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Iodobenzene Diacetate Mediated Oxidation of N-Substituted Hydrazones of Chalcones: An Efficient Regioselective Synthesis of 1,3,5-Trisubstituted Pyrazoles

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Iodobenzene Diacetate Mediated Oxidation of N-Substituted Hydrazones of Chalcones: An Efficient Regioselective Synthesis of 1,3,5-Trisubstituted Pyrazoles

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Abstract: Iodobenzene diacetate, a relatively benign nonmetallic oxidant, has been utilized efficiently for the oxidation of N-substituted hydrazones of chalcones to afford 1,3,5-trisubstituted pyrazoles under mild reaction conditions.

Keywords: Iodobenzene diacetate, oxidative cyclization, regioselective, N-substituted hydrazones of chalcones, 1,3,5-trisubstituted pyrazoles

INTRODUCTION

Generally, regioselective synthesis of 1,3,5-trisubstituted pyrazoles are accomplished by the oxidation of 4,5-dihydropyrazoles, obtained by condensation of hydrazines with chalcone derivatives using a number of oxidizing agents.[1–4] But the versatility of this reaction is somewhat limited because the hydrazines with electron-withdrawing groups such as 4-nitrophenyl and 2,4-dinitrophenyl do not cyclize to 4,5-dihydropyrazoles; instead, formation of corresponding hydrazones has been witnessed even in strongly acidic conditions.[5] Cyclization of these hydrazones to 4,5-dihydropyrazoles has been achieved only in an extremely strong acidic medium (HBr-AcOH).[6] Oxidative cyclization of aryl hydrazones of

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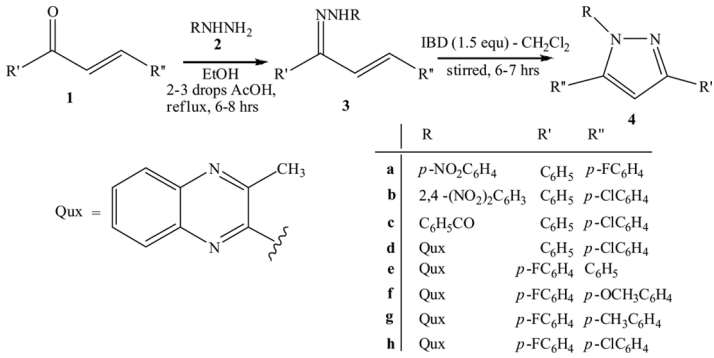
chalcones to pyrazoles has been induced using lead tetraacetate,[1] manganese dioxide,[2] thianthrene cation radical,[7] and anodic oxidation.[8] We herein report oxidative transformation of N-substituted hydrazones of chalcones **3** to 1,3,5-trisubstituted pyrazoles **4** with iodobenzene diacetate (IBD) that leads to the expeditious formation of the title compounds in excellent yields.

RESULTS AND DISCUSSION

Synthesis of 1,3,5-trisubstituted pyrazoles **4** is depicted in Scheme 1. The key intermediates, hydrazones **3**, were prepared in varying yields by condensation of N-substituted hydrazines **2** with appropriately substituted chalcones **1** in refluxing ethanol containing two or three drops of acetic acid. Efforts to cyclize the hydrazones **3** to the corresponding 4,5-dihydropyrazoles failed in high-boiling solvents such as dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) and also by conventional methods (i.e., refluxing in EtOH/AcOH–EtOH/glacial AcOH). Subsequently, oxidative intramolecular cyclization of hydrazones **3** with 1.2 equivalents of IBD in dichloromethane furnished the corresponding pyrazoles **4** but in small yields. The optimum yields of the products were obtained when 1.5 equivalents of IBD were used. It is worth mentioning here that the reaction between 2-hydrazino-3-methylquinoxaline with unsymmetrical aryl- and heteroaryl diketones to achieve the title compounds resulted in the formation of isomeric pyrazoles as the major products, along with formation of triazolo[4,3-*a*]quinoxaline.[9]

Formation of hydrazones **3** and pyrazoles **4** was confirmed on the basis of their IR, NMR (^{1}H, ^{13}C, ^{19}F), elemental analysis, and mass spectrometry (MS) data. In IR, **3** showed a characteristic absorption



	R	R'	R"
a	*p*-$NO_2C_6H_4$	C_6H_5	*p*-FC_6H_4
b	2,4 -$(NO_2)_2C_6H_3$	C_6H_5	*p*-ClC_6H_4
c	C_6H_5CO	C_6H_5	*p*-ClC_6H_4
d	Qux	C_6H_5	*p*-ClC_6H_4
e	Qux	*p*-FC_6H_4	C_6H_5
f	Qux	*p*-FC_6H_4	*p*-$OCH_3C_6H_4$
g	Qux	*p*-FC_6H_4	*p*-$CH_3C_6H_4$
h	Qux	*p*-FC_6H_4	*p*-ClC_6H_4

Scheme 1. Synthesis of 1,3,5-trisubstituted pyrazoles.

band for NH group at $\sim$3350 cm^{-1} and two bands at $\sim$1600 and $\sim$1550 cm^{-1} due to the C=C and C=N stretch. The ^1H NMR of **3d–h** exhibited two doublets of one proton intensity each at around δ 6.8 and 8.1 ($J_{trans} = 16.5$ Hz) due to the trans olefinic protons, whereas in case of chalcones **1**, the corresponding protons resonated at about δ 7.5 and 7.8 ($J = 15.6$ Hz). In ^{13}C NMR of **3**, two olefinic carbons resonated at 113 and 139 Hz. ^1H NMR of pyrazoles **4** showed the disappearance of both olefinic protons rather a singlet of one proton intensity corresponding to pyrazole 4-H was observed at about δ 6.85. Also, in ^{13}C NMR, C-4 carbon of pyrazole resonated at δ 104 Hz, indicating the formation of pyrazole. The known compounds were confirmed by comparison of their melting points with those reported in the literature.[8]

It is quite likely that the reaction mechanism does not involve the intermediacy of 4,5-dihydropyrazoles because no trace of them has been detected in the reaction mixture. Moreover, the reaction requires only 1.5 equivalents of IBD to transform **3** into **4**. Had the dihydropyrazoles been the intermediate, the reaction would have consumed more than 2 equivalents of IBD.

CONCLUSION

In conclusion, we have developed a general, practical, and efficient procedure for the regioselective synthesis of 1,3,5-trisubstituted pyrazoles using IBD as an oxidizing agent. The present protocol has several advantages: mild reaction conditions, operational and experimental simplicity, optimum yields, and use of an ecofriendly reagent.

EXPERIMENTAL

The IR spectra of the compounds were recorded on a Buck Scientific IR M-500 spectrophotometer using KBr pellets (ν_{max} in cm^{-1}); ^1H and ^{13}C NMR spectra were measured on a Bruker instrument at 300 and 75 MHz, respectively. Chemical shifts are expressed in δ-scale downfield from tetramethylsilane (TMS) as an internal standard.

Typical Procedure for the Preparation of Chalcone Hydrazone 3

Chalcone **1** (0.1 mmol) was added to a solution of hydrazine **2** (0.1 mmol) in ethanol (20 ml). The solution was warmed, and then two or three drops of acetic acid were added to it. It was refluxed for 6 h. The progress of the

reaction was monitored by thin-layer chromatography (TLC). A yellow solid separated out during refluxing. The reaction mixture was cooled; the solid thus separated was filtered, washed with cold ethanol, and recrystallized from ethanol to give **3**. All the hydrazones (**3d–h)** were prepared following this procedure.

Data for 3

4-Nitrophenyl Hydrazone of 1-(Phenyl)-3-(*p*-fluorophenyl)propenone **3a**

Yield 56%; mp 128°C. MS m/z 361 (M+). Anal. calcd. for $C_{21}H_{16}FN_3O_2$: found C, 69.78; H, 4.25; N, 11.69, required C, 69.80; H, 4.46; N, 11.63. IR (KBr): 3355, 1597, 1552 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.29 (d, $J = 16.8$ Hz, 1H, 2-H), 7.03–7.06 (m, 3H, 2′, 6′, 4‴-H), 7.17 (d, $J = 16.8$ Hz, 1H, 3-H), 7.33–7.90 (m, 8H, 2″, 3″, 5″, 6″, 2‴, 3‴, 5‴, 6‴-H), 8.16 (d, 2H, 3′, 5′-H, $J = 8.7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 112.30, 116.68 (d, $^2J_{C\text{-}F} = 21.75$ Hz), 124.53, 125.89 (d, $^3J_{C\text{-}F} = 8.25$ Hz), 126.58, 128.81, 128.98, 130.02, 130.66, 130.77, 132.31, 144.65, 151.09, 153.36, 158.52 (d, $^1J_{C\text{-}F} = 240.5$ Hz).

4-Benzoyl Hydrazone of 1-(Phenyl)-3-(*p*-chlorophenyl)propenone **3c**

Yield 65%; mp 120°C. MS m/z 360 (M+), 362 (M + 2). Anal. calcd. for $C_{22}H_{17}ClN_2O$: found C, 73.12; H, 4.55; N, 7.58, required C, 73.23; H, 4.75; N, 7.76. IR (KBr): 3354, 1643, 1600, 1575 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.40 (d, $J = 16.5$ Hz, 1H, 2-H), 7.293–7.41 (m, 9H, 2″, 3″, 5″, 6″, 2‴, 3‴, 4‴, 5‴, 6‴-H), 7.48–7.66 (m, 6H, 3, 2′, 3′, 4′, 5′, 6′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 122.51, 128.20, 128.33, 128.49, 128.67, 129.02, 129.25, 129.58, 129.96, 130.33, 133.39, 134.50, 138.04, 143.30, 158.6, 170.5.

3-Methylquinoxalin-2-yl Hydrazone of 1-Phenyl-3-(*p*-chlorophenyl)propenone **3d**

Yield 78%; mp 138°C. MS m/z 398 (M+), 400 (M + 2). Anal. calcd. for $C_{24}H_{19}ClN_4$: found C, 72.15; H, 4.75; N, 13.65; required C, 72.27; H, 4.80; N, 14.05, IR (KBr): 3351, 1592, 1550 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.58 (s, 3H, CH_3), 6.83 (d, $J = 16.5$ Hz, 1H, 2-H), 6.91–7.09 (m, 2H, 6′, 7′-H), 7.21–7.25 (m, 3H, 8′, 3″, 5″-H), 7.38–7.43 (m, 5H, 2″, 6″, 2‴, 4‴, 6‴-H), 7.56–7.60 (m, 3H, 5′, 3‴, 5‴-H), 8.04 (d, $J = 16.5$ Hz, 1H, 3-H);^{13}C NMR (75 MHz, $CDCl_3$): δ 21.04, 113.05, 119.98, 121.82,

127.44, 127.85, 128.02, 128.06, 128.23, 128.48, 128.64, 129.13, 129.99, 133.90, 133.97, 136.40, 139.41, 142.30, 158.52, 162.04.

3-Methylquinoxalin-2-yl Hydrazone of 1-(*p*-Fluorophenyl)-3-phenylpropenone **3e**

Yield 78%; mp 132°C. MS m/z 382 (M+). Anal. calcd. for $C_{24}H_{19}FN_4$: found C, 75.25; H, 4.95; N, 14.34; required C, 75.37; H, 5.01; N, 14.65; IR (KBr): 3364, 1598, 1553 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.65 (s, 3H, CH_3), 6.92 (d, $J = 16.5$ Hz, 1H, 2-H), 6.99–7.20 (m, 4H, 6′, 7′, 3‴, 5‴-H), 7.28–7.41 (m, 4H, 8′, 2″, 4″, 6″-H), 7.52–7.55 (m, 2H, 3″, 5″-H), 7.64–7.69 (m, 3H, 5′, 2‴, 6‴-H), 8.11 (d, $J = 16.5$ Hz, 1H, 3-H); ^{19}F NMR ($CDCl_3$) δ: −111.89; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.04, 114.30, 115.58 (d, $^2J_{C\text{-}F} = 21.7$ Hz), 120.87, 123.08, 127.32, 127.85, 128.70, 129.12, 129.45, 129.54, 131.55 (d, $^3J_{C\text{-}F} = 8.25$ Hz), 133.59, 134.39, 136.81, 140.15, 145.72, 158.51, 163.77 (d, $^1J_{C\text{-}F} = 247.5$ Hz), 162.32.

3-Methylquinoxalin-2-yl Hydrazone of 1-(*p*-Fluorophenyl)-3-(*p*-methoxyphenyl) Propenone **3f**

Yield 82%; mp 144°C. MS m/z 412 (M+). Anal. calcd. for $C_{25}H_{21}FN_4O$: found C, 72.78; H, 5.01; N, 14.20; required C, 72.80; H, 5.13; N, 13.58. IR (KBr): 3365, 1602, 1561 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.65 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 6.82 (d, $J = 16.5$ Hz, 1H, 2-H), 6.91 (d, $J = 8.7$ Hz, 2H, 3″, 5″-H), 7.02–7.20 (m, 4H, 6′, 7′, 3‴, 5‴-H), 7.26–7.31 (m, 1H, 8′-H), 7.48 (d, $J = 8.7$ Hz, 2H, 2″, 6″-H), 7.63–7.68 (m, 3H, 5′, 2‴, 6‴-H), 7.99 (d, $J = 16.5$ Hz, 1H, 3-H); ^{19}F NMR ($CDCl_3$) δ: −112.10; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.08, 55.35, 113.91, 114.31, 115.23 (d, $^2J_{C\text{-}F} = 21.7$ Hz), 118.42, 122.65, 128.40, 129.06, 129.29, 130.99, 131.29 (d, $^3J_{C\text{-}F} = 8.25$ Hz), 133.25, 134.30, 134.32 (d, $^4J_{C\text{-}F} =$ 3 Hz), 139.64, 145.30. 158.57, 160.65, 162.31, 163.40 (d, $^1J_{C\text{-}F} = 246.7$ Hz).

3-Methylquinoxalin-2-yl Hydrazone of 1-(*p*-Fluorophenyl)-3-(*p*-methylphenyl) Propenone **3g**

Yield 83%; mp 134°C. MS m/z 396 (M+), Anal. calcd. for $C_{25}H_{21}FN_4$: found C, 75.78; H, 5.25; N, 14.62; required C, 75.74; H, 5.34; N, 14.13, IR (KBr): 3354, 1596, 1549 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.38 (s, 3H, CH_3) 2.65 (s, 3H, CH_3), 6.98 (d, $J = 16.5$ Hz, 1H, 2-H), 7.02–7.20 (m, 6H, 6′, 7′, 3″, 5″, 3‴, 5‴-H), 7.26–7.31 (m, 1H, 8′-H), 7.43 (d, $J = 8.1$ Hz, 2H, 2″, 6″-H), 7.64–7.69 (m, 3H, 5′, 2‴, 6‴-H), 8.08 (d,

$J = 16.5$ Hz, 1H, 3-H); ^{19}F NMR ($CDCl_3$) δ: -112.01; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.10, 21.40, 113.93, 115.26 (d, $^2J_{C\text{-}F} = 21.7$ Hz), 119.59, 122.70, 127.54, 128.42, 129.11, 129.56, 130.93, 131.29 (d, $^3J_{C\text{-}F} = 8.25$ Hz), 133.27, 133.77, 134.22, 139.95, 139.51, 145.37, 158.57, 162.17, 163.54 (d, $^1J_{C\text{-}F} = 245.0$ Hz).

3-Methylquinoxalin-2-yl Hydrazone of 1-(*p*-Fluorophenyl)-3-(*p*-chlorophenyl) Propenone **3h**

Yield 75%; mp 156°C. MS m/z 416 (M+), 418 (M + 2). Anal. calcd. for $C_{24}H_{18}ClFN_4$: found C, 69.36; H, 4.25; N, 13.69; required C, 69.15; H, 4.35; N, 13.44. IR (KBr): 3362, 1598, 1559 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.67 (s, 3H, CH_3), 6.88 (d, $J = 16.5$ Hz, 1H, 2-H), 7.03–7.23 (m, 4H, 6′, 7′, 3‴, 5‴-H), 7.32–7.34 (m, 1H, 8′-H), 7.37 (d, $J = 8.4$ Hz, 2H, 3″, 5″-H), 7.48 (d, $J = 8.4$ Hz, 2H, 2″, 6″-H), 7.66–7.69 (m, 3H, 5′, 2‴, 6‴-H), 8.11 (d, $J = 16.5$ Hz, 1H, 3-H); ^{19}F NMR ($CDCl_3$) δ: -111.74; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.10, 113.98, 115.35 (d, $^2J_{C\text{-}F} = 21.0$ Hz), 121.04, 122.84, 128.47, 128.67, 129.05, 129.19, 130.81, 131.23 (d, $^3J_{C\text{-}F} = 8.25$ Hz), 133.31, 134.01, 134.96, 135.06, 138.23, 145.54, 158.39, 161.50, 163.43 (d, $^1J_{C\text{-}F} = 240.0$ Hz).

General Procedure for the Preparation of Pyrazole 4 from Chalcone Hydrazone 3

Iodobenzene diacetate (0.48 g, 0.0015 mol) in portions was added to a solution of **3** (0.001 mol) in dichloromethane (20 ml) over a period of 10 min. The resulting mixture was allowed to stir for 6 h at room temperature. The progress of reaction was monitored with the help of TLC. When the reaction was complete, excess solvent was distilled off in a vacuum to give a gummy residue containing the product and iodobenzene. The residue was triturated with petroleum ether to remove iodobenzene; a yellow compound was obtained, which was recrystallized from methanol to give **4**.

Data for 4

3-Phenyl-1-(4-nitrophenyl)-5-(*p*-fluorophenyl)pyrazole **4a**

Yield 69%; mp 110°C. MS m/z 359 (M+). Anal. calcd. for $C_{21}H_{14}FN_3O_2$: found C, 67.18; H, 3.55; N, 12.01; required C, 67.12; H, 3.75; N, 11.69. IR (KBr): 1497, 1445 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$):

δ 6.86 (s, 1H, 4-H), 7.10–8.44 (m, 13H, 2′, 3′, 5′, 6′, 2″, 3″, 5″, 6″, 2‴, 3‴, 4‴, 5‴, 6‴-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 102.41, 116.45 (d, $^2J_{C\text{-}F} = 21.75$ Hz), 124.17, 124.52, 125.91, 128.60, 128.68 (d, $^3J_{C\text{-}F} = 7.5$ Hz), 130.67, 131.96, 132.07, 138.62, 144.61, 146.71, 150.72, 158.92 (d, $^1J_{C\text{-}F} = 240.7$ Hz).

3-Phenyl-1-benzoyl-5-(*p*-chlorophenyl)pyrazole **4c**

Yield 58%; mp 137°C. MS m/z 358 (M+), 360 (M + 2). Anal. calcd. for $C_{22}H_{15}ClN_2O$: found C, 73.56; H, 4.13; N, 7.67; required C, 73.64; H, 4.21; N, 7.81. IR (KBr): 1496, 1453 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93 (s, 1H, 4-H), 7.23–7.41 (m, 9H, 2″, 3″, 5″, 6″, 2‴, 3‴, 4‴, 5‴, 6‴-H), 7.87–7.97 (m, 5H, 2′, 3′,4′, 5′, 6′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 103.41, 127.40, 128.45, 128.65, 129.01, 129.07, 129.44, 129.73, 133.82, 134.35, 134.68, 136.51, 136.78, 142.32, 152.2, 180.2.

3-Phenyl-1-(3-methylquinoxalin-2-yl)-5-(*p*-chlorophenyl)pyrazole **4d**

Yield 56%; mp 145°C. MS m/z 396 (M+), 398 (M + 2). Anal. calcd. for $C_{24}H_{17}ClN_4$: found C, 72.66; H, 4.26; N, 14.24; required C, 72.63; H, 4.32; N, 14.12. IR (KBr): 1497, 1452 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.6 (s, 3H, CH_3), 6.9 (s, 1H, 4-H), 7.16–7.28 (m, 4H, 2″, 3″, 4″, 5″-H), 7.33–7.42 (m, 5H, 2‴, 3‴, 4‴, 5‴, 6‴-H), 7.67–7.74 (m, 2H, 6′, 7′-H), 7.85–8.01(m, 2H, 5′, 8′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.68, 104.9, 126.01, 127.79, 128.51, 128.72, 128.94, 129.05, 129.45, 130.00, 130.13, 130.83, 130.98, 131.09, 135.32, 139.54, 139.70, 142.05, 151.43, 153.10.

3-(*p*-Fluorophenyl)-1-(3-methylquinoxalin-2-yl)-5-phenylpyrazole **4e**

Yield 65%; mp 158°C. MS m/z 380 (M+). Anal. calcd. for $C_{24}H_{17}FN_4$: found C, 75.74; H, 4.65; N, 14.60; required C, 75.77; H, 4.50; N, 14.73. IR (KBr): 1487, 1442 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.47 (s, 3H, CH_3), 6.84 (s, 1H, 4-H), 7.04–7.09 (m, 2H, 3‴, 5‴-H), 7.19 (m, 5H, 2″, 3″, 4″, 5″, 6″-H), 7.60–7.77 (m, 2H, 6′, 7′-H), 7.82–7.87 (m, 2H, 2‴, 6‴-H), 7.94–8.02 (m, 2H, 5′, 8′-H); ^{19}F NMR ($CDCl_3$) δ: −113.51; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.60, 104.36, 115.62 (d, $^2J_{C\text{-}F} = 21.75$ Hz), 127.75 (d, $^3J_{C\text{-}F} = 7.5$ Hz), 128.69 (d, $^4J_{C\text{-}F} = 3.75$ Hz), 128.13, 128.29, 128.30, 128.93, 129.22, 129.62, 129.89, 130.25, 139.86, 142.12, 146.78, 146.84, 151.98, 152.47, 162.96 (d, $^1J_{C\text{-}F} = 249$ Hz).

3-(*p*-Fluorophenyl)-1-(3-methylquinoxalin-2-yl)-5-(*p*-methoxyphenyl)-pyrazole **4f**

Yield 62%; mp 148°C. MS m/z 410 (M+). Anal. calcd. for $C_{25}H_{19}FN_4O$: found C, 73.02; H, 4.72; N, 14.05; required C, 73.16; H, 4.67; N, 13.65. IR (KBr): 1489, 1450 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.50 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 6.77 (d, $J = 7.8$ Hz, 2H, 3″, 5″-H), 6.84 (s, 1H, 4-H), 7.13–7.27 (m, 4H, 2″, 6″, 3‴, 5‴-H), 7.76–7.82 (m, 2H, 6′, 7′-H), 7.92–7.94 (m, 2H, 2‴, 6‴-H), 8.08–8.11 (m, 2H, 5′, 8′-H); ^{19}F NMR ($CDCl_3$) δ: −113.70; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.50, 55.20, 103.69, 114.20, 115.56 (d, $^2J_{C\text{-}F} = 21.75$ Hz), 121.99, 127.72 (d, $^3J_{C\text{-}F} = 7.5$ Hz), 128.36, 129.02 (d, $^4J_{C\text{-}F} = 3.75$ Hz), 129.28, 129.45, 129.86, 130.85, 139.95, 142.13, 146.64, 146.72, 152.10, 152.42, 159.87, 163.05 (d, $^1J_{C\text{-}F} = 247.5$ Hz).

3-(*p*-Fluorophenyl)-1-(3-methylquinoxalin-2-yl)-5-(*p*-methylphenyl)-pyrazole **4g**

Yield 67%; mp 138°C. MS m/z 394 (M+). Anal. calcd. for $C_{25}H_{19}FN_4$: found C, 76.15; H, 4.68; N, 14.38; required C, 76.12; H, 4.86; N, 14.20. IR (KBr): 1494, 1455 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.29(s, 3H, CH_3), 2.51 (s, 3H, CH_3), 6.89 (s, 1H, 4-H), 7.05–7.10 (m, 2H, 3‴, 5‴-H), 7.11–7.18 (m, 4H, 2″, 3″, 5″, 6″-H), 7.75–7.86 (m, 2H, 6′, 7′-H), 7.90–7.95 (m, 2H, 2‴, 6‴-H), 8.10–8.11 (m, 2H, 5′, 8′-H); ^{19}F NMR ($CDCl_3$) δ: −113.64; ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.97, 18.62, 101.43, 113.04 (d, $^2J_{C\text{-}F} = 21$ Hz), 125.19 (d, $^3J_{C\text{-}F} = 8.25$ Hz), 125.42, 125.82, 126.1, 126.4, 126.75, 126.90, 127.32, 128.31, 136.2, 137.3, 137.4, 138.9, 144.4, 149.9, 150.1, 162.05 (d, $^1J_{C\text{-}F} = 232.5$ Hz).

3-(*p*-Fluorophenyl)-1-(3-methylquinoxalin-2-yl)-5-(*p*-chlorophenyl)-pyrazole **4h**

Yield 72%; mp 165°C. MS m/z 414 (M+), 416 (M + 2). Anal. calcd. for $C_{24}H_{16}ClFN_4$: found C, 69.78; H, 3.99; N, 14.04; required C, 69.48; H, 3.89; N, 13.50. IR (KBr): 1498, 1456 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.53 (s, 3H, CH_3), 6.82 (s, 1H, 4-H), 7.04–7.09 (m, 2H, 3‴, 5‴-H), 7.15–7.20 (m, 4H, 2″, 3″, 5″, 6″-H), 7.65–7.78 (m, 2H, 6′, 7′-H), 7.81–7.86 (m, 2H, 2‴, 6‴-H), 7.90–8.04 (m, 2H, 5′, 8′-H); ^{19}F NMR ($CDCl_3$) δ: −113.27;^{13}C NMR (75 MHz, $CDCl_3$): δ 20.73, 103.67, 114.68 (d, $^2J_{C\text{-}F} = 21.75$ Hz), 126.75 (d, $^3J_{C\text{-}F} = 7.5$ Hz), 127.17, 127.42, 127.70, 127.98, 128.14, 128.45, 129.05, 129.99, 133.7, 138.6, 141.13, 144.6, 145.4, 150.7, 151.9, 162.95 (d, $^1J_{C\text{-}F} = 232.5$ Hz).

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