

TOTAL SYNTHESIS OF OBTUSENOL¹⁾

A.G. González, J.D. Martín, C. Pérez, M.A. Ramírez and F. Ravelo

Departamento de Química Orgánica, Universidad de La Laguna,
 Instituto de Productos Naturales Orgánicos, CSIC, Tenerife, Spain.

Summary.— The total synthesis of obtusenol (9), a dibrominated sesquiterpene isolated from the red alga *Laurencia obtusa*, has been achieved by a three-step synthesis starting from commercial farnesol.

In connection with a programme directed towards the biogenetic-type synthesis of marine terpenoids, we are interested in exploring an approach to the selective C-Br bond formation with concomitant ring closure on acyclic polyenes^{2,3)}. In this article we record the obtaining of a simple synthesis of obtusenol (9)⁴⁾. Some of the results obtained by N-bromosuccinimide oxidation of *trans,trans*-farnesol acetate under argon and in the dark are represented in the Table. Compound 4, which only forms when cupric acetate is added, probably occurs by radical cyclization of the C-7 Me oxidized acyclic intermediate.

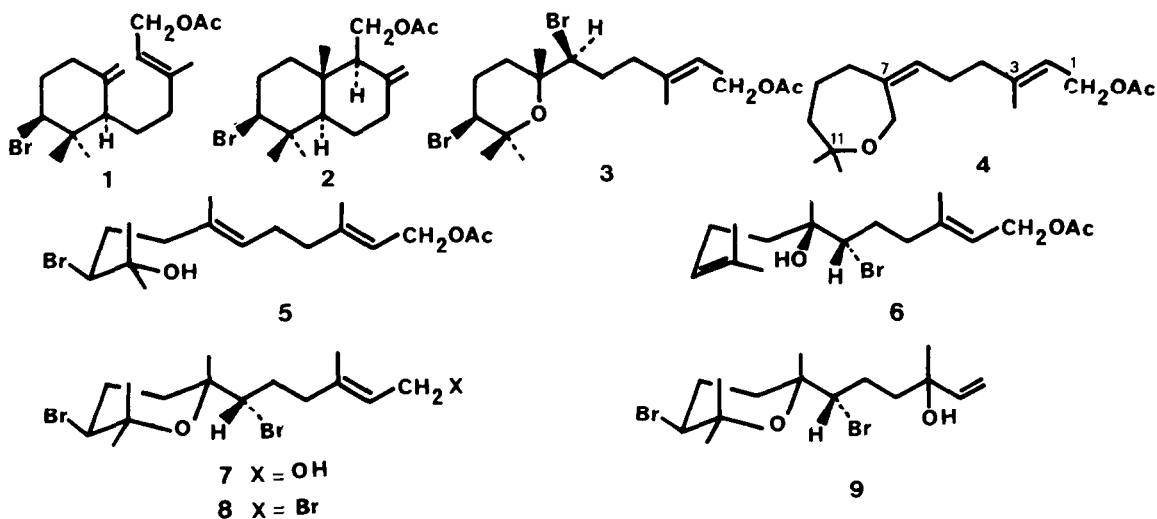
TABLE: Bromonium ion-induced cyclization of *trans,trans*-farnesol acetate.

Exp.	Solvent	temp., °C	time, h	Comp. <u>1</u> yield(%)	Comp. <u>2</u> yield(%)	Comp. <u>3</u> yield(%)	Comp. <u>4</u> yield(%)
1	t-BuOH	0	24	5	-	-	-
2	t-BuOH, (AcO) ₂ Cu	20	12	5.5	-	-	12
3	t-BuOH, (AcO) ₂ Cu	50	12	6	-	-	16
4	t-BuOH, AcOH	0	24	12	1	-	-
5	t-BuOH, AcOH	20	24	7	1	-	-
6	CH ₃ NO ₂ , I ₂ , KI	0	12	8	4	-	-
7	Dioxane	0	24	8	-	-	-
8	Dioxane	20	24	7	-	-	-
9	Acetone-H ₂ O	0	12	10	2	14	-
10	Acetone-H ₂ O	20	12	12	1	10	-

When aqueous acetone was used as solvent (Table, line 9), together with the carbocyclization products 1 and 2, the dibromo-tetrahydropirane derivative 3 was obtained in 14% yield.

The structure of 3 was determined by the following data: a composition of C₁₇H₂₂Br₂O₃ was indicated by the mass spectrum (M⁺ at m/e 438, 440, 442) and confirmed by elemental analysis. Further peaks in the MS were found at m/e (%): 378, 380, 382(4); 299, 301(14); 285, 287(87); 205, 207(100). The IR spectrum $\nu_{\text{max}}^{\text{CCl}_4}$ 1749, 1410, 1385, 1370, 1250, 1125, 1105, 1025 cm⁻¹. The PMR spectrum (100 MHz, CCl₄, δ -value) exhibited singlets for five Me groups at 2.10, 1.73, 1.45, 1.38 and 1.33; two protons deshielded by α -halogens at 3.90 (*dd*, $J = 11$ and 6 Hz) and 3.66 (*dd*,

$J = 11$ and 11.5 Hz); two α -acetoxy protons at 4.65 (d , $J = 8$ Hz); and one olefinic proton at 5.45 (t , $J = 8$ Hz). Treatment of the readily isolable bromohydrin 5⁵⁾ with *N*-bromosuccinimide in aqueous acetone under different reaction conditions failed to give any cyclization products. Compound 3 must then arise by bromonium ion cyclization of the non-isolable bromohydrin 6 at the terminal double bond. Base hydrolysis of 3 with K_2CO_3 in acetone gave the alcohol 7 which on treatment with a slight equivalent excess of PBr_3 in hexane at 0° gave the tribromide 8. Water hydrolysis of 8 provided the racemic natural compound 9⁴⁾ in 60% yield. When compound 8 in hexane was stirred for 12 h. at room temp. over silica gel which had been impregnated with 2% water by weight, (\pm)obtusenol (9) was formed quantitatively⁶⁾.



ACKNOWLEDGMENTS: This research was supported by Grant No. 4125-79, awarded by the C.A.I.C.T.

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- 6 The racemic synthetic material gave identical NMR, MS, and IR spectra with those of a natural sample kindly provided by Professor R.H. Thomson.

(Received in UK 28 September 1981)