

## Bisabolangelone from *Angelica* spp.\*

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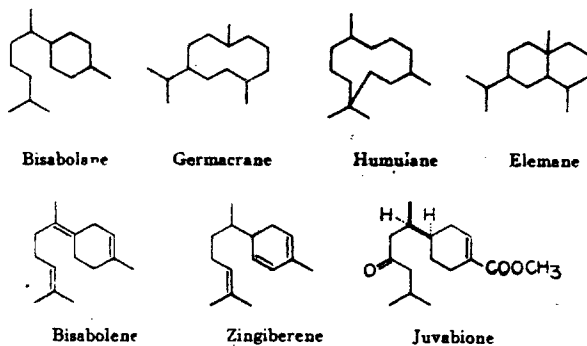
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Sesquiterpenoid which can be separated from plant volatile oils with high boiling points is either aliphatic or aromatic compound containing 15 carbon atoms. Sesquiterpenes occur in nature as hydrocarbons, alcohols, ketones, aldehydes or lactones.

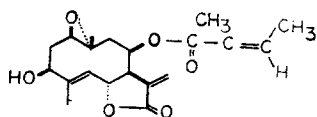
Generally essential oils obtained from medicinal plants consist of mostly monoterpenoids and only about 5~10% sesquiterpenes. Oils from patchouli, vetiva, sandal wood etc. contain sesquiterpenes as their major components. However it is a very difficult task to isolate pure components, because the absolute amount of sesquiterpenoid in essential oils is in small. In addition, they consists of several kinds of sesquiterpenoids which are similar structure and in physical properties. The utilization of gas chromatography, column chromatography, counter current and other modern techniques made the separation and purification of this group of compound much easier.

Sesquiterpenoids can be divided into four classes. 1) Acyclic 2) monocyclic 3) bicyclic and 4) tricyclic. Cyclic sesquiterpenoids are biosynthesized from farnesyl pyrophosphate through several steps of reactions; elimination of pyronic acid ester resulting cyclization, Wagner-Meerwein transformation, 1, 2, shift of methyl group, lactonization and elimination of proton resulting double bond.

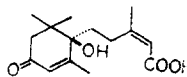
Monocyclic sesquiterpenoids are again divided into several groups: 1) Bisabolane 2) germ-



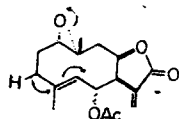
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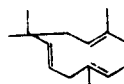
Heliangine



Abscisic acid



Pyrethrosin



Humulene

acrane 3) humulane and 4) elemene groups. Bisabolene from bergamot oil and bisabol-myrth oil<sup>1)</sup>, zingiberene from ginger oil<sup>2)</sup>, and juvabione from *Abies balsamea*<sup>3)</sup> belong to bisabolane group. Juvabione is the first known juvenile hormone. These groups of compounds show such various biological activities as inhibitory activity of juvabione against transformation of insects, antiauxin and antigiberellin activities of heliangine<sup>4)</sup> inducing activity of abscisic acid of falling blossom in cotton-plant and inhibitory activity of abscisic acid against growth of paddy.<sup>5)</sup> It is of interest to us to study the biological activities of this class compounds systematically.<sup>6)</sup>

A study on bisabolane group sesquiterpenoids was carried out on *Angelica* spp., one of Korean Qianghuo(韓國羌活), by the author and coworkers. Separation and determination of chemical structure of bisabolangelone (Angelikoreanol)<sup>7,8)</sup> were reported elsewhere. The preliminary tests on the biological activities were also carried out.

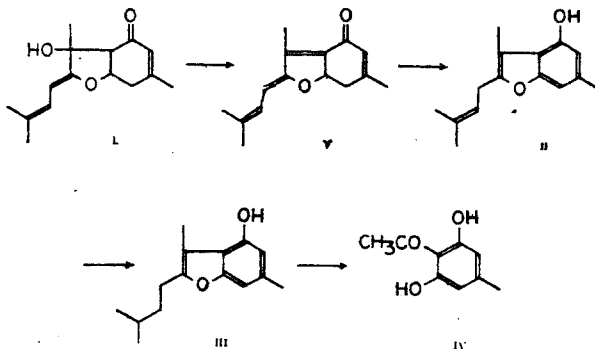
Korean Qianghuo(韓國羌活) in the market can be divided into two classes; 1) *Angelica koreana* Max.(Umbelliferae) which has violet side shoots contains coumarins. 2) *Angelica* spp. which has only one node and peculiar odor contains bisabolangelone and ferulic acid.

On column chromatography (Silica gel, *n*-Hexane: EtOAc=1:2), the ether extract of *Angelica* spp. afforded yellowish crystal, I, mp 157-8°, C<sub>15</sub>H<sub>20</sub>O<sub>3</sub>, and ferulic acid, mp 167-8°, C<sub>10</sub>H<sub>10</sub>O<sub>4</sub>.

I was characterized as an  $\alpha,\beta$ -unsaturated ketone with a hydroxyl group. Conventional acetylation method failed to acetylate I but afforded yellow resinous material. The spectral data suggested dehydration rather than acetylation resulted in an unsaturated bond. The treatment of I with *p*-toluene sulfonic acid in anhydrous benzene at room temperature until the fluorescence almost disappeared compound II, mp 107-107.5°, C<sub>15</sub>H<sub>18</sub>O<sub>2</sub>, in fairly good yield.

Compound II was characterized as phenolic material containing 5-methylresorcinol skeleton. It was proved with the fact that orcinol was identified from the alkali fusion product of II. In addition, II showed negative reaction toward carbonyl reagents and exhibits no absorption band corresponding to carbonyl group in the IR spectrum. These findings sugge-

sed that **II** was produced from **I** by dehydration following the transformation of the ketone on a six membered ring to phenolic hydroxyl group with the aromatization of the compound. The NMR spectrum of **II** showed a series of signals which can be assigned to the protons of isopentenyl group. Compound **II** took up 1 mole of hydrogen in ethanol over Adams catalyst to yield dihydro derivative of mp 95-96°,  $C_{15}H_{20}O_2$ , **III** which yielded *p*-acetophenone **IV** by ozonolysis and 4-methyl-*n*-valeric acid.



Scheme 1-Bisabolangelone and its derivatives.

The results mentioned above suggested the chemical structure of **III** as 2-(3'-methylbutyl)-3,6-dimethyl-4-hydroxybenzofuran. The NMR spectrum of **II** indicated the presence of isopentenyl group. Moreover, when the treatment of **I** with *p*-toluene sulfonic acid was stopped while the intense fluorescence was observed in the reaction mixture, an orange colored product of mp 97-98° formed. The NMR spectrum of this product agreed with the structure of formula **V**. On the basis of these evidences, the only possible structure for compound **I** is formula **I**, a sesquiterpenoid as is shown in Scheme 1. The NMR data also agree with the structure.

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