Supporting Information:

Diversity-Oriented Synthesis of Acyclic Nucleosides via Ring-Opening of Vinyl Cyclopropanes with Purines

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1. General information:

All reactions were carried out in oven-dried Schlenk tube filled nitrogen, and monitored by thin layer chromatography (TLC). All reagents were reagent grade quality and purchased from commercial sources unless otherwise indicated. Anhydrous dioxane was freshly distilled from sodium/ benzophenone before used. NMR spectra were recorded with a 400 MHz spectrometer for $^1$H NMR, 100 MHz for $^{13}$C NMR. Chemical shifts $\delta$ are given in ppm relative to tetramethylsilane as internal standard. Multiplicities are reported as follows: singlet(s), doublet(d), doublet of doublets(dd), triplet(t), quartet(q), multiplet(m). High resolution mass spectra were taken with a 3000 mass spectrometer, using Waters Q-TofMS/MS system. For column chromatography silica gel (200-300 mesh) was used as the stationary phase. 1c$^1$, 1d-f$^2$, 1g-h$^3$, 1m$^4$, 2a-e$^5$ were synthesized following reported methods.

2. General procedure for the 1,5-ring-opening reaction of Pd$_2$(dba)$_3$·CHCl$_3$:

![Scheme S1](image)

Scheme S1 General procedure for the 1,5-ring-opening reaction of Pd$_2$(dba)$_3$·CHCl$_3$.

To an oven-dried Schlenk tube equipped with a magnetic stir bar, was added 2-vinylcyclopropane-1,1-dicarboxylic acid diethyl ester 2a (0.1 mmol, 21.2 mg), 6-chloropurine 1a (0.15 mmol, 23.2 mg), Pd$_2$(dba)$_3$·CHCl$_3$ (5.2 mg, 5 mol%), DIOP (5.0 mg, 10 mol%). The Schlenk tube sealed with threaded stopper was evacuated and backfilled with N$_2$ (this process was repeated for 3 times), and then dioxane (2.0 mL) were added via syringe. The mixture stirred at 30 $^\circ$C for 18 h, it was then filtered through Celite and concentrated under vacuum. The resulted residue was purified by flash chromatography over silica gel (ethyl acetate / petroleum ether) to give the desired product 3aa (82 %).

3. General procedure for the 1,3-ring-opening reaction of AlCl$_3$:
General procedure for the 1,3-ring-opening reaction of AlCl₃.

To an oven-dried Schlenk tube equipped with a magnetic stir bar, was added 2-vinylcyclopropane-1,1-dicarboxylic acid diethyl ester 2a (0.3 mmol, 63.6 mg), 6-chloropurine 1a (0.1 mmol, 15.5 mg), AlCl₃ (0.1 mmol, 13.4 mg). The Schlenk tube sealed with threaded stopper was evacuated and backfilled with N₂ (this process was repeated for 3 times), and then dioxane (2.0 mL) were added via syringe. The mixture stirred at 85 °C for 18 h, it was then filtered through Celite and the organic phase was washed with cooled water. The organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The resulted residue was purified by flash chromatography over silica gel (ethyl acetate / petroleum ether) to give the desired product 5aa (79 %).

General procedure for the 1,3-ring-opening reaction of MgI₂:

To an oven-dried Schlenk tube equipped with a magnetic stir bar, was added 2-vinylcyclopropane-1,1-dicarboxylic acid diethyl ester 2a (0.5 mmol, 106.1 mg), 6-chloropurine 1a (0.1 mmol, 15.5 mg), MgI₂ (2.8 mg, 10 mol%). The Schlenk tube sealed with threaded stopper was evacuated and backfilled with N₂ (this process was repeated for 3 times), and then dioxane (2.0 mL) were added via syringe. The mixture stirred at 85 °C for 18 h, it was then filtered through Celite and the organic phase was washed with cooled water. The organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The resulted residue was purified by flash chromatography over silica gel (ethyl acetate / petroleum ether) to give the desired product 6aa (72 %).

Hydrogenation of adduct 3aa and 5aa.

Hydrogenation of adduct 3aa.
To a solution of acyclic nucleoside analogue 3aa (110.0 mg, 0.3 mmol) in MeOH (10.0 mL) at 0 °C, NaBH₄ (68.0 mg, 1.8 mmol) was added. After 3aa was consumed (determined by TLC), saturated NH₄Cl aq. (10.0 mL) was added. The aqueous phase was extracted with CH₂Cl₂ (10.0 mL×3) and the combined organic phases were dried and concentrated. The residue was purified by silica gel flash chromatography (CH₂Cl₂/MeOH) to afford product 7aa (53 %).

Scheme S5 Hydrogenation of adduct 5aa.

To a solution of acyclic nucleoside analogue 5aa (110.0 mg, 0.3 mmol) in MeOH (10.0 mL) at 0 °C, NaBH₄ (68.0 mg, 1.8 mmol) was added. After 5aa was consumed (determined by TLC), saturated NH₄Cl aq. (10.0 mL) was added. The aqueous phase was extracted with CH₂Cl₂ (10.0 mL×3) and the combined organic phases were dried and concentrated. The residue was purified by silica gel flash chromatography (CH₂Cl₂/MeOH) to afford product 8aa (47 %).

6. Proposed mechanism for Pd-catalyzed ring-opening reaction

A possible catalytic cycle for the palladium-catalyzed 1,5-ring-opening of vinyl cyclopropane 2a with 6-chloro-purine 1a was shown in Scheme S6. Initially, palladium (0) coordinated with the vinyl cyclopropane 2a to generate the zwitterionic π-allylpalladium complex A by cleavage of the three-membered ring. Subsequently, the proton transfer from the 6-chloro-purine 1a to intermediate A afforded nucleophilic anions C and D. The anion C attacked the less substituted carbon of the π-allyl moiety in intermediate B will produce the 1,5-ring-opening N9-adduct 3aa. Meanwhile, the nucleophilic addition between anion D with less substituted carbon of intermediate B will generate 1,5-ring-opening N7 adduct 4aa. If the anions C or D attacked the more substituted carbon of the intermediate B, the 1,3-ring-opening N9 adduct 5aa and N7 adduct 6aa will be obtained, respectively.
7. Control experiment and proposed mechanism for Al-catalyzed ring-opening reaction

The control experiment with 6-nitro-benzoimidazole 1s as a nucleophile was carried out in the presence of AlCl₃, and the 1,3-ring-opening products were afforded in 82% total yield, in which the ratio of the N1 to N3 adducts was 45:37 (Scheme S7a). Thus, we proposed that the N3 in purine participated in the coordination with aluminium and resulted in the high regioselectivity.⁶ As shown in Scheme S7b, the bidentate vinyl cyclopropane 2a and N3 in 6-chloro-purine 1a coordinated with aluminium to form complex E. Thus, the N9 position was close to vinyl cyclopropane 2a to proceed with 1,3-ring-opening reaction to generate the 1,3-ring-opening N9-adduct 5aa.

8. Control experiment and proposed mechanism for Mg-catalyzed ring-opening reaction

The control experiments with 6-chloro-benzoimidazole 1t as nucleophiles was explored, and the corresponding 1,3-ring-opening products were obtained in a poor ratio of N1 to N3 adducts
Thus, we proposed that the N3 in purine also participated in the coordination with magnesium and resulted in the high regioselectivity. As shown in Scheme 8b, the bidentate vinyl cyclopropane 2a and bidentate N3, N9 in 6-chloro-purine 1a coordinated with magnesium to form an octahedral geometry as the intermediate F. Thus, the N7 position could attack vinyl cyclopropane 2a to afford the N7-adduct 6aa.

**Scheme S8** (a) The control experiment; (b) The proposed mechanism for the magnesium-catalyzed ring-opening reaction

**9. Characterization of compounds**

*(E)-Diethyl 2-(4-(6-chloro-9H-purin-9-yl)but-2-en-1-yl)malonate (3aa)*

Colorless oil; 82% yield.

**1H NMR** (400 MHz, CDCl₃): δ 8.75 (s, 1H), 8.12 (s, 1H), 5.88-5.75 (m, 2H), 4.84 (d, J = 5.2 Hz, 2H), 4.21-4.14 (m, 4H), 3.42 (t, J = 7.2 Hz, 1H), 2.68 (t, J = 6.4 Hz, 2H), 1.24 (t, J = 6.8 Hz, 6H) ppm. **13C NMR** (100 MHz, CDCl₃): δ 168.3, 151.7, 151.4, 150.7, 144.7, 132.7, 131.3, 125.5, 61.4, 51.0, 45.4, 31.0, 13.9 ppm. HRMS: calcd for C₁₆H₁₉ClN₄O₄Na [M+Na]⁺ 389.0987, found 389.0987.
(E)-Dimethyl 2-(4-(6-chloro-9H-purin-9-yl)but-2-en-1-yl)malonate (3ab)

Colorless oil; 82% yield.

$^1$H NMR (400 MHz, DMSO): $\delta$ 8.78 (s, 1H), 8.63 (s, 1H), 5.83-5.76 (m, 1H), 5.67-5.60 (m, 1H), 4.85 (d, $J = 6.0$ Hz, 2H), 3.63 (t, $J = 7.6$ Hz, 1H), 3.58 (s, 6H), 2.49 (m, 2H) ppm. $^{13}$C NMR (100 MHz, DMSO): $\delta$ 169.3, 152.1, 152.0, 149.5, 147.6, 131.2, 131.1, 127.1, 52.8, 50.8, 45.6, 31.3 ppm. HRMS: calcd for C$_{14}$H$_{15}$ClN$_4$O$_4$Na $[M+Na]^+$ 361.0674, found 361.0677.

(E)-Diisopropyl 2-(4-(6-chloro-9H-purin-9-yl)but-2-en-1-yl)malonate (3ac)

Colorless oil; 75% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.75 (s, 1H), 8.12 (s, 1H), 5.88-5.74 (m, 2H), 5.07-4.98 (m, 2H), 4.83 (d, $J = 5.6$ Hz, 2H), 3.34 (t, $J = 7.2$ Hz, 1H), 2.65 (t, $J = 6.4$ Hz, 2H), 1.21 (t, $J = 3.2$ Hz, 12H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.0, 152.0, 151.6, 151.0, 144.8, 133.1, 131.6, 125.4, 69.2, 51.5, 45.6, 31.1, 21.6, 21.5 ppm. HRMS: calcd for C$_{18}$H$_{23}$ClN$_4$O$_4$Na $[M+Na]^+$ 417.1300, found 417.1301.

(E)-Di-tert-butyl 2-(4-(6-chloro-9H-purin-9-yl)but-2-en-1-yl)malonate (3ad)

Colorless oil; 56% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.75 (s, 1H), 8.13 (s, 1H), 5.87-5.74 (m, 2H), 4.84 (d, $J = 5.2$ Hz, 2H), 3.22 (t, $J = 7.2$ Hz, 1H), 2.59 (t, $J = 6.4$ Hz, 2H), 1.42 (s, 18H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 167.9, 152.0, 151.0, 144.8, 133.4, 125.0, 81.8, 53.1, 45.7, 31.2, 27.9 ppm. HRMS: calcd for C$_{20}$H$_{27}$ClN$_4$O$_4$Na $[M+Na]^+$ 445.1613, found 445.1606.
(E)-Bis(2,2,2-trifluoroethyl) 2-(4-(6-chloro-9H-purin-9-yl)but-2-en-1-yl)malonate (3ae)

Colorless oil; 37% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.75 (s, 1H), 8.09 (s, 1H), 5.88-5.72 (m, 2H), 4.85 (d, $J = 5.6$ Hz, 2H), 4.53 (q, $J = 8.0$ Hz, 4H), 3.67 (t, $J = 7.2$ Hz, 1H), 2.76 (t, $J = 6.8$ Hz, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 166.1, 152.1, 151.2, 144.7, 130.6, 127.2, 61.3, 60.9, 50.3, 45.4, 31.0 ppm. HRMS: calcd for C$_{16}$H$_{13}$ClF$_6$N$_4$O$_4$Na [M+Na]$^+$ 497.0422, found 497.0412.

(E)-Dimethyl 2-(4-(6-iodo-9H-purin-9-yl)but-2-en-1-yl)malonate (3bb)

Colorless oil; 63% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.63 (s, 1H), 8.12 (s, 1H), 5.80 (q, $J = 5.3$ Hz, 2H), 4.81 (d, $J = 4.6$ Hz, 2H), 3.72 (s, 6H), 3.46 (t, $J = 7.2$ Hz, 1H), 2.68 (t, $J = 6.2$ Hz, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.9, 152.0, 147.8, 144.1, 138.6, 132.6, 125.8, 122.1, 52.7, 50.9, 45.6, 31.2 ppm. HRMS: calcd for C$_{14}$H$_{15}$IN$_4$O$_4$Na [M+Na]$^+$ 453.0030, found 453.0032.

(E)-Diethyl 2-(4-(6-(propylthio)-9H-purin-9-yl)but-2-en-1-yl)malonate (3ca)

Colorless oil; 92% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.69 (s, 1H), 7.91 (s, 1H), 5.81-5.71 (m, 2H), 4.77 (d, $J = 4.4$ Hz, 2H), 4.22-4.10 (m, 4H), 3.41-3.34 (m, 3H), 2.66 (t, $J = 6.4$ Hz, 2H), 1.86-1.77 (m, 2H), 1.22 (t, $J = 7.2$ Hz, 6H), 1.07 (t, $J = 7.2$ Hz, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.5, 161.6, 151.9, 148.1, 142.0, 131.9, 131.3, 126.3, 61.6, 51.3, 45.0, 31.2, 30.6, 22.9, 14.0, 13.4 ppm. HRMS: calcd for C$_{19}$H$_{26}$N$_4$O$_4$SNa [M+Na]$^+$ 429.1567, found 429.1569.
(E)-Diethyl 2-(4-(2-chloro-6-(pyrrolidin-1-yl)-9H-purin-9-yl)but-2-en-1-yl)malonate (3da)

Colorless oil; 67% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.63 (s, 1H), 5.77-5.69 (m, 2H), 4.68 (s, 2H), 4.17-4.16 (m, 6H), 3.74 (s, 2H), 3.39 (t, $J = 7.2$ Hz, 1H), 2.64 (t, $J = 6.4$ Hz, 2H), 2.06-1.97 (m, 4H), 1.23 (t, $J = 7.2$ Hz, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.6, 154.2, 153.3, 151.1, 138.6, 131.4, 126.7, 119.0, 61.5, 51.4, 48.9, 47.7, 44.8, 31.2, 26.1, 24.1, 14.0 ppm. HRMS: calcd for C$_{20}$H$_{26}$ClN$_5$O$_4$Na $[M+Na]^+$ 458.1566, found 458.1563.

(E)-Diethyl 2-(4-(2-chloro-6-(piperidin-1-yl)-9H-purin-9-yl)but-2-en-1-yl)malonate (3ea)

Colorless oil; 89% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.63 (s, 1H), 5.78-5.66 (m, 2H), 4.66 (d, $J = 4.8$ Hz, 2H), 4.23-4.14 (m, 4H), 3.39 (t, $J = 7.2$ Hz, 1H), 2.65 (t, $J = 6.4$ Hz, 2H), 1.70 (s, 6H), 1.23 (t, $J = 7.2$ Hz, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.6, 154.0, 153.9, 151.8, 137.8, 131.4, 126.6, 118.5, 61.5, 51.3, 44.8, 31.2, 26.1, 24.6, 14.0 ppm. HRMS: calcd for C$_{21}$H$_{28}$ClN$_5$O$_4$Na $[M+Na]^+$ 472.1722, found 472.1728.

(E)-Diethyl 2-(4-(2-chloro-6-morpholino-9H-purin-9-yl)but-2-en-1-yl)malonate (3fa)

Colorless oil; 89% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.66 (s, 1H), 5.73 (dd, $J = 7.6$, 5.0 Hz, 2H), 4.68 (d, $J = 4.3$ Hz,
2H), 4.22-4.15 (m, 8H), 3.82 (t, \(J = 4.8\) Hz, 4H), 3.40 (t, \(J = 7.2\) Hz, 1H), 2.70-2.60 (m, 2H), 1.24 (t, \(J = 7.2\) Hz, 6H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 168.6, 154.0, 153.9, 152.0, 138.4, 131.7, 126.5, 118.7, 66.9, 61.6, 51.4, 44.9, 31.2, 14.1 ppm. HRMS: calcd for C\(_{20}\)H\(_{26}\)ClN\(_5\)O\(_5\)Na [M+Na]\(^+\) 474.1515, found 474.1518.

\((E)\)-Dimethyl 2-(4-(6-phenyl-9\(H\)-purin-9-yl)but-2-en-1-yl)malonate (3gb)

\[\text{3gb} \]

Colorless oil; 67% yield.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 9.02 (s, 1H), 8.77 (d, \(J = 7.6\) Hz, 2H), 8.10 (s, 1H), 7.60-7.51 (m, 3H), 5.87-5.75 (m, 2H), 4.86 (d, \(J = 4.4\) Hz, 2H), 3.71 (s, 6H), 3.47 (t, \(J = 7.2\) Hz, 1H), 2.69 (t, \(J = 6.4\) Hz, 2H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 168.9, 154.9, 152.4, 152.2, 143.9, 135.6, 131.8, 131.0, 129.7, 128.6, 126.5, 52.7, 51.0, 45.0, 31.3 ppm. HRMS: calcd for C\(_{20}\)H\(_{20}\)N\(_4\)O\(_4\)Na [M+Na]\(^+\) 403.1377, found 403.1371.

\((E)\)-Diethyl 2-(4-(6-(phenanthren-9-yl)-9\(H\)-purin-9-yl)but-2-en-1-yl)malonate (3ha)

\[\text{3ha} \]

Colorless oil; 69% yield.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 9.17 (s, 1H), 8.77 (dd, \(J = 19.6, 8.4\) Hz, 2H), 8.27 (s, 1H), 8.22 (d, \(J = 8.0\) Hz, 1H), 8.11 (s, 1H), 7.98 (d, \(J = 7.6\) Hz, 1H), 7.75-7.55 (m, 4H), 5.92-5.83 (m, 2H), 4.92 (d, \(J = 3.2\) Hz, 2H), 4.23-4.14 (m, 4H), 3.45 (t, \(J = 7.2\) Hz, 1H), 2.71 (t, \(J = 5.6\) Hz, 2H), 1.24 (t, \(J = 7.2\) Hz, 6H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 168.5, 158.0, 152.3, 151.9, 144.4, 132.9, 132.3, 131.3, 131.3, 131.1, 130.9, 129.6, 129.6, 128.5, 127.7, 126.8, 126.8, 126.7, 126.5, 126.2, 122.9, 122.6, 61.6, 51.3, 45.2, 31.2, 14.1 ppm. HRMS: calcd for C\(_{30}\)H\(_{28}\)N\(_4\)O\(_4\)Na [M+Na]\(^+\) 531.2003, found 531.2002.
(E)-Diethyl 2-(4-(1,3-dimethyl-2,6-dioxo-2,3-dihydro-1H-purin-7(6H)-yl)but-2-en-1-yl)malonate (3ia)

Colorless oil; 94% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.53 (s, 1H), 5.84-5.73 (m, 2H), 4.87 (d, $J = 4.0$ Hz, 2H), 4.21-4.13 (m, 4H), 3.58 (s, 3H), 3.42-3.38 (m, 4H), 2.66 (t, $J = 6.4$ Hz, 2H), 1.24 (t, $J = 7.2$ Hz, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.6, 155.2, 151.7, 148.8, 140.5, 132.2, 126.8, 106.8, 61.6, 51.3, 48.3, 31.2, 29.8, 28.0, 14.1 ppm. HRMS: calcd for C$_{18}$H$_{24}$N$_4$O$_6$Na [M+Na$^+$] 415.1588, found 415.1587.

(E)-Dimethyl 2-(4-(2-chloro-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)malonate (3jb)

Yellow oil; 68% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.71-7.69 (m, 1H), 7.30-7.26 (m, 3H), 5.71-5.56 (m, 2H), 4.76 (d, $J = 5.2$ Hz, 2H), 3.66 (s, 6H), 3.41 (t, $J = 7.2$ Hz, 1H), 2.64 (t, $J = 7.2$ Hz, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.9, 141.7, 140.3, 134.8, 130.2, 126.1, 123.2, 122.7, 119.5, 109.6, 52.5, 51.1, 45.8, 31.2 ppm. HRMS: calcd for C$_{16}$H$_{17}$ClN$_2$O$_4$Na [M+Na$^+$] 359.0769, found 359.0763.

(E)-Diethyl 2-(4-(4-nitro-1H-imidazol-1-yl)but-2-en-1-yl)malonate (3ka)

Yellow oil; 75% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.00 (s, 1H), 7.58 (s, 1H), 5.79-5.68 (m, 2H), 4.91 (d, $J = 4.4$ Hz, 2H), 4.22-4.14 (m, 4H), 3.39 (t, $J = 6.4$ Hz, 1H), 2.65 (t, $J = 7.2$ Hz, 2H), 1.25 (t, $J = 7.2$ Hz, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.5, 140.7, 133.5, 132.7, 125.9, 61.6, 51.2, 49.4, 31.1, 14.0 ppm. HRMS: calcd for C$_{14}$H$_{19}$N$_3$O$_6$Na [M+Na$^+$] 348.1166, found 348.1174.

(E)-Diethyl 2-(4-(6-chloro-7H-purin-7-yl)but-2-en-1-yl)malonate (4aa)
Diethyl 2-(2-(6-chloro-9H-purin-9-yl)but-3-en-1-yl)malonate (5aa)

Colorless oil; 79% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.74 (s, 1H), 8.12 (s, 1H), 6.23-6.14 (m, 1H), 5.38 (d, $J = 10.4$ Hz, 1H), 5.32-5.28 (m, 2H), 4.23-4.03 (m, 4H), 3.24 (t, $J = 7.6$ Hz, 1H), 2.75 (t, $J = 7.6$ Hz, 2H), 1.26-1.17 (m, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.1, 168.1, 151.9, 151.8, 151.0, 143.8, 134.1, 131.6, 119.6, 61.9, 61.8, 56.5, 48.6, 32.6, 13.9, 13.8 ppm. HRMS: calcd for C$_{16}$H$_{19}$ClN$_4$O$_4$Na [$M$+Na]$^+$ 389.0978, found 389.0978.

Dimethyl 2-(2-(6-chloro-9H-purin-9-yl)but-3-en-1-yl)malonate (5ab)

Colorless oil; 87% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.74 (s, 1H), 8.12 (s, 1H), 6.23-6.14 (m, 1H), 5.38 (d, $J = 10.4$ Hz, 1H), 5.32-5.28 (m, 2H), 3.73 (s, 3H), 3.63 (s, 3H), 3.24 (t, $J = 7.2$ Hz, 1H), 2.75 (t, $J = 7.6$ Hz, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.5, 168.5, 151.9, 151.5, 151.2, 143.8, 134.0, 131.7, 119.8, 56.5, 52.9, 52.9, 48.3, 32.8 ppm. HRMS: calcd for C$_{14}$H$_{16}$ClN$_4$O$_4$Na [$M$+Na]$^+$ 361.0674, found 361.0664.
Diisopropyl 2-(2-(6-chloro-9H-purin-9-yl)but-3-en-1-yl)malonate (5ac)

Colorless oil; 67% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.73 (s, 1H), 8.13 (s, 1H), 6.23-6.14 (m, 1H), 5.37 (dd, $J = 10.4$, 0.7 Hz, 1H), 5.31-5.27 (m, 2H), 5.10-5.00 (m, 1H), 4.98-4.89 (m, 1H), 3.11 (t, $J = 7.2$ Hz, 1H), 2.70 (t, $J = 7.2$ Hz, 2H), 1.24-1.14 (m, 12H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 167.8, 167.7, 151.9, 151.5, 151.2, 143.8, 134.2, 131.7, 119.7, 69.7, 69.6, 56.6, 49.0, 32.6, 21.6, 21.5, 21.4 ppm. HRMS: calcd for C$_{18}$H$_{23}$ClN$_4$O$_4$Na [M+Na]$^+$ 417.1300, found 417.1292.

Di-tert-butyl 2-(2-(6-chloro-9H-purin-9-yl)but-3-en-1-yl)malonate (5ad)

Colorless oil; 63% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.74 (s, 1H), 8.13 (s, 1H), 6.23-6.14 (m, 1H), 5.36 (d, $J = 10.0$ Hz, 1H), 5.30-5.26 (m, 2H), 2.99 (t, $J = 7.2$ Hz, 1H), 2.62 (t, $J = 7.6$ Hz, 2H), 1.45 (s, 9H), 1.39 (s, 9H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 167.6, 167.5, 151.9, 151.6, 151.2, 143.8, 134.4, 131.8, 119.5, 82.4, 82.4, 56.6, 50.5, 32.8, 27.8, 27.8 ppm. HRMS: calcd for C$_{26}$H$_{27}$ClN$_4$O$_4$Na [M+Na]$^+$ 445.1613, found 445.1605.

Dimethyl 2-(2-(6-iodo-9H-purin-9-yl)but-3-en-1-yl)malonate (5bb)

Colorless oil; 44% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.62 (s, 1H), 8.12 (s, 1H), 6.22-6.14 (m, 1H), 5.39-5.24 (m, 3H), 3.73 (s, 3H), 3.63 (s, 3H), 3.23 (t, $J = 7.4$ Hz, 1H), 2.74 (t, $J = 7.4$ Hz, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.6, 168.5, 152.0, 147.8, 143.1, 138.7, 134.0, 122.4, 119.8, 56.6, 53.0, 52.9, 48.3, 32.8 ppm. HRMS: calcd for C$_{14}$H$_{13}$IN$_4$O$_4$Na [M+Na]$^+$ 453.0030, found 453.0029.
Diethyl 2-(2-(6-ethoxy-9H-purin-9-yl)but-3-en-1-yl)malonate (5la)

![Diagram](5la)

Colorless oil; 48% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.50 (s, 1H), 7.90 (s, 1H), 6.22-6.13 (m, 1H), 5.33-5.21 (m, 3H), 4.66 (q, $J = 7.2$ Hz, 2H), 4.22-4.03 (m, 4H), 3.17 (t, $J = 7.2$ Hz, 1H), 2.70 (t, $J = 7.4$ Hz, 2H), 1.51 (t, $J = 7.2$ Hz, 3H), 1.21 (dt, $J = 19.9$, 7.1 Hz, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.4, 168.3, 160.9, 152.1, 151.8, 140.6, 134.8, 121.6, 118.8, 63.1, 61.9, 61.9, 55.8, 48.6, 32.9, 14.5, 14.0, 13.9 ppm. HRMS: calcd for C$_{18}$H$_{24}$N$_4$O$_5$Na [M+Na]$^+$ 399.1639, found 399.1642.

Diethyl 2-(2-(2-chloro-6-(piperidin-1-yl)-9H-purin-9-yl)but-3-en-1-yl)malonate (5ea)

![Diagram](5ea)

Colorless oil; 89% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.66 (s, 1H), 6.15-6.06 (m, 1H), 5.32-5.21 (m, 2H), 5.19-5.15 (m, 1H), 4.28-4.01 (m, 8H), 3.16 (dd, $J = 8.0$, 6.4 Hz, 1H), 2.70-2.51 (m, 2H), 1.72-1.69 (m, 6H), 1.26 (t, $J = 7.4$ Hz, 3H), 1.19 (t, $J = 7.4$ Hz, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.4, 168.3, 154.0, 153.8, 151.9, 136.5, 135.0, 118.5, 61.9, 61.8, 54.7, 48.6, 33.1, 26.1, 24.6, 13.9, 13.9 ppm. HRMS: calcd for C$_{21}$H$_{28}$ClN$_5$O$_4$Na [M+Na]$^+$ 472.1722, found 472.1713.

Diethyl 2-(2-(6-cyclopentyl-9H-purin-9-yl)but-3-en-1-yl)malonate (5ma)

![Diagram](5ma)

Colorless oil; 62% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.87 (s, 1H), 8.00 (s, 1H), 6.24-6.15 (m, 1H), 5.35-5.25 (m, 3H), 4.22-4.14 (m, 2H), 4.11-3.99 (m, 2H), 3.93-3.84 (m, 1H), 3.22 (t, $J = 7.2$ Hz, 1H), 2.79-2.67 (m, 2H), 2.17-1.76 (m, 8H), 1.23 (t, $J = 7.2$ Hz, 3H), 1.16 (t, $J = 7.2$ Hz, 3H) ppm. $^{13}$C NMR (100
MHz, CDCl₃): δ 168.4, 168.3, 166.4, 152.5, 150.4, 142.0, 134.8, 132.3, 119.0, 61.9, 61.8, 55.7, 48.8, 42.6, 32.8, 32.8, 26.3,14.0, 13.9 ppm. HRMS: calcd for C₂₁H₂₈N₄O₄Na [M+Na]⁺ 423.2003, found 423.1996.

Diethyl 2-(2-(6-(phenanthren-9-yl)-9H-purin-9-yl)but-3-en-1-yl)malonate (5ha)

Colorless oil; 82% yield.

¹H NMR (400 MHz, CDCl₃): δ 9.16 (s, 1H), 8.77 (dd, J = 20.0, 8.0 Hz, 2H), 8.29-8.25 (m, 2H), 8.12 (s, 1H), 7.99 (d, J = 7.6 Hz, 1H), 7.73-7.56 (m, 4H), 6.32-6.24 (m, 1H), 5.44-5.35 (m, 3H), 4.27-4.07 (m, 4H), 3.33 (t, J = 7.2 Hz, 1H), 2.88-2.76 (m, 2H), 1.29-1.20 (m, 6H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ 168.4, 168.3, 158.2, 152.3, 151.9, 143.3, 143.3, 134.6, 132.9, 131.3, 131.2, 131.2, 131.0, 129.6, 127.8, 126.8, 126.8, 126.7, 126.5, 122.9, 122.6, 119.4, 62.0, 61.9, 56.0, 48.8, 32.8, 14.0, 14.0 ppm. HRMS: calcd for C₃₀H₂₉N₄O₄ [M+H]⁺ 509.2183, found 509.2174.

Diethyl 2-(2-(1H-benzo[d]imidazol-1-yl)but-3-en-1-yl)malonate 5na

Yellow oil; 61% yield.

¹H NMR (400 MHz, CDCl₃): δ 7.93 (s, 1H), 7.83-7.80 (m, 1H), 7.42-7.40 (m, 1H), 7.31-7.28 (m, 2H), 6.12-6.04 (m, 1H), 5.35 (dd, J = 10.4, 1.2 Hz, 1H), 5.23 (dd, J = 17.2, 1.2 Hz, 1H), 5.06-5.01 (m, 1H), 4.21-4.03 (m, 4H), 3.18 (dd, J = 8.0, 6.4 Hz, 1H), 2.73-2.59 (m, 2H), 1.24-1.18 (m, 6H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ 168.6, 168.4, 144.0, 141.4, 135.0, 133.1, 123.0, 122.4, 120.6, 118.7, 110.5, 61.9, 61.8, 56.1, 48.5, 32.6, 14.0, 13.9 ppm. HRMS: calcd for C₁₉H₂₁N₄O₄Na [M+Na]⁺ 353.1472, found 353.1467.
Diethyl 2-(2-(5,6-dimethyl-1H-benzo[d]imidazol-1-yl)but-3-en-1-yl)malonate 5oa

Yellow oil; 35% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.79 (s, 1H), 7.55 (s, 1H), 7.13 (s, 1H), 6.09-6.01 (m, 1H), 5.30 (dd, $J = 10.4$, 1.2 Hz, 1H), 5.18 (dd, $J = 17.2$, 1.2 Hz, 1H), 4.98-4.93 (m, 1H), 4.21-4.05 (m, 4H), 3.16-3.13 (m, 1H), 2.69-2.56 (m, 2H), 2.36-2.35 (m, 6H), 1.23-1.16 (m, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.5, 168.3, 142.4, 140.6, 135.1, 132.0, 131.4, 131.3, 130.3, 110.5, 61.7, 61.7, 55.9, 48.4, 32.4, 20.5, 20.1, 13.8, 13.8 ppm. HRMS: calcd for C$_{20}$H$_{27}$N$_2$O$_4$ [M+H$^+$] 359.1965, found 359.1957.

Diethyl 2-(2-(1H-benzo[d][1,2,3]triazol-1-yl)but-3-en-1-yl)malonate 5pa

Yellow oil; 87% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.06 (d, $J = 8.4$ Hz, 1H), 7.52-7.44(m, 2H), 7.39-7.35 (m, 1H), 6.22-6.14 (m, 1H), 5.50-5.44 (m, 1H), 5.32 (d, $J = 10.4$ Hz, 1H), 5.23 (dd, $J = 16.8$, 0.8 Hz, 1H), 4.20-4.03 (m, 4H), 3.22 (dd, $J = 8.4$, 6.4 Hz, 1H), 2.96-2.88 (m, 1H), 2.80-2.73 (m, 1H), 1.22-1.17 (m, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.6, 168.4, 146.1, 134.8, 133.5, 132.5, 127.3, 124.1, 120.1, 118.9, 109.7, 61.7, 61.7, 59.7, 48.4, 32.4, 13.9 ppm. HRMS: calcd for C$_{17}$H$_{21}$N$_3$O$_4$Na [M+Na$^+$] 354.1424, found 354.1419.

Diethyl 2-(2-(6-nitro-1H-benzo[d]imidazol-1-yl)but-3-en-1-yl)malonate (5sa)

Yellow oil; 45% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.38 (d, $J = 2.0$ Hz, 1H), 8.23 (dd, $J = 9.2$, 2.0 Hz,1H), 8.17 (s, 1H), 7.88 (d, $J = 8.8$ Hz, 1H), 6.13-6.05 (m, 1H), 5.46 (dd, $J = 10.4$, 1.2 Hz, 1H), 5.31 (dd, $J = 4.0$ Hz, 1H), 1.23-1.16 (m, 6H) ppm.
1H NMR (400 MHz, CDCl3): δ 8.73 (d, J = 2.0 Hz, 1H), 8.24 (dd, J = 8.8, 2.0 Hz, 1H), 8.11 (s, 1H), 7.52 (d, J = 9.2 Hz, 1H), 6.12-6.04 (m, 1H), 5.44 (dd, J = 10.4, 1.2 Hz, 1H), 5.28 (dd, J = 17.2, 1.2 Hz, 1H), 5.14-5.08 (m, 1H), 4.21-4.07 (m, 4H), 3.20 (t, J = 7.2 Hz, 1H), 2.72-2.59 (m, 2H), 1.22 (q, J = 7.2 Hz, 6H) ppm. 13C NMR (100 MHz, CDCl3): δ 168.2, 168.2, 144.7, 143.8, 143.2, 137.2, 134.0, 119.8, 118.8, 117.2, 110.6, 62.0, 62.0, 56.7, 48.3, 32.5, 13.9 ppm. HRMS: calcd for C18H21N3O6Na [M+Na]+ 398.1323, found 398.1323.

**Diethyl 2-(2-(6-chloro-7H-purin-7-yl)but-3-en-1-yl)malonate (6aa)**

Colorless oil; 72% yield.

1H NMR (400 MHz, CDCl3): δ 8.90 (s, 1H), 8.35 (s, 1H), 6.12-6.03 (m, 1H), 5.74 (q, J = 7.2 Hz, 1H), 5.41 (d, J = 10.4 Hz, 1H), 5.22 (d, J = 17.2 Hz, 1H), 4.23-4.05 (m, 4H), 3.31 (t, J = 7.2 Hz, 1H), 2.77-2.68 (m, 2H), 1.25-1.19 (m, 6H) ppm. 13C NMR (100 MHz, CDCl3): δ 168.0, 167.9, 161.6, 152.3, 146.9, 142.7, 134.8, 122.1, 119.8, 62.1, 62.0, 57.3, 48.5, 33.5, 13.8 ppm. HRMS: calcd for C18H17ClN4O4Na [M+Na]+ 389.0987, found 389.0978.

**Dimethyl 2-(2-(6-chloro-7H-purin-7-yl)but-3-en-1-yl)malonate (6ab)**

Colorless oil; 84% yield.
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.93 (s, 1H), 8.36 (s, 1H), 6.13-6.05 (m, 1H), 5.76 (d, $J = 7.6$ Hz, 1H), 5.44 (dd, $J = 10.4$, 1.2 Hz, 1H), 5.25 (dd, $J = 17.2$, 1.2 Hz, 1H), 3.75 (s, 3H), 3.68 (s, 3H), 3.38 (t, $J = 7.2$ Hz, 1H), 2.78-2.67 (m, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.4, 168.3, 161.6, 152.5, 146.8, 142.8, 134.7, 122.1, 120.0, 57.3, 53.1, 53.0, 48.2, 33.7 ppm. HRMS: calcd for C$_{14}$H$_{15}$ClN$_4$O$_4$Na [M+Na]$^+$ 361.0674, found 361.0668.

**Diisopropyl 2-(2-(6-chloro-7$H$-purin-7-yl)but-3-en-1-yl)malonate (6ac)**

Colorless oil; 64% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.90 (s, 1H), 8.36 (s, 1H), 6.11-6.03 (m, 1H), 5.76-5.07 (m, 1H), 5.40 (dd, $J = 10.4$, 1.2 Hz, 1H), 5.20 (dd, $J = 16.8$, 1.2 Hz, 1H), 5.07-4.91 (m, 2H), 3.24 (t, $J = 7.2$ Hz, 1H), 2.76-2.63 (m, 2H), 1.22-1.15 (m, 12H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 167.6, 161.7, 152.5, 146.9, 142.8, 135.0, 122.2, 119.7, 69.9, 69.9, 57.5, 48.9, 33.4, 21.5, 21.5, 21.4 ppm. HRMS: calcd for C$_{18}$H$_{23}$ClN$_4$O$_4$Na [M+Na]$^+$ 417.1300, found 417.1290.

**Di-tert-butyl 2-(2-(6-chloro-7$H$-purin-7-yl)but-3-en-1-yl)malonate (6ad)**

Colorless oil; 41% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.90 (s, 1H), 8.36 (s, 1H), 6.10-6.01 (m, 1H), 5.70 (q, $J = 7.2$ Hz, 1H), 5.38 (dd, $J = 10.4$, 0.8 Hz, 1H), 5.17 (dd, $J = 17.2$, 0.8 Hz, 1H), 3.15 (t, $J = 7.2$ Hz, 1H), 2.68-2.59 (m, 2H), 1.44 (s, 3H), 1.40 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 167.5, 167.4, 161.7, 152.4, 146.9, 142.9, 135.3, 122.3, 119.5, 82.7, 57.7, 50.5, 33.4, 27.9, 27.8 ppm. HRMS: calcd for C$_{20}$H$_{27}$ClN$_4$O$_4$Na [M+Na]$^+$ 445.1613, found 445.1606.

**Dimethyl 2-(2-(6-iodo-7$H$-purin-7-yl)but-3-en-1-yl)malonate (6bb)**
Colorless oil; 31% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.77 (s, 1H), 8.37 (s, 1H), 6.09-6.03 (m, 2H), 5.40 (d, $J = 9.2$ Hz, 1H), 5.16 (d, $J = 15.6$ Hz, 1H), 3.75 (s, 3H), 3.65 (s, 3H), 3.39 (t, $J = 7.2$ Hz, 1H), 2.83-2.71 (m, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.4, 168.4, 159.0, 152.7, 146.9, 135.0, 127.6, 119.6, 108.3, 55.0, 53.2, 53.1, 48.2, 33.5 ppm. HRMS: calcd for C$_{14}$H$_{15}$IN$_4$O$_4$Na [M+Na]$^+$ 453.0030, found 453.0023.

Diethyl 2-(2-(2,6-dichloro-7H-purin-7-yl)but-3-en-1-yl)malonate (6qb)

Colorless oil; 33% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.35 (s, 1H), 6.10-6.01 (m, 1H), 5.68 (q, $J = 6.8$ Hz, 1H), 5.44 (dd, $J = 9.2$, 1.2 Hz, 1H), 5.23 (dd, $J = 15.6$, 1.2 Hz, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.35 (t, $J = 7.2$ Hz, 1H), 2.74-2.69 (m, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.3, 168.3, 163.3, 153.3, 148.1, 143.6, 134.4, 121.4, 120.3, 57.6, 53.2, 53.1, 48.1, 33.6 ppm. HRMS: calcd for C$_{14}$H$_{14}$Cl$_2$N$_4$O$_4$Na [M+Na]$^+$ 395.0284, found 395.0277.

Diethyl 2-(2-(2-methyl-1H-benzo[d]imidazol-1-yl)but-3-en-1-yl)malonate (6ra)

Yellow oil; 71% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.70-7.67 (m, 1H), 7.35-7.33 (m, 1H), 7.23-7.16 (m, 2H), 6.14-6.06 (m, 1H), 5.29 (dd, $J = 10.4$, 1.2 Hz, 1H), 5.13-5.06 (m, 2H), 4.23-4.06 (m, 2H), 3.98 (q, $J = 7.2$ Hz, 2H), 3.12-3.01 (m, 1H), 2.84-2.76 (m, 1H), 2.72-2.64 (m, 1H), 2.57 (s, 3H), 1.20 (t, $J = 7.2$ Hz, 3H), 1.13 (t, $J = 7.2$ Hz, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.6, 168.3, 151.6, 142.7, 1346, 133.5, 122.1, 122.0, 119.3, 118.0, 111.1, 61.8, 61.8, 55.6, 48.5, 31.2, 14.6, 13.9, 13.8 ppm. HRMS: calcd for C$_{19}$H$_{25}$N$_2$O$_4$ [M+H]$^+$ 345.1809, found 345.1800.

Diethyl 2-(2-(4-nitro-1H-imidazol-1-yl)but-3-en-1-yl)malonate (6ka)
Yellow oil; 95% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.79 (s, 1H), 7.48 (s, 1H), 5.99-5.91 (m, 1H), 5.44 (d, $J$ = 10.4 Hz, 1H), 5.30 (d, $J$ = 17.2 Hz, 1H), 4.83-4.77 (m, 1H), 4.23-4.17 (m, 4H), 3.21 (t, $J$ = 7.2 Hz, 1H), 2.53-2.48 (m, 2H), 1.29-1.25 (m, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.1, 168.0, 135.1, 134.1, 120.4, 117.6, 62.2, 62.2, 59.1, 48.2, 33.4, 14.0, 14.0 ppm. HRMS: calcd for C$_{14}$H$_{21}$N$_3$O$_6$Na $[M+Na^+]$ 348.1166, found 348.1165.

Diethyl 2-(2-(6-chloro-1H-benzo[d]imidazol-1-yl)but-3-en-1-yl)malonate (6ta)

Yellow oil; 45% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.91 (s, 1H), 7.71 (d, $J$ = 8.8 Hz, 1H), 7.38 (d, $J$ = 1.2 Hz, 1H), 7.24 (d, $J$ = 1.6 Hz, 1H), 6.10-6.01 (m, 1H), 5.38 (d, $J$ = 10.4 Hz, 1H), 5.24 (d, $J$ = 17.2 Hz, 1H), 5.00-4.96 (m, 1H), 4.23-4.07 (m, 4H), 3.15 (t, $J$ = 7.2 Hz, 1H), 2.63 (t, $J$ = 7.2 Hz, 2H), 1.25-1.19 (m, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.5, 168.3, 142.6, 142.2, 134.6, 133.7, 128.9, 123.2, 121.4, 119.0, 110.6, 62.0, 61.9, 56.2, 48.5, 32.6, 13.9, 13.9 ppm. HRMS: calcd for C$_{18}$H$_{22}$ClN$_2$O$_4$Na $[M+Na^+]$ 387.1082, found 387.1080.

Diethyl 2-(2-(5-chloro-1H-benzo[d]imidazol-1-yl)but-3-en-1-yl)malonate (6ta')

Yellow oil; 39% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.92 (s, 1H), 7.79 (d, $J$ = 1.6 Hz, 1H), 7.33 (d, $J$ = 8.4 Hz, 1H), 7.24 (s, 1H), 6.10-6.01 (m, 1H), 5.37 (dd, $J$ = 10.4, 0.8 Hz, 1H), 5.22 (dd, $J$ = 17.2, 0.8 Hz, 1H), 5.04-4.99 (m, 1H), 4.21-4.05 (m, 4H), 3.18-3.14 (m, 1H), 2.70-2.57 (m, 2H), 1.24-1.18 (m, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.4, 168.3, 144.8, 142.6, 134.6, 131.7, 128.1, 123.6, 120.3, 119.0, 111.3, 61.9, 61.9, 56.4, 48.4, 32.5, 14.0, 13.9 ppm. HRMS: calcd for C$_{18}$H$_{22}$ClN$_2$O$_4$ $[M+H^+]$ 365.1263, found 365.1266.
(E)-2-(4-(6-Chloro-9H-purin-9-yl)but-2-en-1-yl)propane-1,3-diol (7aa)

Colorless oil; 53% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.76 (s, 1H), 8.14 (s, 1H), 5.89-5.70 (m, 2H), 4.87 (d, $J = 6.4$ Hz, 2H), 3.81-3.77 (m, 2H), 3.69-3.65 (m, 2H), 2.16 (t, $J = 7.2$ Hz, 4H), 1.88-1.61 (m, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 152.0, 144.9, 135.0, 131.7, 124.4, 65.3, 46.0, 41.7, 31.0 ppm. HRMS: calcd for C$_{12}$H$_{15}$ClN$_4$O$_2$Na [M+Na]$^+$ 305.0776, found 305.0776.

2-(2-(6-Chloro-9H-purin-9-yl)but-3-en-1-yl)propane-1,3-diol (8aa)

Colorless oil; 47% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.74 (s, 1H), 8.19 (s, 1H), 6.20-6.12 (m, 1H), 5.43-5.26 (m, 3H), 3.80-3.64 (m, 4H), 2.46 (d, $J = 19.1$ Hz, 2H), 2.30-2.16 (m, 2H), 1.58-1.52 (m, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 151.8, 151.5, 151.2, 143.9, 135.2, 131.6, 119.1, 64.4, 64.4, 56.3, 38.8, 32.7 ppm. HRMS: calcd for C$_{12}$H$_{15}$ClN$_4$O$_2$Na [M+Na]$^+$ 305.0776, found 305.0776.

10. References:


11. Copies of $^1$H NMR and $^{13}$C NMR spectra

$^1$H-NMR for 3aa

$^{13}$C-NMR for 3aa
$^1$H-NMR for 3ab

$^{13}$C-NMR for 3ab
HSQC for 3ab

HMBC for 3ab
Noesy for 3ab
$^1$H-NMR for 3ac

$^{13}$C-NMR for 3ac
$^{1}H$-NMR for 3ad

$^{13}C$-NMR for 3ad
$^1$H-NMR for 3ae

$^{13}$C-NMR for 3ae
$^1$H-NMR for 3da

$^{13}$C-NMR for 3da
$^1$H-NMR for 3ea

$^{13}$C-NMR for 3ea
**1H-NMR for 3fa**

![1H-NMR spectrum for 3fa](image)

**13C-NMR for 3fa**

![13C-NMR spectrum for 3fa](image)
$^1$H-NMR for 3gb

$^{13}$C-NMR for 3gb
$^1$H-NMR for 3ha

$^{13}$C-NMR for 3ha
$^{1}\text{H-NMR for 3ia}$

$^{13}\text{C-NMR for 3ia}$
$^1$H-NMR for 3jb

$^{13}$C-NMR for 3jb
$^1$H-NMR for 3ka

$^{13}$C-NMR for 3ka
$^1$H-NMR for 4aa

$^{13}$C-NMR for 4aa
$^1$H-NMR for 5aa

$^{13}$C-NMR for 5aa
$^1$H-NMR for 5ab

$^{13}$C-NMR for 5ab
Noesy for 5ab
$^1$H-NMR for 5ac

$^{13}$C-NMR for 5ac
$^1$H-NMR for 5ad

$^{13}$C-NMR for 5ad
$^1$H-NMR for 5bb

$^{13}$C-NMR for 5bb
$^1$H-NMR for 5la

$^{13}$C-NMR for 5la
$^1$H-NMR for 5ea

$^{13}$C-NMR for 5ea
$^{1}$H-NMR for 5ha

$^{13}$C-NMR for 5ha
**1H-NMR for 5na**

![1H-NMR spectrum](image)

**13C-NMR for 5na**

![13C-NMR spectrum](image)
$^1$H-NMR for 5oa

$^{13}$C-NMR for 5oa
1H-NMR for 5pa

13C-NMR for 5pa
**1H-NMR for 5sa**

![1H-NMR spectrum for 5sa](image)

**13C-NMR for 5sa**

![13C-NMR spectrum for 5sa](image)
$^1$H-NMR for 5sa'

![1H-NMR spectrum for 5sa'](image)

$^{13}$C-NMR for 5sa'

![$^{13}$C-NMR spectrum for 5sa'](image)
Noesy for 5sa'}
$^1$H-NMR for 6aa

$^{13}$C-NMR for 6aa
\[ ^1\text{H-NMR for 6ab} \]

\[ ^{13}\text{C-NMR for 6ab} \]
HSQC for 6ab

HMBC for 6ab
$^1$H-NMR for 6ac

$^{13}$C-NMR for 6ac
$^1$H-NMR for 6ad

$^{13}$C-NMR for 6ad
$^1$H-NMR for 6bb

$^{13}$C-NMR for 6bb
$^{1}$H-NMR for 6qb

$^{13}$C-NMR for 6qb
\textbf{\textsuperscript{1}H-NMR for 6ra}

\textbf{\textsuperscript{13}C-NMR for 6ra}
$^1$H-NMR for 6ka

$^{13}$C-NMR for 6ka
Noesy for 6ka
$^1$H-NMR for 6ta

$^{13}$C-NMR for 6ta
Noesy for 6ta
$^{1}$H-NMR for 6ta'

$^{13}$C-NMR for 6ta'
Noesy for 6ta'}
$^1$H-NMR for 7aa

$^{13}$C-NMR for 7aa
$^1$H-NMR for 8aa

$^{13}$C-NMR for 8aa