Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters
Tetrahedron Letters 48 (2007) 4785–4788

A new method for the synthesis of dithiocarbamates by CuI-catalyzed coupling reaction

Yunyun Liu and Weiliang Bao*

Department of Chemistry, Xi Xi Campus, Zhejiang University, Hangzhou, Zhejiang 310028, PR China

Received 18 January 2007; revised 9 March 2007; accepted 30 March 2007
Available online 4 April 2007

Abstract—The Ullmann-type coupling reaction of sodium dithiocarbamates with aryl iodides and vinyl bromides catalyzed by CuI/*N*,*N*-dimethylglycine proceeds smoothly in DMF at 110 °C to give corresponding dithiocarbamates in good yields.

Organic dithiocarbamates have received much attention due to their pivotal role in agriculture[1] and their intriguing biological activities.[2] They have also been used as protection groups in peptide synthesis,[3] as linkers in solid-phase organic synthesis[4] and recently in the synthesis of ionic liquids.[5] Furthermore, dithiocarbamates are broadly employed in medicinal chemistry and have been used in cancer treatment.[6] Therefore, the synthesis of dithiocarbamates has attracted a lot of attention recently. Conventionally, protocols for the synthesis of dithiocarbamates involve the use of costly and toxic reagents, such as thiophosgene and its substituted derivatives.[7] The one-pot reaction of amines with carbonyl sulfide and alkyl halides in organic solvents or without solvent was reported by Chaturvedi, Saidi and their co-workers recently.[8,9] However, most of the above described methods focused on the alkylation of dithiocarbamic acid and obtained alkyl dithiocarbamate. General methods for the synthesis of aryl and vinyl esters of dithiocarbamic acids are based upon the reactions of hypervalent iodine compounds with sodium salt of dithiocarbamic acid,[10] or certain organometallic reagents with tetramethylthiuram disulfide.[11] The synthesis of vinyl esters of dithiocarbamic acids can also be achieved by the reactions of allyl esters of dithiocarbamic acids under strong basic conditions,[12] and phosphonium ylides with aldehydes.[13]

During the past years, great progress has been achieved on the development of copper-catalyzed Ullmann-type coupling reaction. Buchward and other groups have reported the formation of aryl-carbon, aryl-nitrogen, aryl-oxygen and aryl-sulfur bonds based on copper(I) catalysts as alternatives to palladium(0) catalysts.[14] Ma et al. found that α- and β-amino acids could accelerate copper-catalyzed coupling reactions. By using these special ligands many reactions could be carried out at relatively low temperatures.[15] As far as we know, the application of copper-catalyzed coupling reaction of aryl and vinyl halides with dithiocarbamates has not been developed. Herein, we wish to report a novel and efficient method for the synthesis of dithiocarbamates using CuI as the catalyst and amino acids as the ligands.

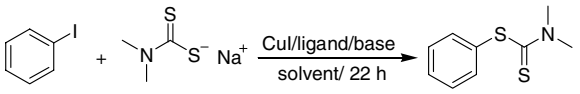
As indicated in Table 1, we chose the coupling of phenyl iodide with sodium dimethylcarbamodithioate as a model reaction to optimize the reaction condition. Because effective activities of amino acids were recently found in the coupling reactions catalyzed by CuX,[15c,e] *N*,*N*-dimethylglycine and L-proline were checked as the ligands for the present reaction. It was found that the reaction proceeded at 90 °C in DMF in the presence of 15 mol % CuI , 30 mol % *N*,*N*-dimethylglycine and K_2CO_3 (entry 1). The reaction also worked well without the addition of K_2CO_3 (entry 3), and gave the coupling product in excellent yield by raising the reaction temperature (entry 8). Among the solvents tested, DMSO and [Bmim]BF_4 were effective (entries 4 and 6) and DMF gave the best result (entry 3), while no conversion was observed in toluene and dioxane (entries 5 and 7).

On the basis of the above results, the scope and the limitations of the coupling reaction were explored with various aryl and vinyl halides and other sodium dithiocarbamates, and the results are summarized in Table 2.

* Corresponding author. Fax: +86 571 88911554; e-mail: wlbao@css.zju.edu.cn

0040-4039/$ - see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.tetlet.2007.03.168

Table 1. CuI-Catalyzed coupling reaction of phenyl iodide with sodium dimethylcarbamodithioate under different catalytic conditions



Entry	Solvent	Base	Ligand	Temperature (°C)	Yield[a,c] (%)
1	DMF	K_2CO_3	*N*,*N*-Dimethylglycine	90	70
2	DMF	K_2CO_3	L-Proline	90	55
3	DMF	No	*N*,*N*-Dimethylglycine	90	70
4	DMSO	No	*N*,*N*-Dimethylglycine	90	50
5	Toluene	No	*N*,*N*-Dimethylglycine	90	0
6	[Bmim]BF_4	No	*N*,*N*-Dimethylglycine	90	60[b]
7	Dioxane	No	*N*,*N*-Dimethylglycine	90	0
8	DMF	No	*N*,*N*-Dimethylglycine	110	95

[a] Isolated yield.
[b] Bmim = 1-butyl-3-methylmidazolium.
[c] Reaction conditions: CuI (15 mol %); *N*,*N*-dimethylglycine (30 mol %); K_2CO_3 (2 mmol); aryl iodide (1 mmol); sodium dimethylcarbamodithioate (1.2 mmol); solvent (2 mL).

Table 2. Coupling reaction of aryl and vinyl halides with sodium dithiocarbamates under the catalysis of CuI/*N*,*N*-dimethylglycine

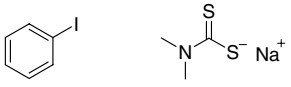
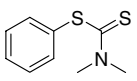
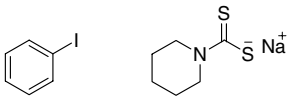
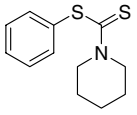
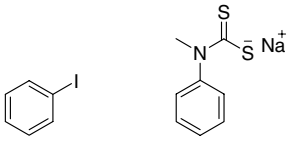
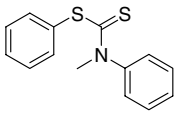
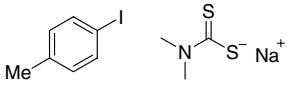
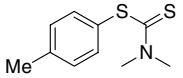
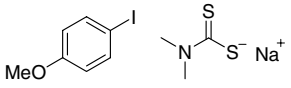
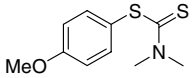
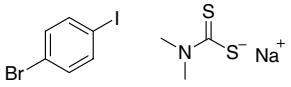
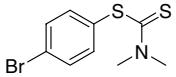
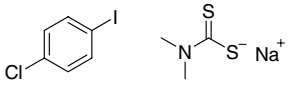
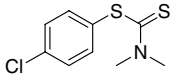
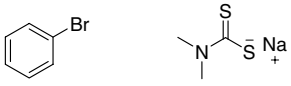
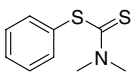
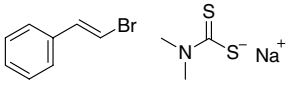
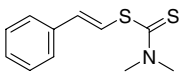
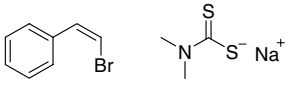
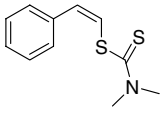
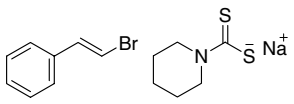
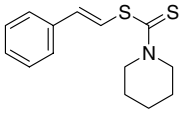
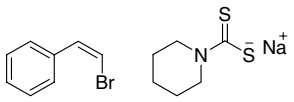
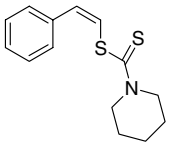
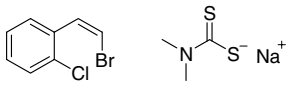
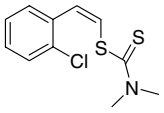
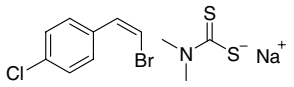
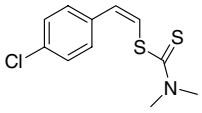
Entry	Substrates	Product	Yield[a,c] (%)	*E*:*Z*[b]
1			95	
2			82	
3			75	
4			83	
5			82	
6			87	
7			91	
8			Trace	
9			75	90:10
10			90	5:95

Table 2 (*continued*)

Entry	Substrates	Product	Yield[a,c] (%)	*E*:*Z*[b]
11			70	90:10
12			77	3:97
13			81	7:93
14			90	6:94

[a] Isolated yield.
[b] The ratio was based on ^{1}H NMR spectrum.
[c] CuI (15 mol %); *N*,*N*-dimethylglycine (30 mol %); aryl iodide or vinyl bromides (1 mmol); sodium dithiocarbamates (1.2 mmol); in DMF (2 mL) at 110 °C for 22 h.

Aryl iodide delivered arylation products in good yields by coupling with sodium piperidine-1-carbo-dithioate, sodium 2-phenylpropanedithioate (entries 2 and 3). The electron-deficient aryl iodides (entries 6 and 7) were generally superior to the electron-rich ones (entries 4 and 5), as demonstrated by better yields. Unfortunately, bromobenzene gave only trace amounts of product under the conditions described (entry 8). Because the general methods for the synthesis of vinyl esters of dithiocarbamic acids have some disadvantages such as difficult accessible starting materials, or lack of stereoselectivity, we wish to report a milder, more stereoselective and convenient method for the synthesis of vinyl esters of dithiocarbamic acids from vinyl bromides catalyzed by CuI/*N*,*N*-dimethylglycine in DMF. It was found that both (*E*)- and (*Z*)-vinyl bromides were suitable for this reaction, giving the desired coupling products in good yields and high stereoselectivities (entries 9–14). The (*Z*)-vinyl bromides gave a higher stereoselectivity in comparison to the (*E*)-vinyl bromides (comparing entries 9 and 10, as well as entries 11 and 12). The steric hindrance of vinyl bromides is slightly disfavoured for this reaction. For example, when (*Z*)-1-(2-bromovinyl)-2-chlorobenzene was used as the substrate, the reaction gave a relatively lower yield in comparison to that of less hindered vinyl bromide (compare entries 13 and 14). The mechanism of the reaction maybe similar with that described by Ma and co-workers.[16]

In conclusion, we have reported a mild and efficient method for the synthesis of aryl and vinyl dithiocarbamates under Ullmann coupling.[17] The materials used are relatively cheap and the procedure is straightforward. It is applicable to both electron-deficient and electron-rich aryl iodides, and even to sterically hindered vinyl bromides. The yields are from good to excellent, and the stereoselectivity is satisfactory.

Acknowledgement

This work was financially supported by the Natural Science Foundation of China (No. 20372058).

References and notes

1. (a) Rafin, C.; Veignie, E.; Sancholle, M.; Postal, D.; Len, C.; Villa, P.; Ronco, G. *J. Agric. Food Chem.* **2000**, *48*, 5283; (b) Len, C.; Postal, D.; Ronco, G.; Villa, P.; Goubert, C.; Jeufrault, E.; Mathon, B.; Simon, H. *J. Agric. Food Chem.* **1997**, *45*, 3; (c) Mizuno, T.; Nishiguchi, I.; Okushi, T.; Hirashima, T. *Tetrahedron Lett.* **1991**, *32*, 6867.
2. (a) Caldas, E. D.; Hosana Conceicüa, M.; Miranda, M. C. C.; Souza, L.; Lima, J. F. *J. Agric. Food Chem.* **2001**, *49*, 4521; (b) Erian, A. W.; Sherif, S. M. *Tetrahedron* **1999**, *55*, 7957; (c) Bowden, K.; Chana, R. S. *J. Chem. Soc., Perkin Trans. 2* **1990**, 2163.
3. Greene, T. W.; Wuts, P. G. M. *Protecting Groups in Organic Synthesis*, 3rd ed.; Wiley Interscience: New York, 1999, p 484.
4. (a) Morf, P.; Raimondi, F.; Nothofer, H.-G.; Schnyder, B.; Yasuda, A.; Wessels, J. M.; Jung, T. A. *Langmuir* **2006**, *22*, 658; (b) Bongar, B. P.; Sadavarte, V. S.; Uppalla, L. S. *J. Chem. Res. (S)* **2004**, *9*, 450.
5. Zhang, D.; Chen, J.; Liang, Y.; Zhou, H. *Synth. Commun.* **2005**, *35*, 521.
6. (a) Ronconi, L.; Marzano, C.; Zanello, P.; Corsini, M.; Miolo, G.; Macca, C.; Trevisan, A.; Fregona, D. *J. Med. Chem.* **2006**, *49*, 1648; (b) Elgemeie, G. H.; Sayed, S. H. *Synthesis* **2001**, 1747; (c) Walter, W.; Bode, K.-D. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 281.

7. (a) Burke, J. T. R.; Bajwa, B. S.; Jacobsen, A. E.; Rice, K. C.; Streaty, R. A.; Klee, W. A. *J. Med. Chem.* **1984**, *27*, 1570; (b) Walter, W.; Bode, K.-D. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 281; (c) Tilles, H. *J. Am. Chem. Soc.* **1959**, *81*, 714.
8. (a) Chaturvedi, D.; Ray, S. *Tetrahedron Lett.* **2006**, *47*, 1307; (b) Salvatore, R. N.; Sahaba, S.; Jung, K. W. *Tetrahedron Lett.* **2001**, *42*, 2055.
9. Azizi, N.; Aryanasab, F.; Saidi, M. R. *Org. Lett.* **2006**, *8*, 5275.
10. (a) Chen, D. J.; Chen, Z. C. *J. Chem. Res. (S)* **2000**, 352; (b) Yan, J.; Chen, Z. C. *Synth. Commun.* **1999**, *29*, 2875; (c) Chen, Z. C.; Jin, Y. Y.; Stang, P. J. *J. Org. Chem.* **1987**, *52*, 4117.
11. (a) Krasovskiy, A.; Gavryushin, A.; Knochel, P. *Synlett* **2005**, 2691; (b) Jen, K.; Cava, M. P. *Tetrahedron Lett.* **1982**, *23*, 2001; (c) Grunwell, J. R. *J. Org. Chem.* **1970**, *35*, 1500.
12. (a) Hayashi, T.; Fujitaka, N.; Oishi, T.; Takeshima, T. *Tetrahedron Lett.* **1980**, *21*, 303; (b) Hori, I.; Hayashi, T.; Midrorikawa, H. *Synthesis* **1975**, 727.
13. (a) Wu, L. L.; Huang, X. *Chin. Chem. Lett.* **1995**, *6*, 751; *Chem. Abstr.* ***1996****, 7*, 86531n; (b) Huang, Z. Z.; Wu, L. L. *Synth. Commun.* **1996**, *26*, 509; (c) Galli, R. *J. Org. Chem.* **1987**, *52*, 5349.
14. (a) Hennessy, E. J.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 269; (b) Zanon, J.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 2890; (c) Klapars, A.; Antilla, J. C.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7727; (d) Kwong, F. Y.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 581; (e) Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 793; (f) Nordmann, G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 4978; (g) Kwong, F.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 3517.
15. (a) Ma, D.; Zhang, Y.; Yao, J.; Wu, S.; Tao, F. *J. Am. Chem. Soc.* **1998**, *120*, 12459; (b) Ma, D.; Xia, C. *Org. Lett.* **2001**, *3*, 2583; (c) Ma, D.; Qian, C. *Org. Lett.* **2003**, *5*, 3799; (d) Zhu, W.; Ma, D. *J. Org. Chem.* **2005**, *70*, 4693; (e) Xie, X.; Cai, G.; Ma, D. *Org. Lett.* **2005**, *7*, 4693.
16. Zhang, H.; Cai, Q.; Ma, D. *J. Org. Chem.* **2005**, *70*, 5164.
17. *Typical procedure:* To a solution of *N*,*N*-dimethylglycine (30 mol %), sodium dimethylcarbamodithioate (1.2 mmol), aryl iodide (1 mmol), in anhydrous DMF (2 mL) was added CuI (15 mol %). Under N_2 atmosphere, the mixture was stirred at 110 °C for 22 h. The reaction mixture was then cooled to rt, dissolved in water and extracted with ethyl acetate. The combined organic layer was dried over $MgSO_4$. The product was further purified by column chromatography (v/v = 4/1, petroleum ether/ethyl ether).