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SYNTHESIS OF IMIDAZO[4,5-*C*] AND TRIAZEPINO[6,5-*C*]CINNOLINES

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ABSTRACT

Hofmann degradation of 4-amino-8-methylcinnoline-3-carboxamide (**1**) gave 3,4-diaminocinnoline **2** which was employed to prepare imidazo and 2-substitutedimidazo[4,5-*c*]cinnolines **3**. On the other hand, reaction of 4-aminocinnoline-3-carboxylic acid hydrazides **4** with ethyl chloroformate or potassium O-ethyl dithiocarbonate afforded 2,3,4,5-tetrahydro-1*H*-1,2,4-triazepino[6,5-*c*]cinnoline-2,5-diones **6** and the corresponding 2-thiones **7**, respectively. Furthermore, reacting **4** with excess orthoesters gave mixtures of 4,5-dihydro-1*H*-1,2,4-triazepino[6,5-*c*]cinnolin-5-ones **9** and 3-(ethoxyalkylidenamino)pyrimido[5,4-*c*] cinnoline-4-ones **10** which were separated and characterized.

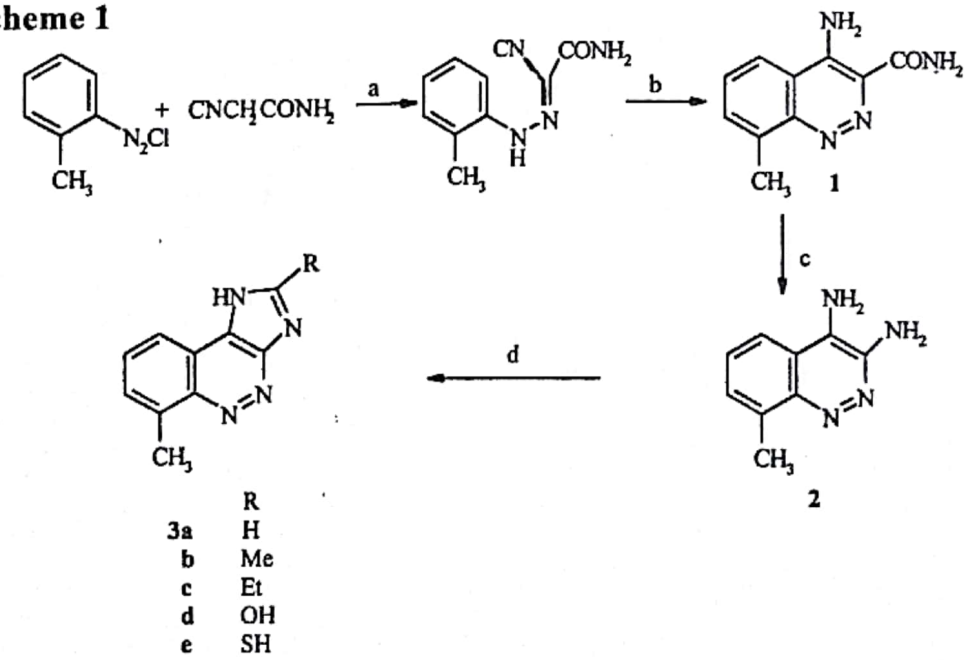
INTRODUCTION

Increasing interest in 5, 6 and 7-membered fused hetarylcinnolines as possible therapeutic agents has been reported.[1-3] No precedent publication, however, described the synthesis of imidazo[4,5-*c*]cinnoline ring system. In addition, The only reported 1,2,4-triazepino[6,5-*c*]cinnoline was obtained by Stanczak et al in 1998 by reacting 4-aminocinnoline-3-carboxylic acid hydrazide with cynogen bromide and was reported as a potential anxiolytic agent [3]. This report describes the synthesis of imidazo[4,5– *c*]cinnolines 3 and 1,2,4 – triazepino [6,5- *c*] cinnolines 6, 7 and 9.

Chemistry

3,4-Diaminocinnoline has already been prepared starting from 2-aminobenzaldehyde in a tedious multistep sequence in 21% overall yield.[4] Herein, it was speculated that Hofmann degradation might be a short and efficient route for preparation of the novel key compound 3,4-diamino-8-methylcinnoline (2) from 4-amino-8-methylcinnoline-3-carboxamide[1,5] (**1**) in a unique one-step synthesis (Scheme 1). Attempts to prepare the respective diamine **2** using bromine/aqueous sodium hydroxide failed whereas the use of aqueous potassium hydroxide (6 folds) while heating the reaction mixture at 75 °C for 5 hours afforded **2** as a minor product alongside imidazo[4,5-*c*]cinnolin-2-one **3d** which was identified by its spectral data and was subsequently synthesized from the diamine.

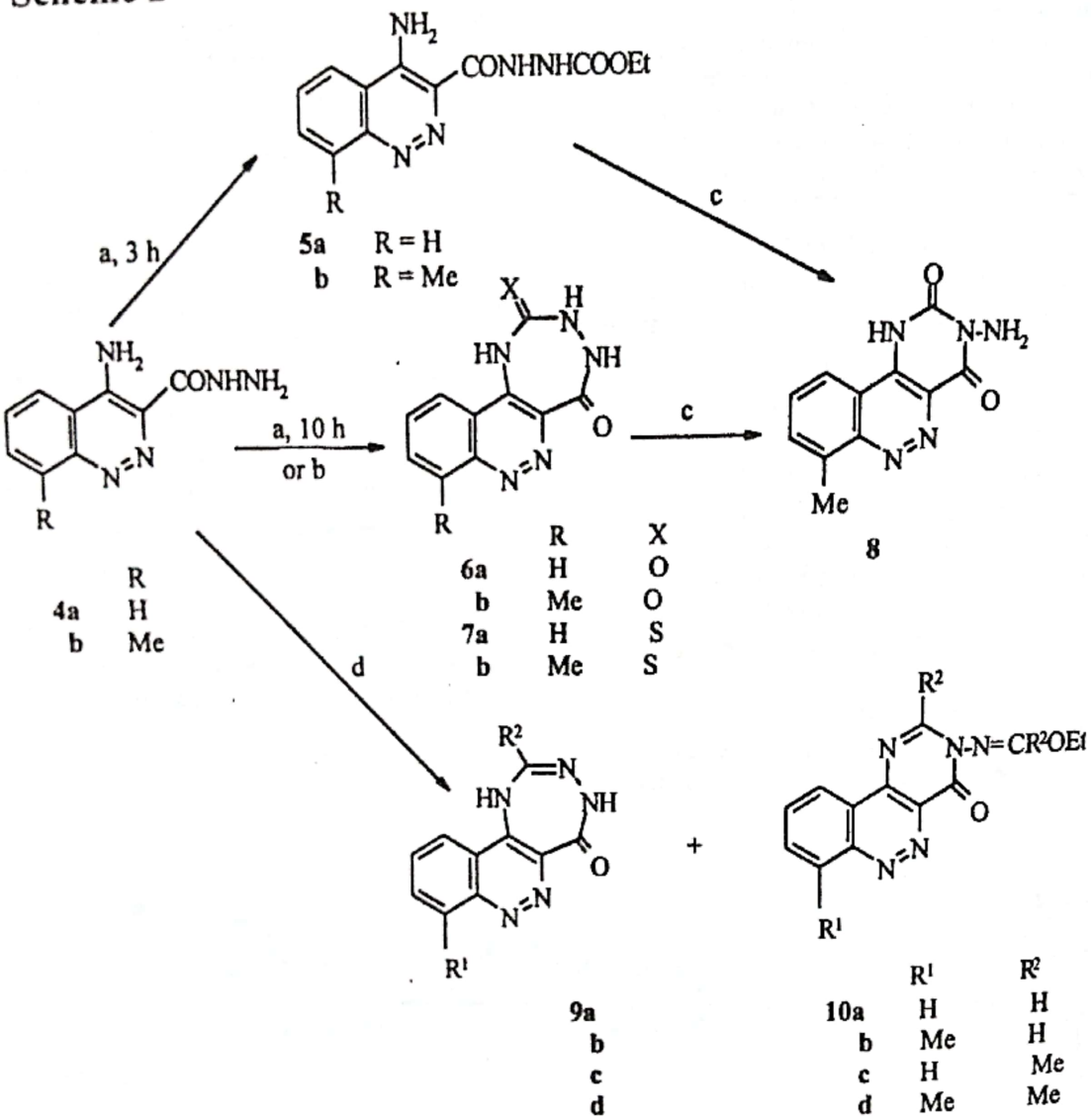
Scheme 1



	R
3a	H
b	Me
c	Et
d	OH
e	SH

(a) AcONa; (b) $AlCl_3$, PhCl ; (c) Br_2 , KOH, MeOH; (d) RC $(OEt)_3$, Na_2CO_3 for **3a-c** , or Ac_2O, Na_2CO_3 for **3b** ; $ClCO_2Et$, pyridine for **3d**; CS_2 , EtOH, KOH for **3e**

Scheme 2



(a) $ClCO_2Et$, pyridine, DMF; (b) CS_2, EtOH, KOH; (c) tetralin, reflux ; (d) $R^2C(OEt)_3$, Na_2CO_3, DMF.

Although it was possible to hydrolyze **3d** to the diamine **2**, the overall yield was only 20 %. Nevertheless, when the reaction solvent was altered from water to methanol, 3,4-diamino-8-methylcinnoline (**2**) was obtained in good yield. The formation of **3d** during the Hofmann degradation of **1** was probably due to nucleophilic addition of the neighboring 4-NH_2 group on the isocyanate intermediate which forms during the reaction. It is likely that in methanolic KOH, MeO attack on this intermediate and subsequent hydrolysis of the formed urethane to **2** was faster than the formation of **3d**.

The reaction of diaminocinnoline **2** and the appropriate reagent (Scheme 1) in acetonitrile or in absolute ethanol for ascending periods failed to afford the respective imidazo compounds. Likewise, no reaction occurred when **2** was refluxed in excess of the used orthoester. Only when DMF was used as a solvent that the reaction proceeded to give imidazocinnolines **3** in 40-60 % yield. Prolonged heating was essential and further reflected the weak nucleophilicity of the diamine. In an alternative route for the synthesis of 2-methylimidazo derivative **3b**, diamine **2** was reacted with acetic anhydride and the isolated monoacetylated product was then refluxed in DMF/Na_2CO_3 to affect cyclization.

The synthesis of triazepinocinnolines **6**, **7** and **9** were carried out as outlined in Scheme 2. Reacting 4-aminocinnoline-3-carboxyhydrazides[3] **4** with ethyl chloroformate in refluxing DMF for 3 hours afforded the ethoxycarbonyl derivatives **5** as the major isolated products. However, when heating was continued for 10 hours, triazepinocinnoline-2,5-diones **6** were obtained in 50-60 % yield. The 2-thione derivatives **7**, on the other hand, were prepared by reacting **4** with potassium O-ethyl dithiocarbonate for 24 hours.

Reported studies on 3,4-dihydro-1*H*-1,3,4-benzotriazepine-2,5-diones indicated that this ring system tends to undergo thermal or base-promoted rearrangement to the thermodynamically more stable 3-amino-2,4(1*H*,3*H*)-quinazolinediones[6-8]. In the present investigation, it was also found that refluxing triazepinocinnoline **6b** in tetralin (bp 207 °C) affected ring contraction to 3-aminopyrimido[5,4-*c*]cinnoline-2,4-dione **8**. Furthermore, pyrimidocinnoline **8** was the exclusive product when **5b** was heated in tetralin.

The transformation of 1,2,4-triazepinocinnoline to 3-aminopyrimidocinnoline was further demonstrated upon reacting hydrazides **4** with excess triethyl orthoformate or triethyl orthoacetate in DMF for 10 hours. Under these conditions, the reaction afforded a mixture of dihydrotriazepinocinnolin-5-ones **9** (25% yield) and 3-(ethoxymethylidene or ethylideneamino) pyrimidocinnolines **10** (40% yield) which were readily separated and characterized. Based on reported studies[9,10] on the reaction of 2-aminobenzoyl hydrazides with orthoesters, it is propable that the reaction of **4** proceeded via initial nucleophilic attack by the β-nitrogen atom of the hydrazide function on the orthoester with subsequent ring closure by the 4-amino group to give the kinetically- controlled triazepino products **9**. Ring contraction of **9** afforded 3-aminopyrimido derivatives which in presence of excess orthoester gave iminoethers **10**. The use of excess orthoesters in this reaction, in addition to the aprotic and polar nature of the reaction solvent (DMF) probably ceased the formation of 4-amino-3-oxadiazolylcinnoline as an expected additional product of the reaction between *o*-aminohydrazides and orthoesters.[10]

EXPERIMENTAL

Mp (uncorrected): Griffin or Stuart Scientific apparatus. IR: Shimadzu-IR 435. ^{1}H NMR: Jeol FXQ-90, Jeol EX-270 or Varian-200, using tetramethylsilane as an internal standard. EIMS: Hewlett Packard 5988 or Finnigan SSQ 7000. TLC: UV-Fluorescent plastic-backed sheets with silica (Merck 60 F254); solvent system: PhH: MeOH: $CHCl_3$: triethylamine (9 : 3 : 1.5 : 0.1). Elemental analyses were carried out at the Microanalytical Center, Cairo University, Cairo, Egypt.

The following compounds were prepared according to literature methods: 4-Aminocinnoline-3-carboxamide[1,5] (1); 4-amino-8-methyl- cinnoline-3-carboxamide[1,11], 4-aminocinnoline-3-carboxylic acid[1],4-amino-8-methylcinnoline-3-carboxylic acid[cf 1] [mp 287-289 °C (water); yield 80 % ; IR (KBr) 3450, 3300, 3100-2700, 1680 cm^{-1}. Anal calcd for $C_{10}H_9N_3O_2$ (203.2): C, 59.11; H, 4.46; N, 20.67. Found: C, 58.8; H, 4.1; N, 20.8], ethyl 4-aminocinnoline-3-carboxylate[12] and ethyl 4-amino-8-methylcinnoline-3-carboxylate[cf 12] [mp 220-223 °C (benzene); IR (KBr) 3400, 3300, 3180, 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.2-6.8 (m, 5H, ArH + D_2O exchangeable NH_2), 4.53 (q, 2H, CH_2), 2.97 (s, 3H, 8-CH_3), 1.49 (t, 3H, CH_3) ppm. Anal calcd for $C_{12}H_{13}N_3O_2$ (231.2): C, 62.32; H, 5.66; N, 18.17. Found: C, 62.5; H, 5.5; N, 17.9]. Potassium O-ethyl dithiocarbonate[13] was prepared and used in situe.

3,4-Diamino-8-methylcinnoline (2).

To a well stirred ice-cold solution of KOH (5 g, 0.09 mol) in MeOH (50 ml), bromine (1 ml, 0.02 mol) and finely powdered **1** (3 g, 0.015 mol) were added sequentially. The mixture was refluxed for 12 h, cooled, filtered and the solid was crystallized from ethanol to give 2.1 g (81%) of **2**: mp 280-282 °C; R_f 0.43; IR (KBr) 3450; 3330, 3250, 3180 (NH_2), 1650, 1615 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 9.8-7.2 (m, 7H, ArH + D_2O exchangeable NH_2), 2.86 (s, 3H, 8-CH_3) ppm; EIMS *m/z* 174 $(M)^+$ (2.0%), 157 $(M\text{-}NH_3)^+$ (55%), 142 $(M\text{-}N_2H_4)^+$ (15.8%), 129 $(M\text{-}NH_3, N_2)^+$ (61.0%), 102 $(M\text{-}NH_3, N_2, HCN)^+$ (89%), 69 (100%). Anal calcd for $C_9H_{10}N_4$ (174.2): C, 62.05; H, 5.78; N, 32.16. Found: C, 61.8; H, 6.0; N, 32.3.

6-Methylimidazo[4,5-*c*]cinnoline(3a), 2,6-Dimethylimidazo[4,5-*c*]cinnoline (3b; method A) and 2-Ethyl-6-methylimidazo[4,5-*c*]cinnoline (3c).

A mixture of 2 (0.005 mol) and the appropriate orthoester (0.05 mol) was refluxed in dry DMF (25 ml) for 20 h. The reaction mixture was filtered while hot, filtered while hot, concentrated filtered and the solid was purified by crystallization to give 60% of 3a-c.

3a: mp > 300 °C (acetone); R_f 0.30; IR (KBr) 3400 (NH), 1590, 1570, 1500 cm^{-1}; EIMS *m/z* 185 $(M+1)^+$ (5.8 %), 157 $(M-HCN)^+$ (4.2 %), 129 $(M-HCN, N_2)^+$ (16.1%), 69 $(C_3H_3N_2)^+$ (100 %). Anal calcd for $C_{10}H_8N_4$ (184.2): C, 65.20; H, 4.37; N, 30.41. Found: C, 65.4; H, 4.0; N, 30.6.

3b: mp > 300 °C (DMF); R_f 0.34; IR (KBr) 3400 (NH), 2920 (CH), 1590, 1570, 1510 cm^{-1}; ^1H NMR (DMSO-d_6) δ 8.56 (m, 1H, C-9 H), 7.72 (m, 2H, ArH), 2.95 (s, 3H, 6-CH_3), 2.42 (s, 3H, 2-CH_3) ppm; EIMS *m/z* 197 $(M-1)^+$ (3.8 %), 149 (100 %), 111 (42.4 %), 97 (69.4 %), 83 (71.2 %), 69 (84.5 %). Anal calcd for $C_{11}H_{10}N_4$ (198.2): C, 66.65; H, 5.08; N, 28.26. Found : C, 66.5; H, 4.8; N, 28.7.

3c: mp > 300 °C (EtOH); R_f 0.35; IR (KBr) 3500 (NH), 2980, 2920 (CH), 1600, 1570, 1510 cm^{-1}; ^1H NMR DMSO-d_6) δ 8.57 (d, 1H, ArH), 7.85-7.65 (m, 2H, ArH), 2.93 (s, 3H, 6-CH_3), 2.66 (q, 2H, CH_2), 1.26 (t, 3H, CH_3) ppm. Anal calcd for $C_{12}H_{12}N_4$ (212.2): C, 67.90; H, 5.69; N, 26.39. Found: C, 68.0; H, 5.9; N, 26.0.

2,6-Dimethylimidazo [4,5-*c*] cinnoline (3b; method B).

A mixture of 2 (0.87 g, 0.005 mol) and acetic anhydride (20 ml, 0.21 mol) was refluxed for 2 h. The mixture was cooled, filtered and the solid was crystallized from ethanol to give 0.63 g (59 %) of the monoacetylated product: mp 295-297 °C; R_f 0.32; IR (KBr) 3420, 3400, 3300, 1690 cm^{-1}; Anal calcd for $C_{11}H_{12}N_4O$ (216.2): C, 61.09; H, 5.59; N, 25.91. Found: C, 60.8; H, 5.8; N, 25.6. A mixture of this product (0.22 g, 0.001 mol), anhydrous Na_2CO_3 (0.52 g, 0.005 mol) and dry DMF (15 ml) was refluxed with stirring for 4 h. The mixture was filtered while hot, and the filtrate was concentrated, cooled, filtered and the solid was crystallized from DMF to give 0.1 g (50 %) of 3b.

6-Methyl-2,3-dihydro-1*H*-imidazo [4,5-*c*] cinnolin-2-one (3d).

A mixture of 2 (0.87 g, 0.005 mol), $ClCO_2Et$ (1ml, 0.01 mol), pyridine (3 ml, 0.037 mol) and dry DMF (20 ml) was heated to reflux for 20 h. The mixture was concentrated, cooled, filtered and the precipitate was crystallized from DMF to give 0.44 g (45%) of 3d: mp > 300 °C; R_f 0.29; IR (KBr) 3400-3180 (NH, OH), 1710 (C=O), 1610 cm^{-1}; EIMS *m/z* 200 (45.5%) $(M)^+$, 69 (100%).

6-Methyl-2,3-dihydro-1*H*-imidazo [4,5-*c*] cinnoline-2-thione (3e).

A mixture of KOH (0.6 g, 0.01 mol), CS_2 (2 ml, 0.033 mol), water (5 ml) and ethanol (60 ml) was refluxed for 1 h then evaporated to dryness. To the residue was added a solution of 2 (0.87 g, 0.005 mol) in dry DMF (30 ml) and the mixture was refluxed for 24 h. The mixture was evaporated to dryness under reduced pressure and the residue was dissolved in the least amount of water with warming. The solution was cooled, acidified to litmus with AcOH and the mixture was set aside in the refrigerator for overnight. The separated solid was filtered, washed with cold water, dried and crystallized from MeCN to give 0.42 g of 3e (40%): mp > 300 °C; R_f 0.12; IR (KBr) 3400, 3200, 2700 (NH, SH), 1640, 1590 cm^{-1}; ^1H NMR (DMSO-d_6) δ 13.12 (s, 2H, NH, SH), 8.71 (d, 1H, ArH), 7.89 (m, 2H, ArH), 2.94 (s, 3H, CH_3) ppm.

Anal calcd for $C_{10}H_8N_4S$ (216.2): C, 55.53; H, 3.72; S, 14.82. Found: C, 55.7; H, 3.8; S, 14.6.

4-Aminocinnoline-3-carboxylic acid hydrazide (4a) and 4-Amino-8-methylcinnoline-3 carboxylic acid hydrazide (4b).

Compounds 4 were prepared by modification of reported [9] procedures for 4a; Hydrazine hydrate (99 %, 0.06 mol) was added to a solution of the corresponding aminocinnoline carboxylic acid ethyl ester[12] (0.01 mol) in absolute EtOH (30 ml) and the mixture was refluxed for 5 h. The mixture was cooled, filtered and the solid was dried and purified by crystallization.

4a: yield 75 % (reported [9] 65 %); mp > 300 °C (DMF) (reported [9] mp > 320 °C; DMF); IR (KBr) 3350, 3330, 3100, 1630 cm^{-1}.

4b: yield 78 %; mp 285-288 °C (DMF); IR (KBr) 3400, 3350, 3320, 1650-1630 cm^{-1}; ^1H NMR (DMSO-d_6) δ 10.13 (s, 1H, NH, D_2O exchangeable), 9.0-7.5 (br, 4-NH_2, D_2O exchangeable), 8.22 (d, 1H, ArH), 7.71-7.60 (m, 2H, ArH), 4.58 (s, 2H, NH_2, D_2O exchangeable), 2.82 (s, 3H, CH_3) ppm. Anal calcd for $C_{10}H_{11}N_5O$ (217.2): C, 55.29; H, 5.10; N, 32.23. Found: C, 55.6; H, 5.1; N, 32.5.

4-Amino-3-ethoxycarbonylhydrazinocarbonyl-cinnoline (5a) and 4-Amino-3-ethoxycarbonyl-hydrazinocarbonyl-8-methylcinnoline (5b).

A mixture of carboxylic acid hydrazide 4a or 4b (0.01 mol), $ClCO_2Et$ (1.4 ml, 0.015 mol), pyridine (3 ml, 0.037 mol) and dry DMF (20 ml) was refluxed for 3 h. The mixture was filtered while hot and the filtrate was concentrated and cooled. The separated solid was filtered, washed with cold water, dried and purified by crystallization.

5a: yield 63 %; mp 238-240 °C (benzene); IR (KBr) 3400, 3300, 3250, 1730, 1715, 1660, 1615 cm^{-1}; ^1H NMR (DMSO-d_6) δ 10.76 (s, 1H, NH, D_2O exchangeable), 9.18 (s, 1H, NH, D_2O exchangeable), 8.8 (br, 2H, NH_2, D_2O exchangeable), 8.52 (d, 1H, ArH), 8.25 (d, 1H, ArH), 7.93 (t, 1H, ArH), 7.77 (t, 1H, ArH), 4.10 (q, 2H, CH_2), 1.23 (t, 3H, CH_3) ppm.

Anal calcd for $C_{12}H_{13}N_5O_3$ (275.2): C, 52.36; H, 4.76; N, 25.44. Found: C, 52.5; H, 4.4; N, 25.7.

5b: yield 60%; mp 225-227 °C (benzene); IR (KBr) 3400-3800, 1720-1640 cm^{-1}; ^1H NMR (DMSO-d_6) δ

10.72 (s, 1H, NH, D_2O exchangeable), 9.18 (s, 1H, NH, D_2O exchangeable), 8.8 (br, 2H, NH_2, D_2O exchangeable), 8.27 (d, 1H, ArH), 7.8-7.6 (m, 2H, ArH), 4.11 (q, 2H, CH_2), 2.85 (s, 3H, 8-CH_3), 1.24 (t, 3H, CH_3) ppm; EIMS *m/z* 289 $(M)^+$ (100%), 186 $(M-NHNHCOOEt)^+$ (64.9%). Anal calcd for $C_{13}H_{15}N_5O_3$ (289.2): C, 53.97; H, 5.22; N, 24.20. Found: C, 53.8; H, 5.4; N, 24.3.

2,3,4,5-Tetrahydro-1*H*-1,2,4-triazepino[6,5-*c*]cinnoline-2,5-dione (6a) and 8-Methyl-2,3-4,5-tetrahydro-1*H*-1,2,4-triazepino[6,5-*c*]cinnoline-2,5-dione (6b).

These compounds were prepared from 4a,b using the previous procedures for 5a,b except that the reflux time was continued for 10 h.

6a: yield 50 %; mp > 300 °C (EtOH / benzene); R_f 0.38; IR (KBr) 3550-2700, 1680-1660, 1590 cm^{-1}. Anal calcd for $C_{10}H_7N_5O_2$ (229.2): C, 52.40; H, 3.07; N, 30.55. Found : C, 52.7; H, 3.4; N, 30.2.

6b: yield 59 %; mp > 300°C (acetone); R_f 0.45; IR (KBr) 3400, 3150, 1670-1655 cm^{-1}; ^1H NMR (DMSO-d_6) δ 13.61 (s, 1H, NH, D_2O exchangeable), 11.94 (s, 1H, NH, D_2O exchangeable), 7.89 (d, 1H, ArH), 7.75 (br s, NH, D_2O exchangeable), 7.49 (m, 2H, ArH), 2.59 (s, 3H, CH_3) ppm; EIMS *m/z* 244 $(M+1)^+$ (5.7 %), 243 $(M)^+$ (4 %), 213 $(M-N_2H_2)^+$ (1%), 186 $(M-CHN_2O)^+$ (100 %). Anal calcd for $C_{11}H_9N_5O_2$ (243.2): C, 54.32; H, 3.72; N, 28.79. Found: C, 54.0; H, 4.0; N, 28.4.

2-Mercapto-4,5-dihydro-1*H*-1,2,4-triazepino[6,5-*c*]cinnolin-5-one (7a) and 2-Mercapto-8-methyl-4,5-dihydro-1*H*-1,2,4-triazepino[6,5-*c*]cinnolin-5-one (7b).

A mixture of KOH (0.6 g, 0.01 mol), CS_2 (2 ml, 0.033 mol), water (5 ml) and ethanol (60 ml) was refluxed for 1 h. Hydrazide 4a or 4b (0.01 mol) was then added and reflux was continued for a further 15 h. The reaction mixture was evaporated to dryness and the residue was dissolved in the least amount of water with warming. The solution was acidified to litmus with HCl and set aside in the refrigerator overnight. The separated solid was filtered, washed with cold water, dried and crystallized from ethanol to give 7a,b in 65 % yield.

7a: mp > 300 °C; R_f 0.08; IR (KBr) 3400-2300, 1640 cm^{-1}. Anal calcd for $C_{10}H_7N_5OS$ (245.2): C, 48.97; H, 2.87; S,13.07. Found: C, 48.6; H, 2.7; S, 13.2.

7b: mp > 300 °C; R_f 0.19; IR (KBr) 3300-2300, 1640 cm^{-1}; ^1H NMR (DMSO-d_6) δ 8.33 (d, 1H, ArH), 8.1 (br, 2H, D_2O- exchangeable), 7.72 (m, 2H, ArH), 2.84 (s, 3H, CH_3) ppm; EIMS *m/z* 257 $(M-2)^+$ (5.6 %), 185 $(M-CH_2N_2S)^+$ (8.1 %), 149 (20.3 %). 111 (33.0 %), 69 (100 %). Anal calcd for $C_{11}H_9N_5OS$ (259.2): C, 50.95; H, 3.49; S, 12.36. Found : C, 51.1; H, 3.5; S, 12.3.

3-Amino-7-methylpyrimido[5,4-*c*]cinnoline-2,4-dione (8).

A mixture of 6b or 5b (0.001 mol) and tetralin (15 ml) was refluxed for 5 h. The reaction mixture was cooled, filtered and the precipitate was crystallized from DMF to give 8 (55-60 % yield): mp 285-287 °C; R_f 0.40; IR (KBr) 3400, 3300, 3200, 1680-1660 cm^{-1}. ^1H NMR (DMSO-d_6) δ 8.27 (d, 1H, ArH), 7.8 (br, 2H, NH_2, D_2O-exchangeable), 7.67 (m, 2H, ArH), 4.1 (br s, NH, D_2O-exchangeable), 2.84 (s, 3H, CH_3) ppm; EIMS *m/z* 243 $(M)^+$ (100 %). Anal calcd for $C_{11}H_9N_5O_2$ (243.2): C, 54.32; H, 3.72; N, 28.79. Found: C, 54.7; H, 3.9; N, 28.5

4,5-Dihydro-1*H*-1,2,4-triazepino[6,5-*c*]cinnolin-5-ones (9a-d) and 3-(Ethoxyalkylideneamino) pyrimido[5,4-*c*]cinnolin-4-ones (10a-d).

A mixture of carboxylic acid hydrazide 4a or 4b (0.01 mol), anhydrous Na_2CO_3 (0.42 g, 0.004 mol) and either triethyl orthoformate or triethyl orthoacetate (0.06 mol) in dry DMF (15 ml) was refluxed for 10 h. The mixture was filtered while hot and the filtrate was evaporated under reduced pressure. The residue was repeatedly boiled with $CHCl_3$ and filtered. The solid was dried and crystallized from ethanol to give triazepinocinnolines 9a-d (25%). The filtrate was dried (anhydrous Na_2SO_4), evaporated and the residue was crystallized from benzene to give pyrimidocinnolines 10a-d (40%).

9a: mp > 300 °C; R_f 0.30; IR (KBr) 3400, 3300, 3150, 1645, 1615-1600 cm^{-1}. Anal calcd for $C_{10}H_7N_5O$ (213.1): C, 56.33; H, 3.30; N, 32.84. Found: C, 56.5; H, 3.6; N, 32.9.

9b: mp > 300 °C; R_f 0.34; IR (KBr) 3400, 3300, 3200, 3150, 1640, 1560 cm^{-1}; ^1H NMR (DMSO-d_6) δ 9.48 (s, 1H, C-2 H), 8.56-8.31 (m, 3H, C-11 H + D_2O exchangeable 2NH), 7.81-7.57 (m, 2H, C-10 H + C-9 H), 2.86 (s, 3H, CH_3) ppm. Anal calcd for $C_{11}H_9N_5O$ (227.2): C, 58.14; H, 3.99; N, 30.82. Found: C, 57.7; H, 3.8; N, 30.4.

9c: mp > 300 °C; R_f 0.32; IR (KBr) 3300, 3100, 1620 cm^{-1}. Anal calcd for $C_{11}H_9N_5O$ (227.2): C, 58.14; H, 3.99; N, 30.82. Found: C, 58.4; H, 4.0; N, 30.6.

9d: mp > 300 °C; R_f 0.35; IR (KBr) 3400, 3300, 3200, 1630, 1590 cm^{-1}; ^1H NMR (DMSO-d_6) δ 8.5-8.2 (m, 3H, C-11 H + 2NH), 7.80-7.55 (m, 2H, C-9 H and C-10 H), 2.86 (s, 3H, CH_3), 2.69 (s, 3H, CH_3) ppm; EIMS *m/z* 242 $(M+1)^+$ (15.6 %), 241 $(M)^+$ (100 %), 200 $(M-MeCN)^+$ (2.5%), 157 (2%). Anal calcd for $C_{12}H_{11}N_5O$ (241.2): C, 59.74; H, 4.59; N, 29.02. Found: C, 59.3; H, 4.3; N, 28.9.

10a: mp 196-198 °C; R_f 0.53; IR (KBr) 3050, 2950, 1705-1680, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.51 (s, 1H, C-2 H), 8.30 (m, 2H, ArH), 7.80 (m, 2H, ArH), 7.35 (s, 1H, olefinic H), 4.16 (q, 2H, CH_2), 1.27 (t, 3H, CH_3) ppm. Anal calcd for $C_{13}H_{11}N_5O_2$ (269.2) : C, 57.98; H, 4.11; N, 26.00. Found: C, 58.1; H, 4.3; N, 25.8. 10b: mp 181-184 °C; R_f 0.54. Anal calcd for $C_{14}H_{13}N_5O_2$ (283.2): C, 59.35; H, 4.62; N, 24.72.

Found: C, 59.5; H, 4.4; N, 24.6. 10c: mp 180-182 °C; R_f 0.56. Anal calcd for $C_{15}H_{13}N_5O_2$ (297.3) : C, 60.95; H, 5.08; N, 23.55. Found: C, 60.3; H, 4.9; N, 23.5. 10d: mp 165-168 °C; R_f 0.61; IR (KBr) 2980, 2920, 1680, 1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ 782-7.38 (m, 3H, ArH), 4.47 (q, 2H, OCH_2CH_3), 3.06 (s, 3H, 7-CH_3), 2.69 (s, 3H, 2-CH_3), 1.82 (s, 3H, N=C-CH_3), 1.46 (t, 3H, OCH_2CH_3) ppm; EIMS *m/z* 311(M)$^+$ (10.4 %), 296 (M-Me)$^+$ (2.3 %), 282 (M-Et)$^+$ (6.1 %), 266 (M-OEt)$^+$ (17.4%), 69 (100%). Anal calcd for $C_{16}H_{17}N_5O_2$ (311.3): C, 61.72; H, 5.50; N, 22.49. Found: C, 61.9; H, 5.2; N, 22.8.

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تشييد مركبات الإيميدازو(٤,٥-جـ) سينولين والترايزيبينو(٦,٥-جـ) سينولين

خديجة منصور غنيم ، محمد يسرى حافظ عيسوى ، سلوى السيد محمد المليجى ، علياء محمد كمال
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تم فى هذا البحث تشييد عدد من مركبات الإيميدازو(٤,٥-جـ)- سينولين (٣) ذات النظام الحلقى الجديد وذلك بتفاعل ٤،٣-ثنائى أمين السينولين (٢) مع ثلاثى ايثيل الأورثوفورمات، إيثيل كلوروكاربونات وبوتاسيوم إيثيل ثنائى ثيوكاربونات. وقد تم تشييد المركب الأولى (٢) بتطبيق تفاعل "هوفمان" على الأمينوسينولين كاربوكساميد (١) كذلك تم تحضير مركبات الترايزيبينوسينولين (٩,٧,٦) بدءاً من حمض الأمينوسينولين هيدازيد وتفاعله مع إيثيل كلوروكابونات ، ثلاثى الأورثوفورمات و بوتاسيوم إيثيل ثنائى كربونات. وقد أظهرت هذه التفاعلات إمكانية حدوث تقلص نواه الترايزيبينوسينولين المستهدفة الى البيريميدوسينولين (١٠,٦).