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

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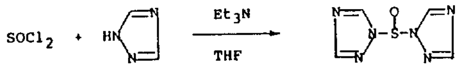
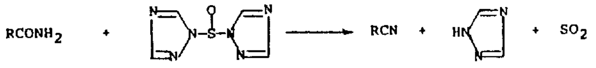
The conversion of carboxamides to nitriles is a well-known reaction and a number of methods for carrying out such conversion have been reported. This reaction can be generally carried out with various dehydrating agents. They include thionyl chloride,[1] phosphorous pentoxide,[2] cyanuric chloride,[3] aluminum chloride,[4] trifluoroacetic anhydride,[5] and diphosgene.[6] 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.[7] 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,[1] 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-butyldimethylsilyl 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_a 2.2)[9] as the only other product formed is a very weak base, as compared with imidazole (pK_a 6.95).

Table 1. Preparation of Nitriles from Carboxamides[a]

amide $RCONH_2$	time, min	isolated yield, %[e] RCN
$CH_3(CH_2)CONH_2$	10	89
$CH_3(CH_2)_3CH(CH_2CH_3)CONH_2$	20	93
$Br(CH_2)_5CONH_2$	10	86
$c\text{-}C_6H_{11}CONH_2$[b]	10	85
$C_6H_5CH=CHCONH_2$	20	90
$C_6H_5CONH_2$	20	82
$C_6H_5CH_2CONH_2$	20	80
$p\text{-}CH_3\text{-}C_6H_4CONH_2$	20	91
$p\text{-}CH_3O\text{-}C_6H_4CONH_2$	20	99
$p\text{-}O_2N\text{-}C_6H_4CONH_2$	180	0
$THP\text{-}O(CH_2)_5CONH_2$[c]	20	80
$TBDMS\text{-}O(CH_2)_5CONH_2$[d]	20	85

[a] The reaction was carried out with 1.2 equiv of the reagent in methylene chloride at room temperature. [b] $c\text{-}C_6H_{11}$ refers to cyclohexyl group. [c] THP: tetrahydropyranyl. [d] TBDMS: t-butyldimethylsilyl. [e] 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[10] 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 samll amout of (9%) of octanoyl imidazole, resulting apparently from the transfer of imidazolyl group. Such phenomenon has been previously noted with N-chlorosulfinylimidazole.[11]

References

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