Original Article

# Synthesis, and biological activity of some new 1,3 - bis ( 4 - nitro benzyl -2 - aryl hydro pyrimidine

Aabd Alrazaaq Khazeal Nasih[1], Khaled Fahd Ali[2*]
[1,2]Department of Chemistry, Ibn Al-Haitham, University of Baghdad, Baghdad 61023, Iraq
Email: drkhalidfahad@yahoo.com

## Abstract

According to bright importance's showed by pyrimidine and hydro pyrimidine derivatives a newly series of hydro pyrimidine derivatives was synthesized by three steps. The first step by synthesized bis Schiff base from reaction two equivalents of p-nitro benzaldehyde with one equivalent of 1,3-propane diamine (1,3-diaminopropane) to afford compound 1. The next step was to reduction the imine group by NaBH4 to afford compound 2. The finally step by cyclization compound 2 during reaction it with some arylaldehyde in constated acetic acid and refluxing the mixture for 24 to 72 hours to afford compounds 3a-h. The resulting compounds were characterized by FT-IR, 1H NMR, 13C NMR, moreover, their structures confirmed by elementary analysis (CHN). The antibacterial activity for newly synthesis compounds 3a-h screened using Staphylococcus aureus as Gram positive bacteria and Escherichia coli as Gram negative bacteria. Compounds 3a and 3h exhibited highest inhibition zone as well compounds 33 and 3g showed moderated antibacterial activity.

**Keywords:** hydro pyrimidine, antibacterial, antifungal, Bis benzyl, bis Schiff base

## Introduction

Hydro pyrimidines and own derivatives have recently gain considerable interest due to their wide pharmacological activities such as anticancer[1] antiviral [2], calcium channel modulation[3] and antimicrobial Agents [4, 5], antioxidant [6], anticonvulsant activity [7],anticancer [8], lipoxygenase inhibitors and cancer chemopreventive agents[9] , anti - inflammatory and Analgesic Activity [10, 11]. In the other hand, the existence of nitro benzyl in chemical structure found it introduce or enhanced diverse biological activity likewise ; Antimicrobial Activity[12, 13], antitumor activity[14, 15] in addition to some of these compounds obtained drug delivery properties [16, 17]. Furthermore, substituted phenyl group in different group in chemical structure add additional biological activity. For instance, existence of hydroxyl group or phenolic group and its substituted donate additional biological activity such as antioxidant activity[18-20], anti-inflammatory activity [21, 22], Antibacterial Activity[23] and anticancer activities [24, 25]. This work offered synthesis new hydro pyrimidine containing bis N-nitro benzyl group as well containing aryl group with difference substituted group and study their antibacterial activity.

Access this article online

Quick Response Code:

Website: www.pnrjournal.com

DOI: 10.47750/pnr.2022.13.04.101

## 2 Experimental

### 2.1 General Chemistry

All chemicals and solvent were used without purification and purchasing from mercantile companies. The melting points of the materials were fixed by the open capillary tube method employed OMEGA MPS10 melting point apparatus and were uncorrected.

**Address for correspondence:** Khaled Fahd Ali, Department of Chemistry, Ibn Al-Haitham, University of Baghdad, Baghdad 61023, Iraq,
Email: drkhalidfahad@yahoo.com

Received date: 15 August 2022 Accepted: 10 September, 2022
Published: 11 October, 2022



How to cite this article: Khazeal Nasih A A, Fahd Ali K, Synthesis, and biological activity of some new 1,3 – bis ( 4 – nitro benzyl -2 - aryl hydro pyrimidine, J Pharm Negative Results 2022;13(4):756-764.

The purities of synthesized compounds were affirmed by using thin layer chromatography (silica gel TLC) using plates from Merck, and spots assigned under iodine vapour. were recorded using Shimadzu instrument (FT-IR- 8400S), The data, of samples, were collected at the university of Baghdad College of Education for Pure Sciences Ibn Al-Haytham. The 1D NMR were recorded on Bruker spectrometer (working frequency 400MHz), at the University of Tehran in the Islamic Republic of Iran, with tetramethyl silane (TMS) as an internal standard for 1H NMR analysis. DMSO–d6 and CDCl3 were used as a solvent. The CHN was recording by EA1112 for 300 Eager (University of Tehran, Iran).

## 2.2 synthesis

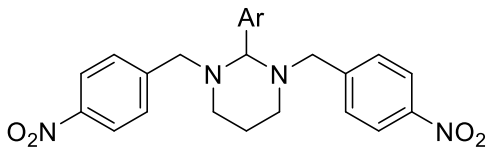
### 2.2.1 Synthesis of N-(3-( 4-nitrobenzylidene)amino)propyl))-1-(4-nitrophenyl)methanimine. 1

The resulting compound was synthesized modified from procedure described by [26-28]. P-nitrobenzaldehyde (9,06g, 60mmol.) in 20 mL absolute ethanol was added in a few batches to warm stirring solution of 1,3-diaminopropane (2,22g, 30mmol.) and three drops of acetic acid in 5mL absolute ethanol. After completion the addition the mixture was heated under reflux for 12h. Upon cooling the precipitate was filtrated and washed with cold ethanol. the crude product recrystallized from isopropanol to afford shiny yellow crystals, Yield 83% (8.78 g), M.P. 159-161˚C.

### 2.2.2 Synthesis of N1,N3-bis(4-nitrobenzyl)propane-1,3-diamine. 2

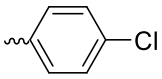
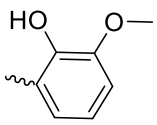
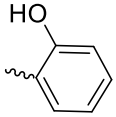
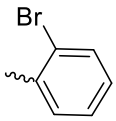
this reaction was synthesized from modified procedure described literature by Shakir et. al. [29]. Sodium borohydride powder (3.75g, 100mmol) was added in a few portions to a stirring solution of N-(3-(((E)-4-nitrobenzylidene)amino)propyl)-1-(4-nitrophenyl) methanimine (8.5g 25mmol.) in 50mL of mixture 1:1 CH3OH-THF at ambient temperature. After completion the addition the stirring mixture left under reflux for 48 hours. Upon cooling crashed ice (100ml) was added and left for stirring half hour. The precipitated was collected by filtration, drying and recrystallized from methanol to produce white precipitate 94.5% , M.P. 300˚C (dec.)

General synthesis of 2-(Aryl)-1,3-bis(4-nitrobenzyl)hexahydropyrimidine.




Appropriate aryl-aldehyde (1.0mmol.) was added to a solution of N1,N3-bis(4-nitrobenzyl)propane-1,3-diamine (0.34g, 1.0mmol.) in 25 mL acetic acid then refluxed for (24-72) h, and the reaction keep tracked by TLC utilizing hexane : ethyl acetate (3-1) as eluent. After cooling the mixture pour in to 150mL crashed ice with vigorous stirring for 15 minutes. The precipitated collected by filtration and washed with cold ethanol then recrystallized from suitable solvent. The yield, M.P. color and aryl ring have been tabulated in Table 1 and Table 2 containing the structure and nomenclature of the synthesis compounds.

**Table 1:** Some physical properties, time of reaction and recrystallization solvent of synthesized compounds 3a-h

| *No.* | *Ar* | *M.P.˚C* | *Yield %* | *Color* | *M.F* | *Recrystallized solvent* | *Time (h)* |
|---|---|---|---|---|---|---|---|
| 3a |  | 123-125 | 71 | white | C24H23ClN4O4 | $C_2H_3N$ | 24 |
| 3b |  | 151-154 | 56 | Off white | C25H26N4O6 | CHCl3 | 72 |
| 3c |  | 130-134 | 69 | yellowish brown | C24H24N4O5 | CH3OH | 48 |
| 3d |  | 220-223 | 64 | Light brown | C24H23BrN4O4 | CH3OH | 72 |

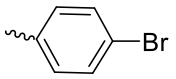
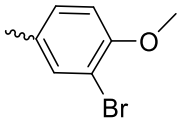
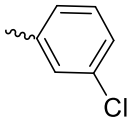
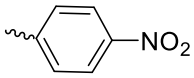
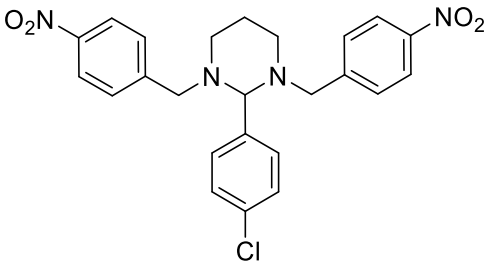
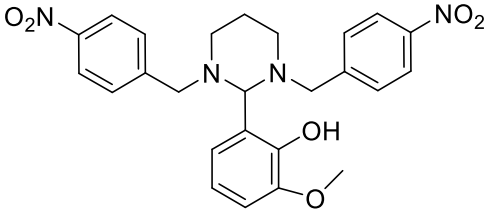
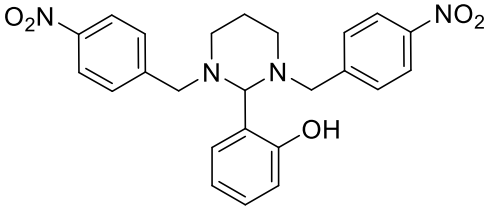
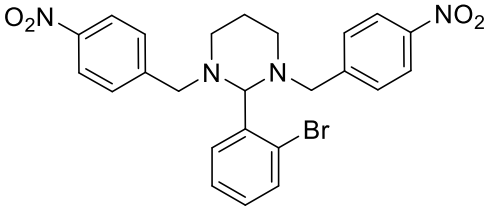
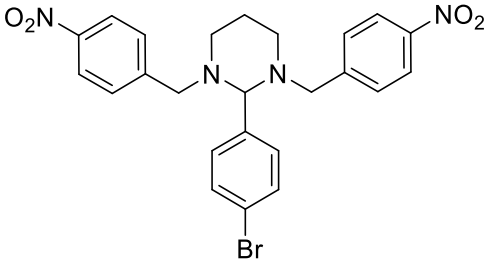
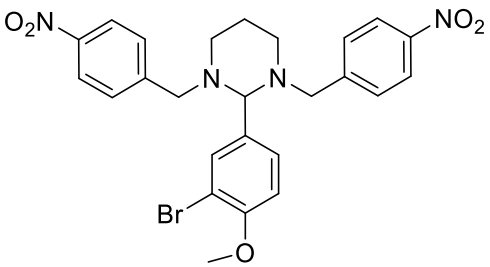
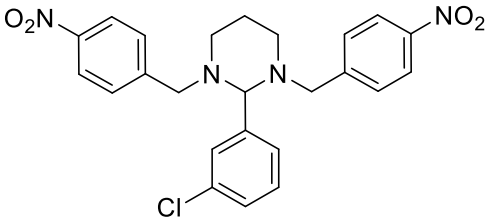
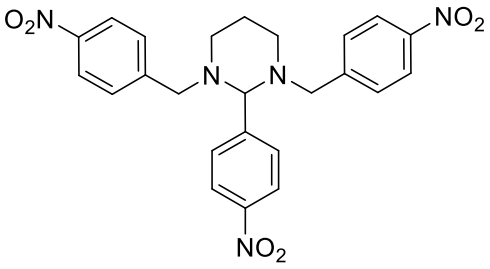
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 3e |  | 294-297 | 70 | Off white | C24H23BrN4O4 | C4H8O2 | 24 |
| 3f |  | 253-256 | 66 | Off white | C25H25BrN4O5 | DCM | 48 |
| 3g |  | 149-151 | 59 | white | C24H23ClN4O4 | $C_2H_3N$ | 72 |
| 3h |  | 183-186 | 61 | yellow | C24H23N5O6 | CHCl3 | 48 |

**Table 2:** Structure and nomenclature of the synthesis compounds 3a-h

| *No.* | *structure* | *Name* |
|---|---|---|
| 3a |  | 2-(4-chlorophenyl)-1,3-bis(4-nitrobenzyl)hexahydropyrimidine |
| 3b |  | 2-(1,3-bis(4-nitrobenzyl) hexahydropyrimidin-2-yl)-6-methoxyphenol |
| 3c |  | 2-(1,3-bis(4-nitrobenzyl) hexahydropyrimidin-2-yl)phenol |
| 3d |  | 2-(2-bromophenyl)-1,3-bis(4-nitrobenzyl)hexahydropyrimidine |
| 3e |  | 2-(4-bromophenyl)-1,3-bis(4-nitrobenzyl)hexahydropyrimidine |

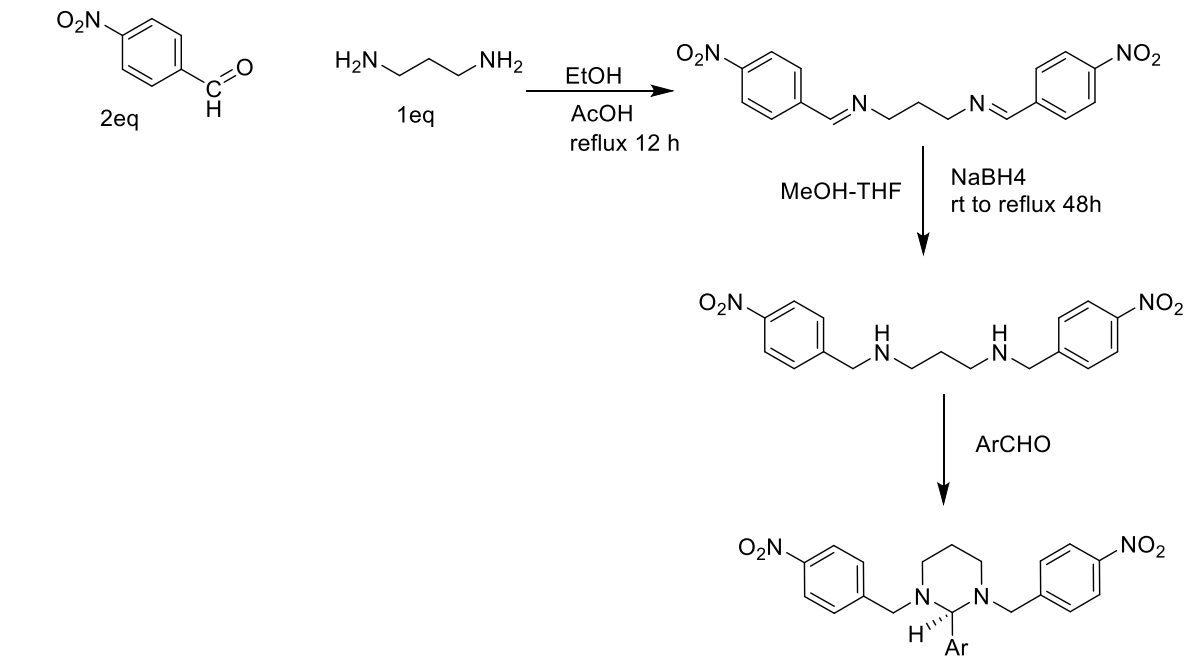
| | | |
|---|---|---|
| 3f |  | 2-(3-bromo-4-methoxyphenyl)-1,3-bis(4-nitrobenzyl)hexahydropyrimidine |
| 3g |  | 2-(3-chlorophenyl)-1,3-bis(4-nitrobenzyl)hexahydropyrimidine |
| 3h |  | 1,3-bis(4-nitrobenzyl)-2-(4-nitrophenyl)hexahydropyrimidine |

### Screening of Antifungal and Antibacterial Activity

The method of screening the effectiveness the synthetic chemical compounds against microbial followed by Ager-well diffusion method was used by using 20ml from media MHA (pathogenic bacteria) or PDA media pathogenic fungi for each Petri dish the diameter of the dish 90mm, then pollinate the medium using (0.1ml) for each Petri dish, the diameter of the dish is then inoculated with the medium by using a bacterial suspension or a fungal suspension through the use of a sterile glass diffuser. Then the dishes were left for a period of time ranging from 15-30 munities until drying holes were made by using a cork borer with a diameter of about 7mm, and 15µL, the solutions of the synthesized compounds 3a-h cyclic Schiff base, were added at a concentration of one 100mg/ml for each hole. Whereas, 50µmol of DMSO solvent as a control were placed in one of the hole, and the samples were placed in an incubator for 24hrs at a temperature 28+2 ºC and 30 +1 ºC, respectively in the incubator, then the dishes were taken out, and the radii of the inhibition zone were measured in mm, as the activation area is the area in which there is no bacterial or fungal infection.

## 3 Results And Discussion

The target compounds were synthesized by utilizing three stages the first one by synthesis bis Schiff bases form reaction 4-nitrobenzaldehyde with 1,3-di amino propane the next stage was reduction of bis Schiff bases N-(3-(4-nitrobenzylidene)amino)propyl))-1-(4-nitrophenyl) methanimine. (Compound 1) utilizing sodium borohydride in mixture of CH3OH-THF (1:1). The progress of reaction reviled by gradually demolitions of yellow color and the end of reaction was determined from convert the solution to off white then to colorless. Ice water was added at end of reaction to remove any excess of sodium borohydride and to remove sodium borate. compounds were 3a -h synthesized by cyclization compound 2 with several aryl aldehydes in concentration acetic acid as , Scheme 1 demonstrated the route of synthesized 3a-h.




**Scheme 1;** Synthetic route of Synthesis newly compounds 3a-h

The FTIR of compound 1 interesting band at 1620cm-1 attributed to two C=N groups, as will the spectrum shows band at 2997, 2945cm-1 for CH aliphatic. The bands of CH aromatic, C=C located at 3049 and 3026cm-1, the Band of NO2 group was located at 1444, 1300cm-1. disappearing the band of C=N from the FT-IR of compound 2 was good primary evidence for success of reduction of bis Schiff bases besides to appearing the NH band in IR spectrum at 23288 cm-1. The 1H NMR spectra of compound 1and compound 2 as well confirm the structure through appearing all protons peaks and their integration. The peak of imine group in compound located at 9.77 ppm and the two doublet peaks for 4-nitrophenyl group located at 7.4 ppm and 7.7 ppm with coupling constant equal 8.0 and 8.2 Hz respectively. Furthermore, all protons of tree CH2 for 1,3-propyl and the two CH2 of benzyl group were located at δ =2.31, 3.22 and 3.64ppm. the 1HNMR spectrum of compound 2 also exhibited all proposed protons peak besides to disappearing the peaks of imine group and new interested peak of NH was located at 4.04 ppm. The 13C NMR spectrum as well exhibited all carbons peaks and it assigned at the proposed location. The three different type carbons of CH2 recognized at 25.07, 26.91 and 35.04 ppm. Moreover, the four aromatic carbons were assigned at =152.55, 128.79, 114.27 and 112.15ppm. the absence band of NH from FT-IR spectra of compounds 3a-h considers good primary evidence for success cyclization reaction of compound 2 with proper aldehyde. Furthermore, existence bands belong to the substituted group for the aryl aldehyde was in agreement with the proposed structure. For example, the IR spectrum of compound 3b shows the band of OH at 3207 cm-1, while the OH of compound 3c located at 3438 cm-1, the rest bands were tabulated in Table 3.

**Table 3:** The FT-IR band for synthesis compounds 3a-3h

| No. | C-H aromatic | C-H aliphatic | C=C | NO2 symmetrical &asymmetrical | other bands |
|---|---|---|---|---|---|
| 3a | 3070 | 2924&2862 | 1595 | 1477,1373, | 739(C-Cl st.) |
| 3b | 3086, 3033 | 2972,2852 | 1610 | 1481,1406 | 3207 (OH st.) 1174 (Ar-O-C) |
| 3c | 3055 | 2952, 2837 | 1597 | 1466, 1379 | 3438 (OH st.) |
| 3d | 3083 | 2954,2864 | 1599 | 1473, 1363 | 869 (C-Br) |
| 3e | 3079 | 2997, 2831 | 1616, 1568 | 1408, 1336 | 872 (C-Br) |
| 3f | 3067 | 2891, 2854 | 1595 | 1431,1361 | 1174(Ar-O-C) 843(C-Br) |
| 3g | 3078 | 2981,2885 | 1593 | 1437,1360 | 812(C-Cl) |
| 3h | 3078 | 2927,2852 | 1610 | 1469, 1308 | - |

The 1H NMR for the synthesized hydro pyrimidines shows new peaks. the interested peak of CH for the hydro pyrimidines ring at rang 4.04-5.54 ppm. Furthermore, the 1H NMR spectra of these compounds depicted all protons of aryl attached the hydro pyrimidines ring at position two and their substituted group such as the proton of hydroxyl in compound 3b and 3c and the three protons of methomyl group in compounds 3f and 3b. The OH of compound 3b assigned at 10. 31ppm and the protons of OCH3 assigned at 3.88 ppm, the proton OH of compound 3c assigned at 10.03 ppm as well the three protons of 4-methoxyl group for compound 3f was located at 3.79 ppm. The CH2 group of 4-nitobenzyl appeared as multiplet and not as singlet peak and that attributed to 1,3- splitting with the CH2 at position four and six in pyrimidine ring as well 1,3-spliting with CH at position two of the pyrimidine ring[30]. Table 4 demonstrated the 1H NMR peaks for compounds 3a-h

**Table 4:** 1H NMR peaks of compounds 3a-h

| *No.* | *CH2 , ppm* | *CH of pyrimidine, ppm* | *Aromatic protons, ppm* | *Another peak ppm* |
|---|---|---|---|---|
| 3a | 2.21-2.25(m,2H), 4.3-4.35(m,8H) | 4.04( s,1H) | 6.75-6.83(m,3H), 7.23-7.38(m,7H), 7.9(d,2H, J=8.8 | - |
| 3b | 1.98-2.12(m ,2H) 3.68-3.98(m,8H) | 5.36 | 6.65-7.48(m, 11H) | 3.88(s,3H,OCH3) 10.31 (bs.1H,OH) |
| 3c | 2.21(m,2H),2.96-3.14(m,4H), 3.97-4.04(m,4H) | 5.0 (s,1H) | 7.45-7.56(m,4H), 7.15(d, 2H),7.93-7.97(m,6H) | 10.03(bs,1H,OH) |
| 3d | 2.70(m,2H),3.98-4.16(m,8H) | 5.21(s,1H) | 7.26-8.3(m,12H) | - |
| 3e | 1.94-2.13(m,2H),2.77-3.36(m,8H) | 5.34(s,1H) | 6.88-7.86(m,12H) | - |
| 3f | 2.14-2.33(m,2H), 3.84-4.04(m,4H),4.33-4.65(m,4H) | 5.54(s,1H) | 7.02-7.51(m,4H), 7.82-8.37(m,7H) | 3.79(s,3H, OCH3) |
| 3g | 1.34-1.56(m,2H), 3,31-3.37(m,4H),4.30-4.35 (m,4H) | 5.51(s,1H) | 6.95-8.45(m,12H) | |
| 3h | 1.37-1.46 (m, 2H), 3.2-3.65 (m,4H), 4.26-4.45 (m,45.4H) | 5.24(s,1H) | 7.24-7.52(m,12H) | |

the 13C NMR spectrum of these compound exhibited all expected carbons in the 2-Aryl hydro hydro pyrimidines ring including the carbons of substituted group in compound 3b and 3f. For example, Figure 1 depicted the 13C NMR spectrum of compound 3g

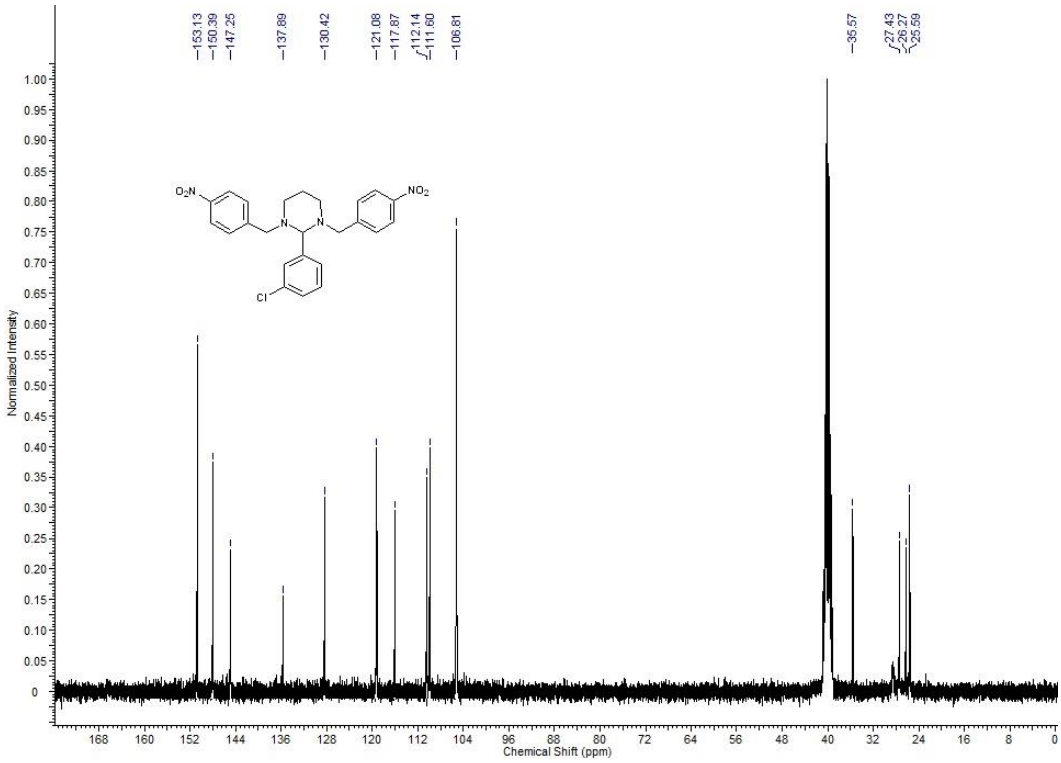



**Figure 1:** The 13C NMR spectrum of compound 3g in DMSO-d6.

the elemental analysis (CHN) for these compounds was in agreement with the proposed structure. the theoretical percentage value of CHN was matched the practical percentage value as demonstrated in Table 5.

**Table 5**: The elemental analysis (CHN) of synthesized compounds 3a-h

| *No.* | *Theoretical* | | | *Practical* | | | |
|---|---|---|---|---|---|---|---|
| | *% C* | *%H* | *%N* | *%C* | *%H* | *% N* | *Molecular wight* |
| 3a | 61.74 | 4.97 | 12 | 61.38 | 5.01 | 11.89 | 466.92 |
| 3b | 62.75 | 5.48 | 11.71 | 62.81 | 5.59 | 11.92 | 478.51 |
| 3c | 64.28 | 5.39 | 12.49 | 64.16 | 5.47 | 12.57 | 448.48 |
| 3d | 56.37 | 4.53 | 10.96 | 56.15 | 4.71 | 11.03 | 511.38 |
| 3e | 56.37 | 4.53 | 10.96 | 56.59 | 5.84 | 10.87 | 511.38 |
| 3f | 55.46 | 4.65 | 10.35 | 55.68 | 5.21 | 10.08 | 541.40 |
| 3g | 61.74 | 4.97 | 12.0 | 61.95 | 5.36 | 11.88 | 466.92 |
| 3h | 60.37 | 4.86 | 14.67 | 60.67 | 5.04 | 14.83 | 477.48 |

## Biological Activity

Heterocyclic rings considered an important class of cyclic Schiff base compounds having a wide spectrum of biological activity, the heterocyclic compounds are well known for antibacterial activity. The antibacterial activity and anti-fungal of the synthesized compounds were performed according to the agar diffusion method (241), using two types of bacteria; Escherichia coli (G-) and Staphylococcus aureus (G+). The prepared agar and petri dishes were sterilized by autoclaving for 20 min at 37oC. Each of tested compounds was dissolved in DMSO (which was used as a solvent and as control) to give concentration 10-2M. The zones of inhibition formed were measured in millimeter. The results in general showed that most of the tested compounds possess biological activity against the two types of the

bacteria and one type of antifungal. The biological activity of the synthesized compounds, which were exhibited good inhibition zones could be related to the type of heterocyclic cyclic Schiff base unit and active groups. Figures, 2and 3 showed the effect of these compounds on two types of bacteria. The results of heterocyclic cyclic Schiff base compounds are presented in Table 6.


**Figure 2**: Antibacterial activity of compounds against, Staphylococcus aureus (G+).

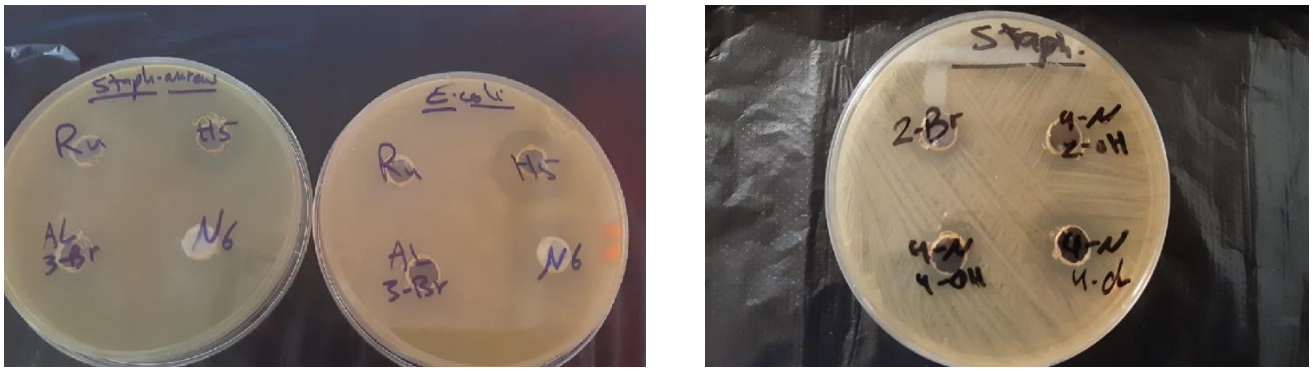



**Figure 3**: Antibacterial activity of compounds against Escherichia coli (G-).

**Table 6:** Inhibition Zones of cyclic Schiff base [3a-3h] compounds.

| *No.* | *Chemical Formula:* | *Inhibition Zone (mm.)* *Bacillius Staphylococcus G +* | *E. Coli G -* |
|---|---|---|---|
| 3a | C24H23ClN4O4 | 17 | 18 |
| 3b | C25H26N4O6 | 18 | 20 |
| 3c | C24H24N4O5 | 16 | 14 |
| 3d | C24H23BrN4O4 | 13 | 12 |
| 3e | C24H23BrN4O4 | 17 | 17 |
| 3f | C25H25BrN4O5 | 14 | 12 |
| 3g | C24H23ClN4O4 | 17 | 14 |
| 3h | C24H23N5O6 | 18 | 16 |

## Conclusion

synthesis of 2-(Aryl)-1,3-bis(4-nitrobenzyl)hexahydropyrimidine (3a-h) successfully synthesized from cyclization of N1,N3-bis(4-nitrobenzyl)propane-1,3-diamine. (2) with proper arylaldehyde in acetic acid. The proposed structure of this compounds was characterized from their IR, NMR spectrum besides to their CHN analysis. The antibacterial activity was tested against Escherichia coli (G-) and Staphylococcus aureus (G+). Compound 3b exhibited the highest inhibition, while compound 3d exhibited the less inhibition.

## Acknowledgment

The authors would like to acknowledge university of Baghdad four supporting this work, as well we would like to express deep thanks to Dr. Raied Mustafa Shakir for his cooperation and advices.

## References


Ghorab, M. M.; Abdel-Gawad, S. M.; El-Gaby, M. S. A., Synthesis and evaluation of some new fluorinated hydroquinazoline derivatives as antifungal agents. Il Farmaco 2000, 55, (4), 249-255.

Kappe, C. O., Biologically active dihydropyrimidones of the Biginelli-type — a literature survey. European Journal of Medicinal Chemistry 2000, 35, (12), 1043-1052.

Atwal, K. S.; Rovnyak, G. C.; O'Reilly, B. C.; Schwartz, J., Substituted 1,4-dihydropyrimidines. 3. Synthesis of selectively functionalized 2-hetero-1,4-dihydropyrimidines. The Journal of Organic Chemistry 1989, 54, (25), 5898-5907.

Lal, K.; Paliwal, L. J.; Bagade, M. B., New Dihydropyrimidines as Antimicrobial Agents. Materials Today: Proceedings 2017, 4, (4, Part E), 5657-5662.

Zohdi, H. F.; Rateb, N. M.; Elnagdy, S. M., Green synthesis and antimicrobial evaluation of some new trifluoromethyl-substituted hexahydropyrimidines by grinding. European Journal of Medicinal Chemistry 2011, 46, (11), 5636-5640.

Sapozhnikova, T. A.; Borisevich, S. S.; Kireeva, D. R.; Gabdrakhmanova, S. F.; Khisamutdinova, R. Y.; Makara, N. S.; Gibadullina, N. N.; Khursan, S. L.; Zarudii, F. S., Effects of novel hexahydropyrimidine derivatives as potential ligands of M1 muscarinic acetylcholine receptor on cognitive function, hypoxia-induced lethality, and oxidative stress in rodents. Behavioural Brain Research 2019, 373, 112109.

Sahu, M.; Siddiqui, N.; Sharma, V.; Wakode, S., 5,6-Dihydropyrimidine-1(2H)-carbothioamides: Synthesis, in vitro GABA-AT screening, anticonvulsant activity and molecular modelling study. Bioorg. Chem. 2018, 77, 56-67.

Tawfik, H. O.; El-Moselhy, T. F.; El-Din, N. S.; El-Hamamsy, M. H., Design, synthesis, and bioactivity of dihydropyrimidine derivatives as kinesin spindle protein inhibitors. Biorg. Med. Chem. 2019, 27, (23), 115126.

Venugopala, K. N.; Govender, R.; Khedr, M. A.; Venugopala, R.; Aldhubiab, B. E.; Harsha, S.; Odhav, B., Design, synthesis, and computational studies on dihydropyrimidine scaffolds as potential lipoxygenase inhibitors and cancer chemopreventive agents. Drug Des Devel Ther 2015, 9, 911-921.

Ramesh, B.; Bhalgat, C. M., Novel dihydropyrimidines and its pyrazole derivatives: Synthesis and pharmacological screening. European Journal of Medicinal Chemistry 2011, 46, (5), 1882-1891.

Khan, M. S. Y.; Gupta, M., Synthesis, Antiinflammatory and Analgesic Activity of New Hexahydropyrimidine Derivatives. ChemInform 2002, 33, (39), 156-156.

Mohamed, M. S.; Maki, T.; Shah, M. M.; Ichinose, Y., Synthesis and Antimicrobial Activity of Nitrobenzyl-oxy-phenol Derivatives. Biological & pharmaceutical bulletin 2016, 39, (11), 1888-1892.

Mohamed, M. S.; Maki, T.; Shah, M. M.; Ichinose, Y., Synthesis and Antimicrobial Activity of Nitrobenzyl-oxy-phenol Derivatives. Biol. Pharm. Bull. 2016, 39, (11), 1888-1892.

Gravatt, G. L.; Baguley, B. C.; Wilson, W. R.; Denny, W. A., DNA-Directed Alkylating Agents. 6. Synthesis and Antitumor Activity of DNA Minor Groove-Targeted Aniline Mustard Analogs of Pibenzimol (Hoechst 33258). J. Med. Chem. 1994, 37, (25), 4338-4345.

Soderlind, K.-J.; Gorodetsky, B.; Singh, A. K.; Bachur, N. R.; Miller, G. G.; Lown, J. W. J. A.-c. d. d., Bis-benzimidazole anticancer agents: targeting human tumour helicases. 1999, 14, (1), 19-36.

Yao, W.; Liu, C.; Wang, N.; Zhou, H.; Shafiq, F.; Yu, S.; Qiao, W., O-nitrobenzyl liposomes with dual-responsive release capabilities for drug delivery. J. Mol. Liq. 2021, 334, 116016.

Wang, X.; Yang, Y.; Liu, C.; Guo, H.; Chen, Z.; Xia, J.; Liao, Y.; Tang, C.-Y.; Law, W.-C., Photo- and pH-responsive drug delivery nanocomposite based on o-nitrobenzyl functionalized upconversion nanoparticles. Polymer 2021, 229, 123961.

Raied Mustafa Shakir; Khalid Fahad Ali; Dhuha Faruk Hussain, Synthesis and Antioxidant Ability of Some New 6-amino-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazin-3-yl) Derivatives Bearing 2,6-Dimethoxy-4-(methoxymethyl)Phenol. Oriental Journal Of Chemistry 2017, 33, (5), 2492-2500.

shaimaa Abed Saoud; Khalid Fahad Ali; Raied Mustafa Shakir, Relationship Between the Structure of Newly Synthesized Derivatives of 1,3,4-Oxadiazole Containing 2-Methylphenol and their Antioxidant and Antibacterial Activities. . Orient J Chem 2017, 33, (4), 1781-1798.

Raied M. Shakir; Shaimaa A. Saoud; Husam S. Jasim; Dhuha F. Hussain, Synthesis, Antioxidant Activity And Molecular Docking Study of 1,2,4-Triazole And Their Corresponding Fused Rings Containing 2-Methylphenol. IJDDT 2021, 11, (2), 501-511.

MURAKAMI, Y.; KAWATA, A.; KATAYAMA, T.; FUJISAWA, S., Anti-inflammatory Activity of the Artificial Antioxidants 2-Tert-butyl-4-methoxyphenol (BHA), 2,6-Di-tert-butyl-4-methylphenol (BHT) and 2,4,6-Tri-tert-butylphenol (TBP), and their Various Combinations. In Vivo 2015, 29, (2), 197-206.

Zhang, T.-T.; Hu, T.; Jiang, J.-G.; Zhao, J.-W.; Zhu, W., Antioxidant and anti-inflammatory effects of polyphenols extracted from Ilex latifolia Thunb. RSC Advances 2018, 8, (13), 7134-7141.

Maddox, C. E.; Laur, L. M.; Tian, L., Antibacterial activity of phenolic compounds against the phytopathogen Xylella fastidiosa. Curr Microbiol 2010, 60, (1), 53-58.

Attar, U. A.; Ghane, S. G., In vitro antioxidant, antidiabetic, antiacetylcholine esterase, anticancer activities and RP-HPLC analysis of phenolics from the wild bottle gourd (Lagenaria siceraria (Molina) Standl.). South African Journal of Botany 2019, 125, 360-370.

Naqi Ahamad, M.; Iman, K.; Raza, M. K.; Kumar, M.; Ansari, A.; Ahmad, M.; Shahid, M., Anticancer properties, apoptosis and catecholase mimic activities of dinuclear cobalt(II) and copper(II) Schiff base complexes. Bioorg. Chem. 2020, 95, 103561.

Shukla S.N., G. P., Gupta J.P., Mathews S. and Rai N., SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL ACTIVITY OF COMPLEXES OF PALLADIUM WITH SCHIFF BASES DERIVED FROM 1, 3-DIAMINOPROPANE International Journal of Basic and Applied Chemical Sciences 2015, 5, (1), 18-28.

Bomfim, J. A. S.; Wardell, J. L.; Low, J. N.; Skakle, J. M. S.; Glidewell, C., [pi]-Stacked hydrogen-bonded sheets in N,N'-bis(4-nitrobenzylidene)ethane-1,2-diamine and [pi]-stacked hydrogen-bonded chains in N,N'-bis(4-nitrobenzylidene)propane-1,3-diamine. Acta Crystallographica Section C 2005, 61, (1), o53-o56.

Shakir, R. M.; Ariffin, A.; Ng, S. W., Ethyl 4-[(3,5-di-tert-butyl-2-hy-droxy-benzyl-idene)-amino]-benzoate. Acta Crystallogr Sect E Struct Rep Online 2010, 66, (Pt 11), o2915.

Shakir, R. M.; Ariffin, A.; Ng, S. W., Ethyl 4-[(3,5-di-tert-butyl-2-hydroxy-benzyl)amino]-benzoate. Acta Crystallogr Sect E Struct Rep Online 2010, 66, (Pt 11), o2916.

Robert M. Selverstein, F. X. W., Spectromeetric Identification Of Organic Compounds. Jon Wiley & Sons Inc. : New York, 1998; p 90-91.