Supplementary Information

Enantioselective total synthesis of bioactive natural product Sch 642305: A structurally novel inhibitor of bacterial DNA primase and HIV-1 Tat transactivation

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Compound 6:

$[\alpha]_D^{23} = +77.3^0$ (*c*,1.1, $CHCl_3$)

IR (neat) $\overline{\nu}_{max}$ 3457, 2955, 2857, 1638, 1087 cm^{-1}

^1H NMR (300MHz, $CDCl_3$): δ 5.93-5.77(m, 3H), 5.54-5.45(m, 2H), 5.17-5.11(m, 2H), 4.35(d, *J* = 7.8 Hz, 1H), 2.97(s, 1H), 2.94(s, 1H), 2.69-2.61 (m, 1H), 2.51(dd, , *J* = 9.9 and 3.1 Hz, 1H), 2.34-2.21(m, 2H), 2.09(bs, 1H), 1.34-1.27(m, 2H), 0.91(s, 9H), 0.08(s, 3 H), 0.05(s, 3H).

^{13}C NMR (75MHz, $CDCl_3$): 135.51, 135.10, 134.00, 133.70, 132.40, 118.85, 71.32, 66.27, 49.33, 47.69, 45.84, 45.73, 43.66, 25.86(3C), 18.03, -4.77(2C).

HRMS calcd for $C_{20}H_{32}O_2SiNa$ (M+Na): 355.2069 found: 355.2056.

Compound 7:

$[\alpha]_D^{24} = -10.9^0$ (*c*,1.1, $CHCl_3$)

IR (neat) $\overline{\nu}_{max}$ 2957, 2856, 1703, 1090 cm^{-1}

^1H NMR (300MHz, $CDCl_3$): δ 6.19(dd, *J* = 5.7 and 3.0 Hz, 1H), 6.04(dd, *J* = 5.7 and 3.0 Hz, 1H), 5.70-5.56(m, 1H), 5.02-4.94(m, 2H), 3.92-3.84(m, 1H) 3.33(s, 1H) 3.15(s, 1H), 2.88-2.79(m, 2H), 2.49-2.44(m, 1H), 2.29(d, *J* = 13.2 Hz, 1H), 1.88-1.58(m, 3H), 1.37(d, *J* = 7.8 Hz, 1H), 1.26(d, *J* = 7.8 Hz, 1H), 0.96(s, 9 H), 0.15 (s, 3H), 0.09(s, 3H).

^{13}C NMR (75MHz, $CDCl_3$): 212.41, 136.88, 135.86, 135.69, 116.84, 73.36, 52.14, 49.45, 47.28, 45.94, 44.79, 43.57, 37.01, 36.83, 25.92(3C), 18.11, -3.87, -4.89.

HRMS calcd for $C_{20}H_{32}O_2SiNa$ (M+Na): 355.2069 found: 355.2065.

Compound 8:

$[\alpha]_D^{24} = -127.4^0$ (*c*,1.35, $CHCl_3$)

IR (neat) $\overline{\nu}_{max}$ 2928, 1687, 1099 cm^{-1} .

^1H NMR (300MHz, $CDCl_3$): δ 6.79(dd, *J* = 1.8 and 10.2 Hz, 1H), 5.92(d, *J* = 10.2 Hz, 1H), 5.78-5.64(m, 1H), 5.10-5.03(m, 2H), 4.21(d, *J* = 6.3 Hz, 1H), 2.62-2.50(m, 2H), 2.20-1.90(m, 3H), 0.93(s, 9 H), 0.14(s, 3H), 0.13(s, 3H).

^{13}C NMR (75MHz, $CDCl_3$): 198.96, 153.61, 134.89, 128.60, 117.61, 71.31, 43.67, 40.84, 36.20, 25.73 (3C), 18.01, -4.23, -4.72.

HRMS calcd for $C_{15}H_{26}O_2SiNa$ (M+Na): 289.1600 found: 289.1606.

Compound 9

$[\alpha]_D^{24} = -85.7^0$ (*c*, 0.7, $CHCl_3$)

IR (neat) $\bar{\nu}_{max}$ 2957, 2932, 1733, 1685 cm^{-1}.

^1H NMR (300MHz, $CDCl_3$): δ 6.78(dd, *J* = 1.8 and 10.2 Hz, 1H), 5.95(dd, *J* = 1.8 and 10.2 Hz, 1H), 5.87-5.74(m, 1H), 5.14(d, *J* =14.7 Hz, 2H), 4.41(d, *J* = 8.7 Hz, 1H), 4.31-4.06(m, 2H), 2.82-2.67(m, 2H), 2.62-2.50(m, 2H), 2.35-2.22(m, 2H), 1.26(t, *J* = 6.9 Hz, 3H), 0.92(s, 9 H), 0.15(s, 3H), 0.13(s, 3H).

^{13}C NMR (75MHz, $CDCl_3$): 199.16, 172.05, 152.11, 133.59, 127.57, 118.31, 69.45, 60.47, 46.16, 45.56, 32.16, 31.58, 25.69 (3C), 17.93, 14.11, -3.98, -4.66.

HRMS calcd for $C_{19}H_{32}O_4SiNa$ (M+Na): 375.1968 found: 375.1957.

Compound 10:

$[\alpha]_D^{25} = -89.0^0$ (*c*, 1.0, $CHCl_3$)

IR (neat) $\bar{\nu}_{max}$ 3430, 2956, 1734 cm^{-1}.

^1H NMR (300MHz, $CDCl_3$): δ 5.85-5.66(m, 3H), 5.15-5.07(m, 2H), 4.17-4.09(m, 4H), 2.74(dd, *J* = 15.9 and 3.6 Hz, 1H), 2.53-2.26(m, 4H), 1.98-1.87(m, 1H), 1.78-1.69(m, 1H), 1.26(t, *J* = 7.2 Hz, 3H), 0.89(s, 9 H), 0.09(s, 3H), 0.07(s, 3H).

^{13}C NMR (75MHz, $CDCl_3$): 173.95, 134.43, 132.04, 130.76, 117.65, 71.65, 69.58, 60.62, 44.08, 41.83, 34.71, 31.63, 25.82(3C), 17.99, 14.16, -3.78, -4.57.

HRMS calcd for $C_{19}H_{34}O_4SiNa$ (M+Na): 377.2124 found: 377.2103

Compound 11:

$[\alpha]_D^{24} = -12.0^0$ (*c*, 1.0, $CHCl_3$)

IR (neat) $\bar{\nu}_{max}$ 3451, 2929, 1734 cm^{-1}.

^1H NMR (300MHz, $CDCl_3$): δ 5.86-5.66(m, 3H), 5.13-5.07(m, 2H), 4.17-4.09(m, 3H), 3.96(d, *J* = 6.6 Hz, 1H), 2.59(d, *J* = 7.5 Hz, 2H), 2.39-2.30(m, 1H), 2.21-2.06(m, 3H), 1.87-1.78(m, 1H), 1.26(t, *J* = 6.9 Hz, 3H), 0.89(s, 9 H), 0.08(s, 3H), 0.06(s, 3H).

^{13}C NMR (75MHz, $CDCl_3$): 174.20, 135.30, 132.91, 128.44, 117.27, 68.91, 65.17, 60.48, 41.11, 37.32, 33.79, 32.95, 25.79(3C), 17.96, 14.18, -4.03, -4.64.

HRMS calcd for $C_{19}H_{34}O_4SiNa$ (M+Na): 377.2124 found: 377.2137

Compound 12:

$[\alpha]_D^{24} = +31.0^0$ (*c*, 1.0, $CHCl_3$)

IR (neat) $\bar{\nu}_{max}$ 2930, 2857, 1734 cm^{-1}.

^1H NMR (300MHz, $CDCl_3$): δ 7.71-7.65(m, 4H), 7.44-7.35(m, 6H), 5.78-5.65(m, 1H), 5.50-5.34(m, 2H), 4.99-4.89(m, 2H), 4.32(s, 1H), 4.17-4.02(m, 2H), 3.81(bs, 1H), 2.83(dd, *J* = 2.7 and 7.2 Hz, 2H), 2.29-2.21(m, 1H), 2.12-1.95(m, 3H), 1.25(d, *J* =6.9 Hz, 3H), 1.06(s, 9H), 0.89(s, 9 H), 0.03(s, 3H), 0.02(s, 3H).

^{13}C NMR (75MHz, $CDCl_3$): 173.91, 136.12, 135.97, 135.81, 134.26, 133.44, 130.13, 129.74, 129.70, 129.51, 127.62, 127.42, 116.73, 68.10, 66.64, 59.96, 41.30, 36.98, 34.51, 32.04, 26.96(3C), 25.78 (3C), 19.33, 17.93, 14.15, -4.39, -4.74.

HRMS calcd for $C_{35}H_{52}O_4Si_2Na$ (M+Na): 615.3302 found: 615.3327

Compound 13:

$[\alpha]_D^{24} = +21.0^0$ (*c*, 0.95, $CHCl_3$)

IR (neat) $\bar{\nu}_{max}$ 2928, 2856, 1731 cm^{-1}.

^1H NMR (300MHz, $CDCl_3$): δ 7.70-7.64(m, 4H), 7.45-7.34(m, 6H), 5.83-5.62(m, 2H), 5.50-5.34(m, 2H), 5.11-4.88(m, 5H), 4.31(bs, 1H), 3.81(bs, 1H), 2.84(d, *J* = 7.2 Hz, 2H), 2.42-2.16(m, 3H), 2.12-1.95(m, 3H), 1.20(d, *J* =6.3 Hz, 3H), 1.06(s, 9H), 0.89(s, 9H), 0.03(s, 3H), 0.02(s, 3H).

^{13}C NMR (75MHz, $CDCl_3$): 173.40, 136.20, 135.96, 135.84, 134.28, 133.88, 133.46, 130.13, 129.84, 129.74, 129.51, 127.63, 127.43, 117.55, 116.69, 69.60, 68.10, 66.57, 41.32, 40.37, 36.91, 34.67, 31.81, 26.99(3C), 25.86 (3C), 19.36, 17.95, -4.41, -4.67.

HRMS calcd for $C_{38}H_{56}O_4Si_2Na$ (M+Na): 655.3615 found: 655.3629

Compound 15:

$[\alpha]_D^{23} = +66.0^0$ (*c*, 0.5, $CHCl_3$)

IR (neat) $\bar{\nu}_{max}$ 2929, 2857, 1726 cm^{-1}.

^1H NMR (300MHz, $CDCl_3$): δ 7.72-7.67(m, 4H), 7.43-7.33(m, 6H), 5.73(dt, *J* = 5.1 and 11.1 Hz, 1H), 5.63-5.50(m, 2H), 5.28(dd, *J* = 5.1 and 10.2 Hz, 1H), 5.07(m, 1H), 4.25(m, 1H), 3.92(t, *J* = 4.2 Hz, 1H), 2.94-2.80(m, 1H), 2.73(dd, *J* = 11.1 and 6.8 Hz, 1H),

2.43(dd, *J* = 16.8 and 2.1 Hz, 1H), 2.27-2.06(m, 4H), 1.93-1.80(m, 1H), 1.21(d, *J* = 6.6 Hz, 3H), 1.04(s, 9H), 0.94(s, 9 H), 0.12(s, 3H), 0.11(s, 3H).

^{13}C NMR (75MHz, $CDCl_3$): 173.07, 136.28, 135.92, 134.34, 133.74, 133.41, 129.79, 129.36, 128.04, 127.73, 127.17, 123.91, 69.54, 69.32, 69.25, 42.47, 39.96, 38.44, 27.06(3C), 25.86 (3C), 19.66, 18.08, 17.63, -3.44, -4.20.

HRMS calcd for $C_{36}H_{52}O_4Si_2Na$ (M+Na): 627.3302 found: 627.3329.

Compound 16:

$[\alpha]_D^{26} = +77.5^0$ (*c*, 0.4, $CHCl_3$)

IR (neat) $\overline{\nu}_{max}$ 2929, 2857, 1727, 1677 cm^{-1}.

^{1}H NMR (300MHz, $CDCl_3$): δ 7.71-7.68(m, 2H), 7.59-7.55(m, 2H), 7.50-7.34(m, 6H), 6.47(dd, *J* = 9.9 and 5.7 Hz, 1H), 5.93(d, *J* = 9.9 Hz, 1H), 5.56-5.46(m, 1H), 5.38-5.32(m, 1H), 5.05-5.01(m, 1H), 4.15(d, *J* =5.4 Hz, 1H), 3.04-2.85(m, 3H), 2.72-2.58(m, 2H), 2.45-2.17(m, 2H), 1.77(dd, *J* = 14.1 and 6.3 Hz, 1H), 1.17(d, *J* = 6.6 Hz, 3H), 1.04(s, 9H).

^{13}C NMR (75MHz, $CDCl_3$): 200.39, 172.56, 147.34, 136.06, 135.94, 133.52, 132.73, 130.92, 130.30, 130.23, 129.94, 128.00, 127.60, 123.88, 68.79, 68.55, 47.14, 40.15, 39.66, 29.05, 27.01(3C), 24.90, 19.54, 17.58.

HRMS calcd for $C_{30}H_{36}O_4SiNa$ (M+Na): 511.2281 found: 511.2285.

Compound 17:

$[\alpha]_D^{24} = -31.4^0$ (*c*, 0.7, $CHCl_3$)

IR (neat) $\overline{\nu}_{max}$ 2959, 2858, 1724, 1712 cm^{-1}.

^{1}H NMR (300MHz, $CDCl_3$): δ 7.71-7.64(m, 4H), 7.47-7.36(m, 6H), 5.00(m, 1H), 4.10(bs, 1H), 2.85-2.69(m, 2H), 2.60-2.42(m, 2H), 2.23-2.03(m, 5H), 1.92-1.63(m, 4H), 1.31-1.25(m, 2H), 1.21(d, *J* = 6.6 Hz, 3H), 1.11(s, 9H), 1.02-0.84(m, 1H).

^{13}C NMR (75MHz, $CDCl_3$): 210.88, 171.50, 136.04, 135.89, 133.85, 133.09, 130.02, 129.94, 127.81, 127.68, 72.95, 72.00, 50.17, 40.47, 40.40, 35.32, 31.06, 29.46, 27.27(3C), 23.16, 22.98, 21.63, 19.56, 18.24.

HRMS calcd for $C_{30}H_{40}O_4SiK$ (M+K): 531.2333 found: 531.2339

Compound 18:

$[\alpha]_D^{25}$= +140.0^0 (*c*, 0.35, $CHCl_3$)

IR (neat) $\bar{\nu}_{max}$ 2928, 2856, 1725, 1678 cm^{-1}.

^{1}H NMR (300MHz, $CDCl_3$): δ 7.72-7.57(m, 4H), 7.48-7.34(m, 6H), 6.48(dd, *J* = 9.9 and 5.1 Hz, 1H), 5.87(d, *J* = 9.9 Hz, 1H), 5.05(m, 1H), 4.20(m, 1H), 2.84-2.67(m, 3H), 2.51-2.38(m, 1H), 2.17-2.05(m, 2H), 1.76-1.50(m, 4H), 1.44-1.25(m, 1H), 1.22(d, *J* = 6.6 Hz, 3H), 1.06(s, 9H), 1.00-0.83(m, 1H).

^{13}C NMR (75MHz, $CDCl_3$): 200.44, 171.47, 147.31, 136.01, 135.92, 133.49, 132.75, 130.20, 130.02, 129.92, 127.99, 127.60, 73.15, 68.25, 46.62, 39.08, 37.47, 29.67, 27.03(3C), 23.34, 22.65, 21.70, 19.51, 18.26.

HRMS calcd for $C_{30}H_{38}O_4SiNa$ (M+Na): 513.2437 found: 513.2461.

Compound 1:

$\alpha]_D^{26}$ = +71.0^0 (*c*, 0.31, CH_3OH)

IR (neat) $\bar{\nu}_{max}$ 3423, 2933, 1722, 1677 cm^{-1}

^{1}H NMR (300MHz, $CDCl_3$): δ 7.03(dd, *J* = 9.9 and 5.7 Hz, 1H), 5.96(d, *J* = 9.9 Hz, 1H), 5.05(m, 1H), 4.22(dd, *J* = 5.7 and 3.6 Hz, 1H), 2.88-2.78(m, 1H), 2.72-2.62(m, 2H), 2.53(dd, *J* = 16.8 and 11.7 Hz, 1H), 2.23-2.06(m, 2H), 1.93-1.78(m, 1H), 1.65-1.50(m, 1H), 1.48-1.32(m, 2H), 1.28(d, *J* = 6.6 Hz, 3H), 1.23(m, 1H), 1.14-1.05(m, 1H).

^{13}C NMR (75MHz, $CDCl_3$): 202.30, 173.69, 149.39, 130.57, 74.63, 67.08, 47.68, 39.77, 37.75, 30.69, 24.13, 24.05, 22.52, 18.52

HRMS calcd for $C_{14}H_{20}O_4Na$ (M+Na): 275.1259 found: 275.1268.

Table 1. Comparison of ^{13}C spectral data of Sch 642305 (natural and synthetic)

natural [a]	**synthetic**	**natural** [a]	**synthetic**
202.6	202.3	39.9	39.8
173.9	173.7	37.9	37.7
149.6	149.4	30.8	30.7
130.7	130.6	24.2	24.1
74.8	74.6	24.1	24.0
67.2	67.1	22.6	22.5
47.8	47.7	18.7	18.5

[a] see ref. 4 in the manuscript.