Synthesis of 1,2,4-Triazolo[1,5-*a*]pyrimidine Supported under Ultrasound Irradiation

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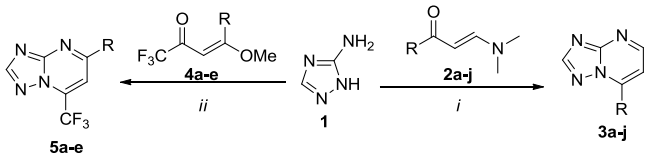
Keywords: Triazolo[1,5-a]pyrimidine, 3-amino-1,2,4-triazole, Ultrasound Irradiation

INTRODUCTION

For many years now, the chemistry of 1,2,4-triazolo[1,5-*a*]pyrimidine derivatives has been of considerable interest for applications in the areas of medicinal and agricultural chemistry.[1-3] The synthesis of triazolopyridines from the cyclocondensation of aminotriazole and 1,3-dieletrophiles, such as enaminones, chalcones, dicarbonyl, and substituted vinyl ketones, is conventionally performed in the reflux of acetic acid, acetonitrile, ethanol, or pyridine/HCl. However, significant variations in yields and reaction times limit the choice of substrates that can be utilized. Consequently, the development in the last few years of synthetic protocols employing ultrasound irradiation has led to an important change in organic reactions and has permitted the activation of substrates with poor reactive properties.[4,5] Considering the importance of triazolo[1,5-*a*]pyrimidine and the restrictions to its synthesis, in this paper we present an efficient approach to the highly regioselective synthesis of 1,2,4-triazolo[1,5-*a*]pyrimidines from the reaction of 3-amino-1,2,4-triazole with β-enamino-dimethyl vinyl ketones or 1,1,1-trifluoro-4-alkoxy-3-alqken-2-ones), under ultrasound irradiation.

RESULTS AND DISCUSSION

The 1,2,4-triazolo[1,5-*a*]pyrimidines **3a-j** and **5a-e** were prepared from the cyclocondensation reaction between either β-dimethylaminovinyl ketones **2a-j** (1.0 mmol) or 1,1,1-trifluoro-4-alkoxy-3-alken-2-ones **4a-e** and 3-amino-1,2,4-triazole 2 (1.0 mmol), in acetic acid (5 mL), at 99ºC for 5–17 min, using ultrasound irradiation (**Figure 1**). The products were extracted with dichloromethane (5 mL), washed with water (3 x 5mL), and then dried on magnesium sulfate. The products were obtained at moderate to good yields at a high degree of purity and without an additional purification step (**Table 1**). The structure of the 1,2,4-triazolo[1,5-*a*]pyrimidines was determined by ^{1}H and ^{13}C NMR spectroscopy, and X-ray diffraction.



i: AcOH, 99 °C, amplitude 20 %.17 min,
ii:AcOH, 99ºC, amplitude 20%. 5-15min.

Figure 1. Synthesis of 1,2,4-triazolo[1,5-a]pyrimidine **3a-j**, **5a-e**.

Table 1. Yield of 1,2,4-triazolo[1,5-*a*]pyrimidine **3a-j** and **5a-e**.

Prod	R	Yield	Prod.	R	Yield
3a	Ph	65%	**3i**	Tien-2-il	76%
3b	4-F-C_6H_4	76%	**3j**	Pirrol-2-il	74%
3c	4-Br-C_6H_4	83%	**5a**	Ph	84%
3d	4-I-C_6H_4	90%	**5b**	4-F-C_6H_4	82 %
3e	4-CH_3-C_6H_4	96%	**5c**	4-Br-C_6H_4	81%
3f	4-OMe-C_6H_4	96%	**5d**	4-OMe-C_6H_4	78%
3g	Ph-Ph	91%	**5e**	4-CH_3-C_6H_4	80%
3h	Naphth-2-yl	94%			

aYield of isolated product.

CONCLUSION

In summary, the synthesis of 7-aryl(alkyl)1,2,4-triazolo[1,5-*a*]pyrimidines described in this paper is highly regioselective. The method is practical and simple, and results in products with moderate to *good yields.*

ACKNOWLEDGEMENTS

The authors are grateful to Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS) and CAPES for financial support and fellowships.

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