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$K_2S_2O_8$ (Potassium Persulfate)-Mediated Heterocyclic Ring Formations

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Dedicated to Dr. Srinivas and R. Adapa

A variety of oxidants that have demonstrated effective application in the oxidative transformation reactions include molecular oxygen, DDQ, *p*-benzoquinone, TBHP, $PhI(OAc)_2$, I_2, metal oxidants, oxone, persulfates, and others. Among these oxidants, which include both inorganic and organic types, potassium persulfate ($K_2S_2O_8$) has emerged as a cost-effective and easily accessible inorganic oxidant suitable for the purpose. Its applications span from laboratory experiments to industrial processes. This mini-review discusses the role of $K_2S_2O_8$ in the formation of heterocyclic rings, specifically focusing on the synthesis of diverse heterocyclic scaffolds, including simple, fused, and spirocyclic heterocycles. In addition to the advantages, the limitations of the methodologies were also discussed.

1. Introduction

Among the various oxidants, including both organic and inorganic options such as molecular oxygen, TBHP, I_2, Selectfluor, IBX, $NaIO_4$, TEMPO, oxone, persulfates, DDQ, *p*-benzoquinone, PIDA, and DTBP, stable persulfate salts, particularly potassium persulfate ($K_2S_2O_8$), have shown significant interest and effectiveness in comparison to conventional oxidants.[1,2] It has not only gained extensive use in palladium catalysis due to Minisci's contributions, but it has also been employed to perform a range of innovative oxidative transformations independently of any metal catalyst.[3–5] Compared to $K_2S_2O_8$, alternatives like $Na_2S_2O_8$ and $(NH_4)_2S_2O_8$ are considerably less commonly employed. The higher solubility of the potassium salt in organic solvents facilitates a more efficient transformation.[6]

$K_2S_2O_8$ is a stable, cost-effective, odorless inorganic salt characterized by its strong oxidizing properties and low hygroscopic nature, making it easily manageable (Figure 1).[7] In recent decades, $K_2S_2O_8$ has proven to be a highly effective oxidant in various oxidative transformations, generating reactive species, typically the sulfate radical anion (SO_4^{-}), under thermal or photocatalytic conditions.[8] With a redox potential of 2.531 V, SO_4^{-} is recognized as an exceptionally potent one-electron oxidant. In recent years, a significant amount of literature has emerged, emphasizing the potential application of this oxidant in various *metal*-catalyzed and *metal*-free organic reactions.[9,10]

Laha and colleagues documented a range of applications of $K_2S_2O_8$ in both *metal*-catalyzed and *metal*-free oxidative transformations up until 2017.[11] Padala and Kumar outlined the developments in $K_2S_2O_8$-mediated cyclization and coupling reactions through oxidative transformation in organic synthesis up to the year 2020.[12] Mir and Rajamanickam discussed the function of $K_2S_2O_8$ as an environmentally friendly *metal*-free oxidant for a range of oxidative transformations up until mid-2021.[13] The present study concentrates on the application of $K_2S_2O_8$ in oxidative organic transformations, and the review is organized into categories according to the reactions that lead to the formation of pharmacologically significant heterocycles. We anticipate that chemists engaged in or intending to pursue the development of $K_2S_2O_8$-based methodologies for various oxidative processes will find this compilation beneficial, facilitating significant scientific progress in this field.

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*Abbreviations: AIE, Aggregation-induced emission; BIM, Bis(indolyl) methane; BQ, 1,4-Benzoquinone; DDQ, 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone; DHPs, Dihydropyridines; DTBP, Di-*tert*-butyl peroxide; EDG, Electron donating group; EWG, Electron withdrawing group; EPR, Electron Paramagnetic Resonance; HCRF, Heterocyclic ring formation; HEs, Hantschz esters; IBX, 2-Iodoxybenzoic acid; $K_2S_2O_8$, Potassium persulfate; $KHSO_5$, Oxone (Potassium peroxymonosulfate); LED, Light emitting diode; PIDA, Phenyliodine (III) diacetate or (diacetoxyiodo)benzene; PTC, Phase transfer catalyst; TBAB, Tetrabutyl ammonium bromide; TBAI, Tetrabutyl ammonium iodide; TBHP,* tert*-Butyl hydroperoxide; TBPB,* tert*-Butyl peroxybenzoate; TEMPO, 2,2,6,6-Tetramethylpiperidin-1-yl)oxidanyl; ND, Not detected; NR, No reaction.*