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THE PREPARATION OF D-NORSTEROIDAL SKELETAL TYPE FROM A DITERPENIC PRECURSOR

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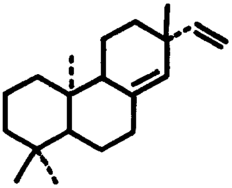
Among the many modifications to which the steroidal skeleton has been subjected, a few have been concerned with the contraction of the D-ring to a four membered ring. The motivation behind this work has been largely the hope of discovering hormone analogs with modified biological activities. This transformation has been achieved by two routes: the first one involves the action of ultraviolet light on 16-17-ketosteroids,[1] while a more recent method is based on a pinacol-type rearrangement of 16-methanesulphonates of $16\alpha,17\alpha$-dihydroxy-17β-ethyl steroids.[2]

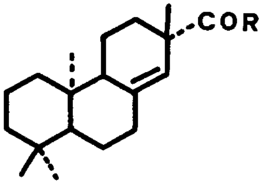
We wish now to report a novel approach to the preparation of this unusual steroidal skeletal type based on the intramolecular C-alkylation of the diazocarbonyl intermediate 3 prepared starting from pimarene 1.[3,4]

While the acid-catalyzed decomposition of unsaturated diazo-ketones has been largely utilized for the incorporation of a bicyclo[3.2.1.] or [2.2.1.]octane moiety in a variety of systems,[5] only one example has been reported concerning the formation of a four membered ring system.[6] Diterpenic compounds with a C(8), C(14) double bond such as 1, are good models for this transformation which involves a π-bond participation in the displacement of nitrogen from the protonated diazomethyl carbonyl function. In order to make the foothold for the bridge formation, pimarene 1 was converted into the carboxylic acid derivative 2 [δ: 0.70, 0.85, 0.88, 1.25 (each s, Me_4), 9.35 (m, COOH), ν_{max}: 1705][7] by the permanganate-periodate oxidation of the vinyl side chain.[8] The sodium salt of 2 was then sequentially treated with oxalyl chloride (1.5 molar equiv.) and diazomethane (3 molar equiv.)[9] to give the diazo-ketone 3 in 90% yield [ν_{max}: 1630, 2110, 3120].

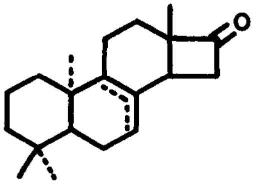
The diazo-ketone was then converted quantitatively to a mixture (45:55) of the two isomeric cyclobutanones 4 [δ: 0.80, 0.93, 0.98, 1.18 (each s, Me_4), 5.53 (m, 7-H); ν_{max}: 1778] and 5 [δ: 0.88, 0.93, 0.98, 1.15 (each s, Me_4); ν_{max}: 1778] by stirring with silica gel in benzene at r.t..[10] The more stable cyclobutanone 5 (m.p. 103-105°) was obtained as the only product when the reaction mixture was treated with hydrogen chloride gas in chloroform at r.t..[11]



1



2 R = OH
3 R = CHN$_2$



4 Δ^7
5 Δ^{8-9}

The above route gives a new, easy access to the preparation of the D-norsteroidal skeletal-type and opens the way to further synthetic applications in the relatively unexplored field of the diterpenes-steroids ring system conversion.

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FOOTNOTES AND REFERENCES

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