A Novel Cyclization of Geraniol and Nerol Initiated by Tris(*p*-bromophenyl)ammoniumyl Radical Cation

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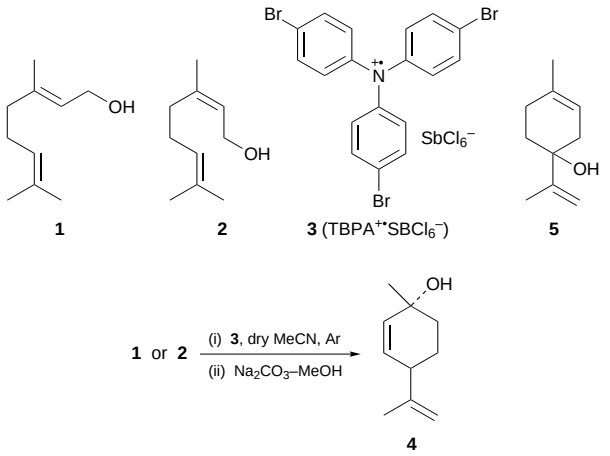
Geraniol (**1**) and nerol (**2**) undergo a novel cyclization to *cis*-*p*-mentha-2,8-dien-1-ol (**4**) by reaction with tris(*p*-bromophenyl)ammoniumyl radical cation (**3**) and the reaction mechanism is discussed.

Tris(*p*-bromophenyl)ammoniumyl hexachloroantimonate ($TBPA^{+\bullet}SbCl_6^-$, **3**) has been used as a one-electron oxidant in a variety of electron transfer reactions. Investigations have shown that **3** can initiate some radical cation cycloadditions, such as the Diels–Alder reaction,[1] cyclopropanation[2] and Cope rearrangement.[3] We have studied the radical cation initiated cyclization of squalene with **3**.[4] In this article, we wish to report a novel cyclization of the monoterpenol geraniol (**1**) and nerol (**2**) to *cis*-*p*-mentha-2,8-dien-1-ol (**4**) by **3,** which is reduced to the neutral tris(*p*-bromophenyl)amine (TBPA) (Scheme 1).



Scheme 1

1 or **2** was treated with excess **3** in dry acetonitrile at room temperature under an argon atmosphere for several hours. After quenching of the reaction with sodium carbonate–methanol solution, the main product was isolated and identified as **4**. The structure of **4** was determined by mass spectrometry, IR, ^1H and ^{13}C NMR spectroscopy and elemental analysis. The results of a ^{13}C-DEPT NMR determination established the structure of **4** and excluded the possibility of structure **5**, which was considered as a reasonable alternative. Fig. 1 illustrates the ^{13}C NMR spectra of compound **4**. Comparing the three spectra of **4** [(a) ordinary ^{13}C NMR spectrum, (b) DEPT-135 spectrum and (c) DEPT-90 spectrum], it can be seen that **4** has two different CH_3, three CH_2, three CH and two *tert*-C groups, which clearly indicate the presence of two differently substituted carbon–carbon double bonds, i.e. CHR , CHR and CR_2 , CH_2, and their relative positions. The ^{13}C NMR chemical shifts assignments for **4** are shown in Fig. 1(*a*). The spectroscopic data are consistent with those reported for **4** obtained from unsensitized photoxidation of limonene.[5]

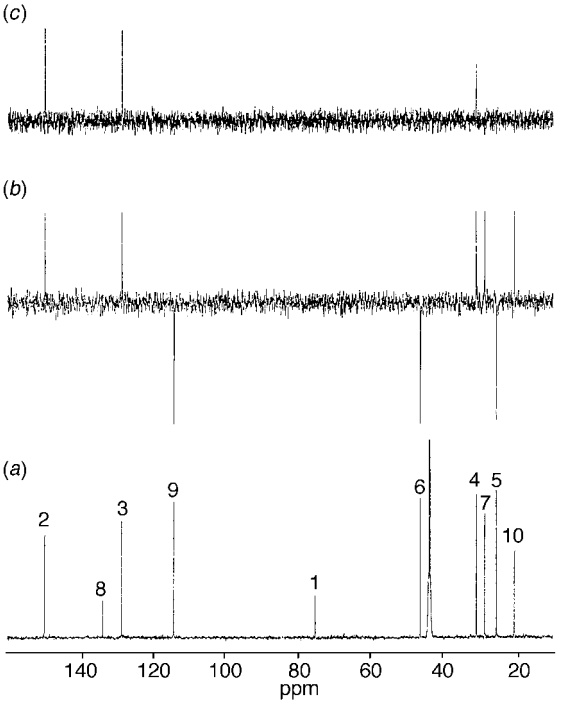


Fig. 1 ^{13}C NMR spectra of product **4**. (a) Normal ^{13}C NMR spectrum; (b) DEPT-135 spectrum; (c) DEPT-90 spectrum

Although the cyclization of acyclic monoterpenes has been known for a long time,[6] and the acid-catalysed rearrangements of **1** and **2** and solvolyses of their derivatives have been studied as models for terpenoid biosynthesis,[7] the title cyclization is of interest because it is initiated by a radical cation. It is also interesting to note that the product **4** obtained from this reaction is rarely observed in most cyclizations of monoterpenes but has been formed by unsensitized photooxidation of limonene.[5] Moreover, most of the reactions reported are assumed to involve carbocationic intermediates, and subsequent intramolecular electrophilic cyclizations or rearrangements of these intermediates lead to complicated mixtures that contain products having the *p*-menthene skeleton without additional unsaturation.[8]

Recently, the radical cation cyclization of hexa-1,5-diene and its derivatives,[9] as well as polyenes[10] containing olefinic bonds at 1,5-positions, have been reported. All-*trans*-geranylgeraniol was converted *via* radical cation intermediates into fused six-membered ring products by photoinduced cyclization in sodium dodecyl sulfate (SDS) micelle. It was proposed that radical cationic intermediates could potentially play a role in the biogenesis of natural products in addition to the cationic intermediates invoked in classical concepts and especially in the cyclization processes for terpene biosynthesis.[10] Accordingly, the title reaction may proceed *via* a radical cation intermediate as shown in Scheme 2.

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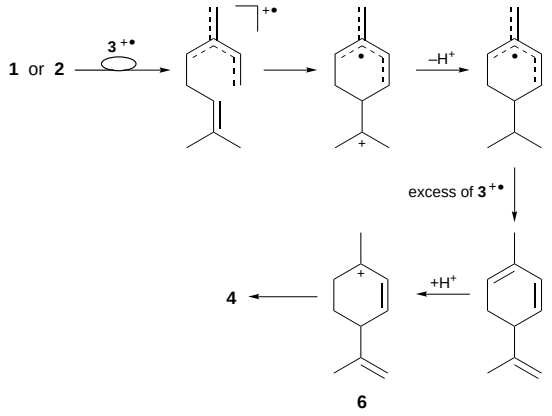

Scheme 2

The radical cation intermediate formed initially undergoes cyclization, deprotonation and dehydrogenation (by excess of $\mathbf{3}^{+\bullet}$) to give a cyclic triene, which protonates to form the carbocationic intermediate **6**. Attack by a water molecule at the cationic centre opposite the isopropenyl group and deprotonation would produce **4**.

Experimental

Melting points were uncorrected. Elemental analyses were carried out on an Italian-1106 elemental analytical apparatus. IR spectra were recorded on a Nicolet FT-170SX spectrometer. ^{1}H and ^{13}C NMR and ^{13}C-DEPT spectra were obtained on a Bruker DMX-500 spectrometer (500.0 MHz for ^{1}H NMR, 125.0 MHz for ^{13}C NMR and ^{13}C-DEPT) using [$^2H_6$]DMSO as solvent and tetramethylsilane (TMS) as internal reference. Mass spectra were determined on a VG-ZAB-HS mass spectrometer (EI).

1 and **2** were purchased from TCI Chemical Co. and used without further purification. Compound **3** was synthesized as described;[11] mp 143–144 °C (decomp.) (Found: C, 26.58; H, 1.46. $C_{18}H_{12}Br_3Cl_6NSb$ requires C, 26.50; H, 1.50%). All solvents were purified and dried according to standard procedures.[12]

cis-p-*Mentha*-2,8-*dien*-1-*ol* (**4**). To a solution of **1** or **2** (2.0 mmol) in anhydrous acetonitrile (35.0 ml) **3** (4.8 mmol) was added. The mixture was stirred at room temperature for 2 h under argon and checked by TLC. It was then poured into saturated sodium carbonate–methanol solution (15.0 ml), and extracted with trichloromethane (total 75 ml). The organic layer was washed with water and dried with anhydrous magnesium sulfate and the solvent was removed. The oily residue was separated by column chromatography on silica gel (eluent: light petroleum–ethyl acetate, from 40:1 to 15:1 v/v) to give **4** as a yellow oil in yields of 61 to 72% (Found: C, 78.81; H, 10.32. $C_{10}H_{16}O$ requires C, 78.94; H, 10.53%). ν_{max}/cm^{-1} (film): 3340 (O•H), 1440 (C,C), 1220 (C,CH$_2$). δ_H ([$^2H_6$]DMSO) 1.24 (3 H, s), 1.52 (1 H, m), 1.73 (2 H, m), 1.81 (3 H, s), 2.13 (2 H, m), 3.45 (1 H, br s, OH), 4.68 (2 H, m), 5.20 (1 H, m), 5.72 (1 H, d, *J* 10.7 Hz). δ_C ([$^2H_6$]DMSO) 149.9, 134.3, 128.2, 114.2, 75.4, 46.1, 31.7, 29.0, 26.2, 21.7; *m*/*z* 152 (M^+), 134, 119, 91, 79, 43, 41. The ^{1}H NMR spectroscopic data are consistent with those reported for **4**.[5]

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