

Three-Component [2+2+1] Cross-cyclotrimerization of Carboryne, Unactivated Alkene, and Trimethylsilylalkyne Co-mediated by Zr and Ni

Yangjian Quan, Jiji Zhang, and Zuowei Xie*

Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

S Supporting Information

ABSTRACT: A three-component [2+2+1] cross-cyclotrimerization of carboryne, alkene, and trimethylsilylalkyne has been achieved under the cooperative action of zirconium and nickel, leading to the synthesis of a series of dihydrofulvenocarboranes. The bulkiness of the alkyne and phosphine ligand plays a key role in the selective formation of the products.

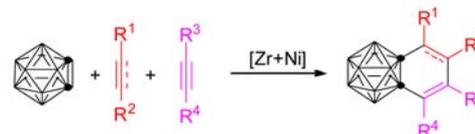
Transition-metal-mediated/catalyzed [2+2+2] cyclotrimerization of alkynes/alkenes serves as a very powerful strategy for the synthesis of substituted cyclic compounds.¹ The challenge in this field of research is how to control the chemoselectivity in the intermolecular [2+2+2] cyclotrimerization of different components. A few successful examples have been reported via either pre-installed functionalities in alkynes² or unsymmetrical zirconacyclopentadiene intermediates.³ In view of the growing interest in applications of carborane derivatives in boron neutron capture therapy,⁴ supramolecular design,⁵ catalysis,⁶ and materials,⁷ we extended such a [2+2+2] protocol to include carborynes (1,2-dehydro-*o*-carboranes⁸ and 1,3-dehydro-*o*-carboranes,⁹ which can be viewed as a three-dimensional relative of benzyne) to develop a toolbox for the synthesis of a variety of functionalized carboranes from readily available starting materials via a simple operation.¹⁰

Subsequently, nickel-mediated/catalyzed two-component [2+2+2] cross-cyclotrimerization of carboryne with alkynes was developed in our laboratory.¹¹ Furthermore, through cooperative mediation by both Zr and Ni, we achieve a three-component [2+2+2] cross-cyclotrimerization of *o*-carboryne with two different alkynes or with one alkene and one alkyne (Scheme 1).^{12,13} During the course of this study, an unprecedented dihydrofulvenocarborane, *E*-5a, was isolated together with the expected dihydrobenzocarboranes from the reaction of zirconacyclopentane 1,2-[Cp₂ZrCH₂CH(^{*n*}Bu)]-1,2-C₂B₁₀H₁₀ (**1**) with TMS—≡—Ph (**3a**) in the presence of NiCl₂(PMe₃)₂ (Table 1). Compound *E*-5a obviously resulted from a three-component [2+2+1] cyclotrimerization of carboryne, alkene, and alkyne (Scheme 1). We were intrigued to investigate such a brand new [2+2+1] reaction, and the results are reported in this Communication.

We screened various reaction conditions for the reaction of **1** with 3 equiv of TMS—≡—Ph (**3a**) in the presence of 1 equiv of nickel complex NiCl₂L₂. The results were summarized in Table 1. All nickel(II) complexes examined could effectively

Scheme 1. Transition Metals Co-mediated Cross-cyclotrimerization

previous work [2+2+2]



this work [2+2+1]

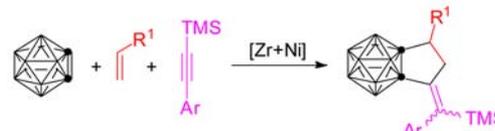


Table 1. Optimization of Reaction Conditions^a

entry	ligand (L ₂)	solvent	T [°C]	conversion [%] ^b	4a/4'a/E-5a ^c
1	PMe ₃	toluene	r.t.	96	35/1/64
2	PMe ₃	Et ₂ O	r.t.	90	33/1/66
3	PMe ₃	THF	40 ^d	93	35/1/64
4	PMe ₃	DME	40 ^d	97	35/1/64
5	PMe ₃	CH ₂ Cl ₂	r.t.	88	42/2/56
6	PPh ₃	toluene	r.t.	95	92/4/4
7	P ^{<i>n</i>} Bu ₃	toluene	r.t.	73	35/4/61
8	PMe ₂ Ph	toluene	r.t.	87	50/1/49
9	PMePh ₂	toluene	r.t.	94	50/3/47
10	dppf	toluene	r.t.	0	none

^aReaction conditions: **1** (0.05 mmol), [Ni] (0.05 mmol), and **3a** (0.15 mmol) in 0.6 mL of solvent in a closed vessel, 48 h. ^bGC yield.

^cDetermined by GC-MS. ^dNo reaction was observed at room temperature.

mediate this reaction in common organic solvents in very good to excellent conversions but with different molar ratios of **4a**/**4'a**/*E*-**5a**. In general, the formation of **4'a** could be neglected due to the polarity of **3a** regardless of phosphines used. On the

Received: October 5, 2013

Published: November 29, 2013

Table 2. Synthesis of Dihydrofulvenocarboranes^a

entry	R ¹	R ²	yield [%] ^b	entry	R ¹	R ²	yield [%] ^b
1	ⁿ Bu	(3a)	46 (E-5a)	14	ⁿ Bu	(3n)	72 (Z-5n)
2	ⁿ Bu	(3b)	72 (E-5b)	15	ⁿ Bu	(3o)	50 ^d (E-5o)
3	ⁿ Bu	(3c)	81 ^c (5c E/Z = 1:3)	16	ⁿ Bu	(3p)	34 (E-5p)
4	ⁿ Bu	(3d)	86 ^c (5d E/Z = 1:2)	17	ⁿ Bu	(3q)	4 (E-5q)
5	ⁿ Bu	(3e)	50 (E-5e)	18	ⁿ Bu	(3r)	30 ^d (5r)
6	ⁿ Bu	(3f)	56 (E-5f)	19	ⁿ Bu	(3s)	N.R.
7	ⁿ Bu	(3g)	38 (E-5g)	20	ⁿ Bu	(3t)	N.R.
8	ⁿ Bu	(3h)	70 (E-5h)	21	H	(3c)	38 ^c (5u E/Z = 1:2)
9	ⁿ Bu	(3i)	85 (Z-5i)	22	CH ₂ Ph	(3m)	81 (E-5v)
10	ⁿ Bu	(3j)	80 (Z-5j)	23	ⁿ Bu	(3m)	76 (E-5w)
11	ⁿ Bu	(3k)	80 ^c (5k E/Z = 1:5)	24	ⁿ Bu	(3i)	71 (Z-5x)
12	ⁿ Bu	(3l)	71 ^c (5l E/Z = 2:1)	25	CH ₂ OMe	(3m)	49 (E-5y)
13	ⁿ Bu	(3m)	73 (E-5m)	26	CH ₂ NMe ₂	(3m)	64 (E-5z)

^aReaction conditions: **1** (0.5 mmol), NiCl₂(PMe₃)₂ (0.5 mmol), and **3** (1.5 mmol) in 10 mL of toluene in a closed vessel, 48 h. ^bIsolated yields. ^cE/Z ratio was determined by GC-MS with authentication. ^dReaction was heated at 110 °C.

other hand, triphenylphosphine offered an excellent selectivity for **4a**, whereas trimethylphosphine gave the best selectivity for **E-5a** (entry 6 vs 1, Table 1). In view of **E-5a**'s selectivity, conversion rate, and reaction temperature, entry 1 in Table 1 was chosen as the optimal reaction conditions.

A variety of trimethylsilylalkynes were examined under the chosen optimal reaction conditions, and the results are compiled in Table 2. *Ortho*-substituents on arenes played a

crucial role in the formation of **5**. When R² in TMS—C≡C—R² was changed from phenyl to *o*-tolyl to *o*-isopropylphenyl, the isolated yield of **5** was increased from 46% to 72% to 81% at the expense of E/Z selectivity, from only *E* isomers for **5a** and **5b** to E/Z = 1:3 for **5c**. Such E/Z selectivity was dependent not only on the relative size of TMS/R² (entries 1–4, Table 2) but also on the nature of R² (entry 8, Table 2). *Ortho*-substituents bearing donor functionality favored the formation of *E* isomers

(entry 3 vs 8 and entry 9 vs 11, Table 2) owing to the possible coordination of the heteroatom to the Ni center. For 2,6-disubstituted aryls **3i** and **3j**, only *Z* isomers, *Z*-**5i** and *Z*-**5j**, were isolated in >80% yield because of steric reasons (entries 9 and 10, Table 2). In the case of pentafluorophenyl substituent, both *E*- and *Z*-isomers were formed, with *E*-**5l**:*Z*-**5l** = 2:1, as the F atom is bigger than a H atom and smaller than a CH₃ group (entry 12, Table 2). The *E*- and *Z*-selectivity was reversed for **3m** and **3n** owing to steric reasons (entries 13 and 14, Table 2).

This reaction was compatible with heteroaromatics such as **3o** and **3p**, affording *E*-**5o** and *E*-**5p** in relatively low yields (entries 15 and 16, Table 2). Alkyl alkyne TMS—≡—"Bu (**3q**) gave *E*-**5q** in only 4% isolated yield with [2+2+2] cross-cyclotrimerization compound dihydrobenzocborane as the major product (entry 17, Table 2). On the other hand, bis(trimethylsilyl)acetylene (**3r**) offered 100% selectivity of **5r** with 35% conversion rate at 110 °C, whereas no reaction was observed for R² = Et₃Si or ^tBuMe₂Si even under forced reaction conditions (entries 18–20, Table 2), suggesting the importance of steric effects in this reaction.

Effects of R¹ on reaction results were also examined. For R¹ = CH₂Ph and ^tBu, products with single isomer *E*-**5v**, *E*-**5w**, and *Z*-**5x** were obtained in high yields, which is very compatible with those of R¹ = ⁿBu (entries 22–24 vs 9 and 13, Table 2). If R¹ contains heteroatom such as CH₂OMe and CH₂NMe₂, single isomers *E*-**5y** and *E*-**5z** were isolated in relatively low yields (entries 25 and 26, Table 2) probably owing to the interaction of the heteroatom with the metal center. Replacement of R¹ = ⁿBu by H resulted in the loss of the chirality, preventing the formation of diastereoisomers (entry 21, Table 2; also see Supporting Information). It was noted that a small amount of dihydrobenzocboranes (**4**) was observed as minor products in most of reactions, which were formed via [2+2+2] cycloaddition reaction as shown in Scheme 1.¹³

Compounds **5** were fully characterized by ¹H, ¹³C, and ¹¹B NMR spectroscopy as well as high-resolution mass spectrometry. The molecular structures of *E*-**5a**, **5b**, **5l**, **5p**, *Z*-**5d**, **5i**, **5u**, and **5r** were further confirmed by single-crystal X-ray analyses. Figure 1 shows the representative structures of *E*-**5b** and *Z*-**5d**.

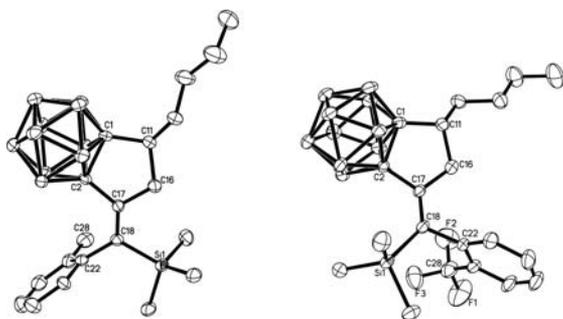
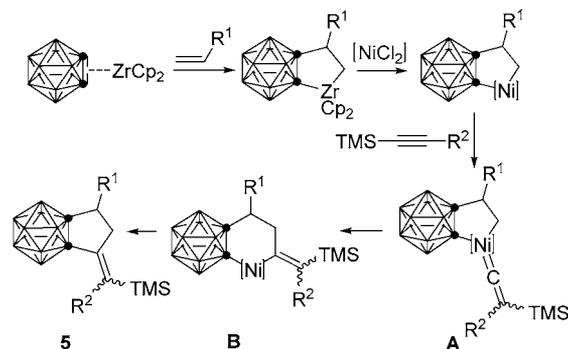


Figure 1. Molecular structures of *E*-**5b** (left) and *Z*-**5d** (right).

As the above [2+2+1] cross-cyclotrimerization¹⁴ works only for trimethylsilylalkynes, and such alkynes are known to react with nickel complexes to give nickelvinylidene species,^{15,16} a plausible reaction mechanism is thus proposed in Scheme 2. Transmetalation of zirconacycle to nickel generates the corresponding nickelacyclopentane.¹³ Coordination of alkyne to the nickel and 1,2-trimethylsilyl shift gives a nickelvinylidene intermediate **A**. Migratory insertion of the vinylidene carbene forms intermediate **B**. Reductive elimination affords the final

Scheme 2. Proposed Reaction Mechanism



product **5**. The *E/Z* selectivity (configuration of alkenes in **5**) is dominated by the relative size of R²/TMS. If R² > TMS, *Z*-configuration is favored; otherwise, *E*-isomers are the major products. On the other hand, *E*-configuration is favored if R² bears a donor atom that can coordinate to the Ni atom. As this reaction can be done in one pot starting from *o*-carborane, it is rational to view this as an equivalent to three-component [2+2+1] cross-cyclotrimerization of carboryne, alkene, and alkyne mediated by transition metals.

In summary, we have developed a novel transition-metal-mediated three-component [2+2+1] cross-cyclotrimerization reaction for the preparation of a series of dihydrofulvenocboranes. In view of the demonstrated similarities between metal-benzynes and metal-carboryne complexes,¹⁰ it is anticipated that a similar benzyne analogue might undergo the same type of reactions. This work may also shed some light on how to control chemoselectivity among alkenes and alkynes in chemical transformations.

ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures, complete characterization data, and X-ray data in CIF format for *E*-**5a**, **5b**, **5l**, **5p**, *Z*-**5d**, **5i**, **5u**, and **5r**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Author

zxie@cuhk.edu.hk

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by grants from the Research Grants Council of The Hong Kong Special Administration Region (Project No. CUHK7/CRF/12G) and National Basic Research Program of China (973 Program, Grant No. 2012CB821600).

REFERENCES

- (1) For reviews on the synthesis of ring systems using [2+2+2] cycloaddition, see: (a) Kotha, S.; Brahmachary, E.; Lahiri, K. *Eur. J. Org. Chem.* **2005**, 4741–4767. (b) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901–2915. (c) Chopade, P. R.; Louie, J. *Adv. Synth. Catal.* **2006**, *348*, 2307–2327. (d) Tanaka, K. *Synlett* **2007**, *10*, 1977–1993. (e) Shibata, T.; Tsuchikama, K. *Org. Biomol. Chem.* **2008**, *6*, 1317–1323. (f) Yamamoto, Y. *Curr. Org. Chem.* **2005**, *9*, 503–519. (g) Heller, B.; Hapke, M. *Chem. Soc. Rev.* **2007**, *36*, 1085–1094. (h) Varela, J. A.; Saá, C. *Chem. Rev.* **2003**, *103*, 3787–3801. (i) Henry, G. D. *Tetrahedron* **2004**, *60*, 6043–6061. (j) Agenet, N.; Busine, O.;

Slowinski, F.; Gandon, V.; Aubert, C.; Malacria, M. *Org. React.* **2007**, *68*, 1–302. (k) Galan, B. R.; Rovis, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 2830–2834. (l) Domínguez, G.; Pérez-Castells, J. *Chem. Soc. Rev.* **2011**, *40*, 3430–3444. (m) Vollhardt, K. P. C. *Angew. Chem., Int. Ed.* **1984**, *23*, 539–556.

(2) (a) Yamamoto, Y.; Ishii, J.; Nishiyama, H.; Itoh, K. *J. Am. Chem. Soc.* **2004**, *126*, 3712–3713. (b) Yamamoto, Y.; Ishii, J.; Nishiyama, H.; Itoh, K. *J. Am. Chem. Soc.* **2005**, *127*, 9625–9631.

(3) (a) Dufková, L.; Kotorá, M.; Císarová, I. *Eur. J. Org. Chem.* **2005**, 2491–2499. (b) Takahashi, T.; Tsai, F. Y.; Li, Y.; Nakajima, K.; Kotorá, M. *J. Am. Chem. Soc.* **1999**, *121*, 11093–11100.

(4) (a) Hawthorne, M. F. *Angew. Chem., Int. Ed.* **1993**, *32*, 950–984. (b) Armstrong, A. F.; Valliant, J. F. *Dalton Trans.* **2007**, 4240–4251. (c) Issa, F.; Kassiou, M.; Rendina, L. M. *Chem. Rev.* **2011**, *111*, 5701–5722.

(5) Selected examples: (a) Yang, X.; Jiang, W.; Knobler, C. B.; Hawthorne, M. F. *J. Am. Chem. Soc.* **1992**, *114*, 9719–9721. (b) Jude, H.; Disteldorf, H.; Fischer, S.; Wedge, T.; Hawkridge, A. M.; Arif, A. M.; Hawthorne, M. F.; Muddiman, D. C.; Stang, P. J. *J. Am. Chem. Soc.* **2005**, *127*, 12131–12139. (c) Dash, B. P.; Satapathy, R.; Gaillard, E. R.; Maguire, J. A.; Hosmane, N. S. *J. Am. Chem. Soc.* **2010**, *132*, 6578–6587.

(6) (a) Hosmane, N. S.; Maguire, J. A. In *Comprehensive Organometallic Chemistry III*; Crabtree, R. H., Mingos, D. M. P., Eds.; Elsevier: Oxford, 2007; Vol. 3, Chapter 5. (b) Xie, Z. *Coord. Chem. Rev.* **2002**, *231*, 23–46. (c) Xie, Z. *Acc. Chem. Res.* **2003**, *36*, 1–9. (d) Deng, L.; Xie, Z. *Coord. Chem. Rev.* **2007**, *251*, 2452–2476. (e) Hosmane, N. S. *Boron Science: New Technologies and Applications*; Taylor & Francis Books/CRC: Boca Raton, FL, 2011.

(7) Selected examples: (a) Wee, K.-R.; Cho, Y.-J.; Jeong, S.; Kwon, S.; Lee, J.-D.; Suh, I.-H.; Kang, S. O. *J. Am. Chem. Soc.* **2012**, *134*, 17982–17990. (b) Cioran, A. M.; Musteti, A. D.; Teixidor, F.; Krpetić, Ž.; Prior, I. A.; He, Q.; Kiely, C. J.; Brust, M.; Viñas, C. *J. Am. Chem. Soc.* **2012**, *134*, 212–221. (c) Visbal, R.; Ospino, I.; López-de-Luzuriaga, J. M.; Laguna, A.; Gimeno, M. C. *J. Am. Chem. Soc.* **2013**, *135*, 4712–4715. (d) Yinghuai, Z.; Peng, A. T.; Carpenter, K.; Maguire, J. A.; Hosmane, N. S.; Takagaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 9875–9880.

(8) (a) Gingrich, H. L.; Ghosh, T.; Huang, Q.; Jones, M., Jr. *J. Am. Chem. Soc.* **1990**, *112*, 4082–4083. (b) Jeon, J.; Kitamura, T.; Yoo, B.-W.; Kang, S. O.; Ko, J. *Chem. Commun.* **2001**, 2110–2111. (c) Lee, T.; Jeon, J.; Song, K. H.; Jung, I.; Baik, C.; Park, K.-M.; Lee, S. S.; Kang, S. O.; Ko, J. *Dalton Trans.* **2004**, 933–937. (d) Wang, S. R.; Qiu, Z.; Xie, Z. *J. Am. Chem. Soc.* **2010**, *132*, 9988–9989. (e) Wang, S. R.; Qiu, Z.; Xie, Z. *J. Am. Chem. Soc.* **2011**, *133*, 5760–5763.

(9) Qiu, Z.; Xie, Z. *J. Am. Chem. Soc.* **2010**, *132*, 16085–16093.

(10) Qiu, Z.; Ren, S.; Xie, Z. *Acc. Chem. Res.* **2011**, *44*, 299–309.

(11) (a) Deng, L.; Chan, H.-S.; Xie, Z. *J. Am. Chem. Soc.* **2006**, *128*, 7728–7729. (b) Qiu, Z.; Xie, Z. *J. Am. Chem. Soc.* **2009**, *131*, 2084–2085. (c) Qiu, Z.; Wang, S. R.; Xie, Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 4649–4652.

(12) Ren, S.; Qiu, Z.; Xie, Z. *J. Am. Chem. Soc.* **2012**, *134*, 3242–3254.

(13) Ren, S.; Qiu, Z.; Xie, Z. *Angew. Chem., Int. Ed.* **2012**, *51*, 1010–1013.

(14) Selected examples of the synthesis of ring systems using one- or two-component [2+2+1] cycloaddition of alkynes: (a) Shibata, Y.; Tanaka, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 10917–10921. (b) Burrows, A. D.; Green, M.; Jeffery, J. C.; Lynam, J. M.; Mahon, M. F. *Angew. Chem., Int. Ed.* **1999**, *38*, 3043–3045. (c) Kim, H.-J.; Choi, N.-S.; Lee, S. W. *J. Organomet. Chem.* **2000**, *616*, 67–73. (d) O'Connor, J. M.; Hiibner, K.; Merwin, R.; Gantzel, P. K.; Fong, B. S.; Adams, M.; Rheingold, A. L. *J. Am. Chem. Soc.* **1997**, *119*, 3631–3632. (e) Becker, E.; Mereiter, K.; Puchberger, M.; Schmid, R.; Kirchner, K.; Doppiu, A.; Salzer, A. *Organometallics* **2003**, *22*, 3164–3170. (f) Wen, T. B.; Zhou, Z. Y.; Jia, G. *Angew. Chem., Int. Ed.* **2006**, *45*, 5842–5846.

(15) (a) Kang, Y.; Lee, J.; Kong, Y. K.; Kang, S. O.; Ko, J. *Organometallics* **2000**, *19*, 1722–1728. (b) Naka, A.; Okazaki, S.;

Hayashi, M.; Ishikawa, M. *J. Organomet. Chem.* **1995**, *499*, 35–41. (c) Naka, A.; Hayashi, M.; Okazaki, S.; Kunai, A.; Ishikawa, M. *Organometallics* **1996**, *15*, 1101–1105.

(16) (a) Kline, E. S.; Kafafi, Z. H.; Hauge, R. H.; Margrave, J. L. *J. Am. Chem. Soc.* **1987**, *109*, 2402–2409. (b) Shiba, T.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2013**, *135*, 13636–13639.