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## Selective Nitration of Styrenes with Clayfen and Clayan: A Solvent-free Synthesis of $\beta$ -Nitrostyrenes

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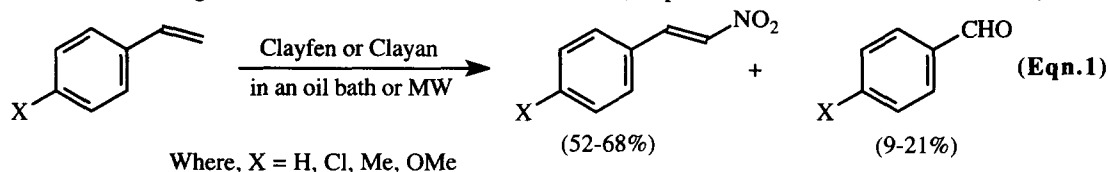
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**Abstract:** A facile solvent-free synthesis of  $\beta$ -nitrostyrenes is described from styrene and its substituted derivatives using inexpensive 'doped' clay reagents, clayfen and clayan. © 1998 Elsevier Science Ltd. All rights reserved.

$\beta$ -Nitrostyrene and its derivatives are vital starting materials for the synthesis of a variety of useful building blocks and valuable precursors such as nitroalkanes, amines, ketoximes, hydroxylamines and aldoximes.<sup>1</sup> The title compounds are generally prepared by direct nitration of styrenes or by the condensation of appropriate aldehydes with nitroethane.<sup>2</sup> However, it is quite challenging to achieve direct transformation of styrenes to  $\beta$ -nitrostyrenes due to the highly sensitive nature of the vinylic side chain. The literature to date embodies only a few scattered reports, which include the treatment of styrene with sodium or potassium nitrate in polyphosphoric acid,<sup>3</sup> nitrohalogenation with nitril halides ( $\text{NO}_2\text{X}$ ) followed by dehydrohalogenation with triethylamine,<sup>4</sup> the reaction of styrene with tetranitromethane (TNM) in the presence of pyridine<sup>5</sup> and nitration of a deactivated styrene with nitric acid (98%) in concentrated sulfuric acid.<sup>6</sup> Nitration reagents such as  $\text{HgCl}_2\text{-NaNO}_2$ <sup>7</sup> lead to varying degrees of ring nitration as well as the desired reaction at the olefinic bond. The photochemical charge transfer activation of the electron donor-acceptor (EDA) complex, derived from TNM and styrenes in acetonitrile, has been reported to give different products depending on the nature of styrenes, e.g.  $\beta$ -nitrostyrene from *p*-methoxy-styrene, isoxazolidines from styrene and *p*-methylstyrene and an  $\alpha$ -nitroacetophenone from *p*-chlorostyrene.<sup>8</sup> Other reagents employed for nitration of styrenes include  $\text{AgNO}_2/\text{PhSeBr}/\text{HgCl}_2$ ,<sup>9</sup>  $\text{AgNO}_2/\text{I}_2$ /ethylene glycol<sup>10</sup> and an ultrasound promoted reaction in a sealed tube with  $\text{NaNO}_2\text{-Ce}(\text{NH}_4)_2(\text{NO}_3)_6\text{-AcOH}$ .<sup>11</sup> A relatively clean reaction of styrene has been reported recently using nitrogen monoxide in 1,2-dichloroethane followed by treatment with activated acidic alumina;<sup>12</sup> the protocol, however, calls for the requirement of 4 equivalents of nitrogen monoxide for the introduction of each nitro group.

In continuation of our ongoing research program on solvent-free organic transformations,<sup>13</sup> we decided to explore the direct conversion of styrenes to  $\beta$ -nitrostyrenes using clay doped with nitrate salts. The heterogeneous reaction with clayfen [iron(III) nitrate on clay]<sup>14</sup> in various solvents failed to generate  $\beta$ -nitrostyrenes but the solid state neat reactions readily provided the desired side chain nitrated styrenes. Herein, we report the details of this simple and inexpensive nitration method using clayfen<sup>14</sup> and clayan [ammonium nitrate on clay]<sup>15</sup> that proceeds under solvent-free conditions. Clayfen has been shown to be an efficient ring nitrating agent for a wide variety of phenols and nitrogen heterocyclic compounds<sup>14</sup> but no side chain nitration has been demonstrated. Additionally, we found that the related clayan<sup>15</sup> is equally useful for nitration of styrene and its *p*-substituted derivatives.

In a typical example, the neat styrene and clayfen or clayan are mixed well in a glass container and then heated in an oil bath (~100-110 °C, 15 min) or irradiated in a microwave oven (~100-110 °C, 3 min) in solid state (Eqn. 1). In the case of clayfen, the reaction mixture is irradiated continuously for 3 min whereas for clayan intermittent warming is recommended with 30 second intervals (temperature should not exceed ~ 60-70 °C).



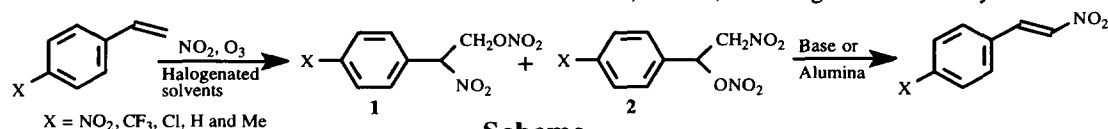
**Table: Product distribution in solventless nitration of styrenes using clayfen and clayan<sup>a</sup>**

Entry	Substrate	$\beta$ -Nitrostyrene <sup>b</sup>	Aldehyde <sup>b</sup>	Polymer/others
<b>Using Clayfen</b>				
1	Styrene	68(56)	21(35)	11(09)
2	<i>p</i> -Chlorostyrene	52(41)	10(22)	38(37)
3	<i>p</i> -Methylstyrene	52(41)	11(24)	37(35)
4	<i>p</i> -Methoxystyrene	14(14)	09(15)	77(71)
<b>Using Clayan</b>				
5	Styrene	59(47)	20(35)	21(18)
6	<i>p</i> -Chlorostyrene	49(37)	11(23)	40(40)
7	<i>p</i> -Methylstyrene	44(35)	15(26)	41(39)
8	<i>p</i> -Methoxystyrene	13(12)	12(15)	75(73)

<sup>a</sup>Reaction conditions: for clayfen, either in oil bath (15 min) or in microwave, MW, (3 min) at 100-110 °C and for clayan, either in oil bath (15 min) or in MW (3 min) at 60-70 °C. <sup>b</sup>The relative amounts of product formation are determined by GC-MS analysis and the results in the parentheses refer to the corresponding yields obtained using MW irradiation; the products are identified by comparison of their m.p. and NMR spectra with those reported for the known compounds in the literature.

Our results for styrene and its various *p*-substituted derivatives such as *p*-chloro-, *p*-methyl- and *p*-methoxy-styrene using both the nitrating agents, clayfen and clayan, are depicted in the Table. In the case of styrene, *p*-chloro- and *p*-methylstyrene, respectable yields (52-68%) of corresponding  $\beta$ -nitrostyrenes are obtainable. In contrast, the electron rich *p*-methoxystyrene resulted in the major formation of polymeric and other unidentified products with only 14% of *p*-methoxy- $\beta$ -nitrostyrene (entries 4 and 8, Table). In all the cases, considerable amount of the corresponding aldehyde (9-21%) formation is observed along with some nitrile (2-3%) from GC-MS analysis. At room temperature, the reaction is found to be very slow and also leads to the major formation of polymeric products. Of the two nitrating reagents, clayfen delivered relatively better results (Table).

A recent report details the side chain nitration of styrenes with nitrogen dioxide and ozone in slightly lower yields<sup>16</sup> wherein the reaction proceeds *via* the formation of nitro-nitrate intermediates (**1** and **2**, Scheme) which, in turn, are converted to the required  $\beta$ -nitrostyrenes using alumina or a base. Our solventless method, however, does not reveal the formation of such nitro-nitrate intermediates, **1** and **2**, according to GC-MS analysis.



**Scheme**

The investigation of the same reaction under the identical conditions using clay that is impregnated with  $\text{NaNO}_3$ ,  $\text{KNO}_3$  and  $\text{NaNO}_2$  does not produce  $\beta$ -nitrostyrene; instead substantial amounts of polymeric products are observed as discerned by GC-MS analysis. In order to improve the formation of nitrated product, we explored the use of *m*-chloroperbenzoic acid which suppresses the formation of polymeric products but results in the formation of nitro-nitrates, **1** and **2** (scheme) as the major product; only minor amounts (~10-15%) of side chain nitrated product were obtained. Changes in other reaction parameters such as conducting the reaction for a longer duration of time or the additional use of a strong base ( $\text{NaNH}_2$ ) does not transform the nitro-nitrate intermediates, **1** and **2**, as reported earlier.<sup>16</sup>

The reaction with clayfen is investigated under heterogeneous conditions in a variety of solvents. In contrast, we observed the following results; (a) in ether at room temperature (16 h), 1% of  $\beta$ -nitrostyrene, 15% aldehyde and 11% starting material; (b) in dichloromethane under refluxing condition (5 h), 1-2% of  $\beta$ -nitrostyrene, 2-3% of aldehydes; (c) upon ultrasound irradiation in dichloromethane at room temperature (2 h), 26% of  $\beta$ -nitrostyrene, 31% of aldehyde. The remaining material in all cases is the polymeric products.

In conclusion, the solid state reaction of styrene and its *p*-substituted derivatives with clayfen and clayan is a very facile method to produce  $\beta$ -nitrostyrenes. The operational simplicity, the use of inexpensive reagents, and a rapid reaction that avoids the undesirable polymerization of styrene (typical heterogeneous reactions in solvents), makes this a useful procedure and attractive alternative to the currently available methods.

**General.** A Sears Kenmore microwave (MW) oven operating at 2450 MHz (power 900 watt) was used for all the experiments. Styrenes were purchased from Acros Organics and were used as received.  $^1\text{H}$  NMR spectra were recorded in  $\text{CDCl}_3$  on Jeol 300 MHz spectrometers using TMS as an internal standard. Clayfen (0.75g  $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ /1g clay) and clayan (1g  $\text{NH}_4\text{NO}_3$ /1g clay) were prepared according to the published procedures.<sup>14,15</sup>

**CAUTION.** Although we did not encounter any accident during these studies, we recommend extreme caution for reactions conducted on larger scales because of the possible higher localized temperatures attained in the microwave (MW) oven, especially for clayan that should not be heated beyond 70 °C in oil bath or MW oven.

**General procedure for the conversion of styrene to  $\beta$ -nitrostyrene:** In a typical experiment, styrene (180 mg, 1.74 mmol) was admixed with clayfen or clayan (300 mg) in a glass tube. The reaction mixture was placed in an oil bath for 15 min or irradiated for 3 min in an alumina bath<sup>17</sup> inside an unmodified household microwave oven (900 watt) at its medium power. On completion of the reaction, followed by TLC examination (hexane:EtOAc, 4:1, v/v), the product was extracted into dichloromethane (45 mL), the combined organic extract dried with anhydrous sodium sulfate and solvent removed under reduced pressure. The relative amounts of product distribution (Table) were calculated from GC-MS analysis (Hewlett-Packard model 5890 gas chromatograph with a mass spectrometer). Alternatively, the crude material was chromatographed on a silica gel column and eluted with hexane:EtOAc (4:1, v/v) to afford the pure product (147 mg, 57%).

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  17. Alumina bath (neutral alumina: 125 g, mesh ~150, Aldrich; bath: 5.7 cm diameter) has three functions: (i) serves as a heat sink in the MW chamber; (ii) houses the small reaction vessels, and (iii) allows the easy measurement of the bulk temperature after completion of the reaction.