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Aquaticol, a Novel Bis-sesquiterpene from *Veronica anagallis-aquatica*

Bao-Ning Su, Qi-Xiu Zhu and Zhong-Jian Jia*

Department of Chemistry, National Laboratory of Applied Organic Chemistry,
Lanzhou University, Lanzhou, 730000, People's Republic of China

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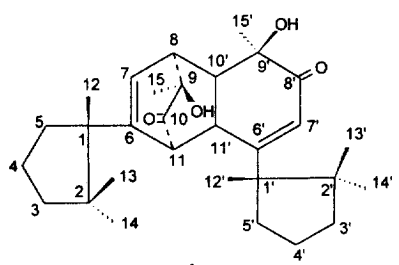
Abstract: Aquaticol, an unusual novel bis-sesquiterpene with a new carbon skeleton was isolated from the medicinal plant *Veronica anagallis-aquatica*. Its structure was determined by spectroscopic means and X-ray crystallographic analysis. The biosythetic route to this bis-sesquiterpene skeleton is discussed. © 1998 Published by Elsevier Science Ltd. All rights reserved.

The genus *Veronica* (Scrophulariaceae) is represented in China by 61 species.[1] Sticher et al.[2] have reported a range of iridoid glucosides in the genus *Veronica*. Phenylpropanoid and flavonoid glycosides have also been isolated from *Veronica*.[3,4] *Veronica anagallis-aquatica* is a well-known traditional Chinese medicine used for the treatment of many diseases such as influenza, hemoptysis, leryngopharyngitis and hernia and is mainly distributed in northwest and southwest of China.[5] In this communication, we wish to report an unusual novel bis-sesquiterpene isolated from *Veronica anagallis-aquatica*, its structure having been determined by spectroscopic methods and finally confirmed by X-ray diffraction.

Veronica anagallis-aquatica[6] has been collected in Huzhu county, Qinhai province of China. The MeOH extract (34g) of air-dried whole plants(900g) was chromatographed over a polyamide column and eluted with H_2O-MeOH, four fractions being obtained. Fraction 4 (H_2O:MeOH; 1:3) was then chromatographed on a silica gel column and eluted with petroleum ether-Me_2CO (6:1), we obtained 60mg of compound **1**,[7] named as aquaticol.



1

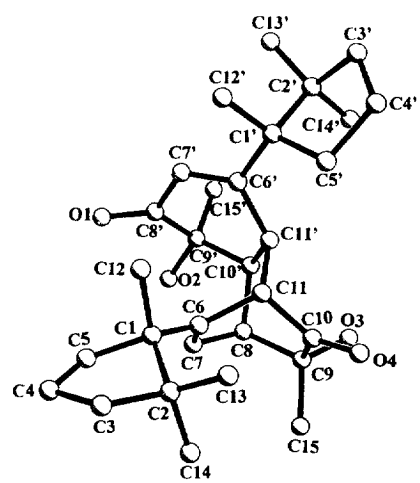


Fig. 1 X-ray structure of aquaticol(**1**)

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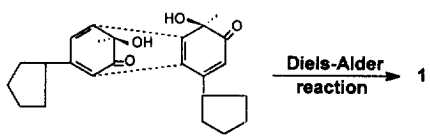
Aquaticol (**1**), colourless needles, mp 194-196°C (uncorrected), $[\alpha]_D^{20}$ +28.3 (c, 0.60; $CHCl_3$), and its UV spectrum showed $\lambda_{max}^{CHCl_3}$ at 247nm, the IR spectrum (KBr) of **1** showed absorption for hydroxy (3447cm^{-1}), olefine (1674cm^{-1}), carbonyl (1724cm^{-1}). The molecular ion peak at m/z 468 in the EI mass spectrum suggested the molecular fomula to be $C_{30}H_{44}O_4$, which was confirmed by the ^{13}CNMR , DEPT and C, H analysis data.[7] The ^{1}HNMR revealed eight singlet methyl signals, in addition to two olefinic protons (δ6.16, 1H, s, H-7';δ6.09, 1H, d, J=7.0Hz, H-7) and four methine protons. The ^{13}CNMR and DEPT indicated that there are ×8CH_3, ×6CH_2, ×6CH and ten quaternary carbons, among them, the characteristic signals are two carbonyl carbons (δ201.6, C-8'; δ211.0, C-10) and two double bonds(δ141.5, C, C-6, δ131.1, CH, C-7; δ164.7, C, C-6', δ124.7, CH, C-7'). It was easy to determine that there is a α,β-unsaturated carbonyl group, two quaternary carbons (δ73.2, δ72.1) were connected with an oxygen atom and a methyl respectively in compound **1** by 2DNMR (^{1}H-^{1}H COSY, HMQC, HMBC), but the structure of **1** was difficult to determine by 2DNMR as the signals of H-8, H-11and H-11' overlapped each other. Fortunately, colorless crystals of aquaticol could be obtained for X-ray crystallographic analysis (Fig. 1),[8] which confirmed the structure of **1**.

We speculate that a biosythetic route to aquaticol could be by intermolecular Diels-Alder reaction (Fig. 2) of the cuparane type sesquiterpene **2**.[9]



2 2

Fig. 2

References and notes

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6. The plant was identified by Prof. Z.-X. Peng(Lanzhou university), to whom we are very grateful. The present research was supported by the National Naturul Science foundation of China.
7. ^{1}HNMR(400MHz, $CDCl_3$, δ, ppm, TMS): 6.16(1H, brs, H-7'), 6.09(1H, d, J=7.0Hz, H-7), 3.40-3.43(3H, m, H-8, H-10, H-11'), 3.01(1H, dd, J=8.6, 3.2Hz, H-10'), 1.34(3H, brs, H-15'), 1.28(3H, brs, H-15), 1.12(3H, brs, H-12'), 0.91(3H, brs, H-13), 0.89(3H, brs, H-13'), 0.87(3H, brs, H-14'), 0.76(3H, brs, H-12),0.51(3H, brs, H-14), 1.22-2.35(12H, m, H-3,H-4,H-5,H-3',H-4',H-5'). ^{13}CNMR(100MHz, $CDCl_3$):49.4(C), 44.4(C), 38.7(CH_2), 18.7(CH_2), 34.0(CH_2), 141.5(C), 131.1(CH), 45.6(CH), 72.1(C), 211.0(C=O), 41.1(CH), 21.3(CH_3), 26.1(CH_3), 21.6(CH_3), 26.2(CH_3), from C-1 to C-15 respectively. 52.1(C), 47.6(C), 39.7(CH_2), 19.4(CH_2), 35.1(CH_2), 164.7(C), 124.7(CH), 201.6(C=O), 73.2(C), 39.7(CH), 53.6(CH), 21.9(CH_3), 26.0(CH_3), 23.9(CH_3), 33.2(CH_3), from C-1' to C-15' respectively. The elemental analysis results: C% 76.67, H%9.50 (Cal. C% 76.88,H% 9.46, O% 13.66).
8. The crystal data for **1** are as follows: orthorhombic crystals from pure $CHCl_3$ with trace petroleum ether. Crystal size=0.50×0.36×0.36mm, cell parameters: a=10.416(2), b=14.124(3), c=18.365(3)Å, space group $P2_12_12_1$ z=4. The diffraction intensities were collected on a Simens-P_4 diffractometer using monochromated M_oK_α radiation. The structure was solved by direct methods and the final R and R_w values were 0.0357 and 0.0613 for 2993 reflections.
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