1.37 (*s*, Me–C(5)); 1.36 (*s*, Me–C(5)). ^{13}C-NMR ($CDCl_3$, 101 MHz)[6]): 173.4 (*s*, C(1)); 60.8 (*d*, ^1J(H,C) = 176.8, C(3)); 60.0 (*d*, ^1J(H,C) = 174.4, C(4)); 58.8 (*s*, C(2)); 58.2 (*s*, C(5)); 24.3 (*q*, ^1J(H,C) = 126.8, C(6)); 19.5 (*q*, ^1J(H,C) = 126.9, *Me*–C(5)); 13.4 (*q*, ^1J(H,C) = 129.1, *Me*–C(2)). GC-MS: 127 (15), 100 (13), 98 (3), 87 (6), 85 (13), 59 (6), 44 (16), 43 (100), 41 (10).

Methyl (2RS,3SR,4SR,5SR)- and (2RS,3SR,4RS,5RS)-2,3:4,5-Diepoxy-2-ethyl-6,6-dimethylheptanoate (*e*- and *t*-**8**, resp.). Methyl (2*E*,4*Z*)-2-ethyl-6,6-dimethylhepta-2,4-dienoate/methyl (2*E*)-2-ethyl-6,6-dimethylhept-2-enoate 7:2 (**16**/**17**; 0.66 g; 2.6 mmol of **16** [15]) was refluxed together with 55% 3-$ClC_6H_4CO_3H$ (4.22 g, 13.4 mmol) in 40 ml of CH_2Cl_2 for 10 d. The mixture was then cooled to 0°, and the precipitate filtered off and washed with ice-cold Et_2O. The filtrate was washed 3 times with 10% $NaHSO_3$ soln. and twice with 10% $NaHCO_3$ soln. The washings were reextracted with 2 × 100 ml of Et_2O and the combined org. extracts washed twice with H_2O, dried, and evaporated. Separation of the products was achieved by 8 successive FC's (*Florisil*, petroleum ether/1–2% acetone or cyclohexane/1–5% acetone): 0.12 g (20%) of *e*-**8** and 0.19 g (32%) of *t*-**8**.

Data of e-**8**: IR (film): 2950, 2870, 1730, 1480, 1460, 1430, 1360, 1310, 1250, 1235, 1190, 1170, 1115, 1060, 1040, 985, 945, 920, 840, 820, 800, 745. ^{1}H-NMR ($CDCl_3$, 400 MHz): 3.77 (*s*, MeO); 3.38 (*d*, *J* = 6.2, H–C(3)); 2.89 (*dd*, *J* = 6.2, 4.3, H–C(4)); 2.81 (*d*, *J* = 4.3, H–C(5)); 2.16 (*dq*, *J* = 14.6, 7.3, 1 H, MeCH_2); 1.80 (*dq*, *J* = 14.6, 7.3, 1 H, MeCH_2); 1.13 (*t*, *J* = 7.4, *Me*CH_2); 1.08 (*s*, *t*-Bu). ^{13}C-NMR (101 MHz, $CDCl_3$): 170.3 (*s*, C(1)); 65.3 (*d*,

[6]) Measurement with *e*/*t*-**7** 1:4.

^1J(H,C) = 167.2, C(5)); 62.9 (*s*, C(2)); 59.2 (*d*, ^1J(H,C) = 170.6, C(3)); 53.2 (*d*, ^1J(H,C) = 172.9, C(4)); 52.7 (*q*, ^1J(H,C) = 147.8, MeO); 31.4 (*s*, C(6)); 27.3 (*q*, ^1J(H,C) = 126.0, Me_3C(6)); 21.8 (*t*, ^1J(H,C) = 129.4, MeCH$_2$); 9.5 (*q*, ^1J(H,C) = 127.4, *Me*CH$_2$. CI-MS (NH_3): 247 (14), 246 (100, $[M + NH_4]^+$), 229 (25, $[M + 1]^+$), 211 (12, $[M - 17]^+$), 188 (3), 169 (5, $[M - CO_2Me]^+$), 155 (4), 143 (4), 129 (3), 128 (5), 99 (11), 76 (3). Anal. calc. for $C_{12}H_{20}O$ (228.29): C 63.13, H 8.83; found: C 62.70, H 9.08.

Data of t-**8**: IR (film): 2965, 2890, 1740, 1485, 1465, 1440, 1370, 1310, 1260, 1245, 1195, 1175, 1125, 1060, 1035, 995, 950, 925, 845, 805, 745. ^{1}H-NMR ($CDCl_3$, 400 MHz): 3.77 (*s*, MeO); 3.34 (*d*, *J* = 5.2, H–C(3)); 2.82 (*t*, *J* = 4.8, H–C(4)); 2.79 (*d*, *J* = 4.4, H–C(5)); 2.30 (*dq*, *J* = 14.5, 7.2, 1 H, MeC*H*$_2$); 1.55 (*dq*, *J* = 14.5, 7.2, 1 H, MeC*H*$_2$); 1.11 (*t*, *J* = 7.4, *Me*CH$_2$); 1.01 (*s*, *t*-Bu). ^{13}C-NMR (101 MHz, $CDCl_3$): 169.9 (*s*, C(1)); 65.1 (*d*, ^1J(H,C) = 167.7, C(5)); 61.4 (*s*, C(2)); 60.4 (*d*, ^1J(H,C) = 180.8, C(3)); 56.3 (*d*, ^1J(H,C) = 173.4, C(4)); 52.7 (*q*, ^1J(H,C) = 147.9, MeO); 31.4 (*s*, C(6)); 27.3 (*q*, ^1J(H,C) = 126.0, Me_3C(6)); 21.9 (*t*, ^1J(H,C) = 128.9, MeCH$_2$); 9.5 (*q*, ^1J(H,C) = 127.4, *Me*CH$_2$). CI-MS (NH_3): 247 (14), 246 (100, $[M + NH_4]^+$), 229 (42, $[M + 1]^+$), 211 (12, $[M - 17]^+$), 169 (4, $[M - CO_2Me]^+$), 143 (8), 129 (3), 128 (5), 113 (3), 111 (3), 99 (11). Anal. calc. for $C_{12}H_{20}O_4$ (228.29): C 63.13, H 8.83; found: C 62.45, H 9.25.

*(2*RS*,3*SR*,4*SR*,5*SR*)-2,3:4,5-Diepoxy-2-ethyl-6,6-dimethylheptanamide* (*e*-**9**). For 3 d, *e*-**8** (50 mg, 0.2 mmol) was left at r.t. in 5 ml of *ca.* 6M NH_3/MeOH. After evaporation, the crude product was subjected to FC (silica gel, cyclohexane/AcOEt 3:2): 35 mg (75%) of *e*-**9**. Colorless crystals: M.p. 91–94°. ^{1}H-NMR ($CDCl_3$, 400 MHz): 6.27 (br. *s*, 1 H, NH_2); 5.88 (br, *s*, 1 H, NH_2); 3.22 (*d*, *J* = 5.7, H–C(3)); 2.94 (*dd*, *J* = 5.5, 4.4, H–C(4)); 2.80 (*d*, *J* = 4.3, H–C(5)); 2.46 (*dq*, *J* = 14.7, 7.4, 1 H, MeC*H*$_2$); 1.54 (*dq*, *J* = 14.5, 7.3, 1 H, MeC*H*$_2$); 1.10 (*t*, *J* = 7.4, *Me*CH$_2$); 1.07 (*s*, *t*-Bu). ^{13}C-NMR (101 MHz, $CDCl_3$): 172.4 (*s*, C(1)); 65.2 (*d*, ^1J(H,C) = 167.6, C(5)); 65.2 (*s*, C(2)); 60.7 (*d*, ^1J(H,C) = 178.2, C(3)); 52.9 (*d*, ^1J(H,C) = 173.1, C(4)); 31.4 (*s*, C(6)); 27.2 (*d*, ^1J(H,C) = 126.0, Me_3C(6)); 21.0 (*t*, ^1J(H,C) = 129.4, MeCH$_2$); 9.2 (*q*, ^1J(H,C) = 127.2, *Me*CH$_2$). CI-MS (NH_3): 232 (12, $[M + 19]^+$), 231 (100, $[M + 18]^+$), 214 (8, $[M + 1]^+$), 196 (22), 171 (6), 146 (5), 129 (5), 128 (68), 124 (8), 112 (8), 86 (28). EI-MS: 169 (7), 114 (19), 101 (19), 99 (37), 98 (6), 86 (9), 84 (28), 83 (5), 71 (5), 70 (13), 69 (31), 57 (100), 56 (47), 55 (37), 53 (5), 44 (16), 43 (27), 42 (21), 41 (61), 39 (20).

*(2*RS*,3*SR*,4*RS*,5*RS*)-2,3:4,5-Diepoxy-2-ethyl-6,6-dimethylheptanamide* (*t*-**9**). For 2 d, *t*-**8** (72 mg, 0.32 mmol) was left at r.t. in 10 ml of *ca.* 6M NH_3/MeOH. After evaporation, the residue was purified by FC (silica gel, cyclohexane/AcOEt 3:2): 30 mg (44%) of *t*-**9**. Colorless crystals: M.p. 117.5–118°. IR (KBr): 3420 (NH), 3190 (br., NH), 2980, 2875, 2770, 1690 (br., C=O), 1615, 1580, 1485, 1460, 1425, 1400, 1365, 1200, 1095, 1055, 960, 925, 910, 865, 840, 815, 725, 695, 615. ^{1}H-NMR ($CDCl_3$, 400 MHz): 6.33 (br. *s*, 1 H, NH_2); 5.81 (br, *s*, 1 H, NH_2); 3.20 (*d*, *J* = 5.1, H–C(3)); 2.83 (*t*, *J* = 4.7, H–C(4)); 2.80 (*d*, *J* = 4.4, H–C(5)); 2.51 (*dq*, *J* = 14.6, 7.3, 1 H, MeC*H*$_2$); 1.36 (*dq*, *J* = 14.4, 7.2, 1 H, MeC*H*$_2$); 1.08 (*t*, *J* = 7.4, *Me*CH$_2$); 1.01 (*s*, *t*-Bu). ^{13}C-NMR (101 MHz, $CDCl_3$): 171.8 (*s*, C(1)); 65.3 (*d*, ^1J(H,C) = 167.7, C(5)); 63.4 (*s*, C(2)); 61.7 (*d*, ^1J(H,C) = 179.0, C(3)); 56.4 (*d*, ^1J(H,C) = 173.7, C(4)); 31.4 (*s*, C(6)); 27.3 (*q*, ^1J(H,C) = 126.0, Me_3C(6)); 20.9 (*t*, ^1J(H,C) = 128.8, MeCH$_2$); 9.1 (*q*, ^1J(H,C) = 127.1, *Me*CH$_2$). CI-MS (NH_3): 232 (6, $[M + 19]^+$), 231 (54, $[M + 18]^+$), 214 (9, $[M + 1]^+$), 197 (5), 196 (42), 146 (17), 129 (7), 128 (100), 112 (8), 110 (5), 86 (18). EI-MS: 169 (10), 114 (19), 101 (15), 99 (42), 98 (6), 86 (9), 70 (13), 69 (17), 57 (100), 55 (23), 44 (19), 43 (18), 42 (6), 41 (36), 39 (15).

X-Ray Structure Analyses of e- *and* t-**4**, e-**6**, e- *and* t-**7**, *and* e- *and* t-**9**. The X-ray structures of *e*- and *t*-**4**, *e*-**6**, *e*- and *t*-**7**, and *e*- and *t*-**9** are shown in *Figs. 1–7*. Crystal data and parameters of the data collection are compiled in *Table 3*. Unit-cell parameters were determined by accurate centering of 25 strong independent reflections by the least-squares method. Reflection intensities were collected at r.t. on a four-circle diffractometer *Enraf-Nonius CAD4* equipped with a graphite monochromator and using MoK_α radiation. Four standard reflections monitored every h during data collection showed no intensity loss. The usual corrections were applied. Diffraction absorption correction was calculated with DIFABS [18] (for *e*/*t*-**4**, *e*-**6**, and *e*/*t*-**9**) or was determined by Psi-Scans (*e*/*t*-**7**). The structures were solved by direct-method strategies using the programs SHELXS-86 [19] (*e*/*t*-**4**, *e*-**6**, and *e*/*t*-**9**) and SIR88 [20] (*e*/*t*-**7**), resp. Anisotropic least-squares full-matrix refinements were carried out on all non-H-atoms using the program CRYSTALS [21] (*e*/*t*-**4**, *e*/*t*-**7**, and *e*/*t*-**9**); the structure of *e*-**6** was refined using SHELX-76 [22]. Positions of H-atoms were calculated with the exception of those used for the determination of torsion angles. They were refined isotropically restraining their distances to 1.0 Å. Scattering factors were taken from *International Tables of Crystallography Vol. IV* or were those implemented in the SHELX-76 program. Fractional coordinates are deposited in the *Cambridge Crystallographic Data Base*.

Table 3. *Crystal Data and Parameters of Data Collection for* e-**4**, t-**4**, e-**6**, e-**7**, t-**7**, e-**9**, *and* t-**9**

	e-**4**	*t*-**4**	*e*-**6**	*e*-**7**	*t*-**7**	*e*-**9**	*t*-**9**
Molecular formula	$C_6H_9N_1O_3$	$C_6H_9N_1O_3$	$C_9H_{14}O_4$	$C_8H_{13}N_1O_3$	$C_8H_{13}N_1O_3 \cdot \frac{1}{2}C_3H_6O$	$2\,C_{11}H_{19}N_1O_3 \cdot C_6H_{12}$	$C_{11}H_{19}N_1O_3$
Crystal system	monoclinic	monoclinic	monoclinic	monoclinic	orthorhombic	triclinic	monoclinic
Space group	$P2_1/n$	$P2_1/a$	$P2_1/n$ (14)	$P2_1/a$ (14)	*Pbna* (60, *Pbcn*)	$P\bar{1}$	$P2_1/n$
a [Å]	7.729(3)	8.851(1)	6.352(3)	7.803(1)	7.624(2)	10.228(6)	10.032(18)
b [Å]	5.018(2)	4.455(1)	20.710(2)	27.739(3)	10.417(1)	10.483(2)	6.850(4)
c [Å]	19.216(5)	18.692(3)	7.889(8)	8.547(1)	28.530(4)	16.191(3)	18.129(7)
α [°]	90.00(0)	90.00(0)	90.00(0)	90.00(0)	90.00(0)	108.73(2)	90.00(0)
β [°]	95.03(2)	98.29(2)	109.08(7)	97.36(1)	90.00(0)	98.86(3)	101.04(9)
γ [°]	90.00(0)	90.00(0)	90.00(0)	90.00(0)	90.00(0)	90.38(3)	90.00(0)
V [Å^3]	742.2(4)	729.3(2)	980.9	1834.6(4)	2266.0(6)	1618.7(1.1)	1222.8(2.5)
Z	4	4	4	8	8	2	4
Crystal dimensions [mm]	0.15 × 0.15 × 0.3	0.2 × 0.2 × 0.3	0.2 × 0.2 × 0.3	0.2 × 0.4 × 0.5	0.2 × 0.4 × 0.4	0.1 × 0.1 × 0.25	0.15 × 0.4 × 0.5
Temperature [K]	298	298	298	298	298	298	298
Θ_{max} [°]	27	27	26	28	26.2	27	28
Radiation	MoK_α, $\lambda = 0.71069$ Å	MoK_α, $\lambda = 0.71069$ Å	MoK_α, $\lambda = 0.71069$ Å	MoK_α, $\lambda = 0.71069$ Å	MoK_α, $\lambda = 0.71069$ Å	MoK_α, $\lambda = 0.71069$ Å	MoK_α, $\lambda = 0.71069$ Å
Scan type	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$
No. of independent refl.	1564	1532	1580	4412	2272	7063	2892
No. of refl. in refinement	885	645	1284	2001	1032	2071	1600
No. of variables	107	107	118	233	143	310	148
Final R	3.99	7.39	5.54	3.82	5.27	6.28	6.71
Final R_w	2.88	4.32	–	4.09	6.40	6.46	6.15
Weighting scheme	weight × $[1-(\Delta F/6\sigma F)^2]^2$	weight × $[1-(\Delta F/6\sigma F)^2]^2$	unit weights	weight × $[1-(\Delta F/6\sigma F)^2]^2$	weight × $[1-(\Delta F/6\sigma F)^2]^2$	weight × $[1-(\Delta F/6\sigma F)^2]^2$	weight × $[1-(\Delta F/6\sigma F)^2]^2$

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