

## DEMONSTRATION OF HETEROARYLMETHANE OXIDATION IN A BENZIMIDAZOLE DERIVATIVE WITH THE USE OF UV SPECTROPHOTOMETRY AND X-RAY DIFFRACTION

Khalid Attar<sup>1</sup>, Youssef Kandri Rodi<sup>2</sup>, Mohamed Benchidmi<sup>1</sup>, Amal  
Haoudi<sup>2</sup>, Frédéric Capet<sup>3</sup>, Christian Rolando<sup>4</sup>, El Mokhtar Essassi<sup>1,5\*</sup>

<sup>1</sup>Laboratory of Heterocyclic Organic Chemistry, URAC 21,  
“Mohammed V” University, Agdal-Rabat, Morocco

<sup>2</sup>Laboratory of Applied Organic Chemistry, Organic Chemistry  
Department, Faculty of Science and Techniques,  
“Sidi Mohammed Ben Abdellah” University, Fès, Morocco

<sup>3</sup>Unité de Catalyse et de Chimie du Solide (UCCS), UMR 8181,  
Ecole Nationale Supérieure de Chimie de Lille, France

<sup>4</sup>USR 3290, Miniaturisation pour l'Analyse, la Synthèse et la Protéomique,  
Université Lille 1, 59655 Villeneuve d'Ascq Cedex, France

<sup>5</sup>Institute of Nanomaterials and Nanotechnology, MAScIR, Rabat, Morocco

\* Corresponding author: [emessassi@yahoo.fr](mailto:emessassi@yahoo.fr)

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**Abstract:** In this work, we present the synthesis of a copper complex of 1-benzyl-2-[(5-methyl-isoxazol-3-yl)methyl]-benzimidazole, by using simultaneously UV spectrophotometry and X-ray diffraction. It has been possible for us to highlight an original oxidation of benzylbenzimidazole group in such complex leading to ketone. A kinetic study carried out by UV spectrophotometry shows well that the oxidation reaction proceeds according to the first-order kinetic law:  $K = 9.4 \times 10^{-4} \text{ s}^{-1}$  and  $t_{1/2} = 12.4 \text{ min}$ .

**Keywords:** complexation, functionalised benzimidazole, kinetic, UV spectrophotometry, X-ray study

## INTRODUCTION

Due to the vast applications that could be found in the coordination complex with benzimidazole, last decades, the synthesis of this compound aroused the interest of scientific research [1-10].

Indeed, it was shown that such compounds intervened at complex fields as varied in organic synthesis (catalysts [11, 12], renewable energies [13, 14] and complexant properties [15]). Thus, in the last years, much of the works concerning the synthesis of this coordination complex were brought back in literature showing the molecules with very varied structures [16-19].

Moreover, the synthesis of heterocyclic systems containing the benzimidazole motif often aroused the passion for researchers. Indeed, the studies showed that such compounds are largely implied in several fields such as pharmacology area: they have shown antibacterial [20], anticancerous [21, 22] and antiulcerous [23, 24] properties.

In a similar way, in this work, we endeavoured to prepare a new complex of coordination likely to find important application thereafter.

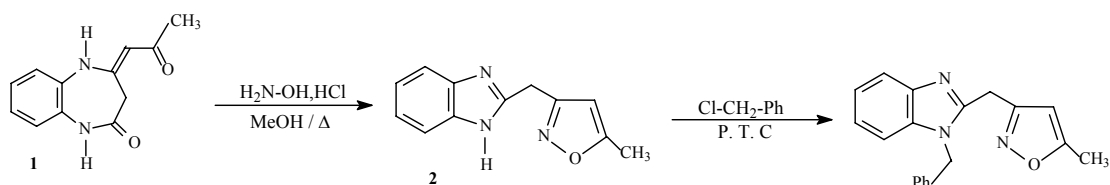
## EXPERIMENTAL

Melting points were taken using an electrothermal machine. The infrared spectra (IR) were carried out with Perkin-Elmer 1760x spectrometer. Single crystal X-ray diffraction data were collected on a SMART Apex II 4K CCD diffractometer (Bruker AXS). This instrument uses graphite monochromatic MoK $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ) and was operating at  $50\text{kV} \times 30 \text{ mA}$ . A green single crystal of complex **4** was analyzed at room temperature. The program Saint V7.34A [25] was used to extract the reflections from collected frames and to correct the corresponding intensities for Lorentz and polarization effects. The data were then corrected for absorption (SADABS [26] 2008/1). The study of systematic absences was performed using Bruker's Xprep [27] program and confirmed the monoclinic space group  $P2_1/c$ . The crystal structure was solved by direct methods (Shelxs97 [28]). Refinements were carried out by full matrix least squares method with the Shelxl97 [28] program. Hydrogen atoms were placed in theoretical positions and refined riding on their parent atoms.

To a solution of ligand **3** ( $1.65 \times 10^{-4} \text{ mol}$ ) in methanol (4 mL) we added a quantity of copper perchlorate corresponding to stoichiometry (1/1). After completion of the reaction the complex was dried under reduced pressure.

## RESULTS AND DISCUSSIONS

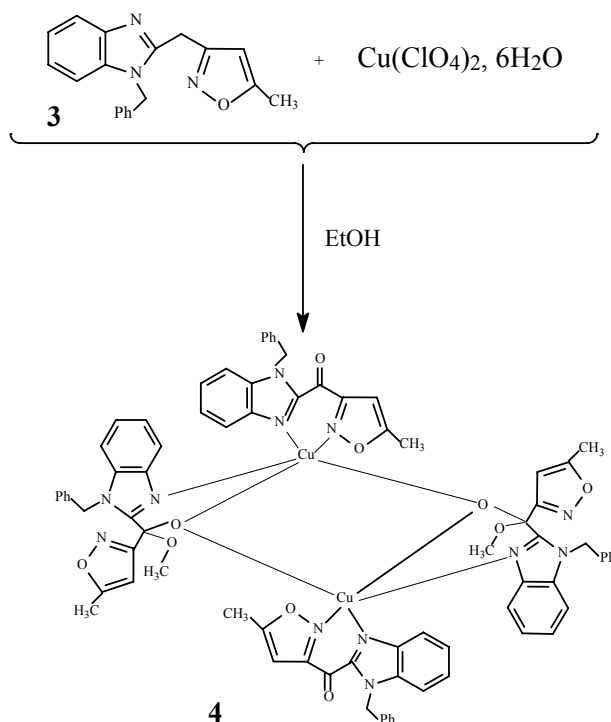
In a previous work we have showed that 1,5-benzodiazepines constitute an interesting precursors in the synthesis of recoveral heterocyclic systems [29-31]. In particular the 1,5-benzodiazepin-2-one **1** reacted with hydroxylamine hydrochloride in methanol giving rise to compound **2** presenting a benzimidazole and an isoxazole motifs. The alkylation reaction carried out on compound **2** by benzyl chloride using liquid-solid phase transfer catalysis [32-36] led to awaited compound with good yields (Figure 1).



**Figure 1.** Synthesis of compound **3** from 1,5-benzodiazepin-2-one

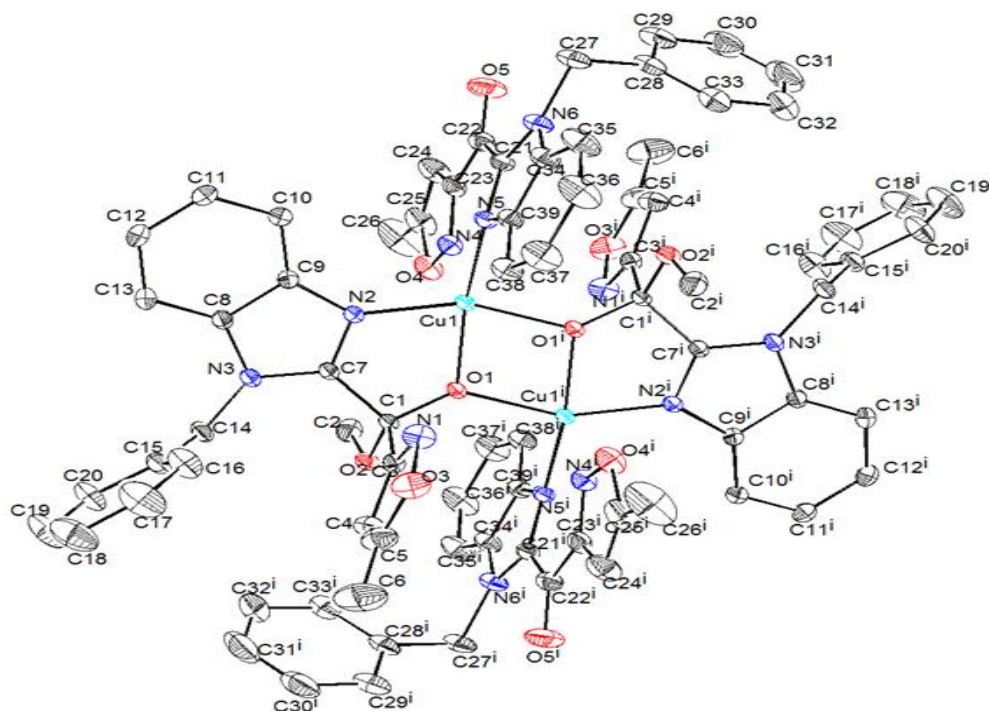
### Reaction of complexation

The ligand **3** prepared and also characterized, it was interesting to be able to study its potentialities of complexation. Indeed, the reaction of compound **3** with hexahydrated copper perchlorate, at ambient temperature, in methanolic medium gave rise to complex **4** (Figure 2).



**Figure 2.** Complexation of ligand **3** with hexahydrated copper perchlorate

The structural study by X-ray diffraction (Figure 3) carried out on complex **4**, emerged certain important points: initially, the complex **4** arises as a binuclear in which each pentacoordinated copper atom can be described as deformed pyramid, with an environment defined by three atoms of nitrogen and two atoms of oxygen.



**Figure 3.** ORTEP diagram of compound **4** with numbering scheme

The crystal data and the experimental conditions have been assembled in Table 1.

The compound **4** crystallizes in monoclinic system. The determination of the structure and refinement are treated in  $P2_1/c$  space group. The structure parameters are:  $a = 11.9675(2)$  Å;  $b = 19.5247(5)$  Å;  $c = 17.0103(4)$  Å;  $\alpha = 90^\circ$ ;  $\beta = 108^\circ 13'$ ;  $\delta = 90^\circ$ . The structure resolution revealed a perchlorate molecule and a water molecule. Unfortunately, the parameters for those molecules were very difficult to refine because of disorder. Therefore, we have used the program SQUEEZE from PLATON [37] to suppress this solvent contribution.

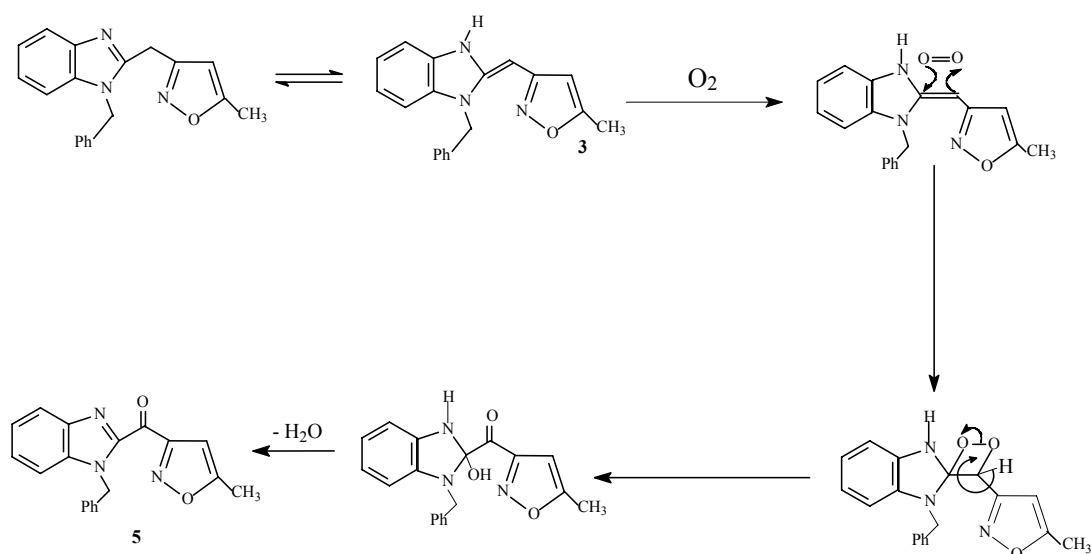
The oxygen atoms implied in this coordination come from oxidation of methylene group out of carbonyl group. In this reaction, the methanol plays at the same time the role of solvent and as nucleophilic agent.

The oxidation of methylene group as revealed by X-ray diffraction can be interpreted by cycloaddition [2+2] of oxygen molecule on the enaminic tautomer form **3a**. The rearrangement of intermediate dioxetane led to  $\alpha$ -hydroxycetone which through dehydration process provides the compound **5** (Figure 4).

A study by infrared spectroscopy of complexation reaction shows that the  $\nu_{C=O}$  vibration band at  $1692\text{ cm}^{-1}$  appears only after a metal addition. This confirms well that the methylene bridge oxidation reaction is closely related to the complexation.

**Table 1.** Crystal data and experimental conditions for compound **4**

Formula	C <sub>78</sub> H <sub>66</sub> Cu <sub>2</sub> N <sub>12</sub> O <sub>10</sub>
Formula weight	1458.51
Crystal system	Monoclinic
Crystal size (mm <sup>3</sup> )	0.49×0.45×0.42
Space group	P2 <sub>1</sub> /c
a (Å)	11.9663 (6)
b (Å)	19.5120 (9)
c (Å)	16.9908 (8)
β (°)	107.959 (2)
V (Å <sup>3</sup> )	3773.8 (3)
Z	2
Density (g/cm <sup>3</sup> )	1.284
F (000)	1512
M (MoKα) (mm <sup>-1</sup> )	0.63
Diffractometer	Bruker AXS Smart APEX II
T (K)	295(2)
Scan mode	ω –scans and φ -scans
θ <sub>max</sub> (°)	33.2
Measured reflection	132508
Independent reflection	14300
R <sub>int</sub>	0.047
Absorption correction	Multi-scan (sadabs 2008/ 1 Bruker AXS)
Reflection parameters	463
Reflection used for reference [I > 2σ (I)]	9455
H atoms	Prameters constrained
R [F <sup>2</sup> > 2σ(F <sup>2</sup> )]	0.043
wR (F <sup>2</sup> )	0.123
W	1/[σ <sup>2</sup> (F <sub>o</sub> <sup>2</sup> )+(0.0677P) <sup>2</sup> ] where P = (F <sub>o</sub> <sup>2</sup> +2F <sub>c</sub> <sup>2</sup> )/3
Goodness of fit	1.04



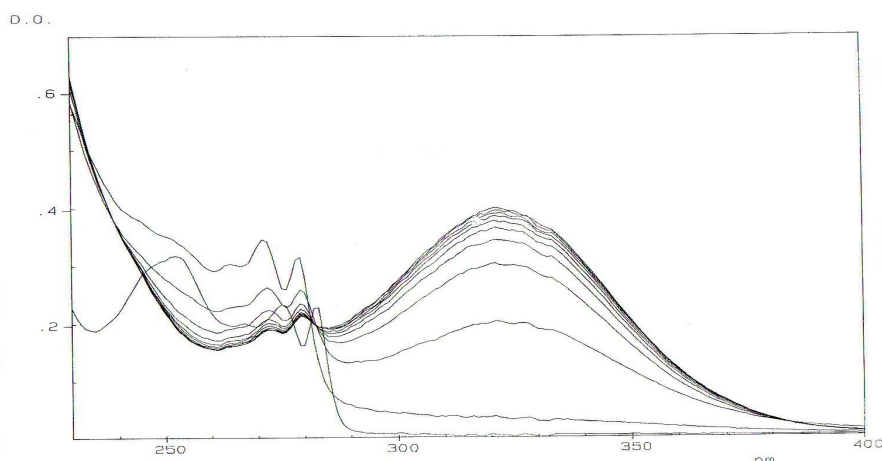
**Figure 4.** Formation of compound **5**

### Kinetic studies of oxidation reaction

The oxidation phenomenon revealed by IR is also confirmed by UV spectrophotometry. However, we noted considerable reaction acceleration. The optical density  $OD = f(\lambda)$  for  $\phi = 1$  curve of absorption is recorded every 10 minutes (Table 2 and Figure 5).

**Table 2.** Parameters of oxidation reaction

	Time, min	Height of the peak (H), mm	$H_{\infty} - H_t$	$\text{Log}(H_{\infty} - H_t)$
1	00	8	82	1.91
2	10	46	44	1.64
3	20	68	22	1.34
4	30	78	12	1.07
5	40	82	8	0.90
6	50	85	5	0.69
7	60	87	3	0.48
8	70	88.5	1.5	0.18
9	80	89	1	0.00
10	90	90	0	-



**Figure 5.** Oxidation of ligand 3 with hexahydrated copper perchlorate

### CONCLUSION

In this work, the study by infra-red spectroscopy enabled us to highlight, initially, an original oxidation of the methylene bridge out of carbonyl during the complexation of  $\text{Cu}^{2+}$  ion by 1-benzyl-2[5-(methylisoxazol-3-yl)-methyl] benzimidazole in acetonitrile. This oxidation phenomenon could be explained by the capturing character of methylene group.

It is worth noting that the compound 4 presents an original structure. It is a complex of  $\text{ML}_2$  type. The first ligand involves nitrogenous atoms of benzimidazole and of pyrazole. The second ligand engages in complexation reaction nitrogenous atom of benzimidazole and hemiacetale oxygen formed by the action of methanol over the formed ketone. Moreover, it was possible for us, in this type of reactions, to trap a

hemiacetal. It is well known that hemi-acetals are generally unstable and react with another alcohol molecule ending up with correspondent acetals.

The kinetic study of oxidation reaction carried out by UV spectrophotometry detected a clear acceleration in these conditions compared to the infra-red one. This difference of reactivity between UV and IR shows well the photochemical character of reaction.

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