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Cascade 1,3-dipolar Cycloaddition/SO_2 extrusion approach for the rapid synthesis of tetraaryl-substituted pyrazoles with Aggregation Induced Emission characteristics

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ABSTRACT

A highly efficient strategy was developed for the straightforward synthesis of tetraaryl-substituted pyrazoles. The cascade process consists of a regioselective 1,3-dipolar cycloaddition of benzosultam-3-ylidenes with nitrile imines and a subsequent elimination of SO_2. The title compounds exhibit high fluorescence quantum yields and Aggregation Induced Emission (AIE) characteristics.

1. Introduction

Pyrazoles represent an important class of five-membered heterocycles composed of three carbons and two nitrogens in adjacent positions. They exist in natural products [1] (L-α-Amino-β-(pyrazolyl-*N*)-propanoic acid, Pyrazofurin, Formycin, Fluviol A, etc), commercial drugs [2] (rimonabant and celebrex) and display a wide range of remarkable pharmacological—anti-hyperglycemic, analgesic, antipyretic, anti-inflammatory, antibacterial, hypoglycemic and sedative-hypnotic—activities [3]. Furthermore, these compounds show intriguing photophysical properties as optical brighteners [4], UV stabilizers [5], fluorescence sensors [6] and OLED materials (Fig. 1). [7].

Although many synthetic strategies have been reported for the construction of substituted pyrazole derivatives [8], the methods devoted to tetraaryl-substituted pyrazoles are still limited [9]. In recent years, the most frequently used methods include the condensation of dicarbonyl compounds with substituted hydrazines and stepwise arylation of the pyrazole scaffold. Peruncheralathan [9a] and Venkatasubbaiah [9b] synthesized tetraaryl-substituted pyrazoles in three steps involving cyclocondensation of dibenzoylmethane with aryl hydrazines, bromination with *N*-bromosuccinimide and Suzuki coupling with arylboronic acids (Scheme 1, eq 1). Foroumadi reported a novel condensation method between benzoin and phenyl hydrazine followed by cyclization with aryl aldehydes to afford corresponding tetraaryl-substituted pyrazoles as promising 15-lipoxygenase inhibitors [9c]. Fuse's group accomplished the tetraaryl-substituted pyrazole synthesis through a sequential cross-coupling approach based on 3-iodo-1*H*-pyrazole [9d] and unsubstituted pyrazole [9e] respectively (Scheme 1, eq 2). These approaches generally suffer from several additional drawbacks, such as multistep synthetic operations, limited substrate scope and the use of transition metal catalyst. Therefore, developing a new protocol for the synthesis of tetraaryl-substituted pyrazoles with mild conditions, a short synthetic route and broad substrate applicability is always highly desirable.

The 1,3-dipolar cycloaddition reaction is among the most prominent reactions to build five-membered heterocycles with good regio-, diastereo-, and enantioselectivity in a single step [10]. Benzosultam-3-ylidenes have been reported as highly efficient dipolarophiles to react with azomethine ylide [11,12] and nitrones [13] leading to spiropyrrolidinyl-benzosultams and spiroisoxazolidinyl-benzosultams respectively. In our previous

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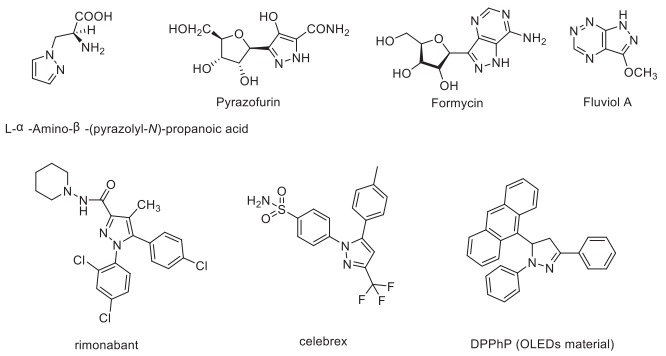
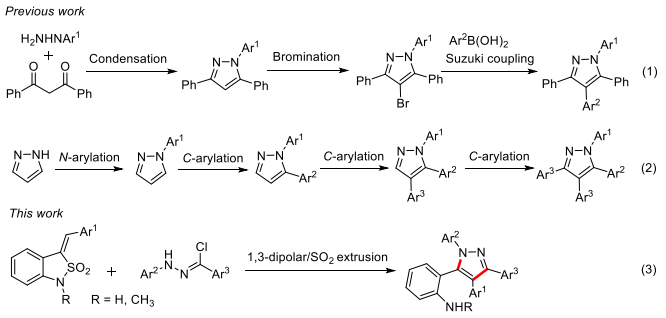


Fig. 1. Some pyrazoles and derivatives with biological and optical properties.



Scheme 1. Representative synthetic approach to tetraaryl-substituted pyrazoles.

research, we found that benzosultam-3-ylidenes, having exocyclic double bond and sulfamoyl group, are of special interest in the synthesis of five-membered heteroaromatic compounds as they can be easily transformed into sprio-frameworks and further extrude SO_2 to afford trisubstituted isoxazoles [14]. With respect to the reported interesting electronic properties of polysubstituted pyrazoles as potential intense blue light emitters [15], the continuing quest for tailor-made functional tetraaryl-substituted pyrazoles by highly efficient methods, and as part of our previous efforts on exploring important heterocyclic compounds, we herein wish to report a cascade 1,3-dipolar cycloaddition/SO_2 extrusion approach using benzosultam-3-ylidenes, which should facilitate the synthesis of tetraaryl-substituted pyrazoles (Scheme 1, eq 3). Furthermore, the photophysical properties of obtained compounds and their Aggregation Induced Emission (AIE) behaviour are investigated.

2. Results and discussion

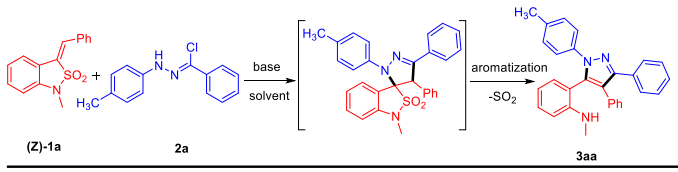
Initially, the reaction of isolable (*Z*)-3-benzylidene-1-methyl-benzosultam **1a** [11] and nitrile imine precursor **2a** [16] were used as a model to optimize reaction conditions including the solvents, bases and reaction temperature as reported in Table 1. In all of the reactions examined, HRMS and ^{1}H NMR spectroscopy analyses on the isolated product revealed a proposed aromatization of the initially formed spirobenzosultam-pyrazoline to a tetraaryl-substituted pyrazole. To our delight, a highly regioselective conversion was observed, and a single product **3aa** was obtained exclusively. The effect of six different solvents was first investigated using triethylamine as the base at 25 °C (entries 1–6). Among them were the apolar and aprotic dichloromethane and toluene, in which the desired 1,3-dipolar cycloaddition/SO_2 extrusion are generally performed leading to tetraaryl-substituted pyrazole **3aa** (entries 1–2). Furthermore, polar and aprotic solvents could also afford **3aa** in slightly lower yields (entries 3–4). It is interesting to see that the cascade reactions are accelerated in polar and protic solvents because of solvent hydrogen bonding [17] and that methanol proved to be the best solvent (entries 5–6). Several bases were tested in methanol (entries 7–10) and it was shown that K_2CO_3 gave the best result, whereas when using pyridine as a single base, none of the desired product was detected in the reaction mixture. When the reactions were performed at lower temperature (0 °C) and higher temperature (50 °C), the yield of tetraaryl-substituted pyrazole was slightly decreased (entries 11–12). Use of K_2CO_3 as base at 25 °C provided tetraarylpyrazole in 86% yield, and as such was established as the optimal protocol for this 1,3-dipolar cycloaddition/SO_2 extrusion study.

Having established the optimized reaction conditions, we tested a variety of nitrile imine precursors and benzosultam-3-ylidenes to probe the versatility of our newly developed 1,3-dipolar cycloaddition/SO_2 extrusion approach to tetraaryl-substituted pyrazoles (Table 2). In reactions of 3-phenylidenebenzosultam **1a**, hydrazonoyl chlorides **2a-b** derived from electron-rich hydrazines are more reactive than hydrazonoyl chlorides **2c-d** derived from electron-poor analogues and afford tetraaryl-substituted pyrazoles in better yields. The electronic effect of *C*-substituted-phenyl imines from **2e-h** on the activity of 1,3-dipolar cycloaddition/SO_2 extrusion was then investigated. The hydrazonoyl chlorides **2e-f** bearing electron-donating (methyl, methoxyl) substituents on the benzoyl chloride moiety gave the corresponding products in better yields than hydrazonoyl chlorides **2g-h** bearing electron-withdrawing (chloro, fluoro) substituents. Hydrazonyl chlorides **2i** containing electron-donating substituent both on the benzoyl chloride moiety and the phenylhydrazone moiety participated in the reaction successfully to afford the desired product **3ai** in excellent yields.

As shown in Table 2, it was found that a variety of 3-(*para*-substituted-phenylidene)-benzosultams **1a-f** underwent smooth cycloaddition/SO_2 extrusion with *C*-phenyl-*N*-phenyl nitrile imine precursor **2j** and provided tetraaryl-substituted pyrazoles **3aj-3fj** in good yields (80–85%). The structural assignment of the tetraaryl-substituted pyrazole **3bj** was based on X-ray analysis [18], and the regiochemistry of other products was assigned by analogy. Benzosultam-3-ylidenes containing ortho-substituted phenyl (**1g, 1h**), meta-substituted phenyl (**1i**) and heteroaryl moiety (**1j**) were also suitable substrates for this reaction and gave products **3gj** and **3ha-3ja**. It is particularly worth noting that pyrazoles containing a 2-aminophenyl group (**3lj, 3la**) were also smoothly prepared in moderate yields. Hydrazonyl chlorides containing heteroaryl moiety (**2k**) gave the tetraaryl-substituted pyrazoles **3hk** in moderate yield. However, hydrazonoyl chlorides **2l-m** bearing strong electron-withdrawing (nitro, trifluoromethyl) substituents can not afford corresponding tetraaryl-substituted pyrazoles.

Although tetraaryl-substituted pyrazoles have been reported to show an important enhancement in their light emission upon aggregation [9a], our interest is in the potential improvement of electronic properties of tetraaryl-substituted pyrazoles containing a 2-methylamino-phenyl group. The photophysical properties of tetraaryl-substituted pyrazoles **3** were examined in THF solution. The electronic absorption spectra of the tetraaryl-substituted pyrazoles display absorption maxima ($\lambda_{max,abs}$) between 233 and 293 nm with molar extinction coefficients ranging from 9400 to 118,700 l mol^{-1} cm^{-1} (see the Supporting Information). All investigated representatives exhibited strong blue luminescence in THF with emission maxima ($\lambda_{max,em}$) between 415 and 429 nm with large Stokes shifts ranging from 10,400 to 14,000 cm^{-1}. Five tetraaryl-substituted pyrazoles (**3aa, 3ah, 3aj, 3ej, 3fj**) reveal high fluorescence efficiency with fluorescence quantum yields Φf ranging between 0.62 and 0.83. It should be noted that the pyrazole

Table 1
Optimization of the 1,3-dipolar cycloaddition/SO_2 extrusion strategy.[a].



(Z)-1a 2a 3aa

Entry	Solvent	Base	Temp (°C)	Time(h)	Yield[b](%)
1	DCM	Et_3N	25	5	73
2	Toluene	Et_3N	25	5	71
3	THF	Et_3N	25	5	66
4	DMF	Et_3N	25	5	68
5	MeOH	Et_3N	25	0.5	81
6	EtOH	Et_3N	25	0.5	80
7	MeOH	Pyridine	25	10	NR
8	MeOH	DBU	25	2	74
9	MeOH	KOH	25	0.5	84
10	MeOH	K_2CO_3	25	0.5	86
11	MeOH	K_2CO_3	0	0.5	83
12	MeOH	K_2CO_3	50	0.5	84

[a] Reaction condition: (*Z*)-alkene **1a** (0.2 mmol), hydrazonoyl chloride **2a** (0.3 mmol), base (0.5 mmol), solvent (1 mL).
[b] Isolated yields. The other regionisomer was not detected by ^1H NMR.

3fj exerted higher fluorescence quantum yield (Φf = 0.83) compared with other tetraaryl-substituted pyrazoles reported before [9a,9e].

The synthesized tetraaryl-substituted pyrazoles are soluble in THF, but insoluble in water. When excited at 270 nm, the dilute solution of **3ae** in THF shows a weak emission band at 421 nm with fluorescence quantum yield (Φf) of 0.38. Excitingly, a sustainable increase in fluorescence emission intensity was observed when the water fraction was increased from 0% to 70% in the H_2O-THF mixture (Fig. 2). The quantum yields of the aggregates of tetraaryl-substituted pyrazole **3ae** at 70: 30 (H_2O: THF) composition increased to 0.93 which is about 2.5 fold higher than that in pure THF.

Owing to the possibility of benzosultam-3-ylidenes **1** undergoing *E-Z* isomerisation under the reaction conditions, we then turned our attention to test the reactivity of *E*-alkene **1a** with nitrile imine precursor **2j** in order to validate its applicability (Scheme 2). Importantly, (*E*)-**1a** was also suitable for this reaction delivering tetraaryl-substituted pyrazoles **3aj** in 80% yield. Encouraged by this result, we chose a mixture of *E-Z* isomers **1a** (mole ratio 1:1) as the substrate and performed the reaction under the optimized conditions to give product **3aj** in 83% yield. In addition, we have extended the scope of the reaction to the formation of 1,3,5-triaryl-4-alkyl-pyrazoles **3mj-3nj** by using 3-alkylene-benzosultams **1m-1n**.

To further demonstrate the utility of this cascade strategy in organic synthesis, we carried out the 1,3-dipolar cycloaddition/SO_2 extrusion of ethyl 2-(benzosultam-3-ylidene)-acetate (*Z*)-**1o** with hydrazonyl chloride **2k** (Scheme 3a). Compared with previous method [19], the reaction is highly regioselective and only one tetraaryl-substituted pyrazole derivative **3ok** was isolated. After cyclization under basic conditions, the pyrazolo [[4,5]-c]quinoline-4-one **4ok**, which was found to exhibit significant inhibitory towards [^{3}H]flunitrazepam binding from bovine brain membranes [19], was obtained in 84% yield (70% total isolated yield two steps from **1o**). Thus, the procedure reported herein could provide reliable methodology for testing the relationship between structure and pharmacological activity of pyrazolo [[4] [3-c]]quinolin-4-ones. Finally, by treating compound **3gj** in Buchwald-Hartwig reaction conditions, dibenzo [*b,f*]pyrazolo [3,4-*d*]azepine **5gj** can be obtained in 88% yield (Scheme 3b).

In order to further test the scalability of this cascade procedure, a gram-scale synthesis was carried out under the optimized conditions. Gratifyingly, the desired tetraaryl-substituted pyrazole derivative **3aa** could be obtained in 78% yield (1.2 g, Scheme 4).

Basis on the experimental results above and the previous studies of cycloaddition reactions involving hydrazonoyl chloride [20], we proposed the following plausible mechanism for this cascade 1,3-dipolar cycloaddition/SO_2 extrusion reaction, as shown in Scheme 5. In the presence of K_2CO_3, the nitrile imine was generated from the dehydrochlorination of hydrazonyl chloride **2a** with two zwitterionic resonance forms [21]. In keeping with a $HOMO_{dipolar}$-$LUMO_{dipolarophile}$ interaction, allenic **6b** proceeds a regioselective 1,3-dipolar reaction with 3-phenylidenebenzosultam **1a** to give spiro [pyrazolin-3,3′-benzosultam] intermediate **7**. Extrusion of SO_2 from intermediate **7** generates azaxylylene **8**, which undergoes [1,5]-sigmatropic hydrogen shift [22] to furnish the aromatic tetraaryl-substituted pyrazole **3aa**.

3. Conclusions

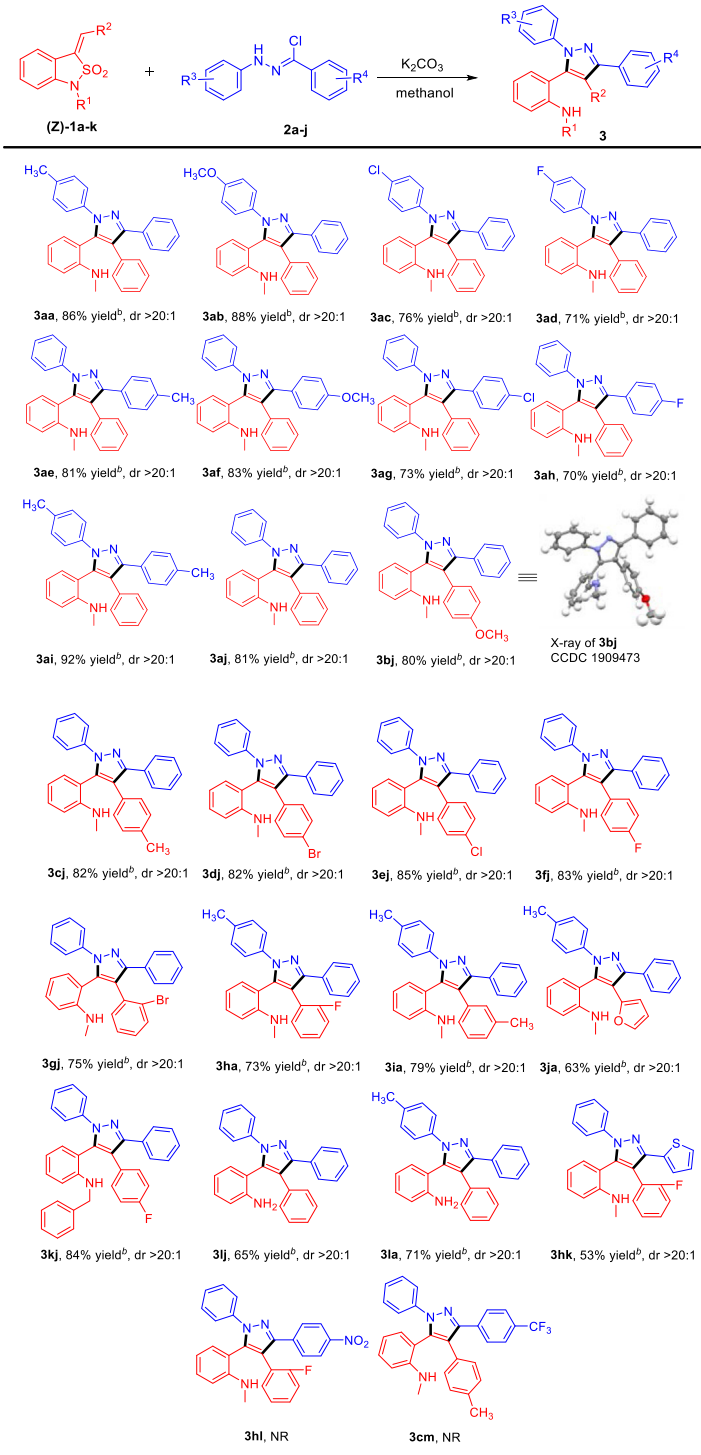
In summary, we have developed an efficient protocol for the construction of tetraaryl-substituted pyrazoles by a cascade 1,3-dipolar cycloaddition/SO_2 extrusion of benzosultam-3-ylidenes with nitrile imines. Compared with traditional syntheses, our new method has the advantages of step economy, milder reaction conditions, transition-metal free process, and higher overall yields. This approach was successfully applied in the convenient synthesis of a potent inhibitor of benzodiazepine (BZD) receptor and tetracyclic dibenzo [*b,f*]pyrazolo [3,4-*d*]azepine derivative. In addition, the absorption and emission spectra of the new tetraaryl-substituted pyrazoles (containing 2-methylamino-phenyl group) were measured. Compound **3fj** showed high fluorescence quantum yields (Φ_f = 0.83). Tetraaryl-substituted pyrazole **3ae** was demonstrated to be AIE active when aggregated. We expect that these results will have great impact on the drug discovery and on the development of tailor-made luminescent materials.

4. Experimental section

4.1. General

All reagents were purchased from commercial suppliers and

Table 2
Substrate scope of tetraaryl-substituted pyrazoles.[a].



[a] Reaction conditions: (*Z*)-**1** (0.2 mmol), **2** (0.3 mmol) and potassium carbonate (0.5 mmol) in methanol (1 mL) were stirred at room temperature for 0.5 h [b]Isolated yield.

used without purification. All reactions were monitored by TLC. Chromatography refers to open column chromatography on silica gel (100–200 mesh). Melting points were uncorrected values. ^{1}H NMR spectra were recorded at 500 MHz and ^{13}C NMR spectra were recorded at 125 MHz by using a Bruker Avance 500 M spectrometer and referenced internally to solvent signals. Mass spectra were performed on an Ultima Global spectrometer with an ESI source. The X-ray single-crystal diffraction was performed on Saturn 724+ instrument. The absorbance spectra were recorded on a Hitachi U-4100 spectrometer. The fluorescence spectra were recorded on a Hitachi F-4600 Fluorescence Spectrometer. The fluorescence spectra were corrected for the instrumental response.

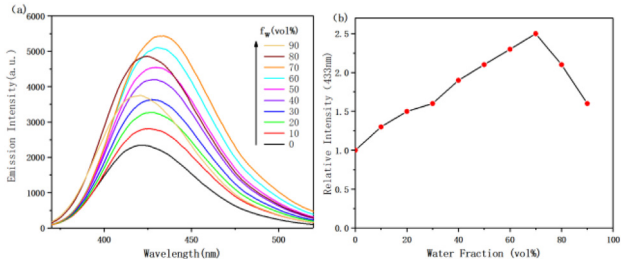
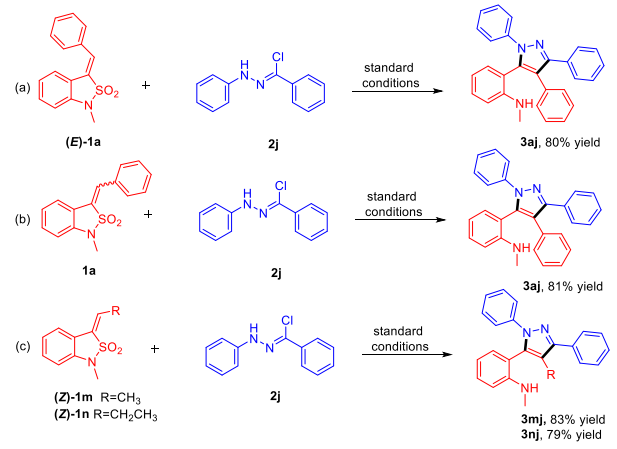
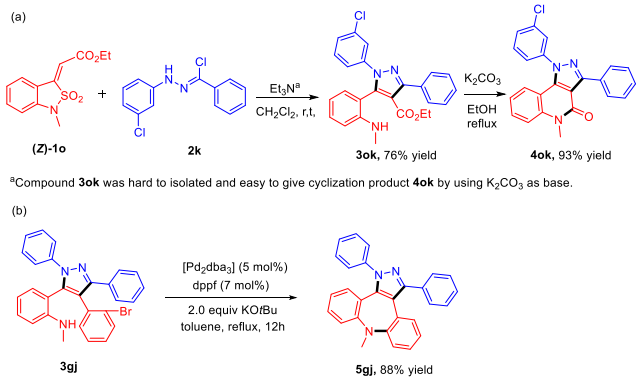


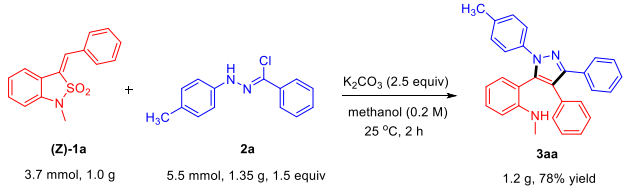
Fig. 2. (a) Fluorescence spectra of **3ae** (10^{-5} M) in water/THF mixtures with increasing amounts of water (f_w = 0–90 vol%). (b) The changes in the fluorescence emission relativeintensities of **3ae** with the water contents in the water/THF mixture vs intensity in pure THF.



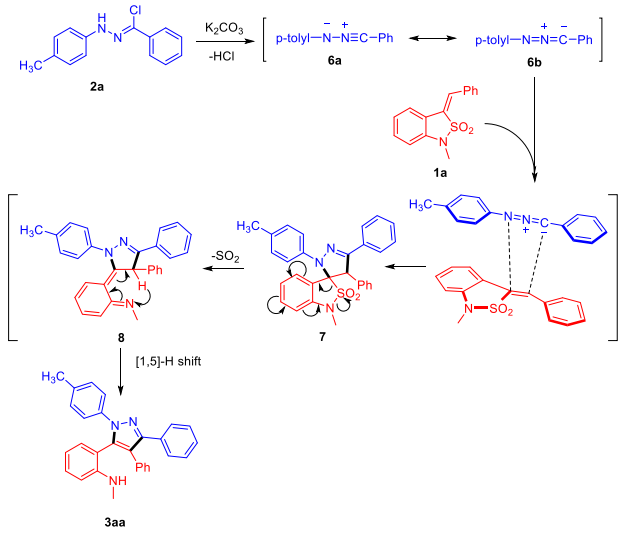
Scheme 2. Scope of benzosultam-3-ylidenes.



Scheme 3. Derivatization of 1,3-dipolar cycloaddition/SO_2 extrusion strategy.



Scheme 4. Gram-scale reaction for the synthesis of **3aa**.



Scheme 5. Plausible mechanism for the 1,3-dipolar cycloaddition/SO_2 extrusion reaction.

The relative fluorescence quantum yields were determined with Quinine sulfate as a standard and were calculated using the following Equation:

$$\Phi_x = \Phi_s(F_x / F_s)(A_s / A_s)(\lambda_{exs} / \lambda_{exx})(n_x / n_s)$$

in which Φ represents the quantum yield, F stands for the integrated area under the corrected emission spectrum, A is the absorbance at the excitation wavelength, λ_{ex} is the excitation wavelength, n is the refractive index of the solution (because of the low concentrations of the solutions (10^{-5} molL^{-1}), the refractive indices of the solutions were replaced with those of the solvents), and the subscripts x and s refer to the unknown and the standard, respectively.

4.2. General procedure for the synthesis of starting materials **1** and **2**

Benzosultam-3-ylidenes **1a-k** and **1m-n** were synthesized according to the reference, [11] and benzosultam-3-ylidene **1l** was synthesized according to the procedure [23]. Nitrile imine precursor **2** were synthesized according to the literature [24].

4.3. General procedure for the synthesis of **3**

In a 5 mL round-bottom flask, benzosultam-3-ylidenes **1** (0.2 mmol) and hydrazonoyl chloride **2** (0.3 mmol, 1.5 equiv) were dissolved in methanol (1 mL, 0.2 M). Then, to this solution potassium carbonate (69 mg, 0.5 mmol, 2.5 equiv) was added slowly at 0 °C. Then the reaction mixture was stirred at room temperature for 0.5 h. After that, saturated aqueous NH_4Cl (2 mL) was added and the organics extracted with ethyl acetate (1 mL × 3). The combined organic layers were dried over Na_2SO_4 and evaporated to remove solvent under reduced pressure. The residue was subjected to column chromatography on silica gel (100–200 mesh) using petroleum ether/ethyl acetate (30:1–80:1) as eluent to afford the corresponding compound **3.**

4.3.1. 5-(2-methylamino-phenyl)-3,4-diphenyl-1-p-tolyl-1H-pyrazole (**3aa**)

71 mg, 86% yield, white solid, petroleum ether/ethyl

acetate = 50:1, R_f = 0.2, mp 154–156 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59–7.57 (m, 2H), 7.34–7.31 (m, 3H), 7.27–7.21 (m, 3H), 7.20–7.18 (m, 3H), 7.11–7.08 (m, 4H), 6.93 (d, 1H, *J* = 7.4 Hz), 6.62 (t, 1H, *J* = 7.4 Hz), 6.57 (d, 1H, *J* = 8.2 Hz), 2.51 (s, 3H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.0, 147.4, 138.7, 137.4, 137.0, 133.1, 132.8, 131.8, 130.3, 129.6, 129.3, 128.5, 128.3128.2, 127.7, 126.7, 124.0, 120.8, 117.1, 115.7, 110.7, 30.6, 21.0; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{29}H_{26}N_3$ [(M + H)$^+$]: 416.2127. Found: 416.2125.

4.3.2. 5-(2-methylamino-phenyl)-3,4-diphenyl-1-(4-methoxy phenyl)-1H-pyrazole (**3 ab**)

76 mg, 88% yield, white solid. Petroleum ether/ethyl acetate = 30:1, R_f = 0.2, mp 170–172 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57–7.56 (m, 2H), 7.30–7.28 (m, 5H), 7.24–7.21 (m, 1H), 7.19–7.18 (m, 3H), 7.10–7.09 (m, 2H), 6.93 (d, 1H, *J* = 7.3 Hz), 6.80 (d, 2H, *J* = 8.4 Hz), 6.63 (t, 1H, *J* = 7.3 Hz), 6.58 (d, 1H, *J* = 8.1 Hz), 3.78 (s, 3H), 2.51 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 158.6, 149.9, 147.1, 138.6, 133.1, 133.0,132.8, 131.8, 130.3, 129.6, 128.5, 128.3, 128.2, 127.7, 126.7, 125.6, 120.6, 117.3, 115.8, 113.9, 110.9, 55.4, 30.7; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{29}H_{26}N_3O$ [(M + H)$^+$]: 432.2076. Found: 432.2075.

4.3.3. 5-(2-methylamino-phenyl)-3,4-diphenyl-1-(4-chlorophenyl) -1H-pyrazole

(**3ac**) 66 mg,76% yield, white solid, petroleum ether/ethyl acetate = 60:1, R_f = 0.2, mp 179–180 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57–7.55 (m, 2H), 7.33–7.31 (m, 5H), 7.26–7.24 (m, 3H), 7.19–7.18 (m, 3H), 7.09–7.08 (m, 2H), 6.92 (d, 1H, *J* = 7.5 Hz), 6.64 (t, 1H, *J* = 7.4 Hz), 6.59 (d, 1H, *J* = 8.2 Hz), 2.52 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.6, 147.2, 138.7, 138.3, 132.8, 132.7, 132.4, 131.7, 130.7, 129.5, 128.9, 128.4, 128.3, 128.2, 127.9, 126.9, 125.1, 121.4, 117.4, 115.3, 110.9, 30.6; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{28}H_{23}ClN_3$ [(M + H)$^+$]: 436.1581. Found: 436.1582.

4.3.4. 5-(2-methylamino-phenyl)-3,4-diphenyl-1-(4-fluorophenyl)-1H-pyrazole (**3ad**)

59 mg, 71% yield, white solid, petroleum ether/ethyl acetate = 40:1, R_f = 0.2, mp 166–167 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50–7.49 (m, 2H), 7.29–7.23 (m, 5H), 7.18–7.14 (m, 1H), 7.12–7.10 (m, 3H), 7.03–7.01 (m, 2H), 6.90 (t, 2H, *J* = 8.5 Hz), 6.84 (d, 1H, *J* = 7.5 Hz), 6.54 (t, 1H, *J* = 7.4 Hz), 6.49 (d, 1H, *J* = 8.3 Hz), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.5 (d, $^1J_{C\text{-}F}$ = 245 HZ), 150.3, 147.4, 138.9, 136.0, 132.9, 132.5, 131.7, 130.6, 129.5, 128.4, 128.3, 128.2, 127.9, 126.9, 125.9 (d, $^3J_{C\text{-}F}$ = 8.4 HZ), 121.1, 117.1, 115.6 (d, $^2J_{C\text{-}F}$ = 22.9 HZ) 115.2, 110.6, 30.5; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{28}H_{23}FN_3$ [(M + H)$^+$]: 420.1876. Found: 420.1872.

4.3.5. 5-(2-methylamino-phenyl)-1,4-diphenyl-3-p-tolyl-1H-pyrazole (**3ae**)

67 mg, 81% yield, white solid, petroleum ether/ethyl acetate = 50:1, R_f = 0.2, mp 170–171 °C;^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (d, 2H, *J* = 7.9 Hz), 7.37 (d, 2H, *J* = 7.9 Hz), 7.30–7.26 (m, 2H), 7.24–7.18 (m, 5H), 7.13–7.09 (m, 4H), 6.92 (d, 1H, *J* = 7.4 Hz), 6.61 (t, 1H, *J* = 7.4 Hz), 6.57 (d, 1H, *J* = 8.2 Hz), 2.50 (s, 3H), 2.36 (s, 3H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.2, 146.3, 138.8, 137.6, 136.4, 131.8, 130.7, 129.3, 129.1, 128.5, 127.9, 127.6, 127.3, 127.1, 126.0, 125.6, 123.0, 119.9, 116.1, 114.6, 109.7, 29.5, 20.2; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{29}H_{26}N_3$ [(M + H)$^+$]: 416.2127. Found: 416.2128.

4.3.6. 5-(2-methylamino-phenyl)-1,4-diphenyl-3-(4-methoxy phenyl)-1H-pyrazole (**3af**)

71 mg, 83% yield, white solid, petroleum ether/ethyl acetate = 30:1, R_f = 0.2, mp 156–158 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (d, 2H, *J* = 8.7 Hz), 7.37 (d, 2H, *J* = 7.8 Hz), 7.30–7.27 (m, 2H), 7.24–7.18 (m, 5H), 7.11–7.09 (m, 2H), 6.92 (d, 1H, *J* = 7.5 Hz), 6.86 (d, 2H, *J* = 8.7 Hz), 6.62 (t, 1H, *J* = 7.5 Hz), 6.58 (d, 1H, *J* = 8.2 Hz), 3.82 (s, 3H), 2.50 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.3, 150.0, 147.2, 139.8, 138.6, 132.8, 131.7, 130.4, 129.7, 129.6, 128.7, 128.2, 127.1, 126.7, 125.6, 124.1, 120.7, 117.3, 115.7, 113.7, 110.9, 55.2, 30.6; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{29}H_{26}N_3O$ [(M + H)$^+$]: 432.2076. Found: 432.2075.

4.3.7. 5-(2-methylamino-phenyl)-1,4-diphenyl-3-(4-chlorophenyl) -1H-pyrazole (**3 ag**)

63 mg, 73% yield, white solid, petroleum ether/ethyl acetate = 70:1, R_f = 0.2, mp 158–160 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52–7.51 (m, 2H), 7.38–7.36 (m, 2H), 7.31–7.27 (m, 4H), 7.24–7.20 (m, 5H), 7.10–7.08 (m, 2H), 6.91 (d, 1H, *J* = 7.3 Hz), 6.61 (t, 1H, *J* = 7.4 Hz), 6.57 (d, 1H, *J* = 8.2 Hz), 2.51 (s, 3H)· ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.1, 147.4, 139.7, 139.0, 133.7, 132.4, 131.7, 131.6, 130.5, 129.7, 129.5, 128.8, 128.5, 128.4, 127.3, 127.0, 124.1, 121.1, 117.1, 115.2, 110.7, 30.5; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{28}H_{23}ClN_3$ [(M + H)$^+$]: 436.1581. Found: 436.1577.

4.3.8. 5-(2-methylamino-phenyl)-1,4-diphenyl-3-(4-fluorophenyl)-1H-pyrazole (**3ah**)

59 mg, 70% yield, white solid, petroleum ether/ethyl acetate = 50:1, R_f = 0.2, mp 141–143 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56–7.53 (m, 2H), 7.38–7.36 (m, 2H), 7.30–7.27 (m, 2H), 7.25–7.19 (m, 5H), 7.09–7.08 (m, 2H), 7.01 (t, 2H, *J* = 8.7 Hz), 6.91 (d, 1H, *J* = 7.3 Hz), 6.60 (t, 1H, *J* = 7.4 Hz), 6.56 (d, 1H, *J* = 8.2 Hz), 2.51 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ162.6 (d, $^1J_{C\text{-}F}$ = 246.8 HZ), 149.4, 147.5, 139.7, 138.9, 132.5, 131.7, 130.5, 130.2 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 129.5, 129.2, 129.1, 128.8, 128.3, 127.2, 126.9, 124.1, 120.9, 117.0, 115.3, 115.2 (d,$^2J_{C\text{-}F}$ = 21.5 HZ), 110.6, 30.5; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{28}H_{23}FN_3$ [(M + H)$^+$]: 420.1876. Found: 420.1873.

4.3.9. 5-(2-methylamino-phenyl)-4-phenyl-1,3-di-p-tolyl-1H-pyrazole (**3ai**)

79 mg, 92% yield, white solid, petroleum ether/ethyl acetate = 40:1, R_f = 0.2, mp 153–175 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (d, 2H, *J* = 7.9 Hz), 7.26–7.18 (m, 6H), 7.13–7.07 (m, 6H), 6.92 (d, 1H, *J* = 7.4 Hz), 6.62 (t, 1H, *J* = 7.4 Hz), 6.58 (d, 1H, *J* = 8.2 Hz), 2.50 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.0, 147.2, 138.5, 137.4, 136.8, 132.8, 131.7, 130.2, 129.5, 129.3, 128.9, 128.3, 128.1, 126.6, 124.0, 120.6, 117.2, 115.8, 110.7, 30.6, 21.3, 21.0; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{30}H_{28}N_3$ [(M + H)$^+$]: 430.2283. Found: 430.2283.

4.3.10. 5-(2-methylamino-phenyl)-4-phenyl-1,3-diphenyl-1H-pyrazole (**3aj**)

65 mg, 81% yield, white solid, petroleum ether/ethyl acetate = 60:1, R_f = 0.2, mp 148–151 °C;^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60–7.58 (m, 2H), 7.40–7.38 (m, 2H), 7.32–7.28 (m, 5H), 7.25–7.19 (m, 5H), 7.12–7.10 (m, 2H), 6.93 (d, 1H, *J* = 7.4 Hz), 6.62 (t, 1H, *J* = 7.4 Hz), 6.57 (d, 1H, *J* = 8.3 Hz), 2.51 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.3, 147.4, 139.8, 138.8, 133.1, 132.7, 131.7, 130.4, 129.6, 128.7, 128.5, 128.3, 128.2, 127.8, 127.1, 126.8, 124.1, 121.1, 117.1, 115.5, 110.7, 30.5. HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{28}H_{24}N_3$ [(M + H)$^+$]: 402.1970. Found: 402.1967.

4.3.11. 5-(2-methylamino-phenyl)-4-(4-methoxyphenyl)-1,3-diphenyl-1H-pyrazole (**3bj**)

69 mg, 80% yield, white solid, petroleum ether/ethyl acetate = 50:1, R_f = 0.2, mp 189–191 °C;^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61–7.60 (m, 2H), 7.39–7.38 (m, 2H), 7.33–7.32 (m, 3H), 7.29–7.27 (m, 2H), 7.25–7.22 (m, 2H), 7.03 (d, 2H, *J* = 8.4 Hz), 6.93 (d, 1H, *J* = 7.4 Hz), 6.75 (d, 2H, *J* = 8.4 Hz), 6.62 (t, 1H, *J* = 7.4 Hz), 6.58 (d, 1H, *J* = 8.2 Hz), 3.76 (s, 3H), 2.55 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 158.4, 150.2, 147.5, 139.9, 138.5, 133.2, 131.8, 130.7, 130.4,

128.7, 128.4, 128.3, 127.7, 127.1, 124.9, 124.1, 120.7, 117.0, 115.6, 113.7, 110.6, 55.1, 30.6. HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{29}H_{26}N_3O$ [(M + H)$^+$]: 432.2076. Found: 432.2078.

4.3.12. 5-(2-methylamino-phenyl)-4-(4-methylphenyl)-1,3-diphenyl-1H-pyrazole (**3cj**)

68 mg, 82% yield, white solid, petroleum ether/ethyl acetate = 60:1, R_f = 0.2, mp 180–182 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59–7.58 (m, 2H), 7.38–7.30 (m, 5H), 7.26–7.21 (m, 4H), 7.00–6.98 (m, 4H), 6.93 (d, 1H, *J* = 7.4 Hz), 6.62 (dd, 2H, *J* = 7.8, 18.4 Hz), 2.51 (s, 3H), 2.29 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.2, 147.5, 139.9, 138.6, 136.3, 133.2, 131.7, 130.3, 129.6, 129.4, 129.0, 128.7, 128.5, 128.3, 127.7, 127.1, 124.1, 121.1, 117.0, 115.6, 110.6, 30.5, 21.2. HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{29}H_{26}N_3$ [(M + H)$^+$]: 416.2127. Found: 416.2125.

4.3.13. 5-(2-methylamino-phenyl)-4-(4-bromophenyl)-1,3-diphenyl-1H-pyrazole (**3dj**)

79 mg, 82% yield, petroleum ether/ethyl acetate = 50:1, R_f = 0.2, white solid, mp 157–159 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56–7.55 (m, 2H), 7.39–7.22 (m, 11H), 6.96 (d, 2H, *J* = 8.3 Hz), 6.91 (d, 1H, *J* = 7.4 Hz), 6.63 (t, 1H, *J* = 7.4 Hz), 6.59 (d, 1H, *J* = 8.3 Hz), 2.55 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.3, 147.3, 139.6, 138.8, 132.8, 131.7, 131.6, 131.4, 131.2, 130.7, 128.8, 128.5, 128.4, 128.0, 127.3, 124.0, 120.9, 119.9, 117.3, 115.1, 110.8, 30.6. HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{28}H_{23}BrN_3$ [(M + H)$^+$]: 480.1075. Found: 480.1072.

4.3.14. 5-(2-methylamino-phenyl)-4-(4-chlorophenyl)-1,3-diphenyl-1H-pyrazole (**3ej**)

74 mg, 85% yield, white solid, petroleum ether/ethyl acetate = 60:1, R_f = 0.2, mp 164–165 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59–7.57 (m, 2H), 7.40–7.35 (m, 5H), 7.32–7.29 (m, 2H), 7.26–7.24 (m, 2H), 7.17 (d, 2H, *J* = 8.3 Hz), 7.04 (d, 2H, *J* = 8.4 Hz), 6.92 (d, 1H, *J* = 7.4 Hz), 6.63 (t, 1H, *J* = 7.4 Hz), 6.59 (d, 1H, *J* = 8.3 Hz), 2.57 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.3, 147.5, 139.7, 138.9, 132.8, 132.6, 131.6, 131.3, 130.8, 130.6, 128.8, 128.5, 128.4, 128.0, 127.3, 124.0, 120.0, 117.0, 115.0, 110.5, 30.5; HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{28}H_{23}ClN_3$ [(M + H)$^+$]: 436.1581. Found: 436.1576.

4.3.15. 5-(2-methylamino-phenyl)-4-(4-fluorophenyl)-1,3-diphenyl-1H-pyrazole (**3fj**)

70 mg, 83% yield, white solid, petroleum ether/ethyl acetate = 40:1, R_f = 0.2, mp 161–163 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57–7.56 (m, 2H), 7.39–7.29 (m, 7H), 7.27–7.23 (m, 2H), 7.08–7.05 (m, 2H), 6.92–6.88 (m, 3H), 6.61 (t, 1H, *J* = 7.4 Hz), 6.57 (d, 1H, *J* = 8.2 Hz), 2.56 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.8 (d, $^1J_{C\text{-}F}$ = 245.9 HZ), 150.2, 147.6, 139.7, 138.9, 132.9, 131.6, 131.2 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 130.5, 128.8, 128.4, 128.3, 127.9, 127.2, 124.0, 120.1, 116.9, 115.3 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 115.0, 110.4, 30.4. HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{28}H_{23}FN_3$ [(M + H)$^+$]: 420.1876. Found: 420.1877.

4.3.16. 5-(2-methylamino-phenyl)-4-(2-bromophenyl)-1,3-diphenyl-1H-pyrazole (**3gj**)

72 mg, 75% yield, white solid, petroleum ether/ethyl acetate = 60:1, R_f = 0.2, mp 176–177 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55–7.52 (m, 2H), 7.46–7.42 (m, 2H), 7.32–7.26 (m, 6H), 7.21–7.11 (m, 5H), 6.92 (d, 1H, *J* = 7.2 Hz), 6.57 (t, 1H, *J* = 7.4 Hz), 6.52 (d, 1H, *J* = 8.2 Hz), 2.56 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.2, 147.3, 139.7, 139.3, 134.2, 132.9, 132.6, 131.5, 130.4, 129.2, 128.8, 128.3, 127.8, 127.5, 127.1, 127.0, 125.0, 124.0, 123.5, 120.8, 116.7, 114.9, 110.6, 30.5. HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{28}H_{23}BrN_3$ [(M + H)$^+$]: 480.1075. Found: 480.1078.

4.3.17. 5-(2-methylamino-phenyl)-4-(2-fluorophenyl)-3-phenyl-1-p-tolyl-1H-pyrazole (**3ha**)

63 mg, 73% yield, white solid, petroleum ether/ethyl acetate = 70:1, R_f = 0.2, mp 164–165 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62–7.61 (m, 2H), 7.33–7.32 (m, 5H), 7.26–7.20 (m, 2H), 7.15–7.11 (m, 3H), 7.04–7.00 (m, 2H), 6.97 (d, 1H, *J* = 7.4 Hz), 6.60 (t, 1H, *J* = 7.4 Hz), 6.55 (d, 1H, *J* = 8.2 Hz), 2.60 (s, 3H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.3 (d, $^1J_{C\text{-}F}$ = 246.2 HZ), 150.4, 147.7, 139.8, 137.4, 137.0, 133.3, 132.5, 131.4, 130.4, 129.4, 129.3, 128.3, 127.8, 127.3, 124.1, 123.8, 121.0 (d, $^3J_{C\text{-}F}$ = 15.7 Hz), 116.6, 115.6, 115.5, 115.0 (d, $^3J_{C\text{-}F}$ = 11.5 Hz), 110.2, 30.5, 21.1. HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{29}H_{25}FN_3$ [(M + H)$^+$]: 434.2033. Found: 434.2027.

4.3.18. 5-(2-methylamino-phenyl)-4-m-tolyl-3-phenyl-1-p-tolyl-1H-pyrazole (**3ia**) 68 mg

79% yield, white solid, petroleum ether/ethyl acetate = 70:1, R_f = 0.2, mp 135–136 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58–7.57 (m, 2H), 7.31–7.26 (m, 5H), 7.22–7.20 (m, 1H), 7.08–7.05 (m, 3H),6.98 (d, 1H, *J* = 7.5 Hz), 6.92–6.87 (m, 3H), 6.61 (t, 1H, *J* = 7.4 Hz), 6.57 (d, 1H, *J* = 8.2 Hz), 2.51 (s, 3H), 2.31 (s, 3H), 2.17 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ149.9, 147.3, *138.*6, 137.7, 137.4, 136.9, 133.2, 132.6, 131.7, 130.3, 129.3, 128.4, 128.2, 128.1, 127.7, 127.5, 126.7, 124.0, 120.9, 117.3, 115.9, 110.8, 30.7, 21.4, 21.1. HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{30}H_{28}N_3$ [(M + H)$^+$]: 430.2283. Found: 430.2285.

4.3.19. 5-(2-methylamino-phenyl)-4-(furan-2-yl)-3-phenyl-1-p-tolyl-1H-pyrazole (**3ja**)

51 mg, 63% yield, white solid, petroleum ether/ethyl acetate = 70:1, R_f = 0.2, mp 129–130 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (d, 2H, *J* = 6.9 Hz), 7.41–7.36 (m, 3H), 7.31–7.25 (m, 4H), 7.08 (d, 2H, *J* = 8.1 Hz), 6.96 (d, 1H, *J* = 7.4 Hz), 6.68–6.64 (m, 2H),6.29–6.28 (m, 1H), 5.99 (d, 1H, *J* = 3.2 Hz), 2.71 (s, 3H), 2.31 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.3, 147.5, 146.5, 141.7, 139.0, 137.2, 133.1, 131.4, 130.6, 129.4, 128.2, 128.0, 123.9, 117.1, 115.5, 111.8, 111.0, 110.5, 108.2, 30.8, 21.1. HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{27}H_{24}N_3O$ [(M + H)$^+$]: 406.1919. Found: 406.1923.

4.3.20. 5-(2-benzylamino-phenyl)-4-(4-fluorophenyl)-1,3-diphenyl -1H-pyrazole (**3kj**)

83 mg, 84% yield, white solid, petroleum ether/ethyl acetate = 60:1, R_f = 0.2, m. p.: 151–152 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55–7.54 (m, 2H), 7.40–7.37 (m, 2H), 7.31–7.28 (m, 6H), 7.18–7.13 (m, 4H), 7.07–7.04 (m, 2H), 6.96 (d, 1H, *J* = 7.4 Hz), 6.90 (t, 2H, *J* = 8.4 Hz), 6.81–6.80 (m, 2H), 6.62 (t, 1H, *J* = 7.3 Hz), 6.49 (d, 1H, *J* = 8.2 Hz), 4.18–4.10 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ161.9 (d, $^1J_{C\text{-}F}$ = 246.5 HZ), 150.3, 145.9, 139.8, 138.7, 132.8, 132.0, 131.3 (d, $^3J_{C\text{-}F}$ = 7.9 HZ), 130.5, 128.8, 128.5, 128.4, 127.9, 127.2, 127.0, 126.8, 124.0, 120.3, 117.1, 115.4 (d, $^2J_{C\text{-}F}$ = 21.5 HZ), 114.9111.0, 47.4. HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{34}H_{27}FN_3$ [(M + H)$^+$]: 496.2189. Found: 496.2187.

4.3.21. 5-(2-amino-phenyl)-1,3,4-triphenyl-1H-pyrazole(**3lj**)

50 mg, 65% yield, yellow solid, petroleum ether/ethyl acetate = 30:1, R_f = 0.2, m. p.: 160–161 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.05 (s, 1H), 7.94–7.93 (m, 2H), 7.70 (d, 2H, *J* = 7.6 Hz), 7.64 (d, 1H, *J* = 7.8 Hz), 7.59 (s, 1H), 7.48–7.47 (m, 3H), 7.33–7.26 (m, 5H), 7.21–7.18 (m, 3H), 7.09 (t, 1H, *J* = 7.6 Hz), 6.93 (t, 1H, *J* = 7.3 Hz), 6.45 (d, 1H, *J* = 8.0 Hz). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 143.3, 137.3, 132.7, 131.6, 131.1, 131.0, 130.6, 129.2, 129.0, 128.5, 126.3, 124.9, 123.0, 121.3, 120.9, 119.1, 113.7, 111.7. HRMS (ESI-TOF$^+$): *m/z* Calcd. For $C_{27}H_{22}N_3$ [(M + H)$^+$]: 388.1814. Found: 388.1818.

*4.3.22. 5-(2-amino-phenyl)-3,4-diphenyl-1-p-tolyl-1H-pyrazole (**3la**)*

57 mg, 71% yield, yellow solid, petroleum ether/ethyl acetate = 60:1, R_f = 0.2, mp 190–191 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.02 (s, 1H), 7.96–7.94 (m, 2H), 7.72 (d, 2H, *J* = 7.4 Hz), 7.64 (d, 1H, *J* = 7.8 Hz), 7.59 (s, 1H), 7.48–7.47 (m, 3H), 7.34–7.28 (m, 3H), 7.19 (t, 1H, *J* = 7.7 Hz), 7.14–7.07 (m, 5H), 6.46 (d, 1H, *J* = 8.0 Hz), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 140.0, 136.3, 131.9, 130.6, 130.2, 130.1, 130.0, 129.9, 129.6, 128.7, 128.0, 127.5, 127.4, 125.1, 123.1, 122.0, 119.9, 118.0, 112.6, 110.6,19.6. HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{28}H_{24}N_3$ [(M + H)$^+$]: 402.1970. Found: 402.1963.

*4.3.23. 5-(2-methylamino-phenyl)-4-(2-fluorophenyl)-3-(thiophene-2-yl)-1-phenyl-1H-pyrazole (**3hk**)*

45 mg, 53% yield, yellow solid, petroleum ether/ethyl acetate = 100:1, R_f = 0.2, mp 146–148 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44 (d, 2H), 7.33–7.28 (m, 3H), 7.27–7.24 (m, 2H), 7.20 (t, 3H, *J* = 9.5 Hz), 7.12–7.07 (m, 2H), 6.99–6.94 (m, 3H), 6.58 (t, 1H, *J* = 9.2 Hz), 6.53 (d, 1H, *J* = 10.3 Hz), 3.86 (br, 1H), 2.62 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.8 (d, $^1J_{C\text{-}F}$ = 305.9 HZ), 147.8, 146.0, 140.2, 139.7, 135.6, 132.9, 131.4, 130.6, 129.9 (d,$^3J_{C\text{-}F}$ = 10.0 Hz), 128.8, 127.4, 127.3, 125.2, 125.0, 124.3 (d,$^3J_{C\text{-}F}$ = 4.5 Hz), 123.9, 120.5, 120.4, 116.6, 115.7(d,$^2J_{C\text{-}F}$ = 27.4 Hz), 114.7(d,$^2J_{C\text{-}F}$ = 24.1 Hz), 110.2, 30.5; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{26}H_{20}FN_3S$ [(M + H)$^+$]: 426.1440. Found: 426.1143.

*4.3.24. 5-(2-methylamino-phenyl)-4-methyl-1,3-diphenyl-1H-pyrazole (**3mj**) 56 mg*

83% yield, white solid, petroleum ether/ethyl acetate = 40:1, R_f = 0.2, mp 166–168 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, 2H, *J* = 7.5 Hz), 7.50 (t, 2H, *J* = 7.6 Hz), 7.41–7.32 (m, 4H),7.28 (t, 2H, *J* = 7.7 Hz), 7.20 (t, 1H, *J* = 7.3 Hz), 6.97 (d, 1H, *J* = 7.3 Hz), 6.72–6.67 (m, 2H), 2.80 (s, 3H), 2.17 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 151.0, 147.6, 140.1, 138.8, 133.9, 131.4, 130.5, 128.7, 128.5, 127.7, 126.7, 123.3, 116.8, 115.6, 115.4, 110.1, 30.5, 10.0; HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{23}H_{22}N_3$ [(M + H)$^+$]: 340.1814. Found: 340.1816.

*4.3.25. 5-(2-methylamino-phenyl)-4-ethyl-1,3-diphenyl-1H-pyrazole (**3nj**)*

56 mg, 79% yield, white solid, petroleum ether/ethyl acetate = 50:1, R_f = 0.2, m. p.: 118–120 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, 2H, *J* = 7.5 Hz), 7.49–7.45 (m, 2H), 7.40–7.36 (m, 3H), 7.32 (t, 1H, *J* = 7.6 Hz), 7.27–7.24 (m, 2H), 7.18 (t, 1H, *J* = 7.3 Hz), 7.01 (d, 1H, *J* = 7.0 Hz), 6.72–6.68 (m, 2H), 2.77 (s, 3H), 2.66–2.48 (m, 2H), 1.02 (t, 3H, *J* = 7.5 Hz). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.8, 147.7, 140.0, 138.4, 134.0, 131.4, 130.5, 128.7, 128.5, 127.8, 127.7, 126.7, 123.4, 122.0, 116.8, 115.8, 110.1, 30.5, 17.3, 15.2. HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{24}H_{24}N_3$ [(M + H)$^+$]: 354.1970. Found: 354.1972.

*4.4. Synthesis of **3ok***

In a 5 mL round-bottom flask, benzosultam-3-ylidenes **1o** (53 mg, 0.2 mmol) and hydrazonoyl chloride **2k** (79 mg, 0.3 mmol, 1.5 equiv) were dissolved in CH_2Cl_2 (0.5 mL, 0.4 M). Then, a solution of triethylamine (1 M, 0.5 mL, 2.5 equiv) was added dropwise at 0 °C. Then the reaction mixture was stirred at room temperature for 5 h. After that, saturated aqueous NH_4Cl (2 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (1 mL × 2). The combined organic layers were dried over Na_2SO_4 and evaporated to remove solvent under reduced pressure. The residue was subjected to column chromatography (petroleum ether/ethyl acetate = 10:1) to afford the compound **3ok**.

*4.4.1. 5-(2-methylamino-phenyl)-4-ethoxycarbonyl-3-phenyl-1-(3-chlorophenyl)-1H-pyrazole (**3ok**)*

65 mg, 76% yield, white solid, mp 166–168 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ7.90–7.89 (m, 2H), 7.46–7.41 (m, 3H), 7.36 (t, 1H, *J* = 7.3 Hz), 7.26–7.19 (m, 6H), 6.74–6.71 (m, 1H), 3.98–3.76 (m, 2H), 2.97 (s, 3H), 0.97 (t, 3H, *J* = 6.3 Hz). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 153.9, 151.5, 140.4, 140.2, 139.9, 133.4, 131.6, 130.4, 128.9, 128.7, 127.7, 127.2, 127.1, 126.0, 125.9, 124.8, 123.2, 121.0, 105.0, 60.7, 36.6, 13.4. HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{25}H_{23}ClN_3O_2$ [(M + H)+]: 432.1479. Found: 432.1475.

*4.5. Synthesis of **4ok***

A suspension of **3ok** (43 mg, 0.1 mmol) and potassium carbonate (15 mg, 0.11 mmol, 1.1 equiv) in ethanol (0.5 mL, 0.2 M) was stirred at reflux in an oil bath for 1 h. After cooling to the room temperature, The mixture was evaporated to remove solvent under reduced pressure. The residue was purified by column chromatography (petroleum ether/ethyl acetate = 5:1) to afford the compound **4ok**.

*4.5.1. 1-(3-chlorophenyl)-5-methyl-3-phenyl-1H-pyrazolo[[4] [3-c]]quinolin-4(5H)-one (**4ok**)*

36 mg, 93% yield, white solid, mp 157–158 °C;^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (d, 2H, *J* = 7.2 Hz), 7.67 (s, 1H), 7.60–7.53 (m, 4H), 7.48–7.43 (m, 4H), 7.32 (d, 1H, *J* = 7.9 Hz), 7.07–7.06 (m, 1H), 3.79 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ158.6, 152.0, 141.5, 141.4, 139.7, 135.5, 131.4, 130.8, 130.4, 130.2, 129.7, 128.9, 128.0, 127.8, 125.5, 123.1, 121.8, 115.7, 111.6, 110.4, 29.6. HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{23}H_{17}ClN_3O$ [(M + H)$^+$]: 386.1060. Found: 386.1065.

*4.6. Synthesis of **5gj***

[Pd_2dba_3] (4.6 mg, 0.005 mmol, 0.05 equiv), dppf (3.9 mg, 0.007 mmol, 0.07 equiv), and KOtBu (22.4 mg, 0.2 mmol) were added to a 5 mL round-bottom flask and mixed with toluene (2 mL, 0.05 M) and **3gj** (48 mg, 0.1 mmol). The mixture was heated in an oil bath (at 100 °C) for 12 h under argon atmosphere. The mixture was evaporated to remove solvent under reduced pressure. The residue was purified by column chromatography (petroleum ether/ethyl acetate = 30:1) to afford the compound **5gj**.

*4.6.1. N-methyl-1,3-diphenyl-dibenzo[b,f]pyrazolo[[3] [4-d]] azepine (**5gj**)*

35 mg, 88% yield, white solid. m. p.: 204–205 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, 2H, *J* = 6.9 Hz), 7.50 (d, 2H, *J* = 7.6 Hz), 7.42–7.32 (m, 9H), 7.29–7.27 (m, 1H), 7.16 (d, 1H, *J* = 7.5 Hz), 6.93–6.90 (m, 1H), 6.84 (s, 2H), 3.50 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.8, 140.2, 133.2, 129.8, 129.6, 129.5, 129.1, 128.9, 128.3, 128.0, 127.8, 127.5, 125.4, 53.4. HRMS (ESI-TOF$^+$): *m*/*z* Calcd. For $C_{28}H_{22}N_3$ [(M + H)$^+$]: 400.1814. Found: 400.1811.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2020.131568.

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