Sodium Tungstate Dihydrate ($Na_2WO_4·2H_2O$): A Mild Oxidizing and Efficient Reagent in Organic Synthesis

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Sodium tungstate dihydrate ($Na_2WO_4·2H_2O$) is a simple, cheap, commercially available, and water-soluble colorless crystalline solid inorganic material. It is synthesized when excess tungstic acid is added to aqueous sodium hydroxide, dehydrates at 100 °C, and is insoluble in ethanol. The aqueous solution is slightly alkaline (pH 8–9).[1] The solid can be stored in a hermetically closed flask in a dry place. This compound is usually used as an oxidizing agent in chemistry,[2] affording the corresponding peracid in conjunction with hydrogen peroxide, under mild conditions, that can oxidize amines and sulfur-containing substrates (Scheme 1).[3] Sodium tungstate dihydrate is the most common hydrated form and can also be used as an efficient catalyst for epoxidation of alkenes and oxidation of alcohols into the corresponding carbonyl compounds. For example, Payne and Williams described the first use of sodium tungstate dihydrate for epoxidation of α,β-unsaturated acids.[4] In addition, it can be used to form heterocycles. Table 1 presents a series of recent applications of this reagent.

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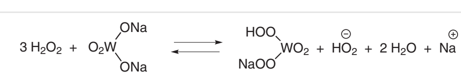
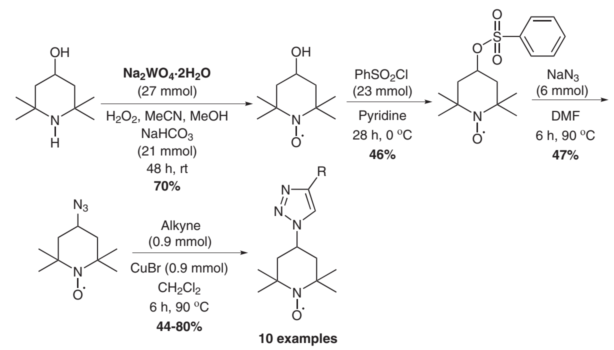


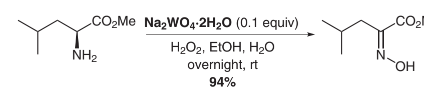
Scheme 1 Peracid formation in the presence of sodium tungstate dihydrate ($Na_2WO_4·2H_2O$)

Table 1 Recent Applications of Sodium Tungstate Dihydrate ($Na_2WO_4{\cdot}2H_2O$)

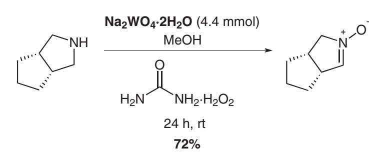
(A) Cunha *et al.* synthesized a series of 4-substituted 1,2,3-1*H*-1,2,3-triazole linked nitroxyl radicals derived from TEMPOL (4-hydroxy-2,2,6,6-tetramethyl-piperidinyl-1-oxy). This class of stable radicals was prepared from 4-hydroxy-2,2,6,6-tetramethylpiperidine with sodium tungstate dihydrate and hydrogen peroxide in 70% yield.[5]



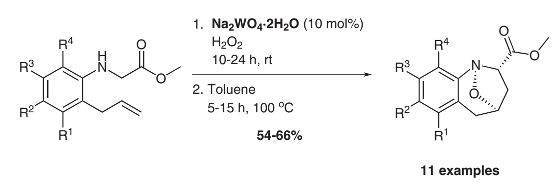
(B) Kuhn *et al.* demonstrated that a primary amine such as methyl L-leucinate could be oxidized with H_2O_2 in the presence of sodium tungstate dihydrate to form the corresponding oxime in excellent yield.[6]



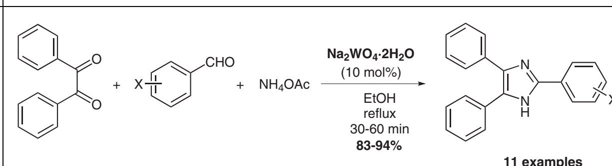
(C) Reddy *et al.* reported the preparation of nitrones by oxidation of bicyclic amines with urea hydrogen peroxide (UHP) at room temperature in methanol in the presence of catalytic sodium tungstate dihydrate.[7]



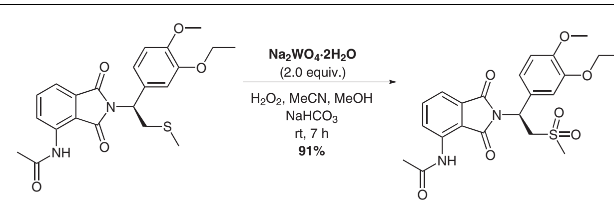
(D) Eleven 1,4-epoxy cycloadducts were prepared in yields of 54–66% by the sequential selective oxidation and intramolecular 1,3-dipolar cycloaddition of methyl 2-(allylaryl)glycinates with an excess of aqueous hydrogen peroxide in the presence of catalytic amounts of sodium tungstate dihydrate.[8]



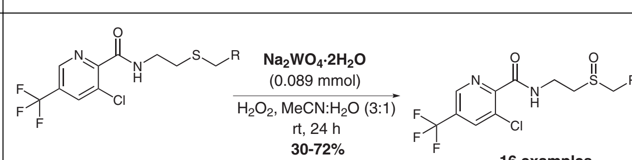
(E) Sodium tungstate dihydrate as a catalyst was disclosed by Kauthale *et al.* in the development of a green protocol for the synthesis of triaryl-substituted imidazoles via one-pot three-component condensation of aldehydes, benzil, and ammonium acetate in ethanol with excellent yields and short reaction times.[9]



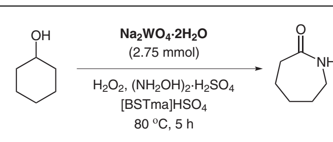
(F) Narode *et al.* published a review of strategies for the synthesis of (*S*)-Apremilast®.[10] One synthetic approach consists of eight steps, with the last being an oxidation in the presence of sodium tungstate dihydrate and 30% hydrogen peroxide to obtain (*S*)-Apremilast® in 91% yield with 99.7% ee.[11]



(G) Synthesis and studies of the biological activities of novel trifluoromethylpyridine amide derivatives containing sulfur moieties was reported by Guo *et al.* Sixteen sulfoxide-containing compounds were chemoselectively obtained by oxidation using sodium tungstate dihydrate in good yields.[12]



(H) Wang *et al.* reported the use of a combination of Na_2WO_4 and the acidic ionic liquid [BSTma]HSO_4 for the one-pot conversion of cyclohexanol into ε-caprolactam. The first step involves oxidation of cyclohexanol to cyclohexanone, followed by reaction with hydroxylamine and subsequent Hoffmann rearrangement.[13]



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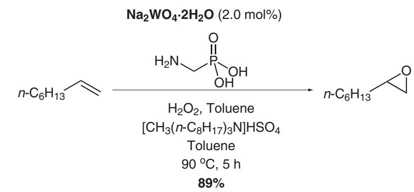
<td>(I) Yada et al. described a tungsten-catalyzed epoxidation of alkenes.[14] This study allowed the catalytic conditions to be optimized.</td>
<td>
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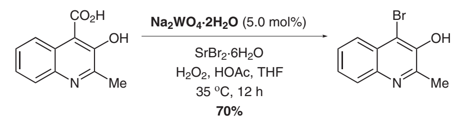
<td>(J) Ma and Chen published the tungstate-catalyzed decarboxylative bromination of 3-hydroxy-2-methylquinoline-4-carboxylic acid to furnish 4-bromo-2-methylquinolin-3-ol.[15]</td>
<td>
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In summary, sodium tungstate dihydrate enables a variety of diverse reactions and functionalizations that include alkene epoxidation, sulfur oxidation, and preparation of nitroxides and nitrones. In the presence of a combination of Na_2WO_4 acidic ionic liquid catalyst, lactams are synthesized from cyclic alcohols. The supported reagent offers additional advantages such mild reaction conditions, increase in reagent stability, ease of workup, and the ability to recycle.

Conflict of Interest

The authors declare no conflict of interest.

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