Selective isomerisation of prop-2-yn-1-ols into α,β-unsaturated aldehydes catalysed by Ru[η³-$CH_2C(Me)CH_2]_2(Ph_2PCH_2CH_2PPh_2$)

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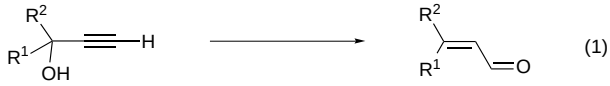
The complex Ru[η³-$CH_2C(Me)CH_2]_2(Ph_2PCH_2CH_2PPh_2$) is an efficient catalyst precursor for the isomerisation of prop-2-yn-1-ols into conjugated enals under mild conditions in the presence of benzoic acid *via* (*Z*)-3-hydroxyprop-1-en-1-yl benzoates.

The isomerisation of propynylic alcohols into α,β-unsaturated aldehydes has the potential to offer access to a variety of terpenoids, *e.g.* vitamin A derivatives, as well as perfume and cosmetic components[1,2] [eqn. (1)].



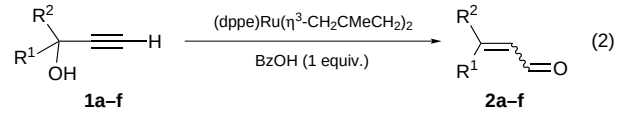
(1)

Such a transformation was first performed in the Meyer–Schuster reaction,[3] which was carried out in acidic medium and catalysed by strong acids.[4] The emergence of metal complex catalysis has allowed the use of catalytic systems based on vanadium(V) oxides[5] or the $Ti(OR)_4$–CuCl–RCO_2H association,[6] operating under milder conditions but still at 125–160 °C. The system Bu_4NReO_4–$MeC_6H_4SO_3H$[7] gives isomerisation at room temperature with alcohol dehydration as a side reaction. A new system $MoO_2(acac)_2$–R_2SO–$ArCO_2H$ operates at 100 °C and appears to be efficient for the formation of prenal.[8] With these metal oxide catalysts, the suggested key steps involve the coordination of the prop-2-ynylic alcohol oxygen atom to the metal and addition of the metal oxide oxygen atom to the alkyne C(1) carbon atom to generate an allenyloxy intermediate. However, in these reactions the required presence of an acid has never been clearly taken into account in the proposed mechanisms.

We now report a new, efficient method for transformation of prop-2-yn-1-ols into α,β-unsaturated aldehydes catalysed by a (diphosphine)ruthenium(II) complex in the presence of benzoic acid, and we show that the key step involves the regioselective catalytic addition of the carboxylate to the terminal carbon atom of the C≡C triple bond, giving a (*Z*)-3-hydroxyprop-1-en-1-yl benzoate intermediate, followed by thermal elimination of the acid.

The ruthenium(II) electrophilic activation concept[9] has allowed the selective preparation of enol esters[10] and furans[11] from terminal alkynes, and β-oxopropyl esters from prop-2-yn-1-ols.[12] Modification of the catalyst precursors has recently made possible control of the regio- and stereo-selective anti-Markovnikov addition of carboxylic acids to terminal alkynes to give (*Z*)-alk-1-en-1-yl carboxylates.[13,14] An attempt to adapt the latter reaction to the addition of benzoic acid to the terminal sp carbon of prop-2-yn-1-ols in the presence of (diphosphine)-ruthenium(II) catalysts led us to discover the formal selective isomerisation of prop-2-yn-1-ylic alcohols into α,β-unsaturated aldehydes [eqn. (2)].

The reaction of the prop-2-yn-1-ol **1a** (R^1, R^2 = Me) with 1 equiv. of benzoic acid in the presence of 1 mol% of Ru[η³-$CH_2C(Me)CH_2]_2$(dppe) **I** (dppe = $Ph_2PCH_2CH_2PPh_2$) at 70 °C for 15 h led to the complete transformation of **1a**. Distillation of

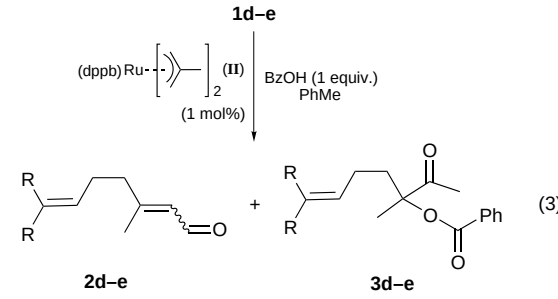


1a–f **2a–f** (2)

a $R^1 = R^2$ = Me **d** R^1 = Me, $R^2 = CH_2CH_2CH{=}CH_2$
b R^1 = Me, R^2 = Ph **e** R^1 = Me, $R^2 = CH_2CH_2CH{=}CMe_2$
c R^1 = Me, $R^2 = Pr^i$ **f** $R^1 = R^2$ = Ph

the crude product led to the sole α,β-unsaturated aldehyde **2a** (prenal), isolated in 56% yield (method A). Complete transformation of the disubstituted prop-2-ynylic alcohols **1b** and **1c** in toluene under similar conditions led after distillation to the unsaturated aldehydes **2b** (68%) and **2c** (37%) (Table 1). Both isomers were formed in the respective ratios *Z*/*E* = 2:1 (**2b**) and 3:4 (**2c**). The unsaturated prop-2-yn-1-ols **1d** and **1e** were good substrates for this isomerisation as they led to the best yields in **2d** (75%) and in the terpenoid citral **2e** (73%), formed as a mixture of the *Z* and *E* isomers in the ratio 1:2 (Table 1).

This reaction is also catalysed by the analogous Ru[η³-CH_2-$C(Me)CH_2]_2$(dppb) complex **II** [dppb = $Ph_2P(CH_2)_4PPh_2$] but the competitive formation of the β-oxopropyl ester **3** was observed [eqn. (3)]. Thus, the reaction of **1e** with BzOH and 1 mol% of **II** afforded **2e** in 18% and **3e** in 50% yield, and **1d** gave 65% of **3d** only.

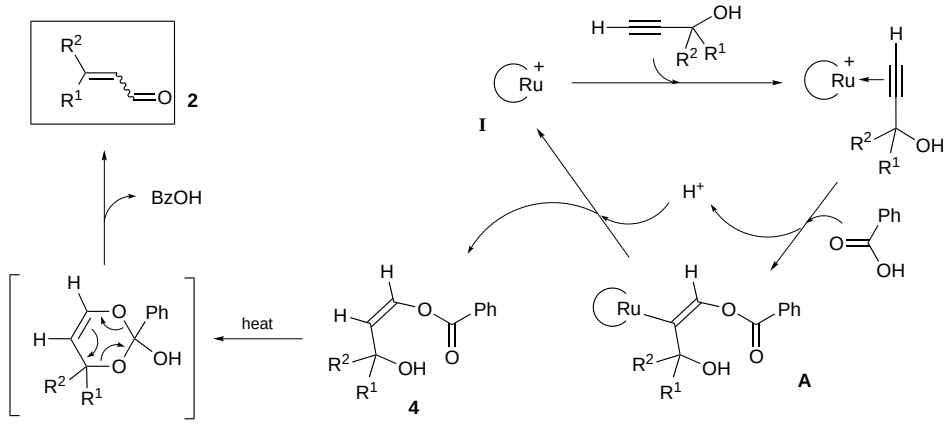


2d–e **3d–e** (3)

1e R = Me → **2e** (18%) + **3e** (50%)
1d R = H → **2d** (traces) + **3d** (65%)

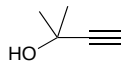
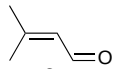
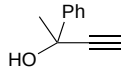
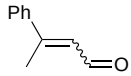
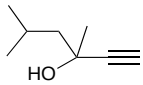
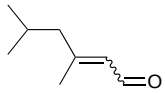
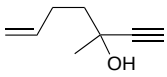
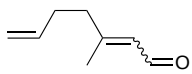
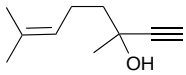
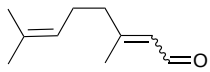
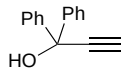
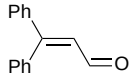
The formation of the keto esters **3** corresponds to the known catalytic addition of benzoate to the C(2) carbon of the triple bond followed by intramolecular transesterification.[12] By contrast, the mechanism of the isomerisation **1** → **2** can be proposed as depicted in Scheme 1. As the catalyst **I** is a known precursor favouring the *trans*-anti-Markovnikov addition of carboxylic acids to terminal alkynes,[13,14] the intermediate **A** corresponding to this first step is likely formed. Its protonolysis leads to the (*Z*)-3-hydroxyprop-1-en-1-yl benzoate **4** which gives the α,β-enal **2** *via* thermal elimination of benzoic acid during distillation (Scheme 1).

This process has been demonstrated in the case of **1a** with the following experiments which were monitored by ^1H NMR spectroscopy: (i) the reaction of **1a** with benzoic acid at 70 °C without a solvent in the presence of the catalyst **I** (1 mol%) gave the complete transformation of the propynol **1a** after 2 h into **2a**



Scheme 1

Table 1 Ruthenium-catalysed isomerisation of prop-2-yn-1-ols[a]

Prop-2-yn-1-ol	Enal	Yield (%) (*Z*/*E*) Method A	Method B
 **1a**	 **2a**	56[b]	68[b]
 **1b**	 **2b**	68 (2:1)	61 (2:1)
 **1c**	 **2c**	37 (3:4)	—
 **1d**	 **2d**	75 (1:2)	—
 **1e**	 **2e**	73 (1:2)	81 (2:3)
 **1f**	 **2f**	—	79[c]

[a] General conditions: prop-2-yn-1-ol (2.5 mmol), benzoic acid (2.5 mmol), catalyst **I** (1 mol%), toluene (2 ml). Method A: 70 °C, 15 h, distillation under reduced pressure. Method B; 70 °C, 2 h, then 100 °C for 3 h (**2a**), 15 h (**2e**), 22 h (**2b**) and 32 h (**2f**), distillation under reduced pressure. [b] Without solvent. [c] Chromatography over silica gel.

and **4a** (*Z*/*E* = 86 : 14) formed in 7 and 93% yields, respectively, as determined by ^{1}H NMR of the crude mixture before distillation; (ii) heating at 100 °C for 3 h of the latter crude mixture containing **2a** and **4a** led to 96% of prenal **2a** (measured by ^{1}H NMR spectroscopy) and isolated in 68% yield. These experiments show that the role of the catalyst is to generate the 3-hydroxyalk-1-en-1-yl benzoate **4a**, and that heating of the latter at 100 °C or during distillation in the presence or absence of the ruthenium derivative is the key step for the transformation of **4a** into the unsaturated aldehyde **2a**.

This sequential heating of the reaction mixture in the presence of catalyst **I**, first at 70 °C (catalytic anti-Markovnikov addition) and then at 100 °C (thermal benzoic acid elimination) appears to be the best method to selectively produce α,β-enals (method B). Thus, **1b**, **1e** and **1f** were converted into 3-hydroxyprop-1-en-1-yl benzoates **2** after treatment with benzoic acid in the presence of a catalytic amount of **I** at 70 °C for 2 h, and further heating in the same pot at 100 °C for 22, 15 and 32 h led to the complete transformation of (*Z*)-**4** and the isolation of the α,β-unsaturated aldehydes **2b**, **2e** and **2f** in 61, 81 and 79% respective yields (Table 1). The ^{1}H NMR spectroscopic monitoring revealed that only the (*Z*)-esters **4** were converted into α,β-enals **2** on heating, whereas the (*E*)-isomers remained almost unchanged except in the case of **4a**. For example, from **1b**, after 2 h at 70 °C, the catalytic reaction afforded 100% of **4b** (*Z*/*E* = 70 : 30) which led after 22 h at 100 °C to 74% of **2b** (*Z*/*E* = 66 : 34) and 26% of (*E*)-**4b**.

The selective synthesis of α,β-unsaturated aldehydes requires the initial regioselective anti-Markovnikov addition of the benzoate to the triple bond, which raises the question of whether such a key step might also be involved in the previous isomerisations of propynylic alcohols promoted by metal oxides.

Footnote

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