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Chiral Phosphoramide-Catalyzed Enantioselective Addition of Allylic Trichlorosilanes to Aldehydes. Preparative and Mechanistic Studies with Monodentate Phosphorus-Based Amides

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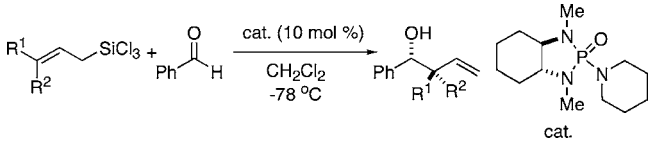

The addition of allylic trichlorosilanes to benzaldehyde promoted by chiral phosphoramides to give the enantioenriched homoallylic alcohol has been investigated. In a survey of Lewis bases as activators for the addition of allyltrichlorosilane to benzaldehyde, phosphorus-based amides have been found to be the most effective promoters. To achieve asymmetric induction, chiral phosphoric triamides derived from chiral diamines have been developed and applied in the allylation reaction albeit with modest enantioselectivities. The addition of 2-butenylsilanes was highly diastereoselective, suggesting a closed, chairlike transition structure. A detailed mechanistic study has been carried out to probe into the origin of activation. From a combination of nonlinear effects and kinetics studies, the reaction was found to likely involve two phosphoramides in both the rate and stereochemistry determining steps. These studies provided the background for the development of highly selective and reactive catalysts.

Introduction and Background

The invention and development of catalytic reactions with a high degree of predictable stereocontrol are among the most challenging and intensively studied frontiers in organic chemistry.[1] The enantioselective addition of allylic organometallic reagents to aldehydes has evolved into a powerful tactic in modern organic synthesis.[2] The high degree of both diastereoselectivity and enantioselectivity achieved, together with the latent functionality of the homoallylic alcohol product, make the reaction ideal for synthetic planning. Among the most common strategies to accomplish asymmetric allylation is the use of allylmetal reagents in which the chiral modifiers are covalently ligated to the metals such as boron,[3] titanium,[4] silicon,[5] and tin.[6] These reagents have been classified as Type I allylation reagents (Scheme 1) and one of the key features common to these reagents is the excellent diastereocontrol observed, which arises from a closed, chairlike transition structure organized around the metal. In addition, the chiral modifier is held in close proximity to the reaction center

(1) *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag: Heidelberg, Germany, 1999; Vols. I−III.

(2) For recent reviews of allylmetal additions see: (a) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 10. (b) Chemler, S. R.; Roush, W. R. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 11. (c) *Stereoselective Synthesis*, *Methods of Organic Chemistry* (*Houben-Weyl*), edition E21; Helmchen, G., Hoffmann, R., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, Germany, 1996; Vol. 3, pp 1357−1602.

(3) (a) Hoffmann, R. W. In *Stereocontrolled Organic Synthesis*; Trost, B. M., Ed.; Blackwell Scientific Publications: Cambridge, UK, 1994; pp 259−274. (b) Roush, W. R. In *Stereoselective Synthesis*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme Stuttgart: New York, 1995; Vol. E 21b, pp 1410−1486.

(4) (a) Duthaler, R. O.; Hafner, A. *Chem. Rev.* **1992**, *92*, 807−832. (b) Duthaler, R. O.; Hafner, A.; Alsters, P. L.; Rothe-Streit, P.; Rihs, G. *Pure Appl. Chem.* **1992**, *64*, 1897−1910. (c) Hoppe, D. In *Stereoselective Synthesis*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme, Stuttgart: New York, 1995; Vol. E 21b, pp 1551−1583.

(5) (a) Wang, Z.; Wang, D.; Sui, X. *Chem. Commun.* **1996**, 2261−2262. (b) Wang, D.; Wang, Z. G.; Wang, M. W.; Chen, Y. J.; Liu, L.; Zhu, Y. *Tetrahedron*: *Asymmetry* **1999**, *10*, 327−338. (c) Kinnaird, J. W. A.; Ng, P. Y.; Kubota, K.; Wang, X.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 7920−7921. (d) Kubota, K. Leighton, J. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 946−948.

(6) (a) Nishida, M.; Tozawa, T.; Yamada, K.; Mukaiyama, T. *Chem. Lett.* **1996**, 1125−1126. (b) Yamada, K.; Tozawa, T.; Nishida, M.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2301−2308.

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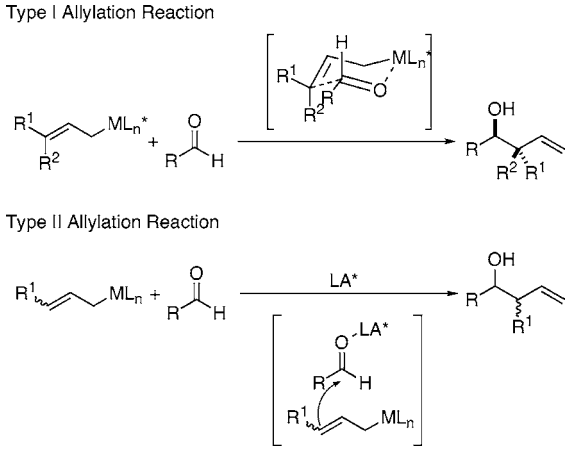
ensuring an effective transfer of stereochemical information for absolute stereocontrol. Despite the excellent selectivities obtained, this approach requires a stoichiometric amount of chiral ligand to modify the organometallic agent.

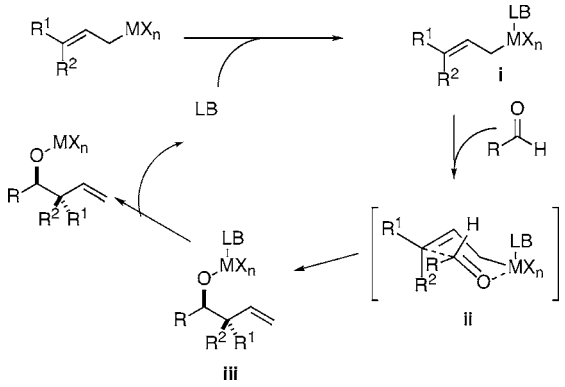
An alternative approach involves the use of chiral catalysts to promote and control asymmetric allylation.[7] This method is more attractive because it allows for the formation of large quantities of desired, enantiomerically pure compounds from simple, relatively small quantities of chiral catalysts. The majority of catalytic enantioselective allylations are the chiral-Lewis acid-catalyzed additions of allyltributylstannane or allyltrimethylsilane to aldehydes. These reactions are know to be classified as Type II allylations (Scheme 1) which proceed through an open transition structure.[8,9] The addition of γ-substituted allyl species generally gives the syn-diastereomer independent of the geometrical purity of the allylic reagent, which render the reaction much less useful for the introduction of γ-substituted species.

SCHEME 1



A mechanistically distinct process that addresses the problem of relative diastereocontrol is the chiral-Lewis base-catalyzed enantioselective addition of allylic trichlorosilanes to aldehydes.[10] The general scheme for this process, illustrated in Scheme 2, requires the coordination of a Lewis base to activate the allylic organometallic reagent. The metal center in the resulting ate complex **i** maintains sufficient Lewis acidity and further coordinates the aldehyde. The complex **ii** of allylmetal, aldehyde, and chiral Lewis base reacts through a closed transition structure. Thus, reaction through intermediate **ii** could provide a mechanism to control diastereoselectivity as well as to transmit the stereochemical information provided by the Lewis base. Finally, the dissociation of the Lewis base from the product trichlorosilyl ether **iii** liberates the ligand to reenter the catalytic cycle. This crucial turnover event is made possible due to the noncovalent association between the chiral Lewis base and chlorosilane substrate. In addition, this step also fundamentally distinguishes chiral Lewis base catalysis from chiral Lewis acid catalysis, which requires dissociation of the entire Lewis acid from the product.

SCHEME 2



The use of anionic activation or strong donor solvents in allylation reactions has been pioneered by Sakurai[11] and Kobayashi.[12] Specifically, the addition of allyl- and crotyltrifluorosilanes promoted by fluoride ion or catecholates has been extensively developed.[11] In these allylations, the intermediacy of five- and six-coordinate siliconate complexes that react through closed, chairlike structures has been convincingly documented (Scheme 2, MXn = SiF_3). In a related study, Kobayashi and co-workers describe the stereoselective allylation of aldehydes with allylic trichlorosilanes in dimethylformamide as the solvent.[12] The stereospecificity observed with 2-butenyltrichlorosilanes ($E \rightarrow$ anti, $Z \rightarrow$ syn) allowed these authors to propose a closed, chairlike transition structure with activation by DMF. The involvement of hypercoordinate silicon species is also supported by ^{29}Si NMR spectroscopic studies. The rate enhancement observed with an external Lewis base activator as well as the involvement of the Lewis base in the rate and stereochemistry determining step suggested the opportunity for asymmetric catalysis.

On the basis of this general conceptual framework and knowledge of the reactivity of allylic trihalosilanes, the first chiral Lewis base-catalyzed enantioselective allylation was reported from these laboratories in 1994.[13a] Since the appearance of that report, the design and development of more efficient catalysts has occupied significant efforts from these laboratories,[13b,c] as well as those of other research groups.[14] As

(7) For reviews on the catalytic enantioselective allylation reaction see: (a) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763−2793. (b) Yanagisawa, A. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag: Heidelberg, Germany, 1999; Vol. II, Chapter 27.

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(9) Recently, Lewis acid-catalyzed addition of allylboronates to aldehydes with high diastereoselectivities has been reported: (a) Kennedy, J. W. J.; Hall, D. G. *J. Am. Chem. Soc.* **2002**, *124*, 11586−11587. (b) (a) Kennedy, J. W. J.; Hall, D. G. *J. Org. Chem.* **2004**, *69*, 4412−4428. (c) Ishiyama, T.; Ahiko, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 12414−12415.

(10) For a highlight of chiral-Lewis base-catalyzed allylation see: Denmark, S. E.; Fu, J. *Chem.* Commun. **2003**, 167−170.

(11) (a) Sakurai, H. *Synlett* **1989**, 1−8. (b) Sakurai, H. In *Proceedings of the 5th International Kyoto Conference on New Aspects of Organic Chemistry*; Yoshida, Z.-I., Ohshiro, Y., Eds.; Kodansha Press: Tokyo, Japan, 1992; pp 129−157 and references therein. (c) Kira, M.; Zhang, L.; Kabuto, C.; Sakurai, H. *Organometallics* **1996**, *15*, 5335−5341.

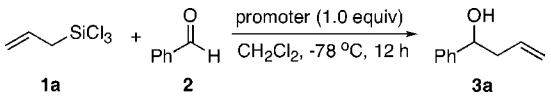
(12) (a) Kobayashi, S.; Nishio, K. *Tetrahedron Lett.* **1993**, *34*, 3453−3456. (b) Kobayashi, S.; Nishio, K. *Synthesis* **1994**, 457−459. (c) Kobayashi, S.; Nishio, K. *J. Org. Chem.* **1994**, *59*, 6620−6628. For additions to hydrazones, see: (d) Kobayashi, S.; Hirabayashi, R. *J. Am. Chem. Soc.* **1999**, *121*, 6942−6943. For propargylation, see: (e) Kobayashi, S.; Nishio, K. *J. Am. Chem. Soc.* **1995**, *117*, 6392−6393. For a recent review see: (f) Kobayashi, S.; Sugiura, M.; Ogawa, C. *Adv. Synth. Catal.* **2004**, *346*, 1023−1034.

is often the case in asymmetric catalysis, the success of this endeavor relies on the combination of empirical experimentation and careful mechanistic analysis. We describe below the interplay of mechanistic and synthetic studies that have led to the development of a highly enantioselective and general catalytic asymmetric allylation reaction.[15]

Results

1. Survey of Achiral Lewis Base Promoters. Although DMF promoted the addition of allylic trichlorosilanes to aldehydes, the necessity of using this agent as the solvent precluded an efficient catalytic process. Thus, as the point of entry, we assayed the ability of other Lewis bases to function as promoters for the addition in stoichiometric quantities. The initial survey included a variety of Lewis bases in the addition of allyltrichlorosilane **1a** to benzaldehyde **2** at room temperature. The reaction conversion was monitored by ^{1}H NMR spectroscopy, and in some cases, the yield of isolated product was determined (Table 1). In the absence of any Lewis base additive, no reaction was observed in C_6D_6 solution. Whereas DMF is an effective allylation promoter when used as solvent, 1.0 and 2.0 equiv of DMF in benzene are relatively ineffective, requiring 70 and 48 h to accomplish ca. 82% conversion (Table 1, entries 1 and 2). It was found that hexamethylphosphoric triamide (HMPA)[16] was much more effective than DMF as a promoter for the addition; 50% conversion was observed after 18 min (entry 2). The more hindered phosphoramide, tris(piperidino)phosphoric triamide (TPPA), was a slightly less potent promoter. Other strongly basic additives such as dimethyl sulfoxide and pyridine *N*-oxide were found to be incompatible with the trichlorosilane reagent.[17] The effect of the solvent on reaction rate was also examined in the allylation promoted by HMPA. The reactions in $CDCl_3$ and CD_3CN were even faster than those in C_6D_6; 63% conversion was observed within 4 min and high yields of the product could be obtained. Finally, the potential of using substoichiometric amounts of the promoter was demonstrated in entries 7−10. In benzene ca. 60% conversion was achieved in 46 h with 0.1 equiv of HMPA, and in other solvents, the reaction proceeded, but stalled in all three cases suggesting the intervention of product inhibition. It was especially encouraging that the reaction could be carried out with a substoichiometric amount of HMPA, which provided the foundation for development of a more efficient, catalytic process.

TABLE 1. Allylation of Benzaldehyde, Using Allyltrichlorosilane with Additives[a]



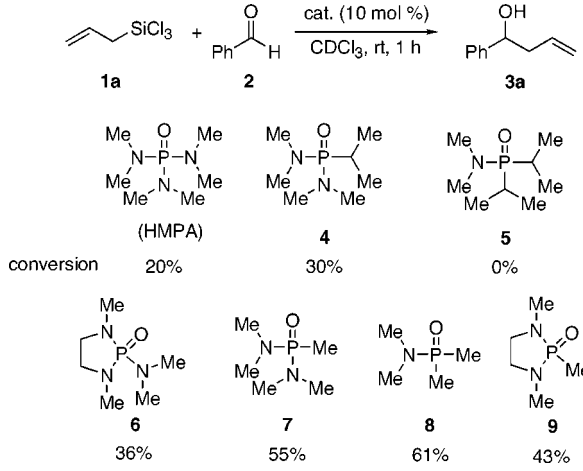
1a **2** **3a**

entry	additive (equiv)	solvent	$t_{1/2}$,[b] min	conversion, % (time)	yield,[c] %
1	DMF (1.0)	C_6D_6		83 (70 h)	
2	DMF (2.0)	C_6D_6		82 (48 h)	
3	HMPA (1.0)	C_6D_6	18		77
4	TPPA[d] (1.0)	C_6D_6	26		71
5	HMPA (1.0)	$CDCl_3$		63 (4 min)	85
6	HMPA (1.0)	CD_3CN		63 (4 min)	86
7	HMPA (0.1)	C_6D_6	529	60 (46 h)	
8	HMPA (0.2)	CD_3CN	397	80 (80 h)	69
9	HMPA (0.1)	$CDCl_3$		20 (1 h)	
10	HMPA (0.1)	d_8-THF	350	80 (124 h)	

[a] Reactions run at 1.0 M concentration. [b] Reaction monitored by ^{1}H NMR. [c] Yield of isolated product after complete consumption of **2**. [d] Tripiperidinophosphoric triamide.

Next, alkylphosphonic and alkylphosphinic amides[18] with different steric and electronic properties were surveyed in these additions (Scheme 3). The allylation of benzaldehyde with **1a** was carried out with 10 mol % of the promoter at 1.0 M in $CDCl_3$ for 1 h, and the formation of product was monitored by ^{1}H NMR spectroscopy.

SCHEME 3



With 10 mol % of HMPA, the addition of **1a** to benzaldehyde gave 20% conversion after 1 h at room temperature. The

(13) For preliminary communications see: (a) Denmark, S. E.; Coe, D. M.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem.* **1994**, *59*, 6161−6163. (b) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc.* **2000**, *122*, 12021−12022. (c) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc.* **2001**, *123*, 9488−9489.

(14) Other chiral Lewis bases have also been employed as promoter in the allylation reaction. For leading references to various promoter structures see: (a) Iseki, K.; Mizuno, S.; Kuroki, Y.; Kobayashi, Y. *Tetrahedron* **1999**, *55*, 977−988. (b) Hellwig, J.; Belser, T.; Muller, J. F. K. *Tetrahedron Lett.* **2001**, *42*, 5417−5419. (c) Nakajima, M.; Saito, M.; Shiro, M.; Hashimoto, S. *J. Am. Chem. Soc.* **1998**, *120*, 6419−6420. (d) Malkov, A. V.; Bell, M.; Orsini, M.; Pernazza, D.; Massa, A.; Hermann, P.; Meghani, P.; Kocovsky, P. *J. Org. Chem.* **2003**, *68*, 9659−9668. (e) Shimada, T.; Kina, A.; Ikeda, S.; Hayashi, T. *Org. Lett*. **2002**, *4*. 2799−2801. (f) Chataigner, I.; Piarulli, U.; Gennari, C. *Tetrahedron Lett.* **1999**, *40*, 3633−3634. (g) Angell, R. M.; Barrett, A. G. M.; Braddock, D. C.; Swallow, S.; Vickery, B. D. *Chem. Commun.* **1997**, 919−920. (h) Massa, A.; Malkov, A. V.; Kocovsky, P.; Scettri, A. *Tetrahedron* **2003**, *44*, 7179−7181. (i) Traverse, J. F.; Zhao, Y.; Hoveyda, A. H.; Snapper, M. L. *Org. Lett.* **2005**, *7*, 3151−3154. (j) Pignataro, L.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Celentano, G. *Chirality* **2005**, *17*, 396−403. (k) Müller, C. A.; Hoffart, T.; Holbach, M.; Reggelin, M. *Macromolecules* **2005**, *38*, 5375−5380. (l) Nakajima, M.; Kotani, S.; Ishizuka, T.; Hashimoto, S. *Tetrahedron Lett.* **2005**, *46*, 157−159.

(15) This paper focuses on the allylation reaction with monophosphoramides and those relevant mechanistic studies. The following paper focuses on the development of bisphosphoramides as catalysts.

(16) General references on the properties and the application of phosphoramides: (a) Normant, H. *Russ. Chem. Rev.* (*Engl. Transl.*) **1970**, *39*, 990−1049. (b) Jensen, W. B. *Chem. Rev.* **1978**, *78*, 1−22. (c) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; VCH: Weinheim, Germany, 1988. (d) Luteric, G. F.; Ford, W. T. *J. Org. Chem.* **1977**, *42*, 820−825. (e) Gutmann, V. *The Donor−Acceptor Approach to Molecular Interaction*; Plenum: New York, 1978.

(17) After our studies other laboratories have successfully employed DMSO and more complex heteroaromatic *N*-oxides as stoichiometric promoters and catalysts for allylation. See refs 12f, 14c, and 14h.

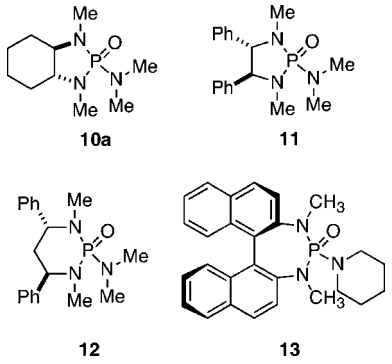
(18) For the preparation of phosphorus amides see: (a) Razvodovskaya, L. V.; Grapov, A. F.; Mel'nikov, N. N. *Zh. Obshch. Khim.* **1969**, *39*, 1260−1263. (b) Bollinger, J.-C.; Faure, R.; Yvernault, T. *Can. J. Chem.* **1983**, *61*, 328−333. (c) Ulrich, H.; Tucker, B.; Sayigh, A. A. R. *J. Org. Chem.* **1967**, *32*, 1360−1362. (d) Koizumi, T.; Haake, P. *J. Am. Chem. Soc.* **1973**, *95*, 8073−8079. (e) Burg, A. B.; Slota, P. J. *J. Am. Chem. Soc*. **1960**, *82*, 2145−2148. (f) Hanessian, S.; Bennani, Y. L.; Leblanc, Y. *Heterocycles* **1993**, *35*, 1411−1424.

isopropylphosphonic diamide **4**[18a] was more reactive than HMPA, reaching a 30% conversion in 1 h. The diisopropylphosphinic amide **5**,[18b] however, did not catalyze the addition at all. Decreasing the steric bulk of the carbon substituents to a methyl group in **6** and **7** led to increased reaction rates. A 55% conversion was observed with methylphosphonic diamide **7**,[18d] and the dimethylphosphinic amide **8**[18e] gave a 61% conversion (compare **7** vs **4** and **8** vs **5**).

The phosphoramide **6**[18c] containing a diazaphospholidine ring was more effective than HMPA in catalyzing the addition to achieve a 36% conversion to **3a**. Replacing the dimethylamino group in **6** with a methyl group in methylphosphonic diamide **9**[18f] led to a further increase in reactivity, but not as dramatically as would have been expected from the increase seen with **7**. These results clearly illustrate that the effectiveness of a promoter is related to a combination of the donor properties of the ligand and the steric accessibility of the oxygen atom. A systematic correlation of ligand structure, Lewis basicity with catalytic activity is in progress.

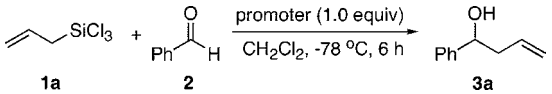
2. Reaction Promoted by Chiral Phosphorus Amides. 2.1. Phosphoramides. Although phosphonic and phosphinic amides showed enhanced reactivity, the gain was not sufficient to offset their lesser synthetic accessibility and the advantage that phosphoramides have in another easily modifiable group. Thus, as point of entry, we turned our efforts to a survey of chiral phosphoramide structures.[19] It was apparent that the nitrogen substituents provided a great opportunity for the preparation of chiral analogues by the use of chiral diamines[20] for the asymmetric modification. Thus, phosphoramides **10a**, **11**, **12**, and **13** (Chart 1) derived from readily available, enantiomerically pure diamines were prepared and evaluated for their ability to promote asymmetric allylation. The results of allylation of benzaldehyde with **1a** promoted by stoichiometric amounts of these promoters are summarized in Table 2. Among these compounds, the chiral phosphoramide (*R*,*R*)-**10a** based on (*R*,*R*)-*trans*-1,2-cyclohexanediamine provided the allylation product **3a** with the highest yet still modest enantioselectivity (er 80.0/20.0).

CHART 1



Encouraged by the enantioselectivity observed with **10a**, we further optimized the structure by varying the R^1 and R^2 substituents on the nitrogen atoms (Table 3). Both the enantioselectivity and reactivity decreased when the methyl groups on the internal nitrogen atoms (R^1) were changed to bulkier groups (Table 3, entries 2−5). For example, the phosphoramide **10b** (R^1 = Et) gave 79.5/20.5 er and the phosphoramide **10d** with a benzyl group at R^1 decreased enantioselectivity at 65.5/34.5. More strikingly, racemic **3a** was obtained in the reaction promoted by **10c** (R^1 = *i*-Pr) and no reaction was observed when **10e** (R^1 = CH_2-*t*-Bu) was used. The selectivity was also found to be sensitive to the substituents on the external nitrogen R^2 (entries 6−8). The phosphoramides **10f**, **10g**, and **10h** with *n*-propyl, isopropyl, or phenyl groups on the external nitrogen gave rather low enantioselectivities. The piperidine derivative **10i**, however, was marginally superior to **10a** (entry 9), providing the adduct with slightly increased yield. The effect of solvent was also briefly studied in the addition promoted by **10a**. Reactions performed in THF, toluene, and propionitrile (entries 10−12) provided similar enantioselectivities compared to that obtained in CH_2Cl_2, revealing little effect of solvent on the enantioselectivity.

TABLE 2. Addition of Allyltrichlorosilane 1a to Benzaldehyde Promoted by Chiral Phosphoramides[a]

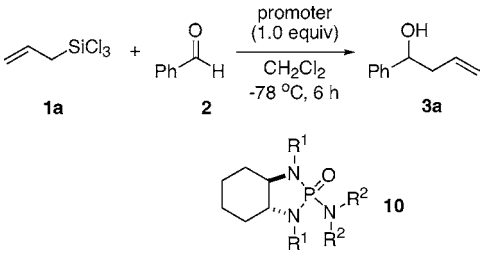


1a 2 3a

entry	promoter[b]	er[c]	yield, %
1	**10a**	80.0/20.0	78
2	**11**	66.5/33.5	
3	**12**	70.5/29.5	
4	**13**	60.0/40.0	43

[a] All reactions carried out at −78 °C for 6 h. [b] 1.0 M in each component. [c] Determined by CSP-GC.

TABLE 3. Allylation of Benzaldehyde, Using Allylic Trichlorosilane and Chiral Phosphoramides[a]



1a 2 3a

entry	promoter[b]	R^1	R^2	solvent[c]	er[d]
1	**10a**	Me	Me	CH_2Cl_2	80.0/20.0
2	**10b**	Et	Me	CH_2Cl_2	79.5/20.5
3	**10c**	*i*-Pr	Me	THF	0[e]
4	**10d**	Bn	Me	CH_2Cl_2	65.5/34.5
5	**10e**	CH_2*t*-Bu	Me	CH_2Cl_2	NR[e]
6	**10f**	Me	*n*-Pr	CH_2Cl_2	59.5/40.5
7	**10g**	Me	*i*-Pr	CH_2Cl_2	58.5/41.5
8	**10h**	Me	Ph	CH_2Cl_2	53.5/46.5
9	**10i**	Me	$-(CH_2)_5-$	CH_2Cl_2	80.0/20.0[f]
10	**10a**	Me	Me	THF	79.5/20.5
11	**10a**	Me	Me	toluene	77.0/23.0
12	**10a**	Me	Me	C_2H_5CN	80.5/19.5

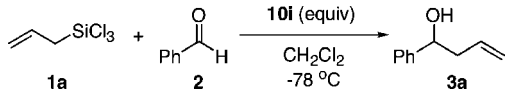
[a] All reactions carried out at −78 °C for 6 h. [b] 1.0 M in each component. [c] Determined by CSP-GC, *R*/*S*. [d] Yield of purified product 78%. [e] Reaction run at −78 °C to room temperature. [f] Yield of purified product 81%.

The absolute configuration of the major enantiomer of **3a** from (*R*,*R*)-**10i** was established to be (+)-(*R*)-**3a** by comparison to the optical rotations in the literature.[21a−c]

(19) Denmark, S. E.; Su, X.; Nishigaichi, Y.; Coe, D. M.; Wong, K.-T.; Winter, S. B. D.; Choi, J. Y. *J. Org. Chem.* **1999**, *64*, 1958−1967.

(20) For recent reviews on chiral 1,2-diamines, see: (a) Bennani, Y. L.; Hanessian, S. *Chem. Rev.* **1997**, *97*, 3161−3195. (b) Shimizu, M.; Fujisawa, T. *J. Synth. Org. Jpn.* **1998**, *56*, 672−680. (c) Lucet, D.; Le Gall, T.; Miokowski, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 2581−2627. (d) Kobayashi, S.; Horibe, M.; Saito, Y. *Tetrahedron* **1994**, *50*, 9629−9642.

TABLE 4. Addition of Allyltrichlorosilane to Benzaldehyde Catalyzed by 10i[a]



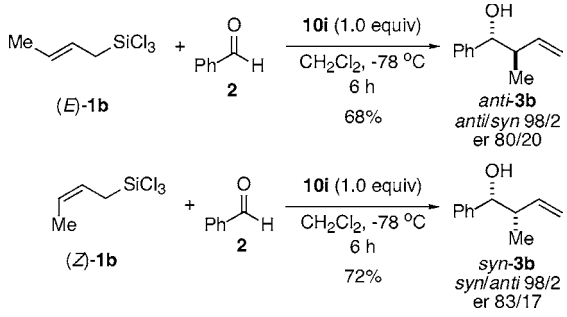
entry	**10i**, equiv	**1a**, equiv	time, h	yield, %[b]	er[c]
1	1.0	1.0	6	81	80.0/20.0
2	0.5	1.0	6	78	78.5/21.5
3	0.25	1.0	6	74	79.5/20.5
4	0.1	1.0	6	40	77.0/23.0
5	0.5	3.0	6	73	76.5/23.5
6	0.1	1.0	24	40	77.0/23.0

[a] All reactions carried out at −78 °C at 1.0 M. [b] Yield of chromatographically purified product. [c] Determined by CSP-GC.

The use of **10i** in substoichiometric quantities also led to decreases in yield and enantioselectivity, Table 4. Attempts to improve the conversion (yield) by increasing the loading of **1a** (entry 5) or extending reaction time (entry 6) were not successful.

To establish that the phosphoramide-promoted process is mechanistically related to the previously described reactions of allylic trihalosilanes, the reactions of benzaldehyde with (*E*)- and (*Z*)-2-butenyltrichlorosilane ((*E*)-**1b** and (*Z*)-**1b**), using **10i** as the promoter, were investigated. The reactions proceeded smoothly at −78 °C to afford the homoallylic alcohols with excellent diastereoselectivities following the expected pattern, *E* → anti and *Z* → syn (Scheme 4). The enantioselectivity in each case was nearly the same as observed in the addition of **1a**. The absolute configuration of the adducts (1*R*,2*R*)-**3b** and (1*R*,2*S*)-**3b** was established by comparison to the optical rotations in the literature.[21d] The high diastereoselectivity observed clearly supported a closed, chairlike transition structure as has been proposed by Sakurai and Kobayashi.[11,12]

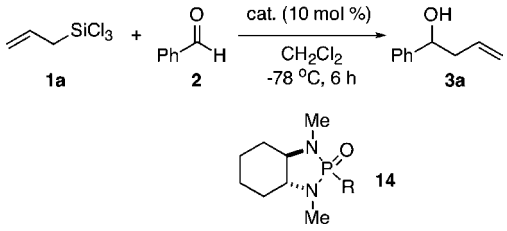
SCHEME 4



2.2. Phosphonamides. In view of the superior reactivity of alkyl phosphoramides **4**, **7**, and **9**, we prepared chiral phosphonic amides **14** derived from (1*R*,2*R*)-*N*,*N*-dimethyl-1,2-cyclohexanediamine for examination in the allylation reaction. The reaction in general gave rather low yields with a catalytic amount of promoter (Table 5). The methylphosphonic amide **14a**[22a] catalyzed the addition with a low enantioselectivity of 57.5/42.5. An improvement of the enantioselectivity was observed when other alkyl groups were utilized. However, the observed enantioselectivity did not correlate well with the bulk of the substituent. The highest enantioselectivity was provided by the phosphonic amide **14b** with an *n*-pentyl substituent. Furthermore, the phosphonic amide **14e**[22b] with a benzyl substituent gave racemic product in the addition.

3. Chiral Phosphoramides Derived from (*S*)-Proline. Chiral phosphoramides **17a**−**e** with pyrrolo[1,2-*c*][1,3,2]diazaphosphole

TABLE 5. Addition of Allyltrichlorosilane to Benzaldehyde Catalyzed by Phosphonic Amides[a]

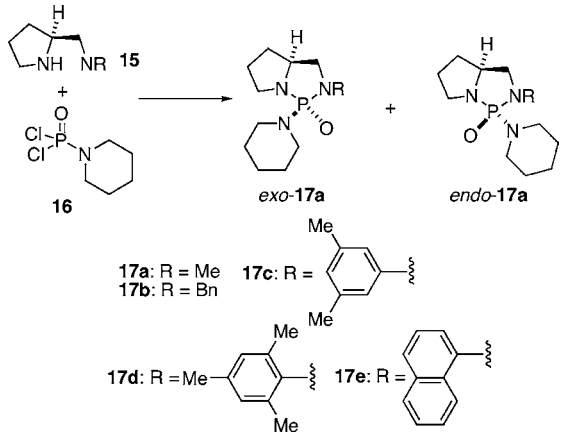


entry	cat.	R	yield, %	er[b]
1	**14a**	Me	28	57.5/42.5
2	**14b**	*n*-pentyl	27	83.0/17.0
3	**14c**	*i*-Bu	20	73.0/26.0
4	**14d**	*i*-Pr	25	77.5/22.5
5	**14e**	Bn	25	50.0/50.0

[a] All reactions carried out at −78 °C for 6 h. [b] Determined by CSP-GC.

skeletons have been synthesized and studied for their potential as catalysts in the allylation reaction.[14a] Mixtures of diastereomers were obtained when coupling the diamines with piperidinophosphoric dichloride, which could be separated by silica gel chromatography (Scheme 5). The configuration at the phosphorus center was assigned by ^{31}P NMR spectroscopy.[23] The ^{31}P NMR chemical shifts of the phosphoramides are listed in Table 6. The general trend is that diastereomers *endo*-**17** with P═O bonds endo to the [3.3.0] ring system (concave face) have ^{31}P NMR chemical shifts downfield with respect to the diastereomers *exo*-**17** with exo P═O bonds (convex face). The differences in the ^{31}P NMR chemical shifts are usually 4−5 ppm. In general, aromatic substituents shifted ^{31}P NMR resonances upfield. An X-ray crystal structure of **17c** (Figure 1) unambiguously established the configuration of *endo*-**17c** at the phosphorus center.[24]

SCHEME 5



(21) (a) Hoffmann, R. W.; Herold, T. *Chem. Ber.* **1981**, *114*, 375−383. (b) Roush, W. R.; Hoong, L. K.; Palmer, M. A.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 4109−4117. (c) Hafner, A.; Duthaler, R. O.; Marti, R.; Rihs, G.; Rothe-Streit, P.; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321−2336. (d) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339−6348.

(22) (a) Lawrence, R. M.; Biller, S. A.; Dickson, J. K. J.; Logan, J. V. H.; Magnin, D. R.; Sulsky, R. B.; DiMarco, J. D.; Gougoutas, J. Z.; Beyer, B. D.; Taylor, S. C.; Lan, S.-J.; Ciosek, C. P. J.; Harrity, T. W.; Jolibois, K. G.; Kunselman, L. K.; Slusarchyk, D. A. *J. Am. Chem. Soc.* **1996**, *118*, 11668−11669. (b) Zhang, Y.; Schuster, G. B. *J. Org. Chem.* **1995**, *60*, 7192−7197.

TABLE 6. Comparison of the ^{31}P NMR Chemical shifts of Phosphoramides *exo*- and *endo*-17

	δ ^{31}P NMR (ppm)[a]				
compd	**a**	**b**	**c**	**d**	**e**
exo-**17**	24.12	23.62	17.11	14.27	18.71
endo-**17**	28.22	28.36	22.51	22.20	22.88

[a] ^{31}P NMR (202 MHz) studies done in $CDCl_3$.

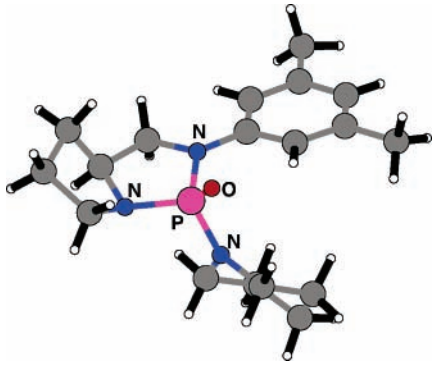
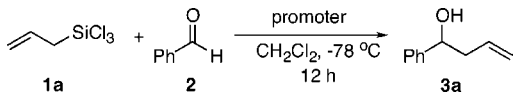


FIGURE 1. ORTEP drawing of *endo*-**17c** (35% thermal ellipsoids).

The selectivities of the chiral phosphoramides in promoting allylation reactions were evaluated with the model reaction between benzaldehyde and allyltrichlorosilane **1a** (Table 7). Originally the reaction was performed with only 1 equiv of **1a** but later it was increased to 5 equiv to reduce the loading of chiral promoters. Most of the phosphoramides (except *endo*-**17b)** promoted the reaction at −78 °C. Efficient conversions were observed in some cases at 25 mol % catalyst loading together with 5.0 equiv of **1a** (entries 5 and 7). Interestingly, in all cases except entry 1, the product (*R*)-**3a** was obtained as the major product regardless of the configuration of the phosphorus center, although the magnitude of enantioselectivity was poor in most cases. The phosphoramide *exo*-**17e** with a 1-naphthyl group on the nitrogen gave the highest enantioselectivity. In addition, the configuration at the phosphorus center does not have a consistent effect on the enantioselectivity, e.g. *endo*-**17c** gave higher er than *exo*-**17c** while *endo*-**17e** is less selective than *exo*-**17e**.

TABLE 7. Asymmetric Allylation with Phosphoramides[a]

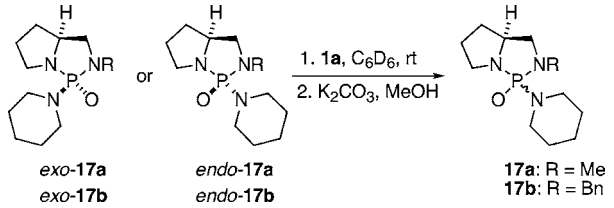


entry	promoter (equiv)	**1a**, equiv	yield,[b] %	er[c]	*R*/*S*[d]
1	*exo*-**17a** (1.0)	1	55	54.5/45.5	*S*
2	*endo*-**17a** (1.0)	1	72	63.0/37.0	*R*
3	*exo*-**17b** (1.0)	1	53	58.3/41.7	*R*
4	*endo*-**17b** (1.0)	1	NR		
5	*exo*-**17c** (0.25)	5	82	52.4/47.6	*R*
6	*endo*-**17c** (0.25)	5	61	79.6/20.4	*R*
7	*exo*-**17d** (0.25)	5	82	65.5/34.5	*R*
8	*endo*-**17d** (0.25)	5	21	52.4/47.6	*R*
9	*exo*-**17e** (0.25)	5	59	85.9/14.1	*R*
10	*endo*-**17e** (0.25)	5	27	66.7/33.3	*R*

[a] All reactions were carried out in CH_2Cl_2 at −78 °C unless otherwise noted. [b] Chromatographically homogeneous material. [c] Enantiomeric ratio determined by CSP-HPLC. [d] Determined by CSP-HPLC elution order and compared to optical rotation.

Interestingly, in the course of the catalyst survey in the allylation reactions, it was discovered that the recovered phosphoramides had suffered an epimerization at the phosphorus center. Thus, a study of this process was undertaken with the hope that some mechanistic insights may be gained for the allylation reaction as well. Solutions of pure phosphoramides (*exo*- and *endo*-**17a**, *exo*- and *endo*-**17b**) in C_6D_6 were mixed with allyltrichlorosilane **1a** and monitored at room temperature by ^{31}P NMR spectroscopy (Scheme 6). The epimerization of *endo*-**17a** by **1a** was observed within 4 min. Three signals in the ^{31}P NMR spectrum were observed (28.1, 24.8, and 21.8 ppm in a ratio of 29/1/3) after about 20 h and no further change was noted thereafter. With *exo*-**17a**, an exothermic reaction was observed and the solution turned yellow rapidly. After 60 h the reaction was quenched with K_2CO_3/MeOH solution and phosphoramides *exo*-**17a** and *endo*-**17a** were recovered in 80% yield in a 1/1 ratio.

SCHEME 6



The reactions of the benzyl phosphoramides *exo*-**17b** or *endo*-**17b** and **1a** were slower than those of the corresponding methyl series. Reaction with either *exo*-**17b** or *endo*-**17b** gave a mixture of both epimers in approximately the same ratio (endo/exo = 14/1) after about 60 h, suggesting that an equilibrium between *endo*-**17b** and *exo*-**17b** was established in the reaction mixture. A combined yield of 70% was recovered when starting with *exo*-**17b**.

4. Mechanistic Studies. Through the use of phosphoramides prepared from C_2-symmetric diamines, the utility of chiral Lewis bases in enantioselective allylation has been demonstrated. Despite significant efforts at improving the enantioselectivity by empirical modification of the promoter structure, a clear mechanistic picture for the origin of rate acceleration and stereoselection was still lacking. Among the important questions that mechanistic analysis should elucidate is the dependence of the enantioselectivity on the loading of phosphoramide **10i**. In the related aldol addition of trichlorosilyl enolates to aldehydes catalyzed by chiral phosphoramides, a similar dependence of selectivity on the promoter loading has been observed.[25] Mechanistic studies on the aldol reactions revealed the existence of two divergent pathways involving both first- and second-order dependence on catalyst and the intermediacy of cationic chlorosilyl species.[25c,d] This mechanistic insight provided an intriguing possibility for the allylation reaction.

(23) Peyronel, J.-F.; Samuel, O.; Fiaud, J.-C. *J. Org. Chem.* **1987**, *52*, 5320−5325.

(24) The crystallographic coordinates of *endo*-**17c** have been deposited with the Cambridge Crystallographic Data Centre; deposition no. CCDC 287231. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

(25) Chiral Lewis base-catalyzed aldol reactions: (a) Denmark, S. E.; Fujimori, S. In *Modern Aldol Reactions*; Mahrwald, R., Ed.; Wiley-VCH: Wienheim, Germany, 2004; Vol. 2, Chapter 7. (b) Denmark, S. E.; Stavenger, R. A. *Acc. Chem. Res.* **2000**, *33*, 432−440. (c) Denmark, S. E.; Su, X.; Nishigaichi, Y. *J. Am. Chem. Soc.* **1998**, *120*, 12990−12991. (d) Denmark, S. E.; Pham, S. M. *Helv. Chim. Acta* **2000**, *83*, 1846−1853.

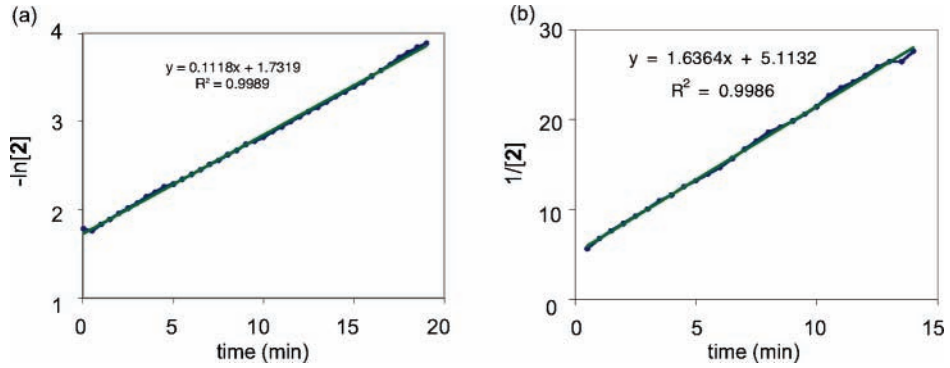


FIGURE 2. (a) Reaction order in **2**. (b) Reaction order in **2** and **1a**.

Because it has been demonstrated that more than one phosphoramide could be involved in the aldol addition transition structure, the mechanistic studies on the allylation reaction commenced on establishing the kinetic rate expression. Toward that end the kinetic parameters of the allylation were determined by in situ monitoring of the consumption of benzaldehyde by the use of a ReactIR 1000 instrument.[26] The order in benzaldehyde was established by using a large excess of **1a** (10 equiv) and 1.0 equiv of (*R*,*R*)-**10i**. Plotting −ln[**2**] versus time gave a straight line (R^2 = 0.9984),[27a] thus establishing first-order dependence in aldehyde (Figure 2). Order in **1a** was established indirectly by determining the overall reaction order at equimolar concentration of **1a**, **2**, and (*R*,*R*)-**10i**. For this experiment, a plot of $[\mathbf{2}]^{-1}$ versus time gave a straight line (R^2 = 0.9986),[27b] indicating that the reaction is overall second order and therefore first order in **1a**.

The reaction order in phosphoramide was established by determining the kinetic rate constants at various promoter concentrations. For these experiments, equimolar amounts of **1a** and **2** were used at catalyst loadings of 50−400 mol %. A ln/ln plot of the second-order rate constants ($\ln(k_{obs})$) versus the catalyst concentration (ln[(*R*,*R*)-**10i**]) gave a straight line (R^2 = 0.9987) with a slope of 1.77 (Figure 3). Clearly the reaction displays a higher order dependence on catalyst. Interestingly, the reaction order is less than 2.0, which could be due to the simultaneous operation of competing pathways involving both one and two phosphoramides.

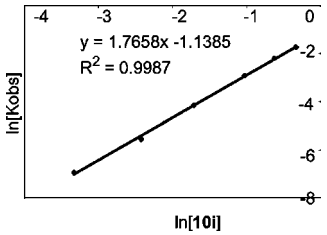


FIGURE 3. Reaction order in phosphoramide **10i**.

To establish if the stereochemistry determining step also involves two molecules of phosphoramide, we made use of the powerful method of asymmetric amplification by nonlinear effects, pioneered by Kagan.[28] Thus, the addition of allylic trichlorosilane **1a** to benzaldehyde was carried out with 1.0 equiv of promoter **10i** at varying enantiomeric composition. The results of this study, graphically depicted in Figure 4, clearly revealed a modest but real, positive nonlinear effect, which suggested that more than one phosphoramide is be involved in the stereochemistry determining step.[29]

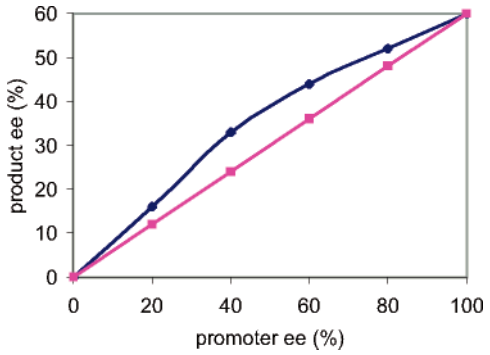


FIGURE 4. Nonlinear effect of allylation with promoter **10i**.

Discussion

1. Transition Structure Assembly. The addition of allylic trichlorosilanes to aldehydes has been reported to be promoted by a number of different Lewis bases such as formamides, phosphoramides, sulfoxides, amines, and amines *N*-oxides. In the addition of (*E*)- or (*Z*)-2-butenyltrichlorosilanes, excellent correlation of the product diastereoselectivities to the geometrical purities of silanes was observed, suggesting a closed, chairlike transition structure. Toward an understanding of the reaction mechanism, the nonlinear effect and kinetics studies provided a crucial insight into the transition structure assembly. Valuable information was provided by the kinetics studies. It was found that the reaction was first order in the allylic trichlorosilane and

(26) ReactIR 1000 fitted with a $^5/_8$ in. DiComp Probe, running software version 2.1a. ASI Applied Systems, Inc., 8223 Cloverleaf Drive, Suite 120, Millersville, MD 21108.

(27) (a) A second-order plot was clearly not linear. (b) A third-order plot was clearly not linear.

(28) (a) Guillaneux, D.; Zhao, S.-H.; Samuel, O.; Rainford, D.; Kagan, H. B. *J. Am. Chem. Soc.* **1994**, *116*, 9430−9439. (b) Fenwick, D.; Kagan, H. B. *Top. Stereochem.* **1999**, *22*, 257−296. (c) Girard, G. L.; Kagan, H. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 2922−2959. (d) Avalos, M.; Babiano, R.; Cintas, P.; Jimenez, J. L.; Palacios, J. C. *Tetrahedron*: *Asymmetry* **1997**, *8*, 2997−3017. (e) Kitamura, N.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028−4036. (f) Kitamura, N.; Suga, S.; Oka, H.; Noyori, R. *J. Am. Chem. Soc*. **1998**, *120*, 9800−9809.

(29) To support the operation of the "two-ligand model", we had to rule out the possibility that the nonlinear dependence was not arising from a reservoir effect[28e,f] or by interaction of the catalyst with the forming product. In the reaction promoted by **10i** of 60% ee, changing the stoichiometry of **1a** or benzaldehyde did not have an effect on the observed enantioselectivity. In addition, the enantiomeric composition of the product did not change with time. Thus, we could rule out both of those alternative interpretations.

aldehyde, respectively; however, most notably, the reaction order in the phosphoramide was 1.77. Clearly, the reaction was higher than first order in phosphoramide and could involve the simultaneous operation of two pathways involving first and second order dependence on catalyst. This conclusion was corroborated by the results of reactions catalyzed by nonenantiopure phosphoramide. The positive nonlinear effect observed suggested the possibility that more than one phosphoramide was also involved in the stereochemistry-determining transition structure. To propose the involvement of two phosphoramides in one of the transition structures requires that the silicon ionizes one chloride anion to produce a hexacoordinate octahedral cationic silicon species (Figure 5a), without this ionization, either a heptacoordinate silicon complex[30] or an open transition structure that does not bind the aldehyde to silicon must be invoked. The first scenario is highly unlikely, and the second is inconsistent with the complementary diastereoselectivity. Such ionization of chloride and intermediacy of cationic siliconate has also been proposed in other reactions with trichlorosilanes such as the aldol addition[25] and epoxide opening reactions.[31]

The involvement of ionic species as intermediates is also supported by the effect of ammonium salts on the reactivity as reported by Berrisford.[31b] It was found that in the addition of allyltrichlorosilane to benzaldehyde, the addition of 1.0 equiv of *n*-Bu_4NI slightly enhances the reaction rate. The rate enhancement may be explained by an increase in the ionic strength of the medium, which stabilizes the ionic transition structure.

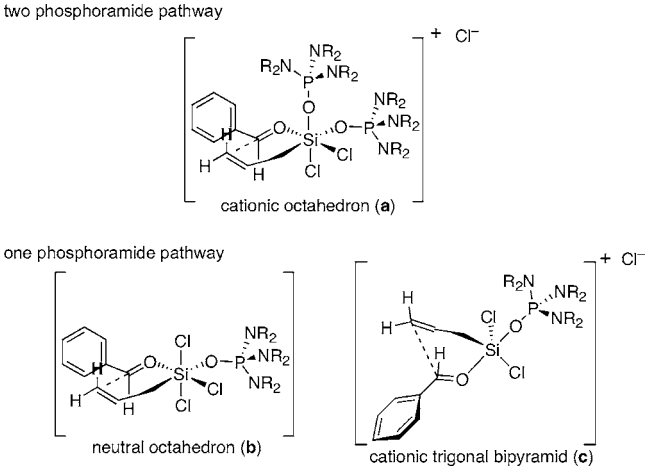


FIGURE 5. Transition structures with one or two phosphoramides.

The reaction order in the phosphoramide **10i** of less than 2.0 suggested the presence of a competing pathway involving only one phosphoramide. Thus, the reaction assembly of phosphoramide, allylic trichlorosilane, and aldehyde could react through a hexacoordinate, octahedral neutral transition structure (Figure 5b). Alternatively, ionization of one chloride anion could also take place, which would then produce a cationic, trigonal bipyramidal transition structure (Figure 5c). However, the lack of a significant drop in enantioselectivity at lower catalyst loadings suggests either (1) the (presumably less enantioselective[25]) one-phosphoramide pathway is not kinetically competent and the order of 1.77 arises from another phenomenon or (2) the one phsphoramide pathway is kinetically competent, but gives rise to the same sense and magnitude of enantioselectivity. At this time we cannot unambiguously eliminate either of these possibilites. Unlike the aldol addition, where a low selectivity, one phosphoramide pathway could be kinetically characterized, we have not been able to identify an analogous pathway here.[32]

2. Origin of Activation. In the allylation reaction, it is most likely that the allyl addition rather than any preequilibrium step is rate determining.[33] Thus, the reaction rates for these pathways would then depend on the reactivities of these complexes but not on the rate of their formation. The major pathway in the allylation reaction involves two phosphoramides and the transition structure is an ionic species (Figure 5a). The formation of such cationic silicon complexes in the presence of Lewis bases has also been documented in the reactions with phosphoramide•$SiCl_4$ complexes, in which the cationic silicon complexes could function as strong Lewis acids and activate aldehydes toward the addition of various nucleophiles. It is conceivable that in the cationic complex shown in Figure 5a the aldehyde is also activated by the strong Lewis acidic silicon toward the nucleophilic addition. Moreover, the coordination of Lewis bases to the silicon could also render the allyl group more nucleophilic.[30] Thus the mode of activation could be viewed as double activation of both aldehyde and allyl group.

In the transition structure with only one phosphoramide, there is no experimental support for either a hexacoordinate octahedral neutral transition structure or a cationic, trigonal bipyramidal transition structure. However, it is possible that the cationic, trigonal bipyramidal transition structure might be favorable due to the involvement of cationic, Lewis acidic silicon, which could activate the aldehyde. In addition, this cationic pathway with one phosphoramide has also been documented in the studies on the aldol reaction with trichlorosilyl enolates.[25]

3. Reaction Promoted by Chiral Phosphoramides. Although phosphoramides, especially hexamethylphosphoric triamide, have found extensive applications in organic chemistry, chiral phosphoramides have not been widely utilized in asymmetric catalysis.[34] Our design and implementation of chiral phosphoramide-promoted allylation clearly demonstrated that the three nitrogen subunits provided a great opportunity for a broad survey of diverse structural types.

In the reaction promoted by chiral phosphoramides, the dual mechanistic pathways have significant implication on the enantioselectivity. As shown in the generalized, hypothetical transition structures for both pathways, it is clear that the

(30) For reviews on the reactivity of hypervalent silicon see: (a) Kost, D.; Kalikhman, I. In *The Chemistry of Organic Silicon Compounds*; Rappoport, Z., Apeloig, Y., Eds.; Wiley: Chichester, UK, 1998; Vol. 2, Chapter 23. (b) Holmes, R. R. *Chem. Rev.* **1996**, *96*, 927−950. (c) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371−1448. (d) Tandura, S. N.; Voronkov, M. G.; Alekseev, N. V. *Top. Curr. Chem.* **1986**, *131*, 99−189.

(31) (a) Denmark, S. E.; Barsanti, P. A.; Wong, K.-T.; Stavenger, R. A. *J. Org. Chem.* **1998**, *63*, 2428−2429. (b) Short, J. D.; Attenoux, S.; Berrisford, D. J. *Tetrahedron Lett.* **1997**, *38*, 2351−2354.

(32) A referee has suggested that the allylation is operating under saturation kinetics. This cannot be the case as the kinetic equation clearly shows first-order behavior in both **1a** and benzaldehyde. Moreover, the order in (*R*,*R*)-**10i** was established from 50 to 400 mol % with respect to **1a**. If **1a** were saturated as a bis-phosphoramide complex, then the reaction rate would level off above 200 mol % of catalyst.

(33) In chiral Lewis base-catalyzed aldol addition reactions, kinetic isotope effect studies performed in these laboratories revealed that the rate determining step is the addition of nucleophile to complexed aldehyde. (a) Pham, S. M. Ph.D. Thesis, University of Illinois at Urbana−Champaign, 2000. (b) Denmark, S. E.; Bui, T. *J. Org. Chem.* **2005**, *70*, 10393−10399.

(34) (a) Buono, G.; Chiodi, O.; Wills, M. *Synlett* **1999**, 377−388. (b) Ansell, J.; Wills, M. *Chem. Soc. Rev.* **2002**, *31*, 259−268.

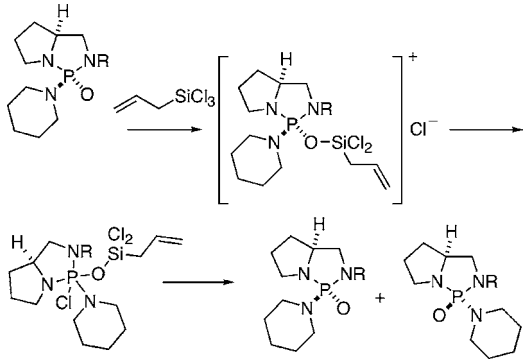
monophosphoramide pathway, if operative through a trigonal bipyramidal pentacoordinate siliconate, would be less enantioselective than a diphosphoramide pathway involving an octahedral hexacoordinate siliconate due to the diminished influence of the singular chiral promoter in the former (Figure 5). This competing, less selective pathway is probably the reason that only modest selectivity is observed in the allylation catalyzed by monophosphoramides.

In our systematic investigation of the effect of the *N*-substituent on the phosphoramide **10**, it was found that increasing the bulk of any substituents reduced the rate and/or selectivity. In the related aldol addition, it was found that the involvement of two phosphoramide pathways was highly dependent on the steric bulk of the phosphoramide.[25] With hindered phosphoramides, only one phosphoramide could coordinate to silicon in the transition structure, which provided the product in a slow reaction rate and low enantioselectivity. Such transition structure with one phosphoramide could also provide a possible explanation for low reactivity/selectivity observed with bulky phosphoramide in the allylation reaction. Thus, the coordination of two phosphoramides to silicon is not sterically accessible and with the activation of single phosphoramide the reaction proceeded through a nonselective and also slower pathway.

4. Phosphonamide and Phosphinamide Catalysts. Phosphonic amides **7** and **9** and unhindered phosphonic amide **8** all displayed enhanced activity as promoters compared to the phosphorus triamide analogues, HMPA and **6**. Analysis of the trends suggests that the steric accessibility of the basic phosphonyl group is largely responsible for the differences (cf. **4** vs **7**, **5** vs **8**, and **6** vs **9**). Clearly there is also an electronic effect from the donor amino groups but it is of lesser magnitude. (cf. HMPA vs **4** and **5**). Unfortunately, this enhanced reactivity did not translate to the chiral analogue **14**, which gave very low conversion (20−18%). Interestingly the *n*-pentyl derivative **14b** gave good selectivity (83.0/17.0) but not significantly superior to the more reactive phosphoric triamide **10i** (80.0/20.0).

5. Epimerization at the Phosphorus Centers. This fascinating observation has not heretofore been noted, most likely because most chiral phosphoramides used are of C_2 symmetry wherein the phosphoryl group is a nonstereogenic center. This isomerization is therefore an identity reaction of no consequence. The following mechanism was envisioned for the epimerization of phosphorus center (Scheme 7). Coordination of the phosphoramide to allyltrichlorosilane resulted in ionization of a chloride ion. Simultaneously, from activation by the Lewis acidic silicon, the phosphorus center was activated toward nucleophilic addition. Thus, association of the chloride ion to the phosphorus generated a pentacoordinate phosphorus species. Pseudorotation at the phosphorus center followed by loss of chloride provides a mechanism for the epimerization. The rate of epimerization, however, was found to be highly dependent on the phosphoramide structure both in the configuration of the phosphorus center and in its steric accessibility. The significance of this isomerization on the interpretation of stereoselectivity with this family of catalysts has not been addressed in the literature.[14a]

SCHEME 7



Conclusion

Phosphoric and phosphonic amides have been established as a class of highly active promoters for the addition of allylic trichlorosilanes to benzaldehyde. Various chiral phosphoric amides derived from chiral diamines have been developed and applied in the allylation reaction. Although a stoichiometric amount of promoter afforded the adduct in high yield, a decreased conversion were obtained when a catalytic amount of promoter was used. The enantioselectivity obtained, however, remained only modest. Nonetheless, the addition of 2-butenylsilanes afforded the adduct with high diastereoselectivity, suggesting a closed, rigid, chairlike transition structure. Mechanistic studies on the addition revealed that there are two phosphoramides in the rate and stereochemistry determining steps. The operation of dual mechanistic pathways has significant implications on the asymmetric catalysis, which suggest a direction for the development of highly selective, reactive catalysts. The successful evolution of dimeric catalyst to achieve this objective is the subject of the following paper.

Experimental Section

General Experimental. See the Supporting Information.

Experimental Procedures: Preparation of Phosphoric Amides Derived from (*R*,*R*)-*trans*-1,2-Cyclohexanediamine; Preparation of (*3aR*,*7aR*)-1,3-Dimethyloctahydro-2-piperidinyl-2*H*-1,3,2-benzodiazaphosphole-2-oxide (10i). A solution of 1-piperidinylphosphonic dichloride[35] (364 mg, 1.8 mmol) in dry ethyl acetate (2.5 mL) was added dropwise to a stirred solution of (*1R*,*2R*)-*N*,*N*-dimethyl-1,2-cyclohexanediamine (253 mg, 1.8 mmol, 1.0 equiv) and triethylamine (0.50 mL, 3.60 mmol, 2.0 equiv) in dry ethyl acetate (15 mL) at 0 °C under an atmosphere of nitrogen. The reaction mixture was allowed to warm slowly to room temperature over 2 h then stirred for an additional 10 h. The white suspension was filtered and the clear filtrate evaporated. The residue was purified by chromatography (silica gel, EtOAc/*i*-PrOH, 10/1) to afford a white solid. Recrystallization from hexane afforded 282 mg (58%) of **10i** as white needle crystals. Data for **10i**: mp 111−112 °C (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.12−2.98 (m, 4 H, $H_2C(1')$, $H_2C(5')$), 2.69−2.61 (m, 1 H, HC(3a or 7a)), 2.54−2.47 (m, 1 H, HC(3a or 7a)), 2.45 (d, J = 9.8 Hz, CH_3N), 2.43 (d, J = 10.7 Hz, CH_3N), 2.00−1.89 (m, 2 H, HC(3), HC(7)), 1.84−1.73 (m, 2 H, HC(3), HC(7)), 1.60−1.04 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) 65.5 (d, J = 9.2 Hz, C(3a) or C(7a)), 62.8 (d, J = 9.2 Hz, C(3a) or C(7a)), 45.31, 45.29, 28.8 (d, J = 1.5 Hz), 28.6 (d, J = 8.4 Hz), 28.43 (d, J = 3.6 Hz), 28.42, 28.3, 26.6 (d, J = 3.8 Hz), 24.7, 24.30, 24.25 (d, J = 1.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.50; IR (NaCl) 2932 (s), 2830 (m), 1443 (s), 1337 (s), 1302 (s), 1254 (s), 1227 (s), 1208 (s), 1177 (s), 1157 (s), 1121 (m), 1065 (s), 1024 (s), 1005 (s), 961 (s), 924 (s), 889 (m), 851 (m), 806 (s), 758 (s) cm^{-1}; MS (EI, 70 eV) 272 (M^+, 12), 271 (M^+, 26), 187 (17), 141 (12), 84 (100); Optical rotation $[\alpha]^{24}_D$ −90.78 (*c* 1.15, $CHCl_3$); TLC R_f 0.20 (EtOAc/*i*-PrOH, 10/1)

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[$KMnO_4$]. Anal. Calcd for $C_{13}H_{26}N_3OP$: C, 57.54; H, 9.66; N, 15.49; P, .11.41. Found: C, 57.49; H, 9.62; N, 15.40; P,11.36.

Addition of Allylic Trichlorosilanes to Benzaldehyde Promoted by 10i: Preparation of 1-Phenyl-3-buten-1-ol (3a). To a solution of (*R*,*R*)-**10i** (273 mg, 1.0 mmol) in 2.0 mL of CH_2Cl_2 under N_2 at −78 °C was added benzaldehyde (100 mL, 1.0 mmol, 1.0 equiv) and allyltrichlorosilane **1a**.[36] The resulting mixture was stirred at this temperature of 6.5 h, before being quenched with 2.0 mL of saturated aqueous $NaHCO_3$ solution and *tert*-butyl methyl ether. The layers were separated and the aqueous layer was extracted with *tert*-butyl methyl ether (3 × 50 mL). The combined organic layers were washed with brine and dried over Na_2SO_4 and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, CH_2Cl_2/pentane, 7/3) followed by Kugelrohr distillation to give 120 mg (81%) of **3a** as a colorless oil. Data for **3a**: bp 115−117 °C (15 mmHg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.25 (m, 5 H, HC(Aryl)), 5.86−5.76 (m, 1 H, HC-(3)), 5.20−5.13 (m, 2 H, H_2C(4)), 4.74 (dd, J = 7.8, 5.1 Hz, 1 H, HC(1)), 2.57−2.46 (m, 1 H, HC(2)), 2.16 (d, J = 3.4 Hz, 1 H, OH); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.8 (C(1′)), 134.4 (C(3)), 128.4 (C(3′)), 127.5 (C(4′)), 125.8 (C(2′)), 118.4 (C(4)), 73.2 (C(1)), 43.8 (C(2)); IR (NaCl) 3398 (b), 3075 (m), 3065 (m), 3030 (m), 2905 (m), 1641 (m), 1493 (m), 1432 (m), 1047 (s), 1000 (s), 988 (m) cm^{-1}; optical rotation $[\alpha]^{24}_D$ +31.7 (*c* 3.5, benzene) (lit.[37] $[\alpha]^{24}_D$ −17.8 (*c* 7.38, benzene) for 30% ee of (*S*)-**3a**); TLC R_f +0.24 (CH_2Cl_2/pentane, 7/3) [$KMnO_4$]; GC (*S*)-**3a**, t_R 26.42 min (20.0%); (*R*)-**3a**, t_R 27.18 min (80.0%) (Astec B−PA 110 °C isotherm).

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Supporting Information Available: Preparation and full characterization of **10a**−**e**, **6**, and **7**, all homoallylic alcohols, a representative allylation procedure, and all kinetic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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