Discovery and Optimization of 1,3,5-trisubstituted Pyrazolines as Potent and Highly Selective Allosteric Inhibitors of Protein Kinase Czeta (PKCζ)

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Supporting Information

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1) Experimental procedures and Analytical data

4-(3-(*Tert*-butyl)-1-(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1b). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 4-fluorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); yellowish white solid; yield: 0.34 g (55%); mp 111-112 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.34 (s, 1H), 7.08 – 7.03 (m, 2H), 6.96 – 6.89 (m, 2H), 6.85 – 6.79 (m, 2H), 6.72 – 6.68 (m, 2H), 4.96 (dd, J = 11.5, 7.5 Hz, 1H), 3.46 (dd, J = 17.4, 11.5 Hz, 1H), 2.64 (dd, J = 17.4, 7.6 Hz, 1H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.18, 156.48, 155.41 (d, $^1J_{C\text{-}F}$ = 233.8 Hz), 142.76, 132.88, 127.02, 115.55, 115.03 (d, $^2J_{C\text{-}F}$ = 22.1 Hz), 113.86 (d, $^3J_{C\text{-}F}$ = 7.4 Hz), 63.85, 42.81, 33.37, 27.91; MS (ESI): m/z = 311.01 $(M\text{-}1)^+$.

4-(1-(4-Bromophenyl)-3-(*tert*-butyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1c). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 4-bromophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); off-white solid; yield: 0.45 g (61%); mp 125-126 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.27 – 7.23 (m, 2H), 7.07 – 7.02 (m, 2H), 6.99 – 6.94 (m, 2H), 5.08 (dd, J = 11.6, 7.7 Hz, 1H), 3.61 (dd, J = 17.2, 11.7 Hz, 1H), 2.91 (dd, J = 17.2, 7.7 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.44, 154.93, 144.82, 134.78, 128.58, 127.18, 123.18, 115.91, 114.40, 64.47, 43.27, 33.82, 28.21; MS (ESI): m/z = 372.71 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1d). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-

1-en-3-one **(E1)** and 4-(trifluoromethyl)phenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); light brown solid; yield: 0.35 g (48%); mp 121-122 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.38 (s, 1H), 7.39 (d, J = 8.5 Hz, 2H), 7.03 – 6.98 (m, 2H), 6.93 (d, J = 8.6 Hz, 2H), 6.75 – 6.65 (m, 2H), 5.21 (dd, J = 11.6, 5.4 Hz, 1H), 3.53 (dd, J = 17.7, 11.7 Hz, 1H), 2.71 (dd, J = 17.7, 5.5 Hz, 1H), 1.18 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.32, 156.62, 147.43, 132.26, 126.76, 125.96, 125.07 (q, $^1J_{C\text{-}F}$ = 270.2 Hz), 116.96 (q, $^2J_{C\text{-}F}$ = 31.8 Hz), 115.66, 111.79, 61.97, 42.65, 33.51, 27.83; MS (ESI): m/z = 362.74 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1e). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and *p*-tolylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4: 1); tan solid; yield: 0.24 g (40%); mp 125.9 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.31 (s, 1H), 7.06 – 7.00 (m, 2H), 6.88 (d, J = 8.2 Hz, 2H), 6.78 – 6.72 (m, 2H), 6.71 – 6.65 (m, 2H), 4.95 (dd, J = 11.5, 7.4 Hz, 1H), 3.43 (dd, J = 17.3, 11.6 Hz, 1H), 2.61 (dd, J = 17.3, 7.4 Hz, 1H), 2.12 (s, 3H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.34, 156.36, 143.76, 133.24, 128.97, 126.97, 126.25, 115.45, 112.95, 63.55, 42.59, 33.34, 27.96, 20.03; MS (ESI): m/z = 308.74 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(4-(isopropyl)phenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1f). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 4-isopropylphenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 3:1); beige solid; yield: 0.19 g (28%); mp 162-163 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.32 (s, 1H), 7.10 – 7.04 (m, 2H), 6.97 – 6.90 (m, 2H), 6.81 – 6.74 (m, 2H), 6.72 – 6.67 (m, 2H), 4.91 (dt, J = 22.8, 11.4

Hz, 1H), 3.43 (dd, *J* = 17.3, 11.5 Hz, 1H), 2.70 (hept, *J* = 6.9 Hz, 1H), 2.60 (dd, *J* = 17.3, 7.9 Hz, 1H), 1.16 (s, 9H), 1.10 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.39, 156.40, 144.17, 137.77, 133.37, 126.98, 126.26, 115.49, 112.90, 63.75, 42.68, 33.34, 32.46, 27.96, 24.09, 24.06; MS (ESI): *m/z* = 337.08 $(M+H)^+$.

4-(3-(*Tert*-butyl)-5-(4-hydroxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)benzoic acid (1g). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 4-hydrazinobenzoicacid hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/MeOH 98:2); white solid; yield: 0.26 g (39%) ; mp 259.1-261 ^oC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.14 (s, 1H), 9.37 (s, 1H), 7.66 (d, *J* = 9.1 Hz, 2H), 7.02 – 6.97 (m, 2H), 6.89 – 6.81 (m, 2H), 6.72 – 6.67 (m, 2H), 5.23 (dd, *J* = 11.6, 5.1 Hz, 1H), 3.53 (dd, *J* = 17.7, 11.7 Hz, 1H), 2.70 (dd, *J* = 17.7, 5.1 Hz, 1H), 1.18 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 167.28, 161.45, 156.59, 147.88, 132.43, 130.67, 126.74, 118.72, 115.63, 111.30, 61.80, 42.58, 33.53, 27.84; MS (ESI): *m/z* = 338.87 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(3-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1h). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); yellowish white solid; yield: 0.2 g (31%); mp 143.3-145.2 ^oC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.37 (s, 1H), 7.09 – 7.04 (m, 1H), 7.04 – 7.00 (m, 2H), 6.88 (t, *J* = 2.1 Hz, 1H), 6.73 – 6.68 (m, 3H), 6.63 (ddd, *J* = 7.9, 2.1, 0.9 Hz, 1H), 5.10 (dd, *J* = 11.6, 6.1 Hz, 1H), 3.49 (dd, *J* = 17.6, 11.6 Hz, 1H), 2.67 (dd, *J* = 17.6, 6.2 Hz, 1H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.34, 156.57, 146.53, 133.29, 132.54, 130.20, 126.85, 116.88, 115.64, 111.85, 110.91, 62.55, 42.67, 33.46, 27.86; MS (ESI): *m/z* = 328.86 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(3-fluorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1i). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 3-fluoropheylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); light brown solid; yield: 0.21 g (35%) ; mp 140.4 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.36 (s, 1H), 7.12 – 6.96 (m, 3H), 6.74 – 6.66 (m, 2H), 6.62 – 6.55 (m, 2H), 6.44 – 6.34 (m, 1H), 5.08 (dd, J = 11.6, 6.3 Hz, 1H), 3.49 (dd, J = 17.6, 11.7 Hz, 1H), 2.67 (dd, J = 17.6, 6.3 Hz, 1H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.81 (d, $^1J_{C\text{-}F}$ = 239.7 Hz), 160.10, 156.56, 147.11 (d, $^3J_{C\text{-}F}$ = 11.1 Hz), 132.69, 130.14 (d, $^3J_{C\text{-}F}$ = 10.1 Hz), 126.86, 115.61, 108.43, 103.61 (d, $^2J_{C\text{-}F}$ = 21.3 Hz), 99.14 (d, $^2J_{C\text{-}F}$ = 26.5 Hz), 62.72, 42.69, 33.43, 27.86; MS (ESI): m/z = 312.10 (M^+).

4-(3-(*Tert*-butyl)-1-(3-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1j). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 3-(trifluoromethyl)pheylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); yellow solid; yield: 0.35 g (49%); mp 130.5 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.37 (s, 1H), 7.27 (t, J = 7.9 Hz, 1H), 7.16 (s, 1H), 7.06 – 7.02 (m, 2H), 6.98 (dd, J = 8.3, 2.1 Hz, 1H), 6.93 – 6.89 (m, 1H), 6.73 – 6.68 (m, 2H), 5.16 (dd, J = 11.6, 6.2 Hz, 1H), 3.52 (dd, J = 17.6, 11.6 Hz, 1H), 2.71 (dd, J = 17.6, 6.2 Hz, 1H), 1.19 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.70, 156.60, 145.54, 132.33, 129.89, 129.49 (q, $^2J_{C\text{-}F}$ = 31.2 Hz), 126.91, 124.33 (q, $^1J_{C\text{-}F}$ = 272.3 Hz), 115.66, 115.45, 113.37, 108.38 , 62.53, 42.69, 33.48, 27.84; MS (ESI): m/z = 362.84 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(*m*-tolyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1k). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and *m*-tolylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The

product was purified by CC (CH_2Cl_2/hexane 4:1); yellowish white solid; yield: 0.25 g (41%); mp 119.3-121.2 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.31 (s, 1H), 7.06 – 7.00 (m, 2H), 6.95 – 6.89 (m, 1H), 6.75 (s, 1H), 6.71 – 6.67 (m, 2H), 6.56 (dd, J = 8.2, 2.1 Hz, 1H), 6.46 – 6.42 (m, 1H), 5.00 (dd, J = 11.6, 6.8 Hz, 1H), 3.45 (dd, J = 17.4, 11.7 Hz, 1H), 2.62 (dd, J = 17.4, 6.8 Hz, 1H), 2.15 (s, 3H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.59, 156.36, 145.66, 137.50, 133.34, 128.39, 126.87, 118.52, 115.49, 113.36, 109.84, 63.01, 42.56, 33.36, 27.96, 21.42; MS (ESI): m/z = 308.94 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(2-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1l). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 2-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); light brown solid; yield: 0.33 g (51%); mp 162-163 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.25 (s, 1H), 7.28 (dd, J = 8.1, 1.5 Hz, 1H), 7.19 (dd, J = 7.9, 1.4 Hz, 1H), 7.11 – 7.05 (m, 1H), 6.90 (d, J = 8.5 Hz, 2H), 6.83 (td, J = 7.8, 1.5 Hz, 1H), 6.53 (d, J = 8.5 Hz, 2H), 5.46 (dd, J = 10.9, 4.7 Hz, 1H), 3.43 – 3.35 (m, 1H), 2.88 (dd, J = 17.2, 4.7 Hz, 1H), 1.22 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.25, 156.47, 143.68, 131.40, 129.72, 127.51, 126.94, 123.63, 123.28, 122.66, 114.94, 65.06, 41.50, 33.60, 27.93; MS (ESI): m/z = 328.86 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(2-fluorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1m). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 2-fluorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); light brown solid; yield: 0.25 g (41%); mp 147.3 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.26 (s, 1H), 7.34 (td, J = 8.3, 1.7 Hz, 1H), 6.98 – 6.88 (m, 4H), 6.73 (dddd, J = 8.1, 7.3, 4.6, 1.7 Hz, 1H), 6.59 – 6.54 (m,

2H), 5.25 (dt, J = 11.0, 3.9 Hz, 1H), 3.40 (dd, J = 17.1, 11.0 Hz, 1H), 2.79 (dd, J = 17.2, 4.3 Hz, 1H), 1.20 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.50, 156.45, 150.79 (d, $^{1}J_{C\text{-}F}$ = 242.7 Hz), 134.19 (d, $^{2}J_{C\text{-}F}$ = 9.3 Hz), 132.21, 127.12, 124.21 , 120.73, 119.22, 115.60 (d, $^{2}J_{C\text{-}F}$ = 20.0 Hz), 115.06, 65.18, 41.91, 33.51, 27.86; MS (ESI): m/z = 312.93 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(2,4-dichlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1n). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 2,4-dichlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 3:1); off-white solid; yield: 0.38 g (52%); mp 137.1-138.5 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.29 (s, 1H), 7.32 – 7.27 (m, 2H), 7.15 (dt, J = 4.1, 2.1 Hz, 1H), 6.91 – 6.84 (m, 2H), 6.56 – 6.52 (m, 2H), 5.49 (dd, J = 10.9, 4.2 Hz, 1H), 3.41 (dd, J = 17.3, 10.9 Hz, 1H), 2.90 (dd, J = 17.3, 4.2 Hz, 1H), 1.22 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.08, 156.59, 142.94, 131.18, 128.96, 127.46, 127.03, 125.92, 123.86, 123.59, 115.04, 64.93, 41.59, 33.64, 27.88; MS (ESI): m/z = 362.82 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(2,4-difluorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1o), The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 2,4-difluorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); yellowish white solid; yield: 0.22 g (33%); mp 163-164 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.29 (s, 1H), 7.29 (td, J = 9.3, 6.1 Hz, 1H), 6.99 (ddd, J = 12.0, 9.0, 2.9 Hz, 1H), 6.93 – 6.88 (m, 2H), 6.88 – 6.82 (m, 1H), 6.59 – 6.54 (m, 2H), 5.15 (ddd, J = 10.8, 4.7, 3.4 Hz, 1H), 3.38 (dd, J = 17.1, 10.9 Hz, 1H), 2.81 (dd, J = 17.1, 4.9 Hz, 1H), 1.19 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.06, 156.55, 156.21 (dd, $^{1}J_{C\text{-}F}$ = 239.3, $^{3}J_{C\text{-}F}$ =11.2 Hz), 150.95 (dd, $^{1}J_{C\text{-}F}$ = 246.7, $^{3}J_{C\text{-}F}$ =12.2 Hz),

131.65, 131.32 (dd, $^{2}J_{C\text{-}F}$ = 9.7, $^{4}J_{C\text{-}F}$= 3.1 Hz), 127.34, 120.21 (dd, $^{3}J_{C\text{-}F}$ = 9.0, 4.9 Hz), 115.07, 110.71 (dd, $^{2}J_{C\text{-}F}$ = 21.5, $^{4}J_{C\text{-}F}$ =3.3 Hz), 104.02 (dd, $^{2}J_{C\text{-}F}$ = 26.4, 24.4 Hz), 65.70, 41.80, 33.53, 27.85; MS (ESI): *m/z* = 330.80 $(M+H)^{+}$.

4-(3-(*Tert*-butyl)-1-(2,4-dimethylphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1p). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 2,4-dimethylphenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); light brown solid; yield: 0.26 g (41%) ; mp 77-79 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.26 (s, 1H), 7.10 – 7.06 (m, 2H), 6.86 – 6.83 (m, 1H), 6.78 – 6.76 (m, 2H), 6.63 – 6.59 (m, 2H), 4.87 (t, *J* = 10.6 Hz, 1H), 3.24 (dd, *J* = 16.5, 10.1 Hz, 1H), 2.65 (dd, *J* = 16.5, 11.1 Hz, 1H), 2.18 (s, 3H), 2.13 (s, 3H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.41, 156.44, 142.97, 131.32, 131.18, 130.79, 128.84, 127.91, 126.04, 118.81, 115.02, 66.78, 41.49, 33.46, 27.97, 20.20, 19.56; MS (ESI): *m/z* = 323.02 $(M+H)^{+}$.

4-(3-(*Tert*-butyl)-1-(2,6-dichlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1q). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 2,6-dichlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 3:1); off-white solid; yield: 0.24 g (33%) ; mp 172-173 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.30 (s, 1H), 7.33 – 7.29 (m, 2H), 7.15 – 7.10 (m, 1H), 7.09 – 7.04 (m, 2H), 6.62 – 6.57 (m, 2H), 5.15 (t, *J* = 10.6 Hz, 1H), 3.35 (dd, *J* = 17.2, 11.1 Hz, 1H), 2.93 (dd, *J* = 17.2, 10.1 Hz, 1H), 1.20 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.02, 156.83, 139.82, 134.06, 130.41, 129.34, 128.87, 127.86, 114.77, 67.20, 40.73, 33.43, 27.87; MS (ESI): *m/z* = 362.79 $(M+H)^{+}$.

4-(3-(*Tert*-butyl)-1-(3-chloro-4-fluorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1r). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 3-chloro-4-fluorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); brown solid; yield: 0.23 g (34%) ; mp 94.2 ^oC; ^1H NMR (500 MHz, DMSO) δ 9.38 (s, 1H), 7.12 (t, J = 9.2 Hz, 1H), 7.05 – 7.01 (m, 2H), 6.93 (dd, J = 6.5, 2.8 Hz, 1H), 6.73 – 6.67 (m, 3H), 5.06 (dd, J = 11.5, 6.6 Hz, 1H), 3.48 (dd, J = 17.5, 11.5 Hz, 1H), 2.68 (dd, J = 17.5, 6.7 Hz, 1H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.44, 156.61, 150.08 (d, $^1J_{C\text{-}F}$ = 236.4 Hz), 142.99 (d, $^4J_{C\text{-}F}$ = 1.8 Hz), 132.31, 126.98, 119.21 (d, $^2J_{C\text{-}F}$ = 18.3 Hz), 116.75 (d, $^2J_{C\text{-}F}$ = 21.6 Hz), 115.65, 113.30, 112.21 (d, $^3J_{C\text{-}F}$ = 6.3 Hz), 63.13, 42.84, 33.44, 27.85; MS (ESI): m/z = 346.91 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(2,3,4-trifluorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1t). The title compound was prepared by reaction of (*E*)-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and 2,3,4-trifluorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 3:1); yellow solid; yield: 0.22 g (32%); mp 159-161 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.34 (s, 1H), 7.11 – 7.02 (m, 2H), 6.94 – 6.89 (m, 2H), 6.63 – 6.58 (m, 2H), 5.24 – 5.18 (m, 1H), 3.42 (dd, J = 17.3, 11.0 Hz, 1H), 2.82 (dd, J = 17.3, 4.8 Hz, 1H), 1.19 (s, 9H); MS (ESI): m/z = 348.99 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (1u) . The title compound was prepared by reaction of *(E)*-1-(4-(*tert*-butoxy)phenyl)-4,4-dimethylpent-1-en-3-one **(E1)** and phenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); yellowish white solid; yield: 0.23 g (39%) ; mp 175-176 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.33 (s, 1H), 7.11 – 6.99 (m, 4H), 6.87 – 6.80

(m, 2H), 6.73 – 6.66 (m, 2H), 6.62 (tt, *J* = 7.3, 1.1 Hz, 1H), 5.01 (dd, *J* = 11.6, 7.0 Hz, 1H), 3.46 (dd, *J* = 17.4, 11.6 Hz, 1H), 2.63 (dd, *J* = 17.4, 7.0 Hz, 1H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.83, 156.42, 145.70, 133.21, 128.55, 126.91, 117.64, 115.52, 112.66, 63.13, 42.63, 33.38, 27.94; MS (ESI): *m/z* = 294.91 $(M+H)^+$.

4-(1-(4-Chlorophenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2a). The title compound was prepared by reaction of (*E*)-3-(4-(*tert*-butoxy)phenyl)-1-phenylprop-2-en-1-one **(E2)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); yellow solid; yield: 0.19 g (28%) ; mp 164-165 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.40 (s, 1H), 7.74 (dt, *J* = 8.3, 1.8 Hz, 2H), 7.47 – 7.31 (m, 3H), 7.21 – 7.14 (m, 2H), 7.09 – 7.03 (m, 2H), 7.02 – 6.95 (m, 2H), 6.75 – 6.67 (m, 2H), 5.36 (dd, *J* = 12.1, 6.1 Hz, 1H), 3.87 (dd, *J* = 17.5, 12.1 Hz, 1H), 3.08 (dd, *J* = 17.5, 6.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.70, 147.99, 143.07, 132.19, 132.15, 128.81, 128.63, 128.55, 127.03, 125.74, 121.98, 115.69, 114.37, 62.73, 43.12; MS (ESI): *m/z* = 348.71 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2b). The title compound was prepared by reaction of (*E*)-3-(4-(*tert*-butoxy)phenyl)-1-phenylprop-2-en-1-one **(E2)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); yield: light brown solid; 0.23 g (33%); mp 161.2-163.3 ^{o}C;^{1}H NMR (500 MHz, DMSO-d_6) δ 9.41 (s, 1H), 7.78 – 7.74 (m, 2H), 7.46 – 7.36 (m, 3H), 7.16 – 7.12 (m, 1H), 7.11 – 7.05 (m, 3H), 6.87 (ddd, *J* = 8.4, 2.2, 0.9 Hz, 1H), 6.75 – 6.66 (m, 3H), 5.40 (dd, *J* = 12.1, 5.9 Hz, 1H), 3.88 (dd, *J* = 17.5, 12.1 Hz, 1H), 3.10 (dd, *J* = 17.5, 6.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.73, 148.56,

145.39, 133.48, 132.12, 132.01, 130.37, 128.98, 128.65, 127.01, 125.88, 117.75, 115.73, 112.32, 111.35, 62.51, 43.10; MS (ESI): *m/z* = 348.74 $(M+H)^+$.

2-(1-(4-Chlorophenyl)-5-(4-hydroxyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl)phenol (2c) . The title compound was prepared by reaction of (*E*)-3-(4-(*tert*-butoxy)phenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one **(E3)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/MeOH 99:1); beige solid; yield: 0.27 g (38%); mp 214.2 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 10.41 (s, 1H), 9.42 (s, 1H), 7.44 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.25 – 7.19 (m, 2H), 7.12 – 7.08 (m, 2H), 6.97 (ddd, *J* = 7.8, 6.9, 1.0 Hz, 1H), 6.95 – 6.88 (m, 3H), 6.74 – 6.69 (m, 2H), 5.35 (dd, *J* = 12.0, 6.4 Hz, 1H), 4.00 (dd, *J* = 17.7, 12.0 Hz, 1H), 3.24 (dd, *J* = 17.8, 6.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.80, 156.19, 150.61, 142.51, 131.77, 130.51, 128.77, 128.17, 127.15, 122.59, 119.54, 116.59, 116.10, 115.73, 114.41, 61.79, 44.11; MS (ESI): *m/z* = 364.34 $(M)^+$.

4-(1-(4-Chlorophenyl)-3-(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2d). The title compound was prepared by reaction of (*E*)-3-(4-(*tert*-butoxy)phenyl)-1-(2-methoxylphenyl)prop-2-en-1-one **(E4)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2); tan solid; yield: 0.31 g (41%) ; mp 205-206 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.37 (s, 1H), 7.87 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.39 – 7.34 (m, 1H), 7.19 – 7.14 (m, 2H), 7.10 – 7.03 (m, 3H), 7.00 (td, *J* = 7.7, 1.0 Hz, 1H), 6.98 – 6.93 (m, 2H), 6.72 – 6.68 (m, 2H), 5.28 (dd, *J* = 12.0, 6.2 Hz, 1H), 3.92 (dd, *J* = 18.1, 12.0 Hz, 1H), 3.79 (s, 3H), 3.15 (dd, *J* = 18.1, 6.3 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.29, 156.62, 147.28, 143.26, 132.39, 130.37, 128.51, 128.14, 126.95,

121.76, 121.08, 120.64, 115.65, 114.31, 112.31, 62.69, 55.61, 46.50; MS (ESI): *m/z* = 378.82 $(M+H)^+$.

4-(1-(4-Chlorophenyl)-3-(2-ethoxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2e). The title compound was prepared by reaction of (*E*)-3-(4-(*tert*-butoxy)phenyl)-1-(2-ethoxylphenyl)prop-2-en-1-one **(E5)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); yellowish white solid; yield: 0.19 g (25%) ; mp 194-196 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.6 Hz, 1H), 7.60 – 7.51 (m, 2H), 7.45 – 7.30 (m, 4H), 7.25 (dd, *J* = 14.2, 7.7 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 1H), 7.10 – 6.98 (m, 2H), 5.37 (dd, *J* = 12.0, 7.0 Hz, 1H), 4.43 (q, *J* = 6.8 Hz, 2H), 4.29 (dd, *J* = 17.8, 12.1 Hz, 1H), 3.55 (dd, *J* = 17.9, 7.0 Hz, 1H), 1.64 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.41, 156.21, 155.02, 143.69, 130.81, 129.06, 128.65, 126.60, 125.80, 122.47,120.73, 115.90, 114.47, 112.32, 109.15, 66.11, 63.89, 46.97, 14.94; MS (ESI): *m/z* = 393.11 $(M+H)^+$.

4-(1-(4-Chlorophenyl)-3-(2-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2f). The title compound was prepared by reaction of (*E*)-3-(4-(*tert*-butoxy)phenyl)-1-(2-chlorophenyl)prop-2-en-1-one **(E6)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 4:1); off-white solid; yield: 0.35 g (46%) ; mp 124-125 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.42 (s, 1H), 7.78 – 7.72 (m, 1H), 7.55 – 7.47 (m, 1H), 7.44 – 7.32 (m, 2H), 7.23 – 7.15 (m, 2H), 7.11 – 7.04 (m, 2H), 7.03 – 6.94 (m, 2H), 6.75 – 6.66 (m, 2H), 5.39 (dd, *J* = 12.1, 6.1 Hz, 1H), 4.00 (dd, *J* = 17.5, 12.1 Hz, 1H), 3.20 (dd, *J* = 17.5, 6.1 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.77, 146.30, 142.89, 131.86, 130.99, 130.86, 130.74, 130.16, 129.90, 128.60, 127.30, 127.07, 122.44, 115.70, 114.61, 62.78, 45.59; MS (ESI): *m/z* = 382.59 $(M+H)^+$.

4-(1-(4-Chlorophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2g). The title compound was prepared by reaction of (*E*)-3-(4-(*tert*-butoxy)phenyl)-1-(thiophen-2-yl)prop-2-en-1-one **(E7)** and 4-chlrorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 3:1); greenish yellow solid; yield: 0.14 g (20%); mp 169.9 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.41 (s, 1H), 7.61 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.26 (dd, *J* = 3.6, 1.1 Hz, 1H), 7.20 – 7.14 (m, 2H), 7.10 (dd, *J* = 5.1, 3.6 Hz, 1H), 7.08 – 7.04 (m, 2H), 6.95 – 6.89 (m, 2H), 6.74 – 6.68 (m, 2H), 5.37 (dd, *J* = 12.0, 6.1 Hz, 1H), 3.87 (dd, *J* = 17.3, 12.0 Hz, 1H), 3.09 (dd, *J* = 17.3, 6.1 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.74, 144.42, 142.85, 135.51, 131.91, 128.58, 127.82, 127.70, 127.61, 127.01, 122.00, 115.71, 114.33, 62.81, 43.88; MS (ESI): *m/z* = 354.47 (M^+).

4-(1-(4-Bromophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2h). The title compound was prepared by reaction of *(E)*-3-(4-(*tert*-butoxy)phenyl)-1-(thiophen-2-yl)prop-2-en-1-one **(E7)** and 4-bromophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 3:1); greenish yellow solid; yield: 0.15 g (19%); mp 162-164 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.40 (s, 1H), 7.62 – 7.59 (m, 1H), 7.31 – 7.25 (m, 3H), 7.11 – 7.08 (m, 1H), 7.07 – 7.03 (m, 2H), 6.89 – 6.85 (m, 2H), 6.74 – 6.69 (m, 2H), 5.37 (dd, *J* = 12.0, 6.0 Hz, 1H), 3.87 (dd, *J* = 17.3, 12.0 Hz, 1H), 3.09 (dd, *J* = 17.3, 6.0 Hz, 1H).^{13}C NMR (125 MHz, DMSO-d_6) δ 156.74, 144.50, 143.15, 135.49, 131.86, 131.41, 127.83, 127.75, 127.65, 126.99, 115.71, 114.82, 109.62, 62.70, 43.87; MS (ESI): *m/z* = 398.70 $(M+H)^+$.

4-(3-(Thiophen-2-yl)-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2i). The title compound was prepared by reaction of (*E*)-3-(4-(*tert*-butoxy)phenyl)-1-(thiophen-2-yl)prop-2-en-1-one **(E7)** and 4-(trifluoromethyl)phenylhydrazine hydrochloride according to

the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 3:1); yellowish white solid; yield: 0.25 g (33%) ; mp 162-163.6 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.43 (s, 1H), 7.65 (dd, J = 5.1, 1.1 Hz, 1H), 7.46 (dd, J = 9.0, 0.5 Hz, 2H), 7.32 (dd, J = 3.6, 1.1 Hz, 1H), 7.12 (dt, J = 7.7, 3.8 Hz, 1H), 7.09 – 7.01 (m, 4H), 6.76 – 6.66 (m, 2H), 5.49 (dd, J = 11.9, 5.3 Hz, 1H), 3.92 (dd, J = 17.4, 12.0 Hz, 1H), 3.15 (dd, J = 17.4, 5.4 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.82, 146.28, 145.86, 135.16, 131.60, 128.39, 128.16, 127.90, 126.91, 126.14, 124.96 (q, $^1J_{C\text{-}F}$ = 270.3 Hz), 117.90 (q, $^2J_{C\text{-}F}$ = 31.9 Hz), 115.78, 112.34, 62.19, 43.86; MS (ESI): m/z = 388.81 $(M+1)^+$.

4-(1-(3-Chlorophenyl)-3-(pyridin-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2j). The title compound was prepared by reaction of (*E*)-3-(4-(*tert*-butoxy)phenyl)-1-(pyridin-2-yl)prop-2-en-1-one **(E8)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/MeOH 98:2); dark yellow solid; yield: 0.25 g (36%); mp 245.9-247 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.42 (s, 1H), 8.56 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H), 8.11 (dt, J = 8.0, 1.1 Hz, 1H), 7.84 (ddd, J = 8.0, 7.5, 1.8 Hz, 1H), 7.35 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H), 7.19 – 7.14 (m, 1H), 7.12 (t, J = 2.1 Hz, 1H), 7.10 – 7.05 (m, 2H), 6.91 (ddd, J = 8.4, 2.2, 0.8 Hz, 1H), 6.76 (ddd, J = 7.9, 2.0, 0.8 Hz, 1H), 6.74 – 6.69 (m, 2H), 5.47 (dd, J = 12.2, 5.8 Hz, 1H), 3.91 (dd, J = 18.1, 12.3 Hz, 1H), 3.14 (dd, J = 18.1, 5.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.75, 151.05, 149.54, 149.25, 144.92, 136.45, 133.54, 131.92, 130.44, 126.97, 123.39, 120.40, 118.34, 115.76, 112.63, 111.63, 62.65, 42.91; MS (ESI): m/z = 349.78 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(1*H*-pyrrol-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2k). The title compound was prepared by reaction of (*E*)-3-(4-(*tert*-butoxy)phenyl)-1-(1*H*-pyrrol-2-yl)prop-2-en-1-one **(E9)** and 3-chlorophenylhydrazine hydrochloride according to the general

procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2); grey solid; yield: 0.094 g (14%); mp 174.6-176.4 ^oC; ^1H NMR (500 MHz, DMSO-d_6) 10.12 (s, 1H), 9.39 (s, 1H), δ 7.78-7.71 (m, 1H), 7.15 – 7.09 (m, 1H), 6.99 (t, J = 2.1 Hz, 1H), 6.98 – 6.92 (m, 2H), 6.84 (ddd, J = 8.4, 2.2, 0.9 Hz, 1H), 6.81 (dd, J = 3.4, 0.7 Hz, 1H), 6.72 (ddd, J = 7.9, 2.1, 0.9 Hz, 1H), 6.68-6.60 (m, 1H), 6.57 – 6.49 (m, 2H), 5.09 (dd, J = 11.5, 5.6 Hz, 1H), 3.69 (dd, J = 17.4, 11.6 Hz, 1H), 2.89 (dd, J = 17.4, 5.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 151.28, 148.15, 146.21, 142.65, 140.47, 134.40, 130.75, 128.46, 126.87, 117.75, 114.22, 113.60, 113.00, 112.93, 112.51, 61.99, 42.03; MS (ESI): m/z = 337.76 $(M+H)^+$.

4-(3-(4-Aminophenyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (2l). The title compound was prepared by reaction of (*E*)-1-(4-aminophenyl)-3-(4-(*tert*-butoxy)phenyl)prop-2-en-1-one **(E10)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/MeOH 98:2); yellow solid; yield: 0.33g (46%) ; mp 181.5 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.36 (s, 1H), 7.42 (d, J = 8.6 Hz, 2H), 7.18 – 7.09 (m, 2H), 7.04 (d, J = 8.6 Hz, 2H), 6.95 – 6.87 (m, 2H), 6.74 – 6.66 (m, 2H), 6.59 (t, J = 11.8 Hz, 2H), 5.49 (s, 2H), 5.21 (dd, J = 11.8, 6.0 Hz, 1H), 3.76 (dd, J = 17.2, 11.8 Hz, 1H), 2.96 (dd, J = 17.2, 6.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.55, 149.91, 149.04, 143.69, 132.56, 128.41, 127.19, 126.98, 120.94, 119.43, 115.61, 113.90, 113.47, 62.30, 43.52; MS (ESI): m/z = 363.85 $(M+H)^+$.

3-(*Tert*-butyl)-1-(4-chlorophenyl)-5-(3-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (3a). The title compound was prepared by reaction of (*E*)-1-(3-methoxyphenyl)-4,4-dimethylpent-1-en-3-one **(E11)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; yellow solid; yield: 0.45 g (66%); MS (ESI): m/z = 342.77 $(M+H)^+$.

3-(*Tert*-butyl)-1,5-bis(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (3b). The title compound was prepared by reaction of 1-(4-methoxyphenyl)-4,4-dimethylpent-1-en-3-one **(E12)** and 4-methoxyphenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; grey solid; yield: 0.40 g (59%); MS (ESI): *m/z* = 338.82 $(M+H)^+$.

3-(*Tert*-butyl)-5-(4-chlorophenyl)-1-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (3c). The title compound was prepared by reaction of 1-(4-chlorophenyl)-4,4-dimethylpent-1-en-3-one **(E13)** and 4-methoxyphenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; brown solid; yield: 0.48 g (71 %); MS (ESI): *m/z* = 342.68 $(M+H)^+$.

3-(*Tert*-butyl)-1-(4-chlorophenyl)-5-(3-fluoro-4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (3d). The title compound was prepared by reaction of (*E*)-1-(3-fluoro-4-methoxyphenyl)-4,4-dimethylpent-1-en-3-one **(E14)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:3); colorless oil; yield: 0.5 g (70%); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.48 – 7.42 (m, 2H), 6.90 – 6.86 (m, 1H), 6.79 (dd, *J* = 12.2, 2.1 Hz, 1H), 6.74 – 6.70 (m, 1H), 6.66 – 6.59 (m, 2H), 5.10 (dd, *J* = 11.6, 5.0 Hz, 1H), 3.56 (s, 3H), 3.32 (dd, *J* = 17.7, 11.7 Hz, 1H), 2.52 (dd, *J* = 17.8, 5.1 Hz, 1H), 1.12 (s, 9H); MS (ESI): *m/z* = 360.71 $(M+H)^+$.

3-(*Tert*-butyl)-5-(3-chloro-4-methoxyphenyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazole (3e). The title compound was prepared by reaction of (*E*)-1-(3-chloro-4-methoxyphenyl)-4,4-dimethylpent-1-en-3-one **(E15)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/ hexane

1:4); yellowish white solid; yield: 0.43g (58%); mp 150-152 ^{o}C; ^{1}H NMR (500 MHz, DMSO) δ 7.18 (d, *J* = 2.1 Hz, 1H), 7.15 – 7.11 (m, 2H), 6.96 (dt, *J* = 6.7, 3.4 Hz, 1H), 6.90 – 6.85 (m, 1H), 6.81 – 6.78 (m, 2H), 5.14 (dd, *J* = 11.7, 6.5 Hz, 1H), 3.82 (s, 3H), 3.48 (dd, *J* = 17.6, 11.6 Hz, 1H), 2.76 (dt, *J* = 21.7, 10.9 Hz, 1H), 1.13 (s, 9H). MS (ESI): *m/z* = 376.78 $(M+H)^{+}$.

3-(*Tert*-butyl)-1-(3-chlorophenyl)-5-(4-fluoro-3-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (3f). The title compound was prepared by reaction of (*E*)-1-(4-fluoro-3-methoxy phenyl)-4,4-dimethylpent-1-en-3-one **(E16)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; yellow oil; yield: 56% (0.4 g); MS (ESI): *m/z* = 360.74 $(M+H)^{+}$.

1-(4-Chlorophenyl)-5-(3,4-dimethoxyphenyl)-3-(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (3g). The title compound was prepared by reaction of 3-(3,4-dimethoxyphenyl)-1-(2-methoxyphenyl)prop-2-en-1-one **(E17)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; brown solid; yield: 0.54 g (64%); MS (ESI): *m/z* = 422.81 $(M+H)^{+}$.

1-(3-Chlorophenyl)-5-(3-fluoro-4-methoxyphenyl)-3-(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (3h). The title compound was prepared by reaction of (*E*)-3-(3-fluoro-4-methoxyphenyl)-1-(2-methoxyphenyl)prop-2-en-1-one **(E18**) and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:3); buff solid; yield: 0.43 g (53%); mp 182-184 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 16.5, 7.8 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.39 (s, 1H), 7.31 –

7.21 (m, 3H), 7.14 (t, *J* = 7.0 Hz, 2H), 6.98 (dd, *J* = 25.1, 8.0 Hz, 2H), 5.33 (dd, *J* = 12.2, 6.9 Hz, 1H), 4.21 (dd, *J* = 20.3, 7.7 Hz, 1H), 4.08 (s, 3H), 4.03 (s, 3H), 3.50 (dd, *J* = 17.9, 6.8 Hz, 1H) ; MS (ESI): *m/z* = 410.76 $(M+H)^+$.

1-(3-Chlorophenyl)-5-(4-ethoxy-3,5-difluorophenyl)-3-(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (3i). The title compound was prepared by reaction of (*E*)-3-(4-ethoxy-3,5-difluorophenyl)-1-(2-methoxyphenyl)prop-2-en-1-one **(E19)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:4); buff solid; yield: 0.55 g (63%); mp 166-167 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.15 (t, *J* = 2.1 Hz, 1H), 7.04 – 6.99 (m, 2H), 6.92 – 6.89 (m, 1H), 6.84 (ddd, *J* = 6.0, 3.4, 2.7 Hz, 2H), 6.77 – 6.73 (m, 1H), 5.07 (dd, *J* = 12.2, 6.7 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.00 (dd, *J* = 20.1, 7.9 Hz, 1H), 3.81 (s, 3H), 3.30 – 3.22 (m, 1H), 1.41 (t, *J* = 7.1 Hz, 3H) ; MS (ESI): *m/z* = 442.71 $(M+H)^+$.

1-(3-Chlorophenyl)-5-(2,3-difluoro-4-methoxyphenyl)-3-(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (3j). The title compound was prepared by reaction of *(E)*-3-(2,3-difluoro-4-methoxyphenyl)-1-(2-methoxyphenyl)prop-2-en-1-one **(E20)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:4); yellowish white solid; yield: 0.62 g (73%); mp 209-210 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.16 (ddd, *J* = 7.7, 3.6, 1.8 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.27 – 7.25 (m, 1H), 7.24 – 7.22 (m, 1H), 7.19 – 7.16 (m, 1H), 7.09 – 7.05 (m, 1H), 6.99 (tt, *J* = 7.1, 3.5 Hz, 1H), 6.91 (dddd, *J* = 8.3, 4.2, 2.1, 0.9 Hz, 2H), 6.79 (ddd, *J* = 13.3, 7.6, 3.9 Hz, 1H), 5.60 (dd, *J* = 12.2, 6.1 Hz, 1H), 4.18 (dt, *J* = 16.5, 7.7 Hz, 1H), 4.02 (s, 3H), 3.99 (s, 3H), 3.45 (dd, *J* = 17.8, 6.1 Hz, 1H) ; MS (ESI): *m/z* = 429.26 $(M+H)^+$.

1-(3-Chlorophenyl)-3-(2,4-dimethoxyphenyl)-5-(3-fluoro-4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (3k). The title compound was prepared by reaction of (*E*)-3-(3-fluoro-4-methoxyphenyl)-1-(2,4-dimethoxyphenyl)prop-2-en-1-one **(E21)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; yellowish white solid; 0.51g (58%); MS (ESI): *m/z* = 440.69 $(M+H)^+$.

3-(*Tert*-butyl)-1-(4-chlorophenyl)-5-(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazole (3l). The title compound was prepared by reaction of 1-(4-fluorophenyl)-4,4-dimethylpent-1-en-3-one **(E22)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:3); yellow solid; yield: 0.18 g (28%); mp 71.2 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.39 (m, 2H), 7.27 – 7.22 (m, 2H), 7.22 – 7.16 (m, 2H), 7.03 – 6.99 (m, 2H), 5.13 (dd, *J* = 11.7, 7.6 Hz, 1H), 3.63 (dd, *J* = 17.2, 11.7 Hz, 1H), 2.89 (dd, *J* = 17.2, 7.6 Hz, 1H), 1.39 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.09 (d, $^1J_{C\text{-}F}$ = 246.0 Hz), 159.25, 144.62, 138.29 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 128.65, 127.44 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 123.41, 115.99 (d, $^2J_{C\text{-}F}$ = 21.5 Hz), 114.35, 64.26, 43.24, 33.82, 28.20;MS (ESI): *m/z* = 331.18 $(M+1)^+$.

3-(*Tert*-butyl)-1,5-bis(4-chlorophenyl)-4,5-dihydro-1*H*- pyrazole (3m). The title compound was prepared by reaction of 1-(4-chlorophenyl)-4,4-dimethylpent-1-en-3-one **(E13)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:5); white solid; yield: 0.34 g (49.5%); mp 85.3-87 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H), 7.21 – 7.17 (m, 2H), 7.10 – 7.05 (m, 2H), 6.85 – 6.80 (m, 2H), 4.94 (dd, *J* = 11.7, 7.6 Hz, 1H), 3.46 (dd, *J* = 17.2, 11.7 Hz, 1H), 2.71 (dd, *J* = 17.2, 7.6 Hz, 1H), 1.21 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

159.25, 144.53, 141.07, 133.26, 129.29, 128.68, 127.24, 123.48, 114.33, 64.28, 43.14, 33.82, 28.20; MS (ESI): *m/z* = 347.16 $(M+H)^+$.

5-(4-Bromophenyl)-3-(*tert*-butyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazole (3n). The title compound was prepared by reaction of 1-(4-bromophenyl)-4,4-dimethylpent-1-en-3-one **(E23)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:5); off-white solid; yield: 0.4 g (52%); mp 108.8 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.43 (m, 2H), 7.15 – 7.11 (m, 2H), 7.10 – 7.05 (m, 2H), 6.85 – 6.79 (m, 2H), 4.92 (dd, *J* = 11.7, 7.6 Hz, 1H), 3.46 (dt, *J* = 17.2, 7.5 Hz, 1H), 2.71 (dd, *J* = 17.2, 7.6 Hz, 1H), 1.21 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.50, 144.76, 141.85, 132.49, 128.94, 127.84, 123.75, 121.57, 114.58, 64.57, 43.34, 34.07, 28.45; MS (ESI): *m/z* = 392.71 $(M+H)^+$.

.**4-(3-(*Tert*-butyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)benzonitrile (3o).** The title compound was prepared by reaction of 4-(4,4-dimethyl-3-oxopent-1-en-1-yl)benzonitrile **(E24)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:1); buff solid; yield: 0.44 g (66%) ; mp 109.5 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 7.83 – 7.78 (m, 2H), 7.42 – 7.38 (m, 2H), 7.16 – 7.10 (m, 2H), 6.83 – 6.77 (m, 2H), 5.33 (dd, *J* = 11.8, 6.3 Hz, 1H), 3.58 (dd, *J* = 17.6, 11.8 Hz, 1H), 2.73 (dd, *J* = 17.6, 6.3 Hz, 1H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.05, 147.90, 143.86, 132.95, 128.61, 126.91, 121.68, 118.58, 113.97, 110.21, 62.66, 42.33, 33.45, 27.83; MS (ESI): *m/z* = 337.03 (M^+).

1-(4-Chlorophenyl)-5-(4-methoxyphenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazole (3p). The title compound was prepared by reaction of 3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one **(E25)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for

pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:3); yellow solid; yield: 0.43 g (59%) ; mp 173-175 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.62 (ddd, *J* = 4.2, 3.5, 1.8 Hz, 2H), 7.38 – 7.33 (m, 1H), 7.32 – 7.28 (m, 2H), 7.14 – 7.07 (m, 3H), 7.05 – 7.00 (m, 2H), 6.92 – 6.88 (m, 1H), 6.79 – 6.74 (m, 2H), 5.10 (dd, *J* = 12.2, 7.1 Hz, 1H), 3.75 – 3.70 (m, 1H), 3.68 (s, 3H), 3.03 (dd, *J* = 17.1, 7.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.08, 147.33, 143.37, 134.05, 130.07, 129.09, 128.76, 127.00, 126.50, 125.75, 123.76, 114.54, 105.03, 63.97, 55.29, 43.6 9; MS (ESI): *m/z* = 362.33 (M^+).

4-(1-(4-Chlorophenyl)-3-methyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (3q) . The title compound was prepared by reaction of the commercially available 4-hydroxybenzylideneacetone and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2); white solid; yield: 0.20 g (35%); mp 184-186 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.35 (s, 1H), 7.12 – 7.07 (m, 2H), 7.05 – 7.01 (m, 2H), 6.82 – 6.77 (m, 2H), 6.72 – 6.68 (m, 2H), 5.02 (dd, *J* = 11.7, 6.9 Hz, 1H), 3.44 (ddd, *J* = 17.7, 11.7, 1.1 Hz, 1H), 2.61 (ddd, *J* = 17.8, 6.9, 1.0 Hz, 1H), 2.00 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.52, 150.03, 144.28, 132.66, 128.37, 126.96, 121.06, 115.58, 113.84, 62.71, 47.40, 15.54; MS (ESI): *m/z* = 286.89 $(M+H)^+$.

3-(3-(*Tert*-butyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenol (4a). The title compound was prepared by demethylation of 3-(*tert*-butyl)-1-(4-chlorophenyl)-5-(3-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole **(3a)** using BBr_3 (3 equiv) according to the general procedure for ether dealkylation. The product was purified by CC (CH_2Cl_2/hexane 4:1); beige solid; yield: 0.21 g (64%); mp 131-133 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.39 (s, 1H), 7.15 – 7.09 (m, 3H), 6.83 – 6.79 (m, 2H), 6.66 (ddd, *J* = 6.5, 3.8, 1.4 Hz, 1H), 6.64 – 6.59 (m, 2H), 5.06 (dd, *J* = 11.7, 6.6 Hz, 1H), 3.52 (dd, *J* = 17.6, 11.8 Hz, 1H), 2.68 (dd, *J* = 17.6, 6.6 Hz, 1H),

1.17 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.84, 157.81, 144.23, 144.05, 129.96, 128.43, 121.18, 116.28, 114.34, 113.83, 112.10, 63.14, 42.65, 33.42, 27.89. MS (ESI): *m/z* = 328.91 $(M+H)^+$.

4,4'-(3-(*Tert*-butyl)-4,5-dihydro-1*H*-pyrazole-1,5-diyl)diphenol (4b). The title compound was prepared by demethylation of 3-(*tert*-butyl)-1,5-bis(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole **(3b)** using BBr_3 (6 equiv) according to the general procedure for ether dealkylation. The product was purified by CC (CH_2Cl_2/MeOH 98:2); grey solid; yield: 0.22 g (73%); mp 104-106 ^oC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.63 (s, 1H), 9.32 (s, 1H), 7.08 (d, *J* = 8.5 Hz, 2H), 7.04 – 6.98 (m, 2H), 6.69 (ddd, *J* = 11.4, 7.7, 3.3 Hz, 2H), 6.55 – 6.50 (m, 2H), 4.77 (dd, *J* = 11.0, 9.2 Hz, 1H), 3.52 (dd, *J* = 17.1, 11.1 Hz, 1H), 2.57 (dd, *J* = 17.1, 9.1 Hz, 1H), 1.15 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.58, 157.95, 157, 139.68, 133.36, 132.05, 121.27, 115.14, 114.93, 65.25, 42.73, 31.77, 27.99; MS (ESI): *m/z* = 311.10 $(M+H)^+$.

4-(3-(*Tert*-butyl)-5-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)phenol (4c). The title compound was prepared by demethylation of 3-(*tert*-butyl)-5-(4-chlorophenyl)-1-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole **(3c)** using BBr_3 (3 equiv) according to the general procedure for ether dealkylation. The product was purified by CC (CH_2Cl_2/hexane 4:1); grey solid; yield: 0.14 g (44%) ; mp 142-143 ^oC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.68 (s, 1H), 7.41 – 7.32 (m, 2H), 7.33 – 7.26 (m, 2H), 6.71 – 6.63 (m, 2H), 6.59 – 6.50 (m, 2H), 4.95 (dd, *J* = 11.3, 8.7 Hz, 1H), 3.45 (dd, *J* = 17.2, 11.4 Hz, 1H), 2.61 (dd, *J* = 17.2, 8.7 Hz, 1H), 1.15 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.11, 150.35, 142.17, 139.24, 131.54, 128.69, 128.05, 115.29, 114.87, 64.66, 42.51, 33.32, 27.96 ; MS (ESI): *m/z* = 328.71 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)-2-fluorophenol (4d). The title compound was prepared by demethylation of 3-(*tert*-butyl)-1-(4-chlorophenyl)-5-(3-fluoro-4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole **(3d)** using BBr_3 (3 equiv) according to the general procedure for ether dealkylation. The product was purified by CC (CH_2Cl_2/hexane 4:1); off-white solid; yield: 0.15 g (44%); mp 130-132 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 9.80 (s, 1H), 7.15 – 7.10 (m, 2H), 6.95 (dd, J = 12.1, 2.0 Hz, 1H), 6.92 – 6.86 (m, 1H), 6.86 – 6.81 (m, 3H), 5.09 (dd, J = 11.5, 6.4 Hz, 1H), 3.48 (dd, J = 17.5, 11.6 Hz, 1H), 2.69 (dd, J = 17.5, 6.4 Hz, 1H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.94, 150.94 (d, $^1J_{C\text{-}F}$ = 241.5 Hz),144.17, 143.96 (d, $^2J_{C\text{-}F}$ = 12.1 Hz), 133.71 (d, $^3J_{C\text{-}F}$ = 5.0 Hz), 128.45, 121.84 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 121.35, 118.17, 114.03, 113.52 (d, $^2J_{C\text{-}F}$ = 18.7 Hz), 62.40, 42.56, 33.42, 27.85.; MS (ESI): m/z = 347.37 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)-2-chlorophenol (4e). The title compound was prepared by demethylation of 3-(*tert*-butyl)-5-(3-chloro-4-methoxyphenyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazole (**3e**) using BBr_3 (3 equiv) according to the general procedure for ether dealkylation. The product was purified by CC (CH_2Cl_2/hexane 4:1); off-white solid; yield: 0.18 g (51%); mp 134-136^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 10.14 (s, 1H), 7.18 (d, J = 2.1 Hz, 1H), 7.15 – 7.11 (m, 2H), 6.96 (dt, J = 6.7, 3.4 Hz, 1H), 6.92 – 6.88 (m, 1H), 6.85 – 6.80 (m, 2H), 5.10 (dd, J = 11.5, 6.4 Hz, 1H), 3.48 (dd, J = 17.6, 11.6 Hz, 1H), 2.69 (dd, J = 17.6, 6.4 Hz, 1H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.99, 152.21, 144.12, 134.11, 128.48, 127.17, 125.36, 121.37, 119.74, 117.08, 114.03, 62.25, 42.58, 33.42, 27.85; MS (ESI): m/z = 362.65 $(M+H)^+$.

4-(1-(4-Chlorophenyl)-3-(2-hydroxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)benzene-1,2-diol (4g). The title compound was prepared by demethylation of 1-(4-chlorophenyl)-5-(3,4-

dimethoxyphenyl)-3-(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (**3g**) using BBr_3 (9 equiv) according to the general procedure for ether the dealkylation. The product was purified by CC (CH_2Cl_2/MeOH 99:1); beige solid; yield: 0.31 g (82%); mp163-164^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 10.20 (s, 1H), 8.74 (s, 1H), 8.67 (s, 1H), 7.21 (dd, J = 7.8, 1.5 Hz, 1H), 7.05 (dt, J = 16.9, 4.9 Hz, 1H), 7.02 – 6.98 (m, 2H), 6.75 (dd, J = 8.2, 0.8 Hz, 1H), 6.72 – 6.66 (m, 3H), 6.46 (d, J = 8.0 Hz, 1H), 6.42 – 6.33 (m, 2H), 5.04 (dd, J = 12.0, 6.3 Hz, 1H), 3.75 (dd, J = 17.8, 12.1 Hz, 1H), 3.01 (dd, J = 17.8, 6.3 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.17, 150.59, 145.72, 144.85, 142.48, 132.49, 130.50, 128.76, 128.16, 122.51, 119.56, 116.91, 116.58, 116.09, 115.87, 114.30, 112.69, 61.85, 44.08; MS (ESI): *m/z*= 380.74 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(2-hydroxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)-2-fluorophenol (4h). The title compound was prepared by demethylation of 1-(3-chlorophenyl)-5-(3-fluoro-4-methoxyphenyl)-3-(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (**3h**) using BBr_3 (6 equiv) according to the general procedure for the ether dealkylation. The product was purified by CC (CH_2Cl_2); beige solid; yield: 0.18 g (49%) ; mp165-167^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 10.32 (s, 1H), 9.89 (s, 1H), 7.48 (dd, J = 7.8, 1.6 Hz, 1H), 7.29 (ddd, J = 8.3, 7.3, 1.6 Hz, 1H), 7.21 (dd, J = 11.0, 5.3 Hz, 1H), 7.12 – 7.07 (m, 1H), 7.00 – 6.89 (m, 5H), 6.85 (ddd, J = 8.4, 2.2, 0.8 Hz, 1H), 6.79 (ddd, J = 7.9, 2.0, 0.8 Hz, 1H), 5.41 (dd, J = 12.0, 6.2 Hz, 1H), 4.01 (dd, J = 17.9, 12.0 Hz, 1H), 3.29 (dd, J = 17.8, 6.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.21, 151.01 (d, $^1J_{C\text{-}F}$ = 241.9 Hz), 150.98, 144.79, 144.28 (d, $^2J_{C\text{-}F}$ = 12.0 Hz), 133.62, 132.86 (d, $^3J_{C\text{-}F}$ = 5.0 Hz), 130.70 (d, $^3J_{C\text{-}F}$ = 6.3 Hz), 128.33,124, 122.05 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 119.55, 118.47, 118.30, 116.61, 116.18, 113.83 (d, $^2J_{C\text{-}F}$ = 18.8 Hz), 112.28, 111.47, 61.12, 44.12; MS (ESI): *m/z*= 382.67 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(2-hydroxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)-2,6-difluorophenol (4i). The title compound was prepared by deprotection of 1-(3-chlorophenyl)-5-(4-ethoxy-3,5-difluorophenyl)-3-(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole **(3i)** using BBr_3 (6 equiv) according to the general procedure for ether dealkylation. The product was purified by CC (CH_2Cl_2); off-white solid; yield: 0.30 g (77%); mp 179-181 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 10.28 (s, 1H), 10.24 (s, 1H), 7.48 (dd, J = 7.8, 1.6 Hz, 1H), 7.29 (ddt, J = 11.1, 5.4, 2.7 Hz, 1H), 7.24 – 7.19 (m, 1H), 7.00 – 6.96 (m, 4H), 6.92 (ddd, J = 7.8, 7.3, 1.2 Hz, 1H), 6.82 (dddd, J = 15.3, 7.9, 2.1, 0.8 Hz, 2H), 5.42 (dd, J = 12.0, 6.2 Hz, 1H), 4.02 (dd, J = 17.9, 12.0 Hz, 1H), 3.31 (dd, J = 17.9, 6.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.21, 152.40 (dd, $^1J_{C\text{-}F}$ = 243.0, $^3J_{C\text{-}F}$ =7.1 Hz), 150.99, 144.73, 133.68, 132.99 (t, $^2J_{C\text{-}F}$ = 16.1 Hz), 132.31 (t, $^3J_{C\text{-}F}$ = 6.9 Hz), 130.78, 130.74, 128.37, 119.53, 118.65, 116.60, 116.21, 112.36, 111.46, 109.47 (dd, $^2J_{C\text{-}F}$ = 16.1, $^4J_{C\text{-}F}$ = 6.4 Hz,), 60.89, 44.03; MS (ESI): m/z = 400.74 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(2-hydroxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)-2,3-difluorophenol (4j). The title compound was prepared by demethylation of 1-(3-chlorophenyl)-5-(2,3-difluoro-4-methoxyphenyl)-3-(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole **(3j)** using BBr_3 (6 equiv) according to the general procedure for ether dealkylation. The product was purified by CC (CH_2Cl_2); off-white solid; yield: 0.27 g (69%); mp 196-197 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 10.48 (s, 1H), 10.30 (s, 1H), 7.50 (d, J = 7.7 Hz, 1H), 7.29 (dd, J = 11.4, 4.0 Hz, 1H), 7.25 – 7.18 (m, 1H), 7.01 – 6.94 (m, 2H), 6.94 – 6.89 (m, 1H), 6.87 – 6.78 (m, 3H), 6.73 (t, J = 8.2 Hz, 1H), 5.61 (dd, J = 12.2, 5.5 Hz, 1H), 4.05 (dd, J = 17.8, 12.5 Hz, 1H), 3.40 (dd, J = 18.0, 5.5 Hz, 1H).; ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.17, 151.20, 148.50 (dd, $^1J_{C\text{-}F}$ = 245.8, $^2J_{C\text{-}F}$ = 10.8 Hz), 146.24, 144.51, 139.84 (dd, $^1J_{C\text{-}F}$ = 243.7, $^2J_{C\text{-}F}$ = 13.6 Hz), 133.72,

130.78, 128.35, 121.67, 119.55, 119.46, 119.38, 118.56, 116.51, 116.19, 113.11, 112.13, 111.22, 56.11, 42.83. ; MS (ESI): *m/z* = 400.81 $(M+H)^+$.

3-(*Tert*-butyl)-1-(4-chlorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (5a). The title compound was prepared by reaction of 4,4- dimethyl-1-(4-nitrophenyl)pent-1-en-3-one **(E26)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:2); orange solid; yield: 0.50 g (71%) ; mp 146-147 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.23 – 8.18 (m, 2H), 7.45 – 7.41 (m, 2H), 7.11 – 7.04 (m, 2H), 6.81 – 6.77 (m, 2H), 5.07 (dd, *J* = 11.9, 7.6 Hz, 1H), 3.53 (dd, *J* = 17.3, 11.9 Hz, 1H), 2.73 (dd, *J* = 17.3, 7.6 Hz, 1H), 1.22 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.23, 149.82, 147.43, 144.18, 128.82, 126.79, 124.50, 123.93, 114.32, 64.23, 42.96, 33.87, 28.17; MS (ESI): *m/z* = 357.75 (M^+).

3-(*Tert*-butyl)-1-(2,4-difluorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (5b). The title compound was prepared by reaction of 4,4-dimethyl-1-(4-nitrophenyl)pent-1-en-3-one **(E26)** and 2,4-difluorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:2); orange oil; yield: 0.34 g (48%); ^1H NMR (500 MHz, $CDCl_3$) δ 8.03 – 7.98 (m, 2H), 7.32 (tt, *J* = 8.9, 4.4 Hz, 1H), 7.26 – 7.20 (m, 2H), 6.64 (dddd, *J* = 9.1, 7.9, 2.8, 1.4 Hz, 1H), 6.56 – 6.49 (m, 1H), 5.26 (ddd, *J* = 11.3, 5.0, 3.3 Hz, 1H), 3.40 (dd, *J* = 17.1, 11.3 Hz, 1H), 2.76 (dd, *J* = 17.1, 5.0 Hz, 1H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.77, 157.40 (dd, $^1J_{C\text{-}F}$ = 242.7, $^3J_{C\text{-}F}$ =11.1 Hz), 151.26 (dd, $^1J_{C\text{-}F}$ = 246.9, $^3J_{C\text{-}F}$ =11.7 Hz), 149.24, 147.29, 130.66 (dd, $^2J_{C\text{-}F}$ = 9.7, $^4J_{C\text{-}F}$ = 3.4 Hz), 127.07, 123.92, 120.47 (dd, $^3J_{C\text{-}F}$ = 8.9, 4.6 Hz), 111.09 (dd, $^2J_{C\text{-}F}$ = 21.6, $^4J_{C\text{-}F}$ =3.4 Hz), 104.27 (dd, $^2J_{C\text{-}F}$ = 26.3, 24.2 Hz), 66.25, 42.48, 33.93, 28.13; MS (ESI): *m/z* = 359.83 $(M+H)^+$.

3-(*Tert*-butyl)-1-(3-chlorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (5c). The title compound was prepared by reaction of 4,4-dimethyl-1-(4-nitrophenyl)pent-1-en-3-one **(E26)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; orange solid; yield: 0.44 g (62%); MS (ESI): *m/z* = 357.92 $(M+H)^+$.

3-(*Tert*-butyl)-1-(4-chlorophenyl)-5-(3-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (5d). The title compound was prepared by reaction of 4,4-dimethyl-1-(3-nitrophenyl)pent-1-en-3-one **(E27)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:2); orange solid; yield: 0.40 g (57%) ; mp 115-116 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 – 8.15 (m, 1H), 8.13 (ddd, *J* = 8.0, 2.3, 1.2 Hz, 1H), 7.58 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.10 – 7.06 (m, 2H), 6.84 – 6.79 (m, 2H), 5.08 (dd, *J* = 11.8, 7.6 Hz, 1H), 3.54 (dd, *J* = 17.3, 11.8 Hz, 1H), 2.75 (dd, *J* = 17.3, 7.6 Hz, 1H), 1.23 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.28, 148.80, 144.76, 144.21, 131.92, 130.25, 128.80, 123.90, 122.70, 121.04, 114.37, 64.16, 43.07, 33.85, 28.16; MS (ESI): *m/z* = 357.80 $(M+H)^+$.

1-(3-Chlorophenyl)-3-cyclopropyl-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (5e). The title compound was prepared by reaction of 1-cyclopropyl-3-(4-nitrophenyl)prop-2-en-1-one **(E28)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; orange solid; yield: 0.35g (51%); MS (ESI): *m/z* = 341.63 $(M+H)^+$.

1-(3-Chlorophenyl)-3-(1-methylcyclopropyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (5f). The title compound was prepared by reaction of (*E*)-1-(1-methylcyclopropyl)-3-(4-

nitrophenyl)prop-2-en-1-one **(E29)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; orange solid; yield: 0.57 g (81%); MS (ESI): *m/z* = 355.75 $(M+H)^+$.

1-(4-Chlorophenyl)-3-cyclohexyl-5-(4-nitrophenyl)-4,5-dihydro-1H-pyrazole (5g). The title compound was prepared by reaction of (*E*)-1-cyclohexyl-3-(4-nitrophenyl)prop-2-en-1-one **(E30)** and 4-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The product was purified by CC (CH_2Cl_2/hexane 1:2); orange solid; yield: 0.49 g (64%); mp 112-113 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.22 – 8.16 (m, 2H), 7.45 – 7.39 (m, 2H), 7.10 – 7.05 (m, 2H), 6.80 – 6.74 (m, 2H), 5.05 (dd, *J* = 11.9, 7.5 Hz, 1H), 3.48 (ddd, *J* = 17.4, 12.0, 0.8 Hz, 1H), 2.69 (ddd, *J* = 17.4, 7.5, 0.8 Hz, 1H), 2.45 – 2.37 (m, 1H), 1.93 – 1.87 (m, 2H), 1.80 (dd, *J* = 9.0, 3.8 Hz, 2H), 1.73 – 1.67 (m, 1H), 1.41 – 1.28 (m, 4H), 1.28 – 1.17 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.25, 149.81, 147.38, 144.06, 128.82, 126.79, 124.48, 123.85, 114.22, 63.55, 44.17, 39.04, 30.57, 30.54, 25.91, 25.74; MS (ESI): *m/z* = 383.83 $(M+H)^+$.

1-(3-Chlorophenyl)-5-(4-nitrophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazole (5h). The title compound was prepared by reaction of 3-(4-nitrophenyl)-1-(thiophen-2-yl)prop-2-en-1-one **(E31)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; orange solid; yield: 0.44 g (58%); MS (ESI): *m/z* = 383.71 $(M+H)^+$.

1-(3-Chlorophenyl)-3-(furan-2-yl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (5i). The title compound was prepared by reaction of 1-(furan-2-yl)-3-(4-nitrophenyl)prop-2-en-1-one

(E32) and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; orange solid; yield: 0.44 g (61%); MS (ESI): *m/z* = 367.66 $(M+H)^+$.

3-(2-Chlorophenyl)-1-(3-chlorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (5j). The title compound was prepared by reaction of 1-(2-chlorophenyl)-3-(4-nitrophenyl)prop-2-en-1-one **(E33)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; orange solid; yield: 0.42 g (51%); MS (ESI): *m/z* = 411.73 $(M+H)^+$.

1-(3-Chlorophenyl)-5-(4-nitrophenyl)-3-(2-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-pyrazole (5k). The title compound was prepared by reaction of (*E*)-3-(4-nitrophenyl)-1-(2-(trifluoromethyl)phenyl)prop-2-en-1-one **(E34)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; orange solid; yield: 0.47 g (53%) ; MS (ESI): *m/z* = 445.67 $(M+H)^+$.

1-(3-Chlorophenyl)-5-(4-nitrophenyl)-3-(*o*-tolyl)-4,5-dihydro-1*H*-pyrazole (5l). The title compound was prepared by reaction of (*E*)-3-(4-nitrophenyl)-1-(*o*-tolyl)prop-2-en-1-one **(E35)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; orange solid; yield: 0.37 g (47.5%); MS (ESI): *m/z* = 391.87 $(M+H)^+$.

1-(3-Chlorophenyl)-3-(2-methoxyphenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (5m). The title compound was prepared by reaction of 1-(2-methoxyphenyl)-3-(4-nitrophenyl)prop-2-en-1-one **(E36)** and 3-chlorophenylhydrazine hydrochloride according to the

general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; orange solid; yield: 0.34 g (42%); MS (ESI): *m/z* = 408.02 $(M+H)^+$.

3-(Benzo[d][1,3]dioxol-5-yl)-1-(3-chlorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (5n). The title compound was prepared by reaction of 1-(benzo[d][1,3]dioxol-5-yl)-3-(4-nitrophenyl)prop-2-en-1-one **(E37)** and 3-chlorophenylhydrazine hydrochloride according to the general procedure for pyrazoline synthesis. The residue obtained after solvent removal was used for the next step without further purification; yield: orange solid; 0.51 g (61%); MS (ESI): *m/z* = 421.71 $(M+H)^+$.

General reduction procedure. A suspension of the nitro derivative (1 mmol) and $SnCl_2 \cdot 2H_2O$ (5 mmol, 1.12 g) in MeOH (40 mL) was heated to reflux for 2 h under argon atmosphere. ThenMeOH was evaporated under reduced pressure and the residue was dissolved in EtOAc (100 mL) and alkalinized with 100 mL aqueous $NaHCO_3$ solution. The resulting mixture was filtered under vacuum followed by separation of organic and water layers. The aqueous layer was extracted with two 20 mL-portions of EtOAc, the organic fractions were combined, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified using column chromatography.

4-(3-(*Tert*-butyl)-1-(4-chlorophenyl)-4,5-dihydro-*1H*-pyrazol-5-yl)aniline (6a). The title compound was prepared by reduction of 3-(*tert*-butyl)-1-(4-chlorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); buff solid; yield: 0.28 g (87%); mp131-132^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 7.13 – 7.07 (m, 2H), 6.89 – 6.85 (m, 2H), 6.85 – 6.80 (m, 2H), 6.51 – 6.46 (m, 2H), 5.00 (s, 2H), 4.95 (dd, *J* = 11.5, 6.5 Hz, 1H), 3.44 (dd, *J* = 17.5, 11.6 Hz, 1H), 2.64 (dd, *J* = 17.5, 6.6 Hz, 1H),

1.17 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.73, 147.86, 144.42, 129.27, 128.28, 126.43, 120.94, 114.14, 113.97, 63.16, 42.73, 33.42, 27.90 ; MS (ESI): *m/z*= 327.77 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(2,4-difluorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6b). The title compound was prepared by reduction of 3-(*tert*-butyl)-1-(2,4-difluorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole **(5b)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); buff solid; yield: 0.24 g (75%); mp 139-140 ^oC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.28 (td, J = 9.3, 6.2 Hz, 1H), 6.98 (ddd, J = 12.1, 9.0, 2.9 Hz, 1H), 6.84 (tdd, J = 9.2, 2.9, 1.2 Hz, 1H), 6.78 – 6.73 (m, 2H), 6.38 – 6.33 (m, 2H), 5.10 – 5.04 (m, 1H), 4.93 (s, 2H), 3.37 – 3.30 (m, 1H), 2.79 (dd, J = 17.1, 4.7 Hz, 1H), 1.20 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.98, 156.17 (dd, $^1J_{C\text{-}F}$ = 239.0, $^3J_{C\text{-}F}$ = 11.2 Hz), 150.99 (dd, $^1J_{C\text{-}F}$ = 246.7, $^3J_{C\text{-}F}$ = 12.0 Hz), 147.88, 131.45 (dd, $^2J_{C\text{-}F}$ = 9.8, $^4J_{C\text{-}F}$ = 3.1 Hz), 128.28, 126.90, 120.26 (dd, $^3J_{C\text{-}F}$ = 9.1, 5.0 Hz), 113.60, 110.62 (dd, $^2J_{C\text{-}F}$ = 21.4, $^4J_{C\text{-}F}$ = 3.2 Hz), 103.94 (dd, $^2J_{C\text{-}F}$ = 26.4, 24.5 Hz), 65.95, 41.67, 33.53, 27.87.; MS (ESI): *m/z* = 329.89 $(M+H)^+$.

4-(3-(*Tert*-butyl)-1-(3-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6c) . The title compound was prepared by reduction of 3-(*tert*-butyl)-1-(3-chlorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole according to the general reduction procedure **(5c)**. The product was purified by CC (CH_2Cl_2); tan solid; yield: 0.20g (62%); mp 136.4 ^oC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.09 – 7.03 (m, 1H), 6.89 – 6.85 (m, 3H), 6.72 (ddd, J = 8.4, 2.2, 0.9 Hz, 1H), 6.61 (ddd, J = 7.9, 2.1, 0.9 Hz, 1H), 6.52 – 6.47 (m, 2H), 5.02 – 4.97 (m, 3H), 3.45 (dd, J = 17.6, 11.6 Hz, 1H), 2.65 (dd, J = 17.6, 6.2 Hz, 1H), 1.18 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.30, 147.90, 146.64, 133.22, 130.12, 129.18, 126.40, 116.71, 114.17, 111.81, 110.94, 62.85, 42.68, , 33.46, 27.88.; MS (ESI): *m/z* = 328.06 $(M+H)^+$.

3-(3-(*Tert*-butyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6d). The title compound was prepared by reduction of 3-(*tert*-butyl)-1-(4-chlorophenyl)-5-(3-nitrophenyl)-4,5-dihydro-1*H*-pyrazole **(5d)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); yellow solid; yield: 0.24 g (74%); mp 104-106 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 7.15 – 7.09 (m, 2H), 6.99 – 6.92 (m, 1H), 6.84 – 6.78 (m, 2H), 6.44 – 6.36 (m, 3H), 5.08 (s, 2H), 4.92 (dd, *J* = 11.8, 7.2 Hz, 1H), 3.50 (dd, *J* = 17.6, 11.8 Hz, 1H), 2.66 (dd, *J* = 17.6, 7.2 Hz, 1H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.79, 149.26, 144.49, 143.42, 128.38, 125.11, 121.11, 115.82, 113.82, 112.99, 110.33, 63.71, 42.78, 33.42, 27.93; MS (ESI): *m/z* = 327.87 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-cyclopropyl-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6e). The title compound was prepared by reduction of 1-(3-chlorophenyl)-3-cyclopropyl-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole **(5e)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); beige solid; yield: 0.24 g (77%) ; mp 90.5-92.5 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 7.08 – 7.02 (m, 1H), 6.89 – 6.83 (m, 3H), 6.69 (ddd, *J* = 8.4, 2.2, 0.9 Hz, 1H), 6.61 (ddd, *J* = 7.9, 2.1, 0.9 Hz, 1H), 6.52 – 6.47 (m, 2H), 5.02 (s, 2H), 4.95 (dd, *J* = 11.6, 6.5 Hz, 1H), 3.27 (dd, *J* = 17.6, 11.6 Hz, 1H), 2.43 (dd, *J* = 17.5, 6.5 Hz, 1H), 1.84 (tt, *J* = 8.3, 5.0 Hz, 1H), 0.87 – 0.81 (m, 2H), 0.81 – 0.69 (m, 2H).^{13}C NMR (125 MHz, DMSO-d_6) δ 155.22, 147.92, 146.49, 133.24, 130.12, 129.01, 126.45, 116.60, 114.16, 111.72, 110.80, 62.36, 43.16, 11.28, 5.84, 5.53; MS (ESI): *m/z* = 311.91 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(1-methylcyclopropyl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6f). The title compound was prepared by reduction of 1-(3-chlorophenyl)-3-(1-methylcyclopropyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole **(5f)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); beige solid; yield: 0.27g (83%); mp 106.2 ^oC; ^1H NMR

(500 MHz, DMSO-d_6) δ 7.09 – 7.03 (m, 1H), 6.89 – 6.84 (m, 3H), 6.71 (ddd, *J* = 8.4, 2.2, 0.9 Hz, 1H), 6.61 (ddd, *J* = 7.9, 2.1, 0.9 Hz, 1H), 6.52 – 6.46 (m, 2H), 5.02 (s, 2H), 4.96 (dd, *J* = 11.5, 6.6 Hz, 1H), 3.27 (dd, *J* = 17.4, 11.5 Hz, 1H), 2.43 (dd, *J* = 17.4, 6.7 Hz, 1H), 1.35 (s, 3H), 0.98 – 0.88 (m, 2H), 0.71 – 0.64 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.32, 147.93, 146.63, 133.22, 130.11, 129.05, 126.44, 116.64, 114.17, 111.76, 110.87, 63.03, 42.94, 21.18, 16.90, 13.71, 13.48; MS (ESI): *m/z* = 325.91 $(M+H)^+$.

4-(1-(4-Chlorophenyl)-3-cyclohexyl-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6g). The title compound was prepared by reduction of 1-(4-chlorophenyl)-3-cyclohexyl-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole **(5g)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); tan solid; yield: 0.31 g (88%); mp 145-146 ^oC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.12 – 7.06 (m, 2H), 6.89 – 6.84 (m, 2H), 6.84 – 6.78 (m, 2H), 6.51 – 6.46 (m, 2H), 5.00 (s, 2H), 4.92 (dd, *J* = 11.6, 6.6 Hz, 1H), 3.44 – 3.34 (m, 1H), 2.59 (dd, *J* = 17.8, 6.4 Hz, 1H), 2.39 – 2.31 (m, 1H), 1.82 (dd, *J* = 16.1, 8.5 Hz, 2H), 1.73 (dt, *J* = 7.0, 4.8 Hz, 2H), 1.63 (d, *J* = 12.4 Hz, 1H), 1.40 – 1.13 (m, 5H); MS (ESI): *m/z* = 353.80 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6h). The title compound was prepared by reduction of 1-(3-chlorophenyl)-5-(4-nitrophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazole **(5h)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); greenish yellow solid; yield: 0.19 g (53%); mp 154.4 ^oC;^{1}H NMR (500 MHz, DMSO-d_6) δ 7.62 (dt, *J* = 5.1, 2.3 Hz, 1H), 7.28 (dd, *J* = 3.6, 1.1 Hz, 1H), 7.28 (dd, *J* = 3.6, 1.1 Hz, 1H), 7.11 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.96 (t, *J* = 2.1 Hz, 1H), 6.94 – 6.90 (m, 2H), 6.84 (ddd, *J* = 8.4, 2.2, 0.9 Hz, 1H), 6.72 – 6.68 (m, 1H), 6.53 – 6.48 (m, 2H), 5.29 (dd, *J* = 11.9, 6.0 Hz, 1H), 5.06 (s, 2H), 3.85 (dd, *J* = 17.3, 12.0 Hz, 1H), 3.08 (dd, *J* = 17.3, 6.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.15, 145.27, 144.91, 135.48, 133.38, 130.34, 130.03, 128.41,

127.84, 127.72, 126.53, 117.65, 114.19, 112.20, 111.41, 62.93, 43.88; MS (ESI): *m/z* = 353.74 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(furan-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6i). The title compound was prepared by reduction of 1-(3-chlorophenyl)-3-(furan-2-yl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole **(5i)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); tan solid; yield: 0.22g (64%) ; mp 115.2-116.9 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 7.82 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.15 – 7.09 (m, 1H), 6.99 (t, *J* = 2.1 Hz, 1H), 6.92 – 6.88 (m, 2H), 6.84 (ddd, *J* = 8.4, 2.2, 0.9 Hz, 1H), 6.81 (dd, *J* = 3.4, 0.7 Hz, 1H), 6.70 (ddd, *J* = 7.9, 2.1, 0.9 Hz, 1H), 6.61 (ddd, *J* = 7.5, 3.4, 1.8 Hz, 1H), 6.52 – 6.47 (m, 2H), 5.27 (dd, *J* = 11.9, 5.8 Hz, 1H), 5.06 (s, 2H), 3.77 (dd, *J* = 17.3, 12.0 Hz, 1H), 2.98 (dd, *J* = 17.3, 5.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.14, 147.30, 145.35, 144.41, 140.46, 133.39, 130.32, 128.27, 126.51, 117.66, 114.18, 112.30, 112.00, 111.41, 111.21, 62.26, 43.03; MS (ESI): *m/z* = 337.85 $(M+H)^+$.

4-(3-(2-Chlorophenyl)-1-(3-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6j). The title compound was prepared by reduction of 3-(2-chlorophenyl)-1-(3-chlorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole **(5j)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2/hexane 4:1); yellow solid; yield: 0.20 g (52%); mp. 170-171 ^oC); ^1H NMR (500 MHz, DMSO-d_6) δ 7.77 – 7.74 (m, 1H), 7.39 (ddd, *J* = 5.4, 2.9, 1.7 Hz, 2H), 7.22 – 7.19 (m, 1H), 7.17 – 7.12 (m, 2H), 7.03 (t, *J* = 2.1 Hz, 1H), 6.88 (ddd, *J* = 8.4, 2.2, 0.8 Hz, 1H), 6.73 (ddd, *J* = 7.9, 2.0, 0.9 Hz, 1H), 6.56 – 6.50 (m, 2H), 6.29 (t, *J* = 5.9 Hz, 1H), 5.33 (dd, *J* = 12.0, 5.9 Hz, 1H), 4.21 (s, Hz, 2H), 3.96 (dd, *J* = 17.6, 12.0 Hz, 1H), 3.18 (dd, *J* = 17.5, 5.9 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.16, 146.86, 145.30, 140.11, 133.41,

131.00, 130.84, 130.72,130.25, 130.00, 128.24, 127.33, 127.19, 126.61, 118.08, 112.51, 111.60, 62.76, 46.44; MS (ESI): *m/z* = 381.72 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(2-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6k). The title compound was prepared by reduction of 1-(3-chlorophenyl)-5-(4-nitrophenyl)-3-(2-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-pyrazole **(5k)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2/hexane 4:1); tan solid; yield: 0.083 (20%); mp 159-160 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 7.87 (d, *J* = 7.8 Hz, 1H), 7.74 – 7.69 (m, 2H), 7.63 – 7.57 (m, 1H), 7.15 (dd, *J* = 10.6, 5.7 Hz, 1H), 7.02 – 6.99 (m, 1H), 6.97 – 6.92 (m, 2H), 6.86 (ddd, *J* = 8.4, 2.2, 0.8 Hz, 1H), 6.73 (ddd, *J* = 7.9, 2.0, 0.8 Hz, 1H), 6.54 – 6.49 (m, 2H), 5.34 (dd, *J* = 12.1, 6.0 Hz, 1H), 5.09 (s, 2H), 3.93 (dd, *J* = 17.5, 12.1 Hz, 1H), 3.08 (dd, *J* = 17.5, 6.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.18, 146.15, 145.35, 133.39, 132.56, 131.31, 130.37, 128.97, 128.33, 127.04, 126.57, 126.53 , 125.97 (q, $^2J_{C-F}$ = 30.8 Hz), 124.10 (q, $^1J_{C-F}$ = 273.3 Hz), 118.10, 114.19, 112.48, 111.47, 62.81, 45.70; MS (ESI): *m/z* = 415.78 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(*o*-tolyl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6l). The title compound was prepared by reduction of 1 1-(3-chlorophenyl)-5-(4-nitrophenyl)-3-(*o*-tolyl)-4,5-dihydro-1*H*-pyrazole **(5l)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); brown solid; yield: 0.21 g (59%); mp 122.2 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 7.45 – 7.41 (m, 1H), 7.34 – 7.31 (m, 1H), 7.30 – 7.23 (m, 2H), 7.18 – 7.13 (m, 1H), 6.98 (t, *J* = 2.1 Hz, 1H), 6.96 – 6.92 (m, 2H), 6.89 (ddd, *J* = 8.4, 2.2, 0.9 Hz, 1H), 6.74 – 6.68 (m, 1H), 6.54 – 6.48 (m, 2H), 5.24 (dd, *J* = 11.9, 5.9 Hz, 1H), 5.06 (s, 2H), 3.92 (dd, *J* = 17.3, 12.0 Hz, 1H), 3.13 (dd, *J* = 17.3, 6.0 Hz, 1H), 2.68 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6)δ 149.35, 148.07, 145.62, 136.48, 133.39, 131.45, 130.66, 130.35, 128.75, 128.51, 128.18, 126.59, 126.00, 117.56, 114.21, 112.20, 111.42, 61.87, 45.24, 23.42 ; MS (ESI): *m/z* = 361.77 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(2-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6m). The title compound was prepared by reduction of 1-(3-chlorophenyl)-3-(2-methoxyphenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole **(5m)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); tan solid; yield: 0.25 g (66%); mp 122.9 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 7.89 (dd, J = 7.8, 1.7 Hz, 1H), 7.37 (ddd, J = 8.4, 7.3, 1.8 Hz, 1H), 7.14 – 7.10 (m, 1H), 7.08 (dd, J = 8.4, 1.0 Hz, 1H), 7.03 – 6.99 (m, 2H), 6.95 – 6.90 (m, 2H), 6.86 (ddd, J = 8.4, 2.2, 0.9 Hz, 1H), 6.71 – 6.67 (m, 1H), 6.53 – 6.48 (m, 2H), 5.21 (dd, J = 12.0, 6.1 Hz, 1H), 5.04 (s, 2H), 3.94 – 3.86 (m, 1H), 3.79 (s, 3H), 3.15 (dd, J = 18.1, 6.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.35, 148.02, 147.82, 145.68, 133.37, 130.44, 130.26, 128.95, 128.22, 126.48, 121.06, 120.67, 117.41, 114.20, 112.30, 112.24, 111.33, 62.78, 55.60, 46.52; MS (ESI): m/z = 377.72 $(M+H)^+$.

4-(3-(Benzo[d][1,3]dioxol-5-yl)-1-(3-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)aniline (6n). The title compound was prepared by reduction of 3-(benzo[d][1,3]dioxol-5-yl)-1-(3-chlorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole **(5n)** according to the general reduction procedure. The product was purified by CC (CH_2Cl_2); brown solid; yield: 0.34 g (87%); mp 140.4 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 7.40 – 7.38 (m, 1H), 7.17 (dd, J = 8.1, 1.7 Hz, 1H), 7.13 – 7.09 (m, 1H), 7.03 (t, J = 2.1 Hz, 1H), 6.97 – 6.94 (m, 1H), 6.93 – 6.89 (m, 2H), 6.87 (ddd, J = 8.4, 2.2, 0.9 Hz, 1H), 6.68 (ddd, J = 7.9, 2.1, 0.9 Hz, 1H), 6.53 – 6.47 (m, 2H), 6.07 (s, 2H), 5.24 (dd, J = 12.0, 6.1 Hz, 1H), 5.04 (s, 2H), 3.78 (dd, J = 17.5, 12.0 Hz, 1H), 3.02 (dd, J = 17.5, 6.1 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.41, 148.09, 148.07, 147.71, 145.61, 133.38, 130.23, 128.77, 126.54, 126.43, 120.62, 117.37, 114.18, 112.19, 111.30, 108.31, 105.42, 101.32, 62.85, 43.36; MS (ESI): m/z = 391.68 $(M+H)^+$.

***N*-(4-(3-(*Tert*-butyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenyl)acetamide (7a).** Acetylchloride (0.14 mL, 2 mmol) was added gradually to a stirred solution of **6a** (0.33 g, 1 mmol) and Na_2CO_3 (0.16 g, 1.5 mmol) in acetone (40 mL) under ice cooling. The mixture was stirred at room temperature under a nitrogen atmosphere for 2h. After pouring to 100 mL of water ice mixture, the solid obtained was separated by filtration followed by CC purification (CH_2Cl_2/MeOH 98:2) to give the title compound as an off-white solid; yield: 0.30 g (81%), mp119-120°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.91 (s, 1H), 7.53 – 7.49 (m, 2H), 7.17 – 7.07 (m, 4H), 6.83 – 6.79 (m, 2H), 5.11 (dd, J = 11.6, 6.6 Hz, 1H), 3.51 (dd, J = 17.5, 11.7 Hz, 1H), 2.68 (dd, J = 17.5, 6.6 Hz, 1H), 2.01 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 168.16, 159.85, 144.25, 138.42, 136.88, 128.41, 126.10, 121.24, 119.50, 113.98, 62.92, 42.64, 33.43, 27.87, 20.73; MS (ESI): m/z= 369.75 $(M+H)^+$.

4-(1-(3-Chlorophenyl)-3-(2-hydroxyphenyl)-4-methyl-4,5-dihydro-1*H*-pyrazol-5-yl)-2-fluorophenol (9). The title compound was prepared by demethylation of 1-(3-chlorophenyl)-5-(3-fluoro-4-methoxyphenyl)-3-(2-methoxyphenyl)-4-methyl-4,5-dihydro-1*H*-pyrazole **(8)** using BBr_3 (6 equiv) according to the general procedure for ether dealkylation. The product was purified by CC (CH_2Cl_2); beige solid; yield: 0.27 g (69%); mp 160.1-161.4 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.30 (s, 1H), 9.87 (s, 1H), 7.56 (ddd, J = 6.1, 4.5, 1.6 Hz, 1H), 7.31 – 7.24 (m, 1H), 7.20 (dd, J = 12.7, 4.6 Hz, 1H), 7.04 (dd, J = 12.0, 2.1 Hz, 1H), 6.99 – 6.96 (m, 2H), 6.93 – 6.90 (m, 1H), 6.90 – 6.85 (m, 2H), 6.84 – 6.80 (m, 1H), 6.78 (ddd, J = 7.9, 2.0, 0.8 Hz, 1H), 5.11 (d, J = 3.5 Hz, 1H), 3.71 (qd, J = 7.1, 3.5 Hz, 1H), 1.35 (d, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.26, 154.88, 150.94 (d, $^1J_{C\text{-}F}$ = 241.8 Hz), 144.47, 144.30 (d, $^2J_{C\text{-}F}$ = 12.1 Hz), 133.70, 131.68 (d, $^3J_{C\text{-}F}$ = 5.0 Hz), 130.71, 130, 128.40, 121.68 (d, $^4J_{C\text{-}F}$ = 2.9 Hz),

119.59, 118.31, 118.27, 116.47, 115.96, 113.63 (d, $^{2}J_{C\text{-}F}$ = 18.8 Hz), 112.15, 111.35, 68.33, 50.92, 18.63 ; MS (ESI): *m/z* = 396.74 $(M+H)^{+}$.

3-(*Tert*-butyl)-5-(3-chloro-4-methoxyphenyl)-1-(4-chlorophenyl)-1*H*-pyrazole (10). A mixture of 0.37 g (1 mmol) of 3-(*tert*-butyl)-5-(3-chloro-4-methoxyphenyl)-1-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazole (**3e**) and 0.34 g (1.5 mmol) of dichlorodicyanoquinone in 10 mL of benzene was heated to reflux for 5h. The mixture was cooled to room temperature and filtered through a plug of silica gel wetted with diethyl ether. The filtrate was concentrated *in vacuo* and the residue was purified by CC (CH_2Cl_2/hexane 1:3) to give the title compound as a white solid (95%, 0.35 g), mp 182-183 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.31 (m, 1H), 7.30 – 7.21 (m, 4H), 6.97 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.84 – 6.81 (m, 1H), 6.31 (s, 1H), 3.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.89, 154.85, 141.56, 138.68, 132.57, 130.38, 129.00, 128.17, 126.19, 124.11, 122.55, 111.77, 104.97, 56.14, 32.23, 30.46; MS (ESI): *m/z* = 374.67 $(M+H)^{+}$.

4-(3-(*Tert*-butyl)-1-(4-chlorophenyl)-1*H*-pyrazol-5-yl)-2-chlorophenol (11). The title compound was prepared by demethylation of 3-(*tert*-butyl)-5-(3-chloro-4-methoxyphenyl)-1-(4-chlorophenyl)-1*H*-pyrazole **(10)** using BBr_3 (3 equiv) according to the general procedure for ether dealkylation. The product was purified by CC (CH_2Cl_2); off-white solid; yield: 0.18 g (50%); mp 176.5-177.5 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.49 (s, 1H), 7.47 – 7.43 (m, 2H), 7.28 – 7.24 (m, 3H), 6.94 – 6.89 (m, 2H), 6.53 (s, 1H), 1.31 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.85, 153.16, 141.69, 138.68, 131.28, 129.72, 128.90, 128.29, 126.36, 122.04, 119.75, 116.60, 104.90, 31.89, 30.23. ; MS (ESI): *m/z* = 360.77 $(M+H)^{+}$.

(*E*)-3-(4-(*Tert*-butoxy)phenyl)-1-phenylprop-2-en-1-one (E2). Synthesized according to the general procedure for enone synthesis using acetophenone and 4-(*tert*-butoxy)benzaldehyde; yellow solid; yield: 2.46 g (88 %); mp 117.5-119 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.18 –

8.08 (m, 2H), 7.85 – 7.79 (m, 3H), 7.72 (d, *J* = 15.6 Hz, 1H), 7.69 – 7.63 (m, 1H), 7.60 – 7.54 (m, 2H), 7.08 – 7.02 (m, 2H), 1.35 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.07, 157.72, 143.77, 137.73, 132.96, 130.11, 129.16, 128.73, 128.41, 123.02, 120.45, 78.89, 28.53.

(*E*)-3-(4-(*Tert*-butoxy)phenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (E3). Synthesized according to the general procedure for enone synthesis using 1-(2-hydroxyphenyl)ethanone and 4-(*tert*-butoxy)benzaldehyde, the product was precipitated after neutralization with 2M HCl; yellow solid; yield: 2.57 g (87 %); mp 137-138 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.35 (s, 1H), 7.89 – 7.84 (m, 1H), 7.76 (d, *J* = 15.9 Hz, 1H), 7.73 – 7.69 (m, 2H), 7.68 (d, *J* = 11.3 Hz, 1H), 7.66 – 7.61 (m, 3H), 6.92 (td, *J* = 7.5, 0.8 Hz, 1H), 6.86 (t, *J* = 7.4 Hz, 1H), 1.39 (s, 9H).

(*E*)-3-(4-(*Tert*-butoxy)phenyl)-1-(2-methoxyphenyl)prop-2-en-1-one (E4). Synthesized according to the general procedure for enone synthesis using 1-(2-methoxyphenyl)ethanone and 4-(*tert*-butoxy)benzaldehyde; yellow oil; yield: 2.51g (81 %); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 8.7, 7.0 Hz, 2H), 7.54 – 7.45 (m, 3H), 7.31 – 7.23 (m, 1H), 7.08 – 6.96 (m, 4H), 3.90 (s,3H), 1.40 (s, 9H).

(*E*)-3-(4-(*Tert*-butoxy)phenyl)-1-(2-ethoxyphenyl)prop-2-en-1-one (E5). Synthesized according to the general procedure for enone synthesis using 1-(2-ethoxyphenyl)ethanone and 4-(*tert*-butoxy)benzaldehyde; yellow oil; yield: 2.65 g (82%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.60 (d, *J* = 15.9 Hz, 1H), 7.51 – 7.47 (m, 2H), 7.44 – 7.40 (m, 1H), 7.38 (d, *J* = 15.9 Hz, 1H), 7.02 – 6.98 (m, 3H), 6.97 – 6.93 (m, 1H), 4.11 (q, *J* = 7.0 Hz, 2H), 1.41 (t, *J* = 7.0 Hz, 3H), 1.38 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.66, 157.66, 157.48, 142.37, 132.66, 130.32, 129.87, 129.46, 129.12, 125.79, 123.58, 120.55, 112.56, 79.13, 64.14, 28.80, 14.74

(*E*)-3-(4-(*Tert*-butoxy)phenyl)-1-(2-chlorophenyl)prop-2-en-1-one (E6). Synthesized according to the general procedure for enone synthesis using 1-(2-chlorophenyl)ethanone and 4-(*tert*-butoxy)benzaldehyde; yellow oil; yield: 2.85 g (91 %); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.58 (d, *J* = 15.9 Hz, 1H), 7.53 – 7.49 (m, 2H), 7.49 – 7.47 (m, 1H), 7.47 – 7.44 (m, 1H), 7.39 – 7.35 (m, 2H), 7.03 (td, *J* = 7.5, 0.9 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 1.36 (s, 9H).

(*E*)-3-(4-(*Tert*-butoxy)phenyl)-1-(thiophen-2-yl)prop-2-en-1-one (E7). Synthesized according to the general procedure for enone synthesis using 1-(thiophen-2-yl)ethanone and 4-(*tert*-butoxy)benzaldehyde; yellowish white solid ; yield: 2.57 g (90 %); mp 128.1 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.30 (dd, *J* = 3.8, 1.1 Hz, 1H), 8.04 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.83 – 7.79 (m, 2H), 7.77 (d, *J* = 15.6 Hz, 1H), 7.70 (d, *J* = 15.6 Hz, 1H), 7.31 (dt, *J* = 10.0, 5.0 Hz, 1H), 7.08 – 7.02 (m, 2H), 1.35 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 181.53, 157.75, 145.66, 142.86, 135.27, 133.36, 130.12, 128.99, 128.85, 122.99, 120.28, 78.91, 28.53.

(*E*)-3-(4-(*Tert*-butoxy)phenyl)-1-(pyridin-2-yl)prop-2-en-1-one (E8). Synthesized according to the general procedure for enone synthesis using 1-(pyridin-2-yl)ethanone and 4-(*tert*-butoxy)benzaldehyde; greenish yellow solid; yield: 2.56 g (91 %); mp 117.1-118.5 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.79 (ddd, *J* = 4.7, 1.7, 0.9 Hz, 1H), 8.17 (d, *J* = 16.1 Hz, 1H), 8.11 – 8.09 (m, 1H), 8.07 – 8.03 (m, 1H), 7.85 – 7.81 (m, 1H), 7.76 – 7.73 (m, 2H), 7.69 (ddd, *J* = 7.5, 4.7, 1.4 Hz, 1H), 7.08 – 7.03 (m, 2H), 1.35 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 188.52, 157.95, 153.55, 149.13, 143.79, 137.69, 129.98, 129.01, 127.50, 123.04, 122.38, 119.12, 78.95, 28.52.

(*E*)-3-(4-(*Tert*-butoxy)phenyl)-1-(1*H*-pyrrol-2-yl)prop-2-en-1-one (E9). Synthesized according to the general procedure for enone synthesis using 1-(1*H*-pyrrol-2-yl)ethanone and 4-(*tert*-butoxy)benzaldehyde; yellowish white solid; yield: 2.26 g (84 %); mp 116.5-118.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.92 (s, 1H), 7.81 (d, *J* = 15.6 Hz, 1H), 7.58 – 7.54 (m, 2H), 7.27 (d, *J* = 15.7 Hz, 1H), 7.11 (td, *J* = 2.7, 1.3 Hz, 1H), 7.07 (ddd, *J* = 3.7, 2.3, 1.3 Hz, 1H), 7.05 – 7.00 (m, 2H), 6.35 (dt, *J* = 3.8, 2.5 Hz, 1H), 1.40 (s, 9H);^{13}C NMR (125 MHz, $CDCl_3$) δ 178.97, 157.75, 141.95, 133.24, 129.81, 129.25, 125.14, 123.76, 120.49, 116.03, 110.88, 79.31, 28.89.

(*E*)-1-(4-Aminophenyl)-3-(4-(*tert*-butoxy)phenyl)prop-2-en-1-one (E10). Synthesized according to the general procedure for enone synthesis using 1-(4-aminophenyl)ethanone and 4-(*tert*-butoxy)benzaldehyde; yellow solid; yield: 2.30 g (78 %); mp 113.7-115.5 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.90 (d, *J* = 8.6 Hz, 2H), 7.77 – 7.69 (m, 3H), 7.57 (d, *J* = 15.5 Hz, 1H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.61 (d, *J* = 8.2 Hz, 2H), 6.09 (s, 2H), 1.35 (s, 9H).

***(E)*-1-(3-Methoxyphenyl)-4,4-dimethylpent-1-en-3-one (E11).** Synthesized according to the general procedure for enone synthesis using pinacolone and 3-methoxybenzaldehyde; yellow oil; yield: 1.87 g (86 %); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 15.6 Hz, 1H), 7.33 – 7.24 (m, 1H), 7.19 – 7.14 (m, 1H), 7.08 (dd, *J* = 5.3, 2.6 Hz, 2H), 6.92 (dt, *J* = 7.2, 3.6 Hz, 1H), 3.83 (s, 3H), 1.23 (s, 9H).

1-(4-Methoxyphenyl)-4,4-dimethylpent-1-en-3-one (E12). Synthesized according to general procedure for enone synthesis using pinacolone and 4-methoxybenzaldehyde; yellow oil; yield: 1.97 g (90.5 %).[1]

1-(4-Chlorophenyl)-4,4-dimethylpent-1-en-3-one (E13). Synthesized according to the general procedure for enone synthesis pinacolone and 4-chlorobenzaldehyde; white solid; yield: 2.11 g (95 %); mp 85-87 °C.[2]

(*E*)-1-(3-Fluoro-4-methoxyphenyl)-4,4-dimethylpent-1-en-3-one (E14). Synthesized according to the general procedure for enone synthesis using pinacolone and 3-fluoro-4-methoxybenzaldehyde; yellowish white solid; yield: 2.22 g (94 %); mp 84.6 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.80 (dd, J = 12.9, 2.1 Hz, 1H), 7.52 (dd, J = 5.5, 4.3 Hz, 1H), 7.48 (d, J = 15.6 Hz, 1H), 7.35 (d, J = 15.6 Hz, 1H), 7.21 – 7.16 (m, 1H), 3.88 (s, 3H), 1.15 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 203.24, 151.53 (d, $^{1}J_{C\text{-}F}$ = 244.2 Hz), 148.83 (d, $^{2}J_{C\text{-}F}$ = 10.9 Hz), 140.80, 127.86 (d, $^{3}J_{C\text{-}F}$ = 6.8 Hz), 126.67 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz), 120.49, 114.79 (d, $^{2}J_{C\text{-}F}$ = 18.4 Hz), 113.66, 56.09, 42.76, 25.76.

(*E*)-1-(3-Chloro-4-methoxyphenyl)-4,4-dimethylpent-1-en-3-one (E15). Synthesized according to the general procedure for enone synthesis using pinacolone and 3-chloro-4-methoxybenzaldehyde; white solid; yield: 2.24 g (89 %); mp 75.2-77.1 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.00 (d, J = 2.1 Hz, 1H), 7.70 (dd, J = 8.7, 2.1 Hz, 1H), 7.47 (d, J = 15.6 Hz, 1H), 7.38 (d, J = 15.6 Hz, 1H), 7.19 – 7.15 (m, 1H), 3.90 (s, 3H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 203.27, 155.89, 140.44, 129.73, 129.26, 128.27, 121.69, 120.52, 112.77, 56.30, 42.77, 25.76.

(*E*)-1-(4-Fluoro-3-methoxyphenyl)-4,4-dimethylpent-1-en-3-one (E16). Synthesized according to the general procedure for enone synthesis using pinacolone and 4-fluoro-3-methoxybenzaldehyde; yellow oil; yield: 1.96 g (83 %); ^{1}H NMR (300 MHz, DMSO) δ 7.91 –

7.83 (m, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.51 (d, J = 15.6 Hz, 1H), 7.27 (dd, J = 15.6, 1.0 Hz, 1H), 6.98-6.93 (m, 1H), 3.80 (s, 3H), 1.16 (s, 9H).

3-(3,4-Dimethoxyphenyl)-1-(2-methoxyphenyl)prop-2-en-1-one (E17). Synthesized according to the general procedure for enone synthesis using 1-(2-methoxyphenyl)ethanone and 3,4-dimethoxybenzaldehyde; yellow oil; yield: 2.38 g (80 %).[3]

(*E*)-3-(3-Fluoro-4-methoxyphenyl)-1-(2-methoxyphenyl)prop-2-en-1-one (E18). Synthesized according to the general procedure for enone synthesis using 1-(2-methoxyphenyl)ethanone and 3-fluoro-4-methoxybenzaldehyde; yellow solid; yield: 2.66 g (93 %); mp 97.5 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.70 (dd, J = 12.7, 2.1 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.47 (dd, J = 7.6, 1.6 Hz, 1H), 7.43 (d, J = 15.9 Hz, 1H), 7.31 (d, J = 15.9 Hz, 1H), 7.23 – 7.16 (m, 2H), 7.07 – 7.02 (m, 1H), 3.88 (s, 3H), 3.85 (s, 3H).^{13}C NMR (125 MHz, DMSO-d_6) δ 192.14, 157.59, 151.53 (d, $^{1}J_{C\text{-}F}$ = 244.5 Hz), 149.04 (d, $^{2}J_{C\text{-}F}$ = 10.9 Hz), 141.58 (d, $^{4}J_{C\text{-}F}$ = 2.2 Hz), 132.82, 129.37, 128.98, 127.77 (d, $^{3}J_{C\text{-}F}$ = 6.8 Hz), 126.40 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz), 126.02, 120.48, 114.99 (d, $^{2}J_{C\text{-}F}$ = 18.4 Hz), 113.85, 112.28, 56.12, 55.78.

(*E*)-3-(4-Ethoxy-3,5-difluorophenyl)-1-(2-methoxyphenyl)prop-2-en-1-one (E19). Synthesized according to the general procedure for enone synthesis using 1-(2-methoxyphenyl)ethanone and 4-ethoxy-3,5-difluorobenzaldehyde; yellow solid; yield: 2.92 g (92 %); mp 85.6 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.64 – 7.58 (m, 2H), 7.55 (ddd, J = 8.4, 7.3, 1.8 Hz, 1H), 7.48 (dt, J = 6.6, 2.4 Hz, 1H), 7.42-7.39 (m, 1H), 7.19 (d, J = 15.9 Hz, 1H), 7.06 (td, J = 7.4, 0.9 Hz, 1H), 6.95 – 6.89 (m, 1H), 4.22 (q, J = 7.0 Hz, 2H), 3.86 (s, 3H), 1.30 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.97, 157.78, 155.28 (dd, $^{1}J_{C\text{-}F}$ = 246.3, $^{3}J_{C\text{-}F}$ 6.5

Hz), 139.87, 135.95 (t, $^{2}J_{C\text{-}F}$ = 14.7 Hz), 133.87, 130.26 (t, $^{3}J_{C\text{-}F}$ = 9.3 Hz), 129.49, 128.68, 128.17, 120.49, 112.54 (dd, $^{2}J_{C\text{-}F}$ = 17.6, $^{4}J_{C\text{-}F}$ = 5.7 Hz), 112.31, 70.11, 55.82, 15.23.

(*E*)-3-(2,3-Difluoro-4-methoxyphenyl)-1-(2-methoxyphenyl)prop-2-en-1-one (E20). Synthesized according to the general procedure for enone synthesis using 1-(2-methoxyphenyl)ethanone and 2,3-difluoro-4-methoxybenzaldehyde; yellow solid; yield: 2.91 g (96 %); mp 128-130 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.66 (td, J = 8.8, 2.2 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.53 – 7.50 (m, 1H), 7.45 (dd, J = 15.6, 13.2 Hz, 2H), 7.20 (dd, J = 8.5, 0.7 Hz, 1H), 7.13 – 7.08 (m, 1H), 7.08 – 7.04 (m, 1H), 3.93 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.57, 157.83, 150.14, 149.45 (dd, $^{1}J_{C\text{-}F}$ = 251.6, $^{2}J_{C\text{-}F}$ =10.6 Hz), 140.16 (dd, $^{1}J_{C\text{-}F}$ = 245.6, $^{2}J_{C\text{-}F}$ 14.3 Hz), 133.60, 133.30, 129.63, 128.48, 127.99, 124.37, 120.60, 116.20, 112.39, 109.51, 56.79, 55.79.

(*E*)-1-(2,4-Dimethoxyphenyl)-3-(3-fluoro-4-methoxyphenyl)prop-2-en-1-one (E21). Synthesized according to the general procedure for enone synthesis using 1-(2,4-dimethoxyphenyl)ethanone and 3-fluoro-4-methoxybenzaldehyde; yellow solid; yield: 2.71 g (86 %); mp 85-86 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.65 (dt, J = 14.9, 3.5 Hz, 1H), 7.59 (d, J = 8.6 Hz, 1H), 7.53 – 7.45 (m, 2H), 7.43 (d, J = 15.8 Hz, 1H), 7.21 (dd, J = 11.0, 6.5 Hz, 1H), 6.68 (d, J = 2.3 Hz, 1H), 6.63 (dd, J = 8.6, 2.3 Hz, 1H), 3.89 (d, J = 2.3 Hz, 6H), 3.85 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.30, 163.83, 160.12, 151.53 (d, $^{1}J_{C\text{-}F}$ = 244.4 Hz), 148.80 (d, $^{2}J_{C\text{-}F}$ = 10.8 Hz), 140.19, 131.91, 128.09 (d, $^{3}J_{C\text{-}F}$ = 6.8 Hz), 126.11, 126.06 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz), 121.50, 114.84 (d, $^{2}J_{C\text{-}F}$ = 18.3 Hz), 113.87, 105.88, 98.60, 56.10, 55.91, 55.56.

1-(4-Fluorophenyl)-4,4-dimethylpent-1-en-3-one (E22). Synthesized according to the general procedure for enone synthesis using pinacolone and 4-fluorobenzaldehyde; yellow solid; yield: 1.73 g (84 %); mp 42.5-44.1 °C.[4]

1-(4-Bromophenyl)-4,4-dimethylpent-1-en-3-one (E23). Synthesized according to the general procedure for enone synthesis using pinacolone and 4-bromobenzaldehyde; white solid; yield: 2.48 g (93 %); mp 102-103 °C.[5, 6]

4-(4,4-Dimethyl-3-oxopent-1-en-1-yl)benzonitrile (E24). Synthesized according to the general procedure for enone synthesis using pinacolone and 4-formylbenzonitrile; white solid; yield: 1.95 g (92 %); mp 131-133 °C.[7, 8]

3-(4-Methoxyphenyl)-1-phenylprop-2-en-1-one (E25). Synthesized according to the general procedure for enone synthesis using acetophenone and 4-methoxybenzaldehyde; yellow solid; yield: 1.88 g (79 %); mp 73-74 °C.[9]

4,4-Dimethyl-1-(4-nitrophenyl)pent-1-en-3-one (E26). Synthesized according to the the general procedure for enone synthesis using pinacolone and 4-nitrobenzaldehyde; beige solid; yield: 2.23 g (96 %); mp 107-109 °C.[10]

4,4-Dimethyl-1-(3-nitrophenyl)pent-1-en-3-one (E27). Synthesized according to the general procedure for enone synthesis using pinacolone and 3-nitrobenzaldehyde; yellow solid; yield: 2.16 g (93 %); mp 92-94 °C.[11]

1-Cyclopropyl-3-(4-nitrophenyl)prop-2-en-1-one (E28). Synthesized according to the general procedure for enone synthesis using 1-cyclopropylethanone and 4-nitrobenzaldehyde; yellowish white solid; yield: 1.82 g (84 %); mp 118.9-120 °C.[12]

(*E*)-1-(1-Methylcyclopropyl)-3-(4-nitrophenyl)prop-2-en-1-one (E29). Synthesized according to the general procedure for enone synthesis using 1-(1-methylcyclopropyl)ethanone and 4-nitrobenzaldehyde; yellowish white solid; yield: 1.96 g (85 %); mp 133.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 – 8.22 (m, 2H), 7.74 – 7.69 (m, 2H), 7.62 (d, *J* = 16.1 Hz, 1H), 6.98 (d, *J* = 16.1 Hz, 1H), 2.26 (s, 3H), 1.24 – 1.18 (m, 2H), 1.07 – 1.01 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.41, 148.46, 140.97, 138.72, 129.77, 128.77, 124.15, 23.12, 20.26, 11.90.

(*E*)-1-Cyclohexyl-3-(4-nitrophenyl)prop-2-en-1-one (E30). Synthesized according to the general procedure for enone synthesis using 1-cyclohexylethanone and 4-nitrobenzaldehyde; beige solid; yield: 2.53 g (98 %); mp 132-134 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 2H), 7.71 (d, *J* = 8.5 Hz, 2H), 7.61 (d, *J* = 16.0 Hz, 1H), 6.93 (d, *J* = 15.9 Hz, 1H), 2.76 – 2.56 (m, 1H), 1.90 (dd, *J* = 22.1, 11.2 Hz, 4H), 1.54 – 1.18 (m, 6H).

3-(4-Nitrophenyl)-1-(thiophen-2-yl)prop-2-en-1-one (E31). Synthesized according to the general procedure for enone synthesis using 1-(thiophen-2-yl)ethanone and 4-nitrobenzaldehyde; yellow solid; yield: 2.14 g (83 %); mp 207-209 °C.[13]

1-(Furan-2-yl)-3-(4-nitrophenyl)prop-2-en-1-one (E32). Synthesized according to the general procedure for enone synthesis using 1-(furan-2-yl)ethanone and 4-nitrobenzaldehyde; yellow solid; yield: 2.13 g (88 %); mp 224.4 °C.[14]

1-(2-Chlorophenyl)-3-(4-nitrophenyl)prop-2-en-1-one (E33). Synthesized according to the general procedure for enone synthesis using 1-(2-chlorophenyl)ethanone and 4-nitrobenzaldehyde; yellow solid; yield: 2.21 g (77 %); mp 162-163 °C.[15]

(*E*)-3-(4-Nitrophenyl)-1-(2-(trifluoromethyl)phenyl)prop-2-en-1-one (E34). Synthesized according to the general procedure for enone synthesis using 1-(2-

(trifluoromethyl)phenyl)ethanone and 4-nitrobenzaldehyde; yellow solid; yield: 2.85 g (89 %); mp 142-144 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 – 8.18 (m, 2H), 7.70 – 7.64 (m, 2H), 7.51 – 7.46 (m, 2H), 7.41 (ddd, *J* = 8.0, 4.4, 1.2 Hz, 2H), 7.34 (ddd, *J* = 7.5, 6.5, 2.1 Hz, 1H), 7.22 (d, *J* = 16.1 Hz, 1H).

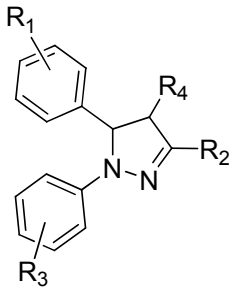
(*E*)-3-(4-Nitrophenyl)-1-(*o*-tolyl)prop-2-en-1-one (E35). Synthesized according to the general procedure for enone synthesis using 1-(*o*-tolyl)ethanone and 4-nitrobenzaldehyde; yellowish white solid; yield: 2.16 g (81 %); mp 128-129 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 – 8.20 (m, 2H), 8.07 – 7.97 (m, 1H), 7.73 – 7.66 (m, 2H), 7.55 – 7.48 (m, 2H), 7.41 (ddd, *J* = 8.9, 6.2, 2.4 Hz, 1H), 7.30 – 7.28 (m, 1H), 7.26 (d, *J* = 16.0 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.98, 148.58, 142.02, 140.84, 138.17, 137.58, 131.64, 129.97, 128.88, 128.59, 128.33, 125.63, 123.74, 20.40.

1-(2-Methoxyphenyl)-3-(4-nitrophenyl)prop-2-en-1-one (E36). Synthesized according to the general procedure for enone synthesis using 1-(2-methoxyphenyl)ethanone and 4-nitrobenzaldehyde; yellowish white solid; yield: 2.43 g (86 %); mp 116.5-118 °C.[16]

1-(Benzo[d][1,3]dioxol-5-yl)-3-(4-nitrophenyl)prop-2-en-1-one (E37). Synthesized according to the general procedure for enone synthesis using 1-(benzo[d][1,3]dioxol-5-yl)ethanone and 4-nitrobenzaldehyde; dark yellow solid; yield: 2.34 g (79 %); mp 182.4 °C.[17]

2) Molecular modeling and docking. All procedures were performed using the Molecular Operating Environment (MOE) software package (v. 2010, Chemical Computing Group). A homology model for the catalytic domain of PKCζ was prepared based on the PDB coordinates 3A8X of the most closely related PKCι isoform. Because of the high identity of 84 %, the following approach was chosen: supported by the rotamer explorer methodology, all amino acid residues different in PKCι were mutated *in silico* to the respective PKCζ counterparts as follows: L251I, T267N, R269Q, N282H, N302S, H303N, E316T, F321L, S350A, S354C, L355I, S379A, R396G, Q496P, S475F, A481S, S482H, S486G, H499R, A505S, G508K, G509S, P511A, N515S, V516I, M520L, M521L, Q523K, V526A, V527L, K531Q, N533Q, S535T, G536D, E537D, F538Y, S545T, N549S, T561A, R563K, K564R. Most of these amino acid residues were located at the protein surface, thus major perturbations of the tertiary structure were not expected. This mutated 3D template was energy minimized using the following parameters: AMBER99 force field, adjust H and LP: enabled, calculate forcefield partial charges: enabled, other settings on default. In the resulting 3D model, the dimensions and topology of the PIF-pocket appeared realistic when compared to the PIF-pockets of other PKC isoforms (e.g., PDB entries 3PFQ, PKCβII; 3IW4, PKCα; 1XJD, PKCθ). Molecular docking simulations were performed using the MMFF94x force field and the "triangle matcher" method, defining the target site by selecting L319 (PKCι notation) which is central to the PIF-pocket. Only the poses with the top 3 affinity scores were further evaluated.

3) Table S1. Inhibition of recombinant PKCζ and the NF-κB pathway in cells by compounds (**6a-6n**)



Cpd No.	R1	R2	R3	R4	Cell free assay		NF-κB reporter gene assay (U937 cells)	
					% inhibition at 62.5 μM[a]	IC_{50}±SD (μM)	% inhibition at 5 μM[a]	IC_{50}±SD (μM)
6a	4-NH_2	*t*-Bu	4-Cl	H	19.0	ND	22.7	ND
6b	4-NH_2	*t*-Bu	2,4-difluoro	H	52.3	ND	23.5	ND
6C	4-NH_2	*t*-Bu	3-Cl	H	53.6	ND	42.3	ND
6d	3-NH_2	*t*-Bu	4-Cl	H	18.7	ND	21.9	ND
6e	4-NH_2	cyclopropyl	3-Cl	H	57.4	ND	24.5	ND
6f	4-NH_2	1-methylcyclopropyl	3-Cl	H	55.6	ND	47.7	ND
6g	4-NH_2	cyclohexyl	4-Cl	H	9.1	ND	30.9	ND
6h	4-NH_2	thiophen-2-yl	3-Cl	H	33.0	ND	44.9	ND
6i	4-NH_2	furan-2-yl	3-Cl	H	48.1	ND	26.1	ND
6j	4-NH_2	2-chlorophenyl	3-Cl	H	1.3	ND	24.4	ND
6K	4-NH_2	2-trifluoromethylphenyl	3-Cl	H	24.0	ND	50.8	ND
6l	4-NH_2	2-methylphenyl	3-Cl	H	30.0	ND	31.3	ND
6m	4-NH_2	2-methoxyphenyl	3-Cl	H	28.3	ND	28.2	ND
6n	4-NH_2	benzo[d][1,3]dioxol-5-yl	3-Cl	H	38.0	ND	22.2	ND

[a]Values are mean of at least two experiments; standard deviation <15%; ND: not determined

4) Table S2. Hit compound **1a** does not inhibit other potential target kinases in the NF-κB pathway nor PKCβII

Kinase (human)	% inhibition at 10 μM of **1a**
IKKβ	n.i.
PKCι	n.i.
RIPK2	n.i.
p38α MAPK	10%
TAK1	n.i.
TBK1	n.i.
PKCβII	n.i.

n.i.: no inhibition. Each value is representative of at least two independent assays which essentially gave the same results.

5) Table S3. Wilcoxon´s signed rank test

Group 1: low potency (less than 75% inhibition at 62.5 μM in the cell free assay)					
compound #	% inhibition at 5 μM (U937 cells)	compound #	% inhibition at 5 μM (U937 cells)	compound #	% inhibition at 5 μM (U937 cells)
1g	40.7	**3n**	9.3	**6e**	24.5
1l	23.5	**3o**	20.1	**6f**	47.7
1m	48.7	**3p**	2.9	**6g**	30.9
1n	50.2	**3q**	50.8	**6h**	44.9
1o	51.8	**4b**	35	**6i**	26.1
1p	41.5	**4c**	37.3	**6j**	24.4
1q	12.3	**5a**	5.9	**6K**	50.8
2d	26.5	**6a**	22.7	**6l**	31.3
2e	48.2	**6b**	23.5	**6m**	28.2
2f	38.7	**6C**	42.3	**6n**	22.2
3l	3.7	**6d**	21.9	**7a**	25.5
3m	5.5				
Group 2: moderate potency (IC_{50} = 5-15 μM in the cell free assay)					
compound #	% inhibition at 5 μM (U937 cells)	compound #	% inhibition at 5 μM (U937 cells)	compound #	% inhibition at 5 μM (U937 cells)
1a	75.1	**1h**	64.6	**4a**	89.9
1b	63.8	**2j**	70.2	**4i**	75.1
1c	58.4	**2l**	42.3	**4j**	81.7
1e	62.9				
Group 3: high potency (IC_{50} <5 μM in the cell free assay)					
compound #	% inhibition at 5 μM (U937 cells)	compound #	% inhibition at 5 μM (U937 cells)	compound #	% inhibition at 5 μM (U937 cells)
1i	73.5	**1t**	84.2	**4f**	92.8
1j	89.7	**2c**	68.2	**4g**	62
1k	73.7	**4d**	95	**4h**	71.7
1r	92	**4e**	85	**4k**	87.4
1s	90.1				

Group 1 *vs.* group 2, exact P value is 0.002; group 1 *vs.* group 3, exact P value is 0.0017; group 2 *vs.* group 3, exact P value is 0.0273

6) Table S4. MTT toxicity assay using RAW 264.7 cells*

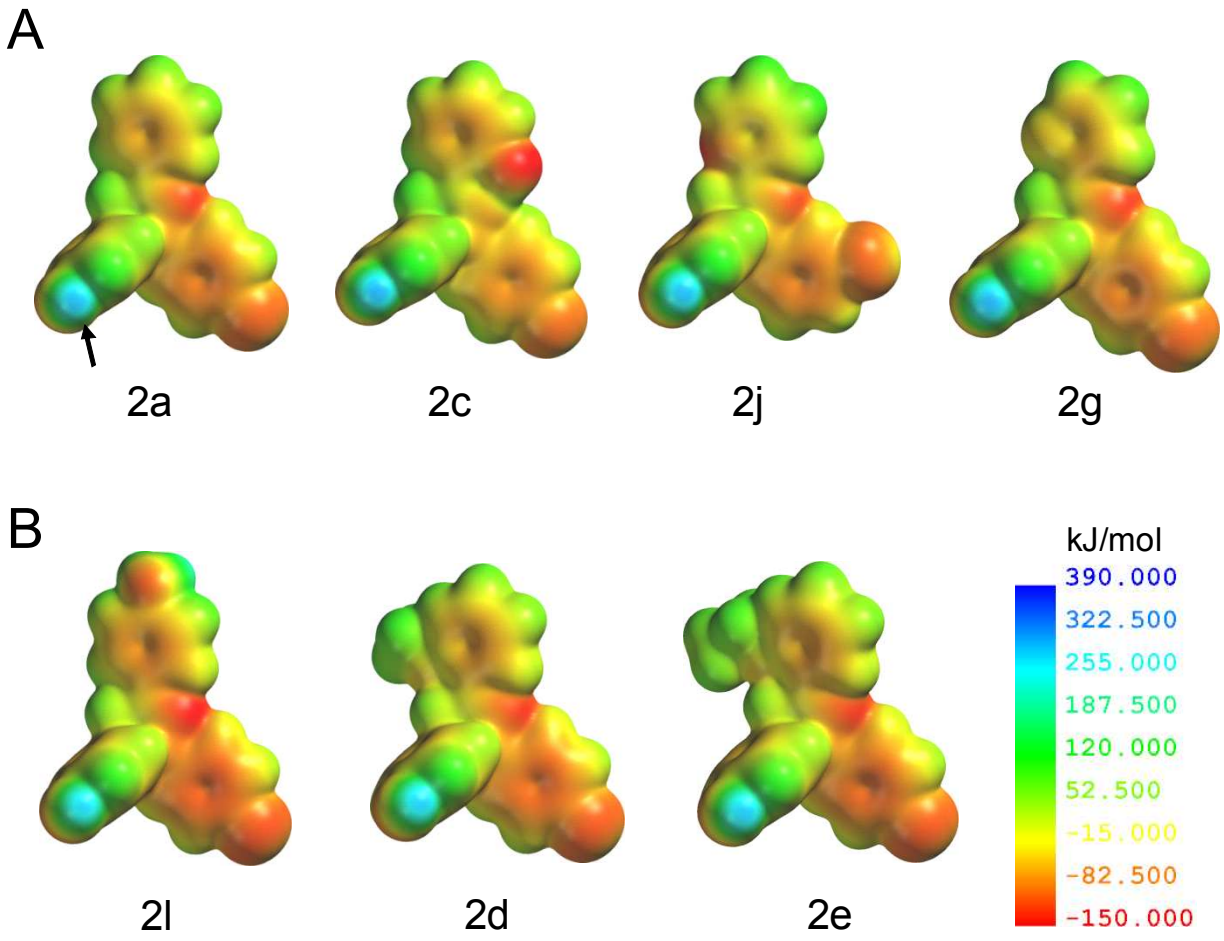
Compound (7.5 µM)	% living cells compared to DMSO control*	Compound (7.5 µM)	% living cells compared to DMSO control*
1a	97	**2e**	92
1b	78	**2f**	95
1c	100	**2g**	94
1d	9	**2h**	90
1e	95	**2i**	94
1f	49	**2j**	89
1g	99	**2k**	100
1h	92	**2l**	92
1i	100	**3o**	88
1j	88	**4a**	92
1k	86	**4b**	63
1l	98	**4d**	100
1m	83	**4e**	99
1n	90	**4f**	98
1o	95	**4g**	99
1p	94	**4h**	100
1q	100	**4i**	92
1r	100	**4j**	84
1s	96	**4k**	100
1t	100	**6a**	91
1u	100	**6c**	85
2a	83	**6h**	84
2b	84	**9**	100
2c	94	**11**	100
2d	93	**Curcumin**	100

* Average of at least two independent experiments

7) Table S5. Selectivity profile of **4f** *vs.* the PKC family and further AGC kinases

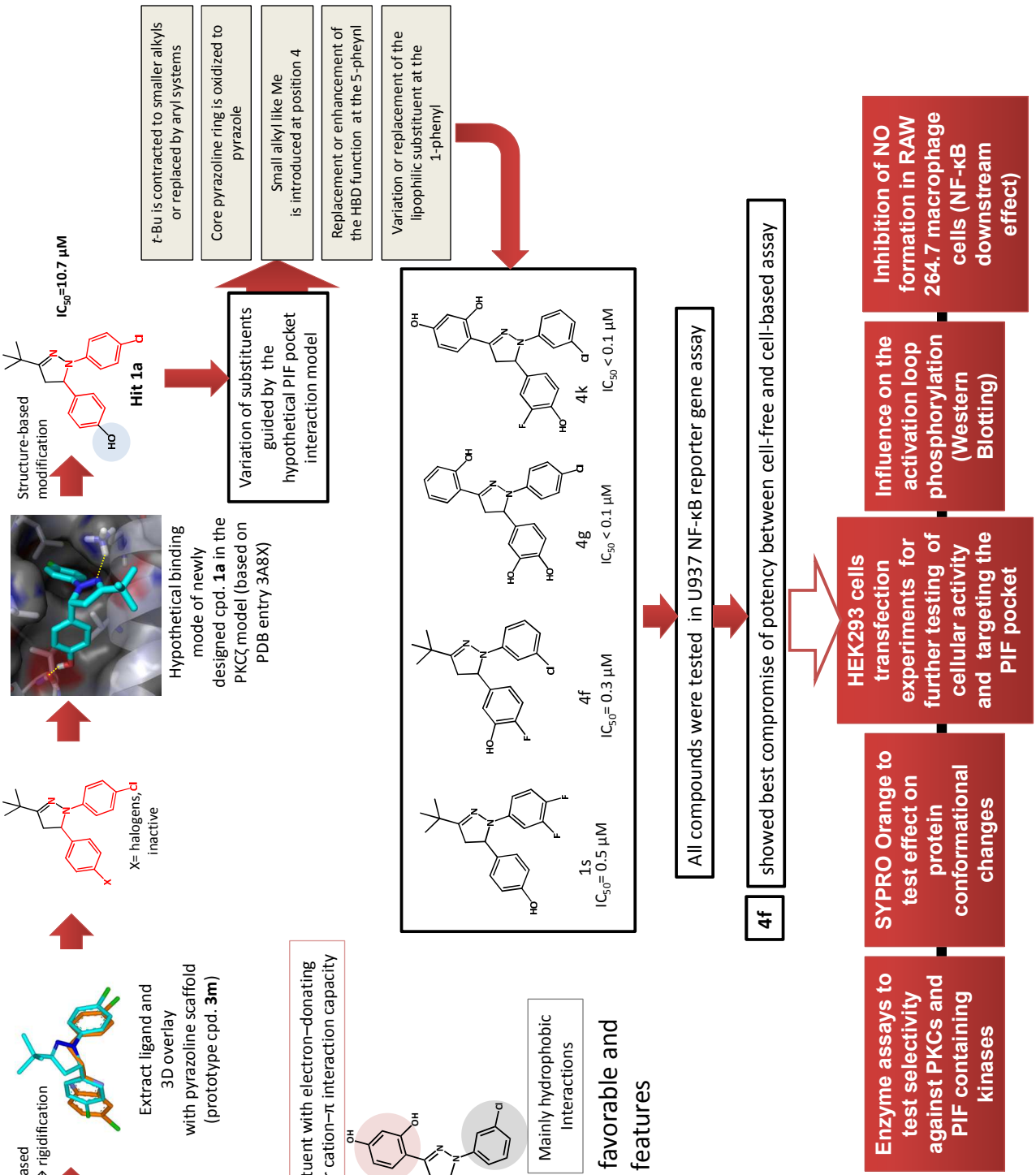
Kinase (human)	% inhibition at 10 μM of **4f**
PKCα	4
PKCβI	n.i.
PKCβII	12
PKCγ	6
PKCδ	n.i.
PKCε	n.i.
PKCη	n.i.
PKCθ	n.i.
PKCι	n.i.
PDK1	8
PKA	n.i.
RSK1	3
MSK1	11
p70S6K	n.i.
SGK1	18

n.i.: no inhibition. Each value is representative of at least two independent assays which essentially gave the same results.



8) Figure S1. Molecular electrostatic potentials (MEP) mapped on the isoelectronic density surfaces of 0.002 e/a_0^3. The *ab initio* calculations of the lowest energy conformers and the electrostatic potentials were carried out at the B3LYP density functional scheme with the 6-31G** basis set in water, as implemented in the Gaussian 03 suite of programs.[18] The color codes were uniformely adjusted to range from -150 to +390 kJ/mol. The arrow points to the hydrogen of the phenolic hydroxyl, which shows a higher positive potential in the compounds from panel (A) than in those from (B). Hence the OH hydrogen in the compounds from (A) is expected to exhibit a higher donor strength.

9) Figure S2. Work-flow chart.



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