Dalton Transactions

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Journal Name

COMMUNICATION

Ruthenium–Indolizinone Complexes as a New Class of Metalated Heterocyclic Compound: Insight into Unconventional Alkyne Activation Pathway, Revelation of Unexpected Electronic Properties and Exploration of Medicinal Application

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

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The two series of ruthenium–indolizinone complexes prepared by Ru-mediated cyclization of pyridine-tethered alkyne represent the first examples of metalated indolizinone complexes. Joint experimental-theoretical investigation suggests an unconventional *5-endo-dig* cyclization pathway as their formation mechanism. They also exhibit moderate cytotoxicity against several human cancer cell lines.

Heterocycles has been a research focus for years in synthetic chemistry due to their versatile applications in medicinal chemistry and materials science.[1] While organic heterocycles represent the mainstream research in the field of heterocyclic chemistry, development of metal-containing heterocyclic compounds have been picking up its pace. More specifically, the modulable coordination spheres together with rich oxidation states offered by the metal centers make the metalated heterocyclic complexes an attractive class of functional compounds. Despite these advantages, studies in metalated heterocyclic complexes are dominated by metal–N-heterocyclic carbene complexes,[2] whereas investigations on other metalated heterocyclic systems are far lagged behind, presumably due to the lack of general synthetic approaches, which hampers further development of metal–heterocycle chemistry.

In recent years, breakthroughs in transition-metal- and Lewis-acid-catalyzed cyclization of alkynes with heteroatom functionalities have dramatically improved the efficiency of organic heterocycle synthesis.[3] While most studies have focused on the cyclization products and reaction efficiencies, efforts on probing and isolating the proposed metalated heterocyclic intermediates are rare. These overlooked intermediates are not only of mechanistic importance but they also offer insights into the preparation of isolable metalated heterocyclic complexes. With this idea in mind, we have recently initiated research activities for isolable metal–heterocyclic complexes from reactions between heteroatom-functionalized alkynes and structurally well-defined low-valent transition-metal complexes. Through this approach, many interesting and unprecedented metal–heterocyclic complexes have been isolated,[4] and this strategy undoubtedly broadens the spectrum of metalated heterocyclic complexes. As an extension of our previous work, we herein report the first examples of isolable and structurally characterized ruthenium–indolizinone complexes prepared by Ru-assisted activation of pyridine-tethered alkynes. Significantly, although the Ru–vinylidene intermediacy is prevalent in numerous Ru(II)-mediated alkyne transformations,[5] this joint experimental-theoretical investigation suggests an unconventional *5-endo-dig* cyclization pathway for the formation of Ru–indolizinone complexes. Besides, the potential application of the Ru–indolizinone complexes as anticancer agents was explored in view of the captivating antitumoral activity of indolizinone-based camptothecins.[6]

Ru(II)–indolizinone complexes (or more correctly Ru(II) complexes bearing indolizinone zwitterion) **1**–**4** were obtained in high yield (73–95%) by reacting pyridyl-ynone RC≡C(C=O)(2-py) with $[Ru([9]aneS3)(bpy)(H_2O)]^{2+}$ and *cis*-$[Ru([14]aneS4)Cl_2]$ respectively (Scheme 1; [9]aneS3 = 1,4,7-trithiacyclononane, bpy = 2,2'-bipyridine, [14]aneS4 = 1,4,8,11-tetrathiacyclotetradecane). Acetonitrile-ligated complexes (**5** and **6**) were obtained from reaction between chloride-ligated complexes (**3** and **4**) and chloride abstracting agent $AgClO_4$ in CH_3CN. All these complexes are stable towards air, moisture, and ambient radiation. The molecular structures for $\mathbf{1}(ClO_4)_2$, $\mathbf{2}(ClO_4)_2{\cdot}(CH_3CN)_2$, $\mathbf{4}(ClO_4)$ and $\mathbf{6}(ClO_4)_2{\cdot}(CH_3CN)_2$ determined by X-ray crystallography (Fig. 1, Table 1) represent the first examples of indolizinone-ligated metal complexes. In each

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‡ Electronic Supplementary Information (ESI) available: Full experimental details, computational details, NMR spectra, CCDC 1832533–1832537 (**1**, **2**, **4**, **6** and **7**). For ESI and crystallographic data in CIF or other electronic format, see DOI: 10.1039/x0xx00000x

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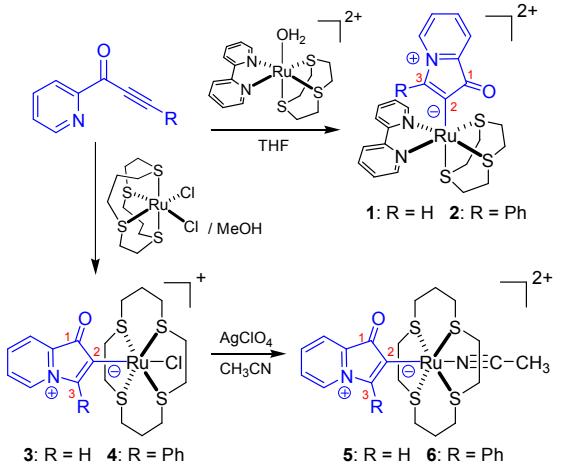
case, the indolizinone moiety behaves as a monodentate ligand and metalates at the *C*-2 position of the indolizinone skeleton, and the ten non-hydrogen atoms on the indolizinone moiety are essentially coplanar. The Ru–C distances (2.019(3)–2.104(3) Å) are indicative of Ru–C single bond character. The slightly longer Ru–C distance in **2** (2.104(3) Å) compared with that in **1** (2.057(4)–2.062(4) Å) is probably originated from the bulkiness of the *C*-3 substituent (Ph for **2** vs. H for **1**). The C–O distances determined (1.204(5)–1.213(4) Å), together with the ν_{CO} for all the indolizinone complexes (1701–1710 cm^{-1}), are standard for carbonyl group.



Scheme 1 Synthetic routes for ruthenium–indolizinone complexes, and the numbering of the ring system.

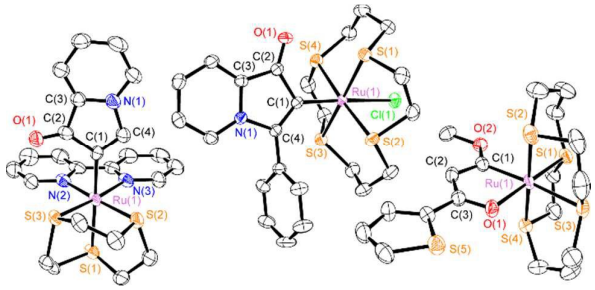


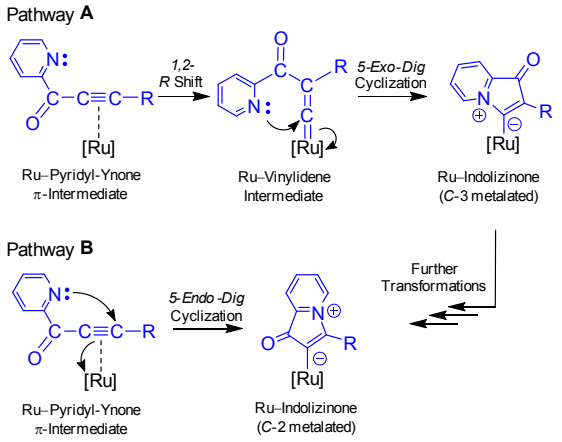
Fig. 1 Perspective view of cations **1** (left), **4** (middle) and **7** (right) as represented by 50% probability ellipsoids; hydrogen atoms are omitted for clarity.

Two plausible mechanisms for the formation of Ru–indolizinone complexes, which are inspired by the mechanisms proposed for metal- or Lewis-acid-catalyzed cyclization of functionalized alkynes, are depicted in Scheme 2. Considering a Ru–pyridyl-ynone π complex as the reactant, Ru–indolizinone complex may be formed via the formation of Ru–vinylidene intermediate followed by some subsequent transformations (pathway **A**) or a direct *5-endo-dig* cyclization (pathway **B**). The former vinylidene-involving pathway is prevalent in Ru-mediated alkyne transformations,[5] whereas the latter one is commonly proposed in coinage-metal- or Lewis-acid-catalyzed cyclization of functionalized alkynes[3] but is rarely known for Ru(II)-mediated alkyne transformations. At this juncture, it is important to note that reacting *cis*-[Ru([14]aneS4)Cl_2] with nucleophile-tethered ynone HC≡C(C=O)(2-thienyl) yields ruthenafuran complex **7** as the only product (Scheme 3(a), Fig. 1), and the formation of ruthenafuran complex from the reaction between *cis*-[Ru([14]aneS4)Cl_2] and HC≡C(C=O)Ph was previously reported to proceed via a vinylidene-involving pathway (Scheme 3(b)).[4c]

Table 1 Selected Bond Lengths (Å) for Cations **1**, **2**, **4**, **6** and **7** Determined by X-ray Crystallography.

	1[a]	**2**	**4**	**6**	**7**
Ru(1)–C(1)	2.057(4), 2.062(4)	2.104(3)	2.019(3)	2.037(3)	2.015(4)
C(1)–C(2)	1.499(5), 1.488(5)	1.499(4)	1.513(4)	1.503(5)	1.377(6)
C(2)–C(3)	1.503(5), 1.517(5)	1.504(4)	1.500(4)	1.499(5)	1.395(6)
C(3)–N(1)	1.345(5), 1.342(5)	1.352(4)	1.358(4)	1.355(5)	–
C(4)–N(1)	1.460(5), 1.441(5)	1.482(3)	1.473(3)	1.475(4)	–
C(1)–C(4)	1.326(5), 1.339(5)	1.351(4)	1.360(4)	1.370(5)	–
C(2)–O(1)	1.212(4), 1.213(4)	1.208(4)	1.210(3)	1.204(5)	–
C(3)–O(1)	–	–	–	–	1.284(5)
Ru(1)–O(1)	–	–	–	–	2.121(3)

[a] The crystal contains two crystallographically independent cations in the asymmetric unit; structural data are listed in the order of Ru(1) moiety, followed by Ru(2) moiety.



Scheme 2 Two plausible reaction mechanisms for the formation of Ru–indolizinone complexes.

The facts that (1) reaction between pyridyl-ynones RC≡C(C=O)(2-py) and *cis*-[Ru([14]aneS4)Cl_2] yields Ru–indolizinone complex instead of ruthenafuran complex, and (2) no *C*-3 metalated Ru–indolizinone complex (proposed in pathway **A**) was isolated in this work, clearly suggest the possibility of non-vinylidene-involving pathway for the formation of Ru–indolizinone complexes. In this regard, density functional theory (DFT) calculations suggest that the formation of **1** from a Ru–pyridyl-ynone π-intermediate **1-π** via a *5-endo-dig* cyclization (pathway **B**) has a lower activation

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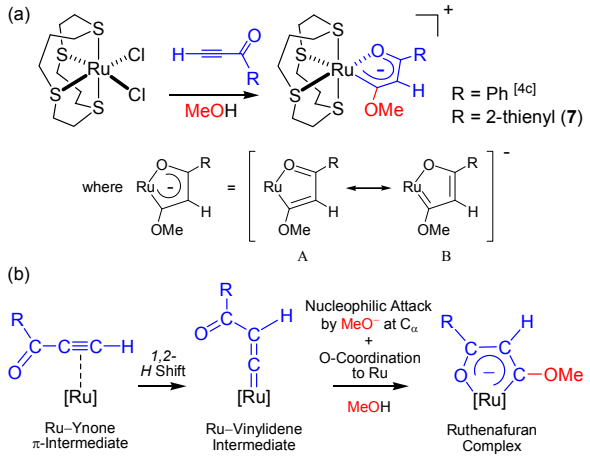
barrier than the formation of Ru–vinylidene species **1v** (Fig. 2): the formation of **1v** from **1-π** via *1,2-H* shift proceeds through the formation of intermediate **1v-INT** with an overall energy barrier of 22.7 kcal mol^{-1} (relative to **1-π**), whereas the energy barrier for the formation of **1** from **1-π** via a direct *5-endo-dig* cyclization pathway is 7.7 kcal mol^{-1}. Even though calculations were not performed on the transformation from **1v** to **1**, the current calculation results signify that pathway **B** is energetically more favorable than pathway **A**.



Scheme 3 (a) Synthetic routes for **7** and (b) plausible formation mechanism for ruthenafuran complexes previously reported.[4c]

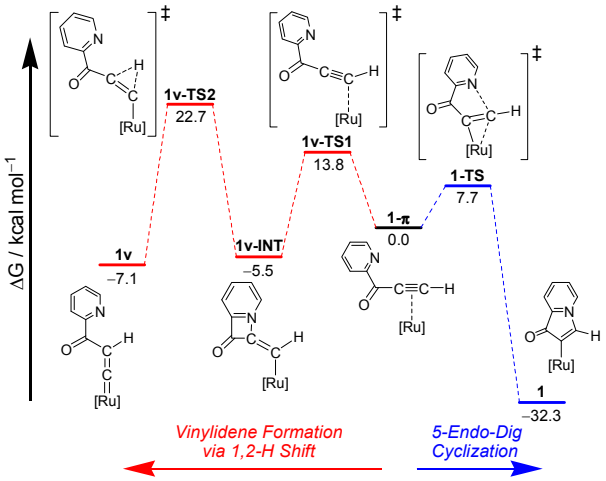


Fig 2. Potential energy surfaces calculated at DFT level (functional = PBE0; solvent = THF) for the formation of **1** via *5-endo-dig* cyclization and **1v** via *1,2-H* shift. [Ru] = [Ru([9]aneS3)(bpy)]$^{2+}$.

Because the chloride ligands for complexes **3** and **4** can be substituted by CH_3CN to give complexes **5** and **6** respectively, spectroscopic and electrochemical studies on Ru–indolizinone complexes in CH_3CN were only performed on complexes **1**, **2**, **5** and **6** (Fig. 3). Each of these complexes feature a low-energy visible absorption band (λ_{max} = 602–663 nm; ε_{max} = 2–4×10^3 dm^3 mol^{-1} cm^{-1}). Time-dependent DFT (TD-DFT) calculation on **5** suggests that this transition mainly originates from the HOMO → LUMO transition. The HOMO has greater Ru contribution (52%) than that in LUMO (3%), whereas the LUMO has greater indolizinone contribution (92%) than that in HOMO (22%). Thus the lowest-energy transitions for **1**, **2**, **5** and **6** are assigned to be d_π(Ru) → π*(indolizinone) MLCT in nature. The electronic difference density plot for **5** in its lowest-energy excited state (generated by taking the difference between the excited state electron density and ground state electron density) also clearly shows that electronic charge is depleted from d_π(Ru) and accumulated at the π*(indolizinone) (Fig. 4). The first oxidation ($E_{1/2}$ = 0.72 to 0.80 V vs $Cp_2Fe^{+/0}$) and reduction couples ($E_{1/2}$ = −0.82 to −0.79 V) for the complexes are assigned to Ru-centered oxidation and indolizinone-centered reduction respectively based on the HOMO and LUMO composition calculated. Surprisingly, these findings reveal that Ru–indolizinone complexes have remarkably low-lying LUMOs when compared with structurally related Ru–indolizine complex [Ru([14]aneS4)(indolizine)(CH_3CN)]$^{2+}$ (d_π(Ru) → π*(indolizine) MLCT absorption at λ_{max} = 426 nm; first reduction at E_{pc} = −1.96 V vs $Cp_2Fe^{+/0}$); where indolizine = 1-hydroxy-1-methyl-1*H*-indolizinium-2-yl.[4b] It is beyond expectation that substitution of a ketone group for a tetrahedral carbon centre contributes to such a starkly different electronic property.

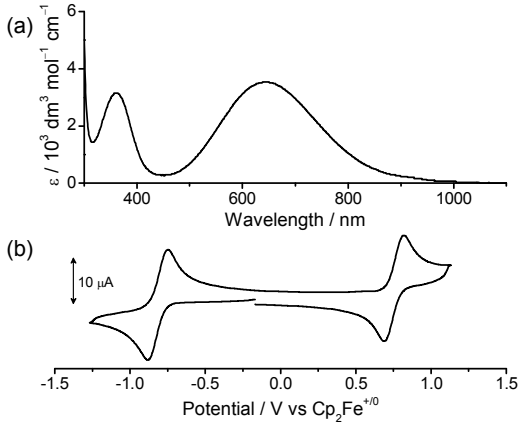


Fig 3. (a) UV/Vis absorption spectrum (CH_3CN, 298 K) and (b) cyclic voltammogram (supporting electrolyte: 0.1 M [Bu_4N]PF_6 in CH_3CN; 298 K; scan rate = 100 mV s^{-1}) of **5**.

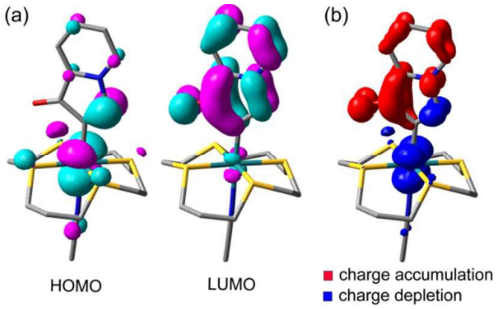


Fig 4. (a) Surface plots of the HOMO and LUMO of **5** (surface isovalue = 0.04 au) and (b) electronic difference density plot of **5** in its lowest-energy excited state (corresponding to the vertical transition marked with * in Fig. S10 (ESI‡); isodensity value = 0.003 au).

The fascinating anticancer properties of indolizinone-based camptothecin[6] prompted us to explore the potential application of metalated indolizinone complexes as anticancer

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agents. The *in vitro* anticancer activity of all the Ru–indolizinone complexes against breast adenocarcinoma (MCF-7), cervical carcinoma (HeLa), fibrosarcoma (HT1080), hepatocarcinoma (HepG2), and lung adenocarcinoma (A549) human cell lines were evaluated by MTT assay and benchmarked against cisplatin (Table 2). Complexes **4** and **6** exhibit moderate cytotoxicity against HepG2, HT1080 and MCF-7 cell lines, whereas **5** shows moderate and low cytotoxicity against MCF-7 and A549 cell lines respectively.

Table 2 Cytotoxicity (IC_{50}, μM) of Ru–indolizinone complexes.[a]

	HeLa	A549	HepG2	HT1080	MCF-7
4(ClO_4)	NC	NC	42 ± 2	61 ± 13	17 ± 1
5$(ClO_4)_2$	NC	219 ± 3	NC	NC	80 ± 2
6$(ClO_4)_2$	NC	NC	75 ± 3	87 ± 5	19 ± 2
cisplatin	18 ± 1	19 ± 1	52 ± 1	15 ± 1	46 ± 4

[a] All indolizinone complexes are non-cytotoxic (NC) against HeLa cells, and **1**$(ClO_4)_2$, **2**$(ClO_4)_2$ and **3**(ClO_4) are NC against all cancer cell lines tested; maximum complex concentration tested = 400 μM (complexes **1**–**6**) and 250 μM (cisplatin).

In conclusion, two series of isolable and structurally characterized Ru–indolizinone complexes were successfully prepared by activation of pyridine-tethered ynone. The reactivity discovered in this work not only represents a general synthetic strategy for a variety of Ru–indolizinone complexes, but also reveals a cyclization pathway which is unconventional in Ru–alkyne chemistry. Work is in progress to explore other metal–indolizinone complexes with interesting electronic properties and potential medicinal applications.

The work described in this paper was supported by the Research Grants Council of Hong Kong SAR (CityU 11228316, CityU 11207117 and T42-103/16-N), the Science Technology and Innovation Committee of Shenzhen Municipality (JCYJ20160229165216275), and by the Shenzhen Research Institute, City University of Hong Kong.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1 *(a) Heterocyclic Chemistry* (Eds.: J. A. Joule, K. Mills), Blackwell Science, Oxford, 2000; *(b) Handbook of Heterocyclic Chemistry* (Eds.: A. R. Katritzky, A. F. Pozharskii), Pergamon, Oxford, 2003; *(c) Comprehensive Heterocyclic Chemistry III,* Vol. 1–15 (Eds.: A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven, R. J. K. Taylor), Pergamon, Oxford, 2008.

2 *(a)* W. Liu, R. Gust, *Chem. Soc. Rev.,* 2013, **42**, 755; *(b)* K. Riener, S. Haslinger, A. Raba, M. P. Högerl, M. Cokoja, W. A. Herrmann, F. E. Kühn, *Chem. Rev.,* 2014, **114**, 5215; *(c)* R. Visbal, M. C. Gimeno, *Chem. Soc. Rev.,* 2014, **43**, 3551; *(d)* M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature*, 2014, **510**, 485; *(e)* F. Lazreg, F. Nahra, C. S. J. Cazin, *Coord. Chem. Rev.,* 2015, **293–294**, 48; *(f)* S. Kaufhold, L. Petermann, R. Staehle, S. Rau, *Coord. Chem. Rev.,* 2015, **304–305**, 73; *(g)* C. I. Ezugwu, N. A. Kabir, M. Yusubov, F. Verpoort, *Coord. Chem. Rev.,* 2016, **307**, 188; *(h)* A. Nasr, A. Winkler, M. Tamm, *Coord. Chem. Rev.,* 2016, **316**, 68; *(i)* W. Liu, R. Gust, *Coord. Chem. Rev.,* 2016, **329**, 191; *(j)* R. Zhong, A. C. Lindhorst, F. J. Groche, F. E. Kühn, *Chem. Rev.,* 2017, **117**, 1970; *(k)* S. Hameury, P. de Frémont, P. Braunstein, *Chem. Soc. Rev.,* 2017, **46**, 632; *(l)* D. Janssen-Müller, C. Schlepphorst, F. Glorius, *Chem. Soc. Rev.,* 2017, **46**, 4845; *(m)* W. Zhao, V. Ferro, M. V. Baker, *Coord. Chem. Rev.,* 2017, **339**, 1; *(n)* V. Charra, P. de Frémont, P. Braunstein, *Coord. Chem. Rev.*, 2017, **341**, 53; *(o)* C. Johnson, M. Albrecht, *Coord. Chem. Rev.*, 2017, **352**, 1.

3 *(a)* F. E. McDonald, *Chem. Eur. J.,* 1999, **5**, 3103; *(b)* I. Nakamura, Y. Yamamoto, *Chem. Rev.,* 2004, **104**, 2127; *(c)* G. Zeni, R. C. Larock, *Chem. Rev.,* 2004, **104**, 2285; *(d)* L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal.*, 2006, **348**, 2272; *(e)* A. S. K. Hashmi, *Chem. Rev.,* 2007, **107**, 3180; *(f)* Z. Li, C. Brouwer, C. He, *Chem. Rev.,* 2008, **108**, 3239; *(g)* E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.,* 2008, **108**, 3326; *(h)* N. T. Patil, Y. Yamamoto, *Chem. Rev.,* 2008, **108**, 3395; *(i)* V. Michelet, P. Y. Toullec, J.-P. Genêt, *Angew. Chem. Int. Ed.,* 2008, **47**, 4268; *(j)* V. Cadierno, J. Gimeno, *Chem. Rev.,* 2009, **109**, 3512; *(k)* E. Soriano, J. Marco-Contelles, *Acc. Chem. Res.,* 2009, **42**, 1026; *(l)* J. J. Vaquero, J. Alvarez-Builla in *Heterocycles Containing a Ring-Junction Nitrogen. In Modern Heterocyclic Chemistry,* Vol. 4 (Eds.: J. Alvarez-Builla, J. J. Vaquero, J. Barluenga), Wiley-VCH, Weinheim, 2011; pp. 1989-2070; *(m)* B. Godoi, R. F. Schumacher, G. Zeni, *Chem. Rev.,* 2011, **111**, 2937; *(n)* A. Marinetti, H. Jullien, A. Voituriez, *Chem. Soc. Rev.,* 2012, **41**, 4884; *(o)* A. Gómez-Suárez, S. P. Nolan, *Angew. Chem. Int. Ed.,* 2012, **51**, 8156; *(p)* I. D. G. Watson, F. D. Toste, *Chem. Sci.,* 2012, **3**, 2899; *(q)* D.-H. Zhang, Z. Zhang, M. Shi, *Chem. Commun.,* 2012, **48**, 10271; *(r)* A. V. Gulevich, A. S. Dudnik, N. Chernyak, V. Gevorgyan, *Chem. Rev.,* 2013, **113**, 3084; *(s)* R. K. Shiroodi, V. Gevorgyan, *Chem. Soc. Rev.,* 2013, **42**, 4991; *(t)* R. Chinchilla, C. Nájera, *Chem. Rev.,* 2014, **114**, 1783; *(u)* C. Obradors, A. M. Echavarren, *Acc. Chem. Res.,* 2014, **47**, 902; *(v)* R. Dorel, A. M. Echavarren, *Chem. Rev.,* 2015, **115**, 9028; *(w)* G. Fang, X. Bi, *Chem. Soc. Rev., 2015*, **44**, 8124; *(x)* B. Sadowski, J. Klajn, D. T. Gryko, *Org. Biomol. Chem.,* 2016, **14**, 7804; *(y)* Y. Li, W. Li, J. Zhang, *Chem. Eur. J.,* 2017, **23**, 467; *(z)* L.-X. Wang, Y.-L. Tang, *Eur. J. Org. Chem.,* 2017, 220.

4 *(a)* L.-H. Chung, C.-Y. Wong, *Organometallics*, 2013, **32**, 3583; *(b)* L.-H. Chung, C.-F. Yeung, D.-L. Ma, C.-H. Leung, C.-Y. Wong, *Organometallics*, 2014, **33**, 3443; *(c)* W.-K. Tsui, L.-H. Chung, W.-H. Tsang, C.-F. Yeung, C.-H. Chiu, H.-S. Lo, C.-Y. Wong, *Organometallics*, 2015, **34**, 1005; *(d)* C.-F. Yeung, L.-H. Chung, H.-S. Lo, C.-H. Chiu, J. Cai, C.-Y. Wong, *Organometallics*, 2015, **34**, 1963; *(e)* S.-W. Ng, L.-H. Chung, C.-F. Yeung, H.-S. Lo, H.-L. Shek, T.-S. Kang, C.-H. Leung, D.-L. Ma, C.-Y. Wong, *Chem. Eur. J.,* 2018, **24**, 1779.

5 *(a)* M. I. Bruce, *Chem. Rev.*, 1991, **91**, 197; *(b)* M. I. Bruce, *Chem. Rev.,* 1998, **98**, 2797; *(c)* C. Bruneau, P. H. Dixneuf, *Acc. Chem. Res.,* 1999, **32**, 311; *(d)* M. C. Puerta, P. Valerga, *Coord. Chem. Rev.,* 1999, **193-195**, 977; *(e)* B. M. Trost, F. D. Toste, A. B. Pinkerton, *Chem. Rev.,* 2001, **101**, 2067; *(f)* F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.,* 2004, **104**, 3079; *(g)* H. Katayama, F. Ozawa, *Coord. Chem. Rev.,* 2004, **248**, 1703; *(h)* B. M. Trost, M. U. Frederiksen, M. T. Rudd, *Angew. Chem. Int. Ed.,* 2005, **44**, 6630; *(i)* C. Bruneau, P. H. Dixneuf, *Angew. Chem. Int. Ed.,* 2006, **45**, 2176; *(j)* B. M. Trost, A. McClory, *Chem. Asian J.,* 2008, **3**, 164; *(k) Metal Vinylidenes and Allenylidenes in Catalysis* (Eds.: C. Bruneau, P. Dixneuf), Wiley-VCH, Weinheim, 2008; *(l)* J. M. Lynam, *Chem. Eur. J.,* 2010, **16**, 8238.

6 *(a)* M. E. Wall, M. C. Wani, C. E. Cook, K. H. Palmer, A. T. McPhail, G. A. Sim, *J. Am. Chem. Soc.*, 1966, **88**, 3888; *(b)* M. E. Wall, *Med. Res. Rev.*, 1998, **18**, 299; *(c)* R. P. Verma, C. Hansch, Chem. Rev., 2009, **109**, 213.

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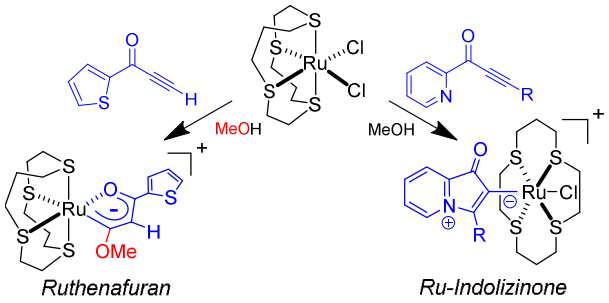

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