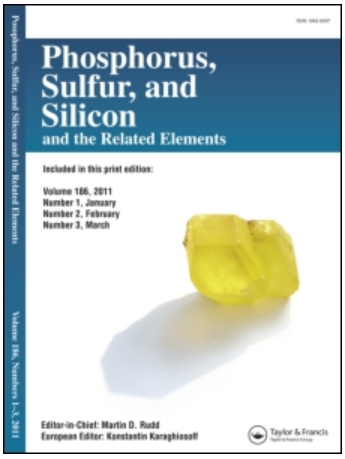

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SYNTHETIC APPROACH TO 6-BENZOYL-2H-[1,2,4] TRIAZINE-3,5-DIONE AND 6-BENZYL-5-THIOXO-3,4-DIHYDRO-2H-[1,2,4] TRIAZIN-3-ONE AND STUDIES ON THEIR TRANSFORMATION TO FUSED [1,2,4]TRIAZINE SYSTEMS

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*Reaction of phenylpyruvic acid with semicarbazide afforded 6-benzyl-2H-[1,2,4]triazine-3,5-dione (**1**) which upon oxidation with potassium dichromate furnished 6-benzoyl-2H-[1,2,4]triazine-3,5-dione (**2**) in good yield. Constructing pyrazolo[3,4-e][1,2,4] triazine system (**4**) was achieved by reacting **2** with arylhydrazines in ethanolic solution. However treatment of **2** with the less reactive heteroarylhydrazines gave only the corresponding hydrazones (**3**). Attempt for constructing 1,2,4,5,10-pentaaza-dibenzo[a,d]cyclohept-3-one (**7**) from **2** was failed and (benzoimidazol-2-yl) [1,2,4] triazine derivative (**6**) was the only product. Reaction of **1** with phosphorus pentasulphide afforded compounds **8** and **9**. Compound **8** was transformed to the hydrazino compound **14**, which led to the construction of triazolo[4,3-d] [1,2,4]triazine system. Thus compounds **15** and **16** were obtained by reacting **14** with carbon disulfide or acetic anhydride respectively. Attempt to couple **8** with chloroacetic acid failed, while it's known isomer **10** led to the formation of thiazolo [2,3-c] [1,2,4]triazine derivative (**13**). Simple theoretical calculation using AM1 and PM3 semiempirical Hamitonian provided rational ways to correlate the reactivity with structure proposed.*

Keywords: AM1; (benzoimidazol-2-yl) [1,2,4] triazine; PM3; pyrazolo[3,4-e][1,2,4]triazine; triazolo [4,3-d] [1,2,4]triazine

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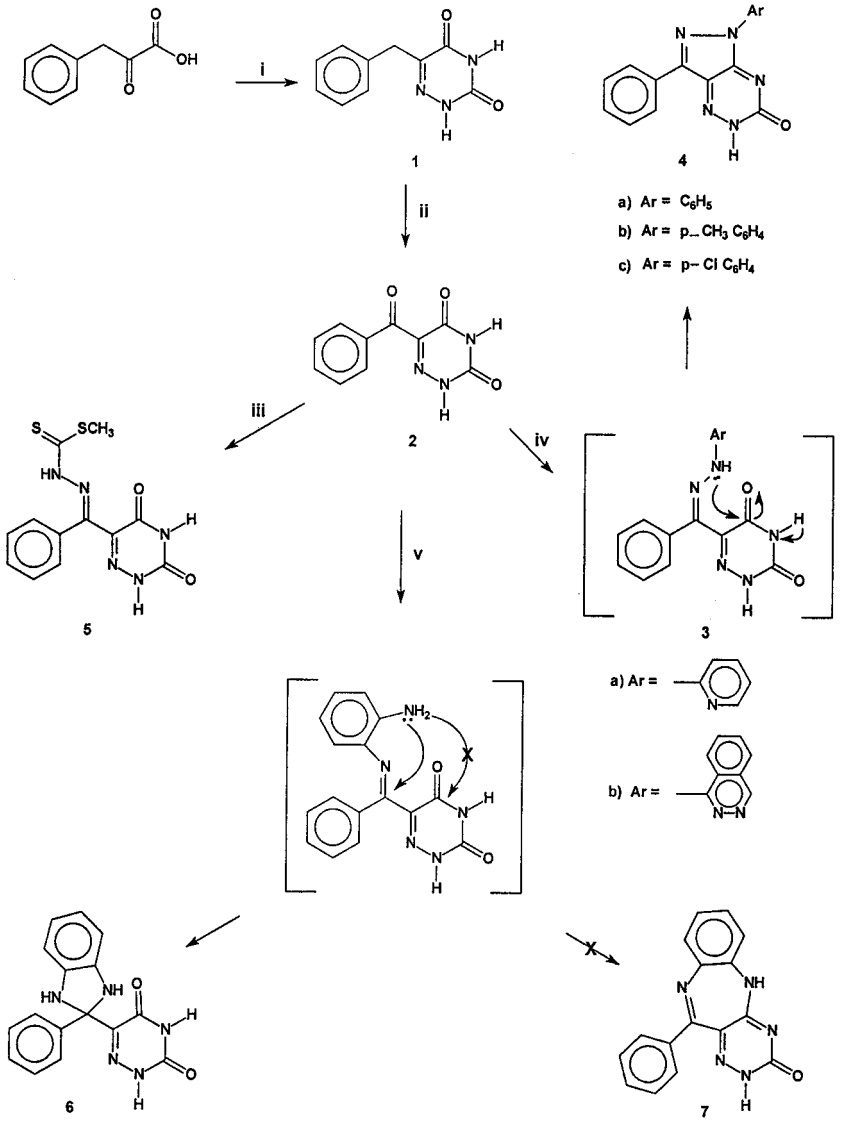
The chemistry of fused 1,2,4-triazines were surveyed in two recent reviews,[1,2] various members of these compounds were reported to posses anti-HIV, anticancer,[3–6], antihypertensive, anesthetic, antidepressant, tranquilizer, sedative, muscle relaxant,[1,2] herbicidal as well as selective weed control in wheat, antibacterial, antiviral, antifungal, anti-inflammatory, anticonvulsant activities, and carragreen-induced edema inhibitor.[1,2]

Such activities and applications furnished the impetus to continue our earlier work[7–12] on the utilization of keto acids and their functionalized analogues as precursors for the preparation of new series of 1,2,4-triazines and condensed derivatives.

DISCUSSION

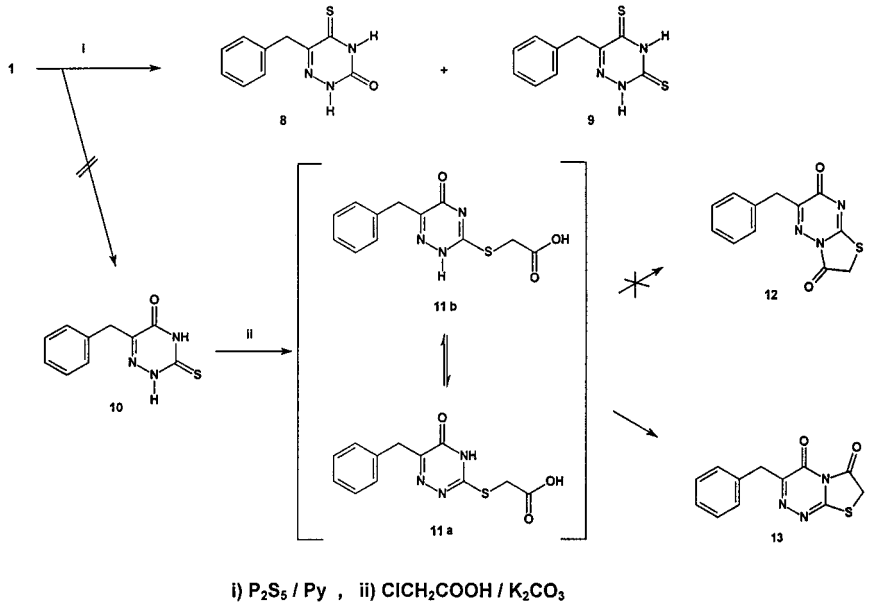
Our initial plan is summarized in Scheme 1. Thus the starting 6-benzyl-2H-[1,2,4] triazine-3,5-dione (**1**) was prepared in good yield by two different methods; the first is slightly modified earlier reported condition[13] through the condensation of phenylpyruvic acid with semicarbazide hydrochloride in aqueous potassium hydroxide solution, the second by the reaction of phenylpyruvic acid thiosemicarbazone with methyl iodide.[14] The oxidation of **1** with potassium dichromate in acetic acid afforded 6-benzoyl-2H-[1,2,4]triazine-3,5-dione (**2**), which revealed IR absorption for the carbonyl group at 1690 cm^{-1}. Its ^{13}C-NMR showed the absence of benzylic carbon signal of the starting material **1** at δ 35 ppm and the appearance of the carbonyl carbon signal at δ 187.6 ppm. Heating **2** with aryl hydrazines (Ar = C_6H_5, p-MeC_6H_4, p-ClC_6H_4) smoothly produced orange precipitates, where the elemental analyses as well as the mass spectrum of **4a** as a prototype showed the elimination of two molecules of water from the sum of the molecular formula of their corresponding starting materials. Their assigned structures 5-aryl-7-phenyl-2,5-dihydro-pyrazolo [3,4-e][1,2,4]triazin-3-ones (**4 a–c**) were confirmed by spectral data analysis. Thus, their ^{1}H-NMR spectra showed only one exchangeable signal at about δ 13.6 ppm due to the remaining NH group. However, reaction of **2** with heteroarylhydrazines afforded the corresponding hydrazones (**3**). Attempts to cyclize the later compounds under acidic conditions met with no success. This could be explained by the delocalization of the electron density of the N atom over the heterocyclic ring which decreases their nucleophilicity. Also the reaction of **2** with hydrazinecarbodithioic acid methyl ester gave the corresponding hydrazone derivative (**5**). On the other hand, reaction of **2** with phenylene-1,2-diamine led to the formation



i) NH_2-NH-CO-NH_2.HCl/KOH, ii) $K_2Cr_2O_7$/HOAc , iii) NH_2-NH-CS-SCH_3, iv) Ar-NH-NH_2, v) Phenylene-1,2-diamine

SCHEME 1

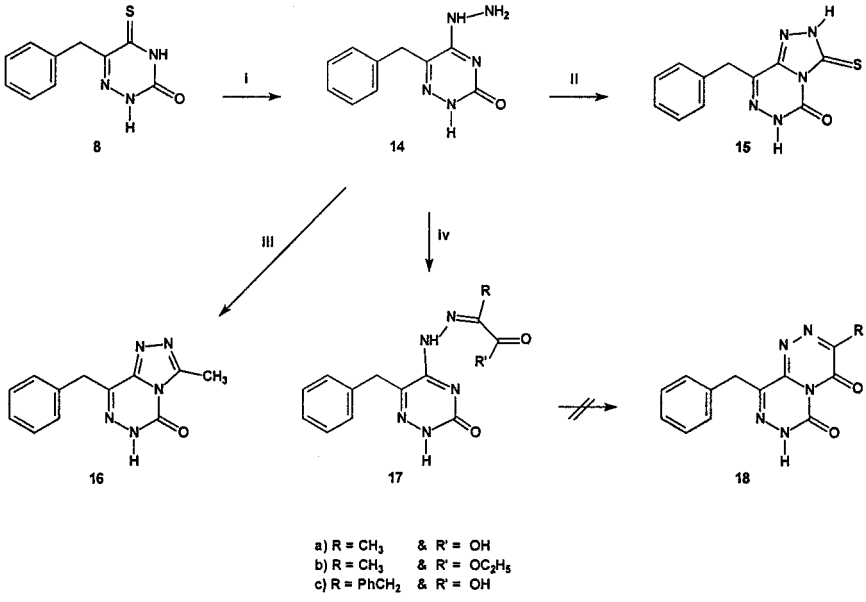
of 6-(2-Phenyl-2,3-dihydro-1H-benzoimidazol-2-yl)-2H-[1,2,4]triazine-3,5-dione (**6**) rather than 11-phenyl-2,5-dihydro-1,2,4,5,10-pentaaza-dibenzo[a,d]cyclohepten-3-one (**7**), where the binucleophilic sites of the diamine attack the side chain carbonyl carbon. The structure



SCHEME 2

assignment of **6** was based on the spectroscopic data as well as the elemental analysis, which indicated the loss of one molecule of water during the condensation process. Heating compound **1** with phosphorus pentasulphide in pyridine under reflux for 3 h afforded a mixture of the hitherto unknown product **8** and the known compound **9**[15] as indicated by TLC. They were separated easily by heating in benzene. The structure of **8** as 6-benzyl-5-thioxo-4,5-dihydro-2H-[1,2,4]triazin-3-one was based on spectroscopic data and secured by comparative study with the known 3-thioxo isomer (**10**) which was prepared by an independent experimental procedure reported earlier by Khamaev et al.[16]

Moreover, attempted coupling of **8** with chloroacetic acid by heating in dry acetone and anhydrous potassium carbonate for 3 h led only to the recovery of the starting materials, while the reaction of its isomer **10** took place and afforded most likely 3-benzyl-thiazolo[2,3-c][1,2,4]triazine-4,6-dione (**13**) as a single product via regiospecific reaction. To better understand why **10** rather than **8** reacts with chloroacetic acid why the former most likely gave **13** rather than its isomeric one **12**, we decided to study the theoretical electron distribution to determine whether the reactivity as well as the regiospecifity are charge controlled. We used a semiempirical approachs, namely PM3 and AM1



i) H_2N-NH_2 / H_20, ii) CS_2 / Py , iii) Ac_2O, iv) RCOCOR'.

SCHEME 3

(MOPAC). The main electronic characteristics of **8** and **10** are shown in Figure 1, which agree with high nucleophilicity of the sulfur atom of **10** over **8**. Next the optimized geometry of the expected reaction intermediate **11** in its two tautomeric forms **11a** and **11b** is represented in Figure 2 using PM3 approach followed by charge density calculations by AM1.[17] The results show that the negative charge density located upon N-4 of **11a** is higher than N-2 of **11b** which prompted us to propose structure **13** over **12**.

In continuation of our goal, compound **8** was allowed to react with hydrazine to afford 6-benzyl-5-hydrazino-2H-[1,2,4]triazin-3-one (**14**). Annelation of five-membered to 1,2,4-triazine ring was achieved upon

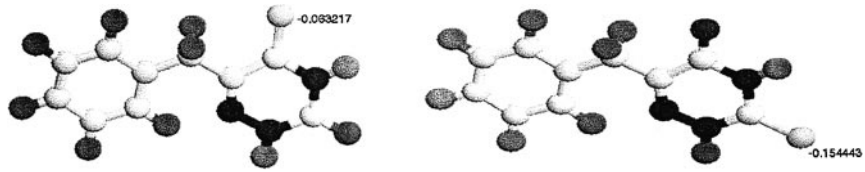


FIGURE 1 Calculated charge densities and optimized geometries of compounds 8 and 10.

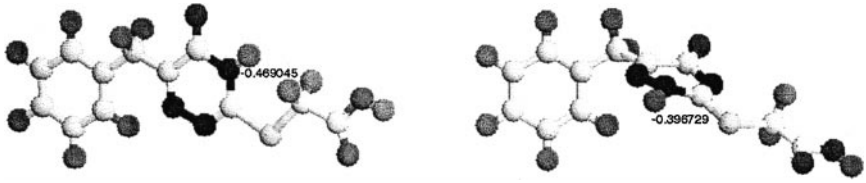


FIGURE 2 Calculated charge densities and optimized geometries of the tautometric forms 11a and 11b.

reacting **14** with carbon disulphide or acetic anhydride to give 8-benzyl-3-thioxo-2,6-dihydro-3H-[1,2,4] triazolo[4,3-d][1,2,4]triazin-5-one (**15**) or 8-benzyl-3-methyl-6H-[1,2,4]triazolo [4,3-d] [1,2,4]triazin-5-one (**16**) respectively.

Attempt to annelate six-membered ring to 1,2,4-triazine ring, namely,1,2,4-triazino-1,2,4-triazine, met with no success. Thus, heating **14** with pyruvic acid, ethyl pyruvate, or phenylpyruvic acid in boiling ethanol gave the corresponding hydrazones (**17a–c**) respectively. Treating compounds **17a** and**17c** with polyphosphoric acid or heating compound **17b** over its melting point led only to the recovery of the starting materials.

EXPERIMENTAL

Melting points were determined with a Mel-Temp apparatus and are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker AC-250 and/or Varian EM-390 spectrometers. Chemical shifts are expressed in δ scale in part per million relative to tetramethylsilane as internal standard. TLC was performed using the ascending technique with EM silica gel 60 F_{254} precoated on plastic sheets. The IR spectra were obtained with Unicam SP 1025 spectrometer. A Hewlett-Packard 5995 Gas chromatograph/Mass spectrometer was used to record Mass spectral data at 70ev. Geometry optimizations were performed initially by PM3/MOPAC in Alchemy 2000 and subsequently the electron density were calculated using the AM1 in Gaussian/98W. The compounds were named using Chem. Draw Ultra version 6, Cambridgesoft Corporation. Elemental analyses were performed in the Chemistry Department, Faculty of Science, Cairo and Beirut Universities.

6-Benzoyl-2H-[1,2,4]triazine-3,5-dione (2)

A mixture of 6-benzyl-2H-[1,2,4]triazine-3,5-dione (2.03 g, 10 mmol) and potassium dichromate (4.42 g, 15 mmol) in glacial acetic acid (40 ml) was heated under reflux for 11 h. The mixture was poured onto crushed

ice and left overnight. The product that precipitated out was filtered off, washed with water, and dried, then crystallized from ethanol to give colorless needles (yield 1.45 g, 66.8%) m.p. 225–227°C; IR (KBr): 3186 (NH), 1757 (CON), 1690 (CO), and 1640 (C=N) cm^{-1}; MS (*m/z*, %): 217 (83), 105 (100), 77 (95), 61 (14). ^{1}H NMR (DMSO-d_6): δ (ppm) 6.93, 7.07, 7.33 (3m, 5H, ArH), 11.76 (s, 1H, NH, D_2O exchangeable), 12.16 (s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 128.8, 129.6, 133.6, 135.1, 140.0, 148.8, 155.2, 187.6. Found: C, 55.1; H, 3.1; N, 19.6%. $C_{10}H_7N_3O_3$ required: C, 55.3; H, 3.2; N, 19.3%.

6-[Phenyl-(pyridin-2-yl)-hydrazono)-methyl]-2H-[1,2,4]triazine-3,5-dione (3a)

To a solution of 6-benzoyl-2H-[1,2,4]triazine-3,5-dione (0.22 g, 1 mmol) in ethanol (30 ml), 2-hydrazinopyridine (0.11 g, 1 mmol) was added. The reaction mixture was heated under reflux for 10 h, concentrated, and allowed to cool. The formed yellow precipitate was filtered off, dried, and crystallized from ethanol to give yellow needles (yield 0.15 g, 48.7%) m.p. 303–304°C; IR (KBr): 3328, 3215 (NH), 1699, 1651 (CO), and 1603 cm^{-1} (C=N). ^{1}H NMR (DMSO-d_6): δ (ppm) 6.89, 7.42, 7.73, 8.19 (t, m, m, d, 9H, ArH), 10.86, 12.13, 12.67 (s, bs, bs, 3H, 3NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 106.9, 115.7, 125.5, 128.2, 128.5, 135.8, 136.7, 138.1, 139.0, 147.6, 149.8, 156.5, 157.1. Found: C, 58.7; H, 4.0; N, 27.0%. $C_{15}H_{12}N_6O_2$ required: C, 58.4; H, 3.9; N, 27.3%.

6-[Phenyl-(phthalazin-1-yl-hydrazono)-methyl]-2H-[1,2,4]triazine-3,5-dione (3b)

To a solution of 6-benzoyl-2H-[1,2,4]triazine-3,5-dione (0.22 g, 1 mmol) in ethanol (30 ml), hydralazine (0.16 g, 1 mmol) was added. The reaction mixture was refluxed for 10 h and allowed to cool. The formed yellow precipitate was filtered off and crystallized from ethanol to give yellow crystals (yield 0.23 g, 64.1%) m.p. 247–249°C; IR (KBr): 3361, 3220, 3129 (NH), 1710, 1685 (CON), and 1612 cm^{-1}, (C=N). ^{1}H NMR (DMSO-d_6): δ (ppm) 7.48, 7.81, 8.14, 8.24 (3m, s, 10H, ArH), 11.78, 12.20, 12.49 (3s, 3H, 3NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 123.7, 126.0, 126.5, 127.1, 127.5, 128.2, 129.5, 132.0, 132.6, 135.8, 138.3, 144.0, 147.8, 149.6, 151.3, 155.9. Found: C, 60.0; H, 3.8; N, 27.1%. $C_{18}H_{13}N_7O_2$required: C, 60.2; H, 3.6; N, 27.3%.

5,7-Diphenyl-2,5-dihydro-pyrazolo[3,4-e]-[1,2,4]triazin-3-one (4a)

To a solution of 6-benzoyl-2H-[1,2,4]triazine-3,5-dione (0.44 g, 2 mmol) in ethanol (18 ml), phenylhydrazine (0.22 g, 2 mmol) was added. The

reaction mixture was refluxed for 6 h and allowed to cool. The formed dark red precipitate was filtered off and recrystallized from acetic acid to give yellow crystals (yield 0.30 g, 51.9%) m.p. 314–316°C (dec.); IR (KBr): 3153 (NH), 1665 (CON), and 1601, 1581 cm^{-1}(C=N); MS (*m/z*, %): 289 (85), 261 (43), 232 (13), 103 (20), 77 (100). ^{1}H NMR (DMSO-d_6): δ (ppm) 6.71, 6.90, 7.67 (t, m, m, 10 H, ArH), 13.63 (s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 119.6, 126.1, 126.7, 128.3, 128.5, 128.7, 130.3, 132.2, 137.2, 145.1, 149.7, 153.8. Found: C, 66.7; H, 3.5; N, 24.0%. $C_{16}H_{11}N_5O$ required: C, 66.4; H, 3.8; N, 24.2%.

7-Phenyl-5-(p-tolyl)-2,5-dihydro-pyrazolo[3,4-e][1,2,4]triazin-3-one (4b)

To a solution of 6-benzoyl-2H-[1,2,4]triazine-3,5-dione (0.22 g, 1 mmol) in ethanol (40 ml), p-tolylhydrazine (0.122 g, 1 mmol) was added. The reaction mixture was heated under reflux for 9 h. The solvent was evaporated under reduced pressure to give a dark precipitate, which upon crystallization from acetic acid gave orange crystals (yield 0.18 g, 59.4%) m.p. 293–295°C; IR (KBr): 3154 (NH), 1672 (CON), and 1592 cm^{-1}(C=N). ^{1}H NMR (DMSO-d_6): δ (ppm) 2.28 (s, 3H, CH_3), 7.39 (d, 2H, ArH), 7.42, 7.62 (m, 3H, ArH), 8.00 (m, 2H, ArH), 8.23 (m, 2H, ArH), 13.90 (s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 21.0, 120.1, 127.1, 129.1, 129.5, 130.0, 131.0, 133.0, 135.5, 136.2, 145.2, 150.5, 154.3. Found: C, 67.0; H, 4.4; N, 22.7%. $C_{17}H_{13}N_5O$ required: C, 67.3; H, 4.3; N, 23.1%.

5-(p-Chlorophenyl)-7-phenyl-2,5-dihydro-pyrazolo[3,4-e][1,2,4]triazin-3-one (4c)

To a solution of 6-benzoyl-2H-[1,2,4]triazine-3,5-dione (0.22 g, 1 mmol) in ethanol (40 ml), p-chlorophenylhydrazine (0.16 g, 1 mmol) was added. The reaction mixture was heated under reflux for 21 h. The solvent was evaporated under reduced pressure to give a dark precipitate, which upon crystallization from acetic acid gave orange crystals (yield 0.11 g, 34.0%) m.p. 303–304°C; IR (KBr): 3153 (NH), 1665 (CON), and 1582 cm^{-1} (C=N). ^{1}H NMR (DMSO-d_6): δ (ppm) 7.68 (m, 5 H, ArH), 8.33 (m, 4H, ArH), 14.69 (s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 121.3, 127.2, 128.8, 129.3, 129.5, 130.8, 131.1, 132.9, 136.7, 145.6, 150.7, 153.9. Found: C, 59.7; H, 3.3; N, 21.4%. $C_{16}H_{10}N_5OCl$ required: C, 59.4; H, 3.1; N, 21.6%.

N-[(3,5-Dioxo-2,3,4,5-tetrahydro-[1,2,4]triazin-6-yl)-phenyl-methylene]-hydrazinecarbodithioc Acid Methyl Ester (5)

A mixture of 6-benzoyl-2H-[1,2,4]triazine-3,5-dione (0.22 g, 1 mmol) and hydrazinecarbodithioic acid methyl ester (0.12 g, 1 mmol) in isopropyl alcohol was heated under reflux for 18 h. The solvent was evaporated under reduced pressure to give yellow precipitate. It was recrystallized from ethyl acetate to give yellow crystals (yield 0.14 g, 43.6%) m.p. 193–195°C (dec.); IR (KBr): 3112, 3047 (NH), 1728, 1699 (CON), 1647 cm^{-1}(C=N). ^{1}H NMR (DMSO-d_6): δ (ppm) 2.49 (s, 3H, CH_3S), 7.39, 7.69 (2m, 5H, ArH), 12.18 (s, 1H, NH, D_2O exchangeable), 12.75 (s, 1H, NH, D_2O exchangeable), 13.00 (s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 17.1, 127.0, 128.8, 130.5, 135.1, 138.0, 142.7, 149.8, 156.5, 201.0. Found: C, 44.7; H, 3.7; N, 21.5%. $C_{12}H_{11}N_5O_2S_2$ required: C, 44.8; H, 3.5; N, 21.8%.

6-(2-Phenyl-2,3-dihydro-1H-benzoimidazol-2-yl)-2H-[1,2,4]triazine-3,5-dione (6)

A mixture of 6-benzoyl-2H-[1,2,4]triazine-3,5-dione (0.22 g, 1 mmol) and o-phenylenediamine (0.11 g, 1 mmol) in ethanol (12 ml) was heated under reflux for 7 h. The reaction mixture was left to cool and the separated red precipitate was filtered off, washed with small amount of cold methanol, and dried (yield 0.12 g , 39.0%) m.p. 185–186°C; IR (KBr): 3398, 3333, 3216, 3138 (NH), 1698 (CON), and 1598 cm^{-1}(C=N); MS (*m/z*, %): 307 (24), 230 (44), 195 (100), 159 (19), 92 (26), 83 (38), 77 (6).^{1}H NMR (DMSO-d_6): δ (ppm) 6.41 (m, 4H, ArH), 6.51 (s, 2H, 2NH, D_2O exchangeable), 7.28, 7.44 (2m, 5H, ArH), 12.05 (s, 1H, NH, D_2O exchangeable), 12.40 (s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 84.0, 107.0, 118.1, 125.5, 127.4, 128.0, 138.7, 143.6, 144.6, 149.6, 156.1. Found: C, 62.2; H, 4.4; N, 22.6%. $C_{16}H_{13}N_5O_2$ required: C, 62.5; H, 4.3; N, 22.8%.

6-Benzyl-5-thioxo-4,5-dihydro-2H-[1,2,4]triazin-3-one (8) & 6-Benzyl-2H-[1,2,4]triazine-3,5-dithione (9)

A mixture of 6-benzyl-2H-[1,2,4]triazine-3,5-dione (7.22 g, 35.5 mmol) and phosphorus pentasulphide (23.8 g, 53.6 mmol) in dry pyridine (130 ml) was heated under reflux for 3 h. The reaction mixture was cooled and poured onto crushed ice. The precipitate was left overnight, filtered off, washed with water, and dried. The dry crude was boiled with about 200 ml of benzene and filtered off. The filtrate was concentrated and left to cool to give dark orange crystals of 6-benzyl-2H-[1,

2,4]triazin-3,5-dithione (yield 2.4 g, 28.8%) m.p. 184–185°C [Lit[15] m.p. 175–176°C].

The precipitate was recrystallized from ethanol to give orange needles of 6-benzyl-5-thioxo-4,5-dihydro-2H-[1,2,4]triazin-3-one (yield 2.9 g, 37.3%) m.p. 218–220°C (dec.); IR (KBr): 3212 (NH), 1728 (CON), and 1662 cm^{-1}(C=N); MS (*m/z*, %): 219 (100), 186 (10), 143 (12), 117 (13), 91 (14), 77 (6). ^{1}H NMR (DMSO-d_6): δ (ppm) 4.03 (s, 2H, CH_2Ph), 7.22 (m, 5H, ArH), 12.60 (s, 1H, NH, D_2O exchangeable), 13.45 (s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 37.6, 126.3, 128.2, 129.0, 137.4, 146.0, 147.5, 184.2. Found: C, 54.7; H, 4.3; N, 19.5%. $C_{10}H_9N_3OS$ required: C, 54.8; H, 4.1; N, 19.2%.

3-Benzyl-thiazolo[2,3-c][1,2,4]triazine-4,6-dione (13)

To a mixture of 6-benzyl-3-thioxo-3,4-dihydro-2H-[1,2,4]triazin-5-one (1.10 g, 5 mmol) and anhydrous potassium carbonate (1.38 g, 10 mmol) in dry acetone (10 ml), a solution of chloroacetic acid (0.47 g, 5 mmol) in dry acetone was added. The mixture was refluxed for 7 h, then poured onto cold dilute hydrochloric acid and left to stand overnight. The formed precipitate was filtered off, washed with water, and dried. It was recrystallized from ethyl acetate to give colorless needles (yield 0.90 g, 69.5%) m.p. 144–146°C; IR (KBr): 1726, 1698 (CON), and 1587 cm^{-1}(C=N); MS (*m/z*, %): 259 (100), 143 (15), 117 (79), 91 (56), 77 (40). ^{1}H NMR (DMSO-d_6): δ (ppm) 3.82 (s, 2H, CH_2Ph), 3.94 (s, 2H, CH_2S), 7.24 (m, 5H, ArH). ^{13}C-NMR (DMSO-d_6): δ 31.8, 35.8, 126.5, 127.8, 128.4, 129.4, 136.8, 151.0, 163.0, 169.1. Found: C, 55.9; H, 3.7; N, 15.9%. $C_{12}H_9N_3O_2S$ required: C, 55.6; H, 3.5; N, 16.2%.

6-Benzyl-5-hydrazino-2H-[1,2,4]triazin-3-one (14)

To a solution of 6-benzyl-5-thioxo-4,5-dihydro-2H-[1,2,4]triazin-3-one (0.22 g, 1 mmol) in ethanol (5 ml) was added hydrazine hydrate 99% (2 ml) in ethanol (25 ml). The mixture was refluxed for 4 h, concentrated, and then allowed to cool to room temperature. The product was filtered off and dried. It was recrystallized from methylene chloride to give colorless needles (yield 0.14 g, 64.5%) m.p. 337–338°C (dec.); IR (KBr): 3355, 3216, 3094 (NH), 1727 (CON), and 1662 cm^{-1}(C=N); MS (*m/z*, %): 217 (100), 143 (37), 128 (63), 106 (73), 91 (99), 77 (90).^{1}H NMR (DMSO-d_6): δ (ppm) 3.65 (s, 2H, CH_2Ph), 5.97 (bs, 2H, NH_2, D_2O exchangeable), 7.19 (m, 5H, ArH), 9.68 (bs, 1H, NH, D_2O exchangeable), 10.74 (s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 35.6, 126.2, 128.1, 128.9, 130.5, 138.0, 144.3, 149.0. Found: C, 55.5; H, 4.9; N, 32.0%. $C_{10}H_{11}N_5O$ required: C, 55.3; H, 5.1; N, 32.2%.

8-Benzyl-3-thioxo-2,6-dihydro-3H-[1,2,4]triazolo-[4,3-d][1,2,4]triazin-5-one (15)

A mixture of 6-benzyl-5-hydrazino-2H-[1,2,4]triazin-3-one (0.22 g, 1 mmol), carbon disulphide (3 ml) in pyridine was refluxed for 18 h. The solvent was evaporated under reduced pressure to give colorless precipitate. It was filtered off and recrystallized from ethyl acetate/n-hexane as colorless crystals (yield 0.20 g, 77.2%) m.p. 202–204°C; IR (KBr): 3114, 3029 (broad NH), 1720 (CON), and 1628 cm^{-1}(C=N); MS (*m/z*, %): 259 (100), 217 (42), 143 (20), 117 (20), 91 (96), 77 (40).^{1}H NMR (DMSO-d_6): δ (ppm) 4.15 (s, 2H, CH_2Ph), 7.25 (m, 5H, ArH), 12.29, 14.43 (s, bs, 2H, 2NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 35.9, 127.0, 128.7, 129.4, 136.3, 139.6, 142.7, 143.9, 164.6. Found: C, 51.3; H, 3.3; N, 27.1%. $C_{11}H_9N_5OS$ required: C, 51.0; H, 3.5; N, 27.0%.

8-Benzyl-3-methyl-6H-[1,2,4]triazolo-[4,3-d][1,2,4]triazin-5-one (16)

A solution of 6-benzyl-5-hydrazino-2H-[1,2,4]triazin-3-one (0.55 g, 2.5 mmol) in acetic anhydride (7 ml) was refluxed for 1.5 h. The reaction mixture was cooled and poured onto crushed ice to give colorless precipitate. It was filtered off, washed with water, dried, and recrystallized from benzene/n-hexane to give colorless needles (yield 0.46 g, 76.3%) m.p. 165–167°C; IR (KBr): 3156 (NH), 1724 (CON), and 1590 cm^{-1}(C=N).^{1}H NMR ($CDCl_3$): δ (ppm) 2.64 (s, 3H, CH_3), 4.28 (s, 2H, CH_2Ph), 7.23, 8.05 (2m, 5H, ArH), 11.23 (s, 1H, NH, D_2O exchangeable). ^{13}C-NMR ($CDCl_3$): δ 14.8, 37.4, 128.7, 129.3, 129.7, 135.7, 141.7, 144.7, 148.8, 166.3. Found: C, 60.0; H, 4.7; N, 28.7%. $C_{12}H_{11}N_5O$ required: C, 59.7; H, 4.6; N, 29.0%.

2-[(6-Benzyl-3-oxo-2,3-dihydro-[1,2,4]triazin-5-yl)hydrazono]-propionic Acid (17a)

To a solution of 6-benzyl-5-hydrazino-2H-[1,2,4]triazin-3-one (0.44 g, 2 mmol) in ethanol (80 ml), pyruvic acid (0.18 g, 2 mmol) was added; the reaction mixture was heated under reflux for 0.5 h and then was allowed to cool to room temperature. The faint yellow product was filtered off, washed with ethanol, and dried (yield 0.4 g, 69.6%) m.p. 227–229°C; IR (KBr): 3240 (OH + NH), 1727 (acid carbonyl + CON), and 1621 cm^{-1}(C=N). ^{1}H NMR (DMSO-d_6): δ (ppm) 2.10 (s, 3H, CH_3), 3.88 (s, 2H, CH_2Ph), 7.25 (m, 5H, ArH), 11.96, 12.23 (s, bs, 3H, 2NH, COOH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 10.7, 33.9, 124.3, 126.1, 126.9, 135.1, 140.9, 144.8, 145.5, 154.1, 163.0. Found: C, 54.1; H, 4.8; N, 24.1%. $C_{13}H_{13}N_5O_3$ required: C, 54.4; H, 4.6; N, 24.4%.

2-[(6-Benzyl-3-oxo-2,3-dihydro-[1,2,4]triazin-5-yl)-hydrazono]propionic Acid Ethyl Ester (17b)

A mixture of 6-benzyl-5-hydrazino-2H-[1,2,4]triazin-3-one (0.44 g, 2 mmol) and ethyl pyruvate (0.24 g, 2 mmol) in ethanol (100 ml) was heated under reflux for 3 h. The reaction mixture was concentrated, left to cool, and the yellow precipitate was filtered off and dried. It was recrystallized from benzene to give yellow needles (yield 0.6 g, 95.2%) m.p. 137–138°C; IR (KBr): 3333, 3234 (NH), 1727 (ester carbonyl), 1711 (CON), and 1628 cm^{-1}(C=N).^{1}H NMR ($CDCl_3$): δ (ppm) 1.35 (t, 3H, CH_3), 2.25 (s, 3H, CH_3), 3.91 (s, 2H, CH_2Ph), 4.34 (q, 2H, CH_2), 7.29 (m, 5H, ArH), 9.27, 9.45 (s, bs, 2H, 2NH, D_2O exchangeable). ^{13}C-NMR ($CDCl_3$): δ 14.6, 15.0, 36.8, 62.4, 127.3, 128.8, 129.6, 136.8, 145.1, 145.2, 147.7, 159.0, 165.1. Found: C, 57.4; H, 5.6; N, 21.9%. $C_{15}H_{17}N_5O_3$ required: C, 57.1; H, 5.4; N, 22.2%.

2-[(6-Benzyl-3-oxo-2,3-dihydro-[1,2,4]triazin-5-yl)-hydrazono]-3-phenyl-propionic Acid (17c)

A mixture of 6-benzyl-5-hydrazino-2H-[1,2,4]triazin-3-one (0.22 g, 1 mmol) and phenylpyruvic acid (0.16 g, 1 mmol) in ethanol (30 ml) was heated under reflux for 1 h. The reaction mixture was left to cool and the yellow precipitate was filtered off and dried. It was recrystallized from ethanol to give yellow crystals (yield 0.3 g, 82.6%) m.p. 223–224°C; IR (KBr): 3239 (OH + NH), 1739 (acid carbonyl), 1695 (CON), and 1621 cm^{-1} (C=N). ^{1}H NMR (DMSO-d_6): δ (ppm) 3.93 (s, 2H, CH_2Ph), 3.99 (s, 2H, CH_2Ph), 7.18 (m, 10H, ArH), 11.78, 12.07, 12.37 (3s, 1H each, 2NH, COOH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6): δ 31.8, 36.0, 126.3, 126.4, 128.3, 128.4, 128.7, 128.9, 136.3, 137.3, 142.7, 147.6, 148.0, 156.7, 164.6. Found: C, 62.6; H, 4.8; N, 19.6%. $C_{19}H_{17}N_5O_3$ required: C, 62.8; H, 4.7; N, 19.3%.

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