Fe^{3+}-K-10 Montmorillonite Clay Catalyzed Friedel–Crafts Reaction of Unactivated Baylis–Hillman Adducts: An Efficient Stereoselective Synthesis of Trisubstituted Alkenes Containing a Benzyl Substituent[1]

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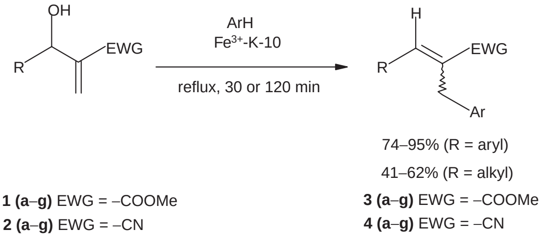
The stereoselective synthesis of trisubstituted alkenes containing a benzyl substituent has been achieved by employing Friedel–Craft reaction of aromatic compounds with unactivated Baylis–Hillman adducts in the presence of Fe^{3+}-K-10 montmorillonite clay as a heterogeneous catalyst. The catalyst can be recovered and reused.

The Baylis–Hillman adducts, 3-hydroxy-2-methylene-alkanoates **1** (derived from acrylate esters) and 3-hydroxy-2-methylene-alkanenitriles **2** (derived from acrylonitrile) are important precursors for stereoselective synthesis of different functionalized molecules.[2,3] In continuation of our work[4] on the preparation of trisubstituted alkenes, we have recently observed that such compounds containing a benzyl substituent can be prepared in stereoselective manner by the Friedel–Craft reaction of the adducts, **1** and **2** with aromatic compounds in the presence of different heterogeneous solid acid catalysts. These target alkenes are useful for the preparation of (*E*)-2-arylideneindane-1-ones which are important synthons in the synthesis of various carbocyclic and heterocyclic molecules of pharmacological importance.[5] These alkenes can also be employed for the preparation of naturally occurring bioactive 1,3-diarylpropanoids.[6] Thus, the present method is an easy access to several biopotent molecules. However, it is difficult to synthesize trisubstituted alkenes having a benzyl substituent and it is also difficult to induce the Friedel–Craft reaction to the Baylis–Hillman adducts to get the products in satisfactory yields—proper selection of catalysts is vital.[7a,7b] Previously, the Friedel–Craft reaction of the unactivated Baylis–Hillman adducts was carried out with concentrated H_2SO_4 under reflux.[7a] The acetyl and *N*-tosylamine derivatives of the adducts were reported to undergo the reaction with $AlCl_3$ and H_2SO_4, respectively.[7b,7c] However, concentrated H_2SO_4 may affect the acid-sensitive groups and $AlCl_3$ yielded side products.[7b] Conversion of the derivatives of the Baylis–Hillman adducts also required two steps.

We initially treated **1a** ($R = 2\text{-Cl-}C_6H_4$; EWG = –COOMe) with benzene under reflux using different heterogeneous-solid-acid catalysts (including various metal doped K-10 clays) to undergo the Friedel–Craft reaction (Table 1). Fe^{3+}-K-10 montmorillonite clay was found to give the best result with the highest yield (95%) of the desired trisubstituted alkene, **3a** (Scheme 1).



Scheme 1.

Table 1. Friedel–Craft reaction of the Baylis–Hillman adduct **1a** ($R = 2\text{-Cl-}C_6H_4$, EWG = –COOMe) with benzene in the presence of different heterogeneous solid acid catalysts[a]

Entry	Catalyst	Reaction time /min	Isolated yield/% of alkene
1	HY-Zeolite	120	61
2	Amberlyst-15	120	75
3	KSF clay	120	84
4	Mont K-10	120	81
5	Fe^{3+}-K-10	30	95
6	Al^{3+}-K-10	30	84
7	Zn^{2+}-K-10	30	63
8	Cu^{2+}-K-10	30	56

[a] **1a** (2 mmol) and a catalyst (100 mg) was taken in benzene (5 mL) and refluxed.

Among the metal doped K-10 clays the order of activity was found as follows: Fe^{3+}-K-10 > Al^{3+}-K-10 > Zn^{2+}-K-10 > Cu^{2+}-K-10 (Table 1). This order depends on the number of Lewis and Brøonsted acid sites present in the catalyst.[8] The highest activity of Fe^{3+}-K-10 clay is due to a compatible mixture of highest number of Lewis and Brøonsted acid sites per its unit volume.[8] Thus Fe^{3+}-K-10 clay was considered to be most suitable for the Friedel–Craft reaction of the unactivated Baylis–Hillman adducts.

In general conversions the trisubstituted alkenes, **3** and **4** were formed in excellent yields from the adducts having the aryl substituents (reaction time: 30 min). However, the adducts (**1** and **2**) with alkyl substituents afforded the alkenes (**3** and **4** respectively) with moderate to good yields (reaction time: 120 min) (Table 2). The structures and stereochemistry of the products were determined from their ^1H and ^{13}C NMR spectra and the ratio of (*E*)- and (*Z*)-isomers from the ^1H NMR spectra of the crude products. A comparison of the ^1H and ^{13}C NMR spectral values of our prepared compounds with those of the same compounds reported[7] earlier guided to establish the stereochemistry and ratio (*E*:*Z* as well as ortho:para)[7a,7c,9] (Table 3) of the products. It was observed that the product **3** was formed with (*E*)-selectivity having trace amount of (*Z*)-isomer when the adduct **1** was derived from an aromatic aldehyde while it (**3**) was obtained as mixtures of (*E*)- and (*Z*)-isomers when **1** was derived from an aliphatic aldehyde. On the other hand, the product **4** was formed with (*Z*)-configuration from the adduct **2** containing both aromatic and alkyl substituents.

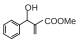
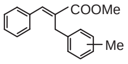
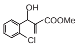
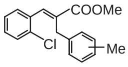
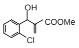
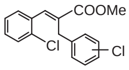
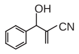
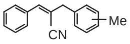
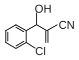
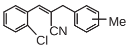
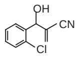
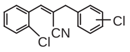
The stereochemistry of the Friedel–Craft reaction can be ex-

Table 2. Stereoselective synthesis of trisubstituted alkenes containing a benzyl substituent **3** and **4** from the adducts **1** and **2** and benzene using Fe^{3+}-K-10 clay[a]

Entry	R	EWG	Time /min	Isolated yield/%	*E*:*Z*
3a	2-Cl-C_6H_4	COOMe	30	95	98:2
3b	C_6H_5	COOMe	30	93	96:4
3c	4-Cl-C_6H_4	COOMe	30	91	98:2
3d	4-Me-C_6H_4	COOMe	30	90	97:3
3e	1-Napth	COOMe	30	74	95:5
3f	*i*-C_3H_7	COOMe	120	62	30:70
3g	*i*-C_4H_9	COOMe	120	56	42:58
4a	2-Cl-C_6H_4	CN	30	92	0:100
4b	C_6H_5	CN	30	89	1:99
4c	4-Cl-C_6H_4	CN	30	86	0:100
4d	4-Me-C_6H_4	CN	30	87	0:100
4e	4-MeO-C_6H_4	CN	30	90	0:100
4f	*n*-C_3H_7	CN	120	41	0:100
4g	*i*-C_3H_7	CN	120	52	0:100

[a]The structures of the alkenes were determined from their spectral (IR, ^1H and ^{13}C NMR, and MS) and analytical data.

Table 3. Friedel–Craft reaction of the Baylis–Hillman adducts with different arenes using Fe^{3+}-K-10 clay under reflux for 30 min

Entry	Substrate	Arene	Product[a]	Isolated yield/%
1		$PhCH_3$		92 *o*:*p* = 45:55
2		$PhCH_3$		91 *o*:*p* = 34:66
3		PhCl		84 *o*:*p* = 42:58
4		$PhCH_3$		89 *o*:*p* = 43:57
5		$PhCH_3$		91 *o*:*p* = 35:65
6		PhCl		87 *o*:*p* = 37:63

[a]alkene (for the Entries 1–3) with opposite stereochemistry was obtained in trace quantity (2–4%).

plained[7c] by considering the plausible mechanism (Figure 1) and transition state models **A**, **B**, and **C** (Figure 2). Model **A** is more favoured than **B** when EWG = –COOMe and R = aryl and (*E*)-products are thus formed from **1**. However, when R = alkyl, due to the steric strain between –CH_2- of the benzyl group and R,[7c] possibly both the transition states **A** and **B** operated to afford the mixture of (*E*)- and (*Z*)-products. On the other hand, model **C** is more favoured than **A** when EWG = –CN (as –CN is linear) and hence (*Z*)-products are formed from **2**.

The present methodology was extended to the Friedel–Craft reaction of other aromatic compounds with the Baylis–Hillman adducts (Table 3). The trisubstituted alkenes were obtained in high yields and in excellent stereoselectivity.

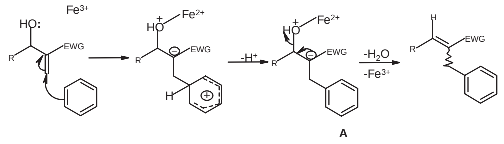


Figure 1.

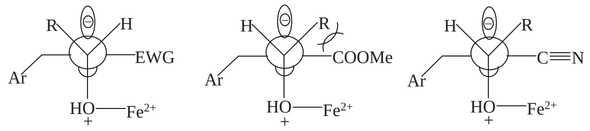


Figure 2.

In conclusion, we have developed a convenient one-pot general methodology for stereoselective synthesis of trisubstituted alkenes containing a benzyl substituent by utilizing the Friedel–Craft reaction of aromatic compounds with the unactivated Baylis-Hillmam adducts using Fe^{3+}-K-10 montmorillonite clay (prepared[10] from $FeCl_3$ and K-10 clay).

The operational simplicity, the application of a heterogeneous and recyclable catalyst, high yield, and excellent stereoselectivity of the products (particularly from the adducts containing aryl substituents) are the great advantages of the present method.

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References and Notes

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