Asian Journal of Chemistry Vol. 19, No. 3 (2007), 2467-2469

NOTE

Efficient Synthesis of 2-Substituted 4*H*-3,1-Benzoxazin-4-ones under Microwave Irradiation

KUROSH RAD-MOGHADAM† and NASSER MONTAZERI*
Chemistry Department, Islamic Azad University of Tonekabon, Tonekabon, Iran
E-mail: montazer50@yahoo.com

A fast synthesis of 2-substituted 4*H*-3,1-Benzoxazin-4-ones is achieved from reaction of acetic anhydride with 2-acylaminobenzoic acid under microwave and solvent-free conditions.

Key Words: 4*H*-3,1-Benzoxazin-4-one, Microwave, Solvent-free, Acetic anhydride.

A majority of the synthesis of biologically active quinazolin-4(3*H*)-ones were based on the use of 4*H*-3,1-benzoxazin-4-one compounds as substrates[1]. In addition, some of the 4*H*-3,1-benzoxazin-4-ones themselves have shown interesting biological activities[2-5]. Owing to these significant features many efforts have been paid to the synthesis of these valuable materials. A literature survey regarding the synthesis of 2-substituted 4*H*-3,1-benzoxazin-4-one derivatives disclosed a variety of methods, including cyclodehydration of N-acylanthranilic acids by acetic anhydride[6], reaction of anthranilic acid with acid chlorides[7], treatment of methyl N-aroylanthranilates or methyl 2-ureidobenzoates with concentrated sulfuric acid[8], rearrangement of *o*-nitrophenylacetic acid in boiling acetic anhydride[9], condensation of *o*-azidobenzoic acid with aldehydes[10] and photoisomerization of 2-arylisatogen[11]. Meanwhile, it was apparent that cyclodehydration of N-acylanthranilic acids in refluxing acetic anhydride has been the prevalent method used for production of 4*H*-3,1-benzoxazin-4-ones. We have also found that beside our previous report[12] on reaction of anthranilic acid with *ortho*-esters under microwave irradiation there is no other report on microwave-assisted synthesis of 4*H*-3,1-benzoxazin-4-ones. Microwave irradiation has proved to be an efficient method of heating that cause to some facilities in performing reactions and improvement of yields[13,14].

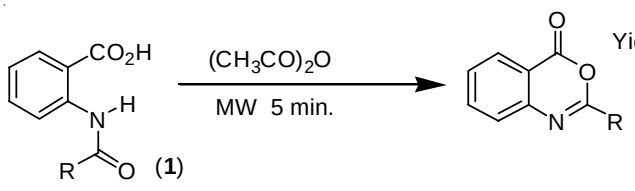
†Chemistry Department, Guilan University, P.O. Box 41335-1914, Rasht, Iran.

Melting points are uncorrected. Infrared spectra were obtained in KBr wafers on Shimadzu IR-470 spectrometer. ^{1}H NMR spectra were recorded on a Brucker DRX-500 Avance spectrometer at 500.13 MHz. Microwave irradiations were carried out in a domestic oven at 2450 MHz. Chemicals were obtained from Merck or Fluka and were used without further purification. In order to control the reaction, irradiations were carried out in two stages with a cooling time between them.

A mixture of 2-acylaminobenzoic acid (5 mmol) and acetic anhydride (1.53 g, 15 mmol) was placed in a tall beaker. The beaker was covered with a stemless funnel and then irradiated in the microwave oven for 2 min with a power of 210 W. After a cooling time of about 5 min to room temperature the beaker was irradiated again for 3 min at 210 W. The resultant residues were dissolved in hot 10 mL heptane, wherefrom the products are precipitated as crystals.

In the present paper, it is reported that under microwave irradiation not only the cyclodehydration of 2-aroylaminobenzoic acid (**1**) by acetic anhydride takes place quickly but also it needs a lower amount of anhydride relative to the conventional heating method[6].

Thus, 2-acylaminobenzoic acids (**2a-c**) cyclodehydrate in reaction with 3 equivalent of acetic anhydride in an open vessel under microwave irradiation to produce the desired 2-substituted 4*H*-3,1-benzoxazin-4-ones in fairly high yields. The reaction takes place quickly, so after a few minutes nearly pure products are obtained. Any reduction in the amount of acetic anhydride from the optimized quantity (3 equivalent) leads to a decrease in yields, however on the other hand increasing the quantity has no sensible effect on the yields but requires some laboratory work up for removing of excess anhydride.



Yield %	R
75	2-Furyl
77	Ph
73	PhCH=CH
80	CH_3CH_2
79	$CH_3CH_2CH_2$

All the products are known compounds and their melting points, IR and ^{1}H NMR spectral data are in good agreement with those of literatures, as well as the authentic samples prepared from the previously reported methods.

In conclusion an eco-friendly and fast method has been introduced for the preparation of 2-substituted 4*H*-3,1-benzoxazin-4-ones under microwave condition. The reactions are clean and perform efficiently.

REFERENCES

1. D.J. Brown, in ed.: E.C. Taylor, The Chemistry of Heterocyclic Compounds, Supl. I, John Wiley & Sons, New York, Vol. 55 (1996).
2. E. Colson, J. Wallach and M. Hauteville, *Biochimie*, **87**, 223 (2005).
3. C.C. Wu, T.W. Wang, W.Y. Wang, P.W. Hsieh and Y.C. Wu, *Eur. J. Pharmacol.*, **527**, 37 (2005).
4. U. Neumann, N.M. Schechter and M. Gütschow, *Bioorg. Med. Chem.*, **9**, 947 (2001).
5. A. Krantz, R.W. Spencer, T.F. Tam, T.J. Liak, L.J. Copp, E.M. Thomas and S.P. Rafferty, *J. Med. Chem.*, **33**, 464 (1990).
6. D.T. Zentmyer and E.C. Wagner, *J. Org. Chem.*, **14**, 967 (1949).
7. D.I. Bain and R.K. Smalley, *J. Chem. Soc. (C)*, 1593 (1968).
8. E.P. Papadopoulos and C.D. Torres, *Heterocycles*, **19**, 1039 (1982).
9. G.N. Walker, *J. Am. Chem. Soc.*, **77**, 6698 (1955).
10. G.S. Reddy and K.K. Reddy, *Indian J. Chem.*, **16B**, 1109 (1978).
11. D.R. Eckroth and R.H. Squire, *J. Org. Chem.*, **36**, 224 (1971).
12. M.S. Khajavi, N. Montazari and S.S. Sadat-Hosseini, *J. Chem. Res. (S)*, 286 (1997).
13. L. Perreux and A. Loupy, *Tetrahedron*, **57**, 9199 (2001).
14. P. Lidstrom, J. Tierney, B. Wathey and J. Westman, *Tetrahedron*, **57**, 9225 (2001).

(*Received*: 23 June 2006; *Accepted*: 13 November 2006) AJC-5271