Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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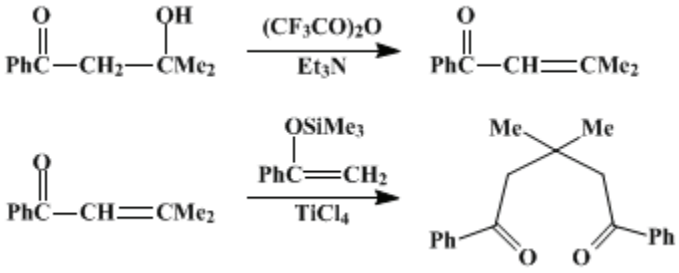
3,3-DIMETHYL-1,5-DIPHENYLPENTANE-1,5-DIONE

[1,5-Pentanedione, 3,3-dimethyl-1,5-diphenyl-]



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1. Procedure

A. *Isopropylideneacetophenone.* A 1-L, three-necked flask is fitted with a 100-mL pressure-equalizing dropping funnel, a mechanical stirrer, and a condenser equipped with a two-way stopcock leading to a balloon of argon gas. To the flask is added a solution of 18.4 g of 3-hydroxy-3-methyl-1-phenyl-1-butanone (Note 1) in 60 mL of dry methylene chloride. The flask is cooled in an ice bath and 28.5 g of triethylamine, a catalytic amount of 4-(*N,N*-dimethylamino)pyridine, and 20 mL of methylene chloride are added. A solution of 25.8 g of trifluoroacetic anhydride (Note 2) in 40 mL of methylene chloride is added dropwise over a period of 15 min, and the mixture is stirred for 2.5 hr.

The ice bath is removed and the mixture is stirred for 21 hr at room temperature (about 30°C). Under vigorous stirring, 100 mL of saturated aqueous sodium carbonate, 100 mL of water, and 300 mL of ether are added to the mixture. The organic layer is separated and the water layer is extracted with 100 mL of ether. The combined ether extracts are washed with brine and dried over magnesium sulfate. The ether solution is condensed using a rotary evaporator and the residue is distilled under reduced pressure to give 14.5–16.0 g (88–97% yield) of isopropylideneacetophenone (Note 3).

B. *3,3-Dimethyl-1,5-diphenylpentane-1,5-dione.* A 500-mL, three-necked flask is fitted with a mechanical stirrer, a rubber septum, and a two-way stopcock equipped with a balloon of argon gas (Note 4). To the flask is added 100 mL of dry methylene chloride, and the flask is cooled in a dry ice–acetone bath. Titanium tetrachloride (7.7 mL) (Note 5) is added by syringe through the septum. The septum is removed and replaced with a 100-mL pressure-equalizing dropping funnel containing a solution of 11.2 g of isopropylideneacetophenone in 30 mL of methylene chloride. This solution is added over a 3-min period, and the mixture is stirred for 4 min. A solution of 13.5 g of the silyl enol ether of acetophenone (Note 1) in 40 mL of methylene chloride is added dropwise with vigorous stirring over a 4-min period, and the mixture is stirred for 7 min. The reaction mixture is poured into a solution of 22 g of sodium carbonate in 160 mL of water with vigorous magnetic stirring (Note 6). The resulting white precipitate is removed by filtration through a Celite pad and the precipitate is washed with methylene chloride.

The organic layer of the filtrate is separated and the aqueous layer is extracted with two 40-mL portions of methylene chloride. The combined organic extracts are washed with 60 mL of brine and dried over sodium sulfate. The methylene chloride solution is concentrated with a rotary evaporator and the residue is passed through a short column of silica gel (Baker 200 mesh, 400 mL) using 1.5 L of a 9 : 1 (v/v) mixture of hexane and ethyl acetate (Note 7). The eluent is condensed and distilled; the first fraction (bp 81–85°C/0.6 mm, 2.04 g) is a mixture of isopropylideneacetophenone and acetophenone; the second fraction (bp 85–172°C/0.6 mm, 0.42 g) is a mixture of the above-mentioned substances and the desired product; the third fraction (bp 172–178°C/0.6 mm) gives 14.0–15.2 g (72–78%) of 3,3-dimethyl-1,5-diphenylpentane-1,5-dione (Note 8).

2. Notes

1. See *Org. Synth., Coll. Vol. VIII* **1993**, 324.
2. Attempted dehydration using an acid catalyst or iodine failed, giving mainly acetophenone. When acetic anhydride is employed instead of trifluoroacetic anhydride, the reaction proceeds very slowly. Dehydration with excess methanesulfonyl chloride and triethylamine gives the product in high yield; however, the distilled product has a strong odor of sulfur compound.
3. The physical properties are as follows: bp 73–75°C/0.4 mm; the NMR spectrum (CCl_4) shows singlets at δ 1.93 (3 H) and 2.13 (3 H) and multiplets at 6.63 (1 H), 7.16–7.48 (3 H) and 7.71–7.91 (2 H).
4. All the apparatuses should be well dried before use.
5. Freshly distilled titanium tetrachloride (bp 136.4°C) is used.
6. Stirring should be continued until the organic and aqueous layers show no acidity.
7. The submitters used Wako gel C-200.
8. The physical properties are as follows. Anal. calcd. for $C_{19}H_{20}O_2$: C, 81.39; H. 7.19. Found: C, 81.34; H, 7.16. The ^1H NMR spectrum ($CDCl_3$) shows singlets at δ 1.22 (6 H, CH_3) and 3.26 (4 H, CH_2), and multiplet signals between 7.17–8.03 (10 H, aromatic CH).

3. Discussion

The preparation of 3,3-dimethyl-1,5-diphenylpentane-1,5-dione has also been achieved from 3,3-dimethylglutaric acid and phenyllithium.[2]

The present method gives 3,3-dimethyl-1,5-diphenylpentane-1,5-dione in better yield and is widely applicable to the preparation of various 1,5-diketones.[3] In addition, when silyl enol ethers of esters are employed instead of those of ketones. δ-keto esters can be obtained.[4]

References and Notes

1. Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo Bunkyo-Ku, Tokyo 113, Japan.
2. Zimmerman, H. E.; Pincock, J. A. *J. Am. Chem. Soc.* **1973**, *95*, 3246.
3. Narasaka, K.; Soai, K.; Mukaiyama, T. *Chem. Lett.* **1974**, 1223; Narasaka, K.; Soai, K.; Aikawa, Y.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 779.
4. Saigo, K.; Osaki, M.; Mukaiyama, T. *Chem. Lett.* **1976**, 163.

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

brine

silyl enol ether of acetophenone

ethyl acetate (141-78-6)

ether (60-29-7)

acetic anhydride (108-24-7)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

iodine (7553-56-2)

methylene chloride (75-09-2)

Phenyllithium (591-51-5)

magnesium sulfate (7487-88-9)

hexane (110-54-3)

titanium tetrachloride (7550-45-0)

triethylamine (121-44-8)

argon (7440-37-1)

3,3-dimethylglutaric acid (4839-46-7)

Methanesulfonyl chloride (124-63-0)

trifluoroacetic anhydride (407-25-0)

4-(N,N-dimethylamino)pyridine (1122-58-3)

3,3-Dimethyl-1,5-diphenylpentane-1,5-dione,
1,5-Pentanedione, 3,3-dimethyl-1,5-diphenyl- (42052-44-8)

3-Hydroxy-3-methyl-1-phenyl-1-butanone (43108-74-3)

Isopropylideneacetophenone (5650-07-7)