

NMR Characterization of Pyribenzoxim

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Pyribenzoxim was developed as a new herbicide by the LG Chemical Ltd. Korea in 1996. This pyrimidinyl-oxybenzoate was known to inhibit acetolactate synthase (ALS), the enzyme involved in the biosynthesis of the branched chain amino acids in plants.¹⁾ No significant adverse effects were reported in toxicology studies²⁾ and a high herbicidal selectivity was observed to control barnyard grass without damages to rice plants.³⁻⁵⁾

This study was carried out to investigate the structure of pyribenzoxim in detail. NMR spectra were obtained on a Bruker ARX 600 instrument in CDCl₃. For the ¹H-NMR experiments, 32 transients were acquired with a 1s relaxation delay using 32 K data points, and the 90 pulse was 12.8 μs, with spectral width of 8,680 Hz. For the ¹³C-NMR and DEPT experiments, 1024 transients were acquired with a 2s relaxation delay using 64 K data points, and the 90 pulse was 7.5 μs with spectral width of 37,594 Hz. Since 1D experiments alone cannot give complete information on chemical shifts, 2D NMR experiments such as COSY, HMQC, and HMBC were carried out. Two-dimensional spectra were acquired with 2048 data points in t₂ and 256 in t₁ increments. The COSY spectrum was collected using the magnitude method.⁶⁾ HMQC and HMBC spectra were collected using the methods as described by Bax.^{7,8)} And phase sensitive NOESY spectrum was measured using a 1.5s mixing time. In order to know the distance in the molecule with low energy state, Computer Aided Molecular Modeling was introduced here. In this study, all computational calculations were performed using Biosym/MSI software (San Diego, CA) on a Silicon Graphics INDY R4400 workstation. The distance was calculated with the discover module of InsightII.

The ¹³C peak at 54.14 ppm should be methoxy groups based on the multiplicity obtained from DEPT, and the chemical shift and the intensity of the ¹H peak. The expected

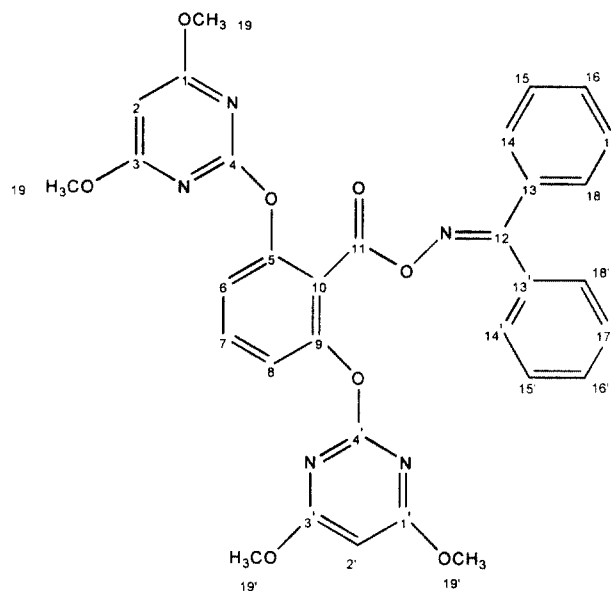


Fig. 1. The structure of the compound.

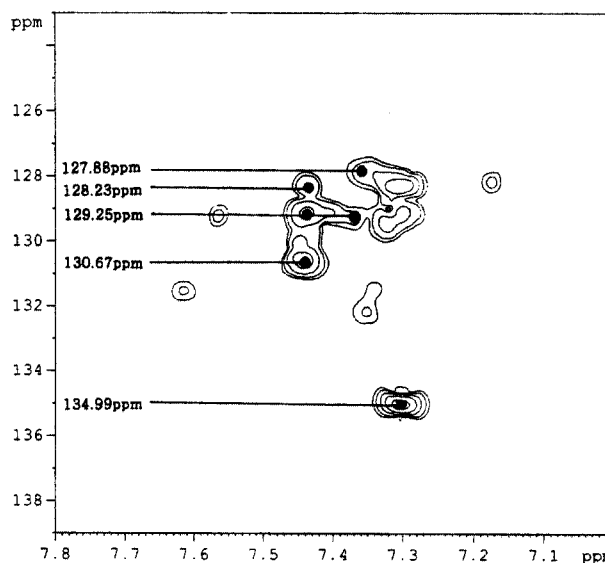


Fig. 2. The HMBC spectrum of the compound.

structure shown in Fig. 1 includes several methine carbons, but only one can be positioned at 85.09 ppm in the ¹³C spectrum, which is C2 or C2'. Since the molecular tumbling rate in chloroform solution at room temperature is too fast to distinguish between C2 and C2', only one peak is given. Eight ¹³C peaks between 120 and 132 ppm belong to methane carbons of benzene rings due to their ¹³C chemical shifts as well as the correlated ¹H chemical shifts. Based on the HMBC spectrum (Fig. 2), C6/C8 and C10 can be assigned because the ¹³C peak of C10 is long ranged coupled with the ¹H peaks of H6/H8 and H7. Comparing the intensity of the peak at 131.52 ppm with that at 120.20 ppm, the former is C7. Even though the peak at 172.75 ppm is

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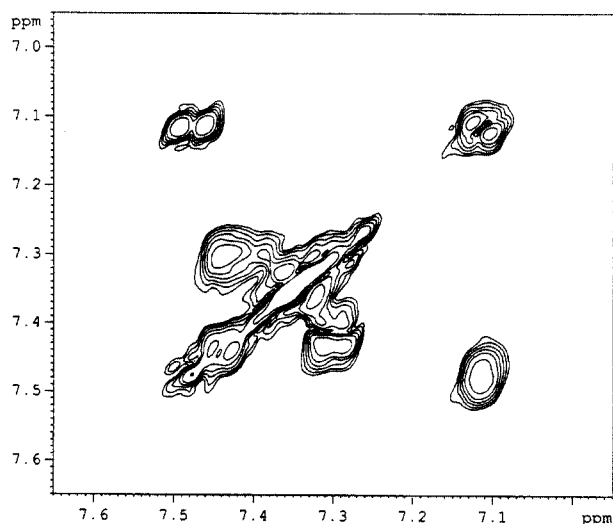


Fig. 3. The COSY spectrum of the compound.

singlet, its intensity is much higher than the others. In addition, the peak is long-ranged coupled to methoxy group in HMBC. Therefore, the peak can be assigned as C1/C1'/C3/C3'. C4/C4' and C11 do not have neighbor protons. Since the peaks at 161.15 and 163.75 ppm are not long-ranged coupled in HMBC, those can be caused by C11 or C4/C4'. The former can be assigned to C11 because it is connected to only two oxygens, while C4/C4' is connected to one oxygen and two nitrogens. The peak at 164.43 ppm is assigned to C12 based on the long-ranged coupling to H14/H14' and H18/H18' which are determined through COSY (Fig. 3). The peak at 151.70 ppm is assigned to C5/C9 because it is long-ranged coupled to H6/H8 and H7. Among the peaks caused by benzene rings, as only the peaks at 132.18 and

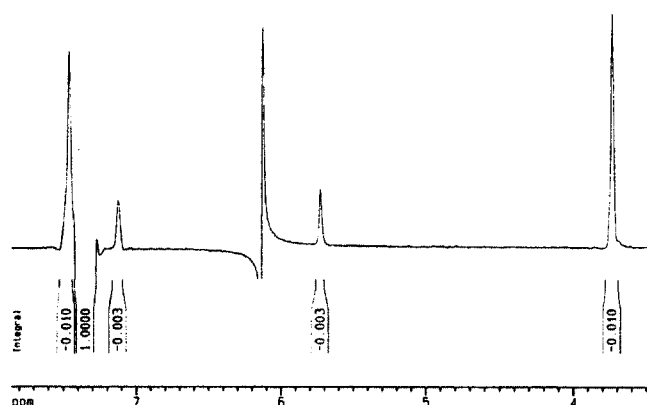


Fig. 4. 1D slice of NOESY at 7.34 ppm.

134.99 ppm are singlet, they can be assigned to C13/C13'. Six doublet peaks can also be assigned based on the COSY experiment. The assignments obtained from the NMR experiments are listed in Table 1.

Since the three dimensional study of the compound may help one to understand its metabolic mechanism, the result is reported here. Even though 2D NOESY spectrum was obtained, 1D slice at 7.34 ppm was selected for the clear observation.

As shown in Fig. 4, the saturation of the peak at 7.34 ppm gave 1% nOe of the peak at 3.80 ppm and 0.3% nOe at 5.75 ppm. This observation results from an approach of H14 to methoxy group and H2. Of course, in our experiments, H14, H14', H18 and H18' are not discriminated so that the approach of H14 mentioned above can take the places of those. In order to clarify this result, the three dimensional structure was calculated using Computer Aided Molecular Modeling (CAMM). As shown in Fig. 5, the refined

Table 1. The NMR assignments of the pyribenzoxim.

δ ^{13}C	multiplicities	δ ^1H	HMBC	COSY	Assignment
54.14	q	3.80(s)	-		C19,C19
85.09	d	5.75(s)	-		C2,C2
119.74	s	-	H6,H8/C10 H7/C10		C10
120.20	d	7.12(d, J = 8.24 Hz)	-	H7/H6,H8	C6,C8
127.88	d	7.35(m)	H16,H16/C15,C17 or C15,C17		C15,C17 or C15,C17
128.23	d	7.31(m)	H14,H18, or H14,H18/C15,C17 or C15,C17 H16,H16/C15,C17 or C15,C17		
129.12	d	7.43(m)	H17,H15 or H17,H15/C14,C18 or C14,C18		C14,C18 or C14,C18
129.25	d	7.34(m)	H17,H15 or H17,H15/C14,C18 or C14,C18		
129.50	d	7.36(m)	H14,H18 or H14,H18/C16 or C16		C16 or C16
130.67	d	7.40(m)	H14,H18 or H14,H18/C16 or C16		
131.52	d	7.48(t, J = 8.24, 8.24 Hz)	-	H6,H8/H7	C7
132.18	s	-	H15,H17 or H15,H17/C13 or C13		C13 or C13
134.99	s	-	H15,H17 or H15,H17/C13 or C13		
151.70	s	-	H6,H8/C5,C9 H7/C5,C9		C5,C9
161.15	s	-	-		C11
163.75	s	-	-		C4,C4
164.43	s	-	H14,H18 or H14,H18/C12		C12
172.75	s	-	H19/C1,C1,C3,C3		C1, C1, C3, C3



Fig. 5. The superimposed structures obtained from CAMM.

structures give the distances of 2.36 and 3.25 for H14 and methoxy group and H2, respectively. That is, nOe among H14, methoxy group and H2 should be observed. As a result, the calculated structures agree with the interpretation of NOESY.

Consequently, the three dimensional structure of pyribenzoxim shows that two 4,6-methoxyprimidine groups cover benzophenone imine group like arms.

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