
Novel and Enantioselective Total Synthesis of Drimane Type Sesquiterpenes

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Two drimane type sesquiterpenoids, (+)-drimane-8,11-diol **1** and (+)-drim-9(11)-en-8-ol **2**, have been synthesized in an optically pure form starting from geraniol.

During work directed towards the synthesis of biologically important terpenoids such as drim-9(11)-en-8-ol **2**¹ and ambrein,² we required a versatile and optically pure common intermediate containing suitable functions. The sesquiterpenoid (+)-drimane-8,11-diol **1**,³ isolated from Greek tobacco, with four contiguous stereogenic centres met our purposes. Here we report an enantioselective total synthesis of **1** from geraniol and its conversion into (+)-**2**, which features the use of a highly diastereoselective intramolecular Diels–Alder reaction.

Sharpless asymmetric epoxidation of geraniol using D-(–)-diethyl tartrate provided the epoxide **3**⁴ (94% ee)† in 97%

yield. Treatment of **3** with isopropenylmagnesium bromide in the presence of cuprous iodide⁵ resulted in the exclusive formation of the 1,3-diol **4**‡ which was converted into the acetone **5** in 83% overall yield. Selective ozonolysis of the trisubstituted olefin in **5** at –78 °C cleanly provided the

† The ee was determined by the ¹⁹F and ¹H NMR spectra of the corresponding MTPA ester.

‡ All new compounds gave spectral data (IR, NMR, MS) in accord with the assigned structure, and satisfactory combustion analysis or accurate mass measurement.

2.52 (3 H, m), 3.70 (1 H, dd, *J* 11.8 and 4.5), 4.00 (1 H, dd, *J* 11.8 and 11.1), 4.75 (1 H, m), 4.93 (1 H, m) and 9.75 (1 H, t, *J* 2.1).

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