SYNLETT
Spotlight 84

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

DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) – A Nucleophillic Base

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Nandita Ghosh was born in Kolkata, West Bengal, India, in 1975. She obtained a MSc in organic chemistry from Visva Bharati University, India, and subsequently joined the department of chemistry, Bose Institute, Kolkata, as a CSIR-Junior Research Fellow in 1999, where she is currently working towards a PhD under the supervision of Professor Manas Chakrabarty. Her research involves the study of the reactions and development of new syntheses of heterocycles including bioactive compounds and dry reactions mediated by montmorillonite clays.

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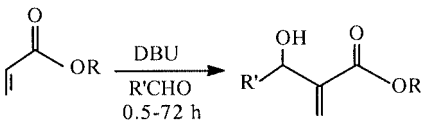
The efficiency of DBU as a non-nucleophilic, sterically hindered, tertiary amine base in organic chemistry has been widely demonstrated.[1] In particular, it has been widely used for carrying out dehydrohalogenation reactions. However, Reed et al. demonstrated for the first time the remarkably strong nucleophilic behavior of DBU in its reaction with halogenated compounds.[2] This nuclephilic behavior of DBU, thus unveiled, also explained many of its so-called unexpected and unusual reactions.[3–5] Subsequently, many other workers have also reported the nucleophilic behaviour of DBU.[6] In many instances, DBU itself reacted with different α,β-unsaturated systems resulting in the formation of ε-caprolactam derivative.[7] The reagent is commercially available and has been extensively used for carrying out a wide range of reactions.[8]

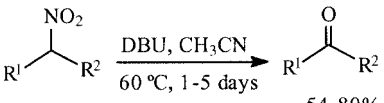
Abstracts

(A) The Baylis–Hillman reaction is of great synthetic utility, as it converts simple starting materials into densely functionalized products. Recently, Agarwal et al. showed the superiority of DBU over other amine catalysts in the Baylis–Hillman reaction, as it was stable under the reaction conditions and gave a clean reaction with the fastest rate.[9]



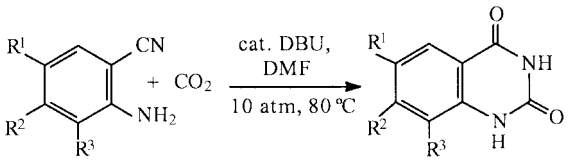
R=Me, Et, *t*-Bu
R'=Aryl, Alkyl
20-95%

(B) The conversion of primary or secondary nitroalkanes into aldehydes or ketones, i.e. Nef reaction originally involved strong acidic conditions. Ballini et al. showed an unprecedented behavior of DBU as a new reagent in acetonitrile solution for the one-step regio- and chemoselective conversion of secondary nitro compounds in the presence of primary nitro compounds into ketones under homogeneous basic conditions in good yields.[10]



R^1, R^2 = alkyl
54-80%

(C) Mizuno et al. developed a new chemical fixation of carbon dioxide in the presence of DBU to form substituted 1*H*-quinazoline-2,4-diones, which are useful for the synthesis of different medicinal intermediates. In this reaction, CO_2 smoothly reacts with 2-aminobenzonitrile under mild conditions, assisted either by an excess of DBU (1 atm, 20 °C) or catalytic amount of DBU (10 atm, 80 °C) to give the corresponding quinazoline derivatives.[11] The authors also synthesized substituted 2,4-dihydroxyquinazolines by chemical fixation of CO_2 (1 atm) of 2-aminobenzonitrile at 20 °C in presence of DBU.[12]



R^1, R^2, R^3 = H, OCH_3, NO_2, Br
1*H*-quinazoline-2,4-dione

SYNLETT 2004, No. 3, pp 0574–0575
Advanced online publication: 26.01.2004
DOI: 10.1055/s-2004-815436; Art ID: V09603ST
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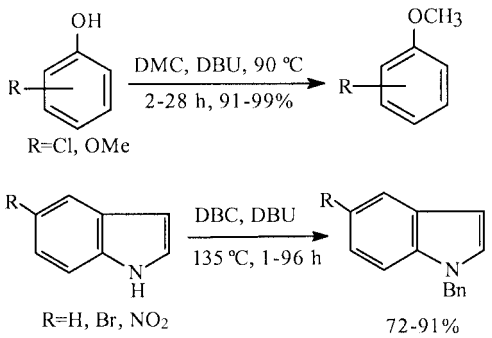
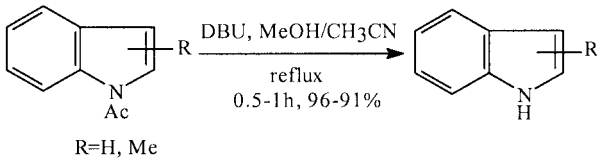
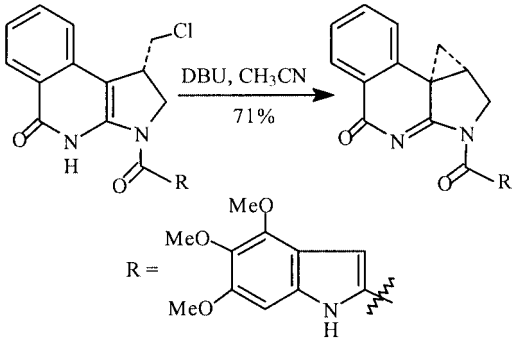
(D) Recently, Shieh et al. showed the efficiency of DBU as a nucleophilic catalyst in the environmentally friendly method for the methylation[13] and benzylation[14] of N-, O- and S-atoms with non-toxic dimethylcarbonate (DMC) and dibenzylcarbonate (DBC), respectively. These authors also showed the superiority of DBU over the commonly used acylation catalyst 4-(dimethylamino)pyridine in the esterification of benzoic acid with DMC.[15]



(E) DBU was also found to smoothly cleave the *N*-acetyl and *N*-benzoyl derivatives of carbazoles, indoles, and nitroanilines in refluxing methanol, and the parent amines were recovered in excellent yields. The cleavage was also accomplished in acetonitrile solution under reflux and under microwave irradiation.[6d]



(F) Recently, in the synthesis of duocarmycin and CC-1065 analogues, the parent members of an important class of potent antitumor antibiotics, Boger and his co-workers used DBU in anhydrous acetonitrile solution to bring about spirocyclization to create a cyclopropane ring in the final step of the synthesis in good yield.[16]



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