

## HETEROSUBSTITUTED ALLYLIC CARBANION BASED STEREOCONTROL. REGIO- AND STEREO-SELECTIVE REACTION OF O AND S SUBSTITUTED ALLYLIC CARBANIONS WITH ALDEHYDES

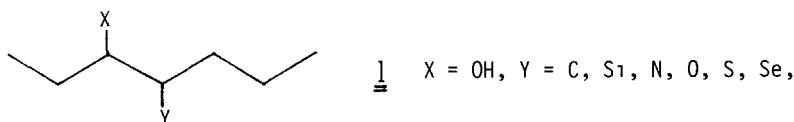
Yoshinori Yamamoto\*, Yoshikazu Saito, and Kazuhiro Maruyama\*

Department of Chemistry, Faculty of Science, Kyoto University

Kyoto 606, Japan

**Summary** Regio- and diastereoselective reaction of oxygen and sulfur substituted allylic carbanions with aldehydes is described. Either threo or erythro isomer can be obtained predominantly or exclusively by merely choosing an additive.

Diastereocontrol between two adjacent substituents in acyclic systems (1) continues to be of a current importance in organic synthesis. Such a stereochemical control between X = OH and Y = C is realized through a number of methods <sup>1</sup>. We now wish to report a convenient method for



diastereocontrol between X = OH and Y = O or between X = OH and Y = S <sup>2</sup>. Our method is based on regio- and stereoselective condensation between heterosubstituted allylic carbanions (2 or 3) and aldehydes under the influence of an additive "M". Our procedure is very simple, either erythro or threo diastereomer can be obtained by merely choosing "M". The results are summarized in the Table.

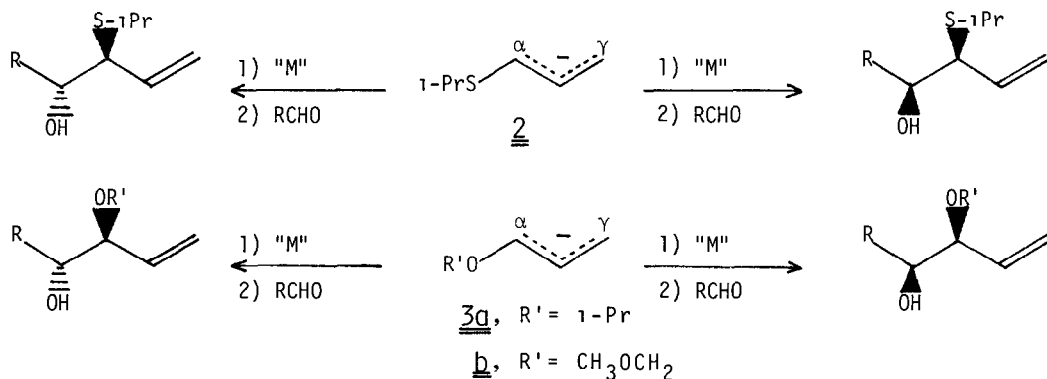
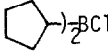
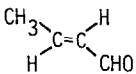


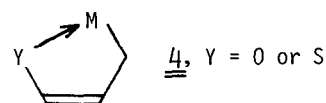
Table Regio- and Stereoselective Coupling through Heterosubstituted Allyl Carbanion <sup>a</sup>

Allyl Carbanion	Aldehyde	Additive "M"	Erythro, %	Threo, %
<u>2</u>	PhCHO	Bu <sub>3</sub> SnCl/BF <sub>3</sub>	90	10
		Ph <sub>3</sub> SnCl/BF <sub>3</sub>	85	15
		Et <sub>2</sub> AlCl	75	25
		Et <sub>3</sub> Al	63	37
		Cp <sub>2</sub> ZrCl <sub>2</sub>	10	90
<u>3a</u>	(CH <sub>3</sub> ) <sub>2</sub> CHCHO	Bu <sub>3</sub> SnCl/BF <sub>3</sub>	~100	-
	PhCHO	Bu <sub>3</sub> SnCl/BF <sub>3</sub>	~100	-
		 BCl	89	11
		EtAlCl <sub>2</sub>	84	16
		Cp <sub>2</sub> ZrCl <sub>2</sub>	27	73
<u>3b</u>	PhCHO	Et <sub>3</sub> Al	92	8
		Cp <sub>2</sub> TiCl <sub>2</sub>	18	82
	CH <sub>3</sub> CH <sub>2</sub> CHO	Et <sub>3</sub> Al	~100	-
	n-BuCHO	Et <sub>3</sub> Al	~100	-
		Et <sub>3</sub> Al	~100	-

<sup>a</sup> All reactions were carried out on a 1 mmol scale as described in the text. An appreciable amount of  $\gamma$ -attacked product, YCH=CHCH<sub>2</sub>CH(OH)R (Y=S or O), was not obtained, and total yields were in a range of 60 - 85 %. The ratio of erythro/threo was determined by GLPC and/or <sup>1</sup>H NMR spectra.<sup>3</sup> Erythro/threo nomenclature is based on Heathcock's convention.

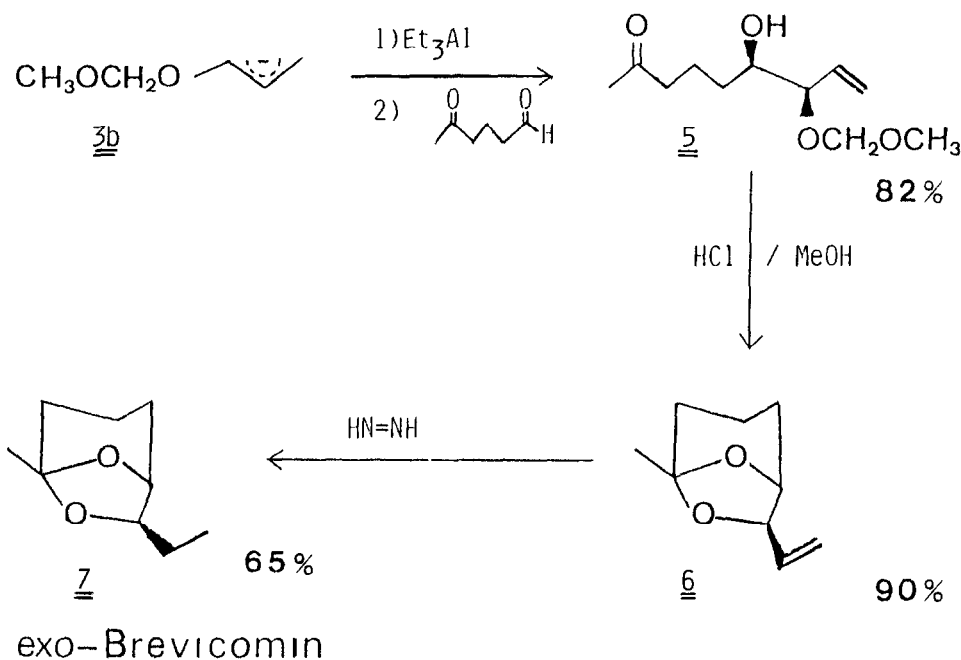
In the reaction of 2, use of Bu<sub>3</sub>SnCl/BF<sub>3</sub><sup>4</sup> as an additive produces erythro isomer either predominantly or exclusively, while use of Cp<sub>2</sub>ZrCl<sub>2</sub><sup>5</sup> gives threo isomer. Other additives such as Et<sub>3</sub>Al<sup>6</sup>, Et<sub>2</sub>AlCl,<sup>7</sup> and R<sub>2</sub>BCl<sup>7</sup> are not effective for stereocontrol, but interestingly they give erythro isomer preferentially. This erythro preference is enhanced in the reaction of 3, boron and aluminum reagents produce erythro isomer with 84 - 100 % stereoselectivity. Such a tendency is in marked contrast with the reaction of carbon<sup>8</sup> or silicon substituted allylic<sup>7</sup> carbanions, which afford threo isomer predominantly under the influence of boron and aluminum reagents. Presumably, "M" attacks the  $\gamma$ -position of 2 or 3, producing an allylic organometallic compound like 4. Oxygen or sulfur atom strongly coordinates to M, so that the double bond is

forced to take cis geometry. Consequently, erythro isomer is produced preferentially. Such a coordination is not expected in  $Y = C$  or  $S$ . In the reaction of 3b, erythro isomer is obtained with very high regio- and stereoselectivity



even under the influence of  $Et_3Al$  which does not produce high stereoselectivity in other reactions as shown in the Table

We next turned our attention to an application of the present method to the stereoselective synthesis of *exo*-brevicomine.<sup>9</sup> Our route is summarized in the following scheme

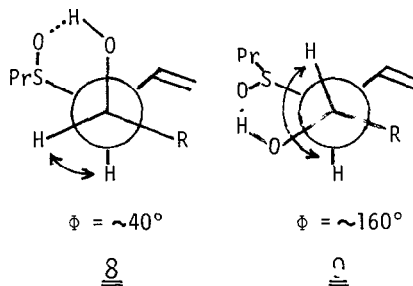


Treatment of MOM-allylic carbanion (3b) with  $Et_3Al$  at  $-78^\circ C$ , followed by the addition of keto-aldehyde produced 5 (erythro/threo = 89/11)<sup>10</sup>. Acid treatment and subsequent reduction gave *exo*-brevicomine (7)

The general procedure is as follows. To a solution of 2<sup>11</sup> in dry ether was added an additive (1 eq), and aldehyde (1 eq) was added after a few minutes. Reaction mixture was allowed to warm to room temperature, and then quenched with aqueous  $NH_4Cl$  solution at  $0^\circ C$ . Similar procedure was used for 3. Generation of 3a is well known reactions,<sup>12</sup> and 3b was generated by the reaction of allyl methoxymethyl ether with  $n-BuLi$  (1 eq) in THF at  $-30^\circ C$

## References and Notes

- 1) For review articles, P. A. Bartlett, *Tetrahedron*, **36**, 3 (1980), Y. Yamamoto and K. Maruyama, *Heterocycles*, **18**, 357 (1982), *J. Syn. Org. Chem. Jpn.*, **40**, 332 (1982)
- 2) Diastereocontrol between X = OH and Y = O, see a) P. G. M. Wuts and S. S. Bigelow, *J. Org. Chem.*, **47**, 2498 (1982), b) R. W. Hoffmann and B. Kemper, *Tetrahedron Lett.*, 845 (1982), c) M. Yamaguchi and T. Mukaiyama, *Chem. Lett.*, 237 (1982), d) T. Mukaiyama and M. Yamaguchi, *ibid.*, 509 (1982), e) M. T. Reetz, R. Steinbach, J. Westermann, R. Urz, B. Wendereth, and R. Peter, *Angew. Chem. Internat. Ed.*, **21**, 135 (1982), f) C. H. Heathcock, J. P. Hagen, E. T. Jarvi, M. C. Pirrung, and S. D. Young, *J. Am. Chem. Soc.*, **103**, 4972 (1981). Diastereocontrol between X = OH and Y = S, see g) R. W. Hoffmann and B. Kemper, *Tetrahedron Lett.*, 4883 (1980). We also learned that Professor H. Yamamoto succeeded stereocontrol between X = OH and Y = O, or between X = OH and Y = S, as mentioned in the 9th round-table conference on organic reactions at Kyoto on August 2, 1982.
- 3) Erythro-, threo-isomer, and  $\gamma$ -adduct of 2 and 3d were separated by GLPC (PEG 6000). The  $\alpha$ -adducts of 2 were converted to the corresponding sulfoxides through NaIO<sub>4</sub> oxidation. The structural determination is based on  $J_{threo}$  <  $J_{erythro}$ , assuming hydrogen bonding as shown in 8 and 9. Stereoisomers from 3h were converted to vinyl epoxides, and then their structures were determined by <sup>1</sup>H NMR spectra, see J.-C. Paladini and J. Chucho, *Bull. Soc. Chim. Fr.*, 187 (1974). Structure determination of isomers from 3d was not unambiguous, but was based on extrapolation from the result of 3h.
- 4) Y. Yamamoto, H. Yatagai, Y. Naruta, and K. Maruyama, *J. Am. Chem. Soc.*, **102**, 7107 (1980).
- 5) Y. Yamamoto and K. Maruyama, *Tetrahedron Lett.*, 2895 (1981)
- 6) Y. Yamamoto, H. Yatagai, and K. Maruyama, *J. Org. Chem.*, **45**, 195 (1980)
- 7) These reagents produced threo isomer either predominantly or exclusively in the reaction of trimethylsilyl substituted allylic carbanion
- 8) Y. Yamamoto, H. Yatagai, and K. Maruyama, *J. Chem. Soc. Chem. Commun.*, 1072 (1980). Et<sub>3</sub>Al reagent gave threo isomer predominantly in the reaction of 2-hydroxybenzimidazole substituted allylic carbanion (ImdO- $\overset{\ominus}{C}H-CH_2$ ), see ref 2c
- 9) When we were nearing completion of our synthesis, related synthesis via allylic boronate derivative was reported (ref 2b).
- 10) The ratio was determined from the ratio of two MeO peaks in NMR spectra. 6;  $\delta$  (CCl<sub>4</sub>) 1.35 (s, 3H), 1.40-2.08 (m, 6H), 4.03 (bs, 1H), 4.24 (d, J=6, 1H), 4.96 (ddd, J=10.0, 2.0, and 1.0, 1H), 5.08 (ddd, J=16.5, 2.0, and 1.0, 1H), 5.69 (ddd, J=16.5, 10.0, and 6.0, 1H). 7;  $\delta$  (CCl<sub>4</sub>) 0.87 (t, J=6.5, 3H), 1.28 (s, 3H), 1.00-2.00 (m, 8H), 3.76 (t, J=6.5, 1H), 3.96 (bs, 1H)
- 11) H. Oshima, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **95**, 7926 (1973)
- 12) See ref 6 and references cited therein



(Received in Japan 14 August 1982)