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Received July 26, 1993

Revised June 23, 1994

The nmr and X-ray diffraction data of the novel ring system furo[3,2-*e*]imidazo[1,2-*c*]pyrimidine are reported in this paper. The crystal and molecular structure of this compound ( $C_9H_7N_3O_2 \cdot 1/2H_2O$ ) has been solved at room temperature. Crystals are monoclinic in a space group of  $P2_1/n$  with cell constants  $a = 9.982(8)$ ,  $b = 13.526(9)$  and  $c = 13.981(9)$  Å,  $\beta = 107.44(5)^\circ$ ,  $V = 1800.9$  Å<sup>3</sup>,  $Z = 8$ ,  $D_x = 1.462$  Mg·m<sup>-3</sup>. The structure was solved by full matrix least square refinement giving a final  $R = 0.054$  ( $R_w = 0.069$ ) for 1263 reflections ( $I > 3.0\sigma(I)$ ). The compound is essentially planar, existing in two slightly structural different forms, A and B. These are held in pairs with symmetry related molecules by hydrogen bonds formed with two water molecules. Then the dimeric units are stacked parallel to the *c* axis to form the tridimensional packing.

*J. Heterocyclic Chem.*, **31**, 1583 (1994).

## Introduction.

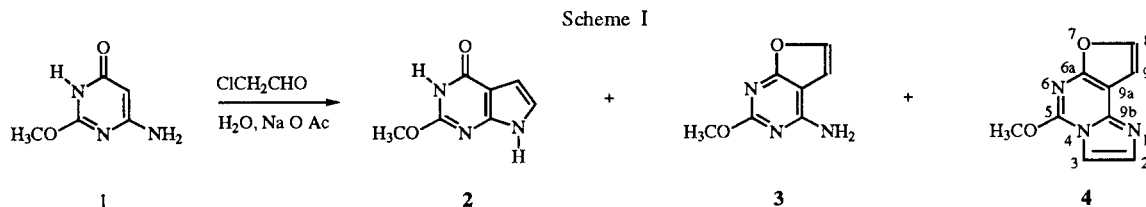
Some time ago, we reported the reaction of 6-amino-3,4-dihydro-2-methoxy-4-oxypyrimidine, **1**, with chloroacetaldehyde in water and sodium acetate [1]. In this reaction three compounds were obtained: 60% of pyrrolo[2,3-*d*]pyrimidine derivative **2**, 6% of furo[2,3-*d*]pyrimidine derivative **3** and 7% of the unknown compound **4** (Scheme I).

On the basis of analytical and spectroscopic data, this compound **4** was initially established as the novel ring system oxazolo[3,2-*c*]pyrrolo[3,2-*e*]pyrimidine, structure **5**. We assumed that such structure should be formed by *N*-alkylation of **2** and subsequent intramolecular cyclization

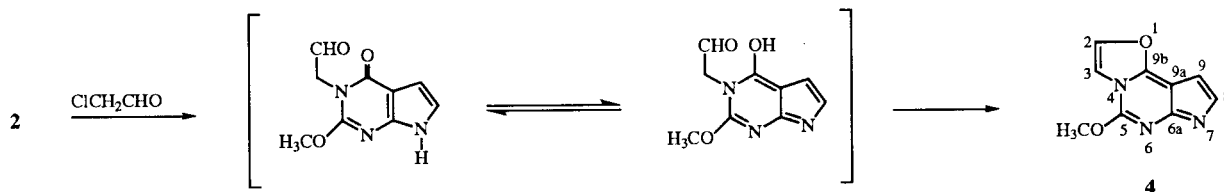
as shown in Scheme II.

In order to improve the yield of this compound and check the outlined route, a similar reaction sequence was carried out using the pyrrolo[2,3-*d*]pyrimidine derivative **2** as starting material. Unfortunately, attempts at the reaction of compound **2** with chloroacetaldehyde under the same (in water and sodium acetate under reflux) or different conditions were unpromising and as a consequence we further investigated the structure of this heterocycle.

The crystalline unknown compound **4** was thoroughly studied by nmr spectroscopy and X-ray diffraction and the data obtained from both techniques seemed to be consistent with the novel ring system furo[3,2-*e*]imidazo[1,2-*c*]-



Scheme II



pyrimidine. No bibliographic accounts were found for this heterocycle type.

Compound **4** can be formed by *N*-alkylation of imidazo[1,2-*c*]pyrimidine or furo[2,3-*d*]pyrimidine **3** (chloroacetaldehyde is in excess) and subsequent intramolecular cyclization. However, imidazo[1,2-*c*]pyrimidine was not detected by reaction of **1** with chloroacetaldehyde under the initial conditions [1] probably due to its fast reaction. The proposed routes are currently under investigation.

## Results and Discussion.

### NMR Section.

The structural elucidation of compound **4** was carried out by  $^1\text{H}$  and  $^{13}\text{C}$  nmr spectroscopy. On the basis of previous analytical and spectroscopic data two potential structures, **4** and **5**, are possible.

The 300  $^1\text{H}$  nmr spectrum of **4** in deuteriochloroform showed the presence of five resonances; a singlet due to the OMe moiety and two AB spin-systems corresponding to four aromatic protons (H-2, H-3 and H-8, H-9, see Table 1).

The 75 MHz proton decoupled  $^{13}\text{C}$  nmr spectrum showed nine resonances; one methyl carbon at 56.1 ppm assigned to the OMe moiety, four methine aromatic carbons at 140.7, 132.7, 109.0 and 105.0 ppm, and four quaternary aromatic carbons at 156.4, 147.2, 143.4 and 100.2 ppm.

In order to assign the protonated carbons a proton-detected heteronuclear multiple quantum correlation (HMQC) spectrum was performed. HMQC [2] provides a heteronuclear correlation spectrum *via* proton detection. The spectrum obtained shows correlations from a proton to the directly bonded carbon. Thus, for the first AB spin system, the proton at 7.57 ppm is bonded to the carbon at 109.0 ppm and the proton at 7.47 ppm is bonded to the carbon at 132.7 ppm. The resonance at 132.7 ppm could

be assigned to a  $\text{sp}^2$  carbon linked to nitrogen (C2). For the second AB spin system, the proton at 7.08 ppm is bonded to the carbon at 105.0 ppm and the proton at 7.48 ppm is bonded to the carbon at 140.7 ppm. The resonance at 140.7 ppm could be assigned to a  $\text{sp}^2$  carbon linked to oxygen (C8).

The remaining quaternary carbons were assigned using the long-range proton-detected heteronuclear correlation experiment (HMBC) [2]. This technique produces a spectrum that shows correlation from proton to carbon atoms which are two or three bonds away. Thus, the proton at 7.47 ppm showed correlations to de carbons at 109.0 ppm and 143.4 ppm, the proton at 7.57 ppm showed correlations to the carbons at 132.7 ppm and 143.4 ppm, the proton at 7.08 ppm showed correlations to the carbons at 100.2, 140.7 and 156.4 ppm and finally the proton at 7.48 ppm showed correlations to the carbons at 100.2 and 105.0 ppm.

On the basis of these results we can establish the structure of the unknown compound. Thus, the existence of a correlation signal for the proton at 7.48 ppm with the carbon at 100.2 ppm, which is the only  $\text{sp}^2$  carbon not bonded to electronegative atoms, is only possible for structure of compound **4**. Table 2 shows the assignment of this spectrum.

Table 2  
 $^{13}\text{C}$  NMR Chemical Shifts (ppm) for Compound **4**

C5	147.2
C9b	143.4
C2	132.7
C3	109.0
C9a	100.2
C6a	156.4
C9	105.0
C8	140.7
OMe	56.1

Table 1

$^1\text{H}$  NMR Chemical Shifts (ppm) and Coupling Constants (Hz) for Compound **4**

H3	7.57
H2	7.47
H9	7.08
H8	7.48
OMe	4.24
$J(\text{H}3, \text{H}2)$	1.64
$J(\text{H}9, \text{H}8)$	2.34

The experimental values of one bond  $^1\text{H}$ - $^{13}\text{C}$  coupling constants obtained from the proton coupled spectra confirm these results (see Table 3). Comparison of one bond experimental coupling constants with the corresponding values for oxazole [3] and pyrrole [3] for compound **5** and furan [3] and imidazole [3] for compound **4** shows a good agreement with the last one.

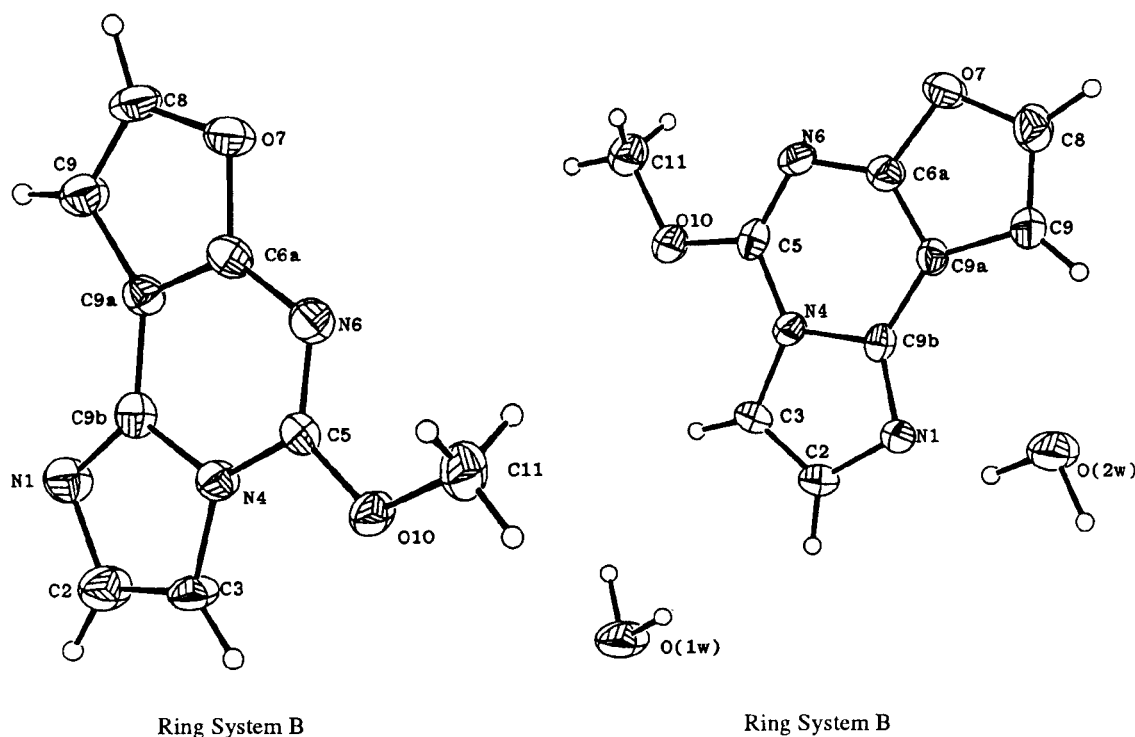


Figure 1: Asymmetric Unit.

Table 3

 $^1\text{H}$ - $^{13}\text{C}$  Coupling Constants (Hz) for Compound 4

$\delta$ $^{13}\text{C}$ (ppm)	$^n\text{J}(\text{C}-\text{H}_2)$	$^n\text{J}(\text{C}-\text{H}_3)$	$^n\text{J}(\text{C}-\text{H}_9)$	$^n\text{J}(\text{C}-\text{H}_8)$
100.2			6.2	3
105.0			180.9	13.1
109.0	16.6	198.6		
132.7	189.9	10.2		
140.7			10.0	206.7
143.4	11.0	5.1		
147.2				
156.4			5.0	

Table 4

Coordinates for Non-Hydrogen Atoms with e.s.d.'s in Parentheses.

$$U_{eq} = (1/3) \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$$

Atom	x/a	y/b	z/c	$U_{eq}(\text{\AA}^2 \times 10^2)$
OW1	0.2500(0)	0.3971(4)	0.2500(0)	7.2(5)
OW2	0.7500(0)	0.7442(5)	0.2500(0)	6.9(4)

System A

N1	0.4626(5)	0.6801(4)	0.1438(4)	3.8(3)
C2	0.3655(7)	0.6052(5)	0.1357(5)	3.6(3)
C3	0.2346(7)	0.6396(4)	0.1218(5)	3.5(3)
N4	0.2473(5)	0.7416(4)	0.1222(3)	3.1(3)
C5	0.1487(6)	0.8156(5)	0.1118(4)	3.4(3)
N6	0.1745(6)	0.9087(4)	0.1093(4)	3.8(3)
C6a	0.3133(7)	0.9265(5)	0.1208(5)	3.8(3)

Table 4 (continued)

O7	0.3547(5)	1.0234(3)	0.1161(3)	4.5(3)
C8	0.4977(8)	1.0172(5)	0.1275(6)	4.8(4)
C9	0.5420(6)	0.9241(5)	0.1389(5)	4.0(3)
C9a	0.4223(6)	0.8644(4)	0.1327(5)	3.2(3)
C9b	0.3889(6)	0.7628(5)	0.1341(4)	3.0(3)
O10	0.0205(4)	0.7792(3)	0.1018(3)	4.4(3)
C11	-0.0905(7)	0.8509(5)	0.0896(5)	4.8(4)
System B				
N1	0.0373(6)	0.5365(4)	0.8566(4)	4.2(3)
C2	0.1334(8)	0.4595(5)	0.8671(6)	4.9(4)
C3	0.2628(7)	0.4929(4)	0.8801(5)	3.8(3)
N4	0.2533(5)	0.5958(3)	0.8764(4)	3.4(3)
C5	0.3556(7)	0.6662(5)	0.8891(4)	3.3(3)
N6	0.3288(5)	0.7606(4)	0.8841(4)	3.6(3)
C6a	0.1914(7)	0.7836(5)	0.8689(5)	3.4(3)
O7	0.1499(5)	0.8790(3)	0.8647(3)	4.0(2)
C8	0.0049(7)	0.8751(5)	0.8504(6)	4.3(4)
C9	-0.0415(7)	0.7823(5)	0.8442(5)	4.1(3)
C9a	0.0801(7)	0.7208(4)	0.8566(4)	3.1(3)
C9b	0.1114(7)	0.6178(5)	0.8612(5)	3.4(3)
O10	0.4829(4)	0.6294(3)	0.9043(3)	4.0(2)
C11	0.5962(7)	0.6993(5)	0.9245(5)	4.9(4)

## X-Ray Section

The titled compound of formulae  $\text{C}_9\text{H}_7\text{N}_3\text{O}_2 \cdot 1/2\text{H}_2\text{O}$  consists of three fused furan-imidazole-pyrimidine rings, with two of these molecules in the asymmetric unit (A and B), together with two molecules of water of crystal-

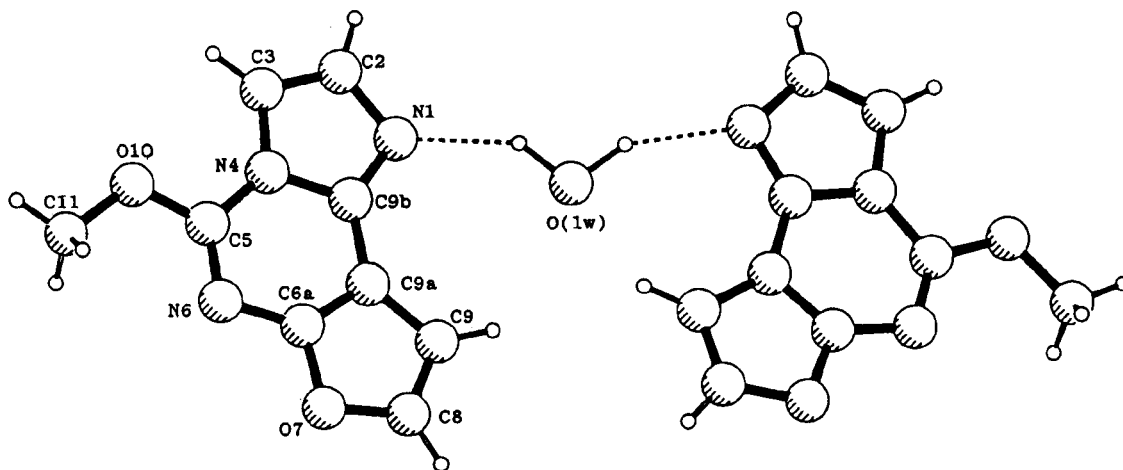


Figure 2: Hydrogen bonding of dimeric units (Molecule A).

Molecule A bonds to Molecule A via  $O(2w) N1 \cdots O(2w)$  2.948(6)Å.

Molecule B bonds to Molecule B via  $O(1w) N1 \cdots O(1w)$  2.938(6)Å.

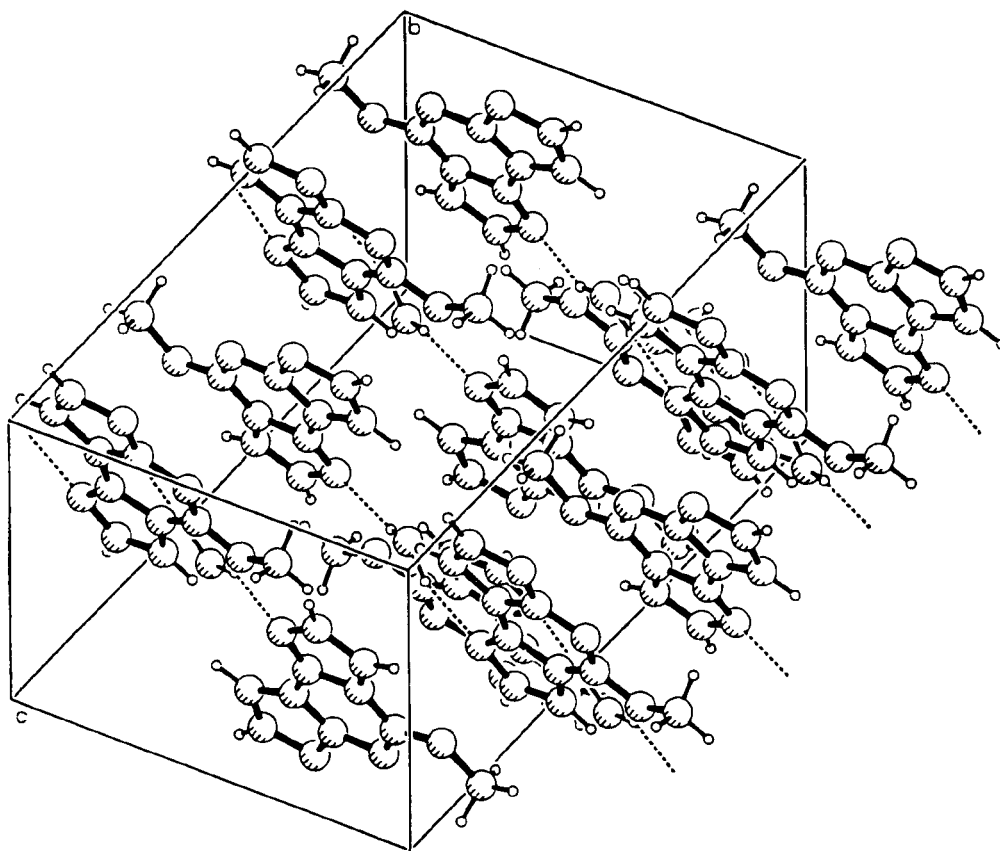


Figure 3. Packing of molecules in the unit cell.

Table 5

Bond Lengths (Å) and Angles (°) with e.s.d.'s in Parentheses

System A		System B	
N1-C2	1.383(8)	N1-C2	1.394(9)
N1-C9b	1.323(8)	N1-C9b	1.315(8)
C2-C3	1.346(10)	C2-C3	1.328(10)
C3-N4	1.385(8)	C3-N4	1.395(7)
N4-C5	1.381(8)	N4-C5	1.369(8)
N4-C9b	1.403(8)	N4-C9b	1.399(8)
C5-N6	1.288(9)	C5-N6	1.302(8)
C5-O10	1.339(7)	C5-O10	1.321(8)
N6-C6	1.368(9)	N6-C6	1.359(9)
C6-O7	1.382(8)	C6-O7	1.352(8)
C6-C9a	1.345(9)	C6-C9a	1.367(9)
O7-C8	1.391(9)	O7-C8	1.401(9)
C8-C9	1.328(10)	C8-C9	1.331(9)
C9-C9a	1.423(8)	C9-C9a	1.439(9)
C9a-C9b	1.415(9)	C9a-C9b	1.425(9)
O10-C11	1.443(8)	O10-C11	1.435(8)
C2-N1-C9a	104.9(5)	C2-N1-C9b	105.1(6)
N1-C2-C3	112.6(6)	N1-C2-C3	111.7(6)
C2-C3-N4	105.1(6)	C2-C3-N4	106.4(6)
C3-N4-C5	131.4(5)	C3-N4-C5	130.5(5)
C3-N4-C9b	107.0(5)	C3-N4-C9b	105.8(5)
C5-N4-C9b	121.6(5)	C5-N4-C9b	123.6(5)
N4-C5-N6	124.8(5)	N4-C5-N6	122.8(6)
N4-C5-O10	111.9(6)	N4-C5-O10	113.8(5)
N6-C5-O10	123.3(6)	N6-C5-O10	123.4(6)
C5-N6-C6	111.9(5)	C5-N6-C6	114.4(6)
N6-C6-O7	117.9(6)	N6-C6-O7	120.4(6)
N6-C6-C9a	131.2(6)	N6-C6-C9a	128.4(6)
O7-C6-C9a	110.9(6)	O7-C6-C9a	111.1(6)
C6-O7-C8	104.4(5)	C6-O7-C8	105.0(5)
O7-C8-C9	111.4(6)	O7-C8-C9	111.7(5)
C8-C9-C9a	106.7(6)	C8-C9-C9a	105.8(6)
C6-C9a-C9	106.6(5)	C6-C9a-C9	106.3(5)
C6-C9a-C9b	115.0(5)	C6-C9a-C9b	116.3(6)
C9-C9a-C9b	138.3(6)	C9-C9a-C9b	137.4(6)
N1-C9b-N4	110.4(5)	N1-C9b-N4	111.0(6)
N1-C9b-C9a	134.1(6)	N1-C9b-C9a	134.6(6)
N4-C9b-C9a	115.5(5)	N4-C9b-C9a	114.4(5)
C5-O10-C11	116.1(5)	C5-O10-C11	116.5(5)

lization, which are on a symmetry plane. A perspective view of the asymmetric unit, including labelling scheme, is shown in Figure 1 [4], while relevant bond lengths and angles are listed in Table 5. Both molecules in the asymmetric unit differ slightly in their structures. The data in Table 5 indicate a large charge delocalization, which is also highlighted by the planarity of both molecules. The maximum deviations from the mean plane are 0.046(6) Å and -0.022(8) Å for C(9a) in A and C(9b) in B, respectively. Each of the three fused rings are almost planar in both molecules, the higher deviations corresponding to molecule A.

Significant hydrogen bond lengths and angles are presented in Table 7. Each of the water molecules links two A or B molecules, by two symmetric hydrogen bonds, through the N atoms of the imidazole rings. This is a consequence of the fact that both water molecules lie on a

symmetry plane. The hydrogen bonding of the dimeric units is shown in Figure 2 [5]

It should be noted that these hydrogen bonding units are almost parallel to the *ab* plane, giving a stacking along the *c* axis, within the tridimensional packing the shortest contact distances between parallel units, N(4)...C(2)<sup>iv</sup>, 3.460 Å (*iv* = -*x*, -*y*, 1-*z*) and N(4)...N(4)<sup>v</sup>, 3.557 Å (*v* = -1/2 +*x*, -*y*, 1/2 +*z*), could suggest the existence of  $\pi$  cloud interactions, as is shown in Figure 3 [5].

Table 6

Angles (°) Formed by the Three Fused Rings in A and B Molecules

Angle	Molecule A	Molecule B
Imidazole/Pyrimidine	1.5°	1.5°
Furan/Pyrimidine	1.9°	3.6°
Furan/Imidazole	1.2°	2.1°

Table 7

Hydrogen bond lengths and angles

Atoms	Bonds lengths (Å)	Atoms	Angle (°)
O(1w)-N(1) [i]	2.948	N(1) [i]-O(1w)-N(1b) [ii]	144.6
O(1w)-N(1) [ii]	2.948	N(1) [i]-O(2w)-N(1b) [iii]	145.7
O(2w)-N(1)	2.938		
O(2w)-N(1) [iii]	2.938		

Equivalent position; [i] = -*x*, 1-*y*, 1-*z*; [ii] = 1/2-*x*, 1-*y*, -1/2+*z*; [iii] = 1/2-*x* 1+*y*, 1/2+*z*.

## EXPERIMENTAL

### NMR Study.

The <sup>1</sup>H and <sup>13</sup>C nmr spectra were carried out on a Varian XL-300 spectrometer operating at 300 MHz and 75 MHz respectively, using deuteriochloroform as the solvent at 30°. Proton spectra were obtained using the following conditions: pulse angle, 77°; acquisition time, 4s; sweep width 4000 Hz and data size, 32 K. Proton-decoupled <sup>13</sup>C nmr spectra were obtained with WALTZ decoupling using the following conditions: pulse angle, 53°; acquisition time, 0.7 s; sweep width, 12000 Hz and data size, 32 K. The proton coupled spectrum was obtained under the same conditions using a relaxation delay of 3 s and the gated decoupling technique. The HMQC experiments were carried out in a Varian Unity 500 operating at 499.843 MHz. The following conditions were used: <sup>1</sup>J(C-H) = 190 Hz; spectral width in <sup>13</sup>C dimension, 15117.2 Hz; spectral width in <sup>1</sup>H dimension, 310.1 Hz; number of experiments, 128; and 512 x 256 points for the data table. The HMBC experiments were carried out under the same conditions and optimized for long-range constants of 5 Hz.

### X-ray Collection and Structure Determination.

The intensity data for a crystal with 0.14 x 0.40 x 0.40 mm were measured at room temperature on a Nicolet P3 diffractometer with MoK $\alpha$  radiation,  $\lambda$  = 0.71069 Å, using the  $\omega$  scan mode. The unit cell parameters were calculated by least-squares refinement of 14 reflections in the  $2\theta$  range 17-20°. The data were collected in the range 0 < 2 $\theta$  < 49.9°. A total of 1263

reflections (with 263 parameters) were considered as observed with  $I > 3\sigma(I_0)$ . No correction was made for absorption. The structure was determined by direct methods using the NRCVAX program [6]. In the final refinements, all non hydrogen atoms were refined anisotropically whereas hydrogen atoms were isotropically refined. Neutral atomic scattering [7] and dispersion factors were included in the program package. The calculation results in a final  $R_F = \Sigma(F_o - F_c) / \Sigma(F_o)$  of 0.054 and a  $R_w = [(\Sigma w(F_o - F_c)^2) / \Sigma(wF_o^2)]^{1/2}$  value of 0.069. Atomic coordinates are given in Table 4.

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