Supplementary Material

Catalyst-free one-pot synthesis of isoindolin-1-imine derivatives via three-component reaction

Sida Shen,[a] Pham Van Khang,[a] Yijia Chen,[b] Min Lei,[b]* and Lihong Hu[a,b]*

[a]School of Pharmacy, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, PR China
[b]Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, PR China

Table of Contents

 ©ARKAT-USA, Inc

General experimental methods

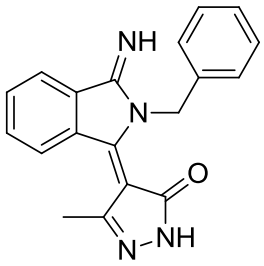
Reagents and all solvents were analytically pure grade and were used without further purification. Column chromatography was performed using silica gel (200–300 mesh). TLC was performed on GF254 silica gel plates (Yantai Huiyou Inc., China). Melting points were determined with a WRS-1B apparatus. ^{1}H (400 MHz) and ^{13}C (100 125 MHz) NMR spectra were recorded on Bruker AMX 400 spectrometer in the solvent indicated. HRMS (ESI) were determined on a Micromass Q-Tif Global mass spectrometer and MS (ESI) were obtained on a Bruker Esquire 3000 Plus spectrometer.

General procedure for the synthesis of 4a-p

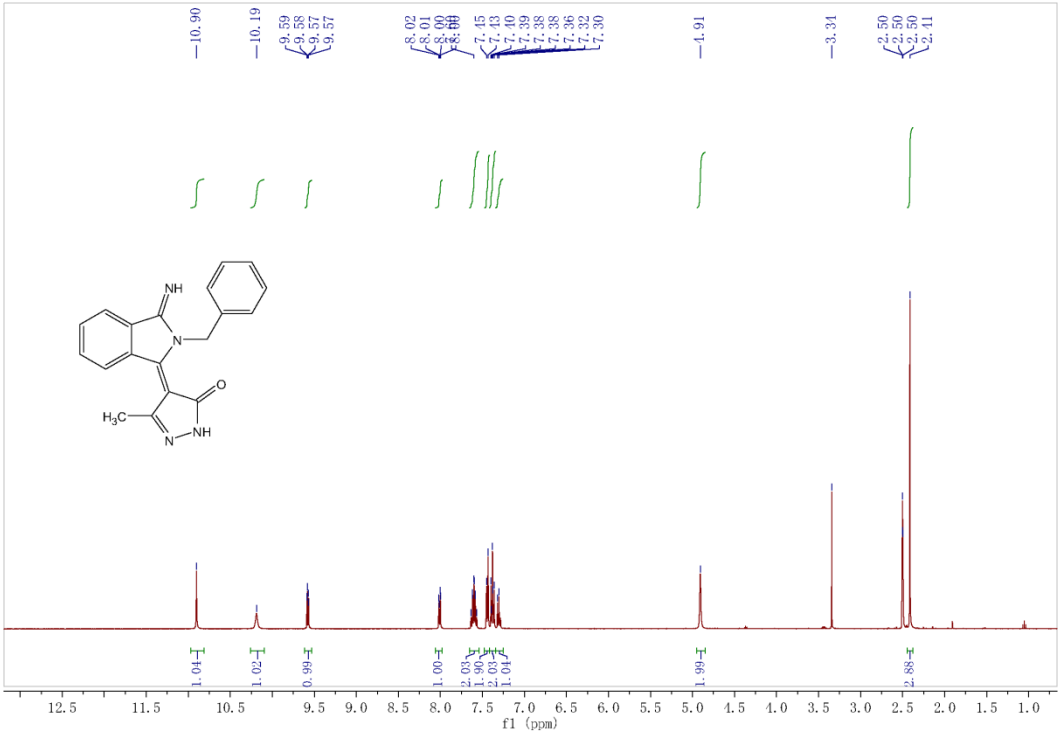
To a stirred ethanol solution of 2-cyanobenzaldehyde (1, 3 mmol) and 3-methyl-1H-pyrazol-5(4H)-one 3a or 1,3-dimethyl-1H-pyrazol-5(4H)-one 3b (3 mmol) was added amine (2, 3mmol). And then the mixture was heated to reflux and stirred for 30 min. After completion of the reaction, the precipitate was filtered off, washed with ethanol, and recrystallized to afford a red solid 4a-p (85-95%).

©ARKAT-USA, Inc

^{1}H NMR of 4-(2-benzyl-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4a)

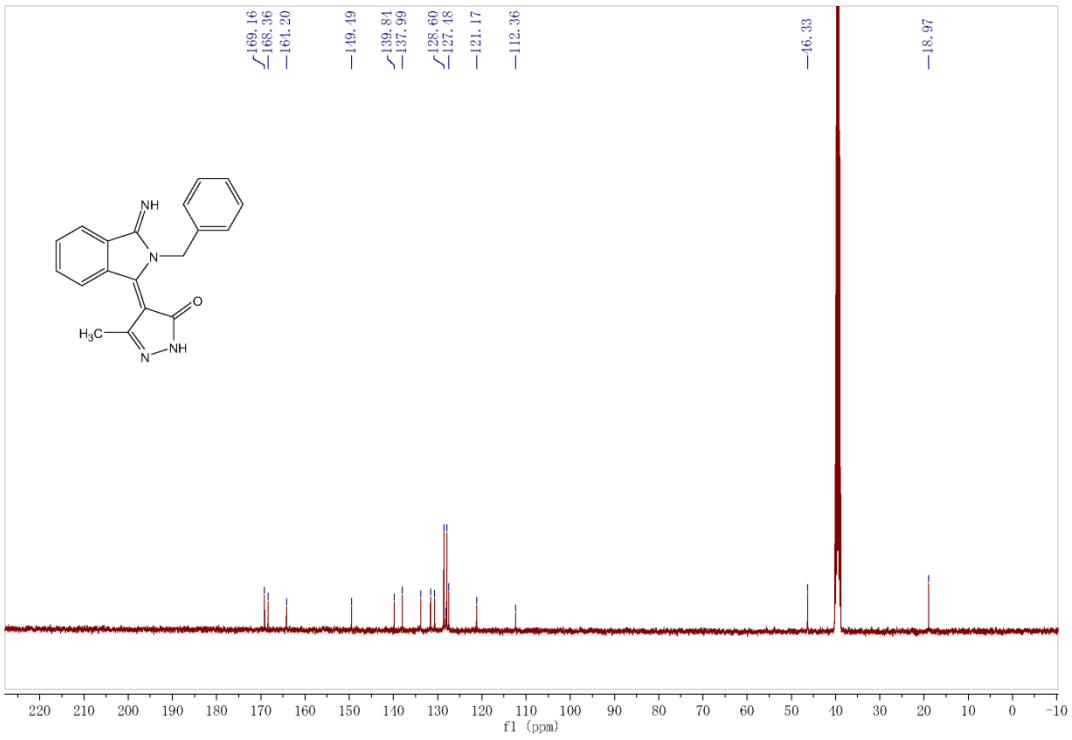


Red solid, yield 93%, mp 243.8–245.1 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.90 (s, 1H), 10.19 (brs, 1H), 9.58 (dd, *J* = 6.2, 1.4 Hz, 1H), 8.01 (dd, *J* = 6.2, 1.8 Hz, 1H), 7.60 (qd, *J* = 7.4, 6.0 Hz, 2H), 7.44 (d, *J* = 7.1 Hz, 2H), 7.42–7.34 (m, 2H), 7.31 (d, *J* = 7.3 Hz, 1H), 4.91 (s, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.2, 168.4, 164.2, 149.5, 139.8, 138.0, 133.8, 131.6, 130.7, 128.6(2C), 128.1, 127.9(2C), 127.5, 121.2, 112.4, 46.3, 19.0; MS (ESI): *m/z* 317.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{19}H_{17}N_4O$ $[M+H]^+$: 317.1397; Found: 317.1407.



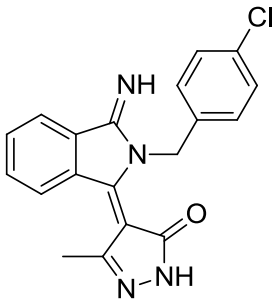
©ARKAT-USA, Inc

^{13}C NMR of 4-(2-benzyl-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4a)

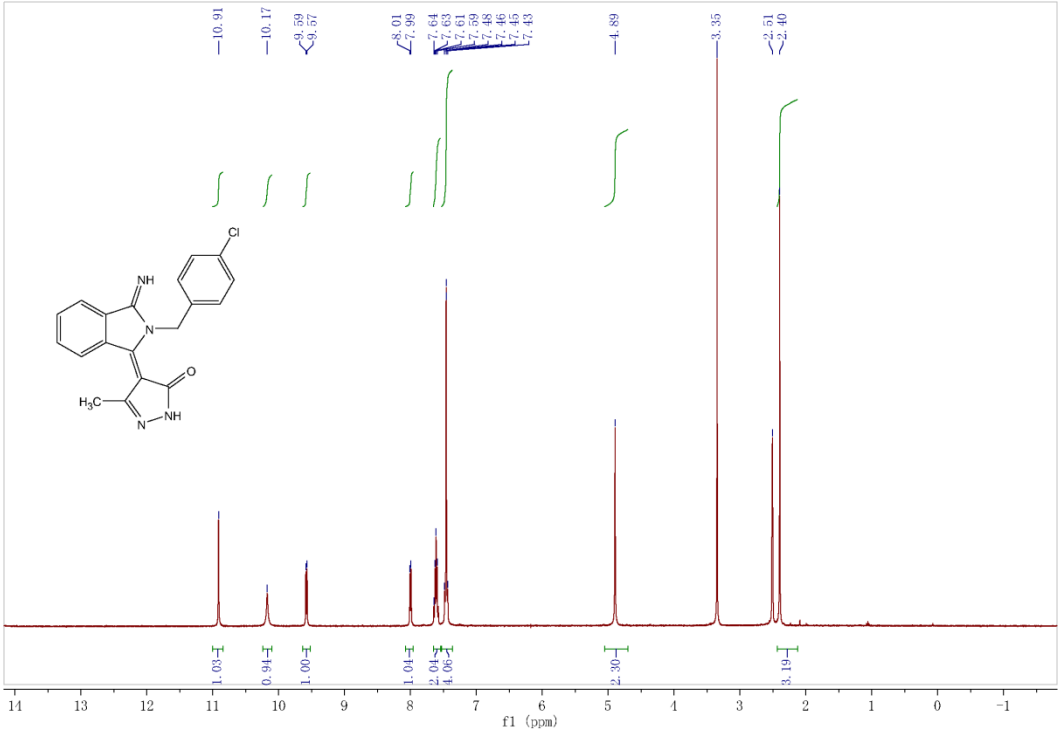


©ARKAT-USA, Inc

^{1}H NMR of 4-(2-(4-chlorobenzyl)-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4b)

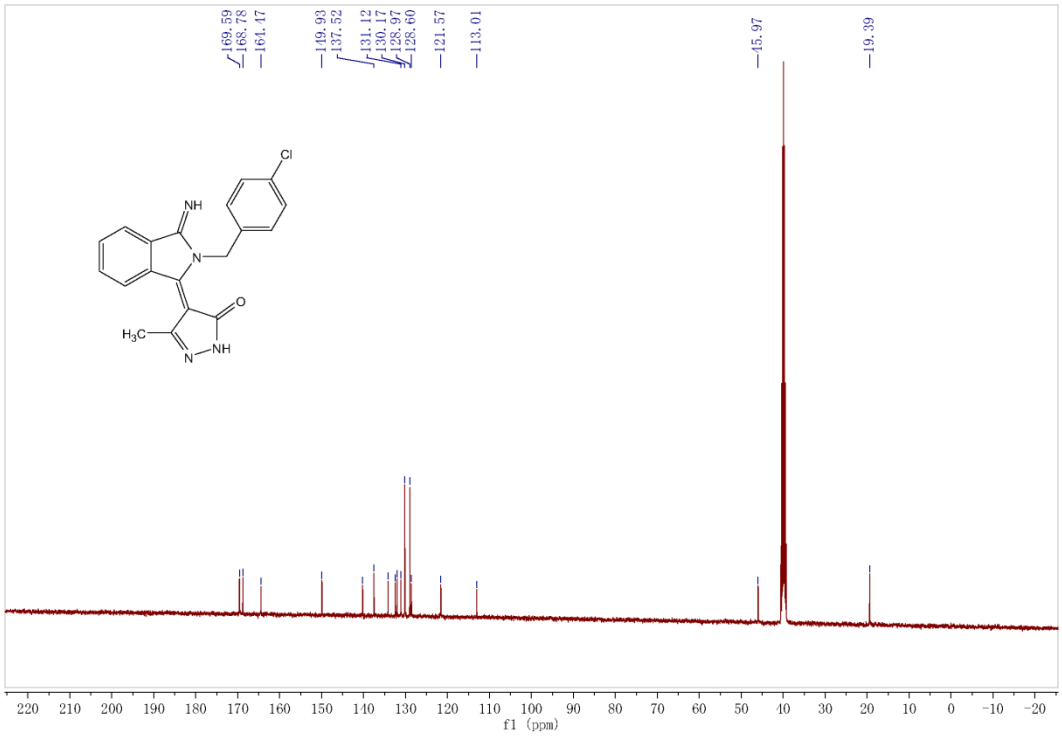


Red solid, yield 94%, mp 234.5–235.7 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.91 (s, 1H), 10.17 (brs, 1H), 9.58 (d, J = 7.0 Hz, 1H), 8.00 (d, J = 6.6 Hz, 1H), 7.62 (dd, J = 13.0, 6.5 Hz, 2H), 7.53–7.36 (m, 4H), 4.89 (s, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.6, 168.8, 164.5, 149.9, 140.2, 137.5, 134.2 132. 5, 132.1 131.1, 130.2(2C), 129.0(2C), 128.6, 121.6, 113.0, 46.0, 19.4; MS (ESI): *m/z* 351.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{19}H_{16}ClN_4O$ $[M+H]^+$: 351.1007; Found: 317.1017.



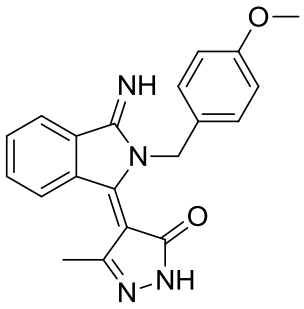
 ©ARKAT-USA, Inc

^{13}C NMR of 4-(2-(4-chlorobenzyl)-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4b)

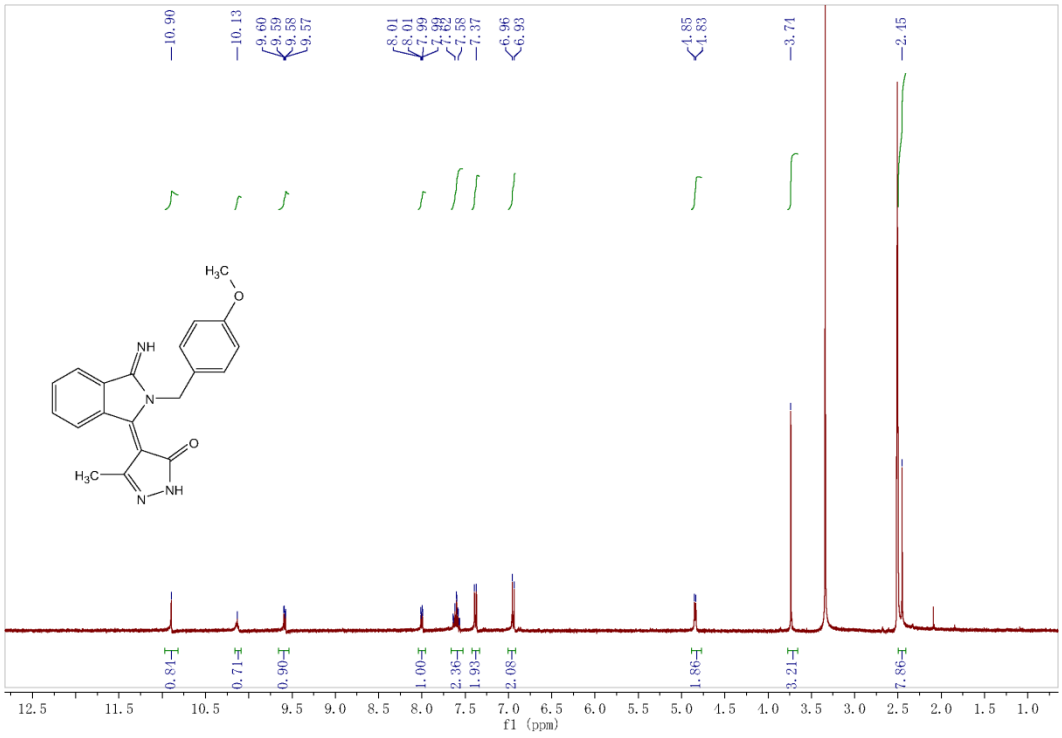


©ARKAT-USA, Inc

^{1}H NMR of 4-(3-imino-2-(4-methoxybenzyl)isoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one(4c)

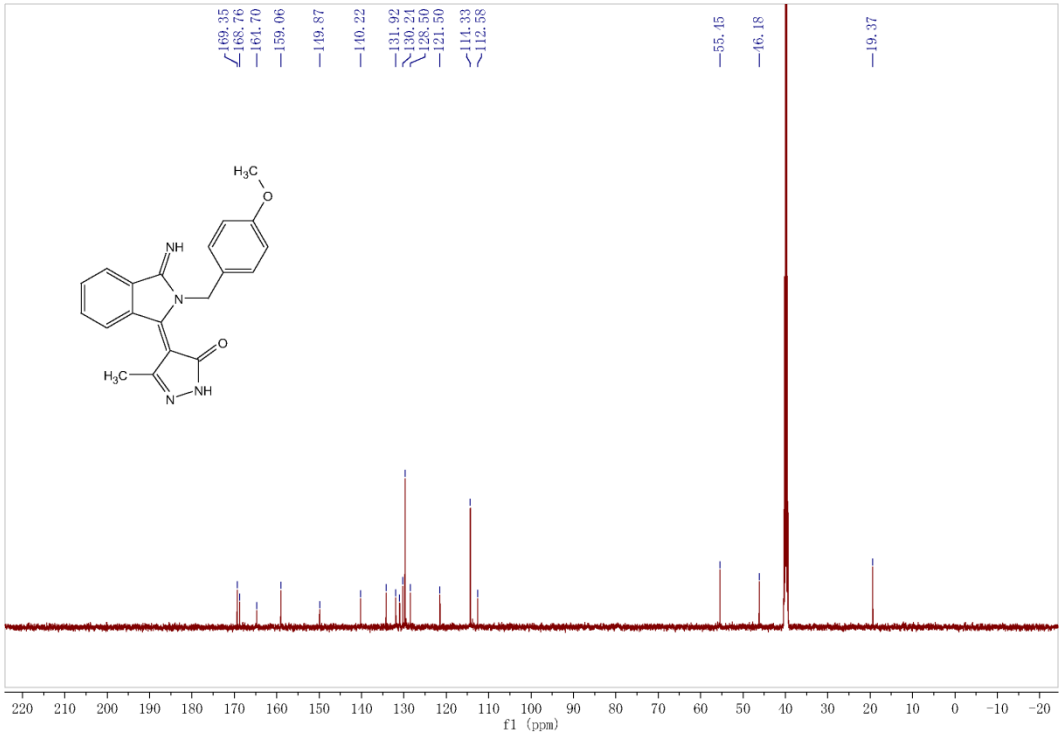


Red solid, yield 92%, mp 216.5–217.8 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.90 (s, 1H), 10.13 (brs, 1H), 9.59 (dd, *J* = 6.7, 1.6 Hz, 1H), 8.00 (dd, *J* = 6.4, 1.4 Hz, 1H), 7.66–7.53 (m, 2H), 7.38 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 4.84 (d, *J* = 6.3 Hz, 2H), 3.74 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.3, 168.7, 164.7, 159.1, 149.9, 140.2, 134.2, 131.9, 131.0, 130.2, 129.7 (2C), 128.5 121.5, 114.3 (2C), 112.6, 55.4, 46.2, 19.4; MS (ESI): *m/z* 347.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{20}H_{19}N_4O_2$ $[M+H]^+$: 347.1503; Found: 347.1516.



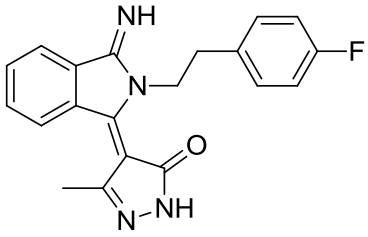
 ©ARKAT-USA, Inc

^{13}C NMR of 4-(3-imino-2-(4-methoxybenzyl)isoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one(4c)

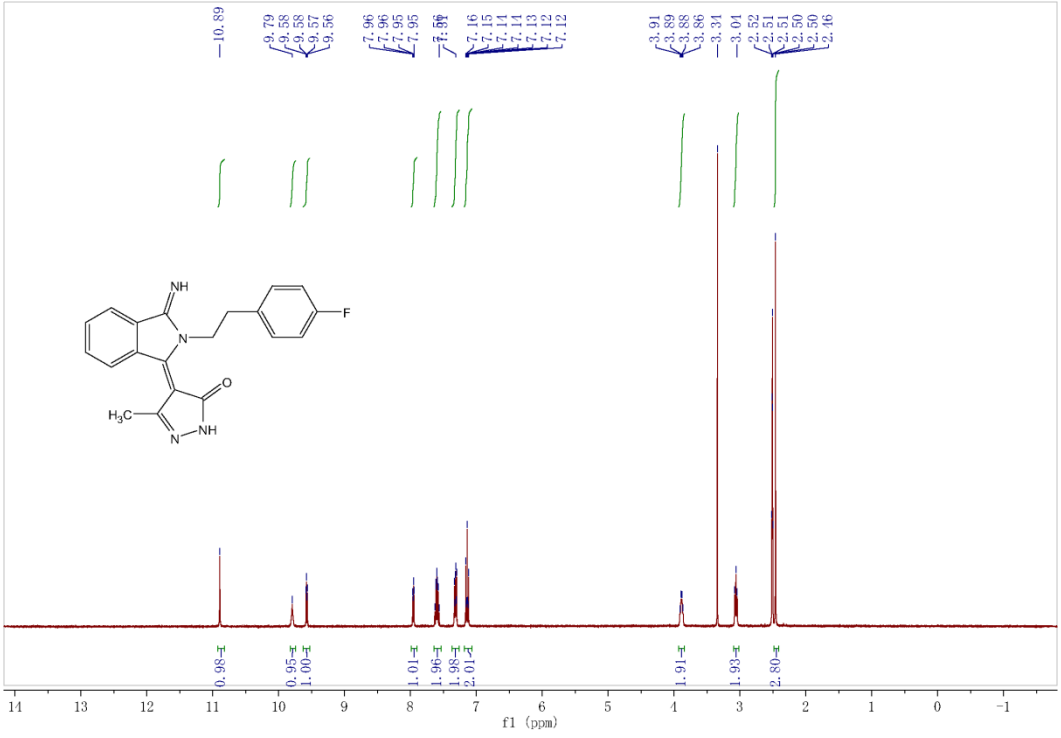


©ARKAT-USA, Inc

^{1}H NMR of 4-(2-(4-fluorophenethyl)-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4d)

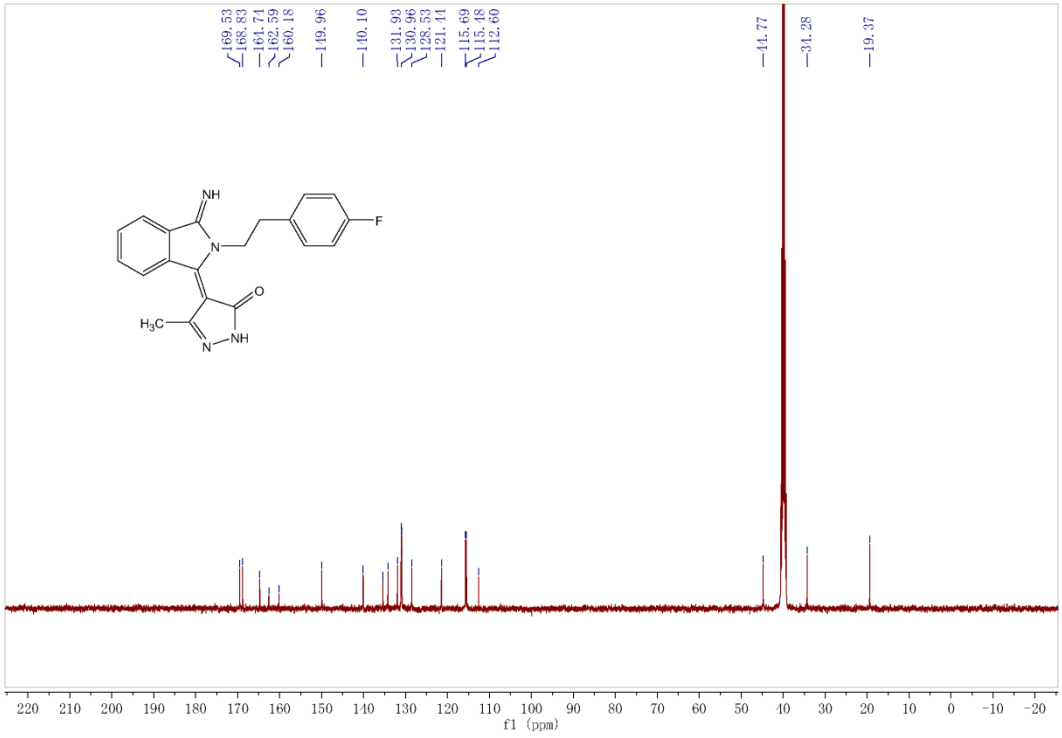


Red solid, yield 89%, mp 258.3–259.5 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.89 (s, 1H), 9.79 (brs, 1H), 9.57 (dd, J = 6.4, 1.8 Hz, 1H), 7.95 (dd, J = 5.7, 1.5 Hz, 1H), 7.64–7.54 (m, 2H), 7.37–7.26 (m, 2H), 7.18–7.07 (m, 2H), 3.89 (dd, J = 11.4, 6.4 Hz, 2H), 3.06 (t, J = 7.4 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.5, 168.8, 164.74, 162.59, and 160.18 ($^1J_{CF}$ = 241.0 Hz), 150.0, 140.1, 135.41, and 135.39 ($^4J_{CF}$ = 2.0 Hz), 134.2, 131.9, 131.1, 130.96, and 130.88 ($^3J_{CF}$ = 8.0 Hz)(2C), 128.5, 121.4, 115.69, and 115.48($^2J_{CF}$ = 21.0 Hz)(2C), 112.6, 44.8, 34.3, 19.4; MS (ESI): *m/z* 349.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{20}H_{18}FN_4O$ $[M+H]^+$: 349.1459; Found: 349.1468.



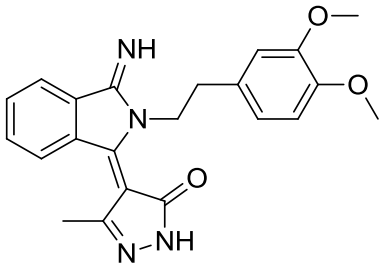
 ©ARKAT-USA, Inc

^{13}C NMR of 4-(2-(4-fluorophenethyl)-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4d)

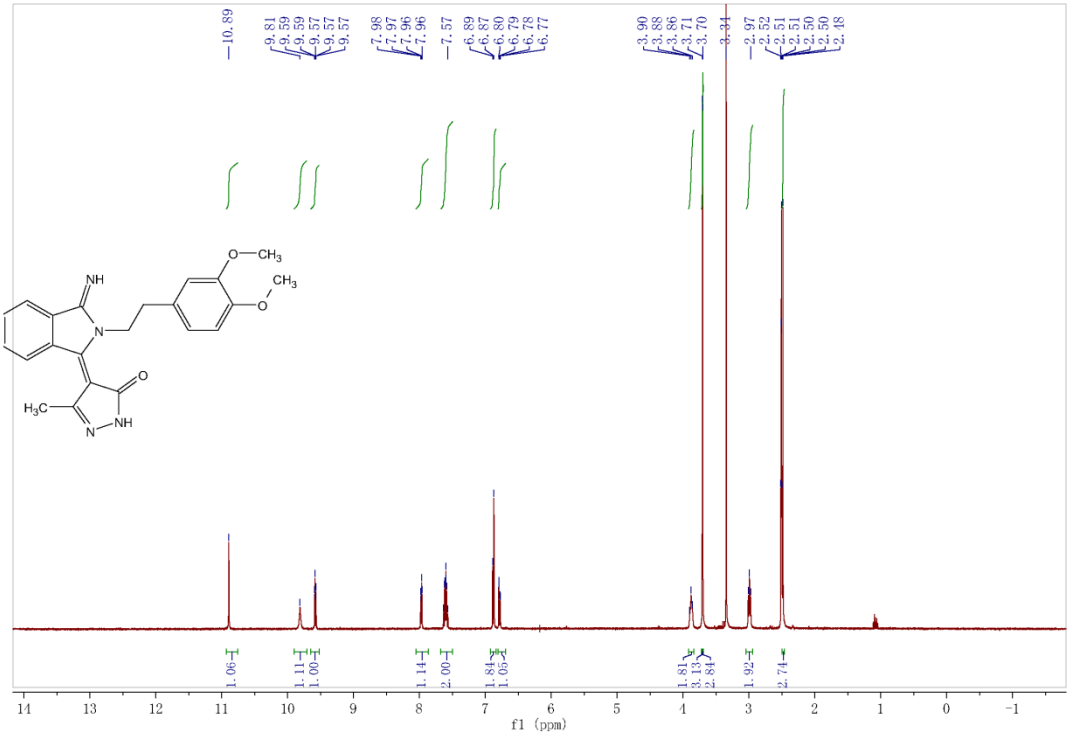


 ©ARKAT-USA, Inc

^{1}H NMR of 4-(2-(3,4-dimethoxyphenethyl)-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4e)

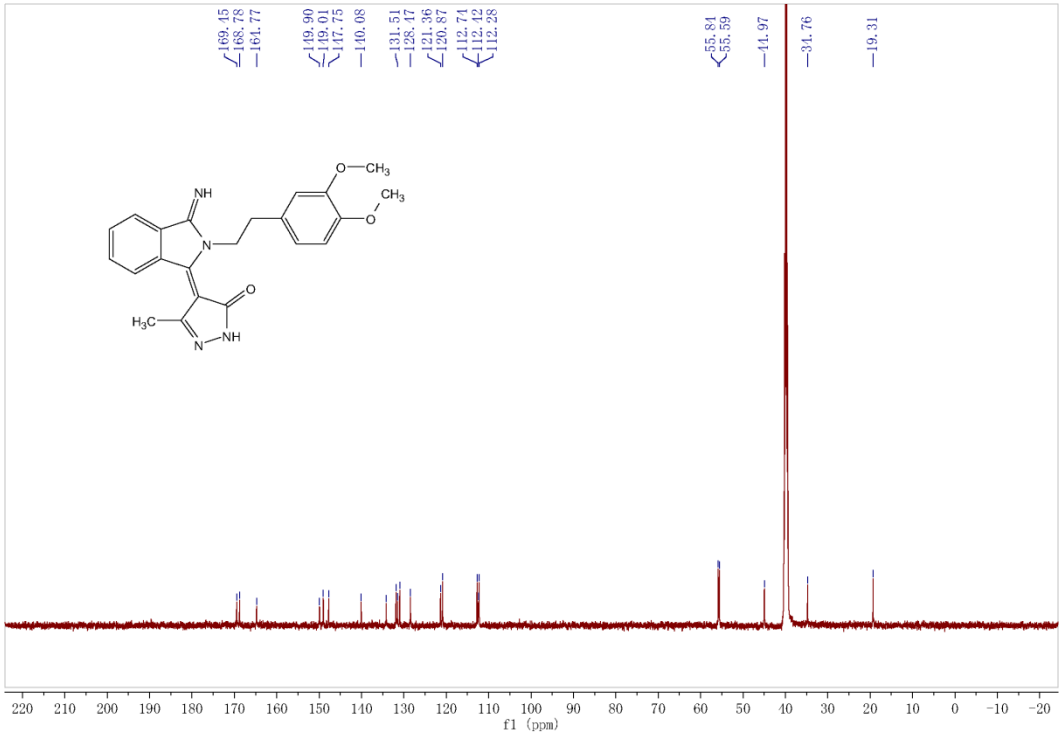


Red solid, yield 87%, mp 229.1–230.6 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.89 (s, 1H), 9.81 (brs, 1H), 9.56 (m, 1H), 7.97 (dd, *J* = 5.6, 1.5 Hz, 1H), 7.67–7.50 (m, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 6.78 (dd, *J* = 8.0, 2.0 Hz, 1H), 33.88 (t, *J* = 8.2 Hz, 2H), 3.71 (s, 3H), 3.70 (s, 3H), 2.99 (t, *J* = 7.4 Hz, 2H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.5, 168.8, 164.8, 149.9, 149.0, 147.7, 140.1, 134.2, 131.8, 131.5, 131.0, 128.5, 121.4, 120.9, 112.7, 112.4, 112.3, 55.8, 55.6, 45.0, 34.7, 19.3; MS (ESI): *m/z* 391.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{22}H_{23}N_4O_3$ $[M+H]^+$: 391.1765; Found: 391.1779.



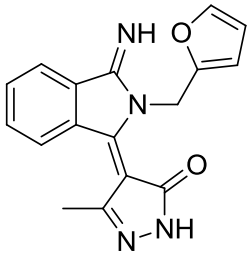
 ©ARKAT-USA, Inc

^{13}C NMR of 4-(2-(3,4-dimethoxyphenethyl)-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4e)

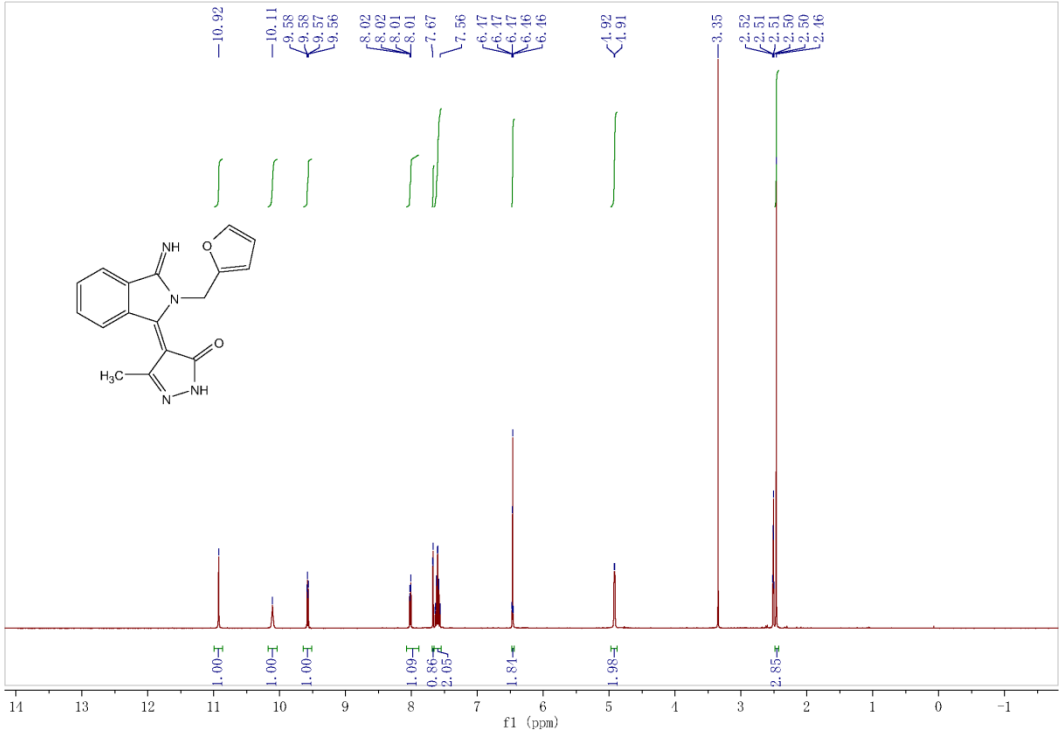


©ARKAT-USA, Inc

^{1}H NMR of 4-(2-(furan-2-ylmethyl)-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4f)

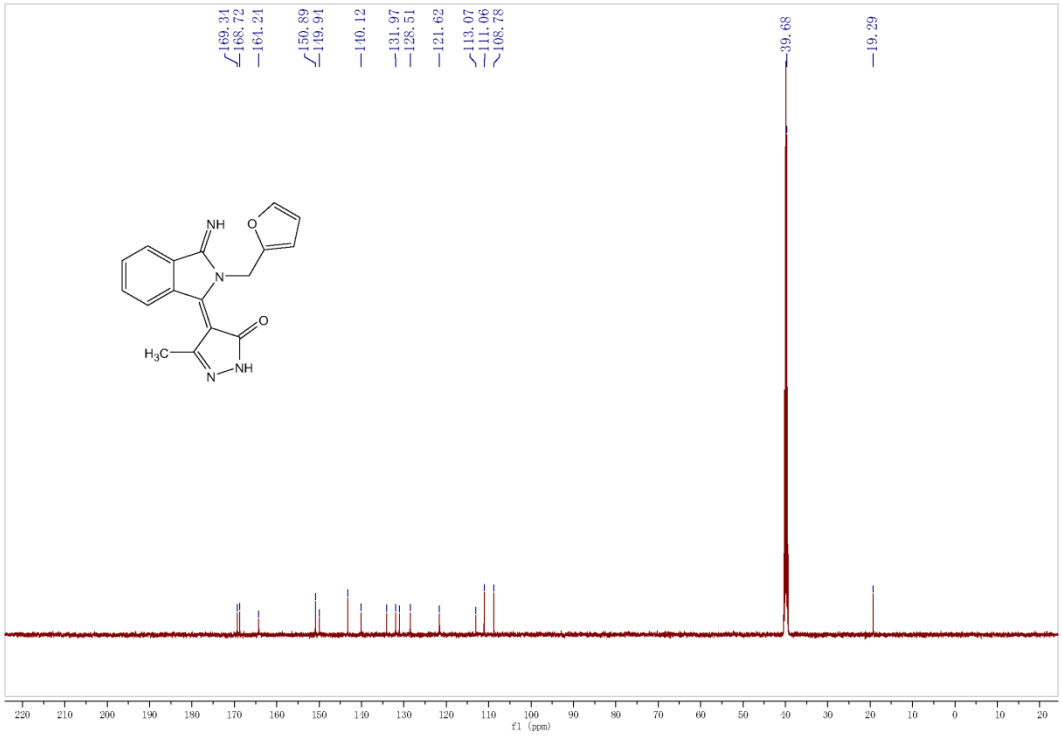


Red solid, yield 85%, mp 219.3–220.6 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.92 (s, 1H), 10.11 (brs, 1H), 9.57 (dd, *J* = 6.6, 1.5 Hz, 1H), 8.01 (dd, *J* = 6.1, 1.3 Hz, 1H), 7.68–7.66 (m, 1H), 7.64–7.56 (m, 2H), 6.48–6.44 (m, 2H), 4.92 (d, *J* = 4.2 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.3, 168.7, 164.2, 150.9, 149.9, 143.5, 140.1, 134.1, 132.0, 131.1, 128.5, 121.6, 113.1, 111.1, 108.8, 39.7, 19.3; MS (ESI): *m/z* 307.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{15}N_4O_2$ $[M+H]^+$: 307.1190; Found: 307.1204.



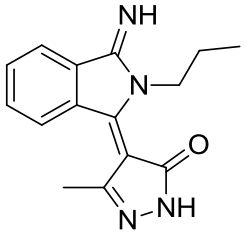
 ©ARKAT-USA, Inc

^{13}C NMR of 4-(2-(furan-2-ylmethyl)-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4f)

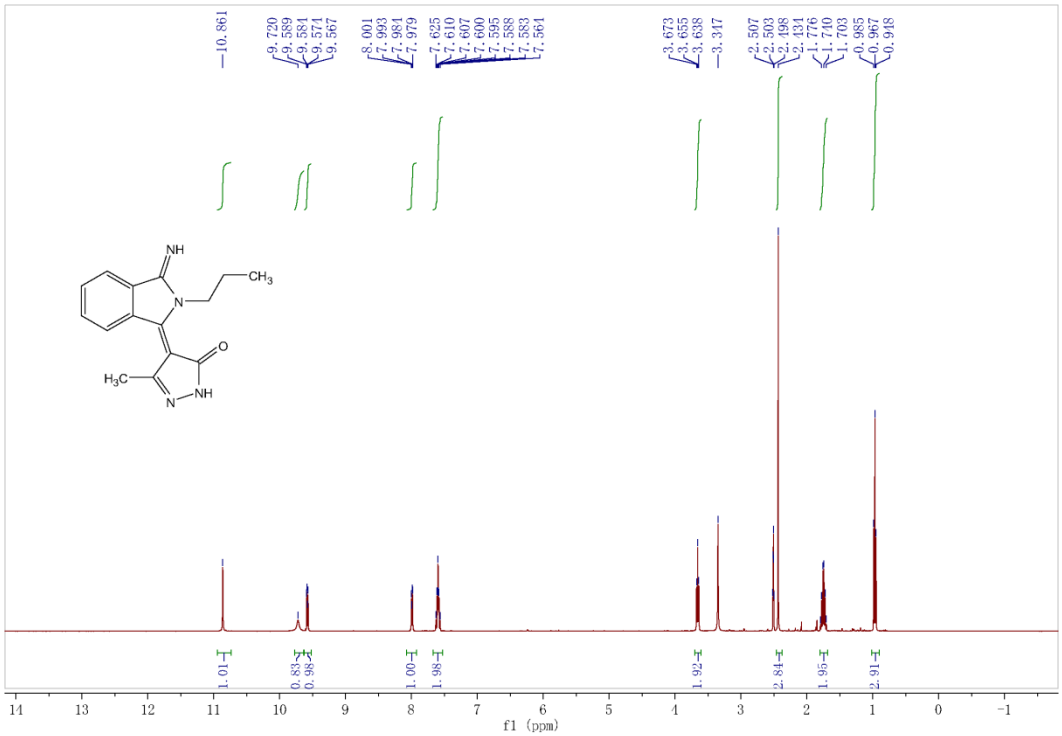


©ARKAT-USA, Inc

^{1}H NMR of 4-(3-imino-2-propylisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4g)

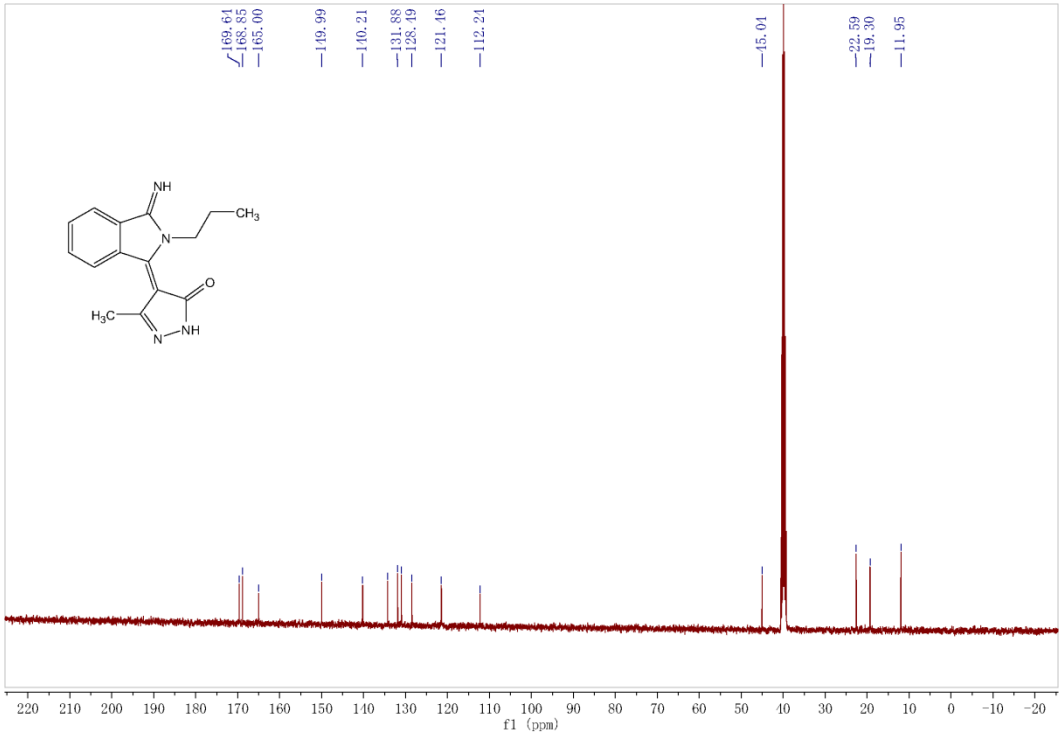


Red solid, yield 94%, mp 255.6–257.3 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.86 (s, 1H), 9.72 (brs, 1H), 9.58 (dd, J = 6.3, 2.4 Hz, 1H), 7.99 (dd, J = 6.0, 2.5 Hz, 1H), 7.67–7.53 (m, 2H), 3.66 (t, J = 7.0 Hz, 2H), 2.43 (s, 3H), 1.75 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.6, 168.8, 165.0, 150.0, 140.2, 134.2, 131.9, 131.0, 128.5, 121.5, 112.2, 45.0, 22.6, 19.3, 11.9; MS (ESI): *m/z* 269.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{15}H_{17}N_4O$ $[M+H]^+$: 269.1397; Found: 269.1409.



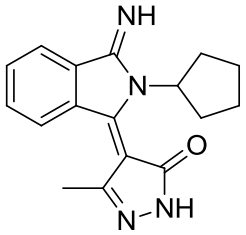
©ARKAT-USA, Inc

^{13}C NMR of 4-(3-imino-2-propylisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4g)

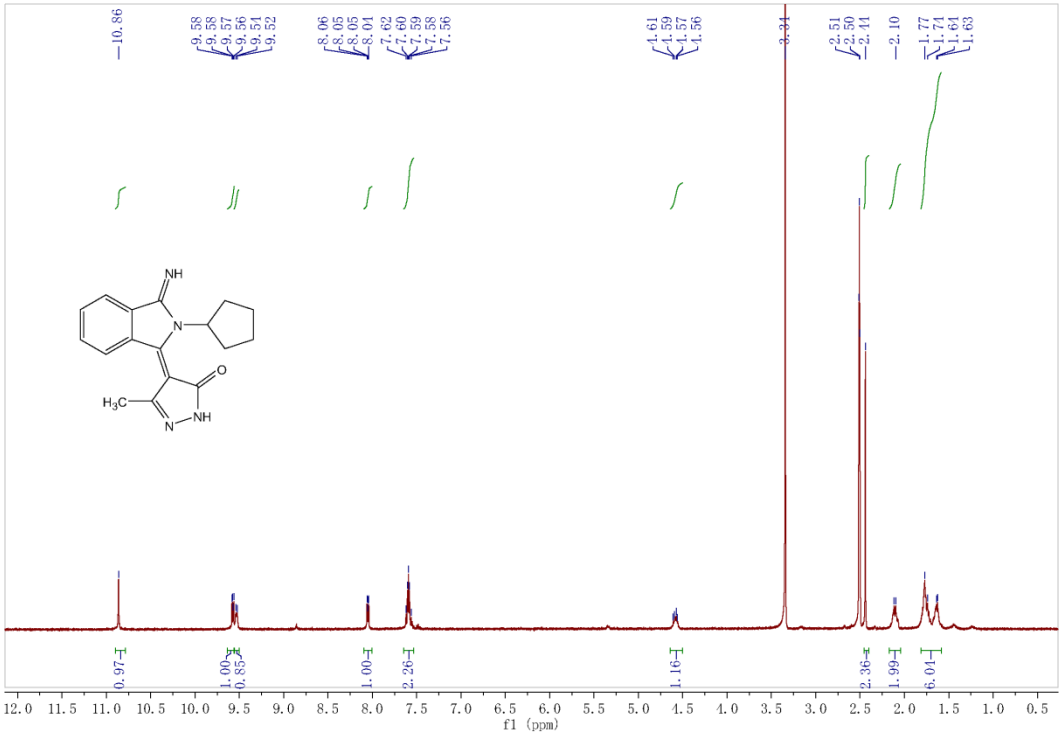


©ARKAT-USA, Inc

^{1}H NMR of 4-(2-cyclopentyl-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4h)

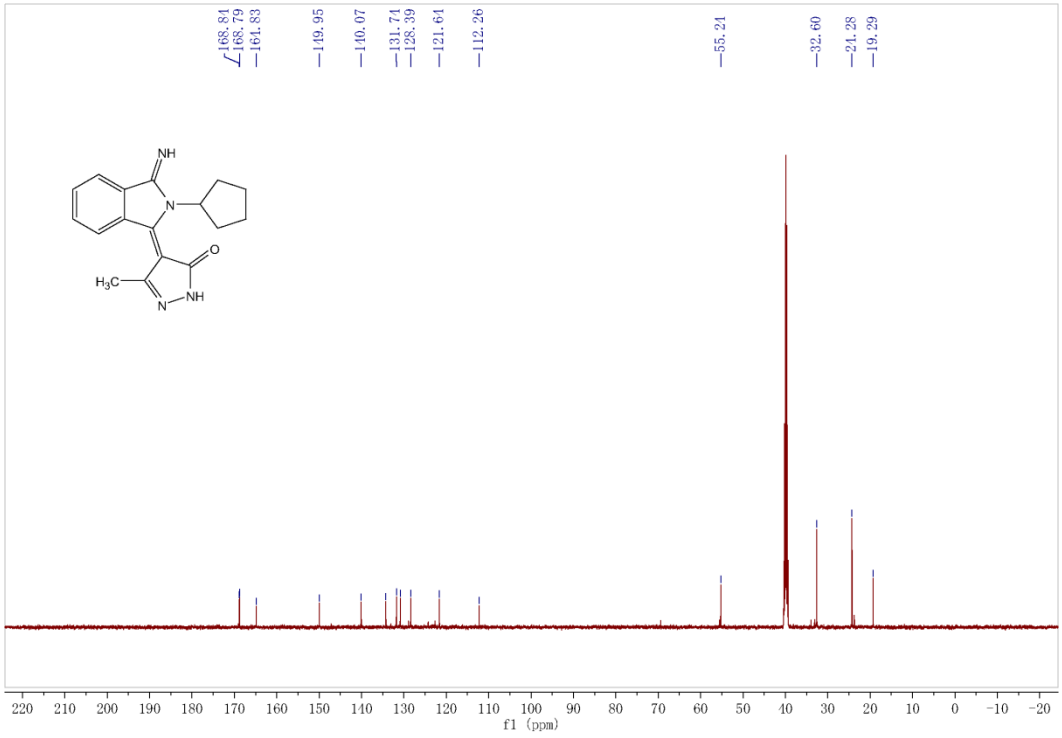


Red solid, yield 91%, mp 269.5–270.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.86 (s, 1H), 9.57 (dd, *J* = 6.0, 2.6 Hz, 1H), 9.53 (d, *J* = 6.4 Hz, 1H), 8.05 (dd, *J* = 5.7, 2.6 Hz, 1H), 7.65–7.53 (m, 2H), 4.58 (dd, *J* = 13.6, 4.9 Hz, 1H), 2.44 (s, 3H), 2.11 (m, 2H), 1.77–1.63 (m, 6H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 168.8, 168.7, 164.8, 149.9, 140.1, 134.2, 131.7, 130.8, 128.4, 121.6, 112.3, 55.2, 32.6(2C), 24.3(2C), 19.3; MS (ESI): *m/z* 295.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{19}N_4O$ $[M+H]^+$: 295.1553; Found: 295.1565.



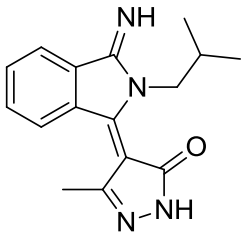
©ARKAT-USA, Inc

^{13}C NMR of 4-(2-cyclopentyl-3-iminoisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4h)

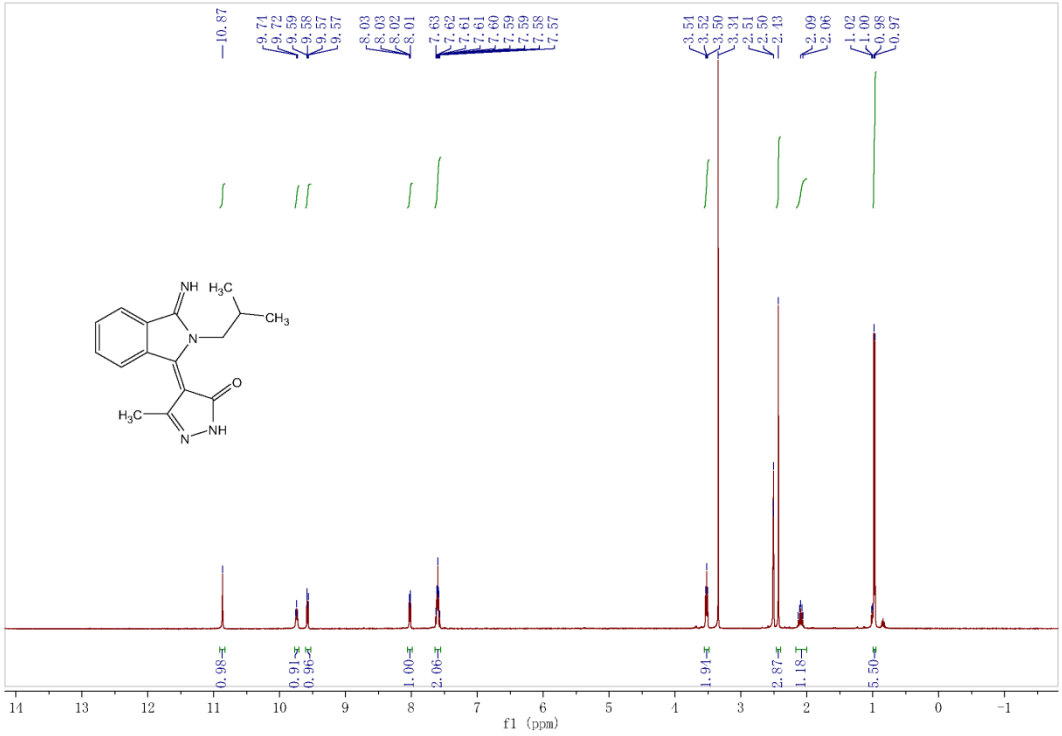


©ARKAT-USA, Inc

^{1}H NMR of 4-(3-imino-2-isobutylisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4i)

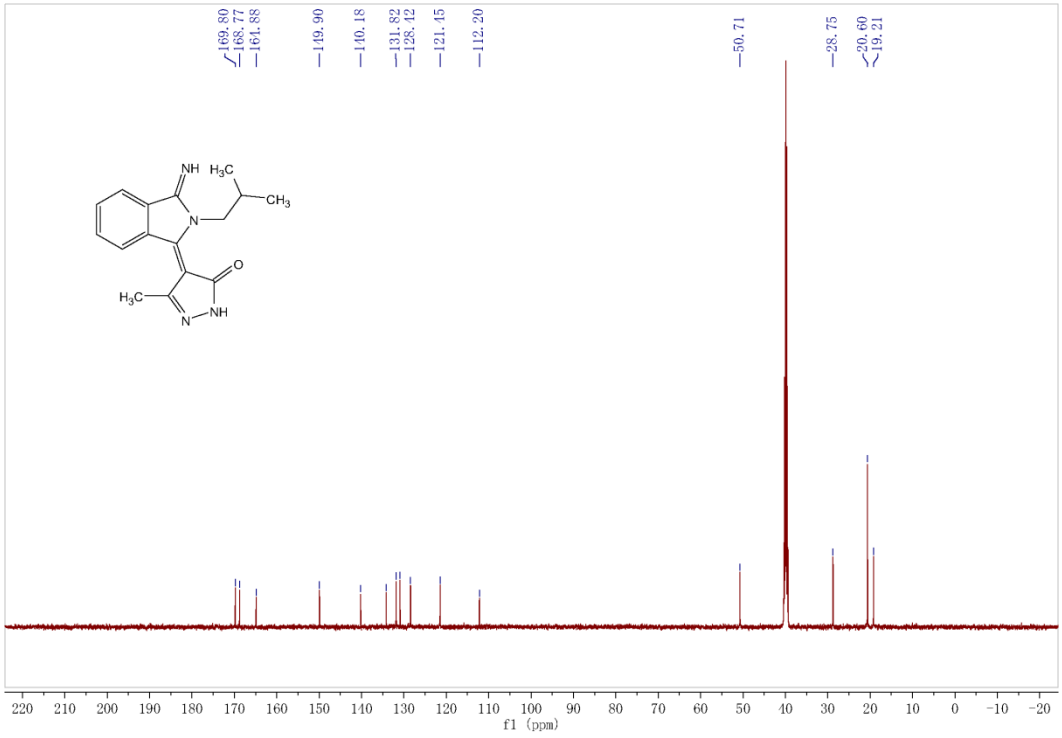


Red solid, yield 90%, mp 278.3–279.7 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.87 (s, 1H), 9.74 (t, J = 6.1 Hz, 1H), 9.58 (dd, J = 5.9, 2.2 Hz, 1H), 8.02 (dd, J = 5.7, 2.4 Hz, 1H), 7.64–7.55 (m, 2H), 3.52 (t, J = 6.5 Hz, 2H), 2.43 (s, 3H), 2.09 (dt, J = 13.4, 6.7 Hz, 1H), 0.97 (d, J = 6.7 Hz, 6H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.8, 168.7, 164.9, 149.9, 140.2, 134.2, 131.8, 130.9, 128.4, 121.4, 112.2, 50.7, 28.7, 20.6(2C), 19.2; MS (ESI): *m/z* 283.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{16}H_{19}N_4O$ $[M+H]^+$: 283.1553; Found: 283.1565.



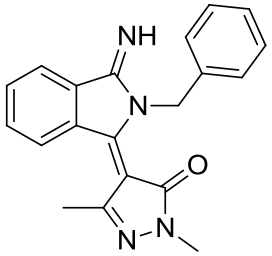
 ©ARKAT-USA, Inc

^{13}C NMR of 4-(3-imino-2-isobutylisoindolin-1-ylidene)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4i)

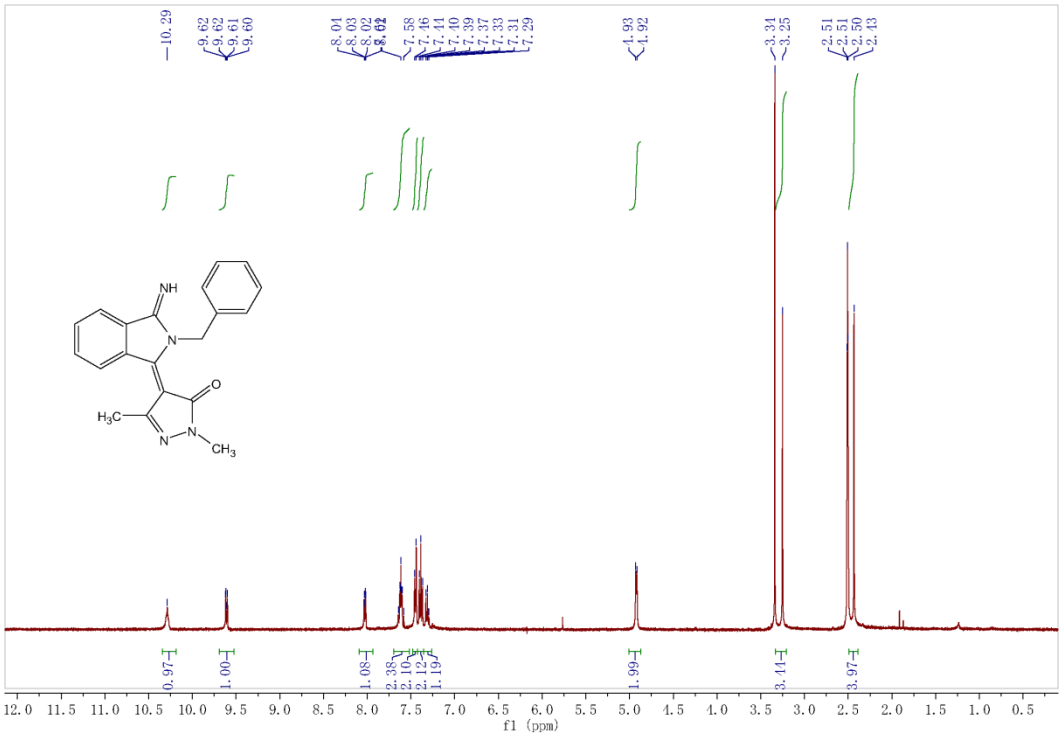


©ARKAT-USA, Inc

^{1}H NMR of 4-(2-benzyl-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4j)

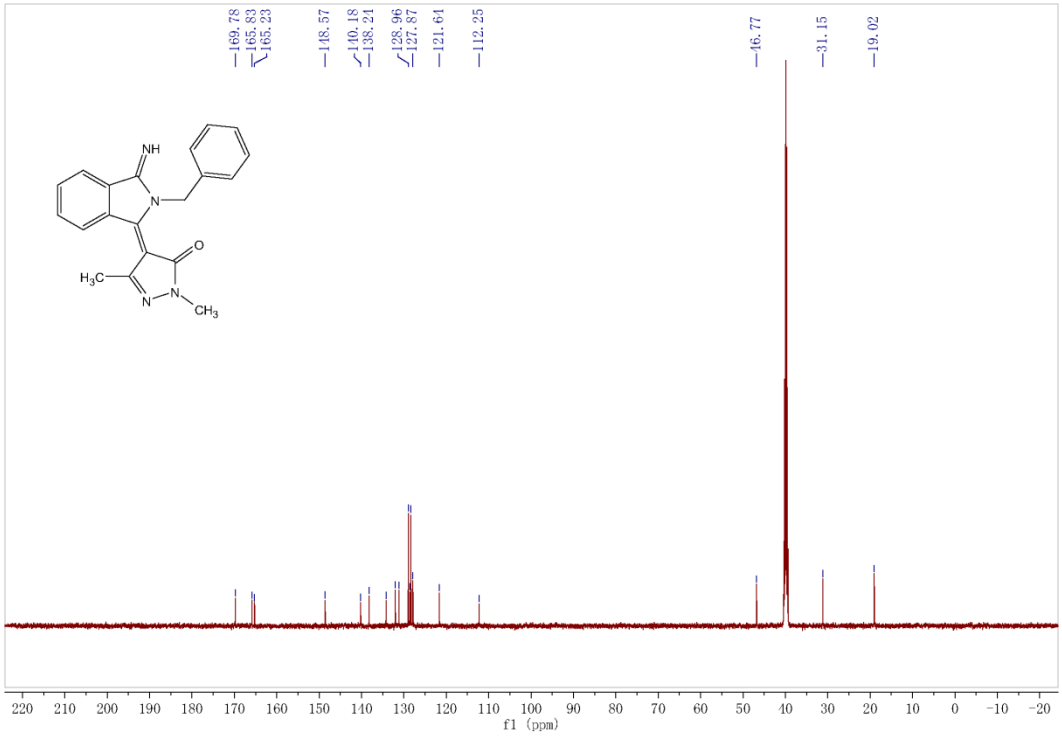


Red solid, yield 94%, mp 118.3–120.1 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.29 (s, 1H), 9.61 (dd, J = 6.2, 2.3 Hz, 1H), 8.03 (dd, J = 5.7, 2.0 Hz, 1H), 7.64–5.59 (m, 2H), 7.45 (d, J = 7.2 Hz, 2H), 7.39 (t, J = 7.4 Hz, 2H), 7.31 (t, J = 7.2 Hz, 1H), 4.92 (d, J = 5.5 Hz, 2H), 3.25 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.8, 165.8, 165.2, 148.6, 140.2, 138.2, 134.2, 132.0, 131.2, 128.9(2C), 128.6, 128.3(2C), 127.8, 121.6, 112.3, 46.8, 31.2, 19.0; MS (ESI): *m/z* 331.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{20}H_{19}N_4O$ $[M+H]^+$: 331.1553; Found: 331.1565.



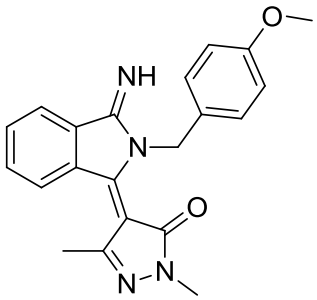
©ARKAT-USA, Inc

^{13}C NMR of 4-(2-benzyl-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4j)

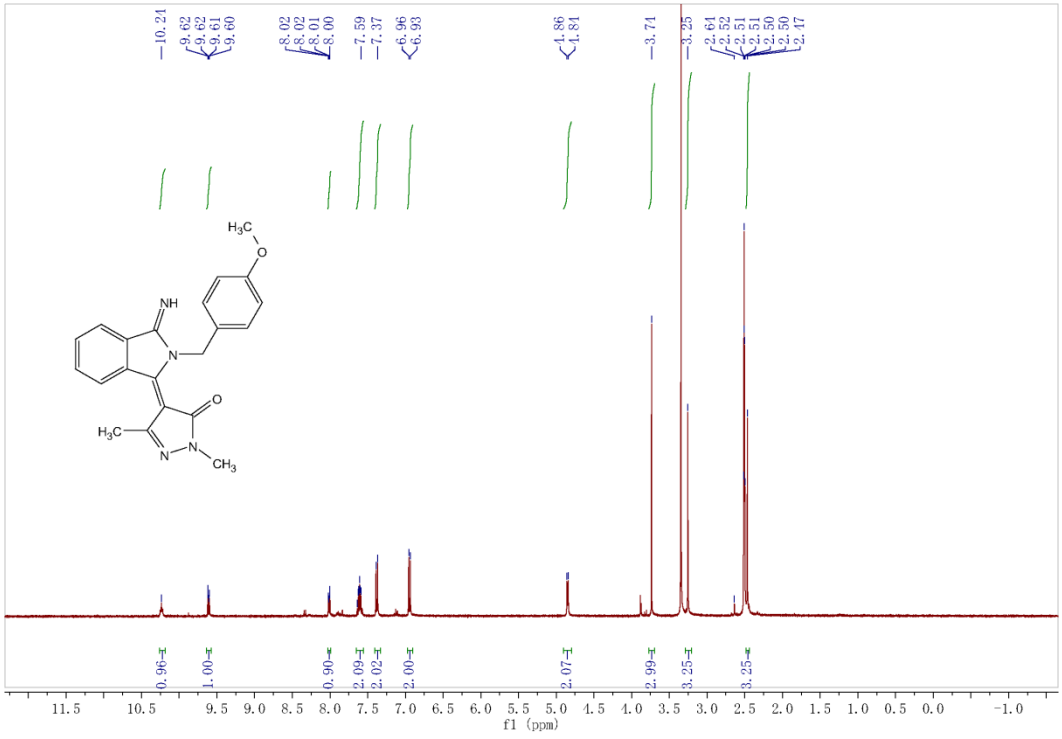


 ©ARKAT-USA, Inc

^{1}H NMR of 4-(3-imino-2-(4-methoxybenzyl)isoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4k)

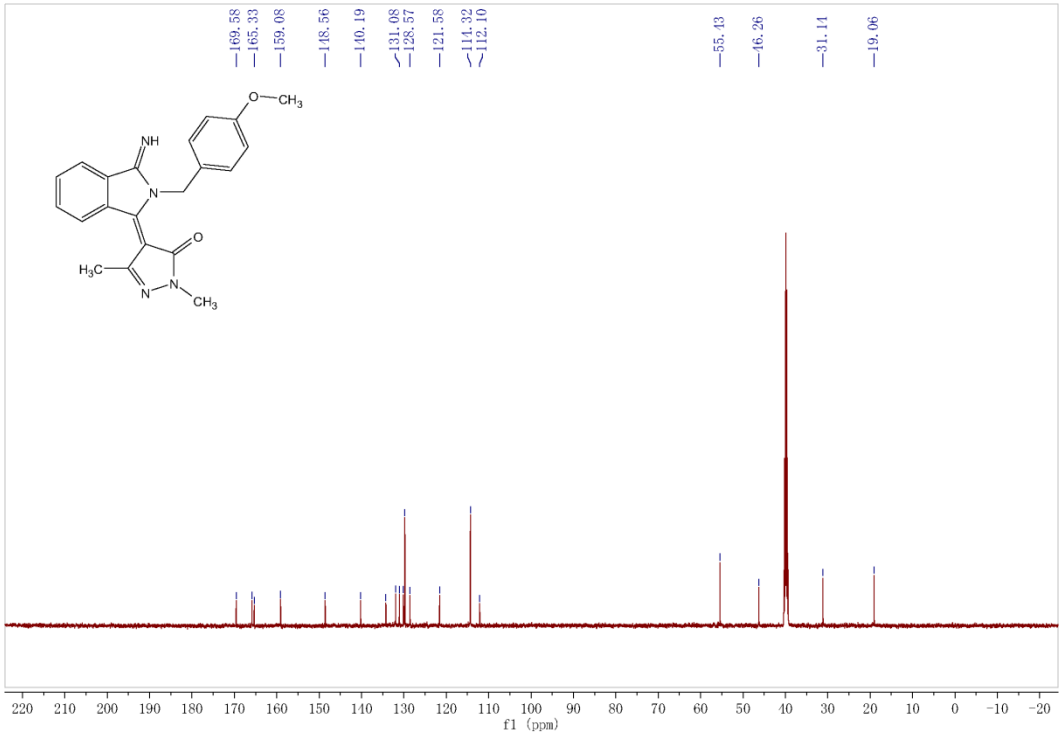


Red solid, yield 93%, mp 93.4–94.2 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.24 (s, 1H), 9.61 (dd, *J* = 6.2, 1.9 Hz, 1H), 8.01 (dd, *J* = 6.4, 2.3 Hz, 1H), 7.64–7.59 (m, 2H), 7.38 (d, *J* = 8.7 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 2H), 4.85 (d, *J* = 5.9 Hz, 2H), 3.74 (s, 3H), 3.25 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.6, 165.8, 165.3, 159.1, 148.6, 140.2, 134.2, 131.9, 131.1, 130.1, 129.8(2C), 128.6, 121.6, 114.3 (2C), 112.1, 55.4, 46.3, 31.1, 19.1; MS (ESI): *m/z* 361.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{21}H_{21}N_4O_2$ $[M+H]^+$: 361.1659; Found: 361.1667.



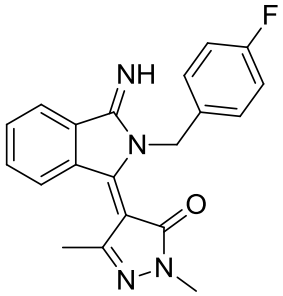
 ©ARKAT-USA, Inc

^{13}C NMR of 4-(3-imino-2-(4-methoxybenzyl)isoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4k)

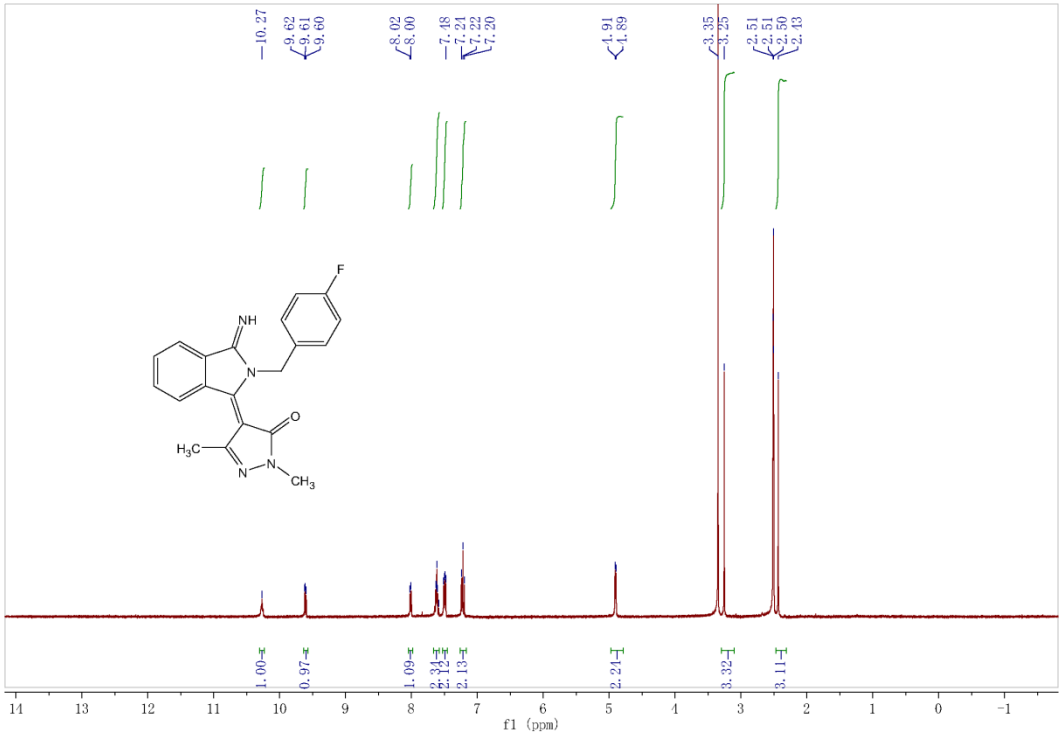


©ARKAT-USA, Inc

^{1}H NMR of 4-(2-(4-fluorobenzyl)-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4l)

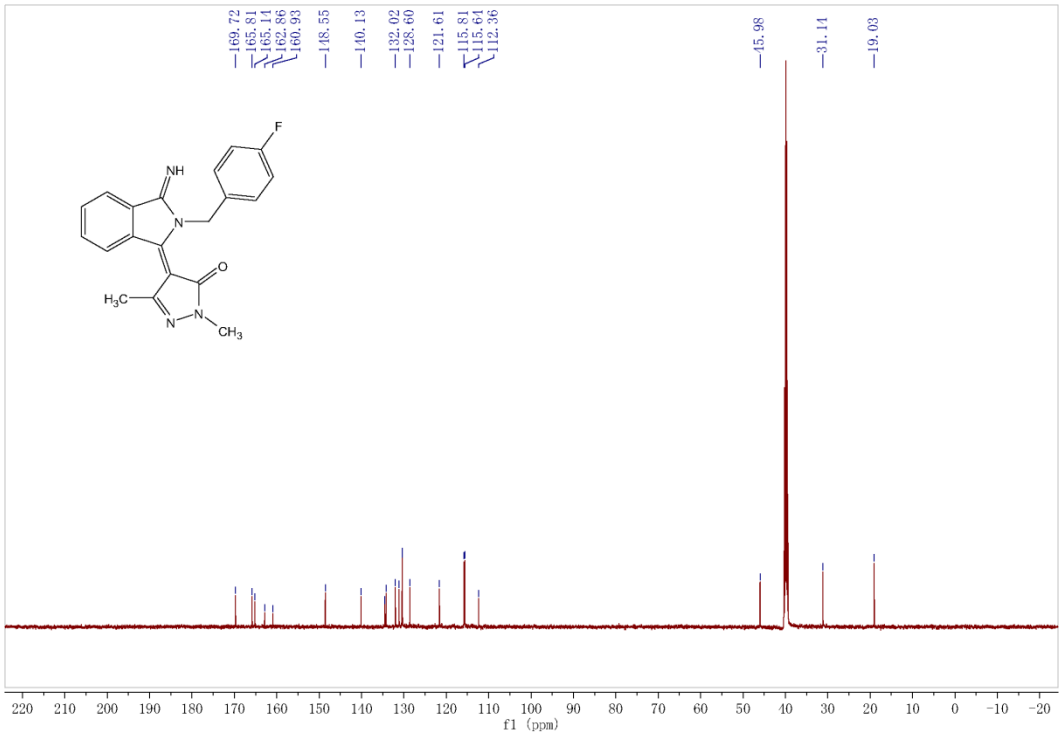


Red solid, yield 90%, mp 146.7–148.3 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.27 (s, 1H), 9.61 (dd, J = 6.1, 2.1 Hz, 1H), 8.01 (dd, J = 6.1, 2.4 Hz, 1H), 7.63–7.59 (m, 2H), 7.49 (dd, J = 8.7, 5.6 Hz, 2H), 7.22 (t, J = 8.9 Hz, 2H), 4.90 (d, J = 5.8 Hz, 2H), 3.25 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.7, 165.8, 165.1, 162.86, and 160.93 ($^1J_{CF}$ = 241.0 Hz), 148.6, 140.1, 134.50, and 134.47 ($^4J_{CF}$ = 3.8 Hz), 134.2, 132.0, 131.2, 130.42, and 130.36 ($^3J_{CF}$ = 7.5 Hz)(2C), 128.6, 121.6, 115.81, and 115.64 ($^2J_{CF}$ = 21.2 Hz)(2C), 112.4, 46.0, 31.1, 19.0; MS (ESI): *m/z* 349.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{20}H_{18}FN_4O$ $[M+H]^+$: 349.1459; Found: 349.1467.



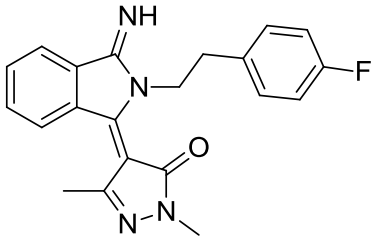
 ©ARKAT-USA, Inc

^{13}C NMR of 4-(2-(4-fluorobenzyl)-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4l)

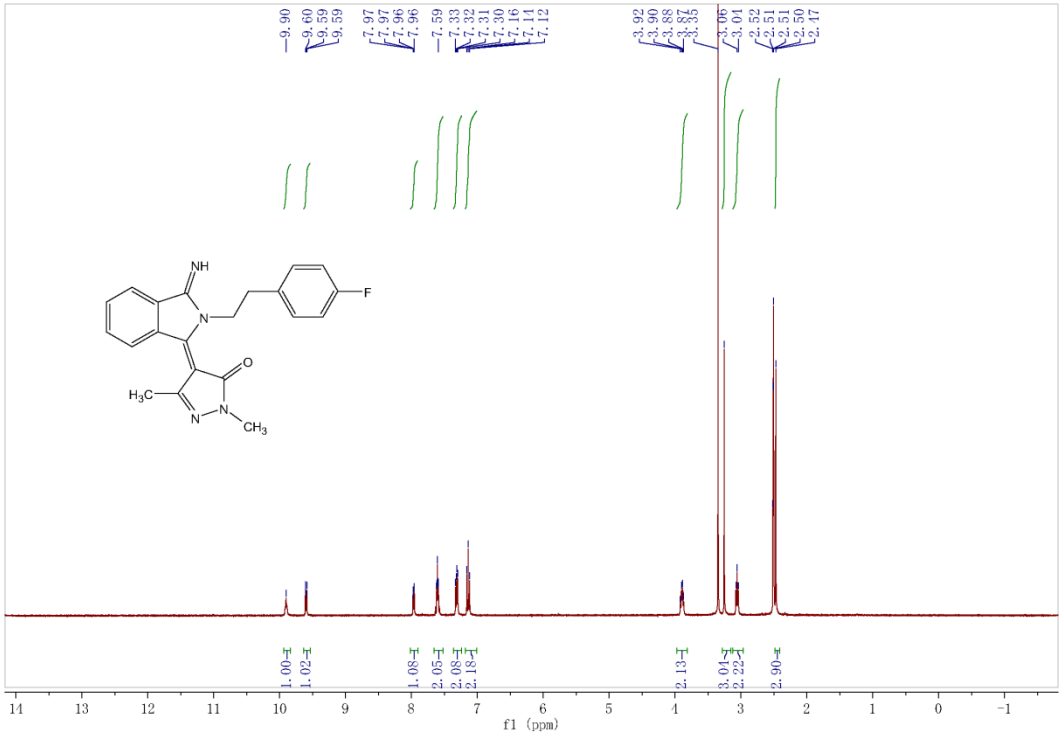


 ©ARKAT-USA, Inc

^{1}H NMR of 4-(2-(4-fluorophenethyl)-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4m)

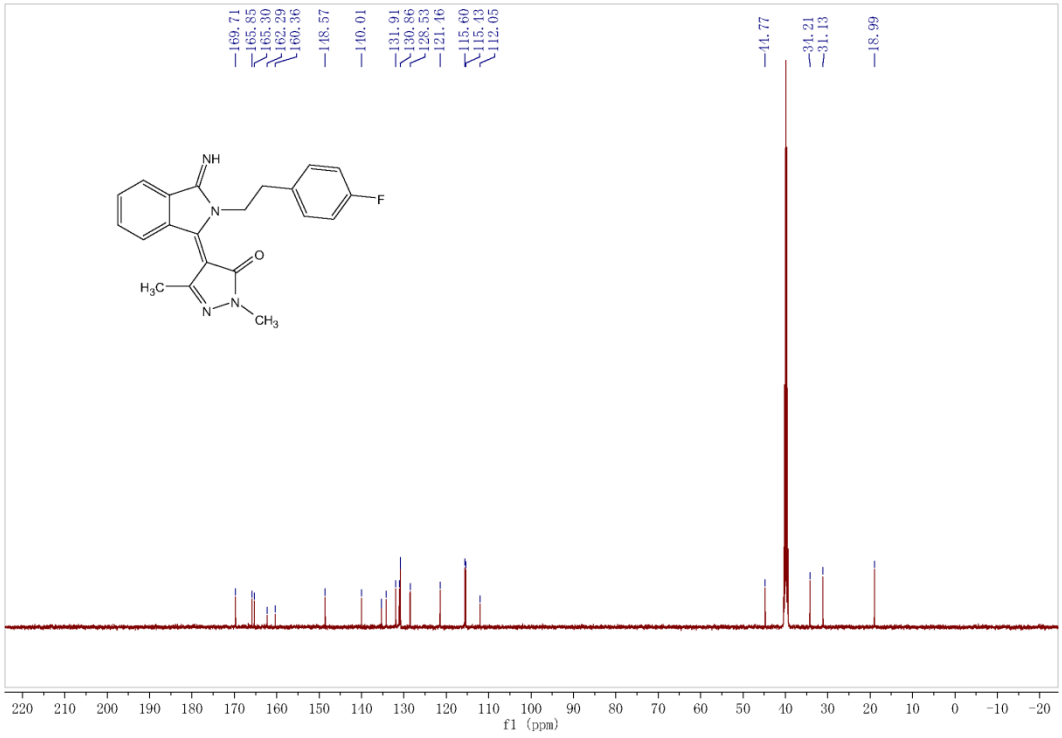


Red solid, yield 92%, mp 196.3–197.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.90 (s, 1H), 9.60 (dd, J = 5.9, 2.3 Hz, 1H), 7.96 (dd, J = 5.2, 1.9 Hz, 1H), 7.63–7.59 (m, 2H), 7.31 (dd, J = 8.7, 5.6 Hz, 2H), 7.14 (t, J = 8.9 Hz, 2H), 3.89 (dd, J = 13.8, 6.8 Hz, 2H), 3.25 (s, 3H), 3.06 (t, J = 7.3 Hz, 2H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.7, 165.9, 165.3, 162.29, and 160.36 ($^1J_{CF}$ = 241.3 Hz), 148.6, 140.0, 135.29, and 135.27 ($^4J_{CF}$ = 2.5 Hz), 134.2, 131.9, 131.1, 130.86, and 130.80 ($^3J_{CF}$ = 7.5 Hz)(2C), 128.5, 121.5, 115.60, and 115.43 ($^2J_{CF}$ = 21.2 Hz)(2C), 112.1, 44.8, 34.2, 31.1, 19.0; MS (ESI): *m/z* 363.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{21}H_{20}FN_4O$ $[M+H]^+$: 363.1616; Found: 363.1623.



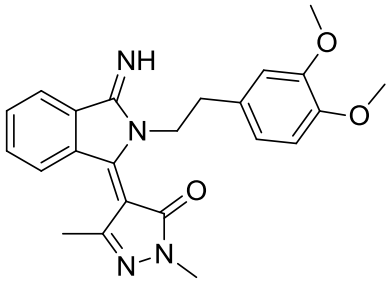
 ©ARKAT-USA, Inc

^{13}C NMR of 4-(2-(4-fluorophenethyl)-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4m)

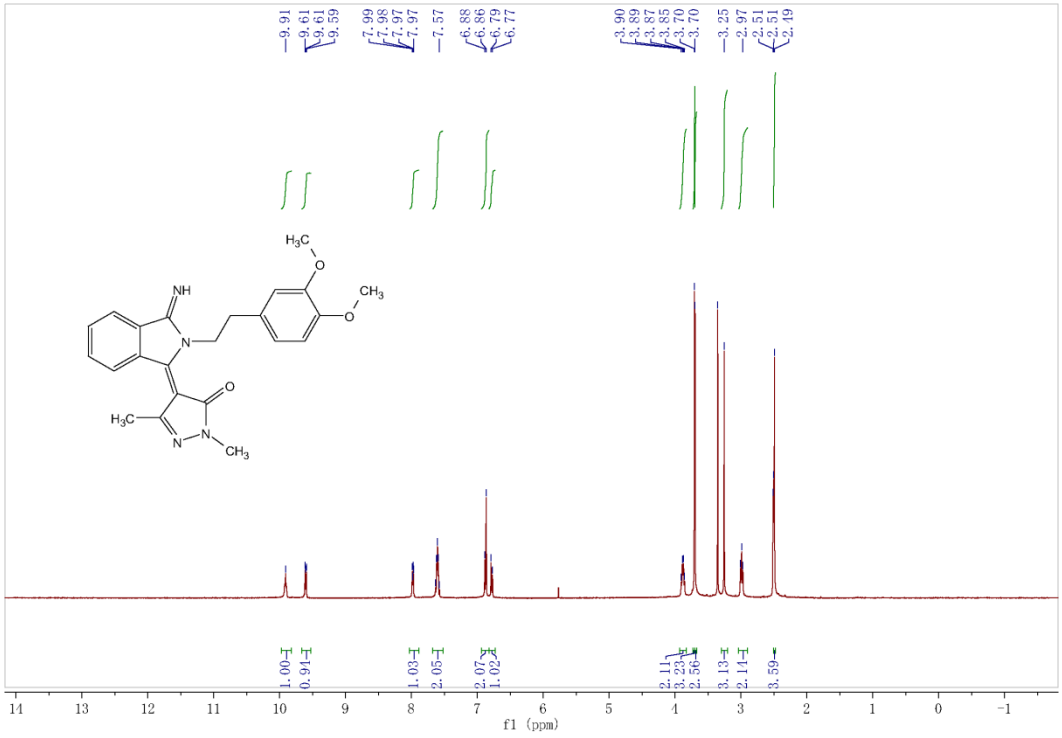


 ©ARKAT-USA, Inc

^{1}H NMR of 4-(2-(3,4-dimethoxyphenethyl)-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4n)

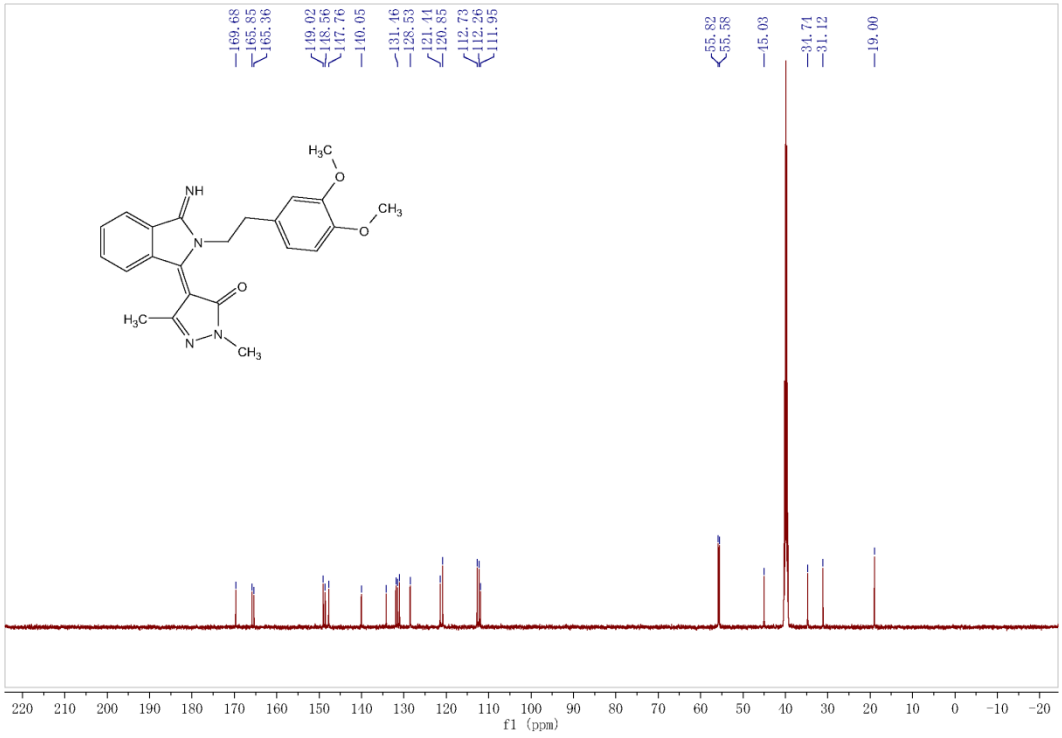


Red solid, yield 88%, mp 98.3–99.6 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.91 (s, 1H), 9.60 (dd, J = 5.6, 2.0 Hz, 1H), 7.98 (dd, J = 5.6, 2.6 Hz, 1H), 7.63–7.59 (m, 2H), 6.87 (d, J = 8.0 Hz, 2H), 6.78 (d, J = 8.1 Hz, 1H), 3.88 (dd, J = 13.4, 7.0 Hz, 2H), 3.70 (s, 3H), 3.70 (s, 2H), 3.25 (s, 3H), 2.99 (t, J = 7.4 Hz, 2H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.7, 165.9, 165.4, 149.0, 148.6, 147.8, 140.1, 134.2, 131.9, 131.5, 131.0, 128.5, 121.4, 120.9, 112.7, 112.3, 111.9, 55.8, 55.6, 45.0, 34.7, 31.1, 19.0; MS (ESI): *m/z* 405.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{23}H_{25}N_4O_3$ $[M+H]^+$: 405.1921; Found: 405.1932.



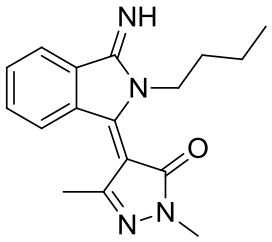
 ©ARKAT-USA, Inc

^{13}H CMR of 4-(2-(3,4-dimethoxyphenethyl)-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4n)

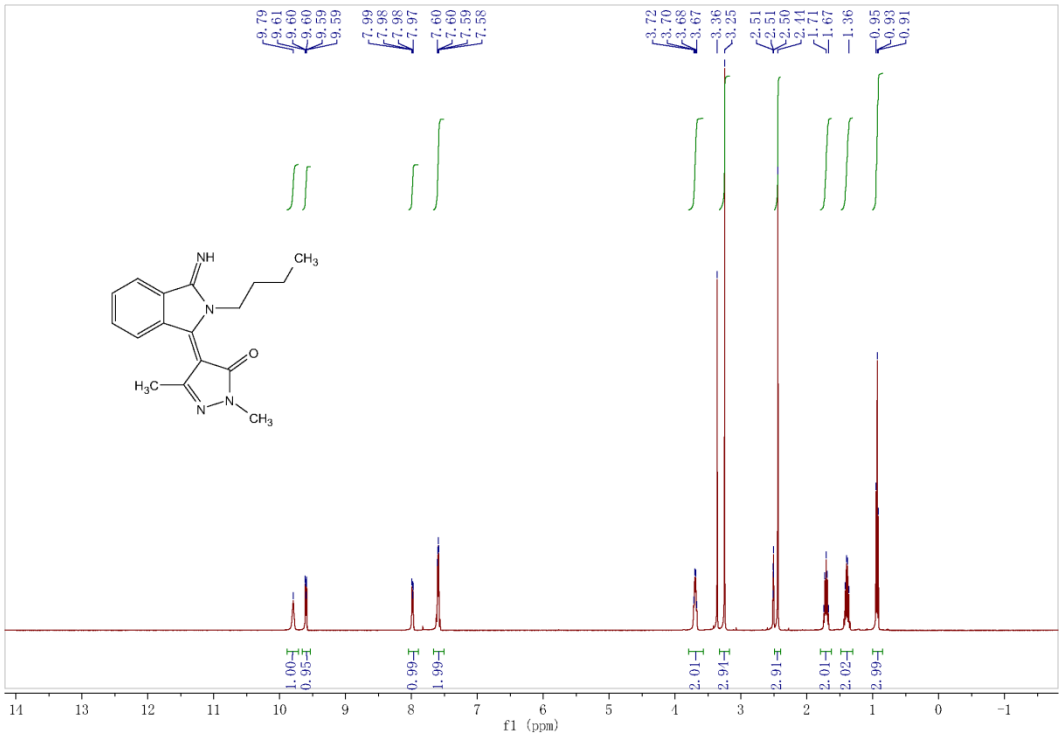


 ©ARKAT-USA, Inc

^{1}H NMR of 4-(2-butyl-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4o)

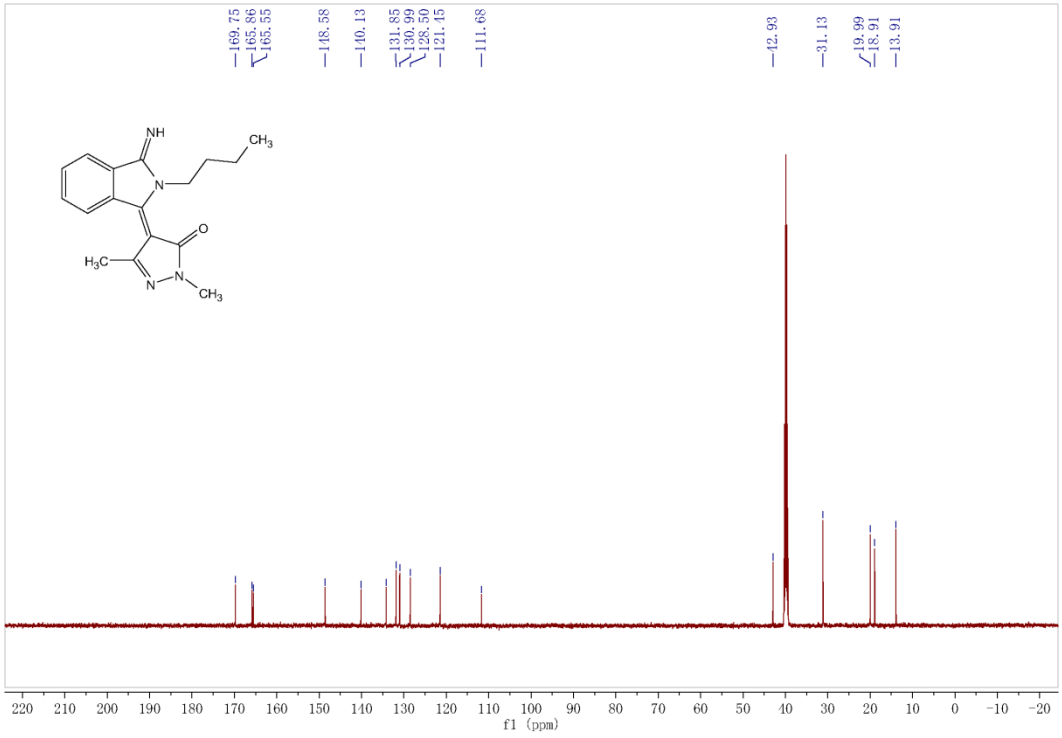


Red solid, yield 92%, mp 91.6–92.8 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.79 (s, 1H), 9.62–9.59 (m, 1H), 7.98 (dd, J = 5.4, 3.1 Hz, 1H), 7.62–7.56 (m, 2H), 3.69 (dd, J = 12.4, 6.4 Hz, 2H), 3.25 (s, 3H), 2.44 (s, 3H), 1.74–1.67 (m, 2H), 1.42–1.36 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.8, 165.9, 165.6, 148.6, 140.1, 134.2, 131.9, 131.0, 128.5, 121.5, 111.7, 42.9, 31.1(2C), 20.0, 18.9, 13.9; MS (ESI): *m/z* 297.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{21}N_4O$ $[M+H]^+$: 297.1710; Found: 297.1723.



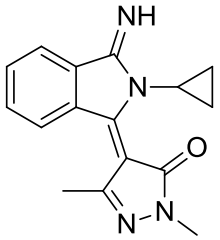
 ©ARKAT-USA, Inc

^{13}C NMR of 4-(2-butyl-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4o)

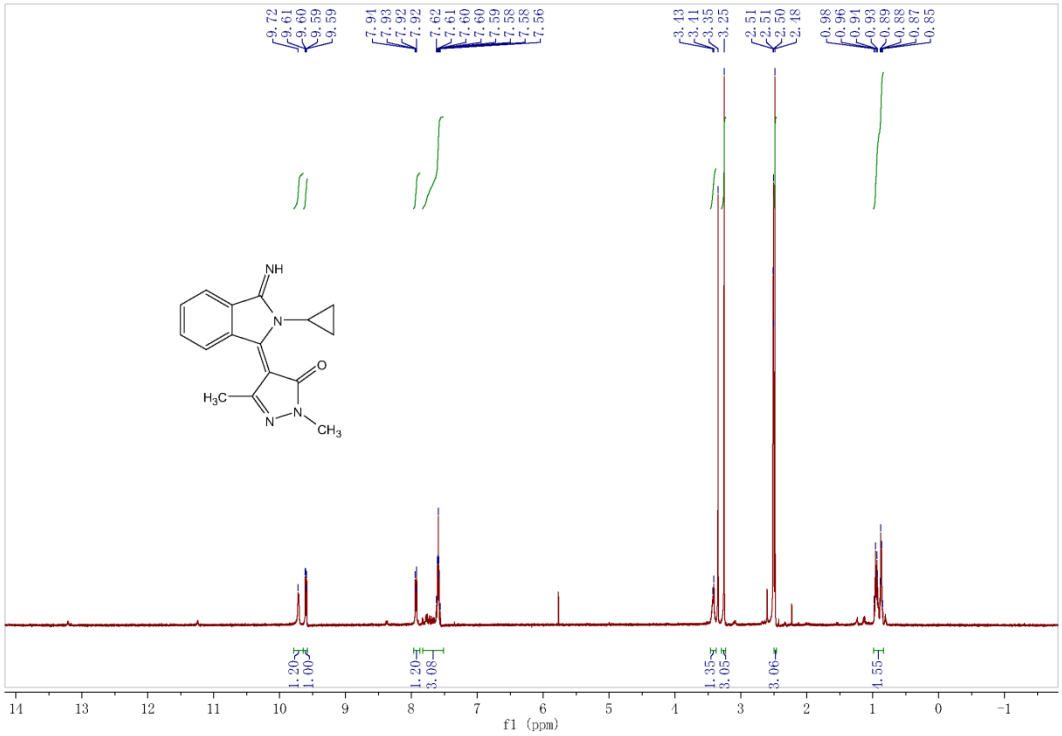


©ARKAT-USA, Inc

^{1}H NMR of 4-(2-cyclopropyl-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4p)

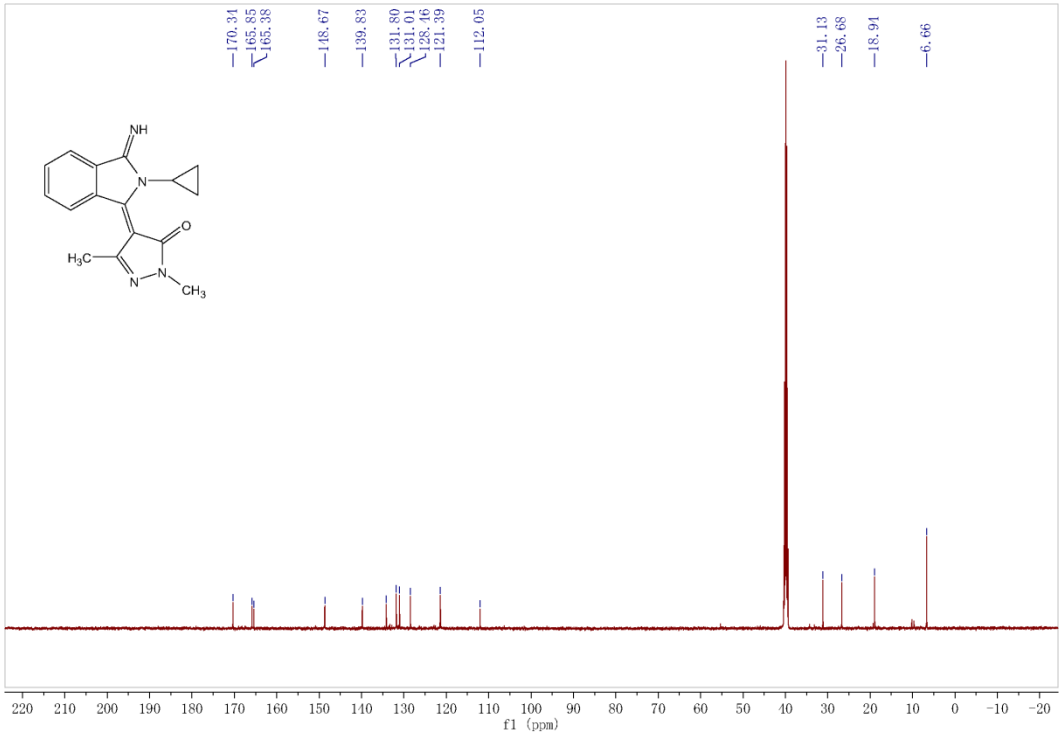


Red solid, yield 85%, mp 171.3–172.5 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.72 (s, 1H), 9.60 (dd, J = 6.1, 2.6 Hz, 1H), 7.93 (dd, J = 5.7, 2.8 Hz, 1H), 7.62–7.56 (m, 3H), 3.45–3.38 (m, 1H), 3.25 (s, 3H), 2.48 (s, 3H), 0.98–0.85 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 170.3, 165.9, 165.4, 148.7, 139.8, 134.1, 131.8, 131.0, 128.5, 121.4, 112.1, 31.1, 26.7, 18.9, 6.7(2C); MS (ESI): *m/z* 281.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{16}H_{17}N_4O$ $[M+H]^+$: 281.1397; Found: 281.1409.



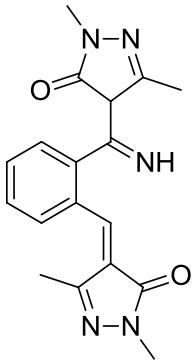
©ARKAT-USA, Inc

^{13}C NMR of 4-(2-cyclopropyl-3-iminoisoindolin-1-ylidene)-1,3-dimethyl-1*H*-pyrazol-5(4*H*)-one (4p)

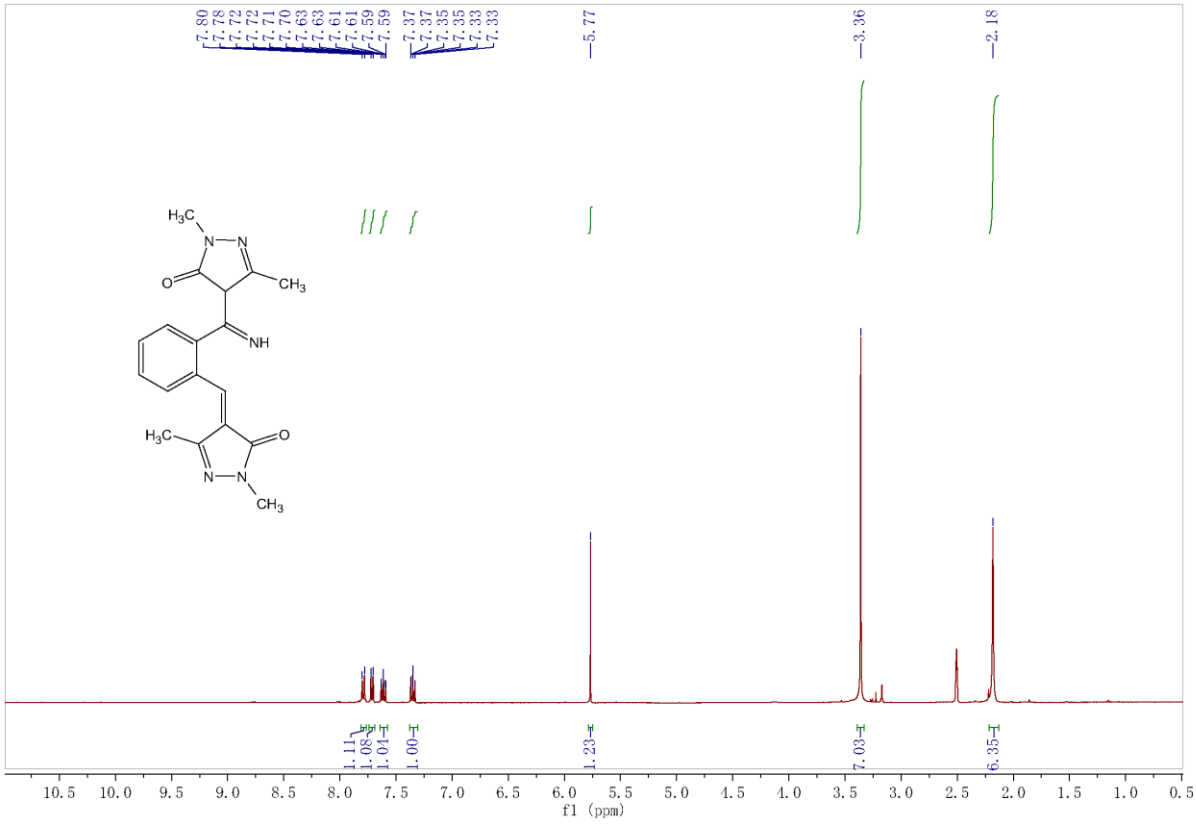


©ARKAT-USA, Inc

^{1}H NMR of compound 6b



^{1}H NMR (400 MHz, DMSO-d_6): δ 7.79 (d, J = 7.9 Hz, 1H), 7.71 (dd, J = 7.7, 1.1 Hz, 1H), 7.61 (td, J = 7.9, 1.4 Hz, 1H), 7.35 (td, J = 7.6, 0.9 Hz, 1H), 5.77 (s, 1H), 3.36 (s, 7H), 2.18 (s, 6H); MS (ESI): *m/z* 338.3 $[M+H]^+$; HRMS (ESI) Calcd for $C_{18}H_{20}N_5O_2$ $[M+H]^+$: 338.1612; Found: 338.1620.



 ©ARKAT-USA, Inc