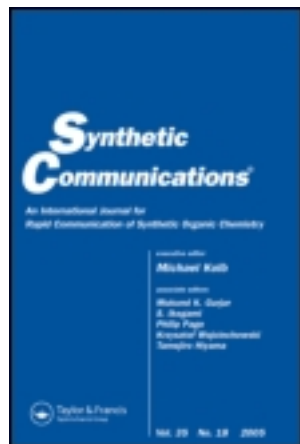


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### Simple and Efficient One-Pot Synthesis of Nitriles from Amides and Oximes Using in Situ-Generated Burgess-Type Reagent

John P. Rappai<sup>a b</sup>, Jayakumar Karthikeyan<sup>a</sup>, Sreedharan Prathapan<sup>a</sup> & Perupparampil A. Unnikrishnan<sup>a</sup>

<sup>a</sup> Department of Applied Chemistry, Cochin University of Science and Technology, Cochin, Kerala, India

<sup>b</sup> Department of Chemistry, Government Victoria College, Palakkad, Kerala, India

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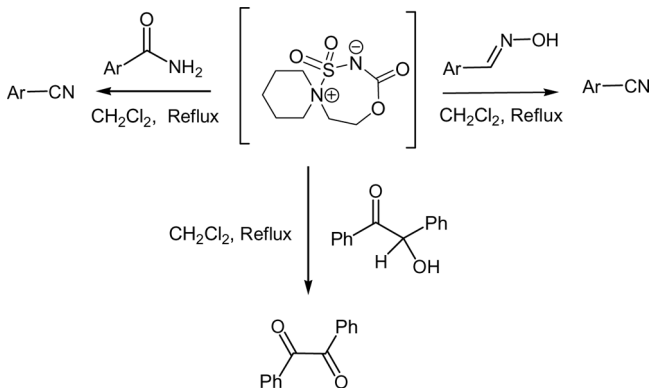
## SIMPLE AND EFFICIENT ONE-POT SYNTHESIS OF NITRILES FROM AMIDES AND OXIMES USING IN SITU-GENERATED BURGESS-TYPE REAGENT

John P. Rappai,<sup>1,2</sup> Jayakumar Karthikeyan,<sup>1</sup>  
Sreedharan Prathapan,<sup>1</sup> and Perupparampil A. Unnikrishnan<sup>1</sup>

<sup>1</sup>Department of Applied Chemistry, Cochin University of Science and Technology, Cochin, Kerala, India

<sup>2</sup>Department of Chemistry, Government Victoria College, Palakkad, Kerala, India

### GRAPHICAL ABSTRACT



**Abstract** The dehydration of aldoximes and amides, and oxidation of benzoin are accomplished in one-pot using in situ-generated Burgess-type reagent.

**Keywords** Amide; benzil; benzoin; Burgess reagent; Burgess-type reagent; dehydration; nitrile; oxidation; oxime

## INTRODUCTION

Burgess reagent<sup>[1]</sup> and its various analogs are extensively used in the field of synthetic organic chemistry. Apart from various dehydration reactions under mild conditions, they are also used for the cyclodehydration of hydroxyamides and thioamides to the corresponding heterocycles.<sup>[2]</sup> Burgess reagent is successfully used for

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Address correspondence to Perupparampil A. Unnikrishnan, Department of Applied Chemistry, Cochin University of Science and Technology, Cochin 682 022, Kerala, India. E-mail: paunni@cusat.ac.in

the synthesis of chiral  $\beta$ -aminoalcohols,<sup>[3]</sup> carbamates of unsaturated  $\beta$ -aminoacids from Baylis–Hillman adducts,<sup>[4]</sup> sulfamidates from epoxides,<sup>[5]</sup> sulfamidates from 1,2-diols or epoxyalcohols,<sup>[6]</sup>  $\alpha$ - and  $\beta$ -glycosylamines from carbohydrates,<sup>[7]</sup> cyclic sulfamidates, and  $\beta^{2,2'}$ -aminoacids.<sup>[8]</sup> Wood et al. developed a modified Burgess reagent for converting primary alcohols to carbamate protected amines.<sup>[9]</sup> Major applications of Burgess reagent and its analogs are based on their remarkable dehydrating property.<sup>[10]</sup>

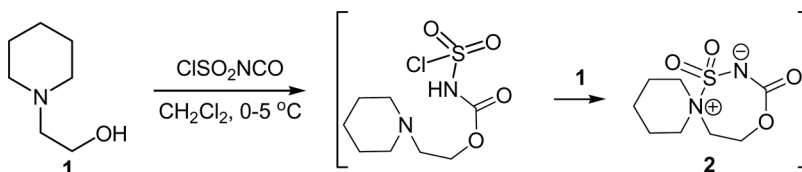
Our group has demonstrated that Burgess reagent can effectively and stereoselectively dehydrate  $\alpha$ -aldoximes to nitriles under very mild conditions.<sup>[11]</sup> We also established that Burgess reagent can efficiently oxidize benzoin to benzils.<sup>[12]</sup> Here, we report a simple and efficient one-pot synthesis of nitriles from amides and oximes using in situ-generated Burgess-type reagent.

Burgess reagent is prepared in two steps by the reaction of chlorosulfonyl isocyanate with an alcohol followed by treatment with a tertiary amine such as triethylamine. The major drawback of conventional Burgess reagent is its limited shelf life. Wipf et al. developed polythelyne glycol (PEG)-supported Burgess reagent to surmount this limitation, but these PEG-supported reagents are found to be less efficient than the conventional one.<sup>[13]</sup> We surmised that treatment of chlorosulfonyl isocyanate with a suitable  $\beta$ -aminoalcohol should yield a cyclic Burgess-type reagent (CBR, **2**) in one step.

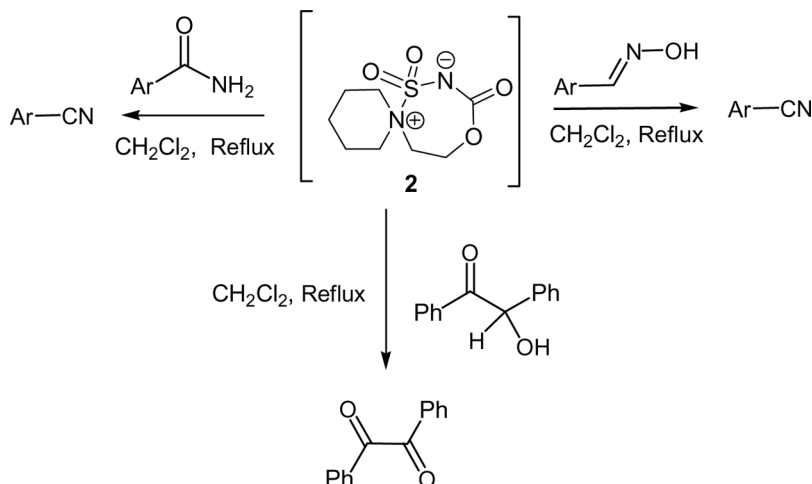
CBRs can be used as such without isolation and purification for effecting various transformations possible with conventional Burgess reagent. With a view to make the procedure simple and more efficient, we carried out the dehydration of aldoximes and primary amides to the corresponding nitriles and oxidation of benzoin to benzil using an in situ-generated Burgess-type reagent in a one-pot synthetic protocol. Because the reactions proceeded smoothly, no attempts were made to isolate the CBR in pure form.

## RESULTS AND DISCUSSION

A few aldoximes<sup>[14]</sup> and amides<sup>[15]</sup> were prepared according to the literature procedures. For the in situ preparation of CBR, a mixture of 1-(2-hydroxyethyl)-piperidine (**1**) and chlorosulfonyl isocyanate was stirred in dry  $\text{CH}_2\text{Cl}_2$  for about 20 min at 0–5 °C. In all the runs, excess of **1** was used to ensure complete consumption of chlorosulfonyl isocyanate and efficient generation of the inner salt. To this mixture, the aldoximes were added and refluxed for 1 h to get the corresponding nitriles in very good yields (Scheme 2). The dehydration reaction is assumed to proceed through a cyclic Burgess-type reagent **2**.



Scheme 1. In situ generation of CBR.



**Scheme 2.** Reactions of CBR.

We found that the same protocol is suitable for dehydration of primary amides to the corresponding nitriles in good yields (Scheme 2).

The substrates, products, and yields are summarized in Table 1.

Interestingly, the same procedure could be adapted to efficiently oxidize benzoin to benzil (Scheme 2).

In all the experiments involving in situ-generated CBR, yields were consistently better than those reported with conventional Burgess reagent. Thus, reactions involving CBRs are simpler, faster, and more efficient than those reported with conventional Burgess reagent. Furthermore, we have demonstrated that CBR solution can be stored in a refrigerator without noticeable loss of activity for several days, attesting to the stability of CBRs.

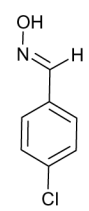
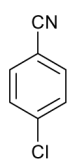
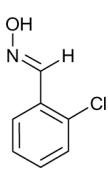
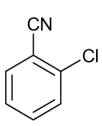
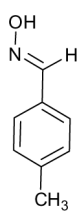
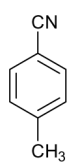
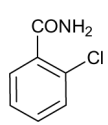
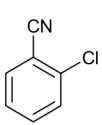
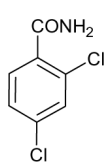
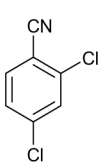
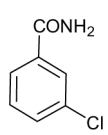
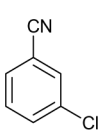
To conclude, we have developed an efficient and quick protocol for the dehydration of aldoximes and amides and oxidation of benzoin by an in situ-generated cyclic Burgess-type reagent.

## EXPERIMENTAL

### General Procedure for Dehydration of Oximes and Amides

Chlorosulfonyl isocyanate (10 mmol) was added dropwise to a solution of 1-(2-hydroxyethyl)piperidine (**1**, 20 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (10 mL) at  $0-5^\circ\text{C}$  and the mixture was stirred for about 20 min. It was then refluxed with aldoximes or amides (5 mmol). The progress of the reaction was monitored by thin-layer chromatography (TLC). After 1 h of refluxing, the reaction mixture was cooled and filtered. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel using a mixture of hexane-dichloromethane (4:1) as eluent, affording the corresponding nitriles in very good yields. These nitriles were characterized by comparing their spectral and analytical data with those of authentic samples.

**Table 1.** Dehydration of aldoximes and amides into corresponding nitriles

Entry	Substrate	Product	Yield (%)
1			90
2			89
3			95
4			93
5			88
6			90

### Procedure for Dehydrogenation of Benzoin

Chlorosulfonyl isocyanate (10 mmol) was added dropwise to a solution of 1-(2-hydroxyethyl)piperidine (**1**, 20 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (10 mL) at  $0-5^\circ\text{C}$  and the mixture was stirred for about 20 min. It was then refluxed with benzoin (5 mmol). The progress of the reaction was monitored by TLC. After 1 h of refluxing, the reaction mixture was cooled and filtered. The solvent was removed, and the residue was purified by column chromatography on silica gel using a mixture of hexane–dichloromethane (4:1) as eluent, affording the corresponding benzil in good yields. Benzil

obtained was characterized by comparing the melting point and spectral data with those of authentic samples.

## ACKNOWLEDGMENT

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