Ruthenium Complex-Catalysed Heck Reactions of Areneboronic Acids; Mechanism, Synthesis and Halide Tolerance

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Abstract: Ruthenium-arene complexes can act as efficient catalysts for the coupling of areneboronic acids with electrophilic alkenes. The chemoselectivity is completely different from palladium coupling, with full tolerance for halogen in the arene. NMR and ES-MS studies have been carried out to elucidate the reaction pathway

Keywords: areneboronic acids; catalysis; ES-MS; Heck reaction; NMR; ruthenium

Introduction

In the late 1960s, R. F. Heck[1] published the coupling reaction between arylmercuric compounds and alkenes catalysed by transition metals, introducing the reaction that would ultimately bear his name. Typically, phenylmercuric chloride reacted with methyl acrylate in the presence of an equivalent of Li_2PdCl_4 to give methyl cinnamate in good yield. It was indicated that Hg-Pd transmetallation was a likely route. Most of the original examples were stoichiometric, since the reaction between a nucleophile and an alkene leading to a new substituted alkene must lead to formal reduction of the palladium catalyst. Notably for the present work, this early publication also indicated that $RuCl_3$ could also promote the reaction, albeit in low yield. The constraint on catalysis was recognized in the first papers, and examples where the palladium is reoxidised by $CuCl_2$ or air allowed up to 50 catalytic turnovers based on palladium salt. An initial example of the complementary protocol, namely the palladium-promoted electrophilic arylation of an alkene, was described by Mizoroki.[2] It is intrinsically catalytic because the oxidation state of the palladium is maintained. The procedure is frequently described, especially but unsurprisingly by Japanese workers, as the "Mizoroki–Heck" reaction. In its modern form, the Mizoroki–Heck reaction is the coupling reaction between an alkene and an aryl or vinyl halide or triflate under palladium complex catalysis to give a substituted alkene. Largely through Heck's early efforts,[3] this reaction has become a standard part of the armoury of synthetic organic chemistry and has been substantially reviewed.[4]

Given the ubiquitous application of palladium complexes in coupling catalysis, we were interested to learn whether ruthenium complexes, intrinsically less expensive but less widely explored in organic synthesis, could fulfil a similar role. Several catalytic reactions seem to depend on the C–C bond-forming transfer of an organic entity from ruthenium to an alkene, encouraging the possibility. The most conspicuous example arises from Murai's demonstration that directed C–H activation by simple Ru phosphine complexes leads to an organoruthenium intermediate which can then be transferred to an alkene.[5] The overall process is reductive, leading to the formal catalytic addition of Ar–H (or its vinylic equivalent) to an alkene. An oxidative variant that does not require a directing group and leads to alkene substitution, but which occurs only under forcing conditions, has been described.[6] Ruthenium complexes can catalyse an analogue of the Baylis–Hillman reaction,[7] the addition of alkynes to alkenes,[8] or Michael addition of dimethyl malonate,[9] by procedures that involve C–H activation. In particular, the alkyne activation chemistry has been applied to good effect through the work of Trost and co-workers.[10] These diverse procedures are summarised in Scheme 1.

Before our preliminary communication on ruthenium-catalysed oxidative Heck reactions,[11] there had been one report of a conventional Heck-type procedure in which the coupling reaction between vinyl halides and electron-poor olefins was carried out in good yield in the presence of (COD)(COT)Ru.[12] Since that publication, catalysis of Heck reactions by ruthenium black under very simple conditions has been demonstrated.[13] Further examples of oxidative Heck reactions involving palladium or rhodium have appeared.[14]

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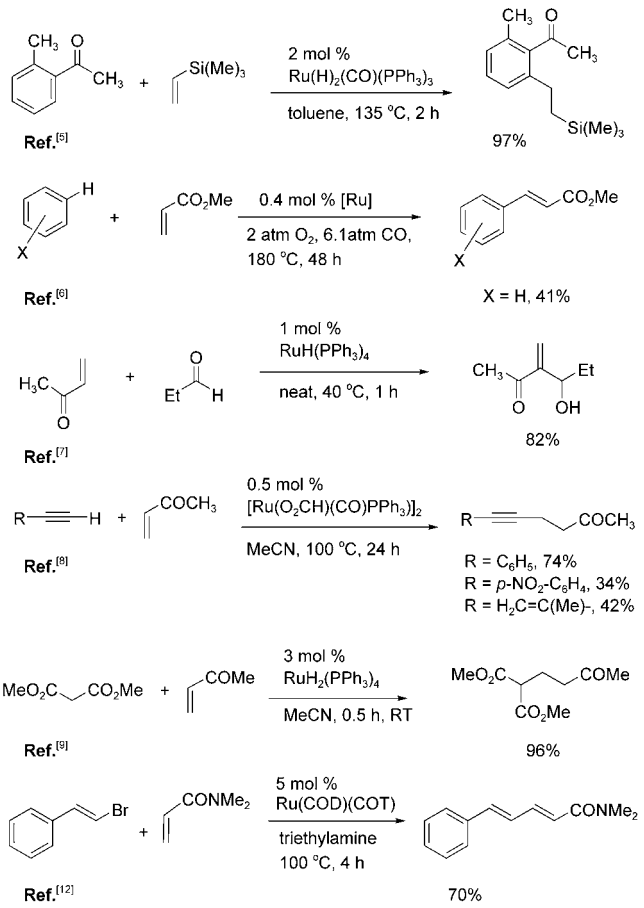
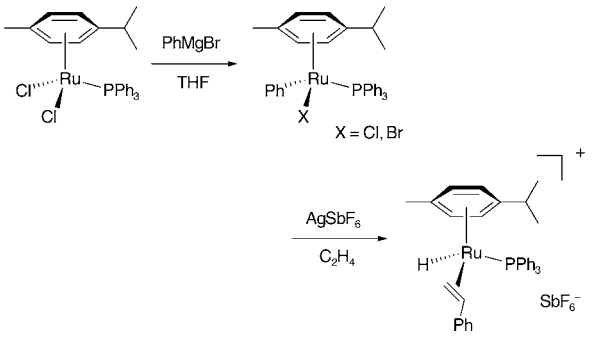


Scheme 1. Prior examples of Ru-catalysed C–C couplings.



Scheme 2. Easy aryl migration/H elimination described in Ref.[15]

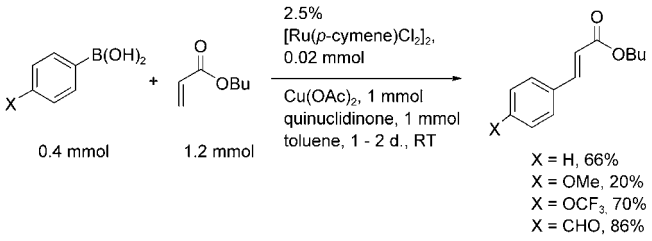
Discussion

Development of a Ruthenium-Catalysed Reaction

Having decided that ruthenium-catalysed coupling was both feasible and desirable, two specific sets of precedent guided our approach. The first was due to Faller and Chase, as shown in Scheme 2.[15] The C–C bond-forming step in their sequence is a clear model for ruthenium Heck chemistry. Thus, (*p*-cymene)(PPh_3)$RuCl_2$ reacted with PhMgBr by single displacement. The halide was removed as its silver salt in the presence of ethene to give the alkene hydride complex, which exists as a pair of diastereomers. An aryl-ethene complex was not detected, although it is a likely intermediate (Scheme 2). Further direct precedent arises from Pfeffer's group, who demonstrate the reactivity of cycloruthenated complexes towards alkene insertion.[16]

These observations demonstrate that a C–Ru bond can indeed be formed by nucleophilic displacement, and that the alkene insertion step is straightforward. In tandem with this, there have been sporadic observations of catalytic alkene coupling with nucleophiles. The most conspicuous example is the rhodium-catalysed asymmetric arylation of α,β-unsaturated carbonyl compounds, first demonstrated by Hayashi and Miyaura.[17] Since this results in ArH addition to the alkene, there is no change in oxidation state of rhodium through the catalytic cycle. In a related case, Lautens has shown that either Ar-H addition or formal displacement of vinyl-H by Ar can occur depending on the structure of the reactant.[18] In palladium catalysis, the best precedent is due to Uemura, who showed that arylboronic acids react with alkenes to give the product expected from a Heck reaction.[19] No re-oxidant was reported in this case (adventitious air?) but the utility of added oxidant has been confirmed in closely related reactions carried out more recently.[14]

The first aim of the present project was to determine whether mild carbon nucleophiles were capable of aryl transfer to ruthenium. Combining $SnBu_3Ph$ with (*p*-cymene)(PPh_3)$RuCl_2$ in dry toluene gave a dark yellow solution which on work-up yielded (*p*-cymene)-(PPh_3)RuClPh as a crystalline yellow solid in 50% yield.[13,20] Likewise, benzeneboronic acid and (*p*-cymene)(PPh_3)$RuCl_2$ were combined in THF in the presence of CsF to give the same product as a yellow solid in 69% yield. Arylboronic acids are more readily available, easier to handle and less toxic than aryltin reagents, making this reaction the preferred approach. In a preliminary experiment, the feasibility of catalysis was demonstrated by reacting $PhB(OH)_2$ with methyl acrylate and Et_3N, in the presence of 0.5 equivalents of (*p*-cymene)(PPh_3)$RuCl_2$. Methyl cinnamate was formed in 28% yield after 24 h at 80 °C. This encouraged further efforts and especially inclusion of $CuCl_2$ as a reoxidant. This led to slow but definable catalysis for the reaction between $PhB(OH)_2$ and butyl acrylate in THF (Scheme 3). Although rather primitive, this represented the first example of a Ru-catalysed oxidative Heck reaction with catalytic turnover. In an assay of reaction conditions involving high-throughput screening (HTPS),[21] it was noted that the phosphine-free complex [(*p*-cymene)$RuCl_2$]$_2$ induced catalytic turnover at ambient temperature, but that Cu(II) remained the preferred oxidizing agent. It was also established through ^{1}H NMR studies that both the dimeric halide and (*p*-cymene)



Scheme 3. The preferred conditions for Ru Heck reactions.

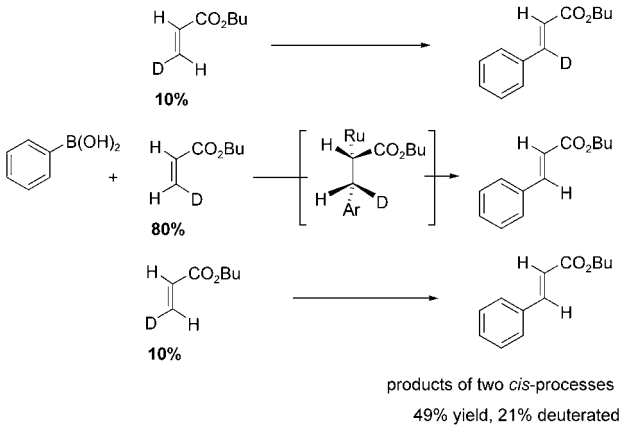
$(PPh_3)RuCl_2$ were responsive to coordinating solvents, with reversible bridge-breaking or phosphine dissociation observed in DMSO and methanol. The aryl complex $ClRuPh(PPh_3)(p\text{-cymene})$ was not altered in these solvents, however. This suggested using the phosphine-free complex as catalyst and a considerable improvement in reactivity was observed, indicating that PPh_3 is in fact an inhibitor of catalytic turnover. The HPTS studies additionally appeared to suggest a unique role for the ruthenium-arene complexes. There are precedents in the literature for the liberating of a coordination site by ring slippage of Ru arenes ($\eta^6-\eta^4$) and this would be expected to facilitate the areneboronic acid addition step.[22]

Finally a systematic assay of bases was carried out, providing the conclusion that quinuclidine, or better its 3-hydroxy or 3-keto derivative, is superior to triethylamine. Under these conditions a satisfactory rate of turnover can be achieved under ambient conditions (Scheme 3), and no further optimisation experiments were attempted.

Mechanistic Studies

Stereoselectivity

One of the main planks used to establish the mechanism of the Heck reaction is the demonstrated stereoselectivity involving *cis*-addition of Pd–Ar and *cis*-elimination of Pd–H. This was first demonstrated by Heck,[23] and reinforced by many later observations although occasional *trans*-elimination of Pd–H has been observed.[24] In order to explore the specificity of the ruthenium-catalysed Heck reaction, the method outlined by Hill and Newkome[25] was modified to give stereoselectively ^2H-labelled butyl acetate. By accurate NMR simulation, the product from the sequence of Scheme 4 was an 8:1:1 mixture of isotopomers, as indicated. The product was subjected to the standard conditions of Ru catalysis and the product butyl cinnamate isolated. It can be seen from the ensuing NMR spectrum that the vinyl signal at 7.72 ppm is reduced in intensity to 0.79 H relative to the undeuterated compound and there is some residual deuterium, revealed by a ^2H-coupled signal at 6.46 ppm under the second vinylic proton, accounting



Scheme 4. Conditions: 2.5 mol % $[Ru(p\text{-cymene})Cl_2]_2$, $Cu(OAc)_2$, quinuclidinone, THF, 24 h, room temperature. Butyl acrylate was present in excess over benzeneboronic acid, allowing the possibility of isotopic fractionation in the starting material and enhancing the deuterium content of the product.

for the missing 21%. A perfectly stereospecific *cis*-addition/cis-elimination process (or, in principle, a *trans*-addition, *trans*-elimination process) would lead to 10% retention of deuterium, and the larger amount indicates imperfect stereoselectivity, e.g., by competing 1,2-migration in the alkylruthenium intermediate. An unselective reaction would lead to a bias towards retention of deuterium, assuming a normal primary kinetic isotope effect. In the absence of phenylboronic acid, there is no scrambling or loss of deuterium observed under the reaction conditions. This indicates that the predominant pathway in ruthenium catalysis parallels that already established for palladium catalysis.

NMR Analysis of Reactive Intermediates

The implication of observations to date is that transmetallation from boron to ruthenium occurs and that the species formed reacts with alkene to form the desired product. Addition of $PhB(OH)_2$ to a solution of $[(p\text{-cymene})RuCl_2]_2$ and Et_3N in $CDCl_3$ led to changes in the ^1H NMR spectrum (especially in Ar-H of cymene) consistent with the formation of a phenylruthenium species. On addition of PPh_3 and work-up, the described phosphine complex, $(p\text{-cymene})(PPh_3)RuClPh$, was characterised. Likewise, if methyl acrylate was added to the solution containing a phenylruthenium species, methyl cinnamate was observed in the spectrum within 30 seconds. In a separate experiment, the phenylruthenium intermediate was generated and both methyl acrylate and *p*-methoxyphenylboronic acid were added simultaneously. The only product formed was methyl cinnamate; the uncomplexed arylboronic acid did not participate.

Further evidence for transmetallation was obtained by the reaction sequence shown in Figure 1, derived

when 2,6-difluorophenylboronic acid was reacted with the standard Ru complex in CD_3CN. In this case the σ-aryl complex gave rise to a broad signal at -85 ppm as the main component in the ^{19}F NMR spectrum, that separated into two distinct ^{19}F signals at $-35\,^{\circ}C$, coalescence being observed at around $-5\,^{\circ}C$. This indicates the formation of a metal-aryl with restricted rotation about the Ru–C bond, providing two distinct magnetic environments for the two ^{19}F nuclei. From the application of standard formulae at the coalescence temperature, the rotation barrier is 49 $kJ \cdot mol^{-1}$.

ES-MS Analysis of Reactive Intermediates

In order to study the transmetallation step, the reacting components including *p*-bromophenylboronic acid were combined in acetonitrile. After 30 minutes, the

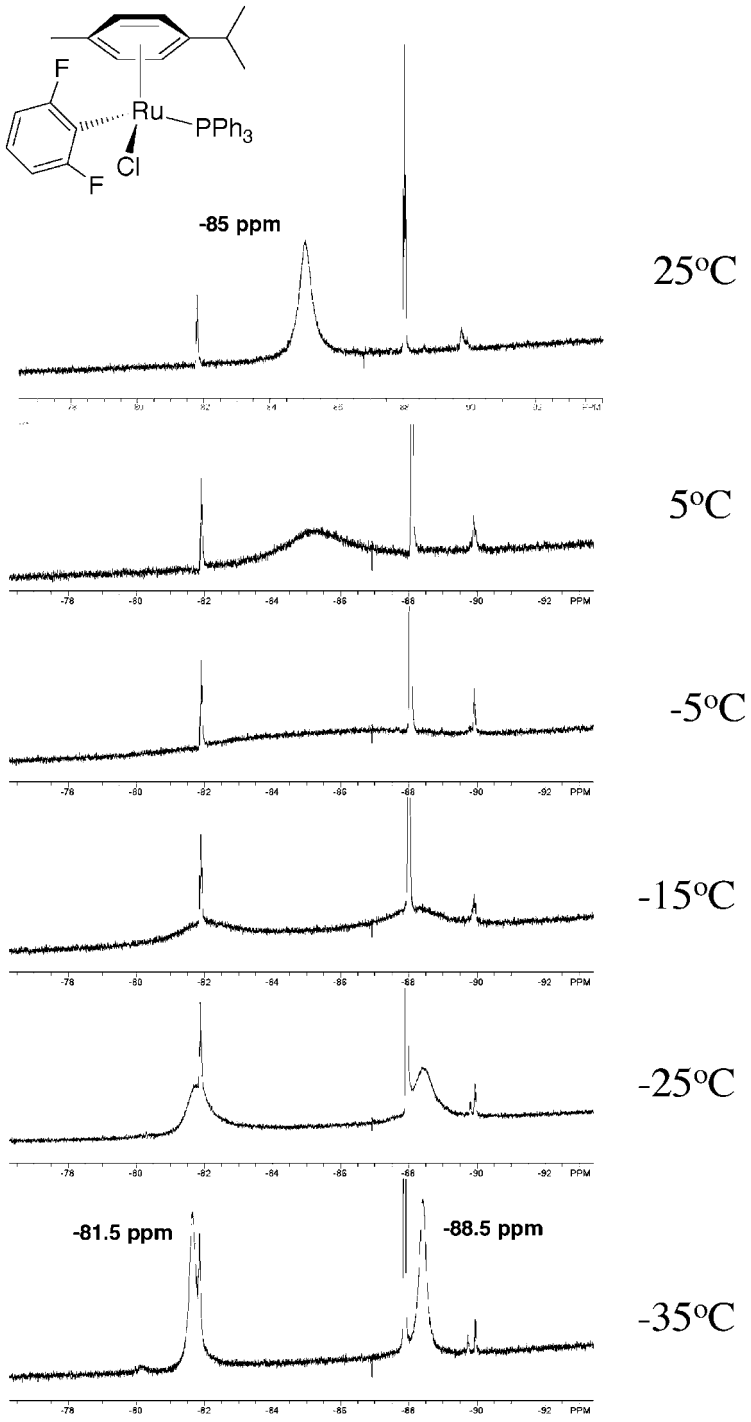
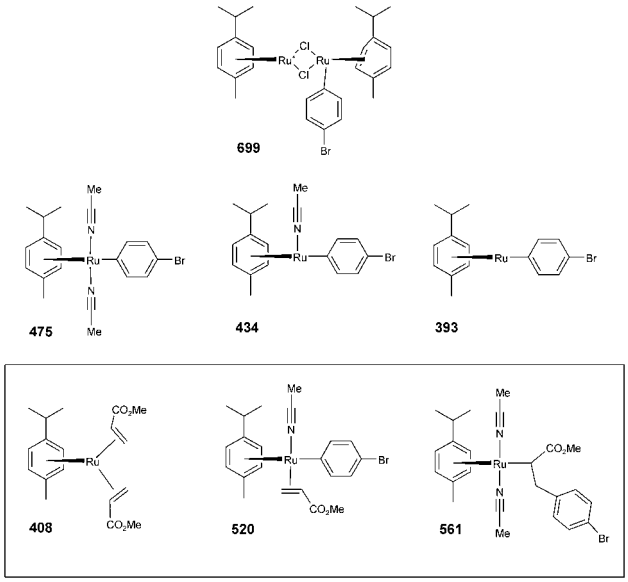


Figure 1. Temperature dependence of the ^{19}F NMR spectrum of the 2,6-diflurophenylruthenium complex in CD_3CN.

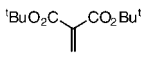


Scheme 5. Cations observed by ES-MS, CV = 5 V; amu values are based on ^{102}Ru, ^{81}Br, ^{35}Cl. The boxed ions are observed in the presence of methyl acrylate, and standing; structures are drawn to indicate likely bonding.

mass spectrum showed monocationic species centred at 393, 434, and 699 amu that correspond to the species shown in Scheme 5. Ruthenium and bromine both give very distinctive isotopic distribution patterns, allowing fragments to be easily identified. The spectra clearly show the presence of various σ-bound aryl-ruthenium complexes; in all cases the *p*-cymene ring is still bound to the metal atom. Both monomeric and dimeric Ar-Ru species are observed, but the dimer is present in very low concentration. No insertion was seen into the C–Br bond and there was no evidence of species containing a metal–$B(OH)_2$ bond. The additional species observed at 353 and 408 amu correspond to $(MeCN)_2(C_{10}H_{14})RuCl$ and $(C_{10}H_{14})(NEt_3)RuCl_2$, respectively. The ratio of (MeCN)(*p*-cymene)RuAr to $(MeCN)_2$(*p*-cymene)RuAr remains approximately constant at 1:1.12 as the cone voltage (CV) increases from +5 V to +30 V. At a CV of +5 V, the signal at 393 amu has an intensity which is 6% of the intensity of (MeCN)(*p*-cymene)RuAr, but its intensity increases dramatically at +20 V. At +30 V, the majority of the Ru is present as (*p*-cymene)RuAr. The variation of the concentration with cone voltage suggests that the complexes observed are the result of fragmentation of $(MeCN)_2$(*p*-cymene)RuBrAr in the inlet cone.

Further ESI-MS experiments were carried out in the presence of methyl acrylate to determine whether alkene coordination to ruthenium could be observed. $[(p\text{-cymene})RuCl_2]_2$ and *p*-bromobenzeneboronic acid were dissolved in acetonitrile:triethylamine solution (100:1) and σ-bound aryl-ruthenium complexes were observed as before. A 10-fold excess of methyl acrylate was added to the yellow-orange solution and the reaction mixture stored at −20 °C for 15 h. As well as the species described above, additional ions were observed in the ESI spectrum centred at 408, 520, and 561 amu. Although only present at low concentration, these correspond to fragments containing one or more alkene molecules bound to ruthenium and are clearly visible and in all cases, *p*-cymene was also bound to Ru. To determine the properties of the alkene which are required for binding to Ru, a variety of alkenes ranging from electron-poor to electron-rich were tested for Ru coordination. A sample of dimer was combined with *p*-bromobenzeneboronic acid in acetonitrile to give a solution for which aryl-ruthenium complexes were observed by ESI-MS as before. This was then split into eight, and an excess of a different alkene was added to each vial. The vials were left at −20 °C for 15 h and the ESI mass spectra were run. The ion corresponding to $(MeCN)_2$(*p*-cymene)RuAr at 475 amu provides a convenient calibration for the spectra, and the values given in Table 1 are the relative intensities of the (MeCN)(alkene)(*p*-cymene)RuAr ions expressed as a percentage of this.

Table 1. Relative intensity (*vs.* 475 amu) of the alkene-bound Ru complex under standard conditions.

Entry	Alkene	%	Entry	Alkene	%
1		39	5		1.6
2		2.6	6		51
3		0	7		0
4		0	8		0

To determine more precisely whether coordination takes place *via* a C=O bond or a C=C bond, a direct comparison was carried out between di-*tert*-butyl methylenemalonate and di-*tert*-butyl malonate. The $[(p\text{-cymene})RuCl_2]_2$ dimer and *p*-bromobenzeneboronic acid were combined in acetonitrile:triethylamine (100:1) and the solution split into two portions. A 10-fold excess of di-*tert*-butylmethylene malonate was added to one sample and a 10-fold excess of di-*tert*-butyl malonate to the other. The samples were left at −20 °C for 15 h and the ESI spectra taken (Figure 2).

The sample containing di-*tert*-butyl methylenemalonate showed a strong signal at 621 amu in the ESI-MS corresponding to coordinated alkene complex. The sample containing di-*tert*-butyl malonate gave a vanishingly weak signal at 609 amu [corresponding to (MeCN)(*p*-cymene)(di-*tert*-butyl malonate)RuAr]. It is clear that

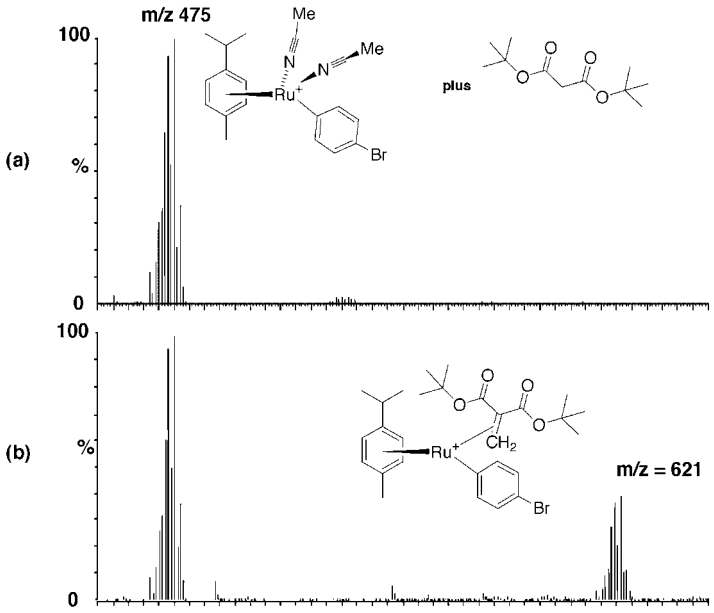
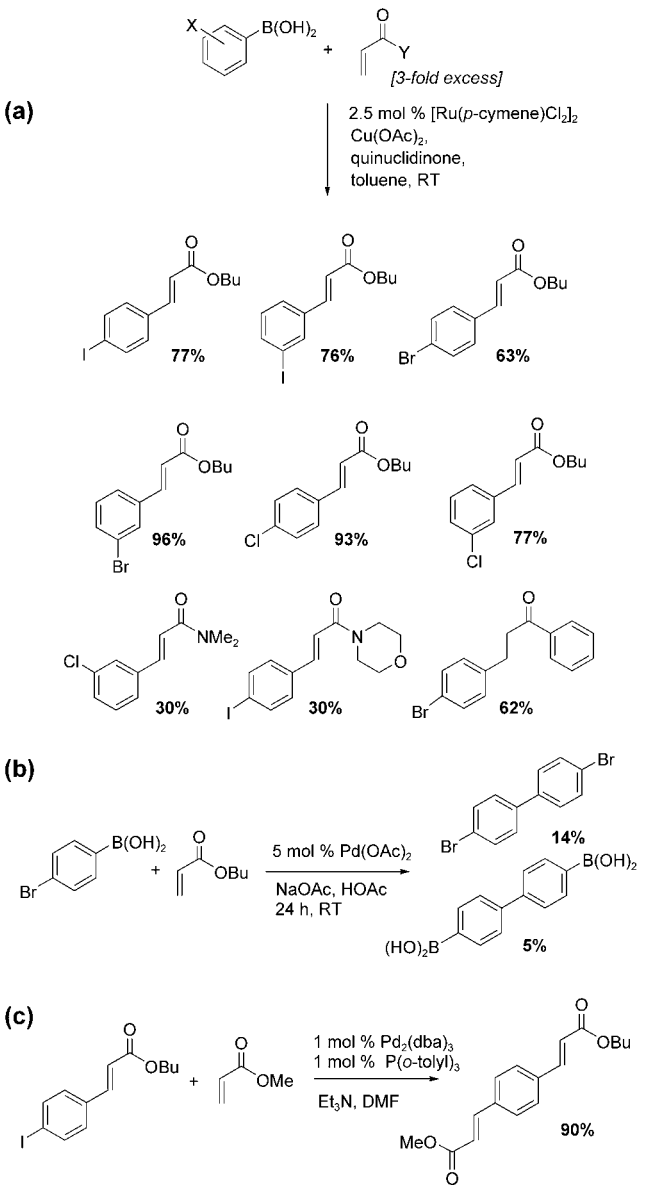


Figure 2. Positive ion electrospray MS (CH_3CN) of bromophenylruthenium complexes taken in the presence of (**a**) di-*tert*-butyl malonate and (**b**) di-*tert*-butyl methylenemalonate at a cone voltage of 5 V. Sample preparation conditions as in text. *m/z* values are quoted for the ^{102}Ru, ^{81}Br, ^{35}Cl isotopomer.

di-*tert*-butyl methylenemalonate binds to the ruthenium arene complex far more effectively than does di-*tert*-butyl malonate. This underpins the suggestion that a C=C double bond is important in order for complexation to occur, and this is also likely to be the case for simple alkenes such as butyl acrylate.

Synthetic Scope

By itself, the ability to react an acrylate and an areneboronic acid under ruthenium catalysis does not constitute a useful synthetic method, since it duplicates what is already readily available in palladium chemistry. Since the ruthenium-based procedure as described here uses an inexpensive and readily available catalyst, and functions at ambient temperature, it would be an attractive alternative if unique regio- or chemoselectivity were observed. The general response to ring-substituents was checked in three cases, shown in Scheme 3 earlier. Interestingly, the most electron-rich boronic acid is least effective. An important aspect of ruthenium chemistry in the formal oxidation state (II) is a reluctance to react with organohalides by oxidative addition. This in turn led us to examine the reaction of butyl acrylate with ring-substituted haloarylboronic acids by ruthenium catalysis under the conditions described above. The results exceeded expectations, in that the halogen was invariably unaffected by the coupling process, and good yields of haloaryl acrylates were obtained. After a simple work-up procedure the products were obtained in a good state of purity (Figure 3). Variation of the alkene component was attempted, but with less success, since the efficiency of turnover was substantially lower with unsaturated amides. Interestingly, the use of methyl vinyl ketone led to a formal addition rather than addition-elimination. This implies that an intermediate palladium enolate formed by the Ru–Ar addition step can then be protonated, releasing the ruthenium in a formal + II oxidation state and obviating the need for reoxidation. The successful reaction sequences are collected in Scheme 6a. The control experiment with a palladium catalyst demonstrated that this outcome was unique to



Scheme 6. (a) Ruthenium-catalysed Heck reactions of haloarylboronic acids under standard conditions. **(b)** Atempted Pd-catalysed haloboronic acid coupling. **(c)** Tandem Ru/Pd catalysis using the product from **(a)** in a conventional Heck reaction.

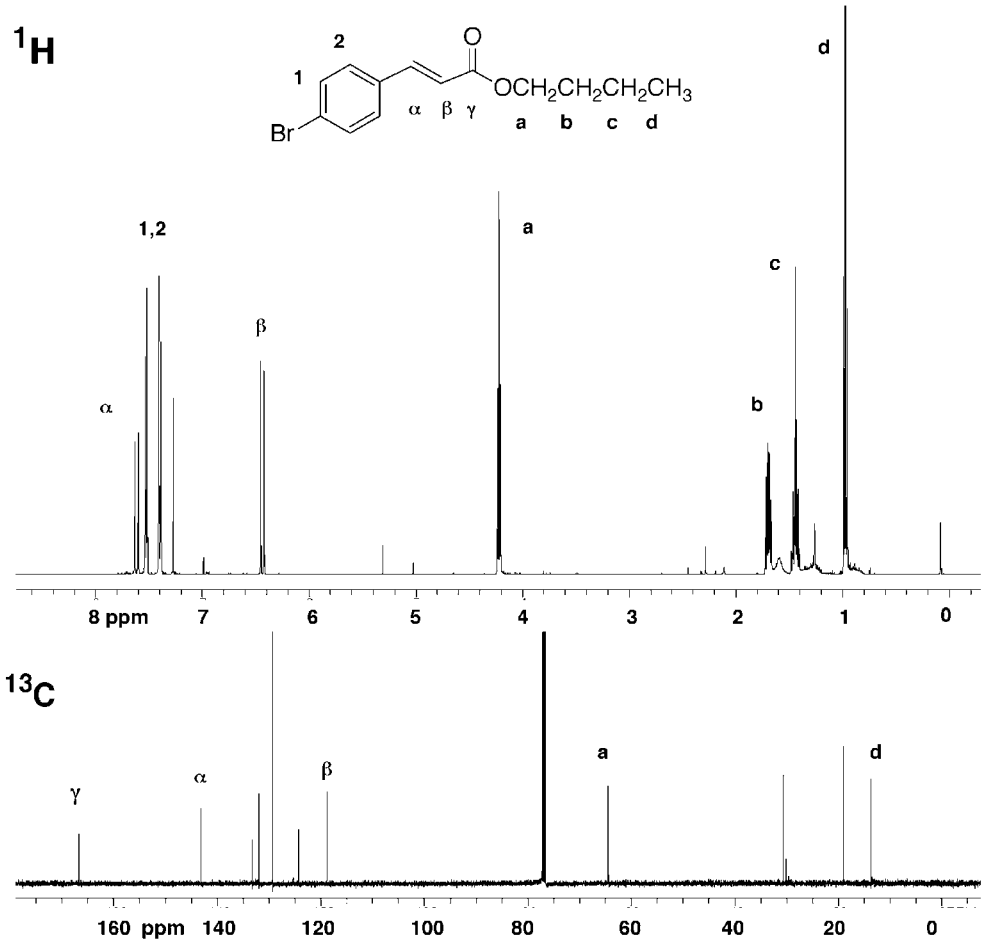


Figure 3. ^{1}H and ^{13}C NMR spectra of the product from the ruthenium Heck reaction of bromobenzeneboronic acid and butyl acrylate after work-up and silica gel filtration.

ruthenium, since an analogous experiment did not afford a useful outcome (Scheme 6b). The distinct chemoselectivity of Ru and Pd catalysts encouraged a tandem reaction, employing the product from Ru-coupling of *p*-iodobenzeneboronic acid and butyl acrylate in a second, Pd-catalysed reaction with methyl acrylate which gave the unsymmetrical bis-cinnamate (Scheme 6c). Phenylene-bis-acrylate esters belong to a well-studied class of compounds that show characteristic photochemical properties in film and solid states and behave as photocrosslinkable monomers in simple polymer mixtures.[26] Polymers containing derivatives of 1,4-phenylene-bis(acrylic acid) show liquid crystalline properties and have been used in applications such as photooptical recorders and photoresists.[27] This technique offers a simple route to unsymmetrical 1,4-phenylene-bis(acrylic acid) derivatives, with scope for variation of the carbonyl functionality.

Summary and Conclusions

As well as extending the boundaries of the conventional Mizoroki–Heck reaction, the results reported here indicate a distinct chemoselectivity associated with ruthenium catalysis. The oxidative addition of ArHal is not competitive with the addition of $ArB(OH)_2$. This permits the development of reaction sequences in which a haloaromatic compound is the nucleophilic partner in the sequence, leaving the C–X bond intact for subsequent transformations.

Experimental Section

Techniques, Materials and Instrumentation

For standard procedures and purifications see recent publications from this laboratory, and standard sources.[28] The following compounds were prepared as previously described: $[(p\text{-cymene})RuCl_2]_2$, $[(benzene)RuCl_2]_2$, $(p\text{-cymene})(PPh_3)RuCl_2$, $(benzene)(PPh_3)RuCl_2$;[29] $(p\text{-cymene})_2Ru(OTf)_2$;[30] di-*tert*-butyl methylenemalonate;[31] β-[^{2}H]-methyl propiolate, and its anthracene Diels–Alder adduct.[32]

Synthesis of (*p*-Cymene)(PPh_3)RuClPh

(*p*-Cymene)(triphenylphosphine)ruthenium dichloride (50 mg, 8.8×10^{-5} mol) was dissolved in dry THF (5 mL) and degassed twice. Benzeneboronic acid (53.6 mg, 4.4×10^{-4} mol) and triethylamine (5 mL) were added against a flow of argon and the mixture stirred at 50 °C for 2 h. The reaction was accompanied by a colour change from red to dark yellow. The solvent was removed under vacuum to yield a dark yellow oil. This was purified by filtration through a short plug of silica gel, eluting with dichloromethane and collecting the yellow band. The solvent was removed under vacuum. Trituration with pentane and removal of the solvent under vacuum afforded (*p*-cymene)(PPh_3)RuClPh as a fine yellow powder (yield: 37 mg, 69%) which was dried under vacuum. X-ray quality crystals were grown by slow precipitation from a dichloromethane solution with heptane at ambient temperature; mp 130 °C (dec.); MS (APCI$^+$): *m/z* = 353.9 [$RuC_{10}H_{14}PhMeCN$]; ^{1}H NMR (500 MHz; $CDCl_3$): d = 0.96 [3H, d, *J* = 6.7 Hz, C(C<u>H</u>$_3$)$_2$], 1.09 [3H, d, *J* = 6.7 Hz, C(C<u>H</u>$_3$)$_2$], 1.56 (3H, s, C<u>H</u>$_3$), 1.94 [1H, m, C<u>H</u>(Me)$_2$], 5.01 (1H, d, *J* = 6.3 Hz, Cy-<u>H</u>), 5.03 (1H, d, *J* = 5.7 Hz, Cy-<u>H</u>), 5.11 (1H, d, *J* = 5.7 Hz, Cy-<u>H</u>), 5.38 (1H, d, *J* = 6.3 Hz, Cy-<u>H</u>), 6.77 (2H, m, Ar-<u>H</u>), 6.84 (1H, m, Ar-<u>H</u>), 6.99 (2H, m, Ar-<u>H</u>), 7.21 (3H, m, PPh_3-<u>H</u>), 7.48 (8H, m, PPh_3-<u>H</u>), 7.55 (2H, m, PPh_3-<u>H</u>), 7.87 (2H, m, PPh_3-<u>H</u>); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 18.7 (<u>C</u>H$_3$), 22.8 [C(<u>C</u>H$_3$)$_2$], 23.5 [C(<u>C</u>H$_3$)$_2$], 30.2 [<u>C</u>(CH$_3$)$_2$], 86.7, 87.3 (Cy-<u>C</u>), 88.0, 88.2 (Cy-<u>C</u>), 109.3, 117.0, 121.8 (Ar-<u>C</u>), 127.5, 128.6, 128.7, 128.9, 129.0, 129.8, 130.6, 131.8, 133.8, 134.9 , 135.0, 136.0, 136.2, 143.1 (br), 160.7, 160.9 (aromatic <u>C</u>); IR (KBr): ν_{max} = 3060 (C–H), 1567, 1436 (C-C), 695, 525, 343 cm^{-1}; elemental analysis: $C_{34}H_{34}PClRu$ requires C 66.8, H 5.57; found: C 66.9, H 5.4.

Use of Ph_4Sn (toluene, 80 °C, 2 h) gave the same product in 51% yield.

Reduction of Diels–Alder Adduct with *p*-Toluenesulphonyl Hydrazide

Methyl 9,10-etheno-9,10-dihydroanthracene-12-[^{2}*H*]-11-carboxylate (the Diels–Alder adduct of methyl 3-[^{2}*H*]-propiolate and anthracene) (1 g, 3.79 mmol) was dissolved/suspended in dry toluene (10 mL) and *p*-toluenesulphonyl hydrazide (1.42 g, 7.5 mmol) added. Triethylamine (2 mL) was added and the reaction mixture was refluxed at 110 °C while monitoring by TLC. After 5 h, the mixture was cooled and a white precipitate formed which was filtered and washed with cold toluene (2 mL). Recrystallisation from methanol afforded white crystals; yield: 0.358 g (36%); mp 126 °C; MS (CI$^+$): *m/z* = 283.2 [MNH_4^+]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.02 (1H, dd, *J* = 2.6 Hz and 10.4 Hz, <u>H</u>2), 2.91 (1H, dd, *J* = 2.6 Hz and 10.4 Hz, <u>H</u>2), 3.61 (3H, s, C<u>H</u>$_3$), 4.36 (1H, d, *J* = 2.68 Hz, <u>H</u>6), 4.7 (1H, d, *J* = 2.68 Hz, <u>H</u>6), 7.13 (4H, m, Ar-<u>H</u>), 7.28 (4H, m, Ar-<u>H</u>); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 43.6 (t, <u>C</u>4), 46.7 (<u>C</u>3), 46.8 (<u>C</u>5) 51.8 (<u>C</u>1), 123.4, 124.5, 125.6, 126.0, 127.5, 129.3, 130.1, 136.4, 139.9, 140.3, 141.9 (<u>C</u>6, <u>C</u>7, <u>C</u>8)), 173.9 (<u>C</u>2); IR (nujol): ν_{max} = 3018, 2960 (C–H), 1731 (C=O), 1481, 1432 (C–C), 1253, 1220, 1080, 757 cm^{-1}.

This product (0.3 g, 1.1 mmol) was dissolved in *n*-butanol and *p*-toluenesulphonic acid (0.19 g, 1.1 mmol) was added. The mixture was refluxed for 24 h in air. The solvent was removed under vacuum to the give butyl ester as a white solid which was purified by recrystallisation from DCM/pentane to give butyl *cis*-9,10-ethano-9,10-dihydroanthracene-12-[^{2}*H*]-11-carboxylate; yield: 0.31 g (91%); mp 118 °C; MS (CI$^+$): *m/z* = 325.1 [MNH_4^+], 308.1 [MH^+]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (3H, t, *J* = 3.4 Hz, C<u>H</u>$_3$), 1.32 (2H, m, C<u>H</u>$_2$), 1.55 (2H, m, C<u>H</u>$_2$), 1.99 (1H, dd, *J* = 2.6 and 8.1 Hz, <u>H</u>3), 2.89 (1H, dd, *J* = 2.6 and 7.8 Hz, <u>H</u>2), 3.97 (2H, t, *J* = 1.7 Hz, OC<u>H</u>$_2$), 4.69 (1H, d, *J* = 2.7 Hz, H4), 4.35 (1H, d, *J* = 2.7 Hz, H4), 7.12 (4H, m, <u>H</u>6, <u>H</u>7), 7.29 (4H, m, <u>H</u>6, <u>H</u>7); ^{13}C NMR (100.6 MHz, $CDCl_3$): d = 13.3 (<u>C</u>H$_3$), 21.5 (<u>C</u>H$_2$), 30.4 (<u>C</u>H$_2$), 44.0 (<u>C</u>3), 43.7 (<u>C</u>2), 44.0 (<u>C</u>4), 46.8 (<u>C</u>4), 64.5 (O<u>C</u>H$_2$), 123.3, 123.5, 125.2, 125.5, 126.0, 142.4 (Ar-<u>C</u>), 173.5 (<u>C</u>5); IR (nujol): ν_{max} = 3026, 2990 (C–H), 1721.1 (C=O), 1501, 1422 (C-C), 1248, 1220 cm^{-1}; HRMS: 308.176 (calcd. for $C_{21}H_{22}O_2D$: 308.176).

This product (0.25 g, 0.8 mmol) was placed in one arm of an A-frame distillation apparatus and flushed with argon. The apparatus was sealed and the first arm was heated to 300 °C in a Wood's metal bath while the second was cooled to −196 °C in liquid nitrogen. After one hour, a colourless liquid had collected in the second arm and white crystals of anthracene had sublimed around the neck of the apparatus. The colourless liquid was slowly warmed to ambient temperature to furnish butyl *cis*-3[^{2}*H*]-acrylate; yield: 42 mg (39%); bp 145 °C; MS (APCI$^+$): *m/z* = 130 [MH^+]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (3H, t, *J* = 3.2 Hz, C<u>H</u>$_3$), 1.40 (2H, m, C<u>H</u>$_2$), 1.62 (2H, m, C<u>H</u>$_2$), 4.19 (2H, t, *J* = 6.7 Hz, OC<u>H</u>$_2$), 5.83 (1H, d, *J* = 10.3 Hz, <u>H</u>3), 6.13 (1H, dt, *J* = 10.3 Hz and 2.5 Hz, <u>H</u>2); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.7 (<u>C</u>H$_3$), 18.7 (<u>C</u>H$_2$), 30.5 (<u>C</u>H$_2$), 64.3 (O<u>C</u>H$_2$), 128.4 (<u>C</u>2), 130 (t, <u>C</u>3), 166.2 (<u>C</u>1).

Coupling of Butyl *cis*-3-[^{2}H]Acrylate with Phenylboronic Acid

Benzeneboronic acid (10 mg, 8.2×10^{-5} mol), [(*p*-cymene)RuCl_2]$_2$ (1.25 mg, 4.1×10^{-7} mol) and copper acetate (40.9 mg, 0.21 mmol) were combined in an MS vial and THF (0.9 mL) and triethylamine (0.1 mL) added. The vial was sealed and the reaction mixture stirred at ambient temperature for 17 h. The solvent was removed under vacuum and the product purified by filtration through a short plug of silica gel, eluting with diethyl ether to afford butyl *trans*-cinnamate; yield: 40 mg (49%); bp 157 °C/15 mmHg); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (3H, t, *J* = 7.3 Hz, C<u>H</u>$_3$), 1.44 (2H, m, C<u>H</u>$_2$), 1.72 (2H, m, C<u>H</u>$_2$), 4.23 (2H, t, *J* = 6.7 Hz, OC<u>H</u>$_2$), 6.48 (1H, d, *J* = 16 Hz, <u>H</u>2), 7.40 (3H, m, <u>H</u>2′, <u>H</u>4″), 7.53 (2H, m, <u>H</u>3′), 7.77 (1H, d, *J* = 16 Hz, <u>H</u>3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.6 (<u>C</u>H$_3$), 19.1 (<u>C</u>H$_2$), 30.6 (<u>C</u>H$_2$), 64.3 (O<u>C</u>H$_2$), 118.2 (<u>C</u>1), 127.9, 128.7, 130.1, 134.3, (<u>C</u>1′, <u>C</u>2′, <u>C</u>3′, <u>C</u>4′), 144.4 (<u>C</u>3), 167.0 (<u>C</u>1); UV/VIS (MeOH): λ = 276 nm (ε = 22000).

Electrospray Mass-Spectrometric Measurements

(a): (*p*-Cymene)ruthenium dichloride dimer (10 mg, 3.26×10^{-5} mol) and *p*-bromobenzeneboronic acid (6.5 mg, 3.26×10^{-5} mol) were combined in acetonitrile (20 mL) and triethylamine (3.3 mg, 3.26×10^{-5} mol) was added. The reaction mixture was subjected to ultrasound for 5 minutes to ensure complete dissolution and left to stand for 30 minutes before the ESI-MS was run.

(b): (*p*-Cymene)ruthenium dichloride dimer (10 mg, 3.26×10^{-5} mol) and *p*-bromobenzeneboronic acid (6.5 mg, 3.26×10^{-5} mol) were combined in acetonitrile (20 mL) and triethylamine (3.3 mg, 3.26×10^{-5} mol) was added. The reaction mixture was subjected to ultrasound for 5 minutes to ensure complete dissolution and left to stand for 30 minutes. ESI-MS showed aryl-ruthenium species as before. Methyl acrylate (28 mg, 0.3 mmol) was added and the solution left at $-20\,^{\circ}C$ for 15 h before the ESI-MS was run.

Synthesis of Coupling Products

Butyl *trans*-cinnamate: Benzeneboronic acid (49.2 mg, 0.4 mmol), $[(p\text{-cymene})RuCl_2]_2$ (6.2 mg, 0.02 mmol), copper acetate monohydrate (199 mg, 1 mmol) and 3-quinuclidinone (126 mg, 1 mmol) were combined in a dry Schlenk tube, which was sealed and placed under vacuum for 30 minutes. The Schlenk tube was flushed with argon then butyl acrylate (155 mg, 1.2 mmol) and freshly distilled toluene (10 mL) were added *via* syringe. The reaction mixture was stirred for 48 h at ambient temperature. The solvent was removed under vacuum and the product purified by silica gel chromatography, eluting with diethyl ether to give butyl *trans*-cinnamate as a colourless liquid; yield: 54 mg (66%); bp 157 °C/15 mmHg); MS (CI^+): *m/z* = 205 [MH^+]; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (3H, t, *J* = 7.3 Hz, C<u>H</u>$_3$), 1.44 (2H, m, C<u>H</u>$_2$), 1.72 (2H, m, C<u>H</u>$_2$), 4.23 (2H, t, *J* = 6.7 Hz, OC<u>H</u>$_2$), 6.48 (1H, d, *J* = 1 6 Hz, <u>H</u>2), 7.40 (3H, m, <u>H</u>2′, <u>H</u>4″), 7.53 (2H, m, <u>H</u>3′), 7.77 (1H, d, *J* = 16 Hz, <u>H</u>3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.6 (<u>C</u>H$_3$), 19.1 (<u>C</u>H$_2$), 30.6 (<u>C</u>H$_2$), 64.3 (O<u>C</u>H$_2$), 118.2 (<u>C</u>2), 127.9, 128.7 (<u>C</u>1′, <u>C</u>4′), 130.1, 134.3 (<u>C</u>2′, <u>C</u>3′), 144.4 (<u>C</u>3), 167.0 (<u>C</u>1); UV-VIS: (MeOH): λ_{max} = 276 nm (ε = 22000).

Butyl *E*-4-iodocinnamate: *p*-Iodobenzeneboronic acid (100 mg, 0.4 mmol), $[(p\text{-cymene})RuCl_2]_2$ (6.2 mg, 0.02 mmol), copper acetate (199 mg, 1 mmol) and quinuclidinone (126 mg, 1 mmol) were combined in a dry Schlenk tube, which was sealed and placed under vacuum for 30 minutes. The Schlenk tube was flushed with argon, then butyl acrylate (155 mg, 1.2 mmol) and freshly distilled toluene (10 mL) were added *via* syringe. The reaction mixture was stirred for 24 h at ambient temperature. The solvent was removed under vacuum and the product purified by silica gel chromatography, eluting with diethyl ether to give butyl-*E*-3-iodocinnamate; yield: 108 mg (77%); MS ($APCI^+$): *m/z* = 349 [MNH_4^+], 332 [MH^+], 274 [MH^+ – Bu], 222, 205 [MH^+ – I]; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.97 (3H, t, *J* = 7.3 Hz, C<u>H</u>$_3$), 1.45 (2H, m, C<u>H</u>$_2$), 1.71 (2H, m, C<u>H</u>$_2$), 4.22 (2H, t, *J* = 6.7 Hz, OC<u>H</u>$_2$), 6.47 (1H, d, *J* = 16 Hz, <u>H</u>2), 7.25 (2H, AA′ of AA′XX′, *J* = 8.3 Hz, <u>H</u>2′), 7.61 (1H, d, *J* = 16 Hz, <u>H</u>3), 7.73 (2H, XX′ of AA′XX′, *J* = 8.3 Hz, <u>H</u>3′); ^{13}C NMR (125.8 MHz, $CDCl_3$): 13.6 (<u>C</u>H$_3$), 19.1 (<u>C</u>H$_2$), 30.6 (<u>C</u>H$_2$), 64.5 (O<u>C</u>H$_2$), 118.9 (<u>C</u>2), 127.3, 133.8 (<u>C</u>1′, <u>C</u>4′), 137.4, 138.0 (<u>C</u>2′, <u>C</u>3′), 143.2 (<u>C</u>3) 166.7 (<u>C</u>1); IR (nujol): ν_{max} = 3054 (sp^2C–H; weak in all such compounds), 2920 (C–H), 1721 (C=O), 1681 (C=C), 1176 cm^{-1} (C–O); HRMS found: 331.0191 (calcd. for $C_{13}H_{16}O_2I$: 331.0195).

Butyl *E*-3-iodocinnamate: As for butyl *trans*-cinnamate, butyl-*E*-3-iodocinnamate; yield: 102 mg (76%); MS ($APCI^+$): *m/z* = 349 [MNH_4^+], 332 [MH^+], 275 [MH^+ – Bu]; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.96 (3H, t, *J* = 7.3 Hz, C<u>H</u>$_3$), 1.44 (2H, m, C<u>H</u>$_2$), 1.68 (2H, m, C<u>H</u>$_2$), 4.18 (2H, t, *J* = 6.7 Hz, OC<u>H</u>$_2$), 6.45 (1H, d, *J* = 16 Hz, <u>H</u>2), 7.12 (1H, dd, *J* = 6.9 Hz and 7.6 Hz, <u>H</u>5′), 7.49 (1H, dd, *J* = 1.5 Hz and 7.6 Hz, <u>H</u>4′) 7.58 (1H, d, *J* = 16 Hz, <u>H</u>3), 7.7 (1H, d, *J* = 1.5 Hz and 6.9 Hz, <u>H</u>6′), 7.88 (1H, dd, *J* = 1.5 Hz, <u>H</u>2′); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.6 (<u>C</u>H$_3$), 19.1 (<u>C</u>H$_2$), 30.8 (<u>C</u>H$_2$), 64.5 (O<u>C</u>H$_2$), 119.5 (<u>C</u>2), 127.3, 130.3, 136.5, 138.8 (<u>C</u>2′, <u>C</u>4′, <u>C</u>5′, <u>C</u>6′), 128.7, 137.4 (<u>C</u>1′, <u>C</u>3′) 142.6 (<u>C</u>3) 166.5 (<u>C</u>1); IR (nujol): ν_{max} = 2859, 1713 (C=O), 1679 (C=C), 1177 cm^{-1} (C–O); HRMS found: 331.0190 (calcd. for $C_{13}H_{16}O_2I$: 331.0195).

Butyl-*E*-4-bromocinnamate:[33] As for butyl *trans*-cinnamate, butyl *E*-4-bromocinnamate; yield: 71.7 mg (63%); MS ($APCI^+$): *m/z* = 226 [M – Bu]; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.97 (3H, t, *J* = 7.3 Hz, C<u>H</u>$_3$), 1.45 (2H, m, C<u>H</u>$_2$), 1.71 (2H, m, C<u>H</u>$_2$), 4.22 (2H, t, *J* = 6.7 Hz, OC<u>H</u>$_3$), 6.45 (1H, d, *J* = 16 Hz, H2), 7.40 (2H, AA′ of AA′XX′, *J* = 8.5 Hz, H2′), 7.52 (2H, XX′ of AA′XX′, *J* = 8.5 Hz, H3′), 7.63 (1H, d, *J* = 16 Hz, H3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.6 (C<u>H</u>$_3$), 19.1 (C<u>H</u>$_2$), 30.6 (C<u>H</u>$_2$), 64.4 (OC<u>H</u>$_2$), 118.9 (<u>C</u>2), 124.3, 133.3 (<u>C</u>1′, <u>C</u>4′), 129.3, 132.0 (<u>C</u>2′, <u>C</u>3′), 143.0 (<u>C</u>3), 166.7 (<u>C</u>1); IR (nujol): ν_{max} = 2960, 1699 (C=O/C=C overlapping) 1173 cm^{-1} (C–O); HRMS found: 283.0335 (calcd. for $C_{13}H_{16}O_2Br$: 283.0335).

Butyl *E*-3-bromocinnamate: As for butyl *trans*-cinnamate, butyl *E*-3-bromocinnamate; yield: 122 mg (96%); MS ($APCI^+$): *m/z* = 284 [MH^+], 226 [M – Bu]; ^{1}H NMR (500 MHz, $CDCl_3$): d = 0.96 (3H, t, *J* = 7.3 Hz, C<u>H</u>$_3$), 1.44 (2H, m, C<u>H</u>$_2$), 1.70 (2H, m, C<u>H</u>$_2$), 4.22 (2H, t, *J* = 6.7 Hz, OC<u>H</u>$_2$), 6.46 (1H, d, *J* = 16 Hz, <u>H</u>1), 7.26 (1H, dd, *J* = 8 Hz and 7.9 Hz, <u>H</u>5′), 7.46 (1H, d, *J* = 1.5 Hz and 8 Hz, <u>H</u>4′), 7.52 (1H, d, *J* = 1.5 Hz and 7.9 Hz, <u>H</u>6′), 7.61 (1H, d, *J* = 16 Hz, <u>H</u>3), 7.68 (1H, dd, *J* = 1.5 Hz, <u>H</u>2′); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.6 (<u>C</u>H$_3$), 19.1 (<u>C</u>H$_2$), 30.6 (<u>C</u>H$_2$), 64.5 (O<u>C</u>H$_2$), 119.7 (<u>C</u>2), 126.5, 130.3, 130.6, 132.9 (<u>C</u>2′, <u>C</u>4′, <u>C</u>5′, <u>C</u>6′), 122.9, 136.4 (<u>C</u>1′, <u>C</u>3′), 142.7 (<u>C</u>3) 166.5 (<u>C</u>1); IR (nujol): ν_{max} = 2921, 1727 (C=O), 1642 (C=C) 1172 cm^{-1} (C–O); HRMS found: 283.0335 (calcd. for $C_{13}H_{16}O_2Br$: 283.0335).

Butyl *E*-3-chlorocinnamate:[34] As for butyl *trans*-cinnamate, butyl *E*-3-chlorocinnamate; yield: 74 mg (77%); MS ($APCI^+$): *m/z* = 257 [MNH_4^+], 240 [MH^+]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (3H, t, *J* = 7.3 Hz, C<u>H</u>$_3$), 1.43 (2H, m, C<u>H</u>$_2$), 1.69 (2H, m, C<u>H</u>$_2$), 4.22 (2H, t, *J* = 6.7 Hz, OC<u>H</u>$_2$), 6.46 (1H, d, *J* = 16 Hz, <u>H</u>2), 7.34 (1H, dd, *J* = 8 Hz and 7.9 Hz, <u>H</u>5′), 7.35 (1H, dd, *J* = 1.5 Hz and 8 Hz, <u>H</u>6′), 7.41 (1H, dd, *J* = 1.5 Hz and 7.9 Hz, <u>H</u>4′), 7.52 (1H, dd, *J* = 1.5 Hz, <u>H</u>2′), 7.63 (1H, d, *J* = 16 Hz, <u>H</u>3); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.1 (<u>C</u>H$_3$), 19.2 (<u>C</u>H$_2$), 30.6 (<u>C</u>H$_2$), 64.5 (O<u>C</u>H$_2$), 119.7 (<u>C</u>2), 126.2, 127.7, 130, 130.1, (<u>C</u>2′, <u>C</u>4′, <u>C</u>5′, <u>C</u>6′), 134.9, 136.2 (<u>C</u>1′, <u>C</u>3′), 142.9 (<u>C</u>3), 166.7 (<u>C</u>1); IR (nujol): ν_{max} = 2924, 1742 (C=O), 1641 (C=C), 1177 cm^{-1} (C–O); HRMS found: 239.0844 (calcd. for $C_{13}H_{16}O_2Cl$: 239.0844).

Butyl *E*-4-chlorocinnamate:[34] As for butyl *trans*-cinnamate, butyl *E*-4-chlorocinnamate; yield: 89 mg (93%: contains *ca.* 5% of biphenyl product); MS ($APCI^+$): *m/z* = 256 [MNH_4^+], 240 [MH^+]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (3H, t, *J* = 7.3 Hz, C<u>H</u>$_3$), 1.45 (2H, m, C<u>H</u>$_2$), 1.7 (2H, m, C<u>H</u>$_2$), 4.22 (2H, t, *J* = 6.7 Hz, OC<u>H</u>$_2$), 6.43 (1H, d, *J* = 16 Hz, <u>H</u>1), 7.36 (2H, AA′ of AA′XX′, *J* = 8 Hz, <u>H</u>2′), 7.49 (2H, XX′ of AA′XX′, *J* = 8 Hz, <u>H</u>3′), 7.68 (1H, d, *J* = 16 Hz, <u>H</u>3); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.6 (<u>C</u>H$_3$), 19.1 (<u>C</u>H$_2$), 30.6 (<u>C</u>H$_2$), 64.5 (O<u>C</u>H$_2$), 118.8 (<u>C</u>2), 128.2, 129.0 (<u>C</u>2′, <u>C</u>3′), 132.8, 134.9 (<u>C</u>1′, <u>C</u>4′), 143.0 (<u>C</u>3), 166.7 (<u>C</u>1); IR (nujol): ν_{max} = 2924, 1725 (C=O), 1643 (C=C), 1173 cm^{-1} (C–O); HRMS found: 239.0844 (calcd. for $C_{13}H_{16}O_2Cl$: 239.0844).

Butyl *E*-4-trifluoromethoxycinnamate: *p*-Trifluoromethoxybenzeneboronic acid (16.9 mg, 0.082 mmol), [(*p*-cymene)-$RuCl_2]_2$ (1.25 mg, 4.1×10^{-6} mmol), copper acetate (40.9 mg, 0.205 mmol) and quinuclidinone (51.5 mg, 0.41 mmol) were combined in a dry Schlenk tube, which was sealed and placed under vacuum for 30 minutes. The Schlenk tube was flushed with argon, then butyl acrylate (10.9 mg, 0.082 mmol) and freshly distilled toluene (1 mL) were added *via* syringe. The reaction mixture was stirred for 24 h at ambient temperature. The solvent was removed under vacuum and the product purified by silica gel chromatography, eluting with diethyl ether to give butyl *E*-4-trifluoromethoxycinnamate; yield: 17 mg (70%); MS (APCI$^+$): *m/z* = 306 [MNH_4^+], 289 [MH^+], 232 [MH^+ – Bu]; ^{1}H NMR (500 MHz, $CDCl_3$): d = 0.98 (3H, t, *J* = 7.4 Hz, C$\underline{H}_3$), 1.44 (2H, m, C$\underline{H}_2$), 1.71 (2H, m, C$\underline{H}_2$), 4.22 (2H, t, *J* = 6.7 Hz, OC$\underline{H}_2$), 6.44 (1H, d, *J* = 16 Hz, $\underline{H}$1), 7.24 (2H, AA′ of AA′XX′, *J* = 8.3 Hz, $\underline{H}$2′), 7.56 (2H, XX′ of AA′XX′, *J* = 8.3 Hz, $\underline{H}$3′), 7.67 (1H, d, *J* = 16 Hz, $\underline{H}$3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.6 (C$\underline{H}_3$), 19.1 (C$\underline{H}_2$), 30.6 (C$\underline{H}_2$), 64.5 (OC$\underline{H}_2$), 119.1 (C$\underline{2}$), 121.0 (C$\underline{F}_3$), 129.3, 142.6 (C$\underline{1}$′, C$\underline{4}$′), 133.0, 134.4 (C$\underline{2}$′, C$\underline{3}$′), 150.2 (C$\underline{3}$) 166.6 (C$\underline{1}$).

Butyl *E*-4-methoxycinnamate: As for butyl *trans*-cinnamate, butyl *E*-4-methoxycinnamate; yield: 8 mg (25%); MS (APCI$^+$): *m/z* = 235 [MH^+], 178 [MH^+ – Bu], 161; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.97 (3H, t, *J* = 7.4 Hz, C$\underline{H}_3$), 1.43 (2H, m, C$\underline{H}_2$), 1.71 (2H, m, C$\underline{H}_2$), 3.84 (3H, s, C$\underline{H}_2$), 4.22 (2H, t, *J* = 6.7 Hz, OC$\underline{H}_2$), 6.33 (1H, d, *J* = 15.9 Hz, $\underline{H}$1), 6.92 (2H, AA′ of AA′XX′, *J* = 8.7 Hz, $\underline{H}$3′), 7.49 (2H, XX′ of AA′XX′, *J* = 8.7 Hz, $\underline{H}$2′), 7.65 (1H, d, *J* = 15.9 Hz, $\underline{H}$3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.6 (C$\underline{H}_3$), 19.1 (C$\underline{H}_2$), 30.8 (C$\underline{H}_2$), 55.3 (OC$\underline{H}_2$), 64.2 (OC$\underline{H}_3$), 114.2 (C$\underline{2}$), 129.6, 133.0, (C$\underline{1}$′, C$\underline{4}$′), 127.1, 128.7 (C$\underline{2}$′, C$\underline{3}$′), 144.1 (C$\underline{3}$), 167.4 (C$\underline{1}$).

Butyl-*E*-4-formylcinnamate: As for butyl *trans*-cinnamate, butyl *E*-4-formylcinnamate; yield: 17 mg (86%); MS (APCI$^+$): *m/z* = 250 [MNH_4^+], 233 [MH^+], 176 [MH^+ – Bu], 159; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (3H, t, *J* = 7.4 Hz, C$\underline{H}_3$), 1.45 (2H, m, C$\underline{H}_2$), 1.72 (2H, m, C$\underline{H}_2$), 4.24 (2H, t, *J* = 6.7 Hz, OC$\underline{H}_2$), 6.58 (1H, d, *J* = 16.1 Hz, $\underline{H}$1), 7.67 (2H, AA′ of AA′XX′, *J* = 8.2 Hz, $\underline{H}$2′), 7.68 (1H, XX′ of AA′XX′, *J* = 16.1 Hz, $\underline{H}$3′), 7.92 (2H, d, *J* = 8.2 Hz, $\underline{H}$3), 10.0 (1H, s, C$\underline{H}$O); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.7 (C$\underline{H}_3$), 19.2 (C$\underline{H}_2$), 30.7 (C$\underline{H}_2$), 64.7 (OC$\underline{H}_2$), 121.4 (C$\underline{2}$), 128.5, 140.1 (C$\underline{1}$′, C$\underline{4}$′), 130.2, 137.1 (C$\underline{2}$′, C$\underline{3}$′), 142.8 (C$\underline{3}$) 166.5 (C$\underline{1}$), 191.5 (C$\underline{H}$O).

Palladium-Catalysed Heck Reaction of Butyl *E*-4-Iodocinnamate with Methyl Acrylate

Butyl *E*-4-iodocinnamate (50 mg, 0.15 mmol), tris(*o*-tolyl)-phosphine (4.56 mg, 0.015 mmol) and tris(dibenzylidineacetone)dipalladium(0) (7.8 mg, 0.0076 mmol) were combined in a dry Schlenk tube under an argon atmosphere. Methyl acrylate (65 mg, 0.76 mmol), triethylamine (76 mg, 0.76 mmol) and dry DMF (5 mL) were added *via* syringe and the reaction mixture was stirred at ambient temperature for 24 h to give a dark yellow solution with a small amount of black precipitate. The solvent was removed under vacuum and the solid residue was filtered through a plug of silica, eluting with diethyl ether to give 3-[4-(2-methoxycarbonylvinyl)-phenyl]acrylic acid butyl ester as an amorphous white solid; yield: 39 mg (90%); mp 69–71 °C; MS (APCI$^+$): *m/z* = 305.2 [MNH_4^+], 235.1 [MH^+ – BuO]; ^{1}H NMR (500 MHz, $CDCl_3$): 0.91 (3H, d, C$\underline{H}_3$), 1.31 (2H, m, C$\underline{H}_2$), 1.7 (2H, m, C$\underline{H}_2$), 3.82 (3H, s, OC$\underline{H}_3$), 4.23 (2H, t, OC$\underline{H}_2$), 6.47 (1H, d, *J* = 16 Hz, $\underline{H}$2), 7.12 (1H, d, *J* = 18 Hz, $\underline{H}$2″), 7.42 (2H, m, $\underline{H}$2′), 7.63 (2H, m, $\underline{H}$3′), 7.71 (1H, d, *J* = 18 Hz, $\underline{H}$3″), 7.77 (1H, d, *J* = 16 Hz, $\underline{H}$3′); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 14.2 (C$\underline{H}_3$), 19.6 (C$\underline{H}_2$), 30.8 (C$\underline{H}_2$), 52.3 (OC$\underline{H}_3$), 65.0 (OC$\underline{H}_2$) 119.3, 119.9 (C$\underline{2}$, C$\underline{2}$″), 126.0, 129.4, 129.2, 132.5 (C$\underline{1}$′, C$\underline{2}$′, C$\underline{3}$′, C$\underline{4}$′), 143.8, 144.2 (C$\underline{3}$, C$\underline{3}$″), 167.3, 167.7 (C$\underline{1}$, C$\underline{1}$″); HRMS found: 288.155 (calcd. for $C_{17}H_{20}O_4$: 288.155).

N-Morpholino *E*-4-Iodocinnamate[35]

p-Iodobenzeneboronic acid (100 mg, 0.4 mmol), (6.2 mg, 0.02 mmol), copper acetate (201 mg, 1 mmol) and quinuclidinone (126 mg, 1 mmol) were combined in a dry Schlenk tube which was sealed and placed under vacuum for 30 minutes. The Schlenk tube was flushed with argon then *N*-acryloylmorpholine (176 mg, 1.2 mmol) and freshly distilled toluene (10 mL) were added *via* syringe. The reaction mixture was stirred for 48 h at ambient temperature under argon. The solvent was removed under vacuum and the product purified by silica gel chromatography, eluting with diethyl ether to give *N*-morpholino *p*-iodo-*trans*-cinnamate as a white solid; yield: 39.9 mg (30%); mp 89 °C; MS (APCI$^+$): *m/z* = 344 [MH^+], 257 [MH^+ – morpholine]; 1H NMR (400 MHz, $CDCl_3$): δ = 3.73 (4H, m, C$\underline{H}_2$), 6.87 (1H, d, *J* = 15.41 Hz, $\underline{H}$2), 7.26 (2H, AA′ of AA′XX′, *J* = 8.4 Hz, $\underline{H}$2′), 7.64 (1H, d, *J* = 15.41 Hz, $\underline{H}$3′), 7.73 (2H, XX′ of AA′XX′, *J* = 8.4 Hz, $\underline{H}$3); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 42.5, 46.2 (C$\underline{H}_2$), 117.2 (C$\underline{2}$), 137.9, 129.3 (C$\underline{2}$′, C$\underline{3}$′), 128.3, 134.6 (C$\underline{1}$′, C$\underline{4}$′), 142.0 (C$\underline{3}$), 165.2 (C$\underline{1}$).

N,N-Dimethyl *E*-3-Chlorocinnamide[36]

3-Chlorobenzeneboronic acid (130 mg, 0.82 mmol), [(*p*-cymene)$RuCl_2]_2$ (12.5 mg, 0.04 mmol), $Cu(OAc)_2$ (410 mg, 2 mmol) and quinuclidinone (513 mg, 4.1 mmol) were combined in a dry Schlenk tube which was sealed and placed under vacuum for 30 minutes. The Schlenk tube was flushed with argon then *N,N*-dimethylacrylamide (81 mg, 0.82 mmol) and freshly distilled toluene (10 mL) were added *via* syringe. The reaction mixture was stirred for 48 h at ambient temperature under argon. The solvent was removed under vacuum and the product purified by silica gel chromatography, eluting with 50:50 ethyl acetate/pentane to give *N,N*-dimethyl *E*-3-chlorocinnamide as a white solid; yield: 52 mg (30%); MS (APCI$^-$): *m/z* = 210 [MH^+]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.11 (3H, s, NC$\underline{H}_3$), 3.21 (3H, s, NC$\underline{H}_3$), 6.75 (1H, d, *J* = 15 Hz, $\underline{H}$2), 7.32 (1H, dd, *J* = 7.8 Hz and 8.1 Hz, $\underline{H}$3′), 7.4 (1H, d, *J* = 1.5 Hz and 8.1 Hz, $\underline{H}$2′), 7.41 (1H, d, *J* = 1.5 Hz and 7.8 Hz, $\underline{H}$4′), 7.52 (1H, dd, *J* = 1.5 Hz, $\underline{H}$6′), 7.53 (1H, d, *J* = 15 Hz, $\underline{H}$3); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 36.4 (NC$\underline{H}_3$), 37.7 (NC$\underline{H}_3$), 113.9 (C$\underline{2}$), 126.9, 129.6, 130.9, 134.6 (C$\underline{2}$′, C$\underline{3}$′, C$\underline{4}$′, C$\underline{6}$′), 135.2, 136.7 (C$\underline{1}$′, C$\underline{5}$′), 141.8 (C$\underline{3}$), 167.0 (C$\underline{1}$).

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