DOI: 10.17344/acsi.2018.4719 *Acta Chim. Slov.* **2019,** *66,* 552–559

Scientific paper

Synthesis and Characterization of Novel Five-Membered Heterocycles and Their Activity against Candida Yeasts

Hiba Maher Tawfeeq,[1] Rasim Farraj Muslim,[2] Obaid Hasan Abid[3] and Mustafa Nadhim Owaid[2,4]

[1] *Department of Chemistry, College of Education for Pure Sciences, University Of Anbar, Anbar 31001, Iraq*

[2] *Department of Ecology, College of Applied Sciences, University Of Anbar, Anbar 31007, Iraq*

[3] *Department of Scientific Affairs and Graduate Studies, University of Fallujah, Anbar, Iraq*

[4] *Department of Heet Education, General Directorate of Education in Anbar, Ministry of Education, Anbar 31007, Iraq*

* *Corresponding author: E-mail: dr.rasim92hmts@gmail.com*

Received: 09-14-2018

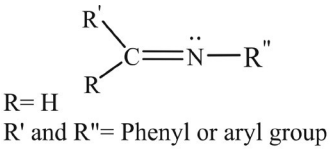
Abstract

Some new tetrazole derivatives were prepared by the reaction between the prepared azomethine compounds $\mathbf{I_6}$–$\mathbf{I_{10}}$ with sodium azide in anhydrous tetrahydrofuran (THF) with a few drops of distilled water and under reflux conditions. Azomethine compounds were prepared by thermal condensation reactions of aromatic aldehydes with primary aromatic amines. The prepared compounds (tetrazole derivatives) were screened for their antibacterial activity (by disc diffusion method). Compound $\mathbf{I_6}$ is the most active derivative that has recorded a significantly (p<0.01) stronger influence to inhibit the growth of *Candida zeylanoides* with an average zone of inhibition of 26.0 mm. Derivatives $\mathbf{I_7}$ and $\mathbf{I_9}$ showed the lowest zone of inhibition of 8.0 mm against *Candida zeylanoides*. This study may be helpful in designing more potential anticandidal agents for therapeutic use in the future.

Keywords: *Candida* sp.; pharmaceutical; azomethine; sodium azide; biological activity.

1. Introduction

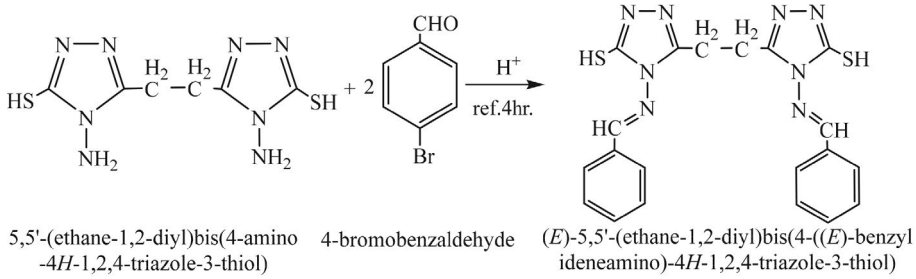
Azomethine compounds discovered by Hugo Schiff in 1864, can be prepared by different methods, one of the more important being the condensation reaction between primary amine with aldehyde.[1] Azomethine compounds contain the N=C group.[2] Some of the azomethine compounds are used as antibacterial agents.[3,4] The structure of azomethine compounds usually includs a phenyl or aryl group with the double bond between the carbon atom and the nitrogen atom.[5,6] (Scheme 1)



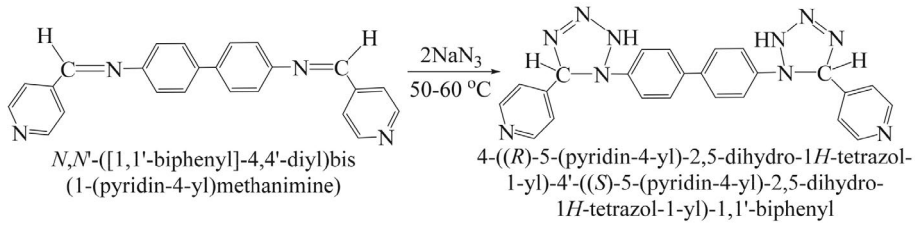
Scheme 1. Structure of azomethine compounds

The reaction of triazole diamine compound with 4-bromobenzaldehyde in the presence of glacial acetic acid gave the next product.[7] (Scheme 2)

Tetrazole derivatives are heterocyclic compounds containing four nitrogen atoms and one carbon atom within one ring.[8] Tetrazoles as a group of heterocyclic compounds appear in IR spectra as broad signals; having peculiar biological activities.[9,10] Tetrazole derivatives have a special structure and can display anti-bacterial properties, such as antiviral and anti-allergic.[11–13] There are several methods to prepare tetrazole derivatives, and each method depends on the constituents of the reaction.[14] Recently, there were many various types of compounds (including such containing a metal centre coordinated with suitable ligands) tested against *Candida albicans*, with a varying degree of success.[15–17] An example of one of tetrazole derivatives is the product from the reaction between azomethine compound (biphenyl bis



Scheme 2. Using glacial acetic acid to prepare the azomethine compound



Scheme 3. Use of sodium azide to prepare tetrazole derivatives

(1-(pyridin-4-yl) methanimine)) with sodium azide.[18] (Scheme 3)

Many of tetrazole derivatives can be prepared by the reaction between a different aldehyde and different amines.[10] (Scheme 4)

In this study, tetrazole derivatives derived from the reaction of the prepared azomethine compounds with sodium azide were evaluated for their biological activity against four types of *Candida* yeasts. The products were identified by their melting points, FT-IR and ^{1}H NMR spectra**.**

2. Experimental

2. 1. Apparatuses

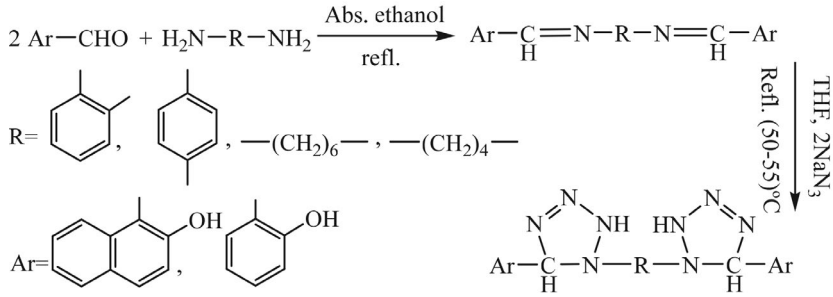
The measurement of melting point was conducted by the electrothermal melting point apparatus. IR spectra were recorded at room temperature in the range of 400–4000 cm^{-1} by a Fourier transform infra-red Spectrophotometer Model Tensor 27 Bruker Co., Germany. The ^{1}H NMR spectra were recorded on Bruker Ac-300 MHz spectrometer.

2. 2. Preparation of Azomethine Compounds I_1–I_5

Azomethine compounds were prepared according to the literature procedure,[19,20] as shown in Table 1. An equimolar mixture 0.02 mole of aldehydes and 0.02 mole of amines and trace of acidic catalyst in 25 mL absolute ethanol were reacted at reflux temperature for 4 hours, whereby a crystalline solid separated out. The products were filtered off and recrystallized from absolute ethanol.

2. 3. Preparation of Tetrazole Derivatives I_6–I_{10}

A mixture of azomethine compounds (0.01 mol) and sodium azide (0.01 mol) was dissolved in 20 mL of THF and 2 mL distilled water and refluxed for 4 hour and left to stand for 24 hour at room temperature, then the solid product separated out.[21] The products were filtered off and recrystallized from absolute ethanol as shwon in Table 2.



Scheme 4. Prepared tetrazole derivatives with double rings

Table 1. Names, structural formulae, symbol, yields, colors and melting points of azomethine compounds I_1–I_5

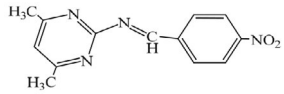
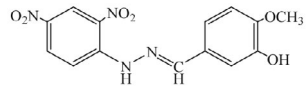
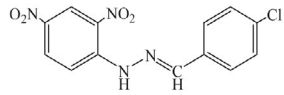
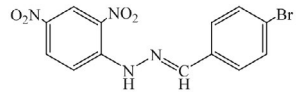
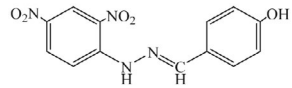
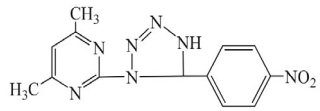
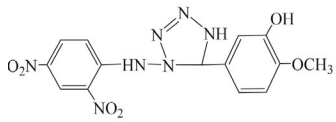
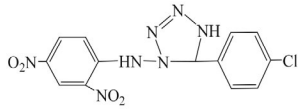
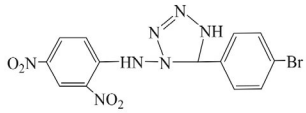
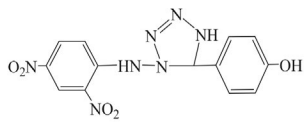
Nomenclature	Structural formula	Compound	Yield %	Color	m.p. °C
(*E*)-4,6-dimethyl-*N*-(4-nitro benzylidene) pyrimidin-2-amine		**I_1**	78%	Bright pale yellow	79–81
(*E*)-5-((2-(2,4-dinitro phenyl) hydrazono)methyl)-2-methoxyphenol		**I_2**	80%	Dark red	250–252
(*E*)-1-(4-chlorobenzylidene) -2-(2,4-dinitro phenyl) hydrazine		**I_3**	82%	Orange	236–238
(*E*)-1-(4-bromobenzyl idene) -2-(2,4-dinitro phenyl) hydrazine		**I_4**	84%	Orange	232–234
(*E*)-4-((2-(2,4-dinitro phenyl) hydrazono) methyl)phenol		**I_5**	80%	Bright Dark red	240–242

Table 2. Names, structural formulae, symbol, yields, colors and melting points of tetrazole derivatives I_6–I_{10}

Nomenclature	Structural formula	Compound	Yield %	Color	m.p. °C
4,6-dimethyl-2-(5-(*p*-nitro phenyl)-4,5-dihydro-1*H*-tetrazol-yl)pyrimidine		**I_6**	76%	Bright tan	96–98
5-((2,4-dinitrophenyl) amino)-4,5-dihydro-1*H*-tetrazol-yl-2-methoxy phenol		**I_7**	83%	Red	276–279
5-(*p*-chlorophenyl)-N-(2,4-dinitrophenyl)-4,5-dihydro -1*H*-tetrazol-1-amine		**I_8**	78%	Orange	256–258
5-(*p*-bromophenyl)-N-(2,4-dinitrophenyl)-4,5-dihydro -1*H*-tetrazol-1-amine		**I_9**	78%	Orange	260–262
4-(1-((2,4-dinitrophenyl) amino)-4,5-dihydro-1*H*-tetrazol-yl) phenol		**I_{10}**	92%	Orange	272–274

2. 4. Activity against *Candida* Yeasts

This test was carried out *in vitro* to investigate the inhibitory effects of the prepared tetrazole derivatives using well diffusion method on Muller-Hinton agar. This experiment was done as mentioned by Owaid *et al.* with some modifications.[22] Four milligrams of the prepared tetrazole derivatives were applied separately in 6 mm-well. After 18 hour at 37 °C, the zone of inhibition was measured using the ruler in millimeters.

3. Results and Discussion

Tables 1 and 2 show structural formulae, names, yields, melting points and color of all prepared compounds **I_1–I_{10}**. The best yield achieved for the prepared azomethine compounds was for compounds **I_3** 82% and **I_4** 84%, while the lowest yield was for compound **I_1** 78% and the best yield of the prepared tetrazole derivatives was for **I_{10}** 92%, while the lowest yield was for **I_6** 76%. The highest melting point for azomethine compounds was for com-

pound $\mathbf{I_2}$, the lowest melting point was for compound $\mathbf{I_1}$, while the highest melting point of the prepared tetrazole derivatives was for compound $\mathbf{I_7}$, the lowest melting point was for compound $\mathbf{I_6}$. The different colors and melting points of the products compared with the raw material are initial evidence of interaction.

3. 1. Azomethine Compounds $\mathbf{I_1}$–$\mathbf{I_5}$

Azomethine compounds were prepared from commercially available aldehydes with primary amines and identified by their melting points and FT-IR spectra. Table 3 shows the appearance of the stretching absorption bands of the characteristic groups of the resulting group (C=N) at 1609–1681cm^{-1} beside the characteristic bands of the residual groups in the structure, being indicative of the formation of the products.[23,24]3, 4, 9a- Tetrahydrobenzo [e] [1,3] oxazepin- 5(5aH

The reaction involves a nucleophile attack of the electron pair of the amino group (NH_2) of aromatic amine on the carbonyl group (C=O) of aromatic aldehydes to form an *N*-substituted hemiaminal; in a suitable medium it can eliminate a water molecule to give the stable compound (azomethine).[20]

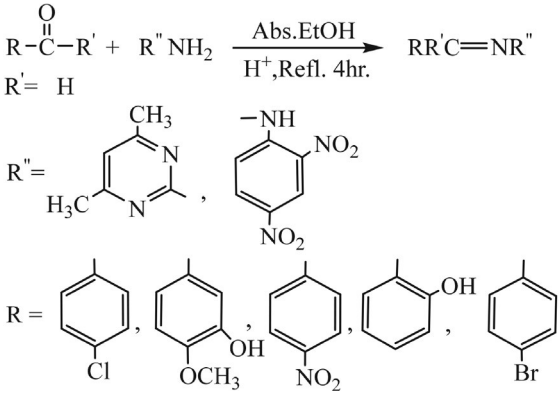
3. 2. Tetrazole Derivatives $\mathbf{I_6}$–$\mathbf{I_{10}}$

In this work, the preparation of tetrazole compounds was achieved by the reaction between prepared azomethine compounds ($\mathbf{I_1}$–$\mathbf{I_5}$) with sodium azide. The resulting products were identified using the melting points, FT-IR and ^{1}H NMR spectra. Table 4 shows characteristic stretching absorption bands at 1219–1286 cm^{-1}, 1007–1083 cm^{-1} and 1487–1509 cm^{-1} indicative of C–N, N–N and N=N bonds of tetrazol rings beside the characteristic stretching absorption bands of the residual groups in their structure.[27]

Table 3. FT-IR of azomethine compounds $\mathbf{I_1}$–$\mathbf{I_5}$

Compound	FT-IR, ν (cm^{-1})						
	C=N	C=C Aromatic	C–H Aromatic	C–H Alkene	C–H Aliphatic Asymmetric	C–H Aliphatic Symmetric	Others
$\mathbf{I_1}$	1681	1601	3042	3105	2969	2849	NO_2 1529, 1340, C=N pyrimidine 1634
$\mathbf{I_2}$	1609	1580	3042	3113	2972	2945	NO_2 1500, 1328 O–H 3491, NH 3278
$\mathbf{I_3}$	1609	1581	3041	3089	–	–	NO_2 1508, 1317 N–H 3283, C–Cl 823
$\mathbf{I_4}$	1611	1581	3042	3087	–	–	NO_2 1505, 1324 N–H 3263
$\mathbf{I_5}$	1615	1592	3042	3112	–	–	NO_2 1508, 1305 O–H 3422, N–H 3257

The general equation (Scheme 5) represents the main reaction through which the prepared azomethine compounds were obtained. The mechanism of azomethine compounds formation was thoroughly studied and established by many authors in the literature.[25,26]



Scheme 5. The main reaction of azomethine compounds

The ^{1}H NMR spectrum of compound $\mathbf{I_7}$ (Fig. 1, in solvent DMSO-d_6) showed the following signals: singlet at δ 1.76 indicating the presence of 3H as o methoxy group (OCH_3), singlet at δ 3.83 indicating the presence of 1H as an NH group (NH outside of the tetrazole ring), singlet at δ 8.55 indicating the presence of 1H as another NH group (NH inside of the tetrazole ring), singlet at δ 9.33 indicating the presence of 1H as one CH group (N-CH), singlet at δ 11.56 indicating the presence of 1H as one hydroxy group (OH), multiplet at δ 8.96–6.99 indicating the presence of 6H of aromatic protons. ^{1}H NMR spectrum of compound $\mathbf{I_8}$ (Fig. 2) shows the following signals: singlet at δ 3.33 indicating the presence of 1H as an NH group (NH outside of the tetrazole ring), singlet at δ 8.71 indicating the presence of 1H as another NH group (NH inside of the tetrazole ring), singlet at δ 11.71 indicating the presence of 1H as one CH group (N-CH), multiplet and doublet of doublet at δ 8.41–7.56 indicating the presence of 7H of aromatic protons.[27] Other chemical shifts for compounds $\mathbf{I_6}$, $\mathbf{I_9}$ and $\mathbf{I_{10}}$ are given in Table 5.

Table 4. FT-IR of tetrazole derivatives $\mathbf{I_6}$–$\mathbf{I_{10}}$

Compound	FT-IR ν (cm^{-1})								
	N–H	N–N	N=N	C–N	C=C Aromatic	C–H Aromatic	C–H Aliphatic Asymmetric	C–H Aliphatic Symmetric	Others
$\mathbf{I_6}$	3383	1007	1500	1286	1606	3044	2976	2849	NO_2 1541, 1345
$\mathbf{I_7}$	3280	1020	1509	1273	1614	3113	2972	2880	O–H b 3497 NO_2 1540, 1339
$\mathbf{I_8}$	3266	1083	1489	1219	1615	3088	–	–	NO_2 1514, 1339 C–Cl 833 C–H 2951
$\mathbf{I_9}$	3299	1083	1487	1269	1585	3067	–	–	NO_2 1512, 1330 C–H 2950 O–H b 3423
$\mathbf{I_{10}}$	3258	1074	1488	1276	1612	3113	–	–	NO_2 1509, 1305 C–H 2977

Table 5. The ^{1}H NMR spectral data of tetrazole derivatives $\mathbf{I_6}$–$\mathbf{I_{10}}$ (in DMSO-d_6).

Compound	Chemical Shifts δ (ppm)
$\mathbf{I_6}$	Singlet at 1.28 (6H, 2 $\underline{CH_3}$), singlet at 8.68 (H, -$\underline{NH}$), singlet at 10.19 (1H, N-$\underline{CH}$), singlet at 9.77 (1H, -$\underline{OH}$), singlet and doublet of doublet at 8.43–8.08 (5H, aromatic protons).
$\mathbf{I_7}$	Singlet at 1.76 (3H, O-$\underline{CH_3}$), singlet at 3.83 (1H, $\underline{NH\ out}$), singlet at 8.55 (1H, $\underline{NH\ in}$), singlet at 9.33 (1H, N-$\underline{CH}$), singlet at 11.56 (1H, -$\underline{OH}$), multiplet at 8.96–6.99 (6H, aromatic protons).
$\mathbf{I_8}$	Singlet at 3.33 (1H, $\underline{NH}$ outside of the tetrazole ring), singlet at 8.71 (1H, $\underline{NH}$ inside of the tetrazole ring), singlet at 11.71 (1H, N-$\underline{CH}$), multiplet and doublet of doublet at 8.41–7.56 (7H, aromatic protons).
$\mathbf{I_9}$	Singlet at 3.26 (1H, $\underline{NH}$ outside of the tetrazole ring), singlet at 8.69 (1H, $\underline{NH}$ inside of the tetrazole ring), singlet at 11.71 (1H, N-$\underline{CH}$), multiplet at 8.41–7.79 (7H, aromatic protons).
$\mathbf{I_{10}}$	Singlet at 3.40 (1H, $\underline{NH\ out}$), singlet at 8.88 (1H, $\underline{NH\ in}$), singlet at 10.07 (H, N-$\underline{CH}$), singlet at 11.57 (1H, -$\underline{OH}$), multiplet and doublet of doublet at 8.59–6.85 fr (7H, aromatic protons).

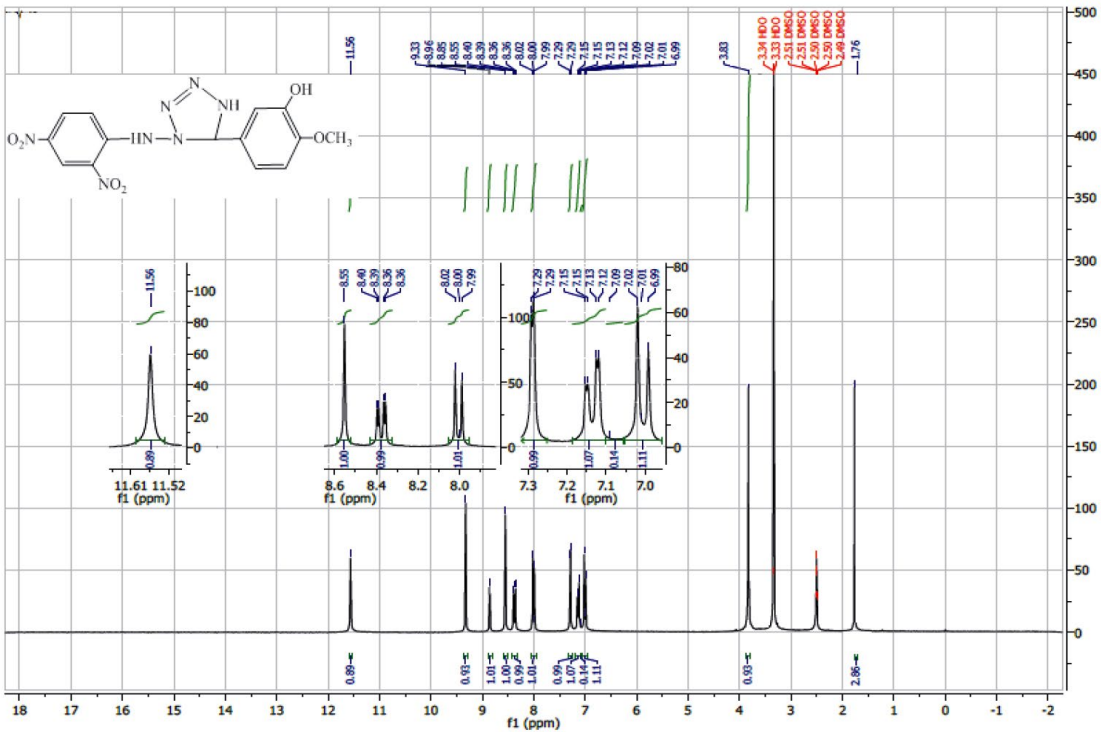


Figure 1. ^{1}H NMR Spectrum of $\mathbf{I_7}$

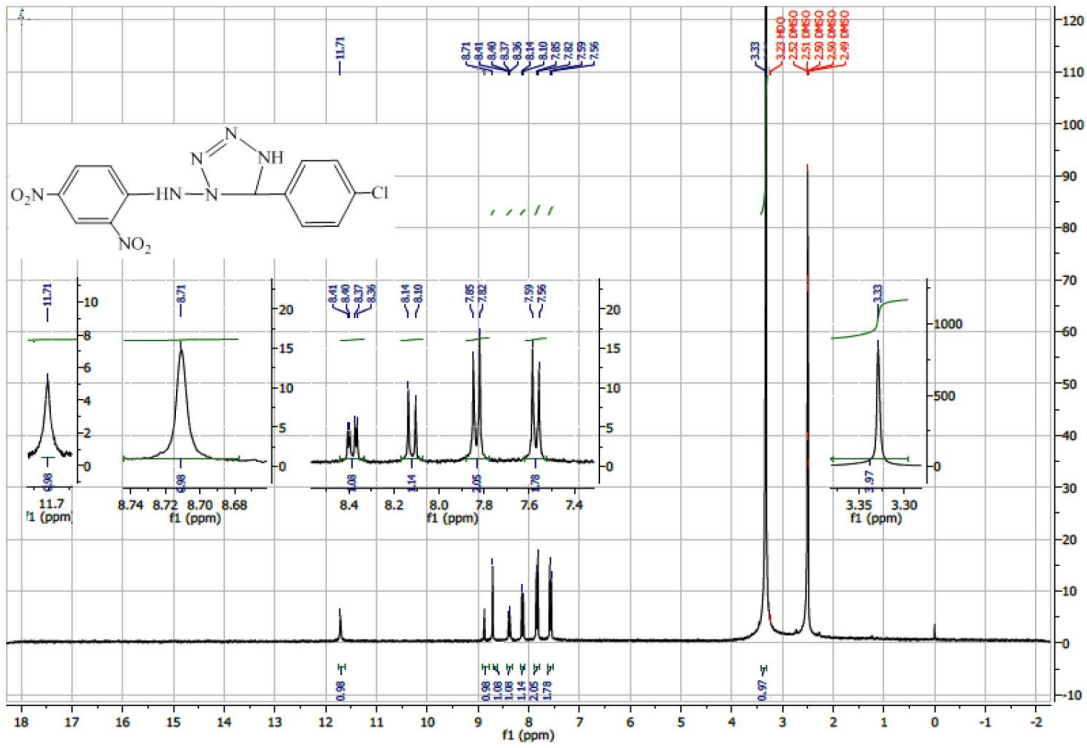
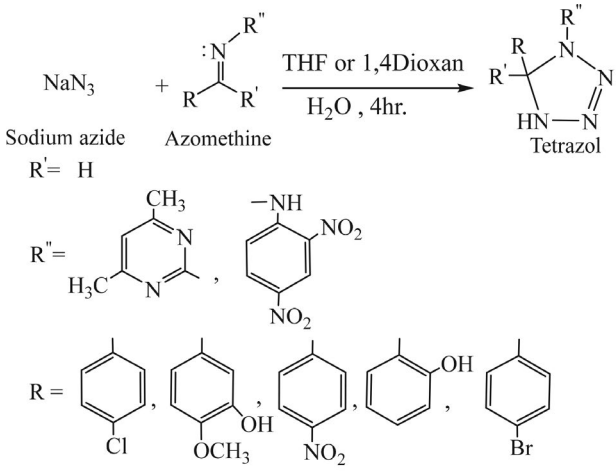


Figure 2. ^{1}H NMR Spectrum of $\mathbf{I_8}$

The reaction of the azomethine compounds with sodium azide is given in the equation in Scheme 6.



Scheme 6. The main reaction of the prepared tetrazole derivatives

From the reaction course and the suggested mechanism it may be concluded that the reaction takes place *via* concerted mechanism (Huisgen 1,3-dipolar cycloaddition).[28]

3. 3. Activity against *Candida* Yeasts

Zone of inhibition of some human pathogenic yeasts was determined by the well-diffusion method and used to test the potential of the prepared tetrazole derivatives ($\mathbf{I_6}$–$\mathbf{I_{10}}$) as shown in Fig. 3 and 4. Compound $\mathbf{I_6}$ was found to be the best derivative that has significantly (p<0.01) recorded a stronger influence to inhibit the growth of *Candida zeylanoides* at an average of the zone of inhibition of 26.0 mm, followed by 24.6–25.6 mm for the rest of the species of *Candida*. Next, $\mathbf{I_8}$ derivative recorded zone of inhibition of 11.0 mm toward *Candida guilliermondii*. Furthermore, $\mathbf{I_7}$ and $\mathbf{I_9}$ showed the lowest zone of inhibition of only 8.0 mm against *Candida zeylanoides.* Additionally, $\mathbf{I_6}$ derivative recorded zone of inhibition of 11.3 mm against *Candida guilliermondii* and *Candida zeylanoides*, respectively. Compound $\mathbf{I_{10}}$ did not inhibit the growth of *Candida* species as shown in Fig. 3. Resistance mechanism depends on which specific paths are inhibited by the drugs

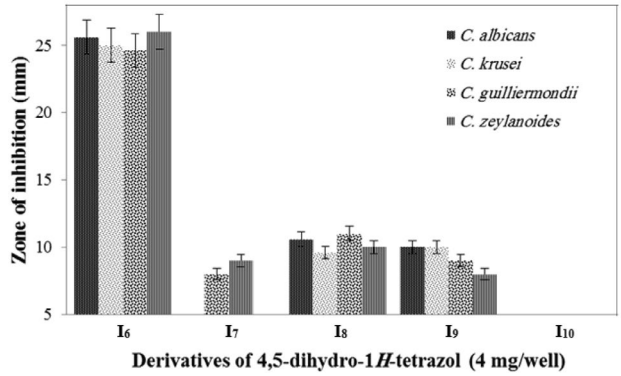


Figure 3. Zone of inhibition of *Candida* sp. using the prepared tetrazole derivatives

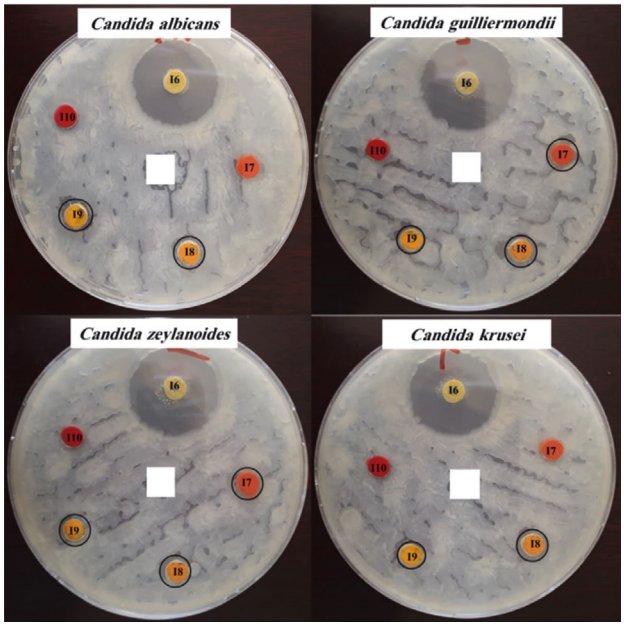


Figure 4. Activity against *Candida* yeasts of the prepared tetrazole derivatives $\mathbf{I_6}$–$\mathbf{I_{10}}$

and if the alternative paths are available to substitute for those paths that the compound has inhibited; in this way the microorganism can modify its pathways and be able to survive by developing resistence.[29,30] These results agree with some recent studies which described the synthesis of hybrid heterocycles proving to have *in vitro* antimicrobial, antibacterial and antifungal activities.

4. Conclusions

The results of FT-IR and ^{1}H NMR showed that the five-membered ring compounds were the least obstructed during all preparation processes and that neither light nor humidity affect the prepared compounds, this proving that the prepared compounds have an excellent stability. $\mathbf{I_6}$ is the best derivative that has significantly ($p < 0.01$) recorded a stronger influence to inhibit the growth of *Candida zeylanoides* at an average zone of inhibition of 26.0 mm. This study may be helpful in designing more potential anticandidal agents for therapeutic use in the future.

5. Acknowledgements

Special thanks to Anbar University's President Professor Dr. Khalid Battal Najim for his continuous support to publishing the research in certified international journals, thanks to Dr. Jalal Abdul Kareem for helping to measure the ^{1}H NMR spectra. Also, grateful is for College of Education for Pure Sciences, University Of Anbar for helping to measurement the FT-IR spectra.

6. References

1. A. Adabiardakani, H. Mohammad, H. Kargar, *World Appl. Progr*. **2012**, *2*, 472–476.
2. M. A. Ashraf, K. Mahmood, A. Wajid, M. J. Maah, I. Yusoff, *Int. Proc. Chem. Biol. Environ. Eng.* **2011**, *10*, 1–7.
3. M. A. Ashraf, A. Wajid, K. Mahmood, M. J. Maah, I. Yusoff, *Orient. J. Chem*. **2011**, *27*, 363–372.
4. A. Golcu, M. Tumer, H. Demirelli, R. A. Wheatley, *Inorg. Chim. Acta* **2005**, *358*, 1785–1797. **DOI:**10.1016/j.ica.2004.11.026
5. K. Brodowska, E. Łodyga-Chruścińska, *Chemik* **2014**, *68*, 129–134.
6. Z. Hussain, Z. Fadhil, H. Adil, M. Khalaf, B. Abdullah, E. Yousif, *Res. J. Pharm. Biol. Chem. Sci.* **2016**, *7*, 1500–1510.
7. A. A. Younus, N. R. Jber, *J. Al-Nahrain Uni-Sci*. **2017**, *20*, 1–6. **DOI:**10.22401/JNUS.20.2.01
8. R. Ranjith, *J. Chem. Pharm. Res*. **2016**, *8*, 505–526.
9. B. Akhlaghinia, S. Rezazadeh, *J. Braz. Chem. Soc*. **2012**, *23*, 2197–2203. **DOI:**10.1590/S0103-50532013005000005
10. H. A. Basheer, A. A. Ibrahim, M. S. Ahmed, *Swift J. Pure Appl. Chem*. **2016**, *2*, 1–3.
11. T. Mavromoustakos, A. Kolocouris, M. Zervou, P. Roumelioti, J. Matsoukas, R. Weisemann, *J. Med. Chem*. **1999**, *42*, 1714–1722. **DOI:**10.1021/jm980499w
12. N. Mekni, A. Baklouti, *J. Fluorine Chem*. **2008**, *129*, 1073–1075. **DOI:**10.1016/j.jfluchem.2008.06.019
13. D. Varadaraji, S. S. Suban, V. R. Ramasamy, K. Kubendiran, J. S. K. Raguraman, S. K. Nalilu, H. N. Pati, *Org. Commun*. **2010**, *3*, 45–56.
14. L. Myznikov, A. Hrabalek, G. Koldobskii, *Chem. Heterocycl. Comp*. **2007**, *43* 1–9. **DOI:**10.1007/s10593-007-0001-5
15. J. Lazarević, A. Kolarević, G. Stojanović, A. Šmelcerović, P. Ciuffreda, E. Santaniello, *Acta Chim. Slov*. **2018**, *65*, 801–810. **DOI:**10.17344/acsi.2018.4380
16. A. Srinivas, M. Sunitha, P. Karthik, K. V. Reddy, *Acta Chim. Slov*. **2017**, *64*, 1030–1041. **DOI:**10.17344/acsi.2017.3805
17. Y. J. Han, L. Wang, Q. B. Li, L. W. Xue, *Acta Chim. Slov*. **2017**, *64*, 179–185.
18. R. M. Al-Juburi, *J. Al-Nahrain Uni-Sci*. **2012**, *15*, 60–67. **DOI:**10.22401/JNUS.15.4.07
19. O. H. Abid, R. F. Muslim, K. M. Mohammed, *J. Uni. Anbar Pure Sci*. **2016**, *10*, 1–9.
20. R. F. Muslim, H. M. Tawfeeq, M. N. Owaid, O. H. Abid, *Acta Pharm. Sci*. **2018**, *56*, 39–57. **DOI:**10.23893/1307-2080.APS.05610
21. B. P. A. M. R. B. Srinivas, *Der Pharma Chemica*. **2016**, *8*, 84–93.
22. M. N. Owaid, J. Raman, H. Lakshmanan, S. S. S. Al-Saeedi, V. Sabaratnam, I. A. Abed, *Mater. Lett*. **2015**, *153*, 186–190. **DOI:**10.1016/j.matlet.2015.04.023
23. R. M. A. K. M. O. Abid, *J. Uni. Anbar Pure Sci*. **2016**, *10*, 8–18.
24. O. H. Abid, H. M. Tawfeeq, R. F. Muslim, *Acta Pharm. Sci*. **2017**, *55*, 43–55.
25. J. Simek, Organic Chemistry, Pearson education, Inc., New York, 2013.

26. O. Abid, A. Ahmed, Spectrometric identification of organic compounds, John Wiley and Sons, Inc., New York, 2005.
28. R. Das, N. Majumdar, A. Lahiri, *Int. J. Radiat. Phys. Chem*. **2014**, *4*, 467–472.
29. F. C. Tenover, *Am. J. Med*. **2006**, *119*, S3–S10. **DOI:**10.1016/j.amjmed.2006.03.011
30. M. N. Owaid, R. F. Muslim, H. A. Hamad, *Jordan J. Biol. Sci*. **2018**, *11*, 401–405.

Povzetek

Z reakcijo natrijevega azida s predhodno pripravljenimi azometinskimi spojinami $\mathbf{I_6}$–$\mathbf{I_{10}}$ smo v brezvodnem tetrahidrofuranu (THF) ob dodatku nekaj kapljic destilirane vode pod pogoji refluksa pripravili nekaj novih derivatov tetrazola. Azometinske spojine smo sintetizirali s termično kondenzacijo aromatskih aldehidov s primarnimi aromatskimi amini. Pripravljenim spojinam (derivatom tetrazola) smo določili antibakterijske aktivnosti (z metodo difuzije v disku). Spojina $\mathbf{I_6}$ se je izkazala za najbolj aktivni derivat z visoko ($p < 0.01$) povečanim vplivom zaviranja rasti organizma Candida zeylanoides (s povprečno vrednostjo premera inhibicije 26.0 mm). Derivata $\mathbf{I_7}$ in $\mathbf{I_9}$ pa sta izkazala najslabše inhibitorno delovanje s premerom inhibicije le 8.00 mm proti istemu organizmu (Candida zeylanoides). Ta študija bi lahko pomagala pri načrtovanju novih bolj učinkovitih spojin proti kvasom iz rodu Candida, ki bi bile v prihodnosti celo uporabne v terapevtske namene.