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α-ONOCERADIENE-SERRATENE ISOMERIZATION AND THE CONFIGURATION OF SERRATENEDIOL

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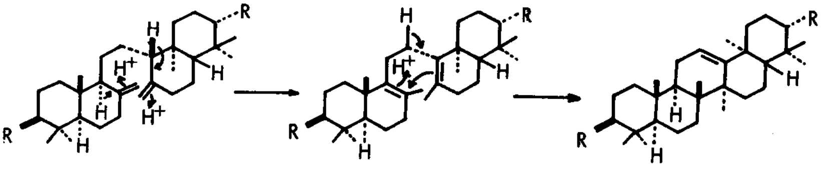
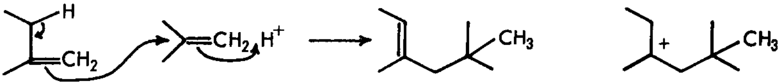
IT has long been known (1) that α-onocerin (I) isomerized by the action of mineral acid into β-(II)* and γ-onocerin (III), and these structures have already been elucidated by Barton and Overton (2). γ-Onocerin is obviously the product from β-onocerin which, in turn, is the product due to double protonation to each double bond in α-onocerin.



(I) (II) (III)

Single protonation to the molecule (I), however, may be expected to cause a complete change of the course, and the product, if followed by scheme 1, should have the structure (B) which we have already assigned to serratenediol (4).



(A) (B) (C)

Scheme 1

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* We have confirmed that the n.m.r. spectrum of β-onocerin diacetate supported the revised structure (II) suggested by Jeger et al. (3).

Re-examination of the isomerization with mineral acid only confirmed the previous results (2). α-Onoceradienediol diacetate (I, R=OAc) even on mild treatment with sulphuric acid gave a single product, β-onoceradienediol diacetate (II, R=OAc) which could be further isomerized to γ-onocerenediol diacetate (III, R=OAc).

Bulky Lewis acid, however, may possibly produce the desired transformation and the validity of this assumption was proved as follows. α-Onoceradienediol diacetate (I, R=OAc) when kept overnight with boron trifluoride in chloroform gave a product of mixture, whose thin layer chromatography showed four spots corresponding to the starting material, β-onoceradienediol diacetate (II, R=OAc), serratenediol diacetate (IV, R=R'=OAc), and γ-onocerenediol diacetate (III, R=OAc) or isoserratenediol diacetate* (V, R=R'=OAc), respectively. Further treatment of this mixture with the same reagent reduced the complexity of the product which in thin layer chromatography gave only two spots corresponding to serratenediol diacetate (IV, R=R'=OAc) and γ-onocerenediol diacetate (III, R=OAc) or isoserratenediol diacetate (V, R=R'=OAc). As these two products were not preparatively separable to characterize, the product was directly hydrolysed, oxidized by chromium trioxide-pyridine complex, and then converted into a mixture of hydrocarbons by Wolff-Kishner reduction. Gas chromatography of this hydrocarbon mixture exhibited two well separable strong peaks which exactly corresponded to γ-onocerene (III, R=H) and serratene (IV, R=R'=H). The ratio of the products was ca. 2:1. The presence of trace isoserratene (V, R=R'=H) in the mixture was also demonstrated from a very small peak near to γ-onocerene.

The preparative separation and characterization of the isomerization products could be achieved when α-onoceradienedione (I, R=O) was used as the starting

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* γ-Onocerenediol diacetate and isoserratenediol diacetate (vide infra) accidentally gave an inseparable spot in thin layer chromatography.

material. The dione (I, R=O), by the same reagent, much more slowly isomerized to produce three well defined compounds, β-onoceradienedione (II, R=O), γ-onocerenedione (III, R=O), and serratenedione (IV, R=R'=O). They were separated from the mixture by repeated fractional crystallizations and their identities with authentic specimens were rigidly confirmed by direct comparisons (m.p., mixed m.p., IR, and ORD). In order to obtain the full information of the components in the product, the crude product was converted into the mixture of hydrocarbons and the resulted mixture was examined by gas chromatography which revealed that the mixture was consisted of α-onoceradiene (I, R=H), β-onoceradiene (II, R=H), γ-onocerene (III, R=H), serratene (IV, R=R'=H), and isoserratene (V, R=R'=H) in ratio of 7, 17, 32, 33 and 11%, respectively.

Serratene derivatives (IV), in turn, isomerized by vigorous treatment with mineral acid into iso-series (V) (R=R'=OH, isoserratenediol, m.p. 267-269° ; R=R'=OAc, diacetate, m.p. 294-296° ; R=R'=O isoserratenedione, m.p. 169-170°; R=R'=H isoserratene, m.p. 174-178°), but could be isomerized only to a negligible extent by the treatment with boron trifluoride. That the double bond had migrated from Δ^{14} to Δ^{13} in iso-compounds was illustrated by its tetrasubstituted nature and the strong positive Cotton effect of isoserratenedione ($a = +70$)* in contrast to serratenedione which gave a weakly negative Cotton effect (6) ($a = -17$). These findings strongly suggested that α-onoceradiene (I)-serratene (IV) isomerization must involve the concerted elimination of proton (A → B) rather than the carbonium ion intermediate (C) which contrary to the results would probably produce iso-compounds (V) by a subsequent loss of proton.

As serratenedione (IV, R=R'=O) could be reduced by sodium and n-propanol

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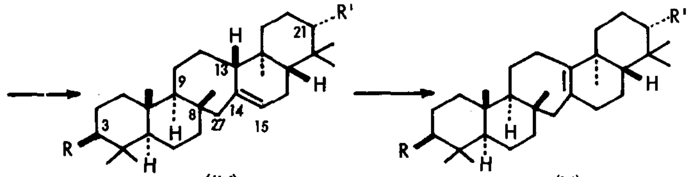
$a = 10^{-2} ([\phi]_1 - [\phi]_2)$ (5).

into serratenediol and α-onocerin has already been synthesised (7), the above transformation means the total synthesis of serratenediol. The main feature of the configuration of serratenediol is naturally derived from the configuration of α-onocerin (2, 3a), and the both hydroxyl groups in serratenediol must be equatorial since they are formed by sodium and propanol reduction of the dione. The same ORD curves of synthetic and natural serratenedione also showed that serratenediol (IV, R=R'=OH) has the same absolute configuration with that of α-onocerin (3a).

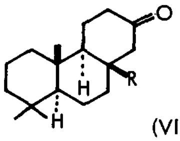
The only remaining problem, the configuration of C_8 methyl group, could be solved from different series of findings.

We have eventually isolated serratenediol monoacetate $C_{32}H_{52}O_3$, m.p. 319-320°, $[\alpha]_D$ -5.7° (c, 1.06 in $CHCl_3$) from the plant together with serratenediol, to which we are going to assign the structure (IV, R=OAc, R'=OH). Oxidation of this monoacetate gave serrateneolone acetate, $C_{32}H_{50}O_3$, m.p. 305-307° which was reduced by Wolff-Kishner method to a mono-ol, serrateneol m.p. 266-267° (acetate, $C_{32}H_{52}O_2$, m.p. 302-305°). Oxidation of serrateneol gave a ketone $C_{30}H_{48}O$, m.p. 204-206°, in which the ketonic function must be situated on the opposite terminal ring respect to serrateneolone acetate.

(I)



(IV) (V)



(VI)

The ORD curve of serrateneolone acetate gave a negative Cotton effect (a = -31), whereas the other ketone gave a positive one (a = +30); the former agrees with those of Δ^7-lanosten-3-one (8) and bauerenone (6) and the latter similar to those of normal triterpene C_3 ketones (9). Thus the position of O-acetyl group in serrateneolone acetate must be at C_3 and the ketonic function at C_{21} as represented by the structure (IV, R=OAc, R'=O). The ketone must be Δ^{14}-serraten-3-one (IV, R=O, R'=H), whose positive Cotton effect suggests that ring B/C is trans junctured and C_8 methyl group is β oriented, since triterpene C_3 ketone of B/C-trans with C_8 β-methyl group always gave a positive Cotton effect (9, 10) which could hardly be changed by a little alternation of Ring C.

The confirmatory evidence of β configuration of this methyl group was provided by the ORD examination of C_{18}-ketone (VI, R=Me) given in the previous communication. The compound gave a positive Cotton effect (a = +55). The sign and the amplitude excellently agreed with those of analogous compounds of which the configurations have already been known (VI, R=H, a = +48; R=CN, a = +65; R=OH, a = +76; R=CO_2Me, a = +80; R=CH_2CO_2Me, a = +32) (5).

Therefore we conclude the absolute configuration of serratenediol as represented by the absolute stereo-structure (IV, R=R'=OH).

There may be a question that serratenediol might be an artifact from α-onocerin during the extraction. The possibility can obviously be eliminated because, by the same extraction procedure, α-onocerin but no serratenediol could be isolated from *Lycopodium clavatum* (11), whereas *Lycopodium serratum* gave serratenediol but no α-onocerin.

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