CHEMISTRY LETTERS, pp. 493-494, 1977. Published by the Chemical Society of Japan

A SYNTHESIS OF β-VETIVONE BY BASE-CATALYZED SPIROANNELATION OF PHENOLIC TOSYLATE

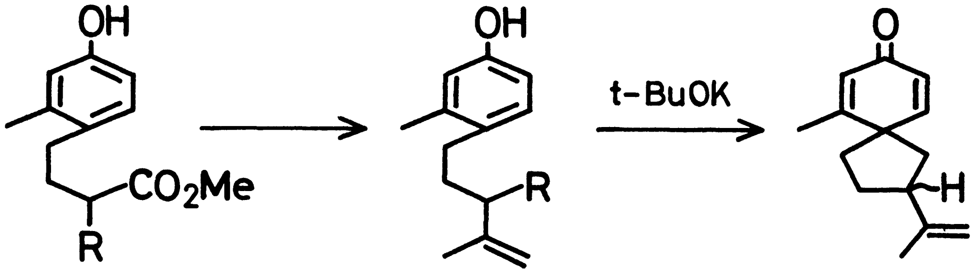
Kenji UNEYAMA, Kaoru OKAMOTO, and Sigeru TORII*

Department of Industrial Chemistry, School of Engineering, Okayama University, Okayama 700

β-Vetivone 8 and C_{10}-epimer were synthesized by base-catalyzed spiroannelation of phenolic tosylate 5.

The discovery of the novel construction of spiro[4.5]deca-1,4-dien-3-one *via* base-catalyzed intramolecular alkylation of 4-(4-hydroxyphenyl)butyl brosylate1) has extensively stimulated the preparation of spiro[n.5]dienones2). However, the spiroannelation has not been applied for β-vetivone synthesis presumably because favorable design of the side chain attached to the phenol ring has not been realized. Here, we describe a novel synthesis of β-vetivone3) and its epimer including a versatile approach to the spirodienones.

Thus, phenolic carboxylate 14), 5) was treated with lithium diisopropylamide in THF-HMPA (12:1) at -70° followed by the addition of dry acetone at the temperature, providing 2 in 86% yield.



1 R = H

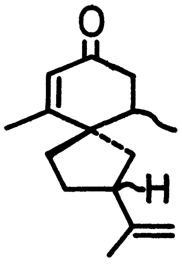
2 R = $C(OH)Me_2$

3 R = CO_2Me

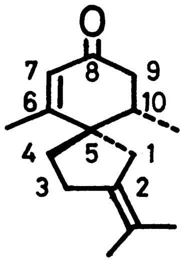
4 R = CH_2OH

5 R = CH_2OTs

6



7



8

The alcohol 2 was then dehydrated to 3 in 80% yield by the action of thionyl chloride in Py-CH_2Cl_2 (3:4) at room temperature for 6 h. Interestingly, the product of 3 was not contaminated with the corresponding α,β-unsaturated ester. The ester 3 was reduced to 4 with LAH in THF and 4 was subsequently tosylated with TsCl in Py affording 5 in 80% yield. The spiroannelation was accomplished by Winstein's method. Thus, the tosylate 5 was refluxed with t-BuOK in dry t-BuOH for 6 h providing 6 in 74% yield. The dienone 6 was methylated with dimethylcopperlithium in dry ether to give 7 6) in 75% yield. Finally, β-vetivone was prepared by isomerization of the terminal double bond of 7 with rhodium chloride 7) in EtOH at 110° for 8 h in 80% yield as an epimeric mixture (1:1) on C_{10}. Pure β-vetivone was separated by HLC and identified spectroscopically (IR and NMR) with authentic data.8)

Acknowledgment We wish to thank Dr. M. Ueda and Mr. I. Akuta, Central Research Lab., Kuraray Co., Ltd. for their generous support of HLC analysis.

References and Note

1) S. Winstein and R. Baird, J. Amer. Chem. Soc., 79, 756 (1957).

2) A. S. Dreiding, Helv. Chim. Acta, 40, 1812 (1957); R. Barner, A. S. Dreiding, and H. Schmid, Chem. & Ind., 1437 (1958); S. Masamune, J. Amer. Chem. Soc., 83, 1009 (1961); S. Dorling and J. Harley-Mason, Chem. & Ind., 1551 (1959); S. Masamune, J. Amer. Chem. Soc., 86, 288 (1964); T. G. Crandall and R. G. Lawton, ibid., 91, 2127 (1969); E. J. Corey, N. N. Girotra, and C. T. Mathew, ibid., 91, 1557 (1969); A. P. Krapcho, Synthesis, 383 (1974) and references cited therein.

3) J. A. Marshall and P. C. Johnson, J. Chem. Soc., Chem. Commun., 391 (1968); Idem, J. Org. Chem., 35, 192 (1970); K. Yamada, H. Nagase, Y. Hayakawa, K. Aoki, and Y. Hirata, Tetrahedron Lett., 4963 (1973); P. M. McCurry, Jr., and R. K. Singh, ibid., 3325 (1973); G. Stork, R. L. Danheiser, and B. Ganem, J. Amer. Chem. Soc., 95, 3414 (1973); G. Bozzato, J. P. Bachmann, and M. Pesaro, J. Chem. Soc., Chem. Commun., 1005 (1974); W. G. Dauben and D. J. Hart, J. Amer. Chem. Soc., 97, 1622 (1975); M. Deighton, C. R. Hughes, and R. Ramage, J. Chem. Soc., Chem. Commun., 662 (1975); G. Büchi, D. Berthet, R. Decorzant, A. Grieder, and A. Hauser, J. Org. Chem., 41, 3209 (1976).

4) The phenol 1 was prepared by demethylation of 4-(4-methoxy-2-methylphenyl)butanoic acid 5) with BBr_3 in CH_2Cl_2 followed by treatment of CH_2N_2 in quantitative yield.

5) R. D. Desai and M. A. Wali, Pro. Indian Acad. Sci., 6A, 144 (1937).

6) D. T. Coxon, K. R. Price, B. Howard, S. F. Osman, E. B. Kalan, and R. M. Zacharius, Tetrahedron Lett., 2921 (1974).

7) J. F. Harrod and A. J. Chalk, J. Amer. Chem. Soc., 86, 1776 (1964); E. Bertele and P. Schudel, Helv. Chim. Acta, 50, 2445 (1967); G. Brieger, T. J. Nestrick, and C. McKenna, J. Org. Chem., 34, 3789 (1969).

8) P. M. McCurry, Jr., R. K. Singh, and S. Link, Tetrahedron Lett., 1155 (1973).

(Received February 21, 1977)