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Synthesis And Characterization Of New Schiff Bases And Their 1,3-Oxazepines Derived From Phthalic Anhydride

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ABSTRACT

In this work one mole of 4-methyl aniline was allowed to react with one mole of phthalic anhydride to produce 2- [N- (4-methyl phenyl)] Phthalamic acid [I]. Which was submitted to esterification via the reaction with dimethylsulphat in anhydrous sodium carbonate in acetone as a solvent to synthesis new ester of 2-[N- (4-methyl phenyl)] Phthalamide acetate [II]. The condensation of ester [II] with hydrazine using ethanol as a solvent led to formation the acorresbonding 2-[N- (4-methyl phenyl)]- Phthalamic acid hydrazide [III] which reacted with aromatic aldehydes (anisaldehyde , N,N dimethyl benzaldehyde , 4-hydroxy benzaldehyde , 4-methyl benzaldehyde) in some drops of glacial acetic acid and ethanol to yield new Schiff bases [IV]a-d . 1,3-oxazepine derivatives [V]a-d can be synthesized form reaction of Schiff bases [IV]a-d with phthalic anhydride in dry benzene to obtain new 1,3-oxazepines [V]a-d. All the synthesized compoundes were characterized by their FTIR and 1HNMR for (some of them).

Keywords: phthalic anhydride, hydrazide, Schiff bases, 1,3-oxazepine

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INTRODUCTION

The widespread applications of phthalic anhydride such as a chemical intermediate in the production of plastics from vinyl c hloride. Phthalate esters, which function as plasticizers, are derived from Phthalic anhydride. Phthalate plasticizers are used f or the production of flexible PVC products such as cables, pipes and hoses, leather cloth, shoes, film for packaging etc[1].
Schiff bases are compounds have an azomethine group (-C=N-), They have important application polymer chemistry and in a ddition of their biological activity such as antibacterial, antifungal, anticancer and another application [2-4].
1,3 –oxazepines is a seven member ring compound (which have two hetero atoms, oxygen atom at position (1) and nitrogen atom at position (3).
Oxazepine derivatives showed various biological activities such as antibacterial [5] and inhibitors for some enzymes action [6].
Also, oxazepine derivatives are used in other applied fields, they have much chemical and biological studies[7]. Many worke rs synthesized the new oxazepines mentioned in the literates[8], [9] ,[10].
The aim of this work is ; synthesis new Shiff bases and their 1,3-oxazepines, derived
from phthalic anhydride by many steps of reaction are given in Scheme 1.

EXPERIMENTAL

Materials: The chemicals were supplied from Merck , Fluka ,GCC and Aldrich chemicals Co.

Techniques: using potassium bromide discs, the FTIR spectra were recorded ona Shimadzo (Ir prestige-21) FTIR spectrosc opy. Uncorrected melting points were determined on Hot-Stage, Gallen Kamp melting point apparatus, ^{1}HNMR spectra were carried out by company : Ultra Shield 300 MHz, Bruker, Switzerland, at University of Al-albayt , Jordan, and NMReady 60 Pro User Manual Version 1.0 are reported in ppm(δ), (TMS) was used as an internal standard with DMSO as a solvent.

General procedures

The compounds were synthesized via Scheme 1.

Synthesis of 2-[N- (4-methyl phenyl)] phthalamic acide [I]

To a solution of phthalic anhydride (1.48g , 0.001mole) in (15mL) acetone , a solution of 4-methyl aniline (1 g ,0.001mole) in (15mL) acetone was added dropwise during one hour. Then, the mixture was left at room temperature with continuous s tirring for 24 hrs . The white product was filtered off and recrystallized by acetone to give a corresponding 2-[N- (4-methy l phenyl)] phthalamic acide [I] [11], yield 87% ,mp 140 -142 ^{0}C.

Synthesis of 2-[N- (4-methyl phenyl)] Phthalamide acetate [II]

A mixture of compound [I]. (1.8g ,0.013mol) anhydrous sodium carbonate (1.2 g ,0.01 mol) were dissolved in 25mL of aceto ne , dimethyl sulphate (0.026 mol) was added to this solution through 20 min , the resulting mixture was heated under refl ux for 4 hrs. The reaction mixture was allowed to cool at room temperature, extraction with chloroform. Collected the pale brown product after evaporating the chloroform [12]. yield 95% ,mp 198-199 ^{0}C.

Synthesis of 2-[N- (4-methyl phenyl)] Phthalamic acid hydrazide [III]

A solution of 2-[N-(4-methyl phenyl)]Phthalamtamide acetate [II] (0.28 g, 0.06 mol), hydrazine hydrate (2mL) in 4 mL of ethanol was heated under reflex for 2 hrs. Cooling the mixture to room temperature, and the obtained off white solid was filt ered dried and recrystallized from ethanol [13] .yield 88% ,mp >300 ^{0}C .

Synthesis of Schiff bases[IV]$_{a-d}$.

Refluxed a mixture of new acid hydrazides [III] (0.05g, 0.001 mole) , different aromatic aldehydes (0.001 mole) , with some d rops of glacial acetic acid (GAA) in ethanol 3 mL for 4hrs. The solvent was evaporated under vaccum and the solid recrystal lized from ethanol [14] .The physical data of new Schiff bases[IV]$_{a-d}$ are listed in Table (1).

Synthesis of 1,3-oxazepine derivatives $[V]_{a-d}$

Schiff bases [IV] (0.001mole) was mixed with phthalic anhydride (0.02g ,0.001 mole) in dry benzene 2mL ,the mixture was h eating under reflux for 6 hrs. The solvent was removed and the resulting colored solid was recrystallized from ethanol to obt ain new 1,3-oxazepines $[V]_{a-d}$. The physical data of all synthesized 1,3-oxazepines are given in Table (2) .

RESULT AND DISCUSSION

2-[N- (4-methyl phenyl)] phthalamic acid [I] was synthesized by the reaction of phthalic anhydride (one mole) with of 4-methyl aniline(one mole) in acetone. The mechanism involves nucleophilic addition reaction[15].

The structure of amic acid was studied by FTIR spectroscopy. The FTIR spectrum of compound [I] showed; disappearance o f absorption bands of NH_2 group and other peaks characterized of cyclic anhydride of the starting materials with appearanc e of new absorption stretching bands due to O-H of carboxyli c moiety at (3350-2720) cm^{-1}, C=O (carboxylic acid) stretching 1695cm^{-1} , C=O (amid) stretching at 1643cm^{-1} [16] and NH stretching band at 3311cm^{-1}.

^{1}HNMR spectrum of compound [I], showed the following characteristic chemical shift: many signals of eight aromatic proto ns appeared at δ (6.79 –7.88) ppm . A good sharp signal at δ 10.23 ppm could be attributed to the a proton of the NH grou p . Finally, a proton of carboxylic moiety appeared as a broad signal weak band at δ 12.4-12.8 ppm [17] ,[18].and a sharp s ingel signal at 2.27 ppm due to three protons of CH3 group .

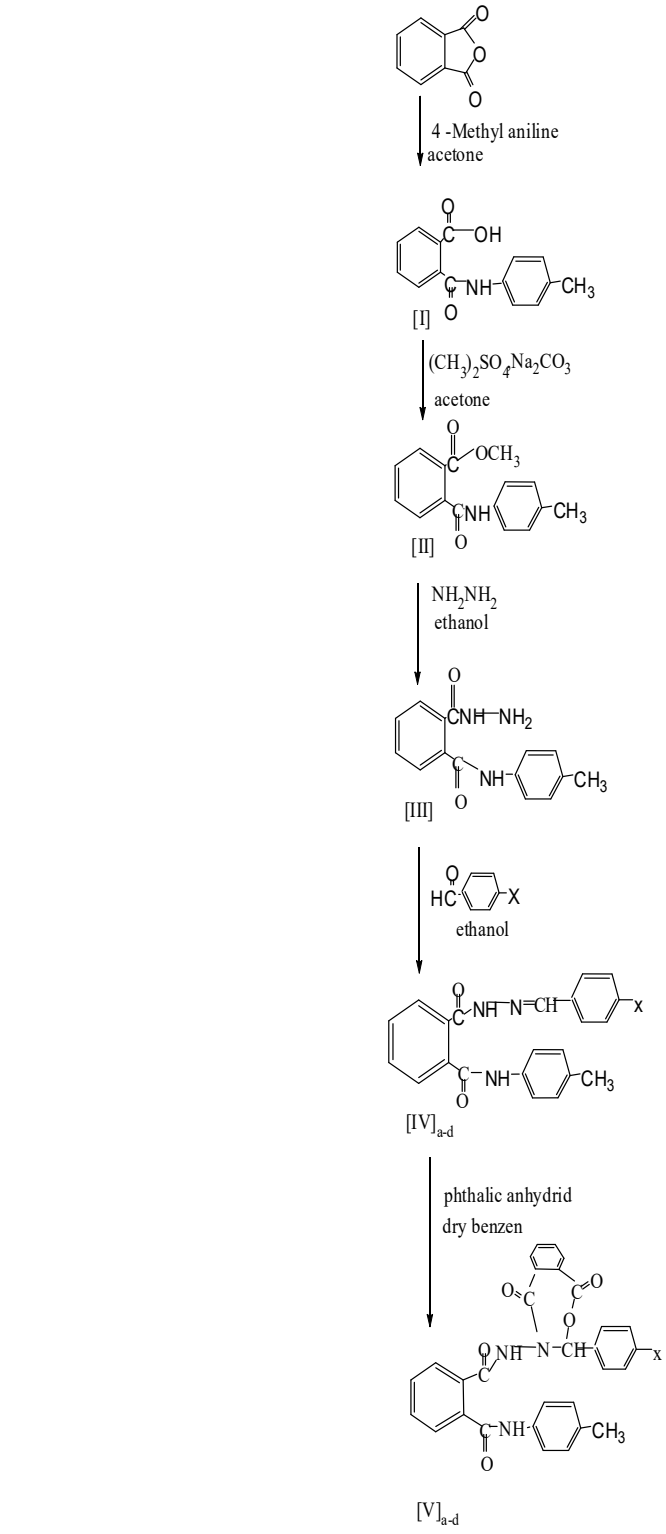
2-[N- (4-methyl phenyl)] phthalamic acide [I] was converted to ester by the common esterifiction prosses using dimethyl sulphate in presence of anhydrous Na_2CO_3 in dry acetone to form 2-[N- (4-methyl phenyl)] Phthalamide acetate [II]. The FTIR spectrum of compound [II] showed a new absorption band at 1716 cm^{-1} due to stretching vibration of the (C=O) f or ester , also appearance band at 1213 cm^{-1} due to (C-O) stretching of ester ,besides, disappearance two bands of O-H an d C=O of carboxylic moiety .

The new 2-[N- (4-methyl phenyl)] Phthalamide acetate [II] was used to synthesis a new compound of acid hydrazide [III], by the refluxing of compound [II] with excess of hydrazine hydrate in ethanol to form compound [III]. This compound was characterized by FTIR spectroscopy. FTIR spectrum exhibited absorption bands at (3350-3161) cm^{-1} due to the asymmetric and symmetric stretching vibration of NH_2 and NH groups besides to a stretching vibration band at 1658cm^{-1} due to (C=O) for amide .

The new Schiff bases were synthesized from condensation of one mole from acid hydrazide [III] and one mole from different aromatic aldehydes in ethanol .

The Schiff bases $[IV]_{a-d}$ were identified by FTIR and ^{1}HNMR spectrum of compound $[IV]_d$. FTIR absorption-spectra showed di sappearance of absorption bands for NH_2 group together with appearance a new absorption band in (1631-1603) cm^{-1} whi ch is assigned to imine group (C=N) stretching. FTIR data of functional groups which are characteristic of these compounds are given in Table (3). The ^{1}HNMR spectrum of compound $[IV]_a$, showed a sharp singlet signal at δ8.63 ppm due to the pr oton of azomethine group CH=N [13] a sharp singlet signal at δ4.10 ppm could be attributed to the three protons of OCH 3 group while the three protons of CH3group appeard at 2.5 ppm two good singlet signals at δ 8.07 ppm and 11.6 ppm d ue to proton of NH group for NHN=C and NHAr [19,20] , respectively and many signals in the region δ (7.04-7.89) ppm for t welve aromatic protons. The refluxing of suitable schiff base $[IV]_{a-d}$ with one mole of phthalic anhydride in dry benzene led to formation new 1,3-oxazepine derivatives $[V]_{a-d}$. The mechanism[10] involves percyclic reaction , the addition of one σ of C-O bond to p-bond (N=C) to give 4-membered cyclic ring and 5-membered cyclic ring of phthalic anhydride in the same transit ion state [T.S] , which opens into phthalic anhydride to give 7-membered cyclic ring.

The characteristic FTIR absorption bands of these compounds were confirmed from the disappearance of stretching band du e to C=N of Schiff bases and other peaks characterized of cyclic anhydride of the starting materials. The appearance two ban ds characteristic of two carbonyl groups of oxazepine ring in the region (1710-1666). The FTIR spectral data of new oxazepi ne compounds are listed in Table (4). The ^{1}HNMR spectrum of compound $[V]_d$, showed a sharp singlet signal at δ12.11 pp m due to the proton of NH group and many signals in the region δ (7.04-7.89) ppm for twelve aromatic protons. While th e proton of CH-N group appeared at δ6.93 ppm, a good singlet signal at δ2.3ppm could be attributed to the six protons of tw o CH_3 groups.



X= OCH_3 , N,N dimethyl , OH and CH_3

Scheme 1

Table (1):The physical properties of Schiff bases $[IV]_{a-d}$

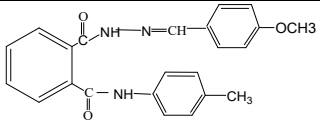
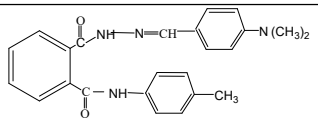
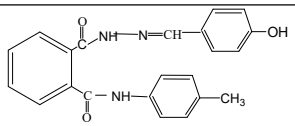
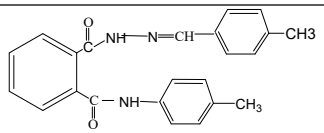
Comp. No.	Nomenclature	Structural formula	Molecuar for mula	M. P 0C	Yiel d %	Color
[IV]a	2-[N-(4-methoxy) benz ylid ene hydrazido]-N'(4'-methyl phen yl)phthalamid '		C21H21N3O3	148-15 0	94	Off white
[IV]b	2-[N-(4-N,N -dimethyl amin o)benzylidenehydrazido]-N '(4'-methyl phen yl)phthala mid		C24H24N4O2	248-25 0	90	brown
[IV]c	2-[N-(4-hydroxy)benzyl ide ne hydrazido]-N'(4'-methyl phenyl)phthalamid		C22H19 N3 O 3	268-27 0	50	Off whit e
[IV]d	2-[N-(4-methy l)benzylid en e hydrazido]-N'(4'-methyl p henyl)phthalamid		C23H21N3O2	164-16 6	81	White

Table (2):The physical properties of 1,3-oxazepine compounds [V]a-d

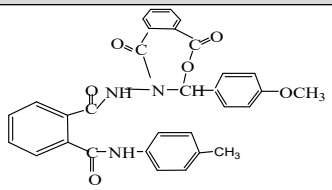
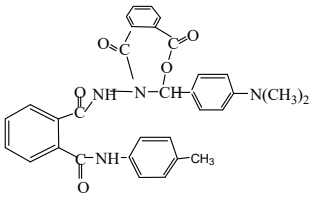
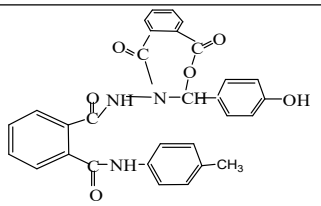
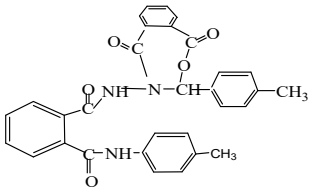
Comp. No.	Nomenclature	Structural formula	Molecuar form ula	M. P 0C	Yield %	Color
[V]**a**	2-[N-[2-(4-methoxyphenyl) -2,3-di hydro benz[1,2]-1,3 -oxazepin-4,7-diones-3-yl] amido]-N'-(4'-methyl phen yl)phthalamide		C31H25 N3O6	>300	83	White
[V]**b**	2-[N-[2-(4-N,N-dimethyl a minophenyl)-2,3-di hydro b enz[1,2]-1,3-oxazepin -4,7-diones -3-yl]amido]-N'-(4'-methyl phenyl)phthalamide		C32H28N4O5	183-185	44	red
[V]**c**	2-[N-[2-(4-hydoxy phenyl)-2,3-di hydro benz[1,2]-1,3-oxazepin -4,7-diones -3-yl] amido]-N'-(4'-methylphen yl)phthalamide		$C_{30}H_{23}N_3O_6$	299-201	50	White
[V]**d**	2-[N-[2-(4-methy l phenyl)-2,3-di hydro benz[1,2]-1,3-oxazepin -4,7-diones -3-yl] amido]-N'-(4'-methylphen yl)phthalamide		$C_{31}H_{25}N_3O_5$	178-180	67	White

Table (3): Characteristic FTIR absorption bands data of new schiff bases compounds[IV]a-d

Comp. No.	Characteristic bands FTIR spectra (cm^{-1})					
	υ (NH)	υ (C-H) aromatic	υ (C=O) amide	υ (C=N)	υ (C=C)	Other stretching bands
[IV]a	3437,3172	3022	1657,1640	1631	1600	C-H aliph. 2914 –2860 C-O 1225
[IV]b	3400-3171	3014	1660	1625	1600	C-H aliph. 2914-2881 C-N 813
[IV]c	3380-3163	3012	1658	1610	1599	υ OH 3261
[IV]d	3319-3161	3020	1666	1603	1590	C-H aliph. 2962-2890

Table (4): Characteristic FTIR absorption bands data of 1,3-oxazepine compounds[V]$_{a-d}$

Comp. No.	Characteristic bands FTIR spectra(cm^{-1})				
	υ (NH)	υ (C-H) Benzelic	υ (C=O) Lacton	υ (C=O) Lactam & amide	υ (C=C)
[V]a	3400,3157	3120	1735	1690-1666	1595
[V]b	3400,3160	3110	1725	1700,1670	1587
[V]c	3163	3115	1710	1680,1666	1585
[V]d	3314 ,3165	3161	1732	1685,1666	1595

REFERENCES

1. Lorz . P , Towae. F, Enke. W, Jäckh .R, Naresh, Hillesheim .W, "Phthalic Acid and Derivatives" in Ullmann's Encyclopedia of Industrial Chemistry, Wiley-VCH, Weinheim ,(2007).
2. Hussain . Z, Khalaf .M, Adil .H, Zageer .D , Hassan .F, Mohammed .S, and Yousif. E. ''Metal Complexes of Schiff's Bases Containing Sulfonamides Nucleus'' , (2016) ,7(5) , 1008.
3. Antony. A, Fasna. F, Ajil .A and Varkey .T , "Amino Acid based Schiff Bases and its Zn (II) Complexes" , Research & Reviews: Journal of Chemistry , (2016) , (5) 2 ,37-44.
4. Kratky. M , Dzurkova .M , Janousek .J, Kone cna . K, Trejtnar. F, Stola rikova .J and Vinsova. J ''Sulfadiazine Salicylaldehyde-Based Schiff Bases: Synthesis, Antimicrobial Activity and Cytotoxicity'' , Molecules, (2017) , 22, 1573.
5. Serrano-Wu. M , D. R. St. Laurent and Y. Chen. , " Bioorganic and Medicinal Chemistry Letters" , (2002),12(19), 2757 .
6. Smith. L, Wong .W and Kiselyov. A, "Bioorganic and Medicinal Chemistry Letters" , 2006 , Available online, (2006).
7. Blain .P, Toxicological Reviews, (2003), 22(2) , 103 .
8. AL-Dujali .A , Karam . N , Tomma .J ,"Synthesis and liquid Crystalline Behaviour Of New Series Containing 1,3 Oxazepine 1,

3 Thiazole ring" , journal of internation academic research for multidisciplinary , (2013) , 1(11),184-169.
9. Muhsen .T , Tomma .J , Mukhlus. J , "Synthesis and Characterization of Novel Compounds Containing of Imidazolidinone a nd Oxazpine rings" , (2012) , 25 (3),276-283.
10. Saued .S , Tomma . J , Ali .E, "Synthesis and Characterization of Novel1,3 Oxazepine derived from Di amic Acid N,N- Bis – (4-methyl phenyl) pyromellit amic Di acid ,(2014), 27 (3) , 329- 381
11. Hussein .Sh , Ali .E , Tomma .J ,Evidence Supports Formation of Isoimides From Pyromellitic Dianhydride" , (2012) , 26(1), 241-249.
12. Saoud.S ,(2007) , ,"Synthesis and Characterization of Some New 1,3,4- Thiadizole and 1,3 Oxazepine Derivatves " MSc. Th esis , College of Education Ibn Al- Haitham University of Baghdad.
13. Muhsin .T, (2012) " "Synthesis and Biological Activity of New Compound Derived from 3-[4 –(4-Methoxybenzoylod benz ylideneamino]-2- thioxo imidazolidin , MSc. Thesis , College of Education Ibn Al- Haitham University of Baghdad.
14. Jamel .N ,(2014) , "Synthesis and Characterization of New Heterocyclic Derived from Chalcon" M.Sc thesis ,college of Edu cation for pur Sccience –Ibn -Al Haitham , Baghdad university.
15. Al-Mamory . Sh (2012) , "Synthesis and Characterization of Some New Asymmetricak Imide /Isoimid Derived From Pyro mellitic Dianhydride", M.Sc thesis ,college of Education for pur Sccience –Ibn –Al Haitham , Baghdad.
16. Silverstein. R, , Bassler .G and Morrill .T , (1981), "Spectrometric Identification of Organic Compounds", 4thed, Johin Wile y and sons ,New York
17. Sharma. P, . Kukereja .P, Choudhary .V and Narula. A , " Ind. J. Engi." , (2005), 12 , 259- 264.
18. Sharma .Y , " Elementary Organic Spectroscopy ",4th Eddition ,Ramnagar , New Delhi Ind. , (2009) , 122,233.
19. AL Aliawy .K , (2011) . "Synthesis and Characterization of Symmetrical and Asymmetrical Pyromellitimides and their Am ic Acids Containing Heterocyclic "Unit M.Sc thesis , college of Education for pur Sccience –Ibn –Al Haitham , Baghdad univ ersity.
20. Alsryfy, A.H., Mosaa, Z.A., Alrazzak, N. “Synthesis and characterization of new schiff base derived from 1,2-Di (indol-2-yl) - 2-hydroxyethanon” Research Journal of Pharmaceutical, Biological and Chemical Sciences, (2015); 6 (2), pp. 798-802.