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## A NEW METHOD FOR THE GENERATION OF NITRILES FROM ALDOXIMES

**Binoy Jose, M. S. Sulatha, P. Madhavan Pillai, Sreedharan Prathapan\***

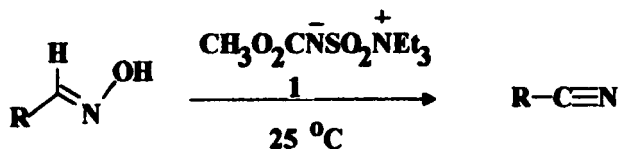
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**Abstract;** A mild and efficient method for the stereoselective dehydration of  $\alpha$ -aldoximes to the corresponding nitriles is described which utilises methyl (carboxysulfamoyl)triethylammonium hydroxide inner salt (Burgess reagent) as the dehydrating agent.

The importance of nitriles as intermediates in organic synthesis is well established. Furthermore, nitriles are reversible inhibitors of thiol protease enzymes.<sup>1</sup> Hence developing a general and mild method for their preparation is of considerable interest. The dehydration of aldoximes offers a convenient approach to nitriles<sup>2</sup>. However, most of the reported procedures require higher temperatures and give poor yields with heteroaromatic aldoximes. We have now discovered that Burgess reagent (methyl (carboxysulfamoyl)triethylammonium hydroxide inner salt<sup>3</sup> 1) is a mild and efficient reagent for the dehydration of  $\alpha$ -aldoximes (Scheme 1).

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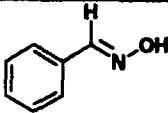
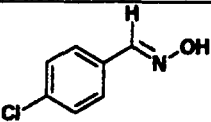
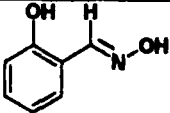
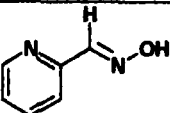
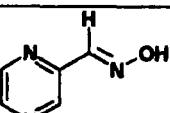
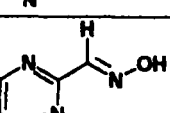
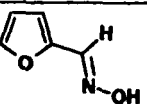
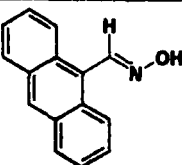
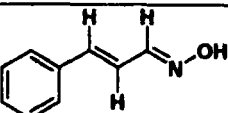
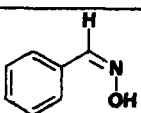


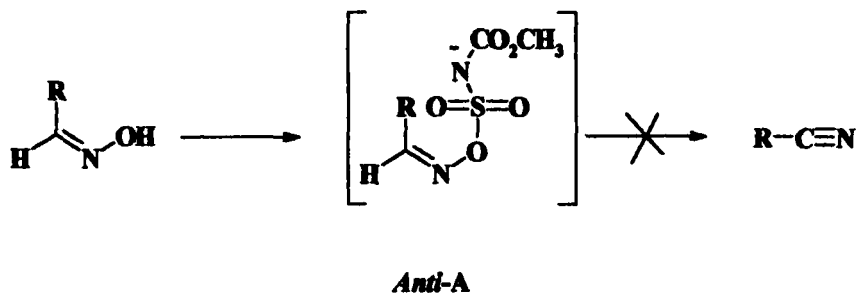
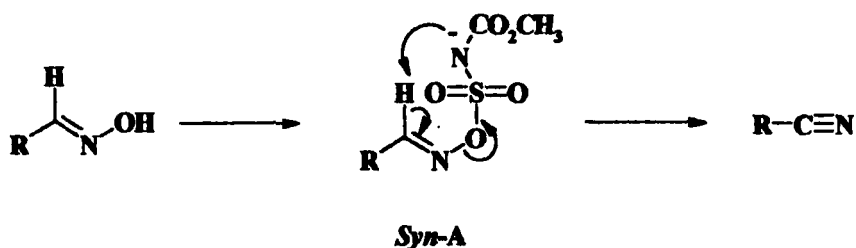
Scheme 1

Burgess reagent has previously been applied for the dehydration of secondary and tertiary alcohols to olefins<sup>4</sup>, the chemoselective conversion of amides to nitriles<sup>5</sup>, stereospecific synthesis of dihydrooxazoles from serine and threonine derivatives,<sup>6</sup> generation of nitrile oxides from primary nitroalkanes<sup>7</sup> and inazole synthesis<sup>8</sup>. It has also been reported that aldoximes undergo Beckmann rearrangement in the presence of the reagent<sup>3</sup>. The observation that amides undergo facile dehydration in the presence of Burgess reagent<sup>5</sup> led us to reinvestigate the reaction of aldoximes with Burgess reagent.

Treatment of  $\alpha$ -benzaloxime with 3 equiv. of Burgess reagent in methylene chloride at room temperature, for 2 h led to the isolation of benzonitrile in a 66% yield. In order to illustrate the wide applicability of this procedure, dehydration experiments were attempted on a variety of aldoximes. It should be noted that heteroaromatic aldoximes are efficiently converted to the corresponding nitriles. The following table summarises our results from the dehydration experiments. Here the interesting observation is that only  $\alpha$ -aldoximes undergo dehydration. We attempted the reaction on  $\beta$ -benzaloxime and the unreacted oxime was recovered almost quantitatively even after prolonged exposure to Burgess reagent. Thus it is clear that the dehydration of aldoximes with Burgess reagent exhibits remarkable stereoselectivity. The method reported by us is the first report on the development of a reagent specific for the dehydration of  $\alpha$ -aldoximes.

Table I

entry	starting oxime	reaction condition	isolated yield
1		3 equiv. Burgess reagent in CH <sub>2</sub> Cl <sub>2</sub> at 25 °C for 2 h	66%
2		3 equiv. Burgess reagent in CH <sub>2</sub> Cl <sub>2</sub> at 25 °C for 2 h	51%
3		3 equiv. Burgess reagent in CH <sub>2</sub> Cl <sub>2</sub> at 25 °C for 2 h	52%
4		3 equiv. Burgess reagent in CH <sub>2</sub> Cl <sub>2</sub> at 25 °C for 2 h	58%
5		3 equiv. Burgess reagent in CH <sub>2</sub> Cl <sub>2</sub> at 25 °C for 2 h	61%
6		3 equiv. Burgess reagent in CH <sub>2</sub> Cl <sub>2</sub> at 25 °C for 2 h	63%
7		3 equiv. Burgess reagent in CH <sub>2</sub> Cl <sub>2</sub> at 25 °C for 2 h	43%
8		3 equiv. Burgess reagent in CH <sub>2</sub> Cl <sub>2</sub> at 25 °C for 2 h	53%
9		3 equiv. Burgess reagent in CH <sub>2</sub> Cl <sub>2</sub> at 25 °C for 2 h	30%
10		3 equiv. Burgess reagent in CH <sub>2</sub> Cl <sub>2</sub> at 25 °C for 8 h	No Reaction



Scheme 2

The mechanism which we propose in Scheme 2 is similar to that for the dehydration of amides proposed by Claremon and Phillips<sup>5</sup>. The observed stereoselectivity of the dehydration experiments provides additional support for the proposed mechanism involving a cyclic transition state.

## EXPERIMENTAL

**Dehydration of  $\alpha$ -aldoximes:** The procedure given below for the dehydration of  $\alpha$ -benzaldoxime is typical.  $\alpha$ -Benzaldoxime (47 mg, 0.30 mmol) was dissolved in 1.5 mL of dry methylene chloride and stirred at 25°C under nitrogen. Methyl (carboxysulfamoyl)triethylammonium hydroxide inner salt (Burgess reagent) was added in five 50 mg portions (1.05 mmol) over 2 h. Stirring was continued for an additional 15 min, and the mixture was applied

directly to a silica gel column. The product formed was separated by eluting with a mixture (2:3) of hexane and methylene chloride. The identity of the products formed was established by GC analysis and comparison of IR spectra with those of authentic samples prepared by known procedures.

**Attempted dehydration of  $\beta$ -aldoxime:**  $\beta$ -benzaloxime (47 mg, 0.30mmol) was dissolved in 1.5 mL of dry methylene chloride and stirred at 25°C under nitrogen. Burgess reagent was added in five 50 mg portions (1.05 mmol) over 2 h. Stirring was continued for an additional 6 h. Work up of the reaction mixture in the usual manner led to the quantitative recovery of unchanged  $\beta$ -benzaloxime.

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