New strategy for the synthesis of Bromacil and their analogous

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Keywords: bromination, 5-bromo uracil, analogous Bromacil

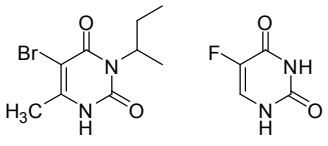
INTRODUCTION

The introduction of halogenes and halogenated groups in organic molecules promotes significant changes in their chemical, physical and biological properties[1]. Halogenation reactions at position 5 of uracils and pyrimidinones has been applied to obtain new substances with biological, industrial and commercial concern.[2,3] As the examples we cited Bromacil (**I**)(Herbicide) and 5-Fluorouracil (**II**)(Antitumor)[4] (**Figure 1**). Furthermore, 5-halouracilas can be used as synthetic intermediates in coupling reactions.[5]

In this work we present the synthesis of 5-bromo uracils (**14-17**), the Bromacil analogous, through a methodology quickly and efficiently.

RESULTS AND DISCUSSION

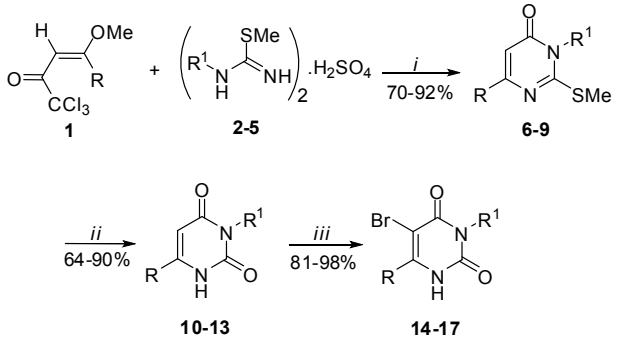
The 5-bromo uracil synthesized in this work, were obtaneid according to Scheme 1. Firstly, the 2-methylthiopyrimidin-4(*3H*)-ones (**6-9**) were obtaneid from the cyclocondensation reaction of β-alkoxyvinyl trihalomethyl ketones (**1**) with asymmetric 1-methylisothiourea sulfates (**2-5**) in solution of Na_2CO_3 1M. The 2-methylthiopyrimidin-4(3H)-ones (**6-9**) were oxidized with OXONE in a mixture of MeOH-H_2O as solvent and refluxing to form uracil of interest (**10-13**). From the bromination reaction between 1.0 mmol of uracil (**10-13**) with 1.5 mmol of Br_2 dissolved in 10 mL of MeOH, the 5-bromo uracils (**14-17**) were synthesized. The reaction is carried at room temperature for 10mim. After completion of the reaction time, the precipitate is filtered and dried under vacuum. All products were obtained off as solids. Purification of the compounds was carried out by recrystallization using $CHCl_3$ and MeOH. The identification of 5-bromo uracils was performed by ^1H and ^{13}C NMR and Mass Spectrometry.



I **II**

Figure 1. Chemistry structure of Bromacil and 5-Fluorouracil

Scheme 1:



i = Na_2CO_3 (1N), t.a, 1-4h; *ii* = OXONE, MeOH/H_2O, Δ, 15h; *iii* = Br_2, MeOH, t.a, 10min

1,14-17	a	b	c	d	e	f
R	Me	Ph	4-Me-C_6H_4	4-OMe-C_6H_4	4-F-C_6H_4	4-Br-C_6H_4

	2,14	3,15	4,16	5,17
R^1	Me	Ph	Bn	*s*-Butil

CONCLUSION

In summary, we presents the synthesis of a new series of 5-bromo uracil (**14-17**), analogous of the Bromacil, through of a methodology quickly, efficiently and high yields.

ACKNOWLEDGEMENTS

The authors acknowledge the financial support of the National Council Scientific and Technological Research (CNPq), CAPES and FAPERGS

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