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STUDIES ON FORSKOLIN RING C FORMING REACTIONS

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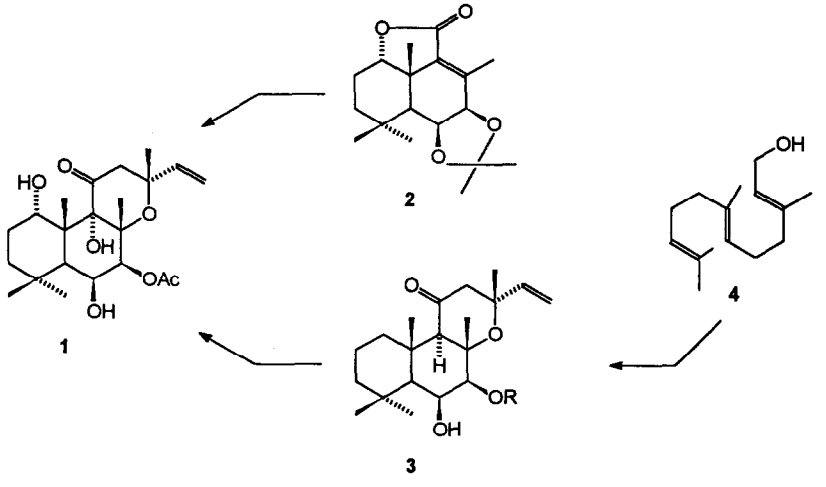
Abstract - Labdane derivative **27** has been prepared from (E,E)-farnesol (**4**). Selenium- and mercury-mediated cyclization of **24** leads to compounds with the opposite configuration at C-8 as found in forskolin.

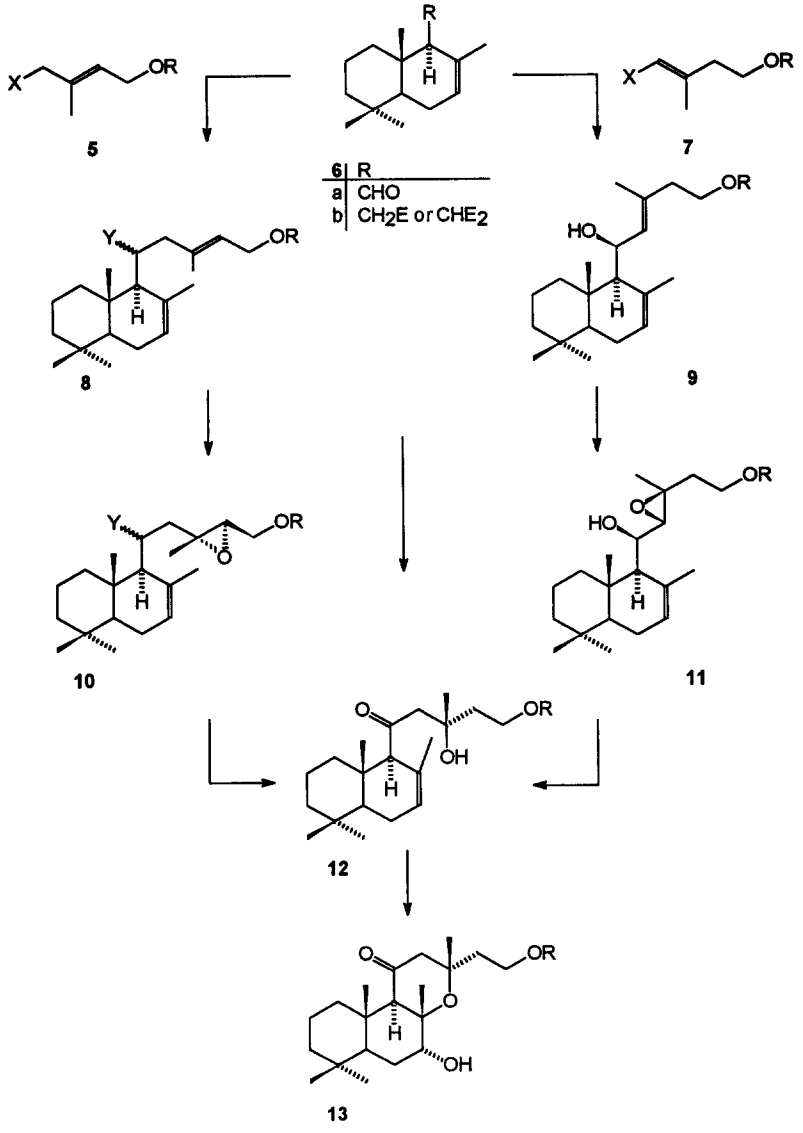
Introduction

Three total syntheses of the pharmacologically important diterpene forskolin (**1**) have been accomplished until now.[1] All of them proceed via the so-called Ziegler lactone (**2**).[2] As detailed in a recent publication we are interested to gain access to forskolin on a different synthetic route where a derivative of 1,9-dideoxy forskolin (**3**, R=Ac) is the key intermediate.[3] **3** can be converted to **1** by a combination of enzymatic and chemical steps. Along these lines 8,13-epoxylabdane derivative *rac*-**13** was prepared in eight steps commencing from (E,E)-farnesol (**4**). Key features are (i) the formation of **9** from (±)-drimenal (*rac*-**6a**) and the organolithium reagent **7** (X=Li), (ii) the stereoselective introduction of the oxygen functionality at C-13 by Sharpless I oxidation of **9**



Scheme 1.

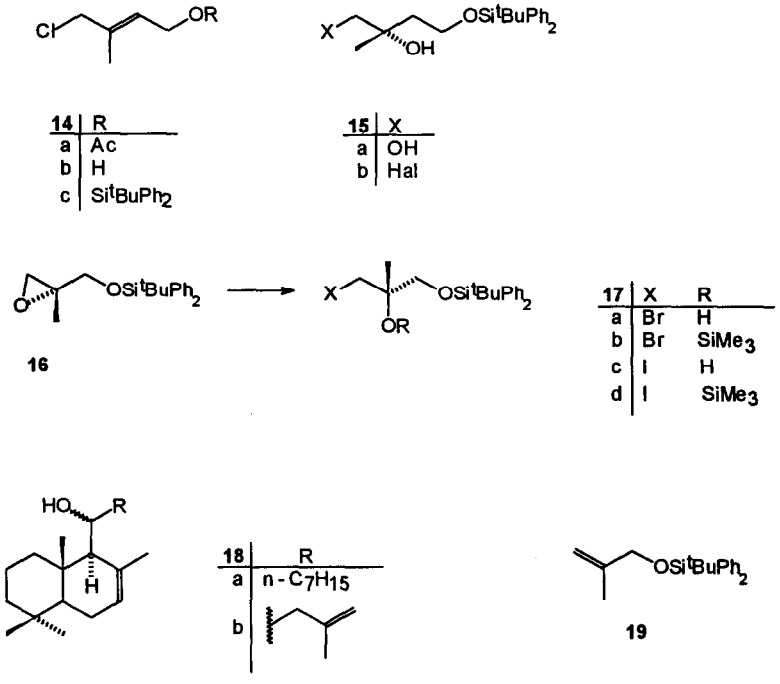
(**9**→**11**), and (iii) the trimethylsilyl triflate-mediated closure of ring C (**12**→**13**).[3] One might consider a related synthetic scheme, in which **6a** on reaction with a nucleophilic reagent **5** would yield **8**. Equivalent would be the use of **5** and **6** with inverted reactivities, i.e. alkylation of **6b** (E=electron withdrawing group) with **5** (X=leaving group) The oxygen functionality at C-13 could then be introduced by Katsuki-Sharpless epoxidation (**8**→**10**) with kinetic resolution at this stage. Coupling of an organometallic reagent of type **15**[4] (X=metal) to **6a** would be even more convergent since this would install directly the OH group at C-13 with the desired configuration at this centre. We describe here results that were obtained based on these ideas.



Scheme 2.

Attempts to add organometallic reagents of type 5 and 15 (X=metal) to drimenal

Since it seemed very probable that reductive 1,4- and ß-eliminations, respectively, as well as Wurtz coupling would plague the formation of organometallic reagents from precursors such as **14** or **15b**,[5,6] recourse was made to the use of highly active magnesium powder obtained from magnesium anthracene.[7] In some model experiments, (±)-drimenal (*rac*-**6a**)[8] was treated with the Grignard reagents obtained from both 1-bromoheptane and methallyl chloride and active magnesium powder at 0°C. **18a** and **18b** were obtained in yields of 34% and 49%, respectively (without optimization). However, all attempts to perform similar reactions using **14a**[9,10] and *rac*-**17b** as precursors of Grignard reagents met with no success. *rac*-**17b** which is readily available from *rac*-**16**[11] by reaction with bromine/triphenylphosphine[12] and subsequent silyl ether formation was used as a model compound for **15**.[4] Some time ago Rao and Periasami[13] reported that the $TiCl_4$-Mg-$BrCH_2CH_2$-Br reagent system behaves as a 1,2-diorganometallic equivalent. We tried, therefore, to obtain the desired nucleophilic reagent from **17b** and active magnesium in the presence of titanium(IV) isopropoxide. At -20°C after 15 min (quench with D_2O) only **19** was detected, and when it was tried to prepare the organometallic reagent at -78°C, after 30 min (quench with D_2O), both **17b** and **19** were identified by ^1H NMR. The deuterated compound expected by quenching the organometallic with D_2O could not be found. A similar set of experiments was performed treating **17d** with ^{t}butyllithium and then quenching with D_2O. Here, too, we only observed the formation of **19**. An approach that has to be pursued involves the use of suitable metalloalkoxides.[14]

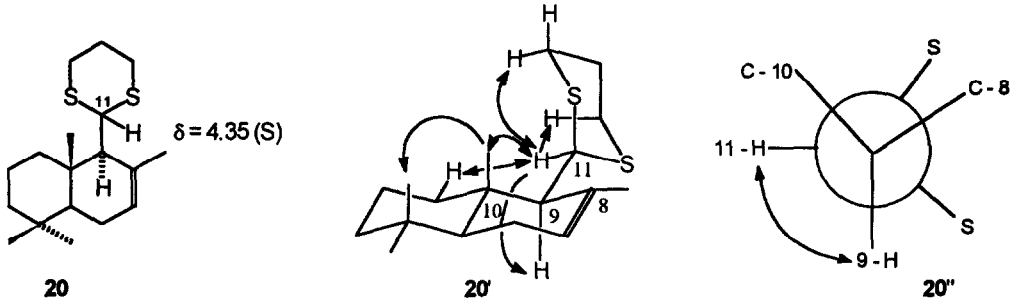


Scheme 3.

Attempted Alkylation of 20

When it was tried to arrive at **8** by alkylation of **6b** with **5** (X=leaving group), the first choice of a synthetic equivalent of **6b** was dithiane **20**. Interestingly, the ^{1}H NMR spectrum of **20** displayed a singlet at δ= 4.35 for 11-H indicating a torsional angle of 90° or -90° between 9-H and 11-H. NOE's between 11-H and CH_3-18, as well as between 11-H and 1ß-H were clearly in favour of the 90° value (see **20'** and **20''**). Force-field calculations[15] yielded a (11-H-)C-11 - C-9(-9-H) torsional angle of 84.4° for the lowest energy conformation. In the crystalline state a similar conformation is adopted. From an X-ray analysis (see Figure 1) the torsional angle was calculated to be 94.5°.

We did not succeed to deprotonate **20**, neither with ^{n}butyllithium in the presence of HMPT or TMEDA nor with ^{t}butyllithium. After quenching with D_2O no deuterium incorporation was observed. It is tempting to speculate, based on the conformation of **20** as discussed above, that proton removal is retarded for steric reasons, but this point has not been further investigated.



20 **20'** **20''**

Scheme 4.

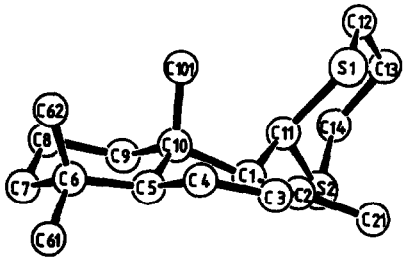
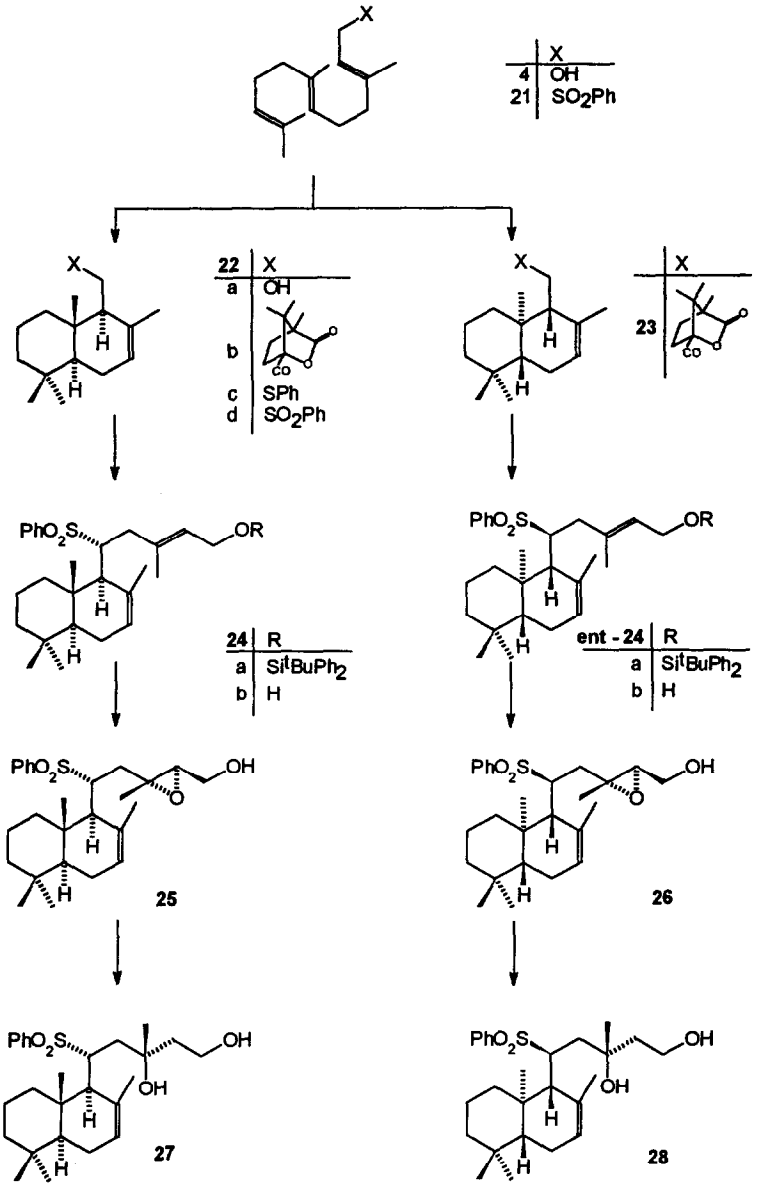


Figure 1. X-ray structure of **20** (SCHAKAL plot)

Sulfone 22d as synthetic equivalent of 6

Primary sulfone **22d** is also a synthetic equivalent of aldehyde **6a** with reversed polarity.[16,17] Racemic **22d** was prepared by cyclization of **21**.[18,4] The synthesis of non-racemic **22d** commenced from racemic drimenol (*rac*-**22a**) obtained from (E,E)-farnesol (**4**) using the Vlad cyclization procedure.[19] Resolution of *rac* **22a** was achieved via chromatographic separation of the diastereomeric camphanoates[20] **22b** and **23**. Ester hydrolysis with methanolic barium hydroxide yielded the two pure drimenol enantiomers. Direct chromatographic resolution of *rac*-**22a** on cellulose triacetate was only partly successful. Polarometric monitoring of the separation indicated only enrichments rather than a base-line separation. From (-)-drimenol (**22a**) sulfide **22c**



Scheme 5.

was obtained by treatment with diphenyl disulfide - triphenylphosphine.[21] Finally, oxidation of the unsaturated sulfide **22c** with Oxone® was chemoselective as described by Trost[22] to yield optically pure sulfone **22d**. TLC indicated fast formation of (probably) the sulfoxide(s), slower oxidation to the sulfone, and after about 2 h the appearance of side products. The reaction was stopped, therefore, after 2 h. **22d** was isolated in 67% yield. The anion, prepared from **22d** with ^{n}butyllithium, was alkylated with **14c** (obtained from **14a** by protecting group exchange) in the presence of tetra-^{n}butylammonium iodide. Two alkylation products were obtained in a 6:1 ratio (total yield: 86%). For the main product (**24a**) the (11R) configuration was established as will be described

below. After silyl ether cleavage (**24a**→**24b**) the stage was set for the catalytic Sharpless asymmetric epoxidation.[23] From optically pure **24b** ($[\alpha]_D$ = + 23.1) a single epoxide (^{1}H NMR analysis) was obtained in 97% yield which was assigned structure **25** on the basis of the well-established steric course of the Sharpless epoxidation reaction. The correctness of this assignment was proven at a later stage (vide infra). When *rac*-**24b** was submitted to the Katsuki-Sharpless epoxidation and the reaction was driven to about 80% consumption of the allyl alcohol (see Table 1), a 1.7:1 mixture of two stereoisomeric epoxides was obtained, **25** being the main product. Thus **25** and the oxidizing complex form the matched pair.[24] The ratio of **25** and **26** (the configuration at the newly created stereogenic centres in **26** was assigned by analogy and is not proven) was determined by ^{1}H NMR analysis (signal of 9-H), the chromatographic separation of the two stereoisomers could not be achieved. When the epoxidation of *rac*-**24b** was stopped after 2 h, 40% of a mixture of **25** and **26** was isolated, and 40% of the non-racemic starting allyl alcohol were recovered (see Table 1). Here, the ratio of **25** and **26** could not be determined by ^{1}H NMR since the 9-H signal of **26** was too small. From the specific rotations of the 4 h (1.7:1) and 2 h mixtures, and the known $[\alpha]_D$ of optically pure **25** a 87:13 ratio was estimated (see Table 1). The reductive hydroxy epoxide → 1,3-diol opening was achieved with RED-AL®.[25] The 1.7:1 mixture of **25** and **26** yielded **27** and **28** whereas from pure **25** only **27** was obtained. At this stage, the separation of the two stereoisomers (**27** and **28**) was readily achieved.

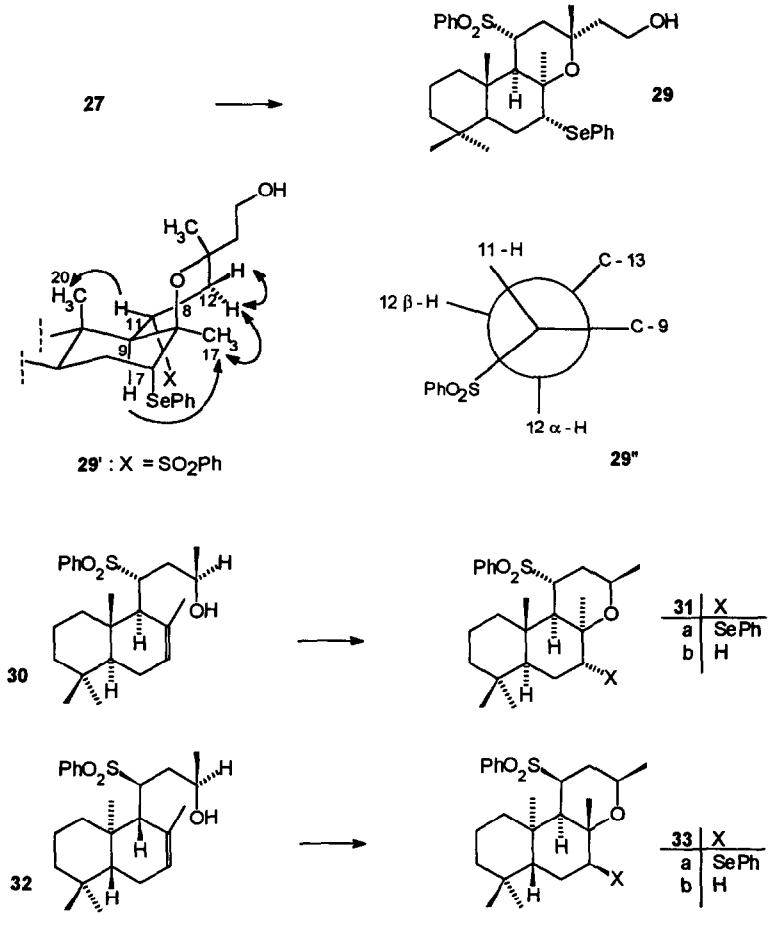
Table 1. Sharpless Epoxidation of *rac*-**24b**

entry	starting allyl alcohol	reaction time	epoxide		recovered allyl alcohol	
			yield	$[\alpha]_D$	yield	$[\alpha]_D$
1	*rac*-**24b**	2h	40%	-0.9	40%	-9.4
2	*rac*-**24b**	4h	83%	+2.1	12%	-11.2
3	**24b**	4h	97%	-2.4	3%	+23.1

Selenium-mediated cyclization of 27

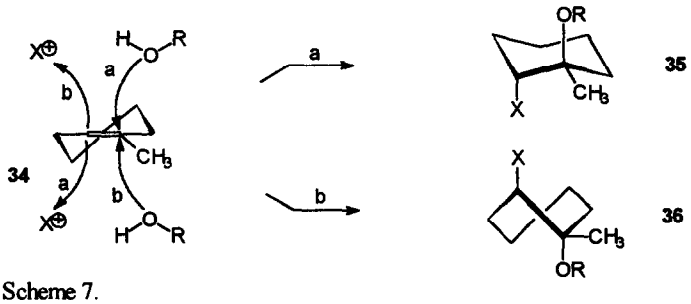
Treatment of **27** at -78°C with N-phenylselenophthalimide (NPSP) in the presence of tin(IV) chloride[26] led to the formation of a major product that was isolated in 73% yield. Structural elucidation is based on NMR experiments including two-dimensional techniques and NOE difference spectra. Both coupling constants $J_{6,7}$ and $J_{6',7}$ were 4.5 Hz which means that 7-H is equatorial. Assuming a chair conformation for ring B the phenylselenyl group must be in the axial 7α position. Under the precondition of an anti addition, the configuration at C-8 should be (R) as indicated in formula **29**. This assumption is supported by a NOE between CH_3-17 and 9-H (see formula **29'**). A NOE between 11-H and CH_3-20 indicates that 11-H is up and that ring C should exist in a boat-type conformation, a view that is confirmed by NOE enhancements between CH_3-17 and 12α-H. 12α-H is deshielded by the neighbouring phenylsulfonyl group. From the quite large coupling constants between 11-H and the two protons at C-12 ($J_{11,12\alpha}$ = 10.2 Hz and $J_{11,12\beta}$ = 8.9 Hz, see formula **29"**) and the

small coupling constant $J_{9,11}$ = 2.5 Hz it is appearent that ring C adopts a *flattened* boat-like conformation. Similar conclusions have been drawn from the NMR spectra of compounds **31** and **33**.[4] The cyclization **27**→**29** allows on the one hand to assign the configuration at C-11 of **24a**, but it also demonstrates, in conjunction with both the selenium and the Hg^{2+}-mediated cyclization reactions **30**→**31** and **32**→**33**,[4] that ring C of **3** cannot be



Scheme 6.

constructed by an electrophile-induced addition of the 13-OH group to the Δ^7 double bond. The reason for this result may be that the addition in the desired stereochemical sense would have to proceed via a boat-like transition state (**34**→**36**) whereas the probably energetically favoured chair-like transition state leads to the cyclization product with the wrong configuration at C-8 (**34**→**35**).



Scheme 7.

Mercuric ion-mediated cyclization of 27

Under kinetically controlled conditions, conformationally fixed cyclohexenes yield diaxial products on solvomercuration. In keeping with this, Hg^{2+}-mediated ring closure of **30** and **32**, followed by reductive demercuration, led to the formation of **31b** and **33b**, respectively.[4] It is, however, known, that under equilibrium conditions the formation of diequatorial addition products may prevail.[27] It appeared, therefore, possible to arrive at the desired cyclization product of **27** by oxymercuration under thermodynamic control. Thus, **27** was treated with mercury(II) trifluoroacetate, and the progress of the reaction was monitored by ^1H and ^{13}C NMR. In tetrahydrofuran-d_8 solution after 30 min the signal of the vinylic proton was unchanged. In contrast, in benzene-d_6 solution after 25 min the olefinic proton signal had completely disappeared. And indeed, the outcome of the reaction was found to be time-dependent. After 25 min both ^1H and ^{13}C NMR indicated the formation of a mixture of products which slowly rearranged to yield an ultimate product which was (with minor impurities) the sole compound that could be detected after seven days (see Figure 2). A careful NMR analysis (H,H COSY, H,C COSY, difference NOE's) permitted to assign structure **37a** to this oxymercuration product. Since the signals of 7-H, 9-H, and 12-H were not sufficiently separated in benzene-d_6 solution, spectra were also taken after addition of $CDCl_3$. In 2:1 and 2:7 C_6D_6-$CDCl_3$ mixtures the signals were well separated. The coupling constants $J_{6,7}$ = 13.7 Hz and $J_{6',7'}$ = 5.3 Hz were indicative of an equatorial position of the Hg substituent. This assignment was corroborated by an NOE between the axial 7α-H and 9-H. The configuration at C-8 was deduced from NOE's between 9-H and CH_3-17 and 7-H and CH_3-17 (see formula **37a'**). A NOE enhancement between 11-H and CH_3-20 allowed to assign the configuration at C-11 in agreement with the result obtained for **29** (cf. **29'**). The coupling constants $J_{9,11}$ = 3.0 Hz, $J_{11,12\alpha}$ = 11.5 Hz, $J_{11,12\beta}$ = 9.0, as well as a NOE between 12α-H and CH_3-17 revealed ring C to be in a similar conformation as deduced for **29**. Structure **37a** is surprising inasmuch as it means that a *syn* addition had taken place, a result which (under kinetic control) is normally only observed for strained olefins.[28] Without knowing the structure of the intermediates on the way to **37a** we would not like to speculate on the mode of its formation. In any case, whereas the Hg substituent is found in the desired equatorial position the more interesting ether oxygen at C-8 is not. Thus, this method cannot be applied to the synthesis of **3**.

When the benzene solution of **37a** was treated with aqueous sodium borohydride, a product was formed that was homogeneous as far as chromatographic behaviour is concerned but could be separated in two fractions according to its solubility behaviour (in benzene, toluene, and CCl_4). Both fractions displayed identical NMR and mass spectra from which the unexpected structure **37b** was deduced. The mass spectrum showed for the signals at m/z = 722 and 580 the typical isotope pattern of Hg containing ions. In the ^{13}C NMR spectrum

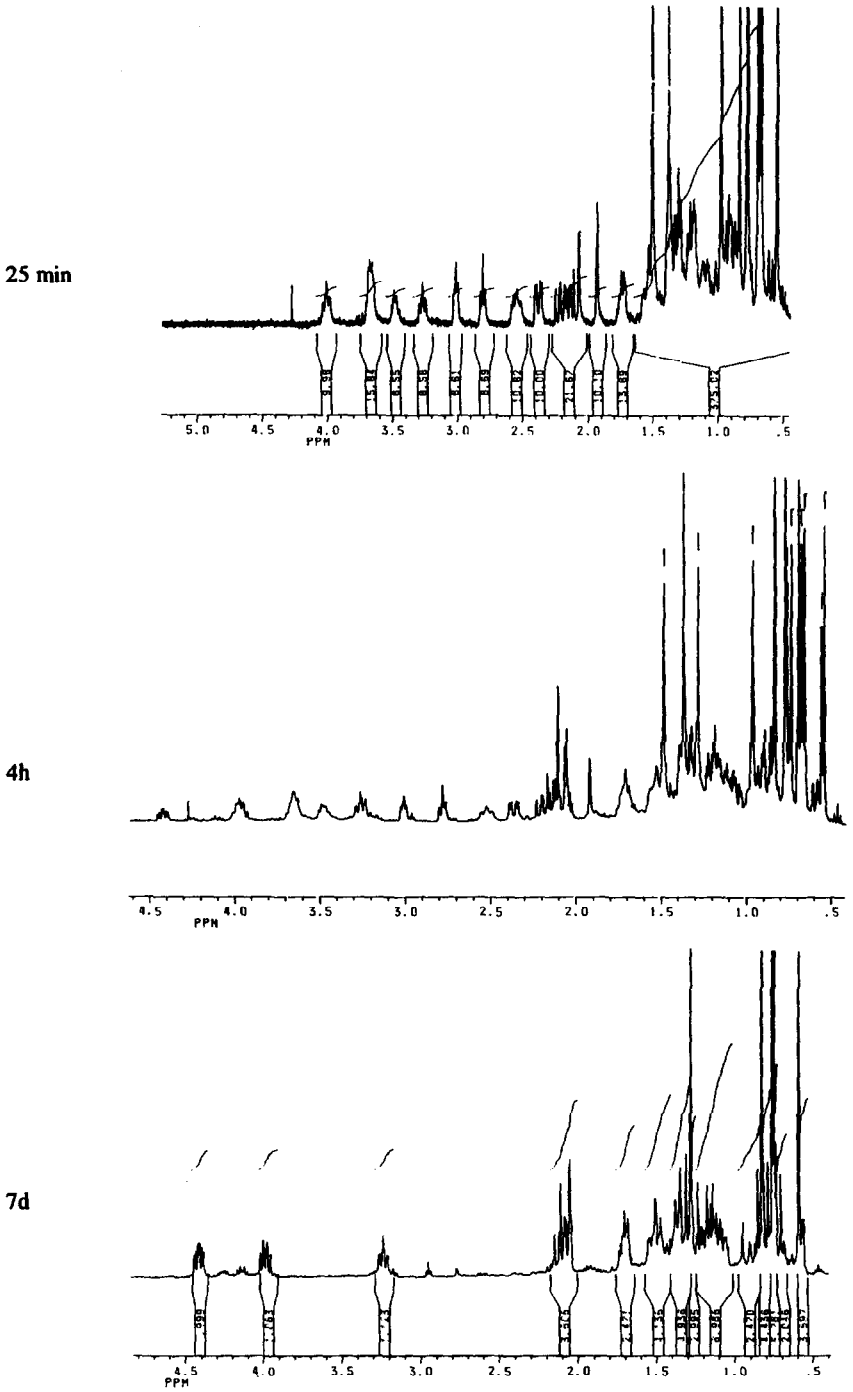
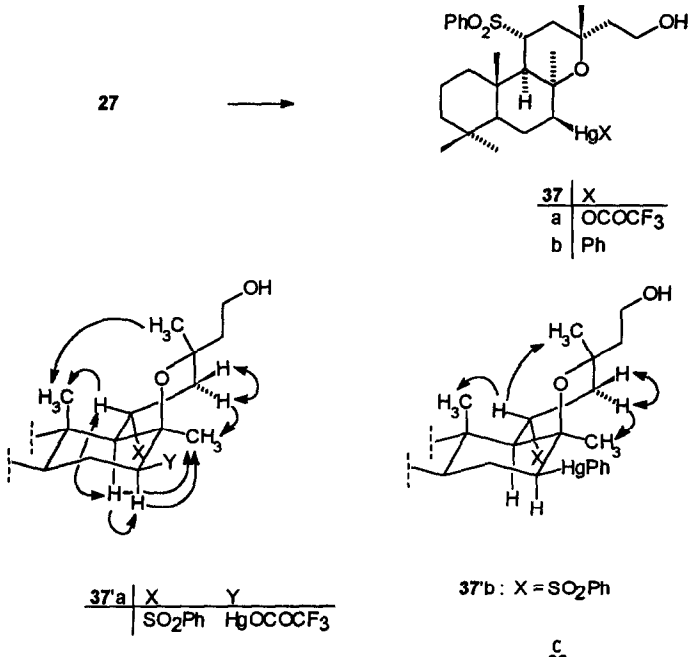


Figure 2. Reaction of **27** with mercury(II) trifluoroacetate in C_6D_6.; ^1H NMR spectra after 25 min, 4h, and 7d.

the absence of the trifluoro acetate ligand was appearent whereas the typical signals of a second aromatic group were observed. The spectrum displayed a quaternary carbon signal at $\delta = 177.9$, characteristic of an aromatic carbon carrying a mercury substituent.[29] Finally, the H,H coupling constants (see Experimental) and the NOE's as summarized in **37b'** are nicely in agreement with the conformation of ring C as depicted in **37b'**. Final proof of the structure was obtained from an X-ray analysis the result of which is shown in Figure 3. The X-ray structure of **37b** serves, at the same time, to confirm all configurational assignments (at C-11, C-13, C-8) discussed above.



Scheme 8.

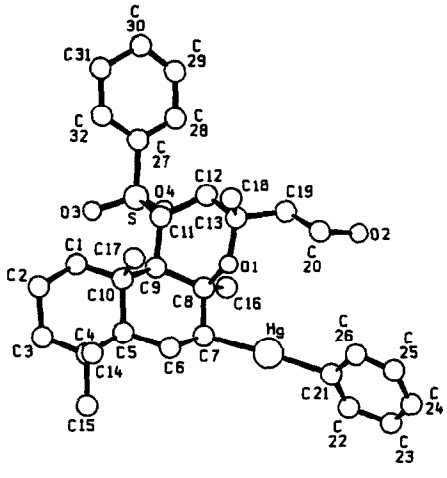
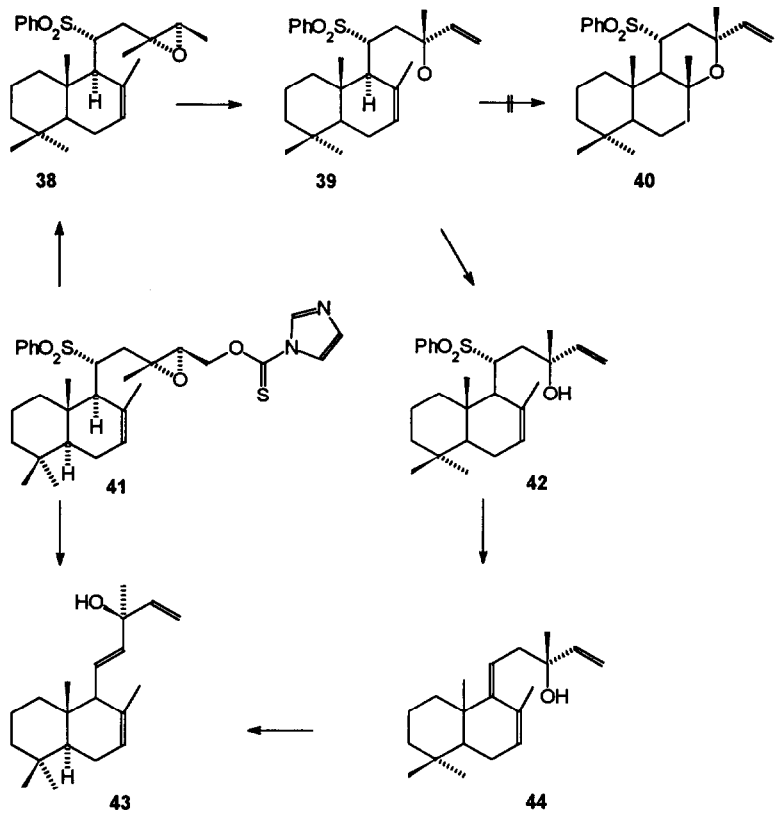


Figure 3. X-ray structure of *rac*-**37b** (SCHAKAL plot); in the crystal, two molecules are connected by a hydrogen bridge [O2...O2' = 2.85(1) Å]

The crystals of **37b** (from the less soluble fraction) used for the X-ray analysis belonged to a centrosymmetric space group, i.e. they were racemic. This explains the above-mentioned solubility behaviour of **37b**. Obviously, from the enantiomerically enriched **37b**[30] the less soluble racemate crystallized first.

Attempted Radical Cyclization of 25

The cleavage of small rings by adjacent radicals has found much attention recently.[31] Thus, it was tried, whether deoxygenation of **25** under the conditions of the Barton-McCombie reaction[32] would lead via **38**, **39**, and **40** to a cyclization product that could be used for the synthesis of **3**. In the event, treatment of thiocarbonylimidazolide **41** (prepared from the **25/26** mixture, see Experimental) led to the formation of **43** in 31% yield. We believe that intermediate **39**, rather than undergoing the desired 6-exo trig cyclization to produce **40**, is converted to **44** by 1,5-hydrogen abstraction[33] followed by extrusion of the phenylsulfonyl radical.[34] **44** might then rearrange to **43** under the reaction conditions.

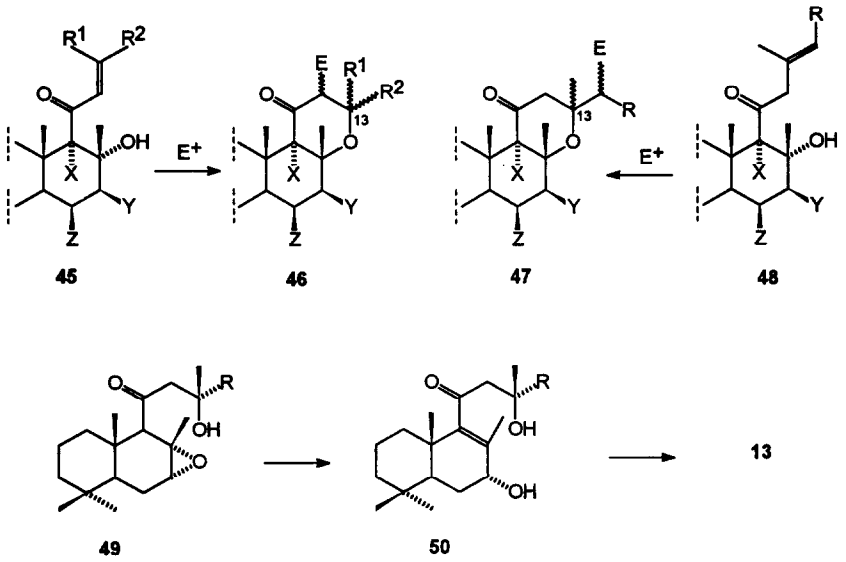


Scheme 9.

Conclusions

Knowledge that has accumulated in recent years seems to indicate that the electrophile-mediated formation of forskolin ring C by both 6-endo-trig and 6-exo-trig processes of type **45**→**46** and **48**→**47** is feasable but furnishes mixtures of 13-stereoisomers in most instances. The addition of the 13-OH group to the Δ^7 double

bond (**27**→**29**, **30**→**31**, **32**→**33**) leads to compounds with the wrong configuration at C-8, probably for the reasons discussed above. The 1,4-addition of the 13-OH group to the enone system present in **50** (structure deduced from the TMS triflate-mediated cyclization of **49**) to give **13** is, on the other hand stereoselective in the desired sense.[35] It might, therefore, be useful, to convert compound **27** into **12** and benefit from (i) the ease with which **24b** is accessible, (ii) the efficient kinetic resolution in the Katsuki-Sharpless epoxidation (*rac*-**24b**→**25**), and (iii) the stereoselective formation of **13** which is triggered by the 11-keto group present in **49** and **50**, respectively.



Scheme 10.

EXPERIMENTAL

For general methods, instrumentation, and abbreviations, see ref.[36] For MPLC the following columns were used: column A (40-60 μ m SiO_2, 9 g), column B (40-60 μm SiO_2, 65 g), column C (40-60 μm, SiO_2, 250 g).- For the preparation of (±)-drim-7-en-11-ol (*rac*-**22a**), the recently described procedure[3] was used. (±)-Drim-7-en-11-al (*rac*-**6a**) was prepared from *rac*-**22a** as described in ref.[37]

HPLC separation of *rac*-22a

Separations were performed using a Chiral Triacel HPLC column 250 mm x 10 mm (Macherey and Nagel, semipreparative) with ethanol-water 96:4 (0.5 mL/min) as eluent. Instrumentation: Shimadzu Chromatography Pump LC-8A, Du Pont UV Photometer (254 nm), Perkin Elmer 241 Polarimeter (80 μL cuvette, 365 nm). 200 μL of a 10 per cent solution of *rac*-**6a** were injected in each run. UV detection showed only one band, whereas the polarometer indicated partial separation. First the (-) enantiomer was eluted.

Formation of camphanoates 22b and 23 from *rac*-22a

A solution of (-)-camphanoyl chloride (5.79 g, 26.7 mmol) in pyridine (20 mL) was added at 0°C to a solution of *rac*-**22a** (2.38 g, 10.7 mmol) in pyridine (15 mL) The reaction mixture was stirred at 20°C for 3 h, then poured onto ice-water (50 mL). Usual work-up (CH_2Cl_2) followed by LC (SiO_2, top of the column covered with Florisil®, petrol-ethyl acetate 30:1),

followed by MPLC (column B, 30 µm silica gel (Grace), 7900 plates, separation in 500 mg batches, toluene-^{t}butyl methyl ether 250:1) yielded **22b** (1.84 g, 43%) and **23** (1.87 g, 44%).

Drim-7-en-11-yl (1R)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate (22b)
$[\alpha]_D^{20}$ = +8.9 (c 4.0, $CHCl_3$).- ^{1}H NMR (400 MHz, $CDCl_3$, H,H COSY): δ = 0.81 (s, 3H, CH_3); 0.84 (s, 3H, CH_3); 0.87 (s, 3H, CH_3); 0.94 (s, 3H, CH_3); 1.03 (s, 3H, CH_3); 1.06 (s, 3H, CH_3); 1.10-1.21 (2H); 1.36-1.60 (4H); 1.60-1.70 {4H with 1.65 ($W_{1/2}$ = 5.6 Hz, 3H, CH_2-12)}; 1.79-2.03 (5H); 2.03-2.10 (m, 1H, 9-H); 2.34 (ddd, J = 4.2 Hz, J = 10.5 Hz, J = 13.3 Hz, 1H); 4.16 (dd, J = 11.9 Hz, J = 6 Hz, 1H, 11α-H); 4.45 (dd, J = 11.9 Hz, J = 3.3 Hz, 1H, 11β-H); 5.47-5.54 (1H, 7-H).- IR (CCl_4): 1795, 1755, 1730 cm^{-1} (C=O).- MS: m/z (%) = 402 ($M^{+\bullet}$, 0.2), 204 (100), 109 (82), 83 (87), 55 (60), 41 (54).-$C_{25}H_{38}O_4$ (402.6), calc C 74.59, H 9.51; found C 74.41, H 9.39.

***ent*-Drim-7-en-11-yl (1R)-4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate (23)**
$[\alpha]_D^{20}$ =-17.1 (c 2.2, $CHCl_3$).- ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (s, 3H, CH_3); 0.84 (s, 3H, CH_3); 0.86 (s, 3H, CH_3); 0.94 (s, 3H, CH_3); 1.03 (s, 3H, CH_3); 1.08 (s, 3H, CH_3); 1.10-1.21 (2H); 1.36-1.59 (4H); 1.59-1.72 {4H, with 1.65, $W_{1/2}$ = 5.6, 3H, CH_3-12)}; 1.77-2.02 (4H); 2.02-2.08 (bs, 1H, 9-H); 2.37 (ddd, J = 4.2 Hz, J = 10.5 Hz, J = 13.3 Hz, 1H); 4.15 (dd, J = 6.1 Hz, J = 11.9 Hz, 1H, 11-H); 4.46 (dd, J = 3.3 Hz, J = 11.9 Hz, 1H, 11-H'); 5.46-5.53 (1H, 7-H).- IR (CCl_4): 1795, 1755, 1730 cm^{-1} (C=O).- MS: m/z (%) = 402 ($M^{+\bullet}$, 0.75), 204 (100), 121 (41), 109 (50), 84 (62).- $C_{25}H_{38}O_4$ (402.6), calc 402.2770; found 402.2774 (HRMS).

Drim-7-en-11-ol (22a)
A solution of **22b** (1.84 g, 4.57 mmol) in 0.25 mol/L methanolic barium hydroxide (50 mL) was left at 20°C for 2.5 h under argon, then water (20 mL) was added. Usual work-up (CH_2Cl_2) and LC (petrol-ethyl acetate 10:1) yielded **22a** (784.1 mg, 88%). $[\alpha]_D^{20}$ = -22.3 (c 0.86, $CHCl_3$), lit.[38]: $[\alpha]_D^{20}$ = -20 (c 10, $CHCl_3$).

***rac*-(11Ξ)-15-Propyl-16-nor-labd-7-en-11-ol (18a)**
To a suspension of Mg* (8.6 mg, 0.35 mmol) in THF (1 mL) 1-bromoheptane (283 µl, 1.8 mmol) was added slowly at 0°C and the mixture was stirred at 0°C for 1h. *rac*-**6a**, dissolved in THF (0.9 mL) was added and the mixture was stirred for 1h being allowed to warm to 20°C. After addition of saturated aq. NH_4Cl (0.5 mL), usual work-up ($CHCl_3$) and LC (petrol-ethyl acetate 30:1) provided **18a** (8.7 mg, 34%).- ^{1}H NMR (80 MHz, $CDCl_3$): δ = 0.89, 0.91, 1.00 (3s, 12H, 4xCH_3); 1.08-2.10 (26H, CH_2, CH_3-17, 5-H, 9-H, OH); 3.80-4.04 (1H, 11-H); 5.51-5.73 (1H, 7-H).- IR (CCl_4): 3610, 3500 cm^{-1} (O-H). MS: m/z (%) = 320 ($M^{+\bullet}$, 0.3), 192 (53), 178 (64), 177 (100), 109 (63), 69 (70), 41 (50). $C_{22}H_{40}O$ (320.6), calc C 82.43, H 12.58; found C 82.44, H 12.55.

***rac*-(11Ξ)-15-Nor-labda-7,13-dien-11-ol (18b)**
To a suspension of Mg* (19.1 mg, 0.78 mmol) in THF (0.7 mL) a solution of methallyl chloride (92.8 µL, 0.94 mmol) in THF (0.3 mL) was added at -65 to -70°C during 1.5 h (20 µL/5min). Then, *rac*-**6a** (39.1 mg, 0.18 mmol), dissolved in THF (0.45 mL) was added, the stirred mixture was allowed to warm to 20°C (1 h), and was then poured into ice-water. Usual work-up ($CHCl_3$), followed by MPLC (column A, petrol-ethyl acetate-ethanol 80:2:0.1) furnished **18b** (24.2 mg, 49 %).- ^{1}H NMR (80 MHz, $CDCl_3$): δ = 0.81, 0.83, 0.86, 0.89 (6H), 0.95, 0.97 (3H) (6s, 9H, 3xCH_3); 1.05 - 2.75 {19H, with δ = 1.76 and δ = 1.88 (CH_3-16, CH_3-17)}; 3.92 - 4.20 (1H, 11-H); 4.70 - 4.92 (2H, CH_2-14); 5.48 - 5.70 (1H, 7-H).- IR (CCl_4): 3580, 3630 cm^{-1} (OH).- MS: m/z (%) = 220 (25, $[M-C_4H_8]^{+\bullet}$), 192 (52), 177 (86), 109 (100), 97 (90), 95 (56), 69 (48), 55 (54), 41 (83).- $C_{19}H_{32}O$ (276.5), calc C 82.55, H 11.67; found C 82.50, H 11.71.

(2RS)-1-Bromo-3-(^{t}butyldiphenylsilyloxy)-2-methylpropan-2-ol (17a)
To a solution of triphenylphosphine (402.9 mg, 1.54 mmol) in CH_2Cl_2 (5 mL) a solution of bromine (79.1 µL, 1.54 mmol) in CH_2Cl_2 (5 mL) was slowly added at 20°C. The epoxide *rac*-**16** (419.4 mg, 1.28 mmol) dissolved in CH_2Cl_2 (5 mL) was added, the stirred mixture was maintained at 20°C for 2 h, and then transferred onto ice-water (pH 7 by addition of $NaHCO_3$). Usual work-up (CH_2Cl_2) followed by LC (petrol-ethyl acetate 10:1) gave **17a** (500.6 mg, 96 %).-^{1}H NMR (80

MHz, $CDCl_3$): δ = 1.08 (s, 9H, ^{t}butyl); 1.28 (s, 3H, CH_3); 3.53 (s, 2H, CH_2-3); 3.53, 3.80 (2H, CH_2-1); 7.28-7.74 (10H, Ar-H's). $|J_{1,1'}|$ = 9.6 Hz.- IR (CCl_4): 3560 (OH), 1110 cm^{-1} (C-O).- $C_{20}H_{27}BrO_2Si$ (407.4), MS: m/z (%) = 351 (3.6), 349 (3.4), 199 (100).

(2RS)-3-(^{t}Butyldiphenylsilyloxy)-1-iodo-2-methylpropan-2-ol (17c)

17c was prepared from *rac*-**16** as described for **17a** using I_2 instead of Br_2. Yield: 98%.- ^{1}H NMR (80 MHz, $CDCl_3$): δ = 1.07 (s, 9H, ^{t}butyl); 1.30 (s, 3H, CH_3); 2.46 (s, 1H, OH), 3.39 (s, 2H, CH_2-3); 3.53, 3.80 (2H, AB, CH_2-1); 7.30-7.72 (10H, Ar-H). $|J_{1,1'}|$ = 9.6 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.29 (C-1), 19.29 ($\underline{C}(CH_3)_3$), 23.30 (CH_3-4), 26.87 ($C(\underline{C}H_3)_3$), 68.70 (C-3), 71.46 (C-2), 127.84, 129.93, 129.96, 135.58, 135.65 (Ar-CH's), 132.60, 132.68 (Ar-C_q's).-IR (CCl_4): 3530 cm^{-1} (OH).- MS: m/z (%) = 397 (18), 199 (100), 139 (18), 57 (18).- $C_{20}H_{27}IO_2Si$ (454.4), calc for $C_{16}H_{18}IO_2Si$: 397.0121; found 397.0120 (HRMS).

(2RS)-1-Bromo-3-(^{t}butyldiphenylsilyloxy)-2-methyl-2-(trimethylsilyloxy)-propane (17b)

To a solution of **17a** (499.2 mg, 1.23 mmol) in THF (11 mL) 2,6-lutidine (287 µL, 2.46 mmol) and trimethylsilyl triflate (357 µL, 1.85 mmol) were added and the mixture was stirred at 20°C for 30 min, then poured onto ice-water (10 mL). Subsequent work-up (diethyl ether) and LC (petrol-ethyl acetate 10:1) furnished **17b** (578 mg, 98 %).- ^{1}H NMR (80 MHz, $CDCl_3$): δ = 0.08 (s, 9H, $Si(CH_3)_3$); 1.05 (s, 9H, ^{t}butyl); 1.35 (s, 3H, CH_3); 3.49-3.62 (4H, 2 AB systems, CH_2-1, CH_2-3); 7.29-7.79 (10H, Ar-H's).- IR (CCl_4): 1110 cm^{-1} (C-O).- MS: m/z (%) = 423 (6), 421 (6, $[M-^t butyl]^+$), 271 (100), 193 (55), 135 (27), 103 (41), 91 (29), 73 (52).- $C_{23}H_{35}BrO_2Si_2$ (479.6), calc for $C_{19}H_{26}{}^{79}BrO_2Si_2$: 421.0655, found 421.0653 (HRMS).

(2RS)-3-(^{t}Butyldiphenylsilyloxy)-1-iodo-2-methyl-2-(trimethylsilyloxy)-propane (17d)

Prepared from **17c** as described for **17b**. Yield: 98%.-^{1}H NMR (80 MHz, $CDCl_3$): δ = 0.08 (s, 9H, $Si(CH_3)_3$); 1.07 (s, 9H, ^{t}butyl); 1.41 (s, 3H, CH_3); 3.43 (s, 2H; CH_2-1), 3.50, 3.62 (2H, AB, CH_2-3); 7.30-7.78 (10H, Ar-H's), $|J_{1,1'}|$ = 10 Hz. - MS: m/z (%) = 469 (18), 271 (100), 193 (44), 135 (36), 73 (58).- $C_{23}H_{35}IO_2Si_2$ (526.6), calc for $C_{19}H_{26}I$: 469.0516, found 469.0513 (HRMS).

Reaction of 17d with ^{t}butyllithium

a) To a solution of **17d** (15 mg 0.03 mmol) in pentane (50 µL) at -78°C ^{t}butyllithium (1.7 mol/L in pentane, 39 µl, 0.066 mmol) was added, and the mixture was stirred for 2 h at the temperatures given in Table 2, D_2O (0.5 mL) was added, and the mixture was then stirred at 0°C for 30 min. After filtration through sodium sulfate and solvent evaporation the reaction products were analyzed by ^{1}H NMR.

b) To a solution of **17d** (14 mg, 0.027 mmol) in pentane (50 µL) at -78°C HMPA (11.3 µl, 0.065 mmol) and ^{t}butyllithium (1.7 mol/L in pentane, 34.7 µl, 0.059 mmol) were added. Then the protocol described above was followed.

Table 2. Reaction of **17d** with ^{t}butyllithium

Solvent	Temperature	Product(s)
pentane	-78°C	**17d**
pentane	-25°C	**17d/19**
pentane	20°C	**19**
pentane-HMPA	-78°C	**19**

Characteristic ^{1}H NMR signals of **19** (80 MHz, $CDCl_3$): δ = 1.64-1.75 (3H, 2-CH_3), 4.00-41.4 (2H, CH_2-3), 4.79-4.92 (1H, 1-H), 5.05-5.20 (1H, 1-H).

Reaction of 17b with activated magnesium in the presence of titanium(IV) isopropoxide

To activated Mg (8.5 mg, 0.35 mmol), suspended in THF (1 mL) titanium(IV) isopropoxide (48 µL, 0.16 mmol) was added and the mixture was set to the temperature indicated in Table 3. Then, **17b** (40 mg, 0.08 mmol), dissolved in THF (0.8 mL), was added and stirring was continued for the time shown in Table 3. D_2O (0.5 mL) was added and the mixture was transferred onto ice-water-aq saturated NH_4Cl (10 mL - 5 mL) and worked up ($CHCl_3$). The reaction products were analyzed by ^1H NMR and ^2H NMR.

Table 3. Reaction of **17b** with activated magnesium in the presence of titanium(IV) isopropoxide

Temperature	Reaction time	Product(s)
0°C	4 h	**19**
0°C	8 h	**19** and decomposition products
0°C	20 h	**19** and decomposition products
-20°C	1 h	**19**[a]
-20°C	0.25 h	**19**[a]
-78°C	0.5 h	**17b** and **19**[a]

[a] A ^2H NMR signal was observed at δ = 3.9.

(E)-4-^{t}Butyldiphenylsilyloxy-1-chloro-2-methylbut-2-ene (14c)

To a solution of (E)-1-chloro-2-methyl-2-buten-2-ol (2.7 g, 22.4 mmol) in CH_2Cl_2 (90 mL) a solution of 4-dimethylaminopyridine (670 mg, 5.5 mmol) in CH_2Cl_2 (10 mL) and triethylamine (4 mL, 28.6 mmol) were added. The mixture was stirred at 20°C for 20 min. ^{t}Butyldiphenylsilyl chloride (7 mL, 27 mmol) was added and the stirred reaction mixture was maintained at 20°C for 3 h. After addition of water (50 mL), usual work-up (CH_2Cl_2), and MPLC (column C, petrol-ethyl acetate 50:1) pure **14c** (5.75 g, 68 %) was obtained.- ^1H NMR (400 MHz, $CDCl_3$, NOE) δ = 1.04 (s, 9H, ^{t}butyl); 1.55 ($W_{1/2}$ = 2.7 Hz, 3H, 2-CH_3); 3.97 (d, J<1Hz, 2H, CH_2-1); 4.24 (dd, J<1Hz and J=6.1Hz, 2H, CH_2-4); 5.70-5.75 (1H, 3-H); 7.35-7.45 (6H, Ar-H's); 7.65-7.69 (4H, Ar-H's).- IR (CCl_4): 700 cm^{-1}(C-Cl).- MS: m/z (%) = 301 (28, [M-^{t}butyl]$^{+\bullet}$), 227 (42), 217 (100), 199 (49), 183 (41), 105 (43), 77 (51), 41 (44).- $C_{21}H_{27}ClOSi$ (359.0), calc C 70.26, H 7.58; found C 70.14, H 7.63

***rac*-(9S)-(1,3-Dithian-2-yl)-11-nor-drim-7-ene (20)**

A solution of ***rac*-6a** (179.2 mg, 0.81 mmol) and 1,3-propanedithiol (77.2 µL, 0.77 mmol) in $CHCl_3$ (2.6 mL) was stirred at 20°C for 70 min. At 0°C boron trifluoride etherate (30.4 µL, 0.24 mmol) was added and the mixture was left at -10°C for 16 h. The product was isolated by washing the organic phase twice with 7 per cent aq. KOH, followed by usual work-up ($CHCl_3$) and MPLC (column B, petrol-ethyl acetate 80:1). 36.6 mg of ***rac*-6b** were recovered, 182.9 mg (91% based on consumed **6b**) of **20** were isolated.- M.p. 72-74°C (from hexane).- ^1H NMR (400 MHz, $CDCl_3$, C,H COSY, NOE, of a slightly impure specimen): δ = 0.84 (s, 3H, CH_3-13); 0.86 (s, 3H, CH_3-14); 1.01 (s, 3H, CH_3-15); 1.02-1.12 (2H, 1-H_{ax}, 5-H); 1.12-1.18 (dd, 1H, J = 4 Hz and J = 13.1 Hz, 3-H); 1.36-1.42 (1H, J=13.1 Hz, 3-H'); 1.42-1.58 (2H, CH_2-2); 1.71-1.84 (1H, 4'-H_{eq}); 1.84-1.91 (2H, CH_2-6); 2.08-2.11 (4H, with 1-H_{eq}, 9-H, 3'-H, and at δ = 2.03, $W_{1/2}$ = 5.7 Hz, CH_2-12); 2.70-2.87 (3H, CH_2-5', 3'-H_{eq}); 3.00 (ddd, J=2.6 Hz, J = 12.7 Hz and J = 13.9 Hz, 1H, 3'-H_{ax}); 4.35 (s, 1H, 11-H); 5.53-5.60 (1H, 7-H).- ^1H NMR (400 MHz, C_6D_6, H,H COSY, NOE): δ = 0.80 (s, 3H, CH_3-13); 0.83 (s, 3H, CH_3-14); 0.98-1.09 (2H with 1-H_{ax}); 1.20 (s, 3H, CH_3-15) 1.29-1.59 (6H, CH_2-2, CH_2-3, CH_2-4'); 1.79-1.88 (2H, CH_2-6); 1.96-2.04 (1H, 1-H_{eq}); 2.21-2.25 (bs, 1H, 9-H); 2.25-2.42 (3H, CH_2-5', 3'-H_{eq}); 2.44 (m, $W_{1/2}$ = 4.3 Hz, 3H, CH_3-12); 2.60-2.68 (ddd, J = 2.6 Hz, J = 12.6 Hz, J = 13.8 Hz, 1H, 3'-H_{ax}); 4.36 (s, 1H, 11-H); 5.58-5.62 (1H, 7-H).- ^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT, slightly impure specimen): δ = 15.64 (CH_3, C-15); 18.76 (CH_2, C-2); 22.40 (CH_3, C-14), 23.25(CH_2, C-6); 23.93 (CH_3, C-12); 26.20 (CH_2, C-4'); 31.84 (CH_2, C-3' or C-5'); 32.91 (C_q, C-4 or C-10); 33.52 (CH_3, C-13); 33.78 (CH_2, C-3' or C-5'); 38.31 (C_q C-4 or C-10); 40.25 (CH_2, C-1); 41.95 (CH_2, C-2); 49.35 (CH, C-3); 50.43 (CH, C-5); 62.05 (CH, C-9); 126.14 (CH, C-7); 131.93 (C_q, C-8).-IR ($CHCl_3$): 1480-1410 (C=C), 1275 cm^{-1} (C-S).- MS: m/z (%) = 310 (6, $M^{+\bullet}$), 235 (10), 119 (100).- $C_{18}H_{30}S_2$ (310.6), calc C 69.62, H 9.74; found C 69.62, H 9.77

11-Benzenesulfanyl-drim-7-ene (22c)

A mixture containing **22a** (774.1 mg, 3.48 mmol), diphenyl disulfide (4.56 g, 20.88 mmol), tri-^{n}butylphosphine (5.2 mL, 20.88 mmol), and THF (40 mL) was heated to 80°C for 9.5 h and to 60°C for 4 h. After cooling to 20°C, usual work-up (CH_2Cl_2) and subsequent MPLC (petrol-ethyl acetate 200:1) furnished **22c** (855 mg, 78%).- $[\alpha]^{D}_{20}$ = +77.9 (c 1.3, $CHCl_3$).- ^{1}H NMR (400 MHz, $CDCl_3$, H,H COSY): δ = 0.82 (s, 3H, CH_3-15); 0.85 (s, 3H, CH_3-14); 0.89 (s, 3H, CH_3-13); 0.89-0.97 (1H); 1.07-1.23 (2H, 5-H and another H); 1.35-1.58 (4H); 1.82 ($W_{1/2}$=4.5 Hz, 3H, CH_2-12); 1.78-2.01 (3H, CH_2-6 and another H) 2.01-2.10 (1H, 9-H); 2.75 (dd, J = 8 Hz, J = 12,3 Hz, 1H, 11-H); 3.08 (dd, J = 2 Hz, J = 12.3 Hz, 1H, 11-H); 5.43-5.48 (1H, 7-H); 7.10-7.20 (1H, Ar-H); 7.21-7.39 (4H, Ar-H's). $|J_{11,11'}|$ = 12.5 Hz; $J_{11,9}$ = 2 Hz; $J_{11',9}$ = 8 Hz.- MS: m/z (%)=314 (M^{+}•,18), 109 (100), 81 (75).- $C_{21}H_{30}S$ (314.5), calc C 80.19, H 9.61; found C 80.19, H 9.54.

11-Benzenesulfonyl-drim-7-ene (22d)

a) *rac*-**22d** was prepared as described in ref.[39]

b) **22d**: To a solution of Oxone® ($KHSO_5$, 586 mg, 0.95 mmol) in water (2 mL) methanol (2 mL) was added (precipitation of inorganic salts). Then a solution of **22c** (48.6 mg, 0.155 mmol) in ether (2 mL) was slowly added. The reaction mixture was stirred at 20°C for 2 h. Addition of water (20 mL) and usual work-up (CH_2Cl_2), followed by LC (petrol-ethyl acetate 5:1) provided **22d** (36.1 mg, 67%).- $[\alpha]^{D}_{20}$ = +28.3 (c 3.0, $CHCl_3$).- ^{1}H NMR (400 MHz, $CDCl_3$, H,H COSY): δ = 0.66 (s, 3H, CH_3-15); 0.82 (s, 3H, CH_3-13); 0.83 (s, 3H, CH_3-14); 0.85-1.02 (3H); 1.12 (dt, J = 4.5 Hz, J = 13.5 Hz, 1H); 1.27 (dd, J = 5.2 Hz, J = 12.3 Hz, 1H, 5-H); 1.31-1.65 (6H); 1.71 (s, $W_{1/2}$=5.2 Hz, 3H, CH_2-12); 1.77-1.88 (1H, 6-H_{eq}); 1.96-2.06 (1H, 6-H_{ax}); 2.59-2.66 (1H, 9-H); 3.12 (d, J = 4.5 Hz, 2H, 11-H); 5.49 (bs, $W_{1/2}$=2 Hz, 1H, 7-H); 7.52-7.95 (5H, Ar-H's).

Alkylation of 22d with 14d

a) To a solution of *rac*-**22d** (952.2 mg, 2.75 mmol) in 1:1 THF-DMPU (20 mL), at -78°C a 1.5 mol/L solution of ^{n}butyllithium (3.66 mL, 5.50 mmol) was added. The colour of the resulting solution was deeply yellow. Then the mixture was stirred at -78°C for 15 min, at 0°C for 45 min, and was then again cooled to -78°C. Sequentially **14d** (5.77 g, 16.0 mmol), dissolved in THF (5 mL), and then tetra-^{n}butylammonium iodide (1.44 g, 3.90 mmol), dissolved in 1:1 THF-DMPU (7 mL), were added. After 5 min the reaction mixture was allowed to warm to 0°C, stirred at that temperature for 1 h and then at 20°C for 18 h. After quenching with water and usual work-up ($CHCl_3$), the products were submitted to a crude separation (petrol-ethyl acetate 40:1). MPLC (petrol-ethyl acetate) then provided pure *rac*-**24a** (1.23g, 67%), its 11-isomer (194.6 mg, 10.6%), and a fraction containing both compounds (150.6 mg).

b) (+)-**22d** was alkylated in the same way.

(11R,13E)-11-Benzenesulfonyl-15-(^{t}butyldiphenylsilyloxy)-labda-7,13-diene (24a)

a) *rac*-**24a**: ^{1}H NMR (400 MHz, $CDCl_3$, C,H COSY): δ = 0.75 (s, 3H, CH_3-20); 0.85 (s, 3H, CH_3-19); 0.87 (s, 3H, CH_3-18); 1.00 (s, 9H, ^{t}butyl); 1.08 (s, 3H, CH_3-16); 1.10-1.21 (2H, 1-H_{ax}, 3-H_{ax}); 1.22-1.28 (1H, 5-H); 1.35-1.43 (1H, 1-H_{eq} or 3H_{eq}); 1.43-1.50 (2H, CH_2-2); 1.62-1.70 (1H, 3H_{eq} or 1-H_{eq}); 1.83-2.02 (5H, CH_2-6 and at δ = 1.88 s, 3H, CH_3-17); 2.25 (d, 1H, 12-H_a); 2.88 (dd, 1H, 12-H_b); 3.15 (bs, 1H, 9-H); 3.64 (d, 1H, 11-H); 3.84, 3.92 (AB part of ABX, 2H, CH_2-15); 5.09-5.16 (X part of ABX, triplet structure, 1H, 14-H); 5.63-5.69 (1H, 7-H); 7.28-7.45 (9H, Ar-H's); 7.59-7.65 (4H, Ar-H's); 7.73-7.76 (2H, Ar-H's); $J_{11,12b}$ = 9.2 Hz, $|J_{12a,12b}|$ = 17.7 Hz, $|J_{15,15'}|$ = 13.0 Hz, $J_{14,15}$ ≈ $J_{14,15'}$ = 6 Hz (first order interpretation)- ^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT): δ = 14.66 (CH_3, C-20); 16.47 (CH_3, C-16); 18.66 (CH_2, C-2[40]); 19.14 (C_q, C-4 or C-10 or $\underline{C}(CH_3)_3$); 22.30 (CH_3, C-19); 23.37 (CH_2, C-6); 26.76 (CH_3, $C(\underline{C}H_3)_3$); 32.96 (C_q, C-4 or C-10 or $C(CH_3)_3$); 33.37 (CH_3, C-18); 36.23 (CH_2, C-12); 38.21 (C_q, C-4 or C-10 or $\underline{C}(CH_3)_3$); 39.45 (CH_2, C-1); 41.62 (CH_2, C-3); 50.37 (CH, C-5); 52.61 (CH, C-9); 60.74 (CH_2, C-15); 61.24 (CH, C-11); 126.22 (CH, C-14); 127.14 (CH, C-7); 127.61, 128.67, 129.60, 129.62, 132.98, 135.51 (Ar-CH); 131.37, 132.24, 133.75, 133.81, 141.37 (Ar-C_q, C-8, C-13).- IR (CCl_4): 1670(C=C), 1320, 1305, 1150 cm^{-1} (SO_2).- MS: m/z (%) = 611 (2.4[M-^{t}butyl]$^{+}$), 263 (34), 199 (100).- $C_{42}H_{56}O_3SSi$ (669.1), calc C 75.40, H 8.44; found C 75.33, H 8.60.

b) **24a**: $[\alpha]^{D}_{20}$ = +17.5 (c 1.9, $CHCl_3$)

(11S,13E)-11-Benzenesulfonyl-15-(^{t}butyldiphenylsilyloxy)-labda-7,13-diene (formula not shown)

a) Racemic specimen: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.75 (s, 3H, CH_3-20); 0.84 (s, 3H, CH_3-19); 0.86 (s, 3H, CH_3-18); 1.04 (s, 9H, ^{t}butyl); 1.09 (s, 3H, CH_3-16); 1.11-1.19 (2H, 1-H_{ax}, 3-H_{ax}); 1.19-1.25 (1H, 5-H); 1.35-1.42 (1H, 1-H_{eq} or 3-H_{eq}); 1.42-1.50 (2H, CH_2-2); 1.58-1.67 (1H, 3-H_{eq} or 1H_{eq}); 1.74 (m, $W_{1/2}$= 5 Hz, 3H, CH_3-17); 1.78-1.92 (2H, CH_2-6); 1.96 (d, 1H, 12-H_a); 2.92 (dd, 1H, 12-H_b); 3.15 (bs, $W_{1/2}$=8.1 Hz, 1H, 9-H); 3.52 (m, $W_{1/2}$=14.7 Hz, 1H, 11-H); 4.25, 4.34 (AB of ABX, 2H, CH_2-15); 5.14-5.20 (X of ABX, triplet structure, 1H, 14-H); 5.55-5.60 (1H, 7-H); 7.32-7.45 (8H, Ar-H's); 7.52-7.58 (1H, Ar-H); 7.63-7.73 (4H, Ar-H's); 7.78-7.82 (2H, Ar-H's). $J_{11,12b}$ = 10.3 Hz, $|J_{12a,12b}|$ = 16.3 Hz, $|J_{15,15'}|$ = 15 Hz, $J_{14,15} \approx J_{14,15'}$ = 7 Hz (first order interpretation).-.^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT): δ = 15.38 (CH_3, C-20); 18.64 (CH_2, C-2); 19.17 (C_q, C-4 or C-10 or $\underline{C}(CH_3)_3$); 21.39 (CH_3, C-16); 22.37 (CH_3, C-19); 23.26 (CH_2, C-6); 23.95 (CH_3, C-17); 26.82 (CH_3, $C(\underline{C}H_3)_3$); 29.47 (CH_2, C-12); 32.91 (C_q, C-4 or C-10 or $\underline{C}(CH_3)_3$); 33.43 (CH_3, C-18); 38.04 (C_q,C-4 or C-10 or $C(CH_3)_3$); 39.63 (CH_2, C-1); 41.57 (CH_2, C-3); 50.57 (CH, C-5); 52.29 (CH, C-9); 60.70 (CH_2, C-15); 61.02 (CH, C-11); 127.02 (CH, C-14); 127.55 (CH, C-7); 127.61, 128.63, 128.67, 129.35, 129.49, 129.53, 133.08, 135.56, 135.61 (Ar-CH's); 131.25, 132.37, 133.73, 133.83, 141.61 (Ar-C_q's, C-8, C-13).- IR (CCl_4): 1320, 1145 cm^{-1} (SO_2).- MS: m/z (%) = 611 (6.3, $[M-^{t}butyl]^{+\bullet}$), 527 (6), 271 (50), 263 (58), 199 (100).- $C_{42}H_{56}O_3SSi$ (669.1), calc C 75.40, H 8.44; found C 75.32, H 8.56.

b) Non-racemic specimen obtained from **22d**: $[\alpha]^{D}_{20}$ = -29 (c 0.93, $CHCl_3$).

(11R,13E)-11-Benzenesulfonyl-labda-7,13-dien-15-ol (24b)

a) To a solution of *rac*-**24a** (75.2 mg, 0.11 mmol) in THF (1.5 mL) was added at 20°C tetra-^{n}butylammonium fluoride (1 mol/L solution in THF, 236 µL, 0.24 mmol), and the mixture was stirred at 20°C for 135 min. After solvent evaporation the crude product was separated by LC (petrol-ethyl acetate=10:1) and furnished pure *rac*-**24b** (43.2 mg, 89 %).- M.p. 154°C (from hexane).- ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.74 (s, 3H, CH_3-20); 0.84 (s, 3H, CH_3-19); 0.86 (s, 3H, CH_3-18); 1.04-1.20 (2H, 1-H_{ax}, 3-H_{ax}); 1.20-1.30 (2H, 5-H, 1-H_{eq} or 3-H_{eq}); 1.37 (s, 3H, CH_3-16); 1.39-1.51 (2H, CH_2-2); 1.61-1.71 (1H, 3-H_{eq} or 1-H_{eq}); 1.86 (s, 3H, CH_3-17); 1.78-2.00 (2H, CH_2-6); 2.32 (d, 1H, 12-H_a); 2.91 (dd, 1H, 12-H_b); 3.12 (bs, 1H, 9-H); 3.68 (d, 1H, 11-H); 3.78-3.90 ($W_{1/2}$= 14.4 Hz, 2H, CH_2-15); 5.05 (overlapping multiplets, probably $J_{14,15a} = J_{14,15b}$ = 6.5 Hz + long range coupling with J =2 Hz, 1H, 14-H) 5.63-5.69 ($W_{1/2}$ = 11 Hz, 1H, 7-H); 7.47-7.53 (2H, Ar-H's); 7.55-7.61 (1H, Ar-H); 7.82-7.87 (2H, Ar-H's); $J_{11,12b}$ = 9.1 Hz, $|J_{12a,12b}|$ = 17.3 Hz.- IR (CCl_4): 3610, 3500 (OH), 1665 (C=C), 1320, 1300, 1145 cm^{-1} (SO_2).- MS: m/z (%) =288 (12), 190 (85), 164 (100), 133 (79), 119 (89).- $C_{26}H_{38}O_3S$ (430.6), calc C 72.52, H 8.89; found C 72.56, H 8.94.

b) **24a** was converted in the same way to **24b** (>99% yield).- $[\alpha]^{D}_{20}$ = +23.1 (c 5.3, $CHCl_3$).

Sharpless Epoxidation of 24b

a) 2 h experiment with *rac*-**24b**: 4Å molecular sieves (powder, 40 mg) in CH_2Cl_2 (1.5 mL) were added sequentially D-(-)-diethyl tartrate (1.3 µL, 7.5 µmol), titanium(IV) isopropoxide (1.5 µL, 5 µmol), and ^{t}butyl hydroperoxide (3.75 mol/L in CH_2Cl_2, 40 µL, 0.15 mmol). The mixture was stirred at -10°C for 10 min. After cooling to -20°C, a solution of *rac*-**24b** (43.2 mg, 0.10 mmol) in CH_2Cl_2 (1 mL) was added within 15 min, and stirring continued at -20°C for 2 h. At 0°C water was added, and after 10 min the mixture was allowed to warm to 20°C. Work-up was performed by washing the organic phase with 3 per cent sodium hydroxide saturated with sodium chloride (2 mL), extracting the aqueous phase with CH_2Cl_2 (3x), drying the combined organic phases (sodium sulfate), solvent evaporation and filtration through Florisil (1 g, CH_2Cl_2 as eluent). HPLC (Merck Si 100, 5 µm, petrol-acetone 3:1, 10 mL/min) gave **25/26** (87:13, 18.3 mg, 40 %, $[\alpha]^{D}_{20}$ = -0.9 (c 1.5, $CHCl_3$), see Table 1), **24b**/*ent*-**24b** (16.2 mg, 40 %, $[\alpha]^{D}_{20}$ = -9.4 (c=1.2, $CHCl_3$), see Table 1), and a fraction (4.8 mg) containing both **24b**/ent-**24b** and **25/26**.

b) 4 h experiment with *rac*-**24b**: This experiment was performed as described above. The reaction was stopped after 4h. 83% of a 1.7:1 mixture (determined by ^{1}H NMR) of **25** and **26** was obtained, see Table 1.

c) 4 h experiment with **24b**, performed as described in b). **25** was isolated in 97 % yield.

(11R,14R)-11-Benzenesulfonyl-13,14-epoxy-labd-7-en-15-ol (25)

$[\alpha]^{D}_{20}$ = -2.4 (c = 0.92, $CHCl_3$).-^{1}H NMR (400 MHz, $CDCl_3$, H,H COSY): δ = 0.79 (s, 3H, CH_3-20); 0.80 (s, 3H, CH_3-19); 0.82 (s, 3H, CH_3-18); 0.85-0.94 (3H, 1-H_{ax}, 3-H_{ax}, 5-H); 1.18-1.41 (4H, CH_2-2, 1-H_{eq}, 3-H_{eq}); 1.39 (s, 3H, CH_3-16); 1.71-1.93 {4H, 6-H_{eq}, and 1.79 (s, 3H, CH_3-17)}; 2.17-2.23 (2H, containing 12-H_a); 2.27 (dd, 1H, 12-H_b); 2.40 (bs, 1H, 9-H); 3.22 (X of ABX, $J_{14,15}$+$J_{14,15'}$= 11.6 Hz, 1H, 14-H); 3.58 (dd, J = 11.3 Hz, J = 2.1 Hz, 1H, 11-H); 3.62-3.78 (2H, CH_2-15); 5.57-5.62 (1H, 7-H); 7.54-7.61 (2H, Ar-H's); 7.63-7.66 (1H, Ar-H); 7.89-7.93 (2H, Ar-H's). $J_{11,12b}$ = 2.1 Hz, $|J_{12a,12b}|$ = 15.6 Hz. The ^{1}H NMR spectra of optically pure **25** and that of the 87:13 **25/26** mixture (2 h experiment) differed only slightly from each other. In the spectrum of 1.7:1 mixture of **25/26** some signals of **26** could be clearly identified (vide infra).- ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.99 (CH_3, C-20); 16.38 (CH_3, C-16); 18.40 (CH_2, C-2); 22.37 (CH_3, C-19); 23.15 (CH_2, C-6); 23.95 (CH_3, C-17); 32.85 (C_q, C-4 or C-10); 33.31 (CH_3, C-18); 35.69 (CH_2, C-12); 38.33 (C_q, C-4 or C-10); 39.40 (CH_2, C-1); 41.45 (CH_2, C-3); 50.32 (CH, C-5); 53.56 (CH, C-9); 59.87 (C_q, C-13); 60.70 (CH_2, C-15); 62.27 (CH, C-11); 64.90 (CH, C-14); 127.91, 128.79, 129.10, 129.41, 133.86 (Ar-CH's); 130.73, 138.82 (Ar-C_q's, C-8).- IR (CCl_4): 3540 (OH), 1320, 1305, 1145 cm^{-1} (SO_2).- MS = m/z (%) = 304 (14), 220 (61), 119 (81), 109 (79), 93 (94), 69 (79), 55 (84), 43 (100).-$C_{26}H_{38}O_4S$ (446.6), calc for $C_{20}H_{32}O_2$: 304.2402, found 304.2407 (HR-MS).

Epoxy alcohol 26 (structure tentatively assigned)

26 was only obtained as a side product in the 4h epoxidation of *rac*-**24a** and could not be separated from **25**. Characteristic ^{1}H NMR signals (400 MHz, $CDCl_3$): δ = 2.59 (9-H), 5.65 (7-H).

Reductive epoxide opening of 25/26

To a solution of a 1.7:1 mixture of **25** and **26** (24.2 mg, 0.054 mmol) in THF (1 mL) at -5°C a 1.6 mol/L solution of RED-Al® in toluene (85 µl, 0.135 mmol) was added. The mixture was stirred at -5°C for 3 h. Usual work-up (CH_2Cl_2) followed by HPLC (Merck Si 100, petrol-ethyl acetate 3:1 + 0.1% triethylamine, 10 mL/min) provided **27** (8.8 mg, 36%) and **28** (7.7 mg, 31%).

Reductive epoxide opening of 25

The reaction was performed as described for the **25/26** mixture. Only **27** was formed in this experiment. Yield: 35% (not optimized).

(11R,13S)-Benzenesulfonyl-labd-7-ene-13,15-diol (27)

a) Sample obtained from the **25/26** mixture: M.p. 118°C (from CH_2Cl_2-hexane).- $[\alpha]^{D}_{20}$ = -1.2 (c 1.15, $CHCl_3$).- ^{1}H NMR (400 MHz, $CDCl_3$, H,H COSY): δ = -0.13 (dt, J = 3.2 Hz, J = 12.8 Hz, 1H, 1-H_{eq}); 0.77 (s, 3H, CH_3-20); 0.78 (s, 3H, CH_3-19); 0.80 (s, 3H, CH_3-18); 0.83-0.90 (1H); 0.94 (dd, J = 4.5 Hz, J = 11.5 Hz, 1H, 5-H); 1.04-1.13 (1H); 1.20-1.32 (3H); 1.41-1.49 {4H, 14-H_a and 1.43 (s, 3H, CH_3-16)}; 1.58 (bs, 1H, OH); 1.73-1.94 {6H, CH_2-6 and 1.78 (s, 3H, CH_3-17), 1.90 (d,, 1H, 12-H_a)}; 2.08 (ddd, J = 4.5 Hz, J = 10.2 Hz, J = 14.4 Hz, 1H, 14-H_b); 2.46 ($W_{1/2}$=7 Hz, 1H 9-H); 2.65 (dd, 1H, 12-H_b); 3.26 (d, 1H, OH); 3.67-3.76 (1H, 15-H); 3.97 (d, 1H, 11-H); 3.98-4.05 (1H, 15-H); 5.58-5.64 (1H, 7-H); 7.54-7.60 (2H, Ar-H's); 7.63-7.68 (1H, Ar-H); 7.90-7.94 (2H, Ar-H's); $|J_{12a,12b}|$ = 16.2 Hz; $|J_{11,12b}|$ = 10.2 Hz.- IR (CCl_4): 3440 (OH), 1295, 1140 cm^{-1} (SO_2).- MS: m/z (%) = 431 (0.1), 218 (100), 203 (25), 89 (99), 43 (64).- $C_{26}H_{40}O_4S$ (448.7), calc C 69.60, H 8.99; found C 69.66, H 9.07.

b) Sample obtained from **25**: The spectral data of this sample were identical with those reported above.- $[\alpha]^{D}_{20}$ = -2.7 (c 0.8, $CHCl_3$). [41]

(11S,13S)-Benzenesulfonyl-labd-7-ene-13,15-diol (28)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.74 (s, 3H, CH_3-20); 0.78 (s, 6H, CH_3-18, CH_3-19); 0.78-0.91 (2H); 0.95-0.99 (1H, 5-H); 1.06-1.18 (2H); 1.18-1.45 {4H with 1.39 (s, 3H, CH_3-16)}; 1.62-1.98 {7H, with CH_2-6, 14-H, 12-H_a and 1.70 ($W_{1/2}$=5.3 Hz, 3H, CH_3-17)}; 2.47 (bs, 1H, 9-H); 2.77 (dd, J = 10.4 Hz, J = 16.7 Hz, 1H, 12-H_b); 3.77-3.97 {2H, 15-H and 3.85 (d, J = 10.4 Hz, 11-H)}; 5.58-5.65 (1H, 7-H); 7.55-7.61 (2H, Ar-H's); 7.63-7.69 (1H, Ar-H); 7.92-7.97 (2H,

Ar-H's).- IR (CCl_4): 3450 (OH), 1300, 1140 cm^{-1} (SO_2).- $C_{26}H_{40}O_4S$ (448.7), MS: m/z (%) = 218 (56), 89 (100), 43 (80).-

(7R,8R,11R,13S)-11-Benzenesulfonyl-8,13-epoxy-7-phenylselanyl-labdan-15-ol (29)

To a -78°C cold solution of **27** (sample with $[\alpha]^D_{20}$ = -2.7, 11.7 mg, 0.026 mmol) in CH_2Cl_2 (250 µL) a solution of NPSP (11.9 mg, 0.039 mmol) in CH_2Cl_2 (360 µL) and a 10 per cent solution of tin(IV) chloride in CH_2Cl_2 (22.3 µL) were added. The mixture was stirred for 3 h being allowed to warm to 20°C. After solvent evaporation and LC (petrol-ethyl acetate 5:1, then 1:1) **29** (11.4 mg, 73 %) was obtained.- $[\alpha]^D_{20}$ = -26.5 (c 0.95, $CHCl_3$).- ^1H NMR (400 MHz, $CDCl_3$, H,H COSY, C,H COSY, NOE): δ = 0.75 (s, 3H, CH_3-19); 0.79 (s, 3H, CH_3-18); 0.82-0.95 (2H); 1.04 (s, 3H, CH_3-20); 1.10-1.25 {7H, with 1.25 (s, 3H, CH_3-16)}; 1.32-1.54 {9H, with 14-H_a, and δ = 1.50 (dd, 12β-H)}; 1.60 (s, 3H, CH_3-17); 1.80 (ddd, J = 3.3 Hz, J = 4.4 Hz, J = 14.3 Hz, 1H, 6-H_{eq}); 2.02 (ddd, J = 4.5 Hz, J = 11.4 Hz, J = 14.3 Hz, 1H, 6-H_{ax}); 2.13 (d, 1H, 9-H); 2.17 (ddd, J = 5.1 Hz, J = 10.4 Hz, J = 14.2 Hz, 1H, 14-H_b); 2.35 (dd, 1H, 12α-H); 3.38 (m, 1H, 11-H); 3.64 (t, 1H, 7-H); 3.65-3.69 (m, J = 4.4 Hz can be observed, 1H, 15-H_a); 3.91-3.99 (m, J = 3.5 Hz, J = 10.4 Hz can be observed, 1H, 15-H_b); 7.21-7.25 (3H, Ar-H's); 7.49-7.69 (5H, Ar-H's); 7.83-7.90 (2H, Ar-H's); $J_{7,6}$ = $J_{7,6'}$ = 4.5 Hz; $J_{9,11}$ = 2.5 Hz; $|J_{12\alpha,12\beta}|$= 15 Hz; $J_{11,12\alpha}$ = 10.2 Hz; $J_{11,12\beta}$ = 8.9 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT): δ = 18.20 (CH_3, C-20); 18.20 (CH_2, C-2); 22.13 (CH_3, C-19); 26.00 (CH_2, C-6); 28.46 (CH_3, C-16); 31.57 (CH_3, C-17); 32.36 (CH_2; C-12); 33.22 (CH_3, C-18); 33.37 (C_q, C-4 or C-10); 39.01 (C_q, C-4 or C-10); 39.92 (CH_2, C-1 or C-2); 41.19 (CH_2, C-1 or C-2); 46.43 (CH_2, C-14); 46.97 (CH, C-9); 49.64 (CH, C-5); 56.69 (CH, C-7); 57.42 (CH, C-11); 59.84 (CH_2, C-15); 74.19 (C_q, C-8 or C-13); 77.74 (C_q, C-8 or C-13); 127.26, 128.70 , 129.08, 129.32, 133.69, 133.85(Ar-CH's); 130.87, 138.94 (ArCq's).- IR (CCl_4): 3610, 3500 (OH), 1315, 1300, 1145 cm^{-1} (SO_2).- MS: m/z (%) = 604 (11, $M^{+\bullet}$ of $C_{32}H_{44}O_4S^{80}Se$), 305 (45), 287 (22), 217 (20), 207 (31), 43(100).- $C_{32}H_{44}O_4SSe$ (603.7), calc C 63.66, H 7.35; found C 63.55, H 7.31

(7S,8R,11R,13S)-11-Benzenesulfonyl-7-trifluoroacetoxymercurio-8,13-epoxy-labdan-15-ol (37a)

A mixture containing mercury(II) trifluoroacetate (15.3 mg, 0.034 mmol), 1,3-diol **27** (29.1 mg, 0.068 mmol), and benzene-d_6 (0.6 mL) was sonicated for 5 min. After filtration the clear solution was left at 20°C for 7 d. After 25 min, 4 h, and 7d ^1H NMR spectra were taken (see Figure 2). The compound that was present after 7d (**37a**) was fully analyzed by NMR techniques.- ^1H NMR (400 MHz, C_6D_6, H,H COSY, C,H COSY, NOE): δ = 0.58 (s, 3H, CH_3-16); 0.74 (s, 3H, CH_3-20); 0.76 (s, 3H, CH_3-19); 0.82 (s, 3H, CH_3-18); 1.02-1.24 (6H with 12-H, 14-H); 1.27 (s, 3H, CH_3-17); 1.29-1.42 (4H); 1.42-1.57 (3H); 1.64-1.75 (2H with 14-H'); 2.02-2.15 (3H, 7-H, 9-H, 12-H); 3.20-3.29 (ddd, J = 3.0 Hz, J = 9 Hz could be identified, 1H, 11-H); 3.92-4.02 (1H, 15-H); 4.38-4.47 (m, J = 4.4 Hz, J = 8.9 Hz, J = 10.9 Hz, 1H, 15-H); 6.98-7.08 (3H, Ar-H's) 7.75-7.82 (2H, Ar-H's).- After addition of $CDCl_3$ the 7-H, 9-H, and 12α-H signals were better separated allowing a more precise assignment of configuration and conformation. The following results were obtained:

Ratio C_6D_6-$CDCl_3$	$\delta_{7\text{-H}}$	$\delta_{9\text{-H}}$	$\delta_{12\alpha\text{-H}}$
1 : 0	≈ 2.07	≈ 2.07	≈ 2.12 (dd)
2 : 1	2.22 (dd)	1.95 (d)	2.07 (dd)
1 : 2	2.45 (dd)	1.98 (d)	2.11 (dd)
2 : 7	2.53 (dd)	1.95 (d)	2.08 (dd)

$J_{9,11}$ = 3.0 Hz; $J_{11,12\alpha}$ = 11.5 Hz; $J_{11,12\beta}$ = 9.0 Hz; $|J_{12\alpha,12\beta}|$ = 15.0 Hz, $J_{6,7}$ = 13.7 Hz; $J_{6',7}$ = 5.3 Hz.- The NOE results summarized in formula **37a'** were obtained from the C_6D_6-$CDCl_3$ 2:7 solution.- ^{13}C NMR (100.6 MHz, C_6D_6, DEPT): δ = 17.05 (CH_3, C-20); 18.15 (CH_2, C-2); 22.27 (CH_3, C-19); 26.08 (CH_2, C-6); 27.25 (CH_3, C-16); 32.46 (CH_2, C-12); 33.20 (C_q, C-4 or C-10); 33.43 (CH_3, C-18); 34.67 (CH_3, C-17); 38.10 (C_q, C-4 or C-10); 39.86 (CH_2, C-1 or C-3); 41.25 (CH_2, C-1 or C-3); 43.27 (CH_2, C-14); 49.28 (CH, C-9); 56.18 (CH, C-5); 57.03 (CH, C-11); 64.30 (CH_2, C-15);

65.40 (CH, C-7); 71.36 (C_q, C-8 or C-13); 75.91 (C_q, C-8 or C-13); 113.75, 116.43, 117.39, 120.26 (CF_3); 128.41, 129.12, 133.36 (Ar-CH's); 139.44 (Ar-C_q); 160.09, 160.87, 160.48, 161.26 ($O\underline{C}OCF_3$ signals).

(7S,8R,11R,13S)-11-Benzenesulfonyl-7-phenylmercurio-8,13-epoxy-labdan-15-ol (37b)

A solution of mercury(II) trifluoroacetate (81.9 mg, 0.191 mmol) and **27** (42.9 mg, 0.096 mmol) in benzene (4 mL) was stirred at 20°C for 6 d. Then, at 0°C an ice-cold solution of $NaBH_4$ (0.1 mol/L in 3 mol/L NaOH, 1.5 mL) was added. The mixture was stirred at 0°C for 5 min and at 20° for 15 min. Usual work-up yielded a product that was separated into two fractions according to their solubility in toluene and CCl_4. Both fractions were purified by HPLC (Merck Si100, toluene-triethylamine 15:1, 10 mL/min). TLC behaviour and spectral data of both fractions were identical, reported are the data of the fraction less soluble in benzene.- ^{1}H NMR (400 MHz, $CDCl_3$, H,H COSY, C,H COSY, NOE): δ = 0.85 (s, 3H, CH_3-19); 0.91 (s, 3H, CH_3-18); 1.00 (dd, J = 11.2 Hz, J = 2 Hz, 1H, 5-H); 1.08 (s, 3H, CH_3-20); 1.16-1.28 {8H with 1.18 (s, 3H, CH_3-16)}; 1.30-1.81 {15H, with 12-H_β, 14-H and 1.52 (s, 3-H, CH_3-17)}; 1.85 (dd, 7-H); 1.93-2.06 (2H, 9-H, 14-H); 2.32 (dd, 1H, 12α-H); 3.45 (m, 1H, 11-H); 3.69-3.76 (1H, 15-H_a); 3.87-3.97 (1H, 1H, 15-H_b); 7.12-7.20 (1H, Ar-H); 7.33-7.43 (3H, Ar-H's); 7.53-7.69 (3H, Ar-H's); 7.85-7.91 (2H, Ar-H's); $J_{9,11}$ = 3 Hz; $J_{11,12\alpha}$ = 11.5 Hz; $J_{11,12\beta}$ = 9 Hz; $|J_{12\alpha,12\beta}|$ = 14.5 Hz; $J_{7,6\alpha}$ = 5 Hz; $J_{7,6\beta}$ = 13.5 Hz.- In $CDCl_3$-C_6D_6 2:1, the 9-H and 14-H signals were separated: 2.15 (9-H), 1.88 (14-H).- ^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT): δ = 17.52 (CH_3, C-20); 18.27 (CH_2, C-2); 22.48 (CH_3, C-19); 25.45 (CH_2, C-6); 28.38 (CH_3, C-16); 32.56 (CH_2, C-12); 33.61 (C_q, C-4 or C-10); 33.97 (CH_3, C-18); 34.99 (CH_3, C.17); 38.37 (C_q, C-4 or C-10); 40.19 (CH_2, C-1 or C-3); 41.63 (CH_2, C-1 or C-3); 48.47 (CH_2, C-14); 51.69 (CH, C-9); 57.86 (CH, C-5); 58.20 (CH, C-11); 59.24 (CH_2, C-15); 68.78 (CH, C-7); 72.14 (C_q, C-8 or C-13); 77.84 (C_q, C-8 or C-13); 127.79, 128.61, 129.26, 133.55, 136.98 (ASr-CH's); 139.32, 177,91 (Ar-C_q's)- IR (CCl_4): 3660, 3520 cm^{-1} (OH).- $C_{32}H_{44}HgO_4S$ (725.4), FABMS: m/z = 725/727 (for $^{200}Hg/^{202}Hg$), 583/585, 93 (100).

(11R,14R)-11-Benzenesulfonyl-13,14-epoxy-labd-7-en-15-yl imidazol-1-carbothioate (41)

Under the exclusion of light to a solution of the **25/26** mixture (obtained from *rac*-**24** in 84% yield after 7 h under the conditions reported above, 163.9 mg, 0.37 mmol) in THF (0.5 mL) a solution of N,N-thiocarbonyldiimidazole (130.8 mg, 0.73 mmol) inTHF (1.5 mL) was added.The mixture was heated to 80°C for 3 h. Solvent evaporation and LC (light exclusion, petrol-ethyl acetate 5:1 → 1:1) furnished **41** (76.3 mg, 37%). ^{1}H NMR showed only one set of signals, probably only one diasteroisomer was isolated. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.10-0.15 (1H); 0.78 (3H, CH_3); 0.82 (3H, CH_3); 0.84 (3H, CH_3); 0.84-0.96 (3H, 5-H, 3-H, 1-H); 1.10-1.41 (4H, CH_2-2, 1-H, 3-H'); 1.43 (s, 3H, CH_3-16); 1.81-1.94 {8H with 1.80 (m, $W_{1/2}$=5 Hz, 3H, CH_3-17)}; 2.25-2.33 (2H, CH_2-12); 2.41 (bs, $W_{1/2}$=8 Hz, 1H, 9-H); 3.48 (dd, 1H, 14-H); 3.52-3.62 (1H, 11-H); 4.55 (dd, 1H, 15-H_a); 4.89 (dd, 1H, 15-H_b); 5.59-5.65 (1H, 7-H); 7.00-7.08 (1H, Ar-H); 7.52-7.73 (4H, Ar-H's); 7.83-7.98 (2H, Ar-H's); 8.35-8.44 (1H, Ar-H); $J_{14,15a}$ = 7.2 +Hz; $J_{14,15b}$ = 3.9 Hz; $|J_{15a,15b}|$ = 12 Hz.- IR (CCl_4): 1725 (C=S), 1325, 1305, 1145 cm^{-1} (SO_2).- MS: m/z (%) = 556 (0.35, $M^{+\bullet}$), 415 (28), 120 (50), 109 (47), 69 (100).- $C_{30}H_{40}N_2O_4S_2$ (556.8), calc for $C_{24}H_{35}N_2O_2S$: 415.2419; found 415.2410 (HRMS).

(11E, 13S)-Labda-7,11,14-trien-13-ol (43)

To a solution of **41** (36.3 mg, 0.065 mmol) in oxygen-free THF tri-^{n}butyltin hydride (34.4 µl, 0.13 mmol) was added (exclusion of light). The mixture was stirred in the dark at 80°C, and in 5 min intervals 10 µl portions of a solution of AIBN (1 mg, 5.9 µmol) in THF (50 µl) were added. Stirring at 80°C was then continued for 3 h. Solvent evaporation and LC (petrol-ethyl acetate 5 : 1) furnished **43** (5.8 mg, 31%). In a further experiment pure **25** was submitted to the two-step deoxygenation and also yielded **43**. This experiment proves the configuration at C-13 in **43**.-^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (s, 3H, CH_3); 0.85 (s, 3H, CH_3); 0.88 (s, 3H, CH_3); 1.38 (s, 3H, CH_3-16); 1.53 (s, 3H, CH_3-17); 1.80-2.06 (2H, CH_2-6); 2.35 (d, 1H, 9-H); 5.04 (dd, 1H, 15-H_a); 5.23 (dd, 1H, 15-H_b); 5.40-5.52 (2H, 7-H, 11-H); 5.58 (d, 1H, 12-H); 5.97 (dd, 1H, 14-H); $J_{15a,14}$ = 10.5 Hz; $J_{15b,14}$ = 17.5 Hz; $|J_{15a,15b}|$ = 1 Hz; $J_{11,12}$ = 15.5 Hz; $J_{9,11}$ = 10 Hz.- IR (CCl_4): 3600 cm^{-1} (OH).- MS: m/z (%) = 288 (4, $M^{+\bullet}$), 164 (46), 121 (57), 106 (50), 81 (100), 55 (70), 43 (95).- $C_{20}H_{32}O$ (288.5), calc 288.2453; found 288.2453 (HRMS).

X-ray Structural Analyses of 20 and 37b[42]

Compound 20: $C_{18}H_{30}S_2$; orthorhombic space group P bca; a = 12.221(4), b = 13.836(4), c = 20.482(4) Å, $\alpha = \beta = \gamma = 90°$; V = 3463.1(1.6) $Å^3$; 8 molecules per unit cell. 2429 unique reflections were measured (diffractometer Enraf-Nonius CAD4, Mo-Kα radiation, $4.00 < 2\Theta < 44°$). The structure was refined by a full-matrix least-squares method (1588 reflections with $I > 2\ \sigma(I)$, hydrogen atoms also refined, 238 variables, R = 0.061, R_w = 0.061, maximum shift/error ratio ≤0.96, residual electron density ≤0.29).

Compound 37b: $C_{32}H_{44}HgO_4S$; monoclinic space group P $2_1/n$; a = 8.524(2), b = 39.043(8), c = 8.764(1) Å, α = 90, ß = 99.29(2), γ = 90°; V = 2878.3(1.7) $Å^3$; 4 molecules per unit cell. 3856 refelctions were measured, of which 3505 were unique (diffractometer Enraf-Nonius CAD4, Mo-Kα radiation, $4.00 < 2\Theta < 44°$). The structure was refined by a full-matrix least-squares method (2614 reflections with $I > 2.5\ \sigma(I)$, hydrogen atoms calculated and included only in structure factor calculation, 343 variables, R = 0.045, R_w = 0.061, maximum shift/error ratio ≤0.06, maximum residual electron density = 0.90 near Hg atom).

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[41] It has not yet been determined whether the different specific rotations of the two samples are due to errors in the $[\alpha]_D$ determinations or indicate a lower optical purity of the sample obtained from the **25/26** mixture than that obtained from pure **25**. In the latter case, the selectivity of the Sharpless epoxidation of ent-**24b** must be lower than that of **24b**, since optically pure **24b** has been demonstrated to yield a single epoxidation product (see text).

[42] Tables of atomic co-ordinates, thermal parameters, bond lengths, and angles have been deposited at the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. The X-ray data are available on request from the Director of the CCDC by quoting the full literature citation of this paper.

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