

SYNLETT Spotlight 311

N,N'-Dimethyl Urea

Compiled by Subrata Das

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

Subrata Das was born in Sabroom, Tripura (India) in 1983. He received his B.Sc. degree in chemistry with honors from Assam University, Silchar, India (2004) and his M.Sc. degree in chemistry from Central University, Tezpur, India (2006). He is currently working as a research fellow towards his Ph.D. in organic chemistry under the supervision of Dr. Ashim J. Thakur at the Central University, Tezpur, India. His research interests are heterocyclic chemistry and the synthesis and pharmacological activity of annelated heterocyclic systems.

Dept. of Chemical Sciences, Central University, Tezpur, Napaam, 784028 Assam, India
E-mail: subrata_das@tezu.ernet.in

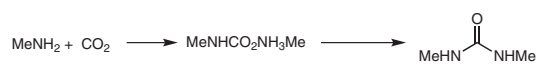


Introduction

N,N'-Dimethyl urea (DMU) (1,3-dimethyl urea, methyl carbamide) is a colourless solid and a non-volatile, versatile and powerful reagent for the synthesis of nitrogen-containing heterocyclic compounds. It is used for the synthesis of caffeine, theophylline, pharmaceuticals, textile aids, herbicides, etc. It also finds application in metal-ion complexation, material science, etc. In 1954, Blick and Godt synthesized the important building block *N,N'*-dimethyl-6-amino uracil from a mixture of DMU, cyanoacetic acid, and acetic anhydride with exclusion of moisture under stirring at 60 °C for 3 h.¹ It is a very important starting material for the synthesis of pyrimidine derivatives.

Preparation

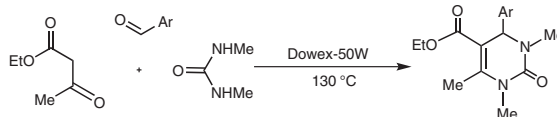
DMU can be prepared by the reaction of methylamine with carbon dioxide (Scheme 1). In 1939, Grinberg reported the first synthesis of alkyl-substituted carbamides by reaction between $\text{NO}_2\text{CONHNO}_2$ and methylamine.² Shigeru and co-workers introduced an easy and reliable method in 1978 by treating methylamine with carbon dioxide at -30 to -50 °C for 24 h, followed by heating at an average rate of 3 °C/min in an autoclave.³



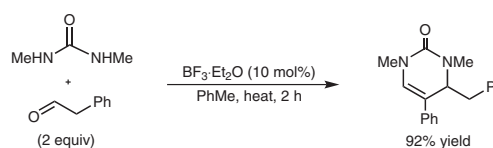
Scheme 1

Abstracts

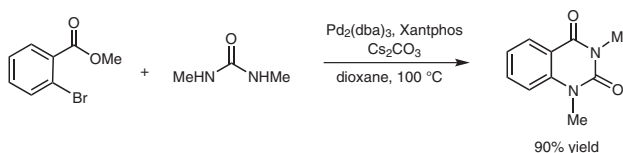
(A) The synthesis of 4-aryl-3,4-dihydropyrimidines (Biginelli compounds, DHPMS) is accomplished by heating a solvent-free mixture of an aldehyde, an active methylene compound, DMU, and Dowex-50W ion-exchange resin.⁴



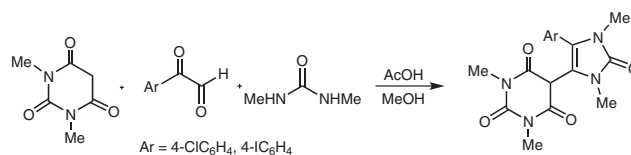
(B) The simple heating of two equivalents of phenyl acetaldehyde with DMU in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ (10 mol%) as a catalyst in toluene afforded dihydropyrimidinone in 92% yield⁵



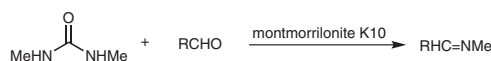
(C) The reaction between *o*-bromo benzoate and DMU in the presence of Xantphos as the initial ligand and the weak base Cs_2CO_3 provided the quinazolinone in 90% yield.⁶



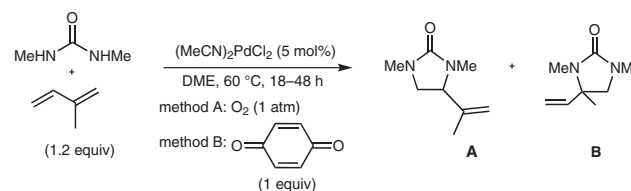
(D) The interaction of 1,3-dimethylbarbituric acid, glyoxals, and DMU in methanol with a catalytic amount of glacial acetic acid led to 5-(5-aryl-1,3-dimethyl-2-oxo-2,3-dihydro-1*H*-imidazol-4-yl)-1,3-dimethylpyrimidine-2,4,6-triones.⁷



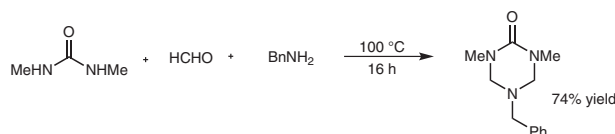
(E) *N*-methyl imines can be synthesized by the reaction of DMU and aldehydes in the presence of solid clay-montmorillonite K10.⁸



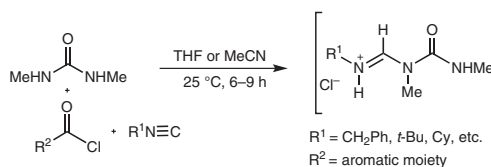
(F) The regioisomeric diene DMU 1,2-adducts **A/B** were synthesized by reacting isoprene with DMU using palladium(II) catalyst (O_2 /cat.) (method A). Switching from oxygen to benzoquinone as reoxidant avoids the generation of water and affords 1,2-adducts **A/B** in good yield (method B).⁹



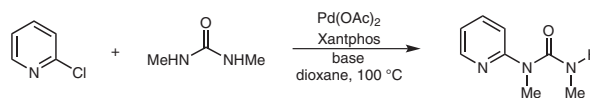
(G) The conversion of benzylamine into the triazone derivative was achieved by reflux condensation with DMU and aqueous formaldehyde under argon atmosphere and heating at 100 °C for 16 h.¹⁰



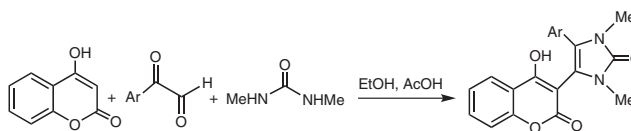
(H) The addition of DMU to a mixture of isocyanide and acid chloride gave formamidine urea salts in pure form.¹¹



(I) The coupling reaction between 2-chloropyridine and DMU gives primarily the corresponding mono-coupled urea.¹²



(J) Kolos and co-workers synthesized 4-aryl-5-(4-hydroxy-2-oxo-2*H*-chromen-3-yl)-1*H*-imidazol-2(3*H*)-ones by one-pot condensation of 4-hydroxycoumarin with arylglyoxals and DMU in ethanol in the presence of a catalytic amount of acetic acid within a short time (15–50 min).¹³



References

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