A New Synthesis of α-Chamigrene

α-Chamigrene has been synthesised via a new spiro-annelation reaction, copper(II) chloride catalysed decomposition of phenolic α-diazoketone (III).

Keywords—total synthesis; α-chamigrene; spiro[5.5]undecane; spiro-annelation; reaction; phenolic α-diazoketone

In a previous paper,1) we described a new synthetic method of spiro[4.5]decane carbon framework via metal catalysed decomposition of phenolic α-diazoketones. Now we extend this reaction to the synthesis of α-chamigrene (I).2)

4-Methyl-4-(p-hydroxyphenyl)pentanoic acid3) was protected at the phenolic hydroxy group by acetylation (Ac₂O, aqueous NaOH) and then converted to the acyl chloride (II) (SOCℓ₂, benzene). Slow addition of II to an ethereal solution of diazomethane4) at 0°, followed by hydrolysis (Na₂CO₃, NaHCO₃, aqueous methanol)5) gave the phenolic α-diazoketone (III) in over all 70% yield. Decomposition of III in the presence of cupric chloride on refluxing benzene gave the spiro-dienone (IV)6) (20%), mp 143–144°, infrared spectrum (IR) νmax cm⁻¹: 1710, 1660, and 1620; ultraviolet spectrum (UV) λmax nm (ε): 241 (1.7 × 10⁴). Partial reduction of IV with sodium borohydride in methanol at 0° gave with stereoselectivity (the trans-alcohol, <5%) the cis-alcohol (V) (80%), mp 193–194°, IR νmax cm⁻¹: 1660 and 1630; UV λmax nm (ε): 248 (1.5 × 10⁴); proton magnetic resonance (PMR) δ (CDCl₃): 4.00 (1H, m, W 1/2 = 8 Hz, -CH-O-). The spiro-dienone (V) was catalytically hydrogenated (H₂/Pd-C, AcOEt) to give the saturated ketone (VI) (90%), mp 96–97°, IR νmax cm⁻¹: 1710, and which was converted to the spiro-undecene (VII)7) (50% from (VI)), mp 52–53°, by warming the corresponding mesylate (VII) (MsCl, pyridine) in dimethyl sulfoxide at 60°. The ketone (VII) was treated with methylmagnesium iodide to give a mixture of distereomeric alcohols (IX) (80%). Without separation, the mixture of alcohol underwent dehydration (silica gel-FeCl₃)8) to give α-

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\begin{align*}
I & : R = \text{Ac}, R' = \text{Cl} \\
II & : R = \text{Ac}, R' = \text{Cl} \\
III & : R = \text{H}, R' = -\text{C} = \text{N}_{2} \text{CH₃} \\
IV & : R = \text{O} \\
V & : R = -\text{O} \\
VI & : R = \text{H} \\
VII & : R = \text{Ms} \\
VIII & : R = \text{O} \\
IX & : R = \text{Me} \text{OH}
\end{align*}
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Chart 1

6) Satisfactory analytical and spectral data were obtained for new compounds.
chamigrene (I). This product was identified by spectral comparison with an authentic α-chamigrene.

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Two New Sesquiterpenoids from *Asarum caulescens*

Two new sesquiterpenoids, caulolactone A(II) and caulolactone B(III) were isolated from *Asarum caulescens*. It was suggested that they were formed via the conformers I-A and I-B of germacrone-4,5-epoxide (I) respectively. Moreover, two configurational isomers of germacrone-1,10; 4,5-diepoxydies (IV and V) were derived from I also via I-A and I-B.

Keywords—sesquiterpenoids; caulolactone A; caulolactone B; transannular rearrangement; *Asarum caulescens*; germacrone-1,10; 4,5-diepoxydies

Previously, the authors have reported the structures of 12 new sesquiterpenoids from essential oil contained in *Asarum caulescens Maxim.* (Aristolochiaceae) collected at various parts of Japan.1) In this report, the authors wish to report the structures of the two new sesquiterpenoids named as caulolactone A (II) and caulolactone B (III), in addition to main component, germacrone-4,5-epoxide (I) from *Asarum caulescens* collected at Mt. Khotsu in Tokushima Prefecture. The subterranean part of the plant were extracted with ether at room temperature. The extract was chromatographed on silica gel by using petroleum ether–diethylether (5:1) to give I (48%), II (1.2%), and III (1.0%). Compounds II and III were also derived from I by treating with anhydrous aluminium chloride in absolute ether, of yields 10% and 8%, respectively (Chart 2).

Caulolactone A(II): Colorless needles, mp 97—98°, C_{12}H_{28}O_2; [α]_D^25=+170° (c, 0.3, MeOH), IR ν_{max} 1715 cm^{-1}, UV λ_{max} 234 nm (ε, 10,000). These data showed the presence of α,β-unsaturated lactone group in the molecule, and also CD (θ_250=+700, [θ]_{120}=+840) supported the presence of this group.2) ^1H-NMR (dCl_4+TMS) 1.18 (tent. methyl on a carbon atom bounded with an oxygenic function), 1.72, 1.81, 2.13 (three olefinic methyls), 4.74 (2H, s, terminal methylene).

II was heated with 10% HCl/aq. methanol to give three compounds: VI being shifted the double bond from terminal to isopropylidene type, mp 105—106°, C_{12}H_{28}O_2; λ_{max} 1715 cm^{-1}, λ_{max} 234 nm (ε, 1600), δ_{ppm} 1.22 (tent. methyl), 1.55, 1.58 (isopropylidene), 1.74, 2.18