Supporting Information

Selective C9orf72 G-quadruplex-binding small molecules ameliorate pathological signatures of ALS/FTD models

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Figure S2. CD spectra of DNA and RNA G4C2 G4s with compounds at different pH.

A. CD spectra (left panels) and CD melting curves (right panels) of DNA (G4C2)$_4$ G4 with compounds cA, cB, and cC at pH6 and pH7, respectively. B. CD spectra (left panels) and CD melting curves (right panels) of RNA (G4C2)$_2$ G4 with compounds cA, cB, and cC at pH6 and pH7, respectively.
**Figure S3.** Isolation of compound chrexanthomycin A (cA) and its UV spectrum.

The purity percentage of compound cA (Peak 2) is 99.2%.

| Peak | Retention time | Area     | %Area | Height |
|------|----------------|----------|-------|--------|
| 1    | 14.225         | 12272    | 0.8   | 1252   |
| 2    | 15.242         | 1529906  | 99.2  | 113437 |
Figure S4. Positive ion HRMS spectrum of cA (Calcd:621.1239, found:621.1235).

HRMS(m/z): calcd for C$_{31}$H$_{25}$O$_{14}$, 621.1239 [M+H]$^+$, found 621.1235.
**Figure S5.** $^1$H NMR spectrum of cA (800 MHz, CD$_3$OD).

$^1$H NMR (800 MHz, Methanol-$d_4$) δ 8.0 (d, $J = 8.2$ Hz, 1H), 7.8 (d, $J = 7.9$ Hz, 1H), 7.4 (t, $J = 8.0$ Hz, 1H), 6.8 (s, 1H), 6.2 (d, $J = 3.7$ Hz, 1H), 5.8 (d, $J = 5.5$ Hz, 1H), 4.3 (t, $J = 4.3$ Hz, 1H), 4.2 (t, $J = 5.1$ Hz, 1H), 2.7 (s, 1H), 1.7 (s, 2H).
Figure S6. $^{13}$C NMR spectrum of cA (200 MHz, CD$_3$OD).

$^{13}$C NMR (200 MHz, Methanol-$d_4$) $\delta$ 182.9, 170.9, 165.1, 160.1, 152.1, 150.6, 148.4, 146.4, 144.8, 142.2, 138.8, 134.2, 134.0, 125.8, 125.0, 122.7, 121.3, 120.2, 118.9, 115.2, 114.9, 113.9, 108.2, 107.6, 72.1, 68.3, 24.3, 22.9.
Figure S7. COSY spectrum of cA (800 MHz, CD$_3$OD).
Figure S8. HSQC spectrum of cA (800 MHz, CD$_3$OD).
Figure S9. HMBC spectrum of cA (800 MHz, CD$_3$OD).
Figure S10. NOESY spectrum of cA (800 MHz, CD$_3$OD).
Figure S11. Isolation of compound chreanthomycin B (cB) and its UV spectrum.

The purity percentage of compound cB (Peak 2) is 99.2%.

| Peak | Retention time | Area   | %Area | Height |
|------|----------------|--------|-------|--------|
| 1    | 17.765         | 13644  | 0.08  | 2650   |
| 2    | 18.079         | 18177452 | 99.2  | 1214549|
Figure S12. Positive ion HRMS spectrum of cB (Calcd: 635.1395, found: 635.1387).

HRMS(m/z): calcd for C\textsubscript{32}H\textsubscript{27}O\textsubscript{14}, 635.1395 [M+H]\textsuperscript{+}, found 635.1387.
Figure S13. $^1$H NMR spectrum of cB (800 MHz, DMSO-$d_6$).

$^1$H NMR (800 MHz, DMSO-$d_6$) δ 13.1 (s, 1H), 11.9 (s, 1H), 7.9 (dd, $J = 8.1$, 1.5 Hz, 1H), 7.8 (d, $J = 8.1$ Hz, 1H), 7.5 (t, $J = 7.9$ Hz, 1H), 6.8 (d, $J = 15.8$ Hz, 1H), 6.1 (d, $J = 4.7$ Hz, 1H), 5.9 (d, $J = 4.4$ Hz, 1H), 4.1 (t, $J = 4.0$ Hz, 1H), 4.0 (t, $J = 3.5$ Hz, 1H), 4.0 (s, 3H), 3.3 (s, 2H), 1.7 (s, 1H).
Figure S14. $^{13}$C NMR spectrum of cB (200 MHz, DMSO-$d_6$).

$^{13}$C NMR (200 MHz, DMSO-$d_6$) $\delta$ 181.7, 169.2, 163.0, 153.4, 149.0, 147.6, 146.7, 145.0, 143.2, 139.9, 138.0, 135.8, 124.5, 123.5, 121.2, 119.1, 117.8, 116.3, 113.6, 113.5, 107.4, 106.3, 99.1, 70.0, 66.0, 61.6, 50.1, 29.5, 23.4, 22.3.
Figure S15. COSY spectrum of cB (800 MHz, DMSO-d$_6$).
Figure S16. HSQC spectrum of cB (800 MHz, DMSO-d$_6$).
Figure S17. HMBC spectrum of cB (800 MHz, DMSO-d$_6$).
Figure S18. *NOESY spectrum of cB (800 MHz, DMSO-d$_6$).*
Figure S19. Isolation of compound chrexanthomycin C (cC) and its UV spectrum.

The purity percentage of compound cC (Peak 2) is 99.84%.

| Peak | Retention time | Area    | %Area | Height |
|------|----------------|---------|-------|--------|
| 1    | 15.191         | 1565    | 0.02  | 256    |
| 2    | 15.6           | 6580915 | 99.84 | 512863 |
| 3    | 16.575         | 9140    | 0.14  | 910    |
Figure S20. Positive ion HRMS spectrum of cC (Calcd: 639.1344, found: 639.1332).

HRMS(m/z): calcd for $C_{31}H_{27}O_{15}$, 639.1344 [M+H]$^+$, found 639.1332.
Figure S21. $^1$H NMR spectrum of cC (800 MHz, CD$_3$OD).

$^1$H NMR (800 MHz, Methanol-$d_4$) $\delta$ 7.71-7.76 (m, 1H), 7.29-7.21 (m, 2H), 6.78-6.71 (m, 1H), 3.8 (s, 1H), 3.7 (t, $J = 8.6$ Hz, 1H), 3.6 (t, $J = 9.4$ Hz, 1H), 3.6 – 3.6 (m, 1H), 1.8 – 1.7 (m, 2H).
Figure S22. $^{13}$C NMR spectrum of cC (200 MHz, CD$_3$OD).

$^{13}$C NMR (201 MHz, Methanol-$d_4$) δ 183.5, 173.0, 172.4, 147.5, 145.8, 134.5, 125.7, 122.3, 121.7, 119.0, 117.5, 116.6, 108.7, 77.4, 76.6, 75.5, 73.0, 31.1, 20.9, 14.5.
Figure S23. COSY spectrum of cC (800 MHz, DMSO-d$_6$).
Figure S24. HSQC spectrum of cC (800 MHz, CD$_3$OD).
Figure S25. HMBC spectrum of cC (800 MHz, CD$_3$OD).
Figure S26. NOESY spectrum of cC (800 MHz, CD$_3$OD).
Figure S27. Open form single-crystal structure of cA.

Figures are 40% probability atom displacement ellipsoids, with labeling schemes.
Figure S28. Cyclic form single-crystal structure of cA.

Figures are 40% probability atom displacement ellipsoids, with labeling schemes.
Figure S29. cA does not bind other G4C2 structures.

A-E. The 1D ¹H-NMR spectra of DNA (G4C2)₂ G4 (A), double-stranded DNA G4C2 (B), single-stranded two-repeat G4C2 (C), RNA G4C2 hairpin form (D), double-stranded RNA G4C2 (E) and those titrated with cA at 1:10 (pink) ratio. The imino region of (A), (B), (D) and (E) and the sugar ring proton region of (C) were shown. To prepare the RNA G4C2 hairpin form, a four-repeat G4C2 sequence was dissolved in 10 mM sodium phosphate buffer with 100 mM LiCl. For single-stranded two-repeat G4C2, oligonucleotide was dissolved in 100% D₂O. Other samples were prepared following the procedure described in Experimental Section.
**Figure S30.** cA does not bind non-G4C2 G4s and AT-rich sequences.

A-F: Imino proton region of 1D $^1$H-NMR spectra of htel21_T18 G4 (A), htel23_hybrid G4 (B), c-kit G4 (C), aptamer RNA hairpin form (D), double-stranded AT-rich DNA (E) and aromatic proton region of single-stranded T rich DNA (F) and those titrated with cA at the ratio of 1:10 (pink). To prepare the single-stranded T-rich DNA, oligonucleotide was dissolved in 100% D$_2$O. Other samples were prepared following the procedure described in **Experimental Section**.
Figure S31. DB1246 non-selectively binds different G4s.

A-D: Imino region of 1D $^1$H-NMR spectra of DNA (G4C2)$_4$ G4 (A), RNA (G4C2)$_2$ G4 (B), DNA (G4C2)$_2$ G4 (C) and human telomeric htel21 T18 G4 (D) and those titrated with DB1246 at 1:5 ratio (pink).
Figure S32. Compound cA could enter cells.

The UPLC-MS spectra of samples from cell lysates and the corresponding culture media of cA-treated Neuro2a cell cultures. The UPLC spectra (Extracted Ion Chromatogram, EIC with the [M+H] of 621.1±0.1) in the top and middle panels in different colors were recognized to be black (pure cA as a positive control), light purple (cA:10 μg/mL ≈ 16.13 μM, 24h, cell lysate), light blue (cA:10 μg/mL ≈ 16.13 μM, 24h, culture medium), red (cA:10 μg/mL ≈ 16.13 μM, 48h, cell lysate), green (cA:10 μg/mL ≈ 16.13 μM, 48h, culture medium), dark red (cA:20 μg/mL ≈ 32.26 μM, 48h, cell lysate), dark blue (cA:20 μg/mL ≈ 32.26 μM, 48h, culture medium). The bottom panel showed the UV Chromatogram of the cA peak (a red triangle and a blue dashed line labeled in the top and middle panels) at the retention time of 9.8 minutes and the MS spectrum of cA (red triangle labeled peak: [M+H] = 621.1239).
Table S1. Crystal data and structure refinement for cA.

| Property                      | Value                          |
|-------------------------------|--------------------------------|
| Identification code           | ye6CuLT                       |
| Empirical formula             | C_{31.5}H_{32}O_{17.5}        |
| Formula weight                | 690.595                       |
| Temperature/K                 | 100.00(10)                    |
| Crystal system                | monoclinic                    |
| Space group                   | P2₁                            |
| a/Å                           | 4.3814(3)                     |
| b/Å                           | 15.5179(7)                    |
| c/Å                           | 22.1729(13)                   |
| α/°                           | 90                             |
| β/°                           | 91.317(5)                     |
| γ/°                           | 90                             |
| Volume/Å³                     | 1507.14(15)                   |
| Z                             | 2                              |
| ρcalc/g/cm³                   | 1.522                          |
| μ/mm⁻¹                        | 1.084                          |
| F(000)                        | 725.0                          |
| Crystal size/mm³              | 0.2 × 0.08 × 0.02              |
| Radiation                     | CuKα (λ = 1.54184)            |
| 2Θ range for data collection/° | 6.96 to 144.9                 |
| Index ranges                  | -3 ≤ h ≤ 5, -19 ≤ k ≤ 18, -24 ≤ l ≤ 27 |
| Reflections collected         | 8054                           |
| Independent reflections       | 5136 [R_{int} = 0.0588, R_{sigma} = 0.1042] |
| Data/restraints/parameters    | 5136/326/608                   |
| Goodness-of-fit on F²         | 1.000                          |
| Final R indexes [I>=2σ (I)]   | R₁ = 0.0598, wR₂ = 0.1153      |
| Final R indexes [all data]    | R₁ = 0.0892, wR₂ = 0.1285      |
| Largest diff. peak/hole / e Å⁻³ | 0.26/-0.29                     |
| Flack parameter               | 0.1(3)                        |
Table S2. Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\AA^2\times 10^3$) for cA.

| Atom | $x$    | $y$    | $z$    | $U(\text{eq})$ |
|------|--------|--------|--------|----------------|
| O1   | 8429(18)| 5751(4)| 2906(3)| 33.2(16)       |
| O1A  | 10096(18)| 5717(4)| 2929(3)| 34.8(17)       |
| O2   | 10549(16)| 6182(4)| 3756(3)| 35.1(14)       |
| O2A  | 8796(16)| 6517(4)| 3689(3)| 32.6(14)       |
| O3   | 5390(20)| 5844(5)| 4396(4)| 26.5(18)       |
| O3A  | 5835(19)| 5911(4)| 4559(4)| 21.8(18)       |
| O4   | 971(7)  | 5651.1(18)| 5087.9(14)| 29.4(7)       |
| O5   | -2009(8)| 6330.6(19)| 5928.7(14)| 33.0(7)       |
| O6   | -547(7) | 4248.6(19)| 8147.2(14)| 29.9(7)       |
| O7   | 1072(7) | 4425.0(18)| 7064.5(13)| 26.0(6)       |
| O8   | 4815(7) | 3161.9(19)| 6719.4(14)| 27.7(7)       |
| O9   | 6328(14)| 3320(4)  | 2451(3)  | 33.8(14)       |
| O9A  | 6439(17)| 4960(5)  | 2373(4)  | 58(2)          |
| O10  | 862(7)  | 4652.2(19)| 9090.4(14)| 31.7(7)       |
| O11  | -2289(7)| 2624(2)  | 8512.9(14)| 34.9(7)       |
| O12  | 679(10) | 2168(2)  | 9662.6(17)| 48.3(10)      |
| O13  | 3510(20)| 4982(7)  | 10589(4) | 36(2)          |
| O13A | 2610(20)| 5013(7)  | 10619(4) | 38(2)          |
| O14  | 3380(20)| 5829(6)  | 9767(4)  | 58(2)          |
| O14A | 4708(15)| 5603(4)  | 9779(3)  | 31.5(14)       |
| C1   | 8880(40)| 5647(9)  | 3422(8)  | 30(2)          |
| C1A  | 8770(40)| 5777(9)  | 3481(8)  | 28(2)          |
| C2   | 7790(30)| 4857(7)  | 3754(7)  | 29.4(17)       |
| C2A  | 7690(30)| 5026(7)  | 3792(7)  | 26.9(16)       |
| C3   | 6090(40)| 5019(9)  | 4280(8)  | 26.6(19)       |
| C3A  | 6270(50)| 5105(9)  | 4350(8)  | 27.8(16)       |
| C4   | 5392(10)| 4350(3)  | 4677(2)  | 26.4(8)        |
| C5   | 4088(9) | 4417(3)  | 5289.4(19)| 23.7(9)       |
| C6   | 2075(9) | 5052(3)  | 5478(2)  | 24.5(9)        |
| C7   | 1024(9) | 5089(3)  | 6077(2)  | 24.5(9)        |
| C8   | -1053(9)| 5755(3)  | 6272(2)  | 25.6(9)        |
| C9   | -1992(9)| 5713(3)  | 6901.1(19)| 23.7(9)       |
| C10  | -3967(10)| 6313(3) | 7154(2)  | 27.5(9)        |
| C11  | -4793(10)| 6238(3) | 7745(2)  | 29.4(10)       |
| C12  | -3683(10)| 5564(3) | 8103(2)  | 28.8(10)       |
| C13  | -1779(9) | 4955(3)  | 7863.2(19)| 23.5(9)       |
| C14  | -889(9) | 5039(3)  | 7258(2)  | 24.1(9)        |
| C16  | 1992(9) | 4452(3)  | 6484.9(19)| 22.9(9)       |
| C17  | 3896(9) | 3789(3)  | 6305.4(19)| 22.5(8)       |
| C18  | 4890(10)| 3758(3)  | 5715(2)  | 24.4(9)        |
| C19  | 6706(10)| 2996(3)  | 5510(2)  | 26.1(9)        |
Table S2. Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{Å}^2\times 10^3$) for cA.

| Atom | $x$      | $y$    | $z$    | $U(\text{eq})$ |
|------|---------|--------|--------|-----------------|
| C20  | 5647(10)| 2770(3)| 4869(2)| 29.2(10)        |
| C21  | 6226(10)| 3524(3)| 4468(2)| 28.5(9)         |
| C22  | 7820(30)| 3354(8)| 3954(6)| 28.0(19)        |
| C22A | 7550(30)| 3486(8)| 3883(6)| 27.6(16)        |
| C23  | 8610(30)| 4028(7)| 3601(6)| 25.7(18)        |
| C23A | 8340(30)| 4214(7)| 3547(6)| 27.4(17)        |
| C24  | 10500(20)| 3869(7)| 3048(4)| 30(2)           |
| C24A | 10050(30)| 4133(7)| 2958(5)| 32(2)           |
| C25  | 8630(20)| 3740(6)| 2452(4)| 33(2)           |
| C25A | 9570(20)| 4941(7)| 2570(5)| 43(2)           |
| C26  | 9810(30)| 4147(10)|1875(5)| 61(4)           |
| C26A | 11760(30)| 5023(8)| 2061(5)| 46(3)           |
| C31  | -1136(10)| 4103(3)| 8752(2)| 27.4(9)        |
| C32  | -375(10)| 3152(3)| 8872(2)| 28.3(9)        |
| C33  | -872(12)| 2955(3)| 9533(2)| 34.3(11)       |
| C34  | 440(12)| 3676(3)| 9912(2)| 38.7(11)       |
| C35  | 1246(11)| 4431(3)| 9683(2)| 34.6(9)        |
| C36  | 2610(40)| 5164(9)| 10011(7)| 40(2)          |
| C36A | 3230(30)| 5069(8)| 10047(7)| 35(2)          |
| O1S  | 1530(40)| 7062(12)|8940(8)| 107(6)         |
| C1S  | 4180(40)| 7654(13)| 8985(7)| 86(5)          |
| O1W  | -48(7)| 2531(2)| 7358.8(14)| 31.2(7)  |
| O2W  | 5931(9)| 6213(2)| 11159(2)| 60.2(11)       |
| O3W  | 1110(30)| 6880(7)| 9167(5)| 63(3)          |
| O4W  | 5970(20)| 7863(6)| 8738(4)| 62(2)          |

$U_{\text{eq}}$ is defined as $1/3$ of the trace of the orthogonalised $U_{ij}$ tensor.
Table S3. Anisotropic displacement parameters ($\text{Å}^2 \times 10^3$) for cA.

| Atom | $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{12}$ | $U_{13}$ | $U_{23}$ |
|------|----------|----------|----------|----------|----------|----------|
| O1   | 40(4)    | 27(3)    | 33(2)    | -4(2)    | 3.9(15)  | 0.7(11)  |
| O1A  | 43(4)    | 24(3)    | 38(3)    | -1(2)    | 11.7(17) | 1.1(14)  |
| O2   | 40(3)    | 31(2)    | 34(3)    | -5.7(17) | 5.8(19)  | -1.8(13) |
| O2A  | 34(4)    | 25.0(19) | 39(3)    | 0.2(15)  | 8(2)     | -0.1(13) |
| O3   | 28(3)    | 25.0(18) | 26(3)    | 1.8(9)   | -0.9(13) | 0.7(9)   |
| O3A  | 24(3)    | 15(2)    | 26(3)    | -0.5(12) | -0.2(13) | 2.7(13)  |
| O4   | 38.9(18) | 18.4(14) | 31.1(17) | 3.6(13)  | 6.6(14)  | 2.1(12)  |
| O5   | 45.1(19) | 18.9(14) | 35.1(18) | 7.5(13)  | 4.6(15)  | 3.0(13)  |
| O6   | 37.2(17) | 24.7(15) | 28.1(16) | 8.9(13)  | 5.0(13)  | 1.9(12)  |
| O7   | 31.9(16) | 18.0(13) | 28.1(16) | 2.3(12)  | 1.6(13)  | -0.1(12) |
| O8   | 30.6(16) | 19.9(13) | 32.7(17) | 4.5(12)  | 1.5(13)  | 0.5(12)  |
| O9   | 30(3)    | 32(3)    | 39(4)    | -6(3)    | 5(3)     | -10(3)   |
| O9A  | 47(4)    | 44(4)    | 82(6)    | -8(4)    | 2(4)     | -2(4)    |
| O10  | 40.0(18) | 24.7(14) | 30.5(17) | -2.2(13) | 7.1(14)  | 0.2(12)  |
| O11  | 44.2(19) | 26.2(14) | 34.4(18) | -4.3(14) | 5.4(15)  | 1.3(14)  |
| O12  | 73(3)    | 25.5(16) | 46(2)    | 0.5(17)  | -6(2)    | 10.2(16) |
| O13  | 36(4)    | 33(3)    | 40(2)    | -1.0(17) | 3.3(13)  | -6.1(11) |
| O13A | 40(4)    | 34(3)    | 38.4(19) | -3.4(17) | 3.1(12)  | -5.2(10) |
| O14  | 84(5)    | 41(2)    | 49(3)    | -18.2(16)| -7.3(18) | 0.7(13)  |
| O14A | 26(3)    | 27(2)    | 42(3)    | 7.0(14)  | 1.7(15)  | -2.0(13) |
| C1   | 33(5)    | 26(2)    | 32(2)    | -0.2(14) | 5.7(13)  | -0.4(10) |
| C1A  | 27(5)    | 25.3(18) | 33(3)    | 1.6(11)  | 3.4(16)  | 1.5(9)   |
| C2   | 31(3)    | 26.2(19) | 31(2)    | -0.2(9)  | 3.9(12)  | -0.1(8)  |
| C2A  | 25(3)    | 26.1(17) | 29.7(19) | 0.6(8)   | 0.3(9)   | 0.4(7)   |
| C3   | 25(4)    | 25.7(15) | 29(2)    | 0.4(8)   | 0.1(14)  | -0.3(7)  |
| C3A  | 26(3)    | 26.9(16) | 30(2)    | -0.0(8)  | 1.1(10)  | -0.1(7)  |
| C4   | 23.7(18) | 26.9(12) | 28.6(14) | -0.8(7)  | -0.9(8)  | -0.6(6)  |
| C5   | 21(2)    | 21.0(19) | 29(2)    | -5.4(16) | -3.8(17) | -3.8(16) |
| C6   | 21.1(19) | 16.7(18) | 36(2)    | -6.2(16) | -2.2(18) | -1.3(17) |
| C7   | 23(2)    | 18.0(18) | 32(2)    | -6.8(16) | -1.1(17) | -2.7(17) |
| C8   | 25(2)    | 18.9(19) | 33(2)    | -5.5(16) | -0.4(18) | 0.0(18)  |
| C9   | 28(2)    | 16.4(18) | 26(2)    | -3.1(17) | -1.0(17) | -2.1(16) |
| C10  | 30(2)    | 18.1(19) | 35(2)    | 1.2(17)  | -0.6(18) | 1.9(17)  |
| C11  | 31(2)    | 22(2)    | 35(3)    | 3.2(18)  | 2.4(19)  | -8.5(18) |
| C12  | 30(2)    | 24(2)    | 32(2)    | 1.2(18)  | 3.5(19)  | -3.1(18) |
| C13  | 22(2)    | 19.8(19) | 29(2)    | -0.2(16) | -1.1(17) | -0.2(17) |
| C14  | 23(2)    | 19.0(19) | 30(2)    | 1.0(17)  | 1.6(17)  | -0.0(17) |
| C16  | 17.9(19) | 21.4(19) | 29(2)    | -6.8(15) | -0.6(17) | -5.0(16) |
| C17  | 21(2)    | 21.3(19) | 25(2)    | -2.7(16) | -4.0(17) | -1.3(16) |
| C18  | 27(2)    | 17.4(18) | 29(2)    | 0.5(16)  | -1.7(17) | -2.3(16) |
| C19  | 25(2)    | 20.9(19) | 33(2)    | -0.1(16) | 2.1(18)  | -4.7(17) |
| C20  | 25(2)    | 23(2)    | 40(3)    | -1.7(17) | 8.4(19)  | -6.2(18) |
Table S3. Anisotropic displacement parameters (Å²×10³) for eA.

| Atom | U_{11}  | U_{22}  | U_{33}  | U_{12}  | U_{13}  | U_{23}  |
|------|---------|---------|---------|---------|---------|---------|
| C21  | 28(2)   | 26.8(12)| 30.3(14)| -0.6(7) | 1.9(9)  | -0.6(6) |
| C22  | 27(4)   | 26(2)   | 30(2)   | -0.7(9) | 1.4(14) | -0.6(8) |
| C22A | 27(3)   | 26.1(18)| 29.5(18)| 0.3(8)  | 1.1(10) | -0.0(7) |
| C23  | 22(4)   | 26.1(19)| 29(2)   | -1.1(10)| -1.2(13)| -0.8(8) |
| C23A | 26(3)   | 26.3(17)| 29.8(19)| 0.7(8)  | 0.9(10) | 0.6(7)  |
| C24  | 30(4)   | 27(3)   | 32(3)   | -0.1(18)| 3.8(16) | -0.1(13)|
| C24A | 36(5)   | 26(3)   | 34(2)   | 1.0(18) | 6.7(16) | 0.7(12) |
| C25  | 33(5)   | 33(5)   | 34(5)   | 6(4)    | 4(4)    | -3(4)   |
| C25A | 43(6)   | 33(5)   | 52(7)   | -9(5)   | 9(5)    | 3(5)    |
| C26  | 70(8)   | 82(9)   | 32(6)   | -29(7)  | 18(6)   | -10(6)  |
| C26A | 50(6)   | 47(6)   | 40(6)   | -1(5)   | 10(5)   | 12(5)   |
| C31  | 27(2)   | 24(2)   | 32(2)   | 3.2(17) | 6.9(18) | 4.8(18) |
| C32  | 32(2)   | 22.6(19)| 31(2)   | -0.1(17)| 5.6(19) | 1.7(17) |
| C33  | 43(3)   | 27(2)   | 34(3)   | -5(2)   | 4(2)    | 2.0(18) |
| C34  | 57(3)   | 34(2)   | 26(2)   | -4(2)   | 5(2)    | 3.1(19) |
| C35  | 38(2)   | 30.7(18)| 35.6(18)| -0.2(12)| 3.6(12) | -3.3(10)|
| C36  | 46(5)   | 33(2)   | 42(2)   | -1.8(14)| 0.0(13) | -5.4(10)|
| C36A | 36(4)   | 30(3)   | 38(2)   | 0.9(16) | 2.7(11) | -4.5(10)|
| O1S  | 105(8)  | 93(8)   | 122(10) | -1(4)   | 3(4)    | -10(4)  |
| C1S  | 99(8)   | 88(9)   | 70(10)  | 5(5)    | 15(7)   | -21(8)  |
| O1W  | 32.4(17)| 28.0(14)| 33.4(17)| 2.3(13) | 2.1(13) | -1.7(13)|
| O2W  | 60(2)   | 32.4(18)| 88(3)   | 3.8(17) | -2(2)   | -16.1(19)|
| O3W  | 107(8)  | 46(5)   | 38(5)   | 35(5)   | 9(5)    | -8(4)   |
| O4W  | 75(6)   | 46(5)   | 65(6)   | 10(4)   | -10(5)  | -4(4)   |

The Anisotropic displacement factor exponent takes the form: -2π²[h²a²U_{11}+2hka*b*U_{12}+...].
| Atom | Atom | Length/Å | Atom | Atom | Length/Å |
|------|------|----------|------|------|----------|
| O1   | C1   | 1.168(19)| C5   | C6   | 1.393(6) |
| O1A  | C1A  | 1.369(18)| C5   | C18  | 1.430(6) |
| O1   | C25A | 1.460(13)| C6   | C7   | 1.418(6) |
| O2   | C1   | 1.320(18)| C7   | C8   | 1.449(6) |
| O2A  | C1A  | 1.238(15)| C7   | C16  | 1.398(6) |
| O3   | C3   | 1.342(14)| C8   | C9   | 1.465(6) |
| O3A  | C3A  | 1.348(14)| C9   | C10  | 1.397(6) |
| O4   | C6   | 1.352(5) | C9   | C14  | 1.391(6) |
| O5   | C8   | 1.240(5) | C10  | C11  | 1.373(7) |
| O6   | C13  | 1.369(5) | C11  | C12  | 1.393(7) |
| O6   | C31  | 1.390(5) | C12  | C13  | 1.376(6) |
| O7   | C14  | 1.359(5) | C13  | C14  | 1.412(6) |
| O7   | C16  | 1.356(5) | C16  | C17  | 1.389(6) |
| O8   | C17  | 1.391(5) | C17  | C18  | 1.390(6) |
| O9   | C25  | 1.201(11)| C18  | C19  | 1.501(6) |
| O9A  | C25A | 1.429(11)| C19  | C20  | 1.526(6) |
| O10  | C31  | 1.424(6) | C20  | C21  | 1.495(6) |
| O10  | C35  | 1.365(6) | C21  | C22  | 1.375(14) |
| O11  | C32  | 1.407(5) | C21  | C22A | 1.434(14) |
| O12  | C33  | 1.424(6) | C22  | C23  | 1.357(16) |
| O13  | C36  | 1.363(19)| C22A | C23A | 1.402(16) |
| O13A | C36A | 1.31(2)  | C23  | C24  | 1.513(16) |
| O14  | C36  | 1.216(18)| C23A | C24A | 1.526(16) |
| O14A | C36A | 1.215(17)| C24  | C25  | 1.551(12) |
| C1   | C2   | 1.51(2)  | C24A | C25A | 1.533(15) |
| C1A  | C2A  | 1.44(2)  | C25  | C26  | 1.527(15) |
| C2   | C3   | 1.42(2)  | C25A | C26A | 1.502(14) |
| C2   | C23  | 1.379(14)| C31  | C32  | 1.534(6) |
| C2A  | C3A  | 1.40(2)  | C32  | C33  | 1.518(6) |
| C2A  | C23A | 1.405(15)| C33  | C34  | 1.505(7) |
| C3   | C4   | 1.399(19)| C34  | C35  | 1.328(7) |
| C3A  | C4   | 1.433(18)| C35  | C36  | 1.470(12) |
| C4   | C5   | 1.489(6) | C35  | C36A | 1.534(12) |
| C4   | C21  | 1.414(6) | O1S  | C1S  | 1.48(2)  |
| Atom Atom Atom | Angle/° | Atom Atom Atom | Angle/° |
|----------------|---------|----------------|---------|
| C25A O1A C1A   | 118.6(9)| C16 C17 O8     | 119.7(4)|
| C31 O6 C13     | 119.6(3)| C18 C17 O8     | 120.3(4)|
| C16 O7 C14     | 118.8(3)| C18 C17 C16    | 119.9(4)|
| C35 O10 C31    | 114.7(3)| C17 C18 C5     | 121.3(4)|
| O2 C1 O1       | 122.9(14)| C19 C18 C5     | 119.2(4)|
| C2 C1 O1       | 122.6(13)| C19 C18 C17    | 119.5(4)|
| C2 C1 O2       | 114.4(14)| C20 C19 C18    | 108.1(4)|
| O2A C1A O1A    | 113.3(13)| C21 C20 C19    | 108.7(3)|
| C2A C1A O1A    | 121.6(11)| C20 C21 C4     | 117.8(4)|
| C2A C1A O2A    | 125.0(13)| C22 C21 C4     | 125.8(6)|
| C3 C2 C1       | 115.6(10)| C22 C21 C20    | 116.0(6)|
| C23 C2 C1      | 123.4(13)| C22A C21 C4    | 116.5(6)|
| C23 C2 C3      | 120.7(13)| C22A C21 C20   | 125.7(6)|
| C3A C2A C1A    | 120.7(11)| C22A C21 C22   | 113.8(6)|
| C23AC2A C1A    | 118.0(12)| C23 C22 C21    | 118.2(10)|
| C23AC2A C3A    | 121.1(12)| C23A C22AC21   | 123.9(11)|
| C2 C3 O3       | 116.9(14)| C22 C23 C2     | 120.4(13)|
| C4 C3 O3       | 122.2(13)| C24 C23 C2     | 120.0(11)|
| C4 C3 C2       | 120.7(10)| C24 C23 C22    | 119.6(10)|
| C2A C3A O3A    | 116.8(14)| C22A C23AC2A   | 117.5(12)|
| C4 C3A O3A     | 122.9(14)| C24A C23AC2A   | 120.9(10)|
| C4 C3A C2A     | 120.3(11)| C24A C23AC22A  | 121.4(10)|
| C3A C4 C3      | 8.7(11)  | C25 C24 C23    | 115.1(9) |
| C5 C4 C3       | 128.0(7) | C25A C24AC23A  | 110.4(9) |
| C5 C4 C3A      | 121.1(7) | C24 C25 O9     | 119.9(9) |
| C21 C4 C3      | 113.9(7) | C26 C25 O9     | 121.4(9) |
| C21 C4 C3A     | 120.1(7) | C26 C25 C24    | 118.6(9) |
| C21 C4 C5      | 118.0(4) | O9A C25AO1A    | 106.8(8) |
| C6 C5 C4       | 125.6(4) | C24A C25AO1A   | 110.5(9) |
| C18 C5 C4      | 117.3(4) | C24A C25AO9A   | 107.9(9) |
| C18 C5 C6      | 117.1(4) | C26A C25AO1A   | 104.1(8) |
| C5 C6 O4       | 120.9(4) | C26A C25AO9A   | 113.1(9) |
| C7 C6 O4       | 116.9(4) | C26A C25AC24A  | 114.1(9) |
| C7 C6 C5       | 122.1(4) | O10 C31 O6     | 106.6(3) |
| C8 C7 C6       | 121.8(4) | C32 C31 O6     | 106.3(3) |
| C16 C7 C6      | 118.5(4) | C32 C31 O10    | 110.8(3) |
| C16 C7 C8      | 119.7(4) | C31 C32 O11    | 109.7(3) |
| C7 C8 O5       | 122.5(4) | C33 C32 O11    | 109.4(3) |
| C9 C8 O5       | 121.2(4) | C33 C32 C31    | 109.1(4) |
| C9 C8 C7       | 116.3(4) | C32 C33 O12    | 106.8(4) |
| C10 C9 C8      | 122.8(4) | C34 C33 O12    | 110.6(4) |
| C14 C9 C8      | 118.3(4) | C34 C33 C32    | 109.1(4) |
Table S5. Bond angles for cA.

| Atom | Atom | Atom | Angle/° | Atom | Atom | Atom | Angle/° |
|------|------|------|---------|------|------|------|---------|
| C14  | C9   | C10  | 118.9(4)| C35  | C34  | C33  | 123.0(5)|
| C11  | C10  | C9   | 120.4(4)| C34  | C35  | O10  | 124.2(4)|
| C12  | C11  | C10  | 120.7(4)| C36  | C35  | O10  | 108.8(8)|
| C13  | C12  | C11  | 120.2(4)| C36  | C35  | C34  | 127.0(8)|
| C12  | C13  | O6   | 127.5(4)| C36A| C35  | O10  | 113.5(7)|
| C14  | C13  | O6   | 113.4(3)| C36A| C35  | C34  | 121.4(7)|
| C14  | C13  | C12  | 119.1(4)| C36A| C35  | C36  | 11.9(10)|
| C9   | C14  | O7   | 124.1(4)| O14  | C36  | O13  | 121.2(11)|
| C13  | C14  | O7   | 115.2(4)| C35  | C36  | O13  | 114.2(12)|
| C13  | C14  | C9   | 120.7(4)| C35  | C36  | O14  | 123.3(13)|
| C7   | C16  | O7   | 122.8(4)| O14A| C36A| O13A | 130.1(11)|
| C17  | C16  | O7   | 116.3(4)| C35  | C36A| O13A | 109.9(11)|
| C17  | C16  | C7   | 120.9(4)| C35  | C36A| O14A | 119.0(11)|
Table S6. Hydrogen bonds for cA.

| D     | H    | A     | d(D-H)/Å | d(H-A)/Å | d(D-A)/Å | D-H-A/° |
|-------|------|-------|-----------|-----------|-----------|---------|
| O2    | H2   | O3    | 0.8399    | 2.133(11) | 2.746(11) | 129.7(3) |
| O3    | H3   | O4    | 0.8400    | 1.70(3)   | 2.517(10) | 162(8)  |
| O3A   | H3A  | O2A   | 0.8400    | 1.87(6)   | 2.530(11) | 134(8)  |
| O4    | H4   | O5    | 0.8400    | 1.83(3)   | 2.531(4)  | 140(4)  |
| O8    | H8b  | O1W   | 0.8400    | 2.16(8)   | 2.765(4)  | 129(9)  |
| O11   | H11  | O1W   | 0.8400    | 1.930(9)  | 2.766(4)  | 173(6)  |
| O12   | H12  | O3W\(^1\) | 0.8400 | 1.946(17) | 2.764(11) | 164(5)  |
| O13   | H13  | O2W   | 0.8400    | 1.73(5)   | 2.512(11) | 154(11) |
| O13A  | H13A | O2W   | 0.8402    | 1.800(11) | 2.634(11) | 171.7(3)|
| O1S   | H1S  | O14   | 0.8399    | 1.94(2)   | 2.76(2)   | 163.8(6)|
| O1W   | H1W  | O8\(^2\) | 0.8694 | 1.956(4)  | 2.808(4)  | 166.16(12)|
| O1W   | H1WaO8 | 0.8704 | 1.944(4)  | 2.765(4)  | 156.71(13)|
| O1W   | H1WbO1A\(^3\) | 0.8704 | 2.030(8)  | 2.887(8)  | 168.3(2)|
| O2W   | H2WaO12\(^4\) | 0.8708 | 1.961(6)  | 2.801(6)  | 161.53(17)|
| O2W   | H2WbO11\(^5\) | 0.8703 | 1.983(5)  | 2.815(5)  | 159.50(16)|
| O3W   | H3WbO14A | 0.8706 | 2.16(11)  | 2.856(13) | 136(14)|
| O4W   | H4WaO3W | 0.8701 | 1.966(17) | 2.802(17) | 160.9(4)|
| O4W   | H4WbO3W\(^6\) | 0.8699 | 2.007(15) | 2.865(15) | 168.8(4)|

\(^1\)\(-X,-1/2+Y,2-Z; \(^2\)\(-1+X,+Y,+Z; \(^3\)\(-1/2+Y,1-Z; \(^4\)\(-X,1/2+Y,2-Z; \(^5\)\(-X,1/2+Y,2-Z; \(^6\)\(-1+X,+Y,+Z)\)
Table S7. Torsion angles for cA.

| A  | B  | C  | D  | Angle/° | A  | B  | C  | D  | Angle/° |
|----|----|----|----|---------|----|----|----|----|---------|
| O1 | C1 | C2 | C3 | -127.8(16) | C1 | C2 | C3 | C4 | -169.4(13) |
| O1 | C1 | C2 | C23 | 58(2) | C1 | C2 | C23 | C22 | 173.1(16) |
| O1A | C1A | C2A | C3A | -178.5(15) | C1 | C2 | C23 | C24 | -4.8(18) |
| O1A | C1A | C2A | C23A | 7.0(19) | C1A | C2A | C3A | C4 | -175.6(14) |
| O1A | C25A | C24A | C23A | 48.5(9) | C1A | C2A | C23A | C22A | 173.7(15) |
| O2 | C1 | C2 | C3 | 56.2(17) | C1A | C2A | C23A | C24A | -1.9(16) |
| O2 | C1 | C2 | C23 | -117.6(12) | C2 | C3 | C4 | C3A | 130(4) |
| O2A | C1A | C2A | C3A | 6(2) | C2 | C3 | C4 | C5 | 169.4(10) |
| O2A | C1A | C2A | C23A | -168.0(16) | C2 | C3 | C4 | C21 | -6.7(17) |
| O3 | C3 | C2 | C1 | 5.8(18) | C2 | C23 | C22 | C21 | -1.0(14) |
| O3 | C3 | C2 | C23 | 179.9(13) | C2 | C23 | C24 | C25 | -88.8(13) |
| O3 | C3 | C4 | C3A | -45(4) | C2A | C3A | C4 | C3 | -40(3) |
| O3 | C3 | C4 | C5 | -6(2) | C2A | C3A | C4 | C5 | 175.6(12) |
| O3 | C3 | C4 | C21 | 178.3(12) | C2A | C3A | C4 | C21 | 6(2) |
| O3A | C3A | C2A | C1A | 3(2) | C2A | C23A | C22A | C21 | -2.4(15) |
| O3A | C3A | C2A | C23A | 177.7(13) | C2A | C23A | C24A | C25A | -26.1(14) |
| O3A | C3A | C4 | C3 | 141(4) | C3 | C4 | C5 | C6 | 31.6(10) |
| O3A | C3A | C4 | C5 | -3(2) | C3 | C4 | C5 | C18 | -150.6(10) |
| O3A | C3A | C4 | C21 | -172.6(12) | C3 | C4 | C21 | C20 | 178.5(9) |
| O4 | C6 | C5 | C4 | 4.2(5) | C3 | C4 | C21 | C22 | 5.5(12) |
| O4 | C6 | C5 | C18 | -173.7(4) | C3 | C21 | C22A | -2.0(11) |
| O4 | C6 | C7 | C8 | -2.2(4) | C3A | C4 | C5 | C6 | 38.1(11) |
| O4 | C6 | C7 | C16 | 176.7(3) | C3A | C4 | C5 | C18 | -144.1(10) |
| O5 | C8 | C7 | C6 | -0.5(5) | C3A | C4 | C21 | C20 | 171.5(10) |
| O5 | C8 | C7 | C16 | -179.3(4) | C3A | C4 | C21 | C22 | -1.4(12) |
| O5 | C8 | C9 | C10 | -0.7(5) | C3A | C4 | C21 | C22A | -8.9(12) |
| O5 | C8 | C9 | C14 | 178.6(4) | C4 | C5 | C6 | C7 | -177.6(4) |
| O6 | C13 | C12 | C11 | -178.6(4) | C4 | C5 | C18 | C17 | 176.9(4) |
| O6 | C13 | C14 | O7 | -1.4(4) | C4 | C5 | C18 | C19 | -6.2(4) |
| O6 | C13 | C14 | C9 | 178.6(3) | C4 | C21 | C20 | C19 | -45.4(4) |
| O6 | C31 | O10 | C35 | -162.2(3) | C4 | C21 | C22 | C23 | -1.7(8) |
| O6 | C31 | C32 | O11 | -62.0(3) | C4 | C21 | C22A | C23A | 7.2(8) |
| O6 | C31 | C32 | C33 | 178.2(3) | C5 | C6 | C7 | C8 | 179.5(3) |
| O7 | C14 | C9 | C8 | 1.6(5) | C5 | C6 | C7 | C16 | -1.6(4) |
| O7 | C14 | C9 | C10 | -179.1(4) | C5 | C18 | C17 | C16 | 2.5(5) |
| O7 | C14 | C13 | C12 | 178.0(3) | C5 | C18 | C19 | C20 | -36.6(4) |
| O7 | C16 | C7 | C6 | -178.9(4) | C6 | C7 | C8 | C9 | 179.3(4) |
| O7 | C16 | C7 | C8 | -0.1(4) | C6 | C7 | C16 | C17 | -1.1(4) |
| O7 | C16 | C17 | O8 | -1.8(4) | C7 | C8 | C9 | C10 | 179.6(3) |
| O7 | C16 | C17 | C18 | 178.6(3) | C7 | C8 | C9 | C14 | -1.2(4) |
| O8 | C17 | C16 | C7 | -179.8(3) | C7 | C16 | C17 | C18 | 0.7(5) |
| O8 | C17 | C18 | C5 | -177.1(4) | C8 | C9 | C10 | C11 | 179.4(4) |

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|   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|
| A | B | C | D | Angle/° | A | B | C | D | Angle/° |
|---|---|---|---|---------|---|---|---|---|---------|
| O8 | C17 | C18 | C19 | 6.0(4) | C8 | C9 | C14 | C13 | -178.4(4) |
| O9 | C25 | C24 | C23 | -40.7(10) | C9 | C10 | C11 | C12 | -0.1(5) |
| O9A | C25A | C24A | C23A | -67.9(10) | C9 | C14 | C13 | C12 | -2.0(5) |
| O10 | C31 | C32 | O11 | -177.4(3) | C10 | C11 | C12 | C13 | -1.1(5) |
| O10 | C31 | C32 | C33 | 62.8(4) | C11 | C12 | C13 | C14 | 2.1(5) |
| O10 | C35 | C34 | C33 | 2.9(6) | C16 | C17 | C18 | C19 | -174.4(4) |
| O10 | C35 | C36 | O13 | -171.0(9) | C17 | C18 | C19 | C20 | 140.4(4) |
| O10 | C35 | C36 | O14 | -3.6(8) | C18 | C19 | C20 | C21 | 60.9(4) |
| O10 | C35 | C36A | O13A | 156.8(9) | C19 | C20 | C21 | C22 | 128.2(8) |
| O10 | C35 | C36A | O14A | -13.3(6) | C19 | C20 | C21 | C22A | 135.1(8) |
| O11 | C32 | C33 | O12 | 76.8(4) | C20 | C21 | C22 | C23 | -174.8(9) |
| O11 | C32 | C33 | C34 | -163.7(4) | C20 | C21 | C22A | C23A | -173.3(11) |
| O12 | C33 | C32 | C31 | -163.2(4) | C21 | C22 | C23 | C24 | 176.9(10) |
| O12 | C33 | C34 | C35 | 130.8(4) | C21 | C22A | C23AC24A | 173.2(12) |
| O13 | C36 | C35 | C34 | 10.2(17) | C22 | C23 | C24 | C25 | 93.3(12) |
| O13 | C36 | C35 | C36A | -55(3) | C22A | C23A | C24AC25A | 158.4(13) |
| O13A | C36AC35 | C34 | -33.3(13) | C23 | C24 | C25 | C26 | 140.0(10) |
| O13AC36AC35 | C36 | 88(3) | C23AC24AC25AC26A | 165.4(10) |
| O14 | C36 | C35 | C34 | 177.6(12) | C31 | C32 | C33 | C34 | -43.7(4) |
| O14 | C36 | C35 | C36A | 112(3) | C32 | C33 | C34 | C35 | 13.6(5) |
| O14AC36AC35 | C34 | 156.5(9) | C33 | C34 | C35 | C36 | -178.4(9) |
| O14AC36AC35 | C36 | -82(3) | C33 | C34 | C35 | C36A | -165.8(8) |
| Atom | x      | y      | z      | U(eq)  |
|------|--------|--------|--------|--------|
| H2   | 9615(16) | 6316(4) | 4069(3) | 53(2)  |
| H3   | 3750(130)| 5865(6) | 4580(40)| 40(3)  |
| H3A  | 7260(120)| 6230(16) | 4440(40)| 33(3)  |
| H4   | -620(70) | 5870(30) | 5227(12)| 44.0(10)|
| H8b  | 3870(180) | 3230(40) | 7042(17) | 41.6(10)|
| H8a  | 3880(7) | 2700.3(19) | 6644.0(14) | 41.6(10)|
| H9A  | 6122(17) | 5423(5) | 2185(4) | 87(3)  |
| H11  | -1690(90) | 2630(30) | 8156(6) | 52.3(11)|
| H12  | 480(140) | 2040(20) | 10028(8) | 72.4(14)|
| H13  | 4800(200) | 5360(40) | 10712(18) | 54(3)  |
| H13A | 3510(20) | 5410(7) | 10809(4) | 57(3)  |
| H10  | -4744(10) | 6775(3) | 6915(2) | 33.0(11)|
| H11a | -6136(10) | 6650(3) | 7912(2) | 35.2(12)|
| H12a | -4243(10) | 5525(3) | 8513(2) | 34.6(11)|
| H19a | 8909(10) | 3138(3) | 5518(2) | 31.3(11)|
| H19b | 6381(10) | 2500(3) | 5782(2) | 31.3(11)|
| H20a | 6776(10) | 2260(3) | 4725(2) | 35.0(12)|
| H20b | 3441(10) | 2630(3) | 4862(2) | 35.0(12)|
| H22  | 8340(30) | 2780(8) | 3849(6) | 34(2)  |
| H22A | 7910(30) | 2934(8) | 3714(6) | 33(2)  |
| H24a | 11890(20) | 4364(7) | 2997(4) | 36(3)  |
| H24b | 11770(20) | 3351(7) | 3121(4) | 36(3)  |
| H24c | 12260(30) | 4055(7) | 3048(5) | 38(3)  |
| H24d | 9310(30) | 3620(7) | 2733(5) | 38(3)  |
| H26a | 8370(130) | 4030(60) | 1541(11) | 92(5)  |
| H26b | 10000(200) | 4771(13) | 1931(17) | 92(5)  |
| H26c | 11800(120) | 3900(50) | 1780(30) | 92(5)  |
| H26d | 13770(60) | 5190(60) | 2222(7) | 68(4)  |
| H26e | 11920(150) | 4468(16) | 1850(20) | 68(4)  |
| H26f | 11000(110) | 5460(40) | 1780(20) | 68(4)  |
| H31  | -3319(10) | 4229(3) | 8841(2) | 32.9(11)|
| H32  | 1805(10) | 3040(3) | 8774(2) | 33.9(11)|
| H33  | -3102(12) | 2890(3) | 9609(2) | 41.2(13)|
| H34  | 703(12) | 3587(3) | 10334(2) | 46.5(14)|
| H1S  | 1980(40) | 6618(12) | 9139(8) | 160(9) |
| H1Sa | 4400(200) | 7850(70) | 9403(15) | 128(7) |
| H1Sb | 6030(60) | 7350(30) | 8860(60) | 128(7) |
| H1Sc | 3830(140) | 8150(50) | 8720(50) | 128(7) |
| H1W  | -1811(7) | 2667(2) | 7197.7(14) | 46.9(10)|
| H1Wa | 1437(7) | 2849(2) | 7228.8(14) | 46.9(10)|
| H1Wb | 213(7) | 1994(2) | 7260.9(14) | 46.9(10)|
Table S8. Hydrogen atom coordinates ($\text{Å} \times 10^4$) and isotropic displacement parameters ($\text{Å}^2 \times 10^3$) for cA.

| Atom  | x     | y     | z     | U(eq)  |
|-------|-------|-------|-------|--------|
| H2Wa  | 6671(9)| 6472(2)| 10846(2)| 90.3(17)|
| H2Wb  | 4969(9)| 6617(2)| 11351(2)| 90.3(17)|
| H3Wa  | -820(100)| 6850(90)| 9250(80)| 95(5)  |
| H3Wb  | 1700(300)| 6350(30)| 9190(70)| 95(5)  |
| H4Wa  | 4280(20)| 7579(6)| 8789(4)| 93(4)  |
| H4Wb  | 7400(20)| 7504(6)| 8848(4)| 93(4)  |
Table S9. Atomic occupancy for cA.

| Atom | Occupancy | Atom | Occupancy | Atom | Occupancy  |
|------|-----------|------|-----------|------|------------|
| O1   | 0.500000  | O1A  | 0.500000  | O2   | 0.500000   |
| H2   | 0.500000  | O2A  | 0.500000  | O3   | 0.500000   |
| H3   | 0.500000  | O3A  | 0.500000  | H3A  | 0.500000   |
| H8b  | 0.500000  | H8a  | 0.500000  | O9   | 0.500000   |
| O9A  | 0.500000  | H9A  | 0.500000  | O13  | 0.500000   |
| H13  | 0.500000  | O13A | 0.500000  | H13A | 0.500000   |
| O14  | 0.500000  | O14A | 0.500000  | C1   |            |
| C1A  | 0.500000  | C2   | 0.500000  | C2A  | 0.500000   |
| C3   | 0.500000  | C3A  | 0.500000  | C22  | 0.500000   |
| H22  | 0.500000  | C22A | 0.500000  | H22A | 0.500000   |
| C23  | 0.500000  | C23A | 0.500000  | C24  | 0.500000   |
| H24a | 0.500000  | H24b | 0.500000  | C24A | 0.500000   |
| H24c | 0.500000  | H24d | 0.500000  | C25  | 0.500000   |
| C25A | 0.500000  | C26  | 0.500000  | H26a | 0.500000   |
| H26b | 0.500000  | H26c | 0.500000  | C26A | 0.500000   |
| H26d | 0.500000  | H26e | 0.500000  | H26f | 0.500000   |
| C36  | 0.500000  | C36A | 0.500000  | O1   | 0.500000   |
| H1S  | 0.500000  | C1S  | 0.500000  | H1S  | 0.500000   |
| H1Sb | 0.500000  | H1Sc | 0.500000  | H1Wa | 0.500000   |
| H1Wb | 0.500000  | O3W  | 0.500000  | H3Wa | 0.500000   |
| H3Wb | 0.500000  | O4W  | 0.500000  | H4Wa | 0.500000   |
| H4Wb | 0.500000  |      |           |      |            |
Table S10. Estimated intermolecular energy of the interaction models of DNA (G4C2)$_4$ G4 with compounds cA, cB, and cC.

| Energy                        | DNA (G4C2)$_4$ G4/cA | DNA (G4C2)$_4$ G4/cB | DNA (G4C2)$_4$ G4/cC |
|-------------------------------|----------------------|----------------------|----------------------|
| van der Waals forces + hydrogen bonds | -8.23 kcal/mol       | -7.99 kcal/mol       | -7.13 kcal/mol       |
| Electrostatic Energy          | -3.21 kcal/mol       | -2.13 kcal/mol       | -1.49 kcal/mol       |
### Table S11. Oligonucleotides adopting different structures used in this study.

| Name                                | Sequence                                                                 |
|-------------------------------------|--------------------------------------------------------------------------|
| two-repeat DNA G4C2 G4\([1, 2]\)     | 5'-GGGGCCGGGGCCG -3'                                                    |
| four-repeat DNA G4C2 G4\([3]\)      | 5'-GGGGCCGGGGCCG -3'                                                    |
| ssDNA G4C2\([1]\)                   | 5'-GGGGCCGGGGCCG -3'                                                    |
| ssDNA T rich (17 bp)\([4]\)         | 5'-GGCCCTTTTTTTTTCTAG -3'                                               |
| dsDNA G4C2\([5]\)                   | 5'-CTAGGGCCTAG -3'                                                      |
| dsDNA AT rich (17bp)\([4]\)         | 3'-GATCCGGGATC -5'                                                      |
| htel21_T18 G4\([6]\)                | 5'-GGGTTAGGGTTAGGGTTAGGG -3'                                            |
| htel23 G4\([7]\)                    | 5'-TAGGGTTAGGGTTAGGGTTAGGG -3'                                          |
| c-kit G4\([8]\)                     | 5'-AGGGAGGGCGCTGGGAGGAGG -3'                                            |
| two-repeat RNA G4C2 G4\([9]\)       | 5'-GGGGCCGGGGCCG -3'                                                    |
| RNA G4C2 hairpin form\([10]\)       | 5'-GGGGCCGGGGCCG -3'                                                    |
| dsRNA G4C2\([5]\)                   | 5'-CUAGGGCCUAG -3'                                                      |
| aptamer RNA hairpin form\([11]\)    | 5'-GGAGAUCGCACUCCA -3'                                                  |
Table S12. Molecular Formula Strings (SMILES) of cA, cB, and cC.

| Compound | SMILE                                                                 | DNA (G4C2) | RNA (G4C2) | Permeability (cm/s) |
|----------|-----------------------------------------------------------------------|------------|------------|---------------------|
| chrexa nthomycin A (cA) | O=C(C(C(O)=C(C(C=CC= C1O[C@@H]2O[C(O)=O]=C[C@H](O ][C@H]2O)=C1O3)=O)C3=C4O)=C4CC 5)=C6)=C6CC(C)=O)O | 2.2 ± 0.1  | 3.0 ± 0.1  | 2.823e-005          |
| chrexa nthomycin B (cB) | O=C(C(C(O)=C(C(C=CC= C1O[C@@H]2O[C(O)=O]=C[C@H](O ][C@H]2O)=C1O3)=O)C3=C4OC)=C4CC 5)=C6)=C6CC(C)=O)O | 3.0 ± 0.1  |           | 2.619e-005          |
| chrexa nthomycin C (cC) | O=C(C(C(O)=C(C(C=CC= C1O[C@@H]2O[C@H](O)[C@H](O)[C@H]2O)=C1O3)=O)C3=C4O)=C4CC5)=C6)=C6CC(C)=O)O | 2.8 ± 0.1  |           | 2.199e-005          |
Refinement model description.

This report has been created with Olex2, compiled on 2021.04.04 svn.r0348f7ac for OlexSys.

Number of restraints - 326, number of constraints - 79.

Details:
1. Fixed Uiso
   At 1.2 times of: All C(H) groups, All C(H,H) groups
   At 1.5 times of: All C(H,H,H) groups, All O(H) groups, All O(H,H) groups, All O(H,H,H) groups

2. Restrained distances
   C25-C24 = C36-C35 1.52 with sigma of 0.02
   O9A-C25A 1.45 with sigma of 0.02
   O3-C3 ≈ O3A-C3  with sigma of 0.02
   O3-C3 ≈ O3A-C3A  with sigma of 0.02
   C22A-C21 ≈ C22-C21  with sigma of 0.02

3. Uiso/Uaniso restraints and constraints
   Uanis(O1S) ≈ Ueq: with sigma of 0.01 and sigma for terminal atoms of 0.015
   Uanis(O3A) ≈ Ueq, Uanis(O3) ≈ Ueq: with sigma of 0.003 and sigma for terminal atoms of 0.005
   Uanis(O3W) ≈ Ueq: with sigma of 0.02 and sigma for terminal atoms of 0.01
   Uanis(O3C) ≈ Ueq, Uanis(C2) ≈ Ueq, Uanis(C3) ≈ Ueq, Uanis(C22) ≈ Ueq: with sigma of 0.005 and sigma for terminal atoms of 0.008
   Uanis(C22A) ≈ Ueq, Uanis(C23A) ≈ Ueq, Uanis(C2A) ≈ Ueq, Uanis(C3A) ≈ Ueq: with sigma of 0.003 and sigma for terminal atoms of 0.005
   Uanis(C36) ≈ Ueq, Uanis(C36A) ≈ Ueq: with sigma of 0.005 and sigma for terminal atoms of 0.002
   Uanis(O13A) ≈ Ueq: with sigma of 0.005 and sigma for terminal atoms of 0.01
   Uanis(O14) ≈ Ueq, Uanis(O14A) ≈ Ueq: with sigma of 0.005 and sigma for terminal atoms of 0.01
   Uanis(C1A) ≈ Ueq: with sigma of 0.008 and sigma for terminal atoms of 0.015
   Uanis(C24) ≈ Ueq, Uanis(C24A) ≈ Ueq: with sigma of 0.01 and sigma for terminal atoms of 0.003
   Uanis(O2W) ≈ Ueq: with sigma of 0.01 and sigma for terminal atoms of 0.002
   Uanis(O13) ≈ Ueq: with sigma of 0.005 and sigma for terminal atoms of 0.01
   Uanis(O14) ≈ Ueq: with sigma of 0.005 and sigma for terminal atoms of 0.01

4. Rigid body (RIGU) restraints
   O1S, C1S, O3, C3, O1, O2, C1, C2, O3A, C3, C1A, C2A, C3A, C4, C21, C22A, C23A, C24A, O13A, O14A, C35, C36A, O1A, O2A, C1A, C2, C3, C4, C21, C22, C23, C24, O13, O14, C35, C36
   with sigma for 1-2 distances of 0.001 and sigma for 1-3 distances of 0.001

5. Others
   Fixed Sos: O1(0.5) O1A(0.5) O2(0.5) H2(0.5) O2A(0.5) O3(0.5) H3(0.5) O3A(0.5) H3A(0.5) H8b(0.5) H8a(0.5) O9(0.5) O9A(0.5) H9A(0.5) O13(0.5) H13(0.5) O13A(0.5) H13A(0.5) O14(0.5) O14A(0.5) C1(0.5) C1A(0.5) C2(0.5) C2A(0.5) C22a(0.5) H22(0.5) C23(0.5) C24(0.5) H24a(0.5) H24b(0.5) C24A(0.5) H24c(0.5) H24d(0.5) C25(0.5) C25A(0.5) C26(0.5) H26a(0.5) H26b(0.5) H26c(0.5) C26A(0.5) H26e(0.5) H26d(0.5) H26f(0.5) C36(0.5) C36A(0.5) H1Wa(0.5) H1Wb(0.5) C1S(0.5) H1Sa(0.5) H1Sb(0.5) H1Sc(0.5) O3W(0.5) H3Wa(0.5) H3Wb(0.5) O4W(0.5) H4Wa(0.5)
H4Wb(0.5) C22A(0.5) H22A(0.5) C23A(0.5) C2A(0.5) C3A(0.5) O1S(0.5) H1S(0.5)
6.a Riding coordinates:
O2(H2), O8(H8a), O9A(H9A), O13A(H13A), O1W(H1W,H1Wa,H1Wb),
O2W(H2Wa,H2Wb),
O4W(H4Wa,H4Wb), O1S(H1S)
6.b Free rotating group: O3W(H3Wa,H3Wb)
6.c Ternary CH refined with riding coordinates:
C31(H31), C32(H32), C33(H33)
6.d Secondary CH2 refined with riding coordinates:
C19(H19a,H19b), C20(H20a,H20b), C24(H24a,H24b), C24A(H24c,H24d)
6.e Aromatic/amide H refined with riding coordinates:
C10(H10), C11(H11a), C12(H12a), C22(H22), C34(H34), C22A(H22A)
6.f Idealised Me refined as rotating group:
C26(H26a,H26b,H26c), C26A(H26d,H26e,H26f), C1S(H1Sa,H1Sb,H1Sc)
6.g Idealised tetrahedral OH refined as rotating group:
O3(H3), O3A(H3A), O4(H4), O8(H8b), O11(H11), O12(H12), O13(H13)
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