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ACID-CATALIZED REARRANGEMENT OF THUJOPSENE II. THE REACTION PATHWAY (1)

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In the preceding paper (2), we described the product analysis of the acid-catalyzed reaction of thujopsene I (3) and have shown that I rearranges much more extensively than reported. The present paper will be concerned with the pathway of the reaction.

Entire course of the reaction is depicted in the CHART starting from I of known conformation (4). The cyclopropylcarbinyl ion A formed by the protonation of I is stabilized by the contribution of three ions, A_1, A_2 and A_3, of the same molecular geometry, thus has a fixed conformation shown. Any process which causes a change in geometry therefore would require energy.

I was heated with perchloric acid at the different temperatures and the reaction was monitored gas chromatographically, in order to estimate the activation energy from the primary ion A to the secondary ions, since protonation, deprotonation and also attack of nucleophile are unlikely to have considerably high activation energy. The result is shown in the TABLE.

The facile formation of widdrol X indicates the process A→B to have the lowest activation energy. Since the existence of the small energy barrier between the ions A and B was clearly demonstrated by Dauben et al.(5), we need not discuss the process any further. The compounds formed next are the isomeric dienes IV and XX. In their formation, the rate-determining process would be the methyl migration from C_7 to C_1, utilizing the empty a-lobe of C_1. Since the conformation is fixed in A, the antiparallel methyl migration followed by the antiparallel elimination of 8β(ax)-hydrogen to give IV would be more favored than the deprotonation at C_6-position with no antiparallel hydrogen. The predominant formation of IV over XX is thus understood. No interconversion between IV and XX occurs under the reaction condition used.

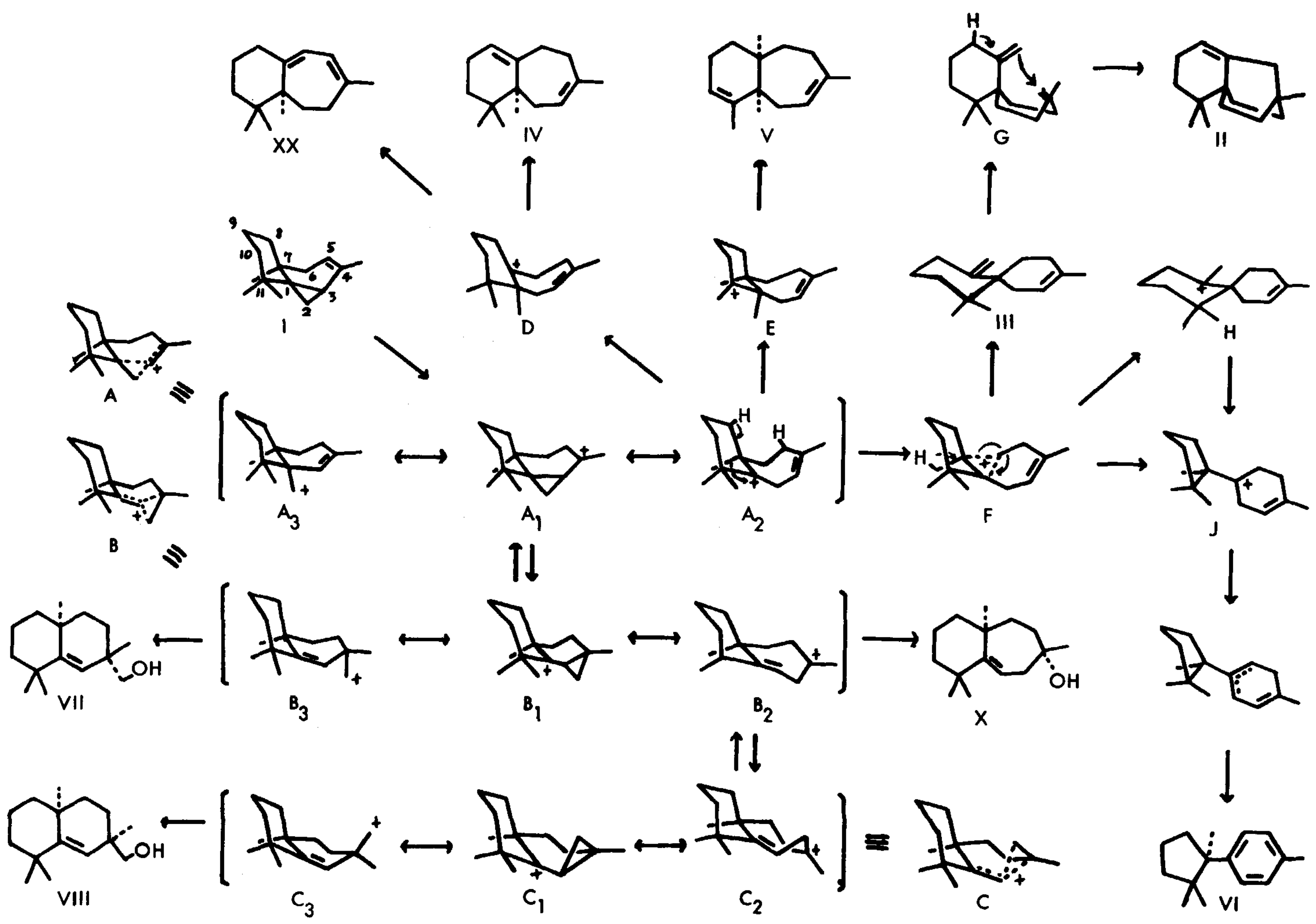

CHART. Acid-catalyzed Rearrangement of Thujopsene

TABLE. Product Ratio in the Reaction of Thujopsene with Perchloric Acid (2 mol. eq.) in 80% Aqueous Dioxane

Temperature		60°										80°			
Time (min.)		5	10	20	30	40	50	60	90	120	140	30	60	90	120
Products and Ratio (%)	I	100	96	89	85	78	75	70	66	55	46	25	16	12	9
	II								1	2	2	2	3	4	5
	III				1	1	2	2	2	2	3	6	8	9	11
	IV			3	4	6	5	7	8	11	12	15	19	21	26
	XX			trace	1	1	1	1	1	1	2	11	14	15	19
	V						1	2	2	3	3	7	8	12	12
	X		3	5	8	15	16	18	19	26	33	34	31	27	18

The formation of the isomeric diene V through the ion E occurs more slowly and involves a similar antiparallel 1,2-migration of 11α-methyl group. The difference in the rate of formation for IV and V can be explained by the steric repulsion between 5β(ax)- and 8β(ax)-hydrogens in the ion A (6): This nonbonded interaction would be more efficiently released by the formation of sp^2 carbon at C_7 rather than at C_{11}, especially when 8β-hydrogen is removed as indicated in the figure A_2.

Another way of releasing the interaction is the formation of β-chamigrene III through the ion F. This involves parallel 1,2-shift of C_6-C_7 bond utilizing β-lobe of C_1 and therefore would be unfavored. In fact, III forms rather slowly. III thus formed however retains 97% of the optical purity (7). This indicates the absence of the allylic rearrangement both in III and the ion F as well as the migration of the α-oriented C_1-C_2 bond in F to an ion of A_2 type. This reaction renders a strong support to the structure depicted for the absolute configuration of III (8). The antiparallel deprotonation of the ion F occurs exclusively, giving only III and not to α-chamigrene (9).

The trisubstituted double bond in III is known (10) to be more reactive than the exocyclic double bond. Thus the ion G have the latter situated above the ionic center and is suitable to form the [2,2,2] bicyclooctane derivative II. In fact, when III was treated with the acid, II was formed together with VI and IV (ratio 29 : 9 : 1).

Although not operating with perchloric acid, another way for the ion F to terminate the reaction is the further 1,2-shift of C_1-C_{11} bond to cuprenenes (11) which suffer aerial oxidation or disproportionation to cuparene VI. This extra 1,2-shift would require more energy: VI was only formed under a vigorous condition with oxalic acid (2). Since VI isolated from the reaction mixture retains only 25% ($[\alpha]_D$ +15.7°) of its optical activity, the majority of VI is resulted from the ion H though some comes directly from the ion F.

The amount of widdrol increases at the earlier stage of the reaction but decreases on prolonged heating especially at higher temperature (see TABLE). This means that the energy barrier B→A is overcome and the reverse reaction, X→B→A→D, E and F, is operating. When X was treated with acid (H_3PO_4, r.t., 20 hrs.), II, III and IV were formed in the ratio of 1 : 3 : 15.

Two alcohols, VII and VIII, of neopentyl type are formed with oxalic acid at higher temperature (2). Although the formation of VII can be explained by the small contribution of B_3 in the ion B, that of VIII indicated the formation of the ion C. This interconversion B→C must require more energy, because delocalization energy in the ion B has to be sacrificed to the stretched B_2 form and then fold to C_2 which is again stabilized. Although the ion C could produce epiwiddrol and trans thujopsene, these compounds (or their equivalents) are known to be less stable than their naturally occurring counterparts (5) thus most part of the ion C would be converted to B, A and further. Both VII and VIII are stable under the condition under which they are formed.

Thus the entire course of the acid-catalyzed rearrangement of I can be rationalized in terms of three discrete but interconvertible cyclopropylcarbinyl ions of fixed geometry, followed by various 1,2-shifts. From the result described in this and the preceding papers, we can estimate the activation energy between the ions in the following order: $A \to B < A \to D < A \to F < A \to E < F \to (H) \to J$.

References and Footnotes

1) Presented at the Symposium on the Chemistry of Natural Products, Fukuoka, October 29, 1970. Abstracts of Papers, p. 174.
2) S. Itô, M. Yatagai and K. Endo, Tetrahedron Letters, 1149 (1971).
3) All compound numbers are in accord with those in reference 2.
4) S. Itô, H. Takeshita, T. Muroi, M. Ito and K. Abe, Tetrahedron Letters, 3091 (1969). S. P. Acharya and H. C. Brown, 15th International Symposium on the Chemistry of Natural Products (London), 1968. Abstracts of Papers, p. 294. G. Ohloff, H. Strickler, B. Willhalm, C. Borer and M. Hinder, Helv. Chim. Acta, **53**, 623 (1970).
5) W. G. Dauben and L. E. Friedrich, Tetrahedron Letters, 1735 (1967).
6) The molecular model having the geometry A indicates the distance between these hydrogens be around 1.8 Å.
7) After several steps of purification, $[\alpha]_D$ of natural β-chamigrene increased to -75.2° (C=1, $CHCl_3$ (10). III obtained in this study shows $[\alpha]_D$ -70.8° (C=1, $CHCl_3$).
8) The sign of $[\alpha]_D$ is in agreement with the chirality caused by the disposition of two isolated double bonds in III. Interaction of the double bonds is demonstrated in the text.
9) α-Chamigrene was not detected by GC. We are grateful to Professor Y. Kitahara and Dr. T. Kato, Tohoku University, for their gift of synthetic α-chamigrene.
10) S. Itô, K. Endo, T. Yoshida, M. Yatagai and M. Kodama, Chem. Comm., 186 (1967). T. Nozoe and H. Takeshita, Tetrahedron Letters, 14 (1960).
11) W. G. Dauben, P. Oberhänsli, J. Org. Chem., **31**, 215 (1966).