44. On Derivatives of α -Thujaplicin. I.¹⁾

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Nozoe and the others^{2a)} synthesized α -thujaplicin (I), i.e. o-isopropyltropolone, m.p. 33–34°, obtained from *Thuja plicata* by Erdtman, et al.³⁾, and ascertained that this compound also possessed semiaromatic properties, similar to hinokitiol (II), i.e. β -thujaplicin (the meta isomer), and tropolone (III) itself. He reported that it is worthy of notice that (I) gave, as substitution products, a di-bromo compound, m.p. 80–81°, and a p-tolylazo compound, m.p. 130–131°, and that the boiling point of (I) was rather low when compared to its meta isomer (II) and para isomer, i.e. γ -thujaplicin³⁾.

The present experiments were undertaken in order to obtain various derivatives of (I) and to compare those with the corresponding derivatives of (II) and (III).

Similar to (II) and (III), (I) gives pale yellow sodium salt less soluble in water and do not form molecular compounds with aromatic amines such as aniline and p-toluidine. It gives a crystalline addition product with ethylenediamine in 2:1 ratio as yellow plates (IVa), m.p. 117–117.8°. (Anal. Calcd. for $C_{22}H_{32}O_4N_2$: N, 7.21. Found: N, 6.42). The ethylenediamine compound of (II) is obtained as pale yellow plates (IVb), m.p. 145–146.5°. (Anal. Calcd. for $C_{22}H_{32}O_4N_2$: N, 7.21. Found: N, 6.72).

Etherification of (I) with ethereal solution of diazomethane yields a neutral substance which does not color by ferric chloride. Distillation of this substance under 4mm. pressure yields two fractions; initial distillate of b.p. 115–118°, and a chief distillate of b.p. 118–120°, which solidifies to colorless needles, m.p. 71.5–72.5°, practically insoluble in water. (Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.20; H, 7.23).

(I) readily submits to azo coupling with p-tolyldiazonium salt and yields p-tolylazo compound (V) of orange prisms, m.p. 130–131°. The yield is almost quantitative. (Anal. Calcd. for $C_{17}H_{18}O_2N_2$: N, 9.39. Found: N, 9.20). However, (V) did not show any tendency to undergo hinopurpurin-type rearrangement^{2b)} when heated for 2.5 hours on a water bath with 50% acetic acid containing a few drops of conc. hydrochloric acid.

Nitrosation of (I) in water as for (III)⁴⁾ ends in an almost total recovery of (I) but nitrosation by alkali nitrite in glacial acetic

acid yields yellow needles (VI) which blackens at 180° and decomposes around 190° . Yield, 97.5% (Anal. Calcd. for $C_{10}H_{11}O_3N$: C, 62.16; H, 5.73; N, 7.25. Found: C, 61.84; H, 5.49; N, 7.14). Catalytic reduction of (V) or (VI) under the presence of Adams' catalyst or PdO.Pd yields p-amino- α -thujaplicin (VII) as yellow prisms, 173 – 174° . Yield, 39% and 82%, respectively. (Anal. Calcd. for $C_{10}H_{11}O_3N$: C, 67.04; H, 7.26; N, 7.81. Found: C, 67.20; H, 7.26; N, 7.59). Picrate: Yellow prisms, m.p. 155 – 156° .

Since the azo group entered the para position in the case of (II) and (III)⁵, it seems certain that the nitroso and amino groups

in (VI) and (VII) are in the para position (A: $X_1 = H$, $X_2 = p\text{-CH}_3\cdot\text{C}_6\text{H}_5$ -, NO or NH_2). Sandmeyer reaction of (VII) yields various p-halogeno compounds (A: $X_1 = H$, $X_2 = \text{Cl}$, Br or I). p-Chloro- α -thujaplicin

(VIII), colorless needles, m.p. 68.2 – 68.6° (Anal. Calcd. for $C_{10}H_{11}O_2\text{Cl}$: C, 60.42; H, 5.58. Found: C, 60.52; H, 5.22). p-Bromo- α -thujaplicin (IX), yellow prisms, m.p. 49.5 – 51° . (Anal. Calcd. for $C_{10}H_{11}O_2\text{Br}$: C, 49.38; H, 4.52. Found: C, 48.72; H, 4.46). p-Iodo- α -thujaplicin (X), yellow needles, m.p. 65 – 66° . (Anal. Calcd. for $C_{10}H_{11}O_2\text{I}$: C, 41.39; H, 3.82. Found: C, 40.90; H, 3.62).

The diazonium salt of (VIII), when left standing at room temperature in an acid solution and then heated on a water bath, yields yellow precipitate which, when sublimated and recrystallized from benzene, gives yellow needle crystals (XIa), m.p. 157 – 159° . Analytical values indicates a hydroxy- α -thujaplicin (A: $X_1 = H$, $X_2 = \text{OH}$), rather than a tropoquinone derivative (B) of $C_{10}H_{11}O_3$, as in the case of (II)⁶. (Anal. Calcd. for $C_{10}H_{11}O_3$: C, 66.64; H, 6.71 or for $C_{10}H_{10}O_3$: C, 67.39; H, 5.65. Found: C, 65.99; H, 6.41). However, since oxidation of (VII) with sodium dichromate also yields yellow needles (XIb), m.p. 155 – 158° , which is assumed to be identical with (XIa), it is thought to be o-isopropyl-p-tropoquinone (B).

Previous dibromination of (I) in ethanol had yielded a dibromo compound (XIIa)³, m.p. 80 – 81° , but the present experiments gave pale yellow needles (XIIb), m.p. 77 – 77.3° , giving a sharper melting point. Mixed fusion of (XIIa) and (XIIb) gave an intermediate value, so that they may be tautomers. Mono-bromination product of (I), when led to a sodium salt almost insoluble in water and then freed, gave pale yellow prisms (XIII), m.p. 21.5 – 22.5° . (Anal. Calcd. for $C_{10}H_{11}O_2\text{Br}$: C, 49.38; H, 4.52. Found: C, 49.40; H, 4.43). This is assumed to be o-monobromo- α -thujaplicin (A: $X_1 = \text{Br}$,

$X_2 = H$). Further bromination of this product gave a dibromo compound of m.p. 77–78°, which, together with (XIII) and (XII), failed to form crystalline addition products with aniline and p-toluidine, but gave crystalline product with ethylenediamine.

Further chlorination of p-chloro- α -thujaplicin (VIII) yields a dichloro- α -thujaplicin (XIV), m.p. 79–80°. (Anal. Calcd. for $C_{10}H_{10}O_2Cl_2$: C, 51.52; H, 4.33. Found: C, 51.32; H, 4.14). Direct chlorination of (I) yields an oily substance which is assumed to be a mixture of mono- and dichloro- α -thujaplicin, and colorless needles (XV), m.p. 120–121° (decomp.), which does not give coloration with ferric chloride. (XV) is assumed to be an aromatic carboxylic acid derivative obtained by rearrangement with halogens.

Sulfonation of (I) with sulfamic acid seemed to be very difficult, contrary to the cases of (II) and (III), the majority of (I) being recovered unreacted. A very small amount of crystals (XVI), m.p. 240–241°, were obtained which were assumed to be p-toluidine salt of a sulfonic acid derivative but they are still under investigation.

As the foregoing shows, electrophilic substitution of (I), such as the halogenation, azo coupling and nitrosation, proceeds as with (II) and (III), but, inspite of the fact that its o' (7)- and p (5)-positions are vacant on α -thujaplicin (I), its sulfonation met with a great difficulty. This fact, together with the rather low boiling point of (I) compared to its meta isomer (II)⁵⁾ and para isomer (α -thujaplicin)⁶⁾, are worthy of notice.

α -Thujaplicin (I), obtained by the authors^{2b)} from the essential oil of *Thujopsis dolabrata* as a complex salt of m.p. 231–232° and then freed, gave a melting point of 23–29° which, when fractionally recrystallized from petroleum ether gave the usual colorless, polygonal large crystals (Ia), m.p. 33–34°, and pale yellow, octagonal large crystals (Ib), m.p. 25.5–26°. Repeated recrystallization of (Ib) failed to raise its melting point so that it must be a simple crystal. (Anal. Calcd. for $C_{10}H_{10}O_2$: C, 73.13; H, 7.37. Found: C, 73.35; H, 7.63). (Ib), when dissolved in conc. sulfuric acid and diluted with water, and the crystals that separated out recrystallized, showed m.p. 33–34°, becoming identical with (Ia). Both (Ia) and (Ib) showed tendency to change to crystals of m.p. ca. 30–32° according to the manner of recrystallization, the use of (Ia) or (Ib) for inoculation, or by allowing the solution to stand for a long periods of time during crystallization. Both (Ia) and (Ib) give the same p-tolylazo compound. From these facts, and from the fact that two dibromo- α -thujaplicins are obtained, (Ia) and (Ib) are assumed to be tautomers. These phenomena are probably due to the steric effect of isopropyl group in the ortho position and are

worthy of attention. Further observations on these interesting facts will be reported in the near future.

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