ENANTIOSELECTIVE SYNTHESIS OF (+)-ACETYLPHOMALACTONE FROM 2-FURYLCARBINOLS

Tetsuji Kametani,[1] Yoko Tatsuzaki, Masayoshi Tsubuki, and Toshio Honda*

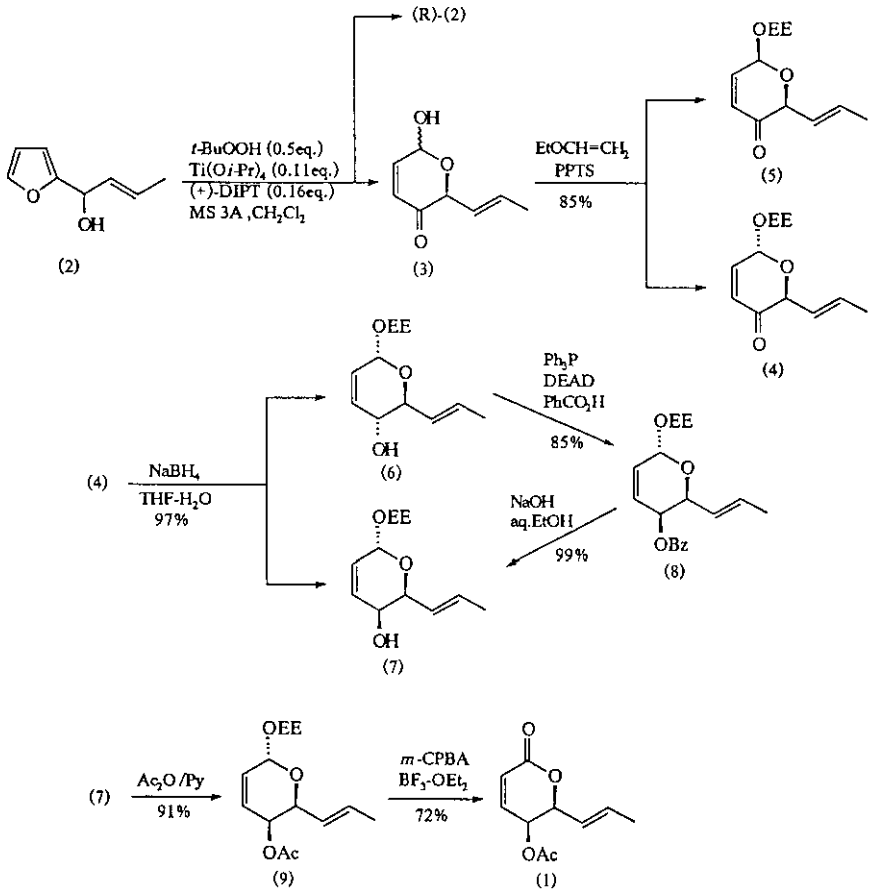
Institute of Medicinal Chemistry, Hoshi University, Ebara 2-4-41, Shinagawa-ku, Tokyo 142, Japan

Abstract——— A facile synthesis of (+)-acetylphomalactone (1) has been developed in seven steps employing the kinetic resolution of the racemic secondary furylcarbinol (2) as a key reaction.

Furylcarbinols have been widely employing as versatile synthons in organic synthesis.[2] Extension of the scope of furylcarbinols as suitable building blocks relies on the development of general methods for the synthesis of optically active furylcarbinols.[3] As a part of our continuing work on the synthesis of physiologically active compounds using furylcarbinols[3ab,4] we here report the enantioselective synthesis of (+)-acetylphomalactone(1),[5] an antimicrobial metabolite from Aspergillus caespitosus. The strategy is based on our previously reported method[3a] involving the kinetic resolution of secondary 2-furylcarbinols under the Sharpless oxidation conditions.[6] The oxidation of (2)[3a] with tert-butyl hydroperoxide, titanium tetra-isopropoxide,and L-(+)-diisopropyl tartrate in dichloromethane in the presence of molecular sieves 3A at -30 °C for 6 h gave the pyranone (3)[7] together with (R)-(2). Compound (3) was converted into (+)-acetylphomalactone (1) as follows. Protection of the lactol(3) with ethyl vinyl ether gave the α - and β -ethoxyethyl ethers (4)[8] and (5) in 72 % and 13% yields, respectively. The ketone (4) was reduced with sodium borohydride to afford the alcohols (6) and (7) in 94 % and 3 % yields, respectively. Conversion of (6) into (7) was carried out by Mitsunobu reaction[9] of (6), followed by hydrolysis of the corresponding benzoate (8)in 84 % yield.[10] Finally, acetylation of (7) provided the acetate (9)(91 %), which on oxidation[11] with m-chloro-perbenzoic acid and boron trifluoride etherate furnished (+)-acetylphomalactone,

mp 53.2 - 54.0 °C, [α]$_D^{23}$ +306.0°(c 0.89, MeOH)[lit.,[5] mp 52.0 - 54.0 °C, [α]$_D$ +311.8°(c 1.02, MeOH)] in 72 % yield.

In summary, we have described a facile enantioselective synthesis of (+)-acetylphomalactone employing the kinetic resolution of the 2-furylcarbinol, and this strategy would be applicable to the synthesis of various types of natural products in optically active forms.



REFERENCES AND NOTES

1 Deceased on October 11th, 1988.

2 For a review, see: B. Lipshutz, Chem. Rev., 1986,86, 795.

3 (a) T.Kametani, M.Tsubuki, Y.Tatsuzaki, and T.Honda, Heterocycles, 1988, 27, 2107; (b) T. Kametani, M. Tsubuki, and T. Honda, Chem. Pharm. Bull., 1988, 36, 3706; (c) P. G. Sammes and D. Thetford, J. Chem. Soc., Perkin Trans. 1, 1988,111; (d) D.G.Drueckhammer, C.F.Barbas III , K.Nozaki, and C. -H. Wong,J. Org. Chem., 1988, 53, 1607; (e) Y. Kobayashi, M. Kusakabe, Y. Kitano, and F. Sato, J. Org. Chem., 1988, 53, 1586;(f) S. F. Martin and D. E. Guinn, J. Org. Chem., 1987, 52, 5588 ;(g) S. F. Martin and P.W.Zinke, J. Am. Chem. Soc., 1989, 111, 2311 and references cited therein.

4 T. Kametani, M. Kigawa, M. Tsubuki, and T. Honda, J. Chem. Soc.,Perkin Trans.1, 1988, 1503; T. Kametani, M. Tsubuki, K. Higurashi, and T. Honda, J. Org. Chem., 1986, 51, 2932.

5 For an isolation of (1), see: S. Mizuba, K. Lee, and J. Jiu, Can. J. Microbial., 1975, 21, 1781; for synthesis of (1), see: T. Murayama, T. Sugiyama, and K.Yamashita, Agric. Biol. Chem., 1987,51, 2055; S. Lesage and A. S. Perlin, Can. J. Chem., 1978, 56, 2889.

6 V. S. Martin, S. S. Woodard, T. Katsuki, Y. Yamada, M. Ikeda, and K. B. Sharpless, J. Am. Chem. Soc., 1981, 103, 6239; Y. Gao, R. M. Hanson, J. M. Klunder, S. Y. Ko, H. Masamune, and K. B. Sharpless, J. Am. Chem. Soc., 1987, 109, 5765.

7 All new compounds exhibited satisfactory analytical and spectral data.

8 The mixture of diastereoisomeric pyranones at the acetal carbon of the ethoxyethyl groups was used without separation in the following reactions since the ethoxyethyl group was removed in the later step of the synthesis.

9 O. Mitsunobu, Synthesis, 1981, 1.

10 Mitsunobu reaction of (6) with triphenylphosphine, diethyl azodicarboxylate, and acetic acid resulted in a mixture of (6) and the desired acetate (9).

11 P. Jarglis and F. W. Lichtenthaler, Tetrahedron Lett., 1982, 23, 3781.

Received, 19th April, 1989