A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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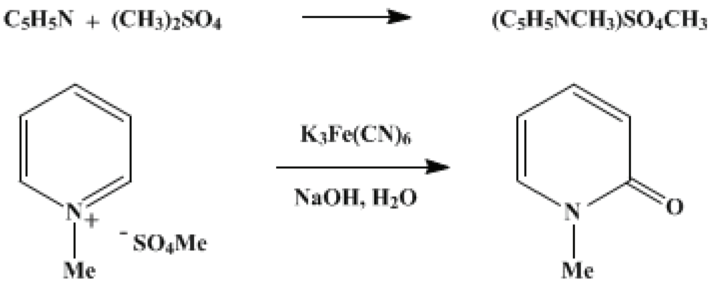
1-METHYL-2-PYRIDONE

[[2(1)-Pyridone, 1-methyl-]]



$C_5H_5N + (CH_3)_2SO_4 \longrightarrow (C_5H_5NCH_3)SO_4CH_3$

Submitted by E. A. Prill and S. M. McElvain.
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1. Procedure

In a 5-l. round-bottomed flask, fitted with a separatory funnel and a reflux condenser, is placed 145 g. (1.83 moles) of dry pyridine (Note 1); 231 g. (1.83 moles) of dimethyl sulfate is added dropwise through the separatory funnel. After the addition of the dimethyl sulfate the flask is heated in a boiling water bath for two hours to complete the reaction.

The flask containing the crude pyridinium salt is removed from the condenser, and the salt is dissolved by adding 400 cc. of water. The flask is fitted with a mechanical stirrer which will stir efficiently any volume of liquid which may be in the flask, and the solution is cooled to 0° in an ice-salt bath. Separate solutions of 1.2 kg. (3.65 moles) of potassium ferricyanide in 2.4 l. of water and of 300 g. (7.5 moles) of sodium hydroxide in 500 cc. of water are prepared and added dropwise from two separatory funnels to the well-stirred solution of the pyridinium salt at such a rate that the temperature of the reaction mixture does not rise above 10°. The rate of addition of these two solutions is regulated so that all the sodium hydroxide solution has been introduced into the reaction mixture when one-half of the potassium ferricyanide solution has been added. This usually requires about one hour. The remaining half of the potassium ferricyanide is then added during another hour. The reaction mixture is allowed to stand five hours, during which time it comes to room temperature.

The 1-methyl-2-pyridone is salted out of the reaction mixture by the addition of 400–500 g. of anhydrous sodium carbonate to the well-stirred solution. When no more sodium carbonate dissolves, stirring is discontinued and the yellow or brown oily layer containing most of the desired pyridone, together with some of the unreacted pyridinium salt, water, and inorganic salts, is separated from the aqueous mixture. The aqueous mixture is filtered (Note 2) to remove the excess sodium carbonate and the precipitated potassium or sodium ferrocyanide. The filtrate is divided into three portions, each of which is extracted twice with 200-cc. portions of technical isoamyl alcohol (Note 3). The alcohol used for the second extraction of the first aqueous portion is satisfactory for the first extraction of a second aqueous portion, et cetera, so that a total volume of 800 cc. is used. The isoamyl alcohol extracts are combined and added to the oily layer which was first separated from the reaction mixture. An aqueous layer usually appears and is separated and extracted with another 100-cc. portion of amyl alcohol.

The combined alcohol extract is distilled under reduced pressure from a modified Claisen flask by heating on a water bath. All the solvent is thus recovered for use in a subsequent preparation.

The residue is transferred to a 250-cc. modified Claisen flask and distilled under diminished pressure from an oil bath. There is almost no low-boiling fraction if the alcohol has been carefully removed. The yield of product boiling at 122–124°/11 mm. is 130–140 g. (65–70 per cent of the theoretical amount) (Note 4) and (Note 5). A small amount of black solid remains in the distillation flask after the pyridone has distilled.

2. Notes

1. A commercial medicinal grade of pyridine was used without further purification.
2. This operation is most satisfactory when a glass-wool plug placed in a glass funnel is used as the filter. The liquid in this funnel should be stirred to prevent the heavy precipitate from settling and clogging the filter.
3. The extraction of the pyridone from the aqueous solution is difficult when benzene or ether is used as a solvent. 1-Methyl-2-pyridone, when dry, is very soluble in ethyl ether, benzene, and most organic solvents. It is, however, practically insoluble in petroleum ether or ligroin. When a mixture of water, benzene, and a little pyridone is shaken together all the pyridone is found in the water layer. When the pyridone is salted out from water by adding a sufficient quantity of potassium carbonate, the oily layer does not dissolve when benzene or ethyl ether is added, but three layers are formed. The pyridone seems to be extracted by ether or benzene only when the aqueous solution is strongly saturated with sodium hydroxide or potassium hydroxide, and then the tendency to form an emulsion is so great that separation of the layers is extremely difficult.

When equal volumes of water, technical isoamyl alcohol, and a little pyridone are shaken together, the pyridone is found to be about equally distributed between the two solvents. Chloroform is also satisfactory for the extraction of pyridone from water.

4. The 1-methyl-2-pyridone when pure is odorless and colorless. It turns dark on standing unless it is kept in a sealed tube.
5. The boiling points at other pressures are given by Fisher and Chur[1] as 250°/740 mm., 130°/14.5 mm., 126°/12.5 mm., and 121°/10 mm.

3. Discussion

1-Methyl-2-pyridone has been prepared by the methylation of 2-pyridone,[2] by the oxidation of 1-methylpyridinium iodide[3] and of 1-methylpyridinium methyl sulfate[4] with a ferricyanide, and by the electrolytic oxidation of 1-methylpyridinium methyl sulfate.[1]

References and Notes

1. Fisher and Neundlinger, Ber. **46**, 2544 (1913); Neundlinger and Chur, J. prakt. Chem. (2) **89**, 466 (1914); Fisher and Chur, ibid. (2) **93**, 363 (1916).
2. v. Pechmann and Baltzer, Ber. **24**, 3144 (1891).
3. Decker, J. prakt. Chem. (2) **47**, 28 (1893).
4. Decker and Kaufmann, ibid. (2) **84**, 435 (1911); Fargher and Furness, J. Chem. Soc. **107**, 690 (1915).

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

2(1)-Pyridone, 1-methyl-

pyridinium salt

potassium or sodium ferrocyanide

petroleum ether or ligroin

alcohol (64-17-5)

potassium carbonate (584-08-7)

Benzene (71-43-2)

ether,
ethyl ether (60-29-7)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

sodium carbonate (497-19-8)

pyridine (110-86-1)

potassium hydroxide (1310-58-3)

dimethyl sulfate (77-78-1)

isoamyl alcohol (123-51-3)

amyl alcohol (71-41-0)

potassium ferricyanide (13746-66-2)

1-Methyl-2-pyridone (694-85-9)

2-pyridone

1-methylpyridinium iodide (930-73-4)

1-methylpyridinium methyl sulfate

ferricyanide