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Synthesis, Spectral Studies and Antimicrobial Activity of 2-Aryl-3-(2′-n-butyl-4′-chloro-1′-H-imidazol-5′-yl)-quinoxazolines †

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Abstract: Quinoxazoline derivatives are renowned for their extensive pharmacological activities and substantial industrial importance. Recognizing their multifaceted applications, this study aims to synthesize novel quinoxazoline derivatives, specifically 2-Aryl-3-(2′-n-butyl-4′-chloro-1′-H-imidazol-5′-yl)-quinoxazoline, and investigate their antimicrobial properties. The synthesis process involved the condensation of a precursor molecule (**1a**–**1j**) with bromine (Br_2) in acetic acid (HAc) and 1,2-diaminobenzene, resulting in the formation of the desired quinoxazoline derivatives (**2a**–**2j**). The structural elucidation of the synthesized compounds was carried out using a combination of spectroscopic techniques, including Nuclear Magnetic Resonance (NMR), Infrared (IR) spectroscopy, and Mass Spectrometry (MS), which confirmed the successful formation of the targeted molecules. The antimicrobial efficacy of these new derivatives was evaluated through a series of bioassays against a diverse panel of bacterial and fungal strains.

Keywords: quinoxazoline derivatives; synthesis; antimicrobial activity; condensation reaction; 2-Aryl-3-(2′-n-butyl-4′-chloro-1′-H-imidazol-5′-yl)-quinoxazoline; spectroscopic characterization; medicinal chemistry; pharmaceutical applications

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1. Introduction

The spontaneous cyclocondensation reaction between ortho-phenylenediamine and α,β-dicarbonyl compounds efficiently produces quinoxazoline and benzopyrazine scaffolds with good yields. This reaction was first explored by Hinsberg and Körner [1–3]. quinoxazoline derivatives can also be synthesized via the condensation of ortho-phenylenediamines with 1,2-dihalocarbonyl compounds.

A significant class of heterocyclic compounds have been known for their broad spectrum of biological activities, including CNS depression [4], anti-tubercular [5], analgesic [6], antiproliferative [7], EGFR inhibitors and radiosensitizers [8], anti-leukemic [9], anticonvulsants [10], anti-viral [11], VEGFR-2 inhibitors [12], and antitubulin agents [13].

Dong and coworkers [14] derived new scaffolds of quinoxazolines derivatives and screened for their anticancer activity against cervical cancer (HeLa), human hepatoma cancer cells (SMMC-7721), and leukemia (K562). Liu and coworkers [15] synthesized potential quinoxazoline derivatives and evaluated for their anticancer activity against different cell lines. Newahie and coworkers [16] synthesized newley designed quinoxazoline derivatives and tested for their potential anticancer activity against the breast cancer cell lines. Recent research has focused on developing synthetic routes for novel quinoxazoline with various activities, including antibacterial [17], antimicrobial [18], potential anxiyolytic agents [19], antidiabetic [20], anti-cancer [21], and anti-tumor [22] activities. Pationate

and coworkers [23] investigated some novel derivatives of quinoxazoline with substituted imidazole-substitution and screened against the melanoma cells A375. S. K. Suthar and co-workers [24] reported pharmacological advancement of novel quinoxazoline derivatives in medicinal chemistry. V. V. Matveevskaya et al. [25] highlighted computational design of quinoxazoline-based scaffolds as potent c-Jun N-terminal kinase 3 (JNK-3) inhibitors demonstrating neuroprotective, anti-inflammatory and anti-arthritic activity.

2. Antimicrobial Activity

The antimicrobial activity was determined by cup plate method at a concentration of 50 μg/mL using DMF as a solvent. The activity was taken by Gram positive bacteria *B.megaterium*, *S. aureus*, Gram negative bacteria *Escherichia coli*, and *S. Taphimarium* and antifungal activity against *Aspergillus niger*. The zone of inhibition was measured in mm. The antibacterial activity was compared with the known standard drugs, viz, Ampicillin, Chloramphenicol, Norfloxacin and antifungal activity was compared with known standard drug viz. Fluconazole. The zone of inhibition that displayed by standard drugs are recorded in Table 2.

3. Experimental

Melting points were determined using the open glass capillary method. IR absorption spectra (in cm^{-1}) were obtained on a SHIMADZU-FT-IR-8400 spectrophotometer, covering a frequency range of 4000–400 cm^{-1} using the KBr disc pellet technique. Proton NMR spectra were recorded on a 400 MHz Bruker Avance-III spectrometer, with DMSO-d_6 as the solvent and tetramethylsilane (TMS) as the internal standard. Mass spectra were acquired using a SHIMADZU-GC-MS QP-2010 Ultra. The purity of the synthesized compounds was routinely monitored by thin-layer chromatography (TLC) on silica gel-G.

*3.1. Spectral Studies of 3-(2′-n-Butyl-4′-chloro-1′-H-imidazol-5′-yl)-1-(4″-methoxy phenyl)-prop-2-ene-1-one (**1i**).*

- FT-IR (KBr) (cm^{-1}): 2968 (C-H str. asym); 2864 (C-H str. sym); 3060 (C-H str. aromatic); 1558 (C=C ring skeletal); 1166 (C-H i.p. def); 751 (C-H-str.def); 1220 (C-N str.); 1515 (C=N str.); 3415 (N-H str); 1600 (N-H bending); 1653 (C=O str.); 1459 (CH=CH); 728 (C-Cl); 1250 (C-O-C str.). ^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm: 0.9 (t, 3H, -C<u>H</u>$_3$); 1.2–1.3 (m, 2H, -C<u>H</u>$_2$-CH$_3$); 1.5–1.6 (m, 2H, -C<u>H</u>$_2$-CH$_2$-CH$_3$); 2.6 (t, 2H, -C<u>H</u>$_2$-CH$_2$-CH$_2$-CH$_3$); 12.8 (s, 1H, -N<u>H</u>); 7.4 (d, 1H, -C<u>H</u>=CH-) 7.6 (d, 1H, -CH=C<u>H</u>-); 7.1 (d, 2H, Ar-<u>H</u>); 8.0 (d, 2H, Ar-<u>H</u>); 3.8 (s, 3H, -OC<u>H</u>$_3$). Mass (m/z): 320, 318, 211, 183, 135, 107.

*3.2. Spectral studies of 2-(4″-Methoxy phenyl)-3-(2′-n-butyl-4′-chloro-1′-H-imidazol-5′-yl)-quinoxazoline (**2i**).*

- FT-IR (KBr) (cm^{-1}): 2924 (C-H str. Asym.); 2857 (C-H str. Sym.); 1457 (C-H str. def.); 3085 (C-H str. aromatic); 1602 (C=C ring skeletal); 1168 (C-H i.p. def.); 730 (C-H o.o.p. str. def.); 1340 (C-N str.); 1553 (C=N str.); 3313 (N-H str.); 1653 (N-H bending); 698 (C-Cl); 1252 (C-O-C str.). ^{1}H NMR (400 MHz, DMSO-d$_6$) δ/ppm: 0.8–0.9 (t, 3H, -C<u>H</u>$_3$); 1.3 (m, 2H, -C<u>H</u>$_2$-CH$_3$); 1.6 (m, 2H, -C<u>H</u>$_2$-CH$_2$-CH$_3$); 2.6 (t, 2H, -C<u>H</u>$_2$-CH$_2$-CH$_2$-CH$_3$); 12.8 (s, 1H, -N<u>H</u>); 3.8 (s, 3H, -OC<u>H</u>$_3$); 7.3–7.4 (d, 2H, Ar-<u>H</u>); 7.6 (d, 2H, Ar-<u>H</u>); 8.0 (d, 2H, Ar-<u>H</u>); 7.1 (d, 2H, Ar-<u>H</u>). Mass (m/z): 395, 393, 285, 157, 128, 107.

4. Materials and Method

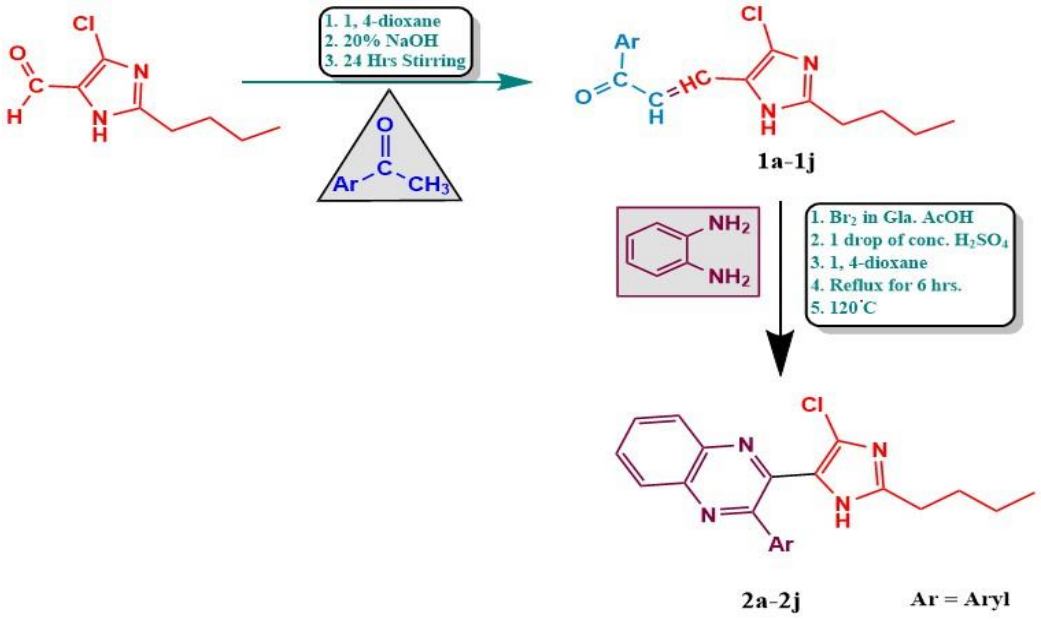
A series of novel quinoxazoline derivatives (**2a**–**2j**), specifically 2-Aryl-3-(2′-n-butyl-4′-chloro-1′H-imidazol-5′-yl)-quinoxazoline, were successfully synthesized through a condensation reaction of 3-(2′-n-butyl-4′-chloro-1′H-imidazol-5′-yl)-1-aryl-prop-2-ene-1-ones with bromine in glacial acetic acid (Gla. HAc) and ortho-phenylenediamine (OPD). The structures of the synthesized products (**2a**–**2j**) were confirmed using IR, ^{1}H NMR, and mass spectrometry, along with TLC analysis.

*4.1. Synthesis of 3-(2′-n-Butyl-4′-chloro-1′-H-imidazol-5′-yl)-1-(4″-methoxy phenyl)-prop-2-ene-1-one (**1i**)*

A mixture of 2-(n-butyl)-4-chloro-5-carboxaldo-1H-imidazole (1.87 gm, 0.01 M); 4-Methoxy acetophenone (1.50 gm, 0.01 M); 1, 4-dioxane (20 mL) and 20% NaOH (20 mL) was stirred for 24 h at room temperature. Completion of reaction was monitored with TLC. The reaction mixture was poured into crushed ice, filtered and dried. The product was crystallized in 1, 4-dioxane. Yield: 77%; M.P.: 87 °C; (*Required*: C: 64.05; H: 6.01; N: 8.79%; $C_{17}H_{19}ClN_2O_2$; Found: C: 64.05; H: 6.01; N: 8.70%). Similarly, other compounds (**1a–1j**) were synthesized. Chalcones physical data and antimicrobial activities are published in another journal.

*4.2. Synthesis of 2-(4″-Methoxy phenyl)-3-(2′-n-butyl-4′-chloro-1′-H-imidazol-5′-yl)-quinoxazoline (**2i**)*

A mixture of 3-(2′-n-butyl-4′-chloro-1′-H-imidazol-5′-yl)-1-(4″-methoxy phenyl)-prop-2-ene-1-one (3.19 gm, 0.01 M); 1, 4-dioxane (20 mL); Br_2 in glacial acetic acid (10 mL); ortho-phenylenediamine (1.08 gm, 0.01 M) and 1 drop of conc. H_2SO_4 was taken in a RBF. The reaction mixture was refluxed in oil bath for 6 h at 120 °C. On successful completion of the above reaction, the solution was poured into ice cold water. The products were formed, filtered and dried (Scheme 1). Crystallization of products was carried out in 1, 4-dioxane. Yield: 79%; M.P.: 289 C; (Required: C: 67.26; H: 5.39; N: 14.26%; $C_{22}H_{21}ClN_4O$; Found: C: 67.24; H: 5.38; N: 14.20%). Similarly, other compounds (**2a–2j**) were synthesized. The physical data and antimicrobial activity of (**2a–2j**) represented in Table 1.



Scheme 1. Synthesis of 2-Aryl-3-(2′-n-butyl-4′-chloro-1′-H-imidazol-5′-yl)-quinoxazolines.

Table 1. The physical data and antimmicrobial activity of compounds (**2a–2j**). Zone of inhibition in mm.

Sr. No.	Ar.	MF	MP	% Nitrogen Yield		Antibacterial Activity				Anti-Fungal Activity
				Calc.	Found	Gram + ve		Gram − ve		
						a	b	c	d	e
2a	C_6H_5-	$C_{21}H_{19}ClN_4$	190	15.44	15.39	14	17	18	12	15
2b	3-OH-C_6H_4-	$C_{21}H_{19}ClN_4O$	122	14.79	14.70	11	16	18	17	18
2c	4-OH-C_6H_4-	$C_{21}H_{19}ClN_4O$	131	14.79	14.65	10	12	15	18	17
2d	3-NH_2-C_6H_4-	$C_{21}H_{20}ClN_5$	211	18.53	18.50	**20**	14	19	15	16

2e	4-Cl-C_6H_4-	$C_{21}H_{18}Cl_2N_4$	236	14.10	14.08	16	**20**	**21**	18	**22**
2f	4-Br-C_6H_4-	$C_{21}H_{18}BrClN_4$	251	12.68	12.60	17	16	17	17	**20**
2g	3-NO_2-C_6H_4-	$C_{21}H_{18}ClN_5O_2$	287	17.17	17.10	13	21	17	17	**20**
2h	4-NO_2-C_6H_4-	$C_{21}H_{18}ClN_5O_2$	256	17.17	17.02	19	13	**20**	18	**21**
2i	4-OCH_3-C_6H_4-	$C_{22}H_{21}ClN_4O$	289	14.26	14.20	**20**	19	18	**21**	19
2j	3-NH_2,2-OH-C_6H_3-	$C_{21}H_{20}ClN_5O$	>300	17.78	17.71	**22**	**23**	17	**25**	17

[1] Ar. = Aryl, MF = Molecular Formula, MP = Melting Point in (°C), a = *Bacillus megaterium*, b = *Stephylococcus aureus*, c = *Salmonella taphimurim*, d = *Escherichia coli*, e = *Aspergillus niger*.

Table 2. Compounds showing comparable antimicrobial activity with known standard drugs.

	Compounds	**Antibacterial Activity**				**Antifungal Activity**
		Gram + ve Bacteria		**Gram − ve Bacteria**		
		B. megaterium	***S. aureus***	***S. taphimurim***	***E. coli***	***A. niger***
	2a–2j	**2d, 2i, 2j**	**2e, 2g, 2j**	**2e, 2h**	**2i, 2j**	**2e, 2f, 2g, 2h**
	Activity of Standard Drugs:					
1	Ampicillin (50 µg/mL)	27	26	25	28	-
2	Chloramphenicol (50 µg/mL)	29	28	27	25	-
3	Norfloxacin (50 µg/mL)	32	30	24	27	-
4	Fluconazole (50 µg/mL)	-	-	-	-	26

5. Results and Discussions

5.1. ^{1}H NMR Spectra

- ^{1}H NMR spectra of 3-(2′-n-butyl-4′-chloro-1′-H-imidazol-5′-yl)-1-(4″-methoxy phenyl)-prop-2-ene-1-one (**1i**) and 2-(4″-Methoxy phenyl)-3-(2′-n-butyl-4′-chloro-1′-H-imidazol-5′-yl)-quinoxazoline (**2i**) have been obtained in solvent DMSO-d_6 are summarized in experimental section. In ^{1}H NMR spectra of chalcone (**1i**), the number of aromatic hydrogens atoms are 7-H (4″-methoxy phenyl), 1-H (1′-H-imidazol) and the number of aliphatic hydrogen atoms are 11-H (2′-n-butyl and prop-2-ene-1-one). Where as in 1H NMR spectra of synthesized quinoxazoline derivative (**2i**), the number of aromatic hydrogen atoms are 11-H (7-H of 4″-methoxy phenyl and 4-H of quinoxazoline), 1-H (1′-H-imidazol) and the number of aliphatic hydrogen atoms are 9-H (2′-n-butyl). The peak of synthesized quinoxazolines are found in the range of 7.3 to 7.6 δ ppm. These hydrohen exhibits doublet of doublet that is not ovserved in chalcones spectra. The peaks of methoxy proton of the methoxy phenyl group in synthesized quinoxazoline and chalcone is appeared at 3.8 δ ppm and the aromatic hydrogen atoms of phenyl protons from methoxy phenyl group appears in the range of 7.1 to 8.0 δ ppm. Two peaks of prop-2-ene-1-one of chalcone in the range of 7.4 to 7.6 δ ppm exhibits doublet splitting which is not appeared in the spectra of synthesized quinoxazoline. Indicating the formation of quinoxazolines.

5.2. FT-IR Spectra

- FT-IR spectral data of chalcone (**1i**) and synthesized quinoxazoline (**2i**) are expressed in the experimental section. The peaks of chalcone containig υ(CH=CH) group is observed at ~1459 cm^{-1} which is not found in the spectra of synthesized quinoxazoline showing formation of quinoxazoline from chalcone. The band of C=C ring skeletal in chalcone is found at ~1558 cm^{-1} which is shifted to ~1602 cm^{-1} for synthesized quinoxazoline. The stretching band due to carbonyl group (C=O) in chalcone is found at ~1653 cm^{-1} which is not found in spectra of quinoxazoline indicating conversion of chalcone in a heterocyclic ring. Aromatic bending peaks (=C-H) of chalcone and synthesized quinoxazoline are observed in the range of 730 to 770 cm^{-1}. The spectra of chalcone and synthesized quinoxazoline show bands in the range of 500 to 800 cm^{-1}, 1050 to 1200 cm^{-1} and 3200 to 3500 cm^{-1} due to (C-Cl), (C-O-C str.) and (N-H str.)

respectively. The υC–$H_{ar.}$ stretching band of the chalcone is observed at 3060 cm^{-1} and shifted to 3085 cm^{-1} in the spectra of quinoxazoline.

5.3. Mass Spectra

- Mass spectral data of chalcone (**1i**) and synthesized quinoxazoline (**2i**) are expressed in the experimental section. The mass spectrum of chalcone (**1i**) shows molecular ion peak at 318 *m*/*z* and 320 *m*/*z* due to $[M]^+$ and [M + 2] respectively. The peak at 211 *m*/*z* indicate loss of 4-methoxy phenyl from chalcone. The peaks at 107 *m*/*z*, 135 *m*/*z*, and 183 *m*/*z* corresponds to 4-methoxy phenyl, 4-methoxy phenone and 2-n-butyl-4-chloro-1-H-imidazol-5-yl respectively.
- The mass spectrum of synthesized quinoxazoline (**2i**) compound shows a molecular ion peak at 393 *m*/*z* and 395 *m*/*z* due to $[M]^+$ and [M + 2] respectively, indicating that one chlorine atom is present in the synthesized compound. The peak at 285 *m*/*z* is due to loss of 4-methoxy phenyl attached to quinoxazoline. The peaks at 157 *m*/*z*, and 107 *m*/*z* is due to 2-n-butyl-4-chloro-1-H-imidazol-5-yl and 4-mehoxy phenyl respectively. The peak at 128 *m*/*z* shows fragment ion of quinoxazoline.

6. Conclusions

The study emphasis on the synthesis, spectral studies and antimicrobial activity of novel quinoxazoline derivatives. The compounds—**2d**, **2e**, **2f**, **2g**, **2h**, **2i**, **2j** have showed potential remarkable antibacterial and antifungal activity with compared to known standard drugs e.g., Ampicillin, Chloramphenicol, Norfloxacin and Fluconazole at same concentration 50 μg/mL.

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References

1. Korner and Hinsberg,; Ber., 17; ref. 593; (1884); Ber., 40; 4830; (1907).
2. Aichhorn, S.; Himmelsbach, M.; Schofberger, W. Synthesis of quinoxalines or quinolin-8-amines from N-propargyl aniline derivatives employing tin and indium chlorides. *Org. Biomol. Chem.* **2015**, *13*, 9373–9380.
3. Zayed, M.F. Chemistry, Synthesis, and Structure Activity Relationship of Anticancer quinoxalines. *Chemistry* **2023**, *5*, 2566–2587.
4. Kanwal, A.; Afzal, U.; Zubair, M.; Imran, M.; Rasool, N. Synthesis of anti-depressant molecules via metal-catalyzed reactions: A review. *RSC Adv.* **2024**, *14*, 6948–6971.
5. Wang, T.; Tang, Y.; Yang, Y.; An, Q.; Sang, Z.; Yang, T.; Liu, P.; Zhang, T.; Deng, Y.; Luo, Y. Discovery of novel anti-tuberculosis agents with pyrrolo [1,2-a] quinoxaline-based scaffold. *Bioorganic Med. Chem. Lett.* **2018**, *28*, 2084–2090.
6. Chawla, G.; Gupta, O.; Pradhan, T. A review on multipurpose potential of bioactive heterocycle quinoxaline. *ChemistrySelect* **2023**, *8*, e202301401.
7. Syam, Y.M.; Anwar, M.M.; El-Karim, S.S.A.; Elokely, K.M.; Abdelwahed, S.H. New quinoxaline-based derivatives as PARP-1 inhibitors: Design, synthesis, antiproliferative, and computational studies. *Molecules* **2022**, *27*, 4924.
8. Ghorab, M.M.; Abdel-Kader, M.S.; Alqahtani, A.S.; Soliman, A.M. Synthesis of some quinazolinones inspired from the natural alkaloid L-norephedrine as EGFR inhibitors and radiosensitizers. *J. Enzym. Inhib. Med. Chem.* **2021**, *36*, 218–238.
9. Guillon, J.; Savrimoutou, S.; Albenque-Rubio, S.; Pinaud, N.; Moreau, S.; Desplat, V. Synthesis, crystal structure and anti-leukemic activity of 1, 3-dihydro-1-{1-[4-(4-phenylpyrrolo [1, 2-a] quinoxalin-3-yl) benzyl] piperidin-4-yl}-2 H-benzimidazol-2-one. *Molbank* **2022**, *2022*, M1333.

10. Abulkhair, H.S.; Elmeligie, S.; Ghiaty, A.; El-Morsy, A.; Bayoumi, A.H.; Ahmed, H.E.A.; El-Adl, K.; Zayed, M.F.; Hassan, M.H.; Akl, E.N.; et al. In vivo-and in silico-driven identification of novel synthetic quinoxalines as anticonvulsants and AMPA inhibitors. *Arch. Pharm.* **2021**, *354*, 2000449.
11. Montana, M.; Montero, V.; Khoumeri, O.; Vanelle, P. quinoxaline derivatives as antiviral agents: A systematic review. *Molecules* **2020**, *25*, 2784.
12. Abdullahi, S.H.; Uzairu, A.; Danazumi, A.U.; Finbarrs-Bello, E.; Umar, A.B.; Shallangwa, G.A.; Uba, S. Computational design of quinoxaline molecules as VEGFR-2 inhibitors: QSAR modelling, pharmacokinetics, molecular docking, and dynamics simulation studies. *Biocatal. Agric. Biotechnol.* **2023**, *51*, 102787.
13. Goel, K.K.; Hussain, A.; Altamimi, M.A.; Rajput, S.K.; Sharma, P.P.; Kharb, R.; Mahdi, W.A.; Imam, S.S.; Alshehri, S.; Alnemer, O.A.; et al. Identification of potential antitubulin agents with anticancer assets from a series of imidazo [1,2-a] quinoxaline derivatives: In silico and in vitro approaches. *Molecules* **2023**, *28*, 802.
14. Qi, J.; Dong, H.; Huang, J.; Zhang, S.; Niu, L.; Zhang, Y.; Wang, J. Synthesis and biological evaluation of N-substituted 3-oxo-1, 2, 3, 4-tetrahydro-quinoxaline-6-carboxylic acid derivatives as tubulin polymerization inhibitors. *Eur. J. Med. Chem.* **2018**, *143*, 8–20.
15. Ahmed, E.A.; Mohamed, M.F.A.; Omran, A.; Salah, H. Synthesis, EGFR-TK inhibition and anticancer activity of new quinoxaline derivatives. *Synth. Commun.* **2020**, *50*, 2924–2940.
16. El Newahie, A.M.S.; Nissan, Y.M.; Ismail, N.S.M.; El Ella, D.A.A.; Khojah, S.M.; Abouzid, K.A.M. Design and synthesis of new quinoxaline derivatives as anticancer agents and apoptotic inducers. *Molecules* **2019**, *24*, 1175.
17. Katariya, D.K.; Vyas, A.K.; Bhanderi, P.; Shah, P.M.; Khoyanee, A.; Mevada, B.; Shah, M.; Khunt, R. Unveiling Synthesis, Characterization, and Assessing Antimicrobial Efficacy of quinoxaline-Based Oxazole Derivatives. *Russ. J. Bioorganic Chem.* **2024**, *50*, 1573–1582.
18. Khatoon, H.; Malek, E.A.; Faudzi, S.M.; Rukayadi, Y. Synthesis of a series of quinoxaline derivatives and their antibacterial effectiveness against pathogenic bacteria. *ChemistrySelect* **2024**, *9*, e202305073.
19. Maltsev, D.V.; Skripka, M.O.; Spasov, A.A.; Vassiliev, P.M.; Perfiliev, M.A.; Divaeva, L.N.; Zubenko, A.A.; Morkovnik, A.S.; Klimenko, A.I.; Miroshnikov, M.V.; et al. Design, Synthesis and Pharmacological Evaluation of Novel C^2,C^3-quinoxaline Derivatives as Promising Anxiolytic Agents. *Int. J. Mol. Sci.* **2022**, *23*, 14401.
20. Bouali, N.; Hammouda, M.B.; Ahmad, I.; Ghannay, S.; Thouri, A.; Dbeibia, A.; Patel, H.; Hamadou, W.S.; Hosni, K.; Snoussi, M.; et al. Multifunctional derivatives of Spiropyrrolidine tethered Indeno-quinoxaline heterocyclic hybrids as potent antimicrobial, antioxidant and antidiabetic agents: Design, synthesis, in vitro and in silico approaches. *Molecules* **2022**, *27*, 7248.
21. Bhat, Z.R.; Kumar, M.; Sharma, N.; Yadav, U.P.; Singh, T.; Joshi, G.; Pujala, B.; Raja, M.; Chatterjee, J.; Tikoo, K.; et al. In Vivo Anticancer Evaluation of 6b, a Non-Covalent Imidazo [1, 2-a] quinoxaline-Based Epidermal Growth Factor Receptor Inhibitor against Human Xenograft Tumor in Nude Mice. *Molecules* **2022**, *27*, 5540.
22. Fan, D.; Liu, P.; Jiang, Y.; He, X.; Zhang, L.; Wang, L.; Yang, T. Discovery and SAR study of quinoxaline–arylfuran derivatives as a new class of antitumor agents. *Pharmaceutics* **2022**, *14*, 2420.
23. Patinote, C.; Deleuze-Masquéfa, C.; Kaddour, K.H.; Vincent, L.-A.; Larive, R.; Zghaib, Z.; Guichou, J.-F.; Assaf, M.D.; Cuq, P.; Bonnet, P.-A. Imidazo [1, 2-a] quinoxalines for melanoma treatment with original mechanism of action. *Eur. J. Med. Chem.* **2021**, *212*, 113031.
24. Suthar, S.K.; Chundawat, N.S.; Singh, G.P.; Padrón, J.M.; Jhala, Y.K. quinoxaline: A comprehension of current pharmacological advancement in medicinal chemistry. *Eur. J. Med. Chem. Rep.* **2022**, *5*, 100040.
25. Matveevskaya, V.V.; Pavlov, D.I.; Kovrizhina, A.R.; Sukhikh, T.S.; Sadykov, E.H.; Dorovatovskii, P.V.; Lazarenko, V.A.; Khlebnikov, A.I.; Potapov, A.S. Experimental and Computational Investigation of the Oxime Bond Stereochemistry in c-Jun N-terminal Kinase 3 Inhibitors 11 H-Indeno [1,2-b] quinoxalin-11-one Oxime and Tryptanthrin-6-oxime. *Pharmaceutics* **2023**, *15*, 1802.