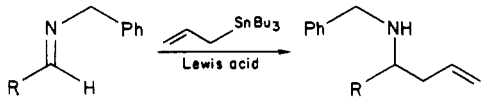
Homoallylamines from Aldimines and Allylstannanes

Summary: Allyltri-*n*-butylstannane adds to aldimines in the presence of Lewis acids to give homoallylamines; for the analogous additions of crotyltri-*n*-butylstannane, bond construction selectivity is a sensitive function of the thermal history of the aldimine–Lewis acid complex.

Sir: Recently considerable attention has been focused on the development of new synthetic methodology for the synthesis of amines.[1] Our own interest in the area of alkaloid synthesis and our recent observations on the stereochemical consequences of Lewis acid mediated additions of allyl- and crotyltri-*n*-butylstannanes to chiral aldehydes has prompted us to examine such organostannane additions to imines as a potential route to homoallylamines, particularly since olefinic amines and various acylated derivatives have proven to be an especially versatile class of compounds with respect to further elaborations.[2] We record herein our observations on this process, some of which are quite surprising.

Initial studies focused on the Lewis acid mediated addition of allyltri-*n*-butylstannane to simple achiral aldimines, as shown in eq 1. Not unexpectedly, such aldimines proved much less reactive than the corresponding aldehydes from which they were derived.[3] In general, little or no immediate reaction was observed at −78 °C in CH_2Cl_2, using either $BF_3{\cdot}Et_2O$ or $TiCl_4$ as Lewis acids (conditions under which aldehydes are rapidly consumed). At least part of the lower reactivity of these aldimines could be shown to be due to sluggish complexation with these Lewis acids, however. Thus, addition of Lewis acid to aldimine at −78 °C, brief warming to 23 °C, recooling to −78 °C, and addition of allyltri-*n*-butylstannane afforded the desired products in reasonable to good yields, as shown in Table I (vide infra).



(1)

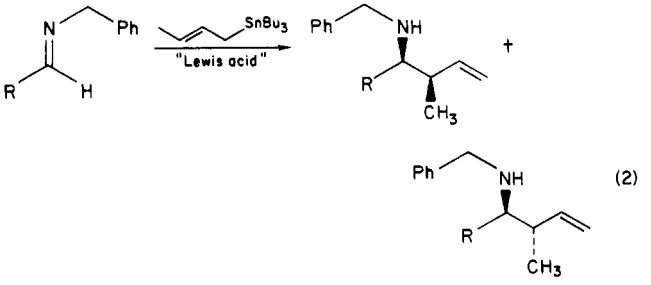
Further evidence for slow complexation in the case of $TiCl_4$ as Lewis acid was easily obtained visually. We have previously reported[4] that $TiCl_4$ reacts with crotyltri-*n*-butylstannane to produce a species which adds to aldehydes with high threo selectivity. Production of this species is accompanied by the development of an intense blue-violet color and appears to require "free" $TiCl_4$, as preformed $TiCl_4$–aldehyde complexes react with crotyltri-*n*-butylstannane with "normal" erythro selectivity,[5] and no blue-violet coloration is observed in such reactions. Parallel observations were made in the $TiCl_4$ mediated additions of allyltri-*n*-butylstannane to aldimines. Addition of $TiCl_4$ to aldimine in CH_2Cl_2 at −78 °C, stirring at −78 °C for ca. 15 min, and addition of allyltri-*n*-butylstannane afforded a deep blue solution from which significant quantities of the desired addition product were not obtained even after warming to room temperature. However, upon brief warming of the $TiCl_4$–aldimine mixture to 23 °C, recooling to −78 °C, and addition of allyltri-*n*-butylstannane, no blue coloration indicative of free $TiCl_4$ was observed, and the expected addition products were obtained in the isolated yields shown in Table I (vide infra).

Table I. Yields and Stereoselectivities for Lewis Acid Mediated Organostannane Additions to Aldimines

R[a]	stannane	Lewis acid	method[b]	yield,[c] %	erythro:threo ratio[d]
cyclohexyl	allyl	$BF_3{\cdot}Et_2O$	A	48	
cyclohexyl	allyl	$TiCl_4$	A	81	
cyclohexyl	crotyl	$TiCl_4$	B	78	23:1
phenyl	allyl	$BF_3{\cdot}Et_2O$	A	73	
phenyl	allyl	$TiCl_4$	A	53	
phenyl	crotyl	$TiCl_4$	B	85	3:1
sec-butyl	allyl	$BF_3{\cdot}Et_2O$	A	53	
sec-butyl	allyl	$TiCl_4$	A	75	
isopropyl	crotyl	$TiCl_4$	B	60	20:1
furanyl	allyl	$BF_3{\cdot}Et_2O$	A	61	
furanyl	allyl	$TiCl_4$	A	88	
furanyl	crotyl	$TiCl_4$	B	84	30:1

[a] Note eq 1 and 2. [b] Method A: 0.2 M in aldimine (CH_2Cl_2) at −78 °C, add 1 equiv of Lewis acid, warm briefly to 23 °C, recool to −78 °C, add 2 equiv of stannane, warm slowly to room temperature. Method B: 0.2 M in aldimine (CH_2Cl_2) at −78 °C, add 1 equiv of Lewis acid, stir 2.5 h at −78 °C, add 2 equiv of stannane, stir 1 h at −78 °C, warm slowly to room temperature. [c] All yields are isolated yields of materials purified by chromatography over silica gel. [d] Product ratios were determined by capillary VPC analysis assuming equal response factors for diastereomeric products.

Attention was next turned to additions of crotyltri-*n*-butylstannane to such aldimines using various Lewis acids and the reaction protocol delineated above. Ratios of erythro (or syn) to threo (or anti) products (note eq 2) were



(2)

determined by capillary VPC analysis using a J & W 30m DB-5 column; assignment of stereochemistry to the products produced was made by unambiguous independent synthesis.[6]

(1) (a) Wada, M.; Sakurai, Y.; Akiba, K. *Tetrahedron Lett.* **1984**, *25*, 1079–1082. (b) Overman, L. E.; Burk, R. M. *Ibid.* **1984**, *25*, 1635–1638. (c) Frankhauser, J. E.; Peevey, R. M.; Hopkins, P. B. *Ibid.* **1984**, *25*, 15–18. (d) Jung, S.-H.; Kohn, H. *Ibid.* **1984**, *25*, 399–402. (e) German, C.; Alexakis, A.; Normant, J. F. *Synthesis* **1984**, 40–43. (f) Bestman, H. J.; Woelfel, G. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 53. (g) Morimoto, T.; Takahashi, T.; Sekiya, M. *J. Chem. Soc., Chem. Commun.* **1984**, 794–795. (h) Hart, D. J.; Kanai, K.; Thomas, D. G.; Yang, T.-K. *J. Org. Chem.* **1983**, *48*, 289–294.

(2) (a) Clive, D. L. J.; Farina, V.; Singh, A.; Wong, C. K.; Keil, W. A.; Menchen, S. M. *J. Org. Chem.* **1980**, *45*, 2120–2126. (b) Danishefsky, S.; Taniyama, E.; Webb, R. R. *Tetrahedron Lett.* **1983**, *24*, 11–14. (c) Parker, K. A.; O'Fee, R. *J. Am. Chem. Soc.* **1983**, *105*, 654–655. (d) Overman, L. E.; McCready, R. J. *Tetrahedron Lett.* **1982**, *23*, 4887–4890. (e) Danishefsky, S.; Webb, R. R. *Tetrahedron Lett.* **1983**, *24*, 1357–1361. (f) Wang, Y.-F.; Izawa, T.; Kobayashi, S.; Ohno, M. *J. Am. Chem. Soc.* **1982**, *104*, 6465–6466.

(3) All aldimines utilized in this study were prepared simply by heating the appropriate aldehyde and benzylamine in toluene with removal (Dean–Stark apparatus) of water and were used without purification.

(4) Keck, G. E.; Abbott, D. E.; Boden, E. P.; Enholm, E. J. *Tetrahedron Lett.* **1984**, *25*, 3927–3930.

(5) Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107–7109.

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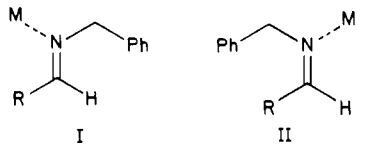
Quite surprisingly, the ratio of erythro to threo products proved essentially independent of the Lewis acid used; all Lewis acids which successfully promoted reaction gave ca. 4:1 mixtures of diastereomeric products in which the erythro product predominated. For the case of R = cyclohexyl, erythro:threo ratios were between 77:23 and 79:21 for all of the following Lewis acids (isolated yields in parentheses[7]) by using the reaction protocol previously described for allyl additions: BF_3·OEt_2 (82%), $TiCl_4$ (83%), $MgBr_2$ (71%), ZnI_2, Et_2AlCl (79%), $ZrCl_4$ (84%), CF_3CO_2H, and CH_3SO_3H.

Fortunately, however, considerable improvement in stereoselectivity could be achieved by allowing sufficient time at −78 °C to effect complexation rather than employing the expedient of warming. Moreover, carefully controlled experiments with respect to time and temperature using $TiCl_4$ as Lewis acid revealed that *stereoselectivity is determined primarily by the history of the Lewis acid–aldimine complex.* Thus, the following results were obtained for experiments conducted by using the following protocol: 0.2 M in substrate at −78 °C in CH_2Cl_2, add 1 equiv of $TiCl_4$, warm to temperature T for the indicated period of time, recool to −78 °C, add 2.0 equiv of crotyltri-*n*-butylstannane, stir at −78 °C for 1 h, and warm slowly to 23 °C overnight.

T	time at T	erythro:threo ratio
23 °C	1.0 h	4.4:1
0 °C	1.5 h	6.7:1
-42 °C	1.0 h	11.3:1
-78 °C	2.5 h	23.6:1

These results quite strongly suggest that, at least for the case of $TiCl_4$, two different aldimine–Lewis acid complexes are undergoing reaction, that these complexes are interconvertible at elevated temperatures, and that the kinetically formed complex exhibits high erythro selectivity in its reaction with crotyltri-*n*-butylstannane, while the erythro selectivity of the other, thermodynamically favored, complex is low. These may be reasonably formulated as I and II, although the identity of which complex exhibits high erythro selectivity is not presently known. However, one would reasonably expect that species I should be



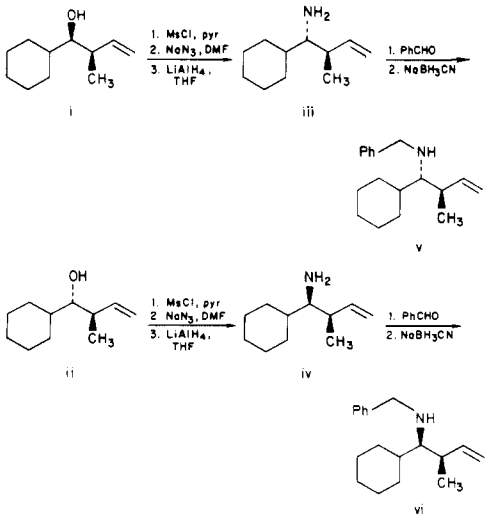
I II

formed initially from an aldimine and Lewis acid. If this is so, the equilibration to II suggests that the $TiCl_4$ moiety may be rather sterically demanding. However, using this hypothesis and the extended transition state proposed by Yamamoto[5] for additions to aldehydes the selectivities observed are not readily explained, since one would then expect higher erythro selectivity for addition to II than for $TiCl_4$–mediated addition to the corresponding aldehyde, which is not the case.[4] Similar difficulties are encountered upon attempting to rationalize the results via synclinal transition states as espoused by Denmark[8] for similar additions to aldehydes. It may be that I and II are not in fact the species undergoing reaction, or that factors other than simple steric interactions are important in controlling the reaction pathway. Efforts to develop a better mechanistic understanding of such reactions are in progress. For the present, however, we note that such organostannane additions to aldimines provide a useful route to homoallylamines and β-methylhomoallylamines with good stereocontrol in the bond construction for the latter case. Product ratios and isolated yields for the $TiCl_4$-mediated addition to other *N*-benzyl aldimines are included in Table I.

Acknowledgment. Support of this research through Grant No. GM-28961 from the National Institutes of Health, by the Alfred P. Sloan Foundation, and by the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

[†]Fellow of the Alfred P. Sloan Foundation, 1981–1985.

(6) Thus, the readily available[4] erythro and threo alcohols i and ii were subjected to mesylation, azide displacement, and reduction to afford amines iii and iv with clean inversion of configuration in each case. Imine formation[3] and sodium cyanoborohydride reduction then afforded the desired *N*-benzylamines v and vi.



(7) For cases where no yield is indicated, conversion to products was 50% or less after ca. 18 h at 23 °C.

(8) Denmark, S. E.; Weber, E. J. *Helv. Chim. Acta* **1983**, *66*, 1655–1660.

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Received August 21, 1984

Desulfurization and Carbonylation of Mercaptans

Summary: The first examples of the carbonylation of mercaptans are described: cobalt carbonyl catalyzes the desulfurization and carbonylation of mercaptans to carboxylic esters by means of carbon monoxide in aqueous alcohol.

Sir: Carbonylation reactions are an important class of organic reactions. Of industrial importance are those transformations utilizing olefins, alkynes, and halides as substrates.[1,2] For example, benzylic halides as well as vinylic mono- or dibromides can be carbonylated to acids by cobalt carbonyl (eq 1)[3] or palladium(0)[4] catalysts under

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(2) Falbe, J., Ed. "New Syntheses with Carbon Monoxide"; Springer Verlag: Berlin, 1980.
(3) Alper, H.; des Abbayes, H. *J. Organomet. Chem.* **1977**, *134*, C11.

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