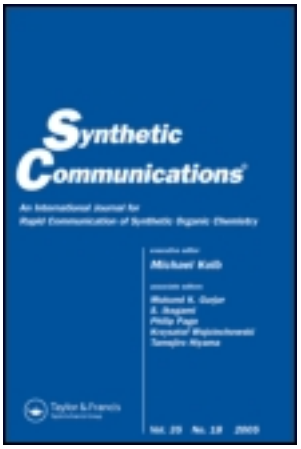

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Tandem One-Pot Conversion of Aldehydes into Ethyl Esters

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TANDEM ONE-POT CONVERSION OF ALDEHYDES INTO ETHYL ESTERS

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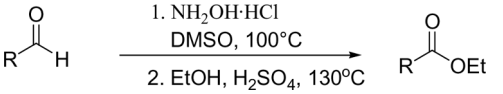
GRAPHICAL ABSTRACT



Abstract *A facile one-pot synthesis of ethyl esters from aldehydes has been developed. This tandem process involves the formation of a nitrile intermediate obtained from the reaction of an aldehyde with hydroxylamine hydrochloride in dimethylsulfoxide (DMSO) at 100 °C and the subsequent reaction of the nitrile with ethanol and sulfuric acid at 130 °C. The resulting ethyl ester products were produced in good yields (65–90%) and high purity (>95%).*

Keywords Aldehyde; ethyl ester; nitrile; nitrile alcoholysis; tandem reaction

Nitriles are versatile synthetic intermediates because they can be transformed into a variety of other functional groups.[1,2] One such transformation is the alcoholysis of nitriles to form esters.[3] Recently,[4] we described a convenient one-pot synthesis of nitriles from aldehydes using hydroxylamine hydrochloride in dimethylsulfoxide (DMSO) at 100 °C. We extended this synthetic methodology to a tandem, one-pot conversion of aldehydes into amides employing basic hydrogen peroxide after formation of the nitrile.[5] We have now further extended this tandem reaction sequence to the one-pot conversion of aldehydes into esters and describe the results in this report. We feel this new method is an attractive alternative to recently described procedures[6] for converting aldehydes into esters including the N-iodosuccinimide-mediated conversion of aldehydes to methyl esters,[7] oxidation of aldehydes to esters with oxone,[8] catalytic oxidative esterification of aldehydes with V_2O_5-H_2O_2,[9] conversion of aldehydes into esters using acetone cyanohydrin,[10] titanosilicate-catalyzed oxidation of aromatic aldehydes to esters,[11] aldehyde to ester through oxidation of acetals,[12] and treatment of aromatic aldehydes with manganese dioxide and sodium cyanide.[13]

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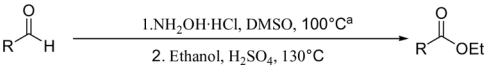
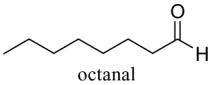
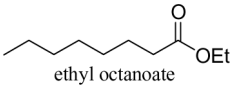
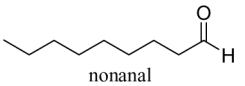
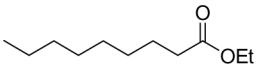
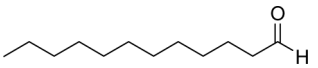
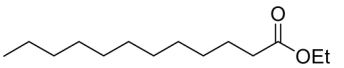
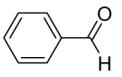
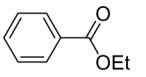
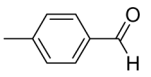
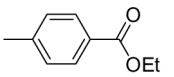
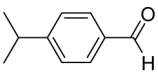
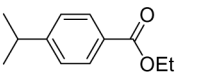
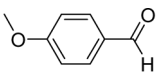
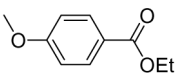
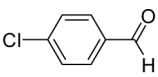
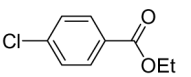
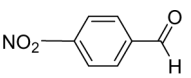
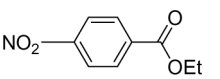
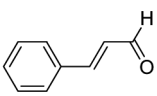
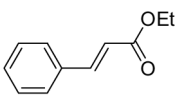
Table 1. One-pot conversion of aldehydes to ethyl esters



Entry	Aldehyde	Ethyl ester	Yield[b] (%)
1	 octanal	 ethyl octanoate	85[c]
2	 nonanal	 ethyl nonanoate	75[c]
3	 dodecanal	 ethyl dodecanoate	90[c]
4	 benzaldehyde	 ethyl benzoate	70[d]
5	 4-methylbenzaldehyde	 ethyl 4-methylbenzoate	74[d]
6	 4-isopropylbenzaldehyde	 ethyl 4-isopropylbenzoate	71[d]
7	 4-methoxybenzaldehyde	 ethyl 4-methoxybenzoate	68[c]
8	 4-chlorobenzaldehyde	 ethyl 4-chlorobenzoate	79[d]
9	 4-nitrobenzaldehyde	 ethyl 4-nitrobenzoate	78[c]
10	 trans 3-phenyl-2-propenal	 ethyl trans-cinnamate	65[c]

[a]Aldehyde (2.0 mmol), $NH_2OH \cdot HCl$ (3.8 mmol), DMSO (4 mL), ethanol (10 mL), and H_2SO_4 (5 mL).
[b]Isolated yields.
[c]Total time for complete reaction = 3 h.
[d]Total time for complete reaction = 3.5 h.

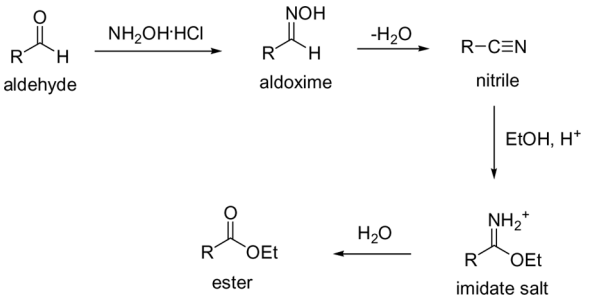


Figure 1. Sequence of possible steps in the conversion of aldehydes into ethyl esters.

The experimental procedure for the one-pot conversion of aldehydes to ethyl esters is simple and straightforward and affords ethyl esters in good isolated yields (Table 1). As an illustrative example, 4-methylbenzaldehyde (2.0 mmol) was added to a solution of hydroxylamine hydrochloride (3.8 mmol) in DMSO (4 mL), and the resulting reaction solution was stirred and heated for 60 min in a sand bath maintained at 100 °C. Complete conversion of octanal, nonanal, dodecanal, 4-methoxybenzaldehyde, 4-nitrobenzaldehyde, and 3-phenyl-2-propenal to their respective nitriles only took 30 min as determined by GC/MS. All other aldehydes took 60 min to reach completion. Ethanol (10 mL) and sulfuric acid (5 mL) were added, and the reaction mixture was stirred while heated in a sand bath held at 130 °C for 2.5 h. After cooling to room temperature, water (15 mL) was added, and the solution was extracted with diethyl ether (4×20 mL). The combined ether layers were washed once with water (20 mL) and dried (K_2CO_3), and the solvent was removed by rotary evaporation and high vacuum to give ethyl 4-methylbenzoate as a light oil (2.43 g, 74% isolated yield). The ^{1}H and ^{13}C NMR spectra and the mass spectrum of the isolated ethyl 4-methylbenzoate were identical to authentic spectra. The ^{1}H and ^{13}C NMR spectra of this ester indicated that its purity was greater than 95%.

As seen in Table 1, this tandem reaction is general for the preparation of both aliphatic and aromatic ethyl esters. All the ethyl esters prepared in this study were confirmed by comparison of ^{1}H and ^{13}C NMR spectra and mass spectra with authentic samples. Furthermore, the ^{1}H and ^{13}C NMR spectra of the ethyl esters indicated that the product purities were greater than 95%.

Although no mechanistic studies were performed, it seems reasonable that this tandem conversion of an aldehyde to an ester first involves the formation of an aldoxime, which we have previously shown dehydrates under the reaction conditions to give a nitrile.[4] Upon the addition of ethanol and acid, alcoholysis of the nitrile leads to an imidate salt, which is further hydrolyzed under the reaction conditions to give an ester.[3]

In conclusion, we have demonstrated that aldehydes can be readily converted into ethyl esters by heating the aldehyde in DMSO containing hydroxylamine hydrochloride followed by selective solvolysis of the subsequent nitrile with ethanol under acidic conditions. This one-pot, tandem process does not involve expensive materials and should offer an attractive alternative for converting aldehydes into esters.

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