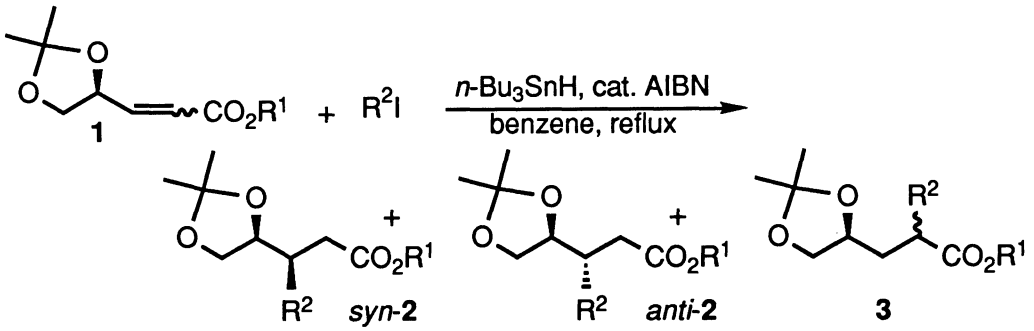
CHEMISTRY LETTERS, pp. 249-250, 1993.

Acyclic 1,2-Asymmetric Induction in Addition Reactions of Alkyl Radicals to Chiral Olefins

Tsutomu MORIKAWA, Yoshiaki WASHIO, Motoo SHIRO,† and Takeo TAGUCHI*
Tokyo College of Pharmacy, 1432-1 Horinouchi, Hachioji, Tokyo 192-03
†Rigaku Corporation, 3-9-12 Matsubara, Akishima, Tokyo 196

Addition reactions of alkyl radicals to chiral (Z)-α,β-unsaturated ester derivatives obtained from (*R*)-2,3-*O*-isopropylidene glyceraldehyde proceeded with high stereoselectivity (1,2-asymmetric induction).

Recently, approaches to acyclic stereochemical control in free-radical reactions have been investigated actively. Effective chirality transfers from chiral auxiliaries have been reported in radical addition reactions of α,β-unsaturated carboxylic acid derivatives.[1] Asymmetric induction by the radical addition reaction to the double bond containing adjacent chiral center [-C*—C=C- + R• → -C*—C*(R)-C•-] would provide a useful method in an acyclic system. Since both enantiomers can be easily prepared, we used 2,3-*O*-isopropylidene glyceraldehyde for asymmetric induction in free-radical promoted C-C bond formation reaction.[2] This paper describes acyclic 1,2-asymmetric induction in the addition reaction of alkyl radicals to chiral α,β-unsaturated ester derivatives (**1**) obtained from (*R*)-2,3-*O*-isopropylidene glyceraldehyde.



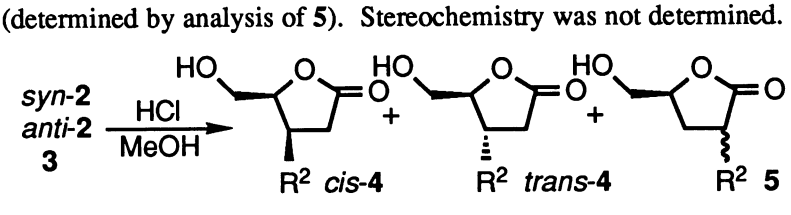
Reactions of chiral α,β-unsaturated ester derivatives **1** with alkyl iodide (R^2I) under free-radical conditions (*n*-Bu_3SnH, cat. AIBN, benzene, reflux) gave β- and α-addition products (**2** and **3**) in 54 - 82% yields as shown in Table 1. The ratios (**2** : **3** and *syn*-**2** : *anti*-**2**) were determined by products analysis (**4** and **5**) of lactonization reactions of addition products (**2** and **3**). β-Attacked products **2** were obtained preferentially in ratios of 2.8 : 1 - 7.4 : 1. The stereochemistry of **2** was determined by correlation with the lactone derivative (**4**), whose stereochemistry was assigned by NOE experiments.[3] In the case of (*E*)-**1** (entries 1 and 2), **2** was obtained as a mixture of stereoisomers (*syn* : *anti* = 1.1 : 1 and 1.3 : 1, respectively). When (*Z*)-**1** was used as the substrate (entries 3 - 8), alkyl radicals (*n*-hexyl, cyclohexyl, and 3-phenylpropyl) added to the β-carbon with high stereoselectivity to give *syn*-**2**.[4] The ratios of *syn*-**2** to *anti*-**2** were 7.9 : 1 - *syn* only. Thus, acyclic 1,2-asymmetric induction was observed in the free-radical promoted C-C bond formation at β-carbon of (*Z*)-**1**.[5]

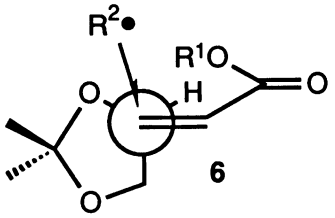
The observed stereoselectivity in the β-attack of radical addition to (*Z*)-**1** can be explained based on a

Table 1. Radical addition reactions of **1** with R^2I[a)]

Entry	Substrate (**1**)	R^2I	Yield of addition products (**2** and **3**)	Ratio[b)] (**2** : **3**[c)])	Ratio[b)] (*syn*-**2** : *anti*-**2**)
1	(*E*)-, R^1=Et	R^2=*n*-C_6H_{13}	55%	3.6 : 1	1.1 : 1
2		R^2=*c*-C_6H_{11}	65%	2.8 : 1	1.3 : 1
3	(*Z*)-, R^1=Me	R^2=*n*-C_6H_{13}	75%	4.9 : 1	8.6 : 1
4		R^2=*c*-C_6H_{11}	82%	3.8 : 1	16.2 : 1
5		R^2=$Ph(CH_2)_3$	54%	7.4 : 1	*syn* only
6	(*Z*)-, R^1=Bn	R^2=*n*-C_6H_{13}	55%	4.8 : 1	9.0 : 1
7		R^2=*c*-C_6H_{11}	79%	3.9 : 1	*syn* only
8		R^2=$Ph(CH_2)_3$	58%	5.6 : 1	14.5 : 1

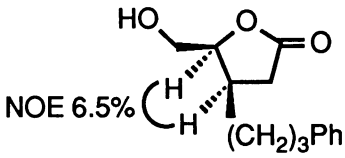
a) A solution of *n*-Bu_3SnH (1.5 mmol) and AIBN (0.3 mmol) in benzene (2.2 mL) was slowly added to a solution of **1** (0.5 mmol) and R^2I (1.5 mmol) in benzene (1.0 mL) over a period of 4-5 h using a syringe pump at reflux temperature, and the reaction mixture was subsequently refluxed for 2 h. b) Ratios were determined by the isolation and/or ^1H NMR of lactone derivatives (**4** and **5**) except for entry 1. Yields of the lactonization: entry 2 (not determined), entry 3 (86%), entry 4 (quant.), entry 5 (88%), entry 6 (83%), entry 7 (95%), and entry 8 (95%), respectively. c) The ratios of the stereoisomers of **3** were 2.3 : 1 - 1 : 1 (determined by analysis of **5**). Stereochemistry was not determined.

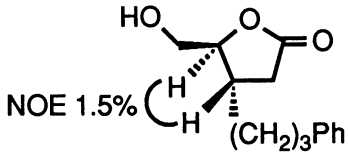


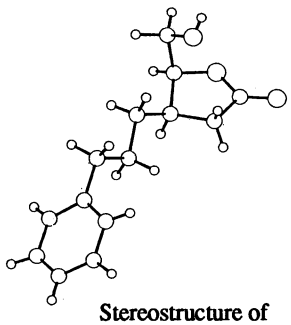


transition state model **6**. Owing to the lack of stereoselectivity with (*E*)-**1**, steric interaction between the dioxolane ring and ester group in (*Z*)-**1** is important for π-facial stereoselectivity at the β-carbon. (*Z*)-Ester group and dioxolane ring take positions so as to minimize steric repulsion due to $A^{1,3}$ strain in the conformer of **6**. The alkyl radical attacks preferentially from the top face without significant steric hindrance from the neighboring dioxolane ring.[6)]

References
1) N. A. Porter, B. Giese, and D. P. Curran, *Acc. Chem. Res.*, **24**, 296 (1991), and references cited therein. 2) J. Jurczak, S. Pikul, and T. Bauer, *Tetrahedron*, **42**, 447 (1986). 3) Crystalline compound (*cis*-**4** obtained from *syn*-**2** in entry 5) was subjected to X-ray crystallographic analysis to confirm its stereostructure.







Stereostructure of *cis*-**4** [R^2=$Ph(CH_2)_3$]

4) *cis*-**4** corresponding to *syn*-**2** was obtained as a major product. In contrast, 1,4-organocuprate addition to 5-hydroxymethyl-2-(5*H*)-furanones derivatives gave *trans*-substituted lactones: J. A. Wurster, L. J. Wilson, G. T. Morin, and D. Liotta, *Tetrahedron Lett.*, **33**, 5689 (1992). 5) The stereoselective addition reaction of hetero atom radicals (silicon and tin) to (*E*)- and (*Z*)-**1**(R^1=Et) was recently reported and the transition state model for the reaction of (*E*)-**1** was proposed: a) W. Smadja, M. Zahouily, M. Journet, and M. Malacria, *Tetrahedron Lett.*, **32**, 3683 (1991); b) W. Smadja, M. Zahouily, and M. Malacria, *ibid.*, **33**, 5511 (1992). However, the stereoselectivity for the reaction of (*Z*)-**1** was not fully clarified and addition reaction of carbon-centered radical was not examined. 6) In the addition reaction of tin-radical to (*E*)-**1**(R^1=Et), the same π-facial stereoselectivity was observed with a modest level of the stereocontrol (2.3 : 1) (see Ref. 5b).

(Received October 19, 1992)