Oblongolide: Synthesis and Absolute Configuration

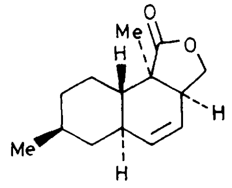
Tony K. M. Shing

Department of Chemistry, University of Manchester, Manchester M13 9PL, U.K.

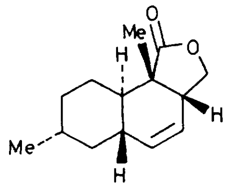
The absolute configuration of oblongolide is shown to be (**1**) by an unambiguous synthesis from (+)-citronellol involving an intramolecular Diels–Alder reaction.

Very recently, oblongolide has been isolated from fungus *Phomopsis oblonga* in low yield,[1] and shown to be a boring/feeding deterrent for elm bark beetles.[1,2] The structure of oblongolide has been shown to be (**1**) or its enantiomer (**2**) by *X*-ray crystallography. The absolute configuration (**2**) was assigned to oblongolide on the basis of a circular dichroism study of its dihydroderivative using the lactone sector rule.[1] We now report, starting from (+)-citronellol, a short and unambiguous synthesis of (**2**) which is identical to the natural oblongolide except for the sign of the optical rotation, thereby demonstrating the absolute configuration of oblongolide to be (**1**).

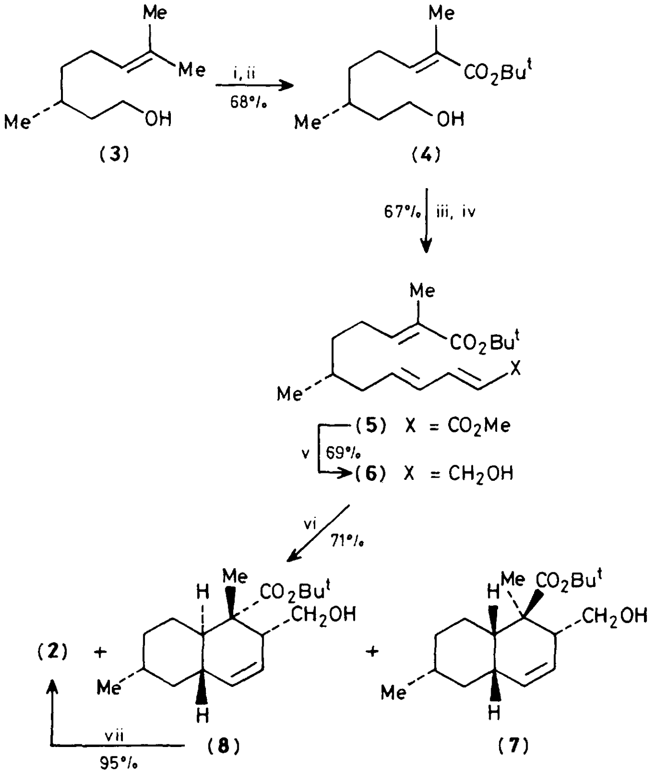
The aldehyde derived from (3*R*)-(+)-citronellol (**3**) ($[\alpha]_D^{20}$ +4.1°, neat) reacted with t-butoxycarbonylethylidenetri-



(1)



(2)



Scheme 1. *Reagents and conditions:* i, catalytic OsO_4, $NaIO_4$, aqueous dioxane; ii, $Ph_3P{=}CMeCO_2Bu^t$, CH_2Cl_2; iii, pyridinium chlorochromate, 3Å molecular sieves, CH_2Cl_2; iv, $(OMe)_2P(O)CH_2CH{=}CHCO_2Me$, lithium di-isopropylamide, tetrahydrofuran, −78 °C; v, di-isobutylaluminium hydride (2 equiv.), tetrahydrofuran, −78 °C; vi, toluene, sealed tube, 155 °C, 7 h; vii, catalytic trifluoroacetic acid, chloroform, reflux, 15 min.

phenylphosphorane to give ester (**4**),† $[\alpha]_D^{20}$ +11.0° (*c* 1.5, $CHCl_3$) (*E*:*Z* ratio 97:3), (Scheme 1). Oxidation of (**4**) followed by condensation with the lithium salt of methyl 4-(dimethylphosphinyl)crotonate provided methyl dienoate (**5**), $[\alpha]_D^{20}$ −12.7° (*c* 1.1, $CHCl_3$) (>96% *E*,*E*).‡ Di-isobutylaluminium hydride reduction of (**5**) proceeded with excellent regioselectivity,§ affording the Diels–Alder precursor (**6**), $[\alpha]_D^{20}$ −10.5° (*c* 1.5, $CHCl_3$), and a trace amount of the regioisomeric allyl alcohol.

Upon heating with toluene (sealed tube), triene (**6**) yielded decalins (**7**), (**8**), and oblongolide (**2**) in the ratio 38 : 24 : 13,¶ indicating preponderant reaction *via* chair conformers with the C-7 methyl substituent[3] disposed in an equatorial orientation. The hydroxy-ester (**8**) was transformed smoothly into (**2**) on mild acid treatment. The crude crystalline oblongolide (**2**) had $[\alpha]_D^{20}$ +141.6° (*c* 0.2, MeOH), 75% enantiomeric excess (e.e.). One recrystallisation from hexane gave needles with spectroscopic data (i.r., ^1H and ^{13}C n.m.r.) identical to those reported,[1] m.p. 102—104 °C; $[\alpha]_D^{20}$ +181.5° (*c* 0.2, MeOH), 96% e.e. The natural oblongolide had m.p. 105—106 °C and $[\alpha]_D^{20}$ −190° (*c* 0.0475).[1] The absolute configuration of natural oblongolide must therefore be (**1**) and the lactone sector rule is inaccurate in this case.

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References

1 M. J. Begley and J. F. Grove, *J. Chem. Soc., Perkin Trans. 1*, 1985, 861.
2 N. Claydon, J. F. Grove, and M. Pople, *Phytochem.*, 1985, **24**, 937.
3 An example of using a methyl-substituent to control the diastereofacial selectivity of an intramolecular Diels–Alder (IMDA) reaction has appeared very recently; D. R. Williams, M. L. Bremmer, D. L. Brown, and J. D'Antuono, *J. Org. Chem.*, 1985, **50**, 2807. For some related IMDA reactions, see W. R. Roush and M. Kageyama, *Tetrahedron Lett.*, 1985, **26**, 4327, and references cited therein.

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† All new compounds gave satisfactory analytical and spectral data.

‡ The *E*,*Z*-isomer was converted into (**5**) with a catalytic amount of iodine in carbon tetrachloride.

§ No selectivity was observed when ethyl ester was used instead of t-butyl ester: the isomeric allyl alcohols were obtained in *ca.* 1 : 1 ratio.

¶ Ratio determined by capillary gas chromatography.