



# A versatile synthesis to trisubstituted nitroalkenes via nitroaldol reaction: Synthesis of Baylis-Hillman type adducts

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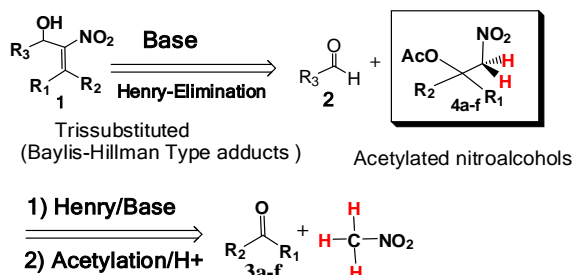
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## INTRODUCTION

Electron deficient nitroalkenes consists of a versatile class of compounds reactive in Michael, Friedel-Crafts, Baylis-Hillman, Diels-Alder, Hetero-Diels-Alder, [3+2]-cycloaddition and Cross Coupling reactions.<sup>1</sup> Usually,  $\beta$ -monosubstituted nitroalkenes and  $\alpha,\beta$ -disubstituted nitroalkenes are synthesized via a nitroaldol reaction between an aldehyde and the nitromethane or a primary nitroalkane, respectively. The hydroxyl group elimination, in its free or active form, leads to the desired nitroalkene. Another usual route consists of nitration of the corresponding nitroalkene with toxic or volatile reagents leading to low regioselectivity. A more convenient method  $\text{NaNO}_2$ -ceric ammonium nitrate has been reported.<sup>2</sup> In the specific case of trisubstituted nitroalkenes, the nitroaldol route is not effective because of the high reversibility of nitroaldol reaction when ketones are employed.

## RESULTS AND DISCUSSION

Here in, we report our preliminary results towards synthesis of various trisubstituted nitroalkenes **1** (Baylis-Hillman adducts) from the nitroaldol reaction between the acetylated nitroalcohols **4a-f** and various aldehydes **2** followed by AcOH elimination Scheme 1. The acetylated nitroalcohols **4a-f** could be obtained via a nitroaldol reaction between diverse ketones (propanone (**3a**), cyclopentanone (**3b**), cyclohexanone (**3c**), 2-pentanone (**3d**), 2-butanone (**3e**) and acetophenone (**3f**)) base catalyzed and the nitromethane, followed by acetylation acid catalyzed.

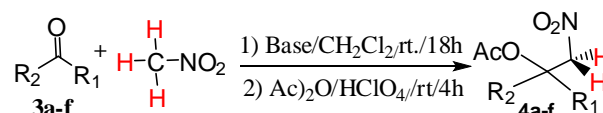


**Scheme 1:** Retrosynthesis to obtainment of **1**.

The results summarized in the table 1 shows that the nitroesters derived from propanone, cyclohexanone and 2-pentanone were obtained in good yields (entries 1,3,4). Cyclopentanone (**3b**) and

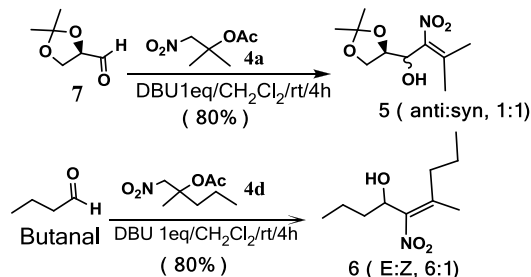
2-butanone (**3e**) furnished **4b** and **4e** in low yield (Entries 2,5). Acetophenone (**3f**) was not reactive (Entry 6).

**Table 1:** Synthesis of acetylated nitroalcohols **4a-f**.



Entry	Ketone	Base	Nitroester Yield (%) <sup>a</sup>
1	<b>3a</b> , R <sub>1</sub> =R <sub>2</sub> =Me	TBAF <sup>b</sup>	<b>4a/50</b>
2	<b>3b</b> , R <sub>1</sub> =R <sub>2</sub> =(CH <sub>2</sub> ) <sub>4</sub>	DBU <sup>c</sup>	<b>4b/21</b>
3	<b>3c</b> , R <sub>1</sub> =R <sub>2</sub> =(CH <sub>2</sub> ) <sub>5</sub>	TBAF	<b>4c/65</b>
4	<b>3d</b> , R <sub>1</sub> =Me, R <sub>2</sub> =Pr	DBU	<b>4d/70</b>
5	<b>3e</b> , R <sub>1</sub> =Me, R <sub>2</sub> =Et	TBAF	<b>4e/30</b>
6	<b>3f</b> , R <sub>1</sub> =Me, R <sub>2</sub> =Ph	TBAF	No reaction

a) After column chromatographic (2 steps). b) 0.5 eq c) 1 eq. Reaction of **4a** with (R)-glyceraldehyde acetone (**7**) and **4d** with butanal, via a nitroaldol-elimination sequence, produced the trisubstituted nitroalkenes **5** and **6** (Baylis-Hillman-type adducts) in 80% yield.



## CONCLUSION

A versatile, simple and efficient route to produce diverse trisubstituted nitroalkenes has been attained.

## REFERENCES

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