

CYCLOPROPYLCARBINYL REARRANGEMENTS IN THE THUJOPSENE SERIES (1)

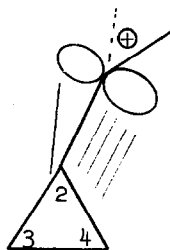
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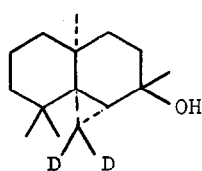
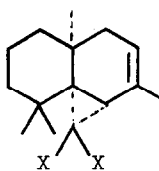
Several reports have recently appeared on the solvolyses of cyclopropylcarbinyl derivatives which are incorporated in a six-membered ring system (4a-e). In each report, a substituted homoallyl ion was indicated to be an intermediate and two of the studies (4c,4e) provided evidence which required that two discrete, rapidly inter-convertible cations must have intervened in the homoallylic rearrangements. We should like to report the preliminary results of a study of the rearrangement of the cyclopropylcarbinyl system in the sesquiterpene thujopsene which require the intervention of a minimum of four isomeric intermediate ions. Although a series of rapidly equilibrating homoallyl ions (4b) would meet this requirement, the four isomeric ions may be more conveniently represented, however, in terms of unsymmetrical homoallyl structures  $\underline{1}$  in which the two lobes of the carbinyl p orbital overlap unequally with the adjacent bonds of the cyclopropyl ring. In this representation, the positive charge of the cat-



$\underline{1}$

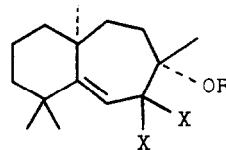
ion is distributed among carbons  $C_1$ ,  $C_3$ , and  $C_4$  and possibly onto carbon  $C_2$ . The preliminary results indicate that there are two stereochemically related pairs of cations; isomerization between ions in each pair is facile as compared to the interconversion between ions of differing pairs.

A solution of (+)-cis-6,6-dideuteriothujopsanol 2 (m.p. 62-63°) (3) in 95% ethanol which was 0.012 N in hydrochloric acid upon heating under reflux for 10 min. gave (+)-cis-6,6-dideuteriothujopsene 3a in quantitative yield. The undeuterated olefin 3b was stable under these acidic conditions in either 95% aqueous ethanol or methanol for as long as 40 min.

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3a, X=D

3b, X=H

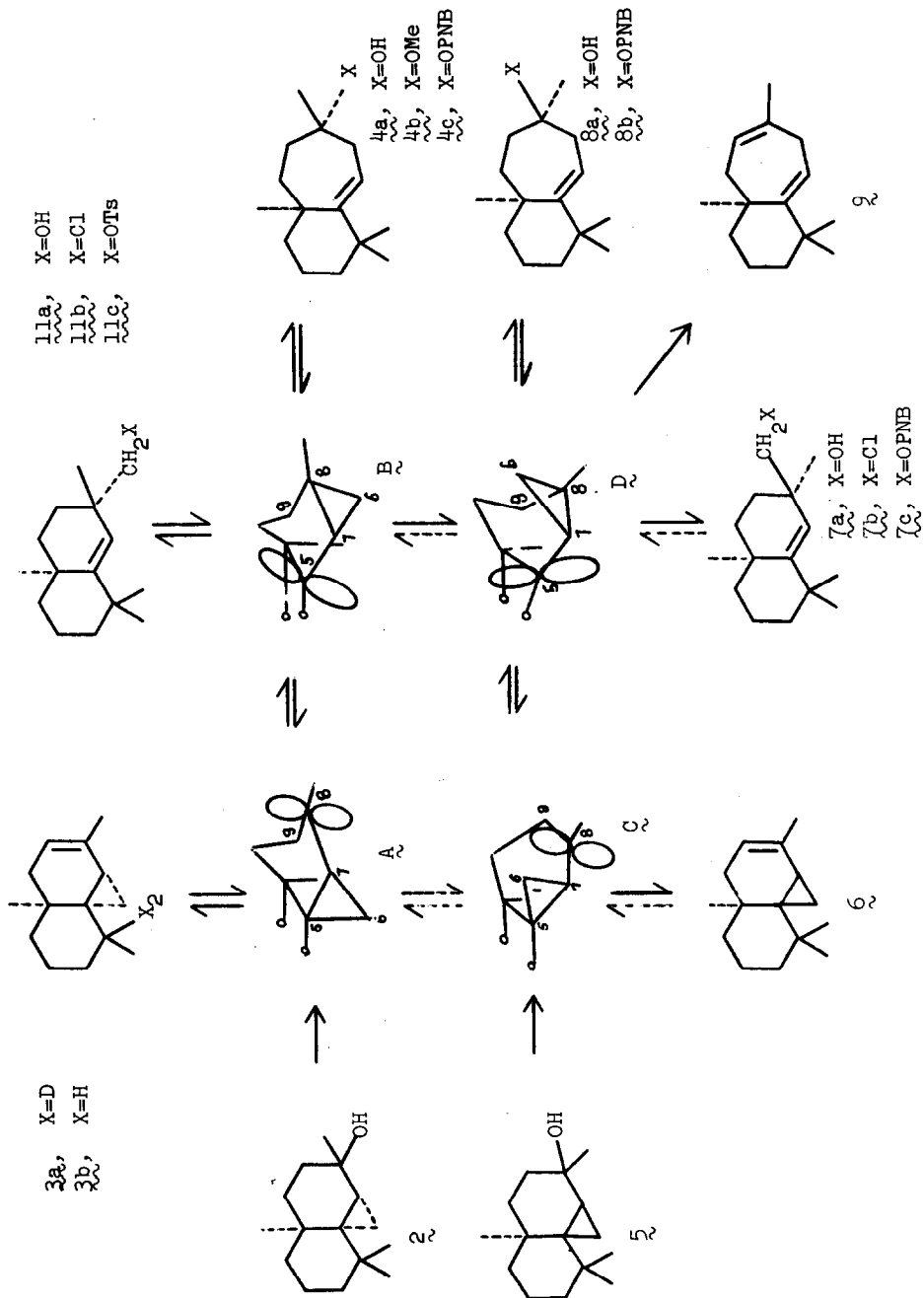


4a, R=H, X=H    4c, R=PNB, X=H

4b, R=Me, X=H    4d, R=H, X=D

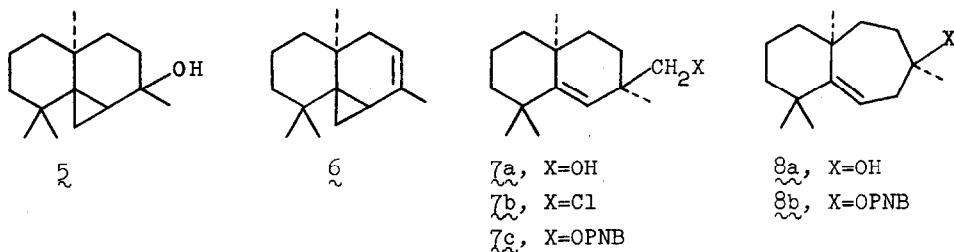
The related homoallylic alcohol, (+)-widdrol 4a, under the same acidic conditions in aqueous methanol led to no rearrangement products in 10 min. and after 40 min. the product mixture consisted of only widdrol 4a and its methyl ether 4b in a ratio of 1:2. Also, solvolysis of the homoallyl p-nitrobenzoate 4c (m.p. 136-137°) in 70% aqueous dioxane gave the unrearranged parent alcohol 4a as the only product.

These reactions demonstrate that the intermediate ion A derived from the cyclopropyl carbinol 2 (see Chart for summary) is structurally different from the ion B derived from the related homoallyl alcohol 4a and that a finite energy barrier for the interconversion must exist between these two unsymmetrical homoallyl ions. The cation from the cyclopropylcarbinol 2 (associated with its counter chloride ion) really eliminates a proton to form the hydrocarbon, thujopsene 3, whereas, the ion derived from the homoallyl alcohol 4a (associated with either a chloride or p-nitrobenzoate counter ion) is stabilized by reaction with the nu-



cleophilic solvent to form the alcohol widdrol  $\underline{4a}$  or a derivative of it.

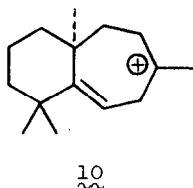
When the (+)-dideuterated cyclopropylcarbinyl olefin  $\underline{3b}$  was heated under reflux in 80% aqueous dioxane which was 0.02 M in perchloric acid, the rearranged homoallyl alcohol, (+)-7,7-dideuterowiddrol  $\underline{4d}$  (3), was the most rapidly formed of the initial products. Similar treatment of homoallyl alcohol widdrol  $\underline{4a}$  or solvolysis of its ester  $\underline{4c}$  in dry dioxane containing lithium perchlorate trihydrate gave the cyclopropylcarbinyl olefin thujopsene  $\underline{3b}$  as the initial product with the fastest rate of formation. These reactions establish that the energy barrier between isomeric ions  $\underline{A}$  and  $\underline{B}$  is finite but not large.



In the stereochemically isomeric series, treatment of (+)-trans-thujopsanol  $\underline{5}$  (5,6) with 0.012 N hydrochloric acid in 95% ethanol under reflux for 10 min. gave only two detectable nonpolar products, (+)-trans-thujopsene  $\underline{6}$  (7) in ca. 80% yield and a neopentyl-type chloride  $\underline{7b}$  (8) in ca. 20% yield. Solvolysis of the related homoallyl alcohol ester, (+)-epi-widdrol p-nitrobenzoate  $\underline{8b}$  (m.p. 57.5-59.0°) (9), in pyridine buffered 70% aqueous dioxane proceeded approximately sixty times more slowly than the epimeric p-nitrobenzoate  $\underline{4c}$ . A 47% yield of hydrocarbons was formed which contained 30% of (+)-trans-thujopsene (7) and approximately an equal amount of the diene  $\underline{9}$ , a material previously prepared from widdrol. The remaining non-hydrocarbon mixture was composed of 15% (+)-epi-widdrol  $\underline{8a}$ , 5% (+)-widdrol  $\underline{4a}$ , 6% trans-neopentyl-type alcohol  $\underline{7a}$ , and 12% of its p-nitrobenzoate  $\underline{7c}$ . (10)

These results in the trans-thujopsene series suggest the intervention of two additional unsymmetrical homoallyl ions  $\underline{C}$  and  $\underline{D}$  which are epimeric with  $\underline{A}$  and  $\underline{B}$  and the activation energy for the isomerization of  $\underline{D}$  to  $\underline{C}$  is less than that

of ion  $\underline{B}$  to  $\underline{A}$ . The kinetic product from the ion  $\underline{C}$  (associated with a chloride anion) generated from trans-thujopsanol is trans-thujopsene. This ion  $\underline{C}$  is readily interconvertible with cation  $\underline{D}$  which is generated by the ionization of epi-widdrol p-nitrobenzoate  $\underline{8b}$ . The kinetically controlled reaction of nucleophiles with ion  $\underline{D}$  (associated with a p-nitrobenzoate anion) gives mainly the trans-neopentyl-type derivatives  $\underline{7}$  and the less stable epi-widdrol derivative  $\underline{8a}$ . The small yield of widdrol from the hydrolysis of ester  $\underline{8b}$  may result from undetected contaminations of the epi-widdrol ester with widdrol p-nitrobenzoate, or from the slow conversion of ion  $\underline{D}$  to  $\underline{B}$ , or from the intervention of the charge localized cation  $\underline{10}$  which could react with solvent from the more hindered side of the molecule to form widdrol.



When either cis-thujopsene ( $\underline{3b}$ ) or widdrol ( $\underline{4a}$ ) was allowed to react with 0.02 M perchloric acid in 80% aqueous dioxane for extended reaction times, the three alcohols  $\underline{7a}$ ,  $\underline{8a}$ , and  $\underline{11a}$  ( $\underline{11}$ ) were formed in about 2% yield, showing a small but significant amount of "leakage" from the set of ions  $\underline{A}$  and  $\underline{B}$  to the set of ions  $\underline{C}$  and  $\underline{D}$ . The cis-chloride  $\underline{11b}$  ( $\underline{12}$ ) was also formed when cis-thujopsene  $\underline{3b}$  was allowed to react with concentrated hydrochloric acid in dioxane for extended reaction times. Therefore, compounds  $\underline{11a-b}$  and  $\underline{7a-b}$  may be regarded as thermodynamic products from the reaction of nucleophiles with ions  $\underline{B}$  and  $\underline{D}$ , respectively, and under thermodynamically controlled reaction conditions, the set of ions  $\underline{A-B}$  slowly convert to the set of ions  $\underline{C-D}$ .

The tosylate ester  $\underline{11c}$  ( $\underline{13}$ ) was solvolyzed in pyridine buffered 80% aqueous dioxane and gave a 98% yield of widdrol  $\underline{4a}$  and a 1% yield of cis-thujopsene  $\underline{3b}$ . Thus, the ionization of the tosylate ester also produces the expected ion  $\underline{B}$  which isomerizes in 1% conversion to ion  $\underline{A}$ .

The difference in structure between ions  $\underline{A}$  and  $\underline{B}$  or ions  $\underline{C}$  and  $\underline{D}$  could or-

iginates from the counter ion locking itself into different positions on a common cationic fragment. Lacking additional evidence, however, we feel the postulated ions adequately account for all of the observed results.

### References

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2. National Science Foundation Predoctoral Fellow, 1963-1966.
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 d. Y. Hiniko and P. de Mayo, Chem. Comm., 550 (1965);  
 e. S. W. Pelletier, S. Nakamura, and Y. Shimizu, Chem. Comm., 727 (1966).
5. W. G. Dauben and A. C. Ashcraft, J. Am. Chem. Soc., 85, 3673 (1963).
6. (±)-Trans-thujopsanol, m.p. 62-66°, was synthesized by the reaction of methyl lithium with 7-keto-4,4,10α-trimethyl-5β,6β-methylenedecalin:  
 (5)
7. (±)-Trans-thujopsene was  $\lambda_{\text{cyclohexane}}^{\text{max}}$  213 mμ (ε 4670); the rotation of (+)-trans-thujopsene is  $[\alpha]_D^{25} +149^\circ$  (c 0.436, CHCl<sub>3</sub>).
8. The n.m.r. spectral features for chloride 7b are: τ 6.63 (1H, doublet, J=11 c.p.s.), 6.77 (1H, doublet, J=11 c.p.s.).
9. (+)-epi-Widdrol, m.p. 54-56°, was obtained from (+)-widdrol via the epoxide of diene 9.
10. The ester 7c (m.p. 99-100°; n.m.r., τ, 5.83 (1H, doublet, J=11 c.p.s.), 6.00 (1H, doublet, J=11 c.p.s.)) was converted by lithium aluminum hydride to alcohol 7a (m.p. 73.0-73.5°; n.m.r., τ, 6.75 (1H, doublet, J=10 c.p.s.), 6.83 (1H, doublet, J=10 c.p.s.)).
11. The cis-neopentyl-type alcohol 11a has the following properties: m.p. 71-72°; n.m.r., τ, 6.86 (2H, singlet).
12. The chloride 11b in the n.m.r. shows a singlet at τ 6.75 (2H).
13. The cis-neopentyl-type tosylate 11c has the following properties: m.p. 87-88°; n.m.r., τ, 6.38 (2H, singlet).