fraction was collected. All other thio compounds and the benzylbutylamines were synthesized by literature procedures. Liquids were purified by fractional distillation under reduced pressure; solids were recrystallized to a constant melting point. Compound 2a was synthesized by the literature procedure.⁶⁷ Compound 2b, N⁵-ethyl-4a-hydroperoxy-N³, N¹⁰dimethylisoalloxazine, was synthesized in a like manner from N^3 , N^{10} dimethylisoalloxazine, prepared by the method of Yoneda,68 While 2b was too unstable for analysis, its precursor, N^5 -ethyl- N^3 , N^{10} -dimethylisoalloxazinium perchlorate, was recrystallized to a constant melting point of 196-197 °C from acetonitrile/ether: IR 1710 (s), 1620 (s), 1610 (s), 1560 (s), 1100 (s), 760 (s) cm⁻¹. Anal. C, H, N, Cl. The *tert*-butyl alcohol for kinetic studies was dried by refluxing over calcium hydride for at least 2 days, usually at least 5, and distilled with protection from moisture. The dioxane was refluxed overnight with sodium and benzophenone, distilled under nitrogen with protection from moisture, and used immediately for kinetic runs.

Isolation of p-Methoxyphenyl Methyl Sulfoxide. A solution of 0.020 g (0.05 mmol) of 2a in 100 mL of *tert*-butyl alcohol was treated with 0.010 g (0.065 mmol) of p-methoxythioanisole in 5 mL of *tert*-butyl alcohol. The mixture was allowed to stand in the dark for several days. Removal of the solvent in vacuo followed by thick-layer chromatography (silica gel GF, ethyl acetate, eluant) gave 0.009 g (106%) of a pale-yellow oil whose infrared spectrum was identical with that of authentic p-methoxyphenyl methyl sulfoxide.⁶⁹ TLC showed that N^5 -ethyl-4a-hydroxy- N^3 -methyl- N^{10} -(2,6-dimethylphenyl)isoalloxazine was the major product from 2a.

Reaction of p-Nitrobenzyl Phenyl Sulfide (6) with 2a in Dry, Degassed 1,4-Dioxane. In a glovebag purged with nitrogen, 12.3 mg (0.051 mmol) of 6 was dissolved in 25 mL of dry, degassed 1,4-dioxane. The solution was magnetically stirred as 20.6 mg (0.052 mmol) of 2a was added. The reaction mixture was monitored by TLC (silica gel, 50:50 hexane/ether), but after 3 days, TLC still showed unreacted 6. The reaction mixture was concentrated in vacuo to approximately 1-2 mL, and a TLC of this

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(68) Yoneda, F.; Sakuma, Y.; Ichiba, M.; Shinomura, K. J. Am. Chem. Soc. 1976, 98, 830-835.

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concentrate showed, besides decomposition products of 2a, only the unreacted 6 and *p*-nitrobenzyl phenyl sulfoxide, by comparison with authentic samples. No *p*-nitrobenzaldehyde or diphenyl disulfide could be detected. Attempts to separate (in the air) the components of the reaction mixture by preparative TLC resulted in extensive decomposition, and no pure products could be isolated.

Kinetic Studies. A known amount of an approximately 2.5×10^{-4} M solution of FlOOH was pipetted into a cuvette. The samples were thermally equilibrated at 30 °C in a Cary 219 spectrophotometer for at least 0.5 h, and then a known amount of neat liquid sulfide or amine or a solution of sulfide of known concentration was pipetted into the cuvette. The concentrations of substrate were approximately 50–500 times that of FlOOH. The absorbance at 400 nm was measured continuously for the fast oxidations and at precise time intervals for the slow oxidations. Almost always the reactions were followed to at least 3 half-lives, and excellent pseudo-first-order kinetics were observed. Plots of first-order rate constants which are reported. All rate constants were determined by the least-squares method. With the exceptions noted, duplicate runs were performed.

Acknowledgment. We thank Prof. Edward Leadbetter for the use of a Cary 219 spectrophotometer and Profs. Wassmundt and Rossi for helpful discussions. This work would not have been possible without the financial support of the University of Connecticut Research Foundation for which we are deeply grateful.

Registry No. 2a, 73475-07-7; **2b**, 96837-33-1; **3** (X = CN), 21382-98-9; **3** (X = PhC(O)), 23405-48-3; **3** (X = Cl), 123-09-1; **3** (X = H), 100-68-5; **3** (X = Me), 623-13-2; **3** (X = AcNH), 10352-44-0; **3** (X = MeO), 1879-16-9; **3** (X = NH₂), 104-96-1; **6**, 7703-38-0; FADMO, 37256-73-8; Me₂S, 75-18-3; Et₂S, 352-93-2; *i*-Pr₂S, 625-80-9; *t*-Bu₂S, 107-47-1; PhSEt, 622-38-8; PhS-*i*-Pr, 3019-20-3; PhS-*t*-Bu, 3019-19-0; PhS-*n*-Pr, 874-79-3; PhS-*i*-Bu, 13307-61-4; *n*-BuNHCH₂Ph, 2403-22-7; *i*-BuNHCH₂Ph, 42882-36-0; *sec*-BuNHCH₂Ph, 46120-25-6; *t*-BuNHCH₂Ph, 3378-72-1; *p*-MeOC₆H₄S(O)Me, 3517-99-5; N^3 , N^{10} -dimethylisoalloxazine, 4074-59-3; N^5 -ethyl- N^3 , N^{10} -dimethylisoalloxazine, 104550-31-4; 4a,5-dihydro- N^5 -ethyl-4a-hydroxy- N^3 -methyl- N^{10} -(2,6-dimethylphenyl)isoalloxazine, 76030-62-1.

Very High 1,2- and 1,3-Asymmetric Induction in the Reactions of Allylic Boron Compounds with Chiral Imines

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Abstract: The reaction of allyl-9-borabicyclo[3.3.1]nonane (allyl-9-BBN) with chiral imines 3 produced the Cram isomer 4 either exclusively or very predominantly. The very high 1,2-asymmetric induction is explained by a six-membered chairlike transition state, in which the imine R group occupies an axial position owing to the stereoelectronic effect of imines (RCH=NR'). The reaction of allyl-9-BBN with the chiral imine 11 also gave the Cram isomer 12 very predominantly. The very high 1,3-asymmetric induction is accounted for by a similar transition state (14), in which the 1,2-axial-equatorial interaction between the R' group and the ligand L plays an important role for the high chiral induction. Very high enantio- and diastereoselective synthesis of amino acid derivatives was realized via the reaction of allylic 9-BBN with α -imino esters (27) having a chiral auxiliary at the R' group. The modified Cram (or Felkin) model (9 or 9') is applicable to explain the 1,2-asymmetric induction. For the 1,3-asymmetric allylboration, the extended Cram model (10) is proposed.

The discovery of new methods for 1,2- and 1,3-asymmetric induction in acyclic systems has been a pressing concern in modern organic chemistry.¹ Especially, the Cram/anti-Cram problem has been one of the longstanding concerns. Although the Cram/anti-Cram selectivity of aldehydes has been intensely investigated during the last decade,² very few attempts have been made to elucidate such selectivity with imines.^{3,4} It was rather

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curious that no such investigation had been performed at the outset of our work. The major reason is presumably owing to the complex

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Table I	High	Cram	Selectivity	v in 1	.2-Asy	mmetric	Induction ^a
				,			

	•	• • •	
entr	imine y 3 , R' ^b	allylorganometal (M)	Cram(4):anti- Cram(5)
1	n-Pr	9-BBN	96:4
2	i-Pr	9-BBN	100:0
3	n-Pr	SnBu ₃ /TiCl ₄	93:7
4	i-Pr	SnBu ₃ /TiCl ₄	92:8
5	n-Pr	MgCl	84:16
6	n-Pr	MgBr	68:32
7	<i>i</i> -Pr	MgCl	70:30
entry	aldehyde	allylorganome	Cram(1):anti- al Cram(2)
8	PhCH(CH ₃)CH	IO 9-BBN	55:45
9		SnBu ₃ /TiCl ₄	69:31
10		MgCl	60:40

^a All reactions were carried out on a 1 mmol scale, and the imine 3 and the aldehyde were used in a racemic form. ^bPhCH(CH₃)CH= NR'.

reactivity of imines toward organometallic compounds. Alkyl Grignard reagents normally abstract the α -hydrogen to give metalloenamines.⁵ The alkylation with organolithium compounds results in low yields.⁶ Frequently, the reductive dimerization is accompanied with the desirable alkylation.

If efficient alkylation and high asymmetric induction are realized, such reactions become undoubtedly very useful for the synthesis of nitrogen-containing natural products, e.g., amino acids, β -lactams, and amino sugars. Previously, we communicated that the reaction of allyl-9-BBN with certain chiral imines gave the allylation product with very high enantiomeric excess in essentially quantitative yields.³ We now report a fully detailed report on the asymmetric induction via organometallic reagents together with its application to the synthesis of amino acids.

Results and Discussion

Very High 1,2-Asymmetric Induction. Generally speaking, the reaction of allyl organometallic compounds with ordinary chiral aldehydes having no ability to be chelated produces low Cram selectivity (eq 1).⁸ To our surprise, however, the reaction of allyl-9-BBN with the corresponding chiral imine produces very high Cram selectivity (eq 2).³ The results are summarized in

$$Ph \underbrace{\downarrow}_{O}^{H} + \underbrace{\downarrow}_{M = \text{Li}, Mg, B, \text{Si}, \cdots} Ph \underbrace{\downarrow}_{I} + Ph \underbrace$$

(2) Excellent 1,2- and 1,3-asymmetric induction through chelation control has been realized in the nucleophilic addition of organometallics to α - and β -alkoxy-substituted aldehydes. Reetz, M. T.; Kesseler, K.; Schmidtberger, S.; Wenderoth, B.; Steinbach, R. Angew. Chem., Int. Ed. Engl. 1983, 22, 989. Reetz, M. T.; Jung, A. J. Am. Chem. Soc. 1983, 105, 4833. Still, W. C.; Schneider, J. A. Tetrahedron Lett. 1980, 21, 1035. Still, W. C.; Mcdonald, J. H. *Ibid.* **1980**, 21, 1031. For α - and β -alkoxyimines: Yamamoto, Y.; Komatsu, T.; Maruyama, K. J. Chem. Soc., Chem. Commun. **1985**, 814. For nonchelation systems: Yamamoto, Y.; Maruyama, K. J. Am. Chem. Soc. 1985, 107, 6411. Maruoka, K.; Itoh, T.; Yamato, H. Ibid. 1985, 107, 4573. (3) Yamamoto, Y.; Komatsu, T.; Maruyama, K. J. Am. Chem. Soc. 1984, 106, 5031.

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Scheme I



Table II. High 1,3-Asymmetric Induction^a

entry	imine	allylorganometal (M)	Cram(12):anti- Cram(13)
1	11	9-BBN	92:8
2	(<i>R</i>)-11	$B(OCH_3)_2$	60:40 ^b
3	(<i>R</i>)-11	B O C	67:33 ^b
4	(<i>R</i>)-11	B Ph 16	80:20 ⁶
5	17	16	80.200
6	11	SnBu₁/TiCl₄	82:18
7	11	SnBu ₃ /BF ₃	67:33
8	11	MgBr	80:20

^a Normally, racemic 11 was used. In entries 2-4, optically active 11 ((R)-11) derived from (R)-1-phenylethylamine was used, and in entry 5, optically active 17 derived from (S)-1-phenylethylamine was utilized. ^bData given by Prof. R. W. Hoffmann.

Table I. As shown in entries 8-10, the Cram selectivity of the aldehvde was very low.⁹ Although the reaction of imines with allylmagnesium compounds exhibited low selectivity (Table I, entries 5-7), the reaction of allyl-9-BBN gave the Cram isomer either exclusively or very predominantly (Table I, entries 1 and 2)

With aldehydes, the α -chiral center goes to the equatorial position of 6 (Scheme I). Therefore, the selectivity is dictated only by the steric factor at the chiral center, and the steric influence of the ligand (L) does not reach the chiral center. On the other hand, the trans geometry¹⁰ of aldimines necessarily forces the metal to coordinate the nitrogen atom syn to the alkyl group (R), and hence the chiral center goes to the axial position of 7. Therefore, the selectivity must depend upon both the original steric factor of the chiral center and the steric influence of L. The conformation of the chiral center is fixed as shown in 7 owing to the steric influence of L, and the allyl group attacks from the less hindered side (7 and 9 (or 9')). The transition state, 8, is highly destabilized owing to the steric repulsion between the methyl group and the 9-BBN ring protons. The bridgehead proton ("H") of the 9-BBN ring covers the six-membered ring. The plane of the imine group (RCH=NR') and the plane of the C-"H" bond intersect with a nearly orthogonal angle.¹¹ Consequently, the anti-Cram attack leading to 5 becomes extremely unfavorable.

The reaction of allyltributylstannane in the presence of TiCl₄ also produced high Cram selectivity (Table I, entries 3 and 4). The reaction was carried out according to Keck's procedure (-78 °C, 2.5 h).¹² An alternative procedure,¹² adding TiCl₄ at -78

⁽⁹⁾ Significantly high Cram selectivity (92:8) has been realized with CH_2 =CHCH₂Ti(NR₂)₃: Reetz, M. T.; Steeinbach, R.; Wenderoth, B.; Westermann, J. Chem. Ind. (London) **1981**, 541.

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^{103, 3229.}

				18:19	:20:21			
entry	imine 3, R'	crotylmetal (M)	18	19	20	21 ^a	Cram:anti-Cram	erythro:three
1	n-Pr	9-BBN	40	45	8	7	85:15	47:53
2	<i>n</i> -Pr	MgCl	18	68	3	11	86:14	29:71
3	<i>n</i> -Pr	ZrCp ₂ Cl	18	70	3	9	88:12	27:73
4	i-Pr	9-BBN	26	51	15	8	77:23	34:66
		<u> </u>		2:	3:24			
entry	imine 22	crotylmetal	(M)	23	24	Сга	am:anti-Cram	erythro:threo
5	22a	9-BBN		75	25		100:0	75:25

Table III. Stereoselectivity in Crotyl Organometallic Reactions

^aCram-erythro:Cram-threo:anti-Cram-threo:anti-Cram-erythro.

°C followed by brief warming to room temperature and recooling to -78 °C, produced the Cram isomer with lower stereoselectivity (85:15). Obviously, the Lewis acid mediated reaction of allylic stannanes with imines does not proceed through a six-membered cyclic transition state as reported previously.^{12,13} Nevertheless, relatively high Cram selectivity is realized. A possible explanation is following. At -78 °C for 2.5 h, the complexation may be incomplete, and hence the transmetalation from allylstannane to allyltitanium reagent may compete during the warming to room temperature. If so, the reaction proceeds through a six-membered cyclic transition state owing to the high affinity of allyltitanium trichloride toward the nitrogen atom. The alternative procedure $(-78 \text{ °C} \rightarrow \text{room temperature} \rightarrow -78 \text{ °C})$ may complete the complexation of TiCl₄ with imines, and the lower selectivity is presumably a reflection of the acyclic transition state. Actually, the reaction of 3 with Bu₂CuLi/BF₃,¹⁴ in which the six-membered transition state cannot be involved, gave a mixture of 4 and 5 in a ratio of 82:18.

Very High 1,3-Asymmetric Induction. The steric interaction between the R group and L in 7 or 8 is a sort of 1,3-diaxial interaction, and this interaction enhances the stereoselectivity. A similar interaction between the R' group and L is conceivable, though it is a sort of 1,2-axial-equatorial interaction. Therefore, we examined the reaction of 11 with allylic organometallic compounds (eq 3). The results are summarized in Table II.



With allyl-9-BBN, the Cram product 12 was obtained very predominantly (Table II, entry 1). The conformation of the chiral center is probably fixed, as shown in 14. The allyl group attacks from the less hindered side (10 and 14). The transition state (15) is destabilized due to the steric repulsion between the methyl group (and/or phenyl group) and L. There may be a question that the bad interaction depicted in 8 and 15 can be avoided by rotating the carbon so that the hydrogen is in the position of the methyl in 8 and the phenyl in 15. Inspection with a Dreiding model clearly indicates that such conformations are destabilized by the steric repulsion between the 9-BBN ring and the phenyl group in 8 and

between the 9-BBN ring and the methyl group in 15.15

Prof. R. W. Hoffmann kindly informed us of their data on the boronate reactions (Table II, entries 2-5).¹⁶ The reactions were very slow: 2-3 weeks at reflux in CH₂Cl₂ led only to 30-40% conversion. Their data clearly indicate that increasing the size of L leads to a higher diastereoselectivity. The 9-BBN residue evidently causes the strongest steric interaction. Further, the chirality of the ligand at boron (16) is not important (Table II, entries 4 and 5). The stereoselectivity is solely determined by the chirality of the phenylethyl moiety.17

The reaction of allylstannane was carried out by Keck's procedure (-78 °C, 2.5 h).¹² The selectivity depended upon the Lewis acids (Table II, entries 6 and 7). A possible explanation is as follows. As mentioned above, the transmetalation to allyltitanium derivative may take place in entry 6 owing to the slow complexation of 11, and hence a cyclic transition state like 14 is presumably involved. With BF₃, (Table II, entry 7), the transmetalation from allylstannane to allylboron derivative does not take place under the reaction condition. Therefore, the reaction proceeds through an acyclic transition state,¹³ resulting in low stereoselectivity.

In conclusion, very high 1,2- and 1,3-asymmetric induction is realized in the reaction of allyl-9-BBN with chiral imines. The 1,2-asymmetric induction (Table I, entry 2) is 100%, while the 1,3-asymmetric induction (Table II, entry 1) is 92%. This is reasonable, since the 1,3-diaxial interaction is normally stronger than the 1,2-axial-equatorial interaction.

Reaction with Crotyl Organometallic Reagents. We next examined the reaction between chiral imines and crotyl organometallic reagents (eq 4 and 5). The results are summarized in Table III. The reaction of 3 ($\mathbf{R}' = n$ -Pr and *i*-Pr) produced four possible isomers, and unsatisfactory selectivities on both Cram/anti-Cram and erythro/threo were obtained (Table III, entries 1-4). The reason for this relatively low selectivity in comparison with the high selectivity in eq 2 is not clear.

The stereostructures of 18-21 were primarily determined by the ¹H NMR analysis of the iodolactonization products as described previously¹³ (Scheme II). Some of these structures were definitely established by X-ray analyses. Drawings of 25 (Cram-trans-cis) derived from 19 (R' = n-Pr) and of 25 (anti-Cram-trans-cis) derived from 20 (R' = i-Pr) are shown in Figure 1. The results of X-ray analyses clearly indicate that the ¹H NMR assignment¹³ is reliable. We also examined X-ray analyses of the iodolactonization products derived from 18, 23, and 24, but unfortunately we could not get nice single crystals.

⁽¹²⁾ Keck, G. E.; Enholm, E. J. J. Org. Chem. 1985, 50, 147.
(13) Yamamoto, Y.; Komatsu, T.; Maruyama, K. J. Org. Chem. 1985, 50,

⁽¹⁴⁾ For a review on RCu/BF₃, R₂CuLi/BF₃, and related reagents, see: Yamamoto, Y. Angew. Chem., Int. Ed. Engl., in press. See also: Wada, M.; Sakurai, Y.; Akiba, K. Tetrahedron Lett. **1984**, 25, 1079.

⁽¹⁵⁾ A referee poses the following question. The steric interaction between Me and L^1 in 7 is more favorable than the interaction between Ph and L^1 in By another conformer of 8, in which the hydrogen is in the position of Me and the Ph is in the position of H: $Me-L^1 < Ph-L^1$ (L¹ is the axial ligand). On the other hand, the interaction between Ph and L² in 14 is more favorable than the interaction between Me and L² in 15', another conformer of 15, in which the hydrogenetic for the state of the He L². the hydrogen is in the position of Ph and Me is in the position of H: $Ph-L^2 < Me-L^2$ (L² is the equatorial ligand). The two conclusions seem to be contradictory. However, the distance between the chiral center and L¹ in 7. 8, and 8' is different from the distance between the center and L^a in 14, 15, and 15'. Therefore, both transition states cannot be compared directly. (16) Eichler, G. Diplomarbeit Marburg, 1980. Y. Y. would like to thank Prof. Hoffmann for providing us with their data and for helpful discussions.

⁽¹⁷⁾ Roush has demonstrated that chiral ligands on boron can be very effective for the chiral induction in the allylation of aldehydes: Roush, W. R.; Walts, A. E.; Hoong, L. K. J. Am. Chem. Soc. 1985, 107, 8186.



The reaction of 22a produced two isomers, 23 and 24, and the anti-Cram isomers were not isolated. Here again, the structures were determined by ¹H NMR analyses of the iodolactonization products. The high Cram selectivity (Table III, entry 5) is inconsistent with the result of Table II, entry 1. Unfortunately, the reaction of 22b with crotyl-9-BBN was quite sluggish, and the starting imine was recovered after 1 day at room temperature.

Consequently, with crotyl organometallic compounds (M = B, Zr, and Mg), the 1,2-asymmetric induction is not so high as that with the allyl system. On the other hand, very high 1,3-asymmetric induction is again realized with crotyl-9-BBN. On simple diastereoselectivity, predominant formation of threo isomers in entries 1–4 of Table III is consistent with the previous observation that the threo selectivity goes up with an increase of the steric bulk of R¹³. The erythro selectivity via **22a** (Table III, entry 5), which possesses a less bulky ethyl group as R, is also in good agreement with the previous result.¹³ We next applied the high 1,3-asymmetric induction to the synthesis of certain amino acids.

Synthesis of Amino Acids. We examined the reaction of α -imino esters (27) with allylic organometallic compounds (eq 6). Previously, Kagan reported the reaction of 27 with Grignard reagents.¹⁸ A major drawback was lack of regioselectivity; the nucleophile attacked three possible electrophilic centers, the imine carbon, ester carbon, and nitrogen atom. We found that the reaction of allylic 9-BBN proceeds regioselectively at the imine carbon in high yields and provides the corresponding amino acid derivatives (28) with very high enantio- and diastereoselectivity (up to 96% enantiomeric excess). The results are summarized in Table IV.



The reaction of allyl-9-BBN with 27a produced 28a in high chemical and optical yield (Table IV, entry 1), though the reaction of allylzinc and magnesium derivatives resulted in very low de (Table IV, entries 2 and 3). The diastereomeric excess increased up to 96% with 27b (Table IV, entry 4). Quite similarly, the reaction of methallyl-9-BBN with 27a and 27b gave 28c and 28d, respectively, in high de (Table IV, entries 6 and 8). With allylic zinc reagents, low diastereoselectivity was obtained as expected (Table IV, entries 5, 7, 9, and 11). The reaction of prenyl-9-BBN with 27a was relatively sluggish and resulted in low chemical and optical yields (Table IV, entry 10). The diastereofacial selectivity



Figure 1. ORTEP stereoviews of 25: (top) 25 (anti-Cram-trans-cis), R' = i-Pr; (bottom) 25 (Cram-trans-cis), R' = n-Pr.

Scheme II



was also examined with crotyl organometallic compounds (Table IV, entries 12–15). Here again, the erythro isomer was produced perferentially as observed previously (Table III, entry 5; ref 12), and the boron reagent exhibited higher diastereoselectivity than other reagents.

The structures of amino acid derivatives (28) were determined as shown in Scheme III. Compound 28a was converted into 29, $[\alpha]^{24}_{\rm D} + 12.6^{\circ}$ (c 0.87, CH₂Cl₂), and authentic L-norvaline (S form) was also transformed into 29, with a comparable $[\alpha]^{24}_{\rm D}$ of +10.2° (c 5.55, CH₂Cl₂). It should be noted that very high 1,3-asymmetric induction is realized by use of a simple and

⁽¹⁸⁾ Fiaud, J.; Kagan, H. B. Tetrahedron Lett. 1970, 1813; 1971, 1019.

Table IV.	Reaction	of 27	with .	Allylic	Organometallic	Compounds
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	27 ^b (R ¹)		allyimet	al		product	yield, %	de, %	erythro:threo
entry		M	R ²	R ³	R ⁴				
 1	27a	9-BBN	Н	Н	Н	28a	92	92	
2	27a	ZnBr	н	Н	н	28a	94	10	
3	27a	MgCl	н	н	н	28a	а	0	
4	27b	9-BBN	н	н	н	28b	94	96	
5	27b	ZnBr	Н	н	н	28b	53	30	
6	27a	9-BBN	Н	н	CH ₃	28c	80	90	
7	27a	ZnBr	Н	н	CH,	28c	83	16	
8	27b	9-BBN	н	Н	CH,	28d	94	78	
9	27b	ZnBr	Н	н	CH ₃	28d	90	14	
10	27a	9-BBN	CH ₁	CH ₁	Н	28e	33	54	
11	27a	ZnBr	CH,	CH ₃	н	28e	60	16	
12	27c	9-BBN	CH ₃	н	н	28f	75		85:15
13	27c	Ti(O- <i>i</i> -Pr) ₃	CH,	Н	Н	28f	75		60:40
14	27c	MgCl	CH ₃	Н	Н	28f	78		59:41
15	27c	Zr(Cp) ₂ Cl	CH	н	Н	28f	73		51:49

^a A major product was the diallylated tertiary alcohol formed via the attack at the ester carbon. ^b 27a, (S)-(-)-CHPhCH₃; 27b, (-)-CH(C₆H₁₁)-CH₃; and 27c, SO₂C₆H₄-p-CH₃.





conventional chiral source and that the direction of chiral induction (from the (S)-amine to the S chirality) is in good agreement with the data of Table II, entry 1 (from the (R)-amine to the R chirality). Quite similarly, **28c** was converted into **30**, $[\alpha]^{24}_{D}$ -16.7° (c 2.51, CHCl₃), and authentic L-leucine (S form) was transformed into the butyl ester. Surprisingly, $[\alpha]^{24}_{D}$ of the authentic sample exhibited +14.6° (c 36.0, CHCl₃). Therefore, we examined again the reaction of methallyl-9-BBN with the imine having (R)-(+)-CHPhMe as the R' group of **27**. The leucine butyl ester derived from this product exhibited $[\alpha]^{24}_{D} + 17.5°$ (c 0.96, CHCl₃). Therefore, the direction of chiral induction is entirely opposite between allylboration and methallylboration.

The absolute configuration of **28b**, **28d**, and **28e** was not determined. The iodolactonization of the major isomer of **28f** produced **31** with $J_{2,3} = 7.62$ Hz (400 MHz), whereas the epimer derived from the minor isomer of **28f** exhibited $J_{2,3} = 5.19$ Hz. From these data, the structure of **31** could not be determined unambiguously. However, the erythro diastereoselectivity in entries 12–15 of Table IV was strongly supported from the following experiment.

Since the reaction of 22a with crotyl-9-BBN produced exceptionally high Cram selectivity (Table III, entry 5), we examined the reaction of 27a and 27b with crotyl-9-BBN (eq 7). The reaction proceeded in essentially quantitative yield to give 32 with an isomer ratio of 93:3:3:1. The relative stereochemistry was determined by the iodolactonization reaction. Although we tried to prepare the six-membered heterocycle as shown in Scheme II, this type of iodolactonization reaction was very sluggish. Therefore, 32 was converted into 33 by the hydrolysis-iodolactonization process. It is known that the vicinal coupling constant of the five-membered ring is in between 0 and 11 Hz for the trans isomer and in between 4.5 and 10 Hz for the cis isomer.¹⁹ The



major isomer of 33 exhibited $J_{2,3} = 0.80$ Hz, indicating trans configuration. The absolute stereochemistry was elucidated by transforming 32 into allo-erythro-isoleucine butyl ester (34) according to the procedure described above: $[\alpha]^{23}_D + 13.5^{\circ}$ (c 7.35, CHCl₃). An authentic sample prepared from L-alloisoleucine had $[\alpha]^{23}_D + 12.0^{\circ}$ (c 8.50, CHCl₃).

Other crotyl organometallic compounds, such as MgCl and Ti $(O-i-Pr)_3$, were also treated with 27a. However, four isomers were obtained in almost equal proportions. The reaction of crotyl-9-BBN with 27b produced four isomers in the ratio 85:6:6:3, but the relative and absolute stereochemistries of these products were not determined.

Extended Cram Model for Chiral Imines. Although the 1,2asymmetric induction in chiral aldehydes is well understood by the Cram and/or Felkin model, there has been no such guiding principle in the corresponding imine series. Now it is clear that the modified Cram model (9) and/or modified Felkin model (9') can be applied to the 1,2-asymmetric induction in chiral imines (eq 2 and 4). For the 1,3-asymmetric induction, we proposed the extended Cram model 10 and this model is applicable to the allylmetalation reactions in eq 3, 5, 6, and 7. However, the methallylboration gave the opposite chiral induction (Table IV, entries 6–9), and the result cannot be explained by the extended Cram model (10).

As shown in Scheme IV, the transition state 35, derived from allyl-9-BBN and 27a, leads to 28a having S,S chirality. On the other hand, 36 derived from methallyl-9-BBN and 27a possesses three 1,3-diaxial interactions, while there is only one 1,3-diaxial interaction in 35. Therefore, 36 is presumably highly destabilized,

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and thus methallylboration provides an opposite chiral induction. The boat transition state 37 may diminish such bad interactions. Consequently, 27 derived from (R)-(+)-PhMeCHNH₂ reacts with methallyl-9-BBN through 37 to produce (SR)-28c with high diastereoselectivity. The direction of chiral induction in aldehydes is identical irrespective of the allylboration, methallylboration, and prenylboration.²⁰ This is reasonable since the chiral group goes to the equatorial position as shown in 6 and the bad 1,3-diaxial interaction does not take place with the methallyl- or prenylboration.

In conclusion, very high 1,2- and 1,3-asymmetric induction is realized via the reaction of allylic 9-BBN with chiral imines. A guideline for predicting the direction of chiral induction is proposed; the modified Cram (or Felkin) model and the extended Cram model can account for the observed asymmetric induction. Finally, the present development provides a new method for very high enantio- and diastereoselective synthesis of amino acids and related compounds via C-C bond formation.

Experimental Section

General information concerning instrumentation and materials is described previously.²¹ Imines were prepared according to the reported procedure.¹³ All amine products, except where the elemental analysis data were described, were analyzed by GC-mass spectroscopy and exhibited the correct exact mass data.³¹

N-(2-Phenylpropylidene)propylamine: bp 81-82 °C/2 mmHg; ¹H NMR (CCl₄) δ 0.87 (t, J = 7.5 Hz, 3), 1.40 (d, J = 7.5 Hz, 3), 1.4–1.8 (m, 2), 3.30 (t, J = 7 Hz, 2), 3.56, (qd, J = 5, 7 Hz, 1), 7.2–7.4 (m, 5), 7.66 (d, J = 4.5 Hz, 1).

N-(2-Phenylpropylidene)isopropylamine: bp 74 °C/2 mmHg; ¹H NMR (CCl₄) δ 1.09 (d, J = 7 Hz, 3), 1.11 (d, J = 7 Hz, 3), 1.36 (d, J= 7 Hz, 3), 3.21 (sp, J = 7 Hz, 1), 3.49 (qd, J = 7, 4.5 Hz, 1), 7.0–7.4 (m, 5), 7.63 (d, J = 4.5 Hz, 1).

N-Isobutylidene-1-phenylethylamine: bp 76-81 °C/5 mmHg; ¹H NMR (CCl₄) δ 1.05 (d, J = 7 Hz, 6), 1.37 (d, J = 7 Hz, 3), 2.40 (sp-d, J = 7, 4 Hz, 1), 4.20 (q, J = 7 Hz, 1), 7.0-7.4 (m, 5), 7.64 (d, J = 4 Hz, 1).

N-n-Propylidene-1-phenylethylamine: bp 63-67 °C/3.5 mmHg; ¹H NMR (CCl₄) δ 1.04 (t, J = 7.5 Hz, 3), 1.38 (d, J = 7 Hz, 3), 2.21 (qd, J = 7.5, 4 Hz, 2), 4.19 (q, J = 7 Hz, 1), 7.0-7.4 (m, 5), 7.72 (t, J = 4 Hz, 1).

Reactions of 3 and 11 with Allylic Organometallic Compounds. The reaction was carried out as described previously.¹³ The reaction with allyl-9-BBN or allylmagnesium halides proceeded smoothly and gave the allylated product in 88-98% isolated yield. On the other hand, the yield via allylstannane was in the range of 60-70% yield. The isomer ratio was determined by ¹H NMR analyses of the crude product and/or by GLPC with a THEED column (tetrakis(hydroxyethyl)ethylenediamine from Wako Chem. Ind.).

N-n-Propyl-2-phenyl-5-hexen-3-ylamine: bp 120-125 °C/1 mmHg (Kugelrohr); ¹H NMR (CCl₄) δ (Cram isomer) 0.72 (brs, 1), 0.87 (t, J = 7 Hz, 3), 1.25 (d, J = 7 Hz, 3), 1.3-1.6 (m, 2), 1.7-3.0 (m, 6), 4.9-5.2 (m, 2), 5.6-6.1 (m, 1), 7.20 (s, 5). It was difficult to distinguish both isomers from the 100-MHz ¹H NMR spectra. However, GLPC examination by THEED column (10%, 2 m, 125 °C) revealed that the retention time of the anti-Cram isomer was 9.4 min, while that of the Cram isomer was 10.5 min. The structure of the major isomer (Cram product) was determined as described below.

N-Isopropyl-2-phenyl-5-hexen-3-ylamine: bp 120–125 °C/0.5 mmHg (Kugelrohr); ¹H NMR (CCl₄) δ (Cram isomer) 0.57 (brs, 1), 0.89 (d, J = 7 Hz, 3), 0.96 (d, J = 7 Hz, 3), 1.25 (d, J = 7 Hz, 3), 1.6–2.3 (m, 2), 2.5–3.0 (m, 3), 4.8–5.2 (m, 2), 5.6–6.1 (m, 1), 7.24 (m, 5). The isomer ratio was determined as described above. The retention time of the anti-Cram isomer was 6.85 min through a THEED column (10%, 2 m, 115 °C), while that of the Cram isomer was 7.40 min.

Stereochemistry of 4 and 5. Iodolactonization. The homoallylamine (4) was protected with the *N*-benzyloxycarbonyl group and then underwent the iodolactonization reaction as described previously.¹³

6-(Iodomethyl)-4-(1-phenylethyl)-3-propylperhydro-1,3-oxazin-2-one: ¹H NMR (CDCl₃, 400 MHz) δ 1.004 (t, J = 7.32 Hz, 3), 1.428 (d, J = 7.02 Hz, 3), 1.635 (ddd, J = 5.49, 11.9, 13.72 Hz, 1), 1.69–1.81 (m, 2), 2.042 (ddd, J = 1.83, 3.97, 12.21 Hz, 1), 2.994 (ddd, J = 6.11, 9.14, 13.63 Hz, 1), 3.10–3.15 (m, 2), 3.227, (dd, J = 3.67, 10.38 Hz, 1), 3.46 (ddd, J = 1.83, 5.49, 8.6 Hz, 1), 3.94–4.07 (m, 2), 7.2–7.6 (m, 5). Anal. Calcd for C₁₆H₂₂NO₂I: C, 49.62; H, 5.73; N, 3.62; I, 32.77. Found: C, 49.61; H, 5.75; N, 3.69; I, 32.69.

6-(Iodomethyl)-3-isopropyl-4-(1-phenylethyl)perhydro-1,3-oxazin-2-one: ¹H NMR (CDCl₃, 400 MHz) δ 1.369 (d, J = 6.71 Hz, 3), 1.377 (d, J = 7.01 Hz, 3), 1.4–1.5 (m, 1), 1.530 (d, J = 6.71 Hz, 3), 1.990 (ddd, J = 1.83, 3.97, 12.21 Hz, 1), 2.98–3.08 (m, 2), 3.132 (dd, J = 3.97, 10.38 Hz, 1), 3.40 (ddd, J = 1.83, 5.34, 8.05 Hz, 1), 3.72–3.81 (m, 2), 7.18–7.52 (m, 5). Anal. Calcd for C₁₆H₂₂NO₂I: C, 49.62; H, 5.73; N, 3.62; I, 32.77. Found: C, 49.65; H, 5.80; N, 3.59; I, 32.68. From these data, it was clear that the *trans*-oxazinone was produced via the iodo-lactonization, as reported in the previous paper.¹³ However, the structure of the side chain (Cram or anti-Cram) could not be determined by this method.

Stereochemistry of 4 and 5. Synthesis of an Authentic Sample. The Cram isomer 1, prepared from the reaction of 2-phenylpropionaldehyde with allyltrimethylsilane in the presence of TiCl₄,⁸ was hydrogenated over Pd-carbon by the conventional method. 2-Phenyl-3-hexanol was obtained in an essentially quantitative yield: bp 150 °C/10 mmHg (Kugelrohr); ¹H NMR (CCl₄) δ 0.9 (t, J = 6 Hz, 3), 1.20 (d, J = 7 Hz, 3), 1.10–1.40 (m, 5), 2.63 (q, J = 7 Hz, 1), 3.42–3.70 (m, 1), 7.2 (br s, 5). This alcohol was converted into the corresponding azide according to the reported procedure²² by use of 1-methyl-2-fluoropyridinium salt/Et₃N and LiN₃. 2-Phenyl-3-hexyl azide was obtained in 75% yield: ¹H NMR (CCl₄) δ 9.0 (t, J = 6 Hz, 3), 1.35 (d, J = 7 Hz, 3), 1.25–1.50 (m, 4), 2.80 (m, 1), 3.30–3.50 (m, 1), 7.30 (br s, 5); IR (CCl₄) 2140 cm⁻¹. Since it is well-known that the substitution with N_3^- proceeds via inversion at the carbon bearing the oxygen atom,²² the anti-Cram isomer is formed in this reaction. The azide was treated with LiAlH₄ (1 equiv) in ether at 0 °C, and then the mixture was refluxed for 1 h. The usual workup followed by Kugelrohr distillation (bp 80-85 $^{\circ}C/2$ mmHg) gave 2-phenyl-3hexylamine in 85% yield: ¹H NMR (CCl₄) δ 0.9 (t, J = 6.5 Hz, 3), 1.22 (d, J = 7 Hz, 3), 1.20-1.60 (m, 6), 2.45-2.90 (m, 2), 7.24 (br s, 5); IR(CCl₄) 3400 cm⁻¹. This anti-Cram amine was treated with propanal in CH₂Cl₂ in the presence of anhydrous MgSO₄, as described previously.¹³ Kugelrohr distillation (bp 95 °C/2 mmHg) gave N-n-propylidene-2-¹H NMR phenyl-3-hexylamine in an essentially quantitative yield: $(CCl_4) \delta 0.80$ (t, J = 6.5 Hz, 3), 0.86 (t, J = 6.5 Hz, 3), 1.08 (d, J =7 Hz, 3), 1.20-1.60 (m, 4), 1.90-2.20 (m, 2), 2.60-2.90 (m, 2), 7.20 (br s, 5), 7.30 (t, J = 4.5 Hz, 1). The reduction of this imine with LiAlH₄ in ether by using the same procedure as described above gave N-npropyl-2-phenyl-3-hexylamine (anti-Cram isomer) in 85% yield: bp 80 °C/1 mmHg; ¹H NMR (CCl₄) δ 0.86 (t, J = 6.5 Hz, 6), 1.21 (d, J = 7 Hz, 3, $Ph\bar{C}CH_3$), 1.20–1.45 (m, 6), 2.00 (br s, 1), 2.36–2.64 (m, 3), 2.70-3.00 (m, 1), 7.22 (br s, 5); IR (CCl₄) 3400 cm⁻¹. The authentic sample of the Cram amine could not be prepared in pure form and was contaminated with the anti-Cram amine, since the anti-Cram homoallyl alcohol (2) was afforded as a minor product and the isolation of pure 2 was difficult. However, the Cram amine could be easily distinguished from the anti-Cram amine with the aid of the ¹H NMR chemical shift of PhC(CH₃): 1.25 (d, J = 7 Hz, 3). For the allylation reaction of N-(2-phenylpropylidene) isopropylamine, the authentic samples were not prepared.

N-(1-Phenylethyl)-2-methyl-5-hexen-3-ylamine (12 and 13). Both isomers could be separated by column chromatography on silica gel (hexane/ether 20:1): ¹H NMR (CCl₄) δ (Cram isomer, **12**) 0.78 (d, J = 6.5 Hz, 3), 0.84 (d, J = 6.5 Hz, 3), 0.89 (br s, 1), 1.24 (d, J = 7 Hz, 3), 1.3-2.3 (m, 4), 3.82 (q, J = 7 Hz, 1), 4.9-5.2 (m, 2), 5.6-6.1 (m, 1), 7.1-7.5 (m, 5), (anti-Cram isomer, **13**) 0.82 (d, J = 6.5 Hz, 3), 0.89 (d, J = 6.5 Hz, 3), 1.00 (br s, 1), 1.24 (d, J = 7 Hz, 3), 1.6-2.4 (m, 4), 3.78 (q, J = 7 Hz, 1), 4.9-5.2 (m, 2), 5.6-6.1 (m, 1), 7.1-7.5 (m, 5). The retention time of **12** through the THEED column (10%, 2 m, 95 °C) was 13.3 min, while that of **13** was 12.5 min.

Stereochemistry of 12 and 13. Iodolactonization. The iodolactonization was carried out as described previously.¹³ Here again, the *trans*-oxazinone was produced. The structure of the side chain (Cram or anti-Cram) could not be determined by this method.

6-(Iodomethyl)-4-isopropyl-3-(1-phenylethyl)perhydro-1,3-oxazin-2-one from 12: ¹H NMR (CCl₄) δ 0.88 (d, J = 7.5 Hz, 3), 0.94 (d, J = 7.5 Hz, 3), 1.28 (ddd, J = 5.5, 11.5, 15.3 Hz, 1), 1.63 (d, J = 8 Hz, 3), 2.00 (sp-d, J = 7, 7 Hz, 1), 2.17 (ddd, J = 2.5, 4.5, 14 Hz, 1), 2.97 (ddd, J = 2.5, 6, 6 Hz, 1), 3.1–3.4 (m, 2), 4.39 (dddd, J = 4.5, 4.5, 7, 11.7 Hz, 1), 5.53 (q, J = 7 Hz, 1), 7.2–7.6 (m, 5). Anal. Calcd for C₁₆H₂₂NO₂I: C, 49.62; H, 5.73; N, 3.62; I, 32.77. Found: C, 49.64; H, 5.64; N, 3.47; I, 32.84. The corresponding oxazinone from 13: ¹H NMR (CDCl₃, 400 MHz) δ 0.779 (d, J = 6.72 Hz, 3), 0.816 (d, J = 6.71 Hz, 3), 1.6–1.8

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(m, 2), 1.724 (d, J = 7.02 Hz, 3), 2.333 (ddd, J = 2.14, 3.97, 14.04 Hz, 1), 3.192 (dd, J = 7.33, 10.38 Hz, 1), 3.24 (m, 1), 3.206 (dd, J = 4.12, 10.23 Hz, 1), 4.307 (dddd, J = 3.97, 4.12, 7.33, 11.2 Hz, 1), 4.967 (q, J = 7.02 Hz, 1), 7.2-7.6 (m, 5). Anal. Calcd for C₁₆H₂₂NO₂I: C, 49.62; H, 5.73; N, 3.62; I, 32.77. Found: C, 49.60; H, 5.68; N, 3.50; I, 32.81.

Stereochemistry of 12 and 13. Synthesis of an Authentic Sample. Palladium hydroxide on carbon was prepared according to the literature procedure.23 To a solution of 20 mg of Pd(OH)₂ on carbon dissolved in distilled methanol was added 0.5 mmol of 12 prepared from N-isobutylidene-(1R)-phenylethylamine ((R)-11). The mixture was stirred for 1 day at room temperature under H_2 and then filtered. Methanol was removed under reduced pressure, and ether was added to the residue. Small amounts of water were added, and the ether extract was dried over anhydrous MgSO₄. The product was purified through column chromatography on silica gel (hexane/ether 15:1). By this procedure, the reduction of the double bond and removal of the 1-phenylethyl group were accomplished to give 2-methyl-3-hexylamine:²⁴ bp 60 °C/130 mmHg (Kugelrohr); ¹H NMR (CCl₄) δ 0.88 (t, J = 6 Hz, 3), 0.90 (d, J = 7 Hz, 6), 1.1–1.5 (m, 7), 2.4–2.6 (m, 1); $[\alpha]^{23}_{D}$ +1.0 (c 0.25, CHCl₃). By use of the same procedure as described above, authentic (3R)-2-methyl-3hexylamine was prepared from (3S)-(-)-2-methyl-5-hexen-3-ol, which was made according to the literature,²⁵ $[\alpha]^{23}_{D}$ +0.85 (c 0.18, CHCl₃). Consequently, it was confirmed that the R chirality is induced from (R)-11.

Reaction of 3 and 22 with Crotyl Organometallic Compounds. The reaction was carried out as described previously.¹³ The resulting four diastereomers were separated through column chromatography on silica gel (hexane/ether 20:1). The isomer ratio was determined by GLPC and/or ¹H NMR analyses. The anti-Cram isomer **20** and **21** was produced as a minor component, and thus the isolation in pure form was difficult. The characteristic ¹H NMR signals of these anti-Cram isomers are shown.

N-Propyl-2-phenyl-4-methyl-5-hexen-3-ylamine: ¹H NMR (CCl₄) Cram-erythro (**18**, $\mathbf{R}' = n$ -Pr) δ 0.60 (br s, 1), 0.82 (t, J = 7 Hz, 3), 0.92 (d, J = 7 Hz, 3), 1.22 (d, J = 7 Hz, 3), 1.1–1.6 (m, 2), 1.9–3.0 (m, 5), 4.8–5.1 (m, 2), 5.6–6.1 (m, 1), 7.18 (m, 5), Cram-threo (**19**, $\mathbf{R}' = n$ -Pr) 0.73 (br s, 1), 0.84 (d, J = 7.5 Hz, 3), 0.98 (d, J = 7 Hz, 3), 1.23 (d, J = 7 Hz, 3), 1.0–1.5 (m, 2), 1.9–2.9 (m, 5), 4.7–5.1 (m, 2), 5.6–6.0 (m, 1), 7.0–7.3 (m, 5), anti-Cram-threo (**20**, $\mathbf{R}' = n$ -Pr) 0.68 (t, J = 7 Hz, 3), 1.21 (d, J = 7 Hz, 3), anti-Cram-erythro (**21**, $\mathbf{R}' = n$ -Pr) 0.68 (t, J = 7.5 Hz, 3), 1.22 (d, J = 7 Hz, 3). The GLPC retention times of these isomers on PEG 6000 (5%, 2 m, 135 °C) were as follows: **20** 6.23 min; **21**, 6.63 min; **19**, 7.55 min; and **18**, 8.07 min.

N-Isopropyl-4-methyl-2-phenyl-5-hexen-3-ylamine: ¹H NMR (CCl₄) Cram-erythro (**18**, R' = i-Pr) δ 0.55 (br s, 1), 0.76 (d, J = 7 Hz, 3), 0.90 (d, J = 7 Hz, 6), 1.21, (d, J = 7.5 Hz, 3), 1.9–2.2 (m, 1), 2.4–2.9 (m, 3), 4.8–5.1 (m, 2), 5.6–6.1 (m, 1), 7.19 (m, 5), Cram-threo (**19**, R' = i-Pr) 0.55 (br s, 1), 0.86 (d, J = 6.5 Hz, 3), 0.94 (d, J = 6.5 Hz, 3), 1.00 (d, J = 7 Hz, 3), 1.22 (d, J = 6.5 Hz, 3), 2.0–2.2 (m, 1), 2.4–2.9 (m, 3), 4.7–5.1 (m, 2), 5.5–6.0 (m, 1), 7.17 (m, 5), anti-Cram-threo (**20**, R' = i-Pr) 0.37 (br s, 1), 0.62 (d, J = 6.5 Hz, 3), 0.82 (d, J = 6.5 Hz, 3), 1.01 (d, J = 7 Hz, 3), 1.25 (d, J = 7 Hz, 3), 1.7–2.9 (m, 4), 4.9–5.1 (m, 2), 5.6–6.0 (m, 1), 7.19 (m, 5), anti-Cram-erythro (**21**, R' = i-Pr) 0.69 (d, J = 6 Hz, 3), 0.93 (d, J = 6.5 Hz, 3), 0.99 (d, J = 7 Hz, 3), 1.23 (d, J = 6.5 Hz, 3), 0.99 (d, J = 7 Hz, 3), 1.23 (d, J = 6.5 Hz, 3), 0.99 (d, J = 7 Hz, 3), 1.23 (d, J = 6.5 Hz, 3), 0.99 (d, J = 7 Hz, 3), 1.23 (d, J = 6.5 Hz, 3), 0.99 (d, J = 7 Hz, 3), 1.23 (d, J = 6.5 Hz, 3). The GLPC retention times of these isomers on PEG 6000 (5%, 2 m, 130 °C) were as follows: **20** and **21** or between **18** and **19** could not be accomplished.

N-(1-Phenylethyl)-4-methyl-5-hexen-3-ylamine. Two isomers, 23 and 24 (R = Et), were detected by ¹H NMR and GLPC analyses: ¹H NMR (CCl₄) Cram-erythro (23, R = Et) δ 0.75 (br s, 1), 0.87 (t, J = 7 Hz, 3), 0.92 (d, J = 7 Hz, 3), 1.24 (d, J = 7 Hz, 3), 1.0–1.6 (m, 2), 2.0–2.3 (m, 1), 2.3–2.7 (m, 1), 3.89 (q, J = 6.5 Hz, 1), 4.9–5.2 (m, 2), 5.6–6.1 (m, 1), 7.1–7.5 (m, 5), Cram-threo (24, R = Et) 0.79 (t, J = 7 Hz, 3), 0.97 (d, J = 7 Hz, 3), 1.26 (d, J = 7 Hz, 3). Other signals were not clearly defined since the minor isomer 24 could not be isolated in pure form.

Stereochemistry of 18–21, 23, and 24. Iodolactonization. The iodolactonization was carried out as described previously.¹³ The stereochemistry was determined by the coupling constants of the oxazinone ring.¹³ Since anti-Cram-erythro 21 was obtained in low yield, the iodolactonization of this isomer was not performed.

6-(Iodomethyl)-5-methyl-4-(1-phenylethyl)-3-propylperhydro-1,3-oxazin-2-one. From 18 (R' = n-Pr), 25 (Cram-cis-trans) and 25 (Cram-

cis-cis) were obtained in a ratio of 82:18. From 19 (R' = n-Pr), 25 (Cram-trans-cis) was obtained as a sole product. From 20 (R' = n-Pr), 25 (anti-Cram-trans-cis) was obtained as a sole product. 25 (Cramcis-trans): mp 121.5-122.5 °C (colorless prism); ¹H NMR (CDCl₃), 400 MHz) δ 0.846 (d, J = 7.019 Hz, 3), 1.067 (t, J = 7.324 Hz, 3), 1.489 (d, J = 7.019 Hz, 3), 1.73–1.83 (m, 2), 2.456 (qdd, J = 7.019, 4.273, and 7.935 Hz, 1), 2.750 (ddd, J = 6.103, 8.239, 14.038 Hz, 1), 3.305 (qi, J = 7.019 Hz, 1), 3.474 (dd, J = 3.052, 11.291 Hz, 1), 3.677 (dd, J =4.273, 7.019 Hz, 1), 3.783 (dd, J = 3.052, 11.291 Hz, 1), 4.022 (ddd, J = 3.052, 3.052, 7.935 Hz, 1), 4.124 (ddd, J = 6.409, 8.545, 14.038 Hz, 1), 7.37–7.51 (m, 5). Anal. Calcd for $C_{17}H_{24}NO_2I$: C, 50.88; H, 6.03; N, 3.49; I, 31.62. Found: C, 50.96; H, 6.06; N, 3.35; I, 31.63. 25 (Cram-cis-cis): oil; ¹H NMR (CDCl₃, 400 MHz) δ 0.904 (t, J = 7.324Hz, 3), 0.990 (d, J = 7.019 Hz, 3), 1.4–1.7 (m, 2), 1.600 (d, J = 7.020Hz, 3), 2.654 (m, 1), 3.111 (ddd, J = 5.188, 10.071, 14.038 Hz, 1), 3.2-3.4 (m, 2), 3.495 (dd, J = 6.408, 10.070 Hz, 1), 3.935 (ddd, J =6.104, 10.071, 14.037 Hz, 1), 4.079 (dd, J = 4.883, 5.88 Hz, 1), 4.564 (ddd, J = 3.052, 6.049, 8.545 Hz, 1), 7.34-7.53 (m, 5). Anal. Calcd for C17H24NO2I: C, 50.88; H, 6.03; N, 3.49; I, 31.62. Found: C, 50.90; H, 6.00; N, 3.56; I, 31.67. 25 (Cram-trans-cis): mp 108-108.5 °C (colorless prism); ¹H NMR (CDCl₃, 400 MHz) δ 0.834 (d, J = 6.714 Hz, 3), 0.959 (t, J = 7.324 Hz, 3), 1.410 (d, J = 7.019 Hz, 3), 1.51–1.58 (m, 1), 1.73-1.80 (m, 1), 2.158 (qdd, J = 6.714, 1.37, 3.051 Hz, 1), 2.88-2.95 (m, 2), 3.045 (qd, J = 7.019, 8.545 Hz, 1), 3.165 (dd, J =1.221, 8.850 Hz, 1), 3.215 (dd, J = 5.34, 9.9 Hz, 1), 3.953 (ddd, J =5.493, 10.986, 13.834 Hz, 1), 4.315 (ddd, J = 3.051, 6.108, 10.68 Hz, 1), 7.17–7.37 (m, 5). Anal. Calcd for $C_{17}H_{24}NO_2I$: C, 50.88; H, 6.03; N, 3.49; I, 31.62. Found: C, 50.89; H, 5.91; N, 3.59; I, 31.37. **25** (anti-Cram-trans-cis): oil; ¹H NMR (CDCl₃, 400 MHz) δ 0.635 (t, J = 7.324 Hz, 3), 0.937 (d, J = 7.019 Hz, 3), 1.357 (d, J = 7.019 Hz, 3), 1.2-1.8 (m, 2), 2.681 (qdd, J = 7.019, 2.136, 3.357 Hz, 1), 2.86-3.24 (m, 4), 3.406 (dd, J = 4.883, 10.071 Hz, 1), 4.694 (ddd, J = 3.357, 4.881, 10.375 Hz, 1), 7.16–7.37 (m, 5). Anal. Calcd for $C_{17}H_{24}NO_2I$: C, 50.88; H, 6.03; N, 3.49; I, 31.62. Found: C, 50.81; H, 5.93; N, 3.60; I. 31.50.

6-(Iodomethyl)-3-isopropyl-5-methyl-4-(1-phenylethyl)perhydro-1,3oxazin-2-one. From 18 (R' = i-Pr) and 20 (R' = i-Pr), 25 (Cram-cistrans) and 25 (anti-Cram-trans-cis) were obtained, respectively, as sole products. 25 (Cram-cis-trans): mp 79-80.5 °C (pale-yellow prism); ¹H NMR (CDCl₃, 400 MHz) δ 0.642 (d, J = 7.019 Hz, 3), 1.219 (d, J = 6.714 Hz, 3), 1.283 (d, J = 7.019 Hz, 3), 1.331 (d, J = 6.714 Hz, 3), 2.122 (qdd, J = 7.019, 4.273, 10.937 Hz, 1), 3.087 (qi, J = 7.019 Hz, 1), 3.250 (dd, J = 3.357, 11.292 Hz, 1), 3.450 (dd, J = 4.273, 7.019 Hz, 1)1), 3.579 (dd, J = 3.051, 11.291 Hz, 1), 3.741 (ddd, J = 3.052, 3.052, 10.937 Hz, 1), 3.822 (sp, J = 6.714 Hz, 1), 7.18–7.31 (m, 5). Anal. Calcd for C₁₇H₂₄NO₂I: C, 50.88; H, 6.03; N, 3.49; I, 31.62. Found: C, 50.78; H, 6.03; N, 3.41; I, 31.55. 25 (anti-Cram-trans-cis): mp 173.5-174.5 °C (yellow needles); ¹H NMR (CDCl₃, 400 MHz) δ 0.843 (d, J = 6.714 Hz, 3), 0.884 (d, J = 6.713 Hz, 3), 1.067 (d, J = 6.714Hz, 3), 1.296 (d, J = 7.019 Hz, 3), 2.573 (qdd, J = 6.714, 1.68, 3.052 Hz, 1), 2.763 (sp, J = 6.714 Hz, 1), 2.964 (qd, J = 7.019, 8.851 Hz, 1), 3.031 (dd, J = 10.071, 10.376 Hz, 1), 3.131 (dd, J = 1.68, 8.70 Hz, 1),3.343 (dd, J = 4.883, 9.766 Hz, 1), 4.597 (ddd, J = 3.052, 4.883, 10.376Hz, 1), 7.19–7.31 (m, 5). Anal. Calcd for $C_{17}H_{24}NO_2I$: C, 50.88; H,

11. (1), 1), 3.49; I, 31.62. Found: C, 50.80; H, 6.04; N, 3.33; I, 31.50. **4-Ethyl-6-(iodomethyl)-5-methyl-3-(1-phenylethyl)perhydro-1,3-oxa zin-2-one.** From **23** (R = Et) and **24** (R = Et), **26** (Cram-cis-trans) and **26** (Cram-trans-cis) were obtained, respectively, as sole products. **26** (Cram-cis-trans): mp 75–77 °C (colorless plate); ¹H NMR (CCl₄) δ 0.77 (d, J = 7 Hz, 3), 0.98 (t, J = 7 Hz, 3), 1.62 (d, J = 7.5 Hz, 3), 1.3–2.0 (m, 3), 2.7–3.0 (m, 1), 3.33 (dd, J = 3.25, 11.75 Hz, 1), 3.64 (dd, J = 3.25, 11.5 Hz, 1), 3.81 (ddd, J = 3.3, 3.3, 10 Hz, 1), 5.82 (q, J = 7.5Hz, 1), 7.48 (s, 5). Anal. Calcd for C₁₆H₂₂NO₂I: C, 49.62; H, 5.73; N, 3.62; I, 32.77. Found: C, 49.89; H, 5.75; N, 3.65; I, 32.71. **26** (Cram-trans-cis): mp 124.5–125.5 °C (yellow plate); ¹H NMR (CCl₄) δ 0.52 (d, J = 7.5 Hz, 3), 0.85 (t, J = 7.5 Hz, 3), 1.65 (d, J = 7.5 Hz, 3), 1.3–2.0 (m, 2), 2.28 (qdd, J = 7, 2.5, 2.5 Hz, 1), 2.78 (ddd, J = 2, 3.8, 10.5 Hz, 1), 3.05 (t, J = 10 Hz, 1), 3.37 (dd, J = 5.5, 10 Hz, 1), 4.60 (ddd, J = 3, 5.5, 10 Hz, 1), 5.60 (q, J = 7.5 Hz, 1), 7.47 (s, 5). Anal. Calcd for C₁₆H₂₂NO₂I: C, 49.62; H, 5.73; N, 3.62; I, 32.77. Found: C, 49.58; H, 5.71; N, 3.64; I, 32.97.

Stereochemistry of 25. X-ray Analysis. The X-ray analyses were carried out at Osaka University, Institute of Protein Research. Y. Y. would like to thank Prof. Yukiteru Katsube for performing the X-ray analyses.

Preparation of α-Imino Esters. *n*-Butyl N-((1S)-Phenylethyl)-αiminoacetate (27a). Freshly prepared *n*-butyl glyoxylate²⁶ (13 g, 0.1 mol)

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and (-)-(1S)-phenylethylamine (12.9 mL, 0.1 mol) were mixed in 50 mL of ether, and the mixture was stirred rapidly at room temperature for 10 h in the presence of small amounts of anhydrous MgSO4. Filtration of MgSO₄ followed by removal of ether in vacuo gave the desired imine in essentially quantitative yield. Without further purification, the imine could be used as the starting material. It was confirmed by the NMR analyses with a chiral shift reagent that 27a did not racemize at room temperature at least for 1 week. Distillation caused racemization to some extent: $[\alpha]^{24}_D - 18.2^\circ$ (neat, 5-cm cell), S form; ¹H NMR (CCl₄) δ 0.95 (t, J = 6.5 Hz, 3), 1.2-1.8 (m, 4), 1.52 (d, J = 6.5 Hz, 3), 4.20 (t, J = 6.5 Hz, 3)6.5 Hz, 2), 4.48 (q, J = 6.5 Hz, 1), 7.29 (s, 5), 7.67 (s, 1); IR (CCl₄) 740, 1090, 1230, 1390, 1450, 1500, 1580, 1620, 1720, 1750/cm⁻

n-Butyl N-((-)-1-Cyclohexylethyl)- α -iminoacetate (27b). Quite similarly, **27b** was prepared in essentially quantitative yield. (-)-1-Cyclo-hexylethylamine was given by BASF Co. Ltd.: $[\alpha]^{24}_{D}$ -17.5° (neat, 5-cm cell); ¹H NMR (CCl₄) δ 0.96 (t, J = 6 Hz, 3), 1.16 (d, J = 6 Hz, 3), 1.4 (m, 4), 1.7 (m, 11), 2.99 (qd, J = 6, 6 Hz, 1), 4.18 (t, J = 6 Hz, 2), 7.50 (s, 1); IR (CCl₄) 750, 890, 1190, 1280, 1390, 1440, 1640, 1720, 1750 cm⁻

n-Butyl N-(*p*-Toluenesulfonyl)- α -iminoacetate (27c).²⁷ In a 300-mL flask were placed n-butyl glyoxylate (6 g, 46 mmol), N-sulfinyl-ptoluenesulfonamide²⁸ (10 g, 46 mmol), and benzene (100 mL). To the mixture were added several drops of AlCl₃ dissolved in nitrobenzene under reflux. After 4.5 h, small amounts of water added, and the organic layer was extracted with ether. Drying and condensing produced a highly viscous oil: ¹H NMR (CCl₄) δ 0.96 (t, J = 7.5 Hz, 3), 1.2–1.8 (m, 4), 2.50 (s, 3), 4.25 (t, J = 6 Hz, 2), 7.30 (d, J = 9.5 Hz, 2), 7.80 (d, J =9.5 Hz, 2), 8.20 (s, 1); IR (CCl₄) 1020, 1090, 1150, 1330, 1600, 1750 cm⁻

Reaction of 27 with Allylic Organometallic Compounds. The reaction was carried out as described previously.^{8,13} Methallylzinc bromide and prenylzinc bromide were prepared from the corresponding Grignard reagents. Methallyl-9-BBN and prenyl-9-BBN were prepared according to the literature procedure.²⁹ All reactions were carried out on a 1 mmol scale under N_2 . To a dry THF solution of 27 cooled at -78 °C was added the metallic reagent (1.1 equiv), and the resulting mixture was warmed to room temperature over a period of 12 h. The reaction was quenched with water except for the reaction of boron reagents, in which a few drops of concentrated HCl were added at 0 °C to hydrolyze the B-N bond. Ethanolamide was then added to remove the BBN moiety. The product was isolated through a short column of silica gel (hexene/ether 10:1). the diastereomer ratio was determined by the 400-MHz ¹H NMR and/or the ¹³C NMR spectrum.

Butyl 2-(N-(1-Phenylethyl)amino)pent-4-enoate (28a): ¹H NMR $(CDCl_{1}, 400 \text{ MHz}) \delta$ (major isomer, Cram) 0.853 (t, J = 7.63 Hz, 3), 1.19-1.28 (m, 4), 1.190 (d, J = 6.41 Hz, 3), 1.876 (br s, 1), 2.260 (m, 2), 3.006 (t, J = 6.41 Hz, 1), 3.666 (q, J = 6.41 Hz, 1), 4.056 (m, 2), 4.96-5.06 (m, 2), 5.59-5.76 (m, 1), 7.233 (s, 5), (minor isomer, anti-Cram) 0.875 (t, J = 7.63 Hz, 3), 1.19–1.28 (m, 4), 1.155 (d, J = 6.1 Hz, 3), 1.876 (br s, 1), 2.339 (m, 2), 3.287 (t, J = 6.1 Hz, 1), 3.725 (q, J =6.1 Hz, 1), 3.924 (m, 2), 4.96-5.06 (m, 2), 5.59-5.76 (m, 1), 7.233 (s, 5); IR (neat) 780, 1160, 1300, 1330, 1410, 1450, 1730, 2920, 3400 cm⁻¹. The reaction with allylmagnesium chloride produced 1-(1-phenylethanimino)-2-(2-propenyl)pent-4-en-2-ol: ¹H NMR (CCl₄) δ 1.28 (d, J = 6 Hz, 3), 2.16 (d, J = 8.5 Hz, 4), 3.56 (br s, 1), 3.86 (q, J = 6 Hz, 1), 4.9–5.2 (m, 4), 5.5–6.1 (m, 2), 7.27 (s, 5), 7.60 (s, 1); IR (CCl₄) 690, 760, 780, 910, 1000, 1370, 1450, 1490, 1660, 2970, 3400 cm⁻¹

Butyl 2-(N-(1-Cyclohexylethyl)amino)pent-4-enoate (28b). Only one isomer was detected by 'H NMR spectroscopy, but ¹³C NMR clearly indicated the presence of only small amounts of isomer. The isomer ratio, 98:2 (96% de), was obtained from the analysis of the ¹³C NMR spectra: ¹H NMR (CCl₄) δ 0.90 (t, J = 6 Hz, 3), 0.99 (d, J = 6 Hz, 3), 1.1-1.8 (m, 15), 2.28 (dd, J = 6.5, 6.5 Hz, 2), 3.24 (t, J = 6.5 Hz, 1), 4.05 (t, J = 6 Hz, 2), 4.95-5.13 (m, 2), 5.56-5.97 (m, 1); ¹³C NMR (CDCl₃) δ (major isomer, Cram) 175.35, 133.90, 117.45, 64.26, 59.43, 56.28, 42.31, 37.99, 30.55, 29.85, 27.38, 26.70, 26.57, 26.36, 18.99, 17.26, 13.51, (minor isomer, anti-Cram) 175.03, 133.72, 117.51, 64.14, 58.64, 55.82, 43.54, 38.17, 30.55, 29.41, 28.17, 26.50, 26.41, 26.36, 18.99, 16.33, 13.51; IR (neat) 770, 790, 1190, 1280, 1460, 1740, 2880, 2950 cm

Butyl 4-Methyl-2-(N-(1-phenylethyl)amino)pent-4-enoate (28c): ¹H NMR (CCl₄) δ (major isomer, anti-Cram) 0.92 (t, J = 7 Hz, 3), 1.29 (d, J = 6 Hz, 3), 1.57 (s, 3), 2.19 (d, J = 7 Hz, 2), 3.03 (t, J = 7 Hz, 2)1), 3.66 (t, J = 6 Hz, 2), 4.02 (q, J = 6 Hz, 1), 4.70 (s, 2), 7.21 (s, 5), (minor isomer, Cram) 0.92 (t, J = 7 Hz, 3), 1.29 (d, J = 6 Hz, 3), 1.74 (s, 3), 2.27 (d, J = 7 Hz, 2), 3.38 (t, J = 7 Hz, 1), 3.92 (t, J = 6 Hz, 2), 4.02 (q, J = 6 Hz, 1), 4.70 (s, 2), 7.21 (s, 5); IR (neat) 780, 1160, 1300, 1370, 1450, 1730, 2920, 3400 cm⁻¹.

Butyl 2-(N-(1-Cyclohexylethyl)amino)-4-methylpent-4-enoate (28d): ¹H NMR (CCl₄) δ (major isomer) 0.86 (t, j = 6 Hz, 3), 0.94 (d, J = 7Hz, 3), 1.0–1.8 (m, 15), 1.73 (s, 3), 2.21 (d, J = 7 Hz, 2), 3.30 (t, J = 77 Hz, 1), 4.02 (t, J = 6 Hz, 2), 4.69 (s, 2), (minor isomer) 0.86 (t, J =6 Hz, 3), 0.94 (d, J = 7 Hz, 3), 1.0–1.8 (m, 15), 1.73 (s, 3), 2.33 (d, J= 7 Hz, 2), 3.37 (t, J = 7 Hz, 1), 4.02 (t, J = 6 Hz, 2), 4.69 (s, 2); IR (neat) 770, 790, 1190, 1270, 1465, 1740, 2880, 3000 cm⁻¹.

Butyl 3,3-Dimethyl-2-(N-(1-phenylethyl)amino)pent-4-enoate (28e): ¹H NMR (CCl₄) δ (major isomer in entry 10, Table IV) 0.90 (t, J = 6 Hz, 3), 1.05 (s, 6), 1.29 (d, J = 6 Hz, 3), 1.2–1.6 (m, 1), 1.74 (br s, 1), 2.96 (s, 1), 3.56 (q, J = 6 Hz, 1), 3.86 (t, J = 6 Hz, 2), 4.86–5.03 (m, 2), 5.66-6.02 (m, 1), 7.23 (s, 5), (minor isomer) 0.90 (t, J = 6 Hz, 3), 0.95 (s, 6), 1.29 (d, J = 6 Hz, 3), 1.2-1.6 (m, 4), 1.74 (br s, 1), 2.65 (s, 1), 3.56 (q, J = 6 Hz, 1), 4.05 (t, J = 6 Hz, 2), 4.86-5.03 (m, 2), 5.66-6.02 (m, 1), 7.23 (s, 5); IR (neat) 780, 1160, 1310, 1350, 1450, 1730, 2925, 3400 cm⁻¹

Butyl 3-Methyl-2-(N-(p-toluenesulfonyl)amino)pent-4-enoate (28f): ¹H NMR δ (erythro isomer) 0.88 (t, J = 6 Hz, 3), 1.09 (d, J = 7 Hz, 3), 1.2–1.6 (m, 4), 1.8–2.0 (m, 2), 2.41 (s, 3), 2.90 (d, J = 5 Hz, 1), 3.81 (t, J = 6 Hz, 2), 4.86-5.0 (m, 2), 5.60-6.0 (m, 1), 7.21 (d, J = 8 Hz, 3.20)2), 7.66 (d, J = 8 Hz, 2), (three isomer) 0.88 (t, J = 6 Hz, 3), 1.02 (d, J = 7 Hz, 3), 1.2–1.6 (m, 4), 1.8–2.2 (m, 2), 2.41 (s, 3), 2.80, (d, J =4 Hz, 1), 3.81 (t, J = 6 Hz, 2), 4.86–5.0 (m, 2), 5.6–6.0 (m, 1), 7.21 (d, J = 8 Hz, 2), 7.66 (d, J = 8 Hz, 2); IR (neat) 960, 1000, 1100, 1350, 1600, 1740, 2920, 3400 cm⁻¹

Stereochemistry of 28. Hydrogenation of 28a by use of Pd(OH)₂ was carried out as described above. The esterification of L-norvaline was carried out as follows. An excess of dry HCl was dissolved in a solution of butanol (50 mL) and L-norvaline (1.17 g, 10 mmol). The mixture was stirred overnight under gentle heating. After the mixture became a clear, pale-yellow solution, the solvent was removed in vacuo. The residue was washed with ether-water and purified by column chromatography in silica gel. 29: ¹H NMR (CCl₄) δ 0.95 (t, J = 6 Hz, 6), 1.2–1.7 (m, 8), 3.33 (br s, 2), 3.71 (d, J = 3 Hz, 1), 4.09 (t, J = 6 Hz, 2); IR (CCl₄) 780, 1220, 1240, 1460, 1520, 1610, 1740, 2960, 3400 cm⁻¹. Quite similarly, **30** was prepared from **28c**: ¹H NMR (CCl₄) δ 0.96 (br s, 9), $1.2-1.9 \text{ (m, 9)}, 3.28 \text{ (dd, } J = 6, 6 \text{ Hz}, 1), 4.02 \text{ (t, } J = 6 \text{ Hz}, 2); IR (CCl_4)$ 750, 840, 960, 1020, 1060, 1140, 1180, 1270, 1360, 1380, 1470, 1740, 2960, 3380 cm⁻¹. Reduction of 28e was carried out similarly to produce butyl 2-amino-3,3-dimethylpentanoate: $[\alpha]^{24}_{D}$ -16.3° (c 2.35, CHCl₃), from 27a bearing a (S)-(-)-1-phenylethylamine group; ¹H NMR (CCl₄) δ 0.78-1.02 (m, 6), 0.86 (s, 6), 1.22-1.68 (m, 8), 3.09 (s, 1), 4.06 (d, J = 6 Hz, 2), IR (CCl₄) 780, 1020, 1080, 1160, 1210, 1470, 1550, 1690, 1740, 2980 cm⁻¹. The corresponding amino acid derived from the imine bearing a (R)-(+)-1-phenylethylamine group exhibited $[\alpha]^{24}_{D}$ +16.6° (c 0.56, CHCl₃). Unfortunately, an authentic amino acid is not available, and thus the absolute stereochemistry cannot be determined. **28f** was converted to **31** according to the literature.³⁰ **31**: ¹H NMR (CDCl₃, 400 MHz) δ (erythro (trans) isomer) 1.171 (d, J = 6.41 Hz, 3), 3.439 (dd, J = 11.60, 3.66 Hz, 1), 3.223 (dd, J = 11.60, 6.10 Hz, 1), 3.878 (ddq, J = 6.41, 9.77, 7.62 Hz, 1), 4.570 (ddd, J = 6.10, 3.66, 9.77 Hz, 1), 5.732 (d, J = 7.62 Hz, 1), other shifts due to NHR' group are omitted, (threo (cis) isomer) 5.490 (d, J = 5.19 Hz, 1), other shifts are omitted; IR (CCl₄) 650, 725, 810, 905, 1090, 1160, 1340, 1450, 1590, 1790, 2920, 2960, 3260 cm⁻¹

Butyl 3-Methyl-2-(N-(1-phenylethyl)amino)pent-4-enoate (32): ¹H NMR (CDCl₃, 400 MHz) δ (Cram-erythro isomer) 0.90 (t, J = 6 Hz, 3), 1.066 (d, J = 6.71 Hz, 3), 1.188 (s, 1), 1.310 (d, J = 6.41 Hz, 3), 1.51-1.62 (m, 4), 2.32-2.54 (m, 1), 3.200 (d, J = 6.40 Hz, 1), 3.711 (q, J)J = 6.41 Hz, 1), 4.106 (t, J = 6 Hz, 2), 4.94–5.07 (m, 2), 5.60–5.80 (m, 1), 7.299 (s, 5); IR (CCl₄) 700, 760, 790, 920, 1160, 1200, 1460, 1480, 1740, 2940, 2980, 3400 cm⁻¹. Three other minor isomers were isolated from the reaction of 27a with crotyltitanium and magnesium reagents. The relative stereochemistries were assigned from the characteristics of the reagents, and hence the assignment was not unambiguous: ¹H NMR δ (Cram-threo isomer) 0.87 (t, J = 6 Hz, 3), 1.022 (d, J = 7.02 Hz, 3), 1.188 (s, 1), 1.318 (d, J = 6.7 Hz, 3), 1.51–1.62 (m, 4), 2.32–2.54 (m, 1), 3.163 (d, J = 6.20 Hz, 1), 3.706 (q, J = 6.71 Hz, 1), 3.985 (t, J =6 Hz, 2), 4.94-5.07 (m, 2), 5.60-5.80 (m, 1), 7.299 (s, 5), (anti-Cramthreo isomer) 0.90 (t, J = 6 Hz, 3), 1.029 (d, J = 7.02 Hz, 3), 1.188 (s, 1), 1.318 (d, J = 6.71 Hz, 3), 1.51–1.62 (m, 4), 2.32–2.54 (m, 1), 2.901 (d, J = 6.41 Hz, 1), 3.647 (q, J = 6.72 Hz, 1), 3.969 (t, J = 6 Hz, 3),4.94-5.07 (m, 2), 5.60-5.80 (m, 1), 7.299 (s, 5), (anti-Cram-erythro isomer) 0.89 (t, J = 3 Hz, 3), 1.060 (d, J = 6.71 Hz, 3), 1.188 (s, 1), 1.310 (d, J = 6.41 Hz, 3), 1.51–1.62 (m, 4), 2.32–2.54 (m, 1), 2.878 (d,

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⁽³⁰⁾ Tschaen, D. M.; Weinreb, S. M. Tetrahedron Lett. 1982, 23, 3015. (31) NMR abbreviations: sp, septet; q, quartet; qd, quartet-doublet; qi, quintet; sp-d, septet-doublet.

J = 6.41 Hz, 1), 3.637 (q, J = 6.41 Hz, 1), 4.123 (t, J = 6 Hz, 2), 4.94-5.07 (m, 2), 5.60-5.80 (m, 1), 7.299 (s, 5).

Stereochemistry of 32. Iodolactonization To Form 33. The iodolactonization was carried out as described above. 33: ¹H NMR (CDCl₃, 400 MHz) δ 0.978 (d, J = 6.71 Hz, 3), 1.339 (d, J = 6.41 Hz, 3), 2.321 (m, 1), 2.601 (ddd, J = 10.37, 1.16, 1.00 Hz, 1), 3.019 (d, J = 0.80 Hz, 1), 3.365 (q, J = 6.41 Hz, 1), 3.451 (dd, J = 7.02, 1.16 Hz, 1), 3.486 (dd, J = 7.02, 1.00 Hz, 1), 7.344 (s, 5); IR (CCl₄) 690, 750, 780, 890, 900, 960, 1070, 1140, 1450, 1490, 1785, 2920, 2960 cm⁻¹. When the reaction product in the ratio 93:3:3:1 was converted into the five-membered ring, 33 was accompanied with small amounts of the isomeric lactones. Although this isomer could not be isolated in pure form, its H-2

peak appeared at δ 3.060 (d, J = 9.77 Hz, 1).

Stereochemistry of 32. Hydrogenation to 34. The hydrogenation was carried out as described above, and an authentic sample was prepared from L-alloisoleucine. **34**: ¹H NMR (CCl₄) δ 0.91 (t, J = 6 Hz, 3), 0.94 (t, J = 6 Hz, 3), 0.96 (d, J = 6 Hz, 3), 1.2-1.7 (m, 9), 3.51 (d, J = 6 Hz, 3), 0.96 (d, J = 6 Hz, 3), 1.2-1.7 (m, 9), 3.51 (d, J = 6 Hz, 3), 1.2-1.7 (m, 9), Hz, 1), 4.07 (t, J = 6 Hz, 2); IR (CCl₄) 780, 840, 950, 1020, 1070, 1170, 1210, 1380, 1460, 1600, 1730, 2860, 2920, 2960, 3360 cm⁻¹.

Supplementary Material Available: Complete listings of positional parameters, bond angles, and bond distances and structures for 25 (Cram-trans-cis) and 25 (anti-Cram-trans-cis) (13 pages). Ordering information is given on any current masthead page.

Reinvestigation of the Chemistry of Arylcarbenes in Polycrystalline Alcohols at 77 K. Secondary Photochemistry of Matrix-Isolated Carbenes

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Abstract: Photolysis of diphenyldiazomethane (DPDM) in frozen alcoholic matrices gives ground-state triplet diphenylcarbene (DPC). At 77 K ³DPC reacts primarily with alcohols by OH insertion to give ethers. Photolysis of ³DPC produces an excited carbene ³DPC* which reacts with the matrix by H-atom abstraction to ultimately give alcohol-type products. Secondary photolysis of triplet fluorenylidene at 77 K is not as prevalent as that of ³DPC.

Photolysis of diphenyldiazomethane (DPDM) in simple alcohols gives near quantitative yields of ethers by formal OH insertion. This reaction is generally believed to proceed via the low-lying singlet state of ¹DPC.² Sensitized photolysis of DPDM in



methanol generates the triplet ground state (3DPC) directly and yields ether 1 in quantitative yields.³ Very similar results are observed on photolysis of phenyldiazomethane.⁴ Several research



groups have explained this result by postulating a rapid triplet-singlet equilibration.⁵⁻⁷ It has also been proposed that ³DPC can react directly with methanol to give 1 by a surface crossing mechanism.⁴

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A near quantitative yield of 1 is observed over a wide temperature interval in fluid solution. Tomioka discovered, however, that photolysis of aryldiazo compounds in alcohols frozen to just below their melting points leads to a dramatic change in the product distribution.⁴ High yields of formal CH insertion products were observed under these conditions in addition to the OH insertion product. Tomioka attributed the change in product

$$\begin{array}{c} \overbrace{}^{\text{VI}}_{\text{H}+} & \underset{\text{CH}_{2}\text{CH}_{2}\text{CH}}{} & \overbrace{}^{\text{CH}_{2}\text$$

distribution to an exaltation in triplet carbene-hydrogen atom abstraction-recombination chemistry. Tomioka's findings and conclusions were consistent with earlier studies of Moss who studied the chemistry of carbenes in olefinic matrices.⁹ It was recognized that the equilibrium population of the low-lying singlet state of the carbene is vanishingly small at very low temperature

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