



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

## Working with Hazardous Chemicals

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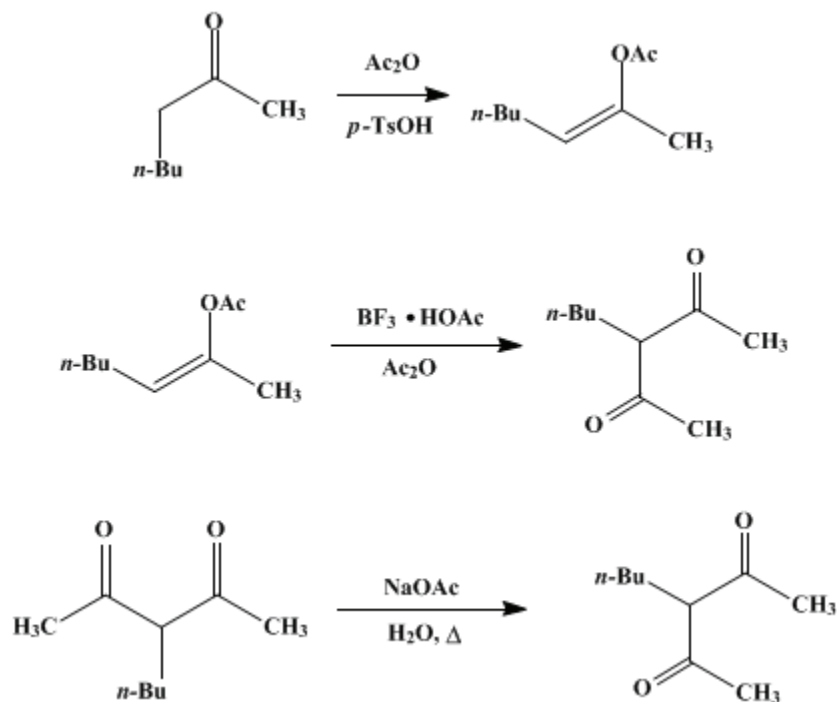
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## **$\beta$ -DIKETONES FROM METHYL ALKYL KETONES: 3-*n*-BUTYL-2,4-PENTANEDIONE**



Submitted by Chung-Ling Mao<sup>1</sup> and Charles R. Hauser<sup>12</sup>.  
Checked by David G. Melillo and Herbert O. House.

### 1. Procedure

A mixture of 28.6 g. (0.251 mole) of 2-heptanone (Note 1), 51.0 g. (0.500 mole) of acetic anhydride (Note 2), and 1.9 g. (0.010 mole) of *p*-toluenesulfonic acid monohydrate (Note 3) contained in a stoppered 500-ml., round-bottomed flask, equipped with a magnetic stirrer, is stirred at room temperature for 30 minutes before 55 g. (0.43 mole) of the solid 1:1 boron trifluoride-acetic acid complex (Note 4) is added, resulting in the evolution of heat. The amber-colored solution is stirred in the stoppered flask at room temperature for 16–20 hours (Note 5), and a solution of 136 g. (1.00 mole) of sodium acetate trihydrate (Note 6) in 250 ml. of water is added. After the flask has been fitted with a reflux condenser, the reaction mixture is heated at reflux for 3 hours and cooled, and the product is extracted with three 100-ml. portions of petroleum ether (b.p. 30–60°). The combined organic extracts are washed successively with aqueous 5% sodium hydrogen carbonate and saturated aqueous sodium chloride and dried over anhydrous calcium sulfate (Drierite). The solvent is removed with a rotary evaporator, and the residual oil is distilled, yielding 25–30 g. (64–77%) of 3-*n*-butyl-2,4-pentanedione as a colorless liquid, b.p; 84–86° (6 mm.),  $n_D^{25}$  1.4422–1.4462 (Note 7).

### 2. Notes

- 2-Heptanone, obtained from Eastman Organic Chemicals, was distilled before use, b.p. 145–147°.
- Acetic anhydride purchased from Merck & Co., Inc., was fractionally distilled and the fraction, b.p. 139–141°, was used.
- p*-Toluenesulfonic acid monohydrate was obtained from Eastman Organic Chemicals and used without purification.
- The submitters employed 75 g. (0.50 mole) of the liquid 1:2 boron trifluorideacetic acid complex obtained from Harshaw Chemical Company. Since the checkers were unable to obtain this complex

from a commercial source, a solid 1:1 complex was prepared according to the literature.<sup>3,4</sup> A 2-l., three-necked flask fitted with a mechanical stirrer, a gas-outlet tube, and a gas-inlet tube extending to the bottom of the flask is charged with a solution of 230 ml. of acetic acid in 750 ml. of 1,2-dichloroethane. A stream of boron trifluoride gas is passed through the reaction flask while the solution is stirred and cooled with an ice bath. After approximately 1 hour, when the mixture is saturated, the addition of boron trifluoride is stopped and the insoluble 1:1 boron trifluoride-acetic acid complex is rapidly collected on a filter, washed with 200 ml. of 1,2-dichloroethane, and transferred to a dry, stoppered container. Since this solid complex tends to liquefy partially on storage, portions to be used in this preparation should be washed with 1,2-dichloroethane immediately prior to use. The amount of catalyst obtained is sufficient to perform this preparation several times.

5. A longer reaction time gives similar results.

6. Sodium acetate trihydrate was obtained from Eastman Organic Chemicals.

7. On a GC column packed with SE-30 silicone gum on Chromosorb P and heated to 150°, the product exhibits a single peak with a retention time of 12.3 minutes; under the same conditions the peak for 2-heptanone has a retention time of 4.4 minutes; The product, which is partially enolic, has IR bands (CCl<sub>4</sub>) at 1725(sh), 1695, and 1605 cm.<sup>-1</sup> with a UV maximum (95% C<sub>2</sub>H<sub>5</sub>OH) at 288 nm. ( $\epsilon$  2560) and <sup>1</sup>H NMR peaks (CCl<sub>4</sub>) at  $\delta$  0.7–2.0 (m, 9H, aliphatic CH), 2.10 (s, 6H, 2COCH<sub>3</sub>), 3.57 (t,  $J$  = 7 Hz., 0.7H, COCHCO), and 16.50 (s, 0.3H, enolic OH). The mass spectrum exhibits a molecular ion at  $m/e$  156 with abundant fragment peaks at  $m/e$  100, 71, 58, 44, and 43 (base peak).

### 3. Discussion

This procedure for the acetylation of methyl alkyl ketones to  $\beta$ -diketones is a modification<sup>5</sup> of an earlier method, which used boron trifluoride gas as the catalyst.<sup>6</sup> 3-*n*-Butyl-2,4-pentanedione has also been prepared by the acetylation of 2-heptanone catalyzed with boron trifluoride gas,<sup>7</sup> by the thermal rearrangement of the enol acetate of 2-heptanone,<sup>7</sup> and by the alkylation of the potassium enolate of 2,4-pentanedione with *n*-butyl bromide.<sup>8</sup>

In this procedure, the ketone is first converted to its enol acetate by reaction with acetic anhydride in the presence of a protic acid. Since enol acetylation is performed under equilibrating conditions, the more stable enol acetate, (usually the more highly substituted isomer) is produced. Acetylation of this enol acetate, catalyzed by boron trifluoride, usually leads to the formation of the enol acetate of a  $\beta$ -diketone, which is cleaved by boron trifluoride, forming acetyl fluoride and the borofluoride complex of the  $\beta$ -diketone. Thus, this procedure offers a convenient and general synthetic route to 3-substituted-2,4-pentanediones.<sup>5</sup> The acylation of 2-butanone to 3-methyl-2,4-pentanedione (48%); 2-pentanone to 3-ethyl-2,4-pentanedione (57%); phenylacetone to 3-phenyl-2,4-pentanedione (68%); and 3-methyl-2-butanone to 3,3-dimethyl-2,4-pentanedione (40–48%) have been reported by the submitters.

A similar acetylation procedure (without *p*-toluenesulfonic acid) has been employed to prepare other  $\beta$ -diketones.<sup>5</sup> For example, cyclohexanone was converted to 2-acetylcyclohexanone (73%); cyclopentanone yielded 2-acetylcyclopentanone (80%); 3-pentanone yielded 3-methyl-2,4-hexanedione (81%); dibenzyl ketone yielded 1,3-diphenyl-2,4-pentanedione (72%); and acetophenone gave benzoylacetone (70%).

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### References and Notes

1. Department of Chemistry, Duke University, Durham, North Carolina 27706.
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**Appendix**  
**Chemical Abstracts Nomenclature (Collective Index Number);**  
**(Registry Number)**

petroleum ether

1:1 boron trifluoride-acetic acid complex

boron trifluorideacetic acid complex

potassium enolate of 2,4-pentanedione

acetic acid (64-19-7)

acetic anhydride (108-24-7)

sodium hydrogen carbonate (144-55-8)

Cyclohexanone (108-94-1)

sodium chloride (7647-14-5)

n-butyl bromide (109-65-9)

1,2-dichloroethane (107-06-2)

calcium sulfate (7778-18-9)

Acetophenone (98-86-2)

Cyclopentanone (120-92-3)

2-Heptanone (110-43-0)

phenylacetone (103-79-7)

2-butanone (78-93-3)

boron trifluoride (7637-07-2)

dibenzyl ketone (102-04-5)

3-methyl-2-butanone (563-80-4)

3-pentanone (96-22-0)

benzoylacetone (93-91-4)  
sodium acetate trihydrate (6131-90-4)  
2-acetylcyclopentanone (1670-46-8)  
3-methyl-2,4-pentanedione (815-57-6)  
3,3-dimethyl-2,4-pentanedione (3142-58-3)  
3-n-BUTYL-2,4-PENTANEDIONE (1540-36-9)  
2-acetylcyclohexanone (874-23-7)  
p-toluenesulfonic acid (104-15-4)  
acetyl fluoride (557-99-3)  
2-pentanone (107-87-9)  
3-ethyl-2,4-pentanedione (1540-34-7)  
3-phenyl-2,4-pentanedione (5910-25-8)  
3-methyl-2,4-hexanedione  
1,3-diphenyl-2,4-pentanedione (19588-08-0)  
p-toluenesulfonic acid monohydrate (6192-52-5)