MANSOURA JOURNAL OF CHEMISTRY
Official Journal of Faculty of Science, Mansoura University, Egypt
E-mail: scimag@mans.edu.eg ISSN: 2974-4938

Synthesis antioxidants and antimicrobial evaluation of new arylazo-triazene hybrids via coupling of aryl diazonium salts with phenolic triazenes

Sonia S. Egeela, Ebrahim Abdel-Galil, and Elsayed M. Afsah

Chemistry Department, Faculty of Science, Mansoura University, Mansoura, Egypt

Correspondence to: *E-mail: msebrahim2002@yahoo.com*

Received:8/3/2023
Accepted:19/3/2023

Abstract: A new series of phenolic triazenes and bis(triazenes), incorporating piperidine was synthesized. Thus, for, 4-(piperidin-1-yldiazenyl)-phenol (3) was synthesized by coupling *p*-hydroxyphenyldiazonium chloride (2) with piperidine. The synthesis of phenolic arylazotriazene and arylazo(bis)triazene hybrids incorporating piperidine moiety was described. The antioxidant and antimicrobial activities of the synthesized new products were evaluated.

Keywords: Triazenes, piperidine, arylazotriazenearylazo(*bis*)triazene, diazonium salts

1.Introduction

As a result of their extensive range of biological and pharmacological activities [1-6], chemistry of triazenes and related compounds has been the subject of an extensive and increasing interest. Several triazenes are receiving attention owing to their promising antibacterial [7, 8], analgesic [9], antiviral [10], antimalarial [11], antitumor and cytotoxic [4, 10, 12] activity. Furthermore, in metal triazenide complexes synthesis, triazenes most often used as ligands [13-16], and in spectrophotometric determination of transition metals [17-19] and mercury [20] as reagents. On the other hand, phenolic compounds are important pharmacophores in the medicinal and pharmaceutical fields. Phenolic compounds for example, coumarins, flavonoids, tannins and phenolic acids possess a potential antioxidant activity [21 – 25], and a large number of these compounds possess antitumor, antiatherosclerotic, antibacterial, anticarcinogenic, antimutagenic, or anti-inflammatory, antiviral activities [26, 27].

From molecular design point of view, the combination of biologically active two pharmacophores or molecules is a well-known process for the drug-like molecules synthesis, which allows the synthesis of more potent agents. Accordingly, the present study has focused on the synthesis of some new phenolic triazenes and bis(triazenes), incorporating a bioactive moiety, such as piperidine, morpholine and piperazine as a structural unit. In addition, the synthesis of some new arylazo phenolic-triazene hybrids and triazene – Mannich base hybrids, of pharmaceutical interest, has been investigated. The new compounds might possess considerable synthetic and pharmaceutical interest**.**

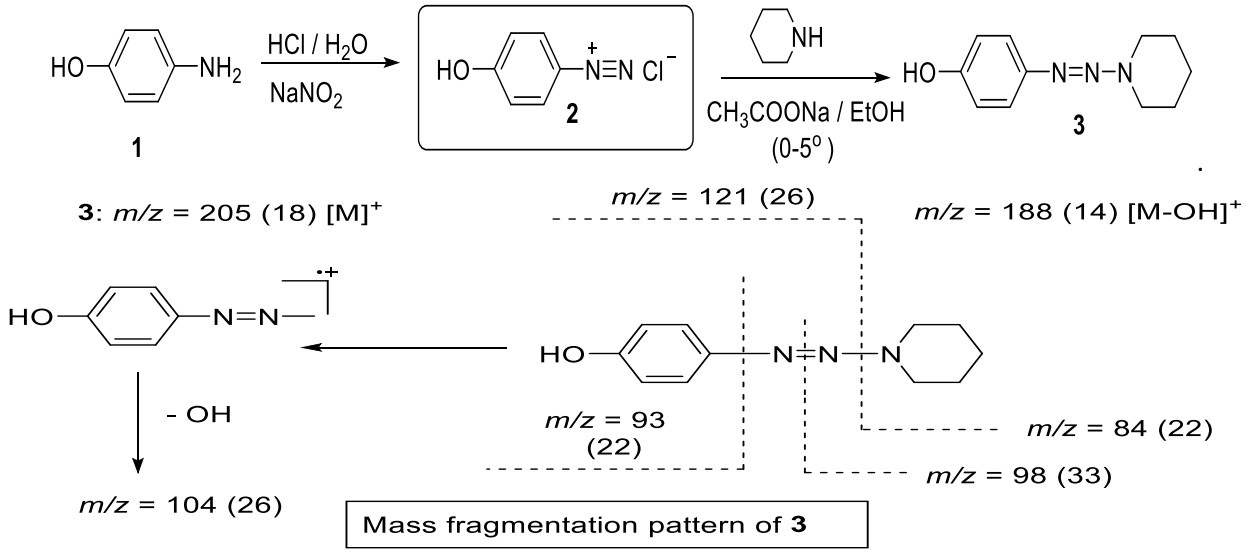
N-Coupling of the suitable diazonium salt with either primary or secondary amine is considered to be the conventional route to the synthesis of triazenes. This reaction proceeds by a two-stage mechanism with a diazonium cation as intermediate state and is subject to general base catalysis. Molecules of solvent or of amine may act as catalyst [28-30].

2. Results and Discussion:

In the present study, the synthesis of a new series of phenolic triazenes incorporating a heterocyclic moiety has been achieved by treating *p*-hydroxyphenyl diazonium chloride (**2**) with the appropriate heterocyclic *sec*-amine. Therefore, *N*-coupling of **2** with piperidine lead to the formation of 4-(piperidin-1-yldiazenyl)phenol (**3**) in the following equation

The formation of the phenolic triazene **3** is of particular interest, because a variety of compounds having a piperidine as a structural unit have been synthesized, because of their potential application in medicinal chemistry. The analytical and spectral data of compound **3** are consistent with its structure. The mass

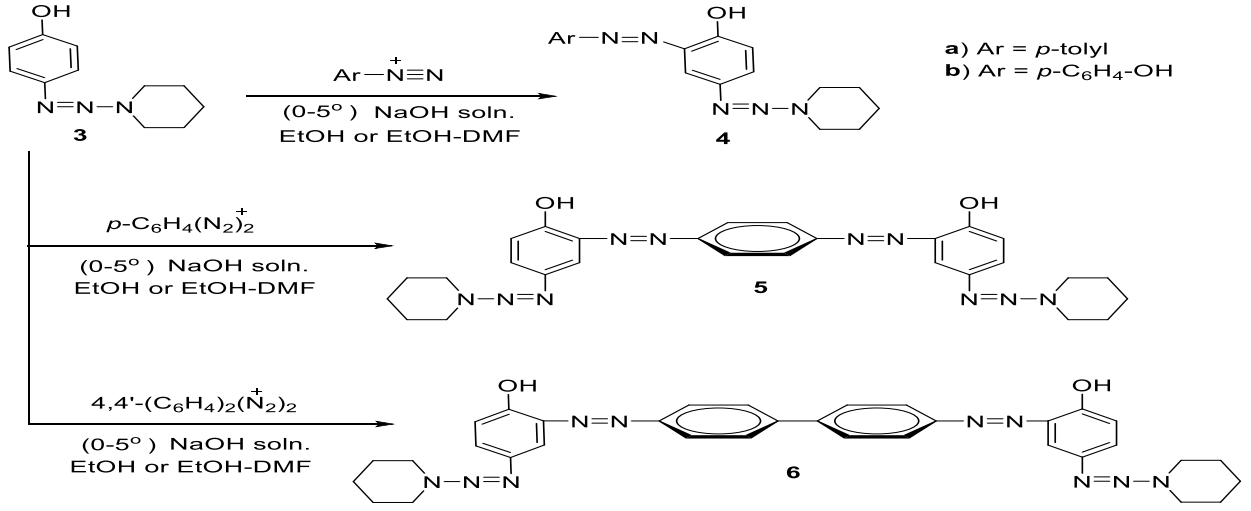
spectra of compound **3** revealed molecular ion peak at *m/z* = 205. The fragmentation pattern of compound **3**, is depicted in the following Scheme.



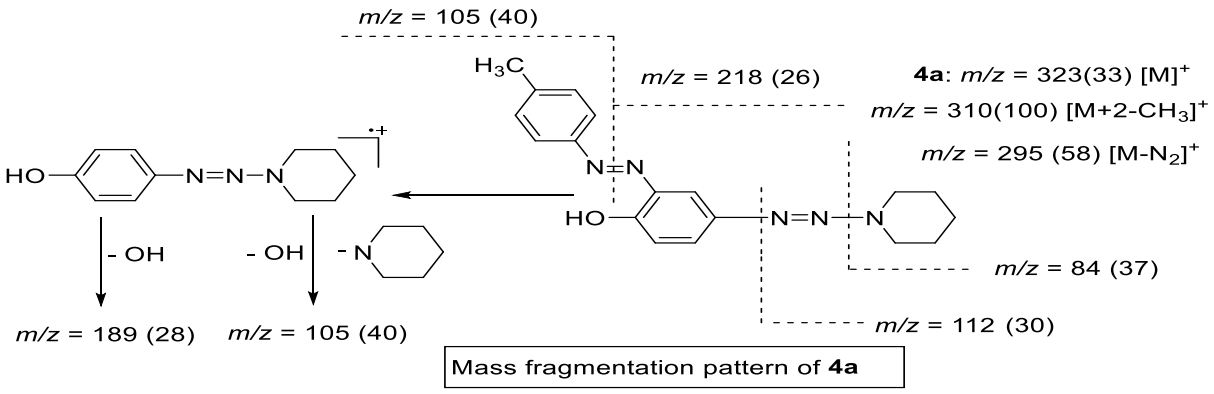
Mass fragmentation pattern of **3**

The synthesis of arylazo compounds and their mode of pharmaceutical activity have been reviewed [31-34]. A variety of compounds having the arylazo moiety as a structural unit have been synthesized and studied with interest centered on their application as dyes and pigments [35, 36]. The literature survey reveals that the arylazo compounds exhibits outstanding biological activities such as, antibacterial [37] antidiabetics [38], antitumor [39] and cytotoxic [40] activities.

In the present work, the possible synthesis of some new arylazo phenolic-triazene hybrids incorporating piperidine moiety as a structural unit has been investigated. Accordingly, coupling of the appropriate diazonium chloride with 4-(piperidin-1-yldiazenyl)-phenol (**3**), afforded a series of 2-(aryldiazenyl)-4-(piperidin-1-yldiazenyl)-phenols (**4a,b**) (Scheme 1). In line with this, coupling of bis(diazotized) *p*-phenylenediamine with 4-(piperidin-1-yldiazenyl)-phenol (**3**) in a molar ratio (1:2), led to the formation of 2,2'-(1,4-phenylenebis(diazene-2,1-diyl))bis(4-(piperidin-1-yldiazenyl)phenol) (**5**). A similar reaction of bis(diazotized)benzidine with **3** gave 2,2'-(biphenyl-4,4'-diylbis(diazene-2,1-diyl))bis(4-(piperidin-1-yldiazenyl)phenol) (**6**) (Scheme 1). Formulation of compounds **4a**,**b** was based on analytical and spectral data. The IR spectrum of **4b** as an example exhibited a strong band at 3425 cm^{-1}. Their mass spectra indicated molecular ion peaks at *m/z* = 323 and 325, respectively, and mass fragmentation patterns which supported their structures. The mass fragmentation pattern of **4a**, as an example, is depicted (Scheme 1A)

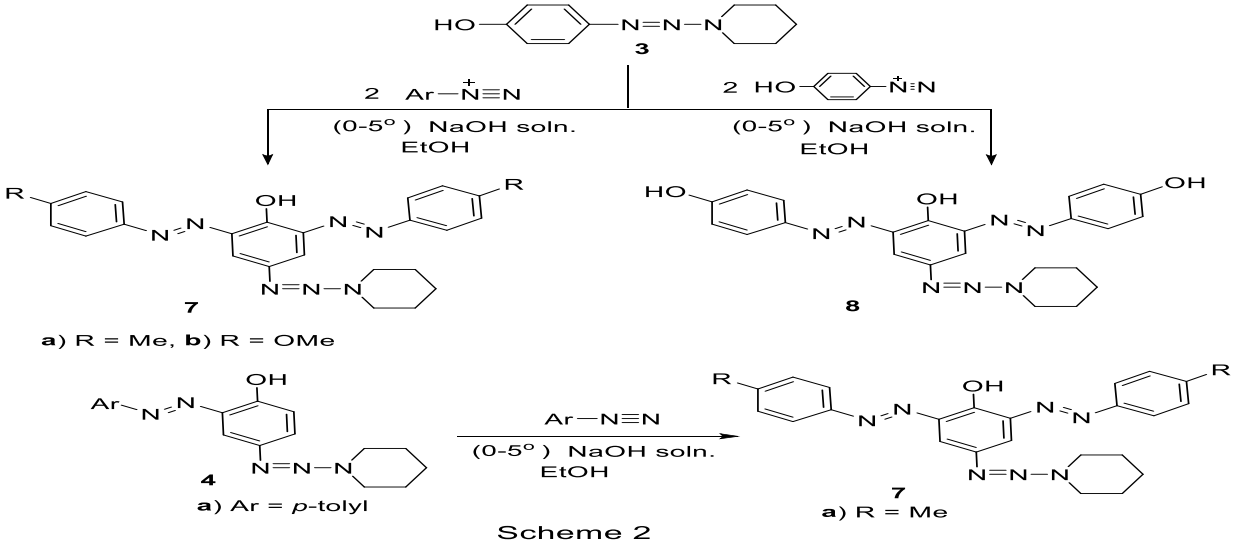


Scheme 1

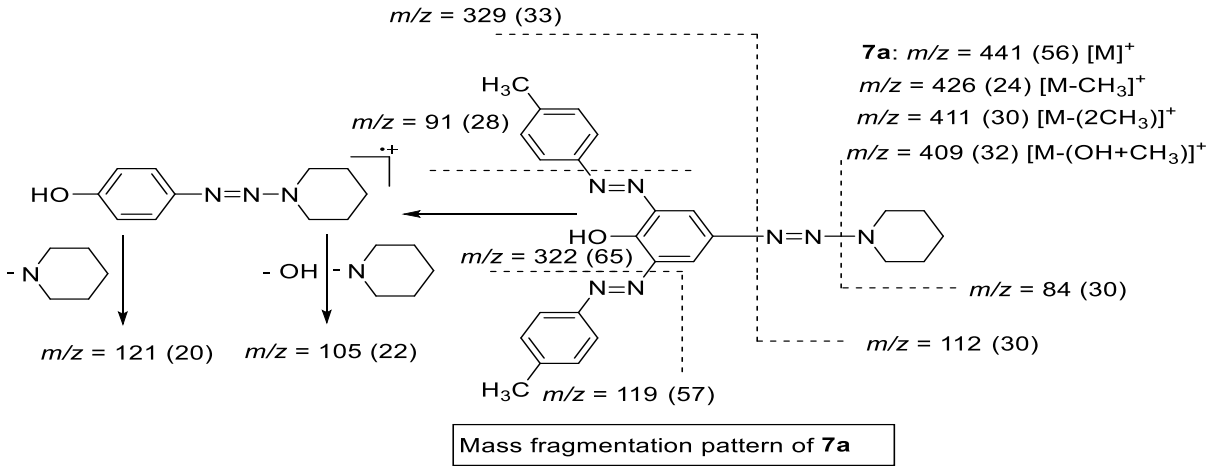


Scheme 1 - A

The synthesis of 2,6-*bis*(arylazo)phenolic triazenes of the type **7a**, **b** and **8** incorporating a piperidine moiety as a structural unit as shown in (Scheme 2), has been achieved by coupling of the appropriate diazonium chloride with 4-(piperidin-1-yldiazenyl)-phenol (**3**) in a molar ratio (2:1). The mass spectra of compounds **7a**, **b** and **8** showed molecular ion peaks at *m/z* = 441, 473 and 445, respectively. In addition, the unambiguous synthesis of **7a** by coupling of diazotized *p*-toluidine with **4a**, supported its assigned structure. The fragmentation pattern of **7a**, as an example, is depicted in Scheme 2-A



Scheme 2

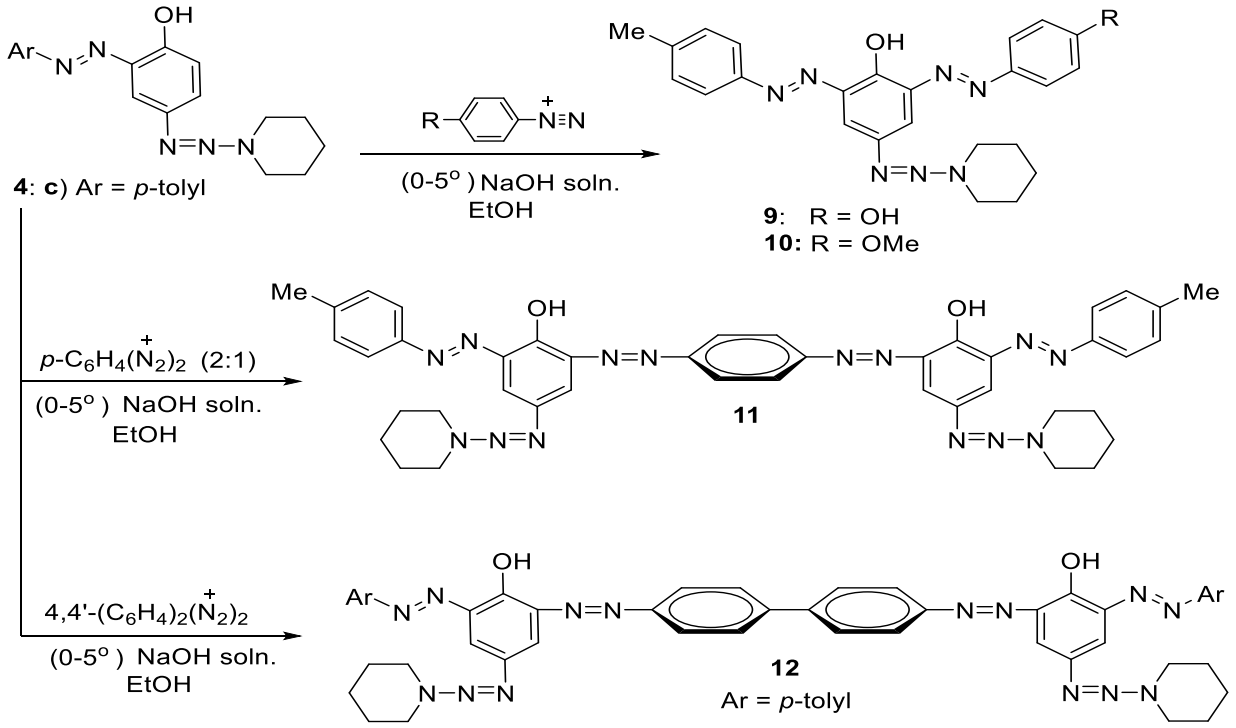


Scheme 2 - A

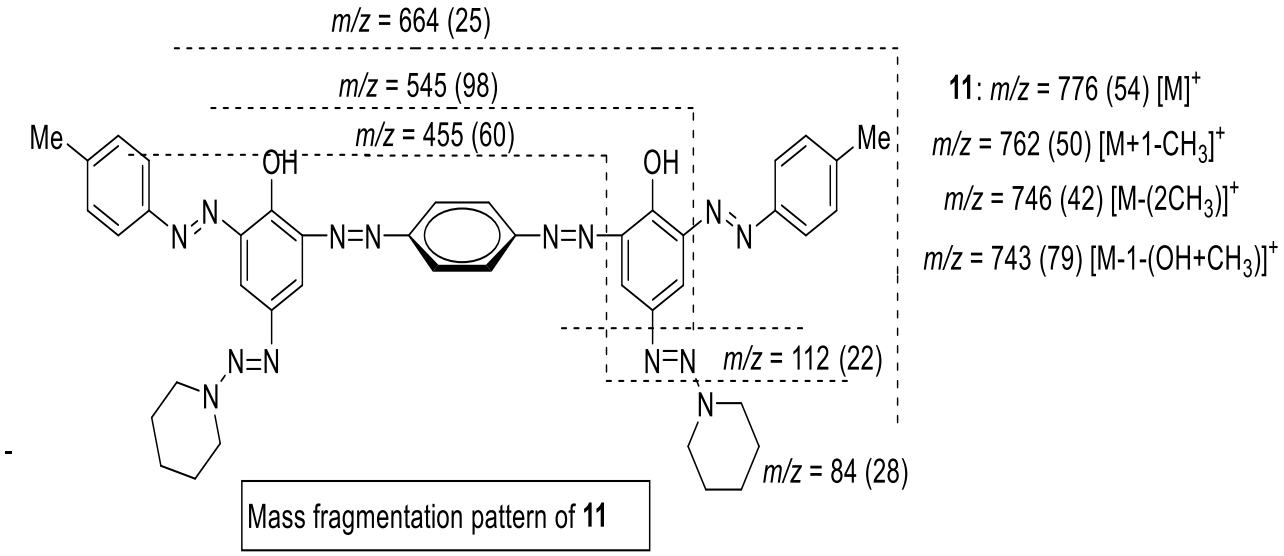
The coupling reaction of 2-(aryldiazenyl)-4-(piperidin-1-yldiazenyl)-phenols of the type **4** with diazonium ions is of particular interest, because it allows the synthesis of a wide range of mixed 2,6-*bis*(arylazo)phenolic triazenes. For instance, coupling of 4-(piperidin-1-

yldiazenyl)-2-(*p*-tolyldiazenyl)phenol (**4a**) with aryl diazonium ions derived from *p*-aminophenol and *p*-anisidine afforded 2-(4-hydroxyphenyl)-diazenyl)-4-(piperidin-1-yldiazenyl)-6-(*p*-tolyldiazenyl)phenol (**9**) and 2-(4-methoxyphenyl) diazenyl)-4-(piperidin-1-yldiazenyl)-6-(*p*-tolyl diazenyl)phenol (**10**), respectively. The advantage of this reaction is further illustrated by the synthesis of 6,6'-(1,4-phenylenebis(diazene-2,1-diyl))bis(4-(piperidin-1-yldiazenyl)-2-(*p*-tolyldiazenyl)-phenol) (**11**) and 6,6'-(biphenyl-4,4'-diylbis(diazene-2,1-diyl))bis(4-(piperidin-1-yldiazenyl)-2-(*p*-tolyldiazenyl)phenol) (**12**), by coupling of (**4a**) with *bis*(diazotized) *p*-phenylenediamine and *bis*(diazotized)-benzidine, as depicted in Scheme 3.

The mass spectra of compounds **9**-**12** indicated molecular ion peaks at *m/z* = 443, 457, 776 and 853, respectively. The mass fragmentation pattern of **11**, as an example, is depicted (Scheme 3A).



Scheme 3



Scheme 3 - A

3.Antioxidant activity:

The antioxidant activities of the synthesiszed new products (**1-12**) shown in (Table 1) were evaluated using 2,2'-azinobis-(3-

ethylbenzthiazoline-6-sulphonic acid) (ABTS) assay that is one of the most common radical scavenging assays.

Table 1. Antioxidant activities of compounds (**1-12**) using ABTS method

Compounds	Absorbance of samples	% inhibition
Control of ABTS	0.510	0
Ascorbic-acid	0.060	88.2%
3	0.068	86.7%
4a	0.175	65.7%
4b	0.093	81.8%
5	0.308	39.6%
6	0.416	18.4%
7a	0.267	47.6%
7b	0.160	68.6%
8	0.089	82.5%
9	0.291	42.9%
10	0.323	36.7%
11	0.353	30.8%
12	0.382	25.1%

From the evaluated products, compound **3** and **8** exihibited the highest inhibition value which is 86.7% and 82.5 respectavelly related to the presence of hydroxyl group and pipridiene group in both structures supported the antioxidant activty. On the other hand, the other evaluated products showed low to moderate inhibition values.

4. Antimicrobial activities:

The antimicrobial activities of compounds under investigation were screened according to the illustrated procedure in literature against *Gram-positive* bacterium (*Staphylococcus aureus*), *Gram-negative* bacterium (*Escherichia coli*) and one fungus (*Candida albicans*) using Ampicillin and Colitrimazole as standard drugs. The procedure which was used in determination is illustrated in details in literature [41-42]. The % activity index for the synthesized new compounds was calculated by the formula:

$$\%\ Activity\ Index = \frac{Zone\ of\ inhibition\ by\ test\ compound\ (diametre)}{Zone\ of\ inhibition\ by\ standard\ (diametre)} x\ 100$$

Table 2. Diameters of inhibition zones (mm), antibacterial and antifungal activities of the new investigated compounds **1-12**

Cpd.No.	*E. coli*		*S. aureus*		*C. Albicans*	
	Diameter of inhibition zone(mm)	% Activity index	Diameter of inhibition zone (mm)	% Activity index	Diameter of inhibition zone (mm)	% Activity index
3	19	76	23	95.8	22	81.5
4a	8	32.0	11	45.8	5	18.5
4b	13	52.0	16	66.7	15	55.5
5	NA	----	3	12.5	NA	----
6	NA	----	NA	----	NA	----
7a	4	16.0	7	29.2	3	11.1
7b	9	36.0	13	54.2	8	29.6
8	15	60.0	17	70.8	13	48.1
9	6	24.0	5	20.8	3	11.1
10	NA	----	NA	----	NA	----
11	NA	----	NA	----	NA	----
12	NA	----	NA	----	NA	----
Ampicillin	26	100	24	100	NA	----
Colitrimazole	NA	----	NA	----	27	100

NA: No Activity

The investigations of antimicrobial screening data which are shown in (Table 2) indicated that, compound **3** exihibited the highest inhibition value which related to the presence of hydroxyl group and pipridiene group in its structure. On the othar hand, most of newly prepared compounds exhibited fair to

good antimicrobial activities compared to that of the standard drugs.

5. EXPERIMENTAL

Melting points were uncorrected and measured by Stuart SMP10 electric melting point apparatus. Infrared spectra were measured on a Mattson 5000 FTIR spectrometer. The ^{1}H NMR spectra were recorded on JEOL 500 MHz NMR Unit Mansoura University in (*DMSO-d*$_6$) solution, with *TMS* as internal reference. Chemical shifts (δ) are measured in ppm and relative to *TMS*. The mass spectra were determined on a GC-MS QP–1000 EX Shimadzu instrument. Elemental analyses were performed by Carlo Erba 1108 instrument. The purity of the new synthesized compounds was established by thin layer chromatography (TLC) on silica gel plates, 0.25 nm, 60 GF 254 (Merck) with visualization by UV lamp. Compounds **5**, **6**, **11** and **12** are insoluble in common ^{1}H NMR solvents.

Synthesis of the triazene 3:

In 100 ml conical flask, prepare a solution of Piperidine (0.5 ml, 5 mmol) dissolved in ethanol (15 mL) and (1.36 g) sodium acetate $CH_3COONa.3H_2O$, cool the solution to 5^o C by immersing in an ice bath. Stir the solution vigorously and add very slowly the cold diazonium salt solution prepared by dissolving 4-aminophenol (**1**) (0.55 g, 5 mmol) in Conc. HCl (1.5 mL, and 5 mL cold H_2O) and diazotized by addition of $NaNO_2$ solution (0.36 g, 5.2 mmol; in 2 mL cold H_2O). When all diazonium salt solution has been added allow the reaction mixture to stand in an ice bath with occasional stirring for about 0.5 hour. The product was filtered, washed with cold water, dried, and crystallized from ethyl alcohol to give compound **3**

4-(Piperidin-1-yldiazenyl)phenol (3).

Yield 50%, (brown powder), mp 151-152^o C; IR (KBr): ν = 3260 (OH), 2928 (-CH_2-aliphatic), 1598, 1511, 1400, 1332, 1102, 766 cm^{-1}; ^{1}H-NMR (DMSO-*d6*) δ = 1.15-1.22 (m, 6H, 3-H_2, 4-H_2, 5-H_2 of piperidine), 2.35-2.73 (m, 4H, 2-H_2, 6-H_2 of piperidine), 6.73-7.70 ppm (m, 4 H, Ar-*H*); 9.44 ppm (s, 1H, OH). MS (EI, 70 eV): *m/z* (%) = 205 (18) [M]$^+$, 188 (14) [M-OH]$^+$, 176 (23) [M-(N_2+1)]$^+$, 160 (22) [M-(N_2+OH)]$^+$, 104 (26) [M-(piperidinyl ion +OH)]$^+$, 121 (26) [M-piperidinyl ion]$^+$, 93 (22) (HOC_6H_4-), 94 (73) [M+1-(piperidinyl ion+N_2)]$^+$, 84 (22) [piperidinyl ion]$^+$, 70 (100). *Anal.* Calcd for $C_{11}H_{15}N_3O$ (205.26): Calcd. C, 64.37; H, 7.37; N, 20.47%. Found: C, 64.30; H, 7.30; N, 20.34%.

Synthesis of the arylazo-triazenes 4a, b.

In 100 ml beaker, prepare a solution of triazene (**3**) (1.03 g, 5 mmol) in 30 ml 10 % sodium hydroxide solution, cool the solution to 5^o C by immersing in an ice bath by direct addition of crushed ice. Stir the solution vigorously and add very slowly the cold diazonium salt solution prepared by dissolving 5 mmol of an appropriate aromatic amine (0.54 gm of *p*-toluidine for compound **4a** and 0.55 gm *p*-aminophenol for compound **4b**) in Conc. HCl (1.5 mL, and water 5 mL) and diazotized by addition of sodium nitrite solution (0.36 g, 5.2 mmol; in 2 mL cold H_2O). When all diazonium salt solution has been added allow the reaction mixture to stand in an ice bath with occasional stirring for about 1 hour. The product was filtered, washed with cold water, dried and crystallized from ethyl alcohol to give compounds **4a**, and **4b**.

4-(piperidin-1-yldiazenyl)-2-p-tolyldiazenyl)phenol (4a):

Yield 55%, (dark brown powder), mp 124-126^o C; IR (KBr): ν = 3459 (OH), 2928 (-CH_2-aliphatic), 1590, 1500, 1441, 1384, 1104, 821 cm^{-1}. ^{1}H-NMR (DMSO-*d6*) δ = 1.38-1.61 (m, 6H, 3-H_2, 4-H_2, 5-H_2 of piperidine), 2.26-2.39 (m, 4H, 2-H_2, 6-H_2 of piperidine), 2.42 (s, 3H, CH_3), 6.89-7.76 (m, 7 H, Ar-*H*); 9.81 ppm (s, 1H, OH). MS (EI, 70 eV): *m/z* (%) = 323 (33) [M]$^+$, 310 (100) [M+2-CH_3]$^+$, 306 (20) [M-OH]$^+$, 291 (32) [M-(CH_3+OH)]$^+$, 218 (26) [M-($CH_3C_6H_4N$)]$^+$, 208 (42) [M+1-(CH_3+OH+piperidinyl ion]$^+$, 201 (28) [M-(OH+$CH_3C_6H_4N$)]$^+$, 189 (28) [C_6H_4N=N-piperidinyl+H]$^+$, 112 (30) [N=N-piperidinyl]$^+$, 105 (40) [$CH_3C_6H_4N$]$^+$, 104 (26) [N=N-C_6H_4-]$^+$, 84 (37) [piperidinyl ion]$^+$. *Anal.* Calcd for $C_{18}H_{21}N_5O$ (323.40): Calcd. C, 66.85; H, 6.55; N, 21.66%. Found: C, 66.98; H, 6.50; N, 21.55%.

2-(4-hydroxyphenyl)diazenyl)-4-(piperidin-1-yldiazenyl)phenol (4b):

Yield 65%, (dark brown powder), mp 170-171^o C; IR (KBr): ν = 3452 (OH), 2930, 2856 (-CH_2-aliphatic), 1590, 1500, 1499, 1446, 1383,

1269, 1129, 839 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 325 (31) $[M]^+$, 297 (18) $[M\text{-}N_2]^+$, 281 (22) $[M+1\text{-}OH\text{-}N_2]^+$, 206 (16) $[M+1\text{-}(HOC_6H_4N_2)]^+$, 196 (12) $[M\text{-}(OH+N_2+piperidinyl)]^+$, 181 (12) $[M+2\text{-}(2OH+N_2+piperidinyl\ ion]^+$, 124 (25) $[[HOC_6H_4N_2+3H]^+$, 119 (15) $[HOC_6H_3N{=}N\text{-}H]^+$, 107 (37) $[HOC_6H_4\text{-}N]^+$, 104 (20) $[N{=}N\text{-}C_6H_4\text{-}]^+$, 84 (10) [piperidinyl ion]$^+$. *Anal.* Calcd for $C_{17}H_{19}N_5O_2$ (325.37): Calcd. C, 62.75; H, 5.89; N, 21.52%. Found: C, 62.61; H, 5.80; N, 21.41%.

2,2'-(1,4-phenylenebis(diazene-2,1-diyl)) bis(4-(piperidin-1-yldiazenyl)phenol) (5):

This compound was obtained following the procedure described above for compound **4** using (1.03 g, 5 mmol) of triazene (**3**) and *p*-phenylenediamine (0.27 gm 2.5 mmol). Yield 50%, (deep brown powder), mp 126-127^o C; IR (KBr): *v* = 3448 (OH), 2930, 2855 (-CH_2-aliphatic), 1594, 1507, 1384, 1271, 1138, 840 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 542 (4) $[M+2]^+$, 541 (5) $[M+1]^+$, 540 (11) $[M]^+$, 458 (7) [M+2-piperidinyl ion]$^+$, 429 (21) $[M+1\text{-}N_2$ - piperidinyl ion]$^+$, 335 (38) $[M\text{-}(HOC_6H_4N{=}N$-piperidinyl ion)]$^+$, 316 (100) [M- (2 N=N-piperidinyl ion)]$^+$, 307 (47) $[M\text{-}(HOC_6H_4N{=}N$-piperidinyl ion$+N_2)]^+$, 122 (10) $[[HOC_6H_4N_2+H]^+$, 119 (8) $[HOC_6H_3N{=}N\text{-}H]^+$, 112 (32) [2 N=N-piperidinyl ion)]$^+$, 107 (37) $[HOC_6H_4\text{-}N]^+$, 105 (27) $[N{=}N\text{-}C_6H_5]^+$, 85 (8) [piperidinyl ion]$^+$. *Anal.* Calcd for $C_{28}H_{32}N_{10}O_2$ (540.63): Calcd. C, 62.21; H, 5.97; N, 25.91%. Found: C, 62.04; H, 5.91; N, 25.80%.

2-(4'-(2-hydroxy-5-(piperidin-1-yldiazenyl)phenyl)diazenyl)-[1,1'-biphenyl]-4-yl)diazenyl)-4(piperidin1yldiazenyl)phenol (6)

This compound was prepared following the procedure described above for compound **4** using (1.03 g, 5 mmol) of triazene (**3**) and benzidine (0.46 gm 2.5 mmol). Yield 65%, (deep brown powder), mp 284-286^o C; IR (KBr): *v* = 3451 (OH), 2934, 2854 (-CH_2-aliphatic), 1589, 1484, 1434, 1385, 1242, 826 cm^{-1}. ^{1}H-NMR (DMSO-*d6*) δ = 1.32-1.65 (m, 12H, 3-H_2, 4-H_2, 5-H_2 of piperidine), 2.22-2.37 (m, 8H, 2-H_2, 6-H_2 of piperidine), 6.85 (s, 2H Ar-*H*), 7.38-7.82 ppm (m, 14 H, 12 Ar-*H* + 2 OH); .MS (EI, 70 eV): *m/z* (%) = 618 (16) $[M+2]^+$, 617 (24) $[M+1]^+$, 616 (21) $[M]^+$, 599 (27) $[M\text{-}OH]^+$, 582 (18) $[M\text{-}(2OH)]^+$, 536 (30) [M+4- piperidinyl ion]$^+$, 514 (54) [M-1-OH-piperidinyl ion]$^+$, 505 (22) [M-(N=N-piperidinyl ion)]$^+$, 498 (40) $[M\text{-}(HOC_6H_4N{=}N$-piperidinyl ion)]$^+$, 422 (18) [M+2-(N=N-piperidinyl ion)-piperidinyl ion]$^+$, 182 (20) $[C_6H_5\text{-}C_6H_4\text{-}N{=}N]^+$, 152 (18) $[\text{-}C_6H_4\text{-}C_6H_4\text{-}]^+$, 120 (29) $[HOC_6H_3N{=}N\text{-}]^+$, 112 (12) [N=N-piperidinyl ion)]$^+$, 92 (30) $[HOC_6H_3\text{-}]^+$, 84 (34) [piperidinyl ion]$^+$. *Anal.* Calcd for $C_{34}H_{36}N_{10}O_2$ (616.73): Calcd. C, 66.22; H, 5.88; N, 22.71%. Found: C, 66.32; H, 5.95; N, 22.87%.

Synthesis of the bisarylazo-triazenes 7a, b and **8**.

These compounds were prepared following the same procedure described above for compound **4** using triazene (**3**) (0.51 g, 2.5 mmol) and an appropriate aromatic amine 5 mmol (0.54 gm of *p*-toluidine for compound **7a**, 0.62 gm of *p*-anisidine for compound **7b**, and 0.55 gm *p*-aminophenol for compound **8**).

4-(piperidin-1-yldiazenyl)-2,6-bis(-p-tolyldiazenyl)phenol 7a

Yield 60%, (red powder), mp 237-238 C; IR (KBr): *v* = 3448 (OH), 2921, 2860 (-CH_2-aliphatic), 1606, 1510, 1449, 1382, 1171, 819 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 441 (56) $[M]^+$, 426 (24) $[M\text{-}CH_3]^+$, 411 (18) $[M\text{-}(2CH_3)]^+$, 409 (32) $[M\text{-}(CH_3+OH)]^+$,355 (85) [M-2-piperidinyl ion]$^+$, 352 (43) $[M+2\text{-}(CH_3C_6H_4)]^+$, 340 (42) [M-(piperidinyl ion +OH)]$^+$, 335 (53) $[M\text{-}(CH_3C_6H_4+CH_3)]^+$, 333 (18) $[M\text{-}(CH_3C_6H_4+OH)]^+$, 329 (65) $[M\text{-}(piperidinylN{=}N)]^+$, 322 (65) $[M\text{-}(CH_3C_6H_4N{=}N)]^+$, 313 (39) $[M+1\text{-}(CH_3+piperidinyl\ N_2)]^+$, 314 (69) $[M\text{-}(piperidinylN{=}N{+}CH_3)]^+$, 231 (33) $[M\text{-}(CH_3C_6H_4N{=}N{+}CH_3C_6H_4\text{-})]^+$,119 (57) $[CH_3C_6H_3N{=}N\text{-}]^+$, 112 (30) [N=N-piperidinyl ion)]$^+$, 91 (28) $[CH_3C_6H_4\text{-}]^+$, 84 (30) [piperidinyl ion]$^+$. *Anal.* Calcd for $C_{25}H_{27}N_7O$ (441.54): Calcd. C, 68.01; H, 6.16; N, 22.21 Found: C, 68.10; H, 6.06; N, 22.30

4-(piperidin-1-yldiazenyl)-2,6-bis(4-methoxyphenyl)diazenyl)phenol (7b)

Yield 60%, (brown powder), mp 84-85^o C; IR (KBr): *v* = 3455 (OH), 2930, 2875 (-CH_2-aliphatic), 1600, 1596, 1500, 1441, 1247, 1144, 839 cm^{-1}. ^{1}H-NMR (DMSO-*d6*) δ = 1.36-1.65 (m, 6H, 3-H_2, 4-H_2, 5-H_2 of piperidine), 2.22-2.35 (m, 4H, 2-H_2, 6-H_2 of piperidine), 3.80 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 6.87 (s, 1 H,

Ar-*H*); 6.89-6.91 (d, 2 H, Ar-*H*); 7.04 (s, 1 H, Ar-*H*);7.07-7.09 (d, 2 H, Ar-*H*); 7.72-7.74 (d, 2 H, Ar-*H*); 7.81-7.79 (d, 2 H, Ar-*H*); 9.94 ppm (s, 1H, OH). MS (EI, 70 eV): *m/z* (%) = 475 (4) $[M+2]^+$, 473 (28) $[M]^+$, 456 (22) $[M-2-(OH)]^+$, 442 (19) $[M-(OCH_3)]^+$, 427 (25) $[M+2-(OCH_3+OH)]^+$, 394 (32) $[M-(2OCH_3+OH)]^+$,390 (23) [M+1-(piperidinyl ion)]$^+$, 340 (16) $[M+2-(CH_3OC_6H_4N=N)]^+$, 335 (16) $[M-(CH_3OC_6H_4+CH_3O)]^+$,284 (38) $[M+2-(CH_3OC_6H_4$+piperidinyl ion)]$^+$, 254 (27) $[M-(CH_3OC_6H_4N=N+$piperidinyl ion)]$^+$ 231 (43) $[M-(CH_3OC_6H_4N=N+CH_3OC_6H_4-)]^+$, 136 (62) $[CH_3OC_6H_4N=N-]^+$, 112 (36) [N=N-piperidinyl ion)]$^+$, 84 (40) [piperidinyl ion]$^+$. *Anal.* Calcd for $C_{25}H_{27}N_7O_3$ (473.54) C, 63.41; H, 5.75; N, 20.71 Found: C, 63.50; H, 5.69; N, 20.65

4-(piperidin-1-yldiazenyl)-2,6-bis(4-hydroxyphenyl)diazenyl)phenol (8)

Yield 65%, (red powder), mp 108-109 C; IR (KBr): *v* = 3456 (OH), 2937 (-CH_2-aliphatic), 1610, 1590, 1499, 1447, 1383, 1245, 839 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 445 (22) $[M]^+$, 417 (25) $[M-(N_2)]^+$, 401 (27) $[M+1-(N_2+OH)]^+$, 363 (54) [M+2-(piperidinyl ion)]$^+$, 361 (15) [M-(piperidinyl ion)]$^+$,333 (45) [M-(N=Npiperidinyl ion)]$^+$, 328 (48) [M+1-(piperidinyl ion+2OH)]$^+$, 324 (13) $[M-(HOC_6H_4N=N)]^+$,315 (19) [M-1 -(OH+N=Npiperidinyl ion)]$^+$, 306 (21) $[M-(HOC_6H_4N=N+OH)]^+$, 121 (35) $[HOC_6H_4N=N-]^+$, 112 (18) [N=N-piperidinyl ion)]$^+$, 84 (31) [piperidinyl ion]$^+$. *Anal.* Calcd for $C_{23}H_{23}N_7O_3$ (445.48) C, 62.01; H, 5.20; N, 22.01 Found: C, 62.11; H, 5.10; N, 22.13

Synthesis of the bisarylazo-triazenes 7a, 9, 10, 11 and **12**.

These compounds were prepared following the same procedure described above for compound **4** using 4-(piperidin-1-yldiazenyl)-2-*p*-tolyldiazenyl)phenol **(4a)** (0.81 g, 2.5 mmol) and an appropriate aromatic amine (0.27 gm (2.5 mmol) of *p*-toluidine for compound **7a**, (0.27 gm (2.5 mmol) of *p*-aminophenol for compound **9**, 0.31 gm (2.5 mmol) of *p*-anisidine for compound **10**, 0.14 gm (1.25 mmol) of *p*-phenylenediamine for compound **11** and 0.23 gm (1.25 mmol) of benzidine for compound **12**).

2-(4-hydroxyphenyl)diazenyl)-4-(piperidin-1-yldiazenyl)-6-(p-tolyldiazenyl)phenol (9)

Yield 75%, (red powder), mp 109-110^o C; IR (KBr): *v* = 3449 (OH), 2929 (-CH_2-aliphatic), 1602, 1510, 1499, 1457, 1384, 1270, 835 cm^{-1}. ^{1}H-NMR (DMSO-*d6*) δ = 1.35-1.62 (m, 6H, 3-H_2, 4-H_2, 5-H_2 of piperidine), 2.19-2.37 (m, 4H, 2-H_2, 6-H_2 of piperidine), 2.45 (s, 3H, CH_3), 6.82-7.91 (m, 11H, 10 Ar-*H* + OH); 9.62 ppm (s, 1H, OH). MS (EI, 70 eV): *m/z* (%) = 443 (27) $[M]^+$, 428 (19) $[M-(CH_3)]^+$, 426 (17) $[M-(OH)]^+$, 359 (17) [M-(piperidinyl ion)]$^+$, 358 (22) [M-1-(piperidinyl ion)]$^+$,352 (52) $[M-(CH_3C_6H_4)$, 331 (23) [M-(N=Npiperidinyl ion)]$^+$, 322 (33) $[M-(HOC_6H_4N=N)]^+$, 314 (36) [M-1-(OH+N=Npiperidinyl ion)]$^+$309 (18) [M-1-(2OH+CH_3+piperidinyl ion)]$^+$, 296 (100) [M-(2OH+N=Npiperidinyl ion)]$^+$ 281 (21) [M-1-(2OH+CH_3+piperidinylN=N ion)]$^+$, 270 (35) [M+2-($CH_3C_6H_4$+piperidinyl ion]$^+$. *Anal.* Calcd for $C_{24}H_{25}N_7O_2$ (443.51) C, 65.00; H, 5.68; N, 22.11 Found: C, 65.11; H, 5.75; N, 22.05

2-(4-methoxyphenyl)diazenyl)-4-(piperidin-1-yldiazenyl)-6-(p-tolyldiazenyl)phenol (10*)*

Yield 70%, (red powder), mp 89-90^o C; IR (KBr): *v* = 3448 (OH), 2921 (-CH_2-aliphatic), 1605, 1510, 1449, 1382, 1270, 820 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 457 (12) $[M]^+$, 427 (35) $[M+1-(OCH_3)]^+$, 413 (25) $[M+2-(CH_3+OCH_3)]^+$, 409 (12) $[M-(CH_3O+$ OH)]$^+$, 359 (18) $[M+1-(CH_3$+piperidinyl ion)]$^+$, 356 (17) [M-(OH+piperidinyl ion)]$^+$,350 (16) $[M-(CH_3OC_6H_4)$, 333 (11) $[M-(OH+CH_3OC_6H_4)]^+$, 324 (61) $[M+2-(CH_3O\ C_6H_4\ N=N\ )]^+$,322 (23) $[M-(CH_3OC_6H_4N=N)]^+$, 321 (52) $[M-(OH+CH_3C_6H_4N=N)]^+$,282 (13) [M-1-($CH_3C_6H_4$+piperidinyl ion)]$^+$, 279 (42) [M-1-(HOC_6H_4+piperidinyl ion)]$^+$, , 255 (26) [M-($CH_3C_6H_4$ +piperidinylN=N ion)]$^+$239 (22) [M-($CH_3OC_6H_4$ +piperidinylN=N ion)]$^+$ 203 (100) $[M-1-(HOC_6H_2N=N$-piperidinyl)]$^+$, 270 (35) [M+2-($CH_3C_6H_4$+piperidinyl ion]$^+$. *Anal.* Calcd for $C_{25}H_{27}N_7O_2$ (457.54) C, 65.63; H, 5.95; N, 21.43 5.68; Found: C, 65.555; H, 5.94; N, 21.53

2-((4-(2-hydroxy-5-(piperidin-1-yldiazenyl)-3-(p-tolyldiazenyl)phenyl) diazenyl) phenyl) diazenyl)-4-piperidin-1-yldiazenyl)-6-p-tolyldiazenyl)phenol (11)

Yield 70%, (red powder), mp 260-261^o C; IR (KBr): *v* = 3449 (OH), 2950 (-CH_2-aliphatic), 1604, 1510, 1449, 1383, 1272, 820 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 776 (54) $[M]^+$,

762 (50) $[M+1-(CH_3)]^+$, 760 (33) $[M+1-(OH)]^+$, 746 (42) $[M-2(CH_3)]^+$, 743 (79) $[M-1-(CH_3+OH)]^+$, 731 (53) $[M+2-(2CH_3+OH)]^+$,692 (32) [M-(piperidinyl ion), 678 (33) [M+1-(piperidinyl ion $+CH_3$)]$^+$, 662 (25) [M-2-(piperidinyl ion N=N)]$^+$,657 (46), $[M-(CH_3C_6H_4N=N)]^+$, 608 (42) [M-2(piperidinyl ion)]$^+$, 580 (33) [M-(piperidinyl+ piperidinyl N=N)]$^+$,545 (98) [M-[M-$(CH_3C_6H_4N=N+$ piperidinyl N=N)]$^+$, 538 (37) [M-$2(CH_3C_6H_4N=N)]^+$, , 455 (60) [M+1-$(CH_3C_6H_4N=N +HOC_6H_2N=N$piperidinyl)]$^+$, 433 (46) [M-$(CH_3C_6H_4N=N$ +2 piperidinylN=N)]$^+$ 112 (24) [piperidinyl N=N)]$^+$, 84 (28) [piperidinyl ion]$^+$. *Anal.* Calcd for $C_{42}H_{44}N_{14}O_2$ (776.91) C, 64.93; H, 5.71; N, 25.24 Found: C, 64.85; H, 5.80; N, 25.33

2-(4'-((2-hydroxy-5-(piperidin-1-yldiazenyl)-3-(p-tolyldiazenyl)phenyl)diazenyl)-[1,1'-biphenyl]-4-yl)diazenyl)-4-(piperidin-1-yldiazenyl)-6-(p-tolyldiazenyl)phenol (12*)* Yield 72%, (red powder), mp 104-105^o C; IR (KBr): *ν* = 3450 (OH), 2934, 2853 (-CH_2-aliphatic), 1599, 1484, 1434, 1355, 1286, 825 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 853 (59) $[M]^+$, 769 (42) [M-(piperidinyl ion)]$^+$, 745 (61) $[M-(CH_3C_6H_4+OH)]^+$, 728 (45) $[M-(CH_3C_6H_4+2OH)]^+$, 710 (83) [M-1-(2CH_3+ piperidinyl ion)]$^+$, 657 (58) [M-(piperidinyl + piperidinyl N=N)]$^+$,649 (41) [M-1-(piperidinyl ion N=N+ $CH_3C_6H_4$), 627 (12) [M-2-2(piperidinyl N=N)]$^+$, 612 (33) [M-2-(piperidinyl N=N)+CH_3]$^+$, N=N)]$^+$. *Anal.* Calcd for $C_{48}H_{48}N_{14}O_2$ (853.01) C, 67.59; H, 5.67; N, 22.99 Found: C, 67.70; H, 5.75; N, 23.10

6. References

1. D. B. Kimball, M. M. Haley (2002), Angew. Chem. Int. Ed., **41**, 3338-3351.
2. K. Vaughan, M. F. G. Stevens, (1978) Chem. Soc. Quart. Rev., , ***7,*** 377-397.
3. V. I. Nifontov, N. P. Bel'skaya, E. A. Shtokareva, *Pharm*(1993). *Chem. J.*, , ***27***, 652-656.
4. V. I. Nifontov, N. P. Bel'skaya, E. A. Shtokareva, *Pharm*(1994). *Chem. J.*, , ***28***, 687-706.
5. K. Vaughan, Triazenes: Synthesis and chemical properties, in Triazenes: Chemical, Biological and Clinical Aspects, eds. T. Giraldi, T. A. Connors and G. Cartei, (1990) Springer Science + Business Media, Plenum Press, New York, , pp. 1-13.
6. (a) K. Vaughan, Triazenes, in Chemistry of Antitumor Agents, ed. D. E. V. Wilman, Blackie, Chapman and Hall, New York, (1990), pp. 159-186., (b) D. Siebert, G. F. Kolar, Mutation Research, 1973, *18*, 267-271.
7. I. S. Hura, N. Naulakha, A. K. Goswami, M. K. Shrivastav, *Indian J. Microbiology*, (2003), **43**, 275-276.
8. M. Horner, V. F. Giglio, B. A. Iglesias, P. R. Martien, T. M. Michelot, L. G. Brenner, G. L. Paraginski, R. Horner, (2008)*Brazilian J. Pharm. Sci*., ***44***, 441-449.
9. L. S. Chauhan, C. P. Jain, R. S. Chauhan, A. K. Goswami, (2007) *Asian J. Chem*., ***19,*** 4684-4688.
10. M. Tonelli, I. Vazzana, B. Tasso, V. Boido, F. Sparatore, M. Fermeglia, M. S. Paneni, P. Posocco, S. Pricl, P. La Colla, C. Ibba, B. Secci, G. Collu, R. Loddo, Bioorg. (2009) Med. Chem., *17*, 4425–4440.
11. K. Nishiwaki, A. Okamoto, K. Matsuo, Y. Kawaguchi, Y. Hayase, K. Ohba, Bioorg. (2007) Med. Chem., ***15,*** 2856–2859.
12. S. Unsalan, S. Rollas, (2007) *Indian J. Chem*., ***26B***, 185-191.
13. K. Paliwal, D. Gorji, S. Kumar, N. Naulakha, A. K. Goswami, D. N. Purohit, (2001**)** *Asian J. Chem*., ***13***, 299-304.
14. S. Ibañez, L. Oresmaa, F. Estevan, P. Hirva, M. Sanaú, M. Angeles Úbeda, Organometallics, (2014**)**, ***33***, 5378–5391.
15. W.-j. Lei, X.-w.Tan, L.-j. Han, S.-z. Zhan, B.-t. Li, (2010**)** Inorg. Chem. Commun., , ***13***, 1325-1328.
16. A. L. Johnson, A. M. Willcocks, S. P. Richards, (2009) Inorg. Chem., , **48**, 8613–8622.
17. Q.-H. Guo, Y.-Y. Zhou, H. Zou, C. Tai, X.-X. Gu, Y.-X. Wang, (2003) Metallurgical Anal., , **20,** 23.
18. X.-H. Zhang, W.-B. Chen, (2013) *Asian J. Chem*., , ***25***, 10360-10362.
19. X.-H. Zhang, W.-B. Chen, (2013) *Asian J. Chem*., , ***25***, 9805-9807.
20. Y. Guo, B. Din, M. Tian, Y. Liu, X. Chang, S. Meng, (2005) *J. Anal. Chem*., , ***60***, 625–628.

21. R. A. Larson, (1988) Phytochemistry, ***27***, 969.
22. N. Cotelle, J. L. Bernier, J. P. Catteau, J. Pommery, J. C. Wallet, E. M. Gaydou, (1996)Free Radical Biology and Medicine, ***20***, 35.
23. Y. S. Velioglu, G. Mazza, L. Gao, B. D. Oomah, *J. Agricul. and Food Chem.* (1998), ***46***, 4113.
24. W. Zheng, S. Y. Wang, (2001) *J. Agricul. and Food Chem.*, *49*, 5165.
25. Y. Cai, Q. Luo, M. Sun, H. Corke, (2004) Life Sciences, ***74***, 2157.
26. R. W. Owen, A. Giacosa, W. E. Hull, R. Haubner, B. Spiegelhalder, H. Bartsch, (2000) *Eur. J. Cancer*, ***36***, 1235.
27. A. Sala, M. D. Recio, R. M. Giner, S. Manez, H. Tournier, G. Schinella, J. L. Rios, (2002) *J. Pharm. Pharmacol*., ***54***, 365.
28. M. Remes, J. Divis, V. Zverina, M. Matrka, *Collect.* Czech. Chem. Commun., (1973), ***38***, 1049-1054.
29. M. Remes, V. Zverina, A. Spevak, (1973)Collect. Czech. Chem. Commun., , ***38***, 1760-11763.
30. I. L. Bagal, S. A. Skvortsov, A.V. El'tsov, (1978)Zh. Obshch. Khim., , ***14***, 361-370.
31. A. Wohl, Ber., (1903), *36*, 4143-4152.
32. E. Weglarz-Tomczak, Ł. Gorecki, CHEMIK (2012), ***66,*** 1298-1307.
33. F. Mo, D. Qiu, L. Zhang, J. Wang, (2021)Chemical Reviews *121*, 5741-5829.
34. C. J. Patil1, S. V. Rajput, (2019)*Intern. J. Recent Scientific Res*., , ***10***, 32144-32156.
35. K. Mezgebe, E. Mulugeta, (2022) RSC Adv., , *12*, 25932–25946.
36. H. Zollinger, Color Chemistry. Syntheses, Properties, and Applications of Organic Dyes and Pigments, Wiley VCH Verlag, Zürich(2003)., 3rd revised edn,
37. P. M. Miladinova, R. K. Vaseva, V. R. Lukanova, (2015) *J. Chem. Technol. Metall*., , *50*, 20–25.
38. U. Pagga, D. Brown, (1986) *Chemosphere*, , *15*, 479-491, DOI:10.1016/0045-6535(86)90542-4.
39. A. Khalid, M. Arshad, D. E. Crowley, (2008),*Appl. Microbiol. Biotech*., *78*, 361-369. [39] H. G. Garg, C. Praksh, (1972) *J. Med. Chem*., , ***15***, 435- 436.
40. J. R. Dimmock, E Erciyas, P. Kumar, M. Hetherington, J. W. Quail, U. Pugazhenthi, S. A. Arpin, S. J. Hayes, T. M. Allen, S. Halleran, E. De Clercq, J. Balzarini, J. P. Stables, (1997) *Eur. J. Med. Chem*., , **32**, 583-594.
41. Refat, H. M.; Fadda, A. A. *Eur*(2013) *J Med Chem*, **70**, 419.
42. Fadda, A. A.; El-Mekawy, R. E.; El-Shafei, A. I. Harold Freeman(2013), Arch Pharm Chem Life Sci, **346**, 53.
43. Rahman, A. U.; Choudhary, M. I.; Thomsen, W. J. Bioassay(2001). Techniques for Drug Development, Harwood Academic Publishers, The Netherlands,