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LETTER - SPECTRAL ASSIGNMENT

WILEY

^{1}H and ^{13}C NMR spectral assignment of 29 *N*′-(3-([1,1′-biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)acylhydrazones

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1 | INTRODUCTION

Doxorubicin (Figure 1a) is an anthracycline drug that has been used for chemotherapy since 1974.[1] In light of its safety and effectiveness for various cancers, several derivatives of doxorubicin have been synthesized.[2,3] Aldoxorubicin (Figure 1b), which is a prodrug of doxorubicin, is the 6-maleimidocap roylhydrazone of doxorubicin.[4] It can be prepared by the addition of 6-maleimidocaproylhydrazide to the ketone of the 1-hydroxypropan-2-one group in doxorubicin. A box marked in Figure 1b indicates the *N*-acylhydrazone moiety in aldoxorubicin. Nifuroxazide (Figure 1c), which has been used to treat diarrhea, colitis, and cancer, also contains the *N*-acylhydrazone moiety.[5] The antimicrobial compound nitrofurazone (Figure 1d)[6] and the hemostatic anti-inflammatory agent carbazochrome (Figure 1e)[7] also have the *N*-acylhydrazone moiety. Furthermore, several compounds containing a pyrazole moiety have been reported to show anticancer activity.[8,9] Based on these considerations, we designed and synthesized 29 compounds containing both the *N*-acylhydrazone and pyrazole moieties (Figure 1f). The compounds were characterized by NMR spectroscopy and high-resolution mass spectrometry. The spectral data presented herein can be used for the characterization of synthetic or natural compounds that contain *N*-acylhydrazone and pyrazole moieties.

2 | EXPERIMENTAL

2.1 | Syntheses

Phenylhydrazine was reacted with biphenylacetophenone in the presence of a catalytic amount of glacial acetic acid to obtain methyl biphenyl hydrazine (**I**). According to literature methods,[10] biphenyl hydrazine (**I**) was transformed into pyrazolo-carbaldehyde (**III**) via a dialdehyde intermediate (**II**) by the Vilsmeier–Haack reaction. Pyrazolo-carbaldehyde (**III**) was functionalized with benzoylhydrazide derivatives (**IV**) to afford a series of pyrazolo-benzohydrazide compounds (**V**) used in this study. The typical procedure for derivative **1** (Table 1) follows. Phenylhydrazine (3 mmol, 0.295 ml, d: 1.098 g/ml) and 4-acetylbiphenyl (3 mmol, 589 mg) were dissolved in 20 ml of ethanol, and the reaction mixture was refluxed for 3 h in the presence of a catalytic amount of acetic acid. The reaction mixture was cooled to room temperature, and the obtained precipitate was filtered and washed with ethanol to afford methyl biphenyl hydrazine (**I**) in 85% yield as a pale-yellow solid. DMF (6 ml) and $POCl_3$ (0.6 ml) were stirred at 0°C for 1 h to form the Vilsmeier reagent; biphenyl hydrazine (**I**, 2 mmol, 570 mg) was added to it and heated at 60°C for 2 h. After the complete disappearance of biphenyl hydrazine (**I**) (confirmed by TLC), the reaction mixture was poured into 200 ml of ice water to give a precipitate of compound **III**. The dried powder of compound **III** (0.5 mmol,

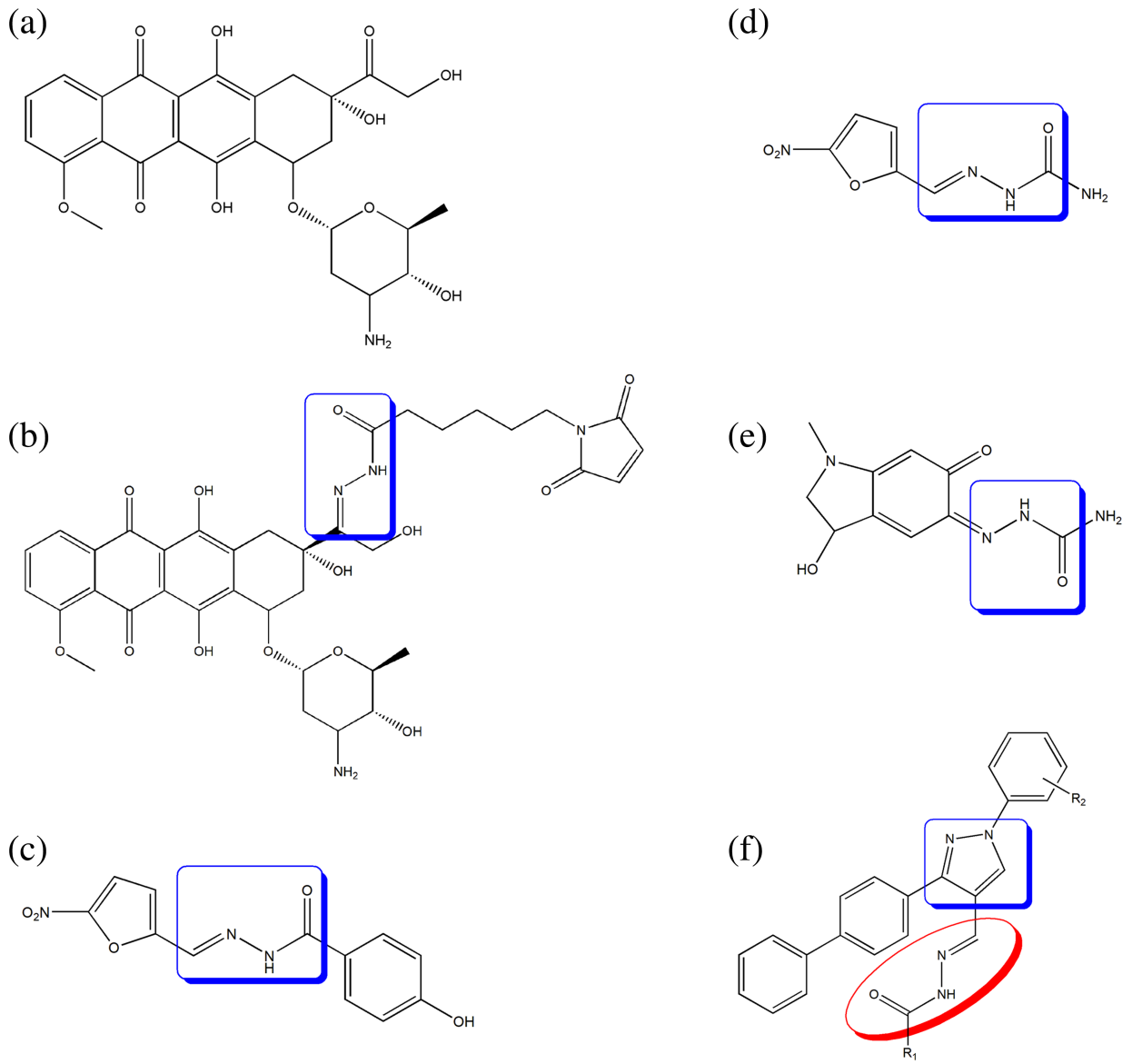


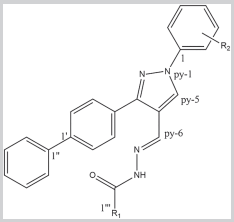
FIGURE 1 Structures of (a) doxorubicin, (b) aldoxorubicin, (c) nifuroxazide, (d) nitrofurazone, (e) carbazochrome, and (f)*N*′-(3-([1,1′-biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)acylhydrazone

150 mg) and 3-anisic hydrazide (0.5 mmol, 85 mg) were added to 10 ml of ethanol in the presence of a catalytic amount of glacial acetic acid, and the reaction mixture was refluxed at 75°C for 4 h. The resulting mixture was cooled to room temperature, and the obtained precipitate washed with ethanol to give derivative **1** in 55% yield. The synthetic procedure for *N*′-(3-([1,1′-biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)acylhydrazone derivatives is provided as Scheme 1.

2.2 | NMR spectra

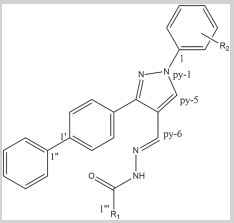
All the derivatives listed in Table 1 were dissolved in dimethylsulfoxide-d_6, except **4**, **17**, **22**, **25**, and **27**, which were dissolved in pyridine-d_5. Their concentrations were adjusted to approximately 50 mM and transferred into 2.5-mm NMR tubes. All the NMR data were collected on an Avance 400 spectrometer system (9.4 T; Bruker, Karlsruhe, Germany) at room temperature, and the chemical shifts were referenced to TMS. The relaxation delay, 90° pulse, spectral width, number of data points, and digital resolution for the ^{1}H NMR experiments were 1 s, 11.6 μs, 5,500 Hz, 32 K, and 0.34 Hz/point, respectively. The same parameters for the ^{13}C NMR experiments were 3 s, 15.0 μs, 21,000 Hz, 64 K, and 0.64 Hz/point, respectively. For the two-dimensional (2D) experiments, including COSY, TOCSY, HMQC, HMBC, and NOESY, 2 K × 256 ($t_2 \times t_1$) data points were acquired.[11] The number of scans per increment was 16 for all 2D experiments.

TABLE 1 Structures and names of *N*′-(3-([1,1′-biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)acylhydrazone derivatives and their high-resolution mass spectroscopic data



Derivative	R_1	R_2	Mass (calc/found)	Name
1	3-Methoxyphenyl	Phenyl	472.1899/473.1986	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)-3-methoxybenzohydrazide
2	4-Methoxyphenyl	Phenyl	472.1899/473.1964	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)-4-methoxybenzohydrazide
3	3-Fluorophenyl	Phenyl	460.1699/461.1795	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)-3-fluorobenzohydrazide
4	4-Fluorophenyl	Phenyl	460.1699/461.1788	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)-4-fluorobenzohydrazide
5	2-Chlorophenyl	Phenyl	476.1404/477.1501	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)-2-chlorobenzohydrazide
6	3-Bromophenyl	Phenyl	520.0899/521.0978	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)-3-bromobenzohydrazide
7	4-Bromophenyl	Phenyl	520.0899/521.0987	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)-4-bromobenzohydrazide
8	3-Pyridinyl	Phenyl	443.1746/444.1822	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)nicotinohydrazide
9	4-Pyridinyl	Phenyl	443.1746/444.1806	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)isonicotinohydrazide
10	Phenyl	Phenyl	442.1794/443.1855	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)benzohydrazide
11	3-Hydroxyphenyl	Phenyl	458.1743/459.1805	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)-3-hydroxybenzohydrazide
12	3-Methoxyphenyl	4-Methoxyphenyl	502.2005/503.2107	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methylene)-3-methoxybenzohydrazide
13	4-Methoxyphenyl	4-Methoxyphenyl	502.2005/503.2085	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methylene)-4-methoxybenzohydrazide
14	3-Fluorophenyl	4-Methoxyphenyl	490.1805/491.1842	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methylene)-3-fluorobenzohydrazide
15	4-Fluorophenyl	4-Methoxyphenyl	490.1805/491.1895	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methylene)-4-fluorobenzohydrazide
16	2-Chlorophenyl	4-Methoxyphenyl	506.1510/505.1418	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methylene)-2-chlorobenzohydrazide
17	3-Pyridinyl	4-Methoxyphenyl	473.1852/474.1949	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methylene)nicotinohydrazide
18	Phenyl	4-Methoxyphenyl	472.1899/ND	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methylene)benzohydrazide
19	3-Hydoxyphenyl	4-Methoxyphenyl	488.1848/489.1898	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methylene)-3-hydroxybenzohydrazide
20	3-Methoxyphenyl	4-Fluorophenyl	490.1805/491.1874	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)methylene)-3-methoxybenzohydrazide
21	4-Methoxyphenyl	4-Fluorophenyl	490.1805/491.1897	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)methylene)-4-methoxybenzohydrazide
22	3-Fluorophenyl	4-Fluorophenyl	478.1605/479.1662	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)methylene)-3-fluorobenzohydrazide
23	2-Chlorophenyl	4-Fluorophenyl	494.1310/495.1358	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)methylene)-2-chlorobenzohydrazide
24	3-Bromophenyl	4-Fluorophenyl	538.0805/539.0876	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)methylene)-3-bromobenzohydrazide
25	3-Pyridinyl	4-Fluorophenyl	461.1652/462.1701	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)methylene)nicotinohydrazide
26	4-Pyridinyl	4-Fluorophenyl	461.1652/462.1772	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)methylene)isonicotinohydrazide
27	Phenyl	4-Fluorophenyl	460.1699/461.1738	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)methylene)benzohydrazide
28	3-Hydroxyphenyl	4-Fluorophenyl	476.1649/477.1739	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)methylene)-3-hydroxybenzohydrazide

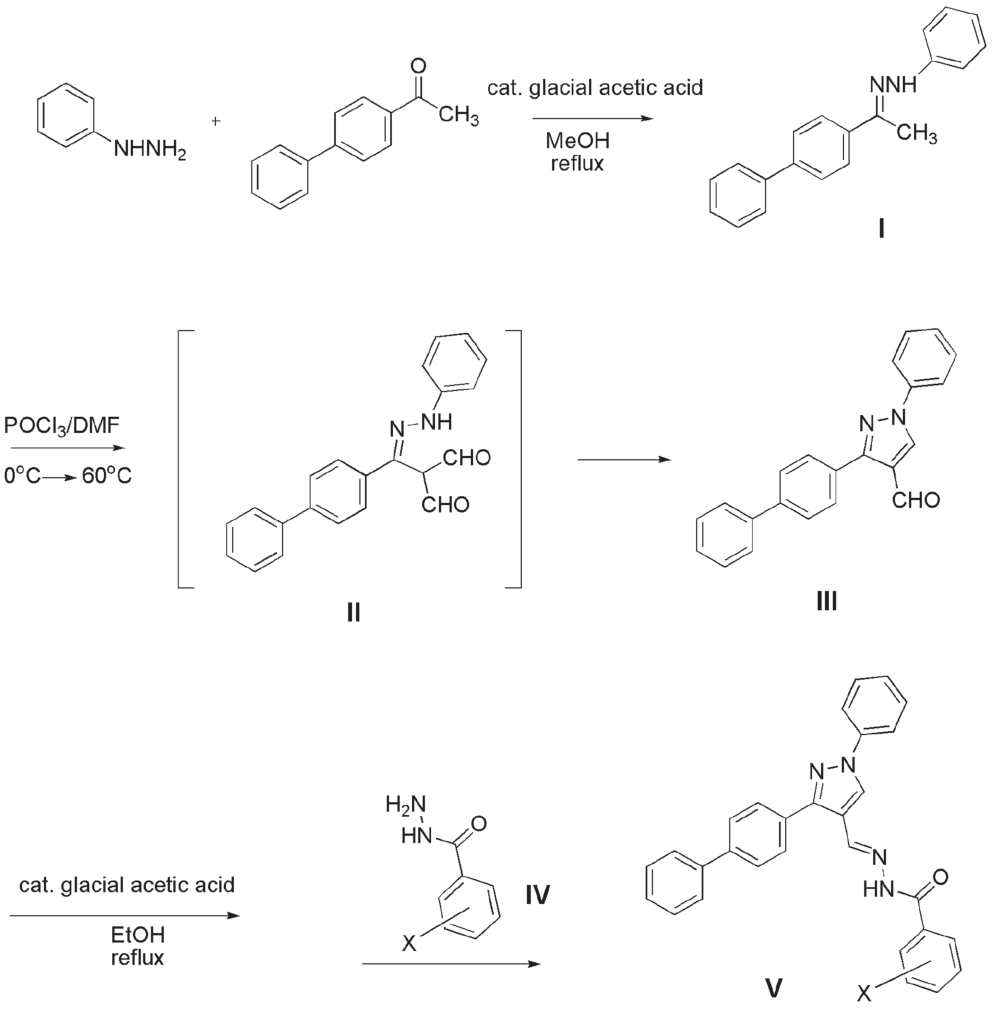
TABLE 1 (Continued)



Derivative	R_1	R_2	Mass (calc/found)	Name
29	4-Bromophenyl	4-Methoxyphenyl	550.1004/551.1115	(*E*)-*N*′-((3-([1,1′-Biphenyl]-4-yl)-1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methylene)-4-bromobenzohydrazide

Note: The calculated mass data denote the exact mass. All the experimental mass data were found in the $[M + H]^+$ mode, except for derivative **16**, which was found in the $[M - H]^-$ mode. ND denotes "not detected."

SCHEME 1 Synthetic procedure for*N*′-(3-([1,1′-biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)acylhydrazone derivatives



The long-range coupling time for HMBC was 70 ms, and the mixing times for TOCSY and NOESY were 400 ms and 1 s, respectively. The NMR data were processed using the NMRPipe program[12] and analyzed using the SPARKY 3 program developed by T. D. Goddard and D. G. Kneller (University of California at San Francisco).

2.3 | General experimental procedures

To confirm the structures of the 29 *N*′-(3-([1,1′-biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)acylhydrazone derivatives determined from the NMR assignments, ultra-performance liquid chromatography-hybrid quadrupole-

time-of-flight mass spectrometry (QTOF-MS) was used on a Waters Acquity UPLC system (Waters Corp., Milford, MA) with the help of Prof. C. H. Lee at Konkuk University, South Korea.[13]

3 | RESULTS AND DISCUSSION

The 29 derivatives have a common structure, where only substituents on the R1 and R2 phenyl groups varied; as a result, NMR assignments of all the *N*′-(3-([1,1′-biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)acylhydrazones were performed similarly. Derivative **1**, (*E*)-*N*′-((3-([1,1′-biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)-3-methoxybenzohydrazide, was chosen as a representative among these. The ^{13}C NMR spectrum of derivative **1** revealed 24 peaks including a methoxy, a carbonyl, and 22 aromatic hydrocarbons. Based on the ^{1}H–^{13}C HMQC spectrum, the 22 peaks were found to consist of 8 quaternary carbons and 14 aromatic methines. The carbonyl carbon at 162.5 ppm was correlated with two ^{1}H peaks at 8.66 ppm (s) and 7.51 ppm (dd, J = 7.7, 1.8 Hz) in the ^{1}H–^{13}C HMBC spectrum; the two proton peaks were assigned as H-Py6 and H-6‴ based on their splitting patterns, respectively. The other carbons and protons in the R1 phenyl group were easily assigned using COSY and HMBC experiments. The ^{1}H peak of H-6‴ was correlated with both C-2‴ (112.9 ppm) and C-4‴ (117.0 ppm) in the HMBC spectrum. In the COSY spectrum, H-4‴ (7.16 ppm) showed a cross peak with H-5‴ (7.51 ppm). The H-5‴ and methoxy protons at 3.82 ppm showed a correlation with the ^{13}C peak at 159.2 ppm in the HMBC spectrum, implying that it could be attributed to C-3‴. Two proton peaks at 8.66 and 9.01 ppm were long range coupled to the ^{13}C peak at 117.3 ppm. Because the former proton was H-Py6, the latter proton and this carbon were assigned H-Py5 and C-Py4, respectively. H-Py5 also showed a correlation with the quaternary carbon peak at 151.4 ppm; the latter was assigned as C-Py3 based on an additional HMBC connection with the ^{1}H peak at 7.84 ppm (d, J = 8.4 Hz). The aromatic protons at 7.84 and 7.86 ppm had identical coupling constants (8.4 Hz) and showed double intensities; thus, they were assigned as H-3′ and H-2′, respectively. It was necessary to compare HMBC correlations (between (H-2′ and C-4′) and (H-3′ and C-1′)) to assign these two ^{1}H signals. The important correlations obtained from the HMBC spectra of derivative **1** are shown in Figure 2. *N*′-(3-([1,1′-Biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)acylhydrazones contain three phenyl groups including *N*-phenyl, biphenyl, and phenyl group attached to acylhydrazone. To distinguish their chemical shifts, the NOESY experiment was performed for derivative **28**. The NOE cross peaks

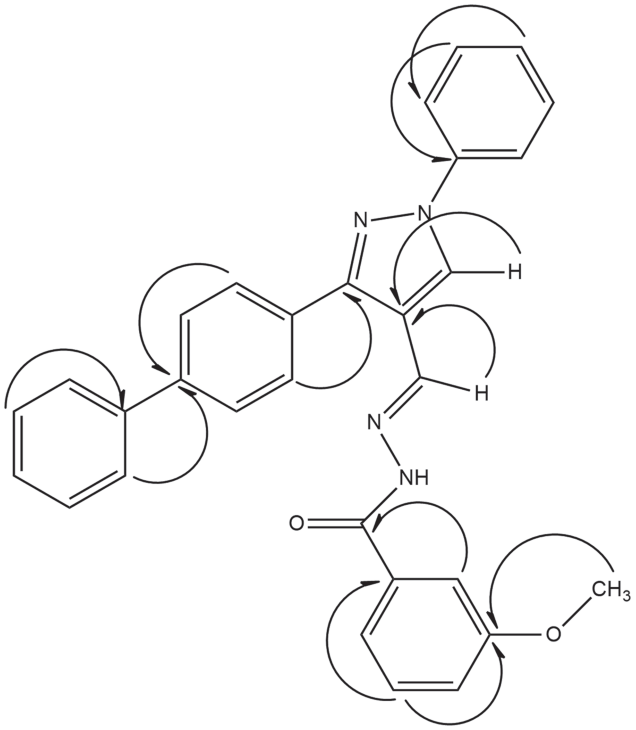


FIGURE 2 Important correlations obtained from the HMBC spectrum of derivative **1**

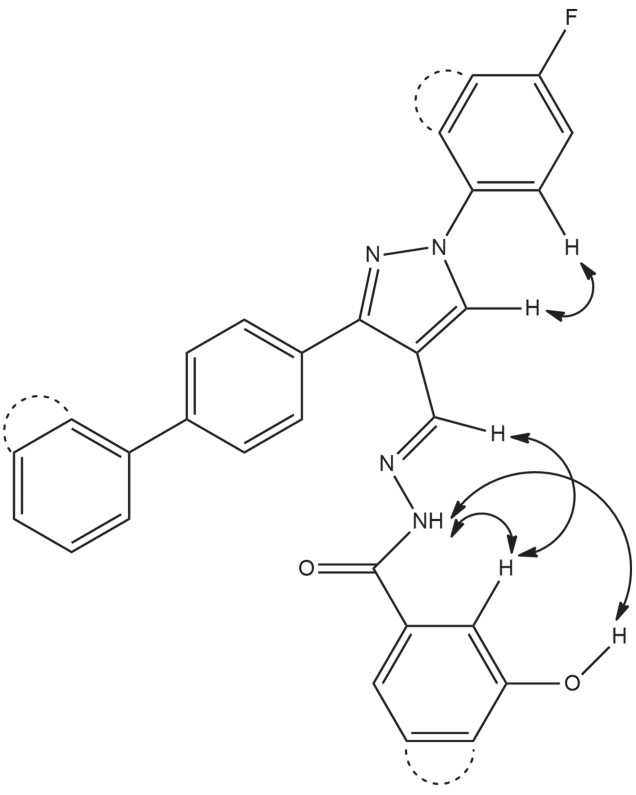


FIGURE 3 The important correlations obtained from the COSY (dot lines) and NOESY (arrow lines) spectra of derivative **28**

TABLE 2 ^{1}H NMR chemical shifts of *N*′-(3-([1,1′-biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)acylhydrazone derivatives **1–29**

Position	1	2	3	4	5
H-2‴	7.47(dd, 2.0, 1.8)	7.93(d, 8.6)	7.74(dd, 9.6, 2.3)	8.37(dd, 8.6, 5.5)	-
H-3‴	-	7.05(d, 8.6)	-	7.21(dd, 8.6, 8.6)	7.57(dd, 7.7, 1.5)
H-4‴	7.16(dd, 8.0, 2.0)	-	7.44(ddd, 8.4, 7.8, 2.3)	-	7.49(ddd, 7.7, 7.5, 1.5)
H-5‴	7.44(dd, 8.0, 7.7)	7.05(d, 8.6)	7.58(ddd, 7.8, 7.8, 5.8)	7.21(dd, 8.6, 8.6)	7.45(ddd, 7.5, 7.5, 1.5)
H-6‴	7.51(dd, 7.7, 1.8)	7.93(d, 8.6)	7.79(d, 7.8)	8.37(dd, 8.6, 5.5)	7.58(dd, 7.5, 1.5)
NH	11.75(s)	11.68(s)	11.82(s)	12.75(s)	11.82(s)
H-Py6	8.66(s)	8.64(s)	8.65(s)	8.96(s)	8.50(s)
H-Py5	9.01(s)	8.98(s)	9.02(s)	9.29(s)	9.05(s)
H-2	8.05(d, 7.9)	8.03(d, 7.9)	8.04(d, 7.9)	8.12(d, 7.9)	8.05(dd, 7.7, 1.2)
H-3	7.55(dd, 7.9, 7.5)	7.55(dd, 7.9, 7.4)	7.55(dd, 7.9, 7.5)	7.52(dd. 7.9, 7.4)	7.58(ddd, 7.7, 7.5, 1.8)
H-4	7.39(dd, 7.5, 7.5)	7.38(dd, 7.4, 7.4)	7.38(dd, 7.5, 7.5)	7.33(dd, 7.4, 7.4)	7.39(dddd, 7.5, 7.5, 1.2, 1.2)
H-5	7.55(dd, 7.9, 7.5)	7.55(dd, 7.9, 7.4)	7.55(dd, 7.9, 7.5)	7.52(dd. 7.9, 7.4)	7.58(ddd, 7.7, 7.5, 1.8)
H-6	8.05(d, 7.9)	8.03(d, 7.9)	8.04(d, 7.9)	8.12(d, 7.9)	8.05(dd, 7.7, 1.2)
H-2′	7.86(d, 8.4)	7.82(d, 8.2)	7.83(d, 8.5)	7.72(d, 7.8)	7.81(d, 8.7)
H-3′	7.84(d, 8.4)	7.85(d, 8.2)	7.86(d, 8.5)	7.93(d, 7.8)	7.84(d, 8.7)
H-5′	7.84(d, 8.4)	7.85(d, 8.2)	7.86(d, 8.5)	7.93(d, 7.8)	7.84(d, 8.7)
H-6′	7.86(d, 8.4)	7.82(d, 8.2)	7.83(d, 8.5)	7.72(d, 7.8)	7.81(d, 8.7)
H-2″	7.74(ddd, 7.8, 1.8, 1.2)	7.73(dd, 7.7, 1.5)	7.74(ddd, 7.8, 1.8, 1.2)	7.72(d, 7.9)	7.73(ddd, 7.9, 1.8, 1.2)
H-3″	7.50(ddd, 7.8, 7.4, 1.5)	7.50(dd, 7.7, 7.5)	7.50(ddd, 7.8, 7.4, 1.8)	7.52(dd, 7.9, 7.4)	7.49(ddd, 7.9, 7.4, 1.5)
H-4″	7.40(dddd, 7.4, 7.4, 1.2, 1.2)	7.40(ddd, 7.5, 7.5, 1.5)	7.40(dddd, 7.4, 7.4, 1.2, 1.2)	7.42(dd, 7.4, 7.4)	7.40(dddd, 7.4, 7.4, 1.2, 1.2)
H-5″	7.50(ddd, 7.8, 7.4, 1.5)	7.50(dd, 7.7, 7.5)	7.50(ddd, 7.8, 7.4, 1.8)	7.52(dd, 7.9, 7.4)	7.49(ddd, 7.9, 7.4, 1.5)
H-6″	7.74(ddd, 7.8, 1.8, 1.2)	7.73(dd, 7.7, 1.5)	7.74(ddd, 7.8, 1.8, 1.2)	7.72(d, 7.9)	7.73(ddd, 7.9, 1.8, 1.2)
3‴-OCH_3	3.82(s)	-	-	-	-
4‴-OCH_3	-	3.82(s)	-	-	-

(Continues)

TABLE 2 (Continued)

Position	6	7	8	9	10
H-2‴	8.11(dd, 1.7, 1.7)	7.88(d, 8.1)	9.09(d, 1.7)	7.88(dd, 4.5, 1.6)	7.94(d, 7.8)
H-3‴	-	7.74(d, 8.1)	-	8.80(dd, 4.5, 1.6)	7.52(dd, 7.8, 7.5)
H-4‴	7.79(dd, 7.9, 1.7)	-	8.76(dd, 4.8, 1.7)	-	7.59(dd, 7.5, 7.5)
H-5‴	7.49(dd, 7.9, 7.9)	7.74(d, 8.1)	7.55(dd, 8.0, 4.8)	8.80(dd, 4.5, 1.6)	7.52(dd, 7.8, 7.5)
H-6‴	7.94(dd, 7.9, 1.7)	7.88(d, 8.1)	8.27(ddd, 8.0, 1.7, 1.7)	7.88(dd, 4.5, 1.6)	7.94(d, 7.8)
NH	11.85(s)	11.82(s)	11.85(s)	12.03(s)	11.79(s)
H-Py6	8.64(s)	8.64(s)	8.64(s)	8.68(s)	8.67(s)
H-Py5	9.02(s)	9.02(s)	9.04(s)	9.05(s)	9.01(s)
H-2	8.04(d, 7.8)	8.04(d, 7.9)	8.05(d, 7.8)	8.05(d, 8.0)	8.04(d, 7.9)
H-3	7.55(dd, 7.8, 7.4)	7.55(dd, 7.9, 7.4)	7.55(dd, 7.8, 7.3)	7.55(dd, 8.0, 7.3)	7.57(dd, 7.9, 7.3)
H-4	7.38(dd, 7.4, 7.4)	7.39(dd, 7.4, 7.4)	7.39(dd, 7.3, 7.3)	7.39(dd, 7.3, 7.3)	7.38(dd, 7.3, 7.3)
H-5	7.55(dd, 7.8, 7.4)	7.55(dd, 7.9, 7.4)	7.55(dd, 7.8, 7.3)	7.55(dd, 8.0, 7.3)	7.57(dd, 7.9, 7.3)
H-6	8.04(d, 7.8)	8.04(d, 7.9)	8.05(d, 7.8)	8.05(d, 8.0)	8.04(d, 7.9)
H-2′	7.83(d, 8.6)	7.83(d, 8.7)	7.84(d, 8.6)	7.83(d, 8.5)	7.81(d, 8.6)
H-3′	7.86(d, 8.6)	7.86(d, 8.7)	7.86(d, 8.6)	7.86(d, 8.5)	7.88(d, 8.6)
H-5′	7.86(d, 8.6)	7.86(d, 8.7)	7.86(d, 8.6)	7.86(d, 8.5)	7.88(d, 8.6)
H-6′	7.83(d, 8.6)	7.83(d, 8.7)	7.84(d, 8.6)	7.83(d, 8.5)	7.81(d, 8.6)
H-2″	7.74(ddd, 7.8, 1.9, 1.2)	7.74(dd, 7.8, 1.2)	7.74(ddd, 7.9, 1.8, 1.2)	7.74(ddd, 7.8, 1.8, 1.2)	7.73(dd, 7.9, 1.3)
H-3″	7.50(ddd, 7.8, 7.4, 1.5)	7.51(ddd, 7.8, 7.5, 1.6)	7.51(ddd, 7.9, 7.4, 1.8)	7.50(ddd, 7.8, 7.5, 1.8)	7.50(dd, 7.9, 7.4)
H-4″	7.41(dddd, 7.4, 7.4, 1.2, 1.2)	7.41(dddd, 7.5, 7.5, 1.2, 1.2)	7.40(dddd, 7.4, 7.4, 1.2, 1.2)	7.40(dddd, 7.5, 7.5, 1.2, 1.2)	7.40(dddd, 7.4, 7.4, 1.3, 1.3)
H-5″	7.50(ddd, 7.8, 7.4, 1.5)	7.51(ddd, 7.8, 7.5, 1.6)	7.51(ddd, 7.9, 7.4, 1.8)	7.50(ddd, 7.8, 7.5, 1.8)	7.50(dd, 7.9, 7.4)
H-6″	7.74(ddd, 7.8, 1.9, 1.2)	7.74(dd, 7.8, 1.2)	7.74(ddd, 7.9, 1.8, 1.2)	7.74(ddd, 7.8, 1.8, 1.2)	7.73(dd, 7.9, 1.3)
3‴-OCH_3	-	-	-	-	-
4‴-OCH_3	-	-	-	-	-

(Continues)

TABLE 2 (Continued)

Position	11	12	13	14	15
H-2‴	7.34(dd, 2.0, 2.0)	7.47(dd, 2.0, 2.0)	7.93(d, 8.8)	7.74(dd, 10.2, 2.2)	8.01(dd, 8.6, 5.6)
H-3‴	-	-	7.05(d, 8.8)	-	7.36(dd, 8.6, 8.6)
H-4‴	6.99(dd, 7.8, 2.0)	7.15(dd, 8.0, 2.0)	-	7.44(ddd, 8.6, 8.0, 2.2)	-
H-5‴	7.31(dd, 7.8, 7.7)	7.43(dd, 8.0, 7.7)	7.05(d, 8.8)	7.58(ddd, 8.0, 8.0, 6.0)	7.36(dd, 8.6, 8.6)
H-6‴	7.36(dd, 7.7, 2.0)	7.51(dd, 7.7, 2.0)	7.93(d, 8.8)	7.78(d, 8.0)	8.01(dd, 8.6, 5.6)
NH	11.71(s)	11.72(s)	11.65(s)	11.78(s)	11.78(s)
H-Py6	8.66(s)	8.65(s)	8.64(s)	8.64(s)	8.63(s)
H-Py5	9.00(s)	8.89(s)	8.86(s)	8.91(s)	8.89(s)
H-2	8.04(dd, 7.9, 1.2)	7.95(d, 9.0)	7.94(d, 9.1)	7.95(d, 9.1)	7.94(d, 9.0)
H-3	7.55(ddd, 7.9, 7.5, 1.8)	7.09(d, 9.0)	7.09(d, 9.1)	7.09(d, 9.1)	7.09(d, 9.0)
H-4	7.38(dddd, 7.5, 7.5, 1.2, 1.2)	-	-	-	-
H-5	7.55(ddd, 7.9, 7.5, 1.8)	7.09(d, 9.0)	7.09(d, 9.1)	7.09(d, 9.1)	7.09(d, 9.0)
H-6	8.04(dd, 7.9, 1.2)	7.95(d, 9.0)	7.94(d, 9.1)	7.95(d, 9.1)	7.94(d, 9.0)
H-2′	7.86(d, 8.5)	7.81(d, 8.6)	7.81(d, 8.6)	7.84(d, 9.1)	7.84(d, 8.9)
H-3′	7.82(d, 8.5)	7.84(d, 8.6)	7.84(d, 8.6)	7.82(d, 9.1)	7.81(d, 8.9)
H-5′	7.82(d, 8.5)	7.84(d, 8.6)	7.84(d, 8.6)	7.82(d, 9.1)	7.81(d, 8.9)
H-6′	7.86(d, 8.5)	7.81(d, 8.6)	7.81(d, 8.6)	7.84(d, 9.1)	7.84(d, 8.9)
H-2″	7.74(ddd, 7.9, 1.9, 1.2)	7.73(ddd, 7.9, 1.8, 1.2)	7.73(ddd, 7.8, 1.8, 1.2)	7.73(ddd, 7.9, 1.9, 1.2)	7.73(ddd, 7.9, 1.8, 1.2)
H-3″	7.50(ddd, 7.9, 7.6, 1.7)	7.50(ddd, 7.9, 7.4, 1.5)	7.50(ddd, 7.8, 7.4, 1.8)	7.50(ddd, 7.9, 7.3, 1.7)	7.50(ddd, 7.9, 7.4, 1.8)
H-4″	7.40(dddd, 7.6, 7.6, 1.2, 1.2)	7.40(dddd, 7.4, 7.4, 1.2, 1.2)	7.40(dddd, 7.4, 7.4, 1.2, 1.2)	7.40(dddd, 7.3, 7.3, 1.2, 1.2)	7.40(dddd, 7.4, 7.4, 1.2, 1.2)
H-5″	7.50(ddd, 7.9, 7.6, 1.7)	7.50(ddd, 7.9, 7.4, 1.5)	7.50(ddd, 7.8, 7.4, 1.8)	7.50(ddd, 7.9, 7.3, 1.7)	7.50(ddd, 7.9, 7.4, 1.8)
H-6″	7.74(ddd, 7.9, 1.9, 1.2)	7.73(ddd, 7.9, 1.8, 1.2)	7.73(ddd, 7.8, 1.8, 1.2)	7.73(ddd, 7.9, 1.9, 1.2)	7.73(ddd, 7.9, 1.8, 1.2)
3‴-OH	9.75(s)	-	-	-	-
3‴-OCH_3	-	3.823(s)	-	-	-
4‴-OCH_3	-	-	3.823(s)	-	-
4-OCH_3	-	3.820(s)	3.817(s)	3.82(s)	3.82(s)

(Continues)

TABLE 2 (Continued)

Position	16	17	18	19	20
H-2‴	-	9.68(d, 1.5)	7.93(d, 7.8)	7.33(dd, 1.9, 1.9)	7.47(dd, 2.0, 2.0)
H-3‴	7.56(dd, 8.0, 1.5)	-	7.52(dd, 7.8, 7.3)	-	-
H-4‴	7.49(ddd, 8.0, 7.4, 1.8)	8.82(dd, 4.7, 1.5)	7.59(dd, 7.3, 7.3)	6.98(dd, 7.8, 1.9)	7.15(dd, 8.0, 2.0)
H-5‴	7.45(ddd, 7.4, 7.4, 1.5)	7.36(dd, 8.0, 4.7)	7.52(dd, 7.8, 7.3)	7.31(dd, 7.8, 7.7)	7.43(dd, 8.0, 7.9)
H-6‴	7.57(dd, 7.4, 1.8)	8.57(ddd, 8.0, 1.5, 1.5)	7.93(d, 7.8)	7.36(dd, 7.7, 1.9)	7.51(dd, 7.9, 2.0)
NH	11.80(s)	12.91(s)	11.74(s)	11.68(s)	11.75(s)
H-Py6	8.50(s)	9.00(s)	8.65(s)	8.65(s)	8.65(s)
H-Py5	8.94(s)	9.25(s)	8.90(s)	8.88(s)	8.99(s)
H-2	7.96(d, 9.0)	8.07(d, 8.9)	7.95(d, 9.1)	7.94(d, 9.0)	8.07(dd, 9.0, 4.7)
H-3	7.10(d, 9.0)	7.18(d, 8.9)	7.09(d, 9.1)	7.09(d, 9.0)	7.38(dd, 9.0, 8.7)
H-4	-	-	-	-	-
H-5	7.10(d, 9.0)	7.18(d, 8.9)	7.09(d, 9.1)	7.09(d, 9.0)	7.38(dd, 9.0, 8.7)
H-6	7.96(d, 9.0)	8.07(d, 8.9)	7.95(d, 9.1)	7.94(d, 9.0)	8.07(dd, 9.0, 4.7)
H-2′	7.80(d, 9.0)	7.74(d, 7.9)	7.82(d, 8.7)	7.84(d, 8.7)	-
H-3′	7.82(d, 9.0)	7.97(d, 7.9)	7.84(d, 8.7)	7.81(d, 8.7)	7.81(d, 8.6)
H-5′	7.82(d, 9.0)	7.97(d, 7.9)	7.84(d, 8.7)	7.81(d, 8.7)	7.84(d, 8.6)
H-6′	7.80(d, 9.0)	7.74(d, 7.9)	7.82(d, 8.7)	7.84(d, 8.7)	-
H-2″	7.73(ddd, 8.0, 1.8, 1.3)	7.73(d, 7.8)	7.74(dd, 7.8, 1.2)	7.74(ddd, 7.9, 1.9, 1.3)	7.73(ddd, 7.9, 1.8, 1.3)
H-3″	7.49(ddd, 8.0, 7.4, 1.8)	7.52(dd, 7.8, 7.4)	7.51(ddd, 7.8, 7.4, 1.5)	7.50(ddd, 7.9, 7.5, 1.5)	7.50(ddd, 7.9, 7.4, 1.5)
H-4″	7.39(dddd, 7.4, 7.4, 1.3, 1.3)	7.42(dd, 7.4, 7.4)	7.40(dddd, 7.4, 7.4, 1.2, 1.2)	7.40(dddd, 7.5, 7.5, 1.3, 1.3)	7.40(dddd, 7.4, 7.4, 1.2, 1.2)
H-5″	7.49(ddd, 8.0, 7.4, 1.8)	7.52(dd, 7.8, 7.4)	7.51(ddd, 7.8, 7.4, 1.5)	7.50(ddd, 7.9, 7.5, 1.5)	7.50(ddd, 7.9, 7.4, 1.5)
H-6″	7.73(ddd, 8.0, 1.8, 1.3)	7.73(d, 7.8)	7.74(dd, 7.8, 1.2)	7.74(ddd, 7.9, 1.9, 1.3)	7.73(ddd, 7.9, 1.8, 1.3)
3‴-OH	-	-	-	9.74(s)	-
3‴-OCH_3	-	-	-	-	3.82(s)
4‴-OCH_3	-	-	-	-	-
4-OCH_3	3.82(s)	3.74(s)	3.82(s)	3.82(s)	-

(Continues)

TABLE 2 (Continued)

Position	21	22	23	24	25
H-2‴	7.93(d, 8.8)	8.16(dd, 10.6, 2.2)	-	8.10(dd, 1.7, 1.7)	9.67(d, 2.0)
H-3‴	7.05(d, 8.8)	-	7.56(dd, 7.8, 1.5)	-	-
H-4‴	-	7.28(ddd, 8.8, 8.4, 2.2)	7.49(ddd, 7.8, 7.5, 1.6)	7.79(dd, 8.0, 1.7)	8.81(dd, 4.7, 2.0)
H-5‴	7.05(d, 8.8)	7.42(ddd, 8.4, 8.2, 5.6)	7.45(ddd, 7.5, 7.3, 1.5)	7.50(dd, 8.0, 7.8)	7.35(dd, 8.0, 4.7)
H-6‴	7.93(d, 8.8)	8.15(d, 8.2)	7.58(dd, 7.3, 1.6)	7.93(dd, 7.8, 1.7)	8.55(ddd, 8.0, 2.0, 2.0)
NH	11.67(s)	12.76(s)	11.82(s)	11.82(s)	12.93(s)
H-Py6	8.63(s)	9.01(s)	8.49(s)	8.62(s)	8.94(s)
H-Py5	8.97(s)	9.30(s)	9.04(s)	9.02(s)	9.29(s)
H-2	8.07(dd, 8.8, 4.7)	8.11(dd, 8.7, 4.5)	8.09(dd, 9.2, 4.7)	8.09(dd, 9.0, 4.7)	8.11(dd, 8.8, 4.7)
H-3	7.38(dd, 8.8, 8.4)	7.34(dd, 8.7, 8.7)	7.37(dd, 9.2, 8.0)	7.39(dd, 9.0, 8.6)	7.33(dd, 8.8, 8.5)
H-5	7.38(dd, 8.8, 8.4)	7.34(dd, 8.7, 8.7)	7.37(dd, 9.2, 8.0)	7.39(dd, 9.0, 8.6)	7.33(dd, 8.8, 8.5)
H-6	8.07(dd, 8.8, 4.7)	8.11(dd, 8.7, 4.5)	8.09(dd, 9.2, 4.7)	8.09(dd, 9.0, 4.7)	8.11(dd, 8.8, 4.7)
H-2′	7.81(d, 8.7)	7.76(d, 8.0)	7.80(d, 8.8)	7.83(d, 8.9)	7.74(d, 7.7)
H-3′	7.84(d, 8.7)	7.97(d, 8.0)	7.83(d, 8.8)	7.85(d, 8.9)	7.94(d, 7.7)
H-5′	7.84(d, 8.7)	7.97(d, 8.0)	7.83(d, 8.8)	7.85(d, 8.9)	7.94(d, 7.7)
H-6′	7.81(d, 8.7)	7.76(d, 8.0)	7.80(d, 8.8)	7.83(d, 8.9)	7.74(d, 7.7)
H-2″	7.74(ddd, 7.9, 1.9, 1.3)	7.74(dd, 7.8, 1.2)	7.72(ddd, 7.8, 1.8, 1.2)	7.73(ddd, 7.9, 1.8, 1.2)	7.74(dd, 7.7, 1.2)
H-3″	7.50(ddd, 7.9, 7.5, 1.5)	7.54(ddd, 7.8, 7.4, 1.5)	7.49(ddd, 7.8, 7.5, 1.6)	7.51(ddd, 7.9, 7.4, 1.7)	7.53(dd, 7.7, 7.4)
H-4″	7.40(dddd, 7.5, 7.5, 1.3, 1.3)	7.44(dddd, 7.4, 7.4, 1.2, 1.2)	7.39(dddd, 7.5, 7.5, 1.2, 1.2)	7.40(dddd, 7.4, 7.4, 1.2, 1.2)	7.43(dddd, 7.4, 7.4, 1.2, 1.2)
H-5″	7.50(ddd, 7.9, 7.5, 1.5)	7.54(ddd, 7.8, 7.4, 1.5)	7.49(ddd, 7.8, 7.5, 1.6)	7.51(ddd, 7.9, 7.4, 1.7)	7.53(dd, 7.7, 7.4)
H-6″	7.74(ddd, 7.9, 1.9, 1.3)	7.74(dd, 7.8, 1.2)	7.72(ddd, 7.8, 1.8, 1.2)	7.73(ddd, 7.9, 1.8, 1.2)	7.74(dd, 7.7, 1.2)
3‴-OH	-	-	-	-	-
4‴-OCH_3	3.80(s)	-	-	-	-
4-OCH_3	-	-	-	-	-

(Continues)

TABLE 2 (Continued)

Position	26	27	28	29
H-2‴	7.83(dd, 4.4, 1.6)	8.38(dd, 8.0, 1.9)	7.33(dd, 2.0, 2.0)	7.88(d, 8.5)
H-3‴	8.78(dd, 4.4, 1.6)	7.46(dd, 8.0, 7.5)	-	7.73(d, 8.5)
H-4‴	-	7.48(dddd, 7.5, 7.5, 1.9, 1.9)	6.98(dd, 7.6, 2.0)	-
H-5‴	8.78(dd, 4.4, 1.6)	7.46(dd, 8.0, 7.5)	7.31(dd, 7.8, 7.6)	7.73(d, 8.5)
H-6‴	7.83(dd, 4.4, 1.6)	8.38(dd, 8.0, 1.9)	7.35(dd, 7.8, 2.0)	7.88(d, 8.5)
NH	11.95(s)	12.77(s)	11.69(s)	11.81(s)
H-Py6	8.64(s)	9.03(s)	8.65(s)	8.63(s)
H-Py5	9.03(s)	9.27(s)	8.99(s)	8.89(s)
H-2	8.08(dd, 9.1, 4.7)	8.09(dd, 8.6, 4.5)	8.06(dd, 9.0, 4.7)	7.94(d, 9.0)
H-3	7.38(dd, 9.1, 8.5)	7.32(dd, 8.6, 8.6)	7.36(dd, 9.0, 8.7)	7.08(d, 9.0)
H-5	7.38(dd, 9.1, 8.5)	7.32(dd, 8.6, 8.6)	7.36(dd, 9.0, 8.7)	7.08(d, 9.0)
H-6	8.08(dd, 9.1, 4.7)	8.09(dd, 8.6, 4.5)	8.06(dd, 9.0, 4.7)	7.94(d, 9.0)
H-2′	7.81(d, 8.8)	7.75(d, 7.9)	7.82(d, 8.7)	7.81(d, 9.0)
H-3′	7.84(d, 8.8)	7.97(d, 7.9)	7.85(d, 8.7)	7.83(d, 9.0)
H-5′	7.84(d, 8.8)	7.97(d, 7.9)	7.85(d, 8.7)	7.83(d, 9.0)
H-6′	7.81(d, 8.8)	7.75(d, 7.9)	7.82(d, 8.7)	7.81(d, 9.0)
H-2″	7.73(ddd, 7.9, 1.8, 1.2)	7.72(d, 7.9)	7.74(ddd, 7.8, 1.8, 1.3)	7.73(dd, 7.9, 1.2)
H-3″	7.50(ddd, 7.9, 7.2, 1.8)	7.52(dd, 7.9, 7.3)	7.50(ddd, 7.8, 7.4, 1.5)	7.50(ddd, 7.9, 7.4, 1.9)
H-4″	7.40(dddd, 7.2, 7.2, 1.2, 1.2)	7.43(dd, 7.3, 7.3)	7.40(dddd, 7.4, 7.4, 1.3, 1.3)	7.40(dddd, 7.4, 7.4, 1.2, 1.2)
H-5″	7.50(ddd, 7.9, 7.2, 1.8)	7.52(dd, 7.9, 7.3)	7.50(ddd, 7.8, 7.4, 1.5)	7.50(ddd, 7.9, 7.4, 1.9)
H-6″	7.73(ddd, 7.9, 1.8, 1.2)	7.72(d, 7.9)	7.74(ddd, 7.8, 1.8, 1.3)	7.73(dd, 7.9, 1.2)
3‴-OH	-	-	9.75(s)	-
4‴-OCH_3	-	-	-	-
4-OCH_3	-	-	-	3.81(s)

Note: Multiplicities and coupling constants are given in parentheses. Multiplicities d and s represent doublet and singlet, respectively.

TABLE 3 ^{13}C NMR chemical shifts of *N′*-(3-([1,1′-biphenyl]-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)acylhydrazone derivatives **1–29**

Position	1	2	3	4	5	6	7	8	9	10
C-1‴	134.9	125.5	135.8(d, 5.9)	131.6(d, 2.1)	135.3	130.7	132.1	129.2	141.1	133.5
C-2‴	112.9	129.5	114.3(d, 22.4)	131.4(d, 7.7)	130.4	130.0	129.7	148.5	121.7	127.5
C-3‴	159.2	113.7	161.9(d, 244.3)	116.3(d, 21.9)	129.7	121.7	131.5	-	149.7	128.4
C-4‴	117.0	162.0	118.5(d, 20.3)	165.4(d, 267.9)	131.3	134.4	125.4	152.2	-	131.6
C-5‴	129.6	113.7	130.6(d, 6.2)	116.3(d, 21.9)	127.2	129.0_2	131.5	123.5	149.7	128.4
C-6‴	119.7	129.5	123.7(d, 2.1)	131.4(d, 7.7)	129.3	126.8	129.7	135.3	121.7	127.5
C═O	162.5	162.3	161.3	164.1	162.0	161.1	161.8	161.2	160.9	162.7
C-Py6	141.1	140.4	141.5	142.4	141.3	141.5	141.4	141.7	142.4	141.0
C-Py3	151.4	151.4	151.5	153.0	151.4	151.5	151.5	151.5	151.6	151.4
C-Py4	117.3	117.2	116.9	118.5	116.7	116.9	117.0	116.8	116.7	117.0
C-Py5	127.2	127.1	127.3	128.0_2	127.4	127.3	127.3	127.4	127.5	127.2
C-1	139.0	139.1	139.0	140.5	139.0	139.0	139.0	139.0	139.0	139.0
C-2	118.8	118.8	118.8	119.8	118.8	118.9	118.9	118.9	118.9	118.8
C-3	129.6	129.6	129.6	130.0	129.6	129.6	129.6	129.6	129.6	129.6
C-4	127.0	127.0	127.0	127.7	127.0	127.0	127.1	127.0	127.0	127.0
C-5	129.6	129.6	129.6	130.0	129.6	129.6	129.6	129.6	129.6	129.6
C-6	118.8	118.8	118.8	119.8	118.8	118.9	118.9	118.9	118.9	118.8
C-1′	140.2	140.2	140.2	141.7	140.2	140.2	140.3	140.3	140.3	140.2
C-2′	128.9	126.9	126.9	127.8	126.9	126.9	127.0	126.9	126.9	126.9
C-3′	126.9	129.0	128.9_6	130.3	128.9	128.9_5	129.0	128.9_7	128.9_8	128.9
C-4′	131.1	131.2	131.0	132.6	131.0	131.0	131.1	131.0	131.0	131.1
C-5′	126.9	129.0	128.9_6	130.3	128.9	128.9_5	129.0	128.9_7	128.9_8	128.9
C-6′	128.9	126.9	126.9	127.8	126.9	126.9	127.0	126.9	126.9	126.9
C-1″	139.5	139.5	139.5	141.1	139.4	139.5	139.5	139.5	139.4	139.5
C-2″	126.6	126.7	126.6	127.9_8	126.6	126.6	126.7	126.6	126.6	126.6
C-3″	129.0	129.1	129.0_2	129.9	129.0	129.0_2	129.1	129.0_3	129.0_3	129.0
C-4″	127.7	127.8	127.7	128.5	127.7	127.7	127.8	127.7	127.7	127.7
C-5″	129.0	129.1	129.0_2	129.9	129.0	129.0_2	129.1	129.0_3	129.0_3	129.0
C-6″	126.6	126.7	126.6	127.9_8	126.6	126.6	126.7	126.6	126.6	126.6
3‴-OCH_3	55.3	-	-	-	-	-	-	-	-	
4‴-OCH_3	-	55.4	-	-	-	-	-	-	-	

(Continues)

TABLE 3 (Continued)

Position	11	12	13	14	15	16	17	18	19	20
C-1‴	134.9	134.9	125.5	135.8(d, 6.7)	129.9(d, 2.6)	135.3	131.2	133.5	134.9	134.9
C-2‴	114.5	112.9	129.4	114.3(d, 22.9)	130.2(d, 9.0)	130.4	150.1	127.5	114.5	112.9
C-3‴	157.4	159.2	113.6	161.9(d, 244.7)	115.4(d, 22.0)	129.7	-	128.4	157.4	159.2
C-4‴	118.6	116.6	161.9	118.5(d, 20.9)	164.1(d, 249.3)	131.3	153.2	131.6	118.6	117.1
C-5‴	129.5	129.6	113.6	130.6(d, 7.9)	115.4(d, 22.0)	127.1	124.3	128.4	129.5	129.6
C-6‴	118.0	119.7	129.4	123.7(d, 2.5)	130.2(d, 9.0)	129.3	136.3	127.5	118.0	119.7
C═O	162.8	162.4	162.1	161.3	161.6	162.0	163.5	162.7	162.7	162.5
C-Py6	140.9	141.2	140.5	141.7	141.2	141.4	143.2	141.2	141.1	141.0
C-Py3	151.4	151.0	150.9	150.1	151.0	151.0	152.7	151.0	151.0	151.4
C-Py4	117.1	117.3	116.7	116.5	116.5	116.3	118.0	116.6	116.7	117.3
C-Py5	127.0	126.9	126.8	127.0	126.9	127.2	127.9_6	126.9	126.8	127.4
C-1	139.0	132.6	132.7	132.6	132.6	132.6	134.2	132.7	132.7	135.6(d, 2.6)
C-2	118.8	120.4	120.4	120.4	120.4	120.4	121.4	120.4	120.4	121.0(d, 8.4)
C-3	129.6	114.6	114.6	114.6	114.6	114.6	115.6	114.6	114.6	116.3(d, 23.0)
C-4	127.1	158.2	158.1	158.2	158.2	158.2	159.6	158.2	158.2	160.7(d, 244.0)
C-5	129.6	114.6	114.6	114.6	114.6	114.6	115.6	114.6	114.6	116.3(d, 23.0)
C-6	118.8	120.4	120.4	120.4	120.4	120.4	121.4	120.4	120.4	121.0(d, 8.4)
C-1′	140.2	140.1	140.0	140.1	140.1	140.1	141.6	140.1	140.1	140.2
C-2′	128.9	126.9	126.9	128.9	128.9	126.9	127.8	126.9	128.9	126.9
C-3′	126.9	128.9	128.9	126.9	126.9	128.8	130.0	128.9	126.9	128.9_5
C-4′	131.1	131.2	131.3	131.2	131.2	131.1	132.7	131.2	131.2	131.0
C-5′	126.9	128.9	128.9	126.9	126.9	128.8	130.0	128.9	126.9	128.9_5
C-6′	128.9	126.9	126.9	128.9	128.9	126.9	127.8	126.9	128.9	126.9
C-1″	139.5	139.5	139.5	139.5	139.5	139.5	141.1	139.5	139.5	139.5
C-2″	126.6	126.6	126.6	126.6	126.6	126.6	127.9_8	126.6	126.6	126.6
C-3″	129.0	129.0	129.0	129.0	129.0	129.0	129.9	129.0	129.0	129.0_2
C-4″	127.7	127.7	127.7	127.7	127.7	127.7	128.5	127.7	127.7	127.7
C-5″	129.0	129.0	129.0	129.0	129.0	129.0	129.9	129.0	129.0	129.0_2
C-6″	126.6	126.6	126.6	126.6	126.6	126.6	127.9_8	126.6	126.6	126.6
3‴-OCH_3	-	55.3	-	-	-	-	-	-	-	55.3
4‴-OCH_3	-	-	55.4_2	-	-	-	-	-	-	-
4-OCH_3	-	55.4	55.3_6	55.4	55.4	55.4	56.0	55.5	55.4	-

(Continues)

TABLE 3 (Continued)

Position	21	22	23	24	25	26	27	28	29
C-1‴	125.5	137.4(d, 7.2)	135.3	130.7	130.9	140.5	135.2	134.9	132.5
C-2‴	129.4	115.9(d, 23.1)	130.4	130.0	150.1	121.4	128.9	114.5	129.6
C-3‴	113.6	163.5(d, 246.4)	129.7	121.7	-	150.3	129.4	157.4	131.5
C-4‴	161.9	119.3(d, 21.5)	131.3	134.4	153.2	-	132.5	118.6	125.4
C-5‴	113.6	131.3(d, 7.6)	127.2	129.0_3	124.2	150.3	129.4	129.5	131.5
C-6‴	129.4	124.7(d, 2.4)	129.3	126.8	136.3	121.4	128.9	118.0	129.6
C═O	162.2	163.8	162.0	161.1	163.6	161.1	165.2	162.8	161.7
C-Py6	140.2	142.8	141.2	141.5	142.8	142.2	142.3	140.8	141.5
C-Py3	151.3	153.0	151.5	151.5	153.0	151.6	152.9	151.4	151.1
C-Py4	117.2	118.5	116.8	116.9	118.4	116.8	118.9	117.1	116.5
C-Py5	127.3	128.2	127.6	127.5	128.3	127.7	128.1	127.4	126.6
C-1	135.6(d, 2.5)	136.9(d, 2.7)	135.6(d, 2.7)	135.6(d, 2.6)	136.9(d, 2.8)	135.6(d, 2.5)	136.9(d, 2.7)	135.6(d, 2.6)	132.6
C-2	120.9(d, 8.4)	121.7(d, 8.3)	120.9(d, 8.4)	121.0(d, 8.2)	121.7(d, 8.2)	121.0(d, 8.4)	121.7(d, 8.3)	120.9(d, 8.6)	120.4
C-3	116.3(d, 23.0)	117.1(d, 23.0)	116.3(d, 23.0)	116.3(d, 22.9)	117.1(d, 23.1)	116.3(d, 22.9)	117.1(d, 23.0)	116.3(d, 23.0)	114.6
C-4	160.7(d, 243.9)	162.1(d, 245.2)	160.7(d, 243.9)	160.8(d, 258.4)	162.1(d, 245.2)	160.7(d, 244.2)	162.1(d, 245.2)	160.7(d, 244.0)	158.2
C-5	116.3(d, 23.0)	117.1(d, 23.0)	116.3(d, 23.0)	116.3(d, 22.9)	117.1(d, 23.1)	116.3(d, 22.9)	117.1(d, 23.0)	116.3(d, 23.0)	114.6
C-6	120.9(d, 8.4)	121.7(d, 8.3)	120.9(d, 8.4)	121.0(d, 8.2)	121.7(d, 8.2)	121.0(d, 8.4)	121.7(d, 8.3)	120.9(d, 8.6)	120.4
C-1′	140.3	141.8	140.2	140.3	141.8	140.3	141.7	140.2	140.1
C-2′	126.9	127.8	126.9	126.9	127.8	126.9	127.8	126.9	126.9
C-3′	128.9	130.0	128.9	128.95	129.9_4	128.9_8	130.0	128.9	128.9
C-4′	131.0	132.5	130.9	130.9	132.5	130.9	132.6	131.0	131.2
C-5′	128.9	130.0	128.9	128.9_5	129.9_4	128.9_8	130.0	128.9	128.9
C-6′	126.9	127.8	126.9	126.9	127.8	126.9	127.8	126.9	126.9
C-1″	139.5	141.1	139.4	139.4	141.1	139.4	141.1	139.5	139.5
C-2″	126.6	128.0	126.6	126.6	128.0	126.6	128.0	126.6	126.6
C-3″	129.0	129.9	129.0	129.0_3	129.9_2	129.0_3	129.9	129.0	129.0
C-4″	127.7	128.6	127.7	127.7	128.6	127.7	128.6	127.7	127.7
C-5″	129.0	129.9	129.0	129.0_3	129.9_2	129.0_3	129.9	129.0	129.0
C-6″	126.6	128.0	126.6	126.6	128.0	126.6	128.0	126.6	126.6
3‴-OCH_3	-	-	-	-	-	-	-	-	-
4‴-OCH_3	55.4	-	-	-	-	-	-	-	-
4-OCH_3	-	-	-	-	-	-	-	-	55.4

Note: Subscripts denote the second decimal places used to distinguish similar chemical shift values.

between H-Py6 (8.65 ppm) and H-2‴ (7.33 ppm), hydroxyl group (9.75 ppm) and NH (11.69 ppm), and H-Py5 (8.99 ppm) and H-2 (8.06 ppm) were observed. The important correlations obtained from the COSY and NOESY spectra of derivative **28** are shown in Figure 3. The remained protons except *N*-phenyl group and phenyl group attached to acylhydrazone can be assigned biphenyl group. All the other derivatives have identical structures and differed only in the R1 and R2 phenyl groups; NMR assignments were performed similarly. The complete NMR assignments for all the derivatives are detailed in Tables 2 and 3. The spectra collected from NMR spectroscopy and high-resolution mass spectrometry and tables assigned based on the 1D and 2D experiments are provided as Supporting Information.

The R1 group alone differed in derivatives **1** to **11**, whereas R2 (phenyl ring) was constant. R2 was a 4″-methoxyphenyl group in derivatives **12** to **19** and **29**, whereas it was a 4″-fluorophenyl group in derivatives **20** to **28**. Derivative **1** has a methoxy substituent at C-3‴ of R1 (*meta* position), whereas derivative **2** has a methoxy substituent at C-4‴ (*para* position). The change in position of the methoxy group leads to slight changes in the ^{1}H and ^{13}C chemical shifts of the common structure. For example, the chemical shifts of C-1‴ and C═O were shifted to higher frequency when the methoxy group was at the *meta* position, compared with the values for methoxy at the *para* position. The ^{1}H signals of the amine also showed a similar trend. The ^{1}H and ^{13}C signals of Py6 also shifted to higher frequency, even though the Py6 is not close to the methoxy group of R1. This was likely due to the resonance effect. This phenomenon was also observed in other derivative pairs (**12** and **13**, **20** and **21**) that differed only in the position of the methoxy group. In contrast, the substitution of the R2 group with methoxy or fluoride at the *para* position had a negligible effect on the chemical shifts of the common structure. Compounds containing pyrazoline moiety, one of the most useful groups in medicinal chemistry, have been known to show anti-inflammatory, antitumor, antiviral, and inhibitory effects on phosphodiesterase and alcohol dehydrogenase.[14] Likewise, various compounds with *N*-acylhydrazone moiety have been developed as antibacterial and hemostatic agents and for the treatment of colitis and diarrhea.[15] Therefore, the spectral data reported here can be useful to characterize synthetic or natural compounds containing *N*-acylhydrazone and pyrazole moieties.

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PEER REVIEW

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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