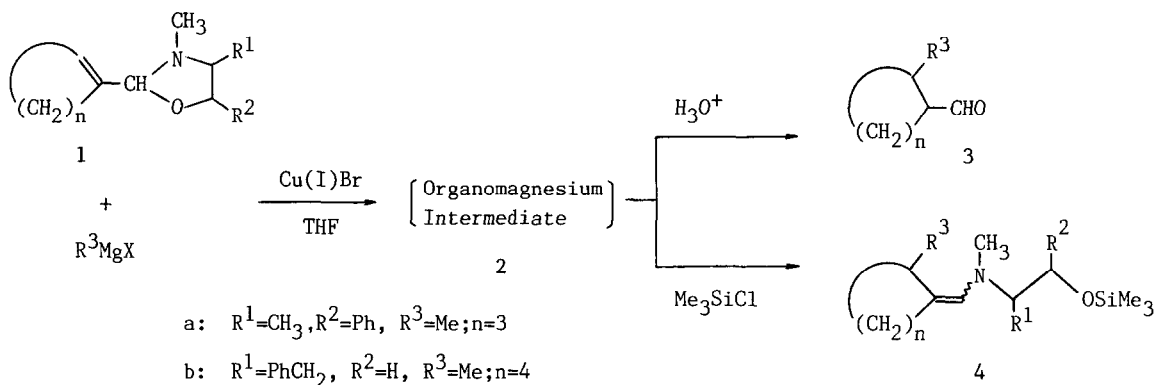


TRIMETHYLCHLOROSILANE INDUCED RING
 OPENING OF 2-ALKYLOXAZOLIDINES TO ENAMINE DERIVATIVES

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Abstract: 2-Alkyloxazolidines (5) were ring-opened by trimethylchlorosilane with N,N-diisopropylamine to give N-[2-(trimethylsilyloxy)alkyl]-enamines (6). A MgCl₂ promoted Michael reaction of chiral enamines thus prepared was achieved with asymmetric induction.

Copper(I) catalyzed addition of Grignard reagents to 2-vinyloxazolidines (1) has been reported to provide alkanals (3), after acid hydrolysis.¹⁾

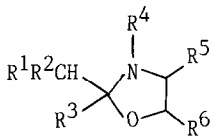
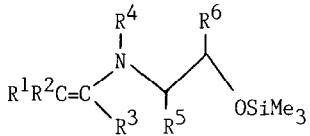
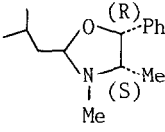
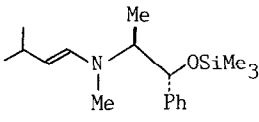
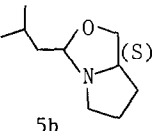
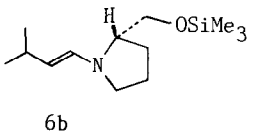
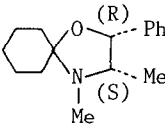
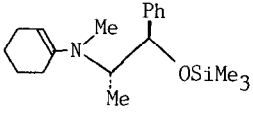
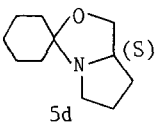
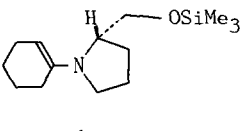


Our attempts to trap the Mg containing intermediate (2), which may conceivably be generated in situ, by Michael acceptor such as methyl vinyl ketone and methyl acrylate have failed. However, we found that the intermediates (2) were trapped on treatment with trimethylchlorosilane to give N-[2-(trimethylsilyloxy)alkyl]-enamines (4).²⁾ Moreover, it was found in the course of the study that 2-alkyloxazolidines (5) themselves were also converted to N-[2-(trimethylsilyloxy)alkyl]-enamines (6) simply by heating with trimethylchlorosilane in the presence of N,N-diisopropylethylamine.

For instance, a mixture of 2-isobutyl-3-methyl-4-methyl-5-phenyl-1,3-oxazolidine (5a)³⁾ (50 mmol), trimethylchlorosilane (100 mmol) and N,N-diisopropylethylamine (75 mmol) was refluxed in benzene (30 mL) for 6 hr. The mixture was concentrated in vacuo and then diluted with benzene to precipitate insoluble ammonium salt. After filtration, the filtrate was distilled in vacuo to give 1-[N-methyl-N-[2-(trimethylsilyloxy)-2-phenyl-1-methylethyl]amino]-

3-methyl-1-(E)-butene (**6a**)⁴⁾ [bp 100°C (1 mmHg)] in 96% yield. Some preparations of enamines (**6**) from 2-alkyloxazolidines (**5**) are summarized in Table 1.

Table 1.

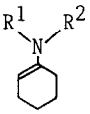
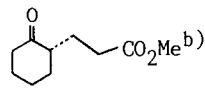
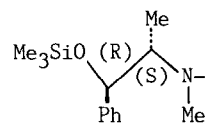
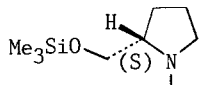
Oxazolidines (5)	Reaction Conditions	Enamines (6) (%)
	$\xrightarrow{\text{Me}_3\text{SiCl}/i\text{-Pr}_2\text{EtN}}$	
 5a	80°C, 6 hr a)	 6a (96)
 5b	80°C, 1 hr a)	 6b (80)
 5c	100°C, 15 hr b)	 6c (100) ^{c)}
 5d	60°C, 1 hr a)	 6d (96) ^{c)}

a) Benzene solvent. b) Toluene solvent. c) 6c and 6d were not distilled.

N-[2-(Trimethylsilyloxy)alkyl]-enamines (**6**) thus prepared did not react with α,β -unsaturated carbonyl compounds in aprotic solvents such as THF, ether and benzene. Noteworthy is that anhydrous MgCl_2 ⁵⁾ and ZnCl_2 efficiently promoted the Michael type reaction with the enamines (**6**). For example, a mixture of enamine (**6a**) (3.0 mmol), 3-penten-2-one (3.3 mmol) and anhydrous MgCl_2 (3.3 mmol) was stirred in THF (5 mL) at room temperature for 15 hr to produce 4-isopropyl-5-methyl-2-cyclohexenone (**7**)⁶⁾ in 95% yield (a 7:3 mixture of two stereoisomers), after extractive workup with ether followed by column chromatography on silica gel ($\text{C}_6\text{H}_{14}\text{-Et}_2\text{O}$ solvent). Some other metal salts such as LiCl , SnCl_2 , CuBr have no effect on the reaction at the comparable reaction conditions. The remarkable effect of MgCl_2 on the Michael type reaction with **6** is not clearly illustrated. But it is likely that MgCl_2 forms a chelate complex with 2-(trimethylsilyloxy)ethylamine moiety of the enamines (**6**), which may be structurally close to those proposed in some chelate metalloenamines⁷⁾.

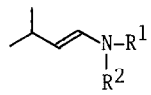
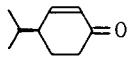
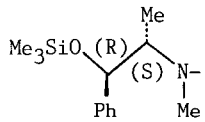
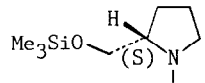
Finally, chiral enamines (**6a**)-(**6d**), which were derived from (1R, 2S)-(-)-ephedrin and (S)-pyrrolidinemethanol, were subjected to the MgCl₂ promoted Michael reactions with methyl acrylate and methyl 1-(trimethylsilyl)vinyl ketone. As shown in Table 2 and 3, the Michael reactions with the chiral enamines considerably improved the chemical yields as well as the optical yields, which were previously reported in the closely related reactions.⁸⁾ Especially, the reaction of chiral 2-[(trimethylsilyloxy)methyl]pyrrolino-1-cyclohexene (**6d**) with methyl acrylate afforded 62% yield of (S)-2-[2-(carbomethoxy)ethyl]cyclohexanone (**8**) with >95% ee ($[\alpha]_{460}^{25} = -12.95$ (CHCl₃)).⁹⁾

Table 2.

 Amino Group	$\xrightarrow[\text{MgCl}_2/\text{THF}]{\text{CH}_2=\text{CHCO}_2\text{Me}^{\text{a}}}$	 Yield(%) / ee(%) ^{c)}
 (6c)	$\xrightarrow[\text{MgCl}_2/\text{THF}]{\text{CH}_2=\text{CHCO}_2\text{Me}^{\text{a}}}$	48/60
 (6d)	$\xrightarrow[\text{MgCl}_2/\text{THF}]{\text{CH}_2=\text{CHCO}_2\text{Me}^{\text{a}}}$	62/>95

a) Reaction conditions : 20°C, 15 hr. b) The reaction product was obtained after hydrolysis on silica gel with H₂O. c) The major enantiomer of **8** has (S)-configuration. (Ref. 9)

Table 3.

 Amino Group	$\xrightarrow[\text{MgCl}_2/\text{THF}]{\text{CH}_2=(\text{SiMe}_3)\text{COCH}_3}$	 Product Yield(%) / ee(%) ^{c)}
 (6a)	$\xrightarrow[\text{MgCl}_2/\text{THF}]{\text{CH}_2=(\text{SiMe}_3)\text{COCH}_3}$	50/53 a),d)
 (6b)	$\xrightarrow[\text{MgCl}_2/\text{THF}]{\text{CH}_2=(\text{SiMe}_3)\text{COCH}_3}$	34/77 b),e)

a) Reaction conditions : 0°C, 24 hr → r.t., 24 hr. b) Reaction conditions : r.t., 15 hr. c) The major enantiomer of **9** has (S)-configuration. (Ref. 10) d) $[\alpha]_{\text{D}}^{20} = +48.5^\circ$ (EtOH). e) $[\alpha]_{\text{D}}^{20} = +70.9^\circ$ (EtOH).

References and Notes

- (1) (a) P. Mangeney, A. Alexakis and J. F. Normant, *Tetrahedron Lett.*, 24, 373 (1983).
 (b) M. Huche, J. Aubouet, G. Pourcelot and J. Berlan, *Tetrahedron Lett.*, 24, 585 (1983).
- (2) Trapping of the intermediate **2** with trimethylchlorosilane was performed as follows. To a stirred mixture of 2-vinyloxazolidine (**1a**) (3 mmol) and Cu(I)Br·SMe₂ (20 mg) in THF (10 mL) was methylmagnesium bromide (4.5 mmol) in ether (2 mL) at -5°C. After 1 hr, the mixture was cooled down to -78°C, to which trimethylchlorosilane (6.0 mmol) and triethylamine (6.0 mmol) were added and allowed to warm up to room temperature. The mixture was diluted with ether, filtered and distilled to afford N-[2-(trimethylsilyloxy)alkyl] enamine **4a** (86% yield) [bp 130-135°C (1 mmHg)]. **4a**: IR (neat) 1660(m), 1250(s), 880(s), 840(s) cm⁻¹; NMR (CDCl₃) δ 5.50-5.66 (broad m, 1H). Similarly, enamine **4b** was prepared in 91% yield. **4b**: IR (neat) 1655(m), 1250(s), 880(s), 840(s) cm⁻¹; NMR (CDCl₃) δ 5.4-5.6 (broad m, 1H).
- (3) Oxazolidines **1** and **5** were prepared by the conventional azeotropic dehydration of ketones or aldehydes with 2-amino alcohols.
- (4) **6a**: IR(neat) 1650, 1250, 1075 cm⁻¹; NMR(CDCl₃) δ 0.05 (s, 9H), 0.96 and 1.00 (two d, 6H), 1.19 (d, 3H, J=7.0 Hz), 1.9-2.6 (m, 1H), 2.53 (s, 3H), 3.17 (qd, 1H, J=7.0 and 5.7 Hz), 4.00 (dd, 1H, J=14.0 and 7.2 Hz), 4.70 (d, 1H, J=5.7 Hz), 6.00 (d, 1H, J=14.0 Hz), 7.36 (s, 5H). **6b**: NMR (CDCl₃) δ 0.14 (s, 9H), 1.04 (d, 6H, J=6.8 Hz), 1.4-4.0 (m, 10H), 4.16 (dd, 1H, J=13.8 and 6.9 Hz), 6.40 (d, 1H, J=13.8 Hz). **6c**: NMR (CDCl₃) δ 0.0 (s, 9H), 1.10 (d, 3H, J=6.8 Hz), 0.9-2.6 (m, 8H), 2.55 (s, 3H), 3.63 (m, 1H), 4.37 (t, 1H, J=3.7 Hz), 4.67 (d, 1H, 6.6 Hz), 7.3 (s, 5H). **6d**: NMR (CDCl₃) δ 0.11 (s, 9H), 1.0-2.5 (m, 12H), 2.5-3.7 (m, 5H), 4.06 (t, 1H, J=3.7 Hz).
- (5) The effect of MgCl₂ was also observed in a reaction of N-(3-methyl-1-butenyl)piperidine with 3-penten-2-one in THF (r.t., 15 hr), which gave **7** in 61% yield. The reaction did not proceed in the absence of MgCl₂ in THF at reflux.
- (6) Compound **7** was a trans and cis mixture, of which ratio was determined by glpc. [ZnCl₂ in Et₂O, r.t., 44 hr: 53% yield (94:6 stereoisomers)]. **7**: IR (neat) 1680 cm⁻¹; NMR (CDCl₃) δ 0.5-1.5 (m, 9H), 1.5-3.0 (m, 5H), 6.08 (d, 1H, J=10.5 Hz), 6.97 (d, 1H, J=10.5 Hz).
- (7) (a) K. Narasaka, T. Miwa, H. Hayashi and M. Ohta, *Chem. Lett.*, 1399 (1984).
 (b) B. De. Jeso and J. Pommier, *Tetrahedron Lett.*, 21, 4511 (1980).
- (8) (a) K. Hiroi, K. Achiwa and S. Yamada, *Chem. Pharm. Bull.*, 20, 246 (1972).
 (b) S. J. Blarer and D. Seebach, *Chem. Ber.*, 116, 2250 (1983).
- (9) The absolute configuration and the enantiomeric excess % were determined, respectively, on the basis of the reported ORD spectrum and a 400 MHz ¹H NMR spectrum of **8** with Eu(hfc)₃ as a chiral shift reagent. The observed [α]₄₆₀²⁵ = -12.95 (c 3.24, MeOH) was larger than the reported maximum rotation.⁸⁾
- (10) The absolute configuration and the enantiomeric excess % were determined on the basis of the reported rotation and configuration of **9**. [(a) D. T. C. Gillespie, A. K. Macbeth and J. A. Mills, *J. Chem. Soc.*, 1948, 996. (b) M. D. Soffer and G. E. Glnay, *Tetrahedron Lett.*, 1963, 389.]

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