Russian Journal of Organic Chemistry, Vol. 41, No. 9, 2005, pp. 1359–1366. Translated from Zhurnal Organicheskoi Khimii, Vol. 41, No. 9, 2005, pp. 1386–1394.

Dedicated to Full Member of the Russian Academy of Sciences N.S. Zefirov on His 70th Anniversary

Palladium-Catalyzed Alkynylation of 2-Iodo-*p*-carboranes and 9-Iodo-*m*-carboranes

I. P. Beletskaya[1], V. I. Bregadze[2], V. A. Ivushkin[1], G. G. Zhigareva[2], P. V. Petrovskii[2], and I. B. Sivaev[2]

[1] *Faculty of Chemistry, Moscow State University, Vorob'evy gory 1, Moscow, 119992 Russia*
e-mail: beletska@org.chem.msu.su

[2] *Nesmeyanov Institute of Organometallic Compounds, Russian Academy of Sciences, Moscow, Russia*

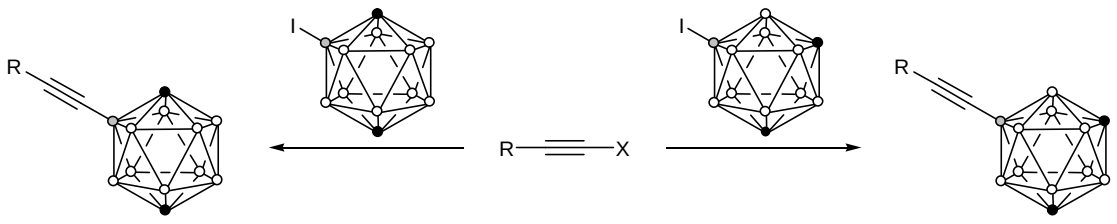
Received April 20, 2005

Abstract—Palladium-catalyzed reaction of ethynyl-substituted pyridine and quinoline derivatives with 2-iodo-*p*-carborane and 9-iodo-*m*-carborane gives the corresponding pyridylethynyl- and quinolylethynyl-substituted carboranes. Carborane-containing steroids in which the carborane fragment is linked to the steroid skeleton through acetylene bridge were synthesized by the Sonogashira reaction.

Although carboranes and other polyhedral boron compounds have been known for more than 40 years, the chemistry of these compounds continuously and extensively develops [1, 2]. The reasons are specific features in their structure and chemical properties and the possibility of using them in the design of new medicines and unique materials. At present, different medical applications of carboranes are known [3]. These include primarily boron-neutron capture therapy of cancer [4–6] and synthesis of compounds possessing various kinds of biological activity [7], in particular antitumor agents [8]. A necessary condition for the preparation of physiologically active compounds on the basis of carboranes is synthesis of their functional derivatives capable of binding to biomolecules which are responsible for delivery of boron-containing fragments to tumor cells. From the viewpoint of design of new molecular and supramolecular materials [9–12], a strong interest is attracted by the synthesis of compounds giving rise to electronic interaction between three-dimensional aromatic systems and various π-electron substituents like vinyl, alkynyl, aryl, or hetaryl group. With the above in mind, we made an attempt to synthesize such compounds via reactions catalyzed by metal complexes. We previously reported the first results on the synthesis of B-hetaryl carborane derivatives by reactions of *p*- and *m*-carboranes having a boron–iodine bond with magnesium and zinc derivatives of furan, thiophene, pyridine, quinoline, and indole in the presence of palladium catalysts [13].

The goal of the present work was to attach a pharmacophoric fragment (heteroring or steroid) to the boron atom of carborane molecule through an acetylenic carbon bridge which should eliminate undesirable effects (steric and electronic) of the bulky carborane core [14] on the biologically active fragment. B-Hetarylalkynyl derivatives of *p*- and *m*-carboranes were synthesized according to the heteroatom version of the

Scheme 1.



● – CH; ○ – BH; ⊚ – B; R = Het; X = H, MgBr.

Table 1. Reaction of 2-iodo-*p*-carborane with 3-quinolylacetylene and 2-pyridylacetylene[a]

Run no.	R in RC≡CH	RC≡CH-to-$IC_2B_{10}H_{11}$ molar ratio	Solvent	Time, h	Ratio of boron-containing products[b] ($RC{\equiv}C$-*p*-$C_2B_{10}H_{11}$/$IC_2B_{10}H_{11}$/NI[c])
1	2-Pyridyl	2	Pyrrolidine	14	36:30:34
2	3-Quinolyl	1.1	Pyrrolidine	22	79:21:0
3	3-Quinolyl	1.1	Benzene	22	46:40:14
4	3-Quinolyl	1.1	DMF	22	25:53:22

[a] A mixture of 2-iodo-*p*-carborane (0.2 mmol), 2-pyridylacetylene or 3-quinolylacetylene, $PdCl_2(PPh_3)_2$ (4 mol %), CuI (4 mol %), and pyrrolidine (0.6 mmol) in 3 ml of the corresponding solvent was heated under reflux in an argon atmosphere. The progress of the reaction was monitored by TLC.

[b] According to the ^{11}B NMR data.

[c] NI stands for nonidentified compounds.

Sonogashira reaction using the corresponding B-iodocarboranes and terminal acetylenes (Scheme 1). 2-Iodo-*p*-carborane was brought into reaction with alkynes under the classical Sonogashira conditions, in the presence of catalytic amounts of $PdCl_2(PPh_3)_2$ and CuI using pyrrolidine as both base and solvent (Table 1). A high yield of the substitution product (~80%) was achieved in the reaction with 3-quinolylacetylene (Table 1, run no. 2). In benzene and DMF the yields were lower (Table 1; run nos. 3, 4) than in pure pyrrolidine. Under analogous conditions, thermally unstable 2-pyridylacetylene reacted with poor selectivity and moderate yield (Table 1, run no. 1).

Unlike 2-iodo-*p*-carborane, 9-iodo-*m*-carborane undergoes complete decomposition on heating in boiling pyrrolidine or pyridine; it also loses boron atoms by the action of strong bases like potassium *tert*-butoxide and lithium hydroxide in boiling anhydrous dioxane. On the other hand, triethylamine, diethylamine, potassium and cesium carbonates, and even sodium methoxide do not induce cleavage of the *m*-carborane skeleton.

On the basis of our data on the stability of 9-iodo-*m*-carborane toward various bases, we tried to find conditions ensuring its reaction with 3-quinolylacetylene (Table 2). 9-Iodo-*m*-carborane almost failed to react with 3-quinolylacetylene in triethylamine or diethylamine (Table 2; run nos. 1, 3). In the latter case, the product yield was as poor as 6%. We also failed to effect the reaction in dioxane in the presence of 50 equiv of amine (Table 2; run nos. 2, 4). No desired results were obtained when the reaction was carried out in anhydrous THF in the presence of such bases as sodium methoxide and anhydrous potassium carbonate (Table 2; run nos. 5, 6): on heating in boiling THF with sodium methoxide, the initial acetylene completely decomposed in 6 h. Nevertheless, we succeeded in raising the yield of 9-[(3-quinolyl)ethynyl]-*m*-carborane to 33% using anhydrous cesium carbonate in anhydrous THF (Table 2, run no. 10). Almost no reaction occurred in dry benzene or acetonitrile (Table 2; run nos. 8, 9). It is known that addition of water often increases the yield of Sonogashira reactions [15]. In our case, addition of water to THF also favored the reaction, and the yield increased to 43% (Table 2, run no. 11). However, further raising the concentration of water led to a poor yield (6%) and separation of palladium black.

2-Pyridylacetylene is unstable under the above conditions (Table 2). Therefore, 9-iodo-*m*-carborane was brought into reaction with 2-pyridylacetylene generated *in situ* by the action of sodium methoxide on 2-(2-pyridylethynyl)-2-propanol in an anhydrous solvent (Scheme 2, Table 3). With sodium methoxide as

Scheme 2.

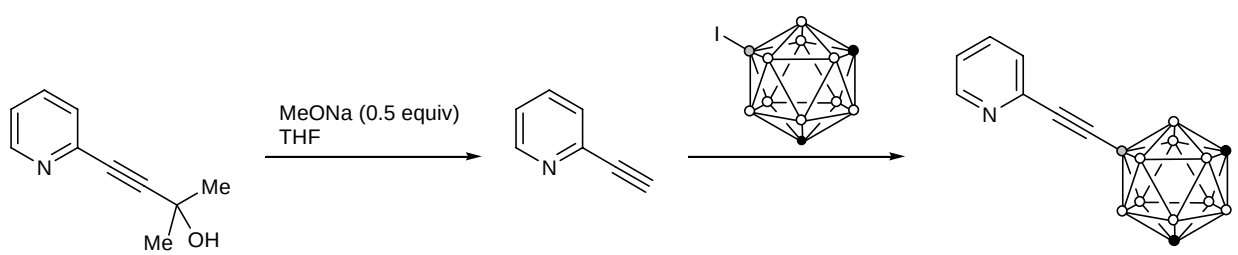


Table 2. Reaction of 9-iodo-*m*-carborane with 3-quinolylacetylene[a]

Run no.	Solvent	Base (equiv)	Reaction time, h	Ratio of boron-containing products[b] (RC≡C-*m*-$C_2B_{10}H_{11}$/$IC_2B_{10}H_{11}$/NI[c])
1	Triethylamine	Et_3N	24	0:100:0
2	Dioxane	Et_3N (50)	24	0:100:0
3	Diethylamine	Et_2NH	24	6:94:0
4	Dioxane	Et_2NH (50)	24	10:90:0
5	THF	MeONa (3)	6	17:83:0
6	THF	K_2CO_3 (3)	24	2:98:0
7	THF–H_2O, 25:1	K_2CO_3 (3)	24	10:90:0
8	Benzene	Cs_2CO_3 (3)	18	3:95:2
9	Acetonitrile	Cs_2CO_3 (3)	18	2:98:0
10	THF	Cs_2CO_3 (3)	18	33:66:1
11	THF–H_2O, 25:1	Cs_2CO_3 (3)	18	43:47:10

[a] The reactions were carried out by heating under reflux in an argon atmosphere in the presence of 1.1 equiv of 3-quinolylacetylene, 5 mol % of CuI, and 5 mol % of $PdCl_2(PPh_3)_2$.

[b] According to the ^{11}B NMR data.

[c] NI stands for nonidentified compounds.

Table 3. Reaction of 9-iodo-*m*-carborane with 2-pyridylacetylene[a]

Run no.	Solvent	Base (equiv)	Ratio of boron-containing products[b] (2-PyC≡C-*m*-$C_2B_{10}H_{11}$/$IC_2B_{10}H_{11}$/NI[c])
1	Benzene	MeONa (1)	3 : 94 : 3
2	THF	MeONa (1)	20 : 70 : 10
3	THF	MeONa (2)	0 : 57 : 43
4	THF	Cs_2CO_3 (3)	24 : 76 : 0

[a] A solution of 2-(2-pyridylethynyl)-2-propanol and 0.5 equiv of sodium methoxide was heated for 1–1.5 h under reflux, 9-iodo-*m*-carborane, $PdCl_2(PPh_3)_2$, CuI, and the corresponding base were added, and the mixture was heated for 18 h under reflux. The progress of reactions was monitored by TLC, following the disappearance of 2-pyridylacetylene.

[b] According to the ^{11}B NMR data.

[c] NI stands for nonidentified compounds.

base, the product yield in THF was as low as 20%, while in benzene only traces (3%) were formed. In the presence of 2 equiv of sodium methoxide, 2-pyridylacetylene decomposed before reaction with 9-iodo-*m*-carborane, and the latter also decomposed subsequently. The reaction was selective in the presence of 3 equiv of cesium carbonate: the yield of 9-(2-pyridylethynyl)-*m*-carborane was 24%, while no other products were detected (Table 3, run no. 4).

Thus the proposed procedure implying preparation of 2-pyridylacetylene *in situ* from 2-(2-pyridylethynyl)-2-propanol and the presence of strong bases (which induce decomposition of both terminal acetylene and 9-iodo-*m*-carborane) cannot be regarded as optimal. To accelerate the cross coupling process and suppress side reactions, the iodine atom in 2-iodo-*p*-carborane and 9-iodo-*m*-carborane was replaced by 2-pyridylethynyl or 3-quinolylethynyl moiety via palladium-catalyzed reaction of magnesium derivative of the corresponding substituted acetylene. Using 3-quinolylethynylmagnesium bromide we succeeded in obtaining cross-coupling products with both *p*- and *m*-carborane derivatives in quantitative yields (Table 4; run nos. 2, 3). Taking into account that the Iotsitch compound is partially consumed for metalation of carborane at the carbon atom and side homocoupling reaction, threefold excess of the organomagnesium compound is necessary to attain high yields.

2-Pyridylethynylmagnesium bromide is extremely unstable under the above conditions, and it readily decomposes at elevated temperature. Therefore, we failed to increase the yield of 2-(2-pyridylethynyl)-*p*-carbo-

Table 4. Reactions of 2-iodo-*p*-carborane and 9-iodo-*m*-carborane with Iotsitch compounds derived from 3-quinolyl- and 2-pyridylacetylenes[a]

Run no.	Carborane	R in RC≡CMgBr	RC≡CMgBr-to-$IC_2B_{10}H_{11}$ molar ratio	Reaction time, h	Ratio of boron-containing products[b] ($RC{\equiv}CC_2B_{10}H_{11}/IC_2B_{10}H_{11}$/NI[c])
1	2-Iodo-*p*-carborane	3-Quinolyl	1.2	20	30:70:0
2	2-Iodo-*p*-carborane	3-Quinolyl	3	12	100:0:0
3	9-Iodo-*m*-carborane	3-Quinolyl	3	48	100:0:0
4	2-Iodo-*p*-carborane	2-Pyridyl	3	8	15:85:0
5	9-Iodo-*m*-carborane	2-Pyridyl	3	48	2:53:45

[a] A mixture of 2-iodo-*p*-carborane or 9-iodo-*m*-carborane (0.2 mmol), 2-pyridyl- or 3-quinolylethynylmagnesium bromide, $PdCl_2(PPh_3)_2$ (4 mol %), CuI (4 mol %), and dioxane (2 ml) was heated under reflux in an argon atmosphere.

[b] According to the ^{11}B NMR data.

[c] NI stands for nonidentified compounds.

rane (it was as poor as 15%), while in the reaction with less active 9-iodo-*m*-carborane the yield did not exceed 2% (Table 4, run nos. 4, 5).

An alternative method for the preparation of carboranylalkynyl derivatives of heterocycles is cross coupling where the carboranyl component is introduced into reaction as carboranylacetylene and the heterocyclic component is the corresponding halogen derivative. Scheme 3 shows the synthesis of 9-ethynyl-*m*-carborane [16] and its reaction with 2-bromopyridine. According to the ^{11}B NMR data, the only boron-containing product was 9-(2-pyridylethynyl)-*m*-carborane (yield 80%).

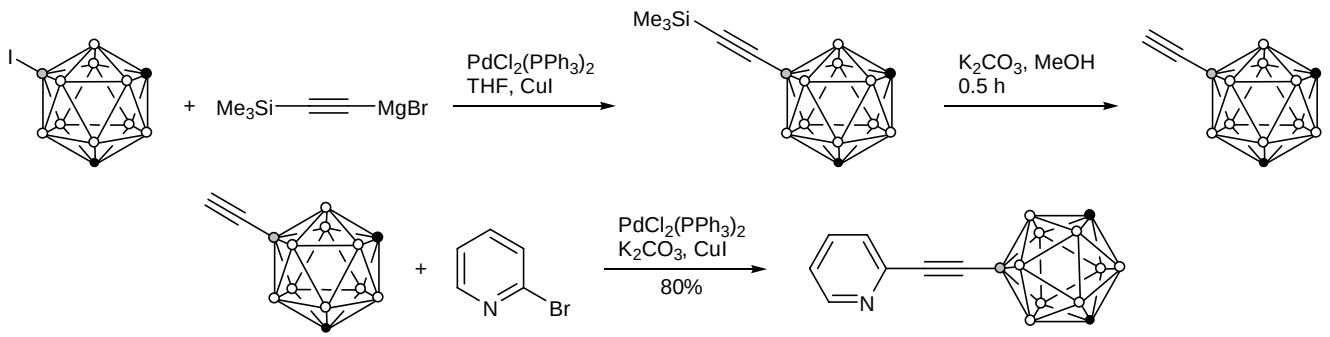
On the basis of the obtained results, we effected cross coupling of 2-iodo-*p*-carborane and 9-iodo-*m*-carborane with ethynyl derivatives of steroids and obtained carboranylethynyl-substituted estrogens and androgens. 2-Iodo-*p*-carborane reacted with 17-α-ethynylestradiol under the classical Sonogashira conditions to give the corresponding carboranylethynyl estradiol derivative in a high yield, the conversion being quantitative (Scheme 4). To avoid decomposition of the carborane polyhedron, the reaction of 17-α-ethynylestradiol with 9-iodo-*m*-carborane was performed in boiling aqueous THF using cesium carbonate as base. However, the yield of the final product was fairly moderate (35%) (Scheme 4).

The palladium-catalyzed reaction of 9-iodo-*m*-carborane with zinc derivative of ethynylestradiol (Scheme 5) was more successful. The zinc derivative was prepared *in situ* by treatment of initial ethynylestradiol in succession with 3 equiv of ethylmagnesium bromide and 3 equiv of zinc bromide. The yield attained 60%.

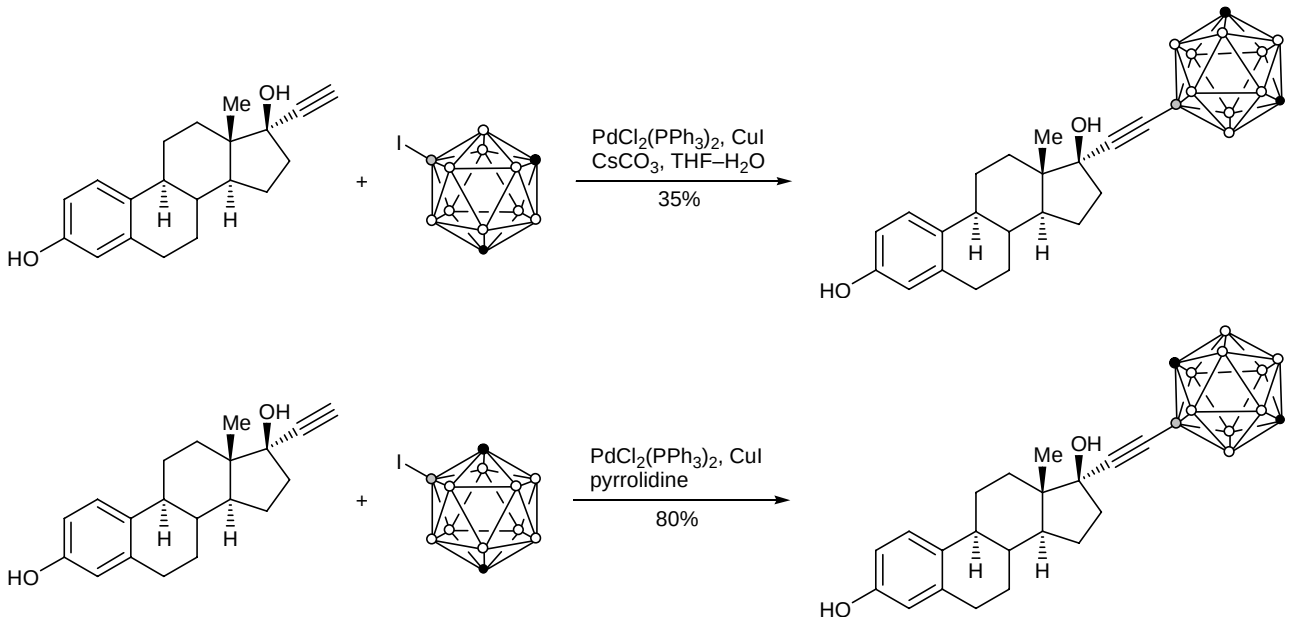
The procedure developed by us for the synthesis of carboranylethynyl derivatives of heterocycles via reaction of halogen-substituted heterocycles with carboranylacetylene was extended to halogen-substituted steroids. By reaction of *m*-carboranylacetylene with 6-bromoandrostenedione in a 3:1 dioxane–water mixture in the presence of 2 equiv of K_2CO_3, 2.2 mol % of $PdCl_2(PPh_3)_2$, and 4.5 mol % of CuI (30 min under reflux) we obtained 60% of *m*-carboranylethynylandrostenedione (Scheme 6).

Thus palladium-catalyzed cross-coupling reactions of ethynyl-substituted heterocycles and steroids allowed us to obtain a series of B-alkynyl derivatives of *p*- and *m*-carboranes.

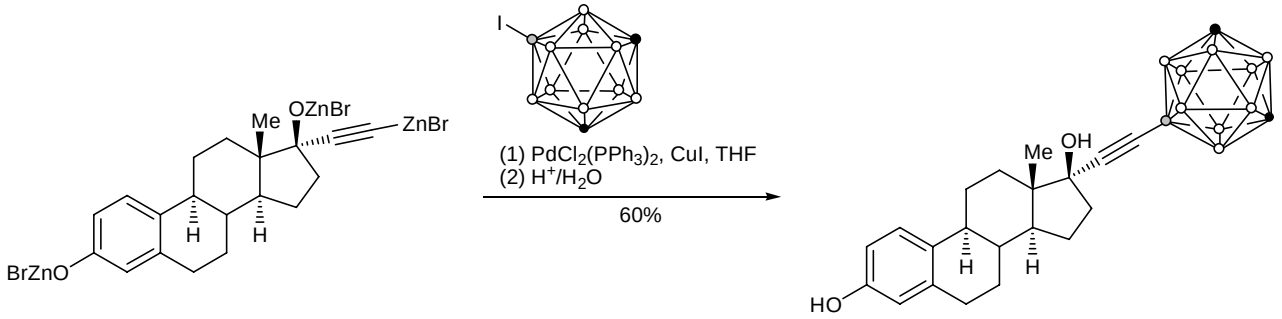
Scheme 3.



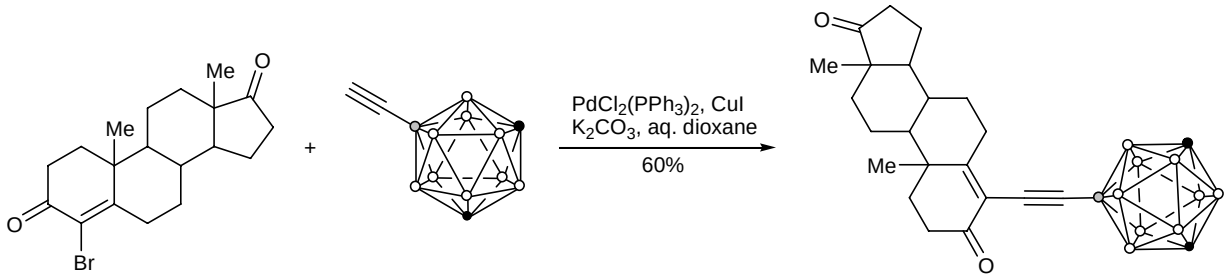
Scheme 4.



Scheme 5.



Scheme 6.



EXPERIMENTAL

All experiments were performed under argon. Tetrahydrofuran and 1,4-dioxane were distilled over potassium diphenylketyl just before use. Zinc chloride was dried for 4 h at 150°C prior to use.

The ^{1}H and ^{11}B NMR spectra were recorded on Bruker AMX-400 and Varian XL-400 spectrometers at 400 and 128.3 MHz, respectively, from solutions in $CDCl_3$ unless otherwise stated. The ^{11}B chemical shifts were measured relative to $Et_2O \cdot BF_3$ as external reference. The mass spectra were obtained on a Finnigan SSQ-7000 instrument.

Reactions of 2-iodo-*p*-carborane with 3-quinolylacetylene and 2-pyridylacetylene. A solution of 0.054 g (0.2 mmol) of 2-iodo-*p*-carborane, 0.034 g (0.22 mmol) of 3-quinolylacetylene or 0.041 g (0.4 mmol) of 2-pyridylacetylene, 5.61 mg (4 mol %)

of $PdCl_2(PPh_3)_2$, 1.52 mg (4 mol %) of CuI, and 0.043 g (0.6 mmol) of pyrrolidine in 3 ml of the corresponding solvent was heated under reflux in an argon atmosphere. The mixture was carefully evaporated under reduced pressure, the solid residue was extracted with diethyl ether, the extract was filtered through a thin layer of celite, and the filtrate was carefully concentrated under reduced pressure. The composition of the reaction mixture was determined from the ^{11}B NMR spectrum.

2-(2-Pyridylethynyl)-*p*-carborane. A solution of 0.540 g (2 mmol) of 2-iodo-*p*-carborane, 0.412 g (4 mmol) of 2-pyridylacetylene, 56.1 mg (4 mol %) of $PdCl_2(PPh_3)_2$, and 15.2 mg (4 mol %) of CuI in 20 ml of pyrrolidine was heated for 14 h under reflux. The mixture was evaporated under reduced pressure, and the residue was subjected to column chromatography using petroleum ether as eluent. Yield 0.112 g (23%). ^1H NMR spectrum, δ, ppm: 1.5–3.0 m (9H), 2.81 s (1H), 3.11 s (1H), 7.22 m (1H), 7.46 m 1(H), 7.63 m (1H), 8.56 m (1H). ^{11}B NMR spectrum, δ_B, ppm: –13.3 (2B), –14.2 (3B), –15.0 (4B), –16.4 (1B). Mass spectrum, *m*/*z* (I_{rel}, %): 241–247 (100) $[M]^+$. Found, %: C 44.06; H 6.29; B 43.98. $C_9H_{15}B_{10}N$. Calculated, %: C 44.06; H 6.16; B 44.07.

2-(3-Quinolylethynyl)-*p*-carborane. A solution of 0.540 g (2 mmol) of 2-iodo-*p*-carborane, 0.612 g (4 mmol) of 3-quinolylacetylene, 56.1 mg (4 mol %) of $PdCl_2(PPh_3)_2$, and 15.2 mg (4 mol %) of CuI in 20 ml of pyrrolidine was heated for 22 h under reflux. The mixture was evaporated under reduced pressure, and the residue was subjected to column chromatography using petroleum ether as eluent. Yield 0.360 mg (61%). ^1H NMR spectrum, δ, ppm: 1.5–3.2 m (9H), 2.85 s (1H), 3.13 s (1H), 7.55 m (1H), 7.71 m (1H), 7.76 m (1H), 8.07 m (1H), 8.27 m (1H), 8.91 m (1H). ^{11}B NMR spectrum, δ_B, ppm: –13.3 (3B), –14.2 (3B), –15.0 (4B). Mass spectrum, *m*/*z* (I_{rel}, %): 291–297 (100) $[M]^+$. Found, %: C 53.7; H 6.12; B 34.01. $C_{13}H_{17}B_{10}N$. Calculated, %: C 52.86; H 5.80; B 36.60.

Reaction of 9-iodo-*m*-carborane with 3-quinolylacetylene. A solution of 0.054 g (0.2 mmol) of 9-iodo-*m*-carborane, 0.034 g (0.22 mmol) of 3-quinolylacetylene, 7.02 mg (5 mol %) of $PdCl_2(PPh_3)_2$, 1.91 mg (5 mol %) of CuI, and 0.6 mmol of appropriate base in 3 ml of the corresponding solvent was heated under reflux in an argon atmosphere. The mixture was carefully evaporated under reduced pressure, the solid residue was extracted with diethyl ether, the extract was filtered through a thin layer of celite, and the filtrate was carefully concentrated under reduced pressure. The composition of the reaction mixture was determined from the ^{11}B NMR spectrum.

Reaction of 9-iodo-*m*-carborane with 2-pyridylacetylene. A solution of 0.035 g (0.22 mmol) of 2-(2-pyridylethynyl)-2-propanol, and 0.007 g (0.13 mmol) of sodium methoxide in 6 ml of THF or benzene was heated for 1–1.5 h under reflux while stirring in an argon atmosphere until initial 2-(2-pyridylethynyl)-2-propanol disappeared (according to the TLC data). The solution was cooled to room temperature, and 0.054 g (0.2 mmol) of 9-iodo-*m*-carborane, 7.02 mg (5 mol %) of $PdCl_2(PPh_3)_2$, 1.91 mg (5 mol %) of CuI, and 0.66 mmol of appropriate base were added. The mixture was heated for 18 h under reflux while stirring in an argon atmosphere until 2-pyridylacetylene disappeared (TLC). The composition of the reaction mixture was determined from the ^{11}B NMR spectrum.

Reaction of 2-iodo-*p*-carborane and 9-iodo-*m*-carborane with magnesium derivatives of 3-quinolylacetylene and 2-pyridylacetylene. 3-Quinolylethynylmagnesium bromide and 2-pyridylethynylmagnesium bromide were prepared by adding at 0°C under argon 0.35 ml (0.6 mmol) of a 1.7 M solution of ethylmagnesium bromide in diethyl ether to a solution of 0.6 mmol of the corresponding hetarylacetylene in 2 ml of dioxane, followed by stirring the resulting suspension for 1 h at 50°C. A solution of 0.054 g (0.2 mmol) of iodocarborane, 5.61 mg (4 mol %) of $PdCl_2(PPh_3)_2$, and 1.52 mg (4 mol %) of CuI in 2 ml of dioxane was added to a freshly prepared suspension of the Iotsitch compound, and the mixture was heated under reflux in an argon atmosphere. The mixture was cooled to room temperature, 0.1 ml of a saturated aqueous solution of NH_4Cl was added, and the mixture was diluted with methylene chloride, filtered through a layer of celite, and carefully evaporated under reduced pressure. The mixture was analyzed by ^{11}B NMR spectroscopy.

9-(3-Quinolylethynyl)-*m*-carborane. 3-Quinolylacetylene, 0.505 g (3.3 mmol), was dissolved in 6 ml of dioxane, and 1.32 ml of a 2.5 M solution of ethylmagnesium bromide in diethyl ether was added dropwise. The mixture was stirred for 1 h at 50°C, a solution of 0.270 g (1 mmol) of 9-iodo-*m*-carborane, 35.1 mg (5 mol %) of $PdCl_2(PPh_3)_2$, and 9.52 mg (5 mol %) of CuI in 6 ml of dioxane was added, and the mixture was heated for 48 h under reflux until the initial iodocarborane disappeared (TLC). The mixture was filtered, the filtrate was evaporated, and the

residue was subjected to column chromatography on silica gel (40–60 μm, Merck) using petroleum ether–ethyl acetate (3:1) as eluent. Yield 0.226 g (77%). ^{1}H NMR spectrum, δ, ppm: 1.5–3.5 m (9H), 2.98 s (2H), 7.53 m (1H), 7.68 m (1H), 7.73 m (1H), 8.05 m (1H), 8.24 s (1H), 8.91 s (1H). ^{11}B NMR spectrum, δ_B, ppm: –19.0 (1B), –17.5 (1B), –13.9 (2B), –12.8 (2B), –9.5 (2B), –6.2 (2B). Found, %: C 52.74; H 5.73; B 36.52. $C_{13}H_{17}B_{10}N$. Calculated, %: C 52.86; H 5.80; B 36.60.

9-(2-Pyridylethynyl)-*m*-carborane. A solution of 0.027 g (0.11 mmol) of 9-trimethylsilylethynyl-*m*-carborane [16] and 0.031 g (0.22 mmol) of K_2CO_3 in 4 ml of methanol was stirred for 0.5 h at room temperature. The mixture was evaporated under reduced pressure, 3.86 mg (5 mol %) of $PdCl_2(PPh_3)_2$ and 1.05 mg (5 mol %) of CuI were added, the reaction flask was purged with argon, and a solution of 0.019 g (0.12 mmol) of 2-bromopyridine in 3 ml of a 3:1 dioxane–water mixture was added. The mixture was heated for 30 min under reflux with stirring, cooled, diluted with 20 ml of water, and extracted with chloroform. The extract was dried over $MgSO_4$ and evaporated, and the residue was subjected to column chromatography on silica gel (40–60 μm, Merck) using chloroform as eluent. Yield 0.022 g (80%). ^{1}H NMR spectrum, δ, ppm: 1.5–4.0 m (9H), 2.96 s (2H), 7.19 m (1H), 7.45 m (1H), 7.62 m (1H), 8.56 m (1H). ^{11}B NMR spectrum, δ_B, ppm: –18.9 (1B), –17.6 (1B), –13.9 (2B), –12.8 (2B), –9.6 (2B), –6.1 (2B). Mass spectrum: *m/z* 241–247 ($(I_{rel}$ 100%) $[M]^+$.

17-(2-*p*-Carboranylethynyl)estra-1(10),2,4-triene-3,17-diol. A solution of 0.270 g (1 mmol) of 2-iodo-*p*-carborane, 0.296 g (1 mmol) of 17α-ethynylestradiol, 28.1 mg (4 mol %) of $PdCl_2(PPh_3)_2$, and 7.62 mg (4 mol %) of CuI in 20 ml of pyrrolidine was heated for 1 h under reflux. The mixture was evaporated under reduced pressure, and the residue was subjected to column chromatography using ethyl acetate–petroleum ether (1:5) as eluent. The product was crystallized from ethyl acetate–petroleum ether. Yield 350 mg (80%). ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 0.88 s (3H), 1.20–2.90 m (24H), 3.40 s (1H), 3.57 s (1H), 4.35 s (1H), 6.50 m (1H), 6.59 m (1H), 7.10 m (1H), 7.95 s (1H). ^{11}B NMR spectrum, δ_B, ppm: –15.3 (3B), –14.8 (2B), –14.5 (2B), –13.5 (3B). Found, %: C 61.40; H 7.79; B 23.58. $C_{22}H_{34}B_{10}O_2$. Calculated, %: C 60.24; H 7.81; B 24.65.

17-(9-*m*-Carboranylethynyl)estra-1(10),2,4-triene-3,17-diol. *a. Sonogashira reaction.* A solution of 0.054 g (0.2 mmol) of 9-iodo-*m*-carborane, 0.059 g (0.2 mmol) of 17-α-ethynylestradiol, 5.62 mg (4 mol %) of $PdCl_2(PPh_3)_2$, 1.52 mg (4 mol %) of CuI, and 0.196 g (0.6 mmol) of Cs_2CO_3 in 20 ml of a 25:1 THF–water mixture was heated for 24 h under reflux. The mixture was evaporated under reduced pressure, the solid residue was dissolved in chloroform, the solution was filtered through a thin layer of celite, and the filtrate was concentrated under reduced pressure. According to the ^{11}B NMR data, the yield was 35%.

b. Negishi reaction. 17α-Ethynylestradiol, 0.120 g (0.4 mmol), was dissolved in 5 ml of THF, and 0.53 ml of a 2.5 M solution of ethylmagnesium bromide in diethyl ether was added dropwise under stirring. The resulting suspension was stirred for 1 h at room temperature under argon, a solution of 0.300 g (1.32 mmol) of $ZnBr_2$ in 2 ml of THF was added, the mixture was stirred for 20 min, and 0.054 g (0.2 mmol) of 9-iodo-*m*-carborane, 7.02 mg (5 mol %) of $PdCl_2(PPh_3)_2$, and 1.91 mg (5 mol %) of CuI were added. The mixture was heated for 26 h under reflux with stirring and evaporated under reduced pressure, the solid residue was dissolved in 30 ml of chloroform, and the solution was washed with water (3×20 ml). The organic phase was separated, dried over $MgSO_4$, and evaporated, and the residue was subjected to column chromatography on silica gel (40–60 μm, Merck) using chloroform as eluent). Yield 0.053 g (60%). ^{1}H NMR spectrum, δ, ppm: 0.88 s (3H), 1.20–2.90 m (25H), 2.95 s (2H), 4.95 s (1H), 6.55 m (1H), 6.65 m (1H), 7.20 m (1H). ^{11}B NMR spectrum, δ_B, ppm: –19.5 (1B), –17.7 (1B), –14.10 (2B), –12.9 (2B), –9.5 (2B), –6.3 (2B). Mass spectrum: *m/z* 435–441 (I_{rel} 100%) $[M]^+$.

4-(9-*m*-Carboranylethynyl)androst-4-ene-3,17-dione. A solution of 0.060 g (0.248 mmol) of 9-(trimethylsilylethynyl)-*m*-carborane [16] and 0.069 g (0.496 mmol) of K_2CO_3 in 6 ml of methanol was stirred for 0.5 h at room temperature. The mixture was evaporated, 3.83 mg (2.2 mol %) of $PdCl_2(PPh_3)_2$, 2.13 mg (4.5 mol %) of CuI, and 0.091 g (0.248 mmol) of 4-bromoandrost-4-ene-3,17-dione were added, the reaction flask was purged with argon, and 8 ml of a 3:1 dioxane–water mixture was added. The mixture was heated for 30 min under reflux with stirring, cooled, diluted with 20 ml of water, and extracted with chloroform. The extract was dried over $MgSO_4$ and evaporated, and the residue was subjected to column chromatography on silica gel (40–60 μm, Merck) using chloroform–ethyl acetate (5:1) as eluent. Yield 0.065 mg (60%). ^{1}H NMR spectrum, δ, ppm: 0.92 s (3H), 1.21 s (3H), 2.94 s (2H), 0.5–3.5 m (28H).

^{11}B NMR spectrum, δ_B, ppm: –19.2 (1B), –17.8 (1B), –14.1 (2B), –13.1 (2B), –10.1 (2B), –6.4 (2B). Mass spectrum: *m*/*z* 448–454 (I_{rel} 100%) $[M]^+$.

The authors thank V.M. Rzheznikov, B.I. Keda, N.V. Lukashev, and G.V. Latyshev for providing samples of steroids. This study was performed under financial support by the Russian Foundation for Basic Research (project nos. 02-03-32680 and 05-03-32359).

REFERENCES

1. Grimes, R., *Carboranes*, New York: Academic, 1970. Translated under the title *Karborany*, Moscow: Mir, 1974, p. 264.
2. Bregadze, V.I., *Chem. Rev*., 1992, vol. 92, p. 209.
3. Valliant, J.F., Guenther, K.J., King, A.S., Morel, P., Schaeffer, P., Sogbein, O.O., and Stephenson, K.A., *Coord. Chem. Rev*., 2002, vol. 232, p. 173.
4. Hawthorne, M.F., *Angew. Chem., Int. Ed. Engl*., 1993, vol. 32, p. 950.
5. Soloway, A.H., Tjarks, W., Barnum, B.A., Rong, F.-G., Barth, R.F., Codogni, I.M., and Wilson, J.G., *Chem. Rev*., 1998, vol. 98, p. 1515.
6. Sivaev, I.B. and Bregadze, V.I., *Ross. Khim. Zh*., 2004, vol. 48, p. 109.
7. Endo, Y., Iijima, T., Yamakoshi, Y., Fukasawa, H., Miyaura, C., Inada, M., Kubo, A., and Itai, A., *Chem. Biol*., 2001, vol. 8, p. 341.
8. Bregadze, V.I., Glazun, S.A., Petrovskii, P.V., Starikova, Z.A., Buyanovskaya, A.G., Takazova, R.U., Gielen, M., de Vos, D., Kemmer, M., Biesemans, M., and Willem, R., *Appl. Organomet. Chem*., 2004, vol. 18, p. 191.
9. Murphy, D.M., Mingos, D.M.P., and Forward, J.M., *J. Mater. Chem*., 1993, vol. 3, p. 139.
10. Jiang, W., Harwell, D.E., Mortimer, M.D., Knobler, C.B., and Hawthorne, M.F., *Inorg. Chem*., 1996, vol. 35, p. 4355.
11. Schöberl, U., Magnera, T.E., Harrison, R.M., Fleischer, F., Pflug, J.L., Schwab, P.F.H., Meng, X., Lipiak, D., Noll, B.C., Allured, V.S., Rudalevige, T., Lee, S., and Michl, J., *J. Am. Chem. Soc*., 1997, vol. 119, p. 3907.
12. Kaszynski, P. and Douglas, A.G., *J. Organomet. Chem*., 1999, vol. 581, p. 28.
13. Beletskaya, I.P., Bregadze, V.I., Ivushkin, V.A., Petrovskii, P.V., Sivaev, I.B., Sjöberg, S., and Zhigareva, G.G., *J. Organomet. Chem*., 2004, vol. 689, p. 2920.
14. Leukart, O., Caviezel, M., Eberle, A., Tun-Kyi, A., and Schwyzer, R., *Helv. Chim. Acta*, 1976, vol. 59, p. 546.
15. Beletskaya, I.P., Latyshev, G.V., Tsvetkov, A.V., and Lukashev, N.V., *Tetrahedron Lett*., 2003, vol. 44, p. 5011.
16. Jiang, W., Knobler, C.B., Curtis, C.E., Mortimer, M.D., and Hawthorne, M.F., *Inorg. Chem*., 1995, vol. 34, p. 3491; Zakharkin, L.I., Kovredov, A.I., and Ol'shevskaya, V.A., *Izv. Akad. Nauk SSSR, Ser. Khim*., 1985, p. 888.