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Synthesis of New Fluorine/Phosphorus Substituted 6-(2'-Amino Phenyl)-3-Thioxo-1,2,4-Triazin-5(2H, 4H)One and Their Related Alkylated Systems as Molluscicidal Agent as against the Snails Responsible for Bilharziasis Diseases

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Abstract

New fluorine substituted 6-(5'-fluoro-2'-triphenylphosphiniminophenyl) 3-thioxo-1,2,4-triazin-5 (2H, 4H) one (2) was obtained via Wittig's reaction of the corresponding 6-(5'-fluoro-2'-amino-phenyl)-3-thioxo-1,2,4-triazinone (1). Behavior of compound 2 towards alkylating agents and/or oxidizing agents was studied were, N-hydroxyl (3), Mannich base (4,5), S-alkyl (6,7,8) and thiazolo [3,2-b][1,2,4] triazinones (10-14) and or 3-disulfide (18), 3-sulfonic acid 19 and 1,2,4-triazin-3,5-Dionne (20) derivatives obtained. Structures of the new products are established by elemental and spectral data. The new targets obtained screened as Molluscicidalagents against Biomophlaria Alexandrina snails responsible for Bilharziasis diseases, in compare with Baylucide as standard drug.

Keywords

Fluorine, Phosphorus, Sulfur-1,2,4-Triazine, Characteristic Properties, Molluscicidal Activity

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1. Introduction

The incorporation of fluorine atoms into a heterocyclic nitrogen molecule frequently provides properties of pharmacological interest as compared to their non-fluorinated analogs [1]-[5]. Also, bonded phosphorus atoms with S, O, N and C-atoms of heterocyclic systems enhance their important properties as herbicides, pesticides and insecticides [6]-[11]. On the other hand, 3-thioxo-1,2,4-triazin-5-one derivatives and their N- and S-alkyl derivatives have gained considerable attention due to their well as medicinal utility such as anti-HIV, anti AIDS and anticancer agents [12]-[16]. Literature reveals that no reports of a molecular scaffold containing these important cores. With this based upon these observations. The present work aims to synthesis and chemical reactivity of 1,2,4-triazinone bearing, fluorine, phosphorus and sulfur atoms through alkylation reactions and the new systems as Molluscicidal agents against Biomophalaria Alexandrina snails by removal from the wastewater (Clean water).

2. Experimental

Melting points were determined with an electro-thermal Bibbly Stuart Scientific Melting point SMPI (UK). A Perkin Elmer (Lambda EZ-210) double beam spectrophotometer (190 - 1100 nm) used for recording the electronic spectra. A Perkin Elmer model RXI-FT-IR 55,529 cm^{-1} used for recording the IR spectra (EtOH as solvents). A Brucker advance DPX 400 MHz using TMS as an internal standard for recording the $^{1}H/^{13}C$ NMR spectra in deuterated DMSO (δ in ppm). AGC-MS-QP 1000 Ex model is used for recording the mass spectra. Hexafluorobenzene was used as external standard for ^{19}F NMR at 8425 MHz and ^{31}P (in $CDCl_3$, 101.25 MHz) [17]. Elemental analysis was performed on Micro Analytical Center of National Reaches Center-Dokki, Cairo, Egypt. Compound **1** was prepared according the reported method [14] and compound **15** as procedure published [18].

6-(5'-Fluor phenyl)2'amino-3-thioxo-1,2,4-triazine-5(2H, 4H)one (1)

Equimolar mixture of 5-fluoroisatin (in 100 ml NaOH, 5%) and thiosemicarbazide (in 10 ml H_2O) reflux for 2 h, then cold and poured onto ice-HCl. The solid result was filtered off and crystallized from EtOH as yellow crystals to give **1**. Yield (80%), m.p. 263˚C - 265˚C. Analytical data, Found C = 44.91, H = 2.90, F = 7.58, N = 23.40, S = 13.29%; Calculated for $C_9H_7FN_4OS$ (238) C = 45.37, H = 2.94, F = 7.98 N = 23.52, S = 13.44%, M/Z (256, M + H_2O, 5%), base peak (68, 100%), 148 (21), 136 (18), 110 (30), 96 (50), 82 (58), 70 (78); UV: (λ_{max} EtOH) 280 nm. IR νcm^{-1} = 3424 (NH_2) 3258, 3169 (NH, NH), 1685 (C=O), 1618 (NH_2), 1545 (C=N), 1263 (C-F): 858, 818 (aryl CH) 685 (C-F) ^{1}H NMR (DMSO) = 14.66, 16.66, 10.90 (each 1H, s, 3NH), 8.68 - 8.06, 7.69 - 7.64, 7.39, 7.39 - 7.30 (3H, aryl protons) ^{13}C NMR = δ 179.47 (C=S), 162 (C=O), 159 - 157 (spin coupling C-F), 138.54 (C=N), 131.82, 121.8, 121.51 (aromatic carbons), 78.14, 77.71 (C5-C6 1,2,4-triazine).

6-[5'-Fluoro-2'(triphenylphosphinimino)phenyl]-3-thioxo-1,2,4-triazine-5(2H, 4H)one (2)

A mixture of 1 (0.01 mol) and triphenyl phosphine (0.01 mol) in acetonitrile (20 ml), THF (20 ml) reflux for 2 h then cold. The solid produced and crystallized from EtOH to give **2** as deep yellowish crystals. Yield (70%) m.p. 249˚C - 250˚C. Analytical date Found C = 64.60, H = 3.96, F = 3.70, N = 11.01, S = 6.33%. Calculated for $C_{27}H_{20}FN_4OPS$ (498): C = 65.06, H = 4.01, F = 3.81, N = 11.24, S = 6.42%, M/Z (498.00) 370 (4), 290 (10), 171 (60), 159 (100), 128 (20), 118 (40), 102 (65), 92 (58), 76 (58), 65 (40); UV: (λ_{max} EtOH) 310 nm. IR νcm^{-1} = 3335 (NH), 1658 (C=O), 1380 (P=N), 1250 (C-F), 1087 (C-S) 1045, (P-N) 879 (aryl CH), 650 (C-F). ^{1}H NMR (DMSO): 14.56, 12.78 (each 1H, s, 2NH), 8.21, 7.76, 7.66, 7.65, 7.65, 7.64, 7.484, 7.840, 7.47, 7.464, 7.460, 7.45, 7.398, 7.391, 7.38, 7.37, 7.29, 7.28, 7.28, 7.27, 7.02, 7.01, 7.009, 7.005, 6.994, 6.990, 6.866, 6.859, 6.852, 6.845, (18H of aromatic protons). ^{13}C NMR (DMSO) = δ 179.74 (C=S), 163.0 (C=O), 138.62 (C-F), 131 (C=N), 118.94 - 107.94 (aromatic carbons), 7.76, 77.21 (C_5-C_6 of 1,2,4-triazine).

2,4-Di(hydroxymethyl)-6-(5'-fluoro-2'-triphenylphosphiniminophenyl)-3-thioxo-1,2,4-triazine-5-one (3)

A mixture of **2** (0.01 mol) and formaldehyde (0.02 mol), in methanol (50 ml) reflux for 2 h, cold. The solid obtained filtered off and crystallized from MeOH to give **2** as faint yellow crystals. Yield = (65%) m.p. 280˚C - 282˚C. Analytical date: Found C = 61.92, H = 4.21, F = 5.23, N = 9.93, S = 5.43% Calculated for $C_{29}H_{24}FN_4PSO_3$ (558): C = 62.36, H = 4.30, F = 3.40, N = 10.03, S = 5.73%. UV: (λ_{max} EtOH) = 363 nm. IR νcm^{-1} = 3346 (b, 2OH) 2974, 2889 ($2CH_2$), 1646 (C=O), 1382 (P=N), 1240 (C-F), 1086 (C-S), 1046 (P-N), 879 (aryl CH), 755 (C-F). ^{1}H NMR (DMSO) δ 8.34 - 6.84 (18 aromatic protons), 4.8, 4.4 (each s, 2H, alcoholic 2OH) 2.62, 2.58 (each s, 4H, $2CH_2$). ^{13}C NMR (DMSO) = δ 179.86 - 179.68 (C=S), 163.07 (C=O), 159.62, 158.03 (C-F), (C-N), 138.60 (C=N), 132.121 - 107.94 (aromatic carbons), 77.75 77.32 (C5-C6 of 1,2,4-triazine), 40.57 -

40.46, 40.32 - 4.14 (2 CH_2).

2,4-Di(Piperidinomethyl)-6-(5'-fluoro-2'-triphenylphosphin-iminophenyl)-3-thioxo-1,2,-4-triazine-5-one (4)

A mixture of **2** (0.01 mol), piperidine (0.02 mol) and formaldehyde (0.02 mol) in methanol (50 ml) reflux for 2 h, cold. The solid produced filtered off and crystallized from MeOH to give **4** as yellow crystals. Yield = (60%) m.p. 179˚C - 180˚C. Analytical date found C = 67.41, H = 5.83, F = 2.55, N = 11.97, S = 4.33%. Calculated for $C_{39}H_{42}FN_6OPS$ (692): C = 67.63, H = 12.13, F = 2.74, N = 12.13, S = 4.62%. IR νcm^{-1} = 3062 (aromatic CH), 2936, 2840 (aliphatic CH_2), 1721 (C=O), 1538 (C=N), 1468 (deform CH_2), 1389) (P=N), 1248 (C-F), 1184 (C=S), 1049 (P-N), 885, 815, 754 (aryl CH), 709 (C-F). ^{1}H NMR (DMSO): δ 8.23 - 6.80 (18H, aromatic), 2.95, 2.92, 2.89 and 2.58 (CH_2 of piperdine, N-CH_2-N). ^{13}C NMR (DMSO) = δ 172 (C=S), 154 (C=O), 147.25 (C-F), 137.54 (C=N), 116.10 - 108 (aromatic carbons), 77.80, 77.39 (C_5-C_6 of 1,2,4-triazine), 40 - 58, 40.47, 40.33, 40.19, 40.05 (CH_2 of piperidine) 39.91 - 39.63 (N-CH_2-N).

2,4-Di(4'-arylaminomethyl)-6-(5'-fluoro-2'-triphenylphosphiniminophenyl)-3-thioxo-1,2,4-triazine-5-ones (5a & 5b)

A mixture of **2** (0.01 mol) and formaldehyde (0.02 mol), 4-fluoroaniline and/or 4-aminoantipyrine (0.02 mol) in methanol (50 ml) warm under reflux for 2 h, then cold. The solid thus obtained, filtered off and crystallized from EtOH to give **5a** & **5b** as yellow crystals.

Compound **5a**, yield (75%) m.p. 210˚C - 212˚C. Analytical data: Found C = 65.80, H = 4.11, F = 7.47, N = 10.89, S = 4.01%. Calculated for $C_{41}H_{32}F_3N_6OPS$ (744), C = 66.12, H = 4.30; F = 7.66; N = 11.29, S = 4.30%. M/Z = 744 (M, 0, 0%), 370 (1), 367 (25), 290 (60), 272 (30), 248 (20), 218 (42), 169 (100), 128 (85), 102 (100), 65 (100). UV: (λ_{max} EtOH) 364 nm; IR νcm^{-1} = 3343 (aryl-NH), 2974, 2889 (CH_2), 1650 (C = O), 1382 (P = N), 1250 (C-F), 1086 (C-S), 1045 (P-N) 879 (aryl CH). ^{1}H NMR (DMSO) = δ 12.71 (s, 1H, NH), 12.55 (s, 1H, NH), 7.41, 7.39, 7.32, 7.06, 7.01, 6.99, 6.98, 6.97, 6.91, 6.90 & 6.89, 6.88, 6.878, 6.873, 6.86 & 6.85, 6.84, 6.83, 6.77 & 6.768, 6.761, 6.754, 6.742, 6.735 (aromatic CH), 5.18 - 5.15 & 5.14 - 5.13 (4H, CH_2 of N CH_2-NH). ^{13}C NMR = (DMSO) = δ 178.0 (C=S), 161.02 (C=O) 144.99 (C-F), 138.37 (C=N), 130.65 - 114.11 (aromatic carbons) 77.57, 77.14 (C_5-C_6 of 1,2,4-triazine), 40.61 - 40.35, 39.94 - 39.66 (2N-CH_2-NH).

Compound **5b**, yield (60%); m.p. 200˚C - 202˚C. Analytical data: Found C = 65.89, H = 4.91, F = 2.04, N = 14.83, S = 3.35%; Calculated for $C_{51}H_{46}FN_{10}O_3PS$ (928), C = 65.94, H = 9.95, F = 2.04, N = 15.08, S = 3.44%. IR νcm^{-1}: 3277 (b, NH), 2974 (aliphatic CH_3) 2840 (CH_2), 1697, 1660 (2C=O), 1604 (C=N), 1542 (C=N), 1482 (deform, CH_2), 1416 (P=N), 1370 (NCSN), 1274 (C-F), 1152 (C-S), 1045 (P-N), 878, 810, 750 (aromatic CH), 650 (C-F). ^{1}H NMR (DMSO) δ 7.48 - 7.26 (aromatic CH) 5.07 (s, 1H, NH), 3.1 - 3.0 (s, 1H, NH), 2.99 - 2.88, 2.84 - 2.82 (2 CH_2), 2.62 - 2.41, 2.34 - 2.23, 2.229 - 2.2221, 2.16 - 2.07 (4 Me). ^{13}C NMR = (DMSO) δ 179.81 (C=S) 159.11 (C=O), 142 (C-F), 138.0 (C=N), 129.38 - 123.31 (aromatic carbons), 77.54, 77.11 (C_5-C_6 of 1,2,4-triazin), 40.61 - 40.08 & 39.94 - 39.66 & 36.75 - 35.49 (N-CH_2), 18.42, 15.15 (N-Me, C-Me).

[6-(5'-Fluoro-2'-triphenylphosphiniminophenyl)-5-oxo-1,2,4-triazine-3-yl]thioacetic acid (6)

Equimolar mixture of **2** and monochloroacetic acid in DMF (20 ml) warm for 30/min, then poured onto ice. The solid yielded filtered off and crystallized form EtOH to give **6** as faint yellow crystals. Yield (80%), m.p. 187˚C - 188˚C. Analytical data: Found: C = 62.42, H = 3.81, F = 3.20, N = 9.85, S = 5.57%; Calculated for $C_{29}H_{22}FN_4O_3PS$ (556). C = 62.58, H = 3.95, F = 3.41, N = 10.07, S = 5.75. IR νcm^{-1} = 3327 (b, OH, NH), 2973, 2884 (CH_2), 1659 (b, 2 C=O), 1440 (deform CH_2), 1380 (P=N), 1250 (C-F), 1087 (C-S), 1045 (P-N) 880 (Ar CH), 810 (Ar CH). ^{1}H NMR (DMSO) δ = 10.31 (s, 1H, NH), 8.06, 8.0, 7.98 - 7.97, 79.86 - 7.84, 7.73, & 7.726, 7.721, 7.14, 7.08, 7.67 & 7.66, 7.65, 7.63, 7.53 - 7.51, 7.48 - 7.35 & 7.34, 6.997, 6.992, 6.838 - 6.824 (18 CH, aromatic) & 4.74 (s, 1H, OH of COOH), 3.86 - 3.24 (2H, CH_2). ^{13}C NMR: (DMSO): δ 168.29 (C=S), 165.40 (C=O), 157.16 (C=O), 142.13 (C-F) 131.35 (C=N), 130.04 - 102.25 (aromatic carbons), 72.43, 72.22 (C_5-C_6 of 1,2,4-traizine), 34.95 - 34.81 (CH_2 carbon).

1,1-Di[6-(5'-Fluoro-2'-triphenylphosphiniminophenyl)-5-oxo-1,2,-4-triazine-3'yl]dimercaptoacetic acid (7)

A mixture of **2** (0.02 mol) and 1,1-dicholoracetic acid (0.01 mol) in DMF (20 ml) reflux for 30 min, cold then poured into ice. The resulted solid filtered off and crystallized from dioxin to give **7** as faint yellow crystals, yield (60%) m.p. 238˚C - 240˚C. Analytical data: Found C = 63.45, H = 3.49, F = 3.39, N = 10.39, S = 5.88%, Calculated for $C_{56}H_{40}F_2N_8O_4P_2S_2$ (1052) C = 63.87, H = 3.80, F = 3.61, N = 10.64, S = 6.08%. IR νcm^{-1} = 3425, 3259, 3170 (OH, NH, NH), 1865, 1680 (C=O), 1618 (C=N), 1476, 1452 (aliphatic CH), 1360 (P=N), 1252 (C-F), 1193 (C-S), 1045 (P-N), 903, 859, 818, 758 (aryl CH) 685 (C-F). ^{1}H NMR (DMSO): δ 12.79, 12.78 (each s, 2NH), 10.75 (s, 1H, OH), 8.21 - 6.84 (18 CH, aromatic), 2.82 - 2.59 (s, 1H, CH) ^{13}C NMR: δ 179.72 (C=S),

163 (C=O), 159 (C-S), 158.0 (C-S), 138.61 (C-F), 132.18 (C=N), 121.12 - 107.94 (aromatic carbons), 77.66, 77.45 (C_5-C_6) of 1,2,4-triazine), 40.57 - 40.46 (-CH-).

Tri[6-(5'-fluoro-2'-triphenxylphosphin-iminophenyl)-5-oxo-1,2,-4-triazine-3'yl]trimercaptoacetic acid (8)

A mixture of **2** (0.03 mol) and 1,1,1-trichloroacetic acid (0.01 mol) in DMF (20 ml) warm for 30 min then cold and poured on to ice. The produced solid filtered off and crystallized from Et OH to give **8** as reddish crystals. Yield (60%); m.p. 189˚C - 190˚C. Analytical data: Found C = 63.89, H = 3.45, F = 3.55 N, 10.67, S = 5.83%. Calculated for $C_{83}H_{58}F_3N_{12}O_5P_3S_3$ (1548); C = 64.34, H = 3.74, F = 3.68, N = 10.85, S = 6.2%. UV (λ_{max} EtOH) 359 nm. IR νcm^{-1} = 3500 - 3100 (b, 3NH, OH) 1716 (C=O), 1624 (NH = OH of 1,2,4-triazinone) 1537 (C=N) 1471 (aliphatic CH). 1390 (P=N), 1300 (NCSN), 1260 (C-F), 1200 (C-S), 1645 (P-N), 920, 850, 780 (aryl CH), 650 (C-F). ^{1}H NMR (DMSO) = δ 12.95, 12.72, 12.33 (each s, 3H, NH), 10.84 (s, 1H, OH), 8.51, 8.23, 8.01, 7.92, 7.89, 7.71, 7.7, 7.69, 7.65, 7.63, 7.59, 7.58, 7.57 - 7.54, 7.50 - 7.47, 7.40 - 7.37, 7.33 - 7.31, 7.02 - 6.98, 6.86 - 6.83 (aromatic CH). ^{13}C NMR = (DMSO) δ 179.61 (C=S), 163 (C=O), 159.5 (C-S), 157 (C-F) 138.58 (C=N), 137.79 (C=N), 132.91 (C=N), 131.99 - 107.93 (aromatic CH), 77.92, 77.49 (C_5-C_6 of 1,2,4-triazine).

6(5'-Fluoro-2'-triphenylphosphin-iminophenyl)2,-4-dihydro-thiazolo[3,2-b][1,2,4]triazine-3,7-dione (9)

Equimolar mixture of **2** and monochloroactic acid in DMF (20 ml) reflux for 2 h then cold and poured onto ice. The solid obtained filtered off and crystallized from dioxan to give **9** as brown ppt, Yield (60%) m.p. 224˚C. Compound **6** (0.50 mg) heat above its melting point (60˚C higher) for 10 min, cold then treat with MeOH. The solid produced filtered off and crystallized from dioxan to give **9** as brown ppt. Yield (58%), m.p. 225˚C - 227˚C. Analytical data Found C = 64.40, H = 3.51, F = 3.35, N = 9.93, S = 5.48% Calculated for $C_{29}H_{20}FN_4O_2PS$ (538); C = 64.68, H = 3.71 F = 3.53, N = 10.40. S = 5.94%. UV: (λ_{max} EtOH) 352 nm. IR νcm^{-1} = 3204 (b-OH), 1694 (C=O), 1623 (C=N), 15,636, 1475 (CH_2), 1380 (P=N), 12,999 (C-F), 1148 (C-S) 816, (aromatic CH), 711 (C-F). ^{1}H NMR (DMSO) = δ 10.79 (s, 1H, Phenolic OH), 8.23 (s, 1H, CH of thazole), 7.95 - 7.47, 7.35, 7.35, 6.98, 6.80 (aromatic CH). ^{13}C NMR = (DMSO): δ 167.21 (C=S), 147.47, (C=O), 136.64 (C-F), 132.97 (C=N), 131.92 - 128.54, 118.80 - 118.14, 113.79 - 113.73 (aromatic carbons), 111.04 - 110.99 (-CH=), 77.80, 77.38 (C_5-C_6 of 1,2,4-triazine).

6(5'-Fluoro-2'-triphenylphosphiniminophenyl)-5-oxo-3-(cyanomethylthia)-2H-1,2,4-triazine (10)

A mixture of **2** (0.01 mol) and chloroacetinitrile (0.01 mol) in DMF (20 ml) warm (10 min) then cold and poured onto ice. The result solid filtered off and crystallized from dioxan to give **10** as faint Yellow crystals. Yield (70%); m.p. 214˚C - 215˚C. Analytical data: Found C = 64.39, H = 3.58, F = 3.11, N, 12.85, S = 5.75%. Calculated for $C_{29}H_{21}FN_5OPS$ (537); C = 64.80, H = 3.91, F = 3.53, N = 13.03, S = 5.95%. M/Z = 537 (5%) 281 (20), 207 (60), 149 (20), 113 (30), 85 (100), 58 (100). UV: (λ_{max} EtOH) 321 nm. IR νcm^{-1} = 3424, 3167 (NH, S-CH=C=NH) 2100 - 2085 (C≡N), 1646 (C=O), 1595 (C=N), 1481 (CH_2), 1370 (P-N), 967, 839, 762 (aryl CH), 700 (C-F). ^{1}H NMR (DMSO) = δ 13.90, (s, 1H, NH), 12.76 (s, 1H, HC=NH), 8.22 - 6.81 (aromatic CH), 4.69 (1H, HC=NH) 2.59 (2H, CH_2). ^{13}C NMR (DMSO): δ 158.11 (C=O), 147.0 (C-F) 132 (C=N), 131.86 - 128.44 (aromatic carbons), 112.21 (C≡N), 77.96, 77.53 (C_5-C_6 of 1,2,4-triazine), 40.133 (-CH=NH), 33.63 (CH_2).

3-Amino-6(5'-fluoro-2'-triphenylphosphiniminophenyl)-thiazolo[3,2-b][1,2,4]triazine-7-one (11)

Compound **10** (0.5 gm) in DMF (20 ml) warm for 2 h then cooled and poured onto ice. The solid produced filtered off and crystallized from EtOH to give **11** as broom ppt, Yield (66%); m.p. 223˚C - 225˚C. Analytical data: Found C = 64.51 H = 3.38, F = 3.21 N = 12.55, S = 5.62%. Calculated for $C_{29}H_{21}FN_5OPS$ (537), C = 64.80, H = 3.91, F = 3.53, N = 13.03, S = 5.95%. M/Z, 537 (2%), 370 (2), 226 (2), 168 (100), 140 (60), 114 (30), 62 (18), 70 (18). IR νcm^{-1} = 3348, (b-NH_2), 16430 (C=O), 1383 (P=N), 1250 (C-F), 1086 (C-S), 1045 (P-N), 878 (aryl CH). ^{1}H NMR (DMSO) = δ 8.11 (s, 1H, = CH thiaszole), 7.72 - 7.011, 6.98 - 6.80 (aromatic CH), 3.99 - 3.84 (2H-NH_2). ^{13}C NMR (DMSO) = 162.54 (C=O), 132.16 (C-F), 132.00 (C=N), 131.99 (C-S), 131.66 - 131.64 (=CH-), 128.61 - 120.55 (aromatic carbons), 77.59, 77.38 (C_5-C_6 of 1,2,4-triazine), 40.51 (-N-C=N).

3-(4'-Fluoro benzoyl)amino-6-(5'-fluoro-2'-triphenylphosphiniminophenyl)-thiazolo[3,2-b][1,2,4] triazine-7-one (12)

Equimolar mixture of **11** and 4-fluorobenzoyl chloride in DMF (20 ml) warm for 10 min then cold and poured onto ice. The resulted solid filtered off and crystallized from EtOH to give **12** as deep-Yellowish crystals. Yield (75%). m.p. 205˚C - 207˚C. Analytical data: Found C = 65.19 H = 3.41, F = 5.49 N = 10.51, S = 4.59%. Calculated for $C_{36}H_{25}F_2N_5O_2PS$ (660), C = 65.55, H = 3.80, F = 5.76, N = 10.60, S = 4.80. IR νcm^{-1} = 3342, (b-NH), 1651 (b, 2C=O), 1381 (P=N), 1326 (NCSN) 1230 (C-F), 1086 (C-S), 1045 (P-N), 879 (aryl CH). ^{1}H NMR (DMSO) = δ 13.70 (s, 1H, NH), 9.89 (s, = CH of thiazole) 8.411, 8.17, 8.07 - 8.05, 8.01, 7.99, 7.95, 7.79, 7.66 -

7.64, 7.44 - 7.42, 7.28, 7.27 (aromatic CH). ^{13}C NMR = (DMSO): δ 167.53 (C=O), 162.54 (C=O) 138.59 (C-F) 132.25 (C-N), 132.19 (C=N), 129.33 - 127.27, 117.78 - 115.17, 112.15, 12.09, 110.52, 108.12, 107.95 (aromatic carbons), 77.64. 77.43 (C_5-C_6 of 1,2,4-triazine).

Schiff base (13)

Equimolar amounts of **11** and 4-fluorobenzaldehyde in absolute ethanol (20 ml) reflux for 30 min then cooled. The solid thus obtain filtered off and crystallized from EtOH to give **13** as Yellowish ppt. Yield (70%); m.p. 248˚C - 250˚C. Analytical data: Found C = 66.85, H = 3.61, F = 5.75 N = 10.59, S = 4.71%. Calculated for $C_{36}H_{24}F_2N_5OPS$ (643), C = 67.18, H = 3.73, F = 5.90, N = 10.88, S = 4.97%. IR νcm^{-1} = 3100, 2880 (aromatic & aliphatic CH), 1700 (C=O), 1600 (C=N), 1483 (C-P), 1370 (P=N), 1230 (C-F), 1200 (C-S), 1045 (P-N), 880, 840, 810 (aryl CH), 650 (C-F) ^{1}H NMR (DMSO) = δ 9.97 (s, 1H, -CH=N-), 8.62 (s, 1H, -CH = thiazole) 8.23, 8.22, 8.09 - 8.00, 7.94 - 7.92, 7.71 - 7.63, 7.56 - 7.53, 7.49 - 7.45, 7.26 - 7.23, 7.12 - 7.10, 7.0 - 6.96, 6.89 - 6.84, 6.81 - 6.79 (aromatic CH).

6-(5'-Fluoro-2'-triphenyl phosphiniminophenyl)-3-oxo-3phenyl-thiazolo[3,2-b][1,2,4]triazine-7-one (14)

A mixture of **2** (0.01 mol) and phenacylbromide (0.01 mol) in ethanolic KOH, (20 ml, 5%) reflux for 2 h, cold then poured onto ice-HCl. The solid produced filtered off and crystallize from dioxan to give **14** as brown ppt. Yield (60%); m.p. > 300˚C. Analytical data: Found C = 69.88, H = 3.59, F = 3.01 N, 9.00, S = 5.13%, Calculated for $C_{35}H_{24}FN_4OPS$ (598); C = 70.23, H = 4.01, F = 3.17, N = 9.36 S = 5.35%. IR νcm^{-1} = 3080, 3030 (aromatic CH), 1680 (C=O), 1380 (P=N), 1240 (C-F), 1180 (C-S), 1045 (P-N), 880, 850 (aryl CH).

Diaylthioether (16)

A mixture of **2** (0.01 mol) and Schiff base **15** (0.01 mol) in dry C_6H_6 (100/ml) reflux 8 h, cold and used peter-either 100˚C - 120˚C to complete precipitation. The solid obtained filtered off and crystallized dioxan to give **16** as Yellowish crystals. Yield (80%); m.p. 204˚C - 205˚C. Analytical data: Found C = 66.53, H = 4.31, F = 4.44, N = 11.88, S = 3.66%, Calculated for $C_{45}H_{36}F_2N_7O_2PS$ (807); C = 66.91, H = 4.46, F = 4.70, N = 12.14, S = 3.96%. M/Z = (807.0.0), 580 (5), 515 (4), 462 (8), 423 (10), 370 (5), 339 (20), 282 (20), 225 (20), 207 (60), 176 (100), 149 (56), 119 (38), 85 (90), 58 (100). UV: (λ_{max} EtOH) 323 nm. IR νcm^{-1} = 3332 (NH), 2973, 2886 (aliphatic CH), 1636 (C = O), 1488 (CH_3), 1381 (P=N), 1324 (NCSN), 1250 (C-F), 1086 (C-S), 1045, (P-N), 880, 755 (aryl CH). ^{1}H NMR (DMSO) = δ 12.77, (s, 1H, NH), 10.75 (s, 1H, NH), 9.68 (s, 1H, S-CH-Ar), 8.23, 7.83 - 7.28, 7.27 - 7.00, 6.99 - 6.84 (aromatic CH), 3.69 (s, CH_3-N) 2.79 (s, CH_3-C).^{13}C NMR (DMSO): δ 164.73 (C=O), 163.08 (C=O), 160.63, 155.18 (C-F), 151.9 (C-S), 134.64, 134.25, 134.23 (C=N), 129.487 - 115.492 (aromatic carbons), 77.72, 77.50 (C_5-C_6 of 1,2,4-triazine), 67.00 (S-CH=NH), 39.95 - 39.81, 39.67 - 39.55 (2 CH_3).

2,3-Diaryl–2,3-dihydro-4-thioxo-7-(5'-fluoro-2'-triphenylphosphiniminophenyl)-1,3,5-thiazolo[3,2-b] [1,2,4] triazine-8-one (17)

A mixture of **16** (0.01 mol) and CS_2 (5 ml) in DMF (20 ml) reflux for 4 h, cold then powered onto ice. The resultant solid filtered off and crystallized from dioxan to give **17** as yellowish crystals. Yield (75%), m.p. 254˚C - 255˚C. Analytical data: Found C = 64.88, H = 3.85, F = 4.38, N = 11.40, S = 7.45%, Calculated for $C_{46}H_{34}F_2N_7O_2PS_2$ (849); C = 65.01, H = 4.00, F = 4.47, N = 11.54, S = 7.53%; M/Z (849, 0.0%), 370 (2), 329 (40), 290 (100), 159 (100), 128 (100), 102 (100), 96 (100), 65 (100). UV: (λ_{max} EtOH) 34.7 nm. IR νcm^{-1} = 2873 (aliphatic CH), 1684 (C=O), 1614. 1593 (C=N) 1475, 1425 (CH_3), 1318 (P=N), 1264 (C-F), 1199 (C=S), 1130 (C-S), 1052 (P-N), 985, 899, 854, 814, 732 (aryl CH). ^{13}C NMR (DMSO) = δ 179.70 (C=S), 163.07 (C=O), 155.08 (C-F), 138.62 (C=N, 1,2,4-triazine), 132.23, 132.13 (C=C pyrazole), 129.43 - 115.44, 112.09 - 107.96 (aromatic carbons), 77.71, 77.28 (C_5-C_6 of 1,2,4-triazine) 66.94 (S-CH-NH), 40.57, 39.76 (2 CH_3).

Di-Heteroaryldisulfide (18)

Compound **2** (0.05 gm) and $FeCl_3$ (0.5 gm) in MeOH (20 ml) reflux for 3 h, then filtered. The solid produced filtered off and crystallized from dioxan to give **18** as deep-yellowish crystals. Yield (80%), m.p. 238˚C - 240˚C. Analytical data: Found C = 64.85, H = 10.89, F = 3.55, N = 10.89, S = 6.22%. Calculated for $C_{54}H_{38}F_2N_8O_2P_2S_2$ (994); C = 65.19, H = 11.26, F = 3.82, N = 11.26, S = 6.43%. IR νcm^{-1} = 3300, 3200 (NH, NH), 1680 (C=O), 1600 (C=N), 1350 (P=N), 1100 (C-S), 1040 (P-N), 900, 850, 800 (aryl CH), 650 (C-F). ^{1}H NMR (DMSO) = δ 14.55, 12.78 (each s, 2H, NH, NH), 8.20 - 6.85 (aromatic CH). ^{13}C CNMR (DMSO): δ 179.90, 179.74 (2C-S), 159 - 66, 158.66 (2C=O), 138.63 (C-F), 132.18 (C=N), 121.12 - 107.95 (aromatic carbons), 77.65, 77.43 (C_5-C_6 of 1,2,4-triazine).

6-(5'-Fluoro-2'-triphenylphosphiniminophenyl)-5-oxo-2H-1,2,4-triazine-3-sulfonic acid (19)

Compound **2** (0.05 gm) in ethanol (10 ml) and H_2O_2, (0.5 ml) add with stirring for 2 h. The solid obtained filtered off and crystallized from EtOH to give **19** as yellowish crystals yield (75%); m.p. 258˚C - 260˚C. Analyti-

cal data: Found C = 59.00, H = 3.44, F = 3.25, N = 9.87, S = 5.45%. Calculated for $C_{27}H_{20}FN_4O_4PS$ (546), C = 59.34, H = 3.66, F = 3.47, N = 10.25, S = 5.86%. IR νcm^{-1} = 3300 (NH), 1696 (C=O), 1390 (NCSN), 1360 (P=N), 879, 820, 780, (aryl CH). 670 (C-F). ^{1}H NMR (DMSO) = δ 12.79 (s, 1H, NH), 10.72 (s, 1H, SO_2-OH), 8.13 - 6.76 (aromatic CH). ^{13}C NMR (DMSO): δ 179.75 (-S=O), 163.09 (C=O), 159.67 (C-F), 138.62 (C=N), 132.23 (C-S), 121.08 - 107.95 (aromatic carbons), 77.60, 77.39 (C_5-C_6 of 1,2,4-triazine).

6-(5'-Fluoro-2'-triphenylphosphiniminophenyl)-1,2,4-triazine-3,5-(2H, 4H)dione (20)

Compound **2** (0.05 gm) in ethanol (10 ml) and $KMnO_4$ solution (ethanolic 1%, 1 ml) add drop wise then stirring for 2 h. The produced solid filtered off and crystallized from Et OH to give **20** as yellowish crystals yield (50%); m.p. 273˚C - 275˚C. Analytical data: Found C = 66.89, H = 4.01, N = 11.35, F = 3.55. Calculated for $C_{27}H_{20}FN_4O_2P$ (482), C = 67.21, H = 4.14, N = 11.61, F = 3.94. M/Z: (482, 0.0%), 370 (10), 206 (101, 148, (16), 128 (24), 110 (35), 96 (55), 83 (78), 68 (100). IR νcm^{-1} = 3426, 3259, 3170 (OH, NH, NH), 1766, 1681 (2C=O), 1619 (C=N) 1452 (C-P) 1301 (P=N), 1252, (C-F) 1048 (P-N), 905, 861, 820, 802, 784, 761 (CH), 687 (C-F), ^{1}H NMR (DMSO) = δ 12.73, 10.82 (each s, NH, OH), 7.88 - 6.84 (aromatic CH). ^{13}C NMR = δ 153.58 (C=O), 152.78 (C=O), 147.84 (C-F). 132.58 (C=N) 130.51 - 111. (Aromatic carbons), 77.85, 77.60 (C_5-C_6 of 1,2,4-triazine).

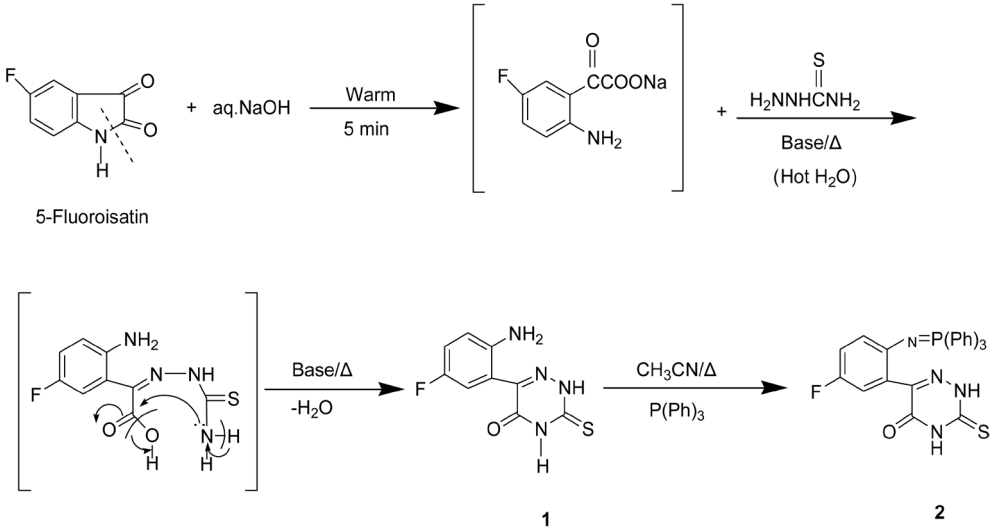
3. Results and Discussion

3.1. Chemistry

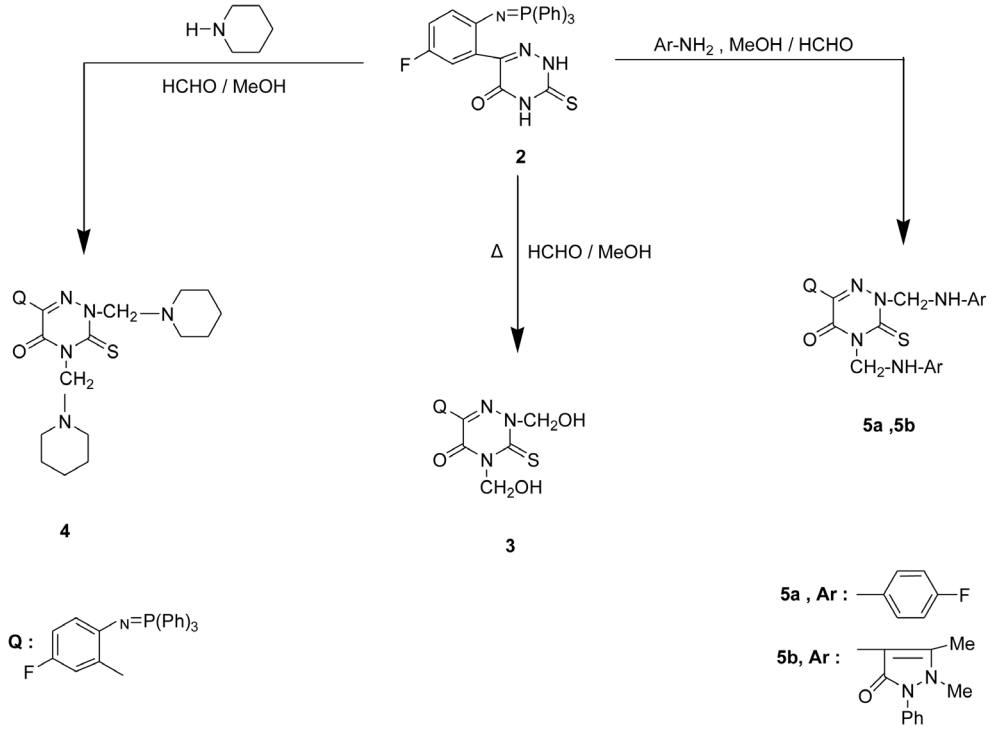
A recent work on the synthesis and chemistry of bioactive sulfur bearing 1,2,4-triazinone moiety was reported [16] [19]. In continuation of this attitude the present investigation reports the synthesis of fluorine and phosphorus-substituted 6-amino-phenyl-3-thioxo-1,2,4-triazin-5-(2H, 4H) one (**1**) and study that behavior towards various alkylating agents. Treatment of 5-fluoroisatin with thiosemicarbozide in alkaline medium [14] [15] produced 6-(2'-amino-5'-fluorophenyl-3-thioxo-1,2,4-triazin-5-(2H'4H) one (**1**). Warm compound **1** with triphenylphosphine in acetonitrile produced the yield **2** (**Scheme 1**).

In the imino [yield, 2] a negative charge of nitrogen is bonded to positive charge of phosphorus stabilized by partial overlap of the filled N-P orbital. This stabilization increase due to the charge on the α-carbon atom is spread by 1,2,4-triazine resonance. Abdel-Rahman [14] [15] reported that N-alkyl of 3-thioxo-1,2,4-triazinones exhibited a wide biological spectrum anti HIV and anticancer properties. Similarly, hydroxyl methylation of compound **2** by boil with formaldehyde-methanolproduced 2,4-di(hydroxylmethyl)-6-(5'fluoro-2'-triphenylphosphiniminophenyl)-3-thioxo-1,2,4-triazin-5-one (**3**). Also, reflux of compound **2** with secondary and primary amines such as piper dine, 4-fluoroaniline and 4-amino-antipyrine in the presence of formaldehyde methanol, furnished the Mannich bases **4** and **5** (**Scheme 2**).

Formation of **3** and **4** was may be as (**Figure 1**).



Scheme 1. Formation of compounds 1 & 2.



Scheme 2. Formation of compounds 3 - 5.

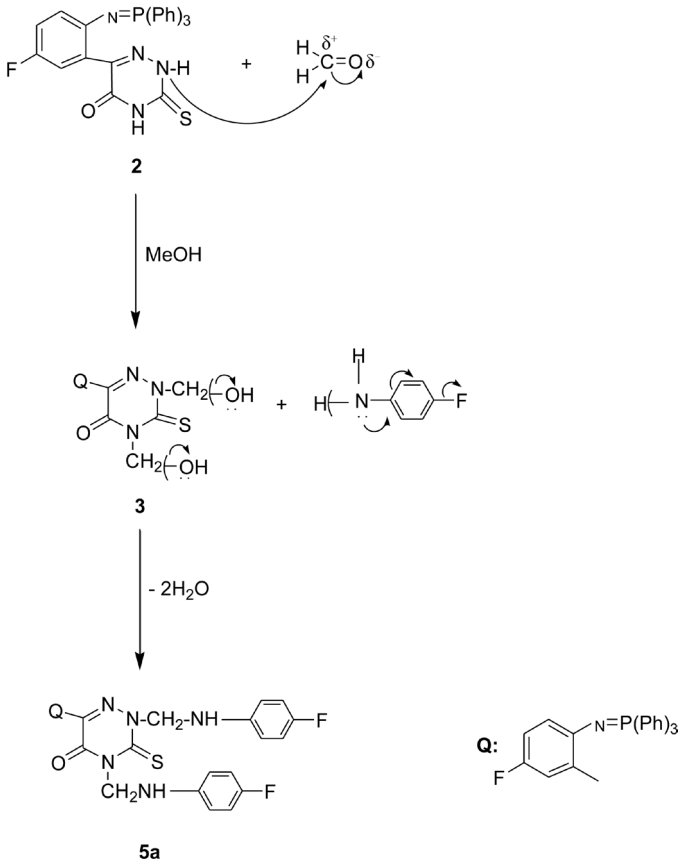


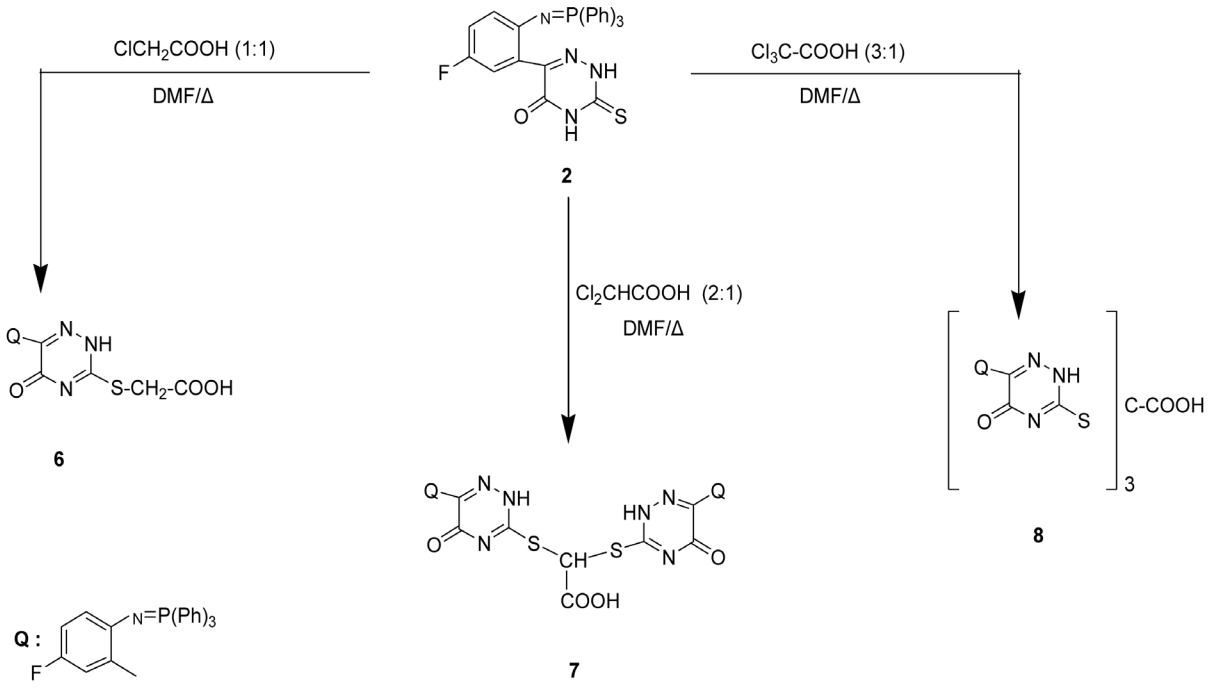
Figure 1. Formation of compounds 3 & 5a.

Due to a higher nucleophilicity of sulfur atoms, the direct displacement of an acidic proton of mercapto group by a simple electrophile can be easily occur via treatment of compound **2** with haloacetic acids. Thus treatment of compound **2** with halo aliphatic acids such as mono/di/trichloroacetic acids in DMF afforded the substituted thiaacetic acids **6**-**8** (**Scheme 3**).

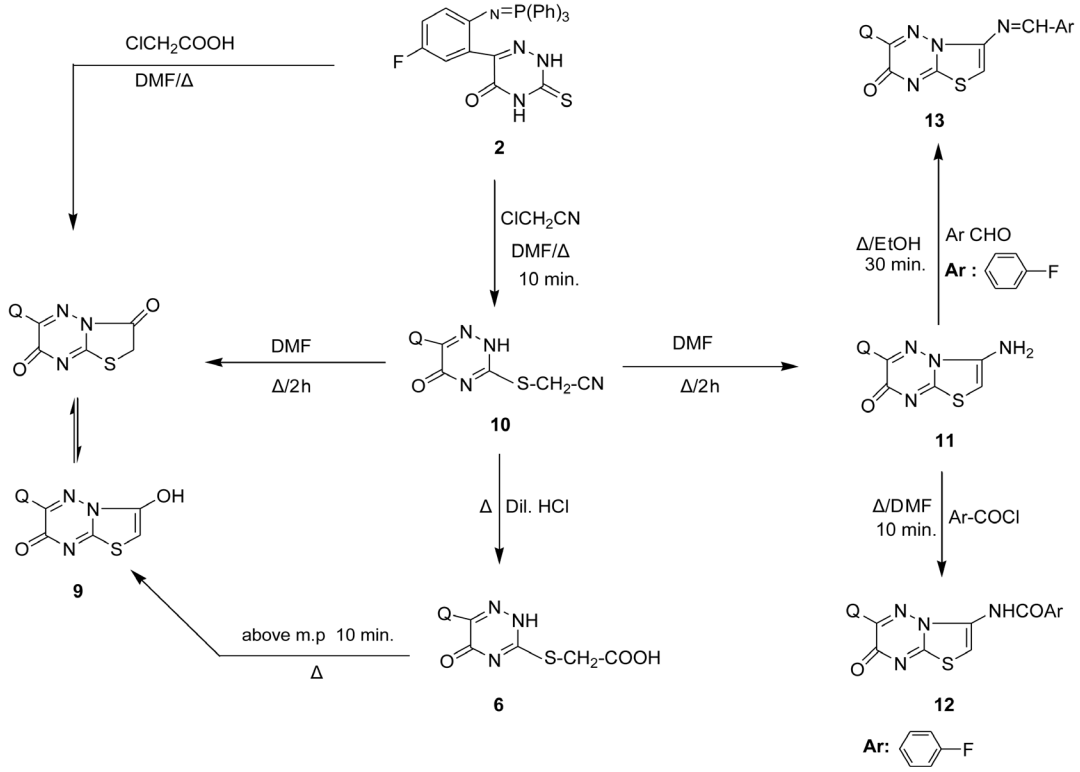
The multicomponent reaction (MCR) was considered as powerful synthetic tool for preparing target molecules of biological relevance in an efficient manner. Thus, treatment of compound **2** with active methylene reagents as chloroacetonitrile in warm DMF [20] produced 3-cyanomethyl thai-6-iminophosphorane-1,2,4-trinazin-5-(2H)one (**10**). The latter compound **10** use for the synthesis of thiazolo [3,2-b][1,2,4]triazinones (**11**-**13**) systems (**Scheme 4**). Acidic hydrolysis of **10** by warm with diluted HCl for short time (10 min) yielded the compound **6**. Boil compound 6 with DMF along time afforded 6-iminophosphorane-2,3-dihydoro-thiazolo [3,2-b] [1,2,4] triazine-3,7-dione (**9**) (**Scheme 4**).

Heat compound **10** on heating with DMF a long time (2 hours), produced 3-aminothiazolo-1,2,4-triazine **11**. Presence of an amino group in structure **11** was deduced from treat with 4-fluorobenzoylchloride (DMF) and/or with 4-fluorobenzaldehyde (EtOH) yield the anilido **12** and/or Schiff's base **13** (**Scheme 4**). Treatment of compound **2** with *α*, *β*-bifunctional oxygen-halogen reagents as phenacyl bromide in ethanolic KOH, yielded 3-phenyl-6-iminophosphorane-thiazolo [3,2-b][1,2,4]triazin-7-one (**14**) (**Scheme 5**). The nitrogen-sulfur containing fused heterobicyclic structures have demonstrated a high degree of binding affinity when they serve as Ligands for various biological receptors [12] [13]. Thus addition of Mercator group (as nucleophilic) of compound **2** to an Schiff's base **15** in boil dry dioxan yielded the thioether**16**, which upon ring closure reaction by reflux with CS_2 in DMF furnished 2,3-diaryl-2,3-dihydro-7-iminophosphorane-4-thioxo-1,3,5-thiadiazino[3,2-b] [1,2,4]-triazin-8-one (**17**) (**Scheme 5**).

Abdel-Rahman *et al.* [21]-[25] reported that thioethers, sulfide and sulfonic acid bearing a 1,2,4-triazine moieties. Exhibited a very interesting medicinal activity as anti-HIV and anticancer agents. Recently, Slawinski *et al.* [25] synthesized 2-mercaptobenzene sulfonamide bearing a 1,2,4-trinzines exhibited a significant activity against cell lines of colon cancer, renal cancer, and melanoma, as well as good selectivity toward non-small cell lung cancer. Similarly, oxidation of compound **2** via treatment with $FeCl_3$ in boiling methanol and/or with H_2O_2 in ethanol by stirred at room temperature furnished the disulfide **18** and/or 3-sulfonic-1,2,4-triazinone **19**. Finally, treatment of **2** with ethanolic $KMnO_4$ at room temperature [21] led to the direct formation of 6-(5'-fluoro-2-triphenylphosphiniminophenyl)-1,2,4-triazin-3,5(2H, 4H)dione (**20**) (**Scheme 5**).



Scheme 3. Formation of compounds 6 - 8.



Scheme 4. Formation of compounds 9 - 13.

3.2. Elucidation the Former Structures

3.2.1. UV Spectra

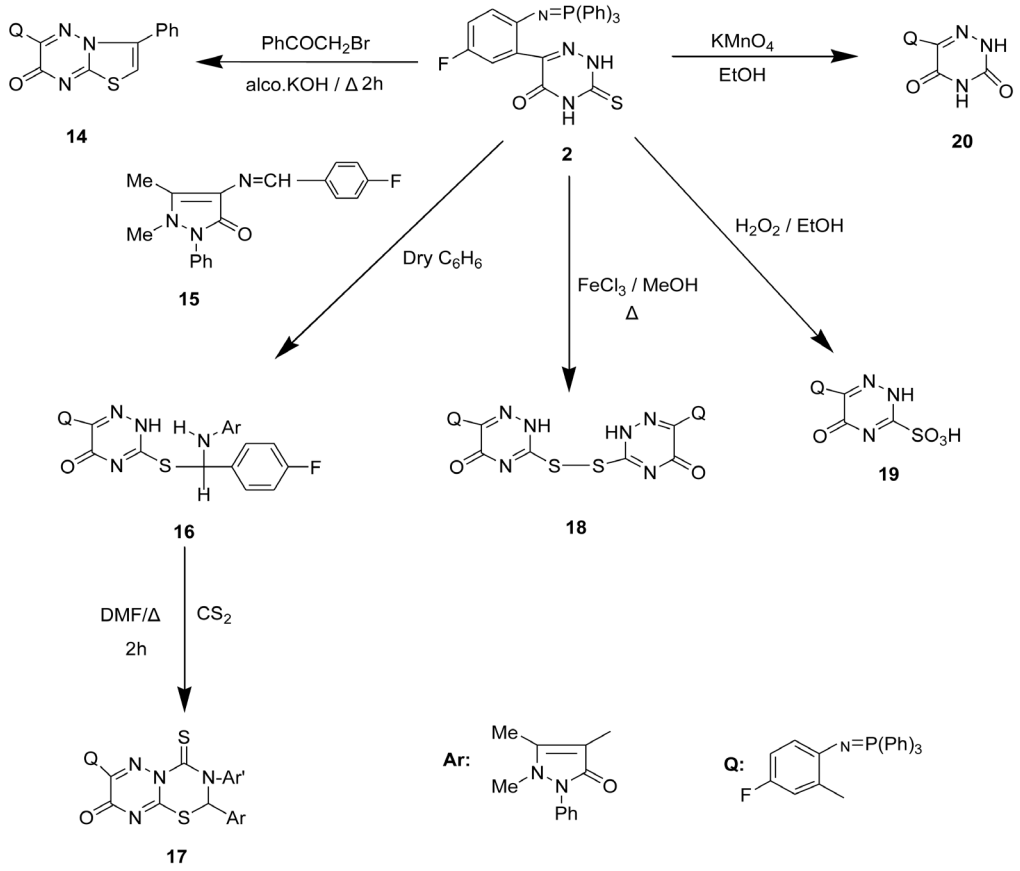
The electronic conjugated molecule of compound **2** exhibited λ_{max} at 310 nm while that of compounds **3** (363), **5a** (364), **8** (359) and **16** (323) nm. A higher absorption bands of new acyclic systems than that of **2** confirm that N- and S-substitution were formed. On the other hand, the absorption bands of fused heterobicycle compounds **9** (352), **17** (347) and **10** (321) nm is higher than the start **2** (310) nm. This is attributing to extension of hetero-conjugation of heterobicylic systems through a type of cylization.

3.2.2. IR Spectra

The new compounds obtained recorded the absorption bands at 1380 - 1390, 1250 - 1230 cm^{-1} due to presence of both P=N and C-F functional groups. Compounds **3-5** showed a lack of band at 3200 - 3100 cm^{-1} for NH=OH of 1,2,4-triazinones, while that of compounds **6-8** and **10** recorded the absorption band at 3343 and 1643 cm^{-1} attributed to presence of ^{4}NH & ^{5}C=O of 1,2,4-triazinone. Only compounds **9-14** showed a lack of the absorption bands at 1200 - 1100 cm^{-1} for C=S, which confirm that heterocyclization. In addition to the compounds **6-9** & **18**, **20** exhibited a two absorption bands at ν 1700 and 1665 cm^{-1} due to the presence of two carbonyl groups. Also, IR absorption spectra of compounds **3-8**, **9-10** and **16** recorded the absorption bands at ν 2975 and 2885 cm^{-1} attributed to aliphatic functional groups [1] [14] [15] [26].

3.2.3. NMR Spectral Study

1) ^{1}H NMR spectrum of **1** showed a resonated signals at δ 14.6, 12.6 and 10.9 ppm for 3NH with δ 8.6 - 0.80, 7.69 - 7.64, 7.41 - 7.31 ppm for three aromatic protons, while that of **3** exhibited a signals at δ 5.24 and 4.98 ppm attributed to two OH with δ 2.92 - 2.88, 2.62 - 2.58 ppm for two CH_2 protons. Compounds **3**, **4** and **5** showed a lack's of ^{4}NH and ^{2}NH of 1,2,4-triazine moiety, while that of **5** recorded additional signals at δ 1.9 and 1.75 ppm of two methyl groups of antipyrine moiety. ^{1}H NMR spectra of **6-8** recorded δ at 12.7, 4.7 ppm for NH and OH protons, while that of **9** showed a signal at δ 10.5 and 8.5 ppm, attributed to OH and CH = of thiazole moiety. In addition to compound **10** recorded a signals at δ 13.90, 2.59 ppm for NH, CH_2 protons, while that of



Scheme 5. Formation of compounds 14 - 20.

11 exhibited only signals at δ 8.01 and 3.99 ppm for = CH thiazole and amino-protons. Moreover ^{1}H NMR spectrum of **16** showed a signals at δ 12.76 and 10.75 ppm for two NH of 1,2,4 trinazine while a lacks of these (2NH) protons of **17**, with presence of CH proton of thiadiazine moiety at δ 9.68 ppm. ^{1}H NMR spectra of compounds **18** recorded the presence of δ at 14.55 and 12.79 ppm attributed to 2NH of 1,2,4-triazine protons, while that of **19** exhibited a signals at δ 12.8 and 10.7 p pm for NH and CH. (SO_2-OH) protons, with signals of aromatic protons. Finally, compound **20** exhibited δ at 12.73 and 10.82 ppm attributed to NH and OH protons [14] [15] [19] [26].

2) ^{13}C NMR spectra of all the synthesized compounds showed a resonated signals at δ 180, 165 - 163, 140 - 138, 135 - 121 and 112 p pm attributed to C=S, C=O, C=N, aromatic and C-F carbons. Also, ^{13}C NMR spectra of compounds **3**-**6**, **9** and **10** recorded signals at δ 39 - 33 ppm for CH_2 carbons. Only the compound **10** showed an additional signal at δ 112 p pm for C≡N carbon. Finally, ^{13}C NMR spectra of the entire compound exhibited a resonated signals at 77 - 75 ppm for C5-C6 of 1,2,4-triazine [27] (**Figure 2**).

3) ^{19}F NMR spectral study recorded a signal at δ −126 to −125 ppm.

4) ^{31}P NMR spectral study exhibited a signal at δ 30 - 29 p pm attributed to P=N [17].

3.2.4. Mass Fragmentation Study

Mass fragmentation pattern study of some selective synthesized compounds indicated that fused heterobiycyclic systems 11 have a more base peak, while that of acyclic structures 1and 16 have only base peak which indicate that their less stability. A higher stability of fused heterobicyclic systems is due to the delocalization of net charge over all the active centers (**Figure 3** to **Figure 5**).

4. Molluscicidal Activity

Based upon the earlier work by Abdel-Rahman *et al.* [7] [16] on the synthesis of phosphono substituted-1,2,4-

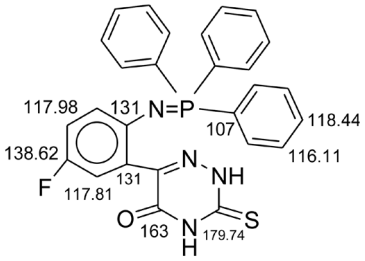


Figure 2. ^{13}C NMR data of compound 2.

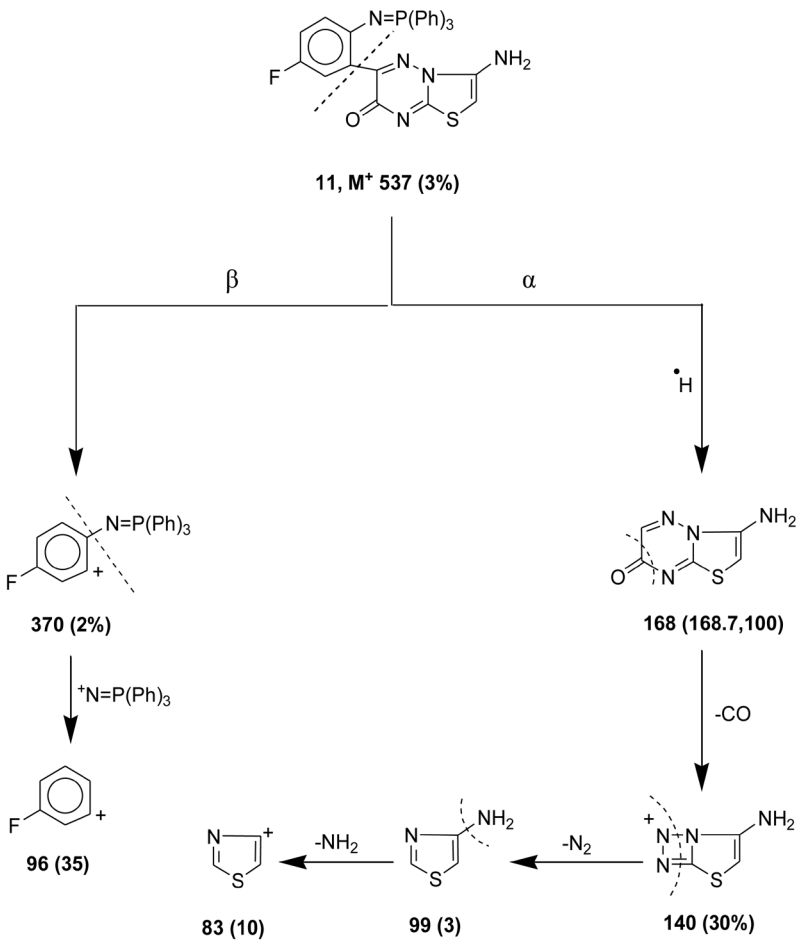


Figure 3. Mass fragmentation pattern of compound 11.

triazine derivative and their molluscicdal activities against Biomophalaria Alexandrina Snails responsible for Bilharziasis diseases, the prepared compounds were tested as killing of that snails (shell in diameter 5 - 8). The intermediate host of sohistosomamausoni in Giza Govern state that was not treated with molluscicides. The snails were adapted to laboratory conditions for two weeks before being used in toxicity tests to be sure that the snails are strong and healthy. Snails were kept in plastic aguaria filled with de chlorinated tap water at room temperature (25˚C - 27˚C). Stock solution (500 $\mu g \cdot ml^{-1}$) of the tested compounds were synthesized in the least volume of ethanol and completed of the least volume of ethanol and completed to the required volume with de chlorinated tap water on the basis of weight volume. A series of more diluted solutions were then prepared following the instructions given by WHO organization [28] [29]. The result given in (**Table 1**) revealed that the high activity towards snails in the following sequences:

18 > **2** > **20** > **3** > **8** and **9** > **10** > **6** > **17** >> **5a** and **5b** > **7** > **14** at 100 ppm in compared with Baylucide as

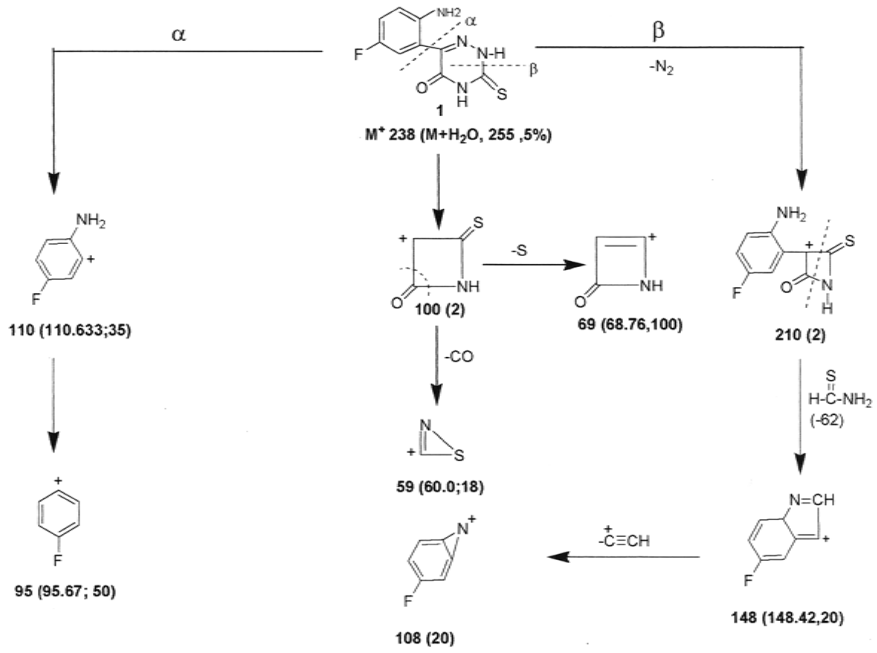


Figure 4. Mass fragmentation pattern of compound 1.

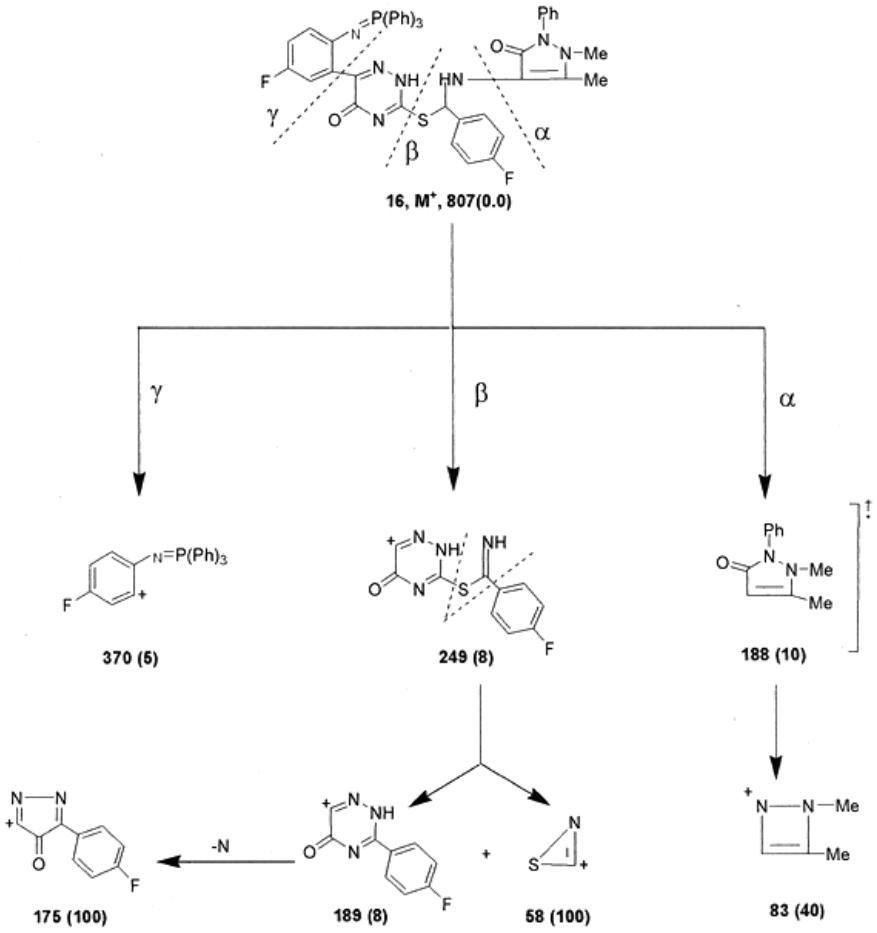


Figure 5. Mass fragmentation pattern of compound 16.

Table 1. The molluscicidal activity of the synthesized systems (2 - 20) mortality of snails various concentration (ppm).

Comp. No.	25 ppm	50 ppm	100 ppm
2	30	60	80
3	30	50	80
4	20	30	60
5a	20	40	70
5b	10	20	50
6	20	40	70
7	20	30	50
8	30	50	80
9	30	50	70
10	30	50	70
12	10	20	30
13a	10	20	30
13b	10	20	30
14	10	30	40
16	10	20	30
17	20	40	70
18	40	60	90
19	30	40	50
20	30	60	80
Reference standard, Baylucide		100	100

standard reference. In general, the strong effect of the compounds **2**, **3**, **8**, **18** and **20** is due to presence both the S-S, S-H and O-H functional groups which agree with bio-oxidation-reduction processes. The moderate effect of the compounds **5a**, **6**, **9**, **10** and **17** is attributed to thioether and cyclic sulfur nitrogen systems. Finally, the lethal effect of the compounds **4**, **5b**, **7**, **11** and **14** may be to absence of SH and/or OH of Mannich base and for thiazolotriazine systems which led to the inhibition of delocalization electron-density over all the center of systems. Also, presence of hetero-elements (F, P, S, O) and N elements in corporated with 1,2,4-trinazines led to increases of electro-negativity, over all the molecular structure and enhance the electrostatic force and hydrophobic properties [17] [18] [31]-[33]. Thus, total electron-barrier of molecular distribution of the evaluated systems synthesized led to highly inhibition of the enzymatic effect on the living processes for the tested snails by causing break of a vital cyclic of that snails, and enhance the possibility killing of these snails. QSAR study of the obtained resulted from (**Table 1**), and based on the introduction of P, S and F in the synthesized 1,2,4-triazines, in compared with the mortality of tested snails, indicated that, increases of P and S percent % led to increase of mortality, while, increase of F percentage % led to decrease of mortality of snails. Also, very high electronegative of fluorine atom can modify the electronic distribution in the molecule affecting its absorption distribution and metabolism. In conclusion, 3-thioxo-1,2,4-triazine-5-ones bearing an P, S and F elements and their related S-alkyl derivatives, enhance the mortality of snails, which cause Bilharziasis Diseases than that their non-fluorinated and non-phosphinated systems. Also, increases of P and S percentage % led to higher mortality of the tested snails, in hope to obtain more clean water from waste water.

5. Conclusion

New fluorine substituted 6-(5'-fluoro-2'-triphenylphosphiniminophenyl) 3-thioxo-1,2,4-triazin-5 (2H, 4H) one (**2**) was obtained via Wittig's reaction of the corresponding 6-(5'-fluoro-2'-aminophenyl)-3-thioxo-1,2,4-triazinone (**1**). 3-thioxo-1,2,4-triazine-5-ones bearing an P, S and F elements and their related S-alkyl derivatives, enhance the mortality of snails, which cause Bilharziasis Diseases than that their non-fluorinated and non-phosphinated systems. Also, increases of P and S percentage % led to higher mortality of the tested snails, in hope to obtain more clean water from waste water.

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