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BIOGENETIC-LIKE REARRANGEMENTS OF ISOSTEVIOL DERIVATIVES A PARTIAL SYNTHESIS OF TRACHYLOBANE

Robert M. Coates and Edward F. Bertram
Department of Chemistry and Chemical Engineering
University of Illinois, Urbana, Illinois 61801

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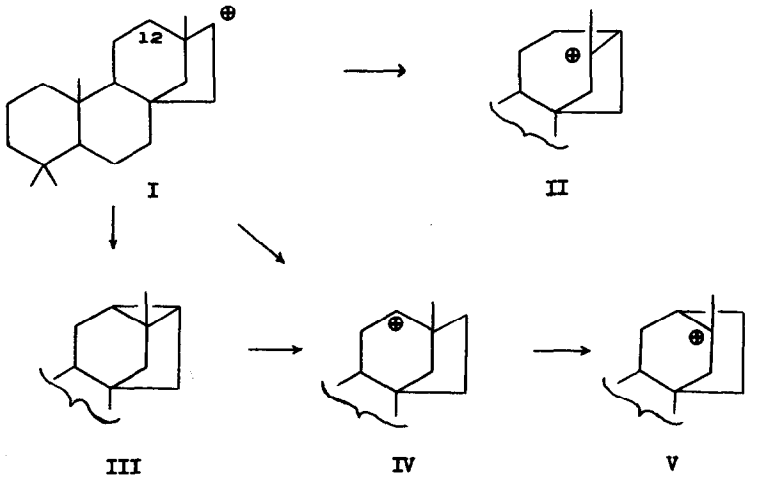
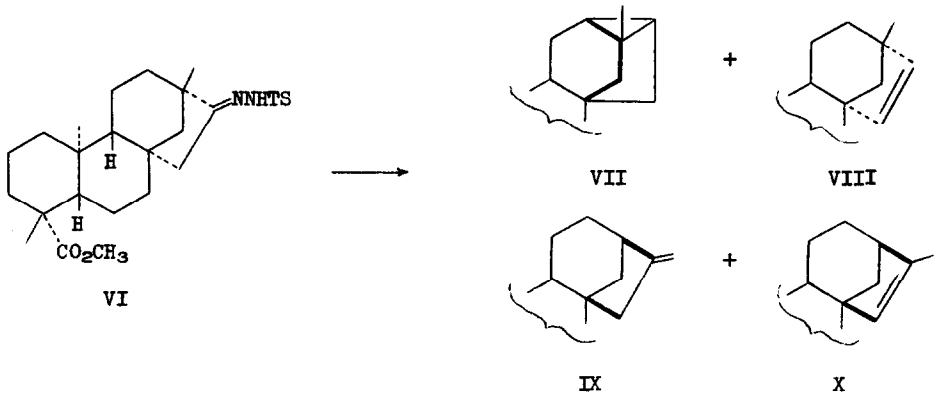
The biogenetic scheme interrelating the various types of tetracyclic diterpenoids (1) involves a sequence of skeletal rearrangements which has been able to account concisely for all of the known structural representatives. The available biosynthetic evidence is also consistent with these relationships (2). Since there are reasonable precedents for the suggested rearrangements, we considered that with the proper selection of experimental conditions, it should be possible to duplicate chemically most, if not all, of the transformations in this biogenetic scheme. In previous studies rearrangements of the types I → II (3,4,5), I → V (4,6), and III → V (4,7) have been observed. We now report the formation of a trachylobane derivative representing the I → III process and another example of the I → II rearrangement.

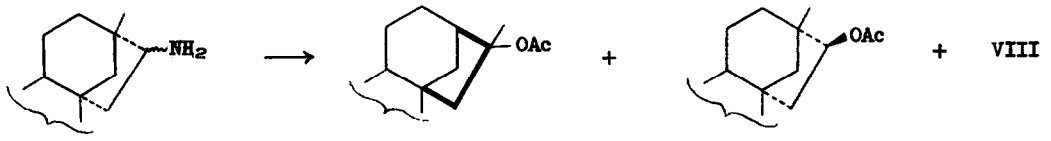


Decomposition of the tosylhydrazone VI (mp 214-215°) of isosteviol methyl ester as its sodium salt in 10% V/V ethylene glycol diethylcarbitol (8) (2 hr. at reflux, 180-190°) affords a mixture of four isomers (40-60%) separable by column chromatography on silica gel impregnated with silver nitrate. The least polar component of this mixture [25%; mp 101-103°, $[\alpha]_D$ -67°; M^+ 316, ϵ^{199} 845; τ 8.87, 8.87, and 9.26 (all S, 3H)] was shown to be methyl trachyloban-19-oate

VII, i.e. C-4 epimer of methyl trachylobanate (9), by its physical properties and conversion to the parent hydrocarbon, trachylobane (mmp, glc, ir, and nmr comparison with a sample supplied by Drs. Hugel and Ourisson). This correlation adds further support to the proposed structure and stereochemistry of this novel pentacyclic diterpene (9,10). The other three compounds proved to be olefinic esters: methyl hibaen-19-oate VIII [37%, mp 115-115.5°, identical to an independently prepared sample (5b)], methyl kauren-19-oate IX [31%, mp 84-85°, identical (mmp, glc, ir, and nmr) to a specimen provided by Dr. P. R. Jefferies (11)], and methyl isokauren-19-oate X [7%, mp 79-80°, $[\alpha]_D$ -54°, τ 4.96 (M, 1H), 8.30 (d, J= 1.8 Hz, 3H), 8.86 and 9.16 (both s, 3H)]. The structure of X was confirmed by a separate synthesis from IX [I_2/xylene, reflux 20 min (5c,d)]. A similar decomposition of VI in the aprotic solvent diglyme (carbenoid conditions) furnishes mainly VIII with small amounts of IX and X.



We have also generated the carbonium ion by deamination of the amine XI (mp 110°), prepared by sodium/isopropyl alcohol reduction of the oxime (mp 153-155°). The reaction of the amine hydrochloride with sodium nitrite in acetic acid yields a mixture of acetates and olefins. The major product is the rearranged tertiary acetate XII [35%; mp 144-148°; τ 8.02, 8.38, 8.81, and 9.14 (all S, 3H)], the constitution of which has been established by dehydration (TsCl/pyridine, reflux 3 hr., 65%) of the corresponding alcohol (mp 154-155°, $[\alpha]_D$ -76°) to a mixture of IX and X. In addition, the unrearranged secondary acetate XIII [18%, mp 91-92°, $[\alpha]_D$ -10.6°, τ 5.4 (M, 1H)], olefin VIII (9%), and a small amount (~5%) of another secondary acetate which appears to be the endo isomer of XIII are obtained. The acetate XIII has been independently synthesized by hydroboration (diisoamylborane/THF, 25°) of VIII followed by acetylation.



XI XII XIII

It is evident from these and previous results (3,4,5) that the Wagner-Meerwein rearrangement I → II which interconverts the hibaene and kaurene structures occurs readily. Although the elimination of a C-12 proton leading to the pentacyclic trachylobane system (I → III) is observed here with an "energized" carbonium ion intermediate (8), this process does not take place to a significant extent under normal solvolytic conditions (3). The rearrangement I → V, although detectable under forcing conditions (4) is apparently much slower than the I → II process and therefore does not occur to a noticeable degree in the irreversible solvolysis (3) and deamination reactions.

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