

Montmorillonite K10 Clay-catalyzed Synthesis of Substituted 1-Aryl Indenes from Baylis–Hillman Adducts

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An eco-friendly method for the synthesis of 1-aryl indenenes from Baylis–Hillman adducts using Mont. K10 and microwave combination as catalyst system and a procedure for the synthesis of β -phenyl-substituted-protected Baylis–Hillman adducts with highly Z-selectivity have been reported.

The Baylis–Hillman reaction¹ is one of the important C–C bond forming reactions and it has been used in organic synthesis for the preparation of a variety of compounds having diverse functional groups. The clay catalysts are known as eco-friendly acid catalysts which have potential for replacing the conventional mineral acids and are non-pollutant.² The advantages of the clay-catalyzed reactions are that they are generally mild, solvent free, and easy work-up.² In continuation of our research work^{3,4} on montmorillonite K10 clay catalyst and Baylis–Hillman adducts in organic synthesis, herein we report the Mont. K10 clay-microwave mediated synthesis of functionalised indenenes by the generation of two types of stabilized allylic carbocation intermediates as shown in Figure 1, structures B and C.

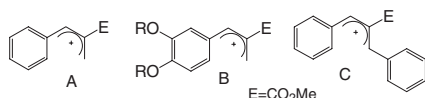
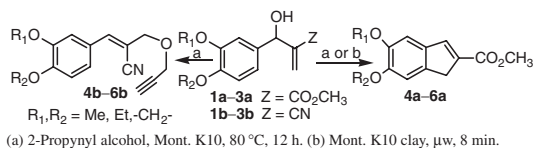


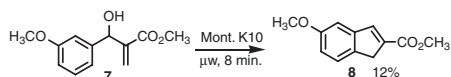
Figure 1. Structure of allylic carbocations. A. Less stabilized B. Stabilized by electron releasing group at phenyl group; C. Stabilized by diaryl group.

During the course of our studies on the synthesis of oxacycles,^{4c–4e} we attempted the preparation of enyne ethers from the Baylis–Hillman adduct **1a** with 2-propynyl alcohol under thermal condition (Mont. K10, heat).^{4b} We did not get the desired enyne ether but indene⁵ **4a** was obtained in 52% yield. The result prompted us to explore the present catalyst system would be a good replacement of the earlier P₂O₅ catalyzed synthesis of indenenes (Scheme 1).⁵ Similarly, under the optimized condition, the other adducts **2a** and **3a** furnished the corresponding indenenes **5a** and **6a** in moderate yields. (Table 1)

In order to compare and examine the difference in the reactivity of the Baylis–Hillman adducts bearing the nitrile substitution, the adduct **1b**, in contrary, afforded only the enyne ether **4b** in 70% yield and not the expected indene derivative (Scheme 1).



Scheme 1.



Scheme 2.

The reason could probably be due to the cumulative effect of stereochemical disfavor of the intermediate carbocation with respect to the arene group and destabilization of the carbocation by the nitrile group (Figure 2). Similarly, the other adducts **2b** and **3b** furnished enyne ethers **5b** and **6b** in good yields (Table 1).

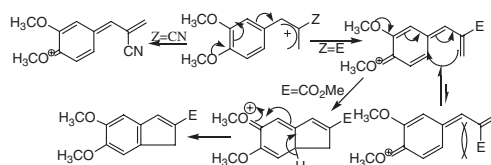


Figure 2.

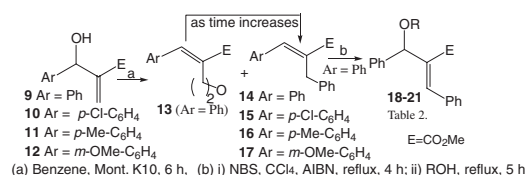
Table 1. Synthesis of indenenes (**4a–6a**) and enyne ethers (**4b–6b**)

Entry	Adduct	R ₁ & R ₂	Product	Yield/%
1	1a	Methyl	4a	52
2	2a	Ethyl	5a	50
3	3a	–CH ₂ –	6a	49
4	1b	Methyl	4b	70
5	2b	Ethyl	5b	69
6	3b	–CH ₂ –	6b	65

According to the reported mechanism,⁵ the reaction proceeded through electrocyclic ring closure facilitated by an alkoxy group at 3-position of the arene. However, the role of 4-alkoxy substitution is not revealed by the mechanism. Hence, we examined the reactivity of adduct with only 3-alkoxy substitution. Accordingly, to our surprise, the 3-methoxy substituted adduct **7** furnished only 12% yield of the indene derivative **8** (Scheme 2). The low yield of the product formation showed the necessity of an electron-releasing group at 4-position and is essential to facilitate the ring closure more effectively for higher yield. Hence, we propose the role of 4-methoxy group in the electrocyclic ring closure based on the mechanism shown in Figure 2.

On the other hand, to achieve the goal for the synthesis of indene derivatives irrespective of whether the aryl ring is substituted or unsubstituted in the Baylis–Hillman adducts, we envisaged by introduction of a phenyl group at the β -position which would stabilize the allylic cation intermediate by both the aryl groups. (Figure 1, structure C). Thus, the suitable precursor for the construction of indenenes would be the β -phenyl substituted Baylis–Hillman adducts **18–21** (Scheme 3).

The literature known Heck coupling⁶ for the synthesis of β -phenyl substituted adduct **18** from acetate adduct **9** failed to afford the desired product and furnished only the isomerized product as evidenced by spectral studies.⁷ Hence, we developed a procedure for the preparation of the adduct **18–21** by a three-step-reaction sequence viz. 1. An intermolecular Friedel–Crafts reaction catalyzed by Mont. K10 clay, 2. Allylic bromination, and 3. An alkoxide substitution (Scheme 3). The side dimerised product **13** was readily converted to compound **14** upon longer heating under Mont. K10 clay catalyst. Accordingly, compounds **9–12** were converted to compounds **14–17**. It should be noteworthy that the procedure de-



Scheme 3.

Table 2. Synthesis of functionalized (*Z*)-β-phenyl-substituted-protected adducts (18–24)

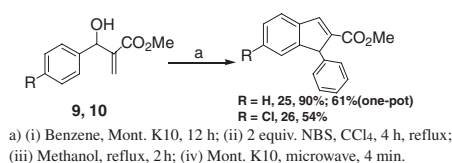
Entry	ROH	Product	Yield/%
1	Methanol	18	82
2	Ethanol	19	81
3	Propargyl alcohol	20	80
4	Homo propargyl	21	76
5	Phenol	22 and 23	74
6	<i>p</i> -Cresol	24	65

scribed herein furnished only the (*Z*)-β-phenyl-substituted-protected adduct **18** as a single product as evidenced by NMR.⁸ The effect of alkoxide substitution at allylic position with various alcohol were also studied and all of them furnished the functionalized products in good yield (Schemes 3 and Table 2).

The stereochemistry of alkene was fixed at the allylic bromination step based on ¹H NMR analysis. Heating the β-phenyl-substituted protected-adduct **18** in the presence of Mont. 10 clay and microwave combination furnished the functionalized indene **25** in 90% yield (Scheme 4). The Mont. K10 clay recovered from the reaction mixture by filtration can be recycled three times without losing its activity by activating the clay at 100 °C for 3 h. In an attempt, we also successfully developed a two-pot synthesis of substituted indenenes **25** and **26** from adducts **9** and **10** respectively without isolation and purification of intermediates (see experimental). Some of the related cyclization reactions involving the Baylis–Hillman adducts are known for organic synthesis.^{9–11}

In conclusion, we have developed an efficient; eco-friendly method for the synthesis of indenenes from the Baylis–Hillman adducts having both electron rich and simple aryl groups through the intramolecular Friedel–Crafts reaction. Thereby we have disclosed the importance of β-phenyl substituted adduct as a precursor for the synthesis of highly substituted indenenes. It is noteworthy that the methodology could be applied for the total synthesis of indatraline¹¹ and related natural products by choosing appropriate substrates. Further work in this direction is under progress.

Synthesis of Indene 4a: A mixture of adduct **1a** (125 mg, 0.5 mmol) and Mont. K10 (75 mg, 30% w/w) was taken in a 25 mL conical flask and irradiated in a microwave oven for 8 min. The mixture was cooled and diluted with 5 mL of CH₂Cl₂. The solvent was removed in vacuo and the crude was purified through silica gel column chromatography using hexane–EtOAc (95:5) to give indene **4a** as crystal in 52% yield. **Synthesis of indene 25:** The adduct **9** (250 mg, 1.3 mmol) in dry benzene (3 mL) and Mont. K-10 (125 mg, 50% w/w) was refluxed for 6 h. The clay was filtered off and 125 mg of fresh clay was added to the mixture and refluxed further 6 h. The clay was filtered out and solvent was removed in vacuo. *N*-bromosuccinimide (231 mg, 2 equiv.), 5 mL of CCl₄ and 50 mg of



Scheme 4.

AIBN were added to the reaction mixture and refluxed for 4 h. Then 3 equiv. of methanol was added and reflux was continued for 2 h. The solvents were removed under vacuum. The crude mixture was treated with Mont. K10 clay (75 mg, 30% w/w) and irradiated in a microwave oven for 4 min. Finally, the mixture was cooled to rt and diluted with 5 mL of CH₂Cl₂ and filtered. The solvent was removed and the crude was purified through silica gel column using hexane–EtOAc (95:5) to give highly functionalized indene **25** as colourless crystal in 61% overall yield.

Compound 4b: ¹H NMR: δ 2.49 (t, 1H, *J* = 2.25 Hz), 3.92 (s, 6H), 4.25 (d, 2H, *J* = 2.25 Hz), 4.31 (s, 2H), 6.87 (d, 1H, *J* = 8.35 Hz), 7.09 (s, 1H), 7.22 (d, 1H, *J* = 8.35 Hz), 7.60 (s, 1H). ¹³C NMR: δ 55.86, 55.89, 57.24, 70.58, 75.51, 78.74, 104.12, 110.59, 110.83, 118.11, 124.17, 125.90, 145.51, 151.41. Mass spectra *m/z*: 257 (M⁺); HRMS (*m/z*): calcd for C₁₅H₁₅NO₃, 257.1052; found: 257.1048. **Compound 8:** White solid; mp 86–88 °C; Yield: 12%; IR (neat) ν_{max}: 1721 cm⁻¹. ¹H NMR: δ 3.6 (s, 2H), 3.82 (s, 6H), 6.86 (1H, dd, *J* = 8.26 and 2.35 Hz), 7.0 (d, 1H, *J* = 2.35 Hz), 7.36 (d, 1H, *J* = 8.26 Hz), 7.64 (s, 1H). ¹³C NMR: δ 37.51, 51.35, 55.18, 107.86, 114.24, 124.57, 136.76, 138.07, 140.98, 143.79, 158.99, 164.90. Mass spectra *m/z*: 204 (M⁺); HRMS (*m/z*): calcd for C₁₂H₁₂O₃, 204.0786; found: 204.0794. **Compound 18:** ¹H NMR: δ 3.29 (s, 3H), 3.52 (s, 3H), 5.06 (s, 1H), 6.64 (s, 1H), 7.15–7.32 (m, 10H). ¹³C NMR: δ 51.51, 57.14, 83.73, 127.36, 128.03, 128.14, 128.31, 133.29, 134.96, 135.23, 138.64, 168.76. Mass spectra *m/z*: 282 (M⁺); HRMS (*m/z*): calcd for C₁₈H₁₈ClO₃, 282.1256; found: 282.1259. **Compound 25:** Colourless solid; mp 126–128 °C; Yield: 61%; IR (neat) ν_{max}: 1702, 1610 cm⁻¹. ¹H NMR: δ 3.69 (s, 3H), 4.85 (s, 1H), 7.06–7.33 (m, 8H), 7.50 (d, 1H, *J* = 7.23 Hz), 7.79 (s, 1H). ¹³C NMR: δ 51.50, 55.64, 123.42, 124.48, 126.87, 127.29, 127.83, 128.31, 128.52, 128.61, 138.31, 141.13, 141.56, 150.41, 164.72. Mass spectra *m/z*: 250 (M⁺); HRMS (*m/z*): calcd for C₁₄H₁₆O₂, 250.0994; found: 250.0992.

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