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Borane catalysed cyclopropenation of arylacetylenes†

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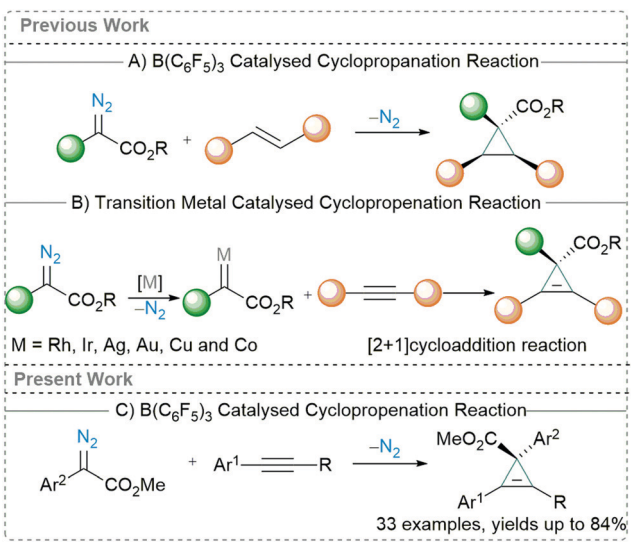
Triarylboranes have gained substantial attention as catalysts for C–C bond forming reactions due to their remarkable catalytic activities. Herein, we report $B(C_6F_5)_3$ catalysed cyclopropenation of a wide variety of arylacetylenes using donor–acceptor diazoesters. A mild reaction protocol has been developed for the synthesis of functionalised cyclopropenes (33 examples) in good to excellent yields.

Transition metal catalysed C–C bond forming reactions overwhelm the chemical literature.[1] Although the use of precious transition metal catalysts has achieved immense success, metal impurities in the final compounds are often unavoidable. This is particularly significant when considering products taken into the body where toxic metal contamination must be kept to a minimum. Over the last few years, main group-based catalysts have been extensively investigated as substantial alternative to the precious transition metals.[2] More precisely, the Lewis acidic triarylboranes[3] have found multitude applications towards C–C bond forming reactions.[4,5] The presence of empty d-orbitals in transition metals allows them to lend or remove electrons from the coupling partners, and thus can be employed as a catalyst for wide variety of reactions.[6] Likewise, the empty p-orbital of the central boron atom of Lewis acids renders them strongly electrophilic in nature and therefore they can readily react with Lewis bases by accepting a lone pair of electrons.[7] Relating to this, an important initial contribution made by Zhang in 2016,[8] showed that $B(C_6F_5)_3$ could act as a catalyst for the *ortho*-selective C–H alkylation of unprotected phenols with α-aryl α-diazoesters. The mechanism for this reaction was revealed computationally to be the activation of the diazoester through O → B adduct formation to generate carbenes.[9] Therefore, by using diazoester precursors, a carbene transfer reactions can be carried out using $B(C_6F_5)_3$ as a catalyst.[10]

Carbene transfer reactions are one of the most fundamental reactions in organic synthesis and widespread studies have been conducted to explore the synthetic utility of carbenes for making a variety of novel compounds.[11] Recently, we[12] and Wilkerson-Hill[13] observed that catalytic amounts of $B(C_6F_5)_3$ enable the cyclopropanation reactions of styrenes (Scheme 1A) using α-aryl α-diazoesters. This exciting outcome motivated us to investigate this reactivity further to see if arylacetylenes could also be used as substrates in reactions with α-aryl α-diazoesters using $B(C_6F_5)_3$ as a catalyst. This reaction, cyclopropenation, has been largely investigated using precious transition metals, such as Rh,[14] Ir,[15] Ag,[16] and Au.[17] Nonetheless, the use of non-precious transition metals, including Cu[18] and Co[19] (Scheme 1B), have also been reported. Typically, in the presence of a metal catalyst, diazoesters afford a metal-carbenoid species



Scheme 1 General approach for cyclopropenation/cyclopropanation reaction.

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which then readily undergoes a [2+1] cycloaddition with an arylacetylene to form the 3-membered carbocycle. Recently, Koenigs *et al.* revealed that cyclopropenation of arylacetylenes using α-aryl α-diazoesters is also possible by employing visible light (blue light; 470 nm).[20]

We initiated our studies into the cyclopropenation reaction using phenylacetylene (1.3 equiv.) and α-aryl α-diazoester **1a** (1 equiv.) as model substrates (Table 1). The reaction between **1a** and phenylacetylene showed no formation of the cyclopropene product (**3i**) in absence of any catalyst at both ambient temperature and at reflux in CH_2Cl_2 (Table 1, entries 1 and 2). Addition of $BF_3{\cdot}OEt_2$ as a Lewis acid catalyst (20 mol%) also showed no formation of the desired carbocycle (**3i**) and only decomposition of the diazo compound into the homocoupled product was observed (Table 1, entry 3). 40 mol% of the Brønsted acid (TfOH, triflic acid) also failed to promote the reaction (Table 1, entry 4). When 20 mol% $B(C_6F_5)_3$ was employed for the reaction, no product formation was observed at ambient temperature, however reaction at 45 °C afforded **3i** in 48% yield after 24 h (Table 1, entries 5 and 6). Switching the solvent from CH_2Cl_2 to $C_2H_4Cl_2$ slightly improved the yield of **3i** to 57% but still did not give satisfactory results (Table 1, entry 7). Increasing the reaction temperature further to 70 °C however was detrimental to the reaction leading to the formation of a complicated reaction mixture and the isolation of the desired product **3i** failed (Table 1, entry 8). Reducing the catalytic loading of $B(C_6F_5)_3$ from 20 mol% to 10 mol% showed improvement in the yield of **3i** to 65%. However, reducing catalytic loadings further to 5 mol% gave lower yields of the desired carbocycle **3i** of 32% (Table 1, entries 9 and 10). Additionally, we tested other triarylfluoroborane catalysts for the cyclopropenation reaction and we observed that although 10 mol% $(2,4,6\text{-}F_3C_6H_2)_3B$ [$(2,4,6\text{-}Ar^F)_3B$] afforded **3i** in poor yields of 28%, the Lewis acidic boranes $(3,4,5\text{-}F_3C_6H_2)_3B$ [$(3,4,5\text{-}Ar^F)_3B$] and $(3,5\text{-}CF_3C_6H_3)_3B$ [$(3,5\text{-}CF_3\text{-}Ar^F)_3B$] completely failed to catalyse the reaction, and no product formation was detected (Table 1, entries 11–13).

Interestingly, the yield of **3i** was further improved to 75% when we used a slight excess of **1a** (1.3 equiv.) (Table 1, entry 14). Thus our optimised reaction conditions were a 1 : 1.3 stoichiometric ratio of phenylacetylene : **1a** and carrying out the reaction in $C_2H_4Cl_2$ at 50 °C using 10 mol% $B(C_6F_5)_3$.

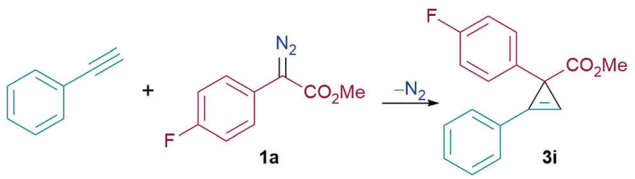
With the optimised conditions in hand, we then explored the scope of the reaction with various α-aryl α-diazoesters (**1**) and arylacetylenes (Scheme 2). Firstly, terminal arylacetylenes were explored bearing electron-withdrawing, neutral, and electron releasing groups, for the cyclopropenation reaction with different α-aryl α-diazoesters (**1a–g**) to generate the products **3a–3ae** in 30–84% yields. Of these, products **3n** and **3o** could be recrystallised by vapour diffusion from CH_2Cl_2/pentane and their structures elucidated by single crystal X-ray diffraction (Fig. 1). Lower yields were observed with strongly electron withdrawing (*p*-CF_3) or electron releasing (*p*-OMe, *p*-Me) arylacetylenes giving **3a,b**, **u–w** in less than 50% yield. Another observation was that the *p*-F or *o*-F substituted α-aryl α-diazoesters (**1a** and **1b** respectively) gave better yields than the *p*-OMe substituted α-aryl α-diazoester (**1g**) when combined with the same arylacetylene. Interestingly, the vinyl diazoacetate (methyl (*E*)-2-diazo-4-phenylbut-3-enoate, (**1h**), symmetrical diisopropyl 2-diazomalonate (**1i**), diazodimedone (**1j**), ethyl 2-diazoacetate (**1k**), and methyl 2-diazo-2-(3-fluorophenyl)acetate (**1l**) failed to react with arylacetylenes to afford the desired carbocycles. Aliphatic terminal acetylenes including *tert*-butylacetylene and hex-1-yne, as well as ethynyltrimethylsilane were also unsuccessful for the reaction.

We then examined the reactivities of the internal alkynes in the cyclopropenation reaction with limited success. However, when 1-phenyl-1-propyne and hex-1-ynylbenzene (**2a**) were reacted with **1c**, the desired carbocycles **3af** and **3ag** were isolated in poor yields of 15% and 26% respectively. Other internal alkynes such as 1,2-diphenylethyne, trimethyl(phenylethynyl)silane, and 1-(prop-1-yn-1-yl)-4-(trifluoromethyl)benzene failed to react completely.

Following this we investigated the selectivity of the carbocycle formation (cyclopropanation *versus* cyclopropenation) when both alkene and alkyne functionalities are present. For this competition study, the intramolecular alkene/alkyne compounds 1-ethynyl-4-vinylbenzene (**2b**) and 1-ethynyl-2-vinylbenzene (**2c**) were tested in the $B(C_6F_5)_3$ catalysed reaction with **1a**. In both cases cyclopropanation was favoured over cyclopropenation giving the cyclopropane carbocycle as a single diastereoisomer in 88% (**3ah**) and 41% (**3ai**) yields, respectively.

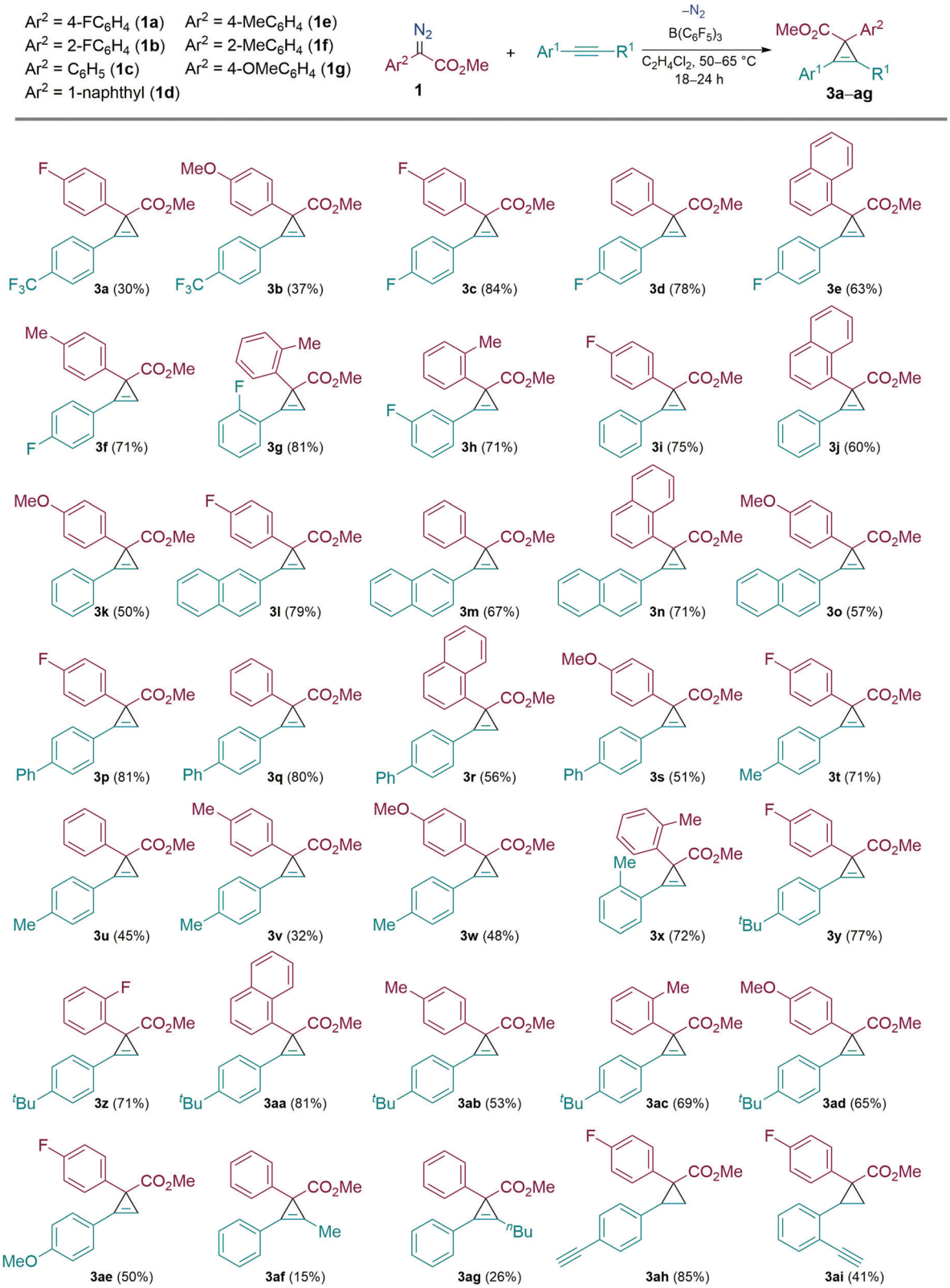
Unfortunately, attempts to synthesise 3-membered heterocycles from the insertion of the carbene into C=O, C=N or C≡N bonds failed. Using the optimised reaction conditions,

Table 1 Optimisation of the reaction conditions



Entry	Catalyst	Loading (mol%)	Solvent	Temp. (°C)	Time (h)	Yield[a] (%)
1	None	—	CH_2Cl_2	r.t.	24	—
2	None	—	CH_2Cl_2	45	24	—
3	$BF_3{\cdot}OEt_2$	20	CH_2Cl_2	45	24	—
4	TfOH	40	CH_2Cl_2	45	24	—
5	$B(C_6F_5)_3$	20	CH_2Cl_2	r.t.	24	—
6	$B(C_6F_5)_3$	20	CH_2Cl_2	45	24	48
7	$B(C_6F_5)_3$	20	$C_2H_4Cl_2$	50	22	57
8	$B(C_6F_5)_3$	20	$C_2H_4Cl_2$	70	18	—
9	$B(C_6F_5)_3$	10	$C_2H_4Cl_2$	50	24	65
10	$B(C_6F_5)_3$	5	$C_2H_4Cl_2$	50	28	32
11	$(2,4,6\text{-}Ar^F)_3B$	10	$C_2H_4Cl_2$	50	24	28
12	$(3,4,5\text{-}Ar^F)_3B$	10	$C_2H_4Cl_2$	40	24	—
13	$(3,5\text{-}CF_3\text{-}Ar^F)_3B$	10	$C_2H_4Cl_2$	50	24	—
14	$B(C_6F_5)_3$[b]	10	$C_2H_4Cl_2$	50	24	75

All the reactions were carried out on a 0.1 mmol scale. **1a** (1 equiv.), phenylacetylene (1.3 equiv.), and 1.5 mL solvent. [a] Reported yields are isolated. [b] Phenylacetylene (1 equiv.), **1a** (1.3 equiv.), and 1.5 mL of solvent.



Scheme 2 Substrate scope for the cyclopropenation of arylacetylenes. Yields reported are isolated. All the reactions were carried out in 0.1 mmol scale, 10 mol% $B(C_6F_5)_3$ was used. **1** (1.3 equiv.), phenylacetylene (1 equiv.), and 1.5 mL of solvents were used.

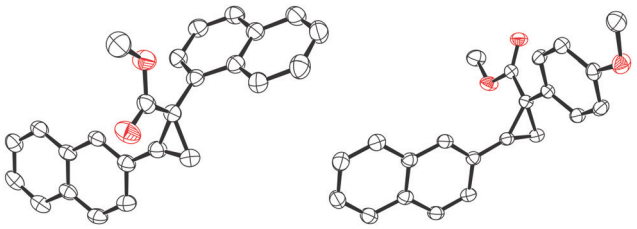


Fig. 1 Solid-state structure of compound **3n** (left) and **3o** (right). Thermal ellipsoids drawn at 50% probability. Carbon: black; oxygen: red. H atoms omitted for clarity.

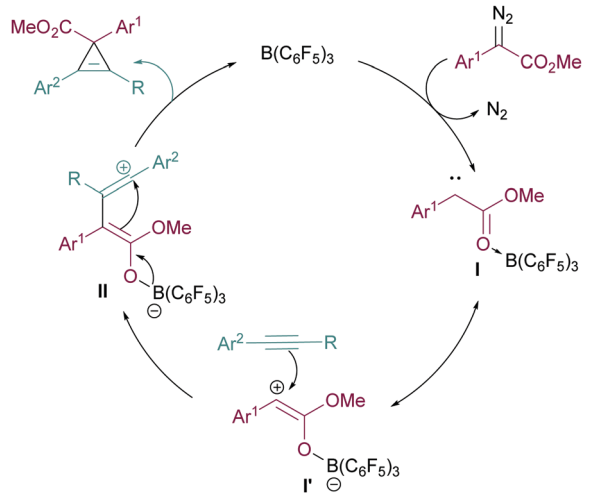


Fig. 2 Proposed reaction mechanism for the cyclopropenation reaction.

the reaction between benzaldehyde and **1c** was examined with the goal to produce the corresponding epoxide. However, multinuclear spectroscopic data of the isolated compound confirmed the formation of methyl 3-oxo-2,3-diphenylpropanoate (see ESI†) formed from the homologation of benzaldehyde with the diazo compound (Roskamp–Feng reaction).[21]

We propose the mechanism of the cyclopropenation reaction to proceed in a similar manner to that for the cyclopropanation reaction reported in our previous studies[12] (Fig. 2). Initially, the Lewis acidic $B(C_6F_5)_3$ binds effectively with the ester functionality of the α-aryl α-diazoester **1**. This facilitates loss of N_2 forming the highly electron deficient intermediate **I** and its resonance form **I′**. Subsequently the reactive carbene intermediate can then react with the nucleophilic arylacetylene forming intermediate **II**. The generation of the carbocationic centre in **II** explains the need for arylacetylenes in the reaction to stabilise this intermediate. Finally, attack of the boron enolate onto the carbocation in **II** then generates the product and regenerates the catalyst.

In conclusion, a metal-free mild reaction protocol has been developed for the cyclopropenation of alkynes using diazo compounds. Our studies demonstrate that catalytic amounts of $B(C_6F_5)_3$ readily react with α-aryl α-diazoesters to promote the carbene transfer reaction when reacted with arylacetylenes generating the desired 3-membered carbocycle. A wide range of substrates were investigated and good to excellent yields of the cyclopropenated products were obtained. This methodology adds to the ever-increasing range of reactions that the Lewis acid $B(C_6F_5)_3$ can catalyse.

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Conflicts of interest

The authors declare no conflict of interest.

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