

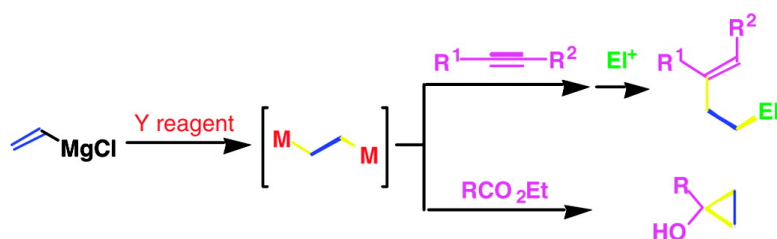
Communication

## Yttrium-Mediated Conversion of Vinyl Grignard Reagent to a 1,2-Dimetalated Ethane and Its Synthetic Application

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## Yttrium-Mediated Conversion of Vinyl Grignard Reagent to a 1,2-Dimetalated Ethane and Its Synthetic Application

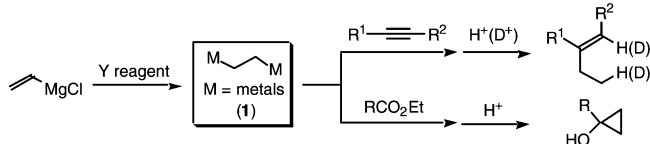
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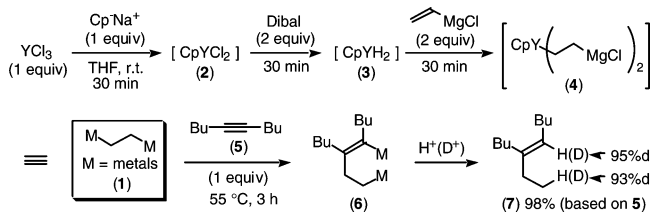
Among the lanthanide reagents used to mediate organic reactions,<sup>1</sup> yttrium reagents are used for hydroxytritation,<sup>2</sup> hydrosilylation,<sup>3</sup> and hydroamination<sup>4</sup> of alkenes and alkynes and show a preference for interaction with carbon–carbon multiple bonds. Here we report that an yttrium reagent can react even with a metalated alkene such as a vinyl Grignard reagent, leading to a new method of generating 1,2-dimetalated ethane **1** (Scheme 1). As there are still limitations in the practical generation of 1,2-dimetalated ethane,<sup>5–7</sup> a fundamental dicarbanionic species and a versatile conjunctive reagent,<sup>6,7</sup> we also demonstrate some synthetic applications of **1** according to Scheme 1.

### Scheme 1. Yttrium-Mediated Generation of **1** and Its Application



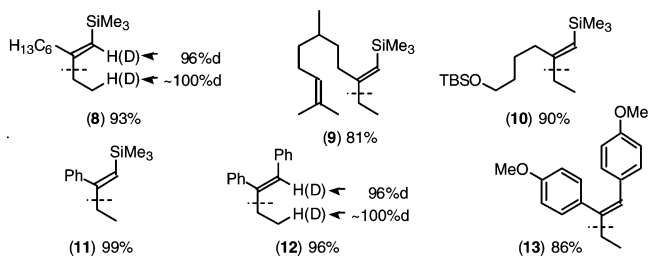
Yttrium(III) chloride was first treated with sodium cyclopentadienide to produce yttrium dichloride **2**,<sup>8</sup> to which diisobutylaluminum hydride (Dibal), vinylmagnesium chloride, and 5-decyne (**5**) were added in this order (Scheme 2). The reaction most likely proceeded via (i) generation of yttrium hydride **3** from **2** and (ii) hydroxytritation of the vinyl Grignard reagent to give **4** (i.e., **1** via metal exchange). Finally, the carbometalation of the acetylene **5** with **1** afforded ethylated alkene **7** in 98% yield with virtually complete stereoselectivity after hydrolytic workup.<sup>9</sup> Other lanthanide trichlorides such as Sm, Sc, Ce, and La in place of Y did not promote this reaction (yield of **7**: 29%, 15%, trace, and trace, respectively). Deuteriolysis of the above reaction mixture produced dideuterated product **7-d<sub>2</sub>**, confirming the presence of a bismetalated intermediate **6**. Additional products obtained by this reaction are summarized in Chart 1 (dotted line refers to ethylated position), which shows that the carbometalation proceeded in a regio- and stereoselective manner, always producing single trisubstituted olefins **8–13**.<sup>10</sup>

### Scheme 2. Yttrium-Mediated ( $\beta$ -Metaloethyl)metalation of Acetylenes

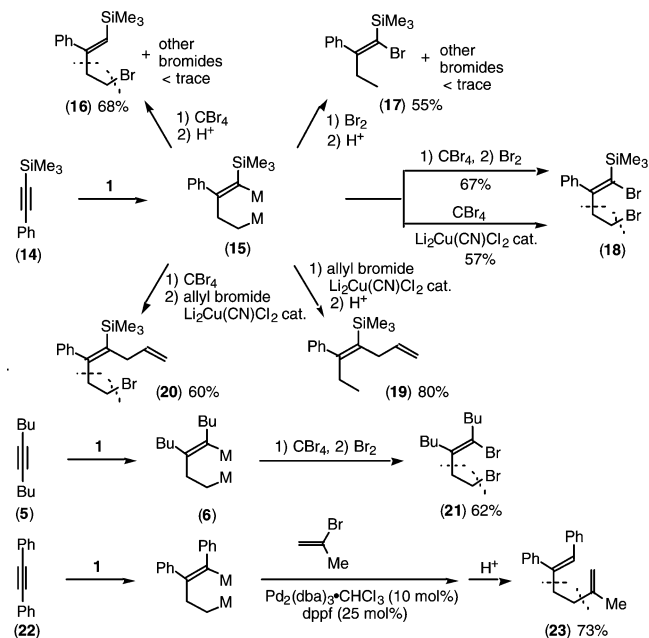


Scheme 3 illustrates the utility of **1** as a conjunctive reagent (dotted lines indicate the ethylene basement and two other frag-

### Chart 1. Products Obtained from Acetylenes According to Scheme 2



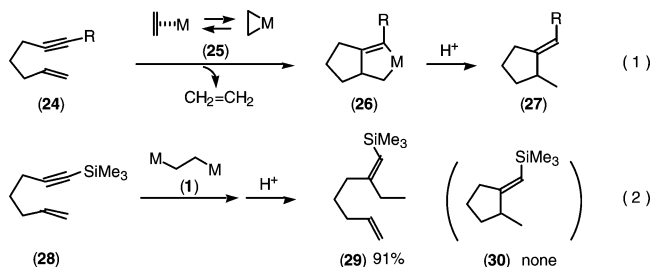
### Scheme 3. Utility of **1** as Conjunctive Reagent



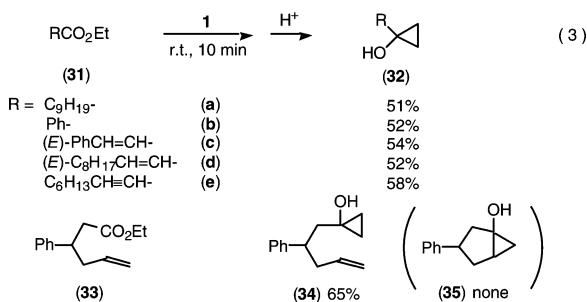
ments). While bromination of **15** (generated from acetylene **14**) with  $\text{CBr}_4$  or  $\text{Br}_2$  selectively afforded monobromide **16** or **17**,<sup>11</sup> respectively, combination of these brominating agents or solely  $\text{CBr}_4$  in the presence of a copper catalyst afforded dibromide **18**. Copper-catalyzed allylation of **15** cleanly produced **19**, and the successive applications of the above bromination and this allylation achieved a four-component coupling process to produce **20**. Two more examples are shown in Scheme 3, which include dibromination of a palladium-catalyzed selective monoalkenylation of the intermediates generated from each acetylene **5** or **22** to give **21** or **23**, respectively.

Although ethylene complexes of group 4 metals, such as **25** ( $\text{M} = \text{Ti}$  or  $\text{Zr}$  with appropriate ligands),<sup>7</sup> are known to constitute a practical and synthetically useful 1,2-dimetalated ethane, these

species usually work as metal transfer reagents toward 1,6-enynes **24** to allow intramolecular cyclization, producing **27** via metalacycle **26**,<sup>7,12,13</sup> instead of ( $\beta$ -metaloethyl)metalation (eq 1). In contrast, with the newly developed reagent **1**, 1,6-enyne **28** underwent clean ( $\beta$ -metaloethyl)metalation to give **29** unaccompanied by the cyclized product **30** (eq 2).



To confirm the nucleophilic nature of this reagent, we investigated its reaction with an electrophile. Actually the reagent **1** underwent double addition to ethyl decanoate to produce 1-nonyl-1-cyclopropanol in one pot, albeit in a low product yield around 20%. After some tuning of its reagent composition,<sup>10</sup> yttrium-based reagent **1** gained improved product yields as shown in eq 3. Even the  $\alpha,\beta$ -olefinic and -acetylenic esters **31c–e** afforded cyclopropanols **32c–e** uniformly in satisfactory yields, which is not attainable with the aforementioned 1,2-dimetalated ethane **25**.<sup>14</sup> Similarly, the reagent **1** and 5-alkenoate **33** cleanly afforded **34**, without contamination with **35** that is usually observed in the reaction with **25**.<sup>14</sup>



In summary, a 1,2-dimetalated ethane was conveniently generated by an yttrium-based multimetallic reagent system. It has new characteristics that are complementary to those of the existing 1,2-dimetalated ethanes already used in organic synthesis. Further synthetic applications are now under investigation.

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**Supporting Information Available:** Experimental procedures and physical properties of products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References

- (1) For reviews, see: (a) Molander, G. A.; Romero, J. A. *C. Chem. Rev.* **2002**, *102*, 2161–2185 and references cited therein. (b) Molander, G. A.; Dowdy, E. D. In *Lanthanides: Chemistry and Use in Organic Synthesis*;

- (c) Kobayashi, S., Ed.; Springer: Berlin, 1999; pp 119–154. (c) Ephritikhine, M. *Chem. Rev.* **1997**, *97*, 2193–2242. (d) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29–68.
- (2) (a) Evans, W. J.; Meadows, J. H.; Hunter, W. E.; Atwood, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 1291–1300. (b) Molander, G. A.; Hoberg, J. O. *J. Org. Chem.* **1992**, *57*, 3266–3268. See also: (c) Zhang, L.; Luo, Y.; Hou, Z. *J. Am. Chem. Soc.* **2005**, *127*, 14562–14563.
- (3) (a) Molander, G. A.; Retsch, W. H. *J. Am. Chem. Soc.* **1997**, *119*, 8817–8825. (b) Molander, G. A.; Dowdy, E. D. *J. Org. Chem.* **1998**, *63*, 3386–3396. (c) Muci, A. R.; Bercaw, J. E. *Tetrahedron Lett.* **2000**, *41*, 7609–7612.
- (4) (a) Hong, S.; Marks, T. J. *Acc. Chem. Res.* **2004**, *37*, 673–686. (b) Kim, J. Y.; Livinghouse, T. *Org. Lett.* **2005**, *7*, 1737–1739. (c) Gribkov, D. V.; Hultzs, K. C.; Hampel, F. *J. Am. Chem. Soc.* **2006**, *128*, 3748–3759. (d) Kim, H.; Livinghouse, T.; Shim, J. H.; Lee, S. G.; Lee, P. H. *Adv. Synth. Catal.* **2006**, *348*, 701–704.
- (5) For 1,2-dimetalated ethanes that attract interest in organometallic and theoretical chemistry, see: (Li): (a) So, S. P. *J. Organomet. Chem.* **1989**, *361*, 283–288. (b) van Eikema Hommes, N. J. R.; Bickelhaupt, F.; Klumpp, G. W. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1083–1084. (c) Schleyer, P.; von R.; Kos, A. J.; Kaufmann, E. *J. Am. Chem. Soc.* **1983**, *105*, 7617–7623. (d) Kos, A. J.; Jemmis, E. D.; Schleyer, P. von R.; Gleiter, R.; Fischbach, U.; Pople, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 4996–5002. (Li, Na, K): (e) Alikhani, M. E.; Hannachi, Y.; Manceron, L.; Bouteiller, Y. *J. Chem. Phys.* **1995**, *103*, 10128–10136. (Al): (f) So, S. P. *J. Organomet. Chem.* **1991**, *420*, 293–301. (g) Olah, G. A.; Farooq, O.; Farnia, S. M. F.; Bruce, M. R.; Clouet, F. L.; Morton, P. R.; Prakash, G. K. S.; Stevens, R. C.; Bau, R.; Lammertsma, K.; Suzer, S.; Andrews, L. *J. Am. Chem. Soc.* **1988**, *110*, 3231–3238. (Cu): (h) Böhme, M.; Wagener, T.; Frenking, G. *J. Organomet. Chem.* **1996**, *520*, 31–43. (Mg): (i) van Eikema Hommes, N. J. R.; Bickelhaupt, F.; Klumpp, G. W. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 393–394. (Zr): (j) Siedle, A. R.; Newmark, R. A.; Schroepfer, J. N.; Lyon, P. A. *Organometallics* **1991**, *10*, 400–404. (Si, Sn, Ge): (k) Matsubara, H.; Schiesser, C. H. *J. Org. Chem.* **2003**, *68*, 9299–9309. (l) Barrau, J.; Hamida, N. B.; Agrebi, A.; Satge, J. *Organometallics* **1989**, *8*, 1585–1593. (m) Henry, M. C.; Noltes, J. G. *J. Am. Chem. Soc.* **1960**, *82*, 558–561. (Ir): (n) Hettterscheid, D. G. H.; Kaiser, J.; Reijerse, E.; Peters, T. P. J.; Thewissen, S.; Blok, A. N. J.; Smits, J. M. M.; de Gelder, R.; de Bruin, B. *J. Am. Chem. Soc.* **2005**, *127*, 1895–1905.
- (6) For a synthetically useful 1,2-dimetalated ethane consisting of Mg and Si, see: (a) Klos, A. M.; Heintzelman, G. R.; Weinreb, S. M. *J. Org. Chem.* **1997**, *62*, 3758–3761. (b) Wilson, S. R.; Shedrinsky, A. *J. Org. Chem.* **1982**, *47*, 1983–1984.
- (7) For reviews on group 4 metal–ethylene complexes that could work as synthetically useful 1,2-dimetalated ethanes, see: (a) Merck, I., Ed. *Titanium and Zirconium in Organic Synthesis*; Wiley-VCH: Weinheim 2002. (b) Sato, F.; Urabe, H.; Okamoto, S. *Chem. Rev.* **2000**, *100*, 2835–2886. (c) Kulinkovich, O. G.; de Meijere, A. *Chem. Rev.* **2000**, *100*, 2789–2834. (d) Negishi, E. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, pp 1163–1184. For a representative example as a conjunctive reagent, see: (e) Lipshutz, B. H.; Segi, M. *Tetrahedron* **1995**, *51*, 4407–4420.
- (8) (a) den Haan, K. H.; Teuben, J. H. *J. Organomet. Chem.* **1987**, *322*, 321–329. (b) Evans, W. J.; Meadows, J. H. In *Organometallic Syntheses*; King, R. B., Eisch, J. J., Eds.; Academic Press: New York, 1986; Vol. 3, pp 1–8.
- (9) The reagent **1** that had been stored under argon for one day at room temperature did not give the product **7** upon reaction with **5**. Attempted generation of 1,2-dimetalated propane from (*E*)- or (*Z*)-1-propenylmagnesium bromide and its addition to **5** are so far unsuccessful.
- (10) For experimental details, see the Supporting Information.
- (11) Bromide **17** is a known key intermediate for the synthesis of an anticancer medicine, tamoxifen. Miller, R. B. A.; Hassan, M. I. *J. Org. Chem.* **1985**, *50*, 2121–2123.
- (12) (a) Fillery, S. F.; Gordon, G. J.; Lucker, T.; Whitby, R. *J. Pure Appl. Chem.* **1997**, *69*, 633–638. (b) Grossman, R. B.; Buchwald, S. L. *J. Org. Chem.* **1992**, *57*, 5803–5805.
- (13) For a recent review on enyne cyclization, see: Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813–834.
- (14) Upon reaction with **25** (M = Ti(OR)<sub>2</sub>),  $\alpha,\beta$ -unsaturated esters afforded the corresponding 1-alkenyl (or alkynyl)-1-cyclopropanols only in 11–26% yields: (a) Kulinkovich, O. G.; de Meijere, A. *Chem. Rev.* **2000**, *100*, 2797–2799. (b) de Meijere, A.; Kozhushkov, S. I.; Savchenko, A. I. In *Titanium and Zirconium in Organic Synthesis*; Merck, I., Ed.; Wiley-VCH: Weinheim, 2002; pp 394–395. (c) de Meijere, A.; Kozhushkov, S. I.; Savchenko, A. I. *J. Organomet. Chem.* **2004**, *689*, 2033–2055. (d) Racouchot, S.; Sylvestre, I.; Ollivier, J.; Kozyrkov, Y. Y.; Pukin, A.; Kulinkovich, O. G.; Salaün, J. *Eur. J. Org. Chem.* **2002**, 2160–2176. These low yields most likely come from the metal transfer from **25** to the carbon–carbon unsaturated bond of these substrates: (e) Urabe, H.; Suzuki, K.; Sato, F. *J. Am. Chem. Soc.* **1997**, *119*, 10014–10027. (f) Hamada, T.; Suzuki, D.; Urabe, H.; Sato, F. *J. Am. Chem. Soc.* **1999**, *121*, 7342–7344.

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