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Highly regioselective ring-opening coupling of diarylmethylenecyclopropa[*b*]naphthalenes with Grignard reagents†

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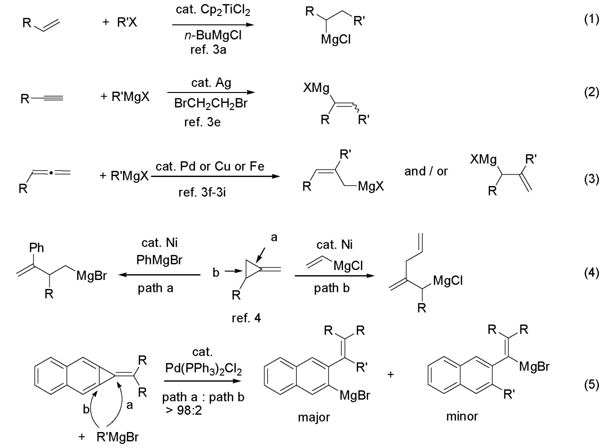
Highly regioselective ring-opening coupling reactions of diarylmethylenecyclopropa[*b*]naphthalenes with Grignard reagents have been developed, which provide differently substituted β-vinylic naphthalenes in moderate to excellent yields.

The addition of organomagnesium compounds across carbon–carbon unsaturated bonds (carbomagnesation) is one of the principal and important methods employed for the generation of Grignard reagents with concomitant C–C bond formation, providing a straightforward entry into Grignard reagents having a unique carbon skeleton.[1,2] Recently, highly regioselective carbomagnesation of carbon–carbon unsaturated systems including alkenes, 1,3-butadienes, alkynes, enynes and allenes by employing transition metal complexes as catalysts has also been achieved, providing a variety of advanced organomagnesium reagents which are ready to be converted to useful compounds by reaction with various electrophiles (Scheme 1, eqn (1)–(3)).[3] In these studies, what should be particularly noted is that Terao and Kambe reported interesting nickel-catalyzed regioselective carbomagnesation of methylenecyclopropanes, wherein the selective cleavage of the proximal or the distal carbon–carbon bond of the MCPs has been achieved with different Grignard reagents (Scheme 1, eqn (4)).[4]

During our recent systematic study on methylenecyclopropane (MCP) chemistry,[5] we became interested in the chemistry of the analogous diarylmethylenecyclopropa[*b*]naphthalenes, which are a class of highly reactive but thermally stable and readily accessible unsaturated hydrocarbons. Because of their unusual structure, which contains a triafulvene, a [3]radialene, and a cycloproparene, they have attracted much attention from physical, theoretical, and synthetic viewpoints.[6,7] In this regard, we have reported a manganese(III) acetate-mediated cyclization of diarylmethylenecyclopropa[*b*]naphthalenes with nucleophiles for the synthesis of 1,2-benzanthracenes and a highly regioselective Pd(0)-catalyzed [3+2] cycloaddition reaction of diarylmethylenecyclopropa[*b*]naphthalenes with alkenes, alkynes or arynes to produce 1(3)-alkylidene-2,3-dihydro-1*H*-cyclopenta[*b*]naphthalene, 1-alkylidene-1*H*-cyclo-penta[*b*]naphthalene and 11-diarylmethylene-11*H*-benzo[*b*]fluorine derivatives.[8] In the continuous exploration of the synthetic utility of these interesting compounds, we are interested in the reaction of diarylmethylenecyclopropa[*b*]naphthalenes with Grignard reagents in the presence of palladium catalysts. Herein, we wish to report such a reaction involving a naphthylmagnesium species through the selective cleavage of the carbon–carbon bond of the three-membered ring controlled by palladium (pre)catalysts (Scheme 1, eqn (5)).



Scheme 1 Previous studies on highly regioselective carbomagnesation of carbon–carbon unsaturated systems and our observation.

In a preliminary experiment, we observed that treatment of 1-(diphenylmethylene)-1*H*-cyclopropa[*b*]naphthalene (**1a**) with *p*-tolylmagnesium bromide (**2a**, 1 M in THF, 1.5 equiv.) in the presence of $Pd(PPh_3)_4$ (5 mol%) in THF at 25 °C for 5 minutes followed by an aqueous workup gave 2-(2,2-diphenyl-1-(*p*-tolyl)vinyl)naphthalene (**3a**)

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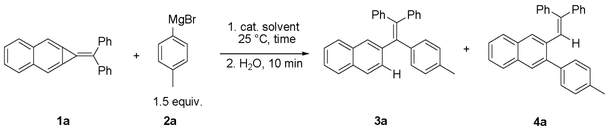
‡ Prof. Huang passed away on March 6, 2010. He had been fully in charge of this project. At this moment, Prof. Luling Wu is helping him to finish all the projects with the help of Prof. Shengming Ma.

Table 1 Optimization of reaction conditions for the Pd-catalyzed ring-opening coupling of **1a** with **2a**[a]



Entry	Catalyst (5 mol%)	Solvent	Time (min)	Yield^b/% (**3a** : **4a**)
1^c	No	THF	5	No reaction
2	$Pd(PPh_3)_4$	THF	5	87 (95 : 5)
3	$Pd(PPh_3)_2Cl_2$	THF	5	91 (98 : 2)
4	$Pd(PPh_3)_2Cl_2$	PhMe	5	93 (99 : 1)
5	$Pd(PPh_3)_2Cl_2$	Dioxane	5	92 (97 : 3)

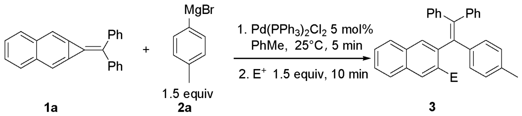
[a] The reaction was conducted with 0.2 mmol of **1a**, 0.01 mmol of the catalyst, 2 mL of solvent, 1.5 equiv. of *p*-tolylmagnesium bromide (1.0 M solution in THF) and 0.1 mL of H_2O. [b] Yields and radios of **3a** and **4a** determined using ^1H NMR using dibromomethane as the internal standard. [c] No reaction occurred in 24 hours.

and 2-(2,2-diphenylvinyl)-3-(*p*-tolyl)naphthalene (**4a**) in 87% with a ratio of 95 : 5 (entry 2, Table 1). When we used $Pd(PPh_3)_2Cl_2$, **3a** was obtained in 91% yield with a better regioselectivity (98 : 2) (entry 3, Table 1). Among the solvents examined, toluene was found to be better than THF, producing **3a** in 93% with an excellent regioselectivity (99 : 1) within 5 minutes (entry 4, Table 1).

We then examined various electrophilic reagents to quench the resulting mixture under the optimized reaction conditions. When D_2O was used, **3a′** was obtained in 83% (98% D) yield. When I_2, NBS, allyl bromide and acetyl chloride were employed, all the reactions proceeded efficiently to give the corresponding products **3b–3e** in moderate to high yields with an excellent regioselectivity (entries 3–6, Table 2). The regioselectivity of the resulting compounds was confirmed using X-ray single crystal diffraction analysis of **3b** and **4b**[9] (Fig. S1, ESI†).

Considering the wide range of applications of aryl iodides, I_2 was used as an electrophile to quench the reaction when we next examined the scope of this reaction with various substrates. In addition to **1a**, diarylmethylenecyclopropa[*b*]naphthalenes **1b–1g**, which bear substituted phenyl rings as the Ar group in **1**, all smoothly generated the corresponding products in high yields with good regioselectivities (entries 1–6, Table 3). However, the reaction of **1h** bearing nitro substituted phenyl rings only gave an unidentified mixture (entry 7, Table 3).

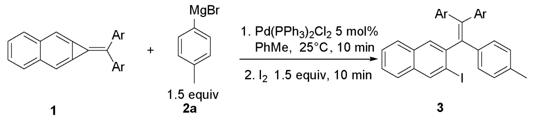
Table 2 Pd-catalyzed ring-opening coupling of **1a** with **2a**, quenching with various electrophilic reagents[a]



Entry	E$^+$	E	Yield of 3^b/%	3/4^c
1	H_2O^d	H	82 (**3a**)	93/1
2	D_2O^e	D	83, 98% D (**3a′**)	95/1
3	I_2	I	87 (**3b**)	94/1
4	NBS	Br	82 (**3c**)	90/1
5	Allyl bromide	Allyl	80 (**3d**)	95/1
6	Acetyl chloride	Ac	87 (**3e**)	95/1

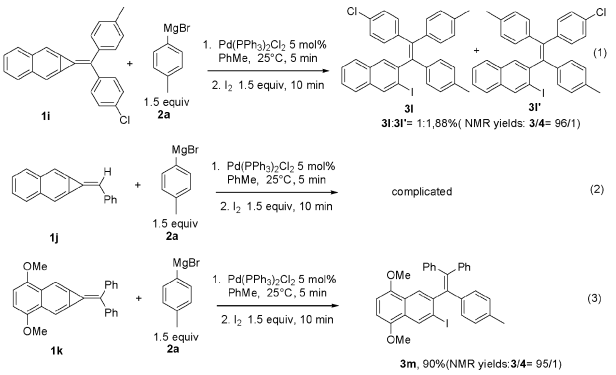
[a] The reaction was conducted with 0.2 mmol of **1a**, 0.01 mmol of the catalyst, 2 mL of solvent, 1.5 equiv. of *p*-tolylmagnesium bromide (1.0 M solution in THF) and 1.5 equiv. of electrophilic reagent. [b] Isolated yield. [c] NMR yields of **3** and **4** determined using NMR using dibromomethane as the internal standard. [d] 0.1 mL of H_2O was used. [e] 0.1 mL of D_2O was used.

Table 3 Pd-catalyzed ring-opening coupling of diarylmethylenecyclopropa[*b*]naphthalenes **1** with **2a** quenching with I_2[a]



Entry	Ar	Yield of 3^b/%	3/4^c
1	$4-MeOC_6H_4$ (**1b**)	78 (**3f**)	86/1
2	$4-MeC_6H_4$ (**1c**)	86 (**3g**)	98/1
3	$3-MeC_6H_4$ (**1d**)	86 (**3h**)	95/1
4	$3,5-(MeO)_2C_6H_3$ (**1e**)	87 (**3i**)	95/1
5	$4-ClC_6H_4$ (**1f**)	85 (**3j**)^d	96/1
6	$4-FC_6H_4$ (**1g**)	86 (**3k**)^d	94/1
7	$4-NO_2C_6H_4$ (**1h**)	Complicated	

[a] The reaction was conducted with 0.2 mmol of **1**, 0.01 mmol of the catalyst, 2 mL of solvent, 1.5 equiv. of *p*-tolylmagnesium bromide (1.0 M solution in THF) and 1.5 equiv. of I_2. [b] Isolated yield. [c] NMR yields of **3** and **4** determined using ^1H NMR using dibromomethane as the internal standard. [d] The reaction time was 5 min.



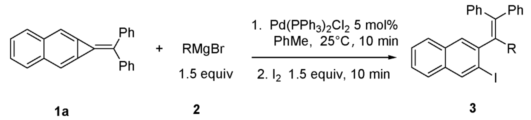
Scheme 2 Reaction of **1i**, **1j** and **1k** with **2a**.

The reaction of **1i** with **2a** gave the desired compounds **3l** and **3l′** as a 1 : 1 mixture of inseparable isomers in 88% overall yield (Scheme 2, eqn (1)). However, the reaction became complicated when **1h** was employed (Scheme 2, eqn (2)). In order to replace the simple naphthalene with other aryl groups, substrate **1k** with two methoxy groups on the naphthalene ring was employed to react with **2a**, the reaction proceeded smoothly to give **3m** in 90% yield.

We further examined the reaction of **1a** using a variety of Grignard reagents. It showed that all aryl magnesium bromides efficiently underwent carbomagnesation to produce the corresponding products in good yields with high regioselectivity (Table 4).

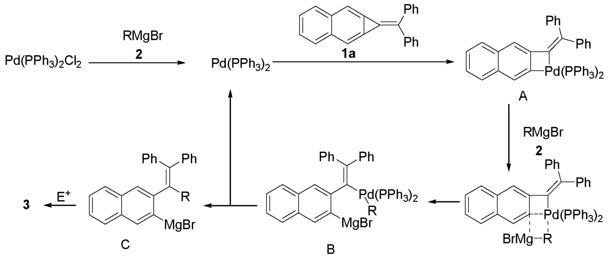
Although the detailed mechanism of the present ring-opening coupling reaction has not yet been clarified, we would like to propose the reaction pathways shown in Scheme 3. First, the reduction of $Pd(PPh_3)_2Cl_2$ with two equivalents of Grignard reagents affords $Pd^0(PPh_3)_2$. Subsequently, oxidative addition of $Pd^0(PPh_3)_2$ with the cyclopropane C–C bond of diarylmethylenecyclopropa[*b*]naphthalene generates metallacyclobutane **A**.[7] This metallacyclobutane **A** leads to the nucleophilic attack of Grignard reagents at the less sterically hindered side to yield dimetallic intermediate **B** with a high regioselectivity.

Table 4 Pd-catalyzed ring-opening coupling of **1a** with various Grignard reagents **2** quenching with I_2[a]



Entry	R	Yield of **3**[b]/%	**3**[c]/**4**
1	C_6H_5 (**2b**)	83 (**3n**)	94/1
2	4-$MeOC_6H_4$ (**2c**)	85 (**3o**)	98/2
3	4-ClC_6H_4 (**2d**)	90 (**3p**)	96/1
4	4-FC_6H_4 (**2e**)	86 (**3q**)[d]	97/2
5	2-naphthyl (**2f**)	89 (**3r**)[d]	97/1

[a] The reaction was conducted with 0.2 mmol of **1a**, 0.01 mmol of the catalyst, 2 mL of solvent, 1.5 equiv. of aryl magnesium bromide (1.0 M solution in THF) and 1.5 equiv. of I_2. [b] Isolated yield. [c] NMR yields of **3** and **4** determined using ^1H NMR using dibromomethane as the internal standard. [d] The reaction time was 5 min.



Scheme 3 Proposed mechanism.

Finally, the products **3** were formed *via* the reductive elimination and quenching with electrophilic reagents.

In conclusion, we have developed highly regioselective ring-opening coupling reactions of diarylmethylenecyclopropa[*b*]naphthalenes with Grignard reagents to produce differently substituted β-vinylic naphthalenes in moderate to excellent yields under mild conditions. Further studies on the scope, mechanism, and synthetic applications of this transformation are being carried out in our laboratory.

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Notes and references

1 P. Knochel, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and F. Ian, Pergamon, NewYork, 1991, vol. 4, pp. 865–911; S. V. Ley and C. Kouklovsky, in *Comprehensive Organic Functional Group Transformations*, ed. A. R. Katritzky, O. Meth-Cohn and C. W. Rees, Pergamon, New York, 1995, vol. 2, pp. 549–603; E. Negishi and D. Choueiry, in *Comprehensive Organic Functional Group Transformations*, ed. A. R. Katritzky, O. Meth-Cohn and C. W. Rees, Pergamon, New York, 1995, vol. 2, pp. 951–995; B. J. Wakefield, in *Organomagnesium Methods in Organic Synthesis*, Academic Press INC, San Diego, 1995, pp. 73–86; A. H. Hoveyda and M. T. Didiuk, *Curr. Org. Chem.*, 1998, **2**, 489.

2 Nickel-catalyzed carbomagnesation: J. G. Duboudin and B. Jousseaume, *J. Organomet. Chem.*, 1972, **44**, C1; B. B. Snider, M. Karras and R. S. E. Conn, *J. Am. Chem. Soc.*, 1978, **100**, 4624; B. B. Snider, R. S. E. Conn and M. Karras, *Tetrahedron Lett.*, 1979, **20**, 1679; copper-catalyzed carbomagnesation: J. G. Duboudin, B. Jousseaume and A. Bonakdar, *J. Organomet. Chem.*, 1979, **168**, 227; titanium-catalyzed carbomagnesation: S. Akutagawa and S. Otsuka, *J. Am. Chem. Soc.*, 1975, **97**, 6870; zirconium-catalyzed carbomagnesation: U. M. Dzhemilev, O. S. Vostrikova and R. M. Sultanov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1983, 218; A. H. Hoveyda and Z. Xu, *J. Am. Chem. Soc.*, 1991, **113**, 5079; T. Takahashi, T. Seki, Y. Nitto, M. Saburai, C. M. Rouusset and E. Negishi, *J. Am. Chem. Soc.*, 1991, **113**, 6266; D. P. Lewis, P. M. Muller and R. J. Whitby, *Tetrahedron Lett.*, 1991, **32**, 6797; R. Fischer, D. Walther, P. Gebhardt and H. Gorls, *Organometallics*, 2000, **19**, 2532; manganesecatalyzed carbomagnesation: K. Okada, K. Oshima and K. Utimoto, *J. Am. Chem. Soc.*, 1996, **118**, 6076; J. Tang, K. Okada, H. Shinokubo and K. Oshima, *Tetrahedron*, 1997, **53**, 5061; iron-catalyzed carbomagnesation: M. Nakamura, A. Hirai and E. Nakamura, *J. Am. Chem. Soc.*, 2000, **122**, 978.

3 S. Nii, J. Terao and N. Kambe, *J. Org. Chem.*, 2004, **69**, 573; J. Terao, H. Watabe and N. Kambe, *J. Am. Chem. Soc.*, 2005, **127**, 3656; H. Todo, J. Terao, H. Watanabe, H. Kuniyasu and N. Kambe, *Chem. Commun.*, 2008, 1332; Y. Fujii, J. Terao, Y. Kato and N. Kambe, *Chem. Commun.*, 2008, 5836; N. Kambe, Y. Moriwaki, Y. Fujii, T. Iwasaki and J. Terao, *Org. Lett.*, 2011, **13**, 4656; Y. Fujii, J. Terao, Y. Kato and N. Kambe, *Chem. Commun.*, 2009, 1115; Y. Fujii, J. Terao, H. Kuniyasu and N. Kambe, *J. Organomet. Chem.*, 2007, **692**, 375; Z. Lu, G. Chai and S. Ma, *J. Am. Chem. Soc.*, 2007, **129**, 14546; G. Chai, Z. Lu, C. Fu and S. Ma, *Adv. Synth. Catal.*, 2009, **351**, 1946; Z. Lu and S. Ma, *Adv. Synth. Catal.*, 2007, **349**, 1225.

4 J. Terao, M. Tomita, S. P. Singh and N. Kambe, *Angew. Chem.*, 2010, **122**, 148.

5 Y. Yang and X. Huang, *J. Org. Chem.*, 2008, **73**, 4702; W. Chen, C. Su and X. Huang, *Synlett*, 2006, 1446; X. Huang, H. Zhou and W. Chen, *J. Org. Chem.*, 2004, **69**, 839; H. Zhou, X. Huang and W. Chen, *J. Org. Chem.*, 2004, **69**, 5471; W. Chen, X. Huang, H. Zhou and L. Ren, *Synthesis*, 2006, 609.

6 B. Halton, *Chem. Rev.*, 2003, **103**, 1327; B. Halton, *Chem. Rev.*, 1989, **89**, 1161; W. E. Billups, W. A. Rodin and M. M. Haley, *Tetrahedron*, 1988, **44**, 1305; B. Halton, C. J. Randall, G. J. Gainsford and P. J. Stang, *J. Am. Chem. Soc.*, 1986, **108**, 5949; B. Halton, S. J. Buckland, Q. Lu, Q. Mei and P. J. Stang, *J. Org. Chem.*, 1988, **53**, 2418; B. Halton, Q. Lu and P. J. Stang, *Aust. J. Chem.*, 1990, **43**, 1277; B. Halton, A. J. Kay, Z. Zhi-mei, R. Boese and T. Haumann, *J. Chem. Soc., Perkin Trans. 1*, 1996, 1445.

7 For the fomation of A-type cyclic intermediates, see: P. J. Stang, L. Song, Q. Lu and B. Halton, *Organometallics*, 1990, **9**, 2149.

8 W. Chen, J. Cao and X. Huang, *Org. Lett.*, 2008, **10**, 5537; Y. Lin, L. Wu and X. Huang, *Eur. J. Org. Chem.*, 2011, 2993; J. Cao, M. Miao, W. Chen, L. Wu and X. Huang, *J. Org. Chem.*, 2011, **76**, 9329.

9 Crystal data for **3b**: $C_{31}H_{23}I$; $M_W = 522.39$; crystal system: triclinic; space group: $P\bar{1}$; final R indices $[I > 2\sigma(I)]$ $R_1 = 0.0359$, $wR_2 = 0.0751$, R indices (all data) $R_1 = 0.0525$, $wR_2 = 0.0821$; $a = 7.2201(4)$ Å, $b = 10.1334(6)$ Å, $c = 17.8528(9)$ Å; $\alpha = 97.658(4)^\circ$, $\beta = 96.136(4)^\circ$, $\gamma = 106.567(5)^\circ$, $V = 1226.28(12)$ Å^3, $T = 293(2)$ K, $Z = 2$; $F(000)$ 524; reflections collected/unique: 9655/4483 $[R_{int} = 0.0279]$; number of observations $[I > 2\sigma(I)]$: 3541; parameters: 290. CCDC 903814. Crystal data for **4b**: $C_{31}H_{23}I$; $M_W = 522.39$; crystal system: triclinic; space group: $P\bar{1}$; final R indices $[I > 2\sigma(I)]$ $R_1 = 0.0318$, $wR_2 = 0.0641$, R indices (all data) $R_1 = 0.0439$, $wR_2 = 0.0707$; $a = 10.1953(6)$ Å, $b = 10.2701(7)$ Å, $c = 13.6377(7)$ Å; $\alpha = 68.376(6)^\circ$, $\beta = 75.947(5)^\circ$, $\gamma = 66.850(6)^\circ$, $V = 1212.54(13)$ Å^3, $T = 293(2)$ K, $Z = 2$; $F(000)$ 524; reflections collected/unique: 8715/4441 $[R_{int} = 0.0284]$; number of observations $[I > 2\sigma(I)]$: 3691; parameters: 290. CCDC 903813.