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# SYNTHESIS, ANTIMICROBIAL AND ANTIVIRAL ACTIVITY OF 1,8-DIOXODECAHYDROACRIDINE DERIVATIVES

Eatedal H. Abdel Aal

Pharmaceutical Organic Chemistry Department, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt.

**ABSTRACT:**

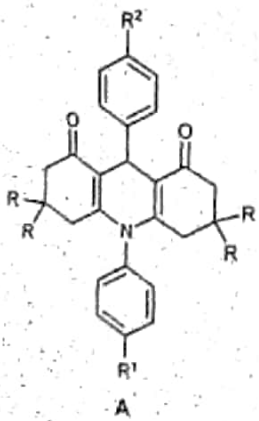
10-(4-Hydroxyphenyl)-9-(4-substituted phenyl)-1,8-dioxo-1,2,3,4,5,6, 7,8,9,10-decahydroacridine and their 3,3,6,6,-tetramethyl derivatives ($II_{1-4}$) have been prepared by reacting 3-(4-hydroxyphenylamino)-2-cyclohexenone or its 5,5-dimethyl derivative ($I_{1,2}$) with the appropriate araldehyde. Alkylation of $II_{1-4}$ with ethyl bromoacetate gave the corresponding esters $III_{1-4}$ which were condensed with hydrazine hydrate to produce hydrazides $IV_{1-4}$. These hydrazides underwent condensation with either 2,5-hexanedione to afford the pyrrole derivatives $V_{1-4}$, or aromatic aldehydes to give the hydrazone derivatives $VI_{1-20}$. Cyclo-condensation of some of the obtained hydrazones $VI_{1,3,5,11-13,15-18}$ with thioglycolic acid afforded the corresponding thiazolidinones $VII_{1-10}$. The antimicrobial activity for thirteen new compounds against either Gram positive or negative bacteria and fungi showed that compounds $IV_{3,4}$ were the most active ones against *Bacillus subtilus*. Moreover, the antiviral activity for twenty compounds performed on Vero cells against *Rinderpest* virus revealed that compounds $IV_3$, $VI_{13}$ and $VII_6$ caused reduction the cytopathic effect of virus by 25, 33 and 50%, respectively at a dose of 1000 µg/ml.

## INTRODUCTION

Many acridines were known to have numerous biological activities such as antitumor[1-5], antiamnestic[6], antimalarial[7], antifungal[8]and some of them were used for treatment of Alzheimer's disease[9,10]. In addition some acridines were found to possess analgesic and antiinflammatory activities[11,12].

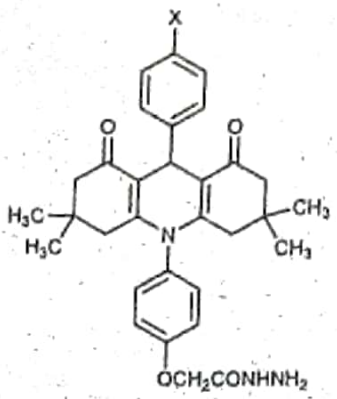
Moreover, some decahydroacridine derivatives [A] have been reported to possess antimicrobial activity [13]. Furthermore, several bis-acridinylated diamides [B] and 9-[4-(5-methylisoxazol-3-yl sulfamoyl) phenylamino] acridine-4-carboxamide [C] were found to have antiviral activity[14,15].

In the present work, new non-classical 1,8-dioxodecahydroacridine derivatives which are structurally related to the aforementioned ones [A,B,C] have been synthesized with the aim to possess better antimicrobial and antiviral activities.



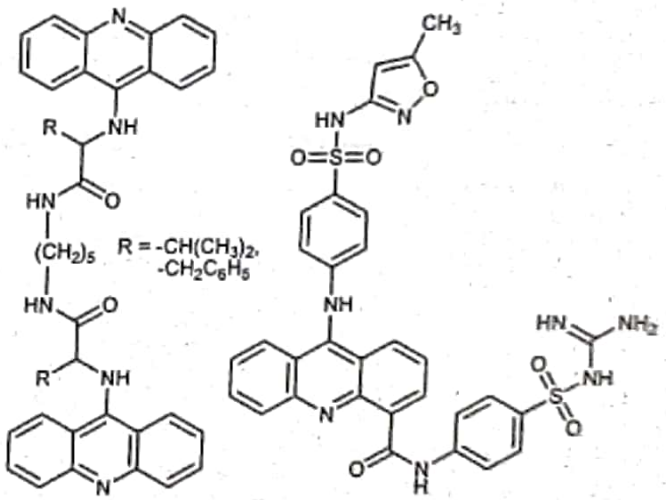
A

R = H, $CH_3$
$R^1$, $R^2$ = H, Br, Cl, $NO_2$, OMe

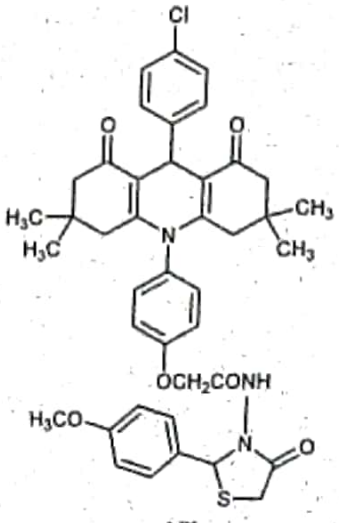


IV

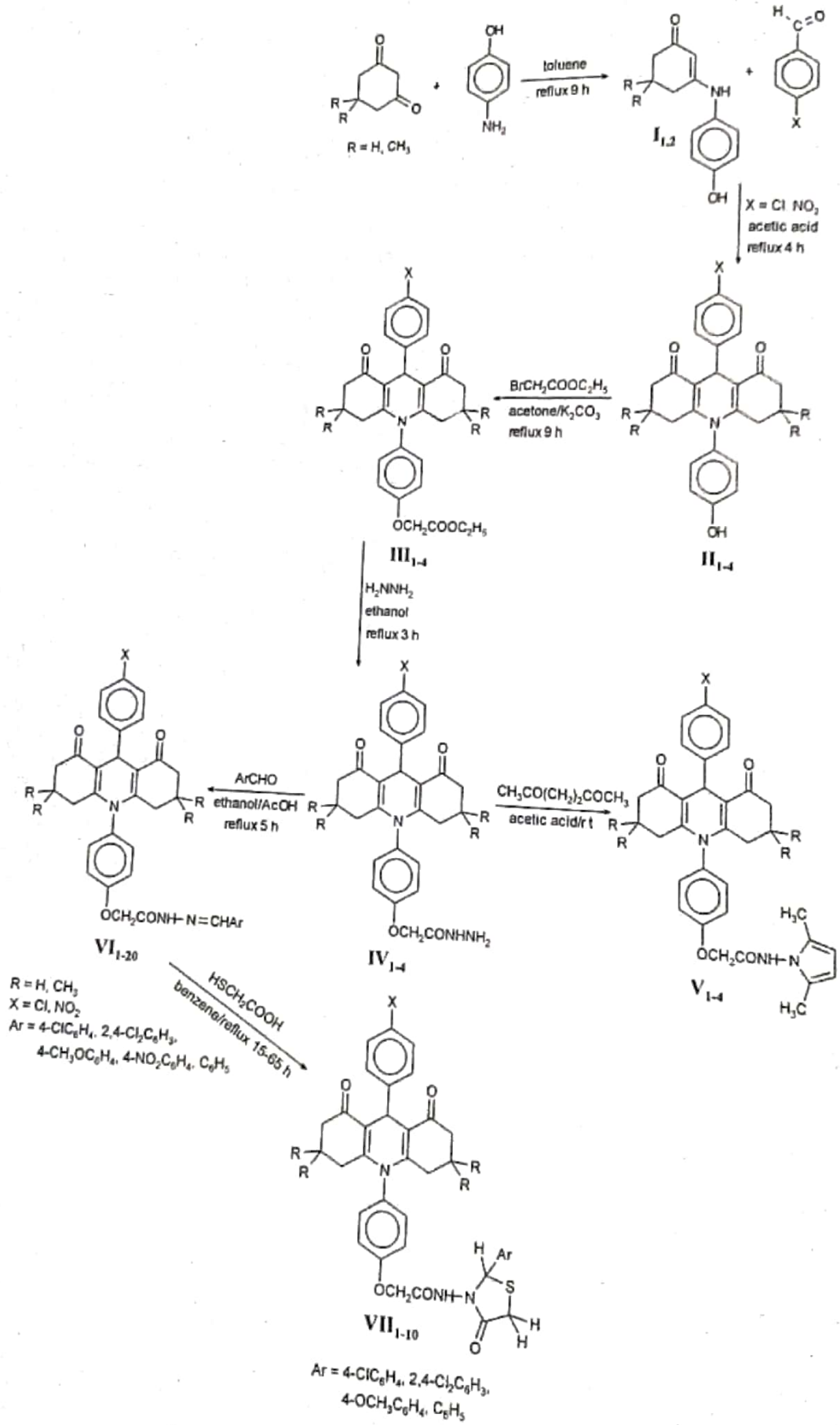
X = Cl, $NO_2$



B C



$VII_6$


R = H, CH3
toluene
reflux 9 h
I1-2
X = Cl NO2
acetic acid
reflux 4 h
II1-4
BrCH2COOC2H5
acetone/K2CO3
reflux 9 h
III1-4
H2NNH2
ethanol
reflux 3 h
IV1-4
ArCHO
ethanol/AcOH
reflux 5 h
VI1-20
CH3CO(CH2)2COCH3
acetic acid/r t
V1-4
HSCH2COOH
benzene/reflux 15-65 h
VII1-10
R = H, CH3
X = Cl, NO2
Ar = 4-ClC6H4, 2,4-Cl2C6H3,
4-CH3OC6H4, 4-NO2C6H4, C6H5
Ar = 4-ClC6H4, 2,4-Cl2C6H3,
4-OCH3C6H4, C6H5

**Scheme 1**

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**Chemistry:**

The novel 1,8-dioxodecahydroacridines were synthesized as illustrated in Scheme 1.

Condensation of 1,3-cyclohexanedione or 5,5-dimethyl-1,3-cyclo-hexanedione (dimedone) with *p*-aminophenol afforded enaminones $I_{1,2}$ in high yield using reported methods[16,17]. The novel decahydroacridinediones $II_{1-4}$ were prepared via heating one mole of the enaminones $I_{1,2}$ and half mole of aromatic aldehydes in glacial acetic acid for 4h according to reported procedure [18].

Alkylation of decahydroacridinediones $II_{1-4}$ using ethyl bromoacetate in acetone containing anhydrous $K_2CO_3$ gave esters $III_{1-4}$.

The hydrazide key intermediates $IV_{1-4}$ were obtained through condensation of the esters $III_{1-4}$ with hydrazine hydrate in refluxing ethanol. These hydrazides $IV_{1-4}$ were cyclized with 2,5-hexanedione in glacial acetic acid at room temperature to afford the novel pyrrole derivatives $V_{1-4}$. Moreover, the hydrazides $IV_{1-4}$ were condensed with different aromatic aldehydes giving the novel compounds 10-[4-arylidenehydrazinocarbonylmethoxyphenyl]-9-[4-substituted phenyl]-1,8-dioxo-1,2,3,4,5,6,7,8,9,10-decahydroacridine and their 3,3,6,6-tetramethyl derivatives $VI_{1-20}$.

Cyclocondensation of ten hydrazones $VI_{1,3,5,11-13,15-18}$ with thioglycolic acid was achieved in refluxing benzene[19] to obtain the desired thiazolidinyl derivatives $VII_{1-10}$.

**Biological activity:**

**(A) Antimicrobial activity:**

The preliminary antimicrobial activity for thirteen newly synthesized compounds $II_3$, $IV_{3,4}$, $V_4$, $VI_{2,4-6,11-13,19}$ and $VII_3$ was performed using disc diffusion method[20]. Generally, all test compounds are active against Gram positive bacteria (*Bacillus subtilus* and *Staphylococcus aureus*) and showed slight activity against Gram negative bacteria(*Escherichia coli*) using ciprofloxacin as a reference drug. On the other hand, all compounds have no inhibitory action against *Candida albicans* compared to the antifungal nystatin (Table 1).

The parent compound $II_3$ as well as derivatives $VI_{2,4-6,11-13,19}$ non significantly inhibited the growth of *Bacillus subtilus* and *Staphylococcus aureus* compared to broad spectrum antimicrobial agent ciprofloxacin whereas the hydrazides $IV_{3,4}$ were significantly active against *Bacillus subtilus* compared to ciprofloxacin. Compounds $V_4$ and $VII_3$ showed lower antimicrobial activity compared to hydrazides $IV_{3,4}$ (Table 1).

**Table (1):** Antimicrobial activity of some new compounds.

| Compounds No. | Antimicrobial activity | | | |
|---|---|---|---|---|
| | *Bacillus subtilus* | *Staphylococcus aureus* | *Escherichia coli* | *Candida albicans* |
| $II_3$ | ++ | ++ | + | - |
| $IV_3$ | +++ | ++ | + | - |
| $IV_4$ | +++ | ++ | + | - |
| $V_4$ | ++ | ++ | + | - |
| $VI_2$ | ++ | ++ | + | - |
| $VI_4$ | ++ | ++ | + | - |
| $VI_5$ | ++ | ++ | + | - |
| $VI_6$ | ++ | ++ | + | - |
| $VI_{11}$ | ++ | ++ | + | - |
| $VI_{12}$ | ++ | ++ | + | - |
| $VI_{13}$ | ++ | ++ | + | - |
| $VI_{19}$ | ++ | ++ | + | - |
| $VII_3$ | ++ | ++ | + | - |
| Ciprofloxacin | ++++ | ++++ | ++++ | - |
| Nystatin | - | - | - | +++ |

*Zone diameter from 7 to 10 mm: +;
zone diameter from 11 to 15 mm: ++
Zone diameter from 16 to 20 mm: +++;
zone diameter >20 mm: ++++
No zone diameter: -

**(B) Antiviral screening**

The *antiviral* activity of twenty new compounds $II_{1,3}$, $III_{2,3}$, $IV_{2-4}$, $V_{2,4}$ $VI_{1,3,5,13,14}$ and $VII_{1,2,4-6,8}$ *against* Rinderpest virus (RPV) performed on Vero cells was investigated. Rinderpest is RNA virus which belongs to the Morbilli viruses and is closely related antigenically to the human measles virus. It causes a fatal disease in cattle, buffaloes and wild ruminants in Africa and Middle East[21].

Firstly, the cytotoxic assays were performed to determine the highest nontoxic concentrations of the test compounds that could be used in the cytopathic effect-reduction assay[22,23]. Subsequently, the antiviral assays were carried out on Vero cell culture which infected with RP virus strain and then the test *compounds* were added in the highest nontoxic concentrations using ribavirin as a reference drug. End point titers (log 10 $TCID_{50}$) were determined by evaluating the cytopathic effect (C.P.E) and were calculated by the accumulative method of Reed and Muench[24], then represented as the % reduction in the cytopathic effects (Table 2).

**Table 2:** Cytopathic effect of Rinderpest bovine old kabete (RBOK) virus on Vero cell cultures previously infected with RBOK alone (control) or treated with different concentrations of the test compounds or ribavirin.

| Compounds | Concentration µg/ml | Virus control titer[1] | Change in virus titer[2] | % reduction in the C.P.E.[3] |
|---|---|---|---|---|
| Ribavirin | 1000 | 6 | 0.00 | 100 |
| | 500 | 6 | 0.00 | 100 |
| | 250 | 6 | 0.00 | 100 |
| Compound $IV_3$ | 1000 | 6 | 4.5 | 25 |
| | 500 | 6 | 4.5 | 25 |
| | 250 | 6 | 4.5 | 25 |
| Compound $VI_{13}$ | 1000 | 6 | 4.0 | 33 |
| | 500 | 6 | 4.0 | 33 |
| | 250 | 6 | 4.0 | 33 |
| Compound $VII_6$ | 1000 | 6 | 3.0 | 50 |
| | 500 | 6 | 3.5 | 42 |
| | 250 | 6 | 4.0 | 33 |

[1]Virus control titer; expressed as mean $Log_{10}TCID_{50}$/ml
[2]Mean $Log_{10}$ change in virus titer
[3] Percentage reduction in the cytopathic effects

Table 2 revealed that compounds $IV_3$, $VI_{13}$ and $VII_6$ showed *in vitro* antiviral activity as they significantly ($P<0.01$) reduced the cytopathic effects of RPV on Vero cell culture at a dose of 1000 µg/ml by 25, 33 and 50% respectively. The rest of compounds did not show any % reduction in the cytopathic effects at the same doses.

It was noticed that:

1) The hydrazone derivative **$VI_{13}$** showed higher antiviral activity (33%) than its corresponding hydrazide derivative **$IV_3$** (25%), as shown in Table 2.
2) The hydrazone derivative bearing electron donating group at 10- position (4-methoxyphenyl, compound **$VI_{13}$**) showed antiviral activity while compound **$VI_{14}$** (4-nitrophenyl) which bearing electron withdrawing group was devoid from such activity.
3) Upon cyclization of hydrazone **$VI_{13}$** gave the thiazolidinone derivative **$VII_6$** which showed higher activity (50%) than its noncyclized derivative **$VI_{13}$** (33%), as shown in Table 2.
4) Derivatives **$VI_{13}$** and **$VII_6$** which showed antiviral activity possess geminal methyl groups at 3,3 and 6,6-positions while their corresponding nonmethylated derivatives (compounds $VI_3$,$VII_2$) did not show any activity.

Thus, all these changes performed on the decahydroacridine skeleton may affect the lipophilicity (e.g. methoxy and geminal methyl groups) or planarity (e.g. geminal methyl groups) of the molecule and/or both which leading to improvement in the antiviral activity.

## CONCLUSION

New decahydroacridine derivatives bearing hydrazino, arylidenehydrazino, pyrrolyl or thiazolidinyl moieties were prepared starting from 3-(4-hydroxyphenylamino)-2-cyclohexenone or its 5,5-dimethyl derivative (**$I_{1,2}$**) to study their *in vitro* antimicrobial and antiviral activity.

The antimicrobial activity showed that the hydrazino derivatives (**$IV_{3,4}$**) were the most active one against Bacillus *Subtilus*. While the antiviral activity performed on Vero cells against *Rinderpest virus* revealed that the thiazolidinyl derivatives **$VII_6$** caused the highest reduction in the cytopathic effect of virus (50% at a dose of 1000 µg/ml).

## EXPERIMENTAL

Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. IR spectra (KBr, $cm^{-1}$) were recorded on Bruker or PU 9700 spectrometers. $^1H$ NMR spectra were determined on a Varian EM-390, 90 MHz, a Varian Gemini-200, 200 MHz and Jeol 270 MHz, JMN-EX270FT spectrometers using TMS as an internal standard and $CDCl_3$ or DMSO-$d_6$ as solvent; the chemical shifts are recorded in δ-units. Electron impact mass spectra were determined using a Mat 1125 at 70 eV spectrometer. Elemental analyses were performed at the Microanalytical Center, Cairo University, Giza, Egypt. TLC was performed on silica gel G for TLC (Merck), and spots were visualized by iodine vapours or by irradiation with UV light (254 nm).

3-[4-Hydroxyphenylamino]-2-cyclohexenone and its 5,5-dimethyl derivative (enaminones) **$I_{1,2}$** were prepared according to reported procedures[16,17].

**10-(4-Hydroxyphenyl)-9-(4-substituted phenyl)-1,8-dioxo-1,2,3,4,5,6,7, 8,9,10-decahydroacridine and their 3,3,6,6-tetramethyl derivatives (**$II_{1-4}$**).**

A solution of an enaminone **$I_{1,2}$** (0.01 mol) and half equivalent of an aromatic aldehyde (0.005 mol) in glacial acetic acid (15 ml) was heated under reflux for 4 h. The reaction mixture was allowed to cool at room temperature then diluted with water. The obtained solid was filtered, washed with water and crystallized from ethanol (Table 3).

**Compound $II_3$:** IR: ν = 3324 (OH), 3065 (CH-Ar), 2957, 2871 (CH-Aliph.), 1636 (C=O), 1571 (C=C) $cm^{-1}$.

**Compound $II_4$:** IR: ν = 3374 (OH), 3068 (CH-Ar), 2927 (CH-Aliph), 1631 (C=O), 1566 (C=C),1510, 1342 ($NO_2$) $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$, 200MHz): δ= 0.72 (s, 6H, $2CH_3$), 0.90 (s, 6H, $2CH_3$), 1.82-2.28 (m, 8H, $4CH_2$), 5.14 (s, 1H, CH), 6.931, 6.969 (d, J = 7.6 Hz, 2H, ArH), 7.235-7.277 (d, J = 8.4 Hz, 2H, ArH), 7.555,7.599 (d, J = 8.8 Hz, 2H, ArH), 8.137 – 8.181 (d, J = 8.8 Hz, 2H, ArH), 10.03 (s, 1H, OH, exch.) ppm.

**10-[4-Ethoxycarbonylmethoxyphenyl]-9-(4-substituted phenyl)-1,8-dioxo-1,2,3,4,5,6,7,8,9,10-decahydroacridine and their 3,3,6,6-tetramethyl derivatives ($III_{1-4}$).**

To a stirred solution of compound $II_{1-4}$ (0.01 mol) in acetone (50 ml) containing anhydrous $K_2CO_3$ (0.02 mol, 2.76 g), ethyl bromoacetate (0.01 mol, 1.67 g) was gradually added. The reaction mixture was refluxed while stirring for 9 h. After cooling, the reaction mixture was diluted with water (50 ml) and the separated solid was filtered and crystallized from ethanol (Table 4).

**Compound $III_1$:** IR: ν = 3040 (CH-Ar), 2950,2920 (CH-Aliph.), 1750 (C=O), 1640 (C=O), 1570 (C=C) $cm^{-1}$.

**Compound $III_2$:** IR: ν = 3050 (CH-Ar), 2950, 2900 (CH-Aliph), 1740 (C=O), 1625 (C=O), 1565 (C=C), 1510, 1350 ($NO_2$) $cm^{-1}$.

**Compound $III_3$:** IR: ν = 3050 (CH-Ar), 2980, 2890 (CH-Aliph.), 1760 (C=O), 1640 (C=O), 1575 (C=C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 90 MHz): δ = 0.8 (s, 6H, $2CH_3$), 0.95 (s, 6H, $2CH_3$), 1.30(t, 3H, $CH_3$), 1.7-2.5 (m, 8H, $4CH_2$), 4.25 (q, 2H, $CH_2$), 4.6 (s, 2H, $CH_2$), 5.1 (s, 1H, CH), 6.8-7.28 (m, 8H, ArH) ppm.

**Compound $III_4$:**
IR: ν = 3040 (CH-Ar), 2980, 2950 (CH-Aliph), 1750 (C=O), 1640 (C=O), 1580 (C=C), 1510, 1340 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 270 MHz): δ = 0.8 (s, 6H, $2CH_3$), 0.95 (s, 6H, $2CH_3$), 1.35(t, 3H, $CH_3$), 1.8-2.24 (m, 8H, $4CH_2$), 4.35 (q, 2H, $CH_2$), 4.75 (s, 2H, $CH_2$), 5.3 (s, 1H, CH), 7.0-7.2 (dd, 4H, ArH), 7.60 (d, 2H, ArH), 8.15 (d, 2H, ArH) ppm; $^{13}C$ NMR ($CDCl_3$, 270 MHz): δ =14 ($CH_2\underline{CH_3}$), 28 ($CH_3$), 30 ($CH_3$), 31 ($CH_2$), 32 (-$\underline{C}(CH_3)_2$), 41 ($CH_2$), 50 (CH), 61 ($OCH_2$), 65 ($OCH_2$), 114 (=C), 116 (=C), 125 (=CH), 129 (=CH), 131 (=CH), 132 (-CH), 146 (=C-), 150 (=C), 154 (=C-), 159 (=C-), 169 (O-C=O), 195 (C=O) ppm; Ms : m/z = 573 ($M^+$, 100%).

**10-[4-Hydrazinocarbonylmethoxyphenyl]-9-(4-substiuted phenyl)-1,8-dioxo-1,2,3,4,5,6,7,8,9,10-decahydroacridine and their 3,3,6,6,-tetramethyl derivatives ($IV_{1-4}$)**

A mixture of compound $III_{1-4}$ (0.01 mol) and hydrazine hydrate (0.015 mol) in absolute ethanol (50 ml) was refluxed for 3 h. The solvent was removed by distillation under reduced pressure and the separated product was filtered, and then crystallized from ethanol (Table 5).

**Compound $IV_4$:**
IR: ν = 3390 (NH), 3340 ($NH_2$), 3062 (CH-Ar), 2957, 2933 (CH-Aliph.), 1676 (C=O), 1637 (C=O), 1575 (C=C), 1511, 1341 ($NO_2$) $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$, 200 MHz): δ =0.72 (s, 6H, $2CH_3$), 0.90 (s, 6H, $2CH_3$), 1.78-2.28 (m, 8H, $4CH_2$), 4.41 (s, 2H, $NH_2$, exch.), 4.62 (s, 2H, $CH_2$), 5.14 (s, 1H, CH), 7.16-7.20 (d, J = 8 Hz, 2H, ArH), 7.409-7.450 (d, J = 8.2 Hz, 2H, ArH), 7.575-7.616 (d, J = 8.2 Hz, 2H, ArH), 8.14-8.18 (d, J = 8 Hz, 2H, ArH), 9.49 (1H, s, NH, exch.) ppm.

**10-[4-[N(2,5-Dimethyl-1-pyrrolyl)aminocarbonyl-methoxy]phenyl]-9-(4-substituted phenyl)-1,8-dioxo-1,2,3,4,5,6,7,8,9,10-decahydroacridine and their 3,3,6,6-tetramethyl derivatives ($V_{1-4}$):**

A mixture of the hydrazide $IV_{1-4}$ (0.001 mol) and 2,5-hexanedione (0.114 gm, 0.001 mol) in glacial acetic acid (5 ml) was stirred at room temperature overnight. The separated solid was filtered and crystallized from the proper solvent (Table 6).

**Compound $V_1$:** $^1H$ NMR (DMSO-$d_6$, 200 MHz):δ =1.66-2.21 (m, 12H, $6CH_2$), 1.96 (s, 6H, $2CH_3$), 4.92 (s, 2H, $CH_2$), 5.13 (s, 1H, CH), 5.67 (s, 2H, 2 =CH), 7.16-7.47 (m, 8H, ArH), 11.05 (s, 1H, NH) ppm; Ms : m/z = 570($M^+$,4.0 %).

**Compound $V_2$:**
IR: ν = 3446 (NH), 3070 (CH-Ar), 2945 (CH-Aliph), 1710 (C=O), 1633 (C=O), 1567 (C=C), 1512, 1346 ($NO_2$) $cm^{-1}$.

Ms: m/z = 580 ($M^+$,57.89 %).

**Compound $V_4$:**
IR: ν = 3448 (NH), 3069 (CH-Ar), 2957, 2871 (CH-Aliph), 1705 (C=O), 1638 (C=O), 1573 (C=C), 1511, 1363 ($NO_2$) $cm^{-1}$;$^1H$ NMR ($CDCl_3$, 200 MHz):δ = 0.78 (s, 6H, $2CH_3$), 0.94 (s, 6H, $2CH_3$), 1.80-2.23 (m, 8H, $4CH_2$), 2.07 (s, 6H, $2CH_3$), 4.85 (s, 2H, $CH_2$), 5.34 (s, 1H, CH), 5.82 (s, 2H, 2=CH), 7.20-7.25 (m, 4H, ArH), 7.56-7.60 (d, J = 8 Hz, 2H, ArH), 8.08-8.12 (d, J = 8 Hz, 2H, ArH), 9.08 (s, 1H, NH) ppm.

**10-(4-Arylidenehydrazinocarbonylmethoxyphenyl)-9-(4-substitutedphenyl)-1,8-dioxo-1,2,3,4,5,6,7,8,9,10-decahydroacridine and their 3,3,6,6-tetramethyl derivatives ($VI_{1-20}$).**

A mixture of equimolecular amounts (0.005 mol) of compounds $IV_{1-4}$ and the appropriate aldehyde was refluxed in ethanol (30 ml) containing acetic acid (2 ml) for 5 h. After cooling, the separated product was filtered and crystallized from the appropriate solvent (Table 7).

**Compound $VI_1$:** IR: ν = 3445, 3217 (NH), 3061 (CH-Ar), 2943, (CH-Aliph.), 1701 (C=O), 1633 (C=O),1568 (C=C)$cm^{-1}$.

**Compound $VI_3$:** IR: ν = 3446, 3215 (NH), 3063 (CH-Ar), 2941, 2836 (CH, Aliph.), 1698 (C=O), 1633 (C=O), 1570 (C=C) $cm^{-1}$.

**Compound $VI_6$:** $^1H$-NMR ($CDCl_3$, 90 MHz): δ =1.60-2.60 (m, 12H, $6CH_2$) 4.6 (s, 1H, $CH_2$), 5.06 (s, 1H, $CH_2$) 5.26 (s, 1H, CH), 6.8-7.92 (m, 12H, ArH), 8.05 (s, 1H, N=CH), 9.7 (s, 1H, NH) ppm.

**Compound $VI_{10}$:** IR: ν = 3441, 3226 (NH), 3059 (CH-Ar), 2943 (CH- Aliph.), 1700 (C=O), 1632 (C=O), 1568 (C=C), 1509, 1343 ($NO_2$) $cm^{-1}$;$^1H$-NMR ($CDCl_3$, 90 MHz): δ =1.6-2.4 (m, 12H, $6CH_2$), 4.6 (s, 1H, $CH_2$),

5.1 (s, 1H, $CH_2$), 5.3 (s, 1H, CH), 6.85-7.95 (m, 13H, ArH), 8.1 (s, 1H, N=CH), 9.5 (s, 1H, NH) ppm.

**Compound $VI_{11}$:** IR: ν=3443, 3216 (NH), 3059 (CH-Ar), 2957, 2871 (CH-Aliph.),1703 (C=O), 1636 (C=O),1573(C=C)$cm^{-1}$.$^1$H-NMR (DMSO, 300 MHz): δ =0.71 (s, 6H, $2CH_3$), 0.88 (s, 6H, $2CH_3$), 1.78-2.17 (m, 8H, $4CH_2$), 4.78 (s, 1H, $CH_2$), 5.01 (s, 1H, $CH_2$), 5.25 (s, 1H, CH), 7.11-7.78 (m, 12H, ArH), 8.03 (s, 1H, HC=N), 11.70 (s, 1H, NH exch.) ppm.

**Compound $VI_{13}$:** IR: ν=3446, 3226 (NH), 3066 (CH-Ar), 2957 (CH-Aliph.), 1701 (C=O), 1638 (C=O), 1574 (C=C) $cm^{-1}$.

**Compound $VI_{14}$:** IR: ν = 3445, 3217 (NH), 3065 (CH-Ar), 2957, 2871 (CH-Aliph.), 1702 (C=O), 1639 (C=O), 1569 (C=C), 1511, 1361 ($NO_2$) $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 90 MHz): δ = 0.6 (s, 6H, $2CH_3$), 0.75 (s, 6H, $2CH_3$), 1.75-2.1 (m, 8H, $4CH_2$), 4.5 (s, 1H, $CH_2$), 5.0 (s, 2H, $CH_2$, CH), 6.7-8.1 (m, 13H, ArH + N=CH), 10.0 (s, 1H, NH) ppm.

**Compound $VI_{15}$:** IR: ν=3442, 3224 (NH), 3064 (CH-Ar), 2958, 2872 (CH-Aliph.),1703 (C=O), 1639 (C=O),1574(C=C) $cm^{-1}$; $^1$H-NMR (DMSO, 300 MHz): δ = 0.71 (s, 6H, $2CH_3$), 0.88 (s, 6H, $2CH_3$), 1.78-2.23 (m, 8H, $4CH_2$), 4.78 (s, 1H, $CH_2$), 5.02 (s, 1H, $CH_2$), 5.25 (s, 1H, CH), 7.14-7.73 (m, 13H, ArH), 8.05 (s, 1H, HC=N), 11.63 (s, 1H, NH) ppm.

**Compound $VI_{17}$:** $^1$H-NMR ($CDCl_3$, 90 MHz): δ = 0.65 (s, 6H, $2CH_3$), 0.85 (s, 6H, $2CH_3$), 1.55-2.1 (m, 8H, $4CH_2$), 4.6 (s, 1H, $CH_2$), 5.05 (s, 1H, $CH_2$), 5.15 (s, 1H, CH), 6.8-8.05 (m, 11H, ArH), 8.4 (s, 1H, N=CH), 9.7 (s, 1H, NH) ppm.

**Compound $VI_{19}$:** $^1$H-NMR ($CDCl_3$, 90 MHz): δ = 0.6 (s, 6H, $2CH_3$), 0.8 (s, 6H, $2CH_3$), 1.7 -2.1 (m, 8H, $4CH_2$), 4.6 (s, 1H, $CH_2$), 5.00 (s, 1H, $CH_2$) 5.10 (s, 1H, CH), 6.8-8.3 (m, 13H, ArH + HC=N), 10.0 (s, 1H, NH) ppm.

**10-[4-(N]2-Substituted phenyl-4-oxo-3-thiazolidinyl)aminocarbonylmethoxy)phenyl]-9-(4-substituted phenyl)-1,8-dioxo-1,2,3,4,5,6,7,8,9,10-decahydroacridine and their 3,3,6,6,-tetramethyl derivatives ($VII_{1-10}$):**

Thioglycolic acid (0.18 gm, 0.002 mol) in dry benzene (7.5 ml) was added dropwise to the hydrazones $VI_{1,3,5,11-13,15-18}$ (0.001 mol) in dry benzene (5 ml) during 5 min. The reaction mixture was heated at the reflux temperture while stirring for 15-65 h and then left overnight at room temperature. The solvent was distilled off and the residue was neutralized with sodium bicarbonate solution (10%), then filtered and crystallized from the proper solvent (Table 8).

**Compound $VII_1$:** IR: ν = 3212 (NH), 3032 (CH-Ar), 2943 (CH-Aliph), 1729 (C=O), 1692 (C=O), 1633 (C=O),1569 (C=C) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 200 MHz):δ =1.68-2.66 (m, 12H, $6CH_2$), 3.76 (s, 1H, $CH_2S$), 3.80 (s, 1H, $CH_2S$), 4.60 (s, 2H, $CH_2$), 5.29 (s, 1H, CH), 5.96 (s, 1H, CH), 6.90-7.51 (m, 12H, ArH), 8.62 (s, 1H, NH) ppm.

**Compound $VII_3$:** $^1$H NMR ($CDCl_3$, 200 MHz):δ= 1.75 – 2.32 (m, 12H, $6CH_2$), 3.77 (s, 1H, $CH_2S$), 3.82 (s, 1H, $CH_2S$), 4.60 (s, 1H, $OCH_2$), 4.74 (s, 1H, $OCH_2$), 5.31 (s, 1H, CH), 5.97 (s, 1H, CH), 6.90-7.87 (m, 13H, ArH), 8.28 (s, 1H, NH) ppm.

**Compound $VII_4$:** IR: ν = 3420, 3269 (NH), 3030 (CH-Ar), 2956, 2927 (CH-Aliph), 1735 (C=O), 1699 (C=O), 1638 (C=O),1575 (C=C) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 200 MHz):δ = 0.78 (s, 6H, $2CH_3$), 0.93 (s, 6H, $2CH_3$), 1.72-2.15 (m, 8H, $4CH_2$), 3.77 (s, 1H, $CH_2S$), 3.81 (s, 1H, $CH_2S$), 4.63 (s, 2H, $CH_2$), 5.21 (s, 1H, CH), 5.97 (s, 1H, CH), 6.93-7.40 (m, 12H, ArH), 8.38 (s, 1H, NH) ppm.

**Compound $VII_5$:** IR: ν = 3229 (NH), 3070 (CH-Ar), 2957, 2872 (CH-Aliph.), 1735 (C=O), 1701 (C=O), 1639 (C=O),1579 (C=C) $cm^{-1}$.

**Compound $VII_6$:** $^1$H NMR (DMSO-$d_6$, 200 MHz):δ = 0.73 (s, 6H, $2CH_3$), 0.89 (s, 6H, $2CH_3$), 1.73-2.29 (m, 8H, $4CH_2$), 3.77 (s, 1H, $SCH_2$), 3.78 (s, 3H, $OCH_3$), 3.82 (s, 1H, $SCH_2$), 4.66 (s, 2H, $CH_2$), 5.03 (s, 1H, CH), 5.82 (s, 1H, CH), 6.95-7.45 (m, 12H, ArH), 10.53 (s, 1H, NH) ppm.

**Compound $VII_7$:** IR: ν = 3414, 3226 (NH), 3040 (CH-Ar), 2957, 2871 (CH-Aliph.), 1697 (2C=O), 1637 (C=O), 1574 (C=C) $cm^{-1}$;$^1$H NMR ($CDCl_3$, 200 MHz) : δ= 0.79 (s, 6H, $2CH_3$), 0.95 (s, 6H, $2CH_3$), 1.73-2.16 (m, 8H, $4CH_2$), 3.78 (s, 1H, $SCH_2$), 3.82 (s, 1H, $SCH_2$), 4.63 (s, 2H, $CH_2$), 5.22 (s, 1H, CH), 5.99 (s, 1H, CH), 6.97-7.46 (m, 13H, ArH), 8.25 (s, 1H, NH) ppm.

**Compound $VII_8$:** $^1$H NMR ($CDCl_3$, 200 MHz) : δ =0.74 (s, 6H, $2CH_3$), 0.94 (s, 6H, $2CH_3$), 1.76-2.16 (m, 8H, $4CH_2$), 3.77 (s, 1H, $SCH_2$), 3.81 (s, 1H, $SCH_2$), 4.64 (s, 2H, $CH_2$), 5.31 (s, 1H, CH), 5.97 (s, 1H, CH), 6.958-7.000 (d, J = 8.4 Hz, 2H, ArH), 7.12-7.16 (d, J = 8 Hz, 2H, ArH), 7.26-7.40 (m, 4H, ArH), 7.548-7.591 (d, J = 8.6 Hz, 2H, ArH), 8.087-8.129 (d, J = 8.4 Hz, 2H, ArH), 8.35 (s, 1H, NH) ppm.

**Compound $VII_9$:** IR: ν = 3220 (NH), 3070 (CH-Ar), 2957, 2871 (CH-Aliph.), 1734 (C=O), 1701 (C=O), 1639 (C=O), 1584 (C=C), 1510, 1363 ($NO_2$) $cm^{-1}$.

**Compound $VII_{10}$:** $^1$H NMR ($CDCl_3$, 200 MHz) : δ =0.74 (s, 6H, $2CH_3$), 0.95 (s, 6H, $2CH_3$), 1.76-2.25 (m, 8H, $4CH_2$), 3.76 (s, 1H, $SCH_2$), 3.83 (s, 3H, $OCH_3$), 3.85 (s, 1H, $SCH_2$), 4.64 (s, 2H, $CH_2$), 5.33 (s, 1H, CH), 5.96 (s, 1H, CH), 6.91-7.55 (m, 8H, ArH), 7.56-7.60 (d, J = 8 Hz, 2H, ArH), 8.09-8.13 (d, J = 8 Hz, 2H, ArH), 9.13 (s, 1H, NH) ppm.

## BIOLOGICAL ACTIVITY

### (A) Antimicrobial activity

The chosen compounds were dissolved in dimethylformamide (DMF) at final concentration 0.2 mg/ml. Susceptibility of Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and Gram-negative bacteria ( *Escherichia coli*) as well as *Candida albicans* against each compound was

performed by a disc diffusion method[20]. Overnight culture was streaked on the surface of Muller-Hinton agar plate. A filter paper disk saturated with a solution of each compound was placed on the agar plate. After incubation at 37°C for 24 h., the inhibition zone diameters of each compound were measured (Table 1).The used concentration of DMF causes no inhibition of bacterial growth. Bacterial and fungal strains were isolated and identified by Department of Microbiology, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt.

**(B) Antiviral screening**

**Materials and methods**

The test compounds ($II_{1,3}$ , $III_{2,3}$ , $IV_{2-4}$ ,$V_{2,4}$, $VI_{1,3,5,13,14}$ and $VII_{1,2,4-6,8}$) were dissolved in dimethyl sulfoxide (DMSO) which is nontoxic to both the virus and Vero cells and then subsequently diluted with the culture media to the required concentration[25].

**Rinderpest virus:**

The Rinderpest bovine old kabete (RBOK) strain of virus was used; being propagated on Vero cells for one passage. The virus titer was $10^6 TCID_{50}/ml$[22].

**Cell culture**

Vero cells are isolated from kidneys of African green monkeys and were used for RBOK propagation[22].

Minimum Essential Medium (MEM) with Hank's salts[26] was used for cell culture preparation and cell passages. It was supplemented with 10 % fetal calf serum. The medium contained 50 µg of streptomycin and 100 units of penicillin/ml of growth medium.

**Cytotoxicity assay**

It was firstly conducted to determine the highest dose of each compound that could be added to Vero cells without causing appreciable cytotoxicity[23].

**Cytopathic effect reduction assays**

These were performed in 96 well microtiter plates[23]. 75 µl of RBOK virus strain prepared in HBSS medium were added to the wells containing Vero cells (100 µl/well) and highest noncytotoxic concentration of each compound or ribavirin (25 µl/well). The test compounds were added 1 h after infection in the highest noncytotoxic concentration. Three replicates per concentration were used. The plates were incubated at 37°C for 7 days. The resulting virus titers were compared with virus control titrations made in parallel. End point titers (log10 $TCID_{50}$) were determined by evaluating the cytopathic effect and were calculated by the accumulative method of Reed and Muench[24] and then represented as the % reduction in the cytopathic effects (Table 2).

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Table 3: Physical data of compounds $II_{1-4}$.

| Comp. No. | R | X | m.p. °C | Yield % | Mol. Form. (M.wt) | Analyses % (Calcd. / Found) | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N |
| 1 | H | Cl | > 300 | 70 | $C_{25}H_{22}ClNO_3$ (419.91) | 71.51<br>71.40 | 5.28<br>5.25 | 3.34<br>3.32 |
| 2 | H | $NO_2$ | > 300 | 75 | $C_{25}H_{22}N_2O_5$ (430.46) | 69.76<br>69.82 | 5.15<br>5.24 | 6.51<br>6.74 |
| 3 | $CH_3$ | Cl | 294-295 | 80 | $C_{29}H_{30}ClNO_3$ (476.01) | 73.17<br>73.35 | 6.35<br>6.92 | 2.94<br>2.82 |
| 4 | $CH_3$ | $NO_2$ | 299-300 | 85 | $C_{29}H_{30}N_2O_5$ (486.57) | 71.59<br>71.42 | 6.21<br>6.33 | 5.76<br>5.55 |

Table 4: Physical data of compounds $III_{1-4}$.

| Comp. No. | R | X | m.p. °C | Yield % | Mol. Form. (M.wt) | Analyses % (Calcd. / Found) | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N |
| 1 | H | Cl | 245-247 | 80 | $C_{29}H_{28}ClNO_5$ (505.947) | 68.84<br>68.30 | 5.58<br>5.10 | 2.77<br>2.90 |
| 2 | H | $NO_2$ | 236-237 | 70 | $C_{29}H_{28}N_2O_7$ (516.55) | 67.43<br>67.54 | 5.46<br>5.65 | 5.42<br>5.51 |
| 3 | $CH_3$ | Cl | 178-180 | 85 | $C_{33}H_{36}ClNO_5$ (562.11) | 70.51<br>70.21 | 6.45<br>5.99 | 2.49<br>2.50 |
| 4 | $CH_3$ | $NO_2$ | 218-220 | 73 | $C_{33}H_{36}N_2O_7$ (572.66) | 69.21<br>69.30 | 6.34<br>6.20 | 4.89<br>4.92 |

Table 5: Physical data of compounds $IV_{1-4}$.

| Comp. No. | R | X | m.p. °C | Yield % | Mol. Form. (M.wt) | Analyses % (Calcd. / Found) | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N |
| 1 | H | Cl | 262-264 | 70 | $C_{27}H_{26}ClN_3O_4$ (491.97) | 65.92<br>66.28 | 5.33<br>5.42 | 8.54<br>8.61 |
| 2 | H | $NO_2$ | 251-253 | 72 | $C_{27}H_{26}N_4O_6$ (502.53) | 64.53<br>64.38 | 5.21<br>5.55 | 11.15<br>11.03 |
| 3 | $CH_3$ | Cl | 209-211 | 75 | $C_{31}H_{34}ClN_3O_4$ (548.09) | 67.93<br>67.88 | 6.25<br>5.75 | 7.67<br>7.85 |
| 4 | $CH_3$ | $NO_2$ | 246-248 | 78 | $C_{31}H_{34}N_4O_6$ (558.59) | 66.65<br>66.99 | 6.13<br>5.91 | 10.03<br>9.73 |

Table 6: Physical data of compounds $V_{1-4}$.

| Comp. No. | R | X | crystallization solvent | m.p. °C | Yield % | Mol. Form. (M.wt) | Analyses % (Calcd. / Found) | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | C | H | N |
| 1 | H | Cl | $CHCl_3$/pet. ether 60-80 | 318-320 | 80 | $C_{33}H_{32}ClN_3O_4$ (570.09) | 69.52<br>69.61 | 5.66<br>5.80 | 7.39<br>7.09 |
| 2 | H | $NO_2$ | DMSO | 279-281 | 70 | $C_{33}H_{32}N_4O_6$ (580.598) | 68.26<br>68.03 | 5.56<br>5.50 | 9.65<br>9.35 |
| 3 | $CH_3$ | Cl | $CHCl_3$/pet. ether 60-80 | 248-250 | 70 | $C_{37}H_{40}ClN_3O_4$ (626.199) | 70.96<br>70.72 | 6.44<br>6.33 | 6.71<br>6.67 |
| 4 | $CH_3$ | $NO_2$ | Ethanol | 328-330 | 65 | $C_{37}H_{40}N_4O_6$ (636.702) | 69.79<br>69.47 | 6.33<br>5.78 | 8.80<br>9.10 |

Table 7: Physical data of compounds $VI_{1-20}$.

| Comp. No. | R | X | Ar | crystallization solvent | m.p. °C | Yield % | Mol. Form. (M.wt) | Analyses % (Calcd. / Found) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | C | H | N |
| 1 | H | Cl | 4-$ClC_6H_4$- | Ethanol | 195-197 | 65 | $C_{34}H_{29}Cl_2N_3O_4$ (614.53) | 66.45<br>66.28 | 4.76<br>4.66 | 6.84<br>6.90 |
| 2 | H | Cl | 2,4-$Cl_2C_6H_3$- | $CHCl_3$/pet. ether | 202-204 | 70 | $C_{34}H_{28}Cl_3N_3O_4$ (648.97) | 62.93<br>62.90 | 4.35<br>4.68 | 6.47<br>6.21 |
| 3 | H | Cl | 4-$CH_3OC_6H_4$- | Ethanol/$H_2O$ | 190-192 | 68 | $C_{35}H_{32}ClN_3O_5$ (610.11) | 68.89<br>68.84 | 5.29<br>5.15 | 6.89<br>6.99 |
| 4 | H | Cl | 4-$NO_2C_6H_4$- | Ethanol | 220-222 | 80 | $C_{34}H_{29}ClN_4O_6$ (625.08) | 65.33<br>65.50 | 4.68<br>4.80 | 8.96<br>8.70 |
| 5 | H | Cl | $C_6H_5$- | Ethanol | 216-218 | 72 | $C_{34}H_{30}ClN_3O_4$ (580.08) | 70.40<br>70.82 | 5.21<br>5.58 | 7.24<br>7.25 |
| 6 | H | $NO_2$ | 4-$ClC_6H_4$- | Ethanol | 226-228 | 74 | $C_{34}H_{29}ClN_4O_6$ (625.08) | 65.33<br>65.51 | 4.68<br>4.80 | 8.96<br>8.66 |
| 7 | H | $NO_2$ | 2,4-$Cl_2C_6H_3$- | $CHCl_3$/pet. ether | 194-196 | 77 | $C_{34}H_{28}Cl_2N_4O_6$ (659.53) | 61.92<br>62.29 | 4.28<br>4.06 | 8.49<br>8.30 |
| 8 | H | $NO_2$ | 4-$CH_3OC_6H_4$- | $CHCl_3$/pet. ether | 182-184 | 75 | $C_{35}H_{32}N_4O_7$ (620.66) | 67.73<br>67.66 | 5.20<br>5.29 | 9.03<br>9.14 |
| 9 | H | $NO_2$ | 4-$NO_2C_6H_4$- | $CHCl_3$/pet. ether | 240-242 | 85 | $C_{34}H_{29}N_5O_8$ (635.59) | 64.25<br>64.40 | 4.60<br>4.70 | 11.02<br>11.32 |
| 10 | H | $NO_2$ | $C_6H_5$- | $CHCl_3$/pet. ether | 230-232 | 72 | $C_{34}H_{30}N_4O_6$ (590.63) | 69.14<br>69.45 | 5.12<br>5.26 | 9.49<br>9.37 |
| 11 | $CH_3$ | Cl | 4-$ClC_6H_4$- | Ethanol | 170-172 | 75 | $C_{38}H_{37}Cl_2N_3O_4$ (670.63) | 68.06<br>68.01 | 5.56<br>5.27 | 6.27<br>6.27 |
| 12 | $CH_3$ | Cl | 2,4-$Cl_2C_6H_3$- | Ethanol/$H_2O$ | 185-187 | 70 | $C_{38}H_{36}Cl_3N_3O_4$ (705.079) | 64.73<br>64.99 | 5.15<br>5.65 | 5.96<br>5.90 |
| 13 | $CH_3$ | Cl | 4-$CH_3OC_6H_4$- | Ethanol | 210-212 | 73 | $C_{39}H_{40}ClN_3O_5$ (666.45) | 70.28<br>70.00 | 6.05<br>5.94 | 6.31<br>6.02 |

Table 7: *continued*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 14 | $CH_3$ | Cl | 4-$NO_2C_6H_4$- | Ethanol/$H_2O$ | 202-204 | 78 | $C_{38}H_{37}ClN_4O_6$ (681.19) | 67.00<br>67.03 | 5.47<br>5.72 | 8.22<br>8.22 |
| 15 | $CH_3$ | Cl | $C_6H_5$- | Ethanol | 214-216 | 70 | $C_{38}H_{38}ClN_3O_4$ (636.19) | 71.74<br>71.54 | 6.02<br>5.73 | 6.60<br>6.52 |
| 16 | $CH_3$ | $NO_2$ | 4-$ClC_6H_4$- | Ethanol | 197-199 | 70 | $C_{38}H_{37}ClN_4O_6$ (681.19) | 67.00<br>66.65 | 5.47<br>5.38 | 8.22<br>8.10 |
| 17 | $CH_3$ | $NO_2$ | 2,4-$Cl_2C_6H_3$- | Ethanol | 218-219 | 68 | $C_{38}H_{36}Cl_2N_4O_6$ (715.625) | 63.78<br>63.76 | 5.07<br>5.14 | 7.83<br>8.37 |
| 18 | $CH_3$ | $NO_2$ | 4-$CH_3OC_6H_4$- | Ethanol | 210-212 | 70 | $C_{39}H_{40}N_4O_7$ (676.761) | 69.22<br>68.88 | 5.96<br>6.44 | 8.28<br>8.12 |
| 19 | $CH_3$ | $NO_2$ | 4-$NO_2C_6H_4$- | Ethanol/$H_2O$ | 236-238 | 80 | $C_{38}H_{37}N_5O_8$ (691.739) | 65.98<br>66.06 | 5.39<br>5.45 | 10.12<br>10.25 |
| 20 | $CH_3$ | $NO_2$ | $C_6H_5$- | Acetone | 231-232 | 80 | $C_{38}H_{38}N_4O_6$ (646.735) | 70.57<br>70.48 | 5.92<br>6.20 | 8.66<br>8.63 |

Table 8: Physical data of compounds $VII_{1-10}$.

| Comp. No. | R | X | Ar | Reflux time / h. | Crystallization solvent | m.p. °C | Yield % | Mol. Form. (M.wt) | Analyses % (Calcd. / Found) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | C | H | N |
| 1 | H | Cl | 4-$ClC_6H_4$- | 18 | Ethanol | 150-152 | 50 | $C_{36}H_{31}Cl_2N_3O_5S$ (688.62) | 62.79<br>63.00 | 4.54<br>4.80 | 6.10<br>6.05 |
| 2 | H | Cl | 4-$CH_3OC_6H_4$- | 30 | Ethanol | 148-150 | 60 | $C_{37}H_{34}ClN_3O_6S$ (684.14) | 64.95<br>64.60 | 5.01<br>4.73 | 6.14<br>6.05 |
| 3 | H | Cl | $C_6H_5$- | 24 | Ethanol | 138-140 | 55 | $C_{36}H_{32}ClN_3O_5S$ (654.12) | 66.09<br>7<br>65.90 | 4.93<br>5.00 | 6.42<br>6.76 |
| 4 | $CH_3$ | Cl | 4-$ClC_6H_4$- | 15 | Benzene/ pet. ether | 180-182 | 70 | $C_{40}H_{39}Cl_2N_3O_5S$ (744.72) | 64.51<br>64.20 | 5.28<br>5.00 | 5.64<br>5.84 |
| 5 | $CH_3$ | Cl | 2,4-$Cl_2C_6H_3$- | 45 | Benzene/ pet. ether | 162-164 | 65 | $C_{40}H_{38}Cl_3N_3O_5S$ (779.21) | 61.65<br>61.70 | 4.91<br>5.00 | 5.39<br>5.46 |
| 6 | $CH_3$ | Cl | 4-$CH_3OC_6H_4$- | 15 | $HCCl_3$/ pet. ether | 168-170 | 72 | $C_{41}H_{42}ClN_3O_6S$ (740.25) | 66.52<br>66.44 | 5.72<br>5.77 | 5.68<br>5.60 |
| 7 | $CH_3$ | Cl | $C_6H_5$- | 25 | Benzene/ pet. ether | 160-162 | 70 | $C_{40}H_{40}ClN_3O_5S$ (710.23) | 67.64<br>67.50 | 5.68<br>5.70 | 5.92<br>5.95 |
| 8 | $CH_3$ | $NO_2$ | 4-$ClC_6H_4$- | 20 | Benzene/ pet. ether | 164-166 | 65 | $C_{40}H_{39}ClN_4O_7S$ (755.22) | 63.61<br>63.52 | 5.20<br>5.00 | 7.41<br>7.31 |
| 9 | $CH_3$ | $NO_2$ | 2,4-$Cl_2C_6H_3$- | 65 | Benzene/pet ether | 172-174 | 60 | $C_{40}H_{38}Cl_2N_4O_7S$ (789.71) | 60.83<br>60.70 | 4.84<br>5.00 | 7.09<br>7.18 |
| 10 | $CH_3$ | $NO_2$ | 4-$CH_3OC_6H_4$- | 22 | Benzene/ pet. ether | 154-156 | 58 | $C_{41}H_{42}N_4O_8S$ (750.75) | 65.59<br>65.70 | 5.64<br>5.40 | 7.46<br>7.35 |

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## تشييد وفحص الفاعلية ضد الميكروبات والفيروسات لمشتقات ١ ، ٨-ثنائى أوكسو ديكاهيدروأكريدين

**اعتدال حسن عبدالعال**

**قسم الكيمياء العضوية الصيدلية – كلية الصيدلة – جامعة الزقازيق – الزقازيق – مصر**

تناول البحث تحضير ١٠-(٤-هيدروكسى الفينيل)-٩-(٤-مستبدل الفينيل)-٨,١-ثنائى أوكسو-١٠,٩,٨,٧,٦,٥,٤,٣,٢,١-ديكاهيدرواكريدين وكذلك مشتقاته من ٦,٦,٣,٣-رباعى الميثيل ($II_{1-4}$) بتفاعل ٣-(٤-هيدروكسى فينيل أمينو)-٢-هكسينون الحلقى ومشتقاته ٥,٥-ثنائى الميثيل ($I_{1,2}$) مع الألدهيدات الأروماتية ولقد تم تفاعل المركبات $II_{1-4}$ مع برومو خلات الإيثيل لتعطى الإسترات المقابلة $III_{1-4}$ والتى تم تحويلها إلى الهيدرازيدات $IV_{1-4}$ بالتفاعل مع هيدرات الهيدرازين وقد استعملت المركبات $IV_{1-4}$ لتحضير بعض مشتقات البيرول $V_{1-4}$ عن طريق تفاعلها مع ٢ ، ٥-هكسان دايون. هذا بالإضافة إلى تكثيفها مع بعض الألدهيدات الأروماتية لتعطى مشتقات الهيدرازون $VI_{1-20}$ . وعلاوة على ذلك تم حلقنه بعض مشتقات الهيدرازون ($VI_{1,3,5,11-13,15-18}$) بتفاعلها مع حمض الثيوجليكوليك إلى الثيازوليدينات المقابلة $VII_{1-10}$ . ولقد تم فحص ثلاثة عشر مركباً جديداً ضد البكتريا العصوية. وعلاوة على ذلك قد تم دراسة النشاط ضد الفطريات ولوحظ أن للمركبات $IV_{3,4}$ فاعلية عالية ضد البكتريا موجبة وسالبة الجرام وكذلك الفيروسات لعشرين مركب جديد ضد فيروس ريندربست وقد أجريت على خلايا الفيرو وقد وجد أن المركبات $IV_3$, $VI_{13}$, $VII_6$ قللت من النشاط الفيروسى بنسبة ٢٥% ، ٣٣% و ٥٠% تباعاً عند جرعة ١٠٠٠ ميكروجرام/مللى.