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A new method for the synthesis of 2,6-dinitro and 2-halo-6-nitrostyrenes

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Abstract

A new method for the synthesis of 2-halo-6-nitrostyrenes from 2-halo-6-nitrotoluenes is disclosed. Also described is a one-pot process for the synthesis of 2,6-dinitristyrene from 2,6-dinitrotoluene.

Keywords: 2,6-dinitrotoluene; 2,6-dinitrostyrene; 2-halo-6-nitrostyrenes and *p*-formaldehyde.

During our efforts to develop an economical process for the production of 5-amino-4-ethyl-benzimidazole **1**, we were interested in evaluating 2,6-dinitrostyrene **2a** as a possible key intermediate.[1] We reasoned that the styrene derivatives **2a–f** might serve as key intermediates for a variety of heterocyclic compounds. We envisioned that these styrene derivatives **2** might easily be synthesized by hydroxymethylation of the corresponding 2-nitrotoluenes[2] **3a–f** followed by elimination of the resulting hydroxyl group. A literature search revealed that Hegedus and Harrington[3] reported the synthesis of 2-bromo-6-nitrostyrene **2c** from 2-bromo-6-nitro toluene **3c** via a three-step sequence in which they used the Wittig olefination reaction as the key step. By using a similar three-step sequence, Soderberg and Shriver[4] recently reported the synthesis of 2,6-dinitrostyrene **2a** from 2,6-dinitrotoluene **3a** with an overall yield of 65%. They also developed a new approach to the synthesis of various indoles from the corresponding styrenes.[4] This prompted us to report on our *one-pot process* for the synthesis of 2,6-dinitrostyrene and the results related to the synthesis of various 2-halo-6-nitro styrene derivatives **2**.

As shown in Scheme 1 and Table 1, treatment of the toluene derivatives **3a–d** with *p*-formaldehyde at room temperature either in dimethylsulfoxide (entry 1) or in *N*,*N*-dimethyl-acetamide (DMAC) (entries 2–5) in the presence of a catalytic amount of potassium hydroxide furnished the hydroxyethyl derivatives **4a–d**. Surprisingly, under similar reaction conditions, the 2-halo-5,6-dinitro

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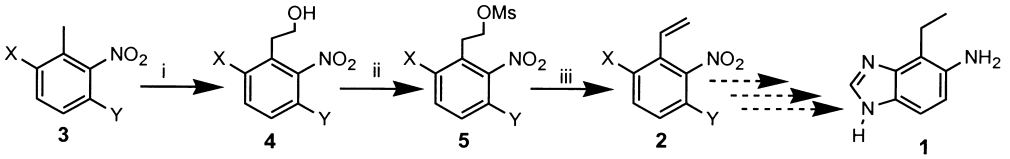

Scheme 1. Reagents and conditions: (i) (HCHO)*n*, KOH, *N*,*N*-dimethylacetamide, rt; (ii) TEA, MsCl, CH_2Cl_2 or DMAC 0–25°C; (iii) TEA or DABCO, CH_2Cl_2 reflux or DMAC, 65–90°C

Table 1

entry	3	X	Y	Yield of 4	Yield of 5	Base Used	Yield of 2
1	**a**	NO_2	H	**95 %**	Used directly	**TEA**	**99 %**
2	**a**	NO_2	H	Used directly	Used directly	**TEA**	**85%**
3	**b**	Cl	H	Used directly	**75 %**	**DABCO**	**82 %**
4	**c**	Br	H	Used directly	**85 %**	**DABCO**	**68 %**
5	**d**	Fl	H	Used directly	Used directly	**DABCO**	**40 %**
6	**e**	Cl	NO_2	No reaction	See Ref. 5	**DABCO**	**50 %**
7	**f**	F	NO_2	No reaction	See Ref. 5	**DABCO**	**35 %**

derivatives[5] **3e**,**f** gave no expected products and remained intact, even after prolonged reaction time. Exposure of the crude hydroxyethyl derivatives **4a**–**d** to triethylamine and methanesulfonyl chloride either in dichloromethane (entry 1) or in DMAC (entries 2–5) gave the mesylate derivatives **5a**–**d**. Heating of the mesylate derivative **5a** with excess triethylamine in the same pot either in dichloromethane at reflux (entry 1) or in DMAC at 70–75°C (entry 2) gave the 2,6-dinitrostyrene **2a** in excellent yield. The styrene **2a** was isolated from the DMAC reaction mixture by simply pouring into water followed by filtration. When we used the above-described reaction conditions to effect the elimination of mesylate from **5b** to furnish **2b**, the reaction was found to be very sluggish and incomplete even after 16 h. But exposure of **5b** to DABCO in DMAC at 70–90°C cleanly furnished **2b**. By using these modified reaction conditions, the mesylate derivatives[5] **5e** and **5f** were also converted into the corresponding styrene derivatives **2e** and **2f**.

General 3-step procedure: (i) To a solution of **3** (14.3 mmol) and *p*-formaldehyde (17.8 mmol) in dimethylacetamide (20 ml) was added powdered potassium hydroxide (1.4 mmol). The reaction mixture was stirred at room temperature for 4–6 h. The product **4** was either isolated after standard work-up[2] or directly used in the next step without any work-up or isolation; (ii) To a stirred solution of hydroxy derivative **4** either in dichloromethane or in DMAC (20 ml) at 0°C was added methanesulfonyl chloride (20 mmol) and triethylamine (45 mmol). The reaction mixture was allowed to warm up to room temperature and stirred until the reaction was complete. The mesylate derivative **5** was either isolated after the usual work up or subjected to the next step without doing any work up; (iii) To a solution of mesylate **5** either in dichloromethane or in DMAC (20 ml) was added either TEA or DABCO, as shown in Table 1 (40 mmol). The reaction mixture was stirred at 65–90°C until the reaction was complete. The styrene **2** was isolated after standard work-up and chromatographic purification.[6]

In conclusion, a general method for the synthesis of 2-halo-6-nitrostyrenes **2** from 2-halo-6-nitro toluenes **3** has been developed. In addition, we have also developed a one-pot process for the synthesis of 2,6-dinitrostyrene from 2,6-dinitrotoluene. This process was found to be advantageous

over the existing method as this method eliminates the use of environmentally unfriendly reagents and is more suitable for large scale synthesis.[4]

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6. All products were identified by proton NMR and Ms spectral data.