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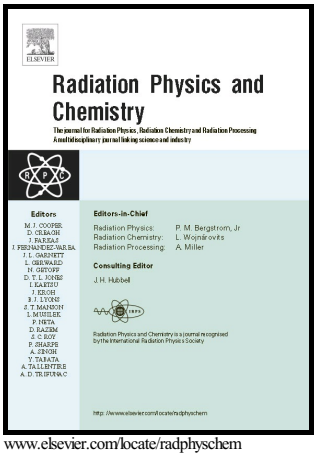

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PII: S0969-806X(18)30272-X
DOI: https://doi.org/10.1016/j.radphyschem.2018.06.004
Reference: RPC7879

To appear in: *Radiation Physics and Chemistry*

Received date: 2 April 2018
Accepted date: 4 June 2018

Cite this article as: Ravi Joshi, Free Radical Induced Redox Reactions of 2,4,6-Triaminopyrimidine: A Pulse Radiolysis Study, *Radiation Physics and Chemistry,* https://doi.org/10.1016/j.radphyschem.2018.06.004

Free Radical Induced Redox Reactions of 2,4,6-Triaminopyrimidine: A Pulse Radiolysis Study

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Abstract

Kinetics and mechanism of reactions of 2,4,6-triaminopyrimidine (TAP) with some free radicals have been studied using pulse radiolysis technique. TAP has been found to react with hydrated electron (3.1×10^8 M^{-1} s^{-1}), hydroxyl radical (4.0×10^9 M^{-1} s^{-1}), trichloromethyl peroxyl radical (1.1×10^8 M^{-1} s^{-1}), and sulfate radical (4.5×10^9 M^{-1} s^{-1}). Density functional calculations have been performed to assign absorption maxima of transients produced on oxidation of TAP as: $TAP^{\bullet+}$ radical cation (~430, ~600, ~720 nm), $TAP(C5)^{\bullet}$ radical (~300, ~320 nm), aminyl $TAP(NH)^{\bullet}$ radical (~300, ~340, ~440 and ~520 nm) and $TAP\text{-}OH^{\bullet}$ radical adduct (640 nm). Almost 72% of TAP transients produced with hydroxyl radical have been found to be oxidizing in nature, which react with tyrosine (8.0×10^7 M^{-1} s^{-1}), glutathione (1.2×10^8 M^{-1} s^{-1}) and bovine serum albumin protein (7.8×10^8 M^{-1} s^{-1}).

Key words

2,4,6-triaminopyrimidine, pulse radiolysis, density functional theory, oxidation, mechanism

1. INTRODUCTION

Pyrimidines (cytosine, uracil and thymine) are part of backbone of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) of all living beings. They are also known to participate in processes as distinct as energy transduction, metabolic cofactors and cell signaling (Brown 1987). A number of synthetic drugs based upon the pyrimidyl structure (5-fluorouracil, 5-thiouracil, flucytosine, tegafur, 1-β-D-arabinosylcytosine, azidothymidine, etc.) show analgesic, anticonvulsant, antiviral, anti-inflammatory, apoptotic, anthelmintic, antibacterial, anti-microbial, anticancer, anti-HIV-1 and anti-rubella virus activities (Botta et al. 2001, Chabner et al. 2001, Rosowsky et al. 2003, Amr et al. 2005, Jain et al. 2006, Naidu et al. 2016). Diaminopyrimidine derivatives like pyrimethamine (antimalarial) and trimethoprim (antibacterial) are used as inhibitors of the enzyme dihydrofolate reductase (DHFR) (Jain et al. 2006). Similarly, 2,4,6-triaminopyrimidine (TAP) (**Scheme 1**) has been widely used to synthesize anti-cancer drugs, such as methotrexate and dyrenium (Jain et al. 2006). Recently, triaminopyrimidine derivatives have also been shown to be promising candidates against plasmodium falciparum, hematological malignancies and inflammatory diseases (Hameed et al. 2015, Patel et al. 2016).