A New, Convenient Method for Labeling Cyclopentadienyl Ligands with Deuterium

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Summary: A new, convenient, and cost-effective method for labeling cyclopentadienyl ligands with deuterium has been developed. Heating a solution of Cp_2Ca-h_{10} in DMSO-d_6 (99.5% D) for 1 h at 150 °C afforded Cp_2Ca-d_{10} (97% D) cleanly in 95% isolated yield. For the ring-substituted bis(1-cyclopentenyl)calcocene, H/D exchange occurred at the 2,5-positions of the 1-cyclopentenyl substituents as well as at the cyclopentadienyl rings. H/D exchange between rac-$Ph_2C_2H_2(C_5H_4)_2$-Ca and DMSO-d_6, by contrast, was extremely inefficient and was accompanied by substantial ansa-calcocene decomposition.

Introduction

A facile method for labeling the cyclopentadienyl ligands of metallocenes with deuterium is desirable for a number of reasons, primary among which is the advantage of ^{2}H NMR over ^{1}H NMR spectroscopy under special circumstances. For instance, deuterium labeling can aid in the characterization of paramagnetic compounds, for which ^{2}H NMR line widths are narrower than corresponding ^{1}H NMR line widths.[1] Solid-state ^{2}H NMR spectroscopy has been useful for examining deuterium-labeled metallocenes in the solid state and in various host matrixes.[2] Deuteration of the cyclopentadienyl rings can also assist with the characterization of metallocenes by other spectroscopic techniques such as vibrational spectroscopy,[3] EPR,[4] and photoelectron spectroscopy.[5] It has also been used to elucidate the kinetics and mechanisms of reactions involving metallocenes.[3a,6]

To date, the preparation of deuterated cyclopentadienyl rings has generally been accomplished by base-catalyzed deuteration of cyclopentadiene in D_2O, followed by extraction of the deuterium-labeled cyclopentadiene,[7] which is then metalated. This method is rather laborious, since the process must be repeated multiple times in order to incorporate a high percentage of deuterium into the cyclopentadienyl ring. Transition-metal-catalyzed H/D exchange directly on the cyclopentadienyl rings of the metallocene has also been demonstrated; however, these processes involve either expensive catalysts or conditions that may be unsuitable for highly reactive cyclopentadienyl transition-metal complexes.[8] Acid-catalyzed ring deuteration has been demonstrated in ferrocenes but is limited to that system.[9] An efficient, one-pot method for preparing 89.4% labeled (C_5D_5)-Tl was reported in 1978.[10] Although cyclopentadienylthallium compounds are versatile reagents for transferring cyclopentadienyl ligands to transition metals, the toxicity of thallium is a significant drawback to this method.

We describe here a new, convenient, and general one-pot method for deuterating cyclopentadienyl ligands via H/D exchange between their calcocene compounds and DMSO-d_6. Among the advantages of this approach is the relative ease of isolation of the deuterium-labeled metallocene product and the ability to transfer the labeled cyclopentadienyl ligands directly from calcium to transition metals and lanthanide metals. It is a nontoxic alternative to the thallium-based method and is just as cost-effective, since DMSO-d_6 is comparable to D_2O in price. Furthermore, the procedure need only be performed once in order to achieve a high (97%) level of deuteration. This method is also applicable to ring-substituted calcocenes, although it is less effective for labeling the cyclopentadienyl rings of *ansa*-calcocene compounds.

Experimental Section

General Considerations. $Cp_2Ca(THF)_{1.5}$ (**1**; Cp = C_5H_5),[11] $\{(C_5H_7)C_5H_4\}_2Ca(THF)_2$ (**3**),[12] $\{Ph_2C_2H_2(C_5H_4)_2\}Ca(THF)_{1.5}$ (**4**),[13] Cp_2Mg,[14] $(C_5Me_5)_2Ca$,[15] and $Me_4C_2(C_5H_4)_2Mg$[16] were prepared as

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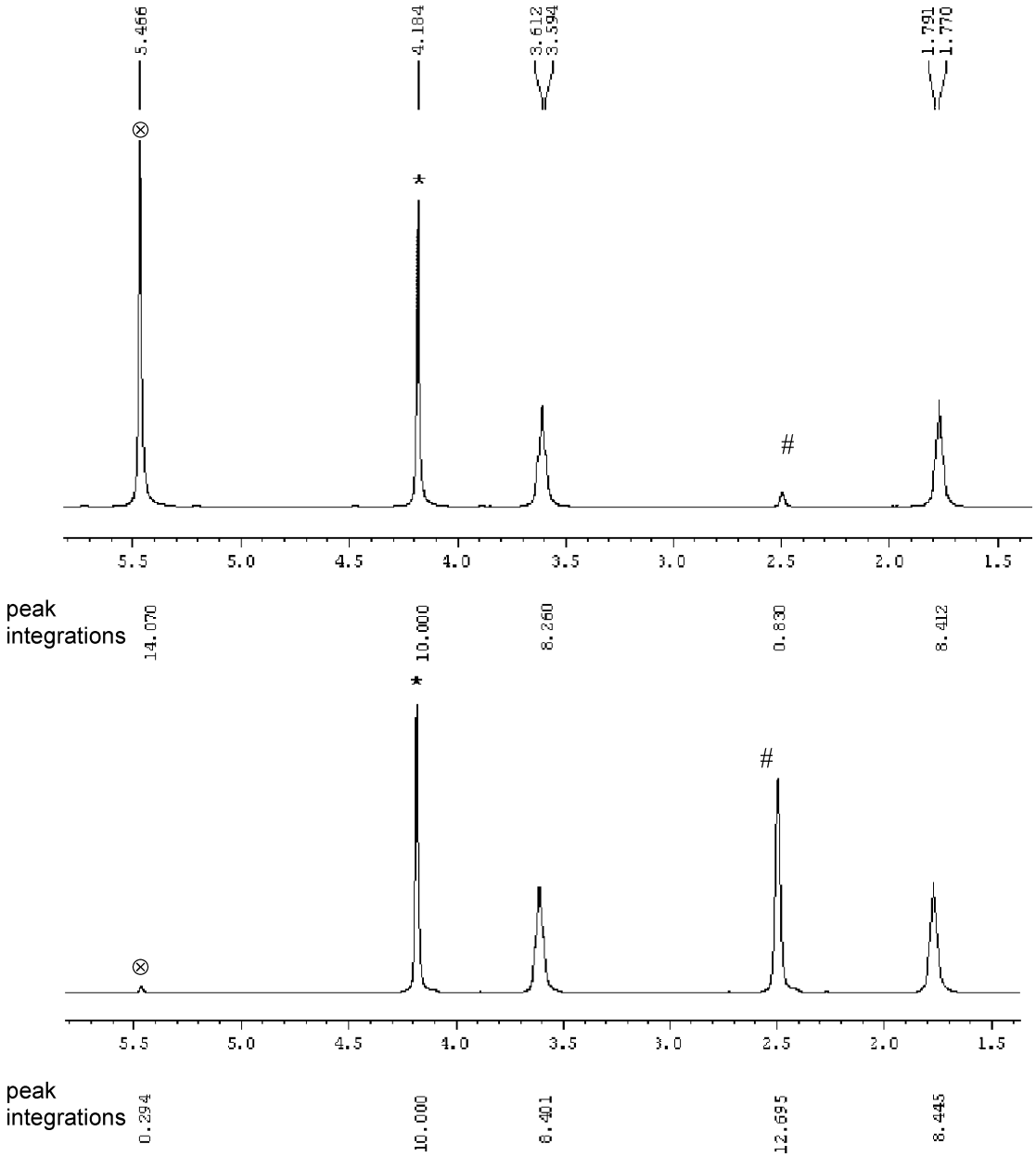

Figure 1. ^{1}H NMR spectra of (top) **1** in DMSO-d_6 before heating and (bottom) the same sample heated for 1 h at 150 °C: (⊗) Cp_2Ca; (#) DMSO; (*) internal Cp_2Fe standard.

described in the literature. Ferrocene and $FeCl_2$ were purchased from Aldrich and used as received. THF and DME (dimethoxyethane) were dried over and distilled from sodium/benzophenone immediately prior to use. DMSO-d_6 (99.5% D) was purchased from ACROS Organics and stored over Linde 4A molecular sieves. All compounds were handled and stored in a nitrogen-filled glovebox and were manipulated using argon and vacuum/Schlenk line techniques. IR spectra of the compounds were recorded as KBr pellets on an Avatar 370 FT-IR Thermo Nicolet spectrometer. NMR spectra were obtained on Bruker AMX 300 (300 MHz ^{1}H) and Bruker AVANCE 500 (500 MHz ^{1}H) spectrometers. All NMR tube scale reactions were performed on solutions of ∼20 mg of the metallocene in ∼0.6 mL of DMSO-d_6 (99.5 or 99.9% D) in sealed J. Young tubes with ferrocene as an internal reference.

Synthesis of $(C_5D_5)_2Ca$-d_{10} (1-d_{10}). A sealable glass reaction vessel was charged with $Cp_2Ca(THF)_{1.5}$ (0.600 g, 2.15 mmol) and 8 mL of DMSO-d_6 (99.5% D). Upon being heated at 150 °C, the calcocene dissolved completely and the reaction mixture turned pink. After 1 h, the solution was cooled to room temperature and a portion of the solution was transferred to an NMR tube. The ^{1}H NMR spectrum of the sample showed 97% deuterium incorporation into cyclopentadienyl rings of the calcocene (using the THF proton signals as an internal reference). No decomposition of the calcocene was apparent. The DMSO was removed from the reaction mixture under reduced pressure, and the remaining solid was heated at 100 °C overnight under a dynamic vacuum to remove any remaining solvent. The product was recrystallized from a 20 mL THF solution cooled at −78 °C, isolated by filtration, and dried overnight at 100 °C under a dynamic vacuum to afford 0.371 g (95% yield) of $(C_5D_5)_2Ca$ (97% D) as a pink-tinged white powder. ^{2}H NMR (THF-h_8, 303 K): 5.53 ppm (s). ^{13}C NMR (DMSO-d_6, 125 MHz,

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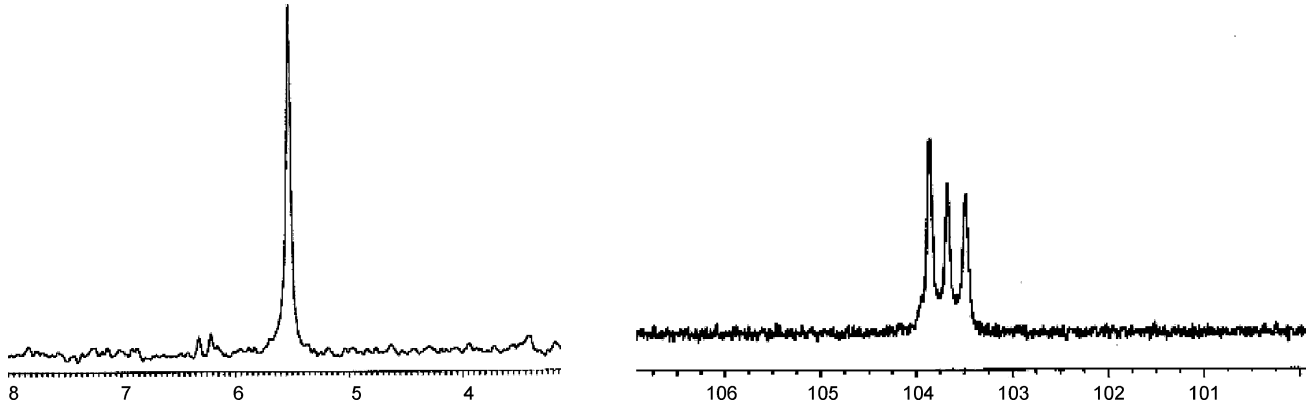


Figure 2. ^{2}H NMR spectrum (left) and ^{13}C NMR spectrum (right) of **1**-d_{10}.

323 K): 103.5 ppm (t, $^1J_{C-D}$ = 24.1 Hz). IR (KBr): 2284, 2250, 2238, 2119 cm^{-1}.

Synthesis of $(C_5D_5)_2Fe$ (2). The synthesis of ferrocene from Cp_2Ca and $FeCl_2$ was first reported in 1973.[17] A Schlenk vessel was charged with Cp_2Ca-d_{10} (50 mg, 0.28 mmol) and $FeCl_2$ (38 mg, 0.28 mmol). The solids were dissolved in 20 mL of DME, and the mixture was refluxed for 1 h under a blanket of argon. The solvent was removed under reduced pressure, and 39 mg (74% yield) of the ferrocene product was obtained by extracting the solid residue with pentane (3 × 10 mL) and drying the extract under reduced pressure. GC/MS analysis of an aliquot of the product dissolved in dichloromethane gave an isotope pattern for the parent ion that was most consistent with the theoretical model for 96% statistically deuterated ferrocene.[18]

Synthesis of *rac*{$Ph_2C_2H_2(C_5D_4)_2$}$Ca(THF)_{0.9}$ (4-d_8). In a sealable glass vessel, 450 mg of {$Ph_2C_2H_2(C_5D_4)_2$}$Ca(THF)_{1.5}$ (1.06 mmol) was partially dissolved in 10 mL of DMSO-d_6 (99.5% D). When the mixture was heated to 120 °C, the compound dissolved completely. After 16 days, the solvent was removed under dynamic vacuum and the solid was dried overnight a 100 °C under dynamic vacuum. The residue was extracted with THF (3 × 30 mL), and the combined extracts were concentrated to 20 mL and cooled to −78 °C. $Ph_2C_2H_2(C_5D_4)Ca(THF)_{0.9}$ crystallized from the solution and was isolated by filtration and dried under vacuum (yield: 172 mg, 43%). The ^{1}H NMR spectrum of the product indicated that 70% deuterium incorporation had occurred uniformly at all C−H positions of the cyclopentadienyl rings.

Deuteration of $[(C_5H_7)C_5H_4]_2Ca(THF)_{1.9}$ (3). The ^{1}H NMR spectrum of a sample of **3** in DMSO-d_6 (99.9% D) that had been heated at 100 °C for 1.5 h revealed a 78% decrease in the intensities of the cyclopentadienyl proton signals. The ^{1}H NMR signals of the protons at the 2- and 5-positions of the cyclopentenyl substituents also decreased in intensity, but only by 23−25%. Heating the sample at 100 °C for an additional 1 h resulted in ca. 10% decomposition of the sample, with no significant change in the intensities of the ^{1}H NMR signals after correcting for decomposition. In a separate experiment, heating a sample of **3** in DMSO-d_6 (99.9% D) for 1 h at 150 °C resulted in complete disappearance of the aforementioned proton signals with no apparent sample decomposition. The ^{2}H NMR spectrum of the sample confirmed the exchange of deuterium into the cyclopentadienyl ring and into the 2,5-positions of the cyclopentenyl subsituents.

Results and Discussion

While examining the reductive coupling of various fulvenes by activated calcium,[12] we discovered that the cyclopentadienyl ^{1}H NMR signals of unbridged calcocenes dissolved in DMSO-d_6 decreased in intensity over time (days) at room temperature, while those of the *ansa*-calcocenes decreased more slowly (weeks). Heating the solutions increased the rate of disappearance of the cyclopentadienyl proton signals in both cases.

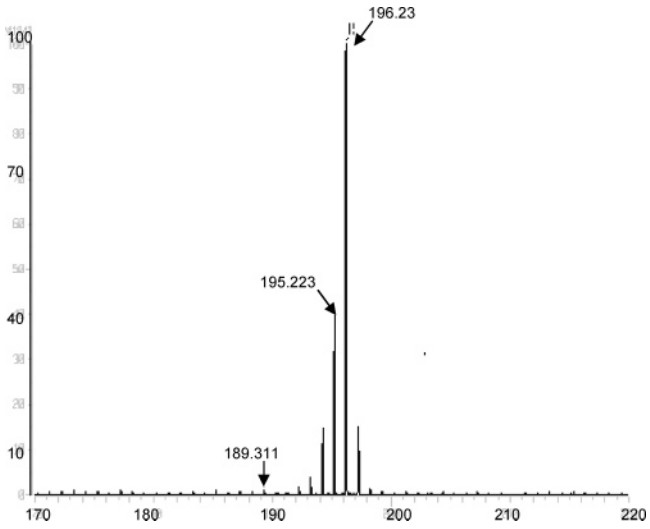
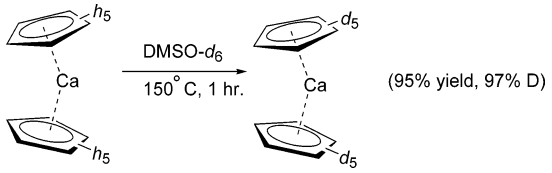


Figure 3. Molecular ion region of the EIMS spectrum of **2**-d_{10} formed from **1**-d_{10}.

We demonstrated that this deuterium labeling could be performed on a preparative scale by isolating $(C_5D_5)_2Ca(THF)_x$ (**1**-d_{10}) in nearly quantitative (95%) yield after heating a solution of **1** in DMSO-d_6 at 150 °C (eq 1). Analysis of the ^{1}H NMR



integrations of an aliquot of the solution after 1 h of heating revealed that 97% of the cyclopentadienyl protons had been replaced with deuterons (Figure 1).

The ^{13}C NMR spectrum of **1**-d_{10} in DMSO-d_6 showed three peaks centered at 103.5 ppm, with a coupling constant ($^1J_{C-D}$ = 24.1 Hz) similar to the $^1J_{C-D}$ value of benzene-d_6 (24 Hz). In addition, a single resonance at 5.53 ppm was observed in the ^{2}H NMR spectrum of **1**-d_{10} in THF-h_8 (Figure 2).The IR spectrum of **1**-d_{10} showed C−D stretching vibrations (2285−2219 cm^{-1}) that were shifted to lower energy from the C−H stretching vibration of **1** (3049 cm^{-1}).

Direct analysis of the level of deuterium incorporation in **1**-d_{10} by either EIMS or FABMS was precluded by the absence of

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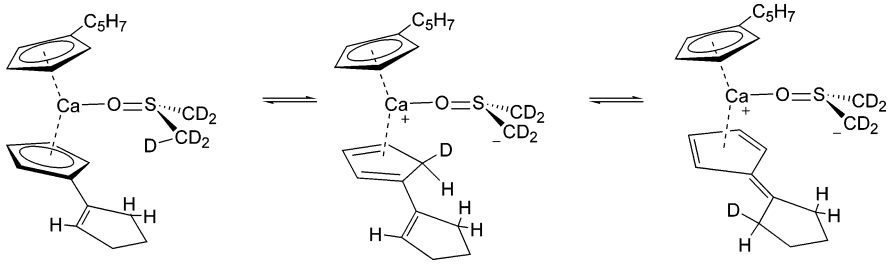
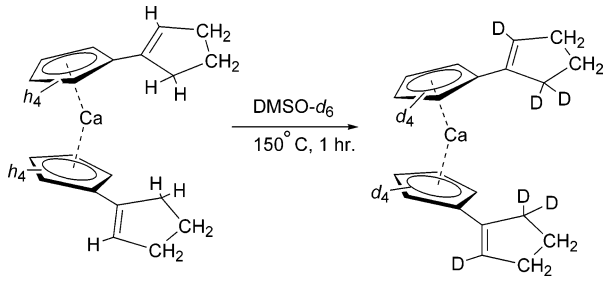


Figure 4. Proposed mechanism for H/D exchange between **3** and DMSO-d_6.

peaks for the molecular ion (M^+). Therefore, to confirm the extent of ring deuteration and the integrity of the labeled calcocene, $(C_5D_5)_2Fe$ (**2**) was prepared by reacting **1**-d_{10} with $FeCl_2$ in refluxing DME and the isotope distribution pattern of the parent ion of **2** was analyzed by EIMS. The isotope ratios for $\mathbf{2}^+$ (Figure 3) corresponded most closely with the theoretical ratios for 96% deuterated ferrocene.[18]

To determine the generality of this method for labeling cyclopentadienyl rings, we monitored the reaction between 1,1′-bis(1-cyclopentenyl)calcocene (**3**) and DMSO-d_6 (99.9%) by ^{1}H and ^{2}H NMR spectroscopy. After 1 h at 150 °C, complete deuterium incorporation was observed in the cyclopentadienyl C−H positions, as well as at the 2-CH and 5-CH_2 positions of the cyclopentenyl substituents (eq 2).



We propose that this H/D exchange proceeds by an acid/base mechanism that is facilitated by the coordination of DMSO-d_6 to the calcium. Labeling of the 2,5-positions of the cyclopentenyl substituents in **3** must occur via a fulvene intermediate, as depicted in Figure 4.

We were particularly interested in applying this deuterium labeling approach to *ansa*-calcocene compounds, which are useful reagents for preparing *ansa*-chromocene complexes,[19] the chemistry of which frequently involves paramagnetic species. Unfortunately, the *ansa*-calcocenes undergo H/D exchange more slowly than the unbridged calcocenes and are less stable to the reaction conditions. Heating a solution of $\{Ph_2C_2H_2(C_5D_4)_2\}Ca(THF)_{1.5}$ (**4**) in DMSO-d_6 at 120 °C for 16 days afforded only 70% deuterated *ansa*-calcocene (**4**-d_8) in 43% yield. ^{1}H NMR analysis of the product indicated that all cyclopentadienyl positions were deuterated to the same extent. No deuterium incorporation at the benzylic hydrogen position of the bridge was observed. The C_{2v} symmetry of the *ansa*-calcocene compound combined with only partial deuteration resulted in ^{13}C and ^{2}H NMR spectra that were too complex to allow definitive assignments. The IR spectrum of **4**-d_8 displayed the expected C−D stretching vibrations at 2241 and 2119 cm^{-1}. Interference of the bridge with H/D exchange in the *ansa*-calcocene is undoubtedly associated with a reduction in the conformational freedom of the cyclopentadienyl rings.

We also explored the possibility of labeling the methyl groups of $(C_5Me_5)_2Ca$[14] by this method. No change in the ^{1}H NMR spectrum was observed after heating an NMR tube sample of the compound in DMSO-d_6 at 150 °C for 3 h.

To determine if this H/D exchange chemistry is unique to calcocene, we also examined the behavior of Cp_2Mg[15] and $Me_4C_2(C_5H_4)_2Mg$[16] in DMSO-d_6. Due to its poor solubility in DMSO, Cp_2Mg was dissolved in a 5:1 mixture of DMSO-d_6 and THF-d_8. H/D exchange proceeded more slowly **(**1.5 h) at 150 °C for Cp_2Mg than it did for Cp_2Ca and led to the formation of free cyclopentadiene-d_6 (ca. 11%) along with Cp_2Mg-d_{10}, as established by ^{2}H NMR. Like the *ansa*-calcocene, the *ansa*-magnesocene compound underwent partial H/D exchange along with decomposition under the same conditions.

In summary, H/D exchange between unbridged calcocenes and DMSO-d_6 offers a convenient, high-yield method for labeling the sp^2 C−H positions of both substituted and unsubstituted cyclopentadienyl ligands. Additional deuterium labeling of substituents on the cyclopentadienyl can also occur at positions that are or can be π-conjugated with the cyclopentadiene via formation of a fulvene tautomer. Since the cyclopentadienyl rings can be transferred directly from calcium to a variety of transition and lanthanide metals,[17,19,20] this method makes deuterium labeling a more accessible tool for probing the structures, physical properties, reactivity, fluxional behavior, and local environments of metallocene complexes.

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