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A Fluorescent Molecular Probe for the Detection of Hydrogen Based on Oxidative Addition Reactions with Crabtree-Type Hydrogenation Catalysts

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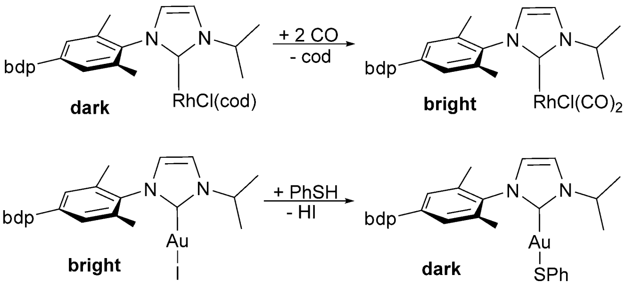
Dedicated to Professor Herbert W. Roesky on the occasion of his 80th birthday

Abstract: *A Crabtree-type Ir^I complex tagged with a fluorescent dye (bodipy) was synthesized. The oxidative addition of H_2 converts the weakly fluorescent Ir^I complex ($\Phi = 0.038$) into a highly fluorescent Ir^{III} species ($\Phi = 0.51$). This fluorogenic reaction can be utilized for the detection of H_2 and to probe the oxidative addition step in the catalytic hydrogenation of olefins.*

Hydrogen is a colorless, odorless, and tasteless gas. The chemistry of hydrogen (H_2) is dominated by its highly exothermic reaction with oxygen. This poses risks when handling hydrogen, but also offers chances for energy production under controlled reaction conditions. As a consequence of the dwindling resources of fossil fuels and excessive CO_2 emissions, a hydrogen-based economy appears to be a desirable target.[1] The increased use of hydrogen in energy production will inevitably create demand for hydrogen sensing to properly address safety issues. Other applications for hydrogen sensing concern the food industry,[2] the detection of certain bacteria,[3] leaks in flexible food packaging,[4] as well as diagnostics for lactose intolerance[5] and hydrogen-metabolizing organisms.[6]

Electrical sensors for hydrogen are well-established,[7] but offer the potential of spark-induced explosions; furthermore, miniaturization is limited. Optochemical sensors for hydrogen have distinct advantages in this respect.[7,8] For example, fluorescent molecular probes are very convenient, since the fluorescence is turned on upon a specific reaction with an analyte.[9] Only a few probes are known for simple gases, such as CO,[10] CO_2,[11] H_2S,[12] NO,[13] NO_2,[14] and ethene,[15] which are important in a biological and chemical context. To the best of our knowledge, a fluorescent molecular probe for hydrogen (H_2) has so far not been reported.[16]

We recently synthesized transition-metal complexes with appended fluorescent tags and realized that the manipulation of the electron density in certain transition-metal complexes enables the modulation of the fluorescence intensity.[17] The brightness of a fluorescent dye attached to organometallic complexes based on Au, Rh, or Ir turned out to be highly sensitive to changes in the electron density at the transition metals. For example, the substitution of a 1,5-cyclooctadiene (cod) ligand by CO (Scheme 1) converts nonfluorescent complexes ($\Phi < 0.01$) into highly fluorescent ones ($\Phi > 0.5$). Alternatively, the substitution of a halide ($\Phi > 0.5$) by a strongly electron-donating thiolato group transforms highly fluorescent gold complexes into partially quenched ones ($\Phi < 0.2$; Scheme 1).



Scheme 1. Modulation of fluorescence intensity as a consequence of ligand-exchange reactions. bdp = pentamethylbodipy.

We set out to test the potential of oxidative addition reactions for the detection of molecules. Such elementary organometallic reactions are highly important steps in various catalytic transformations.[18] Many transition-metal complexes are able to activate H_2 and transfer individual hydrogen atoms to unsaturated substrates.[19]

Iridium-based Crabtree-type complexes are amongst the most popular catalysts[20] for asymmetric hydrogenation reactions.[21] A very important property of Crabtree-type complexes is the lack of reactivity towards oxygen or water. The oxidative addition of H_2 to a transition metal is often the first step in hydrogenation and formally converts an electron-rich Ir^I complex into an electron-deficient Ir^{III} one.[22]

We report here on the synthesis of an Ir^I Crabtree complex with an appended 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (bodipy) fluorophore and on the effect of the oxidative addition of H_2 on the fluorescence intensity. Bodipy and its numerous derivatives are highly useful fluorophores that are characterized by high extinction coefficients, excel-

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lent fluorescence quantum yields, narrow emission bands, high photostability, and good solubility in many organic solvents.[23]

To establish a stable linker between the fluorophore and the transition metal, we chose N-heterocyclic carbenes (NHCs), which are amongst the most prominent ligands in transition-metal chemistry.[24] The synthesis of an (NHC)Ir complex with an appended bodipy fluorophore is outlined in Scheme 2. Trimethylsilylacetylene is coupled in a Sonogashira reaction to monobromo-*N*,*N'*-diaryldiamine (**1**),[25] removal of the trimethylsilyl-protecting group, and another Sonogashira reaction with iodo-bodipy provides the fluorophore-tagged diamine **4**. Hydrogenation of the alkyne group gives diamine **5**, in which the fluorophore is electronically decoupled from the potential metal coordinating site. The cyclization of the diamine with C_6F_5CHO provides imidazolidine **6**. This compound is a useful NHC transfer reagent,[26] whose reaction with $[\{IrCl(cod)\}_2]$ affords complex **7** in excellent yield (Scheme 2). The electrochemical properties of **7** were probed by cyclic voltammetry. Two reversible redox processes were observed: $E_{1/2} = +0.77$ V is a typical Ir^I/Ir^{II} redox potential,[27] while $E_{1/2} = +1.13$ V corresponds to the bodipy oxidation.[28] Exchange of the chloride group by weakly coordinating anions (triflate or BArF) provides the respective "cationic" complexes **8b** and **8c**. A solution of complexes **8** and 100 equiv of pyridine in methanol readily reacts with hydrogen to form the respective cationic dihydride complex **9** within a few minutes. The triflate complex **9b** was isolated and characterized. It displays the characteristic hydride signal at δ −22.4 ppm, but is prone to decomposition in solution. The same highly characteristic hydride shift was observed for the closely related complex $[(IMes)Ir(H)_2(py)_3]^+Cl^-$ (δ −22.5 ppm), which was synthesized by Duckett and coworkers and used in NMR hyperpolarization experiments.[29]

The fluorescence properties of the bodipy-containing compounds **5**–**9** were studied and all found to absorb and emit in a narrow range close to $\lambda_{max}(exc) = 510$ nm and $\lambda_{max}(em) = 524$ nm. The Ir^I complexes **7** and **8** are weakly fluorescent (fluorescence quantum yields $\Phi(\mathbf{7}) = 0.022$, $\Phi(\mathbf{8b}) = 0.038$). A very pronounced increase in the fluorescence intensity was observed in the course of the reactions of solutions of **7** or **8b** or **8c** with hydrogen in methanol (Figure 1). The fluorescence quantum yield of isolated **9c** was determined to be $\Phi = 0.51$. This increase in brightness denotes the formation of the respective Ir^{III} complex **9** following oxidative addition of H_2.[30] This reaction appears to be complete within a few minutes.

A simple paper strip method was employed to demonstrate the hydrogen-sensing properties of the iridium complexes. A filter paper was impregnated with a solution of **8b** in propylene carbonate (b.p. 242 °C; $c = 1.0 \times 10^{-3}$ mol L^{-1}). The solution of complex **8b** in this solvent is highly stable in an ambient atmosphere and the fluorescence of the paper strip does not change in the presence of ambient air. One of the paper strips was exposed to an atmosphere of pure hydrogen. Within a few minutes the highly fluorescent Ir^{III} complex is generated (Figure 2). Using this simple filter paper assay it is

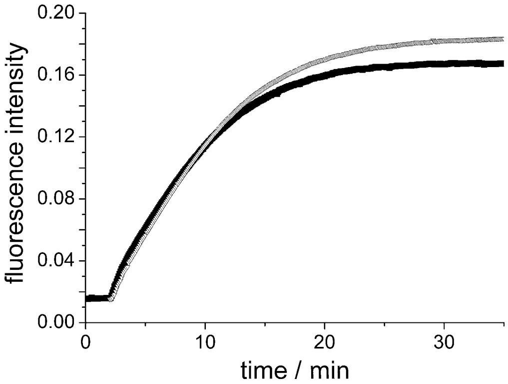
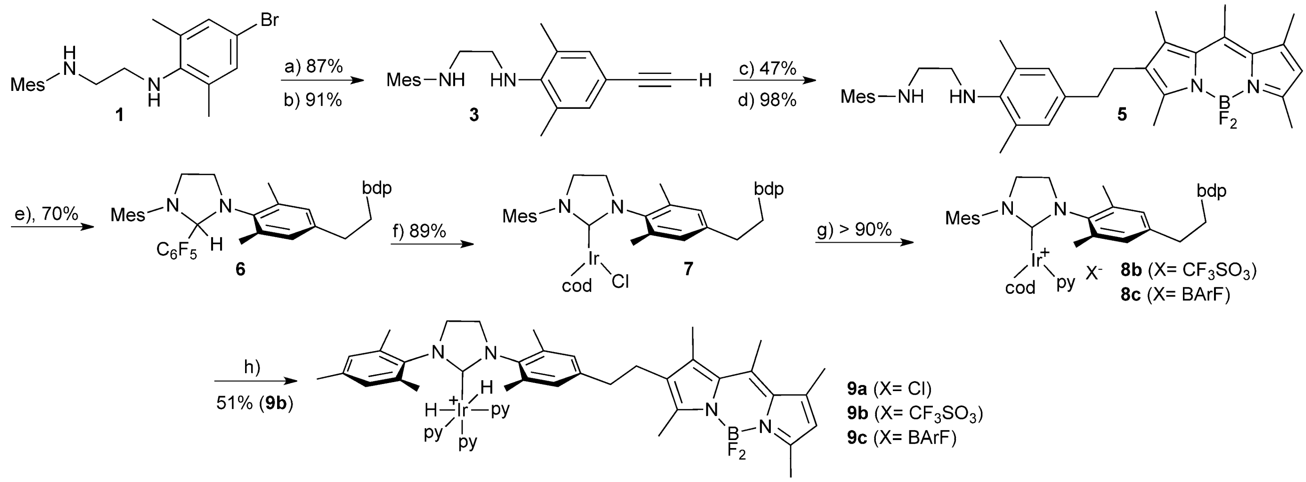


Figure 1. Fluorescence–time plots for the reaction of **8b** (gray) and **8c** (black; 1.0×10^{-6} mol L^{-1}) in methanol containing pyridine (1.0×10^{-4} mol L^{-1}) with hydrogen.



Scheme 2. Synthesis of bodipy-tagged (NHC)Ir complexes. Reagents and conditions: a) $HCCSiMe_3$, Na_2PdCl_4, CuI, $Cy_2PtBu\cdot HBF_4$, $HNiPr_2$, 80 °C, 12 h; b) $NBu_4F\cdot 3H_2O$, THF, RT, 1 h; c) iodo-pentamethyl-bodipy, Na_2PdCl_4, CuI, $Cy_2PtBu\cdot HBF_4$, $HNiPr_2$, 80 °C, 12 h; d) Pd/C, 5 bar H_2, MeOH, RT, 4 h; e) C_6F_5CHO, acetic acid, RT, 12 h; f) $[\{IrCl(cod)\}_2]$, toluene, 70 °C, 2 h; g) **8b** $[Ag(CF_3SO_3)]$, pyridine, CH_2Cl_2, 60 min; **8c** [Na(BArF)], pyridine, CH_2Cl_2, 60 min; h) H_2, MeOH, 100 equiv pyridine. BArF = $[B\{3,5\text{-}(CF_3)_2C_6H_3\}_4]^-$, Mes = 2,4,6-trimethylphenyl, py = pyridyl.

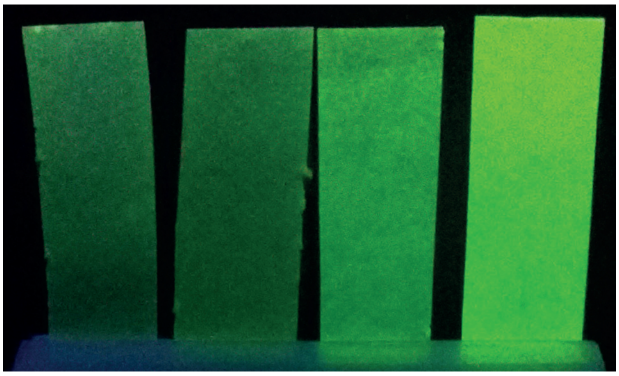


Figure 2. Four filter paper strips (left to right: a–d) impregnated with a solution of **8b** in propylene carbonate and irradiated with broadband UV light. Strip (a) exposed to ambient air; strip (b) exposed to 1% (vol) H_2; strip (c) exposed to 4% (vol) H_2 (lower explosion limit), and strip (d) exposed to pure H_2.

possible to detect hydrogen at a concentration corresponding to the lower explosion limit (4% vol) and to distinguish this from a lower hydrogen concentration (1% vol).

Next the catalytic properties of the new iridium complexes were studied. Catalytic studies were limited to **8b** and **8c** containing weakly coordinating anions, as coordinating anions are detrimental for substrate conversion.[31] The reactions with hydrogen were carried out in 1,2-dichloroethane as solvent, since the donor solvents used for the hydrogen-sensing experiments are known to inhibit olefin hydrogenation, probably by impeding coordination of the olefin to the iridium center. The room-temperature reaction of the test substrate allylbenzene with hydrogen in the presence of **8c** provides the fully hydrogenated product within 10 min in nearly quantitative yield at 0.5 mol% catalyst loading.

Next, the time-dependent fluorescence intensity of **8b** and **8c** during the catalytic hydrogenation reaction with H_2 and allylbenzene in 1,2-dichloroethane as solvent was monitored. For this reaction, a lower loading (0.1 mol%) as well as a much lower concentration of precatalyst **8b** (1.0×10^{-6} mol L^{-1}) was chosen to ensure that the active species is fully consumed during the catalytic reaction. Consequently, the conversion of allylbenzene into the hydrogenation product propylbenzene was only approximately 30%. The catalytic reaction with hydrogen and an olefin is characterized by a pronounced increase in the fluorescence intensity (Figure 3). However, the final level of fluorescence in 1,2-dichloroethane is lower than that observed in MeOH/pyridine (Figure 1), thus indicating the formation of an Ir^{III} species different from complex **9**. This is not surprising, as it is known that, in nonpolar solvents in the absence of the stabilizing cod ligand and after consuming the olefins in the hydrogenation reaction, trimeric[32] as well as higher nuclearity iridium hydride clusters are formed.[33] A hydrogenation experiment carried out in an NMR tube using **8c** and allylbenzene shows the formation of numerous iridium hydride species, as evident by the appearance of a large number of resonances at 0 to −30 ppm in the ^{1}H NMR spectrum, thus confirming findings by Brown and co-workers for related complexes.[33]

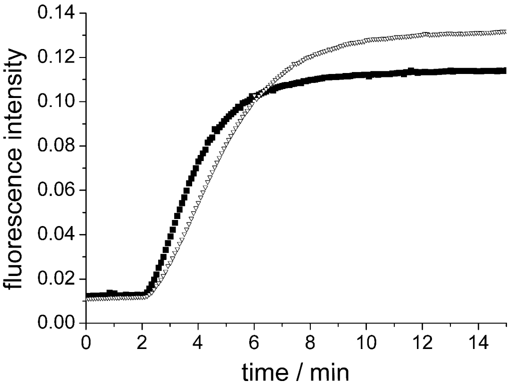


Figure 3. Emission–time plots for the reaction of **8b** (gray) and **8c** (black; 1.0×10^{-6} mol L^{-1}) in 1,2-dichloroethane with hydrogen (fluorescence gain 11.7 and 9). Excitation wavelength 510 nm.

The time-dependent fluorescence intensity of the bodipy was monitored during the catalytic conversion of different substrates (allylbenzene, styrene, cyclohexene, α-terpinene). The increase in the fluorescence intensity during these reactions is virtually the same as observed for the iridium dihydride complex in 1,2-dichloroethane in the absence of an olefinic substrate (Figure 4).[34] One interpretation is that the steps in the catalytic cycle following the oxidative addition of hydrogen do not lead to significant changes in the fluorescence intensity of the iridium complex. Considering the high sensitivity of the fluorescence intensity to changes in the electron density at the metal, this explanation is less likely.[17] The similar fluorescence intensities are more easily explained by assuming that the iridium dihydride species is the dominant one in the catalytic reaction. Previously, a dihydride complex has been suggested to be the resting state of the catalytic reaction, which is in accordance with our data.[35] Notably, the formation of the fluorescent iridium dihydride species occurs faster than substrate conversion (Figures S28, and S29).[36] It is, therefore, less likely that the fluorescent product observed is the decomposition product of the catalyst following substrate conversion.

In conclusion, we have shown that the oxidative addition of hydrogen to an Ir^I complex tagged with a bodipy fluorophore gives rise to a substantial increase in the fluorescence

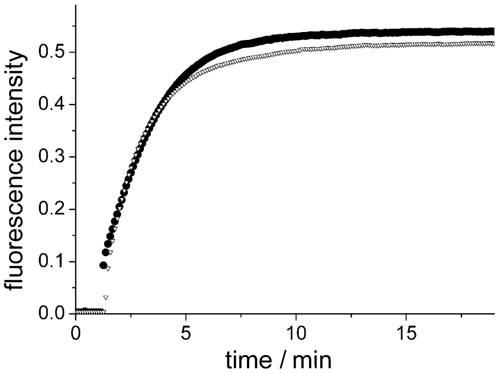


Figure 4. Emission–time plot for the catalytic hydrogenation of 0.1 M allylbenzene (gray) with **8b** (black; 1.0×10^{-5} mol L^{-1}) in 1,2-dichloroethane; same reaction conditions, but without olefin (black).

intensity of the formed $\mathrm{Ir^{III}}$ dihydride complex. This signal enables the detection of hydrogen and is useful for the analysis of catalytic hydrogenation reactions. We, therefore, propose fluorescence spectroscopy to be a useful tool for the analysis of transition-metal-catalyzed reactions, since changes in the electron density at the metal center which translate into changes in the fluorescence intensity occur in numerous metal-catalyzed reactions.

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