Stereoelectronic Effects in Cyclo-octanes: Synthesis of (±)-Dactylol and (±)-Isodactylol

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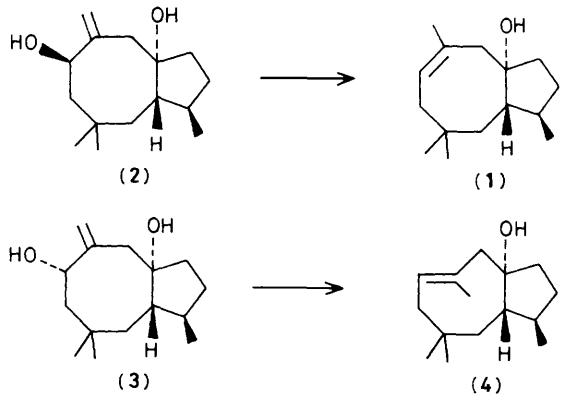
Racemic dactylol and isodactylol were synthesized from racemic poitediol and 4-epipoitediol respectively.

Dactylol (**1**) is an unusual sesquiterpene which has been isolated along with poitediol (**2**) from the red seaweed *Laurencia poitei*.[1] Dactylol has also been isolated from the sea hare *Aplysia dactylomela*.[2] Dactylol and poitediol are relatively simple members of a growing family of cyclo-octanoid natural products which continue to attract interest as challenging synthetic targets.[3] This communication reports the syntheses of dactylol (**1**) and isodactylol (**4**) under stereoelectronically controlled conditions from poitediol (**2**) and 4-epipoitediol (**3**), respectively.

Completion of the total syntheses of poitediol and 4-epipoitediol in this laboratory[4] made possible an investigation of their conversion into dactylol. Although a number of methods could be envisaged to accomplish the required reductive rearrangement, simple treatment with sodium and ethanol in liquid ammonia[5] appeared to be the most straightforward. Based on the observations of Birch[6] concerning allylic alcohol reductions, it was expected that the intermediate allyl anion would be protonated at the less substituted carbon atom so as to afford the desired endocyclic olefin. The reduction of 4-epipoitediol (**3**) (Scheme 1) was initially investigated, since it was available in larger quantities than poitediol (**2**).

Addition of 4-epipoitediol and ethanol to sodium in liquid ammonia did result in formation of dactylol, although in very low yield (7—10%). The major product (50% yield) was instead found to be an isomer of dactylol, based upon high-field n.m.r. and mass spectral data. One of the small but significant differences between the n.m.r. spectrum of this product and that of authentic dactylol was the appearance of the olefinic proton absorption. In dactylol, this absorption

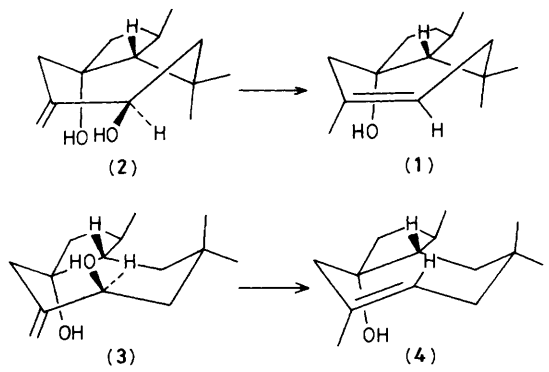


Scheme 1

appears as a broad triplet (J 8 Hz) while the same proton in the isomeric material appears as a broad doublet (J 13 Hz). Based upon its n.m.r. spectrum and stereoelectronic considerations (*vide infra*), this isomeric material has been assigned the isodactylol structure (**4**).

In contrast to the behaviour of 4-epipoitediol, reduction of synthetic poitediol (**2**) under the same conditions led cleanly to dactylol (**1**) in 70% yield. The spectral data of this synthetic material (except of course for optical rotation) were identical with those of authentic dactylol.†

† N.m.r., i.r., and mass spectra of authentic dactylol were kindly provided by Professor F. Schmitz of the University of Oklahoma.



Scheme 2

These results can most easily be interpreted by an analysis of the stereoelectronic requirements of the reduction and the corresponding transition-state conformations of poitediol and 4-epipoitediol. In order for reduction to occur, the cyclo-octane ring must adopt a conformation in which the C–O σ bond is periplanar with respect to the olefinic π system.[7] The best conformations for poitediol (**2**) and 4-epipoitediol (**3**) which meet this requirement are shown in Scheme 2. Selective formation of dactylol and isodactylol from poitediol and 4-epipoitediol, respectively, implies that protonation of the intermediate allyl anion at the methyl carbon atom is faster than bond rotation about the allyl anion. This same phenomenon has been observed in the stereospecific reduction of other allyl alcohols.[8] In the present case, intramolecular proton transfer from the tertiary hydroxy group may be occurring.

Further evidence for the proposed isodactylol structure may be found in the aforementioned appearance of the vinyl proton absorption in the 270 MHz n.m.r. spectrum. The isodactylol structure is fairly rigid, and the conformation (**4**) shown is certainly the favoured solution conformation. In this conformation, the vinyl proton makes a dihedral angle of ~180° with one of the vicinal allylic protons, and a dihedral angle of 70° with the other. The broad doublet (*J* 13 Hz) observed for the vinyl proton of isodactylol is perfectly consistent with this structure.[9]

Finally, the synthesis of dactylol from poitediol fully confirms the structure of dactylol to be correct as previously assigned.[1] Since we have described[4] the total synthesis of substrates (**2**) and (**3**), this transformation constitutes a synthesis of dactylols (**1**) and (**4**).

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