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SKELETAL REARRANGEMENT IN DEHYDROGENATION OF THUJOPSENE AND ITS CONGENERS

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Dehydrogenation of thujopsene and widdrol revealed extensive skeletal rearrangement. The reaction pathway was established by the isolation and dehydrogenation of the stable intermediates.

Although dehydrogenation reaction has quite widely been applied for determining carbon skeleton of natural products, concurrent skeletal rearrangement provides unnecessary complication for the structural study1). In the course of structural elucidation of thujopsene (I) and widdrol (II), 1-isopropyl-4,6-dimethyl-naphthalene (daucalene) (III) was obtained2) by this type of reaction. As the structures of thujopsene and widdrol are now firmly established both by chemical degradation3) and by syntheses4), the present study was undertaken in order to establish the mode of the skeletal rearrangements from I and II to III.

I was heated under N_2 atmosphere with either Se or 5% Pd-Charcoal under the conditions specified in the TABLE. The reaction mixture was separated by column (Al_2O_3, SiO_2 and SiO_2 impregnated with $AgNO_3$) chromatography to afford the products shown in the TABLE5). Six known compounds, the tricyclic hydrocarbon IV6), dihydro-ar-curcumene V7), the tricyclic hydrocarbon VI8a), β-chamigrene VII9), the bicyclic hydrocarbon VIII8a) and cuparene IX10) were identified along with III. The following four hydrocarbons hitherto unknown were characterized11).

Hydrocarbon X. Liquid, λmax 251 nm (ε 11800), ν 1610, 1450, 816 cm^{-1}, $[\alpha]_D=0$, δ 1.27 (6H, s), 2.08 (3H, br.s), 2.30 (3H, s), 5.80 (1H, m), 6.85 (1H, br.d, J=9.0), 6.93 (1H, br.s), 7.15 (1H, d, J=9.0), NMDR irr. at δ 1.27→ NOE (16%) at δ 7.15, MS m/e 200 (M^+), 185 ($M-CH_3$). Hydrocarbon XI. Liquid, λmax 270 (ε 4000), 281 (7200), 293 (9700), 305 nm (7400), ν 1645, 900-800 cm^{-1}, δ 1.34, 1.39, 1.43, 2.31 (each 3H, s), 5.89 (d, J=9.0, H_6), 5.92 (d, J=10.0, H_{10}), 6.06 (br.d, J=9.0, H_7), 6.37 (br.d, J=10.0, H_9), MS m/e 202 (M^+), 187 ($M-CH_3$), 159 (base peak, $M-CH_3-C_2H_4$). Catalytic hydrogenation of XI afforded liquid hexahydro compound which is different (GLC and IR) from tetrahydro-VIII. Hydrocarbon XII. Liquid, λmax 251 nm (ε 10500), ν 1600, 1450, 800 cm^{-1}, $[\alpha]_D=0$, δ 0.98 (6H, s), 2.13 (3H, d, J=1.2), 2.28 (3H, s), 5.87 (1H, br.s), 6.90, 7.10 (each 1H, d, J=8.0), 7.20 (1H, s). MS is almost superimposable with X. Hydrocarbon XIII. Liquid, λmax 281 nm (ε 6400), ν 1600, 1560, 1450 cm^{-1}, δ 1.27 (6H, s), 2.33 (6H, br.s), 5.47 (1H, d, J=10.0), 5.83 (1H, q, J=10.0, 8.0), 6.30 (1H, br.d, J=

TABLE Dehydrogenation of Thujopsene and Widdrol[5)]

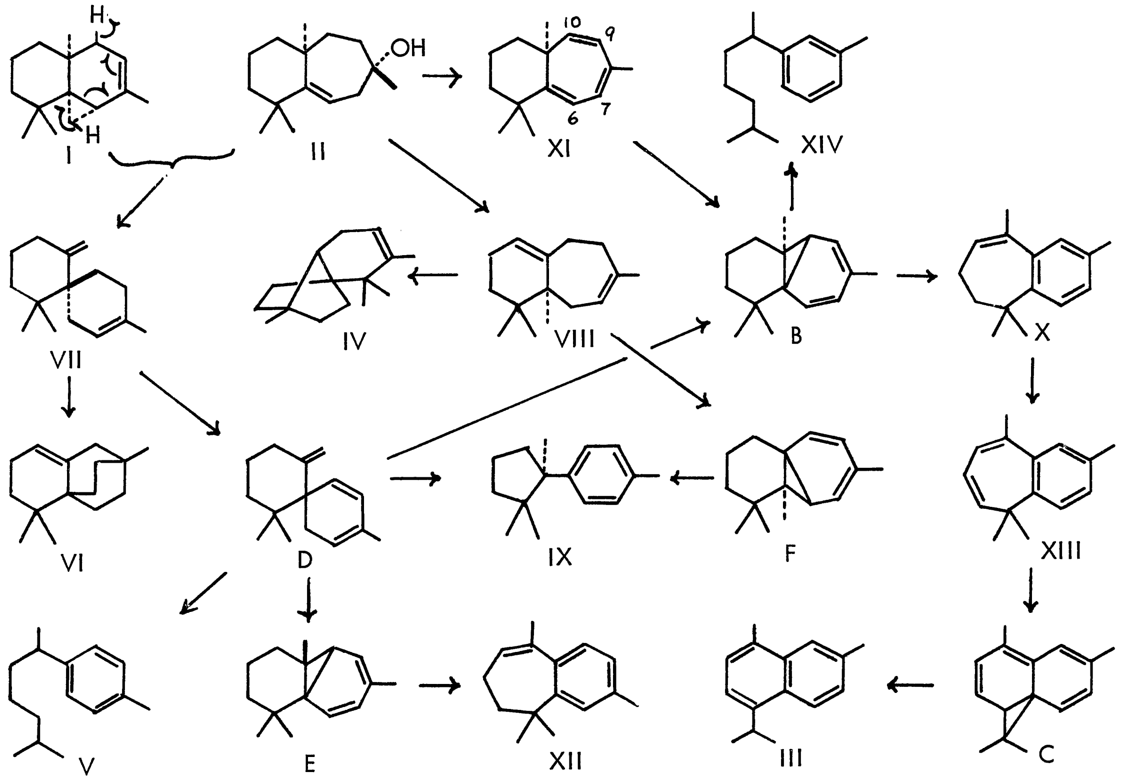
starting materials	reaction conditions	yield of products (%)											
		I	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	III
I	Se, 340° 25 hrs	20		37	8	7		8	4	4	t	1	11
I	Pd, 340° 25 hrs	21	t		6	8	25	19	7	6	t	3	5
I	Pd, 220° 5 hrs	29	t		7	8	32	12	6	1	t	t	
II	Pd, 220° 5 hrs				24	25	11	10	12				

8.0), 7.13 (2H, br.s), 7.30 (1H, br.s), NMDR irr. at δ 1.27→NOE (9%) at 7.13, MS m/e 198 (M^+), 183 (base peak, M-CH_3). Derived from X by bromination with NBS followed by dehydrobromination with dimethylaniline.

As shown in the TABLE, the reactions with both catalysts proceeded similarly at 340°, but the dehydrogenation with Se yielded more of III than that with Pd, and the major product is V in the former reaction and VIII in the latter. Under the milder conditions, the dehydrogenation went to the lesser extent and both I and II afforded the same products in the similar rate implying the general pathway is the same for the two compounds.

In order to establish the reaction sequence, the product obtained was further dehydrogenated. When XI was heated with 5% Pd-C at 220° for 5 hrs, the reaction mixture contains XI (70%), X (29%) and XIII (trace), and from X, the mixture of X (44%) and XIII (56%) was obtained under the same condition. XIII is stable under the condition, but when heated at 320° for 6 hrs in the presence of 5% Pd-C, XIII (26%) and III (63%) were obtained. The fore-going experiments clearly demonstrate the sequence I (II)→XI→X→XIII→III. All the steps can be rationalized as follows: The first steps, I→XI and II→XI, as the allylic hydrogen abstraction followed by the cyclopropane cleavage (arrows in I) and thermal dehydration and dehydrogenation of II; XI→X as the thermal disrotatory electrocyclic reaction of a cycloheptatriene to a norcaradiene (B) followed by the dehydrogenation at α-position to cyclopropyl group, and XIII→III again as the electrocyclic reaction (to C) which is followed by sigmatropic [1,7]-hydrogen shift or allylic hydrogen abstraction and subsequent C-C bond cleavage. The last step has precedences[12)]. No product expected from [1,5] sigmatropic reaction of C was detected contrary to the thermal reaction of 1,2-benzotropylidene[12b)].

The formation of VII and VIII requires no hydrogen abstraction, but hydrogen transfer or rather addition of hydrogen on the double bond of I. As the processes were observed in the acid-catalyzed isomerization of I[6)], it may be cationoid species to cause the rearrangement in the present reaction. VII obtained still retains 86% of its optical activity, revealing ~7% of allylic hydrogen shift in VII during the reaction. The allylic rearrangement occurred to the greater extent compared with the value (3%) observed during the acid-catalyzed isomerization of I[6)]. When VII was



dehydrogenated (Pd-C, 220°, 5 hrs), the product consisted of VI (65%), VII (14%), IX (11%) and X (trace)13,14), disclosing another pathway to III. Again the addition of hydrogen was observed here at the tri-substituted double bond (to VI) as the major course. X and XIV14) may be formed through D and B (or XI and B). IX was formed presumably through D but intervention of B is not likely because XI failed to afford IX. The intervention of D also explains the formation of V and XII. In fact, VII yielded V (Se, 340°, 24 hrs), while IX and XII give no V.

The similar hydrogen transfer reaction was revealed when IV (12%) was found besides VIII (41%) from the reaction of VIII (Pd-C, 220°, 5 hrs). The other product was IX (37%), which can be understood by intervention of F. Thus the two paths to IX were uncovered. IX obtained by the reaction of I has 86% of the optical activity retained. It is rather surprising that, whereas optical activity of IX is only 25% in the acid process6), the both processes, VII→IX and VIII→IX proceeded practically 100% stereochemically controlled, considering the optical purity of the intervening VII. Such stereochemical control can be achieved if the crucial steps occur in concerted fashion on the surface of catalyst.

Thus although the actual oxidation status of leaving hydrogen is now well known1), the dehydrogenation of I and II revealed a variety of reactions involved.

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References and Footnotes

1) Pertinent references can be found in the following reviews: L.M. Jackman in "Advances in Organic Chemistry, Methods and Results", ed. by R.A. Raphael, E.C. Taylor and H. Wynberg, Vol. 2, p. 329. Interscience, New York (1960). Z. Valenta in "Elucidation of Structures by Physical and Chemical Methods", ed. by K.W. Bentley, Vol. 1, p. 581. Interscience, New York (1963). Typical example in sesquiterpene field of the dehydrogenation leading to the incorrect structure is β-vetivone. A.S. Pfau and P.A. Plattner, Helv. Chim. Acta, 23, 768 (1940), the revised structure: J.A. Marshall and P.C. Johnson, J. Am. Chem. Soc., 89, 2750 (1967).

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5) The identity of known compounds was established by comparison of their retention time in GLC, IR and NMR spectra. The yield was determined by GLC, α-methylnaphthalene being used as internal standard. Compounds IV-XIII are numbered in the increasing order of their retention time in GLC.

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11) All the new compounds in this paper gave satisfactory elemental analyses. NMR were measured at 60 MHz or 100 MHz in CCl_4. UV spectra were taken in MeOH, IR spectra in CCl_4 and $[\alpha]_D$ in $CHCl_3$.

12) a) J.C. Joseph and S. Dev, Tetrahedron, 24, 3809 (1968). b) Inter al., S.J. Cristol and R. Caple, J. Org. Chem., 31, 585 (1966).

13) The result is considerably different from that observed by Ohta and Hirose (Tetrahedron Letters, 2483 (1968)). They have isolated IX together with α-chamigrene and isocuparene, which were not detected in our case.

14) The presence of a very small amount of the isomer of V was indicated by IR and NMR. The structure XIV can be assigned to this isomer, but all effort to separate them failed.

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