



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

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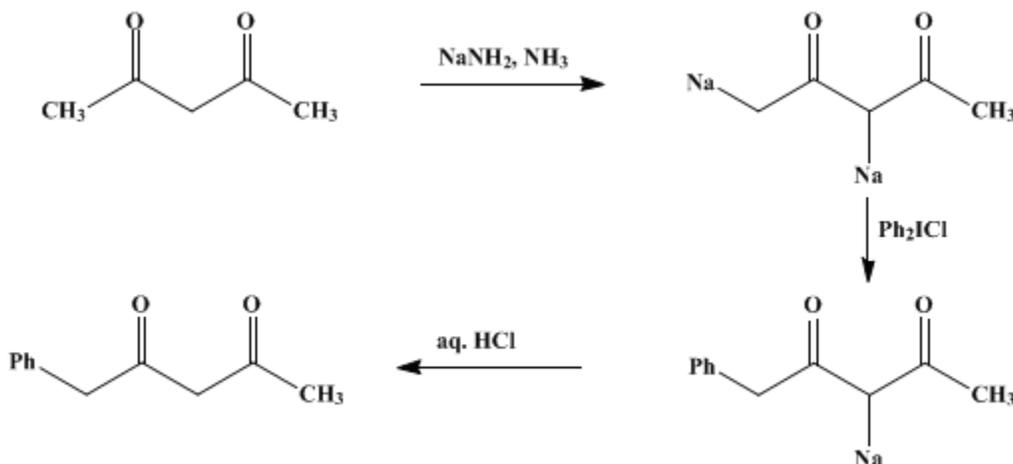
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 6, p.928 (1988); Vol. 51, p.128 (1971).*

## PHENYLATION WITH DIPHENYLIODONIUM CHLORIDE: 1-PHENYL-2,4-PENTANEDIONE

### [2,4-Pentanedione, 1-phenyl-]



Submitted by K. Gerald Hampton<sup>1</sup>, Thomas M. Harris<sup>2</sup>, and Charles R. Hauser<sup>3</sup>.  
Checked by William N. Washburn and Ronald Breslow.

### 1. Procedure

*Caution! This preparation should be carried out in an efficient hood to avoid exposure to ammonia.*

A 1-l., three-necked flask is equipped with an air condenser (Note 1), a ball-sealed mechanical stirrer, and a glass stopper. The stopper is removed, and 800 ml. of anhydrous liquid ammonia is introduced from a cylinder through an inlet tube. The tube is removed and replaced by the stopper. A small piece of sodium is added to the stirred ammonia. After the appearance of a blue color a few crystals of iron(III) nitrate hydrate (about 0.25 g.) are added, followed by small pieces of freshly cut sodium until 18.4 g. (0.800 g.-atom) has been added. After the formation of sodium amide is complete (Note 2), the glass stopper is replaced with a pressure-equalizing dropping funnel containing 40.0 g. (0.400 mole) of 2,4-pentanedione (Note 3) in 30 ml. of anhydrous diethyl ether. The top of the addition funnel is fitted with a nitrogen inlet tube. The reaction flask is immersed at least 3 inches into an acetone-dry ice bath (Note 4), and the slow introduction of dry nitrogen through the inlet tube is begun simultaneously. After the reaction mixture is cooled thoroughly (about 20 minutes), the 2,4-pentanedione solution is added in small portions (Note 4) over 10 minutes. The cooling bath is removed, and the nitrogen flow is stopped. After 30 minutes the addition funnel is removed, and 63.3 g. (0.200 mole) of diphenyliodonium chloride (Note 5) is added through Gooch tubing from an Erlenmeyer flask over 15–25 minutes (Note 6). The reaction mixture is stirred for 6 hours, during which time the ammonia gradually evaporates. The Gooch tubing is replaced with an addition funnel, and 400 ml. of anhydrous ether is added. The remaining ammonia is removed by cautious heating on a warm-water bath. After the ether has distilled gently for 15 minutes, the flask is cooled in an ice-water bath, and 200 g. of crushed ice is added. A mixture of 60 ml. of concentrated hydrochloric acid and 10 g. of crushed ice is then added. The reaction mixture is stirred until the solid material has dissolved (Note 7) and transferred to a separatory funnel, the flask being washed with a little ether and dilute hydrochloric acid. The ethereal layer is separated, and the aqueous layer (Note 8) and (Note 9) is shaken three times with 50-ml. portions of ether. The combined ethereal extracts are dried over anhydrous magnesium sulfate. After filtration and removal of the solvent, the residual oil is purified by vacuum distillation, giving 21.0–22.5 g. (60–64%) (Note 10) of 1-phenyl-2,4-pentanedione, b.p. 133–136° (10 mm.), as a colorless to light yellow liquid (Note 11).

## 2. Notes

1. The flask is insulated with cloth towels to reduce the rate of ammonia evaporation. In addition the towels exclude light, thus reducing the photolytic production of iodine from diphenyliodonium chloride and the reaction products.
2. Conversion to sodium amide is indicated by the disappearance of the blue color. This generally requires about 20 minutes.
3. 2,4-Pentanedione, obtained from Aldrich Chemical Company, Inc., was dried over potassium carbonate and distilled before use, the fraction b.p. 133–135° being used.
4. The addition of 2,4-pentanedione to liquid ammonia is highly exothermic. Also, ammonia vapor reacts with the  $\beta$ -diketone, producing an insoluble ammonium salt which tends to clog the tip of the addition funnel. Cooling the reaction mixture in an acetone–dry ice bath reduces the vigor of the reaction and minimizes the clogging of the addition funnel. The 2,4-pentanedione should be added in spurts which fall on the surface of the reaction mixture rather than on the wall of the flask.
5. Diphenyliodonium chloride prepared by the method of Beringer and co-workers was used,<sup>4</sup> but it can also be prepared by the method described in *Org. Synth., Coll. Vol. 3, 355 (1955)*, or may be purchased from Aldrich Chemical Company, Inc.
6. If the addition is too fast, the reaction mixture will foam out of the flask.
7. A little diphenyliodonium salt may remain which will not dissolve. It will settle between the layers.
8. The aqueous layer should be acidic to litmus paper. If it is basic, more hydrochloric acid should be added until an acidic test is obtained.
9. The ethereal solution is usually dark, but should not have a purple color. A purple color indicates the presence of iodine. Iodine can arise by a light-catalyzed reaction in the latter stages of the reaction and during isolation of the product. For this reason the reaction should be shielded from strong light. In addition it is advisable for the ether employed in the reaction mixture to be peroxide-free. If iodine is present in the reaction product, it must be removed by extraction with aqueous sodium thiosulfate solution, since an adequate separation is not obtained by distillation.
10. The submitters have obtained the product in yields as high as 92% by a similar procedure and 85–91% by this procedure on this scale. The yield is calculated with the assumption that only one of the phenyl groups of diphenyliodonium ion is available for phenylation. This is not rigorously true; however, the magnitude of error is not great.<sup>5</sup>
11. A forerun of 2,4-pentanedione and iodobenzene, b.p. 32–92° (35 mm.), is obtained before the pressure is reduced to 10 mm. The purity of the product may be demonstrated by GC at 130° using a 180-cm. column packed with silicone gum rubber (Hewlett-Packard Co.). The chromatogram obtained showed only traces of iodobenzene and 3-phenyl-2,4-pentanedione.

## 3. Discussion

The method described is that of Hampton, Harris, and Hauser<sup>5</sup> and is an improvement over the benzyne method, which gives poor yields.<sup>5,6</sup> This  $\beta$ -diketone has been prepared by Claisen condensation of ethyl phenylacetate with acetone,<sup>7</sup> but the yield is poorer and the product has been shown by GC to be impure.<sup>5</sup> The  $\beta$ -diketone has also been prepared by hydrolysis of 4-methoxy-5-phenyl-3-penten-2-one<sup>8</sup> and by hydrolysis and decarboxylation of ethyl 1-acetyl-2-oxo-3-phenylbutyrate<sup>9</sup> but these compounds are more difficult to obtain than the starting materials used in the present synthesis.

This procedure represents a novel, convenient, and fairly general method of preparing  $\gamma$ -aryl- $\beta$ -diketones. By this method the submitters have phenylated the dianion of 1-phenyl-1,3-butanedione (61%), 2,4-heptanedione (98%), 2,4-nonanedione (78%), 2,4-tridecanedione (53%), and 3,5-heptanedione (50%).<sup>5</sup> Substituted diaryliodonium salts have also been used to produce 1-(4-chlorophenyl)-2,4-pentanedione (44%), 4-(4-methylphenyl)-1-phenyl-1,3-butanedione (44%), and 1-(4-methylphenyl)-2,4-nonanedione (21%).<sup>5</sup> Under these conditions no more than a trace, if any, of arylation at the  $\alpha$ -position of the  $\beta$ -diketones was observed by GC analysis.

Although the phenylation of monoanions of  $\beta$ -diketones does not proceed at a significant rate under the present conditions, phenylation of monoanions using diphenyliodonium salts under somewhat more vigorous conditions has been observed. The monoanions of 5,5-dimethyl-1,3-cyclohexanedione,<sup>10,11</sup>

dibenzoylmethane,<sup>10</sup> tribenzoylmethane,<sup>10</sup> 1,3-indandione,<sup>12</sup> 2-mesityl-1,3-indandione,<sup>13</sup> and 2-phenyl-1,3-indandione<sup>12</sup> have been phenylated to give the mono- or diphenylated products. Keto esters such as ethyl 1,3-indandione-2-carboxylate,<sup>12</sup> ethyl cyclohexanone-2-carboxylate,<sup>14</sup> and other esters such as ethyl phenylacetate,<sup>14</sup> ethyl diphenylacetate,<sup>14</sup> diethyl acetamidomalonate,<sup>14</sup> diethyl ethylmalonate,<sup>14</sup> diethyl phenylmalonate,<sup>14</sup> and diethyl malonate<sup>15</sup> have been arylated in fair to good yields. Kornblum and Taylor have also found that nitroalkanes can be phenylated in 54–69% yield. These include 1-nitropropane, 2-nitropropane, 2-nitrobutane, 2-nitroöctane, nitrocyclohexane, and ethyl 1-nitroacproate.<sup>16</sup>

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## References and Notes

1. Chemistry Department, Texas A & M University, College Station, Texas 77843. This research was conducted at Texas A & M University and supported in part by the Petroleum Research Fund of the American Chemical Society.
2. Chemistry Department, Vanderbilt University, Nashville, Tennessee 37203.
3. Chemistry Department, Duke University, Durham, North Carolina 27706 (deceased January 6, 1970).
4. F. M. Beringer, E. J. Geering, I. Kuntz, and M. Mausner, *J. Phys. Chem.*, **60**, 141 (1956).
5. K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **29**, 3511 (1964).
6. C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958).
7. C. R. Hauser and R. M. Manyik, *J. Org. Chem.*, **18**, 588 (1953), G. T. Morgan and C. R. Porter, *J. Chem. Soc.*, **125**, 1269 (1924).
8. L. I. Smith and J. S. Showell, *J. Org. Chem.*, **17**, 836 (1952).
9. E. Fischer and C. Bülow, *Ber. Dtsch. Chem. Ges.*, **18**, 2131 (1885).
10. F. M. Beringer, P. S. Forgione, and M. D. Yudis, *Tetrahedron*, **8**, 49 (1960).
11. O. Ia. Neiland, G. Ia. Vanag, and E. Iu. Gudrinietse, *J. Gen. Chem. USSR. (Engl. Transl.)* **28**, 1256 (1958).
12. F. M. Beringer, S. A. Galton, and S. J. Huang, *J. Am. Chem. Soc.*, **84**, 2819 (1962).
13. F. M. Beringer and S. A. Galton, *J. Org. Chem.*, **28**, 3417 (1963).
14. F. M. Beringer and P. S. Forgione, *J. Org. Chem.*, **28**, 714 (1963).
15. F. M. Beringer and P. S. Forgione, *Tetrahedron*, **19**, 739 (1963).
16. N. Kornblum and H. J. Taylor, *J. Org. Chem.*, **28**, 1424 (1963).

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## Appendix

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

potassium carbonate (584-08-7)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

benzyne (71-43-2)

ether,  
diethyl ether (60-29-7)

sodium thiosulfate (7772-98-7)

nitrogen (7727-37-9)

iodine (7553-56-2)

acetone (67-64-1)

sodium (13966-32-0)

Dibenzoylmethane (120-46-7)

diethyl malonate (105-53-3)

Ethyl phenylacetate (101-97-3)

diethyl ethylmalonate (133-13-1)

Iodobenzene (591-50-4)

magnesium sulfate (7487-88-9)

5,5-Dimethyl-1,3-cyclohexanedione (126-81-8)

diethyl phenylmalonate (83-13-6)

sodium amide (7782-92-5)

ethyl cyclohexanone-2-carboxylate (1655-07-8)

2,4-pentanedione (123-54-6)

1-phenyl-1,3-butanedione (93-91-4)

2-nitropropane (79-46-9)

iron(III) nitrate hydrate

Diethyl acetamidomalonate (1068-90-2)

1-nitropropane (108-03-2)

2,4-Nonanedione (6175-23-1)

2,4-tridecanedione

diphenyliodonium chloride (1483-72-3)

3-phenyl-2,4-pentanedione (5910-25-8)

tribenzoylmethane (641-44-1)

1,3-indandione (606-23-5)

2-mesityl-1,3-indandione

2-phenyl-1,3-indandione (83-12-5)

ethyl 1,3-indandione-2-carboxylate

ethyl diphenylacetate

2-nitrobutane (600-24-8)

nitrocyclohexane (1122-60-7)

ethyl 1-nitrocaproate

1-Phenyl-2,4-pentanedione,  
2,4-Pentanedione, 1-phenyl- (3318-61-4)

4-methoxy-5-phenyl-3-penten-2-one

ethyl 1-acetyl-2-oxo-3-phenylbutyrate

2,4-heptanedione (7307-02-0)

3,5-heptanedione (7424-54-6)

1-(4-chlorophenyl)-2,4-pentanedione

4-(4-methylphenyl)-1-phenyl-1,3-butanedione

1-(4-methylphenyl)-2,4-nonanedione

2-nitrooctane