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AN EFFICIENT SYNTHESIS OF NITRILES FROM ALDOXIMES.

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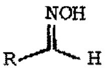
Recently the trifluoromethanesulfonyl (CF_3SO_2-, trifyl) group has proven to be a useful activating functionality in organic synthesis. Reports from this and other laboratories have demonstrated that the trifyl group can activate protons on carbon[1] and nitrogen[2] for bond-forming reactions, and can convert alcoholic-oxygen into an excellent leaving group.[3] Our systematic investigations in this area have led to a new, efficient method for the synthesis of nitriles from aldoximes.

Although many methods for this conversion are known, they have drawbacks such as low yields, harsh reaction and workup conditions, or non-generality for both aryl and alkyl oximes.[4-6] We wish to report that the use of triflic anhydride[7] as a dehydrating agent overcomes these difficulties and results in a high-yield conversion of aldoximes to nitriles under very mild conditions (eq. 1).



$$\xrightarrow[\mathrm{CH_2Cl_2},\ (-78^\circ \rightarrow \mathrm{RT})]{(\mathrm{CF_3SO_2})_2\mathrm{O},\ 2\mathrm{NEt_3}} \mathrm{RCN} + 2(\mathrm{H\overset{+}{N}Et_3}\quad \mathrm{CF_3SO_3^-}) \qquad (1)$$

In a typical procedure, m-nitrobenzaldoxime (10 mM, 1.66 g) and NEt_3 (dist. from CaH_2, 21 mM, 2.12 g) are dissolved in 40 ml of CH_2Cl_2 (dist. from P_2O_5). The flask is flushed with N_2 and cooled (-78°). Triflic anhydride (10 mM, 2.82 g) in 10 ml of CH_2Cl_2 (dist. from P_2O_5) is added over a period of 15 minutes to the oxime solution. The reaction mixture is allowed to warm to RT (ca. 2 hr). The yellow solution is washed with H_2O (3x, 50 ml), satd. brine (3x, 50 ml), dried ($MgSO_4$), and concentrated under reduced pressure to give 1.39 (93.9%) of crude m-nitrobenzonitrile. The crude product was recrystallized from EtOH-H_2O (5:95) to give 1.30 g of colorless needles (87.9%, mp 117°; lit[8] 117-118°).

The results of our experiments are compiled in Table I.

Table I. Synthesis of Nitriles from Aldoximes[a]

Aldoxime	Nitrile	Yield[b]
$PhCH{=}NOH$	$PhCN$	90.3%
$PhCH_2CH_2CH{=}NOH$	$PhCH_2CH_2CN$	91.7%
$Ph(CH_3)CH{=}NOH$	$Ph(CH_3)CHCN$	88.5%
$CH_3CH_2CH_2CH_2CH_2CH{=}NOH$	$CH_3CH_2CH_2CH_2CH_2CN$	93.7%
$m\text{-}NO_2\text{-}PHCH{=}NOH$	$m\text{-}NO_2\text{-}PhCN$	87.9%
(t) $PhCH{=}CHCH{=}NOH$[c]	(t) $PhCH{=}CHCN$	84.5%
(t) $PhCH{=}CHCH{=}NOH$(syn)	(t) $PhCH{=}CHCN$	90.3%
(t) $PhCH{=}CHCH{=}NOH$(anti)	(t) $PhCH{=}CHCN$	92.8%
$Ph_2CHCH{=}NOH$[c]	Ph_2CHCN	92.5%

a) All aldoximes and nitriles had identical physical and spectral properties to those of the known compounds.
b) Distilled or crystallized yields.
c) Mixture of syn- and anti-isomers.

Phenyl triflimide[9] ($PhN(SO_2CF_3)_2$), a much milder triflating agent gives similar yields but is unsatisfactory as a reagent for this conversion due to difficulty in separating the nitrile from triethylammonium phenyltriflamide ($H\overset{+}{N}Et_3\ Ph\overset{-}{N}SO_2CF_3$) formed in the reaction.[10]

As can be seen from the table, the geometry of the oxime is not critical in the reaction. Both syn- and anti- cinnamyl oximes give comparable yields of the nitrile. The high yields obtained for the wide variety of substrates demonstrate the generality of this procedure.

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