Organic Syntheses

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of Organic Compounds

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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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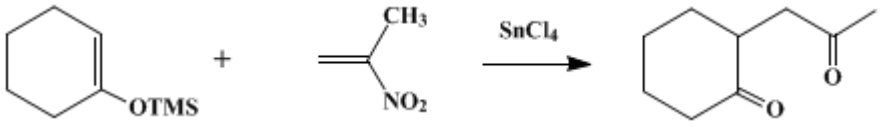
*Organic Syntheses, Coll. Vol. 7, p.414 (1990); Vol. 60, p.117 (1981).*

# SYNTHESIS OF 1,4-DIKETONES FROM SILYL ENOL ETHERS AND NITROOLEFINS: 2-(2-OXOPROPYL)CYCLOHEXANONE

## [Cyclohexanone, 2-(2-oxopropyl)]




Submitted by Masaaki Miyashita, Tetsuji Yanami, and Akira Yoshikoshi[1].
Checked by Donald Hilvert, Stefan Kwiatkowski, and Dieter Seebach.

## 1. Procedure

*Caution! This preparation should be carried out in a hood since 2-nitropropene is a powerful lachrymator and anhydrous stannic chloride is a skin irritant.*

A 1-L, three necked, round-bottomed flask is fitted with a magnetic stirring bar and a pressure-equalizing dropping funnel to which is attached an oil bubbler, a rubber septum, and an argon or nitrogen inlet to maintain a static inert gas atmosphere in the reaction vessel throughout the reaction. The flask and dropping funnel are charged with 500 mL of dry methylene chloride and 40 mL (34 g, 0.20 mol) of 1-trimethylsiloxy-1-cyclohexene (Note 1), respectively. The flask is flushed with dry inert gas and immersed in a cooling bath at ca. −78°C (acetone or 2-propanol-dry ice). Stirring is started and 23 mL (52.1 g, 0.20 mol) of anhydrous stannic chloride (Note 2) is added rapidly through the rubber septum by means of a syringe. Then 20.0 mL (21.0 g, 0.23 mol) of 2-nitropropene (Note 3) is added through the rubber septum by a syringe over a period of 5–10 min, giving a green solution. The reaction mixture is further stirred at −78°C for 20 min, and then the silyl enol ether is added dropwise to the mixture over 1 hr, giving a faint yellow solution. After completion of the addition the resulting solution is stirred at ca. −78°C for an additional hour; then the bath temperature is gradually warmed to −5°C over a period of 3–3.5 hr while the stirring is continued (Note 4). The inert gas flow is stopped, the dropping funnel is replaced by a condenser, the magnetic stirrer is removed, and the flask is equipped with a heating mantle and an overhead stirring device. Then 280 mL of water are added, and the resulting heterogeneous mixture is vigorously stirred at reflux for 2 hr (Note 5). The mixture is subsequently cooled to room temperature and then poured into a 1-L separatory funnel and the methylene chloride layer is separated from the water. The aqueous layer is extracted once with 100 mL of methylene chloride, and the combined organic layers are washed twice with 160-mL portions of cold water (Note 6) and once with saturated brine, dried over anhydrous magnesium sulfate, and filtered. The solvent is removed on a rotary evaporator and the residual oil is distilled through a 10-cm Vigreux column under reduced pressure to yield 18.7–21.5 g (61–70%) of 2-(2-oxopropyl)cyclohexanone as a fragrant yellow liquid, bp 84–85°C (0.8 mm), $n_D^{19}$ 1.4671 [lit.[2] bp 91–93°C (1.1 mm), $n_D^{25}$ 1.4655] (Note 7).

## 2. Notes

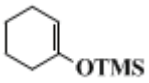
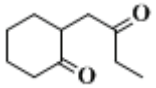
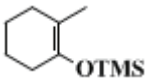
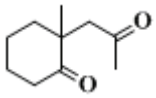
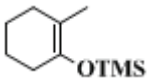
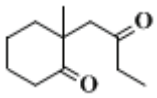
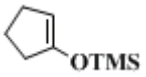
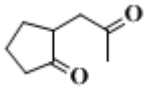
1. This silyl enol ether was prepared according to the procedure of House,[3] 80%, bp 75°C (21 mm) [lit.[3] 74–75°C (20 mm)].
2. A fresh bottle of commercial anhydrous stannic chloride purchased from Wako Pure Chemical Industries, Ltd., Japan, or from Fluka AG, Buchs, Switzerland, was used without purification.
3. 2-Nitropropene[4] was freshly prepared before use.
4. The yellow solution becomes green on warming and finally turns yellow.
5. On addition of water the mixture turns purple, and after refluxing it becomes brown.
6. Although an insoluble white substance appears in the aqueous washings, it is discarded.

7. The checkers found refractive indices $n_D$ 1.468 and 1.4665 or $n_D$ 1.4657 and 1.4649.

## 3. Discussion

This procedure illustrates a recently published, simple, general method for the synthesis of 1,4-diketones from silyl enol ethers and nitroolefins.[5] 2-(2-Oxopropyl)cyclohexanone has been prepared by the reaction of the pyrrolidine enamine of cyclohexanone with bromoacetone (40%)[2] and by several other multistep processes.[6,7,8] However, the overall yields obtained by these routes have never exceeded 50% and some of the methods are laborious for large-scale preparations. The present method illustrates a mild and convenient one-pot reaction for the preparation of 1,4-diketones. In addition, the starting materials are readily accessible, the reaction proceeds regioselectively, and the yields of product are generally high. This process consists of the initial Michael addition of silyl enol ethers to nitroolefins, followed by a Nef reaction of the nitronate esters.[5] The scope of the reaction is shown in Table I. The 1,4-diketones thus obtained have been converted into corresponding cyclopentenones in high yields.[5]

TABLE I
1,4-DIKETONES PREPARED FROM SILYL ENOL ETHERS AND NITROOLEFINS

| Silyl Enol Ether | Nitroolefin | Lewis Acid | 1,4-Diketone | Yield (%) |
|---|---|---|---|---|
|  | 2-Nitro-1-butene | $TiCl_4$ |  | 76 |
|  | 2-Nitropropene | $TiCl_4$ |  | 70 |
|  | 2-Nitro-1-butene | $TiCl_4$ |  | 82 |
|  | 2-Nitropropene | $SnCl_4$ |  | 70 |

[9]

## References and Notes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## Appendix

## Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

brine

pyrrolidine enamine of cyclohexanone

methylene chloride (75-09-2)

Bromoacetone (598-31-2)

stannic chloride (7646-78-8)

magnesium sulfate (7487-88-9)

1-trimethylsiloxy-1-cyclohexene (6651-36-1)

2-Nitropropene (4749-28-4)

2-nitro-1-butene

2-(2-Oxopropyl)cyclohexanone,
Cyclohexanone, 2-(2-oxopropyl) (6126-53-0)