

Enantiomerically Pure Compound Synthesis by Asymmetric Glyoxylate–Ene Reaction with Vinylic Sulfides and Selenides catalysed by a Chiral Titanium Complex

Masahiro Terada, Satoru Matsukawa and Koichi Mikami*

Department of Chemical Technology, Tokyo Institute of Technology, Meguro-ku, Tokyo 152, Japan

Asymmetric catalysis of the glyoxylate–ene reaction with vinylic sulfides and selenides by a binaphthol-derived titanium complex provides enantiomerically pure (e.p.) diastereoisomers (*anti* and *Z*) of β -alkyl- α -hydroxy esters.

The synthesis of enantiomerically pure compounds (EPC-synthesis)¹ has received increasing interest over the past decade. The synthetic efficiency of these processes can be maximized by the asymmetric catalysis thereof.² Herein, we report the asymmetric catalysis of the glyoxylate–ene reaction³ with vinylic sulfides^{4,5} and selenides⁶ by binaphthol-derived titanium complex **1**^{2,7} (Scheme 1). This reaction provides enantiomerically pure (e.p.) diastereoisomers (*anti* and *Z*) of functionalized α -hydroxy esters, which are otherwise difficult to obtain.^{7,8}

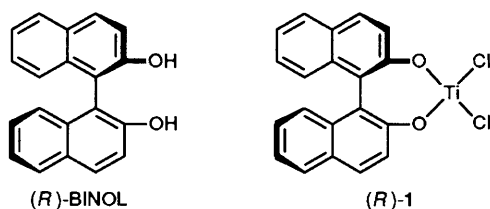
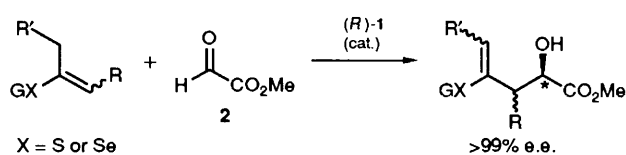
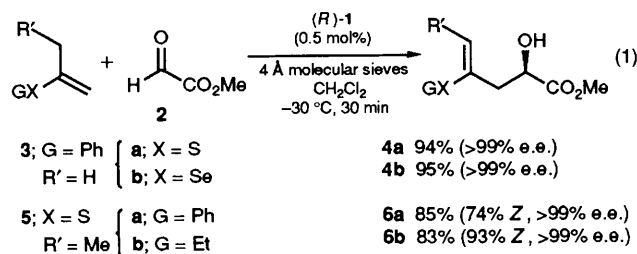
The asymmetric catalytic reaction of glyoxylate **2** was first examined with prop-1-en-2-yl phenyl sulfide **3a** and selenide **3b**, as previously reported with simple olefins⁷ [eqn. (1)]. Both react readily (<30 min) using only 0.5 mol% of chiral catalyst (*R*)-**1** to afford the e.p. (*R*)-hydroxy vinyl sulfide and selenide **4** in good yield.

We next examined, using but-1-en-2-yl sulfides **5**, the diastereocontrol (*E/Z*) over the newly formed double bond. A much higher degree of *Z*-selectivity is obtained with ethyl sulfide **5b** (93% *Z*) than with phenyl sulfide **5a** (74% *Z*).⁹

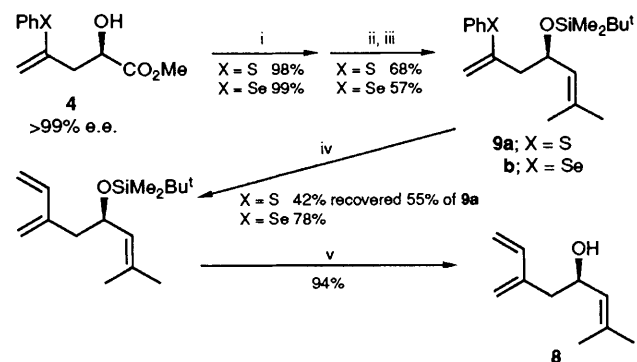
(*E*)-Phenyl sulfides **7** are, in turn, useful for the diastereocontrol over the two new stereogenic centres to provide the e.p. *anti*-diastereoisomer of β -alkyl- α -hydroxy esters (Table 1,

entries 2–4).⁹ The *anti* selectivity increases with the steric bulk of the vinylic substituent R on going from Me to Buⁱ (entries 1–4). However, *Z*-phenyl sulfides exhibit a moderate level of *syn* selectivity (entry 6). Generally, the enantiomeric excesses (e.e.s) of *anti*-diastereoisomers are higher than those of *syn*-isomers (entries 1–6).

By virtue of the vinyl sulfide and selenide products, we accomplished the EPC-synthesis of (*R*)-(-)-ipsdienol **8**, an aggregation pheromone of bark beetles^{10,11} (Scheme 2). Silylation of ene product **4** followed by the sequential treatment with diisobutylaluminium hydride and the Wittig

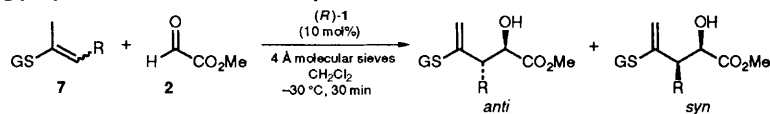


Scheme 1



Scheme 2 Reagents: i, BuⁱMe₂SiOTf–2,6-lutidine; ii, DIBAL-H; iii, [Ph₃PCH(CH₃)₂]⁺I⁻–BuⁿLi; iv, CH₂=CHMgBr–NiCl₂(dmpe) (3 mol%); v, TBAF

Table 1 Asymmetric catalytic glyoxylate–ene reactions with vinyl sulfides **7**^a



Entry	G	Geometry ^b	R	Yield (%)	<i>anti</i> ^c	(% e.e.) ^d	<i>syn</i> ^c	(% e.e.) ^d
1	Ph	>98% <i>E</i>	Me	91	45	(>99)	55	(78)
2	Ph	>98% <i>E</i>	Et	88	81	(>99)	19	(84)
3	Ph	>98% <i>E</i>	Bu ⁿ	90	91	(>99)	9	(>90)
4	Ph	>98% <i>E</i>	Bu ⁱ	94	95	(>99)	5	(>90)
5	Me	78% <i>E</i>	Bu ⁿ	90	48	(>99)	52	(72)
6	Ph	>98% <i>Z</i>	Bu ⁱ	93	12	(>90)	88	(69)

^a All reactions were carried out using 1.0 mmol of glyoxylate **2**, 1.5 mmol of vinyl sulfide **7** and 0.1 mmol of chiral titanium complex **1**.
^b Geometric purity was determined by ¹H NMR analysis. ^c Diastereoisomeric ratio was determined by ¹H NMR analysis. ^d Enantiomeric purity was determined by ¹H NMR analysis after conversion to the corresponding (*R*)- and (*S*)- α -methoxy- α -(trifluoromethyl)phenylacetic acid esters.

reagent furnished the 1,4-dienyl sulfide and selenide **9**. Ni-catalysed coupling reactions^{4a,b,12} with vinyl Grignard reagent and deprotection provided (*R*)-(-)-ipsdienol **8** in e.p. form {[α]_D²¹ -15.6 (c 0.99, MeOH) (lit.^{11a} [α]_D²⁴ -15.3 (c 0.97, MeOH), lit.^{11b} [α]_D²³ -13.2 (c 1, MeOH))}. The coupling reaction proceeds in much higher yield with vinyl selenide **9b** than sulfide **9a**.

Use of vinyl sulfides and selenides extends the scope of the asymmetric catalytic ene reactions with glyoxylates and affords functionally rich synthetically useful ene adducts.

The authors are grateful to Professor Barry B. Snider for his comments and helpful discussions. This research was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Japan, the Asahi-Kasei Award in Synthetic Organic Chemistry, Japan, the Iwaki Scholarship Foundation, and the Joint Studies Program of the Institute for Molecular Science.

Received, 17th November 1992; Com. 2/06111B

References

- 1 For a general discussion and definition of terminology, see: D. Seebach and E. Hungerbühler, *Modern Synthetic Methods*, ed. R. Scheffold, Springer-Verlag, Berlin, 1980, vol. 2, p. 93.
- 2 Reviews on asymmetric catalysis: (a) J. D. Morrison, *Asymmetric Synthesis*, Academic Press, New York, 1984; vol. 3B; (b) R. Noyori and M. Kitamura, in *Modern Synthetic Methods*, ed. R. Scheffold, Springer-Verlag, Berlin, 1989, vol. 5, p. 115; (c) B. Bosnich, *Asymmetric Catalysis*, Martinus Nijhoff Publishers, Dordrecht, 1986; (d) H. B. Kagan, in *Comprehensive Organometallic Chemistry*, ed. G. Wilkinson, Pergamon, Oxford, 1982, vol. 8; (e) K. Narasaka, *Synthesis*, 1991, 1; Y. Hayashi and K. Narasaka, *J. Synth. Org. Chem. Jpn.*, 1990, **48**, 280; (f) K. Mikami, M. Terada, S. Narisawa and T. Nakai, *Synlett.*, 1992, 255; K. Mikami, M. Terada and T. Nakai, *Yukagaku*, 1990, **39**, 837.
- 3 Reviews on ene reactions: H. M. R. Hoffman, *Angew. Chem., Int. Ed. Engl.*, 1969, **8**, 556; B. B. Snider, *Acc. Chem. Res.*, 1980, **13**, 426; *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 2, p. 527; vol. 5, p. 1. K. Mikami and M. Shimizu, *Chem. Rev.*, 1992, **92**, 1021; W. Oppolzer and V. Snieckus, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 476.
- 4 Reviews on vinyl sulfides in organic synthesis: (a) T.-Y. Luh and Z.-J. Ni, *Synthesis*, 1990, 89; (b) T.-Y. Luh, *Acc. Chem. Res.*, 1991, **24**, 257; (c) B. M. Trost and A. C. Lavoie, *J. Am. Chem. Soc.*, 1983, **105**, 5075; (d) C. G. Barret, in *Comprehensive Organic Chemistry*, ed. D. Barton and W. D. Ollis, Pergamon, Oxford, 1979; vol. 3, p. 78.
- 5 For the use of vinyl sulfides as reactive ene components, see: K. Maruoka, Y. Hoshino, S. Shirasaka and H. Yamamoto, *Tetrahedron Lett.*, 1988, **29**, 3967; K. Tanino, H. Shoda, T. Nakamura and I. Kuwajima, *Tetrahedron Lett.*, 1992, **33**, 1337.
- 6 Review: C. Paulmier, *Selenium Reagents and Intermediates in Organic Synthesis*, Pergamon, Oxford, 1986.
- 7 For asymmetric catalytic glyoxylate-ene reaction with simple olefins, see: K. Mikami, M. Terada and T. Nakai, *J. Am. Chem. Soc.*, 1990, **112**, 3949; M. Terada, K. Mikami and T. Nakai, *J. Chem. Soc., Chem. Commun.*, 1990, 1623; K. Mikami, M. Terada and T. Nakai, *J. Am. Chem. Soc.*, 1989, **111**, 1940; K. Mikami and M. Terada, *Tetrahedron*, 1992, **48**, 5671. Unfortunately, the reaction with 1,2-di- and mono-substituted olefins does not proceed.
- 8 Asymmetric aldol reaction catalysed by Sn^{II}-chiral diamine complex to give *syn*- β -hydroxy- α -methyl (thio)esters, see: S. Kobayashi, H. Uchiro, Y. Fujishita, I. Shiina and T. Mukaiyama, *J. Am. Chem. Soc.*, 1991, **113**, 4247; also see: K. Furuta, T. Maruyama and H. Yamamoto, *J. Am. Chem. Soc.*, 1991, **113**, 1041; diastereofacial selective ene reaction of chiral glyoxylate with simple *E/Z* but-2-ene to give *anti*- α -hydroxy- β -methyl ester: J. K. Whitesell, *Acc. Chem. Res.*, 1985, **18**, 280; [2,3]Wittig rearrangement of chiral allylic ethers to give *syn*-(*Z*)- β -alkyl- α -hydroxy esters and amides: K. Mikami, K. Fujimoto, T. Kasuga and T. Nakai, *Tetrahedron Lett.*, 1984, **25**, 6011; O. Takahashi, K. Mikami and T. Nakai, *Chem. Lett.*, 1987, **69**; M. Uchikawa, T. Hanamoto, T. Katsuki and M. Yamaguchi, *Tetrahedron Lett.*, 1986, **27**, 4577.
- 9 These results may reflect the conformational preference of vinyl sulfides: K. Osapy, J. Delhalle and L. Hevesi, *Bull. Soc. Chim. Belg.*, 1986, **95**, 93; see also ref. 4(c).
- 10 For biology activity: A. Bakke, *Naturwissenschaften*, 1976, **63**, 43; J. P. Vite, A. Bakke and P. R. Hughes, *Naturwissenschaften*, 1976, **63**, 550; J. P. Vite, G. Ohloff and R. F. Billings, *Nature*, 1978, **272**, 817; S. A. Teale, F. X. Webster, A. Zhang and G. N. Lanier, *J. Chem. Ecol.*, 1991, **17**, 1145; D. A. Herms, R. A. Haack and B. D. Ayres, *J. Chem. Ecol.*, 1991, **17**, 515; 1705.
- 11 For syntheses of enantiomerically enriched ipsdienol: (a) >96% e.e.: K. Mori and H. Takikawa, *Tetrahedron*, 1991, **47**, 2163; (b) 96% e.e.: H. C. Brown and R. S. Randad, *Tetrahedron*, 1990, **46**, 4463; (c) 91% e.e.: G. Ohloff and W. Giersch, *Helv. Chim. Acta*, 1977, **60**, 1496.
- 12 Ni-catalysed coupling reaction with vinyl sulfides: (a) E. Wenkert, T. W. Ferreira and E. L. Michelotti, *J. Chem. Soc., Chem. Commun.*, 1979, 637; (b) H. Okamura, M. Miura and H. Takei, *Tetrahedron Lett.*, 1979, 43; (c) M. Tiecco, L. Testaferrri, M. Tingoli and E. Wenkert, *Tetrahedron*, 1983, **39**, 2289; (d) M. Tiecco, M. Tingoli and E. Wenkert, *J. Org. Chem.*, 1985, **50**, 3818; (e) V. Fiandanese, G. Marchese, F. Naso and L. Ronzini, *Synthesis*, 1987, 1034; (f) V. Fiandanese, G. Marchese, G. Mascolo, F. Naso and L. Ronzini, *Tetrahedron Lett.*, 1988, **29**, 3708; (g) with vinyl selenides: ref. 12(a); H. Okamura, M. Miura, K. Kosugi and H. Takei, *Tetrahedron Lett.*, 1980, **21**, 87; see also the Ni-catalysed coupling reaction with vinyl and aryl halides: (h) K. Tamao, K. Sumitani, Y. Kiso, M. Zembayashi, A. Fujioka, S. Kodama, I. Nakajima, A. Minato and M. Kumada, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 1958.