Tetrahedron Letters 54 (2013) 975–979

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

An efficient transformation of ethers to *N,N′*-disubstituted ureas in a Ritter type reaction

Veladi Panduranga, Basavaprabhu, Vommina V. Sureshbabu *

#Room 109, Peptide Research Laboratory, Department of Studies in Chemistry, Central College Campus, Bangalore University, Dr. B.R. Ambedkar Veedhi, Bangalore 560001, India

ARTICLE INFO

Article history:
Received 12 November 2012
Revised 8 December 2012
Accepted 9 December 2012
Available online 19 December 2012

Keywords:
Cyanamides
Ethers
Lewis acid
N,N′-disubstituted ureas

ABSTRACT

A simple, mild, and an alternative protocol for the preparation of *N,N′*-disubstituted ureas from readily available ethers and cyanamides as starting materials is described. The protocol explores the reactivity of ether in a Ritter type reaction with cyanamide in the presence of $BF_3{\cdot}Et_2O$ and resulting in the formation of *N,N′*-disubstituted urea. Divinyl ether as well as MTBE (methyl *tert*-butyl ether) can be employed as ether components to afford allyl and *tert*-butyl ureas respectively.

Ureas are the important class of carbonyl compounds which play a significant role in organic, medicinal, supramolecular, and materials chemistry.[1] Urea is the decisive functionality in nature, widespread in biological systems, and monitoring various activities of living beings. Urea derivatives display a wide spectrum of biological activities, in particular several substituted ureas have been shown to possess a marked inhibiting effect on HIV protease enzyme.[2]

There are ample numbers of reports on the synthesis of disubstituted ureas starting from amines. The standard protocol for the preparation of urea generally involves the use of toxic and highly reactive phosgene and its derivatives.[3] However, widely accepted ones include the reaction of two amine components in the presence of carbonylating reagents.[4]

Usually the synthesis of urea is achieved through the condensation of amines with isocyanates,[5] formamides,[6] carbamates,[7] or oxidative carbonylation of amine with carbon monoxide in the presence of transition metal catalysts.[8] Another alternative is the direct carbonylation of amines by CO_2.[9] Because of the cost, toxicity, commercial availability of limited number of isocyanates, hurdles in preparing and handling of the reagents, an alternative and high throughput synthetic protocol is desirable for the synthesis of disubstituted ureas.

Ethers are the most valuable compounds in our day to day life. For example, several applications of GMEs (glycerol methyl ethers) were patented in personal care, cosmetic, laundry, cleaning formulations and in the pharmaceutical field.[10,11] In addition, diaryl ethers constitute an important class of compounds in agricultural and medicinal chemistry.[12] The activation of etheric C–O bonds through transition-metal catalyzed coupling reactions to construct C–C bonds is of significant importance in synthetic organic chemistry.[13]

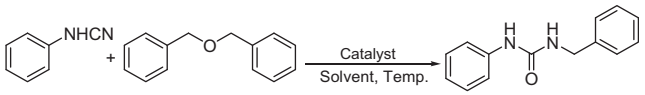
Ritter reaction is the classical C–N bond forming reaction.[14] Variations of the Ritter reaction for variety of organic transformations are well documented.[15] Anatol[16] reported the reaction of *tert*-butyl alcohol with cyanamide under elevated temperature to form urea in less yields (about 30–35%). Recently, the synthesis of di and trisubstituted ureas catalyzed by Fe (III), starting from cyanamides and alcohols through a variation of Ritter reaction has been reported by our group.[17] Currently we are involved in exploring the functionalities like ethers in this case as precursor for the preparation of *N,N′*-disubstituted ureas. Herein, by combining the reactivity of ether in the presence of an acid and utility of cyanamide as nitrile source in Ritter type reaction, we wish to report a simple, mild, and an efficient alternative protocol for the synthesis of disubstituted ureas.

In our previous report[17] we have demonstrated the formation of dibenzyl ether as an intermediate in the preparation of benzyl urea from benzyl alcohol. Similar kind of intermediacy was not observed with other alcohols that is, *tert*-butyl alcohol and allyl alcohol, wherein they react directly through the formation of stable carbocation. However, the formation of dibenzyl ether and its participation in the reaction as masked carbocation source made us to investigate the conversion of ethers to ureas. During the study, it was realized that in the presence of acid, cleavage of C–O bond of ether occurs leading to the formation of a stable

* Corresponding author. Tel.: +91 08 2296 1339/99 8631 2937.
E-mail addresses: hariccb@gmail.com, sureshbabuvommina@rediffmail.com (V.V. Sureshbabu).

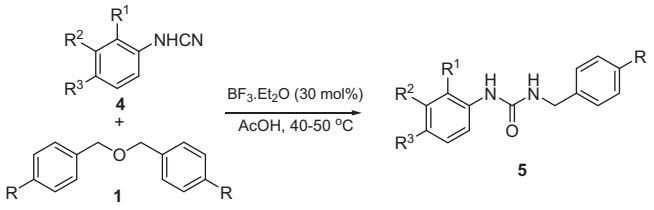
0040-4039/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2012.12.027

Table 1
Optimization of reaction



Entry	Catalyst[a]	Solvent	Yield[b] (%)	Time (h)
1	$AlCl_3$	AcOH	25	6[c]
2	$FeCl_3$	AcOH	48	6[c]
3	$FeCl_3$	DCE	91	2.5[d]
4	$BF_3{\cdot}Et_2O$	AcOH	52	4.5[c]
5	$BF_3{\cdot}Et_2O$	AcOH	94	2[d]
6	$BF_3{\cdot}Et_2O$	ACN	37	4[d]
7	$BF_3{\cdot}Et_2O$	DCE	56	4.5[d]
8	$BF_3{\cdot}Et_2O$	DCM	42	5[d]

[a] 30 mol % of catalyst was used.
[b] Isolated yield.
[c] At room temp.
[d] At temp. 40–50 °C.



Scheme 1. Synthesis of benzyl ureas from dibenzyl ether.

carbocation as reported by Kochetkov et al.[18]Various reagent systems including mineral acids and Lewis acids have been reported for the cleavage of C–O bond of ether.[19] In the present context the choice of the reagent would be such that it has to assist both the cleavage of ethereal C–O bond as well as the catalysis of the Ritter reaction.

Thus the synthesis of *N*,*N*′-disubstituted urea was undertaken employing ether and cyanamide in the presence of Lewis acid catalyst which can assist C–O bond cleavage and catalyze the subsequent Ritter type reaction. The cyanamide required for the present protocol was prepared through the reported methodology[20] wherein the amine was reacted with cyanogen bromide in dry THF/diethyl ether at 0 °C. The product obtained was then purified and used for next step. In order to establish suitable reaction conditions for the above transformation, selection of Lewis acid, solvent, and temperature are critical and need to be optimized (Table 1). In an initial study, dibenzyl ether and phenylcyanamide were chosen as model substrates and various Lewis acids were screened, among which $BF_3{\cdot}Et_2O$ and $FeCl_3$ gave satisfactory results. Before opting acetic acid (AcOH), various solvents such as dichloromethane (DCM), dichloroethane (DCE) and acetonitrile (ACN) were employed for the reaction, except DCE (for $FeCl_3$), remaining solvents did not afford the desired product quantitatively. At room temperature the reaction was very slow and on further increasing the temperature, enhancement in the reaction rate was observed.

In a typical reaction, dibenzyl ether (**1a**) was treated with phenylcyanamide (**4a**) in the presence of $BF_3{\cdot}Et_2O$ in AcOH and the reaction mixture was heated at 40–50 °C. The equivalence of $BF_3{\cdot}Et_2O$ being employed was optimized in order to obtain the urea (**5a**) in good yield (Scheme 1). The progress of the reaction was monitored by IR, where the appearance of strong absorption peaks at ν_{max} 1654 and 1562 cm^{-1} confirms the formation of urea. The resulting mixture was then washed with water and purified through column chromatography to afford the pure product in good yield. The structure of the product was then confirmed by mass and NMR analyses.

Generally, Lewis acid catalyzed Ritter type reaction involves the formation of an oxidative complex which later decomposes to yield a stable carbocation required for the reaction. As described by Anxionnat,[21] the carbocation will be formed through the ether–Lewis acid ($FeCl_3$) complex. In addition, AcOH drives the reaction toward the product formation by reducing the reaction time. AcOH being a strongly ionizable solvent, at an elevated temperature it assists in breaking the oxidative complex of ether and $BF_3{\cdot}Et_2O$ and thus helps in the formation of carbocation with ease (Fig. 1).

Generality of the protocol was further explored, where dibenzyl ethers substituted by methyl (**1b**) and nitro (**1c**) groups at *para*-position were also employed as ether components and afforded corresponding ureas in good to excellent yields.[22] The nitro substituted dibenzyl ether afforded corresponding urea in comparatively lesser yield than its methyl counterpart. Aromatic cyanamides irrespective of their nature of substitution (electron donating or electron withdrawing) furnished corresponding ureas in respectable yields (Table 2). Further, the protocol was extended for the preparation of allyl ureas employing divinyl ether (**2**) as ether component.

We first attempted the reaction of divinyl ether with cyanamide in the presence of $FeCl_3$ in DCE, the product formation was rather slow and furnished the urea in very low yields. When the same reaction was repeated with $BF_3{\cdot}Et_2O$, it served as a better catalyst system in yielding good results with divinyl ether and furnished the allyl ureas (**6**) in good yields (Table 3).[23]

In addition, the synthesis of *tert*-butyl urea was achieved using MTBE (methyl *tert*-butyl ether) as ether component. MTBE (**3**) is

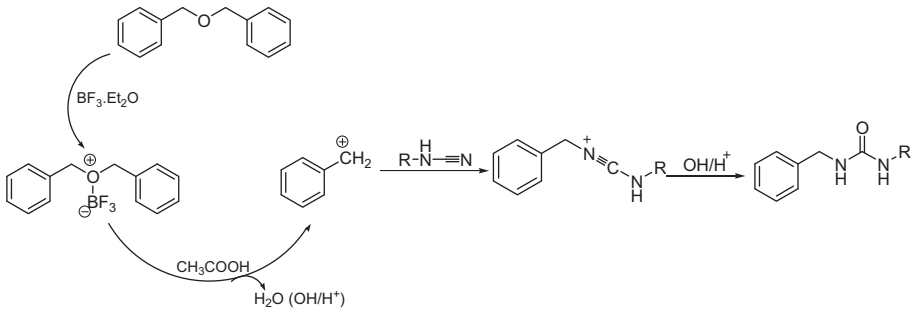
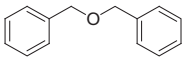
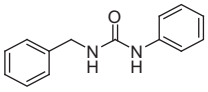
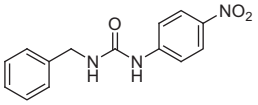
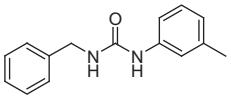
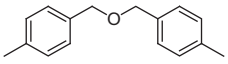
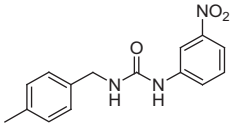
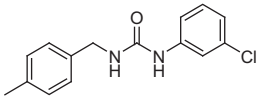
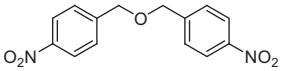
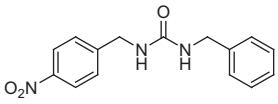
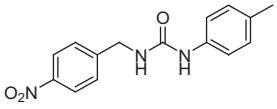


Figure 1. Possible reaction pathway for $BF_3{\cdot}Et_2O$ catalyzed synthesis of *N*,*N*′-disubstituted urea.

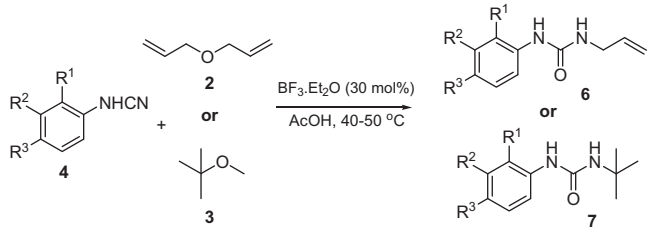
Table 2
List of benzyl ureas prepared

Entry	Ether	Urea	Yield[a] (%)	Time (h)
1	 (**1a**)	 **5a**	94	2
2		 **5b**	68	3.5
3		 **5c**	85	3
4	 (**1b**)	 **5d**	71	4
5		 **5e**	76	3.5
6	 (**1c**)	 **5f**	66	4
7		 **5g**	72	6

[a] Isolated yield.

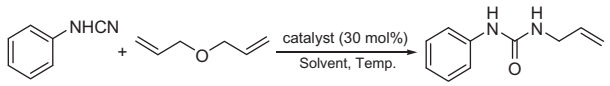
the safe ether available commercially and is cheaper and easy to handle. Kochetkov et al.,[18]reported that MTBE serves as a better source for *tert*-butyl carbocation in the presence of acid catalyst. Thus, we started to investigate it for the present protocol. Under the optimized reaction conditions in presence of $BF_3{\cdot}Et_2O$, MTBE decomposes to *tert*-butyl cation and methoxide ion. Thus formed *tert*-butyl cation took part in the reaction in Ritter like fashion to yield the ureas (**7**). Interesting point noticed with the reaction of MTBE is the selective formation of *tert*-butyl carbocation in the presence of $BF_3{\cdot}Et_2O$ and its participation in the urea formation. With divinyl ether and MTBE, cyanamides possessing electron donating or electron withdrawing groups afforded corresponding ureas in good to excellent yields (Scheme 2), as furnished in Table 4.[24]

Herein we describe a simple, mild, and an alternative methodology which demonstrates the $BF_3{\cdot}Et_2O$ catalyzed cleavage of ethereal C–O bond and the subsequent Ritter type reaction with cyanamides under $BF_3{\cdot}Et_2O$ catalysis resulting in *N*,*N*′-disubstituted ureas in one pot. The protocol would provide an excellent alternative to the existing protocols due to its operational simplicity.



Scheme 2. Synthesis of allyl and *tert*-butyl ureas.

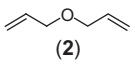
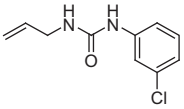
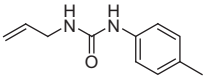
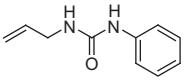
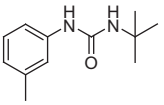
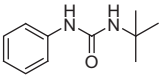
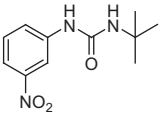
Table 3
Comparison of $FeCl_3$ and $BF_3{\cdot}Et_2O$ for allyl urea preparation



Entry	Catalyst	Solvent	Temp (°C)	Yield[c] (%)
1	$FeCl_3$[a]	AcOH	rt	13
2	$FeCl_3$[b]	AcOH	40–50	23
3	$FeCl_3$	DCE	40–50	47
4	$BF_3{\cdot}Et_2O$[a]	AcOH	rt	38
5	$BF_3{\cdot}Et_2O$[b]	AcOH	40–50	87

[a] 20 mol % of catalyst was used.
[b] 30 mol % of catalyst was used.
[c] Isolated yield.

Table 4
List of allyl and *tert*-butyl ureas prepared

Entry	Ether	Urea	Yield[a] (%) (reacn time in h)
1	 (**2**)	 **6a**	76 (3)
2		 **6b**	79 (3.5)
3		 **6c**	74 (2.5)
4	 (**3**)	 **7a**	86 (2.5)
5		 **7b**	84 (3)
6		 **7c**	67 (6)

[a] Isolated yield.

Acknowledgements

We thank the Department of Science and Technology, Govt. of India (Grant No. SR/S1/OC-52/2011) for the financial assistance and V.P. thanks CSIR for fellowship.

References and notes

1. (a) Gallou, I. *Org. Prep. Proced. Int.* **2007**, *4*, 355; (b) Bigi, F.; Maggi, R.; Sartori, G. *Green Chem.* **2000**, *2*, 140; (c) Vishnyakova, T. P.; Golubeva, I. A.; Glebova, E. V. *Russ. Chem. Rev. (Engl. Ed.)* **1985**, *54*, 249; (d) Matsuda, K. *Med. Res. Rev.* **1994**, *14*, 271; (e) Kishida, T.; Fujita, N.; Sada, K.; Shinkai, S. *Langmuir* **2005**, *21*, 9432. and references cited there in.
2. (a) Dinsmore, C. J.; Hartman, G. D. WO 9,727,752, A1.; (a) Decieco, C. S.; Seng, J. L.; Kennedy, K. E.; Covington, M. B.; Welch, P. K.; Arner, E. C.; Magolda, R. L.; Nelson, D. J. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 2331.
3. (a) Babad, H.; Zeiler, A. G. *Chem. Rev.* **1973**, *73*, 75; (b) Smith, M. B.; March, J. *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 5th ed; Wiley: New York, 2001. p 1191; (c) Knoelker, H. J.; Braxmeier, T. Schlechtingen *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2497.
4. (a) Stabb, H. A. *Liebigs Ann. Chem.* **1957**, *609*, 75; (b) Katritzky, A. R.; Pleynet, D. P. M.; Yang, B. *J. Org. Chem.* **1997**, *62*, 4155; (c) Leung, M.-K.; Lai, J.-L.; Lau, K.-H.; Yu, H.-H.; Hsiao, H.-J. *J. Org. Chem.* **1996**, *61*, 4175.
5. (a) Dominguez, J. N.; Leon, C.; Rodrigues, J.; de Dominguez, N. G.; Gut, J.; Rosenthal, P. J. *J. Med. Chem.* **2005**, *48*, 3654; (b) Bolshan, Y. M.; Tomaszewski, J.; Sanathakumar, V. *Tetrahedron Lett.* **2007**, *48*, 4925; (c) Suzuki, T.; Nagano, Y.; Kouketsu, A.; Matsuura, A.; Maruyama, S.; Kurotaki, M.; Nakagawa, H.; Miyata, N. *J. Med. Chem.* **2005**, *48*, 1019; (d) Lalithamba, H. S.; Narendra, N.; Hemantha, H. P.; Sureshbabu, V. V. *Org. Biomol. Chem.* **2010**, *8*, 835.
6. Williams, A.; Ibrahim, I. T. *Chem. Rev.* **1981**, *81*, 589.
7. (a) Chaturvedi, D.; Mishra, N.; Mishra, V. *Monatsh. Chem.* **2007**, *138*, 57; (b) Azad, S.; Kumamota, K.; Uegaki, K.; Ichikawa, Y.; Kotsuki, H. *Tetrahedron Lett.* **2006**, *47*, 587; (c) McGhee, W.; Riley, D.; Christ, P. Y.; Parnas, B. *J. Org. Chem.* **1995**, *60*, 2820; (d) Hooker, J. M.; Reibel, A. T.; Hill, S. M.; Schueller, M. J.; Fowler, J. S. *Angew. Chem., Int. Ed.* **2009**, *48*, 3482; (e) Matsumura, Y.; Satosh, Y.; Onomura, O.; Maki, T. *J. Org. Chem.* **2000**, *65*, 1549; (f) Azad, S.; Kumamoto, K.; Uegaki, K.; Ichikawa, Y.; Kotsuki, H. *Tetrahedron Lett.* **2006**, *47*, 587; (g) Shi, M.; Shen, Y.-M. *J. Org. Chem.* **2002**, *67*, 16. and references cited therein.
8. (a) Gabriele, B.; Salerno, G.; Mancuso, R.; Costa, M. *J. Org. Chem.* **2004**, *69*, 4741; (b) Sonoda, N.; Yasuhara, T.; Kondo, K.; Ikeda, T.; Tsutsumi *J. Am. Chem. Soc.* **1971**, *93*, 691; (c) Tsuji, Y.; Takeuchi, R.; Watnabe, Y. *J. Organomet. Chem.* **1985**, *290*, 249; (d) Giannoccaro, P. *J. Organomet. Chem.* **1987**, *336*, 271; (e) Pri-Bar, I.; Alper, H. *Can. J. Chem.* **1990**, *68*, 1544; (f) Yang, Y.; Lu, S. *Tetrahedron Lett.* **1999**, *40*, 4845; (g) Mei, J.; Yang, Y.; Xeu, Y.; Lu, S. *J. Mol. Catal. A: Chem.* **2003**, *191*, 135.
9. (a) Hampe, E. M.; Rudkevich, D. M. *Tetrahedron* **2003**, *59*, 9619; (b) Morimoto, Y.; Fujiwara, T. H.; Hori, Y.; Nagano, Y. *Tetrahedron Lett.* **1986**, *1809*, 27; (c) Fournier, J.; Bruneau, C.; Dixneuf, P. H.; Lecolier, J. *J. Org. Chem.* **1991**, *56*, 4456; (d) Gabriele, B.; Mancuso, R.; Salareno, G.; Costa, M. *Chem. Commun.* **2003**, *4*, 486; (e) Ion, A.; Pavulescu, V.; Jacobs, P.; Vos, D. D. *Green Chem.* **2007**, *9*, 158.
10. (a) Shoji, N.; Yuikinaga, Y. **1994**, EP N0624563, Kao Corporation.; (b) Arredondo, V. M.; Back, D. J.; Corrigan, P. J.; Kreuzer, D. P.; Cearley, A. C. WO 2007/113776 (2006), Procter & Gamble Company.
11. (a) Singh, S.; Bhadani, A.; Kamboj, R. *Ind. Eng. Chem. Res.* **2008**, *47*, 8090; (b) Hazra, A. G.; Chatterjee, P. *Ind. Crops Prod.* **2008**, *27*, 39; (c) Erdlenbruch, B.; Jendrossek, V.; Eibl, H.; Lakomek, M. *Exp. Brain Res.* **2000**, *135*, 417; (d) Brohult, A. H.; Brohult, S. F. A. U.S. Patent 3,432,602.
12. Rao, A. V. R.; Gurjar, M. K.; Reddy, K. L.; Rao, A. S. *Chem. Rev.* **1995**, *95*, 2135.
13. (a) Wenkert, E.; Michelotti, E. L.; Swindell, C. S. *J. Am. Chem. Soc.* **1979**, *101*, 2246; (b) Wenkert, E.; Michelotti, E. L.; Swindell, C. S.; Tingoli, M. *J. Org. Chem.* **1984**, *49*, 4894; (c) Dankwardt, J. W. *Angew. Chem., Int. Ed.* **2004**, *43*, 2428; (d) Kakiuchi, F.; Usui, M.; Ueno, S.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **2004**, *126*, 2706; (e) Ueno, S.; Mizushima, E.; Chatani, N.; Kakiuchi, F. *J. Am. Chem. Soc.* **2006**, *128*, 16516; (f) Fumitoshi, K.; Mayumi, U.; Naoto, C.; Shinji, M. *J. Am. Chem. Soc.* **2004**, *126*, 2706.
14. (a) Ritter, J. J.; Minieri, P. P. *J. Am. Chem. Soc.* **1948**, *70*, 4045; (b) Benson, F. R.; Ritter, J. J. *J. Am. Chem. Soc.* **1949**, *71*, 4128; (c) Plaut, H.; Ritter, J. J. *J. Am. Chem. Soc.* **1951**, *73*, 4076.
15. (a) Sanz, R.; Martinez, A.; Guilerate, V.; Alverz-Guiterrez, J. M.; Rodriguez, F. *Eur. J. Org. Chem.* **2007**, 4642; (b) Barbero, M.; Bhazzi, S.; Cadamuro, S.; Dughera, S. *Eur. J. Org. Chem.* **2009**, 430.
16. (a) Anatol, J.; Berecoechea, J. *Bull. Soc. Chim. Fr.* **1975**, *1–2*, 395; (b) Anatol, J.; Berecochea, J. *Synthesis* **1975**, 111; (c) Clark, N. *J. Chem. Res., Synop.* **1981**, *5*, 148; (d) Anatol, J.; Berecoechea, U.S. 4,013,706, March 22, 1977.
17. Basavaprabhu, H.; Sureshbabu, V. V. *Org. Biomol. Chem.* **2012**, *10*, 2528.
18. Kochetkov, H. K.; Derevitskaya, V. A.; Klimov, E. M. *Tetrahedron Lett.* **1969**, *10*, 4769.
19. Guo, Q.; Miyaji, T.; Gao, G.; Hara, R.; Takahashi, T. *Chem. Commun.* **2001**, 1018.

20. (a) Hu, L. Y.; Guo, J.; Magar, S. S.; Fischer, J. B.; Burke-Howie, K. J.; Durant, G. J. *J. Med. Chem.* **1997**, *40*, 4281; (b) Kaupp, G.; Schmeyers, J.; Boy, J. *Chem. Eur. J.* **1998**, *4*, 2467; (c) Chen, C.-Y.; Wong, F. F.; Huang, J.-J.; Lin, S.-K.; Yeh, M.-Y. *Tetrahedron Lett.* **2008**, *49*, 6505; (d) Wong, F. F.; Chen, C.-Y.; Yeh, M.-Y. *Synlett* **2006**, 559; (e) Ghosh, H.; Yella, R.; Ali, A. R.; Sahoo, S. K.; Patil, B. K. *Tetrahedron Lett.* **2009**, *50*, 2407.
21. (a) Anxionnat, B.; Guerinot, A.; Reymond, S.; Cossy, J. *Tetrahedron Lett.* **2009**, *50*, 3470; (b) Wang, Z. D.; Sheik, S. O.; Cox, S.; Zhang, Y.; Massey, K. *Eur. J. Org. Chem.* **2007**, 2243.
22. *General procedure for the preparation of cyanamides (**4**)*
To a solution of amine (1.0 mmol) in dry THF/diethyl ether (10 mL) at 0 °C was added a solution of CNBr (1.5 mmol) in THF/diethyl ether (4 mL). The mixture was stirred till the completion of the reaction as judged by TLC and then the reaction mixture was filtered to remove the residual salt and concentrated to yield corresponding cyanamide. The crude was then diluted with EtOAc and washed twice with 10% HCl (10 mL), water, and brine. Organic extract was dried over anhydrous Na_2SO_4 and evaporation of the solvent in vacuo results in cyanamide which was further purified by silica gel column chromatography (10% EtOAc/hexane system).
23. General procedure for the synthesis of *N*,*N*′-disubstituted ureas (**5**–**7**)
To a stirred solution of ether (1.0 mmol) in AcOH (6 mL), was added 30 mol % of $BF_3{\cdot}Et_2O$ followed by the addition of cyanamide (1.0 mmol). The reaction mixture was refluxed at an elevated temperature (40–50 °C) till the completion of the reaction as monitored by TLC. Upon complete consumption of the cyanamide, the reaction medium was diluted with EtOAc (15 mL). The organic layer was washed with water followed by 5% $NaHCO_3$ (2 × 5 mL), water (2 × 5 mL), and brine (5 mL). The organic layer was then dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuo to afford the crude which was then purified through silica gel column chromatography (30–40% EtOAc/hexane).
24. *Characterization data for selected compounds:*
*1-Benzyl-3-m-tolylurea (**5c**):* White solid; yield = 85%; Mp = 175–177 °C; IR (KBr): 3298, 3037, 1663, 1585 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 2.28 (s, 3H), 4.21 (d, *J* = 5.82 Hz, 2H), 6.46 (s, 1H), 6.90–7.35 (m, 9H), 7.47 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 24.4, 44.5, 120.1, 124.5, 126.2, 128.3, 129.4, 136.5, 137.6, 139.4, 141.2, 158.1; HRMS calcd for $C_{15}H_{16}N_2O$, *m*/*z* 261.1161 (M+Na); found 261.1160.
*1-(4-Methylbenzyl)-3-(3-nitrophenyl)urea (**5d**):* White solid; yield = 71%; Mp = 223–224 °C; IR (KBr): 3311, 3042, 1658, 1582 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 2.31 (s, 3H), 4.28 (d, *J* = 5.88 Hz, 2H), 6.53 (s, 1H), 6.97–7.07 (m, 4H), 7.85–8.16 (m, 4H), 8.32 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 22.4, 48.3, 118.5, 120.2, 126.2, 127.8, 128.4, 129.5, 133.6, 136.6, 141.2, 147.8, 158.2; HRMS calcd for $C_{15}H_{15}N_3O_3$ *m*/*z* 308.1011 (M+Na) found 308.1009.
*1-(4-Nitrobenzyl)-3-benzyl urea (**5f**):* White solid; yield = 66%; Mp = 205–206 °C; IR (KBr): 3331, 3059, 1658, 1590 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 4.26 (d, *J* = 5.95 Hz, 2H), 4.28 (d, *J* = 5.86 Hz, 2H), 6.87 (s,1H), 6.92–7.16 (m,5H), 7.80 (d, *J* = 7.82 Hz, 2H), 8.10 (d, *J* = 8.1 Hz,2H), 8.51 (s,1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 44.8, 119.4, 123.2, 125.4, 127.6, 129.8, 132.4, 139.7, 140.3, 146.8, 157.1; HRMS calcd for $C_{15}H_{15}N_3O_3$ *m*/*z* 308.0930 (M+Na); found 308.0933.
*1-Allyl-3-p-tolylurea (**6b**):* White solid; yield = 79%; Mp = 188–190 °C; IR (KBr): 3334, 3078, 1656, 1562 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 2.36 (s,3H), 3.92 (d, *J* = 6.8 Hz, 2H), 4.64–4.70 (m, 2H), 5.57–5.62 (m, 1H), 6.49 (s, 1H), 6.88 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 8.12 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 23.9, 43.6, 116.2, 118.5, 122.5, 124.8, 129.6.5, 130.3, 134.2, 141.8, 157.1; HRMS calcd for $C_{11}H_{14}N_2O$ *m*/*z* 213.1004 (M+Na); found 213.1003.
*1-tert-Butyl-3-(3-nitrophenyl)urea (**7c**):* White solid; yield = 67%; Mp = 147–149 °C; IR (KBr): 3381, 3054, 1651, 1572 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 1.31 (s, 9H), 6.52 (s, 1H), 7.12–7.81 (m, 4H), 8.03 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 25.2, 51.2, 121.2, 128.3, 129.6, 130.9, 138.4, 146.5, 158.0; HRMS calcd for $C_{11}H_{15}N_3O_3$ *m*/*z* 260.1011 (M+Na); found 260.1009.