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2-Aminoethyl dihydrogen phosphate: As a multi-purpose spacer

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This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research.

Introduction

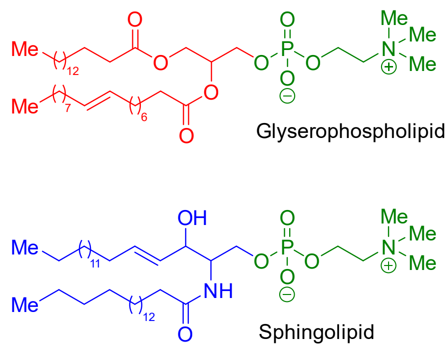
2-Aminoethyl dihydrogen phosphate, phosphorylethanolamine or phosphoethanolamine is known as a polyprotic acid which has two pK_a values of 5.61 and 10.39 (Scheme 1) [1]. This versatile molecule has a striking role for the construction of phospholipids including glycerophospholipids and sphingolipids. Glycerophospholipids and sphingolipids are the main component of cell membranes. Scheme 2 represented the structure of two phospholipids bearing 2-aminoethyl dihydrogen phosphate moiety.

Also, it is demonstrated that the synthetic phosphoethanolamine can acts as anti-leukemia agents. Furthermore, this drug candidate structure is in undergoing human clinical trials [2,3]. The main synthetic form of 2-aminoethyl dihydrogen phosphate is calcium 2-aminoethylphosphate (Ca-AEP or Ca-2AEP) (Scheme 1).

2-Aminoethyl dihydrogen phosphate   Calcium 2-aminoethylphosphate

Scheme 1. Structures of 2-aminoethyl dihydrogen phosphate and calcium 2-aminoethylphosphate phosphate moiety.

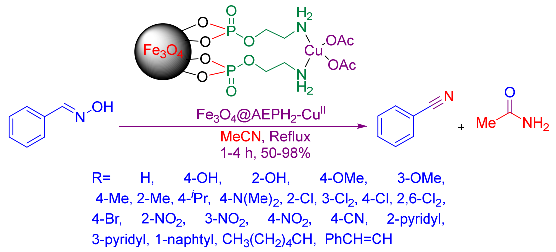
Ca-AEP plays an important role in the structure of cell membrane of human body through improvement of cellular functions. In this spotlight, due to interesting structural features of 2-aminoethyl dihydrogen phosphate, its versatility towards the synthesis of heterogeneous-based catalysts for promoting organic transformations is highlighted.



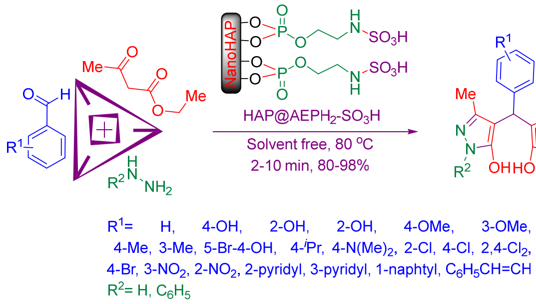
Scheme 2. Structures of two phospholipids bearing 2-aminoethyl dihydrogen phosphate moiety.

Abstracts

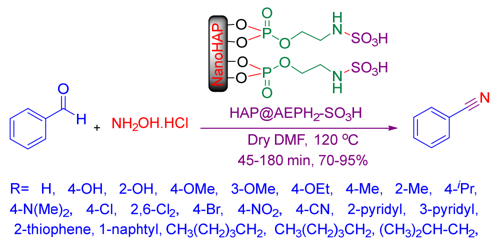
(A) In 2015, Akhlaghinia and co-workers, using 2-aminoethyl dihydrogen phosphate, reported the Cu^{II} immobilization on aminated ferrite nanoparticles. The resulting catalyst was fully characterized by required methods. Experimental investigation demonstrated that the prepared heterogeneous catalyst shows excellent performance for the transformation of aldoximes to nitriles. A wide range of aldoximes including aromatic, aliphatic and heterocyclic aldoximes converted to desired nitriles with good to excellent yields [4].



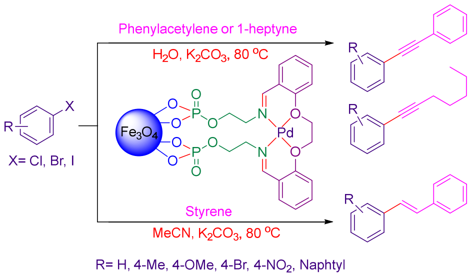
(B) 4,4'-(aryl methylene)bis(1*H*-pyrazol-5-ol) derivatives as biological active structural motifs, prepared in the present of HAP@AEPH$_2$-SO$_3$H through the reaction of phenylhydrazine/or hydrazine hydrate, ethylacetoacetate and aldehydes under mild and solvent free conditions [5].



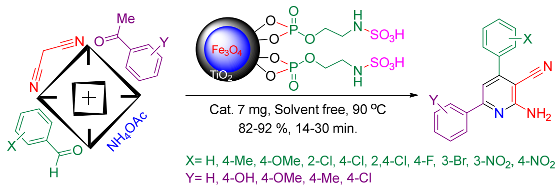
(C) Sulfonated nanohydroxyapatite functionalized by 2-aminoethyl dihydrogen phosphate (HAP@AEPH$_2$-SO$_3$H) represent powerful catalytic activity towards the direct synthesis of nitriles from aldehydes and hydroxylamine hydrochloride. The reported protocol represents a green, useful, and rapid route for the preparation of desired structures with excellent yields [6].



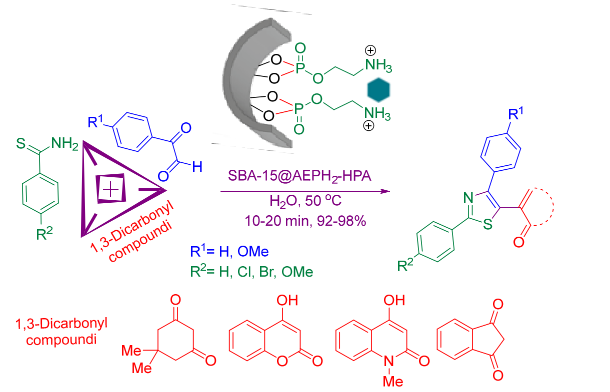
(D) Zolfigol *et al.* in 2016, reported 2-aminoethyl dihydrogen phosphate for synthesis of a novel task-specific nanomagnetic with phosphate spacer as a coating agent for the surface of Fe$_3$O$_4$ nanoparticles. The described magnetic nano particles applied for supporting Pd tags. The resulting catalyst represents elegant performance in Sonogashira and Mizoroki-Heck coupling reactions [7].



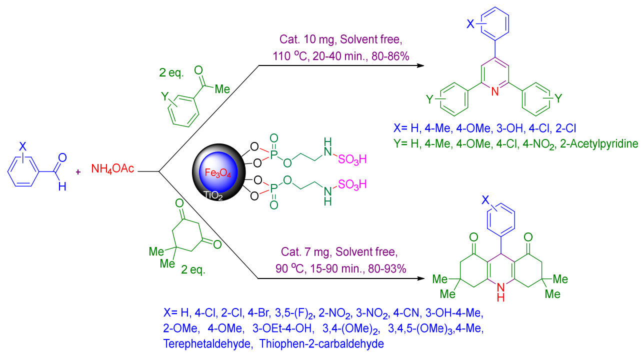
(E) In another investigation, 2-aminoethyl dihydrogen phosphate has been applied for the construction of a reusable nanomagnetic heterogeneous core-shell catalyst namely Fe$_3$O$_4$@TiO$_2$@O$_2$PO$_2$(CH$_2$)$_2$NHSO$_3$H. The achieved recoverable acidic catalyst has been also used as promoter for the synthesis of 2-amino-4,6-diphenylnicotinonitriles *via* anomeric based oxidation (ABO) mechanism [8]. 2-Amino-4,6-diphenylnicotinonitrile derivatives have been obtained with good to high yields in short reaction times upon the reaction of aromatic aldehydes, acetophenone derivatives, malononitrile and ammonium acetate [9].



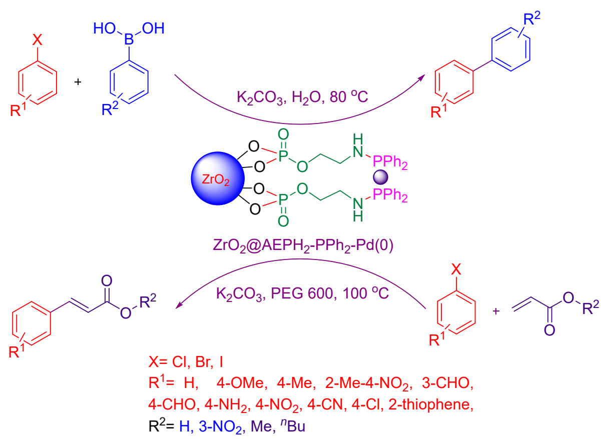
(F) Akhlaghinia *et al.* reported a powerful mesoporous heterogeneous catalyst, heteropolyacid anchored on SBA-15 functionalized with 2-aminoethyl dihydrogen phosphate (SBA-15@AEPH$_2$-HPA). The synthesized catalyst was successfully applied upon the reaction of arylglyoxals, cyclic 1,3-dicarbonyls and thioamides for the three-components preparation of varied trisubstituted 1,3-thiazoles under benign reaction conditions. The applied mesoporous catalyst exhibits superior potential of recyclability over the studied reaction [10].



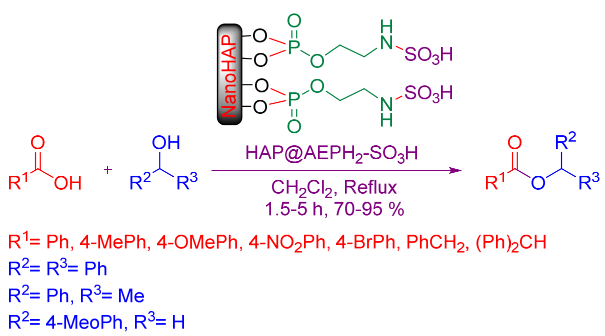
(G) In a separate study, Fe$_3$O$_4$@TiO$_2$@O$_2$PO$_2$(CH$_2$)$_2$NHSO$_3$H has been successfully applied as a robust catalyst for the synthesis of other type of nitrogen-containing heterocyclic molecules such as 2,4,6-triarylpyridines and 1,8-dioxodecahydroacridine derivatives. It is worthy to mention that in this exploration it is demonstrated that the final step of the mechanistic process to 2,4,6-triarylpyridine derivatives proceeds *via* an anomeric based oxidation mechanism [11].



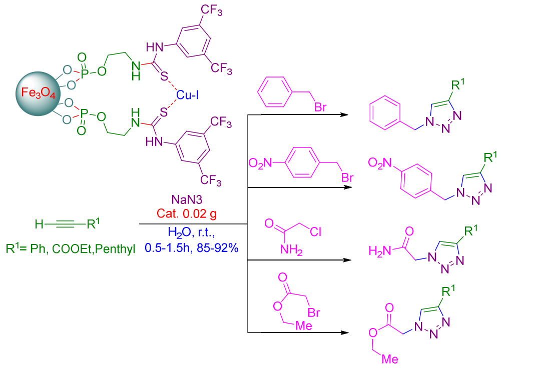
(H) Akhlaghinia and co-workers reported the synthesis and characterization of a novel aminophosphine palladium(0) complex supported on ZrO$_2$ nanoparticles (ZrO$_2$@AEPH$_2$-PPh$_2$-Pd(0)). Further investigations have been revealed that the synthesized catalyst represent elegant activity in the Suzuki-Miyaura and Heck-Mizoroki cross-coupling reactions [12].



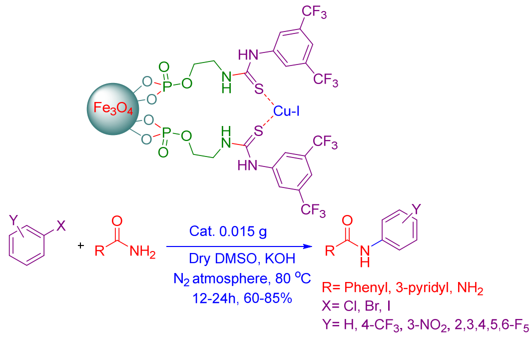
(I) It is reported that the sulfonated nanohydroxyapatite functionalized with 2-aminoethyl dihydrogen phosphate (HAP@AEPH$_2$-SO$_3$H) shows efficient catalytic performance in direct esterification of carboxylic acids and alcohols with high selectivity toward the formation of esters [13].



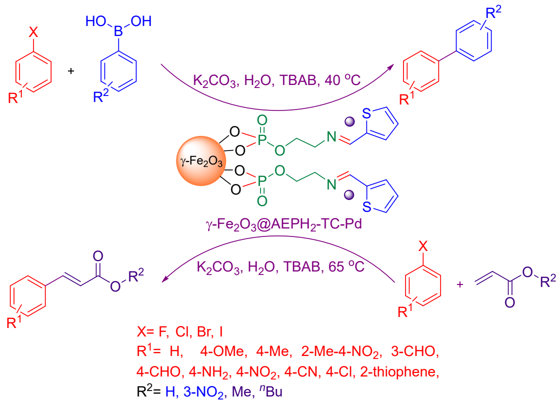
(J) Zolfigol and co-workers reported the design, synthesis and characterization of a novel inorganic-organic Takemoto-like hybrid nanomagnetic catalyst using 2-aminoethyl dihydrogen phosphate as an excellent linker. After structural verification of desired nanomagnetic catalyst, its catalytic performance successfully probed at the synthesis of triazoles through click reaction [14].



(K) In another assay, the abovementioned nanomagnetic supported thiourea-copper(I) has been used as an elegant catalyst at the synthesis of benzamides through coupling reaction under benign reaction conditions. The applied catalyst shows superior potential of recyclability in the tested reaction [14].



(L) In another exploration, thiophene methanimine-palladium Schiff base complex anchored on decorated γ-Fe_2O_3 with 2-aminoethyl dihydrogen phosphate (γ-Fe_2O_3/ $AEPH_2$-TC-Pd) was synthesized. The constructed magnetically separable nanocatalyst was applied as superb promoter for Suzuki-Miyaura and Heck-Mizoroki cross-coupling reactions [15].



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