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The role of germacrene D as a precursor in sesquiterpene biosynthesis: investigations of acid catalyzed, photochemically and thermally induced rearrangements

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Abstract

Germacrene D is considered as a precursor of many sesquiterpene hydrocarbons. We have investigated the acid catalyzed as well as the photochemically and thermally induced rearrangement processes of germacrene D isolated from several *Solidago* species, which contain both enantiomers of germacrene D. Enantiomeric mixtures of sesquiterpenes of the cadinane, eudesmane (selinane), oppositane, axane, isodaucane, and bourbonane group as well as isogermacrene D were identified as main products and made available as reference compounds for structure investigations and stereochemical assignments of plant constituents. δ-Amorphene, one of the rearrangement products, was identified as a natural product for the first time. The absolute configuration of γ-amorphene was revised by correlation with the absolute configuration of germacrene D. The mechanisms of the rearrangement reactions are discussed.

Keywords: Carbocations; Germacrene D; Isogermacrene D; Photochemistry; Rearrangement; Sesquiterpenes; *Solidago* spec.; Thermochemistry

1. Introduction

To date more than 200 different sesquiterpene skeletons are known, which are predominantly formed from farnesyl diphosphate (FDP) as a common acyclic precursor by enzymatic cyclizations and further transformations (Cane, 1990). Using this concept, it was attempted to derive a biogenetic relationship between certain natural sesquiterpene structures on the basis of skeletal rearrangements (Andersen and Syrdal, 1970; Andersen et al., 1978). More recently, feeding experiments with isotopically labeled FDP or mevalonate or incubations of these labeled precursors with isolated sesquiterpene cyclases have become a powerful tool in biogenetic studies (Arigoni, 1975; Cane et al., 1993). However, not all of the correlations discussed in the earlier literature are experimentally proven, and many structures were only tentatively assigned.

The importance of germacrene D (**1**) as a biogenetic precursor of many other sesquiterpene structures was already recognized at its first description in the literature and some acid catalyzed and photochemically induced rearrangements have been reported (Yoshihara et al., 1969). In the past all rearrangement products obtained from germacrene D were eventually also found as natural products. The elucidation of yet unknown rearrangement products should facilitate the discovery of new natural products.

In this work we have attempted to identify the whole band-width of rearrangement products of germacrene D by utilizing modern two-dimensional NMR techniques and enantioselective gas chromatography as an efficient tool for stereochemical assignments.

2. Results and discussion

2.1. Biogenesis of sesquiterpenes involving germacrenyl cations

According to currently accepted hypotheses, in addition to FDP nerolidyl diphosphate (NDP) may be a

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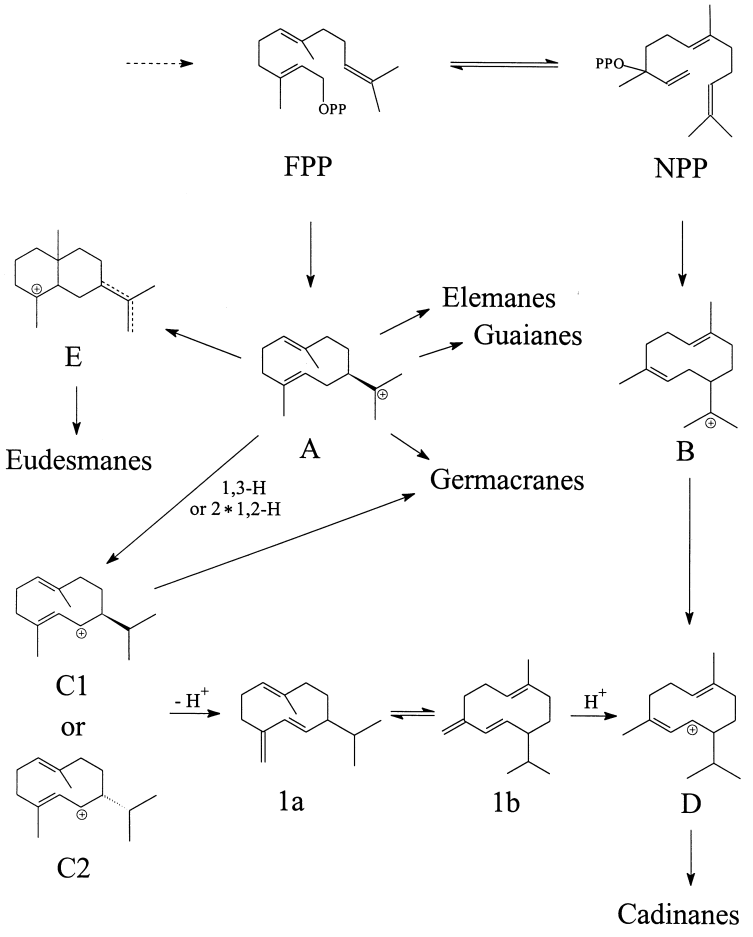
precursor in the enzymatically catalyzed formation of sesquiterpenes in order to allow adequate alignment of π-orbitals for the formation of products with *cis* double bonds (Cane, 1985). It can be assumed that in the cyclisation process after loss of the diphosphate residue the germacrenyl cations **A** and **B** and, after hydride migration, the cations **C** and **D** are formed (Scheme 1). Cation **A** is considered as precursor for the elemanes, guaianes and germacranes. After conversion to cation **E** the eudesmanes (selinanes) may be formed. This suggests that germacrene type sesquiterpenes are biogenetic intermediates for certain groups of sesquiterpenes. As an example (−)-germacrene A (**2**) is assumed as an intermediate in the biosynthesis of (+)-aristolochene (**3**) (Cane, 1990) and in the biosynthesis of bitter sesquiterpene lactones in chicory (de Kraker et al., 1998) (Fig. 2).

For the biosynthesis of cadinane type sesquiterpenes Arigoni suggested two alternatives (Arigoni, 1975). The primarily formed cation **A** may be deprotonated to germacrene D (**1**) after hydride migration to cation **C**. The subsequent conformational change from *cisoid* structure **1a** to *transoid* **1b** is crucial for the formation of cadinane type sesquiterpenes (with a *Z* double bond in the ring) following protonation and rearrangement to cation **D**. It should be mentioned that germacrene D very often occurs in plants together with δ-cadinene (**4**, Scheme 3) (Yoshihara and Hirose, 1978). Investigations of the (+)-δ-cadinene synthase from cotton (*Gossypium hirsutum*), however, did not reveal any germacrene D in the products. This does not exclude **1** as a biosynthetic intermediate, though, as it may be tightly bound to the enzyme as a primary cyclization product and immediately be further rearranged (Davis and Essenberg, 1995; Davis et al., 1996).

As alternative, NDP may serve as a substrate for cadinane type sesquiterpene biosynthesis. In this case the cyclization to the cadinanes would simply proceed via cations **B** and **D**. In fact, for the biosynthesis of the cadinane derivative (+)-1-*epi*-cubenol (**5**, Fig. 2) NDP could be identified as a precursor (Cane and Tandon, 1995).

A series of investigations related to acid catalyzed rearrangements of germacrene D derivatives has led to substituted cadinenes, selinenes, oppositenes and isodaucadienes (Niwa et al., 1976a,b, 1978, 1979; Yamamura et al., 1982; Itokawa et al., 1983; Shizuri et al., 1986) but little is known about the rearrangement to



Scheme 1. Supposed biogenesis of germacrene related sesquiterpenes.

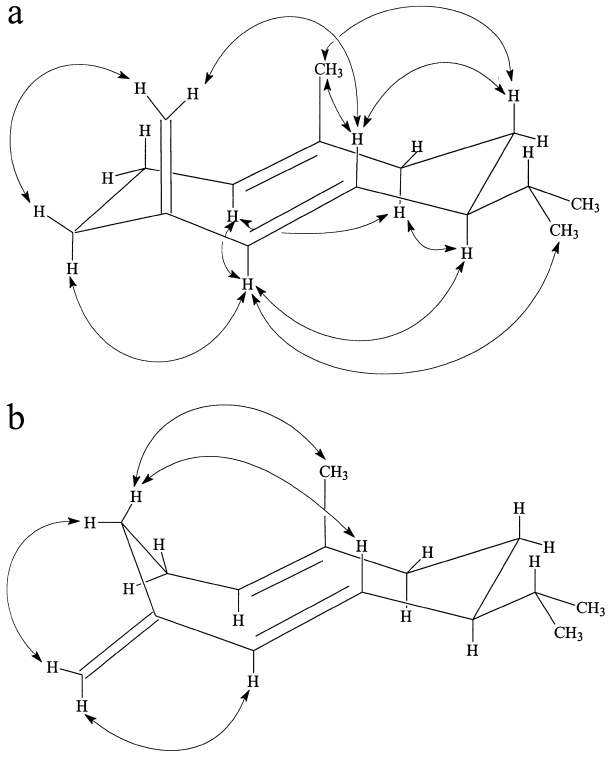


Fig. 1. ^{1}H, ^{1}H-NOESY interactions observed in germacrene D.

sesquiterpene hydrocarbons (Yoshihara et al., 1969; Nishimura et al., 1979; Itokawa et al., 1988). It is likely that new natural compounds will be discovered after identification of new rearrangement products of germacrene D. Moreover, with an enantiomeric mixture of **1** of a defined composition stereochemical and mechanistic aspects of rearrangement processes may be unravelled.

2.2. Occurrence and isolation of germacrene D enantiomers

Although a synthesis of germacrene D was reported (Schreiber and Hawley, 1985) it is more convenient to obtain **1** from natural sources. In most higher plants **1** is present as its (−)-enantiomer, while the (+)-enantiomer is more likely to occur in lower organisms (Beecham and Djerassi, 1978; Lorimer and Weavers, 1987; König et al., 1996). For the higher plants *Solidago altissima* L. (Niwa et al., 1980), *Torilis japonica* D. C. (Itokawa et al., 1983) and *Araucaria bidwillii* (Pietsch and König, 2000) the occurrence of both enantiomers has been described, although we found that 1 is only a minor component in *T. japonica*. To obtain sufficient amounts of both enantiomers of **1** we analysed the "goldenrod" *Solidago canadensis* L. and *S. gigantea* Ait., both very common in central Europe, by enantioselective gas chromatography (König et al., 1996). It turned out that **1** is the main constituent of the sesquiterpene fraction in both plants. Both enantiomers are present in widely varying proportions in dependence on the collection site. In a few cases only one enantiomer was detected. The enantiomeric composition of **1** also varies with the part of the plant. A series of investigations of a plant from the same location during the entire flowering season (July–September) showed that the enantiomeric composition remained constant in different parts of the plant over the whole season and over three years. The investigation of some other *Solidago* species from Europe and the United States gave similar results with respect to the enantiomeric composition of **1** (Bülow and König, 1996; Bülow, 1999). We, therefore, assume that the occurrence of both enantiomers of **1** is common to *Solidago* species.

The biosynthetic pathway of **1** was recently elucidated by incubation of isolated enzymes (Schmidt et al., 1998) with isotopically labeled FDP and mass spectrometric analysis of the products (Schmidt et al., 1999) and proceeds in different steps for both enantiomers as already suspected by Niwa et al. (1980) and as shown in Scheme 1.

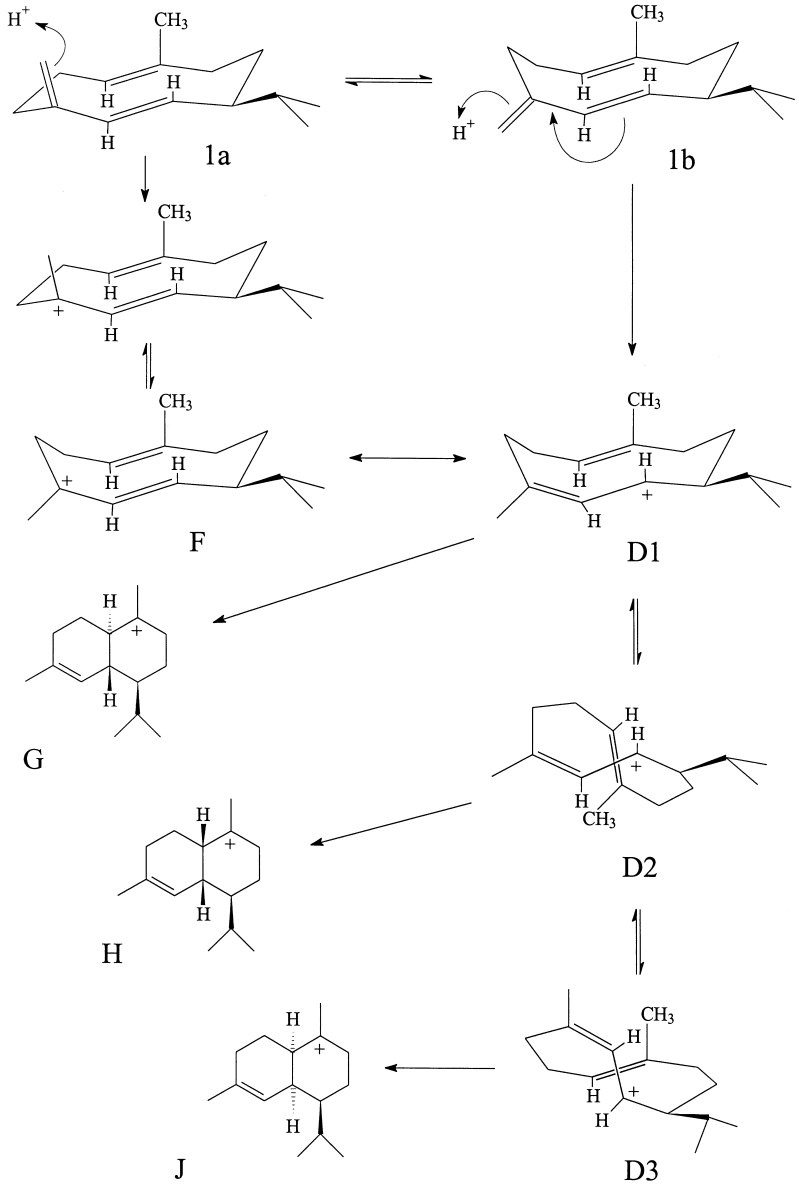
For the following rearrangement reactions germacrene D was isolated from the essential oil of *Solidago* species either by preparative gas chromatography or by silica gel chromatography at low temperature. In cases with over 90% germacrene D in the original oil no further purification was carried out.

2.3. Acid catalyzed rearrangement reactions

Germacrene D completely rearranges to different sesquiterpene hydrocarbons merely by contact with weakly acidic media like silica gel over a period of several days (Yoshihara et al., 1969). Under these conditions cadinane type products are formed almost exclusively. A similar spectrum of compounds was formed under the influence of carboxylic acids, but the yield is lower due to ester formation (Nishimura et al., 1979). A greater variety of products is formed with *p*-toluene sulphonic acid or acidic ion exchange resin. Complete rearrangement can be achieved in only minutes with strong Lewis acids with predominant formation of thermodynamically more stable products (Table 1). The product mixtures obtained in these reactions were preseparated by silica gel chromatography, isolated by preparative gas chromatography and identified by comparison with authentic samples (GC–MS) and/or with published data (NMR).

2.3.1. Cadinane type sesquiterpenes

As main products of acid catalyzed rearrangements cadinenes, muurolenes and amorphenes, which are common in nature, are formed with the cadinenes in predominance, which can be explained by reaction pathways via the cations **G**, **H** and **J** (Scheme 2). According to MM2 molecular mechanics calculations 99% of **1** are

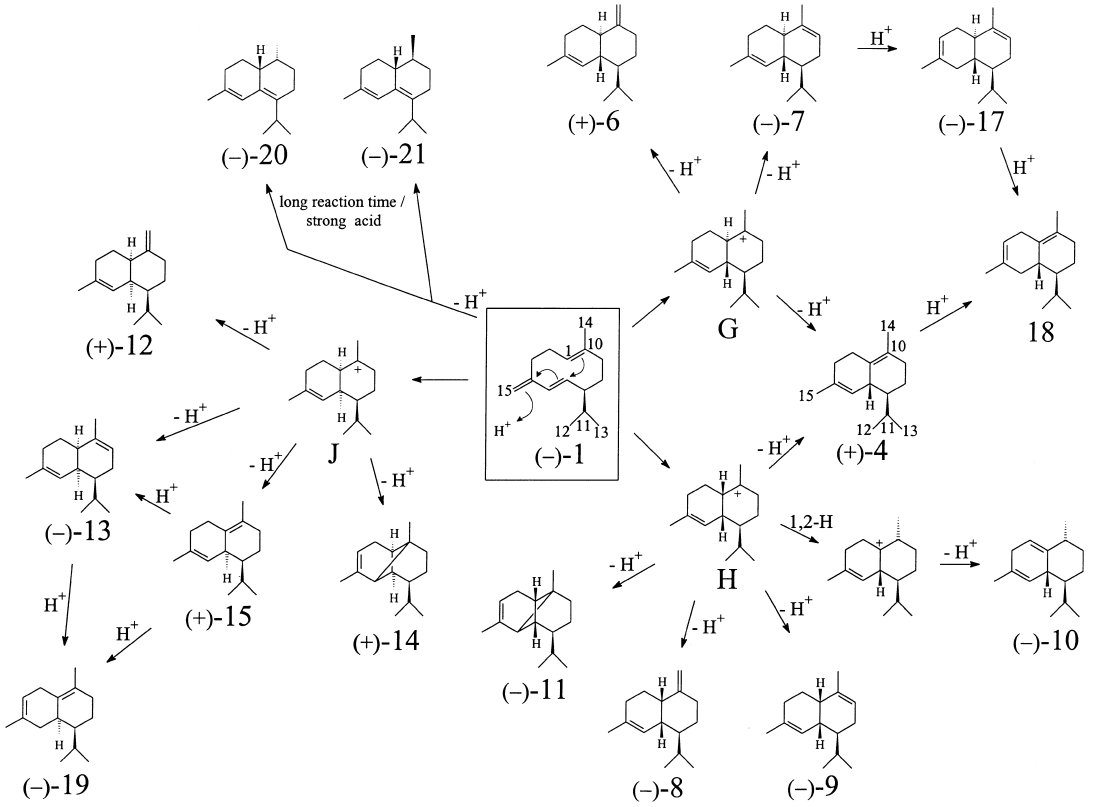


Scheme 2. Protonation of germacrene D resulting in cadinenyl (**G**), muurolenyl (**H**), and amorphenyl (**J**) cations.

present in two preferred conformations **1a** and **1b** in a 82:17 ratio (Shizuri et al., 1986). This result is qualitatively confirmed by ^{1}H-NOESY investigations (Fig. 1). Thus, it can be assumed that in the rearrangement processes at room temperature **1** is attacked by an electrophile in one of the two conformations. Cation **D1** cyclizes to the cadinenyl cation **G**, a step, which could proceed from **1b** in a concerted fashion. In contrast, a conformational change to **D2** or **D3** is necessary for the formation of muurolenyl and amorphenyl cations **H** and **J** (Scheme 2). As a consequence of this thermodynamically unfavourable process to the *cis*-decalin systems, the muurolenes and amorphenes are formed in smaller quantities.

The primary rearrangement products γ-cadinene (**6**) (Andersen and Syrdal, 1970), α-cadinene (**7**) (Naya and Kotake, 1969), δ-cadinene (**4**) (Wenkert et al., 1992), γ-muurolene (**8**) (Beecham and Djerassi, 1978), α-muurolene (**9**) (Beecham and Djerassi, 1978), cadina-1,4-diene (cubenene, **10**) (Connolly et al., 1982), α-copaene (**11**) (Wenkert et al., 1992), γ-amorphene (**12**) (Motl et al., 1966), α-amorphene (**13**) (Gregson and Mirrington, 1976) and α-ylangene (**14**) (Melching et al., 1997) could be identified (Scheme 3). δ-Amorphene (**15**) could not be isolated in a pure state from the product mixture. It was identified by comparison (GC–MS) with **15** prepared by acid catalyzed rearrangement from β-ylangene (**16**, Schemes 11 and 12) (Melching et al., 1997).

With increasing reaction time in the product mixture secondary rearrangement products are formed, which can not be directly related to germacrene D. By isomerization of isolated pure compounds it could be proven



Scheme 3. Sesquiterpenes with cadinane skeleton obtained from germacrene D.

that α-cadinene (**7**) rearranges mainly to β-cadinene (**17**) (Fringuelli et al., 1985), while the latter is isomerized to the thermodynamically more stable ω-cadinene (**18**) (Vlahov et al., 1967; Connell et al., 1968; Nagasampagi et al., 1968). The latter is also formed from δ-cadinene (**4**) in a ratio of 1.4:1. Furthermore, ω-amorphene (**19**) is obtained from **13** and from **15**. The structure assignment of **19** was proven by identical hydrogenation products formed from **15** and **19** and further supported by the finding that the mass spectra of **18** and **19** are identical as are the mass spectra of **4** and **15** (Melching et al., 1997).

The preference of a 2,3-double bond versus a 1,2-double bond in *trans*-decalins has been known before and is associated with the ring strain, which increases when another ring is attached at the α-position of a cyclohexene (Taylor, 1954; Corey and Sneen, 1955; Turner et al., 1957). In a cyclohexene system the substituents at the α-carbon atoms of the double bond are in pseudo-axial and -equatorial orientation. By annelation of another ring to the system, the former pseudo-equatorial substituent is forced into a less favorable position increasing the ring strain (Turner et al., 1957). By the thermodynamically favoured isomerization of an 1,2- to a 2,3-double bond, the second ring is shifted to the β-position resulting in a strain decrease (e.g. compare **7**→**17**).

Since germacrene D was always used in a defined enantiomeric ratio, it was also possible to investigate the products with respect to their enantiomeric composition. It turned out that in most cases the ratio of the enantiomers is retained as long as the stereogenic centres are not involved in the reaction. Minor deviations from the original enantiomeric composition can be explained by the fact that the rearrangements take place in a chiral environment, which may cause some diastereoselective induction.

Assuming the rearrangement mechanism for the formation of the cadinenes to proceed as described above, γ-amorphene (**12**) with the absolute configuration as shown in Scheme 3 is formed from (−)-**1**. This configuration was assigned to (−)-**12** in the original description (Motl et al., 1966). However, by comparison with (−)-**12**, which we obtained from an enantiomeric mixture by preparative GC using a chiral stationary phase (cyclodextrin derivative) and after measuring the optical rotation of the isolated material we could unambiguously prove, that the structure of **12** as depicted in Scheme 3 corresponds to the (+)-enantiomer.

If the rearrangement processes are catalyzed by strong Lewis acids the thermodynamically most stable compounds zonarene (**20**) (Melching et al., 1997) and epizonarene (**21**) (Mehta and Singh, 1977) are predominantly formed. They can either be formed

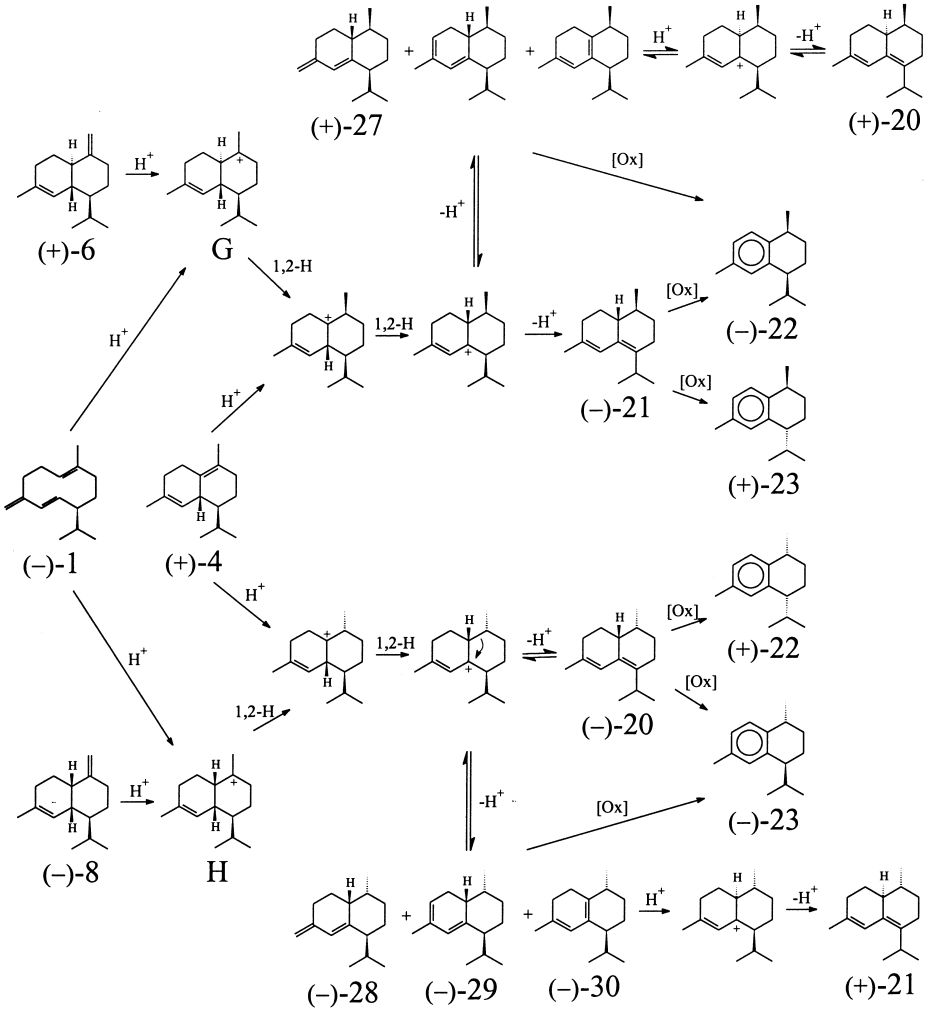
Table 1
Yield (%) of rearrangement products in dependence on the reaction conditions[g]

	SiO_2[a]	Acetic acid[b]	TsOH[c] or Amberlyst®15[d]	dto./longer BF_3[f] reaction time[e]	BF_3[f]	AlCl
δ-Cadinene (**4**)	30	28	13–19	16–23	26–30	0–3
γ-Cadinene (**6**)	14	7	9–17	0–10	9–13	–
α-Cadinene (**7**)	3.5	2	4–6	0–4	7–10	–
γ-Muurolene (**8**)	15	6	8–12	0.5–2	9–13	–
α-Muurolene (**9**)	9	7	3–5	7–8	4–7	–
Cadina-1,4-diene (**10**)	3	1.5	0–1.5	0–1.5	1.5–2.5	–
α-Copaene (**11**)	2.5	1	0.5–2.5	Trace	–	–
γ-Amorphene (**12**)	Trace	2.5	2–6	0–4	1–7	–
α-Amorphene (**13**)	Trace	8	2–6	0–4	5–6	–
α-Ylangene (**14**)	1	0.5	0–1.5	Trace	–	–
δ-Amorphene (**15**)	5.5	5.5	2–4	1–3	3–4	–
β-Cadinene (**17**)	Trace	–	0–0.5	3–8	0–0.5	–
ω-Cadinene (**18**)	Trace	–	Trace	5–12	–	–
ω-Amorphene (**19**)	–	–	–	1–3	–	–
Zonarene (**20**)	–	–	0.5–2	1–7	0–1	5–25
Epizonarene (**21**)	–	–	0.5–8	8–19	3–8	45–80
Calamenene (**22/23**)	–	–	Trace	2–6	Trace	3–15
α-Calacorene (**24**)	–	–	–	0.5–2.5	Trace	1–5
γ-Calacorene (**25**)	–	–	–	Trace	Trace	Trace
Cadalene (**26**)	–	–	–	Trace	–	1–4
cis-Muurola-4(15),5-diene (**27**)	–	–	–	–	Trace	0–2
Bicyclosesquiphellandrene (**28**)	–	–	–	–	–	Trace
Cadina-3,5-diene (**29**)	–	Trace	–	–	Trace	0–2
Cadina-1(6),4-diene (**30**)	–	–	–	–	–	0–1
4S,4aS-1,7-Dimethyl-4-(methylethyl)-2,3,4,4a,5,6-hexahydronaphthalene (**31**)	–	–	–	–	–	0–1
Daucalene (**32**)	–	–	–	–	–	1–4
Selina-4(15),6-diene (**43**)	–	Trace	2–3	0–1.5	0.5–2	–
Selina-4(15),7-diene (**44**)	Trace	Trace	1–6	0–3	0.5–2	–
Selina-4(15),5-diene (**45**)	–	0.5	0.5–2.5	0–1	Trace	–
Selina-3,5-diene (**46**)	4.0	1.0	2–6	0–3	1.5–5	–
δ-Selinene (**49**)	–	–	0–2	12–23	0.5–1	Trace
4(15)-Cycloopositene (**51**)	–	1.5	1–4	0–3	0–1.5	–
Opposita-4(15),7-diene (**52**)	–	0.5	4–11	1–6	1.5–5	–
Opposita-4(15),11-diene (**53**)	–	–	1.5–3	0–2	1–8	–
4(15)-Cycloaxene (**54**)	0.5	0.5	0–1	0–1	–	–
4-Cycloopositene (**57**)	–	–	–	Trace	Trace	–
3-Cycloaxene (**58**)	–	–	–	Trace	Trace	–
Isodauca-4,7(14)-diene (**60**)	–	–	0–0.5	–	1–3	–
Isodauca-4,6-diene (**61**)	1.5	–	0.5–4	0.5–4	0.5–1	–
Unidentified	7.5	26.5	10–18	15–30	5–15	5–10

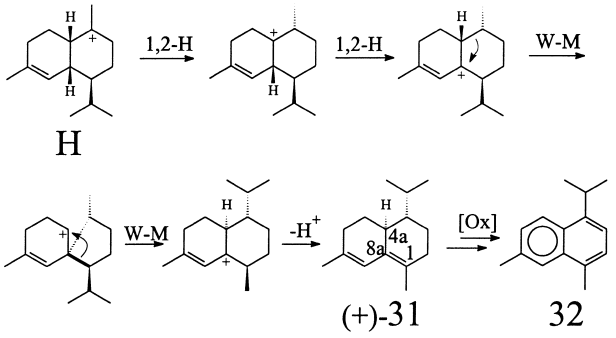
[a] 10 mg SiO_2 in 0.5 ml *n*-hexane, *c*(**1**) = 15 mmol/l, 2 days.
[b] *c*(**1**) in glacial acetic acid = 20 mmol/l, 24 h.
[c] 3–10 mg CH_3PhSO_3H in 5–15 ml CH_2Cl_2, *c*(**1**) = 15- 70 mmol/l, 3 h–4 days.
[d] 2–20 mg Amberlyst®15 in 0.5–1.5 ml *n*-hexane, *c*(**1**) = 15–220 mmol/l, 1–10 days.
[e] 3–7 days and 3–30 days, respectively.
[f] 50 ml BF_3 [60% in dimethyl ether] (24.2 g, 0.36 mol) in 180 ml diethyl ether, *c*(**1**) = 9 mmol/l, 0 °C, 12 min.
[g] 15 mg $AlCl_3$ in 0.5 ml CH_2Cl_2, *c*(1) = 15 mmol/l, 1 h (use of $ZnCl_2$ will give comparable results).

directly from germacrene D (**1**) or from other intermediate cadinenes (Schemes 4 and 5). For **20** and **21** varying enantiomeric proportions are found, which can be explained by the proposed mechanism of formation.

Scheme 4 presents the identified rearrangement products initiating from (−)-**1**, (+)-**4**, (+)-**6**, and (−)-**8**. Thus, from (+)-**6** enantiomerically pure (−)-**21** was formed as the main product (Osadchii et al., 1981), whereas (−)-**20** (Mehta and Singh, 1977; Polovinka et al., 1981) and (+)-**21** as well as the oxidation products *cis*-/*trans*-calamenene **22/23** (Croft et al., 1978; Melching et al., 1997), α-calacorene (**24**, Fig. 2) (Hardt, 1994), γ-calacorene (**25**, Fig. 2) (Adachi and Mori, 1983) and cadalene (**26**, Fig. 2) (Bohlmann and Zdero, 1976) are formed from (−)-**8**. The assumed mechanism of formation is supported by the occurrence of trace components



Scheme 4. Mechanism of formation of products obtained from germacrene D, cadinenes and muurolenes, respectively, with strong Lewis acids.



Scheme 5. Acid catalyzed rearrangement via the muurolenyl cation (**H**) to daucalene derivatives.

as *cis*-muurola-4(15),5-diene (**27**) (Kim et al. 1994), bicyclosesquiphellandrene (**28**) (Melching et al., 1997), cadina-3,5-diene (**29**) (Melching et al., 1997) and cadina-1(6),4-diene (**30**) (Melching et al., 1997). Finally, the rearrangement product **31** (Scheme 5) was identified by comparison with published ^{1}H-NMR data (Polovinka et al., 1981) and by oxidation to daucalene (**32**), which is also a known oxidation product of carotol (**33**, Fig. 2) (Sykora et al., 1961; de Broissia et al., 1972). We got **32** as a reference compound by sulfur induced dehydrogenation from daucene (**34**), a dehydration product of **33** (Hashidoko et al., 1992). **31** was formed by treatment of γ-muurolene (**8**) with super acids according to a mechanism proposed by Polovinka et al. (1981) (Scheme 5). In the reaction with $AlCl_3$ **31** is obtained as a major product from muurolenes or as a minor product from **1** while **32** is formed as a trace compound. An alcohol (**35**, Fig. 2) with this unusual skeleton was already described (Bohlmann and Zdero, 1976).

According to Osadchii et al. (1981) a 1,2-hydride shift is strongly favoured over a 1,3-hydride shift. Correspondingly, (+)-**21** is not formed via the germacrenyl cation **G** (Scheme 4). Alternatively, the formation of (+)-**21** is only possible over a deprotonation/protonation step starting from cation **H**. Andersen et al. (1973) obtained (+)-**21** with only 17% ee by acid treatment of

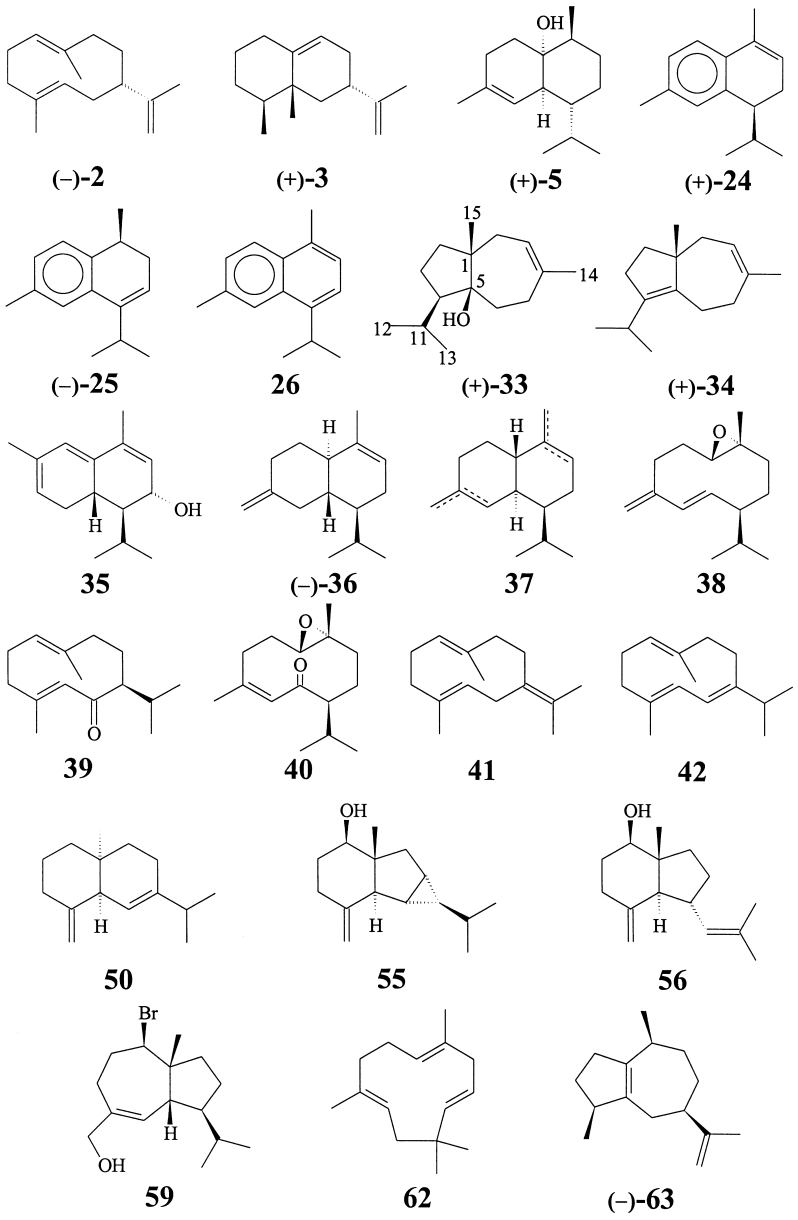


Fig. 2. Sesquiterpenes mentioned in the text.

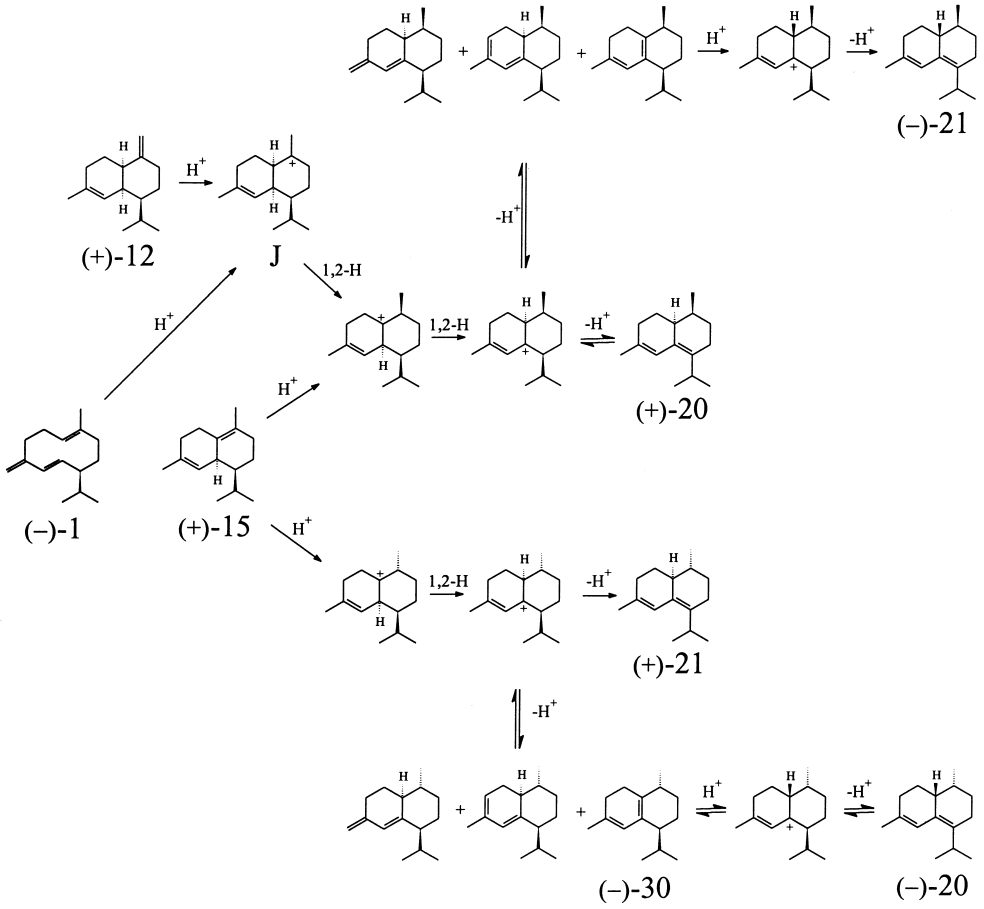
(+)-**4**. By repeating this experiment with (−)-**4**, we got (+)-**21** with 40% ee and (+)-**20** and (−)-**24** with similar enantiomeric composition. Our results confirm that enantiomeric mixtures of **20**, **21** and **24** may be formed from enantiomerically pure **4** and that the less probable process via deprotonation/protonation may lead to the formation of the minor enantiomers. A similar scheme can be established for the amorphenes and the germacrenyl cation **J** according to experimental evidence (Scheme 6).

Although **20** and **21** and their dehydrogenated derivatives are obtained in an unpredictable enantiomeric composition, germacrene D (**1**) is, nevertheless, a suitable educt for the preparation of these isomerization products (see Table 1).

Nishimura et al. (1979) described γ_1-cadinene (**36**, Fig. 2) as an additional rearrangement product. We did not find this component, although it can not be excluded that it is one of the not identified minor products.

The formation of **36** appears rather unlikely since it would imply in **1** a protonation of C-5, whereas the highest electron density and nucleophilicity of a butadiene system should be located at the carbon atom in the 1- or 4-position (Streitwieser et al., 1965).

Interestingly, we obtained no sesquiterpenes with the rare bulgarane skeleton (**37**, Fig. 2), of which only a few



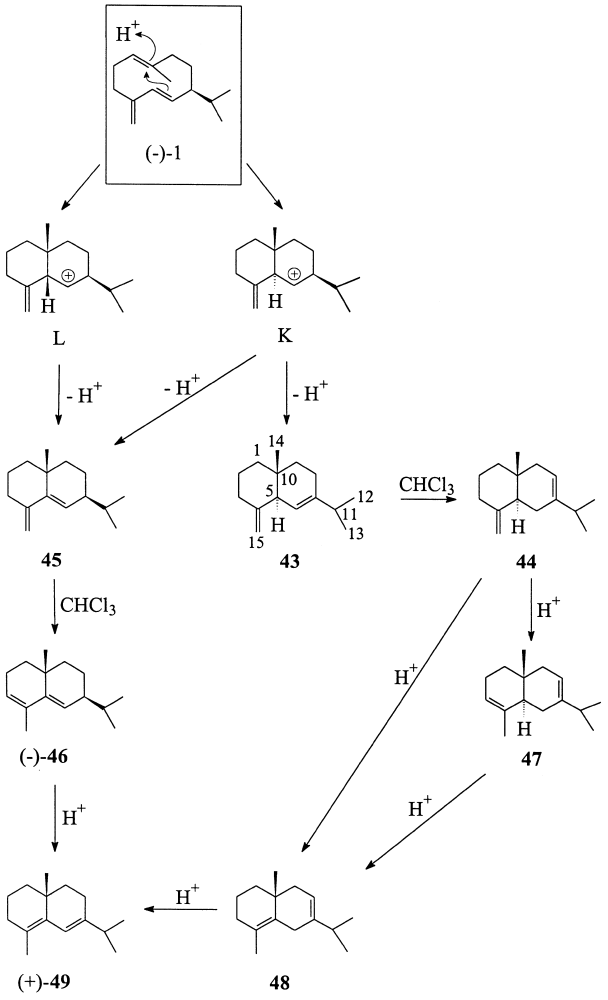
Scheme 6. Mechanism of formation of products obtained from germacrene D and amorphenes with strong Lewis acids.

natural compounds were reported so far (Connolly and Hill, 1991). The fact that bulgarenes can not be formed from germacrene D may explain that they rarely, if at all, occur in nature.

2.3.2. Eudesmane type sesquiterpenes

Protonation of the 1,10-double bond of **1** initiates the rearrangement to sesquiterpenes with eudesmane (selinane) skeleton accounting for approx. 10–20% of the reaction mixture (Scheme 7). Eudesmane derivatives were obtained as main products when epoxygermacrene D (**38**) (Niwa et al., 1978; Shizuri et al., 1986), germacrone (**39**) (Niwa et al., 1976a) and epoxygermacrone (**40**) (Niwa et al., 1976b) (Fig. 2), respectively, were submitted to acid catalyzed rearrangement. Selinenes are furthermore typical rearrangement products of *E*,*E*-1,5-cyclodecadienes, e. g. germacrene B (**41**) (Brown et al., 1967; De Pascual Teresa et al., 1978) and germacrene C (**42**) (Morikawa and Hirose, 1969) (Fig. 2), suggesting the biosynthetic pathway as shown in Scheme 1 (cation **A**→**E**). Rearrangement of germacrene D furnished selina-4(15),6-diene (**43**), selina-4(15),7-diene (vetiselinene, **44**) (Garratt and Porter, 1986), selina-4(15),5-diene (**45**) and selina-3,5-diene (**46**) (Blay et al., 1996) (Scheme 7). At least for the first two products the rearrangement proceeds via cation **K**. For the products **45** and **46** the intermediate *cis*-substituted cation **L** can not be excluded. By acid treatment of **43**, besides **44**, which is already formed under the influence of $CHCl_3$, the intermediates selina-3,7-diene (**47**) and selina-4,7-diene (**48**) (Fricke, 1999) could be identified by GC–MS. **43** is also known as a rearrangement product of germacrene C (**42**, Fig. 2) (Morikawa and Hirose, 1969). The structure of **43** was confirmed by NMR and by comparison with the product mixture of an isomerization experiment of **42** (GC–MS). All products resulted in *δ*-selinene (**49**) (Fricke, 1999) after prolonged acid treatment.

Even more sensitive against acid is the diene **45**, which rearranges in $CHCl_3$ solution even at 0°C mainly to **46**. The structures of these products were confirmed by ^{1}H-^{1}H-COSY-NMR. (−)-**46** was recently synthesized (Blay et al., 1996), while structure **45** had been ascribed to "sibirene" (Pentegova et al., 1966; Ohta and Hirose, 1972), a sesquiterpene known for more than 30 years, but with NMR data differing from those of the germa-



Scheme 7. Sesquiterpenes with selinane skeleton obtained from germacrene D.

crene D rearrangement product. With **46** as a rearrangement product of **45** it is obvious that the structure of sibirene needs to be revised. These facts justify the doubts of Andersen et al. (1977), who proposed structure **50** (Fig. 2) for sibirene.

2.3.3. Oppositane and axane type sesquiterpenes

Oppositane and axane type sesquiterpenes are rarely found in nature. They are formed in similar amounts as the eudesmanes by rearrangement of germacrene D. Substituted oppositanes have been obtained before by rearrangement of epoxygermacrene D (**38**) (Yamamura et al., 1982; Shizuri et al., 1986). As in the case of the structurally related selinanes, cation **K** is formed by ring closure from cation M1 (Scheme 8), which by loss of a proton from C-8 may lead to cyclization and formation of 4(15)-cyclooppositene (**51**) (path a) (Yamamura et al., 1982). Alternatively, a *Wagner–Meerwein* rearrangement results in a ring contraction to cation **N** (path b) that may either immediately be converted to opposita-4(15),7-diene (**52**) or may form opposita-4(15),11-diene (**53**) (after hydride shift via cation **O**) by deprotonation. Cyclization to the axanes with a *cis*-fused indene skeleton is initiated by a conformational change from **M1** to **M2**. 4(15)-Cycloaxene (**54**) is formed by cyclization of cation **P**. Open-chain analogues of **52** and **53** were not observed. All structures were verified by careful NMR studies (HMBC, HMQC and NOESY). The 1-hydroxy compound **55** (Fig. 2, analogous to **51**) was isolated from *Torilis japonica* D.C. **55** is considered as a biogenetic precursor of oppositol type compounds like **56** (Fig. 2), although the cyclopropane ring system is inert against acid treatment (Yamamura et al., 1982). The observed stability can be confirmed: compounds **51** and **54** are almost quantitatively converted to the isomers **57** and **58** with endocyclic double bonds under retention of the cyclopropane partial structure. Although the 1-hydroxy derivative **55** was described, none of the beforementioned oppositane and axane type hydrocarbons could be detected in our samples of *Torilis japonica* D. C. essential oil.

2.3.4. Isodaucadienes

This compound class has been found in functionalized form in several plants and marine organisms (Connolly and Hill, 1991). Isodaucadienes contribute approx. 5% to the reaction mixture of the germacrene D rearrangement products. Interestingly, no isodaucadienes were obtained when carboxylic acids or strong Lewis acids like $AlCl_3$ were used as catalysts (Table 1). Isodaucenol **59** (Fig. 2) was formed by treatment of germacrene D (**1**) with NBS (Shizuri et al., 1986). Epoxygermacrene D (**38**) was isomerized to corresponding isodaucadiene derivatives (Niwa et al., 1979). According to these authors it can be concluded that the acid induced rearrangement proceeds via the *cis*-substituted cation **Q** (Scheme 9). Hydride shift furnishes isodauca-4,7(14)-diene (**60**), which isomerizes under acidic conditions to isodauca-4,6-diene (**61**). This compound is also known to be formed by rearrangement of α-humulene (**62**, Fig. 2) (Naya and Hirose, 1973; Dauben et al., 1975).

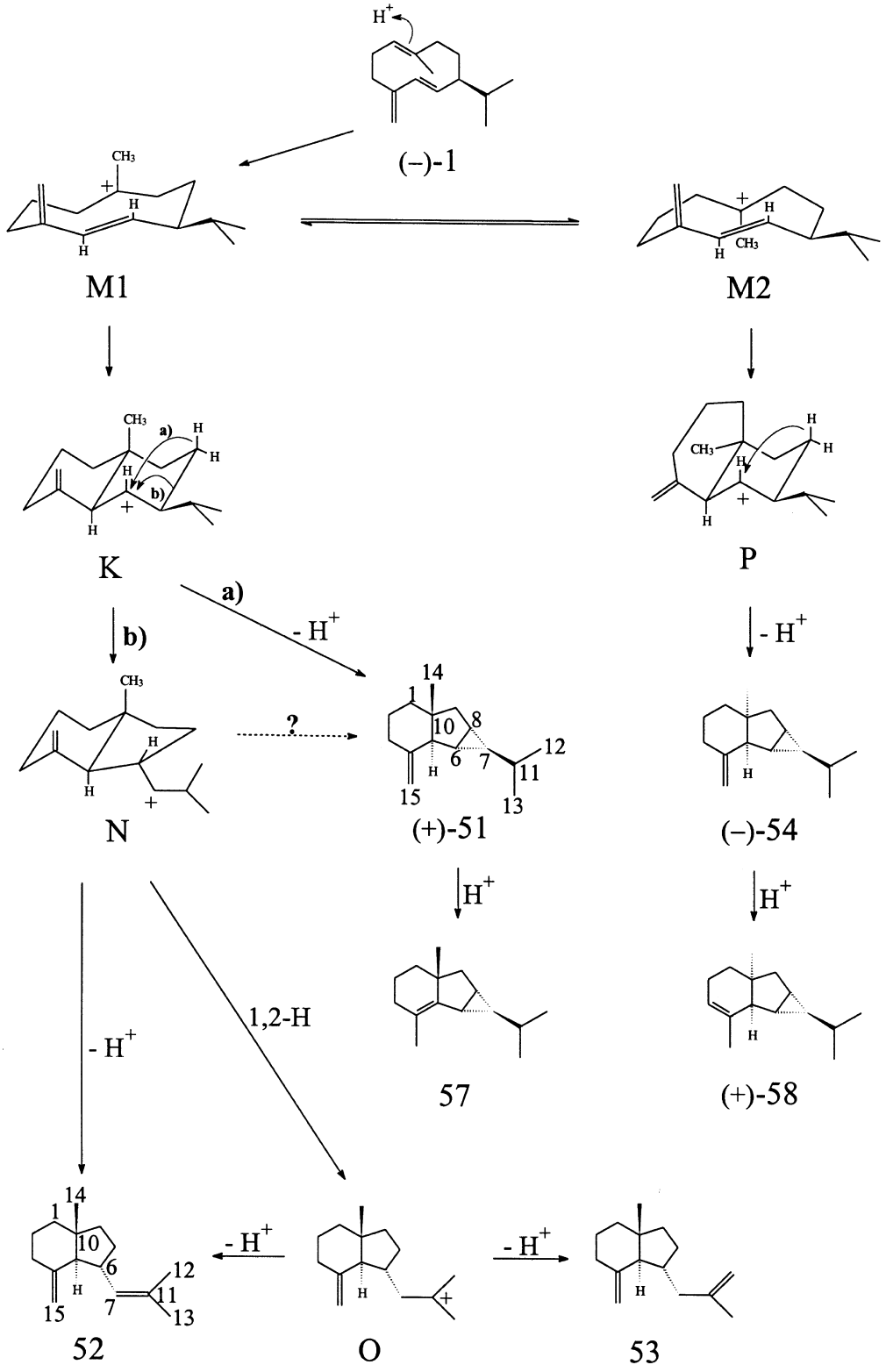
2.3.5. Miscellaneous

Although according to above considerations the acid catalyzed rearrangement of germacrene D proceeds regio- and, in general, stereospecifically to cadinane, eudesmane, oppositane, axane and isodaucane sesquiterpene skeletons, one observes certain transitions between the groups. In the GC–MS investigation of an acid catalyzed rearrangement process of selina-4(15),6-diene (**43**) to δ-selinene (**49**) a small amount of isodauca-4,6-diene (**61**) was detected (Scheme 10). The rearrangement of **61** to **49** under the influence of strong acid has already been described (Mehta and Singh, 1977). When **49** was treated with ion exchange resin Amberlyst®15 over several

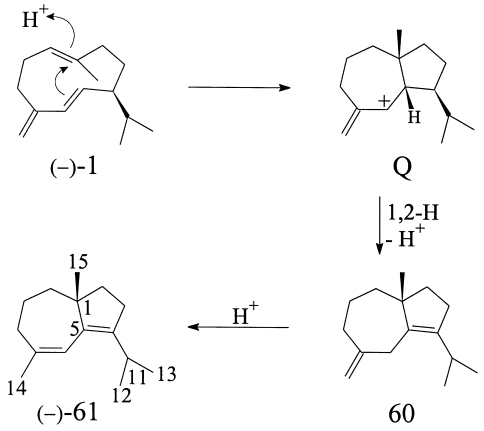
days, we obtained cadalene (**26**) and daucalene (**32**), while **61** only gave **26** among other products. In this context a rearrangement of γ-guaiene (**63**, Fig. 2) to epizonarene (**21**) in concentrated sulfuric acid is remarkable (Mehta and Singh, 1977).

2.4. Biogenesis of sesquiterpenes involving radical intermediates

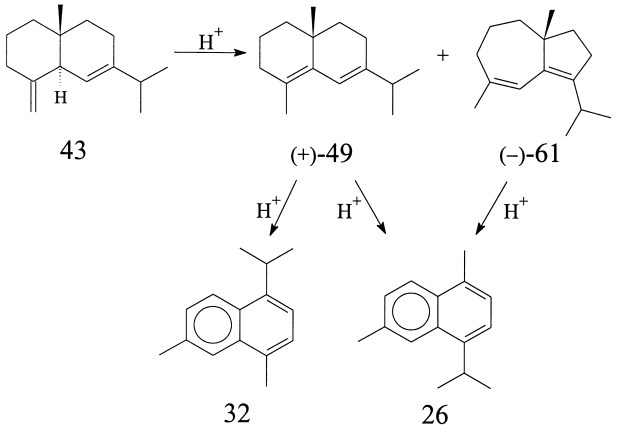
Since the first description of germacrene D (Yoshihara et al., 1969) it is known that it may be converted to



Scheme 8. Sesquiterpenes with the oppositane and axane skeleton obtained from germacrene D.



Scheme 9. Sesquiterpenes with the isodaucane skeleton obtained from germacrene D.



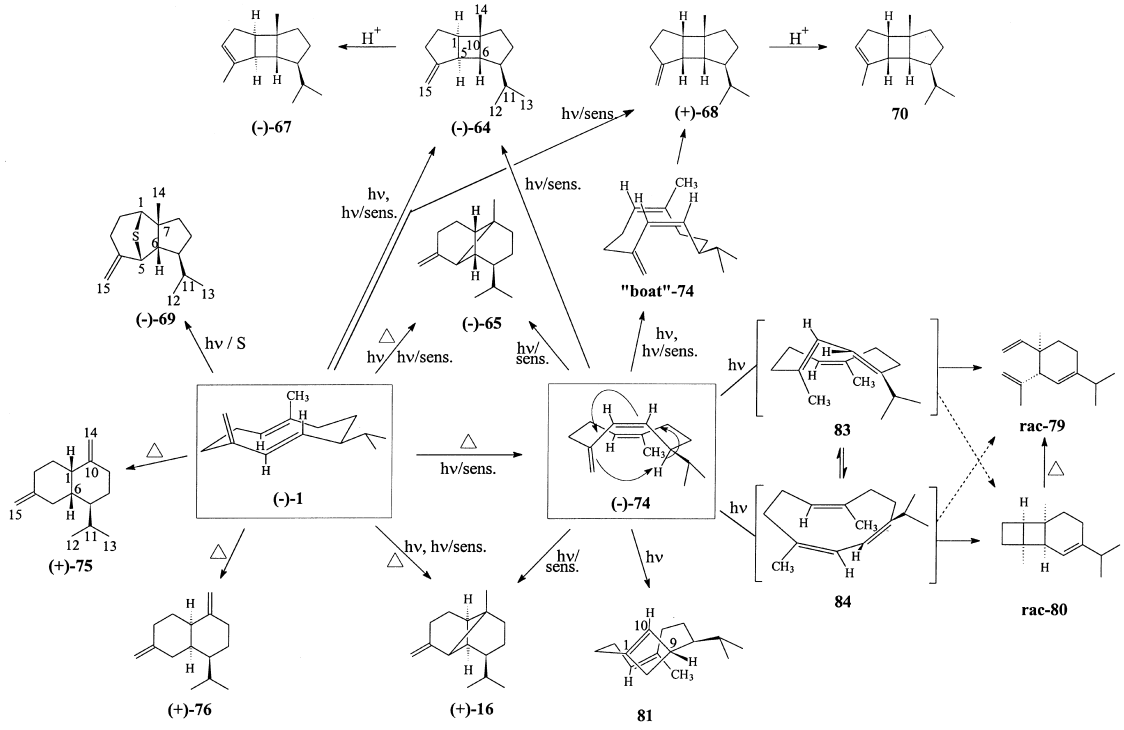
Scheme 10. Acid catalysed transitions between sesquiterpene groups.

β-bourbonene (**64**) (Tomioka et al., 1989) and β-copaene (**65**) (Kulkarni et al., 1987) in photochemical rearrangement reactions (Scheme 11). The biosynthesis of **64** and **65** is still unknown. Due to its molecular geometry (note the spatial proximity of the double bonds, Fig. 1) germacrene D is most suited for intramolecular rearrangement reactions with radical type intermediates. This fact suggests to include radical in addition to cationic intermediates into biogenetic studies. It has been proposed that a pigment-sensitised photocyclization of germacrene D (**1**) or of its endocyclic double bond isomer (**66**) (Fig. 3) could result in the formation of the bourbonene and copaene skeletons (Brown, 1968). As an additional rearrangement mechanism of terpenes lacking a diphosphate moiety photochemically triggered cyclizations via single electron transfer have been suggested (Hoffmann et al., 1993). Although the photochemical rearrangement of germacrene D for the production of β-bourbonene has been an established method for quite some time (Chem. Abstr., 1978, 1981) and thermally induced reactions were reported more than 25 years ago (Lawrence et al., 1972), a reexamination seems reasonable.

2.4.1. Photochemical reactions

2.4.1.1. Irradiaton. Germacrene D (**1**) was irradiated in *n*-hexane solution using a low pressure Hg lamp (254 nm). In addition to β-bourbonene (**64**), which according to the "rule of five" (Brown, 1968), was formed as the major product (Table 2), traces of a compound with a similar mass spectrum as for **64** were formed. By GC–MS comparison this compound was found not to be identical with α-bourbonene (**67**) (White and Gupta, 1968), which can be easily obtained from **64** under acid catalysis (Scheme 11). It was reported (Heathcock and Badger, 1972; Heathcock et al., 1972) that 1,6-cyclodecadienes under irradiation formed not only *cis,anti,cis*-tricyclo[5.3.0.$0^{2,6}$]decanes (corresponding to the bourbonene skeleton) but also *cis, syn, cis*-isomers. For comparison we therefore prepared 1,5-di-*epi*-β-bourbonene (**68**) from mint sulphide (**69**) according to a literature protocol (Uyehara et al., 1981, 1988). **69** can be obtained from **1**, if the irradiation proceeds in the presence of sulphur (Scheme 11) (Yoshida et al., 1979; Takahashi et al., 1981). A GC–MS comparison of 1,5-di-*epi*-β-bourbonene (**68**) and of 1,5-di-*epi*-α-bourbonene (**70**), which is obtained from **69** by acid induced rearrangement, showed no identity with our trace component. It can be assumed that the unknown bourbonene isomer is identical with one of the alternate stereoisomers **71**, **72** or **73** (Fig. 3). **71** has been described as a constituent of the gorgonian *Eunicea succinea* (Gopichand et al., 1984; Tursch et al., 1978). In the case of the *cis,syn,cis*-isomer **72** the isopropyl residue is very likely to cause considerable tensions and repulsion forces in the molecule, while **73** or other isomers with one of the substituents at the four-membered ring in opposite direction compared to the other substituents should be energetically unfavorable because of ring tension. Nevertheless, compounds of this type have been described as products of photochemically induced intramolecular cycloadditions (Orahovats et al., 1983). As additional products of a cross-addition of the endocyclic double bonds β-copaene (**65**) and β-ylangene (**16**) (Kulkarni et al., 1987) are formed (Scheme 11). Their formation can formally be rationalized as shown in Scheme 12 by a 180° turn of the 1,10- and 5,6-double bonds, respectively, following addition of an inner-face to an outer-face olefinic double bond. One should, however, keep in mind, that this is a simplified description and the molecule is present in a photochemically excited state (**1***), with a geometry and electron distribution different from the ground state (Horspool and Arnesto, 1992).

The identified photoisomerization products can be considered as [$2p_s + 2p_s$]-cycloaddition products according to the Woodward–Hoffmann rules (Hoffmann and Woodward, 1965, 1968), in case the reaction proceeds in



Scheme 11. Photochemical and thermal induced rearrangements of germacrene D and isogermacrene D.

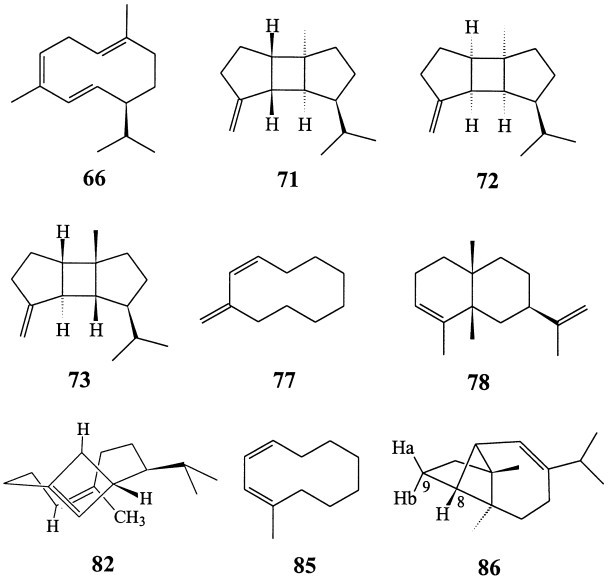
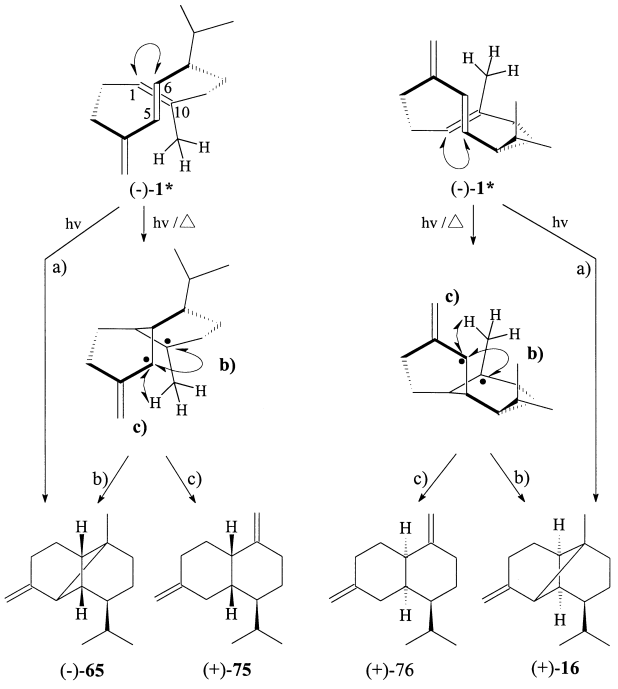


Fig. 3. Sesquiterpenes mentioned in the text.

a concerted fashion (Scheme 12, path a). However, a photo-educt promoted to the S_1-state by direct irradiation is rapidly converted into a T_1-state by intersystem-crossing. Thus, most photochemical reactions proceed in several steps over bi-radical or bi-ionic intermediates (Scheme 12, alternative path b) (Coxon and Halton, 1974; Horspool and Arnesto, 1992). For germacrene D it was reported that the reaction rate and the yield in the formation of β-bourbonene (**64**) is increased when triplet sensitizers were used (Chem. Abstr., 1978). When **1** was irradiated with a medium pressure Hg lamp (300 nm) in acetone as a triplet sensitizer complete conversion was observed after short reaction time. All products obtained in the direct irradiation reaction were also obtained in this reaction, but in a different proportion (Table 2). To make sure that no secondary reactions were induced by the triplet sensitizer acetone in the olefinic photoreaction products, which could be responsible for the differences in the product concentrations, the isolated compounds and the product mixture were irradiated under identical conditions. No conversions or changes in the proportions were observed. Comparing the direct and sensibilized irradiations, it can be assumed that germacrene D reacts at least in part over the S_1-state to its photoproducts. Otherwise we would have expected the same product proportions in both cases. The parallel occurence of triplet transitions in the direct irradiation processes is documented by the formation of the different β-bourbonene isomers. A more detailed comparison with the results obtained under the conditions of triplet sensibilization is questionable since isogermacrene D (**74**) and 1,5-di-*epi*-β-bourbonene (**68**) are formed. **74** is a photo-educt of **68** and of the products also obtained from **1** (Table 2). Therefore, a photochemical equilibrium exists between **1** and **74** under triplet conditions and the product mixture represents the result of the triplet-sensitized rearrangement of **1** and **74**.

Table 2
Results of the irradiation of **1** under several conditiones and of **74** with triplet sensibilization

Experiment/(%/ratio)	**1**, 254 nm	**1** + sulfur, 254 nm	**1**, 300 nm, sensibilized (acetone)	**74**, 300 nm, sensibilized (acetone)
β-Bourbonene (**64**)	78.9/18	10.0/18.3	77.0/12.6	50.2/22.5
Monoepi-β-Bourbonene (**71**, **72** or **73**)	0.9/0.2	0.3/0.6	0.9/0.2	1.8/0.8
1,5-Diepi-β-Bourbonene (**68**)	–	–	6.6/1.1	8.2/3.7
β-Copaene (**65**)	14.9/3.4	1.8/3.3	7.0/1.2	24.0/10.8
β-Ylangene (**16**)	4.4/1	0.6/1	6.1/1	2.2/1
Mintsulfide (**69**)	–	86.2/157	–	–
Isogermacrene D (**74**)	–	–	Trace	–
Unidentified	0.9/0.2	1.1/2	2.3/0.4	13.5/6.1



Scheme 12. Mechanisms of formation of muurolane and amorphane type sesquiterpenes obtained by irradiation and thermal treatment.

2.4.1.2. Thermal treatment. Germacrene D (**1**) is stable up to approx. 180°C. By heating up to 240°C over several hours in n-hexane solution in a sealed tube 1 is rearranged to β-ylangene (**16**), β-copaene (**65**), ϵ-muurolene (**75**) and ϵ-amorphene (**76**) as major products (Köster et al., 1986) (Scheme 12, Table 3). Identical products were obtained when a solution of **1** was injected into the hot injector (400°C) of a gas chromatograph. Lawrence et al. (1972) also found products typical for acid induced rearrangements in the thermal rearrangement of **1** in ethylene glycol at 190°C. We also detected such products in small amounts, of which the formation probably has been induced by the presence of impurities in the liner of the injector, reacting as catalytically active sites.

From a mechanistic point of view it is interesting that, compared to photochemical rearrangement processes, **16** is produced in excess of **65**, while **64** is not obtained at all. No interconversion is observed in the thermal treatment of single components (**16**, **65**, **75**, **76** or **64**) under the same conditions as used for **1**. It should be mentioned that Roth (1966) obtained products with the tricyclo[5.3.0.$0^{2,6}$]decane skeleton (corresponding to **64**) in thermal rearrangements of *trans,trans*- and *cic,cis*-1,6-cyclodecadienes, respectively, whereas no tricyclo[4.$4^{2,7}$.2.0]decanes (corresponding to **16** und **65**) were formed. While **16** and **65** are generated in photochemically induced rearrangements of **1** from excited states, **1** reacts in thermal excitations from the ground state (Horspool and Arnesto, 1992). In a concerted, thermally induced [$2p_s + 2p_a$]-cycloaddition one of the components would react in suprafacial and the other in antarafacial mode. Considering the substituents at the olefinic double bonds, this appears to be highly unlikely in germacrene D (**1**). A non-concerted process and a biradical intermediate can be assumed. According to Hammond (1955) and Streitwieser (1956) the transition state is energetically the lower, the higher the stability of the formed biradical. Accordingly, a reaction pathway (Scheme 12, path b) is proposed, implying a C1–C6-bond formation. In this reaction the more stable biradical is formed (tertiary and allylic radical site *versus* two secondary radical sites). Collapse of the biradical (path b) results in **16** and **65**, respectively. Correspondingly, for the formation of β-bourbonene (**64**) a 1,5- or 6,10-biradical would be necessary. In contrast to the formation of **16** and **65**, a biradical with a less favoured secondary radical site would always be involved, which may explain that **64** is not formed.

ϵ-Muurolene (**75**) and ϵ-amorphene (**76**) can be rationalized as products of an intramolecular *ene*-reaction according to Scheme 12 (Hoffmann, 1969). Probably the reaction does not proceed in a concerted fashion as the same biradical intermediates as in the formation of **16** and **65** can be assumed, however, with an abstraction of the allylic hydrogen from CH_3-14 and without bond formation to a cyclobutane (path c).

Moreover, as a side product a compound was detected, which we identified as a double bond isomer of

Table 3
Results of the thermal induced rearrangement of **1**

	β-Ylangene (**16**)	β-Copaene (**65**)	Isogermacrene D (**74**)	ϵ-Muurolene (**75**)	ϵ-Amorphene (**76**)
%/ratio	39.1/5	13.4/1.7	7.8/1	20.0/2.6	18.0/2.3

germacrene D and which we named isogermacrene D (**74**). The *cis*-configuration of the 5,6-double bond can be established from the vicinal coupling constant of $J = 11.4$ Hz, the configuration of the 1,10-double bond was derived from NOESY measurements (Fig. 4). Accordingly, a chair conformation can be attributed to **74**, as it was already confirmed for similar *cis,cis*-1,6-cyclodecadiene systems (Dale and Moussebois, 1966; Allinger et al., 1972; Ermer and Lifson, 1973; Turner et al., 1973; White and Bovill, 1975). A boat conformation is unfavourable because of the repulsion of π-electrons. Moreover, a bathochromic shift would be expected in the UV spectrum of **74** for the absorption of the 1,10-double bond in the case of a boat conformation. However, the absorption maximum is found slightly below 200 nm ($\epsilon = 7300$) as expected for non-conjugated olefins. It is confirmed by investigations of the photoelectron spectra of 1,6-cyclodecadienes that almost no interactions exist for the *cis,cis*-isomer but very strong transannular interaction of the endocyclic double bonds for the *trans,trans*-isomer (Bischof and Helbronner, 1970), as it is observed for germacrene D (**1**) (Yoshihara et al., 1969). Because of the isolated double bond and based on the equilibrium of the *cisoid* and *transoid* conformations of the conjugated double bonds (**1a** and **1b**, Fig. 1), UV maxima at 208 nm ($\epsilon = 13\,400$) and 258 nm ($\epsilon = 4500$) are observed for **1**. No additional maxima are observed for isogermacrene D (**74**), which shows only weak absorption at higher wave length. This proves that the 4,15- and 5,6-double bonds are not coplanar and conjugation is not possible. These results

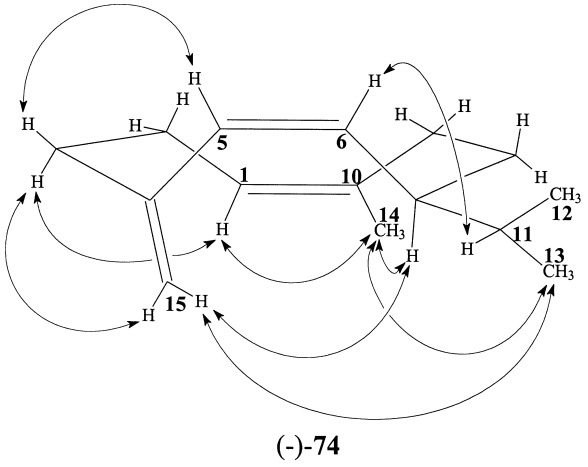


Fig. 4. ^{1}H,^{1}H-NOESY interactions observed in isogermacrene D.

are in agreement with the observation of diene **77** (Fig. 3), for which a dihedral angle between the double bonds of 60° is assumed (Dauben et al., 1970). The rearrangement of the *trans,trans*- to the thermodynamically more stable *cic,cis*-isomer of the 1,6-cyclodecadiene system is supported by experimental results (Dale and Mousesbois, 1966; Roth, 1966).

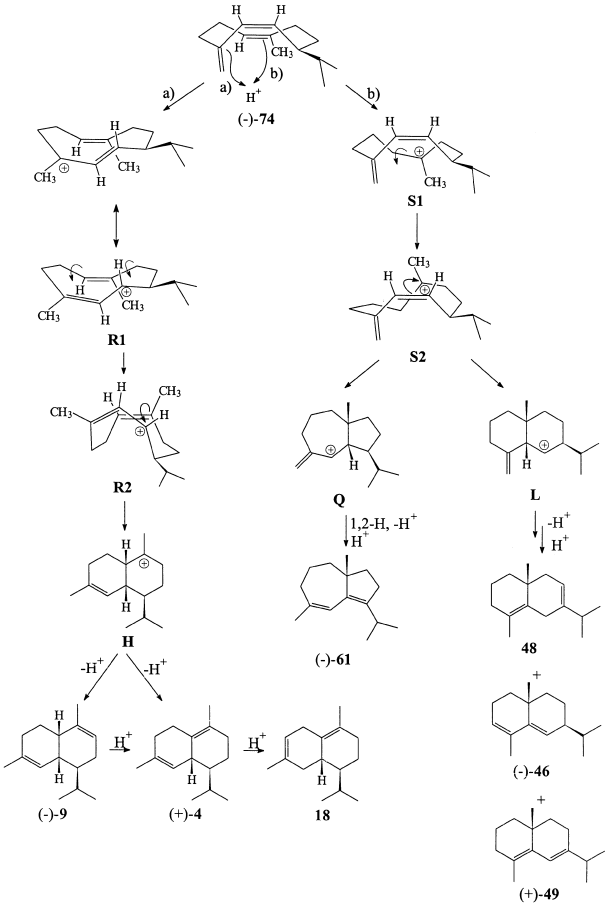
2.5. Rearrangements of isogermacrene D

As germacrene D (**1**) proved to be a very useful source for a multitude of sesquiterpenes, it was prompting to submit isogermacrene D (**74**) to the same rearrangement conditions to investigate, if it could be an educt for new sesquiterpenes with unknown structures. Moreover, it was interesting from a mechanistic point of view to find out, in which way the configuration of the double bonds influences the reaction pathways. Isogermacrene D does not rearrange under the conditions at its formation from germacrene D (240°C). No investigations were performed at temperatures above 240°C.

2.5.1. Acid catalyzed rearrangements

74 was submitted to rearrangement under the influence of acidic ion exchange resin Amberlyst®15 in microscale amounts and the products were investigated by GC–MS and by comparison with a library of reference compounds. We obtained α-muurolene (**9**), δ- (**4**) and ω-cadinene (**18**), 4,7-selinadiene (**48**), 3,5-selinadiene (**46**) and δ-selinene (**49**) in addition to traces of 4,6-isodaucadiene (**61**) (Scheme 13) in proportions as listed in Table 4. Although a major portion of the products could not be identified, it is obvious that the proportion of selinenes is higher than in the case of germacrene D (at least 18% selinenes formed from **74** compared to in total 12% from **1**). Consequently, the electrophilic attack at the 1,10-double bond is more pronounced in the case of **74** and the cyclization to selinenes is favoured. A preference for the protonation at the isolated double bond can be concluded from the considerations about the conformation of **74**. Normally a 1,3-diene, as a conjugated system, exhibits enhanced reactivity towards electrophiles. Since the conjugation between the 4,15- and 5,6-bond in **74** is hindered, the nucleophilicity of the double bonds is solely determined by their relative electron density. The cation **S1**, resulting from protonation of C-1, has to turn around the 1,10-bond to approach the 5,6-double bond to facilitate ring closure via **S2** to cations **L** or **Q** (Scheme 13). **L** is most likely represented

by a 5-*epi*-eudesmane skeleton. Thus, (−)-**74** with a β-orientated isopropyl substituent as depicted in Scheme 13, is rearranged to (+)-δ-selinene (**49**) with a β-orientated C-14 methyl group. The β-position of H-5 consequently follows from the reaction sequence. It is therefore quite conceivable that the majority of the unidentified compounds generated in the acid induced rearrangement of isogermacrene D (**74**) consists of 5-*epi*-selinenes. Such structures have only occasionally been described as natural compounds (Ando et al, 1994a,b). As an example compound **78**, a termite defense substance, should be mentioned (Fig. 3). The acid induced rearrangement to the cadinenes may be described as shown in Scheme 13. As a major product α-muurolene (**9**) was obtained from which the other cadinenes are formed by isomerization. As a consequence of the *cis*-decalin structure of **9** a rotation of the 1,10-double bond is necessary, following the protonation of C-15 in **74**, before cyclization to **H** can take place.



Scheme 13. Sesquiterpenes obtained from isogermacrene D under acid catalysis.

Table 4
Products (%) of the acid catalyzed rearrangement of **74**

α-Muurolene (**9**)	15.7	4,7-Selinadiene (**48**)	0.5
δ-Cadinene (**4**)	1.8	3,5-Selinadiene (**46**)	1.9
ω-Cadinene (**18**)	0.8	δ-Selinene (**49**)	15.2
Unidentified	~63	4,6-Isodaucadiene (**61**)	0.6

2.5.2. Irradiation

74 was directly irradiated under the same conditions as **1**. In the mixture of products (Table 5) δ-elemene (**79**) (Ganter and Keller-Wojkiewicz, 1971) and 1,5-di-*epi*-β-bourbonene (**68**) were identified by comparison of their GC–MS data, while the tricyclic compound **80** and the cyclobutene derivative **81** were identified by NMR. The irradiation of isogermacrene D (**74**), as in the case of **1**, was repeated with acetone as triplet sensitizer. In contrast to **1** the product spectrum of **74** is changed completely, thus proving a process originating from the singlet state for the products of the direct irradiation. The formation of **68** can be explained by a conformational change from *chair*-**74** to *boat*-**74** (Scheme 11) prior to a concerted [$2p_s$-$2p_s$]-cycloaddition. Product **81** is formed by an electrocyclic reaction of the diene system (Hoffmann and Woodward, 1968; Dauben et al., 1970). From the conformation of **74** in its ground state it can be concluded that **81** is formed as 6*S*,7*S*-isomer. However, following a conformational turn of **74** around C-3 and C-7 and subsequent cyclization the diastereoisomer **82** with 6*R*,7*S*-configuration (Fig. 3) may be obtained. Incidentally, inspection of the GC–MS data of some minor constituents reveals a compound with identical mass spectrum and very similar retention time as **81** which could be identical with **82**. The photochemically induced rearrangements to **79** and **80** probably proceed simultaneously. Primarily a 1,5-sigmatropic rearrangement has to take place, which proceeds in a concerted way via an *antarafacial* arrangement and which is favoured by the conformation of **74** as described above. Formally the (not identified) intermediate **83** is formed, which according to the rearrangement mechanism possesses a 4,5-*trans*- and a 6,7-*cis*-double bond (Hoffmann and Woodward, 1968). **83** may exist in a photochemical equilibrium with the *cis,cis*-isomer **84** as it is assumed for the photochemical rearrangement of

Table 5
Results of the irradiation of **74**

	1,5-Diepi-β-bourbonene (**68**)	δ-Elemene (**79**)	Tricyclic compound **80**	Cyclobutene derivative **81**	Unidentified
%/ratio	16.6/4.9	3.4/1	29.8/8.8	26.2/7.7	23

77 to **85** (Fig. 3) (Dauben et al., 1970). Compound **80** may be formed from **84** via a concerted [$2p_s$-$2p_s$]-cycloaddition or from **83** via a biradical intermediate. An alternate cross-addition would generate the tricyclic compound **86** (Fig. 3). The ^{1}H-NMR-spectrum of **80** shows a doublet for H-8 ($J=8.1$ Hz). In the tricyclic compound **86** a triplet would be expected for H-8, since the torsion angle between H-8 and the two H-9 protons should be identical, which should give identical coupling constants for both protons. The doublet in **80** results from a 0° angle for proton H-9a, while the angle to proton H-9b should be close to 90° ($J\approx0$ Hz, Fig. 3). It could further be proved by NOESY measurements that **80**, which shows strong interaction of H-5 and both methyl singlets, has a *cis,syn,cis*- and not a *cis,anti,cis*-configuration. Compounds of type **80** with both *cis,syn,cis*- and *cic,anti,cis*-configurations were obtained by irradiation of germacrene B (**41**) (Reijnenders et al., 1980; Peijnenburg et al., 1988). δ-Elemene (**79**) is a typical Cope rearrangement product easily obtained by thermal treatment of germacrene C (**42**) (König et al., 1996). Here it could be formed from **83** or **84** as an intermediate by a mechanism most likely involving a biradical. **79** is also formed from **80** as a minor constituent by thermal treatment. Therefore, it can not be excluded that **80** is rearranged to **79** by the heat developed during the reaction (≈50°C) over a biradical intermediate.

The photo products obtained from the triplet state of **74** in a qualitative way correspond to those obtained from the triplet-sensitized irradiation of germacrene D (**1**) (Table 2). In comparing the generated product amounts from both experiments it can be concluded that the triplet states of **1** and **74** are not identical. Otherwise identical product amounts should have been obtained. This can be rationalized by the fact that the photochemical excitation primarily effects the 1,3-diene system but does not effect the non-conjugated double bonds which have different configuration in **1** and **74**. From the quantitative comparison of di-*epi*-β-bourbonene (**68**) and of β-copaene (**65**) it can be concluded that **74** as formed by isomerization of **1** is not the only precursor of **68**, but that **68** is also generated from the triplet state of **1**. While **74** could be identified as an intermediate in the photochemical rearrangement of **1**, there is no indication that **74** can isomerize to **1**. However, it should be realized that **1** reacts faster under irradiation than **74** and may be not detected for this reason.

3. Conclusions

It was shown that germacrene D (**1**) is isomerized under acidic conditions to a multitude of naturally occuring cadinane, muurolane and amorphane type sesquiterpene hydrocarbons. Furthermore, the formation of eudesmane and the related oppositane and axane as well as isodaucane type compounds could be proved. In photochemical conversions mainly bourbonane, muurolane and amorphane type sesquiterpene hydrocarbons were obtained. Furthermore, a new germacrene D isomer, isogermacrene D (**74**), was discovered and its reactivity was investigated and compared with that of germacrene D. By specific choice of the rearrangement conditions the use of **1** as a synthetic precursor for certain cadinane type sesquiterpenes can be proposed. Starting from a certain enantiomeric composition of **1**, products of equal or similar enantiomeric composition are obtained, which proved to be very useful reference compounds for the identification and stereochemical investigation of sesquiterpene constituents of essential oils. Thus, it could be proved that not ϵ-bulgarene (Vlahov et al., 1967) but ϵ-amorphene is a constituent of Bulgarian peppermint oil (Bülow, 1999). δ-Amorphene (**15**) was for the first time detected as a natural compound in both enantiomeric forms in various essential oils (Melching et al., 1997). Furthermore, (−)-muurola-4,11-diene was identified as a minor constituent in the essential oil of *Amyris balsamifera* (König et al., 1999) and its (+)-enantiomer as a major constituent of the moss *Mnium hornum* (Musci) (König, 2000) by a chemical correlation with an enantiomeric mixture of γ-muurolene obtained by rearrangement of a corresponding mixture of germacrene D enantiomers. A similar approach was successfully applied in the determination of the absolute configuration of 11-bourbonene, a new sesquiterpene hydrocarbon from the essential oil of liverworts (Warmers et al., 1998).

From a biogenetic point of view a large variety of products were identified for which germacrene D or a germacrenyl cation **D** could be a potential precursor in the enzymatic sesquiterpene biosynthesis. The detection of some new natural compounds, as mentioned above and the correction of erroneous stereochemical assignments, as described for γ-amorphene (**12**), demonstrate the value of systematic studies of sesquiterpene structural correlations.

4. Experimental section

4.1. Collection of plant material and isolation of essential oils

Solidago canadensis L. and *S. gigantea* Ait. were collected at several locations near Hamburg and at Ærö/Denmark (summer 1995 and 1996), species of *S. caesia*, *S. missouriensis*, *S. nemoralis*, *S. oliensis*, *S. rigida*, *S. squarossa* and *S. virgaurea* ssp. praecox were provided by the Botanical Garden of the University of Hamburg (summer 1996), or collected at Zion National Park (Utah/USA) and at Crabtree Falls (Virginia/USA) (summer 1997). Samples of the collected *Solidago*

species are deposited in the Institut für Allgemeine Botanik, University of Hamburg. *S. canadensis* L. essential oil from plants collected at several locations in Poland was kindly provided by Dr. D. Kalemba, Technical University, Lodz/Poland. *Torilis japonica* D.C. was collected at several locations in Germany (autumn 1996). Volatile constituents of the plants were obtained by hydrodistillation (2 h) of aq. homogenates of plant material using n-hexane as collection solvent.

4.2. Isolation of germacrene D (**1**)

Solidago essential oil was either chromatographed on silica gel at −25°C with *n*-pentane as eluent or fractionated by prep. GC to obtain **1** in 99% purity. *Preparative GC* (Hardt and König, 1994). Isolation of all pure compounds was performed by preparative GC on a Varian 1400 instrument, equipped with stainless steel columns (Silcosteel, Amchro). The substances were fractionated using a column with 10% polysiloxane SE 30 on Chromosorb W-HP (1.85 m×4.3 mm). (+)-**6** and (−)-**12** were isolated and **18** and **33** were further purified on a column with 2.5% heptakis(2,6-di-*O*-methyl-3-*O*-pentyl)-β-cyclodextrin in OV-1701 (w/w) on Chromosorb G-HP (2.00 m×5.3 mm; 2,6-Me-3-Pe-β-CD (König et al., 1992a). Helium was employed as carrier gas at a flow rate of 240 ml min^{-1}.

4.3. Enantioselective capillary GC

Capillary columns with cyclodextrin derivatives were prepared as described earlier (König et al., 1992b).

4.4. NMR spectroscopy

NMR measurements were performed with the instruments WM 400 (400 MHz, Bruker) and WM 500 (500 MHz, Bruker) using TMS (δ = 0.00 ppm) as internal standard.

4.5. UV spectroscopy

UV spectra were recorded on a Perkin Elmer 552 spectrometer.

4.6. GC–MS

Electron impact (70 eV) GC–MS measurements were carried out on a Hewlett Packard HP 5890 gas chromatograph coupled to a VG Analytical VG 70-250S mass spectrometer.

4.7. Polarimetry

Optical rotation measurements were performed with a Perkin Elmer 241 polarimeter. The enantiomeric composition of known components was tested by comparison with enantiomerically pure authentic reference material. Only for new compounds with a purity ⩾95% (GC) the optical rotation was determined. Since we obtained enantiomeric mixtures, the values for single enantiomers were extrapolated.

4.8. Photolyses

Irradiations were performed with a Rayonet RPR-100 photoreactor equipped with 254 and 300-nm lamps, respectively.

4.9. Acidic rearrangement of germacrene D (**1**)

(a) *p*-Toluene sulfonic acid: An enantiomeric mixture of **1** [(−):(+) = 1.3:1, 270 mg, 1.32 mmol] in a solution of *p*-toluene sulfonic acid (10 mg) in CH_2Cl_2 (15 ml) was stirred at room temp. (rt) until **1** had completely disappeared. The reaction was controlled by GC. The solution was shaken several times with a saturated aqueous solution of $NaHCO_3$ (2 ml). The solvent was evaporated and the residue was prefractionated by column chromatography on silica gel at −25°C with *n*-pentane as eluent. The fractions were further fractionated by prep. GC. (b) Amberlyst®15 (Fluka): A solution of **1** [(−):(+) = 1.3:1, 61 mg, 0.3 mmol] in *n*-hexane (1.5 ml) was mixed with Amberlyst®15 (8 mg) and left at rt until **1** had completely disappeared (GC control). The solution was filtered, the catalyst washed once with *n*-hexane (0.5 ml) and the solvent evaporated. Isolation of single compounds was performed as described. (c) BF_3: To a solution of **1** [(+):(−) = 1.2:1, 420 mg, 2.06 mmol] in diethyl ether (180 ml) $BF_3{\cdot}Me_2O$ (50 ml, as 60% solution in dimethyl ether, 0.21 mol) was added at 0 °C. The solution was stirred for 12 min. Then ice cooled aqueous 0.5 N KOH (150 ml) was added. The organic layer was washed several times with aqueous 0.5 N KOH, then with satured aqueous NaCl and dried over $MgSO_4$; the solvent was evaporated. Purification and isolation, as described. (d) $AlCl_3$ or $ZnCl_2$: To a solution of 1 [(−):(+) = 2:1, 1.5 mg, 7×10^{-3} mmol] in CH_2Cl_2 (0.5 ml) $AlCl_3$ (15 mg, 0.03 mmol) was added and stirred for 1 h. The mixture was diluted with diethyl ether (0.5 ml) and washed two times with aqueous 0.5 N KOH (0.5 ml), satured aqueous NaCl and dried over $MgSO_4$. The solution was used for GC analysis.

4.10. Germacrene D (**1**)

^{1}H NMR (Kitamura et al., 1976; Mori et al., 1990), ^{13}C NMR (Randriamiharisoa et al., 1968), ^{13}C NMR (125.8 MHz, C_6D_6): δ = 149.2 (*s*, C-4), 136.6 (*d*, C-5), 133.9 (*s*, C-10), 133.4 (*d*, C-6), 130.1 (*d*, C-1), 109.6 (*t*, C-15), 53.8 (*d*, C-7), 41.2 (*t*, C-9), 35.1 (*t*, C-3), 33.2 (*d*, C-11), 29.9 (*t*, C-2), 27.0 (*t*, C-8), 21.2, 19.7 (2 *q*, C-12,-

13), 16.2 (*q*, C-14); MS: *m/z* (%): 204 (16) [M^+], 161 (100) [$M^+-C_3H_7$], 133 (15), 120 (23), 119 (29), 105 (47), 91 (42), 81 (37).

*4.11. δ-Cadinene (**4**)*

^1H, ^{13}C NMR (Wenkert et al., 1992; Randriamiharisoa et al., 1968); MS: *m/z* (%): 204 (42) [M^+], 189 (17) [M^+-CH_3], 161 (100) [$M^+-C_3H_7$], 134 (67), 119 (58), 105 (53), 91 (35).

*4.12. γ-Cadinene (**6**)*

^1H NMR (Andersen and Syrdal, 1970), ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 122.5$ (*d*, C-5), 103.2 (*t*, C-14), 46.9 (*d*, C-7), 45.2 (*d*, C-6), 44.2 (*d*, C-1), 36.3 (*t*, C-9), 30.5 (*t*, C-3), 26.6 (*t*, C-8), 26.2 (*d*, C-11), 25.8 (*t*, C-2), 23.9 (*q*, C-15), 21.6, 15.1 (2 *q*, C-12,-13); MS: *m/z* (%): 204 (15) [M^+], 189 (6) [M^+-CH_3], 161 (100) [$M^+-C_3H_7$], 133 (22), 119 (32), 93 (36), 91 (38), 79 (30).

4.13. α-Cadinene (7)

^1H NMR (Naya and Kotake, 1969), ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.61$ (*br. s*, 1H), 5.40 (*br. s*, 1H), 2.21 (m_c, 1H; H-11), 1.76–2.14 (m, 7H), 1.62 (*br. s*, 6H; H-14,-15), 1.43 (m_c, 1H), 1.25 (m_c, 1H), 0.89, 0.79 (2 *d*, $J_{12/13\text{-}11} = 6.9$ Hz, 6H; H-12,-13); ^{13}C-NMR (100.6 MHz, $CDCl_3$): $\delta = 136.03$ (*s*), 134.85 (*s*), 122.39 (*d*), 121.96 (*d*), 42.62 (*d*), 42.39 (*d*), 41.13 (*d*), 31.37 (*t*), 26.35 (*d*), 26.66 (*t*), 24.96 (*t*), 23.78 (*q*), 20.92 (*q*), 20.72 (*q*), 14.54 (*q*); MS: *m/z* (%): 204 (21) [M^+], 189 (10) [M^+-CH_3], 161 (58) [$M^+-C_3H_7$], 119 (20), 105 (100), 93 (29), 81 (30).

*4.14. γ-Muurolene (**8**)*

^1H NMR (Beecham and Djerassi, 1978), ^{13}C NMR (Weyerstahl et al., 1996; Randmriamiharisoa et al., 1968), ^1H-NMR (400 MHz, $CDCl_3$): $\delta = 5.54$ (*br. d*, $J = 3.6$ Hz, 1H; H-5), 4.65 (*br. s*, 1H; H-14a), 4.59 (*t*, $J = 2.0$ Hz, 1H; H-14b), 2.37 (m_c, 1H; H-1), 2.19 (*dt*, $J_t = 4$ Hz, $J_{AB} = 13.2$ Hz, 1H; H-9 eq), 2.13 (*dtt*, $J_{9ax\text{-}8eq} = 4$ Hz, $J_{9ax\text{-}14} = 1.9$ Hz, $J_{9ax\text{-}9eq,8ax} = 13.2$ Hz, 1H; H-9ax), 1.87–2.10 (*m*, 5H), 1.67 (*s*, 3H; H-15), 1.66 (*dq*, $J_{8eq\text{-}7,9ax/eq} = 4$ Hz, $J_{AB} = 12.2$ Hz, 1H; H-8eq), 1.37–1.45 (*m*, 2 H), 0.91 (*d*, $J_{12\text{-}11} = 6.8$ Hz, 3H; H-12), 0.88–1.07 (*m*, 1H; H-8ax), 0.78 (*d*, $J_{13\text{-}11} = 6.8$ Hz, 3H; H-12); MS: *m/z* (%): 204 (21) [M^+], 189 (5) [M^+-CH_3], 161 (100) [M^+- C_3H_7], 133 (19), 119 (40), 105 (48), 93 (40); ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 154.32$, 133.86 (2 s, C-4,-10), 124.57 (*d*, C-5), 106.51 (t, C-14), 44.80 (*d*, C-7), 43.54 (*s*, C-1), 39.75, 26.71 (2 *d*, C-6,-11), 31.62 (*t*, C-9), 30.86 (*t*, C-3), 25.87 (*t*, C-8), 25.41 (*t*, C-2), 23.89 (*q*, C-15), 21.72, 15.49 (2 q, C-12,-13); MS: *m/z* (%): 204 (19) [M^+], 189 (7) [M^+-CH_3], 161 (100) [$M^+-C_3H_7$], 133 (23), 119 (45), 105 (52), 93 (50), 91 (42), 79 (38).

*4.15. α-Muurolene (**9**)*

^1H NMR (Beecham and Djerassi, 1978), ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.48$ (m_c, 1H), 5.41 (*br. s*, 1H), 2.10–1.70 (*m*, 8H), 1.69 (*br. s*, 6H; H-14,-15), 1.48–1.36 (*m*, 2H), 0.89, 0.83 (2 *d*, $J_{12/13\text{-}11} = 7$ Hz, 6H; H-12,-13); MS: *m/z* (%): 204 (23) [M^+], 189 (9) [M^+-CH_3], 161 (50) [$M^+-C_3H_7$], 105 (100), 94 (31), 93 (34).

*4.16. Cadina-1,4-diene (**10**)*

^1H, ^{13}C NMR (Connolly et al., 1982); MS: *m/z* (%): 204 (22) [M^+], 161 (49) [$M^+-C_3H_7$], 119 (100), 105 (77).

*4.17. α-Copaene (**11**)*

^1H, ^{13}C NMR (Wenkert et al., 1992); MS: *m/z* (%): 204 (15) [M^+], 161 (95) [$M^+-C_3H_7$], 161 (95), 119 (100), 105 (96), 93 (58).

*4.18. γ-Amorphene (**12**)*

^1H NMR, ^{13}C NMR (Weyerstahl et al., 1996); MS: *m/z* (%): 204 (20) [M^+], 189 (6) [M^+-CH_3], 161 (100) [$M^+-C_3H_7$], 133 (21), 119 (50), 105 (56), 93 (60).

*4.19. α-Amorphene (**13**)*

^1H NMR (Gregson and Mirrington, 1976), ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.42$ (m, 1H), 5.17 (s, 1H), 2.64 (br. s, 1H), 2.32 (br. s, 1H), 1.94-2.03 (m, 2H), 1.78–1.89 (m, 1H), 1.63 (m_c, 6H), 1.50–1.71 (m, 4H), 1.09–1.18 (m, 1H), 0.94, 0.91 (2 d, $J_{12/13\text{-}11} = 6.6$ Hz, 6H; H-12,-13); MS: *m/z* (%): 204 (28) [M^+], 189 (10) [M^+-CH_3], 161 (54) [$M^+-C_3H_7$], 119 (26), 105 (100), 94 (58), 93 (56).

*4.20. α-Ylangene (**14**)*

^1H NMR (Melching et al., 1997), ^{13}C NMR (De Buyck et al., 1989); MS: *m/z* (%): 204 (20) [M^+], 189 (8) [M^+-CH_3], 161 (70) [$M^+-C_3H_7$], 120 (70), 119 (91), 105 (100), 93 (82).

*4.21. δ-Amorphene (**15**)*

^1H NMR, MS (Melching et al., 1997).

*4.22. β-Cadinene (**17**)*

^1H NMR (Fringuelli et al., 1985), ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.43$ (m_c, 2H), 2.30 (m_c, 1H), 2.08 (m_c, 1H), 2.00 (*d*sept, $J_{11\text{-}7} = 2.8$ Hz, $J_{11\text{-}12/13} = 6.8$ Hz, 1H; H-11), 1.68, 1.62 (2 s, 6H, H-14,-15), 1.30–1.95 (*m*, 7 H), 0.91, 0.77 (2 *d*, $J_{12/13\text{-}11} = 6.8$ Hz, 6H; H-12,-13);

^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 121.44$, 120.46, 42.83, 41.19, 38.37, 34.60, 30.56, 25.70, 23.41, 23.16, 20.88, 20.20, 14.27; MS: *m/z* (%): 204 (28) [M^+], 161 (46) [$M^+ - C_3H_7$], 119 (41), 105 (62), 93 (100).

*4.23. ω-Cadinene (**18**)*

^{1}H NMR (Vlahov et al., 1967) [these data were originally assigned to **4** which was assumed to be **18** (Connell et al., 1968; Nagasampagi et al., 1968)], ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.36$ (br. s, 1H; H-3), 2.96 (br. d, $J_{AB} = 19.5$ Hz, 1H; H-2a), 2.55 (*br. d*, $J_{AB} = 19.5$ Hz, 1H; H-2b), 1.55-2.15 (m, 12H), 1.04–1.39 (m, 3H), 0.95, 0.82 (2 d, $J_{12/13\text{-}11} = 6.6$ Hz, 6H; H-12,-13); MS: *m/z* (%): 204 (37) [M^+], 161 (63) [$M^+ - C_3H_7$], 119 (100), 105 (72).

*4.24. ω-Amorphene (**19**)*

$[\alpha]_D^{20} = -43$ ($c = 0.002$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.36$ (*br. s*, 1H; H-3), 2.91 (m_c, 1H; H-2a), 2.55 (m_c, 1H; H-2b), 2.35 (m_c, 2H), 1.66, 1.62 (2 *br. s*, 6H; H-14,-15), 1.15–2.10 (*m*, 7H), 0.93 (*d*, $J_{12/13\text{-}11} = 6.6$ Hz, 6H; H-12,-13); MS: *m/z* (%): 204 (38) [M^+], 161 (98) [$M^+ - C_3H_7$], 119 (100), 105 (79).

*4.25. Zonarene (**20**)*

^{1}H, ^{13}C NMR, MS (Melching et al., 1997).

*4.26. Epizonarene (**21**)*

^{1}H NMR (Andersen et al., 1973), ^{1}H-NMR (400 MHz, $CDCl_3$): $\delta = 6.22$ (s, 1H; H-5), 3.03 (sept, $J_{11\text{-}12/13} = 7$ Hz; H-11), 2.19–1.90 (m, 6H), 1.77 (s, 3H, H-15), 1.75–1.55 (m, 2H), 1.21–1.09 (m, 2H), 0.99 (d, $J_{14\text{-}10} = 6$ Hz), 0.96, 0.95 (2 d, $J_{12/13\text{-}11} = 7$ Hz; H-12,-13); MS: *m/z* (%): 204 (57) [M^+], 189 (43) [$M^+ - CH_3$], 161 (100) [$M^+ - C_3H_7$], 147 (18), 133 (23), 119 (39), 105 (58), 91 (36), 81 (67).

*4.27. cis-Muurola-4(15),5-diene (**27**)*

MS (Kim et al., 1994): *m/z* (%): 204 (16) [M^+], 161 (100) [$M^+ - C_3H_7$], 119 (20), 105 (27), 91 (21).

*4.28. Cadina-1(6),4-diene (**30**)*

MS (Melching et al., 1997): *m/z* (%): 204 (29) [M^+], 189 (13) [$M^+ - CH_3$], 161 (100) [$M^+ - C_3H_7$], 134 (15), 119 (24), 105 (36), 91 (18), 81 (29).

*4.29. Cadina-3,5-diene (**29**)*

MS (Melching et al., 1997): *m/z* (%): 204 (22) [M^+], 161 (100) [$M^+ - C_3H_7$], 119 (41), 105 (64), 91 (16), 81 (22).

*4.30. Bicyclosesquiphellandrene (**28**)*

MS (Melching et al., 1997): *m/z* (%): 204 (25) [M^+], 189 (10) [$M^+ - CH_3$], 161 (100) [$M^+ - C_3H_7$], 147 (17), 133 (15), 119 (36), 105 (61), 91 (49).

*4.31. cis-/trans-Calamenene (**22/23**)*

MS (Croft et al., 1978; Melching et al., 1997): *m/z* (%): 202 (8) [M^+], 159 (100) [$M^+ - C_3H_7$], 128 (16).

*4.32. α-Calacorene (**24**)*

^{1}H NMR (Hardt, 1994), ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.12$ (*d*, $J_{2\text{-}3} = 7.6$ Hz, 1H; H-2), 7.00 (m_c, 1H; H-3), 6.92 (*s*, 1H; H-5), 5.66 (*s*, 1H; H-9), 2.29–2.37 (*m*, 6H; H-7,-8a/b,-15), 2.01 (*br. s*, 3H; H-14), 1.88 (m_c, 1H; H-11), 0.89, 0.80 (2 *d*, $J_{12/13\text{-}11} = 6.6$ Hz, 6H; H-12,-13); MS: *m/z* (%): 200 (16) [M^+], 157 (100) [$M^+ - C_3H_7$], 142 (36).

*4.33. γ-Calacorene (**25**)*

MS (Adachi and Mori, 1983): *m/z* (%): 200 (16) [M^+], 157 (100) [$M^+ - C_3H_7$], 142 (36).

*4.34. Cadalene (**29**)*

^{1}H NMR (Bohlmann and Zdero, 1976); MS: *m/z* (%): 198 (42) [M^+], 183 (100) [$M^+ - CH_3$], 168 (13).

*4.35. 4S,4aS-1,7-Dimethyl-4-(methylethyl)-2,3,4,4a,5,6-hexahydronaphthalene (**31**)*

^{1}H NMR (Polovinka et al., 1981), ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.17$ (s, 1H; H-8), 1.80–2.20 (m, 5H), 1.78 (*br. s*, 3H; Me-7), 1.70 (*br. s*, 3H; Me-1), 1.65 (m_c, 1H), 1.00–1.25 (m, 4H), 0.96, 0.74 (2 *d*, $J_{Me(iPr)\text{-}H(iPr)} = 7.1$ Hz, 6H; Me(*i*Pr)); MS: *m/z* (%): 204 (69) [M^+], 189 (15) [$M^+ - CH_3$], 161 (100) [$M^+ - C_3H_7$], 145 (15), 133 (17), 122 (38), 119 (59), 105 (58), 91 (38).

*4.36. Daucalene (**32**)*

MS (Hashidoko et al., 1992): *m/z* (%): 198 (51) [M^+], 183 (100) [$M^+ - CH_3$], 168 (31).

*4.37. Selina-4(15),6-diene (**43**)*

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.41$ (s, 1H; H-6), 4.75, 4.56 (2 *q*, $J = 1.5$ Hz, 2H; H-15), 2.53 (*br.* s, 1H; H-5), 2.32 (*dm*, $J_{AB} = 12.7$ Hz, 1H; H-3eq), 2.20 (*br.* sept, $J_{11\text{-}12/13} = 7.1$ Hz, 1H; H-11), 1.89–2.14 (m, 3H), 1.62–1.73 (*m*, 2H, H-2a/b), 1.40–1.52 (m, 3H), 1.29 (*dt*, $J_{1ax\text{-}2eq} = 5.1$ Hz, $J_{1ax\text{-}1eq,2ax} = 12.7$ Hz, 1H; H-1ax), 1.02 (*d*, $J_{12/13\text{-}11} = 7.1$ Hz, 6H; H-12,-13), 0.63 (s, 3H; H-14); ^{13}C-NMR (100.6 MHz, $CDCl_3$): $\delta = 142.90$, 149.86 (2 s, C-4,-7), 118.58 (d, C-6),

104.74 (t, C-15), 49.09 (*d*, C-5), 40.13 (*t*, C-1), 37.63 (*t*, C-9), 36.77 (*t*, C-3), 35.04 (*d*, C-11), 23.77 (*t*, C-2), 23.28 (*t*, C-8), 21.84, 21.47 (2 *q*, C-12,-13), 15.50 (*q*, C-14); MS: *m/z* (%): 204 (40) [M^+], 189 (27) [M^+-CH_3], 161 (100) [$M^+-C_3H_7$], 133 (42), 119 (31), 105 (52), 91 (49).

*4.38. Selina-4(15),7-diene (vetiselinene, **44**)*

^{1}H, ^{13}C NMR (Garratt and Porter, 1986), ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.29$ (*br. d*, $J = 5.7$ Hz, 1H; H-8), 4.58, 4.78 (2 *br. s*, 2H, H-15), 2.35 (dm, 1H), 2.20 (sep, $J_{11\text{-}12/13} = 6.9$ Hz, 1H; H-11), 1.50–2.05 (m, 9H), 1.30 (*dt*, $J_d = 3.5$ Hz, $J_t = 13.5$ Hz, 1H), 1.01, 1.02 (2 d, $J_{12/13\text{-}11} = 6.9$ Hz, 6H; H-12,-13), 0.67 (s, 3H; H-14); MS: *m/z* (%): 204 (63) [M^+], 189 (37) [M^+-CH_3], 161 (85) [$M^+-C_3H_7$], 147 (32), 133 (68), 119 (42), 105 (100), 93 (82), 91 (73).

*4.39. Selina-4(15),5-diene (**45**)*

^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 5.44$ (*br.s*, 1H; H-6), 4.58, 4.77 (2 *dd*, $J_{15\text{-}3eq} = 2.0$ Hz, $J_{AB} = 3.0$ Hz, 2H; H-15a/b), 2.36 (*ddt*, $J_{3eq\text{-}2eq} = 4$ Hz, $J_{AB} = 13.2$ Hz, $J_{3eq\text{-}2ax,15a} = 2.0$ Hz, 1H; H-3eq), 2.10 (*ddt*, $J_{AB} = 13.2$ Hz, $J_{3ax\text{-}2ax} = 6.1$ Hz, $J_{3ax\text{-}2eq,15a} = 2.2$ Hz, 1H; H-3ax), 2.01–2.10 (*m*, 1H, H-7), 1.69 (*dt*, $J = 13.1$ Hz, $J = 4$ Hz, 1H; H-2b), 1.48–1.69 (m, 5H), 1.35–1.44 (*m*, 2H), 1.32 (*dt*, $J_{1ax\text{-}2eq} = 4.5$ Hz, $J_{1ax\text{-}1eq,2ax} = 13.2$ Hz, 1H; H-1ax), 0.95 (*s*, 3H; H-14), 0.88, 0.90 (2 d, $J_{12/13\text{-}11} = 7.1$ Hz, 6H; H-12,-13); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 149.96$ (*s*), 123.97 (*s*), 118.88 (*d*), 108.07 (t), 42.54 (*d*), 41.32 (*t*), 38.84 (*t*), 35.77 (*t*), 35.51 (*s*), 32.22 (*d*), 24.60 (*q*), 22.44 (*t*), 21.19 (*t*), 19.53 (*q*), 19.09 (*q*); MS: *m/z* (%): 204 (28) [M^+], 189 (9) [M^+-CH_3], 161 (100) [$M^+-C_3H_7$], 133 (38), 119 (25), 105 (50), 91 (46).

*4.40. Selina-3,5-diene (**46**)*

^{1}H NMR, ^{13}C-NMR (Blay et al., 1996); MS: *m/z* (%): 204 (13) [M^+], 189 (3) [M^+-CH_3], 161 (100) [$M^+-C_3H_7$], 119 (17), 105 (25), 81 (30).

*4.41. Selina-3,7-diene (**47**)*

(Fricke, 1999). MS: *m/z* (%): 204 (61) [M^+], 189 (4) [M^+-CH_3], 161 (85) [$M^+-C_3H_7$], 147 (35), 133 (68), 119 (44), 105 (100), 93 (87), 91 (78).

*4.42. Selina-4,7-diene (**48**)*

(Fricke, 1999). MS: *m/z* (%): 204 (85) [M^+], 189 (100) [M^+-CH_3], 161 (75) [$M^+-C_3H_7$], 147 (59), 133 (79), 119 (44), 105 (89), 91 (99).

*4.43. δ-Selinene (**49**)*

^{1}H, ^{13}C NMR (Sun and Erickson, 1978); MS: *m/z* (%): 204 (65) [M^+], 189 (100) [M^+-CH_3], 161 (72) [$M^+-C_3H_7$], 133 (32), 119 (25), 105 (37), 91 (40).

*4.44. 4(15)-Cycloopositene (**51**)*

$[\alpha]_D^{20} = +18.7$ ($c = 1.47$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 4.71$, 4.75 (2 q, $J_{15a\text{-}15b,3a/b} = 1.8$ Hz, 2H; H-15), 2.24 (*dm*, $J_{AB} = 11.7$ Hz, 1H; H-3a), 1.80–1.90 (*m*, 1H; H-3b), 1.75 (*dd*, $J_{9a\text{-}8} = 7.0$ Hz, $J_{AB} = 12.2$ Hz, 1H; H-9a), 1.47–1.60 (*m*, 3H), 1.47 (*br. d*, $J_{5\text{-}6} = 4.9$ Hz, 1H; H-5), 1.25 (*ddd*, $J_{6\text{-}7} = 2.9$ Hz, $J_{6\text{-}5} = 4.9$ Hz, $J_{6\text{-}8} = 7.7$ Hz, 1H; H-6), 1.20–1.29 (*m*, 1H, H-1a), 1.12 (ddt, $J_{8\text{-}7,9b} = 3.6$ Hz, $J_{8\text{-}9a} = 7.0$ Hz, $J_{8\text{-}6} = 7.7$ Hz, 1H; H-8), 0.94 (m_c, 6H; H-12,-13), 0.83–1.00 (m, 2H), 0.79 (*s*, 3H, H-14), 0.51 (*ddd*, $J_{7\text{-}6} = 2.9$ Hz, $J_{7\text{-}8} = 3.6$ Hz, $J_{7\text{-}11} = 8.0$ Hz, 1H; H-7); ^{13}C-NMR (125.8 MHz, $CDCl_3$): $\delta = 148.54$ (*s*, C-4), 103.94 (*t*, C-15), 59.84 (*d*, C-5), 54.77 (*s*, C-10), 48.69 (*d*, C-7), 44.95 (*t*, C-9), 36.96 (*t*, C-1), 35.49 (*t*, C-3), 32.48 (*d*, C-11), 24.79 (*d*, C-6), 24.58 (*d*, C-8), 23.12 (*t*, C-2), 22.00, 21.84 (2 *q*, C-12,-13), 19.71 (*q*, C-14); MS: *m/z* (%): 204 (17) [M^+], 189 (34) [M^+-CH_3], 161 (75) [$M^+-C_3H_7$], 147 (42), 133 (100), 119 (51), 105 (86), 91 (84).

*4.45. Opposita-4(15),7-diene (**52**)*

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.99$ (*d*sept, $J_{7\text{-}12/13} = 1.3$ Hz, $J_{7\text{-}6} = 9.5$ Hz, 1H; H-7), 4.39, 4.73 (2 *q*, $J_{15a\text{-}15b,3eq,5} = 1.9$ Hz, 2H; H-15), 2.75 (*ddt*, $J_d = 6.6$ Hz, $J_{6\text{-}7} = 9.5$ Hz, $J_t = 10.8$ Hz, 1H; H-6), 2.25 (*ddt*, $J_{1eq\text{-}2ax,15a} = 1.6$ Hz, $J_{3eq\text{-}2eq} = 4.7$ Hz, $J_{AB} = 13.5$ Hz, 1H; H-3eq), 1.94–2.04 (m, 1H; H-8b), 1.91 (*br. dt*, $J_{3ax\text{-}2eq} \cong 5.3$ Hz, $J_{3ax\text{-}3eq,2ax} = 13.5$ Hz, 1H; H-3ax), 1.67 (2 d, $J_{12/13\text{-}7} = 1.5$ Hz, 6H; H-12,-13); 1.48–1.73 (*m*, 5H), 1.24–1.40 (*m*, 3H), 0.68 (*s*, 3H; H-14); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 156.1$, 111.6 (2 *s*, C-4,-11), 130.43 (*d*, C-7), 105.42 (*t*, C-15), 59.92 (*d*, C-5), 43.9 (*s*, C-10), 39.72 (*t*, C-1), 39.08 (*t*, C-9), 36.29 (*d*, C-6), 35.99 (*t*, C-3), 29.05 (*t*, C-8), 25.84, 18.22 (2 *q*, C-12,-13), 23.76 (*t*, C-2), 18.52 (*q*, C-14); MS: *m/z* (%): 204 (9) [M^+], 189 (75) [M^+-CH_3], 161 (62) [$M^+-C_3H_7$], 148 (20), 135 (43), 109 (46), 82 (100), 67 (48).

*4.46. Opposita-4(15),11-diene (**53**)*

^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 4.70$, 4.68 (2 m_c, 2H; H-12), 4.78, 4.48 (2 *q*, $J = 1.7$ Hz, 2H; H-15), 2.39 (*d*, $J_{AB} = 14.6$ Hz, 1H; H-7a), 2.27 (*dm*, $J_{AB} = 13.3$ Hz, 1H; H-3a), 2.14 (ddq, $J_{6\text{-}7a} = 2.8$ Hz, $J_{6\text{-}8a} = 5.6$ Hz, $J_{6\text{-}5,7b,8b} = 11.0$ Hz, 1H; H-6), 1.85–1.95 (*m*, 2H), 1.74 (br. s, 3H, H-13), 1.69 (dd, $J_{7\text{-}6} = 10.7$ Hz, $J_{AB} = 14.6$ Hz, 1H; H-7b), 1.65–1.73 (*m*, 1H; H-1a), 1.53–1.64 (*m*, 3H), 1.50 (*dd*, $J = 8.4$ Hz, $J = 10.5$ Hz, 1H; H-9a), 1.22–1.33 (*m*, 3H), 0.66 (*s*, 3H; H-14); ^{13}C-NMR (125.8 MHz, $CDCl_3$): $\delta = 110.45$ (*t*, C-12), 104.41 (*t*, C-15), 59.45 (*d*, C-5), 43.91 (*t*, C-7), 39.52 (*t*, C-1), 39.08 (*t*, C-9), 36.20 (*t*, C-3), 34.48 (*d*, C-6), 27.76 (*t*, C-8), 23.93 (*t*, C-2), 22.77 (*q*, C-13), 18.04 (*q*, C-14); MS: *m/z* (%): 204 (2) [M^+], 189 (100) [M^+-CH_3], 148 (28), 133 (50), 121 (21), 107 (28), 91 (38).

*4.47. 4(15)-Cycloaxene (**54**)*

$[\alpha]_D^{20} = -3.2$ ($c = 12.9$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.68 (m_c, 1H; H-15a), 4.64 (*br. d*, $J_{AB} = 2.8$ Hz, 1H; H-15b), 2.10–2.15 (*m*, 2H; H-3a/b), 1.80 (*dd*, $J_{5\text{-}15b} = 0.5$ Hz, $J_{5\text{-}6} = 3.3$ Hz, 1H; H-5), 1.76 (*dt*, $J_{1eq\text{-}1ax,2ax} = 13.7$ Hz, $J_{1eq\text{-}2eq} = 3.6$ Hz, 1H; H-1eq), 1.66 (*dd*, $J_{9b\text{-}8} = 6.8$ Hz, $J_{AB} = 12.9$ Hz, 1H; H-9b), 1.63 (*d*quin, $J_{2eq\text{-}1,3} = 3.6$ Hz, $J_{AB} = 13.1$ Hz, 1H; H-2eq), 1.29–1.42 (*m*, 1H; H-2ax), 1.22 (*dm*, $J_{AB} = 13.7$ Hz, 1H; H-1ax), 1.16 (*ddt*, $J_{8\text{-}7,9a} = 3.3$ Hz, $J_{8\text{-}9b} = 6.8$ Hz, $J_{8\text{-}6} = 7.6$ Hz, 1H; H-8), 1.08 (*dt*, $J_{6\text{-}5,7} = 3.3$ Hz, $J_{6\text{-}8} = 7.6$ Hz, 1H; H-6), 1.04 (*dd*, $J_{9a\text{-}8} = 3.3$ Hz, $J_{AB} = 12.9$ Hz, 1H; H-9a), 0.92 (2 *d*, $J_{12/13\text{-}11} = 5.1$ Hz, 6H; H-12,-13), 0.88 (m_c, 1H; H-11), 0.80 (*s*, 3H; H-14), 0.45 (*dt*, $J_{7\text{-}11} = 7.7$ Hz, $J_{7\text{-}6,8} = 3.3$ Hz, 1 H, H-7); ^{13}C-NMR (125.8 MHz, $CDCl_3$): δ = 149.44 (*s*, C-4), 108.80 (*t*, C-15), 59.86 (*d*, C-5), 53.82 (*s*, C-10), 47.44 (*d*, C-7), 46.56 (*t*, C-9), 35.06 (*t*, C-1), 32.36 (*d*, C-11), 32.07 (*d*, C-6), 31.99 (*t*, C-3), 24.96 (*d*, C-8), 24.39 (*t*, C-2), 22.77 (*q*, C-14), 21.98, 21.79 (2 *q*, C-12,-13); MS: *m*/*z* (%): 204 (17) [M^+], 189 (22) [M^+CH_3], 161 (38) [$M^+-C_3H_7$], 148 (42), 133 (88), 119 (45), 108 (100), 105 (60), 93 (72), 91 (70).

*4.48. 4-Cycloopositene (**55**)*

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.68 (*br. s*, 3H; H-15), 1.54–1.93 (*m*, 10H), 1.20 (m_c, 1H), 1.03 (*s*, 3H; H-14), 1.00, 0.97 (2 *d*, $J_{12/13\text{-}11} = 6.1$ Hz, 6H; H-12,-13), 0.18 (*dt*, $J_{7\text{-}11} = 8.1$ Hz, $J_{7\text{-}6,8} = 3.1$ Hz, 1H; H-7); MS: *m*/*z* (%): 204 (59) [M^+], 189 (60) [M^+-CH_3], 161 (100) [$M^+-C_3H_7$], 147 (40), 133 (87), 119 (48), 105 (77), 91 (53).

*4.49. 3-Cycloaxene (**58**)*

$[\alpha]_D^{20} = +10$ ($c = 0.02$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.35 (*br. s*, 1H; H-3), 1.94 (m_c, 2H; H-2a/b), 1.77 (*br. d*, $J_{15\text{-}3} = 2.0$ Hz, 3H; H-15), 1.68 (*dd*, $J_{9b\text{-}8} = 7.1$ Hz, $J_{AB} = 13.2$ Hz, 1H; H-9b), 1.66 (*dt*, $J_{1b\text{-}2a} = 6.1$ Hz, $J_{1b\text{-}1a,2b} = 12.2$ Hz, 1H; H-1b), 1.44 (*br. s*, 1H; H-5), 1.19 (*dd*, $J_{9\text{-}8} = 3.1$ Hz, $J_{AB} = 13.2$ Hz, 1H; H-9a), 1.13 (m_c, 1H; H-1a), 1.10 (*ddt*, $J_{8\text{-}6} = 6.6$ Hz, $J_{8\text{-}9eq} = 7.1$ Hz, $J_{8\text{-}7,9ax} = 3.1$ Hz, 1H; H-8), 0.95, 0.93, (2 *d*, $J_{12/13\text{-}11} = 6.1$ Hz, 6H; H-12,-13), 0.97–0.79 (*m*, 2H), 0.79 (*s*, 3H; H-14), 0.39 (*dt*, $J_{7\text{-}11} = 8.6$ Hz, $J_{7\text{-}6,8} = 3.1$ Hz, 1H; H-7); MS: *m*/*z* (%): 204 (45) [M^+], 189 (38) [M^+-CH_3], 175 (15), 161 (76), 147 (32), 133 (83), 121 (68), 108 (90), 105 (69), 93 (100).

*4.50. Isodauca-4,7(14)-diene (**60**)*

^{1}H NMR (500 MHz, C_6D_6): δ = 4.76, 4.75 (2 *br. s*, 2H; H-14), 3.17 (*d*, $J_{AB} = 14.8$ Hz, 1H; H-6a), 2.70 (sept, $J_{11\text{-}12/13} = 6.8$ Hz, 1H; H-11), 2.58 (*d*, $J_{AB} = 14.8$ Hz, 1H; H-6b), 2.19 (m_c, 2H; H-3), 2.12 (m_c, 2H; H-8), 1.32–1.64 (*m*, 6 H), 1.01 (*s*, 3H; H-15), 0.99, 0.95 (2 *d*, $J_{12/13\text{-}11} = 6.9$ Hz, 6H; H-12,-13); ^{13}C-NMR (125.8 MHz, C_6D_6): δ = 150.14 (*s*, C-7), 141.97 (*s*, C-4), 138.01 (*s*, C-5), 110.02 (*t*, C-14), 50.21 (*s*, C-1), 40.90 (*t*, C-10), 38.87 (*t*, C-8), 38.72 (*t*, C-2), 33.60 (*t*, C-6), 27.60 (*t*, C-3), 27.31 (*d*, C-11), 25.03 (*t*, C-9), 24.64 (*q*, C-15), 21.29, 21.00 (2 *q*, C-12,-13); MS: *m*/*z* (%): 204 (17) [M^+], 189 (48) [M^+-CH_3], 161 (100) [$M^+-C_3H_7$], 133 (21), 91 (24).

*4.51. Isodauca-4,6-diene (**61**)*

$[\alpha]_D^{20} = -81$ ($c = 0.28$, $CHCl_3$); ^{1}H, ^{13}C NMR (Naya and Hirose, 1973; Dauben et al., 1975); MS: *m*/*z* (%): 204 (58) [M^+], 189 (100) [M^+-CH_3], 161 (94) [$M^+-C_3H_7$], 133 (31), 119 (30), 105 (43).

*4.52. Hydrogenation of **15** and **19***

Pd/C (10%, 5 mg) was added to a solution of δ-amorphene (**15**) (0.5 mg) in *n*-hexane (1 ml) and a H_2 flow was bubbled through the suspension for 1.5 min. The mixture was stirred under a H_2 atmosphere for 15 min and then filtered through Al_2O_3. The same procedure was repeated for ω-amorphene (19). The resulting solutions were used for GC–MS analysis.

4.53. Isomerization of single compounds

The following sesquiterpenes were used as enantiomeric mixtures. (a) To a solution of δ-cadinene (**4**) (≈0.5 mg) in *n*-hexane (0.5 ml) Amberlyst®15 (3 mg) was added and left at rt. The progress of the isomerization was controlled by GC. The same procedure was repeated for α-cadinene (**7**) (2 mg), β-cadinene (**17**) (0.5 mg), γ-amorphene (**12**) (≈0.25 mg), α-amorphene (**13**) (≈0.25 mg), δ-amorphene (**15**) (1 mg), selina-4(15),6-diene-(**43**) (≈0.25 mg), selina-4(15),7-diene (**44**) (≈0.25 mg), selina-3,5-diene (**46**) (≈0.25 mg), 4(15)-cycloopositene (**51**) (3 mg), 4(15)-cycloaxene (**54**) (3 mg) and isodauca-4,7(14)-diene (**60**) (≈0.25 mg). In the case of **7**, **15**, **51** and **54** the resulting solution was directly used for injection into the prep. GC and **17**, **19**, **57** and **58** were isolated. (b) To a solution of δ-cadinene (**4**) (1.5 mg) in CH_2Cl_2 (0.5 ml) $AlCl_3$ (15 mg) was added and stirred for 1 h at rt. The reaction mixture was worked up as described before. The resulting solution was fractionated by prep. GC to isolate α-calacorene (**24**), cadalene (**26**) and 4*S*,4a*S*-1,7-dimethyl-4-(methylethyl)-2,3,4,4a,5,6-hexahydronaphthalene (**31**). The same procedure was repeated for (−)-δ-cadinene (**4**) (Hardt et al., 1995), (+)-γ-cadinene (**6**), α-cadinene (**7**), (−)/(±)-γ-muurolene (**8**) and (−)/(±)-γ-amorphene (**12**) (each ≈0.25 mg). The resulting solutions were used for GC-MS analysis.

4.54. Isolation of (+)-carotol (**33**)

Minced carrot seeds (200 g) were extracted in a soxhlet apparatus with *n*-pentane/diethyl ether (1:1, 250 ml) for 2 days. The solvent was evaporated and the residue chromatographed on silica gel (400 g) with petrol ether/ethyl acetate (40:1) as eluent. The crude **33** was further purified by prep. GC yielding 30 mg (90% purity). ^{1}H NMR (Hashidoko et al., 1992), ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.32$ (m_c, 1H; H-9), 2.26 (*br. d*, $J_{AB} \cong 16$ Hz, 1H; H-10a), 2.08 (m_c, 2H; H-7a/b), 1.94 (m_c, 1H; H-6a), 1.80 (m_c, 2H; H-4,-11), 1.70 (m_c, 1H; H-10b), 1.67 (*br. s*, 3H; H-14), 1.67–1.43 (m, 4H), 1.30 (*ddd*, $J_d = 7.6$ Hz, $J_d = 8.1$ Hz, $J_{AB} = 12.2$ Hz, 1H; H-2a), 1.14 (*br. s*, 1H; OH), 1.00, 0.94 (2 *d*, $J_{12/13\text{-}11} = 6.6$ Hz, 6H; H-12,-13), 0.95 (*s*, 3H; H-15); ^{13}C-NMR (100.6 MHz, $CDCl_3$): $\delta = 138.60$ (*s*, C-8), 122.13 (*d*, C-9), 84.55 (*s*, C-5), 52.54 (*d*, C-4), 49.09 (*s*, C-1), 39.45 (*t*, C-2), 38.62 (*t*, C-10), 34.45 (*t*, C-6), 29.45 (*t*, C-7), 27.58 (*d*, C-11), 25.23 (*q*, C-14), 24.39 (*t*, C-3), 24.04 (*q*, C-12), 21.38, 21.47 (2 *q*, C-13,-15); MS: *m*/*z* (%): 222 (1) [M^+], 204 (20) [$M^+ - H_2O$], 189 (8) [$M^+ - H_2O$, -CH_3], 179 (7), 161 (100) [$M^+ - H_2O$, -C_3H_7], 151 (14), 137 (21), 123 (28), 119 (35), 107 (29), 105 (31), 97 (33), 84 (33), 81 (32), 69 (29).

4.55. Preparation of (+)-daucene (**34**)

A solution of carotol (**33**) (16 mg, 0.072 mmol) in dry pyridine (1 ml) was cooled down to 0°C and $SOCl_2$ (0.01 ml, 17 mg, 0.14 mmol) was added. The solution was stirred for 15 min. Then water (5 ml) was added and extracted 5 times with *n*-pentane. The organic layer was dried over $MgSO_4$ and the residue fractionated by prep. GC. As main product **34** (4 mg) was isolated. ^{1}H NMR, MS (Andersen et al., 1973).

4.56. Dehydrogenation of **31** and **34**

A solution of 4*S*,4a*S*-1,7-dimethyl-4-(methylethyl)-2,3,4,4a,5,6-hexahydronaphthalene (**31**) (≈0.25 mg) in toluene (1 ml) and sulfur (5 mg) were heated at 280°C for 5 h. The cooled mixture was filtered through Al_2O_3 and carefully evaporated. To the residue was added *n*-pentane (1 ml), the mixture was filtered through Al_2O_3 again and used for GC–MS analysis. The procedure was repeated for daucene (**34**).

4.57. Isomerization of germacrene C (**42**)

Germacrene C (0.5 mg), isolated from *Preissia quadrata* (König et al., 1996), in *n*-hexane (0.5 ml) and silica gel (3 mg) was left at rt for 24 h. The resulting solution was used directly for GC–MS analysis.

4.58. Irradiation of germacrene D (**1**)

(a) An enantiomeric mixture of **1** [(−):(+) = 1.3:1, 20 mg, 0.1 mmol] in *n*-hexane (3 ml) [$c(1) = 32.7$ mmol/l] was degased with argon and irradiated for 3 h at 254 nm. The resulting solution was fractionated by prep. GC. (b) The procedure was repeated in the presence of sulfur (0.8 g) with stirring. The solvent was evaporated and the residue was fractionated by column chromatography on silica gel with petrol ether as eluent. (c) The same enantiomeric mixture of **1** (4 mg, 0.02 mmol) in acetone (1 ml) [$c(1) = 19.6$ mmol/l] was degased and irradiated for 2 min at 300 nm. The resulting solution was used for GC-MS analysis.

4.59. β-Bourbonene (**64**)

^{1}H NMR (Tomioka et al., 1989), ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.69$, 4.71 (2 *s*, 2H; H-15a/b), 2.54 (*m*, 1H; H-3a), 2.40 (*dd*, $J_{5\text{-}1} = 3.6$ Hz, $J_{5\text{-}6} = 7.1$ Hz, 1H; H-5), 2.24–2.33 (*m*, 2H; H-1,-3b), 1.89 (*m*, 1H; H-8a), 1.80 (*dd*, $J = 8.1$ Hz, $J = 13.2$ Hz, 1H; H-2a), 1.45–1.63 (*m*, 6H), 1.24 (*d*sept, $J_{11\text{-}12,13} = 6.6$ Hz, $J_{11\text{-}7} = 9.2$ Hz, 1H; H-11), 0.99 (*s*, 3H; H-14), 0.85, 0.87 (2 *d*, $J_{12/13\text{-}11} = 6.6$ Hz, 6H; H-12,-13); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 157.57$ (*s*, C-4), 103.59 (*t*, C-15), 56.76 (*d*, C-7), 54.96 (*d*, C-6), 47.87 (*d*, C-5), 45.68 (*d*, C-1), 43.15 (*s*, C-10), 42.02 (*t*, C-9), 33.81 (*t*, C-3), 31.14 (*d*, C-11), 29.98 (*t*, C-8), 27.30 (*t*, C-2), 21.56 (*q*, C-14), 21.51, 21.83 (2 *q*, C-12,-13); MS: *m*/*z* (%): 204 (1) [M^+], 161 (25) [$M^+ - C_3H_7$], 123 (50) [$M^+ - C_6H_9$], 81 (100) [$M^+ - C_9H_{13}$], 80 (71) [$M^+ - C_9H_{14}$].

4.60. β-Copaene (**65**)

^{1}H NMR, ^{13}C NMR (Kulkarni et al., 1987); MS: *m*/*z* (%): 204 (7) [M^+], 189 (3) [$M^+ - CH_3$], 161 (100) [$M^+ - C_3H_7$], 120 (21), 119 (22), 105 (37), 91 (33), 81 (28).

4.61. β-Ylangene (**16**)

^{1}H NMR, ^{13}C NMR (Kulkarni et al., 1987); MS: *m*/*z* (%): 204 (9) [M^+], 189 (6) [$M^+ - CH_3$], 161 (100) [$M^+ - C_3H_7$], 120 (88), 105 (53), 91 (47), 79 (31).

4.62. Monoepi-β-Bourbonene (**71**, **72** or **73**)

MS: *m*/*z* (%): 204 (3) [M^+], 189 (4) [$M^+ - CH_3$], 161 (18) [$M^+ - C_3H_7$], 123 (87) [$M^+ - C_6H_9$], 81 (100) [$M^+ - C_9H_{13}$], 80 (86) [$M^+ - C_9H_{14}$].

4.63. Mintsulfide (**69**)

^{1}H NMR (Yoshida et al., 1979), ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.61$, 4.67 (2 *t*, $J_{15a\text{-}b,3a/b} = 2$ Hz, 2H; H-15a/

b), 3.69 (*d*, $J_{5\text{-}6}$ = 6.1 Hz, 1H; H-5), 2.88 (*t*, $J_{1\text{-}2a/b}$ = 3.3 Hz, 1H; H-1), 2.38–2.62 (*m*, 2H; H-3a/b), 2.14–2.25 (*m*, 3H; H-2a/b,-6), 1.24–2.00 (*m*, 6H), 1.35 (*s*, 3H; H-14), 0.86, 0.90 (2 *d*, $J_{12/13\text{-}11}$ = 6.6 Hz, 6H; H-12,-13); MS: *m*/*z* (%): 236 (17) [M^+], 123 (100) [$M^+-C_6H_9S$], 112 (78), 79 (69).

4.64. Synthesis of 1,5-diepi-β-bourbonene (**68**)

8 was prepared from **69** according to described procedures (Uyehara et al., 1981, 1988). **68** and **87** were obtained in a ratio of 2.7:1 and were separated by prep. GC.

4.65. 1,5-diepi-β-Bourbonene (**68**)

^{1}H NMR (Uyehara et al., 1988), ^{1}H NMR: ($CDCl_3$, 400 MHz): δ = 4.71, 4.97 (2 *br. s*, 2H; H-15), 3.09 (*dd*, $J_{5\text{-}1}$ = 8.1 Hz, $J_{5\text{-}6}$ = 9.4 Hz, 1H; H-5), 2.44 (*t*, $J_{1\text{-}2,5}$ = 8.1 Hz, 1H; H-1), 2.42 (m, 1H; H-3a), 2.31 (*dd*, $J_{3b\text{-}2}$ = 9.2 Hz, J_{AB} = 15.7 Hz, 1H; H-3b), 1.87 (*dd*, $J_{6\text{-}7}$ = 6.9 Hz, $J_{6\text{-}5}$ = 9.4 Hz, 1H; H-6), 1.55–1.80 (*m*, 4H, H-2a/b,-8a,-9a), 1.51 (*m*, 1H; H-7), 1.27 (*d*sept, $J_{11\text{-}7}$ = 9.1 Hz, $J_{11\text{-}12,13}$ = 6.6 Hz, 1H; H-11), 1.07–1.17 (*m*, 2H; H-8b,-9b), 1.11 (*s*, 3H; H-14), 0.81, 0.84 (2 *d*, $J_{12/13\text{-}11}$ = 6.6 Hz; 6H; H-12,-13); MS: *m*/*z* (%): 204 (1) [M^+], 161 (26) [$M^+-C_3H_7$], 123 (40) [$M^+-C_6H_9$], 81 (100) [$M^+-C_9H_{15}$], 80 (74) [$M^+-C_9H_{14}$].

4.66. Isodauca-6,9-diene (**87**)

^{1}H NMR (Uyehara et al., 1988), ^{1}H NMR: ($CDCl_3$, 400 MHz): δ = 5.42 (*m*, 2H), 5.31 (*m*, 1H), 2.83, 2.55 (2 *m*, 2H; H-8), 2.0–1.0 (*m*, 7H), 1.70 (*s*, 3H; H-14), 0.82, 0.88 (2 *d*, $J_{12/13\text{-}11}$ = 7.1 Hz, H; H-12,-13); MS: *m*/*z* (%): 204 (13) [M^+], 189 (13) [M^+-CH_3], 161 (84) [$M^+-C_3H_7$], 119 (88), 105 (100), 91 (41).

4.67. Isomerization of β-bourbonene (**64**) and 1,5-diepi-β-bourbonene (**68**)

A solution of **64** [(−):(+) = 1.3:1, 1.5 mg, 7.4×10^{-3} mmol] in $CDCl_3$ (0.6 ml) [*c*(**64**) = 0.12 mol/l] was mixed with Amberlyst®15 (8 mg) and left at rt until **64** had almost disappeared (GC control). The catalyst was filtered off. The procedure was repeated with **68**.

4.68. α-Bourbonene (**67**)

^{1}H NMR (White and Gupta, 1968), ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.26 (*s*, 1H; H-3), 2.43–2.48 (*m*, 2H), 2.31–2.36 (*m*, 2H), 1.95 (*ddt*, J_t = 6.4 Hz, J_d = 9.1 Hz, J_d = 12.7 Hz, 1H), 1.69 (*br. s*, 3H; H-15), 1.65 (*br. s*, 1H), 1.44–1.62 (*m*, 3H), 1.39 (*ddd*, *J* = 6.1 Hz, *J* = 9.2 Hz, *J* = 12.3 Hz, 1H), 1.31 (*ddt*, J_d = 6.6 Hz, J_d = 8.7 Hz, J_t = 13.2 Hz, 1H), 1.02 (*s*, 3H; H-14), 0.86, 0.87 (2 *d*, $J_{12/13\text{-}11}$ = 6.6 Hz, 6H; H-12,-13); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.11 (*s*, C-4), 124.10 (*d*, C-3), 54.77, 53.53, 51.24, 44.95 (*s*, C-10), 43.28, 31.07, 29.70/33.31/41.39 (3 *t*, C-2,-8,-9), 22.50, 21.22, 21.04, 13.82; MS: *m*/*z* (%): 204 (1) [M^+], 123 (42) [$M^+-C_6H_9$], 81 (84) [$M^+-C_9H_{15}$], 80 (100) [$M^+-C_9H_{14}$].

4.69. 1,5-diepi-α-Bourbonene (**70**)

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.39 (*br. s*, 1H; H-3), 3.08 (*br. t*, $J_{5\text{-}1,6}$ = 8.4 Hz, 1H; H-5), 2.44 (*t*, $J_{1\text{-}2a,5}$ = 8.4 Hz, 1H; H-1), 2.31 (*m*, 1H; H-2a), 2.18 (*br. d*, J_{AB} ≈17 Hz, 1H; H-2b), 2.00 (*dd*, $J_{6\text{-}7}$ = 5.6 Hz, $J_{6\text{-}5}$ = 8.4 Hz, 1H; H-6), 1.73 (*m*, 1H; H-8a), 1.68 (*br. s*, 3H; H-15), 1.50–1.65 (*m*, 2H; H-7,-9a), 1.34 (*d*sept, $J_{11\text{-}7}$ = 8.5 Hz, $J_{11\text{-}12,13}$ = 6.6 Hz, 1H; H-11), 1.09–1.26 (*m*, 2H; H-8b,-9b), 1.09 (*s*, 3H; H-14), 0.86, 0.89 (2 *d*, $J_{12/13\text{-}11}$ = 6.6 Hz, 6H; H-12,-13); MS: *m*/*z* (%): 204 (1) [M^+], 189 (2) [M^+-CH_3], 161 (8) [$M^+-C_3H_7$], 123 (62) [$M^+-C_6H_9$], 81 (83) [$M^+-C_9H_{15}$], 80 (100) [$M^+-C_9H_{14}$].

4.70. Thermal treatment of germacrene D (**1**)

(a) In a typical experiment an enantiomeric mixture of **1** [(+):(−) = 5.7:1, 13 mg, 0.06 mmol] in *n*-hexane (0.7 ml) [*c*(1) = 0.91 mol/l] was heated in a sealed tube at 220–240°C for 0.5–2 days. The resulting solution was prefractionated by column chromatography on silica gel at −25°C with *n*-pentane as eluent. The fractions were further separated by prep. GC. (b) 100 μl of the enantiomer mixture of **1** in *n*-hexane was injected in the prep. GC at an injector temperature of 400°C and the rearrangement products were fractionated.

4.71. Isogermacrene D (**74**)

$[\alpha]_D^{20}$ = −320 (*c* = 0.042, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.78 (*d*, $J_{5\text{-}6}$ = 11.4 Hz, 1H; H-5), 5.11 (*dd* = *dt*, $J_{6\text{-}5,7}$ = 11.4 Hz, 1H; H-6), 5.07 (*dd*, J_d = 4.6 Hz, J_d = 11.7 Hz, 1H; H-1), 4.87, 4.88 (2 *br. s*, 2H; H-15), 2.29–2.52 (*m*, 3H; H-7,-2a,-9a), 2.18 (*br. d*, J_{AB} = 13.2 Hz, 1H; H-3a), 2.03 (*dt*, $J_{3b\text{-}2a/b}$ = 3.6 Hz, $J_{3b\text{-}2a/b,3a}$ = 13.2 Hz, 1H; H-3b), 1.79 (*m*, 1H, H-2b), 1.67 (*ddt*, J_d = 3.1 Hz, J_d = 4.1 Hz, J_t = 13.2 Hz, 1H; H-8b), 1.61 (*m*, 1H; H-9b), 1.60 (*br. s*, 3H; H-14), 1.44 (okt, $J_{11\text{-}7,12,13}$ = 6.6 Hz, 1H; H-11), 1.00 (*ddt*, J_d = 2.6 Hz, J_d = 4.1 Hz, J_t = 13.2 Hz, 1H; H-8a), 0.92, 0.94 (2 *d*, $J_{12/13\text{-}11}$ = 6.6 Hz, 6H; H-12,-13); ^{13}C NMR (100.6 MHz, C_6D_6): δ = 146.44 (*q*), 135.57, 134.66 (*q*), 131.88, 125.92, 113.36 (*s*), 41.03, 36.98 (*s*), 32.65, 29.11 (*s*), 28.51 (*s*), 26.23 (*s*), 22.36, 20.94, 20.81; MS: *m*/*z* (%): 204 (23) [M^+], 189 (7), 161 (100) [$M^+-C_3H_7$], 133 (25), 119 (34), 105 (58), 93 (48), 91 (60), 81 (51).

4.72. ε-Muurolene (**75**)

^{1}H NMR, ^{13}C NMR (Köster et al., 1986), ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.64, 4.67 (2 *br. s*, 2H), 4.59 (*m*,

2H), 2.43–2.52 (*m*, 2H), 2.31 (*dm*, $J = 12.7$ Hz, 1H), 1.95–2.19 (*m*, 5H), 1.89 (*dq*, $J_d = 4.7$ Hz, $J_q = 12.6$ Hz, 1H), 1.0–1.73 (m, 5H), 0.89, 0.70 (2 *d*, $J_{12/13\text{-}11} = 7.1$ Hz, 6H; H-12,-13); MS: *m/z* (%): 204 (14) [M^+], 189 (5), 176 (3), 161 (100) [$M^+ - C_3H_7$], 148 (13), 133 (21), 119 (30), 105 (45), 93 (45), 91 (49), 81 (62).

4.73. ϵ-Amorphene (76)

^{1}NMR, ^{13}C NMR (Köster et al., 1986), ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.75, 4.91 (2 *q*, $J = 2.2$ Hz, 2H), 4.56 (*br. s*, 2 H), 2.33–2.44 (*m*, 2H), 2.28 (*br. s*, 1H), 2.20 (*ddt*, $J_t = 2.2$ Hz, $J_d = 5.1$ Hz, $J_d = 13.2$ Hz, 1H), 1.10–2.10 (*m*, 10H), 0.90, 0.91 (2 *d*, $J_{12/13\text{-}11} = 6.6$ Hz, 6H, H-12,-13); MS: *m/z* (%): 204 (23) [M^+], 189 (7), 161 (100) [$M^+ - C_3H_7$], 137 (25), 120 (50), 105 (49), 93 (51), 91 (56), 81 (63).

4.74. Acidic rearrangement of isogermacrene D (74)

A solution of **74** [(+):(−) = 5.7:1, 2 mg, 9.8×10^{-3} mmol] in *n*-hexane (1 ml) [*c*(**74**) = 9.8 mmol/l] was mixed with Amberlyst®15 (8 mg) and left at rt until **74** had almost disappeared (GC control). The solution was filtered, the catalyst washed once with *n*-hexane (0.5 ml) and the resulting solution was used for GC–MS analysis.

4.75. Irradiation of isogermacrene D (74)

(a) An enantiomeric mixture of **74** [(+):(−) = 5.7:1, 8 mg, 0.04 mmol] in *n*-hexane (2 ml) [*c*(**74**) = 19.6 mmol/l] was degassed with argon and irradiated for 3 h at 254 nm. The resulting solution was fractionated by prep. GC. (b) The same enantiomeric mixture of **74** (2.5 mg, 0.01 mmol) in acetone (1 ml) [*c*(**74**) = 12.2 mmol/l] was degassed and irradiated for 2 min at 300 nm. The resulting solution was used for GC–MS analysis.

4.76. rac-δ-Elemene (79)

(Ganter and Keller-Wojtkiewicz, 1971). MS: *m/z* (%): 204 (3) [M^+], 189 (3), 161 (20), 136 (68), 121 (100), 93 (91), 91 (31).

4.77. rac-cis,syn,cis-Tricyclo[6.2.0.0^{2,7}]-1,7-dimethyl-4-(methylethyl)dec-3-ene (80)

^{1}H NMR: (C_6D_6, 400 MHz): $\delta = 5.42$ (*br. s*, 1H; H-3), 2.33 (*dt*, $J_{10a\text{-}9a,10b} = 8.6$ Hz, $J_{10a\text{-}9b} = 11.7$ Hz, 1H; H-10a), 2.15–2.29 [*m*, 2H; H-9a + -C<u>H</u>(CH_3)$_2$], 2.14 (*br. s*, 1 H; H-2), 2.05 (*br. d*, $J_{8\text{-}9b} = 8.1$ Hz, 1H; H-8), 1.82–2.00 (*m*, 4H), 1.61 (m_c, 1H; H-10b), 1.24 (m_c, 1H; H-6b), 1.23 (s, 3H; C1-C<u>H</u>$_3$), 1.08 (*s*, 3H; C7-C<u>H</u>$_3$), 1.06 [*d*, $J_{CH(CH3)2\text{-}CH(CH3)2} = 6.6$ Hz, 6H;-CH(C<u>H</u>$_3$)$_2$]; ^{13}C-NMR: (C_6D_6, 125.8 MHz): $\delta = 123.6$ (*s*, C-4), 119.3 (*d*, C-3), 51.4 (*d*, C-2), 47.4 (*d*, C-8), 39.9, 33.9 (2 *s*, C-1,-7), 36.1 [*d*, <u>C</u>H(CH_3)$_2$], 30.7 (*q*, C7-<u>C</u>H$_3$), 29.0 (*t*, C-6), 27.4 (*t*, C-5), 26.1 (*q*, C1-<u>C</u>H$_3$), 24.0, 19.6 (2 *t*, C-9,-10), 21.8, 21.3 [2 *q*, CH(<u>C</u>H$_3$)$_2$]; MS: *m/z* (%): 204 (5) [M^+], 189 (13), 161 (58) [$M^+ - C_3H_7$], 136 (52), 121 (100), 105 (49), 93 (86), 91 (51).

4.78. cis-Bicyclo[7.1.1]-5-methyl-8-(methylethyl)undeca-1(10),4-diene (81)

^{1}H NMR (400 MHz, C_6D_6): $\delta = 5.66$ (*s*, 1H; H-10), 5.12 (*dd*, $J_d = 7.5$ Hz, $J_d = 8.7$ Hz, 1H; H-4), 3.04 (*br. s*, 1H; H-9), 2.34 (*br. s*, 2H; H-11a/b), 1.83–2.03 (*m*, 6H), 1.71 (*s*, 3H; C5-C<u>H</u>$_3$), 1.64 [*d*sept, $J_{CH(CH3)2\text{-}8} = 2.9$ Hz, $J_{CH(CH3)2\text{-}CH(CH3)2} = 6.6$ Hz, 1H; C<u>H</u>(CH_3)$_2$], 1.56–1.71 (m, 1H; H-6a), 1.21–1.33 (*m*, 2H; H-7a,-8), 0.89, 0.92 [2 d, $J_{CH(CH3)2\text{-}CH(CH3)2} = 6.6$ Hz, 6H; CH(C<u>H</u>$_3$)$_2$]; MS: *m/z* (%): 204 (2) [M^+], 189 (8), 161 (51) [$M^+ - C_3H_7$], 133 (27), 119 (42), 105 (61), 93 (66), 91 (69), 81 (78), 41 (100).

4.79. Thermal treatment of tricyclus 80

rac-**80** (0.5 mg, 2.5×10^{-3} mmol) in *n*-hexane (0.7 ml) [*c*(**80**) = 35.0 mmol/l] was heated in a sealed tube at 50–60°C for 8 h and **79** was identified by GC and GC–MS as a minor compound.

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