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Triarylborane catalysed *N*-alkylation of amines with aryl esters†‡

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The ability of halogenated triarylboranes to accept a lone pair of electrons from donor substrates renders them excellent Lewis acids which can be exploited as a powerful tool in organic synthesis. Tris(pentafluorophenyl)borane has successfully demonstrated its ability to act as a metal-free catalyst for an ever-increasing range of organic transformations. Herein we report the *N*-alkylation reactions of a wide variety of amine substrates including diarylamines, *N*-methylphenyl amines, and carbazoles with aryl esters using catalytic amounts of $B(C_6F_5)_3$. This mild reaction protocol gives access to *N*-alkylated products (35 examples) in good to excellent yields (up to 95%). The construction of a C–N bond at the propargylic position has also been demonstrated to yield synthetically useful propargyl amines. On the other hand, unsubstituted 1*H*-indoles and 1*H*-pyrroles at the C3/C2 positions afforded exclusively C–C coupled products. Extensive DFT studies have been employed to understand the mechanism for this transformation.

Introduction

Over the last decade there has been a surge of interest in the applications of triarylboranes as metal-free catalysts for a range of transformations. This research originates from the seminal work of Piers who, in 1996, demonstrated the use of tris(pentafluorophenyl)borane $[B(C_6F_5)_3]$ as an effective catalyst for the hydrosilylation of carbonyl compounds.[1] A decade later a derivative of this borane, containing a *p*-$PMes_2$ functionality on one of the aryl rings, was reported to be capable of reversibly activating H_2 in the absence of a transition metal.[2] This system, comprising unquenched Lewis acidic and basic sites, was subsequently termed a frustrated Lewis pair (FLP).[3] These two key findings by Piers and Stephan, as described above, have altered the way chemists think about the reactivity of triarylborane Lewis acids prompting the discovery of new catalytic reactivity of these boron compounds.[4,5] Many researchers have investigated the breadth of reactions $B(C_6F_5)_3$ can catalyze, whereas others have focused on catalyst modification through subtle alterations of the aryl rings to influence the accessibility and energy of the empty p-orbital at boron.[5] One of the most studied reactions in FLP chemistry has been the application of $B(C_6F_5)_3$ (and derivatives) for the FLP-catalyzed hydrogenation of imines to generate amines.[6–8] Owing to the importance of nitrogen-containing compounds in nature, new synthetic methods to develop C–N bonds in a mild and efficient manner are continuously being sought.[9] One common approach to synthesize C–N bonds is through reductive amination, a reaction that has been commonly mediated using transition metal catalysts.[10,11] Several groups (including ourselves) have employed a metal-free FLP-catalyzed strategy for reductive amination using the Lewis acidic boranes $B(C_6F_5)_3$, $B(2,6\text{-}Cl_2C_6H_3)(p\text{-}HC_6F_4)_2$, and $B(2,6\text{-}Cl_2C_6H_3)_2(2\text{-}Cl\text{-}6\text{-}FC_6H_3)$ (Scheme 1). In these reactions, the primary or secondary amine is initially condensed with an aldehyde or ketone and, in the second step, the borane catalyzes the reduction of the imine using H_2 (ref. 12) or a silane.[13] Recent studies indicate that $B(C_6F_5)_3$ can also be used as effective catalyst towards the *N*-alkylation of various amines. Chan *et al.* reported the solvent dependent chemoselective *N*-alkylation of aryl amines with alcohols using $B(C_6F_5)_3$ as a catalyst.[14] Furthermore, *N*-alkylation of primary and secondary aromatic amines and amides with primary, secondary, tertiary benzylic alcohols has been demonstrated by Maji *et al.* Activation of the dibenzyl ether intermediate by triarylfluoroboranes was

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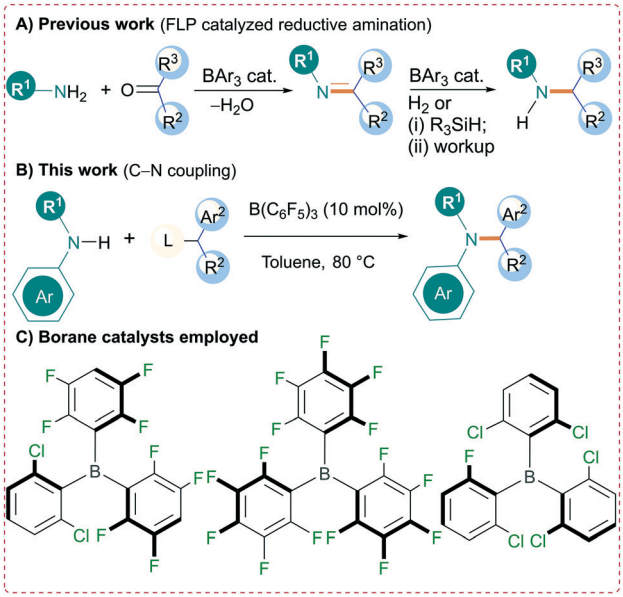
† Electronic supplementary information (ESI) available: Supplementary information includes detailed experimental procedures, NMR spectra, DFT data, and X-ray data. Crystallographic data for **4c** and **5a** have been deposited in the Cambridge Crystallographic Data Centre (CCDC) under accession numbers CCDC: 1996990 and 1996991. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0cy01339k

‡ Information about the data that underpins the results presented in this article, including how to access them, can be found in the Cardiff University data catalogue at http://doi.org/10.17035/d.2020.0117003506



Scheme 1 Amine synthesis catalyzed by triarylboranes. A) Previous work on the use of triarylboranes in reductive amination. B) This work on borane catalyzed *N*-alkylation. C) Borane catalysts employed in current and previous studies.

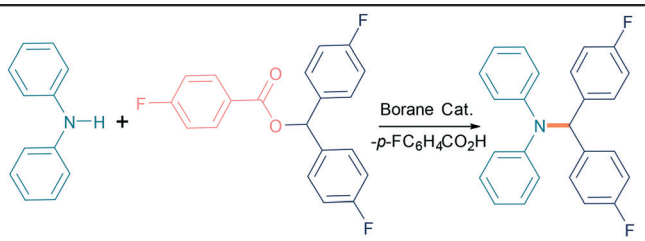
identified as the rate determining step.[15] Here we report an alternative borane catalyzed approach to C_{sp^3}–N bond formation through the *N*-alkylation of an amine with an ester catalyzed by $B(C_6F_5)_3$. Unlike the FLP reductive amination approach, these reactions occur at lower temperatures and do not require the use of hydrogen gas or silane reductants. A mild reaction protocol for synthesis of propargyl amines has also been highlighted.

Initially, we investigated the *N*-alkylation reaction of diphenyl amine (**1a**) with *p*-fluorobenzoate diarylester **2a** as a model system (Table 1). In the absence of a borane catalyst no reaction occurs in toluene. However, addition of 10 mol% $B(C_6F_5)_3$ led to C–N bond formation with elimination of *p*-fluorobenzoic acid to generate the *N*-alkylated product **3a** in excellent isolated yields of 92% after 16 h at 80 °C. The *p*-fluorobenzoate esters were selected due to the ease of reaction monitoring by ^{19}F NMR spectroscopy.

Other boranes, including the more Lewis acidic BCl_3 and less Lewis acidic BPh_3, gave little or no reaction under identical conditions. Likewise, Brønsted acids such as triflic or *p*-fluorobenzoic acid gave low or no conversion. Reaction at higher temperature (110 °C) using 10 mol% $B(C_6F_5)_3$ led to the formation of many other small impurities and lower isolated yields (52%) than the reaction at 80 °C. On the other hand, the room temperature reaction showed no conversion toluene was found to be the best solvent for the reaction with CH_2Cl_2 (56%), α,α,α-trifluorotoluene (TFT) (51%), and hexane (64%) showing only moderate yields. In addition, the more coordinating solvents THF (45%), Et_2O (36%), and acetonitrile (25%) showed a further reduction in yields. Reducing the catalytic loading to 5 mol% also drastically reduced the yield to just 30% after 24 h.

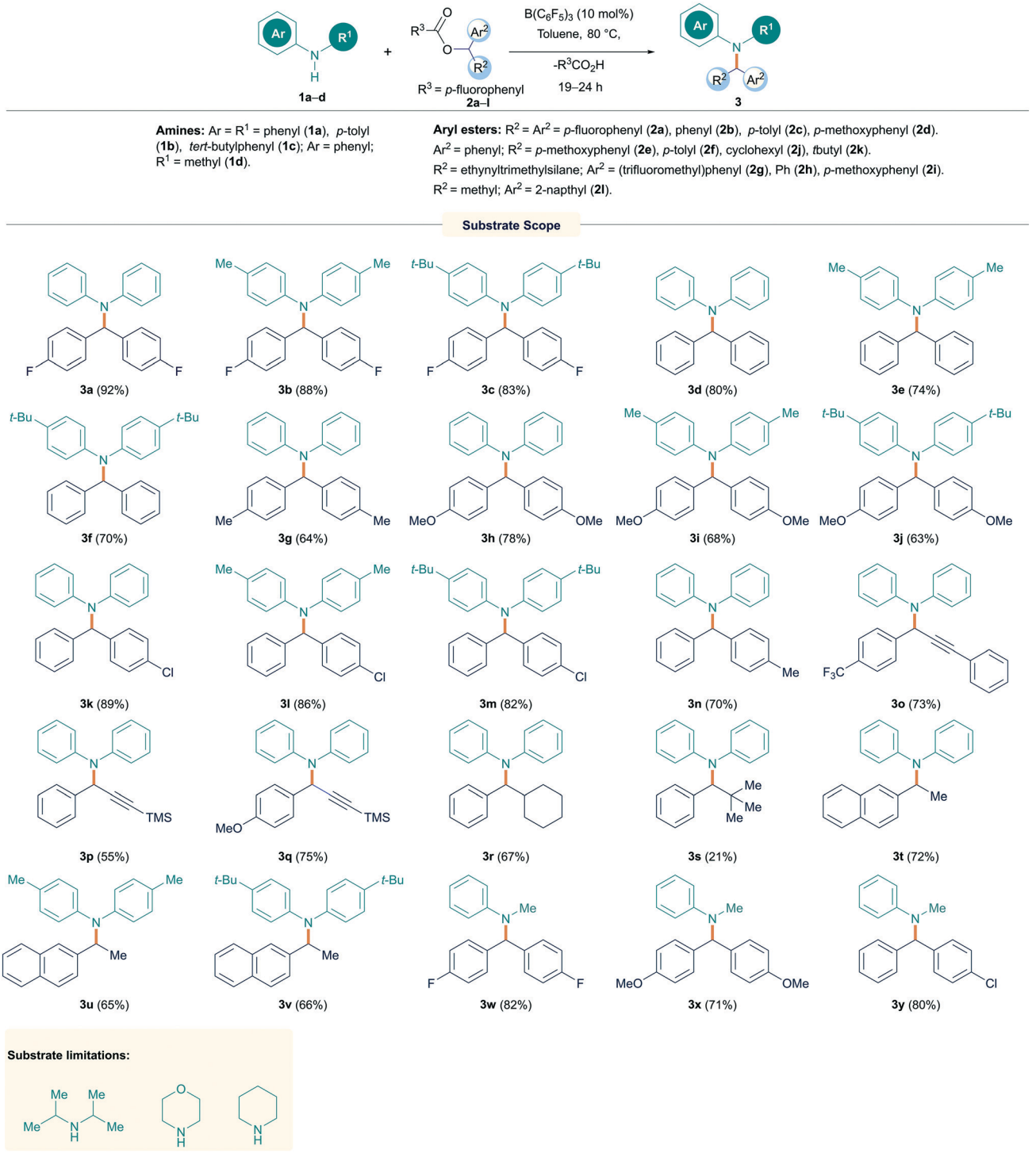
With the optimized conditions in hand, the substrate scope for the reaction was investigated (Scheme 2). Initially, secondary diaryl amines **1a–c** were reacted with a range of symmetrical diaryl esters **2a–d** (see ESI† for details of starting material structures and their synthesis) to generate the

Table 1 Optimization of the reaction conditions



Entry	Catalyst	Solvent	Temperature (°C)	Time (h)	Yield (%)
1	None	Toluene	80	24	NR
2	$B(C_6F_5)_3$	Toluene	80	16	92
3	BCl_3	Toluene	80	24	NR
4	BPh_3	Toluene	80	24	5
5	CF_3SO_3H	Toluene	80	22	39
6	*p*-$FC_6H_4CO_2H$	Toluene	80	22	NR
7	$B(C_6F_5)_3$	Toluene	110	16	52
8	$B(C_6F_5)_3$	Toluene	RT	42	NR
9	$B(C_6F_5)_3$	CH_2Cl_2	45	24	56
10	$B(C_6F_5)_3$	THF	60	24	45
11	$B(C_6F_5)_3$	TFT	80	24	51
12	$B(C_6F_5)_3$	Hexane	65	24	64
13	$B(C_6F_5)_3$	Acetonitrile	80	24	25
14	$B(C_6F_5)_3$	Et_2O	40	24	36
15	$B(C_6F_5)_3$[a]	Toluene	80	24	30

Yields reported are isolated yields. All reactions were carried out in 0.1 mol% scale using 10 mol% catalyst. NR indicates no reaction. [a] 5 mol% catalyst employed.



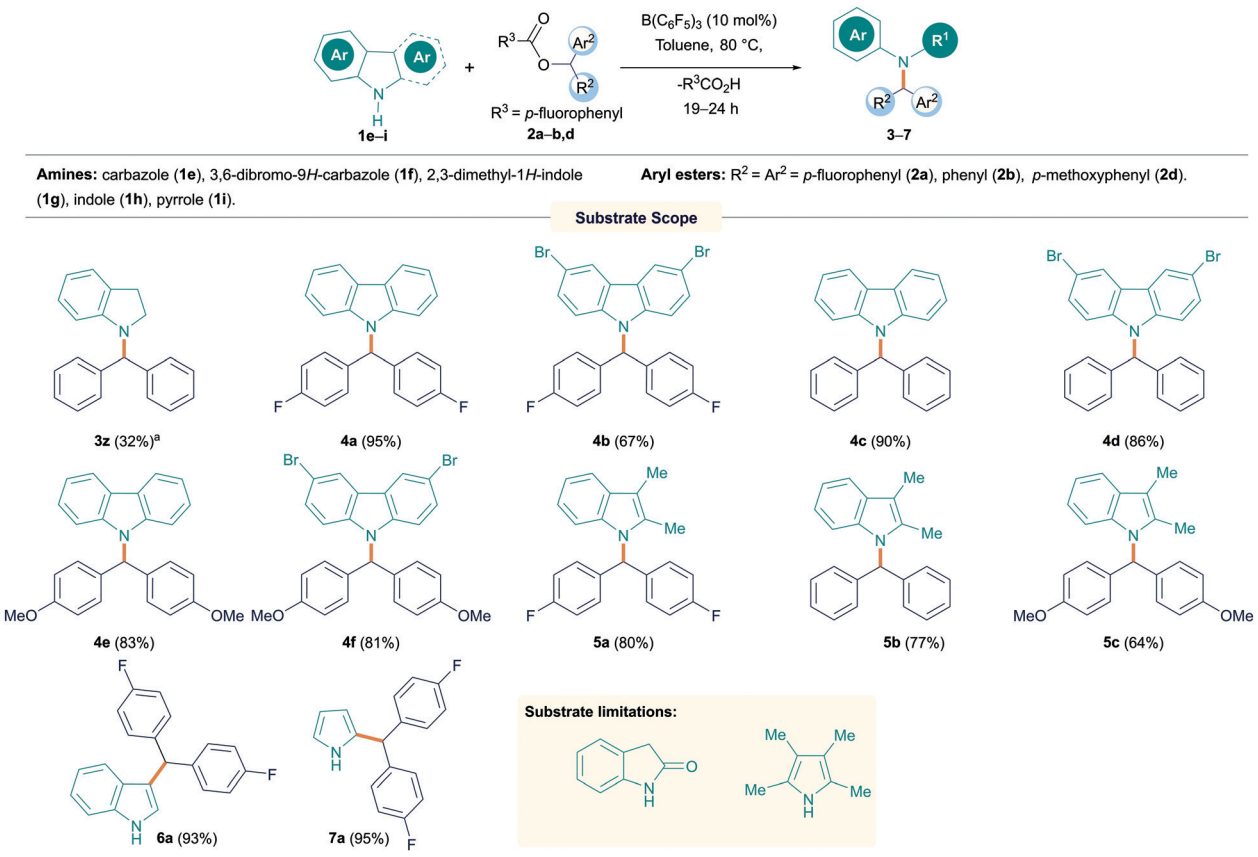
Scheme 2 *N*-Alkylation reactions of amines with diaryl esters. All reactions were carried out on a 0.1 mmol scale. Yields reported are isolated yield. [a]Crude NMR yield.

N-alkylated products **3a–j** in good to excellent yields (63–92%). The reactions were found to be tolerant to electron withdrawing (*p*-F) and electron donating (*p*-OMe) groups on the ester but were generally limited to more electron rich amines. Unsymmetrical diaryl esters **2e–f** also worked well giving products **3k–n** in good to excellent yields (70–89%). Several alkynyl/aryl substituted esters **2g–i** also performed well showing *N*-alkylation at the propargylic position to generate propargyl amines **3o–q** in 55–75% isolated yields. Indeed, the synthesis of propargylic amines is often metal catalyzed[16] and new routes to these compounds are important owing to their prevalence in biologically active compounds, as well as their applications in medicinal and synthetic chemistry. Aryl/alkyl esters **2j–l** could also be

employed; however, with the *tert*-butyl group, the reaction provided the *N*-alkylated product **3s** in only 21% yield. Fortunately, the efficiency of the reaction could be restored by employing cyclohexyl and methyl substituents yielding **3r**, **t–v** in 65–72% isolated yields. Likewise, changing the amine to have an aliphatic group was also successful and reactions of *N*-methyl aniline (**1d**) with esters gave **3w–y** in 71–82% yield. Indoline (**1e**), on the other hand gave poorer yield for the alkylated product **3z** of 32% as calculated from crude NMR. Limitations of this reaction included the aliphatic amines diisopropylamine, morpholine, and piperidine, which showed no reaction even when elevating the temperature to 120 °C. The higher basicity of these aliphatic amines, and the potential to react with $B(C_6F_5)_3$ through hydride abstraction,[17] compared with aromatic amines makes them incompatible with the Lewis acidic boranes to afford the desired *N*-alkylated products. This was also observed in NMR experiments using equimolar mixtures of diisopropyl amine and $B(C_6F_5)_3$ which showed several reaction products in the *in situ* ^{11}B NMR spectrum.

The primary amine, aniline, on the other hand gave a complex mixture of products including the secondary amine product from mono alkylation and the tertiary amine product from double alkylation at the nitrogen atom.

Following this, we turned our attention to *N*-alkylation of aromatic *N*-heterocycles including carbazoles and indoles with aryl esters (Scheme 3). *N*-Alkyl carbazoles are an important class of bioactive heteroaromatic compounds.[18] Their synthesis often relies on an S_N2 reaction, but this is sensitive to more hindered electrophiles, although metal catalyzed processes have recently been reported.[19] Other syntheses typically involve heterocycle generation after incorporation of the alkyl group at nitrogen. This includes precious metal catalyzed routes, benzannulation or oxidative cyclization reactions.[20] We therefore sought to employ our methodology in the synthesis of *N*-alkyl heterocycles. 9*H*-Carbazole (**1f**) and 3,6-dibromo-9*H*-carbazole (**1g**) were reacted with esters **2a**, **b** and **d**, giving excellent yields (81–95%) of the *N*-alkylated products (**4a–f**). As before, the reaction worked well with both electron donating and electron withdrawing groups on the ester. However, when employing electron donating groups on the amine (3,6-dimethoxy-9*H*-carbazole, **1h**), a complicated reaction mixture was obtained, and the presence of unreacted starting material was observed by TLC. The C3 and C2 substituted indole 2,3-dimethyl-1*H*-indole (**1i**) could also be employed giving the products **5a–c** in good to excellent yields (64–80%) when reacted with esters bearing electron donating or electron withdrawing groups. Suitable crystals of **4c** and **5a** were obtained from slow evaporation of saturated CH_2Cl_2 solutions and could be characterized by single-crystal X-ray



Scheme 3 *N*-Alkylation reactions of amines with diaryl esters. All reactions were carried out on a 0.1 mmol scale. Yields reported are isolated yield. [a]Crude NMR yield.

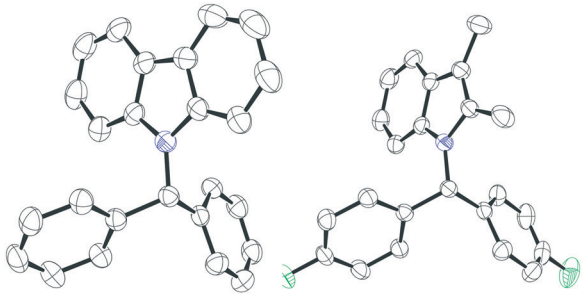
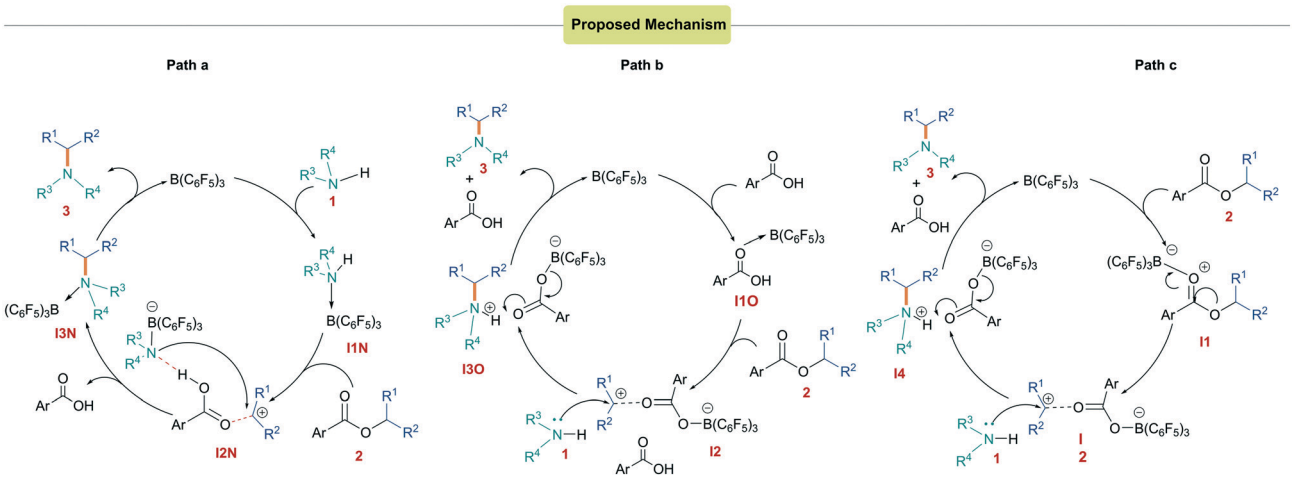


Fig. 1 Solid-state structures of compound **4c** (left) and **5a** (right). Thermal ellipsoids drawn at 50% probability. Carbon: black; nitrogen: blue; fluorine: green.

diffraction (Fig. 1). Surprisingly, when 1*H*-indole (**1j**) was treated with **2a**, no *N*-alkylated product was observed and exclusive formation of the C–C cross-coupled product (**6a**) was isolated in excellent yield (93%). Likewise, 1*H*-pyrrole (**1k**) also exhibited similar reactivity and the C–C cross-coupled product (**7a**) was isolated exclusively in 95% yield. In both cases, addition of further equivalents of the ester **2** still saw no *N*-alkylation reaction. The generation of the C-alkylated product is likely due to the formation of a Lewis acid–base adduct between the indole or pyrrole and the borane which protects the nitrogen centre from alkylation. We have observed similar selectivity in the reactions of these substrates with diazo esters catalyzed by $B(C_6F_5)_3$.[21] Similarly, blocking all other positions as in 2,3,4,5-tetramethyl pyrrole displayed no product formation. 2-Oxyindole was also tested for the *N*-alkylation reaction with **2a** but complicated mixtures of products resulted along with unreacted **2a**.

To investigate the mechanism for the *N*-alkylation reaction, we undertook a series of DFT calculations. We hypothesized that three mechanisms could be possible for the reaction: a Lewis acid-assisted Brønsted acid-catalyzed reaction from activation of the amine (Scheme 4a) or the carboxylic acid by-product (Scheme 4b), or a Lewis acid-catalyzed reaction (Scheme 4c). In all cases, the Lewis/Brønsted acid activates the ester generating a carbenium species that is subsequently trapped by the amine nucleophile. The generation of the carbenium ion corroborates the observation that esters used in the reaction must bear groups able to stabilize a positive charge. Calculations into the first mechanism (Scheme 4a and ESI,† Fig. S115) at the SMD/M06-2X/def2-TZVP//CPCM/ B3LYP/6-31G(d) level of theory show that the borane initially coordinates to the amine generating an acidic proton. This adduct formation was found to be energetically unfavorable relative to the free Lewis acid and base by 4.4 kcal mol^{-1} presumably due to steric hindrance. Upon coordination, the acidity of the amine increases, however, the next step of the reaction (protonation of the ester) had a high activation barrier of 40.5 kcal mol^{-1} (Fig. S115†). An alternative Brønsted acid catalyzed pathway could operate in which the borane activates the 4-fluorobenzoic acid side product, generating an acidic proton (Scheme 4b and Fig. S116†). As in the first case, this protonates the ester **2**, yielding carbenium intermediate **I2**. The activation barrier for the overall reaction was found to be much lower in this case (11.3 to 16.1 kcal mol^{-1}) when calculated at a range of levels of theory (Table 2). However, experimental results (Table 1, entry 6) showed no conversion using *p*-fluorobenzoic acid as a catalyst.

Finally, we turned our attention to the Lewis acid catalyzed pathway in which boron acts as a Lewis acid catalyst to activate the ester (Scheme 4c). DFT studies showed that the formation of a 1 : 1 ester : borane adduct was favorable over a 1 : 2 adduct.[22] Calculations into the reaction indicated that this pathway was also favorable under the reaction conditions with an activation barrier of 18.2 kcal mol^{-1} relative to the starting materials (Fig. 2). It was found that coordination of the borane to the ester **2** was the initial step of the reaction to give the adduct **I1** *via* a low energy transition state ($\mathbf{TS_1}$) of 7.5 kcal mol^{-1}. **I1** was found to have an elongated C–O bond length of 1.510 Å, which results in bond cleavage and the generation of an electrophilic carbenium ion in salt **I2** occurring with an activation barrier



Scheme 4 Catalytic cycles investigated for the reaction. (i) Brønsted acid catalyzed from activation of the amine (a) or carboxylic acid (b). (ii) Lewis acid catalyzed (c).

Table 2 Calculation of the energy barrier to generate the carbenium ion intermediate from **2** at different levels of theory

Level of theory	Lewis acid catalyzed	Brønsted acid catalyzed
CPCM/ωB97XD/def2-TZVP//CPCM/B3LYP/6-31G(d)	10.6 kcal mol^{-1}	12.3 kcal mol^{-1}
CPCM/M06-2X/def2-TZVP//CPCM/B3LYP/6-31G(d)	13.5 kcal mol^{-1}	14.8 kcal mol^{-1}
SMD/ωB97XD/def2-TZVP//CPCM/B3LYP/6-31G(d)	11.1 kcal mol^{-1}	13.5 kcal mol^{-1}
SMD/M06-2X/def2-TZVP//CPCM/B3LYP/6-31G(d)	14.1 kcal mol^{-1}	16.1 kcal mol^{-1}
SMD/ M06-2X-D3/def2-TZVP//CPCM/B3LYP/6-31G(d)	10.8 kcal mol^{-1}	11.3 kcal mol^{-1}

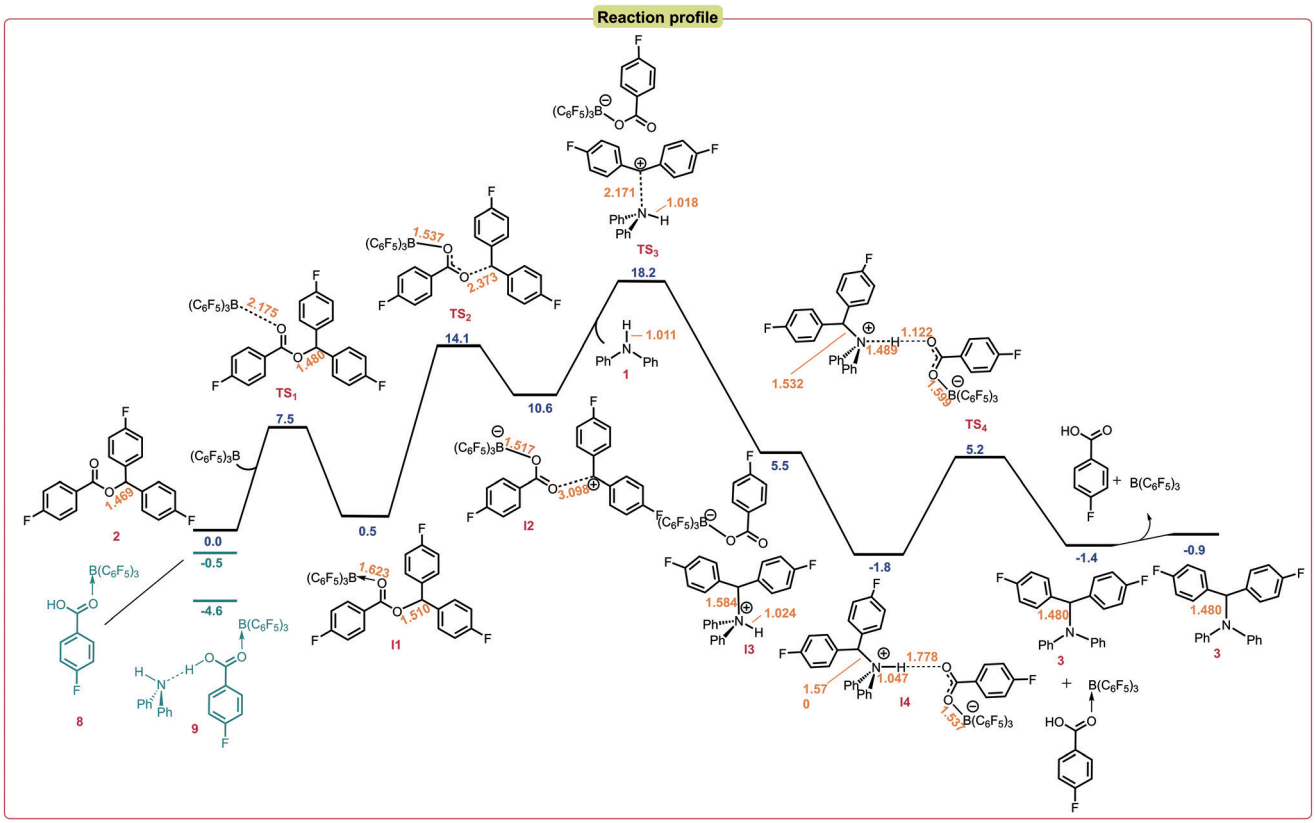


Fig. 2 Reaction profile for the DFT calculated mechanism at the SMD/M06-2X/def2-TZVP//CPCM/B3LYP/6-31G(d) level of theory. Bond lengths shown in Å. Relative energies given in kcal mol^{-1}.

of 13.6 kcal mol^{-1} through $\mathbf{TS_2}$. **I2** exists as a close ion pair and reacts with the amine nucleophile **1** *via* $\mathbf{TS_3}$ (activation barrier 7.6 kcal mol^{-1}) to give **I3** then **I4**. Finally, deprotonation through $\mathbf{TS_4}$ with a low activation barrier of 7.0 kcal mol^{-1} releases the by-product 4-fluorobenzoic acid to generate the *N*-alkylated product and to regenerate the $B(C_6F_5)_3$ catalyst. In the 1 : 1 stoichiometric reaction of the ester with **2a** with $B(C_6F_5)_3$, *p*-fluorobenzoic acid was isolated supporting this pathway.

Since the overall activation energy for formation of carbenium species for latter two pathways (b and c) were quite similar, we compared the energy barrier for this step at various levels of theory (Table 2). In all cases, the energy barrier was slightly lower by 0.5 to 2.4 kcal mol^{-1} for the Lewis acid catalyzed pathway over the Brønsted acid catalyzed pathway. Thus, we propose that the Lewis acid catalyzed pathway predominates in this reaction. It should be noted that the reaction of $B(C_6F_5)_3$ with carboxylic acids can generate $RCO_2B(C_6F_5)_2$ and C_6F_5H.[23] It is therefore possible that an alternative Lewis acid catalyzed pathway could operate with $RCO_2B(C_6F_5)_2$ acting as the active catalyst, however *in situ* NMR studies showed little correlation between the reaction of stoichiometric $B(C_6F_5)_3$ and *p*-fluorobenzoic acid and the catalytic reaction in the ^{19}F NMR spectrum (see ESI† for details).

Lastly, we rationalized why heating is required for the reaction to take place. We hypothesized that several off-cycle catalyst resting states could exist. These include coordination of the borane to the 4-fluorobenzoic acid (**8**) side product which was found to lie 0.5 kcal mol^{-1} lower in energy than free $B(C_6F_5)_3$, and coordination of the borane to the 4-fluorobenzoic acid stabilized by the amine (**9**) which was

calculated to be 4.6 kcal mol^{-1} lower in energy than free $B(C_6F_5)_3$ (Fig. 2). This off-cycle intermediate significantly raises the total overall energy barrier for the reaction, which is in accordance with our reaction conditions.

Conclusions

In conclusion, a simple facile metal-free reaction methodology has been demonstrated for the construction of C–N bond through *N*-alkylation using catalytic amounts of $B(C_6F_5)_3$. A wide range of substrates was tested including secondary amines, carbazoles and indoles to give good to excellent yields of the *N*-alkylated products. Interestingly, when 1*H*-indole and 1*H*-pyrrole were used for the reaction, exclusive C–C cross-coupled products were obtained. DFT studies have shown that the role of the catalyst is to act as a Lewis acid to generate an electrophilic carbenium ion which is then attacked by the amine nucleophile. Overall, this work represents a mild metal-free approach to construct the C–N bond *via* *N*-alkylation reaction and adds to the range of reactions the special Lewis acid $B(C_6F_5)_3$ can catalyze.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

1 D. J. Parks and W. E. Piers, *J. Am. Chem. Soc.*, 1996, **118**, 9440–9441.
2 G. C. Welch, R. R. S. Juan, J. D. Masuda and D. W. Stephan, *Science*, 2006, **314**, 1124–1126.
3 For selected reviews on FLPs see: (*a*) A. R. Jupp and D. W. Stephan, *Trends Chem.*, 2019, **1**, 35–48; (*b*) D. W. Stephan, *Science*, 2016, **354**, aaf7229; (*c*) D. W. Stephan, *J. Am. Chem. Soc.*, 2015, **137**, 10018–10032; (*d*) D. W. Stephan and G. Erker, *Angew. Chem., Int. Ed.*, 2015, **54**, 2–44; (*e*) D. W. Stephan, *Acc. Chem. Res.*, 2015, **48**, 306–316.
4 For selected reviews see: (*a*) Y. Hoshimoto and S. Ogoshi, *ACS Catal.*, 2019, **9**, 5439–5444; (*b*) J. R. Lawson and R. L. Melen, *Inorg. Chem.*, 2017, **56**, 8627–8643; (*c*) G. Erker, *Dalton Trans.*, 2005, 1883–1890; (*d*) W. E. Piers and T. Chivers, *Chem. Soc. Rev.*, 1997, **26**, 345–354.
5 J. L. Carden, A. Dasgupta and R. L. Melen, *Chem. Soc. Rev.*, 2020, **49**, 1706–1725.
6 For the first example of $B(C_6F_5)_3$ in hydrogenation of imines see: P. A. Chase, G. C. Welch, T. Jurca and D. W. Stephan, *Angew. Chem., Int. Ed.*, 2007, **46**, 8050–8053.
7 For selected reviews see: (*a*) J. Lam, K. M. Szkop, E. Mosaferia and D. W. Stephan, *Chem. Soc. Rev.*, 2019, **48**, 3592–3612; (*b*) D. J. Scott, J. M. Fuchter and A. E. Ashley, *Chem. Soc. Rev.*, 2017, **46**, 5689–5700.
8 For selected articles see: (*a*) S. Tussing, K. Kaupmees and J. Paradies, *Chem. – Eur. J.*, 2016, **22**, 7422–7426; (*b*) S. Li, G. Li, W. Meng and H. A. Du, *J. Am. Chem. Soc.*, 2016, **138**, 12956–12962; (*c*) N. Gandhamsetty, J. Jeong, J. Park, S. Park and S. Chang, *J. Org. Chem.*, 2015, **80**, 7281–7287.
9 For examples see: (*a*) A. Maity, B. L. Frey, N. D. Hoskinson and D. C. Powers, *J. Am. Chem. Soc.*, 2020, **142**, 4990–4995; (*b*) O. I. Afanasyev, E. Kuchuk, D. L. Usanov and D. Chusov, *Chem. Rev.*, 2019, **119**, 11857–11911; (*c*) A. Ruffoni, F. Juliá, T. D. Svejstrup, A. J. McMillan, J. J. Douglas and D. Leonori, *Nat. Chem.*, 2019, **11**, 426–433; (*d*) Z. Wu, S. Du, G. Gao, W. Yang, X. Yang, H. Huanga and M. Chang, *Chem. Sci.*, 2019, **10**, 4509–4514; (*e*) Y. Liang, X. Zhang and D. W. C. MacMillan, *Nature*, 2018, **559**(7712), 83–88; (*f*) P. Ruiz-Castillo and S. L. Buchwald, *Chem. Rev.*, 2016, **116**, 12564–12649; (*g*) D. Chusov and B. List, *Angew. Chem., Int. Ed.*, 2014, **53**, 5199–5201.
10 For selected examples see: (*a*) K. Murugesan, Z. Wei, V. G. Chandrashekhar, H. Neumann, A. Spannenberg, H. Jiao, M. Beller and R. V. Jagadeesh, *Nat. Commun.*, 2019, **10**, 5443; (*b*) T. Senthamarai, K. Murugesan, J. Schneidewind, N. V. Kalevaru, W. Baumann, H. Neumann, P. C. J. Kamer, M. Beller and R. V. Jagadeesh, *Nat. Commun.*, 2018, **9**, 4123; (*c*) S. Raoufmoghaddam, *Org. Biomol. Chem.*, 2014, **12**, 7179–7193; (*d*) A. F. Abdel-Magid and S. J. Mehrman, *Org. Process Res. Dev.*, 2006, **10**, 971–1031; (*e*) S. Gomez, J. A. Peters and T. Maschmeyer, *Adv. Synth. Catal.*, 2002, **344**, 1037–1057.
11 (*a*) S. Bhunia, G. G. Pawar, S. V. Kumar, Y. Jiang and D. Ma, *Angew. Chem., Int. Ed.*, 2017, **56**, 16136–16179; (*b*) J. Zheng, T. Roisnel, C. Darcel and J.-B. Sortais, *ChemCatChem*, 2013, **5**, 2861–2864; (*c*) G. B. Giovenzana, D. Imperio, A. Penoni and G. Palmisano, *Beilstein J. Org. Chem.*, 2011, **7**, 1095–1099.
12 (*a*) Y. Hoshimoto, T. Kinoshita, S. Hazra, M. Ohashi and S. Ogoshi, *J. Am. Chem. Soc.*, 2018, **140**, 7292–7300; (*b*) É. Dorko, M. Szabo, B. Kotai, I. Papai, A. Domjan and T. Soos, *Angew. Chem., Int. Ed.*, 2017, **56**, 9512–9516.
13 (*a*) V. Fasano and M. J. Ingleson, *Chem. – Eur. J.*, 2017, **23**, 2217–2224; (*b*) L. C. Wilkins, J. L. Howard, S. Burger, L. Frentzel-Beyme, D. L. Browne and R. L. Melen, *Adv. Synth. Catal.*, 2017, **359**, 2580–2584; (*c*) V. Fasano, J. E. Radcliffe and M. J. Ingleson, *ACS Catal.*, 2016, **6**, 1793–1798; (*d*) M. R. Tiddens, R. J. M. Klein Gebbink and M. Otte, *Org. Lett.*, 2016, **18**, 3714–3717; (*e*) J. M. Blackwell, E. R. Sonmor, T. Scoccitti and W. E. Piers, *Org. Lett.*, 2000, **2**, 3921–3923.
14 S.-S. Meng, X. Tang, X. Luo, R. Wu, J.-L. Zhao and A. S. C. Chan, *ACS Catal.*, 2019, **9**, 8397–8403.
15 M. M. Guru, P. R. Thorve and B. Maji, *J. Org. Chem.*, 2020, **85**, 806–819.

16 For selected examples see: (*a*) C. E. Meyet, C. J. Pierce and C. H. Larsen, *Org. Lett.*, 2012, **14**, 964–967; (*b*) X. Xu and X. Li, *Org. Lett.*, 2009, **11**, 1027–1029; (*c*) V. K.-Y. Lo, Y. Liu, M.-K. Wong and C.-M. Che, *Org. Lett.*, 2006, **8**, 1529–1532.

17 V. Sumerin, F. Schulz, M. Nieger, M. Leskel, T. Repo and B. Rieger, *Angew. Chem., Int. Ed.*, 2008, **47**, 6001–6003.

18 For selected examples see: (*a*) M. Blaess, N. Bibak, R. A. Claus, M. Kohl, G. A. Bonaterra, R. Kinscherf, S. Laufer and H.-P. Deigner, *Eur. J. Med. Chem.*, 2018, **153**, 73–104; (*b*) D. Addla, S.-Q. Wen, W.-W. Gao, S. K. Maddili, L. Zhang and C.-H. Zhou, *Med. Chem. Commun.*, 2016, **7**, 1988–1994; (*c*) Y. Zhang, V. K. R. Tangadanchu, R. R. Y. Bheemanaboina, Y. Cheng and C.-H. Zhou, *Eur. J. Med. Chem.*, 2018, **155**, 579–589.

19 (*a*) J. M. Ahn, T. S. Ratani, K. I. Hannoun, G. C. Fu and J. C. Peters, *J. Am. Chem. Soc.*, 2017, **139**, 12716–12723; (*b*) A. C. Bissember, R. J. Lundgren, S. E. Creutz, J. C. Peters and G. C. Fu, *Angew. Chem., Int. Ed.*, 2013, **52**, 5129–5133; (*c*) R. N. Salvatore, C. H. Yoon and K. W. Jung, *Tetrahedron*, 2001, **57**, 7785–7811.

20 A. Kaga, K. Nogi and H. Yorimitsu, *Chem. – Eur. J.*, 2019, **25**, 14780–14784.

21 A. Dasgupta, R. Babaahmadi, B. Slater, B. F. Yates, A. Ariafard and R. L. Melen, *Chem*, 2020, **6**, 2364–2381.

22 S. Mitu and M. C. Baird, *Can. J. Chem.*, 2006, **84**, 225–232.

23 S. Mitu and M. C. Baird, *Organometallics*, 2006, **25**, 4888–4896.

