Synthesis, Characterization and Study of Biological Activity of Some New Nitrone, Isoxazolidine and Schiff bases Compounds Derived from Nitrofuran

A thesis

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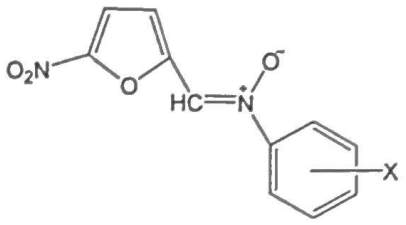
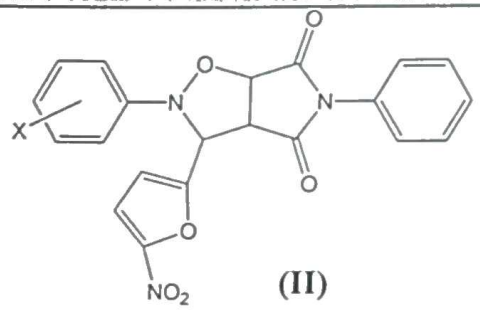
SUMMARY

This study is concerned with the synthesis of three series of new compounds of nitrofuran derivatives. The first series (I), included six of nitrone compounds sythesized from the reaction of 5-nitrofurfural with N-aryl hydroxylamines. The second series (II), is concerned with the synthesis of isoxazolidine compounds by 1,3-dipolar cycloaddition reactions of nitrones with the N-phenylmaleimide. The third series (III) is Schiff bases which were synthesized by the reaction of 5-nitrofurfural with aniline derivatives.



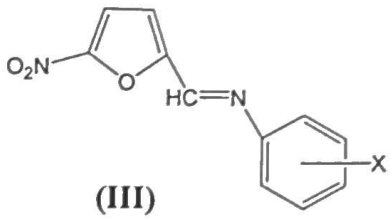
(I)

X=H(N1), p-Br(N2), p-Cl(N3), o-Cl(N4)
m-Me(N5) and o-OMe(N6)



(II)

X=H(I1), p-Br(I2), p-Cl(I3), 0-Cl(I4)
m-Me(I5) and o-OMe(I6)



(III)

X=H(S1), p-Br(S2), p-Cl(S3), o-Cl(S4)
and m-Me(S5)

The synthesized compounds were characterized by using elemental analysis, UV-visible spectroscopy, FT-IR spectroscopy, ^{1}H-NMR spectroscopy and mass spectroscopy.

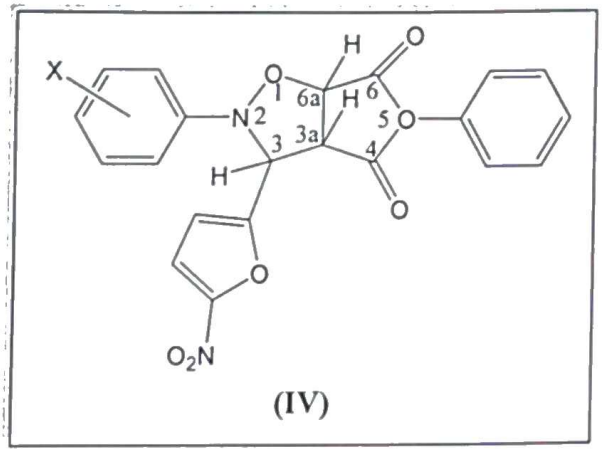
The results of CHN are in a good agreement with the calculated values which indicate that the synthesized compounds are as expected.

UV-visible spectra of nitrones and Schiff bases, showed distinguished absorption bands within the regions (375-390 nm) and (354-365 nm) which attributed to the $\pi \rightarrow \pi^*$ transitions of nitrone and azomethine groups, respectively. On the other hand, the absorption spectra of isoxazolidines showed a disappearance of the absorption band related to nitrone group with the appearance of only two absorption bands which attributed to the electronic transitions $\pi \rightarrow \pi^*$ of aromatic system which confirmed the formation of isoxazloidines.

The IR spectra of nitrones showed two absorption bands in the ranges (1136-1163 cm^{-1}) and (1500-1609 cm^{-1}) which assigned to stretching vibrations of N→O and C=N groups, respectively. The IR spectra of isoxazolidines showed new absorption bands at (1014-1388 cm^{-1}) assigned to isoxazolidine ring in addition to a very strong absorption band at (1718-1727 cm^{-1}) which attributed to the carbonyl group. On the other hand, IR spectra of Schiff bases showed an absorption band in the range (1614-1624 cm^{-1}) related to the C=N group.

The ^{1}H-NMR spectra of nitrones and Schiff bases showed singlet signal in the regions (8.612-9.140 ppm) and (8.605-8.672 ppm), respectively, which attributed to the proton H-α. Protons of the furan ring (H-1′ and H-2′) exhibited spin system type AB in the case of nitrones and spin system type AX in the case of Schiff bases. The spectra also showed that protons of the phenyl rings substituted in para- position exhibited spin systems type AA′XX′ and AA′BB′. The ^{1}H-NMR spectra of isoxazolidines (IV) showed that these compounds have only one type of geometrical form which is *anti-* isomer. The results showed that 1,3-dipolar cycloaddition is an *endo-* type according to the values of coupling constants and dihedral angles between the protons H-3 and H-3a and the protons H-3a and H-6a . Disappearance of the signal of proton H-α confirms the formation of isoxazolidine ring.

In this study, hyperchem 7.5 program was used to find the optimal geometrical forms of isoxazolidines by using PM3 method. This method included the calculation of the energies of HOMO and LUMO levels and the heat of formation of nitrones and isoxazolidines. Also, the angle between the protons H-3 and H-3a and between protons H-3a and H-6a was measured, the theoretical results were identical with the experimental results.



(IV)

Some selected compounds were characterized by mass spectra which indicated that the synthesized compounds were as expected.

The antibacterial activity of the synthesized compounds against Gram positive bacteria *Staphylococcus aureus* (ATCC 25923) and Gram negative *Escherichia coli* (ATCC 25922) showed that most synthesized compounds exhibited a good activity as compared with standard drugs. In nitrones series, compound N6 exhibited good activity against bacteria (*S. aureus*, 25 mm and *E. coli*, 18 mm) as compared with N4 which had lower activity (*S. aureus*, 9 mm and *E. coli*, 10 mm). For isoxazolidines, I5 compound showed good activity (*S. aureus*, 20mm and *E. coli*, 16 mm) as compared with I4 which had lower activity against bacteria (*S. aureus*, 15mm and *E.coli*, no inhibition). Schiff bases, showed very good activity as compared with standard drugs in which compound S5 exhibited higher activity (*S. aureus*, 42 mm and *E. coli*, 28 mm) as

compared with compound S2 (*S. aureus*, 15 mm and *E. coli*, 9 mm). These results showed that compounds substituted with electron-donating groups exhibited good antibacterial activity as compared with the other compounds. The results also showed that the synthesized compounds exhibited bacteriocidal activity and were not bacteriostatic compounds

The antifungal activity of the synthesized compounds against the opportunistic fungal isolate *Aspergillus niger* showed that most synthesized compounds had good activity as compared with standard drugs. Nitrones and Schiff bases exhibited good activity as compared with isoxazolidines in which compound N4 showed good activity (24 mm) in nitrone series and compound S4 had the higher activity (27 mm) among compounds in Schiff bases series. For isoxazolidines, compounds I2 had the higher activity (10 mm).

The results of LD_{50} showed that compounds N5, N6, S1, S4 and S5 are moderately toxic substances, while compounds I3 and I5 are non toxic in the range of graded doses.

The following tables show the name, symbol and structure of synthesized compounds in this study.