

A CONVENIENT SYNTHESIS OF NITRILES FROM PRIMARY AMIDES
UNDER MILD CONDITIONS

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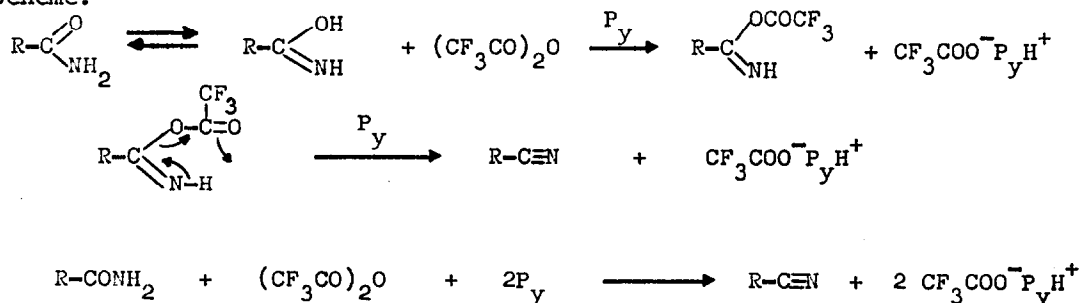
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In the course of our investigations on the dehydration of adducts from 1,2,3-Indantrione with CH-acid compounds (1), we have observed that trifluoroacetic anhydride easily converts the primary carboxamido group into the cyano group.

Many methods for this conversion are known (2-10) but generally they have drawbacks such as unsatisfactory yields, vigorous reaction conditions or difficult workup procedures; more recently the amide dehydration has been obtained with better yields and under milder conditions (11,12,13,14), although the reagents employed were somewhat unusual.

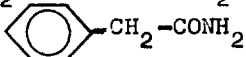
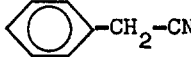
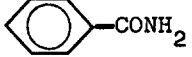





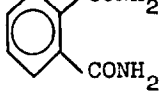
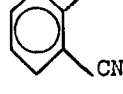
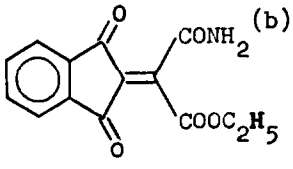
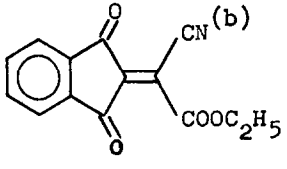
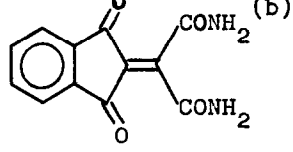
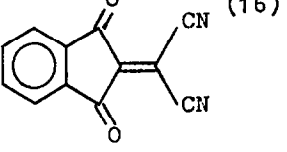
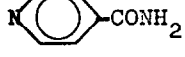

In the present paper we wish to report a new method which, by using the trifluoroacetic anhydride-pyridine system, leads to a rapid amide → nitrile transformation with high yields.

By analogy to the mechanism proposed for the reaction of primary amides with arylsulfonyl chlorides (15), the dehydration reaction probably proceeds according to the pathway and the stoichiometry shown in the following scheme:



P_y = Pyridine

TABLE I (a)

Amides	Nitriles	Method	Yields ^(c)
$\text{CH}_3\text{-CONH}_2$	$\text{CH}_3\text{-CN}$	A	85% ^(f)
$\text{CH}_3\text{-(CH}_2\text{)}_{16}\text{-CONH}_2$	$\text{CH}_3\text{-(CH}_2\text{)}_{16}\text{-CN}$	A	94%
$\text{H}_2\text{NOC-(CH}_2\text{)}_4\text{-CONH}_2$	$\text{NC-(CH}_2\text{)}_4\text{-CN}$	A	70% ^(d)
trans $\text{H}_2\text{NOC-CH=CH-CONH}_2$	trans NC-CH=CH-CN	A	50% ^(e)
		A	97%
		A	99%
		A	88%
		A	94%
		A	85%
		B	91%
		B	92%
		A	90%

a) All known nitriles show physical and spectral properties identical to those reported in the literature.

b) New compounds: the analytical, physical and spectral data are consistent with the indicated structures and will be reported in a forthcoming publication [see reference (1)].

c) Yields of solid nitriles are referred to the crystallized product while gas-chromatographic yields are reported for liquid nitriles.

d) Yield of distilled product.

e) Yield of sublimed product.

f) Gas-chromatographic yield estimated directly on the reaction mixture.

General procedure:

Trifluoroacetic anhydride (ml 3.06, 22m. moles) was added dropwise to a stirred ice-cooled solution (or suspension) of the amide (20 m.moles) in anhydrous dioxane (5-30 ml) and anhydrous pyridine (3.23 ml, 40 m.moles) (17) at such a rate that the temperature was kept below 5°C. Usually the addition was completed over a period of about 45 minutes.

The reaction mixture was then allowed to warm to room temperature and stirred for another 3 hours (18). The resulting thick slurry was worked according to one of the two following methods:

(A) the pyridinium salt was removed by filtration and the filtrate was diluted with chloroform (30 ml), washed with water (2x5 ml) and saturated brine (2x5 ml), dried on Na_2SO_4 and evaporated under vacuum. The crude solid nitriles were then crystallized. The yields of liquid nitriles were estimated by gas-chromatography directly on the foregoing chloroformic solution;

(B) 150-200 g. of ice were added to the reaction mixture and the solid product was removed by filtration, washed with water and crystallized.

The excellent yields shown in table I, and the very mild reaction conditions, demonstrate the usefulness and the versatility of this new synthetic method especially for thermally labile nitriles.

Aldoximes are also utilized as starting materials for nitriles; Hendrickson and co-workers have recently described this conversion by using trifluoromethansulfonyl anhydride (19); the better accessibility of trifluoroacetic anhydride prompted us to extend our procedure also to this dehydration reaction.

In a preliminary trial p-nitrobenzotrile was obtained from the corresponding aldoxime in 85% yield (crystallized product).

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