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Regioselectivity in 1,5-electrocyclization of *N*-[*as*-triazin-3-yl]nitrilimines. Synthesis of *s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-ones

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Abstract—6-Benzyl-3-(arylmethylidenehydrazino)-*as*-triazin-5(4*H*)-ones **4** underwent regioselective cyclization upon treatment with either bromine in acetic acid containing sodium acetate or with ferric chloride in refluxing ethanol to give the respective *s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-ones **7** in overall good yields. The regioselectivity in the studied reactions was elucidated by comparison of ^{13}C NMR spectra of **7** and their methyl derivatives with those of their regioisomers prepared by independent methods.

1. Introduction

Nitrilimines of type **I** whose N-terminals are bonded to heterocyclic imino moiety have been reported to undergo 1,5-electrocyclization to give the corresponding fused *s*-triazoles (Chart 1). In the course of surveying literature in this area, we noticed that almost all of nitrilimines of type **I** used in such reactions have one site for cyclization.[1–3] As part of our continuing research on the chemistry of hydrazonoyl halides, which are the major precursors for nitrilimines,[4–6] we felt it would be interesting to study the 1,5-electrocyclization of nitrilimines characterized by having two different sites for cyclization in an attempt to shed light on their regiochemistry. We wish to report herein the results of our study of the cyclization of nitrilimines **II** (Chart 1) derived from aldehyde *N*-(*as*-triazin-3-yl)hydrazones or their respective hydrazonoyl bromides. As shown in Chart 1, 1,5-electrocyclization of such nitrilimines may provide *s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-ones **III** and/or *s*-triazolo[3,4-*c*]-*as*-triazin-5(7*H*)-ones **IV** or their tautomers.

2. Results and discussion

The required starting 3-hydrazino-6-benzyl-*as*-triazin-5(4*H*)-one **3** was prepared by reacting 3-methylthio-6-benzyl-*as*-triazin-5(4*H*)-one **2** with hydrazine hydrate as previously described.[7,8] Condensation of equimolar quantities of 3-hydrazino-6-benzyl-5(4*H*)-*as*-triazinone **3** with aldehydes gave the corresponding aldehyde *N*-[6-benzyl-5(4*H*)-*as*-triazinon-3-yl]hydrazones **4** (Scheme 1). The elucidation of the structures of compounds **4** was based on spectral evidence and microanalyses. The mass spectra showed the molecular ion peaks in high intensity. The IR spectra of **4** revealed absorption bands in the region 3100–3400 cm^{-1} due to the NH stretches. Their ^{1}H NMR spectra showed the presence of the amide (–CONH–) and the

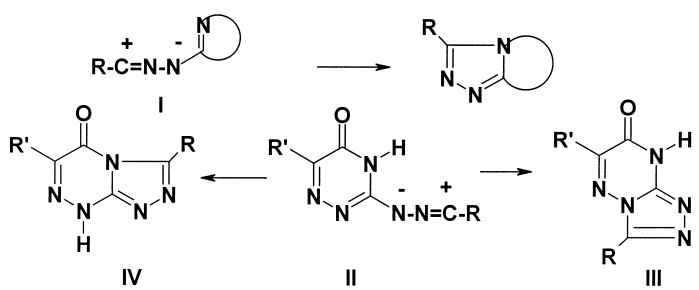

Chart 1.

Keywords: heterocycles; hydrazones; electrocyclization; synthetic methods.

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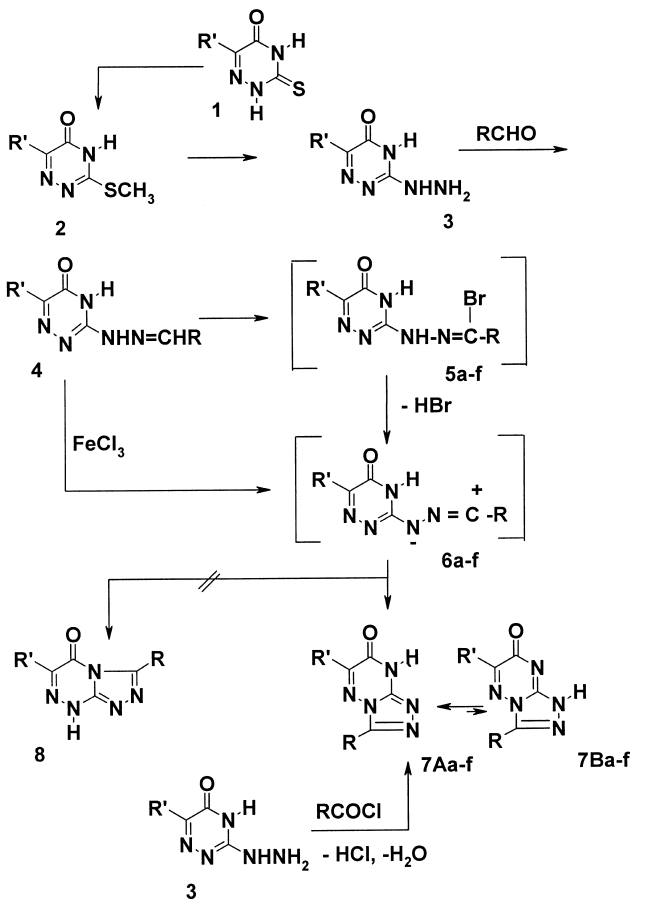


Scheme 1.

hydrazone (–C═N–NH–) protons as two singlets at δ 11.6 and 12.8, respectively. The latter two signals disappeared upon exchange with deuterium oxide. In addition, they showed, in each case, a singlet at δ 3.86–4.02 due to the benzylic (Ph–CH_2–) protons and a multiplet signal at δ 7.06–8.83 due to the aromatic and azomethine (–CH═N–) protons.

Next, the oxidative cyclization of the hydrazone derivatives **4** by two alternative methods was examined. In the first method, compounds **4** were treated with bromine in acetic acid in the presence of sodium acetate at room temperature. In our hands, such treatment yielded the respective triazolotriazines directly (Scheme 1). Attempts to isolate the intermediate hydrazonoyl bromides **5** failed, however. This result indicates that the latter intermediates underwent in situ tandem dehydrobromination, to give the corresponding nitrilimines **6**, and 1,5-electrocyclization as soon as they are formed under the reaction conditions employed to yield the respective triazolotriazines as the end products (Scheme 1). Alternatively, treatment of the hydrazones **4** with iron(III) chloride in ethanol yielded products that proved to be identical in all respects with those obtained above (Scheme 1). This finding suggests that the latter oxidative cyclization of **4** proceeds via the same nitrilimine intermediate **6** as outlined in Scheme 1. This is remeniscent of other related oxidative cyclization of aldehyde *N*-heteroaryl hydrazones with iron(III) chloride.[9]

As pointed out above, there are two directions for 1,5-electrocyclization of **6** towards the N(2) or N(4) atom, thus leading to *s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-ones **7** or *s*-triazolo[3,4-*c*]-*as*-triazin-5(7*H*)-ones **8** or a mixture of both (Scheme 1). TLC analysis of the crude products isolated from either one of the foregoing dehydrogenative cyclization methods indicated that only one product was formed in each case. The mass spectra of the isolated products showed high intensity molecular ion peaks at the expected *m*/*z* values which are less by two than that of the corresponding hydrazones **4**. Their IR spectra, while showing the disappearance of the NH group, they revealed in each case a carbonyl band in the region 1660–1670 cm^{-1}. Also, their ^1H NMR spectra lacked the characteristic signals for the azomethine (–CH═N–) and the hydrazone (–C═N–NH–) protons present in the spectra of **4**. Such data cannot distinguish, however, between the two isomeric structures **7** and **8**. The definite structure assignment of the products isolated was, therefore, made on the basis of the following: (i) chemical evidence, (ii) comparison of ^{13}C NMR spectra of **7** and their methyl derivatives with those of their regioisomers (Chart 2) prepared by independent methods and (iii) chemical reactions as outlined below.

As a first attempt to elucidate the actual structure of the isolated products, an authentic sample of 3-phenyl-6-benzyl-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one **7a** was prepared and compared with the product isolated from the studied dehydrogenative cyclization of **4a**. Thus, reaction of 6-benzyl-3-hydrazino-*as*-triazin-5(4*H*)-one **3** with benzoyl chloride in pyridine at reflux gave a crystalline compound, which proved to be identical in all respects with that obtained from dehydrogenative cyclization of **4a** (Scheme 1). As reactions of 3-hydrazino-6-substituted-*as*-triazin-5(4*H*)-ones with carboxylic acids or acyl chlorides at reflux were reported to give the respective 3,6-disubstituted *s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-ones,[10–13] it is not unreasonable to conclude therefore that oxidative cyclization of hydrazones **4** proceeds via participation of N(2) of *as*-triazine moiety and exclusively affords **7**. This conclusion is in agreement with literature reports which indicate that in *as*-triazin-5(4*H*)-ones the presence of N(1) atom increases the basicity of N(2) in relation to N(4) which is situated between two electron-deficient carbon atoms, and thus the N(2) is more nucleophilic than N(4).[14–16]

The assignment of structure **7** and its tautomeric form **7A** was further confirmed by comparison of the methylation product of **7a** with authentic samples of two isomers namely 6-benzyl-8-methyl-3-phenyl-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one and 6-benzyl-1-methyl-3-phenyl-*s*-triazolo[4,3-*b*]-*as*-triazin-7(1*H*)-one **13a** and **15a**, respectively (Scheme 2). Both isomers **13a** and **15a** have been unreported hitherto and thus they were prepared unambiguously as outlined in Scheme 2.

The synthetic strategy for **13a** was based on oxidation of the hydrazone precursor **12a**. The latter was prepared by

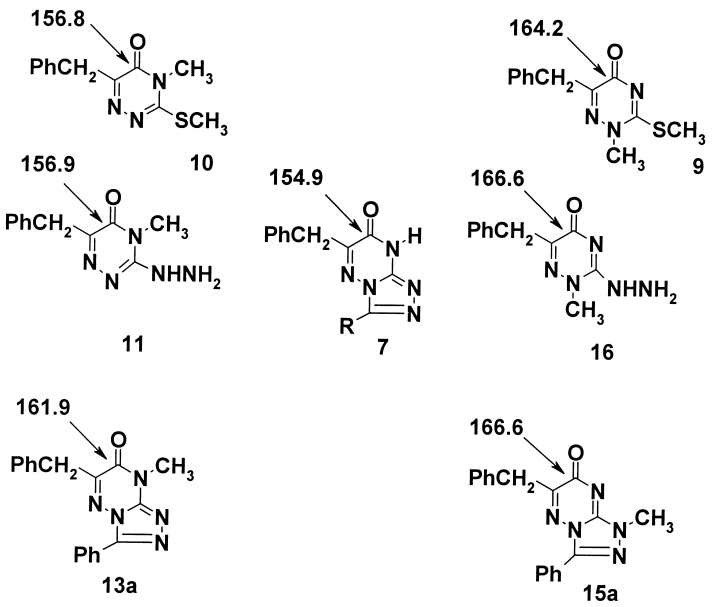
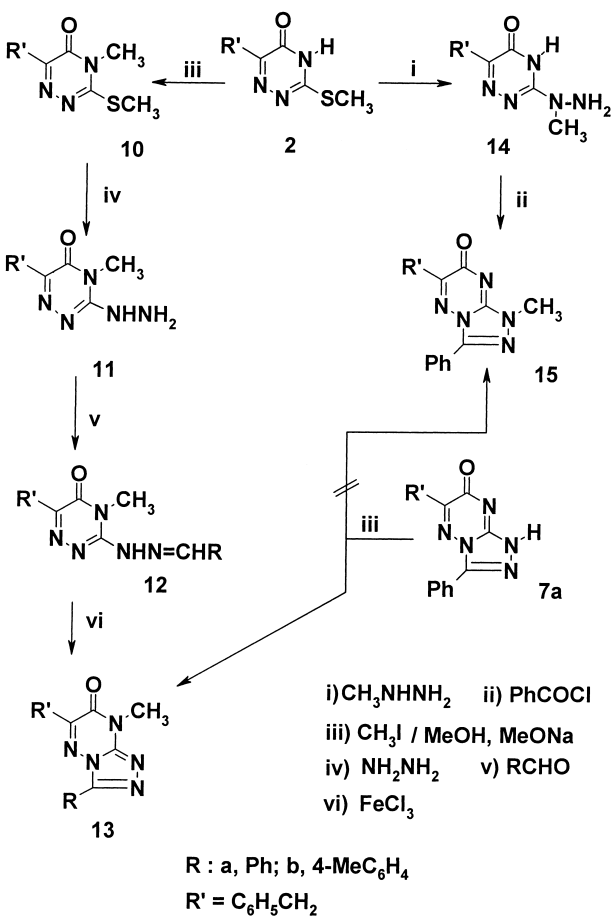


Chart 2.

treatment of **10** with hydrazine hydrate to give the novel hydrazino derivative **11**, and reaction of the latter with benzaldehyde to yield the hydrazone **12a**. Treatment of the latter hydrazone derivative with $FeCl_3$ in EtOH gave 6-benzyl-8-methyl-3-phenyl-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one **13a** (Scheme 2).

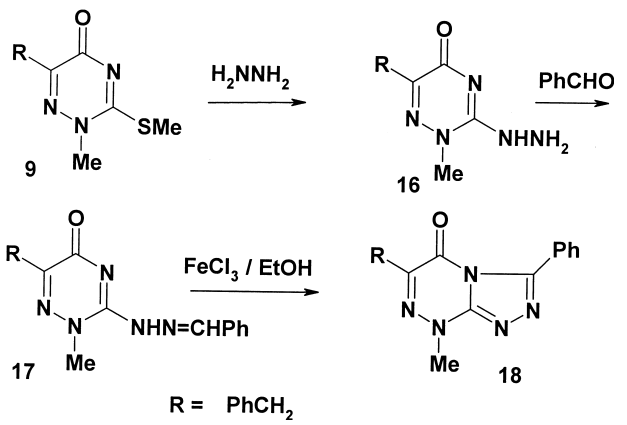


Scheme 2.

The other isomeric compound namely 6-benzyl-1-methyl-3-phenyl-*s*-triazolo[4,3-*b*]-*as*-triazin-7(1*H*)-one **15a** was prepared by reaction of benzoyl chloride with 3-(1-methylhydrazino)-6-benzyl-*as*-triazin-5(4*H*)-one **14** in refluxing pyridine (Scheme 2). The precursor **14** was prepared by reaction of **2** with methylhydrazine. Reactions of methylhydrazine with other 6-substituted-3-methylthio-*as*-triazin-5(4*H*)-ones were reported to give the respective 3-(1-methylhydrazino)-*as*-triazine derivatives.[17] Both **13a** and **15a** proved to have different physical constants as depicted in Section 3.

Treatment of **7a** with methyl iodide in ethanol in the presence of sodium hydroxide yielded a product that proved to be identical in all respects (mp, mixed mp, IR and ^{1}H NMR) with **13a** (Scheme 2). This finding indicates that the products isolated from oxidative cyclization of the hydrazone derivatives **4** have structure **7** and exist predominantly in the tautomeric form **7A**. The predominance of the latter form is compatible with Clar's rule which is used to interpret the relative stability of fused heterocyclic isomers.[18,19] The form **7A**, having one Clar's circle more than the other form **7B** (Scheme 1) is expected to be more stable as it has higher degree of aromatic stability. This same rule can also account for our finding that methylation of **7a** led to the formation of **13a** in preference of **15a** as the former is expected to be more stable than the latter as it has one Clar's circle more than **15a**.

The assigned structure **13a** and in turn structure **7** was further confirmed by its comparison with an authetic sample of its isomer namely 6-benzyl-8-methyl-3-phenyl-*s*-triazolo[3,4-*c*]-*as*-triazin-5(8*H*)-one **18** which was prepared unequivocally by the method depicted in Scheme 3. Thus, treatment of **9** with hydrazine hydrate gave the hydrazino derivative **16**. Reaction of the latter with benzaldehyde



Scheme 3.

afforded the hydrazone derivative **17**. Treatment of the latter with ferric chloride in ethanol or with bromine in acetic acid in presence of sodium acetate yielded **18**. The latter product proved different in all respects (mp, IR and ^{1}H NMR spectra) from **13a** (see Section 3).

In addition to the foregoing chemical evidence, the tautomeric structure **7A** was further confirmed by comparison of ^{13}C NMR spectra of the isolated products with those of some triazinones **9**–**11** and **16** and the triazolotriazinones **13** and **15** (Chart 2). This is because literature reports[14–16] indicate that the chemical shift of the carbonyl carbon in *as*-triazin-5(4*H*)-ones and their annelated analogs is markedly affected by the nature of the adjacent nitrogen, i.e. N(4), pyridine type or pyrrole type, being larger downfield for the former type (Chart 2). The ^{13}C NMR spectrua of **7** revealed the signal for the carbonyl carbon resonance at δ 154.9. This chemical shift value suggests that N(4) atom is sp^3-hybridized nitrogen atom i.e. pyrrole type as it is similar to that found for the triazinones **10** (δ 156.8) and **11** (δ 156.9) and different from those of **9** (δ 164.2), and **15** (δ 166.6) and **16** (δ 166.6) (Chart 2).

In conclusion, all evidence presented in this work points to the fact that cyclization of 6-benzyl-3-(3-arylmethylidene-hydrazino)-*as*-triazin-5(4*H*)-ones **4** is regioselective and leads to *s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-ones **7** in overall good yields and that the latter products exist predominantly in the tautomeric form **7A** (Scheme 1).

3. Experimental

3.1. General

All melting points were determined in open capillary tubes and are uncorrected. The IR spectra were recorded in a Pye-Unicam SP300 instrument in potassium bromide disks. The ^{1}H and ^{13}C NMR spectra were recorded in a Varian Mercury VXR-300 spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C) in $CDCl_3$ or DMSO-d_6 and the chemical shifts were related to that of the solvent. Mass spectra were obtained in a GCMS-Q1000-EX spectrometer, the ionizing voltage was 70 eV. Elemental analyses were carried out by the Microanalytical Center of Cairo University, Giza, Egypt. The identification of compounds from different experiments were secured by mixed mps and superimposable IR spectra. 6-Benzyl-3-methylthio-5(4*H*)-*as*-triazinone **2**,[7] 6-benzyl-3-hydrazino-*as*-triazin-5(4*H*)-one **3**,[8] 6-benzyl-2-methyl-3-methylthio-*as*-triazin-5(2*H*)-one **9**[20] (δ_C (DMSO-d_6) 164.2, 139.4, 130.0, 128.7, 128.5, 127.2, 126.9, 39.5, 38.9, 36.5) and 6-benzyl-4-methyl-3-methylthio-5(4*H*)-*as*-triazinone **10**[21] (δ_C (DMSO-d_6) 156.8, 151.3, 136.9, 132.8, 129.1, 128.2, 126.4, 38.6, 36.6, 35.7) were prepared by literature methods.

3.1.1. 6-Benzyl-3-hydrazino-4-methyl-*as*-triazin-5(4*H*)-one (11) and 6-benzyl-3-hydrazino-2-methyl-*as*-triazin-5(2*H*)-one (16). *General method*. To 6-benzyl-4-methyl-3-methylthio-*as*-triazin-5(4*H*)-one **10** (1 g, 4 mmol) in 2-propanol (10 ml) was added hydrazine hydrate (80% in hydrazine, 2 ml). The reaction mixture was refluxed for 10 h, then cooled. The solid that precipitated was filtered off and crystallized from DMF to give **11** (0.64 g, 69%) as pale yellow needles, mp 271–272°C; (Found: C, 57.2; H, 5.4; N, 30.3. $C_{11}H_{13}N_5O$ (231.3) requires: C, 57.19; H, 5.62; N, 30.30%); ν_{max} (KBr) 3402, 3055, 1674 cm^{-1}; δ_H ($CDCl_3$) 3.39 (s, 3H, NC*H*$_3$), 3.79 (s, 2H, *CH*$_2$Ph), 4.90 (s, 2H, N*H*$_2$), 7.17–7.29 (m, 5H, *Ph*), 12.12 (s, 1H, N*H*); δ_C (DMSO-d_6) 156.9, 147.6, 138.6, 132.8, 129.5, 128.8, 126.7, 38.9, 36.5; MS *m*/*z* (%) 231 (100), 185 (40), 114 (32), 91 (42), 77 (17).

When the above procedure was repeated using 6-benzyl-2-methyl-3-methylthio-*as*-triazin-5(4*H*)-one **9** in lieu of **10**, the hydrazine derivative **16** was obtained as pale yellow needles (0.62 g, 68%); mp 262–264°C; (Found: C, 57.3; H, 5.4; N, 30.2, $C_{11}H_{13}N_5O$ (231.3) requires: C, 57.19; H, 5.62; N, 30.30%); ν_{max} (KBr) 3394, 3030, 1681 cm^{-1}; δ_H ($CDCl_3$) 3.36 (s, 3H, NC*H*$_3$), 3.76 (s, 2H, *CH*$_2$Ph), 7.18–7.23 (m, 5H, *Ph*), 8.54 (s, 2H, N*H*$_2$), 12.11 (s, 1H, N*H*); δ_C (DMSO-d_6) 166.6, 149.1, 138.1, 132.8, 129.7, 128.6, 126.8, 37.3, 36.5; MS *m*/*z* (%) 232 (70), 217 (45), 171 (42), 118 (35), 93 (100), 77 (20).

3.1.2. Synthesis of 6-benzyl-3-(1-methylhydrazino)-*as*-triazin-5(4*H*)-one 14. To a well-stirred solution of **2** (2.2 g, 0.013 mol) in isopropanol (30 ml) was added methylhydrazine (6 g, 0.13 mol). The reaction mixture was refluxed while being stirred for 6 h, then cooled. The solid product that separated was filtered off and crystallized from *i*-propanol to give the hydrazine **14** as colorless needles (1.8 g, 61%), mp 238–239°C; (Found: C, 57.4; H, 5.5; N, 30.1. $C_{11}H_{13}N_5O$ (231.3) requires: C, 57.19; H, 5.62; N, 30.30%); ν_{max} (KBr) 3286, 3170, 1674 cm^{-1}; δ_H ($CDCl_3$) 3.11 (s, 3H, NC*H*$_3$), 3.77 (s, 2H, *CH*$_2$Ph), 7.11–7.29 (m, 5H, *Ph*), 9.90 (s, 2H, N*H*$_2$), 12.12 (s, 1H, N*H*); MS *m*/*z* (%) 231 (42), 93 (100), 77 (33).

3.2. Preparation of hydrazones 4, 12 and 17

General procedure. A mixture of the hydrazine **3** (0.01 mol) and the appropriate aldehyde (0.01 mol) in acetic acid (30 ml) was heated under reflux for 30 min, then cooled. The mixture was diluted with water and the solid produced filtered off, washed with water, dried and crystallized from the proper solvent to give the respective hydrazone **4**.

Repetition of the above procedure using **11** and **16** each in place of **3** afforded the hydrazone derivatives **12** and **17**,

respectively. The physical constants of the hydrazones **4a**–**f**, **12a**, **b** and **17** are listed below.

3.2.1. 6-Benzyl-3-[(phenylmethylene)hydrazino]-*as*-triazin-5(4*H*)-one (4a). (2.4 g, 80%) as yellowish needles, mp 258°C (AcOH); (Found: C, 66.7; H, 4.9; N, 22.9. $C_{17}H_{15}N_5O$ (305.3) requires: C, 66.87; H, 4.95; N, 22.94); ν_{max} (KBr) 3200, 3150, 1660 cm^{-1}; δ_H ($CDCl_3$) 4.01 (s, 2H, CH_2Ph), 7.2–7.8 (m, 11H, 2*Ph*, =*CH*), 8.72 (s, 1H, N*H*), 12.06 (s, 1H, N*H*).

3.2.2. 6-Benzyl-3-[(4-methylphenylmethylene)hydrazino]-*as*-triazin-5(4*H*)-one (4b). (2.6 g, 82%) as white plates, mp 296°C (AcOH); (Found: C, 67.5; H, 5.4; N, 21.8. $C_{18}H_{17}N_5O$ (319.3) requires: C, 67.70; H, 5.37; N, 21.93%); ν_{max} (KBr) 3210, 3100, 1643 cm^{-1}; δ_H ($CDCl_3$) 2.34 (s, 3H, CH_3Ph), 3.87 (s, 2H, CH_2Ph), 7.2–7.8 (m, 9H, *ArH*), 8.0 (s, 1H, =C*H*), 11.6 (s, 1H, N*H*), 12.77 (s, 1H, N*H*).

3.2.3. 6-Benzyl-3-[(4-chlorophenylmethylene)hydrazino]-*as*-triazin-5(4*H*)-one (4c). (2.9 g, 85%) as yellowish needles, mp 312°C (AcOH); (Found: C, 60.3; H, 4.1; N, 20.5. $C_{17}H_{14}ClN_5O$ (339.8); requires: C, 60.09; H, 4.15; N, 20.61%); ν_{max} (KBr) 3200, 3095, 1641 cm^{-1}; δ_H ($CDCl_3$) 3.87 (s, 2H, CH_2Ph), 7.29–8.05 (m, 10H, *ArH*, =C*H*), 11.8 (s, 1H, N*H*), 12.82 (s, 1H, N*H*).

3.2.4. 6-Benzyl-3-[(4-bromophenylmethylene)hydrazino]-*as*-triazin-5(4*H*)-one (4d). (3.2 g, 85%) as yellowish needles, mp 282°C (AcOH); (Found: C, 53.2; H, 3.7; N, 18.1.$C_{17}H_{14}BrN_5O$ (384.2) requires: C, 53.14; H, 3.67; N, 18.22%); ν_{max} (KBr) 3210, 3100, 1641 cm^{-1}; δ_H ($CDCl_3$) 3.86 (s, 2H, CH_2Ph), 7.17–8.64 (m, 10H, *ArH*, =C*H*), 11.7 (s, 1H, N*H*), 12.80 (s, 1H, N*H*).

3.2.5. 6-Benzyl-3-[(2-furanylmethylene)hydrazino]-*as*-triazin-5(4*H*)-one (4e). (2.3 g, 80%) as white solid, mp 248°C (AcOH–H_2O); (Found: C, 61.2; H, 4.6; N, 23.6. $C_{15}H_{13}N_5O_2$ (295.3) requires: C, 61.01; H, 4.44; N, 23.72%); ν_{max} (KBr) 3336, 3100, 1650 cm^{-1}; δ_H ($CDCl_3$) 3.97 (s, 2H, CH_2Ph), 6.48–7.50 (m, 8H, *ArH*, *Het-H*), 8.34 (s, 1H, =C*H*), 12.0 (s, 1H, N*H*), 12.15 (s, 1H, N*H*).

3.2.6. 6-Benzyl-3-[(2-thienylmethylene)hydrazino]-*as*-triazin-5(4*H*)-one (4f). (2.4 g, 80%) as pale brown needles, mp 243°C (AcOH–H_2O); (Found: C, 57.7; H, 4.2; N, 22.3. $C_{15}H_{13}N_5OS$ (311.3) requires: C, 57.86; H, 4.21; N, 22.49%); ν_{max} (KBr) 3400, 3100, 1640 cm^{-1}; δ_H ($CDCl_3$) 4.02 (s, 2H, CH_2Ph), 7.06–7.47 (m, 8H, *ArH*, *Het-H*), 8.83 (s, 1H, =C*H*), 11.49 (s, 1H, N*H*), 11.54 (s, 1H, N*H*).

3.2.7. 6-Benzyl-4-methyl-3-[(phenylmethylene)hydrazino]-*as*-triazin-5(4*H*)-one (12a). (2.8 g, 88%) as pale brown solid, mp 204°C (AcOH); (Found: C, 67.5; H, 5.3; N, 21.7. $C_{18}H_{17}N_5O$ (319.3) requires: C, 67.70; H, 5.37; N, 21.90%); ν_{max} (KBr) 3195, 1690 cm^{-1}; δ_H ($CDCl_3$) 3.19 (s, 3H, NCH_3), 3.82 (s, 2H, CH_2Ph), 7.25–7.94 (m, 11H, ArH, =C*H*), 12.7 (s, 1H, N*H*).

3.2.8. 6-Benzyl-4-methyl-3-[(4-methylphenylmethylene)-hydrazino]-*as*-triazin-5(4*H*)-one (12b). (2.5 g, 76%) as pale yellow solid, mp 221°C (EtOH); (Found: C, 68.3; H, 5.6; N, 21.2. $C_{19}H_{19}N_5O$ (333.4) requires: C, 68.45; H, 5.74; N, 21.01%); ν_{max} (KBr) 3190, 1680 cm^{-1}; δ_H ($CDCl_3$) 2.39 (s, 3H, CH_3Ph), 3.17 (s, 3H, NCH_3), 3.93 (s, 2H, CH_2Ph), 6.3–8.36 (m, 10H, *ArH*), 12.3 (s, 1H, N*H*).

3.2.9. 6-Benzyl-2-methyl-3-[(phenylmethylene)hydrazino]-*as*-triazin-5(2*H*)-one (17). (2.2 g, 70%) as yellow solid, mp 235°C; (Found: C, 67.5; H, 5.4; N, 22.1. $C_{18}H_{17}N_5O$ (319.3) requires: C, 67.70; H, 5.37; N, 21.90%); ν_{max} (KBr) 3209, 1681 cm^{-1}; δ_H ($CDCl_3$) 3.41 (s, 3H, NCH_3), 3.95 (s, 2H, CH_2Ph), 7.02–7.60 (m, 11H, ArH, =C*H*), 11.0 (s, 1H, N*H*).

3.3. Synthesis of *s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-ones (7a–f and 13a, b) and *s*-triazolo[3,4-*c*]-*as*-triazin-5(8*H*)-one (18)

Method A. Bromine (0.44 g, 5.5 mmol) in acetic acid (5 ml) was added dropwise to a stirred mixture of the appropriate hydrazone **4** (5 mmol) and sodium acetate (1.2 g, 15 mmol) in acetic acid (30 ml). The reaction mixture was stirred for 12 h at room temperature. The mixture was then poured onto ice-cold water (250 ml). The solid that precipitated was filtered off, washed with 5% sodium bicarbonate solution and then with water, dried and crystallized from the appropriate solvent to give the respective triazolotriazines **7**.

Method B. To the appropriate hydrazone **4** (14 mmol) in ethanol (40 ml), a solution of ferric chloride (2 M, 5 ml) was added. The mixture was refluxed for 20 min, then left overnight at room temperature. The excess solvent was distilled under reduced pressure, and solid residue left was washed with water several times, dried and finally crystallized from the appropriate solvent to give the respective triazolotriazines **7**.

Repetition of the foregoing procedure using **12** and **17** each in lieu of **4** yielded the corresponding triazolotriazines **13** and **18**, respectively. The physical constants of the triazolotriazines **7a**–**f**, **13a**, **b** and **18** are given below.

3.4. Alternate synthesis of 7a

To a solution of the hydrazine **3** (2.2 g, 0.01 mol) in dry pyridine (20 ml) was added benzoyl chloride (2.1 g, 0.015 mol) and the resulting mixture was refluxed for 1 h, then cooled. The resulting mixture was triturated with ethanol (10 ml) and the solid precipitated filtered off and crystallized from ethanol to give **7a** which proved to be identical in all respects with **7a** prepared above.

3.4.1. 6-Benzyl-3-phenyl-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one (7a). (1.06 g, 70%) as white solid, mp 287°C (EtOH); (Found: C, 67.2; H,4.3; N, 22.9. $C_{17}H_{13}N_5O$ (303.3) requires C, 67.32; H, 4.32; N, 23.09%); ν_{max} (KBr) 3456, 1689 cm^{-1}; δ_H ($CDCl_3$) 4.05 (s, 2H, CH_2Ph), 7.23–8.08 (m, 10H, *ArH*), 13.92 (s, 1H, *NH*); δ_C (DMSO-d_6) 154.9, 136.2, 131.6, 129.5, 129.4, 128.9, 128.3, 127.9, 127.4, 126.6, 123.7, 120.6, 37.1.

3.4.2. 6-Benzyl-3-(4-methylphenyl)-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one (7b). (1.18 g, 75%) as white solid, mp 318°C (AcOH–EtOH); (Found: C, 68.3; H, 4.4; N, 21.9. $C_{18}H_{15}N_5O$ (317.3) requires C, 68.13; H, 4.76; N, 22.07%);

ν_{max} (KBr) 3448, 1659 cm^{-1}; δ_H ($CDCl_3$) 2.40 (s, 3H, CH_3Ph), 4.09 (s, 2H, CH_2Ph), 7.31–8.06 (m, 9H, *ArH*), 14.50 (s, 1H, N*H*).

3.4.3. 6-Benzyl-3-(4-chlorophenyl)-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one (7c). (1.28 g, 76%) as pale brown plates, mp 300°C (EtOH); (Found: C, 60.2; H, 3.7; N, 20.9. $C_{17}H_{12}ClN_5O$ (337.8) requires C, 60.45; H, 3.58; N, 20.73%); ν_{max} (KBr) 3440, 1665 cm^{-1}; δ_H ($CDCl_3$) 3.33 (s, 2H, CH_2Ph), 7.48–7.86 (m, 9H, *ArH*), 13.03 (s, 1H, N*H*).

3.4.4. 6-Benzyl-3-(4-bromophenyl)-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one (7d). (1.47 g, 77%) as brown plates, mp 298°C (AcOH); (Found: C, 53.3; H, 3.3; N, 18.2. $C_{17}H_{12}BrN_5O$ (382.2) requires C, 53.42; H, 3.16; N, 18.32%); ν_{max} (KBr) 3210, 3100, 1661 cm^{-1}; δ_H ($CDCl_3$) 3.9 (s, 2H, CH_2Ph), 7.2–8.4 (m, 9H, *ArH*), 11.99 (s, 1H, N*H*).

3.4.5. 6-Benzyl-3-(2-furanyl)-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one (7e). (1.0 g, 68%) as yellow solid, mp 286°C (AcOH); (Found: C, 61.5; H, 3.6; N, 23.6. $C_{15}H_{11}N_5O_2$ (293.3) requires C, 61.43; H, 3.78; N, 23.88%); ν_{max} (KBr) 3386, 1665 cm^{-1}; δ_H ($CDCl_3$) 3.82 (s, 2H, CH_2Ph), 7.0–8.0 (m, 8H, *ArH*, *Het-H*), 12.10 (s, 1H, N*H*).

3.4.6. 6-Benzyl-3-(2-thienyl)-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one (7f). (1.08 g, 70%) as yellow needles, mp 238°C (EtOH); (Found: C, 58.1; H, 3.7; N, 22.3. $C_{15}H_{11}N_5OS$ (309.3) requires: C, 58.24; H, 3.58; N, 22.64%); ν_{max} (KBr) 3456, 1650 cm^{-1}; δ_H ($CDCl_3$) 3.83 (s, 2H, CH_2Ph), 7.1–8.3 (m, 8H, *ArH*, Het-*H*), 12.6 (s, 1H, N*H*).

3.4.7. 6-Benzyl-8-methyl-3-phenyl-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one (13a). (1.1 g, 70%) as white solid, mp 172°C (AcOH); (Found: C, 68.1; H, 4.6; N, 22.2. $C_{18}H_{15}N_5O$ (317.3) requires: C, 68.13; H, 4.76; N, 22.07%); ν_{max} (KBr) 1675; δ_H ($CDCl_3$) 3.17 (s, 3H, NCH_3), 3.79 (s, 2H, CH_2Ph), 7.25–7.92 (m, 10H, *ArH*); δ_C (DMSO-d_6) 161.9, 153.1, 149.5, 144.5, 137.1, 133.6, 129.5, 128.8, 128.2, 127.8, 127.1, 125.8, 38.5, 35.8.

3.4.8. 6-Benzyl-8-methyl-3-(4-methylphenyl)-*s*-triazolo[4,3-*b*]-*as*-triazin-7(8*H*)-one (13b). (1.1 g, 67% yield) as white solid, mp 216°C (AcOH); (Found: C, 68.6; H, 5.2; N, 21.2. $C_{19}H_{17}N_5O$ (331.3) requires: C, 68.87; H, 5.17; N, 21.13%). ν_{max} (KBr) 1670; δ_H ($CDCl_3$) 2.17 (s, 3H, CH_3Ph), 3.11 (s, 3H, NCH_3), 3.95 (s, 2H, CH_2Ph), 7.2–8.13 (m, 9H, *ArH*).

3.4.9. 6-Benzyl-8-methyl-3-phenyl-*s*-triazolo[3,4-*c*]-*as*-triazin-5(8*H*)-one (18). (1.0 g, 68%) as white solid, mp 247°C (EtOH); (Found: C, 68.1; H, 4.8; N, 21.9. $C_{18}H_{15}N_5O$ (317.3) requires: C, 68.13; H, 4.76; N, 22.07%); ν_{max} (KBr) 1689; δ_H ($CDCl_3$) 3.39 (s, 3H, NCH_3), 4.0 (s, 2H, CH_2Ph), 7.2–8.1 (m, 10H, *ArH*); δ_C (DMSO-d_6) 162.3, 156.8, 149.6, 138.1, 132.8, 132.5, 129.8, 129.2, 128.9, 128.8, 128.6, 126.9, 36.6, 35.8.

3.5. Alternate synthesis of 13a

Compound **7a** (3.1 g, 0.01 mol) was added to a stirred methanolic sodium methoxide solution, prepared by dissolving sodium metal (0.23 g, 0.01 mol) in absolute methanol (10 ml). To the the resulting mixture was added methyl iodide (1.47 g, 0.01 mol). The reaction mixture was left overnight at room temperature while being stirred. The solid that precipitated was filtered off and crystallized from acetic acid to give **13a** (2.1 g, 65%) as white solid, mp 172°C; (Found: C, 68.3; H, 4.4; N, 22.1. $C_{18}H_{15}N_5O$ (317.3) requires: C, 68.13; H, 4.70; N, 22.07%).The latter product proved identical in all respects with **13a** obtained from oxidative cyclization of **12a**.

3.5.1. Synthesis of 6-benzyl-1-methyl-3-phenyl-*s*-triazolo[4,3-*b*]-*as*-triazin-7(1*H*)-one (15a). To a solution of the hydrazine **14** (2.2 g, 0.01 mol) in dry pyridine (20 ml) was added benzoyl chloride (2.1 g, 0.015 mol) and the resulting mixture was refluxed for 2 h, then cooled. The resulting mixture was triturated with ethanol (10 ml) and the solid that precipitated was filtered off and crystallized from acetic acid to give **15a** (2.3 g, 75%) as white needles, mp 228°C; (Found: C, 68.1; H, 4.6; N, 22.0. $C_{18}H_{15}N_5O$ (317.3) requires C, 68.13; H, 4.76; N, 22.07%); ν_{max} (KBr) 1697 cm^{-1}; δ_H ($CDCl_3$) 3.48 (s, 3H, NCH_3), 3.87 (s, 2H, CH_2Ph), 7.19–8.08 (m, 10H, *ArH*); δ_C (DMSO-d_6) 166.6, 162.8, 156.7, 149.1, 138.0, 132.8, 132.5, 129.7, 128.9, 128.8, 128.6, 126.8, 37.3, 36.5.

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