Absolute Configuration of 1,2-Epoxy Menthyl Acetate Isolated from a New Chemical Strain of *M. rotundifolia*[†]

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Received July 23, 1973

In previous papers,¹⁻³⁾ we reported on the principal constituents of the essential oils of two chemical strains of *M. rotundifolia*; one contained rotundifolone (piperitenone oxide) predominantly and the other *neoiso*-isopulegol and piperitone. Recently, we have found a new strain of *M. rotundifolia* containing piperitone oxide and 1,2-epoxy menthyl acetate as its main constituents.

The essential oil was obtained by the steam distillation of stalks and leaves of plants harvested in October, 1972 in a 0.07% yield of the fresh herb. The gaschromatogram of this oil showed two main peaks of retention time (abbr. *Rt.*) 10.5 and 17.3 min (Reoplex 400, 160°C, N₂ gas-1.3 kg/cm²). This oil was subjected to column chromatography on silica gel with benzene. The earlier fraction gave a colorless oil corresponding to the compound of *Rt.* 10.5 min, and also a colorless oil from the later fraction due to the compound of *Rt.* 17.3 min.

The compound of *Rt.* 10.5 min (**III**) was obtained after cooling as colorless crystals, mp 15°C, C₁₀H₁₆O₂ (M⁺ 168), [α]_D²⁰ -147.7° (c=0.4, EtOH), and it has been identified with authentic (-)-(1S:2S:4S)-piperitone oxide from the IR, NMR, [α]_D and GLC data. Furthermore, the semicarbazone of compound (**III**) was colorless crystals, mp 200~201°C, which was identical with authentic semicarbazone by comparing their IR spectra.

The compound of *Rt.* 17.3 min was a color-

less oil of a characteristic odor, C₁₂H₂₀O₃ (M⁺ 212), [α]_D²⁰ +166.4° (c=0.92, EtOH). The IR and NMR spectra and GLC behavior of this compound were identical with those of 1,2-epoxy menthyl acetate isolated from the essential oils of several species in the Genus *Mentha*.^{4~6*)} However, its absolute configuration has not yet been determined by these studies.

Now we investigated the stereochemical structure of this compound by the following method.

SCHEME. Determination Processes of Absolute Configuration of **I**.

The compound of *Rt.* 17.3 min (**I**) was deacetylated to afford the corresponding epoxy alcohol (**II**), which was oxidized with the Jones reagent in an acetone/ether mixture to give the epoxy ketone (**III**). The IR, NMR, GLC and [α]_D of this resulting compound (**III**) were found to be identical with those of (-)-piperitone oxide.³⁾ From the above mentioned fact, it is clear that compound **I** has (1S:2S:4S;-)-configuration.

The configuration of C-3 position was determined by the following method; (-)-piperitone oxide (**III**) was reduced with NaBH₄ to give a mixture of the compound (**II** and **IV**), which was acetylated to afford a mixture containing two acetates (**I** and **V**). This mixture was subjected to silica gel chromatography

[†] Studies on the Essential Oil of *Mentha rotundifolia*, Part VII; see References 1), 2), 3).

* We wish to thank Prof. T. Nagasawa for supplying 1,2-epoxy menthyl acetate.

to give **I** and **V** in the ratio of 1:3. Compound **I** thus obtained was identified with the naturally occurring acetate by the IR, NMR and GLC data. Compound **V** may be an epimer of **I** at C-3 position.

The NMR spectra show that the epoxy methine proton (H_2) of **I** appears at δ 3.30 (t, $J=5.0$ Hz), and that of **V** ($H_{2'}$) appears as a singlet at δ 2.62, while the methine proton (H_3) bearing on C-3 position, appears at δ 5.11 (t, $J=5.0$ Hz), and that of **V** ($H_{3'}$) is a doublet (δ 4.78, $J=8.0$ Hz). On the other hand, the dihedral angle between H_2 and H_3 in **I** is near 0° , and that of **V** is about 90° from the Dreiding model, while the dihedral angle between H_3 and H_4 of **V** are approximately 20° and 150° , respectively.

It is well known that the coupling constant obtained from the signals of the epoxy cyclohexanes are considerably smaller than the values calculated from the Karplus equation with the dihedral angles measured in the Dreiding models, and the revised Karplus equation has been proposed.⁷⁾ From the magnitude of the coupling constant between H_2 and H_3 ($J_{2,3}$) in compound **I**, it is elucidated that the dihedral angle is about 0° according to the revised Karplus equation, and this result is in good agreement with the dihedral angle measured in the Dreiding model. Similarly

the value of the coupling constant, $J_{2,3'}$, agreed with the dihedral angle measured.

From the above evidence, it is concluded that the epoxy ring, the acetoxy group and the isopropyl group in compound **I** are all oriented in *cis* position. And in compound **V**, the epoxy ring and the acetoxy group are arranged to be *trans* and moreover the acetoxy group and the isopropyl group are also oriented in *trans* position.

According to these results, the (1*S*: 2*S*: 3*R*: 4*S*)-configuration can be assigned to (+)-1,2-epoxy menthyl acetate, **I**.

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