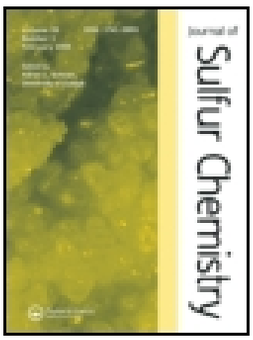


Journal of Sulfur Chemistry

ISSN: 1741-5993 (Print) 1741-6000 (Online) Journal homepage: http://www.tandfonline.com/loi/gsrp20

Synthesis Of di- and tri-substituted thiourea derivatives in water using choline chloride–urea catalyst

Hossein Tavakol, Amir Mahmoudi & Mohammad-Amin Ranjbari

To cite this article: Hossein Tavakol, Amir Mahmoudi & Mohammad-Amin Ranjbari (2018): Synthesis Of di- and tri-substituted thiourea derivatives in water using choline chloride–urea catalyst, Journal of Sulfur Chemistry, DOI: 10.1080/17415993.2018.1533014

To link to this article: https://doi.org/10.1080/17415993.2018.1533014

JOURNAL OF SULFUR CHEMISTRY
https://doi.org/10.1080/17415993.2018.1533014

Taylor & Francis
Taylor & Francis Group

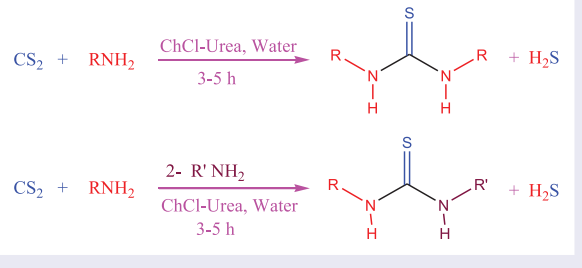
Synthesis Of di- and tri-substituted thiourea derivatives in water using choline chloride–urea catalyst

Hossein Tavakol, Amir Mahmoudi and Mohammad-Amin Ranjbari

Department of Chemistry, Isfahan University of Technology, Isfahan, Iran

ABSTRACT

In this work, di- and tri-substituted thiourea derivatives have been synthesized via a one-pot, three-component reaction from carbon disulfide and aliphatic or aromatic amines using choline chloride-urea deep eutectic solvent as a catalyst in water. Both cyclic and acyclic thiourea derivatives with two or three substituents were synthesized successfully. The reactions were done at 25–100°C, using 5–20 mol% catalyst, in 3–5 h and the GC-Mass yields were between 60% and 95%. All products were characterized using FT-IR, ^{1}H-NMR, ^{13}C-NMR, GC-MS and melting point analyses. The results showed that both water and the DES have important effects on the yield and the rate of this reaction and both of them are necessary to obtain higher yields in less time. The extra experiment, which was designed to study the mechanism of the reaction, showed that an isothiocyanate intermediate was formed in the reaction. Finally, the results showed that by the increase of the amine's nucleophilicity, the reaction occurs faster and gives higher yield.



ARTICLE HISTORY
Received 2 March 2018
Accepted 3 October 2018

KEYWORDS
Green; thiourea; DES; water; carbon disulfide

1. Introduction

Thiourea is a valuable functional group in organic chemistry. Therefore, the syntheses of its derivatives have been the subject of significant interest for many years. These compounds have various applications in medicinal chemistry and biological purposes such

CONTACT Hossein Tavakol h_tavakol@cc.iut.ac.ir

Supplemental data for this article can be accessed here. https://doi.org/10.1080/17415993.2018.1533014

as in fungicides, herbicides [1], phenoloxidase [2] and enzymatic inhibitors [3]. Moreover, thiourea and its derivatives are important building blocks in the synthesis of various heterocycles [4–6] and they have been used as organocatalysts in several synthetic methodologies. The importance of chiral derivatives of thiourea is especially evident from their potencies as enantioselective or stereoselective catalysts [7–9]. However, despite several reported studies of the synthesis and applications of thiourea derivatives [10,11], the existing methodologies for the synthesis of these materials are not sufficient and some of the developed methods suffer synthetic or environmental limitations. Therefore, research in this area is important for synthetic chemists in order to develop new methodologies, especially with less environmental and synthetic problems. During previous decades, many attempts have been made to perform organic reactions in water, [12,13] and this approach has been taken here for the synthesis of these thiourea derivatives. However, finding appropriate catalysts to perform chemical reactions in water is very difficult. However, ionic liquids and their new generation, deep eutectic solvents (DESs) showed promising catalytic abilities in water, as well as potencies in other reaction media.

DESs were introduced in 2003 by Abbott and co-workers [14]. Since then, they have been used extensively in organic synthesis and other applications [15]. These solvents (or mixtures) do not suffer some of the disadvantages of ILs, while they benefit from all the advantages of ILs. Therefore, the use of these solvents has increased in recent years [16], in different scientific and industrial applications such as in the synthesis of organic and inorganic compounds [17,18], extraction of heavy metals [19] and in the construction of solar cells [20]. These solvents are typically made up of a quaternary ammonium or phosphonium salt and a hydrogen bond donor agent such as alcohols or inorganic salts [21]. A lot of DESs have been introduced in recent years and among them, the mixture of choline chloride (ChCl)–urea (mostly in 1:2 ratio) has been considered as an appropriate candidate for synthetic purposes. It can be employed as a catalyst, solvent or both, because of its unique properties such as strong catalytic potency, good solubility and fluidity at room temperature [21]. Therefore, in the continuation of our studies on organic synthesis development, especially using DESs [22–24], and due to the valuable properties of thiourea derivatives, we have focused on their preparation using ChCl–urea DES.

Various methods have been reported in the literature for the synthesis of these compounds, including reactions starting from isothiocyanates, carbon disulfide, thiophosgene or urea [25]. In this work, the reaction between amine and carbon disulfide has chosen for the synthesis of thiourea derivatives, because of the high atom economy and the high overall yield of this method. The green reaction media (water) and the green and inexpensive catalyst (choline chloride–urea DES) were selected to perform this transformation. Various thiourea derivatives with 2 and 3 substitutions have been synthesized successfully via this method. The results of this study and the details of the employed methodologies are mentioned in the next sections.

2. Materials and methods

Chemical compounds were purchased from Merck (Germany) and Dae-Jung (South Korea) companies. The employed amines were purified before the first use and the other starting materials were used without further purifications. Melting points were determined using Gallen Kamp apparatus. Thin-layer chromatography (TLC) was employed

to monitor the reaction and check the purities. FT-IR spectra were recorded using KBr pellets by JASCO FT-IR instrument. ^{1}H-NMR and ^{13}C-NMR spectra were recorded using Brucker Ultrashield 400 MHz NMR instrument and $CDCl_3$ or DMSO were used as solvents. Chemical shifts were expressed in ppm versus the chemical shift of tetramethylsilane (TMS) as a reference. Mass spectra and GC-Mass analyses were recorded on Agilent GC-MS-5975C with Triple-Axis Detector.

2.1. Preparation of ChCl–urea DES

ChCl–urea chloride eutectic solvent was prepared according to the reported procedure in the literature. For this preparation, ChCl was dried under vacuum at 120°C for three hours. Then, ChCl (10 mmol) was mixed with urea (20 mmol) and heated to 100°C in air with stirring until a clear liquid was obtained. This mixture was used in the next experiment without needing further purification.

2.2. General procedure for the synthesis of thiourea derivatives from one amine

In a 10 mL round-bottom flask (equipped with a basic gas trap to neutralize exhausted hydrogen sulfide), 2 mmol amine was added to 3 mL distilled water and 0.1 mmol of DES (ChCl–urea). The flask was placed in an ice bath over the magnetic heater-stirrer and the mixture was stirred vigorously. Then, 1 mmol carbon disulfide was added to the mixture during the stirring. The reaction was monitored by TLC, with ethyl acetate-hexane (3:7) mixture as eluent, up to the completion of the reactant. The ice bath was then removed and replaced with an oil bath, the flask was equipped with a condenser and the reaction was heated to 100°C and stirred for 3 h with refluxing. Then, the heating was stopped and the reaction was allowed to reach to room temperature. The precipitated product (during the cooling), was purified by recrystallization in ethanol and used for the next analyses. All products are known compounds and their structures were confirmed by comparison of their mass specta, IR, ^{1}H-NMR and ^{13}C-NMR spectra, and melting points with the reported values in the literature [26–30]. The selected physical properties, GC-Mass results and spectroscopic data for all products are listed in section 2.4 and all original spectral data (IR, NMR and mass spectrometry) are shown in the supplementary information.

2.3. General procedure for the synthesis of thiourea derivatives from two different amines

In a 10 mL round-bottom flask (equipped with a basic gas trap to neutralize exhausted hydrogen sulfide), 1 mmol amine (first amine) was added to 3 mL distilled water and 0.1 mmol of DES (ChCl–urea). The flask was placed on an ice bath over a magnetic heater-stirrer and the mixture was stirred vigorously. Then, 1 mmol carbon disulfide was added to the mixture at low temperature during stirring. The reaction was monitored by TLC with ethyl acetate-hexane (3:7) mixture as eluent up to the completion of the reaction. After this, 1 mmol of the second amine was added to the reaction mixture, the ice bath was removed and replaced with an oil bath, the flask was equipped with a condenser and the reaction was heated to 100°C and stirred for 3 h (or more, in some derivatives) with refluxing. The heating was stopped and the reaction was allowed to reach room temperature.

The precipitated product (during the cooling), was purified by recrystallization in ethanol and used for the next analyses. All products are known compounds and their structures were confirmed by comparison of their mass spectrometry, IR, ^{1}H-NMR and ^{13}C-NMR spectroscopy, and melting points with the reported values in the literature [26–30]. The physical properties, GC-Mass results and spectroscopic data for all products are listed in section 2.4 and the original spectra (IR, NMR and mass spectrometry) are shown in the supplementary information.

2.4. Physical and spectroscopic data for products

2.4.1. 1,3-dibenzylthiourea (3a)

White crystal (Yield: 90%); m.p. 145°C. FT-IR (KBr): 3289, 3080, 2983, 1553, 1500, 1452, 1393, 1280, 740 cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.73 (s, 4H), 7.34 (m, 10H), 7.97 (s, 2H) ppm; ^{13}C-NMR (100 MHz, CDCl3): δ 48.5, 127.6, 128.0, 129.0, 136.7, 182.2 ppm; GC-MS: *m/z* (%):65 (18.0), 79 (20.1), 91 (83.2), 106 (100), 256 50.9) [M +].

2.4.2. 1,3-diphenylthiourea (3b)

White crystal (Yield: 80%); m.p. 150–153°C. FT-IR (KBr): 3200, 3035, 1660, 1450, 1380, 930, 750, 630 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) 7.1–7.5 (m, 10H), 9.79 (s, 2H) ppm. ^{13}C-NMR (101 MHz, $CDCl_3$) δ 124.11, 124.89, 128.91, 139.94, 180.10 ppm. GC-MS: *m/z* (%): 65, 91, 134, 169, 226 [M^+].

2.4.3. 1,3-bis(3-hydroxyphenyl)thiourea (3c)

Yellow oil (Yield: 60%). FT-IR (KBr): 3350, 3000, 1600, 1550, 1200 cm^{-1}. ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.90, 157.34, 140.43, 129.10, 113.89, 111.42, 110.25. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.65 (s, 2H), 9.46 (s, 2H), 7.10 (t, J = 8.0 Hz, 2H), 7.01 (t, J = 2.2 Hz, 2H), 6.86 (d, J = 8.0 Hz, 2H), 6.52 (dd, J = 7.7, 1.9 Hz, 2H). ^{13}C-NMR (101 MHz, DMSO-d_6) 110.25, 111.42, 113.89, 129.10, 149.43, 157.34, 178.90 ppm. The signals of ethyl acetate (purification solvent) were remained in both NMR spectra.

2.5. 1,3-bis(3,4-dimethoxyphenethyl)thiourea (3d)

White crystal (yield: 90%); m.p. 145–146°C. FT-IR (KBr): 3350, 3250, 2990, 1630, 1550, 1280 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.40 (s, 2H), 6.86 (d, J = 8.1 Hz, 2H), 6.81 (d, J = 2.0 Hz, 2H), 6.72 (dd, J = 8.2, 2.0 Hz, 2H), 3.74 (s, 6H), 3.72 (s, 6H), 3.67–3.50 (m, 4H), 2.72 (t, J = 7.3 Hz, 4H). ^{13}C-NMR (101 MHz, DMSO-d_6) 34.31, 44.98, 55.32, 55.46, 111.80, 112.44, 120.42, 131.74, 141.17, 148.55, 180.10 ppm.

2.5.1. Tetrahydropyrimidine-2(1H)-thione (5a)

White crystal (Yield: 90%); m.p. 183°C. FT-IR (KBr): 3250, 3160, 3090, 2950, 1550, 1425, 1310, 1190 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.72 (m, 2H), 3.1 (m, 4H), 7.8 (s, 2H); ^{13}C-NMR (101 MHz, DMSO-d_6) δ 19.69, 40.25, 176.10 ppm. GC-MS: *m/z* (%): 60 (12.6), 74 (9.9), 116 (100) [M +] [28].

2.5.2. 1,3-dihydro-2H-benzo[d]imidazole-2-thione (5b)

White crystal (Yield: 75%); m.p. 145°C. FT-IR (KBr):1200, 1315, 1550, 3150, 3235 cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6) 7.2 (m, 4H), 12.32 (s, 2H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ 109.93, 122.76, 132.71, 168.59 ppm. GC-MS: *m/z* (%): 45, 78, 105, 150.0 (99.74) [M^+].

2.5.3. 1-benzyl-3-phenylthiourea (7a)

White crystal (Yield: 60%); m.p. 159–163°C. FT-IR (KBr): 3450, 3300, 3230, 3190, 1650, 1610, 1490, 960, 790 cm^{-1}; GC-MS: *m/z* (%): 28 (18.0), 51(7.1), 79 (19.9), 106 (100), 149 (22.3), 207 (6.8), 240 (44.1), 242 (7.30) [M +] [29].

2.5.4. N-benzylmorpholine-4-carbothioamide (7b)

White crystal (Yield: 65%)„ m.p. 85°C. FT-IR (KBr): 3200, 3025, 1460, 1540, 1100, 940, 730, 690 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.77 (t, 4H), 3.88 (t, 4H), 4.9 (d, 2H), 5.63 (s, 1H), 7.34 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 47.54, 50.48, 66.15, 127.93, 128.22, 128.90, 137.66, 182.76 ppm. GC-MS: *m/z* (%): 57, 65, 87, 91, 149 (87 + 149 = 236) [M^+].

2.5.5. N-phenylmorpholine-4-carbothioamide (7c)

White crystal (Yield: 65%), m.p. 115°C. FT-IR (KBr): 3390, 3035, 3950, 1550, 1500, 1213, 950, 740, 690 cm^{-1}. ^{1}H-NMR (400 MHz): 3.65 (t, 4H), 3.76 (t, 4H), 7.06–7.29 (m, 5H), 7.2 (s, 1H) ppm. ^{13}C-NMR (101 MHz, $CDCl_3$) δ 49.72, 66.12, 123.02, 125.40, 129.26, 139.84, 183.75 ppm. GC-MS: *m/z* (%): 42, 51, 57, 71, 87, 108, 135 (135 + 87 = 222) [M^+].

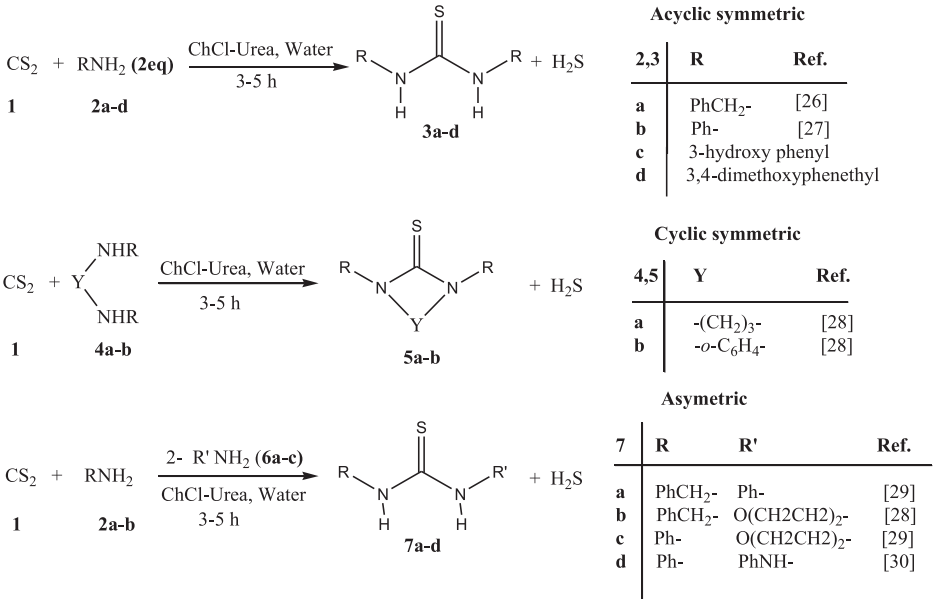
2.5.6. N-benzylhydrazinecarbothioamide (7d)

White crystal (Yield: 75%); m.p. 133°C. FT-IR (KBr): 3450, 3300, 3230, 3190, 1650, 1610, 1490, 960, 790 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 3.78 (2H, bs), 4.87 (2H, d), 7.2–7.45 (overlapping with solvent signal, 5H, m), 7.75 (2H, s) [30].

3. Results and discussion

After the synthesis of the catalyst (ChCl–urea DES), it was characterized using melting point and FT-IR spectroscopy (the results are shown in Fig. S1 in supporting information) and compared to the results from previous reports. Then, the DES was used to prepare various thiourea derivatives in water solution. The general reactions for these syntheses are shown in Scheme 1. As shown in the above scheme and in the experimental section, products from one amine or from two different amines were prepared using different procedures. In addition, the reactivity's of aliphatic and aromatic amines were not the same. Therefore, we had to separately obtain the optimized parameters for each category of reaction. To obtain these optimized parameters, a model reaction was employed, consisting of the reaction between benzyl amine as the aliphatic amine and aniline as the aromatic amine and carbon disulfide in water at different reaction temperatures, times and catalyst amounts.

First, we examined this reaction without catalyst, using only ChCl (20 mol%) and using only urea (20 mol%). Under these conditions, the reaction did not go to completion. Therefore, the use of DES is necessary for completion of this reaction. In addition, using urea as catalyst gave better results than ChCl, showing higher, but not sufficient, catalytic ability.



Scheme 1. The general reactions for the synthesis of various thiourea derivatives.

After this step, the other reaction parameters were changed to obtain the optimized conditions for both steps of the model reaction using both aliphatic and aromatic amines. Brief results of these optimizations are listed in Table 1 (many extra experiments were done that were not mentioned here to save space). For each part, the bolded row shows the optimized condition. It should be noticed that for all optimizations, temperatures less than room temperature and times less than 5 min have not been examined.

Optimizations (Table 1) of the reactions using a single amine to give products 3a,b and 5a,b demonstrated that the aliphatic or aromatic amines showed different results. The reactions of the aliphatic amines, which reacted faster, were optimized using 5 mol% catalyst at 25°C and were complete in 5 min, while the reactions of the aromatic amines, which are less reactive, were optimized using 10 mol% catalyst at 25°C and were complete in 45 min. The reactions using two different amines (products 7a-d) precede much slower and required harsher conditions. Optimization with two aliphatic amines, required 10 mol% catalyst, 100°C temperature and 3 h. Optimization with two aromatic amines required twice the catalyst (20 mol% catalyst) but the same temperature (100°C) and time (3 h) as the aliphatic amines. In addition, it was demonstrated that exclusion of water decreased both the reaction rate and yield.

Various derivatives of thiourea were synthesized using these optimized conditions but with variable reactions times to maximize the yields, and the results are reported in Table 2. The primary amines were more nucleophilic, reacting more rapidly than the secondary amines probably due to their less hindered structures. In addition, they produced fewer byproducts and their yields are higher than those of secondary amines. The highest yield (90%) were observed during preparation of thiourea derivatives from benzyl amine or 1,3-propane diamine (3a and 5a) while the lowest yields were observed in producing the derivatives obtained from two different amines (7a-7d). There is a guess that this decrease

Table 1. The brief results of optimization processes for the reaction according to the model reaction[a].

For 3a, 5a (products obtained from one aliphatic amine)				For 3b, 5b (products obtained from one aromatic amine)			
% Catalyst[b]	Temp. (°C)	Time (min)	Yield (%)	% Catalyst[b]	Temp. (°C)	Time (min)	Yield (%)
20	25	30	> 95	5	25	15	30
20	25	10	> 95	5	25	30	50
10	25	30	> 95	10	25	15	80
10	25	10	> 95	10	25	30	90
5	25	30	> 95	**10**	**25**	**45**	**> 90**
5	25	10	> 95	20	25	15	80
5	**25**	**5**	**> 95**	20	25	45	> 90
Urea (20%)	25	5	> 95	Urea(20%)	25	60	Trace
ChCl (20%)	25	5	> 95	ChCl(20%)	25	60	Trace
Free catalyst	25	5	> 95	Freecatalyst	25	30	Trace
For 7b (product obtained from two aliphatic amines)[c]				For 7a, 7c, 7d (products obtained from one aliphatic and one aromatic amines)[c]			
5	25	60	10	5	25	60	< 10
10	25	60	20	10	25	60	20
20	25	60	25	20	25	60	25
10	60	60	40	20	60	60	40
10	80	60	55	20	80	60	50
10	90	60	60	20	100	60	60
10	100	60	70	20	100	120	75
10	100	120	80	**20**	**100**	**180**	**> 80**
10	**100**	**180**	**> 90**	20	100	240	> 80
10	100	240	> 90	30	100	180	> 80
Urea (20%)	60	60	Trace	Urea(20%)	60	60	Trace
ChCl (20%)	60	60	-	ChCl(20%)	60	60	-
Free catalyst	60	60	-	Freecatalyst	60	60	-

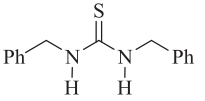
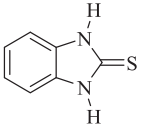
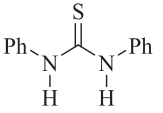
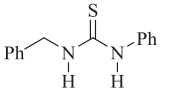
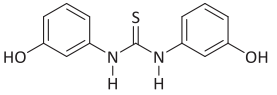
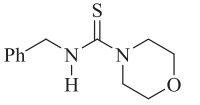
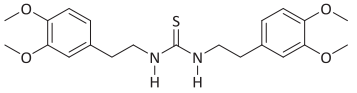
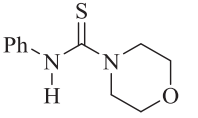
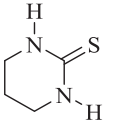
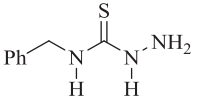
[a]The model reaction involved 2 mmol (1 mmol for each step) of aliphatic (benzyl) amine or aromatic amine (aniline), 1 mmol CS_2 in 3 mL distilled water.
[b]in mol%, for ChCl–urea DES or as defined.
[c]for derivatives with two different amines. Symmetric derivatives are consisted of only 1 step.

in the yield is maybe because of the formation of symmetrical thiourea derivatives (as byproduct) from the reaction of each of two existed amines with carbon disulfide. This guess was confirmed by the comparison of the TLC of the mixture of product with the possible symmetric amines.

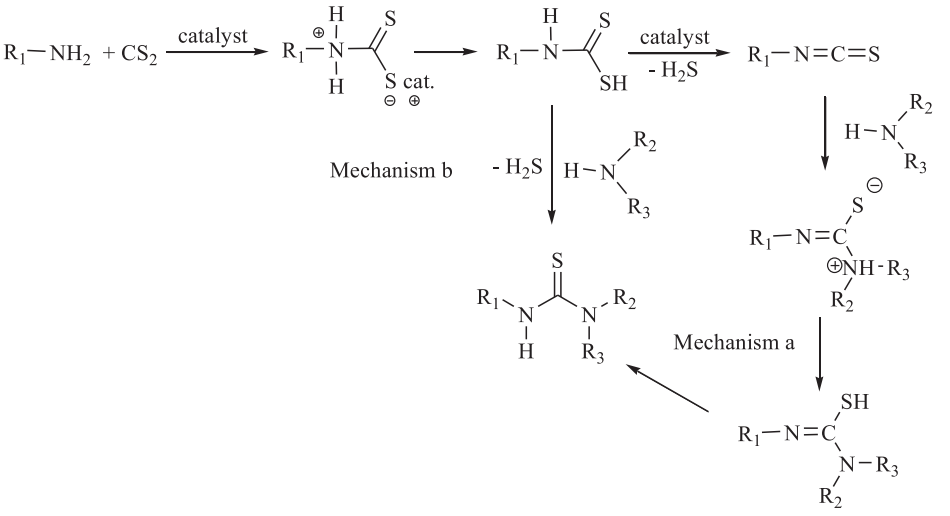
In order to determine the effect of the strength of the amine's nucleophilicity on the efficiency of this reaction, several nitrogen-containing compounds such as amino acids, amides, aromatic amines and the presence of electron withdrawing groups have been used. In accordance with our prediction, no products have been observed in any of these reactions due to the very low nucleophilicity of these compounds, even in the presence of higher concentration of catalyst and higher temperatures during a reaction time of 24 h.

Finally, we have conducted some studies to examine the mechanism for the formation of thiourea under our reported reaction conditions. According to published studies, several mechanisms have been proposed for this reaction as shown in Scheme 2. In the first suggested mechanism, the amine and carbon disulfide in the presence of the catalyst initially form dithiocarbamic acid which decomposed to form isothiocyanate as the main reaction intermediate [24] (Scheme 2(a)). In another proposed mechanism (Scheme 2(b)), the isothiocyanate was not produced as an intermediate in the reaction process [25]. Instead,

Table 2. The list of prepared thiourea derivatives with the yield of each product.

Entry	Time (h)	Product	Yield (%)[a]	Ref	Entry	Time (h)	Product	Yield (%)[a]	Ref
3a	3		90	[26]	**5b**	4		75	[28]
3b	5		80	[27]	**7a**	4.5		60	[29]
3c	5		60	-	**7b**	4		65	[28]
3d	3		90	-	**7c**	5		65	[29]
5a	3		90	[28]	**7d**	3		75	[30]

[a]GC-Mass yields.



Scheme 2. Suggested mechanism for preparation of thiourea derivatives from carbon disulfide.

the second equivalent of amine directly attacks the dithiocarbamic acid intermediate and produces the corresponding thiourea derivative after the removal of H_2S.

To provide evidence for the confirmation or rejection of the reported mechanisms in Scheme 2, we have analyzed the intermediates of the reaction before the addition of the second equivalent of amine with FTIR spectroscopy. Indeed as reported [31], the isothiocyanate signals were observed consistent with mechanism a. This conclusion is consistent with the previously reported evidence [32,33]. Nevertheless, we decided to do an additional study to confirm the operation of mechanism a. We decided to switch the order of addition of the amines by adding the secondary amine in the first step followed by the addition of the primary amine in the second step. Our hypothesis was that, since the secondary amine could not produce the isothiocyanate intermediate, if the thiourea product was formed the isothiocyanate is not a necessary intermediate in this reaction. However, we observed that the reaction did not produce any product using these conditions. Therefore, we concluded that the isothiocyanate is a necessary intermediate in this reaction providing confirmation for mechanism **a**.

4. Conclusion

In this work, di- and tri-substituted thiourea derivatives from carbon disulfide and amines were successfully synthesized using ChCl–urea DES as a catalyst in the green media water. Both cyclic and acyclic products with two or three substituents were synthesized using aliphatic and aromatic amines. The reactions were done at 25–100C, using 5–20 mol% catalyst, in 3–5 h and yields between 60% and 95% (obtained by GC-Mass) were obtained. The results showed that both water and the DES have important effects on the yield and rate of the reaction and are both required for the reactions to go to completion. The study we designed to examine the order of addition of secondary and primary amines provided compelling evidence that an isothiocyanate is a required intermediate. Finally, the

results show that the reaction rate increases and higher yields are obtained with increasing nucleophilicity of the amine.

Acknowledgements

We acknowledge the Institute of organic chemistry, University of Innsbruck (UIBK) for providing NMR facility. We have special thanks to Professor Ronald Micura (the head of the institute) and Professor Christoph Kreutz for their valuable assistances.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was supported by the research affairs of Isfahan University of technology.

ORCID

Hossein Tavakol http://orcid.org/0000-0002-3296-9575

References

[1] Walpole C, Ko SY, Brown M, et al. 2-Nitrophenylcarbamoyl-(S)-prolyl-(S)-3-(2- aphthyl)alanyl-N-benzyl-N- methylamide (SDZ NKT 343), a potent human NK1 tachykinin receptor antagonist with good oral analgesic activity in chronic pain models. J Med Chem. 1998;41(17):3159–3173.
[2] Kumavat PP, Jangale AD, Patil DR, et al. Green synthesis of symmetrical N, N′-disubstituted thiourea derivatives in water using solar energy. Environ Chem Let. 2013;11(2):177–182.
[3] Makhsumov AG, Safaev AS. Abidova SV. Chem Abstr. 1969;71:101668v.
[4] Kearney PC, Fernandez M, Flygare JA, et al. Solid-Phase synthesis of 2-aminothiazoles. J Org Chem. 1998;63(1):196–200.
[5] Lindenmaier M, Pollex A, Heinelt U, et al. A convenient method for the synthesis of 2-amino substituted aza-heterocycles from N,N′-disubstituted thioureas using TsCl/NaOH. Tetrahedron. 2004;60(44):9883–9888.
[6] September R, Patil DG, Chedekel MR. Synthesis and analysis of pheomelanin degradation products. J Org Chem. 1984;49(6):997–1000.
[7] Madarász Á, Dósa Z, Varga S, et al. Thiourea derivatives as brønsted acid organocatalysts. ACS Catal. 2016;6(7):4379–4387.
[8] Cai Q, Liang W, Wang S, et al. Ring-Closing metathesis/isomerization/pictet–spengler cascade via ruthenium/chiral phosphoric acid sequential catalysis. Org Lett. 2012;14(19):5022–5025.
[9] Kimura T, Eto T, Takahashi D, et al. Stereocontrolled photoinduced glycosylation using an aryl thiourea as an organo photoacid. Org Lett. 2016;18(13):3190–3193.
[10] Saeed A, Flörke U, Erben MF. A review on the chemistry, coordination, structure and biological properties of 1-(acyl/aroyl)-3-(substituted) thioureas. J Sulf Chem. 2014;35(3):318–355.
[11] Aly AA, Ahmed EK, El-Mokadem KM, et al. Update survey on aroyl substituted thioureas and their applications. J Sulf Chem. 2007;28(1):73–93.
[12] Linsenmeier AM, Braje WM. Efficient one-pot synthesis of dihydroquinolinones in water at room temperatu. Tetrahedron. 2015;71(38):6913–6919.
[13] Saidhareddy P, Shaw AK. Shaw chiron approach to the total synthesis of amaryllidaceae alkaloid (+)-lycoricidine. Tetrahedron. 2017;73(14):6773–6779.
[14] Abbott AP, Capper G, Davies DL, et al. Novel solvent properties of choline chloride/urea mixtures. Chem Comm. 2003;1:70–71.

[15] Handy S, Wright M. An acid-free pictet–spengler reaction using deep eutectic solvents (DES). Tetrahedron Lett. 2014;55(23):3440–3442.
[16] Jenkin GRT, Al-Bassam AZM, Harris RC, et al. The application of deep eutectic solvent ionic liquids for environmentally-friendly dissolution and recovery of precious metals. Miner Eng. 2016;87(3):18–24.
[17] Shahabi D, Tavakol H. One-pot synthesis of quinoline derivatives using choline chloride/tin (II) chloride deep eutectic solvent as a green catalyst. J Mol Liq. 2016;220(8):324–328.
[18] Abbott AP, Barron JC, Frisch G, et al. Double layer effects on metal nucleation in deep eutectic solvents. Phys Chem Chem Phys. 2011;13(21):10224–10231.
[19] Abbott AP, Capper G, Davies DL, et al. Solubility of metal oxides in deep eutectic solvents based on choline chloride. Chem Eng Data. 2006;51(4):1280–1282.
[20] Shahbaz K, Mjalli FS, Hashim MA, et al. Using deep eutectic solvents based on methyl triphenyl phosphunium bromide for the removal of glycerol from palm-oil-based biodiesel. Energy Fuel. 2011;25(6):2671–2678.
[21] Tang B, Row KH. Recent developments in deep eutectic solvents in chemical sciences. Monatsh Chem. 2013;144(10):1427–1454.
[22] Heydari A, Tavakol H, Aslanzadeh S, et al. A general one-pot, three-component mono N-alkylation of amines and amine derivatives in lithium perchlorate/diethyl ether solution. Synthesis (Mass). 2005;2005(4):627–633.
[23] Keshavarzipour F, Tavakol H. Deep eutectic solvent as a recyclable catalyst for three-component synthesis of b-amino carbonyls. Cat Lett. 2016;145(4):1062–1066.
[24] Shahabi D, Tavakol H. Synthesis of 14H–dibenzo xanthene derivatives using choline chloride/tin(II) chloride deep eutectic solvent and Fe3O4/ƛ –carrageenan/Zn(II). J Iran Chem Soc. 2017;14(1):135–142.
[25] Varma RS, Kumar D. Solvent-free organic syntheses. using supported reagents and microwave irradiation. Green Chem. 1999;1(1):43–55.
[26] Halimehjani AZ, Farahbakhsh F. Synthesis of thioureas in ionic liquid medium. J Sulf Chem. 2013;34(3):284–288.
[27] Azizi N, Khajeh-Amiri A, Ghafuri H, et al. Toward a practical and waste-free synthesis of thioureas in water. Mol Diver. 2011;15(1):157–161.
[28] Tan W, Wei J, Jiang X. Thiocarbonyl surrogate via combination of sulfur and chloroform for thiocarbamide and oxazolidinethione construction. Org Lett. 2017;19(8):2166–2169.
[29] Ramadas K, Srinivasan N, Janarthanan N. A facile conversion of symmetrical to unsymmetrical thioureas. Tetrahedron Lett. 1993;34(40):6447–6450.
[30] Singh K, Sharma S. An isocyanide based multi-component reaction under catalyst-and solvent-free conditions for the synthesis of unsymmetrical thioureas. Tetrahedron Lett. 2017;58(3):197–201.
[31] Vallejos S, Erben MF, Ge MF, et al. Conformational behavior of CH3OC (O) SX (X = CN and SCN) pseudohalide congeners. A combined experimental and theoretical study. J Phys Chem A. 2010;114(10):3703–3712.
[32] Douglass IB, Dains FB. Some derivatives of benzoyl and furoyl isothiocyanates and their Use in synthesizing heterocyclic compounds. J Am Chem Soc. 1934;56(3):719–721.
[33] Saeed A, Qamar R, Fattah TA, et al. Recent developments in chemistry, coordination, structure and biological aspects of 1-(acyl/aroyl)-3-(substituted) thioureas. Res Chem Intermed. 2017;43(5):3053–3093.