Digest Journal of Nanomaterials and Biostructures Vol. 5, No 2, April 2010, p. 331 – 333

ONE-POT PROTOCOL FOR THE PREPARATION OF ARYL-SULFONYLSEMICARBAZIDES FROM SULFONYLHYDRAZIDES

JAVAD SAFAEI-GHOMI*
Department of Organic Chemistry, Faculty of Chemistry, University of Kashan, 51167 Kashan, I. R. IRAN

An efficient and rapid procedure for the preparation of sulfonylsemicarbazide from Sulfonylhydrazides and triphosgene in one-pot sequence is described. In the two-steps sequence: sulfonylhydrazides and acetylsulfanilylhydrazide were transformed into the corresponding intermediates using triphosgene in 1,4-dioxan/water or tetrahydrofuran medium and then the intermediates were converted in situ into sulfonylsemicarbazide in high yields and shorter times related to previous methods.

(Received March 16, 2010; accepted April 21, 2010)

Keywords: Sulfonylsemicarbazides/ Sulfonylhydrazides/ Triphosgene, Acetylsulfanilylhydrazide.

1. Introduction

Sulfonylsemicarbazides are important compounds as blowing agents in cellular rubber and plastics [1]. These compounds have antidiabetic activity [2] and also are characterized by low toxicity and prolonged hypoglycemic activity [3]. Recently the new derivatives of aryl-sulfonylsemicarbazides as a new lead-candidate to antithrombotic agents were prepared from natural safrole [4]. Different methods for the preparation of these compounds have been reported. For example, sulfonylsemicarbazides are prepared by the reaction of sulfinic acid salts with azodicarbonamide in water [5] and of sulfonyl chlorides with semicarbazide [6,7]. These methods give poor yields [6,7], utilize solvents such as pyridine [6]; moreover, the sulfinic acid salts as starting material are not commercially available [5]. Recently, triphosgene [bis(trichloromethyl)carbonate], a crystalline solid which can be easily handled, has been reported as a safe stable reagent, successfully used for the synthesis of large variety of organic compounds [8]. The present paper reports a highly versatile and efficient one-pot method in two-step sequence for the synthesis of sulfonylsemicarbazides utilizing commercially available triphosgene from sulfonylhydrazides and ammonium chloride in organic and aqueous solvent [9].

2. Experimental

Melting points were determined on a Kofler block. FT-IR spectra were recorded on a Nicolet Magna 550 spectrometer (KBr); values are reported in cm-1. 1H NMR spectra were determined on Bruker DRX-500 AVANCE (500 MHz) spectrometer using DMSO-d6 as solvent and TMS as internal standard. Starting materials were either commercially available or prepared according to literature procedure [10].

*Corresponding author: safaei@kashanu.ac.ir

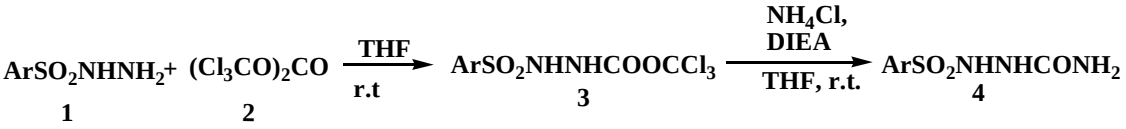
2. 1 General procedure for the preparation of Sulfonylsemicarbazides (4a-e).

A solution of the sulfonylhydrazide (0.7 mmol) in THF (6 mL) was slowly added to a stirred solution of triphosgene (0.148 gr, 0.5 mmol) in THF (2 mL) over a period of 40 min at room temprature. (For **4a** and **4b**, the sulfonylhydrazide dissolved in 1,4-dioxane/water (2:1/6 mL). After a further 5 min of stirring, a solution of ammonium chloride (3 mmol), diisopropylethylamine (DIEA, 3 mmol) and THF (3 mL) was added in one portion. The reaction mixture was stirred for 10 min at room temperature. The mixture was evaporated to dryness by rotary evaporator and the residue was washed with 5% aq. HCl and water and then dried under reduced pressure to yield the colorless product. The crude products were recrystalized from EtOH and water as white crystals.

(**4a**) IR (cm^{-1}): 1163, 1332 (SO_2), 1654 (C=O), 3385, 3482 (NH, NH_2), ^1H NMR (δ ppm): 2.1 (s, 3H, -NHCOC*H*$_3$), 5.9 (s, 2H, -CON*H*$_2$,), 7.7 (m, 4H, Ar*H*), 7.9 (s, 1H, -N*H*CONH$_2$), 9.3 (s, 1H, SO_2N*H*-), 10.3 (s, 1H, -N*H*COCH$_3$).
(**4b**) IR (cm^{-1}): 1157, 1326 (SO_2) 1680 (C=O), 3170, 3359 (NH, NH_2), ^1H NMR (δ ppm): 2.1 (s, 3H, -NHCOC*H*$_3$), 4.5 (s, 2H, ArC*H*$_2$), 6.1 (s, 2H, -CON*H*$_2$,), 7.8 (m, 4H, Ar*H*), 8.4 (s, 1H, -N*H*CONH$_2$), 9.2 (s, 1H, SO_2N*H*-), 10.6 (s, 1H, -N*H*COCH$_3$).
(**4c**) IR (cm^{-1}): 1157, 1342 (SO_2), 1659 (C=O), 3318, 3421 (NH, NH_2), ^1H NMR (δ ppm): 6.0 (s, 2H, -CON*H*$_2$,), 8.01 (d, 2H, Ar*H*, *J*= 8.41), 8.06 (d, 2H, Ar*H*, *J*= 8.41), 8.2 (s, 1H, -N*H*CO), 9.9 (s, 1H, SO_2N*H*-).
(**4d**) IR (cm^{-1}): 1192, 1365 (SO_2), 1664 (C=O), 3380, 3472 (NH, NH_2), ^1H NMR (δ ppm): 5.9 (s, 4 H, -CON*H*$_2$,), 7.2 (d, 4 H, Ar*H*, *J*= 8.6), 7.8 (d, 4 H, Ar*H*, *J*= 8.41), 7.9 (s, 2H, -N*H*CO), 9.4 (s, 2H, SO_2N*H*-).
(**4e**) IR (cm^{-1}): 1135, 1300 (SO_2), 1655 (C=O), 3366, 3444 (NH, NH_2), ^1H NMR (δ ppm): 5.5 (s, 4 H, -CON*H*$_2$,), 7.7 (d, 4 H, Ar*H*, *J*= 7.56), 7.9 (d, 4 H, Ar*H*, *J*= 7.56), 8.0 (s, 2H, -N*H*CO), 9.1 (s, 2H, SO_2N*H*-).

3. Results and discussion

A cooled solution of triphosgene **2** was treated with a solution of sulfonylhydrazide **1** in THF at room temprature. The solution of ammonia and diisopropylethylamine is then added to the above solution in one portion to provide sulfonylsemicarbazides **4** (Scheme).



Scheme

*Table 1: The preparation of sulfonylsemicarbazides **4** using triphosgene **2***

Entry	Ar	Yield (%)	Mp (°C)
a	4-CH_3CONH-C_6H_4	90	227-228 (227) [3]
b	4-$CH_3CONHCH_2$-C_6H_4	85	194-196 (194)[4]
c	4-Cl-C_6H_4	80	228-230 (228)[2]
d	NH_2NHSO_2-C_6H_4-O-C_6H_4	90	223-224 (222)[2]
e	NH_2NHSO_2-C_6H_4-C_6H_4	95	268-270 (270)[2]

There are several literature precedents for the preparation of urea using triphosgene as the starting material [11, 12]. In the first step of this procedure sulfonylhydrazide was added to prepare an intermediate **3**. Ammonium chloride was used in the second step to prepare the products. In order to prevent of the production of undesirable product (urea), the less reactive sulfonylhydrazides was added in the first step, followed by reaction with ammonia. The generality of this reaction was established by preparing various sulfonylsemicarbazides from corresponding

sulfonylhydrazides and ammonia (Table 1). Importantly, excellent transformations were obtained when **2** reacts with water-soluble acetamidosulfonylhydrazides (**4 a**, **b** in Table 1).

In sum, we report here a rapid procedure for the preparation of sulfonylsemicarbazide from sulfonylhydrazides and triphosgene in one-pot sequence with high yields and shorter times related to previous methods.

Acknowledgements

The author gratefully acknowledge the financial support of this work by the Research Affairs Office of the University of Kashan, Kashan, I. R. Iran

References

[1] a) H. R. Lasman, "Blowing Agent" in Encyclopedia of Polymer Science and Technology, N. M. Bikales, ed., John Wiley & Sons, Inc., New York, 1965, Vol 12, p. 532. b) B. A. Hunter, F. B. Root, G. Morrisey, J. Cellular Plastics **3**, 268 (1967).
[2] V. P. Chernykh, Pharm. Chem. J. **12**, 13 (1978). [Chem. Abstr. **89**, 190592 (1978)].
[3] H. J. Ahr, "Oral Antidiabetics" in Handbook of Experimental Pharmac., W. Puls, J. Kuhlman, ed., Springer Verlag, 1996, p. 69.
[4] L. M. Lima, C. B. Ormelli, C. A. M. Fraga, A. L. P. Mirandaa, E. J. Barreiroa, J. Braz. Chem. Soc. **10**, 421 (1999).
[5] B. A. Hunter, Sulfonylsemicarbazides. US Patent 3,903,157, September 2 (**1975**); [Chem. Abstr. **83**, 192800 (1975)].
[6] J. S. Roth, E. F. Degering, J. Am. Chem. Soc. **67**, 126 (1945).
[7] E. Niemiec, J. Am. Chem. Soc. **70**, 1067 (1948).
[8] W. Su, W. Zhong, G. Bian, X. Shi, J. Zhang, Org. Prep. Proc. Int. **36**, 499 (2004).
[9] J. Safaei-Ghomi, A. Bamoniri, A, Abbaszadeh, Z. Naturforsch., B **62b**, 721-724 (2007).
[10] L. Friedman, R. L. Litle, W. R. Reichle, Org. Synth., Coll., Vol., **5**, 1055 (1973).
[11] A. Jayanthi, V. K. Gumaste, A. R. A. S. Deshmukh, Synlett, 979, (2004).
[12] P. Majer, R. S. Randad, J. Org. Chem., **59**, 1937, (1994).