DOI: 10.1002/chem.200801382

A Gold-Catalyzed Entry into the Sesquisabinene and Sesquithujene Families of Terpenoids and Formal Total Syntheses of Cedrene and Cedrol

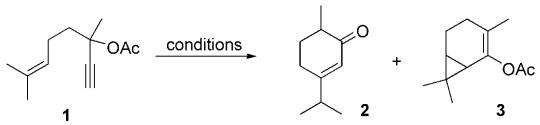
Alois Fürstner* and Andreas Schlecker[a]

Abstract: A concise entry into the bicyclic cyclopropyl ketone derivatives **5** and **6** by way of a gold-catalyzed Ohloff–Rautenstrauch-type enyne cycloisomerization is described. The required substrates were prepared by an asymmetric addition of the branched allylzinc reagent **21** to the alkynyl aldehyde **17** mediated by the deprotonated bisoxazoline (BOX) ligand **22**. Compounds **5** and **6** were then converted into a host of different members of the sesquisabina- and sesquithuja families of terpenoids, inter alia with the aid of iron-catalyzed cross-coupling reactions. As the relative and absolute configuration of **5** and **6** could be unambiguously established, the synthetic samples allowed the previously unknown stereostructures of various such terpenoids to be unraveled, including *cis*-sesquisabinene hydrate (**33**), 7-*epi*-sesquithujene (**36**), sesquisabinene B (**37**) and epoxysesquithujene (**45**). Moreover, the preparation of **6** also constitutes a formal total synthesis of cedrene (**11**) and cedrol (**12**).

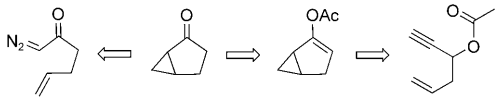
Keywords: cyclopropanes · gold · natural products · rearrangement · terpenoids

Introduction

Even though the cycloisomerization of enynes with migratory participation of a propargylic carboxylate group was originally discovered by Ohloff with the aid of $ZnCl_2$ as stoichiometric promoter,[1] the true value of such transformations can only be garnered since the superior performance of carbophilic π-acid catalysts has been recognized (Scheme 1).[2,3] In conceptual terms, platinum- or gold-catalyzed Ohloff-type reactions open entry into cyclopropyl carbonyl derivatives and as such represent a safe and convenient alternative to the cyclization of unsaturated α-diazoketones (Scheme 2).[4–10]



Scheme 1. Comparison of the greatly different efficiencies of a conventional Lewis acid and a π-acidic gold catalyst in the original Ohloff cycloisomerization reaction.



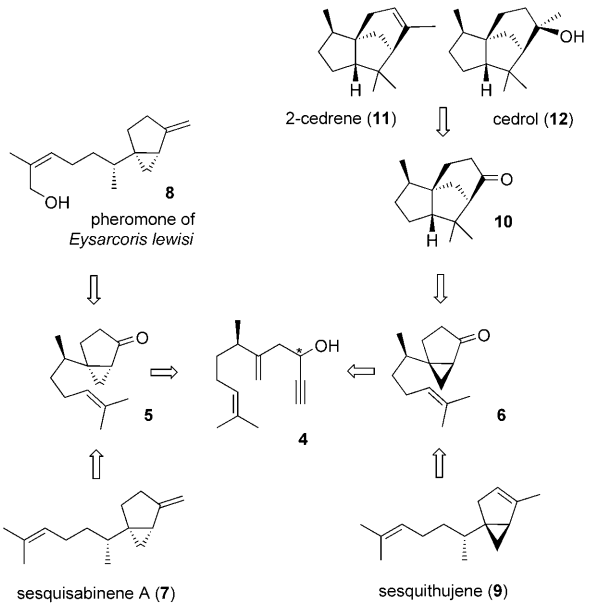
Scheme 2. Synthetic equivalence of classical α-diazoketone methodology and noble metal catalyzed propargyl acetate rearrangements.

In pursuit of our previous investigations in this field,[5,6,8,11–14] we now present a concise approach to bisabolane-type sesquiterpenes by way of stereospecific gold-catalyzed cycloisomerizations (Scheme 3). Since the first isolation of sesquisabinene (**7**) from pepper (*Piper nigrum*)[15] and of sesquithujene (**9**) as a major constituent of the essential oil of ginger (*Zingiber officinale*),[15] many relatives of these natural products have been isolated which differ from the parent compounds in the peripheral functionalization pattern and/or in stereochemical terms;[16] in many cases, however, remained the stereostructures of these congeners uncertain or even completely unknown. It is also remarkable that such bicyclic compounds are not only prevalent in the plant kingdom but were also isolated from animals as exemplified by the aggregation pheromone of the bug *Ey-*

[a] Prof. A. Fürstner, Dipl. Chem. A. Schlecker
Max-Planck-Institut für Kohlenforschung
45470 Mülheim/Ruhr (Germany)
Fax: (+49) 208-306-2994
E-mail: fuerstner@mpi-muelheim.mpg.de

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200801382.

sarcoris lewisi (Distant) (**8**), a severe pest in rice fields in Northern Japan.[17,18] Finally, it should be mentioned that the key synthetic intermediate **6** required for the preparation of sesquithujene and relatives also constitutes a known precursor of cedrene (**11**) and cedrol (**12**).[19,20] Our stereoselective approach to **6** hence represents a formal total synthesis of these renowned targets too (Scheme 3).

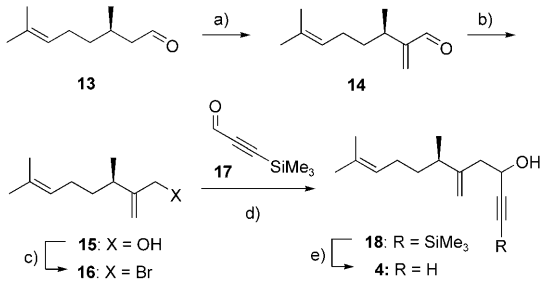


Scheme 3. Descent of prototype terpenoids of the sesquisabina and sesquithuja families as well as of cedrene and cedrol from the two diastereomeric [3.1.0]-bicyclohexanone derivatives **5** and **6**.

Results and Discussion

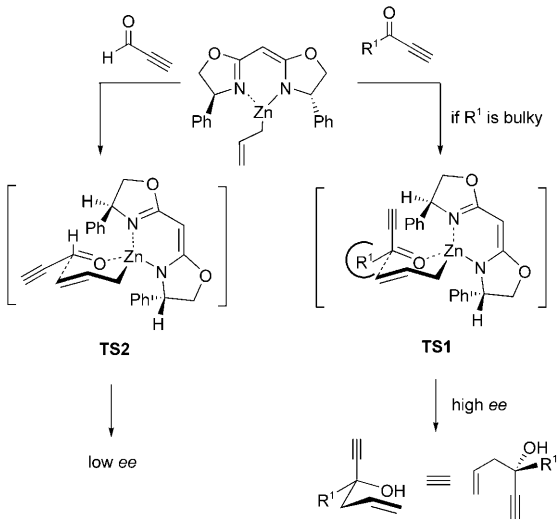
Asymmetric synthesis of the cyclization precursors: The preparation of the required substrates for the envisaged noble metal catalyzed cycloisomerization reaction commenced with the large scale adaptable methylenation of (*R*)-citronellal (**13**) (Scheme 4).[21] Reduction of the resulting enal **14**[22] and subsequent conversion of alcohol **15** into the corresponding allylic bromide **16** set the stage for the addition of a derived organometallic reagent onto aldehyde **17**. Since noble metal-catalyzed rearrangements are known to transmit the configuration of the propargylic center of enynes of type **4** into the product stereostructure,[3–9] it was of utmost importance to control the course of this addition step. Unfortunately, however, some of the most widely practiced asymmetric allylation reactions for aldehydes either failed in this particular case or resulted in disappointingly low diastereomeric ratios.[23]

As a consequence, we faced the need to develop an alternative method for the selective preparation of either isomer of product **4**. Inspiration was provided by a paper published by Nakamura et al., who were the first to describe highly asymmetric allylations of alkynyl carbonyl derivatives with the aid of allylzinc reagents endowed with a bisoxazoline



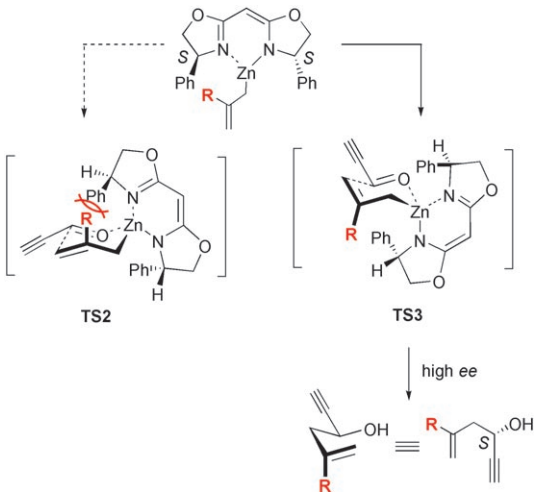
Scheme 4. a) *para*-Formaldehyde, pyrrolidine, propionic acid, *i*PrOH, 45 °C, 88 %; (ref. [21]); b) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH, 0 °C, 98 %; c) Br_2, PPh_3, imidazole, CH_2Cl_2, 0 °C, 87 %; d) see text and Table 1; e) K_2CO_3, MeOH.

(BOX) derived ligand set (Scheme 5).[24,25] In this transformation, however, the best selectivities were observed for ketones bearing bulky R^1 substituents (e.g. R^1 = adamantyl, *tert*-butyl), whereas aldehydes gave rather poor results.[24] This fact is deemed to reflect the peculiarities of a chair-like transition state **TS1**, wherein the massive R^1 group forces the alkynyl moiety into an axial orientation such that it can be recognized by the local chiral environment of the C_2-symmetric BOX ligand (Scheme 5).[24] Aldehydes (R^1 = H) obviously will not attain this crucial array; their alkynyl group prefers the equatorial position in **TS2**, wherein it points away from the stereodetermining ligand framework.



Scheme 5. Asymmetric allylation of alkynyl ketones ($R^1 \neq$ H) according to Nakamura et al., cf. ref. [24].

Even though the recorded data for aldehydes seem to speak against the use of this method en route to **4**, a more careful analysis is warranted. Nakamura et al. reported the transfer of unsubstituted allyl groups to aldehydes only,[24] whereas in our case a large substituent R will reside on the central carbon atom of the allylzinc reagent. Its presence should render **TS2** highly unfavorable due to a clash of R with the ligand's phenyl substituent (Scheme 6). As a result,

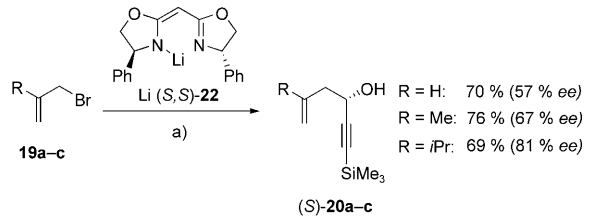


Scheme 6. Proposed asymmetric allylation of alkynyl aldehydes with substituted allylzinc reagents (R ≠ H).

a transition-state topology of type **TS3** with an inverted chair might ensue, wherein the R group should engage in a productive crosstalk with the chiral ligand sphere of the zinc atom. As this interaction renders the equatorial disposition of the aldehyde's alkynyl group inconsequential, appreciable levels of stereoinduction can be expected.[26]

The experimental results nicely matched the predictions of this model. As evident from Scheme 7, the addition of allylzinc reagents to aldehyde **17** under Nakamura conditions become increasingly enantioselective with increasing bulk of the substituent at C2. Likewise, addition of the chiral zinc reagent **21** to the same aldehyde partner showed appreciable levels of diastereocontrol (Scheme 8 and Table 1). Whereas the reaction of unmodified **21** gave a ≈1:1 mixture (entry 1), ligation with deprotonated (*S*,*S*)-**22**[27] provided the forecasted *S*-configured alcohol (*S*)-**18** with good selectivity (dr 10.4:1, entry 3). Importantly, the course of the addition is reagent-controlled, as the (*R*,*R*)-configured ligand furnished the opposite isomer as the major product (dr 1:5.2, entry 4). Separation of the enriched samples by preparative HPLC followed by cleavage of the silyl group afforded (*S*)-**4** and (*R*)-**4** in diastereomerically pure form each. In both cases was the configuration of the newly formed chiral center unambiguously established by the Mosher method (cf. Supporting Informaton).[28] In line with the proposed transition-state model, more encumbered BOX-type ligands, which are unable to acquaint the axial R group for steric reasons, were found inappropriate (Table 1, entries 5 and 6).

Gold-catalyzed cycloisomerizations, stereochemical calibration, and total synthesis of the insect aggregation pheromone 8: Conversion of the propargylic alcohols (*S*)-**4** and (*R*)-**4** into the corresponding *p*-nitrobenzoates (*S*)-**23** and (*R*)-**23**, respectively, followed by $AuCl_3$(pyridine)[29]-catalyzed cycloisomerization furnished the desired [3.1.0]bicyclohexane derivatives **5** and **6** after hydrolysis of the enol esters primarily formed (Scheme 9).[30,31]

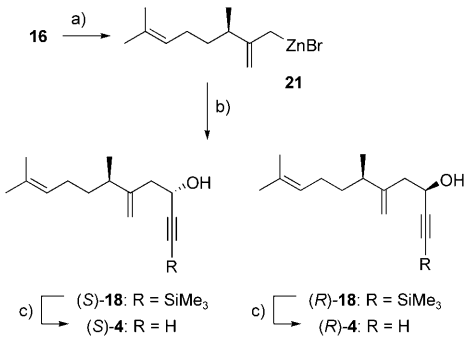


Scheme 7. Asymmetric allylation of aldehyde **17** with differently substituted allylzinc reagents: a) i) Zn, THF; ii) (*S*,*S*)-**22**, *n*BuLi; iii) aldehyde **17**, −100 °C.

Table 1. Addition of the allylzinc reagent **21** to aldehyde **17** in the absence or presence of deprotonated BOX-type ligands.[a]

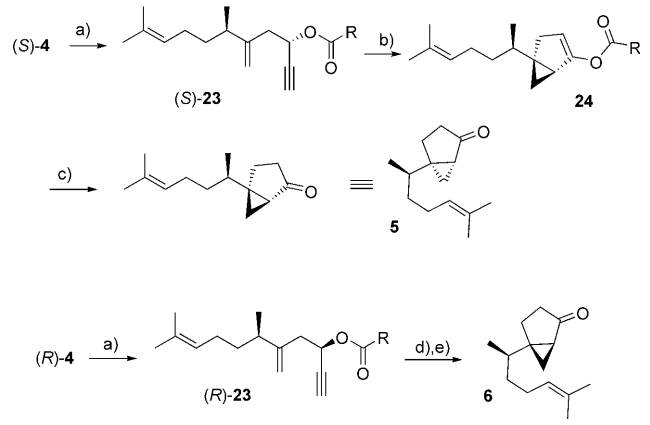
Entry	Ligand	Yield [%]	(*S*)-**18**/(*R*)-**18**
1	–	77	1:1[b]
2	(*S*,*S*)-**22**	74	8.8:1[c]
3		70	10.4:1
4	(*R*,*R*)-**22**	72	1:5.2
5		[d]	1:1
6		[e]	

[a] Unless stated otherwise, all reactions were performed by syringe pump addition of aldehyde **17** to the organozinc reagent at −100 °C in THF; the material was then desilylated with K_2CO_3 in MeOH. The yield refers to the overall yield over both operations; [b] at 0 °C; [c] at −78 °C; [d] as the reaction was unselective according to GC, the product was not isolated; [e] no reaction.



Scheme 8. Reagent-controlled asymmetric allylation: a) Zn, THF, 40 °C; b) see Table 1; c) K_2CO_3, MeOH, 99 %.

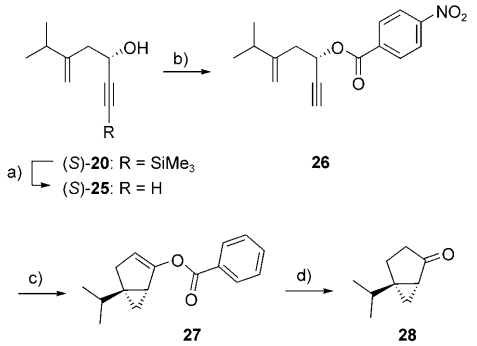
The stereochemical relationship between the newly formed cyclopropane ring and the methyl branch in the side chain of **5** and **6** is by no means trivial to assign because of the conformational freedom in this part of the molecules. Even the detailed analysis of high field NMR spectra and



Scheme 9. a) 4-Nitrobenzoyl chloride, pyridine, DMAP, CH_2Cl_2, 0 °C → RT, 58 % (*S*)-**23**; 62 % (*R*)-**23**; b) $AuCl_3$(pyridine) (10 mol %), CH_2Cl_2, 73 % (dr ≈ 19:1); c) LiOH, THF/H_2O, 91 %; d) $AuCl_3$(pyridine) (10 mol %), CH_2Cl_2, 76 % (dr 15:1); e) LiOH, THF/H_2O, 89 %.

NOESY data remains ambiguous. These difficulties also transpire from previous isolation papers, wherein the stereostructure of several members of the sesquisabina- or sesquithuja families either remained undetermined or were merely inferred by analogy to sister compounds which themselves are more or less well characterized; in these cases, the assigned structures should be met with caution (see below).

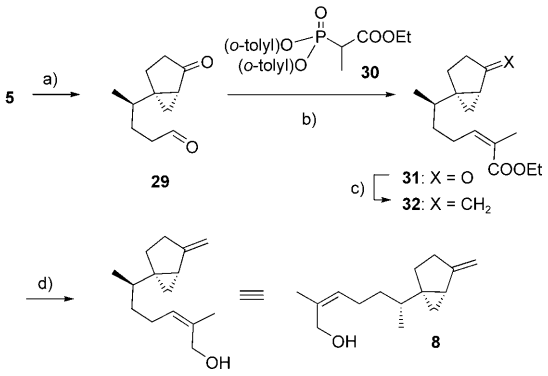
As **5** and **6**, however, constitute the corner stones of our projected synthesis of all natural products of these classes of terpenes, it was of utmost importance to determine the stereochemical course of the gold-catalyzed cycloisomerization beyond doubt. The assignments shown in Scheme 9 were initially made by analogy to recorded cases.[8] Additional information was gathered by conversion of (−)-(*S*)-**20c** into sabina ketone (+)-(1*R*,5*S*)-**28**,[32,33] a product of known stereostructure and parent compound of the entire family of terpenoids embodying a bicyclo[3.1.0]hexane skeleton (Scheme 10).



Scheme 10. a) K_2CO_3, MeOH, 89 %; b) 4-nitrobenzoyl chloride, DMAP, CH_2Cl_2, pyridine, 0 °C → RT, 91 %; c) $AuCl_3$(pyridine) (10 mol %), CH_2Cl_2, 89 %; d) LiOH, THF/H_2O, 53 %.

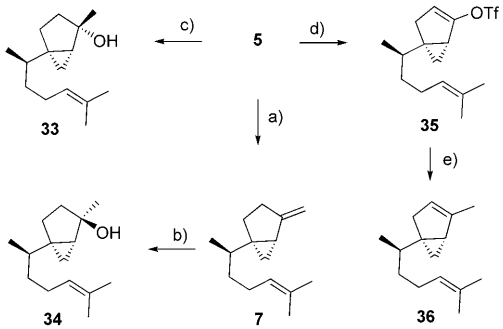
Even though this example provides compelling evidence, further confirmation for the assignments made in Scheme 9 was sought. To this end, we turned our attention to the aggregation pheromone **8** produced by male *Eysarcoris lewisi* (Distant) bugs, which cause severe damage in rice fields in Japan.[17] Mori and coworkers have previously prepared this compound and could determine its stereostructure by chiroptical means.[18] Therefore **8** constitutes an additional stereochemical calibration point.

Its synthesis from ketone (+)-**5** was accomplished by a minor modification of the published route (Scheme 11).[18] The analytical and spectroscopic properties of our samples of synthetic **8** were in excellent agreement with the reported data,[18] including the $[\alpha]_D$. This comparison firmly establishes the stereochemical course of the gold-catalyzed cycloisomerization reactions shown in Scheme 9 and hence sets a sound basis for the preparation of all other sesquiterpenoids of the sabina- and thuja series.



Scheme 11. a) O_3, CH_2Cl_2, −78 °C, then Me_2S, Et_3N, 84 %; b) **30**, NaH, THF, −78 °C → 0 °C; c) [Ph_3PCH_3]Br, *n*BuLi, THF, −78 °C → RT, 50 % (over both steps); d) Dibal-H, toluene/THF, −78 °C, 88 %.

Total synthesis of sesquisabinene, sesquithujene and relatives: With the stereostructure of ketone **5** being secured, it required only the treatment of this compound with Ph_3P=CH_2 in THF to obtain (−)-**7** (Scheme 12). Its spectroscopic data are in full agreement with those of sesquisabinene.[15,16,34] It is unfortunate, however, that the rotatory power of this natural product has not been reported in the



Scheme 12. a) Ph_3P=CH_2, THF, −78 °C → RT, 69 %; b) $Hg(OAc)_2$, THF/H_2O, then $NaBH_4$, NaOH, 53 %; c) MeMgBr, Et_2O, 0 °C, 95 %; d) LDA, THF, −78 °C, then 2-pyridyl-NTf_2, 0 °C; e) MeMgBr, Fe(acac)$_3$ (10 mol %), THF/NMP, −30 °C, 60 % (over both steps).

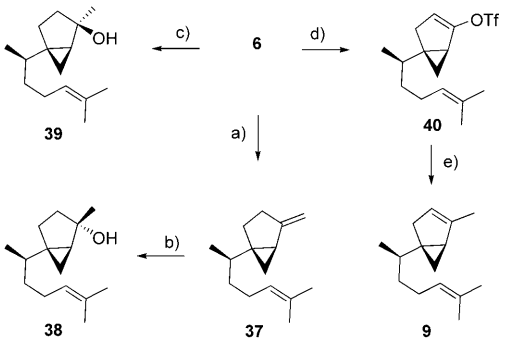
literature. Therefore we cannot decide whether (−)-**7** corresponds to the natural product or its enantiomer.

Reaction of ketone **5** with MeMgBr in Et_2O at 0 °C afforded alcohol **33** as a single isomer in high yield. Its spectra matched those of *cis*-sesquisabinene hydrate, an ingredient of the essential oils of *Zingiber officinale*,[15] *Hedychium gardnerianum* Roscoe ("Kahili ginger"),[35] *Nectandra globosa* ("Ayou" or "canella preta"),[36] and the sub-Himalayan aromatic shrub *Strobilanthes auriculatus*.[37] Whereas the $[\alpha]_D$ of synthetic (−)-**33** and the natural product are in good agreement, the literature actually depicts the opposite enantiomer.[37] Our synthesis, however, is unambiguous in stereochemical regard; therefore the previously proposed configuration of *cis*-sesquisabinene hydrate is incorrect and needs to be revised to what is shown in Scheme 12.

The diastereomeric alcohol **34** was obtained by hydroxymercuration[38] of synthetic sesquisabinene A (**7**). The NMR spectra are sufficiently different from those of **33** and were found to be in accord with the data of *trans*-sesquisabinene hydrate published in the literature.[35,36] As no chiroptical data of this particular natural product are available, the assignment of the absolute configuration must remain open.

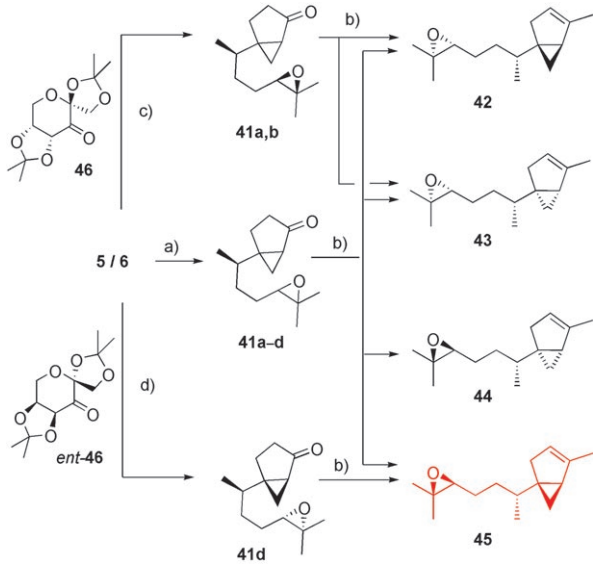
Finally, ketone **5** was transformed into the corresponding enol triflate **35** which underwent an iron-catalyzed cross-coupling with MeMgBr to give endocyclic olefin derivative (+)-**36**. This methodology had previously been developed in our laboratory as a cheap, effective and benign alternative to established cross-coupling protocols and already served other total syntheses with considerable success.[39–41] Comparison of the NMR data shows that synthetic **36** is identical with 7-*epi*-sesquithujene, the stereostructure of which was previously unknown.[16,34] However, as the $[\alpha]_D$ of natural **36** has not been communicated, we cannot establish the absolute configuration of this volatile component produced by the Brazilian tree *Phoebe porosa*.

Next, the diastereomeric ketone **6** derived from (*R*)-**4** was subjected to the same set of reactions (Scheme 13). Wittig olefination delivered (+)-**37**, which corresponds to sesquisabinene B according to its spectral data. The relative stereostructure of this compound isolated from the leaves of *Amyris diatrypta* Sprengel, was previously unknown.[16] Subsequent hydroxymercuration gave 7-*epi*-*trans*-sesquisabinene hydrate (**38**),[35,42] whereas direct addition of MeMgBr furnished the diastereomeric alcohol 7-*epi*-*cis*-sesquisabinene hydrate (**39**),[16,34] both of which are found inter alia in *Helichrysum* oil. The iron catalyzed cross coupling of enol triflate **40** derived from **6** provided sesquithujene (**9**) itself.[15,16] Because we lack information on the rotatory power of all of these naturally occurring sesquiterpenes,[43] their absolute stereochemistry cannot be assigned at this point.



Scheme 13. a) $Ph_3P{=}CH_2$, THF, −78 °C → RT, 66 %; b) $Hg(OAc)_2$, THF/H_2O, then $NaBH_4$, NaOH, 49 %; c) MeMgBr, Et_2O, 0 °C, 97 %; d) LDA, THF, −78 °C then 2-pyridyl-NTf_2, 0 °C; e) MeMgBr, $Fe(acac)_3$ (10 mol %), THF/NMP, −30 °C, 58 % (over both steps).

Epoxysesquithujene: Epoxysesquithujene was recently isolated from the fresh roots of *Valeriana hardwickii* var. *hardwickii*, a rare aromatic Himalayan herb used in traditional medicine.[44] Interestingly, this compound represents about 50 % of the essential oil extracted from this plant but had previously never been found in any other *Valeriana* sp. While its constitution could be firmly established, the stereochemical relationship between the cyclopropane, the methyl branch and the remote epoxide remained undetermined.[44] To answer this question, we first prepared a mixture of all four possible isomers **42**–**45** by epoxidation of a 1:1 mixture of **5** and **6** with *m*CPBA followed by conversion of the ketone groups in **41a–d** into the corresponding endocyclic olefins (Scheme 14). Gratifyingly, the ^{13}C NMR spectra of **42**–**45** are sufficiently resolved such that all four compounds are discernable in the mixture. Next, the epoxidation was performed with the aid of the D-fructose derived catalyst **46**, which delivers isomers **41a**,**b** as the major products according to its well established facial selectivity in oxidations of trisubstituted alkenes.[45] None of the two epoxides



Scheme 14. a) *m*CPBA, 85 %; b) i) LDA, THF, −78 °C, then 2-pyridyl-NTf_2, 0 °C; ii) MeMgBr, $Fe(acac)_3$ (10 mol %), THF/NMP, −35 °C, 72 % (for **41d** → **45**); c) **46** (0.5 equiv), Oxone, Bu_4NHSO_4, $Na_2B_4O_7{\cdot}7H_2O$, K_2CO_3, dimethoxymethane, MeCN/H_2O, 51 %; d) *ent*-**46** (2 equiv), Oxone, Bu_4NHSO_4, $Na_2B_4O_7{\cdot}10H_2O$, K_2CO_3, dimethoxymethane, MeCN/H_2O, 74 % (dr 8:1).

42 and **43** thus formed, however, corresponds to epoxysesquithujene. Therefore, this natural product must be one of the remaining structures **44** or **45**. One of them was then selectively prepared by Shi epoxidation of ketone **6** with the enantiomeric (formally L-fructose derived)[46] catalyst *ent*-**46** (dr 8:1). Subsequent conversion of the carbonyl group of the resulting ketone **41d** into the corresponding triflate and cross-coupling with MeMgBr furnished product **45** in 72% yield after only 5 min reaction time at −35 °C. The fact that the iron-based methodology tolerates the reactive oxirane ring of the substrate is noteworthy and attests to the relevance of this new methodology.[39–41] The NMR spectra of the major diastereomer of the resulting 8:1 mixture of products matched the reported data very well.[44] Therefore we confidently assign structure **45** to epoxysesquithujene derived from *Valeriana hardwickii* var. *hardwickii*.

Conclusion

A short and efficient entry into the cyclopropyl carbonyl derivatives **5** and **6** was established by combining the power of asymmetric synthesis with noble metal catalyzed cycloisomerization chemistry. Specifically, a conceptual extension of an allylation method reported by Nakamura and coworkers using allylzinc derivatives modified by BOX-type ligand **22** allowed the diastereomeric enyne derivatives (*R*)-**4** and (*S*)-**4** to be formed in good yield and appreciable levels of diastereocontrol. Catalytic amounts of $AuCl_3$(pyridine) rearranged these substrates stereospecifically into the bicyclo[3.1.0] ketones **5** and **6** after saponification of the enol ester derivatives primarily formed. These compounds could then be converted into a host of sesquisabina and sesquithuja derivatives. Since the stereochemistry of the synthetic materials is unambiguous, the as yet unknown structure of several members of these families of terpenoids could be established by comparison with the published data. Moreover, it should be pointed out that ketone **6** previously served as the key intermediate en route to cedrene (**11**) and cedrol (**12**).[19] Therefore the new gold-catalyzed access to **6** also represents a formal total synthesis of these challenging targets.

Experimental Section

General methods: All reactions were carried out under argon in flame-dried glassware. The solvents used were purified by distillation over the drying agents indicated and were stored and transferred under argon: THF, Et_2O (Mg/anthracene), CH_2Cl_2, Et_3N, hexanes, benzene, toluene (Na/K), DMF (Desmodur 15, dibutyl tin dilaurate). Flash chromatography (FC): Merck silica gel 60 (230–400 mesh). NMR: Spectra were recorded on a Bruker DPX 300, AMX 300 or AV 400 spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δ_C= 77.0 ppm; residual $CHCl_3$ in $CDCl_3$: δ_H=7.26 ppm; CD_2Cl_2: δ_C= 53.8 ppm; residual CH_2Cl_2 in CD_2Cl_2: δ_H=5.32 ppm; C_6D_6: δ_C= 128.1 ppm; residual C_6H_6 in C_6D_6: δ_H=7.26 ppm; $[D]_8$-toluene: δ_C= 137.9 ppm; residual toluene in $[D]_8$-toluene: δ_H=2.09 ppm). IR: Nicolet FT-7199 spectrometer, wavenumbers (ν) in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: Finnigan MAT 95, accurate mass determinations: Bruker APEX III FT-MS (7 T magnet). Melting points: Büchi melting point apparatus B-540 (corrected). Elemental analyses: H. Kolbe, Mülheim/Ruhr. All commercially available compounds (Fluka, Lancaster, Aldrich) were used as received. Compounds **14** and **15** were prepared according to literature methods.[21,22] The Supporting Information of this paper details the analysis of the Mosher esters derived from (*R*)-**4** and (*S*)-**4**, contains a tabular comparison of the published and the recorded NMR spectra of the individual natural products, and shows copies of their ^1H and ^{13}C NMR spectra.

Compound 16: Bromine (0.64 mL, 13 mmol) was slowly added to a solution of Ph_3P (3.4 g, 13 mmol) in CH_2Cl_2 (60 mL) and the resulting mixture was transferred via cannula to a solution of alcohol **15** (2.0 g, 12 mmol) and imidazole (1.0 g, 14 mmol) in CH_2Cl_2 (80 mL) at 0 °C. After stirring for 10 min at that temperature, the mixture was poured into ice water and stirred for 1 h. A standard extractive work up followed by flash chromatography of the crude material (3% Et_2O in pentanes) gave bromide **16** as a colorless oil (2.4 g, 87%). $[\alpha]_D^{20}=-16.6$ (c=1.04 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ=5.21 (d, J=0.7 Hz, 1H), 5.12–5.08 (m, 1H), 5.00 (br s, 1H), 3.99 (br s, 2H), 2.38 (q, J=6.9 Hz, 1H), 2.00–1.94 (m, 2H), 1.69 (d, J=0.9 Hz, 3H), 1.60 (s, 3H), 1.58–1.49 (m, 1H), 1.42–1.32 (m, 1H), 1.10 ppm (d, J=6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=150.4, 131.6, 124.3, 114.2, 36.5, 36.3, 35.9, 25.7, 25.7, 20.0, 17.7 ppm; IR (film): $\tilde{\nu}$ = 2965, 2919, 2855, 1637, 1452, 1376, 1208, 905 cm^{-1}; MS (70 eV): m/z (%): 232 (0.1) [M^+], 189 (3), 151 (26), 109 (22), 95 (100), 82 (38), 69 (41), 55 (33), 41 (59); HRMS (EI): m/z: calcd for $C_{11}H_{23}NBr$ [M^++NH_4]: 248.1014, found: 248.1012; elemental analysis calcd (%) for $C_{11}H_{19}Br$ (231.2): C 57.15, H 8.28; found: C 57.06, H 8.26.

Compound (*R*)-18: A suspension containing bromide **16** (0.28 g, 1.2 mmol) and zinc dust (0.21 g, 3.0 mmol) in THF (3 mL) was stirred for 1 h at 40 °C. At this time, GC/MS indicated complete conversion of the substrate into the allylzinc reagent **19** and the reaction mixture was allowed to cool to ambient temperature. In a second Schlenk tube, *n*BuLi (1.6 M in hexane, 0.8 mL) was added dropwise to a solution of 2,2′-methylene-bis-[(4*R*)-4-phenyl-2-oxazoline] [(*R*,*R*)-**22**, 0.39 g, 1.3 mmol] in THF (4 mL) at 0 °C. The solution of the organozinc reagent was then added via cannula and the resulting mixture was stirred for 30 min at 0 °C, before it was cooled to −100 °C. A solution of 3-trimethylsilylpropinal (**17**; 0.16 mL, 1.1 mmol) in THF (1 mL) was introduced via syringe pump over a period of 1 h. Once the addition was complete, the reaction was quenched with MeOH/H_2O 1:1 (0.8 mL), the mixture was diluted with Et_2O (5 mL) and allowed to warm to ambient temperature. The organic phase was washed with NaOH (0.5 M, 1 mL), dried over Na_2SO_4, adsorbed on silica gel and purified by flash chromatography (10% Et_2O in pentanes) to give compound (*R*)-**18** as a colorless oil (250 mg, 72%, dr 5.2:1). Analytically pure (*R*)-**18** was obtained by preparative HPLC (250 mm YMC, ∅ 30 mm, MeCN/H_2O 60:40, 35.0 mL min^{-1}, 6.9 MPa, 308 K, UV, 210 nm). $[\alpha]_D^{20}=-3.9$ (c=0.78 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ=5.11–5.07 (m, 1H), 4.93 (s, 1H), 4.92 (d, J= 1.1 Hz, 1H), 4.48 (t, J=6.9 Hz, 1H), 2.43 (dd, J=6.8, 0.5 Hz, 2H), 2.18 (q, J=6.9 Hz, 1H), 1.94 (q, J=7.6 Hz, 2H), 1.79 (br s, 1H), 1.68 (s, 3H), 1.56 (s, 3H), 1.53–1.44 (m, 1H), 1.35–1.26 (m, 1H), 1.04 (d, J=6.9 Hz, 3H), 0.17 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=149.6, 131.5, 124.5, 111.5, 106.4, 89.5, 61.3, 42.8, 39.1, 35.8, 25.8, 25.7, 19.7, 17.7, −0.2 ppm; IR (film): $\tilde{\nu}$ = 3349, 2961, 2923, 2176, 1643, 1454, 1376, 1249, 1033, 883, 837, 759 cm^{-1}; MS (70 eV): m/z (%): 263 (3), 217 (4), 151 (9), 136 (10), 127 (10), 109 (20), 99 (33), 95 (20), 82 (100), 73 (61), 69 (24), 55 (21), 41 (36); HRMS (ESI): m/z: calcd for $C_{17}H_{30}OSiNa$ [M^++Na]: 301.1958, found: 301.1955; elemental analysis calcd (%) for $C_{17}H_{30}OSi$ (278.51): C 73.31, H 10.86; found: C 73.42, H 10.78.

Compound (*S*)-18: Prepared analogously using 2,2′-methylene-bis-[(4*S*)-4-phenyl-2-oxazoline] (*S*,*S*)-**20** as the ligand. Colorless oil (290 mg, 70%, dr 10.4:1). $[\alpha]_D^{20}=-28.9$ (c=0.95 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ=5.11–5.07 (m, 1H), 4.94 (br s, 1H), 4.92 (d, J=1.1 Hz, 1H), 4.49 (dd, J=7.2, 6.1 Hz, 1H), 2.45–2.42 (m, 2H), 2.18 (q, J=6.9 Hz, 1H),

1.94 (q, $J=7.5$ Hz, 2H), 1.68 (s, 3H), 1.59 (s, 3H), 1.53–1.44 (m, 1H), 1.36–1.27 (m, 1H), 1.04 (d, $J=6.9$ Hz, 3H), 0.17 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=149.7$, 131.5, 124.4, 111.5, 106.4, 89.5, 61.2, 42.7, 39.3, 35.7, 25.9, 25.7, 19.9, 17.7, −0.2 ppm; IR (film): $\tilde{\nu}$ = 3380, 2961, 2923, 2177, 1642, 1454, 1376, 1249, 1034, 883, 839, 759 cm^{-1}; MS (70 eV): m/z (%): 263 (2), 217 (5), 151 (8), 136 (10), 127 (9), 109 (19), 99 (32), 95 (20), 82 (100), 73 (60), 69 (24), 55 (21), 41 (36); HRMS (ESI): m/z: calcd for $C_{17}H_{30}OSiNa$ [M^++Na]: 301.1958, found: 301.1957.

(*S*)-1-(Trimethylsilyl)hex-5-en-1-yn-3-ol [(*S*)-20a, R=H]: Colorless oil (93 mg, 70%, *ee* 57%). The enantiomeric excess was determined by GC analysis on chiral stationary phase (25 m Hydrodex-B-TBDAc 0.25/df, ∅ 0.25 mm, 220/105iso, 0.8 bar H_2, FID). The absolute stereochemistry was assigned by comparison of the optical rotation. $[\alpha]_D^{20}=-22.1$ ($c=1.3$ in $CHCl_3$), Lit:[47] $[\alpha]_D^{RT}=-29$ ($c=0.85$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=5.93$–5.83 (m, 1H), 5.21–5.19 (m, 1H), 5.17 (brs, 1H), 4.41 (t, $J=6.1$ Hz, 1H), 2.47 (t, $J=7.0$ Hz, 2H), 1.79 (brs, 1H), 0.17 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=132.9$, 119.0, 105.9, 89.8, 62.0, 42.1, −0.2 ppm; IR (film): $\tilde{\nu}$ = 3351, 3073, 2960, 2901, 2175, 1643, 1250, 1027, 837, 759 cm^{-1}; MS (70 eV): m/z (%): 168 (0.1) [M^+], 127 (98), 99 (100), 75 (33), 59 (11), 45 (16); HRMS (CI): m/z: calcd for $C_9H_{20}NOSi$ [M^++NH_4]: 186.1314, found: 186.1316.

(*S*)-5-Methyl-1-(trimethylsilyl)hex-5-en-1-yn-3-ol [(*S*)-20b, R=Me]: Colorless oil (109 mg, 76%, *ee* 67%). The enantiomeric excess was determined by GC analysis on chiral stationary phase (25 m Hydrodex-B-TBDAc 0.25/df, ∅ 0.25 mm, 220/105iso, 0.8 bar H_2). The absolute stereochemistry was assigned in analogy to (*S*)-**20a**. $[\alpha]_D^{20}=-38.5$ ($c=1.4$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.93$–4.90 (m, 1H), 4.86–4.83 (m, 1H), 4.49 (t, $J=6.6$ Hz, 1H), 2.44 (d, $J=6.6$ Hz, 2H), 1.80 (s, 3H), 0.17 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=140.9$, 114.4, 106.3, 89.5, 60.8, 46.1, 22.6, −0.2 ppm; IR (film): $\tilde{\nu}$ = 3351, 3073, 2961, 2896, 2175, 1647, 1249, 1063, 1019, 883, 837, 759 cm^{-1}; MS (70 eV): m/z (%): 182 (1) [M^+], 167 (21), 151 (17), 127 (44), 111 (15), 99 (100), 91 (29), 75 (56), 45 (20); HRMS (CI): m/z: calcd for $C_{10}H_{22}NOSi$ [M^++NH_4]: 200.1471, found: 200.1473.

(*S*)-6-Methyl-5-methylene-1-(trimethylsilyl)hept-1-yn-3-ol [(*S*)-20c, R=*i*Pr]: Colorless oil (94 mg, 69%, *ee* 81%). The enantiomeric excess was determined by GC analysis on chiral stationary phase (25 m Hydrodex-B-TBDAc 0.25/df, ∅ 0.25 mm, 220/90iso, 0.5 bar H_2). The absolute stereochemistry was assigned by Mosher-ester analysis. $[\alpha]_D^{20}=-18.1$ ($c=0.5$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta=4.93$ (brs, 1H), 4.56 (brs, 1H), 4.47–4.43 (m, 1H), 2.45–2.43 (m, 2H), 2.32 (qt, $J=6.8$ 1H), 1.96 (d, $J=5.2$ Hz, 1H), 1.04 (dd, $J=6.7$, 1.1 Hz, 6H), 0.16 ppm (s, 9H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=151.7$, 110.5, 107.1, 89.4, 61.7, 43.5, 34.0, 21.9, 21.8, −0.2 ppm; IR (film): $\tilde{\nu}$ = 3349, 2961, 2896, 2175, 1642, 1249, 1033, 882, 837, 759 cm^{-1}; MS (70 eV): m/z (%): 210 (1) [M^+], 195 (26), 167 (21), 151 (59), 127 (44), 111 (11), 105 (25), 99 (95), 84 (79), 73 (100), 69 (95), 55 (20), 41 (32); HRMS (ESI): m/z: calcd for $C_{12}H_{22}ONaSi$ [M^++Na]: 233.1332, found: 233.1334.

Compound (*R*)-4: K_2CO_3 (0.34 g, 2.4 mmol) was added to a solution of (*R*)-**18** (0.23 g, 0.82 mmol) in MeOH (10 mL) and the resulting mixture stirred for 2 h before the reaction was diluted with water (10 mL) and extracted with Et_2O (3×10 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, evaporated and the residue purified by flash chromatography (10% Et_2O in pentanes) to give product (*R*)-**4** as a colorless oil (170 mg, 99%). $[\alpha]_D^{20}=+0.4$ ($c=0.87$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta=5.13$–5.08 (m, 1H), 4.94 (brs, 1H), 4.92–4.91 (m, 1H), 4.52–4.47 (m, 1H), 2.50 (d, $J=2.1$ Hz, 1H), 2.44–2.43 (m, 2H), 2.17 (q, $J=6.9$ Hz, 1H), 2.03 (d, $J=5.0$ Hz, 1H), 1.95 (q, $J=7.7$ Hz, 2H), 1.68 (d, $J=1.0$ Hz, 3H), 1.59 (s, 3H), 1.52–1.43 (m, 1H), 1.35–1.26 (m, 1H), 1.04 ppm (d, $J=6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=150.1$, 131.8, 124.8, 111.5, 85.3, 72.9, 61.0, 43.1, 39.5, 36.1, 26.2, 25.8, 19.9, 17.8 ppm; IR (film): $\tilde{\nu}$ = 3377, 3309, 2964, 2918, 2855, 1643, 1453, 1376, 1031, 896 cm^{-1}; MS (70 eV): m/z (%): 206 (0.1) [M^+], 145 (6), 109 (8), 95 (19), 82 (100), 67 (32), 55 (24), 41 (42); HRMS (ESI): m/z: calcd for $C_{14}H_{22}ONa$ [M^++Na]: 229.1563, found: 229.1561; elemental analysis calcd (%) for $C_{14}H_{22}O$ (206.32): C 81.50, H 10.75; found: C 81.40, H 10.66.

Compound (*S*)-4: Prepared analogously as a colorless oil (190 mg, 99%). $[\alpha]_D^{20}=-35$ ($c=1.52$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta=5.13$–5.08 (m, 1H), 4.94 (brs, 1H), 4.92–4.91 (m, 1H), 4.52–4.47 (m, 1H), 2.50 (d, $J=2.1$ Hz, 1H), 2.45–2.42 (m, 2H), 2.16 (q, $J=6.9$ Hz, 1H), 2.03 (d, $J=5.1$ Hz, 1H), 1.95 (q, $J=7.5$ Hz, 2H), 1.68 (d, $J=0.9$ Hz, 3H), 1.59 (s, 3H), 1.52–1.43 (m, 1H), 1.37–1.28 (m, 1H), 1.03 ppm (d, $J=6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=150.2$, 131.8, 124.8, 111.5, 85.2, 72.9, 61.0, 43.0, 39.7, 36.0, 26.2, 25.8, 20.0, 17.7 pm; IR (film): $\tilde{\nu}$ = 3376, 3309, 2963, 2918, 2855, 1643, 1452, 1376, 1029, 896 cm^{-1}; MS (70 eV): m/z (%): 206 (0.1) [M^+], 145 (6), 109 (8), 95 (19), 82 (100), 67 (32), 55 (23), 41 (41); HRMS (ESI): m/z: calcd for $C_{14}H_{22}ONa$ [M^++Na]: 229.1563, found: 229.1561.

Compound (*R*)-23: Pyridine (0.12 mL, 1.5 mmol), 4-nitrobenzoyl chloride (0.27 g, 1.5 mmol) and DMAP (30 mg, 0.25 mmol) were successively added to a solution of compound (*R*)-**4** (100 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) at 0°C and the resulting mixture was allowed to reach ambient temperature. After stirring for 1 h, the reaction was quenched with pH 7 buffer (5 mL) and Et_2O (5 mL), the aqueous phase was extracted with Et_2O (3×5 mL), the combined organic layers were washed with brine, dried over Na_2SO_4, evaporated and the residue was purified by flash chromatography (20% Et_2O in pentanes) to give product (*R*)-**23** as a colorless oil (110 mg, 62%). $[\alpha]_D^{20}=+20.1$ ($c=0.93$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta=8.29$ (d, $J=9.0$ Hz, 2H), 8.21 (d, $J=9.0$ Hz, 2H), 5.75 (ddd, $J=7.7$, 6.5, 2.1 Hz, 1H), 5.12–5.07 (m, 1H), 4.95 (d, $J=1.0$ Hz, 1H), 4.94 (brs, 1H), 2.72 (dd, $J=14.9$, 7.2 Hz, 1H), 2.64 (dd, $J=14.9$, 6.5 Hz, 1H), 2.59 (d, $J=2.1$ Hz, 1H), 2.21 (q, $J=6.9$ Hz, 1H), 1.98–1.92 (m, 2H), 1.67 (s, 3H), 1.58 (s, 3H), 1.52–1.45 (m, 1H), 1.37–1.27 (m, 1H), 1.04 ppm (d, $J=6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=163.9$, 151.1, 148.8, 135.6, 131.9, 131.2, 124.7, 123.9, 112.0, 81.1, 74.6, 64.5, 39.8, 39.6, 36.0, 26.2, 25.8, 19.9, 17.8 ppm; IR (film): $\tilde{\nu}$ = 3293, 2963, 2923, 2855, 1729, 1528, 1345, 1261, 1099, 1014, 872, 718 cm^{-1}; MS (70 eV): m/z (%): 355 (0.3) [M^+], 150 (30), 145 (20), 104 (14), 91 (11), 82 (100), 67 (18), 55 (17), 41 (29); HRMS (CI): m/z: calcd for $C_{21}H_{25}NO_4$ [M^+]: 356.1862, found: 356.1859.

Compound (*S*)-23: Prepared analogously from (*S*)-**4** (0.13 g, 0.63 mmol) as a colorless oil (0.13 g, 58%). $[\alpha]_D^{20}=-42.7$ ($c=0.72$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta=8.29$ (d, $J=9.0$ Hz, 2H), 8.21 (d, $J=9.0$ Hz, 2H), 5.75 (ddd, $J=8.7$, 6.6, 2.2 Hz, 1H), 5.10–5.06 (m, 1H), 4.95 (d, $J=1.1$ Hz, 1H), 4.94 (brs, 1H), 2.74–2.63 (m, 2H), 2.59 (d, $J=2.1$ Hz, 1H), 2.45–2.16 (m, 1H), 1.93 (q, $J=7.5$ Hz, 2H), 1.66 (s, 3H), 1.55 (s, 3H), 1.51–1.44 (m, 1H), 1.39–1.30 (m, 1H), 1.05 ppm (d, $J=6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=163.9$, 151.1, 148.8, 135.6, 131.8, 131.2, 124.7, 123.9, 112.0, 81.1, 74.6, 64.5, 39.8, 39.6, 35.9, 26.2, 25.7, 20.0, 17.7 ppm; IR (film): $\tilde{\nu}$ = 3289, 2963, 2923, 2855, 1729, 1528, 1345, 1264, 1099, 1014, 872, 718 cm^{-1}; MS (70 eV): m/z (%): 355 (0.3) [M^+], 150 (31), 145 (21), 104 (14), 91 (11), 82 (100), 67 (19), 55 (17), 41 (29); HRMS (ESI): m/z: calcd for $C_{21}H_{25}NO_4$ [M^+]: 356.1862, found: 356.1858.

Compound 26: Prepared analogously from (*S*)-**25** (29 mg, 0.2 mmol) as a colorless oil (55 mg, 91%). $[\alpha]_D^{20}=-29.9$ ($c=0.8$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta=8.31$–8.27 (m, 2H), 8.23–8.19 (m, 2H), 5.75 (ddd, $J=8.6$, 5.6, 1.2 Hz, 1H), 4.94 (brs, 1H), 4.91 (brs, 1H), 2.78–2.66 (m, 2H), 2.59 (d, $J=2.2$ Hz, 1H), 2.34 (qt, $J=6.8$ Hz, 1H), 1.06 (d, $J=6.8$ Hz, 3H), 1.06 ppm (d, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=163.9$, 151.1, 150.2, 135.6, 131.2, 123.9, 111.0, 81.0, 74.5, 64.5, 40.2, 34.0, 21.9, 21.7 ppm; IR (film): $\tilde{\nu}$ = 3293, 2963, 2870, 1727, 1526, 1343, 1259, 1098, 1013, 871, 717 cm^{-1}; MS (70 eV): m/z (%): 272 (<1) [M^+-15], 150 (100), 120 (21), 105 (50), 76 (12), 41 (11); HRMS (CI): m/z: calcd for $C_{16}H_{18}NO_4$ [M^++H]: 288.1236, found: 288.1235.

Compound 24: $AuCl_3$(pyridine) (14 mg, 40 μmol) was added to a solution of compound (*S*)-**23** (0.13 g, 0.37 mmol) in CH_2Cl_2 (4 mL) and the resulting mixture was stirred for 5 h at ambient temperature. Silica gel was added and the solvent removed under reduced pressure. Purification of the product by flash chromatography (20% Et_2O in pentanes) gave enol ester **24** as a pale yellow syrup (95 mg, 73%, dr ≈19:1). $[\alpha]_D^{20}=+19.4$ ($c=0.75$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta=8.31$ (d, $J=9.1$ Hz, 2H), 8.25 (d, $J=9.1$ Hz, 2H), 5.27–5.25 (m, 1H), 5.14–5.10 (m, 1H), 2.50 (dd, $J=17.2$, 2.4 Hz, 1H), 2.30 (dt, $J=14.4$, 2.8 Hz, 1H), 2.04 (q, $J=7.5$ Hz, 2H), 1.82–1.78 (m, 1H), 1.68 (d, $J=0.8$ Hz, 3H), 1.61 (s, 3H),

1.57–1.49 (m, 1H), 1.39–1.23 (m, 2H), 0.98 (d, $J=6.8$ Hz, 3H), 0.88 (dd, $J=7.2$, 4.1 Hz, 1H), 0.48 ppm (t, $J=3.5$ Hz, 1H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=162.6$, 154.4, 151.1, 135.6, 131.6, 131.3, 125.1, 124.9, 110.1, 38.2, 35.3, 32.2, 31.7, 27.3, 26.4, 25.8, 21.3, 17.8, 17.7 ppm; IR (film): $\tilde{\nu}=$ 2962, 2915, 2870, 1740, 1528, 1347, 1259, 1143, 715 cm^{-1}; MS (70 eV): m/z (%): 355 (7) [M^+], 270 (22), 150 (100), 104 (18), 69 (24), 41 (14); HRMS (ESI): m/z: calcd for $C_{21}H_{25}NO_4Na$ [M^++Na]: 378.1676, found: 378.1677.

Compound 27: Prepared analogously as a pale yellow solid (42 mg, 89%). M.p. 95–97 °C; $[\alpha]_D^{20}=+7.0$ ($c=0.9$ in CH_2Cl_2); ^{1}H NMR (300 MHz, CD_2Cl_2): $\delta=8.31$ (d, $J=9.1$ Hz, 2H), 8.25 (d, $J=9.2$ Hz, 2H), 5.26 (bt, $J=2.2$ Hz, 1H), 2.51 (dt, $J=17.2$, 2.4 Hz, 1H), 2.31 (dt, $J=17.2$, 2.8 Hz, 1H), 1.79–1.74 (m, 1H); 1.55–1.46 (m, 1H), 1.01 (d, $J=6.8$ Hz, 3H), 0.95 (d, $J=7.3$ Hz, 1H), 0.94 ppm (d, $J=6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=162.6$, 154.5, 135.6, 131.4, 131.3, 124.0, 110.0, 33.1, 32.7, 32.6, 26.2, 21.4, 19.9, 19.4 ppm; IR (film): $\tilde{\nu}=$ 3115, 3060, 2959, 2870, 1735, 1526, 1343, 1262, 1139, 1073, 873, 845, 713 cm^{-1}; MS (70 eV): m/z (%): 287 (6) [M^+], 244 (12), 150 (100), 104 (16); HRMS (ESI): m/z: calcd for $C_{16}H_{17}NO_4Na$ [M^++Na]: 310.1050, found: 310.1052.

Compound 5: LiOH (18 mg, 0.76 mmol) was added to a solution of compound **24** (90 mg, 0.25 mmol) in THF (5 mL) and water (0.5 mL) and the resulting mixture stirred for 2 h at ambient temperature. Silica gel was added and the THF removed in vacuo. The loaded silica was added on top of a silica gel column and the product eluded with 20% Et_2O in pentane to give ketone **5** as a colorless oil (47 mg, 91%). $[\alpha]_D^{20}=+16.2$ ($c=$ 1.62 in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta=5.10$–5.05 (m, 1H), 2.15–1.89 (m, 6H), 1.67 (d, $J=0.9$ Hz, 3H), 1.61–1.60 (m, 1H), 1.59 (s, 3H), 1.53–1.44 (m, 1H), 1.37–1.28 (m, 2H), 1.12–1.08 (m, 1H), 1.05 (dd, $J=4.5$, 3.2 Hz, 1H), 0.96 ppm (d, $J=6.5$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=214.4$, 131.9, 124.7, 38.9, 37.6, 34.7, 34.6, 33.4, 26.2, 25.7, 23.6, 19.3, 17.7, 17.1 ppm; IR (film): $\tilde{\nu}=$ 2956, 2916, 2873, 1727, 1450, 1377, 1295, 1181, 1023, 914, 775 cm^{-1}; MS (70 eV): m/z (%): 206 (28) [M^+], 163 (20), 149 (14), 136 (17), 123 (67), 109 (21), 93 (34), 82 (52), 69 (92), 55 (54), 41 (100); HRMS (EI): m/z: calcd for $C_{14}H_{22}O$ [M^+]: 271.1671, found: 271.1669.

Compound 6: Prepared analogously as a colorless oil (33 mg 89%). $[\alpha]_D^{20}=-27.2$ ($c=1.36$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta=5.12$–5.08 (m, 1H), 2.14–1.94 (m, 5H), 1.88 (dd, $J=10.6$, 9.2 Hz, 1H), 1.68 (s, 3H), 1.61 (s, 3H), 1.52 (dd, $J=8.9$, 3.4 Hz, 1H), 1.48–1.40 (m, 1H), 1.35–1.23 (m, 2H), 1.19–1.13 (m, 2H), 0.98 ppm (d, $J=6.6$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=214.4$, 131.8, 124.8, 38.9, 37.8, 34.6, 33.5, 33.5, 26.3, 25.8, 22.7, 21.4, 17.7, 17.6 ppm; IR (film): $\tilde{\nu}=$ 2962, 2916, 2874, 1724, 1450, 1377, 1294, 1181, 1021, 917, 773 cm^{-1}; MS (70 eV): m/z (%): 206 (27) [M^+], 163 (22), 149 (13), 136 (16), 123 (55), 109 (21), 93 (34), 82 (53), 69 (96), 55 (75), 41 (100); HRMS (EI): m/z: calcd for $C_{14}H_{22}O$ [M^+]: 206.1671, found: 206.1668.

Sabina ketone (28): Prepared analogously as a colorless oil (8 mg, 53%, *ee* 80%). $[\alpha]_D^{20}=+18.1$ ($c=0.8$ in $CHCl_3$); Lit:[32] $[\alpha]_D^{25}=+27.3$ ($c=2.34$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=2.19$–2.07 (m, 2H), 1.99–1.95 (m, 2H), 1.64 (dd, $J=9.0$ Hz, 3.0 Hz, 1H), 1.57 (qt, $J=6.8$ Hz, 1H), 1.17 (dd, $J=8.9$, 4.5 Hz, 1H), 1.08–1.05 (m, 1H), 0.98 (d, $J=6.8$ Hz, 3H), 0.93 ppm (dd, $J=6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta=214.9$, 39.5, 33.8, 33.2, 32.2, 23.6, 19.5, 19.3, 19.1 ppm; IR (film): $\tilde{\nu}=$ 2960, 2874, 1721, 1466, 1178, 1020, 910, 772 cm^{-1}; MS (70 eV): m/z (%): 138 (8) [M^+], 123 (15), 96 (72), 81 (100), 67 (49), 55 (54), 41 (43), 27 (18); HRMS (ESI): m/z: calcd for $C_9H_{14}O$ [M^+]: 138.1047, found: 138.1045.

Sesquisabinene (7): A solution of ketone **5** (7.0 mg, 30 μmol) in THF (0.5 mL) was added to a solution of Ph_3P=CH_2 (14 mg, 50 μmol) in THF (1 mL) at −78 °C and the resulting mixture was allowed to warm to ambient temperature. After stirring for 45 min, the reaction was quenched with aq. sat. NH_4Cl (1 mL) and extracted with Et_2O (3×2 mL). The combined organic phases were dried over Na_2SO_4, adsorbed on silica gel and purified by flash chromatography (pentanes) to give product **7** as a colorless oil (4.8 mg, 69%). $[\alpha]_D^{20}=-48.5$ ($c=1.22$ in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=5.12$–5.06 (m, 1H), 4.80 (s, 1H), 4.62 (s, 1H), 2.14 (dd, $J=16.1$, 7.3 Hz, 1H), 2.06–1.92 (m, 3H), 1.77–1.66 (m, 2H), 1.68 (d, $J=1.1$ Hz, 3H), 1.60 (brs, 4H), 1.51–1.42 (m, 1H), 1.35–1.18 (m, 2H), 0.93 (d, $J=6.7$ Hz, 3H), 0.66 (dd, $J=4.3$, 3.5 Hz, 1H), 0.57 ppm (ddd, $J=$ 0.6, 4.6, 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=154.2$, 131.1, 125.0, 101.8, 37.8, 36.7, 34.6, 31.2, 28.8, 26.7, 26.1, 25.7, 18.0, 17.7, 16.1 ppm; IR (film): $\tilde{\nu}=$ 3073, 2957, 2927, 2867, 1652, 1446, 1375, 862 cm^{-1}; MS (70 eV): m/z (%): 204 (21) [M^+], 161 (49), 133 (30), 120 (30), 109 (19), 93 (60), 79 (23), 69 (100), 55 (30), 41 (58); HRMS (EI): m/z: calcd for $C_{15}H_{24}$ [M^+]: 204.1878, found: 204.1879.

Sesquisabinene B (37): Prepared analogously as a colorless oil (4.6 mg, 66%). $[\alpha]_D^{20}=+53.6$ ($c=0.92$ in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=5.13$–5.07 (m, 1H), 4.80 (s, 1H), 4.62 (s, 1H), 2.15 (dd, $J=15.8$, 9.2, 1H), 2.08–1.94 (m, 3H), 1.82–1.71 (m, 1H), 1.68 (s, 3H), 1.65–1.59 (m, 1H), 1.61 (s, 3H), 1.52 (dd, $J=8.2$, 3.4 Hz, 1H), 1.47–1.35 (m, 1H), 1.30–1.16 (m, 2H), 0.94 (d, $J=6.5$ Hz, 3H), 0.74 (dd, $J=4.4$, 3.5 Hz, 1H), 0.66 ppm (ddd, $J=8.2$, 4.6, 1.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 154.5, 131.2, 124.9, 101.6, 38.0, 36.8, 35.2, 29.7, 29.0, 26.3, 26.2, 25.7, 18.3, 17.7, 17.4 ppm; IR (film): $\tilde{\nu}=$ 3073, 2957, 2927, 2867, 1652, 1446, 1375, 862 cm^{-1}; MS (70 eV): m/z (%): 204 (19) [M^+], 161 (42), 133 (29), 120 (32), 109 (19), 93 (59), 79 (23), 69 (100), 55 (31), 41 (56); HRMS (EI): m/z: calcd for $C_{15}H_{24}$ [M^+]: 204.1878, found: 204.1880.

***cis*-Sesquisabinene hydrate (33)**: MeMgBr (3 M in Et_2O, 23 μL) was added to a solution of compound **5** (6.7 mg, 30 μmol) in Et_2O (0.5 mL) at 0 °C and the resulting mixture stirred for 5 min before it was quenched with aq. sat. NH_4Cl (0.5 mL). The mixture was filtered through Na_2SO_4 and the filtrate evaporated to give product **33** in analytically pure form as a colorless oil (6.8 mg, 95%). $[\alpha]_D^{20}=-10.3$ ($c=1.2$ in $CHCl_3$); $[\alpha]_D^{22}=-10.4$ ($c=0.4$ in $CHCl_3$), lit.:[36] $[\alpha]_D^{20}=-12$ ($c=1.3$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=5.10$–5.06 (m, 1H), 2.07–1.98 (m, 1H), 1.95–1.85 (m, 1H), 1.68 (s, 3H), 1.64–1.52 (m, 3H), 1.60 (s, 3H), 1.49–1.38 (m, 2H), 1.35 (s, 3H), 1.30–1.22 (m, 2H), 1.10 (dd, $J=7.6$, 3.4 Hz, 2H), 0.89 (d, $J=$ 6.8 Hz, 3H), 0.65 (dd, $J=4.8$, 3.7 Hz, 1H), 0.29 ppm (dd, $J=7.6$, 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=131.3$, 124.8, 79.4, 37.6, 36.1, 34.3, 33.9, 33.2, 28.1, 26.1, 25.8, 25.7, 17.7, 17.1, 11.3 ppm; IR (film): $\tilde{\nu}=$ 3349, 2959, 2924, 2866, 1451, 1374, 1127, 985, 925 cm^{-1}; MS (70 eV): m/z (%): 222 (5) [M^+], 207 (36), 189 (10), 161 (30), 151 (11), 137 (26), 119 (60), 109 (29), 93 (54), 82 (82), 69 (100), 55 (43), 29 (11); HRMS (ESI): m/z: calcd for $C_{15}H_{26}ONa$ [M^++Na]: 245.1876, found: 245.1877.

7-*epi*-*cis*-Sesquisabinene hydrate (39): Prepared analogously from ketone **6** as a colorless oil (6.7 mg, 97%); $[\alpha]_D^{20}=+26.3$ ($c=1.2$ in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=5.10$–5.07 (m, 1H), 2.00 (q, $J=7.6$ Hz, 2H), 1.68 (s, 3H), 1.64–1.53 (m, 3H), 1.60 (s, 3H), 1.45–1.36 (m, 2H), 1.34 (s, 3H), 1.30–1.17 (m, 2H), 1.05 (q, $J=6.9$ Hz, 1H), 1.00 (dd, $J=7.5$, 3.7 Hz, 1H), 0.93 (d, $J=6.7$ Hz, 3H), 0.73 (dd, $J=4.7$, 4.0 Hz, 1H), 0.34 ppm (dd, $J=7.9$, 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 131.2, 124.9, 79.4, 37.8, 36.1, 34.9, 33.1, 32.4, 27.9, 26.2, 25.7, 24.6, 17.7, 17.4, 13.1 ppm; IR (film): $\tilde{\nu}=$ 3359, 2959, 2925, 2865, 1451, 1374, 1125, 985, 925 cm^{-1}; MS (70 eV): m/z (%): 222 (3) [M^+], 204 (31), 161 (23), 137 (20), 119 (48), 109 (27), 93 (53), 82 (80), 69 (100), 55 (48), 42 (91), 29 (15); HRMS (ESI): m/z: calcd for $C_{15}H_{26}ONa$ [M^++Na]: 245.1876, found: 245.1876.

7-*epi*-Sesquithujene (36): A freshly prepared solution of LDA (1 M in THF, 50 μmol) was added to a solution of ketone **5** (8.0 mg, 40 μmol) in THF (0.5 mL) at −78 °C and the resulting mixture was stirred for 30 min before a solution of 2-pyridyl-NTf_2 (Comins reagent, 18 mg, 50 μmol) in THF (0.5 mL) was introduced. The mixture was allowed to reach ambient temperature and stirred for 30 min until TLC showed full conversion. The solution was then cooled to −30 °C before NMP (35 μL, 0.39 mmol) and Fe(acac)$_3$ (1.4 mg, 4 μmol) were introduced. MeMgBr (3 M in Et_2O, 40 μL) was added dropwise and the resulting mixture stirred for 45 min at that temperature. A standard extractive work up followed by flash chromatography (pentanes) afforded product **36** as a colorless oil (4.7 mg, 60%). $[\alpha]_D^{20}=+30.2$ ($c=0.7$ in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=5.13$–5.06 (m, 1H), 4.95 (brs, 1H), 2.40–2.33 (m, 1H), 2.18–2.10 (m, 1H), 2.00–1.93 (m, 2H), 1.75 (q, $J=1.9$ Hz, 3H), 1.68 (d, $J=$ 1.1 Hz, 3H), 1.59 (s, 3H), 1.51–1.38 (m, 2H), 1.35–1.13 (m, 2H), 0.93 (d, $J=6.7$ Hz, 3H), 0.68 (dd, $J=7.5$, 3.5 Hz, 1H), 0.01 ppm (t, $J=3.2$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=145.0$, 131.0, 125.2, 120.9, 38.0, 36.1, 35.2, 33.2, 32.5, 26.1, 25.7, 21.5, 18.1, 17.6, 16.3 ppm; IR (film): $\tilde{\nu}=$ 3043, 2963, 2913, 2855, 1448, 1376, 1025, 1009, 806, 778 cm^{-1}; MS (70 eV): m/z (%): 204 (7) [M^+], 119 (100), 105 (17), 93 (89), 77 (20), 69 (32), 56 (15),

41 (29); HRMS (EI): *m/z*: calcd for $C_{15}H_{24}$ [M^+]: 204.1878, found: 204.1878.

Sesquithujene (9): Prepared analogously from ketone **6** as a colorless oil (4.6 mg, 58%). $[\alpha]_D^{20} = -8.9$ ($c = 0.6$ in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.15$–5.08 (m, 1H), 4.94 (brs, 1H), 2.43–2.35 (m, 1H), 2.15–2.00 (m, 3H), 1.77–1.75 (m, 3H), 1.69 (d, $J = 1.0$ Hz, 3H), 1.60 (s, 3H), 1.49–1.38 (m, 1H), 1.34–1.23 (m, 2H), 1.19–1.11 (m, 1H), 0.93 (d, $J = 6.6$ Hz, 3H), 0.76 (dd, $J = 7.5$, 3.5 Hz, 1H), 0.10 ppm (t, $J = 3.3$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 145.2$, 131.0, 125.1, 120.9, 38.1, 35.5, 35.3, 33.1, 30.9, 26.2, 25.7, 23.7, 17.9, 17.6, 16.3 ppm; IR (film): $\tilde{\nu} = 2963$, 2913, 2851, 1641, 1447, 1376, 1026, 779 cm^{-1}; MS (70 eV): *m/z* (%): 204 (7) [M^+], 119 (100), 105 (20), 93 (94), 77 (22), 69 (34), 56 (16), 41 (32); HRMS (EI): *m/z*: calcd for $C_{15}H_{24}$ [M^+]: 204.1878, found: 204.1877.

***trans*-Sesquisabinene hydrate (34)**: A solution of compound **7** (3 mg, 15 μmol) in THF (0.1 mL) was added to a solution of $Hg(OAc)_2$ (4.6 mg, 15 μmol) in water (0.1 mL) and THF (0.1 mL). The yellow color of the reaction mixture disappeared instantaneously and the reaction was quenched after 5 minutes upon addition of aq. NaOH (3 M, 0.1 mL) and $NaBH_4$ (0.5 M in 3 M NaOH, 0.1 mL). A standard extractive work up gave product **34** as a colorless oil (1.7 mg, 53%). $[\alpha]_D^{20} = -7.8$ ($c = 0.84$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.12$–5.06 (m, 1H), 2.10–1.94 (m, 2H), 1.89–1.78 (m, 1H), 1.67 (d, $J = 1.0$ Hz, 3H), 1.62 (d, $J = 8.1$ Hz, 1H), 1.60 (s, 3H), 1.57–1.43 (m, 2H), 1.39 (brs, 1H), 1.35–1.23 (m, 2H), 1.30 (s, 3H), 1.21–1.14 (m, 1H), 1.09 (ddd, $J = 8.3$, 4.8, 3.5 Hz, 1H), 0.91 (d, $J = 6.7$ Hz, 3H), 0.34 (ddd, $J = 8.4$, 5.2, 0.7 Hz, 1H), 0.22 ppm (dd, $J = 5.1$, 3.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 131.2$, 124.9, 80.6, 37.3, 36.5, 34.9, 34.3, 26.1, 25.8, 25.7, 25.2, 17.7, 13.6 ppm; IR (film): $\tilde{\nu} = 3387$, 2962, 2927, 2866, 1452, 1374, 1106, 916 cm^{-1}; MS (70 eV): *m/z* (%): 222 (1) [M^+], 204 (38), 161 (20), 137 (16), 121 (80), 107 (30), 93 (65), 82 (100), 69 (84), 55 (39), 43 (73), 29 (10); HRMS (ESI): *m/z*: calcd for $C_{15}H_{26}ONa$ [$M^+ + Na$]: 245.1876, found: 245.1874.

7-*epi*-*trans*-Sesquisabinene hydrate (38): Prepared analogously from alkene **37** as a colorless oil (1.6 mg, 49%). $[\alpha]_D^{20} = +24.6$ ($c = 1.66$ in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.11$–5.07 (m, 1H), 2.01 (q, $J = 7.5$ Hz, 2H), 1.90–1.82 (m, 1H), 1.68 (s, 3H), 1.60 (s, 3H), 1.56–1.50 (m, 2H), 1.47–1.39 (m, 2H), 1.31–1.19 (m, 2H), 1.29 (s, 3H), 1.16–1.08 (m, 1H), 1.01–0.98 (m, 4H), 0.41 (dd, $J = 7.7$, 5.3 Hz, 1H), 0.31 ppm (dd, $J = 5.1$, 3.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 131.2$, 124.9, 80.5, 37.5, 36.6, 35.4, 34.0, 33.8, 26.2, 25.7, 24.9, 24.8, 17.8, 17.7, 15.5 ppm; IR (film): $\tilde{\nu} = 3399$, 2963, 2926, 2866, 1452, 1375, 1115, 918 cm^{-1}; MS (70 eV): *m/z* (%): 222 (9) [M^+], 204 (29), 161 (21), 137 (20), 121 (59), 107 (27), 93 (58), 82 (100), 69 (93), 55 (41), 43 (79), 29 (11); HRMS (ESI): *m/z*: calcd for $C_{15}H_{26}ONa$ [$M^+ + Na$]: 245.1876, found: 245.1874.

Compound 29: Ozone was bubbled through a solution of compound **5** (45 mg, 0.22 mmol) in CH_2Cl_2 (2 mL) at −78 °C until a pale blue color persisted. The mixture was purged with argon to remove excess ozone before Me_2S (36 μL, 0.44 mmol) and Et_3N (60 μL, 0.42 mmol) were introduced. After stirring for 10 min at −78 °C, the mixture was allowed to reach ambient temperature and additional Et_3N (60 μL, 0.42 mmol) was added. After stirring for 30 min, the mixture was adsorbed on silica and the product eluded with 50% Et_2O in pentanes to give compound **29** as a colorless oil (33 mg, 84%). $[\alpha]_D^{20} = +37.5$ ($c = 2.0$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 9.73$ (t, $J = 1.5$ Hz, 1H), 2.51–2.35 (m, 2H), 2.16–2.01 (m, 2H), 1.98–1.95 (m, 2H), 1.86–1.77 (m, 1H), 1.65–1.55 (m, 2H), 1.39–1.30 (m, 1H), 1.11 (tdd, $J = 9.0$, 4.7, 1.1 Hz, 1H), 1.07 (dd, $J = 4.7$, 3.3 Hz, 1H), 0.97 ppm (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta = 214.0$, 202.4, 42.2, 38.4, 37.5, 34.5, 33.3, 26.4, 23.6, 19.0, 17.0 ppm; IR (film): $\tilde{\nu} = 2956$, 2933, 2875, 2723, 1714, 1461, 1446, 1379, 1259, 1176, 1025, 916, 776 cm^{-1}; MS (70 eV): *m/z* (%): 180 (7) [M^+], 147 (23), 136 (88), 123 (73), 105 (13), 96 (33), 79 (79), 67 (77), 55 (100), 41 (86), 29 (54); HRMS (EI): calcd for $C_{11}H_{16}O_2Na$ [$M^+ + Na$]: 180.1150, found: 180.1151.

Compound 32: NaH (6 mg, 0.23 mmol) was added to a solution of phosphonate **30** (91 mg, 0.25 mmol)[48] in THF (0.5 mL) at 0 °C and the resulting mixture stirred for 30 min before it was transferred via cannula into a solution of **29** (30 mg, 0.17 mmol) in THF (0.5 mL) at −78 °C. The mixture was stirred for 30 min and then allowed to reach 0 °C. After stirring for 1 h, the reaction was quenched with the minimum amount of aq. sat. NH_4Cl, the entire mixture adsorbed on silica gel and product **31** eluded with 50% Et_2O in pentanes. This material was used in the next step without further characterization. A solution of $Ph_3P{=}CH_2$ (14 mg, 0.05 mmol) in THF (1 mL) was added to a solution of compound **31** thus obtained in THF (0.5 mL) at −78 °C and the mixture allowed to reach ambient temperature. After stirring for 45 min, the reaction was quenched with aq. sat. NH_4Cl, the mixture adsorbed on silica gel and the product eluded with 20% Et_2O in pentanes to give compound **32** as a colorless oil (22 mg, 50%). $[\alpha]_D^{20} = -53.8$ ($c = 1.44$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 5.89$ (qt, $J = 7.4$, 1.3 Hz, 1H), 4.78 (brs, 1H), 4.61 (brs, 1H), 4.16 (q, $J = 7.1$ H, 2H), 2.46–2.32 (m, 2H), 2.17–2.10 (m, 1H), 2.05–1.94 (m, 1H), 1.86 (dd, $J = 2.7$, 1.3 Hz, 3H), 1.76–1.67 (m, 2H), 1.61–1.50 (m, 2H), 1.41–1.34 (m, 1H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.25–1.21 (m, 1H), 0.93 (d, $J = 6.8$ Hz, 3H), 0.66 (dd, $J = 4.3$, 3.4 Hz, 1H), 0.58 ppm (dd, $J = 8.0$, 4.3 Hz, 1H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta = 168.3$, 154.5, 142.8, 127.5, 101.9, 60.3, 38.4, 37.0, 34.5, 31.4, 29.1, 28.1, 27.1, 20.8, 17.9, 16.3, 14.5 ppm; IR (film): $\tilde{\nu} = 3073$, 2954, 2931, 2868, 1714, 1651, 1456, 1372, 1220, 1185, 1139, 1098, 1026, 862 cm^{-1}; MS (70 eV): *m/z* (%): 262 (6) [M^+], 216 (12), 141 (16), 133 (16), 119 (100), 105 (19), 93 (65), 77 (28), 67 (16), 55 (18), 41 (22), 29 (17); HRMS (ESI): *m/z*: calcd for $C_{17}H_{26}O_2Na$ [$M^+ + Na$]: 285.1825, found: 285.1823.

Compound 8: Dibal-H (1.0 M in toluene, 0.12 mL) was added to a solution of compound **32** (20 mg, 0.08 mmol) in THF (1 mL) at −78 °C and the mixture was allowed to warm to 0 °C. After stirring for 5 min, additional Dibal-H (1.0 M in toluene, 0.08 mL) was introduced and stirring continued for 30 min. The reaction was quenched by the slow addition of MeOH (1 mL) followed by an aq. sat. solution of Rochelle salt (1 mL). After stirring for 30 min, a clear separation of the phases was reached. The aqueous layer was extracted with Et_2O, the combined organic phases were evaporated and the product purified by flash chromatography (20% Et_2O in pentanes) to give alcohol **8** as a colorless oil (15 mg, 88%). $[\alpha]_D^{27} = -38.9$ ($c = 1.1$ in hexanes), lit.:[18a] $[\alpha]_D^{27} = -37.9$ ($c = 1.19$ in hexanes); ^{1}H NMR (300 MHz, C_6D_6): $\delta = 5.18$ (t, $J = 7.3$ Hz, 1H), 5.00 (brs, 1H), 4.79 (brs, 1H), 3.97 (s, 2H), 2.10–1.86 (m, 4H), 1.76 (d, $J = 1.2$ Hz, 3H), 1.67–1.55 (m, 2H), 1.51–1.39 (m, 2H), 1.29–1.17 (m, 1H), 1.08–1.01 (m, 2H), 0.86 (d, $J = 6.7$ Hz, 3H), 0.58 (dd, $J = 4.2$, 3.5 Hz, 1H), 0.42 ppm (ddd, $J = 7.7$, 4.6, 1.1 Hz, 1H); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 153.8$, 135.1, 102.5, 61.5, 38.1, 36.6, 35.3, 31.8, 29.1, 26.7, 25.9, 21.4, 18.3, 16.3 ppm; IR (film): $\tilde{\nu} = 3310$, 3073, 2954, 2928, 2867, 1709, 1652, 1455, 1375, 1251, 1110, 1005, 862, 837 cm^{-1}; MS (70 eV): *m/z* (%): 220 (17) [M^+], 161 (17), 145 (10), 133 (32), 121 (52), 105 (26), 93 (100), 79 (46), 69 (40), 55 (34), 43 (79), 20 (17); HRMS (EI): *m/z*: calcd for $C_{15}H_{24}O$ [M^+]: 220.1827, found: 220.1825.

Compound 41d: Ketone *ent*-**46** (50 mg, 0.2 mmol), Bu_4NHSO_4 (3.4 mg, 0.01 mmol) and $Na_2B_4O_7{\cdot}10H_2O$ (0.05 M in Na_2EDTA_{aq} (0.4 mM), 2.4 mL) were successively added to a solution of compound **6** (20 mg, 0.1 mmol) in dimethoxymethane/MeCN (2/1, 2 mL). The resulting mixture was vigorously stirred at 0 °C while solutions of K_2CO_3 (0.15 g, 1.1 mmol) in H_2O (1.2 mL) and Oxone (0.17 g, 0.3 mmol) in aq. Na_2EDTA (0.4 mM, 1.2 mL) were added dropwise. Once the addition was complete, the reaction was allowed to stir for 20 min at 0 °C before it was diluted with water (1 mL). The aqueous phase was extracted with Et_2O (3×5 mL), the combined organic layers were dried over Na_2SO_4 and evaporated, and the residue purified by flash chromatography (40% Et_2O in pentanes) to give compound **41d** as a colorless oil (17 mg, 74%). The diastereomeric ratio (dr 8:1) was determined by GC (50 m SE-54 0.32/0.53df G/358, ∅ 0.32 mm, 220/105 410 min, 8 min 320, 5 min 350 °C, 0.63 bar H_2). $[\alpha]_D^{20} = -29.1$ ($c = 0.5$ in CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 2.68$–2.64 (m, 1H), 2.20–1.84 (m, 4H), 1.67–1.52 (m, 4H), 1.43–1.30 (m, 2H), 1.27 (s, 3H), 1.24 (s, 3H), 1.20–1.14 (m, 2H), 1.00 ppm (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta = 214.2$, 64.5, 58.2, 38.8, 38.3, 33.5, 33.4, 31.3, 27.5, 25.0, 22.7, 21.3, 18.8, 17.5 ppm; IR (film): $\tilde{\nu} = 2959$, 1875, 1719, 1459, 1378, 1177, 1119, 1023, 863, 775 cm^{-1}; MS (70 eV): *m/z* (%): 222 (0.2) [M^+], 136 (100), 123 (71), 107 (13), 93 (20), 79 (33), 67 (26), 55 (26), 41 (73), 27 (32); HRMS (EI): *m/z*: calcd for $C_{14}H_{22}O_2Na$ [$M^+ + Na$]: 245.1512, found: 245.1510

Compound 45: A freshly prepared solution of LDA (0.1 M in THF, 0.5 mL) was added to a solution of compound **41d** (dr 8:1, 11 mg,

50 μmol) in THF (0.5 mL) at −78 °C. After stirring for 20 min at this temperature, 2-pyridyl-NTf_2 (Comins reagent, 24 mg, 60 μmol) was introduced and the resulting mixture allowed to reach ambient temperature. Stirring was continued for 30 min before the mixture was cooled to −35 °C. NMP (46 μL, 0.50 mmol), $Fe(acac)_3$ (2 mg, 5 μmol) and MeMgBr (3 M in Et_2O, 27 μL) were then added successively and the ensuing cross coupling reaction quenched after 5 min at −35 °C by addition of aq. sat. NH_4Cl (100 μL). The mixture was adsorbed on silica which was placed on top of a flash column packed with silica gel. The product was eluded with 10% Et_2O in pentanes to give compound **45** as a colorless oil (8 mg, dr 8:1, 72%). $[\alpha]_D^{20} = -17.9$ ($c = 0.5$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.94$ (brs, 1H), 2.73–2.70 (m, 1H), 2.40 (dt, $J = 17.0$, 2.2 Hz, 1H), 2.14–2.09 (m, 1H), 1.76 (d, $J = 1.7$ Hz, 3H), 1.65–1.57 (m, 3H), 1.36–1.30 (m, 2H), 1.31 (s, 3H), 1.27 (s, 3H), 1.20–1.16 (m, 1H), 0.95 (d, $J = 6.8$ Hz, 3H), 0.76 (dd, $J = 7.5$, 3.5 Hz, 1H), 0.11 ppm (t, $J = 3.2$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 145.1$, 120.9, 64.7, 58.1, 38.4, 35.4, 33.1, 31.9, 31.0, 27.1, 24.9, 23.7, 18.7, 17.8, 16.3 ppm; IR (film): $\tilde{\nu} = 3038$, 2959, 2925, 2846, 1687, 1641, 1447, 1377, 1220, 1126, 776 cm^{-1}; MS (70 eV): m/z (%): 220 (1) [M^+], 145 (19), 132 (84), 119 (72), 105 (47), 93 (100), 77 (36), 71 (35), 55 (19), 43 (38), 29 (10); HRMS (EI): m/z: calcd for $C_{15}H_{24}O$ [M^+]: 220.1827, found: 220.1820.

Acknowledgement

Generous financial support by the MPG and the Fonds der Chemischen Industrie is gratefully acknowledged. We thank our NMR and chromatography departments for excellent support, Dr. T. Yamamoto, Takasago, for a gift of enantiopure citronellal, and Umicore AG & Co KG, Hanau, for a gift of noble metal salts.

[1] H. Strickler, J. B. Davis, G. Ohloff, *Helv. Chim. Acta* **1976**, *59*, 1328–1332.
[2] For an early study on related reactions of 1,5- (rather than 1,6-) enynes catalyzed by Pd^{II}, see: V. Rautenstrauch, *J. Org. Chem.* **1984**, *49*, 950–952.
[3] Reviews: a) A. Fürstner, P. W. Davies, *Angew. Chem.* **2007**, *119*, 3478–3519; *Angew. Chem. Int. Ed.* **2007**, *46*, 3410–3449; b) D. J. Gorin, F. D. Toste, *Nature* **2007**, *446*, 395–403; c) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Commun.* **2007**, 333–346; d) A. S. K. Hashmi, G. J. Hutchings, *Angew. Chem.* **2006**, *118*, 8064–8105; *Angew. Chem. Int. Ed.* **2006**, *45*, 7896–7936; e) V. Michelet, P. Y. Toullec, J.-P. Genêt, *Angew. Chem.* **2008**, *120*, 4338–4386; *Angew. Chem. Int. Ed.* **2008**, *47*, 4268–4315; f) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal.* **2006**, *348*, 2271–2296; g) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211.
[4] a) E. Mainetti, V. Mouriès, L. Fensterbank, M. Malacria, J. Marco-Contelles, *Angew. Chem.* **2002**, *114*, 2236–2239; *Angew. Chem. Int. Ed.* **2002**, *41*, 2132–2135; b) S. Anjum, J. Marco-Contelles, *Tetrahedron* **2005**, *61*, 4793–4803; c) C. Blaszykowski, Y. Harrak, M.-H. Gonçalves, J.-M. Cloarec, A.-L. Dhimane, L. Fensterbank, M. Malacria, *Org. Lett.* **2004**, *6*, 3771–3774; d) Y. Harrak, C. Blaszykowski, M. Bernard, K. Cariou, E. Mainetti, V. Mouriès, A.-L. Dhimane, L. Fensterbank, M. Malacria, *J. Am. Chem. Soc.* **2004**, *126*, 8656–8657; e) X. Shi, D. J. Gorin, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 5802–5803; f) B. A. B. Prasad, F. K. Yoshimoto, R. Sarpong, *J. Am. Chem. Soc.* **2005**, *127*, 12468–12469; g) K. Kato, Y. Yamamoto, H. Akita, *Tetrahedron Lett.* **2002**, *43*, 6587–6590; h) for an intermolecular version see: K. Miki, K. Ohe, S. Uemura, *J. Org. Chem.* **2003**, *68*, 8505–8513; i) K. Miki, K. Ohe, S. Uemura, *Tetrahedron Lett.* **2003**, *44*, 2019–2022.
[5] V. Mamane, T. Gress, H. Krause, A. Fürstner, *J. Am. Chem. Soc.* **2004**, *126*, 8654–8655.
[6] A. Fürstner, P. Hannen, *Chem. Commun.* **2004**, 2546–2547.
[7] a) S. Anjum, J. Marco-Contelles, *Tetrahedron* **2005**, *61*, 4793–4803; b) E. Soriano, P. Ballesteros, J. Marco-Contelles, *Organometallics* **2005**, *24*, 3182–3191; c) A. Correa, N. Marion, L. Fensterbank, M. Malacria, S. P. Nolan, L. Cavallo, *Angew. Chem.* **2008**, *120*, 730–733; *Angew. Chem. Int. Ed.* **2008**, *47*, 718–721; d) O. N. Faza, C. S. López, R. Álvarez, A. R. de Lera, *J. Am. Chem. Soc.* **2006**, *128*, 2434–2437; e) E. Soriano, J. Marco-Contelles, *J. Org. Chem.* **2005**, *70*, 9345–9353; f) E. Soriano, J. Marco-Contelles, *J. Org. Chem.* **2007**, *72*, 1443–1448; g) E. Soriano, P. J. Marco-Contelles, *J. Org. Chem.* **2007**, *72*, 2651–2654.
[8] A. Fürstner, P. Hannen, *Chem. Eur. J.* **2006**, *12*, 3006–3019.
[9] C. Fehr, J. Galindo, *Angew. Chem.* **2006**, *118*, 2967–2970; *Angew. Chem. Int. Ed.* **2006**, *45*, 2901–2904.
[10] For pioneering studies on α-diazoketone cyclization reactions, see: a) G. Stork, J. Ficini, *J. Am. Chem. Soc.* **1961**, *83*, 4678; reviews: b) M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*, Wiley, New York, **1998**; c) H. M. L. Davies in *Comprehensive Organic Synthesis, Vol. 4* (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**, pp. 1031–1067; d) A. Padwa, K. E. Krumpe, *Tetrahedron* **1992**, *48*, 5385–5453.
[11] a) A. Fürstner, H. Szillat, B. Gabor, R. Mynott, *J. Am. Chem. Soc.* **1998**, *120*, 8305–8314; b) A. Fürstner, H. Szillat, F. Stelzer, *J. Am. Chem. Soc.* **2000**, *122*, 6785–6786; c) A. Fürstner, F. Stelzer, H. Szillat, *J. Am. Chem. Soc.* **2001**, *123*, 11863–11869; d) A. Fürstner, V. Mamane, *J. Org. Chem.* **2002**, *67*, 6264–6267; e) A. Fürstner, V. Mamane, *Chem. Commun.* **2003**, 2112–2213; f) V. Mamane, P. Hannen, A. Fürstner, *Chem. Eur. J.* **2004**, *10*, 4556–4575; g) A. Fürstner, P. W. Davies, T. Gress, *J. Am. Chem. Soc.* **2005**, *127*, 8244–8245; h) A. Fürstner, P. W. Davies, *J. Am. Chem. Soc.* **2005**, *127*, 15024–15025; i) A. Fürstner, C. Aïssa, *J. Am. Chem. Soc.* **2006**, *128*, 6306–6307; j) A. Fürstner, J. W. J. Kennedy, *Chem. Eur. J.* **2006**, *12*, 7398–7410; k) A. Fürstner, E. K. Heilmann, P. W. Davies, *Angew. Chem.* **2007**, *119*, 4844–4847; *Angew. Chem. Int. Ed.* **2007**, *46*, 4760–4763.
[12] A. Fürstner, C. C. Stimson, *Angew. Chem.* **2007**, *119*, 9001–9005; *Angew. Chem. Int. Ed.* **2007**, *46*, 8845–8849.
[13] A. Fürstner, L. Morency, *Angew. Chem.* **2008**, *120*, 5108–5111; *Angew. Chem. Int. Ed.* **2008**, *47*, 5030–5033.
[14] A. Fürstner, M. Alcarazo, R. Goddard, C. W. Lehmann, *Angew. Chem.* **2008**, *120*, 3254–3258; *Angew. Chem. Int. Ed.* **2008**, *47*, 3210–3214.
[15] S. J. Terhune, J. W. Hogg, A. C. Bromstein, B. M. Lawrence, *Can. J. Chem.* **1975**, *53*, 3285–3293.
[16] For a compilation, see: D. Joulain, W. A. König, *The Atlas of Spectral Data of Sesquiterpene Hydrocarbons*, EB Verlag, Hamburg, **1998**.
[17] a) M. Takita, *Jpn. J. Appl. Entomol. Zool.* **2007**, *51*, 231–233; b) M. Takita, H. Sugie, J. Tabata, S. Ishii, S. Hiradate, *Appl. Entomol. Zool.* **2008**, *43*, 11–17.
[18] a) K. Mori, T. Tashiro, T. Yoshimura, M. Takita, J. Tabata, S. Hiradate, H. Sugie, *Tetrahedron Lett.* **2008**, *49*, 354–357; b) K. Mori, *Tetrahedron: Asymmetry* **2007**, *18*, 838–846.
[19] E. J. Corey, R. D. Balanson, *Tetrahedron Lett.* **1973**, *14*, 3153–3156.
[20] Structure determination: a) G. Stork, R. Breslow, *J. Am. Chem. Soc.* **1953**, *75*, 3291; b) P. A. Plattner, A. Fürst, A. Eschenmoser, W. Keller, H. Kläui, S. Meyer, M. Rosner, *Helv. Chim. Acta* **1953**, *36*, 1845–1862; c) G. Büchi, R. E. Erickson, N. Wakabayashi, *J. Am. Chem. Soc.* **1961**, *83*, 927–938.
[21] A. Erkkilä, P. M. Pihko, *J. Org. Chem.* **2006**, *71*, 2538–2541.
[22] J. D. White, L. R. Jayasinghe, *Tetrahedron Lett.* **1988**, *29*, 2139–2142.
[23] Specifically, attempted Brown-, Duthaler-Hafner- and Keck allylation of **17** with the corresponding boron, titanium or tin reagents derived from bromide **16** gave poor yields and/or diastereomeric ratios close to 1:1. For leading references concerning these classical methods, see: a) U. S. Racherla, H. C. Brown, *J. Org. Chem.* **1991**, *56*, 401–404; b) A. Hafner, R. O. Duthaler, R. Marti, G. Rihs, P. Rothe-Streit, F. Schwarzenbach, *J. Am. Chem. Soc.* **1992**, *114*, 2321–2336; c) G. E. Keck, K. H. Tarbet, L. S. Geraci, *J. Am. Chem. Soc.* **1993**, *115*, 8467–8468.
[24] M. Nakamura, A. Hirai, M. Sogi, E. Nakamura, *J. Am. Chem. Soc.* **1998**, *120*, 5846–5847.

[25] For other applications of chiral zinc reagents of this type, see: a) M. Nakamura, T. Inoue, A. Sato, E. Nakamura, *Org. Lett.* **2000**, *2*, 2193–2196; b) S. Hanessian, R.-Y. Yang, *Tetrahedron Lett.* **1996**, *37*, 8997–9000; c) M. Nakamura, M. Arai, E. Nakamura, *J. Am. Chem. Soc.* **1995**, *117*, 1179–1180; d) M. Nakamura, A. Hirai, E. Nakamura, *J. Am. Chem. Soc.* **1996**, *118*, 8489–8490; e) for a short review on the use of monoanionic bisoxazolinate ligands in asymmetric synthesis, see: S. Dagorne, S. Bellemin-Laponnaz, A. Maisse-François, *Eur. J. Inorg. Chem.* **2007**, 913–925.

[26] A similar rational was provided to explain the results of certain addition reactions of substituted allylzinc reagents to cyclic aldimines, cf. ref. [25d].

[27] a) R. E. Lowenthal, A. Abiko, S. Masamune, *Tetrahedron Lett.* **1990**, *31*, 6005–6008; b) D. A. Evans, K. A. Woerpel, M. M. Hinman, M. M. Faul, *J. Am. Chem. Soc.* **1991**, *113*, 726–728; c) E. J. Corey, N. Imai, H. Y. Zhang, *J. Am. Chem. Soc.* **1991**, *113*, 728–729; d) D. Müller, G. Umbricht, B. Weber, A. Pfaltz, *Helv. Chim. Acta* **1991**, *74*, 232–240; e) G. Helmchen, A. Krotz, K.-T. Ganz, D. Hansen, *Synlett* **1991**, 257–259; f) J. Hall, J.-M. Lehn, A. DeCian, J. Fischer, *Helv. Chim. Acta* **1991**, *74*, 1–6.

[28] Review: J. M. Seco, E. Quiñoá, R. Riguera, *Chem. Rev.* **2004**, *104*, 17–118.

[29] a) C. S. Gibson, W. M. Colles, *J. Chem. Soc.* **1931**, 2407–2416; b) H.-N. Adams, J. Strähle, *Z. Anorg. Allg. Chem.* **1982**, *485*, 65–80; c) for a recent application in catalysis, see:A. S. K. Hashmi, J. P. Weyrauch, M. Rudolph, E. Kurpejović, *Angew. Chem.* **2004**, *116*, 6707–6709; *Angew. Chem. Int. Ed.* **2004**, *43*, 6545–6547.

[30] The corresponding acetates can also be employed. Although they afforded higher yields (89%), the chirality transfer during the cycloisomerization reaction was lower (dr 5:1 rather than $\geq$15:1 in the *p*-nitrobenzoate case). Therefore the *p*-nitrobenzoates were used for our preparative purposes; for previous applications of *p*-nitrobenzoates in Ohloff-type reactions, see refs. [4a,b,d]

[31] $PtCl_2$ in toluene is also effective but results in somewhat lower isolated yields (ca. 60%).

[32] E. A. Mash, K. A. Nelson, *Tetrahedron* **1987**, *43*, 679–692.

[33] For previous syntheses of optically active sabina ketone, see ref. [4d] and the following: a) M. Barberis, J. Pérez-Prieto, *Tetrahedron Lett.* **2003**, *44*, 6683–6685; b) D. M. Hodgson, Y. K. Chung, J.-M. Paris, *J. Am. Chem. Soc.* **2004**, *126*, 8664–8665 and references therein.

[34] P. Weyerstahl, H.-C. Wahlburg, U. Splittgerber, H. Marschall, *Flavour Fragrance J.* **1994**, *9*, 179–186.

[35] P. Weyerstahl, H. Marschall, K. Thefeld, G. C. Subba, *Flavour Fragrance J.* **1998**, *13*, 377–388.

[36] P. Weyerstahl, H. Marschall-Weyerstahl, C. Christiansen, *Flavour Fragrance J.* **1989**, *4*, 93–98. This paper also corrects the erroneous $[\alpha]_D^{20}$ of *cis*-sesquisabinene hydrate reported in ref. [37].

[37] P. Weyerstahl, H. Marschall-Weyerstahl, V. K. Kaul, E. Manteuffel, L. Glasow, *Liebigs Ann. Chem.* **1987**, 21–28.

[38] H. C. Brown, P. Geoghegan, *J. Am. Chem. Soc.* **1967**, *89*, 1522–1524.

[39] a) A. Fürstner, R. Martin, *Chem. Lett.* **2005**, 624–629; b) B. D. Sherry, A. Fürstner, *Acc. Chem. Res.* **2008**, DOI: 10.1021/ar800039x.

[40] a) B. Scheiper, M. Bonnekessel, H. Krause, A. Fürstner, *J. Org. Chem.* **2004**, *69*, 3943–3949; b) for a discussion of the nature of the reactive intermediate formed form iron salts and methyl donors, see: A. Fürstner, H. Krause, C. W. Lehmann, *Angew. Chem.* **2006**, *118*, 454–458; *Angew. Chem. Int. Ed.* **2006**, *45*, 440–444; c) A. Fürstner, R. Martin, H. Krause, G. Seidel, R. Goddard, C. W. Lehmann, *J. Am. Chem. Soc.* **2008**, *130*, 8773–8787.

[41] Applications: a) A. Fürstner, A. Leitner, M. Méndez, H. Krause, *J. Am. Chem. Soc.* **2002**, *124*, 13856–13863; b) A. Fürstner, A. Leitner, *Angew. Chem.* **2003**, *115*, 320–323; *Angew. Chem. Int. Ed.* **2003**, *42*, 308–311; c) A. Fürstner, D. De Souza, L. Parra-Rapado, J. T. Jensen, *Angew. Chem.* **2003**, *115*, 5516–5518; *Angew. Chem. Int. Ed.* **2003**, *42*, 5358–5360; d) G. Seidel, D. Laurich, A. Fürstner, *J. Org. Chem.* **2004**, *69*, 3950–3952; e) B. Scheiper, F. Glorius, A. Leitner, A. Fürstner, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 11960–11965; f) O. Lepage, E. Kattnig, A. Fürstner, *J. Am. Chem. Soc.* **2004**, *126*, 15970–15971; g) A. Fürstner, L. Turet, *Angew. Chem.* **2005**, *117*, 3528–3532; *Angew. Chem. Int. Ed.* **2005**, *44*, 3462–3466; h) A. Fürstner, D. Kirk, M. D. B. Fenster, C. Aïssa, D. De Souza, O. Müller, *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 8103–8108; i) A. Fürstner, E. Kattnig, O. Lepage, *J. Am. Chem. Soc.* **2006**, *128*, 9194–9204.

[42] R. P. Adams, T. A. Zanoni, T. A. van Beek, M. A Posthumus, C. van de Haar, *J. Essent. Oil Res.* **1998**, *10*, 175–178.

[43] Actually, an $[\alpha]_D$ for sesquithujene is reported in: K. Wihstutz, Diplomarbeit, Universität Hamburg, **1997**; its sign is identical to the $[\alpha]_D$ recorded for the synthetic sample but the magnitude is different. However, this literature data point is problematic because the $[\alpha]_D$ was recorded at an unusually low concentration of $c = 0.001\ g\,mL^{-1}$.

[44] C. S. Mathela, C. S. Chanotiya, S. Sati, S. S. Sammal, V. Wray, *Fitoterapia* **2007**, *78*, 279–282.

[45] a) Review: M. Frohn, Y. Shi, *Synthesis* **2000**, 1979–2000; b) O. A. Wong, Y. Shi, *Chem. Rev.* **2008**, *108*, DOI: 10.1021/cr068367; c) Y. Tu, Z.-X. Wang, Y. Shi, *J. Am. Chem. Soc.* **1996**, *118*, 9806–9807; d) see also: Z. Xiong, E. J. Corey, *J. Am. Chem. Soc.* **2000**, *122*, 4831–4832.

[46] M.-X. Zhao, Y. Shi, *J. Org. Chem.* **2006**, *71*, 5377–5379.

[47] S. A. Burova, F. E. McDonald, *J. Am. Chem. Soc.* **2002**, *124*, 8188–8189.

[48] K. Ando, *J. Org. Chem.* **1998**, *63*, 8411–8416.

Received: July 8, 2008
Published online: September 11, 2008

