Supporting Information

The structure-based design of SARS-CoV-2 nsp14 methyltransferase ligands yields nanomolar inhibitors

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1. General information

Reagents were purchased from Sigma Aldrich and Fluorochem and used as received without any further purification or prepared according to published procedures. THF was dried and distilled from sodium and benzophenone, and CH₂Cl₂ was distilled from P₂O₅ and kept over 4Å molecular sieves. Thin layer chromatography (TLC) was performed on silica gel 60 F₂₅₄ plates (Merck). Compounds were visualized on the TLC plates by irradiation with UV light. For normal flash column chromatography (VWR International Silica gel 60 from, particle size 0.040–0.063 mm) as well as for reverse-phase flash column chromatography (C18 RediSep Rf columns), a CombiFlash® Rf from Teledyne ISCO was used. UPLC samples were measured on Waters UPLC H-Class Core System (column Waters Acquity UPLC BEH C18 1.7 μm, 2.1 mm × 100 mm), Waters Acquity UPLC PDA detector, mass spectrometer Waters SQ D2, and MassLynx mass spectrometry software. ¹H and ¹³C NMR spectra for the reported compounds were recorded on a Bruker Avance III™ HD 400 instrument (400.0 MHz for ¹H and 101 MHz for ¹³C) using inverse broadband probe with ATM module (5 mm BBO-¹H Z-GRD) or Bruker Avance III™ HD 400 instrument with broadband PRODIGY cryoprobe with ATM module (5 mm CPBBO BB-¹H/¹⁹F/D Z-GRD). Chemical shifts (δ) and coupling constants (J) are expressed in ppm and Hz, respectively. The NMR experiments were performed in DMSO-d6 and referenced to the solvent signal (δ 2.50 for ¹H NMR and 39.70 for ¹³C NMR). Complete assignment of all NMR signals was performed using a combination of 2D NMR (H,H-COSY, H,C-HSQC, and H,C-HMBC) experiments. The numbering of structures was inspired by numbering of nucleosides (normal digits for nucleobase, prime digits for carbohydrate moiety and double prime digits for aromatic substituent), and for amino acid moiety, symbols from Greek alphabet (α, β, γ) were used. High resolution mass spectrometry (HRMS) analyses were carried out on an LTQ XL Orbitrap XL (Thermo Fisher Scientific) using electrospray ionization (ESI). Purity of all final SAH analogues was determined by analytical HPLC using LCMS-2020 system from Shimadzu equipped by CORTECS column (C18 2.7 μm, 50 × 4.6 mm).
2. Synthetic procedures

2.1. Synthesis of (het)aryl acetylenes

\[
\begin{align*}
R-\text{Br} & \xrightarrow{\text{a,b}} R-\equiv R1-R5 \\
\end{align*}
\]

Reagents and conditions: (a) (Triisopropyl)acetylene, Pd(PPh\(_3\))\(_4\), CuI, Et\(_3\)N, THF, 60 °C. (b) TBAF, THF, r.t.

**General procedure A: Preparation of (het)aryl acetylenes.** To a suspension of bromo (het)arene, (triisopropylsilyl)acetylene (3 equiv.), CuI (0.3 equiv.) and tetrakis(triphenylphosphine)-palladium(0) (0.1 equiv.) in dry THF (4 mL per 1 mmol) was added triethylamine (3 equiv.) at r.t., and the mixture was stirred under argon atmosphere at 60 °C for 1 h. The solution was then filtered through a plug of silica gel, washed with 9:1 cyclohexane/EtOAc, and concentrated under reduced pressure. The residue was dissolved in THF (4 mL per 1 mmol), and tetrabutylammonium fluoride (1 M in THF, 1.5 equiv.) was added. After stirring for 1 h at r.t., the volatiles were removed in vacuo and the crude mixture was subjected to flash column chromatography.

**2-Ethynylnaphthalene (R1)**

Heterocycle R1 was prepared from 2-bromonaphthalene (400 mg, 1.9 mmol) using the general procedure A. Flash column chromatography (0 to 5 % of EtOAc in cyclohexane) gave compound R1 (234 mg, 1.5 mmol, 79 %) as a yellow powder. All characteristics were consistent with published data.\(^3\)

**1-Ethynylnaphthalene (R2)**

Compound R2 was prepared from 1-bromonaphthalene (400 mg, 1.9 mmol) according to the general procedure A. Flash column chromatography (0 to 5 % of EtOAc in cyclohexane) furnished desired heterocycle R2 (225 mg, 1.5 mmol, 78 %) as a yellow oil. \(^1\)H and \(^13\)C NMR spectroscopy was consistent with the published data.\(^3\)

**3-Ethynylquinoline (R3):**

Substituted heterocycle R3 was prepared via Sonogashira cross-coupling reaction from 3-bromoquinoline (400 mg, 1.9 mmol) using the general procedure A. Flash column chromatography (0 to 5 % of EtOAc in cyclohexane) gave compound R3 (213 mg, 1.5 mmol, 75 %) as a yellow powder. All characteristics were consistent with published data.\(^3\)
chromatography (0 to 40 % of EtOAc in CH₂Cl₂) afforded compound R₃ (181 mg, 1.2 mmol, 62 %) as a brown powder. All characteristics matched to those described.⁴

2-tert-Butyl 2-ethynyl-1H-benzo[d]imidazole-1-carboxylate (R₄):

Heterocycle R₄ was prepared from tert-butyl 2-bromo-1H-benzo[d]imidazole-1-carboxylate (600 mg, 2.0 mmol) according to the general procedure A. The crude mixture was purified by flash column chromatography on silica gel (0 to 10 % of EtOAc in cyclohexane) to give desired product R₄ (360 mg, 1.5 mmol, 73 %) as a purple powder. All characteristics were consistent with published data.⁵

5-Ethynylbenzo[b]thiophene (R₅):

Substituted heterocycle R₅ was prepared via Sonogashira cross-coupling reaction from 5-bromobenzo[b]thiophene (400 mg, 1.9 mmol) following the general procedure A. The mixture was purified by flash column chromatography on silica gel (0 to 5 % of EtOAc in cyclohexane) to afford compound R₅ (192 mg, 1.2 mmol, 64 %) as a white powder. All characteristics matched to those described.⁶

2.2. Synthesis of 7-substituted analogues of S-adenosyl homocysteine

(2R,3R,4R,5R)-5-(4-Amino-5-iodo-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-bis((tert-butyldimethylsilyl)oxy)tetrahydrofuran-2-yl)methanol (2):

Persilylated nucleoside 1 (4.1 g, 5.6 mmol) was dissolved in THF (150 mL), and solution of trichloroacetic acid (46 g, 282 mmol) in water (46 mL) was added dropwise at 0 °C. After stirring for 4 h at 0 °C, the mixture was neutralized using anhydrous Na₂CO₃, diluted with water (200 mL) and extracted three times with EtOAc (500 mL). Organic layers were combined, dried over anhydrous MgSO₄, and the volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (20 to 60 % of EtOAc in CH₂Cl₂) to afford desired product 2 (2.5 g, 4 mmol, 72 %) as a yellowish foam.

¹H NMR (400 MHz, DMSO-d₆) δ 8.09 (1H, s, H₂), 7.69 (1H, s, H₈), 6.68 (2H, br s, NH₂), 6.05 (1H, d, J = 7.1 Hz, H1′), 5.37 (1H, dd, J = 6.1, 5.4 Hz, 5′-OH), 4.61 (1H, dd, J = 7.1, 4.6 Hz, H2′), 4.23 (1H, dd, J = 4.5, 1.3 Hz, H3′), 3.94–3.89 (1H, m, H4′), 3.67 (1H, dt, J = 12.0, 4.7 Hz, H5′a), 3.56 (1H, ddd, J = 12.0, 6.2 Hz, 3.2 H5′b), 0.91, 0.67 (18H, 2×s, 2×tBuTBS), 0.11, 0.10, −0.15, −0.42 (12H, 4×s, 4×MeTBS). ¹³C NMR (101 MHz, DMSO-d₆) δ 157.4 (C₆), 152.1 (C₂), 150.4 (C₄), 127.5 (C₈), 103.5 (C₅), 86.6 (C₁' and C₄'), 75.2 (C₂'), 73.2 (C₃'), 61.5 (C₅'), 52.0 (C₇), 25.9, 25.6 (2×tBuTBS), 18.0, 17.7 (2×tBuTBS), −4.5, −4.6, −4.7, −5.5 (4×MeTBS). HRMS (ESI) Calculated for C₂₃H₄₂O₄Na₂Si₂, [M + H]⁺ m/z: 621.1784, [M + H]⁺, found 621.1781.
tert-Butyl S-(((2S,3R,4R,5R)-5-(4-amino-5-iodo-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-bis(tert-butylidimethylsilyl)oxy)tetrahydrofuran-2-yl)methyl)-N-(tert-butoxycarbonyl)-L-homocysteinate (3):

To a solution of nucleoside 2 (2 g, 3.22 mmol) and triethylamine (630 μL, 4.52 mmol) in CH₂Cl₂ (40 mL) methanesulfonyl chloride (300 μL, 3.87 mmol) was added dropwise at 0 °C. After stirring for 2 h at r.t., sat. solution of NaHCO₃ (100 mL) was added, and the mixture was extracted twice with CH₂Cl₂ (250 mL). Organic layers were combined and dried over anhydrous Na₂SO₄, and the solvent was removed in vacuo. This mixture was then dissolved in dry NMP (20 mL) and added to the solution of potassium salt of (S)-4-(tert-butoxy)-3-((tert-butoxycarbonyl)amino)-4-oxobutane-1-thiolate [prepared by the slow addition of solution of tert-butyl (tert-butoxycarbonyl)-L-homocysteinate (1.86 g, 6.4 mmol) in dry NMP (15 mL) to a suspension of t-BuOK (0.71 g, 6.4 mmol) in dry NMP (15 mL) at 0 °C and subsequent warming to r.t. and stirring for 30 minutes] at r.t. and stirred under argon atmosphere for 1 h. After dilution with EtOAc (300 mL) the mixture was washed three times with water (150 mL). Organic layer was dried over anhydrous Na₂SO₄, and the volatiles were removed in vacuo. The crude mixture was subjected to reverse-phase flash column chromatography (0 to 100 % of MeCN in water) to give intermediate 3 (2.36 g, 2.64 mmol, 82 % after two steps) as a brownish foam. ¹H NMR (400 MHz, DMSO-d₆) δ 8.10 (1H, s, H₂), 7.67 (1H, s, H₈), 7.15 (1H, d, J = 7.9 Hz, NHBOc), 6.66 (2H, br s, NH₂), 6.10 (1H, d, J = 7.3 Hz, H₁'), 4.74 (1H, dd, J = 7.3, 4.4 Hz, H₂'), 4.17 (1H, d, J = 4.4 Hz, H₃'), 3.99–3.87 (2H, m, H₄', Hu), 3.01 (1H, dd, J = 13.8, 8.5 Hz, H₅'a), 2.81 (1H, dd, J = 13.7, 6.9 Hz, H₅'b), 2.64–2.45 (2H, m, H₇), 1.91–1.76 (2H, m, Hβ), 1.37 (18H, s, tBuBOc, tBu), 0.92, 0.66 (18H, 2×s, 2×tBuTBS), 0.15, 0.11, −0.11, −0.39 (12H, 4×s, 4×MeTBS). ¹³C NMR (101 MHz, DMSO-d₆) δ 171.6 (COterBu), 157.3 (C₆), 155.7 (COCterBuBOc), 153.2 (C₂), 150.8 (C₄), 127.3 (C₈), 103.4 (C₅), 86.1 (C₁'), 84.6 (C₄'), 80.5, 78.2 (tBuqBOc, tBuq), 74.6 (C₂'), 74.1 (C₃'), 53.5 (C₆), 52.5 (C₇), 33.6 (C₅'), 31.2 (Cβ), 28.4 (Cγ), 28.3, 27.8 (tBuqBOc, tBu), 26.0, 25.6 (2×tBuTBS), 17.9, 17.6 (2×tBuqTBS), −4.5, −4.6, −5.5 (4×MeTBS). HRMS (ESI) Calculated for C₅₆H₆₃O₇N₇ISSi₂, [M + H]⁺ m/z: 894.3182, [M + H]⁺, found 894.3179.
**tert-Butyl S-(((2S,3R,4R,5R)-5-(4-amino-5-benzyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-bis((tert-butyldimethylsilyl)oxy)tetrahydrofuran-2-yl)methyl)-N-(tert-butoxycarbonyl)-L-homocysteinate (4):**

Benzylzinc bromide (0.5 M in THF, 0.9 mL, 0.45 mmol) was added to a solution of intermediate 3 (200 mg, 0.22 mmol), tris(dibenzylideneacetone)dipalladium(0) (10 mg, 0.01 mmol) and 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (20 mg, 0.35 mmol) in dry THF (3 mL), and the mixture was stirred under argon atmosphere at 60 °C for 1 h. After cooling to r.t., sat. solution of NaHCO₃ (30 mL) was added, and the mixture was extracted twice with EtOAc (100 mL). Organic layers were combined and dried over anhydrous Na₂SO₄, and the solvent was removed in vacuo. Flash column chromatography on silica gel (0 to 50 % of EtOAc in CH₂Cl₂) furnished protected SAH analogue 4 (155 mg, 0.18 mmol, 81 %) as a yellowish foam. ¹H NMR (400 MHz, DMSO-d₆) δ 8.03 (1H, s, H2), 7.30−7.21 (4H, m, H6″, H5″, H3″, H2″), 7.21−7.13 (2H, m, H4″, NH Boc), 7.09 (1H, s, H8), 6.36 (2H, br s, NH₂), 6.10 (1H, d, J = 7.1 Hz, H1′), 4.70 (1H, dd, J = 7.0, 4.5 Hz, H2′), 4.20−4.10 (3H, m, H3′, CH₂), 3.99−3.88 (2H, m, H4′, Hα), 2.95 (1H, dd, J = 13.9, 7.8 Hz, H5′a), 2.78 (1H, dd, J = 13.8, 5.7 Hz, H5′b), 2.61−2.42 (2H, m, Hγ), 1.88−1.76 (2H, m, Hβ), 1.38, 1.37 (18H, 2×s, tBu Boc, tBu), 0.92, 0.68 (18H, 2×s, 2×tBuTBS), 0.14, 0.11, −0.12, −0.37 (12H, 4×s, 4×MeTBS). ¹³C NMR (101 MHz, DMSO-d₆) δ 171.6 (COtBu), 157.6 (C6), 155.7 (COOtBu Boc), 151.8 (C2), 151.7 (C4), 140.9 (C1′), 128.6, 128.4 (C6″, C5″, C3″ and C2″), 126.2 (C4″), 120.5 (C8), 114.5 (C7), 102.4 (C5), 86.2 (C1′), 84.1 (C4′), 80.5, 78.2 (tBu Boc, tBu), 74.6 (C3′), 74.1 (C2′), 53.5 (Cα), 33.8 (C5′), 31.2 (Cβ), 28.5 (Cγ), 28.3, 27.8 (tBu Boc, tBu), 25.9, 25.7 (2×tBuTBS), 17.9, 17.7 (2×tBu TBS), −4.5, −4.6, −5.3 (4×Me TBS). HRMS (ESI) Calculated for C₄₃H₇₂O₇N₅S₂Si₂, [M + H]⁺ m/z: 858.4686, [M + H]⁺, found 858.4686.

**General procedure B: Sonogashira cross-coupling reaction.** Triethylamine (3 equiv.) was added to a mixture of intermediate 3, (het)aryl acetylene (2 equiv.), CuI (0.3 equiv.) and tetrakis(triphenylphosphine)-palladium(0) (0.1 equiv.) in dry THF (15 mL per 1 mmol) and the suspension was stirred under argon atmosphere at 60 °C for 2 h. After cooling to r.t., the mixture was diluted with EtOAc (100 mL) and washed with H₂O (30 mL). Organic layer was dried over anhydrous Na₂SO₄, and the solvent was removed in vacuo. The crude mixture was subjected to flash column chromatography.
**tert-Butyl S-((2S,3R,4R,5R)-5-(4-amino-5-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-bis((tert-butyldimethylsilyl)oxy)tetrahydrofuran-2-yl)methyl)-N-(tert-butoxycarbonyl)-L-homocysteinate (5):**

Derivative 5 was prepared from compound 3 (200 mg, 0.22 mmol) and commercially available phenylacetylene using the general procedure B. Flash column chromatography on silica gel (0 to 50 % of EtOAc in CH2Cl2) afforded desired product 5 (168 mg, 0.19 mmol, 88 %) as a yellow foam. **1H NMR** (400 MHz, DMSO-**d6**) δ 8.16 (1H, s, H2), 7.91 (1H, s, H8), 7.62–7.56 (2H, m, H6′′, H2′′), 7.46–7.39 (3H, m, H5′′, H4′′, H3′′), 7.17 (1H, d, J = 7.9 Hz, NH**Boc**), 6.14 (1H, d, J = 7.1 Hz, H1′), 4.81 (1H, dd, J = 7.1, 4.4 Hz, H2′), 4.20 (1H, d, J = 4.3 Hz, H3′), 3.98 (1H, dd, J = 7.0 Hz, H4′), 3.92 (1H, q, J = 8.3 Hz, H3′), 3.04 (1H, dd, J = 13.7, 8.4 Hz, H5′a), 2.87 (1H, dd, J = 13.8, 6.1 Hz, H5′b), 2.65–2.44 (2H, m, Hγ), 1.93–1.77 (2H, m, Hβ), 1.37 (18H, s, tBu**Boc**, tBu), 0.93, 0.69 (18H, 2×s, 2×tBu**TBS**), 0.16, 0.13, −0.09, −0.38 (12H, 4×s, 4×Me**TBS**). **13C NMR** (101 MHz, DMSO-**d6**) δ 171.6 (C1), 157.8 (C6), 155.7 (C1′), 153.1 (C2), 150.6 (C4), 131.3 (C6′′, C2′′), 128.9, 128.7 (C5′′, C4′′, C3′′), 127.2 (C8), 122.6 (C1′′), 120.3 (C5), 95.5 (C7), 91.4 (R-**C=C**), 86.6 (C1′), 84.8 (C4′), 83.1 (R-**C=C**), 80.5, 78.3 (tBu**Boc**, tBuq), 74.7 (C3′), 74.3 (C2′), 53.5 (Ca), 33.6 (C5′), 31.2 (Cb), 28.4 (Cy), 28.3, 27.8 (tBu**Boc**, tBu), 26.0, 25.7 (2×tBu**TBS**), 17.9, 17.6 (2×tBu**TBS**), −4.4, −4.5, −4.6, −5.3 (4×Me**TBS**). **HRMS** (ESI) Calculated for C41H70O11N5SSi2, [M + H]+ m/z: 868.4529, [M + H]+, found 868.4524.

**tert-Butyl S-((2S,3R,4R,5R)-5-(4-amino-5-(naphthalen-2-ylethynyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-bis((tert-butyldimethylsilyl)oxy)tetrahydrofuran-2-yl)methyl)-N-(tert-butoxycarbonyl)-L-homocysteinate (6):**

Compound 6 was prepared via Sonogashira cross-coupling reaction from intermediate 3 (300 mg, 0.34 mmol) and aryl acetylene R1 following the general procedure B. The crude mixture was subjected to flash column chromatography on silica gel (0 to 50 % of EtOAc in CH2Cl2) to give compound 6 (255 mg, 0.28 mmol, 83 %) as a yellow foam. **1H NMR** (400 MHz, DMSO-**d6**) δ 8.21 (1H, d, J = 1.2 Hz, H1′′), 8.18 (1H, s, H2), 7.98–7.92 (4H, m, H8, H8′, H5′, H4′), 7.66 (1H, dd, J = 8.5, 1.6 Hz, H3′′), 7.60–7.54 (2H, m, H7′, H6′), 7.17 (1H, d, J = 7.9 Hz, NH**Boc**), 6.16 (1H, d, J = 7.1 Hz, H1′), 4.83 (1H, dd, J = 7.1, 4.4 Hz, H2′), 4.22 (1H, dd, J = 4.3, 0.8 Hz, H3′), 3.99 (1H, t, J = 7.1 Hz, H4′), 3.93 (1H, q, J = 8.2 Hz, Hx), 3.06 (1H, dd, J = 13.7, 8.3 Hz, H5′a), 2.88 (1H, dd, J = 13.8, 6.1 Hz, H5′b), 2.70–2.42 (2H, m, Hγ), 1.94–1.79 (2H, m, Hβ), 1.37 (18H, s, tBu**Boc**, tBu), 0.94, 0.69 (18H, 2×s, 2×tBu**TBS**), 0.17, 0.13, −0.08, −0.37 (12H, 4×s, 4×Me**TBS**). **13C NMR** (101 MHz, DMSO-**d6**) δ 171.6 (C1), 157.8 (C6), 155.8 (C1′), 153.2 (C2), 150.6 (C4), 132.8 (C9′), 132.5 (C10′), 131.0 (C1′′), 128.4, 128.1, 127.91, 127.86, 127.4 (C8, C8′, C5′, C4′, C3′), 127.2, 127.1 (C7′, C6′), 120.0 (C2′′), 102.3 (C5), 95.5 (C7),
91.8 (R=C=O), 86.6 (C1′), 84.8 (C4′), 83.5 (R=C=O), 80.6, 78.3 (tBuBoc, tBuq), 74.7 (C3′), 74.3 (C2′), 53.5 (Ca), 33.6 (C5′), 31.2 (Cβ), 28.4 (Cγ), 28.3, 27.8 (tBuBoc, tBu), 26.0, 25.7 (2tBuTBS) 18.0, 17.7 (2tBuTBS) −4.4, −4.6, −5.3 (4MeTBS). HRMS (ESI) Calculated for C₈₅H₇₂O₇N₅SSi₂, [M + H]+ m/z: 918.4686, [M + H]+, found 918.4683.

tert-Butyl S-(((2S,3R,4R,5R)-5-(4-amino-5-(naphthalen-1-ylethynyl)-7H-pyrrrolo[2,3-d]pyrimidin-7-yl)-3,4-bis((tert-butyldimethylsilyl)oxy)tetrahydrofuran-2-yl)methyl)-N-(tert-butoxycarbonyl)-1-homocysteinate (7):

Protected SAH analogue 7 was prepared from compound 3 (280 mg, 0.31 mmol) and acetylene R2 using the general procedure B. The mixture was purified by flash column chromatography on silica gel (0 to 50% of EtOAc in CH₂Cl₂) to afford protected SAH analogue 7 (205 mg, 0.33 mmol, 73%) as a yellow foam. ¹H NMR (400 MHz, DMSO-d₆) δ 8.32 (1H, d, J = 8.2 Hz, H5′), 8.19 (1H, s, H2), 8.06 (1H, s, H8), 8.02 (1H, d, J = 7.9 Hz, H8′), 8.01 (1H, d, J = 8.4 Hz, H2′), 7.88 (1H, dd, J = 7.2, 1.0 Hz, H4′), 7.68 (1H, td, J = 7.4, 1.3 Hz, H6′′), 7.62 (1H, td, J = 7.5, 1.3 Hz, H7′′), 7.57 (1H, dd, J = 8.2, 7.3 Hz, H3′′), 7.17 (1H, d, J = 7.9 Hz, NHboc), 6.79 (2H, br s, NH₂), 6.18 (1H, d, J = 7.2 Hz, H1′), 4.86 (1H, dd, J = 7.1, 4.4 Hz, H2′), 4.23 (1H, d, J = 4.9 Hz, H3′), 4.01 (1H, t, J = 7.0 Hz, H4′), 3.94 (1H, q, J = 7.9 Hz, Ha), 3.07 (1H, dd, J = 13.7, 8.4 Hz, H5′a), 2.90 (1H, dd, J = 13.9, 6.0 Hz, H5′b), 2.69–2.46 (2H, m, Hγ), 1.94–1.77 (2H, m, Hβ), 1.37, 1.36 (18H, 2×s, tBuBoc, tBu), 0.94, 0.70 (18H, 2×s, 2tBuTBS), 0.17, 0.14, −0.07, −0.34 (12H, 4×s, 4×MeTBS). ¹³C NMR (101 MHz, DMSO-d₆) δ 171.6 (COOrBu), 157.8 (C6), 155.7 (COOrBu), 153.2 (C2), 150.7 (C4), 133.1 (C9′′), 132.5 (C10′′), 130.5 (C4′′), 129.1 (C2′′), 128.8 (C8′′), 127.6 (C8), 127.4 (C6′′), 126.9 (C7′′), 125.8 (C3′′), 125.5 (C5′′), 120.1 (C1′′), 102.4 (C5), 95.5 (C7), 89.3 (R=C=O), 88.0 (R=C=O), 86.6 (C1′), 84.8 (C4′), 80.5, 78.3 (tBuBoc, tBuq), 74.7 (C3′), 74.2 (C2′), 53.5 (Ca), 33.6 (C5′), 31.2 (Cβ), 28.4 (Cγ), 28.3, 27.8 (tBuBoc, tBu), 26.0, 25.7 (2tBuTBS), 17.9, 17.7 (2tBuTBS) −4.4, −4.6, −5.3 (4MeTBS). HRMS (ESI) Calculated for C₈₅H₇₂O₇N₅SSi₂, [M + H]+ m/z: 918.4686, [M + H]+, found 918.4686.

tert-Butyl S-(((2S,3R,4R,5R)-5-(4-amino-5-(quinolin-3-ylethynyl)-7H-pyrrrolo[2,3-d]pyrimidin-7-yl)-3,4-bis((tert-butyldimethylsilyl)oxy)tetrahydrofuran-2-yl)methyl)-N-(tert-butoxycarbonyl)-1-homocysteinate (8):

Derivative 8 was prepared from intermediate 3 (360 mg, 0.4 mmol) and hetaryl acetylene R3 via Sonogashira cross-coupling reaction according to the general procedure B. The mixture was purified by flash column chromatography on silica gel (30 to 100% of EtOAc in CH₂Cl₂) to give compound 8 (303 mg, 0.33 mmol, 82%) as a brownish foam. ¹H NMR (400 MHz, DMSO-d₆) δ 9.04 (1H, d, J = 2.1 Hz, H2′′),
8.65 (1H, d, J = 1.7 Hz, H4′′), 8.18 (1H, s, H2), 8.05 (1H, d, J = 8.4 Hz, H8′′), 8.01 (1H, dd, J = 8.4, 1.1 Hz, H5′″), 8.01 (1H, s, H8), 7.80 (1H, ddd, J = 7.5, 7.0, 1.1 Hz, H7′′), 7.67 (1H, ddd, J = 7.5, 7.0, 1.1 Hz, H6′′), 7.18 (1H, d, J = 7.9 Hz, NH\text{Boc}), 6.85 (2H, br s, NH₂), 6.16 (1H, d, J = 7.1 Hz, H1′), 4.83 (1H, dd, J = 7.1, 4.3 Hz, H2′), 4.22 (1H, d, J = 4.4 Hz, H3′), 4.00 (1H, t, J = 7.0 Hz, H4′), 3.93 (1H, q, J = 8.2 Hz, H2), 3.06 (1H, ddd, J = 13.7, 8.4 Hz, H5′a), 2.89 (1H, ddd, J = 13.8, 6.1 Hz, H5′b), 2.65–2.47 (2H, m, Hγ), 1.93–1.77 (2H, m, Hβ), 1.37 (18H, 2×s, \text{tBu}^{\text{Boc}}, \text{tBu}), 0.94, 0.69 (18H, 2×s, 2×\text{tBu}^{\text{TBS}}), 0.17, 0.13, −0.08, −0.37 (12H, 4×s, 4×\text{Me}^{\text{TBS}}). ¹³C NMR (101 MHz, DMSO-\text{d₆}) δ 171.6 (\text{CO} \text{OrBu}), 157.8 (C6), 155.7 (\text{CO} \text{OrBu}^{\text{Boc}}), 153.2 (C2), 151.8 (C2′), 150.7 (C4), 146.3 (C9′), 138.2 (C4′), 130.5 (C7′), 129.0 (C8′), 128.2 (C5′′), 128.0 (C8), 127.7 (C6′′), 127.1 (C10′′), 117.0 (C3′′), 102.1 (C5), 95.1 (C7), 88.9 (R-\text{C≡C}), 86.7 (C1′), 86.2 (R-\text{C≡C}), 84.9 (C4′), 80.5, 78.3 (\text{tBu}^{\text{Boc}}, \text{tBu}), 74.7 (C3′), 74.3 (C2′), 53.5 (Ca), 33.6 (C5′), 31.2 (Cb), 28.4 (Cy), 28.3, 27.8 (2×\text{tBu}^{\text{Boc}}, \text{tBu}), 26.0, 25.7 (2×\text{tBu}^{\text{TBS}}), 17.9, 17.6 (2×\text{tBu}^{\text{TBS}}), −4.5, −4.6, −5.3 (4×\text{Me}^{\text{TBS}}). HRMS (ESI) Calculated for C₄₇H₅₀O₈N₈S₂₂, [M + H]⁺ m/z: 919.4638, [M + H]⁺, found 919.4630.

tert-Butyl 2-((4-amino-7-((2R,3R,4R,5S)-5-(((S)-4-((tert-butoxycarbonylamino)-4-oxobutyl)thio)methyl)-3,4-bis((tert-butyldimethylsilyl)oxy)tetrahydrofuran-2-yl)-7H-pyrrolo[2,3-d]pyrimidine-5-yl)ethyl)-1H-benzo[d]imidazole-1-carboxylate (9): Compound 9 was prepared from compound 3 (210 mg, 0.24 mmol) and protected acetylene R4 following the general procedure B. The crude mixture was subjected to flash column chromatography on silica gel (0 to 60 % of EtOAc in CH₂Cl₂) to furnish desired product 9 (210 mg, 0.21 mmol, 87 %) as a yellow foam. ¹H NMR (400 MHz, DMSO-\text{d₆}) δ 8.19 (1H, s, H2), 8.18 (1H, s, H8), 7.89 (1H, d, J = 8.0 Hz, H7″ or H4″), 7.71 (1H, d, J = 7.9 Hz, H4′′ or H7″), 7.50–7.44 (1H, m, H6″ or H5″), 7.41 (1H, td, J = 7.7, 1.4 Hz, H5″ or H6″), 7.16 (1H, d, J = 7.8 Hz, NH\text{Boc}), 6.14 (1H, d, J = 7.2 Hz, H1′), 4.88 (1H, dd, J = 7.2, 4.4 Hz, H2′), 4.23 (1H, d, J = 4.4 Hz, H3′), 4.01 (1H, t, J = 7.2 Hz, H4′), 3.93–3.87 (1H, m, Ha), 3.07 (1H, ddd, J = 13.6, 8.4 Hz, H5′a), 2.90 (1H, dd, J = 13.8, 6.0 Hz, H5′b), 2.68–2.46 (2H, m, Hγ), 1.93–1.78 (2H, m, Hβ), 1.69, 1.37 (27H, 2×s, \text{tBu}^{\text{Boc}}, \text{tBu}^{\text{Boc}}, \text{tBu}), 0.94, 0.69 (18H, 2×s, 2×\text{tBu}^{\text{TBS}}), 0.17, 0.13, −0.09, −0.38 (12H, 4×s, 4×\text{Me}^{\text{TBS}}). ¹³C NMR (101 MHz, DMSO-\text{d₆}) δ 171.6 (\text{CO} \text{OrBu}), 157.6 (C6), 155.7 (\text{CO} \text{OrBu}^{\text{Boc}}), 153.6 (C2), 150.8 (C4), 148.0 (\text{CO} \text{OrBu}^{\text{Boc}}), 142.8 (C8′ or C9′), 136.1 (C2′), 131.4 (C8′ or C9′), 130.0 (C8), 126.0 (C6″ or C5″), 125.1 (C5″ or C6″), 120.0 (C7″ or C4″), 115.1 (C4″ or C7″), 102.2 (C5), 93.8 (C7), 89.3 (R-\text{C≡C}), 87.0 (C1′), 86.9 (R-\text{C≡C}), 85.0 (C4′), 83.4, 80.5, 78.2 (\text{tBu}^{\text{Boc}}, \text{tBu}^{\text{Boc}}, \text{tBu}), 74.7 (C3′), 74.2 (C2′), 53.5 (Ca), 33.5 (C5′), 31.2 (Cb), 28.4 (Cy), 28.3, 27.79, 27.77 (2×\text{tBu}^{\text{Boc}}, \text{tBu}^{\text{Boc}}, \text{tBu}), 25.9, 25.6 (2×\text{tBu}^{\text{TBS}}), 17.9, 17.6 (2×\text{tBu}^{\text{TBS}}), −4.46, −4.48, −4.6, −5.4 (4×\text{Me}^{\text{TBS}}). HRMS (ESI) Calculated for C₅₀H₇₀O₈N₈S₂₂, [M + H]⁺ m/z: 1008.5115, [M + H]⁺, found 1008.5112.
**tert-butyl S-((2S,3R,4R,5R)-5-(4-amino-5-(benzo[8]thiophen-5-ylethynyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-bis((tert-butyldimethylsilyloxy)tetrahydrofuran-2-yl)methyl)-N-(tert-butoxycarbonyl)-L-homocysteinate (10):**

Protected SAH analogue 10 was prepared from intermediate 3 (226 mg, 0.25 mmol) and hetaryl acetylene R5 following the **general procedure B.** Flash column chromatography on silica gel (0 to 60 % of EtOAc in CH₂Cl₂) gave compound 10 (153 mg, 0.17 mmol, 66 %) as a yellow foam. **¹H NMR** (400 MHz, DMSO-d₆) δ 8.17 (1H, s, H2), 8.06 (1H, d, J = 8.4 Hz, H7''), 7.92 (1H, s, H8), 7.85 (1H, d, J = 5.4 Hz, H2''), 7.55 (1H, dd, J = 8.4, 1.5 Hz, H6''), 7.49 (1H, dd, J = 5.6, 0.5 Hz, H3''), 7.17 (1H, d, J = 7.9 Hz, H3'), 4.21 (1H, dd, J = 4.3, 0.8 Hz, H3'), 3.99 (1H, t, J = 7.1 Hz, H4'), 3.93 (1H, q, J = 8.2 Hz, Hα), 3.05 (1H, dd, J = 13.7, 8.4 Hz, H5'a), 2.88 (1H, dd, J = 13.8, 6.1 Hz, H5'b), 2.66–2.47 (2H, m, Hγ), 1.93–1.77 (2H, m, Hβ), 1.37 (18H, s, tBuMS, tBu), 0.93, 0.69 (18H, 2×s, 2×tBuTMS), 0.16, 0.13, −0.08, −0.37 (12H, 4×s, 4×tMeTMS). **¹³C NMR** (101 MHz, DMSO-d₆) δ 171.6 (C' butyldimethylsilyl)oxy)tetrahydrofuran), 157.8 (C6), 155.7 (COtBu), 153.1 (C2), 150.6 (C4), 139.8 (C9'), 139.4 (C8''), 129.1 (C2''), 127.1 (C8), 126.9 (C6'), 126.6 (C4'), 124.0 (C3'), 123.7 (C7'), 118.6 (C5'), 102.3 (C5), 95.6 (C7), 91.7 (R-C≡C), 86.6 (C1'), 84.8 (C4'), 82.6 (R-C≡C), 80.5, 78.3 (tBuOOC, tBuQ), 74.7 (C3'), 74.3 (C2'), 53.5 (Cα), 33.6 (C5'), 31.2 (Cβ), 28.4 (Cγ), 28.3, 27.8 (tBuOOC, tBu), 26.0, 25.7 (2×tBuTMS), 17.9, 17.6 (2×tBuQ), −4.46, −4.6, −5.3 (4×tMeTMS). **HRMS** (ESI) Calculated for C₄₈H₇₀O₁₂N₆S₄Si₂, [M + H]^+ m/z: 924.4250, [M + H]^+: found 924.4245.

**tert-Butyl S-((2S,3R,4R,5R)-5-(4-amino-5-(2-(quinolin-3-yl)-ethyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-bis((tert-butyldimethylsilyloxy)tetrahydrofuran-2-yl)methyl)-N-(tert-butoxycarbonyl)-L-homocysteinate (11):**

Mixture of compound 8 (130 mg, 0.14 mmol) and 10% Pd/C (34 mg, 0.03 mmol) in EtOH and EtOAc (10 mL, 1:1) was vigorously stirred under H₂ atmosphere at r.t. for 18 h. Then the reaction mixture was filtered through celite, and the solvent was removed in vacuo. Purification of the residue by flash column chromatography on silica gel (30 to 100 % of EtOAc in CH₂Cl₂) afforded desired SAH analogue 11 (105 mg, 0.11 mmol, 81 %) as a yellowish foam. **¹H NMR** (400 MHz, DMSO-d₆) δ 8.85 (1H, d, J = 2.1 Hz, H2''), 8.19 (1H, d, J = 1.6 Hz, H4''), 8.04 (1H, s, H2'), 7.98 (1H, d, J = 8.5 Hz, H8''), 7.89 (1H, dd, J = 8.3, 0.9 Hz, H5''), 7.68 (1H, td, J = 7.6, 1.4 Hz, H7''), 7.57 (1H, td, J = 7.6, 1.0 Hz, H6''), 7.22–7.12 (2H, m, 8, NHBoc), 6.66 (2H, br s, NH₂), 6.08 (1H, d, J = 7.2 Hz, H1'), 4.67 (1H, dd, J = 7.0, 4.6 Hz, H2'), 4.15 (1H, d, J = 5.2 Hz, H3'), 3.96–3.88 (2H, m, H4', Hα), 3.28–3.18 (2H, m, CH₂BQ), 3.18–3.06 (2H, m, CH₂), 2.93 (1H, dd, J = 13.9, 8.3 Hz, H5'a), 2.71 (1H, dd, J = 13.8, 5.7 Hz, H5'b),
2.64−2.41 (2H, m, Hγ), 1.92−1.75 (2H, m, Hβ), 1.37, 1.36 (18H, 2×s, tBuBoc, tBu), 0.92, 0.64 (18H, 2×s, 2×tBuTBS), 0.14, 0.12, −0.19, −0.47 (12H, 4×s, 4×MeTBS).

\[ ^{13}C \text{ NMR} \text{ (101 MHz, DMSO-} d_6\text{)} \delta 171.6 \text{ (CO}\text{tBu), 157.8 (C6), 155.7 (CO}\text{tBuBoc), 152.1 (C2”), 151.70 (C2), 151.67 (C4), 146.5 \text{ (C9”), 134.4 (C3”), 134.2 (C4”), 128.8 \text{ (C8”),} 128.7 \text{ (C7”), 127.9 (C10”), 126.6 (C6”), 119.3 (C8), 114.9 (C7), 102.4 (C5), 86.0 (C1’), 84.1 (C4’), 80.5, 78.3 \text{ (tBuq} \text{Boc, tBuq), 74.7 (C3’), 74.0 (C2’), 53.5 \text{ (Ca), 33.7 (C5’), 33.4 (CH}^2_2 \text{I), 31.2 (Cβ), 28.4 (Cγ), 28.3, 27.8 \text{ (tBuBoc, tBu), 27.0 (CH}^2_2 \text{II), 26.0, 25.6 (2×tBuTBS), 17.9, 17.6 (2×tBuTBS), −4.5, −4.7, −5.4 (4×MeTBS).} \]

HRMS (ESI) Calculated for C_{47}H_{75}O_{7}N_{6}SSi_{2}, [M + H]^+ m/z: 923.4951, [M + H]^+ found 923.4954.

2.3. Final deprotection

**General procedure C: Protecting group removal under acidic conditions.** To a solution of protected SAH analogue in a mixture of TFA and water (9:1, 15 mL per mmol) at 0 °C. After stirring for 3 h at r.t., the mixture was concentrated under reduced pressure and the residue was co-evaporated twice with MeOH. Then, the crude mixture was re-dissolved in MeOH (3 mL) and neutralized with NH_4OH. The volatiles were removed under reduced pressure, and the residue was purified by reverse-phase flash column chromatography.

S-(((2S,3S,4R,5R)-5-(4-Amino-5-benzyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-l-homocysteine (12):

Free SAH analogue 12 was prepared by deprotection of compound 4 (130 mg, 0.15 mmol) according to the general procedure C. Purification by reverse-phase flash column chromatography (0 to 50 % of MeOH in water) furnished final compound 12 (61 mg, 0.13 mmol, 85 %) as a white powder.

\[ ^{1}H \text{ NMR} \text{ (400 MHz, DMSO-} d_6\text{)} \delta 8.03 \text{ (1H, s, H2), 7.32−7.22 \text{ (4H, m, H6”, H5”, H3” and H2”), 7.18 \text{ (1H, tt,} J = 7.0, 1.4 \text{ Hz, H4”), 7.09 \text{ (1H, s, H8), 6.38 \text{ (2H, br s, NH2), 6.05 \text{ (1H, d,} J = 5.8 \text{ Hz, H1’), 4.36 \text{ (1H, t,} J = 5.5 \text{ Hz, H2’), 4.15 \text{ (2H, s, CH}2\text{), 4.01 \text{ (1H, dd,} J = 5.5, 4.1 \text{ Hz, H3’), 3.95 \text{ (1H, q,} J = 6.0 \text{ Hz, H4’), 3.32−3.22 \text{ (1H, m, Hα), 2.85 \text{ (1H, dd,} J = 13.7, 5.9 \text{ Hz, H5’a), 2.70 \text{ (1H, dd,} J = 13.6, 6.3 \text{ Hz, H5’b), 2.60 \text{ (2H, t,} J = 7.5 \text{ Hz, Hγ), 2.04−1.89 \text{ (1H, m, Hβa), 1.85−1.72 \text{ (1H, m, Hβb).} \text{ }^{13}C \text{ NMR} \text{ (101 MHz, DMSO-} d_6\text{)} \delta 157.7 \text{ (C6), 151.8 \text{ (C2), 151.5 \text{ (C4), 141.0 (C1’), 128.6 (C6”, C5”, C3”, C2”), 126.2 (C4’), 120.3 (C8), 114.5 \text{ (C7), 102.2 \text{ (C5), 86.7 (C1’), 82.8 (C4’), 73.5 (C2’), 72.7 (C3’), 53.4 (Cα), 34.3 (C5’), 32.0 (Cβ), 31.7 (CH2), 28.6 (Cγ).} \text{ } \text{HRMS (ESI) Calculated for} C_{22}H_{26}O_{5}N_{6}SSi_{2}, \text{ [M − H]}^+ \text{ m/z: 472.1660, [M − H]}^+ \text{ found 472.1657.} \]
S-(((2S,3S,4R,5R)-5-(4-Amino-5-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1-homocysteine (13):

Derivative 13 was prepared from protected SAH analogue 5 (145 mg, 0.17 mmol) following the general procedure C. The crude mixture was subjected to reverse-phase flash column chromatography (0 to 50% of MeOH in water) to give desired product 13 (78 mg, 0.16 mmol, 97%) as a white powder. H NMR (400 MHz, DMSO-d6) δ 8.17 (1H, s, H2), 7.89 (1H, s, H8), 7.62–7.57 (2H, m, H6", H2"), 7.46–7.39 (3H, m, H5", H4", H3"), 6.73 (2H, br s, NH2), 6.09 (1H, d, J = 6.0 Hz, H1'), 4.50 (1H, t, J = 5.6 Hz, H2'), 4.07 (1H, dd, J = 5.4, 3.7 Hz, H3'), 3.99 (1H, q, J = 6.5, 3.6 Hz, H4'), 3.31 (1H, dd, J = 7.1, 5.5 Hz, Hα), 2.91 (1H, dd, J = 13.7, 6.4 Hz, H5'a), 2.78 (1H, dd, J = 13.6, 6.7 Hz, H5'b), 2.64 (2H, t, J = 7.7 Hz, Hβ), 2.07–1.96 (1H, m, Hβα), 1.90–1.78 (1H, m, Hβb). C NMR (101 MHz, DMSO-d6) δ 170.2 (COOH), 157.8 (C6), 153.2 (C2), 150.4 (C4), 131.3 (C6", C2"), 128.9, 128.7 (C5", C4", C3"), 127.2 (C8), 122.7 (C1"), 102.2 (C5), 95.3 (C7), 91.4 (R-C=C), 87.0 (C1'), 83.3 (C4'), 83.2 (R-C=C), 73.5 (C2'), 72.8 (C3'), 53.3 (C6), 34.2 (C5'), 31.6 (Cβ), 28.3 (Cγ). HRMS (ESI) Calculated for C22H23O5N5S, [M – H]− m/z: 482.1504, [M – H]− found 482.1500.

S-(((2S,3S,4R,5R)-5-(4-Amino-5-(naphthen-1-ylethynyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1-homocysteine (14):

SAH analogue 14 was prepared from derivative 6 (165 mg, 0.18 mmol) using the general procedure C. The mixture was purified by reverse-phase flash column chromatography (0 to 50% of MeOH in water) to afford compound 14 (80 mg, 0.15 mmol, 83%) as a yellow powder. H NMR (400 MHz, DMSO-d6) δ 8.22 (1H, s, H1''), 8.18 (1H, s, H2), 7.98–7.91 (4H, m, H8, H8'', H5'' and H4''), 7.66 (1H, dd, J = 8.5, 1.5 Hz, H3''), 7.60–7.52 (2H, m, H7'', H6''), 6.79 (2H, br s, NH2), 6.11 (1H, d, J = 6.0 Hz, H1''), 4.52 (1H, t, J = 5.5 Hz, H2''), 4.11–4.07 (1H, m, H3''), 4.04–3.98 (1H, m, H4''), 3.34–3.28 (1H, m, Hα), 2.92 (1H, dd, J = 13.6, 6.3 Hz, H5'a), 2.80 (1H, dd, J = 13.6, 6.6 Hz, H5'b), 2.66 (2H, t, J = 7.7 Hz), 2.09–1.96 (1H, m, Hβa), 1.91–1.79 (1H, m, Hβb). C NMR (101 MHz, DMSO-d6) δ 170.0 (COOH), 157.8 (C6), 153.2 (C2), 150.4 (C4), 132.8 (C9''), 132.5 (C10''), 130.9 (C1''), 128.4, 128.1, 127.90, 127.86 (C8'', C5'', C4'', C3''), 127.4 (C8), 127.1, 127.0 (C7'', C6''), 120.1 (C2''), 102.2 (C5), 95.3 (C7), 91.8 (R-C=C), 87.0 (C1'), 83.6 (R-C=C), 83.3 (C4'), 73.5 (C2'), 72.8 (C3'), 53.2 (C6), 34.2 (C5'), 31.6 (Cβ), 28.3 (Cγ). HRMS (ESI) Calculated for C22H22O5N5S, [M – H]− m/z: 532.1660, [M – H]− found 532.1657.

S-(((2S,3S,4R,5R)-5-(4-Amino-5-(naphthalen-1-ylethynyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1-homocysteine (15):
Compound 15 was prepared from protected SAH analogue 7 (150 mg, 0.16 mmol) according to the general procedure C. Reverse-phase flash column chromatography (0 to 50 % of MeOH in water) furnished SAH analogue 15 (79 mg, 0.15 mmol, 90 %) as a brownish powder.

\[^{1}H\] NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 8.35 (1H, d, \(J = 8.3\) Hz, H5’’), 8.20 (1H, s, H2), 8.06 (1H, s, H8), 8.01 (1H, d, \(J = 8.0\) Hz, H8’’), 7.99 (1H, d, \(J = 8.2\) Hz, H2’’), 7.89 (1H, d, \(J = 6.8\) Hz, H4’’), 7.69 (1H, t, \(J = 7.1\) Hz, H6’’), 7.62 (1H, t, \(J = 7.7\) Hz, H7’’), 7.57 (1H, t, \(J = 7.7\) Hz, H3’’), 6.79 (2H, br s, NH2), 6.13 (1H, d, \(J = 6.0\) Hz, H1’), 4.55 (1H, t, \(J = 5.5\) Hz, H2’), 4.12–4.07 (1H, m, H3’), 4.02 (1H, q, \(J = 6.4\) Hz, H4’), 3.34–3.27 (1H, m, Hα), 2.93 (1H, dd, \(J = 13.6, 6.4\) Hz, H5′a), 2.81 (1H, dd, \(J = 13.6, 6.6\) Hz, H5′b), 2.66 (2H, t, \(J = 7.6\) Hz, Hγ), 2.09–1.92 (1H, m, Hβa), 1.93–1.78 (1H, m, Hβb). \[^{13}C\] NMR (101 MHz, DMSO-\(d_6\)) \(\delta\) 170.0 (COOH), 157.8 (C6), 153.2 (C2), 150.5 (C4), 133.1 (C9’’), 132.5 (C10’’), 130.5 (C4’’), 129.0 (C2’’), 128.8 (C8’’), 127.6 (C8), 127.5 (C6’’), 126.9 (C7’’), 125.8 (C3’’), 125.6 (C5’’), 120.2 (C1’’), 102.3 (C5), 95.4 (C7'), 89.3 (R-C≡C), 88.1 (R-C≡C), 86.9 (C1’), 83.4 (C4’), 73.5 (C2’), 72.8 (C3’), 53.2 (Ca), 34.2 (C5’), 31.6 (Cβ), 28.3 (Cγ). HRMS (ESI) Calculated for C_{27}H_{26}O_{5}N_{5}S, [M – H]− m/z: 532.1660, [M – H]−, found 532.1656.

\(S-(((2S,3S,4R,5R)-5-(4-Amino-5-(quinolin-3-ylethynyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-L-homocysteine (16):\)

Derivative 16 was prepared from compound 8 (130 mg, 0.14 mmol) following the general procedure C. The crude mixture was subjected to reverse-phase flash column chromatography (0 to 40 % of MeOH in water) to give final compound 16 (67 mg, 0.13 mmol, 89 %) as a brown powder. \[^{1}H\] NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 9.05 (1H, d, \(J = 2.1\) Hz, H2’’), 8.66 (1H, d, \(J = 1.7\) Hz, H4’’), 8.19 (1H, s, H2), 8.04 (1H, d, \(J = 8.5\) Hz, H8’’), 8.01 (1H, d, \(J = 8.4\) Hz, H5’’), 7.99 (1H, s, H8), 7.80 (1H, td, \(J = 7.7, 1.4\) Hz, H7’’), 7.66 (1H, td, \(J = 7.4, 0.9\) Hz, H6’’), 6.86 (2H, br s, NH2), 6.12 (1H, d, \(J = 6.0\) Hz, H1’), 4.53 (1H, t, \(J = 5.5\) Hz, H2’), 4.11–4.05 (1H, m, H3'), 4.04–3.98 (1H, m, H4'), 3.37–3.29 (1H, m, Hα), 2.92 (1H, dd, \(J = 13.6, 6.3\) Hz, H5′a), 2.81 (1H, dd, \(J = 13.6, 6.6\) Hz, H5′b), 2.65 (2H, t, \(J = 7.7\) Hz, Hγ), 2.09–1.96 (1H, m, Hβa), 1.93–1.78 (1H, m, Hβb). \[^{13}C\] NMR (101 MHz, DMSO-\(d_6\)) \(\delta\) 170.0 (COOH), 157.8 (C6), 153.3 (C2), 151.9 (C2’’), 150.5 (C4), 146.3 (C9’’), 138.2 (C4’’), 130.5 (C7’’), 129.0 (C8’’), 128.2 (C5’’), 128.0 (C8), 127.7 (C6’’), 127.1 (C10’’), 117.1 (C3’’), 102.1 (C5), 95.0 (C7'), 88.9 (R-C≡C), 87.0 (C1’), 86.4 (R-C≡C), 83.4 (C4’), 73.5 (C2’), 72.8 (C3’), 53.1 (Ca), 34.1 (C5’), 31.5 (Cβ), 28.3 (Cγ). HRMS (ESI) Calculated for C_{26}H_{32}O_{5}N_{6}S, [M – H]− m/z: 533.1613, [M – H]−, found 533.1609.
S-(((2S,3S,4R,5R)-5-(4-Amino-5-(benzol[b]thiophen-5-ylethynyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-l-homocysteine (18):

SAH analogue 18 was prepared from compound 10 (135 mg, 0.15 mmol) according to the general procedure C. Reverse-phase flash column chromatography (0 to 40% of MeOH in water) afforded final compound 18 (70 mg, 0.13 mmol, 89%) as a white powder.

\(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 8.18 (1H, s, H2), 8.15 (1H, d, \(J = 1.0\) Hz, H4"), 8.06 (1H, d, \(J = 8.4\) Hz, H7"), 7.90 (1H, s, H8), 7.85 (1H, d, \(J = 5.4\) Hz, H2"), 7.55 (1H, dd, \(J = 8.3, 1.4\) Hz, H6"), 7.49 (1H, d, \(J = 5.3\) Hz, H3"), 6.76 (2H, br s, NH3), 6.11 (1H, d, \(J = 6.0\) Hz, H1"), 4.51 (1H, t, \(J = 5.6\) Hz, H2"), 4.09 (1H, dd, \(J = 5.3, 4.8\) Hz, H3"), 4.04–3.97 (1H, m, H4"), 3.33 (1H, dd, \(J = 7.4, 6.4\) Hz, Ha), 2.92 (1H, d, \(J = 13.7, 6.3\) Hz, H5'a), 2.79 (1H, dd, \(J = 13.6, 6.7\) Hz, H5'b), 2.65 (2H, t, \(J = 7.7\) Hz, H7), 2.09–1.96 (1H, m, Hβa), 1.92–1.79 (1H, m, Hβb). \(^13\)C NMR (101 MHz, DMSO-\(d_6\)) \(\delta\) 170.2 (COOH), 157.8 (C6), 153.2 (C2), 150.4 (C4), 139.8 (C9"), 139.4 (C8"), 129.1 (C2"), 127.1 (C8), 126.9 (C6"), 126.6 (C4"), 124.0 (C3"), 123.2 (C7"), 118.6 (C5"), 102.3 (C5), 95.4 (C7), 91.7 (R-C≡C), 87.2 (C1'), 83.3 (C4'), 82.6 (R-C≡C), 73.5 (C2'), 72.8 (C3'), 53.2 (Cα), 34.2 (C5'), 31.6 (Cβ), 28.3 (Cγ). HRMS (ESI) Calculated for C\(_{22}\)H\(_{24}\)O\(_3\)N\(_3\)S\(_3\), [M – H]\(^-\) m/z: 538.1224, [M – H]\(^-\), found 538.1221.
Compound 19 was prepared from protected SAH analogue 11 (90 mg, 0.1 mmol) following the general procedure C. Reverse-phase flash column chromatography (0 to 40% of MeOH in water) furnished SAH analogue 19 (45 mg, 0.08 mmol, 86%) as a yellow powder. \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 8.87 (1H, d, \(J = 2.1\) Hz, H2″), 8.24 (1H, d, \(J = 1.5\) Hz, H4″), 8.05 (1H, s, H2), 7.95 (1H, d, \(J = 8.4\) Hz, H5″), 7.91 (1H, d, \(J = 7.5\) Hz, H8″), 7.69 (1H, ddd, \(J = 8.4, 6.9, 1.4\) Hz, H7″), 7.58 (1H, td, \(J = 7.5, 1.1\) Hz, H6″), 7.18 (1H, s, C8), 6.67 (2H, br s, NH\(_2\)), 6.06 (1H, d, \(J = 5.8\) Hz, H1'), 4.38 (1H, t, \(J = 5.5\) Hz, H2'), 4.01 (1H, t, \(J = 4.4\) Hz, H3′), 3.93 (1H, q, \(J = 6.2\) Hz, H4′), 3.36–3.29 (1H, m, H6), 3.25–3.17 (2H, m, CH\(_2\)I), 3.16–3.09 (2H, m, CH\(_2\)I), 2.83 (1H, dd, \(J = 13.6, 6.1\) Hz, H5'a), 2.71–2.57 (3H, m, H5'b, H7), 2.07–1.95 (1H, m, Hβa), 1.89–1.76 (1H, m, Hβb). \(^{13}\)C NMR (101 MHz, DMSO-\(d_6\)) \(\delta\) 169.9 (COO'OH), 157.9 (C6), 152.4 (C2″), 151.8 (C2), 151.4 (C4), 146.5 (C9″), 134.7 (C3″), 134.3 (C4″), 128.81 (C8″ or C7″), 128.78 (C7″ or C8″), 127.9 (C10″), 127.8 (C5″), 126.7 (C6″), 119.0 (C8), 115.0 (C7), 102.3 (C5), 86.6 (C1′), 82.7 (C4′), 73.4 (C2′), 72.8 (C3′), 53.1 (Ca), 34.2 (C5′), 33.3 (CH\(_2\))I, 31.5 (Cβ), 28.4 (Cγ), 27.3 (CH\(_2\)I).

HRMS (ESI) Calculated for C\(_{26}\)H\(_{29}\)O\(_5\)N\(_6\)S, [M − H]− m/z: 537.1926, [M − H]−, found 537.1922.
3. Docking studies

The 3D structures of the compounds 12-19 were prepared using ACD/ChemSketch 12.01 and their geometries were optimized using MOPAC2016 (PM7 method). The homology model was prepared using SWISS-MODEL server (https://swissmodel.expasy.org). The primary amino acid sequence for which templates were searched and models were built was as follows:

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AENVTLFKDCSKVITGLHPTQAPTHLSVDTKFKEGLVDIIPGIPKDMTYRRLISMGMFKMNYYQVNGYPNMFITREEAIRHVRAMIGFDVEGC
HATREAVGTNLQLGLFSTGYNLAVPTGVYDTNNDTFSRVSAKPPPGDQFKHLIPLMYKGLPNVVR1IK1VQMLSDTLKNLSDRVRVFVLWAH
GFEILTSMKYFVKIGPERTCLCDRRATCFSTADTYACWHS1IGFDYYNPFPMDVQQWFTGNYLQSNHDLYCQVHGNAHVASCDAMTRCLAV
HECFVKRVDMT1EYPI1IDGK1NAACRKYH1VKAALADKFPVL1HDI1GPKA1KCVP0AQDWEKHYDAQPCSDKAYKIELFYAYASTSDK
FTDGVCFL0NCHYDWAYANSIVCFDTPVFVL5NLPGCDGSSLYYKNHAFHTPFAFK5AFLNKFQLPFMYSSFCE5GHQCVDSIDYVLKFS
ATCTRCNLGAVCRHHAEYRLYLDAYNMIAGFSLQNYKQFDYTNLWNTFTR
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The model was build based on crystal structure of SARS-CoV nsp14-nsp10 complex described by Ma et al. (PDB ID:5C8T) which has 94.94 sequence identity. The solvent environment was represented by the IGB7 implicit solvent model (for used homology model see Supplementary material – model.pdb). The hydrogen atoms for the docking experiment were added by GOLD 2020.3.0 software and the docking experiments were performed using CHEMPLP scoring function (Diverse Solution Options set to – Cluster size = 10 and R.M.S.D. = 0.5 Å; Search efficiency 100%) with allowed flip ring corners option. The binding pocket was defined by residues: VAL287, ARG289, VAL290, TRP292, ARG310, GLN313, ASP331, ILE332, GLY333, ASN334, LYS336, TYR351, ASP352, ALA353, GLN354, CYS356, LEU366, PHE367, TYR368, SER369, PHE384, TRP385, ASN387, ASN388, VAL389, ASP390, PHE426, HIS427, PRO429. The poses with the highest ranking within the experiments were used for presentation (Figure S1 and Table S1).

4. Molecular modeling

We only considered the residues within 15 Å of SAM in the complex with the homology model of SARS-CoV-2 nsp14 methyltransferase. The fragmentation of the protein of was done by Cuby4,15 software. Hydrogen atoms were added to the homology model and the ligands using the AMBER 14, PROPKA 3.017 and Chimera 1.13.18 software. The model was optimized at the MM level. The FF14SB force field was used for the protein while the GAFF force field was used for ligands. The solvent environment was represented by the IGB7 implicit solvent model. The SAH and compound 16 were modeled from SAM, the crystallographic ligand, and the complexes were reoptimized. The obtained structures were utilized for energy calculations. The binding ‘free’ energies were computed at the PM6-D3H4X/COSMO2 level of theory using MOPAC2016 and Cuby4,15 software. The contribution of the amino acids in the active site to the binding was examined by a “virtual glycine scanning”. The energy contributions (ΔΔG’int) were calculated as the difference between the original ΔG’int at the QM/MM level with the wild-type amino acid and the new ΔG’int with the mutated glycine residue.
5. Supporting Tables

Table S1 Selectivity of compound 15 and 16. Both compounds were tested against a panel of 33 human RNA-, DNA-, and Protein- methyltransferases at 10 µM. Targets highlighted in green were less than 50% active in the presence of the specified compound. Experiments were performed as previously described.\textsuperscript{27}

| MTase      | % Activity at 10 µM of compound |
|------------|---------------------------------|
|            | 15    | 16    |
| G9a        | 94    | 96    |
| GLP        | 96    | 95    |
| SUV39H1    | 93    | 97    |
| SUV39H2    | 99    | 103   |
| SUV420H1   | 98    | 110   |
| SUV420H2   | 95    | 107   |
| SETD2      | 96    | 103   |
| SETD7      | 100   | 111   |
| SETD8      | 90    | 90    |
| SETD8      | 90    | 90    |
| EZH2       | 100   | 111   |
| SMYD2      | 112   | 109   |
| SMYD3      | 102   | 108   |
| SUV420H2   | 95    | 107   |
| MLL1       | 97    | 100   |
| MLL3       | 100   | 91    |
| PRMT1      | 17    | 37    |
| PRMT3      | 9     | 18    |
| PRMT4      | 0     | 2     |
| PRMT5      | 64    | 71    |
| PRMT6      | 0     | 0     |
| PRMT7      | 12    | 12    |
| PRMT8      | 1     | 4     |
| PRMT9      | 93    | 60    |
| PRDM9      | 98    | 100   |
| DOT1L      | 2     | 1     |
| ASH1L      | 85    | 80    |
| NSD1       | 94    | 107   |
| NSD2       | 99    | 104   |
| NSD3       | 102   | 116   |
| DNMT1      | 3     | 2     |
| BCDIN3D    | 16    | 5     |
| DNMT3A/3L  | 0     | 0     |
| DNMT3B/3L  | 0     | 0     |
Table S2 Selectivity of compound 15 and 16. Inhibition of methyltransferase activity of all targets inhibited by compound 15 and compound 16 with more than 50% at 10 µM (Table S1) were evaluated by IC₅₀ determination. Experiments were performed as previously described\(^\text{27}\).

| Methyltransferase | Compound 15 | Compound 16 |
|-------------------|-------------|-------------|
|                   | IC₅₀ (nM)   | Hill Slope  | IC₅₀ (nM) | Hill Slope |
| PRMT1             | 2252        | 0.6         | 516       | 1.2        |
| PRMT3             | 2795        | 0.7         | 761       | 1.1        |
| PRMT4             | 109         | 1.3         | 40        | 1.3        |
| PRMT6             | 79          | 1.3         | 75        | 1.3        |
| PRMT7             | 727         | 0.7         | 2248      | 0.8        |
| PRMT8             | 139         | 1           | 88        | 1          |
| DNMT1             | 107         | 0.9         | 205       | 0.9        |
| BCDIN3D           | 130         | 0.5         | 1276      | 0.7        |
| DOT1L             | 56          | 1.1         | 52        | 1          |
| DNMT3A/3L         | 9           | 1.6         | 11        | 1.8        |
| DNMT3B/3L         | 26          | 2.1         | 29        | 1.9        |
6. Supporting figures

a

b
Figure S1. Characterization of nsp14 hits. (a) Concentration dependent nsp14 methyltransferase inhibition by each compound was assessed using the radioactivity-based assay. Binding of compounds to nsp14 was tested by SPR. (b) The steady state response (black circles) with the steady state 1:1 binding model fitting (red dashed line) and (b) the Sensorgram (solid green) with the kinetic fit (black dots) are shown for each compound. Experiments were performed in triplicate. (c) Sinefungin was used as a control for activity assay and inhibited nsp14 with an IC50 value of 18.2 ± 1.4 nM (Hill Slope of 0.7).

Figure S2. Evaluation of compound 16 binding to nsp14 by SPR. Multi-Cycle Kinetics SPR was performed by injecting increasing concentrations (from 0.003 μM to 0.66 μM) of compound 16 into the sensitised chip. (a) The steady-state response (black circles) with the steady-state 1:1 binding model fitting (red dashed line), and (b) the sensorgram (black dots) with the kinetic fit (solid lines) are shown. The experiments were performed in quadruplicate. The K_D value was 17.9 ± 2.5 nM.
Figure S3 Mechanism of action (MOA) of compound 15 and 16. MOA of compound 15 (A and B) and 16 (C and D) were determined by monitoring the changes in IC₅₀ values at various concentrations of SAM (A and C) and fixed concentration of RNA (250 nM), and varying concentrations of RNA (B and D) at fixed concentration of SAM (1.25 µM). Both compounds showed a SAM competitive and RNA noncompetitive patterns of nsp14 inhibition. Experiments were performed in triplicate.
Figure S4 Selectivity assay by IC₅₀ determination. Effect of (a) compound 15 and (b) compound 16 on targets inhibited by more than 50% at 10 µM were re-evaluated by IC₅₀ determination. IC₅₀ values are presented in Table S2.

Figure S5 Selectivity of compound 15 and 16 against human RNMT. Effect of compound 15 (IC₅₀ of 700 nM) and 16 (IC₅₀ of 500 nM) on activity of human RNMT (amino acids 123 to 476; 354aa) was assessed using a radioactivity-based enzyme assay. Experiments were performed in triplicate.
Figure S6 Docking poses with the highest ranking generated by GOLD software for compounds 12-19, and standards SIN and SAM. The figures and A and B show the highest scored docking poses from two different angles depicting how the aromatic moieties of the compounds occupy the lateral cavity of the enzyme.
Figure S7 The contribution of selected amino acid residues of SARS-CoV-2 nsp14 methyltransferase to the binding obtained by the virtual glycine scan in kcal mol\(^{-1}\) (A). We have examined the binding of 16 to the homology model of SARS-CoV-2 nsp14 methyltransferase at the semiempirical quantum mechanical (SQM) PM6-D3H4XCOSMO\(^{23-25}\) level of theory and compared it to the binding of SAH. The models were built from the SAM (crystallographic ligand) manually and optimized at the AMBER\(^{16}\) level prior the SQM energy calculations. 16 had considerably more favorable (negative) binding ‘free’ energy (\(\Delta G\)’int)\(^{21,22}\) than SAH (-40.3 and -33.5 kcal mol\(^{-1}\), respectively). The contribution of single amino acids of SARS-CoV-2 nsp14 methyltransferase to the binding (\(\Delta \Delta G\)’int) was studied by a virtual glycine scan. \(\Delta \Delta G\)’int was most favorable in the case of Asp352 for both 16 and SAH (\(\Delta \Delta G\)’int of -16.6 and 16.8 kcal mol\(^{-1}\)). The increase in binding towards 16 was mainly due to the Phe367, Asn388 and Pro429 residues (\(\Delta \Delta G\)’int of -5.7, -1.7 and -1.9 kcal mol\(^{-1}\) for 16 and -4.4, -0.6 and 0.5 kcal mol\(^{-1}\) for SAH, respectively). The modeled structures of SARS-CoV-2 nsp14 methyltransferase with 16 (B) and SAH (C).
9. $^1$H and $^{13}$C NMR of new compounds

Figure S8. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 2 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S9. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 3 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S10. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 4 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S11. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 5 measured in DMSO-$d_6$ at r.t.
(25 °C).

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Figure S12. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 6 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S13. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 7 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S14. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 8 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S15. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 9 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S16. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 10 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S17. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 11 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S18. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 12 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S19. \(^1\text{H}\) (top) and \(^{13}\text{C}\) APT (bottom) NMR spectra of compound 13 measured in DMSO-\(d_6\) at r.t. \(25 \, ^{\circ}\text{C}\).
Figure S20. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 14 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S21. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 15 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S22. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 16 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S23. $^1$H (top) NMR spectra of compound 17 measured in DMSO-$d_6$ at r.t. (25 °C) and $^{13}$C APT (bottom) NMR spectra measured in DMSO-$d_6$ 50 °C.
Figure S24. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 18 measured in DMSO-$d_6$ at r.t. (25 °C).
Figure S25. $^1$H (top) and $^{13}$C APT (bottom) NMR spectra of compound 19 measured in DMSO-$d_6$ at r.t. (25 °C).
10. HPLC purity of final SAH analogues

The final free SAH analogues were measured at their absorption maximum as solutions in DMSO (MeOH/H$_2$O in case of compound 19). Water with 0.05% HCOOH was used as mobile phase A, and MeCN with 0.05% HCOOH was used as mobile phase B. Linear gradient of 5 to 95 % of mobile phase B in mobile phase A over 6 minutes was used for the analysis.

Table S3. HPLC purities of final compounds, $\lambda_{\text{max}} = $ absorption maximum, $t_r = $ retention time

| Compound | $\lambda_{\text{max}}$ (nm) | $t_r$ (min) | Purity (%) |
|----------|-----------------------------|-------------|------------|
| 12       | 282                         | 2.67        | 97.4       |
| 13       | 292                         | 3.42        | 98.7       |
| 14       | 311                         | 3.95        | 98.3       |
| 15       | 321                         | 3.91        | 98.1       |
| 16       | 314                         | 3.24        | 97.3       |
| 17       | 330                         | 3.06        | 97.0       |
| 18       | 304                         | 3.83        | 97.3       |
| 19       | 279                         | 3.12        | 97.6       |

Figure S26. HPLC chromatogram of compound 12 measured at $\lambda_{\text{max}} = 282$ nm, $t_r = 2.67$ min, purity 97.4 %.
Figure S27. HPLC chromatogram of compound 13 measured at $\lambda_{\text{max}} = 292$ nm, $t_r = 3.42$ min, purity 98.7%.

Figure S28. HPLC chromatogram of compound 14 measured at $\lambda_{\text{max}} = 311$ nm, $t_r = 3.95$ min, purity 98.3%.
**Figure S29.** HPLC chromatogram of compound 15 measured at $\lambda_{\text{max}} = 321$ nm, $t_r = 3.91$ min, purity 98.1%.

**Figure S30.** HPLC chromatogram of compound 16 measured at $\lambda_{\text{max}} = 314$ nm, $t_r = 3.24$ min, purity 97.3%.
Figure S31. HPLC chromatogram of compound 17 measured at $\lambda_{\text{max}} = 330$ nm, $t_r = 3.06$ min, purity 97.0 %.

Figure S32. HPLC chromatogram of compound 18 measured at $\lambda_{\text{max}} = 304$ nm, $t_r = 3.83$ min, purity 97.3 %.
Figure S33. HPLC chromatogram of compound 19 measured at $\lambda_{\text{max}} = 279$ nm, $t_r = 3.12$ min, purity 97.6%.

11. References

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