Supplementary Data

Synthesis of compound **14**

Compound **14** was synthesized in accordance with the procedure described previously (1) for the synthesis of compound **13** [3-[4-(o-Carboran-1-yl)butyl]thymidine-5′-monophosphate] (Fig. 1).

Compound **B**:

A 374 mg (1 mmol) of bis(2,2,2-trichloroethyl) phosphorochloridate was added to an ice-cooled solution of 455 mg (0.823 mmol) of 3-[5-(2-(2,3-Isopropylidenedioxyprop-1-yl)-o-carboran-1-yl)pentan-1-yl]thymidine [A] (2) and 50 μL (1.04 mmol) of pyridine in 10 mL of acetonitrile. The solution was reacted at 0°C for 5 days and terminated by adding 5 mL methanol and stirring the resulting mixture for 30 min at room temperature. The solution was evaporated to dryness, the residue dissolved in 20 mL of diethyl ether, and extracted 2 × with 10 mL of 0.1 M aqueous HCl. The organic layer was collected, evaporated to dryness, and the residue was purified by silica column chromatography to give B (400 mg, 50 %) as colorless resin; R_f 0.34 (DCM : MeOH); ^{1}H NMR ($CDCl_3$) δ= 1.25 (s, 3H, -CH_3), 1.29 (s, 3H, -CH_3), 1.41-1.60 (m, 4H, alkane), 1.85 (s, 3H,-CH_3), 2.00-2.19 (m, 2H, alkane), 2.24-2.46 (m, 4H, CH_2-$C_{carborane}$), 3.49 (t, J=6, 1H, CH_2-CH), 3.81 (t, J=6, 2H, CH_2-N), 3.87-3.93 (m, 1H, H-3′), 4.00-4.10 (m, 2H, H-5′), 4.16 (t, J=6, 1H, CH-CH_2), 4.41-4.48 (m, 1H, H-4′), 4.51-4.62 (m, 4H, CH_2-CCl_3), 6.27 (t, J=6, 1H, H-1′), 7.89 (s, 1H, H-6), 4.33-4.40 (m, 2H, OCH-CH_2O); ^{13}C NMR δ= 13.18 (CH_3), 25.85 (CH_3), 26.30 (CH_3), 26.71 (CH_2), 26.86 (CH_2), 29.06 (CH_2), 31.43 (CH_2), 34.75 (CH_2), 36.50 (CH_2), 39.26 (CH_2), 40.07 (CH_2-$C_{carborane}$), 40.84 ($C_{carborane}$-CH_2), 68.19 (CH_2-N), 68.28 (C-2′), 68.96 (CH_2), 70.78 (C-3′), 74.32 (CH), 77.51 (C), 79.96 (C), 84.07 (CH_2), 84.19 (CH_2), 85.48 (C-1′), 94.25 (CH_2), 94.42 (CH_2), 109.44 (O-C-O), C-5

(110.49), 133.30 (C-6), 150.66 (C-2), 162.59 (C-4); MS (HR-ESI) $C_{27}H_{47}O_{10}N_2B_{10}Cl_6PNa$ $(M+Na)^+$ calcd.933.1971; found, 933.1896.

Compound **14**:

A 191 mg (0.21 mmol) of compound B was reacted with 21 mg (0.32 mmol) of zinc powder (100 mesh) in 12 mL of acetic acid for 2 hr. The solution was filtered and evaporated to dryness. This crude product was then reacted with 1 mL of 17% HCl in 10 mL of methanol at room temperature for 12 hr to remove the isopropylidene protecting group. The excess acid was neutralized with 0.5 g of K_2CO_3 and the mixture was stirred for 15 min. The solution was filtered, evaporated to dryness. The resulting residue was suspended in 10 mL water and 10% formic acid solution was added in small aliquots to the suspension under vigorous stirring until all the material was dissolved (PH ~ 2-3). The solution was passed through a 2.5 cm x 50-cm column containing Dowex 50X8-100 (Na^+ form). Fractions of 10 mL were collected and those showing UV absorptions (254 nm) were combined and evaporated at room temperature. The residue was dissolved in methanol and purified by reversed phase column chromatography RP 8 or RP 18, using water/methanol (1:1) as the solvent system. The fractions showing UV absorptions were combined and evaporated to dryness to obtain 25 mg (~5%) of the compound. The residue was suspended in distilled water and was freeze-dried to obtain compound **14** as white powder. ^{1}H NMR ($CDCl_3$) δ= 1.44-1.66 (m, 4H, alkane), 1.86 (s, 3H,-CH_3), 2.14-2.35 (m, 4H, CH_2-$C_{carborane}$), 3.50 (t, J=6, 1H, CH_2-CH), 3.88 (t, J=6, 2H, CH_2-N), 4.00-4.05 (m, 1H, H-3′), 4.07-4.16(m, 2H, H-5′), 4.43-4.52(m, 1H, H-4′), 6.34 (t, J=6, 1H, H-1′), 7.76 (s, 1H, H-6); ^{13}C NMR δ= 14.40 (CH_3), 24.19 (CH_3), 24.62 (CH_2), 26.21 (CH_2), 28.19 (CH_2), 29.57 (CH_2), 33.88 (CH_2), 40.56 (CH_2-$C_{carborane}$), 42.39 ($C_{carborane}$-CH_2), 67.78 (CH_2-N), 68.37 (C-2′), 71.45 (C-3′), 85.38 (C-1′), 94.25 (CH_2),

94.42 (CH_2), 109.44 (O-C-O), 110.43 C-5, 129.80 (C-6), 154.33 (C-2), 162.09 (C-4); MS (HR-ESI) $C_{20}H_{39}O_{10}N_2B_{10}PNa_2$ $(M+2Na)^+$ calcd, 655.3146; found, 655.3118. Reversed phase-18 HPLC retention time: 23.34 min, >90% pure.

Reference:

1. Lunato AJ, Wang J, Woollard JE, et al. Synthesis of 5-(carboranylalkylmercapto)-2'-deoxyuridines and 3-(carboranylalkyl)thymidines and their evaluation as substrates for human thymidine kinases 1 and 2. *J Med Chem* 1999; 42(17): 3373-89.
2. Al-Madhoun AS, Johnsamuel J, Yan J, et al. Synthesis of a small library of 3-(carboranylalkyl)thymidines and their biological evaluation as substrates for human thymidine kinases 1 and 2. *J Med Chem* 2002; 45(18): 4018-28.

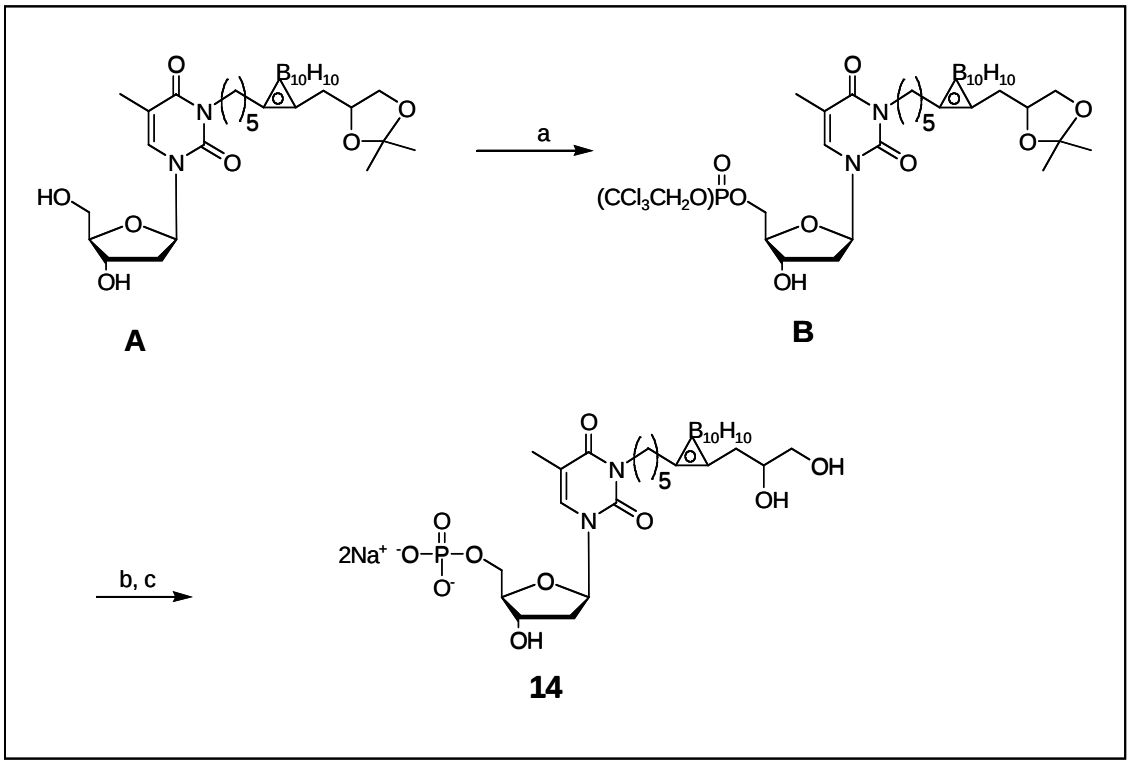

Figure 1. Reagents:

(a) bis(2,2,2-trichloroethyl)phosphochloridate/pyridine/0°C/5 days;

(b) Zn/AcOH/rt/2 h;

(c) 17% HCl in MeOH, room temperature, 12hr/ Dowex 50X8-100 (Na^+-form)