Synthesis of Terpenoid Lactones with the *p*-Menthane System[‡]

Iwona Dams,*[a] Agata Białońska,[b] Zbigniew Ciunik,[b] and Czesław Wawrzeńczyk[a]

Keywords: Antifeedants / Lactones / Natural products / Pulegone / Terpenoids

Starting from (*R*)-(+)- and (*S*)-(−)-pulegone enantiomeric pairs of hydroxy lactones and keto lactones were obtained by Claisen rearrangement of *cis*-pulegols and lactonization of epoxy esters. The hydroxy lactones were reduced with $LiAlH_4$ in order to assign the configuration of the chiral centers. The structures of the synthesized compounds were established on the basis of spectroscopic and crystallographic data.
(© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2004)

Introduction

Terpenoid compounds containing the lactone moiety are widespread in nature. Lactones isolated from plants,[1] microorganisms[2] and insects[3] possess interesting and specific biological properties; the best known is their antifungal,[4] antibacterial[4b][4c,5] and antitumor[4b,6] activity. As they are common secondary metabolites of plants, lactones are also found as part of plants' protective system against predators.[7] Our research in this area involves the synthesis of terpenoid lactones and tests of their activity as insect feeding deterrents. We have synthesized many mono-,[8] bi-[9] and tricyclic[10] lactones which were tested for feeding deterrence against three storage pests — the granary weevil beetle (*Sitophilus granarius* L.), the khapra beetle (*Trogoderma granarium* Ev.) and the confused flour beetle (*Tribolium confusum* Duv.). Some of them (**1**−**8**; Figure 1 exhibit quite good deterrent activity similar to that of the most potent antifeedant, azadirachtin.[11]

Enantiomeric lactones with the *p*-menthane system **5**−**8**, synthesized from optically pure isomers of perillyl alcohol and limonene, appeared to be especially active. Comparison of the biological activity of the corresponding enantiomers indicated that, in general, compounds with the 8*R* configuration are more active than those with the 8*S* configuration.[12] The lactones synthesized were also tested for feeding deterrence against the peach potato aphid (*M. persicae* Sulz.), but only a few of them were significantly active (**3**, **4**, **6b**).[11b,13]

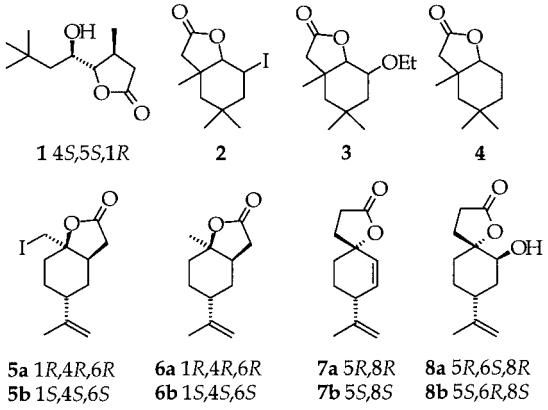


Figure 1. Biologically active lactones

Here we present the synthesis of four enantiomeric pairs of γ-spirolactones with the *p*-menthane system as potential insect feeding deterrents. The lactones were obtained from optically pure isomers of (*R*)-(+)- and (*S*)-(−)-pulegone in order to estimate the influence of the configuration of the chiral centers on their biological activity. Studies of the structure-activity relationship are one of the most important aspects of research on biologically active compounds, and such types of study are especially useful in the search for new synthetic drugs, agrochemicals, food additives, flavours and fragrances.[14]

Results and Discussion

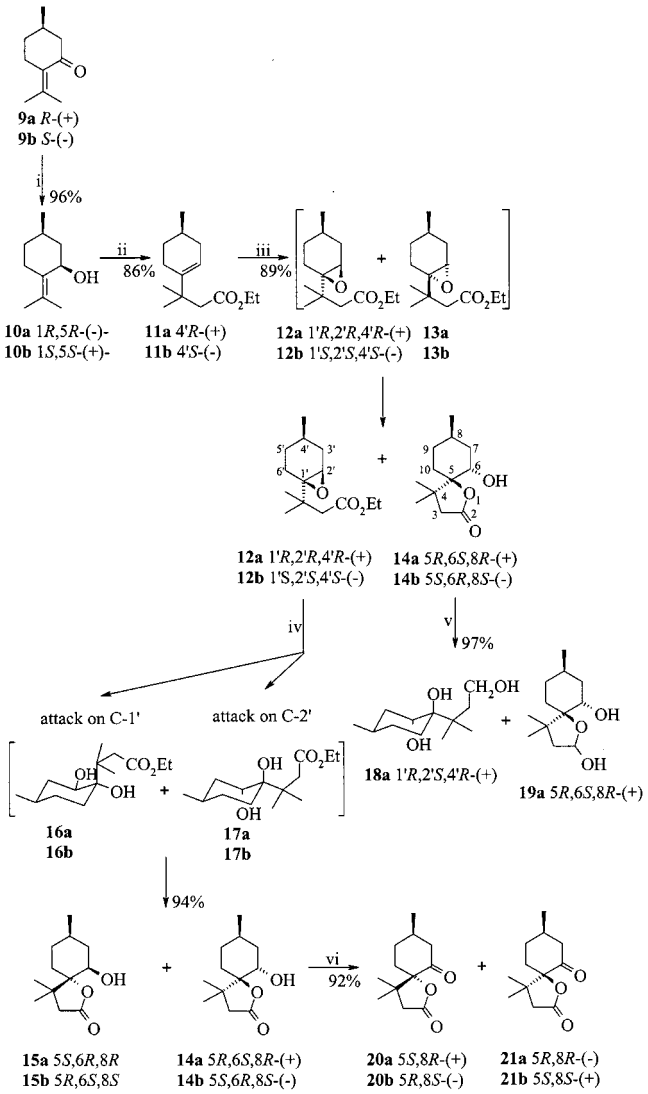
Enantiomeric pairs of δ-hydroxy-γ-lactones (5*R*,6*S*,8*R*)-(+)-**14a**, (5*S*,6*R*,8*S*)-(−)-**14b** and (5*S*,6*R*,8*R*)-**15a**, (5*R*,6*S*,8*S*)-**15b** were obtained in a four-step synthesis from optically pure isomers of (*R*)-(+)- and (*S*)-(−)-pulegone (**9a** and **9b**; Scheme 1). The first step of the synthesis was the reduction of pulegones with sodium borohydride according

[‡] Lactones, 22. Part 21: I. Dams, A. Białońska, Z. Ciunik, C. Wawrzeńczyk, *J. Agric. Food Chem.* **2004**, *52*, 1630−1634.

[a] Department of Chemistry, Agricultural University
Norwida 25, 50-375 Wrocław, Poland
E-mail: iwa_dams@ozi.ar.wroc.pl
[b] Faculty of Chemistry, University of Wrocław
Joliot-Curie 14, 50-383 Wrocław, Poland

 © 2004 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim **DOI: 10.1002/ejoc.200300800**

to the standard procedure.[15] A 5:1 methanol/water mixture as solvent and a small excess of $NaBH_4$ were used to shorten the time of the reaction. The choice of sodium borohydride as a hydride reducing agent was motivated by its high stereoselectivity in the reduction of α,β-unsaturated ketones. The addition of $CeCl_3$ to prevent the formation of saturated alcohols was not necessary. The course of the reactions and the purity of the products were controlled by GC on a capillary column (HP-5). The allylic alcohols *cis*-(1*R*,5*R*)-(−)- and *cis*-(1*S*,5*S*)-(+)-pulegol (**10a** and **10b**) were the main products of the reductions. The stereochemical assignment of the *cis*-pulegols was based on the value of their optical rotation.[16] Their structure was also confirmed by ^{1}H NMR and IR spectroscopy.[17]



Scheme 1. (i) $NaBH_4$, EtOH, MeOH/H_2O, 0 °C, 2 h; (ii) $CH_3C(OEt)_3$, C_2H_5COOH, 138 °C, 8 h; (iii) *m*-CPBA, CH_2Cl_2, 0 °C, 24 h; (iv) THF/$HClO_4$/H_2O (pH = 1.2), 24 h; (v) $LiAlH_4$, Et_2O, 1 h; (vi) CrO_3·2Py, CH_2Cl_2, 24 h.

The crude pulegols, without further purification (according to the GC analysis they had purities of 96% and 97%, respectively), were subjected to the orthoacetate modification of the Claisen rearrangement[18] to give the enantiomerically pure (4′*R*)-(+)-**11a** and (4′*S*)-(−)-**11b** isomers of ethyl 3-methyl-3-(4′-methyl-1′-cyclohexen-1′-yl)butanoate were obtained in good yields (86% and 84%, respectively). Their enantiomeric purity (*ee* 99%) was confirmed by GC on a chiral column (cyclodextrin-β-2,3,6-m-19).

The epoxidation of esters **11a** or **11b** with *m*-chloroperbenzoic acid in dichloromethane[19] afforded a mixture of epoxy ester (1′*R*,2′*R*,4′*R*)-(+)-**12a** and hydroxy lactone (5*R*,6*S*,8*R*)-(+)-**14a** or enantiomeric epoxy ester (1′*S*,2′*S*,4′*S*)-(−)-**12b** and hydroxy lactone (5*S*,6*R*,8*S*)-(−)-**14b** respectively. These mixtures were separable by GC on a capillary column (HP-5). From integration of the signals in the GC chromatograms these mixtures were found to contain 45% of the epoxy ester and 55% of the hydroxy lactone. The mixture of epoxy ester **12a** or **12b** and hydroxy lactone **14a** or **14b** was separated by column chromatography on silica gel. The first fraction, eluted with hexane/acetone (50:1), afforded the epoxy ester **12a** or **12b**. Unfortunately, these epoxy esters undergo partial decomposition on silica gel to unidentified and inseparable products, so their purity after column chromatography was only 86% and 82%, respectively. Their structures were confirmed by the ^{1}H NMR spectra. The presence of the doublet (J = 5.1 Hz) at δ = 3.07 ppm for H-2′ indicates that this proton is coupled with only one proton of the CH_2-3′ group. According to the analysis with a Driding models this is only possible in the half-chair conformation of the cyclohexane ring with the C-1′, C-2′, C-3′, C-4′ and C-6′ atoms in one plane. In such a conformation the dihedral angle between H-2′ and one proton of the CH_2-3′ group is close to 90°. In consideration of the above facts the doublet at δ = 3.07 ppm (J = 5.1 Hz) was ascribed to the H-2′ proton of the *cis* isomer **12a** or **12b**. The *trans*-epoxy ester **13a** or **13b** undergoes lactonization to the hydroxy lactone **14a** or **14b** under epoxidation conditions. Elution with hexane/acetone (5:1) gave the pure hydroxy lactone **14a** or **14b**. The presence of the γ-lactone moiety in **14a** and **14b** was confirmed by the absorption band at 1768 cm^{-1} in the IR spectrum. The shape of the narrow multiplet for H-6 in the ^{1}H NMR spectrum of **14a** or **14b** suggests the equatorial position of this proton and thereby the axial position of the hydroxy group.

The ease of lactonization of epoxy esters **12a** and **12b** was confirmed by their reactions under acidic conditions. The reaction of the epoxy ester **12a** catalyzed by $HClO_4$ in THF/H_2O solution (pH 1.2) after 24 h (when the epoxy ester was no longer detected by TLC analysis) gave the mixture of lactones (5*R*,6*S*,8*R*)-(+)-**14a** (28%) and (5*S*,6*R*,8*R*)-**15a** (72%). In spite of many attempts, the mixture of hydroxy lactones was inseparable by column chromatography. The structure of **14a** was again determined on the basis of spectroscopic data of the mixture of hydroxy lactones **14a** and **15a** and confirmed by the X-ray structure of the triol (1′*R*,2′*S*,4′*R*)-(+)-**18a**. This triol is the product of $LiALH_4$ reduction of the hydroxy lactone **14a** in anhydrous diethyl ether. Lactol (5*R*,6*S*,8*R*)-(+)-**19a** is the minor product of this reduction. The crystals of **19a** were not suitable for X-ray analysis and the absolute configuration was not as-

 © 2004 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

signed to the C-2 atom. The configuration of the chiral centers of the triol **18a** and, indirectly, of the lactone **14a** was provided by the X-ray structural analysis of **18a** (Figure 2). This analysis indicated the presence of two symmetrically independent molecules of **18a** in the crystals. The X-ray structure undoubtedly confirms the axial position of the hydroxy group at C-2′ of the triol **18a** and, indirectly, the axial position of this group at C-6 in the hydroxy lactone **14a**. The structure of diastereoisomeric hydroxy lactones **15a** and **15b** was determined from the ^{1}H NMR and IR spectra of the mixture of hydroxy lactones **14a** and **15a** or **14b** and **15b**. The difference in chemical shift ($\Delta\delta$ = 0.2 ppm) of the two methyl groups at C-4 in the spectrum of **15a** indicates the deshielding effect of the hydroxy group at C-6 on the closer methyl group. Such effective deshielding is only possible when this group is in an equatorial position. The spectrum of **14a** shows the two methyl groups at C-4 as a single six-proton singlet at δ = 1.18 ppm. In this case, as was subsequently confirmed by X-ray analysis of **18a**, the hydroxy group at C-6 occupies the axial position.

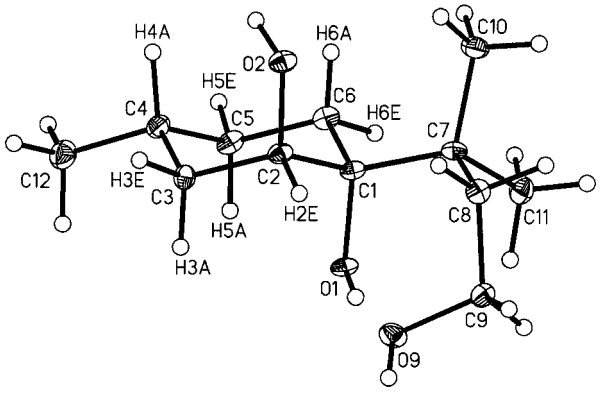


Figure 2. Molecular structure of (1′*R*,2′*S*,4′*R*)-(+)-**18a** with crystallographic numbering

It is generally supposed that lactonization of epoxy esters, induced by H^+ ions, proceeds via the diols **16a** and **16b** or **17a** and **17b** respectively. According to earlier observations concerning the cleavage of an oxirane ring in the limonene system 1,2-oxides,[9a,20] a nucleophile should attack the C-1′ atom from the opposite side of the oxonium ion that is formed after H^+ addition to the oxirane oxygen. In the case of the *trans*-epoxides **13a** and **13b**, this mode of action leads to the *trans*-diaxial diols **17a** and **17b** with the ethoxycarbonyl group in the equatorial position; these diols undergo lactonization to the hydroxy lactones **14a** and **14b**. This was confirmed by the X-ray structure of the triol **18a**, obtained by the reduction of hydroxy lactone **14a** with $LiAlH_4$. In the case of the more stable *cis*-epoxides **12a** and **12b**, attack on C-1′ leads to the *trans*-diequatorial diols **16a** and **16b** with the ethoxycarbonyl group in the axial position. As this conformation is energetically unfavourable, the attack of a nucleophile at C-2′ of the epoxides **12a** and **12b**, leading to the diols **17a** and **17b**, is also reasonable. Such a pattern of diol (**16a** and **16b** or **17a** and **17b**) formation explains the ratio of lactones [**14a** or **14b** (28%) and **15a** or **15b** (72%)] in the products of the lactonization of the pure epoxy esters **12a** or **12b**.

Similar results were obtained when the crude mixture of *cis*-epoxy esters **12a** or **12b** and hydroxy lactones **14a** or **14b** was subjected to lactonization under acidic conditions. From integration of the signals in the GC chromatograms it follows that the mixture of products contains 80% of hydroxy lactone **14a** or **14b** and 20% of **15a** or **15b**. This synthetic path was applied further to avoid decomposition of epoxy esters on silica gel and gain the keto lactones (5*S*,8*R*)-(+)-**20a** or (5*R*,8*S*)-(−)-**20b** and (5*R*,8*R*)-(−)-**21a** or (5*S*,8*S*)-(+)-**21b** in good yields. The mixture of hydroxy lactones **14a** and **15a** or **14b** and **15b** was oxidized with pyridinium dichromate in dichloromethane[21] to give a mixture of keto lactones **20a** and **21a** or **20b** and **21b** (20% and 80% respectively), which was separable on silica gel. The first fraction, eluted with hexane/acetone (20:1), afforded the pure keto lactone **21a** or **21b** as colourless crystals. The X-ray analysis indicated two symmetrically independent molecules of **21b** in the crystals. The crystal structure of (5*S*,8*S*)-(+)-**21b** (Figure 3) shows a *cis* relationship between the CH_3-8 group of the chair-like cyclohexane ring and the C5−O1 bond of the lactone moiety. As the same relative configuration of the corresponding substituents CH_3-4′ and OH-1′ was determined for the triol **19a**, the X-ray structure of keto lactone **21b** indirectly confirms the configuration of the chiral centers of the hydroxy lactones **14a** and **14b**.

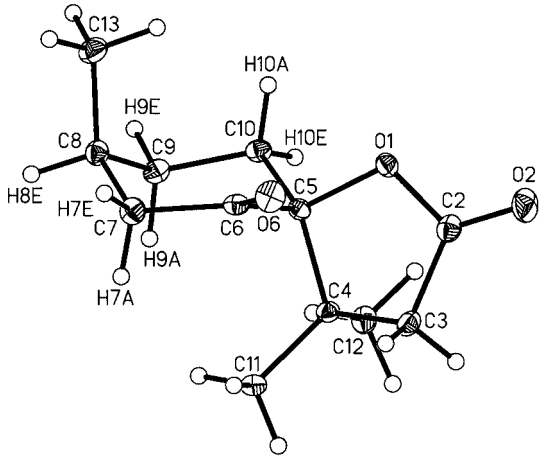


Figure 3. Molecular structure of (5*S*,8*S*)-(+)-**21b** with crystallographic numbering

The second eluted keto lactone was **20a** or **20b**. In the case of (5*S*,8*R*)-(+)-**20a** the X-ray analysis also indicates the presence of two symmetrically independent molecules in the crystals. The crystal structure of **20a** (Figure 4) afforded information about the *trans*-diequatorial orientation of the CH_3-8 group and the C5−O1 bond, thereby confirming the configuration of the chiral centers assigned to the hydroxy lactones **15a** and **15b**.

 © 2004 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

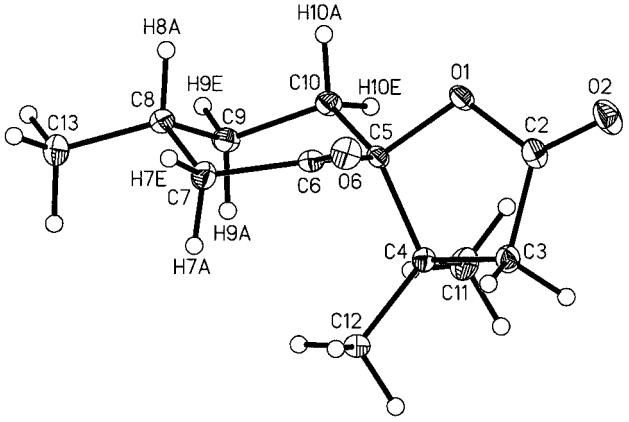


Figure 4. Molecular structure of (5*S*,8*R*)-(+)-**20a** with crystallographic numbering

It is not surprising that esters (4′*R*)-(+)-**11a** and (4′*S*)-(−)-**11b**, containing the *p*-menthane system, possess interesting odors. Their odoriferous properties are slightly influenced by the absolute configuration of the odorant. The fragrance of ester (4′*R*)-(+)-**11a** is intense and fruity with a ripe pear note, whereas its enantiomer (4′*S*)-(−)-**11b** has moderately intense, fruity-pear odor with a woody note.

The lactones synthesized were tested for their deterrent activity against selected storage pest insects (*Sitophilus granarius* L., *Tribolium confusum* Duv., *Trogoderma granarium* Ev.), the peach-potato aphid (*Myzus persicae* Sulz.) and the Colorado potato beetle (*Leptinotarsa decemlineata* Say) according to the procedures described by Paruch et al.,[12] Gabrys et al.[13] and Szczepanik et al.,[22] respectively. The compounds tested showed moderate activity towards all mentioned grain pests (total coefficients of deterrence[12] 66−162) and appeared much more effective antifeedants against the Colorado potato beetle (total coefficients of deterrence 119−184). Among all tested compounds only hydroxy lactones (5*R*,6*S*,8*R*)-(+)-**14a** and (5*S*,6*R*,8*S*)-(−)-**14b** were active against *M. persicae*. The details of these studies will be the subject of a separate publication.

Experimental Section

General: (*R*)-(+)-Pulegone, (*S*)-(−)-pulegone, triethyl orthoacetate and *m*-chloroperbenzoic acid were purchased from Aldrich or Fluka. ^{1}H NMR: Bruker Avance DRX 300 (300 MHz), TMS as internal standard, for solutions ($CDCl_3$ or [D_6]acetone). IR: Specord M 80 spectrophotometer (Carl Zeiss Jena). Melting points: Boetius Apparatus. Optical rotation: Autopol IV automatic polarimeter (Rudolph), in acetone or ethanol, concentrations denoted in g/100 mL. GC analyses: Varian CP-3380 instrument (FID, carrier gas H_2), using the following capillary columns: HP-1 (crosslinked methyl siloxane) 25 m × 0.32 mm × 0.52 μm; HP-5 (crosslinked 5% phenyl methyl siloxane) 25 m × 0.32 mm × 0.52 μm; CP-Cyclodextrin-β-2,3,6-m-19, 25 m × 0.25 mm × 0.25 μm. Analytical TLC: Silicagel DC-Alufolien Kieselgel 60 F_{254} (Merck), hexane, acetone and diethyl ether in various ratios as developing systems, compounds detected by spraying the plates with 1% $Ce(SO_4)_2$/2% $H_3[P(Mo_3O_{10})_4]$ in 10% H_2SO_4, followed by heating to 120 °C. Preparative column chromatography: silica gel (Kieselgel 60, 40−63 μm, 230−400 mesh, Merck), hexane, acetone and diethyl ether in varying ratios as eluents. X-ray structural analyses: X-ray data were collected at low temperature using an Oxford Cryosystem device on a Kuma KM4CCD κ-axis diffractometer with graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å). The crystal was positioned at 65 mm from the CCD camera. Frames (n = 612) were measured at 0.75° intervals with a counting time of 15−20 s. Accurate cell parameters were determined and refined by a least-squares fit of 1800−2000 of the strongest reflections. The data were corrected for Lorentz and polarization effects. No absorption correction was applied. Data reduction and analysis were carried out with the Oxford Diffraction (Poland) programs. The structures were solved by direct methods (program SHELXS-97) and refined by the full-matrix least-squares method on all F^2 data using the SHELXL-97 programs. Non-hydrogen atoms were refined with anisotropic displacement parameters; hydrogen atoms were included from geometry of molecules and Δρ maps. They were refined with isotropic displacement parameters.

***cis*-(1*R*,5*R*)-(−)-Pulegol (10a):** A suspension of $NaBH_4$ (0.4 g, 10.57 mmol) in EtOH (21 mL) was added dropwise to an ice-cooled solution of pulegone (*R*)-(+)-**9a** (1.5 g, 9.85 mmol) in MeOH (18 mL) and water (3.6 mL). Stirring was continued for 2 h at room temperature. When the reaction was complete (TLC, hexane/acetone, 20:1), the mixture was poured into brine and the product was extracted with hexane. The combined extracts were washed with water and dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo and the crude product (1*R*,5*R*)-(−)-**10a** (1.51 g, according to the GC analysis 96% purity) was used for the next step without further purification. $[\alpha]_D^{25}$ = −105.2 (c = 1.9, EtOH), m.p. 30−31 °C (ref. $[\alpha]_D$ = −104, EtOH/H_2O, 95:5; m.p. 29−30 °C[16]). ^{1}H NMR (300 MHz, [D_6]acetone, 25 °C): δ = 1.07 (d, J = 6.8 Hz, 3 H, CH_3-5), 1.33−1.42 (m, 1 H, H-5), 1.49−1.58 (m, 2 H, CH_2-group), 1.62 and 1.74 [two s, 6 H, $(CH_3)_2C$=], 1.66−1.72 (m, 2 H, CH_2-group), 2.11 and 2.34 (two m, 2 H, CH_2-group), 3.25 (br. s, 1 H, −OH), 4.58 (m, 1 H, H-1). IR (nujol): $\tilde{\nu}$ = 3300 cm^{-1} (br. s, OH), 1340 and 1272 (s, C−OH), 1116 (s, OH).

***cis*-(1*S*,5*S*)-(+)-Pulegol (10b):** In the same manner as described for the preparation of (1*R*,5*R*)-(−)-**10a**, pulegone (*S*)-(−)-**9b** (1 g, 6.57 mmol) yielded the crude *cis*-pulegol (1*S*,5*S*)-(+)-**10b** (0.95 g, according to the GC analysis 97% purity). $[\alpha]_D^{25}$ = +103.8 (c = 1.6, EtOH). Its IR and NMR spectra were identical with those of (1*R*,5*R*)-(−)-**10a**.

Ethyl (4′*R*)-(+)-3-Methyl-3-(4′-methyl-1′-cyclohexen-1′-yl)butanoate (11a): A mixture of the crude *cis*-pulegol (1*R*,5*R*)-(−)-**10a** (1.51 g, 9.79 mmol), triethyl orthoacetate (15 mL, 80 mmol) and a catalytic amount of propionic acid (1 drop) was heated at 138 °C for 8 h under the conditions for distillative removal of ethanol. When the reaction was complete (GC, TLC), the mixture was concentrated in vacuo to remove unchanged orthoacetate. The residue was chromatographed on silica gel. Elution with hexane/diethyl ether (80:1) gave the pure ester (4′*R*)-(+)-**11a** (1.89 g, 86% yield). $[\alpha]_D^{25}$ = +44.1 (c = 5.63, acetone), n_D^{20}= 1.4630. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.91 (d, J = 6.1 Hz, 3 H, CH_3-4′), 1.10 and 1.13 [two s, 6 H, $(CH_3)_2C$<], 1.20 (t, J = 7.1 Hz, 3 H, $-OCH_2CH_3$), 1.44−1.66 (m, 4 H, CH_2-groups), 1.96−2.10 (m, 3 H, CH_2-group and H-4′), 2.29 and 2.32 (AB system, J = 13.2 Hz, 2 H, CH_2-2), 4.04 (q, J = 7.1 Hz, 2 H, $-OCH_2CH_3$), 5.41 (m, 1 H, H-2′). IR (film): $\tilde{\nu}$ = 1748 cm^{-1} (s, C=O), 1392 and 1372 [s, $(CH_3)_2C$<], 1232 and 1120 (s, C−O−C). $C_{14}H_{24}O_2$ (224.3): calcd. C 74.97, H 10.78; found C 74.75, H 10.86.

 © 2004 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Ethyl (4′*S*)-(−)-3-Methyl-3-(4′-methyl-1′-cyclohexen-1′-yl)butanoate (11b): According to the procedure described for the preparation (4′*R*)-(+)-**11a**, the crude *cis*-pulegol (1*S*,5*S*)-(+)-**2b** (1.6 g, 10.37 mmol) yielded the unsaturated ester (4′*S*)-(−)-**11b** (1.95 g, 84%): $[\alpha]_D^{25} = -44.4$ (c = 3.87, acetone). Its IR and NMR spectra were identical with those of (4′*R*)-(+)-**11a**.

Ethyl (1′*R*,2′*R*,4′*R*)-(+)-3-Methyl-3-(1′,2′-epoxy-4′-methylcyclohex-1′-yl)butanoate (12a) and (5*R*,6*S*,8*R*)-(+)-6-Hydroxy-4,4,8-trimethyl-1-oxaspiro[4.5]decan-2-one (14a): A solution of *m*-chloroperbenzoic acid (1.46 g, 8.45 mmol) in CH_2Cl_2 (20 mL) was added dropwise to an ice-cooled and stirred solution of the ester (4′*R*)-(+)-**11a** (1.58 g, 7.04 mmol) in CH_2Cl_2 (40 mL). The reaction temperature was gradually raised to room temperature and the mixture was stirred for 24 h. When the reaction was complete (GC, TLC), the excess of *m*-chloroperbenzoic acid was destroyed with saturated $Na_2S_2O_3$ solution. The separated organic layer was washed with 10% Na_2CO_3 solution and brine, dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude mixture of the epoxy ester (1′*R*,2′*R*,4′*R*)-(+)-**12a** and the hydroxy lactone (5*R*,6*S*,8*R*)-(+)-**14a** (according to the GC analysis 45:55) was chromatographed on silica gel. The first fraction, eluted with hexane/acetone (50:1), gave the epoxy ester (1′*R*,2′*R*,4′*R*)-(+)-**12a** (0.79 g, according to the GC analysis 86% purity). $[\alpha]_D^{26} = +46.9$ (c = 4.21, acetone), $n_D^{20} = 1.4652$. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.81 (d, J = 6.0 Hz, 3 H, CH_3-4′), 0.96 and 1.01 [two s, 6 H, $(CH_3)_2C<$], 1.23 (t, J = 7.2 Hz, 3 H, $-OCH_2CH_3$), 2.24 and 2.35 (AB system, J = 13.7 Hz, 2 H, $-CH_2-CO_2$), 3.07 (d, $J_{H\text{-}2',\ H\text{-}3'}$ = 5.1 Hz, H-2′), 4.08 (q, J = 7.2 Hz, $-OCH_2CH_3$). IR (film): $\tilde{\nu}$ = 1740 cm^{-1} (s, C=O), 1232 and 1040 (s, C−O−C). The second fraction, eluted with hexane/acetone (5:1), afforded the pure hydroxy lactone (5*R*,6*S*,8*R*)-(+)-**14a** (0.73 g). $[\alpha]_D^{26} = +22.2$ (c = 3.45, acetone), $n_D^{20} = 1.4865$. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.88 (d, J = 6.3 Hz, 3 H, CH_3-8), 1.18 [s, 6 H, $(CH_3)_2C<$], 1.21−1.34 (m, 2 H, CH_2-group), 1.53−1.96 (m, 6 H, −OH, H-8 and two CH_2-groups), 2.17 and 2.55 (AB system, J = 17.2 Hz, 2 H, CH_2-3), 4.00 (m, 1 H, H-6). IR (film): $\tilde{\nu}$ = 3492 cm^{-1} (m, br., OH), 1768 (s, C=O), 1252 (s, C−O−C), 1164 (s, C−O−H), 1040 (s, C−O−C). $C_{12}H_{20}O_3$ (212.3): calcd. C 67.89, H 9.49; found C 67.67, H 9.24. Total reaction yield was 89%.

Ethyl (1′*S*,2′*S*,4′*S*)-(−)-3-Methyl-3-(1′,2′-epoxy-4′-methylcyclohex-1′-yl)butanoate (12b) and (5*S*,6*R*,8*S*)-(−)-6-Hydroxy-4,4,8-trimethyl-1-oxaspiro[4.5]decan-2-one (14b): According to the procedure described for the preparation of (1′*R*,2′*R*,4′*R*)-(+)-**12a** and (5*R*,6*S*,8*R*)-(+)-**14a**, the unsaturated ester (4′*S*)-(−)-**11b** (1.73 g, 7.71 mmol) yielded the epoxy ester (1′*S*,2′*S*,4′*S*)-(−)-**12b** (0.89 g, according to the GC analysis 82% purity): $[\alpha]_D^{26} = -48.3$ (c = 3.24, acetone) and the pure hydroxy lactone (5*S*,6*R*,8*S*)-(−)-**14b** (0.79 g): $[\alpha]_D^{26} = -21.9$ (c = 3.19, acetone). Their IR and NMR spectra were identical with those of (1′*R*,2′*R*,4′*R*)-(+)-**12a** and (5*R*,6*S*,8*R*)-(+)-**14a**. Total reaction yield was 87% (according to the GC analysis 45% of **12b** and 55% of **14b**).

(5*S*,6*R*,8*R*)-6-Hydroxy-4,4,8-trimethyl-1-oxaspiro[4.5]decan-2-one (15a) and (5*R*,6*S*,8*R*)-(+)-6-Hydroxy-4,4,8-trimethyl-1-oxaspiro[4.5]-decan-2-one (14a): Perchloric acid (60%, 0.5 mL) was added to a solution of the epoxy ester (1′*S*,2′*R*,4′*R*)-(+)-**12a** (0.46 g, according to the GC analysis 86% purity, 1.65 mmol) in THF (24 mL) and water (12 mL). The mixture was stirred for 24 h at room temperature and the products were extracted with diethyl ether. The combined ethereal extracts were washed with saturated $NaHCO_3$ solution and brine, dried over anhydrous $MgSO_4$ and the solvents evaporated in vacuo. The crude mixture of the hydroxy lactones (5*S*,6*R*,8*R*)-**15a** and (5*R*,6*S*,8*R*)-(+)-**14a** (according to the GC analysis 72:28) was chromatographed on silica gel. Elution with various solvent systems (hexane/acetone, 5:1 or hexane/ethyl acetate, 3:1) gave the pure mixture of the hydroxy lactones (5*S*,6*R*,8*R*)-**15a** and (5*R*,6*S*,8*R*)-(+)-**14a** (0.33 g, 94% total reaction yield). Spectral data for the hydroxy lactone (5*S*,6*R*,8*R*)-**15a**. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.97 (d, J = 6.4 Hz, 3 H, CH_3-8), 1.09 and 1.29 [two s, 6 H, $(CH_3)_2C<$], 2.36 and 2.61 (AB system, J = 17.1 Hz, 2 H, CH_2-3), 3.95 (m, 1 H, H-6). IR (film): $\tilde{\nu}$ = 3488 cm^{-1} (m, br., OH), 1768 (s, C=O), 1256 (s, C−O−C), 1164 (s, C−OH), 1052 (s, C−O−C).

(5*R*,6*S*,8*S*)-6-Hydroxy-4,4,8-trimethyl-1-oxaspiro[4.5]decan-2-one (15b) and (5*S*,6*R*,8*S*)-(−)-6-Hydroxy-4,4,8-trimethyl-1-oxaspiro-[4.5]decan-2-one (14b): In the same manner as described for the preparation of (5*S*,6*R*,8*R*)-**15a** and (5*R*,6*S*,8*R*)-(+)-**14a**, the epoxy ester (1′*S*, 2′*S*, 4′*S*)-(−)-**12b** (0.39 g, according to the GC analysis 82% purity, 1.33 mmol) yielded the mixture of hydroxy lactones (5*R*,6*S*,8*S*)-**15b** and (5*S*,6*R*,8*S*)-(−)-**14b** (according to the GC analysis 72:28, 0.26 g, 93% total reaction yield). Spectral data for the hydroxy lactone (5*R*,6*S*,8*S*)-**15b** were identical with those of (5*S*,6*R*,8*R*)-**15a**.

(1′*R*,2′*S*,4′*R*)-(+)-3-Methyl-3-(1′,2′-dihydroxy-4′-methylcyclohex-1′-yl)butan-1-ol (18a) and (5*R*,6*S*,8*R*)-(+)-4,4,8-Trimethyl-1-oxaspiro[4.5]decane-2,6-diol (19a): A solution of the hydroxy lactone (5*R*,6*S*,8*R*)-(+)-**14a** (0.31 g, 1.46 mmol) in anhydrous Et_2O (20 mL) was added dropwise to a solution of $LiAlH_4$ (0.055 g, 1.46 mmol) in Et_2O (20 mL). The reaction mixture was stirred for 1 h at room temperature and then poured into saturated potassium hydrogen tartrate solution. The separated ethereal solution was washed with brine, dried over $MgSO_4$ and the solvents evaporated in vacuo. The crude mixture of (1′*R*,2′*S*,4′*R*)-(+)-**18a** and (5*R*,6*S*,8*R*)-(+)-**19a** (according to the GC analysis 80:20) was chromatographed on silica gel. The first fraction, eluted with hexane/acetone (5:1), gave the pure lactol (5*R*,6*S*,8*R*)-(+)-**19a** (0.069 g) as a white solid. $[\alpha]_D^{26} = +12.7$ (c = 1.11, acetone), m.p. 114−115 °C. ^{1}H NMR (300 MHz, [D$_6$]acetone, 0 °C): δ = 0.79 (d, J = 6.6 Hz, 3 H, CH_3-8), 0.84 and 1.06 [two s, 6 H, $(CH_3)_2C<$], 1.21−1.91 (m, 10 H, H-8, four CH_2-groups and OH-6), 3.67 (m, 1 H, H-6), 4.97 (m, 1 H, H-2), 5.37 (d, J = 6.5 Hz, 1 H, OH-2). IR (nujol): $\tilde{\nu}$ = 3260 cm^{-1} (m, br., OH), 1468 and 1380 [s, $(CH_3)_2C<$], 1072 (s, C−OH) and 1032 (s, C−O−C). $C_{12}H_{22}O_3$ (214.3): calcd. C 67.26, H 10.35; found C 67.16, H 10.34. The second fraction, eluted with hexane/acetone (5:1), gave the crystalline triol (1′*R*,2′*S*,4′*R*)-(+)-**18a** (0.24 g). $[\alpha]_D^{27} = +21.9$ (c = 1.65, acetone), m.p. 127−128 °C. ^{1}H NMR (300 MHz, [D$_6$]acetone, 0 °C): δ = 0.80 (d, J = 6.3 Hz, 3 H, CH_3-4′), 0.96 and 1.05 [two s, 6 H, $(CH_3)_2C<$], 1.22−1.83 (m, 9 H, H-4′, four CH_2-groups), 3.51 (d, J = 4.4 Hz, 1 H, OH-2′), 3.63 (m, 2 H, CH_2-1), 3.84 (s, 1 H, OH-1′), 3.95 (m, 1 H, OH-1), 4.13 (m, 1 H, H-2′). IR (nujol): $\tilde{\nu}$ = 3256 cm^{-1} (s, br., OH), 1468 and 1392 [s, $(CH_3)_2C<$], 1264 and 1080 (s, CH−OH), 1172 (s, C−OH), 1036 (s, CH_2−OH). $C_{12}H_{24}O_3$ (216.3): calcd. C 66.63, H 11.18; found C 66.51, H 11.27. Total reaction yield was 97%.

Crystal Data for (1′*R*,2′*S*,4′*R*)-(+)-18a: $C_{12}H_{24}O_3$, M = 216.31, colourless needle, crystal dimensions 0.30 × 0.25 × 0.20 mm, monoclinic, space group $P2_1$, a = 6.9809(11), b = 10.6061(14), c = 17.174(2) Å, β = 99.331(13)°, V = 1254.7(3) Å^3, Z = 4, D_c = 1.145 Mg·m^{-3}, T = 100 K, R = 0.0844, Rw = 0.1247 (5631 reflections, all data) for 463 variables.

(5*S*,6*R*,8*R*)-6-Hydroxy-4,4,8-trimethyl-1-oxaspiro[4.5]decan-2-one (15a) and (5*R*,6*S*,8*R*)-(+)-6-Hydroxy-4,4,8-trimethyl-1-oxaspiro[4.5]-decan-2-one (14a): Perchloric acid (60%, 0.75 mL) was added to the crude mixture of the epoxy ester (1′*S*,2′*R*,4′*R*)-(+)-**12a** and the

 © 2004 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

hydroxy lactone (5*R*,6*S*,8*R*)-(+)-**14a** (1.72 g, according to the GC analysis 45:55) in THF (36 mL) and water (18 mL). The reaction mixture was stirred for 24 h at room temperature and the products were extracted with diethyl ether. The combined ethereal extracts were washed with saturated $NaHCO_3$ solution and brine, dried ($MgSO_4$) and the solvents evaporated in vacuo. The crude mixture of products (5*S*,6*R*,8*R*)-**15a** and (5*R*,6*S*,8*R*)-(+)-**14a** (according to the GC analysis 20:80) was chromatographed on silica gel with hexane/acetone (5:1) to afford the pure mixture of the hydroxy lactones (5*S*,6*R*,8*R*)-**15a** and (5*R*,6*S*,8*R*)-(+)-**14a** (1.57 g, 96% yield).

(5*R*,6*S*,8*S*)-6-Hydroxy-4,4,8-trimethyl-1-oxaspiro[4.5]decan-2-one (15b) and (5*S*,6*R*,8*S*)-(−)-6-Hydroxy-4,4,8-trimethyl-1-oxaspiro-[4.5]decan-2-one (14b): according to the procedure described for the preparation of (5*S*,6*R*,8*R*)-**15a** and (5*R*,6*S*,8*R*)-(+)-**14a**, the crude mixture of the epoxy ester (1′*R*,2′*S*,4′*S*)-(−)-**12b** and the hydroxy lactone (5*S*,6*R*,8*S*)-(−)-**14b** (1.80 g, according to the GC analysis 45%:55%) yielded the mixture of the hydroxy lactones (5*R*,6*S*,8*S*)-**15b** and (5*S*,6*R*,8*S*)-(−)-**14b** (according to the GC analysis 20:80, 1.60 g, 94% yield). Their IR and NMR spectra were identical with those of (5*S*,6*R*,8*R*)-**15a** and (5*R*,6*S*,8*R*)-(+)-**14a**.

(5*S*,8*R*)-(+)-4,4,8-Trimethyl-1-oxaspiro[4.5]decane-2,6-dione (20a) and (5*R*,8*R*)-(−)-4,4,8-Trimethyl-1-oxaspiro[4.5]decane-2,6-dione (21a): A mixture of the hydroxy lactones (5*S*,6*R*,8*R*)-**15a** and (5*R*,6*S*,8*R*)-(+)-**14a** (according to the GC analysis 20:80, 1.57 g, 7.40 mmol) was added in one portion to a suspension of pyridinium dichromate (3.97 g, 10.55 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred for 24 h at room temperature. The solvent was then distilled off and the residue was extracted with hexane. The hexane solution was filtered through Florisil and the solvents evaporated in vacuo. The crude mixture of (5*S*,8*R*)-(+)-**20a** and (5*R*,8*R*)-(−)-**21a** (according to the GC analysis 20:80) was chromatographed on silica gel. The first fraction, eluted with hexane/acetone (5:1), gave the crystalline keto lactone (5*R*,8*R*)-(−)-**21a** (1.15 g): $[\alpha]_D^{25}$ = −104.9 (*c* = 2.08, acetone). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.02 (d, *J* = 6.2 Hz, 3 H, CH_3-8), 1.15 and 1.20 [two s, 6 H, $(CH_3)_2C<$], 1.36 (m, 1 H, one of CH_2-group), 1.82−2.11 (m, 4 H, H-8 and CH_2-groups) 2.23 and 2.48 (AB system, *J* = 17.1 Hz, 2 H, CH_2-3), 2.36 (ddd, *J* = 14.6, 4.0, 3.2 Hz, 1 H, one of the CH_2-7 group), 2.67 (ddd, *J* = 14.6, 3.8, 2.4 Hz, 1 H, one of the CH_2-7 group). IR (nujol): $\tilde{\nu}$ = 1792 cm^{-1} (s, 2-C=O), 1720 (s, 6-C=O), 1472 and 1424 [s, $(CH_3)_2C<$], 1260 and 1236 (s, C−O−C). $C_{12}H_{18}O_3$ (210.3): calcd. C 68.54, H 8.63; found C 68.39, H 8.58. The second fraction, eluted with hexane/acetone (5:1), gave the crystalline keto lactone (5*S*,8*R*)-(+)-**20a** (0.29 g). $[\alpha]_D^{25}$ = +163.0 (*c* = 2.75, acetone), m.p. 45−46 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.00 (d, *J* = 6.7 Hz, 3 H, CH_3-8), 1.13 and 1.20 [two s, 6 H, $(CH_3)_2C<$], 1.48−2.14 (m, 5 H, CH_2-9, CH_2-10 and H-8), 2.31 and 2.55 (AB system, *J* = 17.0 Hz, 2 H, CH_2-3), 2.40 (ddd, *J* = 13.5, 5.9, 0.9 Hz, H_e-7), 2.48 (dd, *J* = 13.5, 8.6 Hz, 1 H, H_a-7). IR (nujol): $\tilde{\nu}$ = 1788 (s, 2-C=O), 1724 (s, 6-C=O), 1456 and 1428 [s, $(CH_3)_2C<$], 1268 and 1238 (s, C−O−C). $C_{12}H_{18}O_3$ (210.3): calcd. C 68.54, H 8.63; found C 68.41, H 8.68. Total reaction yield was 92%.

Crystal Data for (5*S*,8*R*)-(+)-20a: $C_{12}H_{18}O_3$, *M* = 210.26, colourless block, crystal dimensions 0.30 × 0.30 × 0.30, orthorhombic, space group $P2_12_12_1$, *a* = 7.4689(4), *b* = 14.5042(9), *c* = 21.0854(11) Å, *V* = 2284.2(2) Å^3, *Z* = 8, D_c = 1.223 Mg·m^{-3}, *T* = 100 K, *R* = 0.0376, *Rw* = 0.0806 (5318 reflections, all data) for 415 variables.

(5*R*,8*S*)-(−)-4,4,8-Trimethyl-1-oxaspiro[4.5]decane-2,6-dione (20b) and (5*S*,8*S*)-(+)-4,4,8-trimethyl-1-oxaspiro[4.5]decane-2,6-dione (21b): In the same manner as described for the preparation of (5*S*,8*R*)-(+)-**20a** and (5*R*,8*R*)-(−)-**21a**, the mixture of hydroxy lactones (5*R*, 6*S*, 8*S*)-**15b** and (5*S*,6*R*,8*S*)-(−)-**14b** (1.67 g, 7.87 mmol, according to the GC analysis 20%:80%) yielded the crystalline keto lactones (5*S*,8*S*)-(+)-**21b** (1.23 g). $[\alpha]_D^{25}$ = +105.0 (*c* = 2.98, acetone), m.p. 44−45 °C and (5*R*,8*S*)-(−)-**20b** (0.31 g). $[\alpha]_D^{25}$ = −162.8 (*c* = 3.18, acetone). Their IR and NMR spectra were identical with those of (5*S*,8*R*)-(+)-**20a** and (5*R*,8*R*)-(−)-**21a**. Total reaction yield was 93% (according to the GC analysis 20% of **20b** and 80% of **21b**).

Crystal Data for (5*S*,8*S*)-(+)-21b: $C_{12}H_{18}O_3$, *M* = 210.26, colourless block, crystal dimensions 0.25 × 0.25 × 0.20, monoclinic, space group $P2_1$, *a* = 8.7763(5), *b* = 12.2135(7), *c* = 11.3811(8) Å, β = 112.548(6)°, *V* = 1126.68(12) Å^3, *Z* = 4, D_c = 1.240 Mg·m^{-3}, *T* = 100 K, *R* = 0.0537, *Rw* = 0.0804 (4805 reflections, all data) for 415 variables.

CCDC-226233 (for **18a**), -226235 (for **20a**), -226234 (for **21b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk].

Acknowledgments

This work was supported by the State Committee for Scientific Research (KBN), Grant No. PBZ-KBN-060/T09/2001.

[1] [1a] Y. Asakawa, *Phytochem.* **2001**, *56*, 297−312. [1b] J. R. Hanson, *Nat. Prod. Rep.* **2002**, *19*, 125−132. [1c] H. M. C. Ferraz, L. S. Longo Jr., M. V. A. Grazini, *Synthesis* **2002**, *15*, 2155−2164. [1d] B. M. Fraga, *Nat. Prod. Rep.* **2002**, *19*, 650−672.

[2] [2a] T. J. Simpson, S. A. Ahmed, C. R. McIntyre, F. E. Scott, I. H. Sadler, *Tetrahedron* **1997**, *53*, 4013−4034. [2b] C. Bonini, L. Chiummiento, A. Evidente, M. Funicello, *Tetrahedron Lett.* **1995**, *36*, 7285−7286. [2c] R. Cordova, B. B. Snider, *Tetrahedron Lett.* **1984**, *25*, 2945−2948.

[3] [3a] M. A. Birkett, J. A. Pickett, *Phytochem.* **2003**, *62*, 651−656. [3b] A. J. Hick, M. C. Luszniak, J. A. Pickett, *Nat. Prod. Rep.* **1999**, *16*, 39−54. [3c] K. C. Park, D. Elias, B. Donato, J. Hardie, *Journal of Insect Physiology* **2000**, *46*, 597−604. [3d] B. B. Lohray, S. Venkateswarlu, *Tetrahedron: Asymmetry* **1997**, *8*, 633−638.

[4] [4a] H. Skaltsa, D. Lazari, C. Panagouleas, E. Georgiadou, B. Garcia, M. Sokovic, *Phytochem.* **2000**, *55*, 903−908. [4b] S. D. Lorimer, S. D. Mawson, N. B. Perry, R. T. Weavers, *Tetrahedron* **1995**, *51*, 7287−7300. [4c] H. Tabuchi, A. Ichtihara, *Tetrahedron Lett.* **1992**, *33*, 4933−4936.

[5] [5a] C. L. Cantrell, S. G. Franzblau, N. H. Fischer, *Planta Med.* **2001**, *67*, 685−694. [5b] N. H. Fischer, T. Lu, L. C. Cantrell, J. Castaneda-Acosta, L. Quijano, S. G. Franzblau, *Phytochem.* **1998**, *49*, 559−564.

[6] [6a] A. F. Barrero, J. E. Oltra, M. Álvarez, *Tetrahedron Lett.* **2000**, *41*, 7639−7643. [6b] S. P. Chavan, M. S. Venkatraman, *Tetrahedron Lett.* **1998**, *39*, 6745−6748. [6c] S. De Rosa, R. Puliti, A. Crispino, A. De Giulio, C. De Sena, C. Iodice, C. A. Mattia, *Tetrahedron* **1995**, *51*, 10731−10736. [6d] M. Sanière, I. Charvet, Y. Le Merrer, J.-C. Depezay, *Tetrahedron* **1995**, *51*, 1653−1662.

[7] [7a] Y. Asakawa, G. D. Dawson, D. C. Griffiths, J.-Y. Lallemand, S. V. Ley, K. Mori, A. Mudd, M. Pezechk-Leclaire, J. A. Pickett, H. Watanabe, C. M. Woodcock, Z. Zhong-Ning, *J.*

 © 2004 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Chem. Ecol. **1988**, *14*, 1845−1855. [7b] M. Streibl, J. Nawrot, V. Herout, *Biochem. Syst. Ecol.* **1983**, *11*, 381−382. [7c] J. Harmatha, J. Nawrot, *Biochem. Syst. Ecol.* **1984**, *12*, 95−98. [7d] W. M. Daniewski, M. Gumulka, E. Pankowska, K. Ptaszynska, E. Bloszyk, U. Jacobsson, T. Norin, *Phytochem.* **1993**, *32*, 1499−1502. [7e] W. M. Daniewski, M. Gumulka, D. Przesmycka, K. Ptaszynska, E. Bloszyk, B. Drozdz, *Phytochem.* **1995**, *38*, 1161−1168.

[8] T. Olejniczak, J. Nawrot, Z. Ciunik, C. Wawrzenczyk, *Polish J. Chem.* **2000**, *74*, 673−680.

[9] [9a] E. Paruch, Z. Ciunik, C. Wawrzenczyk, *Eur. J. Org. Chem.* **1998**, 2677−2682. [9b] E. Paruch, Z. Ciunik, J. Nawrot, C. Wawrzenczyk, *J. Agric. Food Chem.* **2000**, *48*, 4973−4977.

[10] E. Paruch, Z. Ciunik, C. Wawrzenczyk, *Liebigs Ann./Recueil* **1997**, 2341−2345.

[11] [11a] T. Olejniczak, M. Grabarczyk, J. Nawrot, C. Wawrzenczyk, *Biotechnologia* **2000**, *3*, 106−117. [11b] C. Wawrzenczyk, M. Grabarczyk, A. Szumny, B. Gabrys, K. Dancewicz, J. Nawrot, A. Pradzynska, A. Halarewicz-Pacan, *Chemistry for Agriculture* **2003**, *4*, 117−129.

[12] E. Paruch, J. Nawrot, C. Wawrzenczyk, *Pest Manag. Sci.* **2001**, *57*, 776−780.

[13] A. Halarewicz-Pacan, B. Gabrys, K. Dancewicz, C. Wawrzenczyk, *Journal of Plant Protection Research* **2003**, *43*, 133−142.

[14] [14a] G. Beck, *Synlett* **2002**, *6*, 837−850. [14b] E. Brenna, C. Fuganti, S. Serra, *Tetrahedron: Asymmetry* **2003**, *14*, 1−42. [14c] A. Mosandl, C. Günther, *J. Agric. Food Chem.* **1989**, *37*, 413−418.

[15] J.-L. Luche, L. Rodriguez-Hahn, P. Crabbé, *J. S. C. Chem. Commun.* **1978**, 601−602.

[16] A. L. Gemal, J.-L. Luche, *J. Am. Chem. Soc.* **1981**, *103*, 5454−5459.

[17] [17a] E. H. Eschinasi, *J. Org. Chem.* **1970**, *35*, 1598−1600. [17b] G. B. Fischer, J. C. Fuller, J. Harrison, S. G. Alvarez, E. R. Burkhardt, C. T. Goralski, B. Singaram, *J. Org. Chem.* **1994**, *59*, 6378−6385.

[18] W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T. Li, D. J. Faulkner, M. R. Petersen, *J. Am. Chem. Soc.* **1970**, *92*, 741.

[19] P. Weyerstahl, H. Marschall-Weyerstahl, J. Penninger, L. Walther, *Tetrahedron* **1987**, *22*, 5287−5298.

[20] H. Kuczynski, K. Piatkowski, *Pol. J. Chem.* **1959**, *33*, 299−310.

[21] E. J. Corey, G. Schmidt, *Tetrahedron Lett.* **1979**, *5*, 399−402.

[22] M. Szczepanik, M. Grabarczyk, A. Szumny, C. Wawrzenczyk, *Journal of Plant Protection Research* **2003**, *43*, 87−96.

Received December 20, 2004

 © 2004 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim