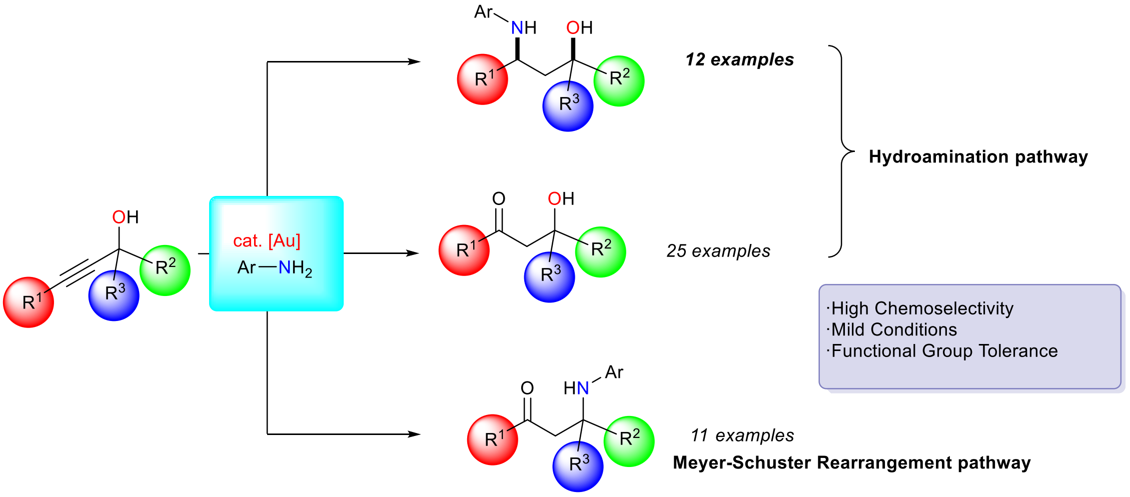
Gold-Catalyzed Hydroamination of Propargylic Alcohols: Controlling Divergent Catalytic Reaction Pathways to Access 1,3-Aminoalcohols, 3-Hydroxyketones or 3-Aminoketones.

Victor Laserna, Michael J. Porter and Tom D. Sheppard*

**Department of Chemistry, University College London, Christopher Ingold Laboratories, 20 Gordon Street, London, WC1H 0AJ, UK*

tom.sheppard@ucl.ac.uk

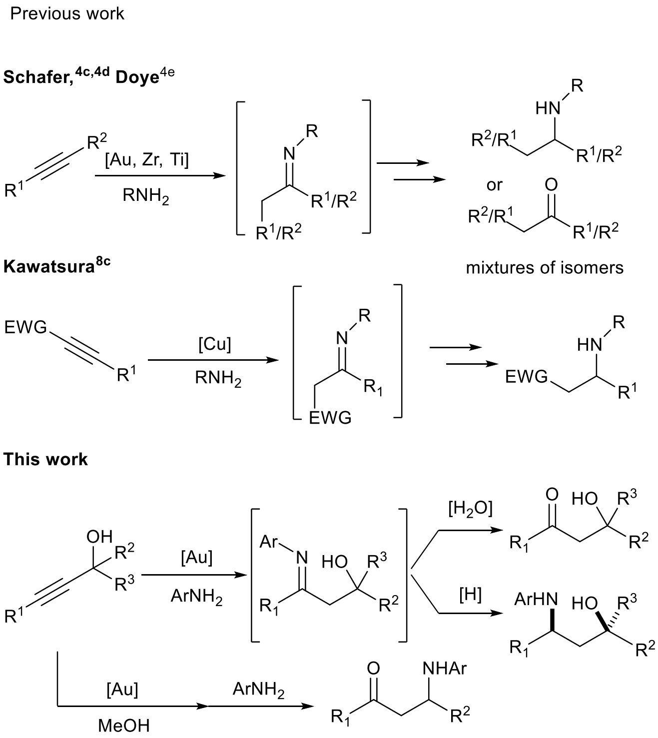


A versatile approach to the valorization of propargylic alcohols is reported, enabling controlled access to three different products from the same starting materials. Firstly, a general method for the hydroamination of propargylic alcohols with anilines is described using gold catalysis to give 3-hydroxyimines with complete regioselectivity. These 3-hydroxyimines can be reduced to give 1,3-aminoalcohols with high *syn* selectivity. Alternatively, by using a catalytic quantity of aniline, 3-hydroxyketones can be obtained in high yield directly from propargylic alcohols. Further manipulation of the reaction conditions enables the selective formation of 3-aminoketones via a rearrangement/hydroamination pathway. The utility of the new chemistry was exemplified by the one-pot synthesis of a selection of *N*-arylpyrrolidines and *N*-arylpiperidines. A mechanism for the hydroamination has been proposed on the basis of experimental studies and DFT calculations.

Introduction

Nitrogen atoms play a key role in many biologically active compounds including natural products and pharmaceuticals, and this has encouraged the development of new synthetic strategies to construct C-N bonds.[1] Hydroamination of alkenes or alkynes is an atom economical and direct method to generate C-N bonds which has attracted considerable interest.[2] Although alkenes yield amines directly, the transformation has often proved challenging. In contrast, the hydroamination of alkynes can be mediated by a range of catalysts based on elements from across the periodic table.[2a,3] This offers an alternative strategy, yielding imines or enamines which can be further transformed through sequential reactions to access useful products.[4] Two key limitations of the hydroamination of alkynes are the low reactivity of internal alkynes and the poor regioselectivity usually observed with these substrates in intermolecular reactions (Scheme 1).[5] Catalyst design has allowed improved regiocontrol for hydroamination of terminal alkynes, with late transition-metal catalysts usually affording Markovnikov products,[6] whereas early transition-metal catalysts predominantly afford anti-Markovnikov products.[3b,7] Internal alkyne hydroamination selectivity has proved to be more challenging, with reactions usually giving mixtures of isomers.[5] A rare exception is the hydroamination of alkynes bearing strongly electron-withdrawing groups,[8] which give high regioselectivities favoring amine attack on the more electron deficient atom of the π-system. The intermolecular hydroamination of internal alkynes using gold catalysts has been challenging, requiring elevated temperatures and yielding mixtures of isomeric products.[5b,6a]

Scheme 1: Hydroamination of Alkynes

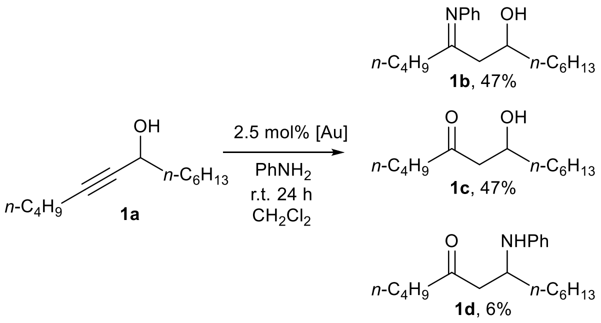


To date, the intermolecular hydroamination of propargylic alcohols to yield 3-hydroxyimines has not been reported, despite the potential utility of the products. The hydroamination of O-protected propargyl alcohol to give hydroxyacetone hydrazone derivatives has been described,[9a] as well as the synthesis of benzodiazepines[9b] or quinolines[9c] via reaction of propargylic alcohols with nitrogen nucleophiles. In this paper, we describe a highly regioselective method for the hydroamination of propargylic alcohols under mild conditions, which can be controlled to provide three different products by varying the reaction conditions. This provides an unusual example of divergent catalysis[10] which employs the same reactant and catalyst to access different products with high levels of selectivity.

Results and Discussion

Propargylic alcohols are readily available alkynes with an adjacent alcohol group which are versatile building blocks due to their diverse reactivity.[11] Through a wide array of different catalytic transformations, using transition metals[12] or organocatalysis,[13] important synthetic targets can be accessed including enones,[14] furans,[15] carbonates,[16] N-heterocycles[17] or geminal dihalides.[18] In a preliminary screen of conditions for hydroamination, we observed that reaction of propargylic alcohol **1a**, aniline and 2 mol% of PPh_3AuNTf_2[19] catalyst at room temperature in CH_2Cl_2 led to complete conversion of starting material within 24 h (Scheme 2), with the formation of three products: 3-hydroxyimine **1b**, 3-hydroxyketone **1c** and 3-aminoketone **1d** in a ratio of 47:47:6 (**1b**:**1c**:**1d**).[‡] No traces of the regioisomeric products (α-hydroxyimine, α-hydroxyketone) resulting from an addition of the aniline to the proximal carbon of the propargylic alcohol were detected. We then decided to explore the reaction conditions to determine if it was possible to selectively obtain each of the three products.

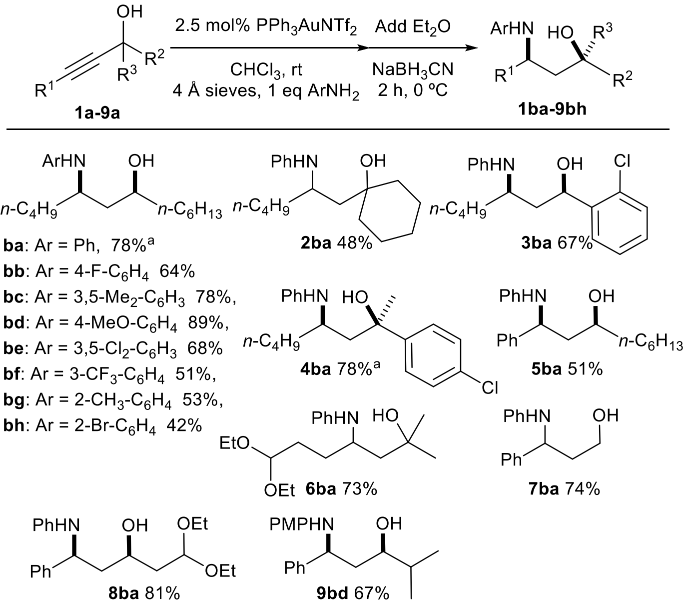
Scheme 2 Initial Discovery of the Hydroamination Reaction



Synthesis of 1,3-Aminoalcohols

During the optimization process (Supporting information), we identified conditions to selectively generate the 3-hydroxyimine **1b** by performing the reaction in chloroform in the presence of molecular sieves. In order to trap the imine intermediate, we carried out a sequential reduction by adding Et_2O and 2 eq of $NaCNBH_3$ at 0 °C. As anticipated, we found that the reduction took place in a stereoselective manner yielding the *syn*-1,3-aminoalcohol in high yield and with excellent selectivity.[20]

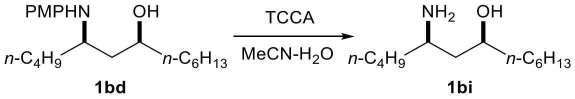
Scheme 3: Synthesis of *syn*-1,3-aminoalcohols via one-pot hydroamination/reduction of propargylic alcohols.



Reactions performed on a 0.5 mmol scale; Yields given are isolated yields of the *syn* diastereoisomer (stereochemistry shown in reaction assumes R^3 is smaller than R^2); (PMP = p-methoxyphenyl); [a]The relative stereochemistry was confirmed by conversion to the corresponding cyclic urethane and analysis of the NOESY spectra (Supporting Information).

We examined a series of different anilines to explore the functional group tolerance of the method (Scheme 3).‡ The reaction tolerates a variety of substitution patterns on the aniline, with groups at the *ortho* (**1bg** and **1bh**), *meta* (**1bc**, **1be** and **1bf**) or *para* (**1bb** and **1bd**) position, with slightly lower yields observed in the first case probably due to steric hindrance. Electron withdrawing groups (**1bb**, **1be**, **1bf** and **1bh**) and electron donating groups (**1bc**, **1bd** and **1bg**) are well tolerated. No hydroamination was observed with alkylamines, presumably because they cause greater deactivation of the cationic gold catalyst.[21] A range of substrates including primary (**7ba**), secondary (**3ba**, **5ba**, **8ba**, **9bd**), tertiary (**2ba**, **4ba**, **6ba**) and benzylic (**3ba**, **4ba**) propargylic alcohols can be transformed into the corresponding amino alcohols effectively. Terminal alkynes did not undergo hydroamination when subjected to the reaction conditions, and only unreacted starting material was observed with these substrates. We were also able to access a primary aminoalcohol **1bi** by oxidative deprotection of *p*-methoxyphenylamine **1bd** using trichloroisocyanuric acid (Scheme 4).[22]

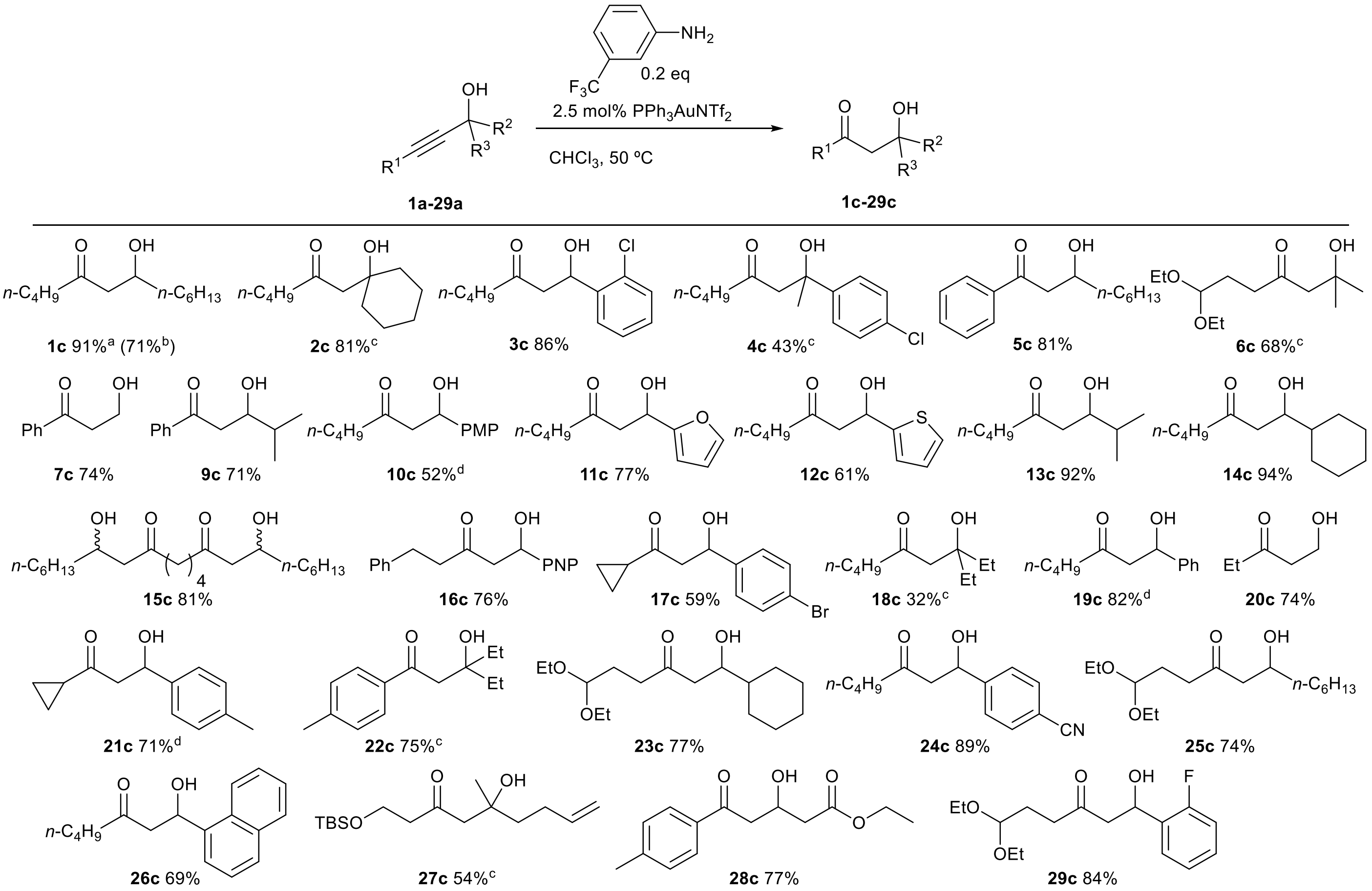
Scheme 4: Synthesis of a primary aminoalcohol via deprotection of a *p*-methoxyphenylamine (PMP = *p*-methoxyphenyl; TCCA = trichloroisocyanuric acid).



Synthesis of 3-Hydroxyketones

During the optimization of the hydroamination reaction we observed that raising the temperature and performing the reaction in non-dried solvents under air favoured the hydrolysis of the imine to yield the 3-hydroxyketone. We hypothesized that *in situ* imine hydrolysis would liberate the aniline, allowing it to participate in further hydroamination reactions. It should therefore be possible to achieve the reaction with a substoichiometric quantity of amine. After examining a small selection of anilines in combination with the gold catalyst (Supporting information), 3-trifluoromethylaniline was identified as a suitable co-catalyst to promote formation of the 3-hydroxyketone. The proposed hydroamination/imine hydrolysis pathway is supported by the fact that in the absence of aniline, Meyer-Schuster rearrangement of the propargylic alcohol is predominant and only small quantities of 3-hydroxyketone are formed.[14a, 23] With these conditions in hand we explored the scope of the hydroamination/hydrolysis reaction for preparing 3-hydroxyketones (Scheme 5). The reaction tolerates a range of substituents on the propargylic alcohol, including carbocycles (**2c**, **14c**, **17c** and **23c**) and branched chains (**9c**, **13c**), and is compatible with primary (**7c** and **20c**), secondary (**1c**, **3c**, **5c**, **9c**-**17c**, **19c**, **21c**, **23c**-**26c**, **28c**, **29c**), tertiary (**2c**, **4c**, **6c**, **18c**, **22c** and **27c**) and benzylic (**3c**, **4c**, **9c**, **11c**, **12c**, **17c**, **21c**, **24c** and **26c**) propargylic alcohols, even though the latter products are often prone to elimination of water to give the corresponding enones.[23] Electron withdrawing (cyano: **24c**, nitro: **16c**, halide: **3c**/**17c**) or electron donating (methoxy: **10c**, methyl: **21c**) substituents could be present on the benzene rings, and alternative aromatic systems such as furan (**11c**), naphthalene (**26c**) or thiophene (**12c**) were also tolerated, as were alkenes (**27c**), protected alcohols (**27c**), esters (**28c**) and acetals (**6c**, **23c**, **25c** and **29c**).

Scheme 5 Synthesis of 3-hydroxyketones via catalytic hydroamination of propargylic alcohols with in situ imine hydrolysis.



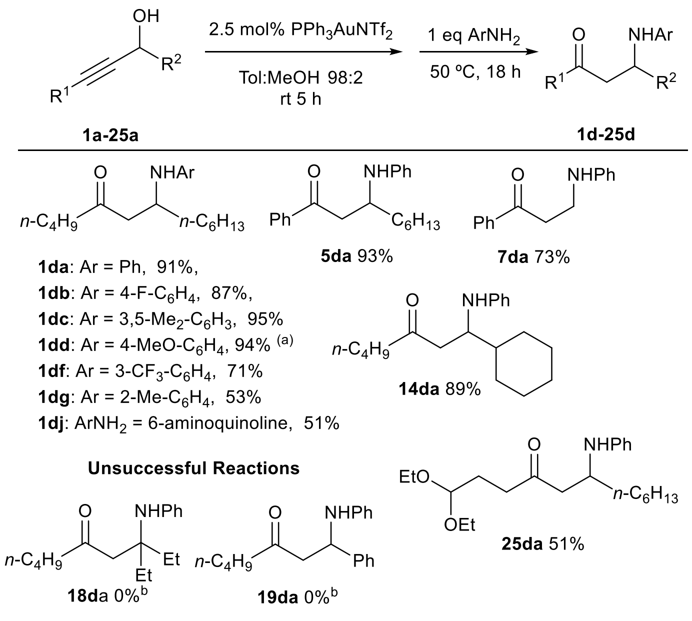
Reactions performed on a 0.5 mmol scale; Undried solvents were used for these reactions; (PMP = *p*-methoxyphenyl; PNP = *p*-nitrophenyl). [a]In other solvents, the yields of **1c** obtained were as follows: MeCN (88%), PhF (86%), $MeOCO_2Me$ (85%), PhMe (88%), EtOAc (82%); [b] 5 mmol scale reaction; [c]0.5 eq of aniline used; [d]Reaction carried out at room temperature for 40 h.

The broad scope of this method for the synthesis of 3-hydroxyketones makes it a useful alternative approach to traditional approaches such as aldol reactions.[24] As chlorinated solvents are often undesirable from an environmental perspective, we examined the reaction in alternative solvents.[25] Pleasingly, the hydroamination/hydrolysis reaction could also be performed efficiently in acetonitrile, fluorobenzene, dimethyl carbonate, toluene or ethyl acetate.

Synthesis of 3-Aminoketones

Finally, we also sought to develop conditions to access the 3-aminoketone **1d**, which was identified as a minor product in our original experiment (Scheme 2). We hypothesized that its formation was due to Meyer-Schuster rearrangement of the propargylic alcohol,[14] followed by conjugate addition of the aniline to the resulting enone. To selectively form the 3-aminoketone, we changed the solvent to a mixture of toluene:MeOH (100:1) which is established to promote gold-catalyzed Meyer-Schuster rearrangement,[14] and then added the aniline to the reaction mixture once the enone had been produced (Scheme 6). Interestingly, the gold catalyst is involved in both steps of the reaction, as it was observed to catalyze conjugate addition of the aniline to the enone (Supplementary information), with a particularly significant effect in the case of less nucleophilic anilines. Whilst the addition of anilines to electron-deficient alkenes can be mediated by a variety of catalysts,[26] this gold-catalysed variant appears to be complementary in scope as previous reports have not included internal enones as substrates.[26]

Scheme 6: Synthesis of 3-aminoketones via Au-catalyzed Meyer-Schuster rearrangement and enone hydroamination.



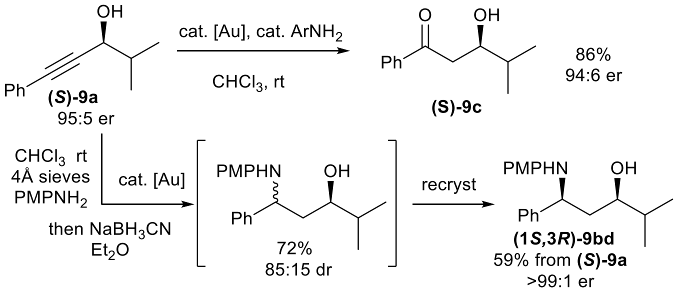
Reactions performed on a 0.5 mmol scale; (a) Reaction was filtered through a silica pad after enone formation; (b) The corresponding enone was obtained as the sole product.

Again, we examined the reaction with a series of different aryl amines on substrate **1a**, and explored the functional group tolerance with respect to the propargylic alcohol component using aniline as the nucleophile (Scheme 6). Although the reaction proved to be tolerant of both electron-deficient and electron-rich anilines (**1da**-**1dj**), only primary (**7da**) and secondary (**5da**, **14da**, **25da**) propargylic alcohols were suitable substrates. While tertiary and benzylic alcohols underwent the Meyer-Schuster rearrangement, no conjugate addition to the resulting enone to give **18da** or **19da** was observed.

Reaction Mechanisms

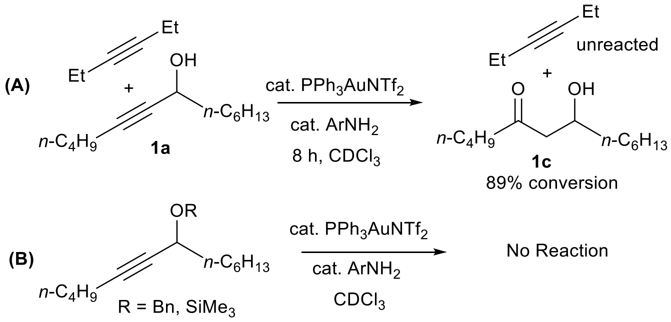
Several gold-catalysed reactions of allylic alcohols with nucleophiles have been reported which proceed via a mechanism in which addition of the nucleophile is concerted with elimination of the adjacent hydroxyl group.[27] In order to exclude the possibility that the hydroamination of propargylic alcohols proceeds in a similar fashion via a planar achiral intermediate (e.g. via Meyer-Schuster rearrangement), we examined the reaction of enantioenriched alcohol **(*S*)-9a**.[28] Pleasingly, alcohol **(*S*)-9a** could be converted into hydroxyketone **(*S*)-9c** in excellent yield and with no significant loss in enantiopurity (Scheme 7). Similarly, hydroamination followed by imine reduction gave the corresponding aminoalcohol in 72% yield as an 85:15 mixture of diastereomers. We were unable to directly determine the enantiopurity of the diastereomeric product mixture by HPLC, so recrystallisation was carried out, affording the aminoalcohol **(1*S*,3*R*)-9bd** as an essentially enantiopure single diastereomer in 59% overall yield (Scheme 7). As analysis of the crude mixture had indicated that only 61% of this diastereomer was present (i.e. 0.85 × 72), it could be concluded that the hydroamination reaction and reduction had taken place without any significant erosion of enantiomeric purity.

Scheme 7: Synthesis of enantioenriched products via hydroamination of an enantioenriched propargylic alcohol.



The alcohol moiety in the propargylic alcohol appears to play an important role in accelerating the hydroamination reaction (Scheme 8), as a competition experiment between propargylic alcohol **1a** and hex-3-yne illustrates **(A)**. Protection of the propargylic alcohol as a benzyl or trimethylsilyl ether appears to stop the hydroamination reaction **(B)**.

Scheme 8: Experiments to probe the relative reactivity of propargylic alcohols in the hydroamination reaction in comparison to other alkyne derivatives.

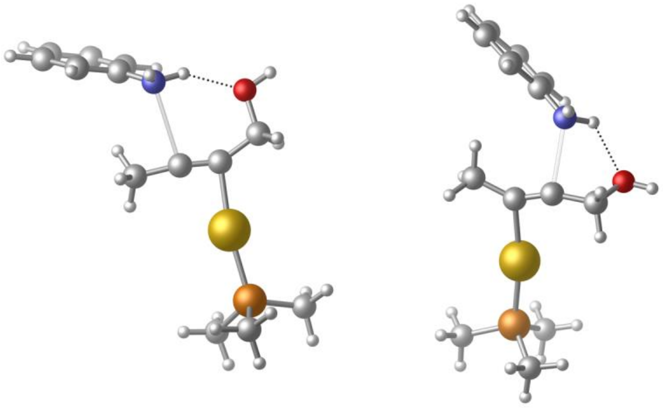


In order to investigate the reaction mechanism further, DFT calculations were carried out. Several computational studies into both inter-[29] and intramolecular[30] hydroamination reactions catalysed by mononuclear gold complexes have been reported previously; we chose to employ the benchmarked method of Ciancaleoni et al.[29c] in which single-point energies are calculated using the hybrid B2PLYP functional[31] on geometries optimized using the GGA functional BP86,[32] with the def2-TZVPP basis set[33] being used throughout. Solution-phase energies were obtained using the SMD solvation model[34] with gas-phase optimized geometries. All calculations were carried out using Gaussian 09.[35]

Initial modelling of but-2-yn-1-ol complexed to an $[\mathrm{Au\text{-}PMe_3}]^+$ fragment indicated that the gold-alkyne complex was slightly lower in energy than a structure with the gold linked to the alcohol oxygen. Transition states were then modelled for addition of aniline to each carbon of the triple bond in this adduct. The transition state for addition to the distal carbon (Figure 1), as observed experimentally, lay only 9.9 kJ mol^{-1} higher in energy than the isolated starting materials, with a hydrogen bond between the aniline N-H and the alcohol oxygen. Conversely, the transition state for addition to the proximal carbon was markedly higher in energy (31.1 kJ mol^{-1} above starting materials).

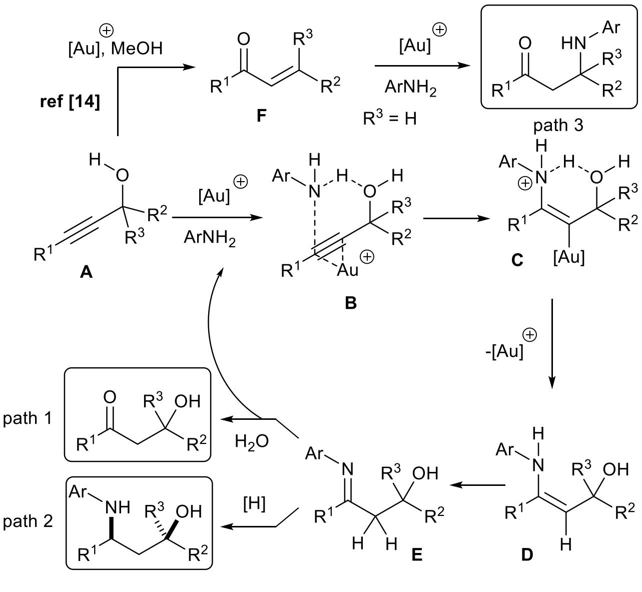
The condensed Fukui functions[36] f_k^+ for these two carbons in the initial gold complex were found to be respectively 0.063 and 0.055 indicating only a small difference in the intrinsic electrophilicity of the two sites. Distortion-interaction analysis[37] (see supporting information) suggested that both potential addition pathways involved similar energetic costs in distorting the starting materials, with the difference between the pathways arising from the more favourable interaction energy for attack at the distal carbon. We tentatively assign this difference to a stronger hydrogen-bonding interaction in the distal attack, due to a more linear geometry for the hydrogen bond in the incipient six-membered ring: at the transition state for distal attack, the O-H-N angle is 145.6° while the corresponding angle for proximal attack is 125.6°.

Figure 1: Transition states for addition of aniline to the distal (left) and proximal (right) carbon atoms of a but-2-yn-1-ol/Au-PMe_3 cationic complex, calculated at the B2PLYP/def2TZVPP//BP86/def2TZVPP level.[38]



For the corresponding addition of aniline to an unfunctionalized alkyne (but-2-yne), the energy barrier was higher still (37.7 kJ mol^{-1} above starting materials), indicating that the hydroxyl substituent plays a role in facilitating the addition reaction as well as determining its regioselectivity.

Scheme 9: Plausible reaction mechanisms for the formation of the three different products. The diastereoselectivity shown assumes R^2 is larger than R^3.



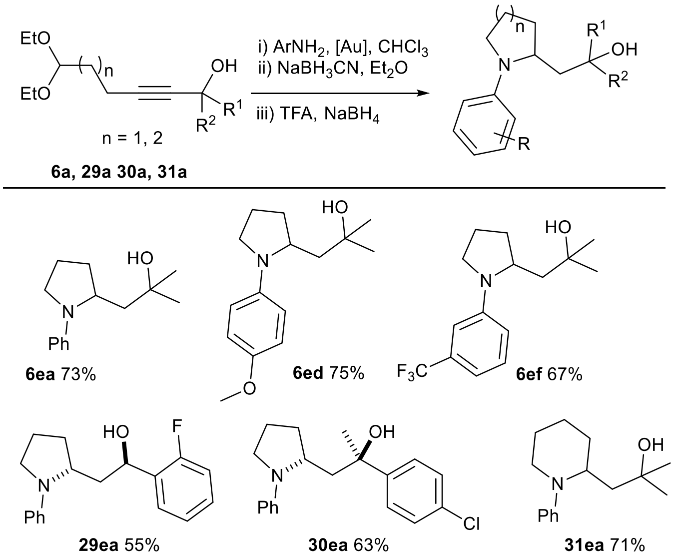
These considerations lead us to suggest the mechanisms shown in Scheme 9. Thus, gold-catalysed addition of the aniline to the complexed alkyne **(B)** is assisted by hydrogen bonding of the aniline to the oxygen lone pair, and this hydrogen bond also controls the regioselectivity of the addition step. After protodeauration of vinylgold intermediate **C**, the resulting enamine **D** can tautomerise to the imine **E** which undergoes hydrolysis to yield the hydroxyketone when water is present (path 1). Under anhydrous conditions, the imine is stable and can be subsequently reduced to the *syn* amino-alcohol (path 2). Further support for these two pathways was obtained from NMR analysis of a reaction of propargylic alcohol **18a** with 0.5 equivalents of 3-trifluoromethylaniline in the presence of PPh_3AuNTf_2

which showed a mixture of 3-hydroxyimine **E** and 3-hydroxyketone **18c** (Supporting Information). The aminoketone product is generated via hydroamination of the enone **F** which is formed readily via Meyer-Schuster rearrangement under conditions similar to those we have previously reported (path 3).[14]

Synthesis of Nitrogen Heterocycles

In order to demonstrate the synthetic potential of the hydroamination reaction, we synthesised a small selection of *N*-arylpyrrolidines/piperidines from the corresponding acetal-containing propargylic alcohols (Scheme 10). We were able to find suitable conditions under which the acetal-containing aminoalcohol was selectively transformed into the pyrrolidine/piperidine product using trifluoroacetic acid and $NaBH_4$. Pleasingly, the heterocycle synthesis could be performed without the need to purify any of the intermediate aminoalcohol compounds.

Scheme 10: Synthesis of *N*-arylpyrrroldines and *N*-arylpiperidines via one-pot gold-catalysed hydroamination of propargylic alcohols, followed by reduction and reductive amination. Yields shown are for the isolated product after the three step sequence.



Conclusions

In conclusion, we report a method for the valorization of propargylic alcohols through gold catalysed hydroamination.[39] In the presence of an aniline and a commercially available gold catalyst, propargylic alcohols undergo regioselective hydroamination yielding a 3-hydroxyimine which can be stereoselectively reduced to a *syn*-1,3-aminoalcohol or hydrolyzed to the corresponding 3-hydroxyketone. By changing to a two-step one-pot process, 3-aminoketones can be obtained via Meyer-Schuster rearrangement and conjugate addition of the aniline to the resulting enone. The latter step is formally a hydroamination of the enone, which is also catalysed by gold. Thus, by using the same substrates and catalyst under different conditions, three different products can be obtained efficiently with high selectivity. This constitutes a highly unusual divergent catalytic reaction.

Experimental Section

General Experimental Procedures

All solvents and chemicals were used as received. Column chromatography was carried out using either Merck Geduran Si 60 (40-63 µm) silica gel or a Biotage purification system using Biotage columns. Analytical thin layer chromatography was carried out using Merck TLC Silica Gel 60 F_{254} aluminium-backed plates. Components were visualised using combinations of ultra-violet lights and potassium permanganate.

Proton magnetic resonance spectra (^{1}H NMR) were recorded at 400, 500 or 600 MHz on a Bruker Avance spectrometer and are reported as follows: chemical shift δ in ppm (number of protons, multiplicity, coupling constant J in Hz, assignment). The solvent used was deuterated chloroform unless stated otherwise. Residual protic solvent was used as the internal reference, setting $CHCl_3$ to δ 7.26. Carbon magnetic resonance spectra (^{13}C NMR) were recorded at 100, 125 or 150 MHz on a Bruker Avance spectrometer using deuterated chloroform using the central reference of $CDCl_3$ to δ 77.0 as the internal standard. Mass Spectrometry data were collected on either TOF or magnetic sector analysers at the Department of Chemistry, University College London. The ionization method is reported in the experimental data.

Preparation of propargylic alcohols

n-Butyllithium (1.6 M in hexanes, 1.2 eq., 3.75 mL) was added dropwise to a stirred solution of the corresponding alkyne (5 mmol) in anhydrous THF (25 mL) at –78 ˚C under an argon atmosphere. After 30 min aldehyde (1 eq.) was added and the resulting solution was stirred for 5 min at 0 ˚C and then 30 min at rt. The reaction was diluted with aq. saturated NH_4Cl and the organic phase extracted with Et_2O. The combined organic phases were washed with brine, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc/Petrol) to give the propargylic alcohol.

The aldehyde used to prepare propargylic alcohol **8a** was synthesized following reported procedures.[40] Alkynes used to prepare **6a**, **23a**, **25a**, **26a**, **27a**, **28a**, **29a** and **30a** were synthesized following reported procedures.[41]

Propargylic alcohols **7a** and **20a** were purchased from commercial suppliers. We have previously reported the synthesis of propargylic alcohols **9a,**[18a] **17a**,[18a] **21a**,[18a] **22a**,[23] and **29a**.[18b] Enantioenriched propargylic alcohol **(*S*)-9a** (e.r. 96:4) was synthesized following reported procedures.[23,28]

Tridec-5-yn-7-ol (1a)[42]

891 mg, 91%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.34 (tt, J = 6.4, 1.9 Hz, 1H), 2.22 (td, J = 7.0, 2.0 Hz, 2H), 1.75–1.58 (m, 2H), 1.53–1.45 (m, 2H), 1.46–1.36 (m, 4H), 1.36–1.22 (m, 6H), 0.91 (t, J = 7.2 Hz, 3H), 0.89 (t, J = 7.3, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 85.6, 81.5, 62.9, 38.3, 31.9, 30.86, 29.1, 25.3, 22.7, 22.0, 18.5, 14.2, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3353 (O-H), 2955 (C-H), 2927 (C-H), 2858 (C-H), 1506, 1431, 1145, 1039, 726.

1-(Hex-1-ynyl)cyclohexan-1-ol (2a)[43]

774 mg, 86%, colourless oil, ^{1}**H NMR** (600 MHz, $CDCl_3$) δ 2.20 (t, *J* = 9.5, 2H), 1.99 (br s, 1H), 1.83 (m, 2H), 1.70–1.61 (m, 2H), 1.58–1.44 (m, 7H), 1.44–1.34 (m, 2H), 1.25-1.18 (m, 1H), 0.89 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 84.8, 84.0, 68.9, 40.4, 31.0, 25.4, 23.57, 22.0, 18.4, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3484 (O-H), 2931 (C-H), 2858 (C-H), 1447, 1340, 1056, 961, 752.

1-(2-Chlorophenyl)hept-2-yn-1-ol (3a)[44]

987 mg, 89%, colourless oil, ^{1}**H NMR** (600 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.37 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.31 (td, *J* = 7.5, 1.3 Hz, 1H), 7.28–7.24 (m, 1H), 5.81 (s, 1H), 2.35 (m, 1H), 2.27 (td, *J* = 7.1, 2.1 Hz, 2H), 1.57–1.47 (m, 2H), 1.46–1.37 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H); **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 138.6, 132.9, 129.8, 129.6, 128.5, 127.3, 88.0, 78.9, 62.3, 30.7, 22.1, 18.6, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3351 (O-H), 2957 (C-H), 2931 (C-H), 2871 (C-H), 1467, 1442, 1052, 1035, 750.

2-(4-Chlorophenyl)hex-3-yn-2-ol (4a)[45]

898 mg, 77%, colourless oil, ^{1}**H NMR** (600 MHz, $CDCl_3$) δ 7.58 (m, 2H), 7.31 (m, 2H), 2.27 (m, 2H), 1.71 (s, 3H), 1.58–1.48 (m, 2H), 1.50–1.37 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 144.9, 133.4, 128.4, 126.6, 86.2, 83.5, 69.7, 33.8, 30.8, 22.1, 18.5, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3425 (O-H), 2995 (C-H), 2933 (C-H), 2889 (C-H), 1497, 1371, 1025, 819.

1-Phenylnon-1-yn-3-ol (5a)[46]

960 mg, 89%, colourless oil, ^{1}**H NMR** (700 MHz, $CDCl_3$) δ 7.45–7.41 (m, 2H), 7.34–7.28 (m, 3H), 4.60 (t, *J* = 6.5 Hz, 1H), 1.92 (br s, 1H), 1.84–1.76 (m, 2H), 1.56–1.47 (m, 2H), 1.40–1.34 (m, 2H), 1.35–1.25 (m, 4H), 0.93–0.86 (m, 3H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 131.8, 128.5, 128.4, 122.8, 90.4, 85.0, 63.2, 38.1, 31.9, 29.1, 25.32, 22.7, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3366 (O-H), 2927 (C-H), 2857 (C-H), 1489, 1457, 1062, 755, 690.

7,7-Diethoxy-2-methylhept-3-yn-2-ol (6a)

834 mg, 78%, colourless oil, ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 4.57 (t, *J* = 5.7 Hz, 1H), 3.64 (dq, *J* = 9.3, 7.1 Hz, 2H), 3.49 (dq, *J* = 9.4, 7.1 Hz, 2H), 2.24 (t, *J* = 7.3 Hz, 2H), 2.12 (br s, 1H), 1.78 (m, 2H), 1.47 (s, 6H), 1.19 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 101.8, 85.5, 81.7, 65.2, 61.5, 32.8, 31.8, 15.4, 14.3. **IR** ν_{max} (solid/cm^{-1}) 3429 (O-H), 2975 (C-H), 2930 (C-H), 2875 (C-H), 1456, 1373, 1127, 1056, 949. **HRMS** (ESI-TOF) *m/z*: $[M+NH_4]^+$ Calcd for $C_{12}H_{26}O_3N^+$, 232.1907; Found, 232.1907.

5,5-Diethoxy-1-phenylpent-1-yn-3-ol (8a)

892 mg, 72%, yellow oil, ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.46–7.36 (m, 2H), 7.33–7.28 (m, 3H), 4.93 (t, *J* = 5.7 Hz, 1H), 4.79 (t, *J* = 5.5 Hz, 1H), 3.87–3.68 (m, 2H), 3.59 (m, 2H), 3.40 (br s, 1H), 2.20–2.10 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 131.7, 128.4, 128.3, 122.7, 101.5, 89.4, 84.8, 62.5, 61.9, 60.0, 40.6, 15.4, 15.4. **IR** ν_{max} (solid/cm^{-1}) 3412 (O-H), 2974 (C-H), 2930 (C-H), 2882 (C-H), 1489, 1374, 1119, 1049, 755, 690, 829. **HRMS** (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{20}O_3Na^+$, 271.1305; Found, 232.1305.

1-(4-Methoxyphenyl)hept-2-yn-1-ol (10a)[42]

1021 mg, 94%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.58–7.38 (m, 2H), 6.95–6.86 (m, 2H), 5.40 (s, 1H), 3.81 (s, 3H), 2.27 (td, *J* = 7.1, 2.0 Hz, 2H), 2.15 (br s, 1H), 1.62–1.49 (m, 2H), 1.47–1.32 (m, 2H), 1.01–0.83 (m, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 159.7, 133.8, 128.2, 114.0, 87.6, 80.2, 64.6, 55.5, 30.8, 22.1, 18.6, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3403 (O-H), 2956 (C-H), 2932 (C-H), 2836 (C-H), 1610, 1509, 1244, 1171, 1031, 634.

1-(Furan-2-yl)hept-2-yn-1-ol (11a)[14b]

703 mg, 79%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41–7.35 (m, 1H), 6.42 (br d, *J* = 3.2 Hz, 1H), 6.34 (dd, *J* = 3.2, 1.8 Hz, 1H), 5.43 (s, 1H), 2.32–2.28 (m, 1H), 2.27 (td, *J* = 7.1, 2.1 Hz, 2H), 1.57–1.48 (m, 2H), 1.41 (m, 2H), 0.96–0.88 (m, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 153.9, 143.0, 110.4, 107.5, 87.0, 77.6, 58.5, 30.6, 22.1, 18.6, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3396 (O-H), 2957 (C-H), 2932 (C-H), 2872 (C-H), 1501, 1148, 1005, 735, 598.

1-(Thiophen-2-yl)hept-2-yn-1-ol (12a)[47]

896 mg, 93%, brown oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.16–7.13 (m, 1H), 6.98–6.94 (m, 1H), 5.62 (s, 1H), 2.35(br s, 1H), 2.28 (td, *J* = 7.1, 2.0 Hz, 2H), 1.63–1.50 (m, 2H), 1.50–1.39 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 145.8, 126.8, 125.9, 125.4, 87.2, 79.7, 60.5, 30.7, 22.1, 18.6, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3381 (O-H), 2956 (C-H), 2933 (C-H), 2877 (C-H), 906, 728, 698.

2-Methylnon-4-yn-3-ol (13a)[42]

692 mg, 90%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.14 (dt, *J* = 5.5, 2.0 Hz, 1H), 2.20 (td, *J* = 7.0, 2.0 Hz, 2H), 1.87–1.79 (m, 1H), 1.55–1.46 (m, 2H), 1.44–1.31 (m, 2H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 86.3, 79.9, 68.3, 68.2, 34.8, 34.8, 30.9, 22.0, 18.5, 18.2, 18.2, 17.5, 17.5, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3383 (O-H), 2958 (C-H), 2931 (C-H), 2872 (C-H), 1671 1466, 1381, 1049, 1021, 779.

1-Cyclohexylhept-2-yn-1-ol (14a)[42]

843 mg, 87%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.15–4.09 (m, 1H), 2.26–2.17 (m, 2H), 1.82 (d, *J* = 12.3 Hz, 2H), 1.75 (d, *J* = 12.6 Hz, 2H), 1.70–1.60 (m, 1H), 1.52–1.44 (m, 3H), 1.45–1.36 (m, 2H), 1.28–1.19 (m, 2H), 1.19–1.09 (m, 2H), 1.09–1.00 (m, 1H), 0.96–0.85 (m, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 86.4, 80.2, 67.6, 44.5, 30.9, 28.7, 28.2, 26.6, 26.0, 22.1, 18.5, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3345 (O-H), 2923 (C-H), 2852 (C-H), 1449, 1008, 892.

Docosa-8,14-diyne-7,16-diol (15a)

1068 mg, 62%, colourless oil, mixture of diastereoisomers (1:1). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.31 (m, 2H), 2.28–2.18 (m, 4H), 1.64 (m, 4H), 1.59–1.56 (m, 4H), 1.46–1.36 (m, 4H), 1.31–1.22 (m, 12H), 0.89–0.83 (m, 6H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 84.9, 81.9, 62.79 (*diastereomer 1*), 62.78 (*diastereomer 2*) 38.3, 31.9, 29.1, 27.8, 25.3, 22.7, 18.3, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3355 (O-H), 2926 (C-H), 2857 (C-H), 1458, 1329, 1039, 735. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{37}O_2^+$, 333.2788; Found, 333.2785.

1-(4-Nitrophenyl)-5-phenylpent-2-yn-1-ol (16a)[48]

1231 mg, 88%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.27–8.10 (m, 2H), 7.64–7.50 (m, 2H), 7.33–7.28 (m, 2H), 7.27–7.22 (m, 1H), 7.20 (dd, *J* = 7.8, 0.9 Hz, 2H), 5.56–5.45 (m, 1H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.60 (td, *J* = 7.4, 2.0 Hz, 2H), 2.33 (d, *J* = 5.8 Hz, 1H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 147.9, 147.8, 140.3, 128.6, 127.5, 127.4, 126.6, 123.8, 88.1, 80.0, 63.9, 34.7, 20.9. **IR** ν_{max} (solid/cm^{-1}) 3405 (O-H), 3029 (C-H), 2930 (C-H), 1519 (C=C), 1343, 1265, 1011, 732, 697.

3-Ethylnon-4-yn-3-ol (18a)[49]

695 mg, 83%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 2.18 (m, 2H), 1.98 (br s, 1H, OH), 1.61 (m, 4H), 1.51–1.41 (m, 2H), 1.39 (m, 2H), 0.99 (t, *J* = 7.20 Hz, 6H), 0.88 (t, *J* = 7.30 Hz 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 84.9, 82.7, 72.3, 34.7, 31.0, 22.0, 18.4, 13.7, 8.7. **IR** ν_{max} (solid/cm^{-1}) 3341 (O-H), 2993 (C-H), 2933 (C-H), 2852 (C-H), 1459, 1019, 871.

1-Phenylhept-2yn-1-ol (19a)[42]

801 mg, 85%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.59–7.52 (m, 2H), 7.38 (m, 2H), 7.35–7.32 (m, 1H), 5.45 (s, 1H), 2.34–2.25 (m, 2H), 1.56–1.51 (m, 2H), 1.47–1.40 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 141.4, 128.7, 128.3, 126.8, 87.8, 80.0, 65.0, 30.8, 22.1, 18.6, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3362 (O-H), 2957 (C-H), 2931 (C-H), 2871 (C-H), 1641, 1497, 1314, 999, 696.

1-Cyclohexyl-6,6-diethoxyhex-2-yn-1-ol (23a)

1045 mg, 79%, colourless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.60 (t, *J* = 5.7 Hz, 1H), 4.12 (d, *J* = 5.9 Hz, 1H), 3.66 (dq, *J* = 9.4, 7.1 Hz, 2H), 3.51 (dq, *J* = 9.4, 7.1 Hz, 2H), 2.30 (td, *J* = 7.3, 2.0 Hz, 2H), 1.88–1.80 (m, 4H), 1.78 (s, 1H), 1.71–1.64 (m, 2H), 1.56–1.47 (m, 1H), 1.33–0.97 (m, 12H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 101.8, 85.43, 80.5, 67.5, 61.6, 44.4, 32.9, 28.7, 28.2, 26.5, 25.98, 25.95, 15.4, 14.5. **IR** ν_{max} (solid/cm^{-1}) 3382 (O-H), 2973 (C-H), 2924 (C-H), 2852 (C-H), 1448, 1374, 1118, 1056, 731. **HRMS** (ESI-TOF) *m/z*: $[M+NH_4]^+$ Calcd for $C_{16}H_{32}O_3N^+$, 286.2377; Found, 286.2376.

4-(1-Hydroxyhept-2-yn-1yl)benzonitrile (24a)[50]

902 mg, 84%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72–7.60 (m, 4H), 5.49 (s, 1H), 2.35 (s, 1H), 2.26 (td, *J* = 7.1, 2.1 Hz, 2H), 1.62–1.46 (m, 2H), 1.50–1.34 (m, 2H), 0.97–0.84 (m, 3H). **^{13}C{^{1}H} NMR** (151

MHz, $CDCl_3$) δ 146.4, 132.5, 127.3, 118.8, 112.0, 88.9, 79.1, 64.1, 30.6, 22.1, 18.6, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3402 (O-H), 2957 (C-H), 2932 (C-H), 2871 (C-H), 2229 (CN) 1608, 1463, 1325, 1134 1013, 887, 562.

1,1-Diethoxydodec-4-yn-6-ol (25a)

952 mg, 71%, colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.59 (t, *J* = 5.7 Hz, 1H), 4.33 (m, 1H), 3.75–3.60 (m, 2H), 3.58–3.45 (m, 2H), 2.28 (td, *J* = 7.3, 1.9 Hz, 2H), 1.81 (m, 2H), 1.65 (m, 2H), 1.48–1.38 (m, 2H), 1.40–1.27 (m, 6H), 1.20 (t, *J* = 7.1 Hz, 6H), 0.88 (t, *J* = 6.8 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 101.8, 84.6, 81.8, 62.8, 61.6, 38.3, 32.8, 31.9, 29.1, 25.3, 22.7, 15.4, 14.5, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3418 (O-H), 2956 (C-H), 2928 (C-H), 2858 (C-H), 1445, 1375, 1127, 1059. **HRMS** (ESI-TOF) *m/z*: $[M+NH_4]^+$ Calcd for $C_{16}H_{34}O_3N^+$, 288.2533; Found, 288.2533.

1-(Naphthalen-1-yl)hept-2-yn-1-ol (26a)[51]

954 mg, 80%, colourless oil **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.5 Hz, 1H), 7.99–7.80 (m, 3H), 7.63–7.43 (m, 3H), 6.20–6.06 (m, 1H), 2.36 (d, *J* = 5.7 Hz, 1H), 2.31 (td, *J* = 7.1, 3.7 Hz, 2H), 1.67–1.50 (m, 2H), 1.49–1.36 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 136.4, 134.2, 130.7, 129.3, 128.8, 126.4, 125.9, 125.4, 124.6, 124.2, 88.5, 79.8, 63.21, 30.8, 22.1, 18.7, 13.7. **IR** ν_{max} (solid/cm^{-1}) 3367 (O-H), 3049, 2956 (C-H), 2930 (C-H), 2870 (C-H), 1687, 1573, 1104, 774.

9-((*tert*-Butyldimethylsilanyl)oxy)-5-methylnon-1-en-6-yn-5-ol (27a)

944 mg, 67%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.87 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.06 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.97 (dq, *J* = 10.2, 1.3 Hz, 1H), 3.70 (t, *J* = 7.1 Hz, 2H), 2.41 (t, *J* = 7.1 Hz, 2H), 2.35–2.21 (m, 2H), 1.79–1.67 (m, 2H), 1.46 (s, 3H), 0.93–0.88 (s, 9H), 0.09–0.04 (s, 6H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 138.6, 114.8, 84.8, 81.2, 68.3, 62.0, 42.9, 30.3, 29.4, 26.0, 23.2, 18.4, -5.2. **IR** ν_{max} (solid/cm^{-1}) 3397 (O-H), 2953 (C-H), 2929 (C-H), 2857 (C-H), 1641, 1470, 1274, 1103, 909, 834, 775. **HRMS** (ESI-TOF) *m/z*: $[M]^+$ Calcd for $C_{16}H_{30}O_2Si^+$, 282.2010; Found, 282.2009.

6,6-Diethoxy-1-(2-fluorophenyl)hex-2-yn-1-ol (29a)

1134 mg, 81%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.62 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.33–7.29 (m, 1H), 7.21–7.11 (m, 1H), 7.09–7.02 (m, 1H), 5.71 (t, *J* = 1.9 Hz, 1H), 4.59 (t, *J* = 5.7 Hz, 1H), 3.71–3.58 (m, 2H), 3.56–3.44 (m, 2H), 2.34 (td, *J* = 7.3, 2.0 Hz, 2H), 1.86–1.81 (m, 2H), 1.29–1.15 (m, 6H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 160.2 (d, $J_{C\text{-}F}$= 248.0 Hz), 130.0 (d, $J_{C\text{-}F}$ = 8.3 Hz), 128.5 (d, $J_{C\text{-}F}$ = 13.1 Hz), 128.3 (d, $J_{C\text{-}F}$ = 3.6 Hz), 124.3 (d, $J_{C\text{-}F}$ = 3.6 Hz), 115.6 (d, $J_{C\text{-}F}$ = 21.3 Hz) 101.8, 86.8, 79.3, 61.7, 59.2 (d, $J_{C\text{-}F}$ = 5.0 Hz), 32.6, 15.4, 14.5. **IR** ν_{max} (solid/cm^{-1}) 3402 (O-H), 2981 (C-H), 2942 (C-H), 2888 (C-H), 1491, 1337, 1057, 762. **HRMS** (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{21}FO_3Na^+$, 303.1367; Found, 303.1369.

2-(4-Chlorophenyl)-7,7-diethoxyhept-3-yn-2-ol (30a)

1072 mg, 69%, colourless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59–7.53 (m, 2H), 7.35–7.27 (m, 2H), 4.59 (t, *J* = 5.7 Hz, 1H), 3.65 (dq, *J* = 9.4, 7.1 Hz, 1H), 3.50 (dq, *J* = 9.4, 7.1 Hz, 1H), 2.34 (t, *J* = 7.3 Hz, 1H), 1.84 (td, *J* = 7.3, 5.7 Hz, 1H), 1.70 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 144.8, 133.4, 128.3, 126.6, 101.7, 85.2, 83.7, 69.6, 61.6, 33.6, 32.7, 15.4, 14.4. **IR** ν_{max} (solid/cm^{-1}) 3415 (O-H), 2975 (C-H), 2930 (C-H), 2883 (C-H), 1487, 1397, 1054, 829. **HRMS** (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{23}ClO_3Na^+$, 333.1228; Found, 333.1224.

8,8-Diethoxy-2-methyloct-3-yn-2-ol (31a)

923 mg, 81%, colourless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.50 (t, *J* = 5.7 Hz, 1H), 3.64 (dq, *J* = 9.4, 7.1 Hz, 2H), 3.49 (dq, *J* = 9.4, 7.1 Hz, 2H), 2.21 (t, *J* = 7.0 Hz, 2H), 1.91 (br s, 1H), 1.70 (m, 2H), 1.66–1.52 (m, 2H), 1.48 (s, 6H), 1.20 (t, *J* = 7.1 Hz, 6H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 102.6, 85.6, 82.2, 65.4, 61.1, 32.8, 31.9, 24.1, 18.6, 15.5. **IR** ν_{max} (solid/cm^{-1}) 3433 (O-H), 2978 (C-H), 2926 (C-H), 2885 (C-H), 1465, 1134, 1056, 949, 761. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{25}O_3^+$, 251.1626; Found, 251.1623.

Preparation of *Syn* 1,3-Aminoalcohols

The corresponding propargylic alcohol (0.5 mmol, 1 equiv.) was dissolved in $CHCl_3$ (0.5 mL), 4 Å molecular sieves (300 mg, previously dried overnight at 120 °C) were added to the mixture. PPh_3AuNTf_2 (8 mg, 2 mol%) was added together with the corresponding amine (0.5 mmol, 1 equiv.) and the reaction was stirred at room temperature until completion (TLC, 18-66 h). Diethyl ether (1 mL) was added followed by $NaCNBH_3$ (62 mg, 1 mmol, 2 equiv.) and the reaction stirred for 2 h at 0 °C. After this time the solvent was removed in vacuo and the product was purified by column chromatography (EtOAc/Petrol) to give the corresponding aminoalcohol.

Different reducing agents were tested for the reduction step including $LiAlH_4$, $NaBH_4$, DIBAL, catecholborane, $LiBHEt_3$ and $NaBH_3CN$. With all of them complete reduction of the imine was achieved, but the best selectivities for the *syn* amino alcohol were obtained using $NaBH_3CN$, which gave complete reduction without significant hydrolysis of the imine.

***syn*-5-(Phenylamino)tridecan-7-ol (1ba)**

After amine addition the reaction was stirred for 18h.
113 mg, 78%, pale yellow solid, , mp 61-62 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.22–7.15 (m, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.69 (m, 2H), 3.89–3.81 (m, 1H), 3.60–3.54 (m, 1H), 1.75–1.69 (m, 1H), 1.56–1.40 (m, 5H), 1.30 (m, 12H), 0.89 (t, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.9, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 147.3, 129.4, 118.8, 115.2, 72.3, 54.6, 41.6, 38.3, 35.4, 32.0, 29.5, 28.0, 25.5, 22.9, 22.7, 14.2, 14.1. **IR** ν_{max} (solid/cm^{-1}) 3367 (O-H), 2923 (C-H), 2853 (C-H), 1598 (C=C), 1497 (C=C), 1463 (C=C), 1317, 745, 691. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{34}O^+$, 292.2635; Found, 292.2633.

***syn*-5-((4-Fluorophenyl)amino)tridecan-7-ol (1bb)**

After amine addition the reaction was stirred for 24h.
98 mg, 64%, white solid, mp 66-67 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.96–6.87 (m, 2H), 6.71–6.62 (m, 2H), 3.92–3.79 (m, 1H), 3.51–3.39 (m, 1H), 1.77–1.67 (m, 1H), 1.54–1.49 (m, 1H), 1.46–1.41 (m, 4H), 1.32–

1.25 (m, 12H), 0.89 (t, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.9, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) 156.7 (d, J_{C-F} = 236.7 Hz), 143.4, 116.5 (d, J_{C-F} = 7.5 Hz), 115.9 (d, J_{C-F} = 22.3 Hz), 72.4, 55.9, 41.4, 38.3, 35.25, 32.0, 29.5, 27.9, 25.5, 22.9, 22.7, 14.2, 14.1. **IR** ν_{max} (solid/cm^{-1}) 3352 (O-H), 2924 (C-H), 2853 (C-H), 1506 (C=C), 1463 (C=C), 1219, 819. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{19}H_{33}FNO^+$, 310.2541; Found, 310.2539.

syn-5-((3,5-Dimethylphenyl)amino)tridecan-7-ol (1bc)

After amine addition the reaction was stirred for 24h.
124 mg, 78%, colourless oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.43 (s, 1H), 6.34 (s, 2H), 3.83 (m, 1H), 3.52 (m, 1H), 2.23 (s, 6H), 1.71 (m, 1H), 1.53–1.46 (m, 1H), 1.45–1.35 (m, 4H), 1.29 (m, 12H), 0.89 (t, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.8, 3H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 147.3, 139.1, 121.0, 113.4, 72.5, 54.9, 41.5, 38.3, 35.4, 32.0, 29.5, 28.0, 25.6, 22.9, 22.8, 21.6, 14.2, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3367 (O-H), 2923 (C-H), 2853 (C-H), 1598 (C=C), 1463 (C=C), 1178. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{21}H_{38}NO^+$, 320.2948; Found, 320.2945.

syn-5-((4-Methoxyphenyl)amino)tridecan-7-ol (1bd)

After amine addition the reaction was stirred for 48h.
143 mg, 89%, white solid, mp 65-67 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.84–6.74 (m, 2H), 6.75–6.67 (m, 2H), 3.85 (m, 1H), 3.75 (s, 3H), 3.42 (m, 1H), 1.78–1.69 (m, 1H), 1.60–1.48 (m, 1H), 1.46–1.38 (m, 4H), 1.32–1.22 (m, 12H), 0.88 (t, *J* = 6.8 Hz, 3H), 0.85 (t, *J* = 6.9, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 153.4, 140.8, 117.4, 114.9, 72.7, 56.8, 55.8, 41.1, 38.3, 35.3, 31.9, 29.5, 27.9, 25.5, 22.8, 22.7, 14.2, 14.1. **IR** ν_{max} (solid/cm^{-1}) 3271 (O-H), 2920 (C-H), 2852 (C-H), 1507 (C=C), 1462 (C=C), 1230, 1040, 817. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{20}H_{36}NO_2^+$, 322.2741; Found, 322.2739.

syn-5-((3,5-Dichlorophenyl)amino)tridecan-7-ol (1be)

After amine addition the reaction was stirred for 48h.
122 mg, 68%, pale brown oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.66 (s, 1H), 6.49 (s, 2H), 3.81 (br s, 1H), 3.74 (m, 1H), 3.53–3.45 (m, 1H), 1.65 (m, 1H), 1.59–1.51 (m, 3H), 1.50–1.42 (m, 2H), 1.33–1.25 (m, 12H), 0.89 (t, *J* = 6.9 Hz, 3H), 0.88 (t, *J* = 6.9, 3H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 149.4, 135.7, 117.4, 112.0, 71.3, 52.9, 41.9, 38.4, 35.0, 31.9, 29.4, 27.9, 25.5, 22.8, 22.7, 14.2, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3449 (O-H), 2924 (C-H), 2853 (C-H), 1583 (C=C), 1507 (C=C), 1451 (C=C), 1110, 725. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{19}H_{32}NOCl_2^+$, 360.1855; Found, 360.1855.

syn-5-((3-(Trifluoromethyl)phenyl)amino)tridecan-7-ol (1bf)

After amine addition the reaction was stirred for 48h.
92 mg, 51%, pale yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.27–7.22 (m, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.86 (s, 1H), 6.79 (m, 1H), 3.84–3.77 (m, 1H), 3.57 (m, 1H), 1.70 (m, 1H), 1.54 (m, 3H), 1.49–1.38 (m, 3H), 1.36–1.25 (m, 12H), 0.89 (t, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.9, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 147.8, 131.8 (q, J_{C-F} = 31.7 Hz), 129.9, 124.4 (q, J_{C-F} = 272.4 Hz), 117.2, 114.5 (d, J_{C-F} = 3.9 Hz), 110.5 (d, J_{C-F} = 3.9 Hz), 71.6, 53.3, 41.8, 38.3, 35.1, 31.9, 29.4, 27.9, 25.5, 22.8, 22.7, 14.2, 14.1. **IR** ν_{max} (solid/cm^{-1}) 3361 (O-H), 2925 (C-H), 2854 (C-H), 1612 (C=C), 1336 (C=C), 1120, 696. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{20}H_{33}F_3NO^+$, 360.2509; Found, 360.2506.

***syn*-5-(*o*-Tolylamino)tridecan-7-ol (1bg)**

After amine addition the reaction was stirred for 66h.
81 mg, 53%, colourless oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.12 (t, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 7.3 Hz, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 6.70 (t, *J* = 7.4 Hz, 1H), 3.83 (m, 1H), 3.61 (m, 1H), 3.46 (br s, 1H), 2.15 (s, 3H), 1.76 (m, 1H), 1.55 (m, 1H), 1.50–1.41 (m, 4H), 1.31 (m, 12H), 0.89 (t, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.9, 3H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 145.2, 130.6, 127.3, 123.5, 118.2, 112.4, 72.4, 54.1, 41.7, 38.3, 35.3, 32.0, 29.5, 28.0, 25.6, 22.9, 22.8, 17.9, 14.2, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3385 (O-H), 2923 (C-H), 2853 (C-H), 1603 (C=C), 1510 (C=C), 1476, 743. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{20}H_{36}NO^+$, 306.2791; Found, 306.2789.

***syn*-5-((2-Bromophenyl)amino)tridecan-7-ol (1bh)**

After amine addition the reaction was stirred for 66h.
78 mg, 42%, colourless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.9 Hz, 1H), 7.17 (t, *J* = 7.3 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.58 (t, *J* = 7.6 Hz, 1H), 3.79 (m, 1H), 3.64–3.58 (m, 1H), 1.74–1.69 (m, 1H), 1.62 (m, 2H), 1.51–1.39 (m, 3H), 1.29 (m, 12H), 0.93–0.84 (m, 6H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 144.5, 132.7, 128.6, 118.5, 113.3, 111.2, 71.2, 53.4, 42.0, 38.3, 35.06, 32.0, 29.5, 27.9, 25.6, 22.9, 22.7, 14.2, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3402 (O-H), 2923 (C-H), 2853 (C-H), 1594 (C=C), 1507 (C=C), 1457 (C=C), 1016, 738. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{19}H_{33}NOBr^+$, 370.1739; Found, 370.1739.

1-(2-(Phenylamino)hexyl)cyclohexan-1-ol (2ba)

After amine addition the reaction was stirred for 18h.
66 mg, 48%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.22–7.12 (m, 2H), 6.77 (tt, *J* = 7.4, 1.0 Hz, 1H), 6.69 (m, 2H), 3.72–3.60 (m, 2H), 1.81 (dd, *J* = 14.7, 2.5 Hz, 1H), 1.71–1.21 (m, 14H), 0.88–0.83 (m, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 147.0, 129.5, 119.0, 115.4, 71.4, 50.7, 40.5, 40.0, 36.9, 35.6, 28.1, 26.1, 22.9, 22.5, 22.3, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3345 (O-H), 2924 (C-H), 2853 (C-H), 1598 (C=C), 1496 (C=C), 1376 (C=C), 1159, 747. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{18}H_{30}NO^+$, 376.2322; Found, 276.2327.

***syn*-1-(2-Chlorophenyl)-3-(phenylamino)heptan-1-ol (3ba)**

After amine addition the reaction was stirred for 18h.
105 mg, 48%, colourless oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.21–7.18 (m, 1H), 6.82 (t, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 7.9 Hz, 2H), 5.33 (m, 1H), 3.74 (m, 1H), 2.09 (m, 1H), 1.65–1.53 (m, 3H), 1.53–1.47 (m, 1H), 1.35–1.24 (m, 3H), 0.86 (t, *J* = 6.7 Hz, 3H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 147.1, 142.2, 131.5, 129.5, 129.4, 128.4, 127.3, 127.1, 119.4, 115.7, 71.5, 55.2, 42.1, 35.2, 27.9, 22.8, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3379 (O-H), 2925 (C-H), 2854 (C-H), 1598 (C=C), 1496 (C=C), 990, 749. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{19}H_{24}NOCl^+$, 318.1619; Found, 318.1614.

(2*RS*,4*RS*)-2-(4-Chlorophenyl)-4-(phenylamino)octan-2-ol (4ba)

After amine addition the reaction was stirred for 18h.
129 mg, 78%, colourless oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.7 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 2H), 6.83 (t, *J* = 7.2 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 2H), 3.78 (m, 1H), 1.99 (d, *J* = 14.7 Hz, 1H), 1.74 (dd, *J* = 14.5, 11.1 Hz, 1H), 1.64 (s, 3H), 1.59–1.49 (m, 1H), 1.39 (dd, *J* = 14.2, 6.9 Hz, 1H), 1.31–1.19 (m, 4H), 0.84 (t, *J* = 6.0 Hz, 3H). **$^{13}C\{^1H\}$ NMR** (176 MHz, $CDCl_3$) δ 148.3, 146.6, 132.4, 129. 6, 128.4, 126.2, 119.8, 115.8, 74.0, 52.3, 47.4, 35.6, 29.1, 28.0, 22.8, 14.1. **IR** ν_{max} (solid/cm^{-1}) 3320 (O-H), 2926 (C-H), 2854 (C-H), 1598 (C=C), 1496 (C=C), 1091, 750. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{27}ClNO^+$, 332.1776; Found, 332.1773.

***syn*-1-Phenyl-1-(phenylamino)nonan-3-ol (5ba)**

After amine addition the reaction was stirred for 18h.
79 mg, 51%, colourless oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.37 (m, 5H), 7.22–7.14 (m, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 6.65 (m, 2H), 5.06–4.96 (dd, *J* = 8.2, 2.8 Hz, 1H), 3.60 (m, 1H), 2.12–2.03 (m, 1H), 1.85–1.78 (m, 1H), 1.37–1.16 (m, 10H), 0.86 (t, *J* = 6.8 Hz, 3H). **$^{13}C\{^1H\}$ NMR** (176 MHz, $CDCl_3$) δ 145.1, 129.5, 128.6, 127.5, 125.7, 118.2, 115.9, 114.3, 71.9, 51.3, 43.7, 35.5, 31.9, 29.4, 26.0, 22.7, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3377 (O-H), 2951 (C-H), 2853 (C-H), 1588 (C=C), 1506 (C=C), 1452 (C=C), 1315, 749. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{30}NO^+$, 312.2322; Found, 312.2326.

7,7-Diethoxy-2-methyl-4-(phenylamino)heptan-2-ol (6ba)

After amine addition the reaction was stirred for 18h.
112 mg, 73%, colourless oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.18 (t, *J* = 7.9 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 2H), 4.41 (t, *J* = 5.4 Hz, 1H), 3.77–3.73 (m, 1H), 3.68 (br s, 1H), 3.59 (m, 2H), 3.46–3.39 (m, 2H), 1.72 (dd, *J* = 14.6, 2.7 Hz, 1H), 1.68–1.58 (m, 4H), 1.50–1.46 (m, 1H), 1.29 (s, 3H), 1.24 (s, 3H), 1.19–1.13 (m, 6H). **$^{13}C\{^1H\}$ NMR** (176 MHz, $CDCl_3$) δ 146.9, 129.5, 119.1, 115.3, 102.9, 70.9, 61.4, 61.1, 51.4, 46.3, 31.5, 30.8, 29.9, 28. 8, 15.4, 15.4. **IR** ν_{max} (solid/cm^{-1}) 3364 (O-H), 2968 (C-H), 2927 (C-H), 1599 (C=C), 1497 (C=C), 1153, 1055. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{32}NO_3^+$, 310.2377; Found, 310.2374.

3-Phenyl-3-(phenylamino)propan-1-ol (7ba)[52]

After amine addition the reaction was stirred for 18h.
84 mg, 74%, colourless oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.38–7.34 (m, 2H), 7.32 (m, 2H), 7.25–7.22 (m, 1H), 7.09 (m, 2H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.56 (t, *J* = 8.6 Hz, 2H), 4.58 (t, *J* = 6.7 Hz, 1H), 3.79 (m, 2H), 2.13–2.01 (m, 2H).**$^{13}C\{^1H\}$ NMR** (176 MHz, $CDCl_3$) δ 147.4, 143.7, 129.3, 128.8, 127.21, 126.4, 117.7, 113.9, 60.9, 57.0, 40.8. **IR** ν_{max} (solid/cm^{-1}) 3393 (O-H), 2938 (C-H), 1599 (C=C), 1501 (C=C), 1315.

***syn*-1,1-Diethoxy-5-phenyl-5-(phenylamino)pentan-3-ol (8ba)**

After amine addition the reaction was stirred for 18h.
138 mg, 81%, colourless oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.42–7.36 (m, 2H), 7.33 (m, 2H), 7.22 (m, 1H), 7.10–7.02 (m, 2H), 6.66–6.61 (m, 1H), 6.60–6.52 (m, 2H), 4.76–4.61 (m, 1H), 4.59–4.44 (m, 1H), 4.04–3.95 (m, 1H), 3.79–3.68 (m, 1H), 3.68–3.59 (m, 1H), 3.58–3.45 (m, 2H), 2.04–1.97 (m, 1H), 1.84–1.71 (m, 3H), 1.26–1.19 (m, 6H). **$^{13}C\{^1H\}$ NMR** (176 MHz, $CDCl_3$) δ 147.6, 144.3, 129.1, 128.8, 127.2, 126.5, 117.7,

114.2, 102.4, 68.1, 62.6, 61.9, 58.4, 46.1, 41.0, 15.5, 15.4. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{30}NO_3^+$, 344.2220; Found, 344.2225.

syn-1-((4-methoxyphenyl)amino)-4-methyl-1-phenylpentan-3-ol (9bd)

After amine addition the reaction was stirred for 48h.
The compound was isolated as a mixture of syn/anti isomers (85:15). The syn isomer was purified by recrystallisation from n-hexane. 97 mg, 67%, colourless crystals, mp 99-101 °C. ^{1}**H NMR** (700 MHz, $CDCl_3$) δ 7.31 (m, 4H), 7.22 (m, 1H), 6.68 (d, *J* = 8.9 Hz, 2H), 6.55 (d, *J* = 8.9 Hz, 2H), 4.46–4.40 (m, 1H), 3.69 (s, 3H), 3.64 (m, 1H), 1.84 (m, 2H), 1.71–1.64 (m, 1H), 1.57 (br s, 1H), 0.91 (m, 6H). ^{13}**C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 152.9, 144.2, 141.1, 128.8, 127.2, 126.3, 116.5, 114.8, 76.9, 60.5, 55.8, 42.1, 34.47, 18.5, 17.4. **IR** ν_{max} (solid/cm^{-1}) 3375 (O-H), 2955 (C-H), 1603 (C=C), 1513 (C=C), 1325.

This compound was synthesized from the corresponding racemic propargylic alcohol and from an enantiomerically enriched sample. From the enantiomerically enriched propargylic alcohol, the yield after crystallization was 59% (84 mg), $[\alpha]_D^{25}$ = +14.2 (c = 1.0, CH_2Cl_2). Only one enantiomer was observed by chiral HPLC.

cis-4-Butyl-6-hexyl-3-phenyl-1,3-oxazinan-2-one (1ba-*URE*)

Compound **1ba** (29 mg, 0.1 mmol, 1 equiv.) was mixed with carbonyldiimidazole (16 mg, 0.1 mmol, 1 equiv.) and dissolved in MeCN (0.5 mL). The mixture was heated to 80 °C. After 14 h the mixture was cooled down to rt and the product was purified by flash column chromatography (AcOEt: Hex). The nOeSY spectrum of the product supports the stereochemical assignment shown above. nOeSY spectrum is included in the supporting information.

28 mg, 85%, pale yellow oil, ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 10.7, 4.5 Hz, 2H), 7.31–7.27 (m, 1H), 7.24 (t, *J* = 3.1 Hz, 2H), 4.40–4.26 (m, 1H), 3.88–3.79 (m, 1H), 2.18 (m, 1H), 1.81–1.62 (m, 3H), 1.54–1.03 (m, 14H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.79 (t, *J* = 7.1, 3H). ^{13}**C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 154.0, 140.2, 129.2, 128.4, 127.4, 76.0, 57.6, 35.2, 34.3, 33.8, 31.8, 29.3, 26.9, 24.8, 22.7, 22.6, 14.2, 14.0. **IR** ν_{max} (solid/cm^{-1}) 2955 (C-H), 2928 (C-H), 2858 (C-H), 1693 (C=O), 1415, 1297, 766, 696. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{32}NO_2^+$, 318.2428; Found, 318.2426.

(4*RS*,6*RS*)-4-Butyl-6-(4-chlorophenyl)-6-methyl-3-phenyl-1,3-oxazinan-2-one (4ba-*URE*)

Compound **4ba** (33 mg, 0.1 mmol, 1 equiv.) was mixed with CDI (16 mg, 0.1 mmol, 1 equiv.) and dissolved in MeCN (0.5 mL). The mixture was heated to 80 °C. After 14 h the mixture was cooled down to rt and the product was purified by flash column chromatography (AcOEt: Hex). The nOeSY spectrum of the product supports the stereochemical assignment shown above. nOeSY spectrum is included in the supporting information.

33 mg, 92%, colourless oil,^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.46–7.39 (m, 2H), 7.34–7.28 (m, 2H), 7.21 (dd, *J* = 8.5, 7.4 Hz, 2H), 6.83 (t, *J* = 7.4 Hz, 1H), 6.72 (dd, *J* = 8.6, 1.0 Hz, 2H), 3.78 (td, *J* = 6.7, 3.3 Hz, 1H), 1.99 (dd, *J* = 14.7, 2.7 Hz, 1H), 1.78–1.68 (m, 1H), 1.63 (s, 3H), 1.41 (d, *J* = 6.8 Hz, 2H), 1.30–1.19 (m, 4H), 0.84 (m, 3H). ^{13}**C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 150.4, 146.6, 139.4, 132.9, 129.4, 129.2, 128.8, 128.6, 126.3, 73.9, 58.5, 46.8, 34.4, 30.4, 29.0, 22.6, 14.1. **IR** ν_{max} (solid/cm^{-1}) 2964 (C-H), 2929 (C-H), 2859 (C-H) 1685 (C=O), 1596 (C=C), 1495 (C=C), 1215, 754, 696. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{25}NO_2Cl^+$, 358.1568; Found, 358.1568.

syn-5-Aminotridecan-7-ol (1bi)

To a solution of aminoalcohol **1bd** (118 mg, 0.5 mmol) in MeCN/H_2O (10 mL, 1:1) trichloroisocyanuric acid (0.13 g, 0.27 mmol) and 1 M aqueous H_2SO_4 (0.5 mL) were added. The mixture was stirred for 16 h. at rt and then the product was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic extracts concentrated. The amino alcohol was purified using flash column chromatography.

78 mg, 72%, brown oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.81 (m, 1H), 3.29 (m, 1H), 1.79 (m, 1H), 1.67 (m, 2H), 1.54 (m, 1H), 1.42 (m, 2H), 1.38–1.22 (m, 12H), 0.89 (t, *J* = 6.8, 1.9 Hz, 3H), 0.87 (t, *J* = 6.9, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 72.6, 53.2, 38.8, 38.6, 34.7, 31.9, 29.4, 27.8, 25.7, 22.7, 22.5, 14.1, 14.0. **IR** ν_{max} (solid/cm^{-1}) 3371 (O-H), 3195 (N-H) 2955 (C-H), 2912 (C-H), 1154, 1092, 752, 692. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{13}H_{30}NO^+$, 216.2322; Found, 216.2323.

Preparation of Hydroxyketones

The corresponding propargylic alcohol (0.5 mmol, 1 equiv.) was dissolved in undried $CHCl_3$ (0.5 mL). After the substrate was completely dissolved, PPh_3AuNTf_2 (8 mg, 2 mol%) and 3-trifluoromethylaniline (16 mg, 0.2 equiv.) were added to the solution. The reaction was then stirred at 50 °C for 18 h. The solvent was removed in vacuo and the product was purified by column chromatography (AcOEt:Hex, 1:4).

7-Hydroxytridecan-5-one (1c)

96 mg, 91%, pale yellow solid, mp 47-49 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.08–3.93 (m, 1H), 3.04 (d, *J* = 3.0 Hz, 1H), 2.58 (dd, *J* = 17.5, 2.7 Hz, 1H), 2.48 (dd, *J* = 17.5, 9.2 Hz, 1H), 2.42 (t, *J* = 7.6 Hz, 2H), 1.59–1.52 (m, 2H), 1.51–1.45 (m, 1H), 1.42–1.35 (m, 2H), 1.33–1.22 (m, 9H), 0.90 (t, 7.3 Hz, 3H), 0.87 (t, 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 212.8, 67.8, 49.0, 43.5, 36.6, 31.9, 29.3, 25.8, 25.5, 22.7, 22.4, 14.2, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3397 (O-H), 2956 (C-H), 2928 (C-H), 2857 (C-H), 1705 (C=O), 1465, 1378, 1164, 732. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{13}H_{27}O_2^+$, 215.2006; Found, 215.2006.

1-(1-Hydroxycyclohexyl)hexan-2-one (2c)

80 mg, 81%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.77 (br s, 1H), 2.56 (s, 2H), 2.41 (t, *J* = 7.4 Hz, 2H), 1.72–1.61 (m, 5H), 1.59–1.52 (m, 3H), 1.45–1.23 (m, 6H), 0.91 (t, *J* = 7.3 Hz, 3H); **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 213.8, 70.8, 44.7, 37.7, 37.7, 25.9, 25.7, 22.4, 22.1, 14.0. **IR** ν_{max} (solid/cm^{-1}) 3497 (O-H), 2931 (C-H), 2859 (C-H), 1698 (C=O), 1447, 1406, 996. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{12}H_{23}O_2^+$, 199.1693; Found, 199.1692.

1-(2-Chlorophenyl)-1-hydroxyheptan-3-one (3c)

103 mg, 86%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.34–7.28 (m, 2H), 7.23–7.18 (m, 1H), 5.49 (dt, *J* = 9.6, 2.7 Hz, 1H), 3.66 (d, *J* = 3.3 Hz, 1H), 2.97 (dd, *J* = 17.6, 2.3 Hz, 1H), 2.63 (dd, *J* = 17.6, 9.6 Hz, 1H), 2.44 (m, 2H), 1.58 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 212.1, 140.3, 131.2, 129.4, 128.7, 127.3, 127.2, 66.9, 49.0, 43.4, 25.8, 22.4, 13.9. **IR** ν_{max}

(solid/cm^{-1}) 3449 (O-H), 2958 (C-H), 2931 (C-H), 2872 (C-H), 1703 (C=O), 1439, 1047, 1032, 753. **HRMS** (ESI-TOF) *m/z*: [M]$^+$ Calcd for $C_{13}H_{17}ClO_2^+$, 240.0912; Found, 240.0911.

2-(4-Chlorophenyl)-2-hydroxyoctan-4-one (4c)

55 mg, 43%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39–7.33 (m, 2H), 7.30–7.27 (m, 2H), 4.71 (s, 1H), 3.10 (d, *J* = 17.1 Hz, 1H), 2.80 (d, *J* = 17.1 Hz, 1H), 2.36 (m, 1H), 2.26 (m, 1H), 1.48 (s, 3H), 1.47–1.40 (m, 2H), 1.20 (m, 2H), 0.84 (t, *J* = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 213.1, 146.1, 132.7, 128.5, 126.0, 73.2, 53.0, 44.5, 30.7, 25.4, 22.2, 13.8. **IR** ν_{max} (solid/cm^{-1}) 3470 (O-H), 2958 (C-H), 2931 (C-H), 2872 (C-H), 1696 (C=O), 1489, 1401, 1164, 1094, 1012, 829, 555. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{14}H_{19}ClO_2Na^+$, 277.0967; Found, 277.0967.

3-Hydroxy-1-phenylnonan-1-one (5c)[53]

95 mg, 81%, yellow oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00–7.91 (m, 2H), 7.63–7.55 (m, 1H), 7.50–7.44 (m, 2H), 4.22 (m, 1H), 3.17 (dd, *J* = 17.7, 2.6 Hz, 1H), 3.04 (dd, *J* = 17.7, 9.0 Hz, 1H), 1.68–1.57 (m, 1H), 1.50 (m, 2H), 1.35–1.24 (m, 7H), 0.89 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 201.1, 136.9, 133.6, 128.7, 128.1, 67.9, 45.1, 36.6, 31.9, 29.3, 25.6, 22.7, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3452 (O-H), 2957 (C-H), 2931 (C-H), 2872 (C-H), 1703 (C=O), 1493, 1379, 1068, 698.

1,1-Diethoxy-6-hydroxy-6-methylheptan-4-one (6c)

60 mg, 78%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.48 (t, *J* = 5.3 Hz, 1H), 3.83 (s, 1H), 3.63 (dq, *J* = 9.4, 7.1 Hz, 2H), 3.55–3.40 (m, 2H), 2.61 (s, 2H), 2.51 (t, *J* = 7.2 Hz, 2H), 1.89 (td, *J* = 7.2, 5.4 Hz, 2H), 1.23 (s, 6H), 1.18 (t, *J* = 7.1 Hz, 6H); **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 212.6, 102.0, 69.8, 61.9, 53.2, 39.3, 29.5, 27.5, 15.4. **IR** ν_{max} (solid/cm^{-1}) 3475 (O-H), 2973 (C-H), 2931 (C-H), 2896 (C-H), 1700 (C=O), 1444, 1373, 1123, 1055. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{12}H_{24}O_4Na^+$, 255.1567; Found, 255.1567.

3-Hydroxy-1-phenylpropan-1-one (7c)[54]

56 mg, 74%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.03–7.93 (m, 2H), 7.63–7.56 (m, 1H), 7.50–7.46 (m, 2H), 4.03 (m, 2H), 3.28–3.20 (m, 2H), 2.65 (t, *J* = 6.5 Hz, 1H); **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 200.7, 136.8, 133.7, 128.8, 128.2, 58.2, 40.5. **IR** ν_{max} (solid/cm^{-1}) 3403 (O-H), 2925 (C-H), 1677 (C=O), 1492, 1327, 1177, 1057, 688.

3-Hydroxy-4-methyl-1-phenylpentan-1-one (9c)[23]

72 mg, 82%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.96 (dt, *J* = 8.5, 1.5 Hz, 2H), 7.62–7.56 (m, 1H), 7.52–7.44 (m, 2H), 4.04–3.97 (m, 1H), 3.21–3.12 (m, 2H), 3.03 (dd, *J* = 17.4, 9.6 Hz, 1H), 1.86–1.76 (m, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 201.5, 137.1, 133.6, 128.8, 128.2, 72.5, 42.1, 33.3, 18.7, 18.0. **IR** ν_{max} (solid/cm^{-1}) 3488 (O-H), 2961 (C-H), 2911 (C-H), 2867 (C-H), 1704 (C=O), 1467, 1355, 1235, 995, 737.

This compound was synthesized from the corresponding racemic propargylic alcohol and from an enantiomerically enriched sample. From the enantiomerically enriched propargylic alcohol, the yield was 86%, $[\alpha]_D^{25}$ = +6.3 (c = 1.0, CH_2Cl_2). An e.r. of 94:6 was observed by chiral HPLC (supporting information).

1-Hydroxy-1-(4-methoxyphenyl)heptan-3-one (10c)[55]

61 mg, 52%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.27 (m, 2H), 6.99–6.77 (m, 2H), 5.09 (dd, *J* = 9.2, 3.0 Hz, 1H), 3.79 (s, 3H), 3.29 (br s, 1H), 2.84 (dd, *J* = 17.3, 9.3 Hz, 1H), 2.75(dd, *J* = 17.3, 3.2 Hz, 1H), 2.42 (t, *J* = 7.6 Hz, 2H), 1.57–1.51 (m, 2H), 1.40–1.24 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 211.8, 159.2, 135.2, 127.0, 114.0, 69.8, 55.4, 51.1, 43.6, 25.8, 22.4, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3433 (O-H), 2957 (C-H), 2931 (C-H), 2872 (C-H), 1704 (C=O), 1611, 1512, 1245, 1033, 830.

1-(Furan-2-yl)-1-hydroxyheptan-3-one (11c)[56]

75 mg, 77%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.32 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.25 (d, *J* = 3.2 Hz, 1H), 5.16 (m, 1H), 3.31 (br s, 1H), 3.02 (dd, *J* = 17.5, 8.9 Hz, 1H), 2.89 (dd, *J* = 17.5, 3.3 Hz, 1H), 2.45 (t, *J* = 7.4 Hz, 2H), 1.63–1.53 (m, 2H), 1.38–1.26 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H); **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 211.2, 155.2, 142.2, 110.4, 106.4, 64.0, 47.2, 43.5, 25.8, 22.4, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3451 (O-H), 2958 (C-H), 2933 (C-H), 2873 (C-H), 1709 (C=O), 1378, 1012, 739.

1-Hydroxy-1-(thiophen-2-yl)heptan-3-one (12c)[57]

60 mg, 61%, brown oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.25–7.22 (m, 1H), 6.97–6.94 (m, 2H), 5.40 (dt, *J* = 8.6, 3.5 Hz, 1H), 3.51 (d, *J* = 3.7 Hz, 1H), 2.98 (dd, *J* = 17.6, 3.6 Hz, 1H), 2.92 (dd, *J* = 17.6, 8.6 Hz, 1H), 2.45 (t, *J* = 7.4 Hz, 2H), 1.65–1.52 (m, 2H), 1.35–1.28 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 211.3, 146.7, 126.8, 124.8, 123.6, 66.4, 50.9, 43.5, 25.7, 22.4, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3433 (O-H), 2957 (C-H), 2931 (C-H), 2872 (C-H), 1706 (C=O), 1404, 1126, 1036, 699.

3-Hydroxy-2-methylnonan-5-one (13c)[58]

79 mg, 92%, colourless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.84–3.77 (m, 1H), 2.63–2.55 (dd, *J* = 17.6, 2.3 Hz, 1H), 2.48 (dd, *J* = 17.6, 9.6 Hz, 1H), 2.44 (t, *J* = 7.4 Hz, 2H), 1.67 (m, 1H), 1.61–1.51 (m, 2H), 1.37–1.26 (m, 2H), 0.95–0.88 (m, 9H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 212.9, 72.4, 46.0, 43.5, 33.1, 25.8, 22.3, 18.4, 17.8, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3397 (O-H), 2959 (C-H), 2932 (C-H), 2873 (C-H), 1702 (C=O), 1333, 1164, 1125, 1070 698.

1-Cyclohexyl-1-hydroxyheptan-3-one (14c)[55]

99 mg, 94%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.79 (m, 1H), 2.96 (d, *J* = 3.5 Hz, 1H), 2.59 (dd, *J* = 17.3, 2.4 Hz, 1H), 2.50 (dd, *J* = 17.3, 9.6 Hz, 1H), 2.43 (t, *J* = 7.5 Hz, 2H), 1.87–1.80 (m, 1H), 1.74 (m, 2H), 1.68–1.60 (m, 2H), 1.60–1.51 (m, 2H), 1.38–1.27 (m, 3H), 1.26–1.09 (m, 3H), 1.07–0.96 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 213.1, 71.9, 46.2, 43.6, 43.1, 29.0, 28.4, 26.6, 26.2, 25.9, 22.4, 14.0. **IR** ν_{max} (solid/cm^{-1}) 3458 (O-H), 2991 (C-H), 2933 (C-H), 2859 (C-H), 1703 (C=O), 1417, 1106, 796.

7,16-Dihydroxydocosane-9,14-dione (15c)

149 mg, 81%, yellow oil, mixture of diastereoisomers (overlapped cannot differentiate most peaks) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.06–3.99 (m, 2H), 2.63–2.54 (m, 2H), 2.54–2.48 (m, 2H), 2.42 (m, 4H), 2.13 (s, 2H), 1.61–1.55 (m, 4H), 1.52–1.47 (m, 2H), 1.44–1.37 (m, 4H), 1.34–1.23 (m, 14H), 0.88 (t, *J* = 6.7 Hz, 6H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 212.0 (*diastereomer 1*), 208.8 (*diastereomer 1*), 67.8, 49.2, 43.5, 36.6, 31.9, 29.3, 25.5, 22.7, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3326 (O-H), 2926 (C-H), 2856 (C-H), 1702 (C=O), 1332, 1166, 1127, 667. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{22}H_{42}O_4Na^+$, 393.2975; Found, 393.2983.

1-Hydroxy-1-(4-nitrophenyl)-5-phenylpentan-3-one (16c)

113 mg, 76%, yellow oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28–8.18 (m, 2H), 7.56–7.45 (m, 2H), 7.29 (m, 2H), 7.24–7.19 (m, 1H), 7.18–7.15 (m, 2H), 5.24 (m, 1H), 3.56 (d, *J* = 3.3 Hz, 1H), 2.93 (m, 2H), 2.79 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 209.9, 150.0, 147.4, 140.4, 128.7, 128.35, 127.1, 126.5, 123.8, 69.1, 51.0, 45.1, 29.6. **IR** ν_{max} (solid/cm^{-1}) 3464 (O-H), 2927 (C-H), 1706 (C=O), 1601, 1515, 1342, 854, 697. **HRMS** (ESI-TOF) *m/z*: [M+Cl]$^+$ Calcd for $C_{17}H_{17}ClNO_4^+$, 334.0846; Found, 334.0851.

3-(4-Bromophenyl)-1-cyclopropyl-3-hydroxypropan-1-one (17c)

79 mg, 59%, pale yellow solid, mp 93-94 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52–7.44 (m, 2H), 7.29–7.20 (m, 2H), 5.12 (m, 1H), 3.58 (d, *J* = 3.0 Hz, 1H), 2.98–2.93 (m, 2H), 1.91 (tt, *J* = 7.8, 4.5 Hz, 1H), 1.16–1.06 (m, 2H), 1.01–0.90 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 211.2, 141.9, 131.7, 127.5, 121.4, 69.4, 51.4, 21.4, 11.6, 11.4. **IR** ν_{max} (solid/cm^{-1}) 3433 (O-H), 2920 (C-H), 2900 (C-H), 1686 (C=O), 1420, 1055, 1027, 819, 532. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{12}H_{13}O_2BrNa^+$, 290.9991; Found, 291.0001.

3-Ethyl-3-hydroxynonan-5-one (18c)

30 mg, 32%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.81 (s, 1H), 2.55 (s, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 1.61–1.47 (m, 6H), 1.35–1.31 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.85 (t, *J* = 7.5 Hz, 6H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 214.2, 74.3, 48.7, 44.7, 31.2, 25.7, 22.4, 14.0, 8.2. **IR** ν_{max} (solid/cm^{-1}) 3463 (O-H), 2960 (C-H), 2930 (C-H), 2874 (C-H), 1698 (C=O), 1488, 1459, 1407, 1126, 1061, 976. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{11}H_{22}O_2Na^+$, 209.1517; Found, 209.1514.

1-Hydroxy-1-phenylheptan-3-one (19c)[55]

84 mg, 82%, colourless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42–7.32 (m, 4H), 7.28 (m, 1H) 5.16 (m, 1H), 3.37 (d, *J* = 3.1 Hz, 1H), 2.92–2.71 (m, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 1.64–1.51 (m, 2H), 1.40–1.23 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 211.8, 142.9, 128.6, 127.7, 125.7, 70.0, 51.1, 43.5, 25.7, 22.3, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3485 (O-H), 2959 (C-H), 2932 (C-H), 2873 (C-H), 1703 (C=O), 1494, 1128, 905, 725, 699.

1-Hydroxyhexan-3-one (20c)[58]

43 mg, 74%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.84 (t, *J* = 5.4 Hz, 2H), 2.72–2.62 (m, 2H), 2.53–2.36 (m, 2H), 1.71–1.55 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H); **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 212.1, 58.0, 45.4, 44.4, 17.2, 13.8. **IR** ν_{max} (solid/cm^{-1}) 3397 (O-H), 2963 (C-H), 2932 (C-H), 1704 (C=O), 1349, 1226, 1189, 729.

1-Cyclopropyl-3-hydroxy-3-*p*-tolylpropan-1-one (21c)

72 mg, 71%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 5.12 (dd, *J* = 8.7, 3.5 Hz, 1H), 3.52–3.37 (m, 1H), 3.04–2.90 (m, 1H), 2.34 (s, 1H), 1.92 (m, 1H), 1.14–1.04 (m, 2H), 0.94–0.89 (m, 2H); **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 211.5, 140.0, 137.4, 129.3, 125.7, 69.9, 51.7, 21.5, 21.2, 11.5, 11.2. **IR** ν_{max} (solid/cm^{-1}) 3430 (O-H), 3009 (C-H), 2923 (C-H), 1686 (C=O), 1514, 1387, 1103, 1056, 815. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{13}H_{16}O_2Na^+$, 227.1043; Found, 227.1049.

3-Ethyl-3-hydroxy-1-*p*-tolylpentan-1-one (22c)

83 mg, 75%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.90–7.81 (m, 2H), 7.30–7.24 (m, 2H), 4.14 (s, 1H), 3.06 (s, 2H), 2.41 (s, 3H), 1.65–1.54 (m, 4H), 0.90 (t, *J* = 7.5 Hz, 6H); **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 202.3, 144.7, 135.2, 129.5, 128.3, 74.6, 44.0, 31.4, 21.8, 8.3. **IR** ν_{max} (solid/cm^{-1}) 3473 (O-H), 2966 (C-H), 2936 (C-H), 2880 (C-H), 1663 (C=O), 1605, 1407, 1122, 781. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{14}H_{21}O_2^+$, 221.1542; Found, 221.1540.

1-Cyclohexyl-6,6-diethoxy-1-hydroxyhexan-3-one (23c)

110 mg, 77%, yellow oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.48 (t, *J* = 5.3 Hz, 1H), 3.80 (m, 1H), 3.63 (m, 2H), 3.53–3.43 (m, 2H), 2.93 (d, *J* = 3.6 Hz, 1H), 2.64–2.58 (dd, *J* = 17.1, 2.6 Hz, 1H), 2.53 (m, 3H), 1.91 (td, *J* = 7.2, 5.3 Hz, 2H), 1.84 (m, 1H), 1.79–1.71 (m, 2H), 1.69–1.61 (m, 2H), 1.39–1.31 (m, 1H), 1.27–1.21 (m, 2H), 1.19 (t, *J* = 6.9 Hz, 3H), 1.18 (t, *J* = 6.9 Hz, 3H), 1.15 (m, 1H), 1.02 (m, 2H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 212.2, 102.1, 71.9, 61.9, 61.8, 46.5, 43.2, 38.5, 29.0, 28.4, 27.7, 26.6, 26.3, 26.2, 15.4. **IR** ν_{max} (solid/cm^{-1}) 3463 (O-H), 2971 (C-H), 2926 (C-H), 2853 (C-H), 1706 (C=O), 1484, 1407, 1123, 1058. **HRMS** Found 309.2038, [$C_{16}H_{30}O_4$+Na]$^+$ requires 309.2036. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{16}H_{30}O_4Na^+$, 309.2036; Found, 309.2038.

4-(1-Hydroxy-3-oxoheptyl)benzonitrile (24c)

103 mg, 89%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 (m, 2H), 7.48 (m, 2H), 5.26–5.12 (m, 1H), 3.79–3.56 (br s, 1H), 2.93–2.71 (m, 2H), 2.58–2.37 (m, 2H), 1.60–1.50 (m, 2H), 1.35–1.26 (m, 2H), 0.89 (t, *J* = 7.6 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 211.3, 148.3, 132.5, 126.5, 118.9, 111.5, 69.3, 50.7, 43.5, 25.7, 22.3, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3472 (O-H), 2958 (C-H), 2932 (C-H), 2872 (C-H), 2228 (CN), 1705 (C=O), 1608, 1328, 1124, 832, 566. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{14}H_{17}O_2Na^+$, 254.1158; Found, 254.1148.

1,1-Diethoxy-6-hydroxydodecan-4-one (25c)

106 mg, 74%, yellow oil, **^{1}H NMR** (400 MHz, CDCl$_3$) δ 4.47 (t, *J* = 5.3 Hz, 1H), 4.01 (m, 1H), 3.62 (m, 2H), 3.46 (m, 2H), 2.60 (dd, *J* = 17.2, 2.8 Hz, 1H), 2.55–2.43 (m, 3H), 1.90 (m, 2H), 1.54–1.22 (m, 8H), 1.18 (m, 6H), 0.89–0.84 (m, 3H). **^{13}C{^{1}H} NMR** (151 MHz, CDCl$_3$) δ 211.9, 102.0, 67.9, 61.9, 61.8, 49.3, 38.4, 36.6, 31.9, 29.3, 27.7, 25.5, 22.7, 15.4, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3453 (O-H), 2956 (C-H), 2927 (C-H), 2857 (C-H), 1708 (C=O), 1409, 1373, 1122, 1057. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{16}H_{32}O_4Na^+$, 311.2193; Found, 311.2197.

1-Hydroxy-1-(naphthalen-1-yl)heptan-3-one (26c)[55]

88 mg, 69%, colourless oil, **^{1}H NMR** (600 MHz, CDCl$_3$) δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.94–7.87 (m, 1H), 7.78 (t, *J* = 8.8 Hz, 1H), 7.69 (d, *J* = 7.1 Hz, 1H), 7.60–7.44 (m, 3H), 5.96 (dt, *J* = 8.4, 2.9 Hz, 1H), 3.47 (d, *J* = 3.1 Hz, 1H), 3.09–2.85 (m, 2H), 2.59–2.40 (m, 2H), 1.73–1.53 (m, 2H), 1.42–1.27 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, CDCl$_3$) δ 212.0, 138.5, 133.9, 130.0, 129.2, 128.2, 126.3, 125.7, 125.7, 123.1, 122.9, 67.0, 50.5, 43.6, 25.8, 22.4, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3451 (O-H), 2957 (C-H), 2931 (C-H), 2872 (C-H), 1706 (C=O), 1264, 1050, 800, 778.

1-((*tert*-Butyldimethylsilanyl)oxy)-5-hydroxy-5-methylnon-8-en-3-one (27c)

81 mg, 54%, colourless oil, **^{1}H NMR** (400 MHz, CDCl$_3$) δ 5.80 (m, 1H), 4.98 (m, 2H), 3.88 (m, 2H), 3.82 (s, 1H), 2.68 (d, *J* = 17.1 Hz, 1H), 2.61 (m, 3H), 2.15–2.07 (m, 2H), 1.62–1.53 (m, 2H), 1.21 (s, 3H), 0.87 (s, 9H), 0.05 (s, 6H). **^{13}C{^{1}H} NMR** (176 MHz, CDCl$_3$) δ 212.4, 138.8, 114.6, 71.7, 58.8, 52.9, 47.4, 41.3, 28.4, 26.9, 26.0, 18.4, -5.4. **IR** ν_{max} (solid/cm^{-1}) 3498 (O-H), 2955 (C-H), 2930 (C-H), 2857 (C-H), 1702 (C=O), 1375, 1331, 1125, 835, 812. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{16}H_{32}O_3SiNa^+$, 323.2013; Found, 323.2014.

Ethyl 3-hydroxy-5-oxo-5-*p*-tolylpentanoate (28c)

97 mg, 77%, yellow solid, mp 86-87 °C **^{1}H NMR** (700 MHz, CDCl$_3$) δ 7.86 (d, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 4.65 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.61 (s, 1H), 3.24–3.16 (m, 2H), 2.62 (d, *J* = 6.4 Hz, 2H), 2.42 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H} NMR** (176 MHz, CDCl$_3$) δ 199.3, 172.0, 144.7, 134.3, 129.5, 128.4, 64.9, 60.9, 44.2, 41.0, 21.8, 14.3. **IR** ν_{max} (solid/cm^{-1}) 3451 (O-H), 2975 (C-H), 2957 (C-H), 2855 (C-H), 1731 (C=O), 1679 (C=O), 1606 (C=C), 1407, 1181, 1059, 810. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{14}H_{18}O_4Na^+$, 273.1097; Found, 274.1096.

6,6-Diethoxy-1-(2-fluorophenyl)-1-hydroxyhexan-3-one (29c)

125 mg, 84%, yellow oil, **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.58–7.48 (m, 1H), 7.26–7.20 (m, 1H), 7.15 (td, *J* = 7.5, 1.1 Hz, 1H), 7.06–6.94 (m, 1H), 5.44 (m, 1H), 4.48 (t, *J* = 5.3 Hz, 1H), 3.70–3.54 (m, 3H), 3.54–3.42 (m, 2H), 2.91 (dd, *J* = 17.4, 2.9 Hz, 1H), 2.81 (dd, *J* = 17.4, 9.2 Hz, 1H), 2.64–2.46 (m, 2H), 1.92 (m, 2H), 1.18 (m, 6H). **^{13}C{^{1}H} NMR** (101 MHz, CDCl$_3$) δ 211.0, 159.4 (d, J_{C-F} = 245.4 Hz), 129.9 (d, J_{C-F} = 13.1 Hz), 129.0 (d, J_{C-F} = 8.2 Hz), 127.3 (d, J_{C-F} = 4.3 Hz), 124.4 (d, J_{C-F} = 3.4 Hz), 115.2 (d, J_{C-F} = 21.5 Hz), 102.0, 64.3 (d, J_{C-F} = 2.8 Hz), 61.8, 61.8, 49.8, 38.2, 27.7, 15.3. **IR** ν_{max} (solid/cm^{-1}) 3433 (O-H), 2974 (C-H), 2930 (C-H), 2897 (C-H), 1710 (C=O), 1487, 1372, 1119, 1055, 757. **HRMS** (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd for $C_{16}H_{23}NFO_4Na^+$, 321.1473; Found, 321.1480.

Preparation of Aminoketones

The corresponding propargylic alcohol (0.5 mmol, 1 equiv) was dissolved in a mixture of toluene:MeOH (98:2, 0.5 mL), and PPh_3AuNTf_2 (8 mg, 2 mol%) was added into the reaction mixture. The mixture was stirred for 5 h and then the corresponding amine (0.5 mmol, 1 equiv.) was added and the reaction heated to 50 °C overnight. The solvent was removed in vacuo and the product was purified by column chromatography (EtOAc/Petrol).

7-(Phenylamino)tridecan-5-one (1da)

131 mg, 91%, pale brown oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19–7.02 (m, 2H), 6.75–6.66 (m, 1H), 6.59 (m, 2H), 3.96–3.77 (m, 1H), 3.67 (s, 1H), 2.67 (dd, *J* = 16.3, 5.0 Hz, 1H), 2.55 (dd, *J* = 16.3, 6.5 Hz, 1H), 2.38 (t, *J* = 7.4 Hz, 2H), 1.53 (m, 4H), 1.36–1.17 (m, 10H), 0.88 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.0, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 210.7, 147.4, 129.5, 117.5, 113.5, 49.9, 47.1, 43.6, 35.4, 31.9, 29.3, 26.4, 25.8, 22.7, 22.4, 14.2, 14.0. **IR** ν_{max} (solid/cm^{-1}) 3367 (N-H), 2924 (C-H), 2854 (C-H), 1704 (C=O), 1599 (C=C), 1498 (C=C), 746. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{32}NO^+$, 290.2478; Found, 290.2478.

7-((4-Fluorophenyl)amino)tridecan-5-one (1db)

133 mg, 87%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.89–6.84 (m, 2H), 6.56–6.51 (m, 2H), 3.79–3.71 (m, 1H), 2.63 (dd, *J* = 16.4, 5.2 Hz, 1H), 2.55 (dd, *J* = 16.4, 6.2 Hz, 1H), 2.38 (t, *J* = 7.4 Hz, 2H), 1.59–1.49 (m, 4H), 1.32–1.22 (m, 10H), 0.88 (t, *J* = 7.0 Hz, 3H), 0.87 (t, *J* = 7.1, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 210.7, 155.9 (d, $J_{C\text{-}F}$ = 245.0 Hz) 143.8 (d, $J_{C\text{-}F}$ = 1.5 Hz), 115.9 (d, $J_{C\text{-}F}$ = 22.3 Hz), 114.5 (d, $J_{C\text{-}F}$ = 7.4 Hz), 50.9, 46.9, 43.7, 35.3, 31.9, 29.3, 26.4, 25.8, 22.7, 22.4, 14.2, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3361 (N-H), 2915 (C-H), 2822 (C-H), 1703 (C=O), 1601 (C=C), 1517 (C=C), 746. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{31}FNO^+$, 308.2384; Found, 308.2385.

7-((3,5-Dimethylphenyl)amino)tridecan-5-one (1dc)

150 mg, 95%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.35 (s, 1H), 6.23 (s, 2H), 3.80 (m, 1H), 3.59 (br s, 1H), 2.65 (dd, *J* = 16.3, 4.8 Hz, 1H), 2.54 (dd, *J* = 16.3, 6.8 Hz, 1H), 2.39 (m, 2H), 2.22 (s, 6H), 1.52 (m, 4H), 1.30 (m, 10H), 0.89 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.2, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 210.8, 147.4, 139.1, 119.5, 111.4, 49.9, 47.2, 43.6, 35.4, 31.9, 29.3, 26.3, 25.9, 22.7, 22.4, 21.6, 14.2, 14.0. **IR** ν_{max} (solid/cm^{-1}) 3387 (N-H), 2952 (C-H), 2853 (C-H), 1704 (C=O), 1597 (C=C), 1463 (C=C), 819. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{36}NO^+$, 318.2791; Found, 318.2797.

7-((4-Methoxyphenyl)amino)tridecan-5-one (1dd)

Propargylic alchohol **1a** (98 mg, 0.5 mmol, 1 equiv) was dissolved in a mixture of toluene:MeOH (98:2, 0.5 mL), and PPh_3AuNTf_2 (8 mg, 2 mol%) was added into the reaction mixture. The mixture was stirred for 5 h and then filtered through a silica pad. The solvent was removed in vacuo and anisidine (62 mg, 0.5 mmol, 1 equiv.) was added and the mixture was dissolved in toluene (0.2 mL) and heated to 50 °C overnight. The solvent was removed in vacuo and the product was purified by column chromatography (EtOAc/Petrol) to give the amino ketone.

149 mg, 94%, colourless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.86–6.68 (m, 2H), 6.63–6.52 (m, 2H), 3.73 (s, 3H), 3.71 (m, 1H), 2.63 (dd, *J* = 16.2, 5.2 Hz, 1H), 2.53 (dd, *J* = 16.2, 6.4 Hz, 1H), 2.37 (t, *J* = 7.4 Hz, 2H), 1.60–1.46 (m, 4H), 1.37–1.22 (m, 10H), 0.87 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 7.2, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 210.9, 152.3, 141.5, 115.2, 115.0, 55.9, 51.2, 47.0, 43.6, 35.3, 31.8, 29.3, 26.3, 25.8, 22.7, 22.3, 14.1, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3365 (N-H), 2925 (C-H), 1703 (C=O), 1508 (C=C), 1462 (C=C), 1233. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{20}H_{34}NO_2^+$, 320.2584; Found, 320.2587.

7-((3-(Trifluoromethyl)phenyl)amino)tridecan-5-one (1df)

126 mg, 71%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.23 (t, *J* = 7.9 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.77 (s, 1H), 6.73 (dd, *J* = 8.2, 2.0 Hz, 1H), 3.97 (br s, 1H), 3.86–3.77 (m, 1H), 2.66 (dd, *J* = 16.6, 5.0 Hz, 1H), 2.59 (dd, *J* = 16.6, 6.1 Hz, 1H), 2.39 (t, *J* = 7.4 Hz, 2H), 1.61–1.49 (m, 4H), 1.35–1.22 (m, 10H), 0.89 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.1, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 210.4, 147.6, 131.8 (q, $J_{C\text{-}F}$ = 31.6 Hz), 129.9, 124.4 (q, $J_{C\text{-}F}$ = 272.4 Hz), 116.1, 113.8 (q, $J_{C\text{-}F}$ = 3.9 Hz), 109.5 (q, $J_{C\text{-}F}$ = 3.9 Hz), 49.8, 46.6, 43.7, 35.2, 31.8, 29.3, 26.4, 25.8, 22.7, 22.4, 14.1, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3378 (N-H), 2925 (C-H), 2855 (C-H), 1704 (C=O), 1612 (C=C), 1339 (C=C), 1119. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{20}H_{31}F_3NO^+$, 358.2353; Found, 358.2352.

7-(*o*-Tolylamino)tridecan-5-one (1dg)

80 mg, 53%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.10 (t, *J* = 8.3 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.66–6.57 (m, 2H), 3.91–3.83 (m, 1H), 2.70 (dd, *J* = 16.4, 4.8 Hz, 1H), 2.60 (dd, *J* = 16.4, 6.6 Hz, 1H), 2.40–2.37 (m, 2H), 2.12 (s, 3H), 1.62–1.57 (m, 2H), 1.57–1.49 (m, 2H), 1.35–1.23 (m, 10H), 0.89 (t, *J* = 7.3, 3H), 0.88 (t, *J* = 7.3, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 210.8, 145.2, 130.4, 127.3, 122.3, 116.8, 110.1, 49.6, 47.0, 43.7, 35.4, 31.9, 29.3, 26.4, 25.8, 22.7, 22.4, 17.7, 14.2, 14.0. **IR** ν_{max} (solid/cm^{-1}) 3369 (N-H), 2924 (C-H), 2871 (C-H), 1705 (C=O), 1587 (C=C), 1489 (C=C), 767. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{20}H_{34}NO^+$, 304.2635; Found, 304.2639.

7-(Quinolin-6-ylamino)tridecan-5-one (1dj)

86 mg, 51%, pale brown oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.59 (dd, *J* = 4.2, 1.5 Hz, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.28–7.20 (m, 1H), 7.05 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.69 (d, *J* = 2.5 Hz, 1H), 3.98–3.92 (m, 1H), 2.73 (dd, *J* = 16.6, 4.8 Hz, 1H), 2.63 (dd, *J* = 16.6, 6.4 Hz, 1H), 2.43–2.34 (m, 2H), 1.64–1.58 (m, 2H), 1.56–1.49 (m, 2H), 1.43 (m, 1H), 1.34–1.21 (m, 9H), 0.89 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.3, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 210.6, 146.3, 145.3, 143.3, 133.9, 130.5, 130.3, 121.8, 121.5, 103.5, 49.9, 46.7, 43.8, 35.3, 31.9, 29.3, 26.4, 25.8, 22.69, 22.4, 14.2, 13.9. **IR** ν_{max} (solid/cm^{-1}) 3380 (N-H), 2952 (C-H), 2923 (C-H), 1703 (C=O), 1620 (C=C), 1517 (C=C), 1377, 826. **HRMS** (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{22}H_{33}N_2O^+$, 341.2587; Found, 341.2584.

1-Phenyl-3-(phenylamino)nonan-1-one (5da)

143 mg, 93%, colourless oil, ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.92 (m, 2H), 7.59–7.51 (m, 1H), 7.50–7.42 (m, 2H), 7.20–7.13 (m, 2H), 6.74–6.66 (m, 1H), 6.62 (m, 2H), 4.03 (m, 1H), 3.77 (br s, 1H), 3.24 (dd, *J* = 16.6, 4.4 Hz, 1H), 3.13 (dd, *J* = 16.6, 6.9 Hz, 1H), 1.75–1.54 (m, 2H), 1.47 (m, 1H), 1.39 (m, 1H), 1.32–1.20 (m, 6H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}**C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 199.7, 147.4, 137.4, 133.3, 129.5, 128.8, 128.2, 117.5, 113.5, 50.2, 42.9, 35.6, 31.9, 29.4, 26.5, 22.7, 14.2. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{28}NO^+$, 310.2165; Found, 310.2168.

1-Phenyl-3-(phenylamino)propan-1-one (7da)[59]

82 mg, 73%, colourless oil, ^{1}**H NMR** (700 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 2H), 6.71 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 2H), 3.62 (t, *J* = 6.0 Hz, 2H), 3.29 (t, *J* = 6.0 Hz, 2H). ^{13}**C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 199.5, 147.9, 136.9, 133.5, 129.5, 128.8, 128.2, 117.7, 113.2, 38.9, 37.8. **IR** ν_{max} (solid/cm^{-1}) 3403 (N-H), 3051 (C-H), 1675 (C=O), 1598 (C=C), 1504 (C=C), 1446.

1-Cyclohexyl-1-(phenylamino)heptan-3-one (14da)

127 mg, 89%, yellow oil; ^{1}**H NMR** (700 MHz, $CDCl_3$) δ 7.14 (m, 2H), 6.65 (t, *J* = 6.8 Hz, 1H), 6.58 (d, *J* = 7.9 Hz, 2H), 3.72 (m, 1H), 2.62 (dd, *J* = 16.2, 5.0 Hz, 1H), 2.56 (dd, *J* = 16.2, 6.3 Hz, 1H), 2.38 (t, *J* = 7.4 Hz, 2H), 2.05-1.86 (m, 2H), 1.75 (m, 3H), 1.68–1.61 (m, 3H), 1.50 (m, 3H), 1.26 (m, 3H), 1.23–1.15 (m, 1H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}**C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 210.8, 147.8, 129.5, 117.2, 113.3, 54.7, 44.8, 43.4, 42.1, 29.7, 29.6, 26.6, 26.4, 25.9, 22.4, 14.0. **IR** ν_{max} (solid/cm^{-1}) 3492 (O-H), 2921 (C-H), 2849 (C-H), 1702 (C=O), 1598 (C=C), 1446 (C=C), 745. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{30}NO^+$, 288.2322; Found, 288.2329.

1,1-Diethoxy-6-(phenylamino)dodecan-4-one (25da)

93 mg, 51%, colourless oil, ^{1}**H NMR** (700 MHz, $CDCl_3$) δ 7.15 (t, *J* = 7.4 Hz, 2H), 6.67 (t, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 7.9 Hz, 2H), 4.45 (t, *J* = 5.2 Hz, 1H), 3.85–3.79 (m, 1H), 3.65 (br s, 1H), 3.63–3.56 (m, 2H), 3.49–3.40 (m, 2H), 2.67 (dd, *J* = 16.2, 5.0 Hz, 1H), 2.58 (dd, *J* = 16.2, 6.3 Hz, 1H), 2.49 (t, *J* = 7.2 Hz, 2H), 1.86 (m, 2H), 1.53 (m, 2H), 1.44–1.37 (m, 1H), 1.27 (m, 9H), 1.17 (t, *J* = 7.0 Hz, 6H), 0.86 (t, *J* = 6.8 Hz, 3H). ^{13}**C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 209.9, 147.4, 129.5, 117.5, 113.5, 102.1, 61.8, 50.0, 47.27, 38.6, 35.4, 31.9, 29.4, 27.6, 26.4, 22.7, 15.4, 14.2. **IR** ν_{max} (solid/cm^{-1}) 3355 (N-H), 2914 (C-H), 2848 (C-H), 1698 (C=O), 1595 (C=C), 1469 (C=C), 1367, 1054 746. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{38}NO_3^+$, 290.2478; Found, 290.2478.

Preparation of Heterocycles

The corresponding propargylic alcohol (0.5 mmol, 1 equiv.) and aniline (0.5 mmol, 1 equiv.) were dissolved in $CHCl_3$ (0.5 mL) and oven-dried molecular sieves were added to the mixture followed by PPh_3AuNTf_2 (8 mg, 2 mol%). The reaction was stirred at room temperature until completion (TLC). Once the reaction was complete, Et_2O (1 mL) and $NaCNBH_3$ (62 mg, 1 mmol, 2 equiv.) were added and the reaction was stirred for 2 h at 0 °C. After this time the mixture was filtered and the solvent removed in vacuo. The residue was dissolved in CH_2Cl_2:TFA (50:1, 2.5 mL) and $NaBH_4$ (46 mg, 1.25 mmol, 2.5 equiv.)

was added. The solution was stirred overnight. The reaction was then quenched with NH_4Cl and extracted with Et_2O. The organic layer was concentrated in vacuo and the product was purified by column chromatography (EtOAc/Petrol).

2-Methyl-1-(1-phenylpyrrolidin-2-yl)propan-2-ol (6ea)

After aniline addition the reaction was stirred for 18h.
78 mg, 73%, colourless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 8.5, 7.3 Hz, 2H), 6.66 (m, 3H), 4.00–3.92 (m, 1H), 3.40 (m, 1H), 3.20–3.07 (m, 1H), 2.08–1.97 (m, 4H), 1.85 (d, *J* = 14.4 Hz, 1H), 1.48 (dd, *J* = 14.4, 10.3 Hz, 1H), 1.36 (s, 3H), 1.31 (s, 3H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 147.1, 129.4, 115.4, 112.2, 71.0, 54.9, 47.9, 45.7, 32.5, 30.6, 30.5, 23.4. **IR** ν_{max} (solid/cm^{-1}) 3405 (O-H), 2965 (C-H), 2928 (C-H), 1705, 1596 (C=C), 1504 (C=C), 1360, 745, 693. **HRMS** (ESI-TOF) *m/z*: $[M]^+$ Calcd for $C_{14}H_{21}NO^+$, 219.1618; Found, 219.1617.

1-(1-(4-Methoxyphenyl)pyrrolidin-2-yl)-2-methylpropan-2-ol (6ed)

After aniline addition the reaction was stirred for 48h.
93 mg, 75%, colourless oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.93–6.80 (m, 2H), 6.66 (d, *J* = 9.0 Hz, 2H), 3.93–3.85 (m, 1H), 3.75 (s, 3H), 3.46–3.35 (m, 1H), 3.11–3.05 (m, 1H), 2.10–1.93 (m, 4H), 1.88–1.81 (m, 1H), 1.50–1.43 (m, 1H), 1.33 (s, 3H), 1.30 (s, 3H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 151.1, 142.5, 115.2, 113.7, 71.0, 56.1, 55.7, 48.9, 46.0, 32.6, 30.8, 30.4, 23.6. **IR** ν_{max} (solid/cm^{-1}) 3420 (O-H), 2965 (C-H), 2929 (C-H), 1708, 1611 (C=C), 1512 (C=C), 1364, 1275, 813. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{24}NO_2^+$, 250.1802; Found, 250.1804.

2-Methyl-1-(1-(3-(trifluoromethyl)phenyl)pyrrolidin-2-yl)propan-2-ol (6ef)

After aniline addition the reaction was stirred for 48h.
95 mg, 67%, colourless oil, **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.93–6.80 (m, 2H), 6.66 (d, *J* = 9.0 Hz, 2H), 3.93–3.85 (m, 1H), 3.75 (s, 3H), 3.46–3.35 (m, 1H), 3.11–3.05 (m, 1H), 2.10–1.93 (m, 4H), 1.88–1.81 (m, 1H), 1.50–1.43 (m, 1H), 1.33 (s, 3H), 1.30 (s, 3H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 146.9, 131.5 (q, J_{C-F} = 31.3 Hz), 129.6, 124.8 (q, J_{C-F} = 272.4 Hz), 115.0, 111.6 (q, J_{C-F} = 3.3 Hz), 108.5 (q, J_{C-F} = 3.8 Hz), 71.0, 55.7 48.9, 46.0, 32.6, 30.8, 30.4, 23.6. **IR** ν_{max} (solid/cm^{-1}) 3434 (O-H), 2969 (C-H), 2930 (C-H), 1710, 1609 (C=C), 1458 (C=C), 1161, 1119, 698. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{21}F_3NO^+$, 288.1570; Found, 288.1570.

1-(2-Fluorophenyl)-2-(1-phenylpyrrolidin-2-yl)ethan-1-ol (29ea)

After aniline addition the reaction was stirred for 48h.
78 mg, 55%, colourless oil, only one diastereoisomer was observed. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.56–7.49 (m, 1H), 7.25–7.21 (m, 3H), 7.16–7.12 (m, 1H), 7.04–6.99 (m, 1H), 6.69 (m, 2H), 6.67 (m, 1H), 5.17–5.10 (m, 1H), 4.14 (m, 1H), 3.41 (m, 1H), 3.21–3.14 (m, 1H), 2.21–2.16 (m, 1H), 2.09–2.00 (m, 4H), 1.99–1.93 (m, 1H), 1.61–1.58 (m, 1H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 159.5 (d, J_{C-F}= 244.9 Hz), 147.3, 132.1 (d, J_{C-F} = 13.2 Hz), 129.4, 129.0 (d, J_{C-F} = 8.2 Hz), 127.0 (d, *J* = 4.3 Hz), 124.5 (d, *J* = 3.4 Hz), 115.6, 115.4

(d, J = 21.7 Hz), 112.1, 66.7, 55.8, 48.2, 41.2, 30.5, 23.4. **IR** ν_{max} (solid/cm^{-1}) 3397 (O-H), 2958 (C-H), 2928 (C-H), 1710, 1642 (C=C), 1554 (C=C), 1454, 756. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{21}FNO^+$, 286.1602; Found, 286.1602.

(*R*,*S*)-2-(4-Chlorophenyl)-1-((*R*,*S*)-1-phenylpyrrolidin-2-yl)propan-2-ol (30ea)

After aniline addition the reaction was stirred for 48h.
99 mg, 63%, colourless oil, only one diastereoisomer was observed. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.46–7.37 (m, 2H), 7.35–7.30 (m, 2H), 7.24–7.11 (m, 2H), 6.66 (t, J = 7.3 Hz, 1H), 6.62–6.50 (m, 2H), 3.94–3.84 (m, 1H), 3.39–3.32 (m, 1H), 3.07 (td, J = 9.0, 7.4 Hz, 1H), 2.11 (dd, J = 14.4, 2.3 Hz, 1H), 1.95–1.80 (m, 2H), 1.76 (dd, J = 14.4, 9.3 Hz, 1H), 1.63 (s, 3H), 1.62–1.55 (m, 2H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 147.4, 146.5, 132.7, 129.3, 128.5, 126.6, 116.0, 112.7, 74.2, 54.8, 48.3, 46.8, 31.6, 31.6, 23.3. **IR** ν_{max} (solid/cm^{-1}) 3406 (O-H), 2966 (C-H), 2925 (C-H), 1712, 1597 (C=C), 1504 (C=C), 1363, 748. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{23}NOCl^+$, 316.1463; Found, 316.1465.

2-Methyl-1-(1-phenylpiperidin-2-yl)propan-2-ol (31ea)

After aniline addition the reaction was stirred for 18h.
82 mg, 71%, colourless oil, **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2H), 7.03 (br d, J = 8.0 Hz, 2H), 6.83 (d, J = 7.3 Hz, 1H), 4.24–4.16 (m, 1H), 3.70 (br s, 1H), 3.51–3.46 (m, 1H), 3.42–3.30 (m, 1H), 2.26 (dd, J = 14.6, 9.7 Hz, 1H), 1.92–1.83 (m, 1H), 1.73 (m, 1H), 1.63 (m, 2H), 1.55–1.38 (m, 3H), 1.25 (s, 3H), 1.23 (s, 3H). **^{13}C{^{1}H} NMR** (176 MHz, $CDCl_3$) δ 150.4, 129.4, 119.4, 117.5, 70.8, 53.1, 43.4, 40.7, 31.2, 29.2, 28.1, 23.2, 19.9. **IR** ν_{max} (solid/cm^{-1}) 3393 (O-H), 2967 (C-H), 2927 (C-H), 1596 (C=C), 1498 (C=C), 1154, 1092, 752, 692. **HRMS** Found 234.1851, $[C_{15}H_{23}NO+H]^+$ requires 234.1852. **HRMS** (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{24}NO^+$, 234.1852; Found, 232.1851.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

We would like to thank the Leverhulme Trust for providing a grant (RPG-2017-221) to support this work.

Supporting Information

Complete optimization tables, details of computational methods and coordinates for all calculated intermediates, chiral HPLC traces for compounds **(*S*)-9c** and **(1*S*,3*R*)-9bd**, and ^{1}H and ^{13}C spectra for all compounds.

Notes and references

[‡] All propargylic alcohols are numbered as **Na**, and all other compounds are labelled with the number of the propargylic alcohol from which they are derived. Thus, all aminoalcohols are numbered **NbX** (where X is a letter used to denote the nitrogen substituent derived from the aniline), all 3-hydroxyketones **Nc**,

all 3-aminoketones **NdX**, and all saturated heterocycles **NeX** (where X in all cases denotes the nitrogen substituent derived from the aniline).

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