Synthesis of (+)-(*S*)-Streptenol A and Biomimetic Synthesis of (2*R*,4*S*)- and (2*S*,4*S*)-2-(Pent-3-enyl)piperidin-4-ol

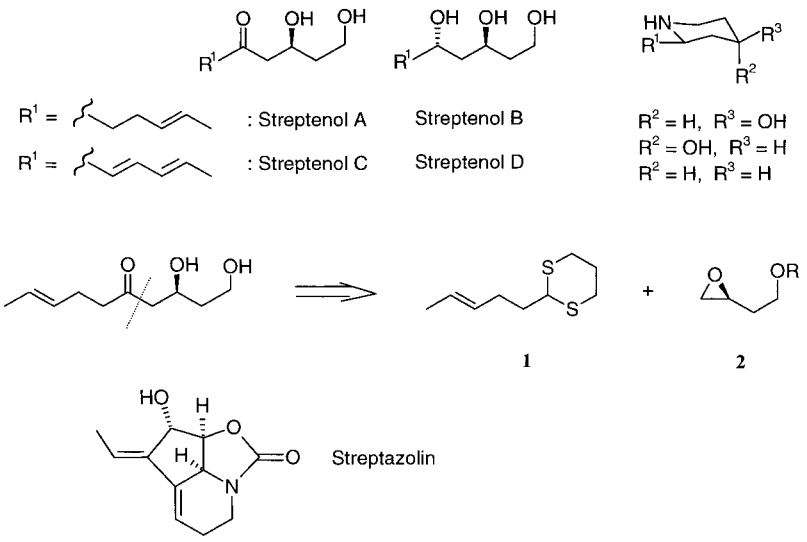
by **Heribert Dollt**[a]), **Peter Hammann**[b]), and **Siegfried Blechert**[c])*

[a]) *F. Hoffmann-La Roche AG*, PRPC-S, Grenzacherstr. 125, CH-4070 Basel
[b]) Core Research Function, DI & A, *HMR Deutschland GmbH*, D-65926 Frankfurt am Main
[c]) Institut für Organische Chemie der TU Berlin, Strasse des 17. Juni 124, D-10623 Berlin

(+)-(*S*)-Streptenol A is synthesized by coupling a 1,3-dithiane with an optically pure epoxide. The absolute configuration of (+)-(*S*)-streptenol A is thereby correlated with that of (*S*)-malic acid. Stereoselective reduction of an oxime that could easily be prepared from streptenol A gave the (3*S*,5*R*)- and (3*S*,5*S*)-aminostreptenols, and after cyclization, configurationally pure 2,4-functionalized piperidine alkaloids.

Introduction. – Product screening of metabolites found in nature is not only an essential feature in the area of pharmacological research, but it is also a valuable tool to enlarge the kit of building blocks for organic syntheses. Nature is thereby very often an exciting guide in synthesis. After a biosynthetic pathway is clarified, it is one of the most challenging fields of interest to find analogous procedures in the laboratory and to transfer them to new synthetic problems in an ensuing step. The secondary metabolite streptenol A (*Scheme 1*) is one of the four known streptenols with antitumor activity and the ability to inhibit the cholesterol biosynthesis and to act as an immunostimulator

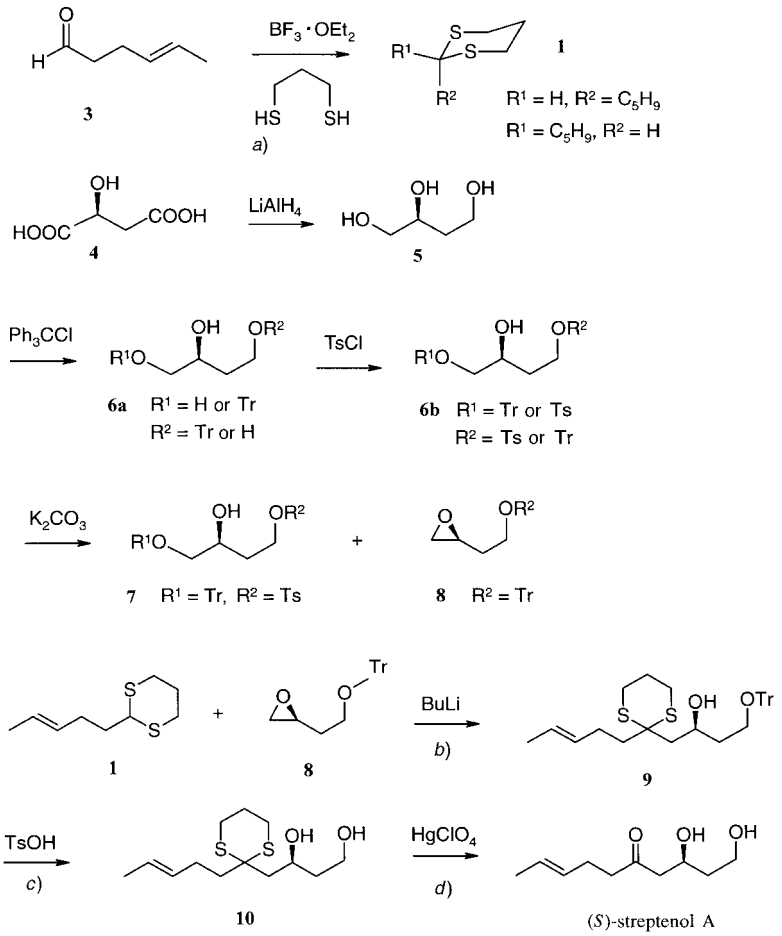
Scheme 1. *Streptenols and Piperidine Alkaloids Obtained During a Fermentation*



[1]. The streptenols are produced by *Streptomyces luteogriseus* during a fermentation reaction [1b][2]. In the culture broth, these streptenols are accompanied by piperidine alkaloids and streptazoline. Feed experiments [3] have thereby shown that the streptenols are metabolized during the fermentation and are thus the biosynthetic precursors of the above-mentioned alkaloids. We describe here the asymmetric synthesis of (+)-(*S*)-streptenol A using a coupling reaction of the *Seebach* aldehyde dithioacetal **1** with the optically pure epoxide **2**. After an N-atom was introduced, the streptenol A skeleton was cyclized, and the piperidine alkaloids were obtained like it is demonstrated by nature.

Results and Discussion. – *(S)-Streptenol A*. The transetherification product from ethyl vinyl ether and but-3-en-2-ol was rearranged to the aldehyde **3** needed for the 'Umpolung' [4] (*Scheme 2*). (*E*)-Selectivity was thereby granted by the six-membered

Scheme 2. *a*) CH_2Cl_2, molecular sieves 4 Å, 0°, 1.5 h. *b*) **1**, BuLi, THF, – 15°, 3 h; then + **8**, 0°, 7 days. *c*) MeOH, r.t., 24 h. *d*) THF, r.t., 5 min.

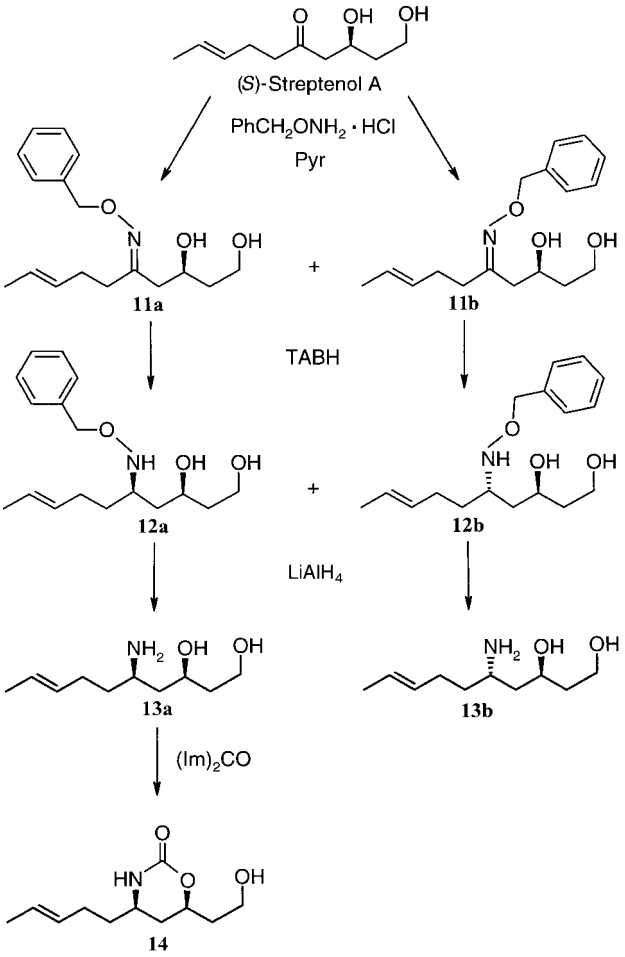


transition state that is passed during the 3,3-sigmatropic rearrangement and that prefers a chair configuration, in which the Me group takes the energetically favorable equatorial position. Treatment of **3** with propane-1,3-dithiol in the presence of boron trifluoride etherate led finally to the 1,3-dithiane **1** as a mixture of diastereoisomers. The absolute configuration of the epoxide **2**, needed as the coupling partner for the 1,3-dithiane **1**, was taken from the chiral pool. Total reduction of (*S*)-malic acid (**4**) resulted in butan-1,2,4-triol **5** [5] which could be transformed into a suitable epoxide for the streptenol synthesis according to a procedure by *Di Fabio* [6]. In a regioselective tritylation ($\rightarrow$ **6a**) followed by a tosylation, a mixture of the products **6b** was obtained. This regioisomer mixture was treated with potassium carbonate, yielding the desired epoxide **8** from one regioisomer besides the unreacted tosylated regioisomers **7** which were finally separated from **8** chromatographically. Thus, purification of **6a**,**b** during the reaction sequence was not necessary.

Known procedures were first used ($-20°$, 12 h) [7] for the ring-opening reaction of **8** with deprotonated **1**. However, it turned out that the epoxide **8** was inert under these conditions which is certainly due to the steric hindrance caused by the bulky trityl group. To force the reaction a little bit more, the temperature was increased, but only up to $0°$ because of the known fact that solutions of deprotonated 1,3-dithianes are stable only for a very short time at a higher temperature [8]. The optimal conditions were found when deprotonated **1** was stirred with **8** at $0°$ for one week yielding 56% of the coupling product **9**, while 38% of the epoxide **8** and 26% of the dithiane **1** could be isolated unchanged. Subsequent acid-catalyzed (TosOH) detritylation of **9** gave the thioketale **10** of streptenol A, and desulfuration was achieved by means of $HgClO_4 \cdot 3\,H_2O$, to profit from the described advantages [9][10] of this system, rather than by means of the classical reagent HgO/HgCl. Thus, after 5 min stirring of **10** with a solution of $HgClO_4 \cdot 3\,H_2O$ in THF/$CHCl_3$ at room temperature, the thioketal cleavage was complete. The target streptenol A had to be removed from the mercury slurry very quickly and completely since the presence of mercury traces caused the destruction of the product after a few days, even at low temperature. The isolated streptenol A showed identical spectroscopic data and optical rotation as the natural product from streptomycetes (see [11]). Thus the absolute configuration of streptenol A was correlated with (*S*)-malic acid.

*Stereoselective Amination of (*S*)-Streptenol A*. The classical one-pot procedure [12] of imine formation and reduction failed when applied to (*S*)-streptenol A, giving only poor yields of aminostreptenol and streptenol B as the main product instead. Therefore, we used the (*E*)- and (*Z*)-*O*-benzyloximes **11a**,**b** of (*S*)-streptenol A, which were obtained in high yield on treatment with *O*-benzylhydroxylamine hydrochloride in pyridine and could be separated chromatographically (*Scheme 3*). Because the (*E*)- and (*Z*)-oximes may lead to a different stereochemistry on oxime reduction, it was important to establish their double-bond configuration. This was successfully done by C,H-COSY NMR experiments. It is known that C(α) (*Z*) to the O-atom appears at higher field than the C(α) (*E*) to the O-atom does [13]. The less polar oxime showed at 36.9 ppm a CH_2 group that possesses a C,H correlation to the *dd* of the $CH_2(\alpha)$ protons, and the more polar one a correlation between the $CH_2(\alpha)$ proton and a CH_2 group at 41.3 ppm; thus, the less polar material is the (*Z*)-oxime **11b**.

Scheme 3. *Stereoselective Reduction of the Oximes of (S)-Streptenol A*



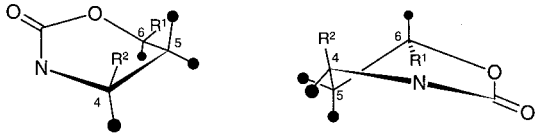
With different reduction methods, it was found in general that the (*E*)-oxime **11a** was reduced under milder conditions faster and smoother than the (*Z*)-oxime **11b** (see *Table 1*). $LiAlH_4$ gave the aminostreptenols in a one-step procedure; however, d.e. values were not satisfying, and an elevated temperature was necessary, especially for the (*Z*)-oxime. To increase the selectivity, the oxime was activated in acidified solutions while the reaction temperature was kept low. Efficient reducing agents under acid conditions were $NaCNBH_3$ and TABH (tetramethylammonium triacetoxyboronhydride). High d.e. values, fast reaction times, and high yields are reported [14] for the resulting (*R*)- or (*S*)-configured secondary hydroxylamines. However, again the oximes **11** of streptenol A reacted much slower than the examples reported in the literature (see *Table 1*). Finally, the obtained hydroxylamines **12a**,**b** were reduced further with $LiAlH_4$, and chromatographic workup gave the pure aminostreptenols **13a**,**b**.

Table 1. *Conditions for the Reduction of the Oximes* **11**

	Reagent	Solvent	Temp [°C]	Time [h]	Ratio **12a/12b**	Yield [%]
11a (*E*)	$LiAlH_4$	THF	−60 to +20	12	39 : 61	67
11b (*Z*)	$LiAlH_4$	THF	+50	72	50 : 50	31
11a (*E*)	TABH[a])	MeCN/HOAc	−15	5	66 : 34	50
11b (*Z*)	TABH[a])	MeCN/HOAc	−15	5	30 : 70	50
11a (*E*)	$NaCNBH_3$	MeCN/HOAc	−20	60	81 : 19	98
11b (*Z*)	$NaCNBH_3$	MeCN/HOAc	−20	108	50 : 50	92

[a]) TABH = Tetramethylammonium triacetoxyboronhydride.

Absolute Configuration of the Aminostreptenols **13a**,**b**. The less polar aminostreptenol **13a** was transformed into the cyclic carbamate **14** on reaction with 1,1′-carbonylbis[1*H*-imidazole]. The ^{1}H-NMR data of the latter established its (4*R*,6*R*)-configuration, which was also supported by PM3 calculations (see *Fig.*).



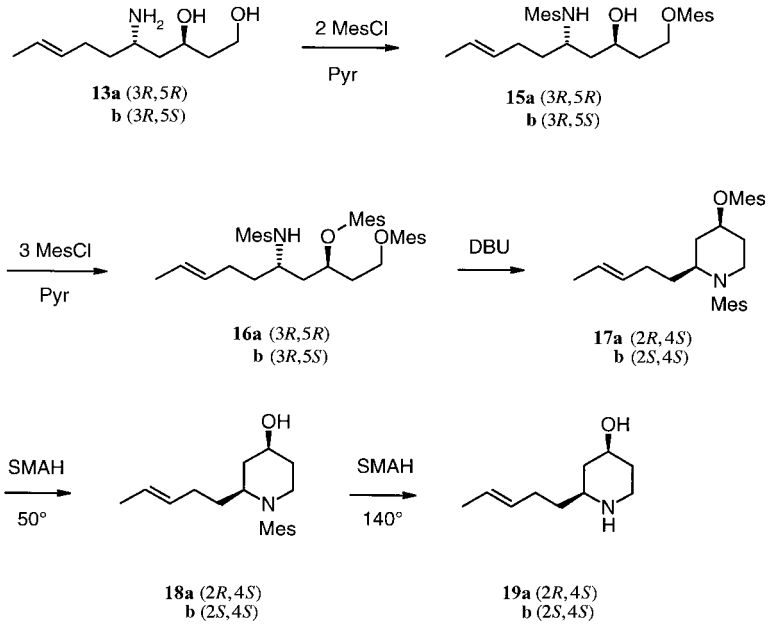
14 (4*R*,6*R*) **14′** (4*S*,6*R*)

Figure. *PM3-Optimized conformations of the (4*R,6R*)- and (4*S,6R*)-carbamates* **14** *and* **14′**, *respectively, of aminostreptenol A*

The CH_2 protons of the ring moiety of **14** showed very different shifts in the ^{1}H-NMR spectrum (1.37 and 2.10 ppm) so that the coupling constants could be measured. Both protons exhibited a *ddd* coupling pattern, typical for the protons at C(5). Because of the anisotropy in cyclic carbamates, the axial proton at C(5) of **14** is the one at higher field. This H_{ax}–C(5) showed three large coupling constants (13.2, 10.8, 10.8 Hz), which is in agreement with a (4*R*,6*R*)-configuration for **14**. Indeed, according to the PM3 calculations (see *Fig.*), the most comfortable conformation of the carbamate **14** is a slightly flat-bottomed boat with eq/eq substituents at C(4) and C(6). The dihedral angle between both protons at the substituted centers and H_{ax}–C(5) is 178.5° and −161.3°. Because of the additional geminal coupling, H_{ax}–C(5) of **14** should show three large coupling constants which is in accord with the ^{1}H-NMR experiment. For the (4*S*,6*R*)-carbamate **14′**, the calculations suggest a twist-boat conformation with eq/ax substituents in which only the protons at C(6) and C(5) exhibit a great dihedral angle (162.7°); therefore, H_{ax}–C(5) of **14′** would show only two large coupling constants in the ^{1}H-NMR.

Piperidine Alkaloids. A leaving group at the primary OH group of the aminostreptenols **13** should allow an intramolecular cyclization involving the nucleophilic N-atom; thereby, the relative configuration of the aminostreptenols should be preserved in the resulting piperidine. For this purpose, the aminostreptenols **13** were mesylated. This could be achieved stepwise in the sequence NH_2, primary OH (→**15**), and secondary OH group (→**16**; *Scheme 4*). However, better yields and smoother reactions were obtained on total mesylation of **13**. Treatment of the resulting trimesyl derivatives **16** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gave the cyclization products **17**. Using the same conditions for the dimesyl derivatives **15**, the piperidinols

Scheme 4. *Biomimetic Synthesis of Piperidine Alkaloids.* The formulae of the **b** series are shown.



18 were formed directly. Finally, the natural products **19** were obtained after reduction with SMAH (sodium methoxy(ethoxy)aluminum hydride) which could be performed stepwise starting with **17**: At 50°, only the *O*-mesyl group was reduced (→ **18**), and at 140° also the *N*-mesyl group was removed.

The coupling constants in the ^{1}H-NMR spectra could be used to determine different conformations of the piperidines **17**–**19**, which were a consequence of their different sterically demanding substituents. The results are listed in *Table 2*.

Table 2. *Coupling Constants and Conformations of the Piperidines* **17**–**19**

	J(H,H) [Hz]	Position[a])	Conformation
17a (2*R*,4*S*)	H–C(2): 5.0, 5.5, < 6.0	ax R–C(2)	chair
	H–C(4): 4.5, 4.5, 11.5, 11.5	eq MesO	
18a (2*R*,4*S*)	H–C(2): 4.5, 4.5, 11.3, 11.3	eq R–C(2)	chair
	H–C(4): 6.2, 6.2, 6.2, 6.2	ax OH	
19a (2*R*,4*S*)	H–C(2): 2.8, 6.4, 6.4, 10.0	eq R–C(2)	chair
	H–C(4): 3.1, 3.1, 3.1, 3.1	ax OH	
17b (2*S*,4*S*)	H–C(2): 6.9, 6.9, 6.9, 6.9	ax R–C(2)	chair
	H–C(4): 3.0, 3.0, 3.0, 3.0	ax MesO	
18b (2*S*,4*S*)	H–C(2): 5.5, 5.5, 5.5, <5.5	ax R–C(2)	twist-boat
	H–C(4): 4.5, 4.5, < 6.0, 12.0	eq OH	
19b (2*S*,4*S*)	H–C(2): 2.4, 7.2, 7.2, 12.0	ax R–C(2)	chair
	H–C(4): 4.5, 4.5, 11.0, 11.0	eq OH	

[a]) R = MeCH=CHCH$_2$CH$_2$.

Experimental Part

General. For molecular calculations, the program package SPARTAN Vers. 2.0. from *Wavefunction Inc.*, Irvine, USA, was used. All solvents were freshly distilled and dried by using standard methods. Column chromatography (CC): silica gel (0.03–0.06 mm) from *Baker*. TLC: foils (silica gel *60F254*, 0.2 mm) from *Merck*. Optical rotations: *Perkin-Elmer-141* polarimeter. IR Spectra: *Perkin-Elmer-881:* rel. intensities are given. NMR Spectra: *Bruker AC200* and *AM400* at 200 and 400 MHz, resp. for ^{1}H; *Bruker AM270* and *AM400* for ^{13}C and DEPT; δ in ppm rel. to the internal standard $SiMe_4$, coupling constants J in Hz; the J of higher spin systems were verified by simulation techniques; isomer ratios of diastereoisomer mixtures were derived from suitable NMR integrals. GC/MS analysis: *HP 5890II* with *MSD 5971A* and a *CP-Sil 5CB* column (12.5 m, 0.2 mm, 0.33 μm film); carrier gas He; the starting temp. 45° for 4 min, then temp. increase with a rate of 8°/min, end temp. 125°; peak intensities are given. Mass spectra: *Variant MAT 711*, ionization potential 70 eV. Microanalyses: elemental analyzer *1106 Carlo Erba*.

*2-[(*E*)-Pent-3-enyl]-1,3-dithiane* (**1**). At 0°, propane-1,3-dithiol (714 mg, 6.6 mmol) was added to **3** (500 mg, 5.1 mmol) and 4-Å molecular sieves (250 mg) in anh. CH_2Cl_2 (20 ml) under Ar. The slow addition of $BF_3 \cdot OEt_2$ (1.283 ml, 10.2 mmol) followed, and the mixture was stirred for 1.5 h. It was quenched with sat. $NaHCO_3$ soln. (12 ml) and extracted with CH_2Cl_2. The extract was washed with sat. $NaHCO_3$ and sat. NaCl soln., dried ($MgSO_4$), and evaporated. Bulb-to-bulb distillation of the residue at 85°/1.5 mbar yielded 549 mg (57%) of **1**. Colorless liquid. R_f (petroleum ether/^{t}BuOMe 10:1) 0.55. IR ($CHCl_3$): 3020 (45.3), 2964 (45.7), 2905 (52.8), 1425 (57.3), 1262 (17.0), 1205 (54.6), 1098 (16.8), 1028 (17.9), 968 (54.4), 720 (0.0). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.33 (*dddd*, J = 6, 1.5, 1.5, 1.5, 6 H, Me(5′)); 1.80 (*dt*, J = 7, 7, 4 H, CH_2(1′)); 1.87 (*dm*, J = 14, 2 H, 1 H–C(5)); 2.12 (*dm*, J = 14, 2 H, 1 H–C(5)); 2.19 (*dddqt*, J = 7, 7, 7, 1.5, 1, 2 H, CH_2(2′)[1]); 2.26 (*dddm*, J = 7, 7, 7, 2 H, CH_2(2′)); 2.79–2.91 (*m*, 8 H, CH_2(4), CH_2(6)); 4.02 (*t*, J = 7, 1 H–C(2))[1]); 4.04 (*t*, J = 7, 1 H–C(2)); 5.39 (*dtq*, J = 15, 7, 1.5, 2 H, H–C(3′)); 5.49 (*dqt*, J = 15, 6, 1, 2 H, H–C(4′)). ^{13}C-NMR (50 MHz, $CDCl_3$): 12.6, 17.8[1]) (*q*, C(5′)); 23.7, 25.8[1]) (*t*, C(2′)); 25.8 (*t*, 2 C(5)); 30.08[1]), 30.12 (*t*, 2 C(4), 2 C(6)); 34.96, 34.99[1]) (*t*, C(1′)); 46.5[1]), 46.7 (*d*, C(2)); 125.1, 125.9[1]) (*d*, C(4′)); 128.6, 129.4[1]) (*d*, C(3′)). GC/MS: t_R 14.448 min; 188 (56, M^+), 133 (26, $[M - C_4H_7]^+$), 119 (100, $[133 - CH_2]^+$), 106 (24, $[119 - CH]^+$, $C_3H_6S_2^+$), 55 (16, $C_4H_7^+$). HR-MS: 188.0694 ($C_9H_{16}S_2^+$; calc. 188.0693).

*(+)-(2*S*)-1-{2-[(*E*)-Pent-3-enyl]-1,3-dithian-2-yl}-4-(trityloxy)butan-2-ol* (**9**). At −40°, 1.6M BuLi (1 ml) was added very slowly to a soln. of **1** (276 mg, 1.47 mmol) in anh. THF (10 ml). Then it was stirred for 3 h at −15°. After cooling to −20°, a soln. of **8** (486 mg, 1.47 mmol) in anh. THF (2 ml) was added dropwise. The mixture was warmed to 0° and stirred for a week. Addition of sat. NH_4Cl soln. (30 ml), extraction with CH_2Cl_2, drying ($MgSO_4$) of the org. layer, and evaporation gave a residue which was purified by CC (silica gel, petroleum ether/^{t}BuOMe 20:1, then 10:1, and finally 2:1): recycled **1** (26%) and **8** (38%), and **9** (430 mg 56%). Slightly yellow solid. R_f (petroleum ether/^{t}BuOMe 2:1) 0.28. $[\alpha]_D = +7.6$ (c = 1.16, CH_2Cl_2). IR ($CHCl_3$): 3483 (76.4), 3017 (33.1), 2934 (30.8), 1450 (28.6), 1228 (16.7), 1076 (0.0), 1034 (21.4), 708 (3.4), 674 (53.1), 633 (50.3). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.64 (*d*, J = 5, Me(5″)); 1.68–1.78 (*m*, 1 H–C(5′)); 1.80–2.12 (*m*, 1 H–C(1), CH_2(1″), CH_2(2″), CH_2(3), 1 H–C(5′)); 2.28 (*dd*, J = 15, 9, 1 H–C(1)); 2.74–2.82 (*ddd*, J = 14.5, 6.5, 3, H_{eq}–C(4′), H_{eq}–C(6′)); 2.88, 2.95 (each *ddd*, J = 14.5, 9.5, 3, H_{ax}–C(4′), H_{ax}–C(6′)); 3.18–3.32 (*m*, 2 H–C(4)); 4.14–4.22 (*m*, H–C(2)); 5.34–5.51 (*m*, H–C(3″), H–C(4″)); 7.20–7.33 (*m*, 9 arom. H); 7.44 (*dd*, J = 8, 1, 6 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 17.9 (*q*, C(5″)); 25.0 (*t*, C(5′)); 26.0, 26.3 (*t*, C(4′), C(6′)); 27.2 (*t*, C(2″)); 38.0 (*t*, C(1″)); 39.5 (*t*, C(3)); 44.7 (*t*, C(1)); 52.0 (*s*, C(2′)); 61.0 (*t*, C(4)); 66.7 (*d*, C(2)); 86.8 (*s*, Ph_3C); 125.6 (*d*, C(4″)); 126.9 (*d*, 3C_p); 127.8 (*d*, 6C_o); 128.8 (*d*, 6C_m); 130.1 (*d*, C(3″)); 144.1 (*s*, 3C_{ipso}). MS (170°): 518 (1, M^+), 463 (6, $[M - C_4H_7]^+$, 275 (38, $[M - Tr]^+$), 243 (100, Tr^+), 187 (18, $[275 - C_4H_8O_2]^+$), 55 (4, $C_4H_7^+$). HR-MS: 518.2313 ($C_{32}H_{38}O_2S_2^+$; calc. 518.2313). Anal. calc. for $C_{32}H_{38}O_2S_2$: C 74.09, H 7.38; found: C 73.77, H 6.72.

*(+)-(2*S*)-4-{2-[(*E*)-Pent-3-enyl]-1,3-dithian-2-yl}butane-1,3-diol* (**10**). A soln. of **9** (420 mg, 0.8 mmol) in MeOH (42 ml) and TsOH (84 mg, 0.5 mmol) were stirred at r.t. for 24 h. Evaporation, CC (petroleum ether/^{t}BuOME 1:2) of the residue yielded **10** (89 mg, 40%). Colorless oil. $[\alpha]_D = +15.4$ (c = 1.78, CH_2Cl_2). R_f (petroleum ether/^{t}BuOME 1:2) 0.35. IR ($CHCl_3$): 3624 (72.6), 3449 (45.5), 3017 (0.0), 3011 (10.7), 2944 (7.8), 1441 (25.2), 1427 (18.9), 1418 (25.9), 1206 (0.3), 1071 (0.0), 968 (33.9), 718 (56.0). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.60–1.70 (*m*, 1 H–C(5′)); 1.66 (*dd*, J = 6.5, 1.5, Me(5″)); 1.73–1.83 (*m*, 1 H–C(5′)); 1.86–1.98 (*m*, CH_2(1″), 1 H–C(2)); 1.98–2.16 (*m*, CH_2(2″), 1 H–C(2)); 2.16–2.34 (*m*, 1 H–C(4)); 2.41 (*dd*, J = 15.5, 9.5, 1 H–C(4)); 2.75–2.88 (*m*, H–C(4′), H–C(6′), OH); 2.96, 3.01 (each *ddd*, J = 14.5, 9.5, 3.5, H_{ax}–C(4′),

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[1]) Data of the more abundant diastereoisomer, else sum of the overlapped signals.

H_{ax}–C(6′)); 3.80–3.86 (*m*, 2 H–C(1)); 3.90 (*d*, *J* = 1, OH); 4.21–4.32 (*m*, H–C(3)); 5.35–5.54 (*m*, H–C(3″), H–C(4″)). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.9 (*q*, C(5″)); 24.8 (*t*, C(5′)); 26.0, 26.3 (*t*, C(4′), C(6′)); 27.2 (*t*, C(2″)); 39.1 (*t*, C(1″)); 39.6 (*t*, C(2)); 44.8 (*t*, C(4)); 51.8 (*s*, C(2′)); 61.2 (*t*, C(1)); 68.7 (*d*, C(3)); 125.8 (*d*, C(4″)); 130.0 (*d*, C(3″)). MS (240°): 276 (21, M^+), 221 (30, $[M - C_4H_7]^+$), 201 (29, $[M - C_3H_7O_2]^+$), 187 (36, $[201 - CH_2]^+$), 169 (18, $[M - C_3H_7S_2]^+$), 151 (57, $[169 - H_2O]^+$), 107 (54, $C_3H_7S_2^+$), 95 (65, $[M - C_3H_6S_2 - C_3H_7O_2]^+$), 75 (39, $C_3H_7O_2^+$), 69 (22, $C_5H_9^+$), 55 (100, $C_4H_7^+$). HR-MS: 276.1218 ($C_{13}H_{24}O_2S_2^+$; calc. 276.1218).

*(*S*)-Streptenol A* (= *(3*S*,8*E*)-1,3-Dihydroxydec-8-en-5-one*). To a soln. of **10** (104 mg, 0.37 mmol) in THF/$CHCl_3$ 2:5 (7 ml), $Hg(ClO_4)_2 \cdot 3\,H_2O$ (367 mg, 0.8 mmol) in THF (6 ml) was added slowly and then stirred for 5 min at r.t. The mixture was neutralized with sat. Na_2CO_3 soln. and extracted with $CHCl_3$, the org. layer washed with brine, dried ($MgSO_4$), evaporated, and the residue purified by CC (silica gel, ^{t}BuOMe/petroleum ether 3:1); 39 mg (57%) of (*S*)-streptenol A. R_f (AcOEt/hexane 4:1) 0.56. $[\alpha]_D = +23.0$ (*c* = 1.05, $CHCl_3$) ([11]: $[\alpha]_D = +23.0$ (*c* = 1.05, $CHCl_3$)). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.64 (*dd*, *J* = 1.0, 5.5, Me(10)); 1.76 (*dddm*, *J* = 6.5, 6.5, 6.5, 2 H–C(2)); 2.26 (*dddm*, *J* = 7.0, 7.0, 7.0, 2 H–C(7)); 2.50 (*t*, 7.0, 2 H–C(6)); 2.60 (*m*, 2 H–C(4)); 4.10–4.30 (*m*, 2 H–C(1), H–C(3)); 5.52–5.34 (*m*, H–C(8), H–C(9)). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.7 (*q*, C(10)); 26.4 (*t*, C(7)); 37.8 (*t*, C(2)); 43.2 (*t*, C(6)); 49.2 (*t*, C(4)); 60.5 (*t*, C(1)); 67.1 (*d*, C(3)); 126.0 (*d*, C(9)); 129.1 (*d*, C(8)); 211.2 (*s*, C(5)). Anal. calc. for $C_{10}H_{18}O_3$: C 64.49, H 9.74; found: C 64.76, H 9.19.

*(+)-(3*R*,5*E*,8*E*)- and (+)-(3*R*,5*Z*,8*E*)-1,3-Dihydroxydec-8-en-5-one* O-*Benzyloxime* (**11a** and **11b**, resp.). To a mixture of *O*-benzylhydroxylamin hydrochloride (840 mg, 5.3 mmol) and pyridine (1.8 ml) in anh. THF (3 ml), a soln. of (*S*)-streptenol A (600 mg, 3.2 mmol) in anh. THF (0.2 ml) was added dropwise. The mixture was stirred for 20 h at r.t. H_2O was added, the mixture extracted with AcOEt, the extract dried ($MgSO_4$) and evaporated, and the residue purified by CC (petroleum ether/^{t}BuOMe 2:1): 891 mg (95%) of slightly yellow oil. Separation of the (*Z*)- and (*E*)-isomer was easily achieved by CC.

Data of **11a**: R_f (AcOEt/hexane/MeOH 1:1:0.2) 0.76. $[\alpha]_D = +11.4$ (*c* = 1, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.64 (*dd*, *J* = 1.0, 6.0, 3 H–C(10)); 1.60–1.98 (*m*, 2 H–C(2)); 2.12–2.21 (*m*, 2 H–C(7)); 2.28 (*d*, *J* = 3.0, 1 H–C(4)); 2.32 (*d*, *J* = 9.0, 1 H–C(4)); 2.37 (*t*, *J* = 8.0, 2 H–C(6)); 3.78–3.84 (*m*, 2 H–C(1)); 4.38 (*dddd*, *J* = 3.0, 3.0, 9.0, 9.0, 1 H–C(3)); 5.06, 5.07 (*s*, PhCH_2); 5.32–5.48 (*m*, H–C(8), H–C(9)); 7.26–7.38 (*m*, 2 H_o, 2 H_m, H_p). ^{13}C-NMR (100 MHz, $CDCl_3$): 17.8 (*q*, C(10)); 28.4 (*t*, C(6)); 29.4 (*t*, C(7)); 37.8 (*t*, C(2)); 41.3 (*t*, C(4)); 61.1 (*t*, C(1)); 68.4 (*d*, C(3)); 75.6 (*t*, Ph*C*H_2); 125.9 (*d*, C(9)); 127.7 (*d*, C_p); 127.9 (*d*, 2 C_o); 128.3 (*d*, 2 C_m); 129.6 (*d*, C(8)); 137.9 (*s*, C_{ipso}); 160.0 (*s*, C(5)). Anal. calc. for $C_{17}H_{25}NO_3$: C 69.29, H 8.36; found: C 69.27, H 8.34.

Data of **11b**: R_f (AcOEt/hexane/MeOH 1:1:0.2) 0.85. $[\alpha]_D = +21$ (*c* = 1, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.64 (*d*, *J* = 6.0, 3 H–C(10)); 1.66–1.74 (*m*, 2 H–C(2)); 2.16–2.26 (*m*, 2 H–C(7)); 2.26–2.32 (*m*, 2 H–C(6)); 2.40 (*dd*, *J* = 4.0, 13.0, 1 H–C(4)); 2.68 (*dd*, *J* = 8.0, 13.0, 1 H–C(4)); 3.74–3.87 (*m*, 2 H–C(1)); 4.14 (*ddm*, *J* = 4.0, 8.0, 1 H–C(3)); 5.08 (*s*, PhCH_2); 5.34–5.51 (*m*, H–C(8), H–C(9)); 7.26–7.40 (*m*, 2 H_o, 2 H_m, H_p). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.8 (*q*, C(10)); 29.2 (*t*, C(7)); 35.2 (*t*, C(6)); 36.9 (*t*, C(4)); 38.8 (*t*, C(2)); 60.9 (*t*, C(1)); 69.3 (*d*, C(3)); 75.5 (*t*, PhCH_2); 125.7 (*d*, C(9)); 127.7 (*d*, C_p); 128.0 (*d*, 2 C_o); 128.3 (*d*, 2 C_m); 129.7 (*d*, C(8)); 137.6 (*s*, C_{ipso}); 158.8 (*s*, C(5)). Anal. calc. for $C_{17}H_{25}NO_3$: C 69.29, H 8.36; found: C 69.21, H 8.37.

*(3*R*,5*R*,8*E*)- and (3*R*,5*S*,8*E*)-5-[(Benzyloxy)amino]dec-8-ene-1,3-diol* (**12a** and **12b**, resp.). The preparation of **12** gave best diastereoselectivities following the procedures below. Starting with **11b** (*Z*) a ratio **12b**/**12a** of 70:30 was obtained if **11b** was added dropwise at −15° to a suspension of 10 equiv. of TABH in AcOH/MeCN 1:1. The mixture was stirred for 5 h, sat. Na_2CO_3 soln. added, and the mixture extracted with AcOEt. Purification by CC (petroleum ether/^{t}BuOMe 1:2) yielded 50% of a colorless oil.

Starting with **11a** (*E*) a ratio **12a**/**12b** of 81:19 was obtained if **11a** was treated with 10 equiv. of $NaCNBH_3$ for 60 h at −20° in AcOH/MeCN 1:1. Yield 98%. R_f (^{t}BuOMe) 0.29. IR ($CHCl_3$): 3624 (85.0), 3015 (11.5), 2939 (0.0), 2857 (21.1), 1455 (12.7), 1439 (18.2), 1365 (37.4), 1205 (45.7), 1074 (15.5) 969 (8.0), 909 (25.9), 700 (6.4). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.65 (*d*, *J* = 5, 6 H–C(10)); 1.34–1.86 (*m*, 4 H–C(2), 4 H–C(4), 4 H–C(6)); 1.94–2.08 (*m*, 4 H–C(7)); 3.00 (*dddd*, *J* = 6.5, 6.5, 6.5, 6.5, H–C(5)); 3.18[1]) (*dddd*, *J* = 7, 7, 7, 3, H–C(5)); 3.76–3.90 (*m*, 4 H–C(1)); 3.96 (*dddd*, *J* = 6, 6, 6, 6, H–C(3)); 4.10[1]) (*dddd*, *J* = 9, 9, 3, 3, H–C(3)); 4.64–4.76 (*m*, PhCH_2); 5.32–5.48 (*dqm*, overlapped, *J* = 15, 5, 2 H–C(8), 2 H–C(9)); 7.24–7.41 (*m*, 4 H_o, 4 H_m, 2 H_p). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.9 (2*q*, C(10)); 28.6, 29.2[1]) (*t*, C(7)); 30.8[1]), 32.8 (*t*, C(6)); 37.4[1]), 38.4 (*t*, C(4)); 38.5[1]), 38.8 (*t*, C(2)); 57.8[1]), 61.2 (*d*, C(5)); 61.5, 61.8[1]) (*t*, C(1)); 69.3[1]), 78.1 (*d*, C(3)); 76.3, 76.4[1]) (*t*, PhCH_2); 125.6, 125.8[1]) (*d*, C(9)); 128.0, 128.1[1]) (*d*, C(4′)); 128.45, 128.5[1]) (2*d*, 2 C_o, 2 C_m); 130.2[1]), 130.4 (*d*, C(8)); 137.2 (2*s*, C_{ipso}). MS (120°): 294 (0.25, $[M + H]^+$), 224 (17, $[M - C_5H_9]^+$), 91 (100, Bn^+), 77 (18,

$C_6H_5^+$), 69 (26, $C_5H_9^+$), 65 (10, $C_5H_5^+$), 55 (46, $C_4H_7^+$), 51 (10, $C_4H_3^+$). HR-MS: 224.1287 ($C_{12}H_{18}O_3N^+$; calc. 224.1287). Anal. calc. for $C_{17}H_{27}NO_3$: C 69.59, H 9.28; found: C 69.36, H 9.35.

*(−)-(3*R*,5*R*,8*E*)- and (−)-(3*R*,5*S*,8*E*)-5-Aminodec-8-ene-1,3-diol* (**13a** and **13b**, resp.). *Method 1:* A (*Z*/*E*)-oxime mixture **11** (1.947 g, 6.7 mmol) in anh. THF (17 ml) was added slowly at r.t. to a suspension of $LiAlH_4$ (1.58 g, 42 mmol) in anh. THF (22 ml). The mixture was stirred for 16 h, a Na_2SO_4 soln. added carefully, and the precipitate that formed filtered. The filtrate was extracted with AcOEt and the org. layer dried ($MgSO_4$) and evaporated: 985 mg of **13a**/**13b** (78%), suitable for further transformations without purification. The diastereoisomers could be separated by CC (CH_2Cl_2/MeOH/NH_3 6:1:0.1).

Method 2: A soln. of **12a** (93 mg, 0.32 mmol) in anh. THF (1 ml) was added at −78° to a suspension of $LiAlH_4$ (50 mg, 1.3 mmol) in anh. THF (1 ml) under Ar. The mixture was slowly warmed to r.t. and then refluxed for 10 h. Workup and CC as described in *Method 1* yielded 46 mg (77%) of **13a** (3*R*,5*R*). R_f (CH_2Cl_2/MeOH/NH_3 90:15:1.5) 0.25. $[\alpha]_D = -15$ ($c = 1$, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.24–1.42 (*m*, 2 H–C(6)); 1.46–1.62 (*m*, 1 H–C(2), 2 H–C(4)); 1.64–1.72 (*m*, 1 H–C(2)); 1.66 (*dd*, *J* = 1.0, 6.0, 3 H–C(10)); 1.96–2.10 (*m*, 2 H–C(7)); 2.88 (*dddd*, *J* = 2.5, 5.0, 7.5, 10.0, H–C(5)); 3.04–3.28 (br., 4 H)); 3.78–3.86 (*m*, 2 H–C(1)); 4.09 (*dddd*, *J* = 2.0, 4.0, 8.0, 10.0, H–C(3)); 5.34–5.50 (*m*, H–C(8), H–C(9)). ^{13}C-NMR (100 MHz, $CDCl_3$): 17.7 (*q*, C(10)); 28.5 (*t*, C(7)); 39.2 (*t*, C(6)); 39.9 (*t*, C(2)); 42.1 (*t*, C(4)); 52.0 (*d*, C(5)); 60.5 (*t*, C(1)); 72.3 (*d*, C(3)); 125.3 (*d*, C(9)); 130.3 (*d*, C(8)). Anal. calc. for $C_{10}H_{21}NO_2$: C 64.13, H 11.38; found: C 64.09, H 11.41.

The procedure described for **13a** was applied to **12b** for the preparation of **13b** (3*R*,5*S*). R_f (CH_2Cl_2/MeOH/NH_3 90:15:1.5) 0.19. $[\alpha]_D = -19.6$ ($c = 1$, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.44–1.64 (5 H), 1.74–1.84 (1 H) (*m*, 2 H–C(2), 2 H–C(4), 2 H–C(6)); 1.65 (*dd*, *J* = 1.0, 6.0, 3 H–C(10)); 1.96–2.10 (*m*, 2 H–C(7)); 2.86–3.18 (br., 4 H); 3.18 (*dddd*, *J* = 3.0, 7.0, 7.0, 7.0, H–C(5)); 3.85 (*t*, *J* = 6.0, 2 H–C(1)); 4.18 (*dddd*, *J* = 3.0, 3.0, 6.0, 9.0, H–C(3)); 5.34–5.52 (*m*, H–C(8), H–C(9)). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.8 (*q*, C(10)); 29.1 (*t*, C(7)); 37.3 (*t*, C(6)); 38.8 (*t*, C(2)); 41.3 (*t*, C(4)); 48.2 (*d*, C(5)); 60.8 (*t*, C(1)); 68.7 (*d*, C(3)); 125.5 (*d*, C(9)); 130.3 (*d*, C(8)). Anal. calc. for $C_{10}H_{21}NO_2$: C 64.13, H 11.38; found: C 64.08, H 11.35.

*(−)-(4*R*,6*R*)-6-(2-Hydroxyethyl)-4-[(*E*)-pent-3-enyl]-1,3-oxazinan-2-one* (**14**). A soln. of **13a** (99 mg, 0.53 mmol) and 1,1′-carbonylbis[1*H*-imidazole] (91 mg, 0.56 mmol) in THF (20 ml) was stirred for 12 h. The volatile components were evaporated. Then, H_2O (130 ml) was added, the mixture extracted with AcOEt (4 × 40 ml), the org. layer dried ($MgSO_4$) and evaporated, and the residue submitted to CC (CH_2Cl_2/MeOH 20:1); 97 mg (85%) of **14** (4*R*,6*R*). R_f (CH_2Cl_2/MeOH 20:1) 0.24. $[\alpha]_D = -46.6$ ($c = 6.5$ mg/ml, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.37 (*ddd*, *J* = 10.8, 10.8, 13.2, 1 H_{ax}–C(5)); 1.60 (*m*, 2 H–C(1″)); 1.63 (*m*, 3 H–C(5″)); 1.85 (*m*, 2 H–C(1′)); 2.05 (*m*, 2 H–C(2″)); 2.10 (*m*, two *J* > 9.0, 1 H_{eq}–C(5)); 3.50 (*m*, H–C(4)); 3.70 (*m*, 2 H–C(2′)); 4.45 (*m*, H–C(6)); 5.45 (*m*, H–C(3″), H–C(4″)). C,H-COSY ($CDCl_3$): 18.0 (*q*, C(5″)); 29.0 (*t*, C(2″)); 34.2 (*t*, C(5)); 36.8 (*t*, C(1″)); 39.1 (*t*, C(1′)); 51.5 (*d*, C(4)); 58.5 (*t*, C(2′)); 75.9 (*d*, C(6)); 126.8 (*d*, C(4″)); 131.2 (*d*, C(3″)); 157.3 (*s*, C(2)). Anal. calc. for $C_{11}H_{19}NO_3$: C 61.94, H 8.98: found: C 62.92, H 9.23.

*(−)-(3*R*,5*R*,8*E*)- and (+)-(3*R*,5*S*,8*E*)-Methanesulfonic Acid 3-Hydroxy-5-[(methylsulfonyl)amino]dec-8-enyl Ester* (**15a** and **15b**, resp.). To **13a** (150 mg, 0.8 mmol) in anh. CH_2Cl_2 (5 ml), Et_3N (235 µl, 1.7 mmol) and finally MesCl (126 µl, 1.6 mmol) were added dropwise at 0°. After 2 h stirring, the mixture was washed with $NaHCO_3$ soln. and extracted with AcOEt. Drying ($MgSO_4$) and evaporation gave a residue which was purified by CC (CH_2Cl_2/MeOH/NH_3 140:5:1). 206 mg (75%) of **15a**. R_f (CH_2Cl_2/MeOH/NH_3 90:5:1) 0.38. $[\alpha]_D = -1.9$ ($c = 8$ mg/ml, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.52–1.70 (*m*, 2 H–C(4), 2 H–C(6)); 1.66 (*dd*, *J* = 1.0, 6.0, 3 H–C(10)); 1.78 (*dddd*, *J* = 5.0, 5.0, 10.0, 15.0, 1 H–C(2)); 1.97 (*dddd*, *J* = 3.0, 6.0, 9.0, 15.0, 1 H–C(2)); 2.04–2.12 (*m*, 2 H–C(7)); 2.97 (*s*, 1 $MeSO_2$); 3.04 (*s*, 1 $MeSO_2$); 3.54 (*m*, 1 H–C(5)); 3.97 (*ddm*, *J* = 3.0, 5.0, 1 H–C(3)); 4.34 (*ddd*, *J* = 5.0, 9.0, 9.5, 1 H–C(1)); 4.46 (*ddd*, *J* = 6.0, 9.5, 10.0, 1 H–C(1)); 4.94 (*m*, NH); 5.35–5.53 (*m*, H–C(8), H–C(9)). ^{13}C-NMR (100 MHz, $CDCl_3$): 17.9 (*q*, C(10)); 28.5 (*t*, C(7)); 35.9 (*t*, C(6)); 36.9 (*t*, C(2)); 37.3 (*q*, $MeSO_3$); 41.7 (*q*, $MeSO_2N$); 42.7 (*t*, C(4)); 52.7 (*d*, C(5)); 66.1 (*d*, C(3)); 67.0 (*t*, C(1)); 126.2 (*d*, C(9)); 129.7 (*d*, C(8)).

As described for **15a**, **15b** was obtained from **13b**. R_f (CH_2Cl_2/MeOH/NH_3 90:5:1) 0.52. $[\alpha]_D = +7.0$ ($c =$ 5 mg/ml, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.9–2.1 (*m*, 2 H–C(2), 2 H–C(4), 2 H–C(6), 2 H–C(7), 3 H–C(10)); 3.01 (*s*, $MeSO_3$); 3.10 (*s*, $MeSO_2N$); 3.60 (*m*, 1 H–C(5)); 3.85 (*m*, 1 H–C(3)); 4.25 (*d*, *J* = 9.0, NH); 4.40 (*m*, 1 H–C(1)); 4.52 (*m*, 1 H–C(1)); 5.95 (*m*, H–C(8), H–C(9)). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.9 (*q*, C(10)); 29.1 (*t*, C(7)); 30.5 (*t*, C(6)); 36.1 (*t*, C(2)); 37.4 (*q*, $MeSO_3$); 40.1 (*t*, C(4)); 41.7 (*q*, $MeSO_2N$); 51.4 (*d*, C(5)); 69.1 (*d*, C(3)); 67.5 (*t*, C(1)); 126.2 (*d*, C(9)); 129.8 (*d*, C(8)).

*(−)-(3*R*,5*R*,8*E*)- and (+)-(3*R*,5*S*,8*E*)-Methanesulfonic Acid 5-[(Methylsulfonyl)amino]-3-[(methylsulfonyl)oxy]dec-8-enyl Ester* (**16a** and **16b**, resp.). To a soln. of **13a** (240 mg, 1.28 mmol) in anh. CH_2Cl_2 (8 ml), Et_3N (720 µl, 5.2 mmol) and MesCl (403 µl, 5.1 mmol) were added at 0°. The mixture was stirred for 2 h, quenched

with sat. Na_2CO_3 soln. and extracted with AcOEt. Drying ($MgSO_4$) and evaporation under high vacuum yielded 505 mg (94%) of **16a**, which could be used without further purification. R_f (^{t}BuOMe/petroleum ether 2:1) 0.06. $[\alpha]_D = -3.54$ ($c = 1$, CH_2Cl_2). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.50–1.85 (*m*, 2 H–C(4), 2 H–C(6)); 1.60 (*d*, *J* = 6.1, 3 H–C(10)); 2.00–2.10 (*m*, 2 H–C(7)); 1.97–2.28 (*m*, 2 H–C(2)); 3.00 (*s*, $MeSO_2$); 3.02 (*s*, $MeSO_2$); 3.10 (*s*, $MeSO_2$); 3.55 (*m*, 1 H–C(5)); 4.28–4.37 (*m*, 2 H–C(1)); 4.63 (*d*, *J* = 8.6, NH); 5.03 (*m*, 1 H–C(3)); 5.30–5.50 (*m*, H–C(8), H–C(9)). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.8 (*q*, C(10)); 28.6 (*t*, C(7)); 33.6 (*t*, C(6)); 35.3 (*t*, C(2)); 37.3 (*q*, $MeSO_3$); 38.4 (*q*, $MeSO_3$); 41.2 (*t*, C(4)); 41.9 (*q*, $MeSO_2N$); 50.6 (*d*, C(5)); 65.4 (*t*, C(1)); 76.2 (*d*, C(3)); 126.3 (*d*, C(9)); 129.3 (*d*, C(8)). Anal. calc. for $C_{13}H_{27}NO_8S_3$: C 37.04, H 6.46; found: C 36.33, H 6.06.

As described for **16a**, **16b** was obtained from **13b**. R_f (^{t}BuOMe/petroleum ether 2:1) 0.14. $[\alpha]_D = +8.76$ (c = 1, CH_2Cl_2). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.45–1.80 (*m*, 2 H–C(4), 2 H–C(6)); 1.65–1.93 (*m*, 2 H–C(2)); 1.70 (*d*, *J* = 5.5, 3 H–C(10)); 2.09–2.16 (*m*, 2 H–C(7)); 3.04 (*s*, $MeSO_2$); 3.08 (*s*, $MeSO_2$); 3.12 (*s*, $MeSO_2$); 3.70 (*m*, 1 H–C(5)); 4.12–4.22 (*m*, 2 H–C(1)); 4.41 (*d*, *J* = 8.0, NH); 4.91 (*m*, 1 H–C(3)); 5.68–5.79 (*m*, H–C(8), H–C(9)). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.8 (*q*, C(10)); 28.5 (*t*, C(7)); 34.8 (*t*, C(6)); 35.4 (*t*, C(2)); 37.3 (*q*, $MeSO_3$); 38.5 (*q*, $MeSO_3$); 40.1 (*t*, C(4)); 42.3 (*q*, $MeSO_2N$); 50.7 (*d*, C(5)); 65.6 (*t*, C(1)); 76.1 (*d*, C(3)); 126.4 (*d*, C(9)); 129.4 (*d*, C(8)).

*(+)-(2*R*,4*S*,3*E*)- and (−)-(2*S*,4*S*,3*E*)-Methanesulfonic Acid 1-(Methylsulfonyl)-2-(pent-3-enyl)piperidin-4-yl Ester* (**17a** and **17b**, resp.). A soln. of **16a** (505 mg, 1.22 mmol) and DBU (4 ml) in anh. THF (42 ml) was stirred for 12 h at r.t. H_2O was added and the mixture extracted with AcOEt. The org. layer was dried ($MgSO_4$) and evaporated and the residue chromatographed (AcOEt/petroleum ether/i-PrOH 1:5:0.25): 390 mg (98%) of **17a**. R_f (AcOEt/petroleum ether/i-PrOH 1:4:0.25) 0.16. $[\alpha]_D = -8.5$ (c = 1, MeOH). IR ($CHCl_3$): 3031 (27.8), 3026 (28.4), 2939 (35.6), 1457 (48.6), 1336 (0.4), 1205 (17.3), 1176 (0.9), 1148 (4.1), 941 (0.0), 851 (25.0), 812 (44.5). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.65 (*dd*, *J* = 6.0, 1.0, 3 H–C(5′)); 1.68–1.76 (*m*, 2 H–C(1′)); 1.80 (*ddm*, *J* = 11.5, 5, 1 H_{eq}–C(3)); 1.88 (*ddd*, *J* = 12, 11.5, 5.5, 1 H_{ax}–C(3)); 2.05 (*td*, *J* = 7, 6.5, 2 H–C(2′)); 2.11–2.20 (*ddmp*, *J* = 15, 2.5, 2 H–C(5)); 2.90 (*s*, $MeSO_2$); 3.03 (*s*, $MeSO_2$); 3.10 (*ddd*, *J* = 15, 15, 2.5, 1 H_{ax}–C(6)); 3.87 (*dm*, *J* = 15, 1 H_{eq}–C(6)); 4.15 (*ddm*, *J* = 5.5, 5, 1 H_{eq}–C(2)); 4.92 (*dddd*, *J* = 11.5, 11.5, 4.5, 4.5, 1 H_{ax}–C(4)); 5.39 (*dqt*, *J* = 15.5, 6.5, 1 H–C(3′)); 5.48 (*dq*, *J* = 15.5, 6, 1 H–C(4′)). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.8 (*q*, C(5′)); 29.2 (*t*, C(2′)); 30.7 (*t*, C(1′)); 32.3 (*t*, C(5)); 35.2 (*t*, C(3)); 38.7 (*t*, C(6)); 38.9 (*q*, $MeSO_3$); 40.9 (*q*, $MeSO_2N$); 52.8 (*d*, C(2)); 74.8 (*d*, C(4)); 126.4 (*d*, C(4′)); 129.2 (*d*, C(3′)). MS (85°): 325 (1.3, M^+), 310 (0.6, $[M - Me]^+$), 256 (13, $[M - C_5H_9]^+$), 230 (11, $[M - OMes]^+$), 189 (2, $[230 - C_3H_5]^+$), 161 (42, $[189 - C_2H_4]^+$), 160 (100, $[161 - H]^+$), 82 (78, $[161 - Mes]^+$), 55 (65, $C_4H_7^+$). HR-MS: 325.1018 ($C_{12}H_{23}NO_5S_2^+$; calc. 325.1018). Anal. calc. for $C_{12}H_{23}NO_5S_2$: C 44.29, H 7.12; found: C 44.25, H 7.20.

As described for **17a**, **17b** was obtained from **16b**. R_f (AcOEt/petroleum ether/i-PrOH 1:4:0.25) 0.10. $[\alpha]_D = +10.7$ (c = 1, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.65 (*d*, *J* = 4.6, 3 H–C(5′)); 1.72–2.16 (*m*, 2 H–C(1′), 2 H–C(2′), 2 H–C(3), 2 H–C(5)); 2.91 (*s*, $MeSO_2$); 3.04 (*s*, $MeSO_2$); 3.35 (*ddd*, *J* = 4.0, 11.5, 15.4, 1 H_{ax}–C(6)); 3.68 (*dm*, *J* = 15.4, 1 H_{eq}–C(6)); 4.02 (*dddd*, *J* = 6.9, 6.9, 6.9, 6.9, 1 H_{eq}–C(2)); 5.10 (*dddd*, *J* = 3.0, 3.0, 3.0, 3.0, 1 H_{eq}–C(4)); 5.34–5.54 (*m*, H–C(3′), H–C(4′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 18.0 (*q*, C(5′)); 29.8 (*t*, C(2′)); 30.6 (*t*, C(1′)); 32.3 (*t*, C(5)); 32.7 (*t*, C(3)); 35.2 (*t*, C(6)); 38.6 (*q*, $MeSO_3$); 40.8 (*q*, $MeSO_2N$); 51.1 (*d*, C(2)); 75.4 (*d*, C(4)); 126.2 (*d*, C(4′)); 129.7 (*d*, C(3′)). Anal. calc. for $C_{12}H_{23}NO_5S_2$: C 44.29, H 7.12; found: C 44.31, H 7.57.

*(+)-(2*R*,4*S*,3*E*)- and (−)-(2*S*,4*S*,8*E*)-1-(Methylsulfonyl)-2-(pent-3-enyl)piperidin-4-ol* (**18a** and **18b**, resp.). *Method 1:* Using compound **15a**, structure **18a** could be obtained as described for **17a**. *Method 2:* A 70% suspension of SMAH in toluene (400 mg) was dried under high vacuum. Under Ar, the residue was dissolved in anh. diglyme (1.5 ml). To this soln., **17a** (50 mg, 0.15 mmol) was added, and the mixture was stirred for 2 h at 60°. Then Na_2SO_4 soln. was added and the precipitate filtered off, washed with sat. NaCl soln., and extracted with AcOEt. Drying ($MgSO_4$) and evaporation gave a residue which was purified by CC (silica gel, AcOEt/MeOH/NH_3 6:1:0.1): 27 mg (72%) of **18a**. R_f 0.57 (CH_2Cl_2/MeOH 20:1). $[\alpha]_D = -34.29$ (c = 16.5 mg/ml, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.62–1.68 (*m*, 2 H–C(1′), 2 H–C(5)); 1.65 (*dm*, *J* = 4.7, 3 H–C(5′)); 1.92–2.08 (*m*, 2 H–C(2′), 2 H–C(3)); 2.90 (*s*, $MeSO_2$); 3.08 (*ddd*, *J* = 2.0, 13.3, 15.4, 1 H_{ax}–C(6)); 3.83 (*ddd*, *J* = 2.0, 4.1, 15.4, 1 H_{eq}–C(6)); 3.95 (*dddd*, *J* = 4.5, 4.5, 11.3, 11.3, 1 H_{ax}–C(2)); 4.10 (*dddd*, *J* = 6.2, 6.2, 6.2, 6.2, 1 H_{eq}–C(4)); 5.36–5.55 (*m*, H–C(3′), H–C(4′)). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.8 (*q*, C(5′)); 29.4 (*t*, C(2′)); 30.9 (*t*, C(1′)); 34.7 (*t*, C(5)); 37.6 (*t*, C(3)); 39.1 (*t*, C(6)); 40.8 (*q*, $MeSO_2N$); 53.1 (*d*, C(2)); 64.5 (*d*, C(4)); 126.1 (*d*, C(4′)); 129.9 (*d*, C(3′)). MS (120°): 247 (0.6, M^+), 178 (100.0, $[M - C_5H_9]^+$), 160 (10, $[178 - H_2O]^+$, 134 (50, $[M - Mes - H_2O - Me]^+$), 55 (44, $C_4H_7^+$). HR-MS: 247.1242 ($C_{11}H_{21}NO_3S^+$, calc. 247.1242). Anal. calc. for $C_{11}H_{21}NO_3S$: C 53.41, H 8.56; found: C 53.19, H 8.47.

As described for **18a**, **18b** was obtained from **17b**. R_f (AcOEt/hexane 1:1) 0.45. $[\alpha]_D = +17.76$ (c = 13 mg/ml, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.54–1.67 (*dm*, *J* = 14.0, 1 H_{ax}–C(5)); 1.64 (*d*, *J* = 6.0, 3 H–C(5′));

1.67–1.80 (*m*, 2 H–C(1′)); 1.86 (*ddd*, *J* = 5.5, 12.0, 12.0, 1 H_{ax}–C(3)); 2.02 (*ddd*, *J* = 7.0, 7.0, 7.0, 2 H–C(2′)); 2.10–2.20 (*dm*, *J* = 12.0, 1 H_{eq}–C(3)); 2.10–2.20 (*dm*, *J* = 2.5, 1 H_{eq}–C(5)); 2.89 (*s*, $MeSO_2$); 3.02 (OH); 3.10 (*ddd*, *J* = 2.5, 14.0, 14.0, 1 H_{ax}–C(6)); 3.88 (*dm*, *J* = 14.0, 1 H_{eq}–C(6)); 4.15 (*dddd*, *J* = 5.5, 5.5, 5.5, < 5.5, 1 H_{eq}–C(2)); 4.90 (*dddm*, *J* = 4.5, 4.5, 12.0, 1 H_{ax}–C(4)); 5.35–5.52 (*m*, H–C(3′), H–C(4′)). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.8 (*q*, C(5′)); 29.2 (*t*, C(2′)); 30.7 (*t*, C(1′)); 32.3 (*t*, C(5)); 35.2 (*t*, C(3)); 38.7 (*t*, C(6)); 40.8 (*q*, $MeSO_2$); 52.8 (*d*, C(2)); 74.7 (*d*, C(4)); 126.4 (*d*, C(4′)); 129.2 (*d*, C(3′)). Anal. calc. for $C_{11}H_{21}NO_3S$: C 53.41, H 8.56; found: C 53.26, H 8.53.

*(+)-(2*R*,4*S*,3*E*)- and (−)-(2*S*,4*S*,3*E*)-2-*(Pent-3-enyl)piperidin-4-ol (**19a** and **19b**, resp.). The procedure for the preparation of **19a** was similar to the preparation of **18a**: **17a** (737 mg, 2.3 mmol) was treated with SMAH (5.9 g) in anh. diglyme (15 ml) as described. However, the temp. was first kept at 60° for 1 h, then increased to 140° and kept for 12 h. Workup as described for **18** and CC (AcOEt/MeOH/NH_3 5 : 1 : 0.1) yielded 289 mg (75%) of **19a**. R_f (AcOEt/MeOH/NH_3 5 : 1 : 0.1) 0.08. $[\alpha]_D = -2.24$ (*c* = 25 mg/ml, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.48–1.65 (*m*, 1 H–C(1′), 1 H–C(3), 1 H–C(5)); 1.65 (*d*, *J* = 4.9, 3 H–C(5′)); 1.68–1.77 (*m*, 1 H–C(1′), 1 H–C(3), 1 H–C(5)); 1.95–2.20 (*m*, 2 H–C(2′)); 2.30–2.60 (br., 2 H); 2.86 (*ddd*, *J* = 3.0, 4.6, 12.2, 1 H_{eq}–C(6)); 2.94 (*dddd*, *J* = 2.8, 6.4, 6.4, 10.0, 1 H_{ax}–C(2)); 3.04 (*ddd*, *J* = 3.1, 12.2, 12.2, 1 H_{ax}–C(6)); 4.14 (*dddd*, *J* = 3.1, 3.1, 3.1, 3.1, 1 H_{eq}–C(4)); 5.37–5.49 (*m*, H–C(3′), H–C(4′)). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.9 (*q*, C(5′)); 29.0 (*t*, C(2′)); 33.3 (*t*, C(1′)); 36.4 (*t*, C(5)); 39.5 (*t*, C(6)); 40.7 (*t*, C(3)); 50.1 (*d*, C(2)); 64.8 (*d*, C(4)); 125.2 (*d*, C(4′)); 130.8 (*d*, C(3′)). MS (100°): 169 (7, M^+), 167 (10, $[M - H_2]^+$), 152 (7, $[M - OH]^+$), 149 (34, $[167 - H_2O]^+$), 140 (23, $[167 - HCN]^+$), 126 (10, $[140 - CH_2]^+$), 113 (20, $[M - C_4H_7]^+$), 100 (100, $[M - C_5H_9]^+$), 97 (8, $C_6H_{11}N^+$, $[M - H_2O$ and *retro-Diels-Alder*$]^+$), 82 (20, $[100 - H_2O^+$), 69 (15, $C_5H_9)^+$, 56 (41, $[97 - C_3H_5]^+$), 55 (32, $C_4H_7^+$). HR-MS: 169.1467 ($C_{10}H_{19}NO^+$; calc. 169.1467). Anal. calc. for $C_{10}H_{19}NO$: C 70.96, H 11.31; found: C 70.43, H 11.11.

As described for **19a**, **19b** was obtained from **17b**. R_f (AcOEt/MeOH/NH_3 5 : 1 : 0.1) 0.24. $[\alpha]_D = +7.3$ (*c* = 25 mg/ml, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.30–1.50 (*m*, 1 H–C(1′), 1 H–C(5)); 1.65 (*dd*, *J* = 1.0, 5.5, 3 H–C(5′)); 1.60–1.80 (*m*, 1 H–C(1′), 1 H–C(5)); 1.90–2.00 (*m*, 2 H–C(3)); 2.00–2.10 (*m*, 2 H–C(2′)); 2.51 (*dddd*, *J* = 2.4, 7.2, 7.2, 12.0, 1 H_{ax}–C(2)); 2.62 (*ddd*, *J* = 2.5, 12.5, 12.5, 1 H_{ax}–C(6)); 3.12 (*ddd*, *J* = 2.7, 4.6, 12.5, 1 H_{eq}–C(6)); 3.64 (*dddd*, *J* = 4.5, 4.5, 11.0, 11.0, 1 H_{ax}–C(4)); 5.40–5.46 (*m*, H–C(3′), H–C(4′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 17.9 (*q*, C(5′)); 29.0 (*t*, C(2′)); 36.2 (*t*, C(1′)); 36.7 (*t*, C(5)); 42.5 (*t*, C(6)); 44.7 (*t*, C(3)); 54.8 (*d*, C(2)); 69.3 (*d*, C(4)); 125.2 (*d*, C(4′)); 130.8 (*d*, C(3′)). Anal. calc. for $C_{10}H_{19}NO$: C 70.96, H 11.31; found: C 70.81, H 11.24.

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