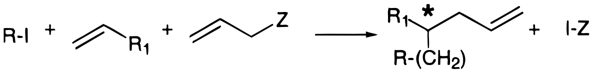
Enantioselective Free Radical Allyl Transfers from Allylsilanes Promoted by Chiral Lewis Acids

Ned A. Porter,* Jason Hongliu Wu, Guiru Zhang, and Aimee D. Reed

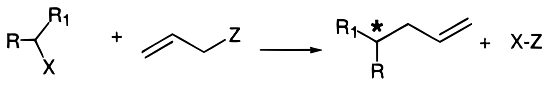
Department of Chemistry, Duke University, Durham, North Carolina 27708

Received July 2, 1997

Free radical reactions have received renewed interest because of recent discoveries demonstrating that control of stereochemistry in these transformations is possible. Diastereoselective reactions involving substrate or chiral auxiliary-controlled processes are now well understood,[1] and very recent examples of enantioselective processes have also been reported.[2] Reaction of prostereogenic radicals with allylstannane radical traps has been one of the most common transformations studied in which control of stereochemistry is at issue (eqs 1 and 2). More recently, trimethylallylsilanes and tris(trimethylsilyl)-allylsilanes have been investigated in radical reactions, some of which involve achiral Lewis acid-controlled transformations.[3] Lewis acids can be used to control the facial bias in reactions of bidentate radicals, and diastereoselectivity can be enhanced or even reversed by selection of an appropriate Lewis acid.[4]



(1)



(2)

X=halide or selenide Z= Sn(Bu)$_3$, Si(Me)$_3$, Si(Si(Me)$_3$)$_3$

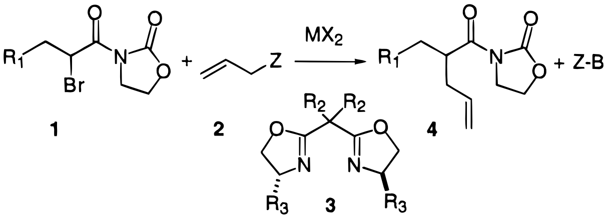
Enantioselective radical reactions such as the one shown in eq 1 have been achieved with enantiomeric excesses of up to 90% by the use of zinc Lewis acid catalysts in combination with alkyl iodides, acrylimides, and chiral bisoxazolines.[2a] The direct transfer sequence with X = Br and Z = Sn(Bu)$_3$ shown in eq 2 proceeds with significantly lower selectivity than the addition−transfer sequence starting from the iodide, eq 1.[5a] We now report experiments analogous to the allylstannane reactions shown in eq 2 but which utilize both zinc and magnesium Lewis acids and a variety of allylsilanes as radical traps. These silane reactions provide products with substantially improved selectivity compared to the allylstannane reactions. We also find that the stannyl bromide byproduct of reaction in eq 2 is detrimental to the overall transformation, yields, and enantiomeric excesses achieved in the silane transfer reactions being reduced in the presence of added stannyl halide.

Table 1. Lewis Acid Promoted Reactions of Allylsilanes and Allylstannane[a]

entry	R$_1$	R$_2$	R$_3$	**3** config	MX$_2$	Z	yield, %	**4***R*:**4***S*
1	CH$_3$	CH$_3$	Ph	(*R*,*R*)	Zn(OTf)$_2$	Sn(Bu)$_3$	84[b]	29:71
2	CH$_3$	CH$_3$	Ph	(*R*,*R*)	Zn(OTf)$_2$	Si(OEt)$_3$	65[b]	20:80
3	^{t}Bu	CH$_3$	Ph	(*R*,*R*)	Zn(OTf)$_2$	Sn(Bu)$_3$	63[b]	87:13
4	^{t}Bu	CH$_3$	Ph	(*R*,*R*)	Zn(OTf)$_2$	Si(Me)$_3$	88[c]	95:5
5	^{t}Bu	CH$_3$	Ph	(*R*,*R*)	MgI$_2$	Si(Me)$_3$	86[b]	16:84
6	^{t}Bu	CH$_3$	^{t}Bu	(*S*,*S*)	MgI$_2$	Si(Me)$_3$	61[c]	89:11
7	^{t}Bu	-(CH$_2$)-	^{t}Bu	(*S*,*S*)	MgI$_2$	Si(Me)$_3$	65[c]	94:6
8	^{t}Bu	CH$_3$	^{i}Bu	(*S*,*S*)	MgI$_2$	Si(Me)$_3$	83[c]	91:9

[a] Reaction as described in eq 3. [b] Isolated yield. [c] Yield based on GC internal standard.

Radical allylations of bromides **1** with several allylsilanes **2** were carried out with 1 equiv of Lewis acid **MX$_2$**/ligand **3** in CH$_2$Cl$_2$ initiated by Et$_3$B at −78 °C, see eq 3. The same product, **4**, was obtained in the silane reactions as was obtained in the corresponding reactions with allylstannane. Table 1 presents the results of reactions of the bromides **1** (R$_1$ = Me and ^{t}Bu) with allyltributylstannane and two allylsilanes. Trimethyl-, trimethoxy-, and triethoxyallylsilanes all gave comparable results while triphenylallylsilane gave low product yields and poor selectivity. The tris(trimethylsilyl)allylsilane (**2**, Z = Si(SiMe$_3$)$_3$) used successfully in allyl transfer reactions by Chatgilialoglu and Curran[3c] proved less effective than simple allylsilanes in the Lewis acid promoted reactions of **1**, product being formed in lower selectivity with this silane as compared to trimethylallylsilane.



(3)

The data presented in Table 1 indicate that the use of allylsilane gives product with superior enantioselectivity as compared to reactions of allylstannane carried out under otherwise identical conditions, compare entries 1 and 2 and entries 3 and 4. The reaction described by eq 3 is promoted by both zinc and magnesium Lewis acids. In accord with our earlier report,[2a] zinc triflate gives the best results when used in conjunction with chiral ligand **3** bearing a phenyl R$_3$ group. Zinc triflate gives product with poor selectivity when used with bisoxazolines **3** having alkyl R$_3$ substituents. In contrast, magnesium salts give moderate to high selectivity when used with

---

* To whom correspondence should be addressed at Department of Chemistry, Duke University, Durham, NC 27708. Tel. (919)660-1550, fax (919)660-1605, email porter@chem.duke.edu.

(1) (a) Porter, N. A.; Giese, B.; Curran, D. P. *Acc. Chem. Res.* **1991**, *24*, 296. (b) Smadja, W. *Synlett* **1994**, 1. (c) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH: Weinheim, 1995.

(2) (a) Wu, J. H.; Radinov, R.; Porter, N. A. *J. Am. Chem. Soc.* **1995**, *117*, 11029. (b) Sibi, M. P.; Ji, J.; Wu, J. H.; Gürtler, S.; Porter, N. A. *J. Am. Chem. Soc.* **1996**, *118*, 9200. (c) Nanni, D.; Curran, D. P. *Tetrahedron: Asymmetry* **1996**, *8*, 2417. (d) Blumenstein, M.; Schwarzkopf, K.; Metzger, J. O. *Angew. Chem.* **1997**, *36*, 235.

(3) (a) Guindon, Y.; Guerin, B.; Chabot, C.; Ogilvie, W. *J. Am. Chem. Soc.* **1996**, *118*, 12528. (b) Guindon, Y.; Guerin, B.; Rancourt, J.; Chabot, C.; Mackintosh, N.; Ogilvie, W. W. *Pure Appl. Chem.* **1996**, *68*, 89. (c) Chatgilialoglu, C.; Ferreri, C.; Ballestri, M.; Curran, D. P. *Tetrahedron Lett.* **1996**, *37*, 6387.

(4) (a) Sibi, M. P.; Jasperse, C. P.; Ji, J. *J. Am. Chem. Soc.* **1995**, *117*, 10779. (b) Renaud, P.; Gerster, M. *J. Am. Chem. Soc.* **1995**, *117*, 6607. (c) Curran, D. P.; Kuo, L. H. *J. Org. Chem.* **1994**, *59*, 3259. (d) Renaud, P.; Moufid, N.; Kuo, L. H.; Curran, D. P. *J. Org. Chem.* **1994**, *59*, 3547. (e) Toru, T.; Watanabe, Y.; Tsusaka, M.; Ueno, Y. *J. Am. Chem. Soc.* **1993**, *115*, 10464. (f) Guindon, Y.; Guerrin, B.; Chabot, C.; Mackintosh, N.; Ogilve, W. W. *Synlett* **1995**, 449. (g) Andrus, M. B.; Argade, A. B.; Chen, X.; Pamment, M. G. *Tetrahedron Lett.* **1995**, *36*, 2945. (h) Newcomb, M.; Ha, C. *Tetrahedron Lett.* **1991**, *32*, 6493. (i) Feldman, K. S.; Romaneli, A. L.; Ruckle, R. E. Jr.; Jean, G. *J. Org. Chem.* **1992**, *57*, 100. (j) Sibi, M. P.; Ji, J. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 190. (k) Sibi, M. P.; Ji, J. *J. Am. Chem. Soc.* **1996**, *118*, 3063. Lett. **1997**, *38*, 2661.

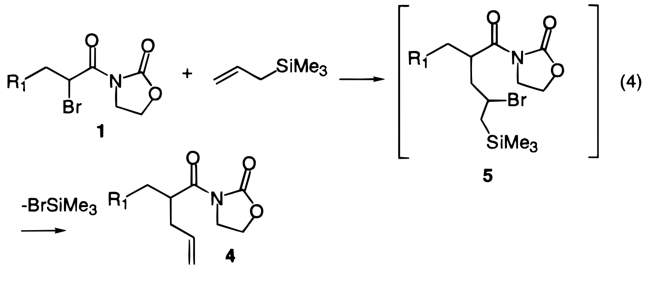
(5) (a) Wu, J. H.; Zhang, G; Porter, N. A. *Tetrahedron Lett.* **1997**, *38*, 2067. (b) Aluminum Lewis acids have also been used in similar transformations with modest selectivity: Fhal, A.-R.; Renaud, P. *Tetrahedron Lett.* **1997**, *38*, 2661.

S0022-3263(97)01199-7 CCC: $14.00

bisoxazolines bearing alkyl or aryl R_3 groups, the iodide giving the best results when used with a new spirocyclopropylbisoxazoline, Table 1, entry 7.[6,7]

Interestingly, bisoxazoline ligands having the same absolute configuration give products with opposite configurations depending on the Lewis acid used, Zn(OTf)$_2$ or MgI$_2$ (see table, entries 4 and 5). This phenomenon has also been observed in previous work in which the stereogenic center is set at the β position of alkenes in addition reactions[2b] and models for the two Lewis acids have been proposed.[7b]

A mechanism consistent with our data is outlined and is analogous to those proposed previously in atom transfer reactions involving very electrophilic radicals,[3a,8] with products like **5** being observed spectroscopically as intermediates in diastereoselective Lewis acid promoted transformations. The β bromosilane **5** undergoes elimination of trimethylsilyl bromide readily[3a] to give product **4** that is formally the result of an allyl transfer **1**. Allylstannanes or the tris(trimethylsilyl)allylsilane presumably provide an intermediate radical that undergoes β fragmentation directly.[9]



(4)

Product **4** enantiomeric excess is higher for the reactions of trimethyl-, trimethoxy-, and triethoxysilanes compared to reactions of allyltributylstannane under all conditions examined. This is presented graphically in Figure 1 where product enantiomeric excess is presented for reactions of trimethylallylsilane and tributylallylstannane under conditions that are otherwise identical.

Tin halides that are formed as a byproduct of reactions of allylstannane radical traps are themselves Lewis acids, and these products may promote nonstereoselective reactions by competing with the transformations controlled by the chiral Lewis acids present in these radical reactions.[10] This would result in products formed with lower selectivity in reactions of allylstannanes than for comparable reactions of allylsilanes. This hypothesis is supported by experiments with allylsilanes in which trialkylstannyl halides are added to the reaction mixture. Trialkyltin chlorides or bromides and dialkyltin dichlorides or dibromides added to reactions utilizing trimethylallylsilane radical traps give products with lower selectivity than reactions that do not include the tin halides. Added tin iodides, on the other hand, have little or no effect on the reaction. In Figure 2 is presented the enantiomeric excess of product formed from transfer to trimethylallylsilane in the presence of trimethyltin bromide. The observation that the product selectivity is inversely proportional to the amount of trimethyltin bromide is consistent with our hypothesis.

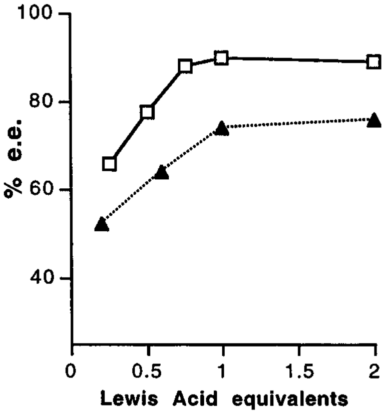


Figure 1. Enantiomeric excess obtained for **4**, (R_1 = ^{t}Bu) in reactions promoted by Zn(OTf)$_2$ and ligand **3** (R_2 = CH_3, R_3 = Ph). ▲ = reaction with allyltributylstannane. □ = reaction with allyltrimethylsilane.

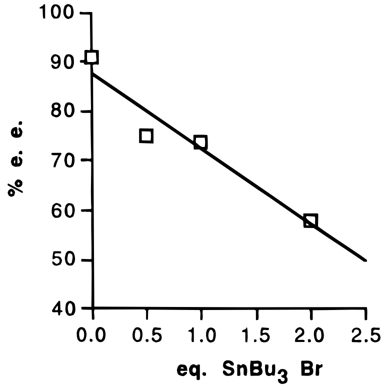


Figure 2. Enantiomeric excess obtained for **4** (R_1 = ^{t}Bu) in reactions promoted by Zn(OTf)$_2$ (1.0 equiv) and ligand **3** (R_2 = CH_3, R_3 = Ph, 1.0 equiv) with added Me_3SnBr.

While magnesium and zinc chiral Lewis acids may be used in free radical reactions to give products with moderate to high enantioselectivities, this report demonstrates that allylsilanes are much more effective reagents than allylstannane for enantioselective free radical allyl transfers and that the use of "standard" tin conditions for allyl transfer reactions should be used with caution.

Acknowledgment. NSF support and the receipt of an NIH MERIT award is gratefully acknowledged. We thank Dr. C. Chatgilialoglu for a sample of tris(trimethylsilyl)allylsilane and helpful discussions.

Supporting Information Available: Synthesis of the new bisoxazoline and NMR spectra (12 pages).

JO971199+

---

(6) The synthesis of this new bisoxazoline is reported in Supporting Information.

(7) The fused indanylbisoxazoline that gives very high selectivity in reactions in which the Lewis acid is complexed to the radical trap gives very low selectivity in reactions such as eq 3 in which the Lewis acid is complexed to the radical in the stereodefining step. See: (a) Davies, I. W.; Gerena, L.; Castonguay, L.; Senanayake, C. H.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *J. Chem. Soc., Chem. Commun.* **1996**, 1753. (b) Sibi, M. P.; Ji, J. *J. Org. Chem.* **1997**, *62*, 6800.

(8) Curran, D. P.; Chen, M.-H.; Spletzer, E.; Seong, C. M.; Chang, C.-T. *J. Am. Chem. Soc.* **1989**, *111*, 8872.

(9) Chatgilialoglu, C. *Chem. Rev.* **1995**, *95*, 1229.

(10) Tin Lewis acids have been shown to promote diastereoselective free radical transformations. See: Sibi, M. P.; Ji, J. G. *J. Am. Chem. Soc.* **1996**, *118*, 3063.