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**, N^5-ethyl-4a-hydroperoxy-N^3,N^{10}-dimethylisoalloxazine, 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 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 vs. concentration of substrate gave the second-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 = NH_2), 104-96-1; **6**, 7703-38-0; FADMO, 37256-73-8; Me_2S, 75-18-3; Et_2S, 352-93-2; *i*-Pr_2S, 625-80-9; *t*-Bu_2S, 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*-$BuNHCH_2Ph$, 2403-22-7; *i*-$BuNHCH_2Ph$, 42882-36-0; *sec*-$BuNHCH_2Ph$, 46120-25-6; *t*-$BuNHCH_2Ph$, 3378-72-1; *p*-$MeOC_6H_4S(O)Me$, 3517-99-5; N^3,N^{10}-dimethylisoalloxazine, 4074-59-3; N^5-ethyl-N^3,N^{10}-dimethylisoalloxazinium perchlorate, 104550-31-4; 4a,5-dihydro-N^5-ethyl-4a-hydroxy-N^3-methyl-N^{10}-(2,6-dimethylphenyl)isoalloxazine, 76030-62-1.

(67) Miller, A.; Bruice, T. C. *J. Chem. Soc., Chem. Commun.* **1979**, 896-897.
(68) Yoneda, F.; Sakuma, Y.; Ichiba, M.; Shinomura, K. *J. Am. Chem. Soc.* **1976**, *98*, 830-835.
(69) Prepared by the method of: Zincke, T.; Frohneberg, W. *Chem. Ber.* **1910**, *43*, 837-848.

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

Yoshinori Yamamoto,*† Shinji Nishii,† Kazuhiro Maruyama,‡ Toshiaki Komatsu,‡ and Wataru Ito‡

Contribution from the Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan, and Department of Chemistry, Faculty of Science, Kyoto University, Kyoto 606, Japan. *Received June 27, 1986*

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

(1) For example: Heathcock, C. H. *Comprehensive Carbanion Chemistry*; Durst, T., Buncel, E. Eds.; Elsevier: New York, 1984. Evans, D. A.; Nelson, J. V.; Taber, T. R. *Topics in Stereochemistry*; Wiley-Interscience: New York, 1982; Vol. 13, p 1. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1983; Vol. 2. Masamune, S. In *Organic Synthesis Today and Tomorrow*; Trost, B. M., Hutchinson, R., Eds.; Pergamon: New York, 1981; p 197. Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357.

†Tohoku University.
‡Kyoto University.

0002-7863/86/1508-7778$01.50/0

Table I. High Cram Selectivity in 1,2-Asymmetric Induction[a]

entry	imine 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*-Pr	MgCl	70:30

entry	aldehyde	allylorganometal	Cram(1):anti-Cram(2)
8	$PhCH(CH_3)CHO$	9-BBN	55:45
9		$SnBu_3/TiCl_4$	69:31
10		MgCl	60:40

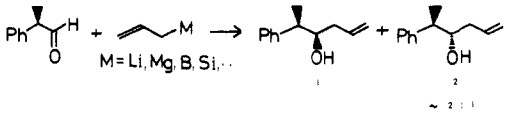
[a] All reactions were carried out on a 1 mmol scale, and the imine **3** and the aldehyde were used in a racemic form. [b] $PhCH(CH_3)CH{=}NR'$.

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.[7]

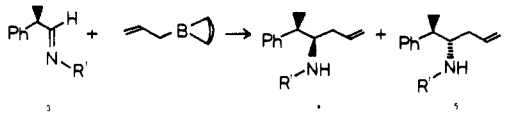
If efficient alkylation and high asymmetric induction are realized, such reactions become undoubtedly very useful for the synthesis of nitrogen-containing natural products, e.g., amino acids, β-lactams, and amino sugars. Previously, we communicated that the reaction of allyl-9-BBN with certain chiral 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



(1)



(2)

Scheme I

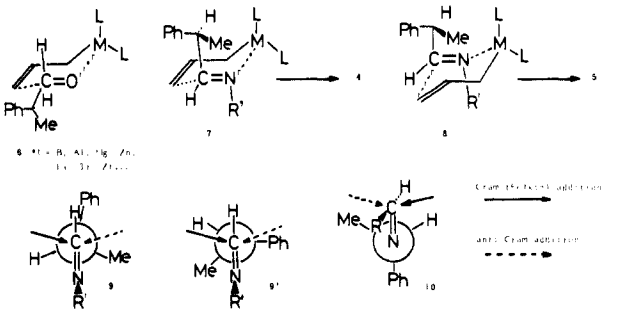
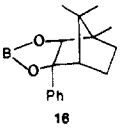


Table II. High 1,3-Asymmetric Induction[a]

entry	imine	allylorganometal (M)	Cram(12):anti-Cram(13)
1	**11**	9-BBN	92:8
2	(*R*)-**11**	$B(OCH_3)_2$	60:40[b]
3	(*R*)-**11**		67:33[b]
4	(*R*)-**11**	 **16**	80:20[b]
5	**17**	**16**	80:20[b]
6	**11**	$SnBu_3/TiCl_4$	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. [b] Data given by Prof. R. W. Hoffmann.

Table I. As shown in entries 8–10, the Cram selectivity of the aldehyde 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 geometry[10] 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 $TiCl_4$ 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 $TiCl_4$ at −78

(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.

(4) (a) Hoffmann, R. W.; Eichler, G.; Endesfelder, A. *Liebigs Ann. Chem.* **1983**, 2000. (b) Wuts, P. G. M.; Jung, Y. W. *Tetrahedron Lett.* **1986**, *27*, 2079.

(5) Layer, R. W. *Chem. Rev.* **1963**, *63*, 489. Stork, G.; Dowd, S. *J. Am. Chem. Soc.* **1963**, *85*, 2178.

(6) Scully, F. E., Jr. *J. Org. Chem.* **1980**, *45*, 1515.

(7) Thies, H.; Schonenberger, H. *Chem. Ber.* **1956**, *89*, 1918.

(8) Yamamoto, Y.; Komatsu, T.; Maruyama, K. *J. Organomet. Chem.* **1985**, *285*, 31. Midland has reported that the reduction of α-phenylpropionaldehyde with $LiBH(sec\text{-}Bu)_3$ proceeds with an exceptionally high Cram selectivity. Midland, M. M.; Kwon, Y. C. *J. Am. Chem. Soc.* **1983**, *105*, 3725.

(9) Significantly high Cram selectivity (92:8) has been realized with $CH_2{=}CHCH_2Ti(NR_2)_3$: Reetz, M. T.; Steeinbach, R.; Wenderoth, B.; Westermann, J. *Chem. Ind. (London)* **1981**, 541.

(10) McCarty, C. G. In *The Chemistry of the Carbon–Nitrogen Double Bond*; Patai, S., Ed.; Interscience: London, 1970; p 363.

(11) Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Am. Chem. Soc.* **1981**, *103*, 3229.

Table III. Stereoselectivity in Crotyl Organometallic Reactions

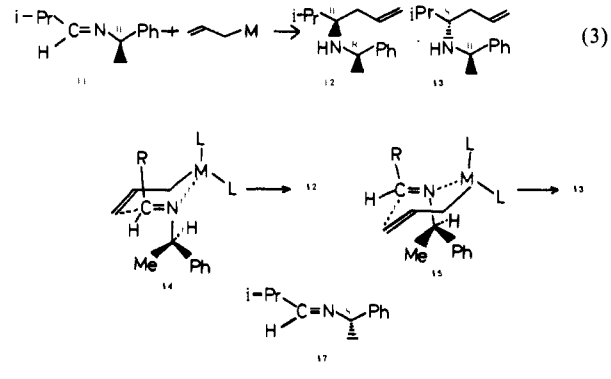
entry	imine 3, R′	crotylmetal (M)	18:19:20:21 18	19	20	21[a]	Cram:anti-Cram	erythro:threo
1	*n*-Pr	9-BBN	40	45	8	7	85:15	47:53
2	*n*-Pr	MgCl	18	68	3	11	86:14	29:71
3	*n*-Pr	$ZrCp_2Cl$	18	70	3	9	88:12	27:73
4	*i*-Pr	9-BBN	26	51	15	8	77:23	34:66

entry	imine 22	crotylmetal (M)	23:24 23	24	Cram:anti-Cram	erythro:threo
5	**22a**	9-BBN	75	25	100:0	75:25

[a] Cram-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 °C → room temperature → −78 °C) may complete the complexation of $TiCl_4$ with imines, and the lower selectivity is presumably a reflection of the acyclic transition state. Actually, the reaction of **3** with Bu_2CuLi/BF_3,[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.



(3)

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 CH_2Cl_2 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 BF_3, (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.

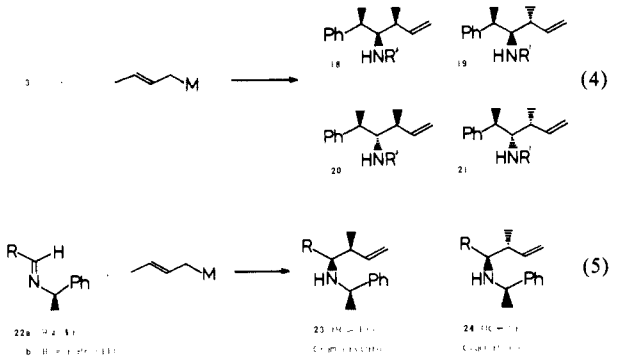
In conclusion, very high 1,2- and 1,3-asymmetric induction is realized in the reaction of allyl-9-BBN with chiral imines. The 1,2-asymmetric induction (Table I, entry 2) is 100%, while the 1,3-asymmetric induction (Table II, entry 1) is 92%. This is reasonable, since the 1,3-diaxial interaction is normally 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** (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 previously[13] (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 assignment[13] 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*, 3115.
(14) For a review on RCu/BF_3, R_2CuLi/BF_3, 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 **8′**, 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 (L^1 is the axial ligand). On the other hand, the interaction between Ph and L^2 in **14** is more favorable than the interaction between Me and L^2 in **15′**, another conformer of **15**, in which the hydrogen is in the position of Ph and Me is in the position of H: Ph–L^2 < Me–L^2 (L^2 is the equatorial ligand). The two conclusions seem to be contradictory. However, the distance between the chiral center and L^1 in **7**, **8**, and **8′** is different from the distance between the center and L^2 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.



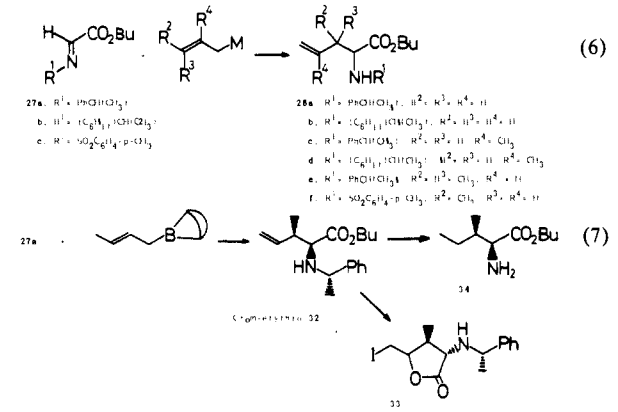
(4)

(5)

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 ^{1}H 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 R[13]. 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.



(6)

(7)

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

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

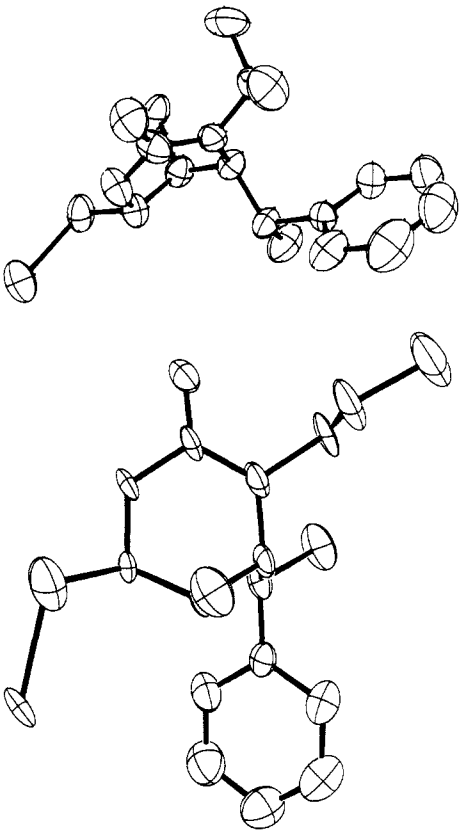
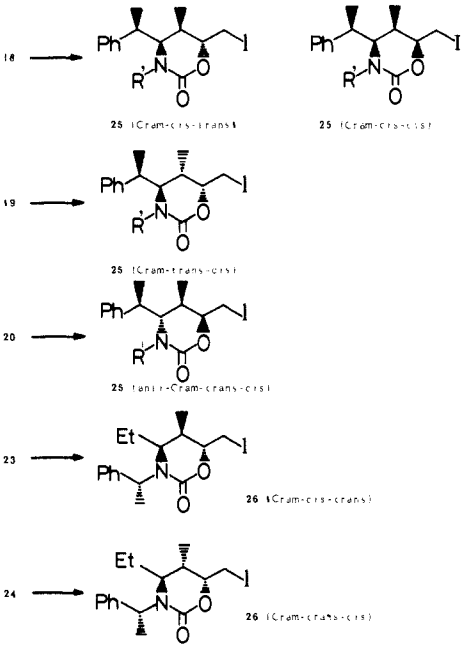


Figure 1. ORTEP stereoviews of **25**: (top) **25** (anti-Cram-trans-cis), R′ = *i*-Pr; (bottom) **25** (Cram-trans-cis), R′ = *n*-Pr.

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.

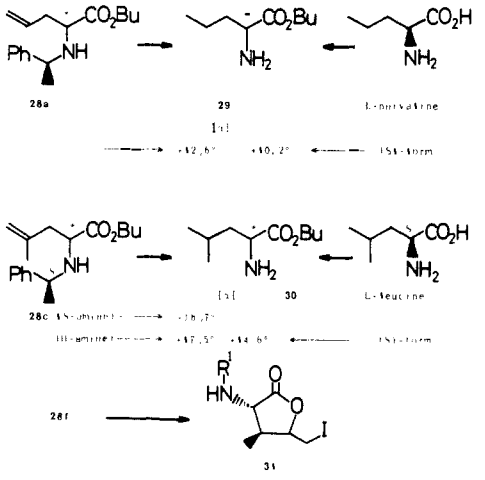
The structures of amino acid derivatives (**28**) were determined as shown in Scheme III. Compound **28a** was converted into **29**, $[\alpha]^{24}_D$ +12.6° (*c* 0.87, CH_2Cl_2), and authentic L-norvaline (*S* form) was also transformed into **29**, with a comparable $[\alpha]^{24}_D$ of +10.2° (*c* 5.55, CH_2Cl_2). It should be noted that very high 1,3-asymmetric induction is realized by use of a simple and

Table IV. Reaction of **27** with Allylic Organometallic Compounds

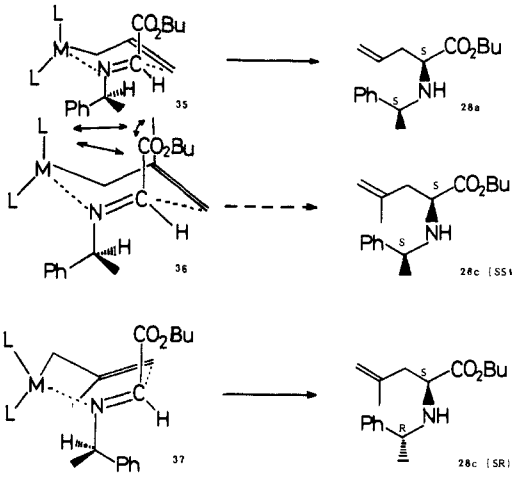
entry	27[b] (R^1)	allylmetal M	R^2	R^3	R^4	product	yield, %	de, %	erythro:threo
1	**27a**	9-BBN	H	H	H	**28a**	92	92	
2	**27a**	ZnBr	H	H	H	**28a**	94	10	
3	**27a**	MgCl	H	H	H	**28a**	*a*	0	
4	**27b**	9-BBN	H	H	H	**28b**	94	96	
5	**27b**	ZnBr	H	H	H	**28b**	53	30	
6	**27a**	9-BBN	H	H	CH_3	**28c**	80	90	
7	**27a**	ZnBr	H	H	CH_3	**28c**	83	16	
8	**27b**	9-BBN	H	H	CH_3	**28d**	94	78	
9	**27b**	ZnBr	H	H	CH_3	**28d**	90	14	
10	**27a**	9-BBN	CH_3	CH_3	H	**28e**	33	54	
11	**27a**	ZnBr	CH_3	CH_3	H	**28e**	60	16	
12	**27c**	9-BBN	CH_3	H	H	**28f**	75		85:15
13	**27c**	$Ti(O\text{-}i\text{-}Pr)_3$	CH_3	H	H	**28f**	75		60:40
14	**27c**	MgCl	CH_3	H	H	**28f**	78		59:41
15	**27c**	$Zr(Cp)_2Cl$	CH_3	H	H	**28f**	73		51:49

[a] A major product was the diallylated tertiary alcohol formed via the attack at the ester carbon. [b] **27a**, (*S*)-(−)-$CHPhCH_3$; **27b**, (−)-$CH(C_6H_{11})$-CH_3; and **27c**, $SO_2C_6H_4$-*p*-CH_3.

Scheme III



Scheme IV



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, $CHCl_3$), 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, $CHCl_3$). 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, $CHCl_3$). 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° (*c* 7.35, $CHCl_3$). An authentic sample prepared from L-alloisoleucine had $[\alpha]^{23}_D$ +12.0° (*c* 8.50, $CHCl_3$).

Other crotyl organometallic compounds, such as MgCl and $Ti(O\text{-}i\text{-}Pr)_3$, 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 1,2-asymmetric 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,

(19) Gaudemer, A. In *Stereochemistry*; Kagan, H., Ed.; George Thieme: Stuttgart, 1977; Vol. 1, p 44.

and thus methallylboration provides an opposite chiral induction. The boat transition state **37** may diminish such bad interactions. Consequently, **27** derived from (*R*)-(+)-$PhMeCHNH_2$ 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; ^{1}H NMR (CCl_4) 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; ^{1}H NMR (CCl_4) 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; ^{1}H NMR (CCl_4) 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; ^{1}H NMR (CCl_4) 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 ^{1}H 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); ^{1}H NMR (CCl_4) 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 ^{1}H 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); ^{1}H NMR (CCl_4) 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: ^{1}H NMR ($CDCl_3$, 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 $C_{16}H_{22}NO_2I$: 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: ^{1}H NMR ($CDCl_3$, 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 $C_{16}H_{22}NO_2I$: 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 iodolactonization, 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 $TiCl_4$,[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); ^{1}H NMR (CCl_4) 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 procedure[22] by use of 1-methyl-2-fluoropyridinium salt/Et_3N and LiN_3. **2-Phenyl-3-hexyl azide** was obtained in 75% yield: ^{1}H NMR (CCl_4) 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 (CCl_4) 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 $LiAlH_4$ (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 °C/2 mmHg) gave **2-phenyl-3-hexylamine** in 85% yield: ^{1}H NMR (CCl_4) 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 (CCl_4) 3400 cm^{-1}. This anti-Cram amine was treated with propanal in CH_2Cl_2 in the presence of anhydrous $MgSO_4$, as described previously.[13] Kugelrohr distillation (bp 95 °C/2 mmHg) gave ***N*-*n*-propylidene-2-phenyl-3-hexylamine** in an essentially quantitative yield: ^{1}H NMR (CCl_4) δ 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 $LiAlH_4$ in ether by using the same procedure as described above gave ***N*-*n*-propyl-2-phenyl-3-hexylamine** (anti-Cram isomer) in 85% yield: bp 80 °C/1 mmHg; ^{1}H NMR (CCl_4) δ 0.86 (t, *J* = 6.5 Hz, 6), 1.21 (d, *J* = 7 Hz, 3, $PhCCH_3$), 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 (CCl_4) 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 ^{1}H NMR chemical shift of $PhC(CH_3)$: 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): ^{1}H NMR (CCl_4) 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: ^{1}H NMR (CCl_4) 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 $C_{16}H_{22}NO_2I$: 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**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.779 (d, *J* = 6.72 Hz, 3), 0.816 (d, *J* = 6.71 Hz, 3), 1.6–1.8

(20) Brown, H. C.; Jadhav, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 2029. Brown, H. C.; Jadhav, J. K. *Tetrahedron Lett.* **1984**, *25*, 1215. Brown, H. C.; Jadhav, P. K; Perumal, P. T. *Ibid.* **1984**, *25*, 5111.

(21) Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Am. Chem. Soc.* **1981**, *103*, 1969.

(22) Hojo, K.; Kobayashi, S.; Soai, K.; Ikeda, S.; Mukaiyama, T. *Chem. Lett.* **1977**, 635.

(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 $C_{16}H_{22}NO_2I$: 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-(1*R*)-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 $MgSO_4$. 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); ^{1}H NMR (CCl_4) 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, $CHCl_3$). By use of the same procedure as described above, authentic (3*R*)-2-methyl-3-hexylamine was prepared from (3*S*)-(−)-2-methyl-5-hexen-3-ol, which was made according to the literature,[25] $[\alpha]^{23}_D$ +0.85 (c 0.18, $CHCl_3$). 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 ^{1}H 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 ^{1}H NMR signals of these anti-Cram isomers are shown.

***N*-Propyl-2-phenyl-4-methyl-5-hexen-3-ylamine**: ^{1}H NMR (CCl_4) Cram-erythro (**18**, 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**, 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**, R′ = *n*-Pr) 0.68 (t, J = 7.5 Hz, 3), 1.02 (d, J = 7 Hz, 3), 1.21 (d, J = 7 Hz, 3), anti-Cram-erythro (**21**, 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**: ^{1}H NMR (CCl_4) 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). The GLPC retention times of these isomers on PEG 6000 (5%, 2 m, 130 °C) were as follows: **20** and **21**, 6.9 min; **18** and **19**, 8.2 min. The separation between **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 ^{1}H NMR and GLPC analyses: ^{1}H NMR (CCl_4) 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** (Cram-cis-trans): mp 121.5–122.5 °C (colorless prism); ^{1}H NMR ($CDCl_3$), 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; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.904 (t, J = 7.324 Hz, 3), 0.990 (d, J = 7.019 Hz, 3), 1.4–1.7 (m, 2), 1.600 (d, J = 7.020 Hz, 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 $C_{17}H_{24}NO_2I$: 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); ^{1}H NMR ($CDCl_3$, 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; ^{1}H NMR ($CDCl_3$, 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-1,3-oxazin-2-one. From **18** (R′ = *i*-Pr) and **20** (R′ = *i*-Pr), **25** (Cram-cis-trans) and **25** (anti-Cram-trans-cis) were obtained, respectively, as sole products. **25** (Cram-cis-trans): mp 79–80.5 °C (pale-yellow prism); ^{1}H NMR ($CDCl_3$, 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), 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 $C_{17}H_{24}NO_2I$: 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); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.843 (d, J = 6.714 Hz, 3), 0.884 (d, J = 6.713 Hz, 3), 1.067 (d, J = 6.714 Hz, 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, 10.376 Hz, 1), 7.19–7.31 (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, 50.80; H, 6.04; N, 3.33; I, 31.50.

4-Ethyl-6-(iodomethyl)-5-methyl-3-(1-phenylethyl)perhydro-1,3-oxazin-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); ^{1}H NMR (CCl_4) 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 = 7.5 Hz, 1), 7.48 (s, 5). Anal. Calcd for $C_{16}H_{22}NO_2I$: 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); ^{1}H NMR (CCl_4) 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 $C_{16}H_{22}NO_2I$: 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*-((1*S*)-Phenylethyl)-α-iminoacetate (27a).** Freshly prepared *n*-butyl glyoxylate[26] (13 g, 0.1 mol)

(23) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, p 782.

(24) Huang, J. *J. Chin. Chem. Soc. (Peding)* **1948**, *15*, 233; *Chem. Abstr.* **1949**, 2166.

(25) Hoffmann, R. W.; Herold, T. *Chem. Ber.* **1981**, *114*, 375.

(26) *Organic Synthesis*; Wiley: New York, 1963; Collect. Vol. IV, p 124.

and (−)-(1*S*)-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 $MgSO_4$. Filtration of $MgSO_4$ 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° (neat, 5-cm cell), *S* form; ^{1}H NMR (CCl_4) 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, 2), 4.48 (q, *J* = 6.5 Hz, 1), 7.29 (s, 5), 7.67 (s, 1); IR (CCl_4) 740, 1090, 1230, 1390, 1450, 1500, 1580, 1620, 1720, 1750/cm^{-1}.

***n*-Butyl *N*-((−)-1-Cyclohexylethyl)-α-iminoacetate (27b).** Quite similarly, **27b** was prepared in essentially quantitative yield. (−)-1-Cyclohexylethylamine was given by BASF Co. Ltd.: $[\alpha]^{24}_D$ −17.5° (neat, 5-cm cell); ^{1}H NMR (CCl_4) 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 (CCl_4) 750, 890, 1190, 1280, 1390, 1440, 1640, 1720, 1750 cm^{-1}.

***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-*p*-toluenesulfonamide[28] (10 g, 46 mmol), and benzene (100 mL). To the mixture were added several drops of $AlCl_3$ 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: ^{1}H NMR (CCl_4) 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 (CCl_4) 1020, 1090, 1150, 1330, 1600, 1750 cm^{-1}.

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 ^{1}H NMR and/or the ^{13}C NMR spectrum.

Butyl 2-(*N*-(1-Phenylethyl)amino)pent-4-enoate (28a): ^{1}H NMR ($CDCl_3$, 400 MHz) δ (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: ^{1}H NMR (CCl_4) 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 (CCl_4) 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 ^{1}H NMR spectroscopy, but ^{13}C 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 ^{13}C NMR spectra: ^{1}H NMR (CCl_4) 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); ^{13}C NMR ($CDCl_3$) 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^{-1}.

Butyl 4-Methyl-2-(*N*-(1-phenylethyl)amino)pent-4-enoate (28c): ^{1}H NMR (CCl_4) 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, 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): ^{1}H NMR (CCl_4) δ (major 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), 2.21 (d, *J* = 7 Hz, 2), 3.30 (t, *J* = 7 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): ^{1}H NMR (CCl_4) 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): ^{1}H 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, 2), 7.66 (d, *J* = 8 Hz, 2), (threo 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**: ^{1}H NMR (CCl_4) 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 (CCl_4) 780, 1220, 1240, 1460, 1520, 1610, 1740, 2960, 3400 cm^{-1}. Quite similarly, **30** was prepared from **28c**: ^{1}H NMR (CCl_4) δ 0.96 (br s, 9), 1.2–1.9 (m, 9), 3.28 (dd, *J* = 6, 6 Hz, 1), 4.02 (t, *J* = 6 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, $CHCl_3$), from **27a** bearing a (*S*)-(−)-1-phenylethylamine group; ^{1}H NMR (CCl_4) 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 (CCl_4) 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, $CHCl_3$). 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**: ^{1}H NMR ($CDCl_3$, 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 (CCl_4) 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): ^{1}H NMR ($CDCl_3$, 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* = 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 (CCl_4) 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: ^{1}H 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-Cram-threo 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,

(27) Albrecht, R.; Kresze, G. *Chem. Ber.* **1965**, *98*, 1431.
(28) Kresze, G.; Wuckerpfenning, W. *Angew. Chem.* **1967**, *79*, 109.
(29) Kramer, G. W.; Brown, H. C. *J. Organomet. Chem.* **1977**, *132*, 9.
(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**: ^{1}H NMR ($CDCl_3$, 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 (CCl_4) 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**: ^{1}H NMR (CCl_4) 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, 1), 4.07 (t, J = 6 Hz, 2); IR (CCl_4) 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.

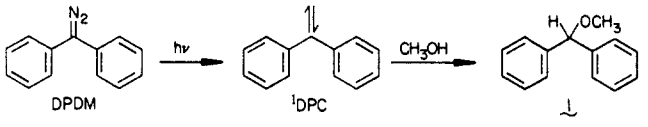
Reinvestigation of the Chemistry of Arylcarbenes in Polycrystalline Alcohols at 77 K. Secondary Photochemistry of Matrix-Isolated Carbenes

Elisa Leyva, Robert L. Barcus, and Matthew S. Platz*[1]

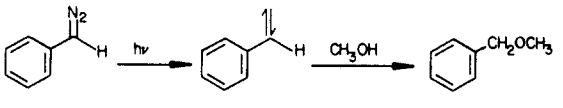
Contribution from the Department of Chemistry, The Ohio State University, Columbus, Ohio 43210. *Received June 23, 1986*

Abstract: Photolysis of diphenyldiazomethane (DPDM) in frozen alcoholic matrices gives ground-state triplet diphenylcarbene (DPC). At 77 K ^{3}DPC reacts primarily with alcohols by OH insertion to give ethers. Photolysis of ^{3}DPC produces an excited carbene ^{3}DPC* 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 ^{3}DPC.

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 ^{1}DPC.[2] Sensitized photolysis of DPDM in

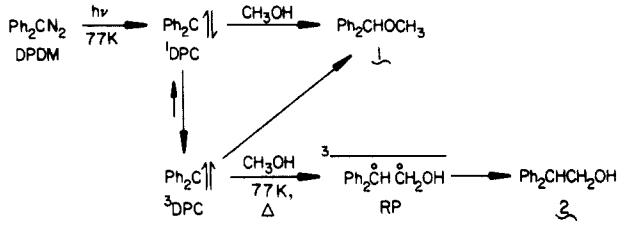


methanol generates the triplet ground state (^{3}DPC) directly and yields ether **1** in quantitative yields.[3] Very similar results are observed on photolysis of phenyldiazomethane.[4] Several research

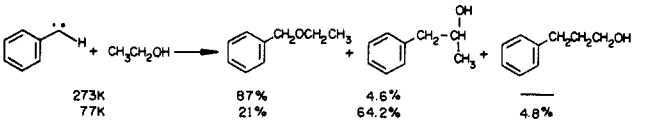


groups have explained this result by postulating a rapid triplet-singlet equilibration.[5-7] It has also been proposed that ^{3}DPC can react directly with methanol to give **1** by a surface crossing mechanism.[8]

Scheme I



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



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

(1) Camille and Henry Dreyfuss Teacher Scholar.
(2) W. Kirmse, *Carbene Chemistry*, 2nd ed; Academic: New York, 1971.
(3) Closs, G. L. *Top Stereochem.* **1968**, *3*, 193.
(4) (a) Tomioka, H.; Izawa, Y. *J. Am. Chem. Soc.* **1977**, *99*, 6128. (b) Tomioka, H.; Griffin, G. W.; Nishiyama, K. *J. Am. Chem. Soc.* **1979**, *101*, 6009.
(5) Bethell, D.; Stevens, G.; Tickle, P. *Chem. Commun.* **1970**, 792.
(6) Closs, G. L.; Rabinow, B. E. *J. Am. Chem. Soc.* **1976**, *98*, 8190.
(7) Eisenthal, K. B.; Turro, N. J.; Sitzmann, E. V.; Gould, I. R.; Hefferon, G.; Langan, J.; Cha, Y. *Tetrahedron* **1985**, *41*, 1543.
(8) Griller, D.; Nazran, A. S.; Scaiano, J. C. *Tetrahedron* **1985**, *41*, 1525.
(9) (a) Moss, R. A.; Joyce, M. A. *J. Am. Chem. Soc.* **1978**, *100*, 4475. (b) Moss, R. A.; Huselton, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 1314. (c) Moss, R. A.; Joyce, M. A. *J. Am. Chem. Soc.* **1977**, *99*, 1262. (d) Moss, R. A.; Dolling, U. *J. Am. Chem. Soc.* **1971**, *93*, 954.

0002-7863/86/1508-7786$01.50/0