Chemoselective Reactivity Study of 6-Hydrazinonicotinic Acid Hydrazide

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INTRODUCTION

Since its discovery, Ferrocene and its derivatives, have been attracting much attention for its use in catalysis, organic synthesis, new materials such as liquid crystals or polymers and supramolecular chemistry.[1] Incorporation of a ferrocene fragment into a molecule of an organic compound often results in unexpected biological activity which is rationalized as being due to its different membrane-permeation properties and anomalous metabolism.[2]

It is well known that certain substituted dihydropyrazole derivatives are highly biologically active and can be used as medications in human and/or veterinary therapy and as insecticides and herbicides in agriculture and horticulture.[1]

Hydrazones are organic compounds characterized by the presence of the NH-N = CHR group in its molecules.[3a] Such molecules have anticonvulsant, antidepressant, analgesic, antibiotic, antitumor, antiviral and anti-platelet properties and it is therefore of great value to develop synthetic methods to access this class of compounds.[3] In this context, this study aims to differentiate the reactivity of 6-hydrazinonicotinic acid hydrazide against ferrocene carboxaldehyde and acetyferrocene in order to obtain, selectively, ferrocenyl hydrazones and subsequently allow the cyclization of the hydrazide moeity with β-alkoxyvinyl trifluoromethyl ketones to obtain a series of pyrazolyl-pyridine ferrocenyl hydrazones.

RESULTS AND DISCUSSION

The ferrocenyl hydrazone nicotinic hidrazides **3** were synthesized according to the reported procedure (scheme 1).[4,5] The pyridine **1** reacted with equimolar amounts of commercially available ferrocene carboxaldehyde **2a** or acetylferrocene **2b** to give **3a-b** in 72 – 77% yields. In a subsequent step, hydrazones **3** reacted with β-alkoxyvinyl trifluoromethyl ketones **4** in ethanol under reflux, to give in 4 hours pyrazolyl-pyridine ferrocenyl hydrazone **5**.[6] All the compounds were characterized by LC-MS/MS, ^{1}H and ^{13}C NMR spectroscopy.

CONCLUSION

In conclusion, we have developed a convenient procedure to selectively react the hydrazinyl sites of **1** obtaining pyrazolyl-pyridine ferrocenyl hydrazones **3**. Subsequently, cyclization reactions with β-alkoxyvinyl trifluoromethyl ketones **4** furnished new ferrocenyl carbonyl heterocycles **5**.

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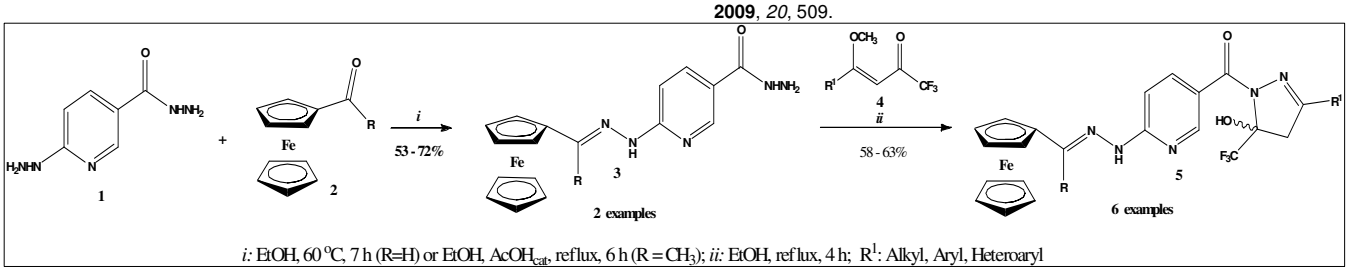
REFERENCES

[1] Fang, J.; Jin, Z.; Li, Z.; Liu, W. *J Organomet. Chem.*. **2003**, *674*, 1.
[2] Hanzlik, R. P.; Soine, P.; Soine, W. N. *J. Med. Chem.* **1979**, *22*, 424.
[3] (a) Angelusiu, M. V.; Barbuceanu, S. F.; Draghici, C.; Almajan, G. L. *Eur. J. Med. Chem.* **2010**, *45*, 2055. (b) Ozkay, Y.; Tunah, Y.; Karaca, H.; Isikdag, I. *Eur. J. Med. Chem.* **2010**, *45*, 3293.
[4] Kuriakose, M.; Kurup, M. R. P.; Suresh, E. *Spectrochim. Acta Part A* **2007**, *66*, 353.
[5] Du, X.; Guo, C.; Hansell, E.; Doyle, P. S.; Caffrey, C. R.; Holler, T. P.; McKerrow, J. H.; Cohen, F. E. *J. Med. Chem.* **2002**, *45*, 2695.
[6] Bonacorso, H. G.; Paim, G. R.; Guerra, C. Z.; Sehnem, R. C.; Cechinel, C. A.; Porte, L. M. F.; Martins, M. A. P.; Zanatta, N. *J. Braz. Chem. Soc.* **2009**, *20*, 509.



Scheme 1. Synthesis of Pyrazolyl-pyridine Ferrocenyl Hydrazones