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of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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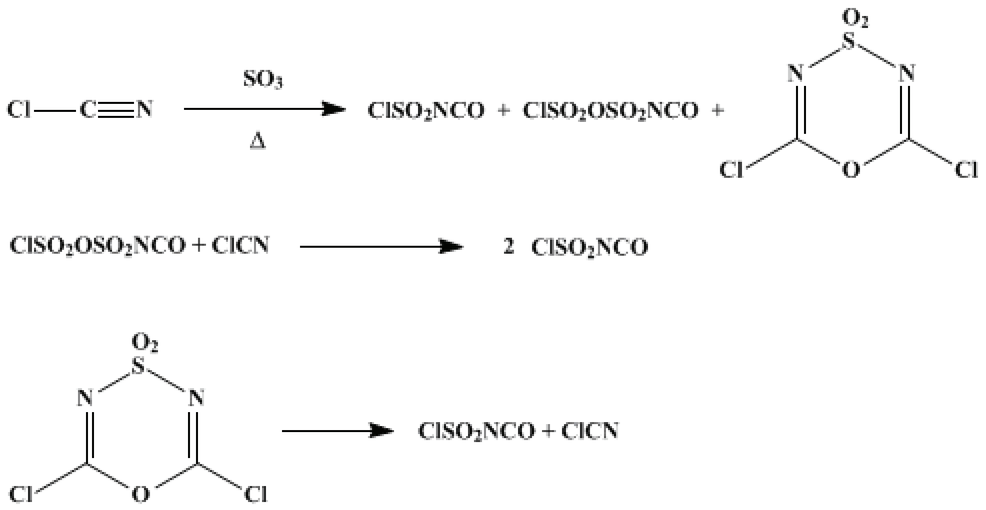
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.046.0023

Organic Syntheses, Coll. Vol. 5, p.226 (1973); Vol. 46, p.23 (1966).

CHLOROSULFONYL ISOCYANATE

[Isocyanic acid, anhydride with chlorosulfonic acid]



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Checked by Jerome F. Levy and William D. Emmons.

1. Procedure

Caution! Cyanogen chloride is extremely toxic. Sulfur trioxide and chlorosulfonyl isocyanate are highly corrosive materials. This preparation should be carried out in an efficient hood, and rubber gloves should be worn throughout.

A 200-ml. four-necked flask is fitted with a mechanical stirrer (Note 1), a thermometer, a Claisen-type adapter bearing a dry ice reflux condenser and a dropping funnel, and a gas-inlet tube consisting of a length of 6-mm. glass tubing extending almost to the bottom of the flask. This gas-inlet tube is connected through a stopcock to a safety trap and then to a cylinder of cyanogen chloride (Note 2). The dropping funnel, protected with a calcium chloride drying tube, is charged with 64 g. (0.80 mole) of liquid sulfur trioxide (Note 3). The outlet from the dry ice condenser is connected to a trap cooled in dry ice.

The flask is charged with approximately 36.9 g. (0.60 mole) of cyanogen chloride while being cooled in a dry ice-methylene chloride slush bath (Note 4). The flask is allowed to warm to −5° to melt the cyanogen chloride, and then the liquid sulfur trioxide is added over a period of 0.75–1.25 hours. The reaction is very exothermic. During the addition the temperature is gradually decreased from −5° to −15° (Note 5). After addition is completed, the reaction mixture is checked for unreacted sulfur trioxide by adding approximately 1–2 g. of cyanogen chloride and noting if a temperature rise takes place. If necessary, this test is repeated until no more unreacted sulfur trioxide is left. The reaction mixture at this point is a pulpy, stirrable mass containing some chlorosulfonyl isocyanate, some chloropyrosulfonyl isocyanate, and much precipitated 2,6-dichloro-1,4,3,5-oxathiadiazine-4, 4-dioxide (Note 6).

The adapter bearing the dry ice condenser and dropping funnel is removed and replaced by a 16 cm. × 2 cm. distillation column packed with glass helices (Note 7) and connected to an efficient air-cooled condenser. The condenser has a 100-ml. receiver and is connected to a trap cooled in dry ice and protected by a drying tube to condense unreacted cyanogen chloride. The reaction flask is heated for about 1 hour while the temperature is gradually increased to 110–115°. At this point, cyanogen chloride is bubbled into the reaction mixture at the rate of about 0.010 mole/min (Note 8). The temperature of the flask is raised to 120–130°, whereupon chlorosulfonyl isocyanate begins to distil at a head temperature of 90–105°. When the distillation rate begins to slacken, and after most of the contents of the flask has distilled, the temperature of the flask is raised to 130–150°. When the residue in the flask is only 3–5 ml., the cyanogen chloride flow is discontinued and the distillation is stopped. This part of the reaction (from the start of the cyanogen chloride feed) requires about 0.4–0.6 mole of cyanogen chloride and takes about 0.75–1 hour.

The crude product, which may contain dissolved cyanogen chloride, is redistilled at a pressure of 100 mm. through the helices-packed column. Heating is done very slowly at first to allow the unreacted cyanogen chloride to distil and be condensed in the dry ice trap. The product is collected at 54–56° (100 mm.); d_4^{20} 1.626, weight 67.7–69.9 g. (60–62%) (Note 9),(Note 10),(Note 11).

2. Notes

1. The lubricant for the ground-glass sleeve of the stirrer may be silicone oil or mineral oil; however, Teflon® oil is preferred. Glycerin should not be used.
2. The checkers used cyanogen chloride supplied in a metal cylinder by the American Cyanamid Co., Bound Brook, New Jersey. The submitter prepared cyanogen chloride beforehand[2] and either charged it as a liquid or allowed it to distil in as is required later in the reaction.[3]
3. The checkers used Sulfan®, a stabilized liquid form of sulfur trioxide which is commercially available from Baker and Adamson, General Chemical Division, Allied Chemical Corp., Morristown, New Jersey. The submitter distilled sulfur trioxide from 65% oleum directly into the reaction flask, a procedure which is described elsewhere.[3]
4. Chlorosulfonyl isocyanate reacts violently with water. For safety reasons, therefore, it is recommended that either air or dry ice mixtures be used for all cooling condensers and cooling baths. The dry ice may be mixed with methylene chloride. Acetone is not recommended, as chlorosulfonyl isocyanate may react with it.
5. Too much cooling in the early stages of the reaction may cause the cyanogen chloride to crystallize. Furthermore, if the reaction mixture is cooled to substantially lower than −15°, *e.g.*, to −30° or −40°, the rate of reaction will decrease to the extent that there is danger of an uncontrollable delayed reaction.
6. At this point the reaction mixture may be stored protected from atmospheric moisture for an unlimited length of time before converting it to chlorosulfonyl isocyanate.
7. It is highly desirable to heat the distillation column with an electrical heating tape to compensate for heat loss. A 6 ft. × ½ in., 288-watt heating tape available from Briscoe Manufacturing Co., Columbus, Ohio, was used by the checkers. This should not be necessary when the reaction is conducted on a larger scale.
8. A flowmeter calibrated for use with air was used. Although this introduces some degree of error, it is adequate for the preparation.
9. The submitter conducted the reaction on ten times the scale indicated here and obtained yields of 88–93%. The checkers, however, on a scale of 0.80 mole, reproducibly obtained the lower yields indicated.
10. For storage over a short time, glass bottles sealed with rubber stoppers that are covered with polyethylene sheet are adequate. Ground-glass stoppers, even if thoroughly coated with silicone grease, will soon become frozen. For storage over moderate periods of time (several weeks) low-pressure polyethylene may be used. If traces of sulfur trioxide are present, the walls of the polyethylene vessel will soon become black; if more than 2% of cyanogen chloride is present, the polyethylene is attacked without a change in color, and its surface is converted to a crumbly mass. For storage over a long period of time, Teflon® FEP bottles available from the Nalge Co., Inc., Rochester, New York, or sealed-glass ampoules may be used.
11. Chlorosulfonyl isocyanate is a colorless, fluid liquid which fumes slightly in moist air. The vapors have a tussive effect. The compound shows an extraordinarily violent, almost explosive-like reaction with water. The contact of a small amount of the compound with the skin has no deleterious effect if it is rapidly removed by rinsing with plenty of water. Contacts which last longer than a few seconds may result in severe burns. Cotton fabrics will char immediately on contact with the compound and produce a dense smoke. A specific toxic effect other than the purely cauterizing effect of the compound has not been observed by the submitter during the past 10 years.

3. Discussion

The present procedure corresponds to the method described earlier by Graf.[3]

4. Merits of the Preparation

The cycloaddition of chlorosulfonyl isocyanate to olefins, followed by removal of the N-sulfonyl chloride group of the resulting β-lactam-N-sulfonyl chloride, offers a convenient synthesis of a large number of β-lactams unsubstituted on nitrogen.[4,5,6] Also produced in the reaction with olefins are unsaturated carboxamide-N-sulfonyl chlorides, which, like the β-lactam-N-sulfonyl chlorides, may be worked up in various ways to give a variety of products.[5,6] The reagent has also been added to 1,3-dienes,[7] cycloheptatriene,[8] and acetylenes.[9] Photochemical reactions with olefins have also been reported.[10] Chlorosulfonyl isocyanate reacts with aldehydes, *e.g.*, benzaldehyde, to give imine-N-sulfonyl chlorides which will undergo cycloaddition reactions with ketene or dimethyl ketene to give, after removal of the sulfonyl chloride group, β-lactams also.[5]

Compounds containing active hydrogens react with chlorosulfonyl isocyanate first at the isocyanate group to give N-substituted sulfamyl chlorides which may react further with more active hydrogen compound at the sulfonyl chloride group.[3,7,8,9,10]

The reactions of chlorosulfonyl isocyanate have been reviewed.[11,12]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 673
- Org. Syn. Coll. Vol. 6, 304
- Org. Syn. Coll. Vol. 6, 465
- Org. Syn. Coll. Vol. 6, 788

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);

(Registry Number)

Isocyanic acid, anhydride

chloropyrosulfonyl isocyanate

chlorosulfonic acid (7790-94-5)

sulfur trioxide (7446-11-9)

glycerin (56-81-5)

nitrogen (7727-37-9)

benzaldehyde (100-52-7)

acetone (67-64-1)

Ketene (463-51-4)

methylene chloride (75-09-2)

cyanogen chloride (506-77-4)

dimethyl ketene (598-26-5)

CHLOROSULFONYL ISOCYANATE (1189-71-5)

2,6-dichloro-1,4,3,5-oxathiadiazine-4, 4-dioxide

cycloheptatriene (544-25-2)