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ON THE FRIEDELENE-OLEANENE REARRANGEMENT

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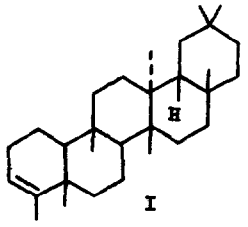
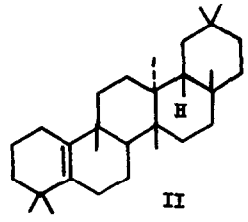
The acid catalyzed rearrangement of Δ^{3}-friedelene I into Δ^{13-18}-oleanene IV(1) is one of the most remarkable transformations in the annals of terpene chemistry.(2) No fewer than six successive 1,2-migrations (four methyl groups and two hydrogen atoms) must occur during the course of this reaction. Of additional interest is the fact that the over-all rearrangement constitutes an exact reversal of the biogenesis of friedelin from a β-amyrin-type intermediate.(1a,3)



I



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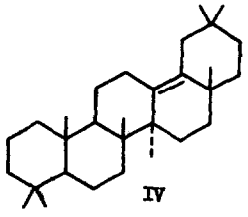

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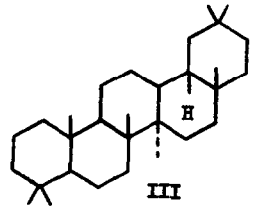

III

With short reaction times it has been possible to isolate Δ^{5-10}-glutinene II and Δ^{12}-oleanene III.(4) However, the extent to which other isomeric intermediates might be involved has not been determined. There are, for example, six other triterpene isomers which could be formed by proton elimination from each carbonium ion site along the rearrangement pathway. On the other hand, the alternating stereochemical disposition of the migrating groups is that required for "a fully concerted process."(5)

In order to define more precisely the course of this complex rearrangement, we have studied the reactions of I, II, and III (0.1%) with zinc chloride (1%) in deuterio-acetic acid at reflux temperature.(1b) The reaction was quenched after various time intervals and the products separated by preparative tlc with silver nitrate (25%)-impregnated silica gel as stationary phase. The identities of II and III have been established by direct comparison [mp, mmp, optical rotation, infrared spectra (KBr), and tlc mobility (silica gel-$AgNO_3$)] with authentic material.* Representative data are collected in Table 1.

Since the major deuterated species (41%) after one hr is III-d_2 (entry 3), the principal pathway for the I → III rearrangement must be a two-stage process. That the intermediate is mainly II follows from its isolation in major amount at 20 min. and independent conversion to III under identical conditions. A rough correction for exchange into II and III increases the proportion of III-d_2 to ca. 50%. The exchange into III, subsequent to rearrangement, is rather accurately provided by the deuterium content of the m/e 218 fragment (cf. entries 6 and 7). This intense ion is known(6) to originate from the C, D, and E rings by a retro-Diels-Alder process and is located in a region of the mass spectrum which is otherwise essentially blank. The rearrangement II → III (entry 4) must proceed mainly without the incursion of isomeric intermediates, for the amount of III-d_1 is about 75% after exchange corrections are applied.

The high percentage of III-d_1 (41%) present at 20 min. demonstrates that in the absence of a large isotopic discrimination ($k_H/k_D > 10$) in a two-step sequence, a significant

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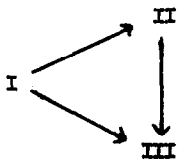
proportion (20-25%) of III must be formed from I without any proton loss during the rearrangement.** The possibility of a large isotope effect in the II → III process has been excluded by carrying out the reaction in a 52:48 mixture of acetic acid and deuterio-acetic acid (entry 5). Any selectivity in favor of proton incorporation is clearly small.

TABLE 1[a]

Entry	Time	Reactant	Products	Approx. Yield (%)	Deuterium Distribution (%)[b] d_0	d_1	d_2	d_3	d_4
1	7 min	I	I	48	93	7			
			II	26	7	84	9		
2	20 min	I	I	9	82	16	2		
			II	43	7	71	20	2	
			III	15	5	41	40	12	2
					85	15[c]			
3	60 min	I	II	28	5	50	35	8	2
			III	28	2	22	41	27	8
					66	31	3[c]		
4	60 min	II	II	26	60	34	6		
			III	24	2	49	40	7	2
					69	31[c]			
5[d]	60 min	II	II	25	82	18			
			III	29	45	43	12		
					86	14[c]			
6	60 min	III	III	74	56	44			
					59	41[c]			
7[e]	10 hr	III	III	65	17	79	4		
					22	78[c]			

[a]The concentration of HOAc in the medium ranged within 2-5% (nmr analysis) unless specified otherwise. [b]The precision of the analysis is about ± 3% and the reproducibility between duplicate experiments within 5% in most cases. Peaks of 1.5% or less abundance have been neglected. [c]Distribution in m/e 218 fragment. [d]Solvent 52-53% HOAc/DOAc. [e]Concentration of HOAc ranged from 2-17%.

**This result does not distinguish a concerted rearrangement from a step-wise mechanism involving either free carbonium ion, acetate, or chloride intermediates.



The specific exchange of a single hydrogen from III is interesting. That this exchange involves the vinyl hydrogen has been established by quantitative integration of the time-averaged nmr absorption in the region δ = 5 to 6 ppm. The intensity of the vinyl triplet in III recovered from the exchange experiments (6 and 7) was reduced to 54-61% and 19% of one hydrogen respectively (benzhydrol served as internal integral standard).

It is evident that Δ^{12}-oleanene is rather resistant to further rearrangement and that the II → III reaction is essentially irreversible. If the intermediate in the vinyl hydrogen exchange process be taken to resemble the hypothetical biosynthetic intermediate (i.e. protonated β-amyrin) in the formation of friedelin and Δ^{5}-glutinone,(1a,3) the enzyme system involved must be able to compensate for the energy deficit apparent in the reverse rearrangement (III → II).

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