amenable to reduction via this method.

The reduction of conjugated dienes is illustrated with **8** and **9**. The sole product of the reduction of **8** is cyclohexenylidenecyclohexane (90%), corresponding to exclusive 1,4-dihydrogenation. However, **9** yields *trans*-1,4-diphenyl-2-butene and *trans*-1,4-diphenyl-1-butene in the ratio 2:1 (75%).

A very attractive ancillary feature of hole transfer promoted hydrogenation is the absence of hydrogenolysis, even of carbon–sulfur bonds. The reduction of **10** is efficient (88%), and the retention of the phenylthio function clearly contrasts with catalytic hydrogenation. Reduction of suitably ionizable aromatics is also feasible. Anthracene affords 9,10-dihydroanthracene (70%), but less ionizable substrates (phenanthrene, naphthalene) are inert.

Hole transfer promoted hydrogenation is experimentally convenient,[11] and the required reagents (**1**$^{+\cdot}$, **2a,b**) are readily available. The unique and superior selectivity characteristics of the reaction suggest potential synthetic utility. Mechanistically, the intervention of cation radical intermediates is strongly supported, but the likely subsequent involvement of carbocations and/or radicals remains to be established.

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Supplementary Material Available: Listings of experimental details and characterization data for the olefin hydrogenations mentioned in the text (6 pages). Ordering information is given on any current masthead page.

(11) The appropriate substrate is dissolved in dichloromethane solution (~0.15 M) and cooled to 0 °C. The hydride reagent (220 mol %) is then added, followed by **1**$^{+\cdot}$ (200 mol %). Both reagents are available from the Aldrich Chemical Company. The reaction mixture is stirred for 1 min to 1 h, depending upon the substrate (**3a** requires 1 h, anthracene ca. 0.5 h, and all other substrates in this study 1–2 min). The reactions are quenched with excess K_2CO_3/CH_3OH. Products are purified by ether/brine extraction followed by flash silica gel chromatography (hexane followed by 8:2 hexane/ethyl acetate).

The Helix-Forming Propensity of D-Alanine in a Right-Handed α-Helix

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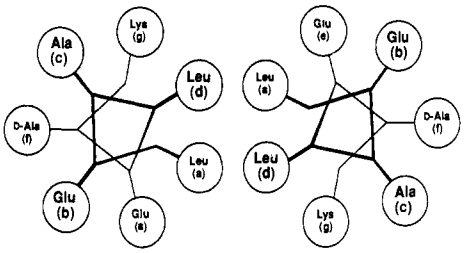
The design of peptides and proteins requires an understanding of the features that stabilize protein secondary, tertiary, and quaternary structures.[1] Toward this goal we have developed a model, two-stranded, coiled-coil peptide that allows one to determine the contributions of individual amino acids to the stability of α-helices[2] (Figure 1). This peptide adopts a random coil as a monomer in dilute aqueous solution, but forms α-helical dimers in more concentrated solution. The free energy of dimerization, $\Delta G°_{dim}$, can be determined by measuring the concentration dependence of α-helix formation as monitored by circular dichroism (CD). Systematic changes on the solvent-exposed face of the helices are then made and the resulting changes in $\Delta G°_{dim}$ measured. These changes can be interpreted in terms of their effect on α-helix formation, an obligatory step in dimerization.[2]



Ac·EWEALEKKLAALE-(D·Ala)·KLQALEKKLEALEHG·CNH$_2$

Figure 1. Helical wheel representation of the heptapeptide repeating unit used in the design of the helical pair. The sequence of the model peptide is shown at the bottom.

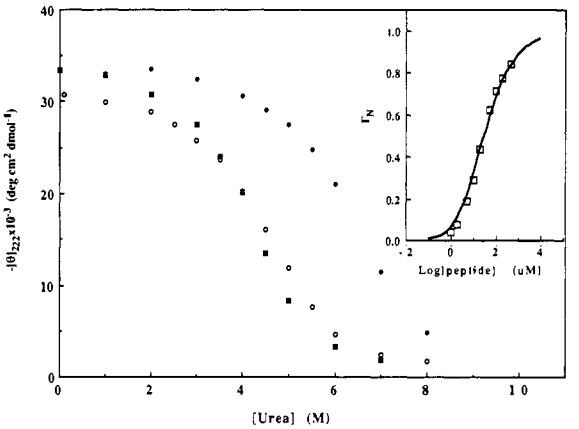


Figure 2. Urea denaturations of the L-Ala peptide (●), Gly peptide (■), and D-Ala peptide (○). $[\theta]_{222}$ was measured as described previously.[2] The helical contents of the peptides in the absence of urea are the same within experimental error (−34 000 ± 2000 deg cm^2 dmol^{-1}) Inset: Peptide concentration dependence[2] for the D-Ala peptide as measured by CD. F_N represents the fraction of coiled coil dimer as calculated from $[\theta]_{222}$. The fitted curve, describing a simple monomer–dimer equilibrium, was generated using MLAB (Civilised Software, Inc., Bethesda, MD).

In this paper, we investigate the effect of substituting D-Ala into our model system. Although D amino acids are used widely in peptides, their effect on the free energy of forming a right-handed α-helix has been unknown.

The model peptide described previously[2] was prepared with D-Ala in the guest site. In aqueous solution, the peptide has a CD spectrum with minima at 208 and 222 nm and a maximum at 192 nm, predictive of a right-handed α-helix. Figure 2 illustrates $[\theta]_{222}$ (a measure of the handedness and extent of α-helix formation) versus [urea] for peptides with Gly, L-Ala, and D-Ala at the guest position. Similar to Gly, D-Ala is destabilizing relative to L-Ala. $\Delta G°_{dim}$ was obtained from the concentration dependence of $[\theta]_{222}$ (Figure 2, inset), and $\Delta\Delta G°$ was found to be unfavorable by 0.95 kcal/mol for D-Ala as compared to 0.77 kcal/mol for Gly, with L-Ala as the standard.

Several features probably account for the destabilizing effect of D-Ala relative to L-Ala. The backbone angles available to D-Ala in the right-handed α-helical portion of the ϕ, ψ map are more restricted and of higher energy than for L-Ala. Also, there are unfavorable steric interactions between the C_β of D-Ala at position i and the carbonyl oxygen atoms from residues i and $i-1$ in a right-handed α-helix.[3]

Hermans and co-workers[3] have recently determined similar values for $\Delta\Delta G°$ between Gly, L-Ala, and D-Ala using perturbational molecular dynamics ($\Delta\Delta G°$ values for Gly and D-Ala are 1.1 and 1.2 kcal/mol, respectively, with L-Ala as the standard state). These theoretical values are in good agreement with our experimental results, given the large differences in the two methods.

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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.

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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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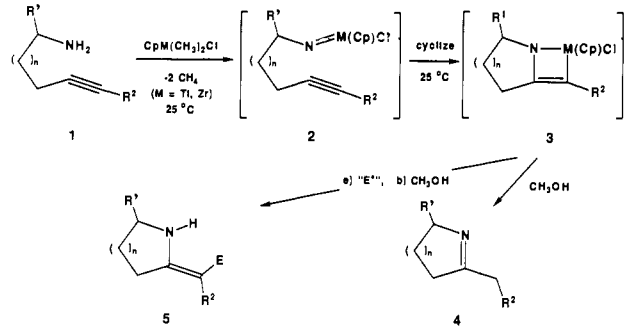
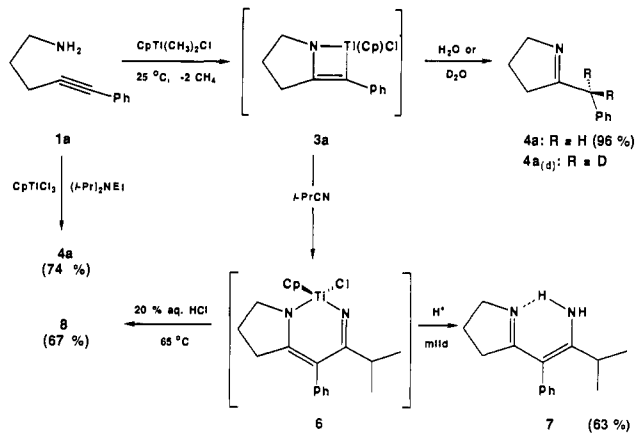
Strained heterometallacycles have recently become the focus of an increasing number of structural and synthetic studies. As a consequence of these investigations, zirconocene thioaldehyde complexes,[2] zirconaaziridines,[3,4] and transient azatitanacyclobutenes[5] have been identified as particularly 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 $(i\text{-Pr})_2NEt$ (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 $CpTi(CH_3)_2Cl$[10] (prepared in situ from $CpTiCl_3$ and 2 equiv of CH_3Li) 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_3OH) gave rise to the anticipated Δ^1-pyrroline **4a** in 96% yield. Deuteration of **3a** (D_2O) provided the corresponding dideuterio derivative $\mathbf{4a}_{(d)}$. 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

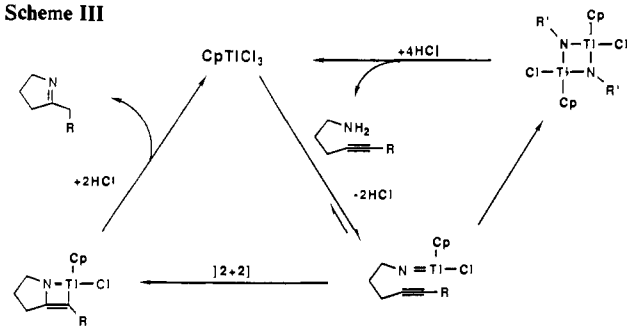
Scheme I



Scheme II



Scheme III



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