The approach taken in this work allows the incorporation of unusual amino acids. In a complementary approach, biosynthetic methods have been developed to introduce unusual amino acids into proteins.[4] However, attempts to introduce D amino acids into β-lactamase[4] or T4 lysozyme[5] using this method have proven unsuccessful.

Acknowledgment. We thank Dr. Robert Woody for helpful discussions. We gratefully acknowledge postdoctoral support from NIH Grants GM14321 (R.F.) and GM13731 (S.J.A.C.).

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Intramolecular [2 + 2] Cycloadditions of Group IV Metal–Imido Complexes. Applications to the Synthesis of Dihydropyrrole and Tetrahydropyridine Derivatives

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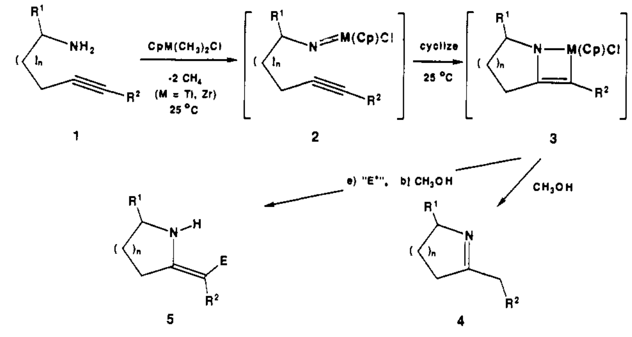
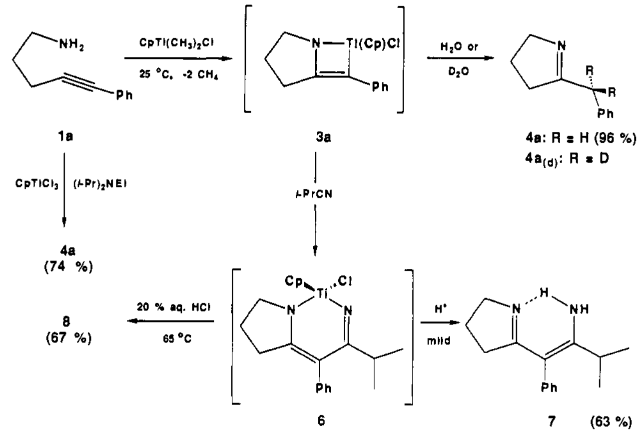
Strained heterometallacycles have recently become the focus of an increasing number of structural and synthetic studies. As a consequence of these investigations, zirconocene thioaldehyde complexes,[2] zirconaaziridines,[3,4] and transient azatitanacyclobutenes[5] have been identified as particularly versatile synthetic intermediates. The preparative utility of these heterometallacycles derives, in part, from their ability to engage in bond-forming reactions with appropriate electrophiles. Recently, Walsh, Hollander, and Bergman reported the generation of several thermally stable imidozirconocene complexes and described some of the *intermolecular* trapping reactions of these species.[6a] In this communication we wish to report the direct preparation of a related class of group IV metal–imido complexes as well as the first examples of *intramolecular* [2 + 2] cycloadditions involving these intermediates.[7] We further demonstrate that the intermediate azametalletines **3** can serve as conventional organometallics in electrophilic substitution reactions leading to selective C or N functionalization (Scheme I).

Jekel-Vroegop and Teuben have noted that monomeric titanium complexes of the type CpTi(NHR)Cl$_2$ undergo self-condensation to provide the corresponding bridging imido dimers under ambient conditions.[8] The remarkable facility of this reaction strongly suggested the feasibility of performing *internal* [2 + 2] cycloadditions between the imido monomers formed in this process and suitably disposed addends. In an initial experiment designed to test this possibility, 5-phenylpent-4-yn-1-ylamine (**1a**) was slowly added to a solution of CpTiCl$_3$[9] (1.0 equiv) and (i-Pr)$_2$NEt (1.2 equiv) in THF at 25 °C. As had been expected, the Δ^1-pyrroline **4a** was obtained from this reaction as the exclusive product in 74% yield. In an effort to more clearly define the nature of the reactive intermediates en route to **4a**, a series of reactions were performed under rigorously aprotic conditions. To this end, slow addition of **1a** to a preformed solution of CpTi(CH$_3$)$_2$Cl[10] (prepared in situ from CpTiCl$_3$ and 2 equiv of CH$_3$Li) in THF at 25 °C gave a dark red solution of the putative titanacycle **3a** with concomitant evolution of CH$_4$.[11] Protonation of **3a** (CH$_3$OH) gave rise to the anticipated Δ^1-pyrroline **4a** in 96% yield. Deuteration of **3a** (D$_2$O) provided the corresponding dideuterio derivative **4a**$_{(d)}$. Direct trapping of **3a** with isobutyronitrile[5b] followed by simple protonation (5% aqueous HCl, 25 °C) furnished the vinylogous amidine **7** in 63% isolated yield. As expected, direct hydrolysis of the presumed metallacyclic intermediate **6** under more vigorous conditions (20% aqueous HCl, 65 °C, 2 h) gave rise to vinylogous amide **8** in 67% isolated yield (Scheme II). Unfortunately, all

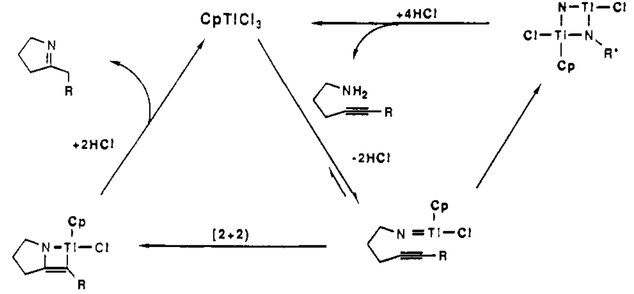
Scheme I



Scheme II



Scheme III



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[1] Fellow of the Alfred P. Sloan Foundation 1989–1991.

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[11] The production of methane in these reactions was confirmed by GLC on a 6 ft × 2 mm i.d. glass column packed with 100–120 mesh alumina by coinjection with an authentic sample.

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Scheme IV

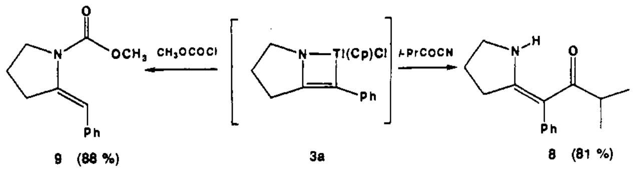
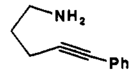
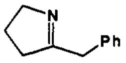
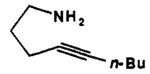
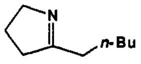
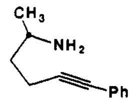
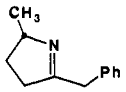
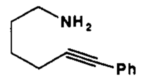
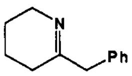
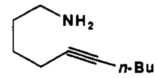
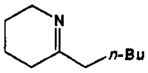


Table I

	substrate 1	product 4	procedure^a	yield, %
a.			A B C	94 96 83
b.			A B C	94 94 82
c.			B C	92 77
d.			C O	69 88
e.			C O	74 89

^{a}A: 20 mol % $CpTiCl_3$, 40 mol % i-Pr_2NEt, THF, 25 °C. B: $CpTi(CH_3)_2Cl$, THF, 25 °C. C: $CpZr(CH_3)_2Cl$, THF, 25 °C. D: 20 mol % $CpTiCl_3$, 40 mol % $PhN(CH_3)_2$, C_7H_8, 80 °C.

attempts to date to isolate and characterize bicyclic azatitanetines such as **3a** have been frustrated by the high reactivity of these species.[12]

Subsequent to these studies this cyclization procedure was extended to a range of representative alkynylamines (e.g., **1a–e**). That an analogous procedure could be utilized for the generation of mono Cp imidozirconium complexes was demonstrated by the treatment of $CpZr(CH_3)_2Cl$ (prepared in situ from $CpZrCl_3\cdot DME$[13] and 2 equiv of CH_3Li) with **1b** in THF at 25 °C to afford **4b** (82% isolated) after methanolysis. *It is of particular significance in a preparative context that the generation of $CpM(X)=NR$ complexes from the precursors $CpM(CH_3)_2X$ and H_2NR proceeds rapidly at temperatures ≤25 °C.* By way of contrast, the corresponding reactions of hindered primary amines with $Cp_2Zr(CH_3)_2$ require 3 days at 85 °C to produce imidozirconocene complexes of the type $Cp_2Zr{=}NR$.[6a] Moreover, exposure of the relatively unhindered amine **1a** to $Cp_2Zr(CH_3)_2$ resulted in no appreciable reaction at 25 °C and only minimal reaction at higher temperatures (e.g., 80 °C, 24 h). *It is of particular interest that heteroannulations of the above variety can be readily effected using catalytic quantities of $CpTiCl_3$ at 25 °C* (Scheme III).

The synthetic generality of this new transition metal based method for heteroannulation was subsequently tested by its application to the construction of a variety of representative ring systems (Table I).[14]

The reactive azametalletines **3** formed as intermediates in stoichiometric cyclization reactions could be *selectively* functionalized on carbon or nitrogen by the use of appropriate carbon-centered electrophiles. Accordingly, treatment of representative azametalletines (e.g., **3a**) with acyl cyanides[15] or nitriles gave rise to exclusive functionalization at carbon, leading to the formation of vinylogous amides (e.g., **8**) or vinylogous amidines [(e.g., **7** (vide infra)], respectively. By way of contrast, acylation of azametalletines with acyl chlorides led to selective functionalization at nitrogen to provide enamides such as **9** (Scheme IV).

The foregoing examples provide a concise illustration of the synthetic potential of this new approach to heterocycle annulation. The utilization of this novel heteroannulation procedure for the synthesis of representative indolizidine alkaloids[16] as well as related naturally occurring ring systems will be described in future accounts from these laboratories.

Acknowledgment. Support for this research by grants from the Alfred P. Sloan Foundation, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation is gratefully acknowledged.

Supplementary Material Available: Listings of spectroscopic and analytical data for the compounds **1a–e**, **4a–e**, and **7–9** (7 pages). Ordering information is given on any current masthead page.

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(12) This is not surprising in that the only reported examples of isolable group IV metalletines are derived from the reaction of imidozirconocene complexes that possess a bulky R group on nitrogen with diphenylacetylene.[6a] Attempts to directly characterize the adduct **6** by ^1H NMR spectroscopy were complicated by the presence of trace amounts of paramagnetic impurities.

(13) Lund, E. C.; Livinghouse, T. *Organometallics* **1990**, *9*, 2426.

(14) A representative experimental procedure is as follows for **3,4-dihydro-5-benzyl-2*H*-pyrrole (4a)**. **Method A**: To $CpTiCl_3$ (44 mg, 0.2 mmol) in THF (3 mL) was added i-Pr_2NEt (70 μL, 0.4 mmol) followed by dropwise addition of a solution of **1a** (159 mg, 1 mmol) in THF (2 mL). After 30 min, a few drops of 5% methanolic NaOH were added, and the reaction mixture was taken to dryness. The solids were triturated with hexane, and the organic phase was filtered through powdered K_2CO_3. Concentration of the organic phases afforded 149 mg (94%) of **4a** as the sole reaction product. **Method B**: To $CpTiCl_3$ (219 mg, 1 mmol) in THF (3 mL) at 0 °C was added CH_3Li (1.4 M in Et_2O, 1.43 mL, 2 mmol). The reaction mixture was warmed to 25 °C over 15 min, and **1a** (159 mg, 1 mmol) in THF (2 mL) was added dropwise over 5 min. After 1 h, 5% methanolic NaOH (0.5 mL) was carefully added, and the reaction mixture was taken to dryness. Trituration with hexane, followed by filtration through powdered K_2CO_3 and concentration afforded **4a** in 96% yield. In cases where filtration through K_2CO_3 was not sufficient, the product was filtered through a small plug of silica (1:1 Et_2O–hexane). **Method C**: To $CpZrCl_3\cdot DME$ (176 mg, 0.5 mmol) suspended in THF (1.5 mL) maintained at 0 °C was added CH_3Li (1.4 M in Et_2O, 0.71 mL, 1 mmol). After 1.5 h, the reaction mixture was warmed to 25 °C, and **1a** (80 mg, 0.5 mmol) in THF (0.4 mL) was added. After 10 min the reaction mixture was diluted with hexane, stirred for 20 min, and then allowed to settle. The organic phase and one 1:1 Et_2O–hexane wash of the solids were filtered through silica gel and concentrated to give **4a** (66 mg, 83%): ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (m, 5 H, Ph), 3.83 (m, 2 H, NCH_2), 3.68 (s, 2 H, $PhCH_2$), 2.39 (m, 2 H, $N{=}CCH_2$), 1.83 (m, 2 H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.56, 137.12, 129.02, 128.57, 126.57, 61.05, 40.75, 36.53, 22.29; IR (film) 3100–2850, 1604, 1496 cm^{-1}; high-resolution mass spectrum calcd for $C_{11}H_{13}N$ (M^+) 159.1048, found 159.1046.

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(16) McGrane, P. L.; Livinghouse, T. *J. Org. Chem.* **1992**, *57*, 1323.

Group-Transfer Polymerization Using Cationic Zirconocene Compounds

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The chemistry of cationic metallocene compounds (e.g, **1**) of the group 4 transition elements has attracted recent attention; such compounds function as useful models for the catalytic intermediates involved in Ziegler–Natta (Z–N) polymerization and hydrogenation of simple olefins.[1] These compounds have also been shown to be potentially useful in organic synthesis. For example, such compounds function as catalysts for the preparation of substituted pyridines,[2] and related heteroatom derivatives function

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(1) For leading references, see: (a) Jordan, R. F.; Bajgur, C. S. *J. Am. Chem. Soc.* **1986**, *108*, 7410. (b) Bochmann, M.; Wilson, L. M. *J. Chem. Soc., Chem. Commun.* **1986**, 1610. (c) Jordam R. F.; LaPointe, R. E.; Bajgur, C. S.; Echols, S. F.; Willett, R. *J. Am. Chem. Soc.* **1987**, *109*, 4111. (d) Bochmann, M.; Wilson, L. M.; Hursthouse, M. B.; Short, R. L. *Organometallics* **1987**, *6*, 2556. (e) Jordan, R. F. *J. Chem. Educ.* **1988**, *65*, 285. (f) Hlatky, G. G.; Turner, H. W.; Eckman, R. R. *J. Am. Chem. Soc.* **1989**, *111*, 2728. (g) Jordan, R. F.; LaPointe, R. E.; Bradley, P. K.; Baenziger, N. *Organometallics* **1989**, *8*, 2892. (h) Jordan, R. F.; LaPointe, R. E.; Baenziger, N.; Hinch, G. D. *Ibid* **1990**, *9*, 1539. (i) Park, J. W.; Henling, L. M.; Schaefer, W. P.; Grubbs, R. H. *Ibid.* **1990**, *9*, 1650.

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