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# Titanocene(III) Chloride-Mediated Reductions of Oxazines, Hydroxamic Acids, and *N*-Hydroxy Carbamates

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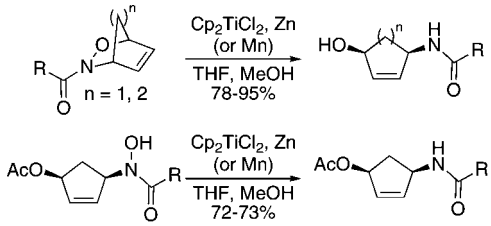
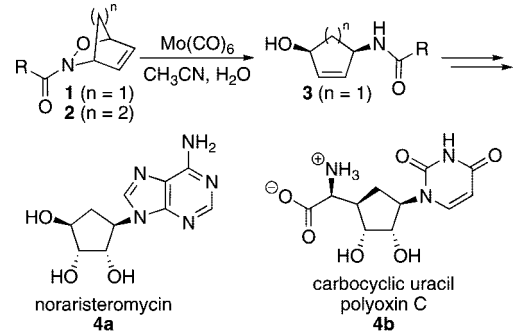



Titanocene(III) chloride ($Cp_2TiCl$), generated in situ, reduces N−O bonds of various substrates in good to excellent yields (72−95%). Reactions may be performed with stoichiometric $Cp_2TiCl$ or with catalytic $Cp_2TiCl$.

Reduction of N−O bonds with titanium(III) is a useful transformation that has been applied to nitro groups,[1] oximes,[2] *N*-hydroxyazetidinones, hydroxamic acids, and *N*-hydroxycarbamates.[3] Mechanistically, the reduction proceeds by single-electron transfer and requires 2 equiv of the titanium(III) source for each N−O bond. The preferred source of titanium(III) is titanium trichloride, commercially available as a solution in hydrochloric acid. Unfortunately, the concentration of titanium(III) in solution is variable, and methods for determining the concentration by titration are limited.[4] Also, Ti(IV) salts are formed in the reaction mixture, which often complicate the workup. Additionally, the reaction conditions may not be compatible with acid-sensitive functionalities.

Our continued interest in hydroxamic acids and the syntheses of biologically relevant molecules from oxazine **1** and *N*-hydroxyazetidinones led us to develop an improved and versatile method for N−O bond reductions. We report herein the use of an alternative source of titanium(III), titanocene monochloride ($Cp_2TiCl$), for the selective reduction of N−O bonds under mild conditions and provides products in good to excellent yields. Titanocene monochloride is readily generated in situ from titanocene dichloride ($Cp_2TiCl_2$) and zinc dust. Although this reagent has been used in reductive openings of epoxides,[5] carbonyl-coupling reactions,[6] and reduction of α,β-unsaturated carbonyls,[7] $Cp_2TiCl$ has not been investigated as a reagent for the reduction of N−O bonds.

**SCHEME 1. Syntheses of Carbocyclic Nucleosides from 3**




We selected several substrates containing N−O bonds, including oxazines, *N*-hydroxyazetidinones, hydroxamic acids, and *N*-hydroxycarbamates, as these compounds often serve as key intermediates in the synthesis of carbocyclic nucleosides,[8] β-lactam antibiotics,[9] and benzodiazepines.[10]

Acylnitroso-derived hetero-Diels−Alder adducts **1** and **2**, generated from the reaction of a transient acylnitroso species with cyclopentadiene and cyclohexadiene,[11] respectively, are synthetically important precursors to a variety of bioactive molecules. For example, oxazine **1** may be reduced with $Mo(CO)_6$ to afford *syn*-1,4 aminocyclopentenol **3**,[12] a key intermediate in the synthesis of norearisteromycin **4a**[8c] and carbocyclic uracil polyoxin C **4b**[8b] (Scheme 1).

In order to access diversified cyclopentene scaffolds, several metal-mediated ring-opening strategies have been established with key cycloadduct intermediate **1** to introduce different functionalities as well as defined stereo- and regiochemistries.[13−15]

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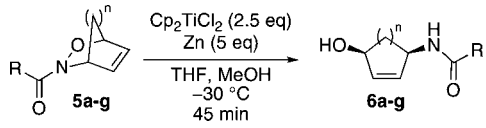
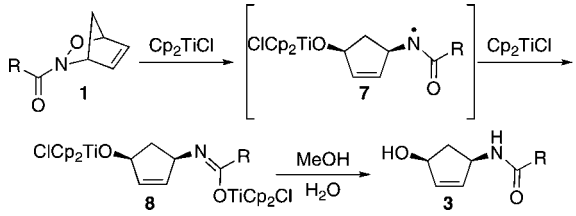
**TABLE 1. $Cp_2TiCl$-Mediated Reductions of Cycloadducts 5a−g**




| entry | cycloadduct | R | n | product | isolated yield (%) |
|---|---|---|---|---|---|
| 1 | **5a** | Ph | 1 | **6a** | 95 |
| 2 | **5b** | (*R*)-CH(OH)Ph | 1 | **6b** | 78 |
| 3 | **5c** | $CH_2Ph$ | 1 | **6c** | 79 |
| 4 | **5d** | $OC(CH_3)_3$ | 1 | **6d** | 79 |
| 5 | **5e** | 4-$NO_2$Ph | 1 | **6e** | 0 |
| 6 | **5f** | $CH_2Ph$ | 2 | **6f** | 86 |
| 7 | **5g** | $OC(CH_3)_3$ | 2 | **6g** | 77 |

**SCHEME 2. Proposed Mechanism for $Cp_2TiCl$-Mediated Reductions**




In all cases, these metal-mediated ring openings furnish hydroxamic acids or *N*-hydroxycarbamates that may serve as appropriate substrates for $Cp_2TiCl$-mediated reductions.

A series of acylnitroso-derived hetero-Diels−Alder cycloadducts **1** and **2** were subjected to $Cp_2TiCl$-mediated reduction conditions (Table 1). Benzoyl-derived cycloadduct **5a** was added to a cooled solution of $Cp_2TiCl_2$ and zinc. The reaction was complete within 45 min and *syn*-1,4 aminocyclopentenol **6a** was observed as the exclusive product in 95% yield. An identical outcome was obtained for [2.2.1] bicyclic systems **5b−d** although in slightly decreased yield.

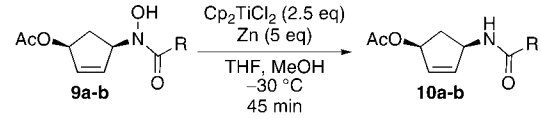
Titanium(III) is known to reduce nitro groups;[1] however, we were interested to learn if the strained oxazine system could be preferentially reduced in the presence of an aromatic nitro group. Unfortunately, when nitro-containing cycloadduct **5e** was exposed to $Cp_2TiCl$ in solution, a complicated mixture resulted and no desired product was observed.

We also investigated [2.2.2] cycloadducts **5f** and **5g**. *syn*-1,4-Aminocyclohexenol products **6f** and **6g** were observed in 86% and 77% yields, respectively.

The $Cp_2TiCl$-mediated reduction may proceed by the proposed reaction mechanism (Scheme 2).[16,17] Single-electron transfer from $Cp_2TiCl$ to **1** cleaves the weak N−O bond and generates radical intermediate **7**. A second equivalent of $Cp_2TiCl$ transfers an electron to the radical species to form reduced product **8,** which is protonated in the presence of MeOH/$H_2O$ to reveal *syn*-1,4-aminocyclopentenol **3**.

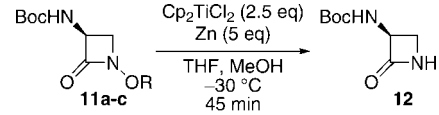
The successful reductions of oxazine systems **5a−g** encouraged us to evaluate hydroxamic acid **9a** and *N*-hydroxycarbamate **9b** as substrates for reduction with $Cp_2TiCl$ (Table 2). The C−O bonds of cycloadducts **5c** and **5d** were cleaved in the presence of Pd(0) and the transient $\pi$-allyl species trapped with acetic acid to provide **9a**[13] and **9b**, respectively. When hydroxamate **9a** was introduced to a solution of $Cp_2TiCl_2$ and zinc, reduction occurred smoothly to afford amide **10a**. Similarly, *N*-hydroxycarbamate **9b** was readily reduced to carbamate **10b**.

**TABLE 2. $Cp_2TiCl$-Mediated Reductions of Substrates 9a,b**




| entry | substrate | R | product | isolated yield (%) |
|---|---|---|---|---|
| 1 | **9a** | $CH_2Ph$ | **10a** | 72 |
| 2 | **9b** | $OC(CH_3)_3$ | **10b** | 73 |

**TABLE 3. $Cp_2TiCl$-Mediated Reductions of Substrates 11a−c**




| entry | substrate | R | product | isolated yield (%) |
|---|---|---|---|---|
| 1 | **11a** | H | **12** | 80 |
| 2 | **11b** | Me | **12** | no reaction |
| 3 | **11c** | $CH_2Ph$ | **12** | no reaction |

**TABLE 4. $Cp_2TiCl$-Catalyzed Reductions of Selected Substrates**

| entry | substrate | conditions | product | isolated yield (%) catalytic | isolated yield (%) stoich. |
|---|---|---|---|---|---|
| 1 | **5c** | B[a] | **6c** | 50 (70[20]) | 79 |
| 2 | **5c** | C[a] | **6c** | incomplete rxn[b] | 79 |
| 3 | **5d** | B[a] | **6d** | 71 | 79 |
| 4 | **5d** | C[a] | **6d** | incomplete rxn[b] | 79 |
| 5 | **9a** | B[a] | **10a** | 48 | 72 |
| 6 | **9a** | C[a] | **10a** | 43 | 72 |
| 7 | **9b** | C[a] | **10b** | 44 | 73 |
| 8 | **11a** | B[a] | **12** | no rxn[c] | 80 |
| 9 | **11a** | C[a] | **12** | no rxn[c] | 80 |

[a] Procedure B: (i) $Cp_2TiCl_2$ (0.2 equiv), Mn (8 equiv), 2,4,6-trimethylpyridine (8 equiv), TMSCl (4 equiv); (ii) TBAF. Procedure C: $Cp_2TiCl_2$ (0.2 equiv), Mn (8 equiv), 2,4,6-trimethylpyridinium HCl (2 equiv), 1,4-cyclohexadiene (4 equiv). [b] Incomplete reaction after 18 h. [c] Unreactive toward catalytic $Cp_2TiCl$.

Our group has previously reported the reduction of *N*-hydroxyazetidinones with $TiCl_3$.[3] Therefore, we were not surprised to find that *N*-hydroxyazetidinone **11a** was reduced to the corresponding azetidinone **12** with $Cp_2TiCl$ (Table 3). Consistent with our group's previous report,[3] *N*-alkoxyazetidinone **11b** and *N*-benzyloxyazetidinone **11c** were unreactive toward Ti(III)-reduction conditions.

These observations demonstrated that $Cp_2TiCl$-mediated reductions of several N−O bond-containing substrates proceed in good to excellent yields.

In order to regenerate Ti(III) from Ti(IV), 2,4,6-trimethylpyridine and chlorotrimethylsilane may be used in the presence of excess reductant (usually zinc or manganese metal).[16] An alternative method to regenerate Ti(III) from Ti(IV) requires 1,4-cyclohexadiene, 2,4,6-trimethylpyridinium hydrochloride, and excess manganese powder.[5b] Several $Cp_2TiCl$-catalyzed reactions have been reported,[5b,6b,17] and we decided to apply these methods to reduce several types of N−O bonds (Table 4).

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In a typical reaction, a degassed THF solution of 20 mol % of $Cp_2TiCl_2$ and excess manganese (8 equiv)[18] was charged with a degassed THF solution of substrate and 2,4,6-trimethylpyridine, followed by introduction of chlorotrimethylsilane (TMSCl).[19] Reduced amounts of $Cp_2TiCl_2$ (i.e., 5 and 10 mol %) resulted in incomplete reactions after 18 h. Excess manganese (8 equiv) with 20 mol % of $Cp_2TiCl$ provided the highest yields and shortest reaction times. The $Cp_2TiCl$-catalyzed reduction of phenylacetyl cycloadduct **5c** and Boc cycloadduct **5d** were complete within 2 h. The resultant silylated alcohols were easily deprotected with tetrabutylammonium fluoride (TBAF) to afford the corresponding alcohols **6c** (50−70% yield)[20] and **6d** (71% yield). $Cp_2TiCl$-catalyzed reduction of Boc cycloadduct **5d** was performed on large scale (25 mmol), and an identical isolated yield was obtained (71% yield). Hydroxamic acid **9a** may be directly reduced to amide **9b** without exposure to TBAF.

Substrates **9a** and **9b** may be reduced to **10a** (43% yield) and **10b** (44% yield), respectively, via a $Cp_2TiCl$-catalyzed reduction with 1,4-cyclohexadiene, 2,4,6-trimethylpyridinium hydrochloride, and excess manganese powder. When cycloadducts **5c** and **5d** were exposed to identical $Cp_2TiCl$-catalyzed reduction conditions, incomplete reactions were observed after 20 h. *N*-Hydroxyazetidinone **11a** was unreactive toward catalytic amounts (20 mol %) of $Cp_2TiCl$.

In conclusion, we have applied $Cp_2TiCl$ methodology to reduce N−O bonds in diverse substrates, including oxazines, *N*-hydroxyazetidinones, hydroxamic acids, and *N*-hydroxycarbamates. Reductions may be performed with stoichiometric $Cp_2TiCl$ as well as catalytic $Cp_2TiCl$. We intend to use this methodology to synthesize biologically significant molecules such as carbocyclic nucleoside analogues and novel benzodiazepines.

## Experimental Section

**General Procedure A: Stoichiometric $Cp_2TiCl$-Mediated Reduction of 5a−g, 9a,b and 11a.** A clean, flame-dried, 25 mL round-bottom flask equipped with a stir bar was evacuated and purged with Ar. A degassed THF solution (6.3 mL) of $Cp_2TiCl_2$ (1.24 mmol) and activated zinc (2.49 mmol) was stirred at rt under Ar for 45 min. The reaction mixture changed color from dark red to olive green. The reaction mixture was cooled to −30 °C and charged with a MeOH solution (5 mL) of substrate (0.50 mmol) dropwise over 3 min. The reaction mixture was stirred for 45 min as the bath temperature was maintained between −10 and −30 °C. The reaction mixture was warmed to rt and partitioned between satd $K_2CO_3$ (5 mL) and EtOAc (20 mL). The organic layer was removed via pipet and filtered through a Whatman glass microfiber filter (type GF/F) to remove insoluble titanium salts. The aqueous layer was extracted with EtOAc (4 × 20 mL), and the organic layer was filtered through a Whatman glass microfiber filter (type GF/F) after each extraction. The combined filtered organics were dried over $MgSO_4$ and again filtered through a Whatman glass microfiber filter (type GF/F), and the filtrate was adsorbed on silica gel and concentrated to solids. The adsorbed material was purified by silica gel chromatography to afford the desired product.

**General Procedure B: Catalytic $Cp_2TiCl$-Mediated Reduction of 5c,d and 9a.** A clean, flame-dried, 25 mL round-bottom flask equipped with a stir bar was evacuated and purged with Ar. A degassed THF solution (3.7 mL) of $Cp_2TiCl_2$ (0.09 mmol) and manganese powder (3.7 mmol) was stirred at rt under Ar for 15 min. Meanwhile, a clean, flame-dried, 10 mL round-bottom flask was evacuated and purged with Ar. A degassed THF solution (1 mL) of substrate (0.46 mmol) and 2,4,6-trimethylpyridine (3.7 mmol) was prepared and then transferred to the $Cp_2TiCl_2$ reaction mixture. Finally, chlorotrimethylsilane (1.9 mmol) was added to the reaction mixture and the reaction proceeded under Ar for 2 h. The reaction mixture was filtered through a Whatman glass microfiber filter (type GF/F) to remove manganese salts. The filtrate was partitioned between 10% w/v citric acid (5 mL) and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organics were washed with brine (20 mL), dried over $Na_2SO_4$, filtered, and concentrated to an oil. The resultant crude material was dissolved in THF (2 mL) and charged with 1 M tetrabutylammonium fluoride in THF (1.86 mL, 1.86 mmol), and the reaction was stirred at rt for 1 h. The reaction mixture was concentrated to a slurry and partitioned between 1 M HCl (2 mL) and EtOAc (5 mL). The aqueous layer was extracted with EtOAc (4 × 5 mL). The combined organics were washed with brine (15 mL), dried over $Na_2SO_4$, filtered, and concentrated to an oil. The resultant residue was purified by silica gel chromatography to afford product.

**General Procedure C: Catalytic $Cp_2TiCl$-Mediated Reduction of 9a and 9b.** A clean, flame-dried, 25 mL round-bottom flask equipped with a stir bar was evacuated and purged with Ar. A degassed THF suspension (3.3 mL) of 2,4,6-trimethylpyridinium hydrochloride (0.62 mmol) was charged with $Cp_2TiCl_2$ (0.06 mmol), manganese powder (2.49 mmol), and substrate (0.31 mmol). 1,4-Cyclohexadiene (1.24 mmol) was added to the reaction mixture, and the reaction proceeded under Ar for 18 h. The reaction mixture was filtered through a Whatman glass microfiber filter (type GF/F) to remove manganese salts. The filtrate was partitioned between 10% w/v citric acid (5 mL) and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organics were washed with brine (20 mL), dried over $Na_2SO_4$, filtered, and concentrated to an oil. The resultant residue was purified by silica gel chromatography to afford product.

**(±)-*cis*-(*Z*)-4-Hydroxycyclopent-2-enyl)benzamide 6a.** Prepared according to general procedure A. Crude material was purified by silica gel chromatography (50−70% EtOAc/hexanes) to afford the product as white solids (95%). An analytical sample was recrystallized from EtOAc to provide a white powder from which all data was obtained: mp = 94−95 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.68 (ddd, 1H, $J$ = 14.2, 3.7, 3.7 Hz), 2.29 (d, 1H, $J$ = 6.8 Hz), 2.83 (ddd, 1H, $J$ = 14.4, 8.2, 7.2 Hz), 4.78−4.82 (m, 1H), 4.93 (ddddd, 1H, $J$ = 7.2, 7.0, 3.7, 1.8, 0.7 Hz), 5.94 (ddd, 1H, $J$ = 5.4, 2.4, 1.0 Hz), 6.08 (ddd, 1H, $J$ = 5.6, 1.8, 1.8 Hz), 6.41 (d, 1H, $J$ = 7.0 Hz), 7.40−7.44 (m, 2H), 7.48−7.51 (m, 1H), 7.73−7.76 (m, 2H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 41.5, 54.6, 75.6, 127.1, 128.8, 131.8, 134.1, 134.6, 137.0, 167.2; IR (thin film, cm$^{-1}$) 3295, 2361, 1638, 1578, 1535, 1490; HRMS (FAB) *m*/*z* (M + H) calcd for $C_{12}H_{14}NO_2^+$ 204.1025, found 204.1009.

**(*R*)-2-Hydroxy-*N*-((1*R*,4*S*)-4-hydroxycyclopent-2-enyl)-2-phenylacetamide 6b.** Prepared according to general procedure A. Crude material was purified by silica gel chromatography (30−50% EtOAc/hexanes) to afford the product as a tan gum (78%). An analytical sample was recrystallized from EtOAc/hexanes to provide a white powder from which all data was obtained: mp = 120−121 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.56 (ddd, 1H, $J$ = 14.4, 3.8, 3.8 Hz), 2.73 (ddd, 1H, $J$ = 14.4, 8.4, 7.3 Hz), 2.80 (d, 1H, $J$ = 7.5 Hz), 3.46 (d, 1H, $J$ = 7.5 Hz), 4.66 (ddddd, 1H, $J$ = 8.8, 7.8, 3.9, 2.9, 2.3 Hz), 4.71−4.74 (m, 1H), 5.77 (ddd, 1H, $J$ = 5.6, 2.3, 1.2 Hz), 6.01 (ddd, 1H, $J$ = 5.6, 2.0, 2.0 Hz), 6.43 (d, 1H, $J$ = 8.8 Hz), 7.33−7.40 (m, 5H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 41.2, 54.4, 74.5, 75.5, 127.1, 129.0, 129.2, 133.4, 137.2, 139.5, 171.8; IR (thin

(18) $Cp_2TiCl$-catalyzed reactions were also conducted with zinc as the excess reductant. However, starting materials were not completely consumed within 18 h.

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(20) Compound **6c** was isolated in 70% yield when the reaction solids were continuously extracted with a Soxhlet apparatus prior to workup. Continuous extraction was accomplished with a 10% MeOH/$CH_2Cl_2$ solution (bath temperature 60 °C) for 18 h to directly afford desilylated product **6c**.

film, $cm^{-1}$) 3378, 1651, 1526; HRMS (FAB) *m*/*z* (M + H) calcd for $C_{13}H_{16}NO_3^+$ 234.1130, found 234.1125.

**(±)-*cis*-(*Z*)-4-Hydroxycyclopent-2-enyl)-2-phenylacetamide 6c.** Prepared according to general procedures A and B. Crude material was purified by silica gel chromatography (50−70% EtOAc/hexanes) to afford the product as white solids (79% and 50%, respectively). An analytical sample was recrystallized from EtOAc to provide a white powder from which all data was obtained: mp = 118−119 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.47 (ddd, 1H, *J* = 14.2, 3.8, 3.8 Hz), 2.71 (ddd, 1H, *J* = 13.4, 9.3, 7.3 Hz), 2.74 (d, 1H, *J* = 7.5 Hz), 3.55 (s, 2H), 4.62 (dddd, 1H, *J* = 7.3, 3.8, 1.9 Hz, 0.7 Hz), 4.68−4.71 (m, 1H), 5.59 (bs, 1H), 5.75 (ddd, 1H, *J* = 6.6, 2.2, 0.9 Hz), 5.98 (ddd, 1H, *J* = 5.6, 1.9, 1.9 Hz, 7.23−7.26 (m, 2H), 7.28−7.31 (m, 1H), 7.34−7.37 (m, 2H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 41.3, 44.2, 54.4, 75.5, 127.7, 129.3, 129.6, 133.7, 134.8, 136.9, 170.9; IR (thin film, $cm^{-1}$) 3292, 1632, 1537; HRMS (FAB) *m*/*z* (M + H) calcd for $C_{13}H_{16}NO_2^+$ 218.1181, found 218.1182.

**(±)-*cis*-(*Z*)-4-Hydroxycyclohex-2-enyl)-2-phenylacetamide 6f.** Prepared according to general procedure A. Crude material was purified by silica gel chromatography (70% EtOAc/hexanes) to afford the product as a clear oil (70%): $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.55−1.61 (m, 2H), 1.72 (bs, 1H), 1.76−1.85 (m, 2H), 3.56 (s, 2H), 4.12−4.17 (m, 1H), 4.40−4.45 (m, 1H), 5.43 (d, 1H, *J* = 6.5 Hz), 5.61 (ddd, 1H, *J* = 10.0, 2.8, 0.6 Hz), 5.84 (ddd, 1H, *J* = 10.0, 3.7, 2.1 Hz), 7.23−7.25 (m, 2H), 7.27−7.31 (m, 1H), 7.33−7.36 (m, 2H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 25.3, 29.2, 44.1, 45.2, 64.4, 127.7, 129.3, 129.6, 130.9, 132.7, 134.9, 170.7; IR (thin film, $cm^{-1}$) 3282, 2929, 1648, 1542; HRMS (FAB) *m*/*z* (M + H) calcd for $C_{14}H_{18}NO_2^+$ 232.1338, found 232.1356.

**(±)-*cis*-(*Z*)-*tert*-Butyl-4-hydroxycyclohex-2-enylcarbamate 6g.** Prepared according to general procedure A. Crude material was purified by silica gel chromatography (50% EtOAc/hexanes) to afford the product as a clear oil (86%): $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.44 (s, 9H), 1.65−1.72 (m, 2H), 1.79−1.89 (m, 2H), 4.07−4.13 (m, 1H), 4.14−4.19 (m, 1H), 4.57−4.64 (m, 1H), 5.74 (ddd, 1H, *J* = 10.1, 2.2, 0.6 Hz), 5.86 (ddd, 1H, *J* = 10.1, 3.4, 1.9 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 25.9, 28.6, 29.2, 46.0, 64.9, 79.7, 131.4, 132.4, 155.4; IR (thin film, $cm^{-1}$) 3306, 2930, 2360, 1682, 1504; HRMS (FAB) *m*/*z* (M + H) calcd for $C_{11}H_{20}NO_3^+$ 214.1443, found 214.1480.

**(±)-*cis*-(*Z*)-4-(2-Phenylacetamido)cyclopent-2-enyl Acetate 10a.** Prepared according to general procedures A−C. Crude material was purified by silica gel chromatography (50−70% EtOAc/hexanes) to afford the product as white solids (72%, 48%, and 43%, respectively). An analytical sample was recrystallized from EtOAc/hexanes to provide a white powder from which all data was obtained: mp = 97−99 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.40 (ddd, 1H, *J* = 14.6, 4.0, 4.0 Hz), 1.96 (s, 3H), 2.76 (ddd, 1H, *J* = 14.6, 7.6, 7.6 Hz), 3.57 (s, 2H), 4.94−5.00 (m, 1H), 5.40 (bd, 1H, *J* = 6.5 Hz), 5.47−5.51 (m, 1H), 5.91−5.95 (m, 2H), 7.23−7.26 (m, 2H) 7.28−7.32 (m, 1H), 7.34−7.38 (m, 2H); $^{13}$C NMR (150 MHz, $CDCl_3$) d 41.3, 44.2, 54.4, 75.5, 127.7, 129.3, 129.6, 133.7, 134.8, 136.9, 170.9; IR (thin film, $cm^{-1}$) 3284, 3030, 1734, 1633, 1537, 1494, 1454; HRMS (FAB) *m*/*z* (M + H) calcd for $C_{15}H_{17}NO_3^+$ 260.1287, found 260.1279.

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**Supporting Information Available:** General methods and experimental details for the preparation of **6d**, **9b**, **10b**, and **12**. $^1$H and $^{13}$C NMR spectra for compounds **6a**−**c**, **6f**−**g**, **9b**, and **10a**. Proposed catalytic cycles for $Cp_2TiCl$-mediated N−O bond reductions. This material is available free of charge via the Internet at http://pubs.acs.org.

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