

Triple C–H/N–H Activation by O₂ for Molecular Engineering: Heterobifunctionalization of the 19-Electron Redox Catalysts Fe^ICp(arene)

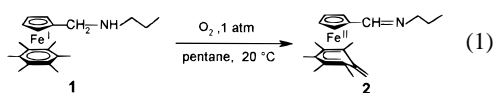
Stéphane Rigaut, Marie-Hélène Delville, and Didier Astruc*

Laboratoire de Chimie Organique et Organométallique,
UMR CNRS N°5802
Université Bordeaux I
33405 Talence Cedex, France

Regiospecific C–H activation is one of the most challenging problems in molecular chemistry. Fundamental recent discoveries have led to considerable advances in this field.¹ One of the next major steps is to adapt and use C–H activation systems to molecular engineering en route toward applications. We know that single benzylic C–H activation of the most acidic hydrogen atom can be achieved by O₂ in the 19-electron complexes Fe^I-Cp(arene).² Since these complexes also catalyze the cathodic reduction of nitrate and nitrite to ammonia in water,³ we have attempted to use this simple and powerful benzylic C–H activation system to attach these redox catalysts onto star molecules and dendrimers.⁵ We report here an unexpected but extremely mild and very useful triple C–H/N–H activation whose principle is derived from that of the benzylic C–H activation by O₂ indicated above. This leads to the heterobifunctionalization of the redox catalyst at room temperature and ultimately to both its solubilization in water and its attachment to star molecules without loss of catalytic activity.

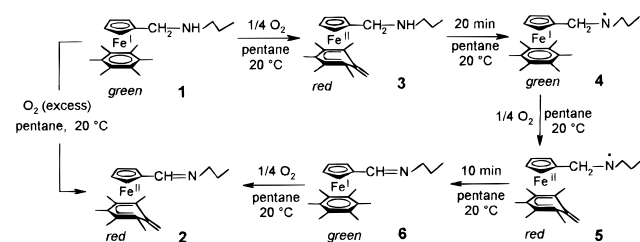
The starting 18-electron complex **1**⁺ was synthesized by the reaction of Fe^{II}(C₅H₄CO₂H)(C₆Me₆)PF₆³ with SOCl₂ (reflux), then with propylamine (0–20 °C), and finally with BH₃ in THF (reflux) in 65% overall yield. Single-electron reduction to the 19-electron isostructural complex **1** was achieved by reaction with Na/Hg in THF in 20 °C.^{4a} The ESR spectrum of **1** shows the characteristic 3-line pattern for the Jahn–Teller active Fe^I state with rhombic distortion:^{4b} $g_x = 1.978$, $g_y = 2.068$, and $g_z = 1.850$. Evidence that the structure is unchanged at this point was obtained by quantitative ferricinium oxidation back to **1**⁺. Much to our surprise, the reaction of the forest-green complex **1** with O₂ in pentane at 20 °C consumed 0.75 equiv of O₂ and gave the red complex **2** resulting from triple H-atom abstraction. On a preparative scale, excess O₂ was bubbled into the solution,

and the reaction took only a few seconds (eq 1). The structure



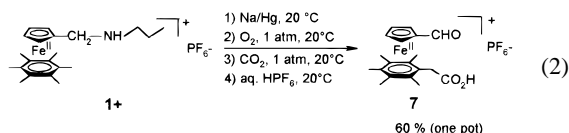
of **2** is shown by ¹H and ¹³C NMR. In order to better understand the reaction of **1** with O₂, we performed it stepwise since we knew that single C–H activation in Fe^ICp(C₆Me₆) only consumed 0.25 equiv of O₂ at 20 °C.² Indeed, reaction of **1** with 0.25 equiv of O₂ instantaneously gave a red complex **3** (the usual color of cyclohexadienyl Fe^{II} complexes with an exocyclic double bond); **3** is not thermally stable and rapidly turned green at 20 °C, giving **4**. Addition of 0.25 equiv of O₂ to **4** instantaneously gave the red color again, forming **5**; this complex is not thermally stable at 20 °C either and gave the green complex **6**. Addition of 0.25 equiv of O₂ to **6** gave the red complex **2** which was relatively stable (thermally and toward O₂). That the green species **4** and **6** are also d⁷, 19-electron

Scheme 1



complexes was indicated by their ESR spectra showing, as for **1**, the classic rhombic distortion (g values are 2.002, 2.074, and 1.858 for **4** and 2.009, 2.074, and 1.904 for **6**). Since the C–H activation by O₂ proceeds by electron transfer from Fe^I to O₂ followed by deprotonation of the cationic organo-Fe^{II} intermediate by superoxide radical anion in the cage-ion pair,² we have also achieved the first C–H activation giving **3** starting from **1**⁺ and KH in THF at –20 °C. This reaction also gave **3**, and at 20 °C, **3**, generated in this way, also turned green and reacted twice with 0.25 equiv of O₂ exactly as above to give **2**. The color change from red **3** to green **4** occurred even at –10 °C in pentane upon transfer by cannula and upon shaking the Schlenk flask, which suggests a radical mechanism (Scheme 1). The synthesis of **3** from **1**⁺ and KH at –30 °C in THF-*d*₈ allowed the recording of its ¹H and ¹³C NMR spectra, which unambiguously showed its cyclohexadienyl structure. Given this information, it is probable that formal H-atom abstraction proceeds each time at the benzylic position to give the red cyclohexadienyl complexes which rearrange by H-atom transfer from the amine chain to the methylene group. This latter thermal process is at least in part intermolecular since it became faster as concentration was increased. In the ESR spectrum of **4**, the expected line around $g = 2.00$ for the nitrogen-centered radical is presumably hidden by the unusually broad central line.

For further synthetic use, **2** could be carboxylated in the benzylic position by reaction with CO₂ (1 atm) at 20 °C and then acidification with aqueous HPF₆ gave the aldehyde **7**. From **1**⁺, the one-pot reaction of eq 2 proceeded in a 60% overall yield of **7**.



The heterobifunctional complex **7** could be attached to the extremities of the branches of the star-shaped molecule **8** to

(1) (a) Bergman, R. G.; Mobley, J. A.; Peterson, T. H. *Acc. Chem. Res.* **1995**, *28*, 154. (b) Arndten, B. A.; Bergman, R. G. *Science* **1995**, *270*, 1970. (c) Brookhart, M.; Green, M. L. H. *J. Organomet. Chem.* **1983**, *250*, 395. (d) Watson, P. L.; Parshall, G. W. *Acc. Chem. Res.* **1985**, *18*, 51. (e) Thompson, M. E.; Bercaw, J. E. *Pure Appl. Chem.* **1984**, *56*, 1. Stahl, S. S.; Labinger, J. A.; Bercaw, J. E. *J. Am. Chem. Soc.* **1996**, *118*, 5961. (f) Brown, S. H.; Crabtree, R. H. *J. Am. Chem. Soc.* **1989**, *111*, 2935, 2946. Crabtree, R. H. *Chem. Rev.* **1995**, *95*, 987. (g) Barton, D. H. R.; Doller, D. *Acc. Chem. Res.* **1992**, *25*, 504. (h) Saillard, J.-Y.; Hoffmann, R. *J. Am. Chem. Soc.* **1984**, *106*, 2006. (i) Lin, M.; Hogan, T.; Sen, A. *J. Am. Chem. Soc.* **1997**, *119*, 6048. (j) *Activation and Functionalization of Alkanes*; Hill, C. L., Ed.; Wiley: New York, 1989. (k) Shilov, A. E. *Activation of Saturated Hydrocarbons by Transition Metal Complexes*; Reidel: Dordrecht, The Netherlands, 1984. (l) *Selective Hydrocarbon Activation*; Davies, J. A.; Watson, P. L.; Liebman, J. F.; Greenberg, A., Eds.; VCH: New York, 1990.

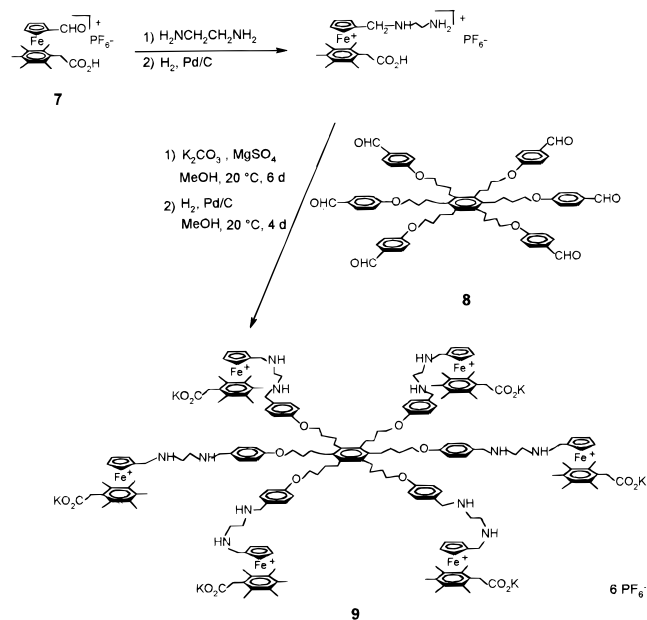
(2) (a) Astruc, D.; Hamon, J.-R.; Román, E.; Michaud, P. *J. Am. Chem. Soc.* **1981**, *103*, 7502. (b) Astruc, D. *Electron Transfer and Radical Processes in Transition-Metal Chemistry*; VCH: New York, 1995. (c) See, for instance, the first step in Scheme 1. This reaction produces 0.5 equiv of H₂O.

(3) Buet, A.; Darchen, A.; Moinet, C. *J. Chem. Soc., Chem. Commun.* **1979**, 447.

(4) (a) Hamon, J.-R.; Astruc, D.; Michaud, P. *J. Am. Chem. Soc.* **1981**, *103*, 758–766. (b) Rajasekharan, M. V.; Giezyński, S.; Ammeter, J. H.; Hamon, J.-R.; Michaud, P.; Astruc, D. *J. Am. Chem. Soc.* **1982**, *104*, 2400.

(5) (a) Newkome, G. R.; Moorefield, C. N.; Vögtle, F. *Dendritic Molecules: Concepts, Syntheses and Perspectives*; VCH: New York, 1996. (b) Tomalia, D. A.; Dupont Durst, H. *Top. Curr. Chem.* **1993**, *165*, 193. (c) Ardoin, N.; Astruc, D. *Bull. Soc. Chim. Fr.* **1995**, *132*, 875.

Scheme 2



give the hexametallalike complex **9**, soluble in basic aqueous medium, according to Scheme 2 (40% overall yield). Complex **9** gave a single reversible wave at -1.80 V vs SCE in cyclic voltammetry in 0.1 M aqueous LiOH showing that, as expected, the six redox centers are independent. The complex **9** catalyzes the cathodic reduction of nitrates and nitrites to ammonia on mercury cathode in aqueous LiOH as indicated by the enhancement of the intensity of the reduction wave upon addition of one of these salts. Using the Nicholson and Shain equation,⁶ this enhancement allowed the calculation of the rate constant of the reduction of the substrate by the 19-electron form of **9**. The values found in the catalysis by **9** are 10^3 L mol⁻¹ s⁻¹ for NO₃⁻ and 2.7×10^3 L mol⁻¹ s⁻¹ for NO₂⁻. They are close to the values reported using Fe(C₅H₄CO₂H)(C₆Me₆) in 0.1 M aqueous LiOH which are 4×10^2 L mol⁻¹ s⁻¹ for NO₃⁻ and 2×10^3 L mol⁻¹ s⁻¹ for NO₂⁻ respectively.^{3a} Thus, no decrease in efficiency was observed with the star-shaped complex **9** when compared to the mononuclear catalyst of analogous driving force.

(6) Nicholson, R. S.; Shain, I. *Anal. Chem.* **1964**, *36*, 706.

In conclusion, although true 19-electron complexes are scarce,⁴ their chemistry illustrated here is rich and promising for further applications of the concept of electron reservoirs in redox catalysis. It should be underlined that very few catalysts^{7,8} or redox catalysts⁹ have so far been attached to dendrimers, most probably due to the difficulty of branching. In the present case, the powerful triple C–H activation found under ambient conditions provided heterofunctionalization allowing for both branching and solubilization in water¹⁰ without loss of catalytic activity. The extremely mild conditions found here for the oxidation of the amine to the imine by O₂ contrast with the well-documented conditions required which are usually harsh or difficult to control.^{11,12}

Acknowledgment. We thank Pr. C. Coulomb and J. Amiel (CRPP, Bordeaux) for the ESR spectra, Dr. J. Losada (Madrid) for helpful discussions, and the Institut Universitaire de France, the Université Bordeaux I, the CNRS, the Région Aquitaine, and Rhône-Poulenc for financial support.

Supporting Information Available: Procedures for the preparation and analytical and spectroscopic characterization of **1**⁺, **2**, **7**, and **9** and experimental details of the triple C–H activation reaction in **1** with O₂ including ¹H and ¹³C NMR data for **3** and ESR spectra of **1**, **4**, and **6** (8 pages). See any current masthead page for ordering and Internet access instructions.

JA9725458

(7) (a) Knapen, J. W. J.; van der Made, A. W.; de Wilde, J. C.; van Leeuwen, P. W. N. M.; Wijkens, P.; Grove, D. M.; Van Koten, G. *Nature* **1994**, *372*, 659.

(8) Bhyrappa, P.; Young, J. K.; Moore, J. S.; Suslick, K. S. *J. Am. Chem. Soc.* **1996**, *118*, 5708.

(9) (a) Herring, A. M.; Steffey, B. D.; Miedaner, A.; Wander, S. A.; Dubois, D. L. *Inorg. Chem.* **1994**, *33*, 5482. (b) Herring, A. M.; Steffey, B. D.; Miedaner, A.; Wander, S. A.; Dubois, D. L. *Inorg. Chem.* **1995**, *34*, 1100.

(10) For the reduction of water-soluble substrates by 19-electron complexes, see also: MacKenzie, V.; Tyler, D. R. *J. Chem. Soc., Chem. Commun.* **1987**, 1783.

(11) (a) Challis, B. C.; Butler, B. R. In *The Chemistry of the Amino Group*; Patai, S., Ed.; Wiley, New York, 1968; Chapter 6, pp 321–338. (b) Murahashi, S. I. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2443.

(12) For the dehydrogenation of transition-metal-coordinated amines to imines, see: Bernhardt, P.; Bull, D. J.; Bürgi, H.-B.; Osvath, P.; Raselli, A.; Sargeson, A. M. *Inorg. Chem.* **1997**, *36*, 2804 and references cited therein.