Short Communication

Synthesis and Absolute Configuration of Nematicidal Constituent of *Cirsium japonicum**

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9,10-*cis*-Epoxyheptadec-16-ene-4,6-diyn-8-ol (**I**) was isolated by Kawazu *et al.* as a nematicidal constituent of *Cirsium japonicum*.¹⁾ It is a kind of C₁₇ polyacetylenic compounds²⁾ bearing epoxyalcohol moiety at the center of the molecule. A closely related analog **II** had also been isolated from other kinds of *Compositae* by Bohlmann and Lam.³⁾ Though their partial stereochemistry was estimated, their whole absolute configuration remained obscure. It is interesting to clarify and compare their absolute stereochemistry from the viewpoint of their biogenetic routes

and chemotaxonomy. This communication deals with the synthesis and absolute configuration of **I**.

Isopropylidene-D-glyceraldehyde (**III**)⁴⁾ was used as a starting chiral synthon. In general, nucleophilic reaction of **III** was known to produce a mixture of *threo* and *erythro* isomers.⁵⁾ When a reaction of **III** with Grignard reagent **IV** was carried out in THF-HMPT at -70°C , *erythro* isomer **V** was obtained in 90% selectivity. Mesylation of **V**⁶⁾ gave **VI** which yielded (2*R*)-*trans*- β,γ -epoxyalcohol (**VII**) as the main product by successive treatment with *p*-toluenesulfonic acid and potassium hydroxide. To obtain the *cis*-epoxide **IX**, mesylate **VI** was converted to the corresponding chloride **VIII** accompanied with inversion of C-3 configuration. The chloride **VIII** was successively treated as in the case of the synthesis of *trans*-isomer **VII** to yield (2*R*)-*cis*-epoxide (**IXa**) which was purified as 3,5-dinitrobenzoate (**IXb**). Then **IXa** was oxidized with chromium trioxide-ether-celite-dichloromethane⁷⁾ to *cis*- α,β -epoxyaldehyde (**X**), which, on reaction with 1-lithio-1,3-heptadiyne, gave diastereomeric mixture of **Ia** and **Ib** in the ratio of 1 : 2. **Ia** was identical to the natural product with respect to

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their spectra and specific rotation:

The stereochemistry of hydroxyl group on

C-8 was determined by two methods using **Ib**.⁸⁾ It was hydrogenated and treated successively with acetic anhydride in pyridine, periodic acid, lithium aluminum hydride and finally (–)- α -methoxy- α -trifluoromethylphenylacetyl chloride in pyridine. The resulting diester **XI** was proved to be identical with authentic specimen prepared from (*S*)-nonan-1,2-diol* tested by the method of Nakanishi (NMR)⁹⁾ and that of Marumo (HPLC).¹⁰⁾ This means that the alcoholic carbon of **Ib** possesses (*S*)-configuration and consequently the hydroxyl group is *threo* against epoxide ring. On the other hand, it is well-known that an allylic alcohol such as **XII** gives *threo*-epoxyalcohol stereoselectively in more than 90% of the mixture when treated with peracid.¹¹⁾ The epoxyalcohol **XIII** thus obtained was identical to perhydro-**Ib** with respect to their NMR and IR spectra. From the above results, it is no doubt that **Ib** is *threo* isomer with (*S*)-configuration at alcoholic carbon and that **Ia** is *erythro* isomer with (*R*)-configuration at C-8.

Therefore it is concluded that the natural product, which is identical with **Ia**, is (8*R*,9*R*,10*S*)-9,10-epoxyheptadec-16-ene-4,6-diyn-8-ol.^{12,13)} The specific rotation of synthetic **Ia** was +98° in benzene, meaning 96% optical purity. Synthesis and chemical property of **II** and analogs are now in progress and the details will be published later.

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- 12) Satisfactory spectral data have been obtained for intermediates and products. Selected characteristics are summarized here: **V**: bp 110 ~ 119°C (1.5 mmHg); $[\alpha]_D^{90} + 11^\circ$ ($c=2.0$, benzene). **VII**: mp 30°C; $[\alpha]_D^{21} + 40.3^\circ$ ($c=2.85$, CHCl_3). **IXa**: $[\alpha]_D^{20} - 6.49^\circ$ ($c=1.85$, benzene). **IXb**: mp 60.5 ~ 61.5°C; $[\alpha]_D^{20} + 36.5^\circ$ ($c=2.3$, benzene). **X**: $[\alpha]_D^{20} - 65.8^\circ$ ($c=3.1$, benzene). **Ia**: $[\alpha]_D^{20} + 98^\circ$ ($c=1.92$, benzene); IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3420, 3080, 2975, 2940, 2860, 2255, 1640, 1380, 1340, 1315, 1230, 1045, 1028, 995, 910, 835; $^1\text{H NMR}$ δ : 0.99 (3H, t, $J=7.2$ Hz), 1.2 ~ 1.8 (10H, $-\text{CH}_2-$), 2.02 (2H, br-t, $-\text{CH}_2\text{CH}=\text{}$), 2.26 (2H, t, $J=7.0$ Hz, $-\text{CH}_2\text{C}\equiv$), 2.66 (–OH), 3.08 (2H, epoxide protons), 4.32 (1H, m, $-\text{CH}-\text{OH}$), 4.89, 4.98 and 5.06 (2H, $=\text{CH}_2$), 5.81 (1H, d-d-t, $J=17.3$, 9.8, 6.4 Hz, $-\text{CH}=\text{}$). **Ib**: $[\alpha]_D^{22} - 189^\circ$ ($c=2.0$, benzene); IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3420, 3080, 2975, 2940, 2860, 2255, 1640, 1465, 1380, 1340, 1315, 1230, 1045 (shoulder), 1028, 995, 910, 835; $^1\text{H NMR}$ δ : 0.99 (3H, t, $J=7.2$ Hz), 1.2 ~ 1.7 (10H, $-\text{CH}_2-$), 2.02 (2H, br-t, $-\text{CH}_2\text{CH}=\text{}$), 2.27 (2H, t, $J=6.8$, $-\text{CH}_2\text{C}\equiv$), 3.07 (2H, $-\text{OH}$ + epoxide proton), 3.19 (1H, d-d, $J=7.2$, 4.4 Hz, epoxide proton), 4.25 (1H, d-d, $J=4.1$, 7.2 Hz, $-\text{CH}-\text{OH}$), 4.90, 5.00 and 5.08 (2H, $=\text{CH}_2$), 5.81 (1H, d-d-t, $J=17.3$, 9.8, 6.4 Hz, $-\text{CH}=\text{}$).
- 13) In ref. 1 the absolute configuration of C-8 was proposed to be (*S*), which must be revised to (*R*).

* Prepared from (*S*)-pentan-1,2,5-triol (U. Ravid and R. M. Silverstein, *Tetrahedron Letters*, **1977**, 423).