STEREOSTRUCTURE OF PLAGIOCHILINE A AND CONVERSION OF PLAGIOCHILINE A AND STEAROYLVELUTINAL INTO HOT-TASTING COMPOUNDS BY HUMAN SALIVA

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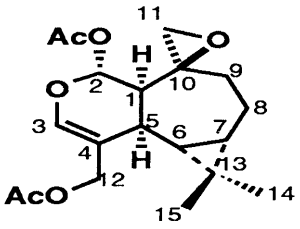
The stereostructure of plagiochiline A (**1**) isolated from the liverwort *Plagiochila fruticosa* has been established by X-ray crystallographic analysis. Plagiochiline A was converted into plagiochilal B (**2**) and furanoplagiochilal (**3**) by human saliva, and stearoylvelutinal (**4**) isolated from the fungus *Lactarius vellerus* was converted into velleral (**5**), also by human saliva.

KEYWORDS plagiochiline A; X-ray crystallographic analysis; human saliva; pungent unsaturated aldehyde; furanoplagiochilal; velleral

Pungent compounds such as polygodial (**6**) and sacculatal (**7**) from *Porella* and *Pellia* species (liverwort)[1,2] and velleral (**5**) from *Lactarius* species (mushroom)[3] have an unsaturated dialdehyde in the molecule, and show interesting biologial activities such as antifungal, antimicrobial, piscicidal and anti-cancer promotion. When one chews a whole plant of *Plagiochila fruticosa* and a fruit body of *Lactarius vellerus* which contain plagiochiline A (**1**)[1] and stearoylvelutinal (**4**),[4] respectively, one feels a potent pungent taste slowly. It is suggested that **1** and **4** might be converted into pungent unsaturated dialdehydes by human saliva. In this paper, we report the stereostructure of **1** , and the conversion of **1** and **4** into hot-tasting compounds by human saliva.



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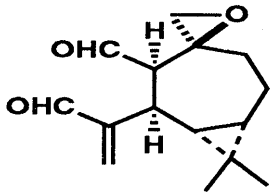

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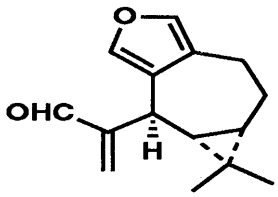

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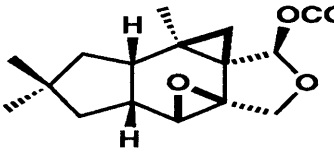

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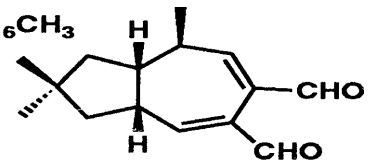

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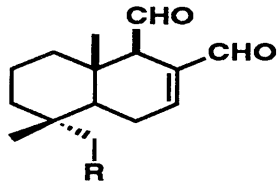
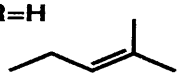


6 : R=H

7 :



Dry material (1.09 kg) of *P. fruticosa* was extracted with ether, and the extract (19.33 g) was chromatographed on silica gel and Sephadex LH-20 to afford plagiochilide (**8**; 1.13 g) , plagiochiline C (**9**, 0.24 g) and plagiochiline A (**1**, 1.36 g). This was the first time plagiochiline A was isolated in the crystalline form, and the relative configuration was established as depicted in formula **1** by X-ray crystallographic analysis.[5]

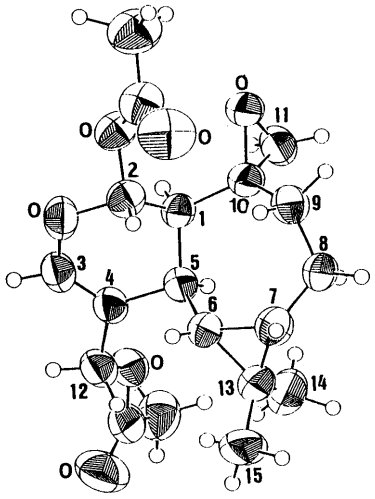
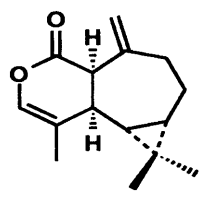


Fig. 1. ORTEP Drawing of Plagiochiline A (1)



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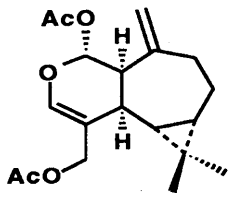

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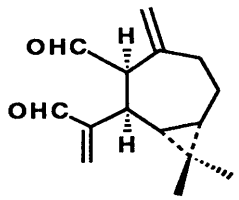

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Compound **1** was treated with human saliva (pH 6.9) at 37°C for 24 hr to give plagiochilal B (**2**)[6] (22.0 %) and furanoplagiochilal (**3**)[7] (7.5%) as shown in Table I. Compound **3** immediately shows a more pungent taste than that of unsaturated dialdehyde **2.** The spectral data of **2** and **3** were identical with those of authentic samples[6, 7]. Human saliva consists of α-amylase, peroxidase, catalase, lipase and sulfatase as enzymes, and sodium, potassium, magnesium, calucium cations, chlorine anion and phosphoric acid as inorganic substances. Compound **1** was treated with α-amylase in phosphate buffer (pH 6.8) at 20°C for 1 day to afford the main product **2** (53.9 %) and minor product **3** (1.8%), as shown in entry 2. At 37°C, the yield of **3** increased ten times, as shown in entry 3. With only phosphate buffer, almost the same result was obtained as shown in entry 4. With only water, **2** was obtained as a single compound in high yield (75%) as shown in entry 6. When **1** was treated with potassium hydrogen carbonate at 20°C for 67 h, compound **2** was obtained as minor product (8.8%) and **3** as major product (35.6 %), as shown in entry 7. At 37°C, the same reaction as **1** gave complex mixtures. Compound **2** was treated with phosphate buffer at 20°C for 1 day to afford **3** (25 %), and the starting material **2** (75 %) was recovered.

Plagiochiline C (**9**) shows no pungent taste, compared with plagiochiline A (**1**). Therefore, it is suggested that the reaction for **9** did not convert into pungent plagiochilal A (**10**)[7] when treated with human saliva at 37°C for 1 day under the same conditions as with **1.**

Table I. The Conversion of Plagiochiline A (**1**) into Plagiochilal B (**2**) and Furanoplagiochilal (**3**)

Entry No.	Reagent	Time (h)	Temp.	**2** (yield)#	**3** (yield)#
1	human saliva	24	37°C	22.0 %	7.5 %
2	α-amylase+phophate buffer*	24	20°C	53.9 %	1.8 %
3	α–amylase+phophate buffer*	24	37°C	52.8 %	12.5 %
4	phophate buffer*	24	37°C	52.8 %	12.5 %
5	α-amylase+dist. H_2O	24	37°C	49.0 %	2.3 %
6	dist. H_2O	24	37°C	75.0 %	0.0 %
7	$KHCO_3$ / MeOH-H_2O	67	20°C	53.9 %	1.8 %

*Phosphate buffer : 0.1M KH_2PO_4+0.1M Na_2HPO_4. #Isolated yield .

From these results, the reaction mechanism for formation of dialdehyde (**2**) and furanoaldehyde (**3**) from plagiochiline A (**1**) in human saliva can be presumed. Hydroxy anion or water molecule will attack the C-3. Then two acetoxy groups will be easily hydrolyzed and deacetoxylated with water to give a hemiacetal (**11**), which will be converted into plagiochilal B (**2**). Compound **2** can be easily converted into furanoplagiochilal (**3**) with weak base such as Na_2HPO_4 contained in the human saliva.

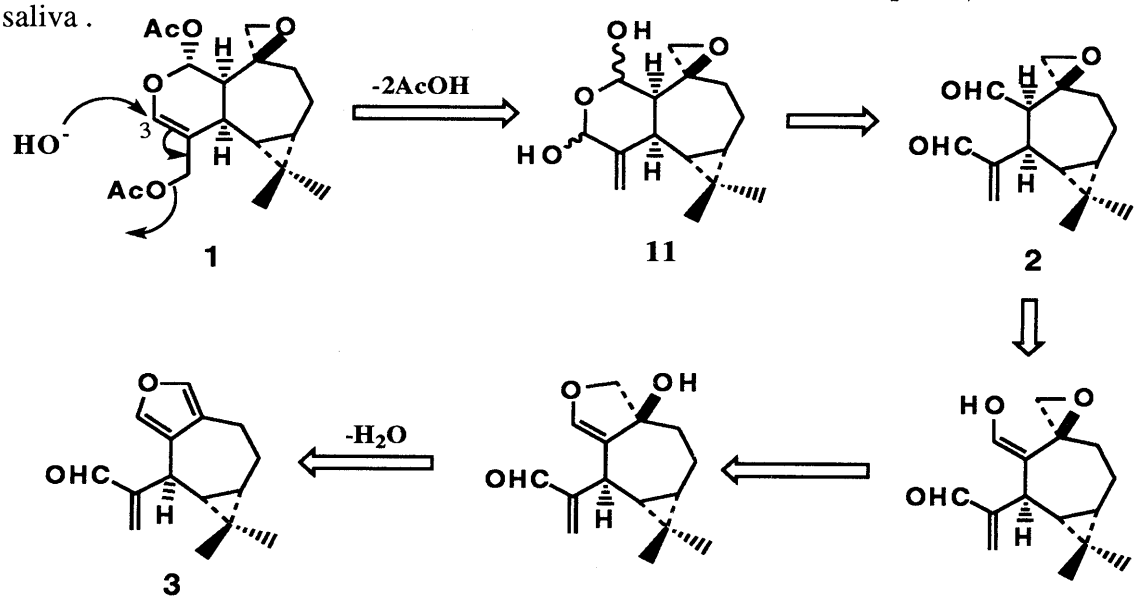

Fig. 2 Possible Conversion Mechanism of 1 into 2 and 3 by Human Saliva

Stearoylvelutinal (**4**) was also treated with human saliva under the same conditions as shown in Table I to give a pungent unsaturated dialdehyde, velleral (**5**) (32%).

In spite of the absence of the unsaturated dialdehyde moiety, **1** and **4** showed potent pungent taste, and several interesting biological activities including potent insect antifeedant and piscicidal activities.[1,3] It has been considered that these biological activities may occur due to the unsaturated aldehyde moiety generated from **1** and **4** which have a hemiacetal group. In conclusion, compounds **1** and **4** were treated with human saliva to yield hot-tasting unsaturated aldehydes **2**, **3** and **5**, which are responsible for the pungent taste. The relative configuration of **1** was established by X-ray crystallographic analysis. The relative configuration of **2** and **3** isolated from *Plagiochila* species (liverwort) was deduced from this.

REFERENCES AND NOTES

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5) The crystal data for **1** (mp 62-63°C; $C_{19}H_{26}O_6$) are as follows : Orthorhombic; space group $P2_12_12_1$ with a=8.641 (2), b=26.269 (6), c=8.436 (2) Å, V=1915(8)Å^3, Z=4, and Cu K-α (λ=1.54178) by Mac Science MXC 18 instrument. Final R value was 0.046 for 1753 reflections.
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(Received May 17, 1994; accepted June 6, 1994)