

# Articles

## Mechanism of Mercuration of Ferrocene: General Treatment of Electrophilic Substitution of Ferrocene Derivatives

Allan F. Cunningham, Jr.

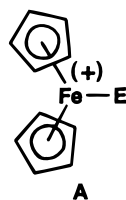
Additives Division, Ciba Specialty Chemicals Research Marly SA, P.O. Box 64, 1723 Marly, Switzerland

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The mercuration of (pentadeuteriocyclopentadienyl)cyclopentadienyliron(II), **1**, occurs preferentially at the C<sub>5</sub>H<sub>5</sub> ring. The ratio of C<sub>5</sub>H<sub>5</sub>:C<sub>5</sub>D<sub>5</sub> attack ranges from 5.2–6.5, depending upon the mercurating agent employed. In contrast to the Friedel–Crafts acetylation of **1**, mercuration does not give rise to intramolecular interannular proton transfers. Under certain conditions, a complex, **6**, can be isolated that contains both carbon–mercury and iron–mercury bonds. Taking these facts into account, a mechanism for the mercuration of ferrocene is proposed whereby precomplexation of the mercurating agent to the iron atom precedes the rate determining formation of the carbon–mercury bond with concomitant loss of H<sup>+</sup>. Combined with our previous work concerning the acetylation and proton exchange of ferrocene, this study allows the formulation of a general mechanism of electrophilic substitution of ferrocene, based on the reactivity of the electrophile and the basicity of the iron atom of the resulting ferrocene product.

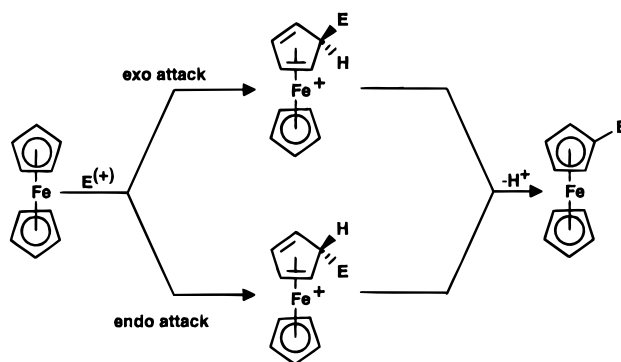
### Introduction

Interest in the special reactivity and properties of ferrocene and its derivatives has not subsided, even more than four decades after the discovery of this metallocene.<sup>1</sup> One of the special features of this compound is its aromaticity,<sup>2</sup> which is instrumental in the synthesis of a wide variety of substituted ferrocenes via electrophilic substitution. Not surprisingly, the mechanisms of these useful transformations have also attracted considerable attention.<sup>3</sup> In principle, electrophilic attack can occur at two different sites: at a carbon atom of a cyclopentadienyl ring either on the face opposite to the metal–carbon bonds (exo attack) or on the same face as the metal–carbon bonds (endo attack, Scheme 1). In addition, intermediates such as **A**, having an iron–electrophile bond, may be involved in either pathway.



Previous work in our laboratory has focused upon the mechanistic course of the Friedel–Crafts acylation of ferrocene.<sup>4</sup> Acetylation of both 1,1'-bis(trimethylsilyl)-

### Scheme 1



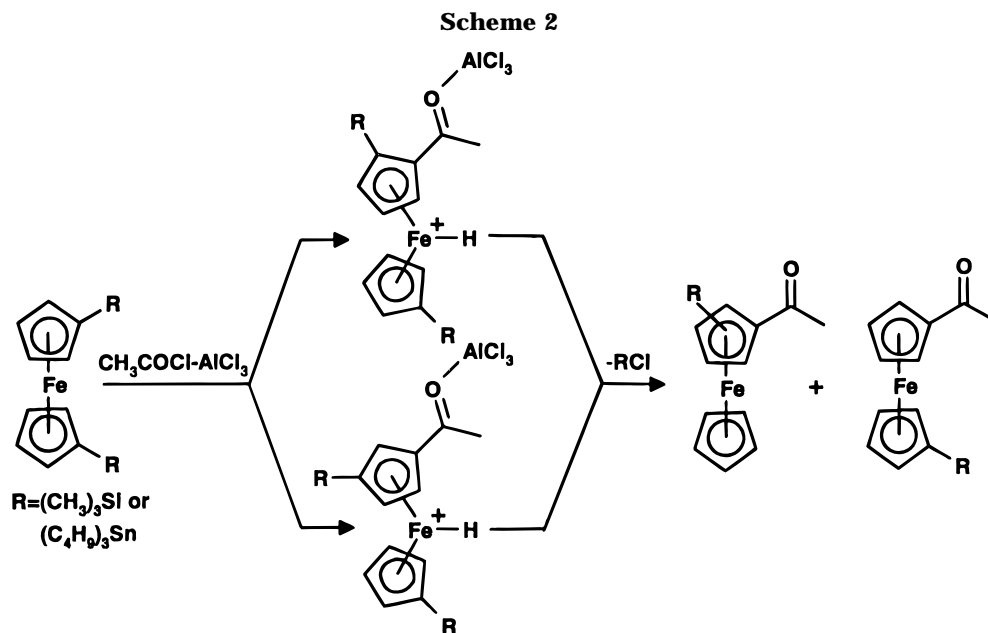
and 1,1'-bis(tributylstannyl)ferrocene led to mixtures of three isomeric acetylferrocenes.<sup>4a</sup> Since such product mixtures could not result from a simple endo displacement of a trimethylsilyl or tributylstannyl group by the acylating agent, the nature of the intermediate was probed via deuterium labeling. This revealed that attack of the acyl chloride–AlCl<sub>3</sub> complex occurred at the exo face of the cyclopentadienyl ring and, subsequent to proton transfer from carbon to iron, afforded two isomeric cationic iron hydrides (Scheme 2). A second heteroannular or homoannular proton transfer resulted in the elimination of trimethylsilyl or tributyl-

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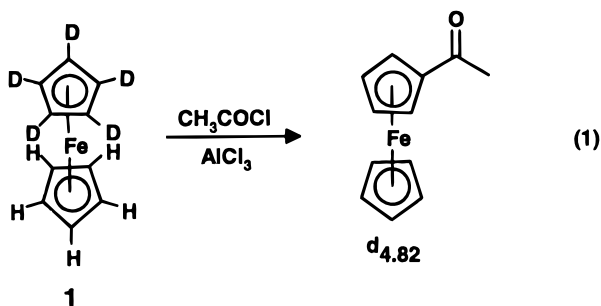
(2) Woodward, R. B.; Rosenblum, M.; Whiting, M. C. *J. Am. Chem. Soc.* **1952**, *74*, 3458.

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stannyl chloride and formation of the observed products. The fact that the deuterium content of the products was identical to that of the reactant indicated that direct deprotonation of the iron hydride does not occur.

In order to exclude that the exo acylation and the ensuing ring to metal to ring proton transfers were specific to the aforementioned ferrocene derivatives, we prepared and studied the acetylation of the pentadeuterated ferrocene **1**.<sup>4b</sup> Here again, the exo attack of the acylating agent could be easily demonstrated. Whereas <sup>1</sup>H NMR analysis showed that acylation occurred indiscriminately at both cyclopentadienyl rings, the deuterium content of the acetylferrocene obtained was 4.82 atoms (eq 1). Clearly, a metal deuteride is engendered



which undergoes preferential loss of HCl with the concomitant formation of a C–D bond. In fact, evidence for both proton and deuteron transfer products was obtained through mass spectral analysis: the *m/e* 122 (C<sub>5</sub>H<sub>4</sub>D<sub>1</sub>Fe) and *m/e* 125 (C<sub>5</sub>H<sub>1</sub>D<sub>4</sub>Fe) fragments of the product were enriched relative to acetylferrocene-*d*<sub>0</sub> and acetylferrocene-*d*<sub>9</sub>. Therefore, the occurrence of intramolecular proton transfers is not an isolated phenomena and is indicative of an exo attack of an electrophile.

With respect to the process of hydrogen exchange of ferrocene, the principle of microscopic reversibility

requires that protonation also occurs via exo attack of H<sup>+</sup>. Further evidence for the exo protonation of ferrocenes has been obtained through the study of the formation of dihydrogen from [1.1]ferrocenophane in acidic media.<sup>3j</sup> Treatment of this dimetalloocene with BF<sub>3</sub>–D<sub>2</sub>O results in its oxidation and the generation of predominately H<sub>2</sub>. If direct protonation of the metal center was operative, the exclusive generation of D<sub>2</sub> would be expected.

Armed with this diagnostic tool for identifying an exo attack, we then considered the electrophilic mercuration of ferrocene. The interaction of various mercury(II) compounds with ferrocene has been the subject of a number of publications. Although the precise structure of ferrocene–mercuric salt adducts is yet to be resolved, the presence of an iron–mercury bond has been detected by infrared,<sup>5</sup> Mössbauer,<sup>3i,6,7</sup> solid state <sup>13</sup>C NMR,<sup>7</sup> and ultraviolet spectroscopy.<sup>8</sup> Indeed, the kinetic evaluation of the acetoxymercuration of ferrocene in acetic acid seemed to indicate the rapid formation of a related 1:1 adduct of ferrocene:mercuric acetate (**A**, E = Hg(OCOCH<sub>3</sub>)<sub>2</sub>) followed by the rate determining formation of the carbon–mercury bond (endo attack).<sup>3h</sup> However, apart from the reasonable correlation of the observed reaction rate with the kinetic expression for the proposed transformation, only a shift in the <sup>1</sup>H NMR signal of ferrocene upon addition of mercuric acetate and a transient color change to red upon mixing concentrated solutions of the two reactants could be offered as proof for precomplexation of mercuric acetate to the iron atom of ferrocene. In contrast, the lack of a direct correlation between the rate of mercuration and the number of ferrocene alkyl substituents has been used as evidence against prior precomplexation.<sup>3f</sup> Whereas the addition

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(6) (a) Roberts, R. M. G.; Silver, J.; Azizian, J. *J. Organomet. Chem.* **1986**, *303*, 387. (b) Watanabe, M.; Motoyama, I.; Sano, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2103. (c) Silver, J. *J. Chem. Soc., Dalton Trans.* **1990**, 3513.

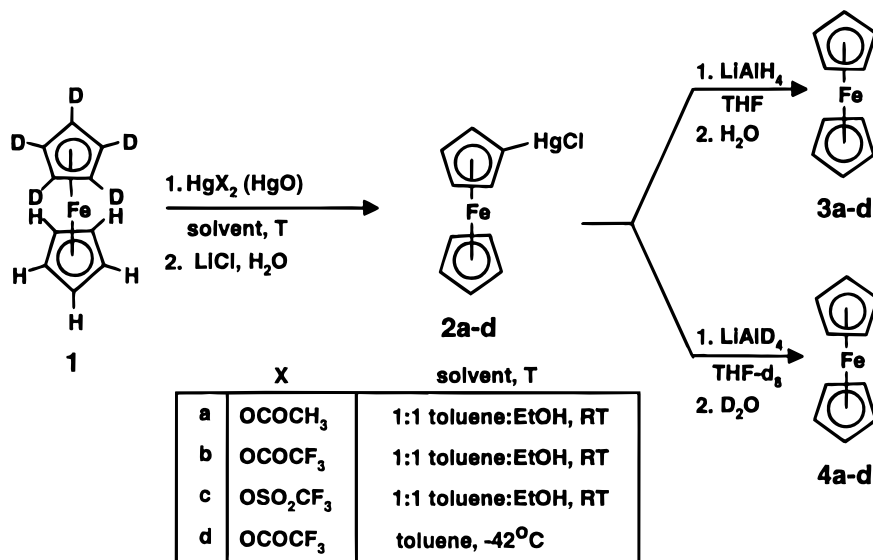
(7) (a) Watanabe, M.; Masuda, Y.; Motoyama, I.; Sano, H. *Chem. Lett.* **1987**, 1981. (b) Watanabe, M.; Masuda, Y.; Motoyama, I.; Sano, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3479. (c) Watanabe, M.; Masuda, Y.; Motoyama, I.; Sano, H. *Hyperfine Interact.* **1988**, *40*, 355.

(8) Traverso, O.; Chiorboli, C.; Mazzi, U.; Zucchini, G. L. *Gazz. Chim. Ital.* **1977**, *107*, 181.

Silver, J.; Morrison, I. E. G. *J. Organomet. Chem.* **1981**, *209*, 385. (j) Mueller-Westerhoff, U. T. *Angew. Chem.* **1986**, *98*, 700. (k) Mueller-Westerhoff, U. T.; Haas, T. J.; Swiegers, G. F.; Leipert, T. K. *J. Organomet. Chem.* **1994**, *472*, 229.

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Scheme 3

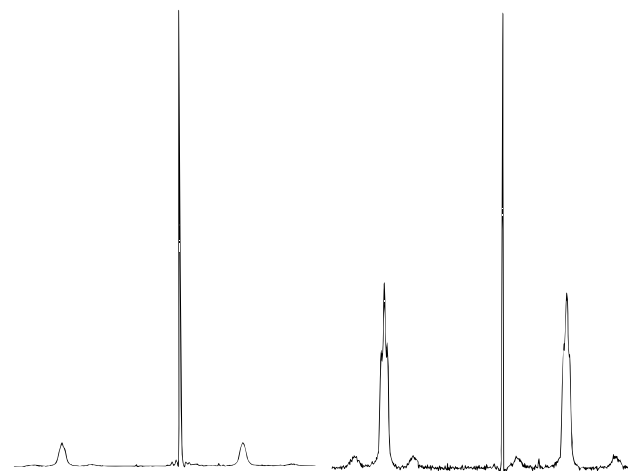


of one ethyl group to ferrocene engenders an approximately 2-fold increase in the reaction rate, the introduction of the second ethyl group promotes a further increase of only 25%. Mercuration via an endo attack without precomplexation had been previously advanced in an earlier study in which the rates of various electrophilic substitution reactions were shown to correlate with  $\sigma^+$  constants determined for the endo and exo attack of ferrocene derivatives. According to this mechanistic interpretation, weak electrophiles such as Hg(II) should preferentially attack the more electron-rich endo face of the cyclopentadienyl ring.<sup>3c</sup>

We now report our work concerning the mercuration of (pentadeuterocyclopentadienyl)cyclopentadienyliron (**1**) which unequivocally confirms that mercuration proceeds via precomplexation and subsequent endo transfer of the electrophile. In addition, these results allow the formulation of a general mechanism for the electrophilic substitution of ferrocene and its derivatives, based not only on the strength of the electrophile but also on the basicity of the iron atom.

### Results and Discussion

Treatment of a 0.33 M solution of **1** in 1:1 toluene:ethanol with 0.5 equiv of mercuric acetate followed by ligand exchange with LiCl led to the isolation of chloromercurioferrocene **2a** in 35% yield (based on **1**, Scheme 3).<sup>9</sup> An additional 58% of unreacted **1** could be recovered; the balance of the material was presumably converted to the insoluble 1,1'-bis(chloromercurio)ferrocene. Inspection of the <sup>1</sup>H NMR clearly shows that mercuration occurs preferentially on the C<sub>5</sub>H<sub>5</sub> ring of **1** (Figure 1). In the absence of interannular proton transfers, indiscriminate mercuration of **1** would afford a spectrum identical with that of undeuterated chloromercurioferrocene: the ratio of each broad triplet (representing the two pairs of protons of C<sub>5</sub>H<sub>4</sub>HgCl) to the singlet (C<sub>5</sub>H<sub>5</sub>) would be 1:2.5. In the case at hand, the ratio of C<sub>5</sub>H<sub>5</sub> attack to C<sub>5</sub>D<sub>5</sub> attack is 6.5:1, again if potential interannular proton transfers are disregarded. An isotope effect of 3.2 has previously been reported for



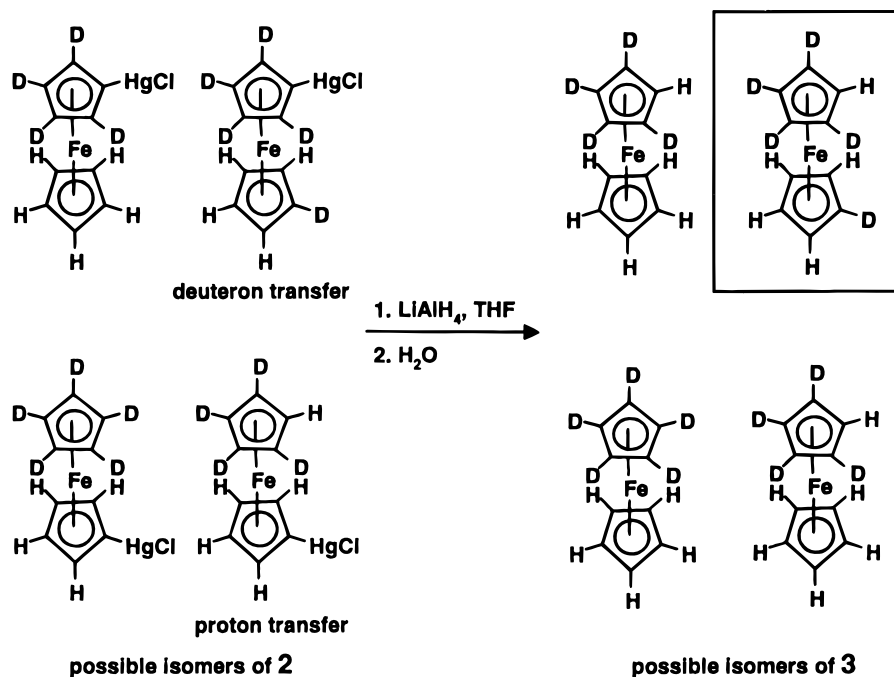
**Figure 1.** <sup>1</sup>H NMR spectrum of chloromercurioferrocene-*d*<sub>0</sub> (left) and **2a** (right) between 4.0 and 4.6 ppm, with constant amplitude of the unsubstituted cyclopentadienyl singlet.

the mercuration of ferrocene with Hg(OAc)<sub>2</sub>,<sup>3c</sup> although the exact reaction conditions were not specified.

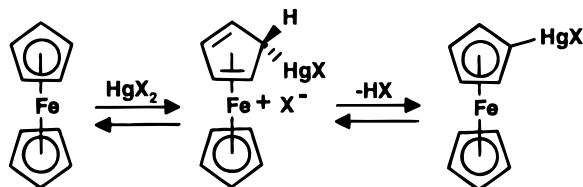
Although a large isotope effect is observed upon mercuration, the question of whether mercuration proceeds via an endo or exo attack remains open. Due to the absence of the C<sub>5</sub>H<sub>5</sub>Fe fragment in the mass spectrum of chloromercurioferrocene, **2a** had to be converted into ferrocene to allow for the analysis for proton transfers. Toward this goal, **2a** was reduced with LiAlH<sub>4</sub> in THF followed by hydrolysis with H<sub>2</sub>O to provide **3a** and reduced similarly with LiAlD<sub>4</sub>/THF-*d*<sub>8</sub>/D<sub>2</sub>O to furnish **4a**. Comparison of the mass spectrum of **3a** with that of **1** allows for the identification of the C<sub>5</sub>H<sub>4</sub>D<sub>1</sub>Fe fragment (*m/e* 122) that would arise from an exo attack of the mercurating agent of the C<sub>5</sub>D<sub>5</sub> ring followed by interannular deuteron transfer. This would lead to an enrichment of this fragment relative to the C<sub>5</sub>H<sub>5</sub>Fe fragment (*m/e* 121), which is obtained from the other three potential mercuration products upon reduction with LiAlH<sub>4</sub> (Scheme 4, only reduction with LiAlH<sub>4</sub> is shown). As can be seen, the percentage of this fragment in the spectra of **3a** and **1** is practically identical; therefore, no deuteron transfer has occurred

(9) Fish, R. W.; Rosenblum, M. *J. Org. Chem.* **1965**, *30*, 1253. These authors employ methanol/benzene.

Scheme 4

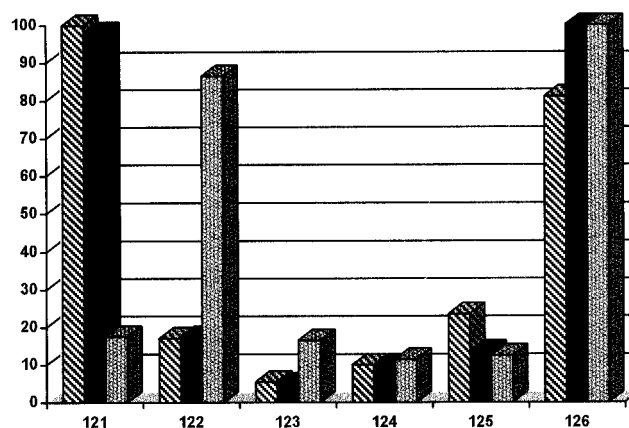


Scheme 5



(Figure 2). A similar analysis reveals, as would be expected, that no proton transfer occurs during the mercuration of **1**. Given the lack of intramolecular proton (deuteron) transfers, the mass spectra of **3a** and **4a** also permit a second, albeit less accurate, evaluation of the ratio of  $\text{C}_5\text{H}_5$  attack to  $\text{C}_5\text{D}_5$  attack. Inspection of the molecular ions of **3a** and **4a** indicate that the former is composed of 12% ferrocene- $d_4$  and 88% ferrocene- $d_5$  whereas the latter consists of 83% ferrocene- $d_6$  and 17% ferrocene- $d_5$ . This translates into a  $\text{C}_5\text{H}_5$ : $\text{C}_5\text{D}_5$  attack ratio of  $\sim 5.9$ :1, which is in unison with that obtained through analysis of the  $^1\text{H}$  NMR spectrum of **2a**, 6.5:1. It is important to note that recovered **1** exhibited a mass spectrum identical to that of the original sample.

These results imply that the acetoxymercuration of ferrocene proceeds via a rate determining endo attack of the mercurating species with a concerted or stepwise exo loss of  $\text{H}^+$ , although it is yet unclear whether a species with an iron–mercury bond serves as an intermediate (Scheme 5). The preferred endo attack of the mercurating agent may be the result of the instability of the intermediate **5**, which would arise from an exo attack and a ring to iron transfer of a proton, toward demercuration. Whereas ferrocene can only be protonated with strong acids such as  $\text{BF}_3\text{--H}_2\text{O}$ ,<sup>10</sup> the hydrolysis of chloromercurioferrocene can be accomplished under mildly acidic conditions, 0.01 M HCl in dioxane–



**Figure 2.** Comparison of the mass spectra of **3a** (lined bar), **1** (solid bar), and **4a** (dotted bar) in the  $m/e$  121–126 region (normalized to 100%).

water.<sup>11</sup> The activation energy determined for this demercuration was 19.1 kcal/mol. Indeed, demercuration should not require the formation of a metal protonated ferrocene intermediate since, according to the mechanism proposed, it must proceed via an exo attack by  $\text{H}^+$  of the carbon atom bound to mercury (the microscopic reverse). The desilylation and deborylation of ferrocene derivatives under mildly acidic conditions must also proceed in a similar manner.<sup>3e</sup>

At this juncture, the course of the reductive demercuration of **2** merits comment. There is some confusion in the literature regarding the mechanism of the reaction of aryl- and alkylmercuric halides with  $\text{LiAlH}_4$ . Publications in the 1950's concerning phenylmercuric chloride and diphenylmercury claimed that the ethereal  $\text{LiAlH}_4$  reduction of both of these compounds afforded tetraphenylaluminum.<sup>12</sup> Subsequent hydrolysis of the

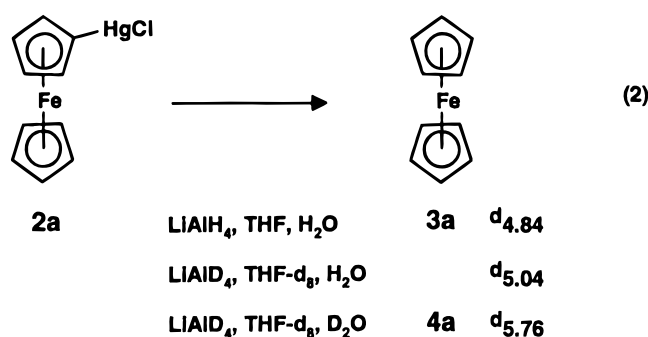
(10) Curphey, T. J.; Santer, J. O.; Rosenblum, M.; Richards, J. H. *J. Am. Chem. Soc.* **1960**, *82*, 5249.

(11) Nesmeyanov, E. G.; Perevalova, E. G.; Gubin, S. P.; Kozlovskii, A. G. *J. Organomet. Chem.* **1968**, *11*, 577.

(12) (a) Barton, D. H. R.; Rosenfelder, W. J. *J. Chem. Soc.* **1951**, 2385. (b) Winstein, S.; Traylor, T. G. *J. Am. Chem. Soc.* **1956**, *78*, 2597. (c) Traylor, T. G. *Chem. Ind.* **1959**, 1223.

latter yielded benzene. A more detailed study, published over 20 years later, discounted the formation of intermediate aluminates by demonstrating that the benzene content of the product mixture was the same before and after hydrolysis.<sup>13</sup> To account for the product mixture of diphenylmercury, benzene, and biphenyl, these authors suggested an initial electron transfer from LiAlH<sub>4</sub> to phenylmercuric chloride, which provides the corresponding radical anion. Subsequent loss of chloride anion and elemental mercury provides a phenyl radical. Interaction of the phenyl radical with phenylmercuric chloride eventually yields diphenylmercury, whereas hydrogen abstraction from LiAlH<sub>4</sub> affords benzene. Biphenyl, obviously, is obtained via dimerization of the phenyl radicals. Absent from this analysis is phenylmercuric hydride: the formation of this product was deemed thermodynamically unfavorable. This, however, is in stark contrast to the recent preparation and NMR analysis of phenylmercuric hydride and related species at low temperature.<sup>14</sup> In fact, the decomposition of phenylmercuric hydride was shown to afford diphenylmercury—one of the products observed in the aforementioned study.

Our observations indicate that, at least in the case of chloromercurioferrocene, the reduction is not uniquely radical in nature. In separate trials, **2a** was treated with LiAlD<sub>4</sub> in THF-*d*<sub>8</sub> and hydrolyzed with either H<sub>2</sub>O or D<sub>2</sub>O (eq 2). Workup with H<sub>2</sub>O afforded ferrocene

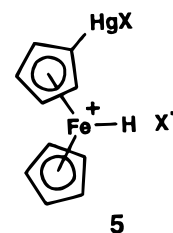


having a deuterium content of 5.04 atoms, whereas a much higher deuterium content (5.76 atoms: +0.72 D) resulted from the D<sub>2</sub>O workup. In contrast, reduction of **2a** with LiAlH<sub>4</sub> followed by H<sub>2</sub>O hydrolysis led to ferrocene having 4.84 deuterium atoms. This suggests that approximately 22% of **2** undergoes reduction via the ferrocenyl radical, either through hydrogen (deuterium) abstraction from the reducing agent or from THF. The vast majority of **2**, however, is converted to an anionic derivative, be it an alanate or ferrocenyllithium, which is quenched with water.

Having established that acetoxymercuration of ferrocene is achieved via the endo attack of the electrophile, we then considered the use of mercurating agents of higher electrophilicity. It is conceivable that a very reactive mercury(II) species would attack exo to the cyclopentadienyl ring to afford the iron hydride **5**. The high instability of the mercury(II) fragment could disfavor the reverse reaction that regenerates the starting materials and lead to the preferential loss of a proton (via iron to ring transfer) to afford **2**.

The mercuration of ferrocene with mercuric trifluoroacetate is best carried out in the presence of mercuric oxide.<sup>15</sup> Mercuric oxide reacts with the trifluoroacetic acid released upon mercuration to regenerate mercuric trifluoroacetate, thereby preventing proton exchange and/or oxidation of ferrocene. Reaction of **1** with 0.1 equiv of Hg(O<sub>2</sub>CCF<sub>3</sub>)<sub>2</sub> and 0.1 equiv of HgO under the same conditions employed for the acetoxymercuration described above furnished **2b**, after ligand exchange with lithium chloride (Scheme 3). The yield of **2b** was 70% based on the total mercury(II) employed and 14% based on **1**. The latter was recovered in 74% yield. <sup>1</sup>H NMR analysis of **2b** indicated a high preference for attack of the C<sub>5</sub>H<sub>5</sub> ring of **1**. Nonetheless, mercury trifluoroacetate is slightly less selective than the corresponding acetate, as would be expected: the ratio of C<sub>5</sub>H<sub>5</sub> to C<sub>5</sub>D<sub>5</sub> attack is 6.2:1. In light of the results obtained with mercuric acetate, the high isotope effect suggests a mechanism based on the endo attack of the mercury(II) species. This is also confirmed by mass spectral analysis of **3b** and **4b**: no evidence of a proton transfer can be detected.

The mercuration of **1** with Hg(O<sub>3</sub>SCF<sub>3</sub>)<sub>2</sub><sup>16</sup> was investigated in a similar manner (Scheme 3). The high isotope effect of 5.2, although less pronounced than in the two previous examples, 6.2 with Hg(O<sub>2</sub>CCF<sub>3</sub>)<sub>2</sub> and 6.5 with Hg(O<sub>2</sub>CCH<sub>3</sub>)<sub>2</sub>, indicates that the desired change in the mechanism from an endo to exo attack did not occur. Apparently, regardless of the counterion bound to mercury, the energy required for the formation of **5** is much too high in relation to that for the endo attack of mercury(II) with direct exo loss of a proton.



In a last attempt to force a change in the mechanistic course of mercuration, we reevaluated the reaction of **1** with Hg(O<sub>2</sub>CCF<sub>3</sub>)<sub>2</sub> in toluene. The replacement of an alcohol by an aromatic solvent leads to higher conversions in the vinyl mercuration of 1,1-diarylethylenes.<sup>17</sup> This effect has been ascribed to the enhanced electrophilicity of the mercury species due to weaker solvent–mercury interactions. Addition of 1.0 equiv of solid Hg(O<sub>2</sub>CCF<sub>3</sub>)<sub>2</sub> to a solution of **1** in toluene at –42 °C led to the precipitation of deep red solid over a 2 h period (Scheme 3). Quick transfer of this suspension into vigorously stirred aqueous LiCl resulted in a color change from red to yellow-orange. After purification, a 19% yield of **2d** was obtained along with the recovery of 80% of unreacted **1** (~100% mass balance). Analysis of **2d** in the usual way suggested that under these conditions, the endo mode of electrophilic substitution was again preferred. The observed isotope effect was 6.6, slightly higher than that of the corresponding

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(14) (a) Bellec, N.; Guillemin, J.-C. *Tetrahedron Lett.* **1995**, 6883.

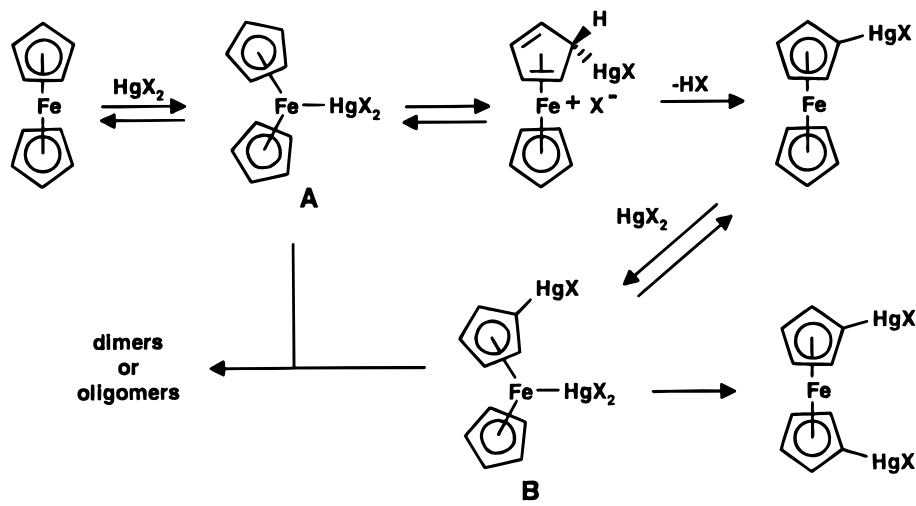
(b) Kwetkat, K.; Kithching, W. J. *Chem. Soc., Chem. Commun.* **1994**, 345.

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(17) Sokolov, V. I.; Bashilov, V. V.; Reutov, O. A. *J. Organomet. Chem.* **1978**, 162, 271.

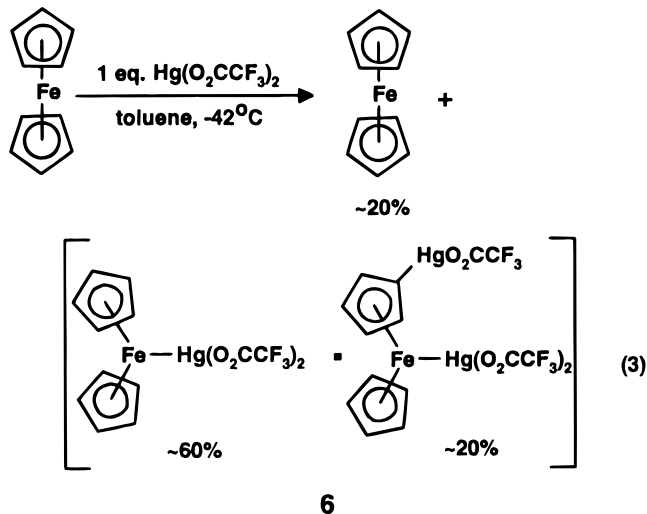
Scheme 6



reaction in 1:1 ethanol:toluene at room temperature. It appears that the enhanced electrophilicity of  $\text{Hg}(\text{O}_2\text{CCF}_3)_2$  in pure toluene is more than compensated for by the decrease in temperature. Attempts to carry this reaction out at room temperature, however, led to the oxidation of **1**.

To develop a better understanding of the course of the mercuration of ferrocene with  $\text{Hg}(\text{O}_2\text{CCF}_3)_2$  in toluene, the reaction was repeated on a larger scale with ferrocene-*d*<sub>0</sub>. The red solid was filtered at low temperature and washed several times with cold toluene ( $-42^\circ\text{C}$ ). The cold toluene filtrate was treated with LiCl, as previously described. From the organic phase, ferrocene was recovered in 22% yield, as well as a trace of chloromercurioferrocene (<0.5%). Concentration of the aqueous phase afforded a white solid containing less than 0.1 mg of mercury, representing far less than 0.1% of the mercury employed in the reaction. Therefore, the red solid contains ferrocene derivatives and mercury species in a 4:5 ratio. Taking into account that mercuration must already occur at  $-42^\circ\text{C}$  (chloromercurioferrocene is detected in the filtrate) and that mercuration proceeds in ~20% yield (previous experiment), the composition of the red solid must be a 3:1 mixture of the ferrocene- $\text{Hg}(\text{O}_2\text{CCF}_3)_2$  complex and the trifluoroacetoxymercurioferrocene- $\text{Hg}(\text{O}_2\text{CCF}_3)_2$  complex **6** (eq 3).<sup>18</sup> When the solid is allowed to warm, a color change from red to blue occurs at  $0^\circ\text{C}$  (oxidation). Treatment of the blue oily substance with aqueous LiCl then affords 11% chloromercurioferrocene (based on total ferrocene employed) and 26% of recovered ferrocene; the remaining 41% of the ferrocene derivatives undergo oxidation.

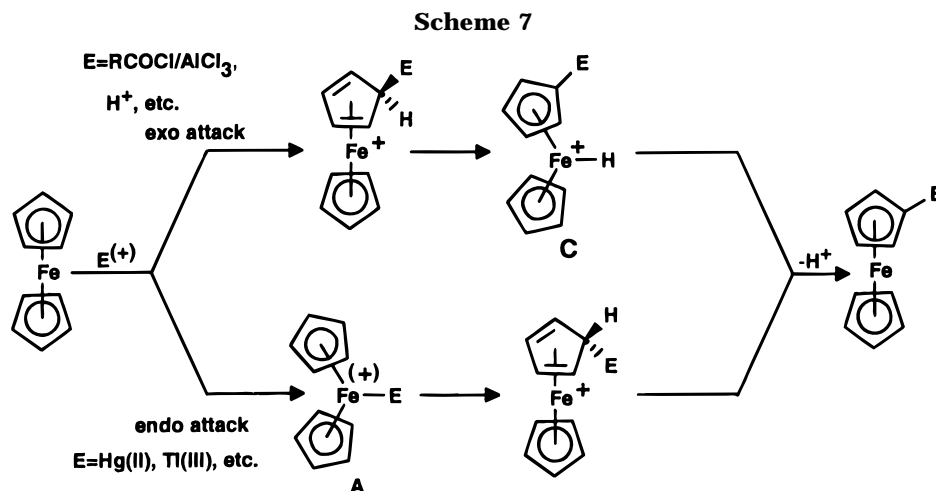
Combining these results with those obtained with **1** allows for the conception of a mechanism for the mercuration, which includes precomplexation of the electrophile at the metal center. The treatment of ferrocene with a mercury(II) species establishes an equilibrium between free ferrocene and complex **A** (Scheme 6). In the rate determining step, formation of the carbon-mercury bond is achieved via a metal to ring transfer of Hg(II) and dissociation of a mercury ligand. This process is either concomitant with or prior to an exo loss of a proton to afford the substituted product.



The aforementioned lack of correlation of the rate of mercuration with the number of ferrocene alkyl substituents can be attributed to increased steric repulsions during the iron to carbon migration of the mercurating species.<sup>3f</sup> It should also be noted that the kinetic study in question was monitored by UV spectroscopy, and no thorough product analysis was carried out. As ferrocene readily undergoes polymermercuration,<sup>9,15</sup> monomercurated ferrocene can also compete with ferrocene for complexation with the free mercurating agent to furnish **B**. Depending upon the reaction conditions (at low temperatures or in apolar solvents), the precipitation of dimers (oligomers) of complexes **A** and **B** may occur. In fact, the red complexes of ferrocene and its derivatives with various mercuric halides have been isolated and studied by various techniques.<sup>5-7</sup> In alcoholic solvents, the precipitation of dimers of complexes **A** and **B** or compounds of other stoichiometry is disfavored and the mercuration proceeds as expected. It is apparent, however, that the solubility of ferrocene- $\text{HgX}_2$  adducts depends on both the solvent and the nature of X. The mercuration of ferrocene with  $\text{Hg}(\text{O}_2\text{CCF}_3)_2$  in toluene is unique in that both dimerization (oligomerization) of the complexes and mercuration occur simultaneously. Under identical conditions, the reaction of with  $\text{Hg}(\text{O}_3\text{SCF}_3)_2$  affords only dimers (oligomers) of complex **A** ( $\text{X} = \text{O}_3\text{SCF}_3$ ).

In view of our previous work on the electrophilic

(18) Both mercuric trifluoroacetate and ferrocene are perfectly soluble in toluene at this temperature; therefore, it is unlikely that the precipitate contains any uncomplexed mercury species.

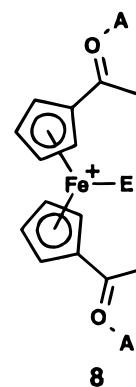


substitution of ferrocene, this mercuration study permits a general understanding of the mechanisms of such reactions. In effect, the course of these reactions is very similar to that first proposed by Traylor almost 30 years ago, with the important exception that the iron atom plays an essential role (Scheme 7). Highly reactive electrophiles, typified by  $\text{RCOCl}-\text{AlCl}_3$  (and possibly  $\text{RX}-\text{AlCl}_3$ ), undergo an exo attack of the cyclopentadienyl ring of ferrocene to afford an iron hydride intermediate **C**. Various cationic iron hydride species,<sup>3d,10,19</sup> including those related to the intermediate proposed for acetylation of ferrocene, **C** ( $\text{E} = \text{C}^+(\text{OH})\text{CH}_3$ ),<sup>4b,20</sup> have been characterized by  $^1\text{H}$  NMR. These reactions, being relatively exothermic, should have early transition states characterized by a low extent of carbon–electrophile bond formation and, therefore, exhibit no isotope effect. As shown by Rosenblum,<sup>3b</sup> the attack of such electrophiles may also occur at the metal center (endo) if an exo attack is excluded by steric constraints. Deprotonation of **C** then proceeds via metal to carbon proton transfer with the exo loss of  $\text{H}^+$ . As previously discussed, the occurrence of these interannular proton transfers is proof in itself that the proton exchange of ferrocene proceeds via an exo attack of  $\text{H}^+$ . Further evidence is provided by the formation of predominately  $\text{H}_2$  through oxidative deuteration of ferrocenophane in  $\text{BF}_3-\text{D}_2\text{O}$ .

With electrophiles that are weaker than  $\text{H}^+$ , for example mercury(II) or thallium(III), substitution occurs via precomplexation of the electrophile to afford **A** followed by the rate determining endo attack of a cyclopentadienyl ring of ferrocene. As such reactions are less exothermic, the extent of bond formation in the transition state is much greater than that with strong electrophiles and an isotope effect is observed. The endo mode is favored not only because of the interaction of these soft electrophiles (soft acids) with the easily oxidized iron atom of ferrocene (soft base) but also since the cationic iron hydride **C**, which would result from

an exo attack, is unstable with respect to elimination of the electrophile.

Whereas this interpretation is valid for ferrocene itself, the mode of electrophilic substitution of ferrocene derivatives depends strongly upon the nature of the substituent(s). It has been shown by a similar labeling experiment that the acetylation of acetylferrocene with  $\text{CH}_3\text{COCl}-\text{AlCl}_3$  (strong electrophile) must occur via an endo attack, although it proceeds without an isotope effect (exothermic reaction with an early transition state).<sup>4b</sup> The generation of the iron hydride **8a** that would result from an exo attack is disfavored due to the low basicity of the iron atom. This is in accord with



- 8**  
**a**  $\text{A}=\text{AlCl}_3$ ,  $\text{E}=\text{H}$   
**b**  $\text{A}=\text{H}^+$ ,  $\text{E}=\text{H}$   
**c**  $\text{A}=\text{AlCl}_3$ ,  $\text{E}=\text{CH}_3\text{COCl}-\text{AlCl}_3$

the lack of exchange of cyclopentadienyl protons of 1,1'-diacetylferrocene with triflic acid-*d*<sub>1</sub><sup>21</sup> (which should occur via **8b**) and the resistance of diacetylferrocene to further acetylation.<sup>22</sup> The addition of two electron-donating methyl groups to diacetylferrocene, however, suffices to stabilize the intermediate **8c**: a triacetylferrocene has been isolated from the reaction of 1,1'-

(19) Bitterwolf, T. *Inorg. Chim. Acta* **1986**, *117*, 55 and other papers in this series, including ref 3d.

(20) (a) Rimmelin, P.; Sommer, J.; Sandström, J.; Seita, J. *J. Organomet. Chem.* **1976**, *114*, 175. (b) Olah, G. A.; Mo, Y. K. *J. Organomet. Chem.* **1973**, *60*, 311. The essential difference between the two species is that the acid complexed to the carbonyl: the acetylation intermediate is an aluminum chloride complex of acetylferrocene protonated at the iron.

(21) Roberts, R. M. G.; Silver, J.; Wells, A. S. *Inorg. Chim. Acta* **1986**, *119*, 171. Here again, the bis(aluminum chloride) complex of diacetylferrocene protonated at the iron is being compared to the triprotonated species.

(22) (a) Only diacetylferrocenes were isolated: Nesmeyanov, A.; Leonova, E. V.; Kochetkova, N. S.; Malkova, A. I. *J. Organomet. Chem.* **1975**, *96*, 271 (10 equiv of  $\text{CH}_3\text{COCl}-\text{AlCl}_3$ ,  $\text{CH}_2\text{Cl}_2$ , RT). (b) Rausch, M. D.; Fischer, E. O.; Grubert, H. *J. Am. Chem. Soc.* **1960**, *82*, 76 (3 equiv  $\text{CH}_3\text{COCl}-\text{AlCl}_3$ ,  $\text{CH}_2\text{Cl}_2$ , reflux). The reported tetraacetylation of ferrocene with acetic anhydride and trifluoroacetic acid (Sweeney, US Patent 2,852,542, February 29, 1956) has been revealed to be irreproducible: Bell, W.; Glidewell, C. *J. Chem. Res., Synop.* **1991**, 44.

dimethylferrocene with excess  $\text{CH}_3\text{COCl}-\text{AlCl}_3$ .<sup>23</sup> Arguments refuting alternative mechanisms based on the endo attack of strong electrophiles without precomplexation have been set forth in a previous publication.<sup>24</sup>

To define the exact point at which the mechanism for electrophilic substitution changes from exo to endo by the proton affinity or oxidation potential of the resulting ferrocene product is difficult: the stability of the iron hydride intermediate depends not only upon the Lewis acid species employed for the reaction but also on the strength of the complex formed between the Lewis acid and the ferrocene substituent(s).

In conclusion, the reaction of ferrocene with various mercurating agents has been shown to proceed via precomplexation of the mercury(II) species at the metal center followed by the rate determining formation of the carbon–mercury bond (endo attack). For the first time, direct evidence was obtained for the formation of an intermediate ferrocene– $\text{HgX}_2$  adduct whose conversion to a ferrocene having a carbon–mercury bond was competitive with the precipitation of a mixed ferrocene– $\text{HgX}_2$ /ferrocene( $\text{HgX}$ )– $\text{HgX}_2$  dimer (oligomer). The mechanistic details of the mercuration complemented earlier studies based on the acetylation and protonation of ferrocene derivatives and allowed the formulation of a general treatment of electrophilic substitution for this metallocene. Important aspects of this mechanistic interpretation are the reactivity of the electrophile and the basicity of the iron atom of the resulting ferrocene product.

## Experimental Section

**General Methods.** The solvents were used as obtained from the suppliers with the exception of toluene which was distilled from  $\text{CaH}_2$ . The preparation of (pentadeuteriocyclopentadienyl)cyclopentadienyliron(II) has been previously described.<sup>4b</sup> Routine monitoring of the reactions was carried out with glass-backed TLC plates of Merck 60 F<sub>254</sub> silica gel. Flash column chromatography was performed on Merck 60H F<sub>254</sub> silica gel. <sup>1</sup>H NMR spectra were recorded on a Bruker 250 AC (250 MHz) or a Bruker 300 AC spectrometer (300 MHz). Chemical shifts are reported in ppm relative to internal tetramethylsilane. Mass spectra were recorded on a Finigan MAT 212-SS300 spectrometer at 70 eV.

**Mercuration of 1 with Mercuric Acetate.** To a solution of 0.19 g (0.001 mol) of **1** in 1:1 toluene:ethanol (3 mL) was added 0.16 g (0.0005 mol) of solid mercuric acetate. The resulting solution was allowed to stir for 24 h at room temperature. At this time a solution of 0.20 g (0.047 mol) of LiCl in H<sub>2</sub>O (10 mL) was added, and the reaction mixture was stirred vigorously for 0.5 h. The reaction mixture was diluted with H<sub>2</sub>O (~50  $\mu\text{L}$ ) and extracted with  $\text{CH}_2\text{Cl}_2$  (3  $\times$  20 mL). The combined organic extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to give a yellow solid. Chromatography ( $\text{SiO}_2$ , 2:1 hexane: $\text{CH}_2\text{Cl}_2$ ) gave 0.11 g (58% recovery) of **1** and 0.15 g (35% based on **1**, 70% based on mercuric acetate) of **2a**: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  4.47 (br t, 2,  $J = 1.5$  Hz, mercury satellites at 4.53 and 4.41), 4.24 (s, 0.77), 4.11 (br t, 2,  $J = 1.5$  Hz, mercury satellites at 4.21 and 4.01) ppm. The mass spectrum of recovered **1** is identical to that of the starting material: MS (70 eV)  $m/e$  (194–188) 194 (0), 193 (1.5), 192 (13.5), 191 (100), 190 (4), 189 (7.5), 188 (1);  $m/e$  (126–121, normalized to 100) *126 (100)*, *125 (13.5)*, 124 (10), 123 (5), *122 (17.5)*, *121 (98%)*. The italicized values are used to determine whether a proton

( $m/e$  126 and 125) or a deuteron ( $m/e$  122 and 121) transfer has occurred.

**Reduction of 2a with  $\text{LiAlH}_4$ .** To a solution of ~0.02 g of **2a** in THF (0.5 mL) at room temperature was added ~0.05 g of  $\text{LiAlH}_4$ . Gas was evolved, and the gray suspension was allowed to stir for 0.5 h. The reaction mixture was quenched carefully with a minimum amount of H<sub>2</sub>O and then diluted with hexane. The organic phase was removed from the solids and placed directly on a small column of silica gel. The ferrocene **3a** formed was obtained via elution with hexane: MS (70 eV)  $m/e$  (194–188) 194 (0), 193 (1.5), 192 (13.5), 191 (100), 190 (14), 189 (8), 188 (2);  $m/e$  (126–121, normalized to 100) 126 (81), 125 (23.5), 124 (10), 123 (5.5), *122 (17)*, *121 (100)*.

**Reduction of 2a with  $\text{LiAlD}_4$ .** This was carried out as described for the reduction with  $\text{LiAlH}_4$ , with the exception that THF- $d_8$  was used as the solvent and that quenching was accomplished with D<sub>2</sub>O. **4a**: MS (70 eV)  $m/e$  (194–188) 194 (1.5), 193 (14.5), 192 (100), 191 (20.5), 190 (8), 189 (2), 188 (0.5);  $m/e$  (126–121, normalized to 100) *126 (100)*, *125 (12.5)*, 124 (11.5), 123 (16.5), 122 (86.5), 121 (17.5).

**Mercuration of 1 with Mercuric Trifluoroacetate.** This reaction was performed as described above for mercuric acetate, with the exception that 0.04 g (0.0001 mol) of mercuric trifluoroacetate and 0.02 g (0.0001 mol) of yellow mercuric oxide were employed. Chromatography gave 0.14 g (74% recovery) of unchanged **1** and 0.06 g (14% based on **1**, 74% based on mercury(II)) of **2b**: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  4.47 (br t, 2,  $J = 1.5$  Hz, mercury satellites at 4.53 and 4.41), 4.24 (s, 0.81), 4.11 (br t, 2,  $J = 1.5$  Hz, mercury satellites at 4.21 and 4.01) ppm.

Compounds **3b** and **4b** were obtained as described above for **3a** and **4a**. MS (70 eV) of **3b**:  $m/e$  (194–188) 194 (0), 193 (1), 192 (13.5), 191 (100), 190 (19), 189 (8), 188 (2);  $m/e$  (126–121, normalized to 100): 126 (88), 125 (26), 124 (11), 123 (7), *122 (18)*, *121 (100%)*. MS (70 eV) of **4b**:  $m/e$  (194–188) 194 (1), 193 (13.5), 192 (100), 191 (26.5), 190 (9), 189 (3), 188 (1);  $m/e$  (126–121, normalized to 100) *126 (100)*, *125 (15)*, 124 (12), 123 (16), 122 (82), 121 (21%).

**Mercuration of 1 with Mercuric Trifluoromethylsulfonate.** This reaction was performed as described above for mercuric acetate, with the exception that 0.38 g (0.002 mol) of **1**, 0.10 g (0.0002 mol) of mercuric trifluoroacetate, and 0.06 g (0.0003 mol) of yellow mercuric oxide in 6 mL of 1:1 toluene:ethanol were employed. Chromatography gave 0.30 g (80% recovery) of unchanged **1** and 0.02 g (14% based on **1**, 9% based on mercury(II)) of **2c**: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  4.47 (br t, 2,  $J = 1.5$  Hz, mercury satellites at 4.53 and 4.41), 4.24 (s, 0.95), 4.11 (br t, 2,  $J = 1.5$  Hz, mercury satellites at 4.21 and 4.01) ppm. Given the high isotope effect upon mercuration, the analysis for proton transfers (reduction of **2c** with  $\text{LiAlH}(\text{D})_4$  and mass spectral analysis) was deemed unnecessary.

**Mercuration of 1 with Mercuric Trifluoroacetate in Toluene at –42 °C.** To a solution of 0.19 g (0.001 mol) of **1** in toluene (5 mL) maintained at –42 °C by means of a dry ice–acetonitrile bath was added 0.43 g (0.001 mol) of solid mercuric trifluoroacetate. As the mercuric trifluoroacetate slowly dissolved, a deep red solid formed. The reaction mixture was allowed to stir for 2.5 h at –42 °C, at which time it was poured into a vigorously stirred solution of 0.20 g (0.047 mol) of LiCl in H<sub>2</sub>O (10 mL). The solution continued to stir for 0.5 h. The toluene phase was separated, and the aqueous phase was extracted with toluene (2  $\times$  20 mL). The combined organic extracts were dried ( $\text{MgSO}_4$ ) and concentrated to give a yellow solid. Chromatography ( $\text{SiO}_2$ , 2:1 hexane: $\text{CH}_2\text{Cl}_2$ ) gave 0.17 g (80%) of unchanged **1** and 0.08 g (19%) of **2d**: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  4.47 (br t, 2,  $J = 1.5$  Hz, mercury satellites at 4.53 and 4.41), 4.24 (s, 0.75), 4.11 (br t, 2,  $J = 1.5$  Hz, mercury satellites at 4.21 and 4.01) ppm.

Compounds **3d** and **4d** were obtained as described above for **3a** and **4a**. MS (70 eV) of **3d**:  $m/e$  (194–188) 194 (0), 193 (1), 192 (13.5), 191 (100), 190 (22), 189 (8.5), 188 (2.5);  $m/e$  (126–121, normalized to 100) 126 (87), 125 (28), 124 (11), 123

(23) Nesmeyanov, A. N.; Perevalova, E. G.; Beinoravichute, Z. A.; Malygina, I. L. *Dokl. Akad. Nauk. SSSR* **1958**, *120*, 1263.

(24) See ref 3a, footnote 17.



(6.5), 122 (18), 121 (100). MS (70 eV) of **4d**: *m/e* (194–188) 194 (1), 193 (14), 192 (100), 191 (25.5), 190 (9), 189 (2.5), 188 (1); *m/e* (126–121, normalized to 100) 126 (100), 125 (15), 124 (12), 123 (15), 122 (82), 121 (23.5).

**Mercuration of Ferrocene-*d*<sub>0</sub> with Mercuric Trifluoroacetate in toluene at -42 °C.** To a solution of 0.93 g (0.005 mol) of ferrocene in toluene (25 mL) maintained at -42 °C by means of a dry ice-acetonitrile bath was added 2.13 g (0.005 mol) of solid mercuric trifluoroacetate. As the mercuric trifluoroacetate slowly dissolved, a deep red solid formed. The reaction mixture was allowed to stir for 2.5 h at -42 °C and then filtered under argon through a externally-cooled (dry ice) sintered glass filter. The red solid (**6**) was washed several times with cold (-42 °C) toluene and then dried under vacuum, while warming to room temperature. At ~0 °C, the red solid became a blue viscous oil; the weight of the oil was 2.70 g. This oil was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) and poured into a vigorously stirred solution of 1.00 g (0.0235 mol) of LiCl in H<sub>2</sub>O (50 mL). The solution continued to stir for 2.5 h. The organic phase was separated, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated to give an orange solid. Chromatography (SiO<sub>2</sub>, 2:1 hexane:CH<sub>2</sub>Cl<sub>2</sub>) gave 0.25 g (27%) of ferrocene and 0.24 g (11%) of chloromercurioferrocene. The filtrate, which was maintained

at -42 °C, was also poured into a vigorously stirred solution of 1.00 g (0.0235 mol) of LiCl in H<sub>2</sub>O (50 mL). The solution continued to stir for 0.5 h. The organic phase was separated, dried (MgSO<sub>4</sub>), and concentrated to give an orange solid. Chromatography (SiO<sub>2</sub>, 2:1 hexane:CH<sub>2</sub>Cl<sub>2</sub>) gave an additional 0.20 g (22%) of ferrocene and a trace (<0.01 g) of chloromercurioferrocene. The aqueous phase was concentrated to give 0.83 g of a white solid. The mercury content of this solid was 110 mg/kg, i.e., the solid contains less than 0.01 mg of mercury (it is predominately LiCl).

A similar reaction was carried out with mercuric trifluoromethylsulfonate. The red suspension was directly poured into LiCl/H<sub>2</sub>O. Only ferrocene, no trace of chloromercurioferrocene, could be detected by TLC analysis, and the blue color of the aqueous phase indicated that oxidation of ferrocene had occurred.

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