This observation indicated that the configurational relationship between two hydroxyl groups at C₈ and C₁₅ in serratandine is trans. However, it is still obscure which hydroxyl group is situated in the β configuration. This ambiguity was solved by the following experiment.

Treatment of serratandine (IV) with phosgene in pyridine afforded serratandine carbonate (XIII), mp 277—278°, C₁₇H₂₉O₅N, IR νmax cm⁻¹: 3050 (OH), 1747 (C=O). IR spectral data showed that the carbonyl group in this carbonate ester is situated on the six membered ring or larger. The formulae (XIII) and (XIV) for serratandine carbonate are still possible but the latter was excluded by the following NMR observations. The NMR spectrum of the carbonate in DMSO revealed three signals at 6.28 (1H, br. d., J=4 cps, >CH–OH), 5.55 (1H, br. d., J=4.3 cps, >CH–OCO–), 4.26 (1H, d., J=4 cps, –OH) and the last signal disappeared by treatment with D₂O, suggesting that the free hydroxyl group in the carbonate is the secondary one. The double resonance technique supported also the correctness of this assignment. These observations show clearly the cis relationship between the C₁₅ and C₁₅ hydroxyl group.

Since the absolute configuration of serratinine (I) which was correlated with serratandine through the compound (VI) with the original hydroxyl group at C₁₅ intact, has been firmly established, the absolute stereoregistration of serratandine should be represented by the formula (IV) and cis–diox–A which seems to arise from (VIII) by attack of OsO₄ from the less hindered α side, is depicted by the formula (IX).

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Synthesis of Ecdysone

Insect molting hormone ecdysone (I) was isolated in pure state in 1954 by Butenandt and Karlson¹) and its chemical structure was elucidated as \( 2β,3β,14α,22β, 25\)-pentahydroxy-\( 5β\)-cholest-7-en-6-one (I) by X-ray analysis in 1965.²) Only one year after establishment of structure, two groups³,⁴) succeeded in the synthesis of ecdysone. In our program to synthesize ecdysone, its chemical structure was divided into three partial structures, namely, A-ring (II), B,C–ring (III) and side chain (IV) structure, and novel and improved methods of preparation of these partial structures were developed, two of these methods being already reported. We now succeeded in synthesis of ecdysone by using above-mentioned methods.

Stigmaster-22-ene-3,6-dione (V) was served as a starting material, which was introduced into diketal (VI) (mp 119–121°, $[\alpha]_D^\infty +3$) by the usual method. Ozonolysis of VI, followed by treatment with zinc dust in acetic acid, gave diketal aldehyde (VII) (mp 172–175°, $[\alpha]_D^\infty -2$). Reaction of VII with ethynylmagnesium bromide afforded ethynyl compound (VIII) as a mixture of 22-isomers, which was treated with methylmagnesium bromide and then shaken with carbon dioxide to give unsaturated acid (IX). Without isolation of isomeric carboxylic acids, IX was catalytically hydrogenated with 10% palladium-charcoal and hydrolyzed by 50% acetic acid to a mixture of isomeric dioxa lactone. This mixture was again converted into 3,6-diketal, which was treated with hydrochlordic acid in mild condition to give a sparingly soluble 3-monomethyl of dioxolactone (X) (mp 314–317°, $[\alpha]_D^\infty +9$). This monomethyl (X) was found to be 23β-lactone and, accordingly, an important key intermediate in edysone synthesis. From mother liquor, another isomeric dioxa lactone (XXIII) (mp 270–277°, $[\alpha]_D^\infty +28$) was isolated as completely hydrolyzed compound (3,6-dione).

The 3-monomethyl (X) was hydrolyzed with $p$-toluenesulfonic acid in aqueous acetone to 3,6-dione (XI) (mp 243–246°, $[\alpha]_D^\infty +6$), which was partially reduced with one equivalent volume of sodium borohydride in ethanol-methylene chloride at $-5$° for 30 minutes to give 3β-hydroxy-6-one (XII) (mp 222–223°, $[\alpha]_D^\infty -7$). Ketalization of XII into oily 6-ketal (XIII), followed by oxidation with pyridine-chromium trioxide complex, led to 6-monomethyl of 3,6-dione (XIV) (mp 224–228°, $[\alpha]_D^\infty +28$).

Introduction of 2β,3β-dihydroxyl grouping in this lactone series was made according to the method reported already from this laboratory. Autoxidation of XIV in the presence of potassium tert-butoxide in tert-butanol afforded a mixture of two possible enol compounds of 2,3-dione (XV) as oily substance. Reduction of enol mixture (XV) with sodium borohydride in methanol, followed by treatment with $p$-toluenesulfonic acid in methanol, led to a mixture of 2,3-diol, from which pure 2β,3β-dihydroxy-6-one (XVI) (mp 254–258°, $[\alpha]_D^\infty 0$°) was isolated in pure state by preparative thin-layer chromatography in satisfactory yield. The proof of the structure depends upon the fact that this diol (XVI) could be converted easily into an acetone (XXIV) (mp 238–241°, $[\alpha]_D^\infty +17$), which on hydrolysis recovered the starting material (XVI), and analogy with chemical transformations in the corresponding cholestane series. Acetylation of XVI with hot acetic anhydride gave the diacetate (XVII) (mp 230–233°, $[\alpha]_D^\infty +4$).

Bromination of XVII with one equivalent volume of bromine in acetic acid and successive warming at 50° for 2 hours afforded crude 7-bromo compound (XVIII). Crude XVIII

7) The assignment of the configuration of C-22 hydroxyl group in X and XXIII was based upon the fact that edysone and isoe Crypsis were synthesized from X and XXIII, respectively.
was treated with lithium carbonate in dimethylformamide to afford 7-en-6-one (XIX) (mp 271—274°, \([\alpha]_{D}^{20} +20^\circ\), UV \(\lambda_{max}^{E} (e) 244 \text{ m}_{\mu} (14200)\)). A hydroxyl group was introduced at C-14 in XIX by a novel method developed in this laboratory,\(^9\) that is, enol acetylation of XIX with acetic anhydride in the presence of a small amount of perchloric acid in ethyl acetate\(^{10}\) afforded an enol acetate (XX) as an oily substance, which was oxidized with 1.3 equivalent of monoperphthalic acid in ether–tetrahydrofuran mixture to 14α-hydroxy-7-en-6-one (XXI) (mp 269—272°, \([\alpha]_{D}^{20} +70^\circ\), UV \(\lambda_{max}^{E} (e) 240 \text{ m}_{\mu} (12700)\)).

Hydrolysis and isomerization (at C-5) of XXI with 0.6% potassium carbonate in 90% methanol at reflux temperature for 30 minutes gave 2β,3β,14α-trihydroxy-7-en-6-ones as an equilibrium mixture. From this equilibrium mixture, which consisted of 5β- and 5α-compound at a ratio of 4:1,\(^{11}\) 5β-isomer (XXII) (mp 264—266°, \([\alpha]_{D}^{20} +79^\circ\), UV \(\lambda_{max}^{E} (e) 243 \text{ m}_{\mu} (10600)\)) was isolated by preparative thin-layer chromatography. Grignard reaction of XXII with a large excess of methylmagnesium bromide in tetrahydrofuran at 0° for 30 minutes afforded ecdysone (I) (mp 238—239°, \([\alpha]_{D}^{20} +62^\circ\), UV \(\lambda_{max}^{E} (e) 243 \text{ m}_{\mu} (11600)\)) identical in all physical properties (melting point, optical rotation, UV, IR, NMR and MS) with those reported for the natural product.

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11) Stereochemistry of this type of equilibrium was discussed in detail in reference 8 and 9.

Ferricyanide Oxidation of dl-N-Methylisalsosoline and Its Methiodide\(^{1}\)

In connection with a preceding work,\(^{2}\) ferricyanide oxidation of dl-N-Methylisalsosoline (I) and its methiodide (II) was examined.

To a stirred solution of I (1.56 g, 7.5 mmole) in dioxane (64 ml) and 2.8% aq. NH₄OH (160 ml) was added powdered K₃Fe(CN)₆ (5.6 g, 17.0 mmole). After two hr's agitation at room temperature followed by standing for 1 hr, the reaction mixture was treated with K₂CO₃ (powder) and the product was extracted with CHCl₃.

\(^{1}\) All melting points were uncorrected using a Yanagimoto micro melting point measuring apparatus. All nuclear magnetic resonance (NMR) spectra were taken with a JNR-C60S spectrometer and the chemical shifts were \(\tau\)-value measured from DSS as internal standard. Mass spectrometry (MS) spectrum was measured with a Hitachi mass spectrometer Model RMU-6D. Gas liquid chromatography (GLC) was run with a Shimadzu GC-1C gaschromatograph (hydrogen flame ionization detector) on 1.5% OV-17 as stationary phase. Thin-layer chromatography (TLC) were carried out on silicagel G (Merck), developing solvents: a) conc. NH₄OH–MeOH (1:20) for tertiary and b) 10% HCl–MeOH (1:2) for quaternary amines.