Synthesis of an *o*-Carboranyl Derivative of 4-[5-(4-Methyl-1-piperazinyl)-2,5′-bi-1*H*-benzimidazol-2′-yl]phenol

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Received May 4, 1998

Synthesis of an *o*-carboranyl derivative of 4-[5-(4-methyl-1-piperazinyl)-2,5′-bi-1*H*-benzimidazol-2′-yl]phenol (**1**), a candidate for application in boron neutron capture therapy for cancer treatment, is described. Decaborane was introduced into 3-(*p*-cyanophenoxy)-1-propyne (**11**) to form 1-(4-cyanophenoxymethyl)-1,2-dicarba-*closo*-dodecaborane(12) (**12**), which was transformed into the corresponding imidate **10** in order to be coupled with 4-cyano-*o*-phenylenediamine (**13**) to give 1-[4-(5′-cyano-1*H*-benzimidazol-2′-yl)phenoxymethyl]-1,2-dicarba-*closo*-dodecaborane(12) (**14**). The latter was reacted to the related imidate salt **15** and condensed with 5-(4-methyl-1-piperazinyl)-*o*-phenylenediamine (**6**) to the title compound 1-{4-[5-(4-methyl-1-piperazinyl)-2,5′-bi-1*H*-benzimidazol-2′-yl]phenoxymethyl}-1,2-dicarba-*closo*-dodecaborane(12) (**2**).

Introduction

Boron neutron capture therapy (BNCT) is a binary process: the stable boron isotope ^{10}B has to be introduced and trapped in the tumor cell, and after neutron irradiation, it emits an α particle and a ^{7}Li nucleus. Both particles have a high linear energy transfer (LET) and may consequently induce disturbances in the tumor cell division. This process was proposed in 1936[1] and has been used for therapeutic applications for many years. The main advantages of this therapy are that no radioactive materials are involved and that, in principle, the supply of neutrons can be controlled with respect to their energy, intensity, and space distribution.[2]

Many attempts have been made to design an efficient tumor-targeting compound as a boron carrier.[3] To date, only two compounds, the ^{10}B-enriched disodium undecahydromercapto-*closo*-dodecaborate, $Na_2{}^{10}B_{12}H_{11}SH$ (sodium borocaptate, BSH), and the ^{10}B-enriched L-4-(dihydroxyboryl)phenylalanine (BPA) are routinely used in BNCT, the former for glioma and the latter for skin melanoma treatment. An increase in the radiotherapeutic effectiveness of ^{10}B, however, could be expected if a carrier compound were designed which enters the cell nucleus or, most favorably, binds directly to the DNA.[4] Thus, the strategy of many research groups is to load potential DNA ligands with as many boron atoms as possible.

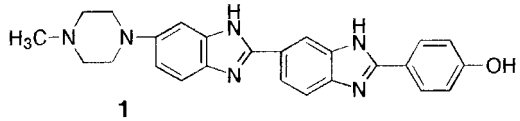

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Figure 1. 4-[5-(4-Methyl-1-piperazinyl)-2,5′-bi-1*H*-benzimidazol-2′-yl]phenol (**1**, "Hoechst 33258").

Boron-containing DNA ligands such as the following compounds were synthesized: (i) pyrimidine derivatives that act as surrogates for thymidine and, hence, can be introduced directly into the DNA of the tumor cell[5] and (ii) well-known dyes that can adhere to the DNA. Among these were boronated netropsin, distamycin, some phenanthridine and acridine derivatives, and the fluorescence marker 4-[5-(4-methyl-1-piperazinyl)-2,5′-bi-1*H*-benzimidazol-2′-yl]phenol (**1**, in the literature known as Hoechst 33258).[6]

1 (Figure 1) was developed in the 1960s for potential application as a chemotherapeutically active drug.[7] So far, however, it is merely used as a fluorescent stain for in vitro DNA studies.[8] It binds to the minor grooves of DNA, preferentially to A−T base pairs. As is shown by X-ray structure analyses,[9] hydrogen bridges are formed between the

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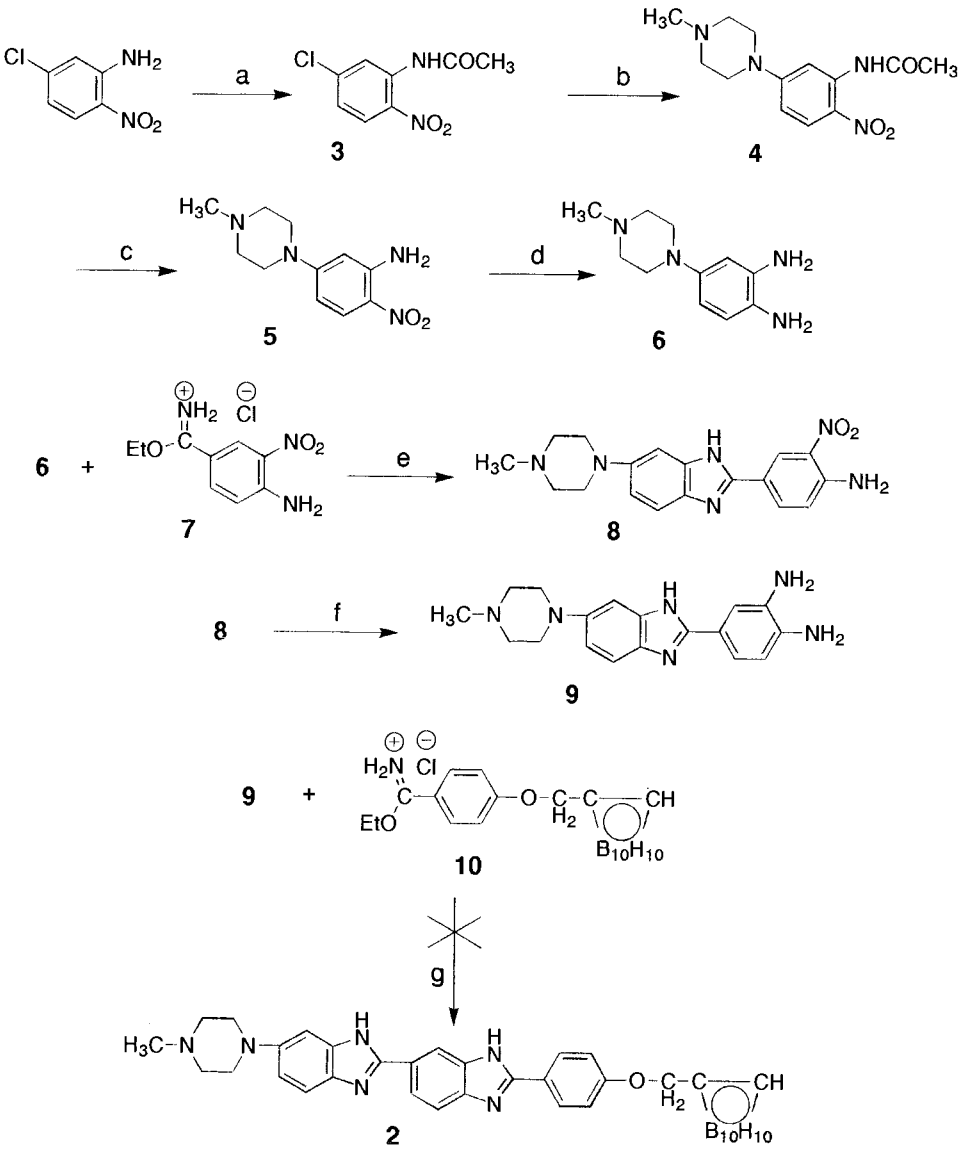
10.1021/ic980505e CCC: $15.00
Published on Web 10/22/1998

Scheme 1[a]



[a] (a) acetyl chloride, reflux; (b) 1-methylpiperazine, K_2CO_3, reflux; (c) 6 M HCl, reflux; (d) Ru (5%)/charcoal, $N_2H_4 \cdot H_2O$/EtOH, reflux; (e) **6**, AcOH, reflux; (f) Pd (10%)/charcoal, 1 M AcOH, reflux; (g) AcOH, reflux.

NH groups of the bis(benzimidazole) system and the adenine and thymine bases of the DNA. The piperazine group, however, tends to bind to the cytosine and guanine residues of the DNA.

Consequently, it was the aim of this work to synthesize a DNA ligand containing as many boron atoms as possible because of the potential value for BNCT. On the basis of the X-ray structure data,[9] it seemed advantageous to choose the compound 1-{4-[5-(4-methyl-1-piperazinyl)-2,5′-bi-1*H*-benzimidazol-2′-yl]phenoxymethyl}-1,2-dicarba-*closo*-dodecaborane-(12) (**2**) as an *o*-carboranyl derivative of **1**.[10,11] In this molecule, the bulky residue of the *o*-carborane is located far away from the bis(benzimidazole) region. Thus, no appreciable steric hindrances in the coupling to the DNA should occur, and the formation of the above-mentioned hydrogen bridges should generally be possible.

Results and Discussion

Our previous attempts to synthesize an *o*-carboranyl derivative of **1** in a way similar to that described in the patents of **1**[7] were unsuccessful (Scheme 1).[11]

The synthesis carried out according to Scheme 2 gave the expected results. In this new route, the first step consisted of the condensation of the commercially available *p*-hydroxybenzonitrile with propargyl bromide in the presence of potassium carbonate in acetone to form 3-(*p*-cyanophenoxy)-1-propyne (**11**). From this by condensation with the previously prepared decaborane/bis(acetonitrile) complex[12] in boiling toluene, 1-(4-cyanophenoxymethyl)-1,2-dicarba-*closo*-dodecaborane(12) (**12**) was obtained.[13] This reaction gave many side products that were not investigated in detail. It might be of interest to mention

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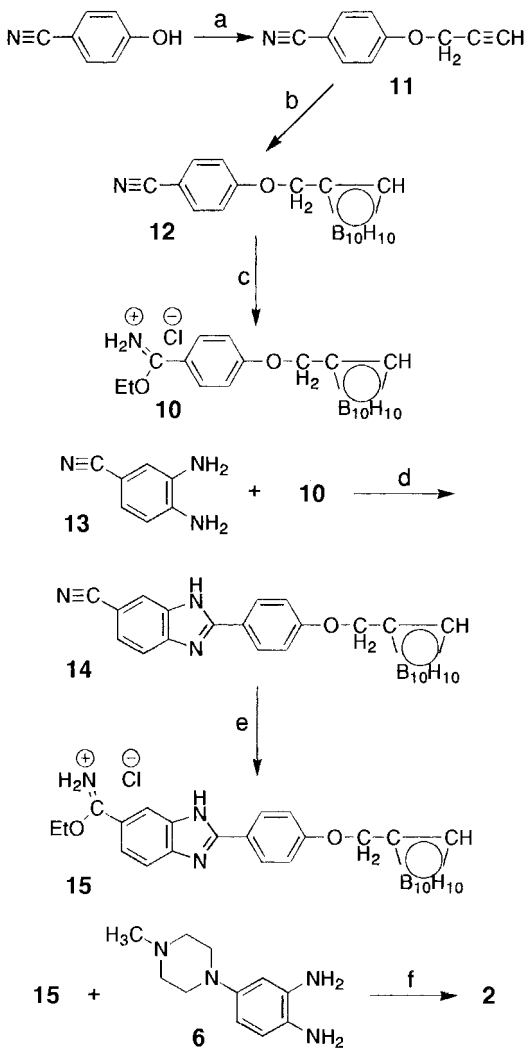
Scheme 2[a]



[a] (a) propargyl bromide, K_2CO_3, acetone, reflux; (b) (6,9-$CH_3CN)_2B_{10}H_{12}$, toluene, reflux; (c) EtOH−benzene/dry HCl; (d) AcOH, reflux; (e) EtOH−benzene/dry HCl; (f) AcOH, reflux.

that when the decaborane/bis(acetonitrile) complex is prepared in situ, no reaction occurs. To avoid a substantial decrease in the yield of **10**, or even the total lack of formation of any **14**, careful purification of **12** is important.

The transformation of highly purified **12** to 1-{4-[imino-(ethoxy)methyl]phenoxymethyl}-1,2-dicarba-*closo*-dodecaborane-(12) (**10**) with dry hydrogen chloride in a dry ethanol/benzene mixture[14] was achieved in a smooth reaction and led to a very pure salt in nearly quantitative yield. The condensation in glacial acetic acid of this pure product with 4-cyano-1,2-phenylenediamine[15] (**13**, obtained by reduction of commercially available 4-cyano-2-nitroaniline with hydrazine hydrate and ruthenium on charcoal in ethanol[16]) is also a straightforwarded reaction, and 1-[4-(5′-cyano-1*H*-benzimidazol-2′-yl)phenoxymethyl]-1,2-dicarba-*closo*-dodecaborane(12) (**14**) crystallized directly from the reaction mixture as very pure fine colorless needles.

The transformation to the corresponding 1-{4-[5′-(imino-(ethoxy)methyl)-1*H*-benzimidazol-2′-yl]phenoxymethyl}-1,2-dicarba-*closo*-dodecaborane(12) (**15**) was achieved in nearly quantitative yields as well when dry hydrogen chloride was bubbled through a dry ethanol/benzene mixture. The final step, consisting of the condensation between the 5-(4-methyl-1-piperazinyl)-*o*-phenylenediamine (**6**), which was freshly prepared by reduction of 5-(4-methyl-1-piperazinyl)-2-nitroaniline (**5**) with hydrazine hydrate and ruthenium on charcoal in ethanol, and the imidate **15**, was carried out in boiling glacial acetic acid, from which the *o*-carboranyl derivative **2** crystallized in pure form.

Experimental Section

General. Starting materials and reagents were purchased from Aldrich Chemical Co., Fluka Chemie AG, or Merck AG as reagent grade. The decaborane was purchased from Alfa, a subsidiary of Johnson Matthey Co. The decaborane/bis(acetonitrile) complex (6,9-$CH_3CN)_2B_{10}H_{12}$ was prepared according to a method described previously.[12] All melting points were determined on a Büchi 535 apparatus, and the values are uncorrected. IR spectra were recorded on a Perkin-Elmer 298 spectrometer using KBr pellets, and the signals are given in cm^{-1}. The ^1H NMR spectra were measured with a Varian Gemini 2000 at 300 MHz. The signals are given in ppm, δ, and are referred to the residual ^1H present in deuterated solvents, and the coupling constants J are given in Hz. The ^{11}B NMR spectra were measured with a Bruker AMX-600 spectrometer, and the signals are given in ppm, δ. The mass spectra (MS) were measured in the following way: EI with a Varian MAT 112s at 70 eV and ESI with a Fison VG TRIO 2000 at 40 eV, with ions in m/z (rel %). Column chromatography was performed with silica gel (Merck grade 60, 35−70-mesh ASTM) and TLC by using silica gel (60 F_{254}, Merck, coated plates 0.25-mm thick). The carboranyl compounds were stained with a solution of palladium chloride (300 mg of palladium chloride was dissolved in 12.5 mL of concentrated hydrochloric acid, diluted with 500 mL of water, and filtered).[17] Stain visualization was improved by heating the coated plates. The *closo*-*o*-carborane is evidenced by a brownish-black area on the plate. In the presence of the *nido*-*o*-carborane, the staining appears nearly immediately, without heating.[17] HPLC analysis was carried out using a Waters 600E multisolvent delivery system fitted with a Nova-Pak C_{18} column (4 μm, 3.9 × 150 mm). The UV spectra were obtained by an Ultrospec 2000 spectrometer (Pharmacia S.A., Uppsala, Sweden).

Synthesis of 5-Chloro-2-nitroacetanilide, 3. A mixture of 5-chloro-2-nitroaniline (145 mmol, 25 g) and acetyl chloride (100 mL) was refluxed for 2 h. The reaction mixture was cooled to room temperature, and acetyl chloride was removed under reduced pressure. The residue was then dissolved in acetone and evaporated to dryness at reduced pressure. This step was repeated until no more acetyl chloride was detectable. Product **3** crystallized as pale yellow needles from ethanol. Yield: 28 g (90%). Mp: 117−118 °C [115 °C (ethanol)[18]].

Synthesis of 5-(4-Methyl-1-piperazinyl)-2-nitroaniline, 5. A mixture of **3** (125 mmol, 26.75 g), 1-methylpiperazine (300 mmol, 30 g), and potassium carbonate (130 mmol, 18 g) was refluxed for 2 h. After being cooled to room temperature, the reaction mixture was poured into distilled water (500 mL). The brownish oil formed in this step solidified on standing overnight at room temperature. The resulting crude product, a mixture of 5-(4-methyl-1-piperazinyl)-2-nitroacetanilide (**4**) and 5-(4-methyl-1-piperazinyl)-2-nitroaniline (**5**), was filtered, washed with water, and refluxed for 2 h in 6 M HCl (500 mL). After the solution was cooled to room temperature, its pH was adjusted to 9−10 using solid NaOH pellets. The resulting precipitate was collected

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on a Büchner funnel, washed with water, and dried in vacuo. The final product recrystallized from ethyl acetate in yellow prisms. Yield: 25 g (85%). Mp: 155−156 °C [155 °C (not cryst)[7a,c]]. ^{1}H NMR (DMSO-d_6): 2.20 (s, 3 H, N−CH_3), 2.38 [t, J = 5.2, 4 H, $(-H_2C)_2N-CH_3$]; 3.32−3.29 [t, J = 4.99, 4 H, $(-H_2C)_2N-Ar$], 6.21 (d, $J_{4,6}$ = 2.6, 1 H, H-6), 6.36 (dd, $J_{4,6}$ = 2.6, $J_{3,4}$ = 9.7, 1 H, H-4), 7.26 (s, 2 H, Ar−NH_2), 7.78 (d, $J_{3,4}$ = 9.7, 1 H, H-3). IR: 3440, 3280, 3150, 2930, 2840, 2800, 1620, 1570, 1500, 1470, 1440. EI MS: 236.2 (7.7, M^+), 71.2 (37), 70.2 (100), 65.1 (14.4). Anal. Calcd for $C_{11}H_{16}N_4O_2$ (236.28): C, 55.93; H, 6.78; N, 23.73. Found: C, 56.08; H, 6.56; N, 23.46.

Synthesis of 5-(4-Methyl-1-piperazinyl)-*o*-phenylenediamine, 6. **5** (8.5 mmol, 2 g) was reduced in the presence of hydrazine hydrate (99%, 2.2 mL) and ruthenium (5%) on charcoal (25%, 0.5 g) in ethanol (50 mL) at reflux for ≈1.5 h or until the foam of the reaction mixture became colorless. After being cooled, the reaction mixture was filtered, and the filtrate was evaporated to dryness. The residue was suspended in water (100 mL) and extracted with chloroform (3 × 100 mL). The organic phase was dried (sodium sulfate), and the combined organic phases were evaporated under reduced pressure to give a yellow-brownish oil which rapidly crystallized. This product **6** can be used without further purification in the following reaction step. Yield: 1.56 g (89%).

Synthesis of 4-Amino-3-nitro-benziminoethyl Ester Hydrochloride, 7. In a flask (250 mL; equipped with a magnetic stirrer and a gas inlet tube), 4-amino-3-nitrobenzonitrile (61.35 mmol, 10 g) was dissolved in a mixture of dry ethanol (100 mL) and dry benzene (100 mL) under stirring. At room temperature, dry hydrogen chloride was bubbled through the solution until saturation was attained. The reaction mixture was left to stand overnight at room temperature, and diethyl ether (300 mL) was added. The crystals were filtered off, washed with diethyl ether, and dried at 60 °C. Yield: 10.84 g (72%). Mp: 288.2−289.4 °C. ^{1}H NMR (DMSO-d_6): 1.46 (t, J = 7.0, 3 H, $-CH_3$), 4.58 (q, J = 7.0, 2 H, $-O-CH_2-$), 7.18 (d, J = 9.2, 1 H, H-5), 8.11 (dd, $J_{5,6}$ = 9.3, $J_{2,6}$ = 2.3, 1 H, H-6), 8.36−8.40 (s, 2 H, $-NH_2$), 8.79 (d, $J_{2,6}$ = 2.3, 1 H, H-2). IR: 3420, 3240, 3150, 1670, 1625, 1490.

Synthesis of 2-(4-Amino-3-nitrophenyl)-5-(4-methyl-1-piperazinyl)-1*H*-benzimidazole, 8. A mixture of **6** (1.7 mmol, 0.35 g) and **7** (1.6 mmol, 0.4 g) was refluxed in glacial acetic acid (55 mL) for 2 h. Glacial acetic acid was removed under reduced pressure, and the residue was dissolved in water and filtered off. The crude product was precipitated with a concentrated aqueous NH_3 solution. The product was purified by redissolution in a mixture of MeOH (250 mL) and CH_3COOH (30 mL) and reprecipitation with a concentrated aqueous NH_3 solution. Yield: 0.44 g (73%). Mp: 183.3−185.4 °C. ^{1}H NMR (DMSO-d_6): 2.4 (s, 3 H, N−CH_3), 2.5 [br, 4 H and DMSO, $(-H_2C)_2N-CH_3$], 3.10 [br, 4 H, Ar−N($-CH_2)_2$], 6.92 (d, $J_{6,7}$ = 8.6, 1 H, H-6), 6.94 (s, 1 H, H-4), 7.13 (d, $J_{5,6}$ = 8.9, 1 H, H-5 ortho to $-NH_2$), 7.40 (d, $J_{6,7}$ = 8.6, 1 H, H-7), 7.80 (s, 2 H, $-NH_2$), 8.15 (d, $J_{5,6}$ = 8.9, 1 H, H-6 para to $-NO_2$), 8.76 (s, 1 H, ortho to $-NO_2$). IR: 3485, 3450, 3358, 2970, 2925, 2860, 2840, 2800, 1635, 1588, 1560, 1505, 1480, 1350, 1240.

Synthesis of 2-(3,4-Diaminophenyl)-5-(4-methyl-1-piperazinyl)-1*H*-benzimidazole, 9. A mixture of **8** (16.34 mmol, 5.75 g) and palladium (10%) on charcoal (≈20%, 1.15 g) in 1 M aqueous acetic acid (70 mL) was hydrogenated at 2.5 kg/cm^2 pressure for 24.5 h. The mixture was filtered on Hyflo (prewashed with ethanol and conditioned with 1 M aqueous acetic acid). The solvent was removed, and the residue was dissolved in water. Concentrated aqueous ammonia solution was added under stirring, the precipitate was filtered off, and the red crystals obtained were washed with diethyl ether. The precipitation was repeated twice. Yield: 3.85 g (73%). Mp: 259.5−264 °C [268 °C (not cryst)[7c] decomp[7a,b]]. IR: 3420, 3400, 3310, 2960, 2920, 2870, 2800, 1625, 1585, 1500, 1455, 1415, 1370, 1150.

Synthesis of 1-{4-[Imino(ethoxy)methyl]phenoxymethyl}-1,2-dicarba-*closo*-dodecaborane(12) Hydrochloride, 10. **12** (36.1 mmol, 10 g) was dissolved in a mixture of dry ethanol (100 mL) and benzene (150 mL). After the solution was cooled to 5−10 °C, dry hydrogen chloride (prepared by dropping 200 mL of concentrated hydrochloric acid into 300 mL of sulfuric acid)[19] was bubbled through for 2 h. The reaction mixture was left for 5 h at room temperature. Then the solvent was removed under reduced pressure, and the residue was triturated in dry diethyl ether (500 mL) and was left to stand overnight at room temperature. The colorless hydrochloride ($C_{12}H_{23}B_{10}NO_2$·HCl) obtained was filtered, washed with diethyl ether, and dried in vacuo. Yield: 12.2 g (94%). This compound was used in the next step without further purification. ^{1}H NMR (DMSO-d_6): 1.46 (t, J = 6.9, 3 H, $-CH_3$), 4.58 (q, J = 6.9, 2 H, $-CH_2-CH_3$), 4.80 (s, 2 H, $-OCH_2-$), 5.45 (s, 1 H, $-CB_{10}H_{10}C-H$), 7.24 [AA′XX′, $J_A(J_X)$ = 9, 2 H, H-3 and H-5], 8.13 [AA′XX′, $J_X(J_A)$ = 9, 2 H, H-2 and H-6]. IR: 2980, 2580, 1600, 1440, 1385, 1255, 1190, 1030, 840.

Synthesis of 3-(*p*-Cyanophenoxy)-1-propyne, 11. *p*-Hydroxybenzonitrile (80 mmol, 9.6 g) was allowed to react with propargyl bromide (80 mmol, 6.4 mL) in the presence of potassium carbonate (80 mmol, 11.2 g) in acetone for 24 h under reflux. After being cooled to room temperature, the solution was evaporated to dryness. The residue was recrystallized from ethanol/water (1:1, v/v) to give pale yellow needles. Yield: 11.3 g (90%). Mp: 109−110 °C. ^{1}H NMR (DMSO-d_6): 2.57 (t, J = 2.4, 1 H, $-C\equiv C-H$), 4.75 (d, J = 2.4, 2 H, $-O-CH_2-C$), 7.04 [AA′XX′, $J_A(J_X)$ = 9, 2 H, H-3 and H-5], 7.61 [AA′XX′, $J_X(J_A)$ = 9, H-2 and H-6]. IR: 3394, 3100, 2918, 2124, 1574, 1372, 1330, 1296, 1120, 968, 840, 812, 746, 720, 665. EI MS: 157.1 (42, M^+), 156.1 (94), 129.1 (53), 128.0 (100). Anal. Calcd for $C_{10}H_7NO$ (157.1): C, 76.43; H, 4.46; N, 8.92. Found: C, 76.35; H, 4.51; N, 8.78.

Synthesis of 1-(4-Cyanophenoxymethyl)-1,2-dicarba-*closo*-dodecaborane(12), 12. 3-(*p*-Cyanophenoxy)-1-propyne (**11**; 20 mmol, 3.1 g) and the decaborane/bis(acetonitrile) complex (40 mmol, 8.2 g) were allowed to react in toluene (500 mL) for 5 h under reflux. After being cooled to room temperature, the reaction mixture was filtered off and evaporated to dryness. The residue was dissolved in chloroform and purified by column chromatography on silica gel 60 (35−70 mesh, length = 20 cm, diameter = 8 cm) with chloroform. This process was repeated, generally three times, or until only one spot was detected by TLC (silica gel, chloroform). **12** crystallized from toluene in colorless crystals. Yield: 2.2 g (40%). Mp: 194−196 °C. ^{1}H NMR (DMSO-d_6): 4.72 (s, 2 H, $-O-CH_2-$), 5.33 (s, 1 H, $-CB_{10}H_{10}C-H$), 7.16 [AA′XX′, $J_A(J_X)$ = 8, 2 H, H-3 and H-5], 7.80 [AA′XX′, $J_X(J_A)$ = 8, 2 H, H-2 and H-6]. IR: 2580, 2200, 1605, 1505, 1300, 1250, 1170, 1030, 825, 710. EI MS: 277.2 (40), 276.6 (91.3), 275.3 (100), 274.2 (72.7), 273.3 (36.4), 272.2 (14.4). Anal. Calcd for $C_{10}H_{17}B_{10}NO$ (277.2): C, 43.32; H, 6.13; N, 5.05. Found: C, 43.45; H, 6.00; N, 4.98.

Synthesis of 4-Cyano-*o*-phenylenediamine, 13. 4-Amino-3-nitrobenzonitrile (38.17 mmol, 5 g) was reduced in the presence of hydrazine hydrate (99%, 6 mL) and ruthenium (5%) on charcoal (28%, 1.4 g) in ethanol (100 mL) at reflux for ≈1.5 h or until the foam of the reaction mixture became colorless. After being cooled, the reaction mixture was filtered, and the filtrate was evaporated to dryness, giving a white powder that turned rapidly reddish-brown by air oxidation. This compound was used without further additional purification. Yield: 3.9 g (77%). Mp: 139−140 °C [140.0−140.5 °C (not cryst)[20]].

Synthesis of 1-[4-(5′-Cyano-1*H*-benzimidazol-2′-yl)phenoxymethyl]-1,2-dicarba-*closo*-dodecaborane(12), 14. **10** (28 mmol, 10 g) and 4-cyano-*o*-phenylenediamine (**13**; 28 mmol, 3.7 g) were allowed to react in glacial acetic acid (150 mL) under reflux for 5 h and then were left standing overnight at room temperature. **14** crystallized from glacial acetic acid as fine colorless needles. Yield: 7.9 g (68%). Mp: 278−279 °C. ^{1}H NMR (DMSO-d_6): 4.76 (s, 2 H, $-O-CH_2-$), 5.4 (br, 1 H, $-CB_{10}H_{10}C-H$), 7.25 [AA′XX′, $J_A(J_X)$ = 8.7, 2 H, Ar−H ortho to $-O-CH_2-$], 7.68 (dd, $J_{4',6'}$ = 1.4, $J_{6',7'}$ = 8.4, 1 H, H-6′), 7.79 (d, J = 8.4, 1 H, H-7′), 8.17 (m, 1 H, H-4′), 8.2 [AA′XX′, $J_X(J_A)$ = 8.7, 2 H, Ar−H meta to $-O-CH_2-$]. ^{11}B NMR (DMSO-d_6): −3.99, −5.83, −10.30, −12.09, and −13.80. IR: 3042, 2586, 2220,

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1698, 1608, 1500, 1394, 1252, 1188, 1058, 820, 620. EI MS: 393.3 (49.5), 392.3 (45), 391.3 (100), 390.2 (59.6), 389.3 (29.5).

Synthesis of 1-{4-[5′-(Imino(ethoxy)methyl)-1*H*-benzimidazol-2′-yl]phenoxymethyl}-1,2-dicarba-*closo*-dodecaborane(12), 15. 14 (12.7 mmol, 5 g) in a mixture of dry ethanol/benzene was treated according to the preparation of **10**. The resulting compound, **15**, proved to be a white substance and was used without further purification for the next step. Yield: 5.9 g (98%). ^{1}H NMR (MeOH-d_4): 1.86 (t, J = 7.2, 3 H, $-CH_3$), 4.55 (q, J = 7, 2 H, $-CH_2CH_3$), 4.96 (s, 2 H, $-O-CH_2-$), 5.10 ($-CB_{10}H_{10}C-H$ under HDO), 7.55 [AA′XX′, $J_A(J_X)$ = 9, 2 H, Ar−H ortho to $-O-CH_2$], 8.24 (dd, $J_{4',7'}$ = 0.6, $J_{5',7'}$ = 9, 1 H, H-7′), 8.35 [AA′XX′, $J_X(J_A)$ = 9, 2 H, Ar−H meta to $-O-CH_2$], 8.42 (dd, $J_{4',6'}$ = 1.8, $J_{6',7'}$ = 9, 1 H, H-6′), 8.73 (dd, $J_{4',7'}$ = 0.6, $J_{4',6'}$ = 1.8, 1 H, H-4′). No further spectral data were taken.

Synthesis of 1-{4-[5-(4-Methyl-1-piperazinyl)-2,5′-bi-1*H*-benzimidazol-2′-yl]phenoxymethyl}-1,2-dicarba-*closo*-dodecaborane-(12), 2. The freshly prepared **6** (11.2 mmol, 2.3 g) and **15** (11.2 mmol, 5.3 g) were allowed to react in glacial acetic acid (250 mL) under reflux for 6 h. After 15−20 min, a yellow substance began to precipitate. After 6 h, the heat was switched off, and the reaction mixture was allowed to stand overnight at room temperature. The crystallized yellow precipitate was collected in a Büchner funnel, washed with glacial acetic acid, and dried in vacuo (if necessary, it can be recrystallized from glacial acetic acid in the dark, because this substance is light-sensitive). Yield: 4 g (62%). Mp: ≥290 °C. UV spectra (H_2O/ethanol, 90:10, v/v) for **1** ("Hoechst 33258"): λ_{max} 261 nm (log ϵ = 4.24) and 342 nm (log ϵ = 4.45), λ_{min} 295 nm (log ϵ = 3.97). UV spectra for **2** ("Hoechst-Carborane"): λ_{max} 262 nm (log ϵ = 4.25) and 342 nm (log ϵ = 4.41), λ_{min} 295 (log ϵ = 3.95). HPLC analysis [acetonitrile/methanol/20 mM KH_2PO_4 buffer (pH 3.36), 50:15:35, v/v, flow rate 1 mL/min, retention time 5.3 min] showed that **2** was obtained in ≥99% purity. ^{1}H NMR (MeOH-d_4 and TFA-d): 3.23 (t, J = 12, 2 H, H_3CN-CH_2-), 3.36 (t, J = 15, 2 H, H_3CN-CH_2-), 3.69 (d, J = 12, 2 H, $ArN-CH_2-$), 4.00 (d, J = 15, 2 H, $ArN-CH_2-$), 4.76 (s, 2 H, $-OCH_2-$), 4.87 ($-CB_{10}H_{10}C-H$ under HDO), 7.35 [AA′XX′, $J_A(J_X)$ = 9, 2 H, Ar−H ortho to $-OCH_2$], 7.38 (d, $J_{4',6'}$ = 1.8, 1 H, H-4′), 7.47 (dd, $J_{4',6'}$ = 1.8, $J_{6',7'}$ = 9, 1 H, H-6′), 7.78 (d, $J_{6',7'}$ = 9, 1 H, H-7′), 8.11 (d, $J_{4,7}$ = 0.6, $J_{6,7}$ = 9, 1 H, H-7), 8.22 [AA′XX′, $J_X(J_A)$ = 9, 2 H, Ar−H meta to $-OCH_2$], 8.28 (dd, $J_{4,6}$ = 1.8, $J_{6,7}$ = 9, 1 H, H-6), 8.60 (dd, $J_{4,7}$ = 0.6, $J_{4,6}$ = 1.8, 1 H, H-4). ^{11}B NMR (DMSO-d_6): −3.99, −5.83, −10.28, −12.20, and −13.77. ESI MS: 584.1 (30), 583 (36), 582.2 (75), 581.3 (50), 579.1 (32).

Acknowledgment. The authors are indebted to the Krebsforschung Schweiz (KFS 176-9-1995) for generous support.

IC980505E