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An efficient one pot three component synthesis of fused pyridines via electrochemical approach

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ABSTRACT

A convenient and economical method is developed for the synthesis of pyrido[2,3-*d*]pyrimidine derivatives by electrochemically induced condensation of various aromatic aldehydes, dimedone or malononitrile and 6-amino uracil. The reaction is carried out in an undivided cell, at a constant current in the presence of NaBr as supporting electrolyte and ethanol as solvent.

Multicomponent reactions have been recently recognized as a powerful tool in synthetic organic chemistry. They allow one-pot reaction in which three or more reactants are combined together to form a new desired compound in sort duration. Multicomponent reactions (MCRs) play an important role in atom economy and green chemistry [1]. These reactions dramatically reduce the generation of chemical waste and the cost. MCR strategies offer significant advantages over conventional linear type synthesis [2]. It provide powerful dais to access diversity as well as complexity in few reaction steps. The conventional multi-step synthesis of compounds involve purification of compounds after each individual step [3], which leads to two main disadvantages, synthetic inefficiency and the production of large amount of waste.

The derivatives of 6-amino uracil have received considerable attention over the last few years due to their vast range of biological and pharmacological properties such as, antimicrobial [4], antibacterial [5], antifungal [6], antiallergic [7], anti-inflammatory [8], analgesic [9], antihypertensive [10] and antitumor [11]. The synthesis of pyrido[2,3-*d*]pyrimidine derivatives (Fig. 1) has been explored extensively in recent years. Various methods such as using microwave [12], magnesium oxide [13], diammonium hydrogen phosphate (DAHP) [14], bismuth(III)-nitrate pentahydrate [15] and palladium-catalyzed oxidative coupling [16] have been reported. However, conventional methods for the synthesis of these products suffer from various drawbacks such as harsh reaction conditions, prolonged reaction time, low yield, use of toxic organic solvents, expensive reagents and catalysts. Therefore simple, efficient and environmentally benign approaches for synthesis of pyrido[2,3-*d*]pyrimidine are desirable.

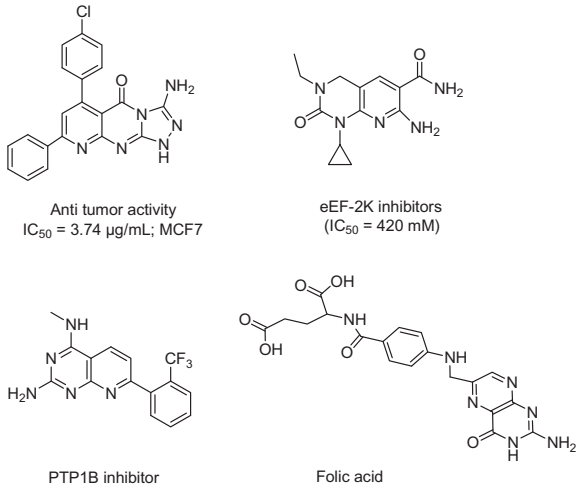

Figure 1. Several biologically active pyrido[2,3-*d*]pyrimidine compounds.

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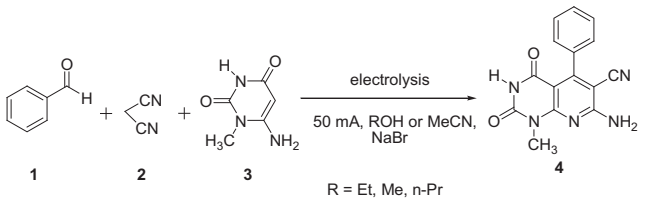
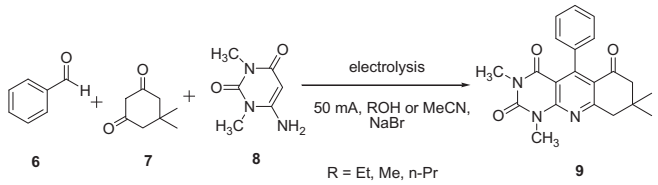
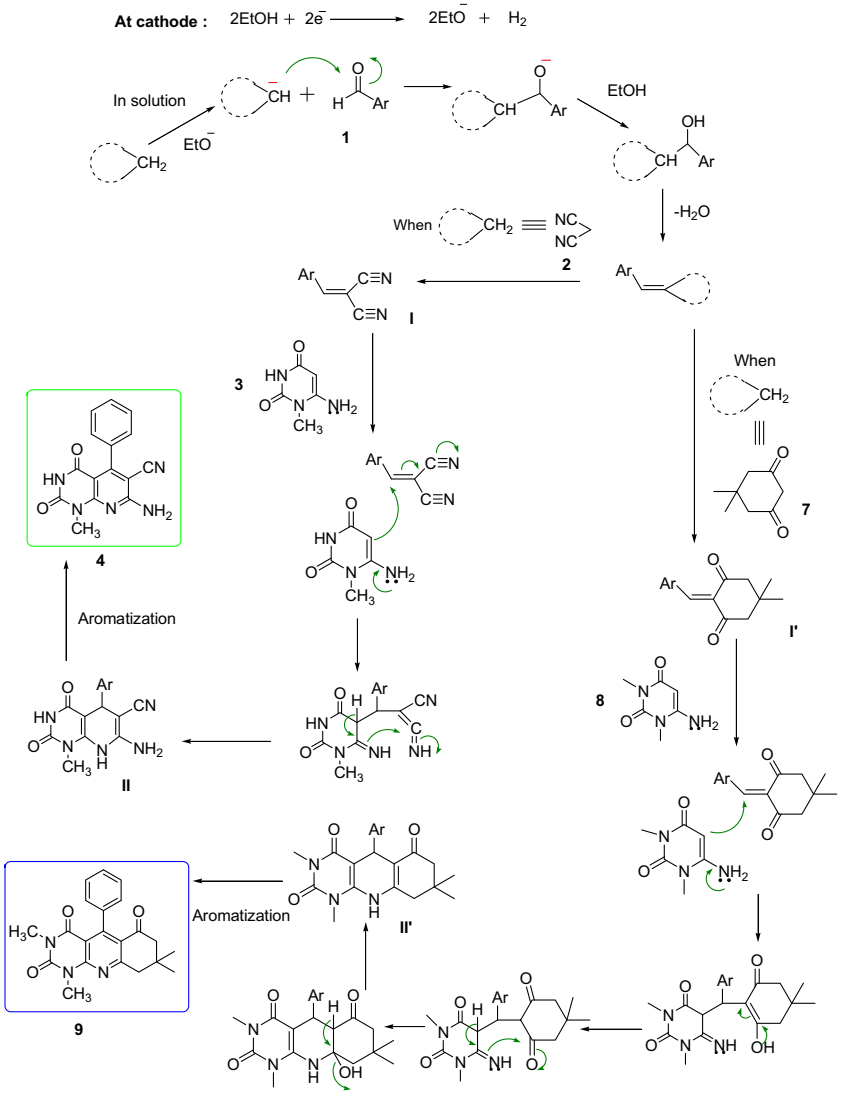
In electrochemistry electron serve as sole reagent hence there is no need of acid, base or catalyst, electrogenerated base (EGB) promote reactions in good yields. Electrosynthesis have many advantages with atom economy, mild reaction conditions, decreased energy requirements and reduced waste production, and the ability to perform a wide range of precisely tuned oxidation and reduction reaction. As a part of our ongoing efforts towards synthesis of medicinally important compound [17], we developed a convenient and environmentally friendly method for multicomponent synthesis of pyrido[2,3-*d*]pyrimidine-6-carbonitrile derivatives and 8,9-dihydro-1,3,8,8-tetramethyl 5-phenylpyrimido[4,5-*b*]quinoline-2,4,6(1*H*,3*H*,7*H*)-trione derivatives by the electrochemical transformation using 6-aminouracil, various aromatic aldehydes, malononitrile or dimedone as starting material in an undivided cell at 40 °C under a constant current density.



Scheme 1. Synthesis of 7-amino-1,2,3,4-tetrahydro-1methyl-2,4-dioxo-5-phenylpyrido[2,3-*d*]pyrimidine-6-carbonitrile.



Scheme 2. Synthesis of 8,9-dihydro-1,3,8,8-tetramethyl-5-phenylpyrimido[4,5-*b*]quinoline-2,4,6-(1*H*,3*H*,7*H*)-trione.



Scheme 3. A plausible mechanism for the formation of pyrido[2,3-*d*]pyrimidine **4** and pyrimido[4,5-*b*]quinoline **9** compounds.