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THE STRUCTURE OF SHIONONE

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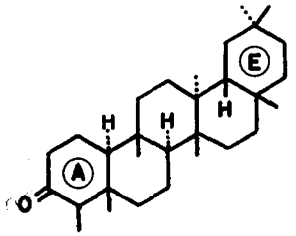
SHIONONE is a tetracyclic triterpene ketone, $C_{30}H_{50}O$, isolated from the roots of Aster tataricus L.[1)] The ORD and CD curves (negative Cotton effect) of shionone are superimposable[2a,4a,5)] upon those of friedelin (1). The partial structure 2 has been deduced[2b)] for shionone on the basis of chemical degradations[2,4)], coupled with spectral studies. The presence of both an unusual side-chain [2b,4c)] and of rings A and B analogous to friedelin[2a,2b,4b)] is characteristic of shionone. This structure (2) has been extended to 3 [2b,3)] by means of biogenetic considerations (FIGURE 1)[2b)]. This is compatible with a detailed NMR study[2c)]. However, no rigid proof for the structure around rings C and D has yet been furnished.

The present paper reports evidence which leads without the help of biogenetic considerations to the structure 3 for shionone.

Pentanorshionanoic acid (4, without 3-oxo group) was obtained from shionone by known procedures[2b)]. Pentanorshionanoyl chloride (5) was transformed into the carboxylic azide, and the azide was submitted to the Curtius rearrangement to yield hexanorshionanyl isocyanate (6), $C_{25}H_{41}ON$[6)], m.p. 150 -151°, IR : 2268 cm^{-1}. Hexanorshionanylamine (7), $C_{24}H_{43}N$, m.p. 192 -193°, was obtained by hydrolysis of 6. The amine (7), when treated with formalin and formic



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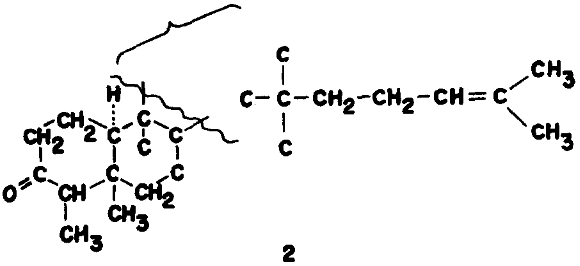

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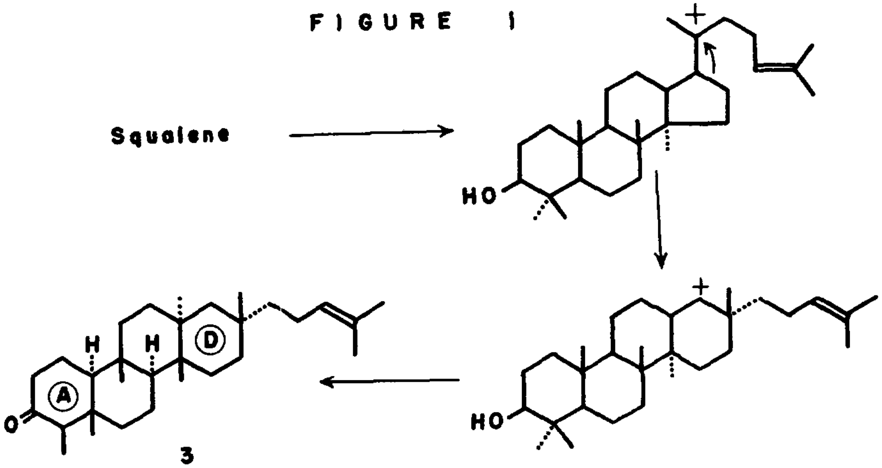
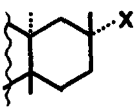
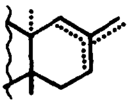




4. X = COOH
5. X = COCl
6. X = NCO
7. X = NH_2
8. X = $NHCH_3$
9. X = $N(CH_3)_2$
10. X = $N^+(CH_3)_3\,I^-$



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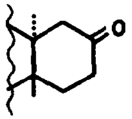

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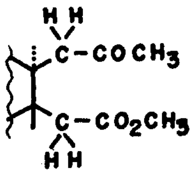

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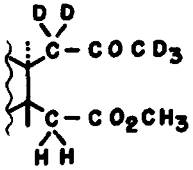

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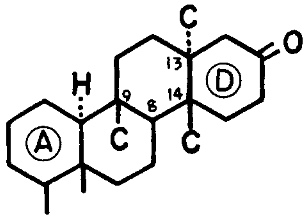
acid at 100 - 110°C , afforded a dimethylamine (9), $C_{26}H_{47}N$, m.p. 177 - 178° (yield, ca. 18 %), and a mixture of olefins (11) (yield, ca. 45 %). Treatment of 9 with the same reagent furnished the same mixture 11 (yield, ca. 94 %). The reduction of 6 with lithium aluminum hydride gave a monomethylamine (8), $C_{25}H_{45}N$, m.p. 123 - 124°, which was methylated with methyl iodide to afford 9. Hofmann degradation of the methiodide (10), $C_{27}H_{50}NI$, m.p. 202.5 - 204°, proceeded mainly to give 9.

The ozonolysis of 11 yielded, after separation by thin layer chromatography, a saturated tetracyclic ketone, heptanorshionanone (12), $C_{23}H_{38}O$, M^+ 330, $\nu_{C=O}$ 1704 cm^{-1} (in CS_2), $[\Phi]^{peak}_{316\ m\mu}$ + 3500°, $[\Phi]^{trough}_{273\ m\mu}$ - 2800° (a = + 63) in dioxane). The acidic fraction of the ozonolysis product afforded after methylation the seco-keto-ester (13), $C_{25}H_{42}O_3$, M^+ 390, m.p. 82 - 82.5°, $\nu_{C=O}$ 1733 and 1707 cm^{-1}, NMR (in C_6D_6): δ = 1.78 (3H, singlet, $COC\underline{H}_3$), 1.99 and 2.25 (2H, quartet, J = 14 Hz, $C\text{-}\overset{C}{\underset{C}{C}}\text{-}C\underline{H}_2\text{-}CO\text{-}CH_3$), 2.08 (2H, singlet, $C\text{-}\overset{C}{\underset{C}{C}}\text{-}C\underline{H}_2\text{-}CO_2CH_3$), and 3.31 (3H, singlet, $CO_2C\underline{H}_3$). When 13 was treated with NaOD-D_2O-dioxane followed by methylation, it gave a deuteriated product 14, NMR (in C_6D_6): δ = 2.08 (2H, singlet, $C\text{-}\overset{C}{\underset{C}{C}}\text{-}C\underline{H}_2\text{-}CO_2CH_3$), and 3.31 (3H, singlet, $CO_2C\underline{H}_3$).

M. Takahashi and W. Kamisako[4b)] have described the formation of a chrysene derivative on selenium dehydrogenation of 3-shionene. Considering the possible transformations which occur during dehydrogenation[7)], these authors have suggested perhydrochrysene or a cyclopentanoperhydrophenanthrene skeleton for shionone.

The IR and ORD data of the C_{23} ketone indicate that the ring D of 12 must be a six membered ring with a ring fusion (C/D) of 5α-cholestan-3-one or 5α-cholestan-2-one type[8)]. Thus, perhydrochrysene represents the framework of shionone; a cyclopentanoperhydrophenanthrene skeleton is eliminated. The NMR spectrum of the keto-ester (13) shows that both $-CH_2CO_2CH_3$ and $-CH_2COCH_3$ groups are attached to tertiary carbon atoms. With this information, the two alternative structures 15 and 16 were derived for the C_{23} ketone (12).

The NMR spectrum of shionone in deuteriobenzene shows the presence of five tertiary methyl groups, two allylic methyl groups and one secondary methyl group[2b)]. This requires the presence of five methyl groups for 12. As the



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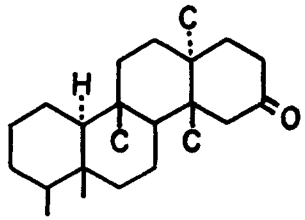

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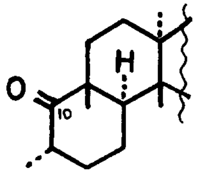

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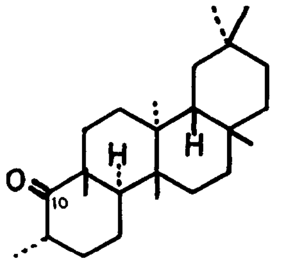

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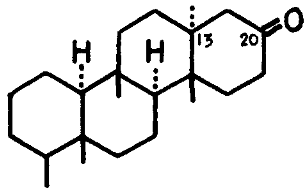

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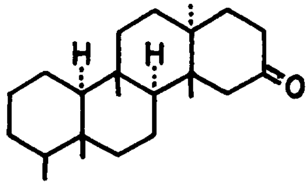

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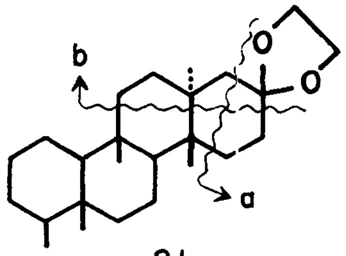

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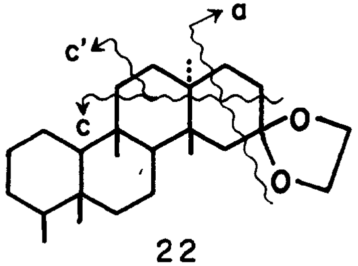

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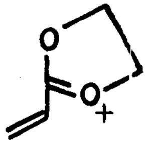

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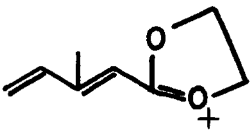

b

nature of twenty carbon atoms among twenty-three is already clarified, the substituents at C_9, C_{13} and C_{14} of 15 or 16 must be methyl groups, and the presence of one hydrogen atom at C_8 is required. The ORD and CD curves of des-A-10-oxoshionane (17) are superimposable[2b)] upon those of des-A-10-oxofriedelane (18). This favors for 17 the ring fusion B/C as in friedelin[2b)]. These observations lead to two alternative structures 19 and 20 for the C_{23} ketone (12).

The mass spectrum of heptanorshionanone ethylene ketal obtained from 12 shows a peak at *m/e* 99 (*a*)[9)] (base peak) together with a strong peak at *m/e* 139 (*b*), of nearly the same intensity. Formula 21 could represent this ethylene ketal: cleavage " b " would give a fragment *b*. The alternative structure (22) would suffer cleavages " a " and " c " (or " c' "), of *m/e* different from " b ". Thus the C_{23} ketone (12) must be 20-oxoheptanorshionane (19)[3)]. The side-chain is therefore attached to C_{20}.

The NMR studies[2c)] on a series of compounds of shionane show that the side-chain bears a 1,3-*diaxial* relationship to one of the tertiary methyl groups on the skeleton. With the α (axial) orientation deduced already for a methyl group at C_{13}, the configuration of the side-chain must be α (axial). Structure 3 follows for shionone. The partial synthesis of norshionene from friedelin will be described in the next paper. This synthesis confirms the above conclusion.

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