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.

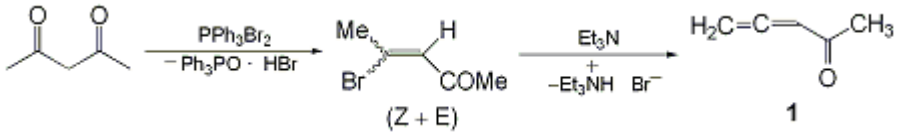
*September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

DOI:10.15227/orgsyn.078.0135

*Organic Syntheses, Coll. Vol. 10, p.595 (2004); Vol. 78, p.135 (2002).*

# SYNTHESIS OF PENTA-1,2-DIEN-4-ONE (ACETYLALLENE)

## [3,4-Pentadien-2-one]




Submitted by Thierry Constantieux and Gérard Buono[1] .
Checked by Dawn M. Bennett and Rick L. Danheiser.

## 1. Procedure

A 1-L, three-necked flask, equipped with a mechanical stirrer, reflux condenser fitted with an argon inlet adapter, and pressure-equalizing dropping funnel is charged with 151 g (0.58 mol) of triphenylphosphine (Note 1) and 350 mL of dichloromethane (Note 2). The mixture is cooled with an ice-salt bath to −5°C, and maintained under an argon atmosphere.

A solution of 92 g (0.58 mol) of bromine (Note 3) in 60 mL of dichloromethane is added dropwise over 1 hr while the reaction mixture is vigorous stirred. Instantaneous decoloration of bromine and formation of a precipitate of dibromotriphenylphosphorane($Ph_3PBr_2$) is observed. After the addition, the reaction mixture is stirred for an additional 30 min while being cooled in the ice bath.

A solution of 57.2 g (0.570 mol) of acetylacetone (Note 4) in 60 mL of dichloromethane is then added dropwise over 1 hr. An exothermic reaction occurs. At the end of the addition, the solution is allowed to warm very slowly to room temperature (Note 5) and stirred at that temperature for 17 hr (Note 6).

The resulting clear yellow-orange solution is transferred to a 1-L, one-necked, round-bottomed flask and concentrated at ca. 20 mm with a rotary evaporator. Anhydrous diethyl ether (230 mL) is added to precipitate triphenylphosphine oxide hydrobromide ; the solid is separated by suction filtration and washed with two 100-mL portions of anhydrous ether. The filtrate is concentrated under reduced pressure and the resulting orange liquid is taken up in 350 mL of anhydrous diethyl ether . This solution is filtered to separate any remaining salt and transferred to a 500-mL, three-necked flask equipped with a magnetic stir bar, reflux condenser fitted with an argon inlet adapter, a rubber septum, and a pressure-equalizing dropping funnel.

A solution of 56.7 g (0.56 mol) of triethylamine (Note 7) in 60 mL of anhydrous diethyl ether is added dropwise to the reaction mixture over 1 hr, and the resulting mixture is stirred at room temperature for 12 hr.

The triethylamine hydrobromide precipitate is filtered and washed with two 60-mL portions of diethyl ether . The filtrate is washed with three 30-mL portions of 5% hydrochloric acid to remove unreacted triethylamine, and then washed with 25 mL of cold water (Note 8), dried over anhydrous magnesium sulfate , and filtered.

Diethyl ether is removed by distillation (Note 9) and the residual product is distilled under reduced pressure (Note 10) to afford 30.5 g (65%) of acetylallene (Note 11) as a colorless liquid.

## 2. Notes

1. Triphenylphosphine was purchased by the submitters from Fluka Chemical Corp. or Aldrich Chemical Company, Inc. , and used without further purification.
2. Dichloromethane was purchased from SDS Co. or Mallinckrodt Inc. and distilled from calcium hydride . The distilled solvent was passed through a plug of silica gel immediately before use.

3. Bromine obtained from Janssen Chimica or Aldrich Chemical Company, Inc. , was used as received.
4. Acetylacetone (obtained from Labosi Co. or Aldrich Chemical Company, Inc.) was distilled prior to use.
5. If the internal temperature is allowed to rise too quickly, rapid decomposition of 2-bromo-4-oxo-pent-2-ene occurs.
6. The reaction was monitored by $^{31}P$ NMR spectroscopic analysis. The two organophosphorus compounds in the reaction mixture show the following spectral properties (40.54 MHz, $CDCl_3$, external reference: $H_3PO_4$, 85% aqueous solution, δ ppm): $PPh_3Br_2$, δ = 50.2 and ($PPh_3OH^+$, $Br^-$), δ = 47.4 . Complete formation of ($PPh_3OH^+$, $Br^-$) was observed after about 12 hr.
7. Triethylamine from Fluka Chemical Corp. or Aldrich Chemical Company, Inc. , was distilled from potassium hydroxide prior to use.
8. It is essential to use a minimum of water for these washes because of the high solubility of acetylallene .
9. To minimize polymerization of acetylallene , ca. 100 mg of hydroquinone is added to the ether solution prior to concentration.
10. *Caution: The highly volatile product must be trapped in a flask cooled in liquid nitrogen.* Acetylallene distills at 48-50°C (60 mm) and is obtained with a purity of 96.5% as determined by gas chromatographic analysis using a 25-m SE30 capillary column at 80°C (Vector gas : He, 1 bar; retention time: 4.09 min).
11. The checkers obtained acetylallene in 59-65% yield, while the submitters report isolating the product in 75% yield. *Caution: Acetylallene is an allergen and is highly lachrymatory*. The product exhibits the following spectral properties: IR (film) $cm^{-1}$: 3025, 1940, 1660, 850 ; $^1H$ NMR (500 MHz, $CDCl_3$) δ: 2.26 (s, 3 H), 5.25 (d, 2 H, J = 6.4), 5.77 (t, 1 H, J = 6.4) ; $^{13}C$ NMR (125 MHz, $CDCl_3$) δ: 27.0, 79.9, 97.7, 198.6, 217.7 .

## Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

## 3. Discussion

Acetylallene (**1**) behaves as an excellent dienophile in Diels-Alder reactions and induces peculiar orienting effects, allowing reactions with high regio- and stereo-selectivities.[2] Retro Diels-Alder reactions of modified adducts of furan and **1** afford a general method of synthesis of α-functionalized allenes.[3]

Hydrochlorination of acetylallene in the presence of N,N'-dimethylhydrazine dihydrochloride leads stereoselectively to the corresponding β-chloroenone that is a valuable intermediate in organic synthesis.[4] Recently, it was disclosed that the hydrohalogenation reaction of 3,4-pentadien-2-one with metal halides in acetic acid at room temperature selectively afforded 4-halo-4-penten-2-ones in high yields17.[5]

Transition metal-catalyzed dimerization of acetylallene leads to the expected dimeric product in mixture with 2-methylfuran .[6] The latter compound may be also obtained by thermal intramolecular cyclization of **1**.[7]

1,3-Dipolar cycloaddition of diazoalkanes to acetylallene leads to five-membered heterocycles containing two nitrogen atoms,[8] e.g., pyrazole and pyrazoline derivatives. Addition of trivalent phosphorus reagents to **1** allows entry to the exomethylene 1,2-oxaphospholene ring system.[9] Triphenylphosphonio groups may also be used as umpolung agents to change the regioselectivity of the addition of nucleophilic compounds on acetylallene. In this case, α,β-unsaturated ketones are obtained with heteroatomic substituents in the γ-position.[10]

Acetylallene is a valuable starting material in α,β-unsaturated γ-lactones synthesis: the tandem nucleophilic addition-aldol reaction of **1**, iodide ion and aldehydes gives 3-iodohomoallylic alcohols in good yields, which can be further transformed to α,β-unsaturated γ-lactones by palladium-catalyzed cyclocarboxylation.[11]

Various complex and low yield procedures for the preparation of acetylallene have been described: oxidation of homopropargylic alcohol with chromium trioxide in sulfuric acid ,[12] mild acid hydrolysis of conjugated ethoxyenyne,[13] reaction of propargyltrimethylsilane with acyl halide,[14] flash vacuum thermolysis of β-keto trimethylsilyl enol ether [15] and cycloelimination of β-silylethyl sulfoxide.[16]

The method reported here is a modification of a previously published procedure by Buono.[17] The yields have been increased by control of the reaction temperature during the first step, i.e., zero to room temperature instead of heating, and by direct dehydrobromination of the non-purified bromo intermediate. By monitoring the reaction by $^{31}P$ NMR spectroscopy, the submitters have determined precisely the end time of the first step, and that the triphenylphosphine oxide generated in the medium is immediately protonated by the hydrogen bromide. One of the major advantages of this procedure lies in the commercial availability of the starting materials. Moreover, only two steps, without purification of the intermediates, are required. Thus, the submitters have developed a new, efficient and cheap procedure for the preparation of acetylallene in large scale (0.5 mol up to 1 mol).

## References and Notes


1. Ecole Nationale Supérieure de Synthèse, de Procédés et d'Ingénierie Chimiques d'Aix-Marseille (ENSSPICAM), U.M.R. 6516 Synthèse, Catalyse, Chiralité, Faculté des Sciences et Techniques de St. Jérôme, Université Aix-Marseille, Avenue Escadrille Normandie-Niemen, 13397 Marseille Cedex 20, France.
2. Gras, J. L. *J. Chem. Res., Synop.* **1982**, 300.
3. Bertrand, M.; Gras, J.-L.; Galledou, B. S. *Tetrahedron Lett.* **1978**, 2873; Gras, J. L.; Galledou, B. S.; Bertrand, M. *Bull. Soc. Chim. Fr.* **1988**, *4*, 757.
4. Gras, J. L.; Galledou, B. S. *Bull. Soc. Chim. Fr.* **1983**, (3-4, Pt. 2), 89.
5. Ma, S.; Li, L.; Xie, H. *J. Org. Chem.* **1999**, *64*, 5325.
6. Hashmi, A. S. K. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1581.
7. Hunstman, W. D.; Yin, T.-K. *J. Org. Chem.* **1983**, *48*, 1813.
8. Battioni, P.; Vo Quang, L.; Vo Quang, Y. *Bull. Soc. Chim. Fr.* **1978**, (7-8, Pt. 2), 401.
9. Buono, G.; Llinas, J. R. *J. Am. Chem. Soc.* **1981**, *103*, 4532.
10. Cristau, H. J.; Viala, J.; Christol, H. *Bull. Soc. Chim. Fr.* **1985**, 980.
11. Zhang, C.; Lu, X. *Tetrahedron Lett.* **1997**, *38*, 4831.
12. Bertrand, M. *C.R. Acad. Sci., Ser. C* **1957**, *244*, 1790; Bertrand, M.; Le Gras, J. *Bull. Soc. Chim. Fr.* **1962**, 2136; Bardone-Gaudemar, F. *Ann. Chim. (Paris)* **1958**, *3*, 52.
13. Bertrand, M.; Rouvier, C. *Bull. Soc. Chim. Fr.* **1968**, 2533.
14. Pillot, J.-P.; Bennetau, B.; Dunoguès, J.; Calas, R. *Tetrahedron Lett.* **1981**, *22*, 3401.
15. Jullien, J.; Pechine, J. M.; Perez, F.; Piade, J. J. *Tetrahedron* **1982**, *38*, 1413.
16. Fleming, I.; Goldhill, J.; Perry, D. A. *J. Chem. Soc., Perkin Trans. I* **1982**, *7*, 1563.
17. Buono, G. *Synthesis* **1981**, 872.


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

Penta-1,2-dien-4-one:
Acetylallene:
3,4-Pentadien-2-one (8,9); (2200-53-5)

Triphenylphosphine:
Phosphine, triphenyl- (8,9); (603-35-0)

Bromine (8,9); (7726-95-6)

Dibromotriphenylphosphorane:
Phosphorane, dibromotriphenyl- (8,9); (1034-39-5)

Acetylacetone: Aldrich:
2,4-Pentanedione (8,9); (123-54-6)

Triphenylphosphine oxide hydrobromide:
Phosphine oxide, triphenyl-, compd. with
hydrobromic acid (1:1) (9); (13273-31-9)

Triethylamine (8);
Ethanamine, N,N-diethyl- (9); (121-44-8)

Triethylamine hydrobromide (8);
Ethanamine, N,N-diethyl-, hydrobromide (9); (636-70-4)