



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

## Working with Hazardous Chemicals

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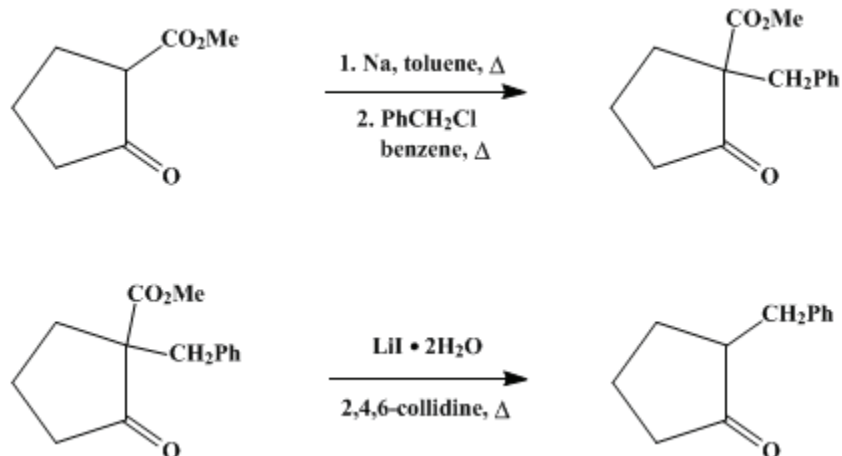
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## 2-BENZYL-CYCLOPENTANONE



Submitted by Fritz Elsinger<sup>1</sup>

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### 1. Procedure

A. *2-Benzyl-2-carbomethoxycyclopentanone*. A dry 2-l. three-necked flask is fitted with a Vibromischer stirrer (Note 1), a reflux condenser, and a 250-ml. dropping funnel with a pressure-equalizing side tube.<sup>2</sup> A nitrogen-inlet tube is connected to the top of the dropping funnel, and an outlet tube is placed on the top of the condenser and connected to a mercury valve. The latter consists of a U-tube the bend of which is just filled with mercury.

To the flask are added 13.4 g. (0.58 mole) of clean sodium and 200 ml. of absolute toluene. The Vibromischer stirrer is activated, the toluene heated to reflux, and the agitation continued at this temperature until all the sodium is pulverized into a very fine sand. The agitation is ceased, and the solution is allowed to cool to room temperature. The nitrogen flow rate is increased, the Vibromischer stirrer is replaced with a conventional sealed mechanical stirrer with a Teflon<sup>®</sup> blade, and a solution of 85 g. (0.6 mole) of 2-carbomethoxycyclopentanone (Note 2) in 450 ml. of absolute benzene is placed in the addition funnel.

The stirrer is started, and the solution in the addition funnel is added over a 2-hour period without external heating (Note 3). After the addition is complete, the mixture is heated under reflux for 2.5 hours, at the end of which time the mixture has a pasty consistency. A solution of 106 g. (0.84 mole) of benzyl chloride in 100 ml. of dry benzene is added in one portion, the mixture heated under reflux for 14 hours, and the solution (Note 4) poured into 600 ml. of water. The benzene layer is separated, the aqueous layer extracted twice with ether, and the combined benzene-ether extract washed with 100 ml. of water and dried over anhydrous sodium sulfate. The solvent is removed under reduced pressure using a rotary evaporator, and the residual liquid distilled to yield 108–116 g. (81–86%) of colorless 2-benzyl-2-carbomethoxycyclopentanone, b.p. 126–128° (0.5 mm.) (Note 5).

B. *2-Benzylcyclopentanone*. A mixture of 30 g. (0.177 mole) of lithium iodide dihydrate (Note 6) and (Note 7) and 140 ml. of dry 2,4,6-collidine (Note 8) in a 300-ml. three-necked flask fitted with a dropping funnel, a reflux condenser, and a nitrogen-inlet system (as in step A) is heated to reflux. As soon as all the lithium iodide has dissolved (Note 9), 30 g. (0.129 mole) of 2-benzyl-2-carbomethoxycyclopentanone dissolved in 30 ml. of 2,4,6-collidine (Note 10) is added to the boiling, faintly yellow solution; and during this process the solution turns darker in color and a precipitate forms (Note 11). Evolution of carbon dioxide begins immediately, and its formation can be followed by passing the nitrogen flush through a saturated barium hydroxide solution. The mixture is heated under reflux and a nitrogen atmosphere for 19 hours, at the end of which time the evolution of carbon dioxide

is very slow (Note 12).

The mixture is cooled and poured onto a mixture of 200 ml. of 6*N* hydrochloric acid, 200 ml. of ether, and 100 g. of ice. The residue in the flask is dissolved in a mixture of 6*N* hydrochloric acid and methylene chloride, and this mixture is added to the main reaction. The aqueous layer is separated and extracted with two 100-ml. portions of ether. The combined ethereal solution is washed once with 70 ml. of 6*N* hydrochloric acid, once with 2*N* sodium carbonate solution, twice with saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The solvent is removed under reduced pressure, and the residue is distilled to yield 16–17 g. (72–76%) of colorless 2-benzylcyclopentanone, b.p. 83–85° (0.3 mm.), 108–110° (0.75 mm.) (Note 13).

## 2. Notes

1. This stirring apparatus is available from Ag. für Chemie Apparatebau, Mannedorf, Zurich, Switzerland.
2. The submitter prepared the material from dimethyl adipate following the procedure published by Pickney<sup>3</sup> for the diethyl ester. The checkers obtained their material by fractional distillation of mixed carbomethoxy- and carbethoxycyclopentanone available from Arapahoe Chemical Co., Boulder, Colorado.
3. If the 2-carbomethoxycyclopentanone is added in one portion, the yield of the product drops to 67%.
4. At the end of the reflux period, the reaction mixture is a nonviscous solution containing a white precipitate.
5. The semicarbazone melts at 168–170°.
6. Lithium iodide dihydrate is available from Fluka A. G., Buchs, S. G., Switzerland. The checkers used the trihydrate and, by means of a Dean Stark trap<sup>4</sup> attached between the flask and the condenser, 1 mole of water was removed via azeotropic distillation with collidine.
7. In cases where a carbomethoxy group is desired to be selectively cleaved in the presence of a readily hydrolyzed ester group, such as an acetate of a secondary alcohol, anhydrous lithium iodide must be employed.<sup>5</sup> In order to avoid partial decomposition of the salt to iodine, it is best dried by slowly heating it to 150° in a high vacuum. The solubility of anhydrous lithium iodide in boiling collidine or lutidine is slightly less than that of the dihydrate, but it still is adequate for the reaction. In the present case, the use of the anhydrous salt lowers the yield of the 2-benzylcyclopentanone to 67%, and a large amount of a product, believed to be a dimer, boiling around 200° (0.5 mm.) is obtained.
8. For the cleavage of less hindered esters, the lower-boiling 2,6-lutidine (b.p. 143°) can be used as the solvent.
9. The development of a small amount of iodine is difficult to avoid. The nitrogen atmosphere is essential to keep this salt decomposition to a minimum.
10. Methyl esters react more rapidly with lithium iodide than do ethyl esters, which in turn react more rapidly than esters of secondary alcohols. On the other hand, *t*-butyl esters are cleaved very readily with a catalytic amount of lithium iodide.
11. A precipitate remains throughout the reaction.
12. By using three mole equivalents of lithium iodide dihydrate, at the end of 6.5 hours of reflux a 77% yield of 2-benzyl-cyclopentanone is obtained.
13. The semicarbazone melts at 204–205°.

## 3. Discussion

This preparation of 2-benzyl-2-carbomethoxycyclopentanone is based on a procedure described by Baker and Leeds<sup>6</sup> for the ethyl ester, and the methyl ester has not been previously prepared. The ethyl ester, also, has been prepared by the alkylation of 2-carbomethoxycyclopentanone with benzyl chloride in the presence of potassium hydroxide in acetaldehyde dipropylacetal.<sup>7</sup> The preparation and isolation of the potassium salt of 2-carbomethoxycyclopentanone can be readily achieved in a very simple way using aqueous alcoholic potassium hydroxide; by reaction of this salt with a variety of different halides in anhydrous media many 2-alkyl-2-carbomethoxycyclopentanones have been prepared.<sup>8,9</sup>

The preparation of 2-benzylcyclopentanone from 2-benzyl-2-carbomethoxycyclopentanone has not been previously reported. Starting with the ethyl ester, however, the compound has been prepared by

heating the ester for many hours with concentrated [hydrochloric acid](#).<sup>6,10</sup> The direct alkylation of [cyclopentanone](#) with [benzyl chloride](#) in the presence of [sodium amide](#) in liquid [ammonia](#) goes only in a poor yield.<sup>11</sup>

#### 4. Merits of the Preparation

This procedure illustrates a general method for the selective splitting of a carbomethoxy group in the presence of easily hydrolyzed esters of other alcohols, such as the easily hydrolyzed equatorial acetoxy group. The specificity of the reaction is not affected by steric hindrance, and a highly hindered methyl ester can be split in the presence of other less hindered esters of secondary alcohols. Normal alkaline saponification goes in exactly the opposite way.

The present case simply illustrates another utility of the ester cleavage reaction, *i.e.*, the cleavage of a  $\beta$ -keto ester with concomitant decarboxylation under only slightly basic conditions. The method should be particularly applicable to systems which are prone to undergo reverse Claisen reactions.

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#### References and Notes

1. Oesterr. Institut für Hämoderivate, Industriestrasse 72, Wien XXII, Austria.
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4. See ref. 2, p. 215.
5. F. Elsinger, J. Schreiber, and A. Eschenmoser, *Helv. Chim. Acta*, **43**, 113 (1960).
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#### Appendix

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

diethyl ester

carbomethoxy- and carbethoxycyclopentanone

potassium salt of 2-carbethoxycyclopentanone

[hydrochloric acid](#) (7647-01-0)

[ammonia](#) (7664-41-7)

[Benzene](#) (71-43-2)

[ether](#) (60-29-7)

[sodium chloride](#) (7647-14-5)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

mercury (7439-97-6)

carbon dioxide (124-38-9)

acetate

iodine (7553-56-2)

potassium hydroxide (1310-58-3)

toluene (108-88-3)

sodium (13966-32-0)

benzyl chloride (100-44-7)

Cyclopentanone (120-92-3)

barium hydroxide (17194-00-2)

2,6-Lutidine (108-48-5)

lutidine (583-61-9)

methylene chloride (75-09-2)

2-Carboethoxycyclopentanone (611-10-9)

sodium amide (7782-92-5)

2,4,6-collidine (108-75-8)

collidine

2-Benzylcyclopentanone,  
2-benzyl-cyclopentanone (2867-63-2)

2-carbomethoxycyclopentanone (10472-24-9)

2-benzyl-2-carbomethoxycyclopentanone (10386-81-9)

lithium iodide dihydrate

lithium iodide (10377-51-2)

dimethyl adipate (627-93-0)

acetaldehyde dipropylacetal (105-82-8)

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