Fourth International Electronic Conference on Synthetic Organic Chemistry (ECSOC-4), www.mdpi.org/ecsoc-4.htm, September 1-30, 2000

[A0008]

Crystal and molecular structures of N-benzyl-C-(2-pyridyl) nitrone and its ZnBr$_2$ complex.

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Received: 8 July 2000 / Uploaded: 26 July 2000

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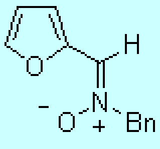
Introduction

Lewis acid modulated reactions play a very important role in organic synthesis as they provide versatile intermediates, sometimes dictating the stereochemistry of the products (1). Nitrones are substrates rather sensitive to Lewis-acid modulation as we have amply demonstrated during the last years (2) in nucleophilic additions to chiral nitrones. For instance, it has been demonstrated in our laboratory that by employing either ZnBr$_2$ or Et$_2$AlCl, one can produce hydroxylamines with either *syn* or *anti* stereochemistry (with respect to the alfa group), respectively (3).

1,3-Dipolar cycloaddition reactions with nitrones are also susceptible to be influenced by the presence of Lewis acids. In fact, Lewis acids catalyzed nitrone cycloadditions have been extensively studied (4). Kanemasa and Tsuruoka have suggested the participation of nitrone-MgBr$_2$ complexes in some cycloaddition reactions with allylic alcohols (5). The scope and limitations of chiral Mg(II) and Cu(II) complexes on the selectivity of cycloaddition of nitrones with alkenes have been studied by Jorgensen and coworkers (6). Activation of nitrones by chiral Lewis acids towards cycloadditions with electron-rich alkenes have also been reported (7).

In the context of cycloaddition chemistry, we have recently reported the 1,3-dipolar cycloaddition of several hetaryl nitrones **1-5** with both electron-rich (8) and electron-deficient alkenes (9). The asymmetric version of the cycloaddition reaction between C-(2-furyl)-N-benzyl nitrone **1** and acrylates has been used in the preparation of various protected derivatives of 4-hydroxy-pyroglutamic acids of synthetic utility (10).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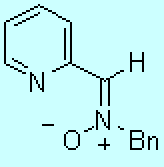
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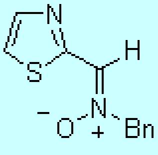
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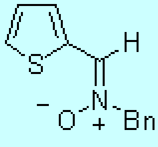
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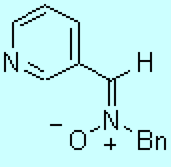
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With the aim of modulating the reactivity of hetaryl nitrones **1-5** we have started a project directed to understand the properties of Lewis acid complexes with compounds **1-5**. Stable complexes of nitrones have already been studied. Nitrone complexes of iron have been full-characterized and their acidic hydrolysis studied by Pierre and coworkers (11). The same authors have also reported the electrochemical reduction of such complexes (12). Several tin (IV) complexes with nitrones giving pentacoordinated metal compounds have been prepared (13). Crist and coworkers (14) have prepared and characterized complexes of N-tert-butyl-C-(2-pyridyl) nitrone with Cu(II), Mn(II), Co(II), Ni(II), Fe(II) and Fe(III). The X-ray structures of some complexes have also been determined (15). Boron chelates with some particular aryl nitrones have also been described (16).

In this communication we describe the structural and theoretical studies of both (Z)-N-benzyl-C-(2-pyridyl) nitrone and its ZnBr$_2$ complex. Additionally, we also compare the reactivity of the nitrone alone and the isolated complex in cycloaddition reactions with vinyl acetate.

Synthesis and Structural Analysis

The N-benzyl-C-(2-pyridyl) nitrone **2** was prepared by condensation of pyridine-2-carbaldehyde (17) and N-benzylhydroxylamine (18) following our previously reported procedure (19). Compound **2** was a crystalline stable product and showed a Z-configuration as demonstrated by nOe experiments and X-ray crystallography. Transparent blocks of **2** were grown at room temperature by slow evaporation of a 1:1 hexane/EtOAc mixture. X-ray diffraction data were obtained at 173 K and the structure is given in Figure 1. Selected data are given in Table 1.

The reaction of **2** with ZnBr$_2$ in acetone for 1 h gave the crystalline chelate **6** after precipitation with diethyl ether (Scheme 1) which displayed a signal for the azomethine proton at d 5.40 ppm in contrast to the signal at d 5.19 ppm displayed by nitrone **2** for the same proton. This result indicated the different orientation of the nitrone group induced by the complexation with the Lewis acid.

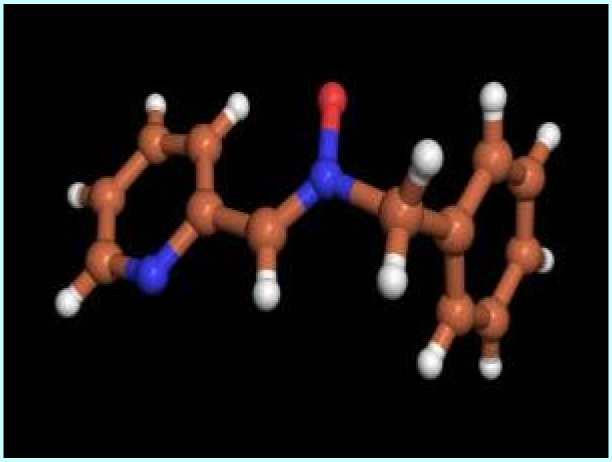


Figure 1. X-ray structure of nitrone **2**

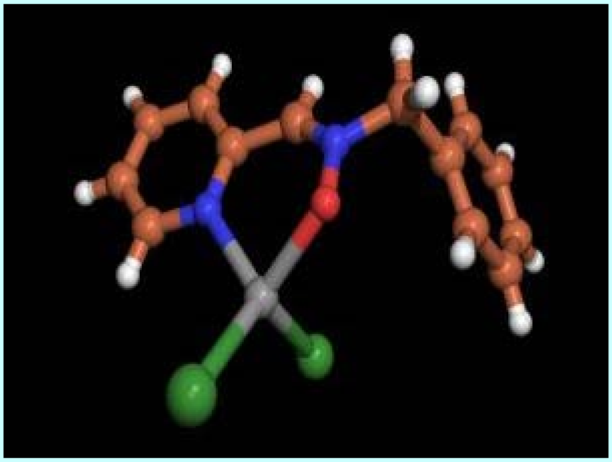
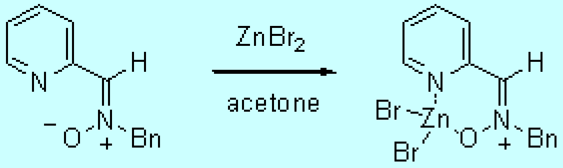


Figure 2. X-ray structure of complex **6**

The complex **6** crystallized as transparent blocks suitable for X-ray analysis from a 1:1 CH$_2$Cl$_2$/hexane mixture. The X-ray diffraction data were obtained at 243 K (due to some instability of the crystal at lower temperatures) and the structure is given in Figure 2. This structure provided an opportunity to compare the structure of **6** with **2**. In fact, the features of the solid-state geometry of **6** summarized in Table 1, are discussed in comparison with the values for **2**.



2 **6**

Scheme 1

A coplanarity is seen, as in other hetaryl nitrones (20), between the planes of the heterocycle moiety and the nitrone function in both the nitrone alone and the chelate with ZnBr$_2$. As expected, formation of the complex resulted in some bond length and bond angle differences between **2** and **6** (Table 1). It is worthwhile noting the change of the N2-C3-

C4-N5 dihedral angle as a consequence of the formation of the chelate. In the complex the metal atom adopts an almost tetrahedral disposition the bond angles with bromine atoms being larger than those with nitrogen and oxygen atoms.

X-ray diffraction data

Crystallographic data for compounds **2** and **6** appear in Table 1. The final unit-cell parameters were obtained by least squares on the settings angles for 39 reflections with $q_{min/max}$ = 9.49-24.75 deg. for **2** and 32 reflections with $q_{min/max}$ = 10.35-24.56 deg. for **6**. Intensity data were measured on a Siemens P4 diffractometer using the w-2q scan technique. The structures were solved by direct methods and all non-hydrogen atoms were refined anisotropically. The hydrogen atoms were located at calculated positions.

Selected acquisition data

	2	**6**
Formula	$C_{13}H_{12}N_2O$	$C_{13}H_{12}Br_2N_2OZn$
FW	212.25	437.44
Crystal system	orthorhombic	triclinic
Space group	Pbcn	P-1
a (Å)	11.033 (5)	7.303 (2)
b (Å)	11.107 (5)	8.135 (3)
c (Å)	17.414 (5)	12.970 (6)
a (deg.)	90	87.01 (3)
b (deg.)	90	80.56 (3)
g (deg.)	90	84.60 (3)
V (Å^3)	2134.0 (15)	756.2 (5)
Z	8	2
r_{calc} (g/cm^3)	1.321	1.921
F(000)	896	424
m (Mo-K$_a$), cm-1	0.086	6.900
crystal size, mm	0.38x0.20x0.16	0.24x0.10x0.08
measurement T (K)	173 (2)	243 (2)
q_{max} (deg.)	25.11	25.0
crystal decay (%)	6.86	15.4
total reflections	2446	5169
total unique reflections	1886	2628
R_{merge}	0.072	0.097
reflections I>2s(I)	1083	1333
No. parameters	147	174
R	0.0474	0.1007
R_w	0.0847	0.2432
GoF (S)	1.084	1.162

Siemens P4 diffractometer. Mo-Ka radiation (l=0.71609Å), normal focus sealed tube, graphite monochromator. Values given for R, Rw and GoF are based on total unique reflections. Computing data collections: Siemens XSCANS (21). Structure solution: SIR-97 (22). Structure refinement: SHELXL-97 (23). Molecular Graphics: PovChem v 2.1 (24)

Theoretical Calculations

In order to assess the various factors contributing to the structural differences between **2** and **6** we have carried out ab initio energy calculations. The optimized structures for **2** and **6** are shown in Figures 3 and 4.

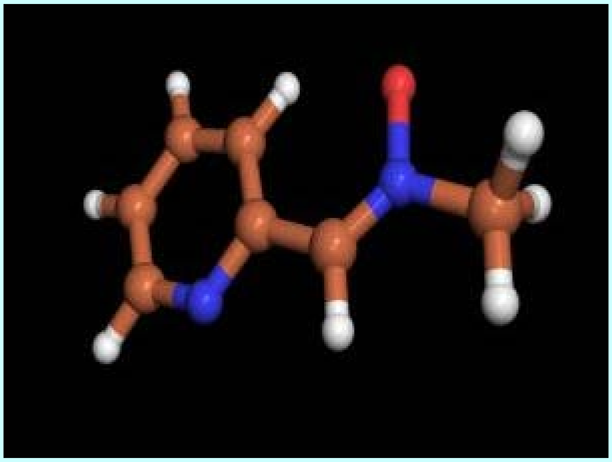


Figure 3. Optimized structure (HF/3-21G) for **2**

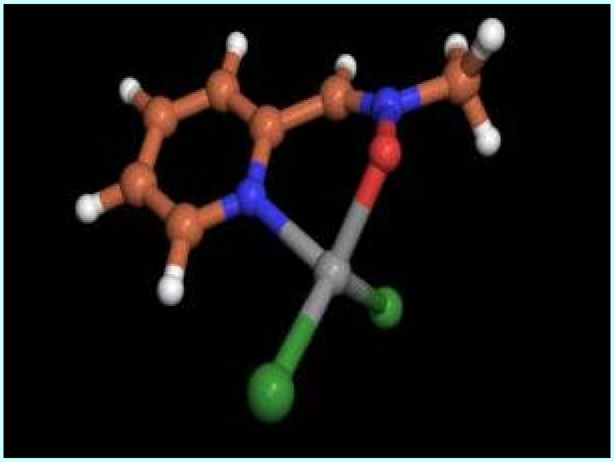


Figure 4. Optimized structure (HF/3-21G) for **6**

The molecular structures found with ab initio calculations agree with those observed in the crystalline state although some differences were observed. For instance, theoretical calculations gave longer O1-N2 bonds and shorter N2-C3 bonds than those found in crystalline state, presumably due to the consideration of resonance for the nitrone function. Nevertheless, the modeled structures showed a good overlap with the X-ray structures (Figures 5 and 6).

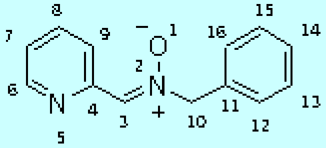
Figure 5. Comparison of the modeled structure of nitrone **2** with the X-ray structure.

Figure 6. Comparison of the modeled structure of complex **6** with the X-ray structure.

Ab initio calculations

Calculated structures were optimized at HF/3-21G level using Gaussian98 (25). All internal coordinates were free. In both **2** and **6** the benzyl group has been replaced for a methyl group, and in the case of **6** the Br atoms have been replaced by Cl atoms. The X-ray data were used (after replacement of the indicated groups) to generate guessed structures which were pre-optimized at semiempirical level (PM3) using MOPAC97 as implemented in CS ChemOffice (26). In the case of the nitrone alone a complete conformational analysis has been carried out in order to determine the preferred orientation of the nitrone function with respect to the pyridine ring.

Table 1. Selected bond lengths (Å), bond angles (°) and dihedral angles (°) for **2** and **6**.



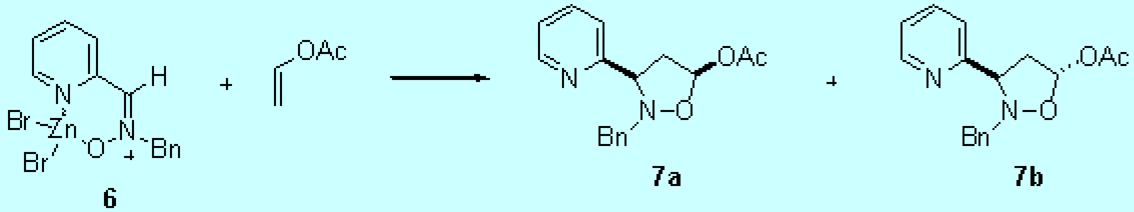
numbering scheme

	Nitrone **2**	Complex **6**

	X-ray data	HF / 3-21G	X-ray data	HF / 3-21G
bond lenghts				
O1-N2	1.299	1.383	1.396	1.326
N2-C3	1.300	1.268	1.261	1.228
C3-C4	1.451	1.458	1.469	1.501
C4-N5	1.365	1.337	1.318	1.318
N2-C10	1.488	1.472	1.477	1.500
O1-Zn	--------	--------	1.993	1.930
N5-Zn	--------	--------	2.055	2.029
Zn-Br1	--------	--------	2.321	2.287
Zn-Br2	--------	--------	2.357	2.333
bond angles				
O1-N2-C3	126.1	125.6	127.3	123.5
N2-C3-C4	126.3	126.4	129.8	125.7
C3-C4-N5	113.2	113.8	118.6	119.6
O1-N2-C10	114.4	111.2	111.1	111.2
C3-N2-C10	119.5	123.2	121.0	125.3
O1-Zn-N5	--------	--------	89.7	87.5
N2-O1-Zn	--------	--------	118.1	111.1
N5-Zn-Br1	--------	--------	108.1	105.3
O1-Zn-Br2	--------	--------	113.7	126.1
dihedral angles				
O1-N2-C3-C4	3.1	0.0	2.6	2.9
N2-C3-C4-N5	175.6	180.0	13.0	23.7
O1-N2-C10-C11	112.6	--------	--------	85.0
N2-O1-Zn-N5	--------	--------	122.8	141.5
O1-Zn-N5-C4	--------	--------	37.2	30.7

Reactivity

The reactivity of the complex was studied by condensing it with vinyl acetate in a 1,3-dipolar cycloaddition reaction. We have recently reported (8) the reaction between nitrones **1-5** and vinyl acetate to give the corresponding isoxazolidines. It might be expected a difference of reactivity between **2** and **6**. However, only slight differences in both reactivity and selectivity were found. Data for the reactivity are illustrated in Scheme 2. The results of the same reaction with nitrone **2** are also given for comparison.



Scheme 2

1,3-Dipole	**7a : 7b**	yield (%)
2	85 : 15	85
6	89 : 11	87

Conclusion

In summary, this preliminary results showed the possibility of using complexed nitrones as suitable 1,3-dipoles in cycloaddition reactions. Similar structures were found in the crystal structure and by the ab initio calculations both for nitrone **2** and ZnBr -complex **6**. The reactivity of those compounds were compared by condensing them with vinyl

$_2$

acetate. Only slight differences of reactivity were observed between the nitrone alone and the complex. Further investigations with other complexes are now in progress.

Acknowledgements

The authors gratefully acknowledge the financial support given by the DGES (Project PB97-1014. Madrid. Spain)

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