Organic Syntheses

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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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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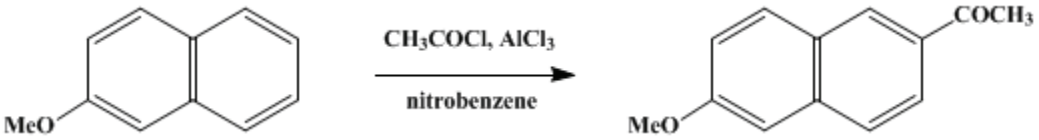
2-ACETYL-6-METHOXYNAPHTHALENE

[Ethanone, 1-(6-methoxy-2-naphthalenyl)-]



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1. Procedure

A 1-l., three-necked, round-bottomed flask is fitted with a mechanical stirrer and a thermometer; the third neck of the flask is fitted with a 50-ml., pressure-equalizing addition funnel, carrying a drying tube attached to a gas trap. The flask is charged with 200 ml. of dry nitrobenzene (Note 1), followed by 43 g. (0.32 mole) of anhydrous aluminum chloride. After the aluminum chloride has dissolved, 39.5 g. (0.250 mole) of finely ground 2-methoxynaphthalene (nerolin, (Note 2)) is added. An ice bath is used to cool the stirred solution to about 5° before 25 g. (23 ml., 0.32 mole) of redistilled acetyl chloride (Note 3) is added dropwise over a 15–20 minute period, with stirring and at a rate which holds the temperature between 10.5 and 13° (Note 4). After addition of the acetyl chloride is complete, the flask is kept immersed in the ice water while stirring is continued for 2 hours. The mixture is then allowed to stand at room temperature for at least 12 hours.

The reaction mixture is cooled in an ice bath, poured with stirring into a 600-ml. beaker containing 200 g. of crushed ice, and treated with 100 ml. of concentrated hydrochloric acid. The resulting two-phase mixture and 50 ml. of chloroform are transferred to a 1-l. separatory funnel (Note 5); the chloroform-nitrobenzene layer is separated and washed with three 100-ml. portions of water. The organic layer is transferred to a 2-l., round-bottomed flask, and steam-distilled. A fairly rapid flow of steam is used, and the distillation flask is heated in an oil bath at about 120°. After about 3 hours (3–4 l. of water) the distillation is stopped, and the residue in the flask is allowed to cool. Residual water in the flask is decanted from the solid organic material and extracted with chloroform. The solid residue in the flask is dissolved in 100 ml. of chloroform and separated from any water left in the flask, and the chloroform layers are combined and dried over anhydrous magnesium sulfate. The chloroform is removed on a rotary evaporator, and the solid residue, weighing 50–65 g. (still slightly wet with chloroform), is distilled under vacuum (Note 6). The receiving flask should be immersed in ice water, and the fraction boiling about 150–165° (0.02 mm.) is collected (Note 7).

The yellow distillate (*ca.* 40 g., m.p. 85–95°) is recrystallized from 75 ml. of methanol, cooled in an ice bath (Note 8) and filtered, yielding 22.5–24 g. (45–48%) of white, crystalline 2-acetyl-6-methoxynaphthalene (Note 9), m.p. 106.5–108° (lit. 104–105°).[3]

2. Notes

1. The nitrobenzene may be dried by distilling the first 10% and using the residue directly, or standing over anhydrous calcium chloride overnight and filtering.
2. 2-Methoxynaphthalene (Matheson, Coleman and Bell), m.p. 71.5–73°, was used without further purification.
3. Acetic anhydride may be used instead of acetyl chloride. However, it is then necessary to use two molecular equivalents of aluminum chloride per mole of anhydride and increase the amount of nitrobenzene by about 30%. About the same yield of ketone is obtained.
4. Temperature control is very important (see discussion).
5. The addition of chloroform is not always indispensable, but very useful to prevent emulsification and facilitate separation of the nitrobenzene layer. The reaction vessel and beaker are rinsed with this

chloroform before it is added to the nitrobenzene layer. If an emulsion does form and phase separation becomes inconveniently slow, as much nitrobenzene as possible is withdrawn, and the emulsion and water layers are filtered by suction through a Celite cake wet with chloroform. The phases should then separate easily.
6. The material may be distilled from a two-bulb distillation flask as described in *Org. Synth.*, **Coll. Vol. 3**, 133 (1955), or from a small Claisen flask.
7. Care must be taken to prevent solidification and possible blocking in the condenser. A small burner may be used to keep the adapter just hot enough to melt the distillate.
8. If the methanol is cooled below 0°, the 1-acetyl isomer that is formed during the reaction will also crystallize with the product.
9. ^{1}H NMR ($CDCl_3$): δ 2.65 (s, 3H, COC*H*$_3$), 3.92 (s, 3H, OC*H*$_3$), 7.20 (m, 4H, Ar*H*), 7.80 (m, 1H, Ar*H*), 8.30 (m, 1H, Ar*H*).

3. Discussion

The procedure described herein is a modification of that of Haworth and Sheldrick,[3] the efficiency of which has been confirmed by many authors.[4,5,6,7,8,9,10] 2-Acetyl-6-methoxynaphthalene has also been prepared by the action of methylzinc iodide on 6-methoxy-2-naphthoyl chloride.[11]

In this reaction, nitrobenzene has an important function because it causes acylation to occur predominantly at the 6-position, whereas 1-acetyl-2-methoxynaphthalene is the principal product when carbon disulfide is used. The main feature of this procedure is the particular attention given to temperature control in order to obtain reliable results. It has been observed that the ratio of 6-acetylated to 1-acetylated nerolin is dependent on the temperature, the lower temperatures favoring 1-acetylation. Below 0° the yield of 6-acetylated product is only 3–10%; at higher temperatures the 6-acetylated product predominates, but an increased amount of tarry material is formed.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 175

References and Notes

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

nerolin

chloroform-nitrobenzene

calcium chloride (10043-52-4)

hydrochloric acid (7647-01-0)

methanol (67-56-1)

acetic anhydride (108-24-7)

acetyl chloride (75-36-5)

chloroform (67-66-3)

2-methoxynaphthalene (93-04-9)

aluminum chloride (3495-54-3)

Nitrobenzene (98-95-3)

carbon disulfide (75-15-0)

magnesium sulfate (7487-88-9)

methylzinc iodide

2-Acetyl-6-methoxynaphthalene,
Ethanone, 1-(6-methoxy-2-naphthalenyl)- (3900-45-6)

6-methoxy-2-naphthoyl chloride

1-acetyl-2-methoxynaphthalene