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$In(OTf)_3$-mediated synthesis of substituted pyridazines

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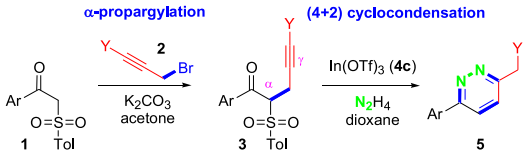
ABSTRACT

$In(OTf)_3$ (**4c**)-mediated one-pot (4+2) cyclocondensation of γ-alkynones **3** with $N_2H_{4(aq)}$ in dioxane affords substituted pyridazines **5** in good yields via a sequential desulfonative or dehydrogenative aromatization. The facile transformation proceeds by a facile synthetic sequence starting with an α-propargylation of β-ketosulfones **1** and a cyclocondensation of γ-alkynones **3** with $N_2H_{4(aq)}$. The method provides a mild and efficient condition. Moreover, this route can be enlarged to multigram scale.

1. Introduction

For transformation from terminal alkynes to methyl ketones, mercuric salts mediating the hydration of alkynes is a classic method used in the presence of acids via Markovnikov regioselectivity.[1,2] However, new catalysts to the synthetic routes of methyl ketones from non-activated alkynes still represent continuing needs in the organic field. Among these protocols, transition-metal complexes (Au,[3] Ag,[4] Ag/Au,[5] Ru,[6] Rh,[7] Pt,[8] Os,[9] Ir,[10] Pd,[11] Fe,[12] Hg,[13] Cu,[14] or In[15]) promoting hydration of alkynes is the major pathway. Notably, few examples have been performed for metal triflates-promoted reactions. Nishizawa et al. reported the traditional synthesis of 2-methylfurans via the $Hg(OTf)_2$-catalyzed cyclization of 1-alkyn-5-ones.[13] Jha et al. reported a microwave-assisted hydration of arylacetylene with $Cu(OTf)_2$.[14a] AgOTf-mediated hydration of alkynes has been developed by Chakraborty and co-workers.[4a] There are only two In(III)-mediated examples of synthesis of substituted furans via the hydration of nonactivated alkynes by Tan[15a] and Nakamura.[15b] To the best of our knowledge, no examples for $In(OTf)_3$-mediated one-pot (4+2) annulation of γ-alkynone with $N_2H_{4(aq)}$ have been reported. In continuation of our investigation on the applications of β-ketosulfones **1** (e.g., 2-arylpyrroles, vinylcyclopropanes, 2,6-diaryltetrahydropyrans, 2-arylfurans and substituted benzenes),[16,17] a facile one-pot synthesis of 2-arylpyridazines **5** is developed, including (1) α-propargylation of **1** with propargylic bromides **2**, and (2) $In(OTf)_3$-promoted cyclocondensation of the resulting γ-alkynones **3** with $N_2H_{4(aq)}$ (see Scheme 1). Pyridazine is a versatile building block in the synthesis of natural products and a useful synthetic intermediate.[18] A number of articles have highlighted fascinating developments based on two C–N bond formations.[19] 2-Arylpyridazines are also known to exhibit versatile biological activities, such as antibacterial activity, antibiotic or anti-depressant activity.[20] After further comparing literature reports on the preparation of substituted pyridazines, herein, we describe one-pot route on the cyclocondensation of the γ-alkynones with $N_2H_{4(aq)}$.



Scheme 1. Synthetic route of **5**.

2. Results and discussion

According to previous literature on metal triflate-mediated hydration of alkynes,[16d] catalytic amounts (2 mol %) of AgOTf (**4a**), $Hg(OTf)_2$ (**4b**), $In(OTf)_3$ (**4c**) or $Cu(OTf)_2$ (**4d**) were first examined for the transformation of model substrate **3a** (R=Tol, Ar=Ph, Y=H) from γ-alkynone to a skeleton of 2-arylpyridazine **5a** in dioxane at 25 °C for 4 h. As shown in Table 1 and entries 1–4, **4c** provided a better yield (80%) than **4a** (72%), **4b** (69%) and **4d** (25%) for generating **5a**. On the basis of a higher yield and activity, low toxicity and relatively low price, **4c** was chosen as the appropriate catalyst for synthesizing **5** via one-pot mild (4+2) cyclocondensation of **3a**

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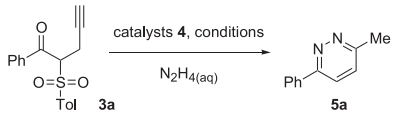
Table 1
One-pot conditions[a]

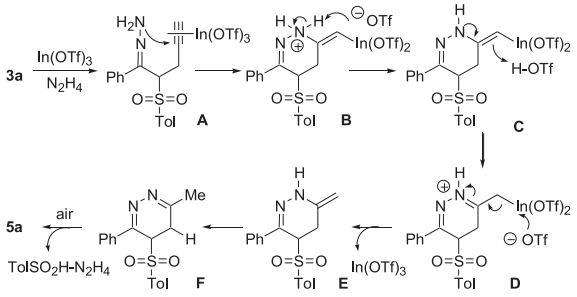


Entry	Catalyst 4 (mol %), solvent (mL), temp (°C)	Yield (%)[b]
1	AgOTf **4a** (2), dioxane (5), 25	72
2	$Hg(OTf)_2$ **4b** (2), dioxane (5), 25	69
3	$In(OTf)_3$ **4c** (2), dioxane (5), 25	80
4	$Cu(OTf)_2$ **4d** (2), dioxane (5), 25	25[c]
5	$InCl_3$ **4e** (5), dioxane (5), 25	60
6	$InBr_3$ **4f** (2), dioxane (5), 25	68
7	In_2O_3 **4g** (2), dioxane (5), 25	12[d] (20)[e]
8	$In(OTf)_3$ **4c** (0), dioxane (5), 25	—[f]
9	$In(OTf)_3$ **4c** (5), dioxane (5), 25	79
10	$In(OTf)_3$ **4c** (10), dioxane (5), 25	77
11	$In(OTf)_3$ **4c** (2), dioxane (10), 25	75
12	$In(OTf)_3$ **4c** (2), dioxane (5), 50	70
13	$In(OTf)_3$ **4c** (2), dioxane (5), 100	63
14	$In(OTf)_3$ **4c** (2), $MeNO_2$ (5), 25	75
15	$In(OTf)_3$ **4c** (2), $(CH_2Cl)_2$ (5), 25	63
16	$In(OTf)_3$ **4c** (2), benzene (5), 25	51
17	$In(OTf)_3$ **4c** (2), EtOH (5), 25	58

[a] Reactions were run on a 1.0 mmol scale with **3a**, $N_2H_{4(aq)}$ (80%, 1 mL), 4 h.
[b] Isolated yields.
[c] 46% of a hydrazone mixture was isolated.
[d] 48% of a hydrazone mixture was isolated.
[e] 40 h and 40% of a hydrazone mixture was isolated.
[f] 88% of a hydrazone mixture was isolated.

in the presence of $N_2H_{4(aq)}$. Then, the use of other In(III) salts was examined (see entries 5–7). In comparison with these In(III) complexes, such as $InCl_3$ (**4e**), $InBr_3$ (**4f**) and In_2O_3 (**4g**), **4c** was still a better catalyst for the generation of **5a**. **4e-f** produced **5a** in 60% and 68% yields, respectively. For **4g**, only 12% of **5a** was isolated along with 48% of a hydrazone mixture. To elongate the reaction time (4 → 40 h), similar results were observed. Furthermore, controlling **4c** as the catalyst, catalyst equivalents, reaction solvents and temperature were further studied. Without the addition of **4c**, no **5a** was yielded (entry 8). When using 5 or 10 mol % of **4c**, the isolated yield was similar to 2 mol % (entries 9–10). By adjusting reaction concentrations (entries 11) or temperature (entries 12–13), poorer yield occurred. To change the reaction solvents from dioxane to $MeNO_2$, dichloroethane, benzene and EtOH, dioxane provided a better yield of **5a** due to good solubility with water (entries 14–17). Based on the above results, we envisioned that 2 mol % of $In(OTf)_3$/dioxane/$N_2H_{4(aq)}$ should be an optimal combination for forming **5a** via one-pot reaction of **3a**.

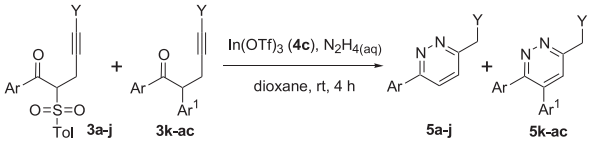
Based on the results, a possible reaction mechanism is shown in Scheme 2. How is **5a** produced? The mechanism should be initiated to form **A** by complexation of an alkynyl motif of a hydrazone skeleton (in situ generated from condensation of **3a** with N_2H_4) with **4c**, and participation of an amino group of hydrazone could lead to an ammonium ion **B** via intramolecular 6-*exo*-*dig* annulation. Deprotonation of **B** should give vinyl indium intermediate **C**. Then, protonation by in situ generated HOTf leads to an alternative iminium cation **D**, which, following loss of $In(OTf)_3$, is able to provide **E** and the recovery of $In(OTf)_3$. Tautomerization of **E** affords **F**. Subsequently, desulfonylative aromatization of the resulting **F** generates **5a** under air atmosphere.



Scheme 2. Possible mechanism.

With optimized conditions in hand (Table 1, entry 3), we further explored the substrate scope of the reaction, and the results are shown in Table 2. For adjusting the Ar and Y substituents of α-sulfonyl γ-alkynones **3a**–**j**, arylpyridazines **5a**–**j** (Ar=Ph, 4-FC_6H_4, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-$CF_3C_6H_4$, 4-PhC_6H_4, 2-naphthalene, 2-thiophene; Y=H, Me, Et) were provided in 72–85% yields (entries 1–10). To demonstrate the utilization of the route, α-aryl γ-arylalkynones **3j**–**ab** were prepared from α-propargylation of substituted deoxybenzoins with propargyl bromide. By this combination of $In(OTf)_3$/dioxane/$N_2H_{4(aq)}$, diarylpyridazines **5j**–**ab** (Ar=Ph, 4-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 2,3,4-$(MeO)_3C_6H_2$; Ar^1=Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-FC_6H_4, 4-$CF_3C_6H_4$, 3,5-$F_2C_6H_3$, 4-PhC_6H_4, 2-naphthalene, 4,7-$(MeO)_2$-1-naphthalene, Y=H) were isolated in 75–85% yields under the above conditions (entries 11–28). Changing a sulfonyl group to an aryl group, no obvious yield changes were observed for the generation of **5**. For the Ar and Ar^1 groups of **3**, the phenyl ring, with both electron-withdrawing and electron-donating substituents, was well tolerated, providing the desired product **5** in moderate to good yields. The structures of **5h**, **5n**, **5p**, **5u**, **5w**, **5z** and **5aa** were determined by single-crystal X-ray crystallography.[21] However, treatment of **3ac** (Ar=Ar^1=Y=Ph) with the α-phenylacetylene group (an internal alkyne) afforded the

Table 2
Synthesis of **5**[a]

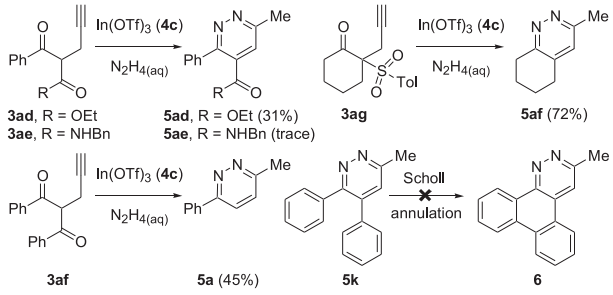


Entry	**3**, Ar=, Ar^1=, Y=,	**5**, yield%[b]
1	**3a**, Ph, —, H	**5a**, 80
2	**3b**, 4-FC_6H_4, —, H	**5b**, 82
3	**3c**, 4-$MeOC_6H_4$, —, H	**5c**, 85
4	**3d**, 4-MeC_6H_4, —, H	**5d**, 83
5	**3e**, 4-$CF_3C_6H_4$, —, H	**5e**, 82
6	**3f**, 4-PhC_6H_4, —, H	**5f**, 81
7	**3g**, 2-naphthalene, —, H	**5g**, 75
8	**3h**, 2-thiophene, —, H	**5h**, 72
9	**3i**, Ph, —, Me	**5i**, 73
10	**3j**, Ph, —, Et	**5j**, 72
11	**3k**, Ph, Ph, H	**5k**, 85
12	**3l**, 4-$MeOC_6H_4$, Ph, H	**5l**, 83
13	**3m**, 4-$MeOC_6H_4$, 4-MeC_6H_4, H	**5m**, 83
14	**3n**, 4-$MeOC_6H_4$, 4-$MeOC_6H_4$, H	**5n**, 80
15	**3o**, 4-$MeOC_6H_4$, 4-FC_6H_4, H	**5o**, 78
16	**3p**, 4-$MeOC_6H_4$, 4-$CF_3C_6H_4$, H	**5p**, 75
17	**3q**, 4-$MeOC_6H_4$, 3,5-$F_2C_6H_3$, H	**5q**, 82
18	**3r**, 4-$MeOC_6H_4$, 4-PhC_6H_4, H	**5r**, 83
19	**3s**, 4-$MeOC_6H_4$, 2-naphthalene, H	**5s**, 84
20	**3t**, 3,4-$(MeO)_2C_6H_3$, Ph, H	**5t**, 85
21	**3u**, 3,4-$(MeO)_2C_6H_3$, 4-MeC_6H_4, H	**5u**, 80
22	**3v**, 3,4-$(MeO)_2C_6H_3$, 4-$MeOC_6H_4$, H	**5v**, 82
23	**3w**, 3,4-$(MeO)_2C_6H_3$, 4-FC_6H_4, H	**5w**, 81
24	**3x**, 3,4-$(MeO)_2C_6H_3$, 4-PhC_6H_4, H	**5x**, 82
25	**3y**, 3,4-$(MeO)_2C_6H_3$, 3,5-$F_2C_6H_3$, H	**5y**, 75
26	**3z**, 2,3,4-$(MeO)_3C_6H_2$, Ph, H	**5z**, 80
27	**3aa**, 2,3,4-$(MeO)_3C_6H_2$, 4-FC_6H_4, H	**5aa**, 82
28	**3ab**, 4,7-$(MeO)_2$-naphthalene, 2,3-$CH_2O_2C_6H_3$, H	**5ab**, 75
29	**3ac**, Ph, Ph, Ph	**5ac**, —[c]

[a] The pyridazine synthesis was run on a 1.0 mmol scale with **3**, $In(OTf)_3$ (**4c**) (2 mol %), dioxane (5 mL), $N_2H_{4(aq)}$ (80%, 1 mL), 4 h at 25 °C.
[b] Isolated yield.
[c] Complex mixture was observed.

complex mixture. No desired **5ac** was isolated (entry 29). Moreover, when 5.0 g of **3a** (16.0 mmol) was treated with the combination at 25 °C, 2.04 g of **5a** was isolated in a 75% yield. This route can be enlarged to multigram scale for producing **5a**.

Changing the α-substituent from sulfonyl and aryl groups to ethyl ester, benzyl amide and benzoyl groups (see Scheme 3), **5ad** and **5a** were isolated in 31% and 45% yields, respectively, by the treatment of **3ad** and **3af** with the one-pot protocol. For β-ketoamide group of **3ae**, trace **5ae** was observed. For the generation of **5a**, the major reason should be that N_2H_4 promoted a retro-aldol debenzoylation of **3af** with a β-diketone motif followed by the dehydrogenative aromatization process. Additionally, one-pot (4+2) cyclocondensation of cyclic α-sulfonyl γ-alkynone **3ag** was examined. By the above conditions, tetrahydrocinnoline **5af** was isolated in 72% yield. Furthermore, attempts to apply the electrocyclization of **5k** failed to afford a tetracyclic cinnoline **6**[22] under Scholl annulation conditions.[23]



Scheme 3. Reactions of **3ad**–**ag** and **5k**.

3. Conclusion

In summary, we have developed a mild, facile and one-pot synthesis of substituted pyridazines **5** in good yields via an $In(OTf)_3$/dioxane/$N_2H_{4(aq)}$-mediated (4+2) cyclocondensation of γ-alkynones **3** under a desulfonative or dehydrogenative aromatization process. The plausible mechanism has been discussed and proposed. The structures of the key products were confirmed by X-ray crystallography. Further investigation regarding synthetic applications of β-ketosulfones will be conducted and published in due course.

4. Experimental section

4.1. General

All other reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry nitrogen with magnetic stirring. Products in organic solvents were dried with anhydrous magnesium sulfate before concentration in vacuo. Melting points were determined with a SMP3 melting apparatus. ^1H and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer operating at 400 and at 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants (J) are given in Hertz. High resolution mass spectra (HRMS) were measured with a mass spectrometer Finnigan/Thermo Quest MAT 95XL. X-ray crystal structures were obtained with an Enraf-Nonius FR-590 diffractometer (CAD4, Kappa CCD).

4.2. A representative synthetic procedure of 5a–ab, 5ad and 5af is as follows

$In(OTf)_3$ (11 mg, 0.02 mmol) was added to a solution of **3a**-**ag** (1.0 mmol) in dioxane (5 mL) at rt. The reaction mixture was stirred at rt for 10 min. $N_2H_{4(aq)}$ (80%, 1 mL) was added to mixture at 25 °C. The reaction mixture was stirred at rt for 4 h. The reaction mixture was concentrated and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc=10/1∼4/1) afforded **5a**–**ab**, **5ad** and **5af**.

*4.2.1. 3-Methyl-6-phenylpyridazine (**5a**).*[19l] Yield=80% (136 mg); Colorless solid; mp=105–108 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{11}H_{11}N_2$ 171.0922, found 171.0925; ^1H NMR (400 MHz, $CDCl_3$): δ 8.07–8.04 (m, 2H), 7.79 (d, J=8.8 Hz, 1H), 7.54–7.46 (m, 3H), 7.42 (d, J=8.4 Hz, 1H), 2.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.44, 157.32, 136.22, 129.86, 128.97 (2×), 127.59, 126.91 (2×), 124.27, 21.86.

*4.2.2. 3-(4-Fluorophenyl)-6-methylpyridazine (**5b**).*[19h] Yield=82% (154 mg); Colorless solid; mp=138–140 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{11}H_{10}FN_2$ 189.0828, found 189.0832; ^1H NMR (400 MHz, $CDCl_3$): δ 8.08–8.03 (m, 2H), 7.52 (d, J=8.8 Hz, 1H), 7.41 (d, J=8.8 Hz, 1H), 7.22–7.16 (m, 2H), 2.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.02 (d, J=248.6 Hz), 158.43, 156.31, 134.77 (d, J=3.8 Hz), 128.78 (d, J=8.4 Hz, 2×), 127.56, 123.84, 115.99 (d, J=22.0 Hz, 2×), 21.87.

*4.2.3. 3-(4-Methoxyphenyl)-6-methylpyridazine (**5c**).* [19l] Yield=85% (170 mg); Colorless solid; mp=136–139 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{12}H_{13}N_2O$ 201.1028, found 201.1033; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J=8.8 Hz, 2H), 7.68 (d, J=8.8 Hz, 1H), 7.32 (d, J=8.8 Hz, 1H), 7.00 (d, J=8.8 Hz, 2H), 3.85 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.99, 157.78, 156.69, 128.76, 128.11 (2×), 127.24, 123.29, 114.27 (2×), 55.30, 21.85.

*4.2.4. 3-Methyl-6-(4-methylphenyl)pyridazine (**5d**).*[19l] Yield=83% (153 mg); Colorless solid; mp=116–118 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{12}H_{13}N_2$ 185.1079, found 185.1088; ^1H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J=8.0 Hz, 2H), 7.67 (d, J=8.8 Hz, 1H), 7.30 (d, J=8.8 Hz, 1H), 7.26 (d, J=8.0 Hz, 2H), 2.68 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.05, 156.93, 139.70, 133.39, 129.49 (2×), 127.14, 126.54 (2×), 123.54, 21.80, 21.15.

*4.2.5. 3-Methyl-6-(4-trifluoromethylphenyl)pyridazine (**5e**).*[19l] Yield=82% (195 mg); Colorless solid; mp=184–186 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{12}H_{10}F_3N_2$ 239.0796, found 239.0801; ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J=8.4 Hz, 2H), 7.80 (d, J=8.4 Hz, 1H), 7.77 (d, J=8.8 Hz, 2H), 7.44 (d, J=8.8 Hz, 1H), 2.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.30, 155.95, 139.72, 131.60 (q, J=31.9 Hz), 127.49, 127.18 (2×), 125.98 (2×), 125.94 (q, J=3.7 Hz), 124.10, 22.06.

*4.2.6. 3-(4-Biphenyl)-6-methylpyridazine (**5f**).* Yield=81% (199 mg); Colorless solid; mp=188–190 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{17}H_{15}N_2$ 247.1235, found 247.1232; ^1H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J=8.4 Hz, 2H), 7.77 (d, J=8.8 Hz, 1H), 7.73 (d, J=8.8 Hz, 2H), 7.66–7.63 (m, 2H), 7.49–7.44 (m, 2H), 7.40–7.36 (m, 2H), 2.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.43, 156.74, 142.42, 140.20, 135.15, 128.81 (2×), 127.65, 127.55 (2×), 127.26, 127.18 (2×), 127.02 (2×), 123.73, 21.97.

*4.2.7. 3-Methyl-6-(naphthalen-2-yl)pyridazine (**5g**).*[19l] Yield=75% (165 mg); Colorless solid; mp=180–183 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{15}H_{13}N_2$ 221.1079, found 221.1082; ^1H NMR (400 MHz, $CDCl_3$): δ 8.50 (d,

J=1.2 Hz, 1H), 8.22 (dd, *J*=1.6, 8.4 Hz, 1H), 7.98–7.87 (m, 4H), 7.55–7.50 (m, 2H), 7.42 (d, *J*=8.8 Hz, 1H), 2.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.45, 157.13, 133.93, 133.50, 133.29, 128.74, 128.71, 127.70, 127.55, 126.98, 126.55, 126.52, 124.33, 124.10, 21.91.

4.2.8. 3-Methyl-6-(thiophen-2-yl)pyridazine (***5h***).[19n] Yield=72% (127 mg); Colorless solid; mp=138–140 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_9H_9N_2S$ 177.0487, found 177.0488; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J*=8.8 Hz, 1H), 7.63 (dd, *J*=1.2, 3.6 Hz, 1H), 7.46 (dd, *J*=1.2, 5.2 Hz, 1H), 7.33 (d, *J*=8.8 Hz, 1H), 7.14 (dd, *J*=3.6, 5.2 Hz, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.30, 153.08, 140.68, 128.78, 127.94, 127.39, 125.83, 122.61, 21.93; Anal. Calcd for $C_9H_8N_2S$: C, 61.33; H, 4.58. Found: C, 61.54; H, 4.75. Single-crystal X-ray diagram: crystal of compound **5h** was grown by slow diffusion of EtOAc into a solution of compound **5h** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/c, *a*=6.1629(2) Å, *b*=7.9773(3) Å, *c*=16.7489(7) Å, *V*=821.82(5) Å^3, *Z*=4, d_{calcd}=1.424 mg/cm^3, *F*(000)=368, 2θ range 2.437∼26.397°, *R* indices (all data) *R*1=0.0307, w*R*2=0.0778.

4.2.9. 3-Ethyl-6-phenylpyridazine (***5i***). Yield=73% (134 mg); Colorless solid; mp=45–48 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{12}H_{13}N_2$ 185.1079, found 185.1075; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07–8.06 (m, 2H), 7.81 (d, *J*=8.8 Hz, 1H), 7.54–7.46 (m, 3H), 7.43 (d, *J*=8.8 Hz, 1H), 3.08 (q, *J*=7.6 Hz, 2H), 1.42 (t, *J*=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.14, 157.42, 136.23, 129.84, 128.96 (2×), 126.89 (2×), 126.55, 124.40, 28.96, 13.56.

4.2.10. 3-Phenyl-6-n-propylpyridazine (***5j***). Yield=72% (143 mg); Colorless solid; mp=48–50 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{13}H_{15}N_2$ 199.1235, found 199.1238; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09–8.07 (m, 2H), 7.82 (d, *J*=8.8 Hz, 1H), 7.54–7.46 (m, 3H), 7.42 (d, *J*=8.8 Hz, 1H), 3.03 (t, *J*=7.6 Hz, 2H), 1.91–1.82 (m, 2H), 1.03 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.05, 157.39, 136.18, 129.87, 128.97 (2×), 127.10, 126.89 (2×), 124.34, 37.62, 22.80, 13.77.

4.2.11. 6-Methyl-3,4-diphenylpyridazine (***5k***). [19l] Yield=85% (209 mg); Colorless solid; mp=117–120 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{17}H_{15}N_2$ 247.1235, found 247.1233; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.40 (m, 2H), 7.39 (s, 1H), 7.36–7.26 (m, 6H), 7.21–7.18 (m, 2H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.40, 157.96, 139.78, 136.66, 136.49, 129.95 (2×), 129.02 (2×), 128.76, 128.70, 128.67 (2×), 128.27, 128.12 (2×), 21.65.

4.2.12. 3-(4-Methoxyphenyl)-6-methyl-4-phenylpyridazine (***5l***). Yield=83% (229 mg); Colorless gum; HRMS (ESI, M^++1) calcd for $C_{18}H_{17}N_2O$ 277.1341, found 277.1345; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.29 (m, 5H), 7.28 (s, 1H), 7.21–7.17 (m, 2H), 6.80 (d, *J*=8.8 Hz, 2H), 3.78 (s, 3H), 2.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.86, 158.07, 157.25, 138.67, 137.21, 131.25 (2×), 129.18, 128.90 (2×), 128.59 (2×), 128.43, 127.72, 113.50 (2×), 55.15, 21.82; Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84. Found: C, 78.41; H, 5.89.

4.2.13. 3-(4-Methoxyphenyl)-4-(4-methylphenyl)-6-methylpyridazine (***5m***). Yield=83% (241 mg); Colorless solid; mp=110–113 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{19}H_{19}N_2O$ 291.1497, found 291.1502; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J*=8.4 Hz, 2H), 7.28 (s, 1H), 7.13 (d, *J*=8.4 Hz, 2H), 7.08 (d, *J*=8.0 Hz, 2H), 6.82 (d, *J*=8.8 Hz, 2H), 3.80 (s, 3H), 2.77 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.89, 158.02, 157.41, 138.95, 138.57, 134.16, 131.27 (2×), 129.37 (2×), 129.31, 128.84 (2×), 127.83, 113.54 (2×), 55.21, 21.78, 21.22; Anal. Calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25. Found: C, 78.68; H, 6.43.

4.2.14. 6-Methyl-3,4-di(4-methoxyphenyl)pyridazine (***5n***). Yield=80% (245 mg); Colorless solid; mp=112–113 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{19}H_{19}N_2O_2$ 307.1447, found 307.1450; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J*=8.8 Hz, 2H), 7.27 (s, 1H), 7.12 (d, *J*=8.8 Hz, 2H), 6.83 (d, *J*=8.8 Hz, 2H), 6.82 (d, *J*=8.8 Hz, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 2.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.86, 159.84, 158.02, 157.38, 138.51, 131.22 (2×), 130.30 (2×), 129.43, 129.21, 127.55, 114.10 (2×), 113.56 (2×), 55.24, 55.19, 21.78; Anal. Calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92. Found: C, 74.53; H, 6.08. Single-crystal X-ray diagram: crystal of compound **5n** was grown by slow diffusion of EtOAc into a solution of compound **5n** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group P −1, *a*=9.7886(6) Å, *b*=11.7178(7) Å, *c*=14.1885(8) Å, *V*=1590.23(16) Å^3, *Z*=2, d_{calcd}=1.280 mg/cm^3, *F*(000)=648, 2θ range 1.456∼26.432°, *R* indices (all data) *R*1=0.1110, w*R*2=0.1918.

4.2.15. 4-(4-Fluorophenyl)-3-(4-methoxyphenyl)-6-methylpyridazine (***5o***). Yield=78% (229 mg); Colorless solid; mp=130–133 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{18}H_{16}FN_2O$ 295.1247, found 295.1248; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, *J*=8.8 Hz, 2H), 7.28 (s, 1H), 7.20–7.14 (m, 2H), 7.05–6.99 (m, 2H), 6.82 (d, *J*=8.8 Hz, 2H), 3.80 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.84 (d, *J*=247.8 Hz), 160.02, 158.15, 157.32, 137.87, 133.15 (d, *J*=3.0 Hz), 131.27 (2×), 130.81 (d, *J*=8.3 Hz, 2×), 128.90, 127.72, 115.84 (d, *J*=22.0 Hz, 2×), 113.67 (2×), 55.22, 21.79.

4.2.16. 3-(4-Methoxyphenyl)-6-methyl-4-(4-trifluoromethylphenyl) pyridazine (***5p***). Yield=75% (258 mg); Colorless solid; mp=138–140 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{19}H_{16}F_3N_2O$ 345.1215, found 345.1212; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J*=8.4 Hz, 2H), 7.34–7.32 (m, 4H), 7.32 (s, 1H), 6.83 (d, *J*=8.8 Hz, 2H), 3.81 (s, 3H), 2.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.21, 158.21, 157.12, 140.91, 137.55, 131.34 (2×), 129.37 (2×), 128.36, 127.89, 125.71 (d, *J*=3.0 Hz, 2×), 125.64 (d, *J*=3.8 Hz, 2×), 113.80 (2×), 55.24, 21.76; Anal. Calcd for $C_{19}H_{15}F_3N_2O$: C, 66.27; H, 4.39. Found: C, 66.38; H, 4.58. Single-crystal X-ray diagram: crystal of compound **5p** was grown by slow diffusion of EtOAc into a solution of compound **5p** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/n, *a*=6.1166(11) Å, *b*=10.929(2) Å, *c*=24.165(5) Å, *V*=1610.2(5) Å^3, *Z*=4, d_{calcd}=1.420 mg/cm^3, *F*(000)=712, 2θ range 1.691∼26.452°, *R* indices (all data) *R*1=0.0527, w*R*2=0.1147.

4.2.17. 4-(3,5-Difluorophenyl)-3-(4-methoxyphenyl)-6-methylpyridazine (***5q***). Yield=82% (256 mg); Colorless solid; mp=117–119 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{18}H_{15}F_2N_2O$ 313.1153, found 313.1155; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, *J*=8.8 Hz, 2H), 7.27 (s, 1H), 6.85 (d, *J*=8.8 Hz, 2H), 6.80 (t, *J*=2.4 Hz, 1H), 6.76–6.71 (m, 2H), 3.82 (s, 3H), 2.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.99 (d, *J*=248.7 Hz), 162.86 (d, *J*=248.7 Hz), 160.27, 158.24, 156.88, 140.51, 136.57, 131.18 (2×), 128.21, 127.51, 113.84 (2×), 112.12 (d, *J*=26.6 Hz), 112.12 (d, *J*=11.4 Hz), 104.10 (t, *J*=25.0 Hz), 55.25, 21.80; Anal. Calcd for $C_{18}H_{14}F_2N_2O$: C, 69.22; H, 4.52. Found: C, 69.35; H, 4.63.

4.2.18. 4-(4-Biphenyl)-3-(4-methoxyphenyl)-6-methylpyridazine (***5r***). Yield=83% (292 mg); Yellowish gum; HRMS (ESI, M^++1) calcd for $C_{24}H_{21}N_2O$ 353.1654, found 353.1655; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.57 (m, 4H), 7.48–4.35 (m, 6H), 7.29 (d, *J*=8.8 Hz,

2H), 6.84 (d, J=8.8 Hz, 2H), 3.81 (s, 3H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.15, 157.92, 157.50, 141.50, 139.89, 135.73, 131.38 (2×), 129.43 (2×), 128.90 (2×), 128.71, 128.36 (2×), 127.83, 127.33 (2×), 127.00 (2×), 113.70 (2×), 55.24, 21.53; Anal. Calcd for $C_{24}H_{20}N_2O$: C, 81.79; H, 5.72. Found: C, 81.92; H, 5.69.

*4.2.19. 3-(4-Methoxyphenyl)-6-methyl-4-(naphthalen-2-yl)pyridazine (**5s**).* Yield=84% (274 mg); Yellowish gum; HRMS (ESI, M^++1) calcd for $C_{22}H_{19}N_2O$ 327.1497, found 327.1499; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J=8.0 Hz, 1H), 7.89 (d, J=8.4 Hz, 1H), 7.51–7.37 (m, 5H), 7.31 (d, J=8.8 Hz, 2H), 7.25 (dd, J=0.8, 8.4 Hz, 1H), 6.62 (d, J=9.2 Hz, 2H), 3.69 (s, 3H), 2.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.18, 158.45, 157.32, 139.04, 134.42, 133.54, 130.73 (2×), 130.64, 130.52, 129.31, 128.59, 128.29, 127.49, 126.99, 126.40, 125.27, 124.77, 113.52 (2×), 55.12, 21.25.

*4.2.20. 3-(3,4-Dimethoxyphenyl)-6-methyl-4-phenylpyridazine (**5t**).* Yield=85% (260 mg); Colorless solid; mp=117–119 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{19}H_{19}N_2O_2$ 307.1447, found 307.1450; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.32 (m, 3H), 7.30 (s, 1H), 7.22–7.19 (m, 2H), 7.01 (d, J=8.4 Hz, 1H), 6.96 (d, J=2.0 Hz, 1H), 6.77 (d, J=8.0 Hz, 1H), 3.86 (s, 3H), 3.63 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.13, 157.17, 149.38, 148.34, 138.90, 137.36, 129.10, 128.89 (2×), 128.67 (2×), 128.46, 127.86, 122.90, 113.11, 110.60, 55.78, 55.56, 21.80.

*4.2.21. 3-(3,4-Dimethoxyphenyl)-6-methyl-4-(4-methylphenyl)pyridazine (**5u**).* Yield=80% (256 mg); Colorless solid; mp=125–127 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{20}H_{21}N_2O_2$ 321.1603, found 321.1610; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (s, 1H), 7.14 (d, J=8.4 Hz, 2H), 7.09 (d, J=8.0 Hz, 2H), 7.00 (dd, J=2.0, 8.4 Hz, 1H), 6.98 (d, J=2.0 Hz, 1H), 6.77 (d, J=8.4 Hz, 1H), 3.87 (s, 3H), 3.66 (s, 3H), 2.78 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.10, 157.30, 149.36, 148.36, 139.04, 138.53, 134.32, 129.36 (2×), 129.33, 128.81 (2×), 127.83, 122.86, 113.12, 110.61, 55.80, 55.57, 21.78, 21.18. Single-crystal X-ray diagram: crystal of compound **5u** was grown by slow diffusion of EtOAc into a solution of compound **5u** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/n, a=7.8618(3) Å, b=10.9341(4) Å, c=19.6250(7) Å, V=1678.08(11) Å^3, Z=4, d_{calcd}=1.268 mg/cm^3, F(000)=680, 2θ range 2.135∼26.359°, R indices (all data) $R1$=0.0583, w$R2$=0.1234.

*4.2.22. 3-(3,4-Dimethoxyphenyl)-4-(4-methoxyphenyl)-6-methylpyridazine (**5v**).* Yield=82% (276 mg); Yellowish gum; HRMS (ESI, M^++1) calcd for $C_{20}H_{21}N_2O_3$ 337.1552, found 337.1552; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (s, 1H), 7.13 (d, J=8.8 Hz, 2H), 7.03 (d, J=2.0 Hz, 1H), 6.97 (dd, J=2.0, 8.0 Hz, 1H), 6.85 (d, J=8.8 Hz, 2H), 6.77 (d, J=8.4 Hz, 1H), 3.87 (s, 3H), 3.81 (s, 3H), 3.70 (s, 3H), 2.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.90, 158.07, 157.32, 149.34, 148.45, 138.71, 130.27 (2×), 129.42, 129.30, 127.66, 122.84, 114.13 (2×), 113.05, 110.63, 55.80, 55.65, 55.30, 21.76; Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99. Found: C, 71.62; H, 6.12.

*4.2.23. 4-(4-Fluorohenyl)-3-(3,4-dimethoxyphenyl)-6-methylpyridazine (**5w**).* Yield=81% (262 mg); Colorless solid; mp=144–146 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{19}H_{18}FN_2O_2$ 325.1352, found 325.1351; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (s, 1H), 7.20–7.15 (m, 2H), 7.05–6.99 (m, 3H), 6.91 (dd, J=2.0, 8.4 Hz, 1H), 6.76 (d, J=8.4 Hz, 1H), 3.86 (s, 3H), 3.70 (s, 3H), 2.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.76 (d, J=247.9 Hz), 158.21, 157.14, 149.45, 148.53, 137.76, 133.29 (d, J=3.0 Hz), 130.74 (d, J=8.3 Hz, 2×), 128.99, 127.61, 122.88, 115.78 (d, J=22.0 Hz, 2×), 112.99, 110.62, 55.78, 55.64, 21.80. Single-crystal X-ray diagram: crystal of compound **5w** was grown by slow diffusion of EtOAc into a solution of compound **5w** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/c, a=15.8783(8) Å, b=9.1753(5) Å, c=11.1547(6) Å, V=1614.43(15) Å^3, Z=4, d_{calcd}=1.334 mg/cm^3, F(000)=680, 2θ range 1.291∼26.416°, R indices (all data) $R1$=0.0589, w$R2$=0.1236.

*4.2.24. 4-(4-Biphenyl)-3-(3,4-dimethoxyphenyl)-6-methylpyridazine (**5x**).* Yield=82% (313 mg); Yellowish gum; HRMS (ESI, M^++1) calcd for $C_{25}H_{23}N_2O_2$ 383.1760, found 383.1766; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.58 (m, 4H), 7.48–7.44 (m, 2H), 7.40 (s, 1H), 7.40–7.36 (m, 1H), 7.30 (d, J=8.4 Hz, 2H), 7.05 (dd, J=2.0, 8.0 Hz, 1H), 7.04 (br s, 1H), 6.79 (d, J=8.4 Hz, 1H), 3.88 (s, 3H), 3.67 (s, 3H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.01, 157.37, 155.78, 149.65, 148.51, 141.57, 139.90, 139.21, 135.93, 129.42 (2×), 128.95 (2×), 128.32, 127.88, 127.36 (2×), 126.99 (2×), 123.08, 113.12, 110.70, 55.83, 55.64, 21.57.

*4.2.25. 4-(3,5-Difluorohenyl)-3-(3,4-dimethoxyphenyl)-6-methylpyridazine (**5y**).* Yield=75% (257 mg); Colorless gum; HRMS (ESI, M^++1) calcd for $C_{29}H_{17}F_2N_2O_2$ 343.1258, found 357.1608; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (s, 1H), 7.06 (d, J=2.0 Hz, 1H), 6.90 (dd, J=2.0, 8.4 Hz, 1H), 6.84–6.72 (m, 4H), 3.88 (s, 3H), 3.76 (s, 3H), 2.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.02 (d, J=248.7 Hz), 162.89 (d, J=248.6 Hz), 158.35, 156.79, 149.82, 148.79, 140.66 (t, J=9.9 Hz), 136.62, 128.32, 127.50, 122.92, 112.82, 112.08 (d, J=26.5 Hz), 112.08 (d, J=11.3 Hz), 110.75, 104.04 (t, J=25.1 Hz), 55.84, 55.78, 21.82.

*4.2.26. 3-(2,3,4-Trimethoxyphenyl)-6-methyl-4-phenylpyridazine (**5z**).* Yield=80% (269 mg); Colorless solid; mp=156–158 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{20}H_{21}N_2O_3$ 337.1552, found 337.1553; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (s, 1H), 7.28–7.25 (m, 3H), 7.20–7.16 (m, 3H), 6.74 (d, J=8.8 Hz, 1H), 3.88 (s, 3H), 3.63 (s, 3H), 3.35 (s, 3H), 2.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.75, 156.23, 154.62, 151.11, 141.70, 140.38, 137.18, 128.41, 128.37 (2×), 128.27 (2×), 126.63, 125.73, 124.29, 107.13, 60.64, 60.51, 55.99, 21.97. Single-crystal X-ray diagram: crystal of compound **5z** was grown by slow diffusion of EtOAc into a solution of compound **5z** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/c, a=13.0301(7) Å, b=17.7043(10) Å, c=7.4858(4) Å, V=1722.63(16) Å^3, Z=4, d_{calcd}=1.297 mg/cm^3, F(000)=712, 2θ range 1.567∼26.407°, R indices (all data) $R1$=0.0547, w$R2$=0.1192.

*4.2.27. 4-(4-Fluorophenyl)-3-(2,3,4-Trimethoxyphenyl)-6-methylpyridazine (**5aa**).* Yield=82% (290 mg); Colorless solid; mp=173–174 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{20}H_{20}FN_2O_3$ 355.1458, found 355.1455; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (s, 1H), 7.18–7.13 (m, 3H), 6.99–6.93 (m, 2H), 6.74 (d, J=8.8 Hz, 1H), 3.88 (s, 3H), 3.65 (s, 3H), 3.40 (s, 3H), 2.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.77 (d, J=247.1 Hz), 158.79, 156.13, 154.68, 151.04, 141.78, 139.43, 133.22, 133.17 (d, J=8.4 Hz, 2×), 126.47, 125.61, 124.11, 115.36 (d, J=22.0 Hz, 2×), 107.28, 60.71, 60.68, 55.99, 21.97; Anal. Calcd for $C_{20}H_{19}FN_2O_3$: C, 67.79; H, 5.40. Found: C, 67.92; H, 5.62. Single-crystal X-ray diagram: crystal of compound **5aa** was grown by slow diffusion of EtOAc into a solution of compound **5aa** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/c, a=8.5581(9) Å, b=17.768(2) Å, c=12.2073(13) Å, V=1788.4(3) Å^3, Z=4, d_{calcd}=1.316 mg/cm^3, F(000)=744, 2θ range 2.077∼26.373°, R indices (all data) $R1$=0.0732, w$R2$=0.1042.

*4.2.28. 4-(3,4-Methylenedioxyphenyl)-3-(4,7-dimethoxynaphthalen-1-yl)-6-methylpyridazine (**5ab**).* Yield=75% (300 mg); Colorless solid; mp=175–177 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{21}N_2O_4$ 401.1501, found 401.1503;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J=9.2 Hz, 1H), 7.41 (s, 1H), 7.28 (d, J=8.0 Hz, 1H), 7.05 (dd, J=2.4, 9.2 Hz, 1H), 6.76 (d, J=2.4 Hz, 1H), 6.68 (d, J=8.0 Hz, 1H), 6.63 (dd, J=1.6, 8.0 Hz, 1H), 6.58 (s, 1H), 6.56 (d, J=1.6 Hz, 1H), 5.85 (s, 2H), 3.99 (s, 3H), 3.69 (s, 3H), 2.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.68, 158.33, 158.10, 156.25, 147.99, 147.66, 140.24, 133.76, 130.47, 129.96, 127.08, 125.96, 123.89, 122.75, 120.72, 117.37, 108.67, 108.38, 103.79, 101.73, 101.24, 55.48, 55.09, 21.98.

*4.2.29. 4-Ethoxycarbonyl-6-methyl-3-phenylpyridazine (**5ad**).* Yield=31% (75 mg); Colorless oil; HRMS (ESI, M^++1) calcd for $C_{14}H_{15}N_2O_2$ 243.1134, found 243.1138; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.58 (m, 2H), 7.60 (s, 1H), 7.48–7.45 (m, 3H), 4.19 (q, J=7.2 Hz, 2H), 2.83 (s, 3H), 1.08 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.56, 158.91, 156.61, 136.71, 129.98, 129.21, 128.77 (2×), 128.28 (2×), 126.09, 62.22, 21.90, 13.57.

*4.2.30. 3-Methyl-5,6,7,8-tetrahydrocinnoline (**5af**).* Yield=72% (107 mg); Colorless oil; HRMS (ESI, M^++1) calcd for $C_9H_{13}N_2$ 149.1079, found 149.1082; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.99 (s, 1H), 3.07 (t, J=6.4 Hz, 2H), 2.73 (t, J=6.4 Hz, 2H), 2.59 (s, 3H), 1.93–1.87 (m, 2H), 1.82–1.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.26, 157.20, 137.38, 126.78, 29.51, 27.87, 22.44, 21.79, 21.57.

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Supplementary data

Supplementary data (Experimental procedure and scanned photocopies of NMR ($CDCl_3$) spectral data were supported) associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.07.025.

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21.. CCDC 1057388 (**5h**), 1053820 (**5n**), 1053819 (**5p**), 106140 (**5u**), 106141 (**5w**), 1062652 (**5z**) and 1053821 (**5aa**) contain the supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html(or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).
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