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Alkali metal hydride or aqueous hydroxide induced conjugate addition of trimethylsilyl enol ethers to enones. A convenient alternative to Lewis acid mediated reaction.[#]

Vishwanath M. Swamy and Amitabha Sarkar*

Division Of Organic Chemistry (Synthesis)
National Chemical Laboratory
Pune - 411 008, India.

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Abstract : Conjugate addition to enones by enolates derived from base-induced cleavage of O-Si bond of trimethylsilyl enol ethers, yields 1,5-dicarbonyl compounds in good yields.

Titanium chloride mediated addition of silyl enol ethers to α,β–unsaturated compounds was first reported in 1974[1]. This reaction is an important carbon-carbon bond forming reaction and stands out for its advantages in terms of selectivity, regiospecificity and suppression of side reactions, over addition of lithium enolates[2] to enones. Since then, other Lewis acids like $BF_3.OEt_2$[3], $SnCl_4$,[4] lanthanide triflates and scandium triflate[5], have been reported to catalyse this reaction. Even trityl salts[6], Montmorillonite clay[7], CsF[8] mediate such reactions to provide 1,5 diketones in high yields. These diketones are useful intermediates for the synthesis of substituted cyclohexenones[9] , pyridines[10a] and selenium[10b] and phosphorous[10c] containing heterocycles.

Water is scrupulously avoided in all these reactions for obvious reasons ever since Stork described the generation of enolates from silyl enol ethers by the use of methyl lithium[11]. Lubinuea, however, has shown that silyl enol ethers undergo Mukaiyama aldol reaction with aldehydes in water without a catalyst over a period of several days[12]. We now find that simple and readily available base like NaOH or KH can cleave silyl enol ethers such that the enolates generated *in situ* can efficiently add to enones in a conjugate manner in a much shorter time.

A biphasic condition using 50% aq. NaOH and dichloromethane with 10 mol% of tetrabutylammonium bromide as a phase transfer catalyst, was used in the reactions initially performed. In a few instances a molar equivalent of potassium hydride in DMF was also effective (Table-1, condition B). All reactions were conducted at room temperature and completion of reaction was monitored by TLC. The reaction is facile with aromatic as well as aliphatic silyl enol ethers. The reaction works well even with ferrocene enones **5** and **6**. The structures of the products were satisfactorily determined by ^1H and ^{13}CNMR spectroscopy, and were supported by elemental analyses.

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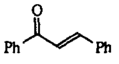
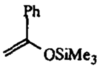
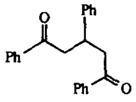
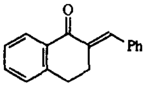
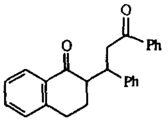
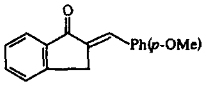
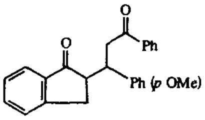
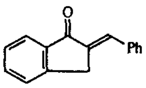
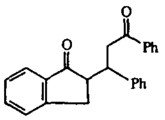
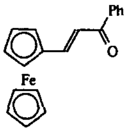
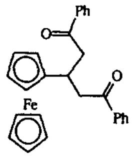
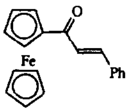
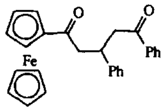
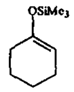
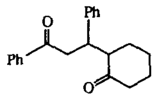
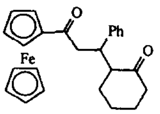
Table I

Enone	Silyl Enol Ether	Product	Conditions	Time (hrs)	Yield (%)
 1	 (A)	 1a	A B	3 2	77 64
 2	(A)	 2a	A B	8 4	74 62
 3	(A)	 3a	A	5	74
 4	(A)	 4a	A B	5 4	76 70
 5	(A)	 5a	A	10	72^{c}
 6	(A)	 6a	A	10	76^{c}
1	 (B)	 7a	A B	4 2	77 66
6	(B)	 8a	A	10	76^{c}

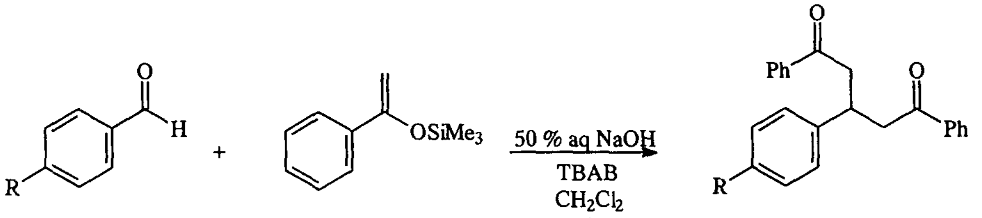
A) 50% aq. NaOH with 10 mol% TBAB as PTC in CH_2Cl_2. B) 1.2 eq. KH in DMF. C) yield based on recovered starting material (< 10%).

Typical procedure for conjugate addition with 50% aq NaOH and PTC (A): The enol silane (1.2 mmol) and the enone (1 mmol) was added successively to a flask containing 4 ml of CH_2Cl_2, 0.5ml of degassed 50% aq NaOH and 10 mol% of tetrabutylammonium bromide (30 mg). The reaction mixture was stirred at room temperature under argon. After completion of the reaction, 10 ml of CH_2Cl_2 was added and the product was extracted with CH_2Cl_2. The organic layer was washed successively with 20 ml of 2N HCl, 10% aq $NaHCO_3$ and water. After drying over sodium sulfate, the solvent was removed *in vacuo* and the product was isolated by column chromatography.

Typical procedure for conjugate addition with KH (B) : To 1.2 mmol of KH in 4 ml of dry DMF was added 1.2 mmol of the enol silane, followed by the enone (1 mmol). The reaction mixture was stirred at room temperature under argon for specified hours. After completion of the reaction, water was added to the reaction mixture, and organic product was extracted with CH_2Cl_2, washed with water to remove DMF, and dried over sodium sulfate. After removal of the solvent *in vacuo*, the product was isolated by column chromatography.

The reaction succeeds with enones that do not have an enolisable hydrogen adjacent to the carbonyl group, e.g. methyl vinyl ketone and cyclohexenone are poor substrates under these conditions. Attempted aldol reaction of enol silane with benzaldehyde under PTC condition led to instantaneous dehydration of the aldol product and a second molecule of the enol silane added to the resultant enone in a conjugate manner (Scheme - I). For the runs given below, two equivalents of enol silane was used, use of equimolar amount returned unreacted starting material.

Scheme - I



(9a-b)

R	time (hrs)	Product	yield %
H	6	9a	62
OCH_3	4	9b	60

In summary, we have described a convenient alternative to Lewis acid and fluoride mediated conjugate addition of enol silyl ethers to enones, which should find wide use in the synthesis of 1,5-diketones.

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