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SYNTHESIS OF ent.-METHYL TRACHYLOBANATE FROM LEVOPIMARIC ACID (1)

Werner Herz, R. N. Mirrington and Harry Young
Department of Chemistry, The Florida State University
Tallahassee, Florida 32306

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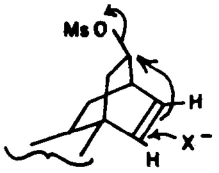
An important new class of pentacyclic diterpenes, discovered by Ourisson and his co-workers (2), is based on the trachylobane (cyclokaurane) skeleton 1a. We describe here the first synthesis of a member of this class, (+)-methyl trachylobanate [2c, ent.-methyl trachylobanate, mirror image of 1c, the methyl ester of the naturally-occurring (-)trachylobanic acid 1b (3)] which confirms structures and configurations assigned to these compounds and possesses features of chemical interest as well.

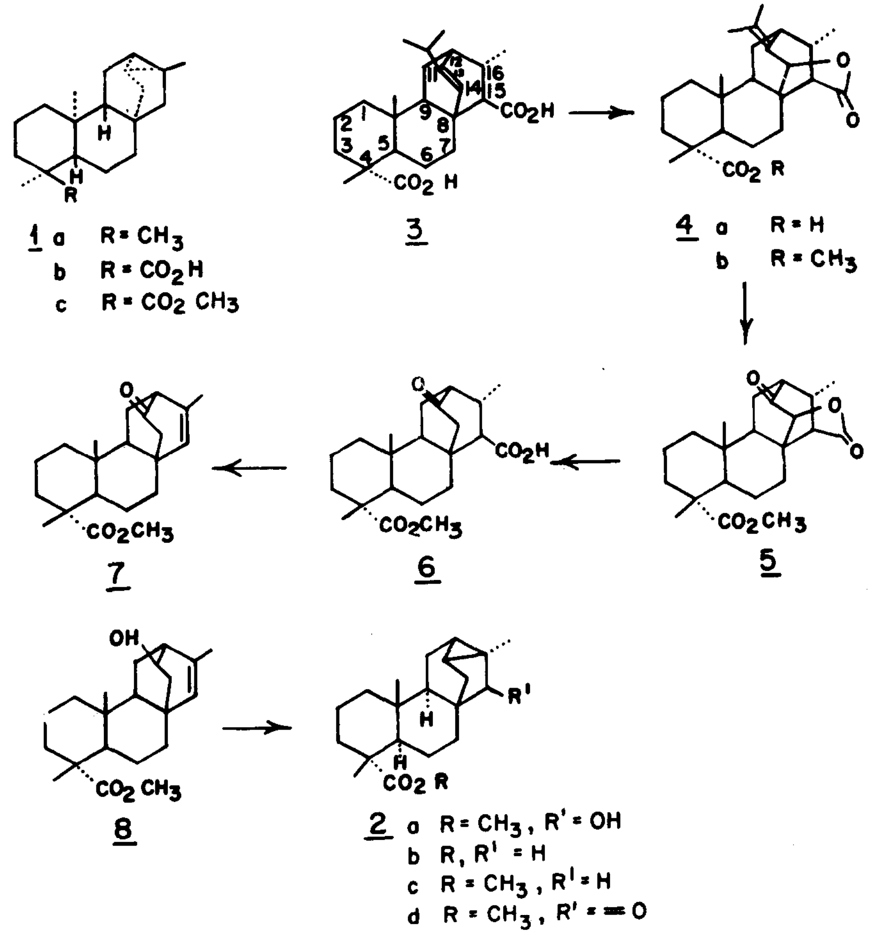
Condensation of methyl levopimarate with n-butyl crotonate at 200° (4) followed by hydrolysis gave a crystalline diacid 3 (5) in 50% yield. $KMnO_4$ oxidation (6) at 0° furnished in variable yield [never higher than 35% conversion (7)] the unsaturated lactone 4a, the ir (1770 cm^{-1}, γ-lactone) and nmr spectrum (broadened singlet at 4.95 ppm, H-14) of whose methyl ester 4b confirmed the attachment and orientation of the carbobutoxy group at C-15 in the Diels-Alder adduct. Ozonolysis of 4b to 5 and reduction of the latter with chromous chloride to 6 proceeded quantitatively. Oxidative decarboxylation of 6 [lead tetraacetate-anhydrous benzene-cupric acetate (8)] resulted in 7 (79%) whose physical properties (vinyl methyl signal allylically coupled to H-15, strong $n \rightarrow \pi^*$ transition of β, γ-unsaturated ketone) showed that no rearrangement had taken place.

Sodium borohydride reduction of 7 gave two epimers in 82% and 16% yield. Attempted conversion of the major product, presumably 8 (deshielded C-10 methyl signal at 1.15 ppm compared with C-10 methyl signal of minor product at 0.88 ppm), to the mesylate and work-up in the usual way revealed that



MsO
H
H
X⁻

A



H
H
R
1 a R = CH3
b R = CO2H
c R = CO2 CH3
1
2
3
4
5
6
7
8
9
11
12
13
14
15
16
CO2H
CO2 H
3
O
O
CO2 R
4 a R = H
b R = CH3
O
O
O
CO2CH3
5
O
CO2H
CO2CH3
6
O
CO2CH3
7
OH
CO2 CH3
8
R'
H
H
CO2 R
2 a R = CH3, R' = OH
b R, R' = H
c R = CH3, R' = H
d R = CH3, R' = O

cationically-induced cyclization (process A,X=H_2O) to 2a had taken place spontaneously in 40% yield (no vinyl proton, new methyl singlet at 1.21 ppm, H-16 singlet at 3.30). This was confirmed by oxidation of 2a to the cyclopropyl ketone 2d (λ_{max} 211, 285 mμ, Σ_{max} 2620, 72).

These findings suggested that mesylation followed by addition of sodium borohydride (9) might result in direct formation of ent.-methyl trachylobanate (process A,X=H^-). Indeed, the crystalline product 2c isolated in 17% yield had properties identical (mp, ir, nmr, tlc and glc) with that of an authentic sample supplied by Professor Ourisson, but the opposite rotation ($[\alpha]_D$+46°).

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4. Choice of ester and temperature represented a compromise between insignificant reaction rates at lower and dissociation of the adduct at higher temperatures.
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