CHEMISTRY LETTERS, pp. 2079-2080, 1987.

Total Synthesis of (±)-Furodysin and (±)-Furodysinin

Hiroshi HIROTA,* Masafumi KITANO, Ken-ichi KOMATSUBARA, and Takeyoshi TAKAHASHI
Department of Chemistry, Faculty of Science, The University of Tokyo,
Hongo, Bunkyo-ku, Tokyo 113

Furodysin and furodysinin, marine origin furanosesquiterpenes having a unique carbocyclic ring system, have been first synthesized as racemic forms from a cis-decalone derivative.

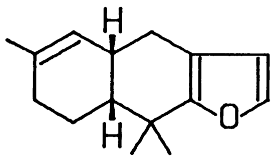
Furodysin (1) and furodysinin (2) are furanosesquiterpenes first isolated from a species of the sponge genus Dysidea in 1978.1) These compounds possess a unique carbocyclic ring system, and would be obtained biogenetically via a skeletal rearrangement of a precursor such as 3, which was also isolated from the sponge D. herbacea.2) In this paper we report the first and short-steps total synthesis of these two compounds (1 and 2).

There have already been known various methods to construct a furan ring. We planned to synthesize these compounds (1 and 2) from a common intermediate such as 4, to which one of these synthetic methods for a furan ring being applied.3) Treatment of a racemic cis-decalone derivative (5), which was prepared stereospecifically via anionic oxy-Cope rearrangement of a bicyclo[2.2.2]octene derivative using a modified procedure from a literature,4) with methyl iodide and potassium t-butoxide in t-butyl alcohol and benzene afforded the objective gem-dimethyl compound (4) regioselectively in 78% yield.5)

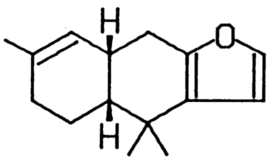
For the synthesis of furodysin (1), the ketone (4) was treated with lithium diisopropylamide (LDA) followed by ethyl bromoacetate to afford keto ester (6; IR: 1735 and 1715 cm^{-1}) in 83% yield as a diastereomeric mixture.6) After hydrolysis of ester (6) with potassium hydroxide in methanol (80% yield), the resulting keto acid was heated with sodium acetate and acetic anhydride to afford unsaturated lactone (7; IR: 1760 and 1655 cm^{-1}) in 83% yield. Racemic furodysin (1) was obtained by the treatment of the lactone (7) with diisobutylaluminum hydride (DIBAL) in THF followed by acidification in 57% yield.3)

On the other hand, the ketone (4) was treated with LDA followed by MoOPH7) to afford a diastereomeric mixture of hydroxy ketone (8; IR: 3500 and 1715 cm^{-1}) in 69% yield, for the synthesis of furodysinin (2). After protection (84% yield) of the hydroxyl group of 8, the methoxymethoxy ketone was treated with lithium enolate of t-butyl acetate to afford 9 as a mixture of four diastereomeric isomers in 97% yield. Treatment of 9 with p-toluenesulfonic acid in benzene afforded dihydroxy acid (10) in 69% yield. When 10 was refluxed with sodium acetate and acetic anhydride followed by DIBAL as the same procedures mentioned above,3) racemic furodysinin (2) was obtained in 55% yield.

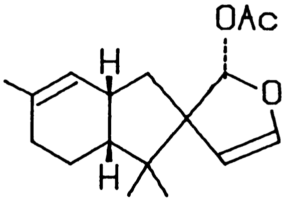
Spectral data of the synthetic **1** and **2** were identical with those of natural ones.1,8) Thus, racemic furodysin and furodysinin have been first synthesized.



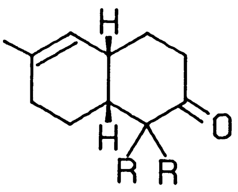
1



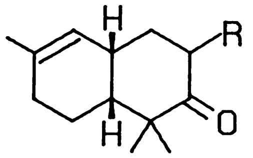
2



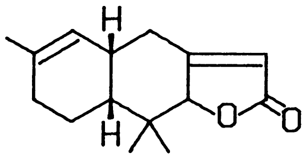
3



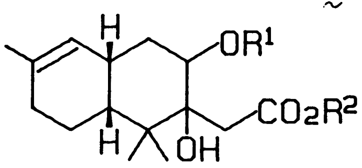
4 R=Me
5 R=H



6 R=CH_2CO_2Et
8 R=OH



7



9 R^1=MOM, R^2=t-Bu
10 R^1=R^2=H

References

1) R. Kazlauskas, P. T. Murphy, R. J. Wells, J. J. Daly, and P. Schönholzer, Tetrahedron Lett., 1978, 4951.

2) R. Kazlauskas, P. T. Murphy, and R. J. Wells, Tetrahedron Lett., 1978, 4949; R. W. Dunlop, R. Kazlauskas, G. March, P. T. Murphy, and R. J. Wells, Aust. J. Chem., 35, 95 (1982).

3) H. Minato and T. Nagasaki, J. Chem. Soc., C, 1966, 377, 1866; 1968, 621.

4) R. P. Gregson and R. N. Mirrington, Aust. J. Chem., 29, 2037 (1976); S. Ranganathan, D. Ranganathan, and A. K. Mehrotra, Synthesis, 1977, 289.

5) The spectral data for all the synthetic compounds were in accord with the structures assigned, and only selected data are cited. **1**: mp 50 °C, IR (KBr) 1640, 1155, 1040, and 895 cm^{-1}; ^{1}H-NMR (CCl_4) δ 1.23 (6H, s), 1.61 (3H, s), 5.50 (1H, d, J=6 Hz), 5.91 (1H, d, J=2 Hz), and 7.05 (1H, d, J=2 Hz); ^{13}C-NMR ($CDCl_3$) δ 19.6, 23.2, 23.8, 27.4, 30.8, 31.7, 31.8, 34.6, 45.8, 109.8, 113.0, 126.5, 133.1, 140.4, and 156.8; $C_{15}H_{20}O$ (m/z 216.1521). **2**: mp 37-40 °C, IR (KBr) 1635, 1200, 1070, 1060, and 900 cm^{-1}; ^{1}H-NMR (CCl_4) δ 1.18 (6H, s), 1.63 (3H, br s), 2.20 (1H, dd, J=17.5 and 12.5 Hz), 2.67 (1H, dd, J=17.5 and 5.5 Hz), 5.55 (1H, br d, J=6 Hz), 6.05 (1H, d, J=2 HZ), and 7.05 (1H, br s); ^{13}C-NMR ($CDCl_3$) δ 19.4, 23.2, 26.3, 27.7, 31.3, 31.8, 32.9, 33.2, 44.7, 108.2, 124.5, 126.5, 133.6, 140.4, and 147.5; $C_{15}H_{20}O$ (m/z 216.1499). **4**: oil, IR (neat) 1715 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.03 (3H, s), 1.30 (3H, s), 1.63 (3H, br s), and 5.36 (1H, br s); $C_{13}H_{20}O$ (m/z 192.1516).

6) Following reactions were run without purification of diastereomers.

7) Complex of MoO_5•pyridine•HMPA; E. Vedejs, D. A. Engler, and J. E. Telschow, J. Org. Chem., 43, 188 (1978).

8) J. Hellou, R. J. Andersen, and J. E. Thompson, Tetrahedron, 38, 1875 (1982).

(Received August 6, 1987)