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DITERPENOID TOTAL SYNTHESIS, AN A→B→C APPROACH.

III. TOTAL SYNTHESIS OF ETHYL *dl*-CARNOSATE DIMETHYL ETHER

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Carnosic acid (XII) (1) is unusual among tricarbocyclic diterpenoids in that its angular substituent is in an oxidation state higher than methyl. We wish to report the substantiation of its structure by total synthesis of its racemic dimethyl ether ethyl ester, using the general diterpenoid synthesis described in the preceding communication (2).

8,8-Dimethyl-10-carbethoxy-*trans*-2-decalone (I) (3) was condensed with ethyl formate and the resulting hydroxymethylene ketone II was dehydrogenated with 2,3-dichloro-5,6-dicyanoquinone (4). Michael addition of *t*-butyl 5-methyl-3-ketohexanoate to the unsaturated aldehyde III, m.p. 94°, followed by treatment of the adduct IV with p-toluenesulfonic acid afforded the enedione V,[**] m.p. 130°, which was dehydrogenated over palladium on carbon to the ketophenol VI, m.p. 193°. Palladium-catalyzed hydrogenolysis affords the phenolic ester VII.

The 11-methoxy substituent was introduced by an adaptation of the sequence applied to structure elucidation of carnosol (5). Treatment of the phenol (as its sodium salt) with diazotized p-nitroaniline afforded the azo compound VIII which was methylated and then reduced with sodium dithionite to the methoxy amine X. Diazotization and methanolysis

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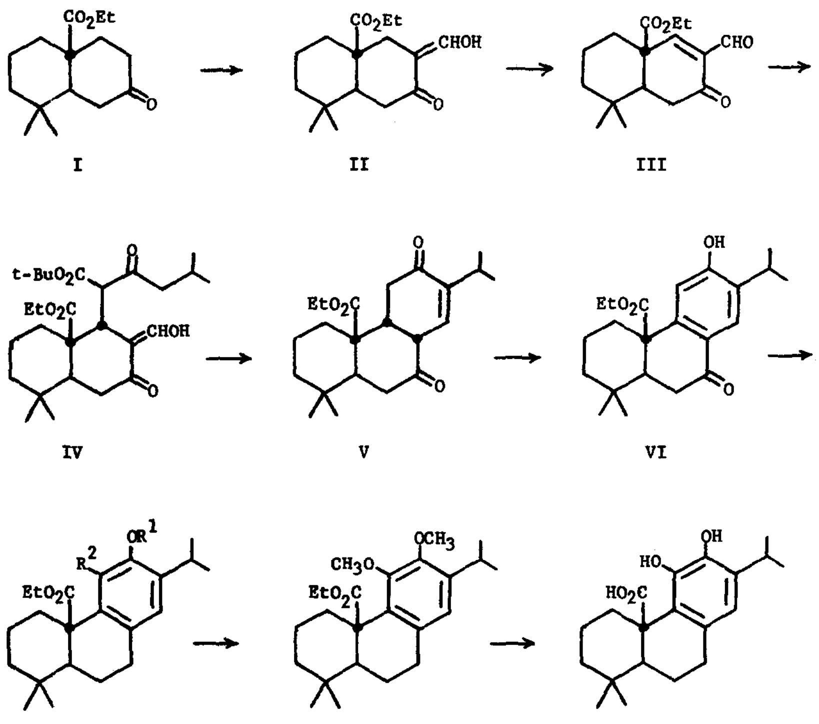
[**] The *trans*-*syn*-*cis* configuration is tentatively assigned on the basis of n.m.r. evidence, *cf*. the accompanying paper.



I

II

III

IV

V

VI

XI

XII

VII, $R^1 = R^2 = H$

VIII, $R^1 = H$, $R^2 = N_2C_6H_4NO_2$

IX, $R^1 = CH_3$, $R^2 = N_2C_6H_4NO_2$

X, $R^1 = CH_3$, $R^2 = NH_2$

afforded ethyl dl-carnosate dimethyl ether (XI), which had infrared and n.m.r. spectral properties and gas chromatographic retention time indistinguishable from those of a sample prepared by treatment of carnosic acid dimethyl ether* with diethyl sulfate.

Potassium t-butoxide in dimethyl sulfoxide (6) converts ethyl

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*We are grateful to Dr. A. Fuchs for the sample of d-carnosic acid.

d-carnosate dimethyl ether to carnosic acid dimethyl ether. Since the dimethyl ether has been converted to the dihydroxy acid by boron tribromide (1), only a resolution step remains unexplored for a total synthesis of carnosic acid itself.

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