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Switchable Ring-Contractive Extrusion Reactions of 2,5-Dihydro-1,4,5-thiadiazepine *S*-Oxides: Entries to Pyridazines or Pyrazoles

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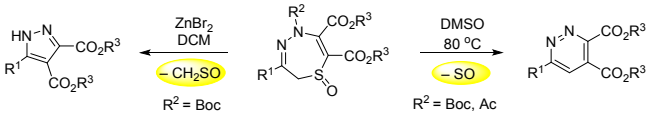
Supporting Information Placeholder

ABSTRACT: Switchable ring-contractive extrusion reactions of 2,5-dihydro-1,4,5-thiadiazepine *S*-oxides are described, which allow expedient access to pyridazines under thermal conditions or pyrazoles under Lewis acid-mediated conditions, respectively.

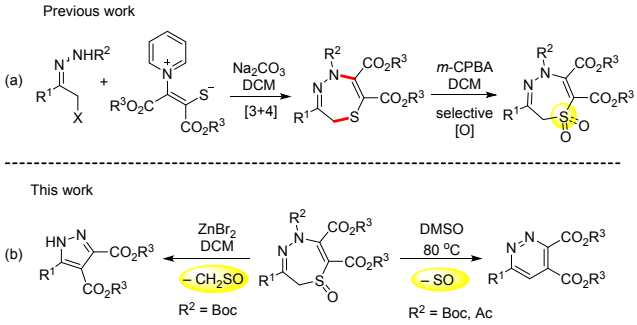


INTRODUCTION

Ring-contraction reactions have been developed as important alternative solutions to access small ring compounds which are inaccessible via direct cyclization reactions from acyclic precursors in modern organic chemistry and great advances had been made by organic chemists in the past decades.[1] Moreover, extrusion reactions (i.e., expulsion of atoms or a group of atoms and reformation of a new bond between the two parts disconnected) are common phenomena in chalcogen and organometallic chemistry, for example, the well-known Ramberg–Bäcklund olefination reaction.[2] As for ring-contractive extrusion reactions, they sometimes could enable the formation of challenging structures (e.g., sterically bulky bonds or strained rings) and have been demonstrated as a kind of useful strategies in synthetic chemistry.[3] For example, Nicolaou had adopted the Ramberg–Bäcklund olefination reaction to access an unusual 13-membered ring in the total synthesis of hirsutellone B.[4a] Corey had disclosed an azo decomposition strategy to construct rare ladderane moiety in the first-generation synthesis of pentacycloanammoxic acid methyl ester.[4b] Thus, to develop new ring-contractive extrusion reactions is highly desired.

Recently we reported the synthesis of 2,5-dihydro-1,4,5-thiadiazepines from pyridinium 1,4-zwitterionic thiolates with 1,2-diaza-1,3-dienes and their *S*-oxides (i.e., sulfoxides and sulfones) via subsequent selective oxidation (eq a, Scheme 1).[5] During our studies, we accidentally discovered two kinds of novel ring-contractive extrusion reactions of 2,5-dihydro-1,4,5-thiadiazepine *S*-oxides, which allow expedient access to pyridazines under thermal conditions or pyrazoles under Lewis acid-mediated conditions (eq b, Scheme 1). Herein we would describe our detailed results on these two interesting transformations.

Scheme 1. Previous work for the synthesis of 2,5-dihydro-1,4,5-thiadiazepine *S*-oxides and this work.

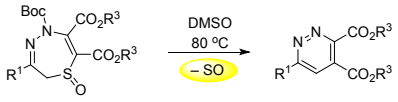


RESULTS AND DISCUSSION

At first, when we checked the spectra of 2,5-dihydro-1,4,5-thiadiazepine *S*-oxides, a serendipitous discovery evoked our great interest. When the samples of sulfoxide **1** were kept in $CDCl_3$ or d^6-DMSO overtime, they would deteriorate apparently and new substances were formed as detected on TLC (thin layer chromatography) and ^{1}H-NMR. The structures of these new substances were finally determined to be **2** after comprehensive identifications including X-ray diffraction analysis of **2a** (Table 1).[6] Pyridazines (**2**) were generated from a ring-contraction reaction via SO extrusion, which was a common phenomenon in chalcogen chemistry.[7] However, this kind of desulfuration transformations only sporadically appeared in the literature for the synthesis of heterocyclic compounds (e.g., indoles, isoquinolines, and so on), owing to the difficulties in preparing ring-contraction precursors. Pyridazines were one of the privileged structural units often recurring in natural products and pharmaceuticals with wide spectrum of bioactive and pharmaceutical applications.[8] After simple optimization of the solvents and temperatures, we

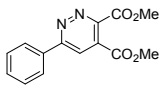
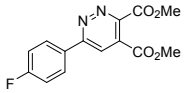
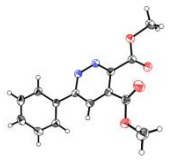
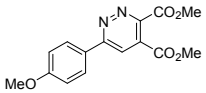
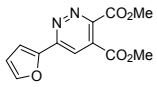
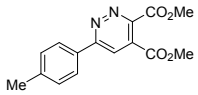
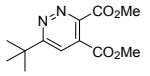
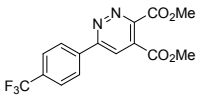
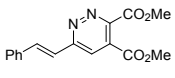
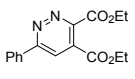
found that a series of sulfoxide analogues prepared according to the reported method[5] could be transformed into functionalized pyridazines (**2a–i**) in DMSO at 80 °C with good yields (Table 1). Among them, electron-withdrawing substituents on the benzene ring induced slightly lower yields (entries 4 and 5). Heteroaryl, alkyl, and alkenyl substituted substrates were all applicable to this transformation (entries 6–8). The *N*-Ac sulfoxide performed well as the *N*-Boc substrate and afforded a comparable yield (see, **2a**). However, when thioether **4a** or sulfone **5a** was examined under thermal conditions, even at 140 °C, the desired pyridazine **2a** was only obtained in low yields. Indeed, these results were in accordance with the empirical extrusion order (SO > SO_2 >S).[7a]

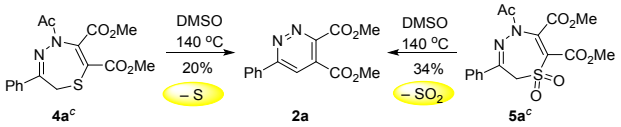
Table 1. Ring-contraction reaction of sulfoxides 1 under thermal conditions [a]



1 2

R^1 = Aryl, Heteroaryl, Alkyl, Alkenyl; R^3 = Me, Et

entry	Product (yield)	entry	Product (yield)
1		5	
	 **2a**, 78% (70%)[b]		**2e**, 59%
2		6	
	2b, 81%		**2f**, 57%
3		7	
	2c, 72%		**2g**, 42%
4		8	
	2d, 65%		**2h**, 68%
		9	
			2i, 74%

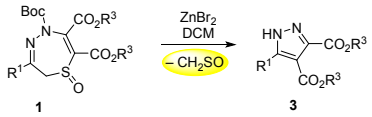


4a[c] 2a 5a[c]

[a] Reaction conditions: ring-contraction precursor (0.3 mmol), DMSO (3 mL), 80 °C unless otherwise noted. Isolated yield. [b] The yield was obtained from the corresponding *N*-Ac analogue. [c]140 °C was employed instead.

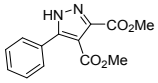
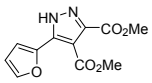
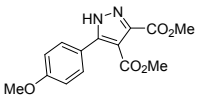
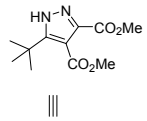
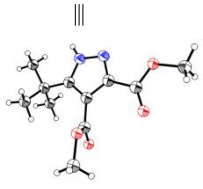
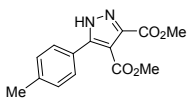
To elucidate the mechanism of our unexpected discovery, we attempted to get the *N*-free analogues of **1**. To our surprise, upon treatment of **1a** with $ZnBr_2$ in DCM at room temperature, the expected *N*-Boc deprotection product was not obtained and pyrazole **3a** was gained instead as the major product via CH_2SO extrusion (entry 1, Table 2). The exact structure of **3a** was subsequently confirmed by analogy with **3g**.[6] This accidental discovery offered a novel synthetic approach to access pyrazoles, which demonstrated a curious and entirely distinct ring-contraction pathway from the identical sulfoxide precursors. Pyrazoles were another fundamentally important class of heterocycles and of great value in organic and medicinal chemistry.[9] By following this Lewis acid-mediated ring-contraction protocol, a library of pyrazoles (**3a–i**) with diverse functional groups were obtained in moderate to good yields. In addition, this ring-contractive extrusion reaction could be scaled up to gram with only a slight loss of the yield (see, **3a**). However, as for thioether **4b** and sulfone **5b** in different oxidant states, **4b** delivered pyrazole **3a** in a low yield of 22%, while **5b** could not afford the extrusion product, even in refluxing DCM.

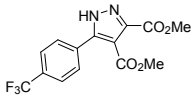
Table 2. Ring-contraction reaction of sulfoxides 1 under Lewis-acid mediated conditions [a]



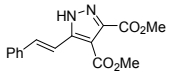
1 3

R^1 = Aryl, Heteroaryl, Alkyl, Alkenyl; R^3 = Me, Et

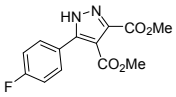
entry	Product (yield)	entry	Product (yield)
1		6	
	3a, 92% (86%)[b]		**3f**, 37%
2		7	
	3b, 85%		
3			
	3c, 78%		**3g**, 78%

4 

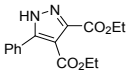
3d, 81%

8 

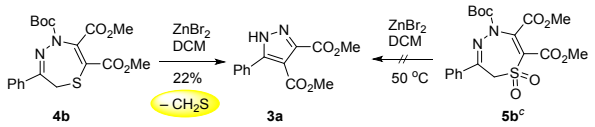
3h, 63%

5 

3e, 76%

9 

3i, 91%

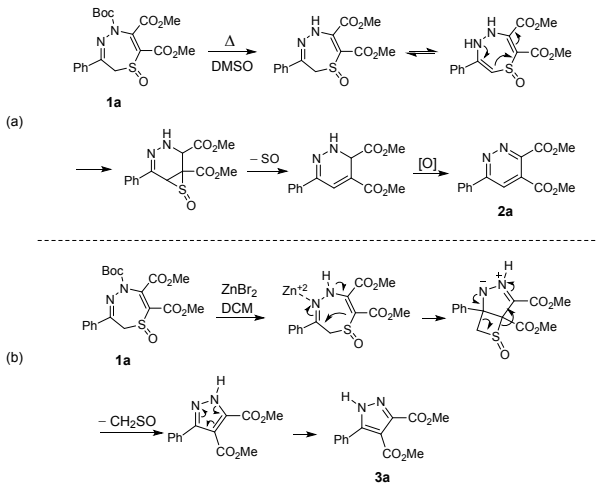


4b 3a 5b[c]

[a] Reaction conditions: ring-contraction precursor (0.3 mmol), $ZnBr_2$ (1.0 equiv), RT (25 °C) unless otherwise noted. Isolated yield. [b] The reaction was conducted in gram-scale. [c] 50 °C was employed instead.

Based on the previous reports and our experimental results, we proposed plausible reaction mechanisms for the switchable ring-contraction reactions as shown in Scheme 2. (a) Initially, sulfoxide **1a** undergoes a deprotection of *N*-Boc under thermal conditions.[10] Then a 1,3-H shift and an intramolecular nucleophilic addition of enamine to activated α,β-unsaturated ester occur to form a 6/3 fused system. After SO extrusion followed by oxidation,[11] pyridazine **2a** is formed (eq a). Whereas, after removal of *N*-Boc assisted with $ZnBr_2$, an intramolecular addition of enamine to imine activated by $ZnBr_2$ furnishes a 5/4 fused system, then CH_2SO extrusion[12] and isomerization occur to afford pyrazole **3a** (eq b).

Scheme 2. Proposed mechanisms for the switchable ring-contraction reactions



CONCLUSIONS

In summary, two bonuses of the ring-contraction reactions of 2,5-dihydro-1,4,5-thiadiazepine *S*-oxides under thermal or acidic conditions via the extrusion of small molecules highlight the utility of sulfur in synthetic chemistry, wherein sulfur sometimes could be adopted as a traceless linker to promote bond-forming and then disappear without a trace.

EXPERIMENTAL SECTION

General Information. All isolated compounds were characterized on Bruker 400 and JEOL 400 spectrometers in $CDCl_3$. Chemical shifts were reported as δ values relative to internal chloroform (δ 7.26 for ^{1}H NMR and 77.00 for ^{13}C NMR). High-resolution mass spectra (HRMS) were obtained on a 4G mass spectrometer by using electrospray ionization (ESI) analyzed by quadrupole time-of-flight (QTof). All melting points were measured with the samples after column chromatography and uncorrected. Column chromatography was performed on silica gel. Anhydrous THF and PhMe were distilled over sodium benzophenone ketyl under Ar. All other solvents and reagents were used as obtained from commercial sources without further purification.

General Procedure for the Preparation of 2,5-Dihydro-1,4,5-thiadiazepines and Their S-Oxides. Compounds (**1a**−**i**, **4a**, **4b**, **5a**, and **5b**) are all known. They were prepared according to the literature.[5]

General Procedure for the Synthesis of Pyridazine (2). A solution of sulfoxide (**1**, 0.3 mmol) in DMSO (3 mL) was heated at 80 °C (oil bath). After completion as monitored by TLC, the mixture was diluted with H_2O and extracted with Et_2O for three times. The combined organic layers were dried over anhydrous Na_2SO_4. After evaporation of solvent, the residue was purified by silica gel column chromatography to get the corresponding pyridazine **2**.

General Procedure for the Synthesis of Pyrazole (3). To a solution of sulfoxide (**1**, 0.3 mmol) in DCM (3 mL) was added $ZnBr_2$ (0.3 mmol, 1.0 equiv) at room temperature. After completion as monitored by TLC, the solvent was removed *in vacuo* and the crude product was purified by silica gel column chromatography to give the corresponding pyrazole **3**.

Scale-up Experiment for 3a. To a solution of sulfoxide **1a** (2.00 g, 4.73 mmol) in DCM (47 mL) was added $ZnBr_2$ (1.06 g, 4.73 mmol), and the resulting solution was stirred at room temperature for 2 h. After removal of the solvent under reduced pressure, the resulting residue was purified by silica gel column chromatography to give **3a** (1.06 g, 86%) as a yellow oil.

Characterization Data of Compounds 2a−i.

Dimethyl 6-phenylpyridazine-3,4-dicarboxylate. Compound **2a** (64 mg, 78%, R_f = 0.40 (PE:EA = 2:1)) was isolated as a yellow solid; mp 97.1−98.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.17–8.11 (m, 2H), 7.58–7.52 (m, 3H), 4.07 (s, 3H), 4.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.5, 160.6, 149.4, 134.4, 131.2, 129.8, 129.2, 127.4, 122.9, 53.6, 53.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{13}N_2O_4$ 273.0870, Found 273.0869.

Dimethyl 6-(4-methoxyphenyl)pyridazine-3,4-dicarboxylate. Compound **2b** (73 mg, Y = 81%, R_f = 0.65 (PE:EA = 1:1)) was isolated as a yellow solid; mp 102.6−103.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 9.2 Hz, 2H), 8.10 (s, 1H), 7.05 (d, J = 8.8 Hz, 1H), 4.06 (s, 3H), 3.99 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.8, 162.2, 160.0, 148.6, 130.0, 129.0, 126.8, 121.9, 114.6, 55.4, 53.5, 53.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{15}N_2O_5$ 303.0975, Found 303.0975.

Dimethyl 6-(p-tolyl)pyridazine-3,4-dicarboxylate. Compound **2c** (62 mg, Y = 72%, R_f = 0.49 (PE:EA = 2:1)) was isolated as a yellow solid; mp 88.2−89.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.06 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 4.07 (s, 3H), 4.00 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 164.7, 160.5, 149.1, 141.8, 131.7, 130.0, 129.9,

127.3, 122.5, 53.6, 53.5, 21.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{15}N_2O_4$ 287.1026, Found 287.1025.

Dimethyl 6-(4-(trifluoromethyl)phenyl)pyridazine-3,4-dicarboxylate. Compound **2d** (66 mg, Y = 65%, R_f = 0.52 (PE:EA = 2:1)) was isolated as a yellow solid; mp 85.2−86.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.4 Hz, 2H), 8.24 (s, 1H), 7.78 (d, J = 8.4 Hz, 2H), 4.04 (s, 3H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 164.1, 159.3, 150.2, 137.8,132.7 (q, J = 32.6 Hz), 129.7, 127.8, 126.1 (q, J = 3.7 Hz),123.6 (q, J = 270.8 Hz), 123.3, 53.6, 53.5; HRMS (ESI) m/z $[M + Na]^+$ Calcd for $C_{15}H_{11}F_3N_2O_4Na$ 363.0563, Found 363.0562.

Dimethyl 6-(4-fluorophenyl)pyridazine-3,4-dicarboxylate. Compound **2e** (51 mg, Y = 59%, R_f = 0.48 (PE:EA = 2:1)) was isolated as a yellow solid; mp 82.3−82.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18–8.12 (m, 3H), 7.26–7.19 (m, 2H), 4.06 (s, 3H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 164.8 (d, J = 251.1 Hz), 164.4, 159.5, 149.4, 130.6 (d, J = 3.1 Hz), 129.9, 129.5 (d, J = 8.8 Hz), 122.5, 116.4 (d, J = 21.8 Hz), 53.6, 53.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{12}FN_2O_4$ 291.0776, Found 291.0774.

Dimethyl 6-(furan-2-yl)pyridazine-3,4-dicarboxylate. Compound **2f** (45 mg, Y = 57%, R_f = 0.56 (PE:EA = 1:1)) was isolated as a red solid; mp 149.3−149.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.65 (d, J = 1.2 Hz, 1H), 7.48 (d, J = 3.6 Hz, 1H), 6.62 (dd, J = 3.6, 1.6 Hz, 1H), 4.03 (s, 3H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 164.4, 153.2, 149.4, 148.5, 145.8, 130.0, 120.5, 113.1, 113.0, 53.5, 53.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{11}N_2O_5$ 263.0662, Found 263.0661.

Dimethyl 6-(tert-butyl)pyridazine-3,4-dicarboxylate. Compound **2g** (32 mg, Y = 42%, R_f = 0.52 (PE:EA = 2:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 4.04 (s, 3H), 3.97 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 165.3, 164.8, 149.1, 129.2, 122.3, 53.4, 53.3, 37.5, 29.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{17}N_2O_4$ 253.1183, Found 253.1183.

Dimethyl (E)-6-styrylpyridazine-3,4-dicarboxylate. Compound **2h** (61 mg, Y = 68%, R_f = 0.40 (PE:EA = 2:1)) was isolated as a yellow solid; mp 149.3−149.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.80 (d, J = 16.4 Hz, 1H), 7.62 (d, J = 6.8 Hz, 2H), 7.46–7.37 (m, 4H), 4.05 (s, 3H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 164.6, 159.7, 148.8, 138.0, 135.2, 129.8, 129.7, 128.9, 127.7, 123.5, 122.9, 53.5, 53.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{15}N_2O_4$ 299.1026, Found 299.1025.

Diethyl 6-phenylpyridazine-3,4-dicarboxylate. Compound **2i** (67 mg, Y = 74%, R_f = 0.45 (PE:EA = 2:1)) was isolated as a yellow solid; mp 149.3−149.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.17–8.10 (m, 2H), 7.58–7.50 (m, 3H), 4.53 (q, J = 7.2 Hz, 2H), 4.45 (q, J = 7.2 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H), 1.40 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 164.0, 160.5, 150.0, 134.7, 131.1, 129.8, 129.2, 127.4, 122.9, 62.9, 62.7, 14.0, 13.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}N_2O_4$ 301.1183, Found 301.1181.

Characterization Data of Compounds 3a−i.

Dimethyl 3-phenyl-1H-pyrazole-4,5-dicarboxylate. Compound **3a** (72 mg, Y = 92%, R_f = 0.29 (PE:EA = 3:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.51 (m, 2H), 7.37–7.32 (m, 3H), 3.81 (s, 3H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 161.1, 146.6, 141.0, 129.6, 128.7, 128.3, 128.0, 113.1, 52.4, 52.4; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{12}N_2O_4Na$ 283.0689, Found 283.0688.

Dimethyl 3-(4-methoxyphenyl)-1H-pyrazole-4,5-dicarboxylate. Compound **3b** (74 mg, Y = 85%, R_f = 0.33 (PE:EA = 1:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 7.6 Hz, 2H), 6.90 (d, J = 7.6 Hz, 2H), 3.81 (s, 6H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 161.4, 160.7, 146.2, 141.6, 129.5, 120.1, 114.1, 112.4, 55.3, 52.4, 52.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O_5$ 291.0975, Found 291.0973.

Dimethyl 3-(p-tolyl)-1H-pyrazole-4,5-dicarboxylate. Compound **3c** (64 mg, Y = 78%, R_f = 0.23 (PE:EA = 2:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 7.6 Hz, 2H), 3.81 (s, 3H), 3.74 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 161.3, 146.2, 141.4, 139.6, 129.3, 127.8, 125.1, 112.6, 52.3, 52.2, 21.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O_4$ 275.1026, Found 275.1027.

Dimethyl 3-(4-(trifluoromethyl)phenyl)-1H-pyrazole-4,5-dicarboxylate. Compound **3d** (80 mg, Y = 81%, R_f = 0.56 (PE:EA = 2:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ, 7.70 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 8.4 Hz, 2H), 3.84 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 160.4, 146.1, 139.6, 132.3, 131.3 (q, J = 32.5 Hz), 128.3, 125.6 (q, J = 3.7 Hz), 123.8 (q, J = 270.6 Hz), 113.8, 52.6, (1C missing); HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{11}F_3N_2O_4Na$ 351.0563, Found 351.0562.

Dimethyl 3-(4-fluorophenyl)-1H-pyrazole-4,5-dicarboxylate. Compound **3e** (63 mg, Y = 76%, R_f = 0.21 (PE:EA = 2:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.52 (m, 2H), 7.06 (t, J = 8.8 Hz, 2H), 3.82 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 163.4 (d, J = 248.6 Hz), 161.0, 145.7, 140.8, 130.1 (d, J = 8.4 Hz), 124.4 (d, J = 3.1 Hz), 115.8 (d, J = 21.7 Hz), 112.8, 52.4 (2C); HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{11}FN_2O_4Na$ 301.0595, Found 301.0593.

Dimethyl 3-(furan-2-yl)-1H-pyrazole-4,5-dicarboxylate. Compound **3f** (28 mg, Y = 37%, R_f = 0.26 (PE:EA = 2:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 1.2 Hz, 1H), 7.24 (d, J = 3.2 Hz, 1H), 6.53 (dd, J = 3.2, 1.6 Hz, 1H), 3.93 (s, 3H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 161.6, 143.5, 142.9, 142.6, 137.7, 112.6, 112.2, 110.1, 52.6, 52.2; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{10}N_2O_5Na$ 273.0482, Found 273.0481.

Dimethyl 3-(tert-Butyl)-1H-pyrazole-4,5-dicarboxylate. Compound **3g** (56 mg, Y = 78%, R_f = 0.24 (PE:EA = 2:1)) was isolated as a white solid; mp 117−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 3H), 3.88 (s, 3H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 161.7, 153.3, 141.5, 112.7, 52.3, 52.1, 32.4, 29.0; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{16}N_2O_4Na$ 263.1002, Found 263.1001.

(E)-dimethyl 3-styryl-1H-pyrazole-4,5-dicarboxylate. Compound **3h** (54 mg, Y = 63%, R_f = 0.20 (PE:EA = 2:1)) was isolated as a white solid; mp 117.5−118.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.2 Hz, 2H), 7.40–7.28 (m, 5H), 3.93 (s, 3H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 161.7, 145.1, 142.8, 135.6, 134.3, 129.0, 128.7, 127.1, 113.7, 111.5, 52.4, 52.0; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{14}N_2O_4Na$ 309.0846, Found 309.0845.

Diethyl 3-phenyl-1H-pyrazole-4,5-dicarboxylate. Compound **3i** (79 mg, Y = 91%, R_f = 0.30 (PE:EA = 2:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.52 (m, 2H), 7.39–7.33 (m, 3H), 4.29 (q, J = 7.2 Hz, 2H), 4.18 (q, J = 7.2 Hz, 2H), 1.26 (t, J = 7.2 Hz, 3H), 1.18 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 160.7, 146.1, 141.0, 129.3, 128.5, 128.4, 127.9, 113.3, 61.4, 61.3, 13.9 (2C); HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{16}N_2O_4Na$ 311.1002, Found 311.1002.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds (PDF), Crystallographic information for **2a** and **3g** (CIF)

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The authors declare no competing financial interest.

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