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AN EASILY ACCESSIBLE CISOID ISOPRENOID SYNTHON

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Summary. Five-step preparation of the cisoid isoprenoid synthon 5 and its use for the two-step C_5-homologation is described.

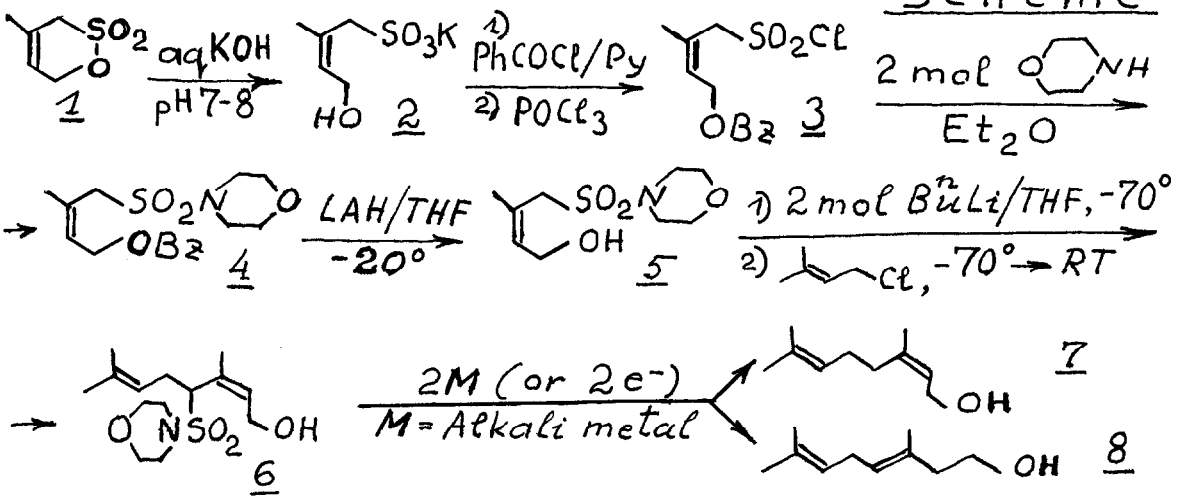
Several efficient syntheses of terpenoids have recently been designed on the basis of five-carbon synthons bearing at C_1 or C_4 an activating, sulfur-containing group, which is easily removable after the chain elongation step.[2,3] The choice of such compounds with trans trisubstituted C=C bond is quite rich whereas their cisoid congeners are still practically unavailable. We describe here a simple transformation of the δ-sultone 1, previously prepared by us[4,5] into an isoprenoid synthon of the cisoid series (Scheme).

Recently we reported the dissolution of 1 in aq. THF gives an oily E,Z-mixture of the respective sulfonic acids.[5] Later we found the pH-controlled saponification of 1 with 0.1N KOH affords the salt Z-2 in ~80% yield.[6,7] Benzoylation of 2 followed by treatment with $POCl_3$ and purification on silica gel afforded the oily sulfonyl chloride 3.[7] Amidation of the latter with 2 mol equiv. of morpholine resulted in the benzoate 4 in 55% overall yield, m.p. 114-6°C (from THF-Et_2O-hexane)[8]; $\delta^{CDCl_3}_{TMS}$: 2.01 (d,J=1.5 Hz,3H,C$\underline{H}_3$), 3.34 (m,4H,C$\underline{H}_2$N), 3.88 (m, 4H,C$\underline{H}_2$O), 4.00(bs,2H,C$\underline{H}_2$S), 4.89 (d,J=7 Hz,2H,C$\underline{H}_2$OBz), 5.84 (tq,J=7 and 1.5 Hz, 1H,$\underline{H}$C=C), 7.5-8.0 ppm (m,5H,$C_6\underline{H}_5$). Mild hydride reduction of 4 gave quantitatively the crystalline sulfonamide 5, m.p. 112-4°C (from CH_2Cl_2-Et_2O-hexane)[8]; $\delta^{CDCl_3}_{TMS}$: 1.99 (d,J=1.5 Hz,3H,C$\underline{H}_3$), 3.34 (m,4H,C$\underline{H}_2$N), 3.74 (m,6H,C$\underline{H}_2$O,C$\underline{H}_2$S), 4.14 (d,J=7 Hz,2H,C$\underline{H}_2$OH), 5.88 ppm(tq,J=7 and 1.5 Hz,1H,$\underline{H}$C=C).

Since sulfonamide is known to be both a good carbanion-stabilizing[9] and reductively removable group[10], the olefin 5 might be expected to be an effective isoprenoid synthon. Indeed it was found this compound was deprotonated and then alkylated whithout allylic shift of the C=C bond. Thus, its prenylation smoothly gives the oily nerol derivative 6[8], $\delta^{CDCl_3}_{TMS}$: 1.66 (bs,6H,C$\underline{H}_3$), 1.81 (d,J= 1.5 Hz,3H,C$\underline{H}_3$ at C_3), 2.60 (m,2H,C$\underline{H}_2$C=C), 3.28 (m,4H,C$\underline{H}_2$N), 3.60 (m,4H,C$\underline{H}_2$O), 4.12 (d,J=7 Hz,2H,C$\underline{H}_2$OH), 4.20 (dd,J=9 Hz,1H,C$\underline{H}$S), 4.92 (bt,J=7 Hz,1H,$\underline{H}$C=C), 5.68 ppm (tq,J=7 and 1.5 Hz,1H,$\underline{H}$ at C_2). The reductive cleavage of 6 or its alkoxide either with alkali metals in amines or with amalgams, or else electrochemically, affords, depending on the conditions employed, nerol 7[11] and/or isogeraniol 8[7,8,12] in high yields.

Thus, such a two-step C_5-homologation using the hydroxy sulfonamide 5

Scheme



opens up promising possibilities for the sterospecific synthesis of a variety of isoprenoid (homo)allylic alcohols, including polyprenols. Examination of the synthetic value of this approach is presently in progress in our laboratory.

References and Notes

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6. The product is contamined with ~15% (NMR data) of the isomeric tertiary allylic alcohol which is formed during the work-up.
7. Satisfactory spectral (IR,NMR) data were obtained for this compound.
8. Satisfactory elemental analyses data were obtained for this compound.
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