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TOTAL SYNTHESIS OF THE β-AMYRIN DERIVATIVES OLEAN-13(18)-ENE AND 18α-OLEAN-12-ENE[1,2]

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We report the total synthesis of the racemic β-amyrin derivatives olean-13(18)-ene (XII) and 18α-olean-12-ene (XIII) by a direct route, not involving relays. Previous syntheses of β-amyrin derivatives using natural materials as relays have been described[4].

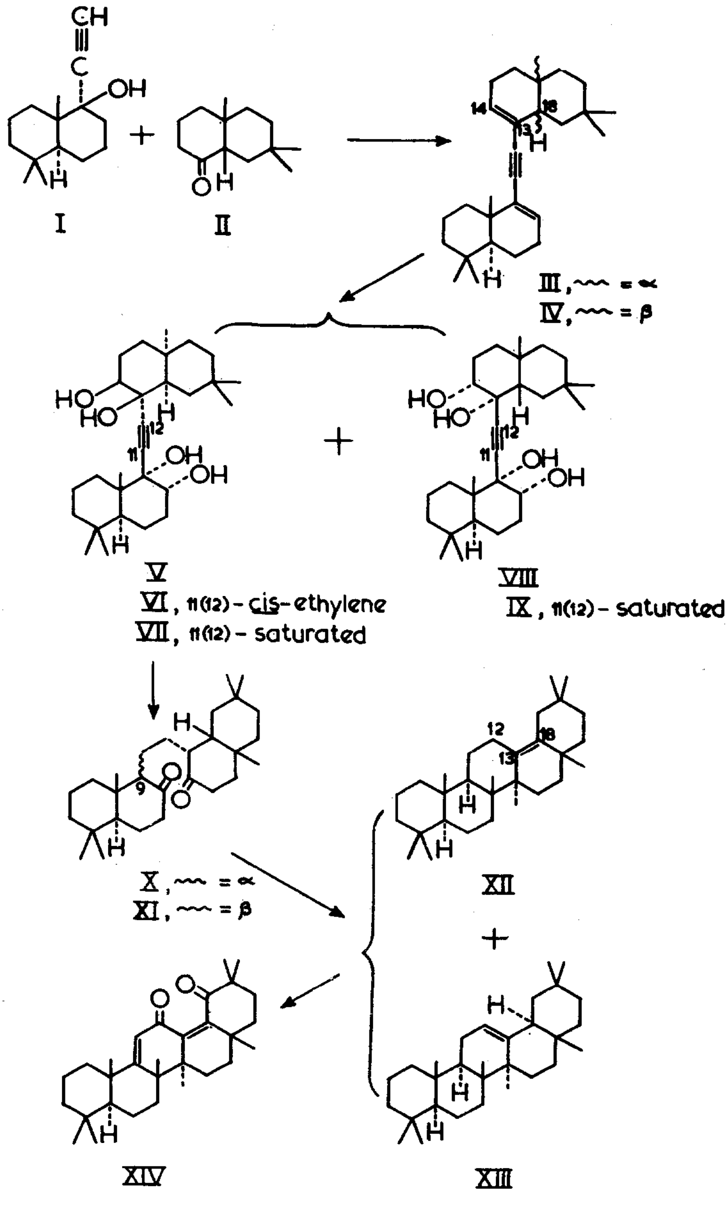
Condensation of the Grignard derivative of the acetylenic carbinol I[5] with the <u>cis</u>-decalone II[6] yielded an isomeric mixture of acetylenic 1,4-diols, which was dehydrated with potassium bisulphate at 180° to the dienynes III and IV [$\lambda_{max}^{isoöctane}$ 265 and 278 mμ (ϵ 16,900 and 13,500)]. Formation of the required $\Delta^{13(14)}$-double bond was predicted on the basis of conformational analysis, whereas use of the <u>trans</u> isomer of II[6] would have resulted in the alternative $\Delta^{13(18)}$-isomer.

Hydroxylation of the double bonds of III and IV with osmium tetroxide in pyridine led to the acetylenic tetrols V and VIII, which were hydrogenated in acetic acid over platinum for 8 hr. The resulting mixture of <u>cis</u>-ethylene VI (m.p. 263 - 265°) and saturated compound IX (m.p. 258 - 259°) could be separated readily by chromatography on alumina, in view of the differing structures. Substance VI, subsequently found to belong to the desired series, could then be fully saturated to VII (m.p. 245 - 246°) by further hydrogenation for several days. Both the saturated tetrols VII and IX gave diacetates (m.p. 229 - 230° and 204 - 206°, respectively) with acetic anhydride in pyridine, showing one of the double bonds in III and IV to have been in the $\Delta^{13(14)}$- and not in the $\Delta^{13(18)}$-position.

The diacetate of VII on being heated with zinc at 170° (Serini reaction, see Ghera *et al*[1] for model experiments) was transformed to the diketone X. Equilibration with potassium *t*-butoxide in *t*-butyl alcohol yielded a mixture of isomers (m.p. 164 - 171°), presumably consisting mainly of the C-9 epimer XI. Reaction with methylmagnesium iodide led to the corresponding ditertiary diols (m.p. 84 - 95°), which were subjected directly to cyclodehydration.

The most effective conditions were found to involve treatment with perchloric acid and acetic anhydride in benzene-acetic acid at room temperature. Gas chromatographic analysis of the product showed that the equilibrium mixture of racemic XII and XIII had been formed in small yield, besides a very complex mixture of other substances, as evidenced by direct comparison with the natural optically active substances[7] (identical retention times on two different stationary phases, no separation on admixture). The presence of the pentacyclic triterpenes in the synthetic mixture was confirmed by the mass spectrum, which showed the characteristic fragmentation pattern of authentic XII and XIII (equilibrium mixture).

Selenium dioxide oxidation of the synthetic mixture led to the racemic diene-dione XIV[8]. The latter was identified with the optically active substance (prepared



CH
C
OH
H
O
I
II
14
18
13
III, ~~~ = α
IV, ~~~ = β
HO
HO
12
11
OH
OH
V
VI, 11(12)-cis-ethylene
VII, 11(12)-saturated
VIII
IX, 11(12)-saturated
9
X, ~~~ = α
XI, ~~~ = β
12
13
18
XII
XIII
XIV

by selenium dioxide oxidation of authentic XII and XIII)[8] by comparison of the ultraviolet spectra (λ_{max}^{EtOH} 279 mμ , λ_{min}^{EtOH} 241 mμ)[8] and thin layer chromatographic behaviour (identical Rf values, no separation on admixture).

The fact that the saturated tetrol IX and precursors belong to the "unnatural" series was confirmed as follows. The diacetate of IX on Serini reaction gave a diketone (m.p. 150 - 151°), inverted to the corresponding C-9 epimer (m.p. 138 - 139°), which was treated with methylmagnesium iodide and then dehydrated, as previously. The complex mixture of products was shown to contain no detectable amounts of XII and XIII, as evidenced by gas chromatography, mass spectrometry and selenium dioxide oxidation.

Satisfactory analytical data were obtained for all compounds for which melting points are recorded. We are indebted to Dr. J. McLean (University of Strathclyde, Glasgow) for samples of authentic XII and XIII, and to Dr. H. Budzikiewicz (Stanford University, California) for the mass spectral data.

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