

The Formation of Aldehydes from the Photochemically Activated Reaction of Cp*Ir(CO)(Cl)(CH₂R) Complexes with Water

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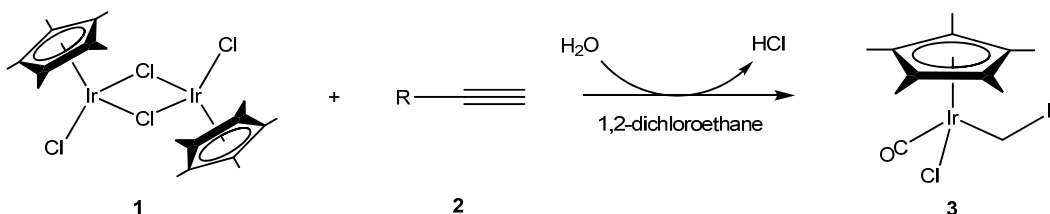
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Abstract

The iridium complexes Cp*Ir(CO)(Cl)(CH₂R), which do not contain any β-hydrogen atoms, react with water to form aldehydes. This reaction was found to be photochemically activated, and a possible pathway involving radical intermediates has been proposed and studied experimentally and computationally.

1. Introduction

The dimeric iridium complex [Cp*IrCl₂]₂ (**1**) reacts with terminal alkynes (**2**) in the presence of water to form the alkyl carbonyl complexes Cp*Ir(CO)(Cl)(CH₂R) (**3**) via a C≡C bond cleavage reaction (Scheme 1). This reaction proceeds with a variety of aromatic and aliphatic alkynes, and the possible reaction pathway has been studied experimentally and computationally [1].



Scheme 1

When R contains a β-hydrogen, the complexes **3** decompose via β-hydrogen elimination to give Cp*Ir(CO)(Cl)₂ (**4**). Such a decomposition pathway is well-known in transition metal alkyl chemistry, and it is equally well-known that if this pathway is shut off,

then the complexes are likely to be stable. Transition metal alkyl complexes are also known to decompose via α -H elimination and abstraction, but this mode of decomposition is generally not common for late transition metal complexes. In the case of iridium complexes, there are very few reports of α -H elimination and, in general, they appear to occur for sterically encumbered iridium centers [2,3,4,5].

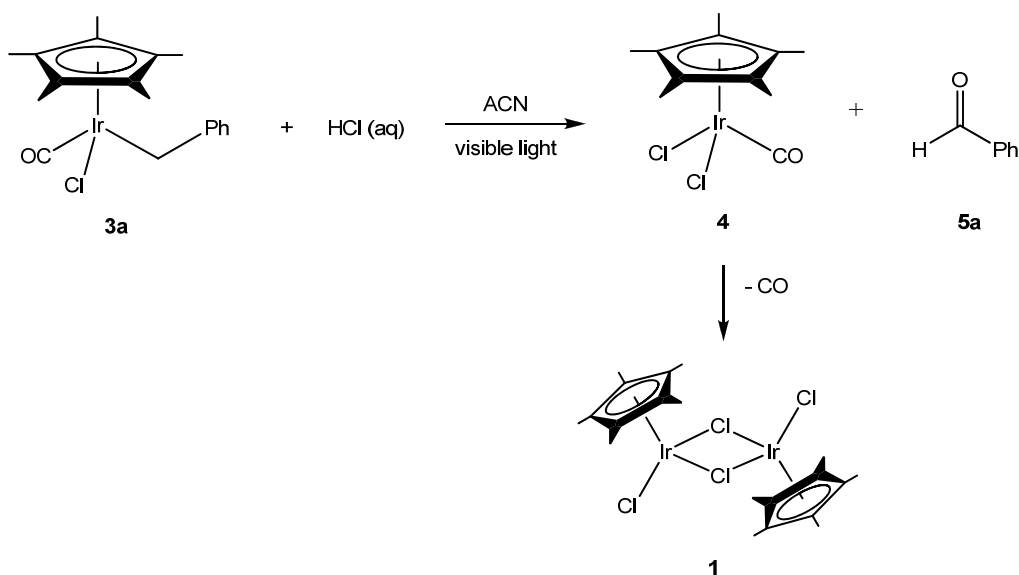
We thus expected that those complexes not containing an R group with a β -hydrogen, for instance, Cp*Ir(CO)(Cl)(CH₂Ph) (**3a**), should be stable. Instead, we invariably obtained small amounts of Cp*Ir(CO)Cl₂ (**4**) and benzaldehyde (**5a**) from its synthesis according to scheme 1. We have now found that **3** reacted with water under photochemical activation via homolytic Ir-Cl bond fission and radical abstraction. The details of our study into this reaction are presented.

2. Results and Discussion

As mentioned above, small amounts of **4** and **5a** were observed to be formed during the synthesis of **3a**. The same products were obtained if purified **3a** was allowed to stand in chloroform. The identity of **4** was confirmed by an independent synthesis involving stirring **1** under a CO atmosphere, as well as by a comparison of the spectroscopic data with literature values [6], while the identity of **5a** was confirmed by comparison of its NMR and GC-MS spectra with an authentic sample.

As the formation of **3a** generates HCl, our initial conjecture was that **4** resulted from the reaction of HCl with **3a**. Indeed a mixture containing **3a** and **4** in roughly equal amounts was obtained when **3a** was stirred with 1 M aqueous HCl in acetonitrile. Monitoring this reaction by NMR over a period of 6 days showed the gradual formation of **4** and **5a**, and the subsequent decarbonylation of **4** to regenerate **1** (Scheme 2). The amount of **5a** formed was slightly less than stoichiometric compared to **4**. The rate and yield of the reaction was not increased by heating, but UV irradiation afforded significant amounts of **5a** in 20 min, while

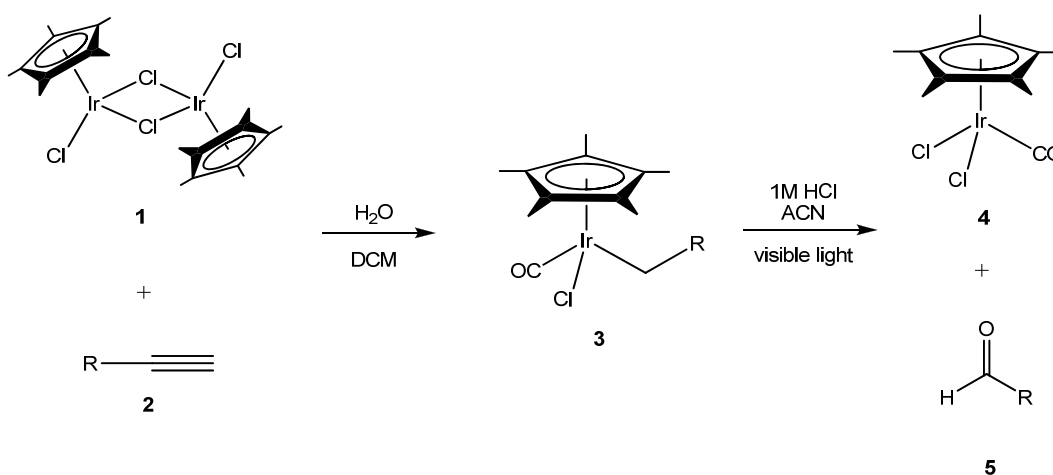
visible light irradiation also gave a better yield of **5a** albeit over a longer reaction time (~20 h to reach completion); no reaction occurred when light was completely excluded. Both irradiation methods also gave rise to small amounts of different unidentified side products. In contrast to this, an attempted synthesis of the C≡C bond cleavage product from the reaction of the bromo analogue of **1**, *viz.*, [Cp*IrBr₂]₂ (**1'**), with **2a** under identical conditions to that above gave Cp*Ir(CO)(Br)₂ (**4'**) as the major product. Resonances which could be attributed to Cp*Ir(CO)(Br)(CH₂Ph) (**3a'**) and **5a** were also observed, and there was no significant improvement to the yield of **3a'** when the reaction was carried out in the dark.



Scheme 2

This reaction to form an aldehyde was tested out with a number of other alkynes; the reaction of **1** with various alkynes to generate the corresponding C≡C bond cleavage product **3**, followed by their subsequent reaction to form **4** and **5** under the optimized conditions, are given in scheme 3. With the exception of 2-ethynylbenzaldehyde, **2g**, all of the aromatic alkynes contained electron donating substituents. Conversion of complexes **3a – d**, and **3f**, to their respective aldehydes was close to stoichiometric. For **3e**, significantly more **1** was present in the crude NMR, which affected proper integration of the CHO resonance of **5e** to the Cp* resonance of **4**. No analogous C≡C bond cleavage product was observed for **2g**, but

instead the aldehyde **5g** was directly obtained from the reaction of **1** with **2g**. This reaction did not require visible light irradiation, and irradiating a mixture of **1** and **2g** gave some unidentified side products. Both **2h** and **2i** failed to react to form **3h** and **3i**, respectively, probably due to interference from the amino and hydroxyl groups; the former, for instance, coordinates strongly to monomeric Cp*IrCl₂ units [7]. In contrast, **3j** showed no tendency towards degradation to the aldehyde **5j**.



	R	Yield of 3 (%)	Integration ratio*
a	C ₆ H ₅	70	1:19
b	<i>p</i> -FC ₆ H ₄	40	1:19
c	<i>p</i> -ClC ₆ H ₄	80	1:20
d	<i>p</i> -BrC ₆ H ₄	72	1:19
e	<i>p</i> -CH ₃ C ₆ H ₄	50	1:5
f	<i>p</i> -CH ₃ OC ₆ H ₄	58	1:11
g**	<i>o</i> -OHCC ₆ H ₄	-	2:15
h	<i>o</i> -NH ₂ C ₆ H ₄	-	
i	<i>o</i> -HOCH ₂ C ₆ H ₄	-	
j	^t Bu	27	

*Integration ratio of the -CHO resonance of **5** to the Cp* signal of **4**.

****5g** obtained directly from the reaction of **1** with **2g**; **3g** not observed.

Scheme 3

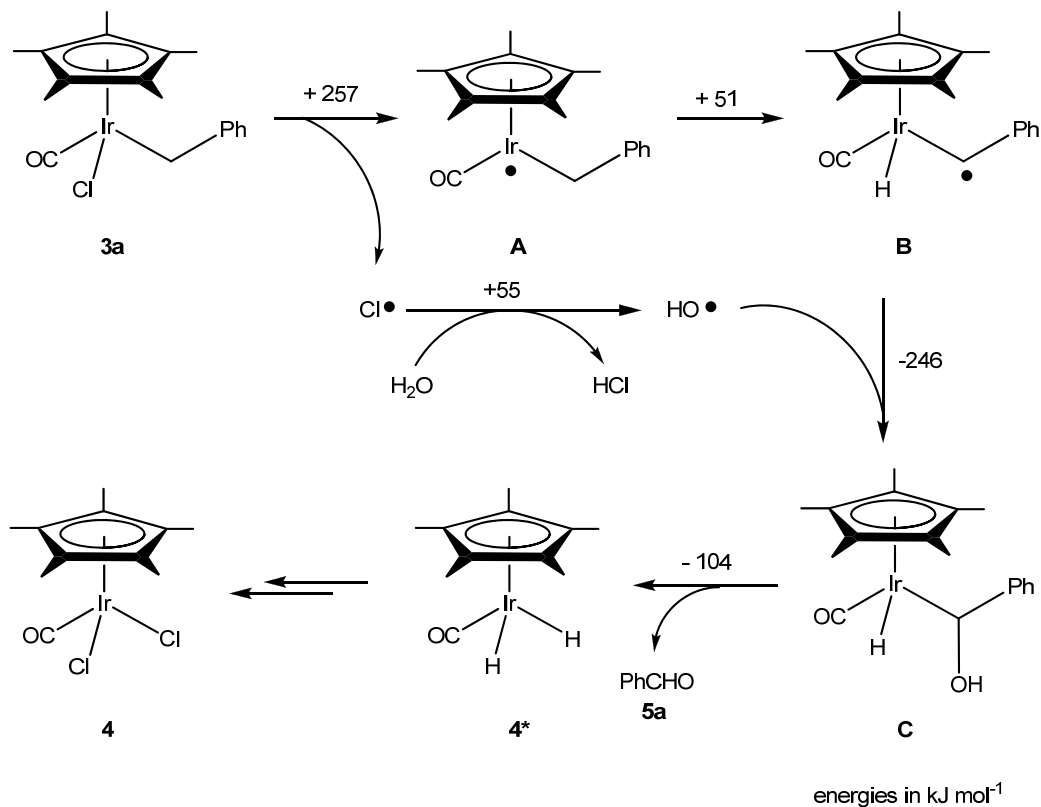
Since **3a** generated **4** upon standing in chloroform, it must indicate that chloroform can act as a chloride source. This was confirmed by a reaction of **3a** with bromoform; the ^1H NMR spectrum showed two Cp* resonances, one corresponding to **4'** and another which could be intrapolated to be that for Cp*Ir(CO)(Br)(Cl) (**4''**), in a 7:1 ratio. On the other hand, the NMR spectrum of a reaction of **1'** with **2a** in chloroform showed only the presence of **3a'** and **4'** but no **4**. This indicates that the conversion of **3a'** to **4'** is more facile than that of **3a** to **4**, and may be attributed to bromide being a better leaving group; presumably, HBr liberated from the formation of **3a'** is responsible for the formation of **4'** in this case.

Visible light irradiation of a mixture of **3a** and aqueous [Et₄N]Cl in acetonitrile showed the formation of **5a** but no **4**. The NMR spectrum also showed a major species containing a Cp* resonance, and the presence of acetamide. The formation of acetamide was mostly likely to be due to the partial hydrolysis of acetonitrile. ESI-MS analysis suggested that the iridium species also contained acetamide ligands but we have otherwise not been able to confirm its identity. A similar result was obtained with aqueous [Et₄N]Br, and when only water was used. These indicated that although an acidic environment is not required for the formation of **5a**, it is required for the formation of **4**.

An isotopic labeling experiment in which **3a** which has been deuterated at the CH₂ protons (**d₂-3a**), afforded **5a** which was deuterated at the aldehyde moiety. This indicated that the CH₂ was transformed into the aldehyde functionality. Similarly, the GC-MS of a reaction using **3d** in 10M HCl which has been diluted with H₂¹⁸O, showed peaks at m/z 186 and 188 in the mass spectrum, indicating the presence of ¹⁸O-**5d**, and thus showing that the source of the oxygen atom in the aldehyde was water.

On the basis of the above observations, we would like to propose a reaction pathway for the reaction from **3a** to **4** and **5a** as shown (Scheme 4). We have investigated this pathway computationally using density functional theory at the B3LYP level using the LANL2DZ

basis set augmented with f polarization functions for the Ir atom and the 6-311+G(2d,p) basis set for all other atoms; the reaction free energy changes, with acetonitrile as the reaction solvent, are also shown in Scheme 4.



Scheme 4

The first step is a photochemical homolytic fission of the Ir-Cl bond from **3a** to give the radical intermediate **A**. The alternative involving loss of the chloride ligand was excluded because performing the reaction in the presence of AgBF_4 in the absence of light resulted in the conversion of **3a** to an unidentified compound with no formation of **5a**. On the other hand, irradiation of **3a** in the presence of TEMPO or acrylonitrile resulted in a mixture of unidentified compounds which did not contain **4** or **5a**, suggesting the presence of radical intermediates. We have also verified that TEMPO did not react with **3a** in the absence of light.

The second step is a hydrogen migration from the CH₂ moiety to the iridium center to produce the radical intermediate **B**, which subsequently picks up a hydroxyl radical to form the intermediate **C**. There are different ways to obtain intermediate **4*** from **C**, but the most likely would be via a β-H elimination similar to that for β-H containing complexes of **3**, thus generating **5a** in the process.

The conversion of **4*** to **4/4'/4''** in the presence of a Cl and/or Br source is then expected to be very fast. It may be expected that this step, or similar steps, would involve elimination of H₂ and/or formation of CH₂Cl₂ (from CHCl₃) [8]. However, we have not been able to detect either; analysis of the headspace gas of the reaction for hydrogen using a residual gas analyzer did not generate any conclusive results when compared to the reading from a blank reaction, nor did an attempt at observing hydrogen gas or CH₂Cl₂ formation via NMR spectroscopy.

We have examined more closely the excited states of **3a**. An excited state computation with the TD method showed that excitations into the first three excited states of **3a** corresponded to absorptions at 362, 302 and 261 nm. The solution (CH₂Cl₂) UV-vis spectrum of **3a** showed two distinct absorption bands centred at ~370 and 320 nm (equivalent to ~323 and 374 kJ mol⁻¹, respectively, in energy), in close accord with the first two computed values. These values suggested that the irradiation could provide sufficient energy for the endergonic step from **3a** to **A**. Visualization of the LUMO of **3a** shows that it is anti-bonding with respect to the Ir-Cl bond (Figure 1), suggesting that excitation into the LUMO would weaken the Ir-Cl bond.

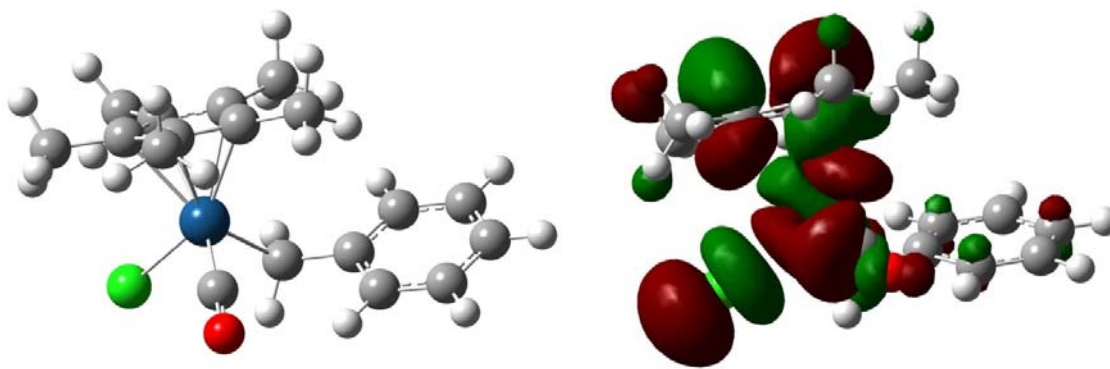


Figure 1. Optimized structure (left) and LUMO (right) of **3a**.

3. Conclusion

Complexes of the general formula $\text{Cp}^*\text{Ir}(\text{CO})(\text{Cl})(\text{CH}_2\text{R})$ react with water under photochemical activation to give the aldehydes RCHO . A pathway for the reaction has been proposed on the basis of experimental and computational studies, and it involves photochemically-activated homolytic fission of the Ir-Cl bond to form an organometallic radical species, which abstracts the α -H. Subsequent reaction with water led, eventually, to elimination of an aldehyde.

4. Experimental

4.1. General procedures

All operations were carried out using standard Schlenk techniques under an inert argon atmosphere unless otherwise stated. Solvents used were of AR grade. Preparative thin layer chromatography was done using Merck 60 F₂₅₄ (20 cm x 20 cm) silica gel plates. ¹H NMR spectra were recorded on a JEOL ECA400 or ECA400SL 400 MHz NMR spectrometer. Chemical shifts were reported with respect to the residual solvent peak in the respective deuterated solvent. Solution IR spectra were obtained as dichloromethane (DCM) solutions on a Bruker Optik GmbH ALPHA FTIR spectrometer at a resolution of 2 cm⁻¹ using a solution IR cell with NaCl windows and pathlength of 0.1 mm. Mass spectra were obtained on a Finnigan MAT95XL-T spectrometer in a 3NBA matrix (FAB). GC – MS analyses were

performed on a ThermoFinnigan DSQII instrument, equipped with Trace gas chromatograph and DSQ II (EI) mass spectrometer, using a DB – 5MS column. All UV and tungsten lamp irradiation experiments were carried out using a Ace Glass medium-pressure, Hanovia, mercury – vapor arc lamp (approx. 254 nm, 450 Watts) and a Phillip N63 tungsten lamp (200 – 400 nm, 60 Watts) respectively. UV–vis absorbance data was obtained using a Varian Cary 300 UV-Vis spectrophotometer. Hydrogen gas was detected using a Balzer Prisma QMS 200 residual mass analyzer. Complexes [Cp*IrCl₂]₂ (**1**), [Cp*IrBr₂]₂ (**1'**) and Cp*Ir(CO)(Cl)₂ (**4**) were synthesized from their respective published methods [9,10].

4.2. Computational Studies

The reaction energetics for the reaction of **3a** to **4** and **5a** was studied by DFT theory utilising the Becke's three parameter hybrid function [11], and Lee-Yang-Parr's gradient-corrected correlation function (B3LYP) [12]. The LANL2DZ (Los Alamos Effective Core Potential Double- ζ) basis set together with an f polarisation function [13], was employed for the Ir atom; the 6-311+G(2d,p) basis set was used for all other atoms. Excited state calculations were carried out with the TD method using the same basis sets [14]. For calculations involving solvated species, the polarized continuum model (PCM) was employed. Harmonic frequencies were calculated at the optimized geometries to characterize stationary points as equilibrium structures, with all real frequencies and to evaluate zero-point energy (ZPE) correction. All calculations were performed using the Gaussian 09 suite of programs [15].

4.3. Reaction of **1** with **2a**

The reaction was modified from a reported procedure [1]. To **1** (25 mg, 0.03 mmol) and **2a** (10 μ L, 0.09 mmol) in DCM (1 mL), water (25 μ L) was added. The orange coloured mixture was stirred at room temperature for 1 d, after which all volatiles were removed *in vacuo*. The residue was redissolved in minimal DCM and subjected to preparative thin layer

chromatography (TLC) using hexane/DCM (1:1, v/v) as the eluent. Recovery of the major yellow band yielded **3a** as a yellow solid.

The reactions of **1a** with **2b** – **2j**, and **1'** with **2a** and **2j**, were performed using this same procedure.

4.4. Synthesis of $Cp^*Ir(CO)(Br)_2$ (**4'**)

The reaction was modified from the reported procedure for the synthesis of **4** [13]. A solution of **1'** (15 mg, 0.021 mmol) in DCM (2 ml) was subjected to three cycles of freeze pump thaw in a carius tube. Carbon monoxide (1 atm) was then introduced into the tube. The orange solution turned yellow instantly and was left to stir for a further 2 h.

1H NMR (δ , $CDCl_3$) = 2.02 (s, 15H, Cp^*). IR (DCM, cm^{-1}) ν_{CO} = 2055 cm^{-1} (vs)

4.5. Synthesis of $Cp^*Ir(CO)(Cl)(CD_2Ph)$ (d_2 -**3a**)

To **1** (25 mg, 0.03 mmol) and **2a** (10 μ L, 0.09 mmol) in dried 1,2-dichloroethane (1 mL) was added D_2O (25 μ L). The orange coloured mixture was stirred at room temperature for 1 d, after which all volatiles were removed *in vacuo*. The residue was redissolved in the minimum volume of DCM and subjected to preparative thin layer chromatography (TLC) using hexane/DCM (1:1, v/v) as the eluent Recovery of the major yellow band yielded $Cp^*Ir(CO)(Cl)(CD_2Ph)$ (d_2 -**3a**) as a yellow solid.

1H NMR (δ , $CDCl_3$) = 1.79 (s, 15H, Cp^*), 6.94-6.99 (m, 1H, aromatic), 7.13-7.26 (m, 4H, aromatic).

Reaction of **3d in d_3 -ACN with $H_2^{18}O$ under visible light irradiation**

In an NMR tube, aqueous HCl (diluted with $H_2^{18}O$) was added to **3d** (10 mg, 0.02 mmol) in d_3 -ACN (0.75 mL). The reaction mixture was irradiated with a tungsten lamp at room temperature for 16 h. Analysis of the reaction mixture showed the presence of **4** and ^{18}O -**5d**.

ATR – IR (DCM, cm^{-1}) ν_{CO} = 1651 cm^{-1} (vs).

¹⁸O-**5d**: ¹H NMR (δ, d₃-ACN) = 7.74 (m, 4H, aromatic), 9.95 (s, 1H, CHO). GCMS: R_T(min) = 6.26; m/z = 186 [M].

Reaction of 3a under various irradiation conditions

To each of two NMR tubes were placed 1 M aqueous HCl (1 drop), **3a** (10 mg, 0.02 mmol), and d₃-ACN (0.5 mL). They were then irradiated at room temperature with UV and tungsten lamps, respectively, for 1 d. Analysis of both reaction mixtures showed the presence of complexes **4**, **5a** and some unidentified organic products.

Complexes **3b-f** and **3j** were irradiated with a tungsten lamp using this same procedure. Complex **3j** showed no reaction.

Reaction of 3a with bromoform

Complex **3a** (20 mg, 0.04 mmol) was stirred with bromoform (1 ml) in a carius tube for 4 d. The yellow solution turned orange after 1 d, and no further colour change was observed over the course of the reaction. After removal of all volatiles *in vacuo*, a ¹H NMR spectrum in CDCl₃ showed the presence of **4'** (2.01 ppm) and **4''** (1.97 ppm, intrapolated from the values for **4** and **4'**) in an integration ratio of 7:1.

Reaction of 3a with aqueous tetraethylammonium chloride under visible light irradiation

In a Wheaton vial, Et₄NCl (4 mg, 0.02 mmol) and deionized water (1 drop) were added to a solution of **3a** (5 mg, 0.01 mmol) in ACN (2 mL). The reaction mixture was irradiated with a tungsten lamp and stirred at room temperature for 1 d. The colour of the solution changed from yellow to green. After removal of all volatiles *in vacuo*, a ¹H NMR spectrum taken in CDCl₃ showed a mixture with an unidentified, major Cp* resonance at 1.61 ppm. Among the mixture, acetamide and **5a** were identified.

Acetamide: ¹H NMR (δ, CHCl₃) = 2.01 (s, 3H, CH₃), 5.37 (br, s, 1H, NH), 5.74 (br, s, 1H, NH).

5a: ^1H NMR (δ , CHCl_3) = 7.54 (t, 2H, aromatic), 7.64 (t, 1H, aromatic), 7.88 (d, 2H, aromatic), 10.02 (s, 1H, CHO).

ESI-MS analysis showed a major set of signals at $m/z = \sim 750$ in the positive region and MS-MS of the peak at 750 showed two fragmentations to 714 (- Cl) and 691 (- CH_3CONH_2).

NMR monitoring of the reaction of 3a in the presence of TEMPO

In a NMR tube, TEMPO (5 mg, 0.03 mmol) was added to a solution of **3a** (15 mg, 0.03 mmol) in d_2 -DCM (0.5 mL). The solution was irradiated with a tungsten lamp at room temperature for 1 d. The colour of the solution changed from yellow to orange. A comparison of the ^1H NMR spectrum collected at 1 d with that collected at 0 d showed that **3a** had completely reacted to form an unknown mixture. A similar observation was made with the reaction was performed using acrylonitrile (2 μL , 0.03 mmol) and **3a** (10 mg, 0.02 mmol) in d_2 -DCM (0.5 mL).

Repeating this reaction with the addition of deionized water (1 drop) did not yield any **5a**.

Repeating this reaction using an amberized NMR tube showed no reaction.

NMR monitoring of the reaction of 3a in the presence of AgBF_4

In an amberized NMR tube, AgBF_4 (4 mg, 0.02 mmol) and deionized water (1 drop) were added to a solution of **3a** (10 mg, 0.02 mmol) in d_2 -DCM (0.5 mL). The solution was left to stand at room temperature for 1 d. The ^1H NMR spectrum collected at 0 d showed that **3a** had reacted instantaneously to form an unknown compound, and no further reaction occurred after 1 d. No **5a** was formed.

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Supporting information available: Spectroscopic data for **3** and **5**, and optimised structures of **3**, **A**, **B** and **4***.

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