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Facile synthesis of alkynyl-, aryl- and ferrocenyl-substituted pyrazoles via Sonogashira and Suzuki–Miyaura approaches

Sedef Karabiyikoglu and Metin Zora*

A concise and efficient synthesis of densely substituted novel pyrazoles with alkynyl, aryl and ferrocenyl functionalities is reported, providing a platform for biological studies. The general strategy involves Sonogashira and Suzuki–Miyaura cross-coupling reactions of easily obtainable 5-ferrocenyl/phenyl-4-iodo-1-phenylpyrazoles with terminal alkynes and boronic acids, respectively. The starting 4-iodopyrazoles were synthesized by electrophilic cyclization of α,β-alkynic hydrazones with molecular iodine. Sonogashira reactions have been achieved by employing 5 mol% $PdCl_2(PPh_3)_2$, 5 mol% CuI, excess Et_3N and 1.2 equiv. of terminal alkyne, relative to 4-iodopyrazole, in tetrahydrofuran at 65 °C, while Suzuki–Miyaura reactions have been accomplished using 5 mol% $PdCl_2(PPh_3)_2$ and 1.4 equiv. of both boronic acid/ester and $KHCO_3$, with respect to 4-iodopyrazole, in 4:1 dimethylformamide–H_2O solution at 110 °C. Both Sonogashira and Suzuki–Miyaura coupling reactions have proven effective for the synthesis of alkynyl-, aryl- and ferrocenyl-substituted pyrazoles and demonstrated good tolerance to a diverse range of substituents, including electron-donating and electron-withdrawing groups. These coupling approaches could allow for the rapid construction of a library of functionalized pyrazoles of pharmacological interest. Copyright © 2016 John Wiley & Sons, Ltd.

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Keywords: pyrazole; ferrocene; alkyne; boronic acid; coupling

Introduction

Pyrazoles represent an important class of nitrogen-containing five-membered heterocycles,[1] which have occupied a unique position in the design and synthesis of novel biologically active agents that exhibit remarkable medicinal activities.[2] In fact, pyrazoles have a profound effect on human health since they are present in a wide range of natural products and drugs used to battle a large number of diseases and pathophysiological conditions.[3] It has been reported that pyrazoles possess a broad spectrum of pharmacological and biological properties such as anti-bacterial,[4] anti-depressant,[5] anti-hyperglycaemic,[6] anti-hypertensive,[7] anti-inflammatory[8] and antitumor[9] properties. In addition, pyrazoles exist as prominent building blocks in the structures of various leading drugs (e.g. Celebrex,[10] Viagra[11] and Zometapine[12]) and pesticides (e.g. Cyenopyrafen,[13] Fenpyroximate[14] and Tebufenpyrad[15]).

In particular, alkynyl-, aryl- and ferrocenyl-substituted pyrazoles have attracted considerable attention due to their broad spectrum of biological and pharmaceutical activities. Alkynylpyrazoles are particularly important for their anti-inflammatory,[16,17] antiviral[18] and muscarinic[19] properties and cyclooxygenase,[20] 5-lipoxygenase,[20] HIV protease[21] and phosphodiesterase[22] inhibitory activities. They are also highly valuable substrates in organic syntheses since their triple bonds are very prone to undergo a variety of reactions, including nucleophilic, electrophilic, radical, and cycloaddition reactions, allowing further functionalization of pyrazole derivatives.[23] Alkynylpyrazoles are commonly synthesized by 1,3-dipolar cycloaddition of diazomethane with 1,3-butadiynes, cycloaddition of hydrazines with diacetylenic ketones, reactions of pyrazolylketones with PCl_5 followed by a base and metal-catalysed cross-coupling of halogenopyrazoles with terminal alkynes (known as Sonogashira reaction).[23,24]

Arylpyrazoles, particularly 1,5-diaryl-substituted pyrazoles, are especially useful for the treatment of inflammation and inflammation-connected disorders, including arthritis, as well as cardiovascular disorders.[25] They are also heat shock protein 90 (HSP90) inhibitors and can be used in the treatment of conditions mediated by HSP90, including cancer.[26] In addition, they are potent CCR2 receptor antagonists.[27] Arylpyrazoles are typically synthesized by the reaction of phenylhydrazine with 1,3-dicarbonyl compounds or their 1,3-dielectrophilic equivalents including alkynals and alkynones, 1,3-dipolar cycloaddition of diazoalkanes and nitrilimines with alkenes and alkynes, and metal-catalysed cross-coupling of halogenopyrazoles with boronic acids (called Suzuki–Miyaura reaction).[28,29]

It is noteworthy that owing to its unique structure, membrane-permeation properties and anomalous metabolism, ferrocene is often integrated into biologically active molecules to enhance their potency or generate new medicinal properties.[30] Indeed, many ferrocene derivatives have proved to be particularly active against a number of animal and human tumours.[30] In this regard, functionally substituted ferrocenylpyrazoles have great potential for

* *Correspondence to: Metin Zora, Department of Chemistry, Middle East Technical University, 06800 Ankara, Turkey. E-mail: zora@metu.edu.tr*

Department of Chemistry, Middle East Technical University, 06800 Ankara, Turkey

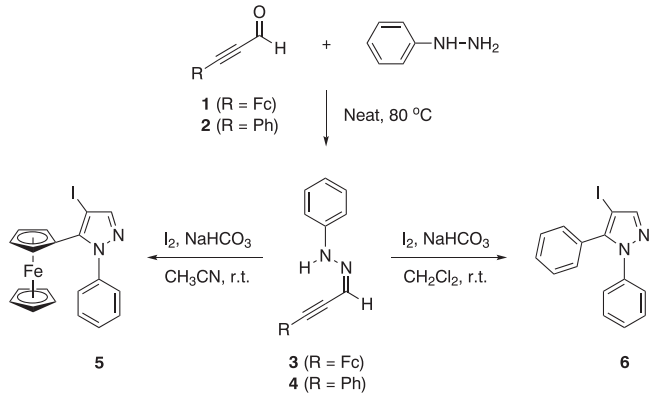
biological studies and it is crucial to provide new methodologies for their construction.[31]

Recently, we have reported the synthesis of α,β-alkynic hydrazones **3** and **4** from propargyl aldehydes **1** and **2**, and their regioselective conversion into pyrazoles **5** and **6**, respectively (Scheme 1).[32] When treated with molecular iodine in the presence of sodium bicarbonate, α,β-alkynic hydrazones **3** and **4** undergo electrophilic cyclization and afford ferrocenyl- and phenyl-substituted 4-iodopyrazole derivatives **5** and **6**, respectively, in high yields. It is noteworthy that iodine-containing pyrazoles are very important building blocks for the synthesis of diverse natural products and pharmaceuticals since they can be easily elaborated to more complex structures by metal-catalysed cross-coupling reactions. In this regard, Sonogashira[33] and Suzuki–Miyaura[34] reactions are among the most widely used C–C bond forming reactions, providing efficient routes to alkynylaryl and biaryl compounds, respectively. In particular, they provide rapid entries to the libraries of alkynylpyrazoles[35] and biarylpyrazoles.[29]

It has been concluded from structure–activity relationships that the number of substituents, such as aryl groups, attached to a potentially bioactive core plays an important role in biological activities.[36] For instance, the corresponding pyridine derivatives bearing more aryl groups exhibit stronger biological activity as compared to those containing fewer aryl groups.[36] Notably, an increase in the number of substituents via introduction of alkynyl and aryl functionalities into ferrocenylpyrazoles could result in beneficial biological properties. We have anticipated that the decoration of a pyrazole core with such functionalities may provide novel derivatives with much enhanced or totally new medicinal properties. Although pyrazoles are among the most intensely studied compounds, to the best of our knowledge, 4-alkynyl/aryl-5-ferrocenyl-substituted pyrazole derivatives are not known. Our continued interest[37] in the synthesis of new carbocyclic, heterocyclic and ferrocenyl compounds as potential pharmaceuticals and scaffolds has prompted us to investigate the Sonogashira and Suzuki–Miyaura cross-coupling reactions of 4-iodopyrazoles **5** and/or **6** with terminal alkynes and boronic acids, respectively. We herein report the full details of this study.

Results and Discussion

We first prepared the required 4-iodopyrazoles **5** and **6** from the corresponding propargyl aldehydes **1** and **2** according to our previous study as shown in Scheme 1.[32] The neat reaction of ferrocenylpropargyl aldehyde (**1**) with phenylhydrazine at 80 °C afforded *Z* and *E* isomers of hydrazone **3** in 54 and 36% yields, respectively. On the other hand, the same reaction with phenylpropargyl aldehyde (**2**) yielded *Z* isomer of hydrazone **4** as the major product (81%); the isolation of the minor *E* isomer was not attempted as it was not adequately stable and mostly converted into *Z* isomer during purification. We next carried out electrophilic cyclizations of hydrazones **3** and **4** using I_2 in the presence of sodium bicarbonate. When reacted with molecular iodine, *Z* and *E* isomers of hydrazone **3** afforded ferrocenyl-substituted 4-iodopyrazole **5** in 90 and 92% yields, respectively. Iodocyclization of *Z* isomer of hydrazone **4** produced phenyl-substituted 4-iodopyrazole **6** in 80% yield (Scheme 1).[32]

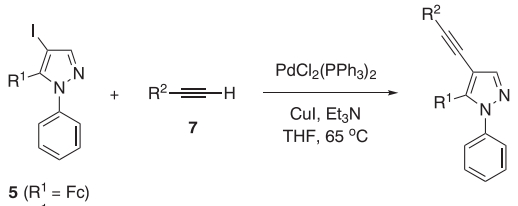


Scheme 1. Synthesis of 4-iodo-substituted pyrazoles.

Subsequently, we investigated the feasibility of metal-catalysed cross-coupling of 4-iodopyrazoles **5** and **6** with terminal alkynes. Although there are many possibilities for the choice of catalyst, co-catalyst and base, one of the most common catalytic systems for Sonogashira reaction consists of a relatively cheap and highly stable palladium(II)–triphenylphosphine complex with CuI in an excess of amine.[33] Accordingly, we chose $PdCl_2(PPh_3)_2$ as catalyst, CuI as co-catalyst and Et_3N as base. The reactions were carried out with 5 mol% $PdCl_2(PPh_3)_2$ and 5 mol% CuI. During the course of such reactions, *in situ* generation of copper acetylide could yield homocoupling product of terminal alkyne when it was exposed to excessive oxidative agents like oxygen. In order to eliminate the homocoupling, reactions were run under argon atmosphere and terminal alkynes were added slowly to the reaction medium in small portions. This prevented the need for high equivalents of alkyne; thus, relative to starting 4-iodopyrazole, only 1.2 equiv. of terminal alkynes was used. Initially, the reaction of 5-ferrocenyl-4-iodopyrazole **5** with phenylacetylene (**7a**) was examined (Table 1, entry 1). The reaction was first performed in tetrahydrofuran (THF) and dimethylformamide (DMF) at room temperature, but these reactions did not produce desired products and approximately 95% of the starting 4-iodopyrazole **5** was recovered with some decomposition. However, the same reaction in refluxing THF at 65 °C for 12 h afforded 4-alkynylpyrazole **8a** in 66% yield. When the reaction was conducted in DMF at 110 °C for 12 h, product formation was not observed and 85% of the starting 4-iodopyrazole **5** was recovered along with some decomposition products. After setting reaction solvent and temperature (THF, 65 °C), the transformation was tested for 4, 6 and 27 h, which yielded 4-alkynylpyrazole **8a** in 55, 64 and 66% yields, respectively, indicating that longer reaction time (27 h) did not improve the yield of **8a** (66%). Although the reaction time for this particular case was around 12 h, the reactions with other terminal alkynes required less or more time as indicated by TLC analyses. In summary, the reactions were performed in refluxing THF at 65 °C by frequent TLC monitoring for completion. Results from a systematic study are given in Table 1.

As evident from Table 1, Sonogashira cross-coupling reactions of **5** were carried out with a variety of terminal alkynes including aryl, heteroaryl, cycloalkyl and ferrocenyl groups as the alkyne substituent (Table 1, entries 1–8). All reactions produced 4-alkynyl-5-ferrocenyl-substituted pyrazole derivatives **8a**–**h**, the yields of which ranged from 37 to 78%. Notably, the couplings with terminal alkynes **7e** and **7f**, bearing alcohol and amine functionalities, resulted in the formation of the corresponding pyrazole derivatives **8e** and **8f**, respectively, in good yields (Table 1, entries 5 and 6). By these Sonogashira reactions, thiophenyl-containing pyrazole **8g** and two-ferrocenyl-bearing pyrazole **8h** were also synthesized in good yields (Table 1, entries 7 and 8). We also carried out the cross-coupling reactions of 4-iodo-5-phenylpyrazole **6** with

Table 1. Synthesis of 4-alkynylpyrazoles from 4-iodopyrazoles



5 (R^1 = Fc)
6 (R^1 = Ph)

8 (R^1 = Fc)
9 (R^1 = Ph)

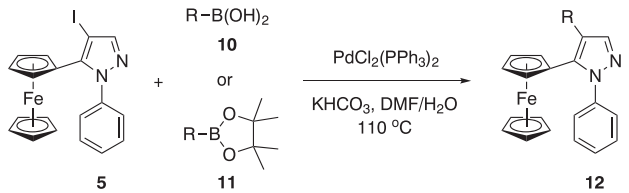
Entry	R^1	R^2	Time (h)	Product	Yield (%)[a]
1[b,c,d]	R^1 = Fc (**5**)	R^2 = Ph (**7a**)	12	**8a**	66
2	**5**	R^2 = 4-MePh (**7b**)	25	**8b**	37
3	**5**	R^2 = 4-MeOPh (**7c**)	8	**8c**	78
4	**5**	R^2 = 4-(Me_2N)Ph (**7d**)	15	**8d**	44
5	**5**	R^2 = 1-hydroxycyclohex-1-yl (**7e**)	14	**8e**	70
6	**5**	R^2 = 1-aminocyclohex-1-yl (**7f**)	20	**8f**	68
7	**5**	R^2 = 3-thienyl (**7g**)	18	**8g**	62
8	**5**	R^2 = Fc (**7h**)	12	**8h**	68
9	R^1 = Ph (**6**)	**7a**	15	**9a**	42
10	**6**	**7b**	24	**9b**	36
11	**6**	**7c**	16	**9c**	76
12	**6**	**7g**	7	**9d**	85
13	**6**	**7h**	13	**9e**	54

[a]Yields are of isolated products.
[b]When the reaction was performed in THF or DMF at room temperature, it did not produce any products and 95% of the starting 4-iodopyrazole **5** was recovered with some decomposition.
[c]When the reaction was performed in DMF at 110 °C, it did not produce any products and 85% of the starting 4-iodopyrazole **5** was recovered along with some decomposition.
[d]When the reaction was performed in THF at 65 °C for 4, 6 and 27 h, it afforded 4-alkynylpyrazole **8a** in 55, 64 and 66% yields, respectively.

terminal alkynes under same conditions (Table 1, entries 9–13). These reactions afforded the corresponding 4-alkynyl-5-phenylpyrazoles **9** in yields ranging from 36 to 85%. In these reactions, the highest yield (85%) was obtained for the pyrazole **9d** bearing a thiophenyl group as the alkyne substituent (Table 1, entry 12). For the pyrazole derivatives containing the same alkynyl group, the yields of 4-alkynyl-5-arylpyrazoles were slightly lower than those of 4-alkynyl-5-ferrocenylpyrazoles except the case of thiophen-3-ylethynyl group. In brief, the coupling reaction was general for a diversity of terminal alkynes and tolerated the presence of aryl, heteroaryl, ferrocenyl and cycloalkyl groups with electron-withdrawing and electron-donating substituents.

Next, we investigated metal-catalysed coupling reactions of 4-iodopyrazole **5** with boronic acids. It is worth mentioning that Suzuki–Miyaura reactions have been tested previously with a large number of solvents, bases and palladium catalysts.[34] Our literature search revealed that bases in bicarbonate salt form and palladium catalysts with triphenylphosphine ligands, especially $PdCl_2(PPh_3)_2$, work quite effectively in these reactions. In addition, DMF–H_2O combination is one of the most widely used solvent systems in such reactions.[38] In the light of this knowledge, the condition involving $PdCl_2(PPh_3)_2$ as catalyst, $KHCO_3$ as base and 4:1 DMF–H_2O as solvent system was adapted for our Suzuki–Miyaura coupling reactions. The reactions were performed with 5 mol% $PdCl_2(PPh_3)_2$ and 1.4 equiv. of both boronic acid/ester and $KHCO_3$, with respect to starting 4-iodopyrazole, and by heating at 110 °C. Results from a systematic study are summarized in Table 2. Initially, the cross-coupling of **5** was carried out with both phenylboronic acid (**10a**) and phenylboronic acid pinacol ester (**11a**) (Table 2, entries 1 and 2). These reactions afforded the corresponding pyrazole **12a** in 72 and 80% yields, respectively. Although boronic ester **11a** gave a higher yield of **12a**, we preferred to use boronic acids in other couplings because they are cheaper and more readily available than boronic esters. As evident from Table 2, the coupling reactions were all successful and produced the expected 4-aryl-5-ferrocenylpyrazole derivatives **12** in good to excellent yields in most cases. The lowest yield (42%) was obtained for 4-(1*H*-indol-6-yl)pyrazole (**12e**) while the highest yield (99%) was observed for 4-(3-nitrophenyl)pyrazole (**12k**) (Table 2, entries 6 and 12). Since the introduction of fluorine-bearing substituents into organic compounds could result in beneficial biological properties,[39] two derivatives of fluorine-containing pyrazoles, **12g** and **12h**, were synthesized (Table 2, entries 8 and 9). For the same reason, indole-containing pyrazole derivative **12e** was synthesized because indoles are very important for pharmaceutical and agricultural applications (Table 2, entry 6).[40] It is noteworthy that during the reactions, homocoupling of arylboronic acids was not observed since the experiments were carried out under argon atmosphere to prevent oxidative homocoupling of boronic acids.[41] Moreover, according to literature studies,[41] the use of a palladium catalyst with triphenylphosphine ligands, instead of a palladium salt such as $PdCl_2$, could have an inhibiting effect on homocoupling of arylboronic acids. In summary, the coupling reaction was found to be general for a wide range of boronic acids and tolerated the presence of aryl groups with electron-withdrawing and electron-donating substituents. Moreover, Suzuki–Miyaura coupling

Table 2. Synthesis of 4-arylpyrazoles from 4-iodopyrazoles



Entry	R	Time (h)	Product	Yield (%)[a]
1	R = Ph (**10a**)	4	**12a**	72
2	R = Ph (**11a**)	6	**12a**	80
3	R = 4-EtPh (**10b**)	5	**12b**	65
4	R = benzo[d] [1,3]dioxol-5-yl (**10c**)	7	**12c**	52
5	R = 3,4,5-trimethoxyphenyl (**10d**)	5	**12d**	78
6	R = 1*H*-indole-5-yl (**10e**)	13	**12e**	42
7	R = 4-ClPh (**10f**)	6	**12f**	91
8	R = 4-ethoxy-3-fluorophenyl (**10g**)	4	**12g**	80
9	R = 3,4,5-trifluorophenyl (**10h**)	5	**12h**	95
10	R = 3-(ethoxycarbonyl)phenyl (**10i**)	5	**12i**	93
11	R = 2-methoxypyridin-5-yl (**10j**)	4	**12j**	94
12	R = 3-NO_2Ph (**10k**)	6	**12k**	99

[a]Yields are of isolated products.

reactions of 4-iodopyrazoles (Table 2) usually required shorter reaction times as compared to their corresponding Sonogashira coupling reactions (Table 1).

Conclusions

In summary, we investigated the Sonogashira and Suzuki–Miyaura cross-coupling reactions of ferrocenyl- and phenyl-substituted 4-iodopyrazoles, prepared by electrophilic cyclization of the corresponding α,β-alkynic hydrazones with molecular iodine in the presence of sodium bicarbonate. Sonogashira reactions of 4-iodopyrazoles were accomplished by employing 5 mol% $PdCl_2(PPh_3)_2$, 5 mol% CuI, excess Et_3N and 1.2 equiv. of terminal alkyne, relative to 4-iodopyrazole, in refluxing THF at 65 °C. From these reactions, 4-alkynylpyrazoles were formed in 36 to 85% yields. Notably, in most cases with the same terminal alkyne, 5-ferrocenyl-4-iodopyrazole yielded the corresponding 4-alkynylpyrazole in higher yield as compared to 4-iodo-5-phenylpyrazole. On the other hand, Suzuki–Miyaura reactions of 4-iodopyrazoles were achieved by using 5 mol% $PdCl_2(PPh_3)_2$ and 1.4 equiv. of both boronic acid/ester and $KHCO_3$, with respect to 4-iodopyrazole, in 4:1 DMF–H_2O solution at 110 °C. These reactions produced 4-arylpyrazoles in 42 to 99% yields. Notably, Suzuki–Miyaura coupling reactions of 4-iodopyrazoles went to completion in shorter times than their corresponding Sonogashira coupling reactions. Both coupling reactions were found to be general for a diverse range of substrates including electron-withdrawing and electron-donating substituents. In conclusion, the chemistry developed here is very versatile and practical and accommodates various functional groups. Moreover, the synthesized heterocycles have potential to act as new pharmacophores and scaffolds in medicinal chemistry.

Experimental

General Information

^{1}H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) downfield from an internal trimethylsilane (TMS) reference or relative to $CDCl_3$ (7.26 and 77.16 ppm in ^{1}H NMR and ^{13}C NMR, respectively). Coupling constants (*J*) are reported in hertz (Hz), and spin multiplicities are presented by the following symbols: s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet). DEPT ^{13}C NMR information is given in parentheses as C, CH, CH_2 and CH_3. Infrared (IR) spectra were recorded using attenuated total reflection. Band positions are reported in reciprocal centimetres (cm^{-1}). MS and high resolution MS (HRMS) were conducted using electrospray ionization (ESI) with Micro-Tof; *m/z* values are reported (for each measurement, the mass scale was recalibrated with sodium formate clusters, and samples were dissolved and measured in MeOH or CH_3CN). Flash chromatography was performed using thick-walled glass columns and 'flash grade' silica (230–400 mesh). TLC was performed using commercially prepared 0.25 mm silica gel plates and visualization was effected with a short-wavelength UV lamp (254 nm). The relative proportions of solvents in chromatography solvent mixtures refer to the volume-to-volume ratio. All commercially available reagents were used directly without purification unless otherwise stated. All the solvents used in reactions were distilled for purity. An inert atmosphere was created by slight positive pressure (*ca* 0.1 psi) of argon. All glassware was dried in an oven prior to use. The starting 4-iodopyrazoles **5** and **6** were synthesized according to a previous study.[32]

General Procedure for Synthesis of 4-Alkynylpyrazoles 8 and 9 via Sonogashira Coupling Reaction (Table 1)

In a two-neck round-bottom flask equipped with a reflux condenser, 4-iodopyrazole **5** or **6** (0.220 mmol), $PdCl_2(PPh_3)_2$ (7.73 mg, 0.011 mmol) and CuI (2.09 mg, 0.011 mmol) were dissolved in a mixture of triethylamine (1.6 ml) and THF (1 ml) by vigorous stirring under argon. Meanwhile, separately in a flask under argon, the corresponding terminal alkyne **7** (0.264 mmol) was dissolved in THF (1 ml) and added slowly to the first reaction flask over 1 h. The resulting reaction mixture was then heated to reflux (65 °C) with stirring. This was continued until TLC revealed the completion of the reaction. After the reaction was over, the solvent was evaporated using a rotary evaporator. Crude product was purified by flash chromatography on silica gel using hexane–ethyl acetate (9:1) as the eluent, which afforded the corresponding 4-alkynylpyrazole **8** or **9** with yield indicated in Table 1.

*5-Ferrocenyl-1-phenyl-4-(phenylethynyl)-1H-pyrazole (**8a**)*

^{1}H NMR ($CDCl_3$): 7.73 (s, 1H in pyrazole), 7.56–7.54 (m, 2H, Ph), 7.35–7.25 (m, 8H, Ph), 4.40 (br s, 2H, Fc), 4.14 (br s, 2H, Fc), 4.04 (s, 5H, Fc). ^{13}C NMR ($CDCl_3$): 143.6 (C–N in Ph), 143.5 (CH in pyrazole), 140.4 (C in pyrazole attached to Fc), 131.2 (CH, Ph), 129.0 (CH, Ph), 128.6 (CH, Ph), 128.5 (CH, Ph), 128.0 (CH, Ph), 126.6 (CH, Ph), 124.0 (C, Ph), 102.5 (C in pyrazole attached to alkyne), 93.4 (C in C≡C attached to Ph), 82.9 (C in C≡C attached to pyrazole), 73.1 (C, Fc), 70.0 (CH, Fc), 68.9 (CH, Fc), 68.6 (CH, Fc). IR (neat): 3729 (m), 3698

(m), 3054 (w), 2228 (vw), 1554 (m), 1495 (s), 1398 (m), 859 (m), 762 (s), 693 (s). Anal. Calcd for $C_{27}H_{20}FeN_2$ (%): C, 75.71; H, 4.71; N, 6.54. Found (%): C, 75.56; H, 4.67; N, 6.53; MS (ESI, *m/z*): 451.09 $[M + Na]^+$, 428.09 $[M]^+$. HRMS (ESI): calcd for $C_{27}H_{20}^{56}FeN_2Na$: 451.0874 $[M + Na]^+$, found: 451.0868; calcd for $C_{27}H_{20}^{56}FeN_2$: 428.0976 $[M]^+$, found: 428.0971.

*5-Ferrocenyl-1-phenyl-4-(p-tolylethynyl)-1H-pyrazole (**8b**)*

^{1}H NMR ($CDCl_3$): 7.84 (s, 1H in pyrazole), 7.55 (d, 2H, J = 7.9 Hz in tolyl), 7.48–7.46 (m, 3H, Ph), 7.41–7.39 (m, 2H, Ph), 7.25 (d, 2H, J = 7.9 Hz in tolyl), 4.56 (s, 2H, Fc), 4.29 (s, 2H, Fc), 4.20 (s, 5H, Fc), 2.44 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): 143.4 (C–N in Ph), 143.3 (CH in pyrazole), 140.4 (C in pyrazole attached to Fc), 138.2 (C in tolyl attached to CH_3), 131.1 (CH, Ph), 129.3 (CH, Ph), 129.0 (CH, Ph), 128.5 (CH, Ph), 126.5 (CH, Ph), 121.0 (C, Ph), 102.8 (C in pyrazole attached to alkyne), 93.5 (C in C≡C attached to tolyl), 82.0 (C in C≡C attached to pyrazole), 73.5 (C, Fc), 70.2 (CH, Fc) 69.0 (CH, Fc), 68.8 (CH, Fc), 21.6 (CH_3). IR (neat): 3733 (m), 3698 (w), 3059 (vw), 2988 (br), 2916 (br), 1500 (s), 1398 (m), 1078 (w), 815 (m), 767 (m), 694 (m). Anal. Calcd for $C_{28}H_{22}FeN_2$ (%): C, 76.03; H, 5.01; N, 6.33. Found (%): C, 75.80; H, 5.39; N, 6.19. MS (ESI, *m/z*): 465.10 $[M + Na]^+$, 442.11 $[M]^+$. HRMS (ESI): calcd for $C_{28}H_{22}^{56}FeN_2Na$: 465.1030 $[M + Na]^+$, found: 465.1025; calcd for $C_{28}H_{22}^{56}FeN_2$: 442.1132 $[M]^+$, found: 442.1127.

*5-Ferrocenyl-4-((4-methoxyphenyl)ethynyl)-1-phenyl-1H-pyrazole (**8c**)*

^{1}H NMR ($CDCl_3$): 7.72 (s, 1H in pyrazole), 7.49 (d, 2H, J = 8.7 Hz in methoxyphenyl), 7.36–7.35 (m, 3H, Ph), 7.29–7.27 (m, 2H, Ph), 6.87 (d, 2H, J = 8.7 Hz in methoxyphenyl), 4.41 (s, 2H, Fc), 4.16 (s, 2H, Fc), 4.06 (s, 5H, Fc), 3.78 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$): 159.5 (C in methoxyphenyl attached to OCH_3), 143.4 (CH in pyrazole), 143.3 (C–N in Ph), 140.4 (C in pyrazole attached to Fc), 132.7 (CH in methoxyphenyl), 129.0 (CH, Ph), 128.5 (CH, Ph), 126.5 (CH, Ph), 116.2 (C in methoxyphenyl), 114.3 (CH in methoxyphenyl), 102.9 (C in pyrazole attached to alkyne), 93.2 (C in C≡C attached to methoxyphenyl), 81.2 (C in C≡C attached to pyrazole), 73.3 (C, Fc), 70.0 (CH, Fc), 68.7 (CH, Fc), 68.6 (CH, Fc), 55.4 (OCH_3). IR (neat): 3057(w), 2969 (w), 2839 (w), 1896 (vw), 1603 (s), 1498 (vs), 1398 (s), 1286 (s), 1245 (vs), 1175 (s), 1027 (s), 966 (s), 878 (m). Anal. Calcd for $C_{28}H_{22}FeN_2O$ (%): C, 73.37; H, 4.84; N, 6.11. Found (%): C, 73.19; H, 5.25; N, 6.20. MS (ESI, *m/z*): 481.09 $[M + Na]^+$, 458.10 $[M]^+$. HRMS (ESI): calcd for $C_{28}H_{22}^{56}FeN_2ONa$: 481.0979 $[M + Na]^+$, found: 481.0974; calcd for $C_{28}H_{22}^{56}FeN_2O$: 458.1082 $[M]^+$, found: 458.1076.

*4-((5-Ferrocenyl-1-phenyl-1H-pyrazol-4-yl)ethynyl)-N,N-dimethylaniline (**8d**)*

^{1}H NMR ($CDCl_3$): 7.82 (s, 1H in pyrazole), 7.54 (d, 2H, J = 8.7 Hz in aniline), 7.47–7.44 (m, 3H, Ph), 7.39–7.37 (m, 2H, Ph), 6.77 (d, 2H, J = 8.7 Hz in aniline), 4.54 (s, 2H, Fc), 4.25 (s, 2H, Fc), 4.18 (s, 5H, Fc), 3.05 (s, 6H, $N(CH_3)_2$). ^{13}C NMR ($CDCl_3$): 150 (C in aniline attached to $N(CH_3)_2$), 143.3 (CH in pyrazole), 142.9 (C–N in Ph), 140.5 (C in pyrazole attached to Fc), 132.4 (CH in aniline), 129.0 (CH, Ph), 128.4 (C, Ph), 126.5 (CH, Ph), 112.1 (CH in aniline), 103.4 (C in pyrazole attached to alkyne), 94.2 (C in C≡C attached to Ph), 80.2 (C in C≡C attached to pyrazole), 73.6 (C, Fc), 70.0 (CH, Fc), 68.7 (CH, Fc), 68.6 (CH, Fc), 40.3 (CH_3 in $N(CH_3)_2$) (one aromatic carbon peak is missing due to overlap). IR (neat): 3831 (w), 3722 (s), 3698 (m), 2988 (s), 2922 (s), 1744 (vw), 1599 (vw), 1219 (vw), 1066 (m), 796 (vw), 668 (m). Anal. Calcd for $C_{29}H_{25}FeN_3$ (%): C, 73.89; H, 5.35; N, 8.91. Found (%): C, 73.71; H, 4.64; N, 8.17. MS (ESI, *m/z*): 472.14 $[M + H]^+$, 471.13 $[M]^+$. HRMS (ESI): calcd for $C_{29}H_{26}^{56}FeN_3$: 472.1476 $[M + H]^+$, found: 472.1443; calcd for $C_{29}H_{25}^{56}FeN_3$: 471.1398 $[M]^+$, found: 471.1389.

*1-((5-Ferrocenyl-1-phenyl-1H-pyrazol-4-yl)ethynyl)cyclohexanol (**8e**)*

^{1}H NMR ($CDCl_3$): 7.65 (s, 1H in pyrazole), 7.38–7.37 (m, 3H, Ph), 7.29–7.27 (m, 2H, Ph), 4.40 (s, 2H, Fc), 4.16 (s, 2H, Fc), 4.08 (s, 5H, Fc), 2.24 (br s, 1H, OH), 2.07–2.02 (m, 2H in C_6H_{10}), 1.74–1.53 (m, 6H in C_6H_{10}), 1.56–1.55 (m, 1H in C_6H_{10}), 1.35–1.25 (m, 1H in C_6H_{10}). ^{13}C NMR ($CDCl_3$): 143.8 (CH in pyrazole), 143.4 (C–N in Ph), 140.5 (C in pyrazole attached to Fc), 129.1 (CH, Ph), 128.7 (CH, Ph), 126.8 (CH, Ph), 101.8 (C in pyrazole attached to alkyne), 97.1 (C in C≡C attached to C_6H_{10}), 73.2 (C, Fc), 70.2 (CH, Fc), 69.3 (C in C≡C attached to pyrazole), 69.0 (CH, Fc), 68.5 (CH, Fc), 40.1 (CH_2 overlapping with C(OH) in C_6H_{10}), 25.3 (CH_2), 23.3 (CH_2). IR (neat): 3725 (w), 3354 (br), 3095 (w), 2930 (vs), 2854 (m), 2218 (w), 1736 (m), 1596 (m), 1505 (s), 1402 (s), 1381 (s), 1255 (m), 1067 (s), 966 (s), 767 (s), 693 (s). Anal. Calcd for $C_{27}H_{26}FeN_2O$ (%): C, 72.01; H, 5.82; N, 6.22. Found (%): C, 71.99; H, 5.92; N, 5.80. MS (ESI, *m/z*): 449.16 $[M + H]^+$. HRMS (ESI): calcd for $C_{27}H_{27}^{54}FeN_2O$: 449.1514 $[M + H]^+$, found: 449.1554.

*1-((5-Ferrocenyl-1-phenyl-1H-pyrazol-4-yl)ethynyl)cyclohexanamine (**8f**)*

^{1}H NMR ($CDCl_3$): 7.63 (s, 1H in pyrazole), 7.38–7.36 (m, 3H, Ph), 7.29–7.26 (m, 2H, Ph), 4.38 (s, 2H, Fc), 4.12 (s, 2H, Fc), 4.03 (s, 5H, Fc), 2.00–1.96 (m, 2H, NH_2), 1.70–1.52 (m, 8H in C_6H_{10}), 1.28–1.15 (m, 2H in C_6H_{10}). ^{13}C NMR ($CDCl_3$): 143.9 (CH in pyrazole), 142.8 (C–N in phenyl), 140.6 (C in pyrazole attached to Fc), 129.1 (CH, Ph), 128.7 (CH, Ph), 126.8 (CH, Ph), 102.2 (C in pyrazole attached to alkyne), 75.8 (C in C≡C attached to C_6H_{10}), 73.1 (C, Fc), 70.0 (CH, Fc), 68.8 (CH, Fc), 68.2 (CH, Fc), 60.4 (C in C≡C attached to pyrazole), 40.6 (C–NH_2 in C_6H_{10}); 25.5 (CH_2 in C_6H_{10}), 23.5 (CH_2 in C_6H_{10}), 14.2 (CH_2 in C_6H_{10}). IR (neat): 3284 (w), 3090 (w), 2927 (vs), 2852 (s), 2222 (w), 1596 (s), 1504 (s), 1381 (m), 1105 (m), 1001 (m), 967 (m), 817 (s), 766 (s), 693 (s). Anal. Calcd for $C_{27}H_{27}FeN_3$ (%): C, 72.17; H, 6.06; N, 9.35. Found (%): C, 71.99; H, 6.21; N, 8.23. MS (ESI, *m/z*): 448.17 $[M + H]^+$. HRMS (ESI): calcd for $C_{27}H_{28}^{54}FeN_3$: 448.1674 $[M + H]^+$, found: 448.1718.

*5-Ferrocenyl-1-phenyl-4-(thiophen-3-ylethynyl)-1H-pyrazole (**8g**)*

^{1}H NMR ($CDCl_3$): 7.72 (s, 1H in pyrazole), 7.50 (d, 1H, J = 2.3 Hz in thiophene), 7.36–7.34 (m, 3H, Ph), 7.29–7.26 (m, 2H in phenyl overlapping with 1H in thiophene), 7.20 (d, 1H, J = 4.8 Hz in thiophene), 4.40 (s, 2H, Fc), 4.16 (s, 2H, Fc), 4.07 (s, 5H, Fc). ^{13}C NMR ($CDCl_3$): 143.6 (C–N in Ph), 143.4 (CH in pyrazole), 140.3 (C in pyrazole attached to Fc), 129.7 (CH, aromatic), 129.0 (CH, aromatic), 128.5 (CH, aromatic), 127.9 (CH, aromatic), 126.5 (CH, aromatic), 125.7 (CH, aromatic), 123.0 (C in thiophene), 102.5 (C in pyrazole attached alkyne), 88.5 (C in C≡C attached to thiophene), 82.1 (C in C≡C attached to pyrazole), 73.3 (C, Fc), 70.1 (CH, Fc), 69.0 (CH, Fc), 68.7 (CH, Fc). IR (neat): 3725 (m), 3691 (m), 2988 (s), 2921 (s), 1489 (s), 1399 (m), 1063 (w), 867 (w), 777 (m), 753 (m), 687 (m). Anal. Calcd for $C_{25}H_{18}FeN_2S$ (%): C, 69.13; H, 4.18; N, 6.45. Found (%): C, 69.06; H, 4.45; N, 6.49. MS (ESI, *m/z*): 457.04 $[M + Na]^+$, 434.05 $[M]^+$. HRMS (ESI): calcd for $C_{25}H_{18}^{56}FeN_2SNa$: 457.0438 $[M + Na]^+$, found: 457.0433; calcd for $C_{25}H_{18}^{56}FeN_2S$: 434.0540 $[M]^+$, found: 434.0535.

*5-Ferrocenyl-4-(ferrocenylethynyl)-1-phenyl-1H-pyrazole (**8h**)*

^{1}H NMR ($CDCl_3$): 7.69 (s, 1H in pyrazole), 7.35–7.27 (m, 5H, Ph), 4.54 (s, 2H, Fc), 4.44 (s, 2H, Fc), 4.28 (s, 5H, Fc), 4.25 (s, 2H, Fc), 4.17 (s, 2H, Fc), 4.13 (s, 5H, Fc). ^{13}C NMR ($CDCl_3$): 143.4 (CH in pyrazole), 143.2 (C–N in Ph), 140.4 (C in pyrazole attached to Fc), 129.0 (CH, Ph),

128.5 (CH, Ph), 126.6 (CH, Ph), 103.2 (C in pyrazole attached to alkyne), 92.0 (C in C≡C attached to Fc), 78.8 (C in C≡C attached to pyrazole), 73.6 (C, Fc), 71.2 (CH, Fc), 70.2 (CH, Fc), 70.0 (CH, Fc), 69.0 (CH, Fc), 68.9 (CH, Fc), 68.7 (CH, Fc), 66.7 (C, Fc). IR (neat): 3725 (m), 3599 (w), 3099 (m), 2988 (m), 2903 (m), 2231 (w), 1595 (s), 1497 (s), 1398 (s), 1105 (s), 1000 (s), 965 (s), 816 (s), 767 (s), 695 (s). Anal. Calcd for $C_{31}H_{24}Fe_2N_2$ (%): C, 69.44; H, 4.51; N, 5.22. Found (%): C, 69.33; H, 4.54; N, 4.73. MS (ESI, *m/z*): 559.05 $[M + Na]^+$, 536.06 $[M]^+$. HRMS (ESI): calcd for $C_{31}H_{24}^{56}Fe_2N_2Na$: 559.0536 $[M + Na]^+$, found: 559.0531; calcd for $C_{31}H_{24}^{56}Fe_2N_2$: 536.0638 $[M]^+$, found: 536.0634.

*1,5-Diphenyl-4-(phenylethynyl)-1H-pyrazole (**9a**)*

^{1}H NMR ($CDCl_3$): 7.84 (s, 1H in pyrazole), 7.35–7.33 (m, 5H, Ph), 7.28–7.20 (m, 10H, Ph). ^{13}C NMR ($CDCl_3$): 144.1 (C–N in Ph), 142.8 (CH in pyrazole), 139.8 (C in pyrazole attached to Ph), 131.3 (CH, Ph), 129.6 (CH, Ph), 129.0 (CH, Ph), 128.9 (CH, Ph), 128.7 (C, Ph), 128.4 (CH, Ph), 128.3 (CH, Ph), 128.0 (CH, Ph), 127.7 (CH, Ph), 125.1 (CH, Ph), 123.6 (C, Ph), 104.5 (C in pyrazole attached to alkyne), 91.6 (C in C≡C attached to Ph), 81.4 (C in C≡C attached to pyrazole). IR (neat): 3693 (w), 3058 (m), 2929 (w), 2223 (m), 1967 (w), 1596 (s), 1495 (s) 1441 (s), 1387 (s), 1063 (m), 962 (m), 907 (s),751 (s), 730 (s), 688 (s). Anal. Calcd for $C_{23}H_{16}N_2$ (%): C, 86.22; H, 5.03; N, 8.74. Found (%): C, 86.00; H, 5.51; N, 8.65. MS (ESI, *m/z*): 321.14 $[M + H]^+$. HRMS (ESI): calcd for $C_{23}H_{17}N_2$: 321.1386 $[M + H]^+$, found: 321.1442.

*1,5-Diphenyl-4-(p-tolylethynyl)-1H-pyrazole (**9b**)*

^{1}H NMR ($CDCl_3$): 7.83 (s, 1H in pyrazole), 7.35–7.32 (m, 2H, Ph), 7.27–7.22 (m, 10H, Ph), 7.04 (d, 2H, J = 7.9 Hz in tolyl), 2.26 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): 144.0 (C–N in Ph), 142.8 (CH in pyrazole), 139.8 (C in pyrazole attached to Ph), 138.1 (C in tolyl attached to CH_3), 131.2 (CH, Ph), 129.5 (CH, Ph), 129.0 (CH, Ph), 128.9 (CH, Ph), 128.7 (C, Ph), 128.3 (CH, Ph), 127.7 (CH, Ph), 125.2 (CH, Ph), 120.5 (C, Ph), 104.7 (C in pyrazole attached to alkyne), 91.7 (C in C≡C attached to tolyl), 80.5 (C in C≡C attached to pyrazole), 21.5 (CH_3) (one aromatic CH carbon peak is missing due to overlap). IR (neat): 3733 (m), 3703 (m), 2988 (s), 2919 (s), 2237 (vw), 1593 (m), 1498 (s), 1442 (m), 1382 (s), 818 (s), 761 (m), 691 (s). Anal. Calcd for $C_{24}H_{18}N_2$ (%): C, 86.20; H, 5.43; N, 8.38. Found (%): C, 86.04; H, 5.64; N, 7.31. MS (ESI, *m/z*): 335.16 $[M + H]^+$. HRMS (ESI): calcd for $C_{24}H_{19}N_2$: 335.1543 $[M + H]^+$, found: 335.1605.

*4-((4-Methoxyphenyl)ethynyl)-1,5-diphenyl-1H-pyrazole (**9c**)*

^{1}H NMR ($CDCl_3$): 7.81 (s, 1H in pyrazole), 7.33–7.31 (m 2H, Ph), 7.25–7.20 (m, 10H, Ph), 6.74 (d, 2H, J = 8.7 Hz in methoxyphenyl), 3.70 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$): 159.4 (C in methoxyphenyl attached to OCH_3), 143.8 (C–N in Ph), 142.7 (CH in pyrazole), 139.8 (C in pyrazole attached to Ph), 132.7 (CH, Ph), 129.6 (CH, Ph), 129.0 (CH, Ph), 128.9 (CH, Ph), 128.7 (C, Ph), 128.3 (CH, Ph), 127.7 (CH, Ph), 125.2 (CH, Ph), 116.0 (C, Ph), 114.0 (CH, Ph), 105.0 (C in pyrazole attached to alkyne), 91.5 (C in C≡C attached to methoxyphenyl), 79.8 (C in C≡C attached to pyrazole), 55.3 (OCH_3). IR (neat): 3838 (vw), 3614 (vw), 3055 (w), 2836 (w), 1605 (s), 1496 (s), 1439 (s), 1383 (s), 1251 (s), 1173 (s), 960 (m), 825 (s), 694 (s). Anal. Calcd for $C_{24}H_{18}N_2O$ (%): C, 82.26; H, 5.18; N, 7.99. Found (%): C, 82.16; H, 5.29; N, 7.36. MS (ESI, *m/z*): 351.16 $[M + H]^+$. HRMS (ESI): calcd for $C_{24}H_{19}N_2O$: 351.1492 $[M + H]^+$, found: 351.1555.

*1,5-Diphenyl-4-(thiophen-3-ylethynyl)-1H-pyrazole (**9d**)*

^{1}H NMR ($CDCl_3$): 7.81 (s, 1H in pyrazole), 7.32–7.29 (m, 3H, aromatic), 7.24–7.20 (m, 8H, aromatic), 7.15 (dd, 1H, J = 4.0, 3.0 Hz in thiophene), 7.0 (dd, 1H, J = 5.0, 1.0 Hz in thiophene). ^{13}C NMR ($CDCl_3$): 144.2 (C–N in Ph), 143.0 (CH in pyrazole), 140.0 (C in pyrazole attached to Ph), 130.0 (CH, aromatic), 129.7 (CH, aromatic), 129.2 (CH, aromatic), 129.1 (C, aromatic), 128.9 (CH, aromatic), 128.6 (CH, aromatic), 128.3 (CH, aromatic), 127.9 (CH, aromatic), 125.5 (CH, aromatic), 125.4 (CH, aromatic), 122.7 (C, aromatic), 104.7 (C in pyrazole attached to alkyne), 86.9 (C in C≡C attached to thiophene), 80.9 (C in C≡C attached to pyrazole). IR (neat): 3614 (vw), 3566 (vw), 3096 (br), 2923 (m), 2851 (m), 2586 (vw), 2215 (vw), 1592 (s), 1498 (vs), 1440 (s), 1386 (s) 960 (s), 771 (s), 761 (s). Anal. Calcd for $C_{21}H_{14}N_2S$ (%): C, 77.27; H, 4.32; N, 8.58. Found (%): C, 77.06; H, 4.65; N, 8.72. MS (ESI, *m/z*): 327.10 $[M + H]^+$. HRMS (ESI): calcd for $C_{21}H_{15}N_2S$: 327.0951 $[M + H]^+$, found: 327.1014.

*4-(Ferrocenylethynyl)-1,5-diphenyl-1H-pyrazole (**9e**)*

^{1}H NMR ($CDCl_3$): 7.78 (s, 1H in pyrazole), 7.33–7.17 (m, 10H, Ph), 4.38 (s, 2H, Fc), 4.14 (s, 2H, Fc), 4.10 (s, 5H, Fc). ^{13}C NMR ($CDCl_3$): 143.8 (C–N in Ph), 142.8 (CH in pyrazole), 140.0 (C in pyrazole attached to Ph), 129.6 (CH, Ph), 129.2 (C, Ph), 129.0 (CH, Ph), 128.7 (CH, Ph), 128.3 (CH, Ph), 127.7 (CH, Ph), 125.1 (CH, Ph), 105.1 (C in pyrazole attached to alkyne), 90.2 (C in C≡C attached to Fc), 71.5 (CH, Fc), 70.1 (CH, Fc), 70.0 (CH, Fc), 65.8 (C, Fc) (one alkyne carbon peak is missing due to overlap). IR (neat): 3648 (vw), 3069 (m), 2225 (w), 1594 (s), 1494 (vs), 1442 (s), 1384 (vs) 961 (s), 762 (vs), 691 (s). Anal. Calcd for $C_{27}H_{20}FeN_2$ (%): C, 75.71; H, 4.71; N, 6.54. Found (%): C, 75.59; H, 4.79; N, 6.12. MS (ESI, *m/z*): 427.11 $[M + H]^+$. HRMS (ESI): calcd for $C_{27}H_{21}^{54}FeN_2$: 427.1095 $[M + H]^+$, found: 427.1136.

General Procedure for Synthesis of 4-Aryl-5-ferrocenylpyrazoles 12 via Suzuki–Miyaura Coupling Reaction (Table 2)

In a two-neck round-bottom flask equipped with a reflux condenser, **5** (100 mg, 0.220 mmol), the corresponding boronic acid **10** or boronic acid ester derivative **11** (0.308 mmol), $PdCl_2(PPh_3)_2$ (7.73 mg, 0.011 mmol) and $KHCO_3$ (30.84 mg, 0.308 mmol) were dissolved in a mixture of DMF (8 ml) and H_2O (2 ml) under argon, and the resulting reaction mixture was heated at 110 °C with stirring. This was continued until TLC revealed the completion of the reaction. Upon completion, the solvent was evaporated, first using a rotary evaporator, then with a high-vacuum pump equipped with two serially connected traps immersed in liquid nitrogen. The obtained crude product was purified by flash chromatography on silica gel using hexane–ethyl acetate (9:1) as the eluent, which afforded the corresponding 4-aryl-5-ferrocenylpyrazole **12** with yield indicated in Table 2.

*5-Ferrocenyl-1,4-diphenyl-1H-pyrazole (**12a**)*

^{1}H NMR ($CDCl_3$): 7.58 (s. 1H in pyrazole), 7.46–7.44 (m, 2H, Ph), 7.40–7.37 (m, 2H, Ph), 7.34–7.30 (m, 6H, Ph), 4.03 (s, 2H, Fc), 4.00 (s, 2H, Fc), 3.63 (s, 5H, Fc). ^{13}C NMR ($CDCl_3$): 141.0 (C–N in Ph), 140.9 (CH in pyrazole), 137.7 (C in pyrazole attached to Fc), 134.3 (C, Ph), 130.5 (CH, Ph), 128.8 (CH, Ph), 128.2 (CH, Ph), 128.0 (CH, Ph), 127.3 (CH, Ph), 126.5 (CH, Ph), 123.3 (C in pyrazole attached to Ph), 75.24 (C, Fc), 70.2 (CH, Fc), 69.4 (CH, Fc), 68.4 (CH, Fc). IR (neat): 3727 (w), 3627 (w), 3106 (vw), 1597 (w), 1497 (s), 1377 (m), 1106 (m), 999 (m), 863 (m), 818 (m), 754 (s), 690 (s). Anal. Calcd for $C_{25}H_{20}FeN_2$ (%): C, 74.27; H, 4.99; N, 6.93. Found (%): C, 74.09; H, 5.18; N, 6.83.

MS (ESI, *m/z*): 403.11 $[M + H]^+$. HRMS (ESI): calcd for $C_{25}H_{21}^{54}FeN_2$: 403.1095 $[M + H]^+$, found: 403.1105.

*4-(4-Ethylphenyl)-5-ferrocenyl-1-phenyl-1H-pyrazole (**12b**)*

^{1}H NMR ($CDCl_3$): 7.56 (s, 1H in pyrazole), 7.34 (d, 2H, J = 7.6 Hz in ethylphenyl), 7.32–7.30 (m, 5H, Ph), 7.22 (d, 2H, J = 7.6 Hz in ethylphenyl), 4.05 (s, 2H, Fc), 4.02 (s, 2H, Fc), 3.67 (s, 5H, Fc), 2.65 (q, 2H, J = 7.6 Hz, CH_2), 1.22 (t, 3H, J = 7.6 Hz, CH_3). ^{13}C NMR ($CDCl_3$): 143.4 (CH in pyrazole), 141.0 (C–N in Ph), 140.9 (C in ethylphenyl attached to CH_2CH_3), 137.5 (C in pyrazole attached to Fc), 131.4 (C, Ph), 130.4 (CH, Ph), 128.7 (CH, Ph), 127.9 (CH, Ph), 127.6 (CH, Ph), 126.5, (CH, Ph), 123.3 (C in pyrazole attached to Ph), 75.6 (C, Fc), 70.3 (CH, Fc), 69.5 (CH, Fc), 68.5 (CH, Fc), 28.7 (CH_2), 15.7 (CH_3). IR (neat): 3928 (w), 3659 (w), 3094 (m), 2962 (s), 2228 (m), 1596 (s), 1499 (vs), 1374 (s), 1107 (s), 951 (s), 820 (s), 762 (s), 728 (s), 693 (s). Anal. Calcd for $C_{27}H_{24}FeN_2$ (%): C, 75.01; H, 5.60; N, 6.48. Found (%): C, 74.90; H, 5.70; N, 6.02. MS (ESI, *m/z*): 431.14 $[M + H]^+$. HRMS (ESI): calcd for $C_{27}H_{25}^{54}FeN_2$: 431.1408 $[M + H]^+$, found: 431.1436.

*4-(Benzo[d] [1,3]dioxol-5-yl)-5-ferrocenyl-1-phenyl-1H-pyrazole (**12c**)*

^{1}H NMR ($CDCl_3$): 7.54 (s, 1H in pyrazole), 7.38–7.29 (m, 5H, Ph), 6.93 (d, 1H, J = 1.2 Hz in benzodioxolyl attached to C and C–O), 6.91 (dd, 1H, J = 8.0, 1.6 Hz in benzodioxolyl attached to C and CH), 6.85 (d, 1H, J = 8.0 Hz in benzodioxolyl attached to CH and C–O), 5.96 (s, 2H, CH_2), 4.05 (s, 2H, Fc), 3.96 (s, 2H, Fc), 3.72 (s, 5H, Fc). ^{13}C NMR ($CDCl_3$): 147.8 (C in benzodioxolyl attached to C–O), 147.3 (C in benzodioxolyl attached to C–O), 141.4 (C–N in Ph), 141.3 (CH in pyrazole), 137.9 (C in pyrazole attached to Fc), 129.2 (CH, Ph), 128.5 (CH, Ph), 128.4 (C in benzodioxolyl), 127.0 (CH, Ph), 124.1 (CH in benzodioxolyl), 123.0 (C in pyrazole attached to benzodioxolyl), 111.3 (CH in benzodioxolyl), 108.5 (CH in benzodioxolyl), 101.6 (CH_2), 75.5 (C, Fc), 70.3 (CH, Fc), 69.7 (CH, Fc), 68.8 (CH, Fc). IR (neat): 3726 (m), 3697 (m), 3627 (m), 2988 (s), 2892 (s), 1596 (w), 1473 (s), 1371 (s), 1230 (s), 1033 (s), 810 (s), 762 (s), 696 (s). Anal. Calcd for $C_{26}H_{20}FeN_2O_2$ (%): C, 69.66; H, 4.50; N, 6.25. Found (%): C, 69.51; H, 4.56; N, 5.68. MS (ESI, *m/z*): 447.10 $[M + H]^+$. HRMS (ESI): calcd for $C_{26}H_{21}^{54}FeN_2O_2$: 447.0994 $[M + H]^+$, found: 447.1021.

*5-Ferrocenyl-1-phenyl-4-(3,4,5-trimethoxyphenyl)-1H-pyrazole (**12d**)*

^{1}H NMR ($CDCl_3$): 7.68 (s, 1H in pyrazole), 7.49–7.42 (m, 5H, Ph), 6.72 (s, 2H in trimethoxyphenyl), 4.16 (s, 2H, Fc), 4.10 (s, 2H, Fc), 3.95 (s, 3H, OCH_3), 3.94 (s, 6H, OCH_3), 3.81 (s, 5H, Fc). ^{13}C NMR ($CDCl_3$): 152.9 (C–O in trimethoxyphenyl), 141.0 (CH in pyrazole), 140.6 (C–N in phenyl), 137.5 (C in pyrazole attached to Fc), 129.7 (C in trimethoxyphenyl), 128.8 (CH, Ph), 128.2 (CH, Ph), 126.7 (CH, Ph), 123.2 (C in pyrazole attached to Ph), 107.8 (CH, Ph), 75.1 (C, Fc), 70.1 (CH, Fc), 69.4 (CH, Fc), 68.5 (CH, Fc), 61.1 (OCH_3), 56.3 (OCH_3) (one aromatic C–O carbon peak is missing due to overlap). IR (neat): 3726 (m), 3698 (m), 3627 (m), 2985 (br), 1581 (s), 1409 (s), 1243 (s), 1123 (vs), 1013 (m), 819 (m), 774 (m), 663 (m). Anal. Calcd for $C_{28}H_{26}FeN_2O_3$ (%): C, 68.03; H, 5.30; N, 5.67. Found (%): C, 67.86; H, 5.87; N, 6.01. MS (ESI, *m/z*): 495.13 $[M + H]^+$, 494.12 $[M]^+$. HRMS (ESI): calcd for $C_{28}H_{27}^{56}FeN_2O_3$: 495.1371 $[M + H]^+$, found: 495.1331; calcd for $C_{28}H_{26}^{56}FeN_2O_3$: 494.1293 $[M]^+$, found: 494.1291.

*6-(5-Ferrocenyl-1-phenyl-1H-pyrazol-4-yl)-1H-indole (**12e**)*

^{1}H NMR (DMSO-d_6): 11.17 (s, 1H, NH), 7.71 (br s, 1H in pyrazole), 7.68 (s, 1H, aromatic), 7.51–7.36 (m, 8H, aromatic), 7.26–7.23 (m, 1H, aromatic), 4.14 (t, 2H, J = 2.0, Fc), 4.01 (t, 2H, J = 2.0 Hz, Fc), 3.65 (s, 5H, Fc). ^{13}C NMR (DMSO-d_6): 140.7 (C–N in Ph), 140.6 (CH in pyrazole), 136.4 (C in pyrazole attached to Fc), 135.1 (C in indole attached to pyrazole), 128.7 (CH, Ph), 127.8 (CH, Ph), 127.6 (CH, Ph), 126.3 (CH in indole), 125.8 (CH in indole), 124.2 (C in pyrazole attached to indole), 124.1 (C in indole), 123.6 (CH in indole), 121.4 (C in indole), 110.9 (CH in indole), 101.2 (CH in indole), 75.2 (C, Fc), 69.6 (CH, Fc), 68.8 (CH, Fc), 67.9 (CH, Fc). IR (neat): 3727 (s), 3698 (s), 3627 (s), 3182 (s), 2988 (vs), 2900 (s), 1407 (m), 1309 (m), 1083 (m), 967 (m), 809 (m), 767 (m), 663 (m). Anal. Calcd for $C_{27}H_{21}FeN_3$ (%): C, 73.15; H, 4.77; N, 9.48. Found (%): C, 73.00; H, 4.90; N, 8.66. MS (ESI, *m/z*): 442.12 $[M + H]^+$. HRMS (ESI): calcd for $C_{27}H_{22}^{54}FeN_3$: 442.1204 $[M + H]^+$, found: 442.1227.

*4-(4-Chlorophenyl)-5-ferrocenyl-1-phenyl-1H-pyrazole (**12f**)*

^{1}H NMR ($CDCl_3$): 7.54 (s, 1H in pyrazole), 7.42–7.32 (m, 9H, Ph), 4.12 (s, 2H, Fc), 4.03 (s, 2H, Fc), 3.75 (s, 5H, Fc). ^{13}C NMR ($CDCl_3$): 140.9 (C–N in Ph), 140.7 (CH in pyrazole), 133.1 (C in pyrazole attached to Fc), 132.8 (C–Cl in chlorophenyl), 131.5 (CH in chlorophenyl), 128.8 (CH, Ph), 128.4 (CH, Ph), 128.3 (CH, Ph), 126.7 (CH, Ph), 126.1 (C, Ph), 121.9 (C in pyrazole attached to chlorophenyl), 74.7 (C, Fc), 70.0 (CH, Fc), 69.3 (CH, Fc), 68.5 (CH, Fc). IR (neat): 3929 (vw), 3737 (vw), 3095 (w), 2230 (vw), 1948 (vw), 1595 (s), 1550 (s), 1498 (vs), 1381 (s), 1088 (s), 952 (s), 822 (vs), 765 (s) 694 (s). Anal. Calcd for $C_{25}H_{19}ClFeN_2$ (%): C, 68.44; H, 4.37; N, 6.38. Found (%): C, 68.26; H, 4.59; N, 7.67. MS (ESI, *m/z*): 437.07 $[M + H]^+$. HRMS (ESI): calcd for $C_{25}H_{20}Cl^{54}FeN_2$: 437.0706 $[M + H]^+$, found: 437.0717.

*4-(4-Ethoxy-3-fluorophenyl)-5-ferrocenyl-1-phenyl-1H-pyrazole (**12g**)*

^{1}H NMR ($CDCl_3$): 7.55 (s, 1H in pyrazole), 7.37–7.28 (m, 5H, Ph), 7.20 (dd, 1H, J = 10.0, 2.0 Hz in fluorophenyl), 7.12 (d, 1H, J = 8.4 Hz in fluorophenyl), 6.99–6.95 (m, 1H in fluorophenyl), 4.1 (q, 2H, J = 7.2 Hz, CH_2), 4.04 (br s, 2H, Fc), 3.93 (br s, 2H, Fc), 3.68 (s, 5H, Fc), 1.42 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR ($CDCl_3$): 150.4 (d, C–F, J = 245.8 Hz in fluorophenyl), 144.4 (d, C–O, J = 10.8 Hz in fluorophenyl attached to C–F), 139.2 (C–N in Ph), 139.0 (CH in pyrazole), 135.9 (C in pyrazole attached to Fc), 127.0 (CH, Ph), 126.3 (CH, Ph), 125.5 (d, CH, J = 5.9 Hz in fluorophenyl attached to CH and C–O), 124.8 (CH, Ph), 124.2 (d, CH, J = 3.3 Hz in fluorophenyl attached to C and CH), 119.9 (C in fluorophenyl attached to pyrazole), 116.4 (d, CH, J = 18.5 Hz in fluorophenyl attached to C–F and C), 112.7 (C in pyrazole attached to fluorophenyl), 73.0 (C, Fc), 68.1 (CH, Fc), 67.4 (CH, Fc), 66.6 (CH, Fc), 63.3 (OCH_2), 13.1 (CH_3). IR (neat): 3726 (m), 2986 (m), 2924 (m), 1566 (m), 1514 (s), 1474 (s), 1262 (s), 1128 (s), 1037 (s), 967 (m), 824 (m), 775 (s), 701 (s). Anal. Calcd for $C_{27}H_{23}FFeN_2O$ (%): C, 69.54; H, 4.97; N, 6.01. Found (%): C, 69.36; H, 5.02; N, 5.52. MS (ESI, *m/z*): 465.13 $[M + H]^+$. HRMS (ESI): calcd for $C_{27}H_{24}F^{54}FeN_2O$: 465.1263 $[M + H]^+$, found: 465.1281.

*5-Ferrocenyl-1-phenyl-4-(3,4,5-trifluorophenyl)-1H-pyrazole (**12h**)*

^{1}H NMR ($CDCl_3$): 7.54 (s, 1H in pyrazole), 7.38–7.32 (m, 5H, Ph), 7.05 (br s, 2H in trifluorophenyl), 4.12 (s, 2H, Fc), 3.94 (s, 2H, Fc), 3.74 (s, 5H, Fc). ^{13}C NMR ($CDCl_3$): 150.9 (ddd, C–F, J = 249.3, 9.0 and 3.9 Hz in trifluorophenyl attached to C–F and CH) 140.7 (C–N in Ph), 140.2 (CH in pyrazole), 139.5 (dt, C–F, J = 245.0 and 4.5 Hz in trifluorophenyl attached to 2 C–F), 130.4 (C in pyrazole attached to Fc), 128.9 (CH, Ph), 128.8 (C in fluorophenyl attached to pyrazole), 128.6 (CH, Ph), 126.9 (CH, Ph), 120.2 (C in pyrazole attached to trifluorophenyl), 113.9–114.1 (m, CH in trifluorophenyl), 74.3 (C, Fc), 70.0 (CH, Fc), 69.5 (CH, Fc), 69.0 (CH, Fc). IR (neat): 3726 (m), 3697 (m), 3628 (m), 3090 (w), 2988 (s), 1526 (s), 1408 (s), 1231 (m),

1046 (s), 846 (m), 754 (m), 695 (m). MS (ESI, *m/z*): 457.08 $[M + H]^+$. HRMS (ESI): calcd for $C_{25}H_{18}F_3^{54}FeN_2$: 457.0813 $[M + H]^+$, found: 457.0840.

*Ethyl 3-(5-ferrocenyl-1-phenyl-1H-pyrazol-4-yl)benzoate (**12i**)*

^{1}H NMR ($CDCl_3$): 8.29 (s, 1H in benzoate), 8.13 (d, 1H, J = 7.6 Hz in benzoate), 7.74–7.72 (m, 2H in pyrazole and benzoate), 7.59–7.55 (m, 1H in benzoate), 7.48–7.41 (m, 5H, Ph), 4.46 (q, 2H, J = 7.2 Hz, OCH_2), 4.14 (s, 2H, Fc), 4.04 (s, 2H, Fc), 3.75 (s, 5H, Fc), 1.45 (t, 3H, J = 7.2, CH_3). ^{13}C NMR ($CDCl_3$): 166.5 (C=O), 140.9 (C–N in Ph), 140.7 (CH in pyrazole), 138.0 (C in pyrazole attached to Fc), 134.6 (C in phenyl attached to C=O), 134.5 (CH, Ph), 131.4 (CH, Ph), 130.5 (C, Ph), 128.8 (CH, Ph), 128.3 (CH, Ph), 128.2 (CH, Ph), 128.1 (CH, Ph), 126.6 (CH, Ph), 122.1 (C in pyrazole attached to benzoate), 74.7 (C, Fc), 69.9 (CH, Fc), 69.2 (CH, Fc), 68.4 (CH, Fc), 61.1 (OCH_2), 14.4 (CH_3). IR (neat): 3925 (w), 3726 (w), 3628 (w), 3094 (m), 2978 (s), 2230 (m), 1714 (vs), 1499 (s), 1367 (s), 1257 (vs), 1104 (s), 908 (s), 757 (s), 726 (vs), 691 (s). Anal. Calcd for $C_{28}H_{24}FeN_2O_2$ (%): C, 70.60; H, 5.08; N, 5.88. Found (%): C, 70.51; H, 5.14; N, 5.37. MS (ESI, *m/z*): 475.13 $[M + H]^+$. HRMS (ESI): calcd for $C_{28}H_{25}^{54}FeN_2O_2$: 475.1307 $[M + H]^+$, found: 475.1345.

*5-(5-Ferrocenyl-1-phenyl-1H-pyrazol-4-yl)-2-methoxypyridine (**12j**)*

^{1}H NMR ($CDCl_3$): 8.37 (s, 1H in pyridine ortho to N), 7.72 (d, 1H, J = 7.6 Hz in pyridine para to N), 7.66 (s, 1H in pyrazole), 7.43–7.40 (m, 5H, Ph), 6.88 (d, 1H, J = 8.4 Hz in pyridine *meta* to N), 4.14 (s, 2H, Fc), 4.04 (br s, 5H, Fc), 3.77 (s, 5H two CH in Fc and OCH_3). ^{13}C NMR ($CDCl_3$): 163.4 (C–O in pyridine), 147.5 (CH in pyridine *ortho* to N), 140.8 (CH in pyrazole), 140.4 (C–N in Ph), 138.1 (C in pyrazole attached to Fc), 128.8 (CH, Ph), 128.1 (CH, Ph), 126.5 (CH, Ph), 123.1 (C in pyridine attached to pyrazole), 119.1 (C in pyrazole attached to pyridine), 110.3 (CH in pyridine *meta* to N), 74.7 (C, Fc), 70.0 (CH, Fc), 69.2 (CH, Fc), 68.5 (CH, Fc), 53.6 (OCH_3) (one CH carbon peak is missing due to overlap). IR (neat): 3726 (m), 3698 (m), 3627 (m), 2988 (s), 2900 (m), 1564 (m), 1477 (m9, 1289 (s), 1017 (s), 948 (m), 810 (m), 668 (m). Anal. Calcd for $C_{25}H_{21}FeN_3O$ (%): C, 68.98; H, 4.86; N, 9.65. Found (%): C, 68.89; H, 4.90; N, 8.83. MS (ESI, *m/z*): 434.12 $[M + H]^+$. HRMS (ESI): calcd for $C_{25}H_{22}^{54}FeN_3O$: 434.1154 $[M + H]^+$, found: 434.1201.

*5-Ferrocenyl-4-(3-nitrophenyl)-1-phenyl-1H-pyrazole (**12k**)*

^{1}H NMR ($CDCl_3$): 8.34 (s, 1H in nitrophenyl), 8.18 (d, 1H, J = 7.2 Hz in nitrophenyl), 7.76–7.74 (m, 1H in nitrophenyl), 7.67 (br s, 1H in pyrazole), 7.57–7.55 (m, 1H in nitrophenyl) 7.38–7.35 (m, 5H, Ph), 4.09 (s, 2H, Fc), 3.94 (s, 2H, Fc), 3.65 (s, 5H, Fc). ^{13}C NMR ($CDCl_3$): 148.1 (C in nitrophenyl attached to NO_2), 140.7 (C–N in Ph), 140.4 (CH in pyrazole), 138.5 (C in pyrazole attached to Fc), 136.1 (C in nitrophenyl attached to pyrazole), 135.9 (CH in nitrophenyl), 129.2 (CH in nitrophenyl), 128.9 (CH, Ph), 128.5 (CH, Ph), 126.7 (CH, Ph), 124.7 (CH in nitrophenyl), 122.0 (CH in nitrophenyl), 120.8 (C in pyrazole attached to nitrophenyl), 74.2 (C, Fc), 70.0 (CH, Fc), 69.3 (CH, Fc), 68.9 (CH, Fc). IR (neat): 3726 (m), 3697 (m), 3628 (m), 3072 (w), 2988 (s), 2900 (s), 1522 (s), 1345 (s), 1081 (m), 809 (m), 768 (m), 683 (m). Anal. Calcd for $C_{25}H_{19}FeN_3O_2$ (%): C, 66.83; H, 4.26; N, 9.35. Found (%): C, 66.76; H, 4.36; N, 8.49. MS (ESI, *m/z*): 448.10 $[M + H]^+$. HRMS (ESI): calcd for $C_{25}H_{20}^{54}FeN_3O_2$: 448.0946 $[M + H]^+$, found: 448.0981.

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