

Progress on Preparation and Application of *p*-Menthane-1,8-diol monohydrate

Xiaoqing YI^{1, 2, a}, Shichao XU^{1, 2, b}, Zhendong ZHAO^{1, 2, c*}

¹Research Institute of Forestry New Technology, CAF, Beijing 100091, China.

²Institute of Chemical Industry of Forest Products, CAF; Key and Open Lab. On Forest Chemical Engineering, SFA; Key Lab. of Biomass Energy and Material, Jiangsu Province; National Engineering Lab. for Biomass Chemical Utilization, Nanjing 210042, China.

^ayxqing1991@163.com, ^btoughxu@163.com, ^czdzha@189.cn

Keyword: *p*-Menthane-1,8-diol monohydrate; preparation; application; progress.

Abstract: This paper provides an elaborate summary and review on the development and progress in the preparation and application of *p*-menthane-1,8-diol monohydrate.

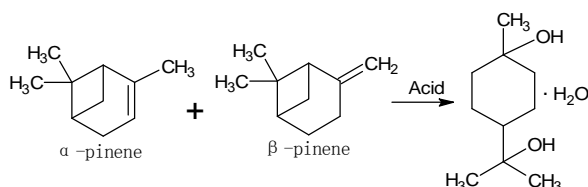
Introduction

p-menthane-1,8-diol monohydrate (so-called terpin hydrate) is one of the most important derivatives of turpentine and used widely as starting material in the preparation of pharmaceutical, pesticide, fragrance and materials¹⁻³. The preparation and application technology of terpin hydrate have made great progress in recent years⁴⁻⁵. However, there isn't any review on this topic.

Preparation of *p*-menthane-1,8-diol monohydrate

Preparation of p-menthane-1,8-diol monohydrate from terpenes and terpineol

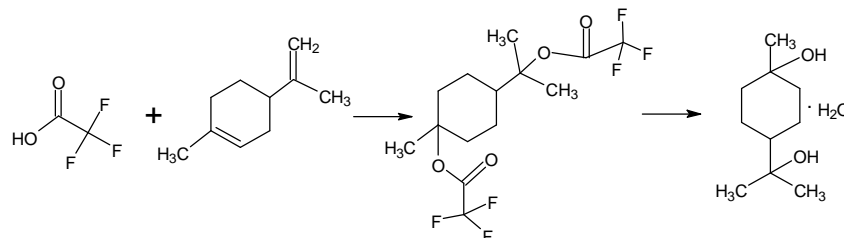
Turpentine, whose main components are α -pinene and β -pinene, is the most abundant natural raw materials used for the synthesis of terpin hydrate in industrial production⁶⁻⁸(scheme 1). Under the catalysis of strong proton acid such as sulfuric acid, nitric acid and phosphoric acid, α -pinene and β -pinene could rearrange and hydrate to *p*-menthane-1,8-diol monohydrate in high yield⁶⁻⁸. Achary and Wheeler got *p*-menthane-1,8-diol from the hydration of α -pinene or β -pinene under the catalysis of nitric acid⁶. Bhushan studied the catalyst performance of phosphoric acid in α -pinene hydration⁷. Sulfuric acid showed higher catalytic performance than nitric acid and phosphoric acid in this reaction. Zhendong Zhao and coworkers⁸ synthesized *p*-menthane-1,8-diol monohydrate from α -pinene with mass yield 107.1% under the catalyst of sulfuric acid.



Scheme1. Synthesis *p*-menthane-1,8-diol monohydrate from α -pinene or β -pinene

Limonene, also known as 1,8-*p*-menthadiene, is a kind of natural essential oil that extract from plants, and it has two unsaturated double bonds, which are easily to be hydrated to *p*-menthane-1,8-diol monohydrate⁹⁻¹¹. Eionhom⁹ catalyzed the hydration of limonene with triflic acid. The yield of *p*-menthane-1,8-diol monohydrate is 3%-18%, which is much low. Yu¹⁰ transformed

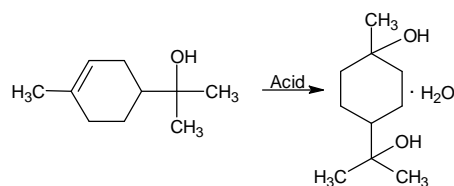
trifluoroacetic acid and limonene to *p*-menthane-1,8-diol monohydrate by a two-step reaction (scheme 2). In the presence of sulfuric acid catalyst, terpin bis-trifluoroacetate could be obtained efficiently from the reaction between trifluoroacetic acid and limonene. Terpin bis-trifluoroacetate could be hydrolyzed to *p*-menthane-1,8-diol monohydrate with a yield of 73% under the catalysis of sodium hydroxide.



Scheme2. Synthesis *p*-menthane-1,8-diol monohydrate from limonene

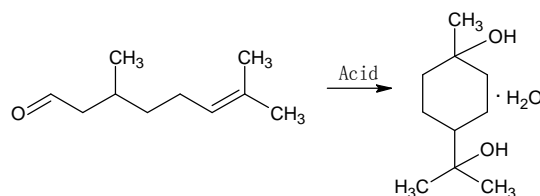
From all procedures mentioned above, *p*-menthane-1,8-diol monohydrate could be obtained in high yield. However, in most procedures, too much inorganic acid and sodium hydrate were adopted, which is harmful to the equipment and environment. Terpinolene has two unsaturated double bonds that can be oxidized to diepoxide and then followed by dehydration under the catalyst of lithium aluminium hydride, which provided an eco-friendly synthetic process for *p*-menthane-1,8-diol monohydrate¹¹. Despite of the low yield of *p*-menthane-1,8-diol monohydrate, the disadvantage of waste water and the corrosion of equipment by acidic catalysts is avoiding in this procedure.

p-Menthane-1,8-diol monohydrate can also be prepared by hydration of the α -terpineol¹² (scheme 3), but it is not valuable in industry because of the more impurities, lower yield and lower economy as it is a inverse reaction of terpineol formation from terpin hydrate.



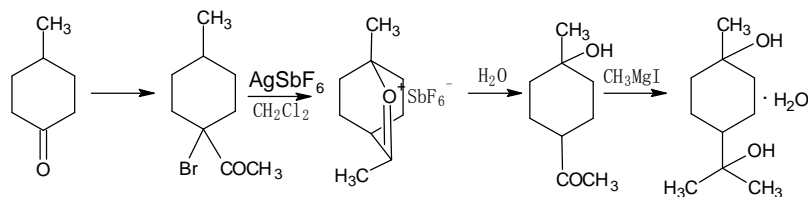
Scheme3. Synthesis *p*-menthane-1,8-diol monohydrate from α -terpineol

Preparation of *p*-menthane-1,8-diol monohydrate from other starting materials



Scheme4. Synthesis *p*-menthane-1,8-diol monohydrate from citronellal

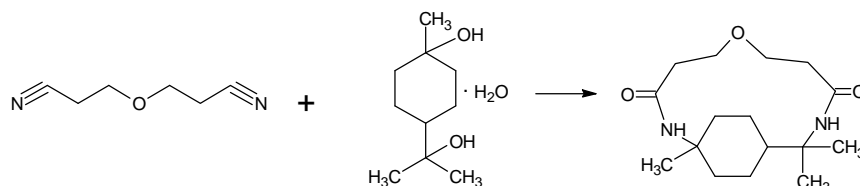
There are other methods to prepare *p*-menthane-1,8-diol monohydrate. Gu¹³ transformed citronellal to *p*-menthane-1,8-diol monohydrate by cyclical reaction catalyzed by solid superacid with a yield of 32% (scheme 4). Begue¹⁴ synthesized *p*-menthane-1,8-diol monohydrate with four-steps reaction from 4-Methylcyclohexanone and the yield of it is 92% (scheme 6). This process provided high efficient method for formation of *p*-menthane-1,8-diol monohydrate. However, this process is complicated with four-step reaction and time-consuming.



Scheme5. Synthesis *p*-menthane-1,8-diol monohydrate from 4-methylcyclohexanone

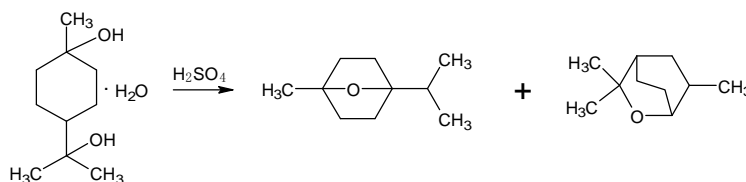
Application of *p*-menthane-1,8-diol monohydrate

Application of *p*-menthane-1,8-diol monohydrate in medical intermediates



Scheme6. Synthesis N, N'-diacyl-*p*-menthane-1,8-diamines from terpin hydrate

In recent years, the synthesis and application of terpene derived biologically active substances has been widely studied. Because of the high reactivity of *p*-menthane-1,8-diol monohydrate, it has been used widely in the synthesis of terpene derived medicines and pesticides. Kovals'skaya¹⁵ and coworkers synthesized N,N'-diacyl-*p*-menthane-1,8-diamines via the interaction of *p*-menthane-1,8-diol monohydrate with various nitriles under the conditions of the Ritter reaction (scheme 6). The spatial structure of the reaction products was confirmed and a mixture of isomeric *cis*- and *trans*-N, N'-diacyl-*p*-menthane-1,8-diamines in a ratio of 1:4 could be obtained. The condensation of *p*-menthane-1,8-diol and 3'-acetoxyolivetol in the presence of fused ZnCl₂ in CH₂Cl₂ gave an important Δ⁹-tetrahydrocannabinol (Δ⁹-THC, an active constituent of marijuana) derivate. The sympatomatology test in mouse and cardiovascular system test in dogs showed that the metabolites produced similar pharmacological effect with higher activity than those of Δ⁹-THC¹⁶. Eucalyptol play an important role in medicine industry, which can be prepared by the intramolecular dehydration of *p*-menthane-1,8-diol monohydrate. Rhein¹⁷ prepared eucalyptol by the dehydration of terpin monohydrate with the catalyzed of sulfuric acid (scheme 7), the product is the mixture of 1,8-epoxy-*p*-menthane (i.e. 1,8-cineole) and 1,4-epoxy-*p*-menthane (i.e. 1,4-cineole).

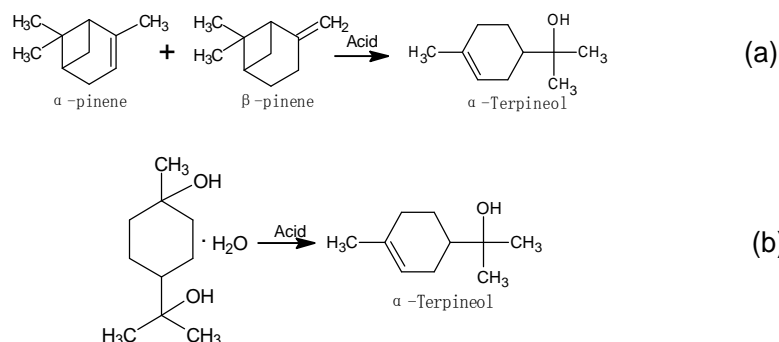


Scheme7. Synthesis encalyptole from *p*-menthane-1,8-diol monohydrate

Application of *p*-menthane-1,8-diol monohydrate in fragrances

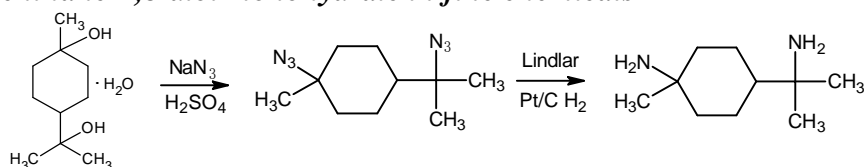
Terpineol is an important synthetic chemical perfume and it has a strong smell of lilac. In industrial production, there are two processes to prepare commercial production of terpineol: with and without the formation and hydrolysis of *p*-menthane-1,8-diol monohydrate. Under the catalysis of acid, turpentine oil could be directly hydrated to terpineol (scheme8, a). 错误! 未定义书签。 However, the terpineol synthesized in one-step process has shortcomings with much by-products, lower purity and poor aroma. If turpentine oil was hydrated to *p*-menthane-1,8-diol monohydrate at the initial step, followed with the hydrolysis of *p*-menthane-1,8-diol monohydrate under the catalysis of sulfuric acid to terpineol (scheme 8, b), the yield and purity of α-terpineol will be remarkably

increased, which significantly improves the aroma of terpineol. The product selectivity can be controlled by the modification of catalyst. Ban¹⁸ chose the solid-liquid mixed acid to catalyze the dehydration of *p*-menthane-1,8-diol monohydrate and the selectivity of terpineol approached to 83%. Under the catalysis of Amberlyst[®]-15¹⁹ *p*-menthane-1,8-diol monohydrate could be hydrolyzed to dipentene and terpinolene. Under the catalysis of presence of halogen-containing catalysts such as magnesium chloride²⁰ *p*-menthane-1,8-diol monohydrate could be transformed to *p*-cymene through hydrogen disproportionation reactions.



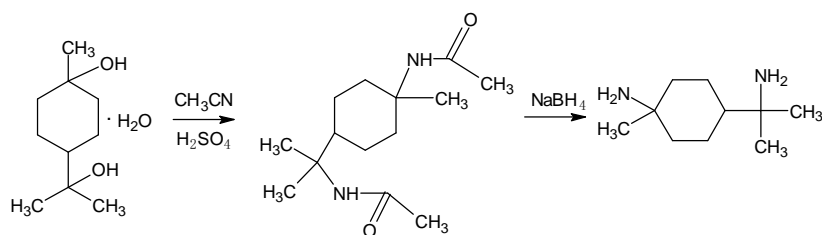
Scheme 8.a: One-step process to synthesis terpineol. b: Two-step process to synthesis terpineol

Application of *p*-menthane-1,8-diol monohydrate in fine chemicals



Scheme 9. Z. Y. FENG's process to synthesis Menthane diamine

Menthane diamine, (1,8-diamino-*p*-menthane) is a primary alicyclic diamine with the same carbon-carbon skeletons to *p*-menthane-1,8-diol monohydrate. Because of its unique chemical structure, menthane diamine used widely as curing agent, antibacterial agent, copolymer and reaction assistant in chemical production industries. Menthane diamine was firstly synthesized and industrialized by Rohm&Hass²¹ Co. Ltd. in America in 1953. However, hypertoxic hydrogen cyanide and excess amount of sulfuric acid were adopted in this protocol, which brought considerable potential hazard to surrounding and environments. Feng *et al.*²² conducted a new way to synthesis 1,8-diamino-*p*-menthane through reacting terpin monohydrate with sodium azide catalyzed by sulfuric acid followed with hydrogenation catalyzed by Lindlar catalyst (scheme 9), the yield reaches to 63.1%. But process is hard to apply in industry because the sodium azide is used as raw material, which is high-risk and explosive. Zhong²³ applied ritter reaction to synthesis 1,8-diamino-*p*-menthane with a two-steps reaction (scheme 10). In the first step, 1,8-diacetamide-*p*-menthane could be obtained from the reaction of *p*-menthane-1,8-diol monohydrate with acetonitrile catalyzed by 60% sulfuric acid solution. Followed with the reduction of 1,8-diacetamide-*p*-menthane with sodium borohydride, menthane diamine could be obtained in high yield. This process provided a relatively more convenient method to avoid the high toxicity and explosive danger existed in other procedures.



Scheme10. X.ZHONG's process to synthesis Menthane diamine

Outlook

Terpin monohydrate is an important derivative of turpentine and plays an important role in the preparation of medicine intermediates, fragrances and other fine chemicals. However, there is a pity in the present investigations to prepare and apply *p*-menthane-1,8-diol monohydrate because there is much poisonous to body and some pollution to environment. Exploring the environmentally friendly and green approach is still a main challenge required to be reserved immediately.

Acknowledgments

This work was supported by National Key Technologies R&D Program (grant No. 2015BAD15B04).

References

- [1] Chunjie QI. Advances in Fine Petrochemicals. 12 (2011) 44-50. (In Chinese)
- [2] Dongmei LI, Zhendong ZHAO, Liangwu BI. Modern Chemistry Industry. 28 (2008) 345-348. (In Chinese)
- [3] Handrik, Duffley, Lambert, et al. Journal of Medicinal Chemistry. 25 (1982) 1447-1450.
- [4] Kai ZHU, Bin XU Gang ZHANG. Chemistry and Industry of Forest Products. 25 (2005) 38-42. (In Chinese)
- [5] Charlyon, Don. Industrial and Engineering Chemistry 29 (1937) 92-95.
- [6] Achary, Wheeler. Journal of the University of Bombay, science, physical science, mathematics, biological sciences, medicine. 6 (1937) 134.
- [7] Bhushan, Gulati, Joshi J. Indian chem. Soc. News. 7 (1944) 62.
- [8] Zhendong ZHAO, Xianzhang LIU, Guixian HU, et al. Chemistry and Industry of Forest Products. 34 (2000) 3-6. (In Chinese)
- [9] Einhorn J, Einhorn C. Luche J.L. Journal of Organic Chemistry. 54 (1989) 4479-4481.
- [10] Yu.G, Shafeeva.M.V, Tamm.L.A. Russian Journal of Organic Chemistry. 49 (2013) 545-550.
- [11] Guoqiang CHEN. Assignee Yunnan Senmeida. 2012. (In Chinese)
- [12] Wallach. Chemische Berichete. 40 (1907) 582
- [13] Yanfei GU, Hong LIU, Fan ZHANG, et al. Journal of Hainan Normal University (Natural Science). 23 (2010) 59-61. (In Chinese)
- [14] J.P.Begue, M.Charpentier-Morize, D.Bonnet-Delponetal. J.Org.Chem. 4 (1980) 3357-3359.
- [15] Kovals'skaya.S.S, Kozlov,N.G, Tikhonova,T.S. Chemistry of Natural Compounds. 25 (1989) 552-557
- [16] G.R.Handrick, R.P.Duffley, G.Lambert. J.Med.Chem. 25 (1982) 1447-150.
- [17] Rhein Kampfer-Fabr. U.S. Patent: 1838456 (1930).
- [18] Weiping Ban, Shiping Gao, Wenjing Song et al. Chemistry and Industry of Forest Products. 28 (2008) 16-20. (In Chinese)

- [19] M.T. Friga,Luis, A.M. Afonso, Carlos. Tetrahedron. 68 (2012) 7414-7421.
- [20] Ono. Chem.Zentrabl. 97 (1926) 1401.
- [21] Bortnick N.M. U.S.Patent:2632022 (1953).
- [22] Zhiyong FENG, Dongmei LI, Zhendong ZHAO, et al. Chemistry and Industry of Forest Products. 28 (2008) 16-20. (In Chinese)
- [23] Xing ZHONG, Tao WU, Jia CHEN, et al. CN Patent: 102746161 (2014). (In Chinese)