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Synthesis of Carboranes Containing Nucleoside Bases

Yoshinori Yamamoto†*, Toshiya Seko, Hiroyuki Nakamura, and Hisao Nemoto

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan.

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ABSTRACT

*The carboranes containing uridine derivatives (**9a, b, c**), and purine base (**8**) were prepared by the reaction of decaborane with the corresponding acetylene precursors (**3a, 3b, 2c** and **5b**, respectively).*

INTRODUCTION

Recently, much attention has been paid to ^{10}B neutron capture therapy (BNCT). The interaction of boron-10 and a thermal neutron, each relatively innocuous, produces intense, ionizing radiation that is confined to single or adjacent cancer cells [1]:

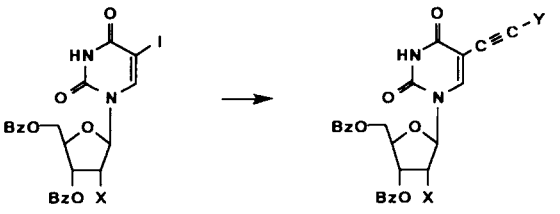
$$^{10}B + {}^{1}n \rightarrow {}^{7}Li + {}^{4}He + 2.4\ MeV$$

Since a practical method for production of highly purified thermal neutrons (^{1}n) has been accomplished, much attention has been paid to the design and synthesis of ^{10}B carriers that deliver an adequate concentration of ^{10}B atoms to tumors. Development of a new synthetic method for ^{10}B carriers with a relatively large number of ^{10}B atoms in the molecule is required in order to deliver a sufficient quantity of ^{10}B atoms to tumor cells. Previously, we reported new synthetic methods for ^{10}B-carriers containing a single boron atom [2]. o-Carborane, one of the most stable boron clusters, is an appropriate candidate for use in ^{10}B carriers [3]. Recently, hydroxyalkylated carboranes [4], glycosyl carboranes [5], carboranylporphyrins [6], and carboranyl nucleoside derivatives [7] have been prepared. We report the synthesis of carboranes containing uridine, deoxyuridine, and 6-methoxypurine derivatives by the reaction of decaborane with the corresponding acetylene precursors [8].

RESULTS AND DISCUSSION

Synthesis of Acetylene Derivatives

Coupling of terminal alkynes with 5-iodouridine derivatives (**1**) and the 2-iodopurine derivative (**4**) proceeded in good yields in the presence of bis(triphenylphosphine)palladium (II) chloride and copper(I) iodide in warm triethylamine (Equation 1, 2) [9] The reaction of **1a** with trimethylsilylacetylene gave **2a** in 75% yield, and the reaction with propargyl acetate produced **2c** in 73% yield. Similarly, the 5-iododeoxyuridine **1b** was converted to **2b** in 80% yield. Treatment of **2a** and **b** with tetrabutylammonium fluoride gave the corresponding desilylated acetylene derivatives **3a** and **b**, respectively, in nearly quantitative yield. In contrast with the reaction of uridine derivatives, the coupling of the 2-iodopurine derivative **4** with trimethylsilylacetylene proceeded



(eq 1)

1a; X = OBz
b; X = H

2a; X = OBz, Y = TMS **3a**; X = OBz, Y = H
b; X = H, Y = TMS **b**; X = H, Y = H
c; X = OBz, Y = CH_2OAc

†This paper is dedicated to Professor Emeritus Herbert C. Brown on the occasion of his 80th birthday.

*To whom correspondence should be addressed.

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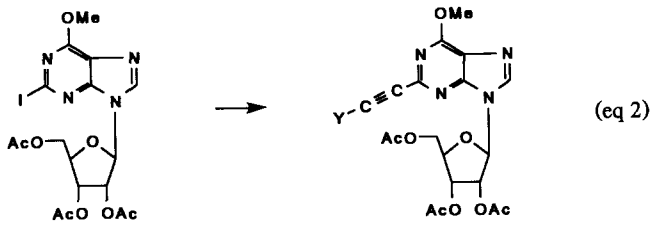
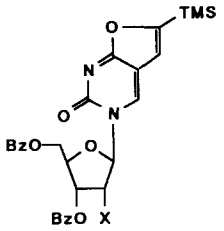


(eq 2)

4

5a; Y = TMS
b; Y = H



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very smoothly to give **5a** in higher yield (94%). The desilylation of **5a** with Bu_4NF produced **5b** in 88% yield. Perhaps, in the case of uridine derivatives, a by-product **6** was produced although the structure was not unambiguously established, leading to relatively lower yield in comparison with that of the purine derivative.

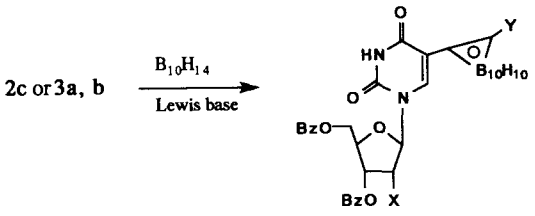
Carborane Formation

The reaction of acetylenes with $B_{10}H_{14}$ requires the presence of Lewis bases (LB), which removes H_2 from $B_{10}H_{14}$ to give $B_{10}H_{12}(LB)_2$. Dissociation of one mole of LB from $B_{10}H_{12}(LB)_2$ affords a reactive intermediate $B_{10}H_{12}(LB)$. The reaction of acetylenes (A) proceeds with this intermediate to produce $B_{10}H_{12}A(LB)$. Elimination of (LB) and H_2 gives a carborane $B_{10}H_{10}A$ [10].

Although the reaction of simple acetylene derivatives with decaborane is a well-known reaction, that of complex molecules is not known. We

$$B_{10}H_{14} + 2(LB) \rightarrow B_{10}H_{12}(LB)_2 + H_2$$
$$B_{10}H_{12}(LB)_2 \rightarrow B_{10}H_{12}(LB) + (LB)$$
$$B_{10}H_{12}(LB) + A \rightarrow B_{10}H_{12}A(LB)$$
$$B_{10}H_{12}A(LB) \rightarrow B_{10}H_{10}A + (LB) + H_2$$

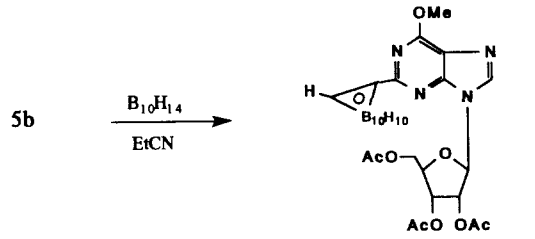
investigated the effect of Lewis bases upon the reaction of **3a** (Equation 3). The results are summarized in Table 1. The reaction time was short when Et_2S or PPh_3 was used as a Lewis base, but the use of C_2H_5CN gave a higher chemical yield.



(eq 3)

7a; X = OBz, Y = H
b; X = H, Y = H
c; X = OBz, Y = CH_2OAc

The reaction of **3b** with $B_{10}H_{14}$ in the presence of EtCN gave **7b** in 74% yield. The reaction of **2c** in the presence of Et_2S produced **7c** in 40% yield; in this case Et_2S was better than EtCN. It seems that the reaction of terminal acetylenes gives a higher yield than that of internal acetylenes. In fact, the reaction of phenylacetylene derivative (**2d**; X = OBz, Y = Ph) in the presence of EtCN or Et_2S did not proceed at all, and the starting material was recovered quantitatively. The reaction of **5b** in the presence of EtCN gave **8** in 40% yield (Equation 4).



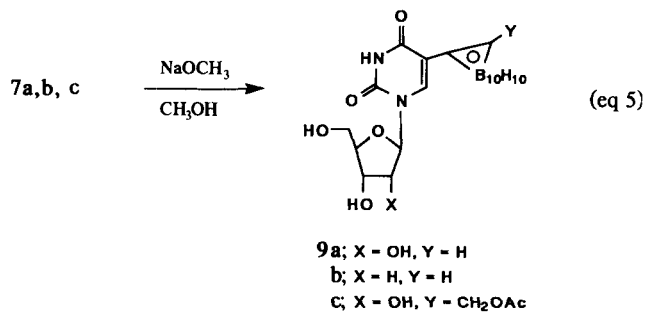
(eq 4)

8

TABLE 1 Effect of Lewis Bases on the Reaction of **3a** with Decaborane.[a]

Lewis Base	*Reaction Time, h*	*Isolated Yield of 7a, %*
CH_3CN	19	57
C_2H_5CN	18	67
PhCN	18	40
Et_2S	4	56
PPh_3	2	40

[a] **3a** (0.25 mmol), $B_{10}H_{14}$ (0.3 mmol), Lewis base (5 mmol), in toluene at reflux



(eq 5)

9a; X = OH, Y = H
b; X = H, Y = H
c; X = OH, Y = CH_2OAc

Removal of Protective Groups

Treatment of **7a, b,** and **c** with sodium methoxide in methanol gave carboranyl uridines **9a, b, c,** respectively, in high yields (Eq 5). Deprotection of **8** was also examined under various conditions, but the deacetylation was accompanied by the cleavage of the CN bond between the purine ring and the ribofuranosyl group. Very interestingly, the carboranyl uridines (**9a** and **b**) exhibited high cytotoxicity toward cancer cells such as P-388, L1210, B-16, MBL-2, and Meth A. IC_{50} values were of the order of 10^{-5}M [11]. These findings suggest that novel boron derivatives such as **9a** and **b** can serve as a neutron capture agents having direct cytotoxicity towards tumor cells, if the cells selectively take up the ^{10}B carriers.

EXPERIMENTAL

General

^1H and ^{13}C NMR spectra were measured on a Jeol GSX-270 NMR at 270 and 67.5 MHz, respectively, using TMS as an internal standard. High resolution mass spectra were measured with a Jeol DX-303 spectrometer using FAB mode. All solvents were dried as usual. Decaborane was purchased from Aldrich and used as such.

*2',3',5'-Tris-O-benzoyl-5-[2-(trimethylsilyl)ethynyl] uridine (**2a**).* To a THF solution (30 mL) of **1a** [12] (2.046 g, 3.0 mmol), $PdCl_2$ (53 mg, 0.30 mmol), triphenylphosphine (158 mg, 0.6 mmol), and copper (I) iodide (114 mg, 0.6 mmol) were added triethylamine (1.2 mL) and trimethylsilylacetylene (0.85 mL, 6.0 mmol) under Ar and the mixture was kept at 40°C for 2 hours. The solvent was removed under vacuum. The crude product was purified by silica gel column chromatography using benzene/AcOEt (5/1) as eluant; **2a** was obtained in 75% yield (1.47 g, 2.25 mmol); mp 237~238°C; IR (KBr) 3450, 3080, 2980, 2160, 1720, 1695, 1460, 1275, 1140, 1100, 850, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.24 (1H, s), 7.74 (1H, s), 7.32–8.14 (15H, m), 6.30 (1H, d, J = 5.9 Hz), 5.86 (1H, dd, J = 5.9, 3.7 Hz), 5.74 (1H, dd, J = 5.9, 5.9 Hz), 4.76 (3H, m), 0.18 (9H, m); ^{13}C-NMR ($CDCl_3$) δ 166.10, 165.29, 160.34, 148.88, 142.60, 133.82, 133.62, 129.93, 129.84, 129.70, 129.06, 128.81, 128.61, 128.35, 101.71, 88.29, 80.89, 73.89, 71.36, 63.99, –0.29; MS (FAB + NBA) m/z 653 (MH^+), 445, 289; Exact mass (MH^+) calcd for $C_{35}H_{33}O_9N_2Si$ m/z 653.1956, found m/z 653.1973.

*3',5'-Bis-O-benzoyl-5-[2-(trimethylsilyl)ethynyl]-2'-deoxyuridine (**2b**).* To a THF solution (100 mL) of **1b** [12] (5.525 g, 9.83 mmol), $PdCl_2$ (174 mg, 0.983 mmol), triphenylphosphine (515 mg, 1.97 mmol), and CuI (187 mg, 0.983 mmol) were added triethylamine (2.7 mL, 19.7 mmol) and trimethylsilylacetylene (2.1 mL, 14.7 mmol) under Ar. The mixture was kept at 40°C for 4 hours. The usual work-up gave **2b** in 80% yield (4.208 g, 7.90 mmol); mp 227 ~ 229°C (white needles); IR (KBr) 3400, 3050, 2950, 2150, 1720, 1685, 1450, 1275, 1120, 1090, 1070, 845, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.32 (1H, bs), 7.43–8.08 (10H, m), 7.88 (1H, s), 6.37 (1H, dd, J = 8.5, 5.5 Hz), 5.60 (1H, m), 4.83 (1H, dd, J = 12.0, 3.5 Hz), 4.67 (1H, dd, J = 12.0, 3.0 Hz), 4.59 (1H, m), 2.78 (1H, ddd, 14.0, 5.5, 1.5 Hz), 2.28 (1H, ddd, J = 14.0, 8.5, 6.5 Hz), 0.14 (9H, s); ^{13}C NMR ($CDCl_3$) δ 166.3, 166.2, 161.5, 149.6, 142.3, 133.9, 133.8, 130.0, 129.8, 129.4, 129.2, 129.0, 128.8, 101.3, 100. 1, 95.2, 86.2, 83.5, 75.3, 64.6, 38.8; Exact mass (MH^+) calcd for $C_{28}H_{29}O_7N_2$ m/z 533.1744, found m/z 533.1722.

*2',3',5'-Tris-O-benzoyl-5-[3-(acetoxy)propynyl]uridine (**2c**).* To a THF solution (30 mL) of **1a** [12] (2.046 g, 3.0 mmol), $PdCl_2(PPh_3)_2$ (63 mg, 0.09 mmol), and CuI (114 mg, 0.6 mmol) were added triethylamine (1.0 mL) and propargyl acetate (0.60 mL, 6.0 mmol) under Ar. The mixture was kept at room temperature overnight. Purification by silica gel column chromatography using hexane-AcOEt (3/2) as eluant gave **2c** in 73% yield(1.44 g, 2.19 mmol) ; mp 173 ~174°C; IR (KBr) 3430, 3070, 1720, 1690, 1450, 1120, 1100, 1070, 1025, cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.50 (1H, bs), 7.77 (1H, s), 7.32–8.14 (15H, m), 6.30 (1H, d, J = 5.9 Hz), 5.88 (1H, dd, J = 5.9, 4.0 Hz), 5.75 (1H, dd, J = 5.9, 5.9 Hz), 4.75 (3H, m), 4.69 (1H, s), 4.68 (1H, s), 2.08 (3H, s); ^{13}C NMR ($CDCl_3$) δ 170.1, 166.0, 165.2, 161.0, 149.1, 143.2, 133.7, 133.6, 133.3, 129.8, 129.7, 129.6, 129.0, 128.6, 128.4, 128.2, 100.2, 88.4, 87.8, 80.7, 76.8, 73.9, 71.7, 63.8, 52.4, 20.5; MS (FAB+NBA) m/z 653 (MH^+), 445; Exact mass (MH^+) calcd for $C_{35}H_{29}O_{11}N_2$ m/z 653.1772, found m/z 653.1736.

*9-[2',3',5'-Tris-O-acetyl-β-D-ribofuranosyl]-2-[2-(trimethylsilyl)ethynyl]-6-methoxypurine (**5a**).* To a THF solution (10 mL) of **4** [13] (450 mg, 0.84 mmol), $PdCl_2(PPh_3)_2$ (29 mg, 0.04 mmol), and CuI (16 mg, 0.08 mmol) were added triethylamine (0.24 mL:, 1.70 mmol) and trimethylsilylacetylene (0.24 mL, 1.70 mmol) under Ar. The mixture was kept at room temperature for 2 hours. Purification by silica

gel column chromatography using n-hexane-AcOEt (1/1) as eluant gave **5a** in 94% yield (398 mg, 0.79 mmol); IR (KBr) 2970, 2170, 1760, 1695, 1680, 1470, 1400, 1370, 1240, 1100, 1050, 870, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.14 (1H, s), 6.33 (1H, d, 5.9 Hz), 5.80 (1H, d, J = 5.9, 5.9 Hz), 5.60 (1H, dd, J = 5.9, 4.0 Hz), 4.38–4.45 (3H, m), 4.22 (3H, s), 2.16 (3H, s), 2.15 (3H, s), 2.08 (3H, s), 0.32 (9H, s); ^{13}C NMR ($CDCl_3$) δ 169.7, 169.0, 168.8, 160.2, 151.2, 144.8, 140.9, 121.2, 102.6, 91.8, 85.3, 80.2, 72.8, 70.3, 62.5, 54.2, 20.3, 20.0, 19.8, −0.82; MS (FAB+NBA) m/z 505 (MH^+); Exact mass (MH^+) calcd for $C_{22}O_{29}O_8N_4Si$ m/Z 505.1755, found m/z 505.1747.

2',3',5'-Tris-O-benzoy-5-ethynyluridine (**3a**). To a THF solution (15 mL) of **2a** (1.10 g, 1.69 mmol) was added dropwise at room temperature a THF solution of Bu_4NF (1.1 M, 1.85 ml), and the mixture was stirred for 30 min. The solvent was removed *in vacuo*. Dichloromethane and water was added. The organic layer was extracted with CH_2Cl_2, washed with sat. aqueous NaCl solution, dried over $MgSO_4$, and concentrated *in vacuo*. Purification by silica-gel column chromatography using CH_2Cl_2-EtOH (50/1) as eluant gave **3a** in 97% yield (954 mg, 1.64 mmol); mp 249°C; IR (KBr) 3430, 3300, 3250, 3110, 3090, 1720, 1450, 1270, 1120, 1090, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.24 (1H, bs), 7.79 (1H, s), 7.34–8.14 (15H, m), 6.34 (1H, d, J = 5.9 Hz), 5.89 (1H, dd, J = 5.9, 4.0 Hz), 5.74 (1H, dd, J = 5.9, 5.9 Hz), 4.83 (1H, dd, J = 14.0, 4.5 Hz), 4.75 (1H, m), 4.73 (1H, dd, J = 14.0, 3.5 Hz), 2.99 (1H, s); ^{13}C NMR ($CDCl_3$) δ 166.1, 165.3, 165.2, 160.9, 149.0, 143.2, 133.8, 133.7, 133.5, 129.8, 129.7, 129.6, 129.0, 128.7, 128.5, 128.2, 100.3, 88.1, 82.3, 80.8, 73.9, 73.7, 71.2, 63.7; MS (FAB+NBA) m/z 581 (MH^+), 445; Exact mass (MH^+) calcd for $C_{32}H_{25}O_9N_2$ m/z 581.1560, found m/z 581.1563.

3',5'-Bis-O-benzoyl-5-ethynyl-2'-deoxyuridine (**3b**). An acetonitrile solution (15 mL) of **2b** (154 mg, 0.29 mmol), Et_4NBr (121 mg, 0.578 mmol), and KF (33 mg, 0.578 mmol) was refluxed for 4 hours. The organic layer was extracted with dichloromethane, washed with sat. aqueous NaCl solution, dried, and concentrated. Purification by silica gel column chromatography using n-hexane-AcOEt (1/1) as eluant gave **3b** in 87% yield (115mg, 0.25mmol); mp 214°C; IR (KBr) 3400, 3300, 3060, 1710, 1685, 1450, 1275, 1120, 1090, 1065, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.00 (1H, bs), 7.91 (1H, s), 7.44–8.09 (10H, m), 6.38 (1H, dd, J= 8.0, 5.5 Hz), 5.63 (1H, m), 4.80 (1H, dd, J = 12.0, 3.5 Hz), 4.71 (1H, dd, J = 12.0, 3.0 Hz), 4.59 (1H, dd, J = 6.5, 3.0 Hz), 3.02 (1H, s), 2.80 (1H, ddd, J = 14.0, 5.5, 1.5 Hz), 2.32 (1H, ddd, J = 14.0, 8.0, 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 166.1, 165.9, 160.8, 148.9, 142.7, 133.8, 133.6, 129.8, 129.6, 129.1, 128.8, 128.6, 99.8, 85.9, 83.3, 82.1, 74.9, 74.0, 64.2, 38.7; Exact mass (MH^+) calcd for $C_{25}H_{21}O_7N_2$ m/z 461.1348, found m/z 461.1344.

9-(2',3',5'-Tris-O-acetyl-β-D-ribofuranosyl)-2-ethynyl-6-methoxypurine (**5b**). A similar procedure as described for the preparation of **3a** was used for **5a** (370 mg, 0.734 mmol), giving **5b** in 88% yield (280 mg, 0.648 mmol); mp 60 ~ 62°C; IR (KBr) 3450, 3260, 2950, 2110, 1750, 1590, 1570, 1470, 1390, 1360, 1240, 1140, 800, 740, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (1H, s), 6.29 (1H, d, J = 5.9 Hz), 5.82 (1H, dd, J = 5.9, 5.9 Hz), 5.61 (1H, dd, J = 5.9, 4.0 Hz), 4.40–4.47 (3H, m), 4.21 (3H, s), 3.09 (1H, s), 2.16 (3H, s), 2.15 (3H, s), 2.08 (3H, s); ^{13}C NMR ($CDCl_3$) δ 169.9, 169.2, 169.0, 160.4, 151.3, 144.4, 141.1, 121.6, 85.6, 81.9, 80.2, 74.3, 72.9, 70.3, 62.7, 54.3, 20.4, 20.2, 20.0; MS (FAB+NBA) m/z 433 (MH^+), 259; Exact mass (MH^+) calcd for $C_{19}H_{21}O_8N_4$ m/z 433.1360, found m/z 433.1362.

2',3',5'-Tris-O-benzoyl-5-carboranyluridine (**7a**). To a toluene solution (10 mL) of **3a** (145 mg, 0.25 mmol) and decaborane (37 mg, 0.30 mmol) was added propionitrile (0.36 mL, 5.0 mmol) under Ar, and the mixture was refluxed for 18 hours. The reaction mixture was cooled to room temperature, and the solvent was removed *in vacuo*. Purification by silica gel column chromatography using CH_2Cl_2-EtOH (100/1) as eluant gave **7a** in 67% yield (117 mg); mp 138 ~ 140°C; IR (KBr) 3450, 3250, 3100, 2610, 1740, 1690, 1460, 1275, 1130, 1100, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.50 (1H, brs), 7.76 (1H, s) 7.34–8.14 (15H, m), 6.19 (1H, d, J = 5.9 Hz), 5.93 (1H, dd, J = 5.5, 4.0 Hz), 5.76 (1H, dd, J = 5.5, 5.5 Hz), 5.61 (1H, brs), 4.81 (1H, dd, J = 11.4, 3.7 Hz), 4.77 (2H, m), 4.68 (1H, dd, J = 11.4, 3.7 Hz), 1.0–3.0 (br); ^{13}C NMR ($CDCl_3$) δ 166.1, 165.4, 165.2, 160.3, 148.6, 142.6, 133.8, 133.7, 133.4, 129.8, 129.7, 129.0, 128.5, 128.4, 128.4, 128.3, 128.0, 107.8, 89.7, 80.7, 73.8, 71.1, 69.2, 64.0, 57.8; MS (FAB+NBA) m/z 701 (MH^+), 445; Exact mass (MH^+) calcd for $C_{32}H_{35}O_9N_2B_{10}$ m/z 701.3277, found m/z 701.3370.

3',5'-Bis-O-benzoyl-5-carboranyl-2'-deoxyuridine (**7b**). A similar procedure as described for the preparation of **7a**, except for the reaction time (6 hours in the case of **7b**), was used for decaboration of **3b** (460 mg, 1.0 mmol). Purification of the crude product by silica gel column chromatography using benzene-AcOEt (9/1) as eluant gave **7b** in 74% yield (427 mg); mp 155 ~ 157°C; IR (KBr) 3425, 3200, 3100, 2600, 1720, 1680, 1460, 1260, 1100, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.90 (1H, bs), 7.43–8.08 (10H, m), 7.95 (1H, s), 6.26 (1H, dd, J = 8.5, 5.4 Hz), 5.65 (1H, d, J = 6.0 Hz), 5.60 (1H, bs), 4.65–4.73 (3H, m), 2.91 (1H, ddd, J = 14.0, 5.4, 1.5 Hz), 2.38 (1H, ddd, J = 14.0, 8.5, 6.0 Hz) 1.0–3.0 (br); ^{13}C NMR ($CDCl_3$) δ 166.1, 165.9, 160.4, 148.8, 141.3, 133.8, 133.7, 129.8, 129.6, 107.5, 86.9, 83.6, 74.9, 69.4, 64.5, 57.9, 39.0; MS (FAB+NBA) m/z 581 (MH^+); Exact mass (MH^+) calcd for $C_{25}H_{31}O_7N_2B_{10}$ m/z 581.3062, found m/z 581.3082.

*2',3',5'-Tris-O-benzoyl-5-(1-acetoxymethyl) carboranyluridine (**7c**).* A toluene solution (10 mL) of **2c** (163 mg, 0.25 mmol), decaborane (37 mg, 0.30 mmol), and diethyl sulfide (0.54 mL, 5.0 mmol) was refluxed under Ar for 4 hours. The usual work-up with silica gel column chromatography using n-hexane-AcOEt (3/1) as eluant gave **7c** in 40% yield (71 mg); mp 110°C; IR (KBr) 3400, 3240, 3060, 2590, 1720, 1700, 1620, 1600, 1450, 1315, 1260, 1210, 1100, 1070, 1020, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.58 (1H, bs), 7.32–8.16 (15H, m), 7.97 (1H, s), 6.30 (1H, d, J = 5.9 Hz), 5.94 (1H, dd, J = 6.2, 4.0 Hz), 5.78 (1H, dd, J = 6.2, 6.2 Hz), 4.83 (1H, dd, J = 11.4, 2.5 Hz), 4.78 (1H, m), 4.71 (1H, dd, J = 11.4, 4.0 Hz), 4.46 (1H, d, J = 13.6 Hz), 4.38 (1H, d, J = 13.6 Hz), 2.00 (3H, s), 1.0–3.0 (br); ^{13}C NMR ($CDCl_3$) δ 169.5, 166.2, 165.5, 165.4, 159.1, 148.7, 147.0, 133.9, 133.9, 133.7, 129.9, 129.9, 129.1, 128.8, 128.6, 128.6, 128.2, 105.4, 88.8, 81.0, 79.6, 75.8, 73.9, 71.2, 64.1, 62.0, 20.2; MS (FAB+NBA) m/z 773 (MH^+), 445; Exact mass (MH^+) calcd for $C_{35}H_{39}O_{11}N_2B_{10}$ m/z 773.3485, found m/z 773.3555.

*9-(2',3',5'-Tris-O-acetyl-β-D-ribofuranosyl) -2-carboranyl-6-methoxypurine (**8**).* A toluene solution (10 mL) of **5b** (101 mg, 0.23 mmol), decaborane (37 mg, 0.30 mmol), and propionitrile (0. 18 mL, 2.5 mmol) was refluxed under Ar for 1.5 hours. The usual work-up using n-hexane-AcOEt (2/1) as eluant gave **8** in 40% yield (52 mg); mp 157°C; IR (KBr) 3400, 2950, 2560, 2500, 1740, 1590, 1480, 1400, 1375, 1220, 1000, 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.78 (1H, s), 6.17 (1H, d, J = 4.0 Hz), 5.80 (1H, dd, J = 5.5, 4.0 Hz), 5.40 (1H, dd, J = 5.5, 5.5 Hz), 4.72 (1H, bs), 4.55 (1H, ddd, J = 5.5, 3.5, 3.0 Hz), 4.45 (1H, dd, J = 12.5, 3.5 Hz), 4.36 (1H, dd, J = 12.5, 3.0 Hz), 4.25 (3H, s), 2.24 (3H, s), 2.17 (3H, s), 2.14 (3H, s), 1.0–3.0 (br); ^{13}C NMR ($CDCl_3$) δ 170.5, 169.5, 169.2, 159.8, 155.9, 149.3, 141.4, 116.7, 88.2, 81.1, 73.6, 73.5, 69.7, 62.2, 57.4, 55.8, 21.1, 20.4, 20.3; MS (FAB+NBA) m/z 553 (MH^+); Exact mass (MH^+) calcd for $C_{19}H_{31}O_8N_4B_{10}$ m/z 553.3075, found m/z 553.3097.

*5-Carboranyluridine (**9a**).* A mixture of **7a** (510 mg, 0.730 mmol) and sodium methoxide (198 mg, 3.67 mmol) in methanol (20 mL) was stirred at room temperature for 3 hours. Then ion exchange resin (Dowex 50 W- × 8 H form) was added until the pH value of this solution became about six. The mixture was filtered and concentrated *in vacuo*. The residual solid was purified by chromatography on SiO_2 (30 g) using dichloromethane-ethanol (15:1) as eluant; **9a** was obtained as a white solid in 83% yield (235 mg, 0.608 mmol), mp 279–280°C; ^1H NMR (CD_3OD) δ 8.49 (s, 1H, H-6), 5.97 (brs, 1H, H-$C_2B_{10}H_{10}$-), 5.94 (d, J = 4.8 Hz, 1H, H-1'), 4.20 (dd, J = 4.8, 4.8 Hz, 1H), 4.15 (dd, J = 4.8, 4.8 Hz, 1H), 4.07 (m, 1H), 3.85 (dd, J = 11.7, 2.6 Hz, 1H), 3.74 (dd, J = 11.7, 2.6 Hz, 1H); ^{13}C NMR (CD_3OD) δ 162.5, 151.0, 144.4, 108.0, 90.9, 86.7, 76.5, 72.3, 71.7, 62.0, 59.8; IR(KBr) 3420, 3100, 2950, 2600, 1700, 1470, 1310, 1300 cm^{-1}; Exact mass (MH^+) calcd for $C_{11}H_{23}O_6N_2B_{10}$ m/z 389.2486, found m/z 389.2477. Anal. Calcd for $C_{11}H_{22}O_6N_2B_{10}$; C: 34.16, H: 5.69, N: 7.25. Found: C: 33.87, H: 5.53, N: 7.05.

*5-Carboranyl-2'-deoxyuridine (**9b**).* This compound was prepared from **7b** by the same method as described for the synthesis of **9a; 9b** was obtained in 91% yield as a white solid; mp 185–187°C; ^1H NMR (CD_3OD) δ 8.45 (s, 1H), 6.26 (dd, J = 6.5, 6.5 Hz, 1H), 5.95 (bs, H-$C_2B_{10}H_{10}$, 1H), 4.41 (ddd, J = 5.7, 3.0, 3.0 Hz, 1H), 4.00 (ddd, J = 3.0, 3.0, 3.0 Hz, 1H), 3.81 (dd, J = 11.5, 3.0 Hz, 1H), 3.74 (dd, J = 11.5, 3.0 Hz, 1H), 2.35 (ddd, J = 13.5, 6.5, 3.0 Hz, 1H), 2.20 (ddd, J = 13.5, 6.5, 5.7 Hz, 1H); ^{13}C NMR (CD_3OD) δ 162.6, 150.8, 144.4, 107.8, 89.5, 87.5, 72.7, 72.4, 62.7, 59.9, 42.1; IR (KBr) 3450, 3060, 2610 (B-H), 1700, 1640, 1470, 1300, 1200 cm^{-1}; Exact mass (MH^+) calcd for $C_{11}H_{23}O_5N_2B_{10}$ m/z 373.2527, found m/z 373.2450.

*5-(1-Hydroxymethyl)carboranyluridine (**9c**).* This compound was prepared from **7c** by the same method as described for the synthesis of **9a**. Chromatography on SiO_2 using dichloromethane-ethanol (6:1) as eluant afforded **9c** as a white solid in 89% yield; mp 254–255°C; ^1H NMR (CD_3OD) δ 8.54 (s, 1H, H-6), 5.94 (d, J = 4.5 Hz, 1H), 4.22 (dd, J = 4.5, 4.5 Hz, 1H), 4.14 (dd, J = 4.5, 4.5 Hz, 1H), 4.08 (m, 1H), 3.93 (d, J = 13.0 Hz, 1H), 3.87 (dd, J = 12.0, 2.5 Hz, 1H), 3.86 (d, J = 13.0 Hz, 1H), 3.76 (dd, J = 12.0, 3.0 Hz, 1H); ^{13}C NMR (CD_3OD) δ 161.0, 151.2, 148.4, 105.6, 91.2, 86.7, 85.6, 77.3, 76.4, 71.7, 64.1, 62.2; IR (KBr) 3420, 2600, 1690, 1460, 1300, 1110, 1080 cm^{-1}; Exact mass (MH^+) calcd for $C_{12}H_{24}O_7N_2B_{10}$ m/z 418.2514, found m/z 418.2528.

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