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Mechanism of Wine Lactone Formation: Demonstration of Stereoselective Cyclization and 1,3-Hydride Shift

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The cyclization mechanism of (*E*)-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid to wine lactone under acidic aqueous conditions was investigated using the two stereoselectively deuterium-labeled precursors (2*E*,6*R*,7*Z*)-[8-^{2}H]-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid and (2*E*,7*E*)-(±)-[8-^{2}H]-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid. A detailed analysis of the generated wine lactone isomers by enantioselective multidimensional gas chromatography (MDGC)/ion trap tandem mass spectrometry demonstrates that the formation of wine lactone proceeds via a nonenzymatic stereoselective cationic cyclization cascade that includes a 1,3-hydride shift. Usually, such mechanisms are features of cyclization reactions that are catalyzed by terpene cyclases. This nonenzymatic conversion of an acyclic precursor to a bicyclic monoterpene under relevant cationic cyclization conditions has rarely been observed and confirms recent suggestions that the precursor itself can provide the chemical functionality required for specific steps in the cyclization cascade.

KEYWORDS: Wine lactone; monoterpenes; stereoselective cyclization; 1,3-hydride shift; deuterium labeling; ion-trap tandem mass spectrometry; enantioselective gas chromatography; flavor

INTRODUCTION

Monoterpenoid benzofuran derivatives are widespread natural products and are well-known as aroma-active flavoring ingredients. Within this group, the *p*-menthane lactones and ethers such as dill ether, linden ether, mintlactone, menthofuran, and wine lactone **1a** are the most prominent examples, and their occurrence, synthesis, and sensory properties have been the topic of several reviews (*1*−*3*). By far, the most active aroma compound within this group is wine lactone **1a**, which has a remarkably low odor threshold of 0.02 pg/L air for its natural 3*S*,3a*S*,7a*R* isomer (see **Figure 6a**). The chemical structure and the absolute configuration of the natural isomer of wine lactone were elucidated by Guth (*4*), and its significant contribution to the aroma of wines made from the varieties Gewürztraminer and Scheurebe was demonstrated by the same author (*5*, *6*).

So far, wine lactone has, inter alia, been detected in black pepper (*7*), apples (*8*), orange juice (*9*), grapefruit juice (*10*), orange essential oil (*11*), clementine peel oil, and several other grape wine varieties (*12*). In all of these foods, wine lactone is present in the parts per billion range but nevertheless contributes to the overall aroma because of its extremely low odor threshold value resulting in high to moderate odor activity values (OAVs; (*13*)).

Despite its importance, only a few investigations of the formation of wine lactone have been performed to date. As a precursor, (*E*)-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, **2** (see **Figure 1** for the chemical structure of its deuterium-labeled isotopomer), could be isolated from a Riesling wine in free form (*3*) and in the form of its glucose ester (*14*, *15*). The formation of wine lactone in acidic medium through the cyclization of (*E*)-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, **2**, has been demonstrated (*14*−*16*), and the enantioselective analysis of wine lactones that are generated from racemic or enantiopure (*R*)-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid has shown the presence of a racemic mixture (*16*). However, it still remains unclear how the enantiomerically pure wine lactone 3*S*,3a*S*,-7a*R* isomer, which was isolated from a Gewürztraminer wine (*4*), is actually generated. In nature, such structural and stereochemical precision is usually achieved by terpene cyclases that control the synthesis of cyclic terpenoids and produce one unique cyclization product (*17*−*19*).

Herein, we present a study of the cyclization mechanism of (*E*)-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, **2**, using two stereoselectively deuterium-labeled precursors. A detailed analysis of the generated wine lactone isomers by enantioselective multidimensional gas chromatography (MDGC)/ion trap tandem mass spectrometry demonstrates that the cyclization is, indeed, stereoselective.

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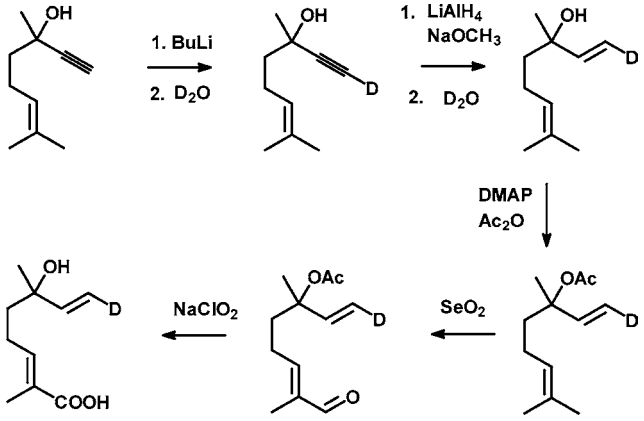
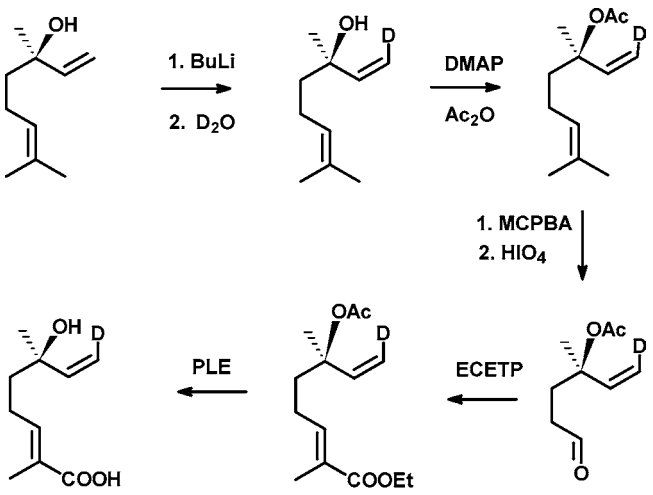


(7*E*)-[8-^{2}H]-2

Figure 1. Synthesis of (2*E*,7*E*)-(±)-[8-^{2}H]-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, (7*E*)-[8-^{2}H]-**2**. BuLi, butyllithium; DMAP, 4-dimethylaminopyridine; Ac_2O, acetic anhydride.



(7Z)-[8-^{2}H]-2

Figure 2. Synthesis of (2*Z*,6*R*,7*E*)-[8-^{2}H]-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, (7Z)-[8-^{2}H]-**2**. BuLi, butyllithium; DMAP, 4-dimethylaminopyridine; Ac_2O, acetic anhydride; MCPBA, *meta*-chloroperbenzoic acid; ECETP, (1-ethoxycarbonylethylidene)triphenylphosphane; PLE, pig liver esterase.

MATERIALS AND METHODS

Chemicals. All reagents were purchased from Fluka (Taufkirchen, Germany) or Aldrich (Steinheim, Germany). Dehydrolinalool as a starting material for the synthesis of (2*E*,7*E*)-(±)-[8-^{2}H]-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, (7*E*)-[8-^{2}H]-**2**, was a gift from Wolfgang Krause (BASF, Ludwigshafen, Germany). Wine lactone cis stereoisomers **1a**−**1c** and trans stereoisomers were synthesized according to Guth (*4*).

Synthesis. (2*E*,7*E*)-(±)-[8-^{2}H]-2,6-Dimethyl-6-hydroxyocta-2,7-dienoic acid, (7*E*)-[8-^{2}H]-**2**, was synthesized by combining several previously published procedures as outlined in **Figure 1**. The key intermediate, (1*E*)-(±)-[1-^{2}H]-linalool, was synthesized according to the method of Croteau et al. by substituting ^3H_2O with ^2H_2O to introduce the deuterium label (*20*). (1*E*)-(±)-[1-^{2}H]-Linalool was converted into (2*E*,7*E*)-(±)-[8-^{2}H]-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, (7*E*)-[8-^{2}H]-**2**, by stepwise oxidation using selenium dioxide and $NaClO_2$, as described by Bonnländer (*16*).

(2*Z*,6*R*,7*E*)-[8-^{2}H]-2,6-Dimethyl-6-hydroxyocta-2,7-dienoic acid, (7*Z*)-[8-^{2}H]-**2**, was synthesized by combining several previously published procedures as outlined in **Figure 2**. The key intermediate, (1*Z*)-(3*R*)-[1-^{2}H]-linalool, was synthesized according to the method of Cuvigny et al. (*21*). (1*Z*)-(3*R*)-[1-^{2}H]-Linalool was converted into ethyl (2*Z*,6*R*,7*E*)-[8-^{2}H]-6-acetyl-2,6-dimethyl-6-hydroxyocta-2,7-dienoate by a reaction sequence previously published by Hiraga et al. (*22*). (2*Z*,6*R*,7*E*)-[8-^{2}H]-6-Acetyl-2,6-dimethyl-6-hydroxyocta-2,7-dienoate was treated with pig liver esterase as previously described (*16*) to yield (7*Z*)-[8-^{2}H]-**2**.

The stereochemistry of the monodeuterated target compounds was assigned via the linalool key intermediates by NMR spectroscopy as previously described (*21*). (1*Z*)-(3*R*)-[1-^{2}H]-Linalool exhibited a $^3J_{1,2}$ coupling constant of 11 Hz, providing evidence for a *Z*-configured double bond between C1 and C2, whereas (1*E*)-(±)-[1-^{2}H]-linalool exhibited a $^3J_{1,2}$ coupling constant of 17 Hz, providing evidence for an *E*-configured double bond between C1 and C2. Target compounds (7*E*)-[8-^{2}H]-**2** and (7*Z*)-[8-^{2}H]-**2** were characterized by GC/MS after acetylation/esterification as the acetoxymethyl ester and had virtually identical mass spectra.

EI-MS (70 eV): 43 (*10*), 56 (*16*), 72 (*25*), 81 (*28*), 94 (*20*), 122 (*33*), 139 (*10*), 149 (*9*), 166 (*13*).

GC/MS and ^{1}H NMR data of all other synthesized compounds are in agreement with previously published data. The degrees of labeling of (7*E*)-[8-^{2}H]-**2** and (7*Z*)-[8-^{2}H]-**2** were estimated to be >95% as determined by GC/MS and ^{1}H NMR analysis of the linalool key intermediates.

(7*E*)-[8-^{2}H]-**2** and (7*Z*)-[8-^{2}H]-**2** were cyclized to wine lactone by simultaneous distillation extraction (SDE) as previously described (*16*, *23*). For this reaction, 100 mg of (7*E*)-[8-^{2}H]-**2** or (7*Z*)-[8-^{2}H]-**2** was added to 100 mL of a citrate buffer (pH 3.2). The cyclization products were extracted into pentane/diethyl ether (1/1 v/v). The distillation was stopped after 4 h, and the extract was dried over anhydrous Na_2SO_4 and concentrated using a Vigreux column at 40 °C.

Gas Chromatography/Mass Spectrometry (GC/MS). The GC/MS analysis of the synthesized compounds was carried out on a Fisons Instruments GC 8065, coupled to a Fisons Instruments MD800 mass spectrometer. Chromatography was performed with a fused-silica column (30 m × 0.25 mm i.d., 0.23 μm) coated with SE 52 and programmed from 60 °C (5 min isothermal) to 260 °C (20 min isothermal) at 5 °C/min with a 2 mL/min He flow rate and a 20 mL/min split. Mass spectra were obtained at 70 eV with an ion source temperature of 200 °C in full-scan mode (50−300 amu).

^{1}H NMR Spectroscopy. NMR spectra were obtained with a Bruker ARX 300 spectrometer, at 300 MHz, in $CDCl_3$ with TMS as the internal standard.

Enantioselective Multidimensional Gas Chromatography/Ion-Trap Tandem Mass Spectrometry (enantio-MDGC/MS/MS). The enantio-MDGC/MS/MS analysis of the labeled cyclization products was performed with a Siemens SiChromat 2-8 instrument coupled to a Finnigan MAT GCQ apparatus. The two capillary columns of the MDGC instrument were coupled to a live-T-switching device. The precolumn was the same as the column of the GC/MS system described above, and the experimental conditions were as follows: carrier gas, He; split, 20 mL/min; injector temperature, 250 °C; detector, FID; oven temperature, 60 °C (5 min isothermal) to 250 °C at 5 °C/min. The chiral main column used was a 30 m × 0.25 mm i.d. column with a 0.25-μm film thickness of DiMe-β [heptakis-(2, 3-di-*O*-methyl-6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin] in SE 52 [carrier gas, He; oven temperature, 60 °C (25 min isothermal) to 200 °C at 2 °C/min]. The main column was coupled to the transfer line of the mass spectrometer using an open split interface with a helium sweeping flow of 1 mL/min (transfer line temperature, 250 °C; EI, 70 eV; ion-trap manifold temperature, 170 °C). The spectra were recorded in full-scan mode (50−250 amu) or in MS/MS mode. The MS/MS operating conditions and collision-induced dissociation (CID) parameters were as follows: EI, 70 eV; isolation width for parent ion: 1.0 *m*/*z*; excitation *q* value: 0.45.

Enantioselective Gas Chromatography/Mass Spectrometry (Enantio-GC/MS). The enantio-GC/MS analysis of the labeled cyclization products was carried out with a Varian GC Series 3400 instrument, coupled to a Finnigan MAT Magnum mass spectrometer. Chromatography was performed with a 30 m × 0.23 mm i.d. column with a 0.23-μm film thickness of DiButyryl-γ [oktakis-(2,3-di-*O*-butyryl-6-*O*-*tert*-butyldimethylsilyl)-γ-cyclodextrin] in OV 1701-vi; the temperature was programmed from 60 °C (5 min isothermal) to 260 °C (20 min

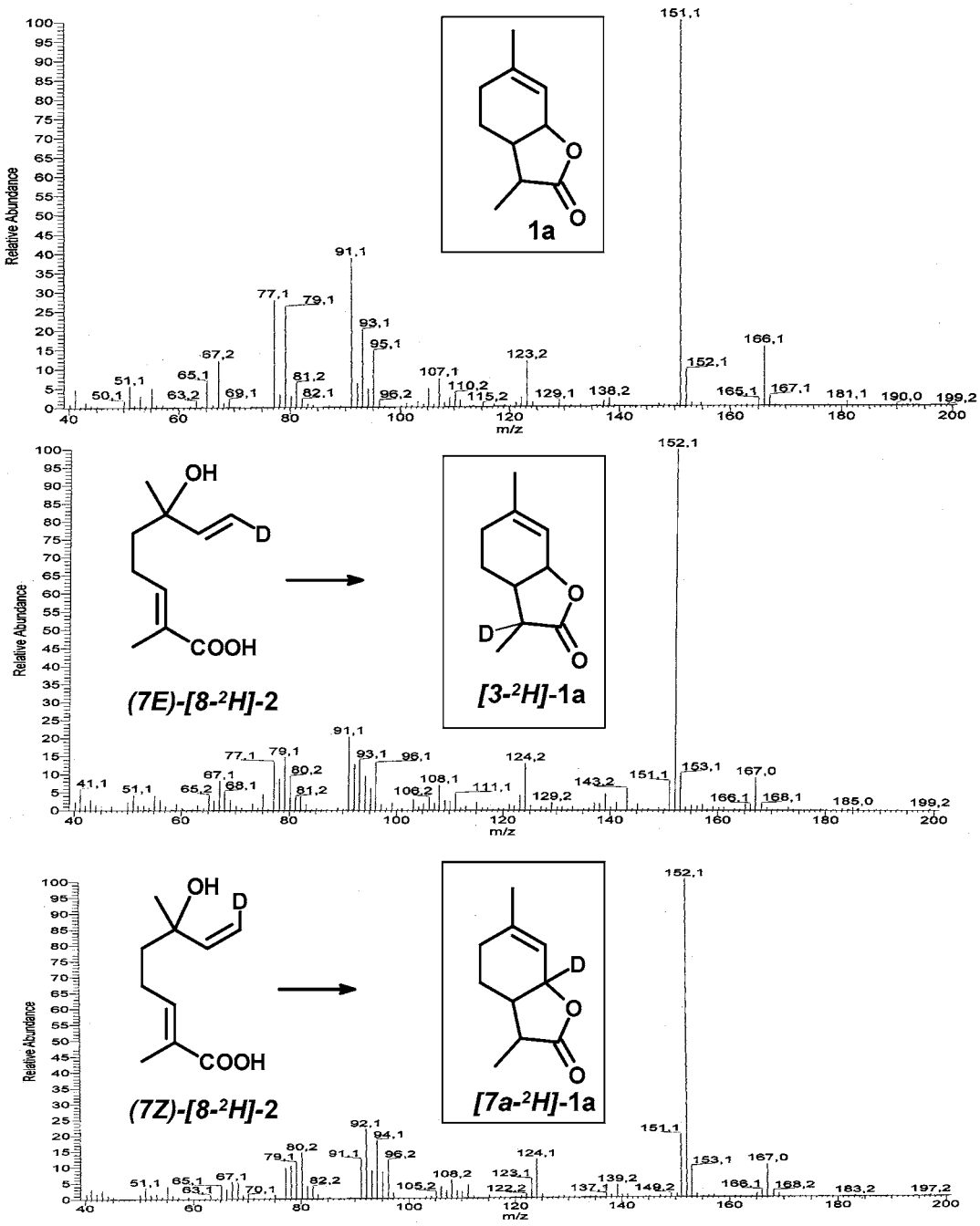


Figure 3. Full-scan mass spectra of wine lactone **1a**; [3-^{2}H]-wine lactone, [3-^{2}H]-**1a**; and [7a-^{2}H]-wine lactone, [7a-^{2}H]-**1a**. The deuterium-labeled isotopomers were generated from the indicated labeled precursors by SDE.

isothermal) at 5 °C/min, and a 2 mL/min He flow rate and 20 mL/min split were used . Mass spectra were obtained at 70 eV with an ion source temperature of 200 °C in full-scan mode (50−300 amu).

RESULTS

To investigate the cyclization mechanism of wine lactone formation from its precursor (*E*)-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid **2** in more detail, the regio- and stereoselectively deuteriated precursors (2*E*,7*E*)-(±)-[8-^{2}H]-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, (7*E*)-[8-^{2}H]-**2**, and (2*E*,6*R*,7*Z*)-[8-^{2}H]-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, (7*Z*)-[8-^{2}H]-**2**, were synthesized according to **Figures 1** and **2**.

(7*E*)-[8-^{2}H]-**2** and (7*Z*)-[8-^{2}H]-**2** were cyclized to wine lactone by simultaneous distillation extraction (SDE). GC/MS analysis on a nonchiral column revealed that both precursors yielded only one cis ring-fused diastereoisomer that coeluted with a wine lactone standard. The trans diastereoisomers were not detectable. These results demonstrate that the cyclization of **2** is highly diastereoselective and confirms earlier findings (*3*, *14*). The full-scan mass spectra of these cis ring-fused diastereomers, denoted as [7a-^{2}H]-**1** and [3-^{2}H]-**1**, are shown in **Figure 3** together with the mass spectrum of a wine lactone standard. The mass spectra reveal that the wine lactone generated from (7*E*)-[8-^{2}H]-**2** and (7*Z*)-[8-^{2}H]-**2** completely retained the deuterium atom of the respective precursor. The M^+ peak at $m/z = 166$ and the $[M - 15]^+$ base peak at $m/z = 151$ are clearly shifted by one mass unit to $m/z = 167$ and $m/z = 152$, respectively. The deuterium-labeled wine lactones show similar but clearly distinguishable mass spectra, providing evidence that the deuterium atom is attached to different carbon atoms of the carbon skeleton.

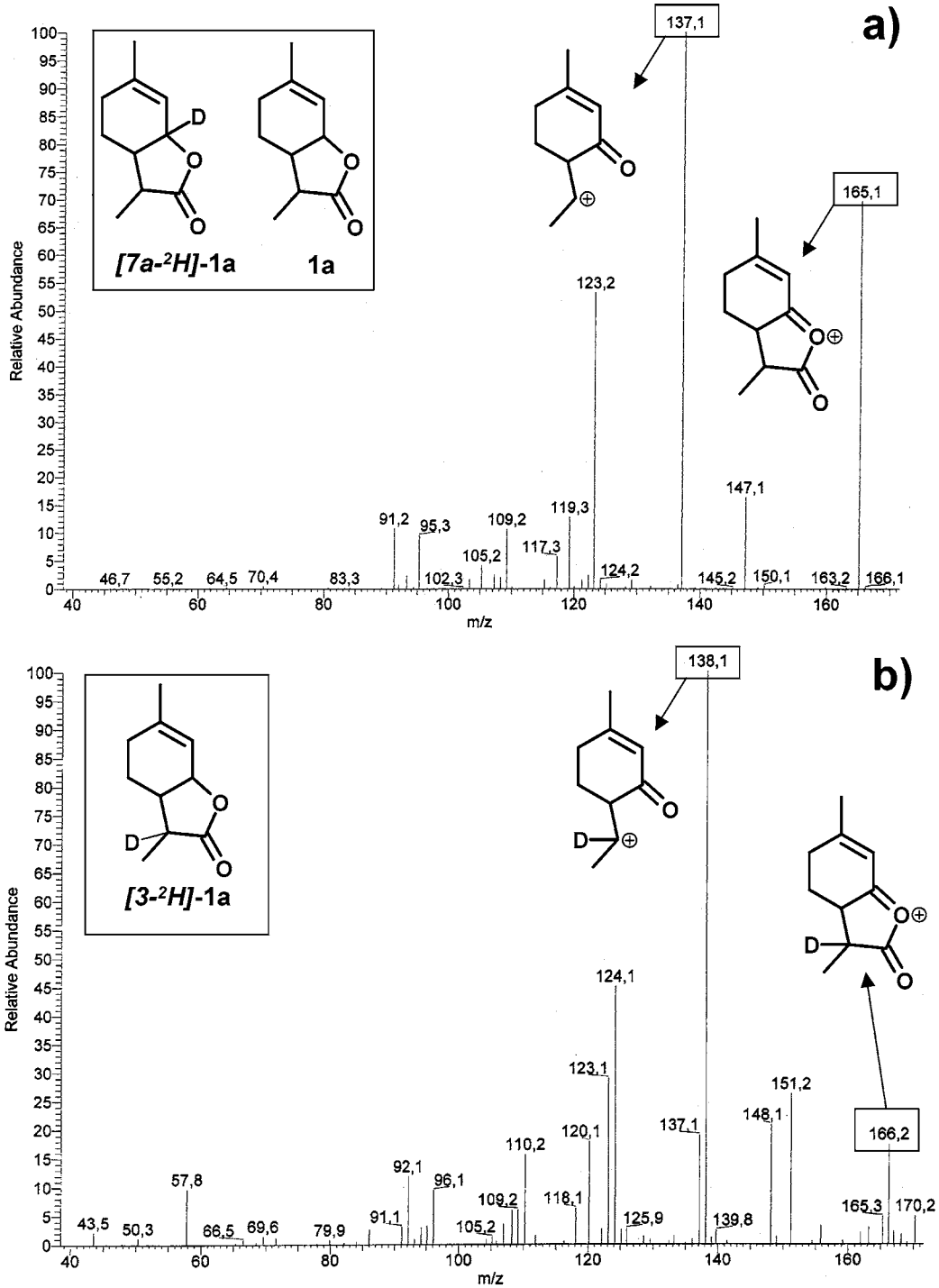


Figure 4. (**a**) MS/MS mass spectrum of wine lactone **1a** and [7a-^{2}H]-wine lactone, [7a-^{2}H]-**1a**; parent ion $m/z = 165$. (**b**) MS/MS mass spectrum of [3-^{2}H]-wine lactone, [3-^{2}H]-**1a**; parent ion $m/z = 166$.

Because the methylene C8 of the precursor **2** becomes the tertiary C7a of wine lactone **1** (for numbering of the carbon skeleton of wine lactone according to IUPAC rules, see **Figure 6a**), the cisoid or transoid hydrogen atom (or deuterium atom) at C8 must be cleaved off and re-bound by an intramolecular hydride or deuterium shift. Thus, (7*E*)-[8-^{2}H]-**2** and (7*Z*)-[8-^{2}H]-**2** yield different monodeuterated wine lactone isotopomers.

The positions of the deuterium atoms in the different wine lactone isotopomers generated from (7*E*)-[8-^{2}H]-**2** and (7*Z*)-[8-^{2}H]-**2** could be determined by elucidation of the mass fragmentation mechanism of wine lactone. This was achieved by combining MS/MS experiments that were carried out in this study (see **Table 1**) with previously published data on the mass spectra of labeled [3-$^2H_3$]-wine lactone (*6*) and high-resolution MS data on the mass fragments of wine lactone (*24*).

The mass fragmentation mechanisms that give rise to the fragments at $m/z = 165$, 151, 137 and 123 are depicted in **Figure 5**. The base peak at $m/z = 151$ is generated by the loss of a methyl group. Surprisingly, this main fragmentation pathway is not initiated by the simple loss of the C3 methyl group, because labeled [3-$^2H_3$]-wine lactone shows a base peak at $m/z = 154$, which means the CD_3 group at C3 is retained. This observation can be explained only by the loss of the C6 methyl group and requires the migration of the double bond between C6 and C7 to another position prior to fragmentation. As outlined in **Figure 5**, the migration is initiated by a rearrange-

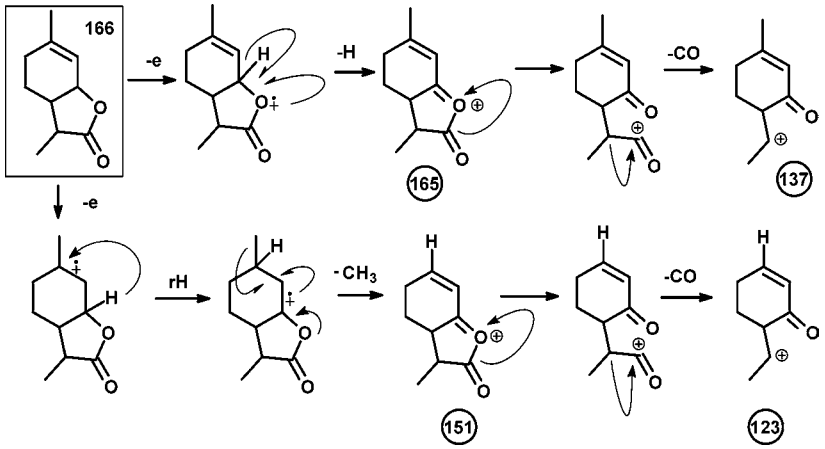


Figure 5. Proposed fragmentation mechanism of wine lactone in electron-impact mass spectrometry. The assignments were made on the basis of ion-trap MS/MS experiments and molecular formulas of the fragments determined by high-resolution mass spectrometry (see also **Table 1**).

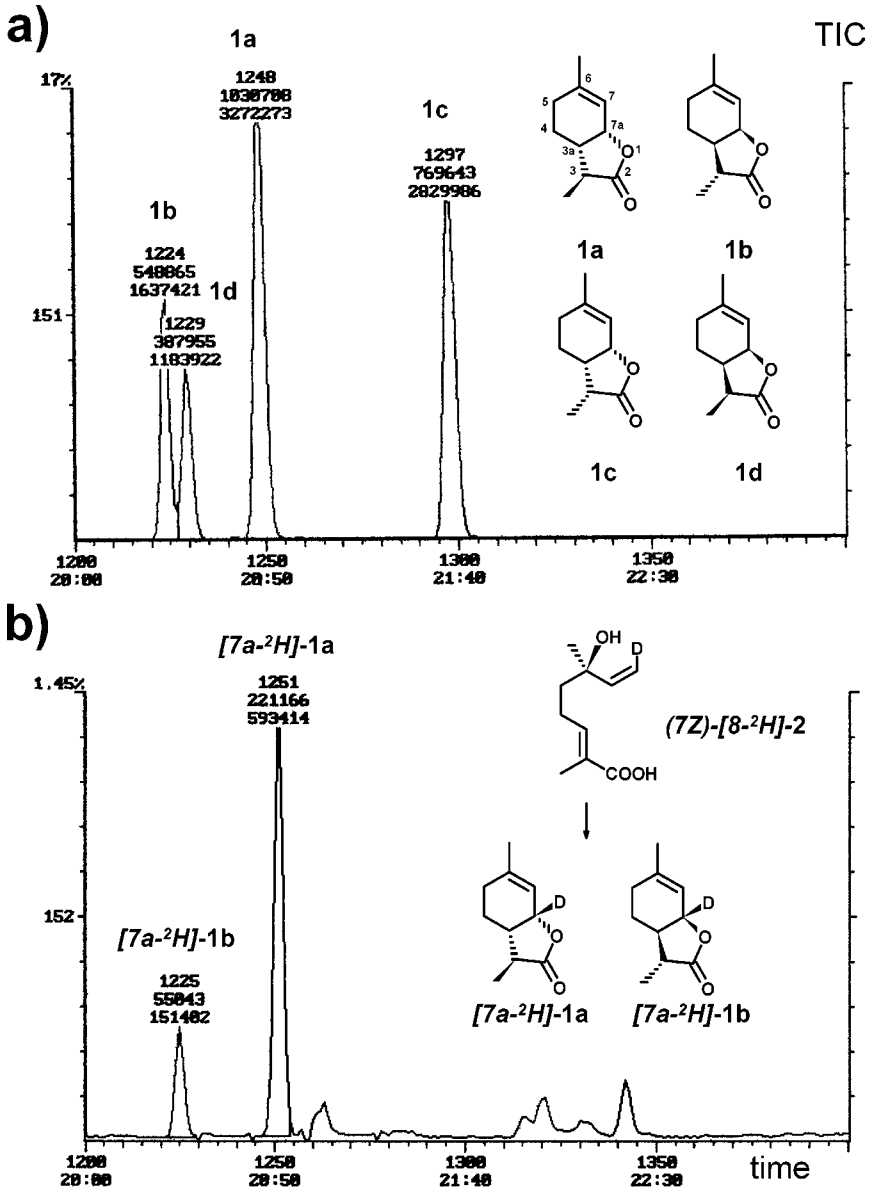


Figure 6. (**a**) Chromatogram obtained from the enantio-GC/MS analysis of all four cis wine lactone isomers **1a**–**1c**. Each peak is also labeled with its retention time in seconds, its peak height, and its peak area. (TIC = total ion count.) (**b**) Chromatogram obtained from the enantio-GC/MS analysis of deuterated cis wine lactone isomers that were generated by cyclization of (2*Z*,6*R*,7*E*)-[8-^{2}H]-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, (7*Z*)-[8-^{2}H]-**2**. Each peak is also labeled with its retention time in seconds, its peak height, and its peak area. The assignments were made on the basis of retention times and MS data. (TIC = total ion count.)

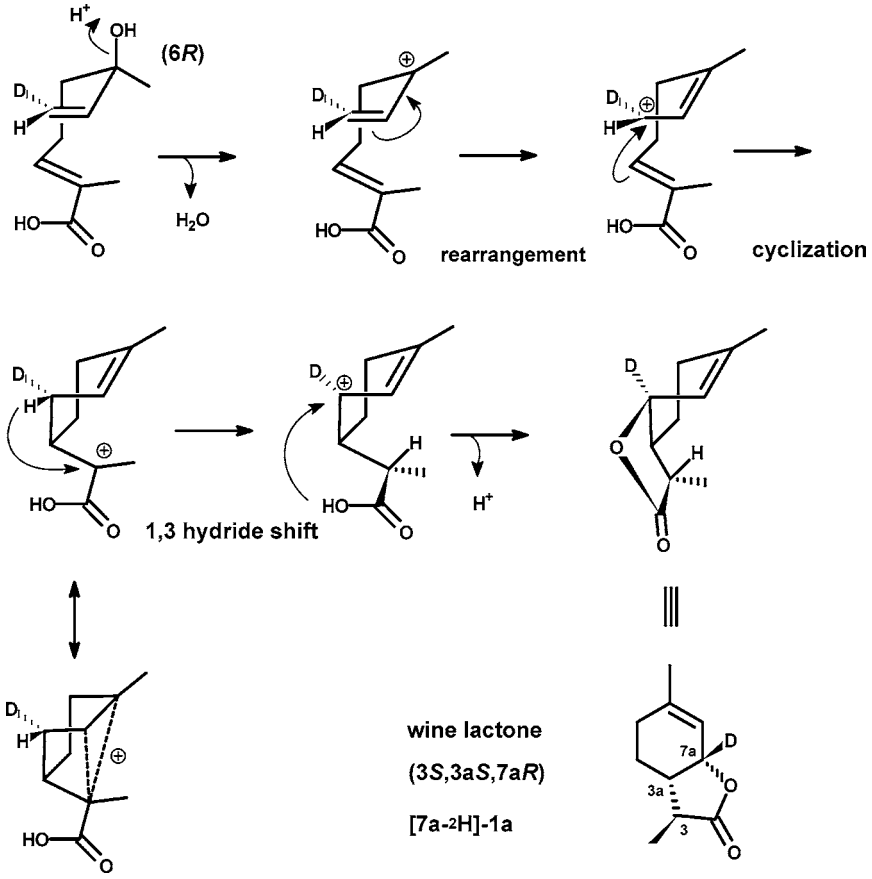


Figure 7. Proposed cyclization mechanism of (2*Z*,6*R*,7*E*)-[8-^{2}H]-2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid, (7*Z*)-[8-^{2}H]-**2**, that gives rise to [7a-^{2}H]-wine lactone, [7a-^{2}H]-**1a**.

Table 1. Results of MS/MS Experiments Performed on Wine Lactone **1** and Its Isotopomers [7a-^{2}H]-**1** and [3-^{2}H]-**1**

compound (*m*/*z* of isolated parent ion)	*m*/*z* of intense daughter ion(s) generated (molecular formula)[a]
1 (166)	151 ($C_9H_{11}O_2$)
1 (165)	137, 123 ($C_8H_{11}O$)
1 (151)	123 ($C_8H_{11}O$), 95 (C_6H_7O/C_7H_{11})
[7a-^{2}H]-**1** (167)	152
[7a-^{2}H]-**1** (166)	137, 123
[7a-^{2}H]-**1** (152)	124, 96
[3-^{2}H]-**1** (167)	152
[3-^{2}H]-**1** (165)	138, 124
[3-^{2}H]-**1** (152)	124, 96

[a] Molecular formulas of the fragment ions were determined by high-resolution MS using a Finnigan 8230 mass spectrometer and data taken from Guth (*24*).

ment of H7a. This is confirmed by the corresponding MS/MS experiment. The parent ion at $m/z = 166$ yields a daughter ion at $m/z = 151$ with the formula $C_9H_{11}O_2$ (see **Table 1**). A similar mechanism has previously been published for the fragmentation of rose oxide (*25*). The labeled wine lactones [7a-^{2}H]-**1** and [3-^{2}H]-**1** showed daughter ions at $m/z = 152$ for the corresponding parent ion at $m/z = 167$, providing evidence that the deuterium label is not attached at the C6 methyl group.

Of special diagnostic interest is the ion at $m/z = 165$ that is generated by loss of the activated allylic H7a (see **Figure 5**). This ion generates an intense daughter ion at $m/z = 137$ by loss of carbon monoxide (see **Figure 4a**). Labeled [7a-^{2}H]-**1** gave the same intense daughter ion at $m/z = 137$ when $m/z = 165$ was chosen as the parent ion, providing evidence that the deuterium atom was lost during formation of this parent ion. The position of the deuterium atom at [7a-^{2}H]-**1** can therefore be assigned to C7a. The control experiment with isotopomer [3-^{2}H]-**1** confirmed this assignment: The parent ion at $m/z = 166$ gave an intense daughter ion at $m/z = 138$ because the deuterium atom was attached not at C7a (see **Figure 4b**) but at C3 (explanation of this assignment is provided below).

[3-^{2}H]-**1** and [7a-^{2}H]-**1** were also analyzed by enantio-GC/MS using a chiral column that allowed for the separation of all four cis isomers of **1** (see **Figure 6a**). Enantiopure 6*R*-configured (7*Z*)-[8-^{2}H]-**2** gave predominately [7a-^{2}H]-**1a** with an enantiomeric purity of 79.6%, demonstrating that the cyclization is stereoselective (see **Figure 6b**). This result is not in agreement with the results of Bonnländer (*16*), who detected racemic wine lactone when using enantiopure synthetic (6*R*)-**2**. In our case, only racemic (7*E*)-[8-^{2}H]-**2** gave racemic [3-^{2}H]-**1ab**, as expected.

DISCUSSION

The results of the experiments using the labeled precursors (7*E*)-[8-^{2}H]-**2** and (7*Z*)-[8-^{2}H]-**2** clearly demonstrate that their cyclization to wine lactone is accompanied by an intramolecular hydrogen shift. Enantiopure 6*R*-configured (7*Z*)-[8-^{2}H]-**2** gave predominately [7a-^{2}H]-**1a**, which is the isotopomer of the natural wine lactone isomer **1a**. Thus, the cyclization is stereoselective.

Stereoselective cyclization reactions that entail hydrogen shifts are usually features of terpenoid cyclases. These enzymes catalyze the most structurally and stereochemically complex reactions in biology. In the case of monoterpene cyclases, loss of diphosphate from the enzyme-bound substrate geranyl

diphosphate results in an allylic carbocation that electrophilically attacks a double bond further down the terpene chain to effect the first ring closure. Additional rearrangements involving transient carbocations can include proton abstractions, hydride and alkyl migrations, and additional electrophilic attacks (*26*). The X-ray crystal structure of bornyl diphosphate synthase demonstrates that the enzyme serves as a template to channel conformation and stereochemistry in the cyclization reaction and the enzyme elegantly protects and stabilizes reactive carbocation intermediates (*18*).

The cyclization of 6*R*-configured (7*Z*)-[8-^{2}H]-**2** to wine lactone [7a-^{2}H]-**1a** shows some features of an enzymatic cyclase reaction but is nevertheless a pure chemical, nonenzymatic reaction. This chemical conversion of an acyclic precursor to a bicyclic monoterpene has rarely been observed and confirms recent suggestions that the precursor itself can provide chemical functionality required for specific steps in the cyclization cascade (*17*).

Because wine lactone **1** is the major degradation product of acid **2** (*3*), **2** must favor a folded conformation in a polar solvent such as water. Usually the linalyl system adopts an anti, endo conformation, giving rise to a stereospecific and stepwise cyclization via a carbocation to yield monocyclic α-terpineol (*27*). It is therefore probable that **2** adopts a similar conformation prior to cyclization. **Figure 7** shows a possible cyclization mechanism of 6*R*-configured (7*Z*)-[8-^{2}H]-**2** to wine lactone **1a** that is in agreement with the results of this study: 6*R*-Configured (7*Z*)-[8-^{2}H]-**2** adopts an anti, endo conformation and generates a carbocation through the acid-catalyzed elimination of water. Allylic rearrangement yields a primary carbocation that attacks the C2−C3 double bond with subsequent ring closure. The driving force for both cyclizations is probably the formation of a relatively strain-free cyclohexenyl ring with concomitant loss of the C2−C3 double bond. This has been shown in an insightful series of experiments for the closely related neryl/linalyl system by Poulter and King (*28*, *29*). A stereoselective 1,3-hydride shift is followed by formation of the lactone ring. The deuterium label ends up at C7a of wine lactone. If (7*E*)-[8-^{2}H]-**2** is used as the precursor, the deuterium label migrates to C3 by a 1,3-deuteride shift.

It is interesting to note that the wine lactone isomers that are epimeric at C3 are not generated. The free rotation of the C2−C3 bond in the first monocyclic intermediate (see **Figure 7**) is obviously blocked. Such rotation would give rise, after H migration and lactonization, to a wine lactone product that would be epimeric at C3. There is some potential for considering a nonclassical cationic intermediate: An unsymmetrical nonclassical bridged ion between C3, C6, and C7 as shown in **Figure 7** would require the relative positioning of the carboxyl and methyl groups to be fixed and would lead to the stereoselective outcome observed.

Because the cyclization of the precursors was carried out under drastic SDE conditions (pH 3.2, 100 °C), a partial racemization at C6 of 6*R*-configured (7*Z*)-[8-^{2}H]-**2** takes place prior to cyclization: The first intermediate that is generated in **Figure 7** is a planar carbocation that can yield the opposite enantiomer by rebinding of a water molecule and subsequent deprotonation. This racemization mechanism is well-known for the linalyl system (*30*) and might explain the rather low enantiomeric purity of 79.6% of [7a-^{2}H]-**1a** compared to the genuine wine lactone **1a** of high enantiomeric purity that was isolated from a Gewürztraminer wine (*4*).

It is noteworthy that the linalool and corresponding derivatives found in grapes are usually (3*S*)-configured (*31*). One would therefore expect that the enantiomer of wine lactone **1b** is the natural isomer because (3*S*)-linalool yields (6*S*)-**2** after oxidation. This is obviously not the case and cannot be explained at the present stage.

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