

Cite this: *Chem. Commun.*, 2019, 55, 13749Received 8th July 2019,
Accepted 26th September 2019

DOI: 10.1039/c9cc05240b

rsc.li/chemcomm

Highly π -extended hetero-cyclic/aromatic skeletons are of great importance as they can be utilized in many organic material based technologies. Therefore, developing efficient, pre-activation-free, synthetic procedures for the rapid build-up of these complex structures remains a high priority objective. The herein presented approach delivers highly fused carbazole skeletons from simple naphthylamine derivatives.

The quest for higher performance aromatic hetero-cyclic fused organic materials imposes increasingly long and tough synthetic routes.¹ Indeed, the desired improved properties often demand ever more complicated scaffolds and/or π -extended/fused aromaticity (compounds **(I)** to **(III)**, Fig. 1).² In this field, the carbazole backbone is of particular importance, as mentioned in some recent patents on electroluminescent materials.² The efficient synthesis of these and related structures is therefore a strategic priority. For example, in a recent and inspiring work from Ito & Itami, a highly annulated carbazole structure (**2a**, Scheme 1) could be accessed from a simple pyrrole (**(IV)**) and a (not so trivial) 2,2'-diiodobiphenyl structure (**(V)**).³ This previous synthetic method operates through a tetra-fold palladium catalyzed Mizoroki–Heck-like reaction.³ The cost associated to the stoichiometric excess of the precious 2,2'-diiodobiphenyl substrate (**(V)**) however, or any other desired diiodo backbone, significantly limits the applicability and price of the final carbazole based target material. In contrast, oxidative C–H bond activation and functionalization strategies⁴

An intermolecular C–H oxidizing strategy to access highly fused carbazole skeletons from simple naphthylamines†

Christian K. Rank,^{‡a} Alexander W. Jones,^{‡b} Tatjana Wall,^c Patrick Di Martino-Fumo,^c Sarah Schröck,^c Markus Gerhards^{‡c} and Frederic W. Patureau^{‡*a}

remain arguably under-appreciated for accessing such highly fused hetero-cyclic π -extended novel materials, in spite of seminal oxidation studies in the middle of the 20th century.⁵ Moreover, inspiring work by Hiroto and Shinokubo showed recently that primary anthramines such as **(VI)** could easily undergo oxidation with DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) to deliver the corresponding annulated carbazole skeleton (**(VII)**, Scheme 1).⁶ Unfortunately, the latter method is limited to very electron rich primary anthramine starting materials. These alternative C–H functionalization strategies are nevertheless essential in order to make the future technologies based on these materials as affordable as possible. We therefore got interested in Ito and Itami's highly annulated carbazole **2a** (Scheme 1), and attempted a more direct C–H oxidative functionalization approach. For this purpose, we inspired ourselves from the historical reports describing the more challenging direct oxidation of *N*-phenyl-2-naphthylamine, wherein the yield of corresponding annulated carbazole **2b** does not exceed 25%.⁵ We thus foresaw that the latter process might be improved by optimizing the oxidizing method, efficiently affording these valuable hetero-cyclic/aromatic skeletons, without pre-activation, from trivial building blocks.

^a Institute of Organic Chemistry, RWTH Aachen University, Landoltweg 1, 52074 Aachen, Germany. E-mail: Frederic.patureau@rwth-aachen.de; Web: www.patureau-oc-rwth-aachen.de

^b FB Chemie, Technische Universität Kaiserslautern, Erwin-Schrödinger Strasse 52, 67663 Kaiserslautern, Germany

^c FB Chemie, Technische Universität Kaiserslautern & Research Center Optimas, Erwin-Schrödinger Straße 52, 67663 Kaiserslautern, Germany

† Electronic supplementary information (ESI) available: Experimental procedures and analytical data. See DOI: 10.1039/c9cc05240b

‡ C. K. Rank and A. W. Jones contributed equally to this work and are considered co-first authors. This work was started at the Technische Universität Kaiserslautern and finished at the RWTH Aachen University.

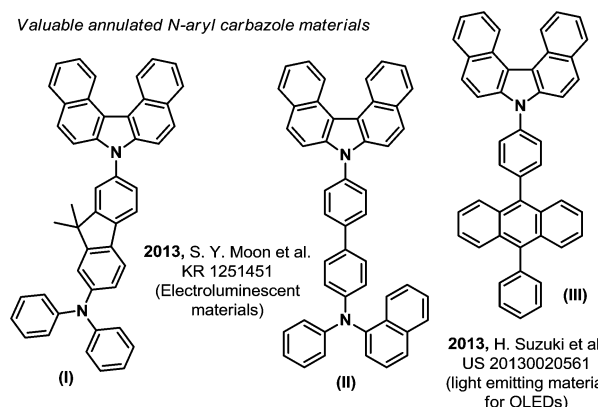
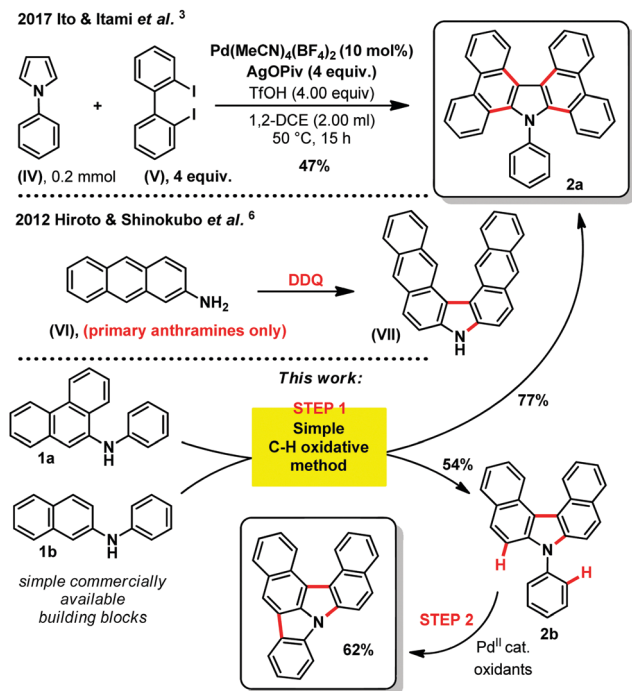


Fig. 1 Some *N*-aryl-dibenzo-carbazole derived electroluminescent materials.





Scheme 1 Strategies for accessing fused carbazole skeletons from naphthylamine derivatives.

While the historical reports focused on potassium permanganate, or peroxides as oxidants, yielding usually only traces of product **2b**,⁵ we turned our attention to silver oxide. The latter is a mild, easy to handle, and relatively basic oxidant, and is therefore well suited for electron-rich and sensitive heterocycles. In addition, silver oxide is one of the cheapest Ag^I salt available. Moreover, in most cases, the reduced silver particles usually precipitate, leading to an easy recovery of the metal through simple filtration. It should otherwise be noted that the reaction does not need any other precious metal catalyst. Elements of optimization are shown in Table 1. Next, we also optimized the solvent system and reaction time (see ESI[†]). We eventually settled for a mixture of toluene, cumene and acetic acid (halide-free system), for a reaction time of two hours, affording product **2b** in 54% isolated yield (Table 1, entry 9). Interestingly, in those conditions two minor side products **2b'** (7%) and **2b''** (4%) could be isolated and identified (Table 1). From these, we assume that this reaction could follow a radical pathway.^{5b} Moreover, TEMPO, a classical radical scavenger, poisons the reaction by either trapping reactive radical intermediates and/or neutralizing the silver oxidant (**2b**, 0%, entry 5). It should be noted that changing the acid to PivOH, CF₃CO₂H, or a mixture of AcOH and NaOAc, did not improve the reaction. Moreover, the addition of any other base led to a significant decrease in conversion towards product **2b** (see ESI[†]). Importantly, any other silver salt or the addition of cationic silver sources to Ag₂O did not have a positive influence on the reaction outcome (see ESI[†]).

With the optimized conditions in hand, we then explored the scope of the reaction (Scheme 2). It was possible to form

Table 1 Reaction optimization^a

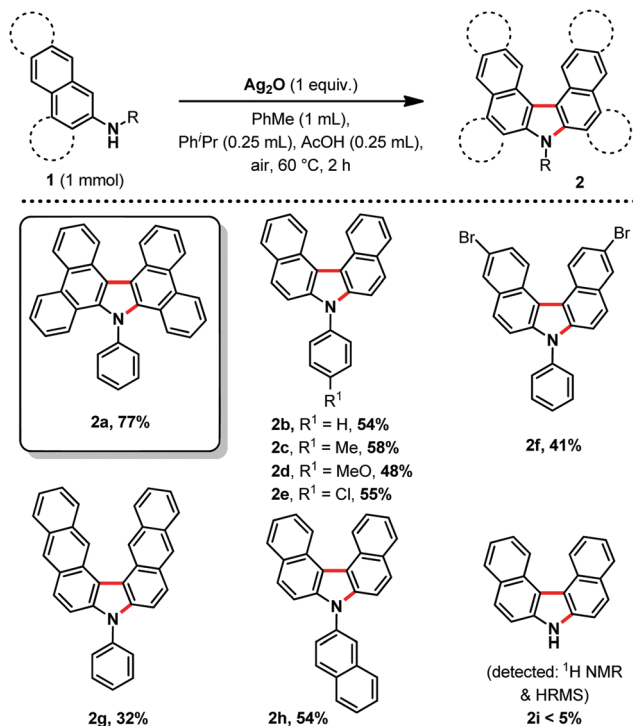
#	Catalyst or oxidant	[mmol]	Atm. [1 bar]	Yield ^d (%)
1 ^c	[Ru(C ₆ Me ₆)Cl ₂] ₂ + Cu(OAc) ₂	0.05 1.10	O ₂	14
2	Ag ₂ O	0.50	Air	42
3	Ag ₂ O	0.75	Air	44
4	Ag ₂ O	1.00	Air	50
5	Ag ₂ O + 1 equiv. TEMPO	1.00	Air	0
6	Ag ₂ O	1.00	O ₂	47
7	Ag ₂ O	1.00	N ₂	50
8	Ag ₂ O	1.25	Air	50
9 ^d	Ag ₂ O	1.00	Air	56(54) ^b

^a All reactions were carried out using **1b** (1 mmol), oxidant, in C₂Cl₄ (1 mL), PhCl (0.25 mL), AcOH (0.25 mL), at 60 °C for 24 h. The yield was determined by ¹H-NMR analysis of the crude reaction mixture using 1,2-DCE (1,2-dichloroethane) as an internal standard. ^b Isolated yields in brackets. ^c 150 °C. ^d C₂Cl₄ and PhCl are replaced by toluene (1 mL) and cumene (0.25 mL), reaction time is reduced to 2 h (see ESI for details).

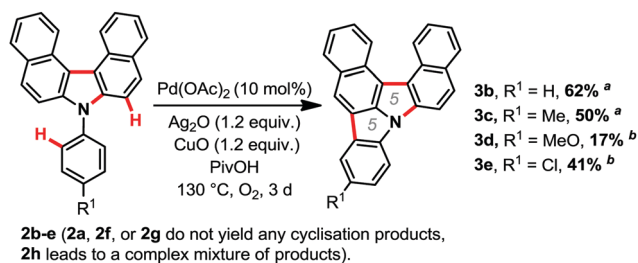
several highly π -extended carbazole derivatives in good yields (for such motifs), and with some functional group tolerance. Importantly, Ito and Itami's highly annulated carbazole product **2a** was isolated with a 77% yield, significantly increasing the previous state-of-the-art yield for this motif (Schemes 1 and 2). Next, we were curious whether we might be able to perform the highly strained dehydrogenative ring closure of the π -extended *N*-aryl-carbazole structure, towards the highly fused indolcarbazole skeleton **3** (nomenclature name: indolo[3.2.1-*jk*]carbazole), with potentially interesting properties.^{7,8} To the best of our knowledge however, dehydrogenative Scholl/Mallory type ring closing systems⁹ have not (yet) been found competent for this type of scaffold. We therefore adapted a palladium catalysed oxidative C–H bond activation method by Patureau.⁸ Satisfyingly, we were able to obtain compound **3b** in 62% isolated yield (Scheme 3), which represents a fairly good yield for this sort of dehydrogenative synthetic method.⁸ No dehydrogenative cyclization product with substrate **2a** was observed however.

Thereafter, we looked at all these novel molecules using DFT calculations^{10–15} (see ESI[†]) as well as UV and fluorescence spectroscopy. Importantly, the DFT calculations show a significant increase of the planarity from backbone **2b** to **3b**, by about a third (torsion angle from -27° to -18° , respectively, see DFT data in the ESI[†]). This is due to an enlargement of the gulf between the two naphthyl moieties in **3b**, allowing for a more planar disposition. The electronic properties of the compounds moreover differ from scaffold **2** to the fused π -system of scaffold **3**. The observed transitions show a $\pi \rightarrow \pi^*$ character. As displayed in the figure for highly fused product **3b**, the LUMO delocalizes over the





Scheme 2 Reaction scope, isolated yields, all reactions were carried out using **1** (1.00 mmol), Ag_2O (1.00 equiv.), PhMe (1.00 mL), Ph'Pr (0.25 mL), AcOH (0.25 mL), under air at 60 °C for 2 h.



Scheme 3 Palladium catalyzed strained dehydrogenative ring closure,^a isolated yields. ^a0.5 mmol scale, PivOH: 1.5 mL. ^b0.12 mmol scale.

entire molecule. In contrast, the HOMO seems to be localized only on the upper carbazole unit (Fig. 2 and 3). The highly fused product **3b** displays a broad absorption band between 250 and 400 nm. Moreover, an emission spectrum ($\lambda_{\text{EX}} = 270 \text{ nm}$) with a maximum emission wave at 428 nm was obtained.

Finally, the quantum yield was determined for the two model systems **2b** and **3b** (see Table 2). The determined values are generally between 0.28 and 0.45, depending on the excitation wavelength. A clear deviation of the additionally annulated system could not be observed. The second cyclization (**3b**) only shows a little influence on the quantum yield. Moreover, these values are somewhat lower compared to other recently appeared fused heterocycles.^{2d}

In summary, we developed an efficient route to synthesize dibenzocarbazole as well as highly fused π -extended dibenzoinolocarbazole derivatives, utilizing only simple oxidative C–H functionalization conditions. In general, the utilization of

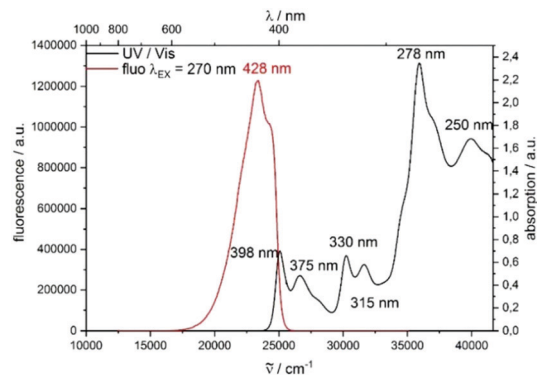


Fig. 2 Normalized UV/vis absorption and emission spectra of **3b** in dichloromethane.

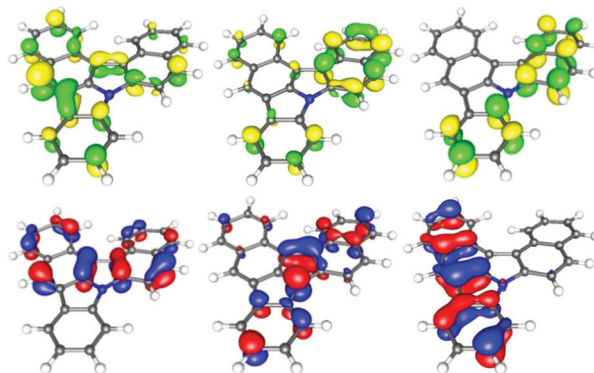


Fig. 3 Frontier molecular orbitals of **3b** (LUMO (3.38 eV), LUMO+1 (4.12 eV) and +2 (4.75 eV), from left to right, top, and HOMO (0 eV), HOMO+1 (–0.26 eV) and +2 (–0.83 eV), from left to right, beneath).

Table 2 Quantum yields for model materials **2b** and **3b**. Equipment and method are described in the ESI

Entry	Substance/wave number	Standard	Quantum yield	Confidence
1	2b /366 nm	POPOP	0.33	± 0.03
2	2b /350 nm	POPOP	0.45	± 0.03
3	2b /280 nm	Tryptophan	0.43	± 0.03
4	3b /375 nm	POPOP	0.43	± 0.03
5	3b /330 nm	POPOP	0.36	± 0.02
6	3b /277 nm	Tryptophan	0.28	± 0.03

simple oxidative C–H bond functionalization strategies can be expected to rise in the next few years. The fluorescence quantum yields are a further aspect for optimization.

DFG-funded transregional collaborative research center SFB/TRR 88 “Cooperative effects in homo and heterometallic complexes” (<http://3MET.de>, B10 in cooperation with C2), DFG funded project PA 2395/2-1, COST Action CA15106 (CHAOS), and ERC project 716136: “2O2ACTIVATION,” are acknowledged for financial support.

Conflicts of interest

There are no conflicts to declare.



Notes and references

- For selected reviews, see: (a) W. Wu, Y. Liu and D. Zhu, *Chem. Soc. Rev.*, 2010, **39**, 1489; (b) A. Narita, X.-Y. Wang, X. Feng and K. Muellen, *Chem. Soc. Rev.*, 2015, **44**, 6616; (c) M. Stepien, E. Gonka, M. Zyla and N. Sprutta, *Chem. Rev.*, 2017, **117**, 3479; (d) M. Krzeszewski, D. Gryko and D. T. Gryko, *Acc. Chem. Res.*, 2017, **50**, 2334; (e) H. Zhylitskaya and M. Stepień, *Org. Chem. Front.*, 2018, **5**, 2395; (f) T. Janosik, A. Rannug, U. Rannug, N. Wahlström, J. Slätt and J. Bergman, *Chem. Rev.*, 2018, **118**, 9058.
- (a) T. Ishisone, S. Seo, Y. Nonaka, T. Kawata and N. Ohsawa, *J. Soc. Inf. Disp.*, 2014, **22**, 404; (b) S. Y. Moon, B. S. Lee, S. H. Lee, G. M. Lee, D. H. Choi, D. H. Kim and J. H. Park, *Preparation of carbazoles for organic electronic element*, *KR Pat.*, 2013106255, 2013; (c) H. Suzuki, S. Seo, S. Kawakami and T. Suzuki, *Dibenzo[*c,g*]carbazole compounds, light-emitting components, light-emitting devices, display devices, lighting devices and electronic devices*, *US Pat.*, 20130020561, 2013; (d) X. Pu, M. Zhang, J. Lan, S. Chen, Z. Liu, W. Liang, Y. Yang, M. Zhang and J. You, *Org. Lett.*, 2019, **14**, 1139.
- (a) W. Matsuoka, H. Ito and K. Itami, *Angew. Chem., Int. Ed.*, 2017, **56**, 12224; (b) H. Kitano, W. Matsuoka, H. Ito and K. Itami, *Chem. Sci.*, 2018, **9**, 7556.
- For some selected reviews, see: (a) C.-L. Sun, B.-J. Li and Z.-J. Shi, *Chem. Commun.*, 2010, **46**, 677; (b) C. S. Yeung and V. M. Dong, *Chem. Rev.*, 2011, **111**, 1215; (c) L. McMurray, F. O'Hara and M. J. Gaunt, *Chem. Soc. Rev.*, 2011, **40**, 1885; (d) P. B. Arockiam, C. Bruneau and P. H. Dixneuf, *Chem. Rev.*, 2012, **112**, 5879; (e) J. Yamaguchi, A. D. Yamaguchi and K. Itami, *Angew. Chem., Int. Ed.*, 2012, **51**, 8960; (f) S. I. Kozhushkov and L. Ackermann, *Chem. Sci.*, 2013, **4**, 886; (g) C. Liu, J. Yuan, M. Gao, S. Tang, W. Li, R. Shi and A. Lei, *Chem. Rev.*, 2015, **115**, 12138; (h) T. Gensch, M. N. Hopkinson, F. Glorius and J. Wencel-Delord, *Chem. Soc. Rev.*, 2016, **45**, 2900; (i) Y. Qin, L. Zhu and S. Luo, *Chem. Rev.*, 2017, **117**, 9433; (j) D.-S. Kim, W.-J. Park and C.-H. Jun, *Chem. Rev.*, 2017, **117**, 8977.
- Early studies on the direct oxidation of *N*-phenyl-2-naphthylamine: (a) J. Rehner Jr., F. W. Baner and S. B. Robison, *J. Am. Chem. Soc.*, 1945, **67**, 605; (b) D. F. Bowman, B. S. Middleton and K. U. Ingold, *J. Org. Chem.*, 1969, **34**, 3456; (c) M. Smrcina, S. Vyskocil, B. Maca, M. Polasek, T. A. Claxton, A. P. Abbott and P. Kocovsky, *J. Org. Chem.*, 1994, **59**, 2156. For related works, see: (d) K. Nakano, Y. Hidehira, K. Takahashi, T. Hiyama and K. Nozaki, *Angew. Chem., Int. Ed.*, 2005, **44**, 7136; (e) N. Ogawa, Y. Yamaoka, H. Takikawa, K. Tsubaki and K. Takasu, *J. Org. Chem.*, 2018, **83**, 7994.
- K. Goto, R. Yamaguchi, S. Hiroto, H. Ueno, T. Kawai and H. Shinokubo, *Angew. Chem., Int. Ed.*, 2012, **51**, 10333.
- Pre-activated route: (a) H. G. Dunlop and S. H. Tucker, *J. Chem. Soc.*, 1939, 1945; (b) C. Niebel, V. Lokshin, A. Ben-Asuly, W. Marine, A. Karapetyanac and V. Khodorkovsky, *New J. Chem.*, 2010, **34**, 1243; (c) M. Rivoal, L. Bekere, D. Gachet, V. Lokshin, W. Marine and V. Khodorkovsky, *Tetrahedron*, 2013, **69**, 3302; (d) S. I. Wharton, J. B. Henry, H. McNab and A. R. Mount, *Chem. – Eur. J.*, 2009, **15**, 5482; (e) J. Lv, Q. Liu, J. Tang, F. Perdih and K. Kranjc, *Tetrahedron Lett.*, 2012, **53**, 5248; (f) P. Kautny, D. Lumpi, Y. Wang, A. Tissot, J. Bintinger, E. Horkel, B. Stoeger, C. Hametner, H. Hagemann, D. Mab and J. Froehlich, *J. Mater. Chem. C*, 2014, **2**, 2069.
- Dehydrogenative route: A. W. Jones, M.-L. Louillat-Habermeyer and F. W. Patureau, *Adv. Synth. Catal.*, 2015, **357**, 945.
- Scholl-type/Mallory-type reactions, see for example: (a) M. Grzybowski, K. Skonieczny, H. Butenschoen and D. T. Gryko, *Angew. Chem., Int. Ed.*, 2013, **52**, 9900; (b) F. B. Mallory and C. W. Mallory, *Org. React.*, 1984, **30**, 1; (c) W. H. Laarhoven, *Org. Photochem.*, 1989, **10**, 163; (d) H. Meier, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 1399; (e) Y. Tominaga and R. N. J. Castle, *Heterocycl. Chem.*, 1996, **33**, 523; (f) S. Hagen and H. Hopf, *Top. Curr. Chem.*, 1998, **196**, 45; (g) K. B. Jørgensen, *Molecules*, 2010, **15**, 4334.
- Methods of Quantum Chemical Calculations: Input structures for the compounds were generated by applying the universal force field (UFF)¹¹ implemented in the Avogadro program.¹² We performed structure optimization in Gaussian 09¹³ with the (TD)-DFT functional B3LYP as implemented in Turbomole 7.3¹⁴ by addition of Grimme's dispersion correction D3.¹⁵ The def2-TZVP basis set was used for all elements. Optimized structures were tested for minimum geometry by application of frequency calculations. No imaginary frequencies were found. The scaling factors 0.956 (CH stretching modes) and 0.97 (fingerprint) were used. To calculate the vertical electronic transitions, TD-DFT was used with the previously mentioned functional and basis set.
- A. K. Rappe, C. J. Casewit, K. S. Colwell, W. A. Goddard and W. M. Skiff, *J. Am. Chem. Soc.*, 1992, **114**, 10024.
- M. D. Hanwell, D. E. Curtis, D. C. Lonie, T. Vandermeersch, E. Zurek and G. R. Hutchison, *J. Cheminf.*, 2012, **4**, 17.
- M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman and D. J. Fox, *Gaussian 09, Revision A.02*, Gaussian, Inc., Wallingford, CT, 2016.
- F. Furche, R. Ahlrichs, C. Hättig, W. Klopper, M. Sierka and F. Weigend, *Wiley Interdiscip. Rev.: Comput. Mol. Sci.*, 2014, **4**, 91.
- S. Grimme, J. Antony, S. Ehrlich and H. Krieg, *J. Chem. Phys.*, 2010, **132**, 154104.

