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Novel Cp_2LnX-mediated coupling–cyclization of propargyl bromide: a new construction of the benzene ring skeleton

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In the presence of Cp_2LnX–$HgCl_2$, the treatment of $RC{\equiv}CCH_2Br$ with Mg leads to the formation of benzene derivatives $C_6H_4R_2$-*1,2* (R = H, Ph) in moderate yield, which provides a new method for the construction of the benzene ring skeleton.

During the past 20 years, tremendous progress has been made in the area of organolanthanide catalysis. It has been found that lanthanocene complexes are highly active and selective catalysts for many unsaturated C–C and C–N bond transformations such as isomerization, hydrogenation, hydroboration, hydrosilylation, hydroamination, hydrophosphination, oligomerization/polymerization and so on.[1–5] However, it is noteworthy that lanthanocene halides are much less used as catalysts than the corresponding alkyls, hydrides and aminates in these transformation reactions, despite being quite easy to prepare and store.[1–6] On the other hand, although the chemistry of propargyl/allenyl complexes has been extensively studied and proven to contribute immensely to organic synthesis, no example of selective synthesis of benzene derivatives by the metal-mediated intermolecular coupling–cyclization of propargyl halides has been reported up to now.[7–10] Additionally, relatively little is also known about organolanthanide propargyl complexes.[11–13] We report herein an unprecedented Cp_2LnCl-mediated coupling–cyclization of propargyl bromide, which provides a convenient way to construct the benzene ring skeleton.

Initially, the synthesis of lanthanide propargyl complexes was attempted by the treatment of Cp_2LnCl with the Grignard reagent $HC{\equiv}CCH_2MgBr$. Interestingly, when propargyl bromide was present in excess, the GC-MS data for hydrolyzed products of the reaction mixture indicated the formation of benzene (**1a**). Apparently, the reaction was promoted by Cp_2ErCl, since no benzene was obtained without Cp_2ErCl under otherwise identical reaction conditions.

This unprecedented bis(cyclopentadienyl)lanthanide chloride-mediated intermolecular coupling–cyclization of unsaturated halides provides a new method for the one-pot formation of benzene derivatives and prompted us to explore other protocols suitable for the catalytic formation of benzene.† The results are summarized in Table 1. As expected, the addition of a small amount of Cp_2LnCl to a mixture of $HC{\equiv}CCH_2Br$ and Mg (entry 2) resulted in the catalytic formation of benzene in 30% GC yield. Furthermore, after stopping the reaction, the catalyst Cp_2ErCl (**A**) may be isolated in an adduct form of $Cp_2Er(\mu\text{-}Cl)(\mu\text{-}Br)MgBr(THF)_3$ (**B**)‡ by directly concentrating and cooling the reaction mixture of entry 1.

Table 1 Cp_2ErCl-catalyzed coupling–cyclization of propargyl bromide

Entry	R	$Cp_2ErCl/Mg/RC{\equiv}CCH_2Br$	$C_6H_4R_2$-*1,2* (Yield, %)
1	H	1:1:2	60[a]
2	H	1:20:20	30[a]
3	Ph	1:1:2	40
4	Ph	1:10:20	23
5	Ph	1:20:20	15

[a] GC yields.

To expand the scope of this remarkable coupling–cyclization and reveal the effect of the substituents, we investigated the reaction of substituted propargyl bromide. In the presence of Cp_2ErCl, the reaction of $PhC{\equiv}CCH_2Br$ with Mg proceeded smoothly to give the corresponding coupling–cyclization product *o*-terphenyl (**1b**) in 15 ~ 40% isolated yield (entries 3–5).§ However, in contrast to the case of unsubstituted propargyl bromide, the generation of **1b** was always accompanied by the formation of a small amount of the coupling product $PhC{\equiv}CCH_2CH_2C{\equiv}CPh$ (**2**) under identical conditions. This may be attributed to the increasing steric repulsive interactions between the substrate phenyl substituent and the catalyst ancillary ligand, which is unfavorable to the occurrence of the cyclization reaction. Notably, if excess Mg is used (entry 5), the yield of **1b** decreases drastically from 30 to 15%. In addition, the yield of **1b** increases with increasing amounts of the catalyst (entries 3 and 5). All these results imply that the reaction of propargyl bromide with Mg is in competition with the coupling–cyclization reaction. Thus, for the organolanthanide-catalyzed coupling–cyclization of propargyl bromide, use of Mg with smaller surface area and more catalyst results in increased cyclization yields. These observations indicate that the coupling–cyclization is sensitive to the nature of the substrates and the stoichiometric ratio.

The diamagnetic Cp_2YCl-catalyzed reaction of $PhC{\equiv}CCH_2Br$ with Mg was closely monitored by ^1H NMR spectroscopy at room temperature and at constant catalyst concentration (Fig. 1).¶ The kinetic data clearly show that some new aryl resonances appear between δ 7.2 and 7.5 ppm and their strength increases with the time, while the resonance at δ 4.32 ppm that is assigned to the CH_2 protons of $PhC{\equiv}CCH_2Br$ fragment weaken gradually.

A plausible reaction pathway for the formation of **1** is given in Scheme 1. In the first step of the catalytic cycle, bis(cyclo-

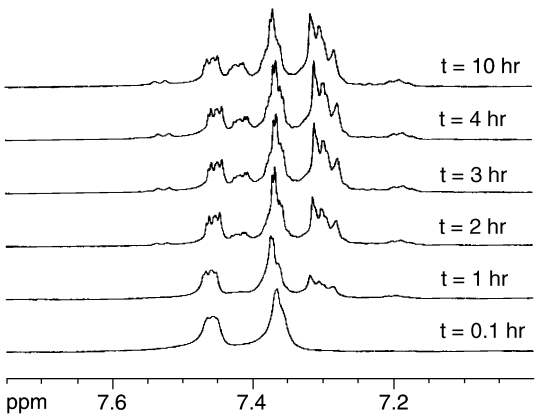

Fig. 1 ^1H NMR chemical shifts of aromatic protons for the progress of the coupling–cyclization using Cp_2YCl as catalyst in THF-d_8 at room temperature.

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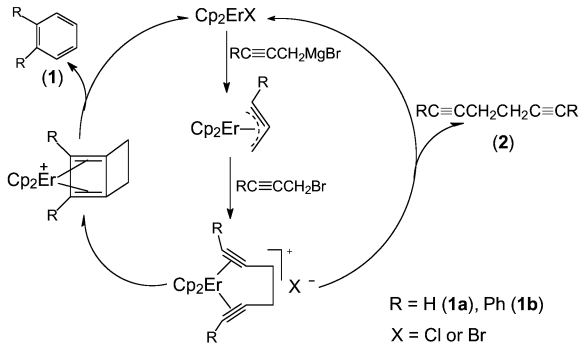

Scheme 1

pentadienyl)lanthanide chloride reacts with the Grignard reagent RC≡CCH_2MgBr to produce the active η^3-propargyl lanthanide intermediate, which can transform into the η^1-proparyglic isomer, and then couples with the remaining propargyl bromide to form the π-1,5-dihexyne lanthanide complex. The subsequent cyclization leads to the formation of **1** *via* [2+2] cycloaddition, followed by rearrangement.[14,15] In accord with this hypothesis, in the case of substituted propargyl bromide, when PhC≡CCH_2Br is combined with Mg in the presence of Cp_2LnCl, the only observable product was **1b**. Surprisingly, reaction of Cp_2ErCl and **2** gave **1b** in rather low yield. Further investigations into the mechanism of the formation of benzene derivatives and its scope and generality are currently in progress.

In conclusion, the benzene ring is an important building block for many organic compounds and of abundant occurrence in natural products. However, the methods for highly selective one-pot synthesis of the benzene ring skeleton are limited.[15] The Cp_2LnX-catalyzed reaction of propargyl bromide and Mg provides a new method for the construction of the benzene ring skeleton due to the ready availability of starting materials with different substitution patterns.

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Notes and references

† All manipulations of air- and moisture-sensitive compounds were performed under purified argon or nitrogen using Schlenk techniques. 60 mg (0.18 mmol) of Cp_2ErCl, 0.22 ml (2.0 mmol) of HC≡CCH_2Br, 25 ml of THF and a minimal amount of $HgCl_2$ (2 mg, 7.4 μmol) were loaded into a reaction vessel equipped with a magnetic stirbar. Next, Mg strip (24.3 mg, 1.0 mmol) was added to the stirring solution. After the Mg strip had disappeared, the reaction was stirred at rt for a further 2 days. The yield of **1a** (30%) was estimated by ^{1}H NMR and GC-MS after the product was isolated from the catalyst by vacuum transfer. ^{1}H NMR (500 MHz, $DCCl_3$): δ 7.36 (s). MS (relative abundance): M^+ (100), 51(21).

‡ Although the rough structure of $Cp_2Er(\mu\text{-}Cl)(\mu\text{-}Br)MgBr(THF)_3$ was confirmed by elemental analysis and X-ray crystallographic data, the refinement of accurate metric parameters was not possible due to severe disorder of chloride and bromide atoms.

§ A procedure analogous to that for **1a** was used in the synthesis of **1b**. After the reaction had completed, saturated aqueous $NaHCO_3$ was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with ether. The extraction was concentrated at reduced pressure and then chromatographed on silica gel using *n*-hexane, then a mixture of *n*-hexane and ethyl acetate in the ratio of 20:1 as the eluent. The eluate was concentrated by rotary evaporation to yield **1b** as a light yellow solid. ^{1}H NMR (500 MHz, $DCCl_3$): δ 7.25 ~ 7.46 (m). ^{13}C NMR (500 MHz, $DCCl_3$): δ 132.75, 130.68, 129.20, 128.37, 127.74, 127.46, 127.28. MS (relative abundance): M^+ (100), 215(58). 202 (20), 115 (23), 77 (3). IR (KBr): 3054, 1597, 1571, 1488, 1442, 1274, 1071, 1028, 918, 755, 692, 530, 510, 453.

¶ A magnesium strip (10 mg, 412 μmol) was weighed into an NMR tube. On the high-vacuum line, THF-d_8 (1.0 ml) was vacuum transferred into the tube. Then, Cp_2YCl (8 mg, 31 μmol) was added. PhCCCH_2Br (120 μl, 830 μmol) was syringed in when the catalyst solution had frozen. The tube was sealed and the frozen reaction mixture was warmed to rt. After the mixture was shaken, the progress of the reaction was monitored by ^{1}H NMR spectroscopy from intensity changes in the substrate and product resonances. The relative concentration of either functional group was measured from the corresponding peak area, standardized to the area of Cp_2YCl.

1 M. Ephritikhine, *Chem. Rev*., 1997, **97**, 2193; X. G. Zhou and M. Zhu, *J. Organomet. Chem*., 2002, **647**, 28.
2 T. Sakakura, H.-J. Lautenschlager and M. Tanaka, *J. Chem. Soc., Chem. Commun*., 1991, 40; P.-F. Fu, L. Brard, Y. Li and T. J. Marks, *J. Am. Chem. Soc*., 1995, **117**, 7157; G. A. Molander and P. J. Nichols, *J. Am. Chem. Soc*., 1995, **117**, 4415; G. A. Molander, E. D. Dowdy and H. Schumann, *J. Org. Chem*., 1998, **63**, 3386; G. A. Molander and W. H. Retsch, *J. Am. Chem. Soc*., 1997, **119**, 8817.
3 J. Soderquist, *Aldrichimica Acta*, 1991, **24**, 15; C. Bied, J. Collin and H. B. Kagan, *Tetrahedron*, 1992, **48**, 3877; M. Murakami and Y. Ito, *J. Organomet. Chem*., 1994, **473**, 93; H. B. Kagan, M. Sasaki and J. Collin, *Pure Appl. Chem*., 1988, **60**, 1725; A. Krief and A. M. Laval, *Chem. Rev*., 1999, **99**, 745.
4 M. R. Gagné and T. J. Marks, *J. Am. Chem. Soc*., 1989, **111**, 4108; Y. Li and T. J. Marks, *J. Am. Chem. Soc*., 1996, **118**, 9295; V. M. Arredondo, F. E. McDonald and T. J. Marks, *J. Am. Chem. Soc*., 1998, **120**, 4871; A. T. Gilbert, B. L. Davis, T. J. Emge and R. D. Broene, *Organometallics*, 1999, **18**, 2125; G. A. Molander and E. D. Dowdy, *J. Org. Chem*., 1999, **64**, 6515; M. R. Bürgstein, H. Berberich and P. W. Roesky, *Organometallics*, 1998, **17**, 1452; V. M. Arredondo, S. Tian, F. E. McDonald and T. J. Marks, *J. Am. Chem. Soc*., 1999, **121**, 3633; Y. Li and T. J. Marks, *J. Am. Chem. Soc*., 1998, **120**, 1757.
5 M. R. Douglass and T. J. Marks, *J. Am. Chem. Soc*., 2000, **122**, 1824; M. R. Douglass, C. L. Stern and T. J. Marks, *J. Am. Chem. Soc*., 2001, **123**, 10221.
6 D. L. Deng, C. T. Qian and J. H. Penn, *Chinese Chem. Lett*., 1994, **5**, 303; J. H. Penn, D. L. Deng and C. T. Qian, *Chinese Chem. Lett*., 1996, **7**, 845; C. T. Qian, A. N. Qiu, D. M. Zhu and X. W. Yang, *J. Mol. Catal*., 1994, **87**, 357.
7 M. E. Welker, *Chem. Rev*., 1992, **92**, 97; A. Wojcicki, *Coord. Chem. Rev*., 1990, **105**, 35; H. L. Stokes, L. M. Ni, J. A. Belot and M. E. Welker, *J. Organomet. Chem*., 1995, **487**, 95; J. T. Chen, *Coord. Chem. Rev*., 1999, **190–192**, 1143; H. Kurosawa and S. Ogoshi, *Bull. Chem. Soc. Jpn*., 1998, **71**, 973; S. Doherty, J. F. Corrigan, A. J. Carty and E. Sappa, *Adv. Organomet. Chem*., 1995, **37**, 39; J. Tsuji and T. Mandai, *Angew. Chem., Int. Ed. Engl*., 1995, **34**, 2589.
8 P. W. Blosser, J. C. Gallucci and A. Wojcicki *J. Organomet. Chem*., 2000, **597**, 125 and refs therein. S. Ogoshi, T. Nishida, K. Tsutsumi, M. Ooi, T. Shinagawa, T. Akasaka, M. Yamane and H. Kurosawa, *J. Am. Chem. Soc*., 2001, **123**, 3223.
9 R. J. Madhushaw, S. R. Cheruku, K. Narkunan, G. H. Lee, S. M. Peng and R. S. Liu, *Organometallics*, 1999, **18**, 748; O. Kuhn, D. Rau and H. Mayr, *J. Am. Chem. Soc*., 1998, **120**, 900.
10 S. Ogoshi and J. M. Stryker, *J. Am. Chem. Soc*., 1998, **120**, 3514; H. G. Shu, L. H. Shiu, S. H. Wang, S. L. Wang, G. H. Lee, S. M. Peng and R. S. Liu, *J. Am. Chem. Soc*., 1996, **118**, 530; A. Wojcicki and C. E. Shuchart, *Coord. Chem. Rev*., 1990, **105**, 35.
11 S. Hajela, W. P. Schaefer and J. E. Bercaw, *J. Organomet. Chem*., 1997, **532**, 45.
12 H. J. Heeres, A. Heeres and J. H. Teuben, *Organometallics*, 1990, **9**, 1508.
13 E. Ihara, M. Tanaka, H. Yasuda, N. Kanehisa, T. Maruo and Y. Kai, *J. Organomet. Chem*., 2000, **613**, 26.
14 M. Lautens, W. Klute and W. Tam, *Chem. Rev*., 1996, **96**, 49; N. E. Schore, *Chem. Rev*., 1988, **88**, 1081; K. P. C. Vollhardt, *Angew. Chem., Int. Ed. Engl*., 1984, **23**, 539.
15 T. Takahashi, F. Y. Tsai, Y. Z. Li, K. Nakajima and M. Kotora, *J. Am. Chem. Soc*., 1999, **121**, 11093.