



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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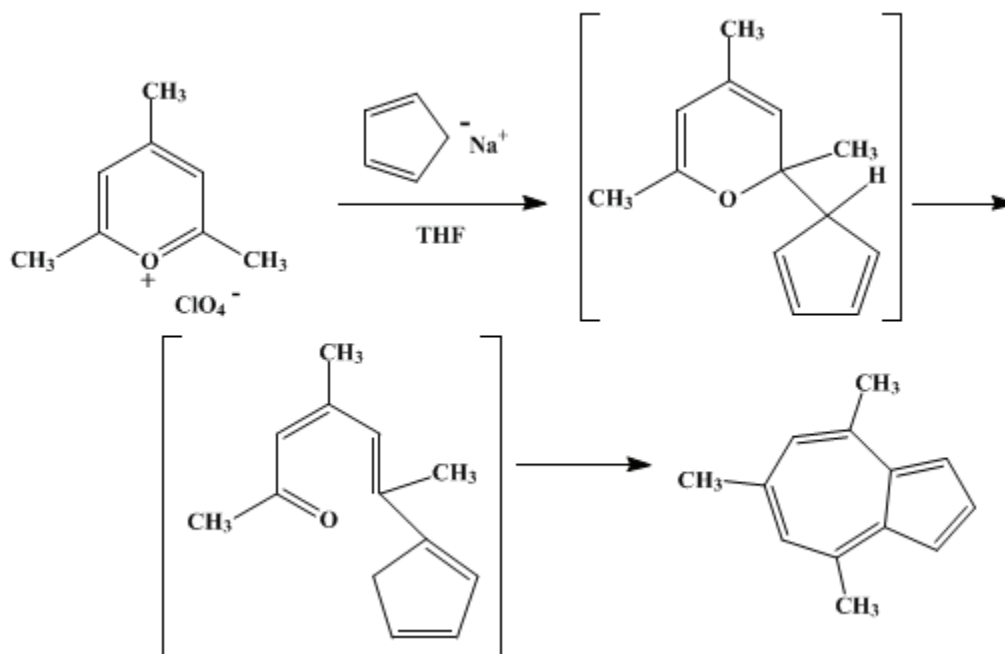
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 5, p.1088 (1973); Vol. 44, p.94 (1964).

4,6,8-TRIMETHYLAZULENE

[Azulene, 4,6,8-trimethyl-]



Submitted by K. Hafner and H. Kaiser¹.

Checked by Karl Bangert and Virgil Boekelheide.

1. Procedure

A. *Cyclopentadienylsodium*. A 1-l. four-necked flask (or a three-necked flask with a Y-tube connection) is outfitted with a Trubore[®] stirrer, a pressure-equalizing dropping funnel, a thermometer reaching to the bottom of the flask, and a reflux condenser in whose outlet is placed a T-tube, one side of which leads to a bubble counter and the other is connected to a source of pure nitrogen. The system is flushed with nitrogen, and a suspension of 23 g. (1.0 mole) of sodium in 350 ml. of dry tetrahydrofuran (Note 1) and (Note 2) is prepared in the flask. There is then added dropwise with stirring 73.0 g. (1.1 moles) of freshly distilled cyclopentadiene (Note 3). As the exothermic reaction begins, evolution of hydrogen through the bubble counter can be observed immediately. The temperature of the reaction mixture should be kept below 35–40° by intermittent cooling of the flask with an ice bath. At the end of the reaction the color of the solution should be a pale rose; exposure to air causes a rapid change in color to dark brown (Note 4).

B. *4,6,8-Trimethylazulene*. **Caution!** *2,4,6-Trimethylpyrylium perchlorate is explosive. Operations with it should be conducted behind a shield.* The arrangements of the reaction flask used in the preparation of cyclopentadienylsodium are now altered for the next step. While increasing the nitrogen flow rate strongly, the dropping funnel is removed and replaced by a wide-mouthed powder funnel. The strong flow of pure nitrogen coming out of the flask and around the powder funnel prevents the atmosphere from diffusing into the flask to any appreciable extent. Then, with strong stirring of the reaction mixture, 142 g. (0.64 mole) of 2,4,6-trimethylpyrylium perchlorate (**Caution! Moistened with dry tetrahydrofuran, (Note 5)**) is added in small portions through the powder funnel at such a rate that the immediate exothermic reaction which ensues maintains the temperature of the reaction mixture between 42° and, at most, 48°. The color of the reaction mixture turns purple immediately on addition of the 2,4,6-trimethylpyrylium perchlorate. Usually the addition requires about 1 hour; then the reaction mixture is stirred for an additional 20 minutes. The powder funnel is replaced with a stopper, the

condenser is turned downward for distillation, and about 130 ml. of [tetrahydrofuran](#) is removed by distillation while stirring is continued. For the distillation the flask is heated on a steam bath, and the temperature of the reaction mixture at the end of the distillation is about 68–70°. The color of the distillate is a weak violet owing to the co-distillation of a small amount of [4,6,8-trimethylazulene](#). After the reaction mixture has cooled, it is transferred to a 3-l. separatory funnel and diluted, first with 75 ml. of [methanol](#) and then with 1 l. of water. This causes the separation of a dark violet oil which is taken up in 400 ml. of petroleum ether (b.p. 60–70°) and separated from the aqueous phase. The aqueous layer is extracted again with 200 ml. of fresh petroleum ether, and the combined petroleum ether extracts are washed five times with 175-ml. portions of water. Since a small quantity of a greasy by-product separates at the interface during the washing with water, the petroleum ether extract, after the final washing, is purified by passing it through a Büchner funnel lined with asbestos fibers as a filtering aid. After the filtrate has been dried over [calcium chloride](#), the solution is concentrated under reduced pressure, and the residue is carefully freed of solvent by heating on a steam bath under reduced pressure for 4 hours.

The crude product is then transferred to an apparatus suitable for distillation of solids ([Note 6](#)), and this is joined to a high-vacuum system capable of a vacuum in the range of 10^{-5} mm. Distillation begins when the bath temperature reaches about 190°; a boiling point of around 120° is usually observed. When the distillate first begins to appear brown rather than violet, the distillation is stopped immediately ([Note 7](#)). The crystalline distillate (ca. 70 g.) is dissolved in 20 ml. of hot [ethanol](#), filtered while hot, and allowed to cool. The solid (about 60 g. of crystals, m.p. 74–76°) is recrystallized from 20 ml. of [ethanol](#) to yield 47–53 g. (43–49%) of [4,6,8-trimethylazulene](#) as dark-violet plates, m.p. 80–81° ([Note 8](#)).

2. Notes

1. The suspension of [sodium](#) is best prepared as follows. In a three-necked flask fitted with a ground-glass stopper, a reflux condenser, and a Vibromischer (available from A. G. für Chemie-Apparatebau, Zurich, Switzerland) are placed 150 ml. of [toluene](#) and 23 g. of [sodium](#). When the [toluene](#) is boiling under reflux, the melted [sodium](#) is dispersed by the Vibromischer, and the flask is quickly cooled. Under [nitrogen](#) atmosphere the [toluene](#) is removed by decantation and is replaced by 350 ml. of dry [tetrahydrofuran](#).
2. The dry [tetrahydrofuran](#) can be prepared by allowing [tetrahydrofuran](#) to stand over [sodium](#), decanting, and distilling from [lithium aluminum hydride](#). (*Caution! See p. 976.*)
3. For the preparation of [cyclopentadiene](#) from its dimer, see M. Korach, D. R. Nielsen, and W. H. Rideout, this volume, p. 414.
4. If desired, the [cyclopentadienylsodium](#) concentration in solution can be determined by withdrawing 1 ml. of solution, diluting this with 100 ml. of water, and titrating the resulting aqueous [sodium hydroxide](#) solution with 0.1N [hydrochloric acid](#) using methyl red as an indicator.
5. The [2,4,6-trimethylpyrylium perchlorate](#), obtained and stored as described by Balaban and Nenitzescu² or by Hafner and Kaiser,³ is used directly.
6. A round-bottomed, standard-taper flask with a Claisen head carrying an ebullition capillary and a thermometer and attached to a two-necked flask with one neck for vacuum takeoff is satisfactory. It is important that the setup allow for heating by either flame or infrared lamp to melt the solid distillate and prevent its clogging the vapor passage.
7. It is helpful to empty the brown tarry residue from the distillation flask while it is still hot. The flask can then be cleaned by using a [sulfuric acid-chromic acid](#) solution.
8. For purification of small amounts of [4,6,8-trimethylazulene](#) it is advantageous to dissolve it in a small amount of [methanol](#) and treat the solution with activated [carbon](#).

3. Discussion

This procedure is adapted from that described earlier by Hafner and Kaiser,⁴ and apparently it is the only method that has been used for synthesizing [4,6,8-trimethylazulene](#).

4. Merits of the Preparation

This procedure illustrates a simple and general method for preparing azulenes. It is far more convenient and proceeds in much better yield than previous syntheses of azulenes involving dehydrogenation.⁵ Also, it is superior to the alternative methods utilizing the monoanil of [glutacondialdehyde](#)⁶ or pyridinium salts.^{7,8} In fact, this procedure has made the azulenes a readily available class of compounds for study and use as starting materials. Illustrative of the latter are the recent syntheses of [pentalene](#),⁹ [heptalene](#),⁹ and *peri*-benzazulene derivatives.¹⁰

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 5, 431](#)
- [Org. Syn. Coll. Vol. 5, 1106](#)
- [Org. Syn. Coll. Vol. 5, 1135](#)
- [Org. Syn. Coll. Vol. 7, 339](#)

References and Notes

1. Institut für Organische Chemie, Munich, Germany.
2. [A. T. Balaban and C. D. Nenitzescu, this volume, p. 1106.](#)
3. [K. Hafner and H. Kaiser, this volume, p. 1108.](#)
4. [K. Hafner and H. Kaiser, *Ann.*, **618**, 140 \(1958\).](#)
5. [V. Prelog and K. Schenker, *Helv. Chim. Acta*, **36**, 1181 \(1953\).](#)
6. [K. Ziegler and K. Hafner, *Angew. Chem.*, **67**, 301 \(1955\).](#)
7. [K. Hafner, *Angew. Chem.*, **67**, 301 \(1955\).](#)
8. [K. Ziegler and K. Hafner, U.S. Patent 2,805,266 \(Sept. 3, 1957\) \[*C. A.*, **52**, 6409 \(1958\)\].](#)
9. [K. Hafner and J. Schneider, *Ann.*, **624**, 37 \(1959\).](#)
10. [K. Hafner and H. Schaum, *Angew. Chem.*, **75**, 90 \(1963\).](#)

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

petroleum ether

Methyl Red

[ethanol \(64-17-5\)](#)

[calcium chloride \(10043-52-4\)](#)

[hydrochloric acid \(7647-01-0\)](#)

[methanol \(67-56-1\)](#)

[hydrogen \(1333-74-0\)](#)

[sodium hydroxide \(1310-73-2\)](#)

[nitrogen \(7727-37-9\)](#)

[carbon \(7782-42-5\)](#)

toluene (108-88-3)

sodium (13966-32-0)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

CYCLOPENTADIENE (542-92-7)

cyclopentadienylsodium

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

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

sulfuric acid-chromic acid

glutacondialdehyde

pentalene

heptalene