A Journal of the Gesellschaft Deutscher Chemiker

Angewandte Chemie

GDCh

International Edition

www.angewandte.org

Title: Continuous Visible Light-Photo-Flow for Manganese-Catalyzed (Het)Arene C−H Arylation

Authors: Yu-Feng Liang, Ralf Steinbock, Long Yang, and Lutz Ackermann

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.201805644
Angew. Chem. 10.1002/ange.201805644

Link to VoR: http://dx.doi.org/10.1002/anie.201805644
http://dx.doi.org/10.1002/ange.201805644

WILEY-VCH

10.1002/anie.201805644

Continuous Visible Light-Photo-Flow for Manganese-Catalyzed (Het)Arene C−H Arylation

Yu-Feng Liang, Ralf Steinbock, Long Yang, and Lutz Ackermann*

Abstract: *Manganese photocatalysts enabled versatile room-temperature C–H arylations by means of continuous visible light-photo-flow, thus allowing for efficient C–H arylations in 30 minutes with ample scope. The robustness of the manganese-catalyzed photo-flow strategy was demonstrated by visible light-induced gram-scale synthesis, clearly outperforming the batch performance.*

The catalytic functionalization of otherwise inert C–H bonds has emerged as a transformative platform in molecular sciences.[1] Considerable recent progress in C–H functionalization chemistry was accomplished with earth-abundant 3d metals,[2] with key contributions in manganese catalysis[3] by Takai/Kuninobu,[4] Wang,[5] and Ackermann,[6] among others.[7] Despite of indisputable advances, the vast majority of manganese-catalyzed C–H functionalizations continue to be limited to rather harsh reaction conditions, with typical reaction temperatures of up to 120 °C.[3-7]

In recent years, light-induced metal catalysis has been identified as a powerful tool for mild single-electron-transfer-based organic transformations.[8] However, photoredox C–H functionalizations were primarily realized with precious[9] iridium and ruthenium catalysts, with notable contributions by Reiser,[10] Rueping,[11] and Stephenson,[12] among others.[13] In sharp contrast, photo-induced room temperature C–H arylations by earth-abundant base-metal manganese catalysis have thus far proven elusive.[14],[15] Within our program on sustainable C–H activation by base-metal catalysis,[16] we have now devised a protocol for unprecedented photo-induced C–H arylations by non-toxic manganese catalysis, on which we report herein. Notable features of our findings include (a) earth abundant base-metal as photoredox catalysis[17] for C–H functionalization, (b) excellent levels of positional control, and (c) visible light-induced manganese catalyzed C–H arylations at room temperature (Figure 1). It is particularly worthy of note that we have also devised the first continuous photo-flow strategy[18],[19] for 3d metal-catalyzed C–H functionalizations, thereby enabling efficient gram-scale C–H arylations, which outperformed the corresponding batch approach.

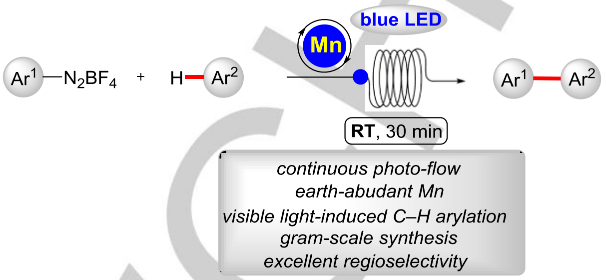
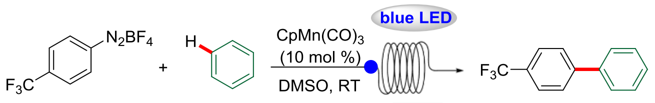


Figure 1. Manganese-catalyzed C−H arylation in continuous photo-flow.

We initiated our studies by probing various reaction conditions for the envisioned manganese-catalyzed C–H arylation of arene **2a** in continuous photo-flow at room temperature (Table 1 and Table S1 in the Supporting Information). We were delighted to observe that the desired C–H arylation product **3aa** was obtained in 62% yield when $CpMn(CO)_3$ was employed as the photocatalyst in DMSO for only 30 minutes (Table 1, entry 1). Control experiments confirmed the essential role of the manganese catalyst and the light (Table 1, entries 2-3). Further optimization studies revealed $MnCl_2$ and $Mn(OAc)_2$ falling short in improving the performance, while Eosin Y, $MnBr(CO)_5$, and $Mn_2(CO)_{10}$ displayed significantly lower catalytic efficacy (Table 1, entries 4-8). Aprotic solvents proved mandatory for the C–H arylation, with DMSO being optimal (Table 1, entries 9-13). The flow rate of the photo-flow C–H functionalization displayed a considerable effect (Table 1, entries 14-15). It is noteworthy that the reaction in batch furnished biaryl **3aa** in significantly lower yields due to the improved mass- and energy transfer in flow, thus highlighting the beneficial assets of photo-flow for C–H functionalizations (Table 1, entry 16).

Table 1. Optimization of reaction conditions in continuous photo-flow.[a]



1a **2a** **3aa**

Entry	Deviation from above	Yield of **3aa** [%][b]
1	None	62
2	Without light	7
3	Without $CpMn(CO)_3$	13
4	$MnCl_2$ instead of $CpMn(CO)_3$	10
5	$Mn(OAc)_2$ instead of $CpMn(CO)_3$	8
6	$MnBr(CO)_5$ instead of $CpMn(CO)_3$	29
7	$Mn_2(CO)_{10}$ instead of $CpMn(CO)_3$	44
8	Eosin Y instead of $CpMn(CO)_3$	35
9	DMF instead of DMSO	41
10	MeOH instead of DMSO	32
11	MeCN instead of DMSO	trace
12	Acetone instead of DMSO	34
13	Benzene instead of DMSO	6
14	With 500 µL/min flow rate for 20 min	49
15	With 250 µL/min flow rate for 40 min	61
16	Reaction in batch instead of flow	33

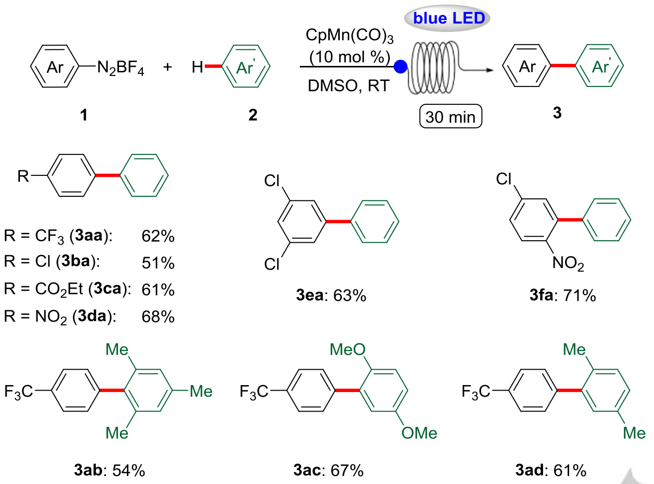
---

[*] Dr. Y.-F. Liang, R. Steinbock, L. Yang, Prof. Dr. L. Ackermann
Institut für Organische und Biomolekulare Chemie
Georg-August-Universität Göttingen
Tammannstraße 2, 37077 Gottingen (Germany)
E-mail: Lutz.Ackermann@chemie.uni-goettingen.de
Homepage: http://www.ackermann.chemie.uni-goettingen.de/

Supporting information for this article is given via a link at the end of the document.

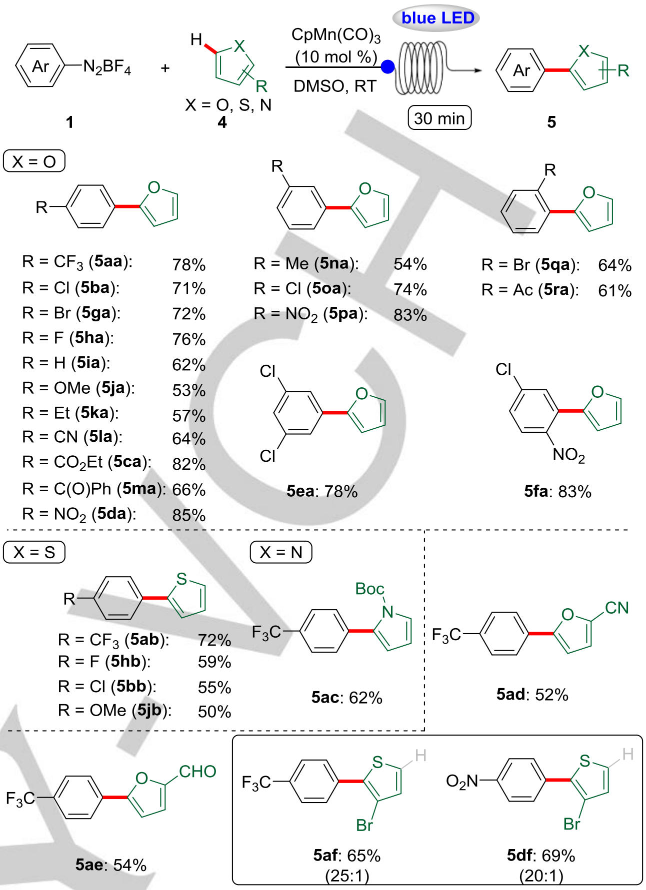
[a] Reaction conditions: **1a** (0.5 mmol), **2a** (7.5 mmol), Cat. (10 mol %), DMSO (0.3 mL), with 330 µL/min flow rate, 30 min, under 24 W blue LED irradiation (λ = 450 nm) in continuous flow at room temperature of 25 ± 3 °C. [b] Yield of isolated product.

With the optimized reaction conditions in hand, we probed the scope of the visible-light-enabled C−H arylation of arenes **2** (Scheme 1). The versatility of the continuous photo-flow C−H arylation was reflected by tolerating valuable functional groups, including fluoro, chloro, ester, and nitro substituents.

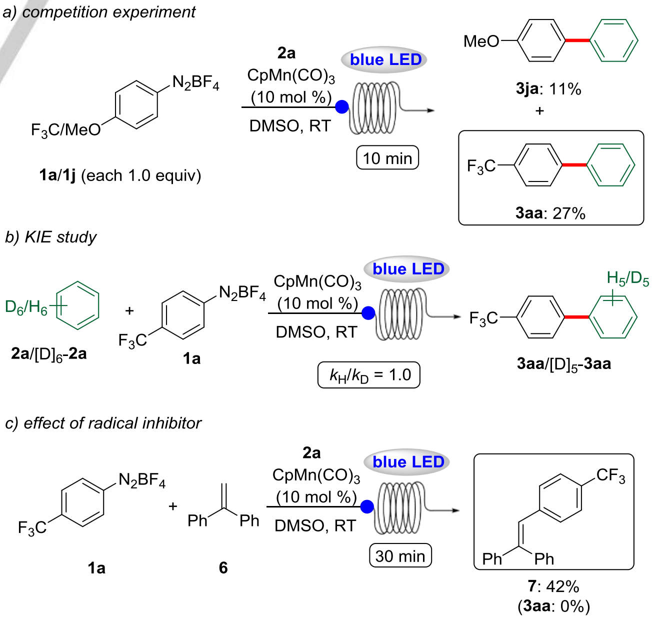


Scheme 1. Manganese-catalyzed C−H arylation by visible-light photo-flow.

The robustness of the manganese-catalyzed C−H functionalization in continuous photo-flow was next explored with heteroarenes **4** (Scheme 2). The manganese-catalyzed C−H arylation was again characterized by ample substrate scope, featuring chloro, bromo, ester, cyano, ketone and nitro functionalities, which should prove invaluable for further late-stage manipulation. The manganese catalysis manifold enabled the direct C−H arylation of substituted furans, pyrolles and thiophenes with improved levels of positional control.



Scheme 2. Room temperature hetroarene C−H arylation by photo-flow.



Scheme 3. Key mechanistic findings.

10.1002/anie.201805644

Subsequently, we conducted mechanistic studies to gain insights into the catalyst's mode of action (Scheme 3). First, intermolecular competition experiments indicated electron-poor arenes **1** to react preferentially (Scheme 3a). This observation can be rationalized by the occurrence of a radical-controlled SOMO–HOMO interaction.[20] A notable intermolecular kinetic isotope effect (KIE, $k_H/k_D \approx 1.0$) was not observed (Scheme 3b), indicating a non-kinetically relevant C–H cleavage. The reaction was completely stopped by the radical inhibitor 1,1-diphenylethylene **6**. Here, the trapped intermediate **7** could be isolated (Scheme 3c), suggesting an aryl radical pathway. Detailed absorption studies provided strong support for the initial formation of an photochemically-competent complex generated by $CpMn(CO)_3$ and the substrates (Figure 2).

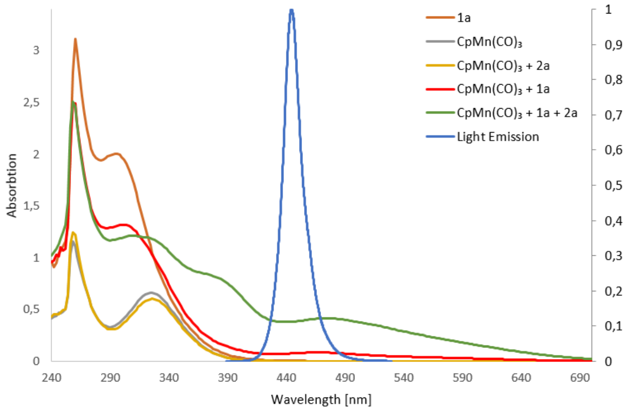
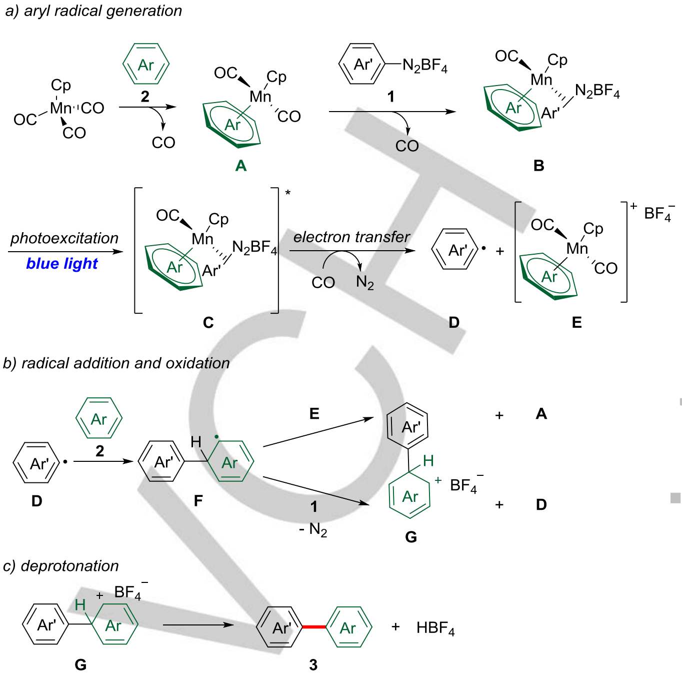


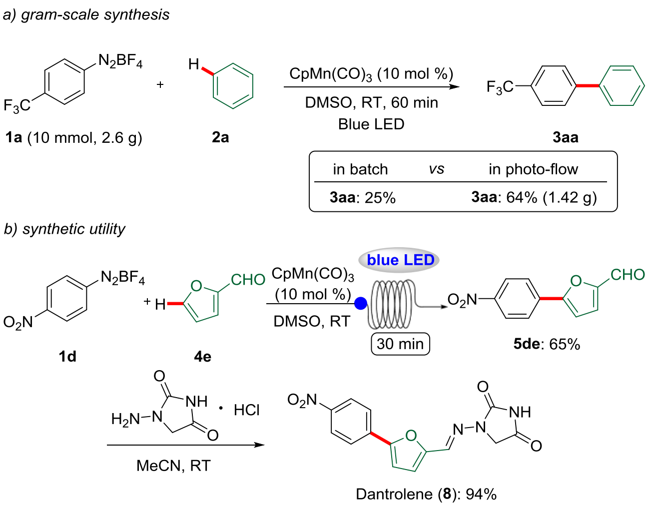
Figure 2. Absorption studies.

Based on our mechanistic studies and literature precedence,[8-13] we propose a plausible reaction mechanism depicted in Scheme 4. First, ligand exchange on $CpMn(CO)_3$ with the arene substrate occurs to afford the manganese species **A**, along with subsequent coordination by substrate **1** to deliver the complex **B**. Then, photoexcitation and electron transfer from excited-state complex **C** gives aryl radical intermediate **D** and manganese radical cation **E**. The addition of aryl radical to arene **2** affords intermediate **F**, which is further oxidized by the manganese radical cation **E** or the aryl diazonium salt **1** to generate carbocation intermediate **G**. Finally, deprotonation delivers the desired arylated product **3**.



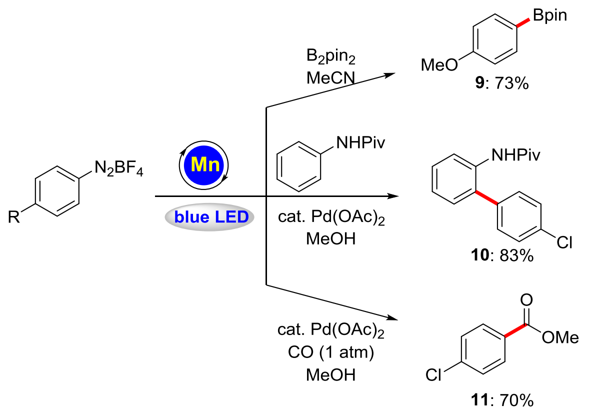
Scheme 4. Proposed mode of action.

Scalable processes continue to be scarce for visible-light photoredox catalysis.[21] The synthetic potential of our manganese-catalyzed C–H arylation in continuous photo-flow was hence illustrated by the gram-scale synthesis of product **3aa** within 60 minutes (Scheme 5a). In sharp contrast, the reaction in batch delivered the biaryl **3aa** in only 25% yield, thus clearly highlighting the beneficial features of the photo-flow approach for scale-up operations. Furthermore, the C–H arylation of biomass-derived furfural **4e**, followed by condensation, afforded Dantrolene **8** (Scheme 5b) – a valuable drug for the treatment of porcine and human malignant hyperthermia.[22]



Scheme 5. Gram-scale synthesis and synthetic utility.

Finally, we explored the manganese visible-light photocatalysis for various transformations (Scheme 6). To this end, the borylation product **9**, the chlation-assisted C–H arylation product **10**, and the alkyoxycarbonylated arene **11** were successfully obtained, demonstrating the versatility of our strategy.



Scheme 6. Versatile manganese-catalyzed photo-induced transformations: [$Mn_2(CO)_{10}$] (10 mol %), RT.

In summary, inexpensive and earth-abundant manganese complexes were employed as photocatalysts for mild visible-light-induced C–H arylations of (het)arenes. Thus, a robust and user-friendly manganese catalyst enabled C–H functionalizations at room temperature, being fully compatible with a wide array of functional groups with excellent position-selectivity. Mechanistic studies provided strong support for an efficient SET process. Our findings highlight the practical value of performing manganese-catalyzed visible light-induced C–H functionalizations in continuous photo-flow for large scale application.

Acknowledgements

Generous support by the Alexander von Humboldt Foundation (fellowship to Y.L.), and the DFG (Gottfried-Wilhelm-Leibniz prize) is gratefully acknowledged.

Conflict of interest

The authors declare no conflict of interest.

Keywords: continuous photo-flow • visible light • manganese • C−H arylation • mechanism

[1] Selected reviews: a) P. Gandeepan, L. Ackermann, *Chem.* **2018**, *4*, 199-222; b) D.-S. Kim, W.-J. Park, C.-H. Jun, *Chem. Rev.* **2017**, *117*, 8977-9015; c) Z. Dong, Z. Ren, S. J. Thompson, Y. Xu, G. Dong, *Chem. Rev.* **2017**, *117*, 9333-9403; d) R. Y. Zhu, M. E. Farmer, Y. Q. Chen, J. Q. Yu, *Angew. Chem. Int. Ed.* **2016**, *55*, 10578-10599; e) O. Daugulis, J. Roane, L. D. Tran, *Acc. Chem. Res.* **2015**, *48*, 1053-1064; f) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, *5*, 369-375; g) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem. Int. Ed.* **2009**, *48*, 9792-9826, and references cited therein.

[2] a) T. Yoshino, S. Matsunaga, *Adv. Synth. Catal.* **2017**, *359*, 1245-1262; b) K. Hirano, M. Miura, *Chem. Lett.* **2015**, *44*, 868-873; c) L. C. M. Castro, N. Chatani, *Chem. Lett.* **2015**, *44*, 410-421; d) K. Gao, N. Yoshikai, *Acc. Chem. Res.* **2014**, *47*, 1208-1219; e) Y. Nakao, *Chem. Rec.* **2011**, *11*, 242-251; f) A. A. Kulkarni, O. Daugulis, *Synthesis.* **2009**, *24*, 4087-4109.

[3] a) Y. Hu, B. Zhou, C. Wang, *Acc. Chem. Res.* **2018**, *51*, 816-827; b) R. Cano, K. Mackey, G. P. McGlacken, *Catal. Sci. Technol.* **2018**, *8*, 1251-1266; c) W. Liu, L. Ackermann, *ACS Catal.* **2016**, *6*, 3743-3752; d) C. Wang, *Synlett* **2013**, *24*, 1606-1613.

[4] a) S. Sueki, Z. Wang, Y. Kuninobu, *Org. Lett.* **2016**, *18*, 304-307; b)Y. Kuninobu, Y. Nishina, T. Takeuchi, K. Takai, *Angew. Chem. Int. Ed.* **2007**, *46*, 6518-6520.

[5] a) X. Yang, C. Wang, *Angew. Chem. Int. Ed.* **2018**, *57*, 923-928; b) B. Zhou, Y. Hu, T. Liu, C. Wang, *Nat. Commun.* **2017**, *8*, 1169; c) X. Yang, X. Jin, C. Wang, *Adv. Synth. Catal.* **2016**, *358*, 2436-2442; d) Y. Hu, C. Wang, *Sci. China Chem.* **2016**, *59*, 1301-1305; e) B. Zhou, Y. Hu, C. Wang, *Angew. Chem. Int. Ed.* **2015**, *54*, 13659-13663; f) B. Zhou, P. Ma, H. Chen, C. Wang, *Chem. Commun.* **2014**, *50*, 14558-14561; g) R. He, Z. T. Huang, Q. Y. Zheng, C. Wang, *Angew. Chem. Int. Ed.* **2014**, *53*, 4950-4953; h) B. Zhou, H. Chen, C. Wang, *J. Am. Chem. Soc.* **2013**, *135*, 1264-1267.

[6] a) Y.-F. Liang, R. Steinbock, A. Münch, D. Stalke, L. Ackermann, *Angew. Chem. Int. Ed.* **2018**, *57*, 5384-5388; b) Y.-F. Liang, L. Massignan, L. Ackermann, *ChemCatChem.* **2018**, DOI: 10.1002/cctc.201800144; c) D. Zell, U. Dhawa, V. Müller, M. Bursch, S. Grimme, L. Ackermann, *ACS Catal.* **2017**, *7*, 4209-4213; d) H. Wang, M. M. Lorion, L. Ackermann, *Angew. Chem. Int. Ed.* **2017**, *56*, 6339-6342; e) Z. Ruan, N. Sauermann, E. Manoni, L. Ackermann, *Angew. Chem. Int. Ed.* **2017**, *56*, 3172-3176; f) W. Liu, G. Cera, J. C. Oliveira, Z. Shen, L. Ackermann, *Chem. Eur. J.* **2017**, *23*, 11524-11528; g) Y.-F. Liang, V. Müller, W. Liu, A. Münch, D. Stalke, L. Ackermann, *Angew. Chem. Int. Ed.* **2017**, *56*, 9415-9419; h) W. Liu, S. C. Richter, Y. Zhang, L. Ackermann, *Angew. Chem. Int. Ed.* **2016**, *55*, 7747-7750; i) W. Liu, S. C. Richter, R. Mei, M. Feldt, L. Ackermann, *Chem. Eur. J.* **2016**, *22*, 17958-17961; j) Y.-F. Liang, L. Massignan, W. Liu, L. Ackermann, *Chem. Eur. J.* **2016**, *22*, 14856-14859; k) W. Liu, D. Zell, M. John, L. Ackermann, *Angew. Chem. Int. Ed.* **2015**, *54*, 4092-4096; l) W. Liu, J. Bang, Y. Zhang, L. Ackermann, *Angew. Chem. Int. Ed.* **2015**, *54*, 14137-14140.

[7] a) C. Wang, B. Maity, L. Cavallo, M. Rueping, *Org. Lett.* **2018**, *20*, 3105-3108; b) C. Zhu, J. L. Schwarz, S. Cembellín, S. Greßies, F. Glorius, *Angew. Chem. Int. Ed.* **2018**, *57*, 437-441; c) Q. Lu, S. Cembellín, S. Greßies, S. Singha, C. G. Daniliuc, F. Glorius, *Angew. Chem. Int. Ed.* **2018**, *57*, 1399-1403; d) C. Wang, A. Wang, M. Rueping, *Angew. Chem. Int. Ed.* **2017**, *56*, 9935-9938; e) J. Ni, H. Zhao, A. Zhang, *Org. Lett.* **2017**, *19*, 3159-3162; f) Q. Lu, F. J. Klauck, F. Glorius, *Chem. Sci.* **2017**, *8*, 3379-3383; g) Q. Lu, S. Greßies, F. J. R. Klauck, F. Glorius, *Angew. Chem. Int. Ed.* **2017**, *56*, 6660-6664; h) Q. Lu, S. Greßies, S. Cembellín, F. J. R. Klauck, C. G. Daniliuc, F. Glorius, *Angew. Chem. Int. Ed.* **2017**, *56*, 12778-12782; i) S.-L. Liu, Y. Li, J.-R. Guo, G.-C. Yang, X.-H. Li, J.-F. Gong, M.-P. Song, *Org. Lett.* **2017**, *19*, 4042-4045; j) S.-Y. Chen, Q. Li, H. Wang, *J. Org. Chem.* **2017**, *82*, 11173-11181; k) S. Y. Chen, Q. Li, X. G. Liu, J. Q. Wu, S. S. Zhang, H. Wang, *ChemSusChem.* **2017**, *10*, 2360-2364; l) S. Y. Chen, X. L. Han, J. Q. Wu, Q. Li, Y. Chen, H. Wang, *Angew. Chem. Int. Ed.* **2017**, *56*, 9939-9943; m) N. P. Yahaya, K. M. Appleby, M. Teh, C. Wagner, E. Troschke, J. T. W. Bray, S. B. Duckett, L. A. Hammarback, J. S. Ward, J. Milani, N. E. Pridmore, A. C. Whitwood, J. M. Lynam, I. J. S. Fairlamb, *Angew. Chem. Int. Ed.* **2016**, *55*, 12455-12459; n) L. Shi, X. Zhong, H. She, Z. Lei, F. Li, *Chem. Commun.* **2015**, *51*, 7136-7139.

[8] For recent reviews on photo chemistry, see: a) L. Marzo, S. K. Pagire, O. Reiser, B. König, *Angew. Chem. Int. Ed.* **2018**, DOI: 10.1002/anie.201709766; b) J. Xie, H. Jin, A. S. K. Hashmi, *Chem. Soc. Rev.* **2017**, *46*, 5193-5203; c) K. L. Skubi, T. R. Blum, T. P. Yoon, *Chem. Rev.* **2016**, *116*, 10035-10074; d) D. Ravelli, S. Protti, M. Fagnoni, *Chem.*

10.1002/anie.201805644

Rev. **2016**, *116*, 9850-9913; e) M. D. Kärkäs, B. S. Matsuura, C. R. Stephenson, *Science* **2015**, *349*, 1285-1286; h) R. Brimioulle, D. Lenhart, M. M. Maturi, T. Bach, *Angew. Chem. Int. Ed.* **2015**, *54*, 3872-3890.

[9] For the use of organic dyes, see: a) N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075-10166; b) D. P. Hari, B. König, *Chem. Commun.* **2014**, *50*, 6688-6699; c) D. Ravelli, M. Fagnoni, A. Albini, *Chem. Soc. Rev.* **2013**, *42*, 97-113.

[10] a) O. Reiser, *Acc. Chem. Res.* **2016**, *49*, 1990-1996; b) D. B. Bagal, G. Kachkovskyi, M. Knorn, T. Rawner, B. M. Bhanage, O. Reiser, *Angew. Chem. Int. Ed.* **2015**, *54*, 6999-7002.

[11] D. C. Fabry, M. Rueping, *Acc. Chem. Res.* **2016**, *49*, 1969-1979.

[12] D. Staveness, I. Bosque, C. R. Stephenson, *Acc. Chem. Res.* **2016**, *49*, 2295-2306.

[13] a) J. C. Tellis, C. B. Kelly, D. N. Primer, M. Jouffroy, N. R. Patel, G. A. Molander, *Acc. Chem. Res.* **2016**, *49*, 1429-1439; b) M. H. Shaw, J. Twilton, D. W. MacMillan, *J. Org. Chem.* **2016**, *81*, 6898-6926; c) S. P. Pitre, C. D. McTiernan, J. C. Scaiano, *Acc. Chem. Res.* **2016**, *49*, 1320-1330; d) S. A. Morris, J. Wang, N. Zheng, *Acc. Chem. Res.* **2016**, *49*, 1957-1968; e) M. Majek, A. Jacobi von Wangelin, *Acc. Chem. Res.* **2016**, *49*, 2316-2327; f) M. N. Hopkinson, A. Tlahuext-Aca, F. Glorius, *Acc. Chem. Res.* **2016**, *49*, 2261-2272; g) A. C. Hernandez-Perez, S. K. Collins, *Acc. Chem. Res.* **2016**, *49*, 1557-1565; h) J.-P. Goddard, C. Ollivier, L. Fensterbank, *Acc. Chem. Res.* **2016**, *49*, 1924-1936; i) I. Ghosh, L. Marzo, A. Das, R. Shaikh, B. König, *Acc. Chem. Res.* **2016**, *49*, 1566-1577; j) E. C. Gentry, R. R. Knowles, *Acc. Chem. Res.* **2016**, *49*, 1546-1556; k) A. Arora, J. D. Weaver, *Acc. Chem. Res.* **2016**, *49*, 2273-2283.

[14] For exmples of light-induced C−H arylations, see: a) M. K. Sahoo, S. P. Midya, V. G. Landge, E. Balaraman, *Green Chem.* **2017**, *19*, 2111-2117; b) S. Crespi, S. Protti, M. Fagnoni, *J. Org. Chem.* **2016**, *81*, 9612-9619; c) D. C. Fabry, M. A. Ronge, J. Zoller, M. Rueping, *Angew. Chem. Int. Ed.* **2015**, *54*, 2801-2805; d) J. Zoller, D. C. Fabry, M. Rueping, *ACS Catal.* **2015**, *5*, 3900-3904; e) D. Cantillo, C. Mateos, J. A. Rincon, O. de Frutos, C. O. Kappe, *Chem. Eur. J.* **2015**, *21*, 12894-12898; f) W. Guo, L.-Q. Lu, Y. Wang, Y.-N. Wang, J.-R. Chen, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2015**, *54*, 2265-2269; g) J. Zoller, D. C. Fabry, M. A. Ronge, M. Rueping, *Angew. Chem. Int. Ed.* **2014**, *53*, 13264-13268; h) D. C. Fabry, J. Zoller, S. Raja, M. Rueping, *Angew. Chem. Int. Ed.* **2014**, *53*, 10228-10231; i) I. Ghosh, T. Ghosh, J. I. Bardagi, B. König, *Science* **2014**, *346*, 725-728; j) M. Tobisu, T. Furukawa, N. Chatani, *Chem. Lett.* **2013**, *42*, 1203-1205; k) J. Yu, L. Zhang, G. Yan, *Adv. Synth. Catal.* **2012**, *354*, 2625-2628; l) D. P. Hari, P. Schroll, B. König, *J. Am. Chem. Soc.* **2012**, *134*, 2958-2961; m) D. Kalyani, K. B. Mcmurtrey, S. R. Neufeldt, M. S. Sanford, *J. Am. Chem. Soc.* **2011**, *133*, 18566-18569, and references cited therein. For mild palladium catalysis, see: n) H. P. L. Gemoets, I. Kalvet, A. V. Nyuchev, N. Erdmann, V. Hessel, F. Schoenebeck, T. Noël, *Chem. Sci*. **2017**, *8*, 1046-1055.

[15] For manganese-enabled light-induced reactions, see: a) P. Nuhant, M. S. Oderinde, J. Genovino, A. Juneau, Y. Gagné, C. Allais, G. M. Chinigo, C. Choi, N. W. Sach, L. Bernier, *Angew. Chem. Int. Ed.* **2017**, *56*, 15309-15313; b) B. C. Gilbert, W. Kalz, C. I. Lindsay, P. T. McGrail, A. F. Parsons, D. T. Whittaker, *J.Chem. Soc., Perkin Trans. 1.* **2000**, 1187-1194; c) H. Chen, J. F. Hartwig, *Angew. Chem. Int. Ed.* **1999**, *38*, 3391-3393.

[16] a) G. Cera, L. Ackermann, *Top. Curr. Chem.* **2016**, *374*, 57; b) M. Moselage, J. Li, L. Ackermann, *ACS Catal.* **2015**, *6*, 498-525; c) L. Ackermann, *J. Org. Chem.* **2014**, *79*, 8948-8954; d) L. Ackermann, *Acc. Chem. Res.* **2014**, *47*, 281-295.

[17] For copper catalysis, see: a) P. Gandeepan, J. Mo, L. Ackermann, *Chem. Commun.* **2017**, *53*, 5906-5909; b) F. Yang, J. Koeller, L. Ackermann, *Angew. Chem. Int. Ed.* **2016**, *55*, 4759-4762.

[18] For reviews on continuous flow technology, see: a) M. B. Plutschack, B. u. Pieber, K. Gilmore, P. H. Seeberger, *Chem. Rev.* **2017**, *117*, 11796-11893; b) B. Pieber, K. Gilmore, P. H. Seeberger, *J. Flow Chem.* **2017**, 1-8; c) K. F. Jensen, *AIChE J.* **2017**, *63*, 858-869; d) D. Cambié, C. Bottecchia, N. J. Straathof, V. Hessel, T. Noël, *Chem. Rev.* **2016**, *116*, 10276-10341.

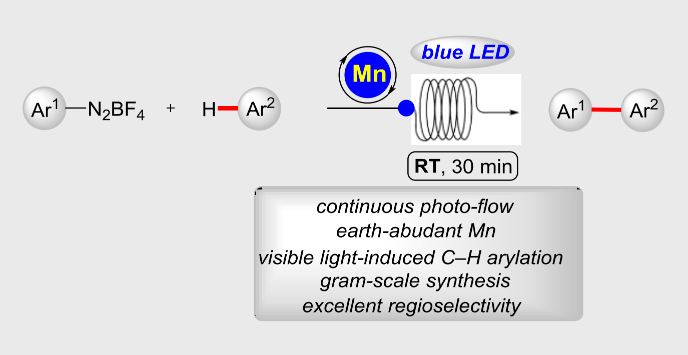
[19] For recent examples on continuous flow, see: a) C. Zhu, J. C. Oliveira, Z. Shen, H. Huang, L. Ackermann, *ACS Catal.* **2018**, *8*, 4402-4407; b) G. Laudadio, S. Govaerts, Y. Wang, D. Ravelli, H. F. Koolman, M. Fagnoni, S. W. Djuric, T. Noël, *Angew. Chem. Int. Ed.* **2018**, *57*, 4078-4082; c) H. Kim, Y. Yonekura, J. i. Yoshida, *Angew. Chem. Int. Ed.* **2018**, *57*, 4063-4066; d) X.-J. Wei, W. Boon, V. Hessel, T. Noël, *ACS Catal.* **2017**, *7*, 7136-7140; e) H. Wang, F. Pesciaioli, J. C. A. Oliveira, S. Warratz, L. Ackermann, *Angew. Chem. Int. Ed.* **2017**, *56*, 15063-15067; f) U. K. Sharma, H. P. Gemoets, F. Schröder, T. Noël, E. V. van der Eycken, *ACS Catal.* **2017**, *7*, 3818-3823; g) H. Seo, A. Liu, T. F. Jamison, *J. Am. Chem. Soc.* **2017**, *139*, 13969-13972; h) H. Seo, M. H. Katcher, T. F. Jamison, *Nat. Chem.* **2017**, *9*, 453-456; i) H. Li, J. W. Sheeran, A. M. Clausen, Y. Q. Fang, M. M. Bio, S. Bader, *Angew. Chem. Int. Ed.* **2017**, *56*, 9425-9429; j) F. Ferlin, S. Santoro, L. Ackermann, L. Vaccaro, *Green Chem.* **2017**, *19*, 2510-2514; k) E. N. DeLaney, D. S. Lee, L. D. Elliott, J. Jin, K. I. Booker-Milburn, M. Poliakoff, M. W. George, *Green Chem.* **2017**, *19*, 1431-1438; l) J. Britton, T. F. Jamison, *Angew. Chem. Int. Ed.* **2017**, *56*, 8823-8827; m) C. Bottecchia, M. Rubens, S. B. Gunnoo, V. Hessel, A. Madder, T. Noël, *Angew. Chem. Int. Ed.* **2017**, *56*, 12702-12707; n) C. Audubert, O. J. Gamboa Marin, H. Lebel, *Angew. Chem. Int. Ed.* **2017**, *56*, 6294-6297; o) N. J. Straathof, S. E. Cramer, V. Hessel, T. Noël, *Angew. Chem. Int. Ed.* **2016**, *55*, 15549-15553; p) J. W. Beatty, J. J. Douglas, R. Miller, R. C. McAtee, K. P. Cole, C. R. Stephenson, *Chem.* **2016**, *1*, 456-472.

[20] S. E. Vaillard, A. Studer, in *Encyclopedia of Radicals in Chemistry, Biology and Materials, Vol. 2,* (Eds.: C. Chatgilialoglu, A. Studer), Wiley, Chichester, **2012**, pp. 1059-1093.

[21] a) O. Reiser, *Chem.* **2016**, *1*, 344-345; b) F. R. Bou-Hamdan, P. H. Seeberger, *Chem. Sci.* **2012**, *3*, 1612-1616.

[22] T. Krause, M. Gerbershagen, M. Fiege, R. Weisshorn, F. Wappler, *Anaesthesia* **2004**, *59*, 364-373.

COMMUNICATION



*Yu-Feng Liang, Ralf Steinbock, Long Yang, and Lutz Ackermann**

Page No. – Page No.

Continuous Visible-Photo-Flow for Manganese-Catalyzed (Het)Arene C−H Arylation

Photo in Flow: Earth-abundant manganese catalysts enabled visible-light-induced C−H arylations at room temperature in a continuous photo-flow manifold.