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tallation of N-1 and N-3 substituted uracil Fischer carbenes.

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

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ABSTRACT

#### A R T I C L E I N F O

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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 glycals [9]. These results stimulated our investigation on base mediated

0022-328X/\$ - see front matter © 2013 Elsevier B.V. All rights reserved. http://dx.doi.org/10.1016/j.jorganchem.2013.09.015 elimination of Fischer tungsten carbene uracil complexes for the preparation of pyrimidine-2-one compounds.

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 deme-

In this communication we describe the preparation of pyrimidin-2-one derivatives **4**,**5** from Fischer carbene complex uracilanalogues **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-4phenylpyrimidin-2(1*H*)-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





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Table 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

Optimization of base-mediated decomposition of Fischer tungsten-carbene 2a.



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

# Table 2

Effect of the base on Fischer tungsten-carbene 3a.



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



Table 3
Study of scope of reaction. Preparation of pyrimidine-2-one derivatives $4b-d$ and $5b.c^{a}$

Entry	Substrate	Pyrimidin-2(1H)-one	NEt <sub>3</sub> (eq. mol.)	Reaction time (d)	Isolated yield (%)
1	W(CO) <sub>5</sub> Ph N O H 2b	Ph NO 4b	1	0.5	95
2	$ \begin{array}{c} W(CO)_{5} \\ W(CO)_{5} \\ N \\ Ph \\ N \\ H \\ 2c \end{array} $	Ph N O 4c	1	10	87
3	W(CO) <sub>5</sub> N <sup>-CH<sub>2</sub>Ph Ph N O H <b>2d</b></sup>	Ph N O 4d	1	1	80
4	W(CO) <sub>5</sub> NH Ph N 3b	Ph N O 5b	10	1	97
5	W(CO) <sub>5</sub> NH Ph N O 3c	Ph N O 5c	10	5	98

<sup>a</sup> All reactions conducted in DCE at 80 °C.

methods [7]. Reaction temperatures were measured externally; reactions were monitored by TLC on Merck silica gel plates (0.25 mm) and visualized by UV light. Flash chromatography was performed on Merck silica gel (60, particle size: 0.040–0.063 mm). Yields refer to chromatographically and spectroscopic (<sup>1</sup>H and <sup>13</sup>C NMR) pure materials. NMR spectra were recorded on a DRX 400 (400 MHz) spectrometer at room temperature. CDCl<sub>3</sub> was used as a solvent and residual chloroform (<sup>1</sup>H  $\delta$  = 7.26; <sup>13</sup>C,  $\delta$  = 77.0) was used as an internal standard. Infrared spectra were obtained at a resolution of 2.0 cm<sup>-1</sup> with a Vector 22 Bruker spectrometer. ESIMS was performed using a Quattro micro API mass spectrometer (Micromass, Manchester, UK) equipped with an electrospray ion source.

#### 4.2. General experimental representative procedure

A solution of metallocarbene (0.4 mmol) and base in dry solvent (8 mL), was stirred, in a round bottomed flask equipped with a condenser, at the temperature of 80 °C until metallocarbene was completely consumed. Then the solvent was evaporated *in vacuo*. The crude mixture was purified by flash chromatography (elution with CHCl<sub>3</sub> and then with CHCl<sub>3</sub>/CH<sub>3</sub>OH mixtures 4:1).

#### 4.2.1. Compound **4a**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 8.05 (d, 2H, *J* = 7.2 Hz), 7.53 (d, 1H, *J* = 6.8 Hz), 7.46 (m, 3H overlapped), 6.76 (d, 1H, *J* = 6.8 Hz), 3.56 (s, 3H). <sup>13</sup>C NMR (100.6 MHz, CDCl<sub>3</sub>)  $\delta$  = 171.5, 157.0, 148.2, 135.8, 131.9, 128.6, 127.7, 101.0, 38.8; IR (CHCl<sub>3</sub>): 1710, 1646, 1388 cm<sup>-1</sup>; EI-MS (70 eV) 185, 157, 115.

#### 4.2.2. Compound 4b

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 8.07 (d, 2H, *J* = 10.4 Hz), 7.68 (d, 1H, *J* = 10.8 Hz), 7.46 (m, 3H overlapped), 6.77 (d, 1H, *J* = 10.8 Hz), 3.92 (t, 2H, *J* = 11.5 Hz), 1.78 (dt, 2H, *J* = 15.0 Hz, *J* = 7.5 Hz), 1.37, 0.94 (t, 3H, *J* = 7.2 Hz). <sup>13</sup>C NMR (100.6 MHz, CDCl<sub>3</sub>)  $\delta$  = 171.1, 156.3, 147.6, 135.7, 131.8, 128.6, 127.7, 100.9, 51.5, 30.1, 19.7, 13.5; IR (CHCl<sub>3</sub>): 2960, 1659, 1616, 1523, 765 cm<sup>-1</sup>; EI-MS (70 eV) 229 (M<sup>+</sup> + H), 228.

#### 4.2.3. Compound 4c

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 8.04 (d, 2H, *J* = 6.8 Hz), 7.69 (d, 1H, *J* = 6.9 Hz), 7.49 (m, 3H overlapped), 6.80 (d, 1H, *J* = 6.9 Hz), 5.99 (m, 1H), 5.31 (m, 2H), 4.56 (m, 3H). <sup>13</sup>C NMR (100.6 MHz, CDCl<sub>3</sub>)  $\delta$  = 171.4, 156.2, 147.1, 135.6, 132.1, 131.4, 128.7, 127.9, 119.4, 101.1, 52.5; IR (CHCl<sub>3</sub>): 1647, 1614, 1493, 1363, 765 cm<sup>-1</sup>; EI-MS (70 eV) 213 (M<sup>+</sup> + H), 199, 164, 153.

#### 4.2.4. Compound 4d

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 8.08 (d, 2H, J = 7.6 Hz), 7.64 (d, 1H, J = 6.9 Hz), 7.46 (m, 3H overlapped), 7.36 (m, 5H overlapped), 6.75 (d, 1H, J = 7.2 Hz), 5.14 (s, 2H). <sup>13</sup>C NMR (100.6 MHz, CDCl<sub>3</sub>)  $\delta = 171.6, 156.9, 147.1, 136.0, 135.3, 132.3, 129.4, 129.0, 128.9, 128.8,$ 128.2, 101.6, 53.6; IR (CHCl<sub>3</sub>): 1645, 1613, 1492, 1362, 763 cm<sup>-1</sup>; El-MS (70 eV) 285 (M<sup>+</sup> + Na), 263 (M<sup>+</sup> + H), 158, 109.

#### 4.2.5. Compound 5a

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 8.55 (d, 2H, J = 4.3 Hz), 7.53 (m, 3H overlapped), 7.37 (m, 3H), 6.23 (d, 1H, *J* = 4.3 Hz), 3.44 (s, 3H). <sup>13</sup>C NMR (100.6 MHz, CDCl<sub>3</sub>)  $\delta$  = 164.3, 160.7, 157.5, 133.0, 130.6, 129.1, 127.7, 105.5, 35.7; IR (CHCl<sub>3</sub>): 1671, 1658, 1358 cm<sup>-1</sup>.

#### 4.2.6. Compound 5b

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 8.51 (d, 2H, J = 5.0 Hz), 7.55 (m, 3H overlapped), 7.40 (m, 2H), 6.15 (d, 1H, *J* = 5.0 Hz), 3.85 (m, 2H), 1.60 (m, 2H), 1.12 (m, 2H), 0.72 (t, 3H, J = 7.5 Hz). <sup>13</sup>C NMR  $(100.6 \text{ MHz}, \text{CDCl}_3) \delta = 164.1, 160.6, 156.7, 133.0, 130.2, 128.8, 127.6,$ 105.6, 47.1, 30.1, 19.7, 13.3.

#### 4.2.7. Compound 5c

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta = 8.60$  (d, 1H, I = 5.0 Hz), 7.51 (m, 3H overlapped), 7.37 (m, 2H), 6.25 (d, 1H, J = 5.0 Hz), 5.90 (m, 1H), 5.18 (d, 1H, J = 10.0 Hz), 4.92 (d, 1H, J = 17.5 Hz), 4.50 (d, 2H, J = 5.0 Hz), <sup>13</sup>C NMR (100.6 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.3, 131.4, 130.7, 128.8, 128.7, 127.7, 118.4, 106.0, 50.1, 47.7.

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