



Preparation of pyrimidin-2-one derivatives via base-mediated decomposition of uracil-analogues Fischer carbene complex



Carmen Bocchino^a, Antonella Carabellese^a, Tonino Caruso^a, Giorgio Della Sala^a, Susagna Ricart^b, Aldo Spinella^{a,*}

^a Dipartimento di Chimica e Biologia, Università di Salerno, Via Giovanni Paolo II, 132 Fisciano, 84084 Salerno, Italy

^b Departament de Materials Moleculars, Institut de Ciència de Materials de Barcelona, CSIC, Campus de la UAB, E-08193 Bellaterra, Spain

ARTICLE INFO

Article history:

Received 12 August 2013

Received in revised form

7 September 2013

Accepted 12 September 2013

Keywords:

Fischer carbene

Pyrimidin-2-one derivatives

Triethylamine

Demetallation

ABSTRACT

A practical and efficient synthesis of pyrimidin-2-one derivatives from Fischer carbene complex uracil-analogues through base-mediated elimination reactions is described. The scope of the protocol has been explored with the preparation of a variety of pyrimidin-2-one derivatives by base mediated demetallation of N-1 and N-3 substituted uracil Fischer carbenes.

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1. Introduction

Pyrimidin-2-one substructure is a part of many compounds showing several biological activities ranging from pharmaceutical to agricultural fields and their preparation has attracted an increasing research interest [1,2].

Fischer carbenes have been widely used in organic synthesis [3–5] and in the course of our studies on the reactivity of alkynyl alkoxy carbene metal complexes, we have prepared several Fischer carbene complex uracil-analogues **2,3** starting from carbene complex **1** and substituted ureas [6,7] (Scheme 1).

These uracil-analogues can be considered as an useful intermediate for the preparation of some heterocyclic derivatives. In fact, uracil derivatives were easily obtained by oxidation of Fischer tungsten–carbene uracil complexes [8]. During this latter study we observed that a pyrimidine-2-one (**4a**) was obtained during the oxidation of **2a** with trimethylamine oxide. We considered the basic condition as an explanation for the formation of elimination product (Scheme 2).

Furthermore, a base mediated elimination of tungsten oxacarbene was described for the preparation of pyranose glycols [9]. These results stimulated our investigation on base mediated

elimination of Fischer tungsten carbene uracil complexes for the preparation of pyrimidine-2-one compounds.

In this communication we describe the preparation of pyrimidin-2-one derivatives **4,5** from Fischer carbene complex uracil-analogues **2,3** through base-mediated elimination reactions.

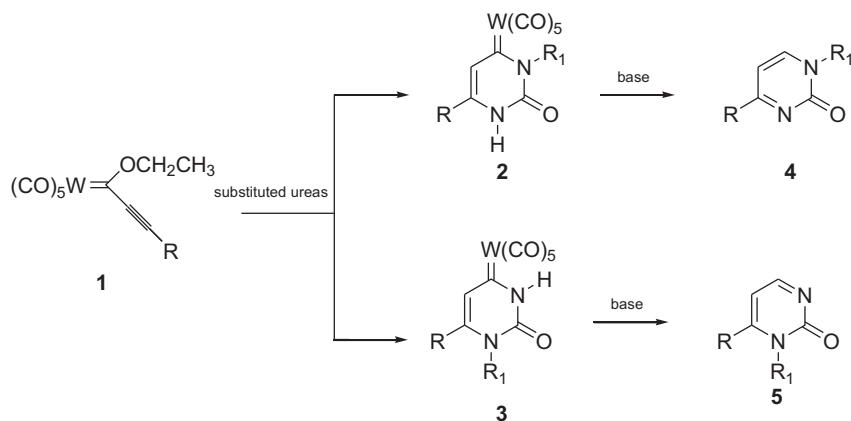
2. Results

We started our study considering the effect of different bases on Fischer tungsten–carbene **2a** for the preparation of 1-methyl-4-phenylpyrimidin-2(1H)-one (**4a**). Several reactions were conducted using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), pyridine and triethylamine (TEA) as base. The results are reported in Table 1. DBU gave quite good results using dichloroethane (DCE) as solvent while reaction conducted in toluene resulted less effective (entries 1,2). Pyridine gave unsatisfactory results while TEA showed best results when used in molar ratio with DCE as solvent (entry 4). In order to optimize the process a catalytic rather than a molar amount of base was used. However, decreasing the amount of base also yield decreases (entry 5). Finally, the reaction was conducted without the base in order to evaluate the heating effect. Under this condition compound **4a** was obtained in 33% yield (entry 6).

With this optimized conditions in our hands, we considered the demetallation of uracil Fischer carbene **3a**. As expected, taking into account the steric hindrance brought about by the presence of the pentacarbonyl moiety, this reaction proved to be more difficult

* Corresponding author. Tel.: +39 089969585; fax: +39 089969603.

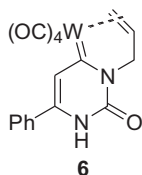
E-mail address: spinella@unisa.it (A. Spinella).



Scheme 1.

giving a mixture containing the desired product together with secondary products. Improvements were obtained using large excess of base. In fact, an excellent yield (91%) was achieved only using 10 eq. of TEA (Table 2).

Finally, we studied the scope of this reaction using different substrates (Table 3). Generally, good results were achieved and only for N-allyl substituted complexes **2c** and **3c** the reaction was slow. In particular **2c** required 10 days in order to give a good yield. Probably this result was due to the initial formation of compound **6** [7] which then is transformed into **4c**.



3. Conclusions

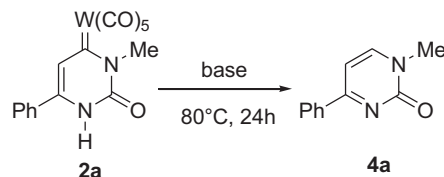
In summary, we have developed a practical and efficient methodology for the preparation of a variety of pyrimidin-2-ones derivatives by base mediated demetallation of N-1 and N-3 substituted uracil Fischer carbenes.

4. Experimental

4.1. General methods

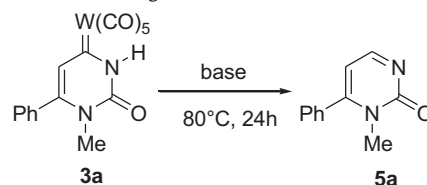
All reactions were carried out using freshly distilled and dried solvents. Starting materials and reagents purchased from commercial suppliers were generally used without purification. Uracil carbenes **2** and **3** were prepared according to literature

Table 1
Optimization of base-mediated decomposition of Fischer tungsten–carbene **2a**.

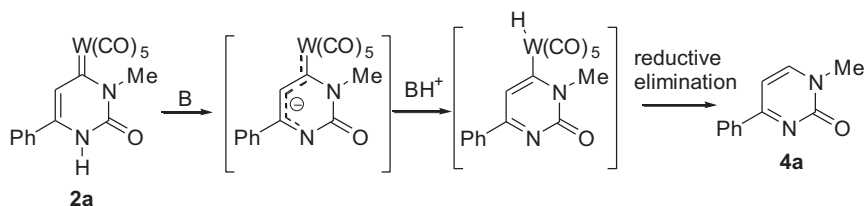


Entry	Base (eq. mol.)	Solvent	4a (%)
1	DBU (1.0)	DCE	79
2	DBU (1.0)	Toluene	63
3	Pyr (1.0)	DCE	34
4	NEt ₃ (1.0)	DCE	96
5	NEt ₃ (0.3)	DCE	35
6	–	DCE	33

Table 2
Effect of the base on Fischer tungsten–carbene **3a**.



Entry	Base (eq. mol.)	Solvent	Yield 5a (%)
1	NEt ₃ (1.0)	DCE	78
2	NEt ₃ (2.0)	DCE	84
3	NEt ₃ (10)	DCE	91
4	NEt ₃ (20)	DCE	100



Scheme 2.

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