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Mini-update on the applications of Hypophosphites in organic synthesis with a special focus on sodium hypophosphite (NaH_2PO_2)

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ABSTRACT

Sodium hypophosphite (NaH_2PO_2) is an inexpensive, abundant, and environmentally friendly reagent widely used in organophosphorus synthesis. Its stability, low toxicity, and ease of handling make it a versatile "green" phosphorus source. This mini-review highlights recent developments (2019–2025) in its applications, including as a phosphorus donor, reducing agent, catalyst, deuterio-deiodinating agent, and deoxyamination reagent. Related reagents such as H_3PO_2 and $Ca(H_2PO_2)_2$ are also briefly discussed. Mechanistic insights are provided where relevant, alongside the advantages and limitations of current methodologies. This concise overview aims to guide researchers in harnessing hypophosphite reagents for efficient and sustainable organic synthesis.

Introduction

The sodium salt of hypophosphorous acid, sodium hypophosphite (NaH_2PO_2, also called sodium phosphinate), is frequently found as the monohydrate $NaH_2PO_2 \bullet H_2O$ (Fig. 1). At room temperature, it appears as odorless white crystals and is a solid. It readily collects moisture from the air and is soluble in water. It is best to store sodium hypophosphite away from oxidizing substances in a cool and dry place. It decomposes into disodium phosphate and phosphine, which irritates the respiratory system [1,2].

Because of its strong reducing nature, sodium hypophosphite is an essential compound utilized in many industrial processes. As a reducing agent, sodium hypophosphite helps deposit metals like copper and nickel on substrates without the need of electrical current, increasing adaptability and efficiency of the process [3,4]. Sodium hypophosphite is "Generally Recognized As Safe" (GRAS) and has good potential as an antibacterial food additive [5]. Sodium hypophosphite is a "non-hazardous substance" for both the people and the environment. Rats' oral LC_{50} is more than 1440 mg/kg, indicating little acute toxicity. Researchers have highlighted the advantages of using sodium hypophosphite as a reducing agent over formaldehyde, owing to its mild pH, ready availability, and enhanced safety profile.

A versatile reducing agent, sodium hypophosphite (NaH_2PO_2) is employed in organic chemistry, namely in hydrodehalogenation, reductive amination, as a precursor for the synthesis of compounds containing phosphorus and in other miscellaneous reactions. The literature on phosphonic and phosphinic acid derivatives as reducing agents was emphasized by Lemaire and others [6]. Yang and colleagues have developed eco-friendly methods for directly converting sodium hypophosphite into organophosphorus compounds [7]. Since there is currently no general and concise evaluation of this versatile reagent, we provide here the applications of NaH_2PO_2, H_3PO_2 and $Ca(H_2PO_2)_2$ in synthetic organic transformations from 2019 forward.

Abbreviations: NaH_2PO_2, Sodium hypophosphite; GRAS, Generally recognized as safe; POPs, Porous organic polymers; POLs, Porous organic ligands; EWG, Electron withdrawing group; EDG, Electron donating group; GCN, Graphitic carbon nitride; XAT, Halogen atom transfer; ADME, Absorption, distribution, metabolism, and excretion; AIBA, 2,2′-Azobis(2-methylpropionamidine) dihydrochloride; KIE, Kinetic isotope effect.

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