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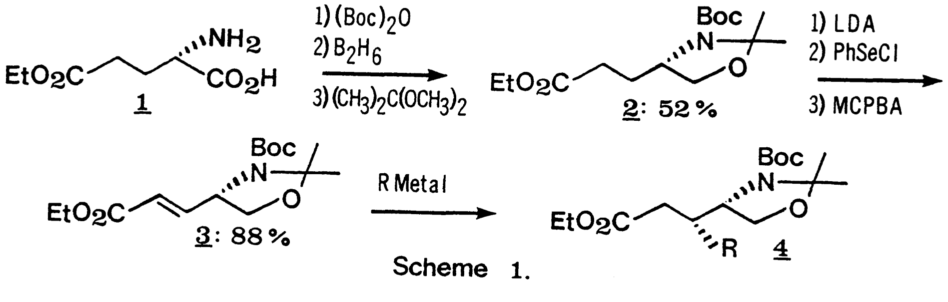
Stereoselective Michael Addition of Organometallic Reagents to α,β-Unsaturated Ester Containing Oxazolidine Ring

Hidemi YODA,* Tsuyoshi SHIRAI, Takao KATAGIRI, Kunihiko TAKABE,*
Kazuhiro KIMATA,† and Ken HOSOYA†
Department of Applied Chemistry, Faculty of Engineering,
Shizuoka University, Hamamatsu 432
†Faculty of Textile Science, Kyoto Institute of Technology, Kyoto 606

Asymmetric conjugate addition of various organometallic reagents to chiral α,β-unsaturated ester derived from L-glutamic acid proceeded cleanly with almost complete diastereoface selection to furnish R-configurated adducts.

Owing to their well documented and important role in the synthesis of biologically active compounds, remarkable utilization of α-amino acids as chiral sources has attracted considerable interest.1) Particularly, chiral synthetic units elaborated from the commercially available proteogenic L-glutamic acid are well known and applied to obtain pharmacologically potent substances.2) During our continual studies to extend the new employment of L-glutamic acid,3) conjugate addition of alkylcuprates to vinylogous ester prepared from serinal was reported to proceed with moderate diastereoselectivity.4) Therefore in this paper we wish to demonstrate that asymmetric Michael addition of suitable organometallic reagents to chiral α,β-unsaturated ester (3) could be accomplished with extremely high diastereoface selection and the absolute configuration was established.

Chiral trans-ester (3;$[\alpha]_D^{25}$+54.3°(c 3.66, $CHCl_3$)) was obtained from γ-ethyl L-glutamate (1) through the successive reactions followed by olefination5) as shown in Scheme 1. Thus, reactions of 3 with a variety of organometallic reagents were examined and the results are listed in Table 1. In the presence of TMSCl,6) the Grignard reagents catalized by CuI as well as



Scheme 1.

the cuprate ones could be added smoothly in satisfied yields. Of particular note is that the conditions under the use of THF as the solvent at low temperatures allow these reactions to provide the products with R configuration exclusively.$^{7)}$

Table 1. Conjugate Addition of Organometallic Reagents to Chiral α,β-Unsaturated Ester (3)

Entry	RM$^{a)}$	Solvent	Temp/°C (Time/h)	Yield of 4 /%$^{b)}$	[R,S]:[S,S]$^{c)}$	$[\alpha]_D$/deg (Temp/°C, c in $CHCl_3$)
1	Bu_2CuLi	THF	-78(1.5)	85(4a)	>99:1	+19.9(24,1.18)
2	Bu_2CuLi	Ether	-78(1.5)	45(4a)	71:29	+19.2(23,0.82)
3	BuMgBr(cat.CuI)	THF	-78--20(4)	55(4a)	>99:1	Entry 1
4	$(CH_3)_2CuLi$	THF	-78(2)	70(4b)	>99:1	+19.8(23,2.18)
5	CH_3MgBr(cat.CuI)	THF	-78(2)	57(4b)	>99:1	Entry 4
6	PrMgBr(cat.CuI)	THF	-78--20(2.5)	62(4c)	>99:1	+22.2(24,1.07)
7	OctMgBr(cat.CuI)	THF	-78--20(2)	52(4d)	87:13	+14.5(25,1.01)

a) 2-5 equiv. of reagents was used in the presence of TMSCl(5 equiv.). b) Isolated yield. c) Determined by ^{13}C NMR and HPLC analyses.

Although the reasonalble explanation for these results is not known at present,$^{4,8)}$ this route would afford new synthetic opportunity for the synthesis of biologically active compounds.

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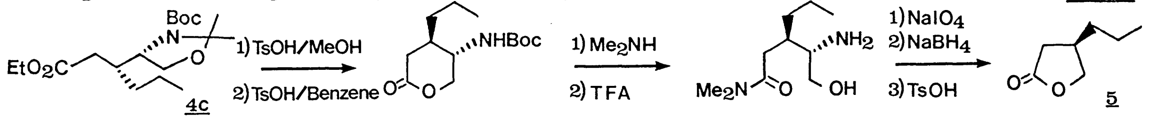
References
1) For excellent reviews see: G. M. Coppola and H. F. Scuster, "Asymmetric Synthesis," John Wiley & Sons, New York (1987); R. M. Williams, "Synthesis of Optically Active α-Amino Acids," Pergamon Press, Oxford (1989).
2) For example see: M. Larcheveque and J. Lalande, Bull. Soc. Chim. Fr., 1987, 116; M. Yanagida, K. Hashimoto, M. Ishida, H. Shinozaki, and H. Shirahama, Tetrahedron Lett., 30, 3799(1989); K. Shimamoto and Y. Ohfune, ibid., 30, 3803(1989); W. Oppolzer and K. Thirring, J. Am. Chem. Soc., 104, 4978(1982).
3) H. Yoda, S. Naito, K. Takabe, N. Tanaka, and K. Hosoya, Tetrahedron Lett., accepted for publication; H. Yoda, S. Naito, K. Takabe, N. Tanaka, and K. Hosoya, Chem. Express, 4, 585(1989).
4) I. Jako, P. Uiber, A. Mann, M. Taddei, and C-G. Wermuth, Tetrahedron Lett., 31, 1011(1990).
5) Cis form of ester (3) was not detected by ^1H and ^{13}C NMR analyses.
6) Y. Horiguchi, M. Komatsu, and I. Kuwajima, Tetrahedron Lett., 30, 7087(1989) and references cited therein.
7) The absolute configuration was determined by the transformation of 4c into known β-propyllactone (5) according to our reported method$^{3)}$: T. Mukaiyama, K. Fujimoto, T. Hirose, and T. Takeda, Chem. Lett., 1980, 635.



8) A. Bernardi, S. Cardini, C. Scolastico, and R. Villa, Tetrahedron, 46, 1987(1990); M. T. Reetz and D. Röhrig, Angew. Chem., Int. Ed. Engl., 28, 1706(1989).

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