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ORIGINAL ARTICLE

Correlation analysis of reactivity in the oxidation of methionine by benzimidazolium fluorochromate in different mole fractions of acetic acid–water mixture

S. Sheik Mansoor [a,*], S. Syed Shafi [b], S. Zaheer Ahmed [a]

[a] *Research Department of Chemistry, C. Abdul Hakeem College, Melvisharam 632 509, Tamil Nadu, India*
[b] *Research Department of Chemistry, Thiruvalluvar University, Vellore 632106, Tamil Nadu, India*

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Abstract The kinetics of oxidation of methionine (Met) by benzimidazolium fluorochromate (BIFC) has been studied in the presence of chloroacetic acid. The reaction is first order with respect to methionine, BIFC and acid. The reaction rate has been determined at different temperatures and activation parameters calculated. With an increase in the mole fraction of acetic acid in its aqueous mixture, the rate increases. The solvent effect has been analyzed using the Kamlet's multi parametric equation. A correlation of data with the Kamlet–Taft solvatochromic parameters (α, β, π^*) suggests that the specific solute–solvent interactions play a major role in governing the reactivity. The reaction does not induce polymerization of acrylonitrile. A suitable mechanism has been proposed.

1. Introduction

The development of oxidizing agents based upon higher-valent transition metal oxo derivatives has been a subject of research in many laboratories and a host of such reagents derived from ruthenium, osmium, iron, manganese, molybdenum, vanadium and chromium have all proven to be capable of oxidation of organic substrates. In particular, there is continued interest in the development of new chromium(VI), Cr(VI) reagents for the effective and selective oxidation of organic substrates under mild conditions. A number of new Cr(VI) containing compounds like quinolinium fluorochromate (Dave et al., 2002) tributylammonium chlorochromate (Mansoor and Shafi, 2010a), quinolinium dichromate (Medien, 2003), tripropylammonium fluorochromate (Mansoor and Shafi, 2010b), imidazolium fluorochromate (Pandurangan et al., 1999), isoquinolinium bromochromate (Vibhute et al., 2009) tetrabutylammonium bromochromate (Ghammamy et al., 2007), tetraheptylammonium bromochromate (Ghammamy et al., 2009), tetrahexylammonium fluorochromate (Koohestani et al., 2008), tetramethylammonium fluorochromate (Sadeghy and Ghammamy, 2005) and tetraethyl ammonium bromochromate (Mansoor and Shafi, 2011) have been used

* Corresponding author. Tel.: +91 9944093020.
E-mail addresses: smansoors2000@yahoo.co.in (S. Sheik Mansoor), suban_shafi@yahoo.com (S. Syed Shafi).

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to study the kinetics and mechanism of various organic compounds.

The oxidation of methionine (Met) plays an important role during biological conditions of oxidative stress as well as for protein stability (Venkataramanan et al., 2007). Oxidation of methionine has been studied extensively using different oxidants (Satsangi et al., 1995; Ghosh et al., 1999; Sharma et al., 1997; Pandeeswaran et al., 2005; Zaheer Khan, 1997; Meenashisundaram and Vinothini, 2003). Methionine (Met) is an important amino acid in human nutrition that is only available from food sources (Lee and Gladydhev, 2011). It is a versatile amino acid at the junction of several metabolic pathways. For example, Met (N-formylmethionine in prokaryotes) is used as the first (N-terminal) amino acid during translation and can often be a limiting factor in protein synthesis, especially under conditions of Met deficiency. Met is also a crucial metabolite that influences redox homeostasis through sulfur metabolism and the transsulfuration pathway (Metayer et al., 2008; Deth et al., 2008). Met is the source of several antioxidants and other sulfur compounds, which function in the defense against oxidative stress, such as glutathione (GSH), taurine, and cysteine (Cys), and therefore, Met is a core amino acid that supplies antioxidants to balance the cellular redox status against the attack by reactive oxygen species (ROS). In addition, S-adenosylmethionine (SAM), another key metabolite produced from Met, is a major methyl donor in cells and an epigenetic regulator (Waterland, 2006). Aerobic organisms generate ROS as products or by-products of mitochondrial respiration, xanthine oxidase, NADPH oxidase, and other metabolic processes and enzymes (Kowaltowski et al., 2009).

Accumulative post translational modification to proteins, mediated by the action of ROS, is thought to be one of the major causes of aging and age related diseases. Thus, mechanisms have evolved to prevent or reverse these protein modifications. While most protein damage by ROS is irreversible, methionine oxidation to proteins can be reversed by the methionine sulfoxide reductase (Msr) system, which consists of MsrA (that reduces *S*-MetO) and MsrB (that reduces *R*-MetO), thioredoxin reductase, thioredoxin, and NADPH (Moskovitz, 2005). ROS may damage macromolecules, such as proteins, lipids, and DNA, which leads to an increased incidence of disease and accelerated aging (Lovell and Markesbery, 2007; Valko et al., 2007). In the case of protein oxidation, all amino acids are subject to oxidative modification (Stadtman, 1993). However, Met is one of two common amino acids (together with Cys) that are most susceptible to oxidation by ROS, and therefore enzymatic systems evolved to counteract this damage. In addition, this amino acid may further contribute to antioxidant function when coupled with reductases (Dalle-Donne et al., 2002; Vogt, 1995). Interestingly, Met has a unique oxidation pattern in that two diastereomers are produced, which require separate enzyme systems for their reduction (Lee et al., 2009). Methionine sulfoxide is a major product of Met oxidation. Met is highly susceptible to oxidation by ROS and reactive nitrogen species (RNS) (Lavine, 1994). Generally, all amino acids are subject to free radical-mediated oxidation by radiation, metal catalyzed reactions, mitochondrial respiration, and many other processes generating ROS, but Met is among the most sensitive to oxidation. In the case of metal ion-catalyzed oxidation, α-carbon of amino acids, including that of Met, can undergo oxidative deamination (Stadtman and Berlett, 1991). However, it appears that only ~10% Met is converted to NH_4^+, $RCOO^-$, and O_2, whereas the major product of Met oxidation is Met sulfoxide.

Literature survey reveals that no report is available on the kinetics of oxidation of methionine by BIFC. In this article, the kinetics and mechanism of the oxidation of methionine by BIFC are reported, with the view to understand the utility of solvent variation studies in the understanding of the mechanism of this biologically important amino acid because it may reveal the mechanism of amino acid metabolism.

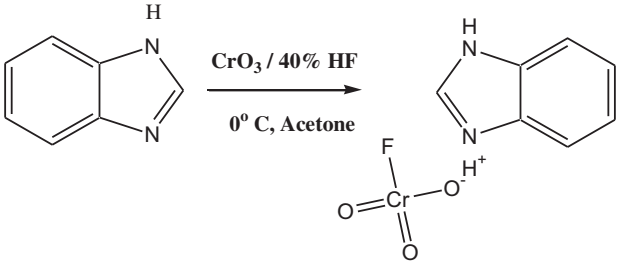
2. Experimental

2.1. Materials and methods

Benzimidazole and chromium trioxide were obtained from Fluka (Buchs, Switzerland). DL-methionine (E Merck, Germany) was used as received. The purities of reagents purchased are 99.9%. Acetic acid was purified by the standard method (Weissberger and Prabankar, 1995) and the fraction distilling at 118 °C was collected. All other chemicals used were of AnalaR grade.

2.2. Preparation of benzimidazolium fluorochromate

Benzimidazolium fluorochromate has been prepared from benzimidazole, 40% hydrofluoric acid and chromium trioxide in the molar ratio 1:1.3:1 at 0 °C. BIFC is obtained as yellow orange crystals. It is non-hygroscopic and light insensitive on storage (Sivamurugan et al., 2005). The purity of BIFC was checked by the iodometric method. The purity is 99.8%. The yield of BIFC was 86%.



Benzimidazole Benzimidazolium fluorochromate (1)

2.3. Stoichiometry and product analysis

The stoichiometry of the reaction was determined by performing the several sets of experiments with varying amounts of BIFC largely in excess over methionine. The disappearance of BIFC was monitored until constant titre values were obtained.

$$Me - S - R + O_2CrFOBIH \rightarrow Me - SO - R + OCrFOBIH \quad (2)$$

$(R = -CH_2CH_2CH(NH_2)COOH)$

The reaction mixture was allowed to stand for a few hours. Then, sodium bicarbonate was added and stirred vigorously, followed by drop wise addition of benzoyl chloride solution. The precipitate N-benzoyl methionine sulphoxide was confirmed by its m.p 183 °C (Goswami et al., 1981). The

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