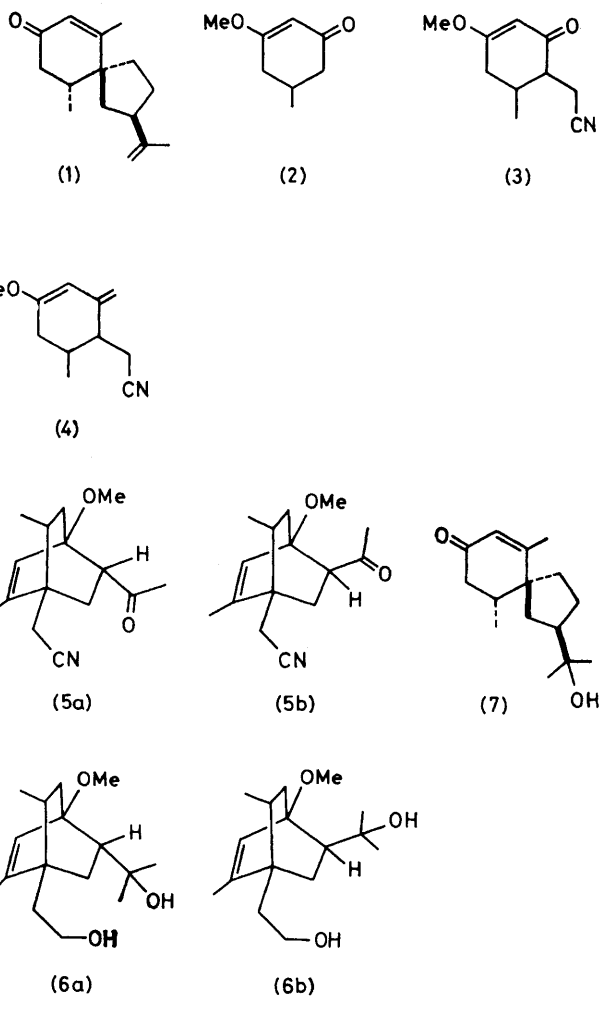
Efficient Synthesis of (±)-Solavetivone[1]

By AKIO MURAI, SHINGO SATO, and TADASHI MASAMUNE*
(*Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo* 060, *Japan*)

Summary An alternative, efficient synthesis of (±)-solavetivone (**1**) is described.

SOLAVETIVONE (**1**)[2] is a representative member of the antifungal spirovetivanes, shown to be phytoalexins,[3] obtained from diseased potatoes[2a] and air-cured tobacco leaves.[4] The biogenetic pathways[5] proposed for the biosynthesis of oxylubimin[6] prompted us to improve our recent synthesis[1] of (±)-(**1**) (12 steps, 3·2% overall yield from 3,5-dimethylanisole). This communication describes an alternative, concise synthesis of (±)-solavetivone (**1**).

Readily available 3-methoxy-5-methylcyclohex-2-enone (**2**)[7]† was treated with lithium di-isopropylamide in tetrahydrofuran (THF) at −78 °C, followed by addition of chloroacetonitrile in hexamethylphosphoramide–THF (1 : 1) at −78 °C. The mixture was warmed to room temperature for 12 h to afford 6-cyanomethyl-3-methoxy-5-methylcyclohex-2-enone (**3**), m.p. 95—97 °C, in 94% yield.‡ The Wittig reaction of compound (**3**) with methylenetriphenylphosphorane in dimethyl sulphoxide[8] (20 °C for 14 h and 45 °C for 6 h) proceeded smoothly to give the dienyl ether (**4**) in 86% yield, which underwent cycloaddition with methyl vinyl ketone in benzene in the presence of dichloromaleic anhydride and 2,6-di-t-butyl-*p*-cresol under reflux for 3 d. The reaction produced a 2·7 : 1 mixture of the *endo*- and *exo*-adducts, each being a 3·5 : 1 mixture of the *anti*- and *syn*-isomers,[9] from which the *anti-endo*-adduct (**5a**), m.p. 64—67 °C, and the *anti-exo*-adduct (**5b**), an oil, could be isolated pure by means of chromatography in 43 and 16% yields, respectively. The *anti-endo*- and *anti-exo*-adducts were transformed by a three-step process [i, methyllithium in diethyl ether, −78 °C, 1 h; ii, di-isobutyl aluminium hydride in diethyl ether, 0 °C, 1 h; and iii, sodium borohydride in THF–water (2 : 1), 0 °C, 10 min] into the corresponding bicyclo-octene diols (**6a**) and (**6b**),



† We prepared compound (**2**) from 5-methylcyclohexane-1,3-dione by reflux with Me_2SO_4 and K_2CO_3 in acetone (89% yield) (*cf.* R. N. Mirrington and G. I. Feutrill, *Org. Synth.*, 1973, **53**, 90).

‡ All new compounds gave satisfactory spectral data.

as oils, in 96 and 75% yields, respectively. These diols were identified as known intermediates[1] which lead to the synthesis of (±)-(**1**) *via* the key spirovetivane compound (**7**), formed stereoselectively by π-cyclization. The present synthesis of (±)-solavetivone (**1**) involves 9 steps and the overall yield is 16·6%.

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[1] For previous paper in the series 'Synthetic Studies of Rishitin and Related Compounds' and 'Studies on the Phytoalexins,' see A. Murai, S. Sato, and T. Masamune, *Tetrahedron Lett.*, 1981, **22**, 1033.
[2] (a) For isolation and structure elucidation, see D. T. Coxon, K. R. Price, B. Howard, S. F. Osman, E. B. Kalan, and R. M. Zacharius, *Tetrahedron Lett.*, 1974, 2921; (b) For absolute configuration, see R. C. Anderson, D. M. Gunn, J. Murray-Rust, P. Murray-Rust, and J. S. Roberts, *J. Chem. Soc., Chem. Commun.*, 1977, 27.
[3] T. Masamune, A. Murai, and N. Katsui, *Kagaku to Seibutsu*, 1978, **16**, 648.
[4] T. Fujimori, R. Kasuga, H. Kaneko, and M. Noguchi, *Phytochemistry*, 1977, **16**, 392.
[5] E. B. Kalan and S. F. Osman, *Phytochemistry*, 1976, **15**, 775; *cf.* A. Stoessl, J. B. Stothers, and E. W. B. Ward, *Can. J. Chem.*, 1978, **56**, 645.
[6] N. Katsui, A. Matsunaga, H. Kitahara, F. Yagihashi, A. Murai, T. Masamune, and N. Sato, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 1217; K. Sato, Y. Ishiguri, N. Doke, K. Tomiyama, F. Yagihashi, A. Murai, N. Katsui, and T. Masamune, *Phytochemistry*, 1978, **17**, 1901.
[7] L. Cleaver, J. A. Croft, E. Ritchie, and W. C. Taylor, *Aust. J. Chem.*, 1976, **29**, 1989.
[8] R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, 1963, **28**, 1128.
[9] *Cf.* A. Murai, S. Sato, and T. Masamune, *Chem. Lett.*, 1981, 429.