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Synthesis and Study Antimicrobial Activities of Some Novel Tetrazole Derivatives

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FOUR (2-phenol derivatives) were coupled with 1*H*-tetrazole-5-diazonium chloride to synthesize four new compounds namely 4-((1H-tetrazol-5-yl)diazenyl)-2-alkylylphenol (T_{a-d}). These prepared Azophenols reacted with two 4-alkoxy acids (8 and 10) to form two new series of 4-((1*H*-tetrazol-5-yl) diazenyl)-2-(alkyl)-phenyl-4-(octyloxy) benzoates T_{8a-d} and 4-((1*H*-tetrazol-5-yl)diazenyl)-2-(alkyl)-phenyl-4-(decyloxy) benzoates T_{10a-d} respectively. The structures of the twelve synthesized compounds were confirmed using the conventional tools of analysis, Elemental Analysis, FT-IR and ^{1}H-NMR spectroscopy. The biological activity of the prepared compounds as anti-fungi and anti-bacteria was studied. Most of the prepared compounds possessed good antimicrobial action for *Gram-positive and Gram-negative* bacteria, whereas they gave no action on *Aspergillus fumigatus* or *Candida albicans*.

Keywords: Tetrazoles, Diazotization, Phenols, ^{1}H-NMR, Biological activity.

Introduction

Lately, research on active nitrogen-rich substances has received considerable attention for several reasons. First, their high positive enthalpies may release a large amount of heat on combustion as dinitrogen (N_2) is one of the major products [1]. Second, the formed nitrogen molecule may achieve a high specific impulse without undesirable smoke or soot. Third, the nitrogen molecule is an environmentally friendly final product. Tetrazoles, with their heterocyclic ring structure, fall within this class of high-nitrogen compounds [2].

In fact, tetrazole is a class of synthetic five membered organic heterocyclic compounds containing four nitrogen atoms and one carbon atom and one hydrogen atom (Fig. 1). The simplest is 1*H*-tetrazole itself CH_2N_4. It is white to pale yellow crystalline solid with weak characteristic odor, soluble in water and alcohol. It is acidic in nature due to presence of four nitrogen atoms. Numbering of tetrazoles were well known [3, 4]. Tetrazoles are usually explosives. They are unknown in nature. They are used as gas generating agent for air bags. Tetrazoles undergo electrophilic as well as nucleophilic substitution [5].

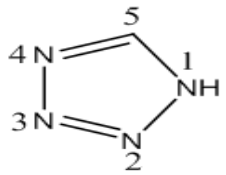

Fig. 1. 1*H*-tetrazole

Due to the higher nitrogen content among the organic substances and the large positive enthalpies of formation, aminotetrazoles are prospective materials to be used, as blowing agents, solid propellants, and other combustible and thermally decomposing systems [6–10]. The number of publications devoted to the study of Tetrazoles increases each year. Significant advances have been made in their use in medicine [11, 12] and biology [13].

They are considered as bioisosteres of cis amides and carboxylic acids in medicinal chemistry with higher liphophilicity [14]. Although tetrazoles and their derivatives rarely occur in nature [15] the clear majority show biological activity [16]. Among them, 5-aminotetrazoles (Fig. 1) show anti-allergic and anti-asthmatic [17]

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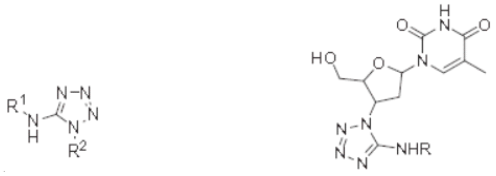
antiviral and anti-inflammatory [18] antineoplastic [19] and cognition disorder activities [20]. Related compounds such as 30-(5-amino-1,2,3,4-tetrazol-1-yl)-30- deoxy-thymidines and its derivatives were developed as anti-HIV drugs (Fig. 2) by Bayer [21].

Since Azo group is considered as a biological active group [22], we prepared in our work different azo tetrazole derivatives and they have been tested for their antimicrobial activity.



5-Aminotetrazoles

Anti-HIV drug

Fig. 2. Structure of 5-aminotetrazoles and related compounds

Experimental

Materials and chemicals

5-Aminotetrazole and 2-alkyl phenols, potassium hydroxide, sodium nitrite, hydrochloric acid, alkyl halides and ethyl-4-hydroxybenzoate purchased from (Sigma-Aldrich). Methylene chloride, ethanol , DCC and DMAP purchased from (Fluka). All chemicals were of analytical grade and used without further purification.

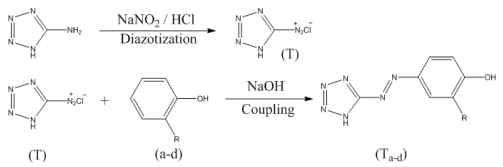
Preparation of compounds Ta-d

Preparation of Diazotetrazole (T)

5 grams of 5-aminotetrazole were dissolved in 30 mL. of water containing 6 mL. of 25% sodium hydroxide solution. To this solution 3.4 grams of sodium nitrite and 170 grams of crushed ice were added while the reaction flask was cooled with a salt-ice bath. Slowly from dropping funnel 16 mL. of 30% cold hydrochloric acid was added at 0 °C. By the end of the diazotization the color of the solution became greenish. Diazotetrazole is very sensitive as even solution with greater concentration than 6-7% at 0° C decomposed explosively [23].

Coupling with Phenol derivatives (a-d)

The prepared diazonium chloride was added to an equimolar amount of alkaline solutions of compounds (a-d) at 0 °C. The resulting precipitate was acidified and crystallized from absolute ethanol to yield compounds T_{a-d}.



Compound	R	Name
Ta	H	4-((1H-tetrazol-5-yl)diazenyl) phenol.
Tb	Me	4-((1H-tetrazol-5-yl)diazenyl)-2-methylphenol.
Tc	C_2H_5	4-((1H-tetrazol-5-yl)diazenyl)-2-ethylphenol.
Td	Tert-butyl	4-((1H-tetrazol-5-yl)diazenyl)-2-(tert-butyl)phenol.

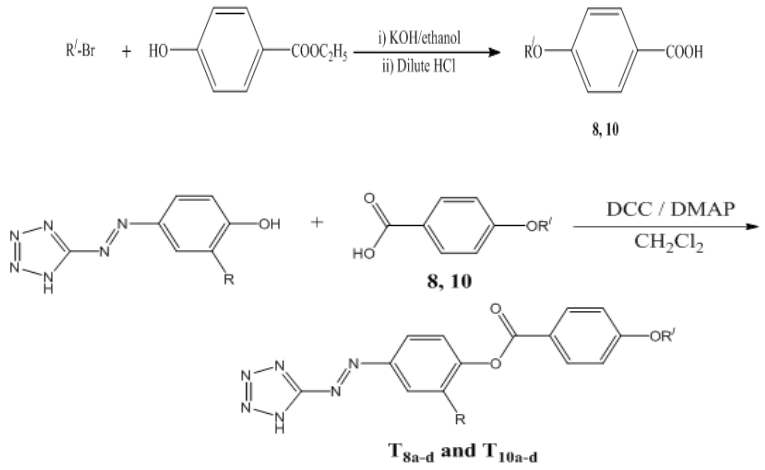
Preparation of Compounds T_{8a-d} and T_{10a-d}

Preparation of 4-(alkoxy) benzoic acids 8 and 10

The 1-bromo alkane (0.030 mol.) was added dropwise to a stirred solution of ethyl -4-hydroxy benzoate (0.030 mol.) in 50 mL ethanolic potassium hydroxide (0.036 mol.). Stirring was continued for two hours at 60 °C. Then the reaction mixture was left overnight at room temperature. The product obtained is hydrolyzed by adding potassium hydroxide (0.030 mol.) and refluxed for three hours. The hydrolyzed product was then cooled and acidified with dilute hydrochloric acid. The resulting alkoxy acids were crystallized from glacial acetic acid and exhibited phase transition temperatures agreed with those reported in the literature [24].

Esterification

Equimolar amount of both (T_{a-d}) and (8, 10), (0.01 mol.) were dissolved in 50 ml methylene chloride. Dicyclohexyl carbodiimide (DCC, 0.011 mol.) and 4-dimethylamino pyridine, (DMAP as catalyst) were added to the solution mixture with stirring overnight at room temperature. The solution was filtered off and vaporized using rotary evaporator. The residue was crystallized from absolute ethanol to give (T_{8a-d} and T_{10a-d}) [25].



Compound	R	R/	Name
T_{8a}	H	$C_8H_{17}O$-	4-((1*H*-tetrazol-5-yl)diazenyl)phenyl 4-(octyloxy)benzoate
T_{8b}	Me	$C_8H_{17}O$-	4-((1*H*-tetrazol-5-yl)diazenyl)-2-methylphenyl-4-(octyloxy)benzoate
T_{8c}	C_2H_5	$C_8H_{17}O$-	4-((1*H*-tetrazol-5-yl)diazenyl)-2-ethylphenyl-4-(octyloxy)benzoate
T_{8d}	Tert-butyl	$C_8H_{17}O$-	4-((1*H*-tetrazol-5-yl)diazenyl)-2-(tert-butyl)phenyl-4-(octyloxy)benzoate
T_{10a}	H	$C_{10}H_{21}O$-	(4-((1*H*-tetrazol-5-yl)diazenyl)phenyl-4-(decyloxy)benzoate
T_{10b}	Me	$C_{10}H_{21}O$-	4-((1*H*-tetrazol-5-yl)diazenyl)-2-methylphenyl-4-(decyloxy)benzoate
T_{10c}	C_2H_5	$C_{10}H_{21}O$-	4-((1*H*-tetrazol-5-yl)diazenyl)-2-ethylphenyl-4-(decyloxy)benzoate
T_{10d}	Tert-butyl	$C_{10}H_{21}O$-	4-((1*H*-tetrazol-5-yl)diazenyl)-2-(tert-butyl)phenyl-4-(decyloxy)benzoate

TABLE 1. Elemental analysis of compounds (T_{a-d}, $T_{8a,b}$ and $T_{10c,d}$)

			Analysis calculations					
Cpd.	**M Formula**	**M. P. °C**	**C%**		**H%**		**N%**	
			Calc.	Obs.	Calc.	Obs.	Clac.	Obs.
T_a	$C_7H_7N_6O$	136-38	44.21	44.58	3.18	3.06	44.19	43.94
T_b	$C_8H_8N_6O$	128-30	47.06	46.95	3.95	4.08	41.16	41.14
T_c	$C_9H_{10}N_6O$	124-25	49.54	48.99	4.62	4.78	38.51	38.9
T_d	$C_{11}H_{14}N_6O$	80-82	53.65	53.38	5.73	6.02	34.13	34.11
T_{8a}	$C_{22}H_{26}N_6O_3$	235-36	62.54	63.01	6.20	6.04	19.89	19.58
T_{8b}	$C_{23}H_{28}N_6O_3$	238-40	63.29	62.99	6.47	6.58	19.25	19.44
T_{8c}	$C_{24}H_{30}N_6O_3$	208-10	63.98	64.21	6.71	6.68	18.65	18.45
T_{8d}	$C_{26}H_{34}N_6O_3$	165-67	65.25	65.85	7.16	6.89	17.56	17.23
T_{10a}	$C_{25}H_{32}N6O_3$	224-25	63.98	64.24	6.71	6.43	18.65	18.67
T_{10b}	$C_{24}H_{30}N_6O_3$	227-30	64.64	63.94	6.94	7.04	18.09	18.69
T_{10c}	$C_{26}H_{34}N_6O_3$	189-90	65.25	65.87	7.16	6.94	17.56	17.16
T_{10d}	$C_{28}H_{38}N_6O_3$	158-60	66.38	66.76	7.56	6.55	16.59	17.22

The data obtained in Table 1 reveals that the experimental results were in good agreement with the calculated values. Infra-Red spectral bands of compounds T_{a-d}, T_{8a-d} and T_{10a-d} Infra-Red spectrum of T_{a-d}

TABLE 2. Characteristic infrared bands for T_{a-d}

				n Cm^{-1}			
Cpd.	R	OH	NH	$CH_{Aromatic}$	$CH_{Aliphatic}$	N=N	C=C
T_a	H	3504	3356	3098	-	1472	1586
T_b	$-CH_3$	3546	3379	3195	2973	1463	1597
T_c	-C2H5	3493	3389	3130	2971	1455	1597
T_d	t-But.	3514	3389	3164	2957	1483	1591

Data obtained in Table 2 illustrate the following:

- The –OH bands of the four compounds appear at (3546 – 3504 cm^{-1}), whereas the –NH streatching bands appear at (3356 – 3389 cm^{-1}).
- The azo group (N=N) for the prepared compounds has the values of (1463 – 1483 cm^{-1}).
- The values of –CH aromatic and –CH aliphatic agree with the theoretical ones.

TABLE 3. Characteristic infrared bands for T_{8a-d} and T_{10a-d}

						ν Cm^{-1}			
Cpd.	R	R/	NH	C=O	$CH_{Aromatic}$	$CH_{Aliphatic}$	N=N	C-O-C	C=C
T_{8a}	H	$-OC_8H_{17}$	3326	1773	3181	2931	1472	1245	1586
T_{8b}	$-CH_3$	$-OC_8H_{17}$	3328	1774	3182	2929	1463	1244	1597
T_{8c}	-C2H5	$-OC_8H_{17}$	3356	1769	3178	2932	1465	1250	1588
T_{8d}	t-But.	$-OC_8H_{17}$	3342	1771	3156	2928	1464	1251	1592
T_{10a}	H	$-OC_{10}H_{21}$	3348	1734	3118	2929	1472	1247	1596
T_{10b}	$-CH_3$	$-OC_{10}H_{21}$	3358	1746	3125	2933	1465	1248	1591
T_{10c}	-C2H5	$-OC_{10}H_{21}$	3326	1728	3117	2930	1474	1252	1597
T_{10d}	t-But.	$-OC_{10}H_{21}$	3332	1745	3123	2927	1483	1244	1591

Infra-Red spectrum of T_{8a-d} and T_{10a-d}

The infra-red absorption bands for compounds T_{8a-d} and T_{10a-d}, (Table 3), explain the following:

- The -NH streatching bands appear at (3326 - 3358 cm^{-1}), whereas the -OH bands disappear (after estrification).
- The carbonyl ester streatching bands appear within the expected ranges (1728 - 1773cm^{-1}). This is due to the π bond character of the carbonyl group (Fig. 3).
- The C-O-C groups have the values ranged from 1244 cm^{-1} to 1252 cm^{-1}.
- The other absorption bands of the eight compounds are reasonable in their values.

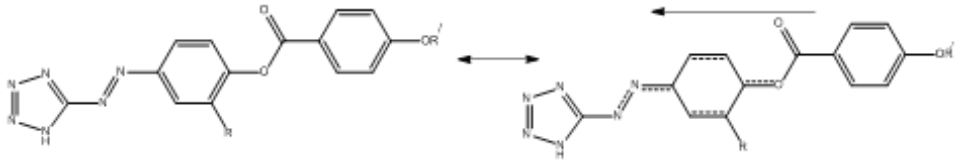
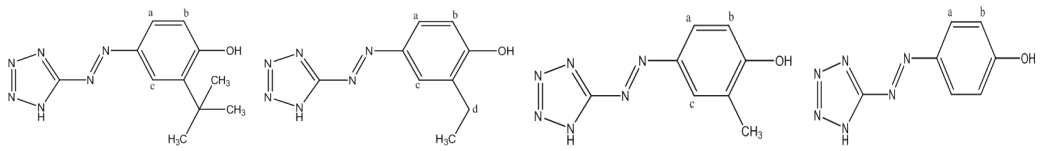


Fig 3. Resonating structure of compounds T_{8a-d} and T_{10a-d}

[1]H-NMR

Nuclear Magnetic Resonance of compounds T_{a-d}



T_a T_b T_c T_d

TABLE 4. Chemical Shifts (d) of compounds T_{a-d}

δ_{ppm} Cpd.	H a	H b	NH	OH	CH_3	H c	H d
Ta	7.898 d	7.019 d	6.235 s	10.895 s	-		
Tb	7.799 d	7.056 d	5.935 d	10.990 s	3.220 s	7.524 dd	
Tc	7.808 d	7.060 d	6.024 s	10.931 s	2.196 t	7.624 dd	2.641 q
Td	7.854 d	6.958 d	6.138 s	11.054 s	2.409 s	7.589 dd	

The spin multiplicity, s = singlet, d = doublet, t = triplet, q = quartet and dd = doublet of doublet and m = multiplet.

Antimicrobial Activity

The antimicrobial activity of the newly synthesized compounds was screened for their antibacterial and antifungal activities using agar well diffusion method [26]. Mean zone of inhibition in mm beyond well diameter (6 mm) produced on a range of pathogenic microorganisms, using DMSO as solvent control, (The regional center of Mycology and Biotechnology, antimicrobial activity unit, Al-Azhar University). The test was done using the diffusion agar technique, Well Diameter: 6.0 mm (100 mL was tested), RCMB. The sample was tested at 5mg/ml concentration.

Results and Discussion

Elucidation of structures of the prepared

Table 4 illustrates the following:

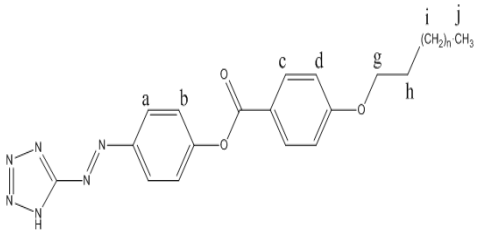
The two aromatic (a) protons, of the benzene ring (T_a) are more deshielded than (b) protons, because of the high electronegative tetrazole ring. In case of compounds (T_{b-d}), the three aromatic protons are not similar in their chemical shifts and the proton (c) appears to have a doublet of doublet splitting.

The nine protons of the tert-butyl group (T_d) appear singlet and having the chemical shift value of 2.409 ppm whereas the three protons of the methyl group (T_c) have triplet spin multiplicity with 2.196 ppm chemical shift value.

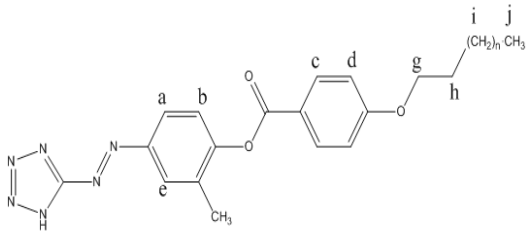
In case of compound T_b, the methyl protons have the chemical shift value of 3.22 ppm with singlet spin multiplicity.

The proton (c) has the spin multiplicity doublet of doublet, due to the unsymmetrical protons (a and b).

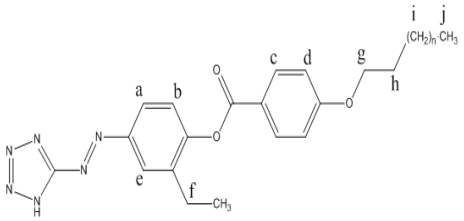
Nuclear Magnetic Resonance of compounds T_{8a-d} and T_{10a-d}



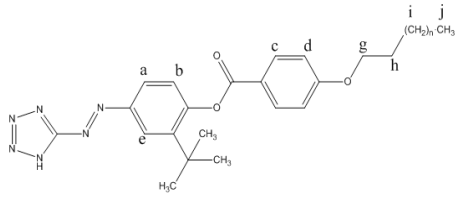
$T_{8,10a}$



$T_{8,10b}$



$T_{8,10c}$



$T_{8,10d}$

Where n = 8 and 10

TABLE 5. Chemical Shifts (d) of compounds T_{8a-d} and T_{10a-d}

d_{ppm} Cpd.	H a	H b	NH	H c	CH_3	H d	H e	H f	H g	H h	H i	H j
T_{8a}	7.824 d	7.028 d	5.573 s	8.248 d	-	6.985 d	-	-	3.318 t	2.254 m	1.728 m	1.135 t
T_{8b}	7.768 d	6.994 d	5.568 s	8.236 d	3.318 3 s	7.024 d	7.682 dd	-	3.468 t	2.232 m	1.684 m	1.136 t
T_{8c}	7.800	7.048	5.582 s	8.324 d	2.224 3 t	7.004 d	7.684 dd	3.428 q	3.382 t	2.248 m	1.728 m	1.048 t
T_{8d}	7.746	7.082	5.604 s	8.286 d	2.186 9 s	7.006 d	7.721 dd	-	3.368 t	2.268 m	1.778 m	0.998 t
T_{10a}	7.814 d	7.112 d	5.582 s	8.198 d	-	6.989 d	-	-	3.408 t	2.264 m	1.804 m	0.986 t
T_{10b}	7.772 d	7.085	5.589 s	8.218 d	3.426 3 s	6.978 d	7.608 dd	-	3.368 t	2.246 m	1.724 m	1.001 t
T_{10c}	7.804 d	7.056 d	5.574 s	8.186 d	2.132 3 t	7.026 d	7.564 dd	3.321 q	3.568 t	2.245 m	1.701 m	1.135 t
T_{10d}	7.689 d	7.068 d	5.591 s	8.195 d	2.229 9 s	6.904 d	7.486 dd	-	3.323 t	2.222 m	1.619 m	1.260 t

The spin multiplicity, s = singlet, d = doublet, t = triplet, q = quartet and dd = doublet of doublet and m = multiplet.

From Table 5 the above data are explained as follows:

The peaks related to the (OH-) proton disappeared which confirm the formation of esters for compounds T_{8a-d} and T_{10a-d}.

The highly deshielded aromatic proton (a) has the values of (7.689 to 7.824 ppm) for the eight compounds.

Proton of the type (e) has the values ranged from (7.486 to 7.682 ppm) with spin multiplicity doublet of doublet (affected by the unsymmetrical protons (a and b) for compounds T_{8b-d} and T_{10b-d}.

The CH_3 protons for compounds T_{8b} and T_{10b} appear singlet with chemical shift values of 3.318 and 3.426 respectively, whereas the CH_3 protons for compounds T_{8c} and T_{10c} appear triplet with chemical shift values of 2.224 and 2.132 ppm respectively. Consequently the CH_3 protons (9 protons) for compounds T_{8d} and T_{10d} appear singlet with chemical shift values of 2.186 and 2.229 ppm respectively.

The proton of type (f), for compounds T_{8c} and T_{10c}, appear quartet with chemical shift values of 3.428 and 3.321 ppm respectively.

Antimicrobial Activity

The pilot study of the antimicrobial Activity for the synthesized azo tetrazole derivatives are illustrated in the following tables.

Antimicrobial Activity of T_{a-d}:

From data obtained in Tables 6 and 7 the antimicrobial work (as a pilot study) illustrates that Compounds T_{a-d}, T_{8a-d} and T_{10a-d} show negative antimicrobial activity versus fungi such as *Aspergillus fumigatus, and Candida albicans.*

Table 6 explains that, with respect to the effect of Gentamycin on *Gram positive* bacteria (*Staphylococcus aureus and Bacillus Subtilis*), and *Gram negative* bacteria (*Salmonella typhimurium* and *Escherichia coli*) the efficiency of T_{a-d} behaves as follows:

In case of *Gram Positive* bacteria **(***Staphylococcus aureus*), the effeciency shows 50 %, 54.16%, 45.83% and 66.67% for the four respective T_a, T_b, T_c, and T_d. However, the efficiency of them on *Gram positive* bacteria (*Bacillus subtilis*) shows 42.31%, 46.15%, 57.69%, and 69.23% respectively.

The effect of T_a, T_b, T_c, and T_d on *Gram negative* bacteria (*Salmonella typhimurium*) get the values of 82.35%, 88.23%, 70.59% and 111.76% (great effect), respectively. In a contrary, in case of *Gram negative* bacteria (*Escherichia coli*)**,** the efficiency get the following values: 43.33%, 36.66, 40%, and 50% for the four respective compounds T_{a-d}.

As illustrated in Table 7, the efficiency of T_{8a-d} and T_{10a-d} on *Gram positive* bacteria (*Staphylococcus aureus and Bacillus subtilis*) and *Gram negative* bacteria (Salmonella typhimurium

and Escherichia coli), with respect to the reference one (Gentamycin), is shown as follows:

Compounds T_{8c} and T_{10c} have no effect on any of the two types of bacteria.

The effect of ($T_{8a, b, d}$ and $T_{10a, b, d}$) on *Gram positive* bacteria (*Staphylococcus aureus*), give the respective values: 37.5%, 41.66%, 37.5%, 41.66%, 50% and 58.33%. While in case of *Gram Positive* bacteria (*Bacillus subtilis*), the effective values of the above six compounds are: 30.77%, 42.31%, 42.31%, 42.31%, 50% and 61.54% respectively.

The sequential effective values for ($T_{8a, b, d}$ and $T_{10a, b, d}$) on *Gram negative* bacteria (*Salmonella typhimurium*) are as follows: 52.94%, 70.59%, 58.82%, 70.59%, 76.47% and 88.23%. Whereas, the effect of them on *Gram negative* bacteria (*Escherichia coli*) shows the following values: 33.33%, 36.67%, 40%, 46.67%, 50% and 66.67% respectively.

Conclusion

The structures of the prepared compounds are elucidated using the conventional tools of analysis, (Elemental Analysis, FT-IR and ^{1}H-NMR spectroscopy).

The net result of using synthesized compounds versus microorganisms, (*Gram +ve* bacteria and *Gram -ve* bacteria) showed high antimicrobial activity.

Instead of the three compounds T_{a-c}, T_d gave higher antimicrobial action for both the two types of bacteria (*Gram +ve* and *Gram –ve*), Table (6).

In case of the eight compounds (T_{8a-d} and T_{10a-d}), Table (7), T_{8d} and T_{10d} gave higher activity for both *Gram +ve* and *Gram –ve* bacteria than

TABLE 6. Antimicrobial activity of T_{a-d} on fungi and bacteria

Sample code **Tested microorganism**	**T_a**	**T_b**	**T_c**	**T_d**	**Control**
Fungi					*Ketoconazol*
Aspergillus fumigatus (RCMB002008)	NA	NA	NA	NA	17
Candida albicans (RCMB005003) (1) ATCC 10231	NA	NA	NA	NA	20
Gram Positive Bacteria					*Gentamycin*
Staphylococcus aureus (RCMB 010010)	12	13	11	16	24
Bacillus subtillis RCMB 015 (1) NRRL B-543	11	12	15	18	26
Gram Negative Bacteria					*Gentamycin*
Salmonella typhimurium RCMB 006 (1) ATCC 14028	14	15	12	19	17
Escherichia coli (RCMB 010052) ATCC 25955	13	11	12	15	30

Antimicrobial Activity of T8a-d and T8a-d

TABLE 7. Antimicrobial activity of T_{8a-d} and T_{10a-d} on fungi and bacteria

Sample code **Tested microorganism**	**T_{8a}**	**T_{8b}**	**T_{8c}**	**T_{8d}**	**T_{10a}**	**T_{10b}**	**T_{10c}**	**T_{10d}**	**Control**
Fungi									**Ketoconazol**
Aspergillus fumigatus (RCMB 002008)	NA	NA	NA	NA	NA	NA	NA	NA	17
Candida albicans (RCMB 005003) (1) ATCC 10231	NA	NA	NA	NA	NA	NA	NA	NA	20
Gram Positive Bacteria									*Gentamycin*
Staphylococcus aureus (RCMB 010010)	9	10	NA	9	10	12	NA	14	24
Bacillus subtillis RCMB 015 (1) NRRL B-543	8	11	NA	11	11	13	NA	16	26
Gram Negative Bacteria									*Gentamycin*
Salmonella typhimurium RCMB 006 (1) ATCC 14028	9	12	NA	10	12	13	NA	15	17
Escherichia coli (RCMB 010052) ATCC 25955	10	11	NA	12	14	15	NA	20	30

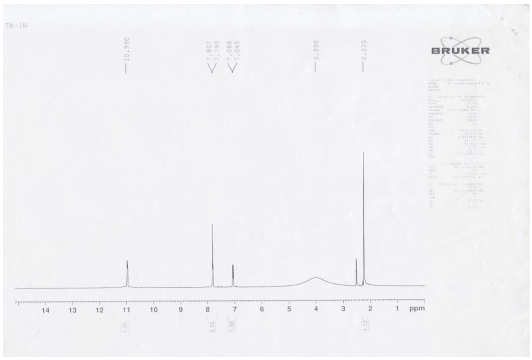


Fig. 3: ^{1}H-NMR Spectra of T_a

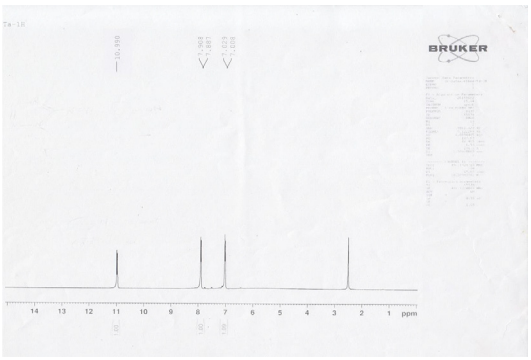


Fig. 4: ^{1}H-NMR Spectra of T_b

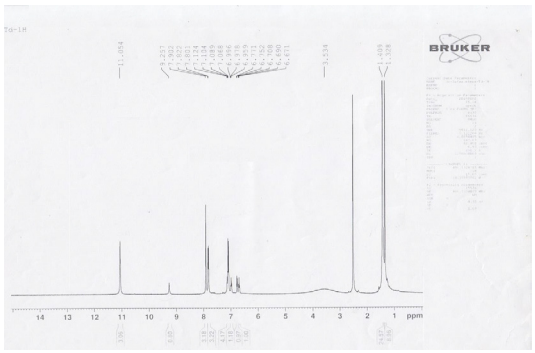


Fig. 5: ^{1}H-NMR Spectra of T_c

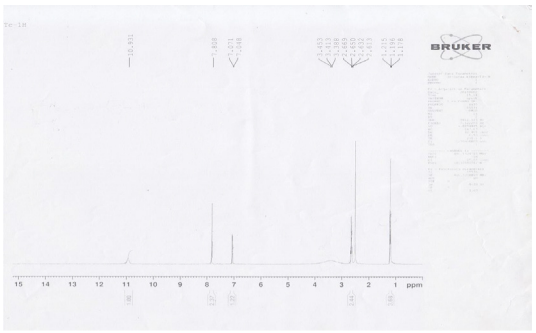


Fig. 6: ^{1}H-NMR Spectra of T_d

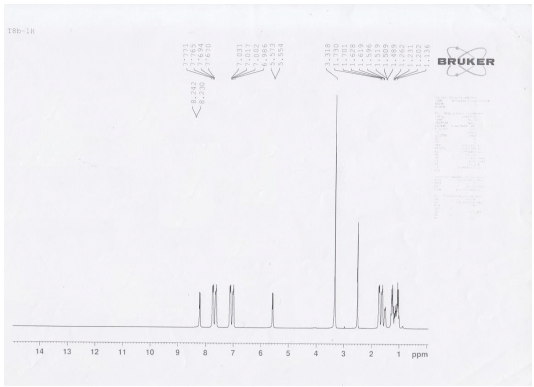


Fig. 7: ^{1}H-NMR Spectra of T_{8a}

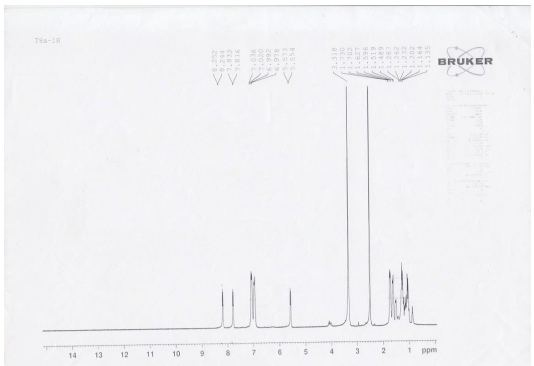


Fig. 8: ^{1}H-NMR Spectra of T_{8b}

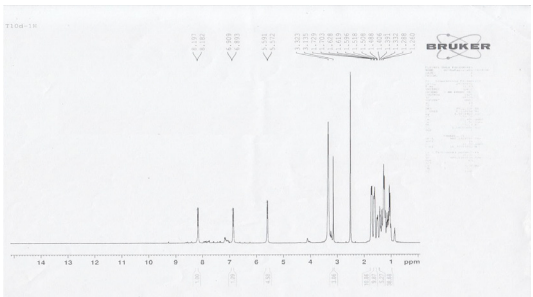


Fig. 9: ^{1}H-NMR Spectra of T_{10c}

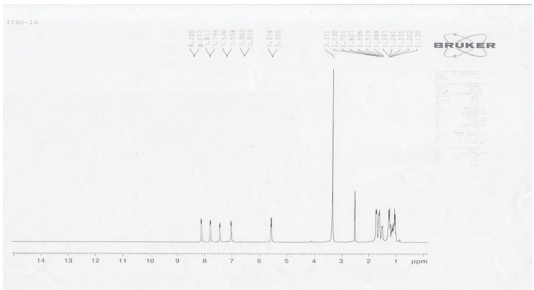


Fig. 10: ^{1}H-NMR Spectra of T_{10d}

the other six compounds

All the twelve prepared compounds have no antifungal activity.

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توليف ودراسة الأنشطة المضادة للميكروبات لبعض المشتقات الجديدة للتترازول

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لقد تم تفاعل أربعة (مشتقات الفينول ٢) مع ١H-تيترازول-٥-ديازونيوم كلوريد لتخليق أربعة مركبات جديدة وهي ٤ - ((H-١-تيترازول -٥-يل) ديازينيل) -٢-ألكيلفينول (T_{a-d}). تفاعلت هذه الأزوفينولات مع اثنين من الأحماض ٤-ألكوكسي (٨ و ١٠) لتشكيل مجموعتين جديدتين من ٤ - (H-١-تيترازول-٥-يل) ديازينيل -٢-(ألكيل)-٤ فينيل- (أوكتيلوكسي) بنزوات $T_{٨a-d}$ و ٤-((H١-تيترازول-٥-يل) ديازينيل) -٢- (ألكيل) --٤فينيل (ديسيلوكسي) بنزوات $T_{١٠,a-d}$ على التوالي. تم التحقق من التركيب البنائى لهذه المركبات الاثني عشر باستخدام الطرق التقليدية للتحليل وهى تحليل العناصر والأشعة تحت الحمراء والرنين النووى المغناطيسى الهيدروجينى. تمت دراسة النشاط البيولوجي للمركبات المخلقة كمضادات للفطريات ومضادة للبكتيريا. معظم المركبات المحضرة تمتلك عمل مضادات الميكروبات جيدة للبكتريا إيجابية الجرام وسالبة الجرام، في حين أنها لم تعط أي تأثير على الفطريات أمثال (*Aspergillus fumigatus*) أو (*Candida albicans*).