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Alkenes from Alcohols by Tandem Hydrogen Transfer and Condensation

Michael I. Hall,[a] Simon J. Pridmore,[a] and Jonathan M. J. Williams[a,*]

[a] Department of Chemistry, University of Bath, Claverton Down, Bath, BA2 7AY, U.K.
Fax/Phone: (+44)-(0)1225-38-62-31
E-mail: J.M.J.Williams@bath.ac.uk

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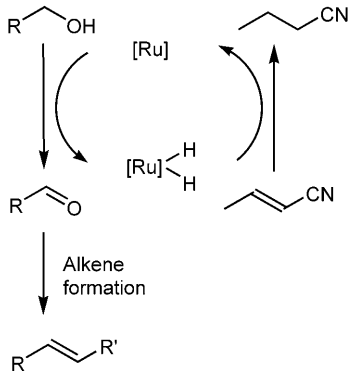
Abstract: A ruthenium-catalysed oxidation of alcohols by hydrogen transfer has been coupled with organocatalysed condensations using pyrrolidine or piperidine, to give α,β-unsaturated esters and nitroalkenes. Reactions proceed with high (*E*)-selectivity and provide an efficient and straightforward route to α,β-unsaturated compounds.

Keywords: alcohols; alkenes; hydrogen transfer; organocatalysis; ruthenium

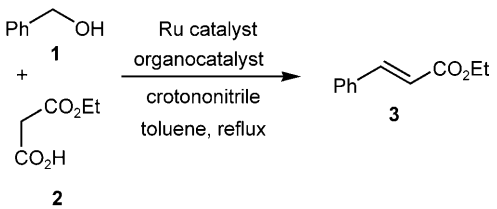


Scheme 1. Tandem oxidation/alkene formation.

We have recently reported that crotononitrile is a useful hydrogen acceptor in the ruthenium-catalysed oxidation of alcohols to methyl esters.[1] Various ruthenium catalysts have also been used by us[2] and by others[3] to allow alcohols to be used as alkylating agents in a sequence involving temporary removal of hydrogen from an alcohol to give an aldehyde which undergoes *in situ* alkene formation followed by return of the hydrogen to provide a new C–C bond.[4,5] We were interested in the possibility of intercepting this pathway by transferring hydrogen to a suitable acceptor providing a route for the conversion of alcohols into alkenes, as shown in Scheme 1.

In order for this approach to be successful, the hydrogen acceptor must be able to accept hydrogen much more readily than the alkene which is being generated, and the alkene-forming reaction must not interfere with the hydrogen-transfer catalysis. Examples of other approaches to the conversion of alcohols into alkenes include oxidation with manganese dioxide and *in situ* Wittig reaction,[6] along with sequential Swern/Wittig[7] and TPAP/Wittig processes.[8]

List and co-workers have recently reported the conversion of aldehydes into unsaturated esters using a decarboxylative condensation of malonate half esters and their salts.[9] These reactions were catalysed by DMAP or pyrrolidine. We were intrigued by the possibility of combining these organocatalytic reactions with ruthenium-catalysed hydrogen transfer reactions. A model reaction involving the conversion of benzyl alcohol **1** and malonic half ester **2** into alkene **3** was chosen, using crotononitrile as the hydrogen acceptor (Scheme 2). We have previously found that the combination of $Ru(PPh_3)_3(CO)H_2$ with Xantphos[10] is useful for hydrogen-transfer processes and chose to use this as the catalyst.[11] The use of triethylamine or dimethylaminopyridine as the base/organocatalyst led to a low conversion into product (16% and 13%) with the major product being benzaldehyde (59% and



Scheme 2. Alkene formation from benzyl alcohol **1**.

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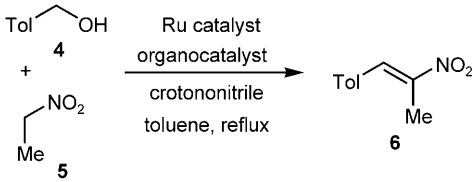
56%). Pyrrolidine and piperidine were both successful as co-catalysts, with both giving complete consumption of starting material after 2 h at reflux using 2.5 mol% catalyst. The use of pyrrolidine afforded product with a trace (<3%) of benzaldehyde, whereas with piperidine, more aldehyde was present (18%).

We then applied these conditions to the formation of a range of alkenes, as shown in Table 1. Methyl, ethyl, benzyl and *tert*-butyl esters were all formed with good isolated yields. The carboxylate salts could be be used in place of the half esters (entries 1 and 3), with the addition of acetic acid. The carboxylate salts of malonate half esters are often cheaper than the acids, and are readily prepared from the diesters by treatment with base.[11]

A variety of substituents could be attached to the starting benzyl alcohol including halides (entries 6–8), electron-donating groups (entries 9 and 10) and electron-withdrawing groups (entry 11) along with the *ortho*-substituted product formed in entry 12. Aliphatic alcohols led to mixtures of α,β- and β,γ-alkene regioisomers, as expected from the corresponding direct reactions of malonate half-esters with aliphatic aldehydes.

As an alternative to the decarboxylative alkene formation using malonate half esters, we chose to investigate the use of nitroalkanes in a tandem alcohol oxidation/nitroaldol condensation process. Nitroalkenes are useful precursors to a range of other functional groups including aldehydes, ketones and amines.[13]

Alcohol **4** and nitroethane **5** were chosen as model substrates for the formation of nitroalkene **6** (Scheme 3). The use of triethylamine, dimethylamino-



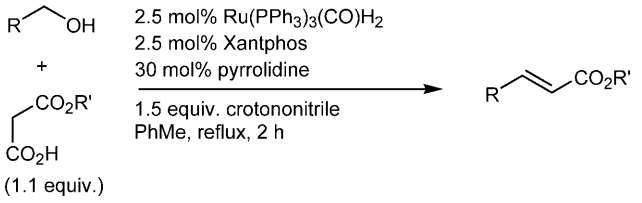
Scheme 3. Tandem oxidation/nitroaldol reaction.

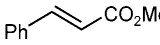
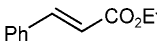
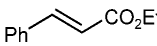
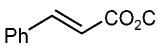
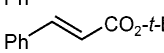
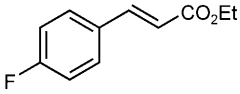
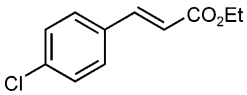
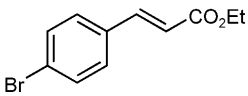
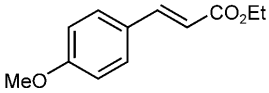
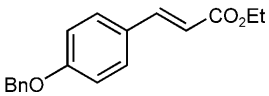
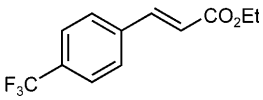
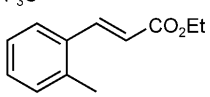
pyridine, pyrrolidine or piperidine led to unreactive systems (a small amount of aldehyde was formed in some cases, but essentially no alkene product). However, the use of piperidinium acetate as co-catalyst provided 100% conversion in the formation of (*E*)-alkene **6**.

These conditions were then applied to the synthesis of other nitroalkenes (Table 2). Whilst nitroethane was used in most cases, nitromethane was also used successfully (entry 1). The tolyl alcohol **4** and its *ortho*-substituted analogue afforded product cleanly (entries 2 and 3). Small amounts of aldehyde were present in some of the other examples, but the products were readily isolated by column chromatography. Furfuryl alcohol was converted cleanly into product, but there was some decompostion during chromatography.

Finally, we have also applied this oxidation/condensation chemistry to the reaction of alcohol **4** with keto nitrile **7** to give the alkene **8** with 100% conversion (Scheme 4). Only one isomer of product was observed by NMR spectroscopy, and an nOe experiment re-

Table 1. Alkenes formed by tandem oxidation/decarboxylative condensation.



Entry	Alkene product	Yield [%][a]
1		74[b]
2		95
3		71[b]
4		84
5		71
6		87
7		90
8		74
9		71
10		83
11		74
12		73

[a] All reactions had reached full conversion as determined by analysis of the ^{1}H NMR spectrum of the crude material which showed only the presence of the (*E*)-isomer of alkene. Products were purified by column chromatography.

[b] The potassium carboxylate salt of the malonate half ester was used, with 1.5 equiv acetic acid.

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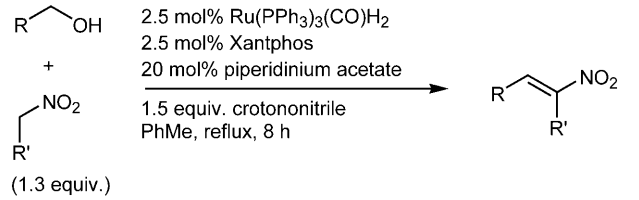
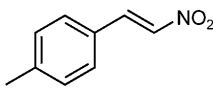
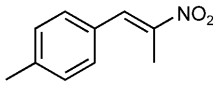
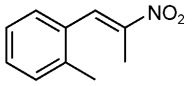
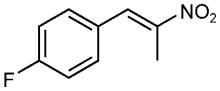
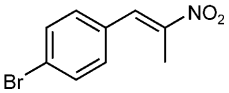
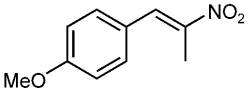
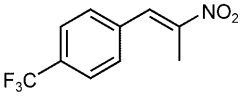
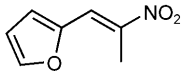
Table 2. Nitroalkenes formed by tandem oxidation/nitroaldol reaction.

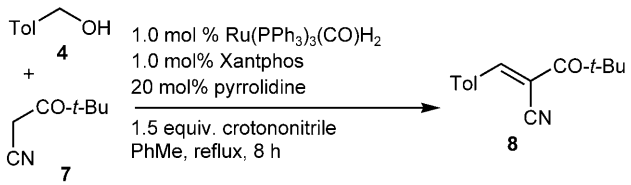


Entry	Alkene product	Yield [%][a]
1		[100][b]
2		84[c]
3		83
4		73
5		62
6		73[c]
7		67
8		[100][b]

[a] All reactions had reached full conversion as determined by analysis of the ^{1}H NMR spectrum of the crude material, which showed only the presence of the (*E*)-isomer of nitroalkene. Products were purified by column chromatography.

[b] Conversion.

[c] These reactions were performed at 1.0 mol% catalyst loading.



Scheme 4. Tandem oxidation/Knoevenagel condensation.

vealed an enhancement of the alkenyl signal upon irradiation of the *tert*-butyl group, indicating the formation of the (*E*)-isomer of product.

In summary, we have used a combination of ruthenium-catalysed hydrogen-transfer with organocatalysed alkene formation to provide new methodology for the conversion of alcohols into alkenes.

Experimental Section

Typical Procedure for the Tandem Oxidation/Decarboxylation Reaction.

To oven-dried, argon-purged Radley's carousel tubes containing $Ru(PPh_3)_3(CO)H_2$ (86 mg, 0.1 mmol, 0.025 equiv.), Xantphos (56 mg, 0.1 mmol, 0.025 equiv.) and pyrrolidine (100 μL, 1.20 mmol, 0.30 equiv.) were added toluene (4 mL), benzyl alcohol (436 μL, 4 mmol, 1 equiv.), crotononitrile (488 μL, 6 mmol, 1.5 equiv.) and monoethyl malonate (581 μL 4.4 mmol, 1.1 equiv.). The reactions were heated to reflux for 2 h, cooled to room temperature and the solvent was removed under vacuum. The resultant oil was purified by column chromatography [9:1 petroleum ether (b.p. 40–60 °C)/diethyl ether, $R_f = 0.31$]. (*E*)-Ethyl cinnamate was obtained as a clear oil; yield: 679.5 mg (95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, 1H, $J = 15.9$ Hz), 7.55–7.36 (m, 5H), 6.45 (d, 1H, $J = 15.9$ Hz), 4.27 (q, 2H, $J = 7.2$ Hz), 1.35 (t, 3H, $J = 7.2$ Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 166.9, 144.5, 130.1, 128.8, 127.9, 118.2, 60.4, 14.2.

Typical Procedure for the Tandem Oxidation/Nitroaldol Reaction.

To oven-dried, argon-purged Radley's carousel tubes containing $Ru(PPh_3)_3(CO)H_2$ (114.5 mg, 0.125 mmol, 0.025 equiv.), Xantphos (72.5 mg, 0.125 mmol, 0.025 equiv.) and piperidinium acetate (181 mg, 1.25 mmol, 0.25 equiv.) were added toluene (5 mL), *para*-methylbenzyl alcohol (611 mg, 5 mmol, 1 equiv.), crotononitrile (610 μL, 7.5 mmol, 1.5 equiv.) and nitroethane (465 μL, 6.5 mmol, 1.3 equiv.). The reaction mixtures were heated to reflux for 8 h, cooled to room temperature and the solvent was removed under vacuum. The resulting oil was purified by column chromatography [9:1 petroleum ether (b.p. 40–60 °C)/diethyl ether, $R_f = 0.40$], affording (*E*)-1-methyl-4-(2-nitroprop-1-enyl)benzene as a pale yellow solid; yield: 744 mg (84%) ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.09 (s, 1H, C*H*), 7.36 (d, 2H, $J = 8.1$ Hz), 7.28 (d, 2H, $J = 8.1$ Hz), 2.47 (d, 3H, $J = 0.9$ Hz), 2.42 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 146.9, 140.5, 133.7, 130.1, 129.6, 129.4, 21.4, 14.1.

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