Double Chiral Induction in *ul*-Selective Michael Additions of Metal Enolates of *N*-Bornylideneglycinates to (*E*)-4,5-Dioxy-2-pentenoates. Exclusive *ul,lk*-1,2-Chiral Induction Leading to *l,u*-Michael Adducts

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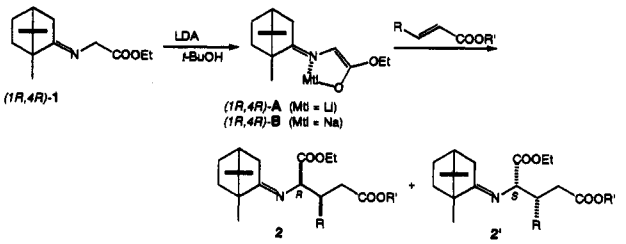
ul-Selective Michael additions of metal enolates of ethyl *N*-[(1*R*,4*R*)-bornylidene]glycinate to optically pure (*E*)-4,5-dioxy-2-pentenoates, such as ethyl (*E*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)propenoate, ethyl (*E*)-3-(1,3-dioxolan-4-yl)propenoate, and ethyl (*E*)-4,5-diacetoxy-2-pentenoate, proceed through *ul,lk*-1,2-induction to provide pure enantiomers of 4-substituted 2-oxopyrrolidine-5-carboxylates as single diastereomers. Exclusive *ul,lk*-1,2-induction is achieved by use of the racemic enolates. Origin of such high stereocontrol is discussed by Kozikowski's antiperiplanar transition model.

Lithium enolates of *N*-arylideneglycinates behave as *N*-lithiated azomethine ylide 1,3-dipoles in reaction with α,β-unsaturated carbonyl compounds.[1,2] There, *endo*-selective cycloadducts are exclusively produced through a frontier orbital- and chelation-controlled rigid transition state. Such high stereochemical integrity based on the rigid transition state has been successfully extended to exclusively *ul*-selective (or *anti*-selective based on product stereochemistry) Michael addition by using sterically hindered imine esters.[3,4] Thus, 3-substituted (*l*)-glutamates are only obtained from lithiated *N*-(2,2-dimethylpropylidene)glycinates and *E*-isomers of α,β-unsaturated esters and ketones. Further employment of the lithium enolates of optically active imine esters, such as *N*-[(1*R*,4*R*)-bornylidene]glycinates, has opened a new entry to an asymmetric version of *ul*-selective Michael additions.[5]

Chart I illustrates a general reaction scheme of exclusively *ul*-selective Michael reaction of the chiral lithium enolate (1*R*,4*R*)-**A**, derived from ethyl *N*-[(1*R*,4*R*)-bornylidene]glycinate (1*R*,4*R*)-**1**, to (*E*)-α,β-unsaturated esters. Two *l*-adducts consisting of 2*R*- and 2*S*-enantiomers, **2** and **2'**, are produced as major and minor products, respectively. Diastereofacial selectivity with respect to the enolate face, *lk*-1,4-chiral induction, is rather independent on the bulk of β-substituent R of acceptor α,β-unsaturated esters.[5b] When methyl esters of α,β-unsaturated carboxylic acids are employed, moderate 2*R*/2*S* ratios are observed: 84:16, 86:14, and 81:19 for R = H, Me, and Ph, respectively. Use of *tert*-butyl esters (R' = *t*-Bu) instead of methyl esters (R' = Me) as acceptor molecules results in better diastereoselectivites which reach to the maximum ratio of 95:5. However, no better selectivities have been observed for β-substituted α,β-unsaturated carbonyl acceptors.[5b] Exclusive diastereofacial selectivity can be achieved only when α,β-unsaturated esters bear an additional α-substituent. Alkylidenemalonates and methacrylates are the cases.[5b]

Chart I



We would like to report here that (*E*)-4,5-dioxy-2-pentenoates, readily available in optically pure forms from naturally occurring D-mannitol, undergo *ul*-selective asymmetric Michael addition to the lithium enolates of *N*-alkylideneglycinates with exclusive *ul,lk*-1,2-chiral induction.

Results and Discussion

One effective approach to attain high chiral induction in organic synthesis is the double chiral induction method. Ethyl (*E*)-3-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]propenoate (**3a**) is an optically active Michael acceptor bearing a heterocyclic chiral auxiliary at the β-position. Although wide use in asymmetric synthesis is familiar, only a limited

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(1) (a) Tsuge, O.; Kanemasa, S.; Yoshioka, M. *J. Org. Chem.* **1988**, *53*, 1384-1391. (b) Kanemasa, S.; Yoshioka, M.; Tsuge, O. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2196-2200. (c) Kanemasa, S.; Uchida, O.; Wada, E.; Yamamoto, H. *Chem. Lett.* **1990**, 105-108. (d) Kanemasa, S.; Yamamoto, H. *Tetrahedron Lett.* **1990**, *31*, 3633-3636. (e) Kanemasa, S.; Yamamoto, H.; Wada, E.; Sakurai, T.; Urushido, K. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2857-2865. (f) Kanemasa, K.; Hayashi, T.; Tanaka, J.; Yamamoto, H.; Sakurai, T. *J. Org. Chem.* **1991**, *56*, 4473-4481.

(2) (a) Barr, D. A.; Grigg, R.; Gunaratne, H. Q. N.; Kemp, J.; McMeekin, P.; Sridharan, V. *Tetrahedron* **1988**, *44*, 557-570. (b) Barr, D. A.; Grigg, R.; Sridharan, V. *Tetrahedron Lett.* **1989**, *30*, 4727-4730. (c) Barr, D. A.; Dorrity, M. J.; Grigg, R.; Malone, J. F.; Montgomery, J. F.; Rajviroongit, S.; Stevenson, P. *Ibid.* **1990**, *31*, 6569-6572. (d) Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L.; Pilati, T. *Tetrahedron Asymm.* **1991**, *2*, 1329-1342. (e) Coulter, T.; Grigg, R.; Malone, J. F.; Sridharan, V. *Tetrahedron Lett.* **1991**, *32*, 5417-5420. (f) Allway, P.; Grigg, R. *Tetrahedron Lett.* **1991**, *32*, 5817-5820.

(3) (a) Kanemasa, S.; Uchida, O.; Wada, E. *J. Org. Chem.* **1990**, *55*, 4411-4417. (b) Yamamoto, H.; Kanemasa, S.; Wada, E. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2739-2743. (c) van der Werf, A.; Kellogg, R. M. *Tetrahedron Lett.* **1991**, *32*, 3727-3730.

(4) According to Heathcock's classification for the Michael addition reaction which occurs at prostereogenic reaction centers, this reaction belongs to the *re,re* or *si,si* (like faces) combination (Oare, D. A.; Heathcock, C. H. Stereochemistry of the Base-Promoted Michael Addition Reaction. In *Topics in Stereochemistry*; Eliel, E. L., Wilen, S. H., Eds.; John Wiley & Sons: New York, 1989; pp 227-407). See also, Seebach, D.; Prelog, V. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 654-660.

(5) (a) Kanemasa, S.; Tatsukawa, A.; Wada, E.; Tsuge, O. *Chem. Lett.* **1989**, 1301-1304. (b) Kanemasa, S.; Tatsukawa, A.; Wada, E. *J. Org. Chem.* **1991**, *56*, 2875-2883.

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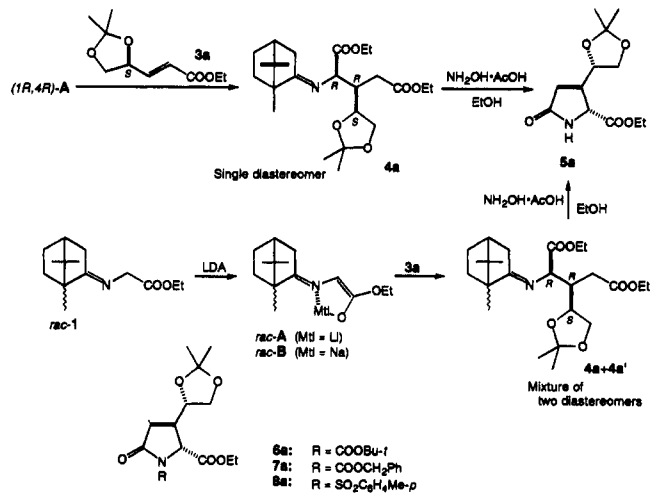
Scheme I



example is known for its use as acceptor molecule in Michael addition of metal enolates.[6,7]

In the present work, chiral α,β-unsaturated ester acceptor **3a** was employed in Michael addition of metal enolates of ethyl *N*-[(1*R*,4*R*)-bornylidene]glycinate [(1*R*,4*R*)-**A**] because combination of (1*R*,4*R*)-**A** and **3a** was expected to form a matching pair according to the previously proposed transition state.[5]

Lithium enolate (1*R*,4*R*)-**A** was generated by treatment of (1*R*,4*R*)-**1** with lithium diisopropylamide (LDA) at −78 °C in tetrahydrofuran (THF) and was allowed to react with **3a** in the presence of *tert*-butyl alcohol[8] at −78 °C for 2 h. The usual aqueous workup, followed by purification by silica gel column chromatography, afforded **4a** as a single diastereomer in 73% yield (Scheme I and Table I, entry 1). Inspection of the crude product mixture by ^{1}H NMR spectrum showed no formation of any other diastereomeric adducts of **4a**, indicating that this Michael addition has taken place in an exclusively diastereoselective manner, probably through a matching combination of both donor and acceptor molecules.

Neither higher reaction temperature nor application of reversible generation procedure affects the selectivity (entry 2). Thus, lithium enolate (1*R*,4*R*)-**A**, generated from (1*R*,4*R*)-**1** and lithium chloride/1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU), reacted with **3a** to give **4a** as a single diastereomer (74%).

The camphor auxiliary was removed from cycloadduct **4a** by treatment with hydroxylamine acetate under reflux in ethanol to give lactam **5a** in a quantitative yield. *N*-Acylation of **5a** afforded **6a** and **7a** and sulfonylation led to **8a**. It was fortunate that recrystallization of **8a** from diethyl ether–hexane gave fine single crystals, one of which was submitted to a single crystal X-ray analysis. Its absolute configuration was determined to be 2*R*,3*R* stereochemistry, indicating that Michael addition of (1*R*,4*R*)-**A** to **3a** has exclusively proceeded in a *ul*-selective manner with *lk*-1,2-chiral induction, a combination between the *re*-face of (1*R*,4*R*)-**A** and the *si*-face of **3a**.

When racemic imine *rac*-**1** was used instead of optical pure (1*R*,4*R*)-**1** in reaction with an equimolar amount of optically active acceptor **3a**, an inseparable 75:25 mixture of two diastereomers **4a** and **4a'** was obtained (entry 3). Major isomer **4a** is identical with the product obtained as a single diastereomer in the aforementioned double chiral induction. Removal of the camphor chiral auxiliary from the mixture of **4a** and **4a'** by treatment with hydroxylamine acetate gave optically pure **5a** as single product, indicating that the two diastereomers **4a** and **4a'** have all the same absolute configurations but that of the camphor auxiliary. It is clear at this stage that the diastereofaces selected in the reaction were only the *re*-face of *rac*-**A** and *si*-face of **3a**, just as observed above between optically pure (1*R*,4*R*)-**A** with **3a**. As a result, chirality of the camphor auxiliary of enolate *rac*-**A** did not play a central role in a chiral induction step. In other words, the *si*-face of chiral acceptor **3a** is always open to the attack by either enolate (1*R*,4*R*)-**A** or (1*S*,4*S*)-**A**. Transition state will be discussed below.

In the reaction of *rac*-**A**, the recovered imine **1** (23%) was enriched with (1*S*,4*S*)-**1**.[9] Even when excess of racemic enolate (1*R*,4*R*)-**A** was employed, virtually the same levels of chiral induction as that observed in entry 3 resulted (entries 4 and 5). Monitoring the reaction of entry 3 shows that diastereomer ratio between **4a** and **4a'** is nearly constant during the course of reaction.[10] A conclusion made on this basis is that the observed diastereoselectivity is a kinetic one resulting from the competitive Michael reaction of (1*R*,4*R*)-**A** to that of (1*S*,4*S*)-**A**. Reaction of (1*R*,4*R*)-**A** is approximately 3 times faster than that of (1*S*,4*S*)-**A**.

Generation of sodium enolate *rac*-**B** was successful from imine *rac*-**1** and sodium hydride in THF. Its reaction with **3a** was also exclusively *ul*-selective, the *re*-face of *rac*-**B** and the *si*-face of **3a** being the only faces selected in the reaction (entries 6 and 7).

Neither the *gem*-methyl groups at the 2-position of the dioxolanyl auxiliary nor the dioxolane ring is requisite for exclusive *ul*,*lk*-1,2-chiral induction. For example, single enantiomers **4b**,**c** were produced in reactions of optically pure lithium enolate (1*R*,4*R*)-**A** with ethyl (*E*)-3-[(*S*)-1,3-dioxolan-4-yl]propenoate (**3b**) and ethyl (*E*,*S*)-4,5-diacetoxy-2-pentenoate (**3c**) (Scheme II and entries 8 and 10). Like the reaction of **3a**, reactions using **3b**,**c** are *re*-face selective with respect to (1*R*,4*R*)-**A** and *si*-face selective with respect to **3b**,**c**. A similar reaction of sodium enolate *rac*-**B** with **3b** (or **3c**) gave a 77:23 mixture of two diastereomers **4b** and **4b'** (or a 75:25 mixture of **4c** and **4c'**), indicating that the kind of base employed for enolate generation does not affect the selectivity of reaction again (entries 9 and 11).

Absolute stereochemistry of **4b** was confirmed to be identical to that of **4a** on the basis of the following interconversions: Removal of the camphor auxiliary of **4b**, followed by cyclization, gave **5b** which was then

(6) Diastereoselective Michael addition to **3a**: (a) Matsunaga, H.; Sakamaki, T.; Nagaoka, H.; Yamada, Y. *Tetrahedron Lett.* **1983**, *24*, 3009–3012. (b) Suzuki, T.; Sato, E.; Kamada, S.; Tada, H.; Unno, K.; Kametani, T. *J. Chem. Soc. Perkin Trans. 1* **1986**, 387–391. (c) Dondoni, A.; Pedro, M.; Ordna, J. *Tetrahedron Lett.* **1991**, *32*, 3247–3250.

(7) Diastereoselective cycloaddition to **3a**: (a) Mulzer, J.; Kappert, M.; Huttner, G.; Jibril, I. *Tetrahedron Lett.* **1985**, *26*, 1631–1634. (b) Trost, B. M.; Lynch, J.; Renaut, P.; Steinman, H. *J. Am. Chem. Soc.* **1986**, *108*, 284–291. (c) Trost, B. M.; Mignai, S. M. *Tetrahedron Lett.* **1986**, *27*, 4137–4140. (d) Trost, B. M.; Mignai, S. M.; Nanninga, T. N. *J. Am. Chem. Soc.* **1988**, *110*, 1602–1608. (e) Wee, A. G. H. *J. Chem. Soc. Perkin Trans. 1* **1989**, 1363–1364. (f) Reference 2d.

(8) Influence of alcohol as an additive was previously discussed (see ref 5b).

(9) The recovered imine **1** showed a plus sign of rotation, $[\alpha]^{24}_D$ = 2.16° (*c* = 1.0, $CHCl_3$) and therefore was assigned to be the 1*S*,4*S*-enriched enantiomer of **1** whose rotation in an optically pure form is $[\alpha]^{24}_D$ = −3.21° (*c* = 1.1, $CHCl_3$).

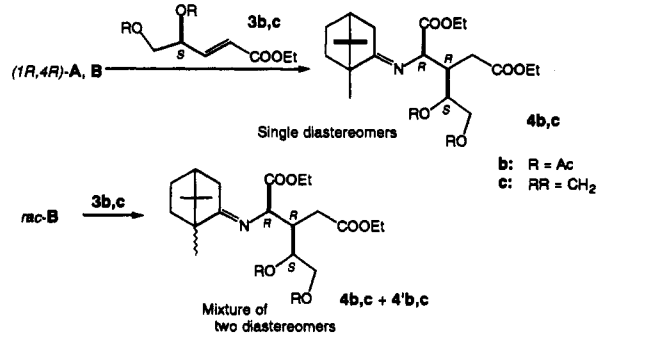
(10) Reaction was monitored by HPLC in every a few minutes from the beginning of reaction. The isomer ratio of **4a** to **4a'** was found to be nearly constant.

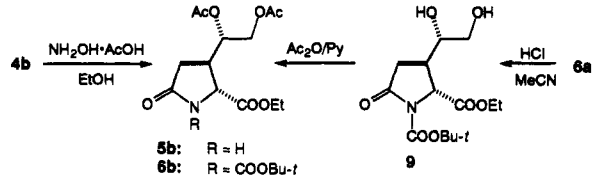
Table I. Absolutely *ul,lk*-1,2-Selective Michael Additions of *N*-Alkylideneglycinate 1 to (*E*)-4,5-Dioxy-2-pentenoates 3a–c[a]

entry	imine 1 (equiv)	base (equiv)	acceptor 3 (equiv)	temp/ °C	time/h	product	yield, %[b]	ratio, 4/4'[c]	recovered 1
1	(1*R*,4*R*)-1 (1)	LDA/*t*-BuOH (1/1)	**3a** (1)	−78	2	**4a**	73	single	
2	(1*R*,4*R*)-1 (2)	LiCl/DBU (1)	**3a** (1)	rt	2	**4a**	74	single	
3	*rac*-1 (1)	LDA/*t*-BuOH (1/1)	**3a** (1)	−78	2	**4a** + **4a'**	74	75:25	23
4	*rac*-1 (1)	LDA/*t*-BuOH (1/1)	**3a** (0.75)	−78	2	**4a** + **4aμ**	61[d]	83:17	
5	*rac*-1 (1)	LDA/*t*-BuOH (1/1)	**3a** (0.5)	−78	2	**4a** + **4a'**	68[d]	83:17	
6	*rac*-1 (1)	NaH (1)	**3a** (1)	0	1	**4a** + **4a'**	58	72:28	16
7	*rac*-1 (1)	NaH (1)	**3a** (0.5)	0	1	**4a** + **4a'**	70[d]	78:22	52
8	(1*R*,4*R*)-1 (1)	LDA/*t*-BuOH (1/1)	**3b** (1)	rt	2	**4b**	57	single	
9	*rac*-1 (1)	NaH (1)	**3b** (0.5)	0	1	**4b** + **4b'**	96[d]	77:23	38
10	(1*R*,4*R*)-1 (1)	NaH (1)	**3c** (1)	0	22	**4c**	68	single	
11	*rac*-1 (1)	NaH (1)	**3c** (0.5)	0	1	**4c** + **4c'**	56[d]	75:25	25

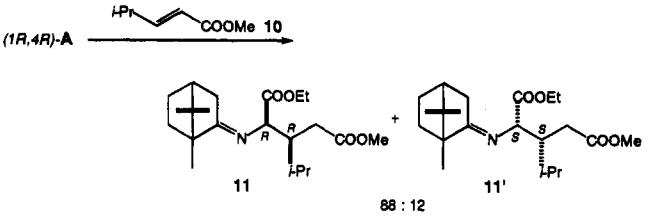
[a] All reactions were performed in THF. [b] Isolated yield. [c] Determined on the basis of ^{1}H NMR spectrum of the crude reaction mixture. [d] Based on 3.

Scheme II





Scheme III

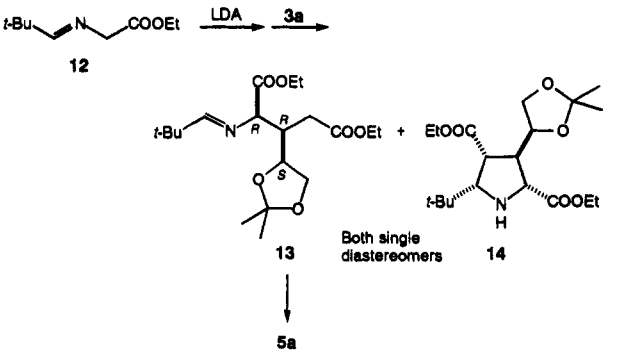


N-acylated producing **6b**. On the other hand, hydrolytic ring cleavage of the dioxolane ring of **6a** and subsequent *O*-acetylation produced the same compound **6b**.

Ester **3a** can be regarded as an acrylate derivative bearing a bulky 1,3-dioxolan-2-yl substituent at the β-position. Bulk of the β-substituent was found not to be important for the exclusive *ul*-selectivity in the Michael addition of enolate (1*R*,4*R*)-**A**. For example, reaction of (1*R*,4*R*)-**A** with ethyl (*E*)-4-methyl-2-pentenoate (**10**), an achiral acrylate bearing a bulky isopropyl substituent at the β-position, at −78 °C in THF was not so high in *lk*-1,4-chiral induction to give an 88:12 mixture of *re*-face adduct **11** and *si*-face adduct **11'** (Scheme III).

Michael addition of an achiral lithium enolate donor to optically pure acceptor **3a** should be also absolutely *si*-face selective with respect to β-carbon of **3a**. The lithium enolate derived from ethyl [(2,2-dimethylpropylidene)-amino]acetate (**12**)[3a] and LDA in the presence of *tert*-butyl alcohol reacted with **3a** at −78 °C for 1 h to give an 82:18 mixture of Michael adduct **13** and cycloadduct **14**, both as single diastereomers, in a combined yield of 49%

Scheme IV



(Scheme IV).[11] They were readily separated from each other by silica gel column chromatography. Absolute structure of **13** was readily determined by its transformation to **5a** through hydrolytic cyclization, while absolute configuration of **14** could not be assigned only on the basis of spectral data. We tentatively propose the 2*R*,3*R*,4*R*,5*S* structure for **14** because it is clear that Michael adduct and cycloadduct, in this case **13** and **14**, are formed competitively through a common adduct enolate intermediate.[3a,12]

The exclusive *ul,lk*-1,2-chiral induction observed in the Michael addition of *rac*-**1** to **3a** may be explained by analogy to the transition states[12] proposed for *endo*-selective 3 + 2 cycloadditions[1] and *anti*-selective Michael additions[3,5] of lithiated *N*-alkylideneglycinates with α,β-unsaturated carbonyl acceptors. The proposed transition state is illustrated in Figure 1.

Coordination of the lithium metal of **A** to the carbonyl oxygen of **3a**, as well as frontier orbital interaction between the reaction centers, makes the transition state rigid. Under such conditions, the sterically less hindered *re*-face of one enantiomer of *rac*-**A**, (1*R*,4*R*)-**A**, combines with the *si*-face of **3a** to form a matching pair **C** leading to **4a**. On the other hand, the *ul*-selective Michael addition of the other enantiomer (1*S*,4*S*)-**A** leads to two mismatching combinations among which the *lk*-1,2-chiral induction **D** under the control of chirality of **3a** became the only pathway providing 2*R*,3*R*-enantiomer **4a'**.

Absolute *ul,lk*-1,2-chiral induction, observed in the double chiral inductive Michael addition of (1*R*,4*R*)-**A** to **3a**, is not surprising. On the other hand, selectivities (*lk*/*ul*) of 1,4-*lk*-induction in Michael additions of *rac*-**A** to **3a**

(11) The reaction in the absence of *tert*-butyl alcohol produced more cycloadduct **14** (13/14 = 63:37).

(12) Kanemasa, S.; Yoshioka, M.; Tsuge, O. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 869–874.

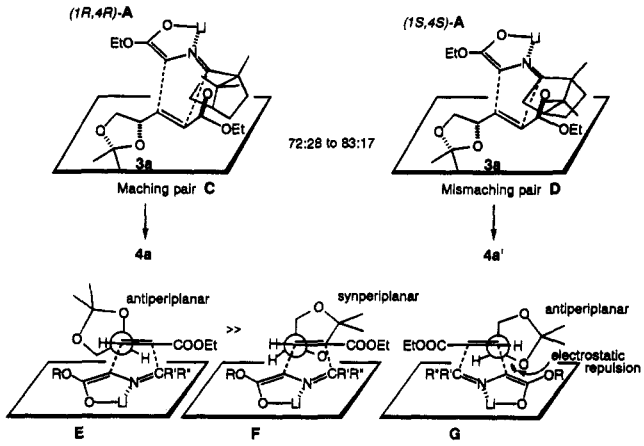


Figure 1. Exclusively *lk*-1,2-inductive Michael additions of lithiated imine esters **A** to ethyl (*E*)-3-(2,2-dimethyl-4-dioxolanyl)propenoate **3a**.

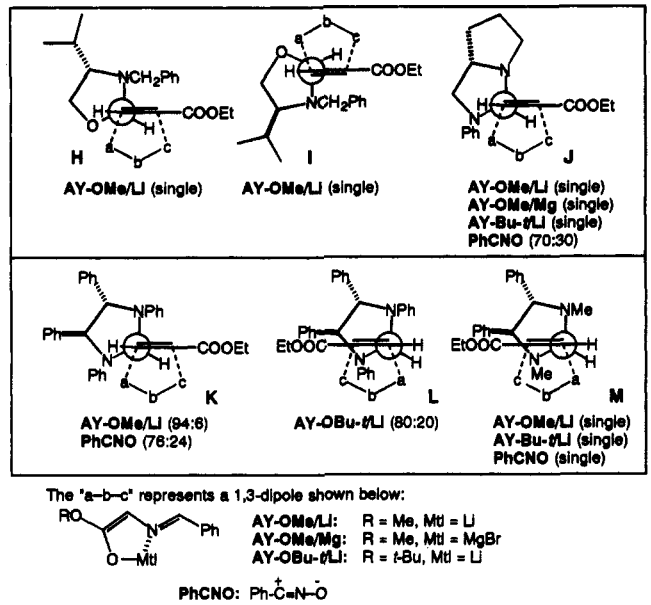


Figure 2. Chiral induction observed in dipolar cycloadditions of *N*-metalated azomethine ylides and benzonitrile oxide to α,β-unsaturated esters bearing a five-membered heterocyclic chiral auxiliary at the β-position.

are ranging from 72:28 to 83:17, comparable to those observed in reactions of lithium enolates **A** with achiral β-substituted methyl acrylates.[5b]

Michael additions of organometallic donors to ethyl (*E,S*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)propenoate (**3a**) are known to be highly *ul*-1,2-selective (or *syn*-selective).[6] So surprising is that the complete reversal of selectivity (*lk*-1,2-selective or *anti*-selective with respect to **3**) was observed in reactions of **3a–c** with metal enolates of *N*-alkylideneglycinates. A few examples are known for *lk*-1,2-selective dipolar cycloadditions of **3** and related derivatives. The reactions recently reported by Annunziata and co-workers are closely related with our results.[2d] Asymmetric cycloadditions of lithiated *N*-benzylideneglycinates to chiral α,β-unsaturated esters bearing a γ-oxygen substituent are the cases. They observed high diastereoselectivities arising from the nucleophilic attack of enolates to the *si,si*-face of an α,β-unsaturated ester similar to **3a**. The observed *si,si*-face selectivities are ranging from 75:25 to 95:5. A number of examples are known for nitrile oxide cycloadditions to γ-oxygen-substituted allylic dipolarophiles,[13] including (*S*)-2,2-dimethyl-4-vinyl-1,3-dioxolane[14] as an analog of **3**. They are also moderately to highly *lk*-1,2-selective. Diels–Alder reaction of **3** is exclusively *si,si*-face selective.[7a]

Exclusive *lk*-1,2-chiral induction of **3a** in our reactions can be explained by a transition state **E** (Figure 1). To account for the *lk*-1,2-induction observed in nitrile oxide cycloadditions to γ-oxygen-substituted allylic dipolarophiles, Kozikowski[15] and Houk[16] have proposed "antiperiplanar model" and "inside alkoxy model". Transition models **E** and **F** correspond to Kozikowski's antiperiplanar model and Houk's inside alkoxy model, respectively. In transition state **E**, the dipolarophile **3a** assumes a thermodynamically more stable antiperiplanar conformation and the nucleophilic enolate carbon attacks the face of **3a** from a side opposite to the ether oxygen. When the dipole attacks from a side opposite to the dioxolanyl methylene moiety, as shown in transition state **G**, the enolate carbon suffers from serious electrostatic repulsion to the ether oxygen. Transition state **F** is also ruled out on the basis of careful analysis of the chiral inductions observed in a series of our dipolar cycloadditions to α,β-unsaturated esters bearing a five-membered heterocyclic chiral auxiliary at the β-position. The previous results[1d–f,17] are summarized in Figure 2.

The sense and degree of chiral induction depend upon either of the following three factors: (1) relative thermodynamic stability among conformations of dipolarophile, (2) electrostatic repulsion working between dipole and dipolarophile, and (3) steric repulsion working between dipole and dipolarophile. Preferred participation of a more stable antiperiplanar conformation, rather than a less stable synperiplanar one, is important (approaches **H–K**). Nucleophilic approach of dipoles to the electron-deficient unsaturated bond of dipolarophiles occurs at a face so as to minimize electrostatic repulsion (approaches **H–J**[1d,e,17]) and steric repulsion (approach **K**[1f,17]). In the cases of approaches **H–J**, ether oxygen and tertiary anilino nitrogen atoms are both less basic than trialkylamine nitrogen.[18] When critical electrostatic or steric repulsion is caused in any approach to the antiperiplanar conformer of dipolarophiles, the less stable synperiplanar conformer participates in the reaction (approaches **L**[1f] and **M**). If the methoxyl group of **AY-OMe/Li** is replaced with a bulky *tert*-butoxyl group in approach **K**, steric repulsion working

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(18) In refs 1d,e and 17, the transition states involving the synperiplanar conformer of methyl (*E*)-3-[(3*R*,7a*S*)-2-phenylperhydropyrrolo[1,2-c]-imidazol-3-yl]propenoate have been proposed. In this report, we would like to revise them with the approaches **J** and **N** involving the antiperiplanar conformer (Figure 2).

between the *tert*-butoxyl and the nearby 4-phenyl group of the chiral auxiliary increases, approach **L** becoming a major path.[1f] The dipolarophile with an *N*-alkyl-substituted chiral auxiliary reacts only in a synperiplanar conformation because any approach in a antiperiplanar one suffers from critical electrostatic repulsion (approach **M**[1f]).

Chiral α,β-unsaturated ester **3a** showed the diastereoselectivity of 80:20 in nitrile oxide.[14c] The exclusive *lk*-1,2-chiral induction of metalated *N*-alkylideneglycinates in reactions with **3a** is consistent with the fact that metalated *N*-alkylideneglycinates are much more selective than nitrile oxides (see approaches **J** and **K**).

Experimental Section

General. Melting points were recorded on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with JASCO IRA-1 and A-702 spectrometers. ^1H and ^{13}C NMR spectra were recorded with Hitachi R-40 (^1H NMR, 90 MHz) and GSX-270 (270 MHz for ^1H NMR and 67.94 MHz for ^{13}C NMR) instruments. Chemical shifts are reported in parts per million downfield (δ) from internal tetramethylsilane. Mass spectra and high resolution mass spectra (HRMS) were recorded with a JEOL-01SG-2 spectrometer operating at an ionization energy of 70 eV. Elemental analyses were performed with a Hitachi 026 CHN analyzer. Optical rotations were recorded with a Horiba SEPA-200 polarimeter. For preparative column chromatography, Wakogel C-200, Wako C-300, and Merck's silica gel 60 were employed. Flash chromatography was performed with an Eyera EF-10 apparatus on a 20 × 180 mm column packed with 0.04–0.063-mm silica gel 60. Gas liquid chromatography (GLC) was accomplished on a Yanaco G-2800 gas chromatograph (Yanagimoto) with an ionization flame detector using a 3 × 2000-mm glass column (SE-30) or a 0.25 × 50000-mm glass capillary column (Silicone GE). Micro vacuum distillation was performed with a Sibata GTO-250R Kugelrohr distilling apparatus.

Ethyl (*E*,*S*)-4,5-Diacetoxy-2-pentenoate (3b). To a solution of **3a** (1 g, 5 mmol) in wet CH_3CN (35 mL containing 2 mL of water) was added at 0 °C 2 M HCl (3.5 mL). The mixture was stirred at rt for 4 h. After treatment with aqueous $NaHCO_3$, the mixture was extracted with EtOAc (15 mL × 2). The combined extracts were dried over $MgSO_4$ and evaporated in vacuo to give ethyl (2*E*,4*S*)-4,5-dihydroxy-2-pentenoate (0.8 g, 100%) as a pale yellow liquid, which was employed for the following reactions without further purification. This compound (0.8 g, 5 mmol) was dissolved in pyridine (10 mL) containing Ac_2O (10 mL). After stirring at rt overnight, the mixture was concentrated in vacuo. The residue was chromatographed on silica gel by using hexane/AcOEt (1:4 v/v) to give **3b** (0.973 g, 80%): colorless liquid; bp 125 °C/1.5 mmHg (bulb-to-bulb); $[\alpha]^{20}_D = 12.9°$ (c = 1.1, EtOH); IR (neat) 2984, 1748, 1665, 1445, 1372, 1221, 1182, 1117, 1044, 980, 866, 716 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3H, t, J = 7.0 Hz, COOEt), 2.07, 2.13 (each 3H, each s, Ac), 4.21 (2H, q, J = 7.0 Hz, COOEt), 4.22 (2H, m, H-5), 5.65 (1H, m, H-4), 6.04 (1H, dd, $J_{2\text{-}3}$ = 15.8 and $J_{2\text{-}4}$ = 1.5 Hz, H-2), 6.84 (1H, dd, $J_{3\text{-}2}$ = 15.8 and $J_{3\text{-}4}$ = 5.1 Hz, H-3); ^{13}C NMR ($CDCl_3$) δ 14.21 (COOEt), 20.76, 20.61 (each Ac), 60.67 (COOEt), 63.94 (C-5), 70.13 (C-4), 123.64 (C-2), 140.77 (C-3), 165.25 (COOEt), 170.16, 169.43 (each Ac); MS m/z (rel inten, %) 244 (M^+, 1), 185 (27), 184 (10), 172 (75), 157 (19), 142 (35), 130 (base peak), 129 (15), 97 (30). Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60%. Found: C, 53.75; H, 6.61%.

Ethyl (*E*)-3-[(*S*)-1,3-Dioxolan-4-yl]acrylate (3c). To a solution of the above obtained ethyl (2*E*,4*S*)-4,5-dihydroxy-2-pentenoate (0.8 g, 5 mmol) in petroleum ether (30 mL) were added paraformaldehyde (0.2 g, 5 mmol) and *p*-TsOH·H_2O (0.014 g). The mixture was refluxed for 20 h. After addition of AcONa (0.014 g), the mixture was dried over $MgSO_4$ and evaporated in vacuo. The residue was chromatographed on silica gel with hexane/AcOEt (1:1 v/v) to give **3c** (0.258 g, 30%): colorless liquid; bp 71 °C/0.4 mmHg (bulb-to-bulb); $[\alpha]^{20}_D = 7.0°$ (c = 1.0, EtOH); IR (neat) 2984, 2876, 1721, 1663, 1468, 1372, 1306, 1269, 1179, 1090, 1034, 982, 939, 868, 718 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (3H, t, J = 7.3 Hz, COOEt), 3.62 (1H, dd, J_{gem} = 8.4 and $J_{5'\text{-}4'}$ = 6.2 Hz, one of H-5 of dioxolanyl), 4.13 (2H, q, J = 7.3 Hz, COOEt), 4.25 (1H, dd, J_{gem} = 8.4 and $J_{5'\text{-}4'}$ = 7.0 Hz, the other of H-5 of dioxolanyl), 4.65 (1H, dddd, $J_{4'\text{-}5'}$ = 7.0, 6.2, $J_{4'\text{-}3}$ = 5.5, and $J_{4'\text{-}2}$ = 1.5 Hz, H-4 of dioxolanyl), 4.98, 5.07 (each 1H, s, H-2 of dioxolanyl), 6.09 (1H, dd, $J_{2\text{-}3}$ = 15.8 and $J_{2\text{-}4'}$ = 1.5 Hz, H-2), 6.87 (1H, dd, $J_{3\text{-}2}$ = 15.8 and $J_{3\text{-}4'}$ = 5.5 Hz, H-3); ^{13}C NMR ($CDCl_3$) δ 14.18 (COOEt), 60.55 (COOEt), 69.18 (C-5 of dioxolanyl), 74.40 (C-4 of dioxolanyl), 95.59 (C-2 of dioxolanyl), 122.45 (C-2), 143.94 (C-3), and 165.74 (COOEt); MS (rel inten, %) 173 ($M + H^+$, 1), 142 (base peak), 127 (20), 97 (22), 84 (42), 69 (67); HRMS calcd for $C_8H_{13}NO_4$ ($M + H^+$) 173.0814, found m/z 173.0836.

Diethyl *N*-[(1*R*,4*R*)-2-Bornylidene]-3-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-(2*R*,3*R*)-glutamate (4a). To a solution of LDA, freshly prepared from *n*-BuLi (1.64 M in hexane; 0.6 mL, 1 mmol) and *N*,*N*-diisopropylamine (0.1 g, 1 mmol) in dry THF (2 mL), were added successively at −78 °C imine (−)-1 (0.237 g, 1 mmol) in THF (1 mL), *t*-BuOH (0.074 g, 1 mmol) in THF (1 mL), and ester **3a** (0.2 g, 1 mmol) in THF (1 mL). After stirring at −78 °C for 2 h, the mixture was quenched with saturated aqueous NH_4Cl and extracted with diethyl ether (3 × 20 mL). The combined extracts were dried over Na_2SO_4 and evaporated in vacuo. The pale yellow residue was purified by silica gel column chromatography (hexane/AcOEt, 4:1 v/v) to give adduct **4a** (0.323 g, 74%): colorless liquid; IR (neat) 2959, 1736, 1372, 1159, 1034, 862 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76, 0.92, 0.94 (each 3H, each s, Me of camphor), 1.25, 1.26 (each 3H, each t, J = 7.0, Hz, COOEt), 1.6–2.0 (6H, m, camphor), 1.32, 1.38 (each 3H, each s, 2-Me of dioxolanyl), 2.34 (1H, m, camphor), 2.56 (1H, dd, J_{gem} = 16.5 and $J_{4\text{-}3}$ = 5.9 Hz, one of H-4), 2.58 (1H, dd, J_{gem} = 16.5 and $J_{4\text{-}3}$ = 5.9 Hz, the other of H-4), 2.81 (1H, quint, J = 5.9 Hz, H-3), 3.76 (1H, dd, J_{gem} = 8.4 and $J_{5'\text{-}4'}$ = 7.3 Hz, one of H-5 of dioxolanyl), 4.03 (1H, dd, J_{gem} = 8.4 and $J_{5'\text{-}4'}$ = 6.6 Hz, the other of H-5 of dioxolanyl), 4.04 (1H, ddd, $J_{4'\text{-}5'}$ = 7.3, 6.6, and $J_{4'\text{-}3}$ = 5.9 Hz, H-4 of dioxolanyl), 4.14 (4H, q, J = 7.0 Hz, 2×COOEt), 4.20 (1H, d, $J_{2\text{-}3}$ = 5.9 Hz, H-2); ^{13}C NMR ($CDCl_3$) δ 11.39, 14.17, 14.21, 19.02, 19.45, 25.30, 26.41, 27.47, 31.88 (camphor, 2-Me of dioxolanyl, and COOEt), 32.64 (C-4), 36.10 (camphor), 41.27 (C-3), 43.92, 47.49, 54.37 (camphor), 60.32, 60.88 (each COOEt), 64.49 (C-2), 67.95 (C-5 of dioxolanyl), 76.17 (C-4 of dioxolanyl), 108.46 (C-2 of dioxolanyl), 171.11, 173.10 (each COOEt), 186.26 (C=N); MS m/z (rel inten, %) 437 (M^+, 4), 422 (11), 336 (15), 264 (9), 238 (17), 237 (base peak), 163 (13), and 43 (13). Anal. Calcd for $C_{24}H_{39}NO_6$: C, 65.88; H, 8.98; N, 3.20%. Found: C, 65.75; H, 8.78; N, 2.90%.

Employment of *rac*-1, instead of (−)-1, afforded an inseparable mixture of **4a** and **4a'**. Configuration of the minor adduct **4a'** was determined on the basis of a partial ^1H NMR spectrum of the mixture with **4a** as well as on the chemical conversion discussed in the text. **4a'**: ^1H NMR ($CDCl_3$) δ 0.75, 0.93, 0.95 (each 3H, each s, camphor), 1.31, 1.37 (each 3H, each s, 2-Me of dioxolanyl), 3.75 (1H, dd, J_{gem} = 8.43, and $J_{5'\text{-}4'}$ = 7.3 Hz, one of H-5 of dioxolanyl). Other signals are overlapping with those of **4a**.

Diethyl *N*-[(1*R*,4*R*)-2-Bornylidene]-3-[(*S*)-1,2-diacetoxyethyl]-(2*R*,3*R*)-glutamate (4b). By a procedure similar to that used for the formation of **4a**, imine (−)-1 (0.237 g, 1 mmol) and ester **3b** (0.244 g, 1 mmol) were converted into Michael adduct **4b** (0.237 g, 49%) as a yellow liquid: IR (neat) 2959, 2878, 1744, 1684, 1447, 1372, 1225, 1182, 1100, 1032, 949, 868 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.78, 0.92, 0.94 (each 3H, each s, Me of camphor), 1.23, 1.27 (each 3H, each t, J = 7.3 hz, COOEt), 1.37 (1H, dd, J = 9.2 and 4.0 Hz, camphor), 1.68 (1H, dt, J = 12.5 and 3.7 Hz, camphor), 1.80–1.96 (4H, m, camphor), 2.04 (6 H, s, OAc), 2.33 (1H, dt, J = 16.9 and 4.0 Hz, camphor), 2.49 (1H, dd, J_{gem} = 16.9 and $J_{4\text{-}3}$ = 7.3 Hz, one of H-4), 2.59 (1H, dd, J_{gem} = 16.9 and $J_{4\text{-}3}$ = 5.1 Hz, the other of H-4), 3.02 (1H, dddd, $J_{3\text{-}4}$ = 7.3, 5.1, $J_{3\text{-}1'}$ = 5.9, and $J_{3\text{-}2}$ = 5.5 Hz, H-3), 4.06 (1H, dd, J_{gem} = 12.1 and $J_{2'\text{-}1}$ = 7.3 Hz, one of H-2 of diacetoxyethyl), 4.09 (1H, d, $J_{2\text{-}3}$ = 5.5 Hz, H-2), 4.14 (4H, q, J = 7.3 Hz, COOEt), 4.33 (1H, dd, J_{gem} = 12.1 and $J_{2'\text{-}1}$ = 3.3 Hz, the other of H-2 of diacetoxyethyl), 5.20 (1H, ddd, $J_{1'\text{-}2'}$ = 7.3, 3.3, and $J_{1'\text{-}3}$ = 5.9 Hz, H-1 of diacetoxyethyl); ^{13}C NMR ($CDCl_3$) δ 11.33, 14.11, 14.20, 19.04, 19.47, 20.78, 20.89, 27.39, 31.96 (camphor, OAc, and COOEt), 32.15 (C-4), 36.26 (camphor), 39.31 (C-3), 43.92, 47.63, 54.50 (camphor), 60.43, 61.12 (each COOEt), 63.49 (C-2), 64.06 (C-2 of diacetoxyethyl), 71.92 (C-1 of diacetoxyethyl), 170.68, 170.74 (each OAc), 170.13, 172.52

(each COOEt), 187.61 (C=N); MS *m/z* (rel inten, %) 482 (M^+ + 1, 13), 481 (M^+, 52), 436 (10), 423 (17), 422 (68), 337 (21), 336 (base peak), 237 (51); HRMS calcd for $C_{25}H_{39}NO_8$ (M) 481.2675, found *m/z* 481.2668.

Diethyl *N*-[(1*R*,4*R*)-2-Bornylidene]-3-[(*S*)-1,3-dioxolan-4-yl]-(2*R*,3*R*)-glutamate (4c). By a procedure similar to that used for the formation of **4a**, imine (−)-1 (0.194 g, 0.82 mmol) and ester **3c** (0.141 g, 0.82 mmol) were converted into Michael adduct **4c** (0.191 g, 57%) as a yellow liquid: IR (neat) 2959, 2876, 2760, 1738, 1684, 1447, 1373, 1248, 1179, 1094, 1030, 943, 860 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77, 0.92, 0.95 (each 3H, each s, Me of camphor), 1.23 (3H, t, *J* = 7.0 Hz, one of COOEt), 1.26 (3H, t, *J* = 7.3 Hz, the other of COOEt), 1.35 (1H, m, camphor), 1.67 (1H, dt, *J* = 11.7 and 3.3 Hz, camphor), 1.83–1.95 (4H, m, camphor), 2.33 (1H, dt, *J* = 16.9 and 3.7 Hz, camphor), 2.56 (1H, dd, J_{gem} = 16.9 and $J_{4\text{-}3}$ = 6.6 Hz, one of H-4), 2.64 (1H, dd, J_{gem} = 16.9 and $J_{4\text{-}3}$ = 6.6 Hz, the other of H-4), 2.82 (1H, dq, $J_{3\text{-}4'}$ = 12.1 and $J_{3\text{-}4}$ = $J_{3\text{-}2}$ = 6.6 Hz, H-3), 3.74 (1H, dd, J_{gem} = 8.4 and $J_{5'\text{-}4'}$ = 6.6 Hz, one of H-5 of dioxolanyl), 3.94 (1H, dd, J_{gem} = 8.4 and $J_{5'\text{-}4'}$ = 6.6 Hz, the other of H-5 of dioxolanyl), 4.10 (1H, dt, $J_{4'\text{-}3}$ = 12.1 and $J_{4'\text{-}5'}$ = 6.6 Hz, H-4 of dioxolanyl), 4.13 (4H, q, *J* = 7.3 Hz, 2×COOEt), 4.15 (1H, d, $J_{2\text{-}3}$ = 6.6 Hz, H-2), 4.80, and 4.98 (each 1H, each s, H-2 of dioxolanyl); ^{13}C NMR ($CDCl_3$) δ 11.39, 14.15, 14.21, 19.01, 19.45, 27.47, 31.92 (camphor and COOEt), 32.74 (C-4), 36.08 (camphor), 41.18 (C-3), 43.90, 47.49, 54.38 (camphor), 60.36, 60.93 (each COOEt), 64.42 (C-2), 68.45 (C-5 of dioxolanyl), 76.34 (C-4 of dioxolanyl), 94.83 (C-2 of dioxolanyl), 170.97, 172.97 (each COOEt), 186.52 (C=N); MS *m/z* (rel inten, %) 409 (M^+, 22), 364 (29), 336 (22), 238 (17), 237 (base peak), 164 (9); HRMS calcd for $C_{22}H_{35}NO_6$ (M) 409.2464, found *m/z* 409.2474.

Ethyl (2*R*,3*R*)-3-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-5-oxopyrrolidine-2-carboxylate (5a). To a solution of **4a** (0.697 g, 1.6 mmol) in EtOH (3 mL) were added NH_2OH·HCl (0.221 g, 3.2 mmol) and NaOAc·$3H_2O$ (0.436 g, 3.2 mmol). The mixture was heated under reflux for 2 h. After evaporation of the solvent, the residue was purified by silica gel column chromatography (hexane/AcOEt, 1:1 v/v) to give **5a** (0.411 g, 100%): pale yellow liquid; $[\alpha]^{20}_D$ = −37.1° (*c* = 1.23, EtOH); IR (neat) 3258, 2986, 2938, 2903, 1705, 1373, 1213, 1061, 856 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (3H, t, *J* = 7.3 Hz, COOEt), 1.44, 1.36 (each 3H, each s, 2-Me of dioxolanyl), 2.43 (1H, dd, J_{gem} = 17.2 and $J_{4\text{-}3}$ = 9.2 Hz, one of H-4), 2.51 (1H, dd, J_{gem} = 17.2 and $J_{4\text{-}3}$ = 6.6 Hz, the other of H-4), 2.70 (1H, dddd, $J_{3\text{-}4}$ = 9.2, 6.6, $J_{3\text{-}2}$ = 5.9, and $J_{3\text{-}4'}$ = 4.8 Hz, H-3), 3.65 (1H, dd, J_{gem} = 8.4 and $J_{5'\text{-}4'}$ = 6.2 Hz, one of H-5 of dioxolanyl), 4.09 (1H, d, $J_{2\text{-}3}$ = 5.9 Hz, H-2), 4.11 (1H, dd, J_{gem} = 8.4 and $J_{5'\text{-}4'}$ = 6.2 Hz, the other of H-5 of dioxolanyl), 4.24 (2H, q, *J* = 7.3 Hz, COOEt), 4.35 (1H, dt, $J_{4'\text{-}5'}$ = 6.2 and $J_{4'\text{-}3}$ = 4.8 Hz, H-4 of dioxolanyl), 6.35 (1H, s, NH); ^{13}C NMR ($CDCl_3$) δ 13.13 (COOEt), 25.36, 24.05 (each 2-Me of dioxolanyl), 30.75 (C-3), 40.93 (C-4), 57.85 (C-2), 61.76 (COOEt), 67.30 (C-5 of dioxolanyl), 75.93 (C-4 of dioxolanyl), 108.81 (C-2 of dioxolanyl), 160.17 (C-5), 176.43 (COOEt); MS *m/z* (rel inten, %) 257 (M^+, 2), 243 (14), 242 (base peak), 200 (16), 199 (64), 184 (74), 169 (53), 168 (13), 155 (11), 154 (23), 126 (15), 102 (10), 101 (91), 84 (9), 72 (9). Anal. Calcd for $C_{12}H_{19}NO_5$: C, 56.02; H, 7.44; N, 5.44%. Found: C, 55.74; H, 7.35; N, 5.01%.

Ethyl (2*R*,3*R*)-3-[(*S*)-1,2-Diacetoxyethyl]-5-oxopyrrolidine-2-carboxylate (5b). By a procedure similar to that used for the formation of **5a**, Michael adduct **4b** (0.237 g, 0.49 mmol) was converted into lactam **5b** (0.148 g, 100%): yellow solid; mp 132.5–134 °C; $[\alpha]^{20}_D$ = −1.38° (*c* = 1.1, EtOH); IR (neat) 3362, 2984, 2922, 1736, 1699, 1437, 1373, 1236, 1122, 1030, 862 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (3H, t, *J* = 7.0 Hz, COOEt), 2.12, 2.07 (each 3H, each s, 2 × OAc), 2.48 (2H, d, $J_{4\text{-}3}$ = 8.4 Hz, H-4), 2.88 (1H, ddt, $J_{3\text{-}4}$ = 8.4, $J_{3\text{-}2}$ = 4.4, and $J_{3\text{-}1'}$ = 4.0 Hz, H-3), 4.10, 4.08 (each 1H, each dd, J_{gem} = 12.1 and $J_{2'\text{-}1'}$ = 6.2 Hz, H-2 of diacetoxyethyl), 4.24 (2H, dq, *J* = 7.0 and 1.1 Hz, COOEt), 4.31 (1H, d, $J_{2\text{-}3}$ = 4.4 Hz, H-2), 5.37 (1H, dt, $J_{1'\text{-}2'}$ = 6.2 and $J_{1'\text{-}3}$ = 4.0 Hz, H-1 of diacetoxyethyl), 6.85 (1H, s, NH); ^{13}C NMR ($CDCl_3$) δ 14.11 (COOEt), 20.85, 20.69 (each Ac), 30.84 (C-3), 39.34 (C-4), 57.55 (C-2), 62.07 (COOEt), 63.51 (C-2 of diacetoxyethyl), 70.78 (C-1 of diacetoxyethyl), 170.48, 170.28 (each Ac), 171.00 (C-5), 176.14 (COOEt); MS *m/z* (rel inten, %) 301 (M^+, 12), 242 (9), 241 (62), 228 (20), 213 (20), 181 (54), 169 (20), 168 (base peak), 153 (11), 126 (32). HRMS calcd for $C_{13}H_{19}NO_7$ (M) 301.1160, found *m/z* 301.1159.

Ethyl (2*R*,3*R*)-*N*-(*tert*-Butoxycarbonyl)-3-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-5-oxopyrrolidine-2-carboxylate (6a). To a suspension of NaH (60% in oil; 0.053 g, 1.32 mmol) in dry THF (2 mL) at 0 °C were added lactam **5a** (0.308 g, 1.2 mmol) and di-*tert*-butyl dicarbonate (0.262 g, 1.2 mmol) in dry THF (4 mL). After being stirred at rt for 12 h, the reaction mixture was worked up according to the usual manner. The crude product was purified by silica gel column chromatography (hexane/AcOEt, 4:1 v/v) to give compound **6a** (0.327 g, 76.3%): colorless liquid; $[\alpha]^{25}_D$ = −14.0° (*c* = 0.53, EtOH); IR (neat) 2984, 2938, 1794, 1717, 1750, 1458, 1372, 1318, 1202, 1155, 1059, 932, 853, 777 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (3H, t, *J* = 7.3 Hz, COOEt), 1.25, 1.09 (each 3H, each s, 2-Me of dioxolanyl), 1.41 (9H, s, *t*-Bu), 1.87 (1H, dddd, $J_{3\text{-}4}$ = 8.4, 4.8, $J_{3\text{-}4'}$ = 5.9, and $J_{3\text{-}2}$ = 3.3 Hz, H-3), 2.32 (1H, dd, J_{gem} = 17.6 and $J_{4\text{-}3}$ = 8.4 Hz, one of H-4), 2.41 (1H, dd, J_{gem} = 17.6 and $J_{4\text{-}3}$ = 4.8 Hz, the other of H-4), 3.23 (1H, dd, J_{gem} = 8.4 and $J_{5'\text{-}4'}$ = 5.9 Hz, one of H-5 of dioxolanyl), 3.48 (1H, dd, J_{gem} = 8.4 and $J_{5'\text{-}4'}$ = 5.9 Hz, the other of H-5 of dioxolanyl), 3.62 (1H, q, $J_{4'\text{-}5'}$ = $J_{4'\text{-}3}$ = 5.9 Hz, H-4 of dioxolanyl), 3.94 (2H, dq, *J* = 7.3 and 0.7 Hz, COOEt), 4.46 (1H, d, $J_{2\text{-}3}$ = 3.3 Hz, H-2); ^{13}C NMR ($CDCl_3$) δ 14.07 (COOEt), 24.80, 26.23 (each 2-Me of dioxolanyl), 27.79 (*t*-Bu), 32.67 (C-3), 37.27 (C-4), 61.63 (COOEt), 61.72 (C-2), 67.18 (C-5 of dioxolanyl), 76.12 (C-4 of dioxolanyl), 83.40 (*t*-Bu), 109.72 (C-2 of dioxolanyl), 148.86 (NCOOBu-*t*), 170.36 (C-5), 171.76 (COOEt); MS *m/z* (rel inten, %) 342 (M^+ − Me, 67), 284 (44), 258 (15), 257 (51), 242 (33), 240 (10), 199 (17), 198 (10), 185 (13), 184 (base peak), 156 (11), 126 (14), 101 (68), 57 (22), 56 (19). Anal. Calcd for $C_{17}H_{27}NO_7$: C, 57.13; H, 7.61; N, 3.92%. Found: C, 56.81; H, 7.51; N, 3.50%.

Ethyl (2*R*,3*R*)-*N*-(*tert*-Butoxycarbonyl)-3-[(*S*)-1,2-diacetoxyethyl]-5-oxopyrrolidine-2-carboxylate (6b). Compound **6** was obtained by either of the following procedures: (1) By a procedure similar to that used for the formation of **6a**, lactam **5b** (0.253 g, 0.84 mmol) was converted into compound **6b** (0.161 g, 47.8%). (2) To a solution of **9** (0.227 g, 0.716 mmol) in pyridine (1.4 mL) at 0 °C was added Ac_2O (1.4 mL). After being stirred at rt for 28 h, the mixture was concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane/AcOEt, 4:1 v/v) to give compound **6b** (0.264 g, 92%): colorless liquid; $[\alpha]^{20}_D$ = 7.9° (*c* = 0.8, EtOH); IR (neat) 2982, 2940, 1796, 1748, 1372, 1316, 1221, 1157, 1046, 945, 851 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (3H, t, *J* = 7.3 Hz, COOEt), 1.50 (9H, s, *t*-Bu), 2.09, 2.07 (each 3H, each s, 2×OAc), 2.50–2.80 (3H, m, H-3 and H-4), 4.10 (1H, dd, J_{gem} = 7.3 and $J_{2'\text{-}1'}$ = 4.4 Hz, one of H-2 of diacetoxyethyl), 4.25 (2H, q, *J* = 7.3 Hz, COOEt), 4.29 (1H, dd, J_{gem} = 7.3 and $J_{2'\text{-}1'}$ = 4.4 Hz, the other of H-2 of diacetoxyethyl), 4.45 (1H, d, $J_{2\text{-}3}$ = 3.7 Hz, H-2), 5.25 (1H, q, $J_{1'\text{-}2'}$ = 4.4 Hz, H-1 of diacetoxyethyl); ^{13}C NMR ($CDCl_3$) δ 14.17 (COOEt), 20.66 (OAc), 27.86 (*t*-Bu), 32.87 (C-3), 35.65 (C-4), 61.65 (COOEt), 62.04 (C-2), 62.89 (C-2 of diacetoxyethyl), 71.29 (C-1 of diacetoxyethyl), 84.01 (*t*-Bu), 148.94 (NCOOBu-*t*), 170.06 (C-5), 170.35, 170.31 (each OAc), 171.61 (COOEt); MS *m/z* (rel inten, %) 386 (M^+ − 15, 1), 301 (34), 272 (17), 241 (33), 228 (15), 181 (19), 169 (11), 168 (base peak), 126 (16), 57 (15). Anal. Calcd for $C_{18}H_{27}NO_9$: C, 53.86; H, 6.78; N, 3.49%. Found: C, 53.62; H, 6.81; N, 3.33%.

Ethyl (2*R*,3*R*)-*N*-(Benzyloxycarbonyl)-3-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-5-oxopyrrolidine-2-carboxylate (7a). To a suspension of NaH (60% in oil, 0.018 g, 0.45 mmol) in dry ether (0.5 mL) were added at 0 °C lactam **5a** (0.105 g, 0.41 mmol) in dry ether (0.5 mL) and benzyloxycarbonyl chloride (0.27 mL, 0.45 mmol) in dry CH_2Cl_2 (1 mL). After being stirred at rt for 24 h, the mixture was worked up according to the usual manner. The crude product was purified by silica gel column chromatography (hexane/AcOEt, 4:1 v/v) to give **7a** (0.048 g, 30%): pale yellow liquid; $[\alpha]^{17}_D$ = −11.53° (*c* = 0.26, EtOH); IR (neat) 2986, 2339, 1797, 1747, 1498, 1456, 1381, 1302, 1203, 1109, 1057, 983, 856, 775, 740, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (3H, t, *J* = 7.3 Hz, COOEt), 1.33, 1.41 (each 3H, each s, 2-Me of dioxolanyl), 2.38 (1H, dddd, $J_{3\text{-}4}$ = 8.8, 4.4, $J_{3\text{-}4'}$ = 5.1, and $J_{3\text{-}2}$ = 3.3 Hz, H-3), 2.63 (1H, dd, J_{gem} = 18.0 and $J_{4\text{-}3}$ = 4.4 Hz, one of H-4), 2.72 (1H, dd, J_{gem} = 18.0 and $J_{4\text{-}3}$ = 8.8 Hz, the other of H-4), 3.66 (1H, dd, $J_{5'\text{-}4'}$ = 8.4 and J_{gem} = 5.5 Hz, one of H-5 of dioxolanyl), 4.24 (1H, dd, $J_{5'\text{-}4'}$ = 11.7 and J_{gem} = 5.5 Hz, the other of H-5 of dioxolanyl), 4.14 (1H, ddd, $J_{4'\text{-}5'}$ = 11.7, 8.4, and $J_{4'\text{-}3}$ = 5.1 Hz, H-4 of dioxolanyl), 4.44 (1H, d, $J_{2\text{-}3}$ = 3.3 Hz, H-2), 5.21,

5.33 (each 1H, each d, J_{gem} = 12.1 Hz, $PhCH_2$), 7.37 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 14.01 (COOEt), 24.79, 26.29 (each 2-Me of dioxolanyl), 32.61 (C-3), 37.68 (C-4), 61.87 (COOEt), 62.00 (C-2), 67.34 (C-5 of dioxolanyl), 68.41 ($PhCH_2$), 76.38 (C-4 of dioxolanyl), 110.10 (C-2 of dioxolanyl), 128.15, 128.46, 128.58, 134.97 (each Ph), 150.78 (NCOO), 170.39 (C-5), 171.90 (COOEt); MS *m/z* (rel inten, %) 391 (M^+, 25), 376 (9), 174 (14), 101 (22), 92 (9), 91 (base peak), 44 (9), 43 (17); HRMS Calcd for $C_{20}H_{25}NO_7$ (M) 391.1631, found *m/z* 391.1632.

Ethyl (2*R*,3*R*)-*N*-(*p*-Tolylsulfonyl)-3-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-5-oxopyrrolidine-2-carboxylate (8a). To a suspension of NaH (60% in oil, 0.029 g, 0.724 mmol) in dry ether (1 mL) were added at 0 °C lactam **5a** (0.169 g, 0.658 mmol) in dry ether (1 mL) and *p*-toluenesulfonyl chloride (0.125 g, 0.658 mmol) in dry CH_2Cl_2 (2 mL). The reaction mixture was worked up according to the usual manner. The crude product was purified by silica gel column chromatography (hexane/AcOEt, 4:1 v/v) to give **8a** (0.178 g, 65.8%): colorless prisms (diethyl ether); mp 118.5–120.5 °C; $[\alpha]^{20}_D$ = –67.17° (*c* = 0.4, benzene); IR (KBr) 2992, 2938, 2905, 1921, 1757, 1597, 1491, 1476, 1262, 1200, 1171, 1152, 1088, 1059, 1017, 961, 856, 816, 704, 667 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26, 1.22 (each 3H, each s, 2-Me of dioxolanyl), 1.32 (3H, t, *J* = 7.3 Hz, COOEt), 2.40 (1H, m, H-3), 2.44 (3H, s, *p*-Me), 2.45 (1H, dd, J_{gem} = 17.6 and $J_{4\text{-}3}$ = 2.9 Hz, one of H-4), 2.64 (1H, dd, J_{gem} = 17.6 and $J_{4\text{-}3}$ = 9.2 Hz, the other of H-4), 4.09 (1H, dd, J_{gem} = 8.8 and $J_{5'\text{-}4'}$ = 6.6 Hz, one of H-5 of dioxolanyl), 4.28 (2H, q, *J* = 7.3 Hz, COOEt), 3.61 (1H, dd, J_{gem} = 8.8 and $J_{5'\text{-}4'}$ = 5.5 Hz, the other of H-5 of dioxolanyl), 4.35 (1H, m, H-4 of dioxolanyl), 4.63 (1H, d, $J_{2\text{-}3}$ = 2.6 Hz, H-2), 7.32 (2H, d, *J* = 8.4 Hz, tolyl), 7.96 (2H, d, *J* = 8.4 Hz, tolyl); ^{13}C NMR ($CDCl_3$) δ 14.11 (COOEt), 21.68 (*p*-Me), 25.93, 24.59 (each 2-Me of dioxolanyl), 31.92 (C-3), 39.06 (C-4), 62.33 (C-2), 62.83 (COOEt), 67.11 (C-5 of dioxolanyl), 76.59 (C-4 of dioxolanyl), 110.03 (C-2 of dioxolanyl), 129.23, 129.05, 135.09, 145.22 (each tolyl), 170.26 (C-5), 171.69 (COOEt); MS *m/z* (rel inten, %) 411 (M^+, 1), 396 (26), 348 (14), 347 (67), 338 (26), 308 (11), 274 (24), 238 (15), 174 (9), 101 (base peak). Anal. Calcd for $C_{19}H_{25}NO_7S$: C, 55.46; H, 6.12; N, 3.40%. Found: C, 56.02; H, 6.02; N, 3.46%.

X-ray Structure Analysis of 8a. The X-ray diffraction data were collected with graphite-monochromatized Mo Kα radiation (λ = 0.71069). Structure analyses were performed with a TEXSAN system.[19] The structure was solved by the MITHRIL[20] direct method and defined by full-matrix least squares. A single crystal of **8a** grown from diethyl ether has a space group $P2_1$, *a* = 11.244(2), *b* = 8.421(2), and *c* = 12.039(2) Å, V = 1049.3(4) Å^3, *Z* = 2. The final *R* factor was 0.050 and 1453 observed reflections.[21]

Ethyl (2*R*,3*R*)-*N*-(*tert*-Butoxycarbonyl)-3-[(*S*)-1,2-dihydroxyethyl]-5-oxopyrrolidine-2-carboxylate (9). To a solution of compound **6a** (0.327 g, 0.915 mmol) in wet MeCN (7 mL containing 0.15 mL of water) was added at 0 °C 2 M HCl (0.7 mL). After stirring at rt for 4 h, the mixture was diluted with AcOEt and treated with $NaHCO_3$ and Na_2SO_4. The mixture was filtered to remove inorganic salts, and the filtrate was evaporated in vacuo to give **9** (0.290 g, 100%): colorless liquid; $[\alpha]^{20}_D$ = –22.2° (*c* = 0.9, EtOH); IR (neat) 2982, 2936, 2342, 1780, 1748, 1651, 1458, 1372, 1314, 1202, 1155, 1096, 1032, 961, 905, 837, 777, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3H, t, *J* = 7.0 Hz, COOEt), 1.48 (9H, s, *t*-Bu), 2.34 (1H, dddd, $J_{3\text{-}4}$ = 9.2, 5.9, $J_{3\text{-}2}$ = 4.8, and $J_{3\text{-}1'}$ = 3.7 Hz, H-3), 2.59 (1H, dd, J_{gem} = 17.9 and $J_{4\text{-}3}$ = 9.2 Hz, one of H-4), 2.61 (2H, br s, 2×OH), 2.73 (1H, dd, J_{gem} = 17.9 and $J_{4\text{-}3}$ = 5.9 Hz, the other of H-4), 3.56 (1H, dd, J_{gem} = 11.0 and $J_{2'\text{-}1'}$ = 7.3 Hz, one of H-2 of dihydroxyethyl), 3.70 (1H, dd, J_{gem} = 11.0 and $J_{2'\text{-}1'}$ = 3.3 Hz, the other of H-2 of dihydroxyethyl), 3.87 (1H, ddd, $J_{1'\text{-}2'}$ = 7.3, 3.3, and $J_{1'\text{-}3}$ = 3.7 Hz, H-1 of dihydroxyethyl), 4.44 (1H, d, $J_{2\text{-}3}$ = 4.8 Hz, H-2); ^{13}C NMR ($CDCl_3$) δ 14.18 (COOEt), 27.88 (*t*-Bu), 32.37 (C-3), 36.80 (C-4), 61.87 (COOEt), 61.96 (C-2), 64.51 (C-2 of dihydroxyethyl), 71.78 (C-1 of dihydroxyethyl), 83.94 (*t*-Bu), 149.21 (NCOOBu-*t*), 171.20 (C-5), 173.33 (COOEt); MS *m/z* (rel inten, %) 244 (M^+ – COOEt, 10), 217 (12), 188 (63), 186 (9), 147 (9), 144 (69), 126 (16), 91 (33), 84 (48), 73 (16), 59 (10), 57 (base peak), 56 (15). Calcd for $C_{14}H_{24}NO_7$ ($M+H^+$) 318.1553, found *m/z* 318.1533.

1-Ethyl 5-Methyl *N*-[(1*R*,4*R*)-2-Bornylidene]-3-isopropyl-(2*R*,3*R*)-glutamate (11). By a procedure similar to that used for the formation of **4a**, imine (–)-**1** (0.237 g, 1 mmol) and methyl 4-methyl-2-heptenoate gave Michael adduct **11** (0.211 g, 48%) and its diastereomer **11'** (0.03 g, 7%). Major product **11** was purified by silica-gel chromatography (hexane/AcOEt, 4:1 v/v), but minor one **11'** was still contaminated by **11** after several attempts of chromatographic separation. No analytical data of **11'** were available [**11'**: Colorless liquid; IR (neat) 2950, 2870, 1740, 1670, 1435, 1390, 1370, 1330, 1250, 1160, 1110, 1065, 1020, 950, 890, 840, 760, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.74 (3H, s, Me of camphor), 3.64 (3H, s, COOMe), 4.06 (2H, q, *J* = 7.3 Hz, COOEt). Other signals are overlapping with those of **11**.] **11**: colorless liquid; IR (neat) 2960, 2880, 1740, 1690, 1440, 1395, 1370, 1330, 1270, 1170, 1115, 1070, 1030, 940, 890, 860, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77 (3H, s, Me of camphor), 0.88, 0.90 (each 3H, each d, *J* = 3.3 Hz, *i*-Pr), 0.92, 0.94 (each 3H, each s, Me of camphor), 1.22 (3H, t, *J* = 7.3 Hz, COOEt), 1.35 (2H, m, camphor), 1.66 (2H, m, camphor), 1.81–1.95 (3H, m, camphor), 2.33 (1H, m, *i*-Pr), 2.38 (1H, dd, J_{gem} = 16.1 and $J_{4\text{-}3}$ = 5.9 Hz, one of H-4), 2.49 (1H, dd, J_{gem} = 16.1 and $J_{4\text{-}3}$ = 8.1 Hz, the other of H-4), 2.63 (1H, m, H-3), 3.65 (3H, s, COOMe), 4.02 (1H, d, $J_{2\text{-}3}$ = 5.9 Hz, H-2), 4.12 (2H, q, *J* = 7.3 Hz, COOEt); ^{13}C NMR ($CDCl_3$) δ 11.37 (Me), 14.17 (COOEt), 19.04, 19.06, 19.45, 20.56 (each Me), 27.54, 29.64, 31.75, 32.92, 36.28, 43.57, 43.92, 47.49 (camphor, C-3, C-4, and *i*-Pr), 51.37 (COOMe), 54.25 (C-1 of camphor), 60.66 (COOEt), 65.84 (C-2), 171.90, 174.25 (each COO), 185.57 (C=N); MS *m/z* (rel inten, %) 365 (M^+, 30), 337 (14), 323 (14), 322 (64), 292 (32), 250 (11), 238 (17), 237 (base peak). Anal. Calcd for $C_{21}H_{35}NO_4$: C, 69.01; H, 9.65; N, 3.83%. Found: C, 68.84; H, 9.55; N, 3.48%.

Diethyl (2*R*,3*R*,4*R*,5*R*)-5-*tert*-Butyl-3-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]pyrrolidine-2,4-dicarboxylate (14). (1) To a suspension of glycine ethyl ester hydrochloride (0.279 g, 2 mmol) in CH_2Cl_2 (10 mL) was added Et_3N (0.202 g, 2 mmol) at rt. The mixture was stirred at rt for 10 min. Then $MgSO_4$ (0.361 g, 3 mmol) and pivalaldehyde (0.172 g, 2 mmol) were added, and the mixture was further stirred for 30 min. After evaporation of the solvent in vacuo, the residue was washed well with ether. Evaporation of the combined ethereal washings gave imine **12** (0.222 g, 65%) which was used in the following reaction without further purification. (2) By a procedure similar to that used for the formation of **4a**, the crude imine **12** (0.222 g, 1.29 mmol) and ester **3a** were allowed to react to give a mixture of **13** and **14** as a yellow oil (0.339 g, 71%). This mixture was treated with $HONH_2$·HCl (0.127 g, 1.825 mmol) and $NaOAc·3H_2O$ (0.248 g, 1.825 mmol) under reflux in EtOH (5 mL). After 1.5 h, the mixture was concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane/AcOEt, 1:2 v/v) to give lactam **5a** (0.067 g, 13%) and cycloadduct **14** (0.161 g, 22%) both as yellow liquids. **14**: $[\alpha]^{25}_D$ = –5.56° (*c* = 0.36, EtOH); IR (neat) 3584, 2984, 2924, 1742, 1728, 1478, 1372, 1312, 1260, 1184, 1123, 1067, 858 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (9H, s, *t*-Bu), 1.26, 1.31 (each 3H, each t, *J* = 7.3 Hz, 2 × COOEt), 1.36, 1.42, (each 3H, each s, 2-Me of dioxolanyl), 2.54 (1H, m, H-3), 2.99 (1H, s, NH), 3.02 (1H, m, H-4), 3.60, (1H, d, $J_{5\text{-}4}$ = 5.1 Hz, H-5), 3.79 (1H, dd, J_{gem} = 8.1 and $J_{5'\text{-}4'}$ = 6.2 Hz, one of H-5 of dioxolanyl), 4.09, (2H, q, *J* = 7.3 Hz, COOEt), 4.13–4.21 (3H, m, H-2, H-4 of dioxolanyl, and the other of H-5 of dioxolanyl), 4.26 (2H, q, *J* = 7.3 Hz, COOEt); ^{13}C NMR ($CDCl_3$) δ 14.19, 13.89 (each COOEt), 26.57, 25.23 (each 2-Me of dioxolanyl), 27.42 (*t*-Bu), 32.55 (*t*-Bu), 47.73 (C-3), 53.34 (C-4), 61.12, 60.44 (each COOEt), 62.88 (C-2), 67.95 (C-5 of dioxolanyl), 72.73 (C-5), 76.88 (C-4 of dioxolanyl), 109.14 (C-2 of dioxolanyl), 172.04, 174.66 (each COOEt); MS *m/z* (rel inten, %) 371 (M^+, 1), 356 (35), 315 (18), 314 (base peak), 298 (13), 268 (34), 257 (13), 256 (87), 171 (13); HRMS calcd for $C_{19}H_{33}NO_6$ (M) 371.2308, found *m/z* 371.2308.

(19) TEXSAN: TEXRAY Structure Analysis Package, Molecular Structure Cor. (1985).

(20) Gilmore, C. J. *J. Appl. Crystallogr.* **1984**, *17*, 42.

(21) Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained on request from the Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.