

Diastereoselective Alkylation Reactions Employing a Camphor-Based Chiral Oxazinone Auxiliary

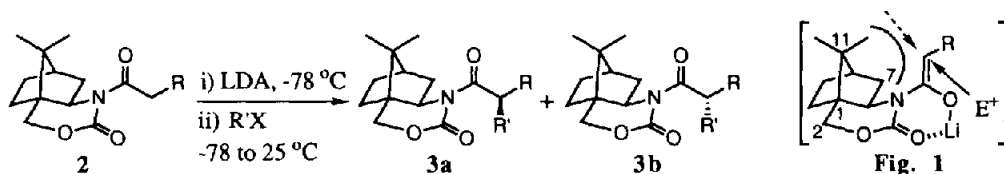
Kyo Han Ahn, * Ankee Lim, and Seungkyu Lee

Department of Chemistry, POSTECH, Pohang 790-600, South Korea

(Received in Japan 4 October 1993)

Abstract: An almost complete π -face selectivity is obtained in asymmetric alkylation reactions of lithium enolates derived from imide **2** which contains a camphor-based chiral oxazinone auxiliary.

Asymmetric reactions employing chiral auxiliaries have been widely used in fundamental carbon-carbon bond forming reactions such as alkylations, aldol condensations, cycloadditions, etc. Recently there has been considerable interest in the development of camphor-based new chiral auxiliaries for both synthetic and mechanistic point of view.^{1a-1g} Camphor-based auxiliaries were known to have good crystallinity, and when the sterically congested camphor moiety was appropriately utilized, a very high level of asymmetric induction was observed. We communicated a new chiral camphorsulfonic acid-derived oxazinone auxiliary and demonstrated indirectly the so-called "chelation-controlled aldol reaction" with it.^{1d} Herein, we wish to report a nearly complete π -face selectivity in alkylation reactions employing the oxazinone auxiliary.^{1h}



The enolization of imide **2** with lithium diisopropylamide (LDA) is believed to generate a *Z*-enolate exclusively, because the corresponding *E*-enolate would receive a severe nonbonded repulsion between the *R* and the camphor moiety. The lithium enolate of **2** comprises two distinct π -faces (C_{α} -re face and C_{α} -si face) because the lithium ion coordinates to both the *N*-acyl and the oxazinone carbonyl oxygens, which was originally demonstrated for oxazoline auxiliaries by Evans and co-workers.² As noted earlier,^{1d} the C_{α} -si face is difficult to access for electrophiles because of the steric hindrance of the syn-11-methyl group and the C-7 methylene group that are locating just above the π -face, which is readily perceivable from Fig. 1. This argument is demonstrated by the nearly complete stereoselectivities in alkylation reactions summarized in Table 1.³ It is notable that most of the alkylation products except for one are crystalline compounds.

Table 1. Stereoselectivity of Alkylation of the Chiral Enolates Derived from Imide **2**

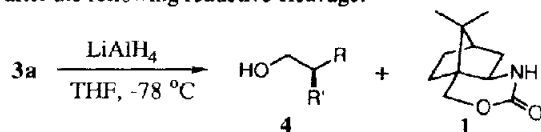
entry	2 R, R'X ^a	3a : 3b ^b	3a		
			[α] _D (c) ^c	mp, °C	% yield ^d
1	Me, PhCH ₂ Br	99.4 : 0.6	-149 (1.1)	90-91	60
2	PhCH ₂ , MeI	99.7 : 0.3	-294 (1.2)	91-92	81
3	Me, CH ₂ =CHCH ₂ I	99.9 : 0.1	-220 (2.2)	79-80	61
4	CH ₂ =CHCH ₂ , MeI	99.9 : 0.1	-248 (0.6)	86-87	49
5	PhCH ₂ , CH ₂ =CHCH ₂ I	99.7 : 0.3	-279 (1.1)	111-112	79
6	CH ₂ =CHCH ₂ , PhCH ₂ Br	99.7 : 0.3	-156 (1.1)	oil	43

^a3.0 molar equiv of R X was used. ^bDetermined by capillary GC analysis. ^cIn CHCl₃ at 23-25 °C.^dYields after column chromatography on SiO₂; Unreacted **2** was recovered in 15-50% yields.

The well-defined π -face structure of the enolate as well as the excellent selectivity foresee a good selectivity in other similar reactions that utilize the oxazinone auxiliary.⁴

REFERENCES AND NOTES

- (a) Yan, T.-H.; Tan, C.-W.; Lee, H.-C.; Lo, H.-C.; Huang, T.-Y. *J. Am. Chem. Soc.* **1993**, *115*, 2613. (b) Yan, T.-H.; Lee, H.-C.; Tan, C.-W. *Tetrahedron Lett.* **1993**, *34*, 3559 and references therein. (c) Tanaka, K.; Uno, H.; Osuga, H.; Suzuki, H. *Tetrahedron: Asymmetry*, **1993**, *4*, 629. (d) Ahn, K. H.; Lee, S.; Lim, A. *J. Org. Chem.* **1992**, *57*, 5065. (e) Banks, M. R.; Blake, A. J.; Cadogan, J. I. G.; Dawson, I. M.; Gosney, I.; Grant, K. J.; Gaur, S.; Hodgson, P. K. G.; Knight, K. S.; Smith, G. W.; Stevenson, D. E. *Tetrahedron*, **1992**, *48*, 7979. (f) Boeckman, Jr. R. K.; Nelson, S. G.; Gaul, M. D. *J. Am. Chem. Soc.* **1992**, *114*, 2258. (g) Bonner, M. P.; Thornton, E. R. *J. Am. Chem. Soc.* **1991**, *113*, 1299. (h) For a recent example of very selective asymmetric alkylation reactions, see: Kimura, K.; Murata, K.; Otsuka, K.; Ishizuka, T.; Haratake, M.; Kunieda, T. *Tetrahedron Lett.* **1991**, *33*, 4461.
- Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737
- The diastereoselectivities are readily determined because both diastereomers are produced from each pair of alkylation experiments (entry 1/2, 3/4, and 5/6). The absolute stereochemistry of the diastereomers was determined by comparing optical rotation of **4** with that of literature value [**4** (R=Me; R'=PhCH₂): [α]_D -11.1 (c 0.83), lit.² value: -11.08 (c 4.6); **4** (R=Me; R'=CH₂CH=CH₂): [α]_D -2.1 (c 1.50), lit. value: -2.3 (c 1.0): Evans, D. A.; Bender, S. L.; Morris, J. *J. Am. Chem. Soc.* **1988**, *110*, 2506], except for **3** (R,R'=PhCH₂, CH₂CH=CH₂, entry 5/6): in this case the assignment was based on the mechanism discussed in the text. The alcohol **4** was obtained in 73-81% yield and the auxiliary **1** was recovered in more than 90% yield after the following reductive cleavage:



- We are grateful to the Korea Science and Engineering Foundation (CBM center) for financial support.