

A Synthesis of Diumycinol

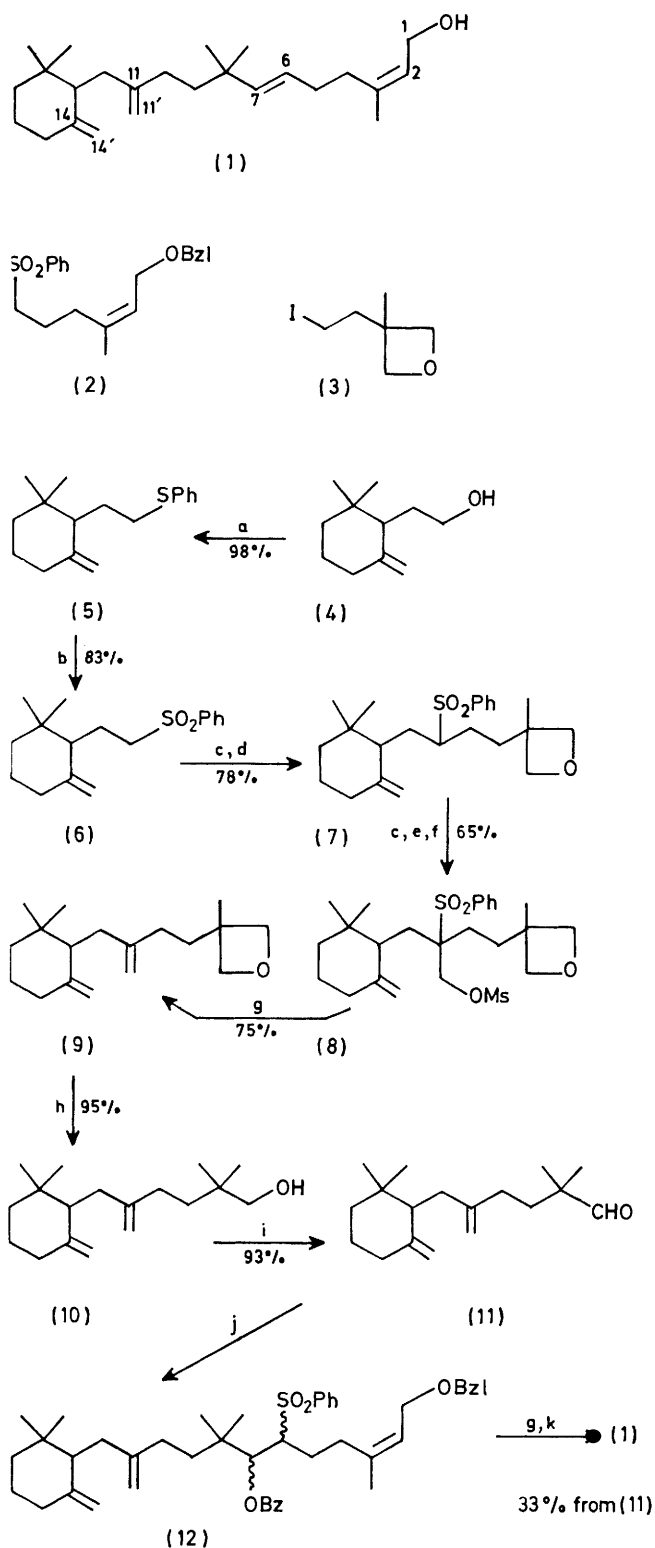
Philip Kocienski* and Michael Todd

Department of Organic Chemistry, The University, Leeds LS2 9JT, U.K.

The reductive-elimination of β -substituted sulphones was used to introduce the hindered alkene bonds at C(6)–C(7) and C(11) of diumycinol.

We report a new synthesis of diumycinol (**1**)¹ which is obtained by hydrolysis of the antibiotic diumycin.² The molecule was assembled from three principal fragments. The sulphone (**2**) was used previously in the synthesis of moenocinol³ and the oxetan (**3**) was prepared by the general method of Castro.⁴

The sulphone (**6**) was prepared in two steps from the known⁵ alcohol (**4**) by first converting (**4**) into the phenyl sulphide (**5**) using *N*-phenylmercaptosuccinimide and Bu^n_3P ⁶ followed by oxidation to the sulphone (**6**) using bis(trimethylsilyl) peroxide^{7,8} in refluxing benzene as shown in Scheme 1.



Scheme 1. Bzl = benzyl, Ms = MeSO₂, Bz = benzoyl. *Reagents and conditions:* a, *N*-Phenylmercaptosuccinimide, Buⁿ₃P-CH₂Cl₂, 0 °C; b, 2.2 equiv. Me₃SiOOSiMe₃-benzene reflux, 18 h; c, BuⁿLi-tetrahydrofuran (THF), -78 °C; d, 1.5 equiv. of (3), -78 °C → 20 °C; e, excess of CH₂O gas, -10 °C; f, MsCl-CH₂Cl₂, Et₃N; g, Na(Hg)-THF:MeOH (3:1), 0 °C; h, Li-H₂NCH₂CH₂-NH₂-Et₂O, 15 °C; i, (Me₂SCl)⁺Cl⁻-CH₂Cl₂, -78 °C followed by Et₃N, -78 °C → 20 °C; j, add (11) to lithium derivative of (2)-THF, -78 °C followed by BzCl, -78 °C → 20 °C; k, Na-NH₃, -78 °C.

Alkylation of the lithium-derivative of the sulphone (6) with the oxetan (3) gave (7). However, a second alkylation of the lithium or potassium derivative of (7) with iodomethyltrimethylsilane under a variety of conditions failed and thereby foiled our use of the β -silylsulphone elimination⁹ which had served as a key step in the similar but sterically less demanding step in the moenocinol synthesis.³ Instead, the lithium derivative of (7) reacted readily with formaldehyde to give a product which underwent methanesulphonation to give a diastereomeric mixture of β -methanesulphonyloxy-sulphones (8). The C(11) methylene group was then introduced by reductive elimination¹⁰ to give the diene (9). Reductive cleavage¹¹ of the oxetan (9) gave the alcohol (10) which was oxidized¹² to the aldehyde (11).

The synthesis was completed by condensing the lithium derivative of sulphone (2) with aldehyde (11). Benzoylation of the adduct gave a diastereomeric mixture of β -benzoyloxy-sulphones (12) which was treated with Na(Hg) to introduce the C(6)-C(7) double bond. Reductive debenzoylation then gave diumycinol (1) whose 400 MHz ¹H n.m.r. spectrum (CDCl₃) gave well resolved ¹H olefinic resonances at δ 5.44 [t with further splitting, *J* 7.5 Hz, C(2)-H], 5.375 [br.d, *J* 16 Hz, C(7)-H], 5.26 [dt, *J* 16, *J'* 6.5 Hz, C(6)-H], and narrow multiplets at 4.725, 4.69 and 4.615, and 4.49 [C(14), H₂ and C(11), H₂ respectively]. There was no evidence for contamination of the product by the *cis*-isomer at C(6)-C(7).

There are three aspects of this synthesis which are noteworthy. Firstly, the reductive-elimination reactions used to introduce the olefinic bonds at C(6)-C(7) and C(11) were successful where alternative methods failed completely⁹ [in the case of the C(11) methylene] or failed to give the *trans*-double bond at C(6)-C(7) selectively.¹³ Secondly, the oxidation of the sulphide (4) to the sulphone (5) by bis(trimethylsilyl) peroxide without affecting the double bond is potentially useful. A similar reaction on phenyl geranyl sulphide gave the corresponding sulphone in 83% yield. Finally, the use of an oxetan as an inert and sterically restricted latent neopentyl alcohol moiety could be useful in the synthesis of crowded complex molecules.

We thank the S.E.R.C. for a post-doctoral award (M. T.) and the Sheffield High Field N.M.R. Service.

Received, 2nd June 1982; Com. 630

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