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Comparison and Bio-Chemical Study of (Imine, Oxazepam, Diazepam, Sulfide) - Derivatives on Microbial

Research Article

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Abstract: This work involves synthesis of (anil, oxazepin, diazepine)–compounds from p-N, N-dimethyl amino benzylideneareneamines (Schiff bases), Compounds $[N_2 - N_{17}]$ were synthesized by condensation of p-N, N-dimethylaminobenzaldehyde with different primary aromatic amines, which reacted with phthalic anhydride to produce other sixteen oxazepine compounds $[N_{34} - N_{49}]$, which reacted with various primary aromatic amines to produce five derivatives of diazepine compounds $[N_{35}, N_{38}, N_{41}, N_{46}, N_{48}]$, four compounds mercaptide compounds $[N_{55} - N_{58}]$. All compounds have been characterized by (FT.IR, C.H.N , some them by H.NMR and biological study).

Keywords: Comparison, sulfide , di ox , di aze

1. Introduction

The Pericyclic reactions involve bond changes in a circle of atoms. In Pericyclic reactions, bonds are made or broken in a concerted cyclic transition state (T.S). This means that there are no intermediates formed in the course of the reaction [1-13]. Pericyclic reactions represent an important class of concerted (single step) process involving pi-systems; a concert rearrangement of the electrons takes place which causes sigma and pi-bonds to simultaneously break and form, the fact that the reactions are concerted gives fine stereo chemical control of the product pericyclic reactivity can be understood in terms of frontier molecular orbital (FMO) theory, it can be predicted using the Woodward-Hoffman rules. Oxazepam and Diazepam (valium) are a class of drugs used as relaxants, minor tranquilizers, hypnotics and muscle relaxant because it is often seen in fortensic and clinical cases [4-13].

1.1. Experimental

- All chemicals used were supplied from Merck and BDH-chemical Company.
- All measurements were carried out by
- Melting points: Electrothermal 9300, melting point Engineering LTD,U.K

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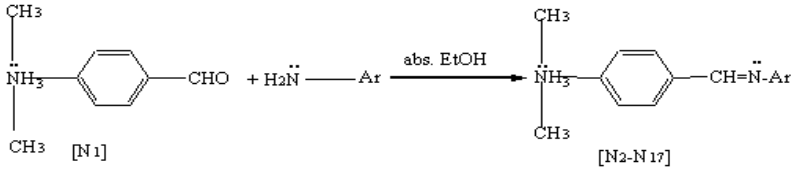
- FI-IR spectra: Fourier transform infrared shimadzu (8300) (FI-IR), Kbr disc was performed by Co. S. Q. Iraq.
- Elemental Analysis (C. H. N) , HNMR spectra
- Biological study in bio- Lab of biology department of science college.

2. Synthetic Methods

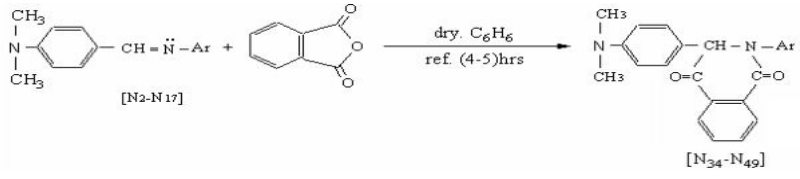
Synthesis of p-N, N-dimethyl amine benzylidenearene amino (Schiff's bases)[$N_2 - N_{17}$] General procedure [12, 13]. A mixture of equimolar amounts (0.05 mole , 6.30 ml) of p-N, N-dimethyl amino benzaldehyde [N_1] and primary aromatic amine dissolved in (50 ml) of absolute ethanol with some drops of acetic acid was refluxed for (3 hrs) . The reaction mixture was then allowed to cool to room temperature and solid product was filtered and recrystallized from ethanol to give colored crystals from compounds [$N_2 - N_{17}$].



Synthesis of 2-(p-N.N-dimethyl amino benzyl)-3-aryl-2,3-dihydrobenz[1,2-e] [1,3]-oxazepine-4-7 diones. (Oxazepine derivatives) [$N_{34} - N_{49}$].

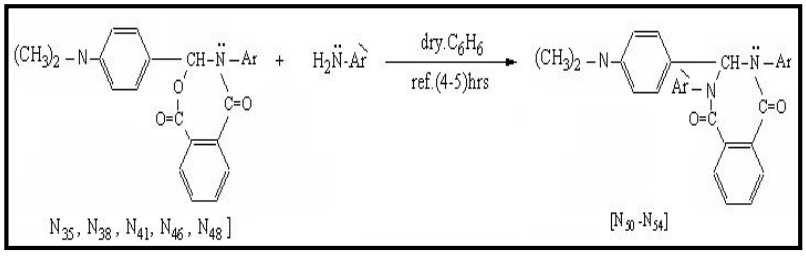
3. General procedure

A mixture of equimolar amounts (0.02 mole) of schiff's bases [$N_2 - N_{17}$] and phthalic anhydride in dry benzene was refluxed for (5-6 hrs), the solvent was removed and the resulting colored crystalline solid was recrystallized from dry 1, 4-dioxane to give the title products of compounds [$N_{34} - N_{49}$].



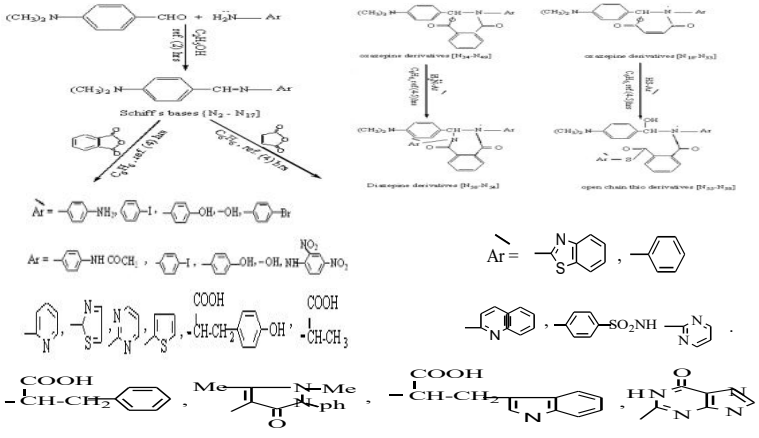
Synthesis of 1(aryl)-2-(p-N,Ndimethylaminobenzyl)-3-aryl1,2,3-trihydrobenzo[1,2-e][1,3]-diazepine-4,7-dionesDiazepine derivatives [$N_{50} - N_{54}$].

A mixture of equimolar amounts (0.02 mole)of oxazepine derivatives $[N_{35}, N_{38}, N_{41}, N_{46}, N_{48}]$ with selected primary aromatic amines in (50 ml) of dry benzene was refluxed (5-6 hrs) , the solvent was removed and the resulting colored crystalline solid was re-crystallized from ethanol to yield diazepine compounds $[N_{50} - N_{54}]$:



4. Results and Discussion

The mechanism for the reaction [12] of phthalic anhydride with Schiff's bases an evidence supporting the 7-membred heterocyclic ring system for the product , will be outlined below: The reaction is initiated by attack the of the azomethine nitrogen at one of the two carbonyl groups of the anhydride, the mechanism involves the addition of one σ-bond to one π-bond to give 4-membered cyclic. Transition state (T.S) which opens into phthalic anhydride (5-membered cyclic ring) to give (7-membered cyclic ring)[12, 13] , synthesized compounds $[N_2 - N_{54}]$ have been characterized by their melting point and spectroscopic methods (UV-Visble, FT.IR , H.NMR spectrum, and (C. H. N)-analysis) .



5. H.NMR-Spectrum

H.NMR-spectrum of compound $[N_2 - N_{54}]$ showed: singlet signal at δ 9.91-9.98 for one proton of anil group [12-14] (-CH=N) in compound $[N_2 - N_{17}]$, singlet signal at δ 10.2 that could be attributed to the proton [11-21] of oxazepine (O-CH-N) group in compound $[N_{34} - N_{49}]$, this signal disappeared in diazepine compounds $[N_{50} - N_{54}]$, and other peaks shown in figures.

6. FT.IR Spectra

FT.IR-showed appearance band at (1610-1630)cm- due to imine [12-23] group (C=N) of compounds [$N_2 - N_{33}$], while this band is disappear and two bands are appear at (1695, 1670) cm-1 due to[11-13] (lactone/lactam) group of oxazepine compounds [$N_{34} - N_{49}$], which disappeared and other bands appeared as evidence to formation of diazepine compounds [$N_{50} - N_{54}$]. Other data of functional groups shown in the following in figures.

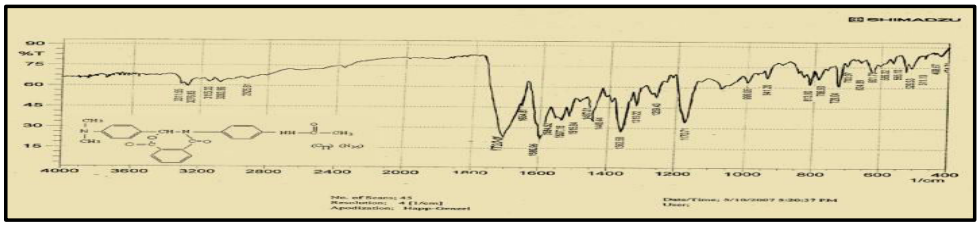


Figure 1. **FT.IR spectrum of compound** [N_{36}]

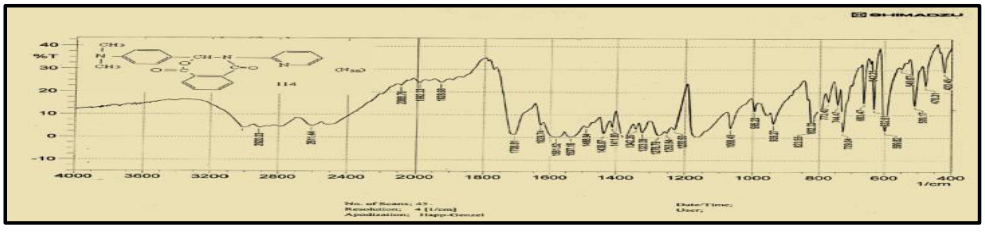


Figure 2. **FT.IR spectrum of compound** [N_{38}]

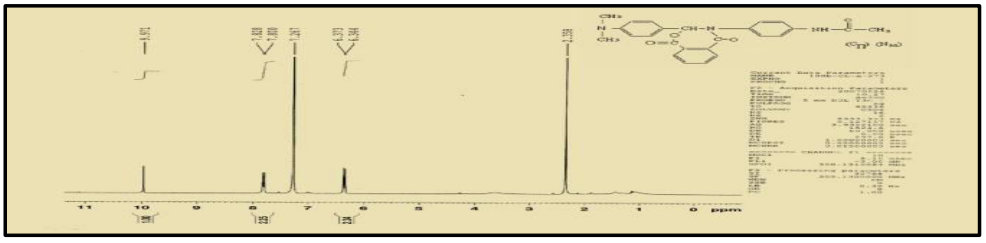


Figure 3. **H-NMR spectrum of compound** [N_{36}]

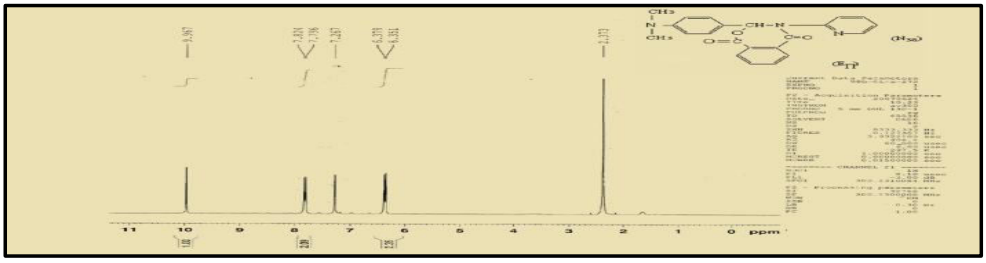


Figure 4. **H-NMR spectrum of compound** $[N_{38}]$

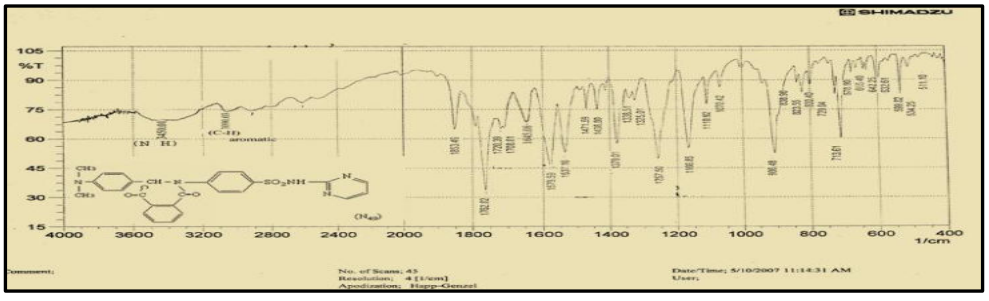


Figure 5. **FT.IR spectrum of compound** $[N_{34}]$

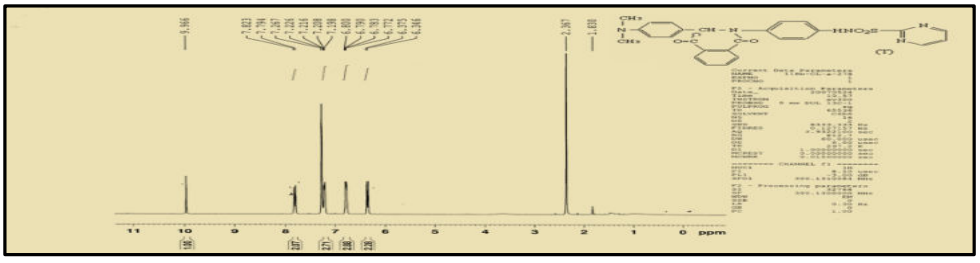


Figure 6. **H-NMR spectrum of compound** $[N_{47}]$

7. UV-spectra & (C. H. N)-Analysis

It was found from (C.H.N)-Analyses, from that compared the experimental data for our compounds are in a good agreement data calculated.Uv-Vis spectrum data of compounds $[N_{34} - N_{49}]$ are listed in Table (1), most of them have chromospheres groups and oxochrom groups (11-13) due to bath chromic shift, and they have electron transition $(n - \pi^*)$ due to the hetro atoms (N, O, S) in these compounds beside of transition $(\pi - \pi^*)$ of conjugated system.

8. Assay of antimicrobial activity

All materials and bacteria supplied from bio-lab in college education. Antimicrobial activity was tested by the filter paper disc diffusion method against gram positive bacteria (Staphylococcus aureus) and gram negative bacteria (Pseudomonas aeruginosa), 0.1 ml of the bacterial suspensions was seeded on agar. To determine minimum inhibitory concentration (MIC) for each compounds were ranged between (10-46) mg/ml by dissolved in (DMSO) and preparation 0.1mg/ml standard antibiotic amoxyline as positive standardand reference. The positive results or sensitivity were established by the presence of clear zone of inhibition around active compounds which were measured with a meter rule and diameters were recorded based on (mm), the assays were performed with two replicates .Generally, The results showed that the compounds have good inhibitory effect against tested bacteria as compared with synthetic antibiotic Amoxyline.

Table (1) showed the zone of inhibition of the compounds in this study ranged (from 34 to 8) mm. From results, we noted that the compounds $[N_{55} - N_{58}]$, then $[N_{50} - N_{54}]$ have higher antibacterial activity against (S.aureus and P.aeruginosa) is due to the presence more than one of nitrogen atoms (N) and sulfur atom (S) in their structures in (thizole, imidazole, pyrimidine)-rings, generally the sulfide compounds and diazepinecmpounds have higher antibacterial activity against (S.aureus and P.aeruginosa) than oxazepine compounds and anil compounds. These compounds become more effective in precipitating proteins on bacteria cell walls.

Compounds	diameter of zone(mm)	
	G+: Staphylococcus aureus	G-: Staphylococcus aureus
compounds[3]	24	18
compounds[4]	20	18
compounds[26]	18	14
compounds[27]	14	10
compounds[34]	20	18
compounds[35]	18	16
compounds[53]	34	20
compounds[45]	34	24
compounds[57]	38	26
compounds[58]	40	30
Amoxyline**	46	34
*Minimum Inhibitory concentration (MIC) of compounds, (5mg/ml).		
**Amoxyline (0.5mg/ml).		

Table 1. **Antibacterial activity of the compounds**

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