Supporting Information For:

**Metallo-Aldehyde Enolates *via* Enal Hydrogenation: Catalytic Cross
Aldolization with Glyoxal Partners as Applied to the Synthesis of 3,5-
Disubstituted Pyridazines**

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Table of Contents:

General Experimental	S2
5-d ₁ -Methyl-3-phenylpyridazine (deuterio-1b)	S3
5-Methyl-3-naphthalen-2-yl-pyridazine 2b	S3
5-Methyl-3-thiophen-2-yl-pyridazine 3b	S4
5-Methyl-3-(1-methyl-1H-pyrrol-2-yl)-pyridazine 4b	S4
5-Ethyl-3-naphthalen-2-yl-pyridazine 6b	S4
¹ H, ¹³ C NMR spectra for compounds 1b , deuterio-1b , 2b , 3b , 4b , 5b , 6b	S6-S10

General.

All reactions were run under an atmosphere of argon, unless otherwise indicated. Anhydrous solvents were transferred by an oven-dried syringe. Flasks were flame-dried and cooled under a stream of argon.

Analytical thin-layer chromatography (TLC) was carried out using 0.2-mm commercial silica gel plates. Preparative column chromatography employing silica gel was performed according to the method of Still.¹ Eluent mixtures are reported as percentages by volume. Infrared spectra are reported in cm^{-1} as strong (s), medium (m), or weak (w). High-resolution mass spectra (HRMS) were obtained from chemical ionization and are reported as m/e (relative intensity). Accurate masses are reported for the molecular ion ($M+1$) or a suitable fragment ion.

All NMR spectra were obtained in CDCl_3 with a 400 MHz (100 MHz ^{13}C) spectrometer. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane or from the center of the triplet at 77.0 ppm for deuteriochloroform. Coupling constants are reported in Hertz (Hz). Multiplicities are reported as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets) or m (multiplet). ^{13}C NMR spectra were routinely run with broadband decoupling.

Noncommercial glyoxals² were made from the selenium dioxide oxidation of the corresponding methyl ketone. The glyoxal was then crystallized from boiling water, and then recrystallized from chloroform. 1,2-Dichloroethane was purified by distillation from CaH_2 . Tetrahydrofuran was purified by distillation from benzophenone ketyl radical.

(1) Still, W. C.; Kahn, M.; Mitra, M. *J. Org. Chem.* **1978**, 43(14), 2923-2925.

(2) (a) Beck, B.; Magnin-Lachaux, M.; Herdtweck, E.; Dömling, A. *Org. Lett.* **2001**, 3(13), 28-25-2878.

(b) Block, M. H.; Harrison, A.; Hargreaves, R. B. *Eur. Pat. Appl.* **1993**, EP 544445. (c) Reed, L. A. *Eur. Pat. Appl.* **1986**, EP 201221.

Ph₃P was crystallized from hexanes. KOAc was flame-dried *in vacuo*. Acrolein was purified by drying over MgSO₄ followed by distillation. Crotonaldehyde was purified by drying over MgSO₄ followed by distillation. Methanol was distilled from Mg/I₂. Compounds **1a** and **2a** are known and fully characterized.³

5-d₁-Methyl-3-phenyl pyridazine (deuterio-1b). The title compound was purified by flash column chromatography using a gradient of 10-30% EtOAc/DCM to yield **1f** as a white solid in 46% yield. Mp 87-88 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.97 (d, *J* = 2.0 Hz, 1H), 8.04 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.63 (m, 1H), 7.48 (m, 3H), 2.38 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 151.6, 136.4, 129.8, 128.9, 127.1 124.2, 18.3 (m). FTIR (neat film): 1596 (m) cm⁻¹. HRMS calcd for C₁₁H₁₀DN₂ (M+1): 172.0985; found 172.0980.

5-Methyl-3-naphthalen-2-yl-pyridazine (2b). The title compound was purified by flash column chromatography using a gradient of 10-30% EtOAc/DCM to yield **1b** as a yellow solid in 59% yield. Mp 137-140 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.96 (d, *J* = 1.7 Hz, 1H), 8.50 (d, *J* = 1.0 Hz, 1H), 8.19 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.92 (m, 1H), 7.86 (m, 1H), 7.72 (m, 1H), 7.51 (m, 2H), 2.38 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 158.5, 151.5, 137.8, 133.9, 133.6, 133.2, 128.6, 128.6, 127.6, 126.9, 126.9, 126.4, 124.2, 124.2, 18.4. FTIR (neat film): 1636 (m) cm⁻¹. HRMS calcd for C₁₅H₁₃N₂ (M+1): 221.1079; found: 221.1083.

(3) South, M. S.; Jakuboski, T. L.; Westmeyer, M. D.; Dukensherer, D. R. *J. Org. Chem.* **1996**, 61(25), 8921-8934.

5-Methyl-3-thiophen-2-yl-pyridazine (3b). The title compound was purified by flash column chromatography using a gradient of 10-30% EtOAc/DCM to yield **1c** as an orange solid in 31% yield. Mp 118-120 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.87 (d, *J* = 1.4 Hz, 1H), 7.65 (dd, *J* = 3.8, 1.0 Hz, 1H), 7.57 (d, *J* = 1.0 Hz, 1H), 7.47 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.14 (dd, *J* = 5.1, 3.8 Hz, 1H), 2.38 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 154.4, 151.4, 140.6, 137.8, 129.0, 128.0, 126.0, 122.4, 18.4. IR (neat film): 1647 (m), 1598 (m), 1445 (w) cm⁻¹. HRMS calcd for C₉H₉N₂S (M+1): 177.0486; found: 177.0489.

5-Methyl-3-(1-methyl-1H-pyrrol-2-yl)-pyridazine (4b). The title compound was purified by flash column chromatography using a gradient of 10-30% EtOAc/DCM to yield **1e** as a yellow oil in 30% yield. ¹H NMR (CDCl₃, 400 MHz): δ 8.81-8.80 (d, *J* = 2.1 Hz, 1H), 7.48-7.47 (q, *J* = 0.91 Hz, 1H), 6.80-6.79 (m, 1H), 6.65-6.63 (m, 1H), 6.22-6.21 (dd, *J* = 2.4, 1.4 Hz, 1H), 4.09 (s, 3H), 2.35 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ 154.1, 150.0, 137.2, 128.9, 127.8, 124.4, 112.0, 108.0, 37.8, 18.3. FTIR (neat film): 2957 (m), 1601 (s) cm⁻¹. HRMS calcd for C₁₀H₁₂N₃ (M+1): 174.1031; found: 174.1032.

5-Ethyl-3-naphthalen-2-yl-pyridazine (6b). The reaction mixture was purified by flash column chromatography using a gradient of 10-30% EtOAc/DCM to yield **2b** a yellow solid in 50% yield. Mp 102-104 °C. ¹H NMR (CDCl₃, 400 MHz): δ 9.03 (s, 1H), 8.53 (s, 1H), 8.23-8.21 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.98-7.94 (m, 2H), 7.88-7.87 (d, *J* = 5.1 Hz, 1H), 7.78 (s, 1H), 7.54-7.52 (m, 2H), 2.77-2.71 (q, *J* = 7.6 Hz, 2H), 1.37-1.33 (t, *J* = 7.7 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ 158.8, 150.8, 143.4, 133.9, 133.7, 133.2, 128.7,

128.6, 127.6, 126.9, 126.8, 126.4, 124.2, 122.9, 25.8, 13.7. FTIR (neat film): 2970 (w),
1642 (m) cm^{-1} . HRMS calcd for $\text{C}_{16}\text{H}_{15}\text{N}_2$ (M+1): 235.1235; found: 235.1227.

^1H , ^{13}C NMR spectra for compounds **deuterio-1b**, **2b**, **3b**, **4b**, **6b**.

5-d₁-Methyl-3-phenyl pyridazine (deuterio-1b)

5-Methyl-3-naphthalen-2-yl-pyridazine (2b)

5-Methyl-3-thiophen-2-yl-pyridazine (3b)

5-Methyl-3-(1-methyl-1H-pyrrol-2-yl)-pyridazine (4b)

5-Ethyl-3-naphthalen-2-yl-pyridazine (6b)