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Synthesis and Biological Screening of New 2-(5-Aryl-1-phenyl-1*H*-pyrazol-3-yl)-4-aryl Thiazole Derivatives as Potential Antimicrobial Agents

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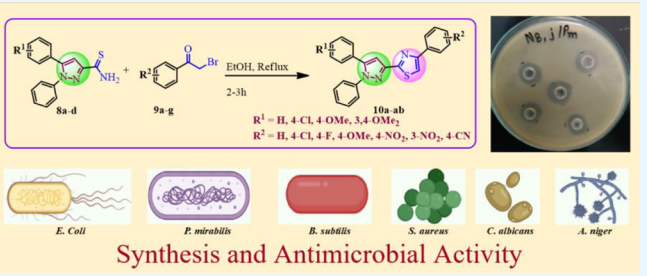
ABSTRACT: A new series of 2-(5-aryl-1-phenyl-1*H*-pyrazol-3-yl)-4-aryl thiazoles (**10a−ab**) have been synthesized by a cyclocondensation reaction of 5-aryl-1-phenyl-1*H*-pyrazole-3-carbothioamide (**7a−d**) with substituted phenacyl bromide (**8a−f**). The structure of newly synthesized 2-(5-aryl-1-phenyl-1*H*-pyrazol-3-yl)-4-aryl thiazole (**10a−ab**) derivatives was characterized by spectroscopic analysis. The compounds **10a−ab** were evaluated for *in vitro* antibacterial activity against *Escherichia coli* (NCIM 2574), *Proteus mirabilis* (NCIM 2388), *Bacillus subtilis* (NCIM 2063), *Staphylococcus aureus* (NCIM 2178), and *in vitro* antifungal activity against *Aspergillus niger* (ATCC 504) and *Candida albicans* (NCIM 3100). Among the twenty-eight pyrazolyl-thiazole derivatives, six compounds, **10g**, **10h**, **10i**, **10j**, **10o**, and **10t**, showed good activity against *P. mirabilis*; four compounds **10q**, **10u**, **10y**, and **10z** showed good activity against *S. aureus*; and twenty-four derivatives showed good antifungal activity against *A. niger*. Compounds **10g**, **10q**, **10r**, **10s**, and **10ab** showed comparable activity with respect to the reference drug Ravuconazole. Thus, the significant antimicrobial activity of 2-(5-aryl-1-phenyl-1*H*-pyrazol-3-yl)-4-aryl thiazole (**10a−ab**) derivatives prompted that these scaffolds could assist in the development of lead compounds to treat microbial infections.



1. INTRODUCTION

Two or more bioactive scaffolds clubbed in one molecule play a significant role in the development of new drugs. Nitrogen-containing heterocyclic scaffolds are continuously utilized in the field of drug discovery and development.[1−3] It is a widely accepted fact that multidrug resistance (MDR) has developed against bacterial and fungal species. In the post-COVID-19 pandemic, this threat attracted significant attention. It has become momentous to explore novel antimicrobial agents to meet the needs of the growing human population and improve overall health. Heterocyclic compounds account for a broad spectrum of biological activities. Among them, five-membered heterocyclic compounds containing nitrogen like pyrazole displayed significant biological activities. Naturally occurring pyrazoles and their synthetic derivatives are well-known to have a broad spectrum of biological activities such as antimycobacterial,[4−6] antimicrobial,[7] anti-inflammatory,[8] anticancer,[9] and antimalarial[10] activities. In recent years, some of the FDA-approved and commercialized drugs, including patented ones, have been developed from pyrazole derivatives (Figure 1).

The thiazole pharmacophore is present in many natural and synthetic compounds. Thiazoles and their derivatives have attracted continuing interest over the years because of their varied biological activities. Representative examples of thiazole-containing marketed drugs are showcased in Figure 1. Its derivatives have a wide range of biological activities such as antimicrobial,[11] antituberculosis,[12] anticancer,[13] antiviral,[14] antidiabetic,[15] antimalarial,[16] antitrypanosomal,[17] anti-inflammatory,[18] analgesic,[19] antioxidant,[20] and anticonvulsant.[21]

The pyrazole ring clubbed with other heterocycles is a privileged pharmacophore for the development of new lead molecules.[22−25] The pyrazole-tethered thiazole (Figure 2) has received much attention in recent years due to its remarkable biological activities such as antimicrobial,[26−30] antibiofilm,[22] as an apoptosis inducer,[31] anti-inflammatory,[29,32] antitubercular,[33] and antimycobacterial[34] activities. Considering the efficiency of pyrazole and thiazole clubbed derivatives, our studies have been focused on the synthesis and bioevaluation of these derivatives by a hybrid approach as possible bioactive molecules. A literature review reveals that the 2-position of thiazole is not clubbed at the 3-position of pyrazole. This information enlightened us to synthesize such pyrazolyl thiazole derivatives and explore their antimicrobial activities. Therefore, in the present work, twenty-eight derivatives of 2-

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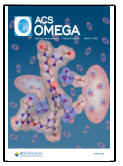

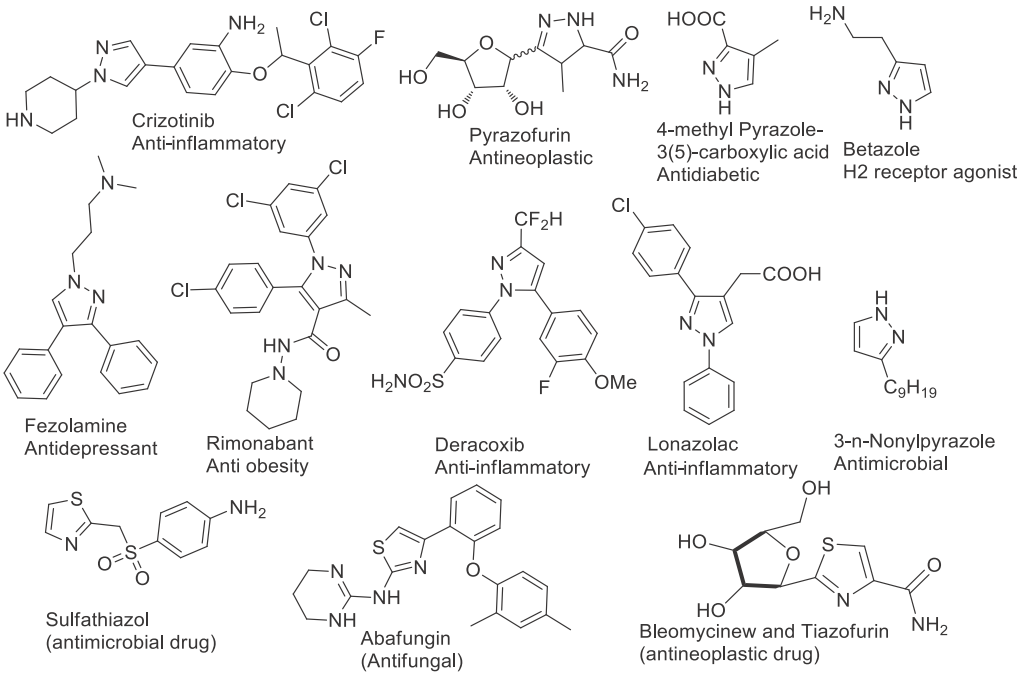

Figure 1. Marketed drugs containing pyrazole, thiazole, and pyrazole-containing natural products.

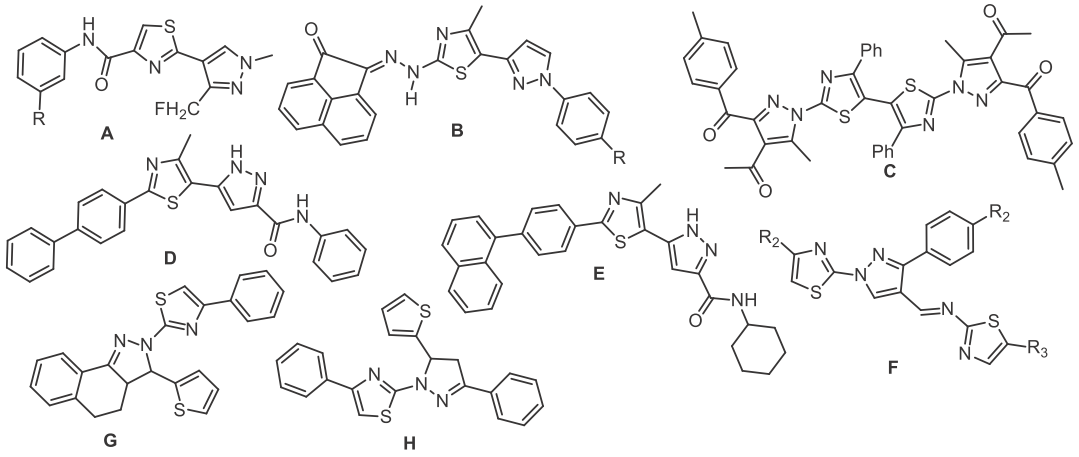

Figure 2. Pyrazole-thiazole clubbed derivatives A−H showing antimicrobial activity.

(5-aryl-1-phenyl-1*H*-pyrazol-3-yl)-4-aryl thiazole were synthesized and screened for their biological activities.

2. RESULTS AND DISCUSSION

2.1. Chemistry. The 2-(5-aryl-1-phenyl-1*H*-pyrazol-3-yl)-4-aryl thiazole (**10a−ab**) derivatives were synthesized as presented in Schemes 1 and 2. Substituted acetophenones **1a−d** upon reaction with diethyl oxalate (**2**) and potassium *t*-butoxide in tetrahydrofuran (THF) at 0 °C to room temperature gave ethyl 2,4- dioxo-4-arylbutanoates **3a−d**. 1,3-Diketoester compounds **3a−d** upon reaction with phenylhydrazine in ethanol gave ethyl 5-aryl-1-phenyl-1*H*-pyrazole-3-carboxylates **4a−d**. The carboethoxy group of pyrazoles **4a−d** was reduced by $LiAlH_4$ in THF and gave (5-aryl-1-phenyl-1*H*-pyrazol-3-yl)methanols, **5a−d**. The pyrazolyl-methanols **5a−d** upon selective oxidation reaction with 2-iodoxybenzoic acid (IBX) in dimethyl sulfoxide gave 5-aryl-1-phenyl-1*H*-pyrazole-3-carbaldehydes, **6a−d**. The aldehyde group of compounds **6a−d** was converted to nitriles **7a−d** by using liq. NH_3 and I_2 in THF.

The pyrazole-3-carbonitriles, **6a−d**, upon reaction with hydrogen sulfide in pyridine gave 5-(4-chlorophenyl)-1-phenyl-1*H*-pyrazole-3-carbothioamides (**8a−d**). The carbothioamides **8a−d** on cyclocondensation reaction with substituted phenacyl bromides **9a−g** in ethanol furnished by reaction with aromatic esters furnished target compounds 2-(5-aryl-1-phenyl-1*H*-pyrazol-3-yl)-4-aryl thiazole (**10a−ab**). The physical data of the synthesized compounds are presented in Table 1. The structure of all synthesized compounds was characterized by IR, NMR, and mass spectral analysis. All the synthesized compounds were screened for antimicrobial activity.

As a representative, the ^{1}H NMR spectrum of 5-(4-chlorophenyl)-3-(4-(4-fluorophenyl)thiazol-2-yl)-1-phenyl-1*H*-pyrazole (**10j**, Figure 3) revealed two singlets in the aromatic region at δ 7.17 and 7.42 assigned to the pyrazole C4 and thiazole C5 protons, respectively. The five protons of the

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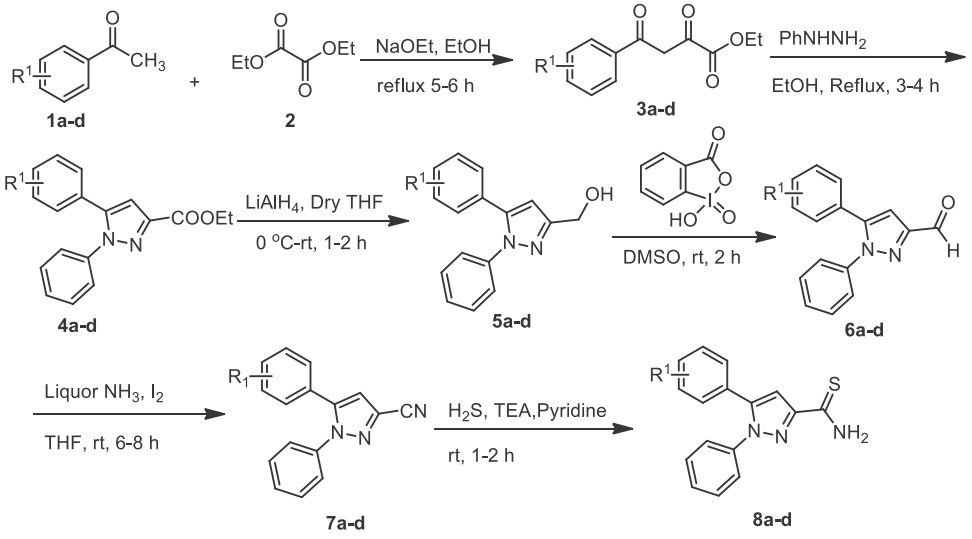
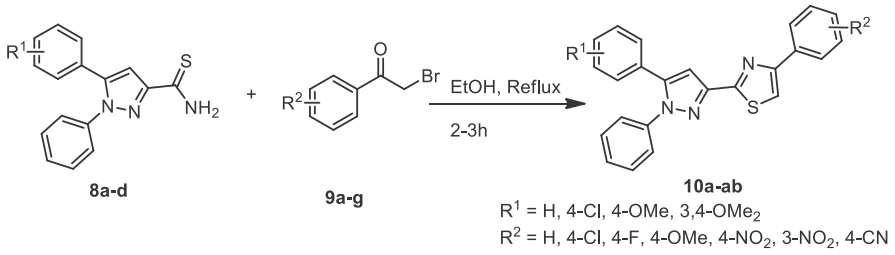
Scheme 1. Synthesis of 5-Aryl-1-phenyl-1*H*-pyrazole-3-carbothioamides, 8a−d



Scheme 2. Synthesis of 2-(5-Aryl-1-phenyl-1*H*-pyrazol-3-yl)-4-aryl Thiazoles, 10a−ab



phenyl ring appeared as multiplates from δ 7.41 to 7.35. The two doublets appeared at δ 7.21 and 7.31, each integrated for two protons assigned to the C2′,C6′ and C3′,C5′ protons of the 4-chlorophenyl ring, respectively. The characteristics of $^{1}H-^{19}F$ coupling are observed for the protons of the 4-fluorophenyl ring. The C2″,C6″ and C3″,C5″ protons of the 4-fluorophenyl ring resonated as a double doublet and a triplet at δ 7.97 and 7.14, respectively. The ^{13}C NMR spectrum of compound **10j** showed characteristic C−F coupling. The signals appeared at δ 163.70, 161.73 ($^{1}J_{C-F}$ = 248.22 Hz) assigned to C4″ carbon, δ 130.73, 130.70 ($^{4}J_{C-F}$ = 3.78 Hz) assigned to C1″ carbon, δ 128.20, 128.13 ($^{3}J_{C-F}$ = 8.82 Hz) assigned to C2″,C6″ carbons, and δ 115.72, 115.55 ($^{2}J_{C-F}$ = 21.42 Hz) assigned to C3″,C5″ carbons. The carbons of phenyl, 4-chlorophenyl, thiazole, and the pyrazole ring resonated from δ 106.08 to 161.24. The structure of compound **10j** was confirmed by HRMS, showing m/z = 432.0738 $(M + H)^+$ and 434.0724 $(M + 2 + H)^+$. The structure of all synthesized compounds was confirmed accordingly.

2.2. Biology. *2.2.1. Antimicrobial Activity.* The newly synthesized 2-(5-aryl-1-phenyl-1*H*-pyrazol-3-yl)-4-aryl thiazole (**10a−ab**) derivatives were screened for antimicrobial activity against Gram-negative bacteria *E. coli* and *P. mirabilis* and Gram-positive bacteria *S. aureus* and *B. subtilis* using the well diffusion method.[35,36] Streptomycin and DMSO were used as the positive and negative control, respectively. All the test solutions were prepared in DMSO at 1000 μg/mL concentrations, and the wells were filled with 80 μL of the samples. The result of antimicrobial activity in the zone of inhibition (mm) has been presented in Table 2. The antimicrobial activity results analysis of compounds **10a−ab** exposed that most of the compounds showed moderate to good activity against *P. mirabilis*, *S. aureus*, and *A. niger* strains and were found to be less active against *E. coli*, *B. subtilis*, and *C. albicans*.

The synthesized compounds were further evaluated for antimicrobial activity in minimum inhibitory concentration (MIC) against *P. mirabilis*, *S. aureus*, and *A. niger*. The results of the MIC are presented in Table 3.

From the structure−activity analysis relationship, the unsubstituted phenyl group at the 5-position of pyrazole and the substituted phenyl group at the 4-position of thiazole, among the compounds 4-aryl-2-(1,5-diphenyl-1*H*-pyrazol-3-yl)thiazoles **10a−g** against the *P. mirabilis* compounds **10a** (R^1 = H), **10c** (R^1 = 4-F), **10d** (R^1 = 4-OCH_3), and **10e** (R^1 = 4-NO_2), showed moderate activity, and compound **10g** (R^1 = 4-CN) showed good activity. All **10a−g** derivatives showed good activity against *A. niger* with an MIC of 62.5−31.25 μg/mL. The phenyl group at the 5-position of pyrazole was substituted by 4-chlorophenyl, from the compounds 4-aryl-2-(5-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-3-yl)thiazoles (**10h−n**), and compounds **10h** (R^1 = H) and **10j** (R^1 = 4-F) showed good activity against *P. mirabilis* and *A. niger* with an MIC of 62.5 μg/mL. Compound **10i** (R^1 = 4-Cl) showed good activity against *P. mirabilis* and *A. niger* with an MIC of 62.5 μg/mL and moderate activity against *S. aureus*. Compound **10k** (R^1 = 4-OCH_3) showed moderate activity against *P. mirabilis*, *S. aureus*, and *A. niger*. Compounds **10l** (R^1 = 4-NO_2), **10m** (R^1 = 3-NO_2), and **10n** (R^1 = 4-CN) showed good activity against *A. niger* with an MIC of 62.5 μg/mL and moderate activity against *P. mirabilis*. The compound **10l** also showed moderate activity

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Table 1. Yield, Melting Point, and Physical Nature of Compounds 10a−ab

compd	R_1	R_2	yield (%)	MP (°C)	physical nature
10a	H	H	85	198−200	Pale pink solid
10b	H	Cl	76	180−182	White solid
10c	H	F	62	174−176	White solid
10d	H	4-OMe	73	156−158	Pale yellow solid
10e	H	4-NO_2	79	>210	Yellow solid
10f	H	3-NO_2	80	160−162	White solid
10g	H	4-CN	82	194−196	Pale pink solid
10h	4-Cl	H	81	170−172	White solid
10i	4-Cl	Cl	79	102−104	White solid
10j	4-Cl	F	65	158−160	White solid
10k	4-Cl	4-OMe	73	150−152	Off-white solid
10l	4-Cl	4-NO_2	68	188−190	White solid
10m	4-Cl	3-NO_2	78	218−220	White solid
10n	4-Cl	4-CN	70	>210	Off-white solid
10o	4-OCH_3	H	75	178−180	Off-white solid
10p	4-OCH_3	Cl	77	110−112	White solid
10q	4-OCH_3	F	69	158−160	White solid
10r	4-OCH_3	4-OMe	76	176−178	White solid
10s	4-OCH_3	4-NO_2	80	160−162	Yellow solid
10t	4-OCH_3	3-NO_2	78	172−174	Pale yellow solid
10u	4-OCH_3	4-CN	63	194−196	Pale pink solid
10v	3,4-$(OCH_3)_2$	H	65	180−182	Pale brown solid
10w	3,4-$(OCH_3)_2$	Cl	78	146−148	Pale brown solid
10x	3,4-$(OCH_3)_2$	F	65	142−144	White solid
10y	3,4-$(OCH_3)_2$	4-OMe	72	158−160	White solid
10z	3,4-$(OCH_3)_2$	4-NO_2	67	154−156	Pale yellow solid
10aa	3,4-$(OCH_3)_2$	3-NO_2	78	160−162	Pale yellow solid
10ab	3,4-$(OCH_3)_2$	4-CN	65	158−160	White solid

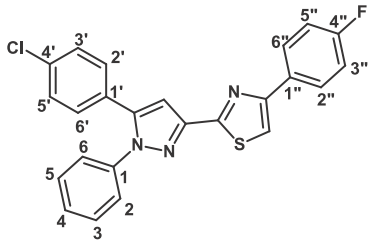

Figure 3. Structure of 5-(4-chlorophenyl)-3-(4-(4-fluorophenyl)-thiazol-2-yl)-1-phenyl-1*H*-pyrazole, **10j**.

against *S. aureus*. The phenyl group at the 5-position of the pyrazole was substituted by 4-methoxy phenyl, from the compounds 4-aryl-2-(5-(4-methoxyphenyl)-1-phenyl-1*H*-pyrazol-3-yl)thiazole (**10o−u**), and against *P. mirabilis* and *A. niger* strains the compounds **10o** (R^1 = H) and **10p** (R^1 = 4-Cl) showed good and moderate activity, respectively. The compounds **10q** (R^1 = F), **10r** (R^1 = 4-OCH_3), and **10s** (R^1 = 4-NO_2) showed good activity against *A. niger* with an MIC of 31.25 μg/mL, which was comparable activity with respect to the reference drug Ravuconazole. These compounds also showed moderate activity against *P. mirabilis*. The compound **10q** also showed good activity against *S. aureus*. Compound **10t** (R^1 = 3-NO_2) showed good activity against *P. mirabilis* and *A. niger* with an MIC of 62.5 μg/mL and moderate activity against *S. aureus*, whereas compound **10u** (R^1 = 4-CN) showed good activity against *S. aureus* and moderate activity against *A. niger*.

The phenyl group at the 5-position of the pyrazole was substituted by 3,4-dimethoxy phenyl, from the compounds 4-aryl-2-(5-(3,4-dimethoxyphenyl)-1-phenyl-1*H*-pyrazol-3-yl)-thiazole (**10v−ab**), and against *P. mirabilis* the compounds were found to be less active. Compound **10v** (R^1 = H) showed moderate activity against *S. aureus*. Compounds **10w** (R^1 = Cl) and **10aa** (R^1 = 3-NO_2) showed good activity against *A. niger*. Compound **10x** (R^1 = 4-F) showed moderate activity against *S. aureus* and good activity against *A. niger*. The compounds **10y** (R^1 = 4-OCH_3) and **10z** (R^1 = 4-NO_2) showed good activity against *S. aureus* and *A. niger* with an MIC of 62.5 μg/mL. Compound **10ab** (R^1 = 4-NO_2) showed good activity against *A. niger* with an MIC of 31.25 μg/mL, which was comparable with respect to the standard drug Ravuconazole.

From the antimicrobial activity analysis, it was noticed that compounds **10g** (R = H, R^1 = CN), **10h** (R = 4-Cl, R^1 = H), **10i** (R = 4-Cl, R^1 = Cl), and **10j** (R = 4-Cl, R^1 = H) showed good activity against *P. mirabilis* with an MIC of 62.5 μg/mL. Compounds **10q** (R = 4-OCH_3, R^1 = F), **10v** (R = 4-OCH_3, R^1 = CN), **10y** (R = 3,4-$(OCH_3)_2$, R^1 = 4-OCH_3) and **10z** (R = 3,4-$(OCH_3)_2$, R^1 = 4-NO_2) showed good activity against *S. aureus* with an MIC of 62.5 μg/mL. Except for compounds **10k**, **10p**, **10u**, and **10v**, all derivatives showed good antifungal activity against *A. niger*. The phenyl or 3,4-dimethoxyphenyl ring at the 5-position of the pyrazole, the 4-cyanophenyl ring at the 4-position of thiazole, the 4-methoxyphenyl ring at the 5-position of the pyrazole, and 4-F/4-OCH_3/4-NO_2-substituted phenyl at 4-position of thiazole showed comparable antifungal activity with respect to the reference drug Ravuconazole.

3. CONCLUSIONS

In conclusion, a new series of 2-(5-aryl-1-phenyl-1*H*-pyrazol-3-yl)-4-aryl thiazole (**10a−ab**) derivatives have been synthesized, and the structure was characterized by spectral analysis and evaluated for antimicrobial activities. **10g**, **10h**, **10i**, **10j**, **10o**, and **10t** pyrazole-thiazole derivatives showed good antimicrobial activity against *P. mirabilis*. Compounds **10q**, **10u**, **10y**, and **10z** showed good antimicrobial activity against *S. aureus*. Twenty-four pyrazole-thiazole derivatives showed good antifungal activity against *A. niger*, from which the compounds **10g**, **10q**, **10r**, **10s**, and **10ab** showed an MIC of 31.25 μg/mL, which is comparable activity with respect to the reference drug Ravuconazole.

4. EXPERIMENTAL SECTION

The chemicals and solvents used were laboratory-grade and were purified as per literature methods. All the reactions have been monitored by thin-layer chromatography (TLC). TLC was performed on the Merck 60 F-254 silica gel plates. Melting points were determined in capillary tubes in a silicon oil bath using a Veego melting point apparatus and were uncorrected. The infrared spectra were recorded on the Shimadzu FTIR (KBr)-408. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ using a Bruker Avance III HD 500 MHz liquid state NMR spectrometer operated at 500 and 125 MHz for ^{1}H and ^{13}C, respectively. HR-MS data were recorded on a Bruker Ascend HD mass spectrometer with TOF. The column chromatography was performed on silica gel for column

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Table 2. Antimicrobial Activity in the Zone of Inhibition (mm) of Synthesized Compounds 10a−ab[a]

comp.	R^1	R^2	*E. coli*	*P. mirabilis*	*B. subtilis*	*S. aureus*	*C. albicans*	*A. niger*
10a	H	H	12	**14.4**	12.6	12.8	12.6	**15.8**
10b	H	Cl	12.2	13	11.2	13.4	13	**15.4**
10c	H	F	13.2	**14**	12	13.8	12.8	**15.6**
10d	H	4-OMe	12	**14.2**	11.6	13	12.4	**15.4**
10e	H	4-NO_2	11.8	**14.2**	12	12.4	12.6	**15**
10f	H	3-NO_2	11.4	13	13.4	13.2	12	**15.4**
10g	H	4-CN	11.8	**15**	13	13	11.6	**16**
10h	4-Cl	H	13	**15.4**	12	12.6	12	**15**
10i	4-Cl	Cl	13.2	**15**	11	**14.6**	11.8	**15.2**
10j	4-Cl	F	**14.2**	**15.8**	12	13.6	12.8	**15**
10k	4-Cl	4-OMe	13	**14**	11	**14**	12.4	**14.4**
10l	4-Cl	4-NO_2	12.8	**14.6**	11	**14.2**	13.2	**15.4**
10m	4-Cl	3-NO_2	12	**14**	12.4	13.4	13	**15.2**
10n	4-Cl	4-CN	11.4	**14.4**	12.6	13.8	13	**15.8**
10o	4-OCH_3	H	13	**15**	13	12.2	12.6	**15.4**
10p	4-OCH_3	Cl	13.2	**14.2**	12.8	13.2	12.6	**14.2**
10q	4-OCH_3	F	12	**14.6**	11	**15**	12	**16.2**
10r	4-OCH_3	4-OMe	10	**14**	12.4	**14**	12	**16.2**
10s	4-OCH_3	4-NO_2	12.2	**14**	11	12.4	12	**16.8**
10t	4-OCH_3	3-NO_2	12.2	**15**	13	**14.4**	12	**15**
10u	4-OCH_3	4-CN	13.8	12.8	12.6	**15.2**	12.8	**14.2**
10v	3,4-$(OCH_3)_2$	H	13.4	**14**	13.6	**14**	13.4	13.8
10w	3,4-$(OCH_3)_2$	Cl	12.6	12.2	12.8	13.4	**14**	**14.6**
10x	3,4-$(OCH_3)_2$	F	12.8	12.4	11.8	**14.2**	**14.4**	**15**
10y	3,4-$(OCH_3)_2$	4-OMe	13.2	13.6	12	**15**	13.6	**15.2**
10z	3,4-$(OCH_3)_2$	4-NO_2	11.8	13.6	12	**15.2**	13.4	**14.8**
10aa	3,4-$(OCH_3)_2$	3-NO_2	13.6	13.8	11.2	13	12.2	**14.6**
10ab	3,4-$(OCH_3)_2$	4-CN	13.4	13.4	11.4	13.6	13.4	**15.4**
Streptomycin			25.0	21.0	18.5	21.0	ND	ND
Fluconazole			ND	ND	ND	ND	21.6	20.3
Ravuconazole			ND	ND	ND	ND	21.6	20.3

[a]ZI: Zone of inhibition (mm). ND: Not determined.

chromatography (100−200 mesh) which was supplied by Thermo Fisher Scientific India Pvt. Ltd.

4.1. Chemistry. *4.1.1. General Procedure for the Synthesis of Ethyl 5-Aryl-1-phenyl-1H-pyrazole-3-carboxylates (**4a−d**).* The solution of ethyl 2,4-dioxo-4-arylbutanoate (0.08 mol) and phenylhydrazine (0.08 mol) in ethanol (50 mL) was refluxed for 3−4 h. After completion of the reaction, the solvent was distilled, and the residue was dissolved in water and extracted with ethyl acetate. The organic layer was distilled on a rotary evaporator. The crude product was purified on column chromatography using ethyl acetate:hexane (2:8) as an eluent to give ethyl 5-aryl-1-phenyl-1*H*-pyrazole-3-carboxylate (**4a−d**) (yield 65−80%).

*4.1.2. General Procedure for the Synthesis of (1,5-Diphenyl-1H-pyrazol-3-yl)methanol Derivatives (**5a**).* Ethyl-1,5-phenyl-1*H*-pyrazole-3-carboxylate (**4a**) (10 mmol) in diethyl ether (20 mL) was added dropwise over a period of 30 min to a cold solution of lithium aluminum hydride (20 mmol) in diethyl ether (20 mL). The resulting reaction mixture was stirred for 1 h at 0 °C. The reaction mixture was monitored by TLC. After completion of the reaction, the reaction mixture was quenched by using the saturated solution of ammonium chloride. The reaction mixture was filtered, and the aqueous layer was extracted with diethyl ether (2 × 30 mL). The combined organic layer was washed with water and brine and dried over sodium sulfate. The solvent was distilled under vacuum given (1,5-diphenyl-1*H*-pyrazol-3-yl)methanol (**5a**) (yield: 88%). The derivatives **5b−d** were synthesized by a similar procedure.

*4.1.3. General Procedure for the Synthesis of 1,5-Diphenyl-1H-pyrazole-3-carbaldehyde Derivatives (**6a−d**).* The solution of (1,5-diphenyl-1*H*-pyrazol-3-yl)methanol (14 mmol) and 2-iodoxybenzoic acid (IBX, 18 mmol) in DMSO (30 mL) was stirred at 0−20 °C for 1 h. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered. The obtained filtrate was diluted with water (90 mL), and the filtrate was extracted with diethyl ether (3 × 30 mL). The organic layer was washed with water and brine and dried over sodium sulfate and distilled under a vacuum to give 1,5-diphenyl-1*H*-pyrazole-3-carbaldehyde (**6a**) (yield: 85%). The derivatives **6b−d** were synthesized by a similar procedure.

*4.1.4. General Procedure for the Synthesis of 1,5-Diphenyl-1H-pyrazole-3-carbonitriles (**7a−d**).* To a solution of 1,5-diphenyl-1*H*-pyrazole-3-carbaldehyde (2.0 g, 9.8 mmol) in tetrahydrofuran (15 mL) and ammonia (20 mL) was added iodine (3.73 g, 29.4 mmol), and the reaction mixture was stirred at ambient temp for 6 h. The progress of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was extracted with ethyl acetate (30 mL × 3); the organic layer was washed with water and dried (Na_2CO_3); and the solvent was removed under vacuum to give 1,5-diphenyl-1*H*-pyrazole-3-carbonitrile (**7a**) (yield 78%). The

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Table 3. Antimicrobial Activity in Minimum Inhibitory Concentration (MIC) in μg/mL of Compounds 10a−ab

comp.	R	R^1	*P. mirabilis*	*S. aureus*	*A. niger*
10a	H	H	125	>250	**62.5**
10b	H	Cl	250	250	**62.5**
10c	H	F	125	250	**62.5**
10d	H	4-OMe	125	>250	**62.5**
10e	H	4-NO_2	125	>250	**62.5**
10f	H	3-NO_2	>250	>250	**62.5**
10g	H	4-CN	**62.5**	>250	**31.25**
10h	4-Cl	H	**62.5**	>250	**62.5**
10i	4-Cl	Cl	**62.5**	125	**62.5**
10j	4-Cl	F	**62.5**	250	**62.5**
10k	4-Cl	4-OMe	125	125	125
10l	4-Cl	4-NO_2	125	125	**62.5**
10m	4-Cl	3-NO_2	125	>250	**62.5**
10n	4-Cl	4-CN	125	250	**62.5**
10o	4-OCH_3	H	**62.5**	>250	**62.5**
10p	4-OCH_3	Cl	125	>250	125
10q	4-OCH_3	F	125	**62.5**	**31.25**
10r	4-OCH_3	4-OMe	125	125	**31.25**
10s	4-OCH_3	4-NO_2	125	>250	**31.25**
10t	4-OCH_3	3-NO_2	**62.5**	125	**62.5**
10u	4-OCH_3	4-CN	>250	**62.5**	125
10v	3,4-$(OCH_3)_2$	H	250	125	250
10w	3,4-$(OCH_3)_2$	Cl	>250	250	**62.5**
10x	3,4-$(OCH_3)_2$	F	>250	125	**62.5**
10y	3,4-$(OCH_3)_2$	4-OMe	250	**62.5**	**62.5**
10z	3,4-$(OCH_3)_2$	4-NO_2	>250	**62.5**	**62.5**
10aa	3,4-$(OCH_3)_2$	3-NO_2	250	250	**62.5**
10ab	3,4-$(OCH_3)_2$	4-CN	250	250	**31.25**
Fluconazole			15.62	15.62	7.81
Fluconazole					7.81
Ravuconazole					31.5

nitriles **7b−d** were synthesized under similar reaction conditions. The nitrile was used without further purification.

*4.1.5. General Procedure for the Synthesis of 1,5-Diphenyl-1H-pyrazole-3-carbothioamides (**8a−d**).* In a solution of 1,5-diphenyl-1*H*-pyrazole-3-carbonitrile (**7a**) (7.5 mmol) were added triethylamine (2 mL) in pyridine (15 mL) and H_2S gas for 2 h at room temperature. The progress of the reaction was monitored by TLC. The reaction mixture was quenched in ice-cold water and neutralized by dilute HCl. The product was filtered and washed with water and dried in air, affording 1,5-diphenyl-1*H*-pyrazole-3-carbothioamides (**8a−d**) (yield 80%).

*4.1.6. General Procedure for the Synthesis of 1,5-Diphenyl-3-(4-phenylthiazol-2-yl)-1H-pyrazole (**10a−ab**).* In the mixture of 1,5-diphenyl-1*H*-pyrazole-3-carbothioamide (0.85 mmol) in 8 mL of ethanol was added 2-bromo-1-phenylethanone (0.71 mmol), and the reaction mixture was refluxed for 2 h. After the reaction (TLC) was completed, the product was filtered and washed with ethanol.

*1,5-Diphenyl-3-(4-phenylthiazol-2-yl)-1H-pyrazole, **10a**.* IR 889, 939, 1000, 1028, 1170, 1205, 1313, 1362, 1403, 1496, 1593, 3028, 3062 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.3, 1.2 Hz, 2H, Ar−H), 7.48 (s, 1H, thiazole C5H), 7.45 (t, J = 7.6 Hz, 2H, Ar−H), 7.38 (dd, J = 3.7, 1.1 Hz, 4H, Ar−H), 7.34 (m, 5H, Ar−H), 7.29 (m, 2H, Ar−H), 7.20 (s, 1H, pyrazole C4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.34 (C, thiazole C-2), 155.96 (C, thiazole C-4), 147.62 (C, pyrazole C-3), 144.79 (C, pyrazole C-5), 139.74 (C, Ar−C1), 134.54 (C, Ar−C1″), 130.02 (C, Ar−C1′), 129.01 (2CH, Ar−C3′,C5′), 128.80 (2CH, Ar−C3,C5), 128.73 (2CH, Ar−C3″,C5″), 128.59 (CH, Ar−C4′), 128.56 (2CH, Ar−C2′,C6′), 128.09 (CH, Ar−C4″), 127.92 (CH, Ar−C4), 126.47 (2CH, Ar−C2″,C6″), 125.47 (2CH, Ar−C2,C6), 112.71 (CH, thiazole C-5), 106.07 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{24}H_{18}N_3S$, $[M + H]^+$, 380.1221 found 380.1232.

*3-(4-(4-Chlorophenyl)thiazol-2-yl)-1,5-diphenyl-1H-pyrazole, **10b**.* IR 833, 892, 971, 1010, 1105, 1168, 1313, 1362, 1400, 1466, 1593, 3035, 3114 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 8.5 Hz, 2H, Ar−H), 7.46 (s, 1H, thiazole C5H), 7.41 (d, J = 8.5 Hz, 2H, Ar−H), 7.36 (m, 5H, Ar−H), 7.31 (m, 5H, Ar−H), 7.18 (s, 1H, pyrazole C4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.61(C, thiazole C-2), 154.72 (C, thiazole C-4), 147.41 (C, pyrazole C-3), 144.85 (C, pyrazole C-5), 139.69 (C, Ar−C1), 133.85(C, Ar−C4″), 132.99 (C, Ar−C1″), 129.93 (C, Ar−C1″), 129.02 (2CH, Ar−C3′,C5′), 128.88 (2CH, Ar−C3,C5), 128.79 (2CH, Ar−C3″,C5″), 128.63 (CH, Ar−C4′), 128.57 (2CH, Ar−C2′,C6′), 127.97 (CH, Ar−C4), 127.72 (2CH, Ar−C2″,C6″), 125.45 (2CH, Ar−C2,C6), 113.01 (CH, thiazole C-5), 106.04 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{24}H_{17}ClN_3S$, $[M + H]^+$, 414.0832 found 414.0845.

*3-(4-(4-Fluorophenyl)thiazol-2-yl)-1,5-diphenyl-1H-pyrazole, **10c**.* IR 803, 895, 1010, 1053, 1170, 1320, 1368, 1405, 1470, 1596, 3002, 3050 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 (dd, J = 8.9, 5.4 Hz, 2H, Ar−H), 7.41 (s, 1H, thiazole C5H), 7.37 (m, 4H, Ar−H), 7.34 (m, 4H, Ar−H), 7.29 (m, 2H, Ar−H), 7.18 (s, 1H, pyrazole C4H), 7.13 (m, 2H), Ar−H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.71and161.75 (C, $^1J_{C-F}$ = 246.96 Hz, Ar−C4″), 161.51 (C, thiazole C-2), 154.95 (C, thiazole C-4), 147.49 (C, pyrazole C-3), 144.83 (C, pyrazole C-5), 139.71 (C, Ar−C1), 130.84 and 130.81 (C, $^4J_{C-F}$ = 3.78 Hz, Ar−C1″), 129.96 (CH, Ar−C4′), 129.02 (2CH, Ar−C3′,C5′), 128.79 (2CH, Ar−C3,C5), 128.62 (C, Ar−C1′), 128.57 (2CH, Ar−C2′,C6′), 128.23 and 128.16 (2CH, $^3J_{C-F}$ = 8.82 Hz, Ar−C2″, C6″), 127.96 (CH, Ar−C4), 125.46 (2CH, Ar−C2,C6), 115.70 and 115.53 (2CH, $^2J_{C-F}$ = 21.42 Hz, Ar−C3″, C5″), 112.29 (CH, thiazole C-5), 106.02(CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{24}H_{17}FN_3S$, $[M + H]^+$, 398.1127 found 434.1522.

*3-(4-(4-Methoxyphenyl)thiazol-2-yl)-1,5-diphenyl-1H-pyrazole, **10d**.* IR 837, 891, 940, 1023, 1096, 1156, 1217, 1240, 1292, 1370, 1396, 1437, 1487, 1530, 1596, 2929, 3080 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.8 Hz, 2H, Ar−H), 7.39−7.27 (m, 12H, Ar−H, thiazole C5H, pyrazole C4H), 6.98 (d, J = 8.9 Hz, 2H, Ar−H), 3.86 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.44 (C, thiazole C-2), 159.68 (C, Ar−C4″), 155.41 (C, thiazole C-4), 147.22 (C, pyrazole C-3), 144.84 (C, pyrazole C-5), 139.71 (C, Ar−C1), 129.94 (C, Ar−C1′), 129.02 (2CH, Ar−C3′,C5′), 128.81 (2CH, Ar−C3,C5), 128.61 (CH, Ar−C4′), 128.56 (2CH, Ar−C3″,C5″), 127.96 (C, Ar−C1″), 127.90 (2CH, Ar−C2′,C6′), 127.03 (CH, Ar−C4), 125.47 (2CH, Ar−C2,C6), 114.12 (2CH, Ar−C2″,C6″), 111.08 (CH, thiazole C-5), 106.39 (CH, pyrazole C-4), 55.36 (C4″-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{25}H_{20}N_3OS$, $[M + H]^+$, 410.1327 found 410.1331.

*3-(4-(4-Nitrophenyl)thiazol-2-yl)-1,5-diphenyl-1H-pyrazole, **10e**.* IR 836, 858, 913, 1043, 1067, 1198, 1330, 1350, 1497, 1505, 1530, 1593, 2930, 3082, 3125 cm^{-1}; ^1H NMR

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(500 MHz, $CDCl_3$) δ 8.31 (d, J = 8.9 Hz, 2H, Ar−H), 8.17 (d, J = 8.9 Hz, 2H, Ar−H), 7.69 (s, 1H, thiazole C5H), 7.36 (m, 8H, Ar−H), 7.29 (m, 2H, Ar−H), 7.19 (s, 1H, pyrazole C4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.32 (C, thiazole C-2), 153.48 (C, thiazole C-4), 147.27 (C, pyrazole C-3), 147.10 (C, Ar−C4″), 145.05 (C, pyrazole C-5), 140.32 (C, Ar−C1), 139.63 (C, Ar−C1′), 129.81(CH, Ar−C4′), 129.08 (2CH, Ar−C3′,C5′), 128.80 (2CH, Ar−C3,C5), 128.75 (C, Ar−C1″), 128.62 (2CH, Ar−C3″,C5″), 128.10 (CH, Ar−C4), 126.98 (2CH, Ar−C2″,C6″), 125.44 (2CH, Ar−C2′,C6′), 124.20 (2CH, Ar−C2,C6), 116.16 (CH, thiazole C-5), 106.05 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{24}H_{17}N_4O_2S$, $[M + H]^+$, 425.1072 found 425.1078.

3-(4-(3-Nitrophenyl)thiazol-2-yl)-1,5-diphenyl-1H-pyrazole, ***10f.*** IR 860, 890, 945, 1001, 1073, 1166, 1202, 1295, 1346, 1410, 1498, 1532, 1595, 2918, 3099 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (t, J = 1.9 Hz, 1H, Ar−H), 8.33 (m, 1H, Ar−H), 8.19 (ddd, J = 8.2, 2.3, 1.0 Hz, 1H, Ar−H), 7.64 (s, 1H, thiazole C5H), 7.62 (t, J = 8.0 Hz, 1H, Ar−H), 7.37 (m, 5H, Ar−H), 7.34 (dd, J = 5.0, 2.2 Hz, 3H, Ar−H), 7.30 (m, 2H, Ar−H), 7.21 (s, 1H, pyrazole C4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.21(C, thiazole C-2), 153.34 (C, thiazole C-4), 148.78 (C, Ar−C3″), 147.19 (C, pyrazole C-3), 145.01 (C, pyrazole C-5), 139.67 (C, Ar−C1), 136.13 (C, Ar−C1″), 132.16 (C, Ar−C1′), 129.84 (CH, Ar−C5″), 129.68 (CH, Ar−C6″), 129.07 (2CH, Ar−C3,C5), 128.80 (2CH, Ar−C3′,C5′), 128.71 (CH, Ar−C4′), 128.61 (2CH, Ar−C2′,C6′), 128.06 (CH, Ar−C4), 125.46 (2CH, Ar−C2,C6), 122.64 (CH, Ar−C2″), 121.34 (CH, Ar−C4″), 114.72 (CH, thiazole C-5), 106.10 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{24}H_{17}N_4O_2S$, $[M + H]^+$, 425.1072 found 425.1078.

4-(2-(1,5-Diphenyl-1H-pyrazol-3-yl)thiazol-4-yl)-benzonitrile, ***10g.*** IR 836, 945, 1005, 1170, 1210, 1362, 1399, 1476, 1594, 2245, 2935, 3062 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 2H, Ar−H), 7.73 (d, J = 8.4 Hz, 2H, Ar−H), 7.63 (s, 1H, thiazole C5H), 7.37 (m, 5H, Ar−H), 7.34 (m, 3H), 7.29 (m, 2H), 7.18 (s, 1H, pyrazole C4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.17 (C, thiazole C-2), 153.82 (C, thiazole C-4), 147.15 (C, pyrazole C-3), 145.01 (C, pyrazole C-5), 139.64 (C, Ar−C1), 138.50 (C, Ar−C1″), 132.63 (2CH, Ar−C3″,C5″), 129.83 (C, Ar−C1′), 129.07 (2CH, Ar−C3,C5), 128.79 (2CH, Ar−C3′,C5′), 128.73 (CH, Ar−C4′), 128.61 (2CH, Ar−C2″,C6″), 128.08 (CH, Ar−C4), 126.89 (2CH, Ar−C2′,C6′), 125.44 (2CH, Ar−C2,C6), 118.99 (CH, Ar−C4″), 115.48 (CH, thiazole C-5), 111.33 (C4″-CN), 106.03 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{25}H_{17}N_4S$, $[M + H]^+$, 405.1174 found 405.1178.

5-(4-Chlorophenyl)-1-phenyl-3-(4-phenylthiazol-2-yl)-1H-pyrazole, ***10h.*** IR 939, 973, 1014, 1072, 1169, 1209, 1321, 1362, 1407, 1440, 1472, 1593, 2965, 3067, 3114 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 7.1 Hz, 2H, Ar−H), 7.48 (s, 1H, thiazole C5H), 7.45 (t, J = 7.6 Hz, 2H, Ar−H), 7.36 (m, 6H, Ar−H), 7.30 (d, J = 8.5 Hz, 2H, Ar−H), 7.21 (d, J = 8.6 Hz, 2H, Ar−H), 7.19 (s, 1H, pyrazole C4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.09 (C, thiazole C-2), 155.99 (C, thiazole C-4), 147.72 (C, pyrazole C-3), 143.56 (C, pyrazole C-5), 139.48 (C, Ar−C1), 134.73 (C, Ar−C4′), 134.47 (C, Ar−C1″), 130.00 (2CH, Ar−C3′,C5′), 129.17 (2CH, Ar−C3,C5), 128.88 (2CH, Ar−C2′,C6′), 128.74 (2CH, Ar−C3″,C5″), 128.43 (C, Ar−C1′), 128.17 (C, Ar−C4), 128.13(C, Ar−C4″), 126.46 (2CH, Ar−C2″,C6″), 125.48 (2CH, Ar−C2,C6), 112.81 (CH, thiazole C-5), 106.16 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{24}H_{17}ClN_3S$, $[M + H]^+$, 414.0832 found 414.0845.

5-(4-Chlorophenyl)-3-(4-(4-chlorophenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10i.*** IR 814, 915, 1045, 1079, 1258, 1320, 1437, 1522, 1595, 2918, 3065, 3118 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 8.6 Hz, 2H, Ar−H), 7.47 (s, 1H, thiazole C5H), 7.41 (d, J = 8.6 Hz, 2H, Ar−H), 7.37 (m, 5H, Ar−H), 7.31 (d, J = 8.6 Hz, 2H, Ar−H), 7.21 (d, J = 8.6 Hz, 2H, Ar−H), 7.17 (s, 1H, pyrazole C4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.37 (C, thiazole C-2), 154.79 (C, thiazole C-4), 147.54 (C, pyrazole C-3), 143.64 (C, pyrazole C-5), 139.44 (C, Ar−C1), 134.80 (C, Ar−C4′), 133.90 (C, Ar−C4″), 132.96 (C, Ar−C1″), 129.99 (2CH, Ar−C3′,C5′), 129.19 (2CH, Ar−C3″,C5″), 128.91 (2CH, Ar−C2′,C6′ and C3C5), 128.36 (C, Ar−C1′), 128.22 (C, Ar−C4), 127.71 (2CH, Ar−C2″,C6″), 125.47 (2CH, Ar−C2,C6), 113.10 (CH, thiazole C-5), 106.12 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{24}H_{16}Cl_2N_3S$, $[M + H]^+$, 448.0442 found 448.0446.

5-(4-Chlorophenyl)-3-(4-(4-fluorophenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10j.*** IR 835, 901, 940, 971, 1027, 1108, 1169, 1220, 1308, 1321, 1358, 1400, 1440, 1497, 1593, 2904, 2953, 3045, 3101 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (dd, J = 8.9, 5.4 Hz, 2H, Ar−H), 7.42 (s, 1H, thiazole C5H), 7.38 (m, 5H, Ar−H), 7.31 (d, J = 8.6 Hz, 2H, Ar−H), 7.21 (d, J = 8.6 Hz, 2H, Ar−H), 7.17 (s, 1H, pyrazole C4H), 7.14 (t, J = 8.7 Hz, 2H, Ar−H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.70 and 161.73 (C, $^1J_{C-F}$ = 248.22 Hz, Ar−C4″), 161.24 (C, thiazole C-2), 154.95 (C, thiazole C-4), 147.56 (C, pyrazole C-3), 143.59 (C, pyrazole C-5), 139.40 (C, Ar−C1), 134.75 (C, Ar−C4′), 130.73 and 130.70 (C, $^4J_{C-F}$ = 3.78 Hz, Ar−C1″), 129.97 (2CH, Ar−C3′,C5′), 129.18 (2CH, Ar−C3,C5), 128.89 (2CH, Ar−C2′,C6′), 128.34 (C, Ar−C1′), 128.20 (CH, Ar−C4), 128.20 and 128.13 (C, $^3J_{C-F}$ = 8.82 Hz, Ar−C2″, C6″), 125.45 (2CH, Ar−C2,C6), 115.72 and 115.55 (C, $^2J_{C-F}$ = 21.42 Hz, Ar−C3″, C5″), 112.39 (CH, thiazole C-5), 106.08 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{24}H_{16}ClFN_3S$, $[M + H]^+$, 432.0737 found 434.1522.

5-(4-Chlorophenyl)-3-(4-(4-methoxyphenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10k.*** IR 834, 913, 939, 971, 1027, 1109, 1198, 1243, 1301, 1358, 1400, 1440, 1593, 2952, 3039 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 8.8 Hz, 2H, Ar−H), 7.37 (m, 5H, Ar−H), 7.35 (s, 1H, thiazole C5H), 7.31 (d, J = 8.5 Hz, 2H, Ar−H), 7.21 (d, J = 8.5 Hz, 2H, Ar−H), 7.18 (s, 1H, pyrazole C4H), 6.98 (d, J = 8.8 Hz, 2H, Ar−H), 3.86 (s, 3H, -OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.91 (C, thiazole C-2), 159.64 (C, Ar−C4″), 155.81 (C, thiazole C-4), 147.79 (C, pyrazole C-3), 143.53 (C, pyrazole C-5), 139.50 (C, Ar−C1), 134.73 (C, Ar−C4′), 130.01 (2CH, Ar−C3′,C5′), 129.17 (2CH, Ar−C3,C5), 128.89 (2CH, Ar−C2′,C6′), 128.47 (C, Ar−C1′), 128.15 (C, Ar−C4), 127.75 (2CH, Ar−C3″,C5″), 127.49 (C, Ar−C1″), 125.49 (2CH, Ar−C2,C6), 114.10 (2CH, Ar−C2″,C6″), 111.10 (CH, thiazole C-5), 106.15 (CH, pyrazole C-4), 55.36 (C4″-OCH_3). HRMS (ESI, m/z): calculated for $C_{25}H_{19}ClN_3OS$, $[M + H]^+$, 444.0937 found 444.0946.

5-(4-Chlorophenyl)-3-(4-(4-nitrophenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10l.*** IR 814, 916, 972, 1015, 1049, 1107, 1170, 1207, 1267, 1338, 1400, 1472, 1507, 1533, 1595, 2931, 3062 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 8.9 Hz, 2H, Ar−H), 8.16 (d, J = 8.9 Hz, 2H, Ar−H), 7.69 (s, 1H, thiazole C5H), 7.38 (m, 5H, Ar−H), 7.32 (d, J = 8.6 Hz, 2H,

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Ar−H), 7.22 (d, J = 8.6 Hz, 2H, Ar−H), 7.18 (s, 1H, pyrazole C4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.08 (C, thiazole C-2), 153.52 (C, thiazole C-4), 147.30 (C, Ar−C4″), 147.21 (C, pyrazole C-3), 143.83 (C, Ar−C1″), 140.26 (C, Ar−C4), 139.38 (C, Ar−C1), 134.93 (C, Ar−C4′), 130.01 (2CH, Ar−C3′,C5′), 129.25 (2CH, Ar−C3,C5), 128.97 (2CH, Ar−C2′,C6′), 128.36 (CH, Ar−C4), 128.24 (C, Ar−C1′), 126.98 (2CH, Ar−C3″,C5″), 125.46 (2CH, Ar−C2,C6), 124.22 (2CH, Ar−C2″,C6″), 116.25 (CH, thiazole C-5), 106.13 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{24}H_{16}ClN_4O_2S$, $[M + H]^+$, 459.0682 found 459.0678.

5-(4-Chlorophenyl)-3-(4-(3-nitrophenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10m.*** IR 890, 945, 1005, 1071, 1168, 1202, 1297, 1347, 1405, 1476, 1533, 1594, 2935, 3099 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (d, J = 11.6 Hz, 1H, Ar−H), 8.39 (t, J = 8.3 Hz, 1H, Ar−H), 8.24−8.16 (m, 1H, Ar−H), 7.92 (s, 1H, Ar−H), 7.71−7.66 (m, 2H, Ar−H, thiazole C5H), 7.45−7.33 (m, 6H, Ar−H), 7.31−7.20 (m, 3H, Ar−H, pyrazole C4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.57 (C, thiazole C-2), 153.00 (C, thiazole C-4), 148.56 (C, pyrazole C-3), 147.04 (C, Ar−C3″), 143.61 (C, pyrazole C-5), 139.19 (C, Ar−C1), 135.92 (C, Ar−C1″), 134.56 (C, Ar−C4′), 132.14 (CH, Ar−C6″), 129.97 (2CH, Ar−C3′, C5′), 129.78 (CH, Ar−C5″), 129.15 (2CH, Ar−C3, C5), 128.79 (2CH, Ar−C2′, C6′), 128.30 (CH, Ar−C4), 128.06 (C, Ar−C1′), 125.32 (2CH, Ar−C2, C6), 122.48 (CH, Ar−C2″), 121.03 (CH, Ar−C4″), 115.37 (CH, thiazole C-5), 105.98 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{24}H_{16}ClN_4O_2S$, $[M + H]^+$, 459.0682 found 459.0678.

4-(2-(5-(4-Chlorophenyl)-1-phenyl-1H-pyrazol-3-yl)-thiazol-4-yl)benzonitrile, ***10n.*** IR 835, 894, 902, 936, 945, 1002, 1072, 1169, 1202, 1297, 1347, 1507, 1491, 1535, 1595, 2250, 2911, 2965, 3067, 3119 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, J = 8.5 Hz, 2H, Ar−H), 7.74 (d, J = 8.5 Hz, 2H, Ar−H), 7.64 (s, 1H, thiazole C5H), 7.38 (m, 5H, Ar−H), 7.32 (d, J = 8.5 Hz, 2H, Ar−H), 7.22 (d, J = 8.5 Hz, 2H, Ar−H), 7.17 (s, 1H, pyrazole C4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.90 (C, thiazole C-2), 153.85 (C, thiazole C-4), 147.25 (C, pyrazole C-3), 143.77 (C, pyrazole C-5), 139.34 (C, Ar−C1), 138.43 (C, Ar−C1″), 134.88 (C, Ar−C4′), 132.63 (2CH, Ar−C3″,C5″), 129.98 (2CH, Ar−C3′,C5′), 129.23 (2CH, Ar−C3,C5), 128.94 (2CH, Ar−C2′,C6′), 128.32 (C, Ar−C1′), 128.22 (C, Ar−C4), 126.86 (2CH, Ar−C2″,C6″), 125.44 (2CH, Ar−C2,C6), 118.97 (C4″-CN), 115.57 (C, Ar−C4″), 111.34 (CH, thiazole C-5), 106.09 (CH, pyrazole C-4). HRMS (ESI, m/z): calculated for $C_{25}H_{16}ClN_4S$, $[M + H]^+$, 439.0784 found 439.0788.

5-(4-Methoxyphenyl)-1-phenyl-3-(4-phenylthiazol-2-yl)-1H-pyrazole, ***10o.*** IR 810, 845, 915, 1003, 1023, 1067, 1109, 1168, 1252, 1366, 1400, 1436, 1485, 1595, 2924, 2961, 3011, 3062 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.3, 1.2 Hz, 2H, Ar−H), 7.48 (s, 1H, thiazole C5H), 7.45 (t, J = 7.6 Hz, 2H, Ar−H), 7.36 (m, 6H, Ar−H), 7.21 (d, J = 8.9 Hz, 2H, Ar−H), 7.14 (s, 1H, pyrazole C4H), 6.85 (d, J = 8.9 Hz, 2H, Ar−H), 3.82 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.47 (C, thiazole C-2), 159.76 (C, Ar−C4′), 155.90 (C, thiazole C-4), 147.50 (C, pyrazole C-3), 144.64 (C, pyrazole C-5), 139.82 (C, Ar−C1), 134.53 (C, Ar−C1″), 130.09 (2CH, Ar−C2′,C6′), 129.00 (2CH, Ar−C3,C5), 128.72 (2CH, Ar−C3″,C5″), 128.07 (C, Ar−C4″), 127.83 (C, Ar−C4), 126.46 (2CH, Ar−C2″,C6″), 125.47 (2CH, Ar−C2,C6), 122.35 (C, Ar−C1′), 113.98 (2CH, Ar−C3′,C5′), 112.67 (CH, thiazole C-5), 105.52 (CH, pyrazole C-4), 55.27 (C4′-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{25}H_{20}N_3OS$, $[M + H]^+$, 410.1327 found 410.1331.

3-(4-(4-Chlorophenyl)thiazol-2-yl)-5-(4-methoxyphenyl)-1-phenyl-1H-pyrazole, ***10p.*** IR 829, 915, 971, 1012, 1066, 1114, 1168, 1204, 1254, 1293, 1362, 1435, 1487, 1593, 2924, 2925, 3032, 3103 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 8.6 Hz, 2H, Ar−H), 7.46 (s, 1H, thiazole C5H), 7.41 (d, J = 8.6 Hz, 2H, Ar−H), 7.36 (m, 5H, Ar−H), 7.20 (d, J = 8.8 Hz, 2H, Ar−H), 7.11 (s, 1H, pyrazole C4H), 6.85 (d, J = 8.8 Hz, 2H, Ar−H), 3.81 (s, 3H, -OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.75 (C, thiazole C-2), 159.82 (C, Ar−C4′), 154.70 (C, Ar−C4′), 147.33 (C, pyrazole C-3), 144.73 (C, pyrazole C-5), 139.81 (C, Ar−C1), 133.82 (C, Ar−C4″), 133.04 (C, Ar−C1″), 130.10 (2CH, Ar−C2′,C6′), 129.01 (2CH, Ar−C3,C5), 128.87 (2CH, Ar−C3″,C5″), 127.88 (C, Ar−C4), 127.72 (2CH, Ar−C2″,C6″), 125.47 (2CH, Ar−C2,C6), 122.30 (C, Ar−C1′), 114.02 (2CH, Ar−C3′,C5′), 112.96 (CH, thiazole C-5), 105.50 (CH, pyrazole C-4), 55.28 (C4′-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{25}H_{19}ClN_3OS$, $[M + H]^+$, 444.0937 found 444.0946.

3-(4-(4-Fluorophenyl)thiazol-2-yl)-5-(4-methoxyphenyl)-1-phenyl-1H-pyrazole, ***10q.*** IR 836, 891, 939, 971, 1023, 1095, 1155, 1217, 1291, 1369, 1395, 1437, 1487, 1530, 1595, 1608, 2930, 3081 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (dd, J = 8.9, 5.4 Hz, 2H, Ar−H), 7.40 (s, 1H, thiazole C5H), 7.36 (m, 5H, Ar−H), 7.20 (d, J = 8.8 Hz, 2H, Ar−H), 7.14 (d, J = 8.7 Hz, 2H, Ar−H), 7.11 (s, 1H, pyrazole C4H), 6.86−6.84 (m, 2H, Ar−H), 3.81 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.70 and 161.73 (C, $^1J_{C-F}$ = 248.22 Hz, Ar−C4″), 161.65 (C, thiazole C-2), 159.81 (C, Ar−C4′), 154.91 (C, thiazole C-4), 147.39 (C, pyrazole C-3), 144.70 (C, pyrazole C-5), 139.82 (C, Ar−C1), 130.86 and 130.83 (C, $^4J_{C-F}$ = 3.78 Hz, Ar−C1″), 130.10 (2CH, Ar−C2′,C6′), 129.01 (2CH, Ar−C3,C5), 128.22 and 128.16 (2CH, $^3J_{C-F}$ = 7.56 Hz, Ar−C2″, C6″), 127.86 (C, Ar−C4), 125.47 (2CH, Ar−C2,C6), 122.33 (C, Ar−C1′), 115.69 and 115.52 (2CH, $^2J_{C-F}$ = 21.42 Hz, Ar−C3″, C5″), 114.01 (2CH, Ar−C3′,C5′), 112.24 (CH, thiazole C-5), 105.49 (CH, pyrazole C-4), 55.28 (C4′-O$\underline{C}H_3$). C25H18FN3OS Exact Mass: 427.1155. HRMS (ESI, m/z): calculated for $C_{25}H_{19}FN_3OS$, $[M + H]^+$, 428.1233 found 428.1237.

5-(4-Methoxyphenyl)-3-(4-(4-methoxyphenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10r.*** IR 880, 941, 985, 1023, 1070, 1109, 1172, 1245, 1299, 1362, 1397, 1437, 1489, 1530, 1593, 2932, 3058, 3110 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 8.9 Hz, 2H, Ar−H), 7.37 (m, 5H, Ar−H), 7.34 (s, 1H, thiazole C5H), 7.21 (d, J = 8.9 Hz, 2H, Ar−H), 7.12 (s, 1H, pyrazole C4H), 6.98 (d, J = 8.9 Hz, 2H, Ar−H), 6.85 (d, J = 8.9 Hz, 2H, Ar−H), 3.86 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.30 (C, thiazole C-2), 159.79 (C, Ar−C4′), 159.60 (C, Ar−C4″), 155.74 (C, thiazole C-4), 147.59 (C, pyrazole C-3), 144.62 (C, pyrazole C-5), 139.88 (C, Ar−C1), 130.11 (2CH, Ar−C2′,C6′), 129.00 (2CH, Ar−C3,C5), 127.81 (CH, Ar−C4), 127.77 (2CH, Ar−C3″,C5″), 127.59 (C, Ar−C1″), 125.50 (2CH, Ar−C2,C6), 122.43 (C, Ar−C1′), 114.08 (2CH, Ar−C2″,C6″), 114.01 (2CH, Ar−C3′,C5′), 110.97 (CH, thiazole C-5), 105.55 (CH, pyrazole C-4), 55.36 (C4′-O$\underline{C}H_3$), 55.29 (C4″-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{26}H_{22}N_3O2S$, $[M + H]^+$, 440.1433 found 440.1435.

5-(4-Methoxyphenyl)-3-(4-(4-nitrophenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10s.*** IR 816, 835, 885, 940, 1005, 1140, 1168, 1209, 1249, 1291, 1340, 1457, 1483, 1510, 1529, 1593,

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2935, 3062 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 9.0 Hz, 2H, Ar−H), 8.16 (d, J = 9.0 Hz, 2H, Ar−H), 7.68 (s, 1H, thiazole C5H), 7.38 (m, 5H, Ar−H), 7.21 (d, J = 8.8 Hz, 2H, Ar−H), 7.12 (s, 1H, pyrazole C4H), 6.86 (d, J = 8.8 Hz, 2H, Ar−H), 3.82 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.46 (C, thiazole C-2), 159.91 (C, Ar−C4′), 153.44 (C, thiazole C-4), 147.26 (C, Ar−C4″), 147.00 (C, pyrazole C-3), 144.92 (C, pyrazole C-5), 140.35 (C, Ar−C1″), 139.74 (C, Ar−C1), 130.11 (2CH, Ar−C2′,C6′), 129.06 (2CH, Ar−C3,C5), 128.00 (CH, Ar−C4), 126.97 (2CH, Ar−C2″,C6″), 125.46 (2CH, Ar−C2,C6), 124.19 (2CH, Ar−C3″,C5″), 122.16 (C, Ar−C1′), 116.12 (CH, thiazole C-5), 114.06 (2CH, Ar−C3′,C5′), 105.51 (CH, pyrazole C-4), 55.30 (C4′-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{25}H_{19}N_4O_3S$, $[M + H]^+$, 455.1178 found 455.1170.

5-(4-Methoxyphenyl)-3-(4-(3-nitrophenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10t***. IR 829, 889, 952, 1025, 1073, 1105, 1170, 1202, 1254, 1295, 1342, 1457, 1526, 1560, 1594, 2909, 2957, 3030, 3108 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.86 (t, J = 1.9 Hz, 1H, Ar−H), 8.32 (ddd, J = 7.8, 1.6, 1.1 Hz, 1H, Ar−H), 8.19 (ddd, J = 8.2, 2.3, 1.0 Hz, 1H, Ar−H), 7.63 (s, 1H, thiazole C5H), 7.61 (d, J = 8.0 Hz, 1H, Ar−H), 7.37 (m, 5H, Ar−H), 7.22 (d, J = 8.9 Hz, 2H, Ar−H), 7.15 (s, 1H, pyrazole C4H), 6.86 (d, J = 8.9 Hz, 2H, Ar−H), 3.82 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.35 (C, thiazole C-2), 159.88 (C, Ar−C4′), 153.30 (C, thiazole C-4), 148.77 (C, Ar−C3″), 147.10 (C, pyrazole C-3), 144.89 (C, pyrazole C-5), 139.78 (C, Ar−C1), 136.15 (C, Ar−C1″), 132.16 (C, Ar−C6″), 130.11 (2CH, Ar−C2′,C6′), 129.67 (C, Ar−C6″), 129.05 (2CH, Ar−C3,C5), 127.96 (CH, Ar−C4), 125.47 (2CH, Ar−C2,C6), 122.61 (CH, Ar−C2″), 122.20 (C, Ar−C1′), 121.34 CH, Ar−C4″), 114.67 (CH, thiazole C-5), 114.05 (2CH, Ar−C3′,C5′), 105.55 (CH, pyrazole C-4), 55.30 (C4′-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{25}H_{19}N_4O_3S$, $[M + H]^+$, 455.1178 found 455.1170.

4-(2-(5-(4-Methoxyphenyl)-1-phenyl-1H-pyrazol-3-yl)-thiazol-4-yl)benzonitrile, ***10u***. IR 833, 894, 939, 971, 1031, 1110, 1202, 1250, 1293, 1364, 1437, 1487, 1533, 1604, 2240, 2931, 2998, 3050, 3110 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, J = 8.6 Hz, 2H, Ar−H), 7.73 (d, J = 8.6 Hz, 2H, Ar−H), 7.62 (s, 1H, thiazole C5H), 7.37 (m, 5H, Ar−H), 7.21 (d, J = 8.8 Hz, 2H, Ar−H), 7.11 (s, 1H, pyrazole C4H), 6.86 (d, J = 8.9 Hz, 2H, Ar−H), 3.82 (s, 3H, -OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.27 (C, thiazole C-2), 159.85 (C, Ar−C4′), 153.76 (C, thiazole C-4), 147.04 (C, pyrazole C-3), 144.85 (C, pyrazole C-5), 139.71 (C, Ar−C1), 138.51 (C, Ar−C1″), 132.61 (2CH, Ar−C3″,C5″), 130.08 (2CH, Ar−C2′,C6′), 129.05 (2CH, Ar−C3,C5), 127.98 (CH, Ar−C4), 126.86 (2CH, Ar−C2″,C6″), 125.44 (2CH, Ar−C2,C6), 122.14 (C, Ar−C1′), 119.01 (C4″-$\underline{C}N$), 115.44 (C, Ar−C4″), 114.03 (2CH, Ar−C3′,C5′), 111.25 (CH, thiazole C-5), 105.46 (CH, pyrazole C-4), 55.29 (C4′-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{26}H_{19}N_4OS$, $[M + H]^+$, 435.1280 found 435.1284.

5-(3,4-Dimethoxyphenyl)-1-phenyl-3-(4-phenylthiazol-2-yl)-1H-pyrazole, ***10v***. IR 855, 890, 939, 1023, 1071, 1136, 1194, 1232, 1291, 1321, 1360, 1407, 1436, 1491, 1593, 2927, 2994, 3056, 3103 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.3, 1.2 Hz, 2H, Ar−H), 7.48 (s, 1H, thiazole C5H), 7.45 (t, J = 7.6 Hz, 2H, Ar−H), 7.37(m, 6H, Ar−H), 7.17 (s, 1H, pyrazole C4H), 6.89 (dd, J = 8.3, 2.0 Hz, 1H, Ar−H), 6.83 (d, J = 8.3 Hz, 1H, Ar−H), 6.72 (d, J = 2.0 Hz, 1H, Ar−H), 3.89 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.42 (C, thiazole C-2), 155.92 (C, thiazole C-4), 149.22 (C, Ar−C4′), 148.62 (C, Ar−C3′), 147.51 (C, pyrazole C-3), 144.71 (C, pyrazole C-5), 139.85 (C, Ar−C1), 134.51 (C, Ar−C1″), 129.03 (2CH, Ar−C3,C5), 128.73 (2CH, Ar−C3″,C5″), 128.09 (CH, Ar−C4″), 127.94 (CH, Ar−C4), 126.46 (2CH, Ar−C2″,C6″), 125.66 (2CH, Ar−C2,C6), 122.40 (C, Ar−C1′), 121.49 (C, Ar−CH6′), 112.71 (CH, Ar−C5′), 111.79 (CH, thiazole C-5), 110.99 (CH, Ar−C2′), 105.35 (CH, pyrazole C-4), 55.86 (C3′-O$\underline{C}H_3$), 55.67 (C4′-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{26}H_{22}N_3O_2S$, $[M + H]^+$, 440.1433 found 440.1435.

3-(4-(4-Chlorophenyl)thiazol-2-yl)-5-(3,4-dimethoxyphenyl)-1-phenyl-1H-pyrazole, ***10w***. IR 836, 890, 939, 1023, 1086, 1139, 1254, 1323, 1362, 1402, 1463, 1498, 1530, 1594, 2924, 3001, 3047, 3112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.6 Hz, 2H, Ar−H), 7.46 (s, 1H, thiazole C5H), 7.41 (d, J = 8.6 Hz, 2H, Ar−H), 7.37 (m, 5H, Ar−H), 7.14 (s, 1H, pyrazole C4H), 6.89 (dd, J = 8.3, 2.0 Hz, 1H, Ar−H), 6.83 (d, J = 8.3 Hz, 1H, Ar−H), 6.71 (d, J = 2.0 Hz, 1H, Ar−H), 3.89 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.72 (C, thiazole C-2), 154.74 (C, thiazole C-4), 149.33 (C, Ar−C4′), 148.70 (C, Ar−C3′), 147.35 (C, pyrazole C-3), 144.81 (C, pyrazole C-5), 139.85 (C, Ar−C1), 133.85 (C, Ar−C4″), 133.03 (C, Ar−C1″), 129.04 (2CH, Ar−C3,C5), 128.89 (2CH, Ar−C3″,C5″), 127.99 (CH, Ar−C4), 127.73 (2CH, Ar−C2″,C6″), 125.66 (2CH, Ar−C2,C6), 122.38 (CH, Ar−C1′), 121.53 (CH, Ar−C6′), 113.00 (CH, Ar−C5′), 111.87 (CH, thiazole C-5), 111.07 (CH, Ar−C2′), 105.34 (C, pyrazole C-4), 55.89 (C3′-O$\underline{C}H_3$), 55.69 (C4′-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{26}H_{21}ClN_3O_2S$, $[M + H]^+$, 474.1043 found 474.1033.

3-(4-(4-Fluorophenyl)thiazol-2-yl)-5-(3,4-dimethoxyphenyl)-1-phenyl-1H-pyrazole, ***10x***. IR 837, 891, 940, 1020, 1082, 1139, 1160, 1230, 1255, 1320, 1360, 1390, 1430, 1455, 1498, 1521, 1593, 2929, 3001, 3047 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 (dd, J = 8.8, 5.4 Hz, 2H, Ar−H), 7.41 (s, 1H, thiazole C5H), 7.38 (m, 5H, Ar−H), 7.14 (dd, J = 12.0, 5.3 Hz, 3H, pyrazole C4H and doublet of Ar−H merged), 6.89 (dd, J = 8.3, 2.0 Hz, 1H, Ar−H), 6.83 (d, J = 8.3 Hz, 1H, Ar−H), 6.71 (d, J = 1.9 Hz, 1H, Ar−H), 3.90 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.69 and 161.73 (C, $^1J_{C-F}$ = 246.96 Hz, Ar−C4″), 161.60 (C, thiazole C-2), 154.91 (C, thiazole C-4), 149.26 (C, Ar−C4′), 148.63 (C, Ar−C3′), 147.39 (C, pyrazole C-3), 144.77 (C, pyrazole C-5), 139.82 (C, Ar−C1), 130.82 and 130.79 (C, $^4J_{C-F}$ = 3.78 Hz, Ar−C1″), 129.04 (2CH, Ar−C3,C5), 128.22 and 128.15 (2CH, $^3J_{C-F}$ = 8.82 Hz, Ar−C2″, C6″), 127.98 (CH, Ar−C4), 125.65 (2CH, Ar−C2,C6), 122.35 (C, Ar−C1′), 121.50 (CH, Ar−C6′), 115.71 and 115.53 (2CH, $^2J_{C-F}$ = 23.94 Hz, Ar−C3″, C5″), 112.30 (CH, Ar−C5′), 111.78 (CH, thiazole C-5), 111.00 (CH, Ar−C2′), 105.30 (C, pyrazole C-4), 55.87 (C3′-O$\underline{C}H_3$), 55.67 (C4′-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{26}H_{21}FN_3O_2S$, $[M + H]^+$, 458.1339 found 458.1350.

5-(3,4-Dimethoxyphenyl)-3-(4-(4-methoxyphenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10y***. IR 805, 855, 920, 980, 1019, 1067, 1110, 1161, 1228, 1260, 1320, 1360, 1400, 1437, 1496, 1593, 2930, 2961, 2991, 3058, 3114 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 8.9 Hz, 2H, Ar−H), 7.38 (m, 5H, Ar−H), 7.35 (s, 1H, thiazole C5H), 7.16 (s, 1H, pyrazole C4H), 6.98 (d, J = 8.9 Hz, 2H, Ar−H), 6.89 (dd, J = 8.3, 2.0 Hz, 1H, Ar−H), 6.82 (d, J = 8.4 Hz, 1H, Ar−H), 6.72 (d, J = 2.0 Hz, 1H, Ar−H), 3.89 (s, 3H, -OCH_3), 3.86 (s, 3H, -OCH_3), 3.66 (s, 3H, -OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$)

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δ 161.26 (C, thiazole C-2), 159.59 (C, Ar−C4″), 155.75 (C, thiazole C-4), 149.23 (C, Ar−C4′), 148.63 (C, Ar−C3′), 147.59 (C, pyrazole C-3), 144.70 (C, pyrazole C-5), 139.88 (C, Ar−C1), 129.04 (2CH, Ar−C3,C5), 127.94 (C, Ar−C4), 127.77 (2CH, Ar−C3″,C5″), 127.54 (C, Ar−C1″), 125.69 (2CH, Ar−C2,C6), 122.45 (CH, Ar−C1′), 121.52 (CH, Ar−C6′), 114.08 (2CH, Ar−C2″,C6″), 111.81 (CH, thiazole C-5), 111.04 (CH, Ar−C5′), 111.00 (CH, Ar−C2′), 105.37 (C, pyrazole C-4), 55.89 (C3′-O$\underline{C}H_3$), 55.69 (C4′-O$\underline{C}H_3$), 55.37 (C4″-O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{27}H_{24}N_3O_3S$, $[M + H]^+$, 470.1538 found 470.1542.

5-(3,4-Simethoxyphenyl)-3-(4-(4-nitrophenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10z***. IR 838, 898, 930, 1023, 1073, 1105, 1142, 1196, 1233, 1269, 1346, 1366, 1414, 1466, 1495, 1529, 1597, 2940, 3002, 3071, 3107 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.35−8.17 (m, 4H, Ar−H), 7.88 (s, 1H, thiazole C5H,), 7.47−7.30 (m, 5H, Ar−H), 7.17−7.09 (m, 1H, Ar−H), 6.94−6.80 (m, 2H, Ar−H and pyrazole C4H), 6.71 (dd, J = 10.9, 2.7 Hz, 1H, Ar−H), 3.87 (s, 3H, Ar-OCH_3), 3.65 (s, 3H, Ar-OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.85 (C, thiazole C-2), 157.96 (C, thiazole C-4), 154.12 (C, Ar−C4′), 153.40 (C, Ar−C3′), 151.85 (C, pyrazole C-3), 151.64 (C, Ar−C4″), 149.70 (C, pyrazole C5), 145.10 (C, Ar−C1″), 144.44 (C, Ar−C1), 133.85 (2CH, Ar−C3,C5), 132.93 (CH, Ar−C4), 131.78 (2CH, Ar−C2″,C6″), 130.35 (2CH, Ar−C2,C6), 128.85 (CH, thiazole C5), 126.78 (C, Ar−C1′), 126.31 (2CH, Ar−C3″,C5″), 121.59 (CH, Ar−C6′), 116.65 (CH, Ar−C5′), 116.03 (CH, Ar−C2′), 109.99 (CH, pyrazole C-4), 60.63 (CH_3, -O$\underline{C}H_3$), 60.42 (CH_3, -O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{26}H_{21}N_4O_4S$, $[M + H]^+$, 485.1284 found 485.1280.

5-(3,4-Dimethoxyphenyl)-3-(4-(3-nitrophenyl)thiazol-2-yl)-1-phenyl-1H-pyrazole, ***10aa***. IR 862, 890, 940, 997, 1026, 1071, 1242, 1168, 1233, 1317, 1341, 1369, 1414, 1457, 1497, 1530, 1593, 2946, 3013, 3099 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.87 (t, J = 1.9 Hz, 1H, Ar−H), 8.32 (ddd, J = 7.8, 1.6, 1.1 Hz, 1H, Ar−H), 8.20 (ddd, J = 8.2, 2.3, 1.0 Hz, 1H, Ar−H), 7.64 (s, 1H, thiazole C5H), 7.62 (t, J = 8.0 Hz, 1H, Ar−H), 7.38 (m, 5H, Ar−H), 7.18 (s, 1H, pyrazole C4H), 6.91 (dd, J = 8.3, 2.0 Hz, 1H, Ar−H), 6.84 (d, J = 8.4 Hz, 1H, Ar−H), 6.73 (d, J = 2.0 Hz, 1H, Ar−H), 3.90 (s, 3H, -OCH_3), 3.68 (s, 3H, -OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.31 (C, thiazole C-2), 153.32 (C, thiazole C-4), 149.38 (C, Ar−C4′), 148.78 (C, Ar−C3″), 148.72 (C, Ar−C3′), 147.11 (C, pyrazole C-3), 144.97 (C, pyrazole C-5), 139.82 (C, Ar−C1), 136.14 (C, Ar−C1″), 132.14 (CH, Ar−C6″), 129.69 (CH, Ar−C5″), 129.09 (2CH, Ar−C3,C5), 128.08 (CH, Ar−C4), 125.66 (2CH, Ar−C2,C6), 122.65 (CH, Ar−C2″), 122.25 (C, Ar−C1′), 121.56 (CH, Ar−C6′), 121.37 (CH, Ar−C4″), 114.72 (CH, Ar−C5′), 111.84 (CH, thiazole C-5), 111.08 (CH, Ar−C2′), 105.38 (C, pyrazole C-4), 55.90 (CH_3, -O$\underline{C}H_3$), 55.72 (CH_3, -O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{26}H_{21}N_4O_4S$, $[M + H]^+$, 485.1284 found 485.1280.

4-(2-(5-(3,4-Dimethoxyphenyl)-1-phenyl-1H-pyrazol-3-yl)thiazol-4-yl)benzonitrile, ***10ab***. IR 866, 903, 960, 1023, 1058, 1131, 1164, 1230, 1254, 1287, 1321, 1362, 1395, 1436, 1495, 1526, 1595, 2223, 2946, 3000, 3056, 3112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 8.6 Hz, 2H, Ar−H), 7.74 (d, J = 8.6 Hz, 2H, Ar−H), 7.63 (s, 1H), 7.39 (m, 5H, Ar−H), 7.15 (s, 1H, pyrazole C4H), 6.90 (dd, J = 8.3, 2.0 Hz, 1H, Ar−H), 6.84 (d, J = 8.4 Hz, 1H, Ar−H), 6.71 (d, J = 2.0 Hz, 1H, Ar−H), 3.90 (s, 3H, -OCH_3), 3.66 (s, 3H, -OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.26 (C, thiazole C-2), 153.82 (C, thiazole C-4), 149.39 (C, Ar−C4′), 148.71 (C, Ar−C3′), 147.08 (C, pyrazole C-3), 144.95 (C, pyrazole C-5), 139.78 (C, Ar−C1), 138.52 (C, Ar−C1″), 132.63 (2CH, Ar−C3″,C5″), 129.08 (2CH, Ar−C3,C5), 128.09 (C, Ar−C4), 126.88 (2CH, Ar−C2″,C6″), 125.64 (2CH, Ar−C2,C6), 122.24 (C, Ar−C1′), 121.55 (C, Ar−C1′), 118.98 (C4″-$\underline{C}N$), 115.47 (C, Ar−C5′), 111.84 (CH, thiazole C-5), 111.32 (C, Ar−C4″), 111.08 (C, Ar−C2′), 105.31 (C, pyrazole C-4), 55.89 (CH_3, -O$\underline{C}H_3$), 55.70 (CH_3, -O$\underline{C}H_3$). HRMS (ESI, m/z): calculated for $C_{27}H_{21}N_4O_2S$, $[M + H]^+$, 465.1385 found 465.1386.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.2c08137.

Biological activity and spectral data of synthesized compounds (PDF)

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All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by Yogesh Nandurkar, Abhijit Shinde, Manish Bhoye, and Shivaji Jagadale. The final version of the manuscript was written by Yogesh Nandurkar and Pravin Mhaske.

Notes

The authors declare no competing financial interest.

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