Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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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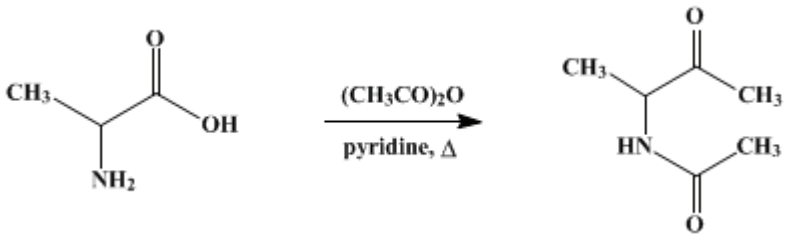
Organic Syntheses, Coll. Vol. 4, p.5 (1963); Vol. 33, p.1 (1953).

3-ACETAMIDO-2-BUTANONE

[2-Butanone, 3-acetamido-]



Submitted by Richard H. Wiley and O. H. Borum[1].
Checked by R. S. Schreiber and B. D. Aspergren.

1. Procedure

A mixture of 156.6 g. (159 ml., 1.98 moles) of pyridine (Note 1), 239.9 g. (224 ml., 2.35 moles) of acetic anhydride (Note 2), and 35.1 g. (0.39 mole) of vacuum-dried alanine (Note 3) and (Note 4) is heated with stirring (Note 5) on the steam bath for 6 hours after solution is complete (Note 6). The excess pyridine and acetic anhydride, and the acetic acid, are removed at reduced pressure. The residue is distilled through a 15-cm. column, packed with glass helices, to give 41.5–47.5 g. of crude product, boiling at 110–125°/3 mm. Refractionation gives 41–45 g. (81–88%) of 3-acetamido-2-butanone; b.p. 102–106°/2 mm.; n_D^{25} 1.4558–1.4561 (Note 7).

2. Notes

1. A commercial C.P. grade can be used. The checkers used Merck A.R. grade.
2. A commercial grade, 95% minimum assay, can be used. The checkers used Merck A.R. grade.
3. Any good commercial grade material appears to be satisfactory.
4. Reducing the molar ratio of pyridine or anhydride to the amino acid reduces the yield.
5. Without stirring the yield is 46%.
6. With other amino acids, notably glycine and sarcosine, it is necessary to reflux the reactants 1–6 hours.
7. The checkers found it necessary to heat the column to obtain the maximum available product.

3. Discussion

This method, an adaptation of a previously described procedure,[2,3,4] has been used with a variety of amino acids and anhydrides to give the following products: 1-phenyl-1-propionamido-2-butanone (75%);[5] acetamidoacetylacetone (60%);[5] N-methylacetamidoacetone;[6] 1-phenyl-2-acetamido-3-butanone (79%);[7] 1-phenyl-2-propionamido-3-pentanone (41%);[7] 1-phenyl-2-butyramido-3-hexanone (27%);[7] α-benzamidopropiophenone (42%);[7] α-benzamido-β-phenylpropiophenone (44%);[7] 1-phenyl-1-acetamidoacetone (72–90%);[8,9] 1-phenyl-1-benzamidoacetone (65%);[8] 1-phenyl-2-benzamido-3-butanone (78%);[8] 3-benzamido-2-butanone (65–88%);[8] and 3-acetamido-5-methyl-2-hexanone (73%).[10]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 27

References and Notes

1. University of Louisville, Louisville, Kentucky.

2. Dakin and West, *J. Biol. Chem.*, **78**, 91, 757 (1928).
3. Levene and Steiger, *J. Biol. Chem.*, **74**, 689 (1927); **79**, 95 (1928).
4. Wiley, *J. Org. Chem.*, **12**, 43 (1947).
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7. Cleland and Niemann, *J. Am. Chem. Soc.*, **71**, 841 (1949).
8. Searles and Cvejanovich, *J. Am. Chem. Soc.*, **72**, 3200 (1950).
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10. Borum, Ph.D. Thesis, University of North Carolina, 1949.

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

acetic acid (64-19-7)

acetic anhydride (108-24-7)

alanine (56-41-7)

pyridine (110-86-1)

sarcosine (107-97-1)

Glycine (513-29-1)

3-Acetamido-2-butanone,
2-Butanone, 3-acetamido- (6628-81-5)

1-phenyl-1-propionamido-2-butanone

acetamidoacetylacetone

N-methylacetamidoacetone

1-phenyl-2-acetamido-3-butanone

1-phenyl-2-propionamido-3-pentanone

1-phenyl-2-butyramido-3-hexanone

α-benzamidopropiophenone

α-benzamido-β-phenylpropiophenone

1-phenyl-1-acetamidoacetone

1-phenyl-1-benzamidoacetone

1-phenyl-2-benzamido-3-butanone

3-benzamido-2-butanone

3-acetamido-5-methyl-2-hexanone