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BROMONIUM ION-INDUCED CYCLIZATION OF METHYL FARNESATE: APPLICATION TO THE SYNTHESIS OF SNYDEROL.

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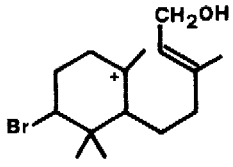
We have previously hypothesized that the wide variety of sesquiterpenes isolated from the marine algae genus Laurencia can be biogenetically rationalized as resulting from the cyclization of the bromo carbenium ion I[1]. This hypothesis has now been supported by the finding, by Fenical et al, of the bromo monocyclonerolidol derivative snyderol (II)[2] in L. snyderae.

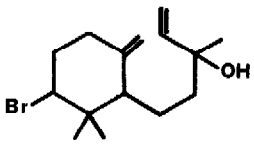
We are very interested in exploring an approach to the selective C-Br bond formation with concomitant ring closure, in connection with a program directed toward the biogenetic type synthesis of marine terpenoids[3]. To the best of our knowledge, only a few examples of bromonium ion-induced carbocyclization of acyclic polyenes has been achieved[4,5]. In this article, we record the obtaining of a simple synthesis of snyderol (II).

Reaction of an equimolecular mixture of freshly crystallized N-bromosuccinimide with methyl trans,trans-farnesate (III) and cupric acetate in tert-BuOH/AcOH yielded 12% of compound IV as a colourless oil. No cyclic compounds other than the exocyclic methylene IV were in evidence.

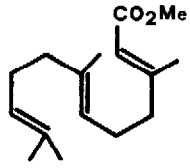
The structure of IV was determined by the following data: a composition of $C_{16}H_{25}O_2Br$ was indicated by the mass spectrum (M^+ at m/e 330,328) and confirmed by elemental analysis; ir: ν_{max} 3080,1650,890 (=CH_2), 1720 (C=O), 1390 and 1360 cm^{-1} (gem-dimethyls); nmr (CCl_4) δ 0.89,1.20 (3H each,s,gem-dimethyls), 2.17 (3H,s,an olefinic methyl), 3.67 (3H,s, a methyl ester), 4.05 (1H,dd,J=12 and 5 Hz, a bromomethine proton), 4.68,4.98 (2H, an exocyclic methylene) and at 5.60 ppm (1H,s, an olefinic proton). In the mass spectrum



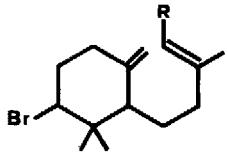
I



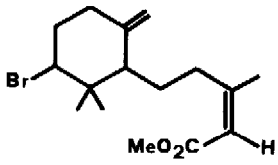
II



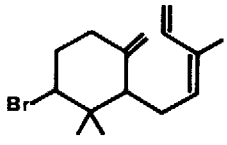
III



IV, R = CO_2Me
V, R = CH_2OH
VI, R = CH_2Br



VII



VIII

of IV, the intense peaks appeared at m/e 248,205,189,173 and 121 (base peak). The reaction was further tested on methyl cis,trans-farnesate which, under identical conditions, gave VII in 10-15% yield [nmr: δ 0.81 and 1.16 (3H each, s), 1.88 (3H,d,J=1.5 Hz), 3.60 (3H,s), 4.05 (1H,dd,J=12,4 Hz), 4.80 and 4.91 (1H each,s), and 5.60 ppm (1H,d,J=1.5 Hz)].

Reduction of IV with LAH in ether yielded the bromo monocyclofarnesol V, which on treatment with a slight equivalent excess of PBr_3 in hexane at 0º gave the bromide VI. Water hydrolysis of VI provided the natural compound II and the conjugated diene VIII in a 1/2 ratio. When compound VI in hexane was stirred for 24hr at 25º over silica gel which had been impregnated with 2% water by weight, snyderol (II) was formed quantitatively.

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