University of Thi-Qar Journal of Science (UTsci)
The 4th Scientific Conference of Science College/ University of Thi_Qar
Volume (7), No.2

Preparation and Characterization of New Heterocyclic Derivatives, Six and Five Ring from Acetanilide

Zainab Amer Sallal
Department of Chemistry, College of Science, University of Baghdad, Iraq
zainabamer34@yahoo.com

***Abstract*-The aim of the study synthesis of new heterocyclic derivatives (six and five ring) from acetanilide. Firstly the chalcones have been synthesized from the reaction acetanilide with aromatic aldehyde [2-nitrobenzaldyhade, 4- dimethylaminobenzaldehyde, 2-naphthaldehyde] in dilute solution of ethanolic sodium hydroxide at room temperature. This reaction occurs depending on Claisen Schmidt condensation, then a new oxazine and thiazine derivatives (six ring) have been synthesized by the reaction chalcones with urea and thiourea. Finally the synthesized chalcones were reacted with hydrazine hydrate to produce new pyrazol derivatives (five ring). All derivatives were characterized by physical properties, FTIR, ^{1}H-NMR and ^{13}C-NMR spectra.**

***Keywords*-** acetanilide, chalcones, thiazine, oxazine, pyrazol.

I. Introduction

Acetanilide is a solid, no having odor chemical and have a peel in appearance. It is also named N-phenylacetamide, acetanilid, acetanil and in the past known the commerce name antifebrin. Acetanilide is applied to a curb of hydrogen peroxide decompositions. It also uses key intermediate for the industry of the sulfa drugs, rubber synthesis, dyes and camphor structure(Baty *et al.*., 1988). Chalcones are appear the important in biosynthesis and can preparation different compounds as pyrazoline, thiazine(Farooque and Zulfequar , 2012), pyrimidine to have heterocyclic ring(Ishwar, 2014). They have α, β- unsaturated keton to responsible for antioxidant(Kamble, 2011) , anti-inflammatory(Hsieh, 2000) and antibacterial activity(Davinder, 2012) Oxazine is heterocyclic compound (six ring) contain N and O in structure, can be prepare form chalcone and posses a large activity such as antimicrobial(Chaitra and Rohini, 2018) , anticancer(Ouberai *et al* ., 2006) , antiviral Anusha1 *et al*., (2015), antimalarial(Beena , 2013), anticoagulant activity(Sawant *et al*., 2012) and antifungal(Sayaji and Pravina, 2013). Thiazine is heterocyclic compound (six ring) contain N and S in structure. It exhibit wide interest to bioactive like antibacterial (Naeemah *et al.*, 2018), hypoglycemic(Alok *et al.*, 2015) and anti-inflammatory(Nagaraj and Reddy, 2008) . Pyrazol heterocyclic derivatives (five ring) have two nitrogen in membered ring(Rana *et al.*, 2018) . It and its derivatives display important of biological activity like anti-depressant, anti-convulsant[Ozdemir *et al.*, 2007), antiamoebic(Budakoti *et al.*, 2006), antibacterial(Korablina *et al.*, 2016)

II. Experimental Methods

1-Synthesis of Chalcones [A_1-A_3] (Choudhary *et al.*, 2011)

Acetanilide (0.01 mole) of dissolved in ethanol (10 ml), then added aqueous sodium hydroxide 40 % (10 ml) and mixed for (25-30 min). After that aromatic aldehyde [m-nitrobenzaldyhade, para-dimethylaminobenzaldehyde, 2-naphthaldehyde] (0.01 mole) was added and mixed for 20 hours at room temperature. After complete this reaction added acetic acid to neutralized solution then put it in crashed ice and precipitated it then filtered the crystal material and recrystallization from ethanol. Table [1] shows the physical data and FT.IR of compounds [A_1-A_3].

2- Synthesis of Oxazine and Thiazine Derivatives [B_1-B_3, C_1-C_3] (Zainab, 2014)

Chalcone [A_1-A_3] (0.01mol) and urea, thiourea (0.01mol) were dissolve it in ethanolic sodium hydroxide (25 ml) was stirred with a magnetic stirrer and refluxed 2-3 hours. Cold distilled water was added with continuous stirring for 1 hour then kept in refrigerator for 20 hours. The precipitated compound was filter and recrystallization from ethanol. Table [2] shows the physical data and FT.IR of compounds [B_1-B_3, C_1-C_3].

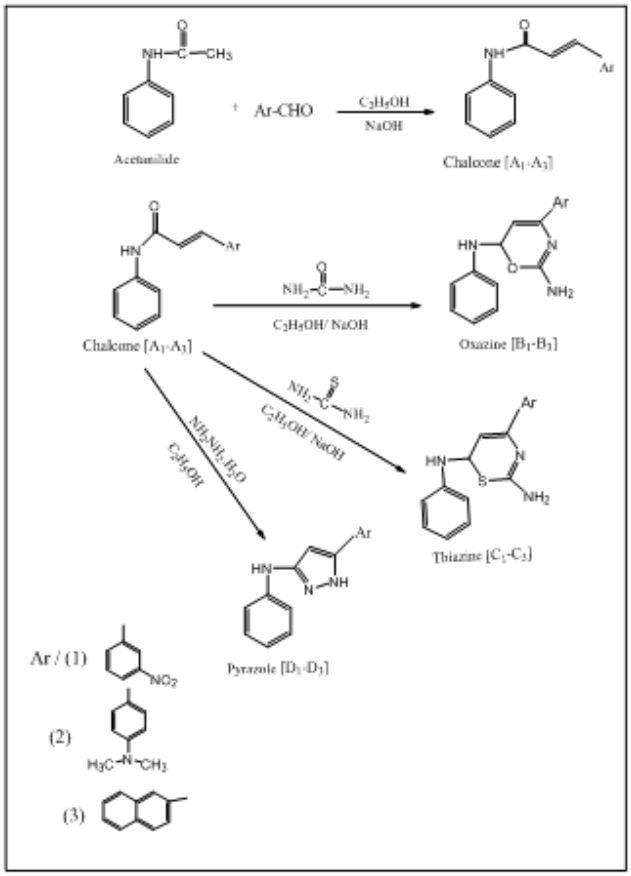
2- Synthesis of Pyrazole Derivatives [D_1-D_3](Zainab, 2014)

Taken from of chalcone [A_1-A_3] (0.01 mol) and hydrazine hydrate (0.01 mol) in ethanol (20 ml) was refluxed for 5 hours. Add of cold distilled water and stirring 1 hour. The precipitation was filtered, then take the crystal and recrystallization from ethyl alcohol. Table [3] shows the physical data and FT.IR of compounds [D_1-D_3].

III. Results and Discussion

New heterocyclic derivatives (six and five ring) from acetanilide have been synthesized. In the begain step chalcones [A_1-A_3] was prepared from the reaction acetanilide with aromatic aldehyde in dilute solution of ethanolic sodium hydroxide in room temperature this reaction occurs depending on Claisen Schmidt condensation, then you synthesized new oxazine and thiazine derivatives [B_1-B_3, C_1-C_3] by the reaction chalcones

with urea and thiourea. Finally chalcones were reacted with hydrazine hydrate to produce new pyrazol derivatives [D_1-D_3], scheme [1]. FTIR spectra of derivatives [A_1-A_3] appear absorpation bands at [(3022-3054) cm^{-1} to (C-H) aromatic, (3334-3456) cm^{-1} to (N-H) and (1639-1662) cm^{-1} to (C=O)] (Silverstein *et al.*, 2005) , other data display in table [1].



Scheme (1) preparation of chalcone and their derivatives

FTIR spectra of derivatives [B_1-B_3 , C_1-C_3] show disappearance of absorption band at (1639-1662) cm^{-1} which belong to the carbonyl group and appear of absorption band at (1610-1632) cm^{-1} due to (C=N) and bands [(3214-3304) sym , (3371-3483) asym] to (NH_2), other data were display in table [2]. ^{1}H-NMR of oxazine [B_2] appear signals at [δ(6.1-7.4) ppm (m, Ar-H), δ 8.7 ppm (s, 2H, NH_2), δ 4.5 ppm (s, H, NH) and δ 3.2 ppm (s, 3H, $2CH_3$)]. ^{13}C-NMR of compound [B_2] notice peaks aromatic carbon at δ(113-135) ppm, δ(150) ppm due to (C-N), δ(60) ppm to (C-O) and δ(45) ppm to (CH_3) group. ^{1}H-NMR of thazine [C_1] display signals at [δ(6.43-7.81) ppm (m, Ar-H), δ 8.3 ppm (s, 2H, NH_2) and δ 4.2 ppm (s, H, NH)] (Rahman and Choudhary, 1991) ^{13}C-NMR of compound [C_1] notice peaks aromatic carbon at δ(122-139) ppm, δ(148) ppm due to (C-N) and δ(35) ppm to (C-S).

FTIR spectra of derivatives [D_1-D_3] appearance of absorption band at (1615-1639) cm^{-1} belong to (C=N) and bands (3300-3354) cm^{-1} due to (N-H), the other data were display in table [3]. ^{1}H-NMR of pyrazol [D_3] display signals at [δ(6.89-8.11) ppm (m, Ar-H), δ 11.9 ppm (s, H, NH pyrazol) and δ 3.9 ppm (s, H, NH)]. ^{13}C-NMR of compound [D_3] appear peaks of aromatic carbon at δ(117-128) ppm and δ(156) ppm due to (C-N).

Table (1) Physical data and FTIR data of compounds [A_1- A_3]

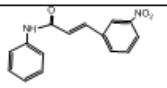
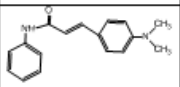
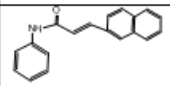
Comp. No.	Compound Structure	M.P. °C	Yield %	Color	FTIR Absorptions cm^{-1}				
					υ (C-H) aromatic	υ(N-H)	υ (C=O)	υ (C=C) Aromatic	Others
A_1		62-64	72	Yellow	3031	3334	1662	1552	υ(NO_2) = 1371
A_2		54-56	90	Brown	3022	3342	1641	1558	υ(C-H) = 2976 aliphatic
A_3		95-97	82	Off white	3054	3356	1639	1550	-

Table (2) Physical data and FTIR data of compounds [B_1- B_3] and [C_1-C_3]

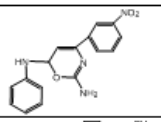
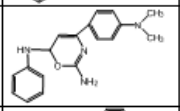
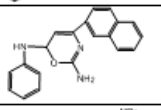
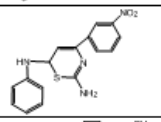
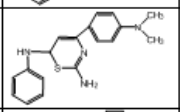
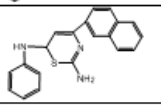
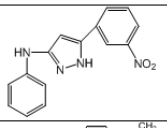
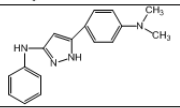
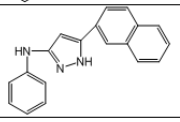
Comp. No.	Compound Structure	M.P. °C	Yield %	Color	FTIR Absorptions cm^{-1}				
					υ (C-H) aromatic	υ(NH_2) asym, sym	υ (C=N)	υ (C=C) aromatic	Others
B_1		195-197	70	Off white	3016	3429 3266	1620	1590	υ(NO_2) = 1366 υ(C-O) = 1125
B_2		173-175	66	white	3024	3371 3214	1632	1591	υ(C-H) = 2891 aliphatic υ(C-O) = 1198
B_3		278-280	60	Off white	3016	3420 3253	1612	1571	υ(C-O) = 1156
C_1		118-120	62	Brown	3060	3483 3303	1625	1570	υ(NO_2) = 1313 υ(C-S) = 2329
C_2		181-183	58	white	3055	3465 3278	1618	1581	υ(C-H) = 2909 aliphatic υ(C-S) = 2256
C_3		262-265	56	white	3011	3454 3280	1610	1592	υ(C-S) = 2279

Table (3) Physical data and FTIR data of compounds [D_1- D_3]

Comp. No.	Compound Structure	M.P. °C	Yield %	Color	FTIR Absorptions cm^{-1}				
					υ (C-H) aromatic	υ(N-H)	υ (C=N)	υ (C=C) aromatic	Others
D_1		260-262	71	Yellow	3061	3354	1623	1590	υ(NO_2) = 1301 υ(C-N) = 1265
D_2		190-192	63	Brown	3049	3331	1639	1594	υ(C-H) = 2910 aliphatic υ(C-N) = 1270
D_3		210-212	59	Brown	3070	3300	1615	1592	υ(C-N) = 1264

IV. References

Alok, S.Th., Ravitas, D., Arvind, K.J. and Sudhir, P.K. 2015. Synthesis and oral hypoglycemic effect of novel

thiazine containing trisubstituted benzenesulfonylurea derivatives. Saudi Pharmaceutical Journal. 23: 475–482.

Anusha1, P., Manichandrika1, P., Shruthi1, S. (2015). Synthesis of schiff's base derivatives of oxazine from chalcones and evaluation of their antibacterial activity. Syeda Uzma Nishat1, Sumaiyya Sultana. (4)11: 886-895.

Baty, J.D., Lindsay, R.M., Fox, W.R. and Willis, R.G. (1988). Stable isotopes as probes for the metabolism of acetanilide in man and the rat, biomed. environ. mass spect. 16: 183-189.

Beena, K.P., Akelesh, T. 2013. Design, synthesis, characterization and evaluation of some 1,3-oxazine derivatives as potent antimicrobial agents. Scholars Research Library. 5(4): 257-260.

Budakoti, A., Abid, M. and Azam, A. 2006. Synthesis and antiamoebic activity of new 1-N-substituted thiocarbamoyl-3,5-diphenyl-2-pyrazoline derivatives and their Pd(II) complexes. Eur J Med Chem. 41: 63-70.

Chaitra, G. and Rohini, R.M. 2018. Synthesis of 1,3-Oxazine derivative from Chalcone and Screening for their Anti-Oxidant and Anti-Inflammatory activity. International Research Journal of Pharmaceutical and Biosciences. 4 (6) 19-27.

Choudhary, A.N., Vijay, J. 2011. Synthesis of chalcone and their derivatives as antimicrobial agents. Int J Pharm Pharm Sci. 3(3) 125-128.

Davinder, P. 2012. Synthesis and Antibacterial evaluation of benzoxazols tethered dihydro oxazines, Indian Journal of chemistry. 51: 739-745.

Farooque, H. and Zulfequar, H. 2012. Synthesis and antimicrobial screening of some 1,3- thiazines, J. Chem. Pharm. Res. 4(4): 2263-2267.

Hsieh, H.K., Tsao, L.T., Wang, J.P. and Lin, C.N. 2000. Synthesis and anti-inflammatory effect of chalcones, J. Pharm Pharmacol. 52(2): 163-171.

Ishwar, K.B. 2014. Synthesis, antitubercular & cytotoxic studies of some pyrimidine derivatives derived from Chalcones, World journal of pharmacy & Ph. Sciences. 3: 1432-1439.

Kamble, V.M. 2011. Synthesis & biological evaluation of Methoxylated chalcones as anti oxidant agents, Journal of chemical & pharmaceutical research. 3: 639-648.

Korablina, D.D., Vorozhtsov, N.I., Sviridova, L.A., Kalenikova, E.I. and Medvedev, O.S. 2016. Pharmacological Activity of 4,5-Dihydropyrazole Derivatives. Pharmaceutical Chemistry Journal. 5: 281-295.

Naeemah Al-Lami, Zainab A. and Rana A.A. 2018. Pryparation, Characterization And Biological Activity of New Derivatives of 2-Biphenyl-3-Aminomethylimidazo (1,2-a) Pyrimidine. Journal of Pharmaceutical Sciences and Research. 10(12): 3344-3350.

Nagaraj, A. and Reddy, C.S. 2008. Synthesis of bis–thiazines or bis–pyrimidines in good yields. The antibacterial, antifungal and anti-inflammatory activities of the compounds have been evaluated. J. Iran. Chem. Soc 5(2): 262 -267.

Ouberai, M., Asche, C., Carrez, D., Croisy, A., Dumy, P. and Demeunynck, M. 2006. 3,4-Dihydro-1H-[1,3]oxazino[4,5-c]acridines as a New Family of Cytotoxic Drugs. Bioorg Med Chem Lett. 16: 4641-4643.

Ozdemir, Z., Kandilici, H.B., Gumusel, B., Calis, U. and Bilgin, A.A. 2007. Synthesis and Studies on Antidepressant and Anticonvulsant Activities of Some 3-(2-furyl)-pyrazoline Derivatives. Eur. J. Med. Chem. 42: 373–379.

Rahman, A. and Choudhary, M. 1991. The Basic of Modern NMR Spectroscopy In Solving problems with NMR Spectroscopy. 2nd ed, New York.

Rana, A.A., Zainab, A. and Entesar, O.Al-Tamimi1. 2018. Synthesis and characterization of substituted 1,2,4-triazole and their derivatives on poly ethylene. Journal of Pharmaceutical Sciences and Research. 10(5): 1079-1084.

Sawant, R.L., Mhaske, M.S., Wadekar, J.B., 2012. A series of Schiff bases of 1,3-oxazines were synthesized via reaction of 1,3-oxazine-2-amine with substituted benzaldehyde and they exhibited significant anti-coagulant activity. International Journal of Pharmacy and Pharmaceutical Science. 4(4):320-323.

Sayaji, S.D. and Pravina, B.P. 2013. Novel synthesis and anti-microbial activity of bis-oxazine derivatives. Journal of Ceramic Processing Research. 5(5): 271-274.

Silverstein, R.M., Webster, F.X. and Kiemle, D.J. 2005. Infrared Spectroscopy in Specteometric Identification of Organic Compounds, New York.

Zainab, A.S. 2014. Synthesis and characterization of new Oxazine, Thiazine and Pyrazol derived from chalcones. Baghdad Science Journal. 11(2): 477-485.