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A SIMPLE STEREOSELECTIVE SYNTHESIS OF (*R*)-RECIFEIOLIDE BY ADOPTION OF (*R*)-METHYLOXIRANE AS A CHIRAL SOURCE

Kiitiro Utimoto, Keiichiro Uchida, Masaaki Yamaya, and Hitosi Nozaki
Department of Industrial Chemistry, Kyoto University, Yoshida, Kyoto, Japan

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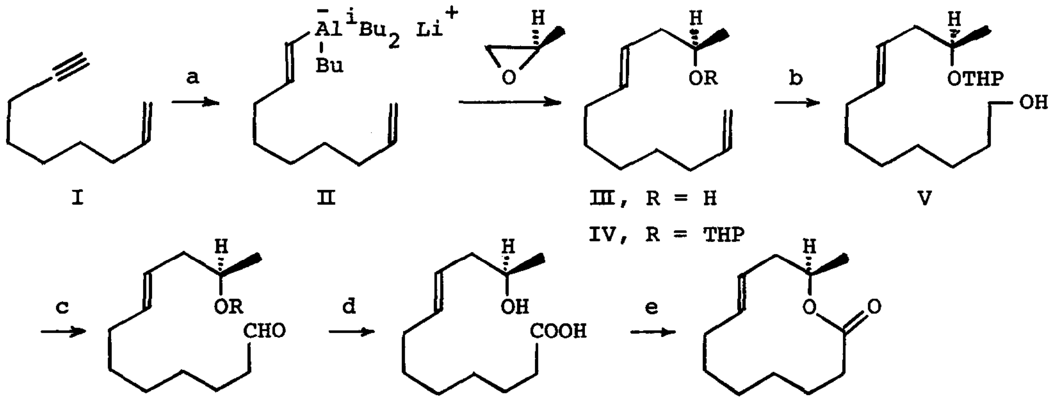
Synthesis of optically pure natural products from easily accessible chiral materials[1] via stereoselective reactions or without disturbance at chiral center has attracted considerable attention since the last decade.[2] This paper describes a simple synthesis of (*R*)-8(*E*)-dodecen-11-olide, (*R*)-recifeiolide,[3,4] along this line from (*R*)-methyloxirane by stereoselective reductive alkenylation of 1-nonen-8-yne via hydralumination.[5]

Successive treatment of 1-nonen-8-yne (I, 7.23 g, 59.2 mmol) with diisobutylaluminum hydride (59.2 mmol, 64 ml of 0.93 M heptane solution; 0°C, 30 min and 50-55°C, 4 hr) and butyllithium (59.2 mmol, 31.5 ml of 1.88 M hexane solution; room temp., 30 min) afforded lithium vinylalanate II[6], which was treated with (*R*)-methyloxirane[7] at room temperature for 24 hr. Hydrolytic work-up of the reaction mixture gave the alcohol III (5.94 g, 32.6 mmol, 55% yield) with over 99% *E* selectivity.[8] Perfect conservation of the chiral center was confirmed by Eu-shifted pmr.[9] After protection of the hydroxy group, hydroboration of the terminal olefin of IV with bis(1,2-dimethylpropyl)borane followed by oxidation with alkaline hydrogen peroxide gave the alcohol V in 74% yield. Oxidation with N-chlorosuccinimide-dimethyl sulfide complex and triethylamine[10] followed by hydrolysis with acetic acid-THF-water gave the hydroxy aldehyde VII (75% yield from V). Oxidation with alkaline silver oxide (VIII,[11] 98%) and lactonization (according to the method of Gerlach[4]) afforded (*R*)-recifeiolide.[12,13]



I

II

III, R = H

IV, R = THP

V

VI, R = THP

VII, R = H

VIII

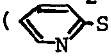
(R)-Recifeiolide

a, (1) $^{i}\text{Bu}_2\text{AlH}$ (2) BuLi

b, (1) $(\text{Me}_2\text{CH-CHMe-})_2\text{BH}$ (2) $\text{H}_2\text{O}_2/\text{NaOH}_{aq}$

c, (1) $\text{NCS-Me}_2\text{S}$ (2) Et_3N

d, Ag_2O

e, (1) ( $\text{S})_2$, Ph_3P (2) AgBF_4

REFERENCES AND NOTES

(1) This kind of materials is called "chiral pool", see ref. 2.

(2) For a summary of recent papers, see D. Seebach and H.-O. Kalinowski, Nachr. Chem. Techn., **24**, 415 (1976).

(3) E. J. Corey, P. Ulrich, and J. M. Fitzpatrick, J. Am. Chem. Soc., **98**, 222 (1976).

(4) H. Gerlach, K. Oertle, and A. Thalmann, Helv. Chim. Acta, **59**, 755 (1976).

(5) Hydralumination of alkynes and synthetic application of alkenylaluminum compounds are discussed: E. Negishi, "New Application of Organometallic Reagents in Organic Synthesis", D. Seyferth ed., Elsevier Scientific Publishing Co., Amsterdam, 1976, p. 93.

(6) Neither isolated nor confirmed by spectroscopy.

(7) $[\alpha]_D^{25} = +11.97°$ (neat) (lit.[7a] $[\alpha]_D^{16} = +12.53°$ (neat)). Enantiomeric excess (97%) could be estimated by Eu(HFC)_3-shifted pmr. (7a) Y. Kumata, J. Furukawa, and T. Fueno, Bull. Chem. Soc. Jpn., **43**, 3920 (1970).

(8) Glc showed more than 99% E selectivity. Cmr [(CDCl_3) δ 22.6, 28.7, 28.8, 29.3, 32.6, 33.8, 42.6, 67.2, 114.3, 125.9, 134.6, 139.1 ppm] also supported homogeneity and the E structure.

(9) $[\alpha]_D^{22} = -1.87°$. Pmr$[\text{Eu(HFC)}_3]$ showed a single doublet for the methyl group whereas two doublets for both R and S isomers were observed with the dl-mixture.

(10) E. J. Corey and C. U. Kim, J. Am. Chem. Soc., **94**, 7586 (1972).

(11) Pmr and ir were identical with the reported ones.

(12) $[\alpha]_D^{28} = +67.5°$ (lit.[12a] $[\alpha]_D^{25} = +73.2°$). Only one doublet (methyl) was observed in Eu(TFC)_3-shifted pmr, whereas two doublets were observed in dl-mixture; (12a) R. F. Vensonder, F. H. Stodola, L. J. Wickerham, J. J. Ellis, and W. K. Rohwedder, Can. J. Chem., **49**, 2029 (1971).

(13) The authors wish to thank The Ministry of Education, Japan, for Grant-in-Aid(110309,203014).