Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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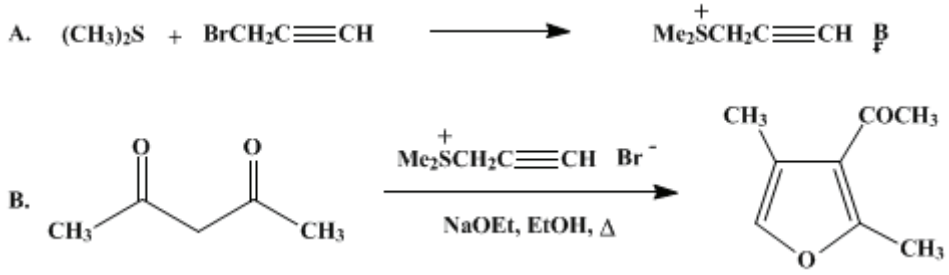
3-ACETYL-2,4-DIMETHYLFURAN

[Ethanone, 1-(2,4-dimethyl-3-furanyl)-]



Submitted by P. D. Howes and C. J. M. Stirling[1].
Checked by C. Reese, M. Uskokovic, and A. Brossi.

1. Procedure

Caution! These reactions should be performed in a hood because of the noxious odors.

A. *Dimethyl-2-propynylsulfonium bromide*. A mixture of 6.2 g. (0.10 mole) of dimethyl sulfide (Note 1), 11.9 g. (0.100 mole) of 3-bromopropyne (Note 2), and 10 ml. of acetonitrile (Note 3) is stirred magnetically for 20 hours (Note 4) in a darkened, 100-ml., round-bottomed flask (Note 5) fitted with a calcium chloride drying tube. The resulting white, crystalline mass is filtered with suction and washed with three 50-ml. portions of dry diethyl ether (Note 6), giving 16.4 g. (90%) of the sulfonium salt, m.p. 105–106°. This material may be used in the next step without purification but, if desired, it may be recrystallized from ethanol-ether (Note 7) with minimal loss, m.p. 109–110°.

B. 3-*Acetyl*-2,4-*dimethylfuran*. To a solution of 8.7 g. (0.087 mole) of acetylacetone (Note 8) in 175 ml. of 0.5 *M* ethanolic sodium ethoxide (0.087 mole), contained in a 500-ml., round-bottomed flask, fitted with a condenser topped with a calcium chloride drying tube, is added a solution of 15.75 g. (0.0870 mole) of dimethyl-2-propynylsulfonium bromide in 150 ml. of ethanol (Note 9). The mixture is refluxed until the odor of dimethyl sulfide is no longer appreciable (Note 10). The reaction flask is then fitted with a 30-cm., helix-packed column, and by heating the flask with a water bath, ethanol is distilled through the column (Note 11). The residue is treated with 200 ml. of ether, and the suspension is filtered. Ether is distilled from the filtrate at atmospheric pressure, and the residue is distilled, giving 9.7 g. (81%) of 3-acetyl-2,4-dimethylfuran (Note 12) and (Note 13), b.p. 90–95° (12 mm.), n_D^{24} 1.4965.

2. Notes

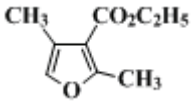
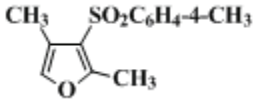
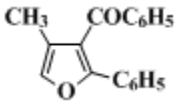
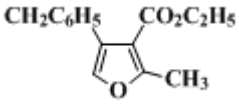
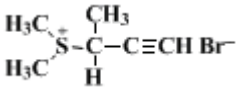
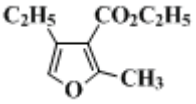
1. Dimethyl sulfide was used as supplied by British Drug Houses.
2. 3-Bromopropyne, supplied by British Drug Houses, was distilled before use (b.p. 84–86°).
3. Acetonitrile (Matheson, Coleman and Bell, spectral grade) was used without further treatment.
4. The maximum yield was obtained after 20 hours. Shorter reaction times give slightly lower yields.
5. If a brown glass flask is unavailable, an ordinary flask wrapped with aluminum foil may be used.
6. The ether was dried over sodium.
7. The salt was dissolved in 10 ml. of ethanol, 75 ml. of ether was added portion-wise, and the mixture was allowed to stand overnight at room temperature.
8. Acetylacetone, supplied by British Drug Houses, was distilled before use (b.p. 137°).
9. The ethanol was dried with magnesium ethoxide.[2]
10. About 6 hours is required on this scale.
11. Distillation through the packed column is essential to prevent loss of furan by co-distillation with ethanol.

12. The product has IR absorption (neat) at 1690 cm.$^{-1}$ (ketone C=O and ^{1}H NMR peaks (CCl_4) at δ 2.20 (s, 3H, $COCH_3$), 2.40 (s, 3H, CH_3), 3.60 (s, 3H, CH_3), and 7.40 (s, 1H, furyl).
13. A convenient modification of this procedure gives the furan in 70–75% yield; the sulfonium salt is preformed in acetonitrile and, without isolation, the other reagents are added.

3. Discussion

This procedure illustrates a recently published,[3] simple, general method for the synthesis of substituted furans. The scope of the reaction is shown in Table I. Many variations of this procedure are clearly possible.

TABLE I
FURANS PREPARED VIA ACETYLENIC SULFONIUM SALTS

Sulfonium Salt	Addend	R_1	R_2	R_3	Yield, %[2]
$CH_3S^+CH_2C{\equiv}CH\ Br^-$	$CH_3COCH_2CO_2CO_2C_2H_5$	CH_3	$CO_2C_2H_5$	CH_3	 86
$CH_3S^+CH_2C{\equiv}CH\ Br^-$	$CH_3COCH_2SO_2C_6H_4$-4-CH_3	CH_3	$SO_2C_6H_4$-4-CH_3	CH_3	 78
$CH_3S^+CH_2C{\equiv}CH\ Br^-$	$C_6H_5COCH_2COC_6H_5$	C_6H_5	COC_6H_5	CH_3	 72
$CH_3S^+CH_2C{\equiv}CC_6H_5\ Br^-$	$CH_3COCH_2CO_2C_2H_5$	CH_3	$CO_2C_2H_5$	$CH_2C_6H_5$	 63
	$CH_3COCH_2CO_2H_5$	CH_3	$CO_2C_2H_5$	C_2H_5	 50

The method described has some features in common with the well-known, but apparently little-used, Feist-Benary furan synthesis,[4] which uses an α-haloketone in place of the sulfonium salt. Acetylenic bromides suitable for preparing the sulfonium salts are readily available by well-documented procedures involving acetylenic organometallic compounds.

The mechanism of furan formation by this route is determined by the structure of the sulfonium salt; the course, hence the end product, is governed by whether an α-substituent is present. This must be

considered when syntheses based on this procedure are being planned. Plausible mechanisms for the reaction have been suggested.[3]

Direct treatment of propargyl halides with β-dicarbonyl compounds and subsequent treatment of the products with zinc carbonate yields 2,3,5-trisubstituted furans.[5]

References and Notes

1. School of Physical and Molecular Sciences, University College of North Wales, Bangor, Caernarvonshire, U.K.
2. D. D. Perrin, W. L. F. Armarego, and D. R. Perrin, "Purification of Laboratory Chemicals," 1st ed., Pergamon Press, New York, 1966, p. 157.
3. J. W. Batty, P. D. Howes, and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 1*, 65 (1973).
4. A. T. Blomquist and H. B. Stevenson, *J. Am. Chem. Soc.*, **56**, 146 (1934).
5. K. E. Schulte, J. Reisch, and A. Mock, *Arch. Pharm. Ber. Dtsch. Pharm. Ges.*, **295**, 627 (1962).

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

ethanol (64-17-5)

ether,
diethyl ether (60-29-7)

acetonitrile (75-05-8)

Salt (7647-14-5)

sodium (13966-32-0)

sodium ethoxide (141-52-6)

sulfonium

dimethyl sulfide (75-18-3)

Acetylacetone (123-54-6)

magnesium ethoxide (2414-98-4)

3-Acetyl-2,4-dimethylfuran,
Ethanone, 1-(2,4-dimethyl-3-furanyl)- (32933-07-6)

3-bromopropyne (106-96-7)

dimethyl-2-propynylsulfonium bromide (23451-62-9)

zinc carbonate (3486-35-9)