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.

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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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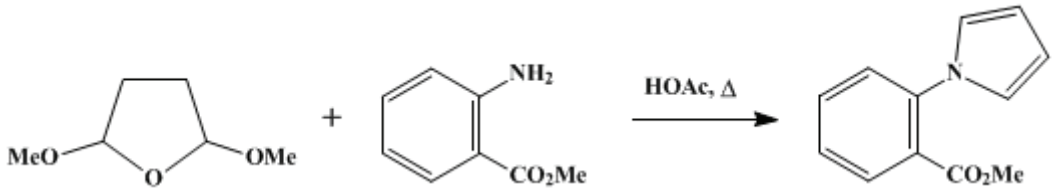
1-(2-METHOXYCARBONYLPHENYL)PYRROLE

[Pyrrole, 1-(2-methoxycarbonylphenyl)-]



Submitted by A. D. Josey[1]
Checked by William G. Dauben and Juraj Hostynek.

1. Procedure

A solution of 90 g. (0.59 mole) of methyl anthranilate (Note 1) in 265 ml. of glacial acetic acid is placed in a 1-l. round-bottomed flask equipped with a reflux condenser and a magnetic stirrer. The stirrer is started, and 78 g. (0.59 mole) of 2,5-dimethoxytetrahydrofuran (Note 2) is added during 10–15 minutes (Note 3). The solution is heated under reflux for 1 hour, during which time the solution turns deep red to black in color. The heating is discontinued, the condenser is replaced with a Vigreux column, and the acetic acid is removed by distillation at aspirator pressure. The dark residue is distilled under reduced pressure through a 25-cm. column packed with glass helices, and 84–96 g. (70–80%) of slightly yellow 1-(2-methoxycarbonylphenyl)pyrrole is collected, b.p. 90–95° (2 mm.), n^{25}D 1.5729.

2. Notes

1. Methyl anthranilate from Eastman Kodak Company was used without further purification.
2. 2,5-Dimethoxytetrahydrofuran from Eastman Kodak Company was used without further purification. This material also can be prepared by catalytic hydrogenation[2] of 2,5-dihydro-2,5-dimethoxyfuran.[3]
3. The submitter reports that much heat is liberated during the addition; the checkers did not find the reaction to be markedly exothermic.

3. Discussion

1-(2-Methoxycarbonylphenyl)pyrrole has not been prepared previously. An attempt to prepare the material via the mucic acid pyrrole synthesis using methyl anthranilate was unsuccessful.[4]

4. Merits of the Preparation

The condensation of primary amines with 2,5-dialkoxytetrahydrofurans to give in one step N-substituted pyrroles is applicable to a variety of substituted aliphatic and aromatic amines.[5] The method, largely developed by Clauson-Kaas and associates, has the advantages of simplicity, mild conditions, and generally excellent yields from readily available starting materials.

The submitter has used the method to prepare the corresponding 1-pyrrolyl derivatives[6] from the following amines in the indicated yields: ethyl β-aminobutyrate 88%, methyl β-aminoglutarate 87%, β-aminopropionitrile 58%, and 2,5-diamino-3,4-dicyanothiophene 22%.

On saponification 1-(2-methoxycarbonylphenyl)pyrrole yields 1-(2-carboxyphenyl)pyrrole, m.p. 106–107°, which on reaction with polyphosphoric acid at 70° is cyclized to 9-keto-9H-pyrrole-(1,2-*a*) indole in 28–32% yield. Through the choice of the appropriate amine and acetal components, the substituted 1-(2-methoxycarbonylphenyl)pyrroles become readily available intermediates in the preparation of a variety of derivatives of the pyrrolo(1,2-*a*)indole ring system.

References and Notes

1. Contribution No. 977 from the Central Research Department, Experimental Station, E.I. du Pont de Nemours and Co., Inc.
2. J. Fakstorp, D. Raleigh, and L. E. Schniepp, *J. Am. Chem. Soc.*, **72**, 869 (1950).
3. D. M. Burness, this volume, p. 403.
4. D. A. Shirley, B. H. Gross, and P. A. Roussel, *J. Org. Chem.*, **20**, 225 (1955).
5. N. Clauson-Kaas and Z. Tyle, *Acta Chem. Scand.*, **6**, 667 (1952); **6**, 867 (1952).
6. A. D. Josey and E. L. Jenner, *J. Org. Chem.*, **27**, 2466 (1962).

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

polyphosphoric

9-keto-9H-pyrrole-(1,2-a)indole

acetic acid (64-19-7)

Pyrrole (109-97-7)

mucic acid

β-Aminopropionitrile (151-18-8)

2,5-Diamino-3,4-dicyanothiophene (17989-89-8)

2,5-Dihydro-2,5-dimethoxyfuran (332-77-4)

2,5-dimethoxytetrahydrofuran (696-59-3)

1-(2-Methoxycarbonylphenyl)pyrrole,
Pyrrole, 1-(2-methoxycarbonylphenyl)- (10333-67-2)

methyl anthranilate (134-20-3)

ethyl β-aminobutyrate (5303-65-1)

methyl β-aminoglutarate

1-(2-carboxyphenyl)pyrrole (10333-68-3)