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McMurry coupling of aryl aldehydes and imino pinacol coupling mediated by $Ti(O\text{-}i\text{-}Pr)_4/Me_3SiCl/Mg$ reagent

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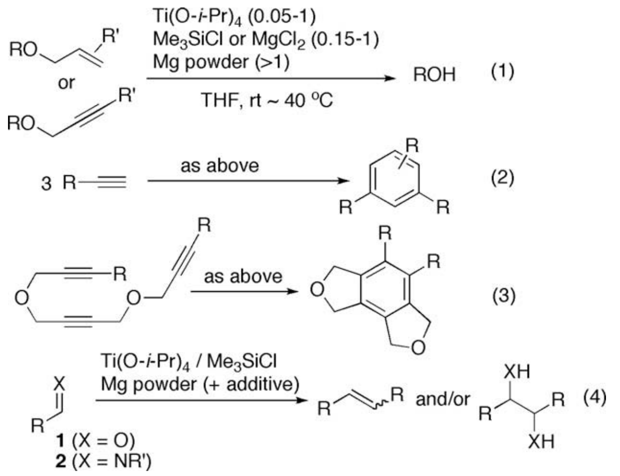
ABSTRACT

$Ti(O\text{-}i\text{-}Pr)_4/Me_3SiCl/Mg$ reagent mediated McMurry coupling of aryl aldehydes to biaryl olefins at near room temperature. This low valent titanium (LVT) reagent also mediated the coupling of aldimines to 1,2-diamines (imino pinacol coupling).

Low valent titanium (LVT) reagents have gained widespread acceptance in organic synthesis.[1] Besides well-defined LVT reagents such as TiX_3, Cp_2TiCl (or its dimer), their aggregates, and solvated derivatives, LVT reagents generated in situ from $TiCl_4$ or $TiCl_3$ by the reaction with various reducing agents have been utilized for a variety of reactions, in which active species is still under debate. Reactivity of the in situ-prepared LVT reagents, including reaction course, reproducibility, chemoselectivity, and stereochemistry, varies greatly with the source of the titanium metal and reducing agent, its procedure for preparation, and the experimental conditions involving the presence of an additional controlling agent (additive).[1,2] Many studies have focused on the ability of the large variety of LVT reagents to mediate the reductive coupling/deoxygenation of carbonyl compounds, known as McMurry coupling,[1a–g] which is one of the most widely utilized synthetic reactions. Conventionally, such LVT reagents have been prepared using Rieke's method involving reduction of $TiCl_4$ or $TiCl_3$ with an alkali metal (Li, Na, or K) in an ethereal or hydrocarbon solvent. These reagents, in general, are prepared prior to the reaction with the substrate(s) and the protocol yields usually heterogeneous colloidal slurries of activated titanium. At low temperature, the reaction of carbonyl compounds with the LVTs gives the corresponding titanium pinacolates. The extrusion of oxygen from the pinacolates to olefins necessitates the conditions of solvent-reflux temperature and prolonged reaction time. In addition to the intricateness of procedure, the functional incompatibility under the refluxing conditions restricts the utility of LVT reagents.

Recently, we have reported that treatment of $Ti(O\text{-}i\text{-}Pr)_4$ with Mg powder in the presence of a halogen source such as R_3SiCl and $MgCl_2$ in THF generates a specific LVT species at room temperature, which catalyzes alkyne [2+2+2] cycloaddition reactions and C–O bond-cleaving reaction of allyl and propargyl ethers (Eqs. 1–3 in Scheme 1).[3] We showed that a LVT(s) could be generated from this combination of reagents $Ti(O\text{-}i\text{-}Pr)_4/MCl_n/Mg$ through the following reaction pathway: (i) titanium *i*-propoxide reacts with halogen source compound to afford a titanium chloride compound(s) and $i\text{-}PrOMCl_{n-1}$, (ii) the resulting titanium chloride(s) can be reduced by the reaction with Mg to generate a lower valent species, (iii) these processes may be repeated with the gradual generation of Ti(III) and lower valent titanium species. As a result, the system generates LVT reagents under mild conditions and the reaction mixture remains homogeneous, except for the Mg powder, to all appearances.

Now we wish to report that a $Ti(O\text{-}i\text{-}Pr)_4/Me_3SiCl/Mg$ reagent mediates McMurry coupling[2,4] of aryl aldehydes **1** to biaryl olefins at near room temperature and the reagent also couples aldimines **2** to 1,2-diamines (imino pinacol coupling)[5] (Eq. 4 in Scheme 1). Application of McMurry coupling with the LVT to the polymeriza-



Scheme 1.

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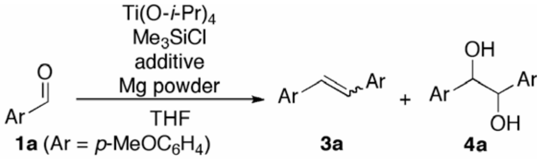
tion reaction starting from di-carbonyl compounds is also disclosed.

Table 1 summarizes the results of optimization of a Ti(O-*i*-Pr)$_4$/Me$_3$SiCl/Mg-mediated reductive coupling of aryl aldehyde **1a**. In the absence of Ti(O-*i*-Pr)$_4$ or Me$_3$SiCl, the reaction did not take place (runs 1 and 2). The reaction with stoichiometric amounts of Ti(O-*i*-Pr)$_4$ and Me$_3$SiCl proceeded to give 1,2-diarylethylene **3a,** but the reaction at room temperature was slow (run 5). The reaction proceeded with a reasonable rate at 40 °C to provide **3a** in 76% NMR yield, but a large amount of 1,2-diol **4a** was also produced (run 6). When the effect of additives was studied (runs 7–11), it was found that the addition of a Lewis base decreased the production of diol **4a**. Among them, the reaction in the presence of Et$_3$N (2.6 equiv) at 40 °C yielded **3a** in 97% NMR yield with a high *E*-selectivity, whereas co-production of **4a** was minimized to be only 2% (run 11).

Table 2 summarizes the results of the reductive coupling of various aryl aldehydes with Ti(O-*i*-Pr)$_4$/Me$_3$SiCl/Mg/Et$_3$N reagent. The reactions afforded 1,2-diarylethylenes predominantly in moderate to good yields. The reaction of benzaldehyde (**1b**) as well as aryl aldehydes **1a**, **1d**, **1e,** and **1g** with an electron-donating group showed good selectivity. However, aldehydes with an electron-deficient group such as **1c** and those with a coordinating group around the carbonyl moiety such as **1f**, **1h,** and **1i** reacted slowly

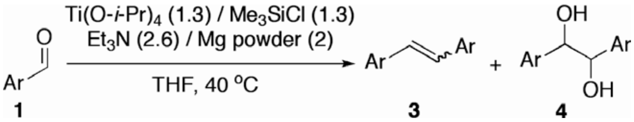
Table 1[a]

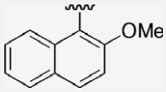
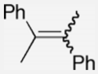


Run	Ti[b] equiv	SiCl[c] equiv	Additive equiv	°C/h	Products, %[d] **3a** (*E*/*Z*)/**4a**/**1a**
1	0	1.3	–	20/24	Trace/trace/>98
2	1.0	0	–	20/24	Trace/trace/>98
3	0.2	1.2	–	40/20	Complex mixture
4	1.0	0.5	–	40/24	Complex mixture
5	1.3	1.3	–	20/48	47 (91:9)/2/51
6	1.3	1.3	–	40/48	76 (99:1)/19/5
7	1.3	1.3	DMA[e] 2.6	40/94	66 (83:17)/30/4
8	1.3	1.3	NMP[f] 2.6	40/94	72 (88:12)/26/2
9	1.3	1.3	Pyridine 2.6	40/38	86 (95:5)/10/4
10	1.3	1.3	Et$_3$N 2.6	20/67	86 (95:5)/9/5
11	1.3	1.3	Et$_3$N 2.6	40/24	97 (99:1)/2/1

[a] Compound **1a** (1.0 mmol), Ti(O-*i*-Pr)$_4$ (0–1.3 mmol), Me$_3$SiCl (0–1.3 mmol), additive (0 or 2.6 mmol), and Mg powder (2.0 mmol) in THF (5 mL).
[b] Equivalent of Ti(O-*i*-Pr)$_4$.
[c] Equivalent of Me$_3$SiCl.
[d] Determined by ^{1}H NMR analysis of the crude mixture using an internal standard.
[e] *N,N*-Dimethylacetamide.
[f] *N*-Methyl-2-pyrrolidinone.

Table 2[a]



Run	Substrate **1**	h	Products, %[b] **3** (*E*/*Z*)/**4**/**1**	Isolated yield of **3**, %[c]
1	**1a**: Ar = 4-MeOC$_6$H$_4$	24	97 (99:1)/2/1	95
2	**1b**: Ar = Ph	48	95 (87:13)/5/0	77
3	**1c**: Ar = 4-ClC$_6$H$_4$	72	75 (61:39)/17/8	58
4	**1d**: Ar = 4-MeC$_6$H$_4$	48	93 (99:1)/6/1	85
5	**1e**: Ar = 3,4-(MeO)$_2$C$_6$H$_3$	48	89 (94:6)/9/2	65
6	**1f**: Ar = 2-MeOC$_6$H$_4$	72	66 (91:9)/15/19	51
7	**1g**: Ar = 2,4,6-Me$_3$C$_6$H$_2$	24	97 (90:10)/3/0	76
8	**1h**: Ar = 2-thienyl	72	61 (10:90)/17/22	53
9	**1i**: Ar = 	48	60 (65:35)/16/24	49
10[d]	Acetophenone	24	 95 (47:53)/0/5	88

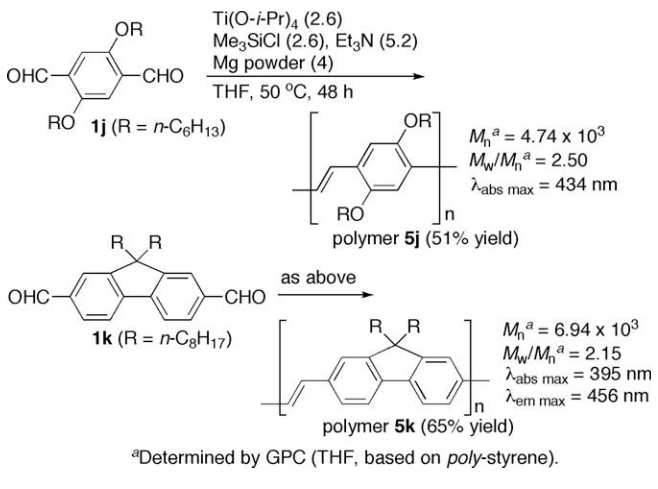
[a] Compound **1** (1.0 mmol), Ti(O-*i*-Pr)$_4$ (1.3 mmol), Me$_3$SiCl (1.3 mmol), Et$_3$N (2.6 mmol), and Mg powder (2.0 mmol) in THF (5 mL) at 40 °C.
[b] Determined by ^{1}H NMR analysis of the crude mixture using an internal standard.
[c] As a mixture of *E* and *Z* isomers of **3** after column chromatography.
[d] The reaction was performed with 1 equiv of Ti(O-*i*-Pr)$_4$ and 2 equiv of Me$_3$SiCl in the absence of Et$_3$N.

and showed low selectivity. Interestingly, the reaction of 2-thiophenecarboxaldehyde (**1h**) gave (*Z*)-**3h** predominantly, presumably due to an effect of coordination of the sulfur atom to the active titanium species (run 8). The reaction of acetophenone with the LVT reagent also proceeded smoothly in the absence of Et_3N to provide 2,3-diphenyl-2-butene in good yield, albeit with low *E*/*Z* selectivity (run 10). The reaction of aliphatic aldehydes gave a complex mixture involving the corresponding primary alcohol generated by simple reduction (data not shown). As a result, the reagent could reductively couple aryl aldehydes and ketones (without Et_3N) at 40 °C by a simple mixing of the reagents and substrate to provide 1,2-diarylethylene derivatives, although somewhat narrow scope on the substrate substitution was observed.

Periasamy and co-workers have reported $TiCl_4/Et_3N$ reagent for reductive coupling of aromatic aldehydes to the corresponding diols, where Et_3N reduces $TiCl_4$ and is converted to the corresponding iminium salt.[6] To confirm this possibility in the present reaction, we carried out the reaction of **1a** with $Ti(O\text{-}i\text{-}Pr)_4/Me_3SiCl/Mg$ in the presence of less-volatile *n*-Bu_3N instead of Et_3N. The NMR analysis of the crude mixture confirmed the production of **3a** (95% NMR yield, $E/Z = 55{:}45$) with less than 5% of diols **4a** and quantitative recovery of *n*-Bu_3N. The result indicates that an added amine did not reduce titanium compound(s) but it might act as a Lewis base to coordinate to the Ti atom in an active species. Since the addition of 1 equiv of Et_3N was found to be inefficient, it can be assumed that the active titanium species stabilized by coordination with two molecules of Et_3N may present as a monomeric form and is suitable for deoxygenation of the titanium pinacolate intermediates. However, the exact role of Et_3N effecting on minimizing production of diols is unclear at this time and its explanation must await further study.

The reaction conditions for the McMurry-type coupling were preliminarily applied to the polymerization reaction starting from aryl dialdehydes **1j** and **1k** (Scheme 2).[7] Thus, a mixture of **1j**[8] and **1k**[9] with $Ti(O\text{-}i\text{-}Pr)_4$ (2.6 equiv), Me_3SiCl (2.6 equiv), Et_3N (5.2 equiv), and Mg powder (4 equiv) in THF was stirred for 48 h at 50 °C to produce polymers **5j** ($M_n = 4.74 \times 10^3$, $M_w/M_n = 2.50$, 51% yield) and **5k** ($M_n = 6.94 \times 10^3$, $M_w/M_n = 2.15$, 65% yield), respectively.

Figure 1 shows UV–vis absorption spectra of polymer **5j**. In the region of longer wavelength, the maximum absorption ($\lambda_{\text{max abs}}$) of **5j** thus obtained was observed at 434 nm. Whereas the polymer **5j** ($M_n = 3.57 \times 10^3$, $M_w/M_n = 2.09$) prepared in the absence of Et_3N has its $\lambda_{\text{max abs}}$ at 373 nm. The polymer **5j** produced by the reaction in the presence of Et_3N had more extended π-conjugation than that derived from the reaction without Et_3N. It can be explained by assuming that conjugation of main chain in polymer **5j** may be broken by 1,2-diol structures and the presence of Et_3N could minimize the formation of 1,2-diol. By comparison with UV–vis data of oligomers of type **5j** reported in the literature,[10] it was estimated that the polymer **5j** generated in the presence of Et_3N involved an extended conjugation length of 4–6 phenylene–vinylene units. The ^1H NMR spectra of polymer **5j** indicated aromatic and olefinic protons of conjugated chain as well as small peaks for diol (and/or its silyl ether) structure around 4.6 ppm (Fig. 2). Similar results were obtained in the case of polymer **5k** (fluorescence: $\lambda_{\text{max em}}$ at 456 nm excited at 385 nm), the conjugation-extending length of which was estimated to be 4–6 arylene–vinylene units by comparison of its UV-absorption and fluorescence data with those of the oligomers of type **5k** reported.[11]



[a]Determined by GPC (THF, based on *poly*-styrene).

Scheme 2. Polymerization of dialdehydes.

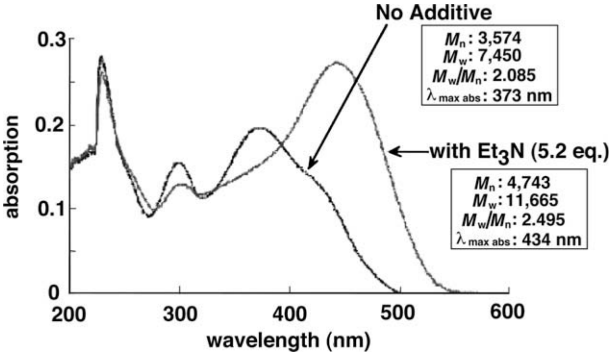


Figure 1. UV–vis absorption spectra of polymer **5j**: In CH_2Cl_2 (10^{-2} mg/mL).

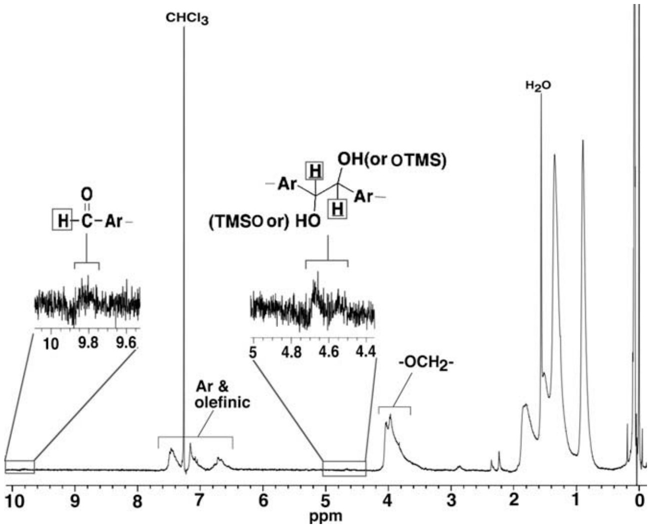
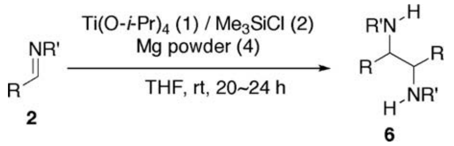


Figure 2. ^1H NMR spectra of polymer **5j** ($CDCl_3$, 500 MHz).

In addition to the McMurry-type coupling, we found that a $Ti(O\text{-}i\text{-}Pr)_4/Me_3SiCl/Mg$ reagent couples aldimines to the corresponding 1,2-diamines.[5] As revealed from Table 3, in which representative results are shown, aromatic as well as aliphatic aldimines[12] were reacted with the reagent to give 1,2-diamines *dl*-selectively, although the yields were not necessarily high. In these reactions, the major side-reaction was reduction of **2** providing the corresponding secondary amines (RCH_2NHR'). Study for improvement of the reaction is underway.

In summary, we have demonstrated that a new low valent titanium reagent, $Ti(O\text{-}i\text{-}Pr)_4/Me_3SiCl/Mg$, enables McMurry coupling of aryl aldehydes to biaryl olefins to be carried out under mild reac-

Table 3
Reactions of aldimines **2**[a]



Run	Substrate **2**		Product **6**	
	R	R'	*dl*:*meso*[b]	Isolated yield, %
1	*n*-Bu	$PhCH_2$	88:12	18
2	*i*-Bu	$PhCH_2$	88:12	23
3	*i*-Pr	$PhCH_2$	91:9	32
4	*cycl*-Hex	$PhCH_2$	>99:1	15
5	*t*-Bu	$PhCH_2$	No reaction	
6	Ph	$PhCH_2$	92:8	74
7	Ph	Ph	76:23	66
8	2-Furyl	$PhCH_2$	61:39	53
9	2-Thienyl	$PhCH_2$	82:18	40

[a] Compound **2** (1.0 mmol), Ti(O-*i*-Pr)$_4$ (1.0 mmol), Me_3SiCl (2.0 mmol), and Mg powder (4.0 mmol) in THF (10 mL).

[b] Determined by ^1H NMR analysis of the crude mixture.

tion conditions with simple operation,[13] where the addition of Et_3N was effective in minimizing the formation of the corresponding 1,2-diols. The reagent also coupled aldimines to 1,2-diamines. Further investigation for improving efficiency of the methods, confirming a role of an additive (Et_3N), and their synthetic application is underway in our laboratory.

Acknowledgment

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References and notes

1. (a) McMurry, J. E.; Fleming, M. P. *J. Am. Chem. Soc.* **1974**, *96*, 4708; (b) Mukaiyama, T.; Sato, T.; Hanna, J. *Chem. Lett.* **1973**, 1041; (c) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513; (d) Lenoir, D. *Synthesis* **1989**, 883; (e) Kahn, B. E.; Rieke, R. D. *Chem. Rev.* **1988**, *88*, 733; (f) Fürstner, A.; Bogdanovic, B. *Angew. Chem., Int. Ed.* **1996**, *35*, 2442; (g) Ephritikhine, M. *Chem. Commun.* **1998**, 2549; (h) Sato, F.; Urabe, H.; Okamoto, S. *Chem. Rev.* **2000**, *100*, 2835; (i) Kulinkovich, O. G.; de Meijere, A. *Chem. Rev.* **2000**, *100*, 2789; (j) Eisch, J. J. *J. Organomet. Chem.* **2001**, *617–618*, 148; (k) Sato, F.; Okamoto, S. *Adv. Synth. Catal.* **2001**, *343*, 759; (l) Sato, F.; Urabe, H. In *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: Weinheim, Germany, 2002; pp 319–354.
2. Rele, A. M.; Nayak, S. K.; Chattopadhyay, S. *Tetrahedron* **2008**, *64*, 7225. and references cited therein.
3. Ohkubo, M.; Mochizuki, S.; Sano, T.; Kawaguchi, Y.; Okamoto, S. *Org. Lett.* **2007**, *9*, 773.
4. For pinacol coupling, see: Lipski, T. A.; Hilfiker, M. A.; Nelson, S. G. *J. Org. Chem.* **1997**, *62*, 4566. and references cited therein.
5. Review for imino pinacol coupling: Lucet, D.; Le Gall, T.; Mioskowski, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 2580.
6. Periasamy, M.; Srinivas, G.; Karunakar, G. V.; Bharathi, P. *Tetrahedron Lett.* **1999**, *40*, 7577.
7. Cooke, A. W.; Wagener, K. B. *Macromolecules* **1991**, *24*, 1404.
8. Demir, A. S.; Reis, Ö. *Tetrahedron* **2004**, *60*, 3803.
9. Anuragudom, P.; Newaz, S. S.; Phanichphant, S.; Lee, T. R. *Macromolecules* **2006**, *39*, 3494.
10. Jiu, T.; Li, Y.; Liu, X.; Liu, H.; Li, C.; Ye, J.; Zhu, D. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 911.
11. Liu, Q.; Liu, W.; Yao, B.; Tian, H.; Xie, Z.; Geng, Y.; Wang, F. *Macromolecules* **2007**, *40*, 1851.
12. Faugeroux, V.; Génisson, Y.; Salma, Y.; Constant, P.; Baltas, M. *Bioorg. Med. Chem.* **2007**, *15*, 5866. and references cited therein.
13. *General procedure for carbonyl coupling with Ti(O-i-Pr)$_4$/Me_3SiCl/Mg/Et_3N reagent*: To a mixture of aldehyde **1** (1.00 mmol), Ti(O-*i*-Pr)$_4$ (0.386 mL, 1.30 mmol), Et_3N (0.360 mL, 2.60 mmol), and Mg powder (49 mg, 2.0 mmol) in THF (5 mL) was added Me_3SiCl (0.165 mL, 1.30 mmol) at 40 °C. The mixture was stirred for 24–72 h at this temperature and then quenched by the addition of aqueous 1 M HCl. The resulting mixture was extracted with AcOEt. The combined organic layers were dried over $MgSO_4$, filtrated through a pad of Celite, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt) to give 1,2-diarylethylene **3**. *Procedure for polymerization with Ti(O-i-Pr)$_4$/Me_3SiCl/Mg/Et_3N reagent*: To a mixture of dialdehyde **1j** or **1k** (0.50 mmol), Ti(O-*i*-Pr)$_4$ (0.385 mL, 1.30 mmol), Et_3N (0.36 mL, 2.60 mmol), and Mg powder (49 mg, 2.0 mmol) in THF (5.0 mL) was added Me_3SiCl (0.165 mL, 1.30 mmol) at 50 °C. The mixture was stirred for 24–96 h at this temperature and then quenched by the addition of aqueous 1 M HCl. The resulting mixture was extracted with $CHCl_3$. The combined organic layers were washed with water, concentrated, and dried in vacuo. The residue was twice reprecipitated from chloroform/methanol or THF/methanol and then dried in vacuo to give **2j** or **2k**. *General procedure for imino-pinacol coupling with Ti(O-i-Pr)$_4$/Me_3SiCl/Mg reagent*: To a mixture of imine **2** (1.00 mmol), Ti(O-*i*-Pr)$_4$ (0.297 mL, 1.00 mmol), and Mg powder (98 mg, 4.0 mmol) in THF (10 mL) was added Me_3SiCl (0.254 mL, 2.00 mmol) at room temperature. The mixture was stirred for 20–24 h at this temperature and then quenched by the addition of aqueous 1 M NaOH (~0.5 mL). After addition of NaF (~1 g) and Celite (~1 g), the resulting mixture was stirred for 1 h and then filtrated through a pad of Celite. The filtrate was concentrated to dryness and the residue was purified by column chromatography on silica gel (hexane/AcOEt) to give 1,2-diarylethylene-1,2-diamine **6**.