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Montmorillonite K-10 Catalyzed Facile Synthesis of 1,3-Disubstituted Ureas from Biuret under Solvent Free Conditions

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ABSTRACT

A proficient synthesis of 1,3-disubstituted ureas from biuret and different amines has been developed using Montmorillonite K-10 as catalyst under solvent free condition using microwave irradiations. The prominent feature of this protocol includes higher yields, shorter reaction times and cleaner procedure with non-toxic and readily available catalyst. Structural confirmation of the products was done on the basis of spectral data- IR, ^{1}H NMR and melting points comparison with the authentic samples.

1. Introduction

Urea and its derivatives are considered as significant organic compounds as they exhibit a wide range of applications as antioxidant, corrosion inhibitors in gasoline, dyes for cellulose fiber, antidiabetic and tranquillizing drugs and agrochemicals [1-3]. Several urea derivatives are associated with diverse pharmaceutical applications such as diuretics [4], antagonists of human vanilloid VR 1 receptors [5], anti-tuberculosis agents [6], anti-melanoma agents[7], potent inhibitors of influenza virus neuraminidase [8], HIV-1 protease inhibitors [9], anti-hyperglycemic agents [10] and as inhibitors of Murine receptor A and Murine receptor B [11]. A large number of methods are reported for the synthesis of urea derivatives including reaction of amines with phosgene and its derivatives [12], carbmates [13], isocynates [14], oxidative carbonylation [15], reductive carbonylation [16] or by reaction of urea or thiourea with amines [17]. In recent times some alternative methods [18-19] are also reported for synthesis of urea derivatives using different catalytic systems as Zinc Chloride [20], $CeCl_3.7H_2O$-KI [21], Iodine [22], Cs_2CO_3 [23], PEG-400 [24], Titanium (IV) isopropoxide and sodium borohydride [25] and zeolite HSZ-360 [3]. Most of the reported methods suffer from limitations of longer reaction times, harsh reaction conditions, tedious isolation and purification procedures, lower yields and use of highly volatile organic solvents. Phosgene and isocynates used during phosgenation are toxic, expensive and hazardous reagents. Similarly CO used during oxidative carbonylation is toxic and difficult to handle. The inadequacies allied with these common methods encouraged us to develop and design some clean and efficient alternative for such type of reactions. Clays are versatile inorganic materials that are used to catalyze a large number of chemical reactions [26-29]. Clays and modified clays are considered as chemical green catalyst as they are readily available, non-toxic, economic, non-corrosive, safe to handle and are easily recovered and reused. Acting as a mild acid catalyst, clays particularly Montmorillonite K-10 act as an efficient heterogeneous catalyst in organic reactions providing higher yield and selectivity with operational ease. Microwave assisted reactions under solvent free conditions has gained considerable attention in synthetic organic chemistry. In comparison to the classical thermal heating, this method has many advantages such as shorter reaction times, higher yields, energy efficiency, ease of reaction condition and enhanced selectivity. In continuation of our efforts towards developing clean and efficient methodologies for various organic transformations [30-31], herein we report a facile synthesis of N, N'- disubstituted ureas by reaction of biuret with differently substituted amines using Mont K-10 as catalyst in the absence of solvent under microwave irradiations.

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2. Experimental Methods

2.1 General Method

Melting points were determined in open capillaries and are uncorrected. All reagents were purchased from Sigma-Aldrich and used without further purification. Mont K-10 was purchased from Fluka Goldie. The reactions were carried out in a Samsung microwave oven operating between 80-800 W Model No. CE745G and were monitored by analytical thin layer chromatography (TLC) performed on glass plates precoated with silica gel G as supplied by Sisco Research Laboratories (SRL). Visualization of the resulting chromatograms was done by looking under iodine chamber followed by dipping in a solution of carbon tetrachloride (CCl4) and ethyl acetate (CH3COOC2H5). IR spectra were recorded on Perkin-Elmer spectrum BX Series FT-IR spectrophotometer with KBr pellets. 1H-NMR was recorded on a 400 MHz spectrometer (Bruker Avance Π 400 using Tetramethylsilane (TMS) as internal standard.

2.2 General Procedure for the Synthesis of 1,3-Disubstituted Ureas

Biuret (0.103 g, 1 mmol) and aniline (0.18 mL, 2 mmol) were taken in a 10 mL Pyrex beaker and mixed thoroughly with the catalyst, Mont K-10 (200 mg). The reaction mixture was agitated for a few minutes at room temperature and then exposed to microwave. The progress of reaction was monitored by TLC (CCl_4: Ethyl acetate / 3: 1) after every 10 seconds. The reaction was found to be completed after 8 min. On completion, the product was extracted using CH_2Cl_2, dried and recrystallized to produce N, N'-diphenylurea in 85% yield.

Identical procedure was followed for the preparation of other 1, 3-disubstituted ureas under similar reaction conditions.

2.3 Data Analysis

N, N'-diphenylurea**:** Mp. 241 °C (lit. 242 °C)[20]; IR (KBr, cm^{-1}): 3215 (N-H), 3079 (C-H), 1699 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6): 8.45 (br, 2H, NH), 7.45 (d, J=8.8 Hz, 4H, ArH), 7.24 (t, 4H, ArH), 6.95 (t, 2H, ArH).

N, N'-bis(2-methylphenyl)urea: Mp. 233 °C (lit. 235 °C)[19]; IR (KBr, cm^{-1}): 3401 (N-H), 3108 (C-H), 1690 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6): 8.57 (br, 2H, NH), 7.48-7.37 (m, 2H, ArH), 7.31-7.16 (m, 4H, ArH), 6.96-6.93 (m, 2H, ArH), 2.09 (s, 6H, CH_3).

N, N'-bis(4-methylphenyl)urea: Mp. 267 °C (lit. 269 °C)[20]; IR (KBr, cm^{-1}): 3305 (N-H), 3032 (C-H), 1640 (C=O); ^1H NMR (400 MHz, DMSO-d_6): 8.28 (br, 2H, NH), 7.34-7.25 (m, 4H, ArH), 7.10-6.99 (m, 4H, ArH), 2.29 (s, 6H, CH_3).

N, N'-bis(2-methoxyphenyl)urea: Mp. 184 °C (lit. 185 °C)[21]; IR (KBr, cm^{-1}): 3415 (N-H), 3040 (C-H), 1668 (C=0); ^1H NMR (400 MHz, DMSO-d_6): 8.90 (br, 2H, NH), 7.23-7.21 (m, 2H, ArH), 7.06-7.02 (m, 2H, ArH), 6.74-6.72 (m, 2H, ArH), 6.69-6.65 (m, 2H, ArH),3.63 (s, 6H, OCH_3).

N, N'-bis(4-methoxyphenyl)urea: Mp. 239 °C (lit. 240 °C)[20]; IR (KBr, cm^{-1}): 3418 (N-H), 3030 (C-H), 1627 (C=0); ^1H NMR (400 MHz, DMSO-d_6): 8.60 (br, 2H, NH), 6.98-6.64 (m, 2H, ArH), 6.54-6.44 (m, 4H, ArH), 3.36 (s, 6H, OCH_3).

N, N'-bis(2-nitrophenyl)urea: Mp. 224 °C (lit. 226-228 °C)[18]; IR (KBr, cm^{-1}): 3370 (N-H), 3085 (C-H), 1687 (C=O); ^1H NMR (400 MHz, DMSO-d_6): 9.09 (br, 2H, NH), 7.82 (d, J=8.4 Hz, 2H, ArH), 7.49 (d, J=8.4 Hz, 2H, ArH), 7.28 (t, 2H, ArH), 7.08 (t, 2H, ArH).

N, N'-bis(4-nitrophenyl)urea: Mp. 303 °C (lit. 305-306 °C)[20]; IR (KBr, cm^1): 3451 (N-H), 3080 (C-H), 1680 (C=0); ^1H NMR (400 MHz, DMSO-d_6): 9.49 (br, 2H, NH), 8.11-7.64 (m, 4H, ArH), 6.70-6.61 (m, 4H, ArH).

N, N'-bis(2-chlorophenyl)urea: Mp. 224 °C (lit. 225-226 °C)[21]; IR (KBr, cm^{-1}): 3338 (N-H), 3095 (C-H), 1695 (C=0); ^1H NMR (400 MHz, DMSO-d_6): 9.38 (br, 2H, NH), 7.53-7.37 (m, 4H, ArH), 7.07-6.80 (m, 4H, ArH).

N, N'-bis(phenylamino)urea: Mp. 172 °C (lit. 171-173 °C)[20]; IR (KBr, cm^{-1}): 3398 (N-H), 3060 (C-H), 1689 (C=0); ^1H NMR (400 MHz, DMSO-d_6): 11.14 (br, 2H, NH), 8.19 (d, 2H, NH),7.97-7.21 (m, 10H, ArH).

N, N'-bis(cyclohexyl)urea: Mp. 203 °C (lit. 205-206 °C)[20]; IR (KBr, cm^{-1}): 3401 (N-H), 3110 (C-H), 1695 (C=0); ^1H NMR (400 MHz, DMSO-d_6): 5.55 (br, 2H, NH), 3.37 (m, 2H), 1.78-1.50 (m, 10H) 1.31-1.18 (m, 10H).

Table 1 Synthesis of N, N'-disubstituted urea derivatives from biuret and various substituted amines (1:2) at 180 W in the presence of Mont K-10 (200 mg)

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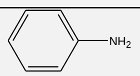
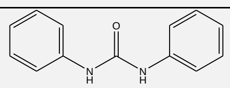
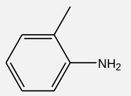
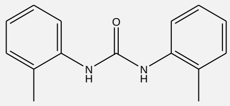
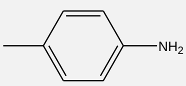
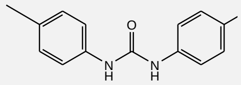
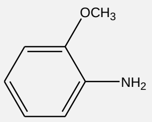
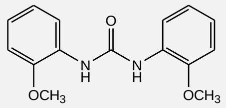
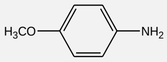
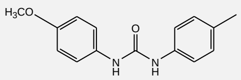
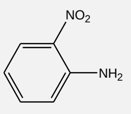
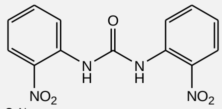
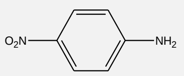
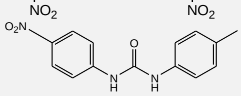
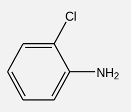
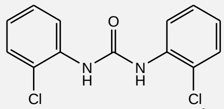
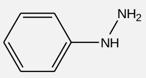
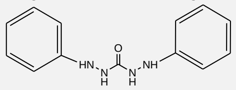
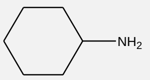
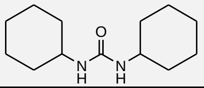
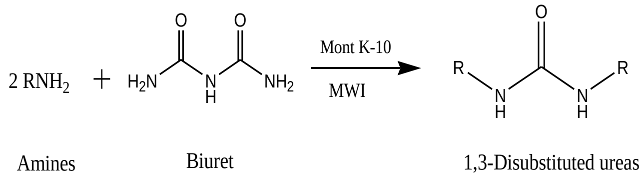
1a			85	8
1b			92	7
1c			70	7
1d			65	8
1e			68	8
1f			64	10
1g			75	12
1h			72	12
1i			80	11
1j			82	9

[a]Yields are of pure product isolated

3. Results and Discussion

We report herein an environmentally acceptable and operationally simple protocol for the synthesis of N, N' – disubstituted urea derivatives from biuret and diverse substituted amines in the presence of Mont K-10 under solvent free condition using microwave irradiations (Scheme 1).



Scheme 1 Synthesis of 1,3-disubstituted ureas catalyzed by Mont K-10

In our preliminary experiment, we selected the synthesis of N, N'-diphenyl urea by reaction of biuret with aniline in the presence of catalytic amount of Mont K-10 under microwave irradiations. The desired product i.e. N, N'- diphenyl urea was formed in 85% yield in 8 min. In this reaction, Mont K-10 provides mild acidic condition as well as a solid support for reaction to take place. Acidic environment makes the carbonyl carbon more susceptible towards the nucleophilic attack of the amines which leads to higher yield with better selectivity.

Similar approach was then extended to get different N, N' - disubstituted urea derivatives from corresponding amines (Table 1). Structural confirmation of all the synthesized compounds was done on the basis of spectroscopic data-IR, ^1H NMR and by comparison of their melting point with the authentic samples [18-21].

4. Conclusion

In conclusion, an eco-friendly green procedure has demonstrated for the synthesis of N, N'-disubstituted urea derivatives in the presence of Montmorillonite K-10 as catalyst under solvent free conditions using microwave irradiation. The protocol is fairly clean, mild and efficient with operational simplicity.

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