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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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SULFONYL CYANIDES: METHANESULFONYL CYANIDE

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1. Procedure

Caution! Since cyanogen chloride is highly toxic, the preparation and isolation of the sulfonyl cyanide should be conducted in a well-ventilated hood.

Benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

A 2-l., three-necked, round-bottomed flask equipped with a sealed mechanical stirrer, a pressure-equalizing dropping funnel capped with a gas-outlet, and a thermometer is charged with 126 g. (0.500 mole) of sodium sulfite heptahydrate, 84.0 g. (1.00 mole) of sodium hydrogen carbonate, and 1 l. of water (Note 1). Stirring is begun, and 57.3 g. (0.500 mole) of freshly distilled methanesulfonyl chloride (Note 2) is added dropwise over 30 minutes. The slightly exothermic reaction is accompanied by the evolution of carbon dioxide. After stirring for 2 hours, gas evolution ceases, and a clear, colorless solution of sodium methanesulfinate (Note 3) is obtained.

The dropping funnel is removed, the solution is cooled to 10° by the addition of ice, and 50 ml. (1.0 mole) of liquid cyanogen chloride (Note 4) is added in one portion with vigorous stirring. Addition of ice keeps the mixture at or below 15°. Within 1 minute the reaction mixture becomes turbid, and methanesulfonyl cyanide separates as a heavy, colorless oil. The mixture is stirred for an additional 15 minutes before 200 ml. of benzene is added (Note 5). After 3 minutes of stirring, the layers are separated in a 2-l. separatory funnel, and the aqueous layer is extracted with two 100-ml. portions of benzene. The combined extracts are washed with water and dried overnight over anhydrous calcium chloride. Filtration and removal of solvent with a rotary evaporator *in a hood* affords an almost pure product (Note 6) which is distilled, yielding 35.4–37.8 g. (67–72%) of methanesulfonyl cyanide, b.p. 68–69° (15 mm.),n_{D}^{20} 1.4301 (Note 7), which may be stored in a well-stoppered bottle, kept at or below 0°, for prolonged times without loss in purity (Note 8).

2. Notes

1. Excess sodium sulfite or sodium hydrogen carbonate should be avoided, since either would react with the sulfonyl cyanide once formed.
2. The procedure given is applicable to many other sulfonyl chlorides as well (see Table I). Solid sulfonyl chlorides are added as such. When heavy frothing occurs in the reduction (*e.g.*, with 4-nitrobenzenesulfonyl chloride), addition of 50 ml. of chloroform to the reaction mixture will eliminate the foam without reducing the final yield. When the sulfonyl chlorides were prepared according to Meerwein and co-workers,[2] it was found advantageous to use the crude, damp sulfonyl chlorides, since these are more easily reduced than the dried or recrystallized materials.

TABLE I
PREPARATION OF SULFONYL CYANIDES FROM SULFONYL CHLORIDES[a]

R =	RSO_2Cl from	m.p.	b.p.	Yield, %
Methyl	Commerce	—	68–69° (15 mm.)	72
Ethyl	$RSCN + Cl_2$[3]	—	80–80.5° (18 mm.)	84
Propyl	$R_2S_2 + Cl_2$[4]	—	81–81.5° (18 mm.)	76
Benzyl	$RSC(NH)NH_2\cdot HCl$[5]	89.5–91°		91
Cyclohexyl	$RH + SO_2Cl_2$[6]		72–73° (0.4 mm.)	85
4-Methoxyphenyl	$RH + SO_2Cl_2$[7]	66–68°		88
p-Tolyl	Commerce	49.5–51°		89
Phenyl	Commerce	19–20°	118–119° (15 mm.)	92
4-Chlorophenyl	$RN_2^+ Cl^- + SO_2$[2]	57.5–59°		65[b]
4-Cyanophenyl	$RN_2^+ Cl^- + SO_2$[2]	123–125°		79[b]
4-Nitrophenyl	$RN_2^+ Cl^- + SO_2$[2]	122–123.5°		66[b]

[a] The preparations were performed on a 0.25 to 1-mole scale.

[b] Overall yield from the corresponding aniline as starting material.

3. When crude sulfonyl chlorides were used as starting materials, on completion of the reduction, and before the addition of cyanogen chloride, the reaction mixture was washed with a suitable solvent (benzene or dichloromethane, or, in some cases, chloroform) to remove organic impurities. In the case of higher-melting, crystalline sulfonyl chlorides, heating to 50° may be necessary to complete their reduction. The solution of the sulfinate salt may be kept overnight, if desired, with no decrease in the yield of sulfonyl cyanide.
4. Cyanogen chloride is commercially available in gas cylinders. It is liquefied by passing the gas through a condenser cooled with ice water. Where difficult to obtain, it may be prepared by passing chlorine gas through a stirred suspension of sodium tetrakis(cyano-C)zincate prepared *in situ* from sodium cyanide and zinc sulfate.[8]
5. If the benzenesulfinates were substituted with electron-withdrawing groups, *e.g.*, 4-nitro- and 4-cyanobenzenesulfinate, the yields were slightly improved when the reaction time with cyanogen chloride was lengthened to 1 hour.

The higher-melting sulfonyl cyanides which separate as solids should be dried when dissolved in a suitable solvent, *e.g.*, benzene. 4-Nitrobenzenesulfonyl cyanide is not readily extracted from the reaction mixture; it is collected on a Büchner funnel, pressed as dry as possible, dissolved in benzene, washed with water, and dried over anhydrous calcium chloride.

6. Solid sulfonyl cyanides show a melting point not more than 1–2° below that of recrystallized material. They may be used without further purification. Analytically pure samples are obtained by recrystallization from dry benzene, dry petroleum ether, or a mixture of the two.
7. The product was further characterized as follows: IR (liquid film) cm.$^{-1}$: 2195 strong, 1370 strong, 1170 strong; ^{1}H NMR resonance ($CDCl_3$), δ 3.43 (s).
8. Contrary to the findings of Cox and Ghosh,[9] methanesulfonyl cyanide may be distilled without decomposition. Samples of benzene-, 4-methoxybenzene-, and 4-chlorobenzenesulfonyl cyanides were kept for over a year without loss in purity.

3. Discussion

Whereas sulfonyl halides have been known for a long time and, especially the chlorides, have become of great synthetic value, sulfonyl cyanides were unknown until 1968. They were first prepared by van Leusen and co-workers from the reaction of sulfonylmethylenephosphoranes with nitrosyl chloride.[10] The same group also investigated part of their chemistry.[11,12,13,14,15] Since then, two more, completely different methods of synthesis have been published: one, involving the reactions of sulfinates with cyanogen chloride,[9] and another, the oxidation of thiocyanates.[16]

The procedure given above for the preparation of methanesulfonyl cyanide is essentially a combination of the sulfite reduction of a sulfonyl chloride, as originally described by Bere and Smiles,[17] and the sulfinate–cyanogen chloride reaction, first published by Cox and Ghosh.[9]

Some sulfinates are commercially available and may be used as starting materials for the preparation of sulfonyl cyanides. Yields, however, are not significantly better than when the much cheaper and more readily available sulfonyl chlorides are used as starting materials. Good to excellent results are obtained, even when starting from rather impure sulfonyl chlorides.[18] Illustrative examples are given in Table I.

Sulfonyl cyanides have an activated cyano group and show many interesting reactions. With a range of *N-, O-, S-*, and *C*-nucleophiles, of the cyano group to these nucleophiles is observed.[11,19,20] Hydroxylamine, hydrazine, and phenylhydrazine (α-effect nucleophiles) add to the cyano group of sulfonyl cyanides, yielding products that could be converted into substituted 1,2,4-oxadiazoles[21] and 1,2,4-triazoles,[15,5] respectively. Dienes show Diels-Alder cycloadditions with sulfonyl cyanides.[12,13,14,19,22] 1,3-Dipolar cycloadditions to the cyano group give rise to substituted tetrazoles (from azides), to substituted 1,2,3-triazoles (from diazo compounds), or to substituted 1,2,4-oxadiazoles (from nitrile *N*-oxides).[12,19] Sulfonyl cyanides undergo free-radical additions to alkenes.[19,23] Chlorine and sulfenyl chlorides add to the cyano group of sulfonyl cyanides.[24,25,26]

References and Notes

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Appendix

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

petroleum ether

sodium tetrakis(cyano-C)zincate

4-nitro- and 4-cyanobenzenesulfinate

benzene-, 4-methoxybenzene-, and 4-chlorobenzenesulfonyl cyanides

mono-, di-, and trichloromethanesulfonyl chloride

ethylene- and 2,4-dinitrophenylsulfonyl chloride

calcium chloride (10043-52-4)

Benzene (71-43-2)

aniline (62-53-3)

sodium sulfite (7757-83-7)

chloroform (67-66-3)

sodium hydrogen carbonate (144-55-8)

sodium cyanide (143-33-9)

ethyl (2025-56-1)

propyl (2143-61-5)

Phenylhydrazine (100-63-0)

carbon dioxide (124-38-9)

chlorine (7782-50-5)

methyl (2229-07-4)

hydrazine (302-01-2)

hydroxylamine (7803-49-8)

dichloromethane (75-09-2)

zinc sulfate (7733-02-0)

nitrosyl chloride (2696-92-6)

benzyl (2154-56-5)

cyanogen chloride (506-77-4)

Cyclohexyl (3170-58-9)

p-tolyl

phenyl

sodium sulfite heptahydrate

Methanesulfonyl chloride (124-63-0)

Methanesulfonyl cyanide (24225-08-9)

sodium methanesulfinate

4-nitrobenzenesulfonyl chloride (98-74-8)

4-Methoxyphenyl

4-Chlorophenyl

4-Cyanophenyl

4-Nitrophenyl

4-Nitrobenzenesulfonyl cyanide

dimethylsulfamoyl chloride (13360-57-1)