SYNTHESIS AND SOME REACTIONS OF QUINOLINO[2,1-b]-QUINAZOLINE DERIVATIVES

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Abstract: The reaction of 2-methylbenzoxazines **1a,b** with methylanthranilate **2** yielded quinolino[2,1-b]quinazoline derivatives **3a,b**. The reaction of compounds **3a,b** with p-nitrobenzaldehyde **4** gave the arylidene derivatives **5a,b**. The reaction of compounds **5a,b** with hydrazine hydrate, hydroxylamine HCl urea and thiourea gave the fused heterocyclic derivatives **6a,b**; **7a,b** and **8a,d** respectively.

Introduction:

Several authors reported the synthesis and the applications of polyfused heterocyclic derivatives incorporated with quinazoline moiety (1-12). From this point of view and in continuation to our previous work (13-17), we report herein the synthesis of some new quinolinoquinazoline derivatives.

Experimental:

The time required for completion of the reaction was monitored by thin layer chromatography (TLC). Melting points were determined in open glass capillaries and are uncorrected. IR spectra were recorded on a Pye-Unicam SP 200G spectrophotometer. ^{1}H-NMR spectra were measured on an EM-360 90 MHz NMR spectrophotometer. Microanalyses were determined on a Perkin-Elmer 240 C microamalyser. EI Mass spectra were recorded on a Varian MAT 311 A spectrometer.

Synthesis of quinolino[2,1-b]quinazoline derivatives 3a,b:

General Procedure:

A mixture of benzoxazine derivatives **1a,b** (0.01 mole) and methyl anthranilate **2** (0.01 mole) was fused at 150°C for one hour. The reaction mixture was cooled to room temperature and then poured into cold water whereby compounds **3a,b** were precipitated, filtered off, dried and recrystallized from acetic acid (Table I).

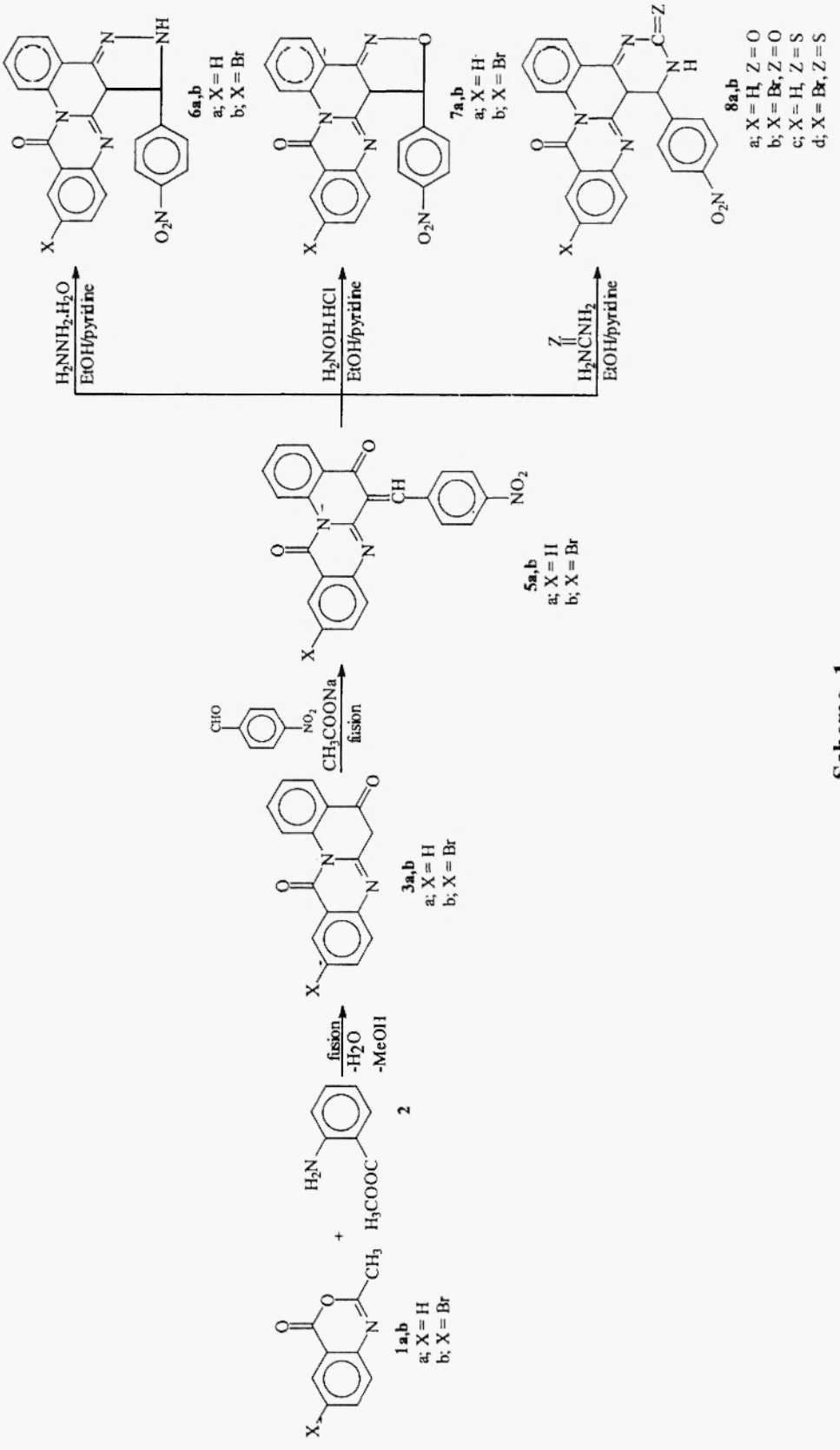
Synthesis of Arylidenoquinolinoquinazoline derivatives 5a,b:

General Procedure:

A mixture of **2a,b** (0.001 mole) and p-nitrobenzaldehyde **4** (0.001 mole) was fused with anhydrous sodium acetate (0.01 mole) for 1 hr., then cooled to room temperature, poured into cold water whereby compounds **5a,b** were precipitated, filtered off, dried and recrystallized from acetic acid (Table I).

Synthesis of pyrazoloquinolinoquinazolines 6a,b, isoxazoloquinolino-quinazolines 7a,b and pyrimido0thiopyrimido)quinolinoquinazolines 8a,d:

General Procedure:



Scheme 1

Table (I) Physical Data of Quinolinoquinazoline Derivatives **3a,b**; **5a,b**; **6a,b**; **7a,b** and **8a-d**.

Compound No.	Yield %	MP (°C)	Molecular Formula (Solvent of Crystallization)	IR (KBr), Cm^{-1}	^1H NMR (Solvent), δ (TMS)
3a	80	135-137	$C_{17}H_{10}N_2O_2$ (acetic acid)	3075(CH arom), 2920(CH aliph), 1711 & 1656(C=O), 1598(C=N).	(DMSO-d_6) 3.50 (2H, s, CH_2), 7.00-8.10 (8H, m, aromatic protons).
3b	75	208-210	$C_{16}H_9N_2O_2Br$ (acetic acid)	3075(CH arom), 2924(CH aliph), 1711 & 1682(C=O), 1600(C=N).	(DMSO-d_6) 3.50 (2H, s, CH_2), 7.00-8.10 (7H, m, aromatic protons).
5a	70	123-125	$C_{23}H_{13}N_3O_1$ (acetic acid)	3055(CH arom), 2924(CH aliph), 1677(C=O), 1591 & 1561 (NO_2).	(DMSO-d_6) 3.80 (1H, s, C-H), 7.00-8.10 (12H, m, aromatic protons).
5b	70	145-147	$C_{23}H_{12}N_3O_1Br$ (acetic acid)	3050(CH arom), 2920(CH aliph), 1682(C=O), 1597 (C=N), 1517 & 1467 (NO_2).	(DMSO-d_6) 3.90 (1H, s, C-H), 7.00-8.00 (11H, m, aromatic protons).
6a	72	215-217	$C_{17}H_{11}N_5O_3$ (acetic acid)	3200(NH), 3050(CH arom), 2921, 2850 (CH aliph), 1680 (C=O), 1632(C=N), 1508 & 1465(NO_2).	(DMSO-d_6) 4.20 (1H, d C-H), 4.40 (1H, d, C-H), 7.00-8.10 (12H, m aromatic protons), 8.30 (1H, d, NH).
6b	70	156-158	$C_{23}H_{14}N_5O_3Br$ (acetic acid)	3200(NH), 3050(CH arom), 2921(CH aliph), 1680 (C=O), 1613(C=N), 1515 & 1467 (NO_2).	(DMSO-d_6) 4.20 (1H, d C-H), 4.50 (1H, d, C-H) 7.10-8.10 (11H, m, aromatic protons), 8.30 (1H, d, NH).
7a	65	147-149	$C_{23}H_{14}N_4O_4$ (acetic acid)	3030(CH arom), 2921 2850 (CH aliph), 1670 (C=O), 1630 (C=O), 1519 & 1484(NO_2).	(DMSO-d_6) 4.20 (1H, d, C-H), 4.40 (1H, d C-H), 7.00-8.10 (12H, m, aromatic protons).
7b	65	140-142	$C_{23}H_{13}N_4O_4Br$ (acetic acid)	3030(CH arom), 2922, 2851 (CH aliph), 1670 (C=O), 1598(C=O), 1518 & 1500 (NO_2).	(DMSO-d_6) 4.25 (1H, d C-H), 4.50 (1H, d, C-H), 7.00-8.10 (11H, m, aromatic protons).
8a	65	183-185	$C_{24}H_{17}N_4O_3$ (acetic acid)	3351(NH), 3030(CH arom), 2921(CH aliph), 1718(C=O) 1634(C=N), 1557 & 1517 (NO_2).	(DMSO-d_6) 4.10 (1H, d C-H), 4.25 (1H, d, C-H), 7.00-8.10 (12H, m, aromatic protons), 8.30(1H, d, NH).
8b	60	130-132	$C_{24}H_{16}N_4O_3Br$ (acetic acid)	3362(NH), 3030(CH arom), 2921(CH aliph), 1718(C=O), 1630(C=N), 1567 & 1517 (NO_2).	(DMSO-d_6) 4.12 (1H, d C-H) 4.25 (1H, d C-H), 7.00-8.10 (12H, m, aromatic protons), 8.30(1H, d, NH).
8c	60	147-149	$C_{24}H_{17}N_5O_3S$ (acetic acid)	3369(NH), 3168(CH arom), 2922(CH aliph), 1685(C=O) 1601(C=N), 1567 & 1517 (NO_2).	(DMSO-d_6) 4.10 (1H, d C-H), 4.50 (1H, d C-H), 7.10-8.10 (11H, m, aromatic protons), 8.30(1H, d, NH).
8d	65	165-167	$C_{24}H_{14}N_5O_3SBr$ (acetic acid)	3348 & 3147(NH), 3030(CH arom), 2921(CH aliph), 1684(C=O), 1597(C=N), 1518, 1457(NO_2).	(DMSO-d_6) 4.10 (1H, d, C-H), 4.25 (1H, d, C-H), 7.10-8.10 (11H, m, aromatic protons), 8.30(1H, d, NH).

Each compound **5a,b** (0.001 mole) was dissolved in 25 ml of an ethanol/pyridine mixture (4:1). To this solution, hydrazine hydrate or hydroxylamine hydrochloride or urea and/or thiourea (0.001 mole) was added portionwise. The reaction mixture was heated under reflux for 6 hrs, then cooled to room temperature, poured into dilute hydrochloric acid solution (10 ml, 10%) whereby the target products were precipitated, filtered off, dried and recrystallized from acetic acid (Table I).

Results and Discussions:

2-Methylbenzoxazines **1a,b** reacted with methylanthranilate **2** to yield quinolino[2,1-b]quinazoline derivatives **3a,b** (Scheme 1). The structures of compounds **3a,b** were established from their elemental analysis and spectroscopic data (Table I). Quinazoline derivatives **3a,b** reacted with p-nitrobenzaldehyde **4** to give the arylidene derivatives 5a,b (Scheme 1). The structures of compounds **5a,b** were confirmed on the basis of their elemental analysis and spectroscopic data (Table I). The arylidene derivatives **5a,b** reacted with hydrazine hydrate, hydroxylamine hydrochloride, urea and thiourea to give the target pyrazoloquinolinoquina-zolines **6a,b**, isoxazoloquinolinoquinazolines, **7a,b** and pyrimido-(thiopyrimido)quinolinoquinazolines **8a-d** respectivly in good yields (Scheme 1). The structures of compounds **6a,b**; **7a,b** and **8a-d** were established from their elemental analysis and spectroscopic data (Table I).

Conclusions:

This work reports a facile method for the synthesis quinolinoquinazoline derivatives.

References:

(1) S.A.H. El-Feky, Zhoughua Yaoxue Zaxhi 43(4), 297-302 (1991), Chem. Abstr. 116: 41398t (1992).
(2) P.S.N. Reddy and G.V. Reddy, Indian J. Chem., Sect. B. 31B(3), 1934 (1992).
(3) H.M. Hassan, Y.M. Darwish and O.M.O. Habib, Rev. Roum. Chim, 37(8), 903-7 (1992); Chem. Abstr. 118: 101912j (1993).
(4) J.W. Chern, P.L. Tao, M.H. Yen, G.Y. Lu, C.Y. Shiau, Y.J. Lai, S.L. Chien and C.H. Chan, J. Med. Chem., 36(15), 2196-2207 (1993).
(5) M.A. Likhate and P.S. Fernandes, J. Indian Chem. Soc., 69(10), 667-8 (1992).
(6) R. Pal, R.N. Handa and H.K. Pujari, Indian J. Chem. Sect., B 32B(9), 929-932 (1993).
(7) J. Reisch and C. Usifoh, J. Heterocycl. Chem., 30(3), 659-661 (1993).
(8) Y.A. Ibrahim and A.H.M. El-Wahy, Heteroat. Chem.; 5(2), 97-101 (1994).
(9) K. Seguchi and S. Tanaka, Heterocycles, 45(4), 707-713 (1997).
(10) S.S. Ghabrial and M.Y. Zaki, J. Chem. Res., Synop., 7, 234-235 (1994).
(11) S.S. Ibrahim, A.M. Abdel-Halim, Y. Gabr, S. El-Edfwy and R.M. Abdel-Rahman, J. Chem. Res., Synop., 5, 154-155 (1997).
(12) J. Kokosi, J. Almasi, B. Podanyi, M. Feher, Z. Bocskei, K. Simon and I. Hermecz, Heterocycles, 48(9), 1851-1866 (1998).
(13) M.S. Al-Thebeiti and M.F. El-Zohry, Indian J. Chem. Sect. B; 37B(8), 804-809 (1998).
(14) M.S. Al-Thebeiti, M.F. El-Zohry, S.S. Al-Lihaibi and F.A.A. Tirkistani, Bulletin of Polish Academy of Sciences, Chemistry, 46(4), 354-357 (1998).
(15) M.F. El-Zohry, A.A. Al-Ahmadi and F.A. Aquily, Phosphorus, Sulfur and Silicon, 175, 1-14 (2001).
(16) M.F. El-Zohry, M.S. El-Thebeiti and G.S. Masaret, Afinidad, LVIII, 495, 355-362 (2001).
(17) M.F. El-Zohry, A.A. Al-Ahmadi and F.A. Aquily, Heterocyclic Communications, 8(2), 187-194 (2002).

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