Experimental

Solvents were HPLC grade and were purified on an MBraun solvent purification system. Ethyl-2-butynoate and n-tributylphosphine were obtained from Sigma-Aldrich and were used without further purification. Anhydrous ethyl alcohol was HPLC grade and was obtained from Commercial Alcohols (Brampton, ON) and used without further purification. All mass spectra were collected on a Micromass Q-ToF micro mass spectrometer in positive mode, using electrospray ionization: capillary voltage, 2900 V; extraction voltage, 0.5 V; source temperature, 70°C; desolvation temperature, 140°C; cone gas flow, 100 L/h; desolvation gas flow, 100 L/h; collision voltage, 2 V for MS experiments and 2-45 V for MS/MS experiments; MCP voltage, 2700 V.

PSI-ESI-MS procedure: Ethyl-2-butynoate, (0.292 mL, 2.50 mmol) and ethanol, (0.730 mL, 12.5 mmol) were added to 5.0 mL of acetonitrile in a Schlenk flask equipped with a stir bar and a septum. PEEK tubing was then inserted into the reaction mixture solution, with the other end of the tubing connected to a T-junction. A syringe pump set at 15 μL/minute pumped acetonitrile through the PEEK tubing to the T-junction where a third piece of tubing, connected to the mass spectrometer, took both solutions into the source. Argon gas was applied to the Schlenk flask at 3 psi and the extra pressure pushed the reaction solution through the tubing to the spectrometer. Spectra were recorded once per second. The catalyst, tri-n-butylphosphine (0.063 mL, 0.25 mmol) was injected by syringe through the septum into the reaction mixture to initiate the reaction.

1H and 31P NMR were conducted in CD$_3$CN. All reagents except ethanol were obtained from Sigma Aldrich and used without further purification. Ethanol was obtained from Commercial Alcohols. Diphenylacetylene (0.0073 g, 0.041 mmol) was used as an internal standard for 1H NMR and was dissolved in CD$_3$CN (500 μL), then added by syringe to an NMR tube equipped with a rubber NMR septum. Ethyl-2-butynoate (0.41 mmol, 47 μL), and anhydrous ethanol (2.05 mmol, 120 μL) were measured by syringe and injected. The solution was sparged with nitrogen. $^8$Bu$_3$P (0.041 mmol, 10 μL) was added to a small flask capped with a septum which previously had been sparged with nitrogen. 285 μL of CD$_3$CN was added to the flask containing $^8$Bu$_3$P. The solution of butynoate and ethanol was placed in the magnet and a spectrum was obtained before the catalyst was added. Spectra were obtained on a 500 MHz Bruker magnet, with spectra collected every 7 minutes for the first hour, with 30 minute wait times between 7 minute scans afterwards, over a total of 4 hours. A 30 degree pulse program was used with a D1 delay time of 20 seconds for 1H NMR, since the T1 relaxation for all species was experimentally determined to be 9.4 seconds, and a D1 of 90 s for 31P as the T1 was experimentally determined to be 13 s. No wait times were used for 31P NMR. This precaution decreased line broadening and gave better shimming results.

1H NMR: Before the addition of catalyst: $\delta$ 7.53-7.37 (10 H, dm), 4.14 (2H, q), 3.54 (2H, q), 3.44 (1H, br s), 1.96 (3H, s), 1.23 (3H, t), 1.11 (3H, t). After addition of catalyst: $\delta$ 7.54-7.38 (10H, dm), 4.99 (1H, s), 4.14 (2H, q), 4.14 (2H, q), 4.06 (2H, q), 3.92 (2H, q), 3.88 (2H, q), 3.82 (2H, q), 3.54 (2H, q), 3.20 (1H, br s), 2.22 (3H, s), 1.96 (3H, s), 1.27 (3H, s), 1.23 (3H, t), 1.23 (3H, t), 1.23 (3H, t), 0.8- 0.9 (m). 31P NMR experiments were conducted in an NMR tube using the same reagents and concentrations that were used for 1H NMR. Spectra were obtained at
202 MHz in CD$_3$CN, and collected every 28 minutes with no wait times between over 4.5 hours. A 30 degree pulse program was used with a delay time of 65 seconds. The T1 relaxation for all species was experimentally determined to be 13 seconds. $^{31}$P NMR: $\delta$ 58.41, 58.30, 50.40, 44.97, 44.18, 43.28, 37.63, 37.00, 36.84, 35.98, 32.91, 31.62, 30.32, 28.13, 27.96, 22.11.

Numerical modelling was accomplished using COPASI 4.11 (Build 64) freeware, using a biochemical time course with a Deterministic (LSODA) method.

(S1). Spectra shows starting alkyne 4.14 (2H, q) (depicted as 1 in the stacked plot below), 1.96 (3H, s), 1.23 (3H, t), and EtOH (3.54 (2H, q), 3.44 (1H, br s), 1.11 (3H, t) before the addition of catalyst. Diphenylacetylene $\delta$ 7.53-7.37 (10 H, dm), was used as an internal standard. The integration of the peaks at 4.14 and 3.82 ppm were used to generate the traces seen in Figure 1.
(S2). 7 minutes after catalyst addition (2 in stacked plot).
(S3). 14 minutes after catalyst addition (3 in stacked plot).
(S4). 61 minutes after catalyst addition (4 in stacked plot).
(S5). 34 minutes after catalyst addition (5 in stacked plot).
(S6). 244 minutes after catalyst addition (6 in stacked plot).
(S7). Stacked plots detailing the disappearance of the methylene protons on the starting alkyne (2H, q 4.14 ppm, spectrum 1) and the appearance of the methylene protons on the product ester (2H, q, 4.06 ppm) and ether (2H, q, 3.82 ppm). Oligomer ester methylene protons appear in the first 7 minutes (spectrum 2) and gradually disappear by 4 hours (spectrum 6).
(S8). $^1$H NMR evidence for existence of oligomers. There are many peaks that arise between 4.25 - 4.10 ppm in low concentration, which have chemical shifts corresponding to the methylene protons in the esters of the oligomers. The pair of quartets at 3.93 and 3.89 ppm grow in quickly at the start and then diminish over the 4 hours as seen in the $^{31}$P NMR and in the MS results. By the time the catalyst is displaced by the alkoxide, solids are forming and drop out of solution, and are no longer detectable by NMR.
(S9). $^{31}$P NMR spectrum, 28 minutes after catalyst added (spectrum 1 in the stacked plot below).
(S10). 56 minutes after catalyst added (2 in stacked spectra)
(S11). 84 minutes after catalyst added (3 in stacked spectra)
(S12). 112 minutes after catalyst added (4 in stacked spectra)
(S13). 140 minutes after catalyst added (5 in stacked spectra)
252 minutes after catalyst added (6 in stacked spectra)
(S15). Stacked plots detailing the changing peak heights of phosphonium species over 4 hours, starting at 28 minutes after the addition of catalyst (spectrum 1) to 4 hours after (spectrum 6). The peak heights were used to generate the $^{31}$P traces of the phosphonium species observed in Figure 3.
(S16). MS combined spectra, first minute after catalyst was added to alkyne, ethanol and solvent mixture.

(S17). MS combined spectra over 3 minutes, 20 minutes after catalyst addition.
(S18). MS combined spectra over 3 minutes, 140 minutes after catalyst addition. EtOH aggregates (m/z 585, 697) are also visible. Collision induced dissociation (CID) of 15 volts caused fragmentation to a loss of 46 Da.
(S19). Expanded model with higher mass oligomers included. Rate constants generated by Copasi Build 64 (4.11) software numerical modelling. Forward constants are in green, reverse constants are in red.
(S20). Optimized parameter estimated traces generated by Copasi (thin lines), compared with experimental 1H NMR data for SM + P (left, crosses) and oligomer MS data (right, thick lines with estimated parameter traces as thin lines).

(S21). Rate constants generated by Copasi using parameter estimation for the starting alkyne/product and oligomer traces.
Effect of a sterically hindered alcohol on product yield

When the sterically hindered neopentyl alcohol is used instead of ethanol, there is a dramatically lower concentration of off-cycle oligomers compared to the on-cycle species observed. This time the main product competitor was from an esterification-type reaction in which the ethoxide from the ester in the starting material could be replaced by the neopentyloxyde generated upon deprotonation of the neopentyl alcohol. This mirrored-cycle competition outpaced the formation of oligomeric species that were observed with EtOH. This confirmed the findings made by Natasha O’Rourke when the same hindered alcohol was used. Throughout the reaction, charged species are observed, separated by 42 amu, which is the mass difference between ethoxide and neopentyloxyde. A list of reacting species, products, intermediates and bi-products is contained in Table S1.
Table S1. Table of starting materials, products, intermediates and bi-products for the reaction with neopentyl alcohol.

<table>
<thead>
<tr>
<th>Species #</th>
<th>Species</th>
<th>m/z</th>
<th>Species #</th>
<th>Species</th>
<th>m/z</th>
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<tr>
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<td></td>
<td>23A</td>
<td>Bu₃⁻O⁻Onp</td>
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</tr>
</tbody>
</table>

According to the data, as illustrated in figure S22, the formation of 6 and 6A occurs nearly simultaneously meaning that the alkoxide switch likely occurred prior to that step. 19 is the next species to be detected, (analogous to 8 from the previous EtOH reaction) and it is the next
species in the same catalytic cycle. 13 again is formed in the same time frame as for the reaction with EtOH, but the concentration increases much more slowly, and stays low over 30 minutes, which was not seen with the unhindered EtOH. Since 13 stays low, the concentration of 6 does not drop to nearly zero until after 25 minutes, where it took 10 minutes to completely deplete in the EtOH reaction. This confirms that the bulkier neopentyl alcohol hinders the formation of the off-cycle oligomers and explains why the % yield of the bulkier product was close to 99%, seen by O’Rourke compared to 30% with EtOH. 6A and subsequently 19A, in the competing cycle, are present at – 10% of the intensity of 6 and 19, which indicates that the formation of 20A is disfavored, as is the formation of the 13A off-cycle oligomer.

The more hindered alcohol does not slow down either the protonation step (3 → 6) or the conjugate addition step (6 → 19) since there is also an immediate and large jump in intensity upon catalyst addition, as was seen with ethanol. 6, 6A and 19 appear to behave with pseudo-first order kinetics, but due to the low concentration of the other species it is more challenging to make that claim. No triple addition oligomer (14) was detected, which indicates that the more hindered alcohol disfavors the formation of oligomers through off-cycle reactions, and the concentrations of on-cycle species remains higher leading to greater product formation. Since 19 and 19A drop off quickly and are present in low intensity, this indicates that the formation of product in the next step is fast, likely the same rate as with ethanol. However, the much lower concentrations of 6A and 19A indicate that the hindered alcohol forestalls the formation of 20A.
(S22). Smoothed MS data for the reaction of ethyl-2-butynoate (0.4 M) with neopentyl alcohol (2.4 M) and PBu$_3$ catalyst (0.04M), and close-up (inset).

The mass spec data suggests a greatly condensed mechanism similar to that which was deduced for the EtOH reaction. The main differences lie in the reduction of off-cycle oligomers and the in the competing cycle due to the presence of 2 different alkoxides, S23.
(S23). Suggested mechanism accounting for the exchange of the two alkoxides present in solution and the formation of the phosphonium intermediates detected by PSI-ESI-MS.