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TOTAL SYNTHESIS OF (±)-FILIFOLONE.

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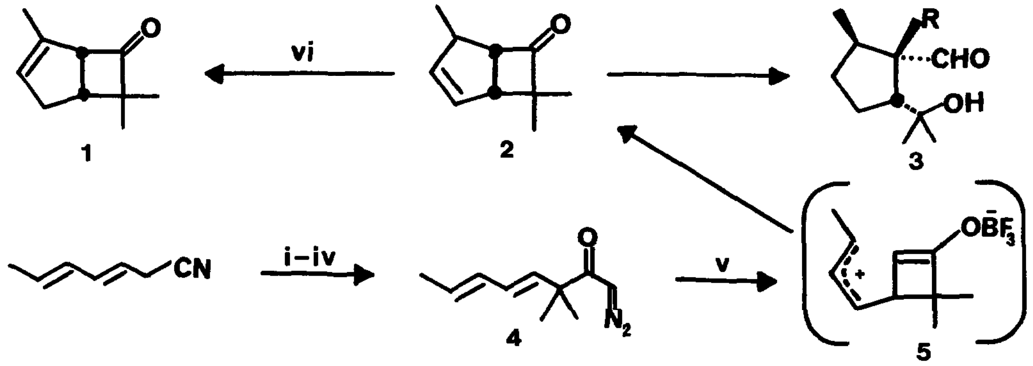
Abstract: Monoterpene filifolone has been synthesized by an intramolecular acid catalyzed alkylation of dienic diazoketone. The potential utility of the key transformation in the synthesis of a new terpene synthon is indicated.

Filifolone 1, a monoterpenoid containing a [3.2.0] bicycloheptane ring system has been subject of several studies since its isolation from *Artemisia filifolia* Torrey.[1] Its formation from geranic acid,[2] chrysanthenone,[3] verbenone,[4] and ocimenone[5] as well as its degradation sequences were described. The chemical reactivity of 1 and the number of modes of rearrangements that are offered through the labile cyclobutanone moiety prompted us to investigate the use of 1 or its isomer 2 as potential terpene synthons, leading to substituted cyclopentanes of the type 3,[6] scheme 1. In connection with our ongoing research in the area of intramolecular carbenoid additions to 1,3-dienes, it appeared that the bicyclic system 2 could be obtained from diazoketone 4, via cyclopropanation-rearrangement sequence.[7] The diazoketone 4 was rapidly synthesized from available heptadienyl nitrile[8] in four steps with an overall yield of 78%, scheme 1.[9]



i LDA/MeI; ii KOH/MeOH; iii $(COCl)_2$; iv CH_2N_2; v BF_3/Benzene/6°C, 5 min.;vi $RhCl_3/EtOH/H_2O$.

Scheme 1

Whereas the copper catalyzed decomposition of 4 led only to fragmentation,[7] its exposure to acid catalysis at low temperature furnished the bicyclic ketone 2 as a mixture of stereoisomers[9] (65% 2β, 35% 2α), presumably via the intermediate zwitter ion 5.

This result is in direct analogy to previously investigated closures of β,γ-unsaturated diazoketones which are known to lead to cyclobutanones[10] or cyclopentanones[11] depending on the substitution of the olefin and thereby on the reactivity of the corresponding cation.

Ketone 2 was isomerized to filifolone 1[12] by treatment with $RhCl_3$ in aqueous ethanol[13] in 30-40% yield and proved spectrally identical to the natural product.

In view of its accessibility and of its troublesome isomerization it would seem that 2 is far better suited for the conversion to cyclopentane 3 than filifolone itself. It appears likely that once the ring strain experienced in 2 is removed by cleavage of the cyclobutanone, isomerization becomes more feasible and with it the possibility of invoking greater stereoselectivity in generating 3. The oxidative conversion of 2 to 3 in which the necessary stereochemical demands of acorane sesquiterpenes have been met, is presently being investigated.

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