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Synthesis and Electrochemical Behavior of Some New Pyridazine Derivatives

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Abstract

One-pot reaction of **1** with ethyl cyanoacetate and/or benzylidenemalono- nitrile afforded pyridazine derivatives **2** and **3**, respectively. Compound **2** was subjected to some reactions to produce other new pyridazine derivatives. Also, treatment of **2** with hydrazine hydrate in ethanol gave the carbohydrazide **7**. Some derivatives of the latter compound have been synthesized. Cyclic voltammograms of compounds **2, 5b, 7** and **8b** using an undivided cell at platinum electrodes are discussed. The antimicrobial activity of some synthesized derivatives has been investigated.

Keywords: *Pyridazine, Carbohydrazide, Carboxamide, Oxidation, Reduction.*

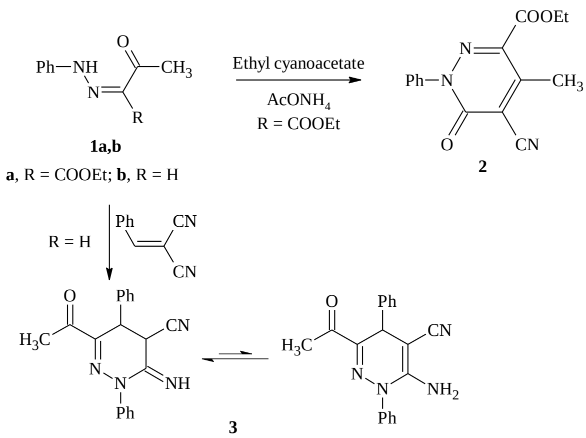
1 Introduction

Several functionalized pyridazines exhibit important biological activity such as: antibacterial, antibiotic, antitumor, antiviral and antidiabetes [1]. Pyridazine derivatives could also find application as ligands in supramolecular chemistry and in metallic complexes which exhibit catalytic properties [2-4]. On the basis of these reports and in continuation of our work [5-8]; we synthesized some novel pyridazine derivatives of expected notable chemical, electrochemical and biological activities.

2 Result and Discussion

We reported here the synthesis of ethyl 5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carboxylate (**2**) by treatment of ethyl 3-oxo-2-

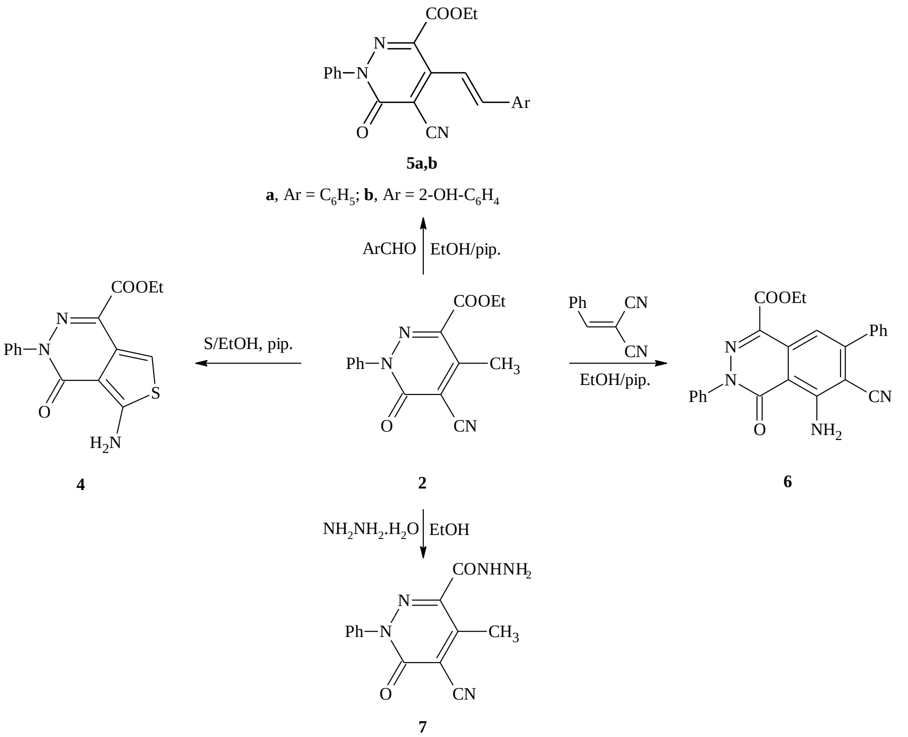
(phenyl- hydrazono)butanoate (**1a**) with ethyl cyanoacetate in the presence of ammonium acetate and acetic acid. Also, 6-acetyl-3-imino-2,5-diphenyl-2,3,4,5-tetrahydropyridazine-4-carbonitrile (**3**) was synthesized by heating of 1-(phenylhydrazono)propan-2-one **1b** with benzylidenemalononitrile in pyridine. The structure of compounds **2** and **3** were established on the basis of their elemental analysis and spectral data. The IR spectrum of compound **2** showed absorption bands at 2230 (C≡N), 1717 (C=O), 1676 (C=O) and 1585 (C=C) cm^{-1}.



Scheme 1

The [1]H NMR spectrum of compound **2** showed signals at δ 1.28 and 2.64 ppm characteristic for $2CH_3$, in addition to signal at δ 4.34 ppm as a quartet for CH_2 of ethyl group. The IR spectrum of compound **3** showed absorption bands at 3407 (NH), 2188 (C≡N) and 1644 cm^{-1} for C=O (amide). [1]H NMR spectrum of **3** showed signals at δ 2.32, 4.75 and 5.99 ppm indicate the presence of CH_3 and 2CH groups, in addition to signal at δ 7.17 ppm for NH.

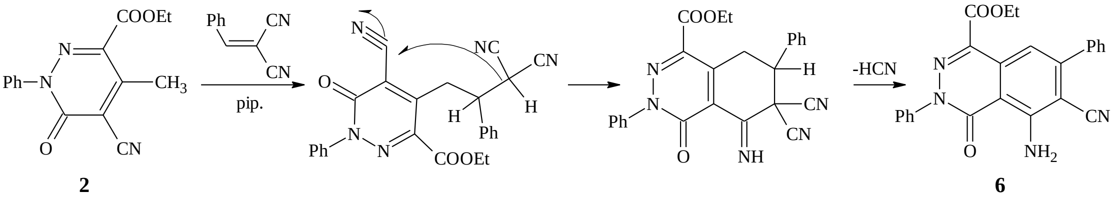
Reaction of compound **2** with different reagents namely, sulphur, benzaldehyde, salicylaldehyde, and/or benzylidenemalononitrile, in absolute ethanol and few drops of piperidine afforded ethyl 5-amino-4-oxo-3-phenyl-3,4-dihydrothieno[3,4-*d*]pyridazine-1-carboxylate (**4**), ethyl 5-cyano-6-oxo-1-phenyl-4-[2-phenylethenyl]-1,6-dihydro-pyridazine-3-carboxylate (**5a**), ethyl 5-cyano-4-[2-(2-hydroxyphenyl)ethenyl]-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carboxylate (**5b**), ethyl 5-amino-6-cyano-4-oxo-3,7-diphenyl-3,4-dihydrophthalazine-1-carboxylate (**6**), respectively.



Scheme 2

The structural assignment of these compounds **4**, **5a** and **5b** were supported by elemental analysis and spectral data in experimental section.

The formation of compound **6** may be proceeding by the following mechanistic equation:



Scheme 3

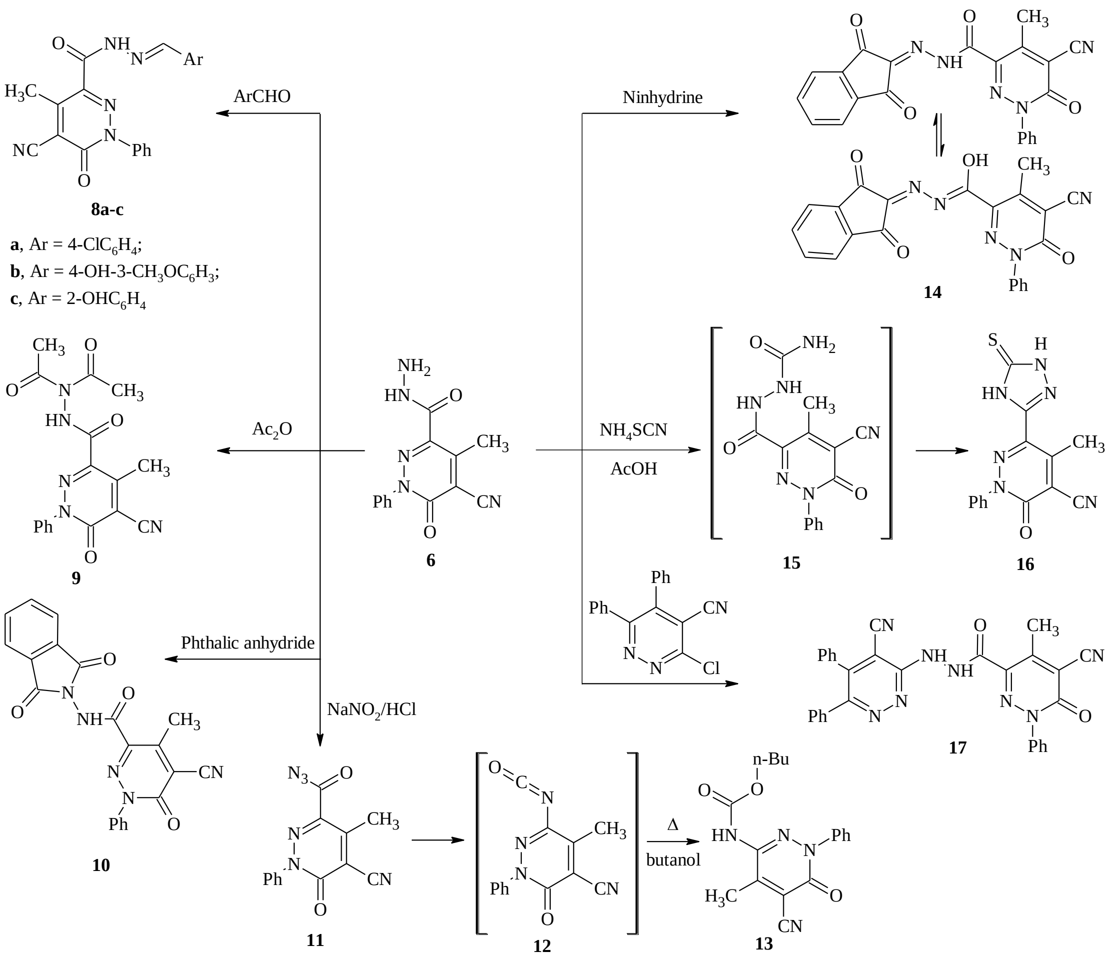
The structure of compound **6** was supported by elemental analysis and spectral data. The IR spectrum showed absorption bands at 3448, 3301 (NH_2), 2204 (C≡N), 1720 (C=O) and 1660 (C=O) cm^{-1}. The ^1H NMR spectrum showed signals at δ 1.31 and 4.39 ppm for ethyl ester group, in addition to signal at δ 8.22 ppm for NH_2.

While, 5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carbohydrazide (**7**) was obtained by reaction of **2** with hydrazine hydrate in refluxing ethanol. The structure of **7** was supported by elemental analysis, absence of IR band and ^{1}H NMR signal for the ester group.

Carbohydrazide **7** was refluxed with benzaldehyde derivatives namely, 4-chlorobenzaldehyde, vanillin and/or salicylaldehyde, in acetic acid to gave the hydrazone derivatives **8a-c**, respectively. The structures of compounds **8a-c** were established on the basis of their elemental analysis and spectral data. The IR spectrums of **8a-c** showed absorption bands at 1595-1613 cm^{-1} for C=N hydrazine band. The ^{1}H NMR spectrum of **8a** (DMSO-d_6) displayed the following δ ppm values: 2.66(s, 3H, CH_3), 7.48-8.42(m, 10H, Ar-H + N=CH), 12.05(s, 1H, NH).

When carbohydrazide **7** was heated under reflux with acetic anhydride and/or phthalic anhydride, it furnished the *N*',*N*'-diacetyl-5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carbohydrazide (**9**) and 5-cyano-*N*-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carboxamide (**10**), respectively.

The structures of compounds **9** and **10** were established on the basis of their elemental analysis and spectral data. IR spectrum of **9** showed absorption bands at 3526 (NH) and 1721 (C=O) cm^{-1}. The ^{1}H NMR spectrum of **9** displayed signal at δ 2.32 ppm characteristic for $2CH_3CO$ in addition to signal at δ 11.08 ppm for NH. The IR spectrum of compound **10** showed absorption bands at 1790, 1741, 1706 and 1672 cm^{-1} characteristic for carbonyl groups.



Scheme 4

Diazotization of **7** with sodium nitrite in glacial acetic acid at 0 °C afforded 5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carbonyl azide (**11**) which showed in its IR spectrum absorption band at 2186 cm^{-1} characteristic for azide group. When compound **11** was boiled in butanol afforded butyl (5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazin-3-yl)carbamate (**13**) without isolation of the intermediate **12**. The IR spectrum of **13** showed absorption band at 1726 cm^{-1} characteristic for ester group. The ^{1}H NMR spectrum of **13** showed signals at δ 0.89, 1.30, 1.56 and 4.09 ppm characteristic for *n*-butyl ester group, in addition to signal at δ 9.84 ppm for NH.

Treatment of compound **7** with ninhydrine and/or ammonium thiocyanate in acetic acid afforded 5-cyano-*N'*-(1,3-dioxo-1,3-dihydro-2*H*-inden-2-ylidene)-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carbohydrazide (**14**) and 5-methyl-3-oxo-2-phenyl-6-(5-thioxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)-2,3-dihydropyridazine-4-carbonitrile (**16**), respectively. The structures of compounds

14 and **16** were established on the basis of their elemental analysis and spectral data. The IR spectrum of **14** showed characteristic absorption bands at 1737 (C=O), 1680 (C=O) and 1585 (C=C) cm^{-1}. ^{1}H NMR spectrum of **14** showed signal at δ 13.84 ppm characteristic for NH. Also, the IR spectrum of **16** showed characteristic absorption bands at 3349, 3168 (NH) and 1374 (C=S) cm^{-1}. ^{1}H NMR spectrum of **16** showed signals at δ 9.49 and 10.53 ppm characteristic for NH.

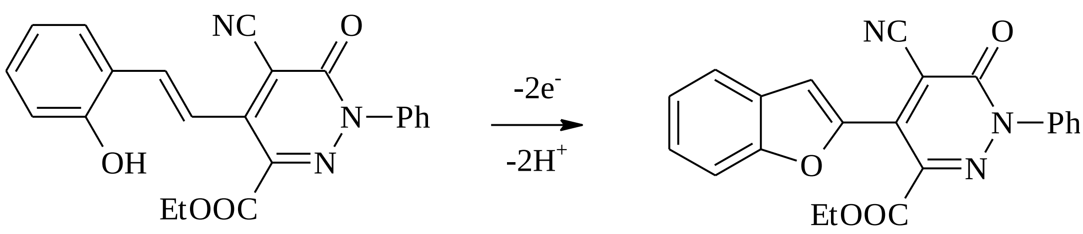
Equimolar amounts of carbohydrazide **7** and 3-chloro-4-cyano-5,6-diphenylpyridazine in n-butanol were refluxed to afford 5-cyano-N'-(4-cyano-5,6-diphenyl-3-pyridazinyl)-4-methyl-6-oxo-1-phenyl-1,6-dihydro-3-pyridazine-carbohydrazide (**17**). The structure of **17** was established by elemental analysis. Also, the IR spectrum exhibited characteristic absorption bands at 3434, 3059 (NH), 2230 (C≡N) cm^{-1} and the ^{1}H NMR spectrum showed characteristic signals at δ 7.23-7.69 ppm for (NH + Ar-H).

2.1 Electroanalytical behavior of some synthesized pyridazines

The simplest behaviour was exhibited by the pyridazine derivative (**2**). Three successive oxidation steps were observed at -1232, 172 and 1056 mV (vs. SCE). While, the reverse scan show three different reduction peaks at -495, -1438 and -2136 mV (vs. SCE). Voltammetric investigation performed at a sweep rate of 0.25 V s^{-1} indicates reversible systems [9].

Figure 1, shows the cyclic voltammogram of ethyl 5-cyano-4-[2-(2-hydroxy-phenyl)ethenyl]-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carboxylate **5b** in DMF/Et_4NClO_4 from -3 V to 2 V at a scan rate of 0.25 Vs^{-1}.

An anodic oxidation peak appears at 211 mV presumably corresponding to formation of ethyl 4-(1-benzofuran-2-yl)-5-cyano-6-oxo-1-phenyl-1,6-dihydro-pyridazine-3-carboxylate [10], while the reverse scan show reduction peaks at -544, -1349 and -2057 mV (Similar to compound **2**).



5b **18**

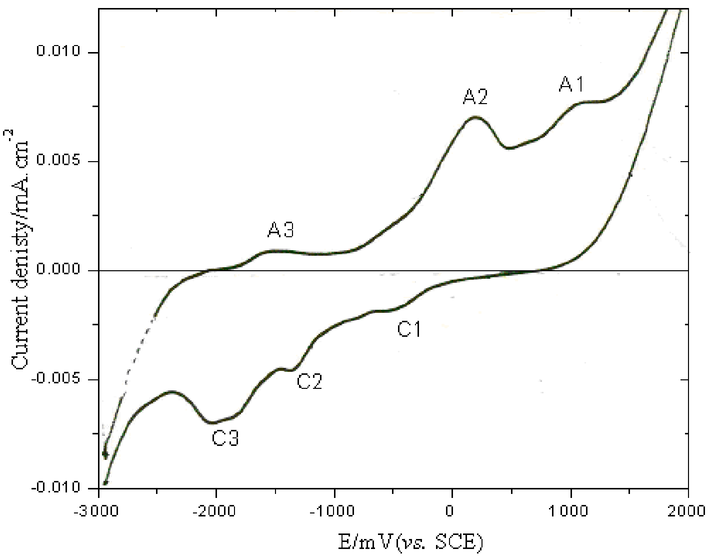


Figure 1: Cyclic voltammogram on 10^{-3} solution of compound **5b** in DMF/Et_4NClO_4 at a platinum electrode with scan rate 0.25 Vs^{-1}.

Clear differences appear for the carbohydrazide derivative **7** (Fig. 2). The second wave A2 corresponds to an irreversible transfer, but is located (398 mV vs. SCE) with high oxidation current at more positive potential than the second oxidation peak of substrate **2**.

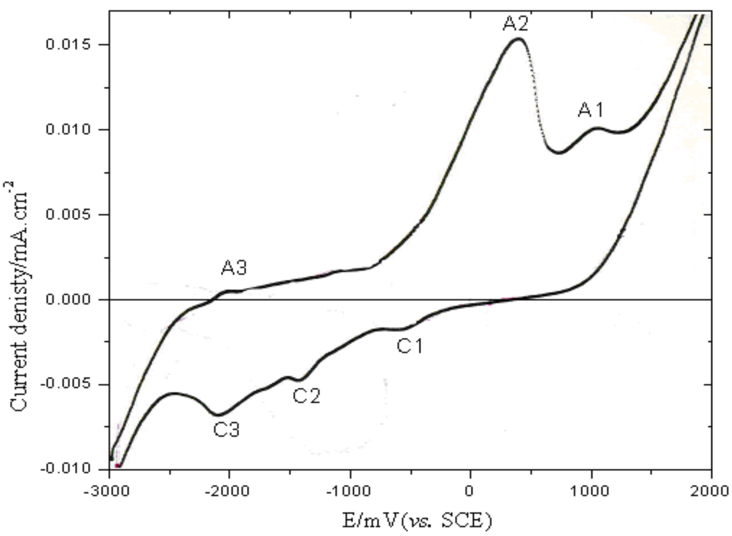
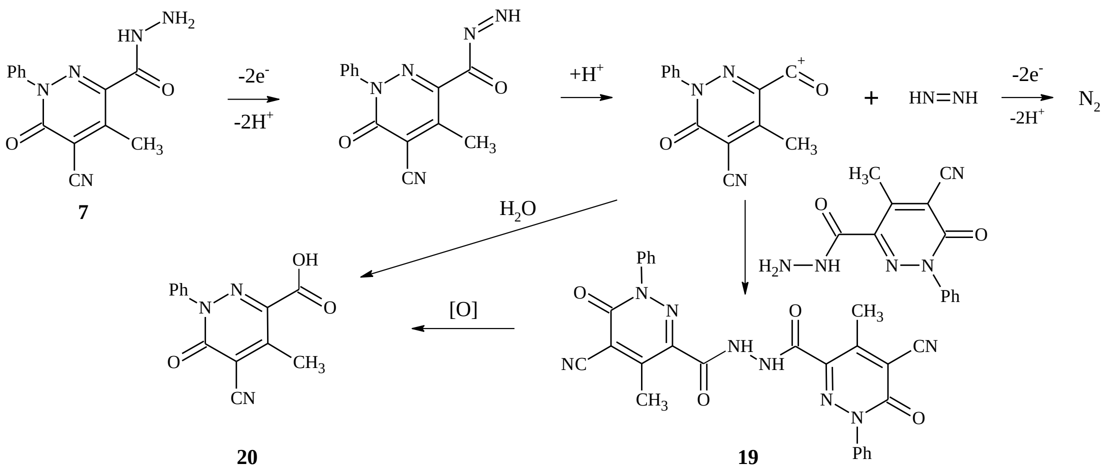


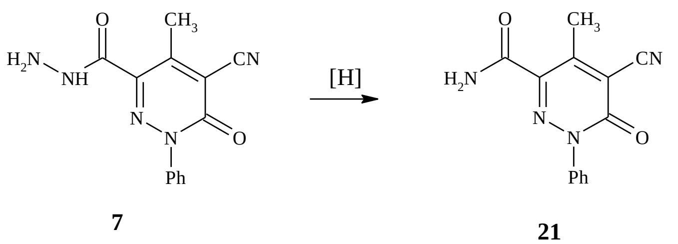
Fig. 2: Cyclic voltammogram on 10^{-3} solution of compound **7** in DMF/Et_4NClO_4 at a platinum electrode with scan rate 0.25 Vs^{-1}.

The mechanism suggested by Lund [11] can explain these results: the electrochemical oxidation is probably a 4-electron process leading to intermediate formation of an acylium cation.

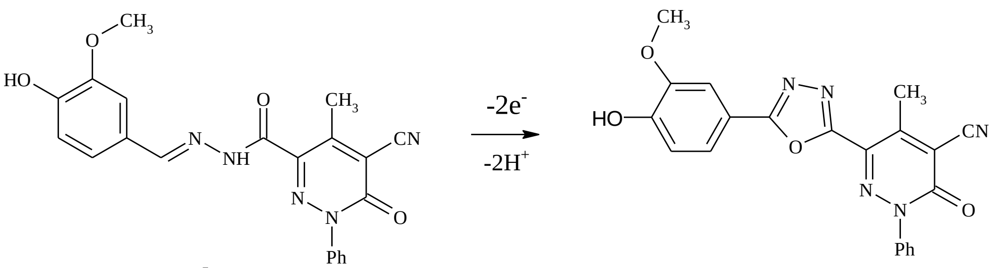


Scheme 5

The latter could react either with water to give the parent acid **20** or with the starting compound leading to 5-cyano-N'-[(5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydro-3-pyridazinyl)carbonyl]-4-methyl-6-oxo-1-phenyl-1,6-dihydro-3-pyridazinecarbohydrazide **19** (which is further oxidized into nitrogen and the parent acid **20**). While, the reverse scan show three different reduction peaks at -564, -1428 and -2098 mV (vs. SCE). Presumably, the hydrazide was reduced to the corresponding amide **21** [12]. The amide may, after uptake of two electrons, lose an amino or a hydroxyl group, and then be further reduced to a methanol or an aminomethylpyridazine derivative, beside the compound may be reduced in the pyridazine ring [13].



The carbohydrazide derivative **8b** displays a totally different behavior. Anodic oxidation peaks of 8b appears at -1340, -73 and 1115 mV (vs. SCE) corresponding to an oxidation processes often leading to formation of oxadiazole derivative 22 [14, 15] with a relatively low oxidation current.



8b **22**

2.2 Screening for an antimicrobial activity

Compounds **2**, **6**, **7**, **8c** and **10** were tested for *in vitro* antimicrobial activity using the method described by Heatly [15]. Tetracycline was used as antibacterial agent and amphotericn B as antifungal agent standards. The zone of inhibition of bacterial growth around the disc was observed. The screening results given in Table 1 indicate that all the compounds have antibacterial activities against Escherichia coli and Staphylococcus aureus except compound **6** but not antifungal activities on tested microorganisms.

Table 1: *In vitro* antimicrobial activities of some of the prepared compounds[a]

Sample		Inhibition zone diameter (mm/mg sample)			
		Escherichia coli (G^-)	*Staphylococcus aureus* (G^+)	*Aspergillus flavus* (Fungus)	*Candida albicans* (Fungus)
Control: DMSO		0.0	0.0	0.0	0.0
Standard	Tetracycline Antibacterial agent	33	31	--	--
	Amphotericn B Antifungal agent	--	--	17	19
2		11	11	0.0	0.0
6		0.0	0.0	0.0	0.0
7		12	13	0.0	0.0
8c		13	13	0.0	0.0
10		14	15	0.0	0.0

3 Experimental

3.1. Instrumentation

All melting points are uncorrected and were determined on Gallenkamp electric melting point apparatus. IR spectra (KBr discs) were recorded on a FT/IR-400 spectrophotometer (Perkin Elmer). ^{1}H NMR spectra were recorded on a varian-300 (DMSO-d6) solution. Chemical shifts were reported as δ values relative to tetramethylsilane (TMS) as internal reference. The analyses and *in vitro* antimicrobial activities were carried out at Micro Analytical Center, Cairo University.

Ethyl 3-oxo-2-(phenylhydrazono)butanoate (**1a**) and 1-(phenylhydrazono) propan-2-one (**1b**) were prepared according to the methods described by [17].

3.2. Synthesis

Ethyl 5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carboxylate (2)

A mixture of compound **1a** (0.01 mol), ethyl cyanoacetate (0.01 mol) and ammonium acetate (2g) in acetic acid (30 ml) was heated under reflux for 3h. The solid product obtained upon cooling was filtered off, dried and recrystallized from ethanol to give **2**.

Yield: 56%; yellow crystals; m.p. 166-168 ^{o}C. IR: 3072, 2980, 2931 (CH), 2230 (C≡N), 1717 (C=O), 1676 (C=O) and 1585(C=C) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 1.28(t, 3H, CH_3), 2.64(s, 3H, CH_3), 4.34(q, 2H, CH_2), 7.54-7.57(m, 5H, Ar-H).

Anal: $C_{15}H_{13}N_3O_3$ (283.28); Calcd: C, 63.60; H, 4.63; N, 14.83; Found: C, 63.40; H, 4.48; N, 14.92.

6-acetyl-3-imino-2,5-diphenyl-2,3,4,5-tetrahydropyridazine-4-carbonitrile (3)

A mixture of compound **1b** (0.01 mol) and benzylidene malononitrile (0.01 mol) in pyridine (30 ml) was heated under reflux for 3h. The reaction mixture was cooled, poured into cold water and neutralized with dil. HCl. The separated solid product was filtered off, dried and recrystallized from ethanol to give **3**.

Yield: 62%; yellow crystals; m.p. 230-232 ^{o}C. IR: 3407 (NH), 3313, 3207, 3066 (CH), 2188 (C≡N), 1644 (C=O) and 1593 (C=C) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 2.32(s, 3H, CH_3), 4.75, 5.99(s, 2H, 2CH), 7.17(s, 1H, NH), 7.20-7.53(m, 10H, Ar-H).

Anal: $C_{19}H_{16}N_4O$ (316.36); Calcd: C, 72.13; H, 5.10; N, 17.71; Found: C, 72.25; H, 4.93; N, 17.50.

Ethyl 5-amino-4-oxo-3-phenyl-3,4-dihydrothieno[3,4-*d*]pyridazine-1-carboxylate (4)

A mixture of compound **2** (0.005 mol), sulphur (0.005 mol) and catalytic amount of piperidine in absolute ethanol (60 ml) was heated under reflux for 4h. The solid product obtained upon cooling was filtered off**,** dried and recrystallized from *n*-butanol to give **4**.

Yield: 59%; orange crystals; m.p. 180-182 ^{o}C. IR: 3419, 3302 (NH_2), 1707 (C=O), 1642 (C=O) and 1588 (C=C) cm^{-1}. ^1H NMR (DMSO-d_6): δ = 1.27(t, 3H, CH_3), 4.33(q, 2H, CH_2), 7.08(s, 2H, NH_2), 7.10-7.61(m, 6H. Ar-H).

Anal: $C_{15}H_{13}N_3O_3S$ (315.35); Calcd: C, 57.13; H, 4.16; N, 13.33; Found: C, 57.21; H, 4.28; N, 13.15.

Ethyl 5-cyano-6-oxo-1-phenyl-4-[2-phenylethenyl]-1,6-dihydro-pyridazine-3-carboxylate (5a) and ethyl 5-cyano-4-[2-(2-hydroxy-phenyl)ethenyl]-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carboxylate (5b)

A mixture of compound **2** (0.005 mol), benzaldehyde and/or salicylaldehyde (0.005 mol) in presence of catalytic amount of piperidine in absolute ethanol (60 ml) was heated under reflux for 4h. The solid product obtained upon cooling was filtered off, dried and recrystallized from the proper solvent to give **5a** and **5b**, respectively.

Compound **5a**

Yield: 76%; from *n*-butanol as Yellow crystals; m.p. 218-220 ^{o}C. IR: 3429, 3064 (CH), 2227 (C≡N), 1723 (C=O), 1671 (C=O) and 1618 (C=C) cm^{-1}. ^1H NMR (DMSO-d_6): δ = 1.28(t, 3H, CH_3), 4.37(q, 2H, CH_2), 7.49-7.74(m, 12H, Ar-H and olefinic protons).

Anal: $C_{22}H_{17}N_3O_3$ (371.39); Calcd: C, 71.15; H, 4.61; N, 11.31; Found: C, 71.26; H, 4.45; N, 11.19.

Compound **5b**

Yield: 31%; from ethanol as violet crystals; m.p. 256-258 ^{o}C. IR: 3352 (OH), 3069, 2973 (CH), 2227 (C≡N), 1734 (C=O), 1654 (C=O) and 1608 (C=C) cm^{-1}.

Anal: $C_{22}H_{17}N_3O_4$ (387.39); Calcd: C, 68.21; H, 4.42; N, 10.85; Found: C, 68.12; H, 4.31; N, 10.67.

Ethyl 5-amino-6-cyano-4-oxo-3,7-diphenyl-3,4-dihydrophthalazine-1-carboxylate (6)

A mixture of compound **2** (0.005 mol), benzylidene malononitrile (0.005 mol) and catalytic amount of piperidine in absolute ethanol (60 ml) was heated under reflux for 3h. The solid product separated during heating was filtered off, dried and recrystallized from DMF to give **6**.

Yield: 34%; yellow crystals; m.p. 284-286 °C. IR: 3448, 3301 (NH_2), 3117, 3061, 2985, 2933 (CH), 2204 (C≡N), 1720 (C=O), 1660 (C=O) and 1598 (C=C) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 1.31(t, 3H, CH_3), 4.39(q, 2H, CH_2), 7.55-8.22(m, 11H, Ar-H and NH_2).

Anal: $C_{24}H_{18}N_4O_3$ (410.42); Calcd: C, 70.23; H, 4.42; N, 13.65; Found: C, 70.12; H, 4.50; N, 13.45.

5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carbohydrazide (**7**)

A mixture of compound **2** (0.005 mol) and hydrazine hydrate (0.01 mol) in ethanol (60 ml) was heated under reflux on a water bath for 5h. The solid product obtained upon cooling was filtered off, dried and recrystallized from *n*-butanol to give **7**.

Yield: 84%; brown crystals; m.p. 236-238 °C. IR: 3437-3331 (NH and NH_2), 2928 (CH), 2242 (C≡N) and 1680 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 2.57 (s, 3H, CH_3), 4.60 (s, 2H, NH_2), 7.48-7.70 (m, 5H, Ar-H), 9.88 (s, broaded, 1H, NH).

Anal: $C_{13}H_{11}N_5O_2$ (269.26); Calcd: C, 57.99; H, 4.12; N, 26.01; Found: C, 58.10; H, 4.28; N, 25.92.

***N*'-[(4-chlorophenyl)methylidene]-5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carbohydrazide** (**8a**)**, 5-cyano-*N*'-[(4-hydroxy-3-methoxyphenyl)methylidene]-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carbohydrazide** (**8b**) **and 5-cyano-*N*'-[(2-hydroxyphenyl)methylidene]-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carbohydrazide** (**8c**)

A mixture of compound **7** (0.005 mol) and benzaldehyde derivatives namely, [4-chlorobenzaldehyde, vanillin and/or salicylaldehyde], (0.005 mol) in acetic acid (30 ml) was refluxed for 3h. The solid product obtained upon cooling was filtered off**,** dried and recrystallized from the proper solvent to give **8a-c**, respectively.

Compound 8a

Yield: 46%; from *n*-butanol as green crystals; m.p. 246-248 °C. IR: 3433 (NH), 3298, 2927 (CH), 2236 (C≡N) and 1685 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 2.66 (s, 3H, CH_3), 7.48-8.42 (m, 10H, Ar-H + N=CH), 12.05 (s, 1H, NH).

Anal: $C_{20}H_{14}ClN_5O_2$ (391.81); Calcd: C, 61.31; H, 3.60; N, 17.87; Found: C, 61.44; H, 3.46; N, 17.93.

Compound 8b

Yield: 84%; from acetic acid as yellow crystals; m.p. 258-260 °C. IR: 3421 (OH), 3072, 2971 (CH), 2230 (C≡N), 1677 (C=O) and 1595 (C=N) cm^{-1}.

Anal: $C_{21}H_{17}N_5O_4$ (403.39); Calcd: C, 62.53; H, 4.25; N, 17.36; Found: C, 62.44; H, 4.15; N, 17.45.

Compound 8c

Yield: 86%; from acetic acid as grey crystals; m.p. 268-270 ^{o}C. IR: 3413 (OH), 3065, 2977 (CH), 2232 (C≡N), 1680 (C=O) and 1613 (C=N) cm^{-1}.

Anal: $C_{20}H_{15}N_{5}O_{3}$ (373.36); Calcd: C, 64.34; H, 4.05; N, 18.76; Found: C, 64.20; H, 3.94; N, 18.91.

***N'*,*N'*-diacetyl-5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydro-pyridazine-3-carbohydrazide (9)**

A mixture of compound **7** (0.005 mol) and acetic anhydride (5 ml) was heated under reflux for 1h. The acetic anhydride excess was evaporated under reduced pressure and the solid product obtained was recrystallized from ethanol to give **9**.

Yield: 10%; pale brown crystals; m.p. 194-196 ^{o}C. IR: 3577, 3526 (NH), 3255, 3071, 3000, 2935 (CH), 2240 (C≡N), 1721 (C=O), 1689 (C=O) and 1592 (C=C) cm^{-1}. ^{1}H NMR (DMSO-*d$_6$*): δ = 2.32(s, 6H, $2CH_3CO$), 2.63(s, 3H, CH_3), 7.51-7.71(m, 5H, Ar-H), 11.08(s, 1H, NH).

Anal: $C_{17}H_{15}N_{5}O_{4}$ (353.33); Calcd: C, 57.79; H, 4.28; N, 19.82; Found: C, 57.62; H, 4.41; N, 19.91.

5-cyano-*N*-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carboxamide (10)

A mixture of compound **7** (0.005 mol) and phthalic anhydride (0.005 mol) in acetic acid (30 ml) was refluxed for 3h. The solid product obtained upon cooling was filtered off**,** dried and recrystallized from acetic acid to give **10**.

Yield: 56%; white crystals; m.p. 264-266 ^{o}C. IR: 3439, 3331 (NH), 3100, 2933 (CH), 2240 (C≡N), 1790-1741 (imidic C=O) and 1672 (cyclic and acyclic amide C=O) cm^{-1}. ^{1}H NMR (DMSO-*d$_6$*): δ = 2.64(s, 3H, CH_3), 7.56-8.01(m, 9H, Ar-H), 11.70(s, 1H, NH).

Anal: $C_{21}H_{13}N_{5}O_{4}$ (399.36); Calcd: C, 63.16; H, 3.28; N, 17.54; Found: C, 63.32; H, 3.11; N, 17.69.

5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carbonyl azide (11)

A stirred cold solution of compound **7** (0.005 mol) in acetic acid (20 ml) was treated dropwise with a cold solution of $NaNO_2$ (0.01 mol) in water (5 ml). The reaction mixture was further stirred for 30 min. and the separated solid product was filtered off**,** washed with water, dried to give **11**, sufficiently pure for direct use in the next stage.

Yield: 36%; yellow crystals; m.p. 109-110 ^{o}C. IR: 3431, 2240 (C≡N), 2186 (N_3), 1686 (C=O) and 1632 (C=N) cm^{-1}.

Anal: $C_{13}H_{8}N_{6}O_{2}$ (280.24); Calcd: C, 55.72; H, 2.88; N, 29.99; Found: C, 55.91; H, 2.69; N, 30.10.

Butyl (5-cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazin-3-yl)carbamate (13)

A solution of compound **11** (0.005 mol) in *n*-butanol (15 ml) is heated under reflux for 3h. The solid product obtained upon cooling was filtered off, dried and recrystallized from *n*-butanol to give **13**.

Yield: 6%; white crystals; m.p. 170-172 ^{o}C. IR: 3226 (NH), 2966 (CH), 2232 (C≡N), 1726 (C=O of carbamate ester), 1640 (C=O) and 1590 (C=C) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 0.89(t, 3H, CH_3), 1.30-1.38(m, 2H, CH_2), 1.56-1.61(m, 2H, CH_2), 2.40(s, 3H, CH_3), 4.09(t, 2H, OCH_2), 7.46-7.58(m, 5H, Ar-H), 9.84(s, 1H, NH).

Anal: $C_{17}H_{18}N_4O_3$ (326.35); Calcd: C, 62.57; H, 5.56; N, 17.17; Found: C, 62.71; H, 5.45; N, 17.30.

5-cyano-*N*'-(1,3-dioxo-1,3-dihydro-2*H*-inden-2-ylidene)-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carbohydrazide (14)

A mixture of compound **7** (0.005 mol) and ninhydrine (0.005 mol) in acetic acid (20 ml) was heated under reflux for 1h. The solid product obtained during heating was filtered off, dried and recrystallized from DMF/EtOH to give **14**.

Yield: 83%; green crystals; m.p. 252-254 ^{o}C. IR: 3432, 3214 (NH), 3064, 2927 (CH), 2239 (C≡N), 1737 (C=O), 1680 (C=O) and 1585 (C=C) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 2.80(s, 3H, CH_3), 7.59-8.02(m, 9H, Ar-H), 13.84(s, 1H, NH).

Anal: $C_{22}H_{13}N_5O_4$ (411.37); Calcd: C, 64.23; H, 3.19; N, 17.02; Found: C, 64.10; H, 3.32; N, 17.11.

5-methyl-3-oxo-2-phenyl-6-(5-thioxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)-2,3-dihydropyridazine-4-carbonitrile (16)

A mixture of compound **7** (0.005 mol) and ammonium thiocyanate (0.005 mol) in acetic acid (20 ml) was heated under reflux for 3h. The solid product separated during heating was filtered off, dried and recrystallized from DMF/EtOH to give **16**.

Yield: 35%; green crystals; m.p. 258-259 ^{o}C. IR: 3349, 3168 (NH), 3119 (CH), 2232 (C≡N), 1681 (C=O), 1632 (C=N) and 1374 (C=S) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 2.63(s, 3H, CH_3), 7.50-7.74(m, 5H, Ar-H), 9.49-10.53(s, broaded, 2H, 2NH).

Anal: $C_{14}H_{10}N_6OS$ (310.33); Calcd: C, 54.18; H, 3.25; N, 27.08; Found: C, 54.30; H, 3.14; N, 26.94.

5-cyano-*N*'-(4-cyano-5,6-diphenyl-3-pyridazinyl)-4-methyl-6-oxo-1-phenyl-1,6-dihydro-3-pyridazinecarbohydrazide (17)

A mixture of compound **7** (0.005 mol) and 3-chloro-4-cyano-5,6-diphenylpyridazine (0.005 mol) in *n*-butanol (30 ml) was heated under reflux for

8h. The solid product separated during heating was filtered off, dried and recrystallized from DMF to give **17**.

Yield: 50%; yellow crystals; m.p. 288-290 ^oC. IR: 3434, 3059 (NH), 2927 (CH), 2230 (C≡N), 1681 (C=O) and 1591 (C=C) cm^{-1}. ^1H NMR (DMSO-d_6): δ = 2.71(s, 3H, CH_3), 7.23-7.69(m, 17H, 2 x NH + Ar-H).

Anal: $C_{30}H_{20}N_8O_2$ (524.53); Calcd: C, 68.69; H, 3.84; N, 21.36; Found: C, 68.81; H, 3.68; N, 21.47.

4 Electrochemistry

Operating conditions used for analytical and small scale preparative electrochemical studies, carried out at a platinum electrode, have been detailed in a preceding paper [17]. Flow-cell electrolysis has been carried out by using a one compartment three electrode electrochemical cell. All CV experiments are carried with stagnant solutions out at a room temperature (25±1°C). The working and the auxiliary platinum electrodes surfaces should be renewed prior to each run. The accessible potential range depends upon the solvent and the supporting electrolyte that are used. Typical cyclic voltammogram (anodic oxidation followed by cathodic reduction) was performed [18-21].

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