Utility Of 6-Azauracils in Synthesis of New Poly Heterocyclic Nitrogen Systems Bearing 1,2,4-Triazine Moiety as Antioxidant Probes

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ABSTRACT

Synthesis of new poly heterocyclic nitrogen systems containing 1,2,4-triazine moiety such as pyrazolines, pyrazolones, phthalazinone and 1,2,4-triazine (9-17) have been deduced from hydrazinolysis of 3,5-dichloro-6,1-dihydro-1,2,4-triazine (2) which produced from the interaction between 6-azauracil (1) with POCl3/PCls. Heterocyclization of 3,5-dihydrazino-1,2,4-triazine (7) by reaction nitrogen / oxygen / halogen bifunctional reagents in different mediums and conditions yielded the targets 9-17 respectively. Former structure of the products has been established from their elemental analysis and spectral data (UV, IR, 1H/13C NMR and Mass). All the new targets obtained evaluated as antioxidant probes in compare with ascorbic acid in 1,1-diphenyl-2-picrylhydrazyl (DPPH) as a standard, were the compounds 11>10>8>12>13 are more active probes.

Key Words: Synthesis; polyheteroaryl; 6-azauracil; antioxidant.

I. INTRODUCTION

In recent years much attention of chemists has arisen for the synthesis, chemistry and biological activity of 6-azauracil and their derivatives as a potential chemotherapeutic agent [1] such as, antibacterial and anti-tumor [2], anti-convulsant [3], inhibitors D-amino acid oxidase [4], imaging probe for 5-HT1A receptor agonist in nonhuman primates [5], [6], antimicrobial [7], and in mutations of the saccharomyces cerevisiae RPB1 gene conferring hypersensitivity to 6-azauracil [8]. Most treatment of 6-azauracils with various electrophilic and/or nucleophilic reagents led to the formation of poly heterocyclic systems [9], [10], in addition produced oligonucleotides [11]-[18] (Fig. 1).

Based on these important observations, in the present study, we extended the scope of use of synthetic substituted 6-azauracils, and used to obtain 3,5-dihydrazino-1,2,4-triazine which upon treated with nitrogen/ oxygen/ halogen bifunctional to give the various new poly heterocyclic nitrogen systems in view of their antioxidant activity.

II. RESULTS AND DISCUSSION

A. Chemistry

In view of the important work of 6-azauracils, the present work tends to obtain a various poly heterocyclic system bearing 1,2,4-triazine moiety derived from 6-azauracil (1) [19]. Thus, chlorination of spiro-5-(fluoren-9'-yl)-6-azauracil (1) by warming with POCl3 / PCls along one hour, yielded 3,5-dichloro-6,1-dihydro-spiro-[5–fluoren-9'-yl]-1,2,4-triazine (2).

Structure of compound 2 can be deduced from refluxing with alcohol and/or H2O, afforded the corresponding asymmetrical ether 3 and/or the compound 1 (Scheme 1).

Former structure of compound 2 can be confirm from that correct elemental analysis and spectral data. IR spectrum showed a lacks of both NH, C=O absorption band, with recorded ν at 700 cm⁻¹ for C-Cl functional group.

**Fig. 1. Some important biological active 6-azauracils.**
Also, $^1$HNMR spectrum showed the disappearance of both NH and OH protons, which confirm that chlorination. A simple nucleophilic attack of removal of chlorine atoms by carbonitrile (DMF), diamino sulfone (DMF), hydrazine hydrate (Fusion) and/or benzene sulfonic acid hydrazide (DMF), led to the direct formation of 3,5-dicarbonyl-1,2,4-triazine (5); 3,5-di(aminosulfonyl amine)-1,2,4-triazine (6); 3,5-dihydrazino-1,2,4-triazine (7) and 3,5-di(benzene sulfonic sulfonyl hydrazino)-1,2,4-triazine (8) respectively (Scheme 2).

![Scheme 1. Formation of compounds 3 and 4 from 2.](image)  

![Scheme 2. Synthesis of compounds 5-8 from 2.](image)

Structures of compounds 5-8 can be deduced from their IR spectra, the presence of $\nu$ at 3100, 2250 cm$^{-1}$ (NH, CN, 5), 3350, 3150, 1350 cm$^{-1}$ (NH, NH$_2$, SO$_2$ 6), 3300,3120 cm$^{-1}$ (NH$_2$, NH, 7) and 3200, 3180, 3080, 1320 cm$^{-1}$ (NHNH, NH, SO$_2$, 8). Also, $^1$HNMR spectra of 5-8 showed a resonated signal at 12.0 and 10.5 ppm for NH of 1,2,4-triazine and a side chain. And compounds 6-8 exhibited $\delta$ at 10.8, 8.8 ppm for the two NH of side chain, in addition to $\delta$ 12 ppm for NH of 1,2,4-triazine moiety. M/S spectra of 7 recorded the molecular ion peak and the base peak at 165 m/z attribute to fluorenyl radical (Fig. 2).

Pyrazoline and pyrazolone derivatives is considered one from a vital unites of biological probes especially if bearing and/or containing 1,2,4-triazine moiety. Thus, the interaction between compound 7 with activated π-acceptor carbonitriles as malononitrile (ETOH/piperidine), cyanoacetic acid (ETOH / piperidine) and/or activated methylene compounds as malonic acid (AcOH), afforded the 3,5-di(3',5'-diaminopyrazol-1'-yl)-1,2,4-triazine (9); 3,5-di(3'-amino-5'-oxo-4',5'-dihydropyrazol-1'-yl)-1,2,4-triazine (10), and/or 3,5-di(3',5'-dioxo-4',5'-dihydropyrazol-1'-yl)-1,2,4-triazine (11) respectively (Schemes 3 and 4). Formation of compounds 9 and 10 maybe takes place via cycloaddition reaction with NH2 and NH of 1,2,4-triazine.

![Fig. 2. Mass fragmentation pattern of compound 7.](image)  

The structural formula of compounds 9-11 can be established from correct elemental analysis and spectral measurements. IR spectra of compounds 10 and 11 showed both $\nu$ at 3150, 3100, 1680~1660 and 2980, 2880, 1488, 1440 cm$^{-1}$ attribute to NH, C=O and CH2 functional groups, while that of compound 9 recorded only $\nu$ at 3380 and 3180 cm$^{-1}$.
for NH2 and NH functional groups. In addition, 1HNMR spectrum give us a good indication about their structures. Both, compounds 10 and 11 showed a resonated signal at 13.0, 10.5 and 5–4.66 ppm attributed to NH-1,2,4-triazine, NH and CH2 of pyrazole. 1HNMR spectrum of 9 recorded δ at 3.5, 7.8 and 12.8 ppm for NH2, CH=pyrazole and NH-1,2,4-triazine.

Cyclocondensation of 3,5-dihydradino-1,2,4-triazine 7 with 1,3-bicarbonyl reagents such as, ethyl acetocetate (THF) and/or diethyl malonate (Dioxane) produced 3,5-di(3’-methyl-5’-oxy-4’,5’-dihydropyrazol-1’-yl)-1,2,4-triazine 12 and/or 3,5-di(3’,5’-dioxo-tetrahydro-pyrazol-1’-yl)-1,2,4-triazine 13 respectively (Scheme 5). Compound 12 only exhibited ν at 1700, 3150, 2980 cm⁻¹ for C=O, NH and CH2, CH3 functional. IR spectrum of recorded only NH- of 1,2,4-triazine with NH pyrazole and C=O functional groups. IR spectrum of 13 recorded only NH of 1,2,4-triazine with NH of pyrazole and C=O functional groups. 1HNMR spectrum of 12 and 13 showed δ at 11.88, 7.8-6.6, and 4–2 & 1.25 ppm for NH, 1,2,4-triazine aromatic and aliphatic protons. 13C NMR spectrum of 12 recorded δ at 160,140, 129-122, 40 and 25 ppm attribute to C=O, C=N, aromatic and aliphatic carbons.

It is interested that reactions of compounds 7 and a cyclic oxygen reagents such as chalcone (ETOH/piperidine) and/or phthalic anhydride (AcOH), gave 3,5-di(3’,5’-diphenyl-4’,5’-dihydropyrazol-1’-yl)-1,2,4-triazine 14 and/or 3,5-di(1’,4’-phthalalazidinone-1’-yl)-1,2,4-triazine 15 respectively (Scheme 6). The structures of the compounds 14 and 15 have been deduced from their correct elemental analysis spectral data. IR spectrum of 14 recorded only NH of 1,2,4-triazine and CH2 of ν at 3100-3080 and 2970,2890 cm⁻¹ with lacks of C=O group, while 1HNMR spectrum showed δ at 8-6.6 (aromatic protons), 5 and 3.8 ppm for CH-Ph and CH2 of pyrazole, in addition, 12.8 ppm for NH-1,2,4-triazine. On other hand, IR spectrum of 15 showed ν at 3150, 1700, 1680 and 1600 cm⁻¹ attribute to NH, C=O, C=N and C=O functional groups. Only 13C NMR spectrum showed δ at 168,155,142 and 130-120 ppm for C=O, O=C-NH (phthalazine), C=N and aromatic carbons.

Finally, treatment of 3,5-dihydradino-1,2,4-triazine 7 with monochloroacetic acid (DMF) and/or 1,1-dichloroacetic acid (DMF), led to the direct formation of fused triheterocyclic systems 16 and 17 respectively (Scheme 7).

[1-spiro(5-fluoren-9’-yl)-1,2,4-triazino[4,3-d][1,2,4]triazinofluorenyl](3,2-e)-[1,2,4]triazino-6.11(13H)dione] (16). Former structure of compounds 16 and 17 established based on correct elemental analysis and their spectral measurements. The difference in structures between compounds 16 than 17 can be deduced from both IR and 1HNMR spectra. Only, compound 17 showed both the ν at 3200-3100, 2980, 2890 and 1700,1670 cm⁻¹ for NH, CH2, CH3, C=O functional groups, while that of 16 recorded only ν at 3180 and 1710 cm⁻¹ for NH and C=O group. 1HNMR of 17 showed δ at 12-8, 11.2,4.5 ppm for NH(1,2,4-triazino), NH(1,2,4-triazone), and CH2 protons, in addition δ at 7.8-6.8 ppm for aromatic protons.

Also, 13C NMR spectrum of 17 recorded δ at 166, 150, 140 and 40 ppm attribute CONH, COCH2, C=N, aromatic and aliphatic carbons respectively. M/S spectral study of 17 showed the molecular ion peak and the base peak at m/z 165 attribute to fluorenyl ion (Fig. 4).

Formation of 17 may be as showed in Figure 5.
Scheme 4. Synthesis of compounds 17 and 18 from 7.

Scheme 5. Synthesis of compounds 14 and 15 from 7.

Fig. 3. Mass Fragmentation Pattern of Compound 11.

Fig. 4. Mass Fragmentation Pattern of Compound 16.

Fig. 5. Mechanism of Compound 7 formation.
III. THE EXPERIMENTAL

The commercial chemicals and solvents used in the synthesis were purchased from Sigma–Aldrich Chemical Co. (St. Louis, MO), Fisher Scientific Inc. (Springfield, NJ), or Lancaster (Windham, NH) and were without further purification. Analytical grade reagents were purchased from standard commercial sources. Melting points determined with an electrothermal Bibby Stuart Scientific melting point sample (UK). A Perkin Elmer Model RXI-FT IR system 55529 was used for recording IR spectra of the prepared compounds. A Bruker advance DPX 400 MHz model uses TMS as internal standard was used for recording the 1H and 13C NMR spectra of the compounds on deuterated DMSO-D6. A GC-MS-GP 1000 Ex model used for recording the mass spectra of the compounds. Electronic spectra recorded in ethanol on Shimadzu UV and visible 310 IPC Spectrophotometer. Elemental analysis was performed in micro analytical center of Cairo University, Cairo, Egypt.

A. 3,5-Dichloro-1H-6-[(spiro(fluoren-9’-yl)]-6,1-dihydro-1,2,4-triazine (2)

A mixture of 1 (0.01 mol), POCI3 (10 ml), and PCi5 (5 gm) warmed at 150 °C for 2h, cooled then poured part, part on the crucible ice with stirring. The solid obtained filtered off and washed with q, Na2CO3, then crystallized from benzene, to give 2 as orange solid, yield 80%; m.p. 240-241 C. UV(λmax, EtOH): 380 nm. IR(csm-1): 3120 (NH), 1580 (C=C), 910, 850 (aromatic ring), 700(C=C). 1HNMR(DMSO-d6) δppm: 12.0(6, 1H, NH, 1.2-4-triazine), 7.2-7.05 (d, 2H, aromatic), 7.0-6.8 (d, 2H, aromatic), 6.6-6.45 (d, 4H, aromatic). 13CNR(DMSO-d6) δppm: 155(C-C), 144 (-C-), 142 (C=N), 141 (C=N), 132, 130, 129, 124, 123, 121(aromatic carbons). Anal.Calecd; C, 59.63; H, 3.00; Cl, 23.46, N, 13.91% for the C15H9Cl2N3(302). Found: C, 59.50; H, 2.88; Cl, 23.19; N, 13.71%.

B. 3,5-Di(ethylloxy)-6-[(spiro (fluoren-9’-yl)]-6,1-dihydro-1,2,4-triazine (3)

A mixture of compound 2 (2gm) and EtOH (20ml) refluxed 2 h, cooled, the solid obtained filtered off and crystallized from THF to give 3, as brown solid yield 66%; m.p. 200-202 C. IRʋmax-1): 3150 (NH), 2970, 2880(alkyl CH), 1600(C=C), 1560 (C=N), 1480, 1420 (deformation R), 1060 (C-O-C), 880, 810 (aromatic ring). 1HNMR(DMSO-d6) δppm: 12.2(6, 1H, NH, 1,2,4-triazine), 4.4, 4.25 (each m, 4H, 2CH2), 1.25 & 1.15 (each δ,6H, 2CH3), 7.6-7.2, 7.0-6.8 &6.7-6.55 (each d, 8H, aromatic). 13CNR(DMSO-d6) δppm: 155(C-O), 143 (C=N), 141 (C=N), 135 (-C-) 132.7, 132.2, 130.7, 129.8, 129.1, 128.3, 125.1(aromatic carbons), 45(CH2), 27(CH3). Anal.Calecd: C,70.13; H,7.18; N, 12.91% for the C19H21N3O2(326). Found: C,70.11; H, 7.11; N, 12.80%.

C. The tautomeric structure 4 ≠ 1

Compound 3 (2 gm) and H2O (20 ml) refluxed for 1h, cooled. The solid obtained filtered off and crystallized from benzene to give 4 as tautomer of compound 1. The same melting point. But IR spectrum showed a lack of OH functional group which confirm that H-bonding formed. UV (λmax EtOH): 280 nm (hetero conjugated systems).

D. 3,5-Dicarbnitrile-1,6-dihydro-6-[(spiro (fluoren-9’-yl)]-1,2,4-triazine (5)

A mixture of compound 2 (0.01 mol) and NaCN (0.02 mol), in few drops H2O and DMF (20 ml) refluxed 2h, cooled, then poured onto ice. The solid produced filtered off and crystallized from dioxane to give 5 as deep brown solid, yield 70%; m.p. 210-212 °C. UV(λmax, EtOH): 320, 270, 220 nm (C=C, C=N, C=C). IR(ʋcm-1): 3110 (NH), 2250(C=N), 16810 (C=C), 1580(C=N), 860, 810 (aromatic rings). 1HNMR(DMSO-d6) δppm: 11.88, 10.55 (each s, 2H, NH, NH), 7.78-7.69, 7.6-7.4, 7.1-6.66 (each m, 8H, aromatic). 13CNMR (DMSO-d6) δppm: 144(C=N), 142.2 (C=N), 141.1(C=N), 138(-C-), 131.1, 132.5, 132.2, 131.5, 129.9, 129.8, 129.2, 127.9, 127.4, 124.6 (aromatic carbons). Anal.Calecd; C,72.08; H,3.20; N, 24.72 for the C17H12N4O2 (284). Found: C, 71.98; H,3.01; N, 24.59%.

E. 3,5-Di(amin sulfon amine)-1,6-dihydro-6-[(spiro (fluoren-9’-yl)]-1,2,4-triazine (6)

A mixture of compound 2 (0.01 mol) and diamino sulfone (0.02 mol), in DMF (20 ml) refluxed 2h, cooled, then poured onto ice. The yielded solid filtered off and crystallized from EtOH to give 6 as dark brown solid, yield 71%; m.p. 260-262 °C. IR(ʋcm-1): 3350 (NH2), 3150(NH), 1600 (C=C), 1580(C=C), 1360 (SO2NH), 880, 810 (aromatic rings). 1HNMR(DMSO-d6) δppm: 12.1, 10.55 (each s, 2H, 2NH), 3.6, 3.8 (each s, 4H, 2NH2SO2), 7.78-7.69, 7.6-7.4(d, 2H, aromatic), 7.1-6.66 (d, 2H, aromatic), 6.5-6.2m, 4H, aromatic) 13CNMR (DMSO-d6) δppm: 144.34(NCN), 142.2 (C=N), 141.1(C=N), 135(-C-), 133.6, 132.6, 132.2, 130.7, 129.9, 128.4, 124.6 (aromatic carbons). Anal.Calecd; C,42.75; H,3.59; N, 23.26; S,15.21 for the C15H12N5O2S (422). Found: C,42.61; H,3.40; N, 23.16; S,15.00%.

F. 3,5-Dihazirazino-1,6-dihydro-6-[(spiro(fluoren-9’-yl)]-1,2,4-triazine (7)

A mixture of compound 2 (0.01 mol) and hydrazine hydrate (0.25 mol) refluxed for 1h at 200 °C, cooled, then treated with cold MeOH. The solid obtained filtered off and crystallized from EtOH to give 7, as deep red solid, yield 65%; m.p. <300 °C. IR(ʋcm-1): 3300 (NH2), 3120(NH), 3050(aromatic CH), 1600 (C=C), 1570(C=N), 860.5, 840 (aromatic rings). 1HNMR(DMSO-d6) δppm: 11.88 (s, 1H, NH), 10.88 (s, 1H, NH), 3.65(s, 2H, NH2), 7.72-7.66, 7.6-7.4(d, 2H, aromatic), 7.55-7.45 (d, 2H, aromatic), 7.35-6.82(m, 4H, aromatic). 13CNMR (DMSO-d6) δppm: 142.34(C=N), 141.1 (C=N), 135.8(C=N), 135.8(-C-), 132.7, 132.2, 130.8, 130.5, 129.9, 129.51, 123.4, 123.6 (aromatic carbons). Anal.Calecd; C,61.42; H,5.15; N, 33.43 for the C13H12N5 (294). Found: C, 61.29; H, 5.05; N, 33.20%.

Fig. 6. The exo- and endo- H-bonding of compound 4
A mixture of compound 2 (0.01 mol) and benzene sulfonic acid hydrizide (0.02 mol) in DMF 20 ml refluxed for 2h at 200 °C, cooled, then poured onto ice. The solid produced filtered off and crystallized from EtOH to give 8, as yellow powder, yield 60%; m.p. <300 °C. IR(vcm⁻¹): 3200 (NH2), 3180(NH), 3088 (NH), 1580 (C=N), 1320 (SO2NH), 870.5, 859.6 (aromatic rings). ¹HNMNR(DMSO-d₆) δ ppm: 11.88 (s, 1H, NH, 1,2,4-triazine), 8.88-8.55 (d, 2H,NH-NHSO₂), 10.88 (s, 1H, NH), 7.65s (2H, NH), 7.88-7.77 (m, 5H, phenyl), 7.55-7.45 (d, 2H, aromatic), 7.4-7.25 (d, 2H, aromatic), 7.1-6.99 (m, 4H, aromatic). ¹³CNMR (DMSO-d₆) δ ppm: 141.19 (C=N), 136.2 (C₂), 135.8(C=N), 135.8(C-2), 132.2, 130.8, 130.5, 129.9, 129.51, 123.4, 123.6 (aromatic carbons). Anal.Caled: C,56.53; H,4.05; N, 17.18. 11.18 for the C₂H₂N₂SO₃ (574). Found: C,56.42; H,3.89; N, 16.91 S, 11.01%. 

H. 3,5-Di(3,5-diaminopyrazol-1'-yl)-1,6-dihydro-6-spiro(fluoren-9'-yl)-1,2,4-triazine (9)

A mixture of compound 7 (0.01 mol) and mononitritile (0.02 mol) in EtOH 50 ml, piperidine (drops) refluxed for 8h, cooled, then poured onto ice. The solid produced filtered off and crystallized from EtOH to give 9, as deep red powder, yield 80%; m.p. 155-157 °C. IR(vcm⁻¹): 3380 (NH2), 3180 (NH), 3010 (aromatic CH), 1590 (C=N), 880.5, 859.6 (aromatic rings). ¹HNMNR(DMSO-d₆) δ ppm: 11.00 (s, 1H, NH, 1,2,4-triazine), 7.9 (s, 1H), cyclic CH=NH, 7.78-7.66 (d, 2H,aromatic),7.6-7.4 (d, 2H, aromatic), 7.2-6.99 (m, 4H, aromatic), 3.55s (each s, 4H,2NH). ¹³CNMR (DMSO-d₆) δ ppm: 160.19 (C-NH₂), 159.2 (C-NH₂), 151.8(N-C=N pyrazole), 142.2(C=N), 141.19(C=N), 135.2(C-2), 133.99(NN-C=N), 132.68, 132.21, 130.79, 129.5, 129.21, 129.18, 123.4, 123.6 (aromatic carbons). Anal.Caled: C,59.28; H,4.50; N, 36.21 for the C₂H₂N₂O₂S (430). Found: C,59.8; H,3.39; N, 22.70.

L. 3,5-Di(3,5-diazo-5-oxo-4,5-dihydropyrazol-1'-yl)-1,6-dihydro-6-spiro(fluoren-9'-yl)-1,2,4-triazine (13)

A mixture of 7 (0.01 mol) and diethylmalonate (0.02 mol) in dioxin (50 ml) refluxed 2 h and cooled. The solid obtained, filtered off and crystallized from EtOH to give 13, as off-white powder, yield 74%; m.p. 204-205 °C. IR (vcm⁻¹) = 3150 (NH), 2980, 2860 (aliphatic CH),1680,1660,1590 (C=N), 880,860,810 (aromatic vinyls). ¹HNMNR (DEMSO-d₆) δ ppm= 11.8 (s,1H,NH)8.8-8.5 (2s,2H, NH) 7.78-7.68 (d, 2H, aromatic) 7.6-7.59 (d, 2H, aromatic) 7.4-6.99 (m, 4H, aromatic) 4.55-4.42 (each d,4H, 2H₂CH₂). ¹³CNMR (DMSO-d₆) δ ppm= 155.14 (C=O), 142.26 (C=N), 141.50, 141.19(C=N), 135.85(C-3), 132.69, 132.48, 130.21, 130.79, 129.88, 129.80, 128.81, 123.4, 123.6 (aromatic carbons) 40.11, 39.65 (CH₂). Anal.Caled; C,58.74; H,3.49; N, 22.04 for the C₂H₂N₂O₂ (429). Found: C,58.80; H,3.39; N, 22.69%.
A mixture of 7 (0.01 mol) and phthalic anhydride (0.02 mol) in glacial AcOH (50 ml), refluxed 4h, cooled then poured onto ice. The solid obtained, filtered off and crystallized from EtOH to give 15, as yellow powder, yield 82%, m.p. 130-132 °C, IR (vmm⁻¹): 3150 (NH), 1700, 1680 (C=O), 1600 (C=C), 1570 (C=N), 880, 810 (aromatic rings).

1H NMR (DMSO-d₆) δ ppm: 11.88 (s, 1H, NH, 1,2,4 triazine), 8.88, 8.68 (each d, 2H, 2NH, phthalazine), 7.88 -7.76, 7.74-7.68 (each m, 8H, benzophthalazine), 7.66-7.48 (d, 2H, aromatic), 7.4-7.2 (d, 2H, aromatic) 7.0-6.8 (m, 4H, aromatic). 13C NMR (DMSO-d₆) δ ppm: 155.14 (C=O), 142.26, 141.19 (C=N), 135.86 (aliphatic CH₃), 132.70, 132.22, 130.79, 129.80, 129.2, 129.1 (aromatic carbons), 121.52, 121.35 (carbons of phthalazine). Anal.Caled: C,61.17; H,3.36; N,17.51%.

A mixture of 7 (0.01 mol) and 1,1-dichloroacetic acid (0.02 mol) in DMF (50 ml), refluxed 2h, cooled then poured onto ice. The solid obtained filtered off and crystallized from EtOH to give 16, as brown powder, yield 30%, m.p. 175-177 °C. UV (λmax): 350 nm. IR (vmm⁻¹): 3110 (NH), 3050 (aromatic CH), 1700, 1690 (C=O), 1610 (C=C), 1580 (C=N), 890, 860, 810 (aromatic rings). 1H NMR (DMSO-d₆) δ ppm: 11.88 (s, 1H, NH, 1,2,4 triazine), 8.88, 8.68 (each d, 2H, 2NH, 2CH=N, 1,2,4- triazine), 7.8 -7.6 (each m, 8H, benzophthalazine), 7.66-7.48 (d, 2H, aromatic), 7.4-7.2 (d, 2H, aromatic) 7.0-6.8 (m, 4H, aromatic). 13C NMR (DMSO-d₆) δ ppm: 155.14 (C=O), 144.36 (C=C), 142.26 (C=N), 141.19 (C=N), 135.14 (aliphatic CH₃), 133.69, 132.69, 132.22, 130.79, 129.79, 129.81, 129.25, 129.18 (aromatic carbons), 124.42, 123.21, 121.7, 121.35 (tricyclic carbons). Anal.Caled: C,61.67; H,3.36; N,26.33%

A mixture of 7 (0.01 mol) and monochloroacetic acid (0.02 mol) in DMF (20 ml), refluxed for 2h, cooled then poured onto ice. The solid yielded filtered off and crystallized from EtOH to give 17, as deep yellow powder, yield 44%, m.p. 188-190 °C. IR (vmm⁻¹): 3120 (NH), 3050 (aromatic CH), 2985, 2890 (aliphatic CH), 1670 (C=O), 1580 (C=N), 1580 (C=N), 1470, 1440 (deformation CH), 860, 810 (aromatic rings). 1H NMR (DMSO-d₆) δ ppm: 12.2 and 11.80 (each s, 2H, 2NH), 7.8 -7.6 (d, 2H, aromatic), 7.5-7.3 (d, 2H, aromatic), 7.1-6.8 (m, 4H, aromatic). 13C NMR (DMSO-d₆) δ ppm: 150.14 (C=O), 144.26, 142.06, 141.8 (C=C), 135.86 (-C), 132.22, 132.69, 132.22, 130.79, 129.79, 129.81, 129.25, 129.18, 124.42, 123.21, 121.7, 121.25 (carbons of tricyclic). Anal.Caled: C,61.12; H,4.05; N,26.26 for the C₁₀H₁₅N₃O₂ (374). Found: C,60.90; H,3.95; N,26.13%

O. Fused heterotricyclic 1,2,4-triazinone (16)

A mixture of 7 (0.01 mol) and 1,1-dichloroacetic acid (0.02 mol) in DMF (50 ml). refluxed 4h, cooled then poured onto ice. The obtained solid, filtered off and crystallized from EtOH to give 15, as yellow powder, yield 82%, m.p. 130-132 °C, IR (vmm⁻¹): 3150 (NH), 1700, 1680 (C=O), 1600 (C=C), 1570 (C=N), 880, 810 (aromatic rings). 1H NMR (DMSO-d₆) δ ppm: 11.88 (s, 1H, NH, 1,2,4 triazine), 8.88, 8.68 (each d, 2H, 2NH, 2CH=N, 1,2,4- triazine), 7.8 -7.6 (each m, 8H, benzophthalazine), 7.66-7.48 (d, 2H, aromatic), 7.4-7.2 (d, 2H, aromatic) 7.0-6.8 (m, 4H, aromatic). 13C NMR (DMSO-d₆) δ ppm: 155.14 (C=O), 142.26, 141.19 (C=N), 135.86 (aliphatic CH₃), 132.70, 132.22, 130.79, 129.80, 129.2, 129.1 (aromatic carbons), 121.52, 121.35 (carbons of phthalazine). Anal.Caled: C,67.27; H,3.46; N,17.71 for the C₃₁H₂₃N₅O₄ (554). Found: C,67.07; H,3.36; N,17.51%.

P. Fused heterotricyclic perhydro-1,2,4-triazinone (17)

A mixture of 7 (0.01 mol) and monochloroacetic acid (0.02 mol) in DMF (20 ml). refluxed for 2h, cooled then poured onto ice. The solid yielded filtered off and crystallized from EtOH to give 17, as deep yellow powder, yield 44%, m.p. 188-190 °C. IR (vmm⁻¹): 3120 (NH), 3050 (aromatic CH), 2985, 2890 (aliphatic CH), 1670 (C=O), 1580 (C=N), 1580 (C=N), 1470, 1440 (deformation CH), 860, 810 (aromatic rings). 1H NMR (DMSO-d₆) δ ppm: 12.2 and 11.80 (each s, 2H, 2NH), 7.8 -7.6 (d, 2H, aromatic), 7.5-7.3 (d, 2H, aromatic), 7.1-6.8 (m, 4H, aromatic). 13C NMR (DMSO-d₆) δ ppm: 150.14 (C=O), 144.26, 142.06, 141.8 (C=C), 135.86 (-C), 132.22, 132.69, 132.22, 130.79, 129.79, 129.81, 129.25, 129.18 (aromatic carbons), 124.42, 123.21, 121.7, 121.35 (tricyclic carbons). Anal.Caled: C,61.12; H,4.05; N,26.26 for the C₁₀H₁₅N₃O₂ (374). Found: C,60.90; H,3.95; N,26.13%.
V. CONCLUSION

In search for some more new antioxidant agent's novel poly heterocyclic nitrogen systems bearing 1,2,4, triazine moiety derived from 6-azaaracyclic via chlorination and hydrazinolysis followed by ring closure reactions with b-functional agents in different medium and conditions. The antioxidant accident evaluation indicated that the compounds containing more hydroxyl groups as pyrazole and 1,2,4-triazine exhibited a high to moderate activity towards scavenging of free radical within the body which prevent diseases.

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