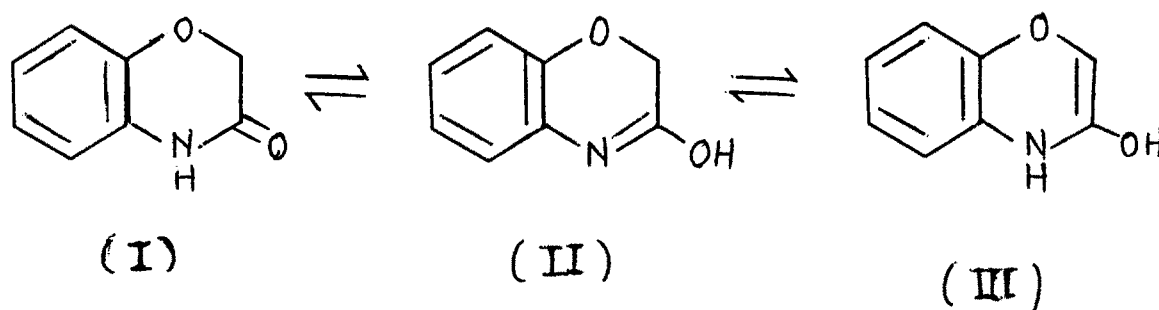


CHAPTER FOUR

SPECTRAL STUDIES AND CONCLUSIONS

STRUCTURAL STUDIES AND CONCLUSIONS

Earlier studies on UV, IR and NMR of the compound 3,4-dihydro-2H-1,4-benzoxazin-3-one have revealed that the compound exists in three different potential lactim-lactam tautomers, where a mobile hydrogen atom can wander from the ring-N to the adjacent hetero atom like oxygen or "keto-enol tautomers" I to III.



Out of these three tautomers the predominant tautomer 'I' became evident from the study of their UV, IR and NMR spectra.

UV-Spectra

The UV spectral data of 3-oxo and substituted-1,4-benzoxazine exhibit an absorption pattern very

similar to that of compound I [λ_{\max} 256.4 nm].
Similarly 2-methyl, N-methyl and 2,4-dimethyl-2H-1,4-benzoxazin-3-one show the UV absorption in 95% ethanol with λ_{\max} 254.6 nm, 256.4 nm and 254.5 nm respectively.

IR-Spectra

Sullivan and Sadler* studied the IR of 3,4-dihydro-2H-1,4-benzoxazin-3-one (Compound I) in solid and solution states. Based on the carbonyl absorption in the 1700 Cm^{-1} region and NH-absorption around 3200 Cm^{-1} in solid state and 3400 Cm^{-1} in solution supported the lactam structure.

NMR Spectra

The NMR spectra are useful to confirm the structure and also to establish the predominant

*D.G. O'sullivan and P.W. Sadler, J. Chem. Soc., 2916 (1957).

tautomer in the potentially tautomeric systems.

C₂-methylene Protons

The presence of a sharp singlet in the region 4.5-5.0, δ (ppm) fixes the C₂-methylene protons and eliminates the possibility of methylene hydrogen atom participating in 'keto-enol' tautomerism. The noninvolvement of C₂-methylene proton in enolization is proved by taking NMR spectra of 2-methyl-3,4-dihydro-2H-1,4-benzoxazin-3-one. If the hydrogen atom at C₂ is involved in tautomerism a singlet should appear for C₂-Me group in above compound and the mobile C₂-proton should give a peak in the 'OH' region; however in this compound the pattern observed is a doublet for C₂-Me and a quartet for C₂-proton, thereby cancelling out the possibility of enolic structures for oxo-compounds.

Aromatic Pattern

The four aromatic protons of 3,4-dihydro-2H-1,4-benzoxazin-3-one appear invariably as a singlet

around 7.0, δ (ppm) indicating that the four aromatic protons in the respective compounds are magnetically equivalent.

Spectral Studies of 6-chloro-3,4-dihydro-2H-1,4-benzoxazin-3-one [Compound II in Scheme 1]

IR: (In KBr)

The IR absorption of 6-chloro-3,4-dihydro-2H-1,4-benzoxazin-3-one in a solid state shows a carbonyl absorption in the 1695 cm^{-1} region and -NH- absorption around 3200 cm^{-1} , indicating the lactam structure. A broad band at 1600 cm^{-1} indicates phenyl-ring in the compound. Peak at 2900 cm^{-1} indicates methylene C-H stretching frequency.

NMR [Fig. 1]

The NMR spectrum was recorded in acetone as a solvent and TMS as an internal reference.

C₂-Methylene Protons

The presence of sharp singlet integrating to two protons in the region 4.5-5.0, δ (ppm) indicates the structure of the Compound-II as shown in

Scheme I and fixes the C₂-methylene protons and eliminates the possibility of methylene protons participating in the 'keto-enol tautomerism'.

Aromatic Pattern

The three aromatic protons are not magnetically equivalent as they are not appearing as singlet around 7.0, δ (ppm). A 'doublet' appeared at 7.25, δ (ppm) with $J = 9.0$ Hz indicates the ortho-coupling of C₈-proton which is highly shielded due to the presence of oxygen at position 1 in the benzoxazin ring. The C₇-proton splits as a 'doublet-doublet' with $J_{ortho} = 9.0$ Hz. due to ortho-coupling with C₈-proton and $J_{meta} = 2.0$ Hz due to meta-coupling with C₅-proton. The doublet at 7.6, δ (ppm) with $J = 2.0$ Hz corresponds to C₅-proton which is meta-coupled with C₇-proton.

A secondary imido proton appeared as a 'broad singlet' integrating to one proton in the region 7-8.9, δ (ppm) corresponding to the -NH- proton of -CONH-group. This establishes the structure

assigned to the Compound II in Scheme I.

6-chloro-4 (Carbethoxy)-3,4-dihydro-2H-1,4-
benzoxazin-3-one [Compound III in Scheme I]

NMR: [In CCl_4] [Fig. 2]

The presence of a 'triplet' integrating to three protons in the region 1.2-1.4, δ (ppm) indicates methyl-protons of an ester. The observed splitting pattern is due to adjacent methylene protons. A 'Quartet' is encountered between 4.1-4.3, δ (ppm) integrating to two protons of methylene group of an ethyl ester. A sharp singlet corresponding to two protons observed at 4.6 δ (ppm) indicates the presence of methylene protons of $-\text{OCH}_2$ -group. This peak appeared at down field region due to the presence of vicinal electronegative oxygen atom. A 'doublet' is observed between 6.7-6.8, δ (ppm) with $J = 8.0$ Hz indicating the ortho-coupling of C_8 -proton with C_7 -proton. Two 'doublets' appeared between 7.05-7.15, δ (ppm) with $J_{\text{ortho}} = 8.0$ Hz and $J_{\text{meta}} = 3.0$ Hz indicating the presence of C_7 -proton ortho-coupled with C_8 -proton and meta-coupled with

C₅-proton in the benzoxazine-ring. A 'doublet' with $J_{\text{meta}} = 3.0$ Hz appeared at 7.35, δ (ppm) proved the presence of C₅-proton meta coupled with C₇-proton. This NMR study proves the structure assigned to the Compound III in Scheme I.

5-chloro-4(hydrazido)-3,4-dihydro-2H-1,4-benzoxazin-3-one [Compound IV in Scheme I]

UV: [Fig. 3]

The UV spectrum was recorded in 95% ethanol. The observed λ_{max} 285 nm of this compound indicates the presence of a chromophoric group which shifts absorption maxima towards longer wavelength as the λ_{max} recorded for the Compound II is 256 nm.



[R = 6-chloro-4(N-substituted)-3,4-dihydro-2H-1,4-benzoxazin-3-one]

IR: (In KBr): [Fig. 4]

A doublet is observed at 3280 Cm^{-1} indicating the presence of NH-NH_2 group in the compound. The presence of a peak at 2880 Cm^{-1} indicates methylene C-H stretching frequency. The peak at 1695 Cm^{-1} indicates the presence of δ -lactam ketone. A peak at 1595 Cm^{-1} - 1600 Cm^{-1} indicates the presence of phenyl-ring in the compound.

NMR: (In CHCl₃) [Fig. 5]

The 'singlet' at 2.1, δ (ppm) indicates the possibility of non-hydrogen bonded $-\text{NH}_2$ group. A 'singlet' observed at 4.52, δ (ppm) indicates the presence of methylene protons of ' O-CH_2 ' group. The aromatic pattern is not indicated, as the spectrum was recorded in CHCl_3 solvent and TMS as an internal reference.

6-chloro-4(nicotinoyl hydrazido)-3,4-dihydro-
2H-1,4-benzoxazin-3-one [Compound V in
Scheme II]

NMR: (In CDCl_3) [Fig. 6]

A singlet at 4.49, δ (ppm) integrating to two protons corresponds to two protons of $-\text{OCH}_2$ group. The 'multiplet' observed between 6.7-7.2, δ (ppm) corresponding to five protons which is in good agreement with the integrated values. A 'multiplet' between 7.7-7.85, δ (ppm) integrated to two protons of pyridine-ring in the compound, which appeared at down field region due to the presence of adjacent nitrogen atom. A sharp signal is observed at 7.2, δ (ppm) probably due to the presence of traces of impurity in CDCl_3 solvent.

6-chloro-4(5'-phenyl-1',3',4'-oxadiazolyl)-
3,4-dihydro-2H-1,4-benzoxazin-3-one:
[Compound VI in Scheme II]

NMR: [Fig. 7]

The NMR spectrum of this compound was recorded

using acetone as a solvent and TMS as an internal reference.

The singlet observed at 4.5, δ (ppm) integrating to two protons indicates the presence of two protons of $-\text{OCH}_2$ group. A 'multiplet' observed between 7.85-8.1, δ (ppm) corresponds to five aromatic protons. A 'multiplet' observed between 8.55-8.7, δ (ppm) integrating to three protons corresponds to C_5 -proton and two ortho protons of phenyl-ring attached at 5'-position of oxadiazole moiety in the Compound VI, which appeared at down field region in NMR.

Conclusions

Thus, the structures of all these compounds were established by elemental analysis and spectral evidences mainly by NMR. All the compounds were obtained in good yields.

The pharmacological functionality of all these derivatives is evident from their nitrogen content. However none of these compounds was tested for its biological activities due to time limitation.