JCRS

Journal of Chemical Reactivity and Synthesis 2021: 11(3) 170-175

Research Article

Facile One-pot Synthesis of Diaryl Thiourea Derivatives Catalyzed by Cu(II)-Schiff base/SBA-15

Ali Saberi

Chemistry Department, Payame Noor University, 19395-4697 Tehran, I. R. of IRAN

ARTICLE INFO:

Received:
19 June 2021

Accepted:
28 July 2021

Available online:
24 August 2021

✉: A. Saberi
saberi@pnu.ac.ir

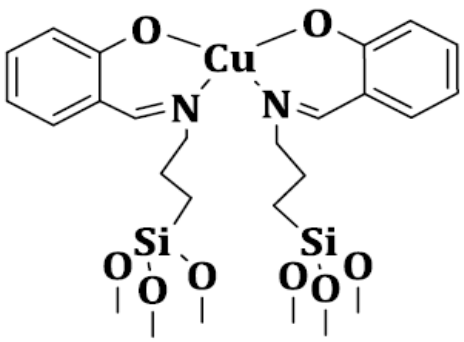
ABSTRACT

Thiourea derivatives are an important group of chemical compounds that play important roles in agriculture, pharmaceuticals, pesticides, and plant growth regulators. Herein a fast synthesis of 1, 3-diaryl-thiourea derivatives by one-pot multi-component reaction of 2-amino-benzoic acid, aryl isothiocyanate, isocyanide, and carbonyl under solvent free condition using Cu(II)-Schiff base/SBA-15 as a reusable heterogeneous catalyst in high yields was reported. These kinds of catalysts are built from mesoporous silica SBA-15 which was covalently anchored with Cu(II) Schiff base complex. The shorter reaction times, good yields, simple work-up procedure and environmentally friendly conditions are the main advantages of this method compared to the last one. This method is also the first example of synthesizing 1, 3-diaryl-thiourea derivatives by Cu(II)-Schiff base/SBA-15 as an efficient catalyst in solvent-free media which can be valuable to be used or investigated for similar systems. The product was identified by its ^{1}H NMR, Mass and IR spectra, which were compared to those reported previously.

Keywords: One-Pot, Synthesis, Diaryl Thiourea Derivatives, Solvent Free Condition, Cu(II)-Schiff base/SBA-15

Introduction

Thiourea derivatives are an important group of chemical compounds that play important roles in agriculture, pharmaceuticals, pesticides, and plant growth regulators [1-4]. Today, the synthesis of urea and thiourea compounds in the chemistry of modern drugs has found a special place. Urea and Thiourea derivatives are used as anti-cancer papers, anti-seizures, and in the novel way of preventing HIV [5-7], and so on. Many Thiourea derivatives have a wide range of biological properties such as fungicides, antiviral, antibacterial and against the protection of khans in agriculture [8-10]. On the other hand, it plays a role in the synthesis of many hydrocarbon compounds [11]. As part of my continuing interest in the development of new synthetic methodologies, herein an efficient and convenient procedure for the synthesis of 1, 3-diaryl-thiourea derivatives in the presence of Cu(II)-Schiff base/SBA-15 catalyst (Scheme 1). These kinds of catalysts are built from mesoporous silica SBA-15 which was covalently bonded with Cu(II) Schiff base complex (Scheme 1) [12]. There are few works of literature about the application of these kinds of catalysts (silica-supported Schiff base cobalt (II) (Co/SBA-15) and copper (II) (Cu/SBA-15) complexes) for synthesis of organic compounds [13] specially for synthesis of thiourea and the reported method is the first example of synthesizing 1, 3-diaryl-thiourea derivatives supported Schiff base metal complexes as an efficient catalyst in solvent-free media which can be valuable to use or investigate for similar systems. The reported examples have demonstrated that the new procedure by solid-supported catalysts are generally faster, give higher yields, and typically require easier work-up processes and simpler equipment than the previously reported methods [14].



Scheme 1. Structure of Cu

2. Experimental

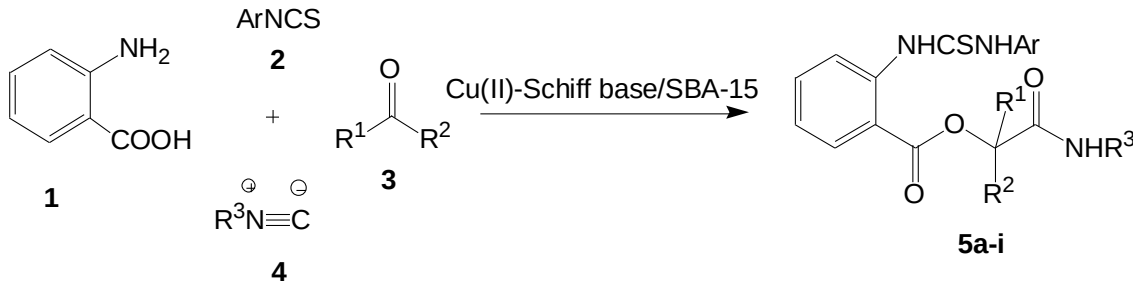
2.1. Preparation of the catalyst Cu (II)-schiff base/SBA-15

The Cu(II)-Schiff base complex was prepared using the pertinent literature procedure with the following modification. Activated silica gel SBA-15 (1.5 g) was suspended in a methanol solution of the Schiff base complex, and the mixture was stirred at the room temperature for 24 h. The solvent was then removed using a rotary evaporator, and the resulting green solid was dried at 80 °C overnight. The final product was washed with MeOH and deionized water until the washings were colourless to ensure that the non-covalently grafted complex and physically adsorbed metal species were removed. Further drying was carried out in an oven at 80 °C for 8 h. Moreover, in order to measure the amount of copper loaded into SBA-15, the catalyst (0.1 g) was digested with HNO_3 by stirring at room temperature for a week. Then the mixture was filtered, and the total amount of copper in SBA-15 in the colorless sample was determined as 0.14 mmol/g by atomic absorption spectroscopy [12-14].

2.2. General procedure for synthesis of 1, 3 diaryl thiourea derivatives (5a-i)

A mixture of 2-amino-benzoic acid (1 mmol) and aryl isothiocyanate derivatives 2 (1 mmol) were mixed thoroughly for half 30 minutes in room temperature. Then carbonyl derivatives 3 (1 mmol) and isocyanide compounds 4 (1 mmol) and Cu(II)-Schiff base/SBA-15 catalyst (0.005 g, 0.007 mmol) added to the resulting mixture and stirred under reflux for

30 minutes to complete the condensation reaction to 5a-i, as monitored by TLC. After cooling, the mixture was washed with EtOH (50 mL) and the catalyst was removed by filtration, rinsed twice with MeOH, and then dried at 80 °C for 60 min for subsequent reuse. Afterwards 20 ml of ethyl acetate was added to the reaction mixture. Then 20 ml of sodium bicarbonate was added. The organic phase was removed and dry with sodium sulfate salt. The solvent was evaporated under vacuum and the residue was purified by column chromatography (3 to 1 hexane to ethyl acetate). The yields are shown in Table 1.

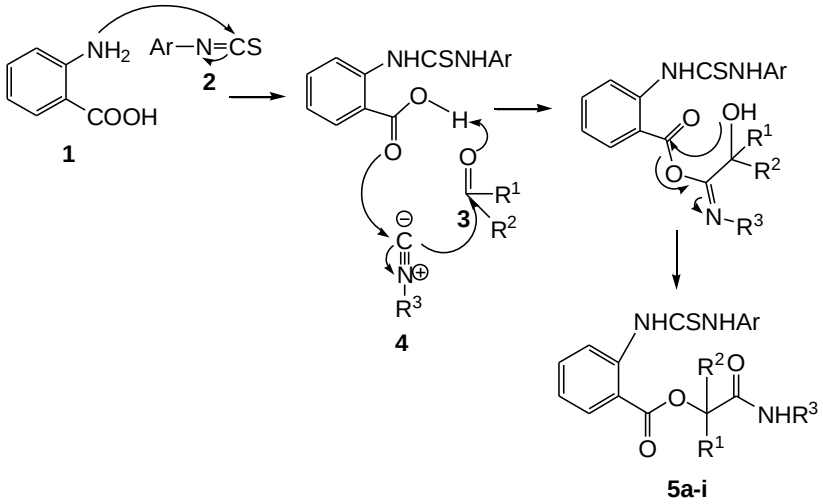


Scheme 2. Synthesis of 1, 3 diaryl thiourea derivatives

Table 1. Synthesis of 1, 3 diaryl thiourea derivatives 5a-i by Cu(II)-Schiff base/SBA-15 catalyst

No.	Product[a]	Ar	R^1	R^2	R^3	Yield (%)b
1	5a	Ph	Me	Me	Cyclohexyl	90
2	5b	Ph	Cyclohexyl	H	Cyclohexyl	87
3	5c	4-OMePh	Cyclohexyl	H	Cyclohexyl	88
4	5d	Ph	Cyclopentyl	H	Cyclohexyl	89
5	5e	4-OMePh	Me	Et	Cyclohexyl	82
6	5f	Ph	Me	Et	2,6-Di Metyl Phenyl	80
7	5g	Ph	p-nitro phenyl	H	Cyclohexyl	70
8	5h	4-OMe Ph	t-But	t-But	Cyclohexyl	81
9	5i	Ph	Ph	H	Cyclohexyl	86

[a] All the products are known compounds and were characterized from their spectroscopic (^{1}H NMR and MS) properties
[b] Isolated yield



Scheme 3-Possible mechanism of the Synthesis of 1, 3 diaryl thiourea derivatives reactions

3. Results and discussion

The duration of this process is about 2 hours and the maximum product efficiency is between 70-90%. According to the results of Table 1, this method has a great variety for the production of new products, so that even with benzaldehyde with a group of fatal electrons is also good (row 6). 5a-i structures have been identified with IR spectra, 1H NMR, and 13C NMR spectra. Although the mechanism of this reaction has not been empirically proven, a possible mechanism for producing a thiourea is shown in Scheme. 3.

4. Conclusion

In conclusion, a fast, one-pot, solvent-free, and high-performance method is presented for simple and accessible raw materials for synthesis of thiourea derivatives. No correction or activation has been performed with the catalyst in this method. In addition, the separation and purification of the products are very easy and high efficiency. One of the main advantages of this method is the introduction of a new group of peptides in the thiourea, which probably increases their biological and antimicrobial properties.

Acknowledgment

The author is grateful to Payam Noor University for financial support.

References

[1] T.P. Vyshnyakova, I.A. Golubeva, E.V. Glebova, *Russ. Chem. Rev. (Engl. Transl.)* 54 (1985) 249.

[2] F.P. Schmidtchen, M. Berger, *Chem. Rev*. 97 (1997) 1609.

[3] A. K. Zafer, T. Z. Gulhan, O. Ahmet, R. Gilbert, *Eur. J. Med. Chem*. 43 (2008) 155.

[4] A. Khalafi-Nezhad, M. N. S. Rad, H. Mohabatkar, Z. Asrari, B. Hemmateenejad, *Bioorg. Med. Chem*. 13 (2005) 1931.

[5] K. J. Hwang, K. H. Park, C. O. Lee, B. T. Kim, *Arch. Pharm. Res*. 25 (2002) 781.

[6] J. A. Shimshoni, M. Bialer, B. Wlodarczyk, R. H. Finnell, B. Yagen, *J. Med. Chem.* 50 (2007) 6419.

[7] Y. Dai, K. Hartandi, Z. Ji, A. A. Ahmed, D. H.; Albert, J. L. Bauch, J. J. Bouska, P. F. Bousquet, G. A. Cunha, K. B. Glaser, C. M. Harris, D.; Hickman, J. Guo, J. P. Li, A. Marcotte, K. C. Marsh, M. D. Moskey, R. L. Martin, A. M. Olson, D. J. Osterling, L. J. Pease N. B. Soni, K. D. Stewart, V. S. Stoll, P. Tapang, D. R. Reuter, S. K. Davidsen, Michaelides, M. R. *J. Med. Chem.* 50 (2007) 1584.

[8] L. P. Duan, J. Xue, L. L. Xu, H. B. Zhang, *Molecules*. 15 (2010) 6941.

[9] Z. M. Zhong, R. Xing, S. Liu, L. Wang, S. B. Cai, P. C. Li, *Carbohydr. Res*. 343 (2008) 566.

[10] Z.Y. Wang, S. Wang, X. J. Song, Y.G. Wang, Chin. *J. Pestic. Sci*. 7 (2005) 282.

[11] B. Yin, Zh. Liu, M. Yi, J. Zhang, *Tetrahedron*, 49 (2008) 3687.

[12] F. Rajabi, B. Karimi, *J. Mol. Catal*. A., 232 (2005) 95-99.

[13] R. Motamedi, B.G. Rezanejade, S. Shakeri, *Heterocycl. Commun*. 20 (2014) 181-184.

[14] R. Motamedi, B. G. Rezanejade, R. S. Makenali, *Asia. J. Green Chem*, (2017) 89- 97.