Sodium Hypochlorite-Dowex 1X8-200: A Convenient Oxidizing Reagent

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ABSTRACT: The polymer supported hypochlorite ion is a facile selective oxidizing agent for the oxidation of various alcohols to aldehydes and ketones. Similarly it successfully oxidizes various Hantzsch type 1,4-dihydropyridines to corresponding pyridines.

KEY WORDS: Oxidation, Supported oxidants, Hantzsch dihydropyridines, Alcohols, Sodium hypochlorite.

INTRODUCTION

There have been a number of important advances in the practical aspects of organic synthesis during recent years. One of these, namely polymer supported reagents, have now been developed to fairly advanced levels [1-3].

The polymeric supports provide particular reaction environments capable of enhancing the reactivity of many reagents, while making the turns work up process very profitable by reducing it to a mere filtration. For example anion exchange resins have been found to be useful in C-alkylation of phenols [4], O-alkylation of carboxylate anions [5], unreactive ketones reduction [6] and many other synthetic applications [2, 3].

Sodium hypochlorite is a readily available and inexpensive oxidant, which has been used for the oxidation of variety of compounds [7]. Unfortunately, the traditional NaClO oxidation methods in this transformation are limited by the very low solubility of NaClO in most organic solvents. In order to overcome this limitation, milder NaClO oxidation methods such as oxidation by phase-transfer catalysts have been developed [8, 9]. However, these methods possess disadvantages, e.g., they require long reaction times, high temperatures and the use of expensive polar aprotic solvents.

We have now here report a polymer supported ClO− that is useful for the oxidation of alcohols to carbonyl compounds and similarly aromatization of Hantzsch 1,4-dihydropyridines to the corresponding pyridines.

Oxidation of alcohols to carbonyl compounds is an important transformation in organic synthesis and because of its significance and in spite of the availability of plethora methods to accomplish this objectives [10-12], a practically simple procedure is yet to be desired.

Hypochlorite ion on Dowex 1X8-200 is an inexpensive alternative for the oxidation of various alcohols to aldehydes and ketones with high selectivity.

Table 1 shows a set of various alcohols, which were oxidized with ClO− supported on the Dowex 1X8-200 anion exchanger resin to the corresponding carbonyl compounds.

Oxidation of 4-substituted-2,6-dimethyl-3,5-pyridine dicarboxylic acid diethyl esters to the corresponding pyridines has been extensively studied in view of the importance of this reaction to the metabolism of Hantzsch esters and the calcium channel blocking drugs used in the treatment of various cardiovascular disorders [13].

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Table 1: Oxidation of alcohols to carbonyl compounds by NaClO⁻ / Dowex 1X8-200

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Time(h)</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃(CH₂)₃OH</td>
<td>CH₃(CH₂)₃CHO</td>
<td>2.0</td>
<td>83</td>
</tr>
<tr>
<td>C₆H₅CH₂OH</td>
<td>C₆H₅CHO</td>
<td>2.0</td>
<td>92</td>
</tr>
<tr>
<td>C₆H₅CH=CHCH₂OH</td>
<td>C₆H₅CH=CHCHO</td>
<td>3.0</td>
<td>89b</td>
</tr>
<tr>
<td>4-ClC₆H₄CH₂OH</td>
<td>4-ClC₆H₄CHO</td>
<td>2.0</td>
<td>85</td>
</tr>
<tr>
<td>(C₆H₅)₂CHOH</td>
<td>(C₆H₅)₂CO</td>
<td>2.5</td>
<td>88</td>
</tr>
<tr>
<td>C₆H₅CHOCH₃</td>
<td>C₆H₅COCH₃</td>
<td>3.0</td>
<td>95</td>
</tr>
<tr>
<td>1,4-hydroquinone</td>
<td>1,4-benzoquinone</td>
<td>1.5</td>
<td>83</td>
</tr>
<tr>
<td>furfuryl alcohol</td>
<td>furfural</td>
<td>1.5</td>
<td>93b</td>
</tr>
<tr>
<td>9-fluorenol</td>
<td>9-fluorenone</td>
<td>3.0</td>
<td>90</td>
</tr>
<tr>
<td>anthrol</td>
<td>anthrone</td>
<td>2.0</td>
<td>87</td>
</tr>
</tbody>
</table>

a: Yield of isolated products  
b: Isolated as the 2,4-dinitrophenylhydrazone.

There are several methods for the oxidation of the compounds[14-20]. Reagents in these regards involve the use of strong oxidants such as KMnO₄[21], CrO₃[22], HNO₃[23] and Bi(NO₃)₃[24] that lead to dealkylation at the 4 -position or formation of side products.

In our laboratory we have successfully developed a mild and efficient method for the oxidation of Hantzsch 1,4 -dihydropyridines to the corresponding pyridines. Hypochlorite ion on Dowex 1X8-200 anion exchanger

Table 2: Aromatization of 1,4 -dihydropyridines to pyridine derivatives using ClO⁻ / Dowex 1X8-200.

<table>
<thead>
<tr>
<th>R</th>
<th>R⁺</th>
<th>time(min)</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Et</td>
<td>15</td>
<td>98</td>
</tr>
<tr>
<td>Me</td>
<td>Et</td>
<td>20</td>
<td>90</td>
</tr>
<tr>
<td>Et</td>
<td>Et</td>
<td>15</td>
<td>97</td>
</tr>
<tr>
<td>n-hexyl</td>
<td>Et</td>
<td>30</td>
<td>93</td>
</tr>
<tr>
<td>2-NO₂C₆H₄</td>
<td>Me</td>
<td>45</td>
<td>92</td>
</tr>
<tr>
<td>4-OCH₃C₆H₄</td>
<td>Et</td>
<td>30</td>
<td>86</td>
</tr>
<tr>
<td>2-pyridyl</td>
<td>Et</td>
<td>30</td>
<td>89</td>
</tr>
<tr>
<td>4-pyridyl</td>
<td>Et</td>
<td>30</td>
<td>93</td>
</tr>
<tr>
<td>2-furyl</td>
<td>Et</td>
<td>30</td>
<td>93</td>
</tr>
<tr>
<td>2-thienyl</td>
<td>Et</td>
<td>30</td>
<td>96</td>
</tr>
<tr>
<td>4-ClC₆H₄</td>
<td>Et</td>
<td>45</td>
<td>90</td>
</tr>
<tr>
<td>C₆H₅</td>
<td>Et</td>
<td>35</td>
<td>92</td>
</tr>
</tbody>
</table>

a: Yields of isolated products

resin aromatize 1,4-dihydropyridines to pyridines with total selectivity and no loss of 4-position substituents (table 2).

EXPERIMENTAL

All chemicals were purchased from Merck (Darmstadt, Germany), Aldrich (Milwaukee, WI, USA) and Riedel Dehauen AG chemical companies and were used without further purification. All products are well known compounds and they were identified their mp, IR, and 1H-NMR spectroscopic properties. All yields refer to the isolated products. 1,4 -dihydropyridines were synthesized according to the refereed procedure[25].

Preparation of ClO⁻ supported on anion exchanger resin

To a stirring solution of 200 ml of 1.85 molar sodium hypochlorite was added 55g of the chloride form of Dowex 1X8-200, a macroreticular anion exchanger resin containing quaternary ammonium groups. Chloride ions were readily displaced and a ClO⁻ form of the resin was quantitatively obtained in 2 hrs. Then the resin was successively rinsed with water, acetone and absolute ethanol and finally dried in vacuum at 65°C for 5 hrs. The capacity of the resin was determined by stirring 1.0g of the resin with 20ml of 2N aqueous potassium hydroxide overnight, filtering off and titrating iodometrically[26]. The average capacity of the dried resin was found 2.2 mmol eq ClO⁻/g of resin.
Oxidation of Alcohols to carbonyl compounds, General Procedure

Benzylic alcohol (2mmol) and dry ClO\textsuperscript{-} form of the resin (1.5g) were refluxed in 25 ml acetonitrile under vigorous stirring for 2h. Reaction mixture was then filtered through a sintered glass and the filtrate concentrated and flash chromatographed (hexane- AcOEt, 10:1) to give 193mg, (1.82mmol, 92% yield) of the pure benzaldehyde.

Oxidation of 1,4-Dihydropyridines to Pyridines, General Procedure

1,4-Dihydroxy-2,6-dimethyl-3,5-pyridine dicarboxylic acid diethyl ester (0.253g, 1mmol) and dry ClO\textsuperscript{-} form of the resin (1.5g) were refluxed in 25 ml acetonitrile under vigorous stirring for 15 minutes. The reaction mixture was then filtered through a sintered glass and the filtrate concentrated and resulting crude product was crystallized from ethanol to afford pure ethyl 2,6-dimethyl-3,5-pyridinedicarboxylate in 98% yield.

In conclusion the hypochlorite ion on Dowex 1X8-200 is a mild and effective alternative for the oxidation of alcohols to carbonyl compounds and oxidative conversion of 1,4-dihydropyridines to the corresponding pyridine derivatives in high yields without formation of side products.

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REFERENCES