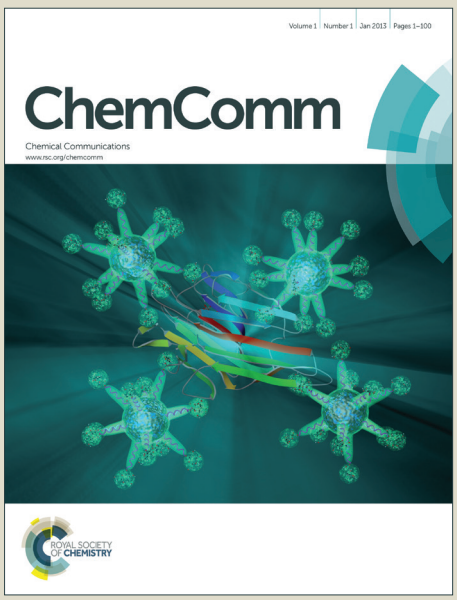
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Chemical Communications

RSCPublishing

COMMUNICATION

Light-driven Au(III)-promoted cleavage of triazole-bearing amine derivatives and its application in the detection of ionic gold

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

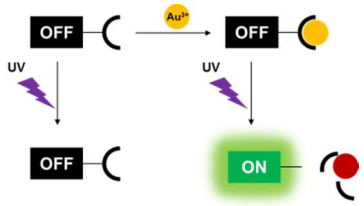
DOI: 10.1039/x0xx00000x

www.rsc.org/

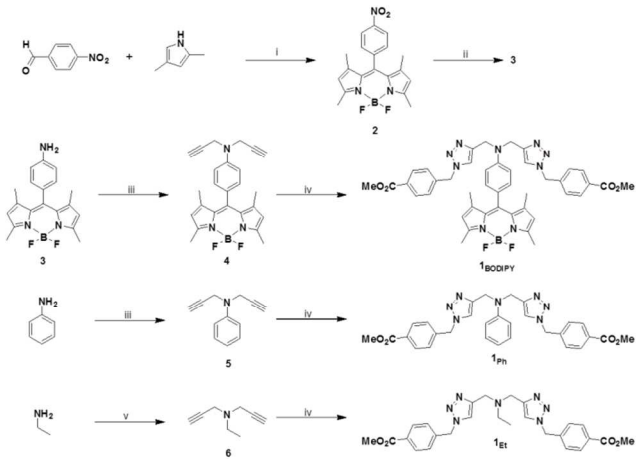
Dajeong Yim,[a] Hongsik Yoon,[a] Chi-Hwa Lee,[a] and Woo-Dong Jang[a] *

Light-driven Au(III)-promoted oxidative cleavage of triazole-bearing amine derivatives is utilized for the detection of ionic gold in aqueous media. A bistriazole-bearing boron dipyrromethane (1_{BODIPY}) exhibited selective and sensitive fluorescence enhancement by the addition of Au^{3+} and subsequent UV irradiation.

Elemental gold is one of the most stable chemical species and has been used since prehistoric periods as a precious metal for the fabrication of jewelry due to its high chemical stability and lustrous, bright yellow color.[1] Due to its superior processability and many other advantageous characteristics, gold is currently a very important material in many industrial fields as well as throughout basic science.[2] Although metallic gold has high chemical stability, ionic forms of gold are very reactive and can be used to catalyze various organic reactions.[3] During the last decade, gold-related chemistry has become particularly active in the field of transition metal catalysis. A large number of gold-catalyzed reactions have been developed due to the versatility and high efficiency of gold complexes.[4] Early studies of gold catalysis mainly focused on the development of methodologies, but current research has expanded to include gold-catalyzed cascade reactions for the total synthesis of natural compounds.[5] The most common pattern in gold-catalyzed organic reactions is the activation of alkyne groups due to the strong Lewis acidity of ionic gold complexes.[1f, 6] Therefore, several gold-sensitive chemosensors have been developed using the gold-catalyzed activation of alkyne groups.[7] Additionally, ionic gold compounds can work as oxidizing agents for some organic species due to their high redox potential.[1g-i] Recently, we discovered a unique Au(III)-promoted oxidative cleavage of triazole-bearing amine derivatives in aqueous media. In this paper, we report the light-driven Au(III)-promoted oxidative cleavage of triazole-bearing amine derivatives and its application in the detection of gold ions in aqueous media. Scheme 1 illustrates the concept of this experiment.



Scheme 1. Schematic expression of light-driven Au(III)-promoted fluorescence enhancement.



Scheme 2. Synthesis of $\mathbf{1}_{BODIPY}$, $\mathbf{1}_{Ph}$, $\mathbf{1}_{Et}$. Reagents and conditions; i) TFA, Chloranil, Et_3N, BF_3-Et_2O, CH_2Cl_2, 25 °C, 12 h, 14%; ii) Fe, HCl, THF, reflux, 7 h, 65%; iii) Propargyl bromide, K_2CO_3, Acetone, reflux, 12 h, 32%; iv) methyl 4-(azidomethyl)benzoate, $CuSO_4.5H_2O$, Na ascorbate, THF, H_2O, 60 °C, 7 h, 85%; v) Ethylamine, triethylamine, propargyl bromide, 0 °C, 60%.

The receptor moiety quenches the emission of fluorescence probe. The light-driven Au^{3+}-promoted chemical reaction transform the chemical structure of receptor moiety and emission of fluorescent probe can be enhanced.

A series of bis((1-(4-methoxycarbonylbenzyl)-1H-1,2,3-triazol-4-yl)methyl)amine derivatives ($\mathbf{1}_{Ph}$, $\mathbf{1}_{Et}$, and $\mathbf{1}_{BODIPY}$) were synthesized from ethynyl-bearing precursors (**4** - **6**) and 4-methoxycarbonylbenzyl azide through the Cu(I)-catalyzed 'click' reaction. The synthetic procedures are outlined in Scheme 2. Briefly, a boron dipyrromethane (BODIPY)-bearing nitrophenyl group (**2**) was prepared by the acid-catalyzed coupling of 4-nitrobenzaldehyde and 2,5-dimethylpyrrole, followed by an oxidation reaction in the presence of BF_3OEt_2. The nitro group of **2** was reduced to an amino group, which was then reacted with propargyl bromide to produce an ethynyl-bearing precursor (**4**). The other two ethynyl-bearing precursors (**5** and **6**) were obtained from the reactions of propargyl bromide with ethylamine and aniline, respectively.

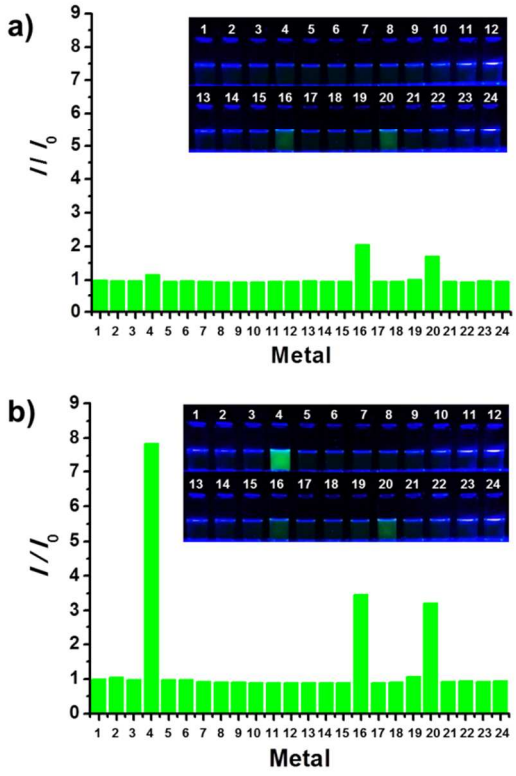


Figure 1. Fluorescence response of $\mathbf{1}_{BODIPY}$ (10 μM) to various metal cation additions (2 eq) in MeCN/H_2O (1:1 v/v); a) without light irradiation; b) after 2 min of UV irradiation by UV-handy lamp (365 nm); 1: blank, 2: Fe^{3+}, 3: Fe^{2+}, 4: Au^{3+}, 5: Hg^{2+}, 6: Zn^{2+}, 7: Pb^{2+}, 8: Ca^{2+}, 9: Co^{2+}, 10: Mn^{2+}, 11: Mg^{2+}, 12: Cu^{2+}, 13: Cd^{2+}, 14: Al^{3+}, 15: Cr^{3+}, 16: Au^{+}, 17: Ag^{+}, 18: Na^{+}, 19: Pt^{2+}, 20: Pd^{2+}, 21: Rh^{2+}, 22: Ni^{2+}, 23: K^{+}, 24: Ba^{2+}, λ_{ex} = 460 nm, λ_{em} = 515 nm.

In this experiment, we choose BODIPY as the fluorescent probe for the detection of Au^{3+} because the fluorescence emission can be easily tuned by structural modification of BODIPY. Although BODIPY is a well-known fluorescent dye, the fluorescence quantum yield of phenylamine-bearing BODIPY is very low due to the photoinduced electron transfer (PET) from the lone pair electron in the amino group to the photo-excited BODIPY unit.[8] $\mathbf{1}_{BODIPY}$ also exhibits a very weak fluorescence emission (Φ = 0.006 in EtOH). Such PET-mediated fluorescence quenching is often utilized as a powerful tool for the design of chemosensors because the metal coordination to the lone pair electron can prevent the PET process.[9] In fact, several examples of amine-bearing BODIPY derivatives have been reported as turn-on fluorescent probes for the detection of metal ions.[10]

Based on the above information, we tested the bindings of various metal ions to $\mathbf{1}_{BODIPY}$ (10 μM) in 50% aqueous MeCN. Two equivalents of various metal ions were added to $\mathbf{1}_{BODIPY}$, and the mixture solutions were incubated for 20 min at 25 °C under dark conditions. None of these solutions showed any fluorescence enhancement or changes in their UV-Vis absorption. In contrast, when exposed to UV light, the solution containing Au^{3+} exhibited great change in absorption as well as fluorescence enhancement. The solution reached its maximum emission intensity within 2 min of UV irradiation by a UV-handy lamp (365 nm) (Figures 1, S1, and Supporting movie). Although the solution containing Au^{+} and Pd^{2+} also exhibited fluorescence enhancement, the reaction rates were relatively slower than that of Au^{3+} containing solution. When fluorescence changes were monitored by a fluorescence photometer, the emission intensity reached its maximum in about 500 s due to the narrow window of light exposure in the fluorescence photometer (Figure 2).

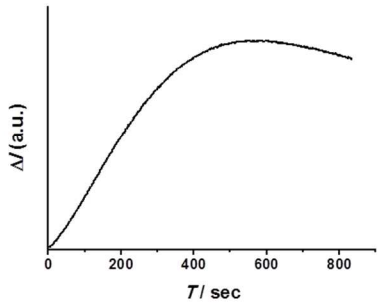


Figure 2. Time dependent fluorescence changes of $\mathbf{1}_{BODIPY}$ with Au^{3+} upon the UV irradiation (365 nm), monitored at 515 nm.

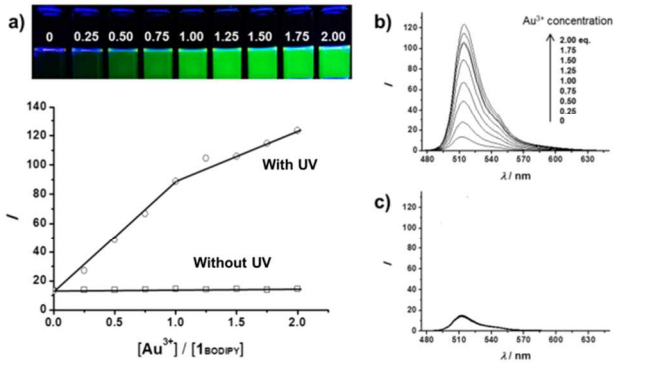


Figure 3. Au^{3+} concentration dependent fluorescence changes of $\mathbf{1}_{BODIPY}$ (10 μM) in MeCN/H_2O (1:1 v/v). a) Fluorescence emission of $\mathbf{1}_{BODIPY}$ after 2 min of UV irradiation (upper) and fluorescence intensity of $\mathbf{1}_{BODIPY}$ (lower; λ_{ex} = 460 nm, λ_{em} = 515 nm) after 2 min of incubation with/without of UV irradiation, b) emission spectra of $\mathbf{1}_{BODIPY}$ after 2 min of UV irradiation (365 nm), c) emission spectra of $\mathbf{1}_{BODIPY}$ after 2 min of incubation without UV irradiation.

Figure 3 exhibits Au^{3+} concentration-dependent fluorescence changes. $\mathbf{1}_{BODIPY}$ does not show a change in fluorescence upon 2 min of incubation without light irradiation, whereas strong fluorescence enhancement was observed upon 2 min of UV irradiation. The fluorescence intensity of $\mathbf{1}_{BODIPY}$ exhibits a linear correlation with the Au^{3+} concentration when the amount of Au^{3+} is less than 1

equivalent of $\mathbf{1}_{\mathbf{BODIPY}}$, indicating the detection limit of $\mathbf{1}_{\mathbf{BODIPY}}$ to Au^{3+} is lower than 2.0 μM.

The fluorescence enhancement of $\mathbf{1}_{\mathbf{BODIPY}}$ by Au^{3+} was also confirmed in the presence of other metal ions. Two equivalents of Au^{3+} were added to a solution containing $\mathbf{1}_{\mathbf{BODIPY}}$ (10 μM) and two equivalents of various metal ions, and the solutions were irradiated with UV light by a UV-handy lamp for 2 min. All solutions exhibited strong fluorescence enhancements, indicating that the fluorescence enhancement of $\mathbf{1}_{\mathbf{BODIPY}}$ caused by Au^{3+} is not influenced by the presence of other metal ions (Figure S2).

^{1}H NMR study was carried out for $\mathbf{1}_{\mathbf{BODIPY}}$ and its structural fragments to investigate the mechanism of photoinduced fluorescence enhancement. Due to solubility problems at high concentrations, the ^{1}H NMR study was conducted using a 5:1 mixture of CD_3CN and D_2O. A slight spectral shift of several proton signals was observed for $\mathbf{1}_{\mathbf{BODIPY}}$, $\mathbf{1}_{\mathbf{Ph}}$, and $\mathbf{1}_{\mathbf{Et}}$ after the addition of excess Au^{3+}. Upon careful observation, all proton signals with major spectral changes can be assigned to the protons neighboring the nitrogen atom in the tertiary amine group. For an example, as shown in Figure 4, the major spectral change of $\mathbf{1}_{\mathbf{Ph}}$ appears at the phenyl and methylene protons. This indicates that the primary binding site of Au^{3+} is the nitrogen atom in the tertiary amine group. Similarly, proton signals in N,N-dimethylaniline also showed a spectral shift with the addition of Au^{3+}. Once again, this indicates that Au^{3+} primarily binds to the tertiary amine group (Figure S3). Upon UV irradiation, a new set of proton signals was generated from the ^{1}H NMR spectra of $\mathbf{1}_{\mathbf{BODIPY}}$, $\mathbf{1}_{\mathbf{Ph}}$, and $\mathbf{1}_{\mathbf{Et}}$ containing Au^{3+}. In contrast, *N,N*-dimethylaniline with Au^{3+} does not show any spectral change, even after lengthy UV irradiation, indicating that the triazole group plays a very important role in the photoinduced chemical reaction. Because the newly generated proton signals from $\mathbf{1}_{\mathbf{BODIPY}}$, $\mathbf{1}_{\mathbf{Ph}}$, and $\mathbf{1}_{\mathbf{Et}}$ exhibited the same chemical shifts (Figures S3 and 4), we expect that the photochemical reaction resulted in the same product from the Au^{3+} complexes of $\mathbf{1}_{\mathbf{BODIPY}}$, $\mathbf{1}_{\mathbf{Ph}}$, and $\mathbf{1}_{\mathbf{Et}}$. Therefore, the reaction product was isolated and identified. Two equivalents of Au^{3+} were added to the $\mathbf{1}_{\mathbf{Ph}}$ solution (in a 5:1 mixture of CH_3CN and H_2O) and then the solution was irradiated with UV light for 20 min. The reaction mixture was chromatographed with a silica column. As result, we isolated an aldehyde-bearing triazole derivative (**7**; Scheme 3) as the major product, which was unambiguously characterized by Tollen's test, ^{1}H NMR, and HR-MS (Figures S4 and 5). We propose that the formation of **7** involves an oxidative cleavage mechanism. As shown in Scheme 3, the $\mathbf{1}_{\mathbf{Ph}}$•Au^{3+} complex transforms into a conjugated imine structure via a cyclic intermediate. This is followed by a hydrolysis reaction which yields the product in **7**. Although the $\mathbf{1}_{\mathbf{Et}}$•Au^{3+} complex also yielded the same product after UV irradiation, the reaction rate was relatively slow compared to that of $\mathbf{1}_{\mathbf{Ph}}$. The cyclic intermediate structures generated from the $\mathbf{1}_{\mathbf{Ph}}$•Au^{3+} and $\mathbf{1}_{\mathbf{Et}}$•Au^{3+} complexes would not be energetically different, but the conjugated imine structure obtained from the $\mathbf{1}_{\mathbf{Ph}}$•Au^{3+} complex would be much more stable compared to the $\mathbf{1}_{\mathbf{Et}}$•Au^{3+} complex due to its expanded π-conjugation. Therefore, we can conclude that UV irradiation accelerates the formation of the conjugated imine structure.

The fluorescence enhancement of $\mathbf{1}_{\mathbf{BODIPY}}$ can also be explained by this mechanism. If the oxidative cleavage reaction proceeded completely, $\mathbf{1}_{\mathbf{BODIPY}}$ would yield aniline-bearing BODIPY and **7**. In fact, after UV irradiation, the ^{1}H NMR spectrum of $\mathbf{1}_{\mathbf{BODIPY}}$•$Au^{3+}$ changes into a similar pattern with a mixture of **7**, aniline-bearing BODIPY (**3**; Scheme 2), and Au^{+} ions (Figure S4). Therefore, we tested the fluorescence response of **3** after the addition of various metals. A slight fluorescence enhancement of **3** was observed after Au^{3+} and Au^{+} additions. However, the fluorescence intensity of **3** after the addition of Au^{3+} was significantly weaker than that of UV-irradiated $\mathbf{1}_{\mathbf{BODIPY}}$•$Au^{3+}$ (Figure S6). This indicates the weak binding of metal ions to the amine group in a polar aqueous solution. Therefore, the observed strong fluorescence enhancement cannot be explained by the simple binding of a metal ion to the lone pair electron in the aniline moiety.

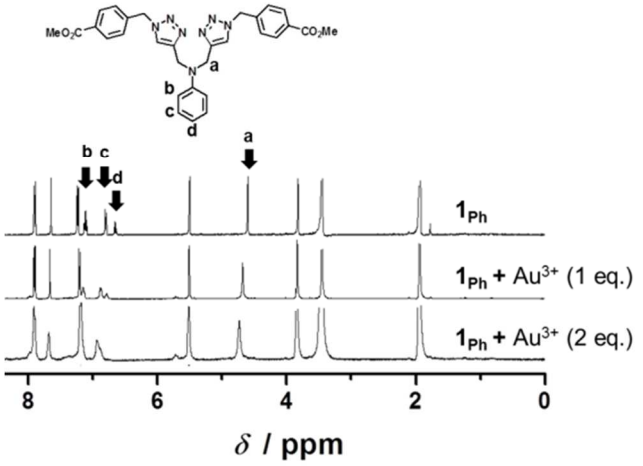
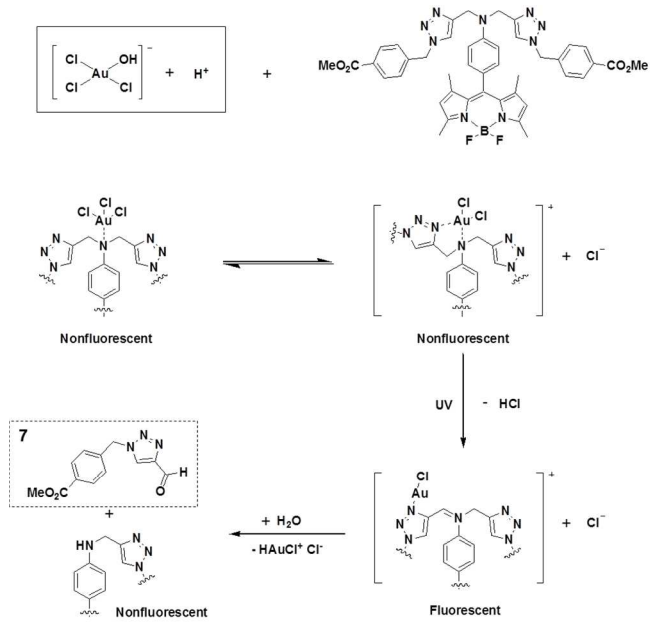


Figure 4. ^{1}H NMR spectral change of $\mathbf{1}_{\mathbf{Ph}}$ by addition of Au^{3+}.



Scheme 3. Proposed mechanism of light-driven Au(III)-promoted cleavage of triazole-bearing amine derivatives

In the reaction mechanism, UV irradiation accelerates the formation of the conjugated imine structure. This conjugated imine structure should have strong fluorescent characteristics, because the PET process is unable to function in this state. However, the final product formed by hydrolysis would have reduced fluorescent intensity. UV irradiation of $\mathbf{1}_{\mathbf{BODIPY}}$•$Au^{3+}$ would result in the accumulation of a highly fluorescent conjugated imine structure, which can be slowly hydrolyzed. In fact, the time-dependent fluorescence change of $\mathbf{1}_{\mathbf{BODIPY}}$•$Au^{3+}$ (Figure 2) also showed a decrease in the fluorescence intensity which indicates the decreasing concentration of the conjugated imine structure by hydrolysis.

In summary, a unique Au(III)-promoted oxidative cleavage of triazole-bearing amine derivatives has been utilized for the detection

of ionic gold in aqueous media. Because the 'turn on' response of $\mathbf{1}_{\mathbf{BODIPY}}$ requires both Au^{3+} binding and UV irradiation, we can greatly reduce the occurrence of false positives by undesirable fluorescence 'turn on' processes for the detection of gold ions. This unique function has the potential to lead to various applications. For example, this system can be applied to the design of fluorescence patterning because the photoirradiation selectively enhances the fluorescence emission of $\mathbf{1}_{\mathbf{BODIPY}}$ (Figure S8).

Notes and references

[a] Department of Chemistry, Yonsei University, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-749, Korea, E-mail: wdjang@yonsei.ac.kr.

† This work was supported by the Mid-Career Researcher Program (No. 2012005565) funded by the National Research Foundation (NRF) of Korea.

Electronic Supplementary Information (ESI) available: [Experimental details, synthesis, and spectral data]. See DOI: 10.1039/c000000x/

1. a) P. Pyykko, *Angew. Chem. Int. Ed.*, 2002, **41**, 3573-3578; b) P. Pyykko, *Annu. Rev. Phys. Chem.*, 2012, **63**, 45-64; c) P. Schwerdtfeger, *Heteroat. Chem*, 2002, **13**, 578-584; d) P. Schwerdtfeger, P. D. W. Boyd, S. Brienne and A. K. Burrell, *Inorg. Chem.*, 1992, **31**, 3411-3422; e) T. E. Jones, S. Piccinin and C. Stampfl, *Mater. Chem. Phys.*, 2013, **141**, 14-17; f) M. Lein, M. Rudolph, S. K. Hashmi and P. Schwerdtfeger, *Organometallics*, 2010, **29**, 2206-2210; g) L. Wang, X. Xie and Y. Liu, *Angew. Chem. Int. Ed.*, 2013, **52**, 13302-13306; h) M. Luty-Blocho, K. Paclawski, M. Wojnicki and K. Fitzner, *Inorg. Chim. Acta*, 2013, **395**, 189-196; i) L. T. Ball, G. C. Lloyd-Jones and C. A. Russell, *J. Am. Chem. Soc.*, 2014, **136**, 254-264.
2. a) C. W. Corti, R. J. Holliday and D. T. Thompson, *Appl. Catal., A*, 2005, **291**, 253-261; b) G. J. Hutchings, M. Brust and H. Schmidbaur, *Chem. Soc. Rev.*, 2008, **37**, 1759-1765; c) H. Schmidbaur, *Chem. Soc. Rev.*, 1995, **24**, 391-&; d) C. W. Corti, R. J. Holliday and D. T. Thompson, *Gold Bull.*, 2002, **35**, 111-136; e) H. Schmidbaur, *Nature*, 2001, **413**, 31-+; f) C. W. Corti, R. J. Holliday and D. T. Thompson, *Top. Catal.*, 2007, **44**, 331-343.
3. A. S. K. Hashmi and G. J. Hutchings, *Angew. Chem. Int. Ed.*, 2006, **45**, 7896-7936.
4. a) P. S. D. Robinson, G. N. Khairallah, G. da Silva, H. Lioe and R. A. J. O'Hair, *Angew. Chem.*, 2012, **124**, 3878-3883; b) O. A. Egorova, H. Seo, Y. Kim, D. Moon, Y. M. Rhee and K. H. Ahn, *Angew. Chem. Int. Ed.*, 2011, **50**, 11446-11450; c) A. S. K. Hashmi, S. Schaefer, M. Woelfle, C. D. Gil, P. Fischer, A. Laguna, M. C. Blanco and M. C. Gimeno, *Angew. Chem. Int. Ed.*, 2007, **46**, 6184-6187; d) C. J. Jones, D. Taube, V. R. Ziatdinov, R. A. Periana, R. J. Nielsen, J. Oxgaard and W. A. Goddard, *Angew. Chem. Int. Ed.*, 2004, **43**, 4626-4629; e) E. Jimenez-Nunez and A. M. Echavarren, *Chem. Commun.*, 2007, DOI: 10.1039/b612008c, 333-346; f) M. N. Hopkinson, A. D. Gee and V. Gouverneur, *Chem. Eur. J.*, 2011, **17**, 8248-8262; g) A. Arcadi, *Chem. Rev.* , 2008, **108**, 3266-3325; h) A. S. K. Hashmi, *Chem. Rev.* , 2007, **107**, 3180-3211; i) E. Jimenez-Nunez and A. M. Echavarren, *Chem. Rev.* , 2008, **108**, 3326-3350; j) Z. Li, C. Brouwer and C. He, *Chem. Rev.* , 2008, **108**, 3239-3265; k) J. C. Fierro-Gonzalez and B. C. Gates, *Chem. Soc. Rev.*, 2008, **37**, 2127-2134; l) A. S. K. Hashmi and M. Rudolph, *Chem. Soc. Rev.*, 2008, **37**, 1766-1775; m) M. K. Samantaray, C. Dash, M. M. Shaikh, K. Pang, R. J. Butcher and P. Ghosh, *Inorg. Chem.*, 2011, **50**, 1840-1848; n) W. Wang, G. B. Hammond and B. Xu, *J. Am. Chem. Soc.*, 2012, **134**, 5697-5705.
5. a) A. S. K. Hashmi, L. Schwarz, J. H. Choi and T. M. Frost, *Angew. Chem. Int. Ed.*, 2000, **39**, 2285-2288; b) T. Wang, S. Shi, M. M. Hansmann, E. Rettenmeier, M. Rudolph and A. S. K. Hashmi, *Angew. Chem. Int. Ed.*, 2014, **53**, 3715-3719; c) M. Rudolph and A. S. K. Hashmi, *Chem. Soc. Rev.*, 2012, **41**, 2448-2462; d) W. Yang and A. S. K. Hashmi, *Chem. Soc. Rev.*, 2014, **43**, 2941-2955; e) A. S. K. Hashmi, T. M. Frost and J. W. Bats, *J. Am. Chem. Soc.*, 2000, **122**, 11553-11554.
6. a) A. S. K. Hashmi, *Gold Bull.*, 2003, **36**, 3-9; b) M. Pernpointner and A. S. K. Hashmi, *J. Chem. Theory Comput.*, 2009, **5**, 2717-2725.
7. a) J.-B. Wang, Q.-Q. Wu, Y.-Z. Min, Y.-Z. Liu and Q.-H. Song, *Chem. Commun.*, 2012, **48**, 744-746; b) Y.-K. Yang, S. Lee and J. Tae, *Org. Lett.*, 2009, **11**, 5610-5613.
8. H. Song, S. Rajendiran, N. Kim, S. K. Jeong, E. Koo, G. Park, T. D. Thangadurai and S. Yoon, *Tetrahedron Lett.*, 2012, **53**, 4913-4916.
9. a) O. A. Bozdemir, R. Guliyev, O. Buyukcakir, S. Selcuk, S. Kolemen, G. Gulseren, T. Nalbantoglu, H. Boyaci and E. U. Akkaya, *J. Am. Chem. Soc.*, 2010, **132**, 8029-8036; b) K. D. Bhatt, B. A. Makwana, D. J. Vyas, D. R. Mishra and V. K. Jain, *J. Lumin.*, 2014, **146**, 450-457; c) S. Goswami, D. Sen and N. K. Das, *Org. Lett.*, 2010, **12**, 856-859; d) H. Wang, J. Lin, W. Huang and W. Wei, *Sens. Actuators, B*, 2010, **150**, 798-805.
10. a) Y. Jeong and J. Yoon, *Inorg. Chim. Acta*, 2012, **381**, 2-14; b) S. C. Dodani, Q. He and C. J. Chang, *J. Am. Chem. Soc.*, 2009, **131**, 18020; c) L. Zeng, E. W. Miller, A. Pralle, E. Y. Isacoff and C. J. Chang, *J. Am. Chem. Soc.*, 2006, **128**, 10-11.

