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Synthesis of some phenylpyrazolo benzimidazolo quinoxaline derivatives

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ABSTRACT

2,3-Diphenyl quinoxalin (NI) is fused with benzimidazole (NII) by a methylene bridge, which is then allowed for acetylation. The acetylated product (NIV) is made to react with different aromatic aldehydes to give chalcones (NV 1-NV 5). Chalcones refluxed with substituted acid hydrazides to afford different phenyl pyrazolo benzimidazole quinoxaline derivatives (NVI 1-NVI 15). The structure of chalcones and phenyl pyrazolo benzimidazole quinoxaline derivatives were confirmed by m.p, TLC and Spectral data. All the synthesized compounds were screened for their pharmacological activities.

Key words: Synthesis, quinoxaline, Benzimidazolo, TLC.

INTRODUCTION

Benzimidazole moiety plays an important role in heterocyclic chemistry largely due to its wide range of biological activities[1, 2, 3, 4] such as antimicrobial, antitubercular, anti-inflammatory, anticancer etc., Quinoxaline derivatives have been reported to possess a wide variety of biological activities[5, 6, 7]. Notable among these are antioxidant, anti-inflammatory antimicrobial, anticancer and antihistamic activities. Drugs having pyrazoline ring system[8,9,10] are well known for their anti-inflammatory, antioxidant, antihistamic, antimicrobial, antidepressant, hypoglycemic, hypotensive, anticarcenogenic activities etc. In view of the above facts, it was contemplated to design and synthesize some phenyl pyrazolo benzothiazolo quinoxaline derivatives by condensing benzimidazole quinoxaline chalcones with different aromatic acid hydrazides. All the synthesized compounds were screened for their pharmacological activities. The structure of chalcones and phenyl pyrazolo benzothiazolo quinoxaline derivatives were confirmed by m.p, TLC, and Spectral data.

MATERIAL AND METHODS

The melting point of the compounds were determined on a Thoshniwal electric melting point apparatus and the values were uncorrected. I.R spectrs of the compounds were recorded on a Thermo Nicolet Nexus670-FTIR, IICT, Hyderabad using KBr Disc method. 1H NMR spectra were recorded on Avance-300, IICT, Hyderabad using $CDCl_3$ as solvent. Mass spectra were recorded on HITACHI RMU GL, IICT, Hyderabad. All the solvents used were of analytical grade.

EXPERIMENTAL

6-((1H-benzo[d]imidazol-5-yl)methyl)-2,3-diphenylquinoxaline NIII[11]

General procedure

2,3 Diphenyl Quinoxalin (NI) and benzimidazole (NII) were prepared following the literature method. NI and NII are linked with a methelyne bridge by treating equimolar quantities of NI and NII in suitable solvent with 35 parts formaldehyde solution and 35% HCl, stirring for 4 hr. at 70°C using magnetic stirrer. Solution was made alkaline using ammonia solution. Filtered the product and recrystallized with aq.ethanol.

Yield: 72%, m.p: 108°C, IR (KBr) in cm^{-1}: 1665 (C=N str.), 1340 (C-N str.), 3085 (Ar-H str.) .^{1}HNMR ($CDCl_3$) δ: 5.0 (S, 1H, N-H of benzimidazole), 3.81 (S, 2H, methylene), 7.5-7.9 (m, 3H, quinoxaline), 7.2-7.4 (m, 10H, Ar-H), 7.0-8.1 (m, 3H, benzimidazole). Mass: m/z: 428 (M+): [Found: C, 81, H, 5.6, N, 13.0 $C_{29}H_{24}N_4$ requires C, 81.28, H, 5.65, N, 13.07%].

1-(5-((2,3-diphenylquinoxalin-6-yl)methyl)-1H-benzo[d]imidazol-1-yl)propan-2-one NIV [12]

General procedure

A solution of NIII (0.01M) and chloroacetone (0.01M) were taken into 250ml round bottom flask. Added to it 150ml of dry acetone and 30g of anhyd. Potassium carbonate and the reaction mixture were refluxed for 6hr. below 75°C. Filterate obtained was concentrated under vaccum and recrystallized with aq.ethanol.

Yield: 68%, m.p: 125°C, IR (KBr) cm^{-1}: 1793 (C=O str.), 1668 (C=N str.), 1340 (C-N str.), 3085 (Ar-H str.), 3323 (C-H str).^{1}HNMR ($CDCl_3$) δ: 2.0 (S, 3H, methyl), 3.8,4.8 (S, 4H, methylene), 7.4-7.9 (m, 3H, quinoxaline), 7.2-7.4 (m, 10H,Ar-H), 7.0-8.0 (m, 4H, benzimidazole). Mass: m/z: 468.2 (M+). [Found C, 79.3, H, 5.1, N, 11.8, O, 3.3, $C_{31}H_{24}N_4O$ requires C, 79.4, H, 5.16, N, 11.9, O, 3.41%].

(Z)-4-phenyl-1-(5-((2,3-diphenylquinoxalin-6-yl)methyl)-1H-benzo[d]imidazol-1-yl)but-3-en-2-one NV1-NV5[13]

General procedure

Method of Aldol Condensation followed. A solution of NaOH / KOH (8ml, 10% in water) was added drop wise to a well-stirred solution of N IV (0.01M) and (0.01M) of appropriate aldehyde in 20ml ethanol. The reaction mixture was stirred for 24h. at cold conditions. Then diluted with ice water and acidified with Concentrated HCl. Filtered the product and recrystallized with aq.ethanol. The purity of the compound was checked by TLC and melting point.

NV 1

Yield: 73%, m.p: 113°C, IR (KBr) cm^{-1}: 1773 (C=O str.), 1668(C=N str.), 1340 (C-N str.), 3085 (Ar-H str.), 3323 (C-H str.) Cm^{-1}.^{1}HNMR ($CDCl_3$) δ: 3.8, 5.3 (S, 4H, methylene), 6.2,7.3(d, 2H,ethylene), 7.5-7.9(m, 3H, quinoxaline), 7.1-7.4 (m, 15H, Ar-H), 7.0-8.1 (m, 4H, benzimidazole). Mass: m/z: 556.2 (M+) [Found C,81.8, H, 5.0, N, 10.0, O, 2.7 $C_{38}H_{28}N_4O$ requires C, 81.99, H, 5.07, N, 10.06, O, 2.87%].

6-((1-((1-benzyl-4, 5-dihydro-5-phenyl-1H-pyrazol-3-yl) methyl)-1H Benzo [d]imidazol-5-yl) methyl)-2, 3-diphenylquinoxaline NVI1– NVI15[14]

General procedure

Chalcone (0.01M) and aromatic acid hydrazide (0.02M) were taken in 20ml glacial acetic acid and refluxed for 10hr. above 130°c. The reaction mixture was concentrated and poured in 300ml of ice-cold water and recrystallized with aq.ethanol. The purity of the compound was checked by TLC and melting point. Physical data are shown in Table 1.

Table 1: Physical data of phenyl pyrazolo benzimidazolo quinoxaline derivatives

Compd.	X	Ar	Molecular formula	Melting point range (°C)	% Yield	R_f value
NVI1	H	C_6H_5	$C_{45}H_{34}N_6O$	122-124	70	0.8
NVI2	OH	C_6H_5	$C_{45}H_{34}N_6O_2$	114-115	67	0.82
NVI3	F	C_6H_5	$C_{45}H_{33}FN_6O$	112-115	66	0.8
NVI4	Cl	C_6H_5	$C_{45}H_{33}ClN_6O$	112-114	78	0.91
NVI5	OCH_3	C_6H_5	$C_{46}H_{36}N_6O_2$	116-118	67	0.8
NVI6	H	OHC_6H_4	$C_{45}H_{34}N_6O_2$	120-124	66	0.81
NVI7	OH	OHC_6H_4	$C_{45}H_{34}N_6O_3$	120-124	80	0.9
NVI8	F	OHC_6H_4	$C_{45}H_{33}FN_6O_2$	108-110	45	0.9
NVI9	Cl	OHC_6H_4	$C_{45}H_{33}ClN_6O_2$	102-105	45	0.8
NVI10	OCH_3	OHC_6H_4	$C_{45}H_{36}N_6O_3$	110-112	67	0.83
NVI11	H	ClC_6H_4	$C_{45}H_{33}ClN_6O$	120-122	56	0.8
NVI12	OH	ClC_6H_4	$C_{45}H_{33}ClN_6O_2$	120-122	78	0.82
NVI13	F	ClC_6H_4	$C_{45}H_{32}ClFN_6O$	131-133	76	0.8
NVI14	Cl	ClC_6H_4	$C_{45}H_{32}Cl_2N_6O$	130-13s4	56	0.98
NVI15	OCH_3	ClC_6H_4	$C_{46}H_{35}ClN_6O_2$	123-126	54	0.81

NVI 1

Yield: 67%, m.p: 121 °C, IR (KBr) cm^{-1}: 1790 (C=O str.), 1668 (C=N str.), 1339 (C-N str.), 3035 (Ar-H str.), 3320 (C-H str.) Cm^{-1}. ^{1}HNMR ($CDCl_3$): 1.79, 2.0 (m, 2H, methylene), 3.8, 3.8 (S, 4H, methylene), 4.9 (m, 1H, methine), 7.5-7.9 (m, 3H, quinoxaline), 7.12-7.95 (m, 20H, Ar-H), 7.9-8.1 (m, 4H, benzimidazole). Mass: m/z: 674.2 (M+) [Found C, 80.0, H, 5.0, N, 12.3, O, 2.3. $C_{45}H_{34}N_6O$ requires C, 80.1, H, 5.08, N, 12.45, O, 2.37 %]

NVI 2

Yield: 64%, m.p: 118 °C, IR (KBr) cm^{-1} :3752 (O-H str.) 1777 (C=O str.), 1664 (C=N str.), 1340 (C-N str.), 3035 (Ar-H str.), 3320 (C-H str.) Cm^{-1}.^{1}HNMR ($CDCl_3$): 1.8,2.0 (m, 2H, methylene), 3.1,3.8(S, 4H, methylene), 4.9 (m, 1H, methine), 5.0 (S, 1H, Ar-OH), 7.5-7.9 (m, 3H, quinoxaline), 6.6-7.9 (m, 19H, Ar-H), 7.0-8.1 (m, 4H, benzimidazole). Mass: m/z: 690.2 (M+) [Found C, 78.0, H, 4.8, N, 12.1, O, 4.6 $C_{45}H_{34}N_6O_2$ requires C, 78.2, H, 4.96, N, 12.17, O, 4.63%]

NVI 5

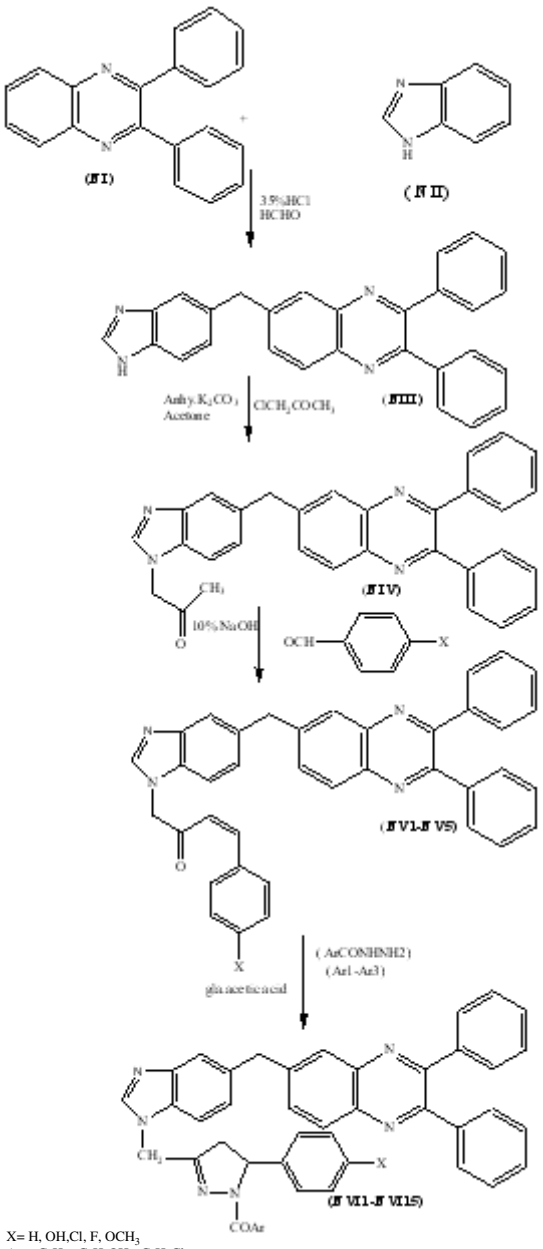
Yield: 60%, m.p: 119 °C, IR (KBr) cm^{-1}: 1770 (C=O str.), 1666 (C=N str.), 1342 (C-N str.), 3037 (Ar-H str.), 3325 (C-H str.) cm^{-1}.^{1}HNMR ($CDCl_3$): 1.8,2.0 (m, 2H, methylene), 3.1,3.8 (S, 4H, methylene), 3.73 (S, 3H, methoxy), 4.9 (m, 1H, methine), 7.5-7.9 (m, 3H, quinoxaline), 6.72-7.9 (m, 19H, Ar-H), 7.06-8.08 (m, 4H, benzimidazole)**.**Mass: m/z: 704.2 (M+) [Found C, 77.9, H, 5.0, N, 11.0, O, 4.3. $C_{46}H_{36}N_6O_2$ requires C, 78.39, H, 5.15, N, 11.92, O, 4.54%].

NVI 6

Yield: 63%, m.p: 109-112°C, IR (KBr) cm^{-1}: 3750 (O-H str.) 1770 (C=O str.), 1666 (C=N str.), 1340(C-N str.), 3037(Ar-H str.), 3325(C-H str.) cm^{-1}. ^{1}HNMR ($CDCl_3$): 1.8,2.0 (m, 2H, methylene), 3.81, 3.8(S, 4H, methylene), 4.9 (m, 1H, methine), 5.1 (S, 1H, Ar-OH), 7.5-7.9 (m, 3H, quinoxaline), 6.9-7.7 (m, 19H, Ar-H), 7.0-8.1 (m, 4H, benzimidazole). Mass: m/z: 690.2 (M+) [Found C, 77.5, H, 4.7, N, 12.2, O, 4.6. $C_{45}H_{34}N_6O_2$ requires C, 78.24, H, 4.96, N, 12.17, O, 4.63%]

NVI 7

Yield: 62%, m.p: 120 °C, IR (KBr) cm^{-1}: 3758 (O-H str.) 1770 (C=O str.), 1666 (C=N str.), 1337 (C-N str.), 3037 (Ar-H str.), 3325 (C-H str.) cm^{-1}. ^{1}HNMR ($CDCl_3$): 1.8,2.0 (m, 2H, methylene), 3.1,3.8(S, 4H, methylene), 4.9 (m, 1H, methine), 5.0 (S, 2H, Ar-OH), 7.5-7.9(m, 3H, quinoxaline), 6.6-7.7(m, 18H,Ar-H), 7.0-8.1 (m, 4H, benzimidazole). Mass: m/z: 706.2 (M+) [Found C, 76.0, H, 4.6, N, 11.2, O, 6.4. $C_{45}H_{34}N_6O_3$ requires C, 76.47, H, 4.85, N, 11.89, O,6.79%].



X= H, OH,Cl, F, OCH_3
Ar= -C_6H_5, -C_6H_4OH, -C_6H_4Cl

Scheme 1

NVI 10

Yield: 59%, m.p: 110-111 °C, IR (KBr) cm^{-1}: 3750 (O-H str.), 1775 (C=O str.), 1660 (C=N str.), 1335 (C-N str.), 3037 (Ar-H str.), 3325 (C-H str.) cm^{-1}. ^{1}HNMR ($CDCl_3$): 1.8,2.0 (m, 2H, methylene), 3.1,3.8 (S, 4H, methylene), 3.73 (S, 3H, methoxy), 4.9 (m, 1H, methine), 5.0 (S, 1H, Ar-OH), 7.5-7.9 (m, 3H, quinoxaline), 6.9-7.7 (m, 18H, Ar-H), 7.0-8.0 (m, 4H, benzimidazole).Mass: m/z: 720.2 (M+) [Found C, 72.0, H, 4.79, N, 11.0, O, 6.64. $C_{46}H_{36}N_6O_3$ requires C, 76.65, H, 5.03, N, 11.66, O, 6.66%]

NVI 11

Yield: 69%, m.p: 110-112 °C, IR (KBr) cm^{-1}: 753 (C-Cl), 1770 (C=O str.), 1660 (C=N str.), 1335(C-N str.), 3037 (Ar-H str.), 3325 (C-H str.) cm^{-1}. ^{1}HNMR ($CDCl_3$): 1.7, 2.0 (m, 2H, methylene), 3.1, 3.8 (S, 4H, methylene), 4.9 (m, 1H, methine), 7.5-7.9 (m, 3H, quinoxaline), 7.0-7.7 (m, 19H, Ar-H), 7.1-8.0 (m, 4H, benzimidazole).Mass: m/z: 708.2 (M+) [Found C, 75.0, H, 4.0, Cl, 4.72, N, 11.0, O, 2.1. $C_{45}H_{33}ClN_6O$ requires C, 76.21, H, 4.69, Cl, 5.0, N, 11.8, O, 2.26%]

NVI 14

Yield: 69%, m.p: 131-132 °C, IR (KBr) cm^{-1}: 750 (C-Cl), 1770 (C=O str.), 1660 (C=N str.), 1335 (C-N str.), 3037 (Ar-H str.), 3325 (C-H str.) cm^{-1}. ^{1}HNMR ($CDCl_3$): 1.8,2.1 (m, 2H, methylene), 3.1,3.8 (S, 4H,methylene), 4.9 (m, 1H, methine), 7.5-7.9 (m, 3H, quinoxaline), 7.0-7.8 (m, 18H, Ar-H), 7.0-8.1 (m, 4H, benzimidazole). Mass: m/z: 742.2 (M+) [Found C, 71.0, H, 4.1, Cl, 9.0, N, 11.0, O, 2.0. $C_{45}H_{32}Cl_2N_6O$ requires C, 72.68, H, 4.34, Cl, 9.53, N, 11.3, O, 2.16%]

NVI 15

Yield: 68%, m.p: 132-124 °C, IR (KBr) cm^{-1}: 755 (C-Cl), 1768 (C=O str.), 1660 (C=N str.), 1332 (C-N str.), 3037 (Ar-H str.), 3325 (C-H str.) cm^{-1}. ^{1}HNMR ($CDCl_3$): 1.8,2.0 (m, 2H, methylene), 3.1,3.8 (S, 4H, methylene), 3.73 (S, 3H,methoxy), 4.9 (m, 1H, methine), 7.5-7.9 (m, 3H, quinoxaline), 6.7-7.8 (m, 18H, Ar-H), 7.0-8.1 (m, 4H, benzimidazole). Mass: m/z: 738.2 (M+) [Found C, 73.0, H, 4.5, Cl, 4.5, N, 11.0, O, 4.10. $C_{46}H_{35}ClN_6O_2$ requires C, 74.74, H, 4.77, Cl, 4.80, N, 11.3, O, 4.33%].

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