Trichloromethyl Carbonochloridate: A Dehydrating Reagent for the Preparation of Nitriles from Aldoximes

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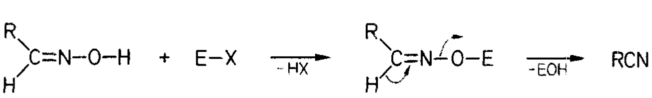
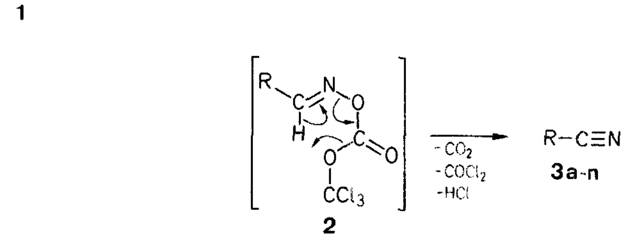
Alkyl, aralkyl, aryl, and heteroaryl aldoximes bearing various functionalities are readily converted to the corresponding nitriles in good yields using trichloromethyl carbonochloridate as dehydrating agent.

Trichloromethyl carbonochloridate (trichloromethyl chloroformate) is also known as „liquid phosgene". Phosgene itself presents a severe hazard in laboratory since it is very volatile, heavier than air, extremely toxic, and not immediately noticed when breathed in. Although trichloromethyl carbonochloridate is also toxic[1,2], it is a dense liquid (b.p. 128 °C) with a vapor pressure of only 10 mm at 20 °C. This reagent has been known for almost a century, however its application to organic synthesis is relatively limited as compared to phosgene. Some of the most recent applications of trichloromethyl carbonochloridate include the preparation of isocyanates[3], isocyanides[4,5], chloroformates[6], active carbonates[7,8], active ureas[9], *N*-carboxy-α-aminoacid anhydrides[10], isocyanatoalkanecarbonyl chlorides[11,12]. We now wish to report the application of trichloromethyl carbonochloridate in the dehydration of aldoximes to nitriles. Considering the general proposed mechanism of the dehydration of aldoximes by a reactive electrophilic reagent[13-22], it is expected that trichloromethyl carbonochloridate would undergo similar reaction pathway. Indeed, when we reacted trichloromethyl carbonochloridate with aldoximes, the reaction proceeded extremely fast to provide nitriles in good yield. Unlike other reagents which require a concomitant base to achieve the 1,2-elimination, trichloromethyl carbonochloridate dehydrates aldoximes without the presence of a base. We attempt to postulate that the driving force for the rapid dehydration is probably due to the powerful electron withdrawing effect of the $-CCl_3$ group which facilitates the decarboxylation and the 1,4-elimination in a concerted process.





The reaction is applicable to alkyl, aralkyl, aryl and heteroaryl aldoximes. Although numerous methods are available for the dehydration of aldoximes to nitriles[23], present method offers several advantages, such as short reaction time, simple work-up, good yield and broad scope.

Table. Preparation of Nitriles From Aldoximes[a]

Product	R	Yield[b] [%]	m.p. [°C] or b.p. [°C]/torr	
			found	reported
3a	c-C_6H_{11}	87	47/1.8	76/16[25]
3b	n-C_6H_{13}	89	53/2.5	71/10[24]
3c	$(CH_3)_3C$	76	105/755	105/760[24]
3d	$C_6H_5CH_2$	86	80/0.5	107/12[24]
3e	$C_6H_5CH{=}CH$	88	70/0.2	135/28[24]
3f	2-Furyl	89	145/755	146/738[24]
3g	2-Thienyl	77	57/2.5	192/760[25]
3h	2,6-$Cl_2C_6H_3$	96	145–146	143[25]
3i	3-$O_2NC_6H_4$	94	115–117	118[24]
3j	2-HOC_6H_4	82	93–95	98[24]
3k	2-BrC_6H_4	92	53–54	55[24]
3l	2,6-$(O_2N)_2C_6H_3$	97	53–55	58[25]
3m	4-$MeOC_6H_4$	87	59–60	61[24]
3n	2-Naphthyl	90	62–64	66[24]

[a] All nitriles prepared are known compounds and were identified by their physical properties and spectral data (m.p., b.p., IR and ^{1}H-NMR).

[b] Yield of pure, isolated product.

Trichloromethyl chloroformate was purchased from Fluka Chemical Corp., Hauppauge, New York. The aldoximes were either purchased commercially or prepared according to conventional methods.

Caution: Since the by-product trichloromethanol decomposes instantaneously into phosgene and hydrogen chloride, care must be exercised at all time. Carbon dioxide is evolved in the reaction, facilitating the escape of phosgene into the atmosphere. It is therefore highly recommended that the escaping gases are passed through a gas washing bottle containing sufficient sodium hydroxide solution to react with the phosgene, carbon dioxide and hydrogen chloride produced.

Preparation of Nitriles from Aldoximes; General Procedure:

In a well ventilated hood, trichloromethyl chloroformate (32.1 g, 0.15 mol) is added dropwise to a stirred solution of aldoxime (0.1 mol) in acetonitrile (50 ml). An increase in temperature is observed. After stirring for 5 minutes, ice-water (200 g) is slowly added to the reaction mixture to destroy any excess chloroformate and the generated phosgene. *Caution*: phosgene is hydrolyzed by water only slowly. Stirring must therefore be continued until no phosgene remains (see the Merck Index for details on the detection of phosgene).

Isolation and Purification:

In the case of solid nitriles, the solid precipitate is filtered, washed with water, air-dried and recrystallized from isopropyl ether to afford an analytically pure product.

In the case of liquid nitriles, ether (200 ml) is added to the mixture, and the organic layer is separated, washed successively with water, 5% sodium hydrogen carbonate, brine, dried over magnesium sulfate, and concentrated to an oil. If desired, the oil could be distilled to afford the pure nitrile.

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