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Excited-state palladium-catalysed reductive alkylation of imines: scope and mechanism†

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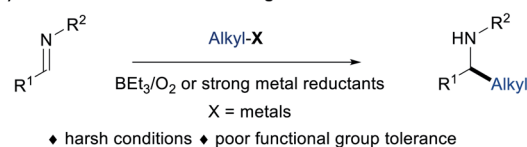
Palladium catalysis induced by visible-light irradiation is a promising tool for promoting unusual chemical transformations. We describe the development of excited-state palladium-catalyzed reductive alkylation of imines with alkyl bromides. The new methodology shows broad functional group tolerance and can additionally be applied in the direct three-component reaction of aldehydes, anilines, and alkyl bromides to give the alkyl amines under mild reaction conditions. Time-resolved photoluminescence experiments allowed the determination of the excited-state reaction kinetics and indicate that the reaction is proceeding *via* the inner-sphere electron transfer mechanism.

Introduction

Alkyl amines are important functional moieties that are presented in a wide range of drugs and natural products.¹ The development of sustainable and environmentally benign strategies for their synthesis has been an enduring area of research. Among the different synthetic approaches available for the synthesis of alkyl amines, the addition of alkyl organometallics to imines is considered one of the most straightforward techniques.^{1a,2} Due to the moisture-sensitive nature of organometallic reagents and the instability of imines, most of the alkyl addition reactions have to be carried out under anhydrous conditions, which may limit their application in organic synthesis. Recently, the visible light-mediated photoredox catalysed alkylation of imines has been realized under mild reaction conditions,³ which has been noticed to be a new and elegant complementary method to the existing classical radical-based strategies [Fig. 1a; classical methods for the alkyl radical generation use alkyl iodides along with Et₃B/O₂ or metal reductants (tin reagents or Zn)].⁴ However, these photoredox methods are mainly applicable to more reactive alkyl-substituted radical precursors such as trifluoroborates, silicates, trimethylsilyl, redox-active esters, and substituted 1,4-dihydropyridines (Fig. 1b).⁵ In addition, the direct reduction of imines with photoredox catalysis to furnish a persistent radical anion intermediate that can undergo radical–radical cross-coupling to give hydroalkylation products has also been reported. However, these systems are limited to C–H activation of substrates with heteroatoms alpha to the site of

functionalization.⁶ Moreover, these C–H activation methods do not provide a general solution for the versatile alkylation of imines. Furthermore, more expensive metal or non-metal alkyl radical precursors or selective heteroatom substituted alkyl derivatives and ruthenium or iridium polypyridyl complexes were often used, thus limiting the scope of the alkyl coupling partner to oxidizable functional groups. As a consequence, the development of new radical-mediated reductive alkylation

a) Classical radical based strategies



b) Photochemical radical based strategies



c) This work: Excited-state palladium catalysed alkylation of imines

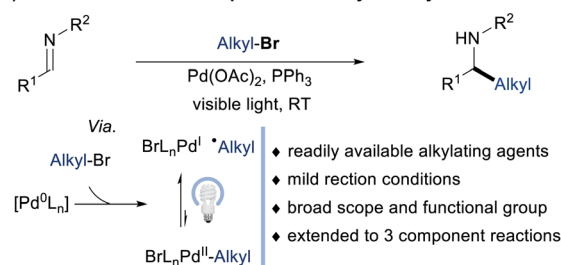


Fig. 1 Strategies for radical-mediated alkylation of imines (a) Classical approach. (b) Photochemical approach. (c) This-work: excited-state Pd-catalysed alkylation of imines.

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reactions of imines using commercially available unactivated alkyl reagents (alkyl bromides) under mild visible light irradiation conditions would be desirable as it remained unexplored.

Advances in visible light-mediated excited-state palladium catalysis have identified competent and versatile manifolds for the selective construction as well as functionalization of structurally diverse organic compounds.⁷ Particularly, the generation of Pd(I)/alkyl radical hybrid species and their reactivity in organic synthesis has been highlighted as a significant process that enables noticeable alkylations under mild reaction conditions, which are hard to realize *via* conventional thermal processes. For instance, excited-state palladium catalysed one-electron reduction of alkyl halides successfully overcomes various long-standing difficulties encountered in two-electron processes involving palladium, such as reluctant oxidative addition to tertiary alkyl halides, fast protonation of alkyl palladium intermediates and the undesired β -H elimination steps. Using this strategy, Gevorgyan,⁸ Shang and Fu,⁹ Glorius,¹⁰ Rueping,¹¹ and others¹² independently reported alkyl radical addition cross-coupling reactions, including the Mizoroki–Heck reactions, difunctionalizations, alkylations, and carbonylations. In most of the cases, a facile addition of Pd(I)/alkyl radical hybrid species to C=C bonds and its application in organic reactions were studied. However, the addition of Pd(I)/alkyl radical hybrid species to polar C=N bond for reductive alkylation of imines using alkyl halides remained elusive (Fig. 1c).¹³ In this regard Gevorgyan's group recently reported the alkyl-Heck reaction of oximes using palladium and indium in the presence of visible light^{14a} as well as a Pd-catalyzed Heck-type alkylation of ester


hydrazones.^{14b} Interestingly, the radical addition to oximes/hydrazones was followed by hydrogen atom transfer by Pd or radical recombination along with β -hydride elimination to give the unsaturated product, while reduced amine was not formed.

Results and discussions

Given the overall interest in the development of imine alkylations with readily available unreactive alkyl bromides we started to investigate the reductive alkylation reaction by reacting imine **1a** and bromocyclohexane **2f** in the presence of Pd(PPh₃)₄ (10 mol%) and Cs₂CO₃ (2 equiv.) in DMSO under irradiation with 34 W blue LEDs which resulted in the desired alkylated amine **3f** in 53% yield (Table 1, entry 1).

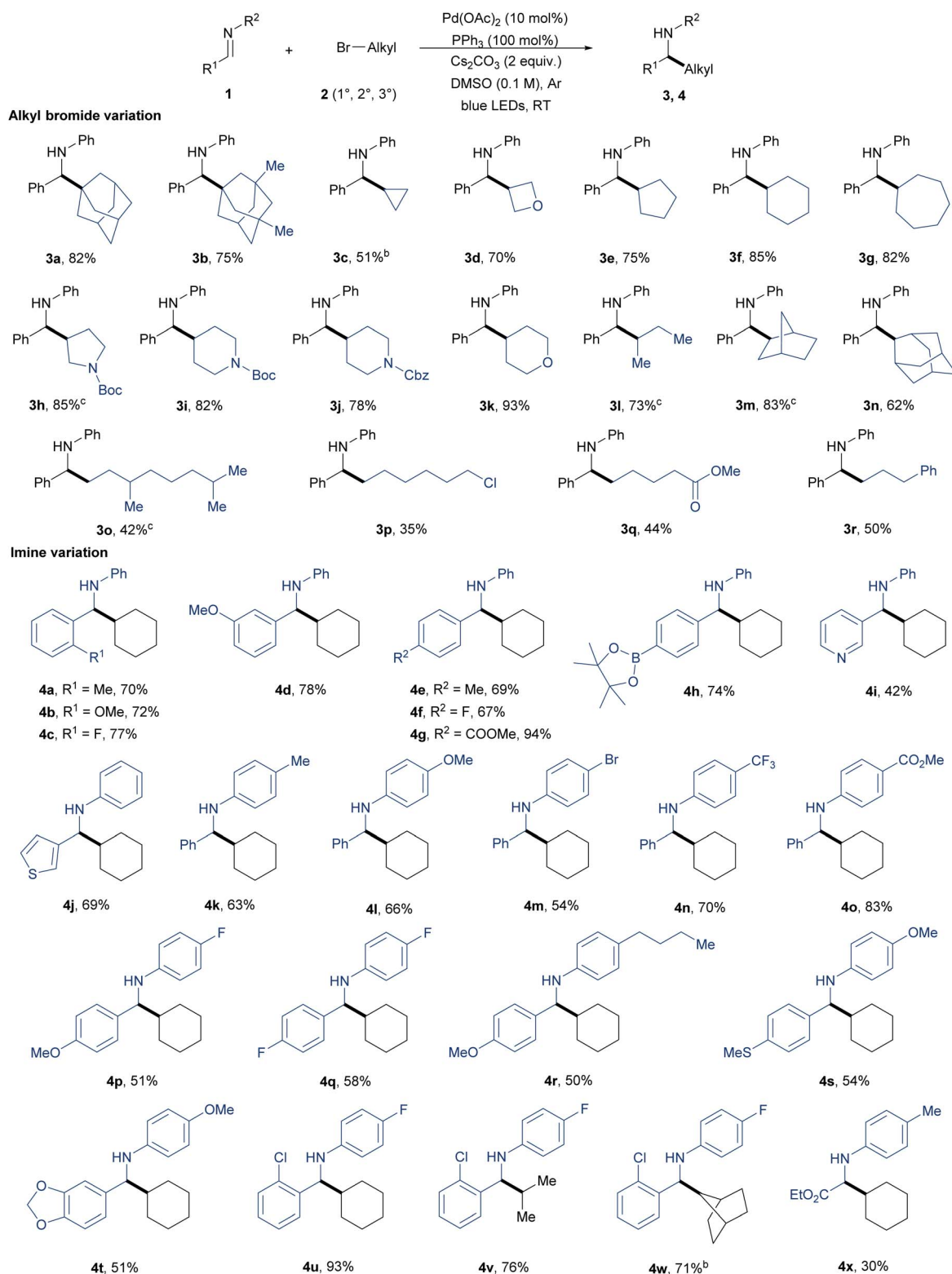
Various protic and aprotic solvents were tested which however did not result in improved yield (Table 1, entry 2, also see ESI†). The use of other acetate, phosphate, and organic bases also did not have a considerable impact on the reaction yield (Table 1, entry 3). However increasing the loading of Pd(PPh₃)₄ from 5 to 15 mol% substantially increased the yield (entry 4, 5). This result along with other control experiments revealed that PPh₃ is playing a dual role both as a ligand and as a reductant (Entry 7–9). To support this observation an extra 10–40 mol% of PPh₃ was added which increased the yield to 89% (entry 6). The use of Pd(OAc)₂ and PPh₃ instead of Pd(PPh₃)₄ is equally effective which gave the product in 85% isolated yield (entry 11). To avoid the excess PPh₃ being used, amines as reducing agents were employed in the reaction which is known

Table 1 Optimization of the reaction conditions^a

		
Entry ^a	Change in the reaction conditions	Yield ^b (%)
1	None	53
2	MeOH or 1,4-dioxane as solvent	40/28
3	CsOAc, K ₃ PO ₄ or TEA as base	43/43/26
4	5 mol% of Pd(PPh ₃) ₄	30
5	15 mol% of Pd(PPh ₃) ₄	81
6	Use of 10–40 mol% PPh ₃ as extra ligand	68–89
7	10 mol% PdCl ₂ and 40 mol% PPh ₃ as catalyst	48
8	10 mol% Pd(PPh ₃) ₂ Cl ₂ and 40 mol% PPh ₃ as catalyst	67
9	10 mol% Pd(PPh ₃) ₂ Cl ₂ and 20 mol% Xantphos as catalyst	28
10	10 mol% Pd(OAc) ₂ and 60 mol% PPh ₃ as catalyst	70
11	10 mol% Pd(OAc) ₂ and 100 mol% PPh ₃ as catalyst	93 (85)
12	5 mol% Pd(OAc) ₂ and 100 mol% PPh ₃ as catalyst	88
13	10 : 40 mol% Pd(OAc) ₂ : PPh ₃ , TEA (4 eq), Na ₂ CO ₃ (1 eq.)	46
14	10 : 40 mol% Pd(OAc) ₂ : PPh ₃ , Zn (3 eq.)	34

^a Reaction conditions: **1** (0.1 mmol), bromocyclohexane **2f** (0.2 mmol), 34 W blue LEDs, RT, Ar, 24 h. RT = 32 ± 2 °C. ^b Yield of product determined by GC-FID using trimethoxybenzene as internal standard. Yield in bracket is the isolated one.



Table 2 Scope of the reaction by varying alkyl bromides and imines^a

^a Reaction conditions: 1 (0.2 mmol), 2 (0.4 mmol), 34 W blue LEDs, Ar, 24 h; RT = 32 ± 2 °C; Yields of isolated products. ^b Reaction time 72 h. ^c d.r. between 1 : 1 to 1.2 : 1.



from nickel catalysis (entry 13).¹⁵ Furthermore, Zn-powder was also used to reduce the amount of PPh₃. However, the yield of the reductive alkylation product was not improved (entry 14,

also see ESI†). Interestingly, apart from the reductive alkylation product, we did not observe alkyl-Heck products, *i.e.* imines, in any of the reactions.¹⁴

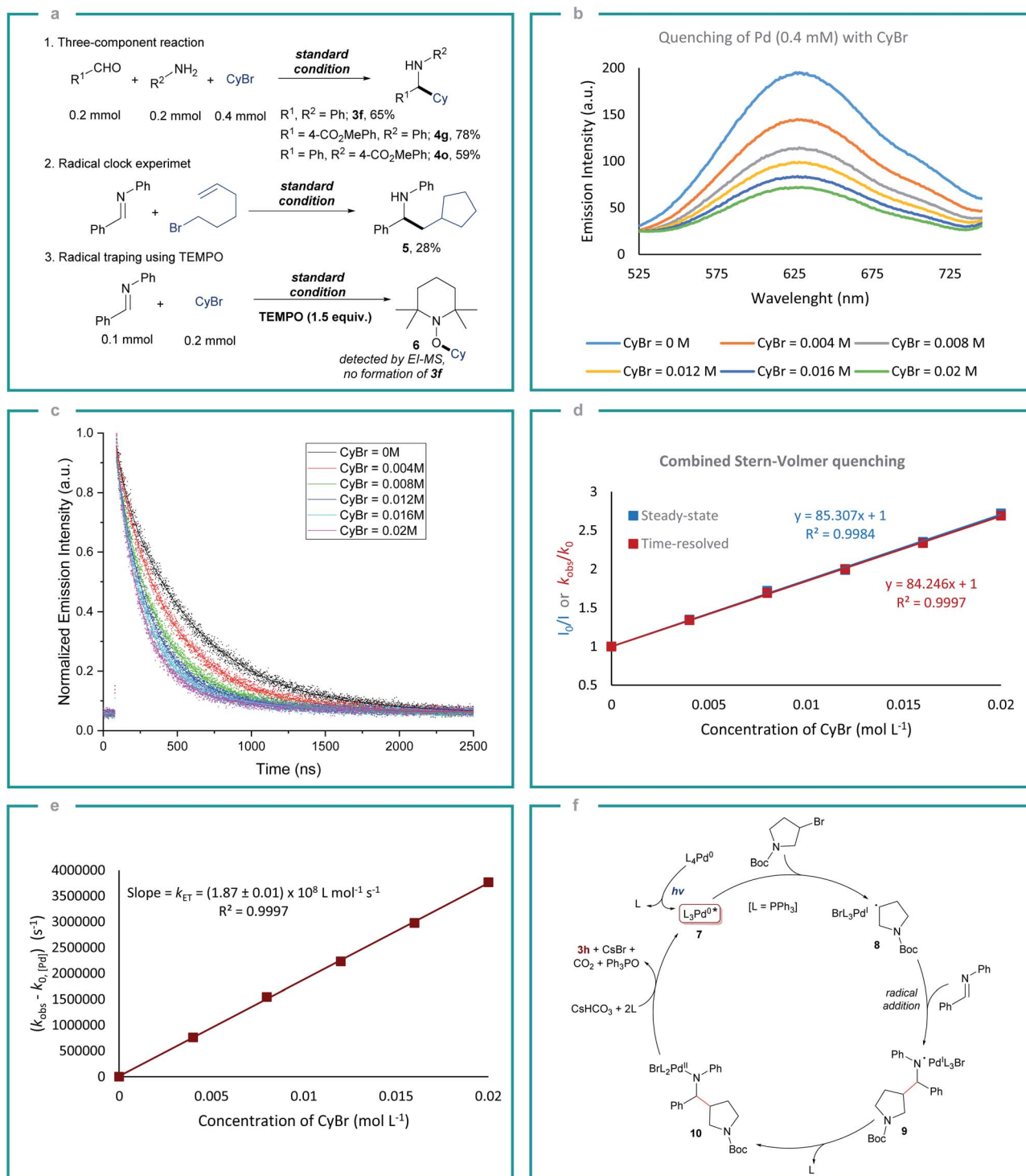


Fig. 2 (a) Mechanistic experiments and the three-component reaction; (b) steady-state quenching of Pd(PPh₃)₄ (0.4 mM) with different concentrations of quencher (bromocyclohexane); (c) decrease in phosphorescence lifetimes of excited-state Pd(PPh₃)₄ (0.4 mM) upon increasing the concentration of bromocyclohexane; (d) steady-state and time-resolved Stern–Volmer quenching of Pd(PPh₃)₄ (0.4 mM) with different concentrations of bromocyclohexane; (e) plot of the observed rate constant (k_{obs}) of *Pd(PPh₃)₄ corrected by its intrinsic ground state recovery rate (k_0) vs. different concentrations of bromocyclohexane to determine the electron transfer rate constant (k_{ET}) between Pd and bromocyclohexane; (f) proposed mechanistic pathway for reductive alkylation of imines.

With the optimized conditions the scope of the reductive alkylation reaction was first evaluated by reacting *N*-benzylideneaniline **1a** with varying alkyl bromides **2** (Table 2). A variety of primary, secondary, and tertiary alkyl bromides were found reactive under the standard reaction conditions. The reactivity of tertiary and secondary alkyl bromides (**3a–n**) was found to be superior compared to primary alkyl bromides (**3o–r**). Cyclic tertiary alkyl bromides that can undergo β -hydride elimination with Pd were also tolerated to give the alkylation product (**3a** and **3b**). However, under the standard conditions employed for the coupling of imine **1a** and *tert*-butyl bromide (non-cyclic), the reaction was not efficient (<20 yield). In this case, the β -hydride elimination seems faster if compared to the radical formation and addition to imine. The reactivity in the case of secondary alkyl bromides was found to increase with the increase in ring size **3c–g**. Heteroatom containing alkyl bromides also underwent the reaction smoothly giving the alkylation product **3d** and **3h–k** in 70–93% yield. Bicyclic and primary alkyl bromides with various functional groups including chloro, ester, and phenyl substituents also gave the alkylated product **3m–r** in good to moderate yields. The selective alkylation of the C–Br bond in the case of 1-bromo-6-chlorohexane provides an opportunity for further functionalization of the reaction product (**3p**).

Next, we started to examine the scope of the reductive alkylation protocol concerning imines under the standard reaction conditions (Table 2). In the first instance, the benzylidene component of the imine was varied which gave the expected product **4a–j** in good to moderate yields. Benzylidene moieties with electron-withdrawing groups at ortho- and para-position gave a better yield compared to electron-donating groups (**4a–c** and **4e–g**). Likewise, an electron-donating group at meta-position (**4d**) gave a better yield compared to ortho- and para-substituents. Aryl boronate which is prone to undergo Suzuki coupling under palladium-catalysed conditions was also well tolerated (**4h**).¹⁶ Heterocyclic substrates also gave the expected product however in moderate yields which are due to the poisoning of the Pd by the strongly coordinating nitrogen and sulfur heteroatoms (**4i** and **4j**).¹⁷ Next, the aniline component of the imine was varied to explore the effect of various substituents on the alkylation reaction (**4k–o**). Similarly, to the benzylidene component variation, electron-withdrawing groups at the para-position (**4m–o**) gave better yields compared to the electron-donating groups (**4k** and **4l**). Additionally, different substituents on the arene ring were tolerated (**4p–x**). Further, the direct three-component reactions of benzaldehydes, anilines, and bromocyclohexane provided the expected reductive alkylation product **3f**, **4g**, and **4o** in 59–78% yield under the standard conditions which highlights the feasibility of the protocol and avoiding the pre-synthesis step of imines (Fig. 2a).

Subsequently, radical clock experiments were performed to understand if the light-mediated single electron oxidative addition of alkyl bromide to the Pd is operative (Fig. 2a). The reaction of 6-bromohex-1-ene with *N*-benzylideneaniline gave product **5** supporting the radical mechanism (Fig. 2a). Further, a radical trapping experiment using TEMPO under standard reaction conditions completely suppressed the product formation which also supports the single electron transfer (SET)

mechanism. To gain insight into the nature of photoinduced SET between $^*\text{Pd}$ and alkyl bromide, steady-state (SSPL) and time-resolved photoluminescence (TRPL) quenching experiments were performed. The excited-state $^*\text{Pd}(\text{PPh}_3)_4$ exhibits a long-lived triplet state with a lifetime of $\tau_0 = 494.85 \pm 1.62$ ns, which may induce an inner-sphere SET with alkyl bromides. The steady-state quenching studies showed that the emission intensity of $^*\text{Pd}(\text{PPh}_3)_4$ decreases with the increase of bromocyclohexane concentration (Fig. 2b). A similar result is also observed in TRPL quenching studies where a decrease in phosphorescence lifetimes of $^*\text{Pd}(\text{PPh}_3)_4$ with increasing bromocyclohexane concentration was observed (Fig. 2c). Both the SSPL and TRPL Stern–Volmer plots displayed a perfect linear correlation which suggests that there is no static quenching between the Pd and alkyl bromide and that the quenching is dynamic (Fig. 2d). The quenching constant calculated from the Stern–Volmer slopes and the lifetime of $^*\text{Pd}$ was found to be $k_q = 1.7 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$.¹⁸ Further, to determine the electron transfer rate constant (k_{ET}), the rate constant plot was plotted by using TRPL measurements (Fig. 2e). The plot of the observed rate (k_{obs}) of $^*\text{Pd}(\text{PPh}_3)_4$ corrected by its intrinsic ground state recovery rate without quencher (k_0) versus different concentrations of bromocyclohexane gave a slope of $(1.87 \pm 0.01) \times 10^8 \text{ L mol}^{-1} \text{ s}^{-1}$ which correlates with the electron transfer rate constant (k_{ET}) (Fig. 2e).^{6c,18}

Based on these observations, a plausible reaction mechanism proceeding *via* an inner-sphere ET pathway is proposed (Fig. 2f). The *in situ* generated $\text{Pd}(\text{PPh}_3)_4$ complex undergoes excitation in the presence of visible light resulting in the triplet state $^*\text{Pd}^0\text{L}_3$ (**7**) that provides an open coordination site for the alkyl bromide association. This results in the inner sphere electron transfer furnishing a hybrid alkyl radical Pd^{I} intermediate.^{11a} The alkyl radical then adds to the imine resulting in an *N*-centered radical intermediate **9** which undergoes radical recombination with Pd^{I} to form a Pd^{II} intermediate **10** with the release of PPh_3 . To realize the product formation and the regeneration of Pd^0 from intermediate **10**, hydrogen and oxygen are required. Therefore, we initially tested the reaction using DMSO- d_6 as a solvent which did not result in any deuterium incorporated alkylation product **3f** which confirmed that the DMSO is not acting as a source of hydrogen. Besides, the formation of triphenylphosphine oxide is observed even in solvents without oxygen (CH_3CN , toluene), leading to the conclusion that DMSO is neither hydrogen nor oxygen source. Thus, $\text{C}_6\text{H}_5\text{CO}_3$ generated in the reaction can be the source of hydrogen and oxygen, which facilitates the release of the hydroalkylation product **3** and Pd^0 from intermediate **10** along with the generation of triphenylphosphine oxide which is observed in comparable yields to the amine **3** formed (Fig. 2f, also see ESI Fig. S8 and S9†). Other plausible pathways for Pd^{II} reduction are also discussed in the ESI (Fig. S8)†.

Conclusions

In summary, we developed a new method for the reductive alkylation of imines with readily available bromoalkanes by the photoexcitation of Pd in the presence of visible light. Imines



with a wide range of functional groups are tolerated in this mild process. The reactivity and utility of this protocol are also demonstrated by the direct three-component reaction of aldehyde, amine, and alkyl bromide. Time-resolved photoluminescence experiments were performed for the first time to determine the excited-state kinetics and to support the formation of the reactive intermediates in photoexcited state Pd catalysis.

Data availability

The data for this work, including optimization tables, experimental procedures, and characterization data for all compounds are provided in the ESI.†

Author contributions

M. R., R. K., and K. M. conceived and designed the project. R. K., and K. M. performed and analysed the experiments. R. K., and K. M. contributed equally to this work. M. R., R. K., and K. M. wrote the manuscript. M. R. directed the whole research.

Conflicts of interest

There are no conflicts to declare.

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References

- (a) D. Ferraris, *Tetrahedron*, 2007, **39**, 9581–9597; (b) J. R. Liddell, *Nat. Prod. Rep.*, 2002, **19**, 773–781; (c) T. C. Nugent and M. El-Shazly, *Adv. Synth. Catal.*, 2010, **352**, 753–819; (d) A. P. Taylor, R. P. Robinson, Y. M. Fobian, D. C. Blakemore, L. H. Jones and O. Fadeyi, *Org. Biomol. Chem.*, 2016, **14**, 6611–6637.
- (a) S. Kobayashi and H. Ishitani, *Chem. Rev.*, 1999, **99**, 1069–1094; (b) M. Hatano, S. Suzuki and K. Ishihara, *J. Am. Chem. Soc.*, 2006, **128**, 9998–9999; (c) K.-i. Yamada and K. Tomioka, *Chem. Rev.*, 2008, **108**, 2874–2886; (d) M. Yus, J. C. Gonzalez-Gomez and F. Foubelo, *Chem. Rev.*, 2011, **111**, 7774–7854; (e) M. Hatano, K. Yamashita, M. Mizuno, O. Ito and K. Ishihara, *Angew. Chem., Int. Ed.*, 2015, **54**, 2707–2711.
- (a) A. Shatskiy, A. Axelsson, E. V. Stepanova, J.-Q. Liu, A. Z. Temerdashev, B. P. Kore, B. Blomkvist, J. M. Gardner, P. Dinér and M. D. Kärkäs, *Chem. Sci.*, 2021, **12**, 5430–5437; (b) J. Wang, Z. Shao, K. Tan, R. Tang, Q. Zhou, M. Xu, Y.-M. Li and Y. Shen, *J. Org. Chem.*, 2020, **85**, 9944–9954; (c) D. P. Plasko, C. J. Jordan, B. E. Ciesa, M. A. Merrill and J. M. Hanna, *Photochem. Photobiol. Sci.*, 2018, **17**, 534–538; (d) H.-H. Zhang and S. Yu, *J. Org. Chem.*, 2017, **82**, 9995–10006; (e) S.-Y. Hsieh and J. W. Bode, *Org. Lett.*, 2016, **18**, 2098–2101; (f) N. R. Patel, C. B. Kelly, A. P. Siegenfeld and G. A. Molander, *ACS Catal.*, 2017, **7**, 1766–1770; (g) J. Jia, Q. Lefebvre and M. Rueping, *Org. Chem. Front.*, 2020, **7**, 602–608; (h) S. T. Cullen and G. K. Friestad, *Org. Lett.*, 2019, **21**, 8290–8294; (i) A. F. Garrido-Castro, H. Choubane, M. Daaou, M. C. Maestro and J. Alemán, *Chem. Commun.*, 2017, **53**, 7764–7767; (j) L. R. Pantaine, J. A. Milligan, J. K. Matsui, C. B. Kelly and G. A. Molander, *Org. Lett.*, 2019, **21**, 2317–2321; (k) J. Yi, S. O. Badir, R. Alam and G. A. Molander, *Org. Lett.*, 2019, **21**, 4853–4858; (l) J. Guo, Q.-L. Wu, Y. Xie, J. Weng and G. Lu, *J. Org. Chem.*, 2018, **83**, 12559–12567; (m) P. Ji, Y. Zhang, Y. Wei, H. Huang, W. Hu, P. A. Mariano and W. Wang, *Org. Lett.*, 2019, **21**, 3086–3092.
- (a) G. K. Friestad, *Tetrahedron*, 2001, **57**, 5461–5496; (b) J. A. Fernandez-Salas, M. C. Maestro, M. M. Rodríguez-Fernández, J. L. García-Ruano and I. Alonso, *Org. Lett.*, 2013, **15**, 1658–1661; (c) J. A. Fernández-Salas, M. M. Rodríguez-Fernández, M. C. Maestro and J. L. García-Ruano, *Eur. J. Org. Chem.*, 2014, **2014**, 5265–5272; (d) S. Fujii, T. Konishi, Y. Matsumoto, Y. Yamaoka, K. Takasu and K.-I. Yamada, *J. Org. Chem.*, 2014, **79**, 8128–8133; (e) K.-I. Yamada, T. Konishi, M. Nakano, S. Fujii, R. Cadou, Y. Yamamoto and K. Tomioka, *J. Org. Chem.*, 2012, **77**, 1547–1553; (f) S. Ni, A. F. Garrido-Castro, R. R. Merchant, J. N. de Gruyter, D. C. Schmitt, J. J. Mousseau, G. M. Gallego, S. Yang, M. R. Collins and J. X. Qiao, *Angew. Chem., Int. Ed.*, 2018, **57**, 14560–14565; (g) M. Ueda, H. Miyabe, O. Miyata and T. Naito, *Tetrahedron*, 2009, **65**, 1321–1326; (h) H. Miyabe, M. Ueda and T. Naito, *Chem. Commun.*, 2000, 2059–2060; (i) H. Miyabe, M. Ueda and T. Naito, *Synlett*, 2004, **2004**, 1140–1157.
- J. A. Leitch, T. Rossolini, T. Rogova, J. A. P. Maitland and D. J. Dixon, *ACS Catal.*, 2020, **10**, 2009–2025.
- (a) D. Hager and D. W. MacMillan, *J. Am. Chem. Soc.*, 2014, **136**, 16986–16989; (b) E. Fava, A. Millet, M. Nakajima, S. Loescher and M. Rueping, *Angew. Chem., Int. Ed.*, 2016, **55**, 6776–6779; (c) J. Jia, R. Kancherla, M. Rueping and L. Huang, *Chem. Sci.*, 2020, **11**, 4954–4959; (d) D. Uraguchi, N. Kinoshita, T. Kizu and T. Ooi, *J. Am. Chem. Soc.*, 2015, **137**, 13768–13771; (e) M. Fernández and R. Alonso, *Org. Lett.*, 2003, **5**, 2461–2464; (f) S. Yang, S. Zhu, D. Lu and Y. Gong, *Org. Lett.*, 2019, **21**, 2019–2024; (g) G. Deng and C.-J. Li, *Tetrahedron Lett.*, 2008, **49**, 5601–5604; (h) B. T. Matsuo, J. T. M. Correia and M. W. Paixao, *Org. Lett.*, 2020, **22**, 7891–7896.
- (a) P. Chuentragool, D. Kurandina and V. Gevorgyan, *Angew. Chem., Int. Ed.*, 2019, **58**, 11586–11598; (b) R. Kancherla, K. Muralirajan, A. Sagadevan and M. Rueping, *Trends Chem.*, 2019, **1**, 510–523; (c) W.-J. Zhou, G.-M. Cao, Z.-P. Zhang and D.-G. Yu, *Chem. Lett.*, 2019, **48**, 181–191; (d) W.-M. Cheng and R. Shang, *ACS Catal.*, 2020, **10**, 9170–9196; (e) K. P. S. Cheung, S. Sarkar and V. Gevorgyan, *Chem. Rev.*, 2022, **122**, 1543–1625; (f) V. M. Chernyshev and V. P. Ananikov, *ACS Catal.*, 2022, **12**, 1180–1200.
- (a) D. Kurandina, M. Parasram and V. Gevorgyan, *Angew. Chem., Int. Ed.*, 2017, **56**, 14212–14216; (b) D. Kurandina,



- M. Rivas, M. Radzhabov and V. Gevorgyan, *Org. Lett.*, 2018, **20**, 357–360; (c) K. P. S. Cheung, D. Kurandina, T. Yata and V. Gevorgyan, *J. Am. Chem. Soc.*, 2020, **142**, 9932–9937; (d) X. Jia, Z. Zhang and V. Gevorgyan, *ACS Catal.*, 2021, **11**, 13217–13222.
- 9 (a) G.-Z. Wang, R. Shang, W.-M. Cheng and Y. Fu, *J. Am. Chem. Soc.*, 2017, **139**, 18307–18312; (b) G.-Z. Wang, R. Shang and Y. Fu, *Org. Lett.*, 2018, **20**, 888–891; (c) B. Zhao, R. Shang, G.-Z. Wang, S. Wang, H. Chen and Y. Fu, *ACS Catal.*, 2019, **10**, 1334–1343; (d) G.-Z. Wang, R. Shang and Y. Fu, *Synthesis*, 2018, **50**, 2908–2914; (e) W.-L. Xing, R. Shang, G.-Z. Wang and Y. Fu, *Chem. Commun.*, 2019, **55**, 14291–14294; (f) W.-M. Cheng, R. Shang and Y. Fu, *Nat. Commun.*, 2018, **9**, 5215.
- 10 (a) M. Koy, F. Sandfort, A. Tlahuext-Aca, L. Quach, C. G. Daniliuc and F. Glorius, *Chem.–Eur. J.*, 2018, **24**, 4552–4555; (b) M. Koy, P. Bellotti, F. Katzenburg, C. G. Daniliuc and F. Glorius, *Angew. Chem., Int. Ed.*, 2020, **59**, 2375–2379; (c) H.-M. Huang, M. Koy, E. Serrano, P. M. Pflüger, J. L. Schwarz and F. Glorius, *Nat. Catal.*, 2020, **3**, 393–400; (d) H.-M. Huang, P. Bellotti, P. M. Pflüger, J. L. Schwarz, B. Heidrich and F. Glorius, *J. Am. Chem. Soc.*, 2020, **142**, 10173–10183.
- 11 (a) R. Kancherla, K. Muralirajan, B. Maity, C. Zhu, P. Krach, L. Cavallo and M. Rueping, *Angew. Chem., Int. Ed.*, 2019, **58**, 3412–3416; (b) K. Muralirajan, R. Kancherla, A. Gimnkhan and M. Rueping, *Org. Lett.*, 2021, **23**, 6905–6910.
- 12 (a) W. J. Zhou, G. M. Cao, G. Shen, X. Y. Zhu, Y. Y. Gui, J. H. Ye, L. Sun, L. L. Liao, J. Li and D. G. Yu, *Angew. Chem., Int. Ed.*, 2017, **56**, 15683–15687; (b) S. Sun, C. Zhou, J.-T. Yu and J. Cheng, *Org. Lett.*, 2019, **21**, 6579–6583; (c) Z. Jiao, L. H. Lim, H. Hirao and J. S. Zhou, *Angew. Chem., Int. Ed.*, 2018, **57**, 6294–6298; (d) G. M. Torres, Y. Liu and B. A. Arndtsen, *Science*, 2020, **368**, 318–323; (e) J.-W. Ma, X. Chen, Z.-Z. Zhou and Y.-M. Liang, *J. Org. Chem.*, 2020, **85**, 9301–9312; (f) D. Kim, G. S. Lee, D. Kim and S. H. Hong, *Nat. Commun.*, 2020, **11**, 5266; (g) Z. Yang and R. M. Koenigs, *Chem.–Eur. J.*, 2021, **27**, 3694–3699; (h) L. Sun, J.-H. Ye, W.-J. Zhou, X. Zeng and D.-G. Yu, *Org. Lett.*, 2018, **20**, 3049–3052; (i) G. S. Lee, D. Kim and S. H. Hong, *Nat. Commun.*, 2021, **12**, 991; (j) W. Yao, G. Zhao, Y. Wu, L. Zhou, U. Mukherjee, P. Liu and M.-Y. Ngai, *J. Am. Chem. Soc.*, 2022, **144**, 3353–3359.
- 13 G. K. Friestad and A. K. Mathies, *Tetrahedron*, 2007, **63**, 2541–2569.
- 14 (a) N. Kvasovs, V. Iziumchenko, V. Palchykov and V. Gevorgyan, *ACS Catal.*, 2021, **11**, 3749–3754; (b) N. Kvasovs and V. Gevorgyan, *Org. Lett.*, 2022, **24**, 4176–4181.
- 15 A. Garcia-Dominguez, Z. Li and C. Nevado, *J. Am. Chem. Soc.*, 2017, **139**, 6835–6838.
- 16 M. R. Netherton, C. Dai, K. Neuschütz and G. C. Fu, *J. Am. Chem. Soc.*, 2001, **123**, 10099–10100.
- 17 Y.-J. Liu, H. Xu, W.-J. Kong, M. Shang, H.-X. Dai and J.-Q. Yu, *Nature*, 2014, **515**, 389–393.
- 18 (a) R. Kancherla, K. Muralirajan, B. Maity, S. Karuthedath, G. S. Kumar, F. Laquai, L. Cavallo and M. Rueping, *Nat. Commun.*, 2022, **13**, 2737; (b) S. Mukherjee, T. Patra and F. Glorius, *ACS Catal.*, 2018, **8**, 5842–5846; (c) M. Teders, C. Henkel, L. Anhäuser, F. Strieth-Kalthoff, A. Gómez-Suárez, R. Kleinmans, A. Kahnt, A. Rentmeister, D. Guldi and F. Glorius, *Nat. Chem.*, 2018, **10**, 981–988; (d) H. Yue, C. Zhu, R. Kancherla, F. Liu and M. Rueping, *Angew. Chem., Int. Ed.*, 2020, **59**, 5738–5746; (e) L. Huang, C. Zhu, L. Yi, H. Yue, R. Kancherla and M. Rueping, *Angew. Chem., Int. Ed.*, 2020, **59**, 457–464.

