

Cite this: *Chem. Sci.*, 2019, 10, 7426

All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 13th April 2019
Accepted 15th June 2019

DOI: 10.1039/c9sc01824g

rsc.li/chemical-science

Rhodium catalyzed template-assisted distal *para*-C–H olefination†Uttam Dutta,^{abc} Sudip Maiti,^a Sandeep Pimparkar,^{abc} Siddhartha Maiti,^a Lawrence R. Gahan,^d Elizabeth H. Krenske,^{id}*^d David W. Lupton^{id}*^{bc} and Debabrata Maiti^{id}*^{ab}

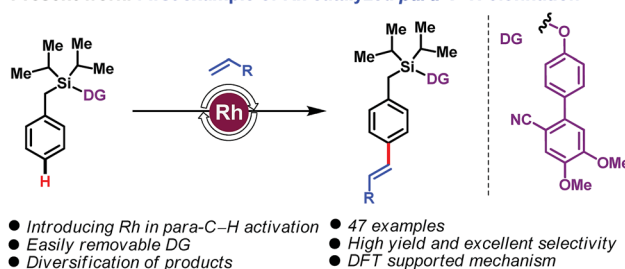
Rhodium catalysis has been extensively used for *ortho*-C–H functionalization reactions, and successfully extended to *meta*-C–H functionalization. Its application to *para*-C–H activation remains an unmet challenge. Herein we disclose the first example of such a reaction, with the Rh-catalyzed *para*-C–H olefination of arenes. The use of a Si-linked cyanobiphenyl unit as a traceless directing group leads to highly *para*-selective arene–olefin couplings.

The transformation of carbon–hydrogen (C–H) bonds into diverse classes of carbon–carbon (C–C) and carbon–heteroatom (C–X) bonds is a cornerstone of organic synthesis. There is intense interest in the discovery of new strategies for regioselective C–H functionalization.¹ A daunting challenge is imposed by the innate inertness of C–H bonds combined with the subtle reactivity differences among the C–H bonds of a given substrate. Directing group (DG)-assisted transition metal-catalyzed C–H activation has proven a successful strategy for regioselective C–H functionalizations in a general and predictable manner.² Most commonly coordination of a directing group to a transition metal to form a kinetically and thermodynamically stable 5- or 6-membered metallacycle is used to achieve *ortho*-C–H functionalization. In sharp contrast, distal C–H activation of *meta*³ and *para*⁴ sites is more challenging. In particular, *para*-C–H activation, which entails the formation of large macrocyclophane type metallacyclic intermediates, has remained elusive.⁵ In a recent breakthrough, palladium-catalyzed systems employing a carefully designed ‘D-shaped’ directing group/linker template, based on a cyanobiphenyl motif, led to the first examples of distal *para*-C–H olefinations and acetoxylations.^{5,6} Subsequent modifications of the 1st generation DGs through steric and electronic tuning led to 2nd generation DGs capable of effecting *para*-selective silylations⁷ and acylations.⁸

To the best of our knowledge, for template assisted *para*-selective functionalization palladium catalysis has been

employed so far; albeit, other transition metals are also known to deliver *para*-selective functionalization relying on steric and electronic governance.^{5–9} As part of our ongoing interest in C–H functionalization, we have now translated this reaction into the realm of rhodium catalysis and we report here the first example of a Rh-catalyzed *para*-C–H olefination. Existing Rh-catalyzed approaches to C–H activation,¹⁰ using Rh(I)/Rh(III) redox cycles, are complementary to the Pd(0)/Pd(II) or Pd(II)/Pd(IV) cycles prevalent in palladium catalysis. The use of Rh offers benefits over Pd: (a) in contrast to Pd catalysis, which usually requires superstoichiometric quantities of silver salts, Rh catalysis can be performed with alternative, often cheaper, oxidants; (b) compared with Pd catalysis, which employ monoprotected amino acids (MPAA) as ligands, the different coordination environment of Rh is expected to provide advantageous opportunities for stereoselective synthesis; and (c) importantly, Rh-catalysis does not require use of hexafluoroisopropanol (HFIP), often unavoidable in Pd-catalysed distal C–H activation. With these thoughts in mind, we set about examining a Rh-catalyzed, DG-assisted distal *para*-C–H olefination, as shown in Scheme 1.

We commenced with the olefination of toluene scaffold DG₁ by ethyl acrylate (Scheme 2). Our first attempt, using

Present work: First example of Rh catalyzed *para*-C–H olefinationScheme 1 Rh-catalyzed *para*-C–H olefination.

^aDepartment of Chemistry, IIT Bombay, Powai, Mumbai 400076, India. E-mail: dmaiti@chem.iitb.ac.in

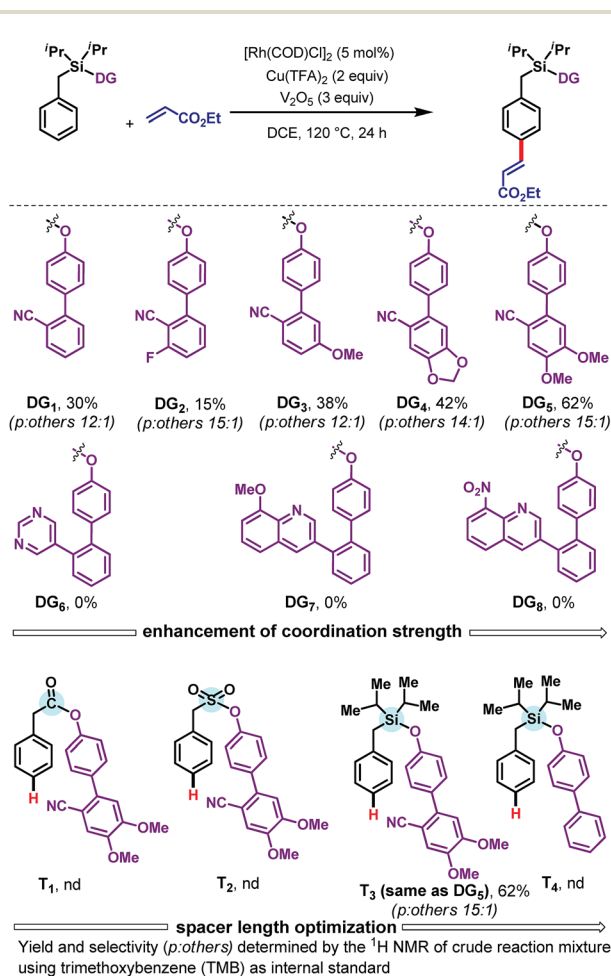
^bIITB-Monash Research Academy, IIT Bombay, Powai, Mumbai 400 076, India

^cSchool of Chemistry, Monash University, Clayton, Victoria 3800, Australia. E-mail: david.lupton@monash.edu

^dSchool of Chemistry and Molecular Biosciences, University of Queensland, Brisbane, Queensland 4072, Australia. E-mail: e.krenske@uq.edu.au

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c9sc01824g

[Rh(COD)Cl]₂ (5 mol%) as catalyst, *N*-Ac-Gly-OH (10 mol%) as ligand, and AgOAc (3 equiv.) as oxidant, was unsuccessful. However, use of copper trifluoroacetate [Cu(TFA)₂] as oxidant with V₂O₅ as a co-oxidant provided the desired *para*-olefinated product in 30% yield. Encouraged by this initial result, we examined how the outcome could be improved by modifying the DG (Scheme 2). Analysis of cyano-based DGs (**DG**₁–**DG**₅) showed that the presence of an electron-withdrawing fluorine substituent (**DG**₂) diminished the yield to 15% whereas an electron donating methoxy group (**DG**₃) elevated the yield to 38%. By further enhancing the electron richness of the DG, the piperonal derivative **DG**₄ afforded a 42% yield of the olefinated product. The dimethoxy-substituted **DG**₅ gave a further improvement in yield, to 62%, with 15 : 1 *para* selectivity. The strong σ -donating DGs **DG**₆–**DG**₈ failed to provide any of the desired olefinated products. A range of different tethers, containing carbonyl (**T**₁), sulfonyl (**T**₂), and silyl (**T**₃) linkers, were tested, as was a nitrile-free biphenyl template (**T**₄); only the silyl based template **T**₃ successfully delivered the desired olefinated product under the Rh-catalyzed conditions. These results indicate that the combination of sterically bulky silyl linker, nitrile group, and alkoxy groups present in **DG**₅ is crucial for obtaining good yields of the *para*-olefinated product.

Scheme 2 Evaluation of directing groups.¹¹

Using best-performing directing group **DG**₅, we optimized the reaction with respect to oxidants. A wide variety of silver and copper salts were tested.¹¹ In contrast to Pd-catalyzed olefinations, silver salts were found to be ineffectual in these Rh-catalyzed reactions, delivering the olefinated products in only trace amounts. Use of Cu(TFA)₂ as the oxidant in conjunction with V₂O₅ as a co-oxidant gave a 62% yield of olefinated product with excellent (15 : 1) *para* selectivity. Use of CuCl₂ provided a lower (30%) yield of product, but a combination of CuCl₂, V₂O₅ and trifluoroacetic acid (TFA) furnished the olefinated product in excellent (85%) yield, with 15 : 1 *para* selectivity.¹¹ Interestingly, in the absence of either V₂O₅ or TFA, the yield was significantly lower (40% and 30%, respectively). Other acidic additives such as acetic acid (AcOH), triflic acid (CF₃SO₃H) and pivalic acid (Piv-OH) failed to yield the *para*-olefinated product.¹¹

With optimized conditions in hand, we explored the scope of the reaction with respect to olefin (Table 1), arene (Tables 2 and 3), and benzylic substituents (Table 4). With respect to the olefin coupling partner (Table 1), a range of acrylates reacted efficiently, including alkyl acrylates **2a**–**2d**, cyclohexyl acrylate **2e**, and trifluoroethyl acrylate **2f**. The olefinated products were obtained in excellent yields with synthetically useful *para*-selectivities ranging from 7 : 1 to 15 : 1. Apart from acrylates, vinyl sulfones including methyl vinyl sulfone (**2g**) and phenyl vinyl sulfone (**2h**) also gave the olefinated products, in 48% and 62% yields, respectively.

Next an array of substituted arenes was examined (Tables 2 and 3). For monosubstituted arenes, excellent yields and selectivities were obtained irrespective of the electronic nature of the substituent (Table 2). Both electron-rich and electron-deficient arenes were well tolerated, providing yields of up to 75% with upto 17 : 1 *para* selectivity.

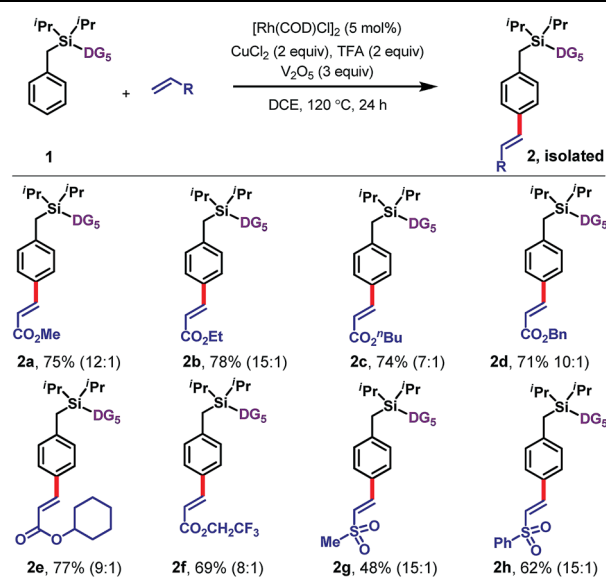
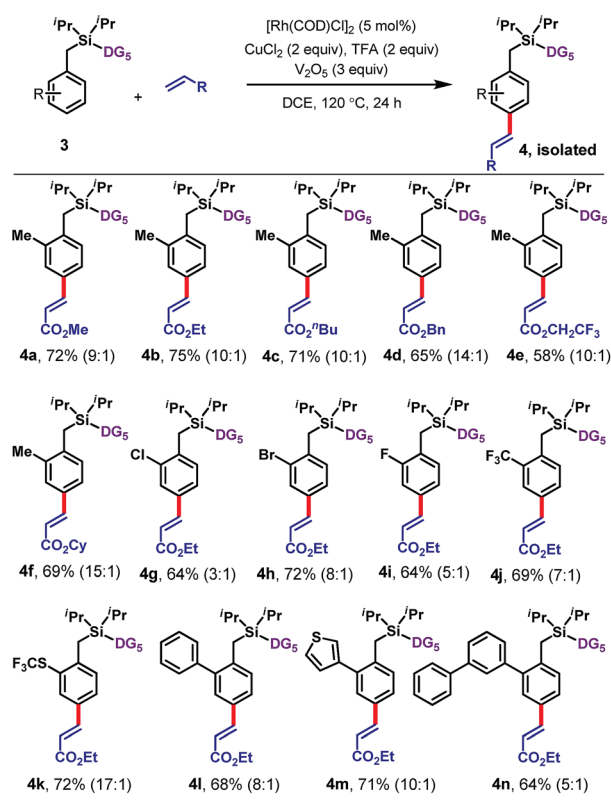
Table 1 Scope of olefin coupling partners^{a11}^a Ratio of *para*: others determined by the ¹H NMR of crude reaction mixture.

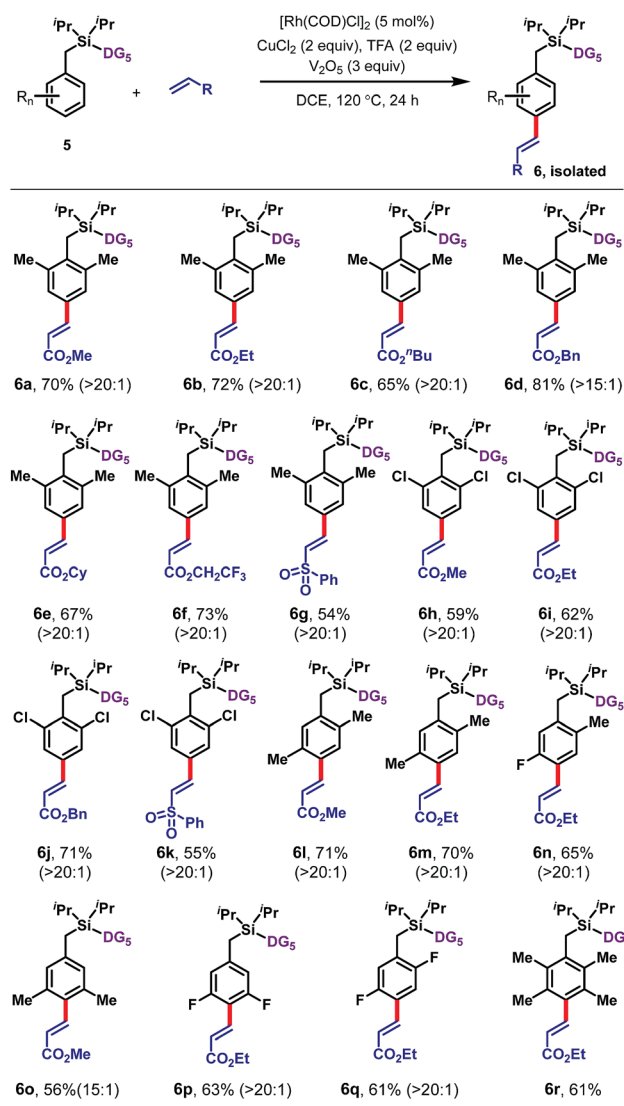
Table 2 Scope of monosubstituted toluene derivatives^{a11}

^a Ratio of *para*: others determined by the ¹H NMR of crude reaction mixture.

Disubstituted arenes were also extremely well tolerated (Table 3). The reaction was successfully applied to a range of 2,2, 2,5, 3,5 and 2,6-disubstituted toluenes containing methyl, fluoro, and/or chloro substituents (6a–6q). The selectivities of these reactions were generally higher than those observed for monosubstituted arenes, with all $\geq 15:1$ *para* selective. Even a tetramethyl-substituted arene was tolerated, reacting with ethyl acrylate to give **6r** in 61% yield.

The protocol is also applicable to α -substituted toluene derivatives (Table 4). Substrates bearing methyl, phenyl, or substituted phenyl substituents at the benzylic position reacted with methyl or ethyl acrylate to afford *para*-olefinated products **8a–8d**. The reaction also worked well with a more complex olefin coupling partner, namely, the acrylate derived from cholesterol, which furnished **8e–8g** in 59–68% yield.

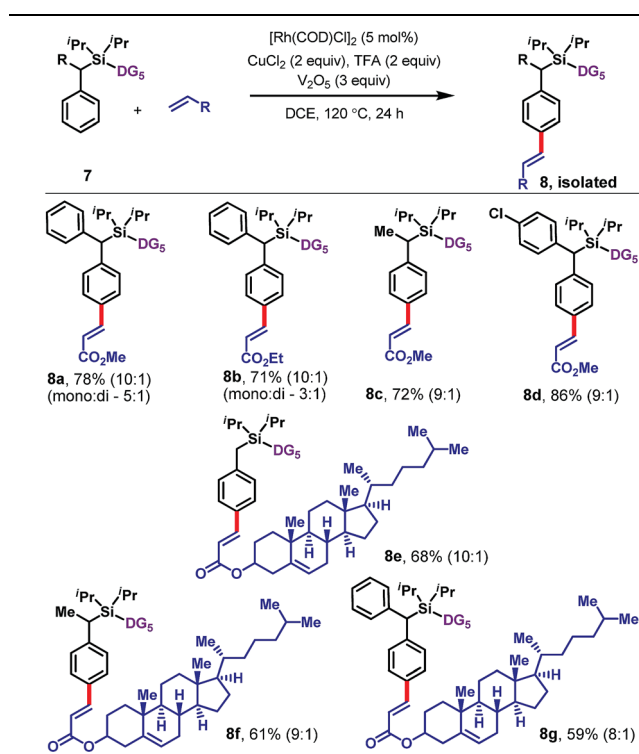
The DG₅ directing group can be readily removed from the olefinated product in several ways (Scheme 3). Treatment of **2b** with TBAF furnished the desilylated product **9** in 92% yield and allowed the DG₅ alcohol **10** to be recovered in 88% yield for reutilization. Alternatively, treatment of **2b** with *p*-TSA generated the corresponding silanol derivative **11** in 82% yield along with an 85% recovery of the DG₅ alcohol. In principle, silanol **11** could be further used as a directing group for *ortho* functionalization. Therefore, the silyl-linked DG₅ represents

Table 3 Scope of disubstituted toluene derivatives in Rh-catalyzed *para*-C–H olefination^{a11}

^a Ratio of *para*: others determined by the ¹H NMR of crude reaction mixture.

a traceless directing group enabling access to multi-functionalized arenes. While the *para*-olefinated product **6g** has been treated with KF, KHCO₃ and H₂O₂, it produced the corresponding silanol (**12**). The silanol derivative was then employed under modified Tamao's oxidation condition to produce corresponding benzyl alcohol (**13**). Another derivative **2c** was treated under similar condition to provide the benzyl alcohol which subsequently oxidized to the corresponding benzaldehyde derivative (**14**) in 76% yield. The silyl based template can act as a nucleophile in presence of TBAF. To demonstrate that, 4-nitrobenzaldehyde (**15**) and 2-naphthaldehyde (**17**) was treated with *para*-olefinated product **2e** and **6c**, respectively to produce corresponding benzyl alcohols (**16** and **18** in 83% and 72%, respectively).



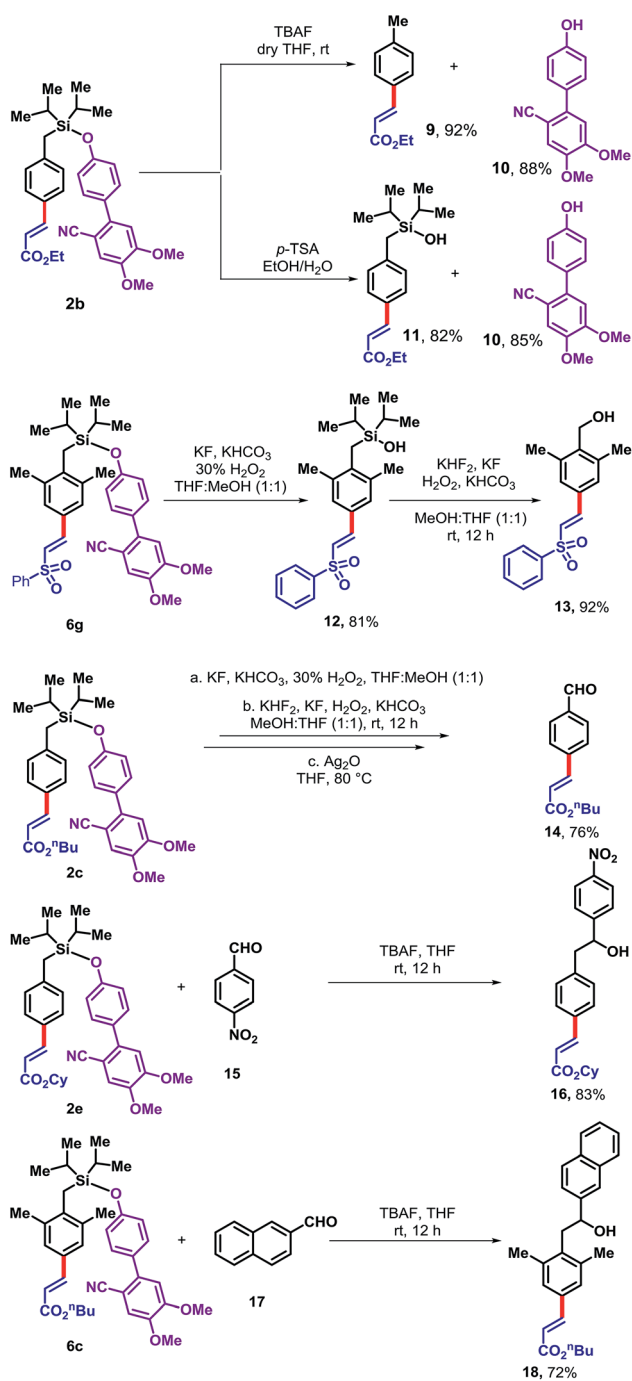
Table 4 Scope of α -substituted toluene derivatives and more complex olefin coupling partners^{a11}

^a Ratio of *para*: others determined by the ^1H NMR of crude reaction mixture.

Isotope labeling experiments were conducted involving an intermolecular competition using substrate **1a** and its deuterated analogue **D₇-1a** and a $P_{\text{H}}/P_{\text{D}}$ value of 2.9 and $k_{\text{H}}/k_{\text{D}}$ value of 2.6 were obtained (Scheme 4).¹¹ Furthermore, a detailed kinetic study indicated that the reaction was first order with respect to the substrate and zero order with respect to the olefin.¹¹ Together, these results suggest that the C–H bond activation is likely to be the rate-determining step of the catalytic cycle. A plausible catalytic cycle for the *para*-olefination is shown in Scheme 5. In this mechanism, the Rh(I) catalyst precursor is first oxidized to Rh(III). The main steps in the cycle consist of C–H activation, migratory insertion, β -hydride elimination, and reductive elimination.¹¹

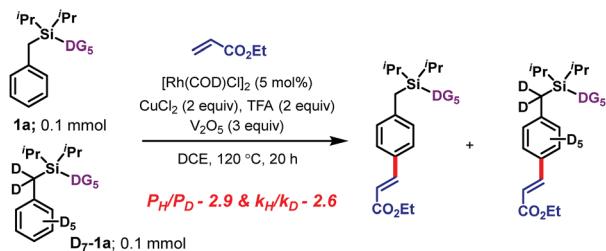
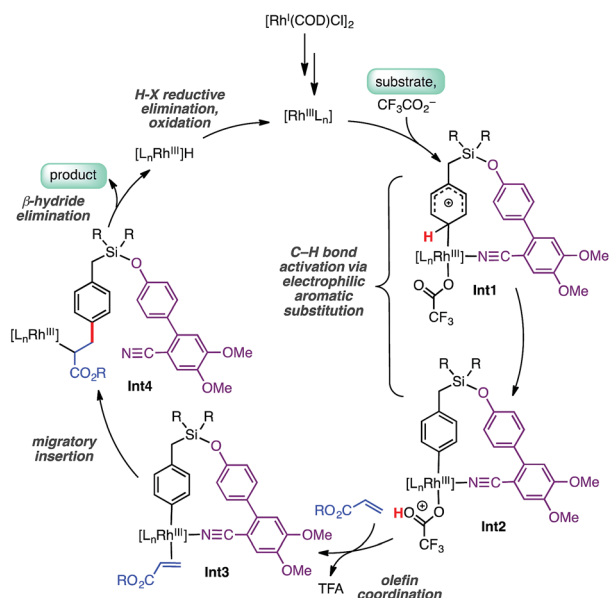
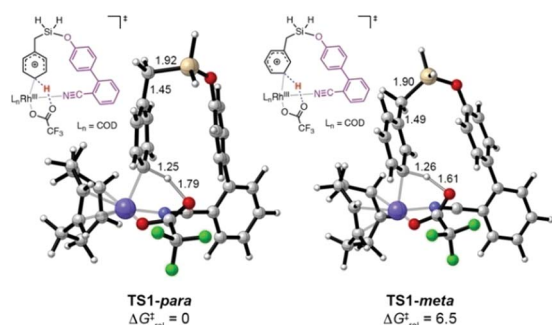
We explored the C–H activation process using density functional theory (DFT) (Fig. 1). Computations with the M06 functional using a model of **DG₁** with trifluoroacetate anion as the base predicted that the C–H bond activation follows an electrophilic aromatic substitution pathway, with a distinct intermediate **Int1**, rather than a concerted metalation–deprotonation pathway.^{10p,12} Transition structures for C–H bond breaking at the *para* and *meta* positions are shown in Fig. 1.

The *para* transition state, **TS1-*para***, is 6.5 kcal mol^{−1} lower in energy than the *meta* transition state **TS1-*meta***. A fragment-based analysis of the TSs¹² reveals that the preference for *para*-C–H activation is due to a β -silicon effect. The interaction of the arene with Rh(III) endows it with arenium cation character, and this interaction is strengthened in **TS1-*para*** because

**Scheme 3** Removal of the directing group and diversification of the *para*-olefinated products.¹¹

the C–Si bond (which lies perpendicular to the ring) stabilizes the positive charge through hyperconjugation. Computations also revealed the roles of the DG methoxy and nitrile substituents.¹² Incorporation of two methoxy groups on the DG activates the substrate toward C–H bond breaking, lowering the barrier by 1.6 kcal mol^{−1} relative to **TS1-*para***. A TS in which the nitrile is not bound to Rh was computed to be 23 kcal mol^{−1} higher in energy than **TS1-*para***, indicating that the coordination of the nitrile to Rh strongly stabilizes the C–H activation transition state.



Scheme 4 Experiments with a deuterium-labeled substrate.¹¹Scheme 5 Possible catalytic cycle for *para*-selective Rh-catalyzed olefination.Fig. 1 Transition states for Rh(III)-mediated *para*-C-H and *meta*-C-H bond activation, computed with M06/6-311+G(d,p)-SDD//M06/6-31G(d,p)-LANL2DZ in SMD dichloroethane. Distances in Å, $\Delta G_{\text{rel}}^{\ddagger}$ in kcal mol⁻¹.

Conclusions

In summary, herein we have reported the first example of a Rh-catalyzed distal *para*-C-H functionalization reaction. The Rh-catalyzed olefination of toluenes using the Si-linked DG₅ directing group displays broad substrate tolerance. Electron-

rich and electron-deficient arenes are coupled with electron-deficient olefins in high yield and selectivity. Mechanistic studies are consistent with a catalytic cycle in which the C-H bond activation is rate-determining. This work reveals the potential of Rh catalysis to diversify the scope of functionalizations in the realm of remote *para*-C-H activation.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

This activity is funded by CSIR, India. Financial support received from IITB-Monash Research Academy (fellowship to UD and SP), UGC-India (fellowship to SM), Australian Research Council (DP180103047 to E. H. K.), and the University of Queensland (fellowship to E. H. K.) is gratefully acknowledged. High-performance computing resources were provided by the Australian National Computational Infrastructure and the UQ Research Computing Centre. Helpful discussions with Dr Romain Lepage (UQ) are gratefully acknowledged.

Notes and references

- (a) S. H. Cho, J. Y. Kim, J. Kwak and S. Chang, *Chem. Soc. Rev.*, 2011, **40**, 5068–5083; (b) C. Jia, T. Kitamura and Y. Fujiwara, *Acc. Chem. Res.*, 2001, **34**, 633–639; (c) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord and F. Glorius, *Angew. Chem., Int. Ed.*, 2012, **51**, 10236–10254; (d) I. A. I. Mkhalid, J. H. Barnard, T. B. Marder, J. M. Murphy and J. F. Hartwig, *Chem. Rev.*, 2010, **110**, 890–931; (e) I. V. Seregin and V. Gevorgyan, *Chem. Soc. Rev.*, 2007, **36**, 1173–1193; (f) C.-L. Sun, B.-J. Li and Z.-J. Shi, *Chem. Rev.*, 2011, **111**, 1293–1314; (g) H. Yi, G. Zhang, H. Wang, Z. Huang, J. Wang, A. K. Singh and A. Lei, *Chem. Rev.*, 2017, **117**, 9016–9085; (h) L. Ackermann, R. Vicente and A. R. Kapdi, *Angew. Chem., Int. Ed.*, 2009, **48**, 9792–9826; (i) T. Gensch, M. N. Hopkinson, F. Glorius and J. Wencel-Delord, *Chem. Soc. Rev.*, 2016, **45**, 2900–2936.
- (a) L. Ackermann, *Acc. Chem. Res.*, 2014, **47**, 281–295; (b) P. B. Arockiam, C. Bruneau and P. H. Dixneuf, *Chem. Rev.*, 2012, **112**, 5879–5918; (c) X. Chen, K. M. Engle, D.-H. Wang and J.-Q. Yu, *Angew. Chem., Int. Ed.*, 2009, **48**, 5094–5115; (d) O. Daugulis, H.-Q. Do and D. Shabashov, *Acc. Chem. Res.*, 2009, **42**, 1074–1086; (e) K. M. Engle and J.-Q. Yu, *J. Org. Chem.*, 2013, **78**, 8927–8955; (f) R. Giri, S. Thapa and A. Kafle, *Adv. Synth. Catal.*, 2014, **356**, 1395–1411; (g) Z. Huang, H. N. Lim, F. Mo, M. C. Young and G. Dong, *Chem. Soc. Rev.*, 2015, **44**, 7764–7786; (h) T. W. Lyons and M. S. Sanford, *Chem. Rev.*, 2010, **110**, 1147–1169; (i) S. R. Neufeldt and M. S. Sanford, *Acc. Chem. Res.*, 2012, **45**, 936–946; (j) M. Pichette Drapeau and L. J. Gooßen, *Chem.–Eur. J.*, 2016, **22**, 18654–18677; (k) A. Ros, R. Fernandez and J. M. Lassaletta, *Chem. Soc. Rev.*, 2014, **43**, 3229–3243; (l) T. Satoh and M. Miura, *Synthesis*, 2011, 3395–3409, DOI: 10.1055/s-0030-1258225; (m) G. Shi and Y. Zhang, *Adv.*



- Synth. Catal.*, 2014, **356**, 1419–1442; (n) J. J. Topczewski and M. S. Sanford, *Chem. Sci.*, 2015, **6**, 70–76; (o) F. W. Patureau, J. Wencel-Delord and F. Glorius, *Aldrichimica Acta*, 2013, 31–41; (p) C. S. Yeung and V. M. Dong, *Chem. Rev.*, 2011, **111**, 1215–1292; (q) F. Zhang and D. R. Spring, *Chem. Soc. Rev.*, 2014, **43**, 6906–6919; (r) Z. Chen, B. Wang, J. Zhang, W. Yu, Z. Liu and Y. Zhang, *Org. Chem. Front.*, 2015, **2**, 1107–1295; (s) M. Zhang, Y. Zhang, X. Jie, H. Zhao, G. Li and W. Su, *Org. Chem. Front.*, 2014, **1**, 843–895; (t) S. Rej and N. Chatani, *Angew. Chem., Int. Ed.*, 2019, **58**, 2–28; (u) S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda and N. Chatani, *Nature*, 1993, **366**, 529–531; (v) F. Kakiuchi and S. Murai, *Acc. Chem. Res.*, 2002, **35**, 826–834; (w) Y. Ogiwara, M. Tamura, T. Kochi, Y. Matsuura, N. Chatani and F. Kakiuchi, *Organometallics*, 2014, **33**, 402–420; (x) F. Kakiuchi, T. Kochi, E. Mizushima and S. Murai, *J. Am. Chem. Soc.*, 2010, **132**, 17741–17750.
- 3 (a) H. Shi, P. Wang, S. Suzuki, M. E. Farmer and J.-Q. Yu, *J. Am. Chem. Soc.*, 2016, **138**, 14876–14879; (b) H.-J. Xu, Y. Lu, M. E. Farmer, H.-W. Wang, D. Zhao, Y.-S. Kang, W.-Y. Sun and J.-Q. Yu, *J. Am. Chem. Soc.*, 2017, **139**, 2200–2203; (c) H.-J. Xu, Y.-S. Kang, H. Shi, P. Zhang, Y.-K. Chen, B. Zhang, Z.-Q. Liu, J. Zhao, W.-Y. Sun, J.-Q. Yu and Y. Lu, *J. Am. Chem. Soc.*, 2019, **141**, 76–79; (d) S. Lee, H. Lee and K. L. Tan, *J. Am. Chem. Soc.*, 2013, **135**, 18778–18781; (e) S. Li, L. Cai, H. Ji, L. Yang and G. Li, *Nat. Commun.*, 2016, **7**, 10443–10450; (f) S. Li, H. Ji, L. Cai and G. Li, *Chem. Sci.*, 2015, **6**, 5595–5600; (g) R.-J. Mi, Y.-Z. Sun, J.-Y. Wang, J. Sun, Z. Xu and M.-D. Zhou, *Org. Lett.*, 2018, **20**, 5126–5129; (h) L. Zhang, C. Zhao, Y. Liu, J. Xu, X. Xu and Z. Jin, *Angew. Chem., Int. Ed.*, 2017, **56**, 12245–12249; (i) S. Bag, R. Jayarajan, U. Dutta, R. Chowdhury, R. Mondal and D. Maiti, *Angew. Chem., Int. Ed.*, 2017, **56**, 12538–12542; (j) M. Bera, S. Agasti, R. Chowdhury, R. Mondal, D. Pal and D. Maiti, *Angew. Chem., Int. Ed.*, 2017, **56**, 5272–5276; (k) M. Bera, A. Maji, S. K. Sahoo and D. Maiti, *Angew. Chem., Int. Ed.*, 2015, **54**, 8515–8519; (l) U. Dutta, A. Modak, B. Bhaskararao, M. Bera, S. Bag, A. Mondal, D. W. Lupton, R. B. Sunoj and D. Maiti, *ACS Catal.*, 2017, **7**, 3162–3168; (m) R. Jayarajan, J. Das, S. Bag, R. Chowdhury and D. Maiti, *Angew. Chem., Int. Ed.*, 2018, **57**, 7659–7663; (n) A. Modak, T. Patra, R. Chowdhury, S. Raul and D. Maiti, *Organometallics*, 2017, **36**, 2418–2423; (o) D. Leow, G. Li, T.-S. Mei and J.-Q. Yu, *Nature*, 2012, **486**, 518–522; (p) R.-Y. Tang, G. Li and J.-Q. Yu, *Nature*, 2014, **507**, 215–220; (q) L. Chu, M. Shang, K. Tanaka, Q. Chen, N. Pissarnitski, E. Streckfuss and J.-Q. Yu, *ACS Cent. Sci.*, 2015, **1**, 394–399; (r) Z. Jin, L. Chu, Y.-Q. Chen and J.-Q. Yu, *Org. Lett.*, 2018, **20**, 425–428; (s) R. J. Phipps and M. J. Gaunt, *Science*, 2009, **323**, 1593–1597; (t) H. A. Duong, R. E. Gilligan, M. L. Cooke, R. J. Phipps and M. J. Gaunt, *Angew. Chem., Int. Ed.*, 2011, **50**, 463–466; (u) J. A. Leitch, Y. Bhonoah and C. G. Frost, *ACS Catal.*, 2017, **7**, 5618–5627; (v) O. Saidi, J. Marafie, A. E. W. Ledger, P. M. Liu, M. F. Mahon, G. Kociok-Köhn, M. K. Whittlesey and C. G. Frost, *J. Am. Chem. Soc.*, 2011, **133**, 19298–19301; (w) N. Hofmann and L. Ackermann, *J. Am. Chem. Soc.*, 2013, **135**, 5877–5884; (x) J. Li, S. Warratz, D. Zell, S. De Sarkar, E. E. Ishikawa and L. Ackermann, *J. Am. Chem. Soc.*, 2015, **137**, 13894–13901; (y) F. Fumagalli, S. Warratz, S.-K. Zhang, T. Rogge, C. Zhu, A. C. Stückl and L. Ackermann, *Chem.-Eur. J.*, 2018, **24**, 3984–3988; (z) M. T. Mihai, H. J. Davis, G. R. Genov and R. J. Phipps, *ACS Catal.*, 2018, **8**, 3764–3769; (aa) M. T. Mihai, G. R. Genov and R. J. Phipps, *Chem. Soc. Rev.*, 2018, **47**, 149–171; (ab) R. Ferraccioli, *Synthesis*, 2013, **45**, 581–591; (ac) M. Catellani, F. Frignani and A. Rangoni, *Angew. Chem., Int. Ed.*, 1997, **36**, 119–122; (ad) F. Faccini, E. Motti and M. Catellani, *J. Am. Chem. Soc.*, 2004, **126**, 78–79; (ae) Z. Dong and G. Dong, *J. Am. Chem. Soc.*, 2013, **135**, 18350–18353; (af) Z. Dong, J. Wang and G. Dong, *J. Am. Chem. Soc.*, 2015, **137**, 5887–5890; (ag) Z. Dong, J. Wang, Z. Ren and G. Dong, *Angew. Chem., Int. Ed.*, 2015, **54**, 12664–12668; (ah) X.-C. Wang, W. Gong, L.-Z. Fang, R.-Y. Zhu, S. Li, K. M. Engle and J.-Q. Yu, *Nature*, 2015, **519**, 334–338; (ai) G.-C. Li, P. Wang, M. E. Farmer and J.-Q. Yu, *Angew. Chem., Int. Ed.*, 2017, **56**, 6874–6877; (aj) Y. Kuninobu, H. Ida, M. Nishi and M. Kanai, *Nat. Chem.*, 2015, **7**, 712–717; (ak) R. Bisht and B. Chattopadhyay, *J. Am. Chem. Soc.*, 2016, **138**, 84–87; (al) J.-Y. Cho, M. K. Tse, D. Holmes, R. E. Maleczka and M. R. Smith, *Science*, 2002, **295**, 305–308; (am) T. Ishiyama, J. Takagi, K. Ishida, N. Miyaura, N. R. Anastasi and J. F. Hartwig, *J. Am. Chem. Soc.*, 2002, **124**, 390–391; (an) D. W. Robbins and J. F. Hartwig, *Angew. Chem., Int. Ed.*, 2013, **52**, 933–937.
- 4 (a) B. E. Haines, Y. Saito, Y. Segawa, K. Itami and D. G. Musaev, *ACS Catal.*, 2016, **6**, 7536–7546; (b) M. E. Hoque, R. Bisht, C. Haldar and B. Chattopadhyay, *J. Am. Chem. Soc.*, 2017, **139**, 7745–7748; (c) J. A. Leitch, C. L. McMullin, A. J. Paterson, M. F. Mahon, Y. Bhonoah and C. G. Frost, *Angew. Chem., Int. Ed.*, 2017, **56**, 15131–15135; (d) S. Okumura and Y. Nakao, *Org. Lett.*, 2017, **19**, 584–587; (e) L. Yang, K. Semba and Y. Nakao, *Angew. Chem., Int. Ed.*, 2017, **56**, 4853–4857; (f) C. Tian, X. Yao, W. Ji, Q. Wang, G. An and G. Li, *Eur. J. Org. Chem.*, 2018, **2018**, 5972–5979; (g) L. Zhu, X. Qi, Y. Li, M. Duan, L. Zou, R. Bai and Y. Lan, *Organometallics*, 2017, **36**, 2107–2115.
- 5 S. Bag, T. Patra, A. Modak, A. Deb, S. Maity, U. Dutta, A. Dey, R. Kancharla, A. Maji, A. Hazra, M. Bera and D. Maiti, *J. Am. Chem. Soc.*, 2015, **137**, 11888–11891.
- 6 T. Patra, S. Bag, R. Kancharla, A. Mondal, A. Dey, S. Pimparkar, S. Agasti, A. Modak and D. Maiti, *Angew. Chem., Int. Ed.*, 2016, **55**, 7751–7755.
- 7 A. Maji, S. Guin, S. Feng, A. Dahiya, V. K. Singh, P. Liu and D. Maiti, *Angew. Chem., Int. Ed.*, 2017, **56**, 14903–14907.
- 8 A. Maji, A. Dahiya, G. Lu, T. Bhattacharya, M. Brochetta, G. Zanoni, P. Liu and D. Maiti, *Nat. Commun.*, 2018, **9**, 3582.
- 9 (a) L. T. Ball, G. C. Lloyd-Jones and C. A. Russell, *Science*, 2012, **337**, 1644–1648; (b) C.-L. Ciana, R. J. Phipps, J. R. Brandt, F.-M. Meyer and M. J. Gaunt, *Angew. Chem., Int. Ed.*, 2011, **50**, 458–462; (c) B. Berzina, I. Sokolovs and E. Suna, *ACS Catal.*, 2015, **5**, 7008–7014; (d) Z. Yu, B. Ma, M. Chen, H.-H. Wu, L. Liu and J. Zhang, *J. Am. Chem. Soc.*, 2014, **136**, 6904–6907.



- 10 (a) D. A. Colby, R. G. Bergman and J. A. Ellman, *Chem. Rev.*, 2010, **110**, 624–655; (b) D. A. Colby, A. S. Tsai, R. G. Bergman and J. A. Ellman, *Acc. Chem. Res.*, 2012, **45**, 814–825; (c) S. Cui, Y. Zhang and Q. Wu, *Chem. Sci.*, 2013, **4**, 3421–3426; (d) C. Feng, D. Feng and T.-P. Loh, *Org. Lett.*, 2013, **15**, 3670–3673; (e) T. K. Hyster, L. Knörr, T. R. Ward and T. Rovis, *Science*, 2012, **338**, 500–503; (f) N. Kuhl, N. Schröder and F. Glorius, *Adv. Synth. Catal.*, 2014, **356**, 1443–1460; (g) B. Li, J. Ma, W. Xie, H. Song, S. Xu and B. Wang, *Chem.–Eur. J.*, 2013, **19**, 11863–11868; (h) G. Li, Z. Ding and B. Xu, *Org. Lett.*, 2012, **14**, 5338–5341; (i) X. Li and M. Zhao, *J. Org. Chem.*, 2011, **76**, 8530–8536; (j) B. Liu, Y. Fan, Y. Gao, C. Sun, C. Xu and J. Zhu, *J. Am. Chem. Soc.*, 2013, **135**, 468–473; (k) S. H. Park, J. Y. Kim and S. Chang, *Org. Lett.*, 2011, **13**, 2372–2375; (l) N. K. Mishra, J. Park, S. Sharma, S. Han, M. Kim, Y. Shin, J. Jang, J. H. Kwak, Y. H. Jung and I. S. Kim, *Chem. Commun.*, 2014, **50**, 2350–2352; (m) K. Nobushige, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2014, **16**, 1188–1191; (n) F. W. Patureau and F. Glorius, *J. Am. Chem. Soc.*, 2010, **132**, 9982–9983; (o) M. Pisset, D. Oehlrich, F. Rombouts and G. A. Molander, *Org. Lett.*, 2013, **15**, 1528–1531; (p) X. Qi, Y. Li, R. Bai and Y. Lan, *Acc. Chem. Res.*, 2017, **50**, 2799–2808; (q) Y. Shen, G. Liu, Z. Zhou and X. Lu, *Org. Lett.*, 2013, **15**, 3366–3369; (r) A. S. Tsai, M. Brasse, R. G. Bergman and J. A. Ellman, *Org. Lett.*, 2011, **13**, 540–542; (s) F. Wang, G. Song and X. Li, *Org. Lett.*, 2010, **12**, 5430–5433; (t) X.-S. Zhang, Q.-L. Zhu, Y.-F. Zhang, Y.-B. Li and Z.-J. Shi, *Chem.–Eur. J.*, 2013, **19**, 11898–11903; (u) J. Zhou, B. Li, F. Hu and B.-F. Shi, *Org. Lett.*, 2013, **15**, 3460–3463; (v) C. Zhu and J. R. Falck, *Chem. Commun.*, 2012, **48**, 1674–1676; (w) K. Shibata, S. Natsui and N. Chatani, *Org. Lett.*, 2017, **19**, 2234–2237; (x) Y. Kita, M. Tobisu and N. Chatani, *Org. Lett.*, 2010, **12**, 1864–1867.
- 11 See the ESI† for detailed descriptions.
- 12 We also considered several other mechanisms in which the CH bond cleavage step is mediated by either Rh(III) or Rh(I), details are provided in the ESI.†

