



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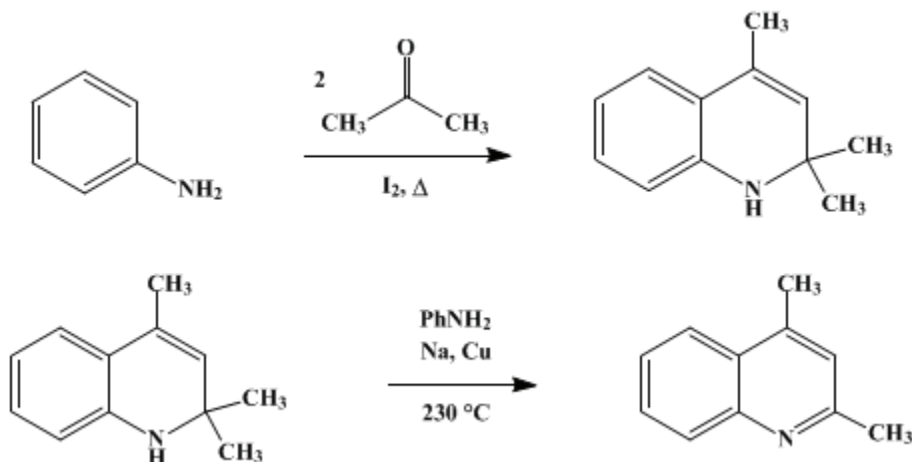
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.329 (1955); Vol. 28, p.49 (1948).

2,4-DIMETHYLQUINOLINE

[Quinoline, 2,4-dimethyl-]



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1. Procedure

A. *"Acetone-anil"* (Note 1). A mixture of 279 g. (3 moles) of aniline and 9 g. of iodine is placed in a 1-l. three-necked round-bottomed flask. The flask is fitted with a dropping funnel (the delivery tube of which extends below the liquid surface), a mercury-sealed stirrer (Note 2), and an adapter carrying a thermometer which extends into the liquid and a condenser system such that most of the aniline will return and all the water produced (as well as excess acetone) will distil (Note 3). The flask is now heated in an oil bath (Note 4) and (Note 5), and the reaction mixture is maintained at 170–175° while acetone is passed in through the dropping funnel at such a rate that no more than 2 drops of liquid distils per second. During the addition the mixture is vigorously stirred. A total volume of 850 ml. (670 g., 11.6 moles) of acetone is added over a 4-hour period, and about 610 ml. of distillate is collected. At the end of this period the reaction mixture is cooled and distilled in vacuum, three fractions being collected (up to 136°/15 mm., 136–141°/15 mm., and 141–146°/15 mm.). The acetone-water distillate is now distilled through a simple column at atmospheric pressure until essentially all the acetone has come over. There remains a mixture of oil and water which is separated after being cooled. The oil is then used as the first fraction for a fractional distillation in vacuum of the reaction product, each of the previous fractions being added in succession. Three new fractions are collected: 78–82°/13 mm. (a little aniline); 82–133°/13 mm. (a small intermediate fraction); and 133–138°/13 mm. (acetone-anil). An appreciable quantity of tarry residue remains in the distillation flask. The yield based upon aniline actually consumed in the reaction is 61–68% (Note 5).

B. *2,4-Dimethylquinoline*. A small quantity of copper powder (Note 6) is added to 4.6 g. (0.2 gram atom) of sodium metal (small pieces) and 56 g. (0.6 mole) of dry aniline (Note 7) contained in a 1-l. round-bottomed flask. The mixture is warmed carefully over a low flame until the evolution of hydrogen ceases, at which time the mixture is usually black. A few boiling chips and 346 g. (2 moles) of acetone-anil are then added. The resulting mixture is heated at the reflux temperature (220–230°) until the evolution of gas (methane) ceases (Note 8). At the end of the reaction the mixture is cooled and then distilled in vacuum. The fraction boiling at 135–140°/12 mm. weighs 252–283 g. (80–90%) (Note 9).

2. Notes

1. The so-called acetone-anil has been assigned the structure indicated in accordance with the work of Craig.²

2. A convenient stirrer may be made from tantalum wire as described by Hershberg.³
3. A Liebig condenser in reflux position is heated with steam and connected at the top to a water-cooled downward condenser.
4. For a reaction temperature of 170–175° the oil is best maintained at about 200° during the addition of the acetone.
5. The reaction may be carried out at any temperature from 70° to 175°. At lower temperature it is much slower and is best carried out by refluxing the theoretical quantities of acetone and aniline with iodine catalyst for an extended time. Regardless of the time or reaction temperature, if due allowance is made for aniline reclaimed at the end of the reaction the yield falls between the limits indicated. At the higher temperature, equilibrium is attained more rapidly, as would be expected, and relatively little aniline is recovered. (A typical run may yield 40 g. of aniline and 297 g. of "anil," with 11 g. of middle fraction.)
6. The exact amount of copper powder used as a catalyst in the preparation of the sodium salt of aniline is not important. Approximately 0.2 g. has been found to be satisfactory in runs of the size described.
7. Aniline which has been recently distilled is satisfactory. An excess of aniline over the sodium is used to minimize decomposition of the 2,4-dimethylquinoline.²
8. The time required for the decomposition of the acetone-anil varies from 3 to 6 hours. The checkers, however, found that essentially all the methane is eliminated after 2 hours.
9. Fractionation of 245 g. of this product through a 14-plate Lecky-Ewell⁴ column yielded 6 g. of aniline, 3 g. of an intermediate fraction, and 218 g. (89%) of 2,4-dimethylquinoline, b.p. 149–150°/20 mm. (controlled). If the material is to be nitrated, the crude product is quite satisfactory.

3. Discussion

The present procedure for the preparation of acetone-anil is described by Reddelien.⁵ A reaction at lower temperature is reported by Craig,² who also describes the alkaline decomposition of the anil to 2,4-dimethylquinoline and methane and gives a method of purification of the final product. Other methods for the preparation of 2,4-dimethylquinoline involve the Beyer⁶ synthesis from aniline hydrochloride and ethylidene acetone, a modification of this synthesis,⁷ a synthesis using 2-chloro-2-pentenone-4,⁸ and the Combes synthesis from acetylacetone and aniline.⁹

References and Notes

1. Work done under contract with the Office of Scientific Research and Development.
2. Craig, *J. Am. Chem. Soc.*, **60**, 1458 (1938).
3. Hershberg, *Ind. Eng. Chem., Anal. Ed.*, **8**, 313 (1936).
4. Lecky and Ewell, *Ind. Eng. Chem., Anal. Ed.*, **12**, 544 (1940).
5. Reddelien and Thurm, *Ber.*, **65**, 1511 (1932).
6. Beyer, *J. prakt. Chem.*, [2] **33**, 401, (1886).
7. Mikeska, Stewart, and Wise, *Ind. Eng. Chem.*, **11**, 456 (1919).
8. Julia, *Compt. rend.*, **228**, 1807 (1949).
9. Combes, *Bull. soc. chim. France*, **49**, 89 (1888).

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

acetone-anil

aniline (62-53-3)

hydrogen (1333-74-0)

aniline hydrochloride (142-04-1)

copper powder (7440-50-8)

iodine (7553-56-2)

acetone (67-64-1)

methane (7782-42-5)

sodium (13966-32-0)

Acetylacetone (123-54-6)

2,4-DIMETHYLQUINOLINE,
Quinoline, 2,4-dimethyl- (1198-37-4)

ethylidene acetone (625-33-2)

2-chloro-2-pentenone-4