REVIEW

Thermal Rearrangements of Monoterpenes and Monoterpenoids

by **Achim Stolle***[a]), **Bernd Ondruschka**[a]), and **Henning Hopf**[b])

[a]) Institute for Technical Chemistry and Environmental Chemistry, Friedrich-Schiller University Jena, Lessingstraße 12, D-07743 Jena
(phone: +49-3691-948413; fax: +49-3641-948402; e-mail: achim.stolle@uni-jena.de)
[b]) Institute for Organic Chemistry, Technical University Braunschweig, Hagenring 30, D-38106 Braunschweig

On the occasion of the 70th anniversary of the *Nobel Prize* in Chemistry awarded to *Leopold Ružička* for his work on polymethylenes and higher terpenes[1])

The thermal conversions of monoterpenes and monoterpenoids are an interesting field of research with respect to mechanistic, kinetic, and theoretical issues. Since the beginning of the 20th century, these reactions have attracted the interest of many research groups, and even today there are sufficient problems and questions to deal with. This review covers the thermal isomerization chemistry of pinanes, pinenes, carenes, and thujenes over the past 70 years. Categorization of these compounds into groups, each of them being represented by a small parent molecule (cyclobutane, vinylcyclobutane, vinylcyclopropane), allows systematization of multitude of publications.

Contents

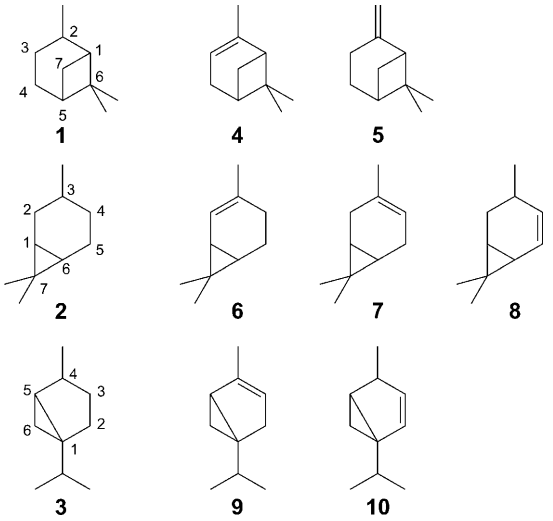
[1]) For a biography, see [1]; *Nobel* lecture: L. Ružička '*Viergliedrige Ringe, höhere Terpenverbindungen und männliche Sexualhormone*' [2].

1. Introduction. – Terpenes and terpenoids are a small and heterogeneous class of naturally occurring compounds and important for laboratory- as well as industrial-scale applications. Due to their nature (odor, taste, chirality), they serve as important synthetic building blocks for the production of flavors, fragrances, pharmaceuticals, and nutraceuticals. Additionally, their derivatives are widely applied in enantioselective reactions as ligands or auxiliaries. Besides these technical applications, the chemistry of terpenes and terpenoids is interesting from both theoretical and mechanistic view points. In addition to catalytic reactions (hydrogenation, oxidation, epoxidation, *etc.*), terpenes and terpenoids offer the opportunity of performing rearrangement reactions in the gaseous, liquid, and supercritical phase [3].

Generally, terpenes are oligomers or polymers of isoprene (C_5H_8), and, depending on the number of isoprene units the molecule consists of, they can be categorized into monoterpenes ($C_{10}H_{16}$; two isoprene units), sesquiterpenes ($C_{15}H_{24}$; three isoprene units), diterpenes ($C_{20}H_{32}$; four isoprene units), sesquiterterpenes, triterpenes, and tetraterpenes. In contrast to terpenes, molecules with a different formula than $(C_5H_8)_n$ are known as terpenoids. Therefore, menthol ($C_{10}H_{22}O$) and citral ($C_{10}H_{16}O$) are monoterpenoids rather than monoterpenes. With respect to occurrence in nature, the monoterpenes and monoterpenoids represent the most important and best investigated class of terpenic compounds. The wide structural diversity and possibility for internal C,C linkage affords a further subcategorization of these molecules [3a – c][4]. Besides a general classification into acyclic, monocyclic, bicyclic, and tricyclic compounds, the molecules with similar structure are classified into subclasses whose names are related to the lead compound of the respective class. Accordingly, citral, nerol, and myrcene are representatives of the 3,6-dimethyloctane subclass, whereas limonene, menthol, and pulegone belong to the *p*-menthane subclass.

The lead compounds for the main subclasses of monoterpenes with constrained rings are pinane (**1**), carane (**2**), and thujane (**3**). The outstanding feature of the chemistry of these basic structures is the ease of skeletal rearrangement. Opening of the cyclobutane (in **1**) or cyclopropane ring (in **2** and **3**) leads to various products, whose distribution is closely related to the mode of activation (thermolysis, photolysis, acidolysis, radiolysis). Thermally induced and acid-catalyzed rearrangements are the most important reactions leading to isomerization products through ring opening in **1** – **3**. Among these compounds the rearrangement chemistry of pinane-type terpenes and terpenoids has been most widely investigated and well-documented, a consequence of the industrial importance of these compounds [5].

Thermal rearrangements of three- and four-membered rings in small molecules have long been known and thoroughly investigated reactions, and they have been the subject of various review articles [6]. Nevertheless, these rearrangements still present challenges, especially since these isomerizations can serve as models for similar

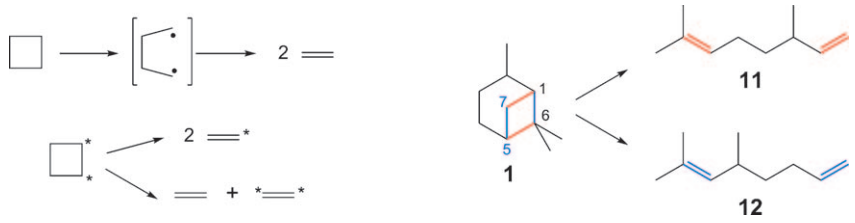


reactions of higher-molecular-weight compounds. Terpenoids **1**–**3** can be classified according to their structural features allowing characteristic thermal isomerizations. Thus, compounds without a C=C bond in α-position to the cyclobutane ring (in **1**) show a thermal behavior similar to that of substituted cyclobutanes, whereas the thermal isomerizations of α- and β-pinene (**4** and **5**, resp.) display similarities to the pyrolysis behavior of vinylcyclobutane (VCB) [6a,e][7][8]. Thermal treatment of Δ^2- and Δ^4-carene (**6** and **8**, resp.), as well as isomerization of α- and β-thujene (**9** and **10**, resp.), yield products similar to those arising from pyrolysis of vinylcyclopropane (VCP) [5f][6a,b,d,e].

2. Isomerizations Related to Cyclobutane. – The outstanding feature of the thermally induced processes of cyclobutane and its derivatives is the ease of degenerative fragmentations leading to substituted ethylene derivatives. According to the rules of conservation of orbital symmetry in pericyclic reactions, these $[\sigma 2 + \sigma 2]$ cycloreversions are thermally forbidden if they proceed *suprafacially*. The *antarafacial* version ($[\sigma 2_s + \sigma 2_a]$) is allowed, but requires severe twisting of the cyclobutane ring. Therefore, the most plausible mechanism is a stepwise fragmentation *via* biradical intermediates (*Scheme 1*). Whereas the pyrolysis of singly or symmetrically 1,3-disubstituted cyclobutanes leads to the formation of one single product (neglecting the stereochemical outcome), fragmentation of 1,2-disubstituted cyclobutanes yields different products, arising from two different fragmentation routes. Since pinane-type compounds are 1,2,2,3-tetrasubstituted cyclobutanes, their thermal fragmentation are expected to yield products of two different pathways. For instance, the pyrolysis of **1** yields β-citronellene (**11**) and isocitronellene (**12**) as primary products [9–11]. The acyclic nature of the products is due to the fact that pinanes are bridged bicyclic cyclobutanes.

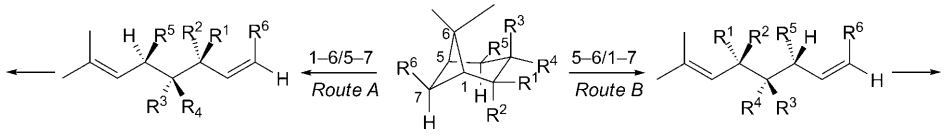
Often the acyclic main pyrolysis products of pinane-type compounds undergo consecutive ene cyclizations forming cyclopentane derivatives. These reactions are

Scheme 1



indicated by an additional reaction arrow and will be discussed in detail in *Chapt. 6*. *Table 1* lists all those compounds the thermal isomerization behavior of which is similar to that of **1** and hence related to the thermochemistry of cyclobutane.

Table 1. *Ratio of Different Fragmentation Routes for Pinane Derivatives Substituted at C(2), C(3), C(4), and/or C(7)*

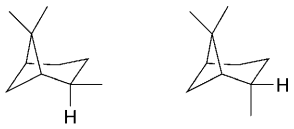


No.	Name	R^1	R^2	R^3	R^4	R^5	R^6	A[a])	B[a])	A/B[b])	Ref.
1a	*cis*-Pinane	Me	H	H	H	H	H	**11**	**12**	90 : 10[c])	[9][10]
										86 : 14[d])	[11]
1b	*trans*-Pinane	H	Me	H	H	H	H	**11**	**12**	55 : 45	[9][10]
13	Norpinane	H	H	H	H	H	H	**14**	[e])		[12]
cis-**15**	*cis*-Pinan-2-ol	Me	OH	H	H	H	H	**15a**	**15b**	95 : 5	[13]
trans-**15**	*trans*-Pinan-2-ol	OH	Me	H	H	H	H	**15a**	**15b**	96 : 4	[13]
16	Isopinocampheol	Me	H	H	OH	H	H	**16a**	**16b**	97 : 3	[14–16]
17	Neoisoverbanol	Me	H	H	H	OH	H	**17a**	**17b**	67 : 33	[15]
18	*cis*-Nopinol	OH	H	H	H	H	H	**18a**	**18b**	76 : 24	[15]
19	Isopinocamphone	Me	H	O		H	H	**19a**	**19b**	93 : 3[c])	[17]
										100 : 0[f])	[14]
20	*cis*-Dihydronopol	HOC_2H_4	H	H	H	H	H	**20a**	–	100	[18]
21	*cis*-Myrtanol	$HOCH_2$	H	H	H	H	H	**21a**	**21b**	62 : 38	[19]
22	*trans*-Myrtanol	H	$HOCH_2$	H	H	H	H	**21a**	**21b**	55 : 45	[19]
23	*endo-cis*-Chrysanthanol	Me	H	H	H	H	OH	**25**	**26**	62 : 38	[20]
24	*endo-cis*-Chrysanthanyl acetate	Me	H	H	H	H	AcO	**25**	**26**	93 : 7	[21]

[a]) Isomerization products arising from *Route A* or *B*. [b]) Relative ratio of products arising from fragmentation *Routes A* and *B* for pinane derivatives in %. [c]) Flow-type pyrolysis (N_2) at ambient pressure. [d]) Flash vacuum pyrolysis (0.07 mbar). [e]) Due to C_s symmetry, the products arising from *Route A* and *B* are identical. [f]) Vacuum pyrolysis (16 mbar).

2.1. *Pyrolysis of Pinane.* The rearrangement of pinane (**1**) leading to β-citronellene (**11**) is a known and thoroughly investigated reaction [9–11][22–29]. Additionally, a few patents and articles have been published on the thermal rearrangement of **1** to **11** as a synthetic step for the production of a multitude of fine and specialty chemicals (*e.g.*,

flavors and fragrances) [30]. Various authors have reported that this reaction is enantioselective, and that the degree of optical rotation of **11** depends on that of **1** used for pyrolysis [9][10][25]. As shown in *Scheme 1*, the fragmentation of the cyclobutane ring in **1** theoretically must lead to two different products: **11** and isocitronellene (**12**). Hydrocarbon **12** as a further product was mentioned only in a few studies [9–11][31]. *Rienäcker* and *Stolle et al.* showed that the ratio **11**/**12** evidently depends on the ratio of *cis*- (**1a**) to *trans*-pinane (**1b**) in the initial mixture [9][10]. Pyrolysis of **1a** predominantly yields **11** (selectivity 90%), whereas reactions under similar conditions carried out with **1b** afforded **11** and **12** in almost equal amounts (*Table 1*). Additionally, both diastereoisomers differ in their reactivity, **1a** being more prone towards thermal cleavage than **1b**.

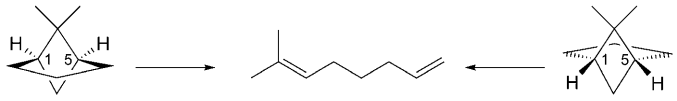


1a **1b**

Recently, *Kinzel* calculated the stepwise fragmentation pathway for both diastereoisomers of **1** using CASSCF methods [32]. The absolute energy differences between concerted [$\sigma 2_s + \sigma 2_a$] and stepwise biradical pathway is *ca.* 200 kJ mol^{-1} in favor of the latter. Computational results also reflect the differences in product distribution and reactivity of **1a** and **1b**. Kinetic pyrolysis experiments gave E_a values of 201.1 and 213.0 kJ mol^{-1} for the rate constants describing the disappearance of **1a** and **1b**, respectively [31]. An *Arrhenius* factor log A of 14.0 (A in s^{-1}) for both diastereoisomers seems to confirm the stepwise pathway *via* biradical intermediates. Activation energies expected from kinetic measurements are comparable with those resulting from *ab initio* calculations on the CASMP2(4,4)/6-31G(d,p) level of theory [32].

2.2. *Pyrolysis of Norpinane and Hydroxypinanes.* The pyrolysis of norpinane (**13**) yields 7-methylocta-1,6-diene (**14**) as the primary pyrolysis product exclusively (*Scheme 2*) [12][33]. Due to the symmetric structure of **13**, the products arising from both possible fragmentation routes are identical. The C_s symmetry of the molecule is due to the absolute configuration of the bridgehead atoms C(1) and C(5). As for all other monoterpenes and monoterpenoids with the pinane skeleton, the configuration of these can either be (1*S*,5*R*) or (1*R*,5*S*). A (*S*,*S*)- or (*R*,*R*)-configuration is sterically impossible, since this would cause severe twisting of the cyclobutane ring comparable to an arrangement in a *trans*-cyclohexene system.

Scheme 2

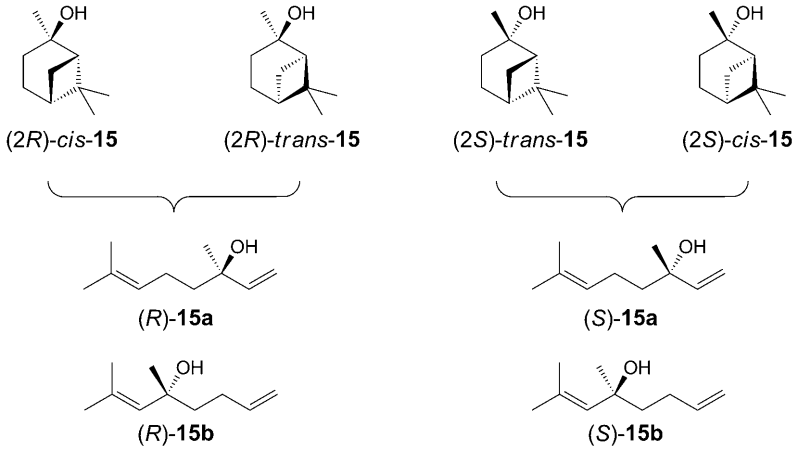


(1*R*,5*S*)-**13** **14** (1*S*,5*R*)-**13**

Pinane-type compounds with a OH group in either 2-, 3-, or 4-position of **1** (*i.e.*, **15**–**17**) are listed in *Table 1*. Among these, pinan-2-ol (**15**) is the most interesting

compound, and its thermal isomerization behavior is well-documented [13][34–40]. Compound **15** is the starting material for the industrially important building block linalool (**15a**; *Scheme 3*). In contrast to the different product spectra arising form **1a** and **1b**, pyrolysis of *cis*- and *trans*-**15** predominantly yielded **15a**, contaminated with minor amounts of isolinalool (**15b**; $<5\%$). Performing this reaction in the standard manner (vacuum or carrier gas pyrolysis) would lead to extensive dehydration yielding monoterpenes ($C_{10}H_{16}$; **4** and **5**) and their pyrolysis products. Use of basic additives (*e.g.*, pyridine, NH_2, *N*,*N*-dimethylaniline) or H_2O suppresses these consecutive reactions very effectively. Reactors made of stainless steel instead of quartz glass also decreased the amount of dehydrated products [34][35][38–40]. Heating **15** under vacuum (1–100 mbar) at high temperatures ($>600°$) and low contact times in a flow-type apparatus yielded up to 90% of **15a** without undesirable formation of side or consecutive products [35].

Scheme 3

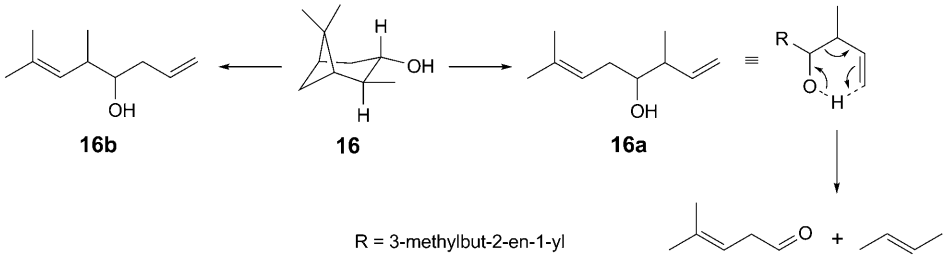


The differences between the two diastereoisomers of **15** concerning the **15a**/**15b** ratio are negligible, whereas the reactivity difference of the diastereoisomers is crucial. Kinetic analysis of the reactions by *Semikolenov et al.* leads to the E_a values of 190 and 215 kJ mol^{-1} for the disappearance of *cis*-**15** and *trans*-**15**, respectively [38]. According to the enantiospecific formation of optically pure **11** and **12** from optically pure **1**, the configuration at C(2) remains unchanged during the pyrolysis of the enantiomers of **15** [34][35]. This effect was used to determine the absolute configuration of **15a** in 1962 by *Ohloff* and *Klein*. Their remarkable study showed that (+)-(3*S*)-**15a** was formed by pyrolysis of either (−)-(2*S*)-*cis*-**15** or (+)-(2*S*)-*trans*-**15**, whereas (−)-(3*R*)-**15a** was formed *via* rearrangement of (+)-(2*R*)-*cis*-**15** or (−)-(2*R*)-*trans*-**15** (*Scheme 3*) [34]. The publication of *Ohloff* and *Klein* is still highly impressive, since it vividly depicts the valid results, although the experimental methods available at the time were limited.

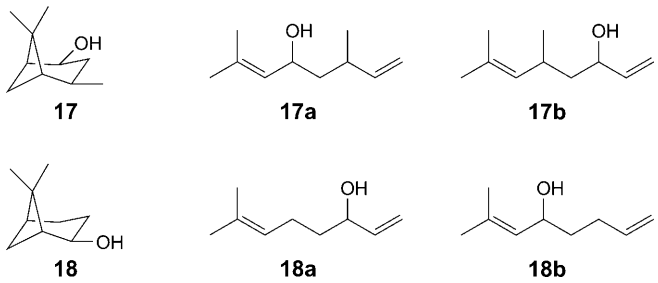
Thermal rearrangement of isopinocampheol **16** at 580° yields the acyclic alcohols **16a** and **16b** with a ratio of 29 : 1 [14–16][41]. Besides the occurrence of isomerization products of **16a**, pyrolysis of **16** at 16 mbar leads also to fragmentation of the primary

product **16a** forming (*E*)-but-2-ene and 4-methylpent-3-enal by a *retro*-ene reaction (*Scheme 4*) [14]. Additionally, the *retro*-ene ring-opening product isodihydrocarveol (*cis*-Δ^8-*p*-menthen-2β-ol) was found in amounts of 6%. These decomposition products were not observed, when the reaction was carried out using a similar contact time regime but at ambient pressure employing N_2 as carrier gas [15].

Scheme 4



Degenerative fragmentation of the cyclobutane ring in neoisoverbanol **17** forms – besides the two expected alcohols **17a** and **17b** – small amounts of 3,7-dimethyloct-6-enal (selectivity $< 5\%$) [15][42]. Experiments in a flow-type apparatus demonstrated that the ratio of the two primarily formed alcohols is temperature-independent and in favor of product **17a**.

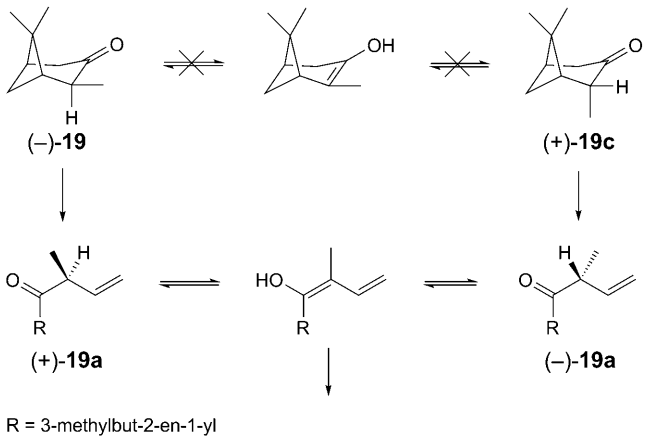


2.3. *Pyrolysis of Nopinol, Isopinocamphone, Dihydronopol, and Myrtanol.* Gas-phase pyrolysis of *cis*-nopinol (**18**) at 580° with an average contact time of 0.1 s primarily gave dienols **18a** and **18b** with a relative ratio of 3.6 [15][43]. Increase of the temperature to 630° did not influence the ratio of the primary fragmentation pathways, but the yields of consecutive reaction products of both alcohols increased.

According to the pyrolysis of **16** in either a flow-type apparatus or at reduced pressure in a batch system, the results from thermal rearrangement of the respective ketone isopinocamphone (**19**) differ also with regard to product selectivity [14][17]. Whereas *Ohloff* and co-workers reported the formation of ketone **19a** and its consecutive reaction products only (450°/16 mbar), experiments by *Hartshorn* and co-workers resulted in the formation of ketone **19b** also (620°, 0.1 s). This product is formed by fragmentation of the cyclobutane ring in **19** by scission of bonds C(5)–C(6) and C(1)–C(7) (*Table 1*). Epimerization of the C-atom C(2) in **19a** was observed, when vacuum pyrolysis experiments were performed at temperatures between 290–

320° [14]. Presumably, this reaction passes through a dienol as a reaction intermediate as shown in *Scheme 5*. This is rationalized by the fact that, besides enantiomerization, formation of further unidentified products was reported resulting from consecutive reactions of the above dienol (*cf. Sect. 6.2*). Remarkably, epimerization of the starting material **19** furnishing pinocamphone (**19c**) was not observed, and pyrolysis experiments at higher temperatures (>400°) afforded products with the same enantiomeric purity as the starting material.

Scheme 5

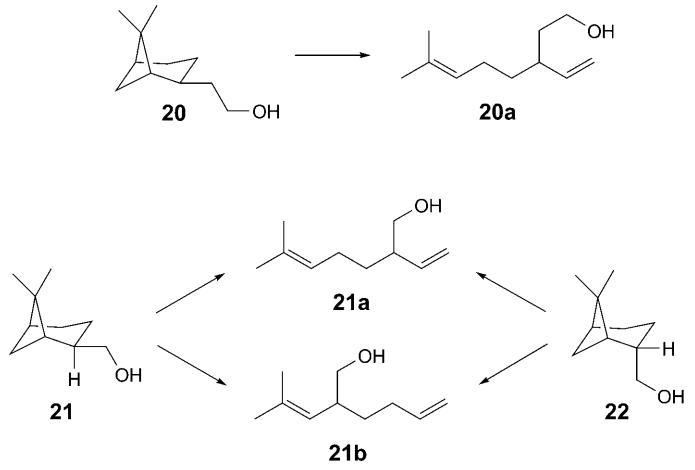


Remarkably, passage of *cis*-dihydronopol (**20**) through a pyrolysis oven heated to 570° yielded only one acyclic primary isomerization product, namely 7-methyl-3-vinyloct-6-enol (**20a**; *Scheme 6*). Compound **20a** was formed with a selectivity of 67% (conversion **20**: 73%), besides dehydration and cyclization products in the presence of a diluting agent (N_2, water vapor, NH_3) [18]. Product formation *via* fragmentation *Route B* (*cf. Table 1*) was not reported.

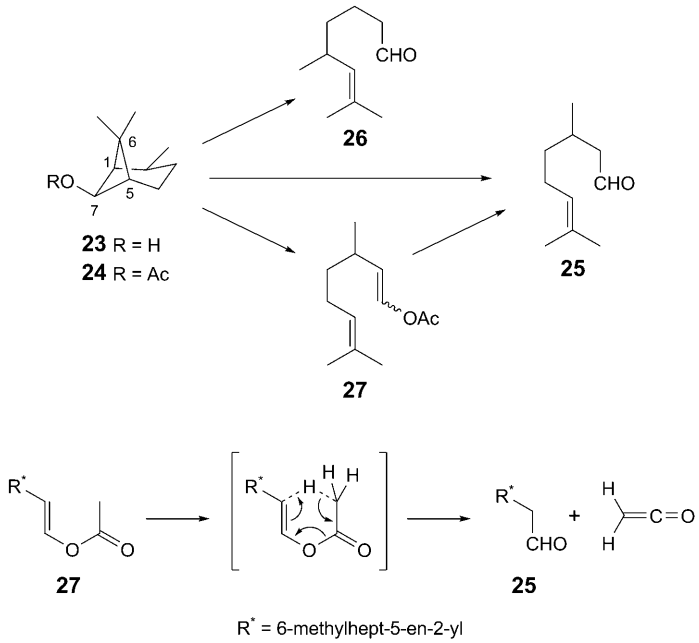
Vacuum pyrolysis of *cis*- and *trans*-myrtanol (**21** and **22**, resp.) at 27 mbar and 750° in a flow apparatus yielded products of both possible fragmentation pathways: 6-methyl-2-vinylhept-5-enol (**21a**) and 2-(isopropen-1-yl)hex-5-enol (**21b**; *Scheme 6*) [19]. Overall conversion of **22** (55%) was lower than for the *cis*-isomer **21**, an indication for the higher reactivity of **21**. The ratio of products **21a** and **21b** is influenced by the configuration of the initially used substrate, *viz.*, **21** yields preferably **21a**, whereas, in the case of **22**, both reaction *Routes* (*cf. Table 1*) occur simultaneously.

2.4. *Pyrolysis of 7-Hydroxypinane Derivatives.* The 7-hydroxypinane derivatives *endo-cis*-chrysanthanol (**23**) and *endo-cis*-chrysanthanyl acetate (**24**) thermally undergo rearrangement to aldehyde **26** and citronellal (**25**; *Scheme 7*) [20][21]. Whereas, in the case of **23**, these are the only products, pyrolysis of **24** also yields the (*E*)- and (*Z*)-enol acetates **27** in a ratio of 28:3. Thermal isomerization experiments with both (*E*)-**27** and (*Z*)-**27** revealed that no interconversion occurred and that the (*E*)-acetate yielded citronellal (**25**) more easily than the other stereoisomer. This indicates that the rearrangement of (*E*)-**27** to **25** proceeds as a *retro*-ene reaction as shown in *Scheme 7*. A

Scheme 6



Scheme 7



R* = 6-methylhept-5-en-2-yl

similar reaction with the (*Z*)-isomer is suppressed due to formation of an unfavorable strained cyclic transition state.

2.5. *Intersystem Comparison.* The data shown in *Table 1* allow the direct comparison of the influence of the substituents on the reactivity of the pinane-type compounds and on the fragmentation routes. Pyrolysis results of both stereoisomers of pinane, **1a** and

1b [10], pinan-2-ol, *cis*-**15** and *trans*-**15** [34], and myrtanol, **21** and **22** [19], demonstrate that *cis*-substituents at C(2) increase the reaction rates, since experiments at similar temperatures and under the same pyrolysis conditions with the *cis*-isomers result in higher conversions (*Table 2*). According to *Stolle et al.*, this is due to the different ground-state conformations of the cyclohexane ring in case of the *cis*- and *trans*-isomers [31]. The semi-chair conformation (*Y*-conformation) with a planar C_3 bridge for the *cis*-isomers results in a higher ring-strain energy due to unfavorable bond angels at the respective C-atoms. The bent-down C-atom C(3) in **1b** results in a chair-type conformation of the cyclohexane ring and, therefore, explains the higher stability towards thermal cleavage of the cyclobutane system.

Table 2. *Stereochemical Influence of the Substituent at C(2) of the Pinane Skeleton on the Reactivity of the Diastereoisomers*

No.	T [°]	p [mbar]	Conversion [%]	Ref.
1a	500	ambient	70	[10]
1b	500	ambient	20	[10]
cis-**15**	600	1.3	96	[34]
trans-**15**	600	1.3	88	[34]
21	750	27	100	[19]
22	750	27	55	[19]

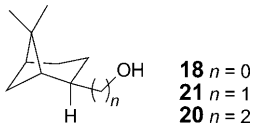
As presented in *Table 1*, the pyrolysis of the cyclobutane ring in pinane type compounds **1** and **13**–**24** leads to products primarily arising from two different fragmentation routes. Apart from **13**, these are different with respect to their configuration of C-atoms along the octa-1,6-diene skeleton, which allows estimation of the ability of different substituents to influence the ratio of the two competing fragmentation routes. *Table 1* summarizes these data by comparing the ratio for *Routes A* (bond scission between C(1)–C(6), C(5)–C(7)) and *B* (C(5)–C(6), C(1)–C(7)) in dependence of different substituents at C(2), C(3), C(4), and C(7). Obviously, the presence of a *cis*-Me group at C(2) strongly favors fragmentation *Route A* (→**1a**), whereas in case of a *trans*-Me group both pathways are equally possible (→**1b**). An additional OH group at C(2) (in **15**) or at C(3) (in **16**) does not show any effect on the ratio, as there is no difference compared to the respective hydrocarbon (*i.e.*, **1a**). The same seems to be valid for a C=O group at C(3) (in **19**). This is likely due to the fact that the substituents at this C-atom are not able to stabilize the biradical intermediate.

Comparison of the results for nopinol (**18**) allows delineation of the substituent effects of OH and H, respectively, indicating that a *cis*-OH group influences the fragmentation pattern three times more effectively than a H-atom. The 2:1 ratio of *Route A* to *B* in case of the pyrolysis of **17** is a strong indicator for the preference of the *cis*-Me group at C(2) over the *cis*-OH group at C(4). Therefore, the following order of substituents can be compiled describing the ability of a substituent at C(2) or C(4) in the pinane skeleton to influence the fragmentation pattern of the respective cyclobutane ring [17]:

$$\textit{cis}\text{-Me} \gg \textit{cis}\text{-OH} > \textit{trans}\text{-Me} = \text{H}.$$

The obviously different behavior of **23** compared to **24** is probably caused by mechanistic differences [20]. In case of **23**, the initial fragmentations are different from those assumed for the respective acetate **24**. Except for **23**, in all cases of cyclobutane fragmentation of the pinanes listed in *Table 1*, the initial step is assumed to either be a bond scission between C(1)–C(6) and C(5)–C(6) for *Routes A* and *B*, respectively. Due to the influence of the OH group at C(7) in **23** (*Scheme 7*), the initial reaction for *Route B* is rather bond breakage between C(1)–C(7) than between C(5)–C(6).

A comparison of the homologous *cis*-C(2)-alcohols nopinol (**18**), myrtanol (**21**), and dihydronopol (**20**) demonstrates the influence of alkyl chains on the reactivity and product selectivity. Generally, the reactivity, *i.e.*, the conversion, decreases with increasing chain length between C(2) and the OH group. The influence on the selectivity for the two fragmentation routes is only vital for **18**. The higher homologs showed a clear preference for the fragmentation induced by cleavage of the C(1)–C(6) bond as observed for **1a** (see *Table 1*).



18 $n = 0$
21 $n = 1$
20 $n = 2$

3. Isomerizations Related to Vinylcyclobutane. – Thermally induced reactions of vinylcyclobutanes (VCB) show a different behavior than their saturated cyclobutane analogs. Whereas cyclobutanes yield fragmentation products only, a competing reaction route exists in the case of VCB pyrolysis, namely a sigmatropic [1,3]-C shift[2]) [6b,d,e][7]. The reactions pass through biradical intermediates leading to ring expansion of VCBs yielding cyclohexenes (*Route A*; *Scheme 8*). The fragmentation pathway of 1,2-disubstituted VCBs is also different from those known from 1,2-disubstituted cyclobutanes, because normally the reaction affords only one set of fragmentation products (*Route B*). This is due to the formation of a resonance-stabilized allyl radical as a reaction intermediate in the rate-determining step (*Scheme 8*).

An additional reaction of VCBs which does generally not occur during the thermal rearrangement of the monocyclic parent system but can be important in the case of bicyclic systems (*e.g.*, **4**) is the 1,5-H shift leading to (*Z*)-hexa-1,4-diene (*Route C*; *Scheme 8*). With respect to the structures of **4** and **5**, the position of the vinylic C=C bond of the VCB system is different and is responsible for the different products arising from their pyrolysis. Therefore, the pinene-type monoterpenes are further classified with respect to the position of the vinylic C=C bond: *i*) the α-pinene class with an endocyclic C=C bond, or *ii*) the β-pinene class containing an exocyclic C=C bond.

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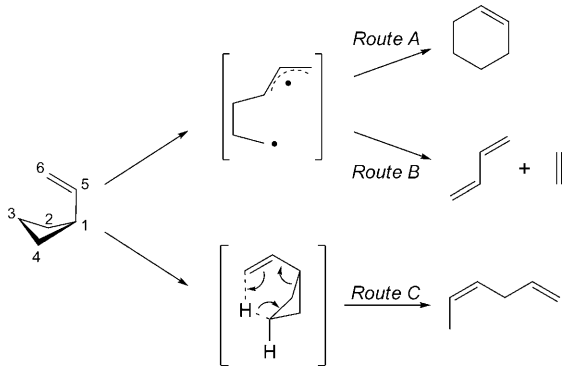
[2]) Due to the occurence of different types of radical, sigmatropic, and electrocyclic reactions some points regarding nomenclature of such reactions have to be stressed out. *i*) Sigmatropic shift reactions are assigned as follows: [*i*,*j*]-X shift (X can either be H or C). *ii*) The assignment for radical shift reactions is as follows: *i*,*j*-X shift. *iii*) Reactions classified as (*i*,*j*)-ene reactions refer to the nomenclature established for intramolecular ene cyclizations (for reviews on intramolecular ene reactions and their nomenclature, see [44]).

Scheme 8[a])



[a]) *Route A:* [1,3]-C Shift; *Route B: retro*-[2+2] cyclization – fragmentation of the cyclobutane ring; *Route C:* 1,5-H shift.

3.1. *α-Pinene-Type Compounds. Table 3* lists all compounds, *i.e.*, **28**–**36**, that have been subjected to pyrolysis studies, which showed similar thermal isomerization behavior as *α*-pinene (**4**). According to *Scheme 8*, these compounds react in VCB-type manner, leading to products arising from three different reaction pathways: *i*) [1,3]-C shift (*Route A*), *ii*) fragmentation of the cyclobutane ring (*Route B*), and *iii*) 1,5-H shift reactions (*Route C*). The primary acyclic pyrolysis products often undergo very fast isomerizations to the fully conjugated isomers by way of sigmatropic [1,5]-H shift reactions (*Route D*).

3.1.1. *Pyrolysis of Norpinene.* Norpinene (= bicyclo[3.1.1]hept-2-ene; **36**) is the simplest monoterpenoid containing the pinene skeleton that showed a similar thermal isomerization behavior as **4**. *Dietrich* and *Musso* suggested that **36a** has to undergo a [1,3]-C shift leading to racemized **36a** (*Scheme 9*) [74]. To investigate this reaction, they synthesized 3-[^{2}H]norpinene (**36b**) and investigated its thermal behavior in quartz ampoules by ^{1}H-NMR spectroscopy. Beside decomposition, they observed rearrangement of **36b** to 1-[^{2}H]norpinene (**37**) with an E_a value of 150.3 kJ mol^{-1}. The similarity of the E_a value for the isomerization with bicyclo[3.1.1]hept-2-ene (**36a**) to that of the bicyclo[2.1.1]hex-2-ene supports a [1,3]-C shift mechanism. Kinetic analysis of the decomposition of **36a** leading to toluene as the main product gave an E_a value of 156.7 kJ mol^{-1}.

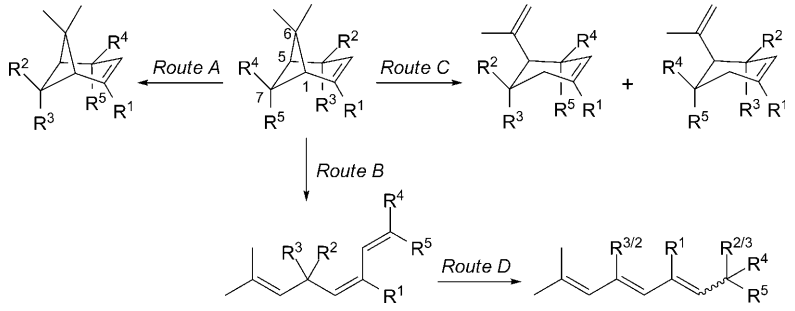
Scheme 9

36a R = H
36b R = D

37 R = D

3.1.2. *Pyrolysis of α-Pinene.* With respect to thermal isomerization of monoterpenes and monoterpenoids, the pyrolysis of **4** is one of the most thoroughly investigated reactions. Starting with the studies of *Smith*, and *Conant* and*Carlson* on racemization of

Table 3. *Compounds with the Pinane Skeleton That Showed Behavior Similar to α-Pinene* (**4**) *Concerning Their Thermal Isomerization* (*Route A:* sigmatropic [1,3]-C shift; *Route B: retro*-[2+2] cyclization; *Route C:* 1,5-H shift; *Route D:* sigmatropic [1,5]-H shift)



No.	Name	R^1	R^2	R^3	R^4	R^5	*A*[a])	*B*[a])	*C*[a])	Ref.
4	α-Pinene	Me	H	H	H	H	obs	obs	obs	[45–65]
28	Myrtenal	CHO	H	H	H	H	no	obs	obs	[66]
29a	Myrtenol	$HOCH_2$	H	H	H	H	obs	obs	obs	[66]
29b	Myrtenyl acetate	$AcOCH_2$	H	H	H	H	no	obs	obs	[66]
30	2-Acetoxy-10-norpin-2-ene	AcO	H	H	H	H	no	obs	obs	[67]
31a	Nopol	HOC_2H_4	H	H	H	H	obs	obs	obs	[68–70]
31b	Nopyl acetate	$AcOC_2H_4$	H	H	H	H	no	obs	obs	[70]
32a	*cis*-Verbenol	Me	OH	H	H	H	no[b])	obs	obs	[71]
32b	*trans*-Verbenol	Me	H	OH	H	H	obs	no	no	[71][72]
33	Verbenone	Me	O		H	H	no	obs	obs	[71][73]
34a	*endo*-Chrysanthenol	Me	H	H	OH	H	no	obs	obs	[20]
34b	*exo*-Chrysanthenol	Me	H	H	H	OH	no	no	no	[20]
35	*exo*-7-Methyl-*endo*-chrysanthenol	Me	H	H	OH	Me	no	obs	obs	[20]
36a[c])	Norpinene	H	H	H	H	H	obs	no	no	[74]
36b[c])	3-[^{2}H]Norpinene	D	H	H	H	H	obs	no	no	[74]

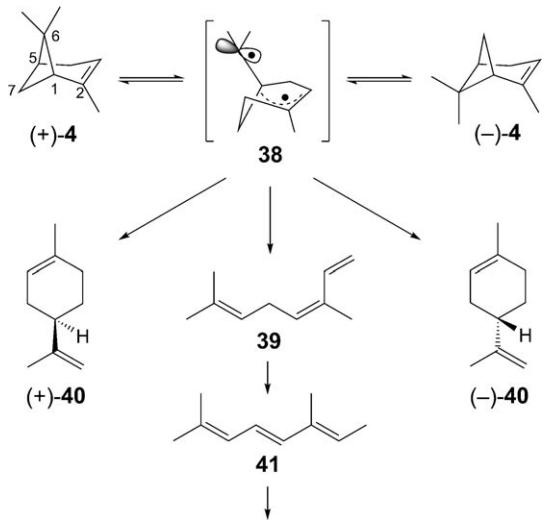
[a]) Occurrence of reaction *Routes A*, *B* or *C*; obs: observed, no: not observed. [b]) Only the isopropyl ether gave small amounts of *endo*-chrysanthenyl isopropyl ether. [c]) In norpinene, the Me groups at C(6) are missing.

4 [45], followed by the studies of the groups of *Goldblatt* and *Hawkins* in the 1940s and 1950s, respectively [46–53], until the extensive kinetic studies of *Riistima* and *Harva*, and *Gajewski et al.* [54][55], these mechanistic studies are still up to date [29][56]. This may be due to the fact that this reaction network remains challenging because of the co-occurrence of the three major reactions of the VCB system in **4** shown in *Table 3* leading to rate equations with feedback routes.

3.1.2.1. *Pyrolysis of α-Pinene and Its Mechanism.* In *Scheme 10*, the products arising from the pyrolysis of **4** are shown. Racemization of **4** occurred in both gaseous and liquid phase at ambient and reduced pressure [45][55]. Remarkably, performing the reaction in a flow apparatus using supercritical EtOH as solvent, no racemization was observed [57][58]. The interconversion of the two enantiomers of **4** *via* biradical **38** is an example of a [1,3]-C shift in a bicyclic system. According to *Scheme 8*, it leads to the

ring-expanded product of the VCB parent system [6b,e][7]. However, due to the bicyclic nature of **4**, this 'ring expansion' of the VCB subsystem is recognizable only on closer inspection.

Scheme 10



The first product rather than racemized substrate observed during the pyrolysis of **4** was alloocimene (**41**) [59]. Further analysis confirmed the formation of **41** and, besides small amounts of (3*Z*)-ocimene (**39**), the pyrolysis additionally furnished racemic limonene (**40**; dipentene) in remarkably high amounts [11][29][46–64]. The formation of dipentene is a consequence of the biradical **38** the reaction passes through. Due to resonance stabilization of one radical position a mirror plane is generated (C_s symmetry) leading to racemic (±)-**40** [55][65]. Hence, pyrolysis in supercritical EtOH yielded racemic **40** without racemization of the starting material [57][58], a prior racemization of **4** does not seem to be the reason for the dipentene formation. Rearrangement to **40** is assumed to proceed through a 1,5-H shift from intermediate **38**, whereas hydrocarbon **39** is the *retro*-[2 + 2] cyclization product of the cyclobutane ring in **4**. Remarkably, the 1,5-H shift and *retro*-[2 + 2] cyclization routes are equivalent in the case of **4**, whereas pyrolysis studies of 2,2-dimethyl-VCB (model compound for **4**) and of other VCBs favor the latter [75]. Therefore, the ratio of **40**/**39** is *ca.* 1:1, independent of reaction temperature, residence time, or *modus operandi*. However, recent studies reveal that the use of H_2O/EtOH mixtures as fluid under supercritical conditions (400°/230 bar) favors dipentene formation over *retro*-[2 + 2] cyclization yielding **39** and **41** [76]. Due to the stronger acidity of supercritical H_2O, an increasing amount of H_2O gave rise to **40** by way of a competitive ionic rearrangement mechanism.

Gajewski et al. used D-labeled **4** for their thorough studies of the stereomutations occurring when **4** is pyrolyzed [55]. Pyrolysis of *syn*-6-CD_3-(1*S*,5*S*)-α-pinene at 275° for 40 min ($< 10^{-3}$ mbar, batch system) yielded two enantiomeric sets of labeled limonene

products **40a** and **40b**. In the first case, one D-atom was transferred to the cyclohexene ring *via* 1,5-H shift, and in the other set no D scrambling occurred (*Table 4*). The relative product ratio of 2 : 1 in favor of the first route indicates that the initial biradical undergoes inversion to a significant extent.

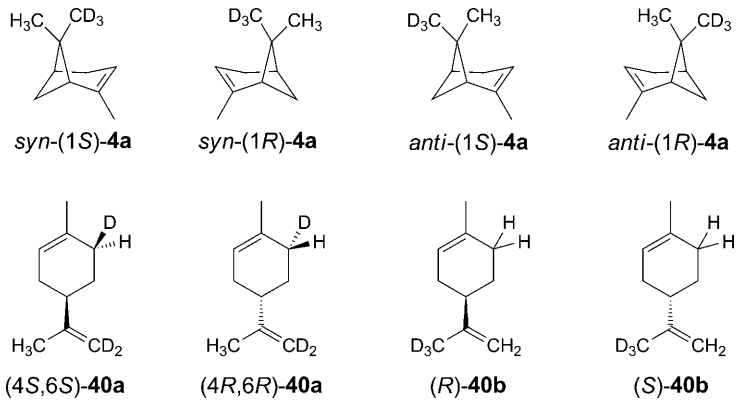
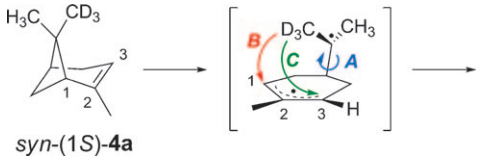


Table 4. *Reaction Pathways for* syn-*(1S)*-**4a** *Including 1,5-H Shifts* (*Route A:* inversion *via* bond rotation; *Routes B* and *C:* 1,5-H shift)

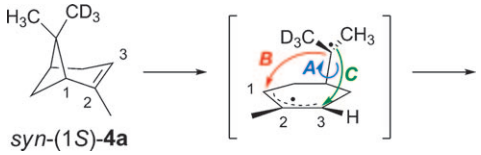


No.	*A*	*B*	*C*
(4*S*,1*S*)-**40a**	–	×	–
(4*R*,1*R*)-**40a**	–	–	×
(*S*)-**40b**	×	–	×
(*R*)-**40b**	×	×	–

Analysis of the reaction products of recovered D-labeled pinene *syn*-(1*S*)-**4a** and separation of the enantiomers by chiral GC revealed for the (1*S*,5*S*)-enantiomers that the *syn*/*anti* ratio of the C(6)–CD_3 group was 95 : 5. The small loss of optical activity of the starting material might be due to the fact that most of the recovered starting material never entered the caldera and, therefore, remained unchanged. In the (*R*)-enantiomers, the *syn*/*anti* ratio was 55 : 45, indicating a slight preference for a sigmatropic [1,3]-C shift accompanied by inversion (*Table 5*).

3.1.2.2. *Kinetic Studies on α-Pinene Pyrolysis.* Kinetic analyses of the thermal reactions of **4** were performed in the liquid and in the gas phase, as well as in supercritical EtOH [29][47][54–56][64]. *Arrhenius* activation parameters for the respective reactions are summarized in *Table 6*. Frequency factors log *A* range from 12.6 to 15.8 (*A* in s^{-1}), indicating that the reaction passes through a transition state

Table 5. *Reaction Pathways for* syn-*(1S)*-**4a** *Including [1,3]-C Shifts* (*Route A:* inversion *via* bond rotation; *Routes B* and *C:* [1,3]-C shift)



No.	*A*	*B*	*C*	Product type[a])
syn-(1*S*)-**4a**	–	×	–	
syn-(1*R*)-**4a**	–	–	×	*si*
anti-(1*S*)-**4a**	×	×	–	*rot*
anti-(1*R*)-**4a**	×	–	×	*sr*

[a]) Assignments as follows: *si*, *suprafacial,inversion*; *rot*, bond rotated; *sr*, *suprafacial,retention*.

typical for radical intermediates with similar degree of freedom as the starting material. Therefore, the biradical mechanism seems to be fairly well established. Except for the results of *Riistima* and *Harva*, E_a and log A for the 1,5-H shift leading to dipentene ($k_{1,5}$) have the smallest values. Similarities in activation parameters for fragmentation to ocimene (k_f) and [1,3]-C shift ($k_{1,3}$) with those for the rate constants describing the disappearance of **4** (k_d) suggest that the overall reactions pass through similar transition states and/or intermediates. E_a Values resulting from experiments in supercritical EtOH are comparatively low indicating that either the rate constants are pressure-dependent or the molecularity of the reaction did change [56].

Table 6. *Kinetic Data for Thermal Isomerization of α-Pinene* (**4**)

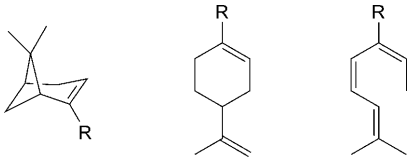
Ref.	Reaction condition	k_i[a])	E_a [kJ mol^{-1}]	log A (A in s^{-1})
[47]	Liquid phase	k_f	179	15.6
		$k_{1,5}$	155	13.3
		$k_{1,3}$	185	15.8
[54]	Liquid phase	k_d	179	14.4
		k_f	171	13.3
		$k_{1,5}$	186	14.7
[55]	Gas phase, vacuum	k_d	179	14.2
		k_f	181	14.1
		$k_{1,5}$	175	13.6
		$k_{1,3}$	188	14.4
[29][64]	Gas phase, N_2	k_d	170	13.7
		k_f	178	14.1
		$k_{1,5}$	161	12.6
[56]	Supercritical EtOH	k_f	137	
		$k_{1,5}$	118	

[a]) k_d, Disappearance of α-pinene (**4**); k_f, *retro*-[2+2] cyclization to ocimene (**39**); $k_{1,5}$, 1,5-H shift to dipentene (**40**); $k_{1,3}$, [1,3]-C shift to racemized α-pinene.

Detailed kinetic studies of *Gajewski et al.* at 257° of the relative rate constants for racemization ($k_{1,3}$), dipentene formation ($k_{1,5}$), and ocimene formation (k_f) showed them to be 1, 2.5, and 3.3, respectively [55]. Pyrolysis of *syn*-6-CD_3-(1*S*,5*S*)-α-pinene at 256.7° for 40 min afforded dipentene, whereas the product resulting from D migration (**40a**) is favored by a 2:1 ratio over the H-migrating product (**40b**; k_H/k_D: 1.49). Isotope effects on loss of starting material and alloocimene formation were 1.16 and 0.89, respectively. Differences in the required ratio *si*/*sr* to rotation products for calculations from experiment (4.6:3.7:1) and theory (4.1:1:1) requires modification of the initially proposed mechanism. The authors concluded that the existence of an equilibrium between a C_s-symmetric diradical (ignoring D-labeling) and the *syn*- and *anti*-forms can rationalize the experimental results.

3.1.3. *Pyrolysis of* C(2)-*Substituted* α-*Pinenes: Myrtenal, Myrtenol, 2-Acetoxy-10-norpin-2-ene, and Nopol*. Vacuum pyrolysis of myrtenal (**28**) at 450°/100 mbar in the presence of Cu–Zn alloy as a catalyst resulted in the formation of perillaldehyde (**42**) exclusively (*Table 7*) [77]. Neither the formation of the [1,3]-C shift product nor the corresponding acyclic product from cycloreversion were reported. Reaction parameters such as temperature, pressure, flow rate, and catalyst amount did not affect the selectivity but only the conversion of **28**. However, in contrast to these results *Klein* reported that, on heating **28** in the gas phase, in the liquid phase, or refluxing it, yielded – besides **42** – also the respective fragmentation product **43** and noticeable amounts of polymeric material [66].

Table 7. *Monocyclic and Open-Chain Isomerization Products* **B** *and* **C**, *Respectively, of Myrtenyl and Nopyl Derivatives* **A**



A **B** **C**

Name	R	**A**	**B**	**C**
Myrtenal	CHO	**28**	**42**	**43**
Myrtenol	$HOCH_2$	**29a**	**44a**	**45a**
Myrtenyl acetate	$AcOCH_2$	**29b**	**44b**	**45b**
2-Acetoxy-10-norpin-2-ene	AcO	**30**	**46**	**47**
Nopol	HOC_2H_4	**31a**	**48a**	**49a**
Nopyl acetate	$AcOC_2H_4$	**31b**	**48b**	**48b**

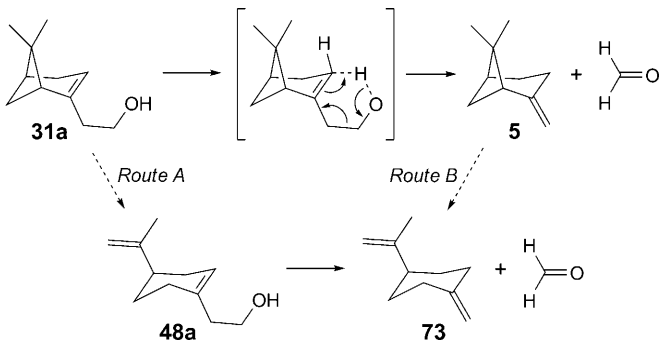
Thermal rearrangement of the related alcohol myrtenol (**29a**) afforded *ca.* 40% of perill alcohol (**44a**), 17% 2-ethylidene-6-methylhepta-3,5-dien-1-ol (**45a**; *Table 7*), and minor amounts of consecutive reaction products of **45a** [66]. The formation of the plausible intermediate 6-methyl-2-vinylhepta-2,5-dienol was not observed. Comparison of the optical rotations for initial **29a** ($\alpha_D^{25} = -49°$) and **44a** isolated by distillation ($-0.84°$) from vapor-phase pyrolysis at 400° indicated a dramatic loss in optical purity. Therefore, the assumption is justified that a [1,3]-C shift occurred, similar to the

reaction leading to racemized **4** in the parent system. Heating **29a** in sealed quartz ampoules or refluxing it in neat form yielded similar products accompanied by higher amounts of polymeric material. Thermal treatment of myrtenyl acetate (**29b**) in the vapor phase under similar conditions described above for **29a** led to similar products, but the amount of the desired *p*-menthane-type target product **44b** was increased by a factor of 1.25 (50%) compared to the yield of **44a** [66].

Passing 2-acetoxy-10-norpin-2-ene (**30**) through a flow reactor at 550° yielded the enol acetates **46** and **47**, besides consecutive reaction products from **47**, such as *o*-ethyltoluene (*Table 7*) [67]. Experiments at lower temperatures lead to similar products, whereby the ratio of 1,5-H shift to *retro*-[2 + 2] cyclization pathways are temperature-independent and *ca.* 40 : 60 favoring the latter. This agrees with the results of the pyrolysis of **4**.

Rearrangement products from pyrolysis of nopol (**31a**) in gase and liquid phase are identical, since the mixtures mainly consist of homoperill alcohol (**48a**) and homoallo-ocimenol (**49a**; *Table 7*) [68–70]. That a sigmatropic [1,3]-C shift in **31a** occurred was shown by partial racemization of the recovered starting material. Although **5** did not racemize on heating, pyrolysis of **31a** yielded partly racemic **5** in low amounts, showing that it originates from elimination of formaldehyde in the (partly) racemized starting material (*Scheme 11*). Hence, isomerization of nopyl acetate (**31b**) at 240° for 5.5 h yielded the enol acetates **48b** and **49b**, but no **5**, the H-atom of the OH group of nopol is crucial for the elimination of formaldehyde by way of a *retro*-ene reaction [70]. The reaction described in *Scheme 11* is, therefore, the reverse of the formation of **31a** by a *Prins* condensation of formaldehyde with **5** (carbonyl-ene reaction). This type of reaction is not restricted to the substrate **31a** only, since similar products originating from elimination of formaldehyde in **48a** are also reported (*Scheme 11*) [78].

Scheme 11[a])

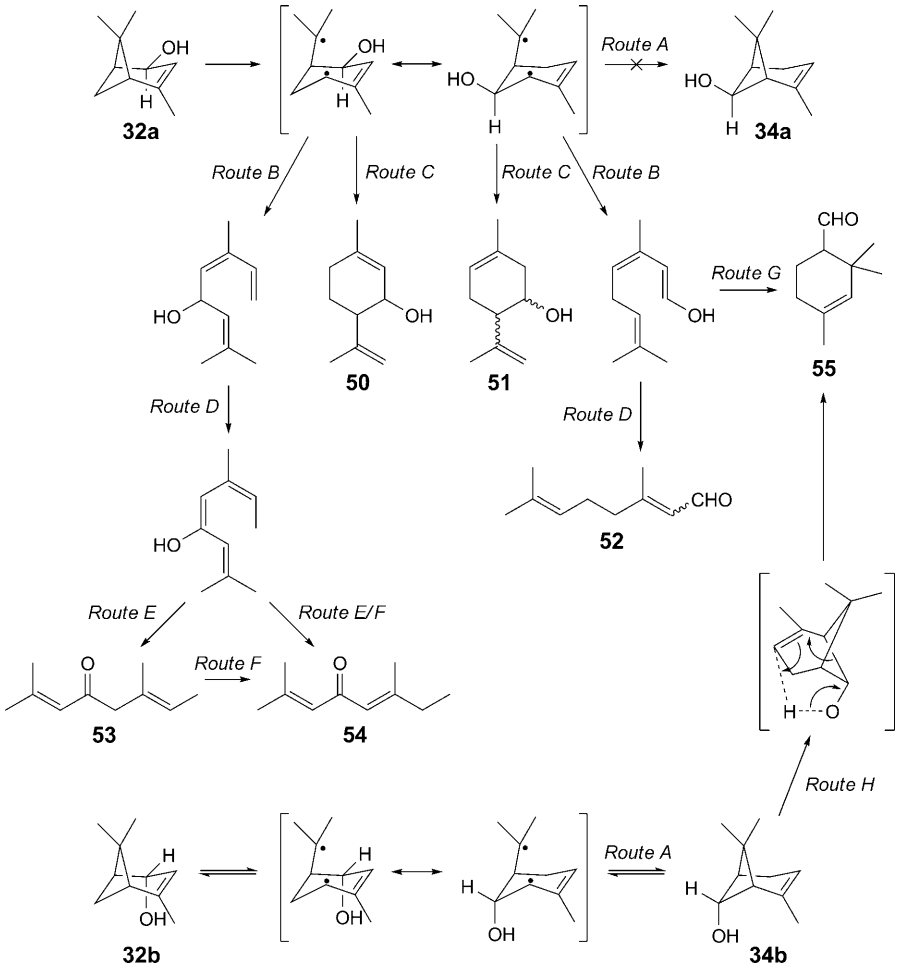


[a]) *Route A:* pyrolysis of **31a**; *Route B:* pyrolysis of **5** (*cf. Sect. 3.2.1*).

3.1.4. *Pyrolysis of* C(4)-*Substituted α-Pinenes: Verbenol, Verbenone, and Derivatives. Bain et al.* showed that the product mixtures resulting from pyrolysis of *cis*-verbenol (**32a**) are rather complex, consisting of a multitude of products (*Scheme 12*). Apart from the [1,3]-C shift product *endo*-chrysanthenol (**34a**), products resulting from cycloreversion and 1,5-H shifts are formed: isopiperitenol (**50**), *cis*- and *trans*-limonen-5-ol (**51**), citral (**52**), α-pseudotagotene (**53**), β-pseudotagotene (**54**), and ψ-cyclocitral

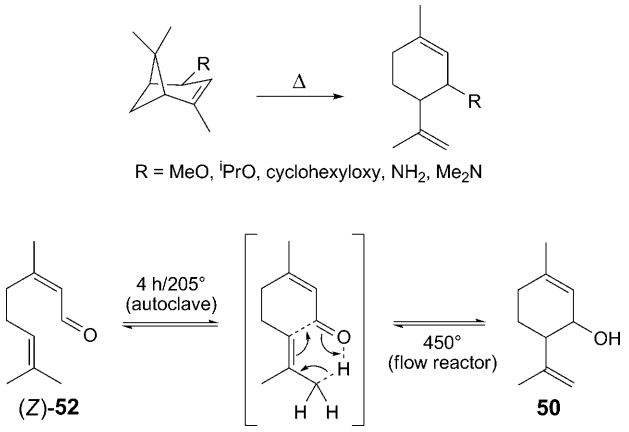
(**55**). Contrarily to gas-phase experiments, rearrangement in the liquid phase (steel autoclave, 250°, 4 h) afforded also appreciable amounts of dehydration and polymerization products. Although the yields of undesirable side products were reduced by passing **32a** through a vertical steel tube (400°, 2 ml min^{-1}), the target products **50** and **52** were still not pure [5e][71]. To increase the yield of the desired alcohol **50**, thermal isomerization of verbenyl ethers and amines proved to be quite a good option (*Scheme 13*). The resulting respective derivatives of **50** can easily be converted into the alcohol by hydrolysis (amines) or hydrogenolysis (ethers).

Scheme 12[a])



[a]) *Route A:* [1,3]-C Shift; *Route B: retro*-[2+2] cyclization – fragmentation of the cyclobutane ring; *Route C:* 1,5-H shift; *Route D:* [1,5]-H shift; *Route E:* keto–enol tautomerization; *Route F:* double-bond isomerization; *Route G:* ene reaction. *Route H: retro*-ene reaction.

Scheme 13



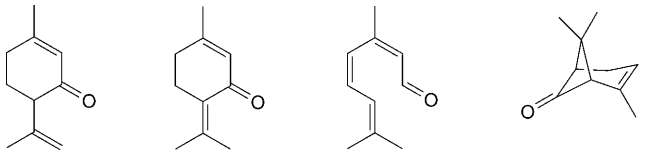
Interestingly, and in contrast to the studies of *Bain et al.*, *Ohloff* reported in 1970 that *trans*-verbenol (**32b**) on heating at 400° is in homolytic equilibrium with *exo*-chrysanthenol (**34b**; *Scheme 12*). Passing through a cyclic transition state, **34b** undergoes a rearrangement *via retro*-ene reaction to the cyclic ketone **55** [72]. This behavior is remarkable, because it revealed an extremely different behavior for the two diastereoisomers of **32**, being in clear contrast to the examples discussed before (**1**, **15**, **21**, and **22**; *cf. Sect. 2.5*), where only different reactivities and ratios of primary pyrolysis products are observed. However, this behavior is reasonable from a stereochemical point of view. Due to an unfavorable orientation of the *endo*-OH group in **34a**, a reaction passing through a transition state as described for the reaction of **34b** to **55** seems not possible. Additionally, the *cis*-orientation in **32a** disfavors a sigmatropic [1,3]-C shift; rather, fragmentation or H-shift routes are more likely. This behavior is in accordance with studies of *Hartshorn et al.* on heating **34a**, since neither the formation of **32a** nor that of **55** has been reported (*cf. Sect. 3.1.5*).

Another interesting aspect within this thermal reaction network is related to the rearrangement of (*E*)- and (*Z*)-citral (**52**) on refluxing in vacuum under Ar [79]. Experiments revealed that the (*Z*)-isomer undergoes rearrangement forming various acyclic isomers, differing in the location of the C(2) double bond, by way of sigmatropic [1,5]-H shifts. Beside these C=C bond isomerizations, products of intramolecular carbonyl-ene reactions (*i.e.*, **50** and **51**) were reported also. For instance, the ene cyclization of (*Z*)-**52** furnishes isopiperitenol (**50**), whereas pyrolysis of **50** at 450° proceeds in the opposite direction, furnishing (*Z*)-**52** (*Scheme 13*) [79][80]. With respect to these results, the general reaction mechanism presented in *Scheme 12* is more complex, since interconversion of products resulting from different primary *Routes A* and *B* do occur.

Vacuum pyrolysis studies with **32a** (10–40 mbar, 450–600°) by *Semikolenov* and co-workers confirm the findings of *Bain et al.*, but the ratio of **50** and **52** to the other undesirable products is strongly increased [71][81]. The independence of the ratio of selectivities for **50** and **52** from contact time, temperature, and flow rate indicates that

both result from competitive parallel reaction pathways of **32a**. Kinetic analysis of the reaction in both gas and liquid phase gave E_a values of 96.7 and 81.4 kJ mol^{-1}, respectively. These values are more consistent with a concerted mechanism rather than with a stepwise biradical process, since the activation energy is clearly too low for bond cleavage of a C–C bond, but is typical for concerted reactions, wherein bond cleavage is accompanied by concomitant bond formation. Probably, performing the pyrolysis of **32a** in octane changes the mechanism, and the reaction is not unimolecular anymore.

Verbenone (**33**) is the keto derivative of alcohol **32** and, therefore, in general its pyrolysis products are similar to those obtained from the corresponding alcohol isomerizations. Gas- (400°) and liquid-phase (230°) experiments afforded a mixture consisting of isopiperitenone (**56**) and piperitenone (**57**) [71]. By treatment of **33** at elevated temperatures (350°) in glass ampoules for 10 min, the amount of monocyclic ketones **56** and **57** decreased in favor of formation of thymol, *m*-cresol, and other degradation products [73]. The consecutive reaction product **58** from the *retro*-[2 + 2] cyclization reaction route was found in low amounts only, whereas the photoisomerization product chrysanthenone (**59**), resulting from a [1,3]-C shift, was absent altogether. Remarkably, pyrolysis obviously passed through the biradical resulting from cleavage of the C(1)–C(6) bond exclusively, rather than that occurring through C(5)–C(6) bond scission (see *Table 3*). Although both biradicals are resonance-stabilized, but of different stability, the route including the exocyclic hetero-VCB system seems to be suppressed completely.

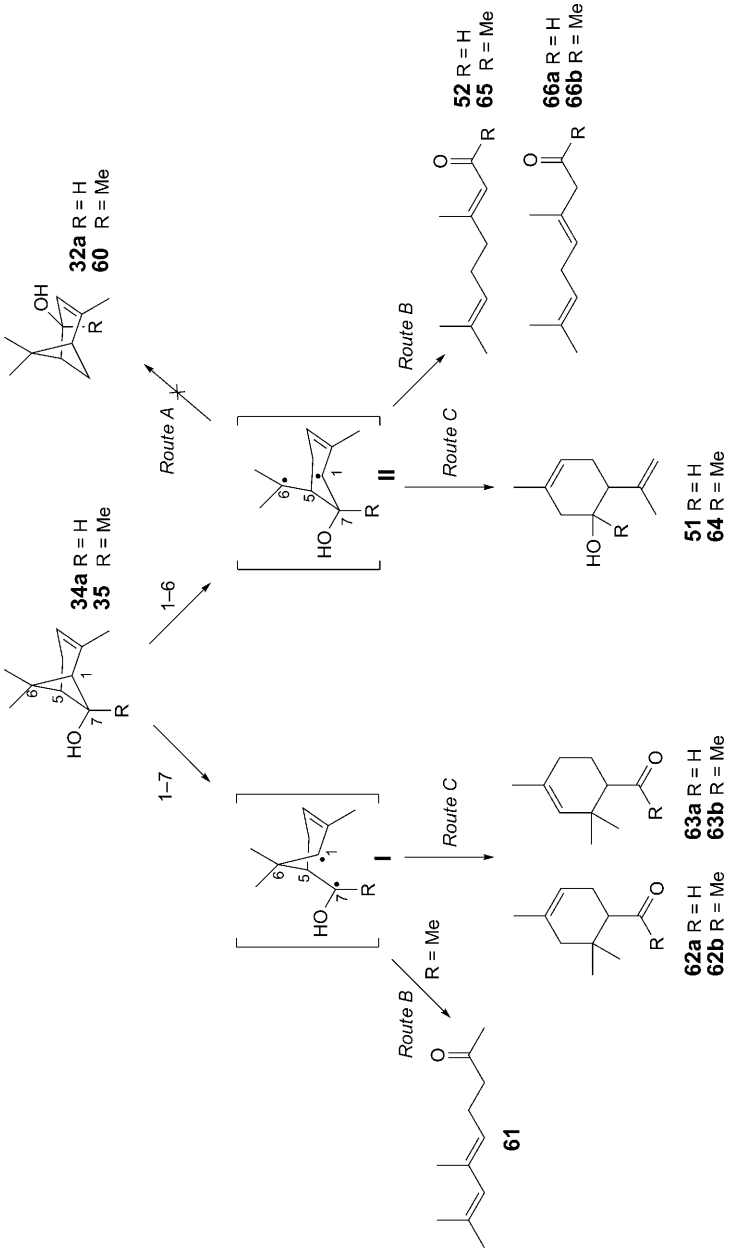


56 **57** **58** **59**

3.1.5. *Pyrolysis of* C(7)-*Substituted* α-*Pinenes:* endo-*Chrysanthenol and* exo-7-*Methylchrysanthenol.* Passing *endo*-chrysanthenol (**34a**) through a stainless steel tube heated up to 430° yielded a crude product mixture consisting of 25% low-boiling products (hydrocarbons), 18% recovered **34a**, and isomerization products aldehyde **62a** (16%), aldehyde **63a** (8%), **51** (9%), **52** (6%), and acyclic aldehyde **66a** (13%; *Scheme 14*) [20]. Studying the influence of other substituents at C(7) of the α-pinene skeleton, *Hartshorn* and co-workers conducted thermolysis experiments of the *exo*-7-methyl derivative (**35**) under similar conditions as described for **34a**. The resulting product distribution was rather complex, and six isomers were identified: acyclic methyl ketones **61**, **65**, and **66b**, as well as the menthane-type products **62b**, **63b**, and **64** (*Scheme 14*). In both cases the formation of the [1,3]-C shift products **32a** and *trans*-4-methyl-*cis*-verbenol (**60**) were not reported, suggesting that this route is suppressed for the *endo*-chrysanthenols in contrast to the *exo*-isomer **34b** (*Scheme 12*).

Analysis of the formation pathways of the products arising from **34a** and **35** leads to the conclusion that two different intermediate biradicals are involved. On the one hand, C(1)–C(7) bond scission generates intermediate **I**, whereas radical **II** results from C(1)–C(6) bond cleavage. The relative ratio of **I** to **II** is 46 : 54 and 56 : 44 for **34a** and **35**, respectively. The small difference is due to the stabilizing effect of the *exo*-Me

Scheme 14[a])

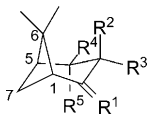


[a]) *Route A*: [1,3]-C Shift; *Route B*: *retro*-[2 + 2] cyclization – fragmentation of the cyclobutane ring; *Route C*: 1,5-H shift.

group in **35**, allowing for more pronounced hyperconjugation than in the case of a H-atom present in **I** resulting from **34a**. Although the monocyclic aldehydes **62a** and **63a** are formed from **34a**, the postulation of biradical **I** as an intermediate is questionable for two reasons: *i*) no acyclic isomer is formed by this route, and *ii*) the relative ratio of **62a** to **63a** was 3 : 1, thus indicating that the mesomeric allylic radical contributes only to a small extent. Since the relative product ratio arising from biradical **II** is independent from substituent R (*Scheme 14*), it can be rationalized that the H-atom at C(7) disfavors formation of intermediate **I**. Thus, the formation of a ring-opened product similar to **61** is suppressed.

3.2. *β-Pinene-Type Compounds. Table 8* lists the compounds with a pinene skeleton, *i.e.*, **67**–**71**, that showed similar thermal behavior like the monoterpene *β*-pinene (**5**). All have in common that the C=C bond of the VCB system is not part of the bicyclic system. Comparison with the parent system indicates an *anti*-orientation of the vinyl group [7]. Therefore, the reaction pathways are limited compared to those principally possible in the case of *syn*-configurated *α*-pinene-type compounds (*cf. Table 3*). Besides stereochemical issues, the sigmatropic rearrangement by a [1,3]-C shift would yield *anti-Bredt* hydrocarbons which are thermally unstable and only isolable in a few cases under special precautions (crowded substituents, low ring strain)[3]). Main reaction pathways are the stepwise fragmentation of the cyclobutane ring leading to open-chain products and 1,*i*-H shift reactions yielding *p*-menthane-type molecules.

Table 8. *Monoterpenes with Thermal Isomerization Behavior Related to β-Pinene* (**5**)

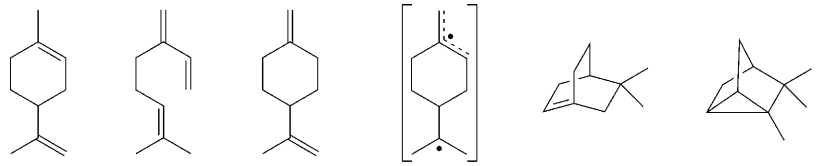


No.	Name	R^1	R^2	R^3	R^4	R^5
5	*β*-Pinene	CH_2	H	H	H	H
67	Nopinone	O	H	H	H	H
68	*cis*-Pinocarveol	CH_2	OH	H	H	H
69a	*trans*-Pinocarveol	CH_2	H	OH	H	H
69b	*trans*-Pinocarvyl acetate	CH_2	H	AcO	H	H
70	*cis*-$\Delta^{2(10)}$-Pinen-4-ol	CH_2	H	H	OH	H
71	*trans*-$\Delta^{2(10)}$-Pinen-4-ol	CH_2	H	H	H	OH

3.2.1. *Pyrolysis of β-Pinene.* Among the compounds with a pinane skeleton the thermal isomerization behavior of which has been studied, the pyrolysis of *β*-pinene (**5**) is – next to *α*-pinene (**4**) – the second most investigated thermal reaction. Beginning with the studies of *Goldblatt* and *Palkin* in the early 1940s and the proposal of biradicals as reactive intermediates by *Burwell* in 1951 [46][65][83], the reaction is still of actual interest [9][11][50][51][84–86] as the recently published studies of *Anikeev* and co-workers in supercritical phase [57][58] and the kinetic analysis by *Stolle et al.* using carrier gas-assisted pyrolysis demonstrate [29][87–90]. The main primary reaction products of the thermal rearrangement of **5** are limonene (**40**), myrcene (**72**), and *ψ*-

[3]) For reviews on *anti-Bredt* hydrocarbons, pyramidalized alkenes, or the *Bredt* rule, see [82].

limonene (**73**). Almost all studies reported that **72** is the main product of the reaction, formed with a selectivity of *ca.* 85%. Under certain conditions (capillary reactor, T: 750°), its overall yield could be increased up to 85% [51]. The ratio of the monocyclic products **40** and **73** is *ca.* 2:1 due to the higher thermodynamical stability of the triply substituted endocyclic C=C bond in the former. Whereas **40** and **73** result from 1,*j*-H shift reactions of the biradical intermediate **74**, the formation of **72** is similar to the ring opening of the cyclobutane ring in **4** leading to **39** (see *Scheme 10*) [29][58][65][87–90]. In contrast to the biradical formed in the case of **4**, **74** is still chiral, and, therefore, the initial optical purity is maintained. Separation of the enantiomers of **40** on a β-cyclodextrin GC column revealed similar enantiomer ratios as found for recovered **5** [57][90]. A [1,3]-C shift would form the *anti-Bredt* hydrocarbon **75**, and, since such compounds are thermally instable, they either form consecutive products or the activation energies needed for their formation are extremely high. Another argument against the formation of **75** from biradical **74** is the long interatomic distance between the isopropenyl radical and the respective mesomeric form of the allyl radical. However, gas-phase studies of *Kolicheski et al.* suggest the presence of tricyclene (**76**) in the product mixtures, which might be produced from **75** [88].



40 **72** **73** **74** **75** **76**

Since **72** is an important substrate for the synthesis of various fine chemicals (flavors, fragrances), its production by thermal cleavage of the cyclobutane ring in **5** is not only important from an academic point of view but also for industrial chemists [3a,b,g,h]. Many protocols have been developed to increase the yields: passage through a capillary reactor [51], carrier-gas-assisted pyrolysis [29][82][87][90], flash vacuum pyrolysis at 0.07 mbar and 900° [11], or thermal cleavage carried out in a flow system using supercritical alcohols as a fluid [57][58]. The results all have in common that performing the reaction at high temperatures (> 600°) and low contact times (< 0.1 s) is advantageous for the yield of **72**. A reaction model based on the combination of kinetic parameters (E_a, log A) with reactor parameters (volume, flow rate, T), published recently, indicates that temperatures higher than 800° and residence times lower than 10^{-5} s would lead to product mixtures consisting of more than 90% of **72**. Unfortunately, these reaction conditions are not readily achieved, since small changes in residence time or temperature would dramatically decrease the yield [90].

Kinetic studies with **5** under different reaction environments lead to the activation parameters listed in *Table 9* [29][50][58][84][90]. Activation energies E_a describing the disappearance of **5** (k_d) and the formation of **72** (k_f) are quite similar regardless of the reactor system used for their determination, thus allowing the conclusion that the transition states are similar. In accordance with the kinetic data calculated from experiments in supercritical phase for **4** (see *Table 4*), its E_a values are different from the values resulting from pyrolysis in gas or liquid phase. This indicates a different

reaction mechanism or a change in the molecularity of the reaction when performed in supercritical alcohols. Perhaps, the reaction is no longer unimolecular and the bath molecules (supercritical EtOH) interact with the substrate molecules because of the high pressures applied to the reaction system (> 100 bar).

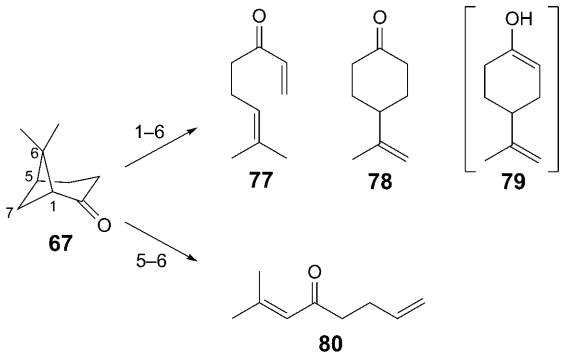
Table 9. *Kinetic Data for Thermal Isomerization of β-Pinene* (**5**)

Ref.	Reaction condition	k_i[a])	E_a [kJ mol^{-1}]	log A (A in s^{-1})
[50]	Liquid phase	k_f	197	15.4
		$k_{1,7}$	209	16.2
[84]	Gas phase	k_d	204	15.6
		k_f	209	15.9
		$k_{1,7}$	189	13.5
[29][90]	Gas phase, N_2	k_d	181	13.9
		k_f	183	14.0
		$k_{1,7}$	169	12.1
		$k_{1,5}$	181	12.6
[58]	Supercritical EtOH	k_f	276	
		$k_{1,7}$	275	
		$k_{1,5}$	215	

[a]) k_d, Disappearance of β-pinene (**5**); k_f, *retro*-[2 + 2] cyclization to myrcene (**72**); $k_{1,7}$, 1,7-H shift to limonene (**40**); $k_{1,5}$, 1,5-H shift to ψ-limonene (**73**).

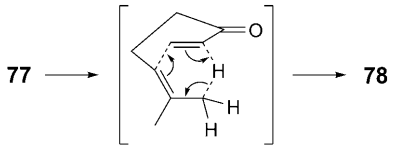
3.2.2. *Pyrolysis of Nopinone.* On heating nopinone (**67**) in the gas phase, the acyclic main product **77** and the monocyclic ketone **78** were found besides daughter products of **77** (*Scheme 15*) [17][29][91]. According to the isomerization of **5**, the corresponding monocyclic isomer with an internal C=C bond (**40** in the case of **5**) is absent, because the intermediate enol **79** undergoes rapid tautomerization to the respective ketone **78**. While passing **67** through a heated tube reactor (580°, 0.1 s), *Hartshorn* and co-workers additionally identified acyclic ketone **80** in low yield (5%) [17]. This product is an artifact of competitive ring opening *via* initial cleavage of the C(5)–C(6) bond. Kinetic analysis of the reaction in N_2 assisted gas-phase pyrolysis leads to E_a values of 166, 170, and 161 kJ mol^{-1} for the disappearance of **67**, the formation of **77**, and the rearrangement to **78**, respectively [29].

Scheme 15

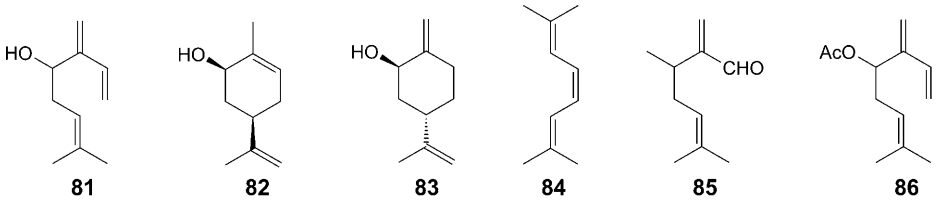


Another small distinction between the studies of *Mayer* and *Crandall*, and the other research groups studying this topic is the fact that they also performed pyrolysis experiments with the products **77** and **78** [91]. These investigations revealed that treatment of **77** (570°) furnished substantial amounts of **78** and other cyclized cyclopentante-type products whose formation will be discussed in *Sect. 6.1*. The authors rationalized their findings with an intramolecular (3,5)-ene cyclization (*Scheme 16*). Apparently **77** and **78** are in thermal equilibrium, since pyrolysis of cyclohexanone **78** at the same temperature (conversion 10%) afforded a mixture of consecutive products of **77**. Comparison of the thermal behavior of **77** with that of the respective monoterpene hydrocarbon **72** shows a marked contrast, since the latter on heating gave only rearrangement products different from **73** [90]. Computational studies on the B3LYP(6-31G*) level of theory did rationalize the isomerization of **77** to **78**, because the theory-based yields agreed with the experimental data [92].

Scheme 16



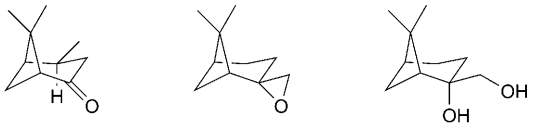
3.2.3. *Pyrolysis of Pinocarveols.* Passing *cis*-pinocarveol (**68**) through a flow reactor at 510° yielded a complex mixture of products consisting of trienol **81**, *cis*-carveol (**82**), triene **84**, and aldehyde **85**. Thermal treatment of the *trans*-isomer **69a** additionally afforded *trans*-isocarveol (**83**) [93][94]. Besides small differences in reactivity of the diastereoisomers and the additional formation of **83** in case of **69a**, the differences in product distribution are negligible, indicating that the configuration at C(3) has little influence on the outcome of the reaction. The occurrence of the unusual products **84** and **85** in both cases is assumed to be a result of the fragmentation of the primarily formed biradical and recombination of the fragments.



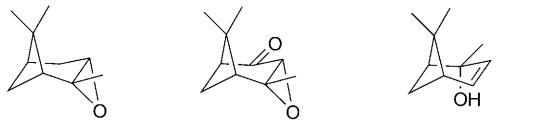
Pyrolysis of *trans*-pinocarvyl acetate (**69b**) is significantly more complex than that of the alcohols **68** and **69a**. The crude product consisted of enol acetates **86**–**88**, and of the $C_{10}H_{14}$ hydrocarbons **89** and **90** [94]. The latter products are due to rearrangement of verbenene (**91**), which is formed intermediately by thermal elimination of AcOH from **69**. The pyrolytic behavior of **91** will be discussed in *Sect. 4.1*.

3.2.4. *Pyrolysis of $\Delta^{2(10)}$-Pinen-4-ol.* Pyrolysis of *cis*- (**70**) or *trans*-$\Delta^{2(10)}$-pinen-4-ol (**71**; isoverbenol) diluted with pyridine at 500–600°/0.01 mbar in a flow apparatus yielded the allylic alcohol ipsdienol (**92**) [95]. In analogy to the enantioselective syntheses of acyclic **11** and **15a** from enantiomerically pure **1** and **15**, respectively, the synthesis of **92** from **70** or **71** takes advantage of the fact that, during the thermal cleavage of the cyclobutane ring, the stereogenic centers remain unchanged (*cf. Scheme 3*). Either enantiomer of the bark beetle aggregation pheromone **92** can be synthesized from (4*R*)-**70** and (4*R*)-**71**, or from (4*S*)-**70** and (4*S*)-**71**, respectively. Surprisingly, this opening of the cyclobutane ring is a very selective reaction, since no formation of any *p*-menthane-type product has been reported.

4. Miscellaneous Isomerizations of Pinanes. – In contrast to the thermal isomerization reactions of pinane-type compounds discussed in the preceding *Chapters*, the rearrangements that will be reviewed in this *Chapter* are more complex, and a categorization is hence difficult. Either two basic functionalities influence the rearrangement, or special functional groups dictate the behavior on heating. In case of verbenene (**91**), two VCB systems are present leading to the desired products, whereas the pinane and the β-pinene subsystem in *cis*-verbanone (**93**) compete with each other. Transformations of functional groups in **94**–**98** mainly influence the behavior of these compounds during pyrolysis.



93 **94** **95**

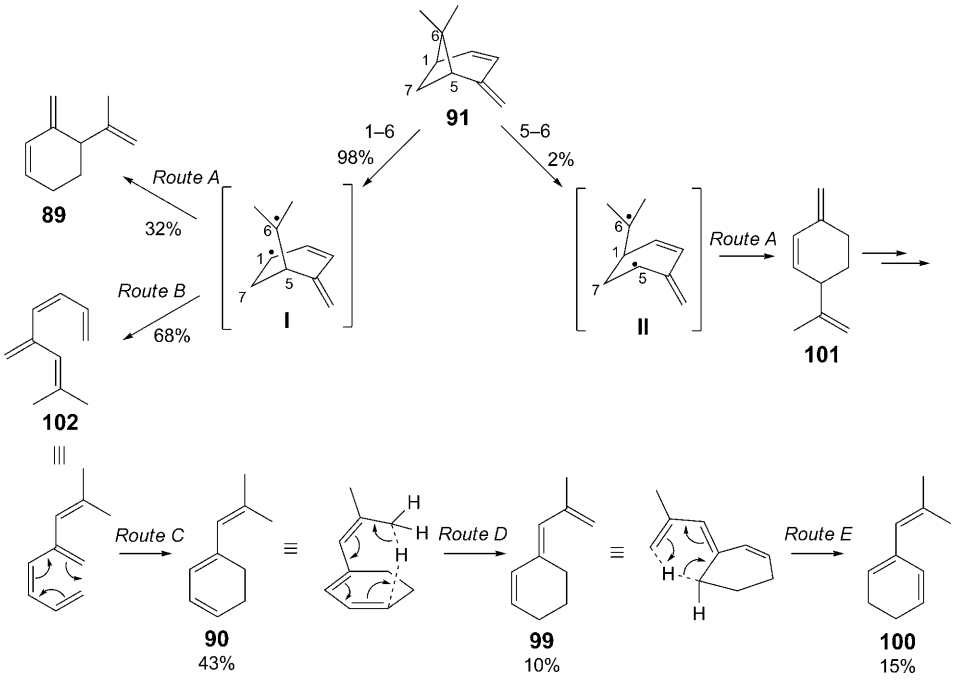


96 **97** **98**

4.1. *Pyrolysis of Verbenene.* As described in *Sect. 3.2.3*, compound **69b** on heating provided the $C_{10}H_{14}$ hydrocarbons **89** and **90**, which are assumed as isomerization products of the intermediary verbenene (**91**), resulting in turn from an electrocyclic thermal elimination of AcOH [94]. Investigation of the pyrolysis of **91** is interesting, because its structure contains both α-pinene and β-pinene moieties. Pyrolysis/GC studies at 380° by *Ohloff* and co-workers in 1969 allowed the identification of further isomerization products: (3*E*)-3-(isobutenylidene)cyclohex-1-ene (**99**), 2-(isobut-1-enyl)-cyclohex-1,3-diene (**100**), and small amounts of *o*-isopropenyltoluene (*Scheme 17*) [96]. Separate pyrolysis of triene **90** yielded **99** and **100** with a similar product ratio,

suggesting that these are consecutive reaction products. Passing a 20% mixture (*w*/*w*) of **91** in benzene through a steel pipe heated up to 370–390°, followed by a detailed product analysis, additionally revealed *p*-$\Delta^{1(7),2,8}$-menthatriene (**101**) and also products obviously arising from disproportionation reactions ($C_{10}H_{16}$ and $C_{10}H_{12}$) [97].

Scheme 17[a])

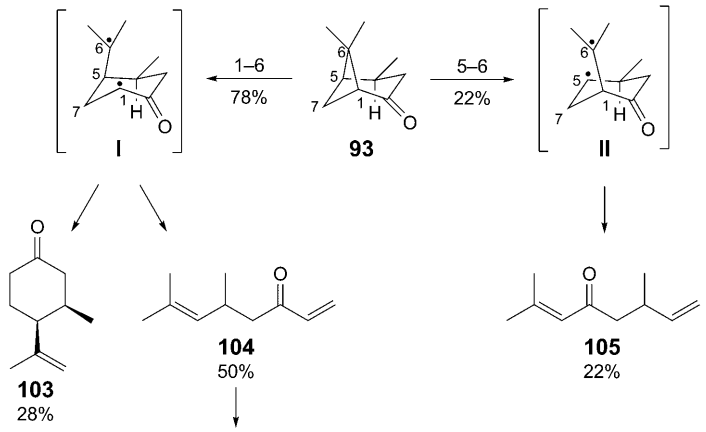


[a]) *Route A:* 1,5-H Shift; *Route B: retro*-[2+2] cyclization – fragmentation of the cyclobutane ring; *Route C:* sigmatropic [3,3] shift – *Cope* rearrangement; *Route D:* 1,7-H shift; *Route E:* [1,5]-H shift.

Differentiation between *p*- (**101**) and *o*-menthane-type products (**89**, **90**, **99**, **100**) lead to the conclusion that the reaction passes through two competitive biradicals either formed by scission of the C(1)–C(6) bond (**I**) or the C(5)–C(6) bond (**II**), with the product ratio indicating a high preference for the former (*cf. Scheme 17*). Likewise, comparative pyrolyses of **4** and **5** have shown that **4** is more prone towards ring cleavage leading to biradical formation [8][29]. The preferred formation of biradical **I** in the combined system **91** is due to the higher reactivity of the internal C=C bond, which raises the ring-strain energy and, therefore, weakens the C(1)–C(6) bond. The cross-conjugated fourfold unsaturated reaction intermediate **102** (*retro*-[2+2] cyclization) presumably underwent a fast [3,3] sigmatropic rearrangement (*Cope* rearrangement) to the cyclic triene **90**. A cap-like orientation of the isobut-1-enyl group in **90** above the flat cyclohexadiene ring opens an opportunity for a 1,7-H shift leading to the conjugated triene **99**. The (*E*)-configuration in **99** is favorable for a sigmatropic *suprafacial*, thermally allowed [1,5]-H shift leading to the formation of **100**.

4.2. *Pyrolysis of* cis-*Verbanone.* Although the monoterpenoid *cis*-verbanone (**93**) unifies two structural entities, *cis*-pinane (**1a**) and nopinone (**67**), the product spectrum is not so complex as in the case of **91**. Subjecting **93** to gas-phase pyrolysis at 580° with a contact time of 0.1 s afforded five main products from which the three primary pyrolysis products are shown in *Scheme 18*: cyclic ketone **103**, and the open-chain ketones **104** and **105** [17][98][99]. Consecutive reactions of **104** will be discussed in *Chapt. 6*. Products arise from two different biradicals either formed as intermediates by cleavage of the C(1)–C(6) or C(5)–C(6) bond of the pinane skeleton. Further fragmentation of the latter yielded **105**, whereas a 1,5-H shift of biradical **I** resulted in the formation of **103**, and *retro*-[2 + 2] cyclization led to the acyclic compound **104**. The ratio of the two main pathways is *ca.* 3 : 1 in favor of the route forming a biradical which is stabilized by mesomeric interaction with the C=O function. The relative product ratio of **103** to **104** of 1 : 2 is in accordance to the favored formation of **77** from **67** [17][91]. Comparison of the results with those derived from thermal rearrangement of isopinocamphone (**19**; *cf. Sect. 2.3*) and **67** indicates that comparable substituents at C(3) have a negligible influence on the reaction pathways, whereas substitution in α-position of the cyclobutane system dramatically affects the product spectrum.

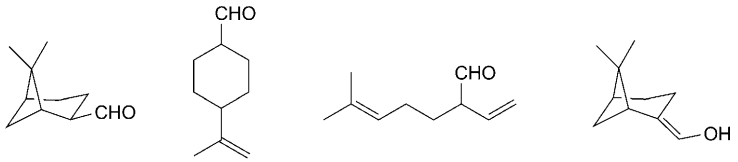
Scheme 18



The different abilities of the C=O and the methylidene function to influence the isomerization behavior are displayed, when the results from the pyrolysis of **5** and **67** are compared with those from **93**. Whereas, in the case of the latter, competing reaction paths exist, rearrangement of the former ones leads to unique products only (*cf. Sect. 3.2.2*), since the resonance stabilization is more pronounced for an allylic radical than a hetero-allylic radical.

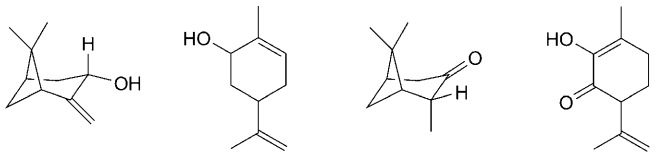
4.3. *Pyrolysis of Epoxy Monoterpenoids.* Subjecting *exo*-β-pinene oxide (**94**) and *exo*-pinane-2,10-diol (**95**) to flash vacuum pyrolysis at 650 and 900° (0.07 mbar), respectively, provides the same products: myrtanal (**106**), 1,2-dihydroperill aldehyde (**107**), and 6-methyl-2-vinylhept-5-enal (**108**) [11]. Since the ratio of acyclic **108** to monocyclic **107** of 1.3 is the same for pyrolysis of both **94** and **95**, it can be concluded that both the epoxide and the diol form **106** as an intermediate, which undergoes ring

cleavage to **108** and *retro*-ene reaction to **107**. Aldehyde **106** is a compound the thermal behavior of which should be comparable to cyclobutane, since the C=O function is in β-position to the four-membered ring. The (for these compounds) unusual formation of a *p*-menthane-type product indicates a reaction intermediate typical for α- or β-pinene-type rearrangements – β-pinen-10-ol (**109**) – which is either formed by epoxide-ring opening (**94**) or thermal elimination of H_2O (**95**).



106 **107** **108** **109**

Passing *exo*-α-pinene oxide (**96**) through a heated iron pipe (400°) or heating it in an autoclave system under autogeneous pressure to 250° yielded pinocamphone (**110**), carveol (**82**), and minor amounts of *trans*-pinocarveol (**69**) [100]. The formed products arise from two different reaction routes: *i*) opening of the epoxide leads to aldehyde **110**, which is thermally stable under the reaction conditions; *ii*) opening by alternative hydride abstraction forms **69**, which itself undergoes *retro*-ene reaction forming **82**, the first route being strongly favored (28 : 1).

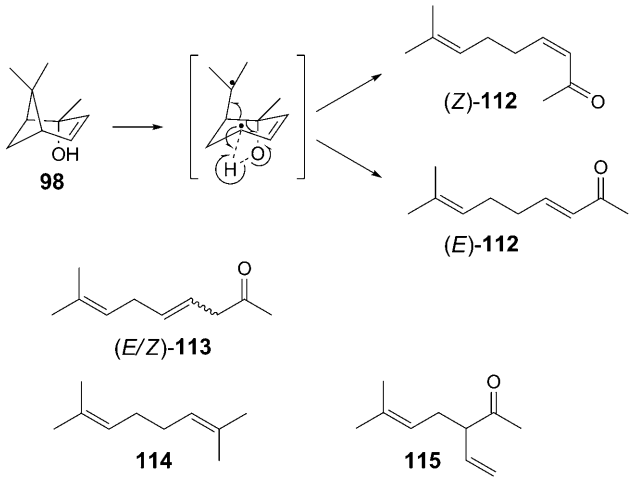


69 **82** **110** **111**

The thermal isomerization of *exo*-verbenone oxide (**97**) mainly yielded 3-isopropyl-6-methyl-*o*-hydroquinone and 3-methyl-*o*-hydroquinone. The main reaction intermediate is assumed to be 2-hydroxy-3-methyl-6-isopropenylcyclohex-2-enone (**111**) [73].

4.4. *Pyrolysis of Δ^3-Pinen-2-ol.* During their studies on substituent effects on the pinane isomerization, *Coxon et al.* investigated the pyrolysis of Δ^3-pinen-2-ol (**98**) at 540° in the gas phase [13]. Besides several hydrocarbons resulting from thermal elimination of H_2O (presumably *via* formation of verbenene (**91**; *cf. Sect. 4.1*)), the product mixture consisted of open-chain methyl ketones **112**, **113**, and **115**, as well as of minor amounts of the diene **114** (*Scheme 19*). Experiments under similar conditions with both (*Z*)-**112** and (*E*)-**112** revealed that both yielded **113**, whereas products **114** and **115** exclusively resulted from rearrangement of the (*E*)-isomer. According to the formation of triene **84** from **68** or **69a** (*cf. Sect. 3.2.3*), and since **114** is an example for a rare tail-to-tail linked isoprenoid, it stands to reason that it resulted from rearrangement of fragmentation products of **112**.

Scheme 19

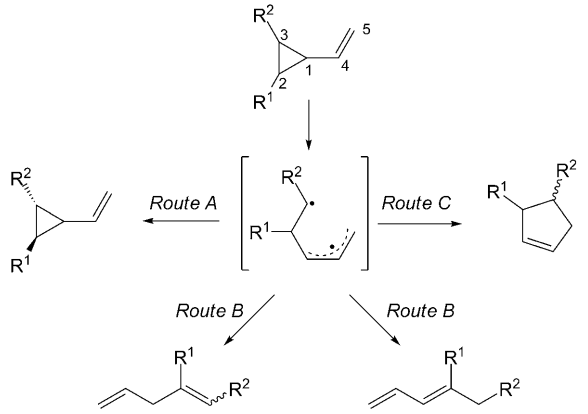


5. Isomerizations Related to Vinylcyclopropane. – All bicyclic monoterpenoid compounds discussed so far have in common that the parent systems contain four-membered rings. In carane (**2**) and thujane (**3**), a cyclopropane ring is part of a bicyclic system, additionally containing a cyclohexane and cyclopentane ring. In contrast to the saturated parent systems **2** and **3**, which can only undergo thermal processes at very high temperatures, the thermal behavior of the unsaturated monoterpenes Δ^2-carene (**6**), Δ^3-carene (**7**), Δ^4-carene (**8**), α-thujene (**9**), and β-thujene (**10**) has been extensively studied at lower temperatures. Besides **7**, these compounds have in common that the parent system vinylcyclopropane (VCP) is part of the bicyclic system. Like vinylcyclobutanes (VCBs), VCPs can undergo various transformations: *i*) *cis–trans* isomerization (*Route A*; *Scheme 20*), *ii*) ring opening *via* 1,*j*-H shift reactions (*Route B*), and *iii*) ring enlargement to cyclopentenes by way of a [1,3]-C shift (*Route C*) [6a,d]. The latter rearrangement of monocyclic VCBs has been part of various interesting review articles [6c,e], whereas the other reactions are less important for the monocyclic systems but become interesting if the system is part of bicyclic molecules or molecules with fused rings. In case of compounds **6**–**10**, the VCB is part of the respective monoterpene skeleton comparable to the VCB in α-pinene-type compounds (*cf. Sect. 3.1*).

5.1. *Carane-Type Compounds.* 5.1.1. *Pyrolysis of Carenes and Hydroxylated Carenes.* The main structural difference among the carenes **6**–**8** is that, in **7**, no VCB system is present, and this is manifested by its inactivity towards ring-opening reactions. However, gas-phase pyrolysis of **7** at temperatures higher than 550° led to the formation of aromatic compounds like benzene, toluene, xylene, cymene, and 8,9-didehydrocymene [101].

Comparison of reaction pathways principally available to carenes **6** and **8** would indicate that the [1,3]-C shift route is the most dominating alternative. Depending on the bond in the cyclopropane ring which is cleaved, two types of products might be

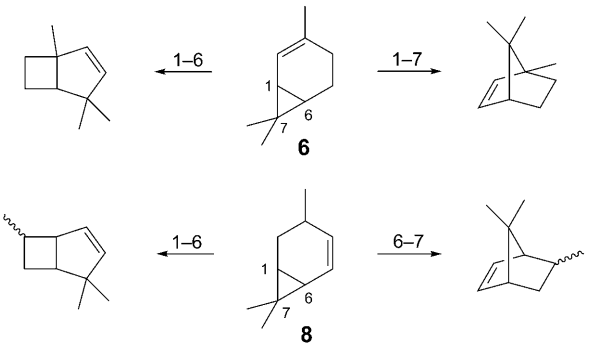
Scheme 20[a])



[a]) *Route A: cis–trans* isomerization; *Route B:* 1,*j*-H shift reactions; *Route C:* [1,3]-C shift.

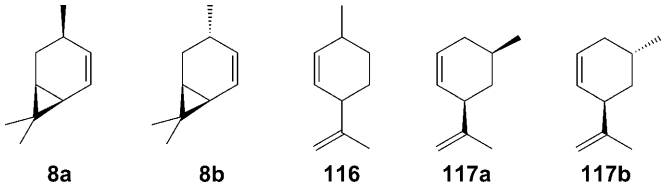
formed. By C(1)–C(6) bond cleavage, 1,4,4- and 4,4,7-trimethylbicyclo[3.2.0]hept-2-ene could be formed from **6** and **8**, respectively. Sigmatropic [1,3]-C shift *via* the biradical resulting from C(1)–C(7) and C(6)–C(7) bond scission would lead to norbornene derivatives (*Scheme 21*). Neither the first nor the second set of products has been found while subjecting **6** or **8** to pyrolysis, however.

Scheme 21



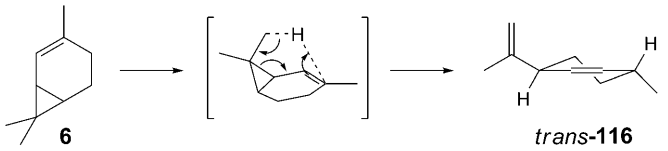
In contrast to the thermal rearrangements of the compounds discussed before, monoterpenes and monoterpenoids of the carane-type undergo *retro*-ene reaction exclusively. In fact, pyrolysis of **6** yielded *trans-p*-$\Delta^{2,8}$-menthadiene **116**, whereas the thermal treatment of *cis*- and *trans*-Δ^4-carene (**8a** and **8b**, resp.) resulted in the formation of *cis*- and *trans-m*-$\Delta^{1,8}$-menthadiene (**117a** and **117b**, resp.), respectively [102–104]. Besides the hydrocarbons **6**–**8**, the isomerization of those carane derivatives was investigated, which are able to be transformed into carenes by thermal elimination of the substituents (H_2O, AcOH) [101–105].

The pyrolysis of **8a** and **8b** stereoselectively yielded the respective isomers **117a** and **117b** [104]. Rearrangement of **6** into **7** or **8** was observed in no case. On the basis of

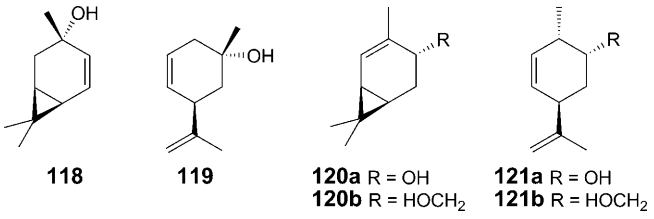


these observations, the authors suggested that the reaction proceeds as a concerted *retro*-ene reaction (sigmatropic *homo*-[1,5]-H shift) as shown in *Scheme 22*. This mechanism readily explains the stereoselective formation of *trans*-**116** from **6**. With respect to the cyclic transition state the *pseudo*-equatorial Me group at C(3) has to end up on the opposite side of the resulting isopropenyl group.

Scheme 22



Performing kinetic pyrolysis experiments with **6** and some other derivatives, the concerted nature of these rearrangements was established by *Ohloff* [103]. The kinetic parameters are typical for reactions passing through rigid cyclic transition states (sigmatropic or pericyclic reactions). Hence, rearrangements starting from bicyclic monoterpenes or monoterpenoids of the carene-type do not involve biradical intermediates. Kinetic analysis of the pyrolysis of *cis*-Δ^4-caren-3-ol (**118**) leading to *cis*-*p*-$\Delta^{3,8}$-menthadien-1-ol (**119**) leads to an activation enthalpy and activation entropy of 118 kJ mol^{-1} and -28 J K^{-1} mol^{-1}, respectively (*Table 10*). These results and those derived from the kinetics of hydroxy derivatives of **6** (*i.e.*, **120a**,**b**) confirm that the concerted mechanism of the *retro*-ene reaction is the main reaction pathway for the isomerization of derivatives of **2**. It has to be pointed out here that the activation enthalpies listed in *Table 10* are distinctly lower than the activation energies (of 218–280 kJ mol^{-1}) found for ring openings of the VCPs, thus indicating different reaction mechanisms (sigmatropic *vs.* stepwise diradical).



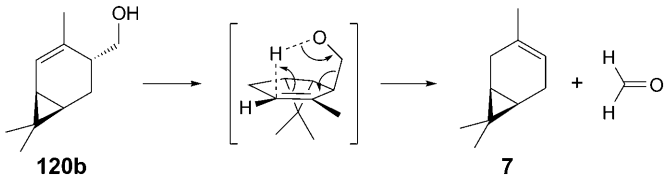
In addition to the formation of **121b**, when **120b** is pyrolyzed, small amounts of **7** have been found in the reaction mixture [102]. The mass difference between **120b** and **7** is 30 amu indicating a loss of formaldehyde. Apparently, thermal treatment leads to loss of formaldehyde similar to the formation of **5** from **31a** (*Scheme 11*). The respective

Table 10. *Kinetic Data for the Thermal Isomerization of Carenes* [99]

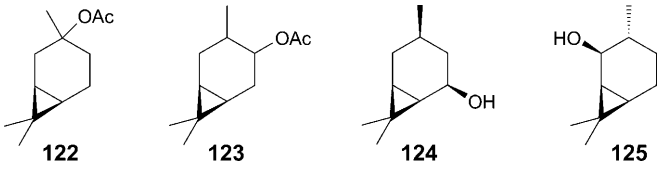
No.	$\Delta^{\ddagger}H^{\circ}$ [kJ mol^{-1}]	$\Delta^{\ddagger}S^{\circ}$ [J K^{-1} mol^{-1}]
6	114	– 72
118	118	– 28
120a	138	– 37
120b	120	– 27

reaction for carene derivative **120b** is shown in *Scheme 23*, exemplifying the observed *retro-Prins* reaction[4]). These thermal fragmentations are typical for β,γ-unsaturated hydroxymethyl compounds long known in the literature [102][106].

Scheme 23



5.1.2. *Pyrolysis of Hydroxycaranes and Their Acetates.* Besides the hydrocarbons **6**–**8**, various O-containing derivatives of carane (**2**) have been pyrolyzed (*i.e.*, **122**–**125**). All these acetates and alcohols yielded $C_{10}H_{16}$ hydrocarbons as intermediary products when thermally treated [101–104]. Therefore, it was concluded that the carenes **6**–**8** are reaction intermediates formed by elimination of either AcOH (in case of **122** and **123**) or H_2O (in case of **124** and **125**). Elimination of AcOH from diastereoisomers of **122** initially afforded both Δ^2- and Δ^3-carene (**6** and **7**, resp.), and a consecutive reaction of **6** led to *trans*-**116** (*Scheme 22*). Pyrolysis of *cis*-**123** and *trans*-**123** selectively led to **117a** and **117b** *via* **8a** and **8b** as reaction intermediates, respectively [104]. Besides these, **7** was also produced, but established to be thermally stable under the reaction conditions. Thermal treatment of *cis*-caran-*cis*-5-ol (**124**) and *trans*-caran-*cis*-2-ol (**125**) yielded selectively the monocyclic hydrocarbons **117a** and *trans*-**116**, respectively [101].

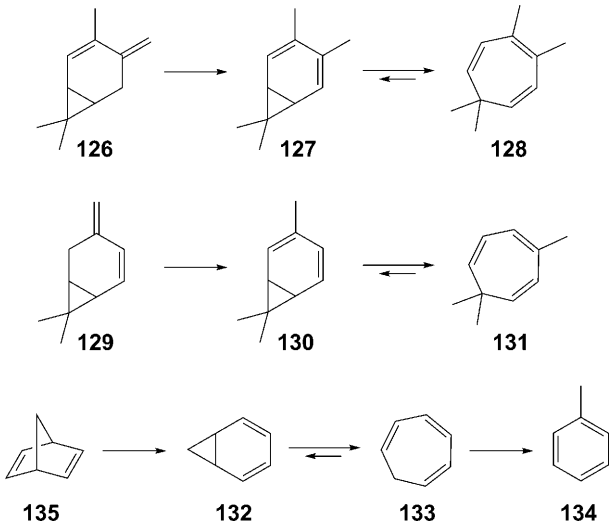


5.1.3. *Rearrangements of the Norcaradiene-Type.* Pyrolyzing 4-methylidene-Δ^2-carene (**126**) in the liquid phase in sealed glass ampoules in a temperature range of 125–210° led to the formation of 4-methyl-$\Delta^{2,4}$-caradiene (**127**) and 3,4,7,7-tetramethylcyclohepta-1,3,5-triene (**128**; *Scheme 24*), which are in thermal equilibrium [107]. Furthermore, the aromatized product 3-methyl-*p*-cymene was identified. On heating

[4]) This reaction is also denoted as 'ricinoleic acid fission' or *English-Zimmerman* cleavage, but naming as *retro-Prins* condensation is more common.

$\Delta^{3(10),4}$-caradiene (**129**), a thermally equilibrated mixture of $\Delta^{2,4}$-caradiene (**130**) and 3,7,7-trimethylcyclohepta-1,3,5-triene (**131**) was formed, besides noticeable amounts of *m*- and *p*-cymene. Apparently **126** and **129** undergo thermal rearrangement to those dienes bearing internal C=C bonds. The equilibrium of these hydrocarbons with the respective cycloheptatrienes is known as the 'norcaradiene–cycloheptatriene rearrangement' named after the parent compounds norcaradiene (**132**) and cycloheptatriene (**133**; *Scheme 24*) [6d][108][109]. The product mixtures showed that the cycloheptatriene is favored in both cases. Presumably, the reaction is initiated by the cleavage of the C(1)–C(6) bond and the formation of a diradical, which, on reorganization, forms the triene. Literature and *ab initio* calculations for the parent system hint at aromatic 6π-intermediates that could be the explanation for the formation of the aromatic side products (toluene (**134**) in case of the parent system), and also the inclusion of norbornadiene (**135**) into this system of degenerate rearrangements, since its thermal isomerization yielded **132** and **133**.

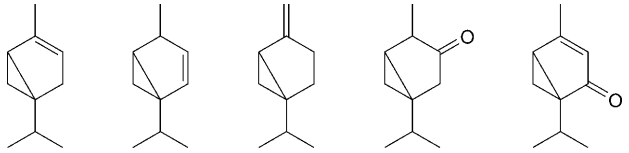
Scheme 24



Kinetic analysis of the thermochemical reactions of **126** and **129** leads to E_a values of 108 and 112 kJ mol^{-1}, respectively. The log A factor of 13.6 (A in s^{-1}) and an activation entropy $\Delta^{\ddagger}S^{\circ}$ of 3.0 J K^{-1} mol^{-1} for these isomerizations indicate a sigmatropic reaction rather than a (bi)radical process. Therefore, the formation of internal dienes **127** and **130** from **126** and **129**, respectively, by a 1,3-H shift was assigned as the rate-determining step.

5.2. *Thujane-Type Compounds.* Monoterpenoids and monoterpenes with a thujane skeleton are interesting compounds from the viewpoint of chemical synthesis. Among other types of isomerization (photolysis, acidolysis), some thujanes have also been the subject of thermolysis studies [5f]. Thujane (**3**) itself has not yet been pyrolyzed. Nevertheless, the thermal rearrangement chemistry of its unsaturated isomers α-thujene (**9**), β-thujene (**10**), and sabinene (**136**), as well as of the ketones thujone (**137**)

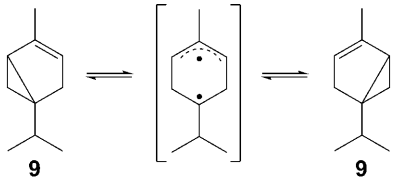
and umbellone (**138**) have been reported. In contrast to the rearrangements discussed above in the carane series, H-shifts do not dominate thujane thermal isomerizations, since no proper H-atom is available to undergo *retro*-ene reaction or other shifts. The predominant reactions are [1,3]-C shifts leading to cyclopentenes in case of VCP (*Scheme 20*) [6d,e]. Due to the bicyclic nature of **9** and **10**, these reactions are often degenerate and not recognizable at first glance.



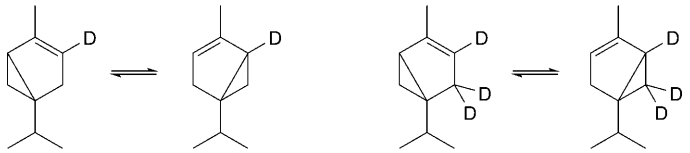
9 **10** **136** **137** **138**

5.2.1. *Pyrolysis of α-Thujene.* Pyrolysis experiments carried out with optically pure **9** in the liquid phase at 200° revealed racemization of the starting material [110]. To study this reaction in greater detail, the thermal rearrangement of D-labeled **9** was investigated. 3-α-[^{2}H]Thujene (**139**) yielded 5-α-[^{2}H]thujene (**140**) without racemization of the starting material, whereas thermal treatment of 3,4,4-α-[$^2H_3$]thujene (**141**) resulted in the formation of a racemic mixture of 5,5,6-α-[$^2H_3$]thujene (**142**; *Scheme 25*) [110][111].

Scheme 25

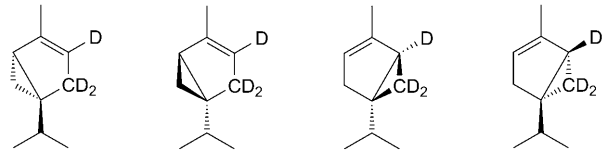


9 **9**



139 **140** **141** **142**

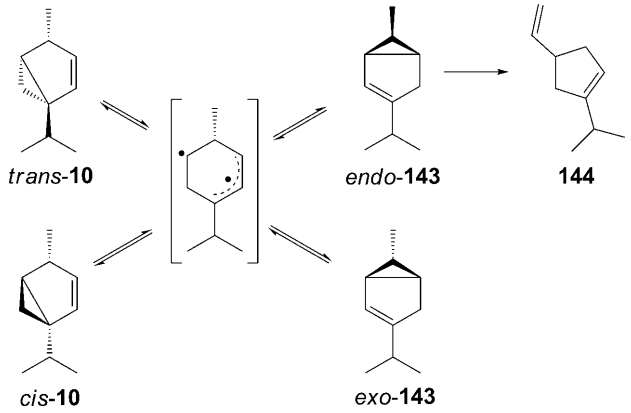
In addition to D-scrambling, enantiomerization ('ring flip') also occurred when **141** was pyrolyzed. Therefore, the four different products shown below are obtained. Starting with the first enantiomer (+)-**141**, the formation of a biradical, similar to the one shown in *Scheme 25* for racemization of **9**, can result in either the sigmatropic [1,3]-C shift product (+)-**142** or in the antipode (−)-**141**, which results from inversion at C(1). Gas-phase pyrolysis revealed a clear preference for the *suprafacial,retention* [1,3]-C shift product (+)-**142** with a relative yield of 49% at 45% conversion. The relative yields of doubly epimerized product (−)-**141** ('ring flip') and the one resulting from an *antarafacial,inversion* by way of a [1,3]-C shift (→ (−)-**142**) were 32% and 19%, respectively [6e][111].



Kinetic analysis of the racemization reaction of undeuterated **9** in the gas phase led to an E_a value of 182 kJ mol^{-1} with a log A value of 14.3 (A in s^{-1}). The activation entropy of 13 J K^{-1} mol^{-1} is an unequivocal hint for a reaction passing through radical intermediates [108]. The suggested reaction mechanism is depicted in *Scheme 25*. Due to the planarity of the biradical intermediate (C_s symmetry) any configurational information of the starting material is lost and the racemate is formed. This reaction is a good example for the non-concerted degenerative rearrangement of a substituted VCP.

5.2.2. *Pyrolysis of β-Thujene.* In contrast to the pyrolysis of **9**, the thermal rearrangement of β-thujene (**10**) is remarkably more complex due to the formation of other pyrolysis products rather than racemized ring-flip products only. First of all, compound **10** exists in two diastereoisomeric forms: *cis*-**10** and *trans*-**10**. Pyrolysis in liquid phase at 250° yielded rearrangement products **143** and **144** in equal amounts, whereas, in experiments at 300°, the formation of **144** was observed almost exclusively (*Scheme 26*). Apparently, hydrocarbon **144** is produced from an unidirectional consecutive reaction of the intermediate product **143** [110]. Kinetic analysis of the reaction steps presented in *Scheme 26* led to an overall E_a value of 188 kJ mol^{-1} [112]. Detailed analysis of the reaction steps revealed that the formation of **144** is only possible from the *endo*-isomer of **143** and apparently proceeds *via* a *retro*-ene reaction. Like the thermal reactions of **9**, **141**, and **142**, the VCP rearrangement of **10** leading to **143** presumably involves biradical intermediates, whereby the mesomeric delocalization causes equilibration at the C(1)-atom. Due to retention of the configuration at C(4), the ring flip is accompanied by a change of relative configuration rather than racemization.

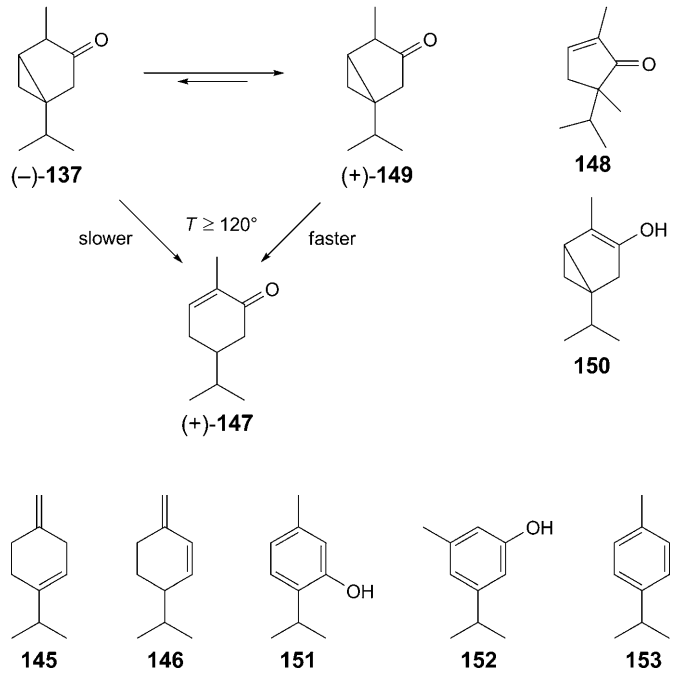
Scheme 26



5.2.3. *Pyrolysis of Sabinene, Thujone, and Umbellone.* Passing sabinene (**136**) through a stainless steel tube heated to 600° resulted in the formation of β-terpinene (**145**) and β-phellandrene (**146**) as major components [113]. The pyrolysis is assumed to proceed through a biradical intermediate resulting from C(1)–C(5) bond scission, which, upon 1,2-H shift, gave the reported products.

On heating optically active thujone (**137**) at 280° in the liquid phase, isomerization to racemic carvotanacetone (**147**) and minor amounts of ketone **148** occurred [114][115]. Experiments carried out at 120° revealed that *d*-(+)-isothujone (**149**) is much more reactive than the diastereoisomeric *l*-(−)-thujone (*Scheme 27*). Therefore, the authors suggested that the reaction passes through a biradical intermediate similar to that postulated in the racemization of **9**. The formation of enol **150** is discussed as a reaction intermediate, since this would favor the racemization of **137** *via* [1,3]-C shift (ring flip).

Scheme 27



Liquid-phase pyrolysis of umbellone (**138**) in sealed *Pyrex* tubes at 280° for several hours resulted in the formation of thymol (**151**; 90–95%), *sym*-thymol (**152**; 5–10%), and traces of *p*-cymene (**153**). Probably, the reaction passes either through ionic intermediates, or H transfer (concerted or *via* biradicals; *retro*-ene reaction) to the keto function is responsible for the rearrangement yielding **151** [116].

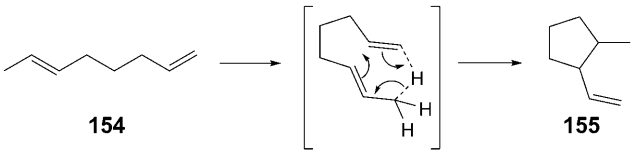
6. Rearrangements of Acyclic Terpenic Compounds. – As suggested in the first *Chapters* of this review, acyclic thermal isomerization products resulting from pyrolysis of monoterpenes and monoterpenoids with pinane skeleton often readily undergo

consecutive reactions. Similar to the classifications of the bicyclic compounds into subclasses (pinane, α-pinene, β-pinene), reactions of open-chain products can be assigned to two major groups represented by the lead compounds octa-1,6-diene (**154**) and (3*Z*)-ocimene (**39**), respectively: *i*) intramolecular ene cyclization, and *ii*) sigmatropic [1,5]-H shift.

The first group is typical for acyclic isomers resulting from isomerization of compounds of the pinane- (*Chapt. 2*) and β-pinene-type (*Sect. 3.2*), whereas the second group of reactions is typical for those open-chain products resulting from ring opening of α-pinene-type compounds (*Sect. 3.1*).

6.1. *Intramolecular Ene Cyclization.* The parent reaction for those types of consecutive reactions, which the acyclic products from pyrolysis of pinane- or β-pinene-type compounds often undergo, is the intramolecular (3,4)-ene reaction of octa-1,6-diene (**154**) to 1-vinyl-2-methylcyclopentane (**155**; *Scheme 28*) [44]. Whereas the respective hepta-1,6-diene failed to cyclize and resulted in decomposition, the formation of *cis*-**155** is stereoselective at 475° with a contact time of 56 s. The rate of cyclization and the preference for *cis*-**155** was reported to be independent from the configuration of **154** [33], which has recently been confirmed by the DFT computational studies of *Das* and co-workers [92].

Scheme 28

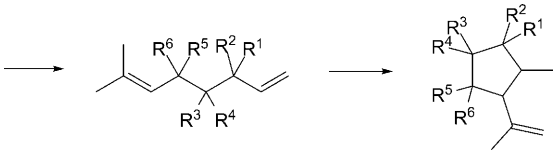


Since many of the acyclic products from thermal isomerization of either pinane-type or β-pinene-type compounds have the same basic structure, it is not astonishing that most of them undergo similar cyclizations to cyclopentane derivatives. *Table 11* lists all these compounds whose isomerization behavior has been discussed in the previous sections, and whose primary acyclic product forms products like **155** in an intramolecular (3,4)-ene reaction.

Kinetic analysis of the cyclizations of β-citronellene (**11**), isocitronellene (**12**), linalool (**15a**), and myrcene (**72**) resulted in E_a values of 134, 139, 122, and 168 kJ mol^{-1}, respectively [31][90][117]. The corresponding log *A* values of 8.7, 9.2, 9.9, and 11.3 (*A* in s^{-1}) are typical for concerted reactions, and, therefore, the presumed cyclic transition state for the archetype of this reaction is confirmed. Authors of almost all studies dealing with the intramolecular (3,4)-ene reactions listed in *Table 11* agree that these cyclopentanes are preferably generated by thermal cyclization of substrates, in which the isopropenyl group and the neighboring Me group can adopt a *cis*-orientation as a prerequisite for a cyclic transition state. The amounts of the respective diastereoisomers with *trans*-orientation of these substituents are always lower.

DFT Computational studies on the cyclization of **14** and **77** resulting from pyrolysis of **13** and **67**, respectively, agree with the results from experimental pyrolysis studies [12][33][91][92]. Whereas the ene reaction of **14** diastereoselectively afforded the *cis*-configured cyclopentane-type product only [12][33], thermal treatment of **77**

Table 11. *Intramolecular (3,4)-Ene Reactions of Acyclic Products Resulting from Thermal Isomerization of Pinane- or β-Pinene-Type Compounds* (*cf. Tables 1* and *8*)



Bicyclus	Acyclic Precursor	R^1	R^2	R^3	R^4	R^5	R^6	Ref.
Pinane (**1**)	β-Citronellene (**11**)	Me	H	H	H	H	H	[9][10][26][29][31]
	Isocitronellene (**12**)	H	H	H	H	Me	H	[10][31]
β-Pinene (**5**)	Myrcene (**72**)	$=CH_2$		H	H	H	H	[29][34][87][90]
Norpinane (**13**)	**14**	H	H	H	H	H	H	[12][33]
Pinan-2-ol (**15**)	Linalool (**15a**)	Me	OH	H	H	H	H	[13][34][38–40]
	Isolinalool (**15b**)[a])	H	H	H	H	Me	OH	[13]
Isopinocampheol (**16**)	**16a**	Me	H	OH	H	H	H	[14–16][41]
Neoisoverbanol (**17**)	**17a**[a])	Me	H	H	H	OH	H	[15]
	17b	OH	H	H	H	Me	H	[15]
Nopinol (**18**)	**18a**	OH	H	H	H	H	H	[15][43]
	18b[a])	H	H	H	H	OH	H	[15][43]
Isopinocamphone (**19**)	**19a**	Me	H	=O		H	H	[14][17]
	19b	H	H	=O		Me	H	[14][17]
Nopinone (**67**)	**77**	=O		H	H	H	H	[29][17][91]
cis-Verbanone (**93**)	**104**	=O		H	H	$=CH_2$		[17][99]

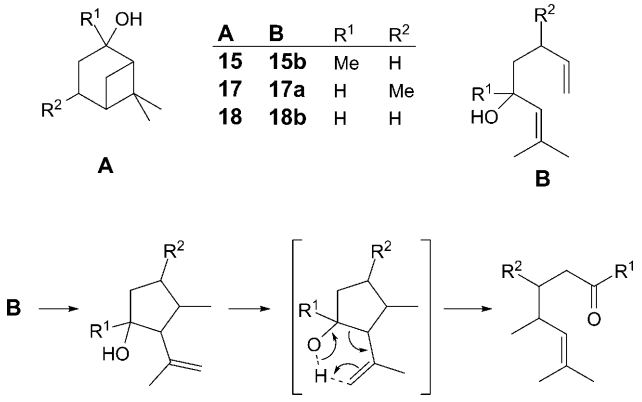
[a]) Cyclization product undergoes further consecutive reactions (see *Scheme 29* and subsequent text).

furnished a mixture of *cis*- and *trans*-(3,4)-ene cyclization products (ratio 4:1) as well as cyclohexanone **78** resulting from an intramolecular (3,5)-ene reaction (*Scheme 15*). Calculation of the relative energies of the respective transition-state structures on a B3LYP(6-31G*) level of theory can explain the formation of (3,4)- and (3,5)-ene-cyclization products.

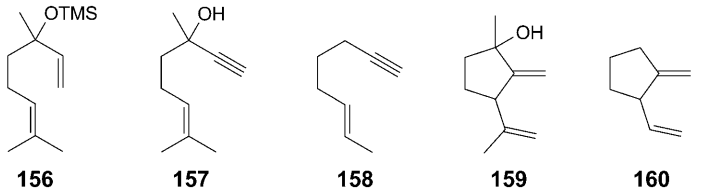
Some of the products listed in *Table 11* are postulated intermediates which undergo further consecutive reactions (*i.e.*, **15b**, **17a**, and **18b**). They have in common that, adjacent to the isopropenyl group of the cyclopentane derivative, a OH group is located. Hydrogen transfer through *retro*-(3,4)-ene reaction then furnished open-chain carbonyl compounds (*Scheme 29*) [15][44]. Compounds showing this behavior resulted from pyrolysis of pinan-2-ol (**15**), neoisoverbanol (**17**), and nopinol (**18**).

Several derivatives of acyclic monoterpenes are listed below, which undergo similar intramolecular ene reactions. Thermocyclization of the Me_3Si (TMS) ether of **15a**, **156**, in the gas phase yielded the respective cyclopentanol TMS ethers, also preferring the *cis*-diastereoisomers [118]. The TMS ether was used instead of pure alcohol **15a** to prevent dehydration. Heating 1,2-didehydrolinalool **157** in an evacuated *Pyrex* flask to 175–227° resulted in the formation of 2-methyl-2-methylidene-3-isopropenylcyclopentanol (**159**) which is an example for an intramolecular ene reaction of an enyne [118]. The parent system for this reaction – oct-6-en-1-yne (**158**) – on passage through a 400° hot *Pyrex* tube gave cyclization product **160** [119]. Kinetic analysis of the reactions

Scheme 29



of **156** and **157** by *Roth* and co-workers confirmed the concerted nature of the process and also the preference for formation of the *cis*-diastereoisomers in the case of TMS ether **156**.



6.2. *Sigmatropic [1,5]-H Shifts.* The possible primary acyclic pyrolysis products from the thermal isomerization of α-pinene-type monoterpenes listed in *Table 3* readily undergo rearrangement to fully conjugated products. These reactions take place so rapidly that the primary products often cannot be detected. The parent system for these reactions is the degenerate rearrangement of (*Z*)-penta-1,3-dienes (*Scheme 30*) [6d]. The [1,5]-H shifts are characterized by low pre-exponential terms ($\log A \approx 11$) and low activation energies (150–160 kJ mol^{-1}). The kinetics of the thermal rearrangement of (3*Z*)-ocimene (**39**) to the fully conjugated regioisomer (4*E*)-alloocimene (**41**) was investigated by *Sasaki et al.* (*Scheme 30*) [120][121]. Liquid-phase pyrolysis experiments (140–160°) provided log *A* and E_a values of 10.4 (*A* in s^{-1}) and 118 kJ mol^{-1}, respectively, leading the authors to conclude that the rearrangement is similar to that of (*Z*)-hexa-1,3-diene to (2*Z*,4*E*)-hexa-2,4-diene. Data have recently been confirmed by kinetic carrier-gas-assisted gas-phase pyrolysis experiments [64]. The reaction can pass through different transition states that determine the configuration of the resulting C=C bonds. Since the axial position of the bulky isobutenyl group in case of **39** would cause steric repulsions, the equatorial conformation is obviously preferred resulting in (4*E*)-**41**. With respect to the cyclic transition state, the configuration of the C(6)=C(7) bond has to be (*Z*), but formation of (4*E*,6*E*)-**41** was reported also when pyrolyzing α-pinene (**4**) [54–58][64].

Scheme 30

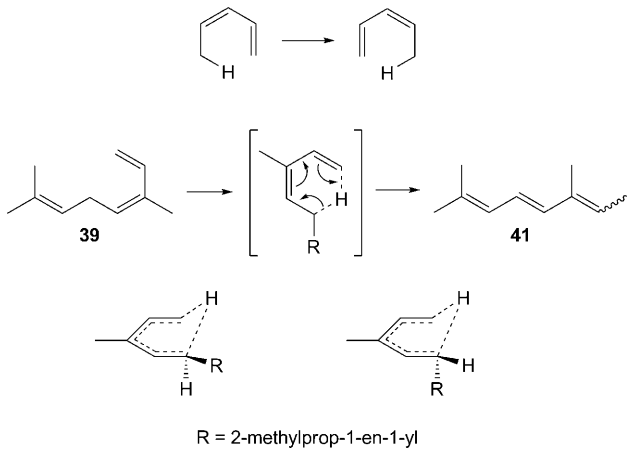


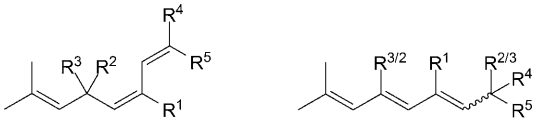
Table 12 lists the acyclic isomerization products resulting from fragmentation of the cyclobutane ring in α-pinene-type compounds. Only in the case of the thermal rearrangement of **4**, the primary product **A** could be identified in low amounts. Pyrolysis of the bicyclic compounds **28**–**33** yielded the H-shift product solely. The acyclic products resulting from isomerization of **34a** and **35** are different in structure from product **A** due to the fact that, in α-position to the first C=C bond (R^4 or R^5), a OH group is located, allowing tautomerization to the respective carbonyl compound [20]. This indicates that the keto–enol tautomerization is much faster than the competing H-shift that would yield the conjugated triene **B**.

It has to be mentioned that the fully conjugated acylic products often undergo further reactions leading to cyclohexadiene derivatives, assumed to result from (sigmatropic or radicalic) C- and/or H-shift reactions. Performing experiments at elevated temperatures causes these cyclohexadienes to form aromatic compounds such as toluene, xylene, or mesitylene [122–124].

7. Conclusions. – Thermally induced rearrangement reactions of monoterpenes and monoterpenoids with strained three- or four-membered rings bridged by a cyclopentane or cyclohexane system are interesting from the mechanistic, kinetic, and synthetic point of view. Regarding the reaction centers, the thermochemistry of these bicyclic systems can be reduced to the thermal behavior of some small parent molecules: cyclobutane, vinylcyclobutane, vinylcyclopropane, and norcaradiene. Among these compounds, the rearrangement of pinane- and pinene-type compounds has been investigated most often due to the fact that these processes are important for the production of starting materials in various branches of the chemical industry.

On heating compounds with a cyclobutane subsystem, fragmentation occurs often leading to two different products, with the substituents in α-position to the bridgehead C-atoms influencing the ratio of competing reaction pathways. Conducting pyrolysis experiments with a vinylcylobutane system yields products arising either from sigmatropic [1,3]-C shifts, fragmentation of the cyclobutane ring, and 1,5-H shift

Table 12. *Acyclic Isomerization Products of Pyrolysis of α-Pinene-Type Compounds* (for assignment of R^1 to R^5, see *Table 3*)



A **B**

Bicyclus	Product **A**	Product **B**	Ref.
α-Pinene (**4**)	**39**	**41**	[45–64][120]
Myrtenal (**28**)		**43**	[66]
Myrtenol (**29a**)		**45a**	[66]
Myrtenyl acetate (**29b**)		**45b**	[66]
2-Acetoxy-10-norpin-2-ene (**30**)		**47**	[67]
Nopol (**31a**)		**49a**	[68–70]
Nopyl acetate (**31b**)		**49b**	[70]
cis-Verbenol (**32a**)		**52**–**55**[a])	[71]
Verbenone (**33**)		**58**	[71][73]
endo-Chrysanthenol (**34a**)	**52**, **66a**[b])		[20]
exo-7-Methyl-*endo*-chrysanthenol (**35**)	**61**, **65**, **66b**[b])		[20]

[a]) Products **53** and **54** are tautomerized products. Products **52** and **55** arise from different [1,5]-H shifts (see *Scheme 12* and *Sect. 3.1.4*). [b]) R^4 or R^5 = OH group; therefore keto–enol tautomerization.

reactions, whereas a C-shift only occurred when the C=C bond system of the vinylcyclobutane moiety is part of the pinene bicycle. Therefore, pyrolysis of compounds similar to β-pinene leads to products resulting from the latter two routes only. Kinetic analysis and careful analysis of products resulting from D-labeling experiments allows deep insights into the reaction mechanisms. Acyclic rearrangement products can participate in consecutive reactions yielding either cyclopentane-type products or fully conjugated open-chain molecules which themselves are able to form cyclohexadienes by sigmatropic-shift and electrocyclic reactions.

The dominant reactions in the case of thermal rearrangements of carenes (and also carane derivatives that yield carenes by thermal elimination of H_2O or AcOH), are sigmatropic [1,5]-H shift reactions furnishing *p*- and/or *m*-menthane derivatives. Ring openings of compounds in the thujane series are good examples for degenerate rearrangements induced by sigmatropic [1,3]-C shifts.

Notwithstanding the multiplicity of monoterpene- and monoterpenoid-type compounds which have been subjected to pyrolysis studies during the last 70 years, systematic and computational studies are still lacking in many cases. Since various sigmatropic reactions in the case of pinane- or pinene-type pyrolysis occur simultaneously, dealing with this topic in computational studies could lead to a better understanding of some important details of the mechanisms of competitive reaction pathways.

REFERENCES[5])

[1] V. Prelog, O. Jeger, *Helv. Chim. Acta* **1983**, *66*, 1307.

[2] 'Nobel Lectures, Chemistry 1922–1941', Elsevier, Amsterdam, 1966; http://nobelprize.org/nobel_prizes/chemistry/laureates/1939/ruzicka-lecture.pdf (June 2009).

[3] a) M. Eggersdorfer, in 'Ullmann's Encyclopedia of Industrial Chemistry', 6th edn., Wiley-VCH, Weinheim, 2002, Vol. 35, pp. 653–671; b) 'Kirk-Othmer Encyclopedia of Chemical Technology', 4th edn., Eds. J. I. Kroschwitz, M. Howe-Grant, John Wiley & Sons, New York, 1997, Vol. 23, pp. 833–882; c) W. F. Erman, 'Chemistry of the Monoterpenes: An Encyclopedic Handbook, Part A and B', in 'Studies in Organic Chemistry', Ed. P. G. Gassman, Marcel Decker, New York, 1985; d) E. Breitmaier, 'Terpene', 2nd edn., Wiley-VCH, Weinheim, 2005; e) K. A. D. Swift, *Top. Catal.* **2004**, *27*, 143; f) N. Ravaiso, F. Zacceria, M. Guidotti, R. Psaro, *Top. Catal.* **2004**, *27*, 157; g) J. L. F. Monteiro, C. O. Veloso, *Top. Catal.* **2004**, *27*, 169; h) H. Surburg, J. Panten, 'Common Fragrance and Flavor Materials', 5th edn., Wiley-VCH, Weinheim, 2006; i) M. B. Erman, B. J. Kane, *Chem. Biodiversity* **2008**, *5*, 910; k) L. Ruzicka, *Helv. Chim. Acta* **1971**, *54*, 1753.

[4] D. V. Banthorpe, B. V. Charlwood, M. J. O. Francis, *Chem. Rev.* **1972**, *72*, 115; D. H. Grayson, *Nat. Prod. Rep.* **1998**, *15*, 439; D. H. Grayson, *Nat. Prod. Rep.* **2000**, *17*, 385; A. Eschenmoser, D. Arigoni, *Helv. Chim. Acta* **2005**, *88*, 3011.

[5] a) G. Egloff, M. Herrman, B. L. Levinson, M. F. Dull, *Chem. Rev.* **1934**, *34*, 287; b) A. A. Frost, R. G. Pearson, 'Kinetik und Mechanismus homogener chemischer Reaktionen', Verlag Chemie, Weinheim 1964, pp. 349–354; c) D. V. Banthorpe, D. Whittaker *Chem. Rev.* **1966**, *66*, 643; d) D. V. Banthorpe, D. Whittaker, *Q. Rev., Chem. Soc.* **1966**, *20*, 373; e) Y. R. Naves, *Russ. Chem. Rev.* **1968**, *37*, 779; f) H. M. Frey, R. Walsh, *Chem. Rev.* **1969**, *69*, 103; g) D. Whittaker, D. V. Banthorpe, *Chem. Rev.* **1972**, *72*, 305; h) R. F. C. Brown, 'Pyrolytic Methods in Organic Chemistry', Academic Press, New York, 1980, pp. 250–253; i) M. Karpf, *Angew. Chem., Int. Ed.* **1986**, *25*, 414; *Angew. Chem.* **1986**, *98*, 413.

[6] a) Z. Goldschmidt, B. Crammer, *Chem. Soc. Rev.* **1988**, *17*, 229; b) P. A. Leber, J. E. Baldwin, *Acc. Chem. Res.* **2002**, *35*, 279; c) J. E. Baldwin, *Chem. Rev.* **2003**, *103*, 1197; d) J. J. Gajewski, 'Hydrocarbon Thermal Isomerizations', 2nd edn., Elsevier, London, 2004; e) J. E. Baldwin, P. A. Leber, *Org. Biomol. Chem.* **2008**, *6*, 36.

[7] B. H. Northrop, K. N. Houk, *J. Org. Chem.* **2006**, *71*, 3.

[8] A. Stolle, B. Ondruschka, *J. Anal. Appl. Pyrolysis* **2009**, *85*, 252.

[9] R. Rienäcker, *Brennst. Chem.* **1964**, *45*, 20.

[10] A. Stolle, B. Ondruschka, W. Bonrath, T. Netscher, M. Findeisen, M. M. Hoffmann, *Chem.–Eur. J.* **2008**, *14*, 6805.

[11] L. Lemée, M. Ratier, J.-G. Duboudin, B. Delmond, *Synth. Commun.* **1995**, *25*, 1313.

[12] H. Pines, N. E. Hoffman, *J. Am. Chem. Soc.* **1954**, *76*, 4417.

[13] J. M. Coxon, R. P. Garland, M. P. Hartshorn, *Aust. J. Chem.* **1972**, *25*, 353.

[14] K. H. Schulte-Elte, M. Gadola, G. Ohloff, *Helv. Chim. Acta* **1971**, *54*, 1813.

[15] J. M. Coxon, R. P. Garland, M. P. Hartshorn, *Aust. J. Chem.* **1972**, *25*, 947.

[16] J. Gebauer, S. Blechert, *Synlett* **2005**, 2826.

[17] J. M. Coxon, R. P. Garland, M. P. Hartshorn, *Aust. J. Chem.* **1972**, *25*, 2409.

[18] A. Bokranz, K. H. Müller, DE Pat. 1234900, 1967.

[19] S. Lemberg, GB Pat. 953776, 1963.

[20] P. A. Euan Cant, J. M. Coxon, M. P. Hartshorn, *Aust. J. Chem.* **1975**, *28*, 621.

[21] P. A. Euan Cant, J. M. Coxon, M. P. Hartshorn, *Aust. J. Chem.* **1975**, *28*, 391.

[22] A. L. Rummelsburg, *J. Am. Chem. Soc.* **1944**, *66*, 1718.

[23] V. N. Ipatieff, W. D. Huntsman, H. Pines, *J. Am. Chem. Soc.* **1953**, *75*, 6222.

[24] H. Pines, N. E. Hoffman, V. N. Ipatieff, *J. Am. Chem. Soc.* **1954**, *76*, 4412.

[25] R. Rienäcker, G. Ohloff, *Angew. Chem.* **1961**, *73*, 240.

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[5]) In case of multiple patent publications of one topic from the same author(s), only the oldest patent reference is given.

[26] J. Tanaka, T. Katagiri, K. Izawa, *Bull. Chem. Soc. Jpn.* **1970**, *44*, 130.
[27] M. Nomura, Y. Fujihara, Y. Matsubara, *Yukagaku* **1979**, *28*, 919 (*Chem. Abstr.* **1980**, *92*, 198534).
[28] J.-B. Lee, C.-B. Kim, *J. Korean Soc. Anal. Sci.* **1992**, *5*, 373 (*Chem. Abstr.* **1993**, *119*, 117556).
[29] A. Stolle, B. Ondruschka, W. Bonrath, *Eur. J. Org. Chem.* **2007**, 2310.
[30] A. L. Rummelsburg, US Pat. 2388084, 1945; K. Ziegler, GB Pat. 910879, 1962; W. Daniewski, A. Dambska, *Tluszcze, Srodki Piorace, Kosmetyki* **1969**, *13*, 229 (*Chem. Abstr.* **1970**, *72*, 100903; A. F. Thomas, *Pure Appl. Chem.* **1990**, *62*, 1369; E. P. Serebryakov, N. C. Hao, M. V. Mavrov, *Pure Appl. Chem.* **1990**, *62*, 2041; V. V. Godin, V. V. Molchanov, R. A. Buyanov, G. A. Tolstikov, RU Pat. 2186758, 2002.
[31] A. Stolle, W. Bonrath, B. Ondruschka, D. Kinzel, L. González, *J. Phys. Chem. A* **2008**, *112*, 5885.
[32] D. Kinzel, Diploma Thesis, Friedrich-Schiller University Jena at Jena, 2008 (available online: http://www.theochem.uni-jena.de/people/thesis/Diplom_Kinzel.pdf); manuscript in preparation.
[33] W. D. Huntsman, V. C. Solomon, D. Eros, *J. Am. Chem. Soc.* **1958**, *80*, 5455.
[34] G. Ohloff, E. Klein, *Tetrahedron* **1962**, *18*, 37.
[35] Studiengesellschaft Kohle mbH (assignee), FR Pat. 1328113, 1963.
[36] J. Texter, E. S. Stevens, *J. Org. Chem.* **1979**, *44*, 3222.
[37] R. Serchelli, A. L. B. Ferreira, L. H. B. Baptistella, U. Schuchardt, *J. Agric. Food Chem.* **1997**, *45*, 1361.
[38] I. I. Il'ina, I. L. Simakova, V. A. Semikolenov, *Kinet. Catal.* **2001**, *42*, 686.
[39] V. A. Semikolenov, I. I. Illína, I. L. Simakova, *Appl. Catal., A* **2001**, *211*, 91.
[40] V. A. Semikolenov, I. I. Illína, I. L. Simakova, *J. Mol. Catal. A: Chem.* **2002**, *182–183*, 383.
[41] K. H. Schulte-Elte, CH Pat. 543464, 1973.
[42] E. A. Klein, U.S. Patent 2972633, 1961.
[43] J. M. Coxon, R. P. Garland, M. P. Hartshorn, *J. Chem. Soc. D* **1970**, 1709.
[44] H. M. R. Hoffmann, *Angew. Chem., Int. Ed.* **1969**, *8*, 556; *Angew. Chem.* **1969**, *81*, 597; W. Oppolzer, V. Snieckus, *Angew. Chem., Int. Ed.* **1978**, *17*, 476; *Angew. Chem.* **1978**, *90*, 506; K. Mikami, M. Shimizu, *Chem. Rev.* **1992**, *92*, 1021.
[45] D. F. Smith, *J. Am. Chem. Soc.* **1927**, *49*, 43; J. B. Conant, G. H. Carlson, *J. Am. Chem. Soc.* **1929**, *51*, 3464.
[46] L. A. Goldblatt, S. Palkin, *J. Am. Chem. Soc.* **1941**, *63*, 3517.
[47] R. E. Fuguitt, J. E. Hawkins, *J. Am. Chem. Soc.* **1945**, *67*, 242.
[48] T. R. Savich, L. A. Goldblatt, *J. Am. Chem. Soc.* **1945**, *67*, 2027.
[49] R. E. Fuguitt, J. E. Hawkins, *J. Am. Chem. Soc.* **1947**, *69*, 319.
[50] H. G. Hunt, J. E. Hawkins, *J. Am. Chem. Soc.* **1950**, *72*, 5618.
[51] T. R. Savich, L. A. Goldblatt, U.S. Patent 2507546, 1950.
[52] J. E. Hawkins, H. G. Hunt, *J. Am. Chem. Soc.* **1951**, *73*, 5379.
[53] J. E. Hawkins, W. A. Burris, *J. Org. Chem.* **1959**, *24*, 1507.
[54] K. Riistama, O. Harva, *Finn. Chem. Lett.* **1974**, *4*, 132.
[55] J. J. Gajewski, C. M. Hawkins, *J. Am. Chem. Soc.* **1986**, *108*, 838; J. J. Gajewski, I. Kuchuk, C. M. Hawkins, R. Stine, *Tetrahedron* **2002**, *58*, 6943.
[56] A. Yermakova, A. M. Chibiryaev, I. V. Kozhevnikov, V. I. Anikeev, *Chem. Eng. Sci.* **2007**, *62*, 2414.
[57] A. M. Chibiryaev, A. Yermakova, I. V. Kozhevnikov, O. I. Sal'nikova, V. I. Anikeev, *Russ. Chem. Bull., Int. Ed.* **2007**, *56*, 1234.
[58] A. Yermakova, A. M. Chibiryaev, I. V. Kozhevnikov, V. I. Anikeev, *J. Supercrit. Fluids* **2008**, *45*, 74.
[59] B. A. Arbusow, *Ber. Dtsch. Chem. Ges.* **1934**, *67*, 563; B. A. Arbusow, *Ber. Dtsch. Chem. Ges.* **1934**, *67*, 569; B. A. Arbusow, *Ber. Dtsch. Chem. Ges.* **1934**, *67*, 1946; B. A. Arbusow, *J. Gen. Chem. USSR* **1936**, *6*, 206 (*Chem. Abstr.* **1937**, *31*, 24981).
[60] J. de Pascual Teresa, I. Sanchez Bellido, M. R. Alberdi Albistegui, A. san Feliciano, M. Grande Benito, *Anal. Quim.* **1978**, *74*, 301.
[61] F. Wattimena, DE Pat. 2744386, 1978.
[62] A. M. Chibiryaev, V. I. Anikeev, A. Yermakova, P. E. Mikenin, I. V. Kozhevnikov, O. I. Sal'nikova, *Russ. Chem. Bull., Int. Ed.* **2006**, *55*, 987.

[63] V. I. Anikeev, A. Ermakova, A. M. Chibiryaev, I. V. Kozhevnikov, P. E. Mikenin, *Russ. J. Phys. Chem. A* **2007**, *81*, 711.
[64] A. Stolle, B. Ondruschka, M. Findeisen, *J. Org. Chem.* **2008**, *73*, 8228.
[65] R. L. Burwell Jr., *J. Am. Chem. Soc.* **1951**, *73*, 4461.
[66] E. A. Klein, U.S. Patent 2821547, 1958.
[67] J. M. Coxon, R. P. Garland, M. P. Hartshorn, *Aust. J. Chem.* **1970**, *23*, 2531.
[68] J. P. Bain, *J. Am. Chem. Soc.* **1946**, *68*, 638.
[69] J. P. Bain, A. H. Best, U.S. Patent 2453110, 1948.
[70] J. P. Bain, A. H. Best, R. L. Webb, *J. Am. Chem. Soc.* **1952**, *74*, 4292.
[71] Glidden Company (assignee), GB Pat. 755667, 1956; J. P. Bain, E. A. Klein, H. G. Hunt, A. B. Booth, W. Y. Gary, DE Pat. 1043324, 1958; J. P. Bain, H. G. Hunt, E. A. Klein, A. B. Booth, U.S. Patent 2972632, 1961.
[72] G. Ohloff, *Angew. Chem., Int. Ed.* **1970**, *9*, 743; *Angew. Chem.* **1970**, *82*, 777; D. Joulain, F. Rouessac, *J. Chem. Soc., Chem. Commun.* **1972**, 314.
[73] J. A. Retamar, *Essenze, Derivati Agrumari* **1991**, *59*, 170 (*Chem. Abstr.* **1991**, *114*, 6830).
[74] K. Dietrich, H. Musso, *Chem. Ber.* **1974**, *107*, 731.
[75] B. V. Carpenter, *J. Am. Chem. Soc.* **1985**, *107*, 5730; J. S. Chickos, H. M. Frey, *J. Chem. Soc., Perkin Trans. 2* **1987**, 365.
[76] A. Ermakova, A. M. Chibiryaev, P. E. Mikenin, O. I. Sal'nikova, V. I. Anikeev, *Russ. J. Phys. Chem. A* **2008**, *82*, 62; V. I. Anikeev, A. Ermakova, P. E. Mikenin, A. M. Chibiryaev, O. I. Sal'nikova, RU Pat. 2320630, 2008.
[77] N. Li, S. Chen, *Huaxue Shijie* **2001**, *42*, 178 (*Chem. Abstr.* **2001**, *136*, 247701).
[78] R. L. Webb, J. P. Bain, *J. Am. Chem. Soc.* **1953**, *75*, 4279.
[79] G. Ohloff, *Tetrahedron Lett.* **1960**, *1*, 10.
[80] A. B. Booth, E. A. Klein, U.S. Patent 2815383, 1957.
[81] N. V. Maksimchuk, I. L. Simakova, V. A. Semikolenov, *React. Kinet. Catal. Lett.* **2004**, *82*, 165.
[82] G. Köbrich, *Angew. Chem., Int. Ed.* **1973**, *12*, 464; *Angew. Chem.* **1973**, *85*, 494; G. L. Buchanan, *Chem. Soc. Rev.* **1974**, *3*, 41; H. Hopf, 'Classics in Hydrocarbon Chemistry', Wiley-VCH, Weinheim 2000; B. R. Bear, S. M. Sparks, K. J. Shea, *Angew. Chem., Int. Ed.* **2001**, *40*, 820; *Angew. Chem.* **2001**, *113*, 864; I. Novak, *J. Chem. Inf. Model.* **2005**, *45*, 334.
[83] L. Steinbach, E. T. Theimer, B. M. Mitzner, *Can. J. Chem.* **1964**, *42*, 959.
[84] J. E. Hawkins, J. W. Vogh, *J. Phys. Chem.* **1953**, *57*, 902.
[85] J. de Pascual Teresa, I. Sanchez Bellido, M. R. Alberdi Albistegui, A. san Feliciano, M. Grande Benito, *Anal. Quim.* **1978**, *74*, 305.
[86] J. Y. Luo, H. Z. Wang, S. J. Peng, *Linchan Huaxue Yu Gongye* **2000**, *20*, 47 (*Chem. Abstr.* **2000**, *134*, 30604).
[87] A. Stolle, C. Brauns, M. Nüchter, B. Ondruschka, W. Bonrath, M. Findeisen, *Eur. J. Org. Chem.* **2006**, 3317.
[88] M. B. Kolicheski, L. C. Cocco, D. A. Mitchell, M. Kaminski, *J. Anal. Appl. Pyrolysis* **2007**, *80*, 92.
[89] A. Stolle, B. Ondruschka, *J. Anal. Appl. Pyrolysis* **2008**, *81*, 136.
[90] A. Stolle, B. Ondruschka, W. Bonrath, *J. Anal. Appl. Pyrolysis* **2008**, *83*, 26.
[91] C. F. Mayer, J. K. Crandall, *J. Org. Chem.* **1970**, *35*, 2688.
[92] S. Roy, K. Chakrabarty, G. K. Das, *J. Mol. Struct. (THEOCHEM)* **2007**, *820*, 112.
[93] J. M. Coxon, R. P. Garland, M. P. Hartshorn, *J. Chem. Soc., Chem. Commun.* **1970**, 542.
[94] J. M. Coxon, R. P. Garland, M. P. Hartshorn, *Aust. J. Chem.* **1971**, *24*, 1481.
[95] G. Ohloff, W. K. Giersch, *Helv. Chim. Acta* **1977**, *60*, 1496; G. Ohloff, W. K. Giersch, DE Pat. 2750604, 1978.
[96] A. F. Thomas, B. William, G. Ohloff, *Helv. Chim. Acta* **1969**, *52*, 1249.
[97] V. V. Bazyl'chik, P. I. Fedorov, E. D. Skakovskii, L. I. Vinogradov, *J. Org. Chem. USSR* **1981**, *17*, 268.
[98] E. A. Klein, U.S. Patent 2945067, 1960.
[99] J. M. Coxon, R. P. Garland, M. P. Hartshorn, *Chem. Commun.* **1971**, 1131.
[100] A. B. Booth, E. A. Klein, U.S. Patent 2803659, 1957.

[101] W. Cocker, D. P. Hanna, P. V. R. Shannon, *Tetrahedron Lett.* **1966**, *7*, 4547; W. Cocker, D. P. Hanna, P. V. R. Shannon, *J. Chem. Soc. C* **1968**, 489.
[102] G. Ohloff, *Chem. Ber.* **1960**, *93*, 2673.
[103] G. Ohloff, *Tetrahedron Lett.* **1965**, *6*, 3795.
[104] K. Gollnick, *Tetrahedron Lett.* **1966**, *7*, 327.
[105] K. Gollnick, G. Schade, *Tetrahedron* **1966**, *22*, 123.
[106] W. Skorianetz, G. Ohloff, *Helv. Chim. Acta* **1975**, *58*, 771.
[107] O. G. Vyglazov, V. A. Chuiko, E. N. Manukov, *Vestn. Akad. Nauk BSSR, Ser. Khim. Nauk* **1988**, 40 (*Chem. Abstr.* **1989**, *111*, 195103), and refs. cit. therein.
[108] G. Maier, *Angew. Chem., Int. Ed.* **1967**, *6*, 402; *Angew. Chem.* **1967**, *79*, 446; J. A. Berson, *Acc. Chem. Res.* **1968**, *1*, 152.
[109] A. A. Jarzęcki, J. J. Gajewski, E. R. Davidson, *J. Am. Chem. Soc.* **1999**, *121*, 6928.
[110] W. von E. Doering, J. B. Lambert, *Tetrahedron* **1963**, *19*, 1989.
[111] W. von E. Doering, E. K. G. Schmidt, *Tetrahedron* **1971**, *27*, 2005.
[112] W. von E. Doering, T. Zhang, E. K. G. Schmidt, *J. Org. Chem.* **2006**, *71*, 5688.
[113] B. M. Mitzner, E. T. Theimer, *J. Org. Chem.* **1962**, *27*, 3359.
[114] R. H. Eastman, A. V. Winn, *J. Am. Chem. Soc.* **1960**, *82*, 5908.
[115] W. von E. Doering, M. R. Willcott, M. Jones Jr., *J. Am. Chem. Soc.* **1962**, *84*, 1224.
[116] J. W. Wheeler Jr., R. H. Eastman, *J. Am. Chem. Soc.* **1959**, *81*, 236, and refs. cit. therein.
[117] W. D. Huntsman, T. H. Curry, *J. Am. Chem. Soc.* **1958**, *80*, 2252.
[118] W. Pickenhagen, G. Ohloff, R. K. Russel, W. D. Roth, *Helv. Chim. Acta* **1978**, *61*, 2249.
[119] W. D. Huntsman, R. P. Hall, *J. Org. Chem.* **1962**, *27*, 1988.
[120] T. Sasaki, S. Eguchi, H. Yamada, *Tetrahedron Lett.* **1971**, *12*, 99.
[121] J. Wolinsky, B. Chollar, M. D. Baird, *J. Am. Chem. Soc.* **1962**, *84*, 2772.
[122] E. D. Parker, L. A. Goldblatt, *J. Am. Chem. Soc.* **1950**, *72*, 2151.
[123] K. J. Crowley, S. G. Traynor, *Tetrahedron Lett.* **1975**, *16*, 3555.
[124] K. J. Crowley, S. G. Traynor, *Tetrahedron* **1978**, *34*, 2783.

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