Tsaokoin, a New Bicyclic Nonane from *Amomum tsao-ko*

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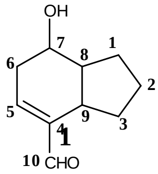
Abstact: 7α-Hydroxy-8β,9β-H- *cis*- bicyclo[4,3,0]non-4-ene-4-aldehyde, a nonane compound with novel skeleton, named tsaokoin, was isolated from the fruits of *Amomum tsao-ko*. Its structure was established on the basis of spectral analysis.

Keywords: 7α-Hydroxy-8β,9β-H- *cis*- bicyclo[4,3,0]non-4-ene-4-aldehyde, tsaokoin, *Amomum tsao-ko*, bicyclononane.

Amomum tsao-ko Crevost *et* Lem., a zingiberaceous plant called “Caoguo” or “Tsao-ko” in Yunnan, China, is a Chinese traditional medicinal herb for treatment of stomach illness and a common spice as well. Some chemical researches on the constituents of its essential oil[1, 2] and antioxidative phenolic compounds[3] have been reported. In this paper, we describe the structure of an unusual bicyclo[4,3,0]nonane derivative, tsaokoin **1**, which was isolated from the chloroform extract of the fruits of this plant.

Tsaokoin was obtained as a pale brown oil, $[\alpha]_D^{10}$ -0.11(c = 0.0221, $CHCl_3$), with a yield of 0.007 %. Its molecular formula was determined as $C_{10}H_{14}O_2$ by HR EI-MS (M^+ 166.0998, calcd. 166.0994) which accounted for 4 degrees of unsaturation. IR spectrum exhibited the presence of one carbonyl group of aldehyde and one hydroxyl group [1682 (C=O), 3441(br, OH) cm^{-1}]. The UV ($CHCl_3$) absorption [λ_{max} 230.5 nm, log ε 3.7) indicated the presence of a typical α, β-unsaturated aldehyde in the form of -CH=C(CHO)-. The aldehyde group (δ_C 193.8, d, δ_H 9.37) and a trisubstituted olefin [δ_C144.1 (s), 147.5(d), δ_H6.69] were also confirmed by NMR spectra. ^{13}C NMR spectrum indicated the presence of four methylenes (δ_C 24.1, 24.3, 30.4 and 31.6), two methines(δ_C 36.6 and 42.3), one oxymethine (δ_C 67.3) besides the double bond and the aldehyde group. The above data suggested that the remaining two degrees of unsaturation were assumed for the presence of two ring systems, and the carbon skeleton of this compound is composed of a six-membered ring and a five-membered ring by the following evidence. Based on the 2D NMR experiment, the α, β-unsaturated methine proton H-5 (δ_H 6.69, ddd, J = 1.4, 4.2, 4.6 Hz) showed correlation with H-6β [δ_H 2.49 (ddd, J = 4.6, 9.3, 15.0 Hz)] and H-6α [δ_H 2.41(ddd, J = 4.2, 4.8, 15.0 Hz)]; ^1H-^1H COSY spectrum showed correlations between H-7 (δ_H 4.03, ddd, J = 4.8, 4.9, 9.3 Hz) and H-6, H-7 and H-8 (δ_H 2.40, m), H-8 and H-9 (δ_H 2.95, m); HMBC spectrum revealed long-rang correlation between H-9 and C-4 (δ_C 144.1), H-9 and C-5 (δ_C 147.5), the proton of aldehyde group (δ_H 9.37) and C-9. These evidence indicated that C-9 is connected to C-4 and the α, β-unsaturated aldehyde group is located on the six-membered ring. The ^{1}H-^{1}H correlations of H-8 with H-1 [δ_H 1.76 (m, H-1$_\alpha$), δ_H 1.54 (m, H-1$_\beta$)] and H-9; H-2 [δ_H 1.52, 1.50 (m, H-2$_{\alpha,\beta}$)] with H-1 and H-3 [δ_H 2.05 (m, H-3$_\alpha$), δ_H 1.41 (m, H-3$_\beta$)]; as well as H-3 with H-9 and H-2, supported the five-membered ring fusing with six-membered ring at C-8 (δ_C 42.3) and C-9 (δ_C 36.6) positions. Furthermore, the assignments of C-6 (δ_C 30.4), C-1 (δ_C 24.1) and C-3 (δ_C 31.6) were confirmed by long-rang correlation of H-6 with both C-4 and C-8, H-1 with C-7 (δ_C 67.3), and H-3 with C-4 in HMBC experiment, respectively. Therefore, the skeleton of **1** was determined as a bicyclic[4,3,0]-non-4-en, similar to part of 7-hydroxy-2,6-cycloxenica-9,13-diene-18,19-dial **2**, which was isolated from the brown alga, *Dictyota dichotoma*[4].



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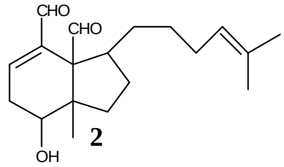

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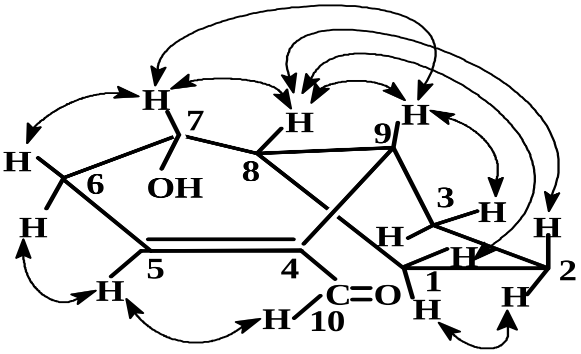
Figure 1 NOE correlation of compound **1** [NOESY, CDCl$_3$, 500 MHz, Mixing time (d8)=0.65 s]

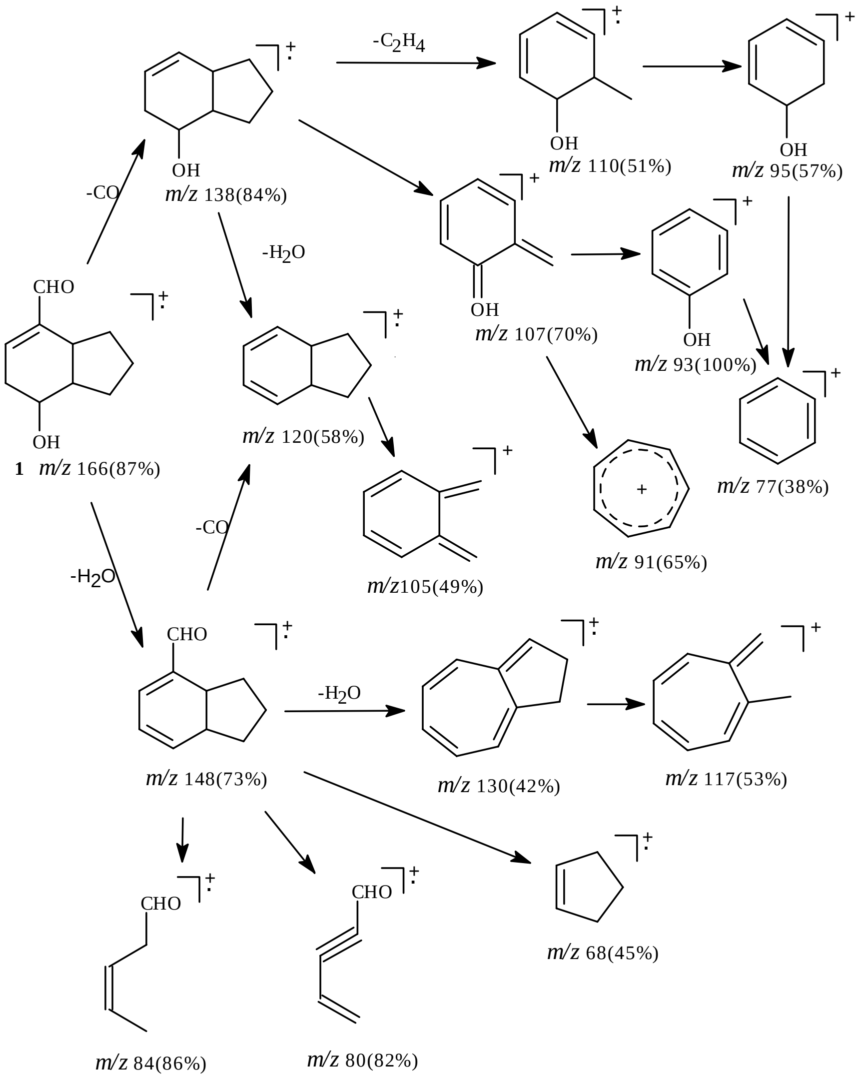


The orientation of C-7 secondary hydroxyl group was determined from the J values of H-7 (4.03, ddd, J=4.9, 4.8, 9.3Hz). The coupling constants of $J_{H\text{-}7/H\text{-}8}$ = 4.9 Hz (*pseudo ae* coupling) and $J_{H\text{-}7/H\text{-}6\alpha,\beta}$ = 4.8, 9.3 Hz (*pseudo ae* and *aa* coupling) express H-7 at *pseudo* α in β orientation. The NOE between H-8 and H-9 suggested that these two protons are on the same side and the two rings are *cis*-fused with each other. NOE enhance between H-7 and H-8 was observed too.

The NOE enhance between the aldehyde proton and H-5 indicates H-5 and the aldehyde group are on the same side of the double bond.

Thus, the structure of the tsaokoin was established as 7α-hydroxy-8β, 9β-H- *cis*-bicyclo[4,3,0]non-4-ene-4-aldehyde (**Figure 1**), which was confirmed by elucidation of the fragmentation of EI-MS spectrum (**Figure 2**).

Figure 2 Elucidation of the Fragmentation of compound **1** in EI-MS spectrum



According to our knowledge, tsaokoin is the first bicyclo[4,3,0] nonane isolated from natural resources. Although its structure is similar to a part of compound **2**, a bicyclic diterpene, its biosynthetic pathway is not clear.

References

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