Synthesis of ent-Herbasolide

Tse-Lok Ho* and Fu-Sen Liang

Department of Applied Chemistry, National Chiao Tung University, Hsinchu, Taiwan, Republic of China

ent-Herbasolide is synthesised by elaboration of (+)-10-camphorsulfonyl chloride which involves homologation at C-10, cleavage of the C-2/C-3 bond, oxidation at C-5 and chain extension at C-3 of the camphor skeleton.

The structure of (+)-herbasolide 1,† a norsesquiterpene lactone of the marine sponge Dysidea herbacea which grows in the waters surrounding Papua-New Guinea has been determined by X-ray diffraction. Biosynthetically this compound is an oxidative catabolite of (+)-herbasydolide 2 which must be also related to spirodysin 3, the progenitor of (+)-furodysinin 4 and (+)-furodysinin 5. Furodysin and furodysinin are most likely derived by elimination of acetic acid from spuodysin, involving a Wagner–Meerwein rearrangement to expand the cyclopentane ring. We have recently devised a concise synthesis of (+)-furodysin 3,† the major isomer; a combined yield of a 11-oxaspiro[4.4]nonane-1,7-dione (mp 88–90 °C, 86% yield) was achieved by the two-step process of Sakurai-Hosomi reaction 6 with allyltrimethylsilane in the presence of Tick, CHzClz; x, PdCl2, CuCl, HOAc, Ac20, heat; iii, 30% HzO2, NaOH; iv, BH3, THF, m). The alcohol was transformed into the exocyclic methylene derivative in two steps via benzylation (BzCl, DMAP→11 (mp 86–87 °C, 92.5% yield) and pyrolysis (→12, mp 54–56 °C, 56% yield). Introduction of an allylic hydroxy group to give 13 (mp 116.5–118.5 °C, 79% for the major isomer; a combined yield of a 11:1 mixture was obtained in 85.5% yield) was performed by oxidation with SeOz-But02H and the product was further oxidized with manganese dioxide to the conjugated ketone 14 (mp 83–85 °C, 82.5% yield). Whilst Michael addition to the enone using acetone enolate equivalents was not too successful, the final conversion of 14 to herbasolide [9,9-dimethyl-8-(3-oxobutyl)-2-oxaspiro[4.4]nonane-1,7-dione (mp 97–98 °C, lit., 97–98 °C) was achieved by the two-step process of Sakurai-Hosomi reaction 6 with allyltrimethylsilane in the presence of TiCl4 (→15, 70% yield) and Wacker oxidation (O2, PdCl2, CuCl, DMF–H2O; 77% yield). The essentially neutral conditions of the oxidation preserved the product by preventing it from undergoing aldol cyclization. The generation of herbasolide in good yield suggests the Sakurai-Hosomi reaction was terminated by C-protonation from the side of the lactone carbonyl.

Using the more readily available (+)-10-camphorsulfonyl chloride in this synthesis resulted in ent-herbasolide. Thus the absolute configuration of (+)-herbasolide, indicated by 1 as arbitrarily assigned, is indeed correct. In view of the fact that (+)-furodysin was elaborated by a Fijian Dysidea sp.,† we strongly suspect that the (-)-isomer† synthesized by us will be found in this other source.

We thank the National Science Council, Republic of China for financial support.

Footnote
† Selected spectroscopic data for ent-1. The mp and all spectral data of synthetic ent-1 are consistent with the assigned structure as well as the data reported in the literature IR vcm−1: 1757, 1740 and 1714. δH (300 MHz, CDCl3): 0.81 (3 H, s), 1.16 (3 H, s), 2.13 (3 H, s), 4.22 (1 H, m) and 4.30 (1 H, m), δC (75 MHz, CDCl3): 18.29 (t), 19.63 (q), 21.11 (q), 29.01 (q), 30.82 (t), 42.18 (t), 44.14 (s), 44.93 (t), 50.68 (s), 55.89 (d), 65.36 (s), 179.39 (s), 208.01 (s) and 215.19 (s). M+ 252.1359 except [M−5.86, [M−134.1

Chem. Commun., 1996 1887

Published on 01 January 1996. Downloaded by National Chiao Tung University on 28/04/2014 15:13:12.
(c 0.1 CHCl₃). The latter value is larger than the reported +95 which might indicate an optical inhomogeneity of the natural product.

References


Received, 10th April 1996; Com. 602485H