Synthesis of some New Quinoxalines with expected Pharmacological Activities

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Síntesis de nuevas quinoxalinas con actividades farmacológicas esperadas

Síntesi de noves quinoxalines amb activitats farmacològiques esperades

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RESUMEN

Se hace reaccionar la 4-metilfenilendiamina 1 con compuestos α-dicarbonílicos para dar las quinoxalinas 2a-g, 4a-d y/o 7a-c. Las quinoxalinas 7a-c se transforman en las dihidropiridazinoquinoxalinas 9a-c, tienoquinoxalinas 10a-c y/o dicloroquinoxalinas 11a-c. Los compuestos 11a-c se convierten en las etoxiquinoxalinas 12a-c, arilaminoquinoxalinas 13a-f y/o quinazolinoquinoxalinas 14a-c. Se describe también la reacción de 11a-c con semicarbazida y/o azida sódica.

Palabras Clave: **Quinoxalinas. Dihidropiridazinoquinoxalinas. Tienoquinoxalinas. Quinazolinoquinoxalinas.**

SUMMARY

4-Methylphenylenediamine 1 was reacted with α-dicarbonyls to give quinoxalines 2a-g, 4a-d and/or 7a-c. Quinoxalines 7a-c were converted into dihydropyridazinoquinoxalines 9a-c, thienoquinoxalines 10a-c and/or dichloroquinoxalines 11a-c. Compounds 11a-c were converted into ethoxyquinoxalines 12a-c, arylaminoquinoxalines 13a-f and/or quinazolinoquinoxalines 14a-c. The reaction of 11a-c with semicarbazide and/or sodium azide was also described.

Key words: **Quinoxalines. Dihydropyridazinoquinoxalines. Thienoquinoxalines, Quinazolinoquinoxalines.**

RESUM

Es fa reaccionar la 4-metilfenilendiamina 1 amb compostos α-dicarbonílics per donar les quinoxalines 2a-g, 4a-d i/o 7a-c. Les quinoxalines 7a-c es transformen en les dihidropiridazinoquinoxalines 9a-c, tienoquinoxalines 10a-c i/o dicloroquinoxalines 11a-c. Els compostos 11a-c es converteixen en les etoxiquinoxalines 12a-c, arilaminoquinoxalines 13a-f i/o quinazolinoquinoxalines 14a-c. Es descriu també la reacció d'11a-c amb semicarbazida i/o azida sòdica.

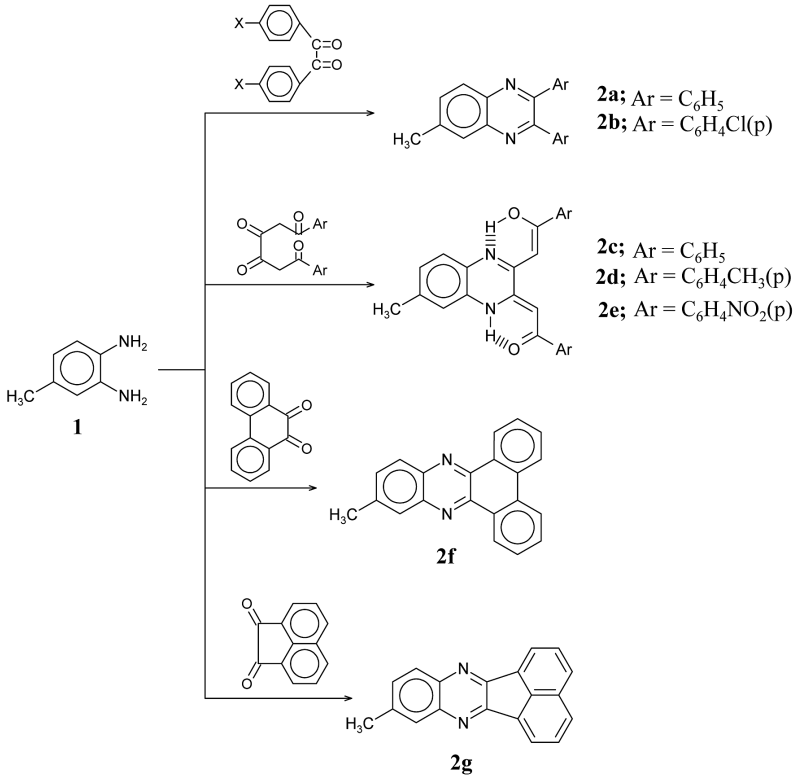
Mots Clau: **Quinoxalines. Dihidropiridazinoquinoxalines. Tienoquinoxalines. Quinazolinoquinoxalines.**

INTRODUCTION

The synthesis of quinoxalines has attracted the attention of medicinal chemists because of their potential pharmacodynamic properties[1-5]. Numerous publications describe the synthesis of quinoxalines possessing a variety of pharmacological activities, such as DNA interactive behaviour[6-8]. Some act as antidiabetic agents[9], anti-HIV agents[10] and NMDA receptor antagonists[11].

RESULTS AND DISCUSSION

Recently, we have reported several new and efficient methods for the synthesis of fused heterocyclic[12-15] from readily available starting compounds. In the present study we report the synthesis of new quinazo-lines and condensed quinazolines. α-Dicarbonyl are versatile building units that have been extensively utilized in organic synthesis[16-18].The reaction of 4-methylphenylenediamine **1** with α-diketones namely benzil, p-dichlorobenzil, tetraketones, 9,10-phenantharenequinone and acenaphthenequinone resulted in cyclocondensation affording the corresponding quinoxaline derivatives **2a-g** respectively (Scheme 1).



Scheme 1

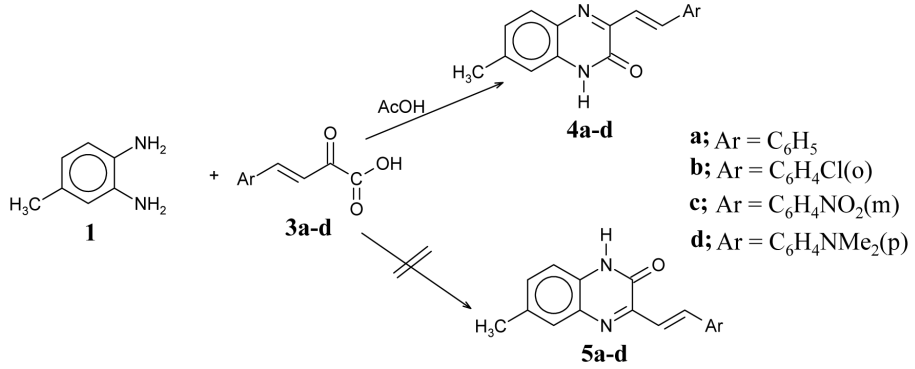
It was reported that 4-methylphenylenediamine **1** reacted with asymmetric dicarbonyl to give 6-methylquinoxaline as major product while 7-isomer as minor product[19]. In the present study it was found that cyclocondensation of arylidenepyruvic acids **3a-d** and 4-methyl-phenylenediamine **1** yielded corresponding 6-methylquinoxalines **4a-d** respectively not the other isomer[19]. (Scheme 2).

When 4-methylphenylenediamine **1** was allowed to react with aroyl pyruvate **6a-c** resulted in cyclocondensation affording 6-methylquin-oxaline derivatives **7a-c** respectively not 7-methylquinoxaline derivatives **8a-c**[19]. The quinoxalines **7a-c** exist in the enol form (no ketonic form can be detected). Thus for **7a-c**, no signal is observed for –CH_2CO- between 3.5 and 4.5 ppm, while a one proton singlet is observed at 6.80 ppm.

Hydrazinolysis of compounds **7a-c** using hydrazine hydrate in ethanolic solution yielded 1,2-dihydropyridazino[3,4-*b*]quinoxaline **9a-c** respectively (Scheme 4). Upon reacting quinoxalines **7a-c** with P_2S_5 in dry pyridine resulted in thiation followed by cyclization affording thienoquinoxaline **10a-c** (Scheme 4). Chlorolysis of quinoxaline derivatives **7a-c** using $POCl_3$ afforded the corresponding dichloro-quinoxaline derivatives **11a-c** (Scheme 4).

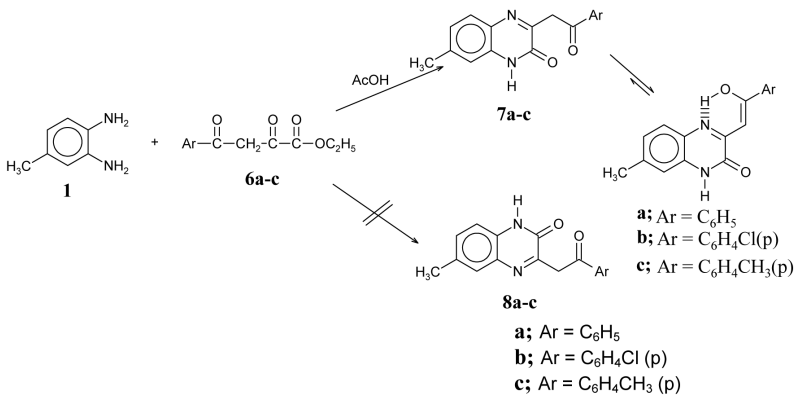
2-Chloroquinoxalines **11a-c** appeared to be versatile starting compound for further functionlization and annulation of the quinoxaline ring. Thus refluxing 2-chloroquinoxalines **11a-c** with ethoxide resulted in 2-ethoxyquinoxalines **12a-c** (Scheme 5). Chloroquinoxalines **11a-c** were now subjected to aminolysis with arylamines namely; aniline and/or anthranilic acid by refluxing in ethanol to give arylaminoquinoxalines **13a-f** (Scheme 5).

When compounds **13d-f** were allowed to react with $POCl_3$ resulted heteroannulation affording quinazolinoquinoxalines **14a-c** (Scheme 5). The semicarbazones **15a-c** were achieved by the reaction of **11a-c** with semicarbazide (Scheme 5). Depending on the reaction conditions compounds **11a-c** were reacted with sodium azide at room temp. yielded the corresponding azido derivatives **16a-c** while upon refluxing compounds **11a-c** with sodium azide yielded the corresponding tetrazoloquinoxaline derivatives **17a-c** presumably via the formation of azido derivatives **16a-c**. The structures of **17a-c** were proved by the disappearance of azido group in IR spectrum.

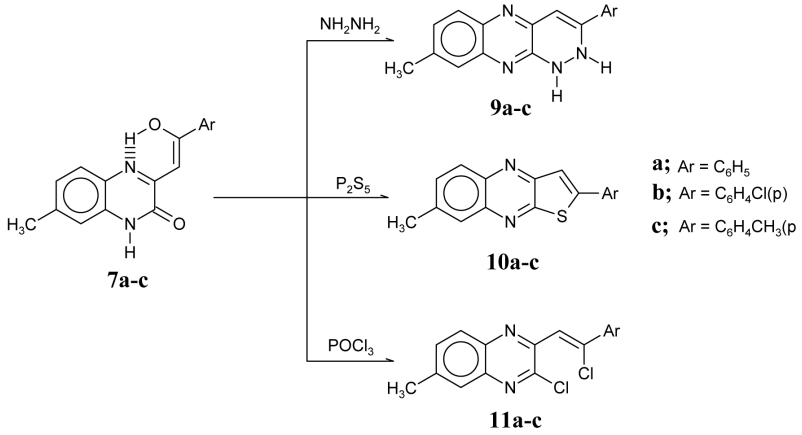


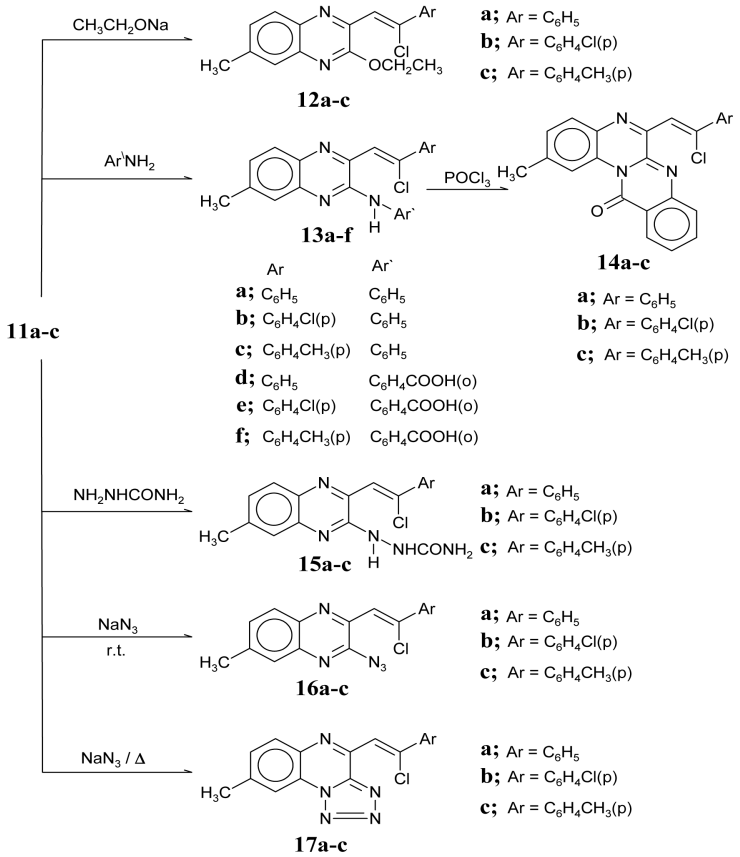
Scheme 2

Scheme 3



Scheme 4





Scheme 5

EXPERIMENTAL

Melting points are uncorrected and were recorded on Büchi 510 apparatus. IR spectra were recorded as KBr disks on a Perkin-Elmer 383 spectrometer and FTIR-spectrometer Nicolet, impact 400. ^{1}H- and ^{13}C-NMR were obtained a Bruker Ac 200F and Ac 250, DRX400 instrument at room temperature using TMS as internal standard. Mass spectra were determined at 70 eV by using AEI MS 30 mass spectrometer and elemental analyses were recorded on LECO-Analyser CHNS-932. Microanalyses were carried out at microanalytical center, Cairo University, Egypt and Friedrich-Schiller University, Jena, Germany.

Quinoxalines 2a-g:

A mixture of **1** (0.01 mole) and appropriate α-diketone (0.01 mole) in acetic acid (20 ml) was refluxed for 3 hours, cooled. The precipitate obtained was filtered and crystallized from ethanol to give crystals of **2a-g** respectively (Tables I and II).

3-Styrylquinoxalines 4a-d:

A mixture of **1** (0.01 mole) and appropriate arylidenepyruvic acid (0.01 mole) in acetic acid (20 ml) was refluxed for 2 hours, cooled. The precipitate obtained was filtered and crystallized from ethanol to give crystals of **4a-d** respectively (Tables I and II).

TABLE I

Spectral analysis data of the synthetic compounds.

Compds	Colour	Yield%	m.p. [°C]	Formula (Molecular mass)	Micro analyses Calcd./Found			IR (Selected bands) cm^{-1}
					C%	H%	N%	
2a	Pale green	84	110-111	$C_{21}H_{16}N_2$ (296.36)	85.10 84.90	5.44 5.21	9.45 9.20	3052 (CH, arom.), 2920, 2843 (CH, aliph.), 1621 (C=N)
2b	White	87	182-183	$C_{21}H_{14}N_2Cl_2$ (365.25)	69.05 69.00	3.86 3.85	7.67 7.70	3058 (CH, arom.), 2922, 2847 (CH, aliph.), 1619 (C=N)
2c	Orange	81	230– 231	$C_{25}H_{20}N_2O_2$ (380.43)	78.92 78.98	5.29 5.30	7.36 7.40	3161 (NH), 3057 (CH, arom.), 2914, 2845 (CH, aliph.), 1685 (C=O), 1596 (C=N).
2d	Yellow	85	240–241	$C_{27}H_{24}N_2O_2$ (408.48)	79.38 79.40	5.92 5.91	6.86 6.89	3158 (NH), 3023 (CH, arom..), 2919, 2830 (CH, aliph.), 1683 (C=O), 1599 (C=N)
2e	Red	79	240-242	$C_{25}H_{18}N_4O_6$ (470.42)	63.83 63.80	3.86 3.87	11.91 11.90	3161 (NH), 3023(CH, arom.), 2919, 2849 (CH, aliph.), 1656 (C=O), 1594 (C=N)
2f	Yellow	89	220–221	$C_{21}H_{14}N_2$ (294.34)	85.69 85.51	4.79 4.80	9.52 9.50	3054 (CH, arom.), 2901, 2829 (CH, aliph.), 1624 (C=N)
2g	White	91	210-211	$C_{19}H_{12}N_2$ (268.31)	85.05 85.00	4.51 4.48	10.44 10.50	3037 (CH, arom.), 2913, 2842 (CH, aliph.), 1620 (C=N)
4a	Brown	80	200-201	$C_{17}H_{14}N_2O$ (262.30)	77.84 77.86	5.38 5.40	10.68 10.71	3160 (NH), 3063 (CH, arom.), 2925, 2851 (CH, aliph.), 1670 (C=O), 1600 (C=N)
4b	Brown	92	234-235	$C_{17}H_{13}N_2OCl$ (296.74)	68.80 68.82	4.41 4.40	9.44 9.42	3161 (NH), 3062 (CH, arom.), 2923, 2854 (CH, aliph.), 1681 (C=O), 1601 (C=N)
4c	Brown	89	250-251	$C_{17}H_{13}N_3O_3$ (307.29)	66.44 66.40	4.26 4.20	13.67 13.72	3162 (NH), 3062 (CH, arom.), 2925, 2850 (CH, aliph.), 1662 (C=O), 1600 (C=N)
4d	Brown	84	> 300	$C_{19}H_{19}N_3O$ (305.36)	74.73 74.80	6.27 6.22	13.76 13.85	3163 (NH), 3013 (CH, arom.), 2923, 2854 (CH, aliph.), 1661 (C=O) 1609 (C=N)
7a	Orange	90	240-241	$C_{17}H_{14}N_2O_2$ (278.30)	73.36 73.14	5.07 5.10	10.06 9.95	3162 (NH), 3056 (CH, arom.), 2920, 2852 (CH, aliph.), 1685 (C=O), 1599 (C=N)
7b	Orange	89	275-276	$C_{17}H_{13}N_2O_2Cl$ (312.74)	65.28 65.45	4.19 4.00	8.96 9.01	3167 (NH), 3062 (CH, arom.), 2918, 2853 (CH, aliph.), 1677 (C=O), 1597 (C=N)
7c	Yellow	80	245-247	$C_{18}H_{16}N_2O_2$ (292.33)	73.95 74.02	5.52 5.49	9.59 9.61	3161 (NH), 3054 (CH, arom.), 2918, 2851 (CH, aliph.), 1677 (C=O), 1599 (C=N)
9a	Pink	65	190-192	$C_{17}H_{14}N_4$ (274.31)	74.43 74.50	5.14 5.19	20.43 20.50	3307, 3263 (NH), 3028 (CH, arom.), 2917, 2851 (CH, aliph.), 1659 (C=N)
9b	Red	71	212-214	$C_{17}H_{13}N_4Cl$ (308.75)	66.13 66.20	4.24 4.21	18.15 18.30	3316, 3253 (NH), 3029 (CH, arom.), 2917, 2848 (CH, aliph.), 1660 (C=N)
9c	Red	69	224-225	$C_{18}H_{16}N_4$ (288.34)	74.97 75.10	5.59 5.60	19.43 19.49	3309, 3261 (NH), 3031 (CH, arom.), 2915, 2850 (CH, aliph.), 1662 (C=N)
10a	Red	67	208-210	$C_{17}H_{12}N_2S$ (276.35)	73.88 74.00	4.38 4.35	10.14 10.20	3055 (CH, arom.), 2919, 2851 (CH, aliph.), 1599 (C=N)
10b	Red	61	203-205	$C_{17}H_{11}N_2SCl$ (310.79)	65.69 65.50	3.57 3.59	9.02 8.98	3061 (CH, arom.), 2917, 2847 (CH, aliph.), 1603 (C=N)
10c	Red	63	174-175	$C_{18}H_{14}N_2S$ (290.37)	74.45 74.50	4.86 4.90	9.65 9.87	3049 (CH, arom.), 2923, 2850 (CH, aliph.), 1596 (C=N)
11a	Green	90	115-116	$C_{17}H_{12}N_2Cl_2$ (315.20)	64.77 64.81	3.84 3.90	8.89 9.00	3056 (CH, arom.), 2918, 2854 (CH, aliph.), 1614 (C=N)
11b	Green	91	118-120	$C_{17}H_{11}N_2Cl_3$ (349.65)	58.39 58.01	3.17 3.20	8.01 7.79	3024 (CH, arom.), 2915, 2853 (CH, aliph.), 1604 (C=N)
11c	Green	89	117-119	$C_{18}H_{14}N_2Cl_2$ (329.22)	65.66 66.01	4.29 4.30	8.51 8.45	3059 (CH, arom.), 2918, 2853 (CH, aliph.), 1605 (C=N)
12a	Yellow	80	190-191	$C_{19}H_{17}N_2OCl$ (324.80)	70.25 70.32	5.28 5.19	8.62 8.60	3055 (CH, arom.), 2922, 2850 (CH, aliph.), 1614 (C=N)
12b	Yellow	86	195-196	$C_{19}H_{16}N_2OCl_2$ (359.25)	63.52 63.49	4.49 4.42	7.80 7.84	3026 (CH, arom.), 2920, 2854 (CH, aliph.), 1603 (C=N)
12c	Yellow	77	205-207	$C_{20}H_{19}N_2OCl$ (338.82)	70.90 70.87	5.60 5.51	8.27 8.40	3051 (CH, arom.), 2919, 2853 (CH, aliph.), 1619 (C=N)

TABLE I *(continued)*

Spectral analysis data of the synthetic compounds.

Compds	Colour	Yield%	m.p. [°C]	Formula (Molecular mass)	Micro analyses Calcd./Found			IR (Selected bands) cm^{-1}
					C%	H%	N%	
13a	Yellow	76	176-178	$C_{23}H_{18}N_3Cl$ (371.87)	74.29 75.10	4.88 3.41	11.30 11.52	3120 (NH), 3065 (CH, arom.), 2920, 2851 (CH, aliph.), 1687 (C=N)
13b	Yellow	78	165-166	$C_{23}H_{17}N_3Cl_2$ (406.31)	67.99 68.90	4.22 2.89	10.34 10.30	3119 (NH), 3026 (CH, arom.), 2920, 2852 (CH, aliph.), 1678 (C=N)
13c	Yellow	70	172-173	$C_{24}H_{20}N_3Cl$ (385.90)	74.70 76.00	5.22 4.01	10.89 10.82	3129 (NH), 3055 (CH, arom.), 2919, 2854 (CH, aliph.), 1677 (C=N)
13d	Yellow	68	198-200	$C_{24}H_{18}N_3O_2Cl$ (415.85)	69.31 69.10	4.36 4.40	10.10 10.37	3433 (OH), 3121 (NH), 3055 (CH, arom.), 2919, 2851 (CH, aliph.), 1679 (C=O), 1617 (C=N)
13e	Yellow	71	180-182	$C_{24}H_{17}N_3O_2Cl_2$ (450.31)	64.01 63.84	3.81 3.50	9.33 9.04	3416 (OH), 3112 (NH), 3025 (CH, arom.), 2918, 2852 (CH, aliph.), 1678 (C=O), 1602 (C=N)
13f	Yellow	68	195-196	$C_{25}H_{20}N_3O_2Cl$ (429.88)	69.85 70.02	4.69 4.43	9.77 9.90	3424 (OH), 3132 (NH), 3058 (CH, arom.), 2920, 2851 (CH, aliph.), 1682 (C=O), 1607 (C=N)
14a	Red	80	160-162	$C_{24}H_{16}N_3OCl$ (397.84)	72.45 72.31	4.05 3.90	10.56 10.20	3075 (CH, arom.), 2921, 2851 (CH, aliph.), 1662 (C=O), 1623 (C=N)
14b	Red	76	155-157	$C_{24}H_{15}N_3OCl_2$ (432.29)	66.68 66.80	3.49 3.13	9.72 9.90	3057 (CH, arom.), 2922, 2852 (CH, aliph.), 1663 (C=O), 1621 (C=N)
14c	Red	69	150-152	$C_{25}H_{18}N_3OCl$ (411.86)	72.90 73.20	4.40 4.29	10.20 9.98	3027 (CH, arom.), 2919, 2852 (CH, aliph.), 1666 (C=O), 1563 (C=N)
15a	Yellow	65	> 300	$C_{18}H_{16}N_5OCl$ (353.80)	61.10 61.00	4.56 4.55	19.80 19.98	3424, 3310 (NH_2), 3256, 3186 (NH), 3064 (CH, arom.), 2920, 2874 (CH, aliph.), 1686 (C=O), 1642 (C=N)
15b	Yellow	62	170-172	$C_{18}H_{15}N_5OCl_2$ (388.25)	55.68 55.61	3.89 3.90	18.04 17.87	3462, 3370 (NH_2), 3279, 3118 (NH), 3029 (CH, arom.), 2921, 2853 (CH, aliph.), 1673 (C=O), 1612 (C=N)
15c	Yellow	60	180-182	$C_{19}H_{18}N_5OCl$ (367.82)	62.04 61.93	4.93 5.10	19.04 19.20	3461, 3373 (NH_2), 3261, 3119 (NH), 3030 (CH, arom.), 2921, 2852 (CH, aliph.), 1677 (C=O), 1639 (C=N)
16a	Brown	71	125-126	$C_{17}H_{12}N_5Cl$ (321.76)	63.45 63.46	3.76 3.70	21.77 21.98	3058 (CH, arom.), 2919, 2854 (CH, aliph.), 2122 (N_3), 1603 (C=N)
16b	Brown	68	133-135	$C_{17}H_{11}N_5Cl_2$ (356.21)	57.32 57.40	3.11 3.15	19.66 19.70	3027 (CH, arom.), 2919, 2853 (CH, aliph.), 2129 (N_3), 1607 (C=N)
16c	Brown	65	165-166	$C_{18}H_{14}N_5Cl$ (335.78)	64.38 64.37	4.20 3.97	20.86 20.81	3091 (CH, arom.), 2920, 2853 (CH, aliph.), 2131 (N_3), 1602 (C=N)
17a	Dark brown	60	180-181	$C_{17}H_{12}N_5Cl$ (321.76)	63.45 63.50	3.76 3.80	21.77 21.24	3061 (CH, arom.), 2918, 2854 (CH, aliph.), 1602 (C=N)
17b	Dark brown	59	140-141	$C_{17}H_{11}N_5Cl_2$ (356.21)	57.32 57.40	3.11 2.97	19.66 19.57	3027 (CH, arom.), 2918, 2853 (CH, aliph.), 1610 (C=N)
17c	Dark brown	63	186-188	$C_{18}H_{14}N_5Cl$ (335.78)	64.38 64.35	4.20 4.21	20.86 20.90	3091 (CH, arom.), 2921, 2851 (CH, aliph.), 1613 (C=N)

3-Benzoylmethylquinoxalines 7a-c:

A mixture of **1** (0.01 mole) and appropriate ethylaroylpyruvate sodium salt (0.01 mole) in acetic acid (30 ml) was refluxed for 3 hours cooled. The precipitate obtained was filtered and crystallized from ethanol to give crystals of **7a-c** respectively (Tables I and II).

1,2-Dihydropyridazino[3,4-*b*]quinoxalines 9a-c:

A mixture of hydrazine hydrate (0.01 mole) and appropriate of compounds **7a-c** (0.01 mole) in dimethylformamide (DMF) was refluxed for 3 hours. The precipitate obtained upon cooling and pouring into ice cooled water was collected by filteration and crystallized from ethanol to give crystals of **9a-c** respectively (Tables I and II).

Thieno[2,3-*b*]quinoxalines 10a-c:

A mixture of P_2S_5 (0.01 mole) and apporopriate quinoxalines **7a-c** (0.01 mole) in dry pyridine (30 ml) was refluxed for 3 hours. The solids obtained upon cooling and acidification with HCl (10 ml, 20%) was collected and crystallized from methanol to give crystals of **10a-c** respectively (Tables I and II).

Dichloroquinoxalines 11a-c:

A mixture of appropriate quinoxalines **7a-c** (0.01 mole) and $POCl_3$ (0.03 mole) was refluxed for 4 hours. The solids that obtained upon cooling and pouring into ice cooled water was collected by filteration and crystallized from benzene to give crystal of **11a-c** respectively (Tables I and II).

2-Ethoxyquinoxalines 12a-c:

A mixture of appropriate **11a-c** (0.01 mole) and sodium ethoxide (0.01 mole) was refluxed for 8 hours. The precipitate obtained upon dilution was collected by filteration and crystallized from ethanol to give crystals of **12a-c** respectively (Tables I and II).

2-Arylaminoquinoxalines 13a-f:

A mixture of appropriate **11a-c**, appropriate aryl amine namely aniline and/or anthranilic acid (0.01 mole) and triethylamine (TEA) was refluxed for 8 hours. The precipitate obtained upon pouring into ice cooled water was collected by filteration and crystallized from toluene to give crystals of **13a-f** respectively (Tables I and II).

Quinazolinoquinoxalines 14a-c:

A solution of appropriate **13d-f** (0.01 mole) in $POCl_3$ (15 ml) was refluxed for 12 hours. The precipitate obtained upon pouring into ice cold water was collected by filteration and crystallized from dichloromethane to give crystals of **14a-c** respectively (Tables I and II).

2-Quinoxalinyl Semicarbazone 15a-c:

A solution of appropriate **11a-c** (0.01 mole), semicarbazidehydro-chloride (0.01 mole), TEA (4 drops) in ethanol (30 ml) was refluxed for 8 hours. The precipitate obtained upon cooling was collected by filteration and crystallized from benzene to give crystals of **15a-c** respectively (Tables I and II).

2-Azidoquinoxalines 16a-c:

A solution of appropriate **11a-c** (0.01 mole) and sodium azide (0.01 mole) in DMF (20 ml) was stirred for 3 hours. The precipitate obtained upon pouring into ice cooled water was collected by filtration and crystallized from ethanol to give crystals of **16a-c** respectively (Tables I and II).

Tetrazoloquinoxalines 17a-c:

A solution of appropriate **11a-c** (0.01 mole) and sodium azide (0.01 mole) in DMF (20 ml) was refluxed for 6 hours. The precipitate obtained upon pouring into ice-cooled water was collected by filteration and crystallized from ethanol to give crystals of **17a-c** respectively (Tables I and II).

TABLE II

Spectral analysis data of the synthetic compounds.

Comp. / Solvent	δppm, ^{1}H-NMR
2a (DMSO-d_6)[a]	2.61 (s, 3H, CH_3), 7.26 – 8.09 (m, 13H, arom.)
2c (DMSO-d_6)[b]	2.38 (s, 3H, CH_3), 6.77 (s, 1H, CH), 7.79 (s, 1H, CH), 6.92 – 7.97 (m, 13H, arom.), 12.00 (s, 1H, NH), 13.75 (s, 1H, OH)
2d (DMSO-d_6)	2.28 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 6.74 (s, 3H, CH), 6.76 (s, 1H, CH), 6.92 – 7.87 (m, 11H, arom.), 11.96 (s, 1H, NH), 13.70 (s, 1H, OH)
2f ($CDCl_3$)[c]	2.17 (s, 3H, CH_3), 7.68 – 9.30 (m, 11H, arom.)
2g ($CDCl_3$)	2.61 (s, 3H, CH_3), 7.58 – 8.40 (m, 9H, arom.)
4b (DMSO-d_6)[d]	2.6 (s, 3H, CH_3), 7.30 – 7.61 (m, 7H, arom.), 7.94 (dd, 1H, CH), 8.03 (dd, 1H, CH), 10.49 (s, 1H, NH)
7a (DMSO-d_6)	2.29 (s, 3H, CH_3), 6.78 (s, 1H, CH), 7.02 – 7.98 (m, 8H, arom.), 12.00 (s, 1H, NH), 13.76 (s, 1H, OH)
7c (DMSO-d_6)[e]	2.28 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 6.74 (s, 1H, CH), 6.95 – 7.87 (m, 7H, arom.), 11.96 (s, 1H, NH), 13.7 (s, 1H, OH)
9c (DMSO-d_6)	2.07 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.99 (dd, 1H, NH), 3.89 (dd, 1H, NH), 6.5 (s, 1H, CH), 6.52 – 7.79 (m, 7H, arom.)
10a ($CDCl_3$)	2.41 (s, 3H, CH_3), 6.92 (s, 1H, CH), 6.98 – 8.07 (m, 8H, arom.)
10b ($CDCl_3$)	2.40 (s, 3H, CH_3), 7.46 (s, 1H, CH), 7.5 – 8.07 (m, 7H, arom.)
10c ($CDCl_3$)	2.44 (s, 3H, CH_3), 2.63 (s, 3H, CH_3), 7.3 (s, 1H, CH), 7.33 – 8.07 (m, 7H, arom.)
11a (DMSO-d_6)[f]	2.55 (s, 3H, CH_3), 7.52 (s, 1H, CH), 7.53 – 8.11 (m, 8H, arom.)
12a (DMSO-d_6)	1.46 (t, 3H, CH_3), 2.29 (s, 3H, CH_3), 4.54 (q, 2H, CH_2), 7.52 (s, 1H, CH), 6.78 – 7.99 (m, 8H, arom.)
13d (DMSO-d_6)	2.5 (s, 3H, CH_3), 6.77 (s, 1H, CH), 6.96 – 8.75 (m, 12H, arom.), 11.99 (s, 1H, NH), 13.76 (s, 1H, OH)
14a (DMSO-d_6)	2.52 (s, 3H, CH_3), 7.17 (s, 1H, CH), 7.29 – 8.05 (m, 12H, arom.)
15a (DMSO-d_6)	2.59 (s, 3H, CH_3), 5.36 (s, 2H, NH_2), 7.09 (s, 1H, CH), 7.11 – 8.08 (m, 8H, arom.), 9.8 (s, 1H, NH), 10.14 (s, 1H, NH)
17a (DMSO-d_6)	2.56 (s, 3H, CH_3), 7.52 (s, 1H, CH), 7.54 – 8.12 (m, 8H, arom.)

a: MS m/z: 296 (M^+, 100%).

b: ^{13}C-NMR : 20.63, 88.6, 115.31, 116.53, 121.88, 123.8, 124.43, 126.67, 126.85, 128.92, 128.67, 131.71, 133.09, 133.66, 138.59, 145.63, 155.71, 188.28.

c: ^{13}C-NMR : 22.03, 122.83, 126.01, 127.8, 127.98, 128.89, 129.96, 130.09, 130.36, 130.40, 131.77, 140.30, 140.73, 141.65, 142.41.

d: ^{13}C-NMR : 21.9, 128, 128.22, 128.62, 128.69, 129, 129.18, 129.83, 129.90, 132.30, 139.18, 139.69, 140.5, 141.25, 152.56, 153, 179.24.

e: ^{13}C-NMR : 20.61, 21.00, 88.52, 115.28, 116.39, 121.94, 124.46, 126.56, 127.03, 129.23, 133.46, 141.89, 145.41, 155.78, 188.17.

f: MS m/z; 319 (M^{+4}, 5%), 317 (M^{+2}, 15%), 315 (M^+, 40%).

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