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FORMAL CHEMICAL CONVERSION OF ENMEIN INTO ent-KAURENE, ATISINE, GARRYINE, AND VEATCHINE

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Recently, we reported[1] the chemical conversion of trichokaurin(I), a diterpene of Isodon trichocarpus Kudo, via compound II into a keto-carboxylic acid III, which had been converted into ent-kaurene*[2], atisine, garryine, and veatchine by Masamune[2]. This communication deals with the chemical transformation of enmein(IV), a major diterpene of Isodon species, into II*[3].

The acyloin condensation with lactone ester V[3] derived from enmein was carried out under metallic sodium-liquid ammonia system to yield 7-hemiketal-6-ol VI as a main product accompanied by other by-products*[4]. The compound VI on acetylation gave acetate VII, m.p. 154.5 ∿ 155.5°, which was dissolved in dry pyridine and photo-chemically oxygenated[4] with O_2 gas using heamatoporphyrin as sensitizer to give an allyl alcohol VIII, m.p. 187 ∿ 189° in 70 % yield. The NMR spectrum($CDCl_3$) of the alcohol gave a singlet signal at δ 4.26 ppm assignable to the C-15 proton and two singlet signals at δ 5.13 and 5.24 ppm assignable to C-17 exo-methylene protons. The C-6 proton signal appeared as a

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*[2] (-)-Kaurene is named like this in accordance with a proposal for nomenclature subscribed to by many workers in diterpene area. (J.W.Rowe, in preparation)

*[3] The analysis and/or mass spectra gave the satisfactory data about all the new compounds reported herein.

*[4] See the preceding communication.

doublet(J = 5.0 Hz) at δ 5.18 ppm. A small amount of an isomer IX, m.p. 204 ∿ 204.5°, whose NMR spectrum(D_5-pyridine) showed a two protons doublet signal(J = 1.5 Hz) coupled to C-15 proton at δ 4.56 ppm assignable to C-17 methylene and a multiplet signal at δ 6.67 ppm assignable to C-15 proton, was isolated on silica gel column chromatography of the mother liquor of VIII. The allylic hydroxy group of VIII resisted against usual acetylation (Ac_2O-pyridine, at room temperature)[5]. Under the more forced conditions (Ac_2O-pyridine, at 110° ; NaOAc-Ac_2O, warming on a water-bath ; or Ac_2O-pyridine-chloroform, at reflux), VIII gave a non-crystalline mixture of diacetates, which on treatment with $LiAlH_4$ in ether gave triol X, m.p. 185 ∿ 186°. In the NMR spectrum($CDCl_3$) of X, the C-15 proton signal appeared as a broad singlet at δ 4.38 ppm and C-6 proton signal as a doublet(J = 4.5 Hz) at δ 3.80 ppm. This triol on usual acetylation gave the original monoacetate VIII. The best procedure for getting diacetate XI was found after detailed investigations ; monoacetate VIII was mixed with a solution of Ac_2O in chloroform (1 : 1) containing NaOAc, and the mixture was heated at gentle reflux on a water bath for 7 to 8 hours to give a crystalline diacetate XI, m.p. 189 ∿ 190°, in 48% yield. It contains two acetoxy-groups, as shown by singlet acetyl methyl protons signals at δ 1.99 and 2.01 ppm and by a C-15 proton doublet signal(J = 3.0 Hz) at δ 5.19 ppm and a C-6 proton doublet signal(J = 5.0 Hz) at δ 5.24 ppm in its NMR spectrum($CDCl_3$). In this reaction, about $\frac{1}{3}$ of the starting material remained unchanged, which was observed on the thin layer chromatogram of the reaction mixture.

The diacetate XI was attempted to convert into ketone XII. Unexpectedly, Remieux-Johnson's reaction on XI resulted in the formation of many kinds of products, hence the material was treated with OsO_4 to give an osmate, which was decomposed by H_2S[6] to afford an unusual glycol XIII[*5]. Its NMR spectrum($CDCl_3$) showed the presence of two acetoxy-groups exhibiting two singlet signals at δ 2.10 and 2.11 ppm. A broad singlet signal at δ 3.60 ppm assignable to C-15 proton, an AB-type signals at δ 3.80 and 3.98 ppm(J = 10.5 Hz) assignable to

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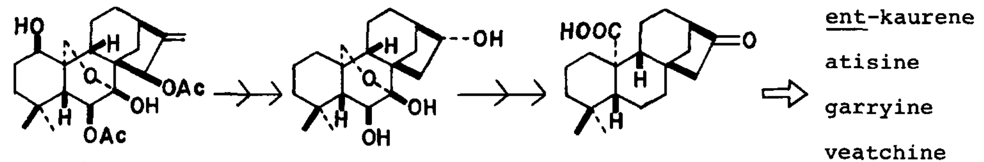
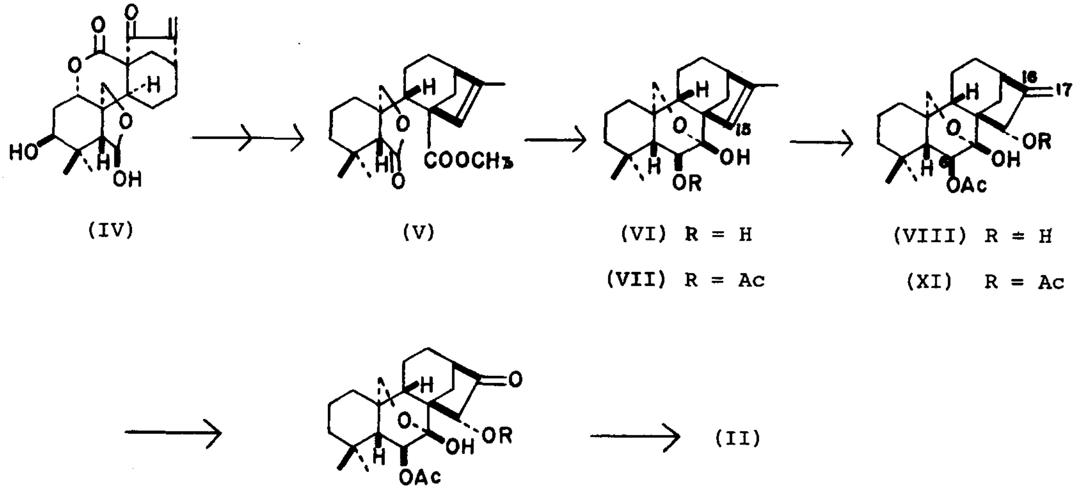
[*5] The same acetyl migration was observed also in a similar reaction with an acetate of photosensitized oxygenation product of lactone ester V.

C-20 methylene protons, a two protons singlet signal at δ 4.18 ppm assignable to C-17 methylene protons, and a doublet signal at δ 5.07 ppm(J = 5.0 Hz) assignable to C-6 proton($CDCl_3$) also appeared. Thus, a rearrangement of the acetyl group[7] was recognized. The glycol XIII on treatment with sodium metaperiodate gave keto-aldehyde XIV, m.p. 152 ∿ 153°. The aldehyde proton singlet signal was observed at δ 9.57 ppm in its NMR spectrum($CDCl_3$) in addition to the



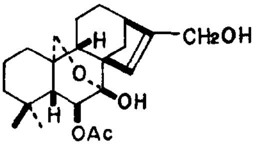
(I) (II) (III)



(IV) (V) (VI) R = H (VII) R = Ac (VIII) R = H (XI) R = Ac

(XII) R = Ac

(XV) R = H



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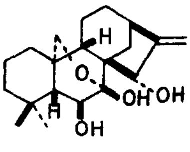
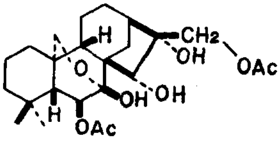


(X)



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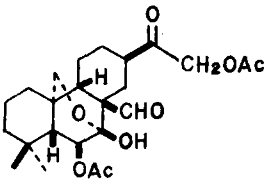

(XIV)

signals of C-17 methylene protons (s, δ 4.67 ppm), two acetoxy methyl protons (δ 2.00 and 2.12 ppm) and C-6 proton doublet (δ 5.00 ppm, J = 5.0 Hz). Now, ozonolysis[8] was tried on the diacetate XI : XI was dissolved in dry EtOAc and cooled to -75°, then an equivalent amount of ozone was passed to yield an ozonide, which was decomposed with prereduced palladium-charcoal. The reaction product was chromatographed on silica gel column to give the desired keto-diacetate XII, m.p. 201 ∿ 204°, in 55% yield and a small amount of keto-monoacetate XV, m.p. 250 ∿ 253°(decomp.). The IR spectrum (KBr) of XII had an absorption band at 1752 cm^{-1} due to a cyclopentanone, and its NMR spectrum($CDCl_3$) showed a doublet signal(J = 2.0 Hz) at δ 4.78 ppm assignable to the C-15 proton. The IR spectrum of XV had also an absorption band at 1750 cm^{-1} and its NMR spectrum($CDCl_3$) showed a broad singlet signal at δ 3.80 ppm assignable to C-15 proton.

Finally, keto-diacetate XII was subjected to hydrogenolysis with an excess amount of calcium in liquid ammonia to afford the known compound II, m.p. 255 ∿ 260°(decomp.), which has been already converted into III[1]. Thus, a formal chemical conversion of enmein into ent-kaurene, atisine, garryine, and veatchine was performed.

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