



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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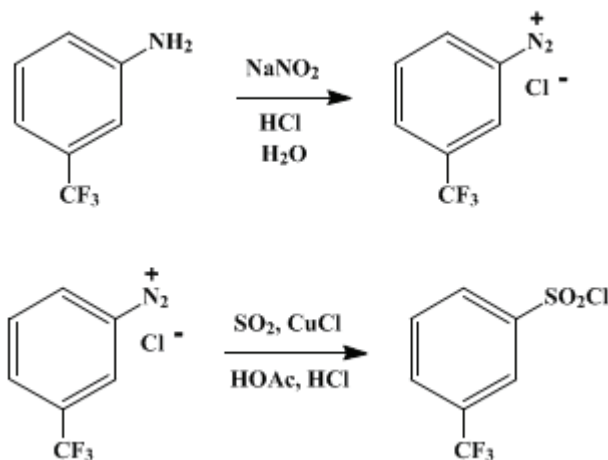
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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***m*-TRIFLUOROMETHYLBENZENESULFONYL CHLORIDE**

[Benzenesulfonyl chloride, *m*-(trifluoromethyl)-]



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1. Procedure

*Caution! All operations should be carried out in a hood! *m*-Trifluoromethylbenzenesulfonyl chloride is a lachrymator. Spills should be treated with saturated sodium carbonate.*

α,α,α -Trifluoro-*m*-toluidine (*m*-aminobenzotrifluoride) (96.7 g, 0.6 mol) (Note 1) is added in one portion to a mixture of concentrated hydrochloric acid (200 mL) and glacial acetic acid (60 mL) in a 1000-mL beaker arranged for efficient mechanical stirring (Note 2). The white hydrochloride salt precipitates (Note 3). The beaker is placed in a dry ice-ethanol bath and, when the temperature of the stirred mixture has reached -10°C , a solution of sodium nitrite (44.8 g, 0.65 mol) in water (65 mL) is added dropwise at such a rate that the temperature does not exceed -5°C (Note 4). After all the sodium nitrite solution has been added, the mixture is stirred for 45 min while the temperature is maintained between -10°C and -5°C (Note 5).

While the diazotization is being completed, glacial acetic acid (600 mL) is placed in a 4000-mL beaker and stirred magnetically. Sulfur dioxide is introduced by a bubbler tube with a fritted end immersed below the surface of the acetic acid until saturation is evident (Note 6). Cuprous chloride (15 g) (Note 7) is added to the solution. The introduction of sulfur dioxide is continued until the yellow-green suspension becomes blue-green. Most of the solids dissolve during this time (20–30 min). The mixture is then placed in an ice bath and cooled with stirring. When the temperature approaches 10°C , the diazotization reaction mixture (Note 8) is added in portions over a 30-min period to the sulfur dioxide solution. Considerable foaming occurs after each addition, and this can be disrupted with a few drops of ether. The temperature rises during the addition, but it should not exceed 30°C . After all the diazonium salt mixture has been added, the mixture is poured into ice water (1 : 1, 2000 mL), stirred magnetically until the ice has melted, and added to a 4000-mL separatory funnel. The product separates as a yellow oil that is drawn off. The reaction mixture is extracted with 200-mL portions of ether until the ether washings are colorless (Note 9), and these washings are added to the initial product. The combined organic fraction is washed with saturated aqueous sodium bicarbonate until neutral (Note 10), then with water, and is then dried with magnesium sulfate. The solvent is removed with a rotary evaporator, and the residue is distilled (bp $54\text{--}55^{\circ}\text{C}$, 0.1 mm) through a 10-cm vacuum-jacketed Vigreux column to give *m*-trifluoromethylbenzenesulfonyl chloride (100–115 g, 68–79%) as a colorless or slightly yellow, clear liquid (Note 11), (Note 12).

2. Notes

1. α,α,α -Trifluoro-*m*-toluidine was obtained from Aldrich Chemical Company, Inc. The checkers distilled this material prior to use (bp 187–189°C).
2. A chain beaker clamp is very satisfactory for supporting the beaker, as it can later be used as a handle to pour the diazonium solution. For efficient stirring the blade of the stirrer was made by trimming the ends of a large Teflon stirring paddle to the diameter of the beaker. The paddle was inverted (straight edge on bottom) and should rotate 1–1.5 cm from the bottom of the beaker.
3. If solid amines are used, they should be thoroughly crushed in a mortar and pestle before adding to the acid mixture.
4. Temperature control during the sodium nitrite addition is essential to the success of the preparation. The temperature can go as low as -15°C but must not exceed -5°C . The addition takes ca. 1 hr. At temperatures greater than -5°C , dark-red by-products form which lower the yield.
5. Temperature control is conveniently accomplished by raising and lowering the dry-ice bath. It does not seem to matter if longer reaction times are employed, but the temperature should be lowered to -10°C or below after 45 min.
6. Saturation, which requires 15–30 min, is conveniently noted by observing that most sulfur dioxide bubbles reach the surface of the acetic acid.
7. The original literature² suggests that copper(II) chloride dihydrate can be used as a catalyst, since it is reduced by the sulfur dioxide to copper(I). It has been noted on several occasions that catalytically inactive mixtures result. If copper(II) chloride dihydrate is used, it is expedient to add copper(I) chloride (1 g) to ensure efficient catalysis in the early stages of reaction.
8. This mixture should be a pale tan suspension, and it should be cooled between additions.
9. The first portion of ether may be larger (400 mL) since much dissolves in the aqueous mixture. A total of 1000 mL of ether is usually sufficient.
10. A considerable amount of acid is present in the ether extracts, so vigorous gas evolution occurs during the sodium bicarbonate extraction. Caution must be exercised at this point.
11. The product is sufficiently pure for most purposes. A second distillation affords a colorless product (lit.³ bp 88–90°C, 6 mm).
12. With many anilines used as precursors in this reaction, the sulfonyl chloride product is a solid and an alternate workup procedure is used. After the reaction is quenched with ice water, the solid product is filtered with suction and washed copiously with cold water. The crude product tends to occlude water and copper salts, which may be detrimental in later reactions. A good washing protocol involves rinsing the solid on the filter with water (200 mL), then suspending the solid in cold water (1000 mL), stirring briskly, and filtering with suction. The latter process should be repeated three times. The final water wash should be only very slightly yellow. After air drying the product can be recrystallized from an appropriate solvent.

3. Discussion

m-Trifluoromethylbenzenesulfonyl chloride has been prepared by treatment of *m*-trifluoromethylbenzenediazonium chloride with sulfur dioxide and hydrochloric acid⁴ and by conversion of benzotrifluoride to *m*-trifluoromethylbenzenesulfonic acid with oleum, followed by chlorination with phosphorus pentachloride.³ Derivatives of this compound, such as esters and amides, are quite useful in that they display reactivities similar to *p*- and *m*-nitrobenzenesulfonyl compounds but have greatly improved solubilities.

The described procedure essentially follows that described by Meerwein et al.² as modified slightly by Yale and Sowinski.⁴ This same method can be used for a great variety of substituted anilines with good results. As evident in Table I, good yields are obtained in most cases, and the reaction works better for anilines with electron-withdrawing substituents. The identical procedure has been used to prepare many other examples, such as *m*-F, *o*-F, 3,5-di-CF₃.⁵ This method readily provides many unavailable arylsulfonyl chlorides; it is experimentally straightforward, and the products are isolated without complications.

There are two general routes to arylsulfonyl chlorides. The first involves the conversion of an

already sulfur-substituted aromatic compound to the sulfonyl chloride. Thus arylsulfonic acids or their alkali metal salts yield sulfonyl chlorides by treatment with a variety of chlorinating agents such as phosphorus pentachloride, thionyl chloride, phosgene, and chlorosulfonic acid. Alternatively, substituted thiophenols or aryl disulfides can be oxidized by chlorine-water to the sulfonyl chloride.⁶

TABLE I
CONVERSION OF ARYLAMINES TO
ARYLSULFONYL CHLORIDES

Amine, XC ₆ H ₄ NH ₂ , X =Yield (%) of XC ₆ H ₄ SO ₂ Cl	
<i>m</i> -CF ₃	72
<i>p</i> -NO ₂	68
<i>m</i> -NO ₂	86
<i>p</i> -Cl	90
<i>p</i> -CO ₂ CH ₃	90
3,5-di-NO ₂	81
<i>m</i> -CH ₃	71
H	53
<i>p</i> -OCH ₃	27

The second route utilizes the introduction of the chlorosulfonyl substituent directly onto the aromatic nucleus. The reaction of substituted benzenes with chlorosulfonic acid gives good yields of arylsulfonyl chlorides; however, the aryl substituent dictates the position of attachment of the chlorosulfonyl function in this electrophilic aromatic substitution.⁷ The method described herein allows replacement of a diazotized amine function by the chlorosulfonyl group. The ready availability of substituted anilines makes this the method of choice for the preparation of arylsulfonyl chlorides.

Arylsulfonyl chlorides are pivotal precursors for the preparation of many diverse functional types including sulfonate esters,⁸ amides,⁴ sulfones,⁹ sulfinic acids,¹⁰ and others.¹¹ Furthermore, sulfonyl fluorides are best prepared from sulfonyl chlorides.¹² The sulfonyl fluorides have many uses, among which is their utilization as active site probes of chymotrypsin and other esterases.¹³ The trifluoromethyl group also plays valuable roles in medicinal chemistry.¹⁴

References and Notes

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13. See ⁵ for a good introduction.
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

sulfonyl chloride

amine

p- and m-nitrobenzenesulfonyl

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

chlorosulfonic acid (7790-94-5)

phosphorus pentachloride (10026-13-8)

thionyl chloride (7719-09-7)

sodium bicarbonate (144-55-8)

sodium carbonate (497-19-8)

sulfur dioxide (7446-09-5)

sodium nitrite (7632-00-0)

phosgene (75-44-5)

cuprous chloride,
copper(I) chloride (7758-89-6)

magnesium sulfate (7487-88-9)

copper(I)

benzotrifluoride (98-08-8)

copper(II) chloride dihydrate (10125-13-0)

m-aminobenzotrifluoride,
 α,α,α -Trifluoro-m-toluidine (98-16-8)

m-Trifluoromethylbenzenesulfonyl chloride,
Benzenesulfonyl chloride, m-(trifluoromethyl)- (777-44-6)

m-trifluoromethylbenzenediazonium chloride

m-trifluoromethylbenzenesulfonic acid