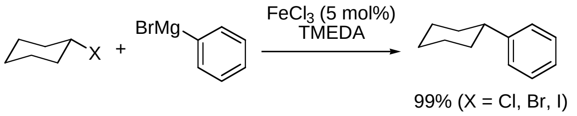
PHYSICAL ORGANIC CHEMISTRY

Annual Research Highlights

(1) "Iron-catalyzed cross-coupling of alkyl halides with Grignard reagents"

Despite its long history and widespread use, C-C bond formation by nucleophilic substitution of an alkyl halide has not been a truly satisfactory synthetic method. Pursuing practical and environmentally benign iron catalysis, we found that primary and secondary alkyl halides and aryl Grignard reagents smoothly undergo cross-coupling reaction in the presence of an iron catalyst.

Extensive studies revealed that a combination of $FeCl_3$ catalyst and *N,N,N',N'*-tetraethylenediamine (TMEDA) and elaborate control of reaction conditions allow quantitative cross-coupling of an aryl Grignard reagent and a secondary alkyl chloride, bromide and iodide (eq 1). While β-hydride elimination and reduction are often problematic side reactions for this class of substrates, no such reaction was observed. Stereochemical probes suggest that the intermediate responsible for the C-C bond-forming step undergoes stereochemical mutation and is rather bulky. One plausible possibility is an "iron-bound radical" intermediate.



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1.(1)-5) *J. Am. Chem. Soc.* **126**, 3686-3687 (2004).

(2) "Mechanism of substitution reaction on sp^2-carbon center with lithium organocuprate"

Substitution of an alkenyl bromide with a lithium diorganocuprate (R_2CuLi) is a groundbreaking reaction that has changed the accepted wisdom that a nucleophilic substitution on an sp^2-hybridized carbon is synthetically impracticable. However, the detailed mechanism of this reaction has been elusive for a long time. Through theoretical and experimental studies, we now revealed the reaction mechanism with a particular focus on the role of copper/lithium aggregate in the carbon-halogen bond cleavage.

Density functional calculations suggested two mechanistic possibilities, which are a conventional three-centered oxidative addition pathway and an "eliminative" pathway (Fig. 1). In the latter, the copper and lithium centers act as a nucleophile and as a Lewis acid, respectively, to effect cooperative, bimetallic carbon-halogen bond cleavage. Experimental kinetic isotope effect measurements, combined with theoretical prediction, showed the eliminative mechanism is operating in the actual reaction.

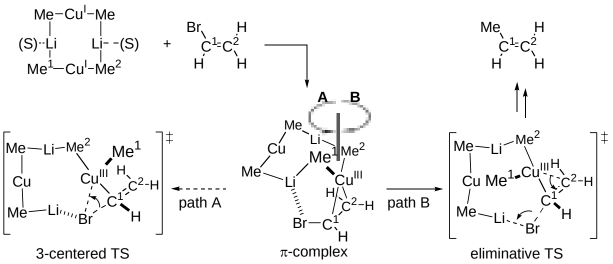


Fig. 1 Pathways of the reaction of $[Me_2CuLi]_2$ and vinyl bromide.

1.(1)-16) *J. Am. Chem. Soc.* **126**, 12264-12265 (2004).

(3) "Selective deposition of a metal cluster in a hole opening of single-wall carbon nanohorn"

Selective synthesis of particles of angstrom to nanometer size consisting of one to many metal atoms is instrumental in various applications, but it has been hampered by the tendency of the metal atom to form large clusters. Because the oxidized edge of carbon nanotube is rich in hydrophilic functional groups, such as hydroxy and carboxyl groups, and hence creates a "locally amphiphilic" structure on a graphene sheet, we considered that selective accumulation of hydrophilic metal ions, one by one through self-assembly, onto a small hole of partially oxidized graphene sheet should be possible. In fact, treatment of single-wall carbon nanohorn possessing hole openings of several angstroms to ~2 nm diameter with methanolic $Gd(OAc)_3$ permits selective deposition of one to several Gd(III) atoms in an opening at the tip of the tube (Fig. 2), or a cluster of an average 1.6-nm diameter in the interior of an opening on the sidewall, as studied by the state-of-the-art electron microscopic technique. Besides the potential utilities of the deposited metal clusters, the metal deposition protocol provides a method to control permeation of molecules through such openings.

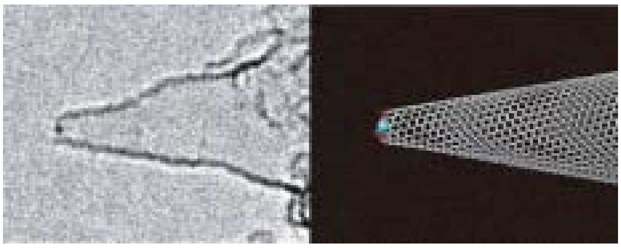


Fig. 2 A Gd atom trapped in a hole of oxidized nanotube. Left: A TEM image of one Gd atom at an open tip. Right: A model representing the TEM image.

1.(1)-10) *Proc. Natl. Acad. Sci.* **101**, 8527-8530 (2004).

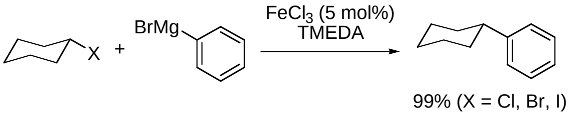
物理有機化学研究室

研究ハイライト

(1)鉄触媒によるハロゲン化アルキルとグリニャール試薬のクロスカップリング反応

ハロゲン化アルキルの求核置換による炭素–炭素結合生成は古典的有機反応であるが，種々の副反応を伴う場合が多く，いまだに有機合成反応としての完成度は低い．近年我々は，鉄触媒による実用的かつ環境調和的な有機合成反応の開発を行っており，一級および二級のハロゲン化アルキルと芳香族グリニャール試薬が鉄触媒のもとで定量的にクロスカップリング（置換）生成物を与えることを見いだした（式１）．

本反応の鍵は添加剤の *N,N,N',N'*-テトラエチレンジアミン（TMEDA）である．反応条件を精密に制御することにより，一般的に β-水素脱離や還元などの副反応を起こしやすい二級の臭化物，さらには反応性の低い塩化物の置換反応を定量的に行うことが可能となった．本反応はエステル等の官能基を有する基質を用いることもできる．反応基質と生成物の立体化学を反応機構のプローブとして検討したところ，本反応は立体反転を伴う S_N2 機構ではなく，ラジカル活性種を経て進行することが示唆された．



(1)

1.(1)-5) *J. Am. Chem. Soc.* **126**, 3686-3687 (2004).

(2)有機銅アート試薬による sp^2 炭素上での置換反応の機構

有機銅アート試薬によるハロゲン化アルケニルの置換反応は，sp^2 炭素上での置換を経る炭素–炭素結合生成反応として最初の例であるが，反応機構は明らかにされていなかった．我々は理論的および実験的手法を併用することにより，本反応の機構，特に炭素ハロゲン結合の切断過程の詳細・銅–リチウム会合構造のはたらきを明らかにした．

密度汎関数計算による反応経路の探索及び速度論的同位体効果の測定および理論予測の結果，本反応の鍵段階である炭素–ハロゲン結合の切断は，従来提唱されていた「３中心型」機構ではなく，銅・リチウムがそれぞれ求核中心・ルイス酸として協働的に関与する「脱離型」機構を経て進行することが分かった（図１）．この結果は sp^2 炭素–ハロゲン結合の遷移金属への酸化的付加の機構として新たな可能性を示唆する．

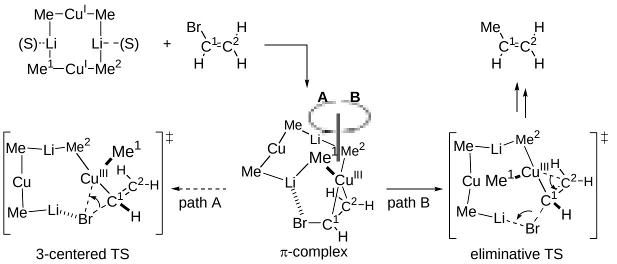


図１　リチウムクプラート$[Me_2CuLi]_2$と臭化ビニルの反応経路

1.(1)-16) *J. Am. Chem. Soc.* **126**, 12264-12265 (2004).

(3)カーボンナノチューブに金属ナノ粒子を閉じこめる「ボトルシップ合成法」

カーボンナノホーンやナノチューブの金属複合化は，燃料電池材料としての実用的応用が目前に迫っているだけでなく，導電材料としての可能性が期待されている．しかし，これまでにチューブ上の望みの位置に金属をつける方法がなく，思った通りの分子構造をもつ複合材料をつくることはできなかった．

我々は今回，一つの金属原子から数十個の原子からなる金属ナノ粒子をカーボンナノチューブの仲間であるカーボンナノホーンの中に集積することに成功した（図２）．

まず，カーボンナノホーンのチューブの壁に直径数オングストローム程度の小さな孔をあけ，この小さな穴に金属原子（Gd）を一つ一つ付着させ，電子顕微鏡によってその原子を観察すること，またその数を数えることに成功した．またナノチューブにあける孔のサイズを１ナノメートル以上にまで大きくすると，今度はその穴から３０個程度の金属原子を次々に導入して，「ボトルシップ（ship-in-bottle）」をつくるように内部に１－２ｎｍサイズの粒子（金属集合体）を合成できた．「ボトルシップ合成法」により，カーボンナノチューブの壁にあけた孔に選択的に金属イオンを集積させることが可能となり，炭素と金属を組み合わせた複合材料の実用化に向けて大きく前進した．

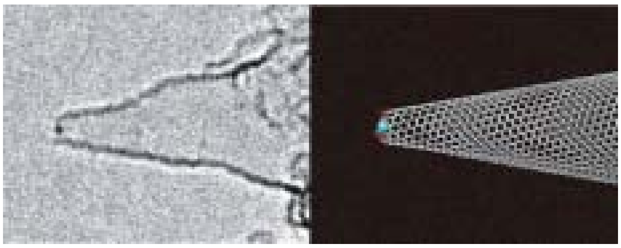


図２　ガドリニウム一原子を捕えたナノチューブ．電子顕微鏡写真（左）とその３次元分子モデル（右）

1.(1)-10) *Proc. Natl. Acad. Sci.* **101**, 8527-8530 (2004).

１．原著論文

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４. その他

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