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CONJUGATE ADDITIONS OF FURANS TO ENONES MEDIATED BY IODOTRIMETHYLSILANE

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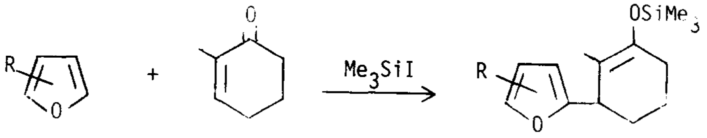
Summary: Furans undergo facile addition to γ-iodoenolsilyl ethers to afford either the ketone or the enol silyl ether.

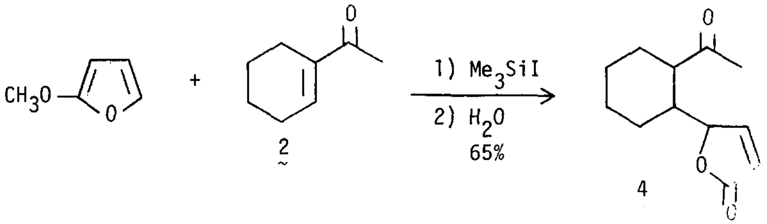
Furans have often been employed as sources of latent functionality in organic synthesis. Accordingly, several procedures have been developed for converting furans into various carbonyl compounds.[1] However, a longstanding problem associated with this strategy has been the lack of a general method for the introduction of the furan subunit under mild conditions. While the acid mediated addition of simple furans to enones does proceed in modest yields, this reaction is limited by competing side reactions such as polymerization of the furan or enone and polysubstitution.[2] Notably, it does not proceed when the enone contains an α-substituent. In conjunction with our studies on the synthetic applications of furans,[3] we have developed a useful solution which is illustrated in Figure 1. An attractive feature of this method is that either the ketone or its corresponding enol silyl ether can be isolated depending on the workup conditions. The method is based on the already documented addition of iodotrimethylsilane to enones to form the unstable γ-iodoenolsilyl ethers.[4] We anticipated that this moiety would react efficiently with furans in polar aprotic solvents. In a related reaction, Godleski has independently observed that iodotrimethylsilane mediates the intramolecular cyclization of activated methylenes to enones.[5] Additionally, Marino has

Figure 1



recently utilized the iodotrimethylsilane-enone addition product in an elegant variant of the Nazarov cyclization.[6]

The scope of the reaction is depicted in Table I. While a variety of enones react effectively, the reaction fails with aldehydes. The use of 2-methyl-2-butene is essential for a successful reaction with enones 2 and 3. Presumably it traps the hydrogen iodide generated in the reaction and averts the polymerization of the furan. Alternate acid traps afforded dramatically lower yields.[7] The regioselective reaction 3-bromo furan is also notable.[8] The reaction of 1-acetyl-cyclohexene (3) with 2-methoxyfuran provides the interesting ketobutenolide 4[9] in 65% yield after hydrolysis. This was the only case in which the furan was transformed into a butenolide.



The availability of these adducts assumes added significance in view of the rapidly expanding methodology involving enolsilylethers.[10] The adduct obtained in entry 3 undergoes selective halogen metal exchange with n-butyl lithium at -78°C in ether. We are presently studying its reactions with bifunctional electrophiles. The γ-iodoenolsilyl ethers also react with electron rich alkenes. The reaction of the enolsilyl ether of acetophenone produces diketone **5** after hydrolysis of the reaction mixture.

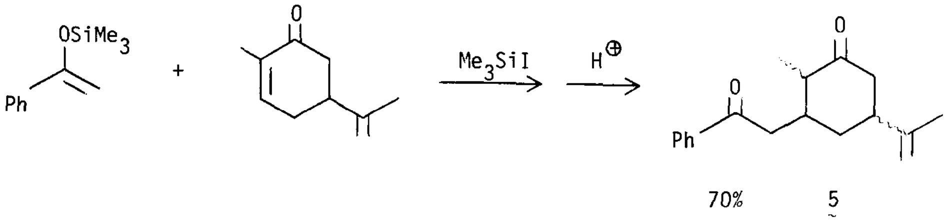
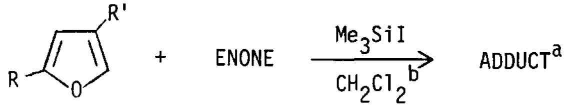


Table I - Iodotrimethylsilane Mediated Additions.



Entry	R	R^1	enone	% yield^c enol silyl ether	% yield^c of ketone
1	H	H	1	96^d	92
2	CH$_3$	H	1	100	89
3	H	Br	1	100	95
4	H	H	2	50^e	95
5	CH$_3$	H	2	70	90
6	H	Br	2	75	80
7	PhS	H	2	67	90
8	H	Br	3		67

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[a] Enone 1 = carvone, 2 = 1-acetylcyclohexene, 3 = 2-methylcyclohexenone. The adduct is either the β-furyl enolsilyl ether or the β-furyl ketone.

[b] To a solution of enone (1.0 eq) in CH$_2$Cl$_2$ at -78°C was added Me$_3$SiI (1.1 eq). The solution was stirred 1 h. The furan (1.0 eq) was added, followed by 2-methyl-2-butene (2 eq). The reaction was kept at -78°C for 2-3h until IR showed no enone (0°C for entries 3, 6 and 8). A solution of (Me$_3$Si)$_2$NH in CH$_2$Cl$_2$ was added, the reaction diluted with hexane and filtered through celite. For the ketone, the reaction was quenched with dilute HCl.

[c] Chromatographed yield. All new products exhibited PMR, IR, mass spectra consistent with the assigned structures.

[d] 4% of a 2:1 enone:furan adduct was also obtained.

[e] 50% of a 2:1 enone:furan adduct was also obtained.

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7. The use of hindered bases lowered the yield of the reaction - possibly by promoting the formation of a dienolsilyl ether (see ref. 4).
8. Acylation affords a 4:1 preference of 2- vs. 5-substitution. Gol'dfarb, Ya., L.; Marakatkina, M. A.; Belen'kii, L. I. Khim. Geterotsikl. Soedin., **1970**, 132.
9. This compound is a mixture of diastereomers.
10. For a review, see Colvin, E. Silicon in Organic Synthesis, Butterworths Monographs, London, 1981, Chapter 17.

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