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9-Allyl-1,7-dicarbadodecaborane as a dienophile in aza Diels–Alder reactions of 1,2,4-triazines: synthesis of pyridines bearing a carborane cage

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Abstract

The synthesis of pyridine and bipyridine derivatives of *m*-carborane via aza Diels–Alder reaction of 1,2,4-triazines with 9-allyl *m*-carborane and their structural characterization and photophysical properties are described. The products 3- and 4-(*m*-carborane-9-ylmethyl)-2,2′-bipyridines form Zn(II) complexes on reaction with $ZnCl_2$, which increases significantly their fluorescence intensity.

Carboranes attract significant attention because of their remarkable properties. Their potential application in the fields of heat-stable polymers,[1] non-linear optical,[2] electronic materials,[3] and especially in medicine[4] stimulates the search for new effective methods for carborane functionalization. The syntheses of carborane derivatives containing various substituents attached to the carbon atoms of the carborane cage, including aryl and heteroaryl substituents, are well documented.[5–8] However, only a few examples are known for the synthesis of heteroaromatic compounds bearing a carborane cage through the boron atom, for example, B-heteroarylation via Pd catalyzed cross-coupling reactions of B-iodocarboranes with organometallic compounds.[9–11]

Previously,[12,13] we described the synthesis of *C*-heteroaryl carboranes by aromatic nucleophilic substitution of 1,2,4-triazine 4-oxides using *C*-lithia carboranes as nucleophiles. The so obtained carboranyl-1,2,4-triazines readily undergo aza Diels–Alder reactions yielding the corresponding carboranylpyridines. In general, a combination of the wide variety of methods for the synthesis of substituted 1,2,4-triazines, coupled with the aza Diels–Alder reaction with various dienophiles, allows the synthesis of numerous differently functionalized pyridines.[14] Due to the inverse electron demands of the aza Diels–Alder reaction, the most active dienophiles are electron-rich enamines.[15] (Cyclo)alkenes without electron-donating substituents react with 1,2,4-triazines at much higher temperatures (extended refluxing in xylene or dichlorobenzene), or the reaction does not occur at all.[16]

Here we report a new example of this methodology for the synthesis of pyridines bearing the *m*-carborane cage using 9-allyl-1,7-dicarbadodecaborane **2** as dienophile. The carboranylmethyl group is assumed to be a very weak electron-donating substituent, so it is no wonder that there are no known examples of the Diels–Alder reactions of allylcarborane. However, we found that heating 6-aryl-3-(2-pyridyl)-1,2,4-triazines **2a**,**b**[16e] with an excess of the allylcarborane[17] in *o*-xylene resulted in the substituted pyridines as a mixture of regioisomers 4- and 3-carboranylmethylbipyridines **3a**,**b**[18] and **4a**,**b**[19] (Scheme 1).

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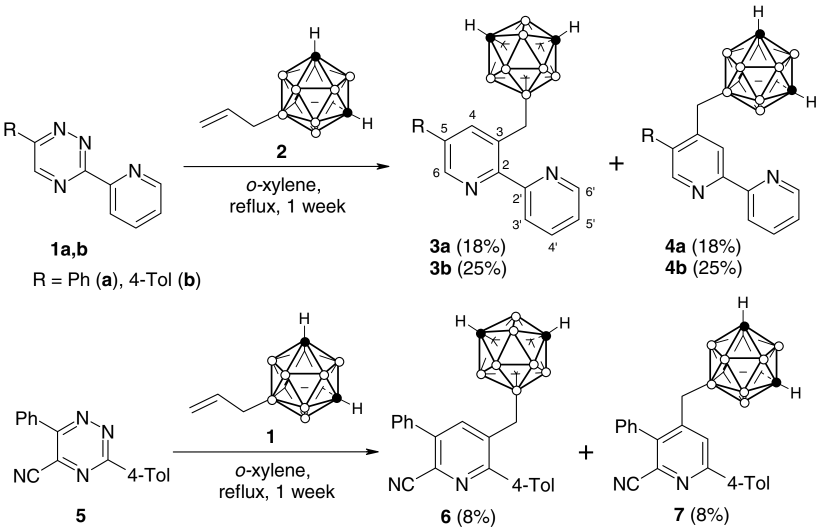


Scheme 1.

The ratios of the isomers in both reactions are close to 1:1, and the total yields were 36–50%. The isomers were separated easily by column chromatography.

The molecular structures of **3b** and **4b** were determined by X-ray diffraction crystallography (Figs. 1 and 2). The bulky carboranylmethyl substituent dictates the geometry of the molecule depending on its position in the pyridine ring. The substitution at position 3 of **3b** disturbs the planarity of the bipyridine moiety. Substitution at position 4 of **4b** leads to significant torsion of the phenyl from the plane of the central pyridine ring, while the pyridine rings are slightly twisted (torsion is 17°). However, the torsion of the pyridine rings of **3b** was significantly less than analogous torsion of the phenyl and the central pyridine of **4b** (torsions are 37° and 60°, respectively). This is due to the fact that repulsion of the bulky pyridyl and the carboranylmethyl is partly compensated by their attraction due to the weak intramolecular interactions between electronegative nitrogen atom of the pyridine and electropositive boron atoms B(2) and B(3) of the carborane cage (distances N(1)–B(2) and N(1)–B(3) are 3.362 Å and 3.382 Å, respectively). Chains of **3b** are formed by linking of the molecules through C–H···N hydrogen bonds (2.334 Å, 3.237 Å, 157°) (Fig. S3, see ESI). The CH-donor is the carborane cage, while the acceptor is the nitrogen atom of the central pyridine. The C–H···N hydrogen bonds in carboranylmethylpyridine **3b** are a little bit shorter than those of ethynylpyridines (C···N distances are 3.275–3.313 Å).[20]

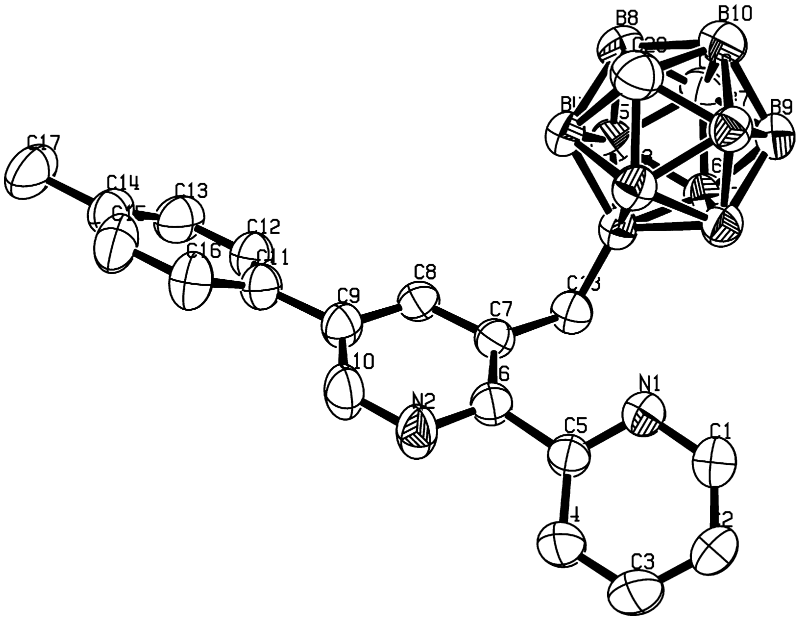


Fig. 1. ORTEP view of **3b** (hydrogen atoms are omitted). Selected bonds length (Å): C(7)–C(18) 1.511, C(18)–B(1) 1.597, C(5)–C(6) 1.495.

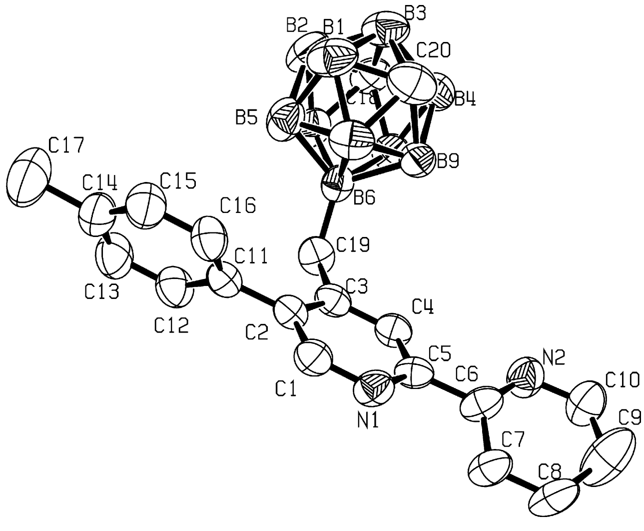


Fig. 2. ORTEP view of **4b** (hydrogen atoms are omitted). Selected bonds length (Å): C(3)–C(19) 1.508, C(19)–B(6) 1.592, C(5)–C(6) 1.480.

As expected, the chemical shifts of the protons at the *o*-positions of the conjugated (hetero)aromatic rings strongly depend on the torsions. In a coplanar configuration they should be shifted downfield compared with those of a twisted configuration due to the anisotropic effect of the aromatic ring. In our case, the H-6 and H-3′ signals are indicative ones. Thus H-3′ of the nearly planar bipyridine **4** is shifted downfield by 0.7 ppm in comparison with twisted **3**, while H-6 of **4** is shifted upfield on comparison with that of **3** ($\Delta\delta$ -0.25 ppm) because of the difference in the torsional angles (60° of **4** and 37° of **3**).

Unfortunately, no regioselectivity was observed. In all the experiments, the ratio of isomers was about 1:1. Allylcarborane reacts with triazine **1** much more slowly than 2,5-norbornadiene.[16e] The relatively low yields of products **3** and **4** are due to decomposition processes at high temperature which compete with the slow aza Diels–Alder reaction.

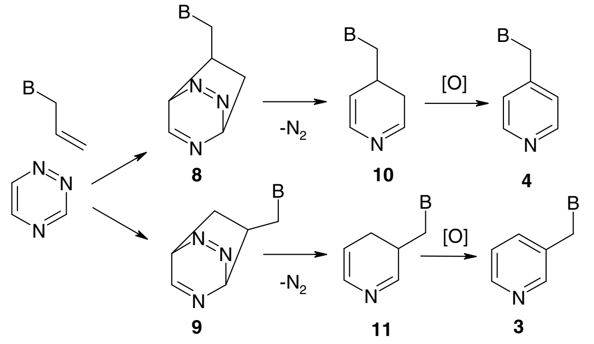
The mechanism of the described reaction should be analogous to the reactions of 1,2,4-triazines with other alkenes.[15] The first step is the cycloaddition of allylcarborane **2** at positions 3 and 6 of the 1,2,4-triazine (Scheme 2). Elimination of nitrogen from cycloadducts **8** and **9** via retro Diels–Alder reaction results in 4- or 3-substituted 3,4-dihydropyridine **10** or **11**. However, these intermediates were neither isolated nor observed by TLC or NMR of the reaction mixture. They undergo spontaneous oxidative rearomatization under the reaction conditions (air atmosphere) to yield pyridines **3** and **4**. Obviously the rate of the process is limited by the formation of dihydropyridines **10** or **11**, while their oxidation is a relatively fast step.

Electron-withdrawing substituents should activate 1,2,4-triazines toward inverse electron demand Diels–Alder reactions. To increase the yields we used 5-cyano-1,2,4-triazine **5**[21] as an active diene in reactions with enamines and 2,5-norbornadiene.[14c] Unfortunately, the cyanotriazine was found to be less stable under the reaction conditions (extended refluxing in xylene) which resulted in lower yields of 4- and 3-carboranylmethylcyanopyridines **6** and **7** (total yield was 16%, while the ratio of regioisomers was 1:1) (Scheme 1; for the crystal structures of **6** and **7** see Figs. S1 and S2, Supplementary data).

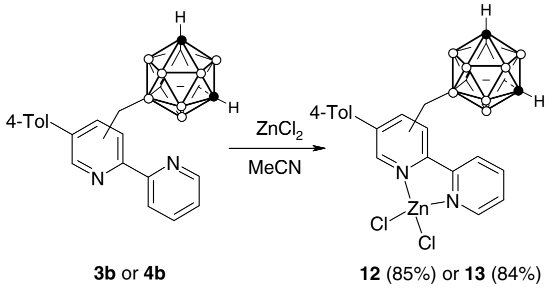
Bipyridines are among the most popular ligands in coordination, analytical, and supramolecular chemistry. They themselves and especially their complexes with several transition metal exhibit photoluminescence from solutions and solids. In particular, 6-aryl-2,2′-bipyridines show significant increasing luminescence quantum efficiency (up to Φ 0.90) upon the addition of Zn^{2+} to the solution.[22] Carboranylmethylbipyridines **3b** and **4b** reacted with $ZnCl_2$ in acetonitrile yielding complexes **12**[23] and **13**,[24] respectively (Scheme 3).

Single crystals of **13** suitable for X-ray diffraction were grown by slow evaporation from a saturated acetonitrile solution. The molecular structure of **13** is shown in Figure 3, and selected bond distances are given in the caption. The Zn atom has distorted tetrahedral coordination. The bipyridine fragment is essentially planar (the torsion angle between the pyridine rings is 1.7°). The torsion angle (63°) between the phenyl and the pyridine rings is nearly the same as that in free ligand **4b** (60°). Chains of **13** are formed because of intermolecular C–H···Cl hydrogen bonds (2.8364 Å, 3.832 Å, 151°) (Fig. S4, see Supplementary data). Similar to ligand **3b**, the CH-donor group in **13** is the carborane cage.

Absorption and emission spectra were recorded for bipyridines **3b** and**4b** and for their Zn(II) complexes **12** and **13** in chloroform at room temperature. The photo-



Scheme 2. Steps of the aza Diels–Alder reaction.



Scheme 3. Synthesis of complexes **12** and **13**.

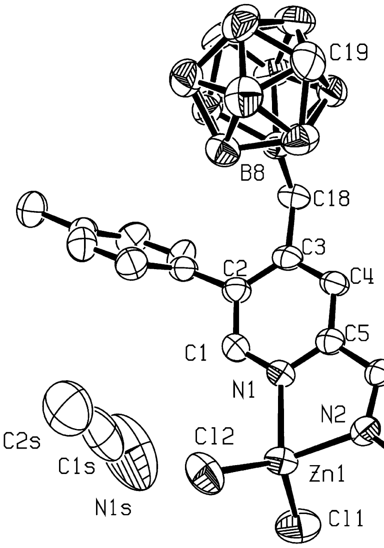


Fig. 3. ORTEP view of **13** (hydrogen atoms are omitted). Selected bonds length (Å): Zn(1)–N(1) 2.054, Zn(1)–N(2) 2.054, Zn(1)–Cl(1) 2.201, Zn(1)–Cl(2) 1.188.

Table 1
Photophysical data for bipyridines **3b** and **4b** and Zn^{II} complexes **12** and **13**

Compound	λ_{max}[a] (nm)	λ_{em}[b] (nm)	Φ_F [c] (%)
3b	298	380	14
4b	293	369	21
[Zn(**3b**)Cl$_2$] (**12**)	336	385	86
[Zn(**4b**)Cl$_2$] (**13**)	315	383	87
tolbpy	303	363	38
[Zn(tolbpy)Cl$_2$]	326	397	91

[a] Absorption maximum in $CHCl_3$.

[b] Emission maximum in $CHCl_3$.

[c] Fluorescence quantum yields were measured using anthracene as standard ($\Phi = 0.27$ in EtOH).

physical data are given in Table 1, and the data for 5-(4-tolyl)-2,2′-bipyridine (tolbpy) and its Zn^{II} complex are included for reference to compare the influence of the carboranylmethyl substituent. The lowest energy absorbance maxima of carboranylmethyl substituted bipyridines **3b** and **4b** are slightly blue-shifted (5–10 nm) if compared with those of unsubstituted tolbpy, which can be attributed to decreased conjugation in **3b** and **4b** because of the disturbed planarity of the aromatic rings. Substitution results in red-shifts of the emission maxima (6–17 nm) and decreasing fluorescence quantum yields. The co-ordination to Zn^{II} results in a small red-shift of the emission maxima, but extremely enhanced emission intensities, similar to the complex of unsubstituted tolbpy (Fig. 4).

In conclusion, allylcarborane **2** can be successfully used as a dienophile in inverse electron demands Diels–Alder reactions with active dienes such as 1,2,4-triazines to obtain pyridines bearing a carborane cage at positions 3 or 4 through the methylene spacer. The position of the allyl group in **2** in this case allows the attachment of the heterocycle to the carborane through the boron atom.

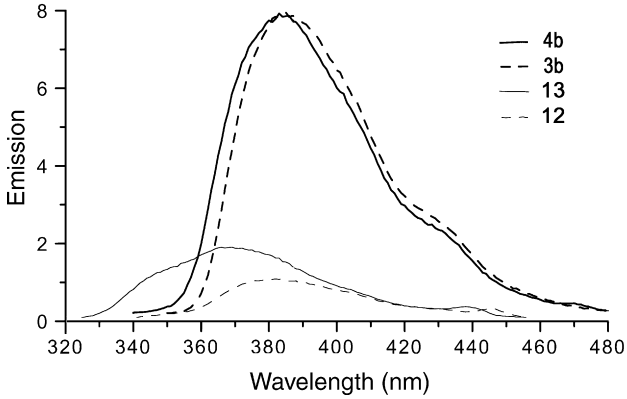


Fig. 4. Fluorescence spectra of **3b**, **4b**, **12**, and **13** in $CHCl_3$.

Acknowledgments

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Supplementary data

CCDC 676908–676910, 679234 and 679235 contain the supplementary crystallographic data for this Letter. Supplementary data (experimental details) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.04.008.

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18. *3-(1,7-Dicarbadodecaborane-9-ylmethyl)-5-phenyl-2,2′-bipyridine* (**3b**): Colorless crystals. Yield 25%. Mp: 125–128 °C (from acetonitrile). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 0.9–3.5 (br q, 9H, BH), 2.41 (s, 3H, CH_3), 2.74 (br s, 2H, BCH), 2.98 (br s, 2H, CH_2), 7.25–7.30 (m, 3H, Tol+H-5′), 7.56 (m, 2H, Tol), 7.71–7.82 (m, 3H), 8.67 (m, 2H, H-6′+H-6). *Crystal data for* **3b**. A single crystal was obtained by slow evaporation of a saturated methanol solution of **3b**. $C_{20}H_{26}B_{10}N_2$, FW = 402.53, monoclinic, $a = 16.167(4)$, $b = 10.0598(7)$, $c = 14.0413(14)$ Å, $\alpha = 90.00°$, $\beta = 99.033(12)°$, $\gamma = 90.00°$, $V = 2255.3(6)$ Å^3, $T = 295(2)$ K, space group $P2(1)/c$, $Z = 4$, 5502 reflections measured, 2144 unique ($R_{int} = 0.0490$) which were used in all calculations. $R_1 = 0.0520$, $wR_2 = 0.0799$.
19. *4-(1,7-Dicarbadodecaborane-9-ylmethyl)-5-(4-methylphenyl)-2,2′-bipyridine* (**4b**): Colorless crystals. Yield 25%. Mp: 141–143 °C (from methanol). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 0.9–3.5 (br q, 9H, BH), 2.42 (s, 3H, CH_3), 2.58 (br s, 2H, CH_2), 2.77 (br s, 2H, BCH), 7.23–7.31 (m, 5H, Tol+H-5′), 7.79 (ddd, $J = 7.8$, 7.8, 1.2 Hz, 1H, H-4′), 8.25 (s, 1H, H-6), 8.39 (m, 2H, H-3′+H-3), 8.69 (dd, $J = 4.7$, 1.2 Hz, 1H, H-6′). *Crystal data for* **4b**. A single crystal was obtained by slow evaporation of saturated methanol solution of **4b**. $C_{20}H_{26}B_{10}N_2$, FW = 402.53, triclinic, $a = 7.0960(11)$, $b = 10.5991(14)$, $c = 16.9295(17)$ Å, $\alpha = 79.809(10)°$, $\beta = 82.526(10)°$, $\gamma = 70.589(13)°$, $V = 1178.5(3)$ Å^3, $T = 295(2)$ K, space group $P\bar{1}$, $Z = 2$, 4617 reflections measured, 2192 unique ($R_{int} = 0.0254$) which were used in all calculations. $R_1 = 0.0479$, $wR_2 = 0.1023$.
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23. *Complex* **12**: Colorless crystals. Yield 85%. Mp: 219–221 °C (from acetonitrile). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 0.9–3.5 (br q, 9H, BH), 2.44 (s, 3H, CH_3), 2.93 (br s, 2H, CH_2), 3.00 (br s, 2H, BCH), 7.33 (m, 2H, Tol), 7.55 (m, 2H, Tol), 7.68 (ddd, $J = 7.8$, 4.7, 1.2 Hz, 1H, H-5′), 8.04 (d, $J = 0.9$ Hz, 1H, H-3), 8.14 (ddd, $J = 7.8$, 7.8, 1.2 Hz, 1H, H-4′), 8.48 (dd, $J = 7.8$, 1.2 Hz, 1H, H-3′), 8.88 (m, 2H, H-6′+H-6).
24. *Complex* **13**: Colorless crystals. Yield 84%. Mp: 244–245 °C (from acetonitrile). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 0.9–3.5 (br q, 9H, BH), 2.43 (s, 3H, CH_3), 2.67 (br s, 2H, CH_2), 2.87 (br s, 2H, BCH), 7.24-7.32 (m, 4H, Tol), 7.70 (ddd, $J = 7.8$, 4.7, 1.2 Hz, 1H, H-5′), 8.02 (s, 1H, H-6), 8.20 (m, 2H, H-3′+H-4′), 8.55 (s, 1H, H-3), 8.83 (dd, $J = 4.7$, 1.2 Hz, 1H, H-6′). *Crystal data for* **13**. A single crystal was obtained by slow evaporation of a saturated acetonitrile solution of **4b** and $ZnCl_2$, mixed in a stoichiometric ratio. $C_{22}H_{29}B_{10}Cl_2N_3Zn$, FW = 579.85, monoclinic, $a = 12.1473(13)$, $b = 11.6461(18)$, $c = 20.624(3)$ Å, $\alpha = 90.00°$, $\beta = 99.052(9)°$, $\gamma = 90.00°$, $V = 2881.4(6)$ Å^3, $T = 295(2)$ K, space group $P2(1)/c$, $Z = 4$, 5866 reflections measured, 2483 unique ($R_{int} = 0.0590$) which were used in all calculations. $R_1 = 0.0444$, $wR_2 = 0.0513$.