Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

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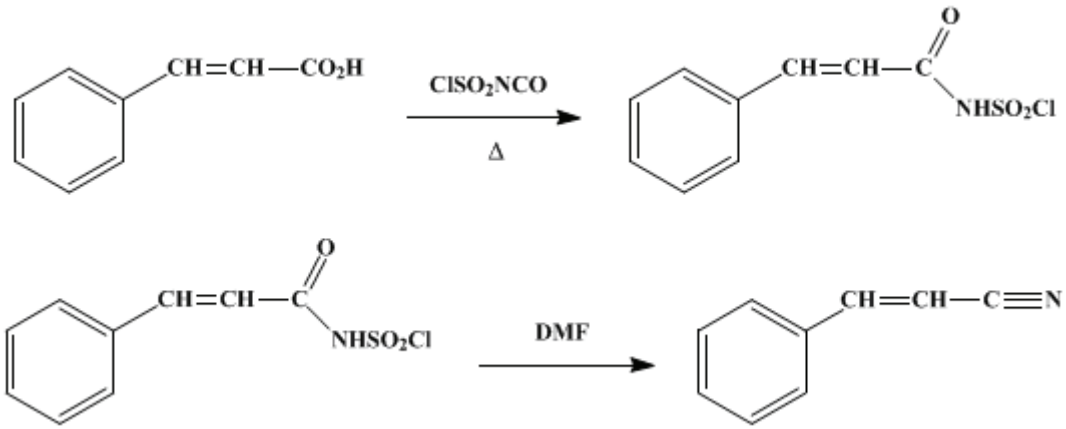
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.050.0018

Organic Syntheses, Coll. Vol. 6, p.304 (1988); Vol. 50, p.18 (1970).

CINNAMONITRILE

[2-Propenenitrile, 3-phenyl-]



Submitted by G. Lohaus[1]
Checked by Frank J. Weigert and Richard E. Benson.

1. Procedure

Caution! Chlorosulfonyl isocyanate is a highly corrosive, irritating compound. This reaction should be carried out in an efficient hood.

A 2-l., four-necked flask equipped with a stirrer, thermometer, dropping funnel, and reflux condenser is charged with 296 g. (2.00 moles) of cinnamic acid and 600 ml. of dichloromethane. The mixture is heated to reflux and a solution of 290 g. (2.05 moles) of chlorosulfonyl isocyanate (Note 1) in 100 ml. of dichloromethane is added dropwise, with stirring, over a period of 45 minutes. After a few minutes the solution becomes clear and, after about one-half of the isocyanate has been added, the carboxylic acid amide *N*-sulfonyl chloride begins to precipitate. At the end of the addition, the reaction mixture is heated for an hour to complete the evolution of carbon dioxide (Note 2). *N,N*-Dimethylformamide (300 g., 4.11 moles) (Note 3) is added, with stirring, over a 15-minute period, while cooling with ice to an internal temperature of 15–20°. The reaction mixture is stirred for an additional 15 minutes and then poured onto *ca.* 800 g. of ice. After the ice has melted, the resulting layers are separated and the aqueous phase is extracted once with 100 ml. of dichloromethane. The organic phases are combined and extracted six times with 100-ml. portions of water to remove most of the *N,N*-dimethylformamide (Note 4). The resulting organic solution is dried for 2 hours with 50 g. of potassium carbonate, decanted from the drying agent, and concentrated by distillation at atmospheric pressure. The resulting oil is distilled through a 10-cm. Vigreux column (Note 5) to give 197–225 g. (78–87%) of cinnamonitrile, b.p. 92–94° (1 mm.), n_D^{25} 1.5998 (Note 6). Its ^{1}H NMR spectrum (60 MHz., CCl_4, 36°) δ, (multiplicity, coupling constant *J* in Hz., number of protons): 5.79 (d, *J* = 17, 1H), 7.29 (d, *J* = 17, 1H), 7.35 (s, 5H).

2. Notes

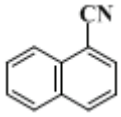
1. Chlorousulfonyl isocyanate, *Org. Synth.*, **Coll. Vol. 5**, 226 (1973), is available from Farbwerke Hoechst AG. The checkers found it necessary to distill the product before use.
2. The rate of evolution of carbon dioxide can be followed easily with a bubble counter attached to the reflux condenser.
3. Other amides also can be used, but *N,N*-dimethylformamide generally is preferred because of its volatility, high solvating ability, and miscibility with water.

4. The checkers found that, if the mixture at this point was allowed to stand overnight, a crystalline product separated that was identified as the *N,N*-dimethylformamide–sulfur trioxide complex.
5. The presence of a crystalline residue at the end of the distillation prevents the use of a spinning band column.
6. GC indicates the purity to be greater than 99.9%. A column containing Chromosorb W/DMCS/AW with 10% Triton X 305 as the stationary phase is used.

3. Discussion

This reaction illustrates a broadly applicable method for converting carboxylic acids to the corresponding nitriles.[2] It avoids the necessity for conversion of the acid to the amide, followed by dehydration with vigorous reagents such as phosphorus pentachloride or phosphorus oxychloride. The reaction is characterized by easy workup, generally good yields, and by mild reaction conditions that permit certain functional groups that may be present to remain unchanged. For example, the half ethyl easter of succinic acid is converted to the corresponding nitrile in 72% yield with this procedure. Aliphatic unsaturation may be present; thus, 2,4-hexadienenitrile is obtained from 2,4-hexadienoic acid in 76% yield. The reaction is operable with chlorine-containg acids, and an aromatic acid has been converted to the nitrile with this procedure. The results are summarized in Table I.[2].

TABLE I
NITRILES DERIVED FROM CORRESPONDING ACID

Nitrile	Yield, %
cyclo-$C_6H_{11}CN$	78
$ClCH_2CH_2CN$	66
$(CH_3)_3CCN$	68
$CH_3CH{=}CHCH{=}CHCN$	76
$C_6H_5CH_2CN$	84
$C_2H_5OCOCH_2CH_2CN$	72
$NC\text{-}(CH_2)_8CN$	86
	63

Other specific procedures for the synthesis of cinnamonitrile include the dehydration of cinnamamide with phosphorus pentachloride[3] or phosphorus oxychloride,[4] the dehydration of cinnamaldehyde oxime with acetic anhydride,[5] and the dehydrochlorination of α-chloro-β-phenylpropionitrile with quinoline,[6,7] *N,N*-diethylaniline,[8] or triethylamine.[9]

References and Notes

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

N-sulfonyl chloride

Chlorousulfonyl isocyanate

potassium carbonate (584-08-7)

acetic anhydride (108-24-7)

phosphorus pentachloride (10026-13-8)

sulfur trioxide (7446-11-9)

carbon dioxide (124-38-9)

Succinic acid (110-15-6)

Phosphorus Oxychloride (21295-50-1)

cinnamic acid (621-82-9)

Quinoline (91-22-5)

N,N-diethylaniline (91-66-7)

dichloromethane (75-09-2)

isocyanate

N,N-dimethylformamide (68-12-2)

2,4-hexadienoic acid (110-44-1)

triethylamine (121-44-8)

CHLOROSULFONYL ISOCYANATE (1189-71-5)

Cinnamonitrile,
2-Propenenitrile, 3-phenyl- (4360-47-8)

2,4-hexadienenitrile

cinnamamide

cinnamaldehyde oxime

α-chloro-β-phenylpropionitrile