

Olefin Metathesis

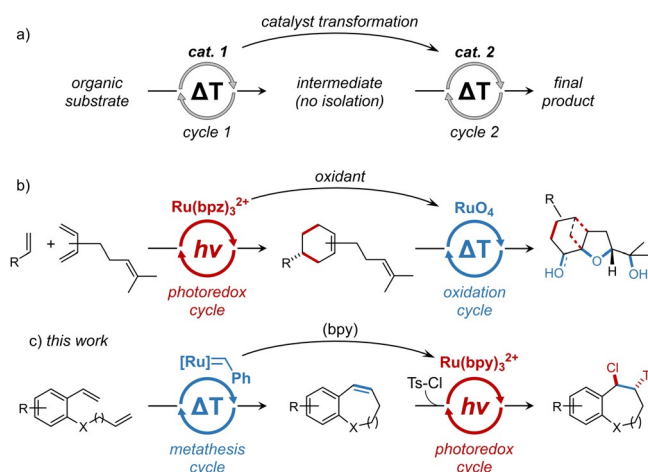
Ligand Substitution of Ru^{II}-Alkylidenes to Ru(bpy)₃²⁺:
Sequential Olefin Metathesis/Photoredox CatalysisMalte Gallhof, Lukas Kell, and Malte Brasholz*^[a]

Dedicated to Professor Rolf Huisgen on the occasion of his 100th birthday

Abstract: Ruthenium(II) alkylidene complexes such as the Grubbs' 1st and 2nd generation catalysts undergo a ligand substitution with 2,2'-bipyridine, which readily leads to the common photoredox catalyst Ru(bpy)₃²⁺. The application of this catalyst transformation in sequential olefin metathesis/photoredox catalysis is demonstrated by way of ring-closing metathesis (RCM)/photoredox ATRA reactions.

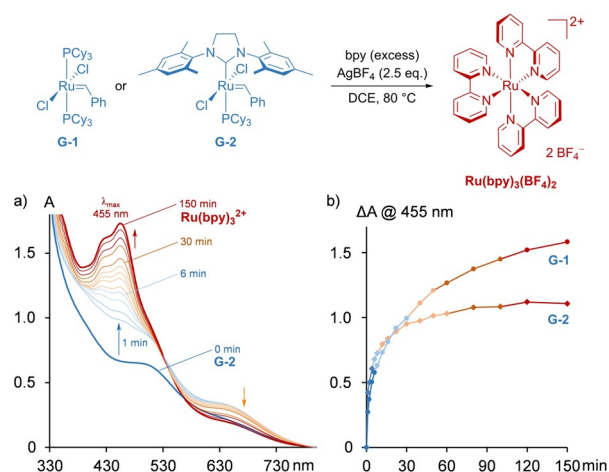
In sequential catalysis,^[1] which may also be referred to as "assisted tandem catalysis",^[2] a single catalytically active metal center is utilized in two (or more) consecutive orthogonal catalytic reactions. Key to this sustainable approach to catalysis is a sufficiently mild ligand substitution of a given metal catalyst in the presence of a respective organic reaction intermediate, which by contrast to conventional multistep synthesis is not isolated between the individual steps, yet avoiding its labor-intensive and waste-generating purification (Scheme 1a). In the context of sequential catalysis, ruthenium-based catalysts, including Ru^{II}-alkylidenes,^[3] have received particular attention. Owing to their large number of stable oxidation states ranging from -2 to +8, ruthenium catalysts can mediate a plethora of synthetically highly useful organic transformations,^[4] and the particularly desired catalytic species are usually readily accessible by relatively simple chemical manipulations.

During the last decade, photoredox catalysis has emerged as a highly useful addition to the chemist's toolbox of synthetic methods, often enabling the synthesis of target structures which are difficult to access by classical approaches.^[5] However, hardly any examples of tandem or sequential catalytic protocols have been disclosed to date which encompass a photo-



Scheme 1. a) Concept of sequential catalysis. b) and c) former and current contributions.

redox reaction as key step. We demonstrated^[6] the successful sequential combination of a photoredox-induced radical cationic Diels–Alder reaction^[7] with an oxidative 1,*n*-diene cyclization.^[8] An in situ oxidation of the photoredox catalyst Ru(bpz)₃²⁺ to the strong oxidant Ru^{VIII} oxide allowed sequencing of the two orthogonal photochemical and thermal trans-



Scheme 2. Ligand substitution of Grubbs' 1st and 2nd generation catalysts with 2,2'-bipyridine (bpy) to photocatalyst Ru(bpy)₃²⁺. a) Time course of the reaction between catalyst G-2 and bpy in the presence of AgBF₄ analyzed by UV/Vis; c) [Ru] = 3.1 × 10⁻⁴ M in DCE. b) Time-dependent development of the absorption at 455 nm for catalysts G-1 and G-2. DCE = Dichloroethane.

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formations in a one-pot procedure, to eventually synthesize highly functionalized *O*-heterocyclic products (Scheme 1 b).

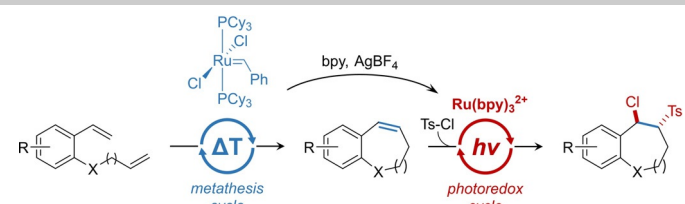
Here, we report the reverse approach: we successfully sequenced a thermal reaction with a consecutive photoredox transformation. An olefin metathesis reaction^[9] was combined in one pot with a photocatalytic radical alkene 1,2-difunctionalization,^[10] this new protocol was enabled by the in situ transformation of a Ru^{II}-alkylidene to Ru(bpy)₃²⁺ (Scheme 1 c).

We investigated the ligand substitution of Grubbs' 1st and 2nd generation catalysts, **G-1** and **G-2**, with 2,2'-bipyridine

(bpy) by UV/Vis monitoring (Scheme 2). For this purpose, dilute solutions of both Ru^{II}-alkylidenes were treated with larger excess of bpy in different solvents at elevated temperatures.

Upon reacting catalyst **G-1**, we observed that the phosphines as well as the carbene ligand were rapidly displaced. However, the thermal reactions of **G-1** with bpy (10 up to 150 equiv with respect to Ru^{II}) in dichloroethane (DCE) at 80 °C, or even in dimethylformamide (DMF) at 140 °C in a sealed tube, would come to a halt at the relatively stable *cis*-

Table 1. One-pot sequential RCM/photoredox chlorosulfonylation reactions.



#	1, <i>n</i> -diene	RCM product	Step 1 yield [%]	Photoredox product	Step 2 yield [%]	Combined yield S1 × S2 [%]	Sequential yield [%]
1			86		80	69	57
2			96		82	79	68
3			97		38	37	36
4			85		69	59	41
5			88		52	46	51
6			80		80	64	69
7			70		57	40	56
8			83		31	26	32
9			65		63	41	18

3i d.r. = 5:1

Experiments were conducted on 0.20 mmol scale. Sequential reactions: Step 1: diene **1** (0.20 mmol), 5 mol% **G-1** (10 μmol), DCE, R.T., 17 h, then bpy (0.10 mmol) and AgBF₄ (25 μmol), 80 °C, 3 h. Step 2: TsCl (0.20 mmol), *hν* 460 nm LED, acetone, R.T., 48 h. Yields refer to isolated yields after chromatography.

[Ru(bpy)₂Cl₂]^[11] (Figure S2). On the other hand, the desired global ligand substitutions of **G-1** and **G-2** could be achieved in the presence of silver(I) tetrafluoroborate (AgBF₄) at 80 °C in DCE (Scheme 2a and Figures S3, S4). In both cases, the characteristic absorption band of Ru(bpy)₃²⁺ at 455 nm evolved rapidly and **G-2** was almost fully converted after 30 min. In case of **G-1**, the reaction required a longer period of 120–150 min and it also generated the blue oxo-bridged dimer [(bpy)₂(Cl)RuORu(Cl)(bpy)₂]²⁺ as a byproduct, which we identified by its absorption spectrum^[12] and which was probably formed by hydrolysis of *cis*-[Ru(bpy)₂Cl₂] with trace amounts of H₂O, followed by Ag^I-mediated oxidative dimerization^[13] (Figure S3). Despite the presence of this side product after the ligand substitution on catalyst **G-1**, the resulting solutions were photochemically active as we could subsequently demonstrate.

The transformation of Grubbs' 1st generation catalyst (**G-1**) to Ru(bpy)₃²⁺ was successfully utilized in tandem olefin metathesis/photoredox reactions. As shown in Table 1, *ortho*-allylstyrenes and further 1,*n*-dienes **1**^[14] were converted to the indenenes and cyclic alkenes **2** by ring-closing metathesis (RCM) in DCE. Subsequent addition of 2,2'-bipyridine (in a reduced excess of 10 equiv with respect to **G-1**) and AgBF₄ (2.5 equiv relative to **G-1**) and heating to 80 °C for 3 h induced the ligand substitution of the Ru^{II}-alkylidene in the presence of the organic intermediate **2**. The resulting reaction mixtures were concentrated to dryness, where after tosyl chloride (TsCl, 1.0 equiv) was added, and acetone as the optimal solvent for the adjacent photoredox step. Irradiation of the homogeneous solutions with blue LED light resulted in the clean chlorosulfonylation of the intermediary alkenes **2** by way of a redox neutral ATRA reaction^[15b,16] of the sulfonyl halide with the alkene. While the presence of silver(I) salts showed no inhibitory effect on the photoredox-induced reaction, the exchange of solvent was found necessary due to the limited solubility of the catalyst Ru(bpy)₃(BF₄)₂ in DCE. When the sequence was carried out in DCE alone, product **3a** was formed in just 26% compared to 57% overall yield using acetone. *trans*-configured products **3** were obtained exclusively in all cases, with the exception of the tetrahydrobenzo[7]annulene **3i** which was formed as a 5:1 mixture of diastereomers. Overall, the sequential protocol generated the 2-chlorosulfones **3** in moderate to good isolated yields of up to 69%, while one C–C and two C–het bonds were consecutively installed. The overall yields are well-correlated with the combined isolated yields of the two individual steps, which were determined in independent experiments after chromatographic purification (see Supporting Information).

In summary, we demonstrated for the first time the combination of olefin metathesis with photoredox catalysis in sequential one-pot protocols, enabled by the in situ ligand substitution of Ru^{II}-alkylidenes to ruthenium(II)-tris(bipyridine). The 2-chlorosulfone products **3** were conveniently prepared by way of exemplary tandem RCM/photoredox ATRA reactions in moderate to good overall yields. Further applications of this concept are currently under investigation.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: ATRA reaction · olefin metathesis · photoredox catalysis · sequential catalysis · tandem catalysis

- [1] a) T. J. J. Müller in *Molecular Catalysts: Structure and Functional Design* (Eds.: L. H. Gade, P. Hofmann), Wiley-VCH, Weinheim, **2014**, pp. 255–280; b) C. Bruneau, S. Dérien, P. H. Dixneuf in *Topics in Organometallic Chemistry, Vol. 19* (Ed.: T. J. J. Müller), Springer, Berlin, **2006**, pp. 295–326; c) A. Ajamian, J. L. Gleason, *Angew. Chem. Int. Ed.* **2004**, *43*, 3754–3760; *Angew. Chem.* **2004**, *116*, 3842–3848.
- [2] According to the taxonomy introduced by Fogg and dos Santos, sequential catalytic protocols may be classified as assisted tandem catalysis: D. E. Fogg, E. N. dos Santos, *Coord. Chem. Rev.* **2004**, *248*, 2365–2379.
- [3] Selected examples: a) Q. Zhao, J. Zhang, M. Szostak, *Chem. Commun.* **2019**, *55*, 9003–9006; b) P. K. Dornan, D. Lee, R. H. Grubbs, *J. Am. Chem. Soc.* **2016**, *138*, 6372–6375; c) N. M. Neisius, B. Plietker, *J. Org. Chem.* **2008**, *73*, 3218–3227; d) L. Ackermann, R. Born, P. Álvarez-Bercedo, *Angew. Chem. Int. Ed.* **2007**, *46*, 6364–6367; *Angew. Chem.* **2007**, *119*, 6482–6485; e) S. Beligny, S. Eibauer, S. Maechling, S. Blechert, *Angew. Chem. Int. Ed.* **2006**, *45*, 1900–1903; *Angew. Chem.* **2006**, *118*, 1933–1937; f) A. A. Scholte, M. H. An, M. L. Snapper, *Org. Lett.* **2006**, *8*, 4759–4762; g) J. Louie, C. W. Bielawski, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 11312–11313.
- [4] Selected reviews: a) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879–5918; b) B. Alcaide, P. Almendros, A. Luna, *Chem. Rev.* **2009**, *109*, 3817–3858; c) B. M. Trost, F. D. Toste, A. B. Pinkerton, *Chem. Rev.* **2001**, *101*, 2067–2096; d) T. Naota, H. Takaya, S.-I. Murahashi, *Chem. Rev.* **1998**, *98*, 2599–2660.
- [5] Selected overviews: a) *Science of Synthesis: Photocatalysis in Organic Synthesis* (Ed.: B. König), Thieme, Stuttgart, **2019**; b) *Visible Light Photocatalysis in Organic Chemistry* (Eds.: C. R. J. Stephenson, T. P. Yoon, D. W. C. MacMillan), Wiley-VCH, Weinheim, **2018**; c) L. Marzo, S. K. Pagire, O. Reiser, B. König, *Angew. Chem. Int. Ed.* **2018**, *57*, 10034–10072; *Angew. Chem.* **2018**, *130*, 10188–10228; d) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322–5363; e) J. Xuan, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 6828–6838; *Angew. Chem.* **2012**, *124*, 6934–6944; f) L. Shi, W. Xia, *Chem. Soc. Rev.* **2012**, *41*, 7687–7697; g) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102–113.
- [6] D. Alpers, M. Gallhof, C. B. W. Stark, M. Brasholz, *Chem. Commun.* **2016**, *52*, 1025–1028.
- [7] a) S. Lin, M. A. Ischay, C. G. Fry, T. P. Yoon, *J. Am. Chem. Soc.* **2011**, *133*, 19350–19353; b) N. J. Saettel, J. Oxgaard, O. Wiest, *Eur. J. Org. Chem.* **2001**, 1429–1439; c) N. L. Bauld, *Tetrahedron* **1989**, *45*, 5307–5363.
- [8] a) J. Adrian, L. J. Gross, C. B. W. Stark, *Beilstein J. Org. Chem.* **2016**, *12*, 2104–2123; b) N. S. Sheikh, *Org. Biomol. Chem.* **2014**, *12*, 9492–9504; c) V. Piccilli, *Synthesis* **2007**, 2585–2607.
- [9] Selected overviews: a) O. M. Ogba, N. C. Warner, D. J. O'Leary, R. H. Grubbs, *Chem. Soc. Rev.* **2018**, *47*, 4510–4544; b) *Handbook of Metathesis* (Eds.: R. H. Grubbs, A. G. Wenzel, D. J. O'Leary, E. Khosravi), Wiley-VCH, Weinheim, **2015**; c) C. Samojłowicz, M. Bieniek, K. Grela, *Chem. Rev.* **2009**, *109*, 3708–3742; d) M. Schuster, S. Blechert, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2036–2056; *Angew. Chem.* **1997**, *109*, 2124–2144.

- [10] Review: X.-W. Lan, N.-X. Wang, Y. Xing, *Eur. J. Org. Chem.* **2017**, 5821–5851.
- [11] *cis*-[Ru(bpy)₂Cl₂] could be identified by its violet color and its UV/Vis spectrum: E. C. Johnson, B. P. Sullivan, D. J. Salmon, S. A. Adeymi, T. J. Meyer, *Inorg. Chem.* **1978**, *17*, 2211–2215.
- [12] T. R. Weaver, T. J. Meyer, S. A. Adeymi, G. M. Brown, R. P. Eckberg, W. E. Hatfield, E. C. Johnson, R. W. Murray, D. Untereker, *J. Am. Chem. Soc.* **1975**, *97*, 3039–3048.
- [13] S. W. Gersten, G. J. Samuels, T. J. Meyer, *J. Am. Chem. Soc.* **1982**, *104*, 4029–4030.
- [14] Syntheses of dienes **1 d–g**: A. Jana, K. Misztal, A. Zak, K. Grell, *J. Org. Chem.* **2017**, *82*, 4226–4234.
- [15] a) T.-F. Niu, D. Lin, L.-S. Xue, D.-Y. Jiang, B.-Q. Ni, *Synlett* **2018**, *29*, 364–368; b) Cu^I- and Cu^{II}-photocatalyzed variant: A. Hossain, S. Engl, E. Lutsker, O. Reiser, *ACS Catal.* **2019**, *9*, 1103–1109.
- [16] a) Overview: T. Courant, G. Masson, *J. Org. Chem.* **2016**, *81*, 6945–6952; b) C.-J. Wallentin, J. D. Nguyen, P. Finkbeiner, C. R. J. Stephenson, *J. Am. Chem. Soc.* **2012**, *134*, 8875–8884.

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