Synthesis of 3,5-dichloro-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacenes (BODIPYs) via $Cu(OTf)_2$ mediated oxidative nucleophilic substitution of hydrogen by chloride

Felicity Frank, Laura Manzoli Alice, Phillip Mauker, Abdulrahman A. Alsimaree, Paul Gordon Waddell, Michael Richard Probert, Thomas James Penfold, Julian Gary Knight, Michael John Hall

PII: S0040-4020(20)30234-9

DOI: https://doi.org/10.1016/j.tet.2020.131113

Reference: TET 131113

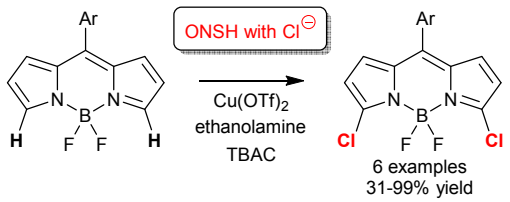
To appear in: *Tetrahedron*

Received Date: 22 January 2020

Revised Date: 26 February 2020

Accepted Date: 6 March 2020

Please cite this article as: Frank F, Alice LM, Mauker P, Alsimaree AA, Waddell PG, Probert MR, Penfold TJ, Knight JG, Hall MJ, Synthesis of 3,5-dichloro-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacenes (BODIPYs) via $Cu(OTf)_2$ mediated oxidative nucleophilic substitution of hydrogen by chloride, *Tetrahedron* (2020), doi: https://doi.org/10.1016/j.tet.2020.131113.



Synthesis of 3,5-Dichloro-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacenes (BODIPYs) via $Cu(OTf)_2$ Mediated Oxidative Nucleophilic Substitution of Hydrogen by Chloride

Felicity Frank,[a] Laura Manzoli Alice,[a,b] Phillip Mauker,[a,c] Abdulrahman A. Alsimaree,[a,d] Paul Gordon Waddell,[a] Michael Richard Probert,[a] Thomas James Penfold,[a] Julian Gary Knight[a]* and Michael John Hall[a]*

[a] Chemistry, School of Natural and Environmental Sciences, Newcastle University, Newcastle upon Tyne, NE1 7RU, UK

[b] Escola de Ciências da Saúde e da Vida, Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Brazil

[c] Faculty for Chemistry and Pharmacy, Ludwig-Maximilians-Universität München, Butenandtstrasse 5-13, 81377, München, Germany

[d] Department of Basic Science (Chemistry), College of Science and Humanities, Shaqra University, Afif, Saudi Arabia

Abstract

Regioselective halogenation is often a key step in the formation of substituted 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY) fluorophores, through the enablement of subsequent downstream C-C or C-X bond forming steps via S_NAr or metal catalyzed cross-coupling reactions. Classical S_EAr halogenation of unsubstituted BODIPYs results in 2/6-substitution, precluding easy access to 3/5-halogenated BODIPYs. Herein we present our development of a 3,5-dihalogenation reaction of unsubstituted BODIPYs, via a double oxidative nucleophilic substitution of hydrogen with chloride. Reaction of a range of *meso*-aryl, but otherwise unsubstituted, BODIPYs with stoichiometric $Cu(OTf)_2$ in the presence of ethanolamine and tetrabutylammonium chloride gives high isolated yields of the corresponding 3,5-dichlorinated BODIPYs, facilitating access to these valuable synthetic intermediates.

Introduction

Since their initial discovery in 1968 the 4,4′-difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY) dyes have become a ubiquitous class of fluorophores (e.g. dye sensitized solar cells, laser dyes, biological imaging agents and displays).[1,2] Their popularity results from the

beneficial combination of superior photophysical properties (high fluorescence quantum yields, extinction coefficients and photostability) and the availability of reliable synthetic strategies for their construction and/or regioselective functionalization (Figure 1).[3]

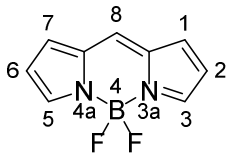
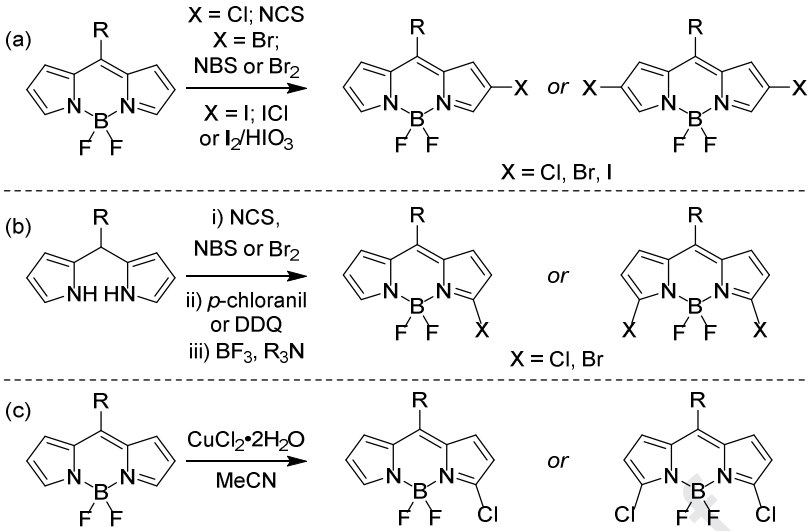


Figure 1. Core structure and IUPAC numbering system for the 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY) fluorophores (Note: the 8-position is also commonly referred to as the *meso*-position).

A common strategy in the synthesis of functionalized BODIPYs involves the initial formation of the core fluorophore (typically via condensation chemistry) followed by regioselective mono- or polyhalogenation. The thus formed halo-BODIPYs are valuable synthetic intermediates capable of further transformation through C-C or C-X bond forming reactions, such as metal catalyzed cross-coupling or nucleophilic aromatic substitutions (S_NAr).[3] Electrophilic halogenation (S_EAr) of unsubstituted BODIPYs results in preferential 2/6-substitution, steric blocking being required to access alternative regiochemistries (Scheme 1: (a)).[4] Thus improved access to the more synthetically elusive 3/5-halogenated BODIPYs would be of significant interest, as they are important intermediates in the synthesis of both red-shifted[5] and chiral BODIPYs architectures.[6] Synthetic access to the 3/5-halogenated BODIPYs typically involves the electrophilic halogenation (S_EAr) of the BODIPY precursor dipyrromethanes, followed by oxidation to the corresponding dipyrromethene and boron chelation (Scheme 1: (b)).[7] However, this reaction sequence is oft capricious due to competing oxidation of the dipyrromethane by the halogenating agent (e.g. NBS) leading to complex product mixtures. Recently a number of new approaches to BODIPY functionalization have been disclosed including direct palladium-catalyzed C–H arylation,[8] radical C-H funtionalization,[9] vicarious nucleophilic substitution (VNS)[10] and oxidative nucleophilic substitution of hydrogen (ONSH).[11] In particular Jiao *et al.* have described a high yielding oxidative 3/5-selective mono-chlorination of BODIPYs using stoichiometric $CuCl_2 \cdot 2H_2O$. However extension of this methodology to the synthesis of 3,5-dichlorinated BODIPYs gave only moderate yields (approx. 60%), which further reduced with increased reaction times and/or the addition of excess $CuCl_2 \cdot 2H_2O$ (Scheme 1:(c)).[12]

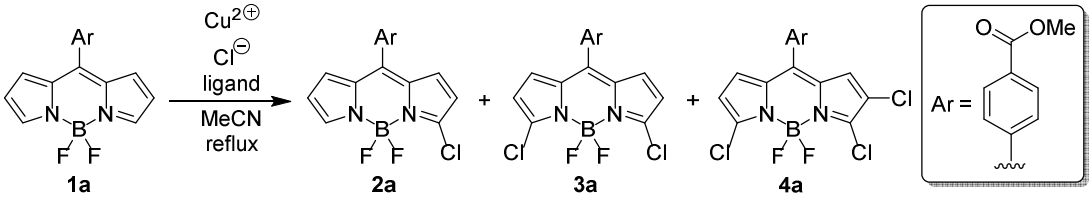


Scheme 1. Regioselective halogenation of BODIPYs: (a) 2/6-halogenation via S_EAr; (b) 3/5-halogenation via, stepwise S_EAr halogentation of precursor dipyrromethenes, oxidation and boron chelation; (c) 3/5-halogenation by oxidative nucleophilic substitution of hydrogen.

Results and Discussion

Due to our ongoing interest in the use of 3,5-dihalogenated BODIPYs as synthetic intermediates,[6] we decided to reexamine the copper mediated double oxidative nucleophilic substitution of hydrogen (ONSH) with chloride, in order to develop an improved and high yielding route to 3,5-dichlorinated BODIPYs. Thus, starting from *meso*-aryl BODIPY **1a**, we have investigated the oxidative 3,5-dichlorination of the BODIPYs in the presence of stoichiometric copper salts (Table 1).

Table 1. Optimization of the copper mediated double ONSH with chloride reaction of BODIPY **1a** to give 3,5-dichloro BODIPY **3a**.



Entry	Copper Source	Additives	Ligand	Time/min	Yield 3a (%)	Yield 4a (%)
1	3 eq. $CuCl_2 \cdot 2H_2O$	-	0	360	-[a]	-
2	10 eq.	-	0	60	29	-

	$CuCl_2 \cdot 2H_2O$					
3	10 eq. $CuCl_2 \cdot 2H_2O$	-	2 eq. Phen	90	-	-
4	10 eq. $CuCl_2 \cdot 2H_2O$	-	1 eq. ETA	60	57	-
5	10 eq. $CuCl_2 \cdot 2H_2O$	-	2 eq. ETA	60	67	-
6	10 eq. $CuCl_2 \cdot 2H_2O$	-	2 eq. ETA	90	69	-
7	5 eq. $CuCl_2 \cdot 2H_2O$/ 5eq. $Cu(OTf)_2$	-	2 eq. ETA	90	63	-
8	5 eq. $CuCl_2 \cdot 2H_2O$/ 5eq. $Cu(OTf)_2$	-	2 eq. ETA	110	99	-
9	10 eq. $Cu(OTf)_2$	5 eq. TBAC	2 eq. ETA	110	96	-
10	10 eq. $Cu(OTf)_2$	5 eq. TBAC	2 eq. ETA	240	49	20
11	10 eq. $Cu(OTf)_2$	2 eq. TBAC	2 eq. ETA	240	20	9
12	10 eq. $Cu(OTf)_2$	5 eq. TBAC	2 eq. ETA	240	59[b]	10
13	10 eq. $Cu(OTf)_2$	5 eq. TBAC	2 eq. ETA	1800	63[b]	15
14	10 eq. $Cu(OTf)_2$	5 eq. TBAC	2 eq. ETA	110	77[c]	2
15	10 eq. $Cu(OTf)_2$	5 eq. TBAC	0	110	37	
16	10 eq. $Cu(OTf)_2$	5 eq. TBAC	2 eq. ETA	110	61[d]	
17	10 eq. $Cu(OTf)_2$	5 eq. TBAC	2 eq. ETA	110	51[d,e]	

18	10 eq. $Cu(OTf)_2$	5 eq. TBAC	2 eq. ETA	110	95[e]	

Reactions carried out on a 0.15 mmol scale in MeCN (6 mL); a) 3-chloro-BODIPY **2a** isolated in 62% yield; b) Reactions carried out at 60 ^{o}C; c) 1.4 mmol scale (i.e. 460 mg of BODIPY **1a**; d) Reaction carried out under an atmosphere of nitrogen; e) Ambient light excluded. Phen = 1,10-phenanthroline, ETA = ethanolamine, TBAC = tetrabutylammonium chloride.

Initial examination of the copper mediated double ONSH with chloride of BODIPY **1a** were based on Jiao's conditions, involving stoichiometric quantities (3 equivalents) of $CuCl_2 \cdot 2H_2O$ in refluxing acetonitrile under an atmosphere of air for 6 hours. However in our hands no conversion to the desired 3,5-dichloro BODIPY **3a** was observed, although 3-chloro BODIPY **2a** could be recovered in moderate yield (62%). Increasing the stoichiometry of $CuCl_2 \cdot 2H_2O$ (10 eq.) did result in the isolation of the desired 3,5-dichloro BODIPY **3a** albeit in a low yield of 29%, however attempts to improve the yield of 3,5-dichloro BODIPY **3a**, either through extended reaction times or further increases in the equivalents of $CuCl_2 \cdot 2H_2O$ failed, in line with Jiao's original observations (Table 1, entries 1 and 2).

We postulated that these low conversions may be in part due to the poor solubility of $CuCl_2 \cdot 2H_2O$ in acetonitrile, prompting us to examine the use of copper chelating ligands. The addition of 2 equivalents of 1,10-phenanthroline to the dichlorination reaction resulted in complete inhibition of the desired ONSH chemistry, even with extended reaction times (Table 1, entry 3), however significant improvements in yield were obtained through the addition of 1 equivalent (57%) or 2 equivalents (69%) of ethanolamine (Table 1, entries 4-6). Alternate Cu^{2+} sources were also examined, the use of a 1:1 mixture of 5 eq. $CuCl_2 \cdot 2H_2O$ and 5 eq. $Cu(OTf)_2$ giving a similar yield of target 3,5-dichloro BODIPY **3a** (63%), which improved (99%) following an extended reaction time of 110 minutes (Table 1, entries 7-8). Complete replacement of $CuCl_2 \cdot 2H_2O$ with 10 eq. of $Cu(OTf)_2$ was also examined, with the addition of 5 eq. of tetrabutylammonium chloride acting as a chloride source, providing a near quantitative yield (96%) of **3a** (Table 1, entry 9).

Extended reaction times (4 hours) resulted in a decrease in isolated **3a** (49 %) due to the formation of trichloro-BODIPY **4a** in 20 % yield (Table 1, entry 10). ^{1}H NMR coupling constant analysis and 1D-NOESY experiments supported a 2,3,5-trichloro-substitution

pattern for BODIPY **4a,** which was confirmed by single crystal X-ray diffraction analysis following crystallization from a DCM solution (Figure 2).[13] We postulate that 2,3,5-trichloro-BODIPY **4a** forms from 3,5-dichloro-BODIPY **3a**, through an S_EAr reaction with chlorine, itself formed *in situ* by copper mediated oxidation of chloride.

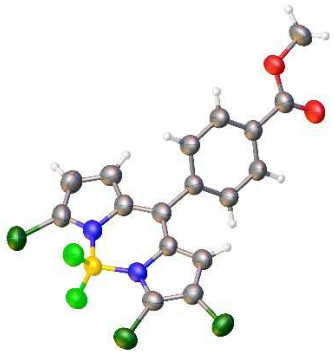


Figure 2: X-ray crystal structure of 2,3,5-trichloro-BODIPY **4a**.

The use of 2 eq. of TBAC, or lower reaction temperatures (60 ^{o}C) in combination with extended reaction times (Table 1, entry 11-13) gave no further improvement in the isolated yield of **3a**. Our optimized conditions also proved scalable, allowing approximately 0.5 grams of 3,5-dichloro-BODIPY **3a** to be prepared in a single reaction (Table 1, entry 14).

To gain further additional insight into our optimized dichlorination conditions, we carried out a series of control experiments (Table 1, entries 15-18). Omission of ethanolamine lead to significant drops in the isolated yield of BODIPY **3a**. The use of a nitrogen atmosphere also resulted in decreased yields, suggesting a role of atmospheric oxygen in the reaction, perhaps through the oxidative recycling of an active copper species. Whilst photochemical reaction pathways could be excluded, as no change in yield is observed when the reaction is carried out in the dark.

Finally, it should be noted that during the optimization of the synthesis 3,5-dichloro-BODIPY **3a** a number of crystallization experiments were undertaken in order to grow single crystals suitable for X-ray diffraction analysis.[13] This resulted in the determination of two different crystal structures for 3,5-dichloro-BODIPY **3a**, one corresponding to a known monoclinic C2/c polymorph (CSD: XEBZIQ),[14] whilst a second was shown to be a new monoclinic $P2_1/c$ polymorph. Together with a previously reported triclinic P-1 polymorph (CSD: XEBZIQ01),[15] this brings the total number of known polymorphs for this compound to three. Interestingly, the three polymorphic forms show little conformational variation in the

individual molecules of **3a** but do show considerable differences in their π···π stacking, resulting in three distinct dimeric units within the crystal structures, each displaying differing levels of overlap of their conjugated cores (Figure 3 and ESI).

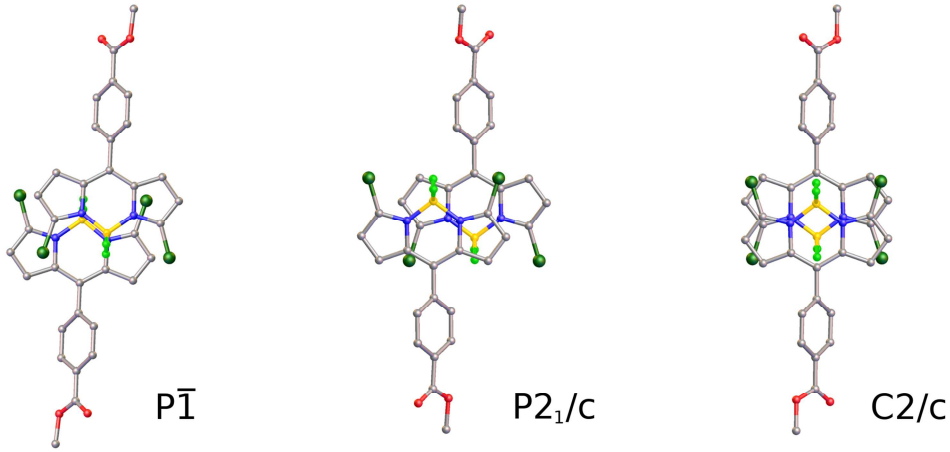
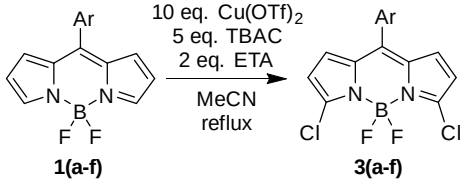


Figure 3: Comparison between the molecules of **3a**, composing the dimeric unit in each of the three polymorphs shown [P-1 polymorph (CSD: XEBZIQ01), $P2_1/c$ polymorph (this work)[13] and C2/c polymorph (CSD: XEBZIQ)].

Next we sought to apply our optimized oxidative 3,5-dichlorination methodology to a more extensive range of *meso*-aryl substituted BODIPYs (Table 2). Synthesis of BODIPYs (**1b-f**) was carried out as previously (see SI), followed by double ONSH with chloride under our previously optimized conditions. Excellent yields were obtained in the case of 3,5-dichloro-BODIPYs (**3a-c**), which contained electron deficient *meso*-aryl groups (Table 2, entries 1-3). However, lower yields (31 %) were observed in the case of *ortho*-tolyl substituted BODIPY (**3d**), potentially through competing chlorination of the tolyl group leading to complex product mixtures. In the case of BODIPYs with electron rich *meso*-aryl groups (**3e-f**) moderate yields were obtained, however these appear to be a consequence of slower rate of reaction as yields could be improved (70%) with longer reaction times (Table 2, entries 4-7).

Table 2. Copper mediated double ONSH with chloride of BODIPYs **1(a-f)**.



Entry	Ar	Reaction Time/min	Product	Yield (%)
1	4-($MeCO_2$)C_6H_4 (**1a**)	110	**3a**	96 %[a]
2	4-(NO_2)C_6H_4 (**1b**)	110	**3b**	92 %
3	3-(NO_2)C_6H_4 (**1c**)	110	**3c**	99 %
4	2-(CH_3)C_6H_4 (**1d**)	110	**3d**	31 %
5	4-(MeO)C_6H_4 (**1e**)	110	**3e**	66 %
6	3-(MeO)C_6H_4 (**1f**)	110	**3f**	56 %
7	3-(MeO)C_6H_4 (**1f**)	150	**3f**	70 %

Reactions carried out on a 0.14-0.25 mmol scale in MeCN (5-6 mL); a) reproduced from table 1 for comparison.

It is notable that the double ONSH with chloride of our BODIPY systems appears to proceed more rapidly for cases containing an electron deficient *meso*-aryl group. In the case of BODIPYs **1a-c** and **1e-f** the *meso*-aryl groups can obtain near co-planarity with the conjugated core, and as such have a significant impact on the electronics of the BODIPY. To further explore this the energy levels of the HOMOs and LUMOs of **1a-c** and **1e-f** were calculated using density functional theory (DFT) within the approximation of the PBE0 exchange and correlation functional[16] as implemented within the Q-Chem quantum chemistry package,[17] employing a Def2-SVP basis set.[18] For these *para*- and *meta*- substituted *meso*-aryl BODIPYs (**1a-c** and **1e-f**) the observed yields (at 110 minutes) correlate well with the calculated energies of the LUMO's (see SI), more rapid chlorination occurring for those compounds with low energy LUMOs. Interestingly this observation appears to contradict the Jiao mechanism,[12] in which the rate determining step is likely the oxidation of the BODIPY to the corresponding radical cation by Cu^{2+}.

In conclusion, we have developed a robust and high yielding double ONSH with chloride for the formation of 3,5-dichloro-BODIPYs with a range of *meso*-substituents. These 3,5-dichloro-BODIPYs are valuable synthetic intermediates, capable of undergoing both transition metal catalyzed couplings and nucleophilic aromatic substitutions (S_NAr), in the synthesis of 3,5-functionalised BODIPY architectures.

Acknowledgments

The authors thank Newcastle University (NCL) for funding a PhD scholarship (F.F.), Shaqra University for PhD scholarship (A.A.A.), Dr. Corinne Wills and Prof. W. McFarlane for NMR support at NCL, the EPSRC for X-ray crystallography facilities at NCL (EP/F03637X/1), the EPSRC UK National Mass Spectrometry Facility at Swansea University and Rebecca G. Clarke and Heinrich Von Koeller (NCL) for supporting studies.

References and Notes

1. A. Treibs and F. Kreuzer, *Justus Liebigs Ann. Chem.*, 1968, **718**, 208–223.

2. (a) A. Loudet and K. Burgess, *Chem. Rev.*, 2007, **107**, 4891-4932; (b) R. Ziessel, G. Ulrich and A. Harriman, *New J. Chem.*, 2007, **31**, 496–501; (c) G. Ulrich, R. Ziessel, A. Harriman, *Angew. Chem., Int. Ed.*, 2008, **47**, 1184-1201.

3. (a) N. Boens, B. Verbelen and W. Dehaen, *Eur. J. Org. Chem.*, 2015, 6577-6595; (b) R. G. Clarke and M. J. Hall in *Advances in Heterocyclic Chemistry*, ed. E. F. V. Scriven and C. A. Ramsden, Academic Press, Elsevier, Amsterdam, 2019, vol. 128, ch. 3, pp. 181-261; (c) N. Boens, B. Verbelen, M. J. Ortiz, L. Jiao and W. Dehaen, *Coord. Chem. Rev.*, 2019, **399**, 213024.

4. (a) L. Jiao, W. Pang, J. Zhou, Y. Wei, X. Mu, G. Bai and E. Hao, *J. Org. Chem.*, 2011, **76**, 9988-9996; (b) G. Duran-Sampedro, A. R. Agarrabeitia, I. Garcia-Moreno, A. Costela, J. Banuelos, T. Arbeloa, I. Lopez Arbeloa, J. L. Chiara and M. J. Ortiz, *Eur. J. Org. Chem.*, 2012, 6335-6350; (c) M. J. Ortiz, A. R. Agarrabeitia, G. Duran-Sampedro, J. Banuelos Prieto, T. A. Lopez, W. A. Massad, H. A. Montejano, N. A. Garcia and I. Lopez Arbeloa, *Tetrahedron*, 2012, **68**, 1153-1162; (d) P. Liu, F. Gao, L. Zhou, Y. Chen and Z. Chen, *Org. Biomol. Chem.*, 2017, **15**, 1393-1399.

5. H. Lu, J. Mack, Y. Yang and Z. Shen, *Chem. Soc. Rev.*, 2014, **43**, 4778–4823.

6. (a) C. Ray, E. M. Sánchez-Carnerero, F. Moreno, B. L. Maroto, A. R. Agarrabeitia, M. J. Ortiz, Í. López-Arbeloa, J. Bañuelos, K. D. Cohovi, J. L. Lunkley, G. Muller, S. de la Moya *Chem. Eur. J.* 2016, **22**, 8805-8808; (b) R. B. Alnoman, S. Rihn, D. C. O'Connor, F. A. Black, B. Costello, P. G. Waddell, W. Clegg, R. D. Peacock, W. Herrebout, J. G. Knight and M. J. Hall, *Chem. Eur. J.*, 2016, **22**, 93-96; (c) R. Clarke, K. L. Ho, A. A. Alsimaree, O. J. Woodford, P. G. Waddell, J. Bogaerts, W. Herrebout, J. G. Knight, R. Pal, T. J. Penfold and M. J. Hall, *ChemPhotoChem*, 2017, **1**,513-517.

7. (a) M. Baruah, W. Qin, N. Basaric, W. M. De Borggraeve and N. Boens, *J. Org. Chem.*, 2005, **70**, 4152-4157; (b) L. Li, J. Han, B. Nguyen and K. Burgess, *J. Org. Chem.*, 2008, **73**, 1963-1970; (c) S. Rihn, P. Retailleau, N. Bugsaliewicz, A. D. Nicola and R. Ziessel, *Tetrahedron Lett.*, 2009, **50**, 7008-7013; (d) L. Jiao, W. Pang, J. Zhou, Y. Wei, X. Mu, G. Bai and E. Hao, *J. Org. Chem.*, 2011, **76**, 9988-9996.

8. B. Verbelen, V. Leen, L. Wang, N. Boens and W. Dehaen, *Chem. Comm.*, 2012, **48**, 9129-9131.

9. (a) B. Verbelen, S. Boodts, J. Hofkens, N. Boens and W. Dehaen, *Angew. Chem. Int. Ed.*, 2015, **54**, 4612-4616; (b) B. Verbelen, L. C. D. Rezende, S. Boodts, J. Jacobs, L. Van Meervelt, J. Hofkens and W. Dehaen, *Chem. Eur. J.*, 2015, **21**, 12667-12675; (c) X. Zhou, Q. Wu, C. Yu, E. Hao, Y. Wei, X. Mu and L. Jiao, *Org. Lett.*, 2016, 18, 736-739; (d) Y. Yu, L. Jiao, J. Wang, H. Wang, C. Yu, E. Hao and N. Boens, *Chem. Commun.*, 2017, **53**, 581-584; (e) H. Zhang, X. Chen, J. Lan, Y. Liu, F. Zhou, D. Wu and J. You, *Chem. Comm.*, 2018, **54**, 3219-3222; (f) F. Lv, B. Tang, E. Hao, Q. Liu, H. Wang and L. Jiao, *Chem. Commun.*, 2019, **55**, 1639-1642.

10. (a) V. Leen, M. Van der Auweraer, N. Boens and W. Dehaen, *Org. Lett.*, 2011, **13**, 1470-1473; (b) J. G. Knight, R. B. Alnoman and P. G. Waddell, *Org. Biomol. Chem.*, 2015, **13**, 3819-3829.

11. (a) V. Leen, V. Zaragozí Gonzalvo, W.M. Deborggraeve, N. Boens and W. Dehaen, *Chem. Comm.*, 2010, **46**, 4908-4910; (b) M. Zhang, E. Hao, J. Zhou, C. Yu, G. Bai, F. Wang and L. Jiao, *Org. Biomol. Chem.*, 2012, **10**, 2139-2145.

12. X. Zhou, C. Yu, Z. Feng, Y. Yu, J. Wang, E. Hao, Y. Wei, X. Mu and L. Jiao, *Org. Lett.*, 2015, **17**, 4632-4635.

13. CCDC 1910572, 1967051, 1967052, 1967296 and 1967297 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

14. M. Laine, N. A. Barbosa, A. Kochel, B. Osiecka, G. Szewczyk, T. Sarna, P. Ziolkowski, R. Wieczorek and A. Filarowski, *Sens. Actuators, B.*, 2017, **238**, 548-555.

15. J. Pliquett, S. Amor, M. Ponce-Vargas, M. Laly, C. Racoeur, Y. Rousselin, F. Denat, A. Bettaieb, P. Fleurat-Lessard, C. Paul, C. Goze and E. Bodio, *Dalton Trans.*, 2018, **47**, 11203-11218.

16. (a) J. P. Perdew, K. Burke and M. Ernzerhof, *Phys. Rev. Lett.*, 1996, **77**, 3865-3868; (b) C. Adamo and V. Barone, *J. Chem. Phys.*, 1999, **110**, 6158-6170.

17. Y. Shao *et al. Mol. Phys.*, 2015, **113**, 184-215.

18. F. Weigend, *Phys. Chem. Chem. Phys.*, 2006, **8**, 1057-1065.

- Regioselective 3,5-dichlorination of unsubstituted BODIPYs is achieved.
- Double oxidative nucleophilic substitution of hydrogen with chloride.
- High yields are obtained for a range of 3,5-dichloro meso-aryl BODIPYs.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: