Tetrahedron Letters, Vol.32, No.37, pp 4929-4932, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

A Novel Synthesis of Acylsilanes

Masahisa Nakada, Sei-ichi Nakamura, Susumu Kobayashi, and Masaji Ohno*

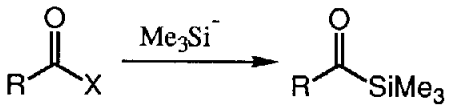
Faculty of Pharmaceutical Sciences, University of Tokyo
Hongo, Bunkyo-ku, Tokyo 113, Japan

Abstract : A mild and general preparative method for acylsilanes is presented. This novel method can be applied without any difficulty to α-chiral, α-alkoxy and multifunctionalized compounds.

Since the discovery of Brook rearrangement in 1958[1], acylsilanes have been recognized as starting materials for silyl enol ethers[2] and useful synthetic intermediates[3]. Acylsilanes are functionally quite unique , possessing various reactivities and selectivity[4]. We also developed a method for 1,2-asymmetric induction in acyclic system utilizing α-chiral acylsilanes as α-chiral aldehyde-equivalents to afford products with high diastereofacial selectivity[5].

The synthesis of acylsilanes via 1,3-dithianes was developed by Brook[6] and Corey[7], and extensive studies on the synthetic methods for acylsilanes were recently reported[4]. However, the reported methods are narrow in scope and have some limitations. For instances, the problem of β-elimination at the lithiation of dithianes derived from α-alkoxy aldehydes is unsolved yet, and partial racemization of α-chiral aldehydes takes place at a converting step. Acid chlorides[8] were found to give some acylsilanes by treatment with tris(trimethylsilyl)aluminum (Al(SiMe3)3)[9], but acid chlorides generally require rather drastic conditions.

Scheme 1



In this communication, we report an efficient and general preparative method of acylsilanes, which can be applied widely to the compounds with various substituents including an alkoxy group at α position of the carbonyl group. Thus, carboxylic acids or their derivatives were chosen as starting materials because of the facile availability in α-chiral form. Also examined was the trimethylsilyl anion source, and among many reagents tested Al(SiMe3)3 was chosen because of the chemoselectivity and the stability.

Reactions of Al(SiMe3)3 with mixed anhydrides[10] were first examined and acylsilanes were obtained in moderate yields in the presence of CuCN. Next, thiol esters, well known as active esters and used in peptide chemistry[11], macrolide synthesis[12], and β-lactam synthesis[13]were tested. No

Table 1 **Synthesis of Acylsilanes from S-2-Pyridyl Thioates**

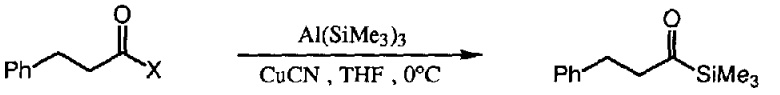


Table 1-1

Entry	X	CuCN (equiv)	Reaction Time(h)	Yield (%)
1	S-Ph-	1.1	24	no reaction
2	S-2-Py-	1.3	0.1	quant.
3		0.1	1	75
4		0	24	trace

Table 1-2 (X= S-2-Py-)

Entry	Additive (equiv)	Temp. (°C)	Reaction Time	Yield
1	LiI(1.1)	0 to r.t.	1h	quant.
2	CuI(1.2)	0 to r.t.	35min	98%
3	CuCN(1.3)	0	1min	quant.
4	AgCN(1.2)	0 to r.t.	3h	trace

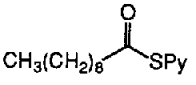
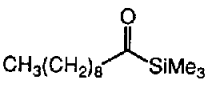
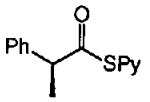
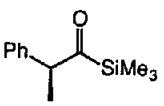
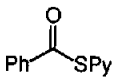
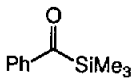
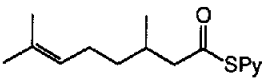
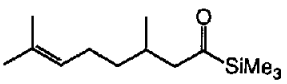
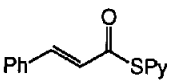
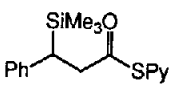
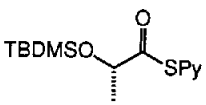
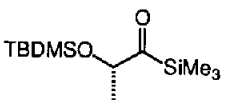
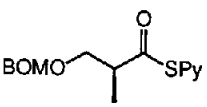
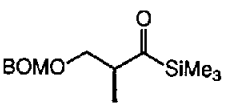
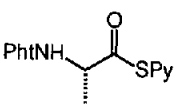
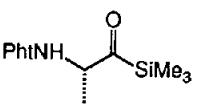
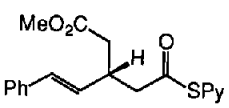
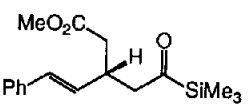
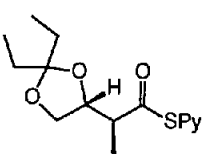
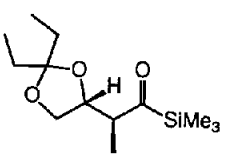
reaction occurred when S-Phenyl esters were treated with Al(SiMe3)3, but S-2-Pyridyl esters were found to react very smoothly with Al(SiMe3)3(0.5 equiv or more) to afford desired acylsilanes in the presence of CuCN (**Table 1-1**). Catalytic amount of CuCN required more prolonged reaction time with moderate yields. Use of Al(SiMe3)3 and CuCN in excess amount was found not to cause any side-reaction. For instance, no α-bis-trimethylsilyl alcohol was detected within a few hours. Among various additives such as Li(I), Cu(I), Ag(I) examined, CuCN was found to accelerate the reaction very smoothly to afford the desired product in excellent yields (**Table 1-2**). Therefore, the condition of entry 3 in **Table 1-2** was generally used for other substrates (**Table 2**). The substrates listed in **Table 2** were prepared by PPh3 and (PyS-)2 starting from carboxylic acids in excellent yields. As shown in **Table 2**, this method was found to be applied to substrates having various substituents such as alkoxyl group, acetal, ester, isolated double bond, and also to α-chiral ones without losing the optical purity (see the following procedure). Especially, the acylsilane of entry 6 in **Table 2** was not prepared by any previous methods. In the case of α,β-unsaturated one (entry 5), SiMe3 group was introduced at β-position, i.e., Michael addition occurred[15].

Though the mechanism of the reaction is not examined in detail, we speculate that Al(SiMe3)3 seems not to react with substrates directly but formation of new reactive species (such as ate complexes) occurred, since the change in color was observed when Al(SiMe3)3 was mixed with CuCN. The following procedure is illustrative.

(S)-3-(Benzyloxymethyl)oxy-2-methylpropionyltrimethylsilane (1)

Under Ar atmosphere, S-2-Pyridyl (S)-3-(Benzyloxymethyl)oxy-2-methylpropanethioate (169mg, 0.53mmol) was dissolved in THF (5ml), then CuCN (58mg, 0.64mmol) was added. To the well stirred solution cooled with an ice bath, Al(TMS)3 in n-hexane (4.0ml, 0.15mmol) was added dropwise (color of the solution turned to dark brown), and the solution was kept at room temperature. Completion of the reaction was checked by tlc, and to the solution cooled with an ice bath acetic acid (ca. 0.1ml) was added dropwise, and stirring was continued for 30min. The precipitate was removed by Celite filtration and the filtrate was partitioned between Et2O and sat.NaHCO3 aq., then the

Table 2

Entry	S-(2-Pyridyl) Thioate	CuCN (equiv)	Product	Yield (%)
1		1.1		quant.
2		1.1		82
3		1.1		61
4		1.1		62
5		1.1		34[*1]
6		1.2		96
7		1.1		98
8		1.3		86
9		1.3		86
10		1.3		76

*1 3-Phenylpropenoyltrimethylsilane and 3-phenyl-3-(trimethylsilyl)-propionyltrimethylsilane were also produced.

organic layer was washed with brine, and dried over anhydrous Na_2SO_4, filtered, concentrated under reduced pressure. The residue was chromatographed on silicagel column (Hexane:AcOEt = 20:1) to afford **1** as pale orange oil (146mg, y.98%). By ^{1}H-NMR(400MHz) study using chiral shift reagent ((+)Eu-DPPM)[14], it was confirmed that the loss of optical purity in overall transformation was less than 1 %.

Acknowledgment : This work was financially supported in part by a Grant-in-Aid for Encouragement of Young Scientists (No. 01771902) from The Ministry of Education, Science and Culture of Japan, and CIBA-GEIGY FOUNDATION(JAPAN) for the Promotion of Science.

References and Notes:

1. Brook, A. G. *J. Am. Chem. Soc.* **1958**, *80*, 1886.
2. a) Enda, J.; Kuwajima, I. *J. Am. Chem. Soc.* **1985**, *107*, 5495 and references cited therein. b) Reich, H. J.; Holtan, R. C.; Borkowsky, S. L. *J. Org. Chem.*. **1987**, *52*, 312. c) Ricci, A.; Degl'Innocenti, A.; Borselli, G.; Reginato, G. *Tetrahedron Lett.* **1987**, *28*, 4093.
3. a) Reich,H. J.; Eisenhart,E. K.; Olson,R. E.; Kelly,M. J. *J. Am. Chem. Soc.* **1986**, *108*, 7791. b) Nowick, J. S.; Danheiser, R. L. *Tetrahedron* **1988**, *44*, 4113.
4. a) Ricci, A.; Degl'Innocenti, A. *Synthesis* **1989**, 647. b) Page, P. C. B.; Klair, S. S.; Rosenthal, S. *Chem. Soc. Rev.* **1990**, *19*, 147.
5. Nakada, M.; Urano, Y.; Kobayashi, S.; Ohno, M. *J. Am. Chem. Soc.* **1988**, *110*, 4826.
6. Brook, A. G.; Duff, J. M.; Jones, P. F.; Davis, N. R. *J. Am. Chem. Soc.* **1967**, *89*, 431.
7. Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1967**, *89*, 434.
8. Kang, J.; Lee, J. H.; Kim, K. S.; Jeong, J. U.; Pyun, C. *Tetrahedron Lett.***1987**, *28*, 3261.
9. a) Rösch, L.; Altnau, G.*Chem. Ber.* **1979**, *112*, 3934. b) Rösch, L.; Altnau, G. *J. Organomet. Chem.* **1980**, *195*, 47. *It can be stored in solution for many months.
10. a) Zaoral, M. *Collect. Czech. Chem. Commun.* **1962**, *27*, 1273. b) Vaugham, Jr., J. R.; Osato, R. L. *J. Am. Chem. Soc.* **1952**, *74*, 676. c) Boissonnas, R. A. *Helv. Chim. Acta* **1951**, *34*, 874.
11. a) Wieland,T.; Schäfer,W.; Bokelman,E. *Justus Liebigs Ann.Chem.* **1951**, *573*, 99. b) Farrington, J. A.; Hextall, P. G.; Kenner, G. W.; Turner, J. M. *J. Chem. Soc.* **1957**, 1407. c) Mukaiyama, T.; Matueda, R.; Suzuki, M. *Tetrahedron Lett.* **1970**, 1901.
12. a) Masamune, S.; Kamata, S.; Schelling, W. *J. Am. Chem. Soc.* **1975**, *97*, 3515. b) Corey, E. J.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1974**, *96*, 5614.
13. Kobayashi, S; Iimori, T.; Izawa, T.; and Ohno, M. *J. Am. Chem. Soc.* **1981**, *103*, 2406.
14. Kawa, H.; Yamaguchi, F.; Ishikawa, N. *Chem. Lett.* **1982**, 153.
15. For synthesis of α,β-unsaturated one, see : Danheiser, R. L.; Fink, D. M.; Okano, K.; Tsai, Y. -M.; Szczepanski, S. W. *J. Org. Chem.* **1974**, *50*, 5393.

(Received in Japan 7 May 1991)