

SYNTHESIS OF FUSED AND NONFUSED HETEROCYCLES FROM 5- AND 8-SUBSTITUTED 3-HYDRAZINO-1,2,4-TRIAZINO[5,6-*b*]INDOLE

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Abstract: The 7- and 10-substituted 1,2,4-triazolo[4',3':2,3][1,2,4]triazino[5,6-*b*]indoles were prepared by the reaction of 5- and 8-substituted-3-hydrazino-1,2,4-triazino[5,6-*b*]indole with formic acid or triethyl orthoformate. Reaction of the hydrazines with acetylacetone, ethyl acetoacetate and ethyl cyanoacetate gave the respective biheterocycles containing pyrazole and pyrazolone rings. Reaction of the hydrazines with carbondisulphide, thiourea, urea, ethyl chloroformate as well as nitrous acid have been investigated. Reaction of 5-allyl-3-methylthio-1,2,4-triazino[5,6-*b*]indole with ethanolamine followed by cyclization gave the imidazotriazinoindole.

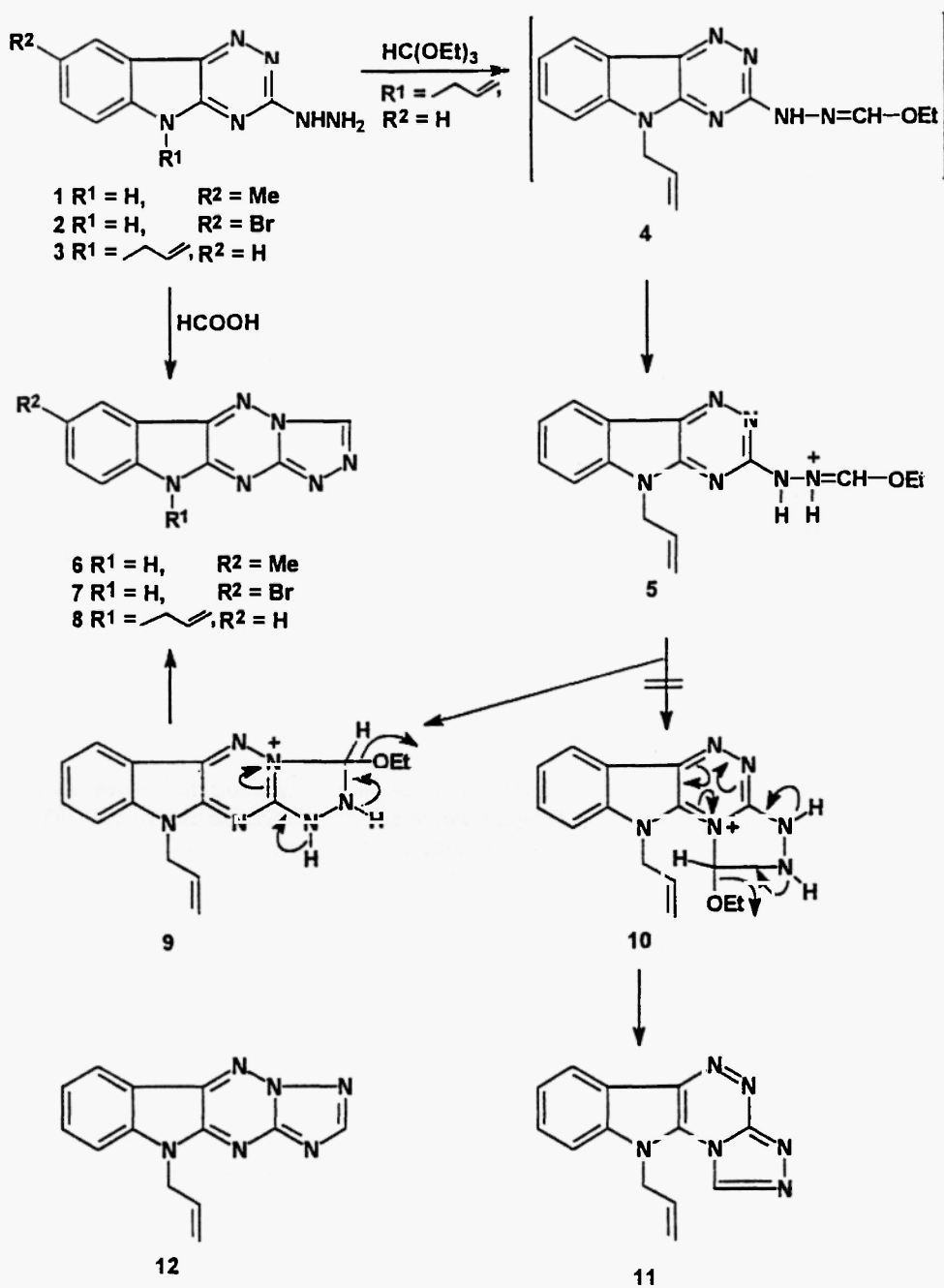
INTRODUCTION

The 1,2,4-triazino[5,6-*b*]indole ring has been found to be a useful carrier for various functional groups for developing antiviral and antibacterial activities [1-8]. The imidazo, pyrimido or triazolo-1,2,4-triazino[5,6-*b*]indoles showed also antiviral and antibacterial properties [9]. The arylidene moiety of 3-arylidene and heterocyclic formylidenehydrazono-1,2,4-triazino[5,6-*b*]indole derivatives has been found to play a role on their activity against *Staphylococcus aureus* and *Bacillus cereus* as well as P 388 lymphocytic leukemia [8]. The 3-hydrazino-1,2,4-triazino[5,6-*b*]indole and 3-hydrazino-5,6-diphenyl-1,2,4-triazine have an effect on the carbohydrate metabolism and lipid components in rat [10,11]. The regioselective annelation of a triazole ring to the 1,2,4-triazino[5,6-*b*] indole either *via* the dehydrative cyclization of the respective hydrazide or the dehydrogenative cyclization of the hydrazones has been reported [12-16]. In the present paper, the formation of heterocycles fused or nonfused to the substituted 1,2,4-triazino[5,6-*b*]indole has been investigated.

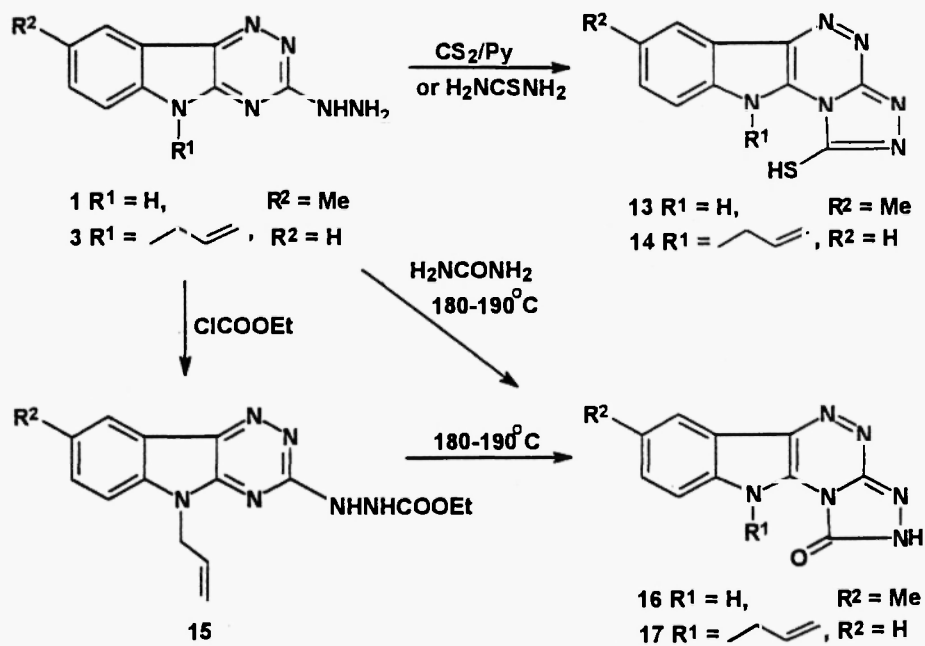
RESULTS AND DISCUSSION

The reaction of hydrazines **1**, **2** and **3** with formic acid afforded the linear triazolotriazinoindoles **6-8**. The reaction of **3** with triethyl orthoformate has been anticipated to give one or both of the isomeric ring systems **8** and/or **11**. The product was found to be identical with the linear isomer **8**, whereas its Dimroth rearrangement to give **12** was ruled out since the condition of cyclization by triethyl orthoformate could not cause such type of rearrangement. Moreover, when **8** was subjected to the action of acid or alkali, no change could be noticed. This means that the ring is stable towards acid or alkali and this was the reason that formic acid afforded identical product with that obtained from triethyl orthoformate. The mechanism of cyclization of **3** with triethyl orthoformate may have taken place *via* the formation of ethoxymethylidenehydrazino intermediate **4** which upon protonation at the imino nitrogen atom gave **5**. Nucleophilic attack of the N-2 of the triazine ring rather than the N-4 to the methylidene carbon atom may take place to give **9** and not **10** (scheme 1). This preference can be attributed to the existence of steric hinderance in **10** which may prohibit its formation and consequently the formation of **9** is the preferred intermediate. This steric effect is more influential than preserving the 10- π electron system in the indole ring. Finally, elimination of EtOH molecule with deprotonation would occur to give **8**.

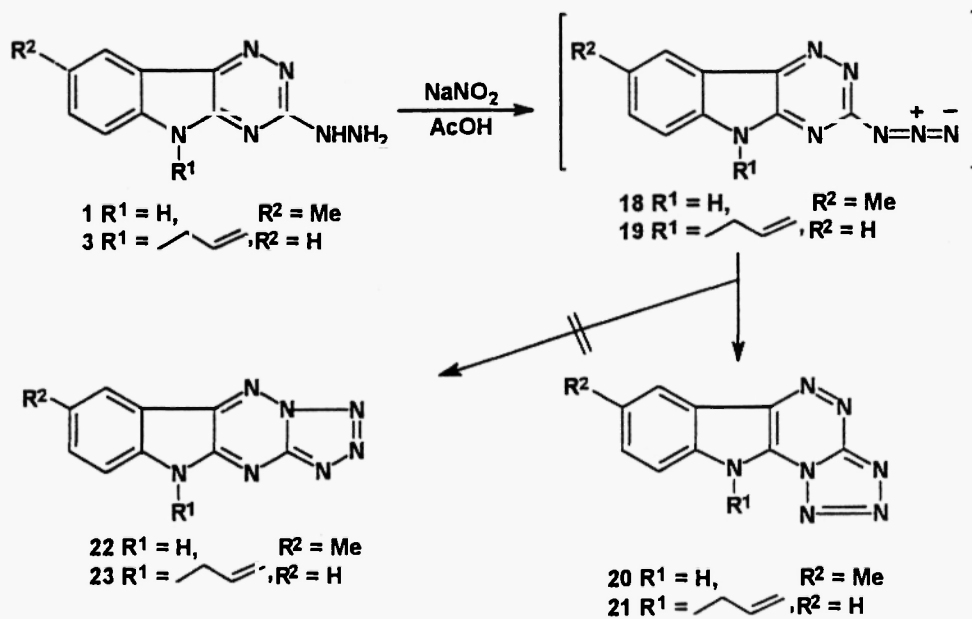
Reaction of **1** and **3** with carbon disulphide in pyridine gave **13** and **14**, respectively (scheme 2). The later can be obtained by fusion of **3** with thiourea. The products were assigned the angular structures as the 10 π -electron system of the indole ring is preserved in a similar manner to that reported [17] for its analogues.



SCHEME 1



SCHEME 2



SCHEME 3



Heating **3** with ethyl chloroformate in pyridine led to ethyl 2-(5-allyl-1,2,4-triazino[5,6-*b*]indol-3-yl)hydrazinocarboxylate (**15**). Fusion of **15** eliminates a molecule of ethanol to give **17**, which was also obtained by fusion of **3** with urea. Similarly, reaction of the hydrazine **1** with urea gave **16**.

Treatment of the hydrazines **1** and **3** with sodium nitrite in acetic acid gave the tetrazoles **20** and **21** through the 3-azido valence tautomers **18** and **19**, respectively (scheme 3). The structures of the isolated products were confirmed by IR spectroscopy which showed the absence of a band due to the azide group. However, this conclusion can only be stated for the solid products as the tetrazole-azide equilibrium for a series of condensed systems [18, 19] indicated that the most stable tetrazole form is present only in the solid state, whereas in solution an equilibrium is often detected with fractions of each form depending on the system, the solvent and the temperature. The products were assigned the angular structures **20** and **21** rather than the linear structures **22** and **23**, because the 10π -electron system of the indole ring is preserved in the former. This view has been supported by isotope labelling studies done by Messmer [20] on the benzo-1,2,4-triazines as well as by the molecular orbital calculations [21]. Reaction of **24** with chloroacetic acid in 20% KOH gave **25**, whose cyclization by heating with $\text{Ac}_2\text{O}/\text{Py}$ was failed.

The reaction of **24** with ethyl chloroformate afforded **26**, whose reaction with hydrazine hydrate did not give the corresponding hydrazide, but the product was found to be **3** (scheme 4). Methylation of the thiol **24** with MeI/NaOH gave **27**, whose reaction with ethanolamine in butanol afforded **28**. Cyclization of **28** by heating with PCl_5 gave the imidazotriazinoindole **29**.

Reaction of **1** with ethyl acetoacetate gave the hydrazone **30**. Heating of **30** in presence of acetic acid caused its cyclization to give **31**. On the other hand, the reaction of hydrazines **1** and **3** with acetyl acetone did not give the respective monohydrazones, but the products were found to be the cyclized ones **36** and **37**, and not the hydrazones **34** and **35**, or their enolic form (scheme 5). Reaction of the hydrazines **1** and **3** with ethyl cyanoacetate gave the pyrazolones **32** and **33**.

EXPERIMENTAL SECTION

7-Methyl-10*H*-1,2,4-triazolo [4',3':2,3][1,2,4] triazino [5,6-*b*] indole (6).

A solution of **1** (0.2 g, 1.0 mmol) in formic acid (20 ml) was boiled under reflux for 8 h. The yellow product was recrystallized from ethanol/ *N,N*-dimethylformamide (DMF) (0.13 g, 58% yield), mp > 300°C. IR (KBr): 1618 cm^{-1} ($\text{C}=\text{N}$ and $\text{C}=\text{C}$). Anal. Calcd. for $\text{C}_{11}\text{H}_8\text{N}_6$ (224.2): C 58.9 H 3.6 N 37.5. Found: C 58.8 H 3.7 N 37.1.

7-Bromo-10*H*-1,2,4-triazolo[4',3':2,3][1,2,4]triazino[5,6-*b*]indole (7).

It was prepared as above (0.23 g, 83% yield), mp > 300°C. IR (KBr): 1610 cm^{-1} ($\text{C}=\text{N}$ and $\text{C}=\text{C}$). Anal. Calcd. for $\text{C}_9\text{H}_5\text{N}_6\text{Br}$ (277.1): C 39.0 H 1.8 N 30.3. Found: C 38.7 H 2.0 N 30.1.

10-Allyl-1,2,4-triazolo[4',3':2,3][1,2,4]triazino[5,6-*b*]indole (8).

A solution of **3** (0.24 g, 1.0 mmol) in triethyl orthoformate (10 ml) was heated under reflux for 4 h. The product was filtered, recrystallized from ethanol as yellow crystals (0.2 g, 80% yield), mp 226-228°C. IR (KBr): 1607 cm^{-1} ($\text{C}=\text{N}$ and $\text{C}=\text{C}$). ^1H NMR (CDCl_3) δ = 4.93 (d, 2 H, $\text{N}-\text{CH}_2$) 5.28 (m, 2 H, $=\text{CH}_2$) 5.99 (m, 1H, $=\text{CH}$), 7.38 (t, 2H, Ar-H), 7.71 (t, 1H, Ar-H), 8.19 (d, 1H, Ar-H), and 9.08 (s, 1 H, CH). Anal. Calcd. for $\text{C}_{13}\text{H}_{10}\text{N}_6$ (250.3): C 62.4 H 4.0 N 33.6. Found: C 62.7 H 4.0 N 33.2.

7-Methyl-10*H*-1,2,4-triazolo[3',4':3,4][1,2,4]triazino[5,6-*b*]indol-1-thiol (13).

A solution of **1** (0.2 g, 1.0 mmol) in pyridine (10 ml) was heated with carbondisulphide (0.2 ml) for 5 h. The product was recrystallized from ethanol/DMF as red crystals (0.21 g, 82% yield), mp > 300°C. IR (KBr): 2838 (SH) and 1619 cm^{-1} ($\text{C}=\text{N}$ and $\text{C}=\text{C}$). Anal. Calcd. for $\text{C}_{11}\text{H}_8\text{N}_6\text{S}$ (256.3): C 51.5 H 3.1 N 32.8. Found: C 51.8 H 2.9 N 32.5.

10-Allyl-1, 2,4-triazolo[3', 4': 3,4][1,2,4]triazino[5,6-*b*]indol-1-thiole (14).

- (a) A solution of **3** was treated as above (0.20 g, 71% yield), mp 298-300°C. IR (KBr): 2933 (SH) and 1610 cm^{-1} (C=N and C=C). ^1H NMR (DMSO- d_6) δ = 4.86 (d, 2 H, N-CH₂), 5.26 (m, 2 H, =CH₂), 5.98 (m, 1H, CH), 7.41 (t, 1H, Ar-H), 7.56 (d, 1H, Ar-H), 7.78 (t, 1H, Ar-H), 8.21 (d, 1H, Ar-H) and 14.4 (brs, 1H, SH). Anal. Calcd. for C₁₃H₁₀N₆S(282.3): C 55.3 H 3.6 N 29.8. Found: C 55.1 H 3.5 N 29.5.
- (b) A mixture of **3** (0.24 g, 1.0 mmol) and thiourea (0.09 g, 1.2 mmol) was heated at 180-190°C in an oil bath for 1 h. The product (0.18 g, 64% yield), was found to be identical with the product from method (a).

Ethyl-2- (5-allyl-1, 2,4-triazino[5,6-*b*] indol-3-yl)hydrazinocarboxylate (15).

A mixture of **3** (0.24 g, 1.0 mmol), ethyl chloroformate (0.2 ml, 2.2 mmol) and pyridine (20 ml) was heated for 8 h. The product was recrystallized from ethanol as yellow needles (0.19 g, 61% yield), mp 194-196°C. IR (KBr): 3198, 3294 (NH), 1724 (NCO) and 1612 cm^{-1} (C=N and C=C). Anal. Calcd. for C₁₅H₁₆N₆O₂(312.3): C 57.7 H 5.2 N 26.9. Found: C 57.9 H 5.0 N 26.6.

7-Methyl-1,2-dihydro-10H-1,2,4-triazolo[3',4':3,4][1,2,4]triazino[5,6-*b*]indol-1-one (16).

A mixture of **1** (0.2 g, 1.0 mmol) and urea (0.07 ml, 1.2 mmol) was heated at 180-190°C in an oil bath for 1 h. The product was recrystallized from ethanol/DMF as red needles (0.14 g, 58% yield), mp > 300°C. IR (KBr): 3209, 3180 (NH), 1707 (NCO) and 1608 cm^{-1} (C=N and C=C). Anal. Calcd. for C₁₁H₈N₆O (240.2): C 55.0 H 3.4 N 35.0. Found: C 55.2 H 3.5 N 34.7.

10-Allyl-1,2-dihydro-1,2,4-triazolo[3',4':3,4][1,2,4]triazino[5,6-*b*]indol-1-one (17).

Compound **15** (0.3 g, 1.0 mmol) was heated at 180-190°C in an oil bath for 1 h. The melt was cooled and recrystallized from ethanol/DMF as red crystals (0.20 g, 75% yield), mp 324-326°C. IR (KBr): 3233 (NH), 1736 (NCO) and 1609 cm^{-1} (C=N and C=C). ^1H NMR (DMSO- d_6) δ = 4.76 (d, 2 H, N-CH₂), 5.25 (m, 2 H, =CH₂), 5.98 (m, 1H, =CH), 7.14 (t, 1H, Ar-H), 7.43 (d, 1H, Ar-H), 7.67 (t, 1H, Ar-H), 8.05 (d, 1H, Ar-H) and 12.0 (NH). Anal. Calcd. for C₁₃H₁₀N₆O(266.3): C 58.6 H 3.8 N 31.6. Found: C 58.6 H 3.9 N 31.5.

7-Methyl-10H-tetrazolo[5',1':3,4][1,2,4]triazino[5,6-*b*]indole (20).

To a solution of **1** (0.2 g, 1.0 mmol) in acetic acid (15 ml) was added sodium nitrite solution (0.09 g, 1.3 mmol) in water (5 ml) at 0-5°C during 30 min. The product was recrystallized from ethanol/DMF as yellow crystals (0.16 g, 71% yield), mp 266-268°C. IR (KBr): 3085 (NH) and 1617 cm^{-1} (C=N and C=C). Anal. Calcd. for C₁₀H₇N₇ (225.2): C 53.5 H 3.1 N 43.5. Found: C 53.6 H 3.3 N 43.7.

10-Allyl-tetrazolo[5',1':3,4][1,2,4]triazino[5,6-*b*]indole (21).

It was prepared as above (0.21 g, 84% yield), mp 220-222°C. IR (KBr): 1597 cm^{-1} (C=N and C=C). ^1H NMR (CDCl₃) δ = 4.90 (d, 2 H, N-CH₂), 5.25 (m, 2 H, =CH₂), 5.90 (m, 1H, =CH), 7.40 (t, 2H, Ar-H), 7.70 (t, 1H, Ar-H), and 8.25 (d, 1H, Ar-H). Anal. Calcd. for C₁₂H₉N₇ (251.2): C 57.4 H 3.6 N 39.0. Found: C 57.3 H 3.9 N 38.8.

5-Allyl-1,2,4-triazino[5,6-*b*]indol-3-thiolacetic acid (25).

A solution of **24** (0.24 g, 1.0 mmol) in 20% KOH (20 ml) was heated with chloroacetic acid (0.09 ml, 1.0 mmol) for 5 h, and neutralized with diluted HCl. The yellow product was recrystallized from ethanol (0.22 g, 73% yield), mp 244-246°C. IR (KBr): 2871 (OH), 1653 (CO) and 1623 cm^{-1} (C=N and C=C). ^1H NMR (CDCl₃) δ = 4.81 (d, 2 H, N-CH₂), 5.27 (m, 2H, =CH₂), 5.93 (m, 1H, =CH), 7.33 (m, 2H, Ar-H), 7.56 (t, 1H, Ar-H), 8.01 (d, 1H, Ar-H) and 11.87 (brs, 1H, COOH). Anal. Calcd. for C₁₄H₁₂N₄SO₂ (300.3): C 56.0 H 4.0 N 18.7. Found: C 56.0 H 4.3 N 19.0.

5-Allyl-3-thiocarbethoxy-1,2,4-triazino[5,6-*b*]indole (26).

A stirred solution of **24** (0.24 g, 1.0 mmol) in DMF (10 ml) was treated with sodium hydride (0.02 g, 1.0 mmol) and then ethyl chloroformate (0.1 ml, 1.1 mmol). The mixture was poured onto crushed ice. The yellow product was recrystallized from ethanol (0.26 g, 83% yield), mp 122-124°C. IR (KBr): 1738 (COOEt) and 1622 cm⁻¹ (C=N and C=C). ¹H NMR (CDCl₃) δ = 1.22 (t, 3 H, Me), 4.31 (q, 2H, CH₂), 4.93 (d, 2H, N-CH₂), 5.14 (m, 2H, =CH₂), 6.0 (m, 1H, =CH), 7.53 (d, 1H, Ar-H), 7.77 (m, 2H, Ar-H), and 8.4 (d, 1H, Ar-H). Anal. Calcd. for C₁₅H₁₄N₄SO₂ (314.4): C 57.3 H 4.5 N 17.8 %. Found: C 57.1 H 4.5 N 18.0.

5-Allyl-3-methylthio-1,2,4-triazino[5,6-*b*]indole (27).

Methyl iodide (0.7 ml, 11.0 mmol) was added during 2-5 min., to a stirred solution of **24** (2.42 g, 10.0 mmol) in sodium hydroxide solution (1N, 11.0 mmol). The mixture was stirred for a further 30 min., and the solid was recrystallized from ethanol as yellow crystals (2.15 g, 84% yield), mp 138-140°C. IR (KBr): 1619 cm⁻¹ (C=N and C=C). Anal. Calcd. for C₁₃H₁₂N₄S (256.3): C 60.9 H 4.7 N 21.9. Found: C 60.6 H 4.5 N 21.6.

5-Allyl-3-(hydroxyethylamino)-1,2,4-triazino[5,6-*b*]indole (28).

A solution of **27** (2.56 g, 10.0 mmol) in *n*-butanol (20 ml) was treated with ethanolamine (15 ml) and the mixture was heated for 8 h. The yellow product was recrystallized from ethanol (2.1 g, 78% yield), mp 204-206°C. IR (KBr): 3308 and 3229 (OH, NH) and 1608 cm⁻¹ (C=N and C=C). Anal. Calcd. for C₁₄H₁₅N₅O (269.3): C 62.4 H 5.6 N 26.0. Found: C 62.4 H 5.4 N 25.9.

10-Allyl-1,2-dihydro-imidazo[2',1':3,4][1,2,4]triazino[5,6-*b*]indole (29).

A mixture of **28** (0.27 g, 1.0 mmol) and phosphorus pentachloride (5 ml) was heated for 2 h. The mixture was diluted with water and neutralized with NaHCO₃ solution. The product was recrystallized from ethanol as red crystals (0.17 g, 68% yield), mp 184-186°C. IR (KBr): 1627 cm⁻¹ (C=N and C=C). ¹H NMR (CDCl₃) δ = 3.94 (t, 2 H, CH₂), 4.20 (t, 2 H, CH₂), 4.58 (d, 2H, N-CH₂), 5.20 (m, 2H, =CH₂), 5.87 (m, 1H, =CH), 7.10 (m, 2H, Ar-H), 7.34 (m, 1H, Ar-H), and 7.68 (d, 1H, Ar-H). Anal. Calcd. for C₁₄H₁₃N₅ (251.3): C 66.9 H 5.2 N 27.9. Found: C 66.5 H 5.0 N 27.6.

3-(Carbethoxymethylethylidenehydrazino)-7-methyl-5H-1,2,4-triazino[5,6-*b*]indole (30).

A solution of **1** (0.2 g, 1.0 mmol) in ethanol (25 ml) was treated with ethyl acetoacetate (0.14 ml, 1.1 mmol). The mixture was heated for 4 h. The product was recrystallized from ethanol/DMF as yellow crystals (0.15 g, 46% yield), mp 154-156°C. IR (KBr): 3278 (NH), 1734 (COOEt) and 1609 cm⁻¹ (C=N and C=C). Anal. Calcd. for C₁₆H₁₈N₆O₂ (326.4): C 58.9 H 5.6 N 25.7. Found: C 59.0 H 5.4 N 25.9.

3-(3-Methyl-5-oxo-4,5-dihydropyrazol-1-yl)-7-methyl-5H-1,2,4-triazino[5,6-*b*]indole (31).

A solution of **30** (0.33 g, 1.0 mmol) in glacial acetic acid (25 ml) was heated under reflux for 10 h. The mixture was poured onto crushed ice. The product was recrystallized from ethanol/DMF as orange crystals (0.23 g, 82% yield), mp 312-315°C. IR (KBr): 1652 (NCO) and 1613 cm⁻¹ (C=N and C=C). Anal. Calcd. for C₁₄H₁₂N₆O (280.3): C 60.0 H 4.3 N 30.0 %. Found: C 59.8 H 4.1 N 30.3.

3-(5-Amino-3-oxo-2,3-dihydropyrazol-1-yl)-7-methyl-5H-1,2,4-triazino[5,6-*b*]indole (32).

A mixture of **1** (0.2 g, 1.0 mmol), ethyl cyanoacetate (0.11 ml, 1.0 mmol) and DMF (10 ml) was heated for 5 h. The product was recrystallized from ethanol/DMF as orange crystals (0.15 g, 56% yield), mp

> 300°C. IR (KBr): 3250 (NH, NH₂), 1679 (NCO) and 1617 cm⁻¹ (C=N and C=C). Anal. Calcd. for C₁₃H₁₁N₆O (267.3): C 58.4 H 4.1 N 31.4. Found: C 58.0 H 3.9 N 31.3.

5-Allyl-3-(5-amino-3-oxo-2,3-dihydropyrazol-1-yl)-1,2,4-triazino[5,6-b]indole (33).

It was prepared as above (0.17 g, 58% yield), mp 290-292°C. IR (KBr): 3365 and 3251 (NH, NH₂), 1728 (NCO) and 1615 cm⁻¹ (C=N and C=C). ¹H NMR (DMSO-*d*₆) δ = 3.4 (brs, 2 H, NH₂), 4.3 (s, 1 H, CH), 5.1 (d, 2H, N-CH₂), 5.3 (m, 2H, =CH₂), 6.0 (m, 1H, =CH), 7.5 (m, 1H, Ar-H), 7.7 (m, 2H, Ar-H), 8.3 (d, 1H, Ar-H) and 8.69 (s, 1H, NH). Anal. Calcd. for C₁₅H₁₃N₆O (293.3): C 61.4 H 4.5 N 28.6. Found: C 61.2 H 4.2 N 28.3.

3-(3,5-Dimethylpyrazol-1-yl)-7-methyl-5H-1,2,4-triazino[5,6-b]indole (36).

A solution of **1** (0.2 g, 1.0 mmol) in ethanol (25 ml) was treated with acetylacetone (0.1 ml, 1.0 mmol) and few drops of glacial acetic acid. The mixture was heated for 2 h. The product was recrystallized from ethanol as pale yellow crystals (0.19 g, 68% yield), mp 305-307°C. IR (KBr): 1624 cm⁻¹ (C=N and C=C). Anal. Calcd. for C₁₅H₁₄N₆ (278.3): C 64.7 H 5.1 N 30.2. Found: C 65.0 H 4.8 N 30.4.

5-Allyl-3-(3,5-dimethylpyrazol-1-yl)-1,2,4-triazino[5,6-b]indole (37).

It was prepared as above (0.21 g, 69% yield), mp 160-162°C. IR (KBr): 1596 cm⁻¹ (C=N and C=C). ¹H NMR (CDCl₃) δ = 2.77 and 2.99 (2s, 6 H, 2 Me), 5.1 (d, 2 H, N-CH₂), 5.28 (m, 2H, =CH₂), 5.97 (m, 1H, =CH), 6.13 (s, 1 H, pyrazolyl-H), 7.49 (m, 2H, Ar-H), 7.7 (t, 1H, Ar-H) and 8.50 (d, 1H, Ar-H). Anal. Calcd. for C₁₇H₁₆N₆ (304.3): C 67.1 H 5.3 N 27.6. Found: C 67.3 H 5.6 N 27.8.

REFERENCES

- [1] E. S. H. El Ashry, N. Rashed, M. Taha, E. Ramadan, *Adv. Heterocycl. Chem.*, **59**, 39 (1994).
- [2] E. S. H. El Ashry, N. Rashed, M. Taha, E. Ramadan, *Adv. Heterocycl. Chem.*, **61**, 207 (1994).
- [3] Allen, Hanburys Ltd., Neth. Pat., 6,410,823 (1965); C.A. **63**, 13295 (1965).
- [4] J. M. Z. Gladych, J. H. Hunt, South African Pat., 6,804,428 (1968); C.A. **71**, 81436 (1969).
- [5] S. Kline, French Lab., Brit. Pat., 1,170,560 (1969); C.A. **72**, 55513 (1970).
- [6] A. W. J. Chow, Ger. Pat., 2,119,375 (1971); C.A. **76**, 25315 (1972).
- [7] J. M. Z. Gladych, R. Hornby, J. H. Hunt, D. Jack, J. J. Boyle, R. J. Ferlauto, R. F. Haff, C. G. Kormendy, F. J. Stanfield, R. C. Stewart, *J. Med. Chem.*, **15**, 277 (1972).
- [8] A. M. M. E. Omar, N. H. Eshba, H. M. Abou Shleib, *J. Heterocycl. Chem.*, **23**, 1731 (1986).
- [9] Allen, Hanburys Ltd., Neth. Pat., 6,410,715 (1965); C.A. **63**, 13294 (1965).
- [10] M. A. El Saadani, B. A. B. El Gamal, G. I. El Koholy, M. M. El Sayed, E. S. H. El Ashry, *J. Med. Res. Inst.*, **14**, 293 (1993).
- [11] B. A. B. El Gamal, M. A. El Saadani, E.K. A. El Sayed, M. M. El Sayed, E. S. H. El Ashry, *J. Med. Res. Inst.*, **15**, 119 (1994).
- [12] A. Mousaad, N. Rashed, E. Ramadan, E. S. H. El Ashry, *Spectroscopy Lett.*, **27**, 677 (1994).
- [13] N. Rashed, A. El Nemr, E. S. H. El Ashry, *Spectroscopy Lett.*, **26**, 1817 (1993).
- [14] A. Mousaad, H. Abdel Hamid, A. El Nemr, E. S. H. El Ashry, *Bull. Chem. Soc. Jpn.*, **65**, 546 (1992).
- [15] E. S. H. El Ashry, N. Rashed, H. Abdel Hamid, E. Ramadan, *Z. Naturforsch.*, **52b**, 873 (1997).
- [16] N. Rashed, H. Abdel Hamid, E. Ramadan, E. S. H. El Ashry, *Nucelosides Nucelotides* **17**, 373 (1998).
- [17] M. I. Younes, A. A. M. Abdel Alim, H. H. Abbas, S. A. Metwally, *Arch. Pharm.*, **320**, 1196 (1987).
- [18] Gy. Hajos, A. Messmer, *J. Heterocycl. Chem.*, **13**, 881 (1976).
- [19] G. A. Reynolds, J. A. von Allen, J. P. Tinker, *J. Org. Chem.*, **43**, 1209 (1978).
- [20] A. Messmer, G. Hajos, J. Tamas, A. Neszmelyi, *J. Org. Chem.*, **44**, 1823 (1979).
- [21] A. N. Asaad, E. S. H. El Ashry, *Z. Naturforsch.*, **51a**, 1012 (1996).

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