

Synthesis of 1-Vinylmenth-4(8)-ene, the Purported Sesquiterpene from *Mentha citrata*

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A synthesis of the title compound from geraniol *via* Claisen rearrangement, Chugaev elimination, and reduction is reported. The synthesized compound shows different spectral properties from those described for such a structure.

A steam-volatile constituent of *Mentha citrata* has been recently identified as 1-vinylmenth-4(8)-ene (1), mainly on a spectroscopic basis.¹ As such, this hydrocarbon is most plausibly derived from oxidative degradation of elemene-type precursors and it can be regarded as a trisnorsesquiterpene. However, it is intriguing to note the low oxidation state of the ring carbon atoms (C-2, -3) as the loss of the three-carbon unit would be expected to require some sort of unsaturation at those sites.

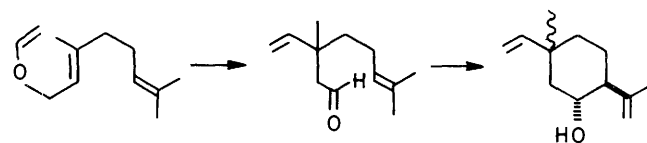
We now wish to report an expedient synthesis of the terpene (1) starting from geraniol (Scheme 1). Thus, the tandem Claisen rearrangement/ene reaction of 3,7-dimethylocta-2,6-dienyl vinyl ether performed at 220 °C for 20 h provided the 1-vinylisopulegols (2) which consisted mainly of two diastereoisomers.² The hydroxy and isopropenyl groups of these major products are likely to be *trans* related, according to the rationale put forth by Dev.²

We proposed to dehydrate the alcohols (2) to obtain the triene (3), and reduce the conjugated diene moiety of the latter compound in a 1,4-manner, resulting in our target molecule (1). In view of the *cis* relationship between the hydroxy group and the vicinal methine hydrogen, dehydration by a pyrolytic method was planned. Both the acetates and xanthates were prepared and pyrolysed. The Chugaev reaction was preferred because smaller amounts of by-products arose and lower temperatures were required. Three olefins were formed predominantly from the Chugaev elimination in a ratio of 21.6 : 11.8 : 66.6. By spinning-band distillation the last compound, identified as the triene (3), can be separated from the other components which proved to be the diastereoisomers (4). It is known that pyrolysis of menthyl *S*-methylxanthate affords a 51% yield of menth-2- and -3-enes in a 1 : 3 ratio.³

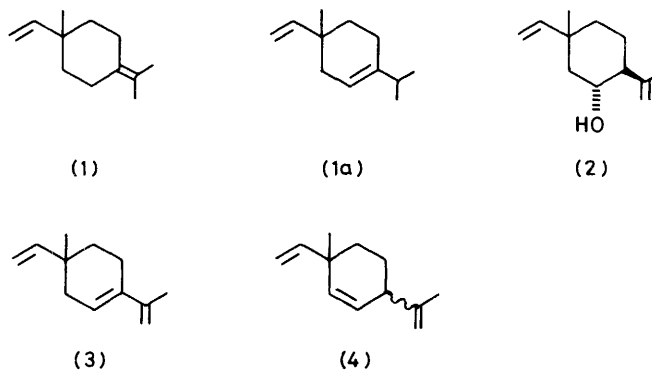
Reduction of the olefin (3) with lithium in liquid ammonia furnished the terpene (1) together with the regioisomer (1a) in a 3 : 1 ratio, as a result of the predominant 1,4-reduction of the conjugated diene system. Interestingly, the vinyl group attached to C-1 also underwent reduction when an excess of lithium was present and the reaction time was prolonged. However, the more highly substituted double bond survived, presumably because of its existence as the allyl anion prior to protonation. Saturation of an isolated double bond by lithium-liquid ammonia is rather unusual.

The spectral data of our synthetic material are similar to those reported, but there are several important differences. In the ¹H n.m.r. spectrum the allylic methylene groups appear as a triplet instead of a multiplet, and the two vinylic methyl groups are magnetically equivalent. Features of both signals are fully consistent with the symmetrical structure. While the mass spectrum of our material shows all fragments corresponding to those reported, the base peak † is *m/z* 81 instead of 149.

Prior to the successful completion of the above synthesis, many other approaches were investigated. The solvolysis of the methanesulphonate (5), which was obtained from the



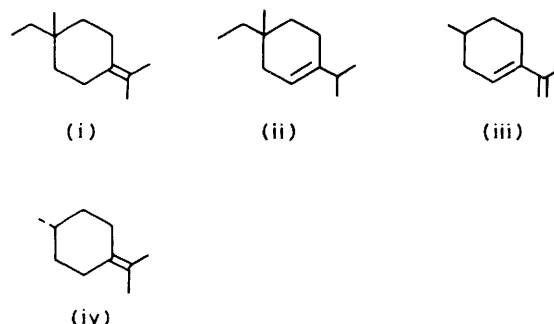
Scheme 1.



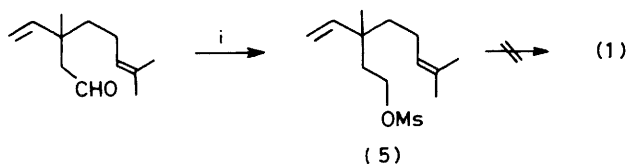
primary Claisen rearrangement product of 3,7-dimethylocta-2,6-dienyl vinyl ether by hydride reduction and methanesulphonylation, did not lead to (1) (Scheme 2).

A route starting from *p*-mentha-1,3-diene, embodying the Prins reaction and acid hydrolysis,⁴ was thwarted (Scheme 3). All efforts to selectively hydrogenate the cyclic double bond of (6) failed. Conditions included di-imide reduction, catalytic hydrogenation with Wilkinson's catalyst, and lithium-liquid

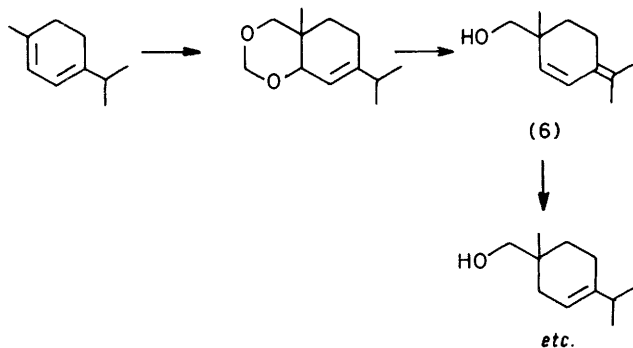
† Our experience shows that *m/z* 81 is the base peak in the mass spectrum of (1a), (i), and (ii), and *m/z* 79 in that of (3), (4), and (iii). The fragment *m/z* 81 is the second most abundant peak in the mass spectrum of (iv).



A referee suggested that the *m/z* 149 peak described by the Indian workers is due to a typical plasticizer (phthalate) contaminant.



Scheme 2. Reagents: i, NaBH₄, MsCl, Et₃N. Ms = methanesulphonyl



Scheme 3.

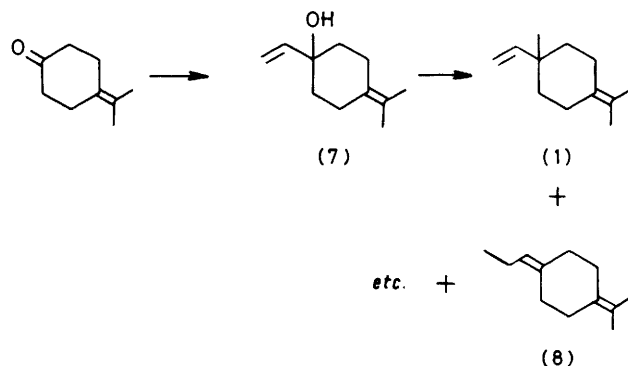
ammonia reduction. Either intractably complex mixtures resulted, or 1,4-reduction occurred. The Koch-Haaf reaction⁵ of *p*-mentha-1,4(8)-diene yielded a complex mixture.

Another attempt involved the Felkin alkylation.⁶ Thus, 4-isopropylidenecyclohexanone⁷ was treated with vinylmagnesium bromide in tetrahydrofuran (THF) at room temperature (24 h) to give the allylic alcohol (7) (Scheme 4); ν_{\max} (neat) 3 400 and 910 cm⁻¹; $\delta(\text{CDCl}_3)$ 1.4–1.8 (5 H, m), 1.63 (6 H, s), 2.0–2.5 (4 H, m), 4.97 (1 H, dd, *J* 10.5, 1.5 Hz), 5.18 (1 H, dd, *J* 16.5, 1.5 Hz), and 5.92 (1 H, dd, *J* 16.5, 10.5 Hz); in almost quantitative yield. However, prolonged exposure of compound (7) to excess of methylmagnesium iodide in the presence of bis(triphenylphosphine)nickel chloride in diethyl ether led to a mixture of products. Although compound (1) was detected as the major component by the g.c.-mass spectrometric matching technique, it was difficult to obtain pure. The most abundant side-product appeared to be the allyl isomer (8).

In summary, the synthesis of 1-vinylmentha-4(8)-ene has been accomplished. The discrepancy in spectral data of our synthetic material with those reported casts doubt on the correctness of the structural assignment by the Indian chemists. Requests for copies of the original spectra did not draw a positive response. Our own investigation by capillary gas chromatography and g.c.-mass spectrometric techniques of a *M. citrata* oil did not reveal the presence of a compound which elutes in the same region as our synthetic material. The limit of detection by our instruments is <0.01%.

Experimental

I.r. spectra were taken with a Perkin-Elmer 137 spectrophotometer for neat samples. ¹H N.m.r. spectra were recorded on a Hitachi/Perkin-Elmer R20B (60 MHz) spectrometer, with tetramethylsilane as internal standard and deuteriochloroform as solvent. Electron-impact mass spectra were measured with a Finnigan MAT 112 spectrometer. Gas chromatograms were run with a Perkin-Elmer Sigma GC equipped with a 30 m × 0.25 mm bonded DB 1 column, programmed at 4 °C per min, from 75 to 250 °C, flow rate 20 cm s⁻¹.



Scheme 4.

1-Vinyl-isopulegols (*p*-mentha-8-en-3-ols) (2).—3,7-Dimethylocta-2,6-dienyl vinyl ether (30 g) was heated at 220 °C for 16 h to give a quantitative conversion into the vinylisopulegols (cf. ref. 2).

1-Vinylmentha-*x*,8-dienes (3) and (4).—To a stirred suspension of sodium hydride (50% dispersion, 20 g; washed with pentane) in diethyl ether (400 ml) was added the 1-vinylisopulegol (60 g) and a drop of methanol. After being refluxed for 16 h, the reaction mixture was cooled, and treated with carbon disulphide (50 ml). Heating was continued for 3 h and iodomethane (30 ml) was then added to the xanthate salt. After 4 h, the reaction mixture was cooled, poured into ice-water, and extracted with diethyl ether. The ether layer was washed with water, dried (Na₂SO₄), and filtered. Concentration of the ether solution gave a mixture of the crude xanthates (75 g) which was directly heated to reflux (bath temp. 230 °C). After 4 h, g.c. analysis showed that complete elimination had taken place. Spinning-band distillation (reflux ratio 59 : 1) afforded 1-vinyl-*p*-mentha-2,8-diene (4) (4.29 g; b.p. 65–70 °C/10 Torr); ν_{\max} (neat) 1 640, 910, 875, and 740 cm⁻¹; $\delta(\text{CDCl}_3)$ 1.00 (3 H, s), 1.45–1.6 (2 H, m), 1.6–1.8 (5 H, m), 2.65 (1 H, m), 4.71 (1 H, narrow m), 4.7–4.9 (1 H, m), 5.02 (1 H, narrow m), 5.51 (1 H, narrow m), and 5.5–6.0 (1 H, m); and 1-vinyl-*p*-mentha-3,8-diene (3) (11.12 g; b.p. 74–79 °C/10 Torr); ν_{\max} (neat) 1 640, 1 610, 910, 875, and 815 cm⁻¹; $\delta(\text{CDCl}_3)$ 0.95 (3 H, s), 1.53 (2 H, t, *J* 6 Hz), 1.87 (3 H, d, *J* 1 Hz), 2.0–2.4 (4 H, m), 4.75–5.10 (4 H, m), 5.84 (1 H, dd, *J* 18, 10 Hz), and 5.80 (1 H, t, *J* 3 Hz); *m/z* (70 ev) 162 (*M*⁺) (Found: *M*⁺ 162.1407. Calc. for C₁₂H₁₈: *M*⁺ 162.1408).

An intermediate fraction containing the products (3) and (4) weighed 4.82 g. The combined yield of the olefins was 37% from 3,7-dimethylocta-2,6-dienyl vinyl ether.

1-Vinylmentha-4(8)-ene (1).—Lithium chips (0.15 g) were added to liquid ammonia (20 ml), followed by, after 2 min stirring, a solution of the triene (3) (0.2 g) in diethyl ether (10 ml). The reduction was allowed to proceed for 10 min, and then quenched with absolute ethanol (10 ml) as rapidly as possible. On addition of ammonium chloride (10 g), ammonia was evaporated at room temperature. The residue was treated with pentane and aqueous ammonium chloride, and filtered. The organic layer was separated, washed twice with water, dried (Na₂SO₄), and evaporated to afford a mixture (0.2 g) containing (1) (68.65%), its isomer (1a) (23.57%) and monoene (0.54%). In a larger run [4.8 g of (3)] the product consisted of (1a) (19.98%), (1) (53.25%), and monoene (11.82%). The diene (1) was further purified by preparative g.c. (neat) 1 630 and 910 cm⁻¹; $\delta(\text{CDCl}_3)$ 1.00 (3 H, s), 1.65 (6 H, br s), 1.1–1.6 (4 H, m), 2.22 (4 H, t, *J* 6 Hz), and an ABX

system 4.99 (*J* 9.5, 1.5 Hz), 5.02 (*J* 19, 1.5 Hz), and 5.87 (*J* 19 9.5 Hz); *m/z* (70 ev) 164 (22.47%), 149 (15.70), 135 (24.94), 122 (25.57), 121 (69.81), 109 (7.44), 108 (19.99), 96 (19.10), 95 (40.18), 94 (14.37), 93 (81.65), 91 (23.53), 82 (16.76), 81 (100), 80 (12.79), 79 (72.32), 77 (21.28), 69 (17.45), 68 (32.58), 67 (85.74), 65 (13.50), 55 (47.21), 53 (27.01), 44 (20.55), 43 (23.05), and 41 (56.28) (Found: 164.1548. Calc. for C₁₂H₂₀: 164.1565).

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