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MODIFICATION OF α-SANTONIN II[1].
SYNTHESIS OF DIHYDROCOSTUNOLIDE[*1].

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In a previous paper[1], we have reported that the 3-hydroxy-4,5-epoxy-6,11βH-eudesm-1-en-6,12-olides are stereospecifically chlorinated to the corresponding 3-chloro derivatives(I) having the inverted configuration of C_3-H by the action of methanesulfonyl chloride or p-toluenesulfonyl chloride.

In this communication, we wish to describe a novel method for the preparation of cyclodecanone intermediate which is useful for the synthesis of not only germacrene-type sesquiterpenoids but guaiane-type sesquiterpenoids, and also describe the synthesis of dihydrocostunolide(IX)[2a),2b),3] isolated from costus root oil.

A diastereomeric mixture of the chlorides(I) was treated with sodium iodide zinc(acetone, reflux, 40-50 min.) to give a dienol(II)[yield: 95%, mp 118-119°, ir: 3500, 1780, uv: λ_{max}^{MeOH} 263 nm, nmr: 5.51(1H, dd, J=9.0, 2.0 Hz; C_1-H), 5.73 (1H, dd, J=5.0, 2.0 Hz; C_3-H), 5.93(1H, dd, J=9.0, 5.0 Hz; C_2-H)], which without purification was submitted to the next reaction because the dienol(II) was rearranged to form hyposantonin[4] and isohyposantonin[4] on silica-gel chromatography

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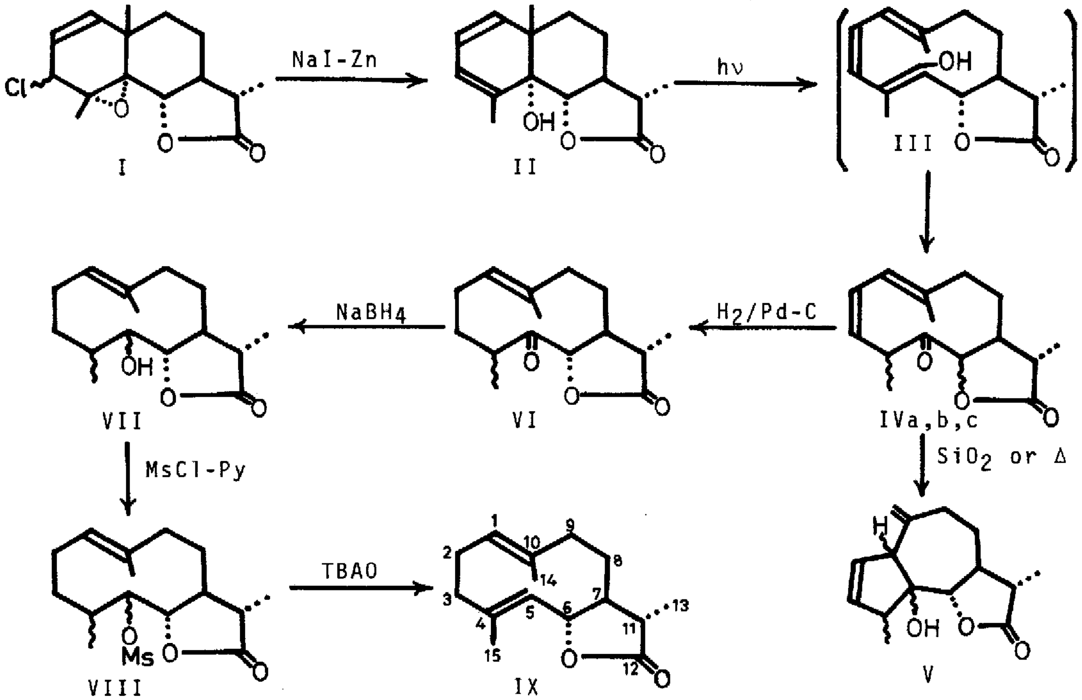
[*1] The new compounds accompanied with physical data in the text gave satisfactory analytical values. The ir spectra(cm^{-1}) of crystallized compounds were taken in KBr and the nmr spectra(δ, 100 MHz) were measured in $CDCl_3$ containing 1% TMS as an internal standard.

While the photolytic cleavage of hexahydronaphthalene derivatives[3,5] usually yields a photostationary equilibrium mixture of the starting material and a cyclodecatriene, the irradiation of the dienol(II)(7 W low-pressure mercury lamp, methanol, 15°)[*2] provided a diastereomeric mixture of dienones(IVa:IVb:IVc= 5:1:1, yield: ∿80%) in good yield because the initially formed cyclodecatrienol (III) was immediately transformed to the stable dienones before equilibration.

The cyclodecadienone structure of the photolytic products was confirmed by the following spectral data and the chemical conversions[IVa; mp 64.5-65.0°, ms: m/e 248; M^+, ir: 1775, 1710, uv: λ_{max}^{MeOH} 214 nm, nmr: 3.49(1H, m; C_4-H), 4.50 (1H, d, J=7.5 Hz; C_6-H), 5.45(1H, m, J=10.2, 4.6, 2.0 Hz; C_3-H), 5.69(1H, m; C_2-H), IVb; oil, ms: m/e 248; M^+, ir: 1770, 1720, uv: λ_{max}^{MeOH} 203 nm, IVc; mp 145-147°, ms: m/e 248; M^+, ir: 1770, 1720, uv: λ_{max}^{MeOH} 203 nm].



[*2] Application of a 10 W or more powerful low-pressure mercury lamp to the photolysis increased the side reactions.

Treatment of IVa with refluxing benzene or silica-gel gave a guaianolide-type derivative(V) in quantitative yield[mp 119-120°, ms: m/e 248; M^+, ir: 3450, 1770, 890, nmr: 5.01, 5.18(1H each, m; C_{14}-H), 5.50(1H, dq, J=5.6, 1.5, 1.0 Hz; C_2-H), 5.97(1H, quint, J=5.6, 2.8, 2.8 Hz; C_3-H)].

Hydrogenation of IVa over palladium on charcoal, followed by treatment of the resulting dihydro derivative(VI)[mp 73-74°, ms: m/e 250; M^+, nmr: 1.66(3H, s; C_{14}-H), 4.98(1H, m; C_1-H)] with sodium borohydride(isopropanol, room temp., overnight) afforded an alcohol(VII)[yield: 57.8%, mp 115-117°, ir: 3380, 1755 (shoulder), 1745, nmr: 3.43(1H, dd, J=5.8, 2.0 Hz; C_5-H), 4.23(1H, dd, J=5.0, 2.0 Hz; C_6-H), 5.35(1H, m; C_1-H)].

Dehydration of the alcohol(VII) with thionyl chloride-pyridine or phosphoryl chloride-pyridine produced a complex mixture and the dihydrocostunolide could not be detected on thin layer chromatograms(tlc) or gas liquid phase chromatograms(glpc) of the reaction products.

Thus, the alcohol(VII) was converted into a mesylate(VIII)[quantitative yield, mp 137-138°, ir: 1360, 1180, nmr: 3.09(3H, s; OSO_2CH_3), 4.82(1H, dd, J=2.0, 1.0 Hz; C_5-H)] which was treated with tetra-n-butylammonium oxalate[*3,6] (TBAO)(acetone, 60-65°, 5 days) to give the dihydrocostunolide(IX)[yield: 39.6%, $[\alpha]_D^{18°}$ +105.2°($CHCl_3$, c. 0.37%)(lit.[7] $[\alpha]_D$ +113.6°($CHCl_3$, c. 3.0%)] after purification by preparative tlc(benzene:AcOEt=5:1).

The synthetic dihydrocostunolide was identical with an authentic specimen in tlc, glpc, and ms, ir and nmr spectra.

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*3. In spite of the extensive efforts, the dihydrocostunolide was not obtained by treatment of mesylate(VIII) with 1,8-diazabicyclo[5,4,0]undecene-7(DBU) or any other organic bases.

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