Pergamon

Tetrahedron Letters 43 (2002) 2511–2513

TETRAHEDRON
LETTERS

First synthesis of hydroxy-pinonaldehyde and hydroxy-pinonic acid, monoterpene degradation products present in atmosphere

Fabienne Fache,[a,]* Olivier Piva[a,]* and Philippe Mirabel[b]

[a]*Laboratoire de Chimie Organique, Photochimie et Synthèse, Université Claude Bernard Lyon I, CNRS UMR 5622, Bâteau J. Raulin, 43 Boulevard du 11 Novembre 1918, F-69622 Villeurbanne cedex, France*

[b]*Centre de Géochimie de la Surface, Université Louis Pasteur Strasbourg I, 1 rue Blessig, F-67084 Strasbourg cedex, France*

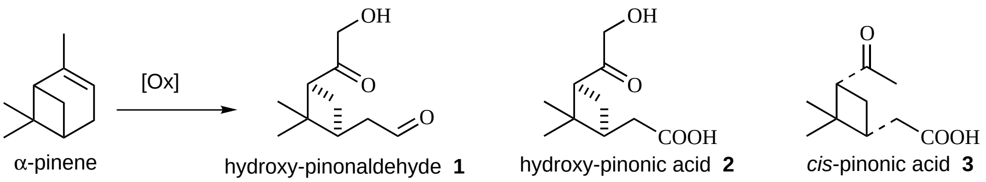
Received 28 January 2002; revised 14 February 2002; accepted 16 February 2002

Abstract—Hydroxy-pinonaldehyde and hydroxy-pinonic acid, monoterpene degradation products have been for the first time isolated by synthesis and fully characterized. The key step of the synthesis is an oxidation using the $RuCl_3/NaIO_4$ system. © 2002 Elsevier Science Ltd. All rights reserved.

Monoterpenes constitute about 10% of the mass of the nonemethane organic compounds emitted into the atmosphere.[1] Their degradation by hydroxyl radicals and ozone produces organic aerosols formed by particulated matter. The terpene double-bond oxidation leads to the formation of numerous products containing carbonyl, carboxy, and/or hydroxy functional groups.[2] All these compounds have been already detected in ionization chambers and identified most of the time only thanks to their GC-EI and GC-CI mass spectra. As some of them exist at trace levels, identification and quantification are extremely difficult. Even if some derivatization techniques[2,3] have been developed to ensure better analyses of these degradation products, we assume that the synthesis of pure samples will be better to confirm the proposed structures. Moreover, other experiments to elucidate the atmospheric hydrocarbon reaction mechanism[4,5] should be performed starting from these authentic compounds. Among all the oxidation products[6] hydroxy-pinonaldehyde **1** and hydroxy-pinonic acid **2** have been often detected in aerosols but neither isolated nor synthesized before, probably because of their high polarity and low stability of the aldehyde derivative, toward oxidative processes (Scheme 1).

We started the synthesis from commercially available (−)-myrtenol **4** and protected the hydroxy function with an acetate group[7] which could resist under oxidative conditions (Scheme 2).

The key step of the synthesis was the oxidation of product **5** into **7**. We tested two different pathways. The first one used the classical OsO_4/NMO dihydroxylation system[8] leading to **6** which after treatment with $NaIO_4$ without further purification, gave the aldehyde **7**. The second method consisted of a one-pot oxidation procedure using $RuCl_3/NaIO_4$. Such a procedure has been already used for the oxidation of (−)-α-pinene into pinonic acid[9] **3**. The authors did not mention the presence of the corresponding aldehyde at the end of the reaction. In our case, we nether isolated the acid

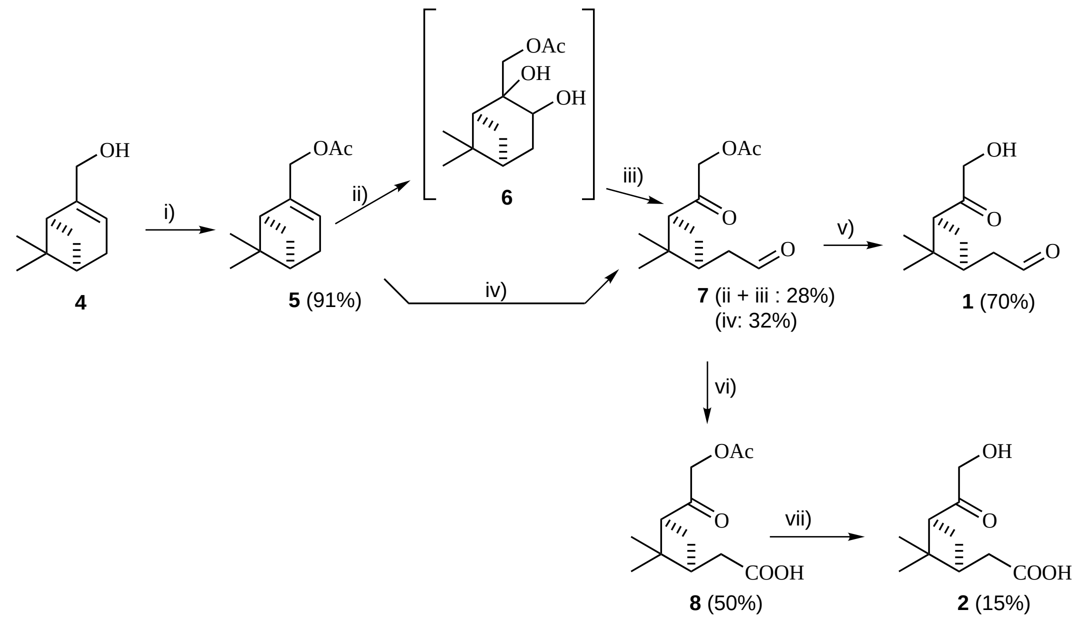


Scheme 1.

Keywords: hydroxy-pinonaldehyde; hydroxy-pinonic acid; monoterpenes; oxidation.

* Corresponding authors. Fax: 00 33 (0)4 72 44 81 36; e-mail: fache@univ-lyon1.fr

PII: S0040-4039(02)00337-4



Scheme 2. (i) CH_3COCl, Et_3N; (ii) OsO_4, NMO tBuOH, H_2O; (iii) $NaIO_4$; (iv) $RuCl_3$, $NaIO_4$; (v) K_2CO_3, MeOH, H_2O (vi) $NaClO_2$, H_2O_2; (vii) K_2CO_3, MeOH, H_2O.

derivative. During the reaction, we detected an intermediate product which should be diol **6** in agreement with the results published by Shing et al.[10] for the synthesis of a diol from alkenes with the same system. After two hours we added a new portion of $NaIO_4$ to go to completion. As the two procedures led to the same isolated yield (30%), we chose the second one, which is easier to carry out. Moreover, catalytic amounts of $RuCl_3$ were necessary (7%) against 20% for OsO_4. Compound **7** was oxidized into **8** with H_2O_2·$NaClO_2$, a mild selective method for the oxidation of aldehyde into acid.[11] We have also tested the procedure developed by Noyori et al.[12] which allowed the selective oxidation by H_2O_2 of an aldehyde in the presence of an hydroxy function on the same molecule but without success. Starting from **1**, we never obtained **2**. In both cases (**7** and **8**) the desired products **1** and **2** were finally obtained by deprotection according to a classical procedure.[13] In the case of the acid **2**, the isolated yield after deprotection was quite low probably due to its high solubility into water. Nevertheless, the conditions have not been optimized. It is noted that both aldehydes **1** and **7** can be stored several days at −15 °C without degradation.

In conclusion, even if the synthesis of these products should be improved, we have realized the first synthesis of hydroxy-pinonaldehyde and hydroxy-pinonic acid, terpene degradation products present in the atmosphere. These products are now currently tested to verify previous studies and to contribute to the elucidation of the terpene atmospheric degradation pathway.

All the compounds have been fully characterized. Selected data:

Product **7**: 1 mmol of **5** (194 mg) was dissolved in 12 mL (v/v) of AcOEt–CH_3CN. Then at 0°C, 0.07 mmol of $RuCl_3$·$3H_2O$ (18.3 mg) and 1.5 mmol of $NaIO_4$ (321 mg) in 2 mL of H_2O were added. After a few minutes, we noticed the appearance of the intermediate diol **6** and after 2 h, all the starting material was consumed. Then 1.3 mmol of $NaIO_4$ (285 mg) in 6 mL of H_2O were added again and the reaction mixture was allowed to stir for 5 additional h. The organic phase was washed with a saturated aqueous solution of $Na_2S_2O_3$ and the aqueous phase extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$. After evaporation and chromatography on silica (AcOEt–petroleum ether: 1/3) the desired product **7** was isolated with 32% yield. ^1H NMR ($CDCl_3$, 300 MHz) 0.85 (s, 3H), 1.31 (s, 3H), 2.05 (m, 3H), 2.15 (s, 3H), 2.4 (m, 2H), 2.95 (dd, $J=7.2$ Hz, $J=12$ Hz, 1H), 4.54 (d, $J=3.7$ Hz, 2H), 9.72 (s, 1H); ^{13}C NMR (75 MHz) 17.7, 20.5, 22.1, 30.5, 35.9, 43.8, 45.1, 50.1, 68.4, 170.1, 201.1, 202.2.

Product **1**: 3.34 mmol of **7** (764 mg) were stirred under nitrogen with 8.54 mmol of K_2CO_3 (1.18 g) in 118 mL of MeOH and 12 mL of H_2O. After 1.5 h the reaction medium was poured into ice water and extracted with CH_2Cl_2 to give 435 mg of pure product **1** (70% isolated yield) without further purification. ^1H NMR 0.82 (s, 3H), 1.28 (s, 3H), 2.05 (m, 3H), 2.47 (m, 2H), 2.91 (dd, $J=7.7$ Hz, $J=12$ Hz, 1H), 3.15 (m, 1H), 4.05 (dd, $J_{AB}=12$ Hz, $J=2$ Hz, 1H), 4.10 (dd, $J_{AB}=12$ Hz, $J=2$ Hz, 1H), 9.72 (s, 1H); ^{13}C NMR: 17.8, 22.3, 30.5, 36.1, 43.8, 45.1, 49.8, 68.7, 201.1, 207.9; $[\alpha]_D^{21}=-39$ (c 0.49, $CHCl_3$).

Product **8**: 8.14 mmol of $NaClO_2$ (80% purity, 920 mg) in 8 mL of water were added dropwise in 15 min to a stirred mixture of 5.8 mmol of **7** (1.3 g) in 5.8 mL of CH_3CN, 1.54 mmol of NaH_2PO_4·H_2O (212 mg) in 2.3 mL of water and 6 mmol of 35% H_2O_2 (575 μL). The temperature was kept below 10°C. The solution became immediately yellow and oxygen evolved from the solution. After a few minutes, a precipitate appeared. After 1 h, 0.36 mmol of $Na_2S_2O_3$ (57 mg) were added to destroy the unreacted HOCl and H_2O_2. The solution was acidified until pH 1 with 10% aqueous HCl. The precipitate was dissolved with CH_2Cl_2 and all the reaction mixture was extracted with the same solvent. The organic layer was dried over $MgSO_4$ and the product was purified by chromatography on silica (AcOEt–petroleum ether: 1/3). Isolated yield 50% (702 mg). ^{1}H NMR 0.90 (s, 3H), 1.3 (s, 3H), 2.08 (m, 3H), 2.16 (s, 3H), 2.37 (m, 2H), 2.92 (dd, $J=8.1$ Hz, $J=10.3$ Hz, 1H), 4.55 (d, $J=2.2$ Hz, 2H).

Product **2** was synthesized from **8** according to the same procedure described for **1**. ^{1}H NMR: 0.81 (s, 3H), 1.24 (s, 3H), 2.05 (m, 3H), 2.32 (m, 2H), 2.85 (dd, $J=7.5$ Hz, $J=10.5$ Hz, 1H), 4.03 (d, $J=15$ Hz, 1H), 4.15 (d, $J=15$ Hz, 1H), ^{13}C NMR: 17.4, 22.4, 30.3, 34.8, 38.0, 43.8, 49.6, 68.5, 177.9, 208.1; $[\alpha]_D^{21}=-25$ (*c* 0.79, $CHCl_3$).

References

1. Guenther, A.; Hewitt, C. N.; Erickson, D.; Fall, R.; Geron, C.; Graedel, T.; Harley, P.; Klinger, L.; Lerdau, M.; McKay, W.; Pierce, T.; Scholes, B.; Steinbrecher, R.; Tallamraju, R.; Taylor, J.; Zimmerman, P. *J. Geophys. Res.* **1995**, *100*, 8873–8892.
2. (a) Yu, J.; Flagan, R.; Seinfeld, J. *Environ. Sci. Technol.* **1998**, *32*, 2357–2370; (b) Jenkin, M.; Shallcross, D.; Harvey, J. *Atmos. Environ.* **2000**, *34*, 2837–2850.
3. Jang, M.; Kamens, R. M. *Atmos. Environ.* **1999**, *33*, 459–474.
4. Dibble, T. *J. Am. Chem. Soc.* **2001**, *123*, 4228–4234.
5. Kamens, R.; Jang, M.; Chien, C.-J.; Leach, K. *Environ. Sci. Technol.* **1999**, *33*, 1430–1438.
6. (a) Glasius, M.; Lahaniati, M.; Calogirou, A.; Di Bella, D.; Jensen, N.; Hjorth, J.; Kotzias, D.; Larsen, B. *Environ. Sci. Technol.* **2000**, *34*, 1001–1010; (b) Larsen, B.; Di Bella, D.; Glasius, M.; Winterhalter, R.; Jensen, N.; Hjorth, J. *J. Atmos. Chem.* **2001**, *38*, 231–276.
7. Bessière-Chrétien, Y. *Bull. Soc. Chim. Fr.* **1971**, 91–4396.
8. Miyano, M. *J. Org. Chem.* **1981**, *46*, 1846–1853.
9. Moglioni, A. G.; Garcia-Exposito, E.; Aguado, G. P.; Parella, T.; Branchadell, V.; Moltrasio, G. Y.; Ortuno, R. M. *J. Org. Chem.* **2000**, *65*, 3934–3940.
10. Shing, T.; Tai, V.; Tam, E. *Angew. Chem., Int. Ed Engl.* **1994**, *33*, 2312–2313.
11. Dalcanale, E.; Montanari, F. *J. Org. Chem.* **1986**, *51*, 567–569.
12. Sato, K.; Hyodo, M.; Takagi, J.; Aoki, M.; Noyori, R. *Tetrahedron Lett.* **2000**, *41*, 1439–1442.
13. Terasawa, T.; Okada, T. *Tetrahedron* **1986**, *42*, 537–545.