



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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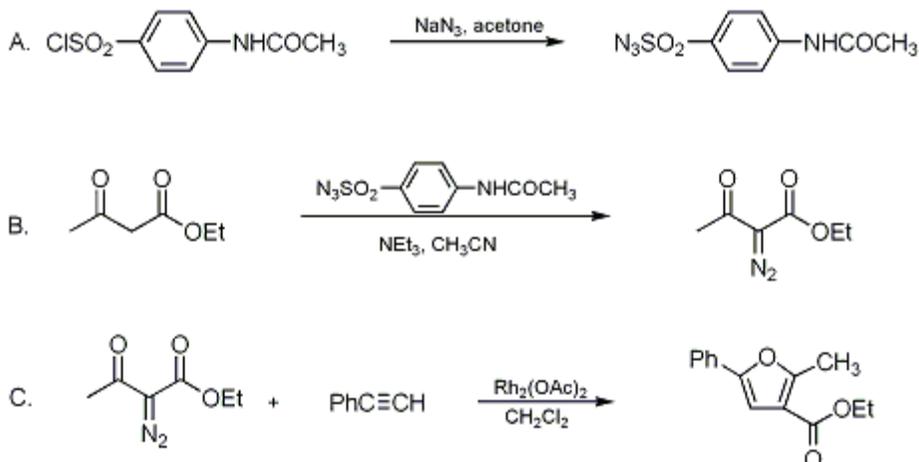
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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SYNTHESIS OF FURANS VIA RHODIUM(II) ACETATE-CATALYZED REACTION OF ACETYLENES WITH α -DIAZOCARBONYLS: ETHYL 2-METHYL-5-PHENYL-3-FURANCARBOXYLATE

[3-Furancarboxylic acid, 2-methyl-5-phenyl-, ethyl ester]



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1. Procedure

CAUTION! These reactions, which involve toxic reagents, should be carried out in an efficient hood. Although p-acetamidobenzenesulfonyl azide exhibited no impact sensitivity,³ proper caution should be exercised with all azide compounds.

A. *p*-Acetamidobenzenesulfonyl azide.³ A 2-L Erlenmeyer flask equipped with a magnetic stirrer is charged with 117.0 g (0.50 mol) of *p*-acetamidobenzenesulfonyl chloride (Note 1) and 1 L of acetone. A solution of 39.0 g (0.60 mol) of sodium azide in 300 mL of water is added with stirring and the resulting mixture is left to stir for 12 hr. Three 2-L beakers equipped with magnetic stirrers are charged with 1.5 L each of water. The reaction mixture is divided into three portions and poured into the beakers with stirring. After the mixture is stirred for 1 hr, the white precipitate is filtered (Note 2) and dried in a desiccator over sodium hydroxide for 24 hr. Recrystallization of this material in four portions from toluene (1.5 L each portion), while the temperature is maintained below 80°C (Note 3), affords 88.9 g (74%) of *p*-acetamidobenzenesulfonyl azide as white crystals, mp 113°-115°C (Note 4).

B. *Ethyl diazoacetoacetate*.³ A 2-L, round-bottomed flask equipped with a magnetic stirrer is charged with 26.0 g (0.20 mol) of ethyl acetoacetate, 49.0 g (0.20 mol) of *p*-acetamidobenzenesulfonyl azide and 1.5 L of acetonitrile. The reaction vessel is cooled in an ice bath, and 60.6 g (0.60 mol) of triethylamine is added to the stirring mixture in one portion. The reaction mixture is warmed to room temperature and stirred for 12 hr. The solvent is removed under reduced pressure, and the residue is triturated with 500 mL of a 1:1 mixture of ether/petroleum ether. The mixture is filtered to remove the sulfonamide by-product, and the filtrate and wash are concentrated under reduced pressure. The crude product is purified by chromatography on silica gel (130 g, (Note 5)) with ether/petroleum ether (1:4) as eluant to yield 28.5 g (91%) of ethyl diazoacetoacetate as a yellow oil (Note 6).

C. *Ethyl 2-methyl-5-phenyl-3-furancarboxylate*.⁴ A 1-L, three-necked, round-bottomed flask equipped with a magnetic stirrer, an addition funnel, and a reflux condenser is flushed with argon (Note 7). The reaction vessel is charged with 44.35 g of phenylacetylene (0.44 mol, (Note 8)), 0.38 g of rhodium(II) acetate dimer (0.00087 mol), and 100 mL of dichloromethane and the mixture is heated to reflux under an argon atmosphere. The addition funnel is charged with 13.57 g of ethyl diazoacetoacetate (0.087 mol) and 200 mL of dichloromethane, and this solution is added dropwise over 1.5 hr to the reaction mixture. After the reaction mixture is heated under reflux for an additional 12 hr, it is cooled and the solvent is removed under reduced pressure. The crude product is purified by chromatography on silica gel (110 g) with ether/petroleum ether (1:19) as eluant, followed by vacuum distillation (10-cm Vigreux column, 130°C, 0.1 mm) to yield 9.95 g (50%) of the furan as a pale yellow liquid (Note 9).

2. Notes

1. The following chemicals were obtained from the Aldrich Chemical Company, Inc., and were used without further purification: *p*-acetamidobenzenesulfonyl chloride, 97%; acetone, 99.9+%, HPLC grade; sodium azide, 99%; ethyl acetoacetate, 99%; triethylamine, 99%; rhodium(II) acetate dimer; phenylacetylene, 98%. The following solvents were obtained from Fisher Scientific and were used without further purification: toluene, certified A. C. S.; ethyl ether (Solvent grade, Concentrated); petroleum ether, certified A. C. S. Dichloromethane was distilled from calcium hydride.
2. The filtrate contains excess sodium azide which should be destroyed prior to disposal.
3. The azide partially decomposes at temperatures exceeding 80°C, and the resulting crystals appear slightly brown.
4. Data for *p*-acetamidobenzenesulfonyl azide are as follows: $R_f = 0.49$ (ether/petroleum ether (1:4)); ¹H NMR (200 MHz, CDCl₃) δ : 2.23 (s, 3 H), 7.75–7.89 (m, 4 H), 8.02 (s, 1 H); IR (nujol) cm⁻¹: 3250, 2110, 1665, 1580. Anal. Calcd for C₈H₈N₄O₃S: C, 40.00; H, 3.36; N, 23.32; S, 13.35. Found: C, 40.10; H, 3.40; N, 23.26; S, 13.40.
5. Silica gel 60 230–400 mesh ASTM was used. Whatman 250-mm layer, UV254, silica gel TLC plates with polyester backing were used to analyze the fractions.
6. Spectral data for ethyl diazoacetoacetate are as follows: ¹H NMR (200 MHz, CDCl₃) δ : 1.29 (t, 3 H, $J = 7.1$), 2.43 (s, 3 H), 4.26 (q, 2 H, $J = 7.1$); IR (neat) cm⁻¹: 2970, 2130, 1700, 1650.
7. The glassware in this reaction is dried with a heat gun and placed in a drying oven for 1 hr prior to use.
8. A smaller amount of phenylacetylene results in inefficient capture of the carbenoid intermediate, leading to lower yields.
9. Data for ethyl 2-methyl-5-phenyl-3-furancarboxylate are as follows: $R_f = 0.51$ (ether/petroleum ether (1:9)); ¹H NMR (200 MHz, CDCl₃) δ : 1.35 (t, 3 H, $J = 7.1$), 2.63 (s, 3 H), 4.30 (q, 2 H, $J = 7.1$), 6.87 (s, 1 H), 7.24–7.40 (m, 3 H), 7.60–7.65 (m, 2 H); IR (neat) cm⁻¹: 3080, 3000, 1725, 1610, 1590, 1565. Anal. Calcd for C₁₄H₁₄O₃: C, 73.03; H, 6.13. Found: C, 73.17; H, 6.09.

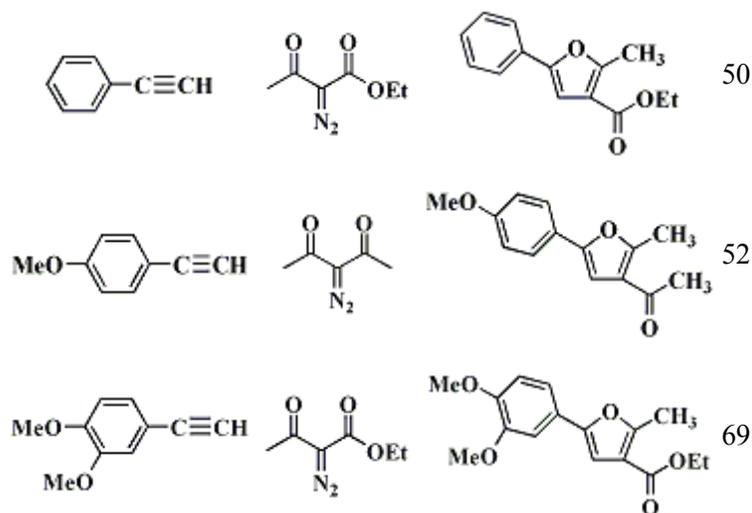
Waste Disposal Information

Excess sodium azide in the filtrate was destroyed by treatment with ammonium cerium(IV) nitrate solution according to the procedure described by Lunn, G.; Sansone, E. B., In "Destruction of Hazardous Chemicals in the Laboratory"; Wiley: New York, 1990; p. 44.

3. Discussion

The procedure described here provides a direct synthesis of highly substituted furans (see Table). Reaction of keto carbenoids with acetylenes is normally an efficient method to prepare cyclopropenes.⁵ In numerous systems, however, the formation of furans was observed as a competing side reaction.^{6 7 8 9} Furan formation is particularly favored when the carbenoid is a pyruvate¹⁰ or contains two electron-withdrawing groups,^{4,11} and when electron-donating groups are present on the acetylene.^{4,11}

TABLE
RHODIUM(II) ACETATE-CATALYZED REACTION OF
ACETYLENES WITH DIAZO CARBONYL COMPOUNDS⁴



The diazo transfer reaction with sulfonyl azides has been used extensively for the preparation of diazo compounds.¹² [Toluenesulfonyl azide](#) is the standard reagent used,¹³ but because of safety problems resulting from its potentially explosive nature, and because of the difficulty of product separation, several alternative reagents have been developed recently. [n-Dodecylbenzenesulfonyl azide](#)¹⁴ has been reported to be very effective for the preparation of crystalline diazo compounds, while [p-naphthalenesulfonyl azide](#)¹⁴ has been used for fairly non-polar compounds. Other useful reagents are [methanesulfonyl azide](#)¹⁵ and [p-carboxybenzenesulfonyl azide](#).¹⁶ [p-Acetamidobenzenesulfonyl azide](#)³ offers the advantages of low cost, safety, and ease of removal of the sulfonamide by-product through a simple trituration.

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 9, 322](#)

References and Notes

1. Department of Chemistry, Wake Forest University, P. O. Box 7486, Winston-Salem, NC 27109.
2. Agricultural Chemical Group, FMC Corporation, P. O. Box 8, Princeton, NJ 08543.
3. Baum, J. S.; Shook, D. A.; Davies, H. M. L.; Smith, H. D. *Synth. Commun.* **1987**, *17*, 1709.
4. Davies, H. M. L.; Romines, K. R. *Tetrahedron* **1988**, *44*, 3343.
5. Petiniot, N.; Anciaux, A. J.; Noels, A. F.; Hubert, A. J.; Teyssié, Ph. *Tetrahedron Lett.* **1978**, 1239.
6. D'yakanov, I. A.; Komendantov, M. I. *J. Gen. Chem. USSR (Engl. Trans.)* **1961**, *31*, 3618; *Chem. Abstr.* **1962**, *57*, 8405f;
7. D'yakanov, I. A.; Komendantov, M. I.; Korshunov, S. P.; *J. Gen. Chem. USSR (Engl. Trans.)* **1962**, *32*, 912; *Chem. Abstr.* **1963**, *58*, 2375e;
8. Komendantov, M. I.; Domnin, I. N.; Bulucheva, E. V. *Tetrahedron* **1975**, *31*, 2495;
9. Hendrick, M. E. *J. Am. Chem. Soc.* **1971**, *93*, 6337.
10. Wenkert, E.; Alonso, M. E.; Buckwalter, B. L.; Sanchez, E. L., *J. Am. Chem. Soc.* **1983**, *105*, 2021.
11. Yoshida, J.-i.; Yano, S.; Ozawa, T.; Kawabata, N. *J. Org. Chem.* **1985**, *50*, 3467.
12. Regitz, M., In "The Chemistry of Diazonium and Diazo Groups"; Patai, S., Ed.; Wiley: New York, 1978; Part 2, p. 751.
13. [Regitz, M.; Hocker, J.; Liedhegener, A. *Org. Synth., Coll. Vol. V* **1973**, 179.](#)
14. Hazen, G. G.; Weinstock, L. M.; Connell, R.; Bollinger, F. W. *Synth. Commun.* **1981**, *11*, 947.
15. Taber, D. F.; Ruckle, Jr., R. E.; Hennessy, M. J. *J. Org. Chem.* **1986**, *51*, 4077.

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

silica gel

petroleum ether

p-naphthalenesulfonyl azide

ether,
ethyl ether (60-29-7)

acetonitrile (75-05-8)

sodium hydroxide (1310-73-2)

p-acetamidobenzenesulfonyl chloride (121-60-8)

acetone (67-64-1)

toluene (108-88-3)

Ethyl acetoacetate (141-97-9)

sodium azide (26628-22-8)

dichloromethane (75-09-2)

Phenylacetylene (536-74-3)

triethylamine (121-44-8)

argon (7440-37-1)

calcium hydride (7789-78-8)

p-carboxybenzenesulfonyl azide (17202-49-2)

ammonium cerium(IV) nitrate

rhodium(II) acetate (5503-41-3)

methanesulfonyl azide

p-Acetamidobenzenesulfonyl azide (2158-14-7)

n-Dodecylbenzenesulfonyl azide (79791-38-1)

Ethyl 2-methyl-5-phenyl-3-furancarboxylate,
3-Furancarboxylic acid, 2-methyl-5-phenyl-, ethyl ester (29113-64-2)

Ethyl diazoacetoacetate (2009-97-4)

Toluenesulfonyl azide