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Nickel-Mediated Three-Component Cycloaddition Reaction of Carboryne, Alkenes, and Alkynes

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Multicomponent cross-coupling reactions are a powerful strategy to assemble complex molecules from very simple precursors in a single operation.[1] For example, transition metal complexes can promote cycloadditions of alkynes and alkenes to construct a wide variety of compounds since complexation of the metal center to an olefin or alkyne significantly modifies the reactivity of this moiety.[2−4] Carboryne (1,2-dehydro-*o*-carborane) is very energetically comparable with its two-dimensional relative benzyne.[5] In view of the unique properties of carboryne,[6] we developed the nickel-mediated two-component [2 + 2 + 2] cycloaddition of carboryne with alkynes to afford benzocarboranes,[7] and cross-coupling reaction of carboryne with alkenes to generate alkenylcarboranes.[8] In the latter case, when methyl acrylate or 2-vinylpyridine was used as the starting material, only alkylcarboranes **1a**,**b** were obtained after hydrolysis (Scheme 1). This result implies that the donor atom of the olefin may stabilize the intermediate, preventing the β-H elimination. These intermediates do not show any activity toward olefins, but react readily with alkynes to give three-component [2 + 2 + 2] cycloaddition products. These findings are reported in this Communication.

In a typical procedure, alkene (1.2 equiv) and alkyne (4 equiv) were added to a THF solution of nickel-carboryne, prepared in situ by the reaction of $Li_2C_2B_{10}H_{10}$ with $NiCl_2(PPh_3)_2$,[8,9] and the reaction mixture was heated at 110 °C in a closed vessel. Standard workup procedures afforded the cyclization products in very good chemo- and regioselectivity (Table 1). An excess amount of alkynes were necessary as hexasubstituted benzenes were isolated from all reactions, which were generated via Ni-mediated cyclotrimerization of alkynes.[2] It is noted that alkynes do not react with nickelacyclopentanes till the reaction temperature reaches ~80 °C, and the optimal temperature is 110 °C as suggested by GC−MS analyses. On the other hand, activated alkenes can react well with Ni-carboryne in THF at room temperature to give the nickelacycles. Therefore, a separate addition of alkene and alkyne is not necessary for this system.

As shown in Table 1, a variety of alkynes are compatible with this nickel-mediated three-component cyclization. Steric factors played an important role in the reactions. Sterically less demanding 3-hexyne offered the highest yield (entries 1 and 9). No reaction proceeded for diphenylacetylene (entries 8 and 12) and bis(trimethylsilyl)acetylene. Unsymmetrical alkynes gave only one isomer of **4** due to the electronic effects as phenyl can be viewed as electron-withdrawing group (entries 3−7).[10] In the case of **3g** ($CH_2{=}CHCH_2C{\equiv}CC_6H_5$), no C=C insertion product was observed (entry 7). It is noteworthy that terminal alkynes quenched the reaction intermediates to afford **1a**,**b**, and nitriles, isonitriles, or carbodiimides did not yield any insertion products. Compounds **4** were fully characterized by ^1H, ^{13}C, and ^{11}B NMR as well as high-resolution mass spectrometry.[11] The molecular structures of **4c** and **4h** were further confirmed by single-crystal X-ray analyses (see Supporting Information).

Scheme 1. Nickel-Mediated Coupling of Carboryne with Alkenes

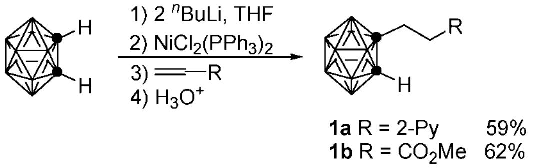
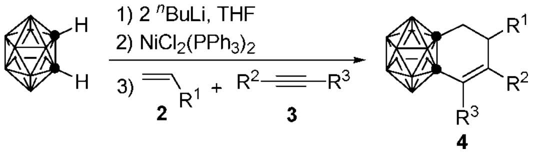


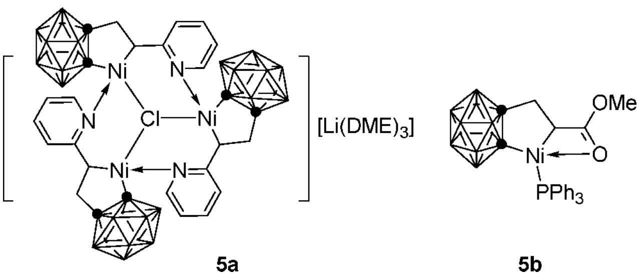
Table 1. Nickel-Mediated Three-Component Cycloaddition



entry	R^1	R^2	R^3	products	yield[a] (%)
1	2-Py	Et	Et	**4a**	57
2	2-Py	^{n}Bu	^{n}Bu	**4b**	32
3	2-Py	Me	Ph	**4c**	40
4	2-Py	Me	*p*-Tolyl	**4d**	35
5	2-Py	Et	Ph	**4e**	39
6	2-Py	^{n}Bu	Ph	**4f**	31
7	2-Py	Ally	Ph	**4g**	36
8	2-Py	Ph	Ph	NR	-
9	CO_2Me	Et	Et	**4h**	59
10	CO_2Me	^{n}Pr	^{n}Pr	**4i**	50
11	CO_2Me	^{n}Bu	^{n}Bu	**4j**	48
12	CO_2Me	Ph	Ph	NR	-

[a] Isolated yields.

Chart 1. Structures of Nickelacyclopentanes



5a **5b**

To gain some insight into the reaction mechanism, the alkene insertion species nickelacyclopentanes **5a**,**b** (Chart 1)[11] were isolated and fully characterized from the reaction of nickel-carboryne with 2-vinylpyridine and methyl acrylate, respectively. Complex **5a** was further confirmed by single-crystal X-ray analyses. It is an ionic complex, in which the anion consists of three square-planar Ni moieties sharing one μ_3-Cl atom (Figure 1). The proposed molecular structure of **5b** is shown in Chart 1, which is supported

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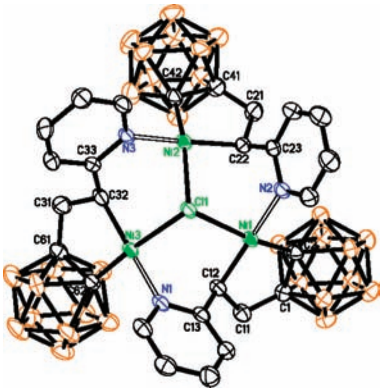
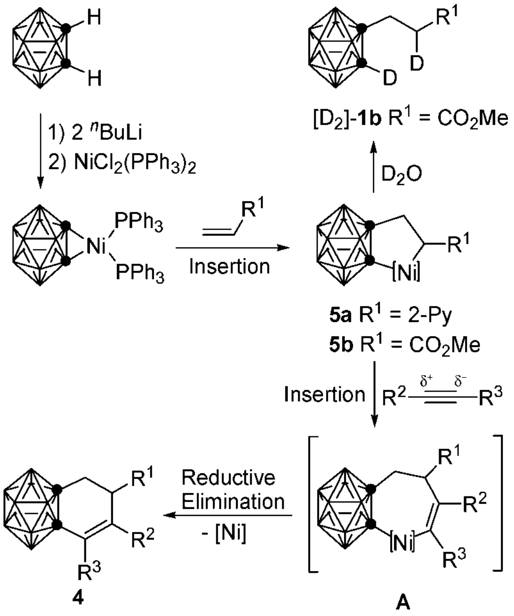


Figure 1. Molecular structure of the anion in $[\{[2\text{-}CH_2CH(o\text{-}C_5H_4N)\text{-}1,2\text{-}C_2B_{10}H_{10}]Ni\}_3(\mu_3\text{-}Cl)][Li(DME)_3]$ (**5a**). Selected bond lengths (Å) and angles (deg): Ni1−C2, 1.884(5); Ni1−C12, 1.966 (5); Ni1−Cl1, 2.292(1); Ni1−N2, 1.937(4); Ni2−C42, 1.884(6); Ni2−C22, 1.970(5); Ni2−Cl1, 2.307(1); Ni2−N3, 1.946(4); Ni3−C62, 1.880(5); Ni3−C32, 1.974(6); Ni3−Cl1, 2.285(1); Ni3−N1, 1.948(4); C2−Ni1−C12, 88.3(2); C42−Ni2−C22, 87.7(2); C62−Ni3−C32, 87.6(2).

Scheme 2. Proposed Mechanism for Three-Component Cycloaddition



by ^1H, ^{13}C and ^{11}B NMR as well as elemental analyses. Hydrolysis of **5b** with D_2O afforded $[D_2]$-**1b** with greater than 95% deuterium incorporation (Scheme 2). Treatment of **5a**,**b** with EtC≡CEt in THF at 110 °C gave **4a** or **4h** in $>$90% yield. This result suggested that the alkyne insertion is much more efficient than the alkene insertion. In view of the similarity in reactivity between **5a** and **5b**, and anionic nature of trinuclear Ni complex in **5a**, it is suggested that **5a** may be dissociated into mononuclear Ni complex during the reaction. Accordingly, the formation of products **4** can be rationalized by the sequential insertion of alkene and alkyne into the Ni−C bond, as illustrated in Scheme 2. The insertion of alkene affords the nickelacyclo-pentane **5**.[8] Subsequent insertion of alkyne into the nickel-C(alkyl) bond gives the seven-membered intermediate **A**.[7,12,13] Reductive elimination yields the final products **4**.

In summary, we have developed a novel nickel-mediated three-component assembling reaction of carboryne with alkenes and alkynes. This work offers a direct route to the synthesis of dihydrobenzocarborane derivatives that cannot be prepared by conventional methods.

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Supporting Information Available: Detailed experimental procedures, full characterization data, and X-ray data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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