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(2 + 1 + 1 + 1)-Annulation Reactions of Aryldiazonium Tetrafluoroborates with Sulfur Ylides to Polysubstituted Pyrazoles

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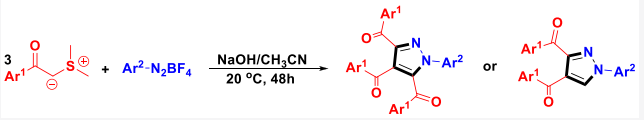
ABSTRACT: Novel divergent domino annulation reactions of sulfur ylides with aryldiazonium tetrafluoroborates have been developed, affording various tetra- and trisubstituted pyrazole derivatives in moderate to good yields. Three molecules of sulfur ylides were applied as C_1 synthon to construct the complex products with five new chemical bonds formed in these one-pot reactions.



INTRODUCTION

Sulfur ylides are readily accessible and classical reagents widely used as one-carbon units. Due to their inherent zwitterionic property and reactivity, sulfur ylide-initiated reactions are considered as effective approaches to achieve varieties of organic transformations in organic chemistry.[1] Over the past decades, the development of tandem reactions with sulfur ylides has provided one of the most advantageous strategies for the construction of structurally diverse carbo- or heterocyclic compounds.[2] Although great progress has been made in sulfur ylide-related chemistry, there is still room for researchers to extend the application of sulfur ylides in organic synthesis, as new reagents or reaction types are emerging successively.

Aryldiazonium salts are known as readily available and inexpensive chemicals that have been applied as versatile building blocks for a number of organic syntheses.[3] One of the reaction modes of aryldiazonium salts is acting as highly reactive electrophiles. Under this mechanism, aryldiazonium salts are usually attacked by nucleophiles to generate a range of nitrogen-containing compounds.[4] Aryldiazonium salts have been reported to react with stabilized sulfur ylides, resulting in nitrilimine intermediates, which could further proceed a 1,3-dipolar dimerization or react with another reactive functional reagent to construct a variety of nitrogen-containing heterocyclic compounds (Scheme 1, eq 1). In the above cases, aryldiazonium salts and sulfur ylides usually reacted equivalently with each other.[5] Recently, Xu's group reported an interesting synthesis of highly functionalized hydrazones using α-diazo-β ketoesters/ketones and dimethylsulfonium ylides as starting materials. In this transformation, zwitterionic intermediates generated from addition of dimethylsulfonium ylides with diazo compounds could be further attacked by another molecule of dimethylsulfonium ylides. As a result, two molecules of dimethylsulfonium ylides were involved during the reaction process (Scheme 1, eq 2).[6]

Inspired by Xu's work, we deduced that new chemical transformations might be realized when aryldiazonium salts are reacting with multiple equivalents of sulfur ylides. In view of our long-standing interests in exploring new methodologies of sulfur ylides,[7] we herein reported a type of (2 + 1 + 1 + 1)-annulation reaction, in which various polysubstituted pyrazoles were obtained from reactions of aryldiazonium tetrafluoroborates with three molecules of sulfur ylides (Scheme 1, eq 3).

RESULTS AND DISCUSSION

Our inquiry began with the reaction of stabilized sulfur ylide **1a** with aryldiazonium tetrafluoroborate **2a**. First, a 2:1 mixture of **1a** and **2a** was stirred in acetonitrile at 20 °C for 48 h in the presence of TEA, DBU, or DABCO; no major products were generated (Table 1, entries 1−3). To our delight, when 3.0 equiv of $NaHCO_3$ was used as an additive, two major products were isolated in 16 and 28% yields, respectively (Table 1, entry 4). A similar result was gained when Na_2CO_3 was applied in the reaction (Table 1, entry 5). The products were further identified as polysubstitutedpyrazole **3a** and **4a**. As we all know, pyrazole is a privileged scaffold with broad pharmaceutical activities in medicinal chemistry. Commercial drugs such as Celecoxib, Difenamizole, Ruxolitinib, as well as Crizotinib are featured with pyrazole moieties.[8] Besides, functional pyrazoles are valuable building blocks which could be further transferred to more complex drug-like molecules by late-stage modifications. In this sense, the development of a synthesis method for functional pyrazoles would be an important advance.

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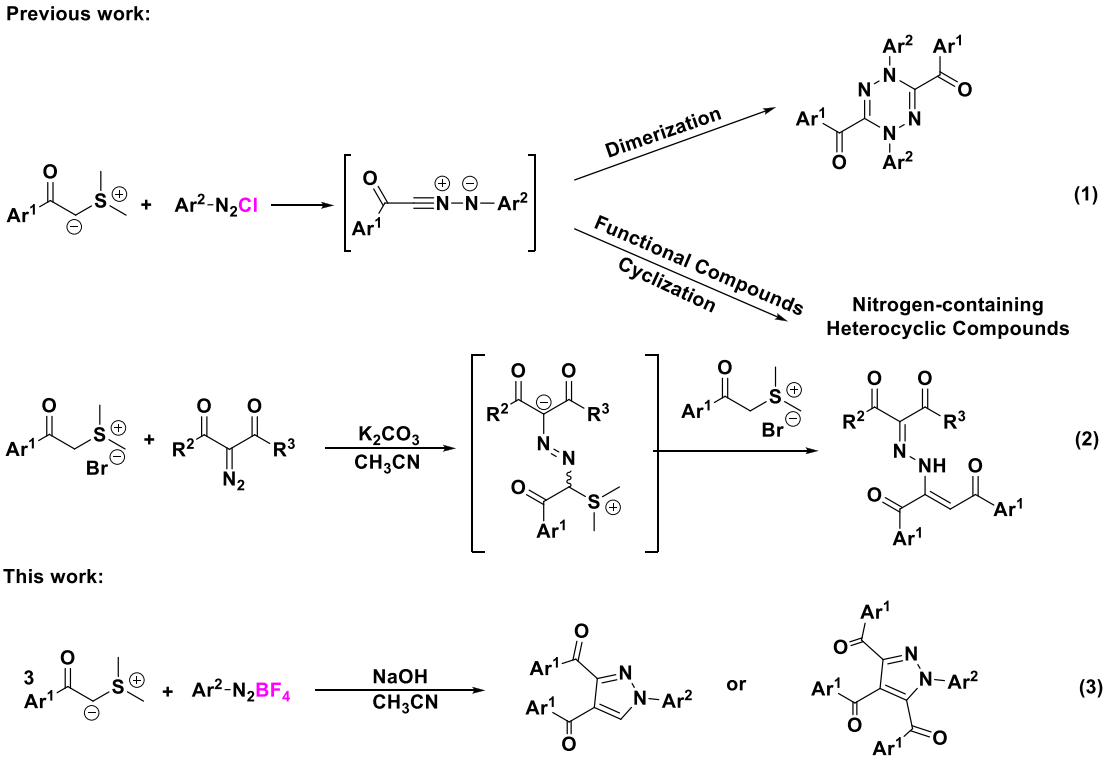
Scheme 1. Reactions of Sulfur Ylides or Sulfonium Ylides with Diazo Compounds



Encouraged by the initial results, other inorganic bases were then screened for further optimization of these transformations. As listed in Table 1, in the presence of K_2CO_3, KOH, NaH, or NaOH, **4a** was obtained as a major product (Table 1, entries 6−9). NaOH was proven to be superior to other bases with an 80% yield of **4a** (Table 1, entry 9). Besides, the amount of base seemed to be an influencing factor for the conversions of these reactions. Reducing the amount of bases led to the formation of major product **3a** (Table 1, entries 10−12), among which NaOH was still the most effective base (Table 1, entry 11). As we expected, increasing the amount of NaOH led to **4a** as the major product with a yield of 64% (Table 1, entry 13). Further screening of solvents showed that acetonitrile was the best solvent (Table 1, entries 9 and 14−20). Furthermore, reducing or increasing the amount of **2a** was not conducive to the yields of products (Table 1, entries 21 and 22). It should be pointed out that each molecule of diazonium salt would react with three molecules of sulfur ylide to afford products theoretically; however, due to the instability of diazonium salts in the presence of bases, the amount of diazonium salts was set to be excessive in comparison with that of sulfur ylides, so a 2:1 ration of **1a** and **2a** was considered to be the most suitable. Based on the above investigation, the optimal conditions for synthesis of **3a** and **4a** were set as entries 11 and 9 in Table 1, respectively. Besides, previous work has been reported that 1,4-dihydrotetrazin-1,2,4,5-tetrazines can be obtained as major products when the methanol solution of sulfur ylides was added dropwise to the solution of diazonium salts.[5b] Interestingly, only a trace of 1,4-dihydrotetrazin-1,2,4,5-tetrazines was detected under the optimal conditions; this is possibly due to the fact that sulfur ylides were always in a higher concentration than the key intermediate during the reaction process, thus effectively avoiding the 1,3-dipolar dimerization of nitrilimine intermediates to form 1,4-dihydrotetrazin-1,2,4,5-tetrazines as the literature reported.

With the optimal conditions in hand, we then explored the scope of substrates for these sequential (2 + 1 + 1 + 1) tandem reactions. As listed in Table 2, some kinds of tetrasubstituted pyrazole derivatives **3** could be obtained in accepted yields in the presence of 1.0 mmol of NaOH. Phenyldiazonium tetrafluoroborate and aryldiazonium tetrafluoroborates with a methyl or methoxyl group on the benzene ring (Table 2, **3a**, **3i**, and **3b**) could be carried out in slightly better yields than that with a fluorine substituent (Table 2, **3k**). A strong electron-withdrawing substitute, such as a nitro group on the benzene ring of aryldiazonium tetrafluoroborate, was intolerant to the reaction, and only a trace of the product was observed (Table 2, **3l**). Sulfur ylides with electron-donating substitutes on the benzene ring led to slightly higher yields than those with halogen substitutes (Table 2, **3f−3h** vs **3c−3e**); however, all of them were obtained in lower yields than unsubstituted sulfur ylides (Table 2, **3b**). As expected, the positions of methyl on the benzene ring of sulfur ylides had little effect on the yields (Table 2, **3f−3h**). In addition, sulfur ylide with 2-naphthyl attached at the carbonyl was found to be tolerable to the reaction (Table 2, **3j**). Unfortunately, when 1-(dimethyl-l4-sulfanylidene)-4-phenylbutan-2-one or methyl 2-(dimethyl-l4-sulfanylidene)acetate was applied as a starting material, only a trace amount of products was detected. Besides, it should be pointed out that trisubstituted pyrazole compounds were detected as major byproducts under the standard reaction conditions when 2.0 equiv of NaOH was used as an additive, which was responsible for the relatively lower yields of some tetrasubstituted pyrazoles **3**.

Trisubstituted pyrazole compounds **4** could be obtained in the presence of 1.5 mmol of NaOH. As listed in Table 3, some kinds of aryldiazonium tetrafluoroborates could be applied in

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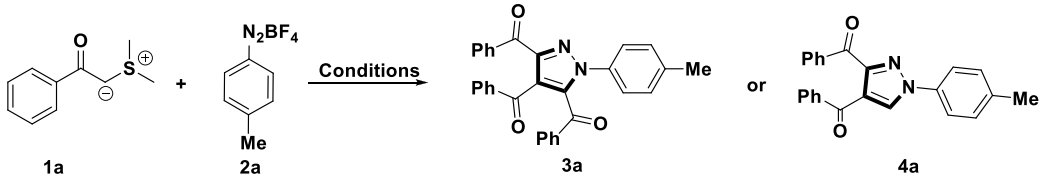
Table 1. Optimization of the Reaction Conditions[a]



entry	solvent	base/equiv	major product (yield, %)[b]
1	CH_3CN	TEA/3.0	**3a** (<5%), **4a** (<5%)
2	CH_3CN	DBU/3.0	**3a** (<5%), **4a** (<5%)
3	CH_3CN	DABCO/3.0	**3a** (<5%), **4a** (<5%)
4	CH_3CN	$NaHCO_3$/3.0	**3a** (16%), **4a** (28%)
5	CH_3CN	Na_2CO_3/3.0	**3a** (22%), **4a** (34%)
6	CH_3CN	K_2CO_3/3.0	**4a** (55%)
7	CH_3CN	KOH/3.0	**4a** (62%)
8	CH_3CN	NaH/3.0	**4a** (69%)
9	CH_3CN	NaOH/3.0	**4a** (80%)
10	CH_3CN	NaOH/1.6	**3a** (51%)
11	CH_3CN	NaOH/2.0	**3a** (70%)
12	CH_3CN	K_2CO_3/2.0	**3a** (65%)
13	CH_3CN	NaOH/4.0	**4a** (64%)
14	Et_2O	NaOH/3.0	**3a** (<5%), **4a** (<5%)
15	CH_2Cl_2	NaOH/3.0	**4a** (30%)
16	THF	NaOH/3.0	**4a** (65%)
17	DMF	NaOH/3.0	**4a** (60%)
18	EtOH	NaOH/3.0	**4a** (57%)
19	MeOH	NaOH/3.0	**4a** (71%)
20	DMSO	NaOH/3.0	**3a** (<5%), **4a** (<5%)
21[c]	CH_3CN	NaOH/3.0	**4a** (30%)
22[d]	CH_3CN	NaOH/3.0	**4a** (71%)

[a]The reaction was carried out with **1a** (0.2 mmol, 2.0 equiv), **2a** (0.1 mmol, 1.0 equiv), base and solvent (2 mL), 20 °C, 48 h, under air atmosphere. [b]Isolated yields were calculated according to **1a** after column chromatography. [c]**1a** (0.2 mmol), **1a**:**2a** = 3:1. [d]**1a** (0.2 mmol), **1a**:**2a** = 3:2. TEA = Triethylamine. DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene. Dabco = 1,4-Diazabicyclo[2.2.2]octane.

the reactions to generate the products **4** in moderate to good yields. Among them, aryldiazonium tetrafluoroborates with electron-donating groups on the benzene ring were generally proceeded better than those with electron-withdrawing substituents (Table 3, **4a** vs **4b**−**4g**; **4q** vs **4i**). The reactions can also be applied to sulfur ylides with −F, −Cl, −Br, $-NO_2$, or −CN on the benzene ring in moderate yields (Table 3, **4h**−**4l**). To our surprise, sulfur ylides bearing an electron-donating group such as a methyl group on the benzene ring were unfavorable for the transformations; tetrasubstituted pyrazoles **3f** and **3g** were obtained as major products instead of the desired products even when increasing the amounts of NaOH or prolonging the reaction time. The possible reason is that a methyl group might weaken the electrophilic ability of a carbonyl group and further affect the subsequent removal of aroyl groups. To our delight, diazonium tetrafluoroborate with biphenyl, sulfur ylides with 2-naphthyl or 2-thienyl attached to the carbonyl can also be well tolerated (Table 3, **4p**, **4o**, and **4m**).

The structures of all products were characterized by ^1H NMR, ^{13}C NMR, and HRMS. Moreover, the structures of **3k** and **4h** were further identified by single-crystal X-ray diffraction (Table 2, **3k**, CCDC 2064733; Table 3, **4h**, CCDC 2064734).

In order to better expand the application of these methods, **4f** was selected for the late-stage modifications. As displayed in Scheme 2, aryl methanol compound **4fa** and pyrazolo[3,4-*d*]pyridazine compound **4fb** could be efficiently obtained in 70 and 97% yield, respectively (Scheme 2, eq 1).

At last, to gain insight into the reaction mechanism, a control experiment was carried out (Scheme 2, eq 2). When **3a** (1.0 equiv) was treated with NaOH (0.5 equiv) in CH_3CN at 20 °C for 24 h, **4a** was generated in 22% yield.

Based on the above-mentioned results, a possible mechanism for this domino reaction is proposed in Scheme 3. Initially, nucleophilic attack of sulfur ylides **1** on aryldiazonium tetrafluoroborates **2** leads to formation of a new C−N bond to generate the intermediate **I′**. Intermediate **I′** would further convert to the zwitterionic nitrilimine **II**,[5b] which could be attacked by the other two molecules of sulfur ylides through a repeated S_N2 reaction process to form intermediate **IV**. A subsequent intramolecular nucleophilic attack of intermediate **IV** provides the dihydropyrazole intermediate **V**. Aromatization of intermediates **V** under the air atmosphere leads to the desired product **3**. However, there may be two possible pathways for the formation of product **4**. In pathway a, breaking of the C−C bond between 5-arylformyl and the pyrazole nucleus in the presence of NaOH results in the transformation from **3** to **4**. However, pathway b cannot be excluded either. In this pathway, intermediate **IV** might undergo a deacylation process in the presence of NaOH to afford intermediate **V′** which would go through an intramolecular cyclization followed by aromatization to provide product **4**.

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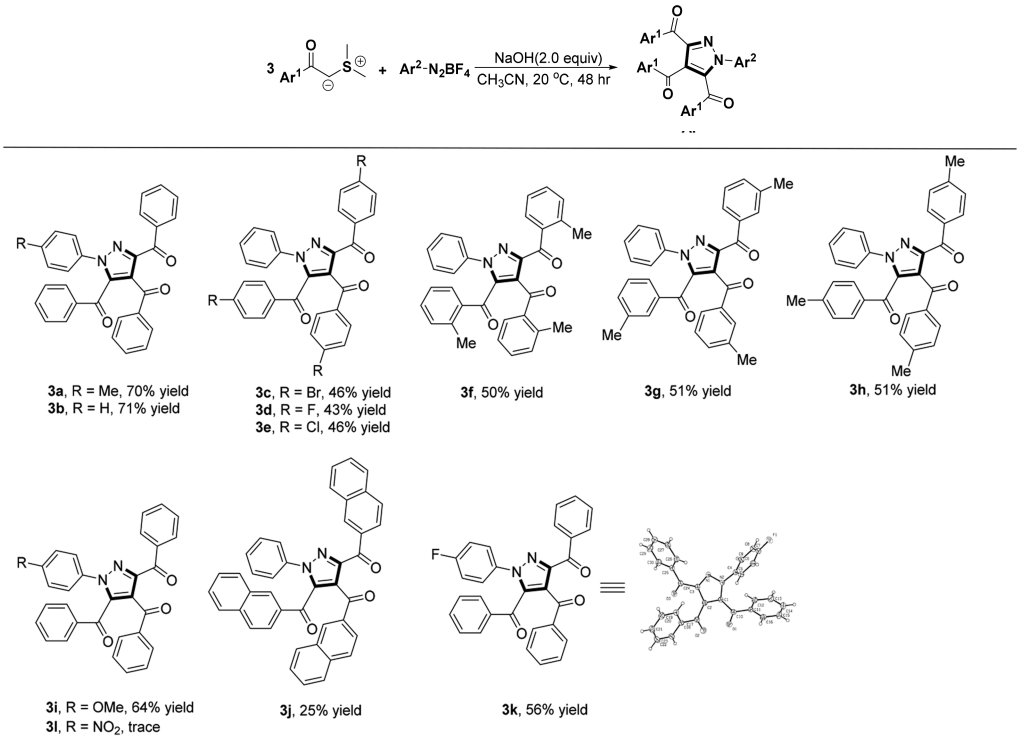
Table 2. Substrate Scope of Tetrasubstituted Pyrazole Compounds 3[a]



[a]Reaction conditions: **1** (1.0 mmol, 2.0 equiv), **2** (0.5 mmol, 1.0 equiv), NaOH (1.0 mmol, 2.0 equiv), and CH_3CN (10 mL), 20 °C, 48 h, under air atmosphere. Isolated yields were calculated according to sulfur ylides after column chromatography.

CONCLUSIONS

In conclusion, we have developed novel divergent domino annulation reactions of stabilized sulfur ylides and aryldiazonium tetrafluoroborates for the synthesis of polysubstituted pyrazole derivatives in moderate to good yields under mild conditions. In these (2 + 1 + 1 + 1)-annulation reactions, three molecules of sulfur ylides were applied as C_1 synthon to construct the complex products with five new chemical bonds formed in the one-pot reactions. Good generality, mild reaction conditions, easily manufactured start materials, as well as no need for precious catalysts are all advantages for this method. We believe that these interesting chemical transformations will be a supplement to the synthetic diversities of sulfur ylides and attract research interest from organic chemists and pharmacologists.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all reagents and solvents were purchased from commercial sources and used without purification. Purifications of reaction products were carried out by chromatography using silica gel (200−300 mesh). Melting points were recorded on a BÜCHI B-540 melting point apparatus. NMR spectra were recorded for ^{1}H NMR at 400 MHz and for ^{13}C NMR at 100 MHz. For ^{1}H NMR, tetramethylsilane (TMS) served as the internal standard (δ = 0) and data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constant(s) in Hz. For ^{13}C NMR, $CDCl_3$ (δ = 77.26) or DMSO-d_6 (δ = 39.6) was used as the internal standard and spectra were obtained with complete proton decoupling. HPLC analysis and the HRMS of all final products were confirmed on an Agilent 1290 HPLC-6224 Time of Fight Mass Spectrometer using a PhenomenexLuna 5μ C_{18}, 100 Å, 150 × 4.60 mm 5 μm column at a flow rate of 0.5 mL/min using linear gradient buffer B in A (B, CH_3OH containing 0.1% formic acid; A, H_2O containing 0.1% formic acid). Mobile phase B was increased linearly from 5 to 95% over 7 min and 95% over the next 2 min, after which the column was equilibrated to 5% for 1 min. The X-ray diffraction measurements were carried out on a Rigaku RAXIS-RAPID single-crystal diffractometer. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF254. Aryldiazonium tetrafluoroborates and sulfur ylides were synthesized according to the literature procedure.[9,10]

Typical Procedure for Synthesis of Product 3. A mixture of sulfur ylide (1.0 mmol, 2.0 equiv), aryl diazonium tetrafluoroborate (0.5 mmol, 1.0 equiv), and NaOH (1.0 mmol, 2.0 equiv) was stirred in 10 mL of CH_3CN at 20 °C for 48 h under an air atmosphere. After the completeness of the reaction, the solvent was removed, and the crude product was carried out by chromatography to afford **3a**−**3k** as desired products.

(1-(*p*-Tolyl)-1*H*-pyrazole-3,4,5-triyl)tris(phenylmethanone) (3a). Purified by column chromatography (silica gel, petroleum:-EtOAc = 8:1), white solid (110 mg, 70%), mp 128.9−130.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 7.2 Hz, 2H), 7.67 (d, J = 7.2 Hz, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.59−7.54 (m, 1H), 7.47−7.42 (m, 4H), 7.37 (d, J = 7.6 Hz, 2H), 7.30−7.26 (m, 4H), 7.19 (d, J = 7.2 Hz, 2H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 189.7, 186.9, 186.8, 149.8, 141.4, 139.5, 138.0, 136.5, 136.5, 136.4, 134.4, 133.5, 133.2, 130.7, 130.1, 129.7, 129.1, 128.8, 128.5, 126.9, 124.5, 21.3. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{31}H_{23}N_2O_3$ 471.1703; found 471.1700.

(1-Phenyl-1*H*-pyrazole-3,4,5-triyl)tris(phenylmethanone) (3b). Purified by column chromatography (silica gel, petroleum:-EtOAc = 8:1), white solid (108 mg, 71%), mp 128.9−130.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 7.2 Hz, 2H), 7.68 (d, J = 7.6 Hz, 2H), 7.64 (d, J = 7.6 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.52−7.38 (m, 9H), 7.30 (d, J = 7.8 Hz, 2H), 7.26 (d, J = 7.6 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 189.5, 186.7, 186.5, 149.8, 141.2, 138.7, 137.8, 136.2, 136.2, 134.3, 133.4, 133.1, 130.5, 129.5, 129.3, 129.1,

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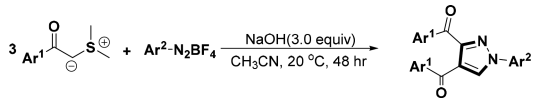
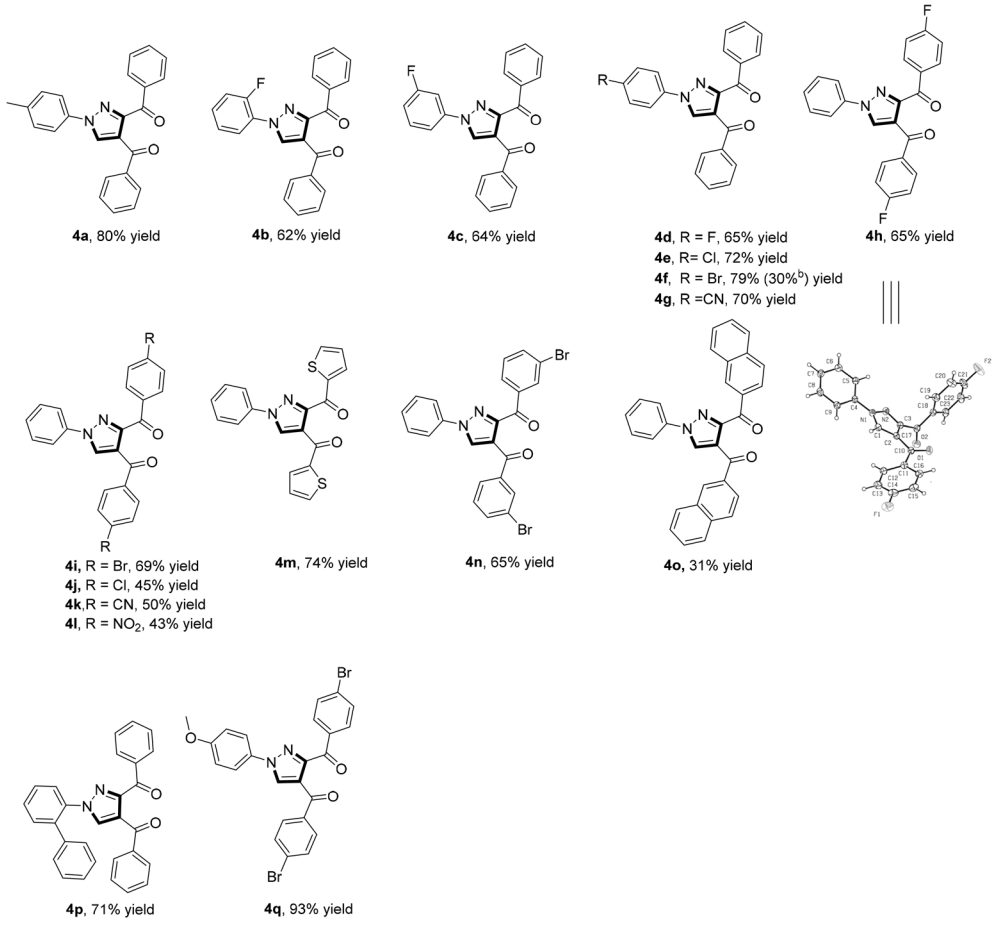
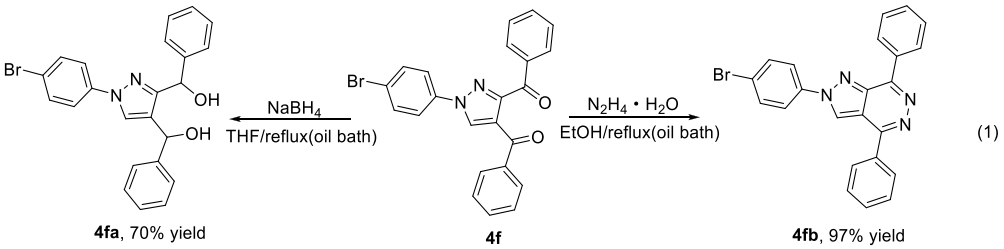
Table 3. Substrate Scope of Trisubstituted Pyrazole Compounds 4[a]

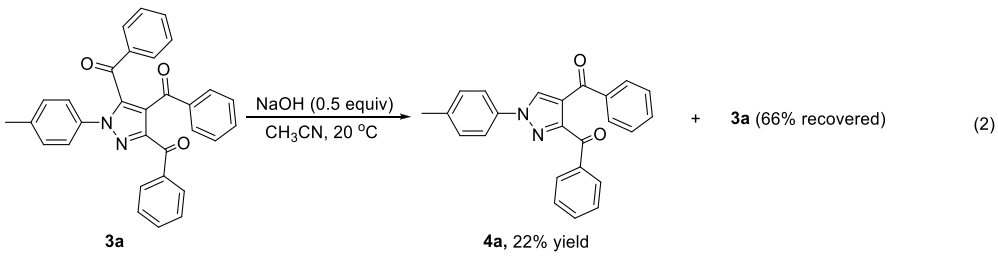




[a]Reaction conditions: **1** (1.0 mmol, 2.0 equiv), **2** (0.5 mmol, 1.0 equiv), NaOH (1.5 mmol, 3.0 equiv), and CH_3CN (10 mL), 20 °C, 48 h, under air atmosphere. [b]Scale-up reaction with 10 mmol of sulfur ylide and 5 mmol of aryldiazonium tetrafluoroborate. Isolated yields were calculated according to sulfur ylides after column chromatography.

Scheme 2. Late-Stage Modifications of 4f and Control Reaction





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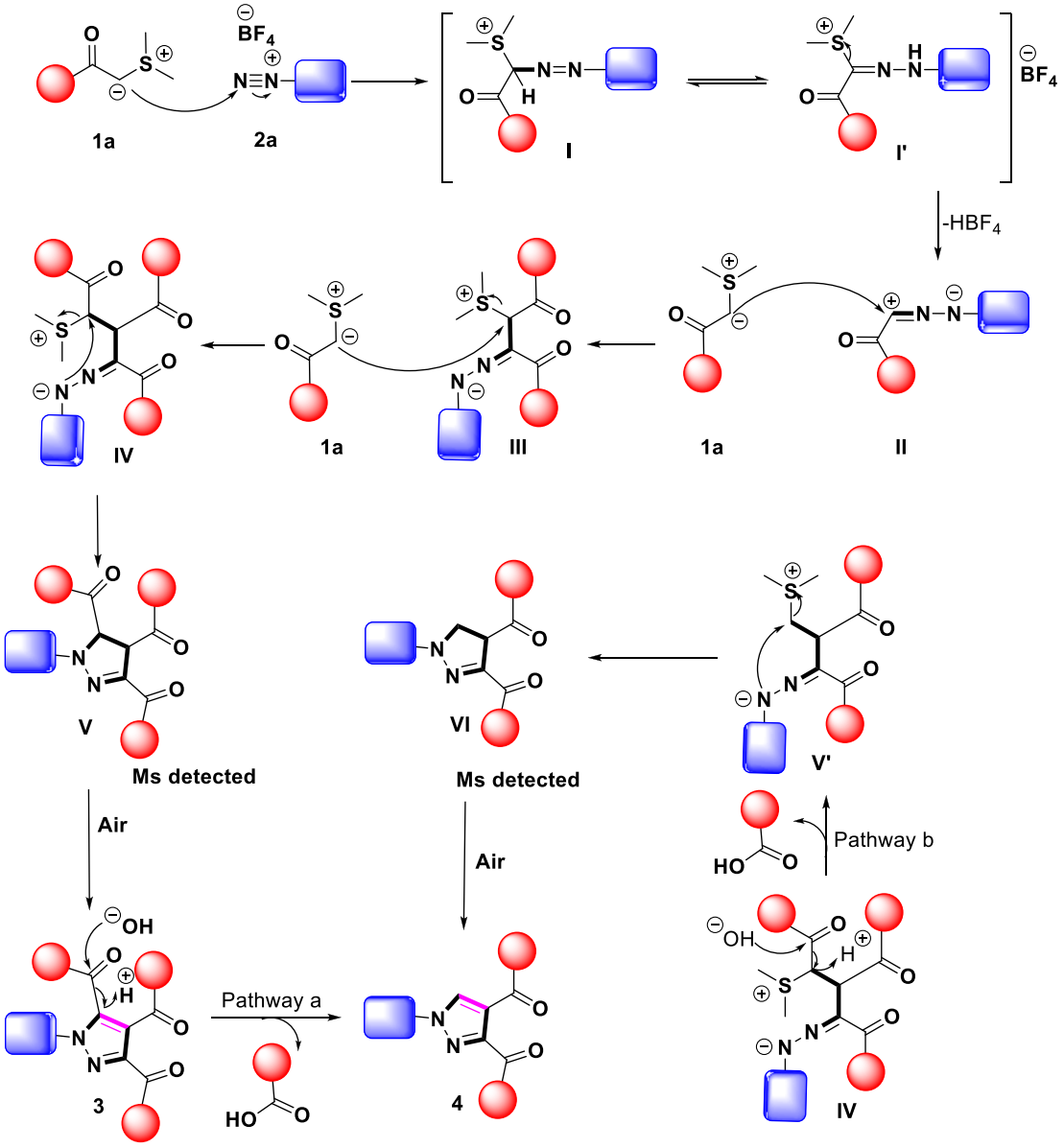
Scheme 3. Plausible Mechanisms for the Formation of 3 and 4



128.9, 128.6, 128.3, 126.9, 124.5. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{21}N_2O_3$ 457.1547; found 457.1550.

(1-Phenyl-1*H*-pyrazole-3,4,5-triyl)tris((4-bromophenyl)-methanone) (3c). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (106 mg, 46%), mp 138.2−140.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H), 7.55 (t, J = 8.8 Hz, 4H), 7.50−7.44 (m, 6H), 7.43−7.40 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 188.5, 185.4, 185.1, 149.4, 140.9, 138.5, 136.3, 134.7, 134.6, 132.2, 132.1, 131.9, 131.8, 130.9, 130.4, 130.2, 129.6, 129.5, 129.2, 128.8, 126.8, 124.4. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{18}Br_3N_2O_3$ 690.8862; found 690.8864.

(1-Phenyl-1*H*-pyrazole-3,4,5-triyl)tris((4-fluorophenyl)-methanone) (3d). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), a white solid (73 mg, 43%), mp 151.0−151.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, J = 8.8, 5.6 Hz, 2H), 7.74−7.70 (m, 4H), 7.49−7.41 (m, 5H), 7.15 (t, J = 8.6 Hz, 2H), 7.02−6.97 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 188.2, 185.0, 184.7, 166.5 (d, J = 256.9 Hz), 166.3 (d, J = 254.5 Hz), 166.0 (d, J = 254.3 Hz), 149.6, 141.0, 138.7, 134.2 (d, J = 2.8 Hz), 133.6 (d, J = 9.5 Hz), 132.6 (d, J = 2.8 Hz), 132.5 (d, J = 10.0 Hz), 132.4 (d, J = 2.8 Hz), 131.8 (d, J = 9.5 Hz), 129.6, 129.5, 127.0, 124.5, 116.3 (d, J = 22.0 Hz), 115.9 (d, J = 22.0 Hz), 115.8 (d, J = 21.7 Hz). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{18}F_3N_2O_3$ 511.1264; found 511.1270.

(1-Phenyl-1*H*-pyrazole-3,4,5-triyl)tris((4-chlorophenyl)-methanone) (3e). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (86 mg, 46%), mp 185.2−187.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 6.8 Hz, 2H), 7.70−7.58 (m, 4H), 7.50−7.38 (m, 7H), 7.35−7.25 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 188.2, 185.1, 184.8, 149.3, 141.3, 140.9, 140.3, 139.9, 138.4, 135.9, 134.3, 134.2, 132.1, 130.8, 130.3, 129.5, 129.5, 129.2, 128.9, 128.8, 126.8, 124.3. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{18}Cl_3N_2O_3$ 559.0378; found 559.0382.

(1-Phenyl-1*H*-pyrazole-3,4,5-triyl)tris(*o*-tolylmethanone) (3f). Purified by column chromatography (silica gel, petroleum:-EtOAc = 8:1), white solid (83 mg, 50%), mp 138.2−140.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 7.2 Hz, 3H), 7.41−7.36 (m, 4H), 7.35−7.29 (m, 2H), 7.23−7.17 (m, 3H), 7.16−7.12 (m, 1H), 7.11−7.06 (m, 2H), 7.01 (d, J = 7.4 Hz, 1H), 2.40 (s, 3H), 2.22 (s, 3H), 2.08 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 190.6, 190.0, 187.6, 151.0, 142.5, 140.6, 139.5, 139.4, 138.7, 137.4, 136.4, 135.8, 133.0, 132.0, 131.8, 131.7, 131.6, 131.5, 131.3, 131.2, 130.8, 129.2, 129.1, 127.5, 125.7, 125.3, 125.2, 124.7,

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20.9, 20.6, 20.5. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{33}H_{27}N_2O_3$ 499.2016; found 499.2020.

(1-Phenyl-1*H*-pyrazole-3,4,5-triyl)tris(*m*-tolylmethanone) (3g). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (85 mg, 51%), mp 150.2−152.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.6 Hz, 1H), 7.87 (s, 1H), 7.53−7.46 (m, 4H), 7.42−7.36 (m, 6H), 7.34−7.38 (m, 2H), 7.25−7.14 (m, 3H), 2.36 (s, 3H), 2.22 (s, 3H), 2.21 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.5, 187.3, 186.7, 150.0, 141.4, 138.8, 138.6, 138.1, 138.1, 137.9, 136.4, 136.3, 135.0, 134.2, 133.7, 130.6, 129.9, 129.3, 129.0, 128.6, 128.2, 127.8, 126.9, 126.8, 126.2, 124.5, 21.3, 21.0, 21.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{33}H_{27}N_2O_3$ 499.2016; found 499.2010.

(1-Phenyl-1*H*-pyrazole-3,4,5-triyl)tris(*p*-tolylmethanone) (3h). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (85 mg, 51%), mp 203.2−204.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.0 Hz, 2H), 7.53−7.47 (m, 2H), 7.39−7.35 (m, 3H), 7.26−7.23 (m, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 2.41 (s, 3H), 2.33 (s, 3H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.2, 186.4, 186.4, 149.9, 145.6, 144.3, 143.9, 141.3, 138.9, 135.4, 133.9, 133.8, 130.7, 129.8, 129.4, 129.3, 129.2, 129.1, 129.0, 129.0, 126.7, 124.4, 21.8, 21.8, 21.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{33}H_{27}N_2O_3$ 499.2016; found 499.2021.

(1-(4-Methoxyphenyl)-1*H*-pyrazole-3,4,5-triyl)tris(phenylmethanone) (3i). Purified by column chromatography (silica gel, petroleum:EtOAc = 6:1), white solid (104 mg, 64%), mp 119.3−121.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 7.2 Hz, 2H), 7.69−7.61 (m, 4H), 7.57 (t, J = 7.4 Hz, 1H), 7.50−7.40 (m, 6H), 7.31−7.28 (m, 2H), 7.27−7.24 (m, 2H), 6.89 (d, J = 9.2 Hz, 2H), 3.79 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.5, 186.8, 186.7, 160.0, 149.5, 141.3, 137.8, 136.3, 136.3, 134.3, 133.7, 133.0, 131.8, 130.5, 129.5, 128.9, 128.6, 128.3, 126.5, 125.9, 114.4, 55.5. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{31}H_{23}N_2O_4$ 487.1652; found 487.1645.

(1-Phenyl-1*H*-pyrazole-3,4,5-triyl)tris(naphthalen-2-ylmethanone) (3j). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), light pink solid (51 mg, 25%), mp 183.9−185.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.25 (s, 1H), 8.13 (d, J = 9.2 Hz, 2H), 7.94 (d, J = 8.0 Hz, 1H), 7.85 (t, J = 8.2 Hz, 2H), 7.78−7.70 (m, 4H), 7.69−7.65 (m, 2H), 7.62−7.58 (m, 5H), 7.56−7.50 (m, 3H), 7.46−7.35 (m, 5H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.6, 186.9, 186.7, 150.3, 141.6, 139.0, 136.2, 135.9, 135.7, 135.5, 133.9, 133.8, 133.3, 133.0, 132.5, 132.3, 132.2, 131.4, 130.1, 129.8, 129.6, 129.5, 129.4, 129.3, 129.0, 128.9, 128.6, 128.5, 128.4, 127.9, 127.8, 127.3, 127.2, 126.8, 126.7, 125.5, 124.6, 124.2, 123.9. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{42}H_{27}N_2O_3$ 607.2016; found 607.2013.

(1-(4-Fluorophenyl)-1*H*-pyrazole-3,4,5-triyl)tris(phenylmethanone) (3k). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (88 mg, 56%), mp 163.9−164.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 6.0 Hz, 2H), 7.66−7.57 (m, 5H), 7.50−7.45 (m, 6H), 7.35−7.26 (m, 4H), 7.14−7.06 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.4, 186.6, 186.4, 162.6 (d, J = 250.2 Hz), 149.8, 141.3, 137.7, 136.2, 136.1, 134.9 (d, J = 3.1 Hz), 134.5, 133.5, 133.2, 130.5, 129.5, 128.9, 128.7, 128.4, 126.9, 126.6 (d, J = 8.9 Hz), 116.4 (d, J = 23.2 Hz). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{20}FN_2O_3$ 475.1452; found 475.1460.

Typical Procedure for Synthesis of Product 4. A mixture of sulfur ylide (1.0 mmol, 2.0 equiv), aryl diazonium tetrafluoroborate (0.5 mmol, 1.0 equiv), and NaOH (1.5 mmol, 3.0 equiv) was stirred in 10 mL of CH_3CN at 20 °C for 48 h under an air atmosphere. After the completeness of the reaction, the solvent was removed, and the crude product was carried out by chromatography to afford **4a**−**4q** as desired products.

Typical procedure for scale-up synthesis of product **4f**. A mixture of 2-(dimethyl-l4-sulfanylidene)-1-phenylethan-1-one (10 mmol, 2.0 equiv), 4-bromobenzenediazonium tetrafluoroborate (5 mmol, 1.0 equiv), and NaOH (15 mmol, 3.0 equiv) were stirred in 80 mL of CH_3CN at 20 °C for 48 h under an air atmosphere. After the completeness of the reaction, the solvent was removed, and the crude product was carried out by chromatography (silica gel, petroleum:EtOAc = 10:1) to afford **4f** as a white solid (430 mg, 30%).

(1-(*p*-Tolyl)-1*H*-pyrazole-3,4-diyl)bis(phenylmethanone) (4a). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (98 mg, 80%), mp 99.3−101.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.14−7.99 (m, 2H), 7.89−7.76 (m, 2H), 7.67 (d, J = 8.4 Hz, 2H), 7.60−7.48 (m, 2H), 7.48−7.35 (m, 4H), 7.31 (d, J = 8.0 Hz, 2H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.2, 188.1, 151.2, 138.3, 138.2, 136.7, 136.7, 133.2, 132.9, 130.2, 130.2, 130.1, 129.1, 128.5, 128.3, 125.0, 119.9, 21.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{19}N_2O_2$ 367.1441; found 367.1438.

(1-(2-Fluorophenyl)-1*H*-pyrazole-3,4-diyl)bis(phenylmethanone) (4b). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (76 mg, 62%), mp 118.3−119.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.08 (d, J = 7.2 Hz, 2H), 7.98 (t, J = 7.4 Hz, 1H), 7.84 (d, J = 7.2 Hz, 2H), 7.65−7.52 (m, 2H), 7.49−7.36 (m, 5H), 7.34−7.25 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.8, 188.2, 154.0 (d, J = 250.3 Hz), 151.5, 138.2, 136.7, 134.3 (d, J = 10.4 Hz), 133.5, 133.1, 130.4, 129.6 (d, J = 7.9 Hz), 129.2, 128.6, 128.5, 127.3 (d, J = 9.5 Hz), 125.4 (d, J = 3.8 Hz), 125.0, 124.9, 117.2 (d, J = 20.2 Hz). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{16}FN_2O_2$ 371.1190; found 371.1183.

(1-(3-Fluorophenyl)-1*H*-pyrazole-3,4-diyl)bis(phenylmethanone) (4c). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (79 mg, 64%), mp 105.6−107.1 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.24 (s, 1H), 8.02 (d, J = 7.6 Hz, 2H), 7.97−7.85 (m, 4H), 7.73−7.66 (m, 2H), 7.64−7.50 (m, 5H), 7.31 (t, J = 8.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 193.4, 193.1, 167.7 (d, J = 244.4 Hz), 156.6, 145.3 (d, J = 10.6 Hz), 142.5, 141.3, 139.1, 138.5, 136.8 (d, J = 9.7 Hz), 135.0, 134.4, 134.0 (d, J = 3.5 Hz), 129.2, 120.9, 119.9 (d, J = 21.0 Hz), 112.5 (d, J = 26.3 Hz), 112.3 (d, J = 3.5 Hz). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{16}FN_2O_2$ 371.1190; found 371.1192.

(1-(4-Fluorophenyl)-1*H*-pyrazole-3,4-diyl)bis(phenylmethanone) (4d). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), a white solid (80 mg, 65%), mp 92.3−94.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 8.06 (d, J = 7.2 Hz, 2H), 7.81 (m, 4H), 7.64−7.48 (m, 2H), 7.46−7.32 (m, 4H), 7.30−6.98 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.0, 188.0, 162.1 (d, J = 248.6 Hz), 151.6, 138.1, 136.6, 135.3 (d, J = 2.8 Hz), 133.4, 133.0, 130.2, 129.1, 128.5, 128.4, 125.3, 121.9 (d, J = 8.5 Hz), 116.7 (d, J = 23.3 Hz). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{16}FN_2O_2$ 371.1190; found 371.1196.

(1-(4-Chlorophenyl)-1*H*-pyrazole-3,4-diyl)bis(phenylmethanone) (4e). Purified by column chromatography (silica gel, petroleum:EtOAc = 10:1), white solid (93 mg,72%), mp 105.6−106.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.06 (d, J = 7.6 Hz, 2H), 7.80 (d, J = 7.6 Hz, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.59−7.45 (m, 5H), 7.44−7.38 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.9, 187.8, 151.6, 138.0, 137.5, 136.5, 133.9, 133.4, 133.0, 130.2, 130.0, 129.9, 129.0, 128.5, 128.3, 125.4, 121.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{16}ClN_2O_2$ 387.0895; found 387.0901.

(1-(4-Bromophenyl)-1*H*-pyrazole-3,4-diyl)bis(phenylmethanone) (4f). Purified by column chromatography (silica gel, petroleum:EtOAc = 10:1), white solid (143 mg, 79% for 1 mmol scale reaction; 430 mg, 30% for 10 mmol scale reaction), mp 115.6−117.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.06 (d, J = 7.2 Hz, 2H), 7.80 (d, J = 7.2 Hz, 2H), 7.71−7.62 (m, 4H), 7.60−7.56 (m, 1H), 7.55−7.51 (m, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.39 (t, J = 7.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.9, 187.8, 151.7, 138.0, 138.0, 136.5, 133.4, 133.0, 132.8, 130.2, 129.9, 129.0, 128.5, 128.3, 125.4, 121.7, 121.3. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{16}BrN_2O_2$ 431.0390; found 431.0397.

4-(3,4-Dibenzoyl-1*H*-pyrazol-1-yl)benzonitrile (4g). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (88 mg, 70%), mp 118.9−120.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.06 (d, J = 7.6 Hz, 2H), 7.95 (d, J = 8.4 Hz,

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2H), 7.87−7.75 (m, 4H), 7.64−7.52 (m, 2H), 7.46 (t, J = 7.4 Hz, 2H), 7.41 (t, J = 7.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.6, 187.6, 152.3, 141.8, 137.8, 136.3, 133.9, 133.6, 133.2, 130.2, 130.0, 129.1, 128.6, 128.5, 126.0, 119.9, 117.8, 111.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{16}N_3O_2$ 378.1237; found 378.1240.

(1-Phenyl-1*H*-pyrazole-3,4-diyl)bis((4-fluorophenyl)-methanone) (4h). Purified by column chromatography (silica gel, petroleum:EtOAc = 10:1), white solid (84 mg, 65%), mp 134.5−136.5 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.26−8.18 (m, 2H), 7.92−7.85 (m, 2H), 7.78 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.6 Hz, 2H), 7.46−7.41 (m, 1H), 7.14 (t, J = 8.6 Hz, 2H), 7.09 (t, J = 8.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 187.9, 186.1, 167.16 (d, J = 254.1 Hz), 164.6 (d, J = 253.5 Hz), 151.1, 139.0, 134.5 (d, J = 2.9 Hz), 133.3 (d, J = 9.4 Hz), 132.9 (d, J = 2.9 Hz), 131.9 (d, J = 9.4 Hz), 130.1, 130.0, 128.5, 125.3, 120.1, 115.9 (d, J = 21.9 Hz), 115.7 (d, J = 21.7 Hz). HRMS (ESI) m/z: $[2M + Na]^+$ calcd for $C_{46}H_{28}F_4N_4NaO_4$ 799.1939; found 799.1946.

(1-Phenyl-1*H*-pyrazole-3,4-diyl)bis((4-bromophenyl)-methanone) (4i). Purified by column chromatography (silica gel, petroleum:EtOAc = 10:1), white solid (117 mg, 69%), mp 182.1−182.7 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.03 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.58−7.50 (m, 4H), 7.46−7.42 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.2, 186.4, 150.7, 138.8, 136.7, 135.1, 131.9, 131.7, 130.5, 130.1, 129.8, 128.8, 128.4, 128.3, 125.0, 119.9. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{15}Br_2N_2O_2$ 508.9495; found 508.9495.

(1-Phenyl-1*H*-pyrazole-3,4-diyl)bis((4-chlorophenyl)-methanone) (4j). Purified by column chromatography (silica gel, petroleum:EtOAc = 10:1), white solid (63 mg, 45%), mp 162.3−164.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.19−8.02 (m, 2H), 7.88−7.65 (m, 4H), 7.56−7.52 (m, 2H), 7.46−7.42 (m, 3H), 7.40−7.35 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.0, 186.2, 150.8, 140.0, 139.6, 138.7, 136.4, 134.8, 131.8, 130.5, 130.1, 129.9, 128.9, 128.8, 128.4, 125.1, 120.0. HRMS (ESI) m/z: $[2M + Na]^+$ calcd for $C_{46}H_{28}Cl_2N_4NaO_4$ 863.0757; found 863.0753.

4,4′-(1-Phenyl-1*H*-pyrazole-3,4-dicarbonyl)dibenzonitrile (4k). Purified by column chromatography (silica gel, petroleum:-EtOAc = 5:1), white solid (67 mg, 50%), mp 140.5−141.6 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.29 (d, J = 8.4 Hz, 2H), 7.94 (d, J = 8.4 Hz, 2H), 7.78 (t, J = 8.6 Hz, 4H), 7.74 (d, J = 8.4 Hz, 2H), 7.56 (t, J = 7.7 Hz, 2H), 7.47 (t, J = 7.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 187.8, 185.5, 150.1, 141.1, 139.3, 138.6, 132.5, 132.2, 130.8, 130.6, 130.0, 129.4, 128.9, 124.9, 120.0, 118.0, 117.8, 116.7, 116.4. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{15}N_4O_2$ 403.1190; found 403.1192.

(1-Phenyl-1*H*-pyrazole-3,4-diyl)bis((4-nitrophenyl)-methanone) (4l). Purified by column chromatography (silica gel, petroleum:EtOAc = 3:1), brown solid (64 mg, 43%), mp 154.3−156.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 8.00 (d, J = 7.6 Hz, 2H), 7.75−7.74 (m, 2H), 7.69 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 7.6 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H). 7.25−7.17 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.1, 186.3, 150.9, 136.7, 135.1, 132.0, 131.9, 131.8, 130.5, 130.2, 128.9, 128.4, 125.2, 122.0, 121.9, 117.0, 116.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{23}H_{14}N_4NaO_6$ 465.0806; found 465.0814.

(1-Phenyl-1*H*-pyrazole-3,4-diyl)bis(thiophen-2-ylmethanone) (4m). Purified by column chromatography (silica gel, petroleum:EtOAc = 7:1), white solid (90 mg, 74%), mp 150.2−152.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.28 (s, 1H), 7.82 (d, J = 7.2 Hz, 2H), 7.74 (d, J = 3.6 Hz, 1H), 7.69 (d, J = 3.6 Hz, 1H), 7.62 (s, 1H), 7.55 (t, J = 6.6 Hz, 2H), 7.43 (t, J = 6.6 Hz, 1H), 7.19 (s, 1H), 7.10 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 181.0, 178.4, 149.9, 144.5, 142.2, 139.0, 135.8, 135.3, 134.5, 134.0, 129.9, 129.3, 128.3, 128.1, 125.0, 119.9. HRMS (ESI) m/z: $[2M + Na]^+$ calcd for $C_{38}H_{24}N_4NaO_4S_4$ 751.0573; found 751.0570.

(1-Phenyl-1*H*-pyrazole-3,4-diyl)bis((3-bromophenyl)-methanone) (4n). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (110 mg, 65%), mp 122.6−125.9 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.24 (s, 1H), 8.05 (d, J = 7.6 Hz, 1H), 7.92 (s, 1H), 7.79 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 7.6 Hz, 2H), 7.67 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 7.8 Hz, 2H), 7.45 (t, J = 7.2 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.29 (t, J = 7.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 187.7, 186.1, 150.7, 139.8, 138.8, 138.2, 136.2, 135.8, 133.1, 131.9, 130.3, 130.1, 129.9, 129.8, 128.8, 128.5, 127.5, 124.8, 122.9, 122.7, 120.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{15}Br_2N_2O_2$ 508.9495; found 508.9499.

(1-Phenyl-1*H*-pyrazole-3,4-diyl)bis(naphthalen-2-ylmethanone) (4o). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (47 mg, 31% yield), mp 138.5−140.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.46 (s, 1H), 8.30 (s, 1H), 8.04−8.01(m, 1H), 7.95−7.73 (m, 9H), 7.68−7.50 (m, 5H), 7.49−7.41 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 187.8, 186.0, 167.3, 167.0, 164.8, 164.5, 151.0, 138.9, 134.4, 134.4, 133.2, 133.1, 132.9, 132.8, 131.8, 131.7, 129.9, 129.9, 128.4, 125.2, 119.9, 115.9, 115.7, 115.6, 115.5. HRMS (ESI) m/z: $[2M + Na]^+$ calcd for $C_{62}H_{40}N_4NaO_4$ 927.2942; found 927.2943.

(1-([1,1′-Biphenyl]-2-yl)-1*H*-pyrazole-3,4-diyl)bis-(phenylmethanone) (4p). Purified by column chromatography (silica gel, petroleum:EtOAc = 8:1), white solid (101 mg, 71%), mp 115.3−116.5 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 4.4 Hz, 2H), 7.72 (s, 1H), 7.59−7.50 (m, 7H), 7.49−7.46 (m, 4H), 7.43−7.38 (m, 2H), 7.35−7.27 (m, 2H), 7.26−7.22 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.4, 188.0, 151.1, 138.3, 137.9, 137.4, 137.3, 136.6, 135.0, 133.2, 132.8, 131.3, 130.3, 129.6, 129.2, 129.0, 128.8, 128.7, 128.4, 128.3, 128.0, 126.4, 123.9. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{29}H_{21}N_2O_2$ 429.1598; found 429.1603.

(1-(4-Methoxyphenyl)-1*H*-pyrazole-3,4-diyl)bis((4-bromophenyl)methanone) (4q). Purified by column chromatography (silica gel, petroleum:EtOAc = 7:1), white solid (167 mg, 93%), mp 158.0−160.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.01 (d, J = 8.8 Hz, 2H), 7.77−7.65 (m, 4H), 7.61 (d, J = 8.6 Hz, 2H), 7.55 (d, J = 8.8 Hz, 2H), 7.03 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.3, 186.4, 159.7, 150.5, 136.9, 135.3, 132.4, 132.0, 131.9, 131.7, 130.5, 130.1, 128.8, 128.2, 121.6, 114.9, 55.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{17}Br_2N_2O_3$ 538.9600; found 538.9605.

General Procedure for Synthesis of Product 4fa. A mixture of **4f** (0.25 mmol, 1.0 equiv) and $NaBH_4$ (1.25 mmol, 5.0 equiv) was stirred in 5 mL of THF at 110 °C (oil bath) for 8 h. After the completeness of the reaction, the reaction mixture was poured into water and then extracted with EtOAc and dried by Na_2SO_4. The crude product was carried out by chromatography to afford **4fa**.

(1-(4-Bromophenyl)-1*H*-pyrazole-3,4-diyl)bis-(phenylmethanol) (4fa). Purified by column chromatography (silica gel, petroleum:EtOAc = 3:1), a white solid (76 mg, 70%), mp 137.0−137.5 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.52−7.45 (m, 7H), 7.44−7.26 (m, 8H), 6.04 (s, 1H), 5.73 (s, 1H), 3.55 (s, 1H), 2.72 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.7, 142.7, 141.9, 138.8, 132.5, 128.7, 128.6, 128.0, 127.3, 127.1, 126.4, 125.1, 120.4, 119.7, 71.1, 68.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{20}BrN_2O_2$ 435.0703; found 435.0700.

General Procedure for Synthesis of Product 4fb. A mixture of **4f** (0.25 mmol, 1.0 equiv) and $N_2H_4{\cdot}H_2O$ (1.0 mmol, 4.0 equiv) was stirred in 5 mL of EtOH at 90 °C (oil bath) for 8 h. After the completeness of the reaction, the product was filtered out to afford **4fb**.

2-(4-Bromophenyl)-4,7-diphenyl-2*H*-pyrazolo[3,4-*d*]-pyridazine (4fb). Filtered to afford **4fb** as a green solid (103 mg, 97%), mp 216.2−217.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 4.4 Hz, 2H), 8.77 (s, 1H), 8.14 (d, J = 4.8 Hz, 2H), 7.90 (d, J = 7.2 Hz, 2H), 7.72 (d, J = 7.6 Hz, 2H), 7.64−7.48 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.2, 150.4, 143.6, 138.6, 136.8, 135.0, 133.2, 130.6, 130.5, 129.6, 129.2, 128.7, 128.5, 123.5, 123.1, 122.6, 118.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{16}BrN_4$ 427.0553; found 427.0549.

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■ ASSOCIATED CONTENT

Supporting Information

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HRMS spectra for the key intermediates in the proposed mechanism and copies of NMR spectra of final products and X-ray-crystallography data of **3k** and **4h** (PDF)

Accession Codes

CCDC 2064733−2064734 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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