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Unexpected C−C Bond Cleavage: A Route to 3,6-Diarylpyridazines and 6-Arylpyridazin-3-ones from 1,3-Dicarbonyl Compounds and Methyl Ketones

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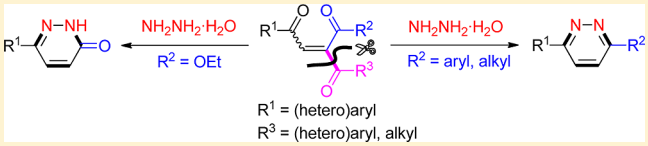
Supporting Information

ABSTRACT: An unexpected C−C bond cleavage has been revealed in the absence of metal. This observation has been exploited to develop an efficient approach toward 3,6-diarylpyridazines and 6-arylpyridazin-3-ones from simple and commercially available 1,3-dicarbonyl compounds and methyl ketones.

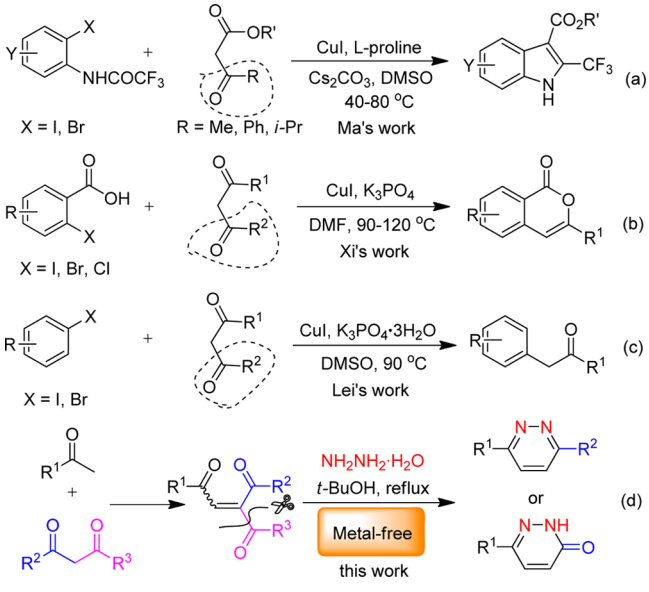


C−C bond formation and cleavage (activation) have attracted considerable attention due to not only fundamental scientific interest but also their potential utility in organic synthesis.[1] Numerous useful C−C bond formation procedures have been developed, and because of its inertness,[2] the cleavage of the C−C single bond has emerged as a tremendous challenge. In recent years, significant progress has been achieved involving two basic strategies to facilitate C−C bond cleavage. One is to use strained molecules[3] bearing three- and four-membered rings, forming more stable complexes to release ring strain. On the other hand, C−C bond cleavage of unstrained molecules is required to generate stable intermediates by chelation assistance[4] or other means.[5]

C−C bond cleavage is frequently found in carbonyl compounds, such as Baeyer−Villiger,[6] haloform,[7] and Haller−Bauer[8] reactions. Until now, few examples of the deacylation of carbonyl compounds have been reported.[9] A novel CuI-catalyzed deacylation process was closely studied by Ma[9a] (Scheme 1a) and Xi[9c] (Scheme 1b). Another interesting CuI-catalyzed deacylation in the arylation/C−C activation process was discovered by Lei's group[9d] (Scheme 1c). Those reports mainly focused on the metal-catalyzed deacylation approaches. Until now, much attention has been paid to metal-free transformations[10] in organic synthesis for significant potential economic and environmental benefits. However, the development of a metal-free process to achieve C−C bond cleavage still represents a fascinating topic. In this paper, a metal-free C−C bond cleavage of 1,4-enediones for accessing pyridazines and pyridazin-3-ones is described (Scheme 1d).

Pyridazines and pyridazin-3-ones are versatile building blocks in natural product syntheses[11] and useful intermediates to construct other heterocycles.[12] Although several general approaches to pyridazines and pyridazin-3-ones are known,[13] to the best of our knowledge, no examples have been reported

Scheme 1. Deacylation Process



on the synthesis of pyridazines and pyridazin-3-ones from 1,3-dicarbonyl compounds and methyl ketones.

In our previous study, we proposed a focusing domino strategy to synthesize various substituted 1,4-enediones.[14] In view of the synthesis of pyridazines involving the reaction of 1,4-dicarbonyl compound with hydrazine, we envisioned a novel one-pot, two-step synthesis of pyridazines from simple and commercially available 1,3-dicarbonyl compounds and methyl ketones.

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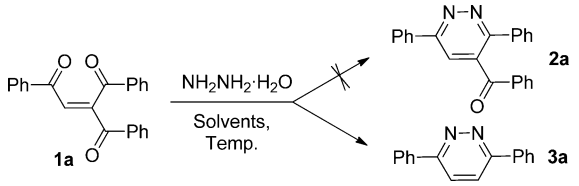
With the above idea in mind, we investigated the reaction of 2-benzoyl-1,4-diphenylbut-2-ene-1,4-dione (**1a**) and hydrazine hydrate ($NH_2NH_2{\cdot}H_2O$) in *t*-BuOH at reflux. Unexpectedly, the condensation product (3,6-diphenylpyridazin-4-yl)-(phenyl)methanone (**2a**) was not the final product; instead, 3,6-diphenylpyridazine (**3a**) was obtained in 40% isolated yield after cleavage of the benzoyl group of **2a** (Table 1, entry 2).

Table 1. Optimization of the Reaction Conditions[a]



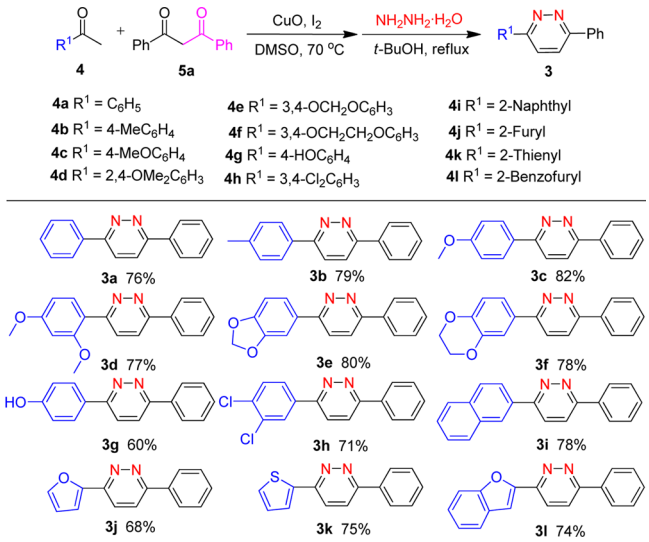
entry	solvent	temp (°C)	molar ratio (**1**: $NH_2NH_2{\cdot}H_2O$)	yield[b] (%)
1	*t*-BuOH	reflux	1:1	<5
2	*t*-BuOH	reflux	1:3	40
3	*t*-BuOH	reflux	1:5	50
4	*t*-BuOH	reflux	1:8	67
5	*t*-BuOH	reflux	1:10	88
7	**t-BuOH**	**reflux**	**1:15**	**94**
8	MeOH	reflux	1:15	85
9	EtOH	reflux	1:15	92
10	*n*-PrOH	reflux	1:15	73
11	*i*-PrOH	reflux	1:15	75
12	*n*-BuOH	reflux	1:15	83
13	DMSO	80	1:15	86
14	DMF	80	1:15	88
15	MeCN	reflux	1:15	72
16	$CHCl_3$	reflux	1:15	55
17	THF	reflux	1:15	60
18	H_2O	reflux	1:15	0
19	Toluene	reflux	1:15	65
20	*t*-BuOH	25	1:15	76
21	*t*-BuOH	25	1:20	76
22	*t*-BuOH	25	1:30	76
23	*t*-BuOH	60	1:15	80

[a]Reaction conditions: **1a** (0.2 mmol), solvent (1 mL). The reaction was performed for 0.5 h. [b]Isolated yields.

Furthermore, **3a** was further identified by X-ray diffraction (Supporting Information, Figure S3). This result indicated that we accidentally discovered a fascinating C–C bond cleavage without any metal, which meanwhile led to an efficient approach toward 3,6-diarylpyridazines under mild condition.

This deacylation process prompted us to investigate the reaction parameters. As shown in Table 1, the effect of solvents, temperature, and molar ratios was examined to optimize the reaction conditions, and we were pleased to find that 1,4-enedione (**1a**) could react with 15 equiv of hydrazine hydrate in *t*-BuOH at reflux for 0.5 h to afford the deacylated product **3a** in 94% yield (Table 1, entry 7). Motivated by our discovery, we considered the possibility for the preparation **3a** via a one-pot, two-step reaction from acetophenone (**4a**) and 1,3-diphenylpropane-1,3-dione (**5a**) (Scheme 1d). Nevertheless, only trace amounts of **3a** were formed. Subsequently, the feasibility of this strategy was verified by reaction of 1.0 mmol of **4a** and 1.0 mmol of **5a** in the presence of 1.1 mmol of CuO and 1.1 mmol of iodine in 5 mL of DMSO at 70 °C for 12 h until complete disappearance of the starting materials. After being extracted with EtOAc and washed with aqueous solution of $Na_2S_2O_3$, the crude product was treated with $NH_2NH_2{\cdot}H_2O$ (15.0 mmol) in *t*-BuOH at reflux for another 0.5 h. The desired pyridazine **3a** was isolated in 76% yield after the workup (Scheme 2).

Scheme 2. Scope of Methyl Ketones[a]



[a]Isolated yields.

The efficient formation of **3a** prompted us to further study the reaction scope. To our delight, different methyl ketones with **5a**, irrespective of their electronic or steric properties, proceeded smoothly to afford their corresponding products in moderate to good yields (60–82%; Scheme 2). For example, substituted methyl ketones bearing electron-neutral (4-Me), electron-rich (4-OMe, 2,4-OMe_2, 3,4-OCH_2O, 3,4-OCH_2CH_2O), electron-deficient (3,4-Cl_2), and sterically hindered (*β*-naphthyl) methyl ketones all performed efficiently to afford the expected pyridazines in good yields (71–82%; **3a–f**, **h**, **i**). It should be noted that an electron-donating substituent attached to the benzene ring caused a considerable increase in yield. Gratifyingly, the sensitive hydroxy group (OH) in **4g** was compatible with these conditions to give the expected product **3g** in 60% yield. Furthermore, heteroaryl ketones were also discovered to be able to efficiently furnish the desired products in moderate yields (68–75%; **3j–l**).

Next, the scope of this reaction was extended to various 1,3-dicarbonyl compounds (Scheme 3). When symmetrical 1,3-diketones such as acetylacetone (**5b**) and 1,3-bis(4-methoxyphenyl)propane-1,3-dione (**5c**) were employed, the desired pyridazines **3m** and **3c** were isolated in 81% and 72% yields, respectively. Interestingly, when unsymmetrical 1,3-diketone (**5d**) was used in this system, the reaction exhibited excellent selectivity and gave **3a** in 89% yield, while 1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione (**5e**) resulted in two products **3a** and **3c** in 78% overall yield with the molar ratio of 1:1. Surprisingly, when ethyl benzoylacetate (**5f**) was used, the C–C bond cleavage was also observed, and the reaction proceeded smoothly to furnish 6-phenylpyridazin-3-one (**6a**) in 75% yield under the standard conditions. Varied *β*-keto esters were effective for this transformation. Both electron-donating (OMe) and electron-withdrawing (NO_2) groups attached to the phenyl rings of **4a** could afford their corresponding products **6b** and **6c** in 72% and 67% yields. Much to our satisfaction, naphthyl and heteroaryl methyl

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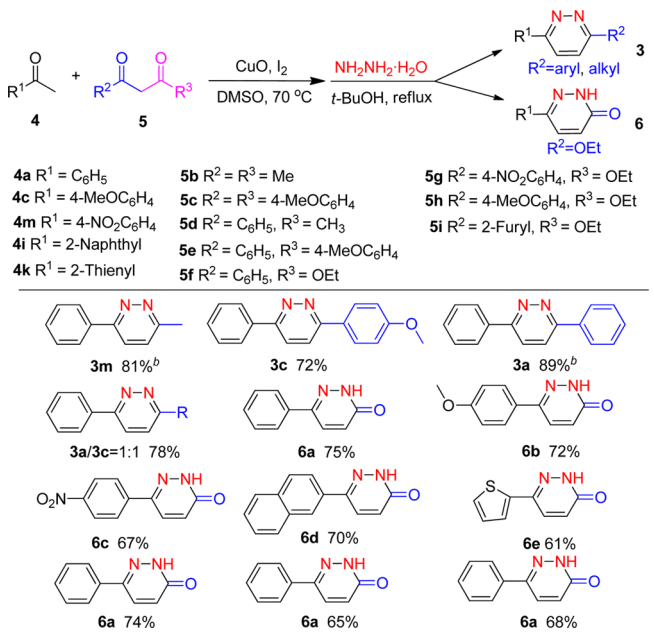
Scheme 3. Scope of Methyl Ketones and 1,3-Dicarbonyl Compounds[a]



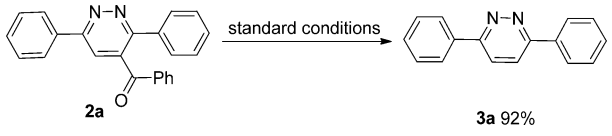
[a]Isolated yields. [b]Reaction conditions: 2,2-dihydroxy-1-phenylethanone **4a′** (1.0 mmol) with **5b** or **5d** (1.0 mmol) was stirred at reflux in CH_3CN (5 mL) for 12 h. After evaporation, the crude product and $NH_2NH_2·H_2O$ (15.0 mmol) were stirred in *t*-BuOH at reflux for another 0.5−1 h.

ketones also proceeded efficiently to give the pyridazin-3-one **6d** and **6e** in 70% and 61% yields. For further investigation, in the case of electron-deficient ethyl 4-nitrobenzoylacetate (**5g**), the reaction delivered **6a** with a satisfactory yield (74%). When electron-donating group was attached to the phenyl ring of the *β*-keto ester ethyl 4-methoxybenzoylacetate (**5h**), the yield slightly dropped (65%; **6a**). Significantly, the heterocycle substrate ethyl 3-(furan-2-yl)-3-oxopropanoate (**5i**) was employed and **6a** was also obtained in 68% yield.

To gain some insights into the mechanism of this reaction process, the reaction of **1a** with hydrazine hydrate was performed under the standard conditions. Benzohydrazide (**7**), phenyl(3-phenyl-1*H*-pyrazol-5-yl)methanone (**8a**), and 5-phenyl-1*H*-pyrazole[15] (**9**) were detected by GC−MS (Supporting Information, Figure S1). In addition, **7** was also isolated and characterized by ^{1}H and ^{13}C NMR. Furthermore, **2a** was synthesized according to the known method,[16] which reacted with hydrazine hydrate under the standard reaction conditions to afford **3a** in 92% yield (Scheme 4). This control experiment indicated that the reaction between **1a** and hydrazine hydrate might undergo the intermediate **2a**.

On the basis of the results described above and previous reports,[8,13] a possible mechanism of the present reaction was described using **1a** and hydrazine hydrate as an example (Scheme 5). Initially, **1a** reacted with hydrazine hydrate to give

Scheme 4. Control Experiment



hydrazone **A** or **B** through a condensation reaction. Subsequently, intramolecular cyclization led to the formation of **2a**. Then excess amount of hydrazine hydrate as a nucleophilic agent could attack the carbonyl group of intermediate **2a** to produce intermediate **C**,[8] which underwent a deacylation process to furnish the desired product. In addition, 6-arylpyridazin-3-ones were formed via a similar process (Supporting Information, Figure S2).

In summary, we have revealed an efficient C−C cleavage process to construct 3,6-diarylpyridazines and 6-arylpyridazin-3-ones without any metal. The reaction gave the desired products from simple and commercially available 1,3-dicarbonyl compounds and methyl ketones under mild conditions. This deacylation has a broad substrate scope and high functional group tolerance.

EXPERIMENTAL SECTION

General Information. All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using precoated glass plates. Flash column chromatography was performed on silica gel (200−300 mesh). IR spectra were recorded as KBr pellets with absorption in cm^{-1}. ^{1}H spectra were recorded in $CDCl_3$ or DMSO-d_6 on 400/600 MHz NMR spectrometers and resonances (δ) are given in parts per million relative to tetramethylsilane. ^{13}C spectra were recorded in $CDCl_3$ or DMSO-d_6 on 100/150 MHz NMR spectrometers and resonances (δ) are given in ppm. HRMS were obtained on an apex-Ultra MS equipped with APCI. MS was recorded using EI (70 eV). Melting points were determined using an electrothermal capillary melting point apparatus and not corrected.

General Procedure for the Synthesis of 3 and 6 (3a as an Example). A mixture of acetophenone **4a** (1.0 mmol), 1,3-diphenylpropane-1,3-dione **5a** (1.0 mmol), iodine (1.1 mmol), and CuO (1.1 mmol) in DMSO (5 mL) was stirred at 70 °C for 12 h until nearly completed conversion of the substrates by TLC analysis and then extracted with EtOAc two times (2 × 30 mL). The extract was washed with 10% $Na_2S_2O_3$ solution (w/w). After drying over Na_2SO_4 and evaporation, hydrazine hydrate (15.0 mmol) was added and the mixture were stirred at reflux in *t*-BuOH (5 mL) for 0.5−1 h. After the reaction complete (as monitored by TLC), the solvent was removed under reduce pressure, 50 mL of water was added to the residue, and then the mixture was extracted with EtOAc three times (3 × 50 mL). The extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford the product **3a**.

*(3,6-Diphenylpyridazin-4-yl)(phenyl)methanone (**2a**):*[16] ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 8.20 (d, J = 7.2 Hz, 2H), 7.92 (s, 1H), 7.72−7.66 (m, 4H), 7.58−7.51 (m, 4H), 7.39−7.34 (m, 2H), 7.32 (br, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 195.1, 157.5, 156.2, 137.1, 135.8, 135.4, 135.2, 134.3, 130.5, 129.8, 129.7, 129.2(4), 129.1(7), 128.8, 128.6, 127.1, 122.6; m/z 337.12 (M + 1, 17.528), 336.09 (M, 72.55).

*3,6-Diphenylpyridazine (**3a**):*[17] white solid; 176.3 mg (yield 76%); mp 226−228 °C; IR (KBr) 3054, 1449, 1408, 868, 758, 744, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.16 (d, J = 6.4 Hz, 4H), 7.94 (s, 2H), 7.60−7.44 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.6, 136.1, 130.0, 129.0, 126.9, 124.2; HRMS (APCI) m/z [M + H]$^+$ calcd for $C_{16}H_{13}N_2$ 233.1073, found 233.1074.

*3-Phenyl-6-(p-tolyl)pyridazine (**3b**):*[18] white solid; 194.3 mg (yield 79%); mp 187−189 °C; IR (KBr) 3054, 1608, 1511, 1428, 1410, 1260, 1248, 1175, 1035, 829, 791, 750, 693, 583 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.15 (d, J = 7.6 Hz, 2H), 8.06 (d, J = 8.0 Hz, 2H), 7.89 (s, 2H), 7.57−7.47 (m, 3H), 7.34 (d, J = 8.0 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 157.5, 157.3, 140.2, 136.1, 133.2, 129.9, 129.8, 129.0, 126.8(4), 126.7(5), 124.1, 123.9, 21.36; HRMS (APCI) m/z [M + H]$^+$ calcd for $C_{17}H_{15}N_2$ 247.1230, found 247.1231.

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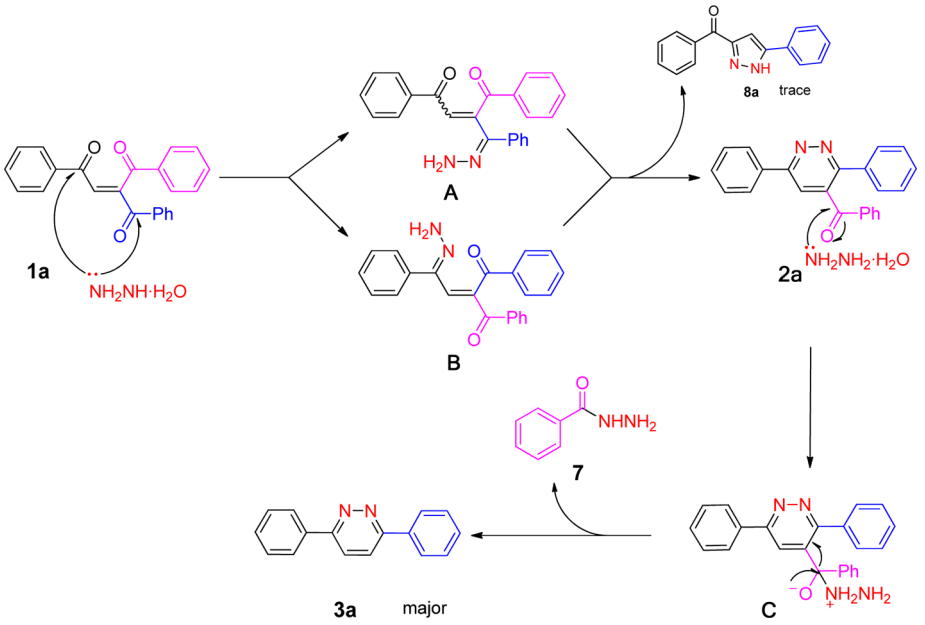
Scheme 5. Possible Mechanism



3-(4-Methoxyphenyl)-6-phenylpyridazine (***3c***):[18] white solid; 214.8 mg (yield 82%); mp 197−199 °C; IR (KBr) 3057, 3031, 1449, 1419, 1398, 822, 785, 747, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.20−8.10 (m, 4H), 7.90−7.87 (m, 2H), 7.58−7.47 (m, 3H), 7.06 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 161.3, 158.7, 157.1, 157.0, 136.2, 129.9, 129.0, 128.3, 126.8, 124.1, 123.5, 114.4, 55.4; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{17}H_{15}N_2O$ 263.1179; found: 263.1180.

3-(2,4-Dimethoxyphenyl)-6-phenylpyridazine (***3d***): white solid; 224.8 mg (yield 77%); mp 157−160 °C; IR (KBr) 3044, 2960, 2934, 2839, 1612, 1408, 1305, 1282, 1212, 1161, 1139, 831, 756, 697 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm) 8.17−8.10 (m, 4H), 7.82 (d, J = 9.0 Hz, 1H), 7.55−7.51 (m, 2H), 7.50−7.46 (m, 1H), 6.69 (d, J = 9.0 Hz, 1H), 6.59 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 162.3, 158.6, 156.8, 156.5, 136.5, 132.0, 129.7, 128.9, 128.2, 126.8, 122.9, 118.5, 105.3, 99.0, 55.5(4), 55.4(9); HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{18}H_{17}N_2O_2$ 293.1285, found 293.1285.

3-(Benzo[d][1,3]dioxol-5-yl)-6-phenylpyridazine (***3e***): white solid; 220.8 mg (yield 80%); mp 174−177 °C; IR (KBr) 3054, 2904, 1506, 1489, 1450, 1267, 1237, 1046, 934, 818, 789,749, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.12 (d, J = 6.8 Hz, 2H), 7.88−7.77 (m, 2H), 7.75−7.71 (m, 1H), 7.62−7.57 (m, 1H), 7.56−7.45 (m, 3H), 6.94 (d, J = 8.0 Hz, 1H), 6.04 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.2, 157.0, 149.4, 148.5, 136.1, 130.3, 129.9, 129.0, 126.8, 124.1, 123.6, 121.1, 108.6, 107.2, 101.5; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{17}H_{13}N_2O_2$ 277.0972, found 277.0973.

3-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)-6-phenylpyridazine (***3f***): white solid; 226.2 mg (yield 78%); mp 170−174 °C; IR (KBr) 3059, 2925, 1586, 1507, 1451, 1412, 1319, 1285, 1257, 1132, 1065, 861, 791, 749, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.13 (d, J = 6.8 Hz, 2H), 7.90−7.78 (m, 2H), 7.72 (s, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.57−7.44 (m, 3H), 7.00 (d, J = 8.0 Hz, 1H), 4.31 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.1, 156.9, 145.5, 144.0, 136.2, 129.8, 129.5, 128.9, 126.8, 124.1, 123.5, 120.2, 117.8, 115.9, 64.5, 64.3; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{18}H_{15}N_2O_2$ 291.1128, found 291.1129.

4-(6-Phenylpyridazin-3-yl)phenol (***3g***): white solid; 148.8 mg (yield 60%); mp 227−229 °C; IR (KBr) 3055, 1609, 1598, 1511, 1443, 1408, 1253, 835, 791, 750, 694 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 10.0 (s, 1H), 8.26−8.16(m, 4H), 8.09 (d, J = 8.4 Hz, 2H), 7.61−7.51 (m, 3H), 6.95 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 159.5, 157.0, 156.3, 136.1, 129.9, 129.1, 128.4, 126.6, 124.6, 123.7, 116.0, 104.8; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{16}H_{13}N_2O$ 249.1022, found 249.1023.

3-(3,4-Dichlorophenyl)-6-phenylpyridazine (***3h***): white solid; 213.7 mg (yield 71%); mp 179−181 °C; IR (KBr) 3040, 2925, 1471, 1449, 1416, 1375, 1030, 832, 793, 756, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.27 (s, 1H), 8.14 (d, J = 6.8 Hz, 2H), 8.01−7.81 (m, 3H), 7.63−7.44 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 158.1, 155.4, 135.9, 135.6, 134.4, 133.4, 131.0, 130.3, 129.1, 128.7, 127.0, 125.9, 124.3, 123.9; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{16}H_{11}Cl_2N_2$ 301.0294, found 301.0295.

3-(Naphthalen-2-yl)-6-phenylpyridazine (***3i***):[19] white solid; 220 mg (yield 78%); mp 196−198 °C; IR (KBr) 3054, 1439, 1408, 1132, 1121, 862, 855, 827, 793, 742, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.62 (s, 1H), 8.38−8.26 (m, 1H), 8.22−8.12 (m, 2H), 8.05−7.90 (m, 5H), 7.54 (br, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.6, 136.1, 134.1, 133.4, 130.1, 129.1, 128.8, 127.8, 127.1, 126.9, 126.7, 126.6, 124.3, 124.2, 124.1; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{20}H_{15}N_2$ 283.1230, found 283.1231.

3-(Furan-2-yl)-6-phenylpyridazine (***3j***):[20] white solid; 151 mg (yield 68%); mp 198−200 °C; IR (KBr) 3059, 1604, 1488, 1448, 1425, 1162, 1080, 1004, 865, 789, 827, 784, 737, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.13 (d, J = 6.8 Hz, 2H), 7.89 (s, 2H), 7.62 (s, 1H), 7.57−7.46 (m, 3H), 7.41 (d, J = 3.2 Hz, 1H), 6.62 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.1, 150.9, 150.7, 144.4, 136.1, 130.0, 129.0, 126.8, 123.9, 122.1, 112.6, 110.3; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{14}H_{11}N_2O$ 223.0866, found 223.0867.

3-Phenyl-6-(thiophene-2-yl)pyridazine (***3k***):[21] white solid; 178.5 mg (yield 75%); mp 160−162 °C; IR (KBr) 3065, 1546, 1450, 1433, 1406,1300, 851, 835, 787, 748, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.10 (d, J = 7.6 Hz, 2H), 7.85−7.76 (m, 2H), 7.69−7.63 (m, 1H), 7.55−7.44 (m, 4H), 7.17−7.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.2, 153.4, 140.5, 135.8, 129.9, 129.1, 128.9, 128.0, 126.6, 126.1, 123.9, 122.6; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{14}H_{11}N_2S$ 239.0637, found 239.0638.

3-(Benzofuran-2-yl)-6-phenylpyridazine (***3l***): white solid; 201.3 mg (yield 74%); mp 215−217 °C; IR (KBr) 3042, 1603, 1580, 1446, 1421, 1260, 1029, 1008, 827, 790, 751, 738, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.15 (d, J = 7.2 Hz, 2H), 8.07 (d, J = 9.2 Hz, 1H), 7.94 (d, J = 8.8 Hz, 1H), 7.77 (s, 1H), 7.71 (d, J = 7.6 Hz, 1H), 7.61−7.43 (m, 4H), 7.41−7.34 (m, 1H), 7.33−7.27 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 157.6, 155.5, 152.3, 150.9, 135.8, 130.1, 129.0, 128.5, 126.8, 125.7, 123.8, 123.5, 122.9, 122.1, 111.5,

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106.2; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{18}H_{13}N_2O$ 273.1022, found 273.1023.

*3-Methyl-6-phenylpyridazine (**3m**):*[22] white solid; 137.7 mg (yield 81%); mp 101−104 °C; IR (KBr) 3061, 1587, 1450, 1416, 1113, 1012, 851, 772, 741, 751, 692, 565 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.05 (d, J = 6.8 Hz, 2H), 7.74 (d, J = 8.8 Hz, 1H), 7.53−7.46 (m, 3H), 7.37 (d, J = 8.4 Hz, 1H), 2.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 158.4, 157.1, 136.3, 129.6, 128.9, 127.2, 126.8, 123.9, 22.0; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{11}H_{11}N_2$ 171.0917, found 171.0918.

*6-Phenylpyridazin-3(2H)-one (**6a**):*[13b] yellow solid; 112.4−129.7 mg (yield 65−75%); mp 199−201 °C; IR (KBr) 2925, 2854, 1650, 1593, 1574, 1007, 856, 775, 736, 687, 587 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.46 (s, 1H), 7.87−7.75 (m, 3H), 7.45−7.48 (m, 3H), 7.11 (d, J = 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.1, 145.7, 134.4, 132.1, 131.7, 130.1, 129.6, 128.9, 125.9; MS (EI) m/z 173.19 (M + 1, 12.00), 172.13 (M, 100.00), 171.11 (M − 1, 16.20), 144.11 (25.18), 116.08 (21.76), 115.08 (99.60).

*6-(4-Methoxyphenyl)pyridazin-3(2H)-one (**6b**):*[13b] yellow solid; 145.4 mg (yield 72%); mp 185−188 °C; IR (KBr) 2931, 2839, 1650, 1594, 1573, 1512, 1251, 1008, 828, 558, 506 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.31 (s, 1H), 7.80−7.69 (m, 3H), 7.07 (d, J = 8.8 Hz, 1H), 6.98 (d, J = 8.4 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 161.8, 160.7, 145.4, 131.5, 130.1, 127.3, 127.0, 114.3, 55.4; MS (EI) m/z 203.14 (M + 1, 12.75), 202.15 (M, 100.00), 201.15 (M − 1, 4.43), 145.11 (66.11), 131.08 (12.13), 115.07 (11.24), 103.08 (11.59), 102.06 (20.63).

*6-(4-Nitrophenyl)pyridazin-3(2H)-one (**6c**):*[23] yellow solid; 145.4 mg (yield 67%); mp 247−249 °C; IR (KBr) 3317, 3222, 1633, 1518, 1342, 857, 756, 697 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ (ppm) 9.95 (s, 1H), 8.55 (d, J = 8.4 Hz, 1H), 8.44 (d, J = 9.0 Hz, 2H), 7.85−7.78 (m, 1H), 7.55 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 164.8, 156.7, 155.2, 148.6, 141.3, 135.9, 134.1, 128.8, 128.6, 128.3, 124.3; MS (EI) m/z 217.14(M, 4.23), 184.15 (69.36), 176.39 (6.65), 166.13 (7.49), 165.23 (5.23), 159.21 (100.00).

*6-(Naphthalen-2-yl)pyridazin-3(2H)-one (**6d**):*[24] yellow solid; 155.4 mg (yield 70%); mp 241−246 °C; IR (KBr) 2925, 2854, 1717, 1655, 1585, 1013, 827, 737, 480 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ (ppm) 13.29 (s, 1H), 8.46 (s, 1H), 8.24 (d, J = 10.2 Hz, 1H), 8.07−7.99 (m, 3H), 7.98−7.94 (m, 1H), 7.61−7.55 (m, 2H), 7.06 (d, J = 9.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 160.4, 143.7, 133.1, 132.9, 132.0, 131.6, 130.3, 128.6, 128.5, 127.6, 127.0, 126.8, 125.2, 123.0; MS (EI) m/z 223.18 (M + 1, 15.60), 222.16 (M, 100.00), 221.17 (M-1, 11.08), 194.15 (16.42), 166.13 (16.03), 165.11 (78.65), 164.10 (17.79), 163.11 (15.52), 152.11 (10.84), 139.12 (10.31), 115.13 (12.94).

*6-(Thiophene-2-yl)pyridazin-3(2H)-one (**6e**):*[25] yellow solid; 108.6 mg (yield 61%); mp 153−157 °C; IR (KBr) 3371, 3081, 3068, 2928, 2850, 1678, 1657, 1587, 1009, 832, 729, 594 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ (ppm) 13.11 (s, 1H), 8.06 (d, J = 9.6 Hz, 1H), 7.71−7.69 (m, 1H), 7.65 (d, J = 4.8 Hz, 1H), 7.18−7.15 (m, 1H), 7.02 (d, J = 9.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 160.0, 140.6, 139.1, 130.7, 130.2, 128.2(4), 128.1(8), 126.5; MS (EI) m/z 179.09 (M + 1, 11.28), 178.10 (M, 100.00), 122.06 (18.83), 121.04 (86.89).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Evidence in support of the hypothetic mechanism and ^1H and ^{13}C NMR spectra of compounds **3a−m** and **6a−e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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