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Multicomponent reactions in the synthesis of phenytoin derivatives for formation of products with potential anticonvulsant activity

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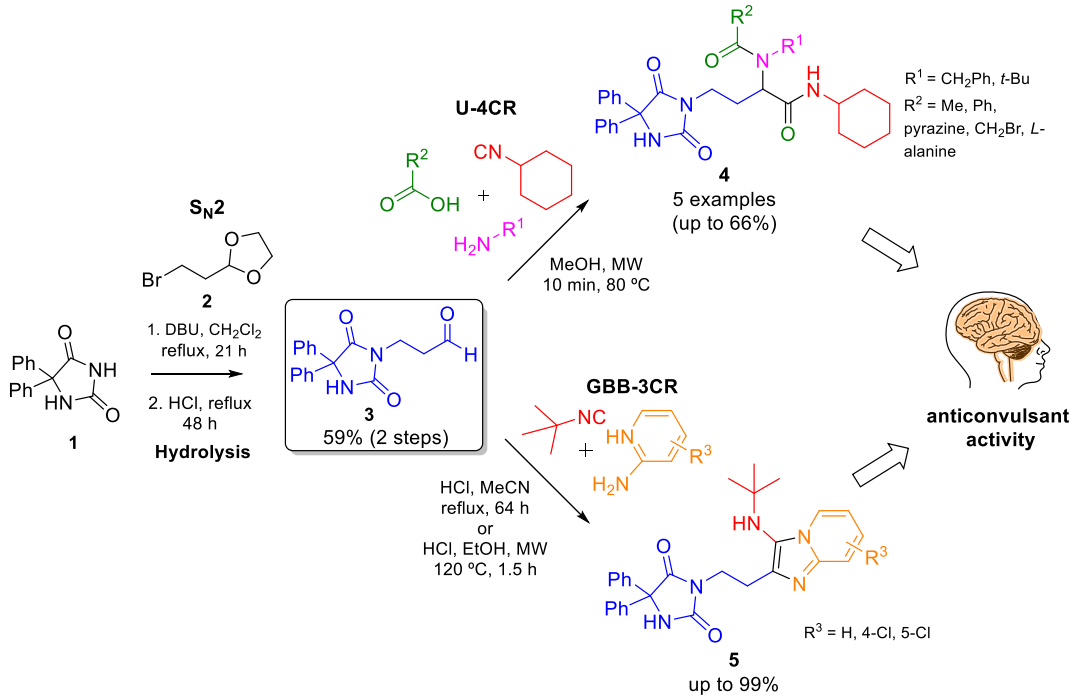
ABSTRACT

Epilepsy is a common neurological disorder that affects people of all ages.[1] Approximately 95% of antiepileptic drugs were approved before 1985 and control seizures in 60-70% of patients.[2] Therefore, the search for safer and more effective drugs is essential in the field of Medicinal Chemistry.[3] Phenytoin is used in the treatment of epilepsy, one of the most widely used anticonvulsants globally and is on the WHO's List of Essential Medicines.[4,5] This study focused on the structural conversion of phenytoin into an aldehyde derivative (**3**) from which new compounds with potential anticonvulsant activity were obtained through Ugi-4CR and GBB-3CR multicomponent reactions. Initially, the synthesis of aldehyde **3** was performed via *N*-alkylation, followed by acetal hydrolysis. This intermediate was then employed in the Ugi reaction with different carboxylic acids, amines, and isocyanides in MeOH under microwave heating, yielding analogs **4** in good yields. The use of aminopyridine derivatives provided GBB adducts **5** in high yields (up to 99%) under HCl catalysis. In both approaches, novel compounds with potential antiepileptic activity (yet to be tested) were synthesized.



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