



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

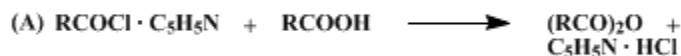
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

ACID ANHYDRIDES



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1. Procedure

A. *Heptoic anhydride (enanthic anhydride)*. In a 250-ml. round-bottomed three-necked flask, equipped with a stirrer, dropping funnel, and thermometer, are placed 15.8 g. (16.1 ml., 0.2 mole) of dry pyridine (Note 1) and 25 ml. of dry benzene (Note 2). Then 14.8 g. (15.5 ml., 0.1 mole) of heptoyl chloride (Note 3) is added rapidly to the stirred solution. The temperature rises only slightly, and a pyridinium complex separates. While stirring is continued, 13.0 g. (14.1 ml., 0.1 mole) of heptoic acid (Note 3) is added from the dropping funnel over a period of 5 minutes. The temperature rises rapidly to 60–65° (Note 4), and pyridine hydrochloride is formed. After stirring for 10 minutes, the solid is collected on a chilled Büchner funnel and washed twice with 25-ml. portions of dry benzene (Note 5).

The filtrate is concentrated under reduced pressure on the steam bath, and the residue is distilled using a 200-ml. modified Claisen flask.¹ The fraction boiling up to 155°/12 mm. is discarded; the anhydride is collected at 155–162°/12 mm. (170–173°/15 mm.). It amounts to 19–20 g. (78–83%).

B. *p-Chlorobenzoic anhydride (benzoic anhydride, p,p'-dichloro-)*. A mixture of 17.5 g. (0.1 mole) of *p*-chlorobenzoyl chloride (Note 6) and 50 ml. (0.6 mole) of pyridine in a loosely stoppered 200-ml. flask is warmed on the steam bath for 5 minutes and poured upon 100 g. of cracked ice and 50 ml. of concentrated hydrochloric acid (sp. gr. 1.18). The anhydride separates at once; as soon as the ice has melted sufficiently the mixture is filtered by suction. The solid is washed once with 15 ml. of methanol, then with 15 ml. of dry benzene. The yield is 14.2–14.6 g. (96–98%). Though suitable for most purposes, the crude product can be purified by recrystallization from 250 ml. of dry benzene; the recovery is 90%; it melts at 192–193°.

2. Notes

1. The pyridine was Eastman grade which was dried by long standing over potassium hydroxide for A but used without further drying in B. Adkins' studies on the mechanism of this reaction indicate that the intermediate complex may react with water or with a molar quantity of the acid to form an anhydride.²
2. The benzene is dried by distilling the first 10% and using the residue directly.
3. The heptoyl chloride, b.p. 173–175°, and the heptoic acid, b.p. 108–109°/9 mm., were obtained from the Eastman Kodak Company.
4. When preparing larger amounts, it would probably be better to control the temperature by external cooling as well as by the rate of addition of the acid.
5. Pyridine hydrochloride is hygroscopic; the filtration should be done rapidly, using a Büchner funnel.
6. *p*-Chlorobenzoyl chloride (m.p. 14–15°) is readily obtained by refluxing and stirring 156 g. (1.0 mole) of *p*-chlorobenzoic acid (obtained by the procedure for the *o*-isomer³) and 200 g. (1.7 moles) of thionyl chloride until solution is complete. The unused thionyl chloride is distilled, under slightly reduced pressure, and the product at 10 to 25 mm.; the yield of *p*-chlorobenzoyl chloride, b.p. 119–120°/22 mm., is 131–142 g. (75–81%). An additional amount can be secured by working up the fore-run and residue.

3. Discussion

These procedures are generally applicable to both aliphatic and aromatic compounds. They are reported to fail for [furoic anhydride](#) and to give poor results for [p-nitrobenzoic anhydride](#) (W. W. Prichard, private communication). They are superior to the common interchange method⁴ in that they avoid the fractional distillation which is very troublesome in the aliphatic series. They have been used in numerous instances^{2,5,6,7,8,9,10,11,12} and can be adapted to give mixed anhydrides.¹³ [Benzoic anhydride](#) has been obtained, by closely related procedures, from [benzoic acid](#) and [benzoyl chloride](#) by heating under reduced pressure¹⁴ or in the presence of [zinc chloride](#).¹⁵ Benzoic, acetic, and propionic anhydrides have been conveniently prepared by the action of [bromine](#) on the sodium salts of the acids in the presence of [sulfur](#).¹⁶

References and Notes

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Appendix

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

Heptoic anhydride (enanthic anhydride)

heptoyl chloride

heptoic acid

p-Chlorobenzoic anhydride (benzoic anhydride, p,p'-dichloro-

Benzoic, acetic, and propionic anhydrides

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

[Benzene](#) (71-43-2)

methanol (67-56-1)
thionyl chloride (7719-09-7)
bromine (7726-95-6)
Benzoic acid (65-85-0)
sulfur (7704-34-9)
benzoyl chloride (98-88-4)
Benzoic anhydride (93-97-0)
pyridine (110-86-1)
potassium hydroxide (1310-58-3)
zinc chloride (7646-85-7)
pyridine hydrochloride (628-13-7)
furoic anhydride
p-chlorobenzoic acid (74-11-3)
p-chlorobenzoyl chloride (122-01-0)
p-nitrobenzoic anhydride