Chemical and Microbiological Remote Oxidation of (−)-Bornyl Acetate

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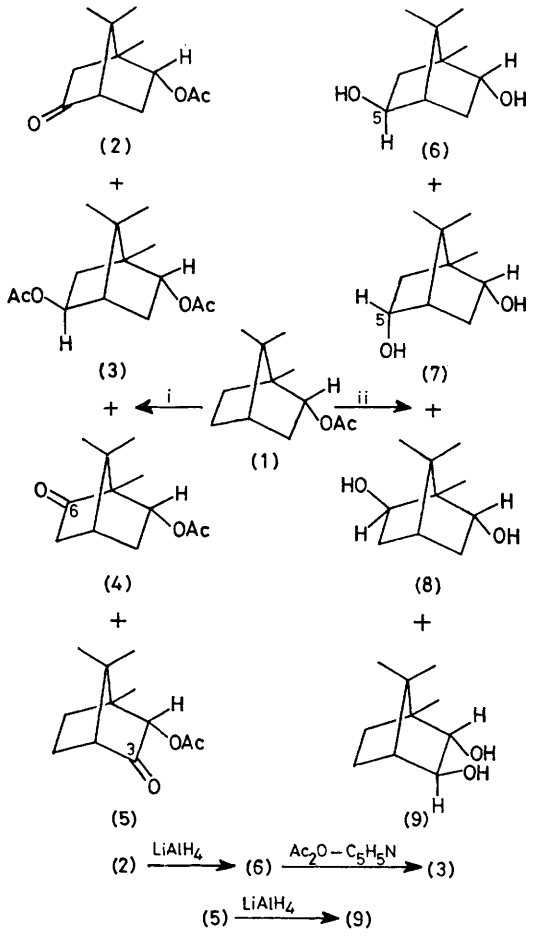
Summary Chemical and microbiological remote oxidation of (−)-bornyl acetate occurs preferentially at the C(5) position.

IN connection with synthetic objectives, we have investigated the feasibility of oxidising certain bicyclic and tricyclic terpenoid systems at positions remote from activating functionality. The literature contains several reports on the remote oxidation of bornyl acetate,[1] isobornyl acetate,[2] and camphor[3] at the C(5) position in 6—40% yields based on recovered starting material. We have re-investigated two of these oxidative transformations in order to understand their mechanism and assess their potential use in synthetic and biosynthetic studies.

Oxidation of (−)-bornyl acetate (**1**) (Scheme 1) with CrO_3–Ac_2O–HOAc for 7 days at room temperature or with CrO_3–HOAc for 2 h at reflux provided a mixture of products (35—45% yield) which were separated and purified by column chromatography and g.l.c. The major product (40—50% of mixture) was identified as 5-oxobornyl acetate (**2**) on the basis of spectral data (i.r. and n.m.r.) and chemical transformation to 5-*exo*-hydroxyborneol (**6**), 5-oxoborneol, and bornane-2,5-dione. Three minor products of the oxidation reaction were identified as 5-*exo*-acetoxybornyl acetate (**3**) (2—3%), 6-oxobornyl acetate (**4**) (10—13%), and 3-oxobornyl acetate (**5**) (1—3%) by chemical correlation with bornane-2,5-, bornane-2,6-, and bornane-2,3-diones (camphorquinone), respectively. The stereochemistry of (**3**) was deduced from its n.m.r. spectrum and by its synthesis from (**2**).

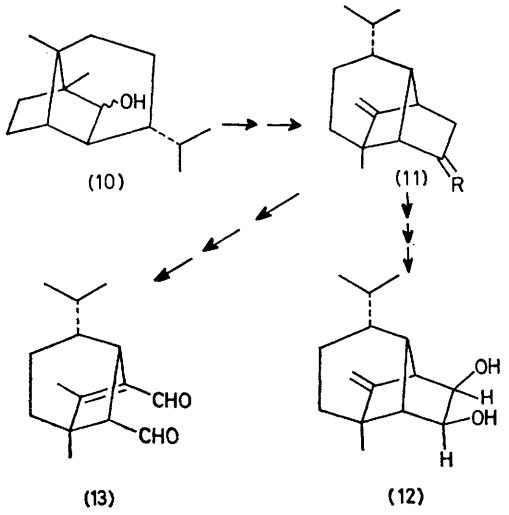
The regiospecific oxidation of bornyl acetate prompted us to consider that similar oxidations could be occurring in nature. For example, introduction of oxygen functionality at C(5) in ylangoborneol (**10**; OH *endo*) or ylangoisoborneol (**10**; OH *exo*) (Scheme 2) followed by Wagner–Meerwein rearrangement to the 5-keto compound (**11**; R = O) or to 5-hydroxysativene (**11**; R = H, OH) could be involved in the biosynthesis of *cis*-sativenediol (**12**),[4] helminthosporal (**13**), and related compounds.[5] A result of these proposals is the prediction that *Helminthosporium sativum*, the fungus responsible for the production of (**13**), should contain



SCHEME 1. i, CrO_3–Ac_2O–HOAc or CrO_3–HOAc; ii, *H. sativum*.

an oxidase or hydroxylase system which may be capable of functionalising bicyclic acetates of appropriate structure and absolute configuration. Support for this prediction has

been obtained by feeding (**1**)† to 3-day-old cultures of *H. sativum*. After 7—10 days, ether extraction of the broth provided (−)-borneol and a crude mixture of bornanediols which were purified and separated by column chromatography. These compounds were identified as bornane-2,3-, bornane-2,5-, and bornane-2,6-diols by n.m.r. data and conversion into the corresponding diketones.‡ The overall yield of diols was *ca.* 50% and the relative proportions of the 2,5-, 2,3-, and 2,6-isomers were estimated to be 5:2:1 by g.l.c. of their diacetates. On the basis of their n.m.r. spectra and chemical correlation with products obtained in the chemical oxidation of (**1**), the various microbiological products were identified as 5-*exo*-hydroxyborneol (**6**), 5-*endo*-hydroxyborneol (**7**), 6-*exo*-hydroxyborneol (**8**), and 3-*exo*-hydroxyborneol (**9**).[6]



SCHEME 2

The results described above illustrate a remarkable correspondence between the chemical and biological oxidation of bornyl acetate and it is hoped that subsequent investigations will provide a general explanation for this phenomenon.

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† This enantiomer corresponds in absolute configuration with the enantiomer of ylangoborneol which we suggest as a possible precursor of helminthosporal (*cf.* Scheme 2). (−)-Borneol is not functionalised under these conditions.

‡ Previous studies on the biological oxidation of bornane systems have shown that camphor can be oxygenated at the C(3), C(5), and C(6) positions (G. A. Fonken and R. A. Johnson, 'Chemical Oxidations with Microorganisms,' Marcel Dekker, New York, 1972, pp. 24 and 25 and references cited therein; K. Kieslich, 'Microbial Transformations of Non-Steroid Cyclic Compounds,' Wiley, 1976, p. 59 and references cited therein).

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