Thermal Isomerization of Isoborneols and Dehydroisoborneols to New Chiral Building Blocks in Terpenoid Synthesis

by **Georg Rüedi**[1])* and **Hans-Jürgen Hansen**

Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich
(phone: +4116354248; fax: +4116356853; e-mail: georg@access.unizh.ch)

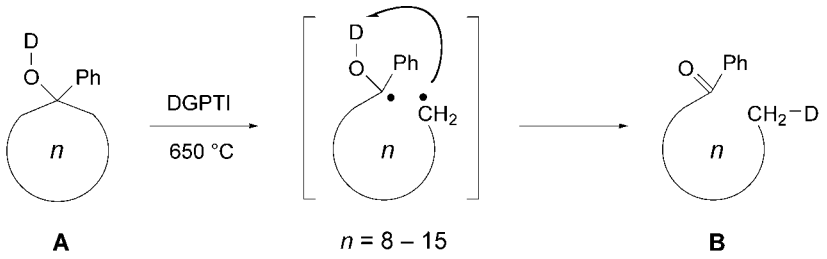
The substituted isoborneols **1a**–**1g** and 5,6-dehydroisoborneols **6a**–**6c**, readily prepared in excellent yields from (+)-camphor and (+)-5,6-dehydrocamphor (**2**) by aryl, vinyl, or alkyl *Grignard* addition in the presence of stoichiometric amounts of $CeCl_3$, were thermally isomerized in a flow reactor system under DGPTI (dynamic gas-phase thermo-isomerization) conditions at temperatures between 480 and 630° to give the enantiomerically pure monocyclic carbonyl compounds **7a**–**7d**, **19a**,**b**, **23**, and **24**. In all cases, product formation proceeded highly regio- as well as stereoselectively. The absolute configurations of the new stereogenic centers were determined by ^{1}H-NOE measurements. DGPTI of the aryl substrates **1a**–**1d** is proposed to effect initial cleavage of the weakest single bond in the molecule under formation of a diradical intermediate state followed by intramolecular H-abstraction to afford the acetophenone derivatives **7a**–**7d**. This reaction path was further supported by a ^{2}H-labeling study showing the OH group to be the exclusive H-source. In contrast, DGPTI of the vinyl substrates **1e** and **6b** allowed concerted *retro*-ene and oxy-*Cope* rearrangements. In the case of 5,6-dehydro-2-phenylisoborneol (**6a**), concomitant diradical and *retro-Diels–Alder* reaction pathways could be observed. In addition, a new route to (+)-*trans*-α-campholanic acid (**9**) and (+)-*trans*-α-dihydrocampholytic acid (**14**) is presented by regioselective *Baeyer–Villiger* oxidation and subsequent hydrolysis of **7c** and **7d**, respectively.

1. Introduction. – Recently, we have reported a diradical-mediated ring-opening reaction of medium- and large-ring 1-phenylcycloalkanones **A** performed under DGPTI (dynamic gas-phase thermo-isomerization) conditions at 650° [1]. A reaction mechanism *via* initial cleavage of the weakest single bond in the molecule resulted in the formation of a α-hydroxybenzyl ω-alkyl diradical. Intramolecular H-abstraction within the transient diradical state furnished open-chain phenones **B** with the corresponding chain length in excellent yields. This reaction pathway has been confirmed by subjecting *O*-deuterated substrates to DGPTI. The label was found to be fully incorporated into ω-position of the alkyl chain (*Scheme 1*).

Impelled by the preparative and mechanistic importance associated with diradical-mediated disproportionation reactions, we extended our investigations to optically active substrates derived from camphor. The main interest of the present work is focused on *1*) whether phenylisoborneols might react under DGPTI conditions in a similar manner to afford the corresponding open-chain products, and, if this is the case, *2*) whether the cleavage of the weakest single bond occurs regioselectively, and *3*) whether the H-transfer proceeds stereoselectively under retention of the geometry of the camphor framework. If this were the case, the procedure would provide a new and

[1]) Part of the PhD thesis of *G. R.*, University of Zürich, 2004.

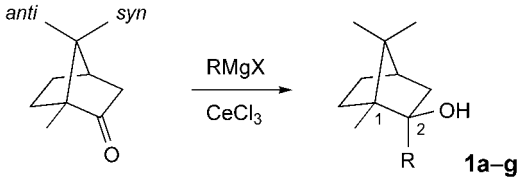
Scheme 1



very convenient access to a broad variety of chiral building blocks in terpenoid synthesis.

2. Results and Discussion. – 2.1. *Synthesis of Monoterpene Substrates* **1a**–**1d** *and* **6a**–**6c**. The addition of both phenyl and vinyl *Grignard* reagents to (+)-camphor in the presence of anhydrous $CeCl_3$ carried out in THF at room temperature provided the optically pure tertiary *exo*-alcohols **1a**–**1e** in good-to-excellent yields (*Table 1*). Except for the 4-methoxyphenyl derivative **1c** [2], which could be crystallized from hexane, all compounds were obtained as liquids. Isoborneols with aliphatic substituents at C(2), such as the i-Pr and the cyclohexyl group, were prepared accordingly in comparable yields, but by means of the corresponding magnesium chlorides instead of the bromides. As reported by *Dimitrov et al.* [3], the employment of a stoichiometric amount of $CeCl_3$ as *Lewis* acid is essential for complete conversion. In the absence of $CeCl_3$, the same alcohols were formed, but with significantly lower conversion rates (30–40%) due to competing enolization, giving back starting material.

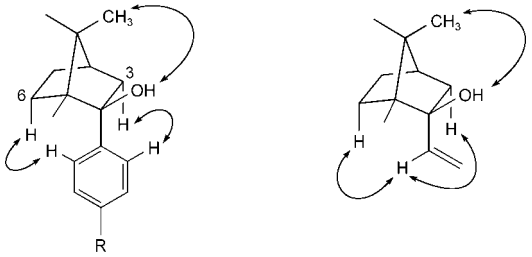
Table 1. *$CeCl_3$-Mediated Addition of* Grignard *Reagents to (+)-Camphor*



R	Product **1**	$CeCl_3$	Time [h]	Yield [%]
Ph	**a**	1.2 equiv.	0.5	95
4-MeC_6H_4	**b**	1.2 equiv.	0.5	92
4-$MeOC_6H_4$	**c**	1.0 equiv.	2.0	88
4-$CF_3C_6H_4$	**d**	0.8 equiv.	1.0	98
Vinyl	**e**	1.2 equiv.	1.0	76
i-Pr	**f**	1.2 equiv.	1.5	81
Cyclohexyl	**g**	1.2 equiv.	1.5	85

The *endo*-configuration of the 2-aryl *Grignard* adducts **1a**–**1d** was established by ^{1}H-NOE experiments. According to *Fig. 1*, NOE effects were observed between the *ortho*-H-atoms of the aromatic ring and both H_{endo}–C(3) and H_{endo}–C(6), respectively,

and between the OH group and Me_{syn}–C(7). Similarly, 2-vinylisoborneol (**1e**) exhibited an NOE effect between the α-H-atom on the vinyl moiety at δ(H) 6.03 and H_{endo}–C(3,6). The exclusive *endo*-attack of *Grignard* reagents on camphor is due to the steric shielding by Me_{syn}–C(7) of the rigid bicyclo[2.2.1]heptane skeleton.



1a–d **1e**

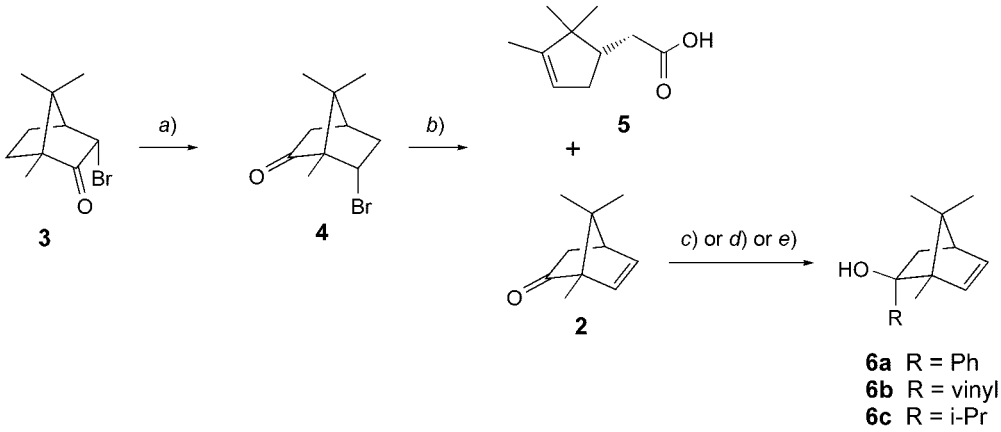
Fig. 1. *^{1}H-NOE Correlations of isoborneols* **1a**–**e** *of* endo-*configuration*

(+)-5,6-Dehydrocamphor (**2**) was prepared according to the procedure described by *Hutchinson et al.* [4][5] by treating commercially available (+)-*endo*-3-bromocamphor (**3**) with chlorosulfonic acid ($ClSO_3H$) at 45° to afford rearranged (–)-*endo*-6-bromocamphor (**4**) in 42% yield after crystallization from hexane (*Scheme 2*). It is noteworthy that this isomerization reaction, involving several *Wagner–Meerwein* rearrangements as well as Me- and hydride-shift reactions, effects inversion of the camphor skeleton. Subsequent dehydrobromination with KOH in DMSO/H_2O 7:1 at 120° yielded the highly volatile dehydrocamphor **2** (45%). The low yield of **2** is due to the competing formation of (–)-α-campholenic acid (**5**), which was produced in 38% yield as the result of a *Grob*-like fragmentation. $CeCl_3$-Assisted addition of phenyl or vinyl magnesium bromide to (+)-5,6-dehydrocamphor (**2**) proceeded smoothly to give the corresponding *endo*-adducts **6a** and **6b**, respectively, in excellent yields (93–96%). The i-Pr-substituted dehydroisoborneol derivative **6c** was synthesized in the same manner, but with i-Pr MgCl. In contrast to camphor as the substrate, only substoichiometric amounts of $CeCl_3$ (0.2 equiv.) were necessary for optimal conversion to the products **6a**–**6c**. Again, the *endo*-selectivity was approved by ^{1}H-NOE measurements (*Fig. 2*). Irradiation of the *ortho*-H-atoms of the aromatic ring in **6a** produced NOE effects for H_{endo}–C(3), H–C(5), and H–C(6). Comparable interactions could be observed with **6b** by irradiating the α-H-atom on the vinyl moiety at δ(H) 6.01, as well as with **6c** when the Me groups at δ(H) 0.8 of the i-Pr moiety were irradiated. Furthermore, each compound exhibited an NOE effect between its OH group and the *syn*-positioned Me group at C(7).

2.2. *Rearrangements by DGPTI.* The thermal isomerization experiments were performed in a flow reactor system under vacuum conditions ($2-4\times10^{-2}$ mbar) at temperatures between 400° and 750°. The substrates were evaporated in a *Kugelrohr* oven heated at 80–130°, while a flow of N_2 was applied (0.8–1.4 l/h). The rearrangement products were collected in a cooling trap filled with liquid N_2 and subsequently subjected to column chromatography (for details, see *Exper. Part*).

2.2.1. *DGPTI of 2-Arylisoborneols.* In order to find the optimal contact time and temperature of the isoborneol substrates at the hot reactor zone, the DGPTI conditions

Scheme 2.



a) $ClSO_3H$, 45°; 42%. *b*) KOH, DMSO, H_2O, 120°; 45% (**2**), 38% (**5**). *c*) PhMgBr, $CeCl_3$, THF; 93%. *d*) C_2H_3MgBr, $CeCl_3$, THF; 96%. *e*) i-PrMgBr, $CeCl_3$, THF; 93%.

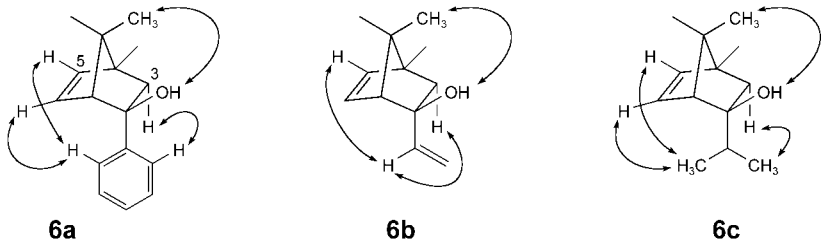
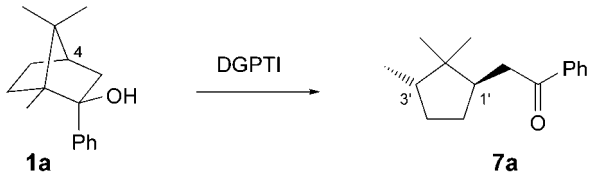


Fig. 2. *^{1}H-NOE Correlations of dehydroisoborneols* **6a**–**c** *of* endo-*configuration*

for each substrate were established by varying both the reactor temperature and the flow rate of the applied carrier gas. The product distribution of each experiment was analyzed by GC/MS. The results of the thermal isomerization of our model compound **1a** are displayed in *Table 2*. Two general tendencies are evident: *1*) the conversion rate is increased, as expected, by raising the reactor temperature and *2*) decreasing by raising the flow rate. However, product formation occurred only in a limited temperature range (580–680°). Almost no product formation was observed at temperatures below 580°, whereas temperatures above 680° provided numerous low-boiling side products, *e.g.*, dehydrated 2-phenylbornene and acetophenone. However, a reactor temperature of 630° in combination with a flow rate of 1.2 l/h provided the best results (73% yield of **7a**).

Examination of the isomerization product **7a** by ^{1}H- and ^{13}C-NMR spectroscopy indicated that only one diastereoisomer had been formed. The ^{13}C-NMR spectrum ($CDCl_3$) exhibited a *singlet* at δ(C) 201.1, which is typical for the C=O C-atom of aliphatic phenones. As the stereogenic center at C(4) in **1a** is not involved in a bond-cleavage/bond-formation process during the isomerization reaction, the (*R*)-configuration is retained in the product ((*R*)-configuration at C(1′)). The relative

Table 2. *Thermal Isomerization of 2-Phenylisoborneol* (**1a**) *to (1*R,*3*S*)-1-Phenyl-2-(2,2,3-trimethylcyclopentyl)-ethanone* (**7a**)



1a **7a**

Temp. [°]	Flow Rate [l/h]	**7a** (%)	**1a** (%)[a])
550	1.2	–	85
580	1.2	21	6
600	1.2	48	29
620	1.2	70	7
630	1.2	73	4
630	0.8	62	2
630	1.4	65	8
650	1.2	59	–
680	1.2	36	–

[a]) Recovered starting material.

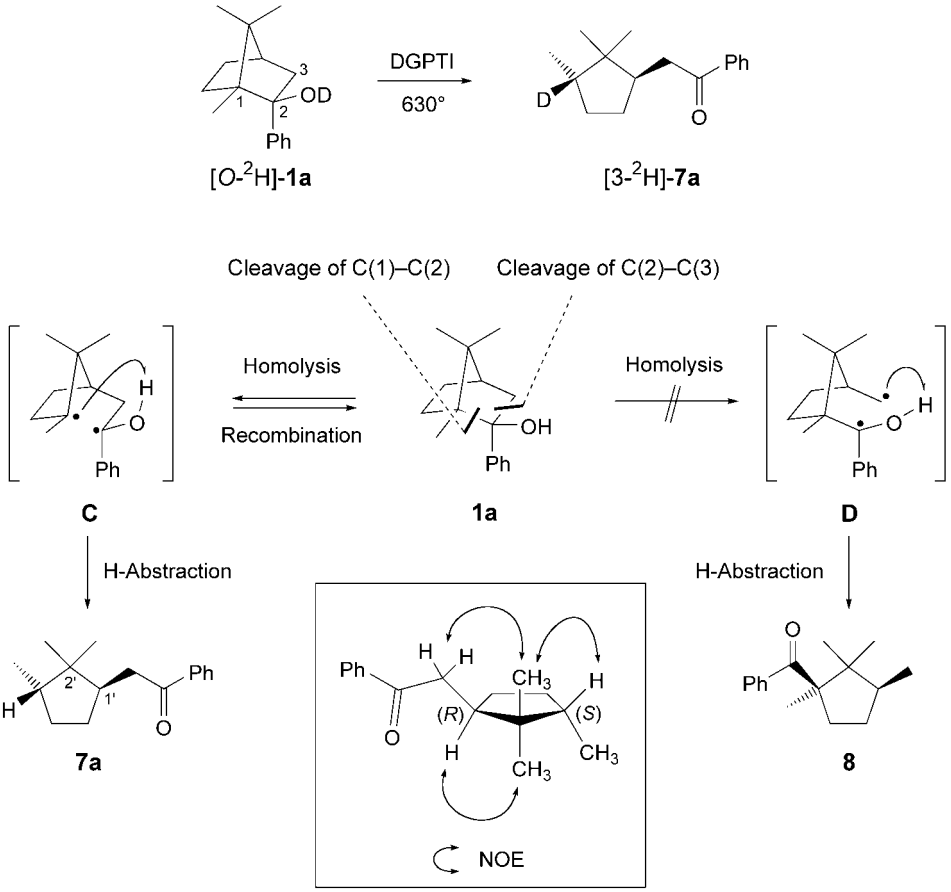
configuration at C(3′) in the tetrasubstituted cyclopentane ring was established by ^{1}H-NOE studies ($CDCl_3$) on a 600-MHz spectrometer. The ^{1}H-NMR spectrum of **7a** displayed three *singlets* for the Me groups on the cyclopentane ring. As displayed in *Scheme 3*, irradiation of the signals of the exocyclic methylidene group, which appeared as the *AB* part of an *ABX* system at δ(H) 3.03 and 2.73, respectively, produced an NOE effect for the *exo*-Me group at C(2′) at 0.88 ppm. Irradiation of the *X* part (H−C(1′)) at δ(H) 1.66 caused an NOE for the signals of the *endo*-Me group at 0.89 ppm. An NOE effect was further observed between Me_{exo}−C(2′) and H−C(3′). These observations provided evidence that the configuration at C(3′) was (*S*), *i.e.*, *trans*-1-phenyl-2-(2,2,3-trimethylcyclopentyl)ethanone (**7a**) was the exclusive isomerization product.

To gain additional insight into the mechanism of this highly regio- as well as stereoselective intramolecular H-transfer reaction, we prepared the *O*-deuterated isoborneol [*O*-^{2}H]-**1a** by repeated treatment of **1a** with MeOD/D_2O. After DGPTI at 630°, the label was found to be fully incorporated into the *exo*-position at C(3′) of [3-^{2}H]-**7a** (*Scheme 3*)[2]). The *sextet* for H−C(3′) of [3-^{2}H]-**7a** at δ(H) 1.66 had vanished while the ^{2}H-NMR spectrum ($CDCl_3$) showed a broad *singlet* at the same ppm value. It is important to state that no reaction or only tar formation occurred, when **1a** was thermolyzed up to 350° under static conditions in a sealed glass tube.

The above findings are consistent with a reaction pathway involving radical structures. Due to the required high thermal-energy impact (630° in the reactor zone), the weakest single bond (C(1)−C(2)) in the molecule is broken homolytically, and this highly regioselective cleavage leads to a stabilized hydroxy benzyl radical on one side of the pentacyclus, and a tertiary alkyl radical on the other side. This monocyclic diradical

[2]) The deuterium content was determined by ^{1}H-NMR and MS to be above 80%.

Scheme 3

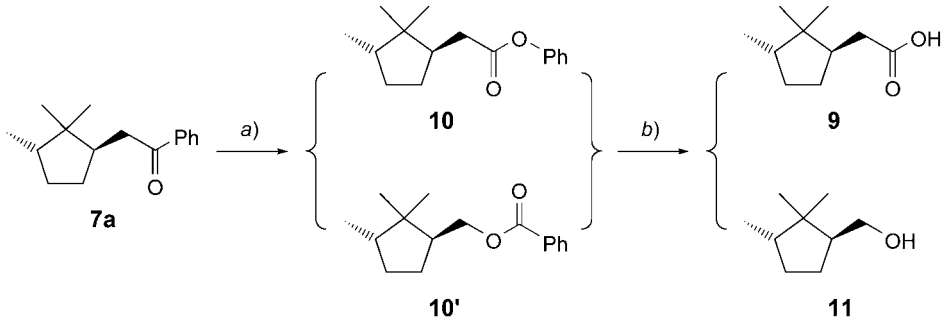


intermediate **C** can relax either way, giving back isoborneol **1a** by recombination, or going forward to the energetically more-stable phenone **7a** by intramolecular H-transfer, which is favored by 16.7 kcal mol^{-1} according to AM1-calculated ΔH_f° values of **1a** (−29.3 kcal mol^{-1}) and **7a** (−46.0 kcal mol^{-1}). AM1 Calculations of **1a** further showed that the C(1)−C(2) bond is longer (157.6 pm) than the C(2)−C(3) bond (155.9 pm), which is in excellent accordance with X-ray crystallographic analyses of reported phenylisoborneol derivatives [6]. Contrarily, cleavage of the stronger C(2)−C(3) bond would result in a disfavored diradical intermediate **D**, containing a primary alkyl radical, which would afford the sterically encumbered *cis*-phenylmethanone **8** (− 34.4 kcal mol^{-1}) through an analogous intramolecular H-transfer. The formation of **8**, however, was not observed even at temperatures of up to 680° (*Table 2*). The labeling experiment further showed the OH group to be the exclusive H-source for the disproportionation reaction. H-abstraction from C(3), forming thereby the enol of **7a**, which on tautomerization would give **7a**, could not be observed. It is further noteworthy that H-abstraction can be accomplished only under retention of

the geometry at bridgehead C(1), which explains the unique diastereoselectivity of this reaction (100% de).

As phenone **7a** represents a versatile chiral building block for the construction of a variety of useful synthetic intermediates, we tried to convert it to α-campholanic acid (**9**) by *Baeyer–Villiger* oxidation and subsequent hydrolysis of the intermediate phenyl ester **10** (*Scheme 4*). In addition, alkyl esters of **9** are reported to smell fruity and floral [7], which make them interesting for applications in the fragrance industry. Unfortunately, any attempts to effect regioselective oxidation of **7a** failed. Hence, treatment of **7a** with MCPBA (3-chlorobenzenecarboperoxoic acid) and 1 equiv. of TFA (trifluoroacetic acid) in CH_2Cl_2 at room temperature [8] yielded both the expected phenyl ester **10** along with benzoate **10′** in comparable amounts. Although hydrolysis of this mixture with LiOH in MeOH/H_2O [9], leading to (+)-*trans*-α-campholanic acid (**9**) and (1*S*,3*S*)-(2,2,3-trimethylcyclopentyl)methanol (**11**), was feasible, this procedure was considered not to be satisfactory due to the lack of regioselectivity in the *Baeyer–Villiger* oxidation.

Scheme 4

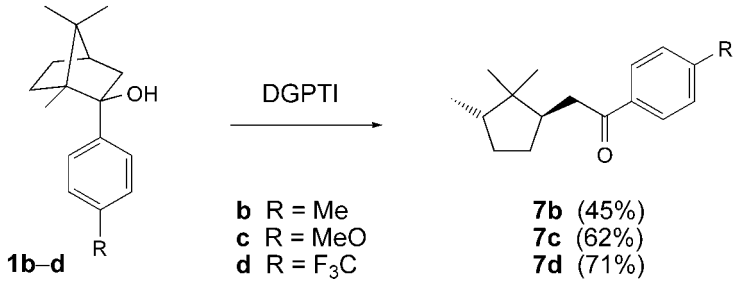


a) MCPBA, TFA, CH_2Cl_2, r.t.; 93%. *b*) LiOH, MeOH, H_2O, r.t.; 91%.

To circumvent this inconvenience, we subjected the freshly prepared *para*-substituted isoborneols **1b–d** to DGPTI at 610–630°, which provided the corresponding phenones **7b–d** in moderate-to-good yields (*Scheme 5*). The optimal conditions for each reaction were determined as described above by means of GC/MS analysis (for details, see *Exper. Part*). The C=O absorptions in the IR spectra of **7b–d** were shifted to lower wave numbers with increasing electron density at the aromatic ring. The lowest value (1677 cm^{-1}) was observed in the case of **7c** with the π-donating MeO group. Conversely, the electron-withdrawing F_3C group in **7d** effected the highest value (1694 cm^{-1}), the C=O absorption in the case of the σ-donating Me group lying in between (1682 cm^{-1}).

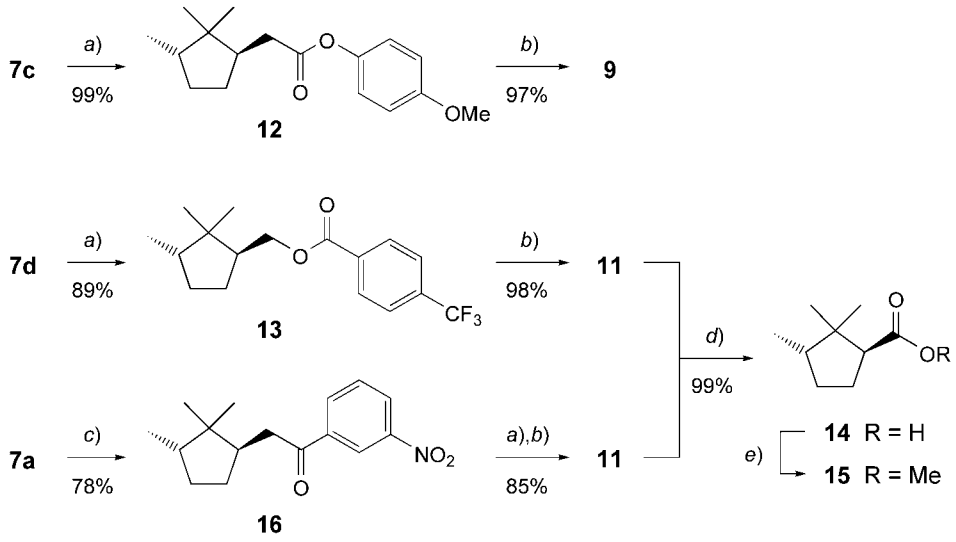
The difference of the substituent-controlled electronic properties of the aromatic rings of **7c** and **7d** enabled us to perform regioselective *Baeyer–Villiger* oxidations, as shown in *Scheme 6*. The oxidizing agent, trifluoroperacetic acid, was generated by the addition of TFA (CF_3COOH) to a solution of MCPBA in CH_2Cl_2 at 0°. Application of this procedure provided, in the case of the electron-rich **7c**, the corresponding methoxyphenyl ester **12** (99%), whereas the electron-deficient **7d** afforded the

Scheme 5



cyclopentylmethyl ester **13** (89%). Subsequent hydrolysis proceeded smoothly in both cases to furnish the desired (+)-*trans*-α-campholanic acid (**9**) and cyclopentylmethanol **11**, respectively[3]), in almost quantitative yields. However, *Baeyer–Villiger* oxidation of substrate **7b** under similar conditions led only to a 3 : 1 mixture of both possible esters as a result of predominant migration of the *p*-tolyl group.

Scheme 6



a) MCPBA, TFA, CH_2Cl_2, r.t. *b*) LiOH, MeOH, H_2O, r.t. *c*) H_2SO_4, HNO_3, $-15°$. *d*) CrO_3, H_2SO_4, $0° \rightarrow$ r.t. *e*) CH_2N_2, Et_2O, r.t.; 96%.

Alternatively, the introduction of electron-withdrawing groups can also be accomplished on the stage of phenone **7a** by electrophilic aromatic substitution, which has been demonstrated by nitration. The NO_2 group of the corresponding electron-deficient phenone **16** was introduced in the *meta*-position ($\tilde{\nu}$(C=O) 1695 cm^{-1}), and subsequent *Baeyer–Villiger* oxidation followed by hydrolysis of the intermediate ester

[3]) Only the corresponding racemic *cis*-compound has been reported so far [10].

led to the desired alcohol **11** (69% over three steps). Oxidation of **11** was achieved quantitatively with *Jones* reagent [11] to afford (+)-*trans*-α-dihydrocampholytic acid (**14**), the normethylene analogue of **9**.

The class of enantiomerically pure α-dihydrocampholytic acid derivatives is still sparsely populated due to the awkward stereocontrol of two stereogenic centers. Among the four possible diastereoisomers of **14**, only *cis*/*trans* mixtures have been reported in the literature, obtained predominantly *via* nonselective hydrogenation of unsaturated precursors (for leading references, see [10] and [12–16]). However, the presented 'DGPTI/*Baeyer–Villiger* procedure' is limited to the preparation of *trans*-configured derivatives of α-campholanic acid (**9**) and α-dihydrocampholytic acid (**14**) due to the stereochemical reasons mentioned above. Attempts to at least partially epimerize methyl ester **15** to the corresponding *cis*-compound by treatment with NaOMe in MeOH were futile.

2.2.2. *DGPTI of 2-Vinylisoborneol*. In sharp contrast to the isomerization of phenylisoborneols **1a–d**, pyrolysis of 2-vinylisoborneol (**1e**) under similar conditions provided an isomerization product exhibiting spectral data that showed no evidence for the expected vinylketone. Instead, an isomeric compound (43% isolated yield) containing a *singlet* at δ(C) 147.7 and a *doublet* at 121.6 in its ^{13}C-NMR spectrum ($CDCl_3$) was observed. Moreover, the upfield-shifted C=O absorption at δ(C) 211.6 indicated the presence of a saturated rather than an α,β-unsaturated ketone, and the ^{1}H-NMR spectrum exhibited a *triplet* at δ(H) 1.06, with a vicinal coupling of 7.3 Hz typical for an ethyl ketone. These data are consistent with the formation of (*R*)-1-(2,2,3-trimethylcyclopent-3-enyl)butan-2-one (**17a**; *Scheme 7*)[4]). In addition, the presence of a minor amount (*ca.* 10%) of the isomeric butanone **17b**, with an exocyclic C=C bond, was evident from ^{1}H- and ^{13}C-NMR analyses.

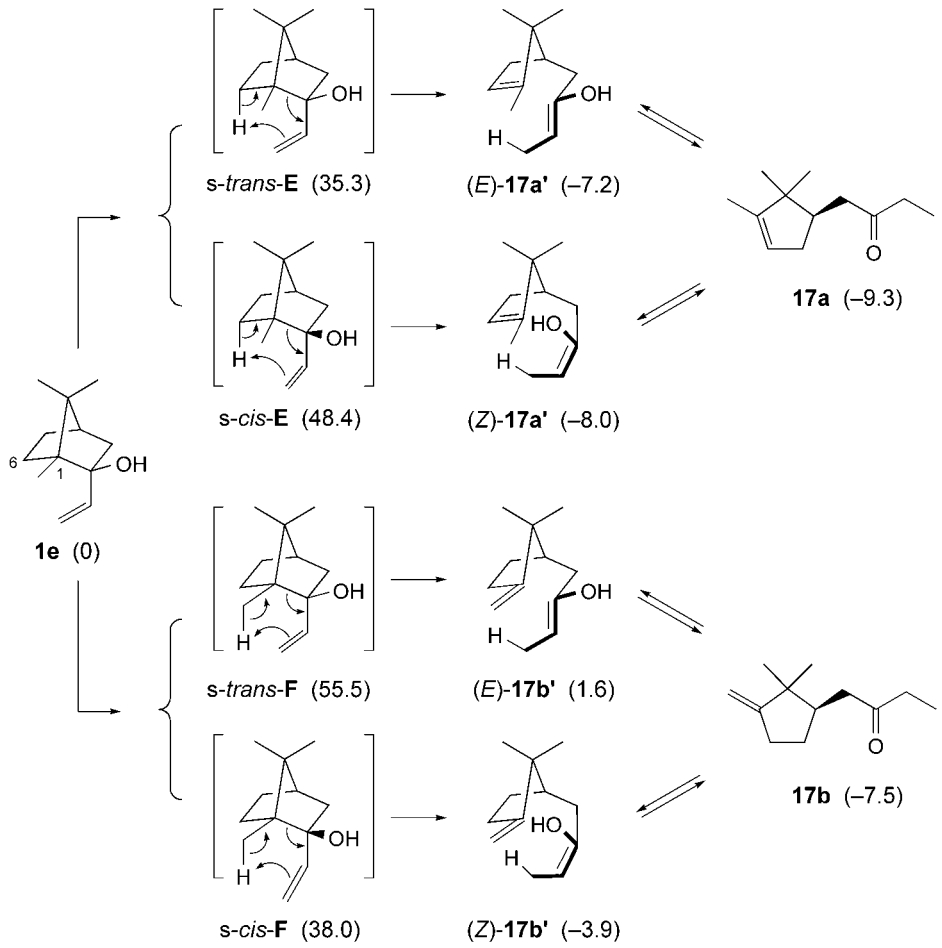
Interestingly, the isomerization reaction occurred already at a relatively low temperature (600°). As the ability to stabilize radicals in α-position is decreasing by passing from phenyl (*ca.* 16 kcal mol^{-1}) to vinyl (*ca.* 14 kcal mol^{-1}) [19–21], one would expect a higher temperature (> 630°) to be required for the thermal isomerization of 2-vinylisoborneol (**1e**) relative to 2-phenylisoborneol (**1a**; 630°). These observations are not compatible, however, with a reaction pathway *via* initial homolysis of the weakest single bond and subsequent H-transfer. Apparently, the proper arrangement in **1e** allows a concerted *retro*-ene reaction, having a lower activation energy than a reaction involving complete dissociation of the weakest single bond. Indeed, our assumption has firmly been corroborated by theoretical calculations using PBE density-functional theory[5]) [22]. All calculated energy values given in *Scheme 7* refer to the applied reactor temperature (600 °C = 873 K). Generally, four six-membered transition states s-*trans*/*cis*-**E** and s-*trans*/*cis*-**F** are possible. The intermediates s-*trans*- and s-*cis*-**E** implicate H_{endo}–C(6), whereas s-*trans*- and s-*cis*-**F** implicate H–CH_2–C(1). The energetically most-favored reaction pathway *via* s-*trans*-**E**, with a *transoid* arrangement

---

[4]) Compound **17a** has previously been prepared by *Siewinsky et al.* by addition of EtMgBr to α-campholenonitrile [17][18].

[5]) PBE Density-functional theory has been implemented in the computer program written by *Laikov* [23]. Full geometry optimizations for energy minima and transition states were followed by harmonic vibrational analysis to get the thermochemical data.

Scheme 7. *Calculated Relative Energies* [22] (in parentheses; kcal mol^{-1}) *for Different Thermo-Isomerization Pathways of* **1e**



of the hydroxyally moiety ($\Delta G^{\ddagger}_{873} = 35.3$ kcal mol^{-1}, *cf. Fig. 3*) affords enol (*E*)-**17a′** ($\Delta\Delta G_{873} = -7.2$ kcal mol^{-1}).

The tautomerization to ketone **17a** is assumed to take place only in the condensed phase (cooling trap) as an intermolecular process. The activation barrier for an intramolecular, symmetry-forbidden 1,3-H-shift, however, would be insurmountable under these conditions. Also, a reaction pathway leading to (*Z*)-**17a′** *via* highly energetic s-*cis*-**E** ($\Delta G^{\ddagger}_{873} = 48.4$ kcal mol^{-1}) can be neglected for the same reasons. In contrast, a pathway *via* the *cisoid* transition state s-*cis*-**F** (*cf. Fig. 3*) was found to be favored over *transoid* s-*trans*-**F** by 17.5 kcal mol^{-1}. Enol (*Z*)-**17b′** is then formed ($\Delta\Delta G_{873} = -3.9$ kcal mol^{-1}), followed by intermolecular tautomerization to ketone **17b**. The ratio for **17a**/**17b** of 10 : 1 determined is in quite good agreement with PBE-calculated $\Delta G^{\ddagger}_{873}$ values for s-*trans*-**E** and s-*cis*-**F**, which accounts for the predominant

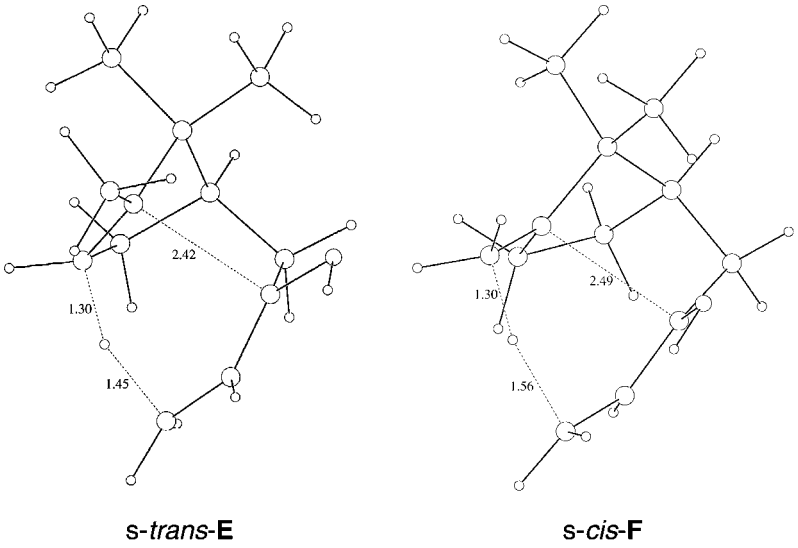
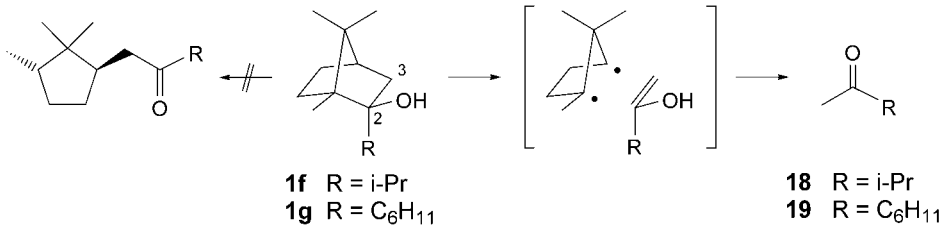


Fig. 3. *DFT-Calculated transition-state structures s*-trans-**E** *and s*-cis-**F** (interatomic distances in Å)

formation of **17a** ($\Delta\Delta G^{\ddagger}_{873} = 2.7$ kcal mol^{-1} corresponds to *ca.* 83% of **17a** and 17% of **17b**, assuming the reaction to occur under kinetic control).

2.2.3. *DGPTI of 2-Alkylisoborneols.* Interestingly, isoborneol substrates such as **1f** and **1g**, having an aliphatic substituent at C(2), could not be thermo-isomerized to the desired monocyclic isopropyl and cyclohexyl ketones, respectively (*Scheme 8*). At elevated temperatures (680–750°), isopropyl methyl ketone (**18**) and 1-cyclohexylethanone (**19**) were the only products isolated (<20%) besides many unidentified low-molecular-weight components (80%) according to GC/MS analysis. Taking into account the high reactor temperatures, concomitant cleavage of the C(1)–C(2) and C(3)–C(4) bonds becomes feasible under formation of the enol forms of **18** or **19**, and a highly reactive 1,4-diyl species undergoing further 1,4-fragmentation. Unfortunately, neither of these compounds could be isolated or characterized. Apparently, aliphatic substituents are not capable to sufficiently stabilize C(2) radicals. In other words, homolytic cleavage of the C(1)–C(2) bond requires higher temperatures (>680°) at which competing homolysis of non-activated single bonds in the molecule can also occur.

Scheme 8

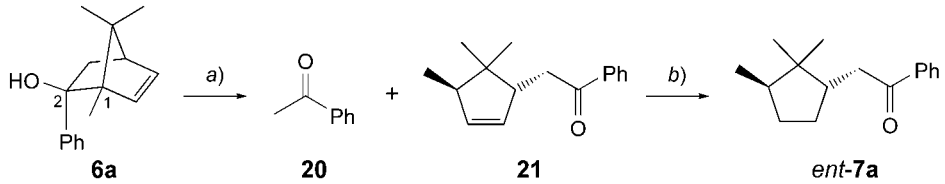


1f R = i-Pr
1g R = C_6H_{11}

18 R = i-Pr
19 R = C_6H_{11}

2.2.4. *DGPTI of 5,6-Dehydrolisoborneols.* In contrast to 2-phenylisoborneol (**1a**), DGPTI of its dehydro analogue **6a** occurred already at 520°, providing the two products **20** and **21** of different molecular weights in a 2 : 1 ratio (*Scheme 9*). Compounds **21** and **22** exhibited M^+ signals at *m*/*z* 228 (18%) and 120 (40%), respectively. The product mixture revealed a typical smell of acetophenone, and, indeed, co-injection of an authentic sample proved **20** to be acetophenone. The ^{13}C-NMR spectrum of **21** showed two signals at δ(C) 136.0 and 132.4, and a broad *singlet* at δ(H) 5.95 appeared in the ^{1}H-NMR spectrum. Apart from that, the spectra were very similar to those of phenone **7a**. These data were in agreement with the cyclopent-2-enyl phenyl ethanone **21**, which, upon hydrogenation, quantitatively afforded *ent*-**7a**. Apart from the optical rotation power (opposite sign of $[\alpha]_D^{23}$), the spectroscopic data of the latter were identical in all respects with those recorded for **7a**. Even though the reactor temperature was remarkably low (520°), the structure of **21** could not be rationalized by a concerted process. Thus, the isomerization reaction is more likely to proceed through diradical transition structures in analogy to that observed in the case of **7a**. Homolytic cleavage of the C(1)–C(2) bond in **6a** results in a stabilized diradical intermediate consisting of a hydroxy benzyl radical and a trisubstituted allyl radical, which, upon intramolecular disproportionation, leads to **21**[6]). Conversely, the formation of acetophenone (**20**) is consistent with a concerted *retro-Diels–Alder* reaction under loss of trimethylcyclopentadiene. The presence of two competing reaction mechanisms was firmly established by varying the reactor temperature. Besides the main product **20**, only traces of **21** were detected up to 450°, but the ratio of **21** to **20** increased with increasing temperature to almost equal amounts (650°).

Scheme 9

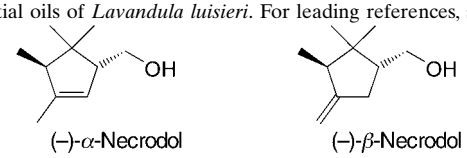


a) DGPTI, 480°; 40% (**20**), 18% (**21**). *b*) H_2, Pd(C), MeOH, r.t.; 98%.

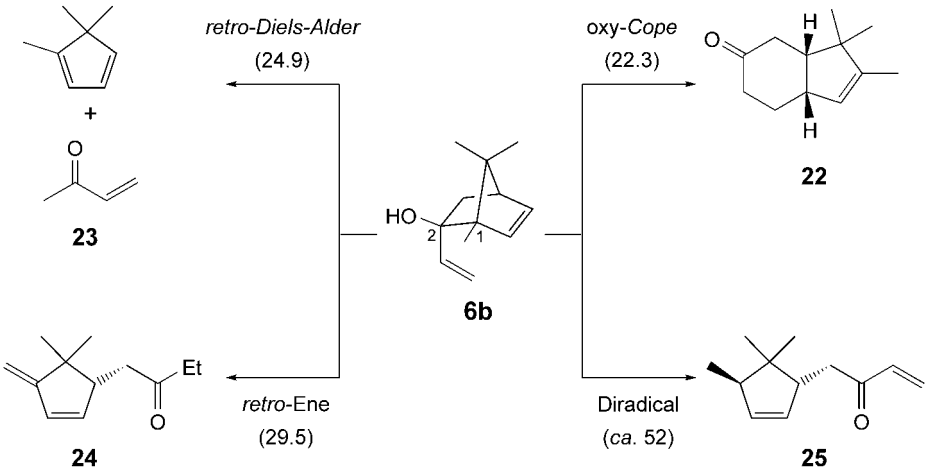
Although 5,6-dehydro-2-vinylisoborneol (**6b**) has been reported to be smoothly converted to the bicyclic ketone **22** (85%) upon treatment with KH in THF at room temperature [28], its thermochemical behavior has apparently not been investigated so far. As outlined in *Scheme 10*, the formation of four different products is possible upon pyrolysis of **6b**, each *via* a separate mechanism. Only the formation of cyclopentyl vinyl

---

[6]) Compound **21** can be viewed as a precursor of necrodanes (1,2,2,3,4-pentamethylcyclopentanes), which are found in the defense spray of *Necrodes surinamensis*, a silphid beetle from Surinam, and as constituents of the essential oils of *Lavandula luisieri*. For leading references, see [24–27]



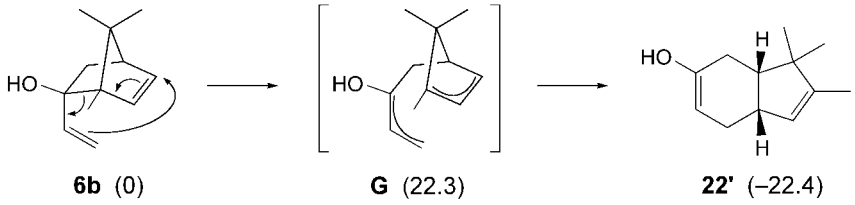
Scheme 10. *Possible Transformations of* **6b**. Numbers in parentheses refer to DFT-calculated $\Delta G^{\ddagger}_{823}$ values (in kcal mol^{-1}).



ketone **25** would require a diradical intermediate, whereas the formation of compounds **22**–**24** involves concerted reactions leading primarily to the corresponding enol compounds. A *retro-Diels–Alder* pathway could well give methyl vinyl ketone **23** and trimethylcyclopentadiene, as was observed for DGPTI of the corresponding phenyl analogue **6a**, while a *retro*-ene process would provide the conjugated diene **24**.

Our interest was focused on whether DGPTI of **6b** could effect homolysis between C(1)–C(2) and give, at least partially, the monocyclic vinylketone **25** *via* a diradical state. However, applying even harsher conditions (> 700°, 0.4 l/h N_2 flow) resulted in the formation of **22** as the sole product. Furthermore, the yield of rearranged **22** reported by *Hutchinson et al.* [28] could be improved to 93% by carrying out the pyrolysis at 550°. Excellent yields were also obtained by heating **6b** in a sealed glass tube under static conditions at 220° (95%), whereas the same transformation under anionic oxy-*Cope* conditions, as reported above, provided lower yields (80%). In addition, DFT calculations referring to a reactor temperature of 550° (823 K) showed that the lowest activation barrier was found for a concerted oxy-*Cope* rearrangement ($\Delta G^{\ddagger}_{823} = 22.3$ kcal mol^{-1}). As depicted in *Scheme 11*, enol **22′** is the actual product of the gas-phase reaction ($\Delta\Delta G_{823} = -22.4$ kcal mol^{-1}). Subsequent intramolecular

Scheme 11. *DFT-Calculated Relative* ΔG_{873} *Values* (in kcal mol^{-1}) *for the Proposed Transition State* **G** *and the Product* **22′**



tautomerization providing hexahydroindenone **22** occurs then in the condensed phase at low temperatures. The DFT-calculated structures of both the oxy-*Cope* transition state **G** and enol **22′** are displayed in *Fig. 4*.

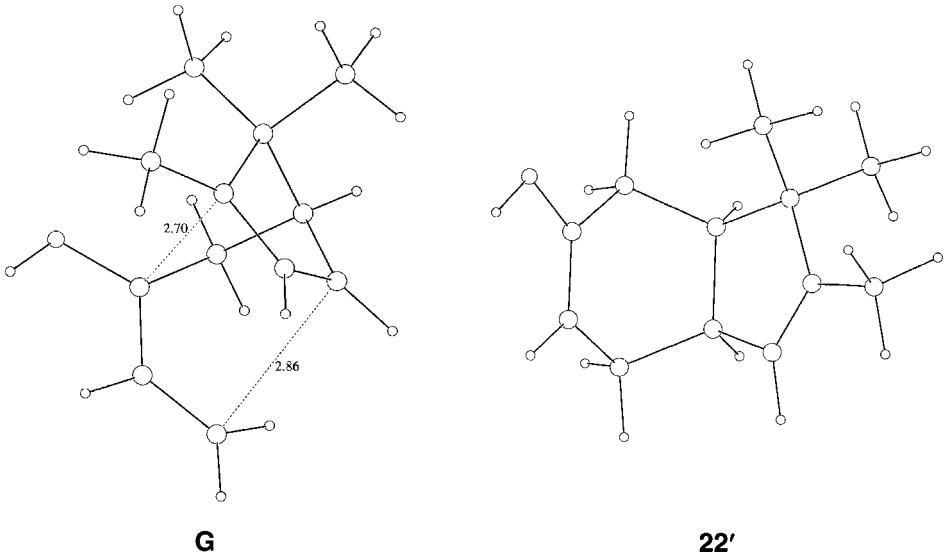


Fig. 4. *DFT-Calculated structures of transition state* **G** *and enol* **22′** (interatomic distances in Å)

Both a *retro-Diels–Alder* ($\Delta G^{\ddagger}_{823} = 24.9$ kcal mol^{-1}) and a *retro*-ene reaction ($\Delta G^{\ddagger}_{823} = 29.5$ kcal mol^{-1}) leading to **23** and **24**, respectively, were found to require higher activation energies. To approximately determine the activation energy for the homolytic cleavage of the C(1)–C(2) bond in **6b** to a hydroxyallyl radical on one side of the chain and a trisubstituted allyl diradical on the other, we used dissociation energy-values of similar compounds reported in the literature. However, the bond-dissociation energies are generally reduced with increasing substitution of one or both of the bond-breaking centers. Thereby, the contribution of π-substituents adjacent to this center is by far the most important due to resonance-stabilizing effects. Taking an average, unactivated C–C single bond (*ca.* 83 kcal mol^{-1}) and subtracting the radical-stabilization-energy values of a hydroxyallyl radical (*ca.* 15 kcal mol^{-1}), a trisubstituted allyl radical (*ca.* 15 kcal mol^{-1}), and some ring strain (*ca.* 5 kcal mol^{-1}) being released upon ring opening, the activation energy is estimated to be in the range of 48 kcal mol^{-1}. Hence, a diradical-mediated mechanism is energetically clearly disfavored in comparison to the symmetry-allowed concerted reactions.

Finally, pyrolysis of 5,6-dehydro-2-isopropylisoborneol (**6c**) in the range of 450–650° produced isopropyl methyl ketone in moderate yields (30–50%), accompanied by a large number of low-boiling side products. In contrast to the phenyl group in **6a**, the radical-stabilization energy provided by the i-Pr group is too small to be in accordance with the formation of a diradical intermediate, but is consistent with a concerted *retro-Diels–Alder* reaction. Apparently, the additional C=C bond in 5,6-dehydroisoborneol substrates not only affects the radical-stabilization energy by means of lowering the

activation energy for the intramolecular H-transfer reactions, but also enables competing concerted pericyclic processes such as *retro-Diels–Alder* reactions and oxy-*Cope* rearrangements.

3. Conclusions. – We have demonstrated that the concept of the 'cleavage of the weakest single bond' can be extended to loco- and stereoselective ring-opening reactions. Easily available monoterpene substrates were thermally isomerized under DGPTI conditions to optically pure monocyclic compounds that can be used as chiral building blocks in terpenoid synthesis or further transformed to valuable odorant molecules by regioselective *Baeyer–Villiger* oxidation. The reaction pathway passes either through diradical intermediates or concerted processes, depending on the substrate framework and the nature of the substituents.

The authors are indebted to the *Swiss National Science Foundation* for financial support and to the analytical department of our institute for specific NMR measurements and elemental analyses. Thanks are due to Dr. *D. Laikov* for DFT calculations and for lively discussions.

Experimental Part

1. *General*. See [29].

2. *Monoterpene Substrates.* – 2.1. *Arylisoborneols* **7a** – **7d**. *General Procedure* (*GP 1*) *for* Grignard *Addition*. A 0.5M soln. of aryl magnesium bromide was prepared by treating a suspension of Mg (0.843 g, 34.68 mmol) in anh. THF (63 ml) with the corresponding aryl bromide (31.53 mmol) at r.t. In a separate flask, (+)-camphor (4.0 g, 26.27 mmol) was added with stirring to a suspension of $CeCl_3$ (0.8 – 1.2 equiv.) in anh. THF (100 ml) at r.t. Stirring was continued for 0.5 – 2 h, after which the initially yellowish-colored suspension became homogenous and yogurt-like. To this mixture, the freshly prepared ArMgBr soln. was added by cannula at r.t., while the temperature rose to 45°. Stirring was continued for 0.5 – 2 h at r.t., and the conversion of the reaction was monitored by TLC and GC (normally more than 95% consumption after 20 min). The resulting ivory-colored suspension was then poured into a separatory funnel containing crushed ice, H_2O (500 ml), and Et_2O (200 ml). A 10% aq. HCl soln. was added with stirring until the mixture became clear (pH < 3). The org. layer was washed twice with H_2O. The aq. layers were extracted with Et_2O (3 × 50 ml). The combined org. layers were washed with sat. aq. $NaHCO_3$ and with brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure.

2.1.1. *(1*R,2S,4R*)-1,7,7-Trimethyl-2-phenylbicyclo[2.2.1]heptan-2-ol* (**1a**). *GP 1*, with 1.2 equiv. of $CeCl_3$. The crude product was purified by CC (hexane/AcOEt 30:1) to give **1a** (5.75 g, 95%). Colorless oil. $[\alpha]_D^{23} = -29.6$ ($c = 0.52$, MeOH). IR (film): 3060*m*, 2958v*s*, 2871v*s*, 1495*m*, 1482*s*, 1458*s*, 1389*m*, 1297*m*, 1146*w*, 1111*m*, 1080*m*, 1059*s*, 1016*m*, 966*s*, 906*m*, 860*m*, 761v*s*, 703v*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.54 (*A* of *AA′BB′C*, H_o of Ph); 7.33 (*B* of *AA′BB′C*, H_m of Ph); 7.25 (*C* of *AA′BB′C*, H_p of Ph); 2.33 (*d*, $^2J(3_{endo},3_{exo}) = 14.0$, H_{endo}–C(3)); 2.19 (*dt*, $^2J(3_{exo},3_{endo}) = 14.0$, $^3J(3_{exo},4) = 4.0$, H_{exo}–C(3)); 1.91 (*t*, $^3J = 4.0$, H–C(4)); 1.75 – 1.64 (*m*, OH, H_{exo}–C(5)); 1.28 (*s*, Me–C(1)); 1.25 – 1.11 (*m*, 2 H); 0.91 (*s*, Me_2C(7)); 0.86 – 0.79 (*m*, H_{endo}–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 146.0 (*s*, C_{ipso} of Ph); 127.5 (*d*, C_o of Ph); 126.7, 126.6 (2*d*, $C_{m/p}$ of Ph); 83.5 (*s*, C(2)); 53.8 (*s*, C(1)); 50.4 (*s*, C(7)); 45.5 (*d*, C(4)); 45.4 (*t*, C(3)); 31.1 (*t*, C(6)); 26.5 (*t*, C(5)); 21.6 (*q*, *Me*$_2$C(7)); 9.7 (*q*, *Me*–C(1)). EI-MS: 230 (2, $M^{+\cdot}$), 212 (100, $[M - H_2O]^{+\cdot}$), 196 (2), 153 (4, $[M - Ph]^{+\cdot}$), 120 (8), 105 (12), 95 (20).

2.1.2. *(1*R,2S,4R*)-1,7,7-Trimethyl-2-(4-methylphenyl)bicyclo[2.2.1]heptan-2-ol* **1b**). *GP 1*, with 1.2 equiv. of $CeCl_3$. The crude product was purified by CC (hexane/AcOEt 30:1) to give **1b** (5.91 g, 92%). Colorless oil. $[\alpha]_D^{23} = -17.4$ ($c = 0.77$, MeOH). IR (film): 3557*m*, 3473*m*, 3023*m*, 2954v*s*, 1511*m*, 1481*m*, 1458v*s*, 1388*s*, 1368*s*, 1214*m*, 1106*m*, 1063v*s*, 1017*m*, 946*s*, 821*s*, 806*s*, 787*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.41 (*A* of *AA′BB′*, H_o of Ar); 7.33 (*B* of *AA′BB′*, H_m of Ar); 2.33 (*s*, 4′-Me); 2.28 (*d*, $^2J(3_{endo},3_{exo}) = 13.8$, H_{endo}–C(3)); 2.17 (*dt*, $^2J(3_{exo},3_{endo}) = 13.8$, $^3J(3_{exo},4) = 4.0$, H_{exo}–C(3)); 1.87 (*t*, $^3J = 4.0$, H–C(4)); 1.75 – 1.67 (*m*, 2 H); 1.26 (*s*, Me–C(1); 1.25 – 1.09 (*m*, OH, H_{exo}–C(5)); 0.90 (*s*, Me_2C(7)); 0.87 – 0.80 (*m*, H_{endo}–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 143.2 (*s*, C_p of Ar); 136.2 (*s*, C_{ipso} of Ar); 128.2, 126.6 (2*d*, $C_{o/p}$ of Ar); 83.4 (*s*, C(2)); 53.3 (*s*, C(1)); 50.3 (*s*, C(7)); 45.6 (*d*, C(4)); 45.4 (*t*, C(3)); 31.2 (*t*, C(6)); 26.5 (*t*, C(5)); 21.6 (2*q*, *Me*$_2$C(7)); 20.8 (*q*, 4′-

Me); 9.8 (*q*, *Me*–C(1)). EI-MS: 244 (1, $M^{+\cdot}$), 226 (100, $[M-H_2O]^{+\cdot}$), 198 (1), 172 (2), 156 (2), 136 (3, $[M-Ar-H]^{+\cdot}$), 120 (9), 108 (5), 95 (2).

2.1.3. *(1*R*,2*S*,4*R*)-2-(4-Methoxyphenyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol* (**1c**). *GP 1*, with 1.0 equiv. of $CeCl_3$. The crude product was crystallized from hexane/AcOEt 40:1 to afford **1c** (6.02 g, 88%). Slightly reddish solid. M.p. 92–94°. $[\alpha]_D^{23} = -19.5$ ($c = 0.50$, MeOH). IR (KBr): 3473v*s*, 2926v*s*, 1605*s*, 1509v*s*, 1460v*s*, 1388*m*, 1369*m*, 1300*s*, 1242v*s*, 1183v*s*, 1106*w*, 1062*s*, 1017*s*, 976*m*, 963*m*, 834*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.43 (*A* of *AA′BB′*, 2 H); 6.85 (*B* of *AA′BB′*, 2 H); 3.80 (*s*, MeO); 2.27 (*d*, $^2J(3_{endo},3_{exo}) = 13.8$, H_{endo}–C(3)); 2.16 (*dt*, $^2J(3_{exo},3_{endo}) = 13.8$, $^3J(3_{exo},4) = 4.0$, H_{exo}–C(3)); 1.88 (*t*, $^3J = 4.0$, H–C(4)); 1.80–1.68 (*m*, OH, H_{exo}–C(5)); 1.26 (*s*, Me–C(1); 1.23–1.09 (*m*, 2 H); 0.903 (*s*, Me_{anti}–C(7)); 0.897 (*s*, Me_{syn}–C(7)); 0.87–0.80 (*m*, H_{endo}–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 158.3 (*s*, C_p of Ar); 138.3 (*s*, C_{ipso} of Ar); 127.7 (*d*, C_o of Ar); 112.7 (*d*, C_m of Ar); 82.2 (*s*, C(2)); 55.2 (*q*, MeO); 53.4 (*s*, C(1)); 50.2 (*s*, C(7)); 45.5 (*d*, C(4)); 45.5 (*t*, C(3)); 31.2 (*t*, C(6)); 26.5 (*t*, C(5)); 21.6, 21.5 (2*q*, Me_2C(7)); 9.8 (*q*, *Me*–C(1)). EI-MS: 260 (3, $M^{+\cdot}$), 242 (100, $[M-H_2O]^{+\cdot}$), 153 (4, $[M-Ar-H]^{+\cdot}$), 134 (8), 109 (6), 95 (4).

2.1.4. *(1*R*,2*S*,4*R*)-1,7,7-Trimethyl-2-[4-(trifluormethyl)phenyl]bicyclo[2.2.1]heptan-2-ol* (**1d**). *GP 1*, with 0.8 equiv. of $CeCl_3$. The crude product was purified by CC (hexane/AcOEt 20:1) to give **1d** (7.68 g, 98%). Colorless oil. $[\alpha]_D^{23} = -21.2$ ($c = 2.16$, hexane). IR (film): 3605*w*, 3470*m*, 3021*m*, 2959v*s*, 2879*s*, 1618*s*, 1459*s*, 1408*s*, 1372*s*, 1330v*s*, 1249*s*, 1168v*s*, 1128v*s*, 1071v*s*, 969*s*, 852*s*, 836v*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.64 (*d*, $^3J(o,m) = 8.5$, H_o of Ar); 7.56 (*d*, $^3J(m,o) = 8.5$, H_m of Ar); 2.30 (*d*, $^2J(3_{endo},3_{exo}) = 14.0$, H_{endo}–C(3)); 2.20 (*dt*, $^2J(3_{exo},3_{endo}) = 14.0$, $^3J(3_{exo},4) = 4.1$, H_{exo}–C(3)); 1.93 (*t*, $^3J = 4.1$, H–C(4)); 1.87 (br. *s*, OH); 1.80–1.73 (*m*, H_{exo}–C(5)); 1.27 (*s*, Me–C(1)); 1.25–1.18 (*m*, 2 H); 0.92 (*s*, Me_{anti}–C(7)); 0.90 (*s*, Me_{syn}–C(7)); 0.80–0.74 (*m*, H_{endo}–C(6)). ^{13}C-NMR (150 MHz, $CDCl_3$): 150.0 (*s*, C_{ipso} of Ar); 128.9 (*q*, $^2J(C_p,F) = 32.1$, C_p of Ar); 127.1 (*d*, C_o of Ar), 124.3 (*q*, $^3J(C_m,F) = 3.8$, C_m of Ar); 124.2 (*q*, $^1J(C,F) = 270.2$, F_3C); 83.3 (*s*, C(2)); 53.5 (*s*, C(1)); 50.5 (*s*, C(7)); 45.6 (*t*, C(3)); 45.5 (*d*, C(4)); 31.0 (*t*, C(6)); 26.4 (*t*, C(5)); 21.4 (*q*, Me_2C(7)); 9.5 (*q*, *Me*–C(1)). EI-MS: 298 (1, $M^{+\cdot}$), 280 (5, $[M-H_2O]^{+\cdot}$), 237 (21), 188 (25), 172 (46), 145 (48, $(F_3C)C_6H_4^+$), 127 (35), 109 (100), 95 (87), 77 (33), 67 (41), 55 (45).

2.2. *(1*R*,2*S*,4*R*)-2-Ethenyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol* (**1e**). To a stirred suspension of anh. $CeCl_3$ (4.86 g, 19.7 mmol) in anh. THF (80 ml) was added (+)-camphor (2.5 g, 16.4 mmol) at r.t. After stirring for 2 h at r.t., the suspension became homogenous and yogurt-like. To this mixture, a 1M soln. of vinyl magnesium bromide (32.8 ml, 32.8 mmol) was added at r.t. Workup in the usual fashion followed by CC (hexane/AcOEt 30:1) provided **1e** (2.25 g, 76%). Colorless oil. $[\alpha]_D^{23} = -46.3$ ($c = 1.0$, MeOH). IR (film): 3038*m*, 2960v*s*, 2871v*s*, 1495*m*, 1480*s*, 1450*m*, 1389*m*, 1293*m*, 1146*w*, 1111*m*, 1088*m*, 1076*s*, 1021*m*, 906*m*, 869*m*, 761*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.03 (*dd*, $^3J_{trans} = 17.3$, $^3J_{cis} = 10.7$, H–C(1′)); 5.23 (*dd*, $^3J_{trans} = 17.3$, $^2J = 1.2$, H_{trans}–C(2′)); 5.07 (*dd*, $^3J_{cis} = 10.7$, $^2J = 1.2$, H_{cis}–C(2′)); 2.01 (*dt*, $^2J(3_{exo},3_{endo}) = 13.3$, $^3J(3_{exo},4) = 4.5$, H_{exo}–C(3)); 1.77 (*t*, $^3J = 4.5$, H–C(4)); (*d*, $^2J(3_{endo},3_{exo}) = 13.3$, H_{endo}–C(3)); 1.64 (br. *s*, OH); 1.37–1.32 (*m*, 1 H); 1.15 (*q*, Me–C(1)); 1.07–0.89 (*m*, 3 H); 0.87, 0.83 (2*q*, Me_2C(7)). ^{13}C-NMR (75 MHz, $CDCl_3$): 143.7 (*d*, C(1′)); 112.0 (*t*, C(2′)); 81.4 (*s*, C(2)); 52.5 (*s*, C(1)); 49.0 (*s*, C(7)); 45.4 (*d*, C(4)); 44.6 (*t*, C(3)); 31.1 (*t*, C(6)); 27.0 (*t*, C(5)); 21.2, 20.8 (2*q*, Me_2C(7)); 9.6 (*q*, *Me*–C(1)). EI-MS: 180 (4, $M^{+\cdot}$), 110 (12), 95 (100), 77 (45), 55 (12).

2.3. O-*Deuteration of Isoborneol* **1a**. To a soln. of **1a** (1.15 g, 4.99 mmol) in MeOD (5 ml), D_2O (0.1 ml) was added, and the soln. was stirred at 40° for 30 min, after which the solvent was evaporated under reduced pressure. This procedure was repeated two more times. The *O*-deuterated phenylisoborneol [*O*-^{2}H]-**1a** was obtained in quant. yield.

2.4. *(1*S*,4*R*,6*S*)-6-Bromo-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one* (**4**). A mixture of chlorosulfonic acid (40 ml) and (+)-3-*endo*-bromocamphor (**3**) (10.0 g, 43.2 mmol) was placed in a three-neck round-bottom flask and stirred at 45° for 20 min, after which the starting material had been entirely consumed (GC analysis). The resulting dark suspension was then carefully poured onto ice (500 g). After extraction with Et_2O (3 × 100 ml), the combined org. layers were washed once each with sat. aq. $NaHCO_3$ soln., H_2O, and brine. The org. phase was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to afford a dark brown solid, which was recrystallized from hexane to give **4** (4.10 g, 42%). Colorless prisms. M.p. 129–131°. $[\alpha]_D^{23} = -9.4$ ($c = 1.0$, CH_2Cl_2). IR (film): 2970v*s*, 2932v*s*, 1746v*s*, 1458*s*, 1430*s*, 1324*m*, 1170*m*, 1054*s*, 1010*s*, 916*s*, 857*m*, 793*s*, 763*s*, 735*m*, 635*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.22 (*dd*, $^3J(6,5_{exo}) = 10.2$, $^3J(6,5_{endo}) = 3.3$, H–C(6)); 2.84 (*dddd*, $^2J(5_{exo},5_{endo}) = 15.1$, $^3J(5_{exo},6) = 10.2$, $^3J(5_{exo},4) = 4.3$, $^4J(5_{exo},3_{endo}) = 3.6$, H_{exo}–C(5)); 2.45 (br. *td*, $^2J(3_{exo},3_{endo}) = 18.5$, $^3J(3_{exo},4) = 3.6$, H_{exo}–C(3)); 2.22 (*dd*, $^3J(4,5_{exo}) = 4.3$, $^3J(4,3_{exo}) = 3.6$, H–C(4)); 2.04 (*d*, $^2J(3_{endo},3_{exo}) = 18.5$, H_{endo}–C(3)); 1.89 (*dd*, $^2J(5_{endo},5_{exo}) = 15.1$, $^3J(5_{endo},6) = 3.3$, H_{endo}–C(5)); 1.00 (*s*, Me); 0.97 (*s*, Me); 0.91 (*s*, Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 213.9 (*s*, C(2)); 71.1 (*s*, C(1)); 50.9 (*d*, C(4)); 47.8 (*s*, C(7)); 42.7 (*t*, C(3)); 42.3 (*d*, C(6)); 39.9 (*t*, C(5)); 20.9 (*q*, Me); 19.2 (*q*, Me); 7.5 (*q*, Me). EI-MS: 230 (5, $M^{+\cdot}$), 175 (18), 151 (75, $[M-HBr]^{+\cdot}$), 109 (100), 93 (26), 81 (31), 67 (19), 53 (9).

2.5. *(1S,4R)-1,7,7-Trimethylbicyclo[2.2.1]hept-5-en-2-one* (=*(+)-5,6-Dehydrocamphor*; **2**). A soln. of **4** (4.0 g, 17.32 mmol) and KOH (4.82 g, 86.5 mmol) in a mixture of DMSO (160 ml) and H_2O (24 ml) was heated at 120° for 2.5 h under vigorous stirring. The resulting orange soln. was allowed to cool to r.t., and H_2O (100 ml) was added. After extraction with Et_2O (3 × 100 ml) the combined org. layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to afford crude **2** as a highly volatile orange oil. Purification by CC (pentane/Et_2O 20:1) provided **2** (1.18 g, 45%). Colorless oil. $[\alpha]_D^{23} = +718$ ($c = 0.6$, CH_2Cl_2). IR (film): 3066*w*, 2968v*s*, 2873v*s*, 1735v*s*, 1467*s*, 1447v*s*, 1380*m*, 1291*m*, 1150*m*, 1111*s*, 1029*s*, 982*m*, 853*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.48 (*dd*, $^3J(5,6) = 5.4$, $^3J(5,4) = 2.0$, H–C(5)); 5.58 (*d*, $^3J(6,5) = 5.4$, H–C(6)); 2.68 (br. *s*, H–C(4)); 2.21 (*ddd*, $^2J(3_{exo},3_{endo}) = 16.7$, $^3J(3_{exo},4) = 3.4$, $^3J(3_{exo},5) = 1.0$, H_{exo}–C(3)); 1.93 (*d*, $^2J(3_{endo},3_{exo}) = 16.7$, H_{endo}–C(3)); 1.21 (*s*, Me); 1.07 (*s*, Me); 1.01 (*s*, Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 216.8 (*s*, C(2)); 142.6 (*d*, C(5)); 133.5 (*d*, C(6)); 65.7 (*d*, C(4)); 65.2 (*s*, C(1)); 60.7 (*s*, C(7)); 48.7 (*t*, C(3)); 19.6 (*q*, Me); 19.2 (*q*, Me); 6.8 (*q*, Me). EI-MS: 150 (12, $M^{+\cdot}$), 108 (100), 93 (75), 77 (26), 65 (18), 53 (14).

2.6. *(1S,2R,4R)-1,7,7-Trimethyl-2-phenylbicyclo[2.2.1]hept-5-en-2-ol* (**6a**). To a stirred suspension of anh. $CeCl_3$ (0.79 g, 3.2 mmol) in anh. THF (30 ml), (+)-5,6-dehydrocamphor (**2**; 2.40 g, 16.0 mmol) was added at r.t. Stirring was continued for 1 h, after which a 1M soln. of PhMgBr (32 ml, 32 mmol) was added at r.t. Workup in the usual fashion followed by CC (hexane/AcOEt 30:1) provided **6a** (3.51 g, 93%). Slightly yellow oil $[\alpha]_D^{23} = +93.8$ ($c = 1.5$, CH_2Cl_2). IR (film): 3448*s*, 3087*w*, 3056*s*, 3025*s*, 2954v*s*, 2871v*s*, 1596*m*, 1492*s*, 1470*s*, 1444v*s*, 1389v*s*, 1365*s*, 1225*s*, 1154*s*, 1120*s*, 1012*s*, 906*s*, 755v*s*, 732v*s*, 702v*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.37 (*A* of *AA′BB′C*, H_o of Ph); 7.24 (*B* of *AA′BB′C*, H_m of Ph); 7.19 (*C* of *AA′BB′C*, H_p of Ph); 6.09 (*dd*, $^3J(5,6) = 5.7$, $^3J(5,4) = 3.2$, H–C(5)); 5.11 (*d*, $^3J(6,5) = 5.7$, H–C(6)); 2.54 (br. *t*, $^3J(4,5) = {}^3J(4,3_{exo}) = 3.2$, H–C(4)); 2.36 (*dd*, $^2J(3_{exo},3_{endo}) = 13.1$, $^3J(3_{exo},4) = 3.2$, H_{exo}–C(3)); 2.27 (*d*, $^2J(3_{endo},3_{exo}) = 13.1$, H_{endo}–C(3)); 1.86 (*s*, OH); 1.31 (*s*, Me_{syn}–C(7)); 1.03 (*s*, Me–C(1)); 0.96 (*s*, Me_{anti}–C(7)). ^{13}C-NMR (150 MHz, $CDCl_3$): 146.9 (*s*, C_{ipso} of Ph); 139.8 (*d*, C(5)); 135.7 (*d*, C(6)); 128.1, 127.1 (2*d*, $C_{o/m}$ of Ph); 126.4 (*d*, C_p of Ph); 83.5 (*s*, C(2)); 61.1, 60.8 (2*s*, C(1,7)); 52.3 (*d*, C(4)); 42.3 (*t*, C(3)); 22.6, 21.8 (2*q*, Me_2C(7)); 7.5 (*q*, *Me*–C(1)). EI-MS: 228 (1, $M^{+\cdot}$), 108 (100, retro-*Diels–Alder*), 93 (71), 77 (16).

2.7. *(1S,2R,4R)-2-Ethenyl-1,7,7-trimethylbicyclo[2.2.1]hept-5-en-2-ol* (**6b**). To a stirred suspension of anh. $CeCl_3$ (0.36 g, 1.46 mmol) in anh. THF (10 ml) was added **2** (1.10 g, 7.32 mmol) at r.t. Stirring was continued for 30 min, after which a 1M soln. of vinyl magnesium bromide (14.6 ml, 14.6 mmol) was added *via* syringe at r.t. Workup in the usual fashion followed by CC (hexane/AcOEt 20:1) provided **6b** (1.25 g, 96%). Colorless oil. $[\alpha]_D^{23} = +69.5$ ($c = 1.75$, CH_2Cl_2). IR (film): 3598*m*, 3060*w*, 3024*w*, 2965v*s*, 2872v*s*, 1452*m*, 1387*m*, 1326*w*, 1214*w*, 1118*w*, 1062*m*, 1009*m*, 891*s*, 745*m*. ^{1}H-NMR (600 MHz, $CDCl_3$): 6.01 (*dd*, $^3J(5,6) = 5.8$, $^3J(5,4) = 3.2$, H–C(5)); 5.84 (*dd*, $^3J_{trans} = 17.3$, $^3J_{cis} = 10.7$, H–C(1′)); 5.62 (*d*, $^3J(6,5) = 5.8$, H–C(6)); 5.15 (*dd*, $^3J_{trans} = 17.3$, $^2J = 1.1$, H_{trans}–C(2′)); 5.00 (*dd*, $^3J_{cis} = 10.7$, $^2J = 1.1$, H_{cis}–C(2′)); 2.42 (br. *t*, $^3J(4,5) = {}^3J(4,3_{exo}) = 3.2$, H–C(4)); 2.15 (*dd*, $^2J(3_{exo},3_{endo}) = 12.7$, $^3J(3_{exo},4) = 3.2$, H_{exo}–C(3)); 1.61 (*d*, $^2J(3_{endo},3_{exo}) = 12.7$, H_{endo}–C(3)); 1.60 (*s*, OH); 1.19 (*s*, Me_{syn}–C(7)); 0.94 (*s*, Me_{anti}–C(7)); 0.92 (*s*, Me–C(1)). ^{13}C-NMR (150 MHz, $CDCl_3$): 146.3 (*d*, C(1′)); 139.8 (*d*, C(5)); 136.1 (*d*, C(6)); 111.9 (*t*, C(2′)); 83.4 (*s*, C(2)); 60.8, 60.1 (2*s*, C(1,7)); 52.0 (*d*, C(4)); 41.3 (*t*, C(3)); 22.3, 21.8 (2*q*, Me_2C(7)); 7.3 (*q*, *Me*–C(1)). EI-MS: 178 (2, $M^{+\cdot}$), 108 (100, retro-*Diels–Alder*), 93 (95), 77 (12), 55 (11).

2.8. *(1S,2R,4R)-1,7,7-Trimethyl-2-(1-methylethyl)bicyclo[2.2.1]hept-5-en-2-ol* (**6c**). To a stirred suspension of anh. $CeCl_3$ (0.17 g, 0.68 mmol) in anh. THF (5 ml) was added **2** (0.52 g, 3.43 mmol) at r.t. Stirring was continued for 30 min, after which a 2M soln. of i-PrMgCl (3.42 ml, 6.84 mmol) was added *via* syringe at r.t. Workup in the usual fashion followed by CC (hexane/AcOEt 30:1) provided **6c** (0.62 g, 93%). Colorless oil. $[\alpha]_D^{23} = +28.1$ ($c = 1.3$, CH_2Cl_2). IR (film): 3523*m*, 2956v*s*, 2874v*s*, 1473*s*, 1386*s*, 1365*s*, 1267*m*, 1209*m*, 1100*m*, 1039*m*, 1004*s*, 954*w*, 926*m*, 905*m*, 858*w*, 742*s*, 715*s*, 650*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.88 (*dd*, $^3J(5,6) = 5.8$, $J = 3.1$, H–C(5)); 5.73 (*d*, $^3J(6,5) = 5.8$, H–C(6)); 2.26 (br. *t*, $J = 3.2$, H–C(4)); 1.92 (*dd*, $^2J(3_{exo},3_{endo}) = 12.5$, $J = 3.7$, H_{exo}–C(3)); 1.62 (*sept.*, $J = 6.9$, Me_2CH); 1.36 (*s*, OH); 1.33 (*d*, $^2J(3_{endo},3_{exo}) = 12.5$, H_{endo}–C(3)); 1.04 (*s*, Me_{syn}–C(7)); 0.98 (*s*, Me_{anti}–C(7)); 0.83 (*s*, Me–C(1)); 0.81, 0.80 (2*d*, $J = 6.9$, Me_2CH). ^{13}C-NMR (75 MHz, $CDCl_3$): 138.8 (*d*, C(5)); 135.9 (*d*, C(6)); 84.9 (*s*, C(2)); 61.1, 60.1 (2*s*, C(1,7)); 50.9 (*d*, C(4)); 40.4 (*t*, C(3)); 38.0 (*d*, Me_2CH); 22.3, 21.4 (2*q*, Me_2C(7)); 18.0, 17.7 (2*q*, Me_2CH); 9.7 (*q*, *Me*–C(1)). EI-MS: 194 (2, $M^{+\cdot}$), 151 (2), 121 (3), 108 (100, retro-*Diels–Alder*), 93 (81), 77 (5).

3. *Thermal Isomerization Reactions and Derivatizations.* – 3.1. *General Procedure* (*GP 2*) *for DGPTI of* **1a**–**1e**, *and* **6a** *and* **6b**. The thermo-isomerization device consisted of an electrically heatable tube furnace (1 m), a condenser unit with a cooling trap at the outlet side, and a *Kugelrohr* oven as the evaporation unit at the inlet side. A quartz tube (110-cm long, 2.5 cm i.d.), which fitted into the furnace, was connected to a trap (cooled with liquid N_2) on one side and to a bulb placed in the *Kugelrohr* oven on the other. The starting material (typically 2 g) was placed in the bulb equipped with a capillary inlet device for the inert gas (N_2) flow and a magnetic

stirrer. After evacuation of the apparatus with a high-vacuum oil pump, the starting material was directly distilled through the preheated reactor tube (1–3 g/h). After all of the starting material had been distilled, the apparatus was vented, and the frozen products were transferred to a bulb using Et_2O as solvent. The resulting soln. was dried ($MgSO_4$) and evaporated under reduced pressure. The following parameters are typical for DGPTI of isoborneol and dehydroisoborneol substrates **1a**–**1e**, and **6a** and **6b**, respectively: *i*) the *Kugelrohr* oven was heated to 80–130°; *ii*) a flow of N_2 was adjusted from 0.8–1.4 l/h; *iii*) the reactor tube was heated up to 450–750°; *iv*) the high vacuum was adjusted at $2-4\times10^{-2}$ mbar.

3.1.1. *2-[(1*R*,3*S*)-(2,2,3-Trimethylcyclopent-1-yl)]-1-phenylethan-1-one* (**7a**). Following *GP 2*, **1a** (2.0 g, 8.68 mmol) was thermo-isomerized at 630°. The dark-yellow crude product was purified by CC (hexane/AcOEt 20:1) to give **7a** (1.46 g, 73%). Slightly yellow oil. $[\alpha]_D^{23}=+54.7$ ($c=0.6$, MeOH). IR (film): 3060*w*, 3027*w*, 2958v*s*, 2871*s*, 1687v*s*, 1598*m*, 1580*m*, 1448*s*, 1366*m*, 1285*m*, 1215*m*, 1180*m*, 1016*m*, 1002*m*, 752*s*, 690*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.95 (*dd*, $^3J(o,m)=8.1$, $^4J(o,p)=1.4$, H_o of Ph); 7.54 (*tt*, $^3J(p,m)=7.4$, $^4J(p,o)=1.4$, H_p of Ph); 7.45 (*t*, $J=8.1$, H_m of Ph); 3.03 (*A* of *ABX*, $^2J_{AB}=16.2$, $^3J=4.0$, H_a–C(2)); 2.73 (*B* of *ABX*, $^2J_{AB}=16.2$, $^3J=10.4$, H_b–C(2)); 2.20 (m_c, H–C(1′)); 1.93 (m_c, H_{endo}–C(5′)); 1.85 (m_c, H_{exo}–C(4′)); 1.66 (*sext.*, $^3J=7.1$, H–C(3′)); 1.25–1.20 (*m*, H_{endo}–C(4′), H_{exo}–C(5′)); 0.89 (*s*, Me_{endo}–C(2′)); 0.88 (*s*, Me_{exo}–C(2′)); 0.86 (*d*, $^3J=7.1$, Me–C(3′)). ^{13}C-NMR (150 MHz, $CDCl_3$): 201.1 (*s*, C(1)); 137.6 (*s*, C_{ipso} of Ph); 133.0 (*d*, C_p of Ph); 128.7 (*d*, C_m of Ph); 128.3 (*d*, C_o of Ph); 44.3 (*d*, C(1′)); 43.7 (*d*, C(3′)); 42.4 (*s*, C(2′)); 40.7 (*t*, C(2)); 31.6 (*t*, C(4′)); 29.7 (*t*, C(5′)); 24.4 (*q*, Me_{exo}–C(2′)); 23.8 (*q*, Me_{endo}–C(2′)); 16.5 (*q*, *Me*–C(3′)). EI-MS: 230 (12, $M^{+\bullet}$), 221 (2), 187 (1), 173 (45), 145 (7), 120 (82, $[M-COPh]^{+\bullet}$), 105 (100, $[M-PhAc]^{+\bullet}$), 95 (23), 77 (30), 69 (11). Anal. calc. for $C_{16}H_{22}O$ (230.35): C 83.43, H 9.63; found: C 83.31, H 9.62.

3.1.2. *1-(4-Methylphenyl)-2-((1*R*,3*S*)-2,2,3-trimethylcyclopent-1-yl)ethan-1-one* (**7b**). Following *GP 2*, **1b** (1.25 g, 5.11 mmol) was thermo-isomerized at 620°. The orange crude product was purified by CC (hexane/AcOEt 30:1) to give **7b** (0.56 g, 45%). Colorless oil. $[\alpha]_D^{23}=+53.2$ ($c=0.6$, hexane). IR (film): 3031*m*, 2958v*s*, 2872v*s*, 1682v*s*, 1608v*s*, 1451*s*, 1366*s*, 1289v*s*, 1224*s*, 1181v*s*, 1016*m*, 806*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.85 (*A* of *AA′BB′*, H_o of Ar); 7.25 (*B* of *AA′BB′*, H_m of Ar); 3.00 (*A* of *ABX*, $^2J_{AB}=15.4$, $^3J=4.0$, H_a–C(2)); 2.70 (*B* of *ABX*, $^2J_{AB}=15.4$, $^3J=10.4$, H_b–C(2)); 2.41 (*s*, *p*-Me); 2.18 (m_c, H–C(1′)); 1.95–1.80 (*m*, H_{exo}–C(4′), H_{endo}–C(5′)); 1.65 (*sext.*, $^3J=7.1$, H–C(3′)); 1.28–1.14 (*m*, H_{endo}–C(4′), H_{exo}–C(5′)); 0.89 (*s*, Me_{endo}–C(2′)); 0.87 (*s*, Me_{exo}–C(2′)); 0.86 (*d*, $^3J=7.0$, Me–C(3′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 200.5 (*s*, C(1)); 143.4 (*s*, C_p of Ar); 134.9 (*s*, C_{ipso} of Ar); 129.1 (*d*, C_m of Ar); 128.1 (*d*, C_o of Ar); 44.2 (*d*, C(1′)); 43.4 (*d*, C(3′)); 42.1 (*s*, C(2′)); 40.3 (*t*, C(2)); 31.3 (*t*, C(4′)); 29.4 (*t*, C(5′)); 24.1 (*q*, Me_{exo}–C(2′)); 23.5 (*q*, Me_{endo}–C(2′)); 21.4 (*q*, *p*-Me); 16.2 (*q*, Me–C(3′)). EI-MS: 244 (4, $M^{+\bullet}$), 187 (12), 173 (2), 134 (91, $ArAc^{+\bullet}$), 119 (100, $COAr^{+\bullet}$), 91 (25).

3.1.3. *1-(4-Methoxyphenyl)-2-[(1*R*,3*S*)-2,2,3-trimethylcyclopent-1-yl)]ethan-1-one* (**7c**). Following *GP 2*, **1c** (1.86 g, 7.14 mmol) was thermo-isomerized at 610°. The dark-yellow crude product was purified by CC (hexane/AcOEt 30:1) to give **7c** (1.15 g, 62%). Yellow oil. $[\alpha]_D^{23}=+50.0$ ($c=0.32$, hexane). IR (film): 2966*s*, 2872*s*, 1677v*s*, 1601v*s*, 1510v*s*, 1418*s*, 1365*s*, 1259v*s*, 1170v*s*, 1032*s*, 829*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.94 (*A* of *AA′BB′*, H_o of Ph); 6.93 (*B* of *AA′BB′*, H_m of Ph); 3.86 (*s*, MeO); 2.97 (*A* of *ABX*, $^2J_{AB}=15.3$, $^3J=4.0$, H_a–C(2)); 2.67 (*B* of *ABX*, $^2J_{AB}=15.3$, $^3J=10.4$, H_b–C(2)); 2.18 (m_c, H–C(1′)); 1.95–1.80 (*m*, H_{exo}–C(4′), H_{endo}–C(5′)); 1.65 (*sext.*, $^3J=7.1$, H–C(3′)); 1.28–1.14 (*m*, H_{endo}–C(4′), H_{exo}–C(5′)); 0.89 (*s*, Me_{endo}–C(2′)); 0.87 (*s*, Me_{exo}–C(2′)); 0.86 (*d*, $^3J=7.0$, Me–C(3′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 199.4 (*s*, C(1)); 163.2 (*s*, C_p of Ar); 130.5 (*s*, C_{ipso} of Ar); 130.2 (*d*, C_o of Ar); 113.5 (*d*, C_m of Ar); 55.3 (*q*, MeO); 44.3 (*d*, C(1′)); 43.4 (*d*, C(3′)); 42.1 (*s*, C(2′)); 40.0 (*t*, C(2)); 31.3 (*t*, C(4′)); 29.4 (*t*, C(5′)); 24.1 (*q*, Me_{exo}–C(2′)); 23.5 (*q*, Me_{endo}–C(2′)); 16.2 (*q*, *Me*–C(3′)). EI-MS: 260 (5, $M^{+\bullet}$), 203 (10), 189 (7), 163 (1), 150 (100), 135 (90), 110 (7, $[M-ArAc-H]^{+\bullet}$), 92 (9), 77 (12), 69 (3), 55 (4).

3.1.4. *1-[(4-Trifluoromethyl)phenyl]-2-[(1*R*,3*S*)-1-(2,2,3-trimethylcyclopent-1-yl)]ethan-1-one* (**7d**). Following *GP 2*, **1d** (1.41 g, 4.73 mmol) was thermo-isomerized at 610°. The dark-yellow crude product was purified by CC (hexane/AcOEt 25:1) to give **7d** (1.0 g, 71%). Colorless oil. $[\alpha]_D^{23}=+40.2$ ($c=0.6$, hexane). IR (film): 2961v*s*, 2874*s*, 1694v*s*, 1512*m*, 1470*m*, 1410*s*, 1367*m*, 1325v*s*, 1289*s*, 1214*m*, 1170v*s*, 1133v*s*, 1110*s*, 1067v*s*, 1016*s*, 994*m*, 857*m*, 825*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.05 (*d*, $^3J(o,m)=8.2$, H_o of Ar); 7.72 (*d*, $^3J(m,o)=8.2$, H_m of Ar); 3.06 (*A* of *ABX*, $^2J_{AB}=15.9$, $^3J=4.1$, H_a–C(2)); 2.75 (*B* of *ABX*, $^2J_{AB}=15.9$, $^3J=10.2$, H_b–C(2)); 2.18 (m_c, H–C(1′)); 1.98–1.82 (*m*, H_{exo}–C(4′), H_{endo}–C(5′)); 1.67 (*sext.*, $^3J=7.2$, H–C(3′)); 1.27–1.14 (*m*, H_{endo}–C(4′), H_{exo}–C(5′)); 0.89 (*s*, Me_{endo}–C(2′)); 0.88 (*s*, Me_{exo}–C(2′)); 0.87 (*d*, $^3J=7.2$, Me–C(3′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 199.7 (*s*, C(1)); 140.0 (*s*, C_{ipso} of Ar); 134.0 (*q*, $^2J(C_p,F)=32.6$, C_p of Ar); 128.6 (*d*, C_o of Ar); 125.4 (*q*, $^3J(C_m,F)=3.5$, C_m of Ar); 123.5 (*q*, $^1J(C,F)=271.2$, F_3C); 44.0 (*d*, C(1′)); 43.4 (*d*, C(3′)); 42.1 (*s*, C(2′)); 40.7 (*t*, C(2)); 31.2 (*t*, C(4′)); 29.4 (*t*, C(5′)); 24.1 (*q*, Me_{exo}–C(2′)); 23.4 (*q*, Me_{endo}–C(2′)); 16.1 (*q*, Me–C(3′)). EI-MS: 298 (4, $M^{+\bullet}$), 279 (5), 241 (88), 213 (8), 188 (81), 173 (100), 145 (95), 125 (16), (22,

$M^{+\bullet}$), 155 (8), 138 (24), 127 (19), 111 (25, [M − COAr + H]$^{+\bullet}$)), 110 (76, [M − ArAc]$^{+\bullet}$), 95 (98), 84 (37), 69 (79), 55 (68).

3.1.5. *1-[(*R*)-(2,2,3-Trimethylcyclopent-3-en-1-yl)]butan-2-one* (**17a**) *and 1-[(*R*)-(2,2-dimethyl-3-methylidenecyclopent-1-yl)]butan-2-one* (**17b**). Following *GP 2*, **1e** (1.25 g, 6.93 mmol) was thermo-isomerized at 600°. The yellow crude product was purified by CC (hexane/AcOEt 60:1) to give **17a**,**b** (0.54 g, 43%; **17a**/**17b** 10:1) as a colorless oil. The presence of a minor amount of the isomeric butanone **17b** was evident from ^{1}H- and ^{13}C-NMR analyses.

Data of **17a**. IR (film): 3038*w*, 2962v*s*, 2876v*s*, 1713v*s*, 1462*s*, 1440*s*, 1412*s*, 1376*s*, 1364*s*, 1271*m*, 1160*m*, 1114*s*, 1032*m*, 988*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.22 (*s*, H−C(4′)); 2.53–2.31 (*m*, 5 H); 2.30–2.19 (*m*, 1 H); 1.84–1.75 (*m*, 1 H); 1.60 (m_c, Me−C(3′)); 1.06 (*t*, ^3J(4,3) = 7.3, Me(4)); 0.99, 0.77 (2*s*, *Me*$_2$C(2′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 211.6 (*s*, C(2)); 147.7 (*s*, C(3′)); 121.6 (*d*, C(4′)); 46.6 (*s*, C(2′)); 45.4 (*d*, C(1′)); 43.3 (*t*, C(1)); 36.1 (*t*, C(3)); 35.6 (*t*, C(1)); 25.4, 19.8 (2*q*, *Me*$_2$C(2′)); 12.4 (*q*, *Me*−C(3′)); 7.7 (*q*, Me(4)). EI-MS: 180 (2, $M^{+\bullet}$), 108 (100, [M − C_4H_8O]$^{+\bullet}$), 93 (61), 77 (6), 57 (26).

Data of **17b**. ^{13}C-NMR (75 MHz, $CDCl_3$): 211.1 (*s*, C(2)); 161.1 (*s*, C(3′)); 103.3 (*t*, *C*H$_2$C(3′)); 46.8 (*s*, C(2′)); 43.6 (*d*, C(1′)); 43.0 (*t*, C(1)); 36.2 (*t*, C(4′)); 30.3 (*t*, C(3)); 28.3 (*t*, C(5′)); 26.4, 24.0, 23.4 (3*q*). EI-MS: 180 (1, $M^{+\bullet}$), 123 (3), 108 (100, [M − C_4H_8O]$^{+\bullet}$), 93 (54), 81 (10), 67 (7), 57 (49).

3.1.6. *1-Phenyl-2-((1*R*,4*R*)-4,5,5-trimethylcyclopent-2-en-1-yl)ethan-1-one* (**21**). Following *GP 2*, **6a** (1.45 g, 6.35 mmol) was thermo-isomerized at 520°. The yellow crude product was purified by CC (hexane/AcOEt 40:1) to give a first fraction of nonpolar, volatile side products (0.2 g), followed by **21** (0.26 g, 18%) as a colorless oil, and acetophenone (**20**) (0.31 g, 40%). $[\alpha]_D = -194.2$ ($c = 1.2$, CH_2Cl_2). IR (film): 3043*w*, 2961v*s*, 2870v*s*, 1686v*s*, 1596*s*, 1448v*s*, 1385*m*, 1363*s*, 1316*m*, 1282*s*, 1218*s*, 1180*m*, 1002*s*, 917*w*, 760v*s*, 690v*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.95 (*A* of *AA′BB′C*, H$_o$ of Ph); 7.55 (*C* of *AA′BB′C*, H$_p$ of Ph); 7.45 (*B* of *AA′BB′C*, H$_m$ of Ph); 5.95 (br. *s*, H−C(2′), H−C(3′)); 3.05 (*A* of *ABX*, $^2J_{AB}$ = 15.8, ^3J = 4.7, H$_a$−C(2)); 2.92 (*dd*, ^3J = 10.0, 4.7, H−C(1′)); 2.81 (*B* of *ABX*, $^2J_{AB}$ = 15.8, ^3J = 10.0, H$_b$−C(2)); 2.37 (*q*, ^3J = 7.2, H−C(4′)); 0.98, 0.97 (2*s*, Me$_2$C(5′)); 0.91 (*d*, ^3J = 7.4, Me−C(4′)). ^{13}C-NMR (150 MHz, $CDCl_3$): 200.6 (*s*, C(1)); 137.6 (*s*, C_{ipso} of Ph); 136.0, 132.4 (2*d*, C(2′,3′)); 133.1 (*d*, C_p of Ph); 128.8 (*d*, C_m of Ph); 128.3 (*d*, C_o of Ph); 50.4 (*d*, C(1′)); 49.3 (*d*, C(4′)); 42.9 (*s*, C(5′)); 38.8 (*t*, C(2)); 24.6, 24.0 (2*q*, *Me*$_2$C(5′)); 14.1 (*q*, *Me*−C(4′)). EI-MS: 228 (5, $M^{+\bullet}$), 213 (2), 157 (3), 108 (63, [M − PhAc]$^{+\bullet}$), 105 (100), 93 (22), 77 (34).

3.1.7. *(3a*R*,7a*R*)-3,3a,4,6,7,7a-Hexahydro-2,3,3-trimethylinden-5(5*H*)-one* (**22**). *a*) Following *GP 2*, **6b** (0.74 g, 4.15 mmol) was thermo-isomerized at 550°. The temp. of the evaporation unit was adjusted to 80° to prevent concerted [3,3]-oxy-*Cope* rearrangements, which may already take place under static conditions above 120°. The yellow crude product was purified by CC (hexane/AcOEt 20:1) to give **22** (0.69 g, 93%) as a colorless oil.

b) Alternatively, **6b** (0.10 g, 0.56 mmol) was added to a suspension of KH (2.80 mmol) in anh. THF (2 ml) at r.t. The mixture was stirred for 30 min at r.t., cooled in an ice bath, and then carefully treated with EtOH (1 ml) *via* rapid injection. H_2O (5 ml) was added, and the resulting slurry was extracted with Et_2O (3 × 10 ml). The combined org. layers were washed with sat. aq. NH_4Cl soln. and brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by CC (hexane/AcOEt 20:1) to give **22** (80 mg, 80%). Colorless oil. $[\alpha]_D^{23} = -126.7$ ($c = 1.6$, CH_2Cl_2). IR (film): 3030*s*, 2958v*s*, 1718v*s*, 1461v*s*, 1436v*s*, 1385*s*, 1376*s*, 1328*s*, 1269*s*, 1184v*s*, 1146*s*, 1083*m*, 1040*m*, 919*m*, 850*s*, 822*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.17 (*s*, H−C(1)); 2.97–2.92 (*m*, H−C(7a)); 2.38 (*dd*, ^3J(4$_a$,4$_b$) = 13.2, ^3J(4$_a$,3a) = 8.6, H$_a$−C(4)); 2.35–2.27 (*m*, H−C(3a), H$_b$−C(4), H$_a$−C(6)); 2.22–2.16 (*m*, H$_b$−C(6)); 2.01 (*dq*, ^3J(7$_a$,7$_b$) = 13.8, J = 5.5, H$_a$−C(7)); 1.69–1.63 (*m*, H$_b$−C(7)); 1.62 (m_c, Me−C(2)); 1.02 (*s*, Me$_{exo}$−C(3)); 0.93 (*s*, Me$_{endo}$−C(3)). ^{13}C-NMR (150 MHz, $CDCl_3$): 214.9 (*s*, C(5)); 147.4 (*s*, C(2)); 125.6 (*d*, C(1)); 48.7 (*s*, C(3)); 47.3 (*d*, C(3a)); 41.2 (*d*, C(7a)); 39.8 (*t*, C(4)); 37.9 (*t*, C(6)); 28.0 (*q*, *Me*$_{exo}$−C(3)); 26.5 (*t*, C(7)); 22.7 (*q*, *Me*$_{endo}$−C(3)); 12.6 (*q*, Me−C(2)). EI-MS: 178 (23, $M^{+\bullet}$), 163 (100, [M − Me]$^{+\bullet}$), 135 (7), 121 (69), 107 (24), 93 (23), 79 (8), 55 (11).

3.2. *4-Methoxyphenyl (1*R*,3*S*)-(2,2,3-Trimethylcyclopent-1-yl)acetate* (**12**). Phenone **7c** (0.34 g, 1.31 mmol) was dissolved in anh. CH_2Cl_2 (7 ml), and MCPBA (80–85%, 0.59 g, 3.40 mmol) was added. The suspension was cooled to 0°, and TFA (0.1 ml, 1.31 mmol) was added dropwise over 15 min. The reaction flask protected from light was stirred over night at r.t., whereupon the ketone was completely consumed (GC analysis). The mixture was diluted with CH_2Cl_2 (50 ml), washed once each with 10% aq. Na_2SO_3 soln., sat. aq. K_2CO_3 soln., and H_2O. The org. phase was dried ($MgSO_4$) and evaporated. The residue was taken up in hexane and filtered over a short pad of silica gel using hexane/AcOEt 50:1 to give **12** (0.36 g, 99%). Colorless oil. $[\alpha]_D^{23} = +27.5$ ($c = 1.0$, MeOH). IR ($CHCl_3$): 2962*s*, 2874*m*, 1747*s*, 1506v*s*, 1467*m*, 1368*w*, 1290*w*, 1249*s*, 1195v*s*, 1145*s*, 1103*m*, 1036*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.98 (*A* of *AA′BB′*, H$_o$ of Ar); 6.88 (*B* of *AA′BB′*, H$_m$ of Ar); 3.79 (*s*, MeO); 2.59 (*A* of *ABX*, $^2J_{AB}$ = 14.5, ^3J = 4.6, H$_a$−C(2)); 2.30 (*B* of *ABX*, $^2J_{AB}$ = 14.5, ^3J = 10.3, H$_b$−C(2)); 2.15

(m_c, H–C(1′)); 2.06–1.95 (m, H_{endo}–C(5′)); 1.92–1.84 (m, H_{exo}–C(4′)); 1.66 (*sext.*, $^3J = 7.2$, H–C(3′)); 1.43–1.19 (m, H_{endo}–C(4′), H_{exo}–C(5′)); 0.89 (s, Me_{endo}–C(2′)); 0.87 (s, Me_{exo}–C(2′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 172.8 (s, C(1)); 157.1 (s, C_p of Ar); 144.2 (s, C_{ipso} of Ar); 122.2 (d, C_o of Ar); 114.3 (d, C_m of Ar); 55.5 (q, MeO); 44.8 (d, C(1′)); 43.4 (d, C(3′)); 42.1 (s, C(2′)); 36.5 (t, C(2)); 31.2 (t, C(4′)); 29.1 (t, C(5′)); 23.8 (q, Me_{exo}–C(2′)); 23.4 (q, Me_{endo}–C(2′)); 15.9 (q, Me–C(3′)). EI-MS: 276 (3, $M^{+\bullet}$), 219 (1), 153 (1), 135 (1), 124 (100), 109 (14, $[M - \text{ArAc}]^{+\bullet}$), 81 (3), 69 (10), 55 (7).

3.3. *(1*R*,3*S*)-(2,2,3-Trimethylcyclopent-1-yl)acetic Acid* (=*(+)*-trans-*α*-*Campholanic Acid*; **9**). To a stirred soln. of **12** (1.27 g, 4.60 mmol) in MeOH (10 ml) at 0° was added sat. aq. LiOH (10 ml). The mixture became immediately dark and cloudy. After stirring for 15 min at r.t., H_2O was added, and the soln. was treated with 10% aq. HCl (pH < 3). The resulting mixture was extracted with sat. aq. $NaHCO_3$ soln. (3×). The aq. layer was acidified again and extracted with Et_2O (3×). The combined org. layers were washed with brine, dried ($MgSO_4$), and evaporated to yield **9** (0.76 g, 97%) as a colorless oil. An anal. sample was purified by bulb-to-bulb distillation. $[\alpha]_D^{23} = +40.6$ ($c = 0.85$, hexane). IR ($CHCl_3$): 3517v*w*, 2961v*s*, 2874v*s*, 2680*m*, 1704v*s*, 1470*m*, 1452*m*, 1412*s*, 1389*m*, 1368*m*, 1296v*s*, 1230*m*, 1178*w*, 1136*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.43 (*A* of *ABX*, $^2J_{AB} = 14.1$, $^3J = 3.5$, H_a–C(2)); 2.12 (*B* of *ABX*, $^2J_{AB} = 14.1$, $^3J = 10.4$, H_b–C(2)); 2.06–1.81 (m_c, H–C(1′), H_{exo}–C(4′), H_{endo}–C(5′)); 1.62 (*sext.*, $^3J = 7.1$, H–C(3′)); 1.31–1.17 (m, H_{endo}–C(4′), H_{exo}–C(5′)); 0.86 (d, $^3J = 6.9$, Me–C(3′)); 0.84 (s, Me_{endo}–C(2′)); 0.81 (s, Me_{exo}–C(2′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 180.6 (s, C(1)); 44.5 (d, C(1′)); 43.3 (d, C(3′)); 42.0 (s, C(2′)); 36.2 (t, C(2)); 31.1 (t, C(4′)); 29.1 (t, C(5′)); 23.7 (q, Me_{exo}–C(2′)); 23.3 (q, Me_{endo}–C(2′)); 16.0 (q, *Me*–C(3′)). EI-MS: 170 (10, $M^{+\bullet}$), 127 (11), 114 (37), 110 (26, $[M - \text{AcOH} - \text{H}]^{+\bullet}$), 95 (42), 84 (67), 69 (100), 55 (23). Anal. calc. for $C_{10}H_{18}O_2$ (170.25): C 70.55, H 10.66; found: C 70.42, H 9.53.

3.4. *[(1*S*,3*S*)-(2,2,3-Trimethylcyclopent-1-yl)]methyl 4-(Trifluoromethyl)benzoate* (**13**). Phenone **7d** (0.30 g, 1.0 mmol) was dissolved in anh. CH_2Cl_2 (5 ml), and MCPBA (80–85%, 0.45 g, 2.6 mmol) was added. The suspension was cooled to 0°, and TFA (77 µl, 1.0 mmol) was added dropwise over 15 min. The mixture, protected from light, was stirred for 10 d at r.t. Workup as described above, followed by filtration over a short pad of silica gel with hexane/AcOEt 50:1, provided **13** (0.28 g, 89%). Colorless oil. $[\alpha]_D^{23} = +27.7$ ($c = 1.0$, hexane). IR (film): 2961*s*, 2874*m*, 1725v*s*, 1469*w*, 1412*m*, 1326v*s*, 1276v*s*, 1170v*s*, 1067v*s*, 1018*s*, 863*m*, 776*m*, 705*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.14 (d, $^3J(o,m) = 8.1$, H_o of Ar); 7.70 (d, $^3J(m,o) = 8.1$, H_m of Ar); 4.39 (*A* of *ABX*, $^2J_{AB} = 10.9$, $^3J = 6.5$, H_a–C(2)); 4.23 (*B* of *ABX*, $^2J_{AB} = 10.9$, $^3J = 7.5$, H_b–C(2)); 2.08 (m_c, H–C(1′)); 1.99–1.83 (m, H_{exo}–C(4′), H_{endo}–C(5′)); 1.68 (*sext.*, $^3J = 7.1$, H–C(3′)); 1.35–1.19 (m, H_{endo}–C(4′), H_{exo}–C(5′)); 0.96 (s, Me_{endo}–C(2′)); 0.92 (s, Me_{exo}–C(2′)); 0.89 (d, $^3J = 7.1$, Me–C(3′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 165.4 (s, C(1)); 134.4 (s, C_{ipso} of Ar); 133.7 (q, $^2J(C_p,F) = 32.2$, C_p of Ar); 129.8 (d, C_o of Ar); 125.3 (q, $^3J(C_m,F) = 3.5$, C_m of Ar); 123.7 (q, $^1J(C,F) = 271.2$, F_3C); 67.5 (t, C(2)); 47.3 (d, C(1′)); 44.1 (d, C(3′)); 41.7 (s, C(2′)); 31.4 (t, C(4′)); 26.8 (t, C(5′)); 24.5 (q, Me_{exo}–C(2′)); 23.6 (q, Me_{endo}–C(2′)); 15.2 (q, *Me*–C(3′)). EI-MS: 314 (1, $M^{+\bullet}$), 295 (6), 258 (3), 231 (3), 211 (1), 173 (100, $[\text{COAr} + \text{H}]^{+\bullet}$), 145 (43), 124 (40), 109 (56), 95 (18), 82 (42), 69 (43), 55 (16).

3.5. *[(1*S*,3*S*)-2,2,3-Trimethylcyclopent-1-yl]methanol* (**11**). To a stirred soln. of **13** (1.40 g, 4.45 mmol) in MeOH (10 ml) was added at 0° sat. aq. LiOH soln. (10 ml). The mixture became immediately dark and cloudy. After stirring for 30 min at r.t., 2N NaOH soln. (10 ml) was added, and the mixture was extracted with Et_2O (3×). The combined org. layers were washed with brine, dried ($MgSO_4$), and evaporated to afford **11** (0.62 g, 98%). Colorless oil. $[\alpha]_D^{23} = +49.9$ ($c = 0.85$, hexane). IR ($CHCl_3$): 3623*m*, 3469*w*, 2961v*s*, 2874v*s*, 1681*s*, 1598*w*, 1581v*w*, 1469*s*, 1450*s*, 1388*m*, 1367*s*, 1285*m*, 1217*m*, 1181*m*, 1022*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.71 (*A* of *ABX*, $^2J_{AB} = 10.4$, $^3J = 5.7$, H_a–C(1)); 3.44 (*B* of *ABX*, $^2J_{AB} = 10.4$, $^3J = 8.2$, H_b–C(1)); 1.91–1.73 (m, H–C(1′), H_{exo}–C(4′), H_{endo}–C(5′)); 1.65 (*sext.*, $^3J = 7.0$, H–C(3′)); 1.53 (br. s, OH); 1.46–1.16 (m, H_{endo}–C(4′), H_{exo}–C(5′)); 0.87 (s, Me_{endo}–C(2′)); 0.85 (d, $^3J = 7.0$, Me–C(3′)); 0.85 (s, Me_{exo}–C(2′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 65.0 (t, C(1)); 50.9 (d, C(1′)); 44.0 (d, C(3′)); 41.5 (s, C(2′)); 31.5 (t, C(4′)); 26.7 (t, C(5′)); 24.2 (q, Me_{exo}–C(2′)); 23.4 (q, Me_{endo}–C(2′)); 15.1 (q, Me–C(3′)). EI-MS: 142 (2, $M^{+\bullet}$), 124 (6, $[M - \text{H}_2\text{O}]^{+\bullet}$), 109 (78), 99 (14), 95 (10), 84 (33), 69 (100), 55 (30).

3.6. *(1*S*,3*S*)-2,2,3-Trimethylcyclopentanecarboxylic Acid* (=*(+)*-trans-*α*-*Dihydrocampholytic Acid*; **14**). *Jones* reagent, prepared by dissolving CrO_3 (1.13 g, 11.30 mmol) in H_2O (3.5 ml) and H_2SO_4 (1 ml), was added dropwise to a soln. of **11** (0.5 g, 3.52 mmol) in acetone (25 ml) at 0°. After stirring for 30 min at r.t., H_2O (20 ml) and Et_2O (30 ml) were added. The mixture was extracted with 2N NaOH soln. (3 × 20 ml), and the aq. layer was acidified with 10% aq. HCl to pH 3. The aq. phase was extracted with Et_2O (2 × 30 ml), and the combined org. extracts were dried ($MgSO_4$) and evaporated. The residual oil was filtered through a short pad of silica gel with hexane/AcOEt 50:1 to provide **14** (0.54 g, 99%). Colorless oil. $[\alpha]_D^{23} = +51.2$ ($c = 1.0$, hexane). IR (film): 2963v*s*, 2875v*s*, 2748*s*, 2668*s*, 1700v*s*, 1471*s*, 1420*s*, 1369*s*, 1291*s*, 1239v*s*, 1190*s*, 941*s*, 713*w*. ^{1}H-NMR (600 MHz, $CDCl_3$): 2.53 (dd, $^3J = 8.4$, 6.0, H–C(1)); 1.97–1.89 (m, H_{exo}–C(4), H_{exo}–C(5)); 1.88–1.79 (m, H–C(3),

H_{endo}–C(5)); 1.35–1.21 (*m*, H_{endo}–C(4)); 0.98 (*s*, Me_{endo}–C(2)); 0.94 (*s*, Me_{exo}–C(2)); 0.86 (*d*, $^3J = 7.0$, Me–C(3)). ^{13}C-NMR (150 MHz, $CDCl_3$): 182.6 (*s*, CO_2H); 54.9 (*d*, C(1)); 44.7 (*s*, C(2)); 43.5 (*d*, C(3)); 32.1 (*t*, C(4)); 25.8 (*t*, C(5)); 24.5 (*q*, Me_{exo}–C(2)); 24.1 (*q*, Me_{endo}–C(2)); 14.9 (*q*, *Me*–C(3)). EI-MS: 156 (6, $M^{+\cdot}$), 138 (4), 123 (4, $[M - CO_2 + H]^{+\cdot}$), 113 (6), 101 (10), 96 (12), 84 (100), 69 (70), 55 (19).

3.7. *Methyl (1S,3S)-2,2,3-Trimethylcyclopentanecarboxylate* (**15**). A soln. of **14** (0.20 g, 1.28 mmol) in Et_2O (5 ml) was treated with a 0.5M soln. of CH_2N_2 in Et_2O (7.68 ml, 3.84 mmol) at 0°. The mixture was allowed to warm to r.t. within 30 min, whereupon the solvent was evaporated under reduced pressure to give **15** (0.21 g, 96%). Colorless oil. $[\alpha]_D^{23} = +68.0$ ($c = 1.0$, hexane). IR (film): 2962v*s*, 2875v*s*, 1733v*s*, 1455*s*, 1435*s*, 1389*m*, 1369*s*, 1357*s*, 1295*m*, 1258*s*, 1216v*s*, 1199v*s*, 1162v*s*, 105*m*, 1037*m*, 918*m*, 735*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 3.65 (*s*, MeO); 2.52 (*dd*, $^3J = 8.4$, 5.9, H–C(1)); 1.97–1.88 (*m*, H_{exo}–C(4), H_{exo}–C(5)); 1.86–1.77 (*m*, H–C(3), H_{endo}–C(5)); 1.31–1.25 (*m*, H_{endo}–C(4)); 0.91 (*s*, Me_{endo}–C(2)); 0.89 (*s*, Me_{exo}–C(2)); 0.85 (*d*, $^3J = 6.9$, Me–C(3)). ^{13}C-NMR (150 MHz, $CDCl_3$): 176.6 (*s*, MeOOC); 54.9 (*d*, C(1)); 51.3 (*s*, MeO); 44.5 (*s*, C(2)); 43.4 (*d*, C(3)); 32.2 (*t*, C(4)); 25.9 (*t*, C(5)); 24.5 (*q*, Me_{exo}–C(2)); 24.1 (*q*, Me_{endo}–C(2)); 14.7 (*q*, *Me*–C(3)). EI-MS: 170 (22, $M^{+\cdot}$), 155 (8), 138 (24), 127 (19), 111 (25, $[M - CO_2Me + H]^{+\cdot}$), 95 (88), 87 (88), 84 (100), 69 (92), 55 (56).

3.8. *1-(3-Nitrophenyl)-2-[(1*R*,3*S*)-2,2,3-trimethylcyclopent-1-yl]ethan-1-one* (**16**). A round-bottom flask containing H_2SO_4 (0.6 ml) was cooled to −15°, and phenone **7a** (0.53 g, 2.28 mmol) was added dropwise. Then, a 3:2 mixture of H_2SO_4/HNO_3 (0.5 ml) was added at such a rate that the temp. of the mixture remained below −5°. Stirring was continued for 15 min at 0°, and the contents of the flask were poured onto ice. The yellow mixture was extracted with Et_2O (2 × 30 ml), and the combined org. extracts were washed with sat. aq. $NaHCO_3$ soln. and brine, dried ($MgSO_4$), and evaporated. The residual oil was filtered through a short pad of silica gel with hexane/AcOEt 50:1 to provide **16** (0.49 g, 78%). Yellow oil. $[\alpha]_D^{23} = +43.5$ ($c = 1.0$, hexane). IR (film): 3086*w*, 2959v*s*, 2872*s*, 1695v*s*, 1613*s*, 1534*s*, 1471*m*, 1439*m*, 1406*m*, 1351v*s*, 1294*m*, 1212*s*, 1086*m*, 1001*m*, 920*w*, 810*m*, 735*s*, 676*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.76 (*t*, $^4J = 1.8$, arom. H); 8.41 (*ddd*, $^3J = 8.2$, $^4J = 2.2$, 1.1, arom. H); 8.28 (*ddd*, $^3J = 7.8$, $^4J = 1.5$, 1.2, arom. H); 7.68 (*t*, $^3J = 8.0$, arom. H); 3.08 (*A* of *ABX*, $^2J_{AB} = 16.1$, $^3J =$ 4.0, H_a–C(2)); 2.79 (*B* of *ABX*, $^2J_{AB} = 16.1$, $^3J = 10.1$, H_b–C(2)); 2.18 (m_c, H–C(1′)); 1.92 (m_c, H_{endo}–C(5′)); 1.86 (m_c, H_{exo}–C(4′)); 1.65 (*sext.*, $^3J = 7.1$, H–C(3′)); 1.26–1.19 (*m*, H_{endo}–C(4′), H_{exo}–C(5′)); 0.91 (*s*, Me_{endo}–C(2′)); 0.90 (*s*, Me_{exo}–C(2′)); 0.87 (*d*, $^3J = 7.1$, Me–C(3′)). ^{13}C-NMR (150 MHz, $CDCl_3$): 198.3 (*s*, C(1)); 148.4 (*s*, C–NO_2); 138.5 (*s*, C_{ipso} of Ar); 133.5 (*d*); 129.7 (*d*); 127.0 (*d*); 122.9 (*d*); 43.9 (*d*, C(1′)); 43.4 (*d*, C(3′)); 42.1 (*s*, C(2′)); 40.7 (*t*, C(2)); 31.2 (*t*, C(4′)); 29.5 (*t*, C(5′)); 24.1 (*q*, Me_{exo}–C(2′)); 23.5 (*q*, Me_{endo}–C(2′)); 16.1 (*q*, Me–C(3′)). EI-MS: 275 (2, $M^{+\cdot}$), 218 (100), 150 (42), 95 (39), 69 (36), 55 (12).

REFERENCES

[1] G. Rüedi, M. Nagel, H.-J. Hansen, *Synlett* **2003**, 1210.
[2] J. M. Coxon, P. J. Steel, *Aust. J. Chem.* **1979**, *32*, 2441.
[3] V. Dimitrov, S. Bratovanov, S. Simova, K. Kostova, *Tetrahedron Lett.* **1994**, *35*, 6713.
[4] J. H. Hutchinson, D. L. F. Li, T. Money, M. Palme, M. R. Agharahimi, K. F. Albizat, *Can. J. Chem.* **1991**, *69*, 558.
[5] W. M. Dadson, J. H. Hutchinson, T. Money, *Can. J. Chem.* **1990**, *68*, 1821.
[6] F. H. Allen, *Acta Crystallogr., Sect. B* **2002**, *52*, 380.
[7] M. Rohr, C. Flynn, U.S. Pat. 4-547315, 1985.
[8] S. S. C. Koch, A. R. Chamberlin, *Synth. Commun.* **1989**, *19*, 829.
[9] F.-Y. Zhang, E. J. Corey, *Org. Lett.* **2000**, *2*, 1097.
[10] M. B. Rubin, A. L. Gutman, *J. Org. Chem.* **1986**, *51*, 2511.
[11] J. T. Welch, J. Lin, *Tetrahedron* **1996**, *52*, 291.
[12] Y. L. Chow, D.-C. Zhao, M. Kitadani, K. Pillay, N. Somasekaren, M. A. Yoursy, T.-I. Ho, *J. Chem. Soc., Perkin Trans. 2* **1990**, 361.
[13] M. D. McCreary, D. W. Lewis, D. L. Wernick, G. M. Whitesides, *J. Am. Chem. Soc.* **1974**, *96*, 1038.
[14] J. R. Lewis, J. L. Simonsen, *J. Chem. Soc.* **1936**, 734.
[15] W. Borsche, W. Sander, *Chem. Ber.* **1915**, *48*, 117.
[16] M. G. Blanc, M. Desfontaines, *Bull. Soc. Chim. Fr.* **1904**, *31*, 381.
[17] A. Siewinski, J. Dmochowska-Gladysz, T. Kolie, A. Zabza, K. Derdzinski, A. Nespiak, *Tetrahedron* **1979**, *35*, 1409.

[18] A. Siewinski, J. Dmochowska-Gladysz, T. Kolie, A. Zabza, K. Derdzinski, A. Nespiak, *Tetrahedron* **1983**, *39*, 2265.
[19] K. W. Egger, D. M. Golden, S. W. Benson, *J. Am. Chem. Soc.* **1964**, *86*, 5420.
[20] K. W. Egger, A. T. Cooks, *Helv. Chim. Acta* **1973**, *56*, 1516.
[21] K. W. Egger, A. T. Cooks, *Helv. Chim. Acta* **1973**, *56*, 1537.
[22] J. P. Perdew, K. Burke, M. Ernzerhof, *Phys. Res. Lett.* **1996**, *77*, 3865.
[23] D. N. Laikov, *Chem. Phys. Lett.* **1997**, *281*, 151.
[24] J. M. Galano, G. Audran, L. Mikolajezyk, H. Monti, *J. Org. Chem.* **2001**, *66*, 323.
[25] M.-I. Garcia-Vallejo, M. C. Garcia-Vallejo, J. Sanz, M. Bernabe, Velasco-Negueruela, *Phytochemistry* **1994**, *36*, 43.
[26] R. T. Jacobs, G. I. Feutrill, J. Meinwald, *J. Org. Chem.* **1990**, *55*, 4051.
[27] W. Oppolzer, P. Schneider, *Helv. Chim. Acta* **1986**, *69*, 1817.
[28] J. H. Hutchinson, D. L. Kuo, T. Mooney, B. Yokohama, *J. Chem. Soc., Chem. Commun.* **1988**, 1281.
[29] G. Rüedi, H.-J. Hansen, *Helv. Chim. Acta* **2004**, *87*, 1628.

Received February 13, 2004