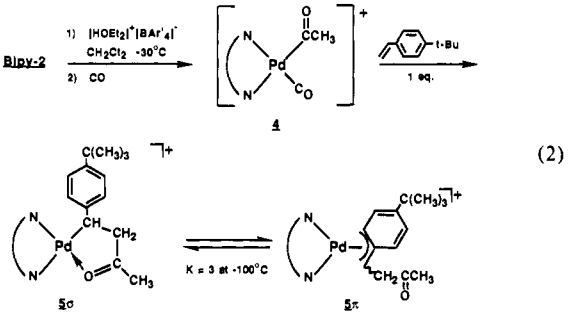
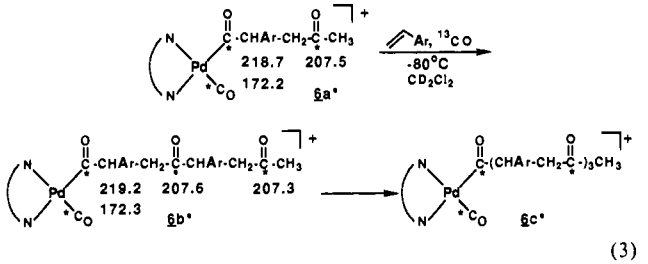
a substantial degree of stereoregularity at C_2.[7] For example, in the decoupled ^{13}C spectrum, CH_2 shows a single major resonance at 43.4 ppm, with minor bands (ca. 5%) appearing at 44.7 and 44.2 ppm. Epimerization of **1** using ($NaOH/CH_3OH$, THF) and reprecipitation yields an atactic polymer which exhibits multiple bands for CH_2: 46.1, 44.9, 44.7, and 43.4 ppm. Similarly, the ^1H NMR spectrum exhibits major doublets for H_{ortho} and H_{meta} at δ 6.16 and 7.10 and minor doublets at δ 6.85, 6.97, 7.16, and 7.25. The atactic polymer shows a complex envelope of bands in the δ 6.5–7.5 range.

A ^{13}C NMR study has revealed details concerning the chain growth process and the catalyst resting state. For the mechanistic study, an acetonitrile-free catalyst **5** was prepared as shown in eq 2. The chelate species **5**σ is in very rapid equilibrium with



(2)

the π-benzyl complex **5**π; static ^1H and ^{13}C spectra can be obtained below −80 °C indicating a **5**σ:**5**π ratio of ca. 3:1.[5,8] Intermediate **4** has been spectrally identified.[9a,b] Preparation of **5*** using 99% ^{13}CO followed by exposure to ^{13}CO (1 atm) in CD_2Cl_2 at −80 °C yields the labeled carbonyl acyl complex **6a*** which shows three characteristic carbonyl bands at 172.2, 218.7, and 207.5 ppm for the PdCO, the α-acyl carbonyl, and $CH_2C(O)CH_3$, respectively. Treatment of a CD_2Cl_2 solution of **6a*** with ca. 6 equiv of *tert*-butylstyrene under 1 atm of ^{13}CO results in chain growth which can be monitored by ^{13}C NMR spectroscopy at temperatures between −80 and −60 °C.[9a] The first species detected upon insertion is **6b*** followed by **6c***. In a related ^{13}C NMR experiment, unlabeled **5** was reacted with ^{13}CO and ca. 10 equiv of 4-*tert*-butylstyrene. The first two insertion products, analogous to **6b*** and **6c*** but with unlabeled end groups, confirmed the assignments for $^{13}C(O)CH_3$ bands in **6a,b*** and allowed identification of the internal carbonyl resonances of **6c***. Further insertions led to an envelope of bands in the 207–208 ppm range continually increasing in intensity relative to the PdCO and PdCO(R) bands. These experiments clearly indicate that the carbonyl acyl complex form of the catalyst, **6**, is the resting state and that olefin insertion is the slow step in chain growth. The structure of **5** establishes the regiochemistry of the insertion reaction which is confirmed by structural assignment of **6a**.



(3)

(7) Stereoregularity has also been noted by Corradini[2c] for insoluble fractions of $(CH(C_6H_5)CH_2CO)_n$ from the mixture of polymers obtained using the Drent procedure.[2a]

(8) For Pd(II) chelate structures related to **5a**, see: (a) Brumbaugh, J. S.; Whittle, R. R.; Parvez, M.; Sen, A. *Organometallics* **1990**, *9*, 1735–57. (b) Ozawa, F.; Hayashi, T.; Koide, H.; Yamamoto, A. *J. Chem. Soc., Chem. Commun.* **1991**, 1469–70.

(9) (a) See supplementary material for complete spectroscopic details. (b) **4**: key NMR parameters $^{13}C(H)$ NMR (CD_2Cl_2, −80 °C) δ 217.4 ($C(O)CH_3$), 172.5 (PdCO), 40.6 (CH_3); ^1H NMR (CD_2Cl_2) δ 2.77 (CH_3). (2,2′-Bipy)Pd(CH_3)CO$^+$$BAr'_4^-$ **7** can be prepared as a stable, isolable precursor to **4**.[5]

These systems[10] represent a rare example of a living alternating copolymerization.[11] The living nature of the polymerization has been verified by demonstrating a linear relationship between $\langle M_n \rangle$ and the degree of monomer conversion together with $\langle M_w \rangle / \langle M_n \rangle$ values for **1** which approach 1.0. Figure 1 illustrates data for a typical polymerization carried out at 4 atm of CO with Phen-**3** as catalyst. The compatability of these catalysts with a variety of functional groups and the presence of readily modified carbonyl groups suggest that a variety of functionalized polymers with well-defined structures and narrow molecular weight distributions will be accessible.

Acknowledgment is made to the National Science Foundation (CHE-8705534) for support of this work. J.C.B. was supported by an NSF-ROA grant and F.C.R. by a Department of Education fellowship. We thank Elise Maury for obtaining GPC data.

Supplementary Material Available: Details of synthesis and listings of spectral data for **1**, Bipy-**3**, Phen-**3**, **4**, **4***, **5**σ, **5**π, **5***, **6a**, **7**, and **7*** and listing of ^{13}C NMR data for chain growth experiments **5** → **6a** → **6b** → **6c** (14 pages). Ordering information is given on any current masthead page.

(10) Other chlorobenzene-soluble co- and terpolymers prepared using these catalysts include norbornene/CO, styrene/ethylene/CO, styrene/propylene/CO, and *p*- and *m*-methylstyrene/CO.

(11) Inoue has reported living alternating copolymerizations using aluminum porphyrin initiators for the synthesis of aliphatic polycarbonates and polyesters: (a) Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1985**, *107*, 1358. (b) Kojima, F.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1986**, *108*, 391. (c) Aida, T.; Ishikawa, M.; Inoue, S. *Macromolecules* **1986**, *19*, 8.

$[Ru(\eta^5\text{-}C_5Me_5)(\eta^5\text{-}C_5F_5)]$: The First Transition-Metal Complex Containing a Perfluorocyclopentadienyl Ligand

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Since the discovery of ferrocene,[1] the η^5-cyclopentadienyl ligand and its substituted analogues have become the most ubiquitous in organometallic chemistry, and many derivatives are now readily accessible.[2] While most cyclopentadienyl complexes are prepared by reaction of the appropriate cyclopentadiene or cyclopentadienyl anion with a suitable transition-metal complex, the first perhalocyclopentadienyl complexes were prepared by repetitive metalation/halogenation exchange reactions.[3] A subsequent approach to complexes containing η^5-C_5X_5 (X = Cl, Br, I) ligands has involved reactions of diazotetrahalocyclopentadienes with the appropriate metal halide,[4] and permercuration/perhalogenation of ferrocene has also been used to prepare perhaloferrocenes.[5]

(1) (a) Kealy, T. J.; Pauson, P. L. *Nature (London)* **1951**, *168*, 1039. (b) Wilkinson, G.; Rosenblum, M.; Whiting, M. C.; Woodward, R. B. *J. Am. Chem. Soc.* **1952**, *74*, 2125.

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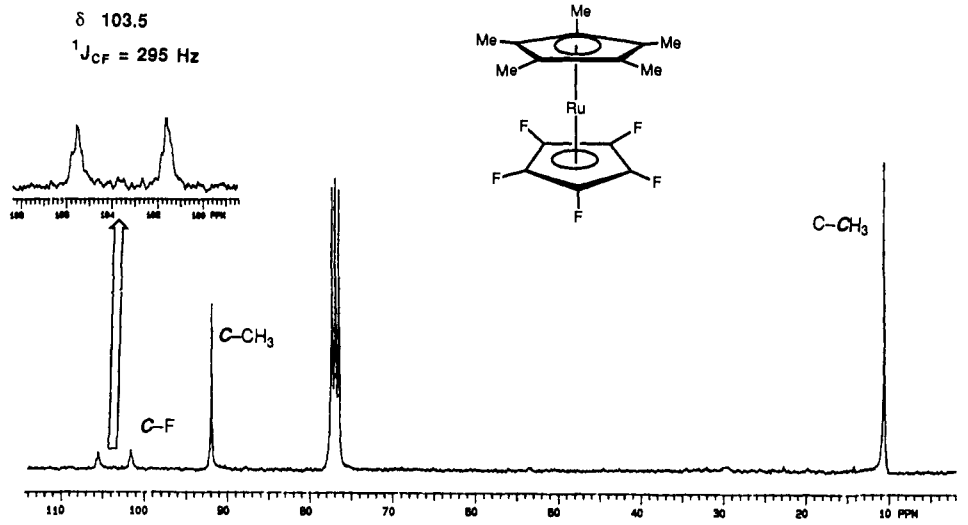
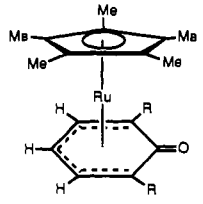
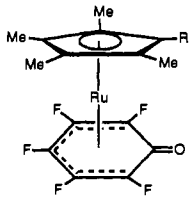


Figure 1. $^{13}C\{^1H\}$ NMR spectrum (75 MHz) of **3a** in $CDCl_3$ solution.

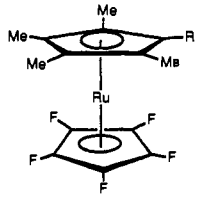
While two examples of monofluorocyclopentadienyl complexes have been reported,[6] the absence of any transition-metal complexes containing a perfluorocyclopentadienyl ligand is notable. Attempts to replace chlorine with fluorine by reactions of F^- sources with perchlorocyclopentadienyl complexes have failed.[3b] Although the $C_5F_5^-$ anion is known,[7] attempts to use it as a precursor to transition-metal complexes have also been frustratingly unsuccessful.[8] Here we report the first successful synthesis of a perfluorocyclopentadienyl complex.



1 a. R = H
b. R = ^{t}Bu



2 a. R = Me
b. R = Et



3 a. R = Me
b. R = Et

Complexes **1a,b**, which contain η^5-oxocyclohexadienyl ligands, have been described recently.[9,10] Reaction of $[RuCp^*(CH_3CN)_3]Cl$[11] ($Cp^* = C_5Me_5$) with the thallium(I) salt of pentafluorophenol in acetonitrile affords the fluorinated analogue **2a**.[12] The ^{19}F NMR spectrum of **2a** contains three multiplet resonances (−186.0, −190.5, and −197.3 ppm), shifted upfield by 20–30 ppm from those of pentafluorophenol[13] and assigned to the meta, ortho, and para F substituents of the η^5-pentafluorooxocyclohexadienyl ligand, respectively. In comparison, coordination of hexafluorobenzene to Cr results in a significant upfield shift in the ^{19}F NMR spectrum (δ −193.3 for $[Cr(\eta^6\text{-}C_6H_6)(\eta^6\text{-}C_6F_6)]$ versus δ −162.9 for C_6F_6).[14] In the infrared spectrum of **2a**, $\nu_{C=O}$ appears at 1620 cm^{-1}, ca. 80 wavenumbers higher than that in the hydrocarbon analogues **1a**[9] and **1b**[10] (both 1542 cm^{-1}). The mass spectrum and microanalytical data for **2a** are also consistent with its formulation. In particular, a significant parent ion peak is observed (49.7%), with a small peak due to loss of CO (4.6%); the base peak results from loss of C_6F_5OH, but a small peak at m/e 257 (7.4%) corresponding to $Ru(C_5F_5)^+$ is observed.[12]

Flash vacuum pyrolysis (FVP) of **2a** at 750 °C under vacuum (10^{-4} Torr) results in CO extrusion and formation of the pentafluorocyclopentadienyl complex **3a** in 20% yield, with **2a** recovered in 60% yield.[15] The ^1H and ^{19}F NMR spectra of **3a** show sharp singlets at 1.68 and −213.24 ppm respectively, consistent with a 5-fold symmetric metallocene. Curiously, the ^{19}F chemical shift is only 4 ppm upfield from that reported for the $C_5F_5^-$ anion (δ −209 ppm).[8] Further structural confirmation is provided by the

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(12) In a typical preparation, $[Tl(OC_6F_5)]$ (0.234 g, 0.604 mmol) was added to an acetonitrile (25 mL) solution of $[RuCp^*(CH_3CN)_3]Cl$ (obtained by refluxing a CH_3CN solution of $[RuCp^*Cl]_4$ (0.157 g, 0.578 mmol Ru) for 2 h) and stirred for 1 h. The solvent was removed in vacuo, and the yellow-orange solid was allowed to sit under vacuum overnight. Extraction with CH_2Cl_2 and filtration through Celite yielded an off-white powder after removal of the solvent. White crystals of **2a** (0.195 g, 80% yield) could be obtained by sublimation under vacuum at 150 °C or by extraction and recrystallization from $MeOH/H_2O$: ^1H NMR (C_6D_6) δ 1.40 (s, Cp*); ^{19}F NMR (C_6D_6) δ −186.0 (m, 2 F, *m*-C_6F_5O), −190.5 (m, 2 F, *o*-C_6F_5O), −197.3 (tt, 1 F, *p*-C_6F_5O), J_{om} = 30.7 Hz, J_{op} = 14.2 Hz, J_{mp} = 42.6 Hz; IR (KBr) $\nu_{C=O}$ 1620 cm^{-1}; EI (70 eV) mass spectrum [m/e using ^{102}Ru (relative intensity)] 420 (49.7) P^+, 392 (4.6) $P^+ - CO$, 377 (4.0) $P^+ - COCH_3$, 373 (4.1) $P^+ - COF$, 257 (7.4) $Ru(C_5F_5)^+$, 236 (100) $P^+ - C_6F_5OH$. Anal. Calcd for $C_{16}H_{15}F_5ORu$: C, 45.83; H, 3.61. Found: C, 45.99; H, 3.71.

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(15) In a typical experiment, **2a** (0.0558 g, 0.133 mmol) is slowly heated to 200 °C under dynamic vacuum (10^{-4} Torr) and allowed to pass through a quartz tube (0.5 cm × 60 cm) at 750 °C. White solid condenses at ambient temperature in the exit tube and can be washed out with CH_2Cl_2. Elution through silica (1 cm) with CH_2Cl_2 (ca. 20 mL) yields $[RuCp^*(C_5F_5)]$ (**3a**: 0.010 g, 20% yield) upon evaporation. Elution with acetone (ca. 30 mL) yields 0.030 g (54%) of unreacted **2a**. For **3a**: ^1H NMR (C_6D_6) δ 1.68 (s, Cp*); ^{19}F NMR (C_6D_6) δ −213.24 (s, C_5F_5); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 103.50 (d, $^1J_{CF}$ = 295 Hz, C_5F_5), 91.97 (s, $C_5(CH_3)_5$), 10.49 (s, $C_5(CH_3)_5$); IR (KBr) 2928 (w), 1571 (s), 1387 (m), 1032 (w), 941 (s), 580 (s), 486 (m) cm^{-1}; EI (70 eV) mass spectrum [m/e using ^{102}Ru (relative intensity)] 392 (100) P^+, 377 (25.7) $P^+ - CH_3$, 373 (21.3) $P^+ - F$, 257 (28.6) $Ru(C_5F_5)^+$, 231 (41.2) $P^+ - C_5F_5H_6$, 134 (98.7) $C_{10}H_{14}^+$, 119 (99.0) $C_9H_{11}^+$. Anal. Calcd for $C_{15}H_{15}F_5Ru$: C, 46.04; H, 3.86. Found: C, 45.93; H, 4.00.

$^{13}C\{^1H\}$ NMR spectrum (Figure 1), which shows two singlets at 91.97 and 10.49 ppm for the Cp* ligand and a somewhat broader doublet ($^1J_{CF}$ = 295 Hz) at 103.50 ppm for the carbons of the C_5F_5 ligand. The single ^{13}C resonance strongly coupled to a single fluorine provides compelling evidence for the pentafluorocyclopentadienyl ligand. The value of $^1J_{CF}$ for the C_5F_5 ligand is similar to that found in $[Cr(\eta^6\text{-}C_6H_6)(\eta^6\text{-}C_6F_6)]$ (303 Hz).[14c] Finally, the mass spectrum of **3a** exhibits fragmentation behavior quite different from that of precursor **2a**, in which the base peak results from loss of the fluorinated portion of the molecule as C_6F_5OH. In contrast, the parent ion peak of **3a** is the most intense, and no peak due to $[Ru(C_5Me_5)]^+$ is observed. However, the peak corresponding to $[Ru(C_5F_5)]^+$ (28.6%) is prominent. Together with the microanalytical data,[15] the NMR and mass spectra provide an unambiguous characterization of **3a**.

Although crystals of **2a** and **3a** suitable for X-ray crystallography were obtained, attempts to refine both structures revealed a 2-fold disorder.[16] In an attempt to circumvent this problem, the η^5-C_5Me_4Et analogues **2b** and **3b** were also prepared[17] and found to have spectroscopic properties similar to **2a** and **3a**. Unfortunately, they were also found to suffer from the same disorder problem.[16]

Further work to extend this methodology to other complexes, to explore the chemistry of the perfluorocyclopentadienyl ligand, and to obtain suitable crystallographic samples is in progress.

Acknowledgment. We are grateful to the Air Force Office of Scientific Research (Grant AFOSR-91-0227) and the National Science Foundation for generous support of our research. We are especially grateful to Professor Arnold L. Rheingold, University of Delaware, for repeated efforts to obtain X-ray crystal structures. A generous loan of ruthenium chloride from Johnson-Matthey Aesar/Alfa is gratefully acknowledged.

(16) Rheingold, A. L. Personal communication.

(17) Data for **2b**: ^1H NMR (C_6D_6) δ 1.90 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 1.44 (s, 6 H, CH_3), 1.42 (s, 6 H, CH_3), 0.64 (t, 3 H, CH_2CH_3); ^{19}F NMR (C_6D_6) δ -185.4 (m, 2 F, *m*-C_6F_5O), -190.1 (m, 2 F, *o*-C_6F_5O), -196.8 (tt, 1 F, *p*-C_6F_5O), J_{om} = 30.4 Hz, J_{op} = 14.1 Hz, J_{mp} = 42.7 Hz; IR (KBr) $\nu_{C=O}$ 1618 cm^{-1}. Anal. Calcd for $C_{17}H_{17}F_5ORu$: C, 47.11; H, 3.95. Found: C, 47.18; H, 3.82. For **3b**: ^1H NMR (C_6D_6) δ 2.13 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 1.71 (s, 6 H, CH_3), 1.69 (s, 6 H, CH_3), 0.85 (t, 3 H, CH_2CH_3); ^{19}F NMR (C_6D_6) δ -212.56 (s, C_5F_5). Anal. Calcd for $C_{16}H_{17}F_5Ru$: C, 47.41; H, 4.23. Found: C, 47.57; H, 4.39.

Probing Qualitative Conformation Differences of Multiply Protonated Gas-Phase Proteins via H/D Isotopic Exchange with D_2O

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We report a method for qualitatively probing the higher order structure of protein molecular ions in the gas phase and demonstrate the ability to distinguish the native and disulfide bond reduced forms in solution by gas-phase reactions of multiply protonated bovine proinsulin and α-lactalbumin. With the recent development of soft ionization methods based upon electrospray ionization (ESI)[1,2] allowing the formation of multiply charged ions from large polypeptides and proteins, new opportunities for probing structural characteristics and reactivity have arisen. Previous studies of multiply protonated cytochrome *c* reactions with dimethylamine[3] and 1,6-diaminohexane[4] in a quadrupole ion trap mass spectrometer have shown differences in the reactivity of various charge states. Chait and co-workers have also shown that H/D isotopic exchange with D_2O in solution can be useful for qualitatively probing protein structure.[5] Recent reports have indicated that various noncovalent associations, and perhaps elements of the higher order structure of macromolecular ions, may be preserved in the gas phase after ESI.[6] The method reported here invokes the use of thermal energy ion/molecule reactions of multiply protonated proteins with D_2O in order to probe *gas-phase* structural differences.

In our studies, multiply protonated protein molecules formed via ESI are transported through a dual "inlet/reaction" capillary interface, described elsewhere.[7] The first (inlet) capillary is temperature-regulated in order to assist droplet evaporation and ion desolvation. At the junction with the second capillary, D_2O (or H_2O) gas is added, and subsequent thermal energy reactions between the partially or completely desolvated ions occur in a second temperature-regulated capillary prior to expansion into vacuum. The extent of deuterium isotopic exchange is determined from the change in molecular weight measured with a triple quadrupole mass spectrometer.[2,7]

The extent of H/D exchange for the individual proteins is dependent upon the reaction temperature. Most of the presented data was obtained with the reaction capillary at an externally measured temperature of 145 °C. Above 145 °C thermally induced dissociation[8] increases for ion formed from the reduced species. When multiply protonated molecules generated via ESI from native bovine proinsulin react with gas-phase D_2O, the measured average molecular mass (M_r) calculated from the ESI *m/z* spectrum is 8715.0 ± 1.4 Da, 33.2 Da higher than the nondeuterated molecule (M_r = 8681.8 ± 1.4 Da).[9] This corresponds to approximately 25.2% deuterium incorporation (based upon 132 potentially labile hydrogens in the native molecule).[10] Upon reduction of the three disulfide bonds in proinsulin with 1,4-dithiothreitol, the number of potentially labile hydrogens increases to 138 and the measured M_r to 8687.8 ± 1.4 Da. However, when this species is electrosprayed and allowed to react with gas-phase D_2O, the measured M_r is 8705.2 ± 1.4 Da. This corresponds to an increase in M_r of only 17.4 Da or approximately 12.6% deuterium incorporation for ions formed from reduced proinsulin. Therefore, the ratio of the differences in molecular weight after reaction with D_2O for ions formed from the native (*N*) and reduced (*R*) proteins, $\Delta N/\Delta R$, is 1.91 ± 0.25,[11] after

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(8) Rockwood, A. L.; Busman, M.; Smith, R. D. *Rapid Commun. Mass Spectrom.* **1991**, *5*, 582.

(9) To ensure that the increase in M_r was not due to the addition of solvent molecules, H_2O was added to the reaction capillary and the M_r of the protein was measured. The M_r value obtained in these experiments matched exactly the M_r measured without H_2O added.

(10) Determined by totaling the number of hydrogens attached to the heteroatoms N, O, and S. The total number of potentially labile hydrogens for α-lactalbumin is 227 for the native form and 235 for the reduced form.

(11) The experimental error associated with the ratio is based on the precision in the *m/z* measurement, obtained from the summation of five scans.

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