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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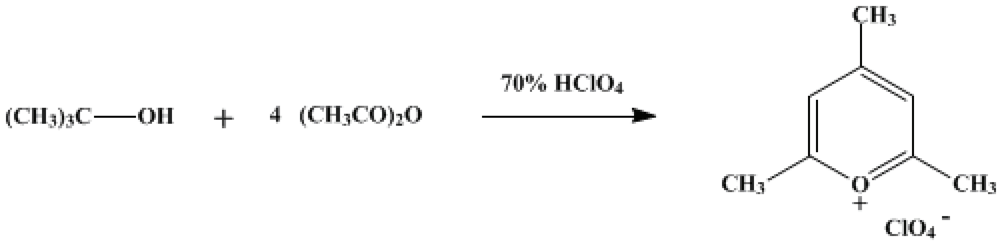
Organic Syntheses, Coll. Vol. 5, p.1106 (1973); Vol. 44, p.98 (1964).

2,4,6-TRIMETHYLPYRYLIUM PERCHLORATE

[Method I]



Submitted by A. T. Balaban[1] and C. D. Nenitzescu[2].
Checked by Karl Bangert and Virgil Boekelheide.

1. Procedure

Caution! 2,4,6-Trimethylpyrylium perchlorate is explosive. Operations should be conducted behind a shield, and directions should be followed closely (see (Note 1) of Method I and Section 4 before carrying out these preparations).

In a 2-l. four-necked flask (or a three-necked flask with a Y-tube connection) outfitted with a stirrer, a short reflux condenser, a dropping funnel, and a thermometer reaching to the bottom of the flask, 148 g. (2.0 moles) of anhydrous *t*-butyl alcohol and 1020 g. (945 ml., 10.0 moles) of acetic anhydride are mixed with stirring and cooled to −10° by means of an ice-salt cooling bath. Then 250 g. (150 ml., 1.75 moles) of 70% perchloric acid is added rapidly from the dropping funnel to the stirred mixture over a period of 5–7 minutes (Note 2). With the first few drops a vigorous reaction begins which is manifested by evolution of fumes, coloration of the reaction mixture to orange and then reddish brown, and a rapid rise in temperature. When the temperature of the reaction mixture reaches 40–50°, crystals of 2,4,6-trimethylpyrylium perchlorate should begin to separate (Note 3); then the temperature is allowed to rise to 100°. The rate of perchloric acid introduction and the use of the cooling bath are then so controlled that the temperature of the reaction mixture is maintained between 100° and 105°. Toward the end of the addition the perchloric acid may be added quite rapidly and the desired temperature may still be maintained. After all the perchloric acid has been added, the cooling bath is removed and stirring of the mixture is continued. The temperature remains at about 90° for 10 or 15 minutes and then falls to about 75° after 30 minutes. The dark-brown stirred mixture is cooled once again until the temperature has fallen to 15°. The crystalline 2,4,6-trimethylpyrylium perchlorate, which has separated, is collected on a Büchner funnel and is washed on the funnel with a 1:1 mixture of acetic acid and ether and then washed twice with ether (Note 4). Suction is stopped before the crystals are dry. The product can be air-dried to give 195–210 g. (50–54%) of yellow crystals, m.p. 244° dec. (Note 1), (Note 5), and (Note 6). For storing or for use in the preparation of 4,6,8-trimethylazulene, however, it is best to place the product in a cork-stoppered flask and moisten it with dry tetrahydrofuran.

2. Notes

1. The impact sensitivity of 2,4,6-trimethylpyrylium perchlorate was examined by Dr. T. E. Stevens at the Redstone Arsenal Division of Rohm and Haas Co., and the compound was found to be slightly more sensitive to detonation by impact than the commercial explosive RDX. This point should be kept constantly in mind. When the crystals are handled as a slurry or are wet with solvent, the hazard is considerably reduced. On the other hand, the dry perchlorate should be handled with great care and should never be crushed, rubbed, or pushed through a narrow opening.
2. The specified order of mixing the three reagents is critical. If the reagent added to the solution of the other two is *t*-butyl alcohol or acetic anhydride, large amounts of triisobutylenes are formed, separating

as a colorless upper layer.

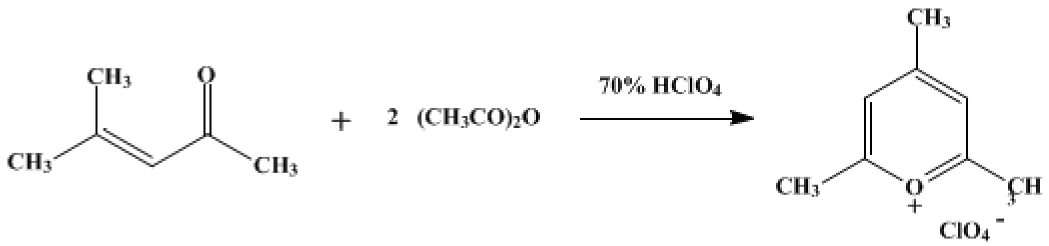
3. The rate of perchloric acid introduction should be slow at first so that in the range of 40–50° crystals of the 2,4,6-trimethylpyrylium perchlorate will begin to appear. Then the rate of addition should be increased to maintain the temperature in the optimum range of 100–105°. If the temperature rises too rapidly, no crystals will appear and the yield will be somewhat lower. Then seeding is helpful.

4. If crystallization is not complete, dilution of the filtrate by the ether washings will cause separation of additional crystals. These are collected separately because they are finer and less pure. Concentration of filtrates is to be avoided because severe explosions[3] have been reported when solutions of perchloric acid in acetic acid were concentrated.

5. The product is of satisfactory purity for use in the 4,6,8-trimethylazulene preparation without further purification. Recrystallization of a small sample of the 2,4,6-trimethylpyrylium perchlorate from a seven-fold amount of hot water, containing a few drops of perchloric acid and some carbon black, gives colorless crystals, m.p. 245–247° dec. However, the recrystallization of larger amounts in this way presents some hazard and is not recommended. Concentration of filtrates should be avoided (see (Note 4)).

6. The preparation of 2,4,6-trimethylpyrylium perchlorate may be carried out on a much smaller scale, such as one-tenth, with only a small lowering of the yield.

[Method II]



Submitted by K. Hafner and H. Kaiser[4].
Checked by Virgil Boekelheide and H. Fleischer.

1. Procedure

Caution! 2,4,6-Trimethylpyrylium perchlorate is explosive. Operations should be conducted behind a shield, and directions should be followed closely (see (Note 1) of Method I and Section 4 before carrying out these preparations.)

In a 2-l. four-necked flask (or a three-necked flask with a Y-tube connector) equipped with a stirrer, a reflux condenser, a dropping funnel, and a thermometer extending nearly to the bottom of the flask is placed 550 ml. (595 g., 5.83 moles) of acetic anhydride which is cooled to 0° with an ice-salt bath. Then 180 ml. (300 g., 2.09 moles) of a 70% solution of perchloric acid is added with stirring at a rate such that the temperature does not rise above 8° (Note 1). This step takes about 3 hours. The mixture is continually cooled and stirred, and 240 ml. (204 g., 2.09 moles) of mesityl oxide is then added slowly. The slow addition of 370 ml. (400 g., 3.92 moles) of acetic anhydride follows. The ice bath is then replaced by a water bath; the temperature of the reaction mixture will usually rise to 50–70° because of the heat liberated by the exothermic reaction, and the reaction mixture will turn dark. The reaction mixture is heated on a steam bath for 15 minutes to complete the reaction, and the mixture is then allowed to cool and stand at room temperature for 2 hours. The crystals, which have separated from the brown solution, are collected on a Büchner funnel and are washed on the funnel twice with 100-ml. portions of acetic acid, twice with 100-ml. portions of absolute ethanol, and twice with 100-ml. portions of absolute ether. This gives 250–260 g. (54–56%) of pale-yellow to light-brown crystals, m.p. 240° dec. (Note 2). For storage the crystals should be transferred, without drying, to an ordinary flask, moistened with dry tetrahydrofuran, and then kept in this state by stoppering the flask with an ordinary cork (Note 3).

2. Notes

1. Since the reaction is quite exothermic, the mixture must be well stirred to avoid developing any local hot spots which could lead to explosions. Although no difficulties were encountered in either the submitters' or checkers' laboratories, it is well to keep in mind that 2,4,6-trimethylpyrylium perchlorate is potentially hazardous; hence due precaution should be exercised at all times.
2. Although a small sample of 2,4,6-trimethylpyrylium perchlorate may with care be recrystallized from acetic acid to give white crystals, m.p. 245–247° dec., it is recommended that this not be done with larger quantities. The 2,4,6-trimethylpyrylium perchlorate is of satisfactory purity for use in the 4,6,8-trimethylazulene preparation without further purification.
3. The hazard of handling 2,4,6-trimethylpyrylium perchlorate is greatly reduced if the crystals are kept moist with a solvent such as tetrahydrofuran. The flask used for storage should be stoppered with a cork rather than a ground-glass stopper to avoid the possibility of initiating an explosion by the grinding action of the stopper.

3. Discussion

2,4,6-Trimethylpyrylium perchlorate has been prepared from 2,6-dimethylpyrone and methylmagnesium halides;[5] from mesityl oxide and sulfoacetic acid;[6] from mesityl oxide (or less satisfactorily from acetone) and a mixture of acetic anhydride and perchloric acid;[7] from mesityl oxide, acetyl chloride, and aluminum chloride;[8] and from *t*-butyl chloride, acetyl chloride, and aluminum chloride.[8] The procedure given under Method I is adapted from that reported by Balaban and Nenitzescu[9] and is similar to that of Praill and Whitear.[10] The procedure given under II is adapted from that reported by Hafner and Kaiser.[11] The methods of preparation have been reviewed.[12]

4. Merits of the Preparation

2,4,6-Trimethylpyrylium perchlorate is a very versatile and useful starting material. Thus its reaction with cyclopentadienylsodium has made 4,6,8-trimethylazulene[13] easily available for general studies of the properties of azulenes[14] and for the synthesis of related compounds.[15] In addition, pyrylium salts are readily converted to a variety of pyridine derivatives,[9,16] 4H- and 2H-pyrans,[17] 2-acylfurans,[18,19] isoxazolines,[20] pyrazolines,[20] 1,2-diazepines,[20,21] 5-cyano-2,4-dien-1-ones,[22] and various benzene and naphthalene derivatives,[23] including derivatives of nitrobenzene[24] and phenol.[9,25,26] It is clear that its value as a starting material is such that it is receiving wide use.

In including this preparation in *Organic Syntheses*, it was felt that standard procedures which have been tested in more than one laboratory without difficulty and which attempt to point out as clearly as possible the potential hazards involved would serve a useful function for those who, despite the hazards, find this a necessary and important starting material.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 1088
- Org. Syn. Coll. Vol. 5, 1114
- Org. Syn. Coll. Vol. 5, 1135

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

carbon black

ethanol (64-17-5)

acetic acid (64-19-7)

ether (60-29-7)

acetic anhydride (108-24-7)

acetyl chloride (75-36-5)

phenol (108-95-2)

acetone (67-64-1)

aluminum chloride (3495-54-3)

Nitrobenzene (98-95-3)

t-butyl chloride (507-20-0)

Mesityl oxide (141-79-7)

Tetrahydrofuran (109-99-9)

cyclopentadienylsodium

t-butyl alcohol (75-65-0)

perchloric acid (7601-90-3)

4,6,8-Trimethylazulene (941-81-1)

2,4,6-Trimethylpyrylium perchlorate (940-93-2)

2,6-dimethylpyrone

sulfoacetic acid (123-43-3)