

Synthesis of poly-substituted nitrobenzene derivatives from Baylis–Hillman adducts via [3+3] annulation protocol

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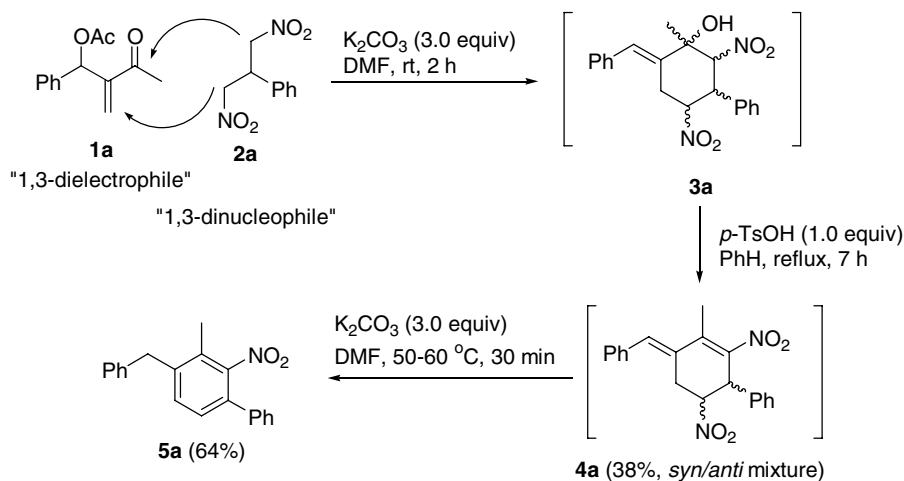
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Abstract—Poly-substituted nitrobenzenes were synthesized from Baylis–Hillman adducts via the [3+3] annulation strategy as the key step. 1,3-Dinitroalkanes served as the 1,3-dinucleophilic component and the Baylis–Hillman acetates as a 1,3-dielectrophilic part.

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Recently, we reported the synthesis of poly-substituted phenols starting from the Baylis–Hillman adducts.¹ In the synthesis, the Baylis–Hillman adducts served as a 1,3-dielectrophilic three-carbon component and dimethyl acetone-1,3-dicarboxylate as the 1,3-dinucleophilic three-carbon unit.¹ During the investigations, we presumed that 1,3-dinitroalkane derivatives could act the role of another effective 1,3-dinucleophilic component in the reaction and could provide poly-substituted nitrobenzene derivatives as shown in **Scheme 1**.

Ballini et al. reported the synthetic applications of 1,3-dinitroalkanes in their synthesis of diarylamines and aromatic compounds.^{2,3} They suggested the formation of nitroarene as the plausible intermediate during the synthesis of the diarylamines, although nitroarene compound was not isolated actually.² Based on the previous results of ours⁴ and others,^{2,3,5} we intended to examine the synthesis of nitroarenes starting from the Baylis–Hillman adducts by following **Scheme 1**.



Scheme 1.

Keywords: Nitrobenzenes; Baylis–Hillman adducts; Nitroalkanes; 1,3-Dinucleophiles.

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Table 1. Synthesis of poly-substituted nitroarenes^a

Entry	1,3-Dielectrophile	1,3-Dinucleophile	Cyclohexene ^b (%)	Product (%)
1				
2				
3				
4				
5				
6				

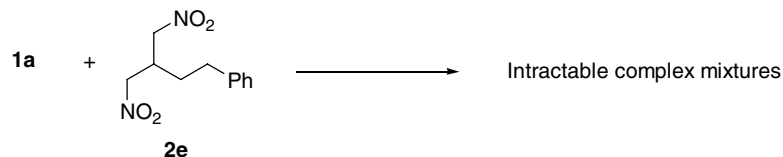
^a Reaction conditions in Scheme 1 were used throughout all entries.

^b Crude diastereomeric mixtures of cyclohexene derivatives.

^c One of the diastereoisomers was isolated and identified the structure.

Initially, we worried about the possibility for the successful formation of cyclohexane ring via the nitroaldol reaction between nitroalkane and ketone moiety.⁶ However, to our delight, we could obtain the desired nitroarenes eventually and wish to report herein the results. The reaction of the Baylis–Hillman acetate **1a** and 1,3-dinitroalkane **2a**⁷ in the presence of K_2CO_3 in DMF at room temperature showed the formation of many compounds on TLC as in our previous paper.^{1,4} These compounds were thought to be as the diastereomeric mixtures of **3a**. From the diastereomeric mixtures of **3a**, we obtained **4a** (*p*-TsOH in benzene) as a *syn/anti* mixture albeit in low yield (38%).⁸ After the column separation of **4a** as a mixture, we subjected **4a** under the conditions of K_2CO_3 /DMF again and could obtain the desired nitroarene **5a** in moderate yield (64%) as shown in Scheme 1.⁹

Based on the successful results, we examined the synthesis of a variety of nitroarenes **5b–f** following the same procedure by applying **1a–d** and **2a–d**. The mechanism for the formation of nitroarenes **5** could be thought as follows: (i) S_N2' type substitution of **2** at the primary position of **1**, (ii) intramolecular nitroaldol reaction to form the diastereomeric mixture of **3**, (iii) *p*-TsOH-catalyzed dehydration to afford **4**, (iv) elimination of HNO_2 and concomitant isomerization of the double bond to **5**. However, unfortunately, the yields of the corresponding cyclohexene derivatives **4b–f** (34–48%) and nitroarenes **5b–f** (56–61%) were moderate to low in all cases (Table 1). All the efforts to improve the yields of products by the modification of solvent, kinds and amounts of base, reaction temperature, etc., were found ineffective. We could not obtain the corresponding cyclohexene or nitroarene from the reaction of **1a** and

**Scheme 2.**

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