Palladium-Catalyzed Coupling Reaction of α-Diazocarbonyl Compounds with Aromatic Boronic Acids or Halides

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Abstract: Efficient palladium-catalyzed cross-coupling reactions of α-diazocarbonyl compounds and arylboronic acids or aryl halides have been developed. The reaction proceeds smoothly for a range of diazo compounds, boronic acids, and halides. The coupling reaction conditions tolerate various substituents on the aromatic rings of the substrates, such as chloro, fluoro, acyl, oxo, ester, and nitro groups. This coupling reaction constitutes a novel access to α-aryl-substituted α,β-unsaturated carbonyl compounds. Mechanistically, palladium–carbene is supposed to be the key intermediate; its formation is followed by migratory insertion of an aryl group to the carbenic carbon of the palladium–carbene complex and subsequent β-hydride elimination. Kinetic isotope effect (KIE) data measured for intra- and intermolecular competition experiments suggest that β-hydride elimination is not involved in the rate-determining step.

Key words: palladium catalysis, cross-coupling, diazo compounds, aryl halides, arylboronic acids

Introduction

α-Diazocarbonyl compounds have attracted great attention due to their wide applications in organic synthesis.[1] The most common application of α-diazocarbonyl compounds is to generate metal–carbene species through transition-metal catalysis. Although many transition metals are known to decompose diazo compounds, extensive investigations in this field have demonstrated that rhodium(II) and copper(I) complexes are the two most successful metals in this chemistry. Rhodium(II) and copper(I) complexes have been proved to be highly efficient in catalyzing dinitrogen extrusion from diazo substrates, generating the corresponding metal–carbene species. The metal–carbene intermediates thus generated are highly reactive, yet very selective in many cases, and undergo a variety of typical metal–carbene reactions, such as cyclopropanations and X–H (X = C, O, N, S, Si, etc.) bond insertions. Those reactions have been developed into standard transformations in organic synthesis. Despite these achievements, the development of novel and efficient synthetic methods based on the reaction of α-diazocarbonyl compounds has still been pursued actively in recent years. One important direction in this area is to look for other transition metals that may lead to novel reactivity of the metal–carbene intermediates.[2]

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Palladium complexes show diverse reactivities in organometallic chemistry. In particular, palladium-catalyzed cross-coupling reactions have become part of the most applied reactions for the formation of carbon–carbon and carbon–heteroatom bonds.[3] In combination with oxidative addition, transmetalation, migratory carbonyl insertion, and reductive elimination, palladium-catalyzed reactions demonstrate striking diversity. Various types of palladium-catalyzed coupling reactions are utilized routinely as key steps in organic synthesis.[4] A variety of nucleophiles (organometallic reagents and carbonyl compounds, amines, alcohols, phosphines, etc.) and electrophiles (halides, triflates, tosylates, etc.) can be applied in the palladium-catalyzed cross-coupling process.

Despite the great success of palladium catalysts, palladium-catalyzed reactions involving palladium–carbenes as reactive intermediates have not received much attention until very recently.[5] Palladium–carbene species have only been sporadically suggested as reactive intermediates in palladium-catalyzed transformations.[6] Although in recent years stable N-heterocyclic carbenes (NHCs) have been widely used as ligands in palladium-catalyzed reactions, the Pd–C bond between the NHC ligand and palladium is found to be closer to being a single bond due to the strong donor and poor π-acceptor properties of NHCs.[7] Recently, Bröring and co-workers reported the first palladium(II) complex of a nonheteroatom-stabilized carbene ligand.[5b] However, this palladium(II)–carbene complex shows no reactivity toward either nucleophiles or electrophiles. Thus, it has not been possible to study the chemical properties of palladium(II)–carbenes from this complex.

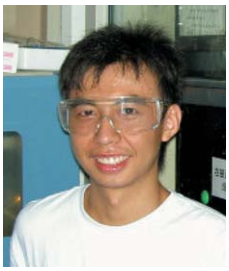
On the other hand, palladium complexes as catalysts for the diazo decomposition reaction were examined quite a long time ago.[1,8] Those studies already demonstrated different reaction patterns of the palladium-catalyzed reaction of diazo compounds when compared with the corresponding rhodium(II)- or copper(I)-catalyzed reactions. For example, in palladium-catalyzed cyclopropanation of diazomethane, it is suggested that the reaction proceeds through electrophilic addition by palladium–olefin complexes to diazomethane, rather than through a palladium–carbene intermediate.[9] Another example is palladium(II)-catalyzed polymerization with diazoesters and diazoketones, which has been studied by Inoue and co-workers.[10] This polymerization is a unique method to construct polymer backbones consisting of one-carbon units. The migratory insertion of the palladium(II)–car-

bene intermediate may be involved as the key step in the chain-propagation process. Palladium(II) catalysts are also effective in the cyclopropanation of α,β-unsaturated esters and nitriles by diazomethane and aryldiazoacetates. In the latter case, the reaction is likely to involve a dipolar cycloaddition, followed by thermal decomposition of the

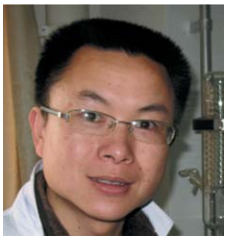
Biographical Sketches

Cheng Peng was born in 1982 in the Jiangsu province, China. After finishing his high school education, he entered Peking University in 2000, where he obtained a B.S. degree, before continuing his graduate studies at the same university in Prof. Jianbo Wang's laboratory. He received his Ph.D. degree in June 2009 and subsequently joined GSK R&D China.

Guobin Yanwas born in the Jiangxi province of China in 1975. He obtained his B.S. degree from the Jingangshan Normal University, his M.Sc. degree from Suzhou University, and his Ph.D. degree from Tongji University in 2010. He spent two years in 2008 and 2009 as visiting student in Prof. Jianbo Wang's laboratory.



Yan Wang was born in the Jiangxi province of China in 1988. After finishing his high school education, he entered Peking University in 2005, where he obtained his B.S. degree, before moving to the USA to continue his graduate studies at the University of Wisconsin-Madison.



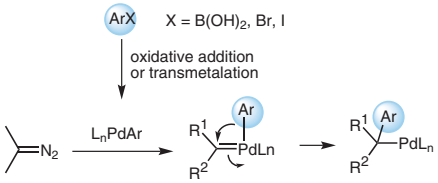
Yubo Jiang was born in the Anhui province of China in 1975. He obtained his B.S. degree from the Huaibei Coal Industry Teachers College and his M.Sc. degree from Tongji University. He is currently a Ph.D. student at Tongji University. He spent one year in 2009 as visiting student in Prof. Jianbo Wang's laboratory.

Yan Zhang was born in the Shandong province of China in 1975. She received her B.S. and Ph.D. degrees from Lanzhou University. She continued her research as a postdoctoral fellow at the Hong Kong University of Science and Technology (2002–2004), the University of Innsbruck & the Leibniz Institute of Surface Modification (IOM) (2004–2005), the University of Missouri-St. Louis (2005–2006), and Auburn University (2006–2008). She has been at Peking University since 2008 as an associate professor. Her research focuses on the application of transition-metal complexes of N-heterocyclic carbenes and the synthesis of small biological compounds.

Jianbo Wang was born in the Zhejiang province of China in 1962. He received his B.S. degree from Nanjing University of Science and Technology in 1983, and his Ph.D. from Hokkaido University (under the supervision of Prof. H. Suginome) in 1990. He was a postdoctoral associate at the University of Geneva from 1990 to 1993 (with Prof. C. W. Jefford) and the University of Wisconsin-Madison from 1993 to 1995 (with Prof. H. E. Zimmerman and F. A. Fahien). He began his independent academic career at Peking University in 1995. His research interests include catalytic metal–carbene transformations.

initially formed pyrazole.[11] In addition, it has been noted that palladium-catalyzed dinitrogen extrusion of α-diazocarbonyl compounds is not efficient in general, and in many cases affords mixtures of products with low selectivity due to harsh reaction conditions such as high temperature and long reaction time.

Palladium-catalyzed reactions of diazo compounds with palladium–carbene proposed as reactive intermediate have recently emerged in the literature.[12] In 2001, Van Vranken and co-workers reported the reaction of (trimethylsilyl)diazomethane with substituted benzylic halides, which leads to the generation of styrene.[12a] The formation of palladium–carbene and the subsequent migratory insertion are proposed as the key steps in the reaction mechanism (Scheme 1). Following this seminal work, several catalytic systems involving similar palladium–carbene formation and subsequent migratory insertion have been reported. Van Vranken and co-workers further reported palladium-catalyzed migratory insertion of the vinyl group to the carbene center to afford an allylpalladium intermediate, which could be incorporated into a three-component reaction with amine nucleophiles or active methylene nucleophiles.[12c] In 2007, Barluenga and co-workers first reported on their palladium-catalyzed coupling of *N*-tosylhydrazone with aryl bromide, in which similar migratory insertion of palladium–carbene was suggested as a key step in the mechanism.[12d] More recently, a palladium-catalyzed coupling reaction of benzyl bromides and α-aryldiazoesters, which gives (*E*)-α,β-diarylacrylates with high stereoselectivity, was reported by Yu and co-workers.[12j] We have reported a similar coupling of *N*-tosylhydrazones with benzyl halides, which affords di- or trisubstituted olefins.[12k]



Scheme 1 Palladium-catalyzed cross-coupling through palladium–carbene migratory insertion

In connection with our long-standing interest in the chemistry of diazo compounds, we have envisaged that it would be worthwhile to revisit the palladium catalyst in this area. Exploration along this line led to the development of a palladium-catalyzed cross-coupling of α-diazocarbonyl compounds with aromatic boronic acids, which was communicated in 2008.[12f] Further studies revealed that this palladium-catalyzed cross-coupling reaction can be extended to aryl iodides and aryl bromides. We present here a full account of this novel palladium-catalyzed coupling reaction.

Results and Discussion

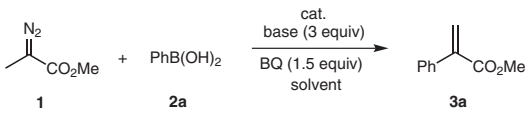
Palladium-Catalyzed Cross-Coupling of α-Diazocarbonyl Compounds with Arylboronic Acids

To explore the possibility of using an α-diazocarbonyl compound as cross-coupling partner in a palladium-catalyzed reaction, our initial studies focused on palladium-catalyzed coupling of α-diazocarbonyl compounds with boronic acids. Since its discovery, Suzuki–Miyaura coupling of aryl and vinyl halides or triflates with organoboron reagents has developed into one of the most important C–C bond-forming reactions.[13] The availability of various boronic acids that are normally nontoxic and stable, as well as easy workup and separation of the products are some of the factors that contribute to the success of the Suzuki–Miyaura reaction. However, to our knowledge, palladium-catalyzed coupling of diazo compounds with boronic acids has not been documented in the literature until our recent report.[12f,14]

Initially, the palladium-catalyzed reaction of methyl α-diazopropionate (**1**) and phenylboronic acid (**2a**) was used to explore the cross-coupling conditions (Table 1). Methyl 2-phenylacrylate (**3a**) was isolated in moderate yield when the reaction was catalyzed by tetrakis(triphenylphosphine)palladium in the presence of benzoquinone (BQ) and potassium carbonate (entry 1). Benzoquinone was found indispensable as oxidant, since in the absence of benzoquinone only a trace amount of **3a** could be detected (entry 2). Further optimization was carried out by screening other reaction parameters (temperature, solvent, and base). The reaction proceeded more efficiently at high temperature (entry 3). Diisopropylamine was found to be the most suitable base, promoting the reaction to provide high yields (entries 6 and 7), although other bases, such as potassium carbonate, cesium carbonate, and triethylamine were also effective. As for the solvent, the polar solvent 1,2-dichloroethane could accelerate the reaction, but led to slightly lower yield (entry 8), while acetonitrile was found to give a poor result (entry 9). Lastly, palladium catalysts were examined. Palladium(II) acetate, dichlorobis(triphenylphosphine)palladium(II), and palladium(II) acetate/phosphine ligands all led to lower yields of **3a** (entries 10–14). As control experiment, the reaction was carried out in the absence of tetrakis(triphenylphosphine)palladium: product **3a** could not be detected under such conditions.

On the basis of the above experiments, it was concluded that methyl α-diazopropionate (**1**) could react well with phenylboronic acid (**2a**) to generate methyl 2-phenylacrylate (**3a**) with tetrakis(triphenylphosphine)palladium as catalyst in the presence of diisopropylamine as base and benzoquinone as oxidant. Table 2 summarizes the reactions of methyl α-diazopropionate (**1**) with a series of arylboronic acids **2a–l** under the optimized reaction conditions. All these reactions were completed in 15 minutes, affording the corresponding α-arylacrylates **3a–l** in moderate to high yields. The presence of *ortho* substituents in arylboronic acids **2** had little negative effect on the

Table 1 Palladium-Catalyzed Reaction of Methyl α-Diazopropionate (**1**) and Phenylboronic Acid (**2a**)[a]



Entry	Cat. (mol%)	Solvent	Base	Temp (°C)	Time	Yield (%)[b]
1	$Pd(PPh_3)_4$ (5)	toluene	K_2CO_3	60	30 min	53
2[c]	$Pd(PPh_3)_4$ (5)	toluene	K_2CO_3	60	3 h	trace
3	$Pd(PPh_3)_4$ (5)	toluene	K_2CO_3	80	30 min	64
4	$Pd(PPh_3)_4$ (5)	toluene	Cs_2CO_3	80	30 min	45
5	$Pd(PPh_3)_4$ (5)	toluene	Et_3N	60	30 min	50
6	$Pd(PPh_3)_4$ (2.5)	toluene	*i*-Pr_2NH	80	15 min	74
7[d]	$Pd(PPh_3)_4$ (2.5)	toluene	*i*-Pr_2NH	80	15 min	82
8[d]	$Pd(PPh_3)_4$ (2.5)	DCE	*i*-Pr_2NH	80	5 min	68
9	$Pd(PPh_3)_4$ (5)	MeCN	K_2CO_3	60	12 h	8
10[d]	$Pd(OAc)_2$ (2.5)	toluene	*i*-Pr_2NH	80	2 h	19
11[d]	$PdCl_2(PPh_3)_2$ (2.5)	toluene	*i*-Pr_2NH	80	30 min	27
12[d]	$Pd_2(dba)_3$ (2.5)/PPh_3 (10)	toluene	*i*-Pr_2NH	80	15 min	41
13[d]	$Pd(OAc)_2$ (2.5)/dppe (2.5)	toluene	*i*-Pr_2NH	80	1 h	34
14	$Pd(OAc)_2$ (5)/PPh_3 (20)	toluene	K_2CO_3	60	3.5 h	51
15[d]	none	toluene	*i*-Pr_2NH	80	15 h	0

[a] Reaction conditions: **1** (1.0 equiv), **2a** (3.0 equiv).
[b] Isolated yield.
[c] The reaction was carried out in the absence of BQ.
[d] *i*-Pr_2NH (5 equiv) was used.

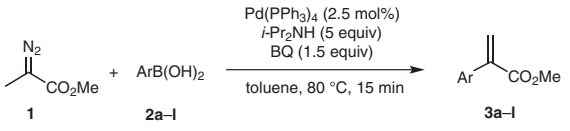
reaction. The coupling products were isolated in high yields that were comparable to *meta*- and *para*-substituted arylboronic acids (entries 2–5). In the case of the reaction with 3,5-dimethyl-substituted arylboronic acid, the slightly lower yield can be attributed to the poor solubility of the boronic acid (entry 6). Notably, the electronic properties of the substituents on the aryl group have an observable effect on the yields. The yields of products with electron-donating groups were higher than those of electron-withdrawing groups (entries 7–9). It is noteworthy that chloro and bromo substituents were inert to the reaction conditions and could be retained on the aryl group after reaction (entries 10 and 11). 1-Naphthylboronic acid also gave the product in good yield (entry 12).

Next we went on to study the scope of the coupling reaction by using various α-diazocarbonyl compounds **4a–i** under the same conditions (Table 3). The results show that diazo compounds with a wide range of substituents could be applied in the reaction with phenylboronic acid (**2a**), affording α,β-unsaturated carbonyl compounds **5a–i** bearing various substituents (Table 3). It is noteworthy that a tetrasubstituted olefin, which is usually difficult to access, can be obtained in moderate yield (entry 5). The reaction with α-alkyl-substituted α-diazoketones also occurred smoothly to afford α,β-unsaturated ketones (entries 6–9). The relatively stable chloride and bromide groups could survive these mild reaction conditions, and these groups could be utilized for further transformations through transition-metal catalysis (entries 7 and 8).

Palladium-Catalyzed Cross-Coupling of α-Diazocarbonyl Compounds with Aryl Iodides

The success of the cross-coupling of α-diazocarbonyl compounds with aromatic boronic acid under mild reaction conditions encouraged us to turn our attention to other coupling partners, such as aryl halides. When aryl halides are used as coupling partners, oxidative addition, instead of transmetalation as in the coupling reaction with boronic acids, must be involved in the catalytic cycle. Thus, a palladium(0) complex will be used as catalyst and an oxidant will not be required in these cases. Initial attempts at utilizing iodobenzene (**6a**) and methyl α-diazopropionate (**1**) under the above-described conditions but in the absence of benzoquinone gave the desired product of methyl 2-phenylacrylate (**3a**) in low yield (Table 4). Optimization experiments were then carried out and the

Table 2 Tetrakis(triphenylphosphine)palladium-Catalyzed Reaction of Arylboronic Acids **2a–l** with Methyl α-Diazopropionate (**1**)[a]



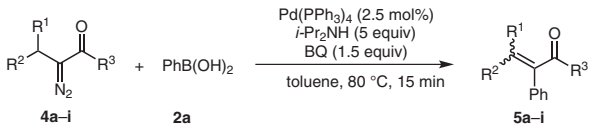
Entry	2	Ar	3	Yield (%)[b]
1	**2a**	C_6H_5	**3a**	82
2	**2b**	2-MeC_6H_4	**3b**	88
3	**2c**	3-MeC_6H_4	**3c**	83
4	**2d**	4-MeC_6H_4	**3d**	83
5	**2e**	4-*t*-BuC_6H_4	**3e**	83
6	**2f**	3,5-$Me_2C_6H_3$	**3f**	49
7	**2g**	4-$MeOC_6H_4$	**3g**	86
8	**2h**	3-$O_2NC_6H_4$	**3h**	58
9	**2i**	4-$OHCC_6H_4$	**3i**	44
10	**2j**	4-ClC_6H_4	**3j**	77
11	**2k**	4-BrC_6H_4	**3k**	77
12	**2l**	1-naphthyl	**3l**	83

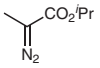
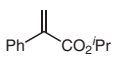
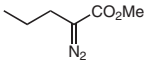
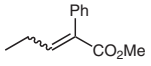
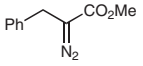
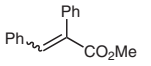
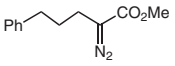
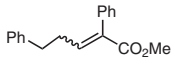
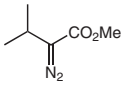
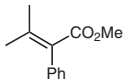
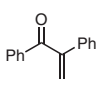
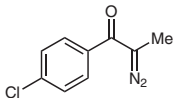
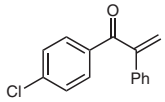
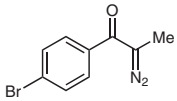
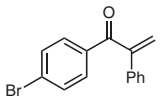
[a] Reaction conditions: **1** (1.0 equiv), **2a–l** (3.0 equiv).
[b] Isolated yield.

results are summarized in Table 4. The polarity of the solvents had a marginal effect on the yields, with 1,2-dichloroethane affording the best results (entries 1–6). The choice of suitable base was found to be very important for this reaction. Organic bases afforded better yields than inorganic bases (entries 6–11). Low temperature slowed down the rate of the coupling reaction, leading to poor yields (cf. entries 6, 12, and 13). We also examined other palladium complexes and ligands. When palladium(II) acetate was used alone, the catalytic activity was diminished, and the reaction afforded the product in low yield (entry 14). In the presence of monophosphine ligands, moderate yields could be obtained (entries 15–17). In contrast, a bidentate phosphine ligand suppressed the coupling reaction (entry 18).

With the optimized reaction conditions in hand, we then moved on to the next stage to investigate the scope of this coupling reaction. First, a variety of substituted aryl iodides **6** were subjected to the reaction under optimized conditions (Table 5). All the substrates that we examined worked well to afford the desired products in moderate to good yields. The alkyl- and phenyl-substituted aryl iodides reacted smoothly to afford coupling products in good yields (entries 2–4). When bromo and chloro substituents were present in the aryl iodides, the reactions occurred selectively at the iodo-substituted carbon (entries 5–8). 4-Methoxy-substituted iodobenzene afforded a low yield, presumably due to its relatively slow rate of oxidative addition (entry 9). Conversely, for the substrate with

Table 3 Tetrakis(triphenylphosphine)palladium-Catalyzed Reaction of **4a–i** with Phenylboronic Acid (**2a**)



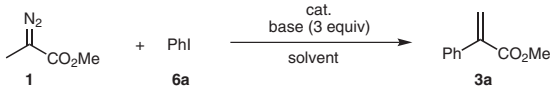
Entry	4	5	Yield (%)[b]
1	 **4a**	 **5a**	84
2	 **4b**	 **5b**	92 (*Z*/*E* = 1:2.5)
3	 **4c**	 **5c**	80 (*Z*/*E* = 1:1.5)[c]
4	 **4d**	 **5d**	97 (*Z*/*E* = 1:2.3)
5	 **4e**	 **5e**	65
6	 **4f**	 **5f**	90
7	 **4g**	 **5g**	87
8	 **4h**	 **5h**	93
9	 **4i**	 **5i**	75

[a] Reaction conditions: **4** (1 equiv), **2a** (3 equiv).
[b] Isolated yield.
[c] Ratio determined by ^{1}H NMR spectroscopy of the crude product.

the phenyl moiety bearing an electron-withdrawing substituent, the reaction proceeded smoothly to afford the coupling product in good yield (entry 10).

We then proceeded to examine the reaction with a series of α -alkyl-substituted α -diazoesters **4** (Table 6). It was found that the α-alkyl-substituted diazoesters all led to the formation of the expected olefin products **5**. Primary alkyl groups gave trisubstituted olefins in good yields; however, *E* and *Z* selectivity was low in all cases (entries 3–5). When the alkyl group was isopropyl, as in the case of **4e**,

Table 4 Conditions for Palladium-Catalyzed Reaction between Methyl α-Diazopropionate (**1**) and Iodobenzene (**6a**)[a]



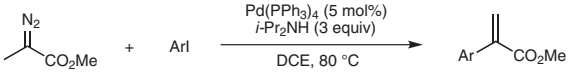
Entry	Cat. (mol%)	Base	Solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	$Pd(PPh_3)_4$ (5)	*i*-Pr_2NH	THF	80	0.5	64
2	$Pd(PPh_3)_4$ (5)	*i*-Pr_2NH	dioxane	80	0.5	72
3	$Pd(PPh_3)_4$ (5)	*i*-Pr_2NH	EtOAc	80	0.5	64
4	$Pd(PPh_3)_4$ (5)	*i*-Pr_2NH	toluene	80	0.5	68
5	$Pd(PPh_3)_4$ (5)	*i*-Pr_2NH	MeCN	80	0.5	76
6	$Pd(PPh_3)_4$ (5)	*i*-Pr_2NH	DCE	80	0.5	86
7	$Pd(PPh_3)_4$ (5)	DBU	DCE	80	0.5	49
8	$Pd(PPh_3)_4$ (5)	DIPEA	DCE	80	0.5	41
9	$Pd(PPh_3)_4$ (5)	Et_3N	DCE	80	0.5	68
10	$Pd(PPh_3)_4$ (5)	K_2CO_3	DCE	80	0.5	27
11	$Pd(PPh_3)_4$ (5)	K_3PO_4	DCE	80	3	35
12	$Pd(PPh_3)_4$ (5)	*i*-Pr_2NH	DCE	60	4	64
13	$Pd(PPh_3)_4$ (5)	*i*-Pr_2NH	DCE	40	12	35
14	$Pd(OAc)_2$ (5)	*i*-Pr_2NH	DCE	80	4	39
15	$Pd(OAc)_2$ (5)/ Ph_3P (20)	*i*-Pr_2NH	DCE	80	0.5	66
16	$Pd(OAc)_2$ (5)/ $(4\text{-Tol})_3P$ (20)	*i*-Pr_2NH	DCE	80	0.5	66
17	$Pd(OAc)_2$ (5)/ $(2\text{-furyl})_3P$ (20)	*i*-Pr_2NH	DCE	80	0.5	70
18	$Pd(OAc)_2$ (5)/ dppf (10)	*i*-Pr_2NH	DCE	80	4	16

[a] Reaction conditions: **1** (1.3 equiv), **6a** (1.0 equiv).
[b] Isolated yield.

the corresponding tetrasubstituted olefin could be obtained in good yield (entry 6).

To further expand the scope of the diazo substrate, α-diazoketones were subjected to the above reaction conditions. Unexpectedly, under the same reaction conditions, unknown mixtures of products were detected by TLC. We speculated that the halide ion generated in the course of the reaction might interfere with this reaction. Thus, silver salts were introduced to the reaction mixture as additive, to eliminate the halide ion dissolved in the reaction solution (Table 7). After screening of several silver salts, it was found that in the presence of silver(I) carbonate coupling product **5f** could be isolated in 90% yield (entry 3). Although silver(I) carbonate is an inorganic base, we confirmed that diisopropylamine was still necessary to promote the reaction. When the reaction was carried out in the absence of diisopropylamine, the yield of **5f** was significantly diminished (entry 5).

Table 5 Palladium-Catalyzed Reaction of Methyl α-Diazopropionate (**1**) with Aryl Iodides **6a–j**[a]



Entry	**6**	Ar	Time	**3**	Yield (%)[b]
1	**6a**	C_6H_5	1 h	**3a**	86
2	**6b**	3-MeC_6H_4	1 h	**3c**	69
3	**6c**	4-MeC_6H_4	1 h	**3d**	74
4	**6d**	4-PhC_6H_4	30 min	**3m**	76
5	**6e**	2-ClC_6H_4	45 min	**3n**	85
6	**6f**	4-ClC_6H_4	45 min	**3j**	74
7	**6g**	4-BrC_6H_4	45 min	**3k**	64
8	**6h**	$3,4\text{-Cl}_2C_6H_3$	45 min	**3o**	62
9	**6i**	4-MeOC_6H_4	1 h	**3g**	57
10	**6j**	$4\text{-MeO}_2CC_6H_4$	30 min	**3p**	80

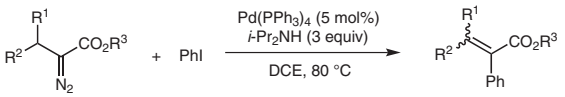
[a] Reaction conditions: **1** (1.3 equiv), **6** (1.0 equiv).
[b] Isolated yield.

Several α-diazoketones **4** were then examined under the optimized reaction conditions. As shown in Table 8, the expected coupling products were obtained in good yields for all the α-diazoketones examined in this study. It was noted again that chloro and bromo substituents on the aromatic ring of the diazo substrates were tolerated under the reaction conditions (entries 2 and 3). The reaction with cyclic α-diazoketone **4i** also occurred smoothly to afford **5i** in a yield of 76% (entry 4).

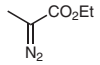
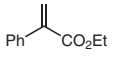
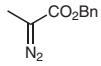
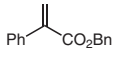
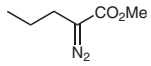
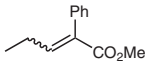
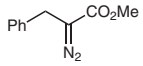
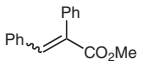
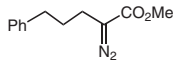
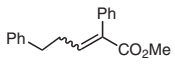
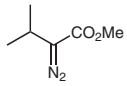
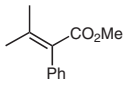
Palladium-Catalyzed Cross-Coupling of α-Diazocarbonyl Compounds with Aryl Bromides

Next, we proceeded to apply aryl bromides as substrates, which are generally less reactive than aryl iodides in palladium-catalyzed reactions. Under the optimized reaction conditions developed for aryl iodides, diazo compounds were indeed decomposed by palladium catalysts, but no corresponding coupling products could be detected. We speculated that the slow rate of oxidative addition of the palladium(0) complex to a phenyl bromide might be responsible for this result. Thus, we decided to examine some electron-rich phosphine ligands, which are well known to promote oxidative addition of palladium(0) complexes to halides. After a series of screening experiments, it was concluded that $[Pd(\pi\text{-allyl})Cl]_2$ ligated by 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (Xphos)[15] could efficiently catalyze the coupling of phenyl bromide (**7a**) with **1**, affording the coupling product in 86% yield.

Table 6 Palladium-Catalyzed Reaction of α-Diazoesters **4** with Iodobenzene (**6a**)



4b–e,j,k 6a 5b–e,j,k

Entry	4	Time (h)	5	Yield (%)[c]
1[a]	 **4j**	1	 **5j**	78
2[b]	 **4k**	0.5	 **5k**	73
3[a]	 **4b**	1.5	 **5b**	86 (*Z*/*E* = 1:4)
4[b]	 **4c**	1	 **5c**	81 (*Z*/*E* = 1:5)[d]
5[b]	 **4d**	1	 **5d**	71 (*Z*/*E* = 1:2)
6[a]	 **4e**	1	 **5e**	84

[a] Reaction conditions: **4b**,**e**,**j** (1.3 equiv), **6a** (1.0 equiv).
[b] Reaction conditions: **4c**,**d**,**k** (1 equiv), **6a** (1.5 equiv).
[c] Isolated yield.
[d] Ratio determined by ^{1}H NMR spectroscopy of the crude product.

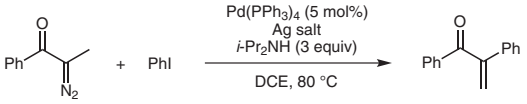
Similarly, a series of substituted aryl bromides **7** was then subjected to the optimized reaction conditions (Table 9). The coupling reaction proceeded smoothly in all cases. It is noteworthy that an *ortho* substituent on the aromatic ring of the bromide had no deleterious effect on this reaction (entry 2). When there is a chloro or fluoro substituent on the arene ring of the aryl bromide, the reaction occurred selectively at the carbon bonded to bromo rather than that bonded to chloro or fluoro (entries 6 and 7). Both electron-donating and -withdrawing substituents were tolerated in the process (entries 8–10). The reaction also took place smoothly with 2-bromonaphthalene and 2-bromo-3-methylthiophene with good yields (entries 11 and 12).

Mechanistic Investigation

One possible reaction pathway for the cross-coupling reaction is a two-step process involving 1,2-H shift of the palladium–carbene species, followed by a Heck–Mizoroki-type reaction.[16] In this process, methyl acrylate should be formed as reaction intermediate, as shown in Scheme 2. To confirm such a reaction pathway, methyl acrylate was subjected to the palladium-catalyzed reaction with phenylboronic acid under the standard conditions (Scheme 2). Methyl cinnamate (**8**) was isolated in very low yield as the product of a Heck–Mizoroki-type reaction. No product **3a** could be detected by TLC or GC-MS for this reaction. Consequently, this pathway could be ruled out.

As discussed in the introduction, for several recently reported palladium-catalyzed reactions of diazo compounds, palladium–carbene generated from the decomposition of the diazo compound has been proposed as a key intermediate.[12] Migratory insertion of palladium–

Table 7 Screening of Silver Salts as Additive[a]

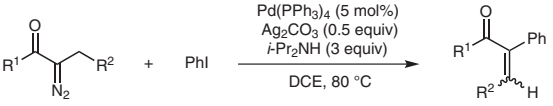


4f 6a 5f

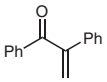
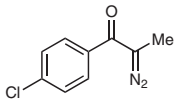
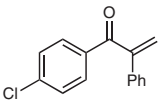
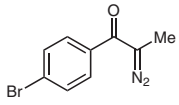
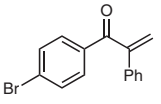
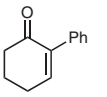
Entry	Ag salt (mol%)	Time (h)	Yield (%)[b]
1	AgF (100)	2	80
2	AgOAc (100)	1.5	67
3	Ag_2CO_3 (50)	1	90
4	Ag_2O (50)	1	50
5	Ag_2CO_3 (50)	1	45[c]

[a] Reaction conditions: **4f** (1.3 equiv), **6a** (1.0 equiv).
[b] Isolated yield.
[c] The reaction was carried out in the absence of *i*-Pr_2NH.

Table 8 Palladium-Catalyzed Reaction of α-Diazoketones **4f–i** with Iodobenzene (**6a**)[a]



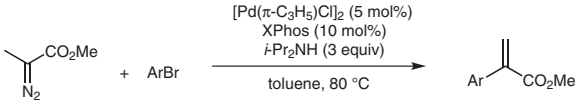
4f–i 6a 5f–i

Entry	4	Time (h)	5	Yield (%)[b]
1	 **4f**	0.5	 **5f**	90
2	 **4g**	0.5	 **5g**	81
3	 **4h**	0.5	 **5h**	75
4	 **4i**	1	 **5i**	76

[a] Reaction conditions: **4** (1.3 equiv), **6a** (1.0 equiv).
[b] Isolated yield.

carbene complexes have been studied previously in stoichiometric reactions.[5] In particular, Barluenga and coworkers proposed that palladium–carbene formation and subsequent migratory insertion took place in their palladium-catalyzed cross-coupling of aryl bromides with *N*-tosylhydrazones.[12d,e] On the basis of this information, we propose a plausible mechanism as shown in Scheme 3. For the coupling with boronic acids, the reaction is initiated by oxidation of palladium(0) by benzoquinone, to afford palladium(II) intermediate **A** (path a). Transmetalation of **A** with arylboronic acid generates intermediate **B**. For the coupling with aromatic halides, the intermediate **B** can be generated by oxidative addition of palladium(0) with aryl halide (via path b). Complexation of the diazo compound to palladium of intermediate **B** and subsequent dinitrogen extrusion would generate palladium–carbene **C**. Migratory insertion of the aryl group to the carbenic carbon leads to intermediate **D**, which could undergo β-hydride elimination to afford the alkene product and to regenerate the catalyst with the assistance of base.

Table 9 Palladium-Catalyzed Reaction of Methyl α-Diazopropionate (**1**) with Aryl Bromides **7a–l**[a]



1 **7a–l** **3a,b,d,f,g,q–w**

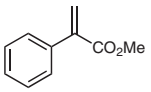
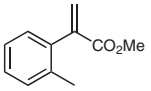
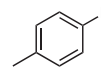
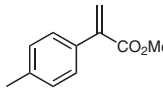
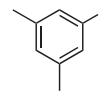
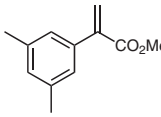
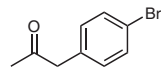
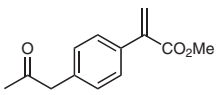
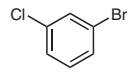
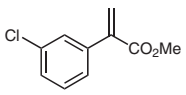
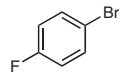
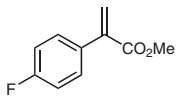
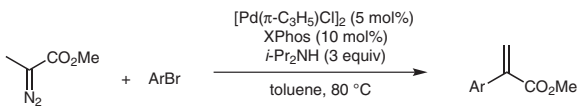
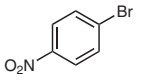
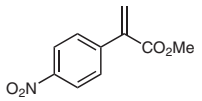
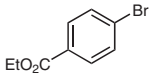
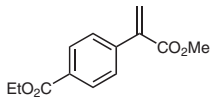
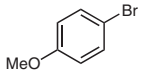
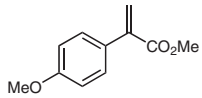
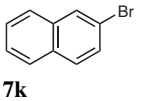
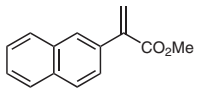
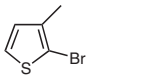
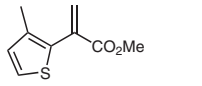
Entry	7	Product 3	Yield (%)[b]
1	 **7a**	 **3a**	86
2	 **7b**	 **3b**	84
3	 **7c**	 **3d**	80
4	 **7d**	 **3f**	86
5	 **7e**	 **3q**	78
6	 **7f**	 **3r**	78
7	 **7g**	 **3s**	77

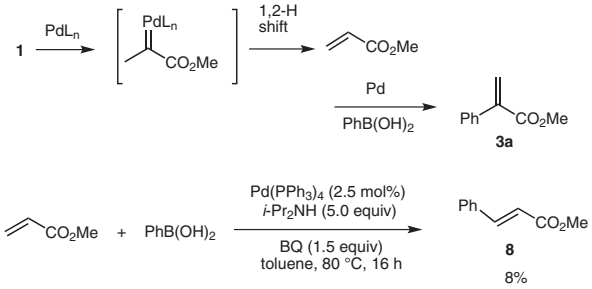
Table 9 Palladium-Catalyzed Reaction of Methyl α-Diazopropionate (**1**) with Aryl Bromides **7a–l**[a] (continued)



1 **7a–l** **3a,b,d,f,g,q–w**

Entry	7	Product 3	Yield (%)[b]
8	 **7h**	 **3t**	47
9	 **7i**	 **3u**	80
10	 **7j**	 **3g**	79
11	 **7k**	 **3v**	94
12	 **7l**	 **3w**	52

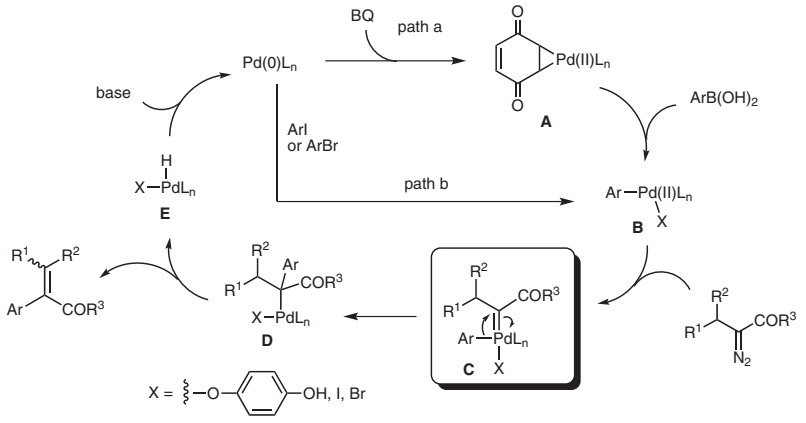
[a] Reaction conditions: **1** (1.5 equiv), **7** (1.0 equiv).
[b] Isolated yield.



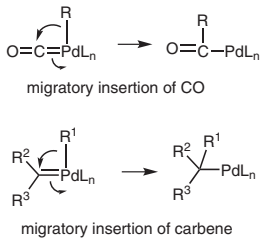
Scheme 2

It is worth noting that the migratory insertion of palladium–carbene may be compared with the migratory insertion of palladium–carbonyl complexes, which is a key step in the palladium-catalyzed carbonylation of aromatic halides (Scheme 4). Palladium-catalyzed migratory carbonyl insertion into the Pd–C bond is a powerful method for introducing a one-carbon unit into an organic molecule.[17]

To gain further insight into the mechanism of this novel coupling reaction, kinetic isotope effect (KIE) experiments were carried out. First, KIE values were measured through intermolecular competition between diazo substrate **9** and deuterated diazo substrate **9**-d_3 (Table 10).



Scheme 3 Mechanistic rationale

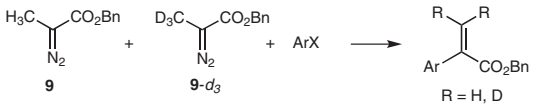


Scheme 4 Comparison of migratory insertion of carbonyl and carbene

Under the standard reaction conditions, equal amounts of **9** and **9**-d_3 were subjected to the reaction with 4-iodotoluene, phenylboronic acid, and 1-(4-bromophenyl)propan-2-one, respectively. In all cases, the measured KIE values were close to 1.0, indicating no kinetic isotope effect for k_{obs}. Furthermore, the KIE values of the β-hydride elimination step were measured though intramolecular competition with monodeuterated diazo substrate **10**-d_1 (Table 11). For the reactions with three different cross-coupling partners, the experiments afforded almost identical k_H/k_D values [k_H/k_D = 2.05, 2.07, 1.95, for reaction with phenyl iodide, phenylboronic acid, and 1-(4-bromophenyl)propan-2-one, respectively]. These values are comparable to the kinetic isotope effects reported for *syn*-β-hydride elimination in other palladium-catalyzed reactions.[18] Furthermore, it is noteworthy that in our recent study on palladium-catalyzed oxidative cross-coupling of diazo compounds with boronic acids, similar kinetic isotopic data were obtained.[12n]

The results of these KIE experiments clearly indicate that the β-hydride elimination is not in the rate-limiting step. From the different reaction times for the reactions with boronic acids, iodides, and bromides, we suppose that the transmetalation or oxidative addition is the slow step in the catalytic cycle. The diazo decomposition, migratory insertion, and β-hydride elimination are all relatively faster processes. The KIE data are consistent with the proposed mechanism shown in Scheme 3.

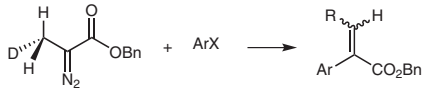
Table 10 Intermolecular Kinetic Isotope Effect Measurement



Ar	X	Conditions[a]	k_H/k_D
4-MeC$_6$H$_4$	I	A	1.0
C$_6$H$_5$	B(OH)$_2$	A	1.0
4-MeC(O)CH$_2$C$_6$H$_4$	Br	B	1.0

[a] Reaction conditions: A. Pd(PPh$_3$)$_4$ (2.5 mol%), *i*-Pr$_2$NH, DCE, 80 °C; B. [Pd(C$_3$H$_5$)Cl]$_2$ (2.5 mol%), XPhos (10 mol%), *i*-Pr$_2$NH (3 equiv), toluene, 80 °C.

Table 11 Intramolecular Kinetic Isotope Effect Measurement



Ar	X	Conditions[a]	k_H/k_D
C$_6$H$_5$	I	A	2.05
C$_6$H$_5$	B(OH)$_2$	A	2.07
4-MeC(O)CH$_2$C$_6$H$_4$	Br	B	1.95

[a] Reaction conditions: A. Pd(PPh$_3$)$_4$ (2.5 mol%), *i*-Pr$_2$NH, DCE, 80 °C; B. [Pd(C$_3$H$_5$)Cl]$_2$ (2.5 mol%), XPhos (10 mol%), *i*-Pr$_2$NH (3 equiv), toluene, 80 °C.

Conclusion

We have developed a novel access to α-aryl-substituted α,β-unsaturated carbonyl compounds by palladium-catalyzed coupling of α-diazocarbonyl compounds with arylboronic acids, aryl iodides, or aryl bromides. The mechanism of the reaction most likely involves a migratory insertion of the aryl group to the carbon of the palladium–carbene, which is generated from the palladium catalyst and the diazo substrate. Although migratory in-

sertion of palladium–carbene species has been studied in stoichiometric reactions, it has attracted attention only recently as a key step in catalytic processes. Incorporation of this process with the well-established rich chemistry of palladium complexes should lead to novel transformations. Moreover, as shown by Barluenga's and our work,[12d,e,k,m,n] extension of the cross-coupling partners from α-diazocarbonyl compounds to other metal–carbene precursors, such as hydrazones, is also possible. On the other hand, organopalladium species can be generated from a variety of precursors, such as allyl halides, 1,4-dienes, allenes, and alkynes. The combination of these processes would significantly expand the scope of this coupling reaction. Novel transformations may also emerge from these combinations. Further studies in this area are underway in our laboratory and the results will be reported in due course.

All reactions were performed under a N_2 atmosphere in flame-dried reaction flasks. All solvents were distilled prior to use. Toluene and THF were dried over Na with benzophenone-ketyl intermediate as indicator. For chromatography, 200–300 mesh silica gel (Qingdao, China) was employed. ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz (or 400 MHz) and 75 MHz (or 100 MHz) on a Varian Mercury 300 or a Bruker ARX400 spectrometer. Chemical shifts are reported with reference to TMS as internal standard. IR spectra were recorded on a Nicolet 5MX-S infrared spectrometer. Mass spectra (EI method) were recorded on a VG-ZAB-HS mass spectrometer. HRMS was carried out on a Bruker APEXIV mass spectrometer. Compounds **3p**,[19] **3r**,[20] **3t**,[19] **3v**,[21] **5j**,[22] **5k**[23] have been reported previously.

Methyl 2-Phenylacrylate (3a) by Palladium-Catalyzed Cross-Coupling between Arylboronic Acids and α-Diazocarbonyl Compounds; Typical Procedure

Under a N_2 atmosphere, methyl α-diazopropionate (**1**; 57 mg, 0.5 mmol) was added to a mixture of phenylboronic acid (**2a**; 183 mg, 1.5 mmol), *i*-Pr_2NH (253 mg, 2.5 mmol), BQ (81 mg, 0.75 mmol), and $Pd(PPh_3)_4$ (14 mg, 0.0125 mmol) in toluene (8 mL). The mixture was stirred at 80 °C until **1** had disappeared as judged by TLC. The solvent was evaporated in vacuo. Purification of the mixture by column chromatography (silica gel, PE–EtOAc, 30:1) gave pure **3a**.

Colorless oil; yield: 66 mg (82%).

Methyl 2-Phenylacrylate (3a) by Palladium-Catalyzed Cross-Coupling between Aryl Iodides and α-Diazocarbonyl Compounds; Typical Procedure

Under a N_2 atmosphere, $Pd(PPh_3)_4$ (27 mg, 0.025 mmol) was added to a mixture of PhI (**6a**; 102 mg, 0.5 mmol), *i*-Pr_2NH (151 mg, 1.5 mmol), and methyl α-diazopropionate (**1**; 74 mg, 0.65 mmol) in DCE (8 mL). The mixture was then stirred at 80 °C until **1** had disappeared as judged by TLC. The solvent was removed in vacuo. Purification of the mixture by column chromatography (silica gel, PE–EtOAc, 30:1) gave pure **3a**.

In the reactions of **4f–i** with **6a**, Ag_2CO_3 (0.25 mmol) was used as additive.

Methyl 2-Phenylacrylate (3a) by Palladium-Catalyzed Cross-Coupling between Aryl Bromides and α-Diazocarbonyl Compounds; Typical Procedure

Under a N_2 atmosphere, a mixture of toluene (8 mL), $[PdCl(C_3H_5)]_2$ (5 mg, 0.0125 mmol), and Xphos (24 mg, 0.05 mmol) was stirred at r.t. After 10 min, *i*-Pr_2NH (151 mg, 1.5 mmol), PhBr (**7a**, 79 mg, 0.5 mmol) and methyl α-diazopropionate (**1**; 86 mg, 0.75 mmol) were added. The mixture was then stirred at 80 °C until **1** had disappeared as judged by TLC. The solvent was removed in vacuo. Purification of the mixture by column chromatography (silica gel, PE–EtOAc, 30:1) gave pure **3a**.

Methyl 2-Phenylacrylate (3a)[24]

Colorless oil; yield: 70 mg (86%).

IR (film): 2952, 1721, 1201 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3 H), 5.89 (d, *J* = 0.9 Hz, 1 H), 6.36 (d, *J* = 0.9 Hz, 1 H), 7.33–7.43 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.2, 126.9, 128.1, 128.2, 128.3, 136.7, 141.3, 167.2.

MS (EI, 70 eV): *m*/*z* (%) = 162 [M$^+$] (49), 131 (13), 103 (100), 77 (30).

Methyl 2-(2-Tolyl)acrylate (3b)[25]

Colorless oil.

IR (film): 2951, 1722, 1209 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3 H), 3.75 (s, 3 H), 5.70 (d, *J* = 1.5 Hz, 1 H), 6.51 (d, *J* = 1.5 Hz, 1 H), 7.11–7.27 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.7, 52.1, 125.6, 128.1, 128.6, 129.4, 129.8, 136.0, 137.1, 141.7, 167.1.

MS (EI, 70 eV): *m*/*z* (%) = 176 [M$^+$] (72), 161 (19), 144 (14), 117 (78), 115 (100), 91 (27).

Methyl 2-(3-Tolyl)acrylate (3c)

Pale yellow oil.

IR (film): 2951, 1724, 1225, 1162 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3 H), 3.82 (s, 3 H), 5.87 (d, *J* = 0.9 Hz, 1 H), 6.34 (d, *J* = 0.9 Hz, 1 H), 7.15–7.26 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4, 52.1, 125.3, 126.6, 128.0, 128.9, 129.0, 136.6, 137.7, 141.4, 167.4.

MS (EI, 70 eV): *m*/*z* (%) = 176 [M$^+$] (70), 145 (8), 117 (100), 91 (16).

Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 75.16; H, 6.94.

Methyl 2-(4-Tolyl)acrylate (3d)[20]

Oil.

IR (film): 2951, 1723, 1202, 1089 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3 H), 3.81 (s, 3 H), 5.85 (d, *J* = 1.2 Hz, 1 H), 6.31 (d, *J* = 1.2 Hz, 1 H), 7.16 (d, *J* = 7.8 Hz, 2 H), 7.30 (d, *J* = 7.8 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.1, 52.1, 126.1, 128.1, 128.8, 133.8, 138.0, 141.1, 167.4.

MS (EI, 70 eV): *m*/*z* (%) = 176 [M$^+$] (63), 117 (100), 91 (16).

Methyl 2-(4-*tert*-Butylphenyl)acrylate (3e)

Colorless oil.

IR (film): 2961, 1724, 1208, 1115 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (s, 9 H), 3.82 (s, 3 H), 5.88 (d, *J* = 1.2 Hz, 1 H), 6.32 (d, *J* = 1.2 Hz, 1 H), 7.34–7.41 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.2, 34.5, 52.1, 125.1, 126.2, 127.9, 133.7, 141.0, 151.2, 167.4.

MS (EI, 70 eV): *m*/*z* (%) = 218 [M$^+$] (20), 203 (100), 159 (5), 143 (24).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{18}O_2$: 218.1307; found: 218.1309.

Methyl 2-(3,5-Dimethylphenyl)acrylate (3f)
Colorless oil.

IR (film): 2951, 1724, 1264, 1163 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 6 H), 3.80 (s, 3 H), 5.84 (d, *J* = 1.2 Hz, 1 H), 6.30 (d, *J* = 1.2 Hz, 1 H), 6.97 (s, 1 H), 7.01 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2, 52.1, 126.0, 126.3, 129.8, 136.6, 137.6, 141.5, 167.4.

MS (EI, 70 eV): *m*/*z* (%) = 190 [M^+] (90), 159(5), 131 (100), 91 (17).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{14}O_2$: 190.0994; found: 190.0994.

Methyl 2-(4-Methoxyphenyl)acrylate (3g)[26]
Colorless oil.

IR (film): 2953, 1721, 1512, 1173 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 3 H), 3.82 (s, 3 H), 5.83 (d, *J* = 1.2 Hz, 1 H), 6.26 (d, *J* = 1.2 Hz, 1 H), 6.88 (d, *J* = 9.0 Hz, 2 H), 7.36 (d, *J* = 9.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.1, 55.2, 113.5, 125.3, 129.1, 129.4, 140.6, 159.6, 167.5.

MS (EI, 70 eV): *m*/*z* (%) = 192 [M^+] (68), 133 (100), 118 (9), 92 (5).

Methyl 2-(3-Nitrophenyl)acrylate (3h)
White solid.

IR (film): 2954, 1724, 1529, 1350, 1207 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.87 (s, 3 H), 6.05 (s, 1 H), 6.55 (s, 1 H), 7.53–7.58 (m, 1 H), 7.76–7.80 (m, 1 H), 8.19–8.23 (m, 1 H), 8.31–8.32 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.4, 122.9, 123.3, 129.0, 129.2, 134.4, 138.2, 139.1, 148.0, 166.0.

MS (EI, 70 eV): *m*/*z* (%) = 207 [M^+] (100), 176(8), 148 (35), 102 (20).

HRMS (EI): *m*/*z* calcd for $C_{10}H_9NO_4$: 207.0532; found: 207.0527.

Methyl 2-(4-Formylphenyl)acrylate (3i)
White solid.

IR (film): 2954, 1709, 1687, 1204, 1090 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H), 6.02 (s, 1 H), 6.51 (s, 1 H), 7.60 (d, *J* = 8.1 Hz, 2 H), 7.89 (d, *J* = 8.1 Hz, 2 H), 10.04 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.3, 128.8, 129.0, 129.4, 135.8, 140.2, 142.6, 166.3, 191.7.

MS (EI, 70 eV): *m*/*z* (%) = 190 [M^+] (100), 159 (13), 131 (72), 103 (24).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{10}O_3$: 190.0630; found: 190.0635.

Methyl 2-(4-Chlorophenyl)acrylate (3j)[27]
Colorless oil.

IR (film): 2952, 1722, 1202, 1094 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3 H), 5.90 (d, *J* = 0.9 Hz, 1 H), 6.39 (d, *J* = 0.9 Hz, 1 H), 7.33–7.36 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.2, 127.3, 128.3, 129.6, 134.2, 135.1, 140.1, 166.8.

MS (EI, 70 eV): *m*/*z* (%) = 196 [M^+] (67), 137 (100), 111 (14).

Methyl 2-(4-Bromophenyl)acrylate (3k)[19]
Colorless oil.

IR (film): 2951, 1722, 1202, 1090 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3 H), 5.90 (d, *J* = 0.9 Hz, 1 H), 6.39 (d, *J* = 0.9 Hz, 1 H), 7.27–7.31 (m, 2 H), 7.47–7.49 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.3, 122.4, 127.4, 129.9, 131.2, 135.5, 140.2, 166.7.

MS (EI, 70 eV): *m*/*z* (%) = 240 [M^+] (97), 181 (94), 102 (100), 75 (29).

Methyl 2-(1-Naphthyl)acrylate (3l)[21]
Colorless oil.

IR (film): 2950, 1721, 1222, cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.71 (s, 3 H), 5.88 (d, *J* = 1.8 Hz, 1 H), 6.72 (d, *J* = 1.8 Hz, 1 H), 7.34–7.37 (m, 1 H), 7.43–7.50 (m, 3 H), 7.71–7.75 (m, 1 H), 7.83–7.87 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.2, 125.2, 125.8, 126.1, 126.9, 128.3, 128.5, 129.9, 131.7, 133.3, 135.2, 140.6, 167.4.

MS (EI, 70 eV): *m*/*z* (%) = 212 [M^+] (28), 153 (100), 84 (27).

Methyl 2-(Biphenyl-4-yl)acrylate (3m)
Colorless oil.

IR (film): 3023, 2945, 1722, 1487, 770 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3 H), 5.94 (d, *J* = 0.9 Hz, 1 H), 6.38 (d, *J* = 0.9 Hz, 1 H), 7.34–7.51 (m, 5 H), 7.57–7.61 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.2, 126.7, 126.8, 127.0, 127.4, 128.6, 128.7, 135.5, 140.5, 140.8, 141.0, 167.2.

MS (EI, 70 eV): *m*/*z* (%) = 238 [M^+] (100), 179 (97), 152 (16).

Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.35; H, 5.99.

Methyl 2-(2-Chlorophenyl)acrylate (3n)
Colorless oil.

IR (film): 2945, 1725, 1207, 763 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.77 (s, 3 H), 5.78. (d, *J* = 0.9 Hz, 1 H), 6.52 (d, *J* = 0.9 Hz, 1 H), 7.26–7.31 (m, 3 H), 7.37–7.40 (m, H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.2, 126.7, 129.1, 129.2, 129.4, 130.8, 133.3, 136.5, 140.1, 166.4.

MS (EI, 70 eV): *m*/*z* (%) = 196 [M^+] (6), 161 (100), 146 (5), 137 (36), 101 (24).

Anal. Calcd for $C_{10}H_9O_2Cl$: C, 61.08, H, 4.61; Found: C, 61.34, H, 4.72.

Methyl 2-(3,4-Dichlorophenyl)acrylate (3o)
White solid.

IR (film): 2951, 1725, 1474, 1091, 825 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3 H), 5.94 (d, *J* = 0.9 Hz, 1 H), 6.43 (d, *J* = 0.9 Hz, 1 H), 7.25–7.28 (m, 1 H),7.41–7.44 (m, 1 H), 7.53–7.54 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.4, 127.7, 128.2, 130.0, 130.2, 132.2, 132.3, 136.5, 139.0, 166.2.

MS (EI, 70 eV): *m*/*z* (%) = 230 [M^+] (72), 199 (13), 171 (100), 136 (45).

Anal. Calcd for $C_{10}H_8O_2Cl_2$: C, 51.98, H, 3.49. Found: C, 51.99; H, 3.61.

Methyl 2-[4-(2-Oxopropyl)phenyl]acrylate (3q)
Oil.

IR (film): 2923, 2852, 1723, 1212, 1173, 1004 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.17 (s, 3 H), 3.71 (s, 2 H), 3.82 (s, 3 H), 5.90 (d, *J* = 0.6 Hz, 1 H), 6.36 (d, *J* = 0.6 Hz, 1 H), 7.20 (d, *J* = 7.8 Hz, 2 H), 7.40 (d, *J* = 7.8 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.2, 50.4, 52.0, 126.7, 128.5, 129.0, 134.1, 135.3, 140.6, 167.0, 205.9.

MS (EI, 70 eV): *m*/*z* (%) = 218 [M$^+$] (20), 176 (63), 159 (10), 145 (9), 116 (53), 43 (100).

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{15}O_3$: 219.1016; found: 219.1018.

Methyl 2-(4-Fluorophenyl)acrylate (3s)
Oil.

IR (film): 2955, 1737, 1510, 1233, 838, 763 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3 H), 5.88 (d, *J* = 0.9 Hz, 1 H), 6.37 (d, *J* = 0.9 Hz, 1 H), 7.02–7.08 (m, 2 H), 7.38–7.42 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.2, 115.0 (d, *J* = 21.4 Hz), 126.9, 130.0 (d, *J* = 8.3 Hz), 132.7 (d, *J* = 3.6 Hz), 140.1, 162.6 (d, *J* = 246 Hz), 166.9.

MS (EI, 70 eV): *m*/*z* (%) = 180 [M$^+$] (46), 149 (8), 121 (100), 101 (40).

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_9FNaO_2$: 203.0479; found: 203.0479.

Ethyl 4-(3-Methoxy-3-oxoprop-1-en-2-yl)benzoate (3u)
Oil.

IR (film): 2979, 2955, 1718, 1274, 1107, 781 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.2 Hz, 3 H), 3.83 (s, 3 H), 4.39 (q, *J* = 7.2 Hz, 2 H), 5.98 (d, *J* = 0.9 Hz, 1 H), 6.46 (d, *J* = 0.9 Hz, 1 H), 7.48–7.51 (m, 2 H), 8.03–8.06 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 52.1, 60.8, 128.1, 129.1, 129.9, 140.3, 140.9, 166.0, 166.4.

MS (EI, 70 eV): *m*/*z* (%) = 234 [M$^+$] (38), 206 (32), 189 (100), 175 (24), 161 (7).

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{15}O_4$: 235.0965; found: 235.0967.

Methyl 2-(3-Methyl-2-thienyl)acrylate (3w)
Oil.

IR (film): 2955, 1733, 1693, 1278, 1028, 715 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3 H), 3.83 (s, 3 H), 5.88 (d, *J* = 1.2 Hz, 1 H), 6.53 (d, *J* = 1.2 Hz, 1 H), 6.88 (d, *J* = 5.1 Hz, 1 H), 7.23 (d, *J* = 5.1 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9, 52.3, 124.3, 129.3, 130.1, 131.7, 134.2, 135.9, 166.6.

MS (EI, 70 eV): *m*/*z* (%) = 182 [M$^+$] (79), 167 (34), 151 (20), 139 (14), 123 (100).

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_9H_{10}NaO_2S$: 205.0294; found: 205.0296.

Isopropyl 2-Phenylacrylate (5a)
Colorless oil.

IR (film): 2981, 1714, 1196, 1091 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (d, *J* = 6.3 Hz, 6 H), 5.17 (m, 1 H), 5.87 (d, *J* = 0.9 Hz, 1 H), 6.32 (d, *J* = 0.9 Hz, 1 H), 7.25–7.45 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7, 68.5, 126.1, 128.0, 128.2, 136.8, 141.8, 166.3.

MS (EI, 70 eV): *m*/*z* (%) = 190 [M$^+$] (35), 148 (55), 132 (23), 103 (100), 77 (35), 43 (52).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{14}O_2$: 190.0994; found: 190.0990.

Methyl (*Z*)-2-Phenylpent-2-enoate (5b)
Colorless oil.

IR (film): 2967, 1721, 1202 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11 (t, *J* = 7.5 Hz, 3 H), 2.45 (m, 2 H), 3.80 (s, 3 H), 6.18 (t, *J* = 7.5 Hz, 1 H), 7.26–7.32 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 23.6, 51.7, 127.2, 127.5, 128.2, 133.9, 137.9, 142.1, 168.6.

MS (EI, 70 eV): *m*/*z* (%) = 190 [M$^+$] (100), 158 (65), 131 (78), 115 (60), 91 (48), 77 (20).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{14}O_2$: 190.0994; found: 190.0999.

Methyl (*E*)-2-Phenylpent-2-enoate (5b)
Colorless oil.

IR (film): 2967, 1716, 1241 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.5 Hz, 3 H), 2.08 (m, 2 H), 3.72 (s, 3 H), 7.07 (t, *J* = 7.5 Hz, 1 H), 7.16–7.18 (m, 2 H), 7.31–7.39 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.2, 22.8, 51.9, 127.3, 127.9, 129.6, 133.1, 135.3, 146.7, 167.7.

MS (EI, 70 eV): *m*/*z* (%) = 190 [M$^+$] (100), 158 (65), 131 (79), 115 (60), 91 (49), 77 (20).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{14}O_2$: 190.0994; found: 190.0992.

Methyl 2,3-Diphenylacrylate (5c)[28]
Obtained as a *Z*/*E* mixture of isomers (1:1.5); white solid.

(*E*)-5c

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.79 (s, 3 H), 7.03–7.48 (m, 10 H), 7.86 (s, 1 H).

Mixture of Isomers 5c
IR (film): 3025, 2949, 1711, 1251, 1168 cm^{-1}.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.2, 52.3, 126.4, 127.8, 128.1, 128.2, 128.3, 128.5, 128.6, 128.7, 129.0, 129.7, 130.5, 131.5, 132.4, 134.5, 134.8, 135.6, 135.8, 136.8, 140.5, 168.3, 170.0.

MS (EI, 70 eV): *m*/*z* (%) = 238 [M$^+$] (89), 207 (8), 179 (78), 121 (100), 103 (14), 77 (21).

Methyl (*Z*)-2,5-Diphenylpent-2-enoate (5d)
Colorless oil.

IR (film): 2920, 1720, 1204 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.75–2.85 (m, 4 H), 3.77 (s, 3 H), 6.21 (t, *J* = 6.9 Hz, 1 H), 7.18–7.32 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.8, 35.4, 51.7, 126.0, 127.3, 127.6, 128.2, 128.4, 128.5, 134.9, 137.9, 139.6, 141.1, 168.4.

MS (EI, 70 eV): *m*/*z* (%) = 266 [M$^+$] (22), 235 (6), 190 (6), 115 (54), 91 (100).

Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.18; H 6.92

Methyl (*E*)-2,5-Diphenylpent-2-enoate (5d)
Colorless oil.

IR (film): 2949, 1715, 1252 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35–2.42 (m, 2 H), 2.72 (t, *J* = 7.5 Hz, 2 H), 3.71 (s, 3 H), 7.03–7.35 (m, 11 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.2, 34.9, 52.0, 126.1, 127.4, 127.9, 128.3, 128.4, 129.5, 134.3, 135.1, 140.8, 144.0, 167.6.

MS (EI, 70 eV): *m*/*z* (%) = 266 [M$^+$] (41), 235 (8), 175 (12), 115 (90), 91 (100), 77 (9).

Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.13; H 6.91.

Methyl 3-Methyl-2-phenylbut-2-enoate (5e)[29]
Colorless oil.

IR (film): 2949, 1714, 1220 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.71 (s, 3 H), 2.16 (s, 3 H), 3.69 (s, 3 H), 7.18–7.20 (m, 2 H), 7.28–7.39 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.6, 23.3, 51.6, 126.9, 128.1, 129.4, 129.7, 138,1 145.7, 168.9.

MS (EI, 70 eV): *m*/*z* (%) = 190 [M$^+$] (100), 158 (57), 131 (79), 115 (57), 73 (84).

1,2-Diphenylprop-2-en-1-one (5f)[30]
White solid.

IR (film): 3059, 1665, 1214 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.64 (s, 1 H), 6.07 (s, 1 H), 7.33–7.57 (m, 8 H), 7.90–7.93 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 120.9, 127.0, 128.3, 128.4, 128.6, 129.9, 133.0, 136.9, 137.0, 148.2, 197.5.

MS (EI, 70 eV): *m*/*z* (%) = 208 [M$^+$] (38), 132 (4), 105 (100), 77 (59).

1-(4-Chlorophenyl)-2-phenylprop-2-en-1-one (5g)
Oil.

IR (film): 3059, 1665, 1586, 1212 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.64 (s, 1 H), 6.06 (s, 1 H), 7.32–7.42 (m, 7 H), 7.82–7.87 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 121.1, 126.9, 128.5, 128.6, 128.7, 131.3, 135.3, 136.7, 139.5, 147.9, 196.2.

MS (EI, 70 eV): *m*/*z* (%) = 242 [M$^+$] (42), 207 (20), 139 (100), 111 (26), 103 (25).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}OCl$: 242.0498; found: 242.0492.

1-(4-Bromophenyl)-2-phenylprop-2-en-1-one (5h)
Oil.

IR (film): 3057, 1665, 1583, 1210 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.65 (s, 1 H), 6.07 (s, 1 H), 7.32–7.42 (m, 5 H), 7.54–7.58 (m, 2 H), 7.74–7.79 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 121.1, 126.9, 128.2, 128.5, 128.6, 131.4, 131.7, 135.7, 136.6, 147.9, 196.3.

MS (EI, 70 eV): *m*/*z* (%) = 286 [M$^+$] (25), 207 (57), 183 (100), 155 (27), 103 (42).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}OBr$: 285.9993; found: 285.9987.

2-Phenylcyclohex-2-enone (5i)[31]
Solid.

IR (film): 2941, 1680, 1154 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.05–2.14 (m, 2 H), 2.50–2.61 (m, 4 H), 7.03 (t, *J* = 4.2 Hz, 1 H), 7.25–7.37 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.8, 26.5, 39.0, 127.5, 127.9, 128.6, 136.5, 140.3, 148.0, 197.9.

MS (EI, 70 eV): *m*/*z* (%) = 172 [M$^+$] (100), 144 (74), 116 (77), 89 (10), 77 (13).

Hydrogen/Deuterium Kinetic Isotope Effect Studies

Benzyl 3,3,3-Trideuterio-α-diazopropionate (9-*d*$_3$)

Benzyl 2-(methyl-*d*$_3$)-3-oxobutanoate (**11**-*d*$_3$): Under a N_2 atmosphere, a soln of benzyl 3-oxobutanoate (2.88 g, 15 mmol) in THF (10 mL) was added dropwise to a stirred suspension of NaH (60% dispersion in mineral oil; 0.6 g, 15 mmol) in THF (10 mL) at r.t. After the mixture had become clear, NaI (4.5g, 30 mmol) was added. Then a soln of CD_3OTs (10 mmol) in THF (10 mL) was added dropwise, and the mixture was stirred at 60 °C. After completion of the reaction as monitored by TLC, sat. aq NH_4Cl (10 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4) and evaporated, and the crude residue was purified by column chromatography (silica gel, PE–EtOAc, 50:1) to afford pure benzyl 2-(methyl-*d*$_3$)-3-oxobutanoate (**11**-*d*$_3$).

Benzyl 3,3,3-trideuterio-α-diazopropionate (**9**-*d*$_3$): A soln of 4-acetamidobenzenesulfonyl azide (*p*-ABSA; 3.12 g, 13 mmol) in CH_2Cl_2 (10 mL) was added dropwise to a soln of benzyl 2-(methyl-*d*$_3$)-3-oxobutanoate (**11**-*d*$_3$; 2.09 g, 10 mmol) and DBU (2.28 g, 15 mmol) in CH_2Cl_2 (30 mL) at r.t., and the mixture was stirred overnight. The soln was filtered through a short column (silica gel) to remove the DBU. The crude product was further purified by column chromatography (silica gel, PE–EtOAc, 10:1) to afford pure **9**-*d*$_3$.

Oil; yield: 75% (1 step); 41% (2 steps).

IR (film): 3032, 2097, 1687, 1295, 1128, 1048, 697 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.21 (s, 2 H), 7.33–7.38 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.2, 128.0, 128.1, 128.5, 136.1.

MS (EI, 70 eV): *m*/*z* (%) = 193 [M$^+$] (2), 165 (2), 147 (2), 135 (22), 121 (6), 91 (100).

ESI-HRMS: *m*/*z* [M + Na]$^+$ for $C_{10}H_7D_3N_2NaO_2$: 216.0823; found: 216.0823.

Benzyl 3-Deuterio-α-diazopropionate (10-*d*$_1$)

Benzyl 3-deuteriopropionate (**12**-*d*$_1$): A soln of benzyl acrylate (3.24 g, 20 mmol) in EtOH (5 mL) was added dropwise to a stirred suspension of $NaBD_4$ (0.42 g, 10 mmol) in EtOH (5 mL) at 0 °C, and the mixture was stirred at 0 °C for 1 h and then at r.t. for another 4 h. After completion of the reaction as monitored by TLC, sat. aq NaCl (10 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layer was dried (Na_2SO_4) and evaporated, and the residue was purified by column chromatography (silica gel, PE–EtOAc, 20:1) to afford benzyl 3-deuteriopropionate (**12**-*d*$_1$); yield: 43%.

Benzyl 2-(methyl-*d*$_1$)-3-oxo-3-phenyl-3-deuteriopropionate (**13**-*d*$_1$): Under a N_2 atmosphere, a soln of **12**-*d*$_1$ (0.66 g, 4 mmol) in THF (10 mL) was added dropwise to a stirred suspension of NaH (60% dispersion in mineral oil; 0.64 g, 16 mmol) in THF (10 mL) and the mixture was then stirred for 30 min at 0 °C. Then a soln of $PhCO_2Bn$ (1.272 g, 6 mmol) in THF (10 mL) was added dropwise, and the mixture was stirred at 80 °C. After completion of the reaction as monitored by TLC, the reaction mixture was quenched by cautious addition of 1.0 M aq HCl to pH = 4. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated, and the residue was purified by column chromatography (silica gel, PE–EtOAc, 40:1) to afford benzyl 2-(methyl-*d*$_1$)-3-oxo-3-phenyl-3-deuteriopropionate (**13**-*d*$_1$); yield: 70%.

Benzyl 3-deuterio-α-diazopropionate (**10**-*d*$_1$): A soln of *p*-ABSA (1.44 g, 6 mmol) in CH_2Cl_2 (10 mL) was added dropwise to a soln of **13**-*d*$_1$ (0.79 g, 3 mmol) and DBU (0.91 g, 6 mmol) in CH_2Cl_2 (30 mL) at r.t. The soln was stirred overnight and then filtered through a short column (silica gel) to remove the DBU. The crude product was further purified by column chromatography (silica gel, PE–EtOAc, 10:1) to afford pure **10**-*d*$_1$; yield: 74%; oil.

IR (film): 3029, 2081, 1687, 1113 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.95 (t, *J* = 2.1 Hz, 2 H), 5.20 (s, 2 H), 7.24–7.36 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.15 (t, *J* = 20.1 Hz), 66.3, 127.9, 128.1, 128.4, 136.1.

MS (EI, 70 eV): *m*/*z* (%) = 191 [M^+] (3), 163 (3), 147 (3), 133 (32), 119 (9), 91 (100).

Anal. Calcd for $C_{10}H_9DN_2O_2$: C, 63.15; H, 5.30, N, 14.73. Found: C, 63.38; H 5.40; N, 14.28.

Kinetic Isotopic Effect (KIE) Experiments

Each experiment was performed twice, and the KIE data were the average of two runs.

Intermolecular KIE Experiment with $PhB(OH)_2$

$Pd(PPh_3)_4$ (17 mg, 0.015 mmol) was added to a soln of **9** (57 mg, 0.3 mmol), **9**-d_3 (57 mg, 0.3 mmol), phenylboronic acid (220 mg, 1.8 mmol), benzoquinone (97 mg, 0.9 mmol), and *i*-Pr_2NH (303 mg, 3.0 mmol) in DCE (8 mL). The mixture was stirred at 80 °C and the reaction was stopped before completion. Then the crude products were purified by column chromatography (silica gel, PE–EtOAc, 30:1). The ratios were determined from the ^1H NMR spectra.

Intermolecular KIE Experiment with Aryl Iodide

$Pd(PPh_3)_4$ (35 mg, 0.03 mmol) was added to a soln of **9** (57 mg, 0.3 mmol), **9**-d_3 (58 mg, 0.3 mmol), 4-iodotoluene (196 mg, 0.9 mmol), and *i*-Pr_2NH (182 mg, 1.8 mmol) in DCE (8 mL). The mixture was stirred at 80 °C and the reaction was stopped before completion. Then the crude products were purified by column chromatography (silica gel, PE–EtOAc, 30:1). The ratios were determined from the ^1H NMR spectra.

Intermolecular KIE Experiment with Aryl Bromide

A soln of $[PdCl(C_3H_5)]_2$ (3 mg, 0.0075 mmol) and Xphos (14 mg, 0.03 mmol) in toluene (8 mL) was stirred at r.t. After 10 min, 1-(4-bromophenyl)propan-2-one (64 mg, 0.3 mmol), *i*-Pr_2NH (91 mg, 0.9 mmol), **9** (86 mg, 0.45 mmol), and **9**-d_3 (87 mg, 0.45 mmol) were added. The mixture was stirred at 80 °C and the reaction was stopped before completion. Then the crude products were purified by column chromatography (silica gel, PE–EtOAc, 30:1). The ratios were determined from the ^1H NMR spectra.

Intramolecular KIE Experiment

$Pd(PPh_3)_4$ (17 mg, 0.015 mmol) was added to a mixture of **10**-d_1 (57 mg, 0.3 mmol), iodobenzene (92 mg, 0.45 mmol), and *i*-Pr_2NH (151 mg, 1.5 mmol) in DCE (8 mL). The mixture was stirred at 80 °C until the **10**-d_1 had completely disappeared as judged by TLC. The ratios of the products were determined from the ^1H NMR spectra. The reactions of **10**-d_1 with phenylboronic acid and 1-(4-bromophenyl)propan-2-one were carried out by following the same procedure as described above.

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