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Amberlyst-15® as a novel and recyclable solid acid for the coupling of aromatic aldehydes with homopropargyl alcohol

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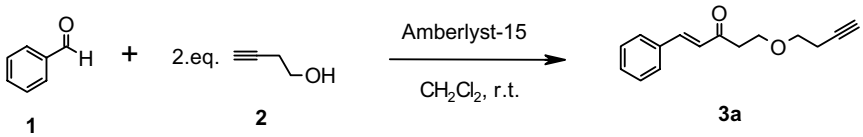
Abstract—Aldehydes undergo smooth condensation with homopropargyl alcohol in the presence of Amberlyst-15® under mild conditions to afford the corresponding β-butynyloxy enones in excellent yields with a high degree of selectivity.

The coupling of alkynes to aldehydes is an important transformation in organic synthesis.[1] Although the addition of alkynylmetal reagents to aldehydes to produce propargyl alcohols has been extensively studied,[1] the reaction between alkynes and aldehydes to generate, α,β-unsaturated ketones has received less attention.[2] Only a few methods are known in literature for the preparation of conjugated enones from alkynes and aldehydes. Lewis acids such as SbF_5, $Yb(OTf)_3$ and $In(OTf)_3$ are employed to promote this reaction.[2,3] The Prins-type cyclization of homopropargyl alcohol with aldehydes has recently been reported using anhydrous $FeCl_3$ to produce 2-alkyl-4-halo-5,6-dihydro-2*H*-pyrans.[4] Other reagents such as $VO(OSiPh_3)_3$ and $InCl_3$ have been used in the coupling of allenyl carbinols with aldehydes to generate β-hydroxy enones.[5,6] However, there have been no reports on the condensation of homopropargyl alcohols with aldehydes to produce conjugated enones using solid acid catalysis.

In this letter, we report a novel and efficient protocol for the synthesis of β-butynyloxy enones from the 2:1 coupling of a homopropargyl alcohol and aldehydes using Amberlyst-15® as an inexpensive and recyclable heterogeneous solid acid catalyst. To the best of our knowledge, this is the first report on the coupling of a homopropargyl alcohol with aldehydes using a Brønsted acid. Initially, we attempted the coupling of benzaldehyde **1** with 3-butyn-1-ol **2** in the presence of an acid resin. The reaction went to completion within 2.5 h and the product, 5-(3-butynyloxy)-1-phenyl-(*E*)-1-penten-3-one **3a** was obtained in 86% yield (Scheme 1).[7]

Encouraged by the results obtained with benzaldehyde and 3-butyn-1-ol, we turned our attention to substituted aldehydes. Interestingly, a large number of substituted benzaldehydes such as the *p*-methyl-, 3,4-dichloro-, *p*-fluoro-, *p*-chloro-, *o*-ethoxy-, *m*-nitro-, 3,4-dimethoxy-, *m*-phenoxy-, and 3,4,5-trimethoxy-derivatives reacted efficiently with 3-butyn-1-ol under similar conditions to afford a wide range of conjugated enones (entries b–k, Table 1). This method is equally effective for both electron-rich as well as electron-deficient aromatic aldehydes. Sterically hindered 2-naphthaldehyde also gave the corresponding enone in 85% yield (entry l, Table 1). In all cases, the reactions proceeded efficiently in high



Scheme 1.

Keywords: Ion-exchange resin; Aldehydes; β-Alkoxy conjugated enones.
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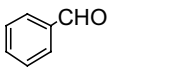
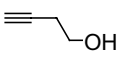
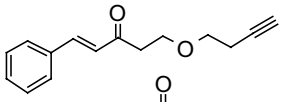
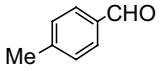
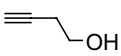
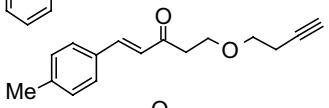
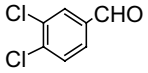
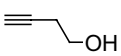
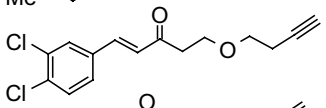
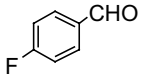
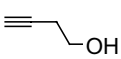
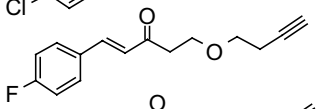
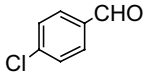
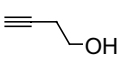
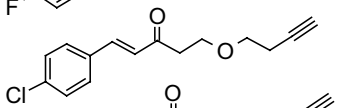
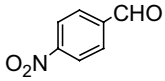
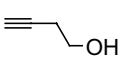
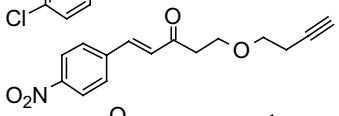
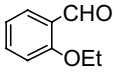
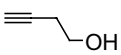
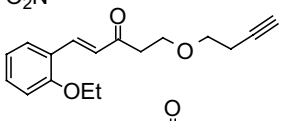
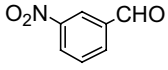
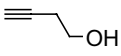
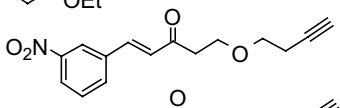
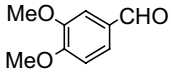
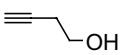
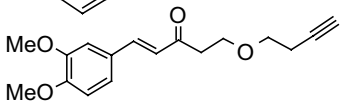
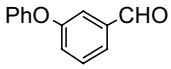
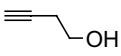
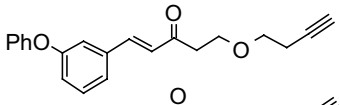
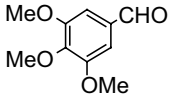
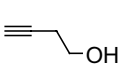
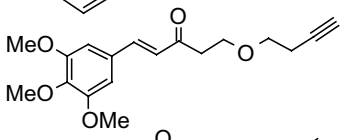
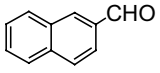
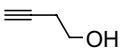
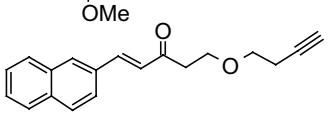
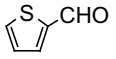
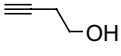
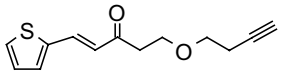
Table 1. Synthesis of α,β-unsaturated ketones from aldehydes and homopropargyl alcohol

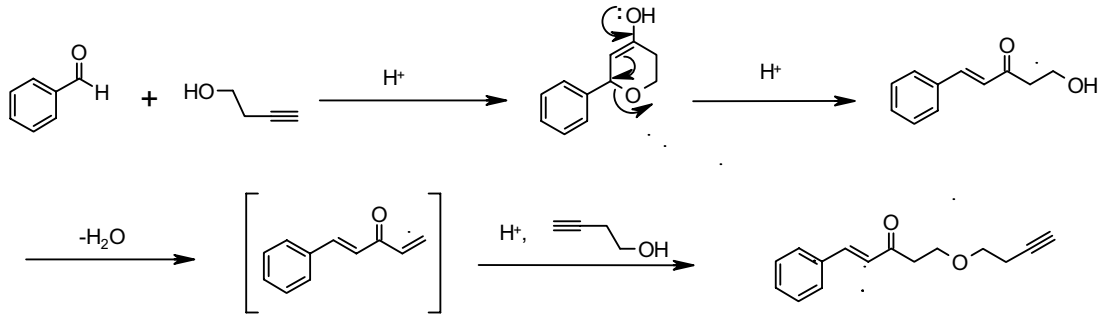
Entry	Aldehyde **1**	Homoallyl alcohol	Product 3[a]	Time (h)	Yield (%)[b]
a				3.0	86
b				2.5	82
c				3.5	90
d				4.0	81
e				3.5	87
f				3.0	85
g				5.0	79
h				3.5	82
i				4.5	75
j				4.0	80
k				5.0	72
l				3.0	85
m				4.0	78

[a]All products were characterized by ^{1}H NMR, IR and mass spectroscopy.
[b]Isolated and unoptimized yields.

yields at ambient temperature under mild conditions. In the absence of an acid resin, no reaction was observed between the aldehydes and homopropargyl alcohol. Furthermore, low conversions (20–35%) were obtained when other solid acid catalysts such as montmorillonite KSF, heteropoly acid $H_3PW_{12}O_{40}$ and H-ZSM were employed. In addition, Lewis acids such as $Sc(OTf)_3$, $Bi(OTf)_3$ and $In(OTf)_3$ were also found to be ineffective for this conversion. Among these reagents, Amberlyst-15® was found to be the most effective in terms of conversion. Other hydroxy alkynes such as propargyl alcohol and 3-octyn-1-ol failed to produce the conjugated enones under the reaction conditions. Similarly, hydroxy protected homopropargyl alcohol also failed to give the desired product. The reaction was successful only with simple homopropargyl alcohol and aromatic aldehydes. The catalyst could be easily separated by simple filtration and the recovered acid resin was reused in subsequent reactions with only gradual decrease in activity. For example, benzaldehyde and homopropargyl alcohol gave 85%, 82%, 76% and 71% yields over four cycles. A possible reaction mechanism is shown in Scheme 2.

The scope and generality of this process is illustrated with respect to various aldehydes and the results are presented in Table 1.

In summary, we have developed a novel and efficient approach for the preparation of β-butynyloxy enones through the 2:1 coupling of homopropargyl alcohol and aldehydes using Amberlyst-15® as a heterogeneous



Scheme 2.

solid acid. The use of an inexpensive and recyclable acid resin makes this method simple, convenient and economically viable.

Acknowledgements

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References and notes

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7. *Experimental procedure*: A mixture of the aldehyde (1 mmol), homopropargyl alcohol (2.2 mmol) and Amberlyst-15® (0.75 g) in dichloromethane (10 mL) was stirred at room temperature for the appropriate time (Table 1). After completion of the reaction, as indicated by TLC, the reaction mixture was filtered and washed with dichloromethane (2×10 mL). The combined organic extracts were concentrated in vacuo and the resulting product was directly charged on a small silica gel column and eluted with a mixture of ethyl acetate/*n*-hexane (1:9) to afford the pure enone. Spectral data for selected products: Compound **3a**: 5-(3-butynyloxy)-1-phenyl-(*E*)-1-penten-3-one: Liquid, IR (KBr): *v* 3017, 2925, 2856, 1691, 1662, 1608, 1451, 1216, 1112, 976, 757 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.90 (m, 1H), 2.40–2.50 (m, 2H), 2.90 (t, $J = 6.9$ Hz, 2H), 3.60 (t, $J = 7.0$ Hz, 2H), 3.80 (t, $J = 7.0$ Hz, 2H), 6.70 (d, $J = 16.7$ Hz, 1H), 7.30–7.40 (m, 3H), 7.50–7.60 (m, 3H). FABMS: *m/z*: 228 [M^+], 189, 145, 137, 131, 109, 97, 83, 69, 53. Compound **3d**: 5-(3-butynyloxy)-1-(4-fluorophenyl)-(*E*)-1-penten-3-one: liquid, IR (KBr): *v* 3019, 2921, 2856, 1685, 1655, 1598, 1508, 1219, 1109, 772 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.87 (m, 1H), 2.36–2.50 (m, 2H), 2.89 (t, $J = 7.0$ Hz, 2H), 3.55 (t, $J = 7.0$ Hz, 2H), 3.80 (t, $J = 7.0$ Hz, 2H), 6.65 (d, $J = 16.8$ Hz, 1H), 7.05–7.15 (m, 2H), 7.45–7.60 (m, 3H). FABMS: *m/z*: 246 [M^+], 177, 149, 137, 109, 97, 83, 69, 53. Compound **3h**: 5-(3-butynyloxy)-1-(3-nitrophenyl)-(*E*)-1-penten-3-one: liquid, IR (KBr): *v* 3020, 2927, 2857, 1698, 1668, 1608, 1527, 1347, 1216, 1112, 972, 757 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.91 (m, 1H), 2.38–2.50 (m, 2H), 2.99 (t, $J = 7.0$ Hz, 2H), 3.60 (t, $J = 7.0$ Hz, 2H), 3.85 (t, $J = 7.0$ Hz, 2H), 6.60 (d, $J = 16.9$ Hz, 1H), 7.55–7.65 (m, 3H), 8.05 (d, $J = 16.9$ Hz, 1H), 8.10 (d, $J = 8.1$ Hz, 1H). FABMS: *m/z*: 274 [$M+H^+$], 189, 145, 109, 97, 83, 69, 53.