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(C₆F₅)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. 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. More precisely, the Lewis acidic triarylboranes have found multitude applications towards C–C bond forming reactions. 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. 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. Relating to this, an important initial contribution made by Zhang in 2016 showed that B(C₆F₅)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. Therefore, by using diazoester precursors, a carbene transfer reactions can be carried out using B(C₆F₅)₃ as a catalyst.

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. Recently, we and Wilkerson-Hill observed that catalytic amounts of B(C₆F₅)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(C₆F₅)₃ as a catalyst. This reaction, cyclopropenation, has been largely investigated using precious transition metals, such as Rh, Ir, Ag, and Au. Nonetheless, the use of non-precious transition metals, including Cu and Co (Scheme 1B), have also been reported. Typically, in the presence of a metal catalyst, diazoesters afford a metal-carbenoid species...
which then readily undergoes a [2+1] cycloaddition with an ary lacetylene to form the 3-membered carbocycle. Recently, Koenigs et al. revealed that cyclopropanation of arylacetylenes using z-aryl z-diazoesters is also possible by employing visible light (blue light; 470 nm).20

We initiated our studies into the cyclopropanation reaction using phenylacetylene (1.3 equiv.) and z-aryl z-diazoester 1a (1 equiv.) as model substrates (Table 1). The reaction between 1a and phenylacetylene showed no formation of the cyclopropane product (3i) in absence of any catalyst at both ambient temperature and at reflux in CH₂Cl₂ (Table 1, entries 1 and 2). Addition of BF₃·OEt₂ 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 Bronsted acid (TfOH, triflic acid) also failed to promote the reaction (Table 1, entry 4). When 20 mol% B(C₆F₅)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 CH₂Cl₂ to C₂H₄Cl₂ 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(C₆F₅)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 triarylfuoroborane catalysts for the cyclopropanation reaction and we observed that although 10 mol% (2,4,6-F₃C₆H₃)₃B [(2,4,6-ArF)₃B] afforded 3i in poor yields of 28%, the Lewis acidic boranes (3,4,5-F₃C₆H₂)₃B [(3,4,5-ArF)₃B] and (3,5-Cl,C₆H₃)₃B [(3,5-ClF₂-ArF)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 C₂H₄Cl₂ at 50 °C using 10 mol% B(C₆F₅)₃.

With the optimised conditions in hand, we then explored the scope of the reaction with various z-aryl z-diazoesters (1) and arylacetylenes (Scheme 2). Firstly, terminal arylacetylenes were explored bearing electron-withdrawing, neutral, and electron releasing groups, for the cyclopropanation reaction with different z-aryl z-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 CH₂Cl₂/pentane and their structures elucidated by single crystal X-ray diffraction (Fig. 1). Lower yields were observed with strongly electron withdrawing (p-CF₃) 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 z-aryl z-diazoesters (1a and 1b) respectively gave better yields than the p-OMe substituted z-aryl z-diazoester (1g) when combined with the same arylacetylene. Interestingly, the vinyl diazoacetate (methyl (E)-2-diazo-4-phenylbut-3-enoate, (1h), symmetrical diisopropyl 2-diazaomalonate (1i), diazidomedone (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 cyclopropanation 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-diphenylethylene, 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 cyclopropanation) when both alkene and alkyne functionalities are present. For this competition study, the intramolecular alkene/alkyne compounds 1-ethyl-4-vinylbenzene (2b) and 1-ethyl-2-vinylbenzene (2c) were tested in the B(C₆F₅)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,
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(C₆F₅)₃ was used. 1 (1.3 equiv.), phenylacetylene (1 equiv.), and 1.5 mL of solvents were used.
of substrates were investigated and good to excellent yields of the cyclopropanated products were obtained. This methodology adds to the ever-increasing range of reactions that the Lewis acid B(C₆F₅)₃ can catalyze.

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Conflicts of interest

The authors declare no conflict of interest.

Notes and references