

## Facile Conversion of Carboxamides to Nitriles with 1,1'-Sulfinylbis-1,2,4-triazole under Mild Conditions

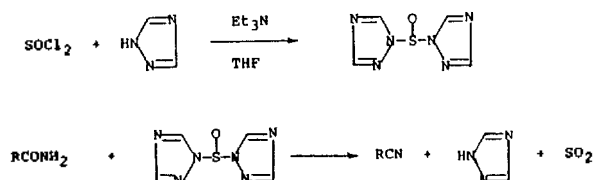
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The conversion of carboxamides to nitriles is a well-known reaction and a number of methods for carrying out such conversion have been reported. This reaction can be generally carried out with various dehydrating agents. They include thionyl chloride,<sup>1</sup> phosphorous pentoxide,<sup>2</sup> cyanuric chloride,<sup>3</sup> aluminum chloride,<sup>4</sup> trifluoroacetic anhydride,<sup>5</sup> and diphosgene.<sup>6</sup> However, each method often involves heating and/or acidic conditions which may not be useful to complex molecules.

In connection with our research program toward the development of new condensing agents, we have reported that di-2-pyridyl sulfite is very effective for the conversion of aromatic carboxamides into the corresponding nitriles under extremely mild conditions.<sup>7</sup> However, this method does not work with aliphatic carboxamides. We wish to report that 1,1'-sulfinylbis-1,2,4-triazole is very effective for a facile conversion of carboxamides into nitriles under mild conditions.



1,1'-Sulfinylbis-1,2,4-triazole was easily prepared by the reaction of thionyl chloride with 2.0 equiv of 1,2,4-triazole and triethylamine in tetrahydrofuran at 0°C for 1 h. Since the reagent was hydrolyzed during aqueous workup or silica gel column chromatographic purification, it was used as a crude form after filtering off triethylamine hydrochloride and subsequent solvent removal. 1,1'-Sulfinylbis-1,2,4-triazole was obtained in 85-95% yields as a pale yellow solid and could be stored in a refrigerator for several weeks without little decomposition.

Table 1 shows some experimental results and illustrates the efficiency and applicability of the present method. The present method works well with aliphatic carboxamides. For instance, 2-ethylhexanamide was smoothly converted into 2-ethylhexanonitrile with the reagent in methylene chloride at room temperature in 20 min, whereas the reaction required 4.5 h at reflux in benzene with thionyl chloride,<sup>1</sup> demonstrating the efficiency of the present method. Similarly, aromatic carboxamides were converted into the corresponding nitriles in high yields under similar conditions. However, p-nitrobenzamide was inert to the reagent and the starting material was recovered unchanged. Carboxamides containing acid-labile protective groups such as tetrahydropyranyl and t-butyltrimethylsilyl ether were cleanly converted into the corresponding nitriles in high yields. Furthermore, another noteworthy feature of the present method includes the possible application in base-sensitive compounds because 1,2,4-triazole (pK<sub>a</sub> 2.2)<sup>9</sup> as the only other product formed is a very weak base, as compared with imidazole (pK<sub>a</sub> 6.95).

Table 1. Preparation of Nitriles from Carboxamides<sup>a</sup>

amide RCONH <sub>2</sub>	time, min	isolated yield, % <sup>e</sup> RCN
CH <sub>3</sub> (CH <sub>2</sub> )CONH <sub>2</sub>	10	89
CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> CH(CH <sub>2</sub> CH <sub>3</sub> )CONH <sub>2</sub>	20	93
Br(CH <sub>2</sub> ) <sub>5</sub> CONH <sub>2</sub>	10	86
c-C <sub>6</sub> H <sub>11</sub> CONH <sub>2</sub> <sup>b</sup>	10	85
C <sub>6</sub> H <sub>5</sub> CH=CHCONH <sub>2</sub>	20	90
C <sub>6</sub> H <sub>5</sub> CONH <sub>2</sub>	20	82
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CONH <sub>2</sub>	20	80
p-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub>	20	91
p-CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub>	20	99
p-O <sub>2</sub> N-C <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub>	180	0
THP-O(CH <sub>2</sub> ) <sub>5</sub> CONH <sub>2</sub> <sup>c</sup>	20	80
TBDMS-O(CH <sub>2</sub> ) <sub>5</sub> CONH <sub>2</sub> <sup>d</sup>	20	85

<sup>a</sup> The reaction was carried out with 1.2 equiv of the reagent in methylene chloride at room temperature. <sup>b</sup> c-C<sub>6</sub>H<sub>11</sub> refers to cyclohexyl group. <sup>c</sup> THP: tetrahydropyranyl. <sup>d</sup> TBDMS: t-butyltrimethylsilyl. <sup>e</sup> Physical and spectral data of the products are in accord with reported values.

Finally, it is of interest to note that conversion of carboxamides to nitriles with 1,1'-sulfinylbisimidazole<sup>10</sup> turned out to be not very effective. Thus, the reaction of octanamide with 2.0 equiv of 1,1'-sulfinylbisimidazole in methylene chloride at room temperature gave 25% of octanonitrile and 25% of starting material along with a significant amount of unidentified black solids and a small amount of (9%) of octanoyl imidazole, resulting apparently from the transfer of imidazolyl group. Such phenomenon has been previously noted with N-chlorosulfinylimidazole.<sup>11</sup>

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- mp 98-101 °C; NMR(CDCl<sub>3</sub>) δ 8.20 (s, 1H), 9.10 (s, 1H).
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