



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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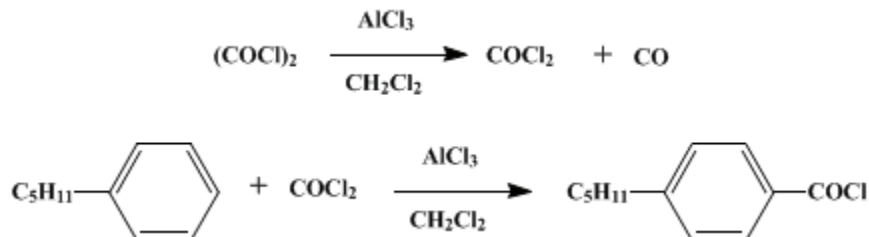
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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PREPARATION OF 4-ALKYL-AND 4-HALOBENZOYL CHLORIDES: 4-PENTYLBENZOYL CHLORIDE

[Benzoyl chloride, 4-pentyl-]



Submitted by Mary E. Neubert and D. L. Fishel¹.
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1. Procedure

Caution! Operations prior to vacuum distillation of the product should be done in a good hood since phosgene, carbon monoxide, and hydrogen chloride are present (Note 1). Rubber gloves should also be used to avoid contact with the reagents.

A 100-mL, three-necked, round-bottomed flask is fitted with a mechanical stirrer, 100-mL pressure-equalized addition funnel (Note 2) to which is attached a drying tube (Note 3), and a rubber septum. Dry methylene chloride (27 mL, (Note 4)) and 8.9 g (0.067 mol) of aluminum chloride (Note 5) are added to the flask, stirring is begun, and 17.1 g (11.5 mL, 0.135 mol) of oxalyl chloride (Note 6) is added over 5 min by means of a syringe introduced through the septum (Note 7). The septum is replaced by a thermometer and a solution of 10 g (11.6 mL, 0.067 mol) of amylbenzene (Note 8) in 40 mL of dry methylene chloride is added dropwise over 1 hr with stirring while the temperature is maintained at 20–25°C. The reaction mixture is reduced to about half of the original volume by distillation of solvent and excess oxalyl chloride and/or phosgene (Note 9). Approximately 40 mL of fresh dry methylene chloride is added to the flask and the solution is cooled to 0°C in an ice-salt bath. The cold solution is slowly poured onto a stirred mixture of 170 g of crushed ice and 10 g of calcium chloride at a rate to maintain the temperature below 5°C (Note 10). The organic layer is rapidly separated from the aqueous layer and dried over anhydrous sodium sulfate. The mixture is filtered and the solvent is removed by distillation at reduced pressure. The residual liquid is dissolved in 50 mL of ether, and the resulting solution is cooled to 0°C, extracted with 5 mL of cold (0°C) 5% potassium hydroxide solution, and then washed twice with 15-mL portions of cold (0°C) water (Note 11). The ether solution is separated and dried over anhydrous sodium sulfate. The mixture is filtered and the solvent is removed by distillation at reduced pressure (Note 12). Distillation through a Vigreux column affords a small forerun and then 7.80–7.82 g (55%) of pure 4-pentylbenzoyl chloride, bp 95°C (0.20 mm) (Note 13) and (Note 14). The acid chloride is stable if kept in a sealed container to prevent hydrolysis.

2. Notes

- Both phosgene and carbon monoxide were identified in IR spectra of gases generated from an equimolar mixture of oxalyl chloride and aluminum chloride at room temperature.
- The submitters used a constant addition funnel.
- Molecular sieves 4A available from Davison Chemical Co. were used.
- The submitters state that the use of predried methylene chloride (stored overnight over 4A molecular sieves) gave the best results.
- Use of either an excess of aluminum chloride or partially hydrolyzed aluminum chloride gives larger amounts of the by-product diaryl ketone at the expense of the acid chloride. The checkers used freshly

opened containers of the anhydrous material available from Fisher Scientific.

6. **Oxalyl chloride** should be distilled if it is colored or contains solid. Studies by the submitters have shown that an excess of **oxalyl chloride** is needed for maximum conversion of the alkylbenzene to acid chloride. The checkers used **oxalyl chloride** available from Eastman Organic Chemicals.

7. The submitters added the **oxalyl chloride** through the funnel used to add **amylbenzene**.

8. The checkers used product available from Aldrich Chemical Company, Inc.

9. If excess **oxalyl chloride** (and/or **phosgene**) is not removed, the vigorous reaction with water during decomposition of the aluminum chloride complex contributes to hydrolysis of the product acid chloride by increasing the time needed to complete this step. The more dilute solution achieved by additional solvent helps to prevent this hydrolysis as does maintenance of a low temperature during decomposition of the complex.

10. The calcium chloride-ice mixture helps to maintain a low temperature.

11. Changing the solvent to **ether** prior to the base extraction step (to remove carboxylic acid formed by hydrolysis) inhibits emulsion formation, particularly with the higher alkyl-substituted products.

12. The procedure may be interrupted at this point if the crude acid chloride is protected from moisture, although highest yields are obtained if distillation is done at once. Failure to remove water (even that associated with the **sodium sulfate** drying agent) before storage may result in anhydride formation during distillation because of the presence of free carboxylic acid.

13. Infrared analysis (neat, film) shows a carbonyl doublet at 1740, 1770 cm^{-1} , typical of 4-substituted benzoyl chlorides and thought to be due to Fermi resonance.^{2,3} Contamination of the product with the anhydride can be detected by a doublet at 1720 and 1780 cm^{-1} , with the ketone by a singlet at 1650 cm^{-1} , and with the acid by a singlet at 1690 cm^{-1} .

14. The submitters obtained the product in 75% yield.

3. Discussion

This method is based on that of Fahim,⁴ who isolated 4-alkylbenzoic acids in 40–60% yields by hydrolysis of the corresponding acid chlorides. The present improved procedure includes those conditions believed to be optimum for a one-step synthesis of 4-substituted benzoyl chlorides in good yields and apparently free of positional isomers, as indicated by gas chromatography/mass spectroscopy as well as ^1H and ^{13}C NMR analyses. The procedure has been used successfully for the synthesis of 4-halobenzoyl chlorides and several other aryl acid chlorides,^{5,6} as well as for 4-alkylbenzoyl chlorides up through the decyl derivative. Some of these results are summarized in Table I. The reaction has been run on a 1-mol scale by the submitters with no difficulty.

The major by-product that can be isolated (3–6%) from the residue after distillation is the 4,4'-disubstituted benzophenone; formation of the ketone is minimized by using excess **oxalyl chloride** and by slow addition of a dilute solution of the alkylbenzene to the acylating agent. Ambient temperatures (20–25°C) appear to give optimum results; higher temperatures favor ketone formation and lower temperatures result in incomplete reaction for reasonable reaction times. Numerous additional reactions using 4-alkyl-benzenes indicate that the alkylbenzene solution can be added more rapidly as long as the temperature is maintained at 20–25°C. Maximum yields are obtained when the addition time is 30–60 min, apparently because longer times lead to loss of **phosgene** and reaction of the acid chloride with the alkylbenzene to give the ketone.

This method cannot be used to prepare acid chlorides of aromatic systems that contain substituents strongly activating for electrophilic substitution such as alkoxy groups (the major product is ketone), deactivating ring substituents (no reaction), or those that form stable acylium ions (major product is carboxylic acid). **Mesitoic acid** rather than the acid chloride was isolated from the acylation of **mesitylene** using these conditions, which confirms the results previously reported using similar conditions.⁷

TABLE I
4-SUBSTITUTED BENZOYL
CHLORIDES FROM
SUBSTITUTED BENZENES

Substituent Yield (%) bp (°C)(mm)

C ₄ H ₉	66.5	113 (1.7)
<i>i</i> -C ₄ H ₉	77.5	115 (1.6)
C ₃ H ₁₁	75.3	136 (3.2)
C ₆ H ₁₃	80.3	143 (1.3)
C ₇ H ₁₅	79.3	160 (5)
C ₉ H ₁₉	71.8	182 (2.6)
C ₁₀ H ₂₁	68.0	169 (0.6)
F	84.4	50 (1.1)
Cl	77.7	86 (2.1)
Br	75.9	103 (2.5)
I	74.1	100 (0.7)

Previously, the most widely used method for preparation of 4-alkylbenzoyl chlorides on a laboratory scale has been from the benzoic acids obtained by oxidation of aromatic ketones, usually 4-alkylacetophenones.^{8,9,10,11,12,13,14} The latter are usually prepared by acylating alkylbenzenes. Although this sequence gives high yields, it is lengthy (three completely separate steps) and the scale is restricted in the second step because of the large volumes required. The submitters state that they were unable to repeat the reported alkylation of **toluic acid**.¹⁵ Methods that lead to formation of ortho and para isomeric intermediates are inconvenient since they require that the isomers be separated.^{16,17,18,19}

This method provides easy access to 4-alkylbenzoyl chlorides, which are useful intermediates in the preparation of diaryl esters that have mesomorphic properties.²⁰ Benzoyl chlorides substituted in the 4-position also serve as starting materials for the preparation of aromatic aldehydes²¹ and nitriles,^{6,22} whereas the acids, derivable quantitatively from the acid chlorides, are good precursors via the Schmidt reaction to 4-substituted anilines.²³ This method has been used to prepare deuterated liquid crystalline anils from the anilines obtained by Schmidt rearrangement of 4-alkylbenzoic acids²⁴ and 4'-cyanobiphenyls²⁵ but was not successful in an attempt to prepare 2-alkyl-7-cyanofluorenes.²⁶

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

4,4'-disubstituted benzophenone

Benzoyl chlorides

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

[hydrogen chloride \(7647-01-0\)](#)

ether (60-29-7)

carbon monoxide (630-08-0)

sodium sulfate (7757-82-6)

aluminum chloride (3495-54-3)

potassium hydroxide (1310-58-3)

phosgene (75-44-5)

Mesitylene (108-67-8)

methylene chloride (75-09-2)

Amylbenzene (538-68-1)

oxalyl chloride (79-37-8)

Mesitoic acid (480-63-7)

toluic acid (99-94-5)

4-Pentylbenzoyl chloride,
Benzoyl chloride, 4-pentyl- (49763-65-7)

