

REACTIONS OF 2-LITHIOSILYLMETHYL-1,3-OXAZINES WITH CARBONYL COMPOUNDS.
A CONVENIENT ROUTE TO STEREOSELECTIVE OLEFIN SYNTHESIS

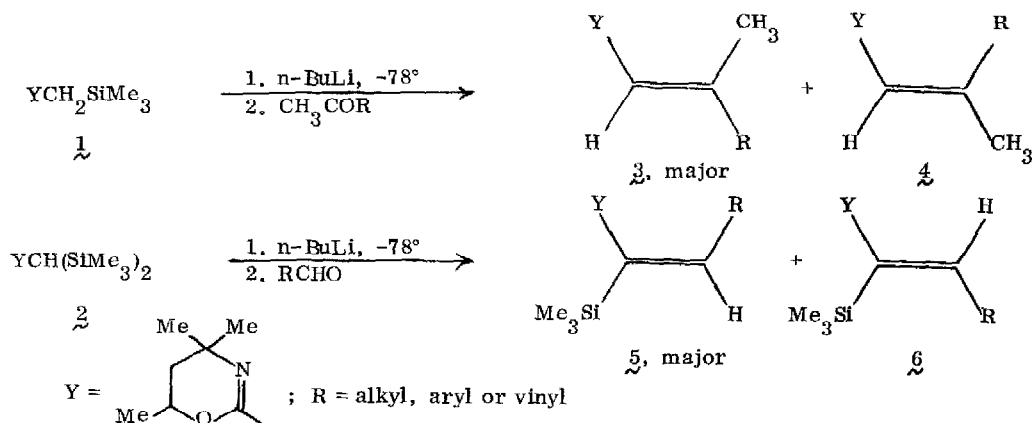
Krishna Sachdev *

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA

(Received in USA 28 July 1976; received in UK for publication 21 September 1976)

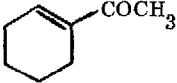

The versatility of organo silicon reagents has been amply demonstrated by their application to the synthesis of olefins, ^{1,2} vinylsilanes ³ and ketenethioacetals, ⁴ etc. This communication is concerned with a high yield "Peterson olefination" using the lithium reagents derived from 2-(trimethylsilyl)methyl-5,6-dihydro-1,3-oxazine (**1**) and the bis-trimethylsilylmethyl derivative (**2**) as expressed by Scheme A.

Scheme A



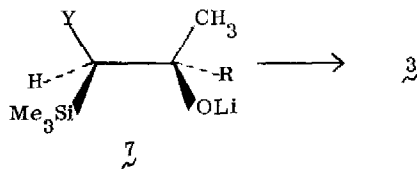
Meyers, *et al.*,⁵ have well established the utility of 2-substituted 1,3-oxazines as useful precursors of highly functionalized carbonyl compounds. The present study complements their synthesis of vinyloxazines via phosphonate $\text{YCH}_2\text{PO}(\text{OC}_2\text{H}_5)_2$ and phosphorane $\text{YCH}_2^+\text{PPh}_3\text{Cl}^-$, which upon reaction with acetophenone give cis-trans mixtures (24:76) and (50:50), in 57 and 70% yields, respectively. We have observed that the lithio reagent derived from **1** upon reaction with unsymmetrical ketones generally affords one major product ⁶ in excellent yields (Table 1). Further, the lithio derivative of **2** is highly selective and reacts smoothly and efficiently with aldehydes (but not with ketones)⁷ to give stereoselectively vinylsilanes **5** as useful intermediates capable of further functionalization.^{8,9}

Table 1

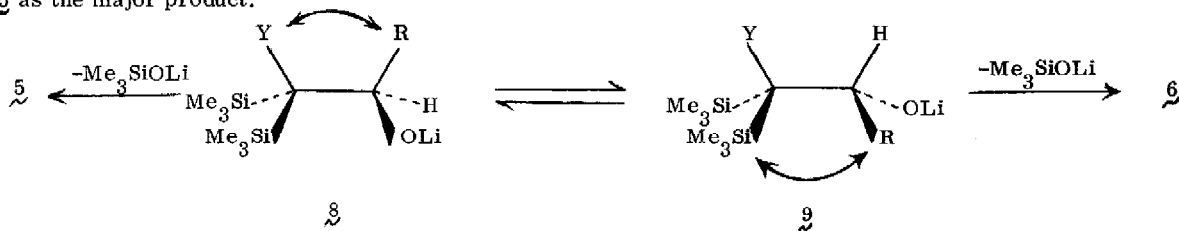
Carbonyl compound	Product ^a b. p. °C/mm	(3:4) ^b	Chemical Shift Values ^c			
			olefinic H		C=C-CH ₃	
			major	minor	major	minor
C ₆ H ₅ COCH ₃	R = -C ₆ H ₅	(96:4)	5.92	6.07	2.09	2.4
		84-86/0.1	q, J=1.5		d, J=1.5	
CH ₃ COCH(CH ₃) ₂	= -CH(CH ₃) ₂	(85:15)	5.63	--	1.8	--
		81-83/2.0	m		d, J=1.5	
	= 	(95:5)	5.6 ^d	--	1.84	--
		76-77/0.1 ^e	q, J=1.5		d, J=1.5	
CH ₃ CH ₂ COCH ₃	= -CH ₂ CH ₃	(75:25)	5.6	--	1.76	--
		62-65/1.0	m		d, J=1.5	
	Product	(5:5)	olefinic H			
			major	minor		
C ₆ H ₅ CHO	R = -C ₆ H ₅	(90:10)	6.68	--		
		92-94/0.1	s			
(CH ₃) ₂ CHCHO	= -CH(CH ₃) ₂	(93:7)	5.7	--		
		53-54/0.2	d, J=9			
CH ₃ CH ₂ CHO	= -CH ₂ CH ₃	(86:14)	5.91	6.57		
		60-62/0.3	t, J=7	t, J=7		
CH ₃ CHO	= -CH ₃	(76:24)	6.06	6.7		
		100-105/15	q, J=7	q, J=7		

- a. Yields based on the distilled products were between 80-95%.
- b. The product ratios were determined by glpc analysis on a 6 ft. x 1/8 in. glass column packed with 3% SE-30 on Gas Chrom Q. The stereochemical assignments are based on the comparison of glpc retention times and nmr spectral data with the products of thermal equilibration.
- c. In ppm downfield from TMS. J values in hertz.
- d. Partly overlaps a multiplet at 5.5 ppm due to the olefinic H of cyclohexene.
- e. Cannot be kept for any considerable length of time as it darkens even at -20°, but can be stored without deterioration as methyl fluoroborate.

In recent studies with diastereomerically pure β -hydroxysilanes it has been demonstrated^{1b} that the base induced β -elimination occurs stereospecifically in a syn fashion. In the present investigation the formation of one major olefin from the reaction of the lithio derivative of 1 with unsymmetrical ketones would require that the initial adduct be formed with an overwhelming preference for the diastereomer 2, which upon syn elimination of Me₃SiOLi would give 3.



The products 5 and 6 (Scheme A) appear to be formed in nearly a thermodynamic ratio as no change was observed when a 10% solution in decalin was heated in a sealed tube at 180–190° for 70 min.¹⁰ The stereochemical assignments in this case are tentative and are based on the assumption that the Me₃Si-R interaction is more destabilizing than the Y-R interaction. The elimination then may proceed through conformer 8 to give 5 as the major product.



Silylation of 2-methyl 4, 4, 6-trimethyl-5, 6-dihydro-1, 3-oxazine (10): preparation of 1 and 2. To a stirred suspension of the lithio reagent prepared at -78° from 7.05 g (50 mmole) of 10 according to Meyers, *et al.*,⁵ was added trimethylchlorosilane (5.5 g, 50 mmole) in dry THF (20 ml) over 15 min. After 2 hr the reaction mixture was allowed to warm to ambient temperature, stirred for another 2 hr, and poured into ice water (50 ml). The organic layer was separated and the aqueous part was extracted with three 50 ml portions of ether. The extracts were combined, washed with brine, dried (MgSO₄), concentrated and distilled at 85°/6 mm to give 8.1 g (80%) of 1 as a colorless liquid: nmr (CDCl₃) shows characteristic signals at 0.1 ppm (s, SiMe₃) and 1.61 ppm (s, C-CH₂-Si).

Disilylmethyloxazine (2) was prepared from 10 by the above procedure without isolating the monosilylation product (1) which was treated with another equiv of *n*-butyllithium at -78° followed after 1 hr by one equiv of trimethylchlorosilane. The usual workup after 2 hr at -78° and 2 hr at 25° gave 2 as a colorless oil, b.p. 95–97°/3.5 mm.

Reaction of lithio derivatives of 1 and 2 with carbonyl compounds. A typical procedure is as follows. To a stirred solution of 1 (6 mmole) in THF (6 ml) at -78° under argon was introduced *n*-butyllithium (2.3 ml, 2.68 M in hexane). After 1 hr freshly distilled acetophenone (0.72 g, 6 mmole) in THF (5 ml) was added over a 5 min period and the reaction mixture was allowed to remain for 2 hr at -78° and 14 hr at 25°. The product mixture was then poured into ether/water (10 ml/5 ml), the organic layer was separated and the aqueous part was extracted with two 10 ml portions of ether. The extracts were washed with brine, dried (anhyd. K₂CO₃), concentrated and distilled to give the products (Table 1). The same procedure was followed with 2 for reactions with aldehydes.

Acknowledgement. We are grateful to Professor Glenn A. Berchtold for providing laboratory facilities including funds and for his encouragement.

REFERENCES AND NOTES

- * Present address: Polaroid Corporation, Research Laboratories, 750 Main St., Cambridge, MA, 02139.
1. (a) D. J. Peterson, J. Org. Chem., 33, 780 (1968); A. W. D. Jarvie, Organometal. Chem. Rev. A, 6, 153 (1970); (b) P. F. Hudrlik and D. Peterson, J. Amer. Chem. Soc., 97, 1464 (1975) and literature cited therein; P. F. Hudrlik, D. Peterson and R. J. Rona, J. Org. Chem., 40, 2263 (1975); (c) P. B. Dervan and M. A. Shippey, J. Amer. Chem. Soc., 98, 1265 (1976); M. T. Reetz and M. Plancky, Synthesis, 199 (1976).
 2. E. J. Corey, D. Enders and M. G. Bock, Tetrahedron Letters, 7 (1976); H. Yamamoto, *et al*, J. Amer. Chem. Soc., 96, 1620 (1974); D. J. Faulkner, Synthesis, 175 (1971); S. L. Hartzell, D. F. Sullivan and M. W. Rathke, *ibid.*, 1403 (1974).
 3. (a) B. T. Grobel and D. Seebach, Angew. Chem. Int. Ed., 13, 83 (1974); (b) H. Sakurai, K. Nishiwaki and M. Kira, Tetrahedron Letters, 4193 (1973); M. A. Cook, J. Organometal. Chem., 24, 529 (1970).
 4. F. A. Carey and A. S. Court, J. Org. Chem., 37, 939, 1926 (1972); D. Seebach, *et al*, Angew. Chem. Int. Ed., 11, 443 (1972); P. F. Jones and M. F. Lappert, Chem. Commun., 526 (1972).
 5. A. I. Meyers, *et al*, J. Org. Chem., 38, 36 (1973); *ibid.*, 39, 618, 623 (1974).
 6. Upon reaction with acetaldehyde, propionaldehyde and isobutyraldehyde, monosilylmethyloxazine (1) gave *cis-trans* mixtures (*ca.* 55:45) while with benzaldehyde the ratio was 70:30.
 7. Attempted reaction with acetophenone and with isopropylmethyl ketone led only to the recovery of the starting materials.
 8. G. Stork and E. Colvin, J. Amer. Chem. Soc., 93, 2080 (1971); *ibid.*, 96, 3682, 3684 (1974); R. K. Boeckman and J. Bruza, Tetrahedron Letters, 3365 (1974); also reference 3a.
 9. K. E. Koenig and W. P. Weber, Tetrahedron Letters, 2533 (1973); J. Amer. Chem. Soc., 95, 3416 (1973); R. B. Miller and T. Reichenbach, Tetrahedron Letters, 543 (1974).
 10. Vinyl oxazines of the type 3 and 4 undergo *cis-trans* equilibration under similar conditions in less than 1 hr, also see reference 5.