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FINAL CLARIFICATION OF THE SATURATED HYDROCARBONS DERIVED FROM HYDROXYHOPANONE, DIPLOPTENE, ZEORIN, AND DUSTANIN

Y. Tsuda, K. Isobe, S. Fukushima
Faculty of Pharmaceutical Sciences, Osaka University
Toyonaka, Osaka

H. Ageta and K. Iwata
Shôwa College of Pharmacy, Setagaya, Tokyo

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ALTHOUGH hydroxyhopanone (I)(1), diploptene (V)(2), zeorin (II)(3,4,5) and dustanin (III)(6) have been considered to have the same hopane skeleton, there is an ambiguity on the identity of the saturated hydrocarbons derived from these compounds (TABLE I)(6).

TABLE I

Author	Name	Source	M.p.°C	$[\alpha]_D$	Method	Ref.
Barton	zeorinane	zeorin	186.5-187.5	+12	(b)(c)	(7)
Halsall	hopane	hydroxyhopanone	198	+43	(b)	(8)
Huneck	zeorinane	zeorin	191.5-192	+ 5.4	(c)	(4)
Ageta	hopane	diploptene	206-207[*1]	+42	(a)	(2)
Huneck	hopane	zeorin	---	---	---	(5)
Tsuda	dustanane	dustanin	179-182	---	(c)	(6)
	zeorinane	zeorin	182-184	---	(b)	

Halsall recognized that his hopane obtained by the hydrogenation of hopenes (V and VI) was different from Barton's zeorinane (9), whereas Huneck supposed his zeorinane prepared by forced Wolff-Kishner reduction of 22-deoxy-zeorinone was identical with Halsall's hopane (4,5). We have confirmed that hopane obtained by the hydrogenation of diploptene (V) shows a single peak in VPC (10); hopane derived from

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[*1] Further recrystallization of the specimen from acetone gave that having m.p. 220-221°. Our m.p.s in this communication were taken on a Kopfler Block and uncorrected.

hydroxyhopanone (I) by Halsall's method gives the same peak when rigorously purified; on the other hand, zeorinane prepared from zeorin (II) by Huneck's method is different from our hopane, while the properties of dustanane [*2] is identical with those of zeorinane (6).

There have been known three methods for the preparation of the saturated hydrocarbons from these naturally occuring triterpenoids; (a) catalytic hydrogenation of hop-22(29)-ene, (b) dehydration of 22-hydroxyhopanes, followed by hydrogenation of the resulting unsaturated compounds, or (c) catalytic hydrogenolysis of 22-hydroxyhopanes in acetic acid. Either method has been assumed to give the same saturated compound (7). We have, however, found that the methods (b) and (c) give a mixture of two saturated compounds, one corresponding to hopane (VII), the other to 21α-hopane (VIII),[*3] the ratio of the two varying with the condition of the reaction and also with the followed purification method for getting the specimen. For example, hydroxyhopane (IV) has given a mixture of VII and VIII in a ratio of ca. 1 : 3 by the method (b); further recrystallization from acetone-ether of the mixture has afforded pure VII as the specimen showing a single peak in VPC, although VII is the minor product. It is summerized in this communication that hopane reported by Ageta (2) and probably the sample by Halsall (8) are almost pure hopane; Huneck's hopane (5),[*4] zeorinane (7,4,6) and dustanane (6) should be 21α-hopane contaminated with a considerable amount of hopane; finally, zeorin and dustanin have the same hopane skeleton as in hydroxyhopanone. To clarifying these situation, the following experiments according to the methods (b) and (c) have been carried out by the aid of VPC. [*5]

Dehydration of 22-hydroxy-hopane (IV) derived from hydroxyhopanone (I) with phosphorous oxychloride in pyridine gave a mixture of

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[*2] Actually our zeorinane and dustanane used for comparison (6) were 21α-hopane (VIII) contaminated with 13% and 7% of hopane (VII), respectively.

[*3] The following notations are used: Hopane (VII) for 17βH, 21βH-; 21α-hopane (VIII) for 17βH, 21αH-; 17α-hopane (XIII) for 17αH, 21βH-configuration.

[*4] The NMR spectrum reported to be that of hopane (5) is different from our observation, but is very similar to that of 21α-hopane (VIII) (TABLE II).

[*5] Vapor phase chromatography was carried out on 1% SE-30 column. Retention time (RRT) was calculated from the solvent peak (n-hexane) and presented relative to cholestane. The value may have deviation depending on the column and the condition used.

two hydrocarbons, hop-21-ene (VI), m.p. 183-185°, RRT 2.86, and hop-22(29)-ene (V), m.p. 212-215°, RRT 2.70, in a ratio of 4 : 1, which was effectively separated by chromatography over $AgNO_3$-silica gel column.[*6] 22-Hydroxy-21α-hopane (IX)(1), m.p. 228-229°, prepared from the stable nor-ketone, isoadiantone (X)(9), similarly gave a mixture of VI and 21α-hop-22(29)-ene (XI), m.p. 215-216°, RRT 2.12, in a ratio of 1 : 4. XI was also obtained directly from X by Wittig reaction confirming the 21α-configuration. V and XI were obviously different, and the former was identical with diploptene (2) and the latter with moretene (11).[*7]

Hydrogenation of V and XI over Adams catalyst in n-hexane and ether afforded single hydrocarbons, hopane (VII), m.p. 216-218°, RRT 2.68, and 21α-hopane (VIII), m.p. double 178-180, 195-196°, RRT 2.15, respectively. VI was difficult to hydrogenate in the same solvent, but easy in acetic acid to give a mixture of VII, VIII and hop-17(21)-ene (XII), m.p. 183-185°, RRT 1.73, in a ratio of 2 : 84 : 14, showing the formation of 21α-compound in its saturated hydrocarbon fraction [*8] at the unexpectedly high rate (97%)(12). The possibility that this result owes to the hydrogenation of XII, since such double bond migration is often observed during the process, was firmly excluded by the independent hydrogenation of XII. XII was practically unaffected in acetic acid and hydrogenated only when acetic acid containing perchloric acid was used as a solvent, the saturated hydrocarbon product being VII, VIII and 17α-hopane (XIII) in a ratio of 6 : $<$40 : $>$54.

The structure of XIII was proved by the synthesis. Hop-17(21)-en-20-one (XIV)(13) was reduced with lithium-liq. NH_3 in ether to give a ca. 4 : 1 mixture of the D:E cis- and trans-ketone (XV, m.p. 198-200°, and XVI, m.p. 210-212°). They were effectively separated by preparative TLC of the corresponding alcohols (XVII, m.p. 171-173°, and XVIII, m.p. 187-191°), reconverted into the ketone with Jones

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[*6] VI and V were not well separable in VPC, but easily distinguishable each other by TLC on $AgNO_3$-silica gel plate. The ratio was calculated from the result of hydrogenation.

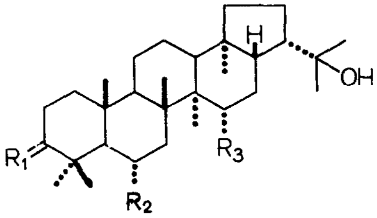
[*7] Although direct comparison with moretene was not available, the identity is doubtless from the result of hydrogenation, the product being 21α-hopane (moretane).

[*8] The saturated hydrocarbon as designated in this communication was obtained after treatment of the mixture with sulfuric acid and acetic anhydride for removing unsaturated impurities and confirmed negative to tetranitromethane.

reagent. Since metal-ammonia reduction of unsaturated ketones favors the formation of the thermodynamically more stable isomers at the β-carbon(14), and since the isopropyl groups of both ketones were found to be stable to base, we were able to assign the major product as XV, and the minor as XVI. Wolff-Kishner reduction of XV or desulfurization of the corresponding ethylene thioketal gave the saturated hydrocarbon, 17α-hopane (XIII), m.p. 156-158°, RRT 1.93, which was readily distinguishable from VII and VIII. Similarly, XVI gave 21α-hopane (VIII) as expected.

The method (c), catalytic hydrogenolysis of 22-hydroxy-hopane (IV) over Adams catalyst in a acetic acid solution, was also reinvestigated. The hydrocarbon fraction of the product consisted of hopane (VII), 21α-hopane (VIII) and hop-17(21)-ene (XII) in a ratio of 4 : 84 : 12. The result shows much less formation of the original 21β-compound than that by the method (b). On the other hand, attempts for the same reaction of 22-hydroxy-21α-hopane (IX) were failed, the starting material being recovered unchanged. These findings conclusively show that the reaction is not a real hydrogenolysis, but proceeds via 21-ene. In IX such dehydration may be more difficult as convincingly evidenced by changing the ratio of 21-ene and 22(29)-ene from 4:1 of IV to 1:4 of IX in phosphorous oxychloride dehydration.

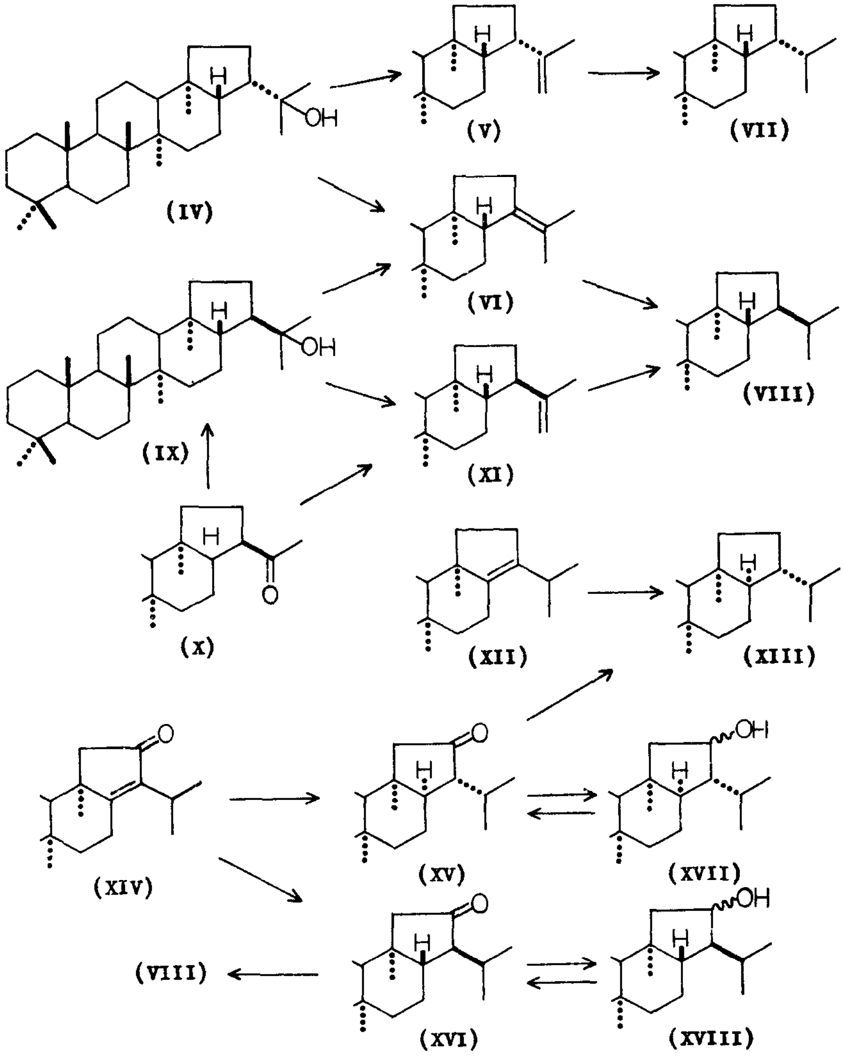
The above evidences suffice to indicate that the parent triterpenoid must be 22-hydroxy-hopane derivative if the VPC peak corresponding to hopane (VII) appears more than 5% in the saturated hydrocarbon fraction prepared by the two methods (b and c). Since our zeorinane and dustanane (6) contained 13% and 7% of hopane, respectively (see ※1), as shown by VPC, zeorin (II) and dustanin (III) are concluded to have the same stereochemistry with that of hydroxyhopanone (I), whereas their 22-deoxy derivatives so far reported (deoxyzeorin, deoxydustanin etc.) should be revised to be 21α-hopane derivatives probably contaminated with a small amount of 21β-compounds. Hydroxyhopanone (I) when reduced over Adams catalyst in acetic acid-ether gave somewhat impure 21α-hopan-3β-ol, m.p. 220-222° (acetate, m.p. 265-268°)(lit. 11, moretanol, m.p. 225-227°, acetate, m.p. 269-270°), the 3α-ol isomer, m.p. 214-216° (acetate, m.p. 212-215°), being also formed in about 10% yield. Although the purity of the products was more than 90% as shown by the VPC of the corresponding ketone, m.p. 186-188° (lit. 11, moretanone, m.p. 190-192°), further



(I) $R_1=O$, $R_2=R_3=H$

(II) $R_1=H$, $R_2=OH$, $R_3=H$

(III) $R_1=H$, $R_2=H$, $R_3=OH$



recrystallizations were not effective to afford the pure specimens.

It is interesting to note that the RRT of the 21β-compounds (VII and V) using SE-30 column are very different from those of the 21α-compounds (VIII and XI), while VII and V / VIII and XI are similar each other. The chemical shifts of the methyl group attached to C(18) in the latters give appreciably higher values than those of the corresponding former compounds as shown in TABLE II.

TABLE II Chemical Shifts of the Methyl Groups (τ-Value)
(Varian A-60, in CCl_4 solution with TMS)

Compound	Methyl Groups attached to C( )				
	4α,4β,10	8	14	18	22
VII	9.16,9.19,9.20	9.05	9.05	9.29	9.11d,9.24d (J=6.5 cps)
VIII	9.16,9.19,9.22	9.04	9.07	9.37	9.11d,9.22d (J=6.5 cps)
V	9.16,9.19,9.20	9.03	9.03	9.22	8.27; 5.23 (2H)
XI	9.16,9.18,9.21	9.02	9.06	9.32	8.37; 5.41 (2H)

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