Supporting Information for

Base-Promoted Cascade Reaction of Isocyanides, Selenium and Amines: A Practical Approach to 2-aminobenzo[d][1,3]selenazines Under Metal-free Conditions

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I. General Information

All reagents were purchased without further purification unless otherwise noted. Reactions were monitored using thin-layer chromatography (TLC). Visualization of the developed plates was performed under UV light (254 nm). Flash column chromatography was performed on silica gel (300-400 mesh). $^1$H and $^{13}$C NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts (δ) were reported in ppm referenced to an internal tetramethylsilane standard or the CDCl$_3$ residual peak (δ 7.26) for $^1$H NMR. Chemical shifts of $^{13}$C NMR are reported relative to CDCl$_3$ (δ 77.16). The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants, J, were reported in Hertz unit (Hz). High resolution mass spectra (HRMS) were obtained on an ESI-MS Spectrometer.

II. Synthesis of Substrates

1. General Procedure for the Synthesis of Isonitriles

Isocyanides were prepared according to the literatures with minor modifications. A representative procedure (synthesis of 1a) is shown below.

**Mizoroki-Heck reaction of 2-iodoanilines.** An Ar-purged 100 mL three-necked flask was charged with tri-o-tolyl phosphine (457 mg, 1.5 mmol), palladium (II) acetate (168 mg, 0.75 mmol), 2-iodoaniline (2.85 g, 13 mmol), methyl acrylate (1.62 mL, 18 mmol), NEt$_3$ (2.29 mL, 16.5 mmol) and CH$_3$CN (60 mL). The system was immersed in an oil bath at reflux. After 24 h, it was removed from the oil bath, diluted with EtOAc (180 mL) and extracted with water (2 x 60 mL) and brine (60 mL). The organic layer was dried over Na$_2$SO$_4$ and volatiles were removed in vacuo. The residue was subjected to column chromatography on silica-gel (eluent : PE/EtOAc = 5/1) to give 3-(2-aminophenyl) acrylic acid methyl ester as a white solid.

**N-Formylation of 2-alkenylanilines.** Acetyl formyl anhydride (prepared by stirring 1 equiv of acetic anhydride and 1.1 equiv of formic acid for 2 h at 55 °C; 5.45mL, 6.11 g, 40 mmol) was added dropwise at 0 °C to a stirred solution of 3-(2-aminophenyl)acrylic acid methyl ester (1.77g, 10 mmol), in THF (20 mL), and the mixture was stirred for 2 h at room temperature. Volatiles were removed in vacuo to give 3-(2-formamidophenyl)acrylic acid methyl ester as a white solid.
Dehydration of formanilides. A THF solution (60 mL) of 3-(2-formamidophenyl)acrylic acid methyl ester (2.05 g, 10 mmol) and NEt₃ (4.80 mL, 30 mmol) was cooled at 0 °C, then POCl₃ (1.27 mL, 12 mmol) was added dropwise. After the reaction was completed, an aqueous saturated Na₂CO₃ solution was added at 0 °C to quench the reaction and the mixture was extracted with CHCl₃. The residue was subjected to column chromatography on silica-gel (eluent : PE/EtOAc = 10/1) to give 3-(2-isocyanophenyl)acrylic acid methyl ester 1a as a white solid.

III . General Procedure and Product Characterization

1. General Procedure for the Formation of 2-aminobenzo[d][1,3]-selenazines

A representative procedure (synthesis of 4a) is shown below.

In a 10 mL round-bottom flask, 3-(2-isocyanophenyl)acrylic acid methyl ester 1a (0.3 mmol, 1 equiv), elemental selenium 2 (0.45 mmol, 1.5 equiv), piperidine 3a (0.45 mmol, 1.5 equiv) were dissolved in 2 mL DCE followed by addition of Et₃N (0.45 mmol, 1.5 equiv). The system was stirred in an oil bath at 25 °C. After 12h, it was removed from the oil bath. The reaction mixture was charged with silica gel and concentrated. The residue was purified by silica gel column chromatography (eluent : PE/EtOAc = 30 : 1) to obtain the desired product 4a as a light yellow oil.

2. Product Characterization

![Chemical Structure of Methyl 2-(2-(piperidin-1-yl)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4a)](image)

Methyl 2-(2-(piperidin-1-yl)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4a)

**Yield:** 90%. Light yellow oil. **IR:** \( \nu_{\text{max}} \) (cm\(^{-1}\)) = 2933, 2851, 1736, 1602, 1550, 1257, 1224, 1122, 758.

**\(^1\)H NMR** (400 MHz, Chloroform-\(d\)) \( \delta \) 7.24 – 7.16 (m, 1H), 7.11 (dd, \( J = 10.8, 8.5 \) Hz, 2H), 6.98 (t, \( J = 7.4 \) Hz, 1H), 4.51 (dd, \( J = 8.5, 7.0 \) Hz, 1H), 3.78 – 3.68 (m, 4H), 3.64 (s, 3H), 2.92 – 2.79 (m, 2H), 1.63 (ddt, \( J = 26.7, 10.6, 5.2 \) Hz, 6H). **\(^13\)C NMR** (100 MHz, Chloroform-\(d\)) \( \delta \) 171.20, 150.82, 146.83, 128.18, 125.67, 125.49, 122.99, 122.00, 77.48, 77.16, 76.84, 51.63, 48.68, 41.91, 35.59, 25.96, 25.08. **HRMS** (ESI⁺, MeCN): found, 353.0765 [M + H]⁺, calcd for C₁₆H₂₁N₂O₂Se, 353.0768.

S3
Methyl 2-(diethylamino)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4b)

**Yield:** 98%. Light yellow oil. **IR:** $\nu_{\text{max}}$ (cm$^{-1}$) = 3061, 3028, 2978, 2904, 1730, 1603, 1546, 1411, 1372, 1189, 759, 697. **$^1$H NMR** (400 MHz, Chloroform-$d$) $\delta$ 7.26 – 7.07 (m, 3H), 6.98 (td, $J = 7.3, 1.4$ Hz, 1H), 4.51 (dd, $J = 8.7, 6.9$ Hz, 1H), 3.73 – 3.52 (m, 7H), 2.93 – 2.79 (m, 2H), 1.22 (t, $J = 7.1$ Hz, 6H). **$^{13}$C NMR** (100 MHz, Chloroform-$d$) $\delta$ 171.43, 149.56, 147.19, 128.32, 125.75, 125.52, 122.73, 122.04, 77.48, 77.16, 76.84, 51.76, 44.35, 41.85, 35.69, 14.33. **HRMS** (ESI$^+$, MeCN): found, 341.0765 [M + H]$^+$, calcd for C$_{15}$H$_{21}$N$_2$O$_2$Se, 341.0768.

Methyl 2-(diisopropylamino)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4c)

**Yield:** 95%. White solid. **Mp:** 53.4 – 54.2 oC. **IR:** $\nu_{\text{max}}$ (cm$^{-1}$) = 3004, 2968, 2952, 2923, 2853, 1742, 1549, 1474, 128.17, 125.64, 125.25, 122.62, 122.13, 77.48, 77.16, 76.84, 51.76, 44.35, 41.85, 35.69, 14.33. **HRMS** (ESI$^+$, MeCN): found, 369.1084 [M + H]$^+$, calcd for C$_{17}$H$_{25}$N$_2$O$_2$Se, 369.1081.

Methyl 2-(pyrrolidin-1-yl)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4d)

**Yield:** 85%. Orange solid. **Mp:** 83.7-84.7 oC. **IR:** $\nu_{\text{max}}$ (cm$^{-1}$) = 3065, 2946, 2867, 1728, 1553, 1474, 1357, 1214, 1169, 764, 736. **$^1$H NMR** (400 MHz, Chloroform-$d$) $\delta$ 7.19 (td, $J = 7.6, 1.6$ Hz, 1H), 7.11 (dd, $J = 7.6, 1.5$ Hz, 2H), 6.96 (td, $J = 7.3, 1.5$ Hz, 1H), 4.46 (t, $J = 7.7$ Hz, 1H), 3.71 (dd, $J = 10.3, 5.8$ Hz, 2H), 3.66 (s, 3H), 3.54 (d, $J = 9.3$ Hz, 2H), 2.90 (d, $J = 7.7$ Hz, 2H), 1.95 (td, $J = 7.9, 6.7, 4.6$ Hz, 4H). **$^{13}$C NMR** (100 MHz, CDCl$_3$) $\delta$ 171.45, 148.82, 147.07, 128.46, 126.01, 125.60, 122.80, 121.74,
Methyl 2-(2-(3,4-dihydroisoquinolin-2(1H)-yl)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4e)
¹H NMR (400 MHz, Chloroform-d) δ 7.26–7.12 (m, 7H), 7.03 (td, J = 7.3, 1.5 Hz, 1H), 5.10 (d, J = 16.7 Hz, 1H), 4.87 (d, J = 16.7 Hz, 1H), 4.55 (p, J = 8.1 Hz, 1H), 3.99 (t, J = 5.9 Hz, 2H), 3.65 (s, 3H), 2.98–2.83 (m, 4H).
¹³C NMR (100 MHz, CDCl₃) δ 171.36, 151.13, 146.67, 134.93, 133.61, 128.69, 128.46, 126.63, 126.40, 125.89, 125.76, 123.44, 122.14, 77.51, 77.19, 76.87, 51.82, 49.09, 45.44, 42.03, 35.93, 29.36. HRMS (ESI⁺, MeCN): found, 339.0626 [M + H]⁺, calcd for C₁₅H₂₁N₂O₂Se, 339.0612.

Methyl 2-(2-(methyl(phenyl)amino)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4f)
Yield: 92%. White solid. Mp: 127.5-128.4 °C. IR : νₘₐₓ (cm⁻¹) = 2980, 1736, 1605, 1555, 1492, 1230, 758, 701. ¹H NMR (400 MHz, Chloroform-d) δ 7.43–7.26 (m, 4H), 7.25–7.14 (m, 5H), 7.04 (dd, J = 7.5, 6.1, 2.6 Hz, 1H), 4.41 (dd, J = 8.7, 7.0 Hz, 1H), 3.62 (s, 3H), 3.60 (s, 3H), 2.89–2.77 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 171.36, 150.51, 146.67, 144.92, 129.31, 128.40, 125.89, 125.76, 123.44, 122.14, 77.51, 77.19, 76.87, 51.82, 49.09, 45.44, 42.03, 35.93, 29.36. HRMS (ESI⁺, MeCN): found, 375.0671 [M + H]⁺, calcd for C₂₀H₂₁N₂O₂Se, 375.0668.

Methyl 2-(2-(3,4-dihydroquinolin-1(2H)-yl)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4g)
Yield: 90%. Light brown solid. Mp: 111.0-111.9 °C. IR : νₘₐₓ (cm⁻¹) = 2943, 2887, 1736, 1536, 1205, 1164, 760, 743. ¹H NMR (400 MHz, Chloroform-d) δ 7.41–7.17 (m, 7H), 7.12 (d, J = 7.6 Hz, 1H), 4.66
– 4.56 (m, 1H), 4.51 (dd, \( J = 12.6, 8.1, 5.9 \) Hz, 1H), 4.10 (dt, \( J = 12.2, 5.8 \) Hz, 1H), 3.66 (s, 3H), 2.96 – 2.76 (m, 4H), 2.25 (dq, \( J = 12.4, 6.0 \) Hz, 1H), 2.04 (dd, \( J = 16.1, 8.2, 4.2 \) Hz, 1H). \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \( \delta 171.15, 148.74, 145.78, 139.48, 132.27, 128.41, 128.24, 126.03, 125.94, 125.83, 124.67, 124.08, 123.67, 123.34, 77.48, 77.16, 76.84, 51.70, 47.77, 41.96, 35.99, 27.41, 24.28. HRMS (ESI\(^+\), MeCN): found, 401.0771 \([M + H]^+\), calcd for C\(_{20}\)H\(_{21}\)N\(_2\)O\(_2\)Se, 401.0768.

**Ethyl 2-(2-(benzyl(methyl)amino)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4h)**

Yield: 98%. Light yellow oil. IR: \( \nu_{\text{max}} \) (cm\(^{-1}\)) = 3061, 3028, 2978, 2904, 1730, 1603, 1546, 1478, 1372, 1189, 759, 732, 697. \(^1H\) NMR (400 MHz, Chloroform-\( d \)) \( \delta 7.39 – 7.26 \) (m, 5H), 7.26 – 7.16 (m, 3H), 7.03 (td, \( J = 7.3, 1.4 \) Hz, 1H), 4.86 (s, 2H), 4.63 – 4.51 (m, 1H), 4.14 (q, \( J = 7.1 \) Hz, 2H), 2.96 – 2.85 (m, 2H), 1.23 (t, \( J = 7.1 \) Hz, 3H). \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \( \delta 170.86, 151.69, 146.99, 137.62, 128.68, 128.39, 127.38, 125.89, 125.74, 123.21, 122.00, 77.48, 77.16, 76.84, 60.74, 55.00, 42.26, 37.02, 36.15, 14.27. HRMS (ESI\(^+\), MeCN): found, 403.0929 \([M + H]^+\), calcd for C\(_{20}\)H\(_{23}\)N\(_2\)O\(_2\)Se, 403.0925.

**Ethyl 2-(2-(diethylamino)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4i)**

Yield: 92%. Light yellow oil. IR: \( \nu_{\text{max}} \) (cm\(^{-1}\)) = 3061, 3028, 2978, 2904, 1730, 1603, 1546, 1478, 1372, 1189, 759, 732, 697. \(^1H\) NMR (400 MHz, Chloroform-\( d \)) \( \delta 7.24 – 7.08 \) (m, 3H), 6.97 (td, \( J = 7.4, 1.4 \) Hz, 1H), 4.51 (dd, \( J = 8.7, 6.9 \) Hz, 1H), 4.14 (qd, \( J = 7.1, 3.2 \) Hz, 2H), 3.62 (tp, \( J = 14.2, 7.1 \) Hz, 4H), 2.90 – 2.78 (m, 2H), 1.23 (td, \( J = 7.1, 3.4 \) Hz, 9H). \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \( \delta 171.00, 149.60, 147.24, 128.29, 125.81, 125.52, 122.70, 122.14, 77.48, 77.16, 76.84, 60.70, 44.35, 42.07, 35.78, 14.35, 14.28. HRMS (ESI\(^+\), MeCN): found, 355.0926 \([M + H]^+\), calcd for C\(_{16}\)H\(_{23}\)N\(_2\)O\(_2\)Se, 355.0925.

**Ethyl 2-(2-(dipropylamino)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4j)**
Yield: 94%. Light yellow oil. IR: $\nu_{max}$ (cm$^{-1}$) = 2961, 2931, 2873, 1732, 1603, 1551, 1368, 1214, 1122, 757. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.23 – 7.08 (m, 3H), 6.97 (t, $J$ = 7.4 Hz, 1H), 4.51 (dd, $J$ = 8.8, 6.8 Hz, 1H), 4.14 (qq, $J$ = 7.3, 3.7 Hz, 2H), 3.53 (ddddd, $J$ = 43.2, 14.3, 8.9, 5.8 Hz, 4H), 2.83 (dd, $J$ = 7.8, 4.9 Hz, 2H), 1.76 – 1.58 (m, 4H), 1.23 (t, $J$ = 7.2 Hz, 3H), 0.94 (t, $J$ = 7.4 Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.00, 150.13, 147.19, 128.25, 125.77, 125.48, 122.66, 122.18, 77.48, 77.16, 76.84, 60.67, 51.87, 42.03, 35.88, 14.26, 11.38. HRMS (ESI$^+$, MeCN): found, 383.1240 [M + H]$^+$, calcd for C$_{18}$H$_{27}$N$_2$O$_2$Se, 383.1238.

Ethyl 2-(2-(dibutylamino)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4k)
Yield: 90%. Light yellow oil. IR: $\nu_{max}$ (cm$^{-1}$) = 2957, 2930, 2871, 1733, 1603, 1552, 1479, 1369, 1203, 1189, 1124, 1108, 757. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.25 – 7.01 (m, 3H), 7.01 – 6.92 (m, 1H), 4.51 (dd, $J$ = 8.7, 6.8 Hz, 1H), 4.14 (q, $J$ = 7.3 Hz, 2H), 3.76 – 3.35 (m, 4H), 2.91 – 2.73 (m, 2H), 1.73 – 1.53 (m, 4H), 1.36 (h, $J$ = 7.4 Hz, 4H), 1.24 (t, $J$ = 7.1 Hz, 3H), 0.97 (t, $J$ = 7.4 Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.02, 150.13, 147.19, 128.25, 125.77, 125.48, 122.66, 122.15, 77.48, 77.16, 76.84, 60.67, 51.87, 42.03, 35.88, 14.26, 11.38. HRMS (ESI$^+$, MeCN): found, 411.1553 [M + H]$^+$, calcd for C$_{20}$H$_{31}$N$_2$O$_2$Se, 411.1551.

Methyl 2-(7-chloro-2-(diethylamino)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4l)
Yield: 88%. Colorless oil. IR: $\nu_{max}$ (cm$^{-1}$) = 2971, 2931, 1736, 1542, 1461, 1357, 1227, 1118, 844, 686. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.14 – 7.01 (m, 2H), 6.92 (dd, $J$ = 8.1, 2.3 Hz, 1H), 4.47 (t, $J$ = 7.8 Hz, 1H), 3.69 – 3.51 (m, 7H), 2.86 – 2.76 (m, 2H), 1.21 (t, $J$ = 7.1 Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.24, 150.05, 147.24, 128.26, 125.79, 125.50, 122.64, 122.15, 77.48, 77.16, 76.84, 60.68, 49.86, 42.08, 35.86, 31.12, 20.20, 14.28, 14.02. HRMS (ESI$^+$, MeCN): found, 401.0390 [M + H]$^+$, calcd for C$_{15}$H$_{29}$N$_2$O$_2$SeCl, 415.0379.
Methyl 2-(7-chloro-2-morpholino-4H-benzo[d][1,3]selenazin-4-yl)acetate (4m)

**Yield:** 68%. White solid. **Mp:** 85.3-86.1 °C. **IR:** ν\text{max} (cm\textsuperscript{-1}) = 2956, 2898, 2858, 1729, 1547, 1208, 1145, 1023, 874, 805. **\textsuperscript{1}H NMR** (400 MHz, Chloroform-d) δ 7.13 – 7.03 (m, 2H), 6.97 (dd, J = 8.1, 2.2 Hz, 1H), 4.50 (p, J = 7.7 Hz, 1H), 3.82 – 3.70 (m, 8H), 3.65 (s, 3H), 2.82 (dd, J = 7.7, 1.8 Hz, 2H). **\textsuperscript{13}C NMR** (100 MHz, CDCl\textsubscript{3}) δ 171.02, 152.65, 147.63, 133.72, 126.96, 125.55, 123.46, 120.55, 77.48, 77.16, 76.84, 66.77, 51.95, 48.11, 42.00, 35.24. **HRMS** (ESI\textsuperscript{+}, MeCN): found, 389.0179 [M + H]\textsuperscript{+}, calcd for C\textsubscript{15}H\textsubscript{18}N\textsubscript{2}O\textsubscript{3}SeCl, 389.0171.

Methyl 2-(2-(diethylamino)-6-fluoro-4H-benzo[d][1,3]selenazin-4-yl)acetate (4n)

**Yield:** 94%. Orange-yellow oil. **IR:** ν\text{max} (cm\textsuperscript{-1}) = 2971, 2932, 2871, 1736, 1611, 1559, 1484, 1230, 1117, 862, 821, 766. **\textsuperscript{1}H NMR** (400 MHz, Chloroform-d) δ 7.03 (dd, J = 8.6, 5.5 Hz, 1H), 6.89 (ddd, J = 17.2, 8.6, 2.9 Hz, 2H), 4.43 (dd, J = 8.5, 7.0 Hz, 1H), 3.67 (s, 3H), 3.59 (dq, J = 24.4, 7.1 Hz, 4H), 2.89 – 2.77 (m, 2H), 1.20 (t, J = 7.1 Hz, 6H). **\textsuperscript{13}C NMR** (100 MHz, CDCl\textsubscript{3}) δ 171.02, 159.64, 157.23, 149.24, 143.57, 143.55, 126.73, 126.66, 123.30, 122.31, 115.09, 114.88, 112.37, 112.14, 77.48, 77.16, 76.84, 51.86, 44.38, 41.51, 35.25, 14.33. **HRMS** (ESI\textsuperscript{+}, MeCN): found, 401.0675 [M + H]\textsuperscript{+}, calcd for C\textsubscript{15}H\textsubscript{20}N\textsubscript{2}O\textsubscript{2}SeF, 359.0674.

Methyl 2-(2-(diethylamino)-6-(trifluoromethyl)-4H-benzo[d][1,3]selenazin-4-yl)acetate (4o)

**Yield:** 80%. Light yellow solid. **Mp:** 49.5-50.3 °C. **IR:** ν\text{max} (cm\textsuperscript{-1}) = 2971, 2933, 1741, 1533, 1327, 1301, 1231, 1163, 1101, 1067, 836. **\textsuperscript{1}H NMR** (400 MHz, Chloroform-d) δ 7.43 (dd, J = 10.3, 2.2 Hz, 2H), 7.15 (d, J = 8.2 Hz, 1H), 4.58 – 4.47 (m, 1H), 3.67 (s, 3H), 3.58 (dq, J = 13.8, 6.8 Hz, 4H), 2.90 – 2.79 (m, 2H), 1.23 (t, J = 7.1 Hz, 6H). **\textsuperscript{13}C NMR** (100 MHz, CDCl\textsubscript{3}) δ 171.06, 151.20, 150.31, 125.72, 125.30, 125.26, 125.22, 125.19, 124.20, 123.88, 123.22, 123.18, 123.15, 123.11, 122.13, 77.48, 77.16,
Methyl 2-(2-(diethylamino)-6-methyl-4H-benzo[d][1,3]selenazin-4-yl)acetate (4p)

**Yield:** 95%. Light yellow oil. **IR:** $\nu$ max (cm$^{-1}$) = 2968, 2931, 1736, 1557, 1491, 1232, 1114, 821, 767.

**$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.05–6.93 (m, 3H), 4.46 (dd, $J = 8.8, 6.7$ Hz, 1H), 3.70–3.52 (m, 7H), 2.85 (dd, $J = 7.8, 3.1$ Hz, 2H), 2.30 (s, 3H), 1.22 (t, $J = 7.1$ Hz, 6H).

**$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.43, 148.91, 144.78, 132.11, 128.98, 126.19, 125.37, 121.77, 77.48, 77.16, 76.84, 51.69, 44.23, 41.87, 35.74, 20.84, 14.29. **HRMS (ESI$^+$, MeCN): found, 355.0934 [M + H]$^+$, calcd for C$_{16}$H$_{23}$N$_2$O$_2$Se, 355.0925.

2-(2-(diethylamino)-4H-benzo[d][1,3]selenazin-4-yl)-1-phenylethan-1-one (4q)

**Yield:** 94%. Yellow oil. **IR:** $\nu$ max (cm$^{-1}$) = 2969, 2929, 1682, 1599, 1547, 1357, 1231, 1116, 756, 689.

**$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.91–7.84 (m, 2H), 7.54 (t, $J = 7.4$ Hz, 1H), 7.42 (t, $J = 7.6$ Hz, 2H), 7.25–7.14 (m, 3H), 6.99 (td, $J = 7.4, 1.5$ Hz, 1H), 4.78 (dd, $J = 9.4, 5.1$ Hz, 1H), 3.68 (tt, $J = 14.2, 8.3$ Hz, 3H), 3.52 (dq, $J = 14.1, 7.0$ Hz, 2H), 3.37 (dd, $J = 17.3, 5.1$ Hz, 1H), 1.19 (t, $J = 7.1$ Hz, 6H).

**$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 197.67, 150.50, 147.43, 136.93, 133.29, 128.61, 128.20, 128.14, 125.50, 125.40, 122.87, 122.67, 77.48, 77.16, 76.84, 45.12, 44.16, 34.95, 14.36. **HRMS (ESI$^+$, MeCN): found, 387.0983 [M + H]$^+$, calcd for C$_{20}$H$_{23}$N$_2$OSe, 387.0976.
methyl 2-((S)-2-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-4H-benzo[d][1,3]selenazin-4-yl) acetate  (4t)

**Yield:** 66%. White solid. **Mp:** 48.7-50.1 °C. **IR:** ν max (cm⁻¹) = 3058, 3023, 2950, 2920, 2849, 1734, 1542, 1480, 1363, 1224, 755, 700. **¹H NMR** (400 MHz, Chloroform-d) δ 8.77 (s, 1H), 7.43 (t, J = 9.5 Hz, 4H), 7.31 (dd, J = 16.2, 8.4 Hz, 6H), 7.18 – 7.06 (m, 3H), 6.97 (t, J = 7.3 Hz, 1H), 5.30 (dd, J = 8.9, 5.0 Hz, 1H), 4.38 (t, J = 7.7 Hz, 1H), 4.38 (s, 3H), 3.38 (q, J = 8.0 Hz, 1H) 3.24 (td, J = 8.8, 5.9 Hz, 1H), 2.81 – 2.69 (m, 2H), 2.19 – 2.03 (m, 2H), 1.48 (hept, J = 8.0 Hz, 1H), 0.93 (dq, J = 13.6, 7.4 Hz, 1H). **¹³C NMR** (100 MHz, CDCl₃) δ 171.37, 146.85, 143.96, 128.59, 128.23, 127.97, 127.81, 127.36, 127.13, 126.01, 124.94, 123.66, 122.42, 81.65, 51.82, 50.75, 41.97, 35.79, 31.17, 22.09. **HRMS** (ESI⁺, MeCN): found, 521.1336 [M + H]⁺, calcd for C₂₈H₂₉N₂O₃Se, 521.1343.

methyl 2-((R)-2-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-4H-benzo[d][1,3]selenazin-4-yl) acetate (4t’)

**Yield:** 25%. White solid. **Mp:** 162.1–163.3 °C. **IR:** ν max (cm⁻¹) = 3061, 3032, 2960, 2851, 1724, 1539, 1481, 1371, 1222, 767, 704. **¹H NMR** (400 MHz, Chloroform-d) δ 8.92 (s, 1H), 7.48 – 7.40 (m, 4H), 7.38 – 7.29 (m, 3H), 7.26 – 7.19 (m, 5H), 7.14 (d, J = 7.1 Hz, 1H), 7.03 (dt, J = 7.6, 4.2 Hz, 1H), 5.63 (dd, J = 8.9, 4.5 Hz, 1H), 4.52 (dd, J = 9.1, 6.3 Hz, 1H), 3.67 (s, 3H), 2.92 – 2.79 (m, 2H), 2.75 (ddd, J = 9.9, 8.0, 5.9 Hz, 1H), 2.23 (dq, J = 13.3, 8.5 Hz, 1H), 2.08 (ddt, J = 13.3, 8.1, 5.1 Hz, 1H), 1.73 – 1.40 (m, 2H), 1.00 – 0.91 (m, 1H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.58, 146.19, 143.96, 128.59, 128.23, 127.97, 127.81, 127.36, 127.13, 126.01, 124.94, 123.66, 122.42, 81.65, 51.82, 50.75, 41.97, 35.79, 31.17, 22.09. **HRMS** (ESI⁺, MeCN): found, 521.1344 [M + H]⁺, calcd for C₂₈H₂₉N₂O₃Se, 521.1343.

**IV. Computational studies**

![S (4t)](image1)

![R (4t’)](image2)
Computational studies at the B3LYP/6-311++G(d,p)/B3LYP/6-31G(d,p) level of theory indicate that the $S$ configuration (4t) is 3.3 kcal/mol lower in energy than the $R$ configuration (4t'). Thus, the $S$ configuration (4t) is more likely to be the major product. Structural inspection shows that the methylene group is present in an axial position for the $S$ configuration and in an equatorial position for the $R$ configuration, respectively. Therefore, the $S$ configuration is preferred due to the less steric effect between the methylene group and the ortho-C-H bond.

V. References
