(*S*)-3,3′-Dimethyl-2,2′-biquinoline *N*,*N*′-Dioxide as an Efficient Catalyst for Enantioselective Addition of Allyltrichlorosilanes to Aldehydes

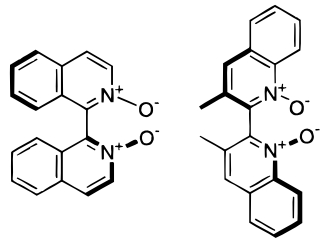
Makoto Nakajima,* Makoto Saito, Motoo Shiro,† and Shun-ichi Hashimoto

Graduate School of Pharmaceutical Sciences Hokkaido University, Sapporo 060-0812, Japan X-ray Research Laboratory, Rigaku Corporation Akishima 196-0003, Japan

Received April 1, 1998

The rational design and synthesis of novel chiral ligands directed toward catalytic, asymmetric reactions is currently the focus of attention in synthetic organic chemistry.[1] Given that amine *N*-oxides possess a notable electron-pair donor property to form complexes with a variety of metals,[2,3] the development of chiral amine *N*-oxides as chiral ligands or catalysts should be a significant addition to the field of asymmetric synthesis; however, there have been reported only a few attempts to use chiral amine *N*-oxides for this purpose.[4] In this context, of particular interest are the recent findings of Kobayashi[5] and Denmark[6] that DMF or HMPA coordinates to the silicon atom of allyltrichlorosilanes to form hypervalent silicates,[7,8] which in turn react with aldehydes via cyclic chairlike transition states to afford the corresponding homoallylic alcohols in a regio- and diastereospecific manner. As a logical extension of this reaction, Denmark has reported the first example of the catalytic, asymmetric version by the use of chiral phosphoramide derivatives as Lewis bases, albeit with modest levels of enantioselectivity.[6,9,10] Since amine *N*-oxides are known to exhibit a significant nucleophilicity toward the silicon atom,[11] we were intrigued by the feasibility of this catalytic, asymmetric process based on chiral amine *N*-oxide. Herein we describe a new catalytic, enantioselective allylation of aldehydes with allyltrichlorosilanes that exploits (*S*)-3,3′-dimethyl-2,2′-biquinoline *N*,*N*′-dioxide ((*S*)-**2**) as a catalyst, which affords homoallylic alcohols in high enantioselectivities of up to 92% ee.

At the outset, we examined addition of allyltrichlorosilane to benzaldehyde using 10 mol % of isoquinoline *N*-oxide as a catalyst. As expected, the reaction in dichloromethane proceeded smoothly at 23 °C for 12 h to afford the corresponding homoallylic alcohol in 76% yield. Encouraged by this finding, we undertook asymmetric allylation, employing 10 mol % of (*S*)-1,1′-biisoquinoline *N*,*N*′-dioxide ((*S*)-**1**),[12] which was patterned after (*S*)-1,1′-binaphthalene-2,2′-diol. However, the optical yield obtained here (23 °C, 2 h) was found to be less satisfactory (82% yield, 52% ee). To improve the enantioselectivity, we then adopted (*S*)-3,3′-dimethyl-2,2′-biquinoline *N*,*N*′-dioxide ((*S*)-**2**)[3a]



(*S*)-**1** (*S*)-**2**

as a chiral catalyst, wherein the *N*-oxide moieties were embedded within a chiral pocket created by the walls of the biaryl unit.[13] Indeed, we were gratified to find that the allylation reaction (23 °C, 2 h) under the influence of (*S*)-**2** (10 mol %) gave the (*R*)-enriched homoallylic alcohol in 90% yield and 71% ee. After considerable experimentation based on (*S*)-**2**,[14] we were very surprised to find that the allylation was notably accelerated by the addition of 5 equiv of diisopropylethylamine (23 °C, 10 min) and virtually the same enantioselectivity as above was obtained (90% yield, 71% ee). The beneficial effect of diisopropylethylamine on the reaction rate made it possible to conduct the reaction at −78 °C, thereby enhancing the enantioselectivity up to 88% ee.[15−17] It is noteworthy that this remarkable activation is obtained specifically with diisopropylethylamine, whereas other amines

* Address correspondence to this author at Hokkaido University.
† Rigaku Corporation.

(1) (a) Ojima, I., Ed. *Catalytic Asymmetric Synthesis*, VCH: New York, 1993. (b) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994.

(2) For a review on amine *N*-oxide complexes, see: Karayannis, N. M.; Pytlewski, L. L.; Mikulski, C. M. *Coord. Chem. Rev.* **1973**, *11*, 93−159.

(3) Studies on bipyridine *N*,*N*′-dioxide derivatives by our group: (a) Nakajima, M.; Sasaki, Y.; Shiro, M.; Hashimoto, S. *Tetrahedron: Asymmetry* **1997**, *8*, 341−344. (b) Nakajima, M.; Sasaki, Y.; Iwamoto, H.; Hashimoto, S. *Tetrahedron Lett.* **1998**, *39*, 87−88.

(4) (a) Diana, M. B.; Marchetti, M.; Melloni, G. *Tetrahedron: Asymmetry* **1995**, *6*, 1175−1179. (b) O'Neil, I. A.; Turner, C. D.; Kalindjian, S. B. *Synlett* **1997**, 777−780.

(5) (a) Kobayashi, S.; Nishio, K. *Tetrahedron Lett.* **1993**, *34*, 3453−3456. (b) Kobayashi, S.; Nishio, K. *J. Org. Chem.* **1994**, *59*, 6620−6628.

(6) Denmark, S. E.; Coe, D. M.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem.* **1994**, *59*, 6161−6163.

(7) For recent reviews on hypervalent silicates, see: (a) Sakurai, H. *Synlett* **1989**, 1−8. (b) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371−1448.

(8) For Lewis base promoted reactions based on hypervalent silicates other than allylation, see: (a) Denmark, S. E.; Barsanti, P. A.; Wong, K.-T.; Stavenger, R. A. *J. Org. Chem.* **1998**, *63*, 2428−2429. (b) Denmark, S. E.; Wong, K.-T.; Stavenger, R. A. *J. Am. Chem. Soc.* **1997**, *119*, 2333−2334. (c) Denmark, S. E.; Winter, S. B. D.; Su, X.; Wong, K.-T. *J. Am. Chem. Soc.* **1996**, *118*, 7404−7405. (d) Kobayashi, S.; Nishio, K. *J. Am. Chem. Soc.* **1995**, *117*, 6392−6393. (e) Kobayashi, S.; Yasuda, M.; Hachiya, I. *Chem. Lett.* **1996**, 407−408. (f) Kobayashi, S.; Tsuchiya, Y.; Mukaiyama, T. *Chem. Lett.* **1991**, 537−540.

(9) Iseki and Kobayashi have recently improved the enantioselectivity by employing a proline-based phosphoramide derivative as a chiral Lewis base. See: (a) Iseki, K.; Kuroki, Y.; Takahashi, M.; Kobayashi, Y. *Tetrahedron Lett.* **1996**, *37*, 5149−5150. (b) Iseki, K.; Kuroki, Y.; Takahashi, M.; Kishimoto, S.; Kobayashi, Y. *Tetrahedron* **1997**, *53*, 3513−3526.

(10) For a review on chiral Lewis acid catalyzed allylation of aldehydes, see: Cozzi, P. G.; Tagliavini, E.; Umani-Ronchi, A. *Gazz. Chim. Ital.* **1997**, *127*, 247−254.

(11) Trimethylamine *N*-oxide is known to cleave carbon−silicon bond via hypervalent silicate intermediate. See: Sato, K.; Kira, M.; Sakurai, H. *Tetrahedron Lett.* **1989**, *30*, 4375−4378.

(12) Homochiral **1** has been prepared via optical resolution with chiral stationary phase column (Fujii, M.; Honda, A. *J. Heterocycl. Chem.* **1992**, *29*, 931−933). We successfully resolved the racemic dioxide via hydrogen-bonding complex with (*R*)-binaphthol (see: ref 3a and Toda, F.; Mori, K.; Stein, Z.; Goldberg, I. *Tetrahedron Lett.* **1989**, *30*, 1841−1844). Absolute configuration was determined by X-ray crystallography of the hydrogen-bonding complex. See the Supporting Information for the crystallographic data.

(13) On the basis of the same concept, Wulff has prepared homochiral 3,3′-diphenyl-2,2′-binaphthalene-1,1′-diol, which exhibited better enantioselectivity than 1,1′-binaphthalene-2,2′-diol in asymmetric Diels−Alder reaction. See: Bao, J.; Wulff, W. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1993**, *115*, 3814−3815.

(14) Dichloromethane has been proven to be the solvent of choice at room temperature. Solvent (% yield, ee): propionitrile (82, 61); tetrahydrofuran (58, 34); ethyl acetate (45, 33); toluene (12, 27).

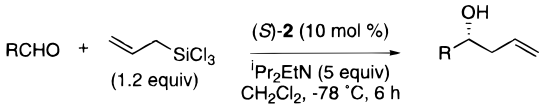
(15) General procedure of enantioselective allylation is as follows. To a solution of (*S*)-**2** (0.16 mmol), diisopropylethylamine (8.0 mmol), and benzaldehyde (1.6 mmol) in dichloromethane (1.5 mL) was added allyltrichlorosilane (1.9 mmol) at −78 °C. The mixture was stirred at the same temperature for 6 h. Aqueous workup followed by silica gel column chromatography afforded (*R*)-enriched α-(2-propenyl)benzenemethanol, the enantiomeric excess of which was determined by HPLC. Amine *N*-oxide (*S*)-**2** was recovered from the column quantitatively without any loss of optical purity.

(16) The allylation promoted by dimethylformamide or triphenylphosphine oxide has recently been reported to be accelerated by the addition of tetraalkylammonium halide. See: Short, J. D.; Attenoux, S.; Berrisford, D. J. *Tetrahedron Lett.* **1997**, *38*, 2351−2354.

(17) Allylation employing stoichiometric amount of (*S*)-**2** without diisopropylethylamine at −78 °C for 24 h afforded the homoallylic alcohol of 88% ee in 90% yield.

S0002-7863(98)01091-9 CCC: $15.00
Published on Web 06/14/1998

Table 1. Enantioselective Allylation of Aldehydes with Allyltrichlorosilane Catalyzed by (*S*)-**2**



entry	R	yield, %[a]	ee, %[b]	(config)[b]	$[\alpha]_D$[c]
1	Ph	85	88	(*R*)	+38.5 (C_6H_6)[19a]
2	4-$MeOC_6H_4$	91	92	(*R*)	+45.1 (C_6H_6)[6]
3	4-$CF_3C_6H_4$	71	71	(*R*)[d]	+24.6 (C_6H_6)[9]
4	2-MeC_6H_4	70	90	(*R*)[d]	+39.2 (EtOH)[6]
5	1-naphthyl	68	88	(*R*)	+84.7 (C_6H_6)[19b]
6	(*E*)-$C_7H_{15}CH{=}CH$	74[e]	81[f]	(*R*)	+3.2 ($CHCl_3$)[19c]
7	(*E*)-PhCH=CH	87	80	(*R*)	−11.3 (Et_2O)[19a]
8	$Ph(CH_2)_2$	30	7	(*S*)	−2.5 ($CHCl_3$)[19a]
9	c-Hex	27	28[g]	(*S*)	−3.5 (EtOH)[19c]

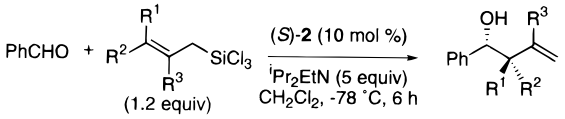
[a] Isolated yield. [b] Determined by HPLC analysis employing a Daicel Chiralcel OD, OJ, or Chiralpak AD. Configuration assignment by comparison to literature values of optical rotations. [c] Observed rotations and literatures. [d] Assignment by analogy. [e] The reaction was carried out with 20 mol % of (*S*)-**2**. [f] Determined by HPLC analysis of the corresponding 4-nitrobenzoate. [g] Determined by HPLC analysis of the corresponding 3,5-dinitrobenzoate.

such as triethylamine, pyridine, and diaza[2.2.2]bicyclooctane showed the relatively modest effects. While the role of diisopropylethylamine is presently unclear, it may be reasonable to assume that the amine promotes a dissociation of (*S*)-**2** from silicon atom in the product by ligand exchange to regenerate (*S*)-**2** because the addition of the amine does not influence the sense and extent of the enantioselection.

The results obtained for the reaction of a variety of aldehydes with allyltrichlorosilane are summarized in Table 1. Allylation of aromatic aldehydes gave results similar to those with benzaldehyde, except in the case of 4-(trifluoromethyl)benzaldehyde bearing an electron-withdrawing group (entry 3). It is worthy of note that the enantioselectivity (92% ee) observed with anisaldehyde is the highest reported to date for enantioselective allylations of aldehydes with allyltrichlorosilane catalyzed by a chiral Lewis base (entry 2). While the present protocol could be extended to α,*β*-unsaturated aldehydes (entries 6 and 7), aliphatic aldehydes (entries 8 and 9) proved to be unsuitable substrates in terms of both chemical yield and enantioselectivity.

To establish the mechanistic profile of the amine *N*-oxide-promoted process, we then examined allylations of benzaldehyde with (*E*)- and (*Z*)-crotyltrichlorosilanes.[18] As shown in Table 2, *γ*-allylated *anti*-homoallylic alcohol was obtained from (*E*)-crotyltrichlorosilane (entry 1) while corresponding *syn*-alcohol was produced from (*Z*)-crotyltrichlorosilane (entry 2), both in virtually complete regio- and diastereoselectivities. In each case, the consistent sense and magnitude of the asymmetric induction at the hydroxy center was observed as in the case of the parent

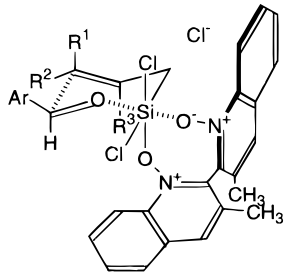
Table 2. Enantioselective Allylation of Benzaldehyde with Allyltrichlorosilanes Catalyzed by (*S*)-**2**



entry	R^1	R^2	R^3	yield, %[a]	ee, %[b]	(config)[b]	$[\alpha]_D$[c]
1[d]	H	CH_3	H	68[f]	86	(1*R*,2*R*)	+94.6 ($CHCl_3$)[19d]
2[e]	CH_3	H	H	64[g]	84	(1*R*,2*S*)	+22.6 ($CHCl_3$)[19d]
3	CH_3	CH_3	H	52	78	(*R*)	+46.4 ($CHCl_3$)[19e]
4	H	H	CH_3	70	49	(*R*)	+24.0 (C_6H_6)[19a]

[a] Isolated yield. [b] Determined by HPLC analysis employing a Daicel Chiralcel OD, OJ, or Chiralpak AD. Configuration assignment by comparison to literature values of optical rotations. [c] Observed optical rotations and literatures. [d] *E*:*Z* = 97:3. [e] *E*:*Z* = 1:99. [f] *syn*:*anti* = 3:97. [g] *syn*:*anti* = 99:1.

allyltrichlorosilane. These results suggest that the allylations of aromatic and unsaturated aldehydes mediated by (*S*)-**2** proceed via cyclic chairlike transition structures **3**, involving hypervalent silicates where one of a pair of *N*-oxide moieties occupies an axial position. In this respect, it is of interest to note that the



3

allylation using sterically congested prenyltrichlorosilane still maintained good enantioselectivity in accord with a general trend (entry 3), whereas a dramatic drop in enantioselectivity was observed with methallyltrichlorosilane (entry 4). On the basis of the above hypothesis, the latter result may also be rationalized by assessing the 1,3-diaxial-type steric repulsion between the methyl group and the wall of the biaryl unit.

In summary, we have demonstrated the effectiveness of (*S*)-3,3′-dimethyl-2,2′-biquinoline *N*,*N*′-dioxide ((*S*)-**2**) as a catalyst for enantioselective addition of allyltrichlorosilanes to aldehydes, wherein the use of diisopropylethylamine as an additive has proven to be crucial for the acceleration of the catalytic cycle. Studies on the mechanism as well as the design of chiral amine *N*-oxides to further enhance enantioselectivity are currently in progress.

Acknowledgment. This research was supported in part by the Special Coordination Funds of the Science and Technology Agency of the Japanese Government.

Supporting Information Available: Preparation of (*S*)-**1**, X-ray crystallographic data of (*S*)-**1**·(*R*)-binaphthol complex, procedure of enantioselective allylation, and ^1H, ^{13}C NMR, HPLC data of all homoallylic alcohols are provided (15 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA981091R

(18) For preparation of allyltrichlorosilanes, see: (a) Furuya, N.; Sukawa, T. *J. Organomet. Chem.* **1975**, *96*, C1−C3. (b) Kira, M.; Hino, T.; Sakurai, H. *Tetrahedron Lett.* **1989**, *30*, 1099−1102.

(19) (a) Minowa, N.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3697−3704. (b) Sugimoto, K.; Aoyagi, S.; Kibayashi, C. *J. Org. Chem.* **1997**, *62*, 2322−2323. (c) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 4109−4117. (d) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowiz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339−6348. (e) Manabe, S. *Chem. Commun.* **1997**, 737−738.