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Rhodium Fluorapatite Catalyst for the Synthesis of Trisubstituted Olefins via Cross Coupling of Baylis−Hillman Adducts and Arylboronic Acids

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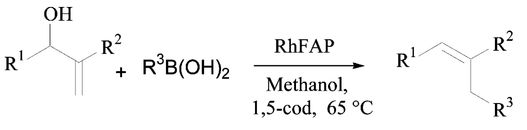

$R^1 = C_6H_5$, 4-Cl C_6H_4 , 4-NO_2 C_6H_4 , 4-CH_3 C_6H_4 , Furyl, $(CH_3)_2CH\text{-}CH_2$
$R^2 = CO_2CH_3$, CO_2Et , CN
$R^3 = C_6H_5$, 4-Cl C_6H_4, 4-NO_2 C_6H_4 , 4-CH_3 C_6H_4, 4-F C_6H_4 , 2,4-OCH_3 C_6H_3
3-NO_2 C_6H_4 , 4-OCH_3 C_6H_4
For R^2 = CN, Z-isomer (99%) was obtained.

Treatment of fluorapatite (prepared by incorporating basic species F^- in apatite in situ by coprecipitation) with an aqueous solution of $RhCl_3$ resulted in rhodium-exchanged fluorapatite catalyst (RhFAP), which successfully promoted cross coupling of Baylis−Hillman adducts with arylboronic acids to yield trisubstituted olefins. A variety of arylboronic acids and Baylis−Hillman adducts were converted to the corresponding trisubstituted olefins, demonstrating the versatility of the reaction. The reaction is highly stereoselective. RhFAP was recovered quantitatively by simple filtration and reused with almost consistent activity.

Rhodium-catalyzed carbon−carbon bond formation via cross coupling of organoboron compounds and organic electrophiles is one of the most important reactions in organic synthesis.[1] The Baylis−Hillman reaction of an aldehyde and an activated olefin produces Baylis−Hillman adducts (BHA), an interesting class of disubstituted olefins possessing both allylic alcohol and α,β-unsaturated ester moieties in which the carbon−carbon double bond is an integral part of both allyl alcohol and α,β-unsaturated ester moieties, which makes it valuable in a number of stereoselective processes[2] and offers multiple opportunities for further transformations.[3] Arylation with trifluoro(organo)borates and organosilanes to α,β-unsaturated ester moieties of BHA was successfully carried out by using palladium catalysts, but such coupling required the activation of the hydroxyl group with acetate or carbonate.[4] The use of nonactivated BHA would be more desirable, particularly from the point of view of atom economy.[5a,b] Recently Darses, Genet, et al. reported the synthesis of trisubstituted olefins using homogeneous rhodium catalyst via an unexpected mechanism involving 1,4-addition/β-hydroxy elimination steps.[1c]

Despite the advantages of homogeneous metal complex catalysts, difficulties in recovering the expensive catalyst metals and ligands from the reaction mixture severely limit their industrial applications. Apatites are metal basic phosphates for which the chemical formula is $M_{10}(PO_4)_6(X)_2$ [M = divalent metal, X = monovalent anion] and various kinds of cations and anions can be readily introduced into their framework due to their large ion exchange ability and such exchanged apatites are already in use in several organic transformations.[5c,6,7] Very recently, we reported the preparation of recyclable heterogeneous Cu-exchanged fluorapatite and copper exchanged *tert*-butoxyapatite catalysts, for *N*-arylation of imidazoles and other heterocycles with iodo-, bromo-, chloro-, and fluoroarenes (EW) with good to excellent yields.[8a,b] We also reported PdFAP catalyst (Fluorapatite-supported palladium catalyst) for the Suzuki and Heck coupling reaction.[8c] Thus in continuation of our work with fluorapatite we herein report the preparation of recyclable heterogeneous rhodium-exchanged fluorapatite catalyst (RhFAP) for cross coupling of Baylis−Hillman adducts with arylboronic acids to yield trisubstituted olefins.

Calcium Fluorapatite (Ca/P) of 1.56 FAP ($Ca_{10}(PO_4)_6(F)_2$) was synthesized according to the literature procedure[9] and exchanged with $RhCl_3$, yielding the RhFAP as a yellowish orange powder. The rhodium content was measured as 0.1 mmol g^{-1} with ICP-AES. XRD and FTIR of the RhFAP were similar to those of parent FAP. The (Rh+Ca)/P ratio of the RhFAP was 1.56, which shows the occurrence of a substitution of Rh for Ca^{2+} at the column of Ca and O atoms parallel to the hexagonal axis. XPS spectra were recorded for the RhFAP catalyst. A high-resolution narrow scan of Rh showed peaks at

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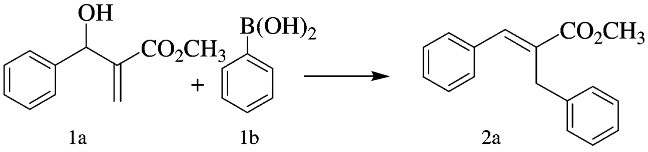
TABLE 1. Screening Reaction Parameters for the Synthesis 2-Benzyl-3-phenylacrylic Acid Methyl Ester[a]



entry	catalyst	solvent	additive	yield (%)[b]
1[d]	$RhCl_3$	methanol	–	–
2[d]	$RhCl_3$	methanol	1,5-cod	–
3	RhFAP	methanol	–	–
4	RhFAP	methanol	1,5-cod	94, 90[c]
5	RhFAP	ethanol	1,5-cod	86
6	RhFAP	water	1,5-cod	trace
7	RhFAP	1,4-dioxane	1,5-cod	42
8	RhFAP	DMF	1,5-cod	58
9	RhFAP	DMSO	1,5-cod	70
10	RhFAP (impregnated)	methanol	1,5-cod	–
11	Rh/SiO_2	methanol	1,5-cod	–

[a] Reaction conditions: **1a** (1 mmol), **2a** (1.2 mmol), catalyst (100 mg), solvent (4 mL), 1,5-cyclooctadiene (1,5-cod) (0.05 mmol), reaction time (6 h), 65 °C. [b] Isolated yields. [c] Yield after fourth recycle. [d] Entries 1 and 2, 2 mol % of $RhCl_3$ was used.

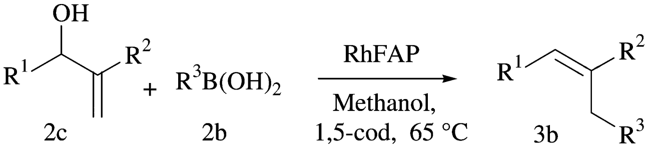
308.8 and 313.6 eV which are due to Rh $5d_{5/2}$ and Rh $5d_{3/2}$, respectively, in the +3 oxidation state (see the Supporting Information). The presence of chlorine was confirmed by XPS and EDAX analyses and the atomic ratio of Rh to Cl was 1:1. Thus the rhodium species in RhFAP are surrounded by oxygen and a chlorine atom, which is in concordance with ruthenium-(III) hydroxyapatite reported earlier.[7a,b]

In an effort to develop a better catalytic system, various reaction parameters were screened for cross coupling of 3-hydroxy-2-methylene-3-phenylpropanoate with phenylboronic acid to yield 2-benzyl-3-phenylacrylic acid methyl ester (**2a**) and are presented in Table 1. RhFAP catalyst combined with 1,5-cyclooctadiene (1,5-cod) in methanol at 65 °C exhibited the highest catalytic activity giving **2**, (Table 1, entry 4), while the reaction conducted in the absence of 1,5-cod did not yield the product **2a** (Table 1, entry 3). There is no reaction with homogeneous $RhCl_3$ catalyst in the presence and absence of 1,5-cod under similar conditions (Table 1, entries 1 and 2). To evaluate the catalytic active species, we conducted the reaction with $RhCl_3$ impregnated on FAP support (RhFAP-impregnated (for catalytic characterization see the Supporting Information)) and there was no reaction (Table 1, entry 10). It clearly emphasizes that the rhodium chemisorbed on the FAP surface is not the active species. Conversely a unique monomeric Rh species (RhFAP) surrounded by oxygen and a chlorine atom on the FAP support (Ca exchanged by Rh) is the real catalytic active species. There is no reaction with Rh/SiO_2 (Table 1, entry 11).

The solvent has a pronounced effect in these reactions. Methanol and ethanol have proven to be good solvents whereas DMF, DMSO, and 1,4-dioxane provided moderate yields. The reaction was also carried out in water but only a trace amount of product **2**a was detected (Table 1, entries 5–9).

The controlled reaction conducted under identical conditions without RhFAP and 1,5-cod gave no coupled product, despite prolonged reaction times. RhFAP was recovered quantitatively by simple centrifugation and reused for four cycles with minimal loss of activity (Table 1, entry 4). Moreover, the absence of rhodium in the filtrate was confirmed by ICP-AES, which confirms no leaching of rhodium during the reaction (detection limit is <1ppb) and provides evidence for heterogeneity throughout the reaction.

TABLE 2. Synthesis of Trisubstituted Olefins Catalyzed by RhFAP Catalyst[a]



entry	R^1	R^2	R^3	yield (%)[b]
1	C_6H_5	CO_2CH_3	C_6H_5	94
2	C_6H_5	CO_2CH_3	4-CH_3-C_6H_4	96
3	C_6H_5	CO_2CH_3	4-OCH_3-C_6H_4	94
4	C_6H_5	CO_2CH_3	4-Cl-C_6H_4	92
5	C_6H_5	CO_2CH_3	4-F-C_6H_4	89
6	C_6H_5	CO_2CH_3	2,4-OCH_3-C_6H_3	91
7	C_6H_5	CO_2CH_3	3-NO_2-C_6H_4	69
8	C_6H_5	CO_2Et	C_6H_5	93
9	C_6H_5	CN	C_6H_5	92[c]
10	4-Cl-C_6H_4	CO_2CH_3	C_6H_5	86
11	4-NO_2-C_6H_4	CO_2CH_3	C_6H_5	79
12	4-CH_3-C_6H_4	CO_2CH_3	C_6H_5	93
13	furyl	CO_2CH_3	C_6H_5	97
14	$(CH_3)_2CH$-CH_2	CO_2CH_3	C_6H_5	95

[a] Reaction conditions: **2c** (1 mmol), **2b** (1.2 mmol), catalyst (100 mg), methanol (4 mL), 1,5-cycloctadiene (0.05 mmol), reaction time (5–7 h), 65 °C. [b] Isolated yields. [c] *Z* isomer (99%) was obtained.

We chose a variety of structurally divergent nonactivated Baylis–Hillman adducts and arylboronic acids possessing a wide range of functional groups to understand the scope and the generality of the RhFAP-promoted cross coupling reaction to yield trisubstituted olefins and the results are summarized in Table 2. Phenylboronic acids with an electron-donating group afforded better yields (Table 1, entries 2, 3, and 6) than those with electron-withdrawing groups (Table 2, entry 7). Among the Baylis–Hillman adducts, electron-donating groups on the aromatic moiety of the adduct gave better yield than that of withdrawing groups such as nitro and chloro which gave moderate yield. An electron-rich Baylis–Hillman adduct such as 2-(furan-2-yl-hydroxy-methyl)-acrylic acid methyl ester reacted faster than a Baylis–Hillman adduct with electron-withdrawing groups on the aromatic moiety to give the corresponding olefin in excellent yields (Table 2, entry 13). The aliphatic Baylis–Hillman adduct 2-(1-hydroxy-3-methylbutyl)-acrylic acid methyl ester was also successfully coupled with phenylboronic acid to give the respective olefin in excellent yields (Table 2, entry 14). The reaction is highly stereoselective. The stereochemistry of the products was established by comparing the NMR of olefinic and methylene protons with the literature value and the *E*/*Z* ratio was determined by both GC-MS and ^1H NMR. The reaction of 3-hydroxy-2-methylenealkanoates with a variety of arylboronic acids yielded 2-substituted 2-aldenoates with *E*/*Z* isomers >96%. Interestingly, when 3-hydroxy-2-methylenealkanenitrile was reacted with phenylboronic acid, only the *Z* isomer (99%) was obtained as the major product (Table 2, entry 9).

The used RhFAP catalyst was well characterized by XRD, FTIR, XPS, ICP-AES, and EDAX analysis. XRD and FTIR of the used RhFAP catalyst were similar to those of fresh RhFAP catalyst. The XPS, high-resolution narrow scan of Rh showed peaks at 308.5 and 312.7 eV which are due to Rh $5d_{5/2}$ and Rh $5d_{3/2}$, respectively, in the +3 oxidation state (see the Supporting

Information). The absence of chlorine was confirmed by XPS and EDAX analyses. The (Rh+Ca)/P ratio of the used RhFAP showed 1.56. The rhodium content of used RhFAP was measured as 0.1 mmol g^{-1} with ICP-AES.

Based on retention of the +3 oxidation state of Rh and the absence of chlorine in the used RhFAP catalyst, we assume that the reaction proceeds via a 1,4-addition type mechanism[1c] involving β-hydroxy elimination resulting in a rhodium hydroxide species. Thus the rhodium species in the used RhFAP catalyst are surrounded by oxygens and a hydroxyl group (see the Supporting Information).

In conclusion, we have developed a simple and efficient method for the preparation of trisubstituted olefins, using RhFAP catalyst. A variety of arylboronic acids and nonactivated Baylis–Hillman adducts were converted to the corresponding trisubstituted olefins, demonstrating the versatility of the reaction. The catalyst can be readily recovered and reused.

Experimental Section

General Procedure for the Synthesis of Trisubstituted Olefins. RhFAP (100 mg or Rh = 0.01 mmol) was added to a mixture of Baylis–Hillman adduct (1 mmol), arylboronic acid (1.2 mmol), and 1,5-cod (0.05 mmol) in methanol (4 mL) at 65 °C, and the mixture was stirred for 6 h. The progress of the reaction was monitored by TLC and on completion of the reaction, the reaction mixture was centrifuged and the centrifugate was concentrated under reduced pressure to give the crude product. The crude product was purified by column chromatography on silica gel to afford the corresponding trisubstituted olefins. The centrifuged catalyst was washed with methanol, dried, and reused for the next cycle.

2-Benzyl-3-phenylacrylic acid methyl ester (Table 2, entry 1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.34–7.31 (m, 10H), 3.91 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 140.9, 139.3, 135.2, 130.5, 129.1, 128.7,128.5, 128.4, 127.8, 126.0, 52.0, 33.1; MS m/z 252 (M^+). Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.81; H, 6.34.

2-Benzyl-3-(4-chlorophenyl)acrylic acid methyl ester (Table 2, entry 10): ^{1}H NMR (300 MHz, $CDCl_3$) δ =7.82 (s, 1H), 7.30–7.10 (m, 9H), 3.89 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 139.6, 139.0, 134.5, 133.7, 131.2, 130.5, 128.8 128.6, 127.8, 126.2, 52.2, 33.1; MS m/z 286 (M^+). Anal. Calcd. for $C_{17}H_{15}ClO_2$: C, 71.20; H, 5.27. Found: C, 71.09; H, 5.23.

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Note Added after ASAP Publication. Structures in Table 1 and 2 were corrected and the corrected version was published December 18, 2007.

Supporting Information Available: Detailed experimental procedures and compound characterization data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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