Tetrahedron Letters,Vol.28,No.40,pp 4649-4652,1987   0040-4039/87 $3.00 + .00
Printed in Great Britain   Pergamon Journals Ltd.

FLUORIDE ION MEDIATED CONJUGATE ADDITION REACTIONS OF 1-ACYLOXY-2-PROPENYLTRIMETHYLSILANE. SYNTHESIS OF 3-(1-ACYLOXY-2-PROPENYL)ALKANONES.

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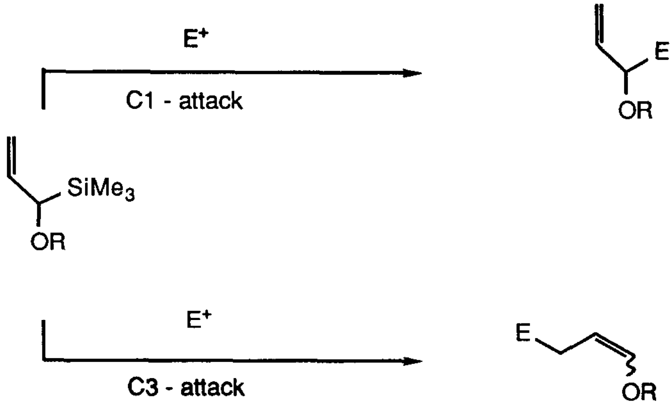
Abstract. The reaction of 1-acyloxy-2-propenyltrimethylsilane (**1**) with α, ß-unsaturated ketones in the presence of tetra-n-butylammonium fluoride has been investigated. In all cases the reaction was regiospecific resulting in the conjugate addition of a 1-acyloxy-2-propenyl function.

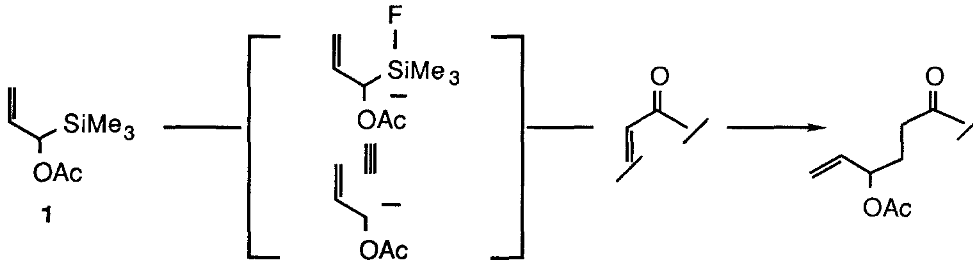
The use of organosilicon reagents has proven to be of considerable value in organic synthesis.[1] It has been well documented that both Lewis acids[2] and fluoride ion[3] promote the conjugate addition of allyltrimethylsilane to α, ß-unsaturated carbonyl compounds leading to the introduction of an allyl group. Metalated allylic ethers participate in nucleophilic addition reactions with α, ß-unsaturated carbonyl compounds in a regioselective manner with reaction occuring at the carbonyl group and preferentially at C1 of the allyl ether.[4] Our initial investigations have focused on the development of the potential utility of C1-oxygenated allylsilanes as bifunctional organometallic reagents wherein reaction with electrophiles may be directed to either C1 or C3 of the oxygenated allylsilane, equation 1.



eq. 1

In this Letter we wish to describe a simple and effective method for the conjugate addition of 1-acyloxy-2-propenyltrimethylsilane (**1**)[5] with α, β-unsaturated ketones mediated by fluoride ion. The reaction makes possible a useful conjugate addition process resulting in incorporation of a 1-acyloxy-2-propenyl function.[6] The reactions are rapid and demonstrate virtual regiospecificity with respect to the oxygenated allylsilane. No products originating from addition of **1** to the carbonyl group of the enone or attack at the C3-position of the allylsilane were detected. The carbon nucleophile adds to the β-carbon of the enone with reaction occuring at the C1-position of the allylsilane leading to a variety of 3-(1-acyloxy-2-propenyl)alkanones.

Still[7a] and McGarvey[7b] have demonstrated the feasibility of generating α-alkoxyorganolithium reagents by low temperature transmetallation from the corresponding geminal alkoxytrialkylstannane. This observation was the basis for our expectation that **1** could behave formally as an α-alkoxy stablized allyl anion and participate in conjugate additions with electrophilic olefins. The reaction of 1-acyloxy-2-propenyltrimethylsilane (**1**) with α, β-unsaturated ketones proceeds through the apparent generation of a reactive hypervalent silicon species. The proposed intermediates are depicted in equation 2.

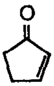
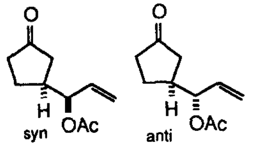
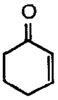
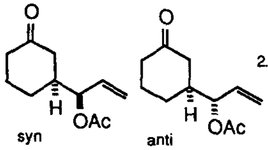
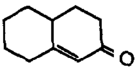
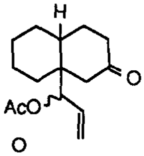
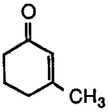
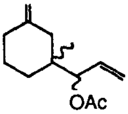
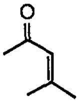
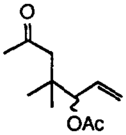
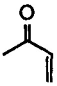
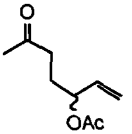
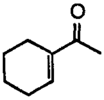
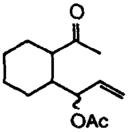


eq. 2

A series of α, β-unsaturated ketones was examined to investigate the scope of this process. The results of this study are detailed in the Table. Of the examples shown, all cases were run at -78° C in tetrahydrofuran (THF), 0.5 to 2.0 **M** substrate concentration employing a catalytic amount of anhydrous $n\text{-Bu}_4\text{NF}$[3a,b] (0.1 to 0.5 equiv) using 1.5 to 5.0 equivalents of **1**. Extractive isolation followed by chromatography (SiO_2) gave the desired conjugate addition products with varying amounts of unreacted enone. The use of cesium fluoride in THF, DMF, toluene or CH_2Cl_2 between -78° C and 25° C, resulted in diminished yields of the conjugate addition products. Also noteworthy, is the promising diastereoselectivity observed in reactions of **1** with 2-cyclopenten-1-one and 2-cyclohexen-1-one (Table, entries 1 and 2).[8]

We had hoped that this process might be extented to include 1,4-additions to ß-disubstituted enones thereby demonstrating the potential of the conjugate addition process for the formation of quaternary carbon centers (Table, entries 3, 4 and 5) and the introduction of an angular 1-acyloxy-2-propenyl function in bicyclic systems. The reaction of $\Delta^{1,9}$ 2-octalone with 1-acyloxy-2-propenyltrimethylsilane (1) in the presence of a catalytic amount of n-Bu_4NF was very rapid and provided the addition product in 25% yield.[9] Similarly, the reactions of 1 with methyl vinyl ketone and 1-acetyl-1-cyclohexene generated the 3-substituted ketones in 25 % and 47% yield.

TABLE FLUORIDE ION CATALYZED CONJUGATE ADDITION REACTIONS

Entry	enone	# Equiv. 1	Time(Temp °C) °	1,4-Addition Products[a]	Ratio[b]	Yield[c]
1.		1.5	5min.(-78)		4:1	54
2.		1.5	5min.(-78)		2.5:1	59
3.		5.0	5min.(-78)		3.5: 1	25
4.		5.0	5min. (-78)			50
5.		5.0	30min. (-78)			37
6.		2.0	30min. (-78)			25
7.		5.0	30min. (-78)			47

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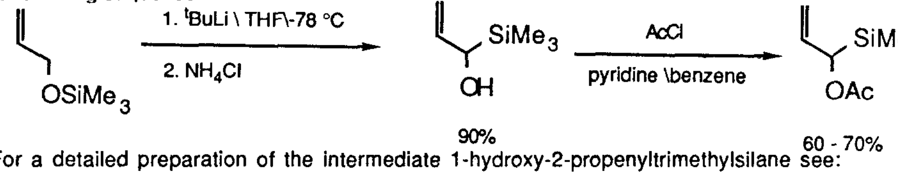
[a] All products gave ^1H NMR (400 MHz); IR and Mass Spectra data consistant with their assigned structures. [b] Ratios were determined by HPLC analysis on the corresponding keto - alcohols. [c] Isolated yields after chromatography on SiO_2.

In conclusion, the reactions of 1 with α, ß-unsaturated ketones described herein lead to variety of 3 substituted alkanones containing a 1-acyloxy-2-propenyl function. The implications of this conjugate addition process are broad and may be utilized in the context of acyclic stereoselection. The use of a homochiral varient of **1** in stereocontrolled nucleophilic addition reactions with chiral aldehydes and epoxides is currently under investigation.[10]

References and Notes

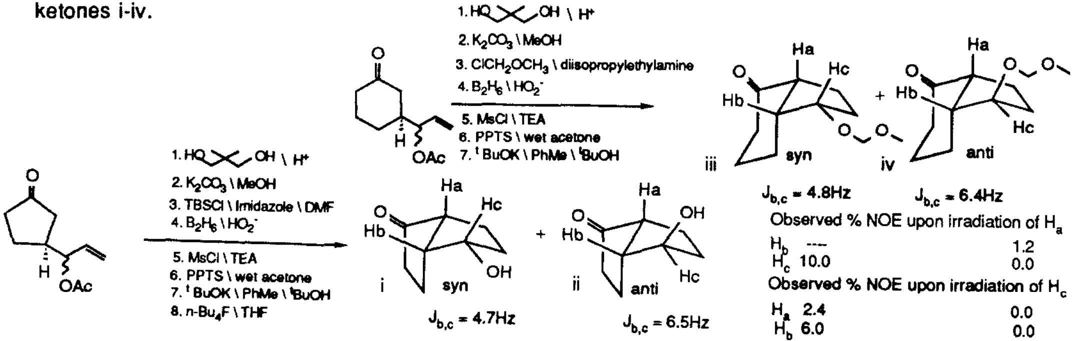
1. (a) For reviews on the use of organosilanes in synthesis, see Sakurai, H. Pure Appl. Chem. **1982**, 54, 1. (b) Parnes, Z. N.; Bolestova, G.I. Synthesis **1984**, 991.
2. Hosomi, A,; Sakurai, H. J. Am. Chem. Soc. **1977**, 99,1673.
3. (a) Majetich, G.; Casares, A.; Chapman, D.; Behnke, M. J. Org. Chem. **1986**, 51, 1745. (b) Majetich, G.; Desmond, R.W.; Soria, J.J. Ibid. **1986**, 51, 1753 and references cited therein.
4. Still, W.C.; Macdonald, T.L. J. Org. Chem. **1976**,22, 3620, (b) Still, W.C.; Macdonald, T.L. J. Am. Chem. Soc. **1974**, 96, 5561. (c) Evans, D.A.; Andrews, G.C.; Buckwalter, B. J. Am. Chem. Soc. **1974**, 96, 5560.
5. Compound **1** was prepared from commerically avaliable allyloxytrimethylsilane (Aldrich) by the following sequence:



1

For a detailed preparation of the intermediate 1-hydroxy-2-propenyltrimethylsilane see: Danheiser, R.L.; Fink, D.M.; Okano, K.; Tsai, Y-M.; Szczepanski, S.W. J. Org. Chem. **1985**, 50, 5393.

6. For the conjugate addition reaction of α-alkoxyorganocuprate reagents see: Linderman, R.J.; Godfrey, A. Tetrahedron Lett. **1986**, 27,4553.
7. (a) Still, W.C.; Sreekumar, C. J. Am. Chem. Soc. **1980**, 102, 1201. (b) Sawyer, J.S.; Macdonald, T. L.; McGarvey, G.L. J. Am. Chem. Soc. **1984**, 106, 3376.
8. The stereochemical assignments for the products in entries 1 and 2 were determined by difference NOE, 2D COSY and Homonuclear 2D J experiments following conversion to their respective bicyclic ketones i-iv.



$J_{b,c} = 4.7Hz$ $J_{b,c} = 6.5Hz$

Observed % NOE upon irradiation of H_a

H_b	2.7	----
H_c	1.0	0.0

Observed % NOE upon irradiation of H_c

H_a	0.6	0.0
H_b	4.2	0.0

$J_{b,c} = 4.8Hz$ $J_{b,c} = 6.4Hz$

Observed % NOE upon irradiation of H_a

H_b	----	1.2
H_c	10.0	0.0

Observed % NOE upon irradiation of H_c

H_a	2.4	0.0
H_b	6.0	0.0

9. Although the stereochemistry of the ring fusion was not rigorously proven, it is presumed to be trans, c.f. Deslongchamps, P. "Stereoelectronic Effects in Organic Chemistry"; Pergamon Press:Oxford, England, **1983**, Chapter 6.
10. This work was financially supported with funds supplied by Boston University. The authors wish to thank Professor John Snyder (Boston University) for helpful discussions concerning the stereochemical assignments of bicyclic ketones i-iv.

(Received in USA 26 May 1987)