a new method of differentiation of one carbonyl group from the other.

Various synthetic applications of the product 4 may be envisaged.[14]

References and Notes

(1) Synthesis via Silyl Alkenyl Ethers. Part 14. Part 13: I. Ryu, S. Murai, and N. Sonoda, *Tetrahedron Lett.*, 4611 (1977).
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(3) Cyanosilylated derivatives of monosilylated β-diketones should have electron rich C=C double bonds to allow interesting reactions with various electrophiles.
(4) **3**: IR (neat) 1640 cm^{-1}; NMR (CCl_4) δ 0.23 (s, 18 H), 1.55 (s, 3 H), 2.18–2.56 (d-d, 2 H), 4.08 (s, 2 H); MS *m/e* 271 (M^+).
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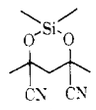
(6) For enolization of β-diketones, see: S. Forsen and M. Nilsson in "The Chemistry of the Carbonyl Group", Vol 2, J. Zabicky, Ed., Interscience, London, 1970, Chapter 3; H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, pp 157–240.
(7) S. Torkelson and C. Ainworth, *Synthesis*, 722 (1976), and references cited therein.
(8) It is not clear whether **9** was formed from dehydrocyanation of **8** or directly from **6**.
(9) **6**: NMR (CH_2Cl_2) δ 0.33 (s, 6 H), 1.34 (s, 6 H), 2.06 (s, 3 H), 2.56 (s, 2 H). **7**: IR 1720 cm^{-1}; NMR (CCl_4) δ 0.07 (s, 6 H), 1.33 (s, 6 H), 2.09 (s, 3 H), 2.48 (s, 2 H), 3.39 (s, 3 H); MS *m/e* 189 (P − 15).
(10) Well accepted 1,6 interaction of silicon and oxygen may be responsible for this: see T. J. Pinnavaia and J. A. McClarin, *J. Am. Chem. Soc.*, **96**, 3012 (1974), and references cited therein.
(11) The possibility that the initial formation of doubly cyanosilylated product i followed by dehydrocyanation might afford **4** is not precluded at the present stage.



i

(12) For example, the parent β-diketone of 5-cyano-1,1,3,5-tetramethyl-2,6-dioxa-1-silacyclohex-3-ene was regenerated on treatment with methanol (2 mL for 4 mmol of **4**) in 85% (room temperature, 20 h).
(13) The reaction of trimethylcyanosilane with 1 equiv of acetylacetone gave the enol silyl ether **1** (*E* + *Z*) in a high yield.
(14) Attempts of cyclopropanation of the product **4**, which may promise the one carbon homologation of β-diketones, are now in progress.

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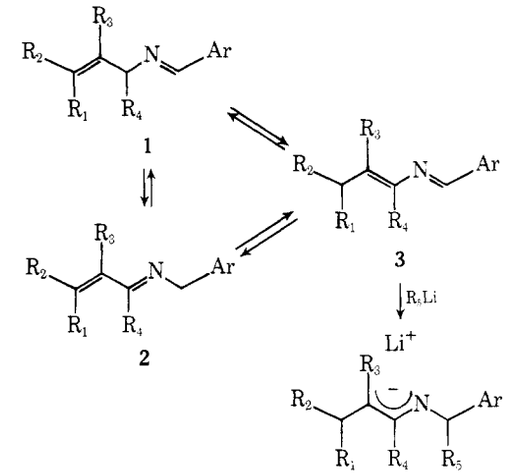
Imine Prototropy: Synthetic Consequences in the Generation of Metalloenamines

Summary: *N*-allylic imines and α,β-unsaturated imines undergo facile prototropic isomerization to *N*-alkenylimines which, upon reaction with *tert*-butyllithium, are converted into metalloenamines; the overall process allows for the regiocontrolled, sterically unimpeded generation of these organometallic intermediates.

Sir: Initial reports from the laboratories of Stork[1a] and Wittig[1b] on the utility of metalloenamines in controlled alkylation and directed aldol processes, respectively, have fostered in subsequent years a rapid expansion of methodology[2] and synthetic strategies[3] based on these intermediates. Notwithstanding this record, the preparation of metalloenamines is confined presently to imine deprotonation with strong base, a procedure which is only useful for metalation (and hence bond formation) at the less-substituted α site of an unsymmetrically substituted ketimine.[4] Moreover, the efficiency of imine metalation with various bases is found to decrease with increasing substitution at the deprotonation site.[1b] We recently reported on methods which circumvent these limitations by the regiospecific, reductive generation of metalloenamines from α,β-unsaturated imines.[5] A further solution to the above noted problems is described herein.

Two studies bear on the genesis of the present method. In 1929, Ingold and associates[6] reported that *N*-benzylimines undergo prototropic isomerization with base to provide a thermodynamic mixture of imine isomers (eq 1). More recently, it has been proposed[7] (albeit not demonstrated) that the enzyme inactivation produced by suicide enzyme substrates, such as propargylamine, involves a similar prototropic isomerization of an active site bound *N*-propargylimine. By analogy with these studies and the results of our previous work, we reasoned that the readily available *N*-allylic imines (**1**) of arylaldehydes would be sufficiently activated for base-catalyzed rearrangement to *N*-alkenylimines (**3**) (eq 2). Nucleophilic addition to these intermediates would then be expected to provide the corresponding metalloenamines in a regiospecific, sterically unimpeded manner.



(2)

In order to explore this rationale the proclivity of imine **1a** to prototropic isomerization was initially examined. Addition of this imine to a solution of potassium *tert*-butoxide (*t*-BuOK) in tetrahydrofuran (THF) was accompanied by an instantaneous reaction which upon workup provided alkenylimine **3a**[8] in essentially quantitative yield. The facility of this transformation at ambient temperature precluded an accurate determination of its half-life; however, at −78 °C a value of ~60 min was obtained. When the isomerization was conducted at 5 °C with 0.33 mol equiv of *t*-BuOK in the presence of 7.6 mol equiv of *t*-BuOD, the reaction was complete within 10 s and provided on workup d_1 and d_0 alkenylimines[9] in a ratio (1:2, respectively, as determined by NMR and mass spectroscopy) which is consistent with competing inter-

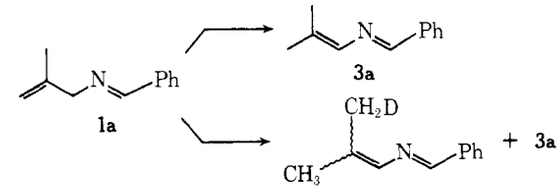


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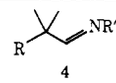
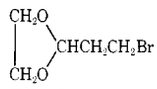
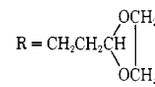
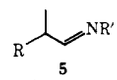
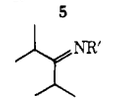
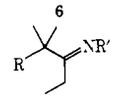
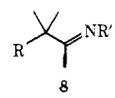
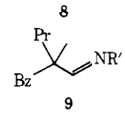
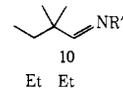
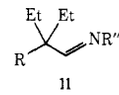
Table I

Entry	Starting material: Ar	R_1	R_2	R_3	R_4		Equilibrium composition, %: 1	2	3
1	Ph	H	H	Me	H	(**1a**)			>95
2	Ph	H	H	H	H	(**1b**)			>95
3	Ph	H	H	H	*i*-Pr	(**1c**)		>95	
4	Ph	H	H	Me	Et	(**1d**)			>95
5	Ph	H	H	Me	Me	(**1e**)			>95
6	Ph	H	Me	H	H	(**1f**)		*a*	
7	Ph	H	$-(CH_2)_4-$		H	(**1g**)		>95	
8	Ph	H	Et	Me	H	(**2h**)			>95
9	Ph	H	Me	Me	H	(**2i**)			>95
10	Ph	H	Me	H	H	(**2f**)		*a*	
11	Ph	H	*i*-Pr	H	H	(**2j**)		>95	
12	Ph	H	Me	Et	H	(**2k**)		>95	
13	PhOMe-*p*	H	Me	Et	H	(**2l**)			>95

[a] Isomerization of this substrate to **3f** was accompanied by polymerization.

Table II

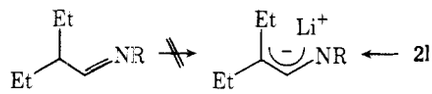
Entry	Starting material	Electrophile	Product[a]		% isolated yield
1	**1a**	MeI	 **4**	R = Me	93
2		BzBr		R = Bz	86
3		*n*-BuI		R = *n*-Bu	95
4		CH_2CHCH_2Br		R = CH_2CHCH_2	83
5		*i*-PrI		R = *i*-Pr	94
6				R = 	60
7		PhCOCl		R = PhCO	81
8		Me_3SiCl		R = Me_3Si	82
9		H_2O		R = H	81
10	**1b**	MeI	 **5**	R = Me	58
11		CH_2CHCH_2Br		R = CH_2CHCH_2	65
12		$CH_2C(Br)CH_2Br$		R = $CH_2C(Br)CH_2$	48
13	**1c**	MeI	 **6**		55
14	**1d**	MeI	 **7**	R = Me	90
15		H_2O		R = H	83
16	**1e**	MeI	 **8**		93
17	**2h**	BzBr	 **9**		86
18	**2i**	MeI	 **10**		87
19	**2l**	EtI	 **11**	R = Et	80
20		BzBr		R = Bz	83

[a] R′ = $-CH[C(CH_3)_3]Ph$; R″ = $-CH[C(CH_3)_3]$PhOMe-*p*.

and intramolecular isomerization processes.[6] Exchange of all nonaromatic hydrogens for deuterium was achieved upon prolonged exposure (>100 h) of imine **1a** to *t*-BuOK/*t*-BuOD. Other bases such as potassium isopropoxide and potassium ethoxide were also found to catalyze the rearrangement, while potassium hydroxide and potassium methoxide were only effective when used in combination with 18-crown-6 ether.

The effect of substitution in the allylic moiety on the above rearrangement is exemplified by the entries in Table I. In general, the isomer (**1**, **2**, or **3**) with the more highly substituted double bond is favored at equilibrium.[10] Whereas appropriately substituted unsaturated imines (**2**) can also be used in the preparation of alkenylimines (**3**) (entries 8 and 9), the equilibrium position is again dependent on substitution on the allylic or unsaturated imine moieties (entries 10–12). However, this limitation may be circumvented by substitution on the aromatic ring. The effectiveness of this modification is exemplified with 2-ethylbut-2-enal: the corresponding *N*-benzylimine **2k** is recovered unchanged under basic equilibrating conditions, whereas under the same conditions the *N*-(*p*-methoxybenzyl)imine **2l** provides the desired *N*-alkenylimine **3l** (>95%).

Transformation of the *N*-alkenylimine into the corresponding metalloenamine is readily performed by reaction of the former with *tert*-butyllithium. The efficiency of this process, as determined by trapping of the metalloenamine with various electrophiles, is illustrated by the entries in Table II. Several features of this tabulation are noteworthy. First, the overall yields are moderate to excellent, even in cases, such as entry 5, where the conjunction of a sterically encumbered nucleophile and electrophile is required in the alkylation step. Secondly, the process is regiocontrolled: imines **1c** and **1d** are converted into imines **6** (>99.5% VPC isomeric purity) and **7** (R = Me, >99.5% VPC isomeric purity), respectively, without evidence of crossover (i.e., metalloenamine equilibration). Similarly, imine **1e** regiospecifically provides the alkylated imine **8** (>99.5% VPC isomeric purity). By contrast, the metalloenamine generated in this process (**1e** → **8**) cannot be prepared from the corresponding methyl ketimine using conventional deprotonation, since such methodology is restricted to metalation "on the methyl group only".[4] Finally, the process is not subject to the steric constraints encountered in imine deprotonation. For example, Wittig[1b] reported that imine **12** (R = c-C_6H_{11}) was not deprotonated by lithium di-

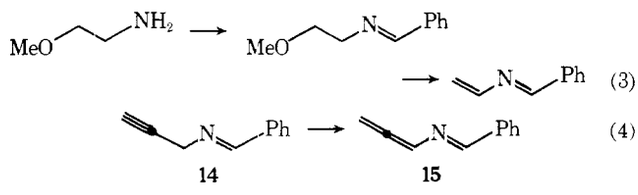


12 **13**

isopropylamide (2 h), tritylsodium, or tritylpotassium (for periods exceeding 4 weeks). Using the present method, the related metalloenamine **13** (R = CH(*t*-Bu)PhOMe-*p*) was efficiently generated from **2l** and converted to **11** (R = Bz) in an overall yield of 83% (isolated).

The *N*-allylic imines used in the present study were formed in >91% yield through condensation of the allylic amine[11] with benzaldehyde and converted to the corresponding metalloenamines using commercially available reagents. The following procedure is representative. Imine **1a** (16.5 mmol, ~1 M THF) was added to a solution of *t*-BuOK (3.4 mmol) in THF (42 mL). The resulting solution was stirred at ambient temperature (10 min), cooled to −78 °C, and transferred via cannula to a well-stirred solution (−78 °C) of *t*-BuLi (25 mmol) in pentane (14.8 mL). After 15 min, *n*-butyl iodide (33.5 mmol) was added. The resulting solution was stirred for 1 h at −78 °C, 1 h at ambient temperature, and treated with an equivalent volume of water. The mixture was extracted with methylene chloride and the combined organic phase was dried (Na_2SO_4) and concentrated. Distillation of the crude oil provided imine **4** (R = Bu, bp 119–129 °C (0.2 mm), 95%).[12] The alkylated imines are readily converted into the carbonyl derivatives by hydrolysis with 2 N hydrochloric acid or by distillative hydrolysis using aqueous oxalic acid.

In addition to the transformations of allylic imines and unsaturated imines into alkylated imines (and thence ketones and aldehydes) noted above, several further consequences of this chemistry are noteworthy. For example, the allylic imine isomerization involves a transient species which is functionally equivalent to a homoenolate. Thus, the method can be used to prepare β-deuteriocarbonyl derivatives (vide supra).[13] Furthermore, the imine functionality can be used to facilitate elimination reactions (eq 3) and, as such, this strategy can be employed as an alternative method for the preparation of alkenylimines.[14] Finally, in vitro analogy for suicide enzyme inhibition has been demonstrated in the conversion of propargylimine **14** into the novel allenylimine **15** (eq 4). Further studies are in progress.



14 **15**

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(1) (a) G. Stork and S. Dowd, *J. Am. Chem. Soc.*, **85**, 2178 (1963); (b) G. Wittig, H. D. Frommeld, and P. Suchanek, *Angew. Chem.*, **75**, 978 (1963); *Angew. Chem., Int. Ed. Engl.*, **2**, 683 (1963); G. Wittig and H. D. Frommeld, *Chem. Ber.*, **97**, 3548 (1964); and as reviewed by G. Wittig and H. Reiff, *Angew. Chem.*, **80**, 8 (1968); *Angew. Chem., Int. Ed. Engl.*, **7**, 7 (1968).

(2) Representative examples include the preparation of (a) α-, β-, γ-, and δ-dicarbonyl compounds, diimines, and derivatives: G. Wittig, S. Fischer, and M. Tanaka, *Justus Liebigs Ann. Chem.*, 1075 (1973); T. Cuvigny, M. Larcheveque, and H. Normant, *Tetrahedron Lett.*, 1237 (1974); M. Larcheveque, G. Valette, T. Cuvigny, and H. Normant, *Synthesis*, 256 (1975); T. Cuvigny and H. Normant, *Ibid.*, 198 (1977); R. M. Jacobsen, R. A. Raths, and J. H. McDonald, *J. Org. Chem.*, **42**, 2545 (1977); S. Danishefsky and A. Zimmer, *ibid.*, **41**, 4059 (1976); and ref 1; (b) β-hydroxy ketones and aldehydes and the related unsaturated carbonyl compounds: W. Nagata and Y. Hayase, *J. Chem. Soc. C*, 460 (1969); G. Stork and J. Benaim, *J. Am. Chem. Soc.*, **93**, 5938 (1971); K. Takabe, H. Fujiwara, T. Katagiri, and T. Tanaka, *Tetrahedron Lett.*, 1237 (1975); E. J. Corey, D. Enders, and M. G. Bock, *ibid.*, 7 (1976); (c) dihydrofurans: W. E. Harvey and D. S. Tarbell, *J. Org. Chem.*, **32**, 1679 (1967); (d) aminocycloalkenes: K. Takabe, H. Fujiwara, T. Katagiri, and J. Tanaka, *Tetrahedron Lett.*, 1239 (1975); (e) pyrroles: G. Wittig, R. Röderer, and S. Fischer, *ibid.*, 3517 (1973). Chiral metalloenamines have been used with unprecedented success in enantioselective alkylations: A. I. Meyers, D. R. Williams, and M. Druelinger, *J. Am. Chem. Soc.*, **98**, 3032 (1976); J. K. Whitesell and M. A. Whitesell, *J. Org. Chem.*, **42**, 377 (1977); M. Kitamoto, K. Hiroi, S. Terashima, and S. Yamada, *Chem. Pharm. Bull.*, **22**, 459 (1974); D. Méa-Jacheet and A. Horeau, *Bull. Soc. Chim. Fr.*, 4571 (1968); and references cited therein.

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(4) M. Larcheveque, G. Valette, T. Cuvigny, and H. Normant, *Synthesis*, 256 (1975), and references cited therein.

(5) P. A. Wender and M. A. Eissenstat, *J. Am. Chem. Soc.*, **100**, 292 (1978).

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(7) For a review on this subject, see R. H. Abeles and A. L. Maycock, *Acc. Chem. Res.*, **9**, 313 (1976).

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(9) The *E* and *Z* isomers of the d_1 alkenylimine were formed in approximately equal amounts.

(10) In the case of **1g** isomerization gave exclusively the unsaturated imine as expected from the general preference for *endo*- over *exo*-olefin in such systems: A. H. Dickens, W. E. Hugh, and G. A. R. Kon, *J. Chem. Soc.*, 1630 (1928); J. C. Aumiller, and J. A. Whittle, *J. Org. Chem.*, **41**, 2959 (1976).

(11) For a convenient preparation of allylic amines, see: L. E. Overman, *J. Am. Chem. Soc.*, **98**, 2901 (1976).

(12) Alternatively, the *N*-alkenylimines can be isolated after the initial isomerization and stored until needed. Generation of the metalloenamine is then simply effected by addition of an aliquot of the reagent stock solution to a solution of *t*-BuLi.

(13) Specific deuteration of the β position of carbonyls has also been accomplished by enone reduction with $Fe(CO)_5$ in deuterated solvents (R. Noyori, I. Umeda, and T. Ishigami, *J. Org. Chem.*, **37**, 1542 (1972)), and with Li in deuterated amines (D. H. Williams, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 2091 (1963) and M. Fetizon and J. Gore, *Tetrahedron Lett.*, 471 (1966)).

(14) For a further route to alkenylimines, see: A. Dehnel, J. P. Finet, and G. Lavielle, *Synthesis*, 474 (1977).

(15) National Science Foundation Predoctoral Fellow, 1975–1977.

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Total Synthesis of (±)-Sarracenin

Summary: The synthesis of the iridoid monoterpene sarracenin is described.

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