Sequential [3+2] annulation reaction of prop-2-ynylsulfonium salts and hydrazonyl chlorides: synthesis of pyrazoles containing functional motifs

Tao Shi,†,a,c Zhaoxiao Wu,†,a,c Tingting Jia,a,c Chong Zhang,a Linghui Zeng,a Rangxiao Zhuang,b Jiankang Zhang,a,c Shourong Liu,*b Jiaan Shao,*a,c and Huajian Zhu*a,c

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1. General information

All the solvents were used from commercially available sources without any purification. White solid, yield referred to isolated compounds, unless noted otherwise. Reactions were monitored by TLC using a UV lamp as a visualizing agent. Low temperature conditions require the use of cryostat. The $^1$H NMR and $^{13}$C NMR spectra were recorded at 400, 500 MHz and 100,125 MHz, respectively, in CDCl$_3$/$_6$-DMSO solutions with shifts referenced to tetramethylsilane (TMS). All J values are in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. LC-MS equipment was used to record mass spectra for isolated compounds where appropriate.

2. General procedure for the synthesis of 1

![Chemical structure](image)

A (20 mmol) and B (20 mmol) were dissolved in 50 mL EtOH and the reaction mixture was stirred at room temperature until consumption of A (about need 5-30 min, monitored by TLC,). Then, by concentrating the reaction system under reduced pressure the solid product C was obtained.

Dissolve NCS (15 mmol) in 100 mL DCM and stir at 0 °C for 5 minutes. A solution of Me$_2$S (20 mmol) in DCM (20 mL) was added dropwise until the white precipitate suddenly appeared. After stirring for 15 minutes, the reaction mixture was cooled to -40 °C. Add solution of C (10 mmol) in DCM (30 mL) dropwise to the above reaction system. After the addition, react at -40 °C for 1 hour and then raise the temperature to 0 °C. After the reaction is complete, the solvent was evaporated and through column chromatography to obtain the solid 1.$^1$

3. General procedure for the synthesis of 2

![Chemical structure](image)

D (20 mmol) and Me$_2$S (40 mmol) were dissolved in 50 mL MeCN and the reaction mixture was stirred at room temperature overnight. The reaction mixture was filtrated and the filter residue was washed with 30 ml petroleum ether and dried under vacuum to obtain 2 as white solid.
4. General procedure for the synthesis of 3

\[ \text{1 (1 mmol), 2 (2 mmol) and K}_2\text{CO}_3 (2 \text{ mmol}) \text{ were added in 10 mL CHCl}_3 \text{ under N}_2, \text{ then the reaction mixture was stirred at 0 °C for 24 h. After the completion of the reaction, the reaction mixture was filtrated. The filtrate was concentrated and purified by flash column chromatography (petroleum ether: ethyl acetate = 80:1) to obtain the product 3.} \]

5. General procedure for the synthesis of 4

\[ \text{1 (1 mmol), 2 (2 mmol), NaI (5.0 eq) and K}_2\text{CO}_3 (2 \text{ mmol}) \text{ were added in 10 mL CHCl}_3 \text{ under N}_2, \text{ then the reaction mixture was stirred at 0 °C for 24 h. After the completion of the reaction, the reaction mixture was filtrated. The filtrate was concentrated and purified by flash column chromatography (petroleum ether: ethyl acetate = 80:1) to obtain the product 4.} \]

6. Synthesis of 5, 6, 7, 8, 9

\[ \text{3a (0.3 mmol), KF (0.6 mmol), CuI (0.45 mmol) and Trifluoromethyltrimethylsilane (0.6 mmol) were dissolved in DMF (2 mL). Reaction mixture was stirred at room temperature for 12 h. Then concentrate the reaction mixture and obtain 5 by column chromatography (petroleum ether: ethyl acetate = 50:1).} \]

Dissolve 3a (0.3 mmol) in 2 mL DMSO, NaN\(_3\) (0.33 mmol) was added, then the reaction mixture was stirred at room temperature for 12h. After completion of the reaction as monitored by TLC, the reaction mixture was extracted by DCM. The DCM layer was concentrated and purified by column chromatography (petroleum ether: ethyl acetate = 50:1) to obtain the 6.
AgSbF$_6$ (0.5 mmol) was added to the solution of 3a in CH$_3$CN (2 mL) and the reaction mixture was stirred at room temperature for 12h. After completion of the reaction as monitored by TLC, the reaction mixture was filtered and the filtrate was concentrated. Then the concentrate was purified by column chromatography (petroleum ether: ethyl acetate = 50:1) to obtain the 7.$^4$

Isopropanol (1mL) was added to the mixture of 3a (0.3 mmol) and FeSO$_4$ (0.3 mmol). Reaction mixture was stirred at 50 ℃ for 4h. After the completion of the reaction, the mixture was filtered. The filtrates was concentrated and the residue was purified by column chromatography (petroleum ether: ethyl acetate = 50:1) to obtain the 8.$^5$

3a (0.3 mmol) and benzylamine (0.3 mmol) were dissolved in CH$_3$OH (2 mL). Reaction mixture was stirred at 40 ℃ for 4h. Then concentrate the reaction mixture and obtain 9 by column chromatography (petroleum ether: ethyl acetate = 50:1)$^6$.

7. The structure of 3u (NOESY)

According to the chemical shifts and the coupling constants in $^1$H NMR spectra, the signals of the key H-6, H-4, H-2’ and H-2” can be identify. Then as shown in NOESY of 3u, there are no correlations between H-6 and H-2’ which indicated that the structure can not be 3u’. Instead, we can find that there have correlations of H-6 with H-2” and H-4. Therefore, the structure of product should be 3u.
8. References


9. Analytical Data

5-(bromomethyl)-1,3-diphenyl-1H-pyrazole (3a)
White solid, yield: 65%, melting point: 95.3–96.2 °C.
$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.86 (dd, $J = 7.2$, 1.6 Hz, 2H), 7.67-7.63 (m, 2H), 7.54 (t, $J = 7.6$ Hz, 2H), 7.47 (t, $J = 7.2$ Hz, 1H), 7.42 (t, $J = 7.2$ Hz, 2H), 7.34 (t, $J = 7.2$ Hz, 1H), 6.85 (s, 1H), 4.51 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 152.2, 140.3, 139.3, 132.8, 129.6, 128.9, 128.8, 128.4, 126.0, 125.5, 106.2, 21.3; HRMS calcd for C$_{16}$H$_{13}$BrN$_2$+H$: 313.0335$, found: 313.0335.

5-(bromomethyl)-1-phenyl-3-(p-tolyl)-1H-pyrazole (3b)
White solid, yield: 64%, melting point: 100.1–100.5 °C.
$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.76 (d, $J = 8.0$ Hz, 2H), 7.68-7.62 (m, 2H), 7.57-7.50 (m, 2H), 7.50-7.43 (m, 1H), 7.23 (d, $J = 8.0$ Hz, 2H), 6.82 (s, 1H), 4.50 (s, 2H), 2.39 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 152.3, 140.2, 139.3, 138.2, 130.0, 129.6, 129.5, 128.7, 125.9, 125.4, 106.0, 21.5, 21.4; HRMS calcd for C$_{17}$H$_{15}$BrN$_2$+H$: 327.0491$, found: 327.0488.

5-(bromomethyl)-3-(4-methoxyphenyl)-1-phenyl-1H-pyrazole (3c)
White solid, yield: 62%, melting point: 108.8–109.2 °C.
$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.81-7.78 (m, 2H), 7.66-7.62 (m, 2H), 7.55-7.51 (m, 2H), 7.47-7.43 (m, 1H), 6.95 (d, $J = 8.8$ Hz, 2H), 6.77 (s, 1H), 4.50 (s, 2H), 3.84 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 159.9, 152.0, 140.2, 139.3, 129.6, 128.7, 127.2, 125.6, 125.4, 114.3, 105.7, 55.5, 21.4; HRMS calcd for C$_{17}$H$_{15}$BrN$_2$O+H$: 343.0441$, found: 343.0443.

5-(bromomethyl)-3-(4-fluorophenyl)-1-phenyl-1H-pyrazole (3d)
White solid, yield: 61%, melting point: 109.5–110.4 °C.
White solid, yield: 65%, melting point: 103.2-104.0 °C. 

1H-NMR (400 MHz, CDCl3): δ 7.85-7.81 (m, 2H), 7.63 (m, 2H), 7.56-7.52 (m, 2H), 7.49-7.45 (m, 1H), 7.10 (t, J = 8.8 Hz, 2H), 6.79 (s, 1H), 4.50 (s, 2H); 13C NMR (100 MHz, CDCl3): δ 163.1 (d, J = 246 Hz), 151.3, 140.5, 139.2, 129.7, 128.9, 127.6 (d, J = 8 Hz), 125.4, 125.3, 115.8 (d, J = 21 Hz), 105.9, 21.2; HRMS calcd for C16H12BrFN2+H+: 331.0241, found: 331.0238.

5-(bromomethyl)-3-(4-chlorophenyl)-1-phenyl-1H-pyrazole (3e) 
White solid, yield: 66%, melting point: 103.2-104.0 °C. 

1H-NMR (400 MHz, CDCl3): δ 7.79 (d, J = 7.2 Hz, 2H), 7.67-7.60 (m, 2H), 7.58-7.51 (m, 2H), 7.50-7.44 (m, 1H), 7.38 (d, J = 7.2 Hz, 2H), 6.81 (s, 1H), 4.49 (s, 2H); 13C NMR (100 MHz, CDCl3): δ 151.1, 140.6, 139.1, 134.2, 131.4, 129.7, 129.1, 129.0, 127.2, 125.4, 106.1, 21.1; HRMS calcd for C16H12BrClN2+H+: 346.9945, found: 346.9941.

5-(bromomethyl)-3-(4-bromophenyl)-1-phenyl-1H-pyrazole (3f) 
White solid, yield: 61%, melting point: 103.2-103.9 °C. 

1H-NMR (400 MHz, CDCl3): δ 7.73 (d, J = 8.4 Hz, 2H), 7.66-7.60 (m, 2H), 7.54 (m, 4H), 7.47 (t, J = 7.3 Hz, 1H), 6.82 (s, 1H), 4.50 (s, 2H); 13C NMR (100 MHz, CDCl3): δ 151.1, 140.6, 139.1, 132.0, 131.9, 129.7, 129.0, 127.5, 125.4, 122.3, 106.0, 21.1; HRMS calcd for C16H12Br2N2+H+: 390.9440, found: 390.9435.

5-(bromomethyl)-1-phenyl-3-(4-(trifluoromethyl)phenyl)-1H-pyrazole (3g) 
White solid, yield: 67%, melting point: 114.2-115.7 °C. 

1H-NMR (400 MHz, CDCl3): δ 7.97 (d, J = 8.0 Hz, 2H), 7.68-7.64 (m, 4H), 7.58-7.54 (m, 2H), 7.49 (d, J = 7.2 Hz, 1H), 6.89 (s, 1H), 4.51 (s, 2H); 13C NMR (100 MHz, CDCl3): δ 150.8, 140.8, , 139.1, 129.7, 129.4 (q, J = 32 Hz), 129.1, 126.1, 125.9 (q, J = 4 Hz), 125.5, 124.1 (q, J = 270 Hz), 106.4, 21.0; HRMS calcd for C13H12BrF3N2+H+: 381.0209, found: 381.0207.

4-(5-(bromomethyl)-1-phenyl-1H-pyrazol-3-yl)benzonitrile (3h) 
White solid, yield: 65%, melting point: 137.5-138.3°C.
$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.95 (d, $J = 7.6$ Hz, 2H), 7.69 (d, $J = 8.0$ Hz, 2H), 7.66-7.60 (m, 2H), 7.59-7.53 (m, 1H), 7.53-7.46, 6.89 (s, 1H), 4.50 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 150.2, 141.1, 138.9, 137.3, 132.8, 129.8, 129.3, 126.3, 125.4, 119.2, 111.7, 106.6, 20.8; HRMS calcd for C$_{17}$H$_{12}$BrN$_3$+H$: 338.0287$, found: 338.0288.

5-(bromomethyl)-3-(3-methoxyphenyl)-1-phenyl-1H-pyrazole (3i)
White solid, yield: 65%, melting point: 103.2~103.9 °C.
$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.67-7.63 (m, 2H), 7.56-7.51 (m, 2H), 7.49-7.46 (m, 1H), 7.45-7.42 (m, 2H), 7.33 (t, $J = 7.8$ Hz, 1H ), 6.91-6.87 (m, 1H), 6.83 (s, 1H), 4.50 (s, 2H ), 3.87 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 160.2, 152.1, 140.3, 139.3, 134.2, 129.9, 129.6, 128.8, 125.5, 118.6, 114.5, 111.0, 106.3, 55.6, 21.3; HRMS calcd for C$_{17}$H$_{15}$BrN$_2$O+H$: 343.0441$, found: 343.0444.

5-(bromomethyl)-3-(2-methoxyphenyl)-1-phenyl-1H-pyrazole (3j)
White solid, yield: 49%, melting point: 117.1~118.1 °C.
$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 8.06 (dd, $J = 7.6$, 1.6 Hz, 1H), 7.68-7.65 (m, 2H), 7.55-7.51 (m, 2H), 7.47-7.43 (m, 1H), 7.36-7.30 (m, 1H), 7.12 (d, $J = 2.4$ Hz, 1H ), 7.04 (dd, $J = 7.6$, 1.2 Hz, 1H), 7.00 (d, $J = 8.0$ Hz, 1H), 4.59 (s, 2H ), 3.94 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 157.1, 149.1, 139.4, 139.2, 129.5, 129.4, 128.9, 128.6, 125.4, 121.7, 121.1, 111.5, 110.4, 55.7, 21.7; HRMS calcd for C$_{17}$H$_{15}$BrN$_2$O+H$: 343.0441$, found: 343.0444.

5-(bromomethyl)-3-(3-chlorophenyl)-1-phenyl-1H-pyrazole (3k)
White solid, yield: 72%, melting point: 108.5~109.1 °C.
$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.88 (s, 1H), 7.72 (d, $J = 6.0$ Hz, 1H), 7.69-7.60 (m, 2H), 7.55 (s, 2H), 7.49 (d, $J = 6.0$ Hz, 1H), 7.35-7.27 (m, 2H ), 6.83 (s, 1H), 4.49 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 150.9, 140.6, 139.1, 134.9, 134.7, 130.2, 129.7, 129.0, 128.3, 126.1, 125.4, 124.1, 106.2, 21.1; HRMS calcd for C$_{16}$H$_{12}$BrClN$_2$+H$: 346.9945$, found: 346.9944.
5-(bromomethyl)-3-(2-chlorophenyl)-1-phenyl-1H-pyrazole (3l)
White solid, yield: 51%, melting point: 119.8~120.1 °C.
\[ \text{^1H-NMR (400 MHz, CDCl}_3\): } \delta 7.91 (dd, J = 7.6, 2.4 Hz, 1H), 7.68-7.64 (m, 2H), 7.56-7.52 (m, 2H), 7.49-7.45 (m, 2H), 7.33-7.27 (m, 2H), 7.10 (s, 1H ), 4.53 (s, 2H); \]
\[ \text{^13C NMR (100 MHz, CDCl}_3\): } \delta 149.8, 139.5, 139.2, 132.5, 131.8, 130.8, 130.6, 129.6, 129.4, 128.9, 127.1, 125.4, 110.1, 21.3; HRMS calcd for C_{16}H_{12}BrClN_{2}+H^+: 346.9945, found: 346.9941.

![Chemical structure of 5-(bromomethyl)-3-(2-chlorophenyl)-1-phenyl-1H-pyrazole (3l)](image)

5-(bromomethyl)-3-(2-fluorophenyl)-1-phenyl-1H-pyrazole (3m)
Pink solid, yield: 35%, melting point: 103.1~103.8 °C.
\[ \text{^1H-NMR (500 MHz, CDCl}_3\): } \delta 8.08 (m, 1H), 7.65 (m, 2H), 7.54 (m, 2H), 7.48 (m, 1H), 7.30 (m, 1H), 7.16 (m, 2H), 7.01 (d, J = 4 Hz, 1H), 4.52 (s, 2H); \]
\[ \text{^13C NMR (125 MHz, CDCl}_3\): } \delta 159.8 (d, J = 248 Hz), 146.6, 139.8, 139.0, 129.6, 129.5, 129.4, 128.7, 128.4 (d, J = 3 Hz), 125.3, 125.2, 124.3 (d, J = 3 Hz), 120.5 (d, J = 12 Hz), 116.1 (d, J = 22 Hz), 109.4 (d, J = 10 Hz), 21.0; HRMS calcd for C_{16}H_{12}BrClN_{2}+H^+: 331.0244, found: 331.0244.

![Chemical structure of 5-(bromomethyl)-3-(2-fluorophenyl)-1-phenyl-1H-pyrazole (3m)](image)

5-(bromomethyl)-3-(naphthalen-1-yl)-1-phenyl-1H-pyrazole (3n)
White solid, yield: 41%, melting point: 98.8~99.3 °C.
\[ \text{^1H-NMR (400 MHz, CDCl}_3\): } \delta 8.63-8.57 (m, 1H), 7.92-7.88 (m, 2H), 7.78 (dd, J = 7.2, 1.2 Hz, 1H), 7.75-7.71 (m, 2H), 7.59-7.53 (m, 4H), 7.52 (t, J = 2.0 Hz, 1H), 7.50-7.46 (m, 1H), 6.87 (s, 1H), 4.59 (s, 2H); \]
\[ \text{^13C NMR (100 MHz, CDCl}_3\): } \delta 152.1, 139.6, 139.3, 134.2, 131.5, 130.9, 129.6, 128.9, 128.8, 128.6, 127.5, 126.7, 126.2, 126.1, 125.6, 125.4, 110.0, 21.3; HRMS calcd for C_{20}H_{15}BrN_{3}+H^+: 363.0491, found: 363.0489.

![Chemical structure of 5-(bromomethyl)-3-(naphthalen-1-yl)-1-phenyl-1H-pyrazole (3n)](image)

2-(5-(bromomethyl)-1-phenyl-1H-pyrazol-3-yl)pyridine (3o)
White solid, yield: 32%, melting point: 94.2~95.4 °C.
\[ \text{^1H-NMR (400 MHz, CDCl}_3\): } \delta 8.64 (d, J = 4.8 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.73 (td, J = 8.0, 1.6 Hz, 1H), 7.67-7.63 (m, 2H), 7.56-7.51 (m, 2H), 7.49-7.46 (m, 1H), 7.25-7.22 (m, 1H), 7.19 (s, 1H), 4.51 (s, 2H); \]
\[ \text{^13C NMR (100 MHz, CDCl}_3\): } \delta 152.4, 151.8, 149.6, 140.7, 139.2, 136.9, 129.6, 129.0, 125.6, 123.1, 120.4, 107.6, 21.2; HRMS calcd for C_{15}H_{12}BrN_{3}+H^+: 314.0287, found: 314.0288.

![Chemical structure of 2-(5-(bromomethyl)-1-phenyl-1H-pyrazol-3-yl)pyridine (3o)](image)
5-(bromomethyl)-3-(furan-2-yl)-1-phenyl-1H-pyrazole (3p)
White solid, yield: 40%, melting point: 76.6~76.9°C.
$^1$H-NMR (400 MHz, CDCl$_3$): δ 7.63-7.60 (m, 2H), 7.53 (t, $J$ = 7.6 Hz, 2H), 7.47-7.44 (m, 2H), 6.77 (s, 1H), 6.75 (d, $J$ = 2.8 Hz, 1H), 6.48-6.47 (m, 1H), 4.47 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 148.3, 144.8, 142.4, 140.2, 139.0, 129.6, 129.0, 125.6, 111.6, 106.7, 105.8, 21.0; HRMS calcd for C$_{14}$H$_{11}$BrN$_2$+H$: 303.0128$, found: 303.0122.

5-(bromomethyl)-3-(tert-buty1)-1-phenyl-1H-pyrazole (3q)
White solid, yield: 65%, melting point: 71.9~72.7°C.
$^1$H-NMR (400 MHz, CDCl$_3$): δ 7.57 (d, $J$ = 7.2 Hz, 2H), 7.49 (t, $J$ = 8.0 Hz, 2H), 7.40 (t, $J$ = 7.2 Hz, 1H), 6.39 (s, 1H), 4.46 (s, 2H), 1.35 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 162.8, 139.6, 138.8, 129.5, 128.3, 125.3, 105.7, 32.4, 30.7, 21.9; HRMS calcd for C$_{14}$H$_{17}$BrN$_2$+H$: 293.0648$, found: 293.0644.

5-(bromomethyl)-3-phenyl-1-(p-tolyl)-1H-pyrazole (3r)
White solid, yield: 57%, melting point: 88.0~88.8°C.
$^1$H-NMR (400 MHz, CDCl$_3$): δ 7.89-7.82 (m, 2H), 7.53-7.49 (m, 2H), 7.45-7.37 (m, 2H), 7.35-7.32 (m, 3H), 6.83 (s, 1H), 4.49 (s, 2H), 2.44 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 152.0, 140.3, 138.9, 136.8, 132.9, 130.2, 128.9, 128.3, 125.3, 105.7, 32.4, 30.7, 21.9; HRMS calcd for C$_{17}$H$_{15}$BrN$_2$+H$: 327.0491$, found: 327.0487.

5-(bromomethyl)-1-(4-methoxyphenyl)-3-phenyl-1H-pyrazole (3s)
White solid, yield: 47%, melting point: 117.4~118.5°C.
$^1$H-NMR (400 MHz, CDCl$_3$): δ 7.85 (d, $J$ = 6.8 Hz, 2H), 7.59-7.50 (m, 2H), 7.45-7.37 (m, 2H), 7.33 (t, $J$ = 6.8 Hz, 1H), 7.03 (d, $J$ = 8.4 Hz, 2H), 6.81 (s, 1H), 4.46 (s, 2H), 3.88 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 160.0, 151.9, 140.4, 133.0, 132.2, 128.9,
128.3, 127.1, 125.9, 114.7, 105.6, 55.8, 21.3; HRMS calcd for C_{17}H_{13}BrN_2O+H^+: 343.0441, found: 343.0443.

5-(bromomethyl)-1-(4-fluorophenyl)-3-phenyl-1H-pyrazole (3t)
White solid, yield: 75%, melting point: 103.7~104.3 °C.

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.84 (dd, J = 7.2, 1.6 Hz, 2H), 7.65-7.60 (m, 2H), 7.42 (t, J = 7.2 Hz, 2H), 7.34 (t, J = 7.2 Hz, 1H), 7.25-7.20 (m, 2H), 6.83 (s, 1H), 4.47 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 152.6, 140.4, 138.3, 132.8, 132.6, 126.9, 128.6, 126.8, 126.0, 106.6, 21.1; HRMS calcd for C_{16}H_{12}BrFNO+H^+: 331.0241, found: 331.0244.

5-(bromomethyl)-1-(4-bromophenyl)-3-phenyl-1H-pyrazole (3u)
White solid, yield: 66%, melting point: 84.6~85.4 °C.

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.84 (d, J = 6.8 Hz, 2H), 7.67 (d, J = 7.6 Hz, 2H), 7.56 (d, J = 7.2 Hz, 2H), 7.42 (t, J = 6.4 Hz, 2H), 7.35 (d, J = 7.2, 1H), 6.84 (s, 1H), 4.49 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 152.6, 140.4, 138.3, 132.8, 132.6, 129.0, 128.6, 126.8, 126.0, 106.6, 21.1; HRMS calcd for C_{16}H_{12}Br_{2}N_2O+H^+: 390.9440, found: 390.9447.

5-(bromomethyl)-1-(4-chlorophenyl)-3-phenyl-1H-pyrazole (3v)
White solid, yield: 63%, melting point: 92.6~93.4 °C.

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.84 (d, J = 7.2 Hz, 2H), 7.66-7.57 (m, 2H), 7.51 (d, J = 8.4Hz, 2H), 7.42 (t, J = 7.2 Hz, 2H), 7.35 (t, J = 7.2 Hz, 1H), 6.84 (s, 1H), 4.49 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 152.5, 140.4, 137.8, 134.6, 132.6, 129.8, 128.9, 128.6, 126.6, 126.0, 106.5, 21.1; HRMS calcd for C_{16}H_{12}BrClN_2O+H^+: 346.9945, found: 346.9941.

5-(bromomethyl)-3-phenyl-1-(4-( trifluoromethyl) phenyl)-1H-pyrazole (3w)
White solid, yield: 70%, melting point: 99.7~100.3 °C.

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.86-7.80 (m, 6H), 7.43 (t, J = 7.2 Hz, 2H), 7.36 (t, J = 7.2 Hz, 1H), 6.88 (s, 1H), 4.54 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 153.0, 142.2 (q, J = 1.6 Hz), 140.5, 132.4, 129.0, 128.7, 126.9 (q, J = 3.6 Hz), 126.0, 125.2,
123.8 (q, \( J = 240.0 \) Hz), 107.2, 21.0; HRMS calcd for C\(_{17}\)H\(_{12}\)BrF\(_3\)N\(_2\)+H\(^+\): 381.0209, found: 381.0204.

![Structure of 5-(bromomethyl)-1-(2-chlorophenyl)-3-phenyl-1H-pyrazole (3x)](image)

**5-(bromomethyl)-1-(2-chlorophenyl)-3-phenyl-1H-pyrazole (3x)**
White solid, yield: 47%, melting point: 99.3~100.2 °C.

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \( \delta 7.85 \) (d, \( J = 7.2 \) Hz, 2H), 7.62 (dd, \( J = 7.2, 1.6 \) Hz, 1H), 7.60-7.55 (m, 1H), 7.51-7.46 (m, 2H), 7.41 (t, \( J = 7.6 \) Hz, 2H), 7.33 (t, \( J = 7.2 \) Hz, 1H), 6.83 (s, 1H), 4.36 (s, 2H); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 152.6, 140.4, 140.3, 135.4, 130.7, 130.5, 128.9, 128.5, 128.0, 126.1, 105.1, 20.5; \)
HRMS calcd for C\(_{16}\)H\(_{12}\)BrClN\(_2\)+H\(^+\): 346.9945, found: 346.9944.

![Structure of 5-(iodomethyl)-1-(2-chlorophenyl)-3-phenyl-1H-pyrazole (3y)](image)

**5-(bromomethyl)-1-(3-chlorophenyl)-3-phenyl-1H-pyrazole (3y)**
White solid, yield: 78%, melting point: 79.5~80.5 °C.

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \( \delta 7.85 \) (d, \( J = 6.0 \) Hz, 2H), 7.71 (s, 1H), 7.63-7.53 (m, 1H), 7.47-7.41 (m, 4H), 7.38-7.33 (m, 1H), 6.85 (s, 1H), 4.51 (s, 2H); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 152.6, 140.4, 140.3, 135.4, 132.6, 130.6, 129.0, 128.9, 128.6, 126.0, 125.7, 123.2, 106.7, 21.0; \)
HRMS calcd for C\(_{16}\)H\(_{12}\)BrClN\(_2\)+H\(^+\): 346.9945, found: 346.9939.

![Structure of 5-(iodomethyl)-1,3-diphenyl-1H-pyrazole (4a)](image)

**5-(iodomethyl)-1,3-diphenyl-1H-pyrazole (4a)**
White solid, yield: 75%.

\(^1\)H-NMR (400 MHz, d6-DMSO): \( \delta 7.85 \) (dd, \( J = 7.2, 1.6 \) Hz, 2H), 7.67 (d, \( J = 7.2 \) Hz, 2H), 7.61 (t, \( J = 6.4 \) Hz, 2H), 7.53 (t, \( J = 7.2 \) Hz, 1H), 7.45 (t, \( J = 7.2 \) Hz, 2H), 7.36 (t, \( J = 7.2 \) Hz, 1H), 7.07 (s, 1H), 4.65 (s, 2H); \(^13\)C NMR (100 MHz, d6-DMSO): \( \delta 150.6, 141.9, 139.2, 132.5, 129.5, 128.8, 128.4, 128.2, 125.3, 124.8, 105.3, -6.4; \)
HRMS calcd for C\(_{16}\)H\(_{13}\)IN\(_2\)+H\(^+\): 361.0196, found: 361.0195.

![Structure of 5-(iodomethyl)-3-(4-methoxyphenyl)-1-phenyl-1H-pyrazole(4b)](image)

**5-(iodomethyl)-3-(4-methoxyphenyl)-1-phenyl-1H-pyrazole(4b)**
White solid, yield: 41%.

\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \( \delta 7.77 \) (d, \( J = 8.8 \) Hz, 2H), 7.64-7.62 (m, 2H), 7.56-7.52 (m, 2H), 7.48-7.44 (m, 1H), 6.94 (d, \( J = 8.8 \) Hz, 2H), 6.75 (s, 1H), 4.43 (s, 2H), 3.84(s,
3H); $^1$C NMR (100 MHz, CDCl$_3$): $\delta$ 159.9, 152.0, 141.4, 139.4, 129.6, 128.7, 127.2, 125.7, 125.5, 114.3, 105.5, 55.6, -8.2; HRMS calcd for C$_{17}$H$_{15}$IN$_2$O+H$: 391.0302, found: 391.0310.

![](image1)

3-(4-fluorophenyl)-5-(iodomethyl)-1-phenyl-1H-pyrazole (4c)
White solid, yield: 35%.
$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.81 (dd, $J$ = 8.8, 5.6 Hz, 2H), 7.62 (d, $J$ = 7.2 Hz, 2H), 7.55 (t, $J$ = 7.6 Hz, 2H), 7.48 (t, $J$ = 7.2 Hz, 1H), 7.09 (t, $J$ = 8.8 Hz, 2H), 6.77 (s, 1H), 4.43 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 163.1 (d, $J$ = 250.0 Hz), 151.2, 141.7, 139.3, 129.7, 129.1, 128.9, 127.7 (d, $J$ = 8.1 Hz), 125.5, 115.8 (d, $J$ = 21.5 Hz), 105.2, -8.6; HRMS calcd for C$_{16}$H$_{12}$FIN$_2$+H$: 379.0102, found: 379.0109.

![](image2)

1-(4-fluorophenyl)-5-(iodomethyl)-3-phenyl-1H-pyrazole (4d)
White solid, yield: 45%
$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.84-7.82 (m, 2H), 7.62 (dd, $J$ = 8.8, 4.8 Hz, 2H), 7.41 (t, $J$ = 7.6 Hz, 2H), 7.34 (t, $J$ = 7.6 Hz, 1H), 7.24-7.21 (m, 2H), 6.81 (s, 1H), 4.40 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 171.9, 161.5, 152.2, 141.7, 135.4 (d, $J$ = 3.1 Hz), 132.7, 128.9, 128.5, 127.6 (d, $J$ = 8.7 Hz), 125.9, 116.7 (d, $J$ = 22.8 Hz), 105.3, -8.8; HRMS calcd for C$_{16}$H$_{12}$FIN$_2$+H$: 379.0102, found: 379.0101.

![](image3)

1,3-diphenyl-5-(2,2,2-trifluoroethyl)-1H-pyrazole (5)
White solid, yield: 32%.
$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.90-7.84 (m, 2H), $\delta$ 7.56-7.50 (m, 2H), $\delta$ 7.50-7.44 (m, 3H), 7.42 (t, $J$ = 7.6 Hz, 2H), 7.34 (t, $J$ = 7.2 Hz, 1H), 6.82 (s, 1H), 3.52 (q, $J$ = 6.0 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 152.1, 138.9, 133.3, 132.7, 129.5, 128.9, 128.7, 128.2, 126.2, 125.8, 123.3 (q, $J$ = 273 Hz), 105.4, 31.6 (q, $J$ = 32 Hz); HRMS calcd for C$_{27}$H$_{13}$F$_3$N$_2$+H$: 302.1031, found: 302.1033.

![image4]

5-(azidomethyl)-1,3-diphenyl-1H-pyrazole (6)
White solid, yield: 65%.
^1^H-NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \) 7.89 (d, \( J = 7.2 \) Hz, 2H), 7.59 (d, \( J = 8.0 \) Hz, 2H), 7.52 (t, \( J = 7.6 \) Hz, 2H), 7.46-7.41 (m, 3H), 7.35 (t, \( J = 7.2 \) Hz, 1H), 6.82 (s, 1H), 4.39 (s, 2H); ^1^C NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \) 152.2, 139.3, 138.1, 132.9, 129.7, 128.9, 128.6, 128.4, 126.0, 125.2, 105.9, 45.5; HRMS calcd for C\textsubscript{16}H\textsubscript{13}N\textsubscript{5}H\textsuperscript{+}: 276.1244, found: 276.1243.

![Diagram of 1,3-diphenyl-1H-pyrazol-5-yl)methanol (7)](image)

Green solid, yield: 35%.

^1^H-NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \) 7.83 (d, \( J = 7.2 \) Hz, 2H), 7.60 (d, \( J = 7.6 \) Hz, 2H), 7.46 (t, \( J = 7.6 \) Hz, 2H), 7.43-7.37 (m, 3H), 7.34 (t, \( J = 7.2 \) Hz, 1H), 6.73 (s, 1H), 4.65 (s, 2H), 2.27 (s, 1H); ^1^C NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \) 152.2, 143.9, 139.6, 132.9, 129.6, 129.0, 128.5, 126.1, 124.8, 105.3, 56.1; HRMS calcd for C\textsubscript{16}H\textsubscript{14}N\textsubscript{2}O\textsuperscript{+}: 251.1179, found: 251.1172.

![Diagram of 5-(isopropoxymethyl)-1,3-diphenyl-1H-pyrazole (8)](image)

White oil, yield: 50%.

^1^H-NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \) 7.88 (dd, \( J = 7.6 \), 1.2 Hz, 2H), 7.72-7.69 (m, 2H), 7.49 (t, \( J = 7.6 \) Hz, 2H), 7.43-7.38 (m, 3H), 7.32 (t, \( J = 7.6 \) Hz, 1H), 6.79 (s, 1H), 4.49 (s, 2H), 3.74-3.68 (m, 1H), 1.21 (d, \( J = 6.0 \) Hz, 6H); ^1^C NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \) 151.8, 141.3, 140.0, 133.4, 129.3, 128.8, 128.1, 128.0, 126.0, 124.9, 106.2, 71.5, 60.7, 22.2; HRMS calcd for C\textsubscript{19}H\textsubscript{20}N\textsubscript{2}O\textsuperscript{+}: 293.1648, found: 293.1655.

![Diagram of N-benzyl-1-(1,3-diphenyl-1H-pyrazol-5-yl)methanamine (9)](image)

White solid, yield: 33%.

^1^H-NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \) 7.80 (d, \( J = 7.2 \) Hz, 2H), 7.55 (d, \( J = 7.6 \) Hz, 2H), 7.38 (t, \( J = 7.6 \) Hz, 2H), 7.35-7.29 (m, 3H), 7.24-7.18 (m, 6H), 6.67 (s, 1H), 3.80 (s, 2H), 3.75 (s, 2H), 1.91 (s, 1H); ^1^C NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \) 151.9, 143.1, 140.1, 133.4, 129.4, 128.8, 128.7, 128.4, 128.1, 128.0, 127.4, 126.0, 125.1, 104.8, 100.2, 53.4, 44.3; HRMS calcd for C\textsubscript{23}H\textsubscript{21}N\textsubscript{3}H\textsuperscript{+}: 340.1808, found: 340.1801.
10. $^1$H and $^{13}$C NMR Spectra