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One pot and metal free protocol for the synthesis of bioactive Natural product based phosphoramidates.

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Phosphoramidates have gained considerable interest from last few decades as they have various applications in different area of medicinal chemistry. They form important pharmacophore of many biologically potent compounds e.g., sofosbuvir (FDA approved drug) used for the treatment of hepatitis C virus (HCV), evofosfamide (TH-302) which is in clinical trials for cancer treatment. Owing to their great utility and potential applications in different area of chemistry particularly in pharmaceutical arena, an efficient synthesis has been developed for the synthesis of primary phosphoramidates using simple azide precursors like benzyl, allyl, alkyl, and propargyl halides in EtOH–H_2O as a green reaction medium. Operational simplicity, metal free, in situ generation of organic azides, and environmental benign conditions are the features of the developed protocol. This reaction has a wide substrates scope and offers the possibility of synthesizing phosphoramidates in good yield under mild conditions. The developed protocol can also be used for synthesis of valuable phosphoramidates of APIs, natural products or their derivatives as prodrugs to enhance their water solubility and therapeutic efficiency.