

Palladium Catalyzed Regioselective B–C(sp) Coupling via Direct Cage B–H Activation: Synthesis of B(4)-Alkynylated *o*-Carboranes

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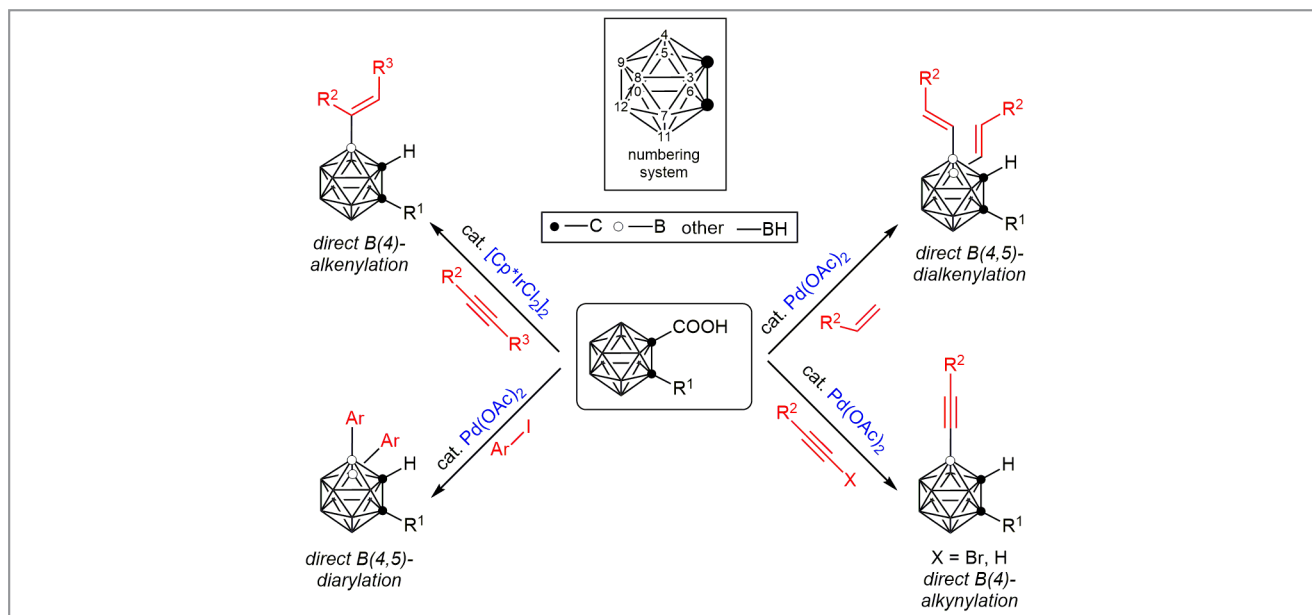
Icosahedral carboranes are a class of polyhedral boron hydride clusters in which one or more of the BH vertices are replaced by CH units, which can be viewed as three-dimensional relatives of benzene. Their exceptional thermal and chemical stabilities as well as 3D structures make them useful building blocks for boron neutron capture therapy agents in medicine, versatile ligands in coordination/organometallic chemistry, and functional units in supramolecular design/optoelectronic materials.¹ As a result, considerable attention has been directed towards the functionalization of carboranes.

Classic routes to functionalized carboranes rely on the polarized cage C–H/B–H bonds: the weakly acidic C–H proton ($pK_a \sim 23$) and basic B–H hydride.¹ Generally, cage C–H bonds can be deprotonated by strong bases, followed by the reaction with electrophiles to give carbon-substituted carboranes. Cage B–H bonds are preferentially subjected to electrophilic substitution reactions, resulting in the formation of cage boron-substituted carborane derivatives. However, the latter suffers from poor regioselectivity due to the presence of different electronic environments of BH vertices.

To tackle the regioselectivity problem, the group of Professor Zuowei Xie from the Chinese University of Hong Kong (P. R. of China) introduced a carboxyl group at the cage carbon to control the regioselectivity and facilitate cage B–H activation. Subsequently, transition-metal-catalyzed cage B(4)-alkenylation,^{2a} B(4,5)-dialkenylation,^{2b} and B(4,5)-diarylation^{2c} have been achieved (Scheme 1).

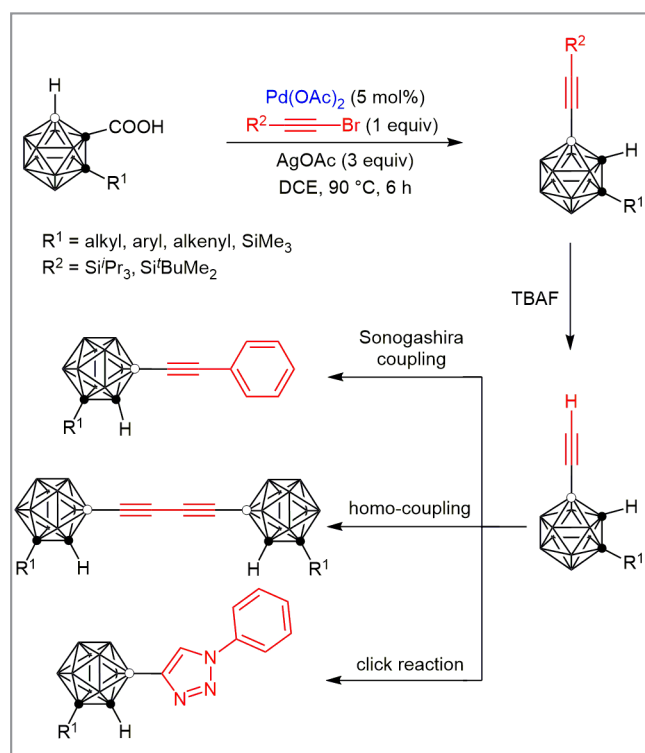
Professor Xie said: “In view of the wide application of carboranyl acetylenes in molecular rods, nanomaterials and metal-organic frameworks,¹ we have developed the first transition-metal-catalyzed regioselective cage B–C(sp) coupling via direct cage B(4)–H activation for the synthesis of B(4)-alkynylated *o*-carboranes.”

In the presence of 5 mol% Pd(OAc)₂ and three equivalents of AgOAc, the reaction of carboranyl carboxylic acid with alkynyl bromide proceeds smoothly in DCE (DCE = 1,2-dichloroethane) at 90 °C to give the desired B(4)-alkynylated *o*-carboranes in moderate to very good isolated yields. “Though this reaction is tolerant of many functional groups R¹ at the cage C(2), it is compatible only with sterically bulky silyl groups



Scheme 1 Carboxylic acid guided, transition-metal-catalyzed cage B–H functionalization

R²,” explained Professor Xie. He continued: “On the other hand, the silyl groups R² can be easily removed by treatment with TBAF (TBAF = tetra-*n*-butylammonium fluoride), giving quantitatively the terminal alkyne 4-(CH≡C)-2-R¹-*o*-C₂B₁₀H₁₀. Like other terminal alkynes, this carboranyl acetylene is a useful synthon for the synthesis of a variety of *o*-carborane derivatives via Sonogashira coupling, homo-coupling and click reactions (Scheme 2).”

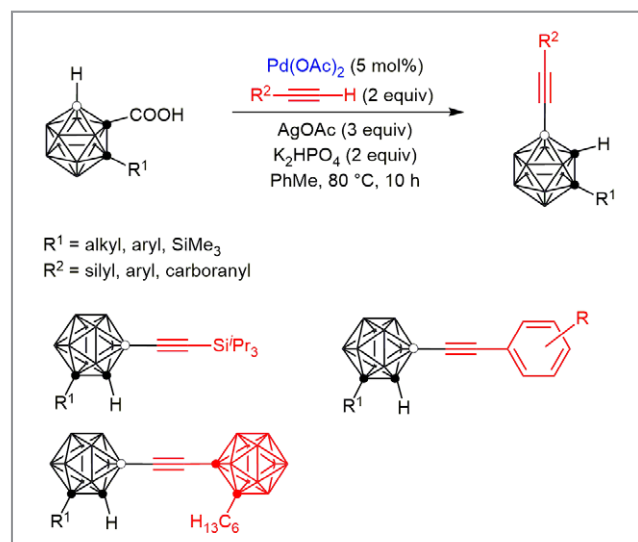


Scheme 2 Pd-catalyzed cage B(4)-H alkynylation using alkynyl bromides as coupling agents and subsequent transformations

“To broaden the substrate scope, another catalytic system, Pd(OAc)₂/AgOAc/K₂HPO₄, has been developed using terminal alkynes as coupling agents (Scheme 3),” remarked Professor Xie. He said: “Such an oxidative dehydrocoupling reaction is compatible with various R² groups like silyl, phenyl and carboranyl, leading to the preparation of different kinds of B(4)-alkynylated *o*-carboranes.”

Professor Xie explained that preliminary mechanistic studies indicate (1) both catalytic cycles are initiated by Pd(II) species, and (2) the traceless directing group –COOH plays a key role not only in regioselectivity but also in monoselectivity of this reaction. Accordingly, two possible catalytic cycles involving Pd(II)–Pd(IV)–Pd(II) and Pd(II)–Pd(0)–Pd(II) processes

were proposed for the aforementioned reaction systems, respectively.



Scheme 3 Pd-catalyzed cage B(4)-H alkynylation using terminal alkynes as coupling agents

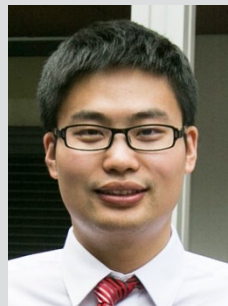
“In conclusion, two catalytic systems for regioselective cage B(4)-H alkynylation of *o*-carboranes have been developed, for the first time, via direct B–H activation, resulting in a variety of previously inaccessible cage B(4)-alkynylated *o*-carborane derivatives,” said Professor Xie. “The current work represents significant advances over the known methods involving multi-step synthesis.” He concluded: “This work also opens avenues to a wide and varied range of new carborane derivatives and sets an excellent example for the development of regioselective B–H functionalization in other boron clusters.”

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About the authors



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C. Tang

Cen Tang received her B.Sc. from Shanghai University (P. R. of China, 2012) and is now pursuing her Ph.D. in chemistry at The Chinese University of Hong Kong (CUHK, P. R. of China) under the supervision of Professor Zuowei Xie. She received a Postgraduate Research Output Award (2015). She is currently working on the cage C–H and B–H functionalization of carboranes.



Prof. Z. Xie

Zuowei Xie received his Ph.D. in chemistry in 1990, working in a special joint program between the Shanghai Institute of Organic Chemistry (P. R. of China), Chinese Academy of Sciences (P. R. of China) and the Technische Universität Berlin (Germany). After a stay as a postdoctoral fellow at the University of Southern California (USA), he joined the chemistry faculty of CUHK (P. R. of China) in 1995, where he is now Choh-Ming Li Professor of Chemistry. He has received several prestigious awards including the State Natural Science Awards in 1997 and 2008, the Chinese Chemical Society Yao-Zeng Huang Award in Organometallic Chemistry in 2010, and the Croucher Award from the Croucher Foundation (Hong Kong) in 2003. He has co-authored over 260 publications and his recent work focuses on the chemistry of carboranes, supercarboranes, and metallacarboranes.