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Nickel-Catalyzed Mizoroki–Heck- versus Michael-Type Addition of Organoboronic Acids to α,β-Unsaturated Alkenes through Fine-Tuning of Ligands

Pao-Shun Lin, Masilamani Jeganmohan, and Chien-Hong Cheng*[a]

Abstract: Various arylboronic acids reacted with activated alkenes in the presence of [Ni(dppe)Br_2], $ZnCl_2$, and H_2O in CH_3CN at 80 °C to give the corresponding Mizoroki–Heck-type addition products in good to excellent yields. Furthermore, 1 equivalent of the hydrogenation product of the activated alkene was also produced. By tuning the ligands of the nickel complexes and the reaction conditions, Michael-type addition was achieved in a very selective manner. Thus, various *p*- and *o*-substituted arylboronic acids or alkenylboronic acid reacted smoothly with activated alkenes in CH_3CN at 80 °C for 12 h catalyzed by $Ni(acac)_2$, P(*o*-anisyl)$_3$, and K_2CO_3 to give the corresponding Michael-type addition products in excellent yields. However, for *m*-substituted arylboronic acids, the yields of Michael-type addition products are very low. The cause of this unusual *meta*-substitution effect is not clear. By altering the solvent or phosphine ligand, the product yields for *m*-substituted arylboronic acids were greatly improved. In contrast to previous results in the literature, the present catalytic reactions required water for Mizoroki–Heck-type products and dry reaction conditions for Michael-type addition products. Possible mechanistic pathways for both addition reactions are proposed.

Keywords: alkenes · arylboronic acids · Michael addition · Mizoroki–Heck addition · nickel

Introduction

The addition reaction of an organometallic reagent to activated alkenes catalyzed by transition-metal complexes is one of the most versatile and well-acknowledged methods for the construction of carbon–carbon bonds in organic synthesis.[1] Various organometallic reagents such as organoboron,[2] organosilane,[3] organotin,[4] organozinc,[5] and organomercury compounds[6] are widely used. Among them, organoboron reagents display multifarious advantages, including easy availability, stability to air and moisture, low toxicity, and simple removal of boron-derived by-products, unlike other organometallic reagents.[7]

Mizoroki–Heck-[8] and Michael-type[2,9] reactions are two familiar categories of metal-catalyzed addition reactions of organoboron reagents to α,β-unsaturated carbonyl compounds. The catalytic reaction proceeds by transmetalation of the organoboron reagent followed by insertion of activated alkenes to give an alkyl metal intermediate. If the alkyl metal intermediate prefers β-hydride elimination,[10] the Mizoroki–Heck-type product is generally obtained under dry reaction conditions. Conversely, if the alkyl metal intermediate readily enolizes to give the oxa-π-allyl species,[9i,11] the O-bound enolate then facilitates hydrolysis in the presence of water to afford the Michael-type addition product. The reaction type is mainly determined by the nature of the metal complex. In general, palladium complexes catalyze Mizoroki–Heck-type reactions of aryl or alkenyl boron reagents with α,β-unsaturated alkenes in the presence of reoxidants such as $Cu(OAc)_2$ or oxygen.[8a–f] Biaryls, homocoupled compounds from organoboron reagents, are formed as by-products. On the other hand, rhodium(I) complexes are the most efficient catalysts for the addition of organoboron reagents to α,β-unsaturated alkenes to give Michael-type reaction products.[9c–j] There are several exceptions to rhodium-catalyzed addition reactions of organoboronic acids with activated alkenes.[8i,j] For instance, Lautens et al. reported a Mizoroki–Heck-type reaction of arylboronic acids with styrenes in moderate yields, but a Michael-type reaction with

[a] P.-S. Lin, Dr. M. Jeganmohan, Prof. C.-H. Cheng
Department of Chemistry
National Tsing Hua University
Hsinchu 30013 (Taiwan)
Fax: (+886) 3-572-4698
E-mail: chcheng@mx.nthu.edu.tw

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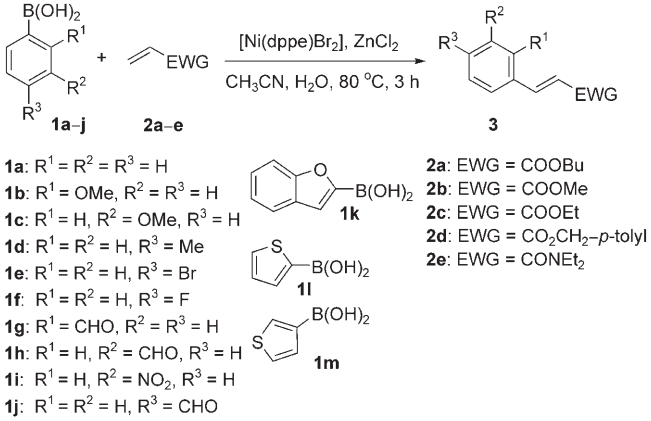
vinylpyridines. In these previous reports, it appears that aqueous conditions are necessary for Michael-type addition.

Our continual interest in nickel-catalyzed coupling reactions[12] prompted us to explore the possibility of using nickel complexes as catalysts for the addition reaction of organoboron reagents with activated alkenes. Herein, we report the nickel-catalyzed Mizoroki–Heck- and Michael-type addition of organoboronic acids to activated alkenes. By fine-tuning the ligands, we were able to control the addition reaction to give either product with remarkable selectivity. In contrast to the previous results, the present catalytic reaction requires water for the Mizoroki–Heck-type product and dry reaction conditions for the formation of the Michael-type addition product.

Results and Discussion

Mizoroki–Heck-Type Addition Reaction

Treatment of phenylboronic acid (**1a**; 1.0 mmol) with butyl acrylate (**2a**; 3.0 mmol) and H_2O (3.0 mmol) in CH_3CN in the presence of [Ni(dppe)Br_2] (5 mol%) and $ZnCl_2$ (15 mol%) at 80°C for 3 h gave (*E*)-butyl cinnamate (**3aa**) in 96% yield (Scheme 1).[13] Besides **3aa**, an equal amount



Scheme 1. Nickel-catalyzed Mizoroki–Heck-type addition reaction of arylboronic acids **1** with activated alkenes **2**. dppe = 1,2-bis(diphenylphosphanyl)ethane.

of butyl propionate, the hydrogenation product of butyl acrylate, was also observed. As a result, more than 2 equivalents of butyl acrylate were used for the present catalytic reaction. This reaction is highly stereoselective and afforded only the *E* isomer as the addition product. Product **3aa** was thoroughly characterized by its ^1H and ^{13}C NMR, IR, and mass spectral data. A control experiment revealed that, in the absence of either nickel complex or $ZnCl_2$, no expected product was observed.

To optimize the reaction conditions, the effects of additive, nickel complex, and solvent were examined (Table 1).

Table 1. Effect of additive, catalyst, and solvent on the Mizoroki–Heck-type addition reaction of phenylboronic acid (**1a**) with butyl acrylate (**2a**).[a]

Entry	Additive	Catalyst	Solvent	Yield [%][b]
1	Na_2CO_3	[Ni(dppe)Br_2]	CH_3CN	42
2	K_2CO_3	[Ni(dppe)Br_2]	CH_3CN	57
3	NEt_3	[Ni(dppe)Br_2]	CH_3CN	0
4	H_2O	[Ni(dppe)Br_2]	CH_3CN	99
5	H_2O	[Ni(dppe)I_2]	CH_3CN	89
6	H_2O	[Ni(dppe)Cl_2]	CH_3CN	19
7	H_2O	[Ni(dppm)Br_2]	CH_3CN	18[c]
8	H_2O	[Ni(dppp)Br_2]	CH_3CN	27
9	H_2O	[Ni(dppb)Br_2]	CH_3CN	0
10	H_2O	[Ni(PPh_3)$_2Br_2$]	CH_3CN	0
11	H_2O	[Ni(PPh_3)$_2Cl_2$]	CH_3CN	0
12	H_2O	[Ni(dppe)Br_2]	THF	54
13	H_2O	[Ni(dppe)Br_2]	1,4-dioxane	0
14	H_2O	[Ni(dppe)Br_2]	ethyl acetate	62
15	H_2O	[Ni(dppe)Br_2]	toluene	19
16	H_2O	[Ni(dppe)Br_2]	EtOH	57
17	H_2O	[Ni(dppe)Br_2]	DCE	0
18	H_2O	[Ni(dppe)Br_2]	DME	32

[a] Reactions were carried out with **1a** (1.00 mmol), **2a** (3.00 mmol), [Ni(dppe)Br_2] (0.050 mmol, 5.0 mol%), $ZnCl_2$ (0.150 mmol, 15.0 mol%), and an additive (3.00 mmol) in a solvent (2.0 mL) at 80°C for 3 h under N_2. [b] Yield of **3aa** was determined by ^1H NMR spectroscopy with mesitylene as an internal standard. [c] Michael-type addition product **4aa** was observed. DCE = 1,2-dichloroethane, DME = 1,2-dimethoxyethane, dppb = 1,4-bis(diphenylphosphanyl)butane, dppm = diphenylphosphanylmethane, dppp = 1,3-bis(diphenylphosphanyl)propane.

Phenylboronic acid (**1a**) and butyl acrylate (**2a**) were used as the substrates in these studies. The yield of **3aa** was determined based on the ^1H NMR signal-integration method with mesitylene as an internal standard. In the reaction with [Ni(dppe)Br_2] (5 mol%) at 80°C for 3 h in CH_3CN, no addition product **3aa** was observed. The addition of a catalytic amount of Lewis acid $ZnCl_2$ (15%) led to the formation of **3aa**, albeit in only 10% yield. Various additives, Na_2CO_3, K_2CO_3, NEt_3, and water, were then tested (Table 1, entries 1–4). Among them, water exhibited the highest activity to afford **3aa** in quantitative yield (Table 1, entry 4). The other additives Na_2CO_3, K_2CO_3, and NEt_3 afforded **3aa** in 42, 57, and 0% yields, respectively (Table 1, entries 1–3). Notably, the presence of a base is generally essential to activate organoboron reagents in coupling reactions. However, in the present case, water was required instead of base.

Besides [Ni(dppe)Br_2], various bidentate and monodentate phosphine nickel complexes were examined for catalytic activity in the reaction of **1a** with **2a** to give **3aa** (Table 1,

Abstract in Chinese:

近幾年來，藉由過渡金屬催化有機硼試劑進行的偶合反應在有機合成上日趨重要。本文中，我們利用鎳金屬錯化合物為觸媒，經由適當的調整配位基團，成功的使有機硼試劑與共軛雙烯類選擇性的進行 Mizoroki–Heck 或 Michael 兩種加成反應。研究結果顯示，配位基團的種類及電子密度對於反應型態有決定性的影響。

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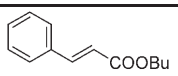
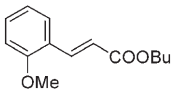
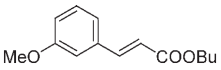
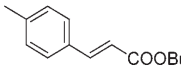
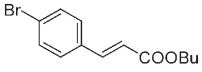
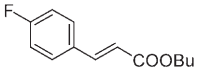
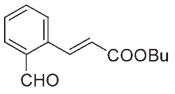
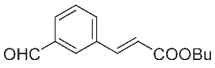
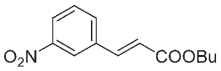
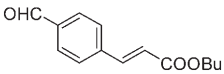
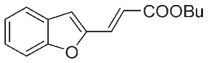
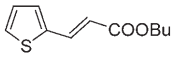
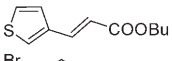
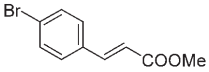
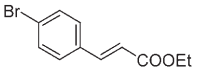
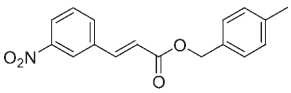
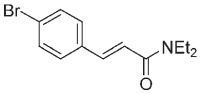
entries 5–11). The results indicate that dppe complexes (Table 1, entries 4–6) are more reactive than the other bidentate phosphine complexes (Table 1, entries 7–9), whereas monodentate PPh_3 complexes are inactive. Several solvents were examined for the present reaction. The results reveal that CH_3CN is the solvent of choice; it gave the highest yield of product **3aa**. Other solvents such as THF, 1,4-dioxane, ethyl acetate, toluene, EtOH, DCE, and DME gave **3aa** in 54, 0, 62, 19, 57, 0, and 32% yield, respectively (Table 1, entries 12–18). On the basis of these optimization studies, we chose [Ni(dppe)Br_2] (5 mol%), $ZnCl_2$ (15 mol%), and water (3 mmol) in CH_3CN at 80°C for 3 h as the reaction conditions for the following catalytic reactions.

Under the optimized reaction conditions, a wide range of arylboronic acids and activated alkenes were investigated. The results are summarized in Table 2. Arylboronic acids **1b–j** efficiently reacted with **2a** to afford the corresponding Mizoroki–Heck-type addition products in good to excellent yields (Table 2, entries 2–10). In all cases, only the *E* stereoisomers were observed. The catalytic reactions tolerated a variety of functional groups such as OMe, Br, F, CHO, and NO_2 on the phenyl ring of arylboronic acids **1**. These results indicate that the catalytic reaction is insensitive to the electronic properties of the substituent, but does depend on the position of the substituent on the ring. For example, 2-methoxyphenylboronic acid (**1b**) gave **3ba** in only 35% yield (Table 2, entry 2), whereas 3-methoxyphenylboronic acid (**1c**) afforded **3ca** in a very high 93% yield (Table 2, entry 3). Likewise, 2-formylphenylboronic acid (**1g**) afforded **3ga** in 67% yield (Table 2, entry 7), but 3-formyl- and 4-formylphenylboronic acid (**1h** and **1j**) gave **3ha** and **3ja** in 87 and 93% yields, respectively (Table 2, entries 8 and 10). The present catalytic reaction was successfully extended to heteroaromatic boronic acids **1k–m**. Thus, treatment of benzo[*b*]furan-2-boronic acid (**1k**) with **2a** under the optimized reaction conditions afforded **3ka** in 93% yield (Table 2, entry 11). Similarly, 2-thienylboronic acid (**1l**) and 3-thienylboronic acid (**1m**) reacted efficiently with butyl acrylate (**2a**) to give the corresponding addition product **3la** and **3ma** in 87 and 81% yield, respectively (Table 2, entries 12 and 13). Besides **2a**, other acrylates such as methyl acrylate (**2b**), ethyl acrylate (**2c**), and 4-methylbenzyl acrylate (**2d**) also reacted with 4-bromophenylboronic acid (**1e**) or 3-nitrophenylboronic acid (**1i**) to afford the corresponding Mizoroki–Heck-type products in 88–96% yield (Table 2, entries 14–16). In contrast to the previous rhodium catalytic system,[8g] *N*,*N*-diethylacrylamide (**2e**) reacted efficiently with **1e** to afford **3ee** in 79% yield (Table 2, entry 17).

Table 2. Results of the nickel-catalyzed Mizoroki-Heck-type addition reaction of arylboronic acids **1** with activated alkenes **2**.[a]

Entry	1	2	Product 3	Yield [%][b]
1	**1a**	**2a**		96
2	**1b**	**2a**		35 62[c]
3	**1c**	**2a**		93
4	**1d**	**2a**		86
5	**1e**	**2a**		98
6	**1f**	**2a**		94
7	**1g**	**2a**		67
8	**1h**	**2a**		87
9	**1i**	**2a**		86
10	**1j**	**2a**		93
11	**1k**	**2a**		93
12	**1l**	**2a**		87
13	**1m**	**2a**		81
14	**1e**	**2b**		93
15	**1e**	**2c**		96
16	**1i**	**2d**		88
17	**1e**	**2e**		79

[a] Reactions were carried out with **1** (1.00 mmol), **2** (3.00 mmol), [Ni(dppe)Br_2] (0.050 mmol, 5.0 mol%), $ZnCl_2$ (0.150 mmol, 15.0 mol%), and H_2O (3.00 mmol) in CH_3CN (2.0 mL) at 80°C for 3 h under N_2. [b] Yield of isolated product. [c] The reaction was carried out at 90°C.

Michael-Type Addition Reaction

In the reaction of phenylboronic acid (**1a**) with butyl acrylate (**2a**) under the optimized reaction conditions above, but with a further 10 mol% acacH (acac = acetylacetonate), an unexpected Michael-type addition product **4aa** was formed in 35% yield. This result prompted us to explore the possibility of using oxygen-based nickel complexes as catalysts for the Michael-type addition reaction.

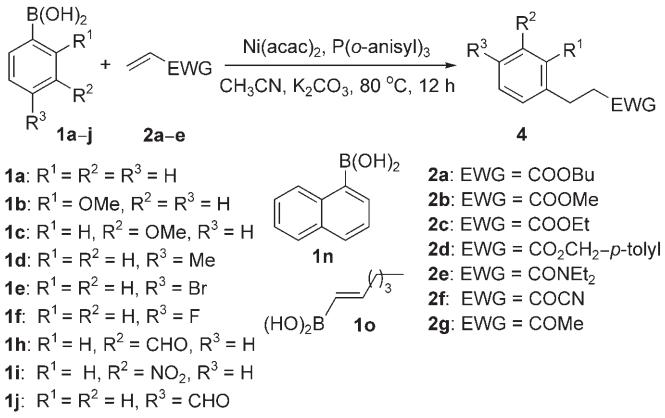
In the following optimization studies, the reactions were carried out with **1a** and **2a** as the substrates and Ni(acac)$_2$/phosphine as the catalyst in the presence of an additive (Table 3). Ni(acac)$_2$ alone does not catalyze the reaction (Table 3, entry 1). In the presence of water with Ni(acac)$_2$/PPh_3 as the catalyst, the Michael-type addition product **4aa**

Table 3. Effect of additive and catalyst on the nickel-catalyzed Michael-type addition reaction of phenylboronic acid (**1a**) with butyl acrylate (**2a**).[a]

Entry	Additive	Catalyst	Yield [%][b]
1	K_2CO_3	$Ni(acac)_2$	0
2	H_2O	$Ni(acac)_2/PPh_3$	10
3	K_2CO_3	$Ni(acac)_2/PPh_3$	78
4	K_2CO_3	$Ni(acac)_2/PCy_3$	90
5	K_2CO_3	$Ni(acac)_2/P(t\text{Bu})_3$	91
6	K_2CO_3	$Ni(acac)_2/P(o\text{-tolyl})_3$	91
7	K_2CO_3	$Ni(acac)_2/P(o\text{-anisyl})_3$	99
8	K_2CO_3	$Ni(acac)_2/P(p\text{-anisyl})_3$	81
9	K_2CO_3	$Ni(acac)_2$/dppe	75
10	K_2CO_3	$Ni(acac)_2$/dppb	60

[a] Reactions were carried out with **1a** (2.00 mmol), **2a** (1.00 mmol), $Ni(acac)_2$ (0.050 mmol, 5.0 mol%), phosphine ligand (0.050 mmol, 5.0 mol%), and an additive (2.00 mmol) in CH_3CN (2.0 mL) at 80°C for 12 h under N_2. [b] Yield of **4aa** was determined by the ^1H NMR signal-integration method with mesitylene as an internal standard. Cy = cyclohexyl.

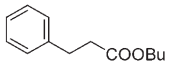
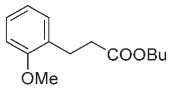
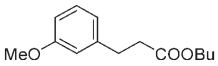
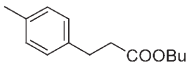
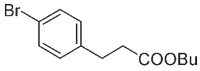
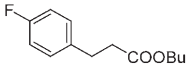
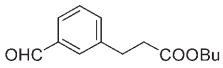
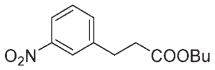
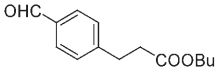
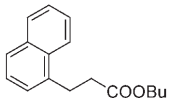
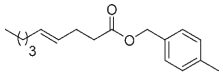
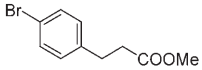
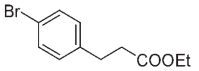
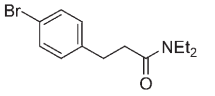
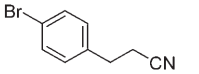
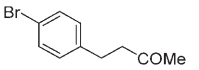
was obtained, but in only 10% yield (Table 3, entry 2). By replacing water with K_2CO_3, **4aa** was obtained in 78% yield (Table 3, entry 3). The addition of phosphine ligand appears to improve the nickel catalytic activity greatly. Consequently, various phosphine ligands such as PPh_3, PCy_3, $P(t\text{Bu})_3$, $P(o\text{-tolyl})_3$, $P(o\text{-anisyl})_3$, $P(p\text{-anisyl})_3$, dppe, and dppb were examined for the reaction (Table 3, entries 3–10). Among them, highly electron-rich and sterically hindered $P(o\text{-anisyl})_3$ gave the best yield at 99% (Table 3, entry 7). Other similar ligands $P(o\text{-tolyl})_3$, PCy_3, and $P(t\text{Bu})_3$ also provided **4aa** in very high yields of 91, 90, and 91%, respectively. Monodentate phosphines with less-hindered ligands such as $P(p\text{-anisyl})_3$ and PPh_3 also gave **4aa** in 81 and 78% yield, respectively. Bidentate phosphine ligands dppe and dppb afforded **4aa** in only 75 and 60% yield, respectively (Table 3, entries 9 and 10). On the basis of these optimization studies, we employed $Ni(acac)_2/P(o\text{-anisyl})_3$ (5 mol%), and K_2CO_3 (2 mmol) in acetonitrile at 80°C for 12 h as the standard reaction conditions for the following catalytic Michael-type addition reactions.



Scheme 2. Nickel-catalyzed Michael-type addition reaction of aryl and alkenylboronic acids **1** with activated alkenes **2**.

This nickel-catalyzed Michael-type addition reaction can be further applied to various aryl- and alkenylboronic acids and α,β-unsaturated alkenes (Scheme 2 and Table 4). Substituted arylboronic acids **1b–f**, **1h–j**, and **1n**, with either an electron-donating or -withdrawing group on the aryl ring, reacted with **2a** to form the corresponding Michael addition

Table 4. Results of nickel-catalyzed Michael-type addition reaction of arylboronic acids **1** with activated alkenes **2**.[a]

Entry	1	2	Product 4	Yield [%][b]
1	**1a**	**2a**		96 (99)
2	**1b**	**2a**		94
3	**1c**	**2a**		8 88[c]
4	**1d**	**2a**		97
5	**1e**	**2a**		98
6	**1f**	**2a**		96
7	**1h**	**2a**		57
8	**1i**	**2a**		17 91[d]
9	**1j**	**2a**		97
10	**1n**	**2a**		0 94[c]
11	**1o**	**2d**		96
12	**1e**	**2b**		90
13	**1e**	**2c**		93
14	**1e**	**2e**		29 85[d]
15	**1e**	**2f**		93
16	**1e**	**2g**		90

[a] Reactions were carried out with **1** (2.00 mmol), **2** (1.00 mmol), $Ni(acac)_2$ (0.050 mmol, 5.0 mol%), $P(o\text{-anisyl})_3$ (0.050 mmol, 5.0 mol%), and K_2CO_3 (2.00 mmol) in CH_3CN (2.0 mL) at 80°C for 12 h under N_2. [b] Yield of isolated product. [c] Reaction was carried out with $Ni(acac)_2$ (0.050 mmol, 5.0 mol%), tris(*p*-fluorophenyl)phosphine (0.050 mmol, 5.0 mol%), and K_2CO_3 (2.00 mmol) in DCE (2.0 mL) at 80°C for 12 h. [d] Reaction was carried out in THF (2.0 mL).

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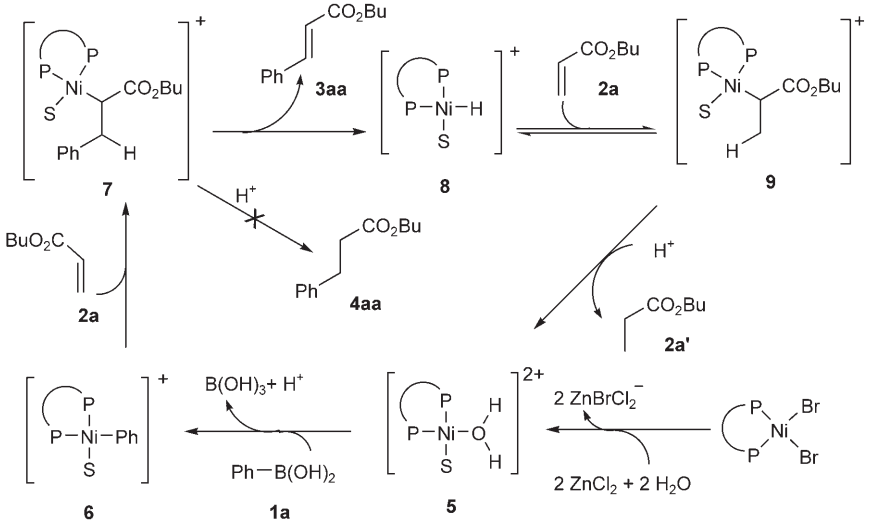
products **4ba–fa**, **4ha–ja**, and **4na** (Table 4, entries 2–10). As with the Mizoroki–Heck-type reaction, this catalytic reaction is compatible with a wide range of functional groups on the phenyl ring, and the product yield is insensitive to the type of functional group. However, the catalytic reaction is very sensitive to the position of the substituent on the ring. According to Table 4, *p*- and *o*-substituted arylboronic acids gave excellent yields of Michael-type products, whereas *m*-substituted arylboronic acids afforded very low product yields under the standard reaction conditions. For example, 2-methoxyphenylboronic acid (**1b**) gave **4ba** in a very high 94% yield (Table 4, entry 2), whereas 3-methoxyphenylboronic acid (**1c**) gave **4ca** in only 8% yield (Table 4, entry 3). Similarly, 3-formylphenylboronic acid (**1h**) and 3-nitrophenylboronic acid (**1i**) gave **4ha** and **4ia** in low yields of 57 and 17%, respectively (Table 4, entries 7–8). These *m*-substituted arylboronic acids remained mostly intact at the end of the reaction. To increase the yield of the addition reaction of **1c** with **2a**, various supporting ligands and different solvents were investigated. The employment of tris(*p*-fluorophenyl)phosphine gave **4ca** in an excellent 88% yield with DCE as the solvent. Similarly, by altering the solvent from CH_3CN to THF, **1i** afforded the expected product **4ia** in 91% yield. On the other hand, no improvement in the yield of **4ha** (Table 4, entry 7) was observed by varying the ligands and solvents. No addition product was observed in the reaction of 1-naphthylboronic acid (**1n**) with **2a** under the optimized reaction conditions (Table 4, entry 10). However, when the same reaction was carried out with tris(*p*-fluorophenyl)phosphine as the ligand in DCE, **4na** was observed in an excellent 94% yield. The observed unusual *meta*-substitution effect of arylboronic acid on the yield of the Michael addition product with $Ni(acac)_2/P(o\text{-anisyl})_3$ as the catalyst system is interesting. It appears to be the first time that such an effect has been reported. The exact reason is not clear, but it is likely that a steric effect arose from the *m*-substituted aryl group and the $P(o\text{-anisyl})_3$ ligand or the solvent.

The present catalytic reaction was further extended to (*E*)-1-hexenylboronic acid (**1o**) with **2d** to afford the Michael-type product **4od** in 96% yield (Table 4, entry 11). Under similar conditions, methyl acrylate (**2b**) and ethyl acrylate (**2c**) also underwent the addition reaction effectively with **1e** to afford **4eb** and **4ec** in 90 and 93% yield, respectively (Table 4, entries 12 and 13). Other activated alkenes such as *N*,*N*-diethylacrylamide (**2e**), acrylonitrile (**2f**), and methylvinylketone (**2g**) can also be used as the substrates. Thus, the reaction of **2e** with **1e** in the presence of $Ni(acac)_2/P(o\text{-anisyl})_3$ in THF provided product **4ee** in 85% yield (Table 4, entry 14). Similarly, the reaction of acrylonitrile (**2f**) and methylvinylketone (**2g**) with **1e** in CH_3CN also proceeded smoothly to give **4ef** and **4eg** in 93 and 90% yield, respectively (Table 4, entries 15 and 16).

Mechanistic Considerations

On the basis of the above observations and the known metal-catalyzed addition reactions of organometallic reagents with activated alkenes,[8,9] a conceivable mechanism is proposed in Scheme 3 to account for the present nickel-catalyzed Mizoroki–Heck-type addition reaction. The catalytic reaction is probably initiated by the formation of $Ni^{II}\cdot H_2O$ species **5** through substitution of coordinated bromide in $[Ni(\widehat{PP})Br_2]$ by water and solvent with the assistance of Lewis acid $ZnCl_2$. Intermediate **5** then undergoes transmetalation with phenylboronic acid (**1a**) to give aryl nickel(II) intermediate **6**. Coordination of butyl acrylate (**2a**) to the nickel center and insertion into the nickel–aryl bond gives intermediate **7**. β-Hydride elimination affords nickel hydride species **8** along with Mizoroki–Heck-type addition product **3**. Insertion of another butyl acrylate molecule into the Ni–H bond of **8** gives intermediate **9**. Protonation of **9** regenerates the active $Ni^{II}\cdot H_2O$ species **5** for the next catalytic cycle and affords hydrogenation product butyl propiolate **2a′**. The formation of **5** and its following transmetalation with **1a** are similar to the pathways suggested for the catalytic reaction of enones with arylboronic acids catalyzed by dicationic palladium complexes.[9b]

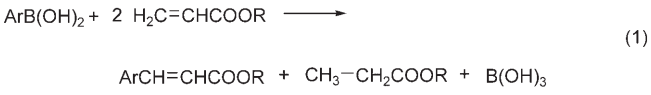
The proposed mechanism shown in Scheme 3 clearly explains the requirement of a catalytic amount of Lewis acid $ZnCl_2$, the observation of equal amounts of Mizoroki–Heck and hydrogenation products of the alkene substrate, and the role of water in the present catalytic reaction. Water not



Scheme 3. Possible mechanism for the nickel-catalyzed Mizoroki–Heck-type addition reaction. $\widehat{PP}$ = bidentate phosphine ligand, S = solvent.

only provides the hydroxy group for the arylboronic acid, but also one of the proton sources for the hydrogenation product **2a′**.

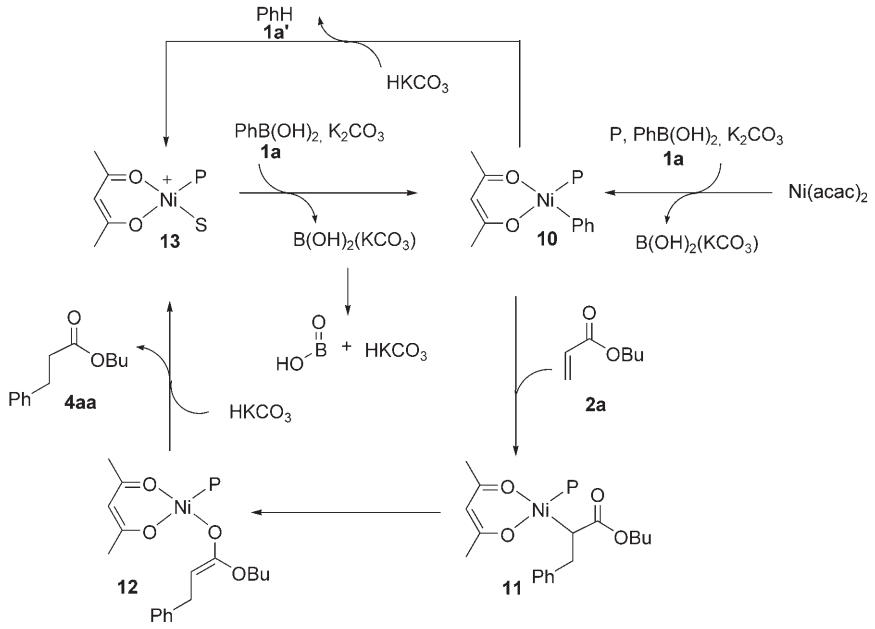
An interesting question for the proposed mechanism is why intermediates **9** and **7**, which are very similar in structure, behave so differently. Intermediate **7** undergoes β-hydride elimination efficiently to give the corresponding Mizoroki–Heck product **3**, but intermediate **9** undergoes protonation to afford only the hydrogenation product. The difference may be rationalized on the basis of the relative rate of β-hydride elimination and protonation of these two intermediates **9** and **7** and the relative rate of insertion of acrylates **2** and **3** into the nickel–hydride bond in **5**. A reasonable hypothesis is that both intermediates **9** and **7** undergo β-hydride elimination much faster than protonation, but the elimination is irreversible to product **3** but reversible to product **2**. This hypothesis explains well the formation of Mizoroki–Heck product **3** without the corresponding hydrogenation product **4**. Furthermore, it also shows clearly that β-hydride elimination of **9** cannot lead to any new product no matter how fast this step is; however, the protonation of **9** results in the hydrogenation product **2a′**. It is possible that in the protonation process of intermediate **9** to give **2a′**, the former is first enolized to form the O-bound nickel enolate before protonation.[9i,11] On the basis of the above results, we propose the stoichiometry of the catalytic reaction in Scheme 1 as that shown in Equation (1).



(1)

In palladium- and ruthenium-catalyzed addition reactions of arylboronic acids to α,β-unsaturated alkenes, the unstable H–Pd or H–Ru species generated is readily reduced to a lower oxidation state, so an additional oxidant such as $Cu(OAc)_2$ or oxygen is necessary.[8] For the present nickel-catalyzed Mizoroki–Heck-type reaction, the Ni–H species is not reduced to a lower oxidation state; throughout the catalytic cycle, it is the nickel(II) species that is involved.

A possible catalytic mechanism for the nickel-catalyzed Michael-type addition reaction is shown in Scheme 4. The catalytic reaction is probably initiated by the reaction of $Ni(acac)_2$ with $PhB(OH)_2$ in the presence of base[14] and a monodentate phosphine ligand to give aryl nickel(II) intermediate **10**. Insertion of an acrylate into the nickel–aryl bond of **10** provides intermediate **11**. Subsequent rearrangement of **11** to O-bound nickel enolate **12** followed by protonation affords the Michael-type addition product **4aa** and intermediate **13** for further transmetalation. A side reaction of this catalytic cycle is the protonation of **10** to give deboronation product PhH (**1a′**) and regenerate the Ni^{II} species **13**. This accounts for the use of excess phenylboronic acid (2 equiv) in the present reaction to obtain a high yield of **4aa**. The initiation step, the transmetalation of $Ni(acac)_2$ with $PhB(OH)_2$ to give **10** in the presence of base,[14] is evidenced by the observation that $Ni(acac)_2$ readily catalyzes the deboronation of $ArB(OH)_2$ to afford ArH in good yield. Furthermore, the observation of a small amount of deboronation product and the absence of biaryl (ArAr) in the catalytic Michael-type addition reaction indicates that the Ni^{II} species is not reduced to Ni^0, and only Ni^{II} species are involved in the catalytic reaction. Previously, in the nickel-catalyzed conjugate addition of zirconium alkenyls to α,β-unsaturated ketones, evidence also indicated that Ni^{II}, not Ni^0, is involved in the catalytic reaction.[15] Recently, a Mizoroki–Heck-type reaction of boronic acids catalyzed by $Pd(OAc)_2$ in the presence of $Cu(OAc)_2$ or oxygen as an oxidant was found to proceed by a Pd^{II}-mediated pathway.[8a–f]



Scheme 4. Possible mechanism for the nickel-catalyzed Michael-type addition reaction. P = monodentate phosphine ligand.

It is very surprising that both intermediates **7** (Scheme 3) and **11** (Scheme 4) are analogues of each other, but that **7** favors β-hydride elimination and intermediate **11** prefers enolization. The exact reason for this contrast is not yet clear. A rationale for the difference lies in the fact that the cationic nickel bidentate phosphine complexes **7** easily offer a vacant site for β-hydride elimination. However, the oxygen-based acac ligand and the bulky electron-donating monodentate phosphine ligand of **11** increase the electron

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density of the nickel center, thus restraining β-hydride elimination and facilitating the O-bound nickel enolate to give the Michael-type addition product.

Conclusions

We have demonstrated a highly efficient nickel-catalyzed addition reaction of organoboronic acids with activated alkenes. By fine-tuning the environment of the nickel complexes, two different types of reaction, Mizo-roki–Heck- and Michael-type addition, can be accomplished in a remarkably selective manner and in good to excellent yields. The Mizoroki–Heck-type addition reaction is highly stereoselective and affords the *E* isomer as the exclusive addition product under base-free conditions. The Michael-type addition showed an unusual *meta*-substitution effect of the arylboronic acids on the product yield when $Ni(acac)_2/P(o\text{-anisyl})_3$ was used as the catalyst. These results reveal that a highly electron-rich nickel complex favors Michael-type addition, whereas an electron-deficient nickel complex prefers Mizoroki–Heck-type addition. This new nickel-catalyzed reaction highlights the potential of using nickel as an inexpensive and efficient catalyst for the addition reaction of organoboron reagents with activated alkenes.

Experimental Section

General

All reactions were conducted under nitrogen atmosphere. ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 400 spectrometer. Chemical shifts are given relative to the center of the solvent resonance ($CDCl_3$: 7.24 (^1H), 77.0 ppm (^{13}C)). FTIR spectra were recorded on a Horiba F2–901 spectrophotometer. High-resolution EI mass spectra were recorded on a JEOL-SX102A spectrometer.

Syntheses

General procedure for the Mizoroki–Heck-type addition reaction of **1** with **2**: A sealed tube containing $[Ni(dppe)Br_2]$ (0.050 mmol, 5.0 mol%), **1** (1.00 mmol), and $ZnCl_2$ (0.150 mmol, 15.0 mol%) was evacuated and purged with nitrogen gas three times. Freshly distilled CH_3CN (2.0 mL), activated alkene **2** (3.00 mmol), and H_2O (3.00 mmol) were added sequentially to the system. After water was injected, the solution turned deep red immediately and was then stirred at 80 °C for 3 h. The mixture was filtered through a celite and silica-gel pad and washed with dichloromethane completely. The filtrate was concentrated, and the residue was purified on a silica-gel column with hexanes/ethyl acetate as eluent to afford the desired product **3**. The spectral data of **3aa**, **3ga**, **3ka**, **3id**, and **3ee** are given below. The spectral data of the remaining compounds and copies of the ^1H and ^{13}C NMR spectra of all compounds are given in the Supporting Information.

3aa: Butyl (*E*)-3-phenyl-2-propenoate: IR (CaF_2): $\tilde{\nu}$ = 2960, 2873, 1714, 1637, 1450, 1311, 1280, 1172, 1072 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, J = 7.2 Hz, 3H; CH_3), 1.38–1.47 (m, 2H; CH_2), 1.68 (quint, J = 6.4 Hz, 2H; CH_2), 4.19 (t, J = 6.4 Hz, 2H; OCH_2), 6.42 (d, J = 16.0 Hz, 1H; HC=), 7.36–7.37 (m, 3H; aromatic CH), 7.50–7.52 (m, 2H; aromatic CH), 7.66 ppm (d, J = 16.0 Hz, 1H; HC=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.1 (C=O), 144.2 (CH), 134.5 (C), 130.2 (CH), 128.8 (CH), 128.0 (CH), 118.3 (CH), 64.4 (CH_2), 30.8 (CH_2), 19.2 (CH_2), 13.7 ppm (CH_3); HRMS (EI): m/z calcd for $C_{13}H_{16}O_2$: 204.1150 $[M]^+$; found: 204.1153.

3ga: Butyl (*E*)-3-(2-formylphenyl)-2-propenoate: IR (CaF_2): $\tilde{\nu}$ = 2960, 2873, 1704, 1635, 1594, 1567, 1465, 1317, 1284, 1178, 1066 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.2 Hz, 3H; CH_3), 1.37–1.47 (m, 2H; CH_2), 1.68 (quint, J = 6.8 Hz, 2H; CH_2), 4.21 (t, J = 6.8 Hz, 2H; OCH_2), 6.36 (d, J = 15.6 Hz, 1H; HC=), 7.51–7.62 (m, 3H; aromatic CH), 7.85 (d, J = 7.2 Hz, 1H; aromatic CH), 8.49 (d, J = 16.0 Hz, 1H; HC=), 10.27 ppm (s, 1H, CHO); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.8 (C=O), 166.3 (C=O), 140.9 (CH), 136.6 (C), 133.9 (C), 133.8 (CH), 132.2 (CH), 129.8 (CH), 127.9 (CH), 123.2 (CH), 64.7 (CH_2), 30.7 (CH_2), 19.2 (CH_2), 13.7 ppm (CH_3); HRMS (EI): m/z calcd for $C_{14}H_{16}O_3$: 232.1099 $[M]^+$; found: 232.1102.

3ka: Butyl (*E*)-3-benzo[b]furan-2-yl-2-propenoate: IR (CaF_2): $\tilde{\nu}$ = 2958, 2933, 2873, 1716, 1639, 1550, 1450, 1382, 1299, 1257, 1162, 1126 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, J = 7.2 Hz, 3H; CH_3), 1.38–1.47 (m, 2H; CH_2), 1.68 (quint, J = 6.8 Hz, 2H; CH_2), 4.20 (t, J = 6.8 Hz, 2H; OCH_2), 6.57 (d, J = 16.0 Hz, 1H; HC=), 6.91 (s, 1H, HC=), 7.21 (t, J = 7.6 Hz, 1H; aromatic CH), 7.34 (t, J = 7.6 Hz, 1H; aromatic CH), 7.46 (d, J = 8.4 Hz, 1H; aromatic CH), 7.52 (d, J = 16.0 Hz, 1H; HC=), 7.57 ppm (d, J = 8.0 Hz, 1H; aromatic CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.7 (C=O), 155.5 (C), 152.3 (C), 131.1 (CH), 128.3 (C), 126.3 (CH), 123.2 (CH), 121.7 (CH), 119.0 (CH), 111.3 (CH), 110.9 (CH), 64.5 (CH_2), 30.7 (CH_2), 19.1 (CH_2), 13.7 ppm (CH_3); HRMS (EI): m/z calcd for $C_{15}H_{16}O_3$: 244.1099 $[M]^+$; found: 244.1086.

3id: 4-Methylbenzyl (*E*)-3-(3-nitrophenyl)-2-propenoate: IR (CaF_2): $\tilde{\nu}$ = 3083, 2923, 2871, 1727, 1712, 1643, 1575, 1531, 1440, 1353, 1176 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3H; CH_3), 5.21 (s, 2H; OCH_2), 6.57 (d, J = 16.0 Hz, 1H; HC=), 7.18 (d, J = 8.0 Hz, 1H; aromatic CH), 7.30 (d, J = 8.0 Hz, 1H; aromatic CH), 7.56 (t, J = 8.0 Hz, 1H; aromatic CH), 7.72 (d, J = 16.0 Hz, 1H; HC=), 7.79 (d, J = 7.6 Hz, 1H; aromatic CH), 8.19–8.22 (m, 1H; aromatic CH), 8.35 ppm (t, J = 2.0 Hz, 1H; aromatic CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9 (C=O), 148.6 (C), 142.0 (CH), 138.3 (C), 136.0 (C),133.5(CH), 132.6 (C), 129.9 (CH), 129.3 (CH), 128.5 (CH), 124.5 (CH), 122.4 (CH), 121.1 (CH), 66.7 (CH_2), 21.2 ppm (CH_3); HRMS (EI): m/z calcd for $C_{17}H_{15}O_4N$: 297.1001 $[M]^+$; found: 297.0998.

3ee: N^1,N^1-Diethyl-(*E*)-3-(4-bromophenyl)-2-propenamide: IR (CaF_2): $\tilde{\nu}$ = 3052, 2981, 1648, 1606, 1488, 1432, 1263, 1139 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.17–1.22 (m, 6H; CH_3), 3.44–3.46 (m, 4H; NCH_2), 6.78 (d, J = 15.2 Hz, 1H; HC=), 7.35 (d, J = 8.4 Hz, 2H; aromatic CH), 7.47 (d, J = 8.4 Hz, 2H; aromatic CH), 7.61 ppm (d, J = 15.6 Hz, 1H; HC=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4 (C=O), 140.9 (CH), 134.4 (C), 131.9 (CH), 129.1 (CH), 123.5 (C), 118.4 (CH), 42.3 (CH_2), 41.1 (CH_2), 15.1 (CH_3), 13.1 ppm (CH_3); HRMS (EI): m/z calcd for $C_{13}H_{16}ONBr$: 281.0415 $[M]^+$ (^{79}Br); found: 281.0420.

General procedure for the Michael-type addition reaction of **1** with **2**: A sealed tube containing $Ni(acac)_2$ (0.050 mmol, 5.0 mol%), $P(o\text{-anisyl})_3$ (0.050 mmol, 5.0 mol%), **1** (2.00 mmol), and K_2CO_3 (2.00 mmol) was evacuated and purged with nitrogen gas three times. Freshly distilled CH_3CN (2.0 mL) and activated alkene **2** (1.00 mmol) were added to the system, and the green reaction mixture was stirred at 80 °C for 12 h. The mixture was filtered through a short celite column and a silica-gel pad and washed with dichloromethane completely. The filtrate was concentrated, and the residue was purified on a silica-gel column with hexanes/ethyl acetate as eluent to give the desired Michael-type addition product **4**. The spectral data of **4aa**, **4od**, **4ee**, **4ef**, and **4eg** are given below. The spectral data of the remaining compounds and copies of the ^1H and ^{13}C NMR spectra of all compounds are given in the Supporting Information.

4aa: Butyl 3-phenylpropanoate: IR (CaF_2): $\tilde{\nu}$ = 2962, 2931, 1735, 1573, 1465, 1427, 1241, 1180 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.2 Hz, 3H; CH_3), 1.28–1.37 (m, 2H; CH_2), 1.57 (quint, J = 6.8 Hz, 2H; CH_2), 2.61 (t, J = 7.6 Hz, 2H; CH_2), 2.94 (t, J = 7.6 Hz, 2H; CH_2), 4.05 (t, J = 6.4 Hz, 2H; OCH_2), 7.17–7.20 (m, 3H; aromatic CH), 7.27 ppm (t, J = 7.6 Hz, 2H; aromatic CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.0 (C=O), 140.6 (C), 128.5 (CH), 128.3 (CH), 126.2 (CH), 64.3 (CH_2), 35.9 (CH_2), 31.0 (CH_2), 30.6 (CH_2), 19.1 (CH_2), 13.7 ppm (CH_3); HRMS (EI): m/z calcd for $C_{13}H_{18}O_2$: 206.1307 $[M]^+$; found: 206.1314.

4od: 4-Methylbenzyl (*E*)-4-nonenoate: IR (CaF_2): $\tilde{\nu}$ = 2956, 2927, 2859, 1778, 1737, 1517, 1455, 1378, 1259, 1160 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.84–0.88 (m, 3H; CH_3), 1.24–1.30 (m, 4H; CH_2), 1.91–1.96 (m, 2H; CH_2), 2.27–2.40 (m, 7H; CH_3, CH_2), 5.05 (s, 2H; CH_2), 5.32–5.46 (m, 2H; HC=), 7.15 (d, J = 7.6 Hz, 2H; aromatic CH), 7.23 ppm (d, J = 8.8 Hz, 2H; aromatic CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.1 (C=O), 138.0 (C), 133.0 (C), 131.8 (CH), 129.2 (CH), 128.3 (CH), 127.7 (CH), 66.0 (CH_2), 34.4 (CH_2), 32.1 (CH_2), 31.5 (CH_2), 27.9 (CH_2), 22.1 (CH_2), 21.1 (CH_3), 13.9 ppm (CH_3); HRMS (EI): m/z calcd for $C_{17}H_{24}O_2$: 260.1776 $[M]^+$; found: 260.1776.

4ee: N^1,N^1-Diethyl-3-(4-bromophenyl)propanamide: IR (CaF_2): $\tilde{\nu}$ = 2971, 2933, 2873, 1641, 1488, 1430, 1263, 1220, 1139, 1099 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.07 (t, J = 7.2 Hz, 3H; CH_3), δ = 2.53 (t, J = 7.6 Hz, 2H; CH_2), 2.91 (t, J = 7.6 Hz, 2H; CH_2), 3.19 (q, J = 7.2 Hz, 2H; NCH_2), 3.33 (q, J = 7.2 Hz, 2H; NCH_2), 7.07 (d, J = 7.6 Hz, 2H; aromatic CH), 7.36 ppm (d, J = 7.6 Hz, 2H; aromatic CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9 (C=O), 140.5 (C), 131.4 (CH), 130.2 (CH), 119.8 (C), 41.9 (CH_2), 40.2 (CH_2), 34.7 (CH_2), 30.9 (CH_2), 14.2 (CH_3) , 13.0 ppm (CH_3); HRMS (EI): m/z calcd for $C_{13}H_{18}ONBr$: 283.0572 $[M]^+$ (^{79}Br); found :283.0569.

4ef: 3-(4-Bromophenyl)propanenitrile: IR (CaF_2): $\tilde{\nu}$ = 2931, 2861, 1589, 1488, 1403, 1203, 1072 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.59 (t, J = 7.6 Hz, 2H; CH_2), 2.89 (t, J = 7.2 Hz, 2H; CH_2), 7.10 (td, J = 7.6, 2.4 Hz, 2H; aromatic CH), 7.45 ppm (td, J = 7.6, 2.4 Hz, 2H; aromatic CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.9 (C), 132.0 (CH), 130.0 (CH), 121.2 (C), 118.7 (C), 31.0 (CH_2), 19.2 ppm (CH_2); HRMS (EI): m/z calcd for C_9H_8NBr: 208.9840 $[M]^+$ (^{79}Br); found: 208.9866.

4eg: 4-(4-Bromophenyl)-2-butanone: IR (CaF_2): $\tilde{\nu}$ = 2925, 1716, 1488, 1436, 1405, 1367, 1286, 1228, 1160 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.11 (s, 3H; CH_3), 2.71 (t, J = 7.2 Hz, 2H; CH_2), 2.82 (t, J = 7.2 Hz, 2H; CH_2), 7.03 (d, J = 8.4 Hz, 2H; aromatic CH), 7.36 ppm (d, J = 8.4 Hz, 2H; aromatic CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.3 (C=O), 140.0 (C), 131.5 (CH), 130.1 (CH), 119.8 (C), 44.8 (CH_2), 30.0 (CH_3), 29.0 ppm (CH_2); HRMS (EI): m/z calcd for $C_{10}H_{11}OBr$: 225.9993 $[M]^+$ (^{79}Br); found: 226.0007.

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