

Gold- and Silver-Catalyzed Reactions of Propargylic Alcohols in the Presence of Protic Additives

Matthew N. Pennell,^[a] Peter G. Turner,^[b] and Tom D. Sheppard*^[a]

Abstract: A wide range of primary, secondary and tertiary propargylic alcohols undergo a Meyer–Schuster rearrangement to give enones at room temperature in the presence of a gold(I) catalyst and small quantities of MeOH or 4-methoxyphenylboronic acid. The syntheses of the enone natural products isoeogonaketone and daphenone were achieved using this reaction as the key step. The rearrangement of primary

propargylic alcohols can readily be combined in a one-pot procedure with the addition of a nucleophile to the resulting terminal enone, to give β -aryl, β -alkoxy, β -amino or β -sulfido ketones.

Keywords: gold • homogeneous catalysis • Meyer–Schuster rearrangement • propargylic alcohols • silver

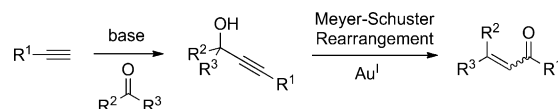
Propargylic alcohols bearing an adjacent electron-rich aryl group can also undergo silver-catalyzed substitution of the alcohol with oxygen, nitrogen and carbon nucleophiles. This latter reaction was initially observed with a batch of gold catalyst that was probably contaminated with small quantities of silver salt.

Introduction

α,β -Unsaturated carbonyl compounds are important building blocks in organic synthesis and are commonly used as substrates in a wide variety of transformations including Michael additions,^[1] Diels–Alder reactions,^[2] cyclopropanations^[3] and a wide variety of organocatalytic processes.^[4] This diversity in application makes them common intermediates in the total synthesis of natural products and the synthesis of drug molecules. Traditionally α,β -unsaturated carbonyl compounds are synthesised by aldol condensation reactions, or by a Wittig,^[5] Horner–Wadsworth–Emmons^[6] or Petersen^[7] olefination reaction. The Meyer–Schuster rearrangement^[8,9] of a propargylic alcohol can provide a convenient alternative to these processes, which avoids the production of stoichiometric by-products such as phosphorous oxides.

The required propargylic alcohol can readily be synthesised through an alkynyl anion addition to an aldehyde or ketone, typically a high yielding process that is also highly

effective even with sterically hindered carbonyls. This two-step process can therefore offer a highly attractive method to synthesise α,β -unsaturated carbonyl compounds (Scheme 1).



Scheme 1. Convenient access to α,β -unsaturated carbonyl compounds.

The classical Meyer–Schuster rearrangement involves heating the alcohol with strong acid, and is hence incompatible with many functional groups.^[8] However, more recently a number of highly effective metal-catalysed methods for achieving this reaction have been reported.^[10–14] The emergence of Au^I catalysis^[15] in particular has revived this reaction, and conditions have been developed that enable the rearrangement to take place under very mild conditions. The first reports required the alcohol to be converted to the corresponding acetate derivative,^[11] but more recently procedures have been developed for the direct rearrangement of the alcohols themselves.^[12] We have previously reported that carrying out the Au-catalyzed rearrangement in a non-coordinating solvent, in the presence of one equivalent of methanol, greatly accelerates the reaction.^[14]

Herein, we report on the full scope of this room temperature Meyer–Schuster rearrangement with regard to the rearrangement of secondary and tertiary propargylic alcohols, and its application to the synthesis of the natural products isoeogonaketone and daphenone. We also report convenient one-pot procedures for the direct conversion of primary propargylic alcohols into β -arylketones, β -alkoxyketones, β -

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aminoketones and β -sulfidoketones via intermediate terminal enones. During the course of these studies it was observed that propargylic substitution reactions of electron-rich propargylic alcohols took place in some cases. This interesting side reaction, which works with a wide range of oxygen, carbon and nitrogen nucleophiles, was shown to be mediated by silver salts, probably present as impurities in some batches of the gold catalyst.

Results and Discussion

Rearrangement of secondary propargylic alcohols: In our preliminary experiments we quickly identified that the Au-

catalyzed Meyer–Schuster rearrangement was more efficient using a cationic gold catalyst^[16] in non-polar solvents in the presence of a small quantity of a protic additive (either a boronic acid or methanol).^[14] A wide range of secondary propargylic alcohols underwent a Meyer–Schuster rearrangement at room temperature upon treatment with Au^I catalyst (2 mol %) and MeOH (1 equiv) in PhMe as the solvent (Table 1). In nearly all cases the enone was obtained as the pure *E* isomer after purification (see the Supporting Information).

A variety of alkyl, alkenyl and aryl substituents at R¹ on the alkyne were tolerated (Table 1, entries 1–7) and the reaction could be run on a 1 g scale without difficulty with only 1 mol % Au catalyst (entry 1). An alkoxy group could

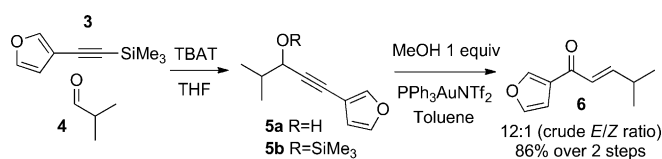
Table 1. Meyer–Schuster rearrangement of secondary propargylic alcohols.

Entry	Propargylic Alcohol	Enone	Yield [%] (<i>E/Z</i>) ^[a]	Entry	Propargylic Alcohol	Enone	Yield [%] (<i>E/Z</i>) ^[a]
1			91 83 ^[b] (17:1)	12			78 (18:1)
2			80 ^[c] (14:1)	13			96 (19:1)
3			43 (7:1)	14			99 (12:1)
4			99 (8:1)	15			15 (8:1)
5			97 (18:1)	16			84 (7:1)
6			99 (6:1)	17			85 (5:1)
7			88 (11:1)	18			98 (13:1)
8			91 ^[d] (20:1)	19			92 (5:1)
9			96 (20:1)	20			93 (24:1)
10			98 (18:1)	21			87 (10:1)
11			77 (15:1)	22			84 (3:2) ^[e]

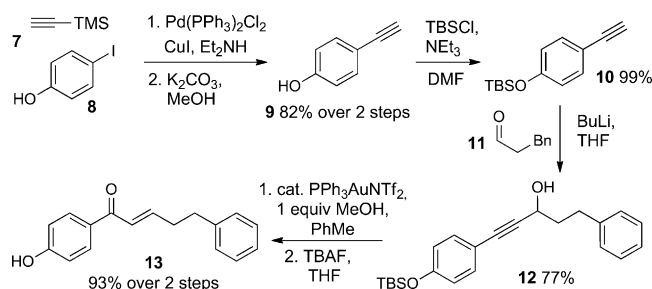
[a] *E/Z* ratio measured by crude ¹H NMR spectroscopy. [b] 1 g scale with 1 mol % catalyst. [c] 16 h at room temperature. [d] EtOH was used instead of MeOH. [e] Crude *E,E/E,Z* ratio, after chromatography the pure *E/Z* isomer was obtained. Bn = benzyl.

be incorporated to give access to an α,β -unsaturated ester (Table 1; entry 8). Compounds containing both electron-rich aromatic groups (Table 1, entry 6) and electron-deficient aromatic groups (Table 1, entry 5) at R^1 rearranged smoothly, as did a substrate containing a thiophene ring (Table 1, entry 7). The sterically congested substrate containing a tertiary butyl substituent (Table 1, entry 2) rearranged to the corresponding enone in very good yield, but required a prolonged reaction time of 16 h. A substrate containing a conjugated alkene at R^1 (Table 1, entry 3) gave a lower yield, but this probably reflects the relative instability of the dienone product **2c** rather than the yield of the reaction itself. A variety of substituents could also be incorporated at the R^2 position (Table 1, entries 9–15). Benzylic alcohols rearrange efficiently (Table 1, entries 9–17) with substrates containing electron-deficient (Table 1, entry 11–13) or moderately electron-donating (Table 1, entry 10) substituents giving excellent yields. Although the electron-rich alcohol **1n** gave the corresponding enone **2n** in excellent yield, dimethylaniline **1o** gave only a 15% yield of the corresponding enone **2o**. This may be due to the presence of the coordinating nitrogen atom, which can potentially interfere with the gold catalyst (see below). Propargylic alcohols containing electron-rich heterocycles gave the corresponding enones in good yield (Table 1, entries 16 and 17), and there was no evidence for the Au-catalyzed reaction of the electron-rich heterocycle with the pendant enone in the product.^[17] Further combinations of substituents could also be incorporated (Table 1, entries 18–22) including cyclopropanes (**1r** and **1v**), which did not undergo ring-opening during the rearrangement reaction. The dienone **2v** (Table 1, entry 22) can be generated in excellent yield from the corresponding propargylic alcohol **1v**. Interestingly the initial major product observed from the rearrangement was the *E,E* isomer. However after purification the pure *E,Z* isomer **1v** was obtained cleanly in good yield. Presumably this latter isomer is actually thermodynamically more stable in this case.

Application to natural product synthesis: Isoegomaketone **6** is an essential oil component of *perilla frutescens britt* and has been shown to exhibit anti-inflammatory properties.^[18–19] The natural product **6** was synthesised in two steps by fluoride-mediated addition^[20] of commercially available silyl acetylene **3** to aldehyde **4**, followed by Meyer–Schuster rearrangement of the resulting mixture of alcohol **5a** and its corresponding TMS ether **5b**, with concomitant silyl deprotection. (Scheme 2). The natural product **6** was obtained in 86% overall yield with high *E/Z* selectivity from the two-step sequence.



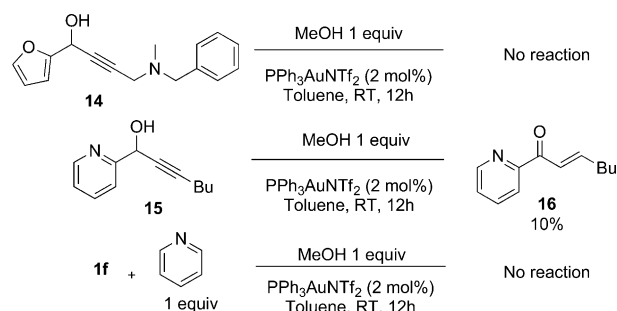
Scheme 2. Two-step synthesis of *E*-isoegomaketone.



Scheme 3. Synthesis of daphenone by a Meyer–Schuster rearrangement.

We also carried out a short synthesis of daphenone **13** (Scheme 3), a natural product isolated from *daphne odora* which showed cytotoxicity against five human tumour cell lines.^[21] Sonogashira coupling of 4-iodophenol (**8**) with trimethylsilyl (TMS)-acetylene (**7**) gave phenol **9**^[22] after desilylation. After protection of the phenol as a silyl ether, the alkyne **10** was lithiated and treated with dihydrocinnamaldehyde **11** to give propargylic alcohol **12**. Meyer–Schuster rearrangement of **12** proceeded cleanly without deprotection of the silyl ether, which was cleaved with fluoride to give the natural product **13** (58% yield over 6 steps from **8**).

Problematic substrates for the Meyer–Schuster rearrangement: As mentioned above, propargylic alcohols containing nitrogen functionality did not undergo efficient Meyer–Schuster rearrangement (Table 1, entry 15 and Scheme 4).



Scheme 4. Attempted Meyer–Schuster rearrangement of nitrogen-containing compounds.

Tertiary amine **14** was completely unreactive, whereas pyridine **15** gave the abnormal rearrangement product **16** in 10% yield. The low reactivity of these substrates is presumably a consequence of the ability of the basic nitrogen atom to coordinate to the Au-catalyst and deactivate it. Addition of one equivalent of pyridine to alcohol **1f** completely inhibited the Meyer–Schuster rearrangement of this otherwise reactive substrate. It should be noted that there are virtually no reports of the Au-catalyzed Meyer–Schuster rearrangement of nitrogen-containing compounds in the literature.^[23]

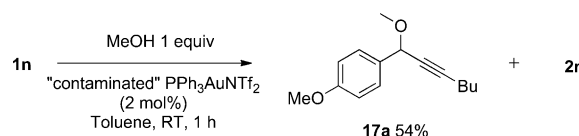
Propargylic substitution reactions: During the course of our evaluation of the substrate scope of the reaction (Table 1),

we initially observed the formation of propargylic substitution product **17a** in 54 % yield when rearrangement of electron-rich alcohol **1n** was attempted, with **2n** being produced as a minor product (Scheme 5). It subsequently transpired that the formation of such products was not reproducible, and appeared to be dependent on the batch of gold catalyst used in the reaction—with a new batch of catalyst the Meyer–Schuster rearrangement proceeded cleanly in good yield (Table 1, entry 14).

We hypothesised that the propargylic substitution reaction was probably mediated by an impurity present in the original batch of gold catalyst.^[24] The most likely candidate seemed to be AgNTf₂,^[25] used during the preparation of the catalyst,^[16] and pleasingly treatment of propargylic alcohol **1n** with AgNTf₂/MeOH in PhMe led to the formation of substitution product **17a** in good yield (Table 2, entry 1). Reaction of alcohol **1n** with HNTf₂/MeOH in PhMe led to a complex mixture of products suggesting that this is not simply an acid-catalyzed process.^[26,27]

These reaction conditions were applied to a range of different nucleophiles to illustrate the scope of the reaction (Table 2). Substitution reactions with oxygen (Table 2, entries 1–3), carbon (Table 2, entries 4–7) and nitrogen nucleophiles (Table 2, entries 8 and 9) were all possible. In the absence of an external nucleophile, dimerisation of the propargylic alcohol took place to form the symmetrical ether as a mixture of diastereoisomers (Table 2, entry 10). The presence of both an alkyne and an electron-rich aromatic ring at R¹ seem to be necessary for the substitution reaction to take place. Propargylic alcohols **1a**, **1f** and **1i** did not react in the presence of AgNTf₂ and MeOH even at 60 °C; similarly, benzhydrol (Ph₂CHOH) and 1-phenylethanol were also unreactive. Note that neither HNTf₂ nor AgNTf₂ were able to mediate the Meyer–Schuster rearrangement of the propargylic alcohols **1a**, **1f** and **1i**, which suggests that an Au catalyst is essential for this reaction.^[27]

It is notable that the Ag-catalyzed substitution reaction must be highly efficient, since it was the dominant reaction pathway in our original experiments, even though the quantity of Ag present as an impurity in the 2 mol % Au-catalyst used must have been very small. We carried out an NMR experiment to determine the relative rates of the silver- and gold-catalyzed reactions (Scheme 6). Treatment of alcohol **1n** with 1 mol % of each of the catalysts in the presence of MeOH (2 equiv) in C₆D₆ gave a 20:1 ratio of substitution product **17a** to Meyer–Schuster rearrangement product **2n** after 10 min at room temperature, illustrating that the substitution reaction is considerably faster than the Meyer–Schuster rearrangement. There are several reports in the literature of metal-catalyzed substitu-

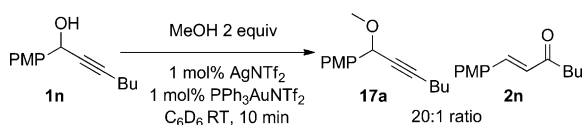


Scheme 5. Substitution of the propargylic alcohol with “contaminated” Au catalyst.

Table 2. Ag-catalyzed substitution reactions of propargylic alcohols.

Entry	Propargylic Alcohol	NuH	Product	Yield [%]
1	1n	MeOH	17a	76
2	1w	MeOH	17b	77
3	1n	BnOH	17c	82
4	1n		17d	77
5	1n		17e	96
6	1n		17f	83
7	1n		17g	98
8	1n	H ₂ NBoc	17h	59 ^[a]
9	1n	H ₂ NTs	17i	74 ^[a]
10	1n	none	17j	80 ^[b]

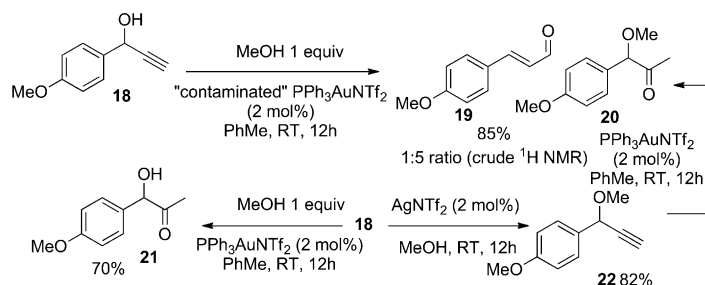
[a] 60 °C overnight. [b] 1.3:1 mixture of diastereoisomers. PMP = 4-methoxyphenyl.



Scheme 6. Competition between the Au and Ag-catalyzed reactions of alcohol **1n**.

tion reactions of alcohols^[25,28] and in light of these results, it is possible that some of these processes may actually be mediated or assisted by trace quantities of Ag-salts that are present, particularly the reactions for which Ag salts have been added as a co-catalyst.^[29] However, it should be noted that Au^{III}-catalyzed substitution reactions have been reported to work with propargylic alcohols that do not contain an electron-rich aromatic substituent.^[28d]

During the course of these investigations, we also explored the rearrangement of terminal propargylic alcohols to see whether it was possible to obtain α,β -unsaturated aldehydes through a Meyer–Schuster rearrangement.^[30] The initial reactions were carried out by treatment of alcohol **18** with the contaminated Au catalyst and gave a mixture of the desired aldehyde **19** and α -methoxyketone **20** (Scheme 7). The latter product is presumably formed by Ag-



Scheme 7. Ag/Au-catalyzed reactions of terminal alkynes in the presence of MeOH.

mediated substitution of the alcohol, followed by Au-catalyzed hydration of the terminal alkyne.^[31] Reaction of **18** with a new batch of catalyst gave α -hydroxyketone **21** as the major product, together with traces of aldehyde **19**. As above (Table 2), treatment of alcohol **18** with catalytic AgNTf₂ in the presence of MeOH gave the substitution product **22** cleanly in good yield. Treatment of **22** with catalytic Au gave ketone **20**, providing evidence that product **20** was formed in our original experiment by two separate steps catalyzed by the two different metals.^[29]

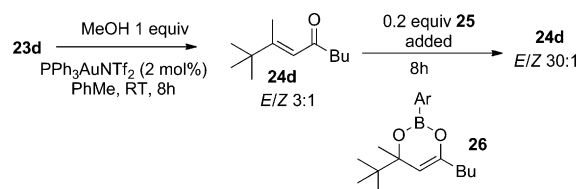
Tertiary propargylic alcohols: Tertiary propargylic alcohols **23** can be easily prepared by addition of alkynyl anions to ketones, and provide access to sterically congested trisubstituted enones **24** upon Meyer–Schuster rearrangement. We were able to demonstrate the formation of a range of symmetrically and unsymmetrically substituted enones **24** in good to excellent yield and with high levels of geometric control in some cases (Table 3). Where there is a large difference in the size of the propargylic substituents, impressive

Table 3. Meyer–Schuster rearrangement of tertiary propargylic alcohols.

Entry	Propargylic Alcohol	Enone	Yield [%] (<i>E/Z</i>) ^[a]
1			24a 75 ^[c]
2			24b 67 (3.5:1) ^[c]
3			24c 78 (2:1) ^[c] 83 (2.3:1) ^[b]
4			24d 74 (3:1) ^[c] 77 (> 30:1) ^[b]
5			24e 72 (1.3:1) ^[c] 83 (2.3:1) ^[b]
6			24f 79 (1.5:1) ^[c] 82 (4.7:1) ^[b]
7			24g 82 ^[c]

[a] Crude ratio determined by ¹H NMR spectroscopy. [b] With 0.2 equiv boronic acid **25**, 16 h at RT. [c] With 1 equiv MeOH, 6 h at RT.

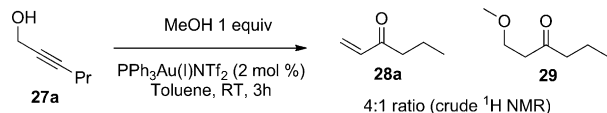
selectivity is observed (Table 3, entry 4), and even when the groups are of similar size moderate selectivity is still obtained (Table 3, entry 2). In general, reactions of tertiary propargylic alcohols were found to be slower than those of secondary propargylic alcohols.



Scheme 8. Enhancement of the *E/Z* ratio by addition of boronic acid **25**.

The use of *p*-methoxyphenyl boronic acid^[13,14,32] **25** rather than MeOH as the reaction additive was found to give higher yields and higher *E/Z* selectivity in many cases, though longer reaction times were necessary. Extending the reaction time with MeOH as the additive did not increase the *E/Z* selectivity however. Interestingly, addition of boronic acid **25** to the 3:1 ratio of enone **24d** obtained from Au/MeOH catalyzed rearrangement, led to further isomerisation of the product to give an enhanced *E/Z* ratio (Scheme 8). This indicates that the boronic acid is involved in the isomerisation of the alkene, possibly through an addition process to give cyclic boronate **26**.

Primary propargylic alcohols: The rearrangement of primary propargylic alcohols should provide a highly effective and mild method for accessing terminal enones. However, during the rearrangement of **27** in the presence of methanol as the additive, some addition of MeOH to enone **28a** was observed to give **29** (Scheme 9).^[12a]



Scheme 9. Meyer–Schuster rearrangement of a primary propargylic alcohols with MeOH as the additive.

Pleasingly, in the presence of boronic acid **25** as an additive, clean rearrangement to the unsubstituted enone **28a** was observed. The reaction provides a mild method for generating highly reactive terminal enones, and the crude product is clean enough to be used directly in further transformations. We therefore developed reaction conditions for the synthesis of a range of functionalised products by addition of nucleophiles to the crude enone, generated in situ from the propargylic alcohol (Table 4). In our preliminary report we outlined how Pd-catalyzed addition of boronic acids^[33] could be used to access β -aryl ketones **30** in moderate to good yield (Table 4, entries 1–4).^[14] β -Alkoxyketones **31** (Table 4, entries 5 and 6), β -aminoketones **32** (Table 4, entries 7–12) and β -sulfidoketones **33** (Table 4, entries 13 and 14) can also be readily prepared by simple one-pot procedures, by addition of the appropriate nucleophile directly to the reaction mixture after the Meyer–Schuster rearrangement reaction is complete.

Conclusion

In the presence of catalytic $\text{PPh}_3\text{AuNTf}_2$ and a protic additive such as MeOH or 4-methoxyphenylboronic acid, the Meyer–Schuster rearrangement of a wide range of propargylic alcohols occurs in generally good to excellent yield. Secondary alcohols rearrange with high selectivity for the *E* isomer of the enone product and tertiary alcohols with moderate to high selectivity. This reaction was employed as a key step in the synthesis of the enone natural products isogomaketone and daphenone. The rearrangement of primary propargylic alcohols can be combined with the addition of carbon, oxygen or nitrogen nucleophiles to the resulting terminal enone to give access to β -substituted ketones in a one-pot procedure. During the course of this work, we also observed that propargylic alcohols bearing an electron-rich aryl group readily undergo substitution of the alcohol, with a variety of oxygen, carbon and nitrogen nucleophiles in the presence of a silver catalyst. This latter reaction was the dominant pathway over the desired Meyer–Schuster rearrangement with a batch of Au^I catalyst that was probably contaminated with Ag^I salts.

Table 4. Rearrangement of primary propargylic alcohols and addition of nucleophiles to the resulting terminal enones.

Entry ^[a]	“Nucleophile”	Product ^[c]		Yield [%]
1	25 /cat. Pd		30a	81
2	25 /cat. Pd		30b	58
3	PhB(OH)_2 /cat. Pd		30c	45
4	<i>o</i> -tolylB(OH) ₂ /cat. Pd		30d	39
5	$\text{BnOH}^{[a]}$		31a	63
6	<i>i</i> PrOH		31b	76
7	HNEt_2		32a	70
8	Bn_2NH		32b	65
9			32c	83
10			32d	79
11			32e	84
12	PhNHMe		32f	52
13	<i>n</i> -hexylSH		33a	41
14	PhSH		33b	46

Experimental Section

All reactions were carried out under an atmosphere of air unless otherwise indicated. Tetrahydrofuran was used following purification from a zeolite drying apparatus. All other chemicals were used as supplied unless otherwise indicated. Column chromatography was carried out using silica gel (40–60 μm) and analytical thin layer chromatography was carried out using aluminium-backed plates coated with silica gel. Components were visualised using combinations of UV light, iodine, ceric ammonium molybdate, phosphomolybdic acid and potassium permanganate. ^1H NMR spectra were recorded at 500 or at 600 MHz in CDCl_3 using residual protic solvent CHCl_3 ($\delta = 7.26$ ppm, s) as the internal standard. Chemical shifts are quoted in ppm using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; qn, quintet; m, multiplet; br, broad or a combination of these. The coupling constants (*J*) are measured in Hertz. ^{13}C NMR spectra were recorded at 125 or 150 MHz in CDCl_3 using the central reference of CHCl_3 ($\delta = 77.0$ ppm, t) as the internal standard.

Meyer–Schuster Rearrangements to give enones 2, 16, and 24

Compounds **2a**, **2b**, **2d**, **2f**, **2r**, **2u**, and **24a–24f** have previously been reported.^[14]

General procedure A (preparation of compounds 2, 6 and 13): [Ph₃PAuNTf₂]₂PhMe (1 mol %) and methanol (1 equiv) or 4-methoxyphenylboronic acid (0.2 equiv) were added to a solution of propargylic alcohol in toluene (10 mL g^{−1}) and the solution stirred magnetically at room temperature until starting material had disappeared (TLC). The solvent was removed in vacuo and the crude product purified by column chromatography.

(E)-1-(Cyclohex-1-en-1-yl)hex-2-en-1-one (2c):^[10c] ¹H NMR (CDCl₃, 600 MHz): δ = 6.91–6.88 (m, 1H), 6.84 (dt, *J* = 15.4, 7.4 Hz, 1H), 6.63 (brd, *J* = 15.4 Hz, 1H), 2.30–2.24 (m, 4H), 2.20 (app q, *J* = 7.4 Hz, 2H), 1.68–1.56 (m, 4H), 1.50 (appsx, *J* = 7.4 Hz, 2H), 0.94 ppm (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 191.6, 147.0, 140.00, 139.96, 125.0, 34.8, 26.3, 23.5, 22.1, 21.7, 21.6, 13.9 ppm; IR (film) $\tilde{\nu}$ = 2962, 2936, 2875, 1711 cm^{−1}; HRMS (EI): *m/z*: calcd for C₁₂H₁₈O: 178.13522 [*M*]; found: 178.13492.

(E)-1-(4-(Trifluoromethyl)phenyl)hex-2-en-1-one (2e): ¹H NMR (CDCl₃, 600 MHz): δ = 8.00 (d, *J* = 8.3 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.12–7.07 (dt, *J* = 15.4, 7.2 Hz, 1H), 6.86–6.83 (brdt, *J* = 15.4, 1.4 Hz, 1H), 2.33 (brqd, *J* = 7.2, 1.5 Hz, 2H), 1.60–1.53 (appsx, *J* = 7.4 Hz, 2H), 0.98 ppm (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 190.2, 151.6, 141.0, 134.0 (q, *J* = 32.5 Hz), 128.9, 125.9, 125.7 (q, *J* = 3.7 Hz), 123.9 (q, *J* = 27.4 Hz), 35.1, 21.5, 13.9 ppm; HRMS (EI): *m/z*: calcd for C₁₃H₁₃OF₃: 242.09130 [*M*]; found: 242.09084.

(E)-1-(Thiophen-3-yl)hex-2-en-1-one (2g): ¹H NMR (CDCl₃, 600 MHz): δ = 8.05 (m, 1H), 7.59 (brd, *J* = 4.9 Hz, 1H), 7.33–7.31 (m, 1H), 7.08 (dt, *J* = 15.5, 7.1 Hz, 1H), 6.77 (brd, *J* = 15.5 Hz, 1H), 2.30–2.25 (m, 2H), 1.54 (appsx, *J* = 7.4 Hz, 2H), 0.96 ppm (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 184.4, 149.1, 142.9, 132.1, 127.6, 126.7, 125.4, 34.9, 21.6, 13.9 ppm; IR (film) $\tilde{\nu}$ = 2963, 2933, 2874, 1665 cm^{−1}; HRMS (EI): *m/z*: calcd for C₁₀H₁₂OS: 180.06034 [*M*]; found: 180.06071.

(E)-Ethyl 5-phenylpent-2-enoate (2h):^[34] ¹H NMR (CDCl₃, 600 MHz): δ = 7.29 (t, *J* = 7.5 Hz, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 2H), 7.00 (dt, *J* = 15.7, 6.9 Hz, 1H), 5.84 (dt, *J* = 15.7, 1.6 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.77 (t, *J* = 7.6 Hz, 2H), 2.55–2.50 (m, 2H), 1.28 ppm (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 166.7, 148.2, 140.9, 128.6, 128.4, 126.3, 121.9, 60.3, 34.4, 34.1, 14.4 ppm; HRMS (EI): *m/z*: calcd for C₁₁H₁₁O: 159.08044 [*M*–OEt]; found: 159.08089.

(E)-1-Phenylhept-1-en-3-one (2i):^[35] ¹H NMR (CDCl₃, 600 MHz): δ = 7.55 (d, *J* = 16.3 Hz, 1H), 7.56–7.53 (m, 2H), 7.41–7.38 (m, 3H), 6.75 (d, *J* = 16.3 Hz, 1H), 2.64 (t, *J* = 7.5 Hz, 2H), 1.69–1.64 (m, 2H), 1.39 (appsx, *J* = 7.5 Hz, 2H), 0.94 ppm (t, *J* = 7.5 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 200.9, 142.4, 134.7, 130.5, 129.1, 128.4, 126.4, 40.8, 26.6, 22.6, 14.1 ppm; IR (film) $\tilde{\nu}$ = 2955, 2942, 2926, 2866, 1649 cm^{−1}.

(E)-1-(4-Tolyl)hept-1-en-3-one (2j):^[35] ¹H NMR (CDCl₃, 500 MHz): δ = 7.53 (d, *J* = 16.3 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.70 (d, *J* = 16.3 Hz, 1H), 2.65 (t, *J* = 7.5 Hz, 2H), 2.38 (s, 3H), 1.65 (qn, *J* = 7.5 Hz, 2H), 1.39 (sx, *J* = 7.5 Hz, 2H), 0.94 ppm (t, *J* = 7.5 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ = 201.0, 142.5, 141.0, 131.9, 129.8, 128.4, 125.5, 40.7, 26.7, 22.6, 21.6, 14.1 ppm; IR (film) $\tilde{\nu}$ = 2955, 2930, 2862, 1648 cm^{−1}.

(E)-1-(4-Fluorophenyl)hept-1-en-3-one (2k):^[10c] ¹H NMR (CDCl₃, 500 MHz): δ = 7.53 (brdd, *J* = 8.6, 5.4 Hz, 2H), 7.50 (d, *J* = 16.2 Hz, 1H), 7.08 (t, *J* = 8.6 Hz, 2H), 6.67 (d, *J* = 16.2 Hz, 1H), 2.65 (t, *J* = 7.4 Hz, 2H), 1.65 (qn, *J* = 7.4 Hz, 2H), 1.38 (appsx, *J* = 7.4 Hz, 2H), 0.94 ppm (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ = 200.5, 162.2 (d, *J* = 250.7 Hz), 141.0, 130.9 (d, *J* = 3.8 Hz), 130.2 (d, *J* = 8.6 Hz), 126.0 (d, *J* = 1.9 Hz), 116.1 (d, *J* = 22.0 Hz), 40.9, 26.5, 22.5, 14.0 ppm; HRMS (CI): *m/z*: calcd for C₁₃H₁₆OF: 207.11806 [*M*+H]; found: 207.11852.

(E)-1-(4-(Trifluoromethyl)phenyl)hept-1-en-3-one (2l):^[10c] ¹H NMR (CDCl₃, 500 MHz): δ = 7.63 (s, 4H), 7.56 (d, *J* = 16.3 Hz, 1H), 6.80 (d, *J* = 16.3 Hz, 1H), 2.68 (t, *J* = 7.4 Hz, 2H), 1.67 (qn, *J* = 7.4 Hz, 2H), 1.38 (appsx, *J* = 7.4 Hz, 2H), 0.95 ppm (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ = 200.2, 141.3, 138.1, 131.9 (q, *J* = 32.7 Hz), 128.4, 128.3, 125.6 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 271.6 Hz), 41.1, 26.3, 22.5, 14.0 ppm;

HRMS (CI): *m/z*: calcd for C₁₄H₁₆OF₃: 257.11532 [*M*+H]; found: 257.11501.

(E)-1-(4-Bromophenyl)hept-1-en-3-one (2m): ¹H NMR (CDCl₃, 500 MHz): δ = 7.52 (d, *J* = 8.5 Hz, 2H), 7.50 (d, *J* = 16.1 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 16.1 Hz, 1H), 2.65 (t, *J* = 7.4 Hz, 2H), 1.65 (appqn, *J* = 7.4 Hz, 2H), 1.38 (appsx, *J* = 7.4 Hz, 2H), 0.94 ppm (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ = 200.4, 140.9, 133.6, 132.2, 129.7, 126.8, 124.7, 41.0, 26.5, 22.5, 14.0 ppm; IR (film) $\tilde{\nu}$ = 2964, 2951, 2930, 2868, 1685 cm^{−1}; HRMS (CI): *m/z*: calcd for C₁₃H₁₆OBr: 267.03845 [*M*+H]; found: 267.03824.

(E)-1-(4-Methoxyphenyl)hept-1-en-3-one (2n):^[10c] ¹H NMR (CDCl₃, 600 MHz): δ = 7.51 (d, *J* = 16.0 Hz, 1H), 7.50 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.63 (d, *J* = 16.0 Hz, 1H), 3.84 (s, 3H), 2.64 (t, *J* = 7.5 Hz, 2H), 1.67 (appqn, *J* = 7.5 Hz, 2H), 1.38 (appsx, *J* = 7.5 Hz, 2H), 0.94 ppm (t, *J* = 7.5 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 200.9, 161.6, 142.2, 130.1, 127.3, 124.2, 114.5, 55.5, 40.7, 26.8, 22.6, 14.1 ppm; IR (film) $\tilde{\nu}$ = 2958, 2934, 2872, 1685 cm^{−1}.

(E)-1-(4-(Dimethylamino)phenyl)hept-1-en-3-one (2o): ¹H NMR (CDCl₃, 600 MHz): δ = 7.50 (d, *J* = 16.0 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 2H), 6.68 (d, *J* = 8.8 Hz, 2H), 6.56 (d, *J* = 16.0 Hz, 1H), 3.03 (s, 6H), 2.62 (t, *J* = 7.5 Hz, 2H), 1.65 (appqn, *J* = 7.5 Hz, 2H), 1.38 (appsx, *J* = 7.5 Hz, 2H), 0.94 ppm (t, *J* = 7.5 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 201.1, 152.0, 143.3, 130.1, 122.3, 121.7, 112.0, 40.4, 40.3, 27.1, 22.7, 14.1 ppm; IR (film) $\tilde{\nu}$ = 2956, 2931, 2871, 1646 cm^{−1}; HRMS (EI): *m/z*: calcd for C₁₅H₂₁ON: 231.16176 [*M*]; found: 231.16240.

(E)-1-(5-Methylthiophen-2-yl)hept-1-en-3-one (2p): ¹H NMR (CDCl₃, 600 MHz): δ = 7.58 (d, *J* = 15.8 Hz, 1H), 7.08 (brd, *J* = 3.6 Hz, 1H), 6.72 (brd, *J* = 3.6 Hz, 1H), 6.41 (dd, *J* = 15.8 Hz, 1H), 2.59 (t, *J* = 7.4 Hz, 2H), 2.50 (s, 3H), 1.63 (appqn, *J* = 7.4 Hz, 2H), 1.38 (appsx, *J* = 7.4 Hz, 2H), 0.93 ppm (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 200.4, 144.4, 138.1, 135.4, 132.5, 126.8, 123.9, 40.9, 26.7, 22.6, 16.0, 14.1 ppm; IR (film) $\tilde{\nu}$ = 2960, 2932, 2873, 1651 cm^{−1}; HRMS (EI): *m/z*: calcd for C₁₂H₁₆OS: 208.09164 [*M*]; found: 208.09115.

(E)-1-(Furan-2-yl)hept-1-en-3-one (2q): ¹H NMR (CDCl₃, 600 MHz): δ = 7.49 (brd, *J* = 1.5 Hz, 1H), 7.32 (d, *J* = 15.8 Hz, 1H), 6.65 (d, *J* = 3.4 Hz, 1H), 6.64 (d, *J* = 15.8 Hz, 1H), 6.47 (brdd, *J* = 3.4, 1.5 Hz, 1H), 2.60 (t, *J* = 7.4 Hz, 2H), 1.67–1.61 (m, 2H), 1.36 (appsx, *J* = 7.4 Hz, 2H), 0.93 ppm (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 200.4, 151.3, 144.9, 128.6, 123.5, 115.7, 112.6, 41.3, 26.6, 22.6, 14.0 ppm; IR (film) $\tilde{\nu}$ = 2961, 2934, 2875, 1611 cm^{−1}; HRMS (EI): *m/z*: calcd for C₁₁H₁₄O₂: 178.09883 [*M*]; found: 178.09903.

1-(4-Methoxyphenyl)hept-2-en-1-one (2s): *Z* enone: ¹H NMR (CDCl₃, 600 MHz): δ = 7.94 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.75 (dt, *J* = 11.6, 1.5 Hz, 1H), 6.26 (dt, *J* = 11.6, 7.5 Hz, 1H), 3.87 (s, 3H), 2.60 (qd, *J* = 7.5, 1.5 Hz, 2H), 1.45 (appqn, *J* = 7.5 Hz, 2H), 1.35 (appsx, *J* = 7.5 Hz, 2H), 0.90 ppm (t, *J* = 7.5 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 191.1, 163.3, 148.7, 131.7, 130.8, 124.5, 113.8, 55.6, 31.6, 29.7, 22.6, 14.1 ppm; *E* enone: ¹H NMR (CDCl₃, 600 MHz): δ = 7.95 (d, *J* = 8.8 Hz, 2H), 6.75 (dt, *J* = 15.5, 7.0 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.89 (dt, *J* = 15.5, 1.5 Hz, 1H), 3.87 (s, 3H), 2.31 (qd, *J* = 7.5, 1.5 Hz, 2H), 1.50 (appqn, *J* = 7.5 Hz, 2H), 1.38 (appsx, *J* = 7.5 Hz, 2H), 0.93 ppm (t, *J* = 7.5 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ = 189.3, 163.3, 149.2, 131.0, 130.9, 125.6, 113.8, 55.6, 32.7, 30.5, 22.5, 14.0 ppm; IR (film) $\tilde{\nu}$ = 2962, 2935, 1600 cm^{−1}; HRMS (CI): *m/z*: calcd for C₁₄H₁₉O₂: 219.13850 [*M*+H]; found: 219.13812.

(E)-1-(4-Methoxyphenyl)-5-phenylpent-2-en-1-one (2t): ¹H NMR (CDCl₃, 600 MHz): δ = 7.91 (d, *J* = 8.9 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.22 (m, 3H), 7.07 (dt, *J* = 15.4, 6.9 Hz, 1H), 6.94 (d, *J* = 8.9 Hz, 2H), 6.88 (dt, *J* = 15.4, 1.3 Hz, 1H), 3.05 (s, 3H), 2.85 (t, *J* = 7.5 Hz, 2H), 2.64 ppm (m, 2H); ¹³C NMR (CDCl₃, 150 MHz): δ = 189.2, 163.4, 147.5, 141.1, 131.0, 130.8, 128.63, 128.55, 126.3, 113.9, 55.6, 34.69, 34.66 ppm; IR (film) $\tilde{\nu}$ = 2965, 2938, 1618 cm^{−1}; HRMS (EI): *m/z*: calcd for C₁₈H₁₈O₂: 266.13013 [*M*]; found 266.13090.

(2E,4Z)-1-Cyclopropylocta-2,4-dien-1-one (2v): ¹H NMR (CDCl₃, 600 MHz): δ = 7.23–7.18 (dd, *J* = 15.4, 9.6 Hz, 1H), 6.21 (d, *J* = 15.4 Hz, 1H), 6.21–6.15 (m, 2H), 2.18–2.14 (m, 2H), 2.14–2.10 (m, 1H), 1.50–1.42 (appsx, *J* = 7.4 Hz, 2H), 1.10–1.06 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.91–

0.87 ppm (m, 2H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 200.6, 145.6, 142.8, 129.2, 128.1, 35.3, 22.0, 19.3, 13.8, 11.1 ppm; IR (film) $\tilde{\nu}$ = 2965, 2936, 2876, 1704 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{11}\text{H}_{16}\text{O}$: 164.11957 [M]; found 164.11993.

(E)-1-(Pyridin-2-yl)hept-2-en-1-one (16): ^1H NMR (CDCl_3 , 600 MHz): δ = 8.71 (m, 1H), 8.12 (d, J = 7.9 Hz, 1H), 7.85 (td, J = 7.9, 1.5 Hz, 1H), 7.58 (dt, J = 15.6, 1.2 Hz, 1H), 7.49–7.45 (m, 1H), 7.24 (dt, J = 15.6, 7.0 Hz, 1H), 2.35 (brqd, J = 7.0, 1.2 Hz, 2H), 1.55–1.48 (m, 2H), 1.41–1.35 (m, 2H), 0.93 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 189.7, 154.3, 150.8, 148.9, 137.1, 126.9, 124.5, 123.0, 32.8, 30.4, 22.5, 14.0 ppm; IR (film) $\tilde{\nu}$ = 2960, 2933, 2831, 1621 cm^{-1} ; HRMS (CI): m/z : calcd for $\text{C}_{12}\text{H}_{16}\text{ON}$: 190.12319 [$M+H$]; found 190.12364.

1,3,3-Triphenylprop-2-en-1-one (24g):^[36] ^1H NMR (CDCl_3 , 600 MHz): δ = 7.91 (brd, J = 7.3 Hz, 2H), 7.49 (brt, J = 7.3 Hz, 1H), 7.41–7.36 (m, 7H), 7.29–7.25 (m, 3H), 7.20–7.17 (m, 2H), 7.12 ppm (s, 1H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 192.8, 154.9, 141.5, 139.1, 138.3, 132.8, 129.9, 129.5, 128.9, 128.7, 128.58, 128.51, 128.49, 128.2, 124.1 ppm; HRMS (CI): m/z : calcd for $\text{C}_{21}\text{H}_{16}\text{O}$: 283.1174 [$M+H$]; found 283.11288.

Synthesis of the natural products isoeogomaktone (6) and daphenone (13)

(E)-Isoeogomaktone (6):^[18,19] Isobutraldehyde (110 mg, 1.52 mmol), (furan-3-ylethynyl)trimethylsilane (500 mg, 3.65 mmol), and tetrabutylammonium triphenyldifluorosilicate (8 mg, 0.15 mmol) were dissolved in dry THF (5 mL). The resultant solution was stirred for 20 min at 0°C. The reaction was quenched with aq. NaHCO_3 and the organic phase extracted with diethyl ether. The combined organic phases were washed with brine, dried (MgSO_4) and concentrated in vacuo to give **5a** and **5b** as a mixture. Compound **5** was submitted without further purification to the Meyer-Schuster rearrangement reaction conditions (general procedure C) to give *E*-isoeogomaktone in 86% yield over the two steps. ^1H NMR (CDCl_3 , 600 MHz): δ = 8.04 (m, 1H), 7.45 (app br t, J = 1.7 Hz, 1H), 7.02 (dd, J = 15.4, 6.8 Hz, 1H), 6.83 (br dd, J = 1.7, 0.8 Hz, 1H), 6.49 (dd, J = 15.4, 1.5 Hz, 1H), 2.53 (app sxd, J = 6.8, 1.3 Hz, 1H), 1.11 ppm (d, J = 6.8 Hz, 6H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 185.0, 154.7, 147.2, 144.3, 128.2, 124.1, 109.3, 31.4, 21.5 ppm; IR (film) $\tilde{\nu}$ = 2966, 2934, 2873, 1667 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{10}\text{H}_{12}\text{O}_2$: 164.08318 [M]; found: 164.08354.

tert-Butyl(4-ethynylphenoxy)dimethylsilane (10):^[37] (4-Hydroxyphenyl)acetylene **9**^[20] (400 mg, 3.43 mmol) and imidazole (230 mg, 3.43 mmol) were dissolved in DMF (10 mL) and *tert*-butyldimethylsilyl chloride (TBSCl) (510 mg, 3.43 mmol) was added. The reactants were stirred at room temperature overnight and then quenched with the addition of water. The resultant slurry was extracted with diethyl ether, the combined organic phases were washed with brine, dried (MgSO_4) and concentrated in vacuo. The residue was purified by flash column chromatography to give the protected acetylene **10**. ^1H NMR (CDCl_3 , 600 MHz): δ = 7.38 (d, J = 8.6 Hz, 2H), 6.78 (d, J = 8.6 Hz, 2H), 2.99 (s, 1H), 0.98 (s, 9H), 0.20 ppm (s, 6H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 156.4, 133.7, 120.3, 114.9, 83.8, 76.0, 25.7, 0.17, –4.3 ppm; IR (film) $\tilde{\nu}$ = 2957, 2930, 2896, 2860, 2157 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{14}\text{H}_{20}\text{OSi}$: 232.12779 [M]; found: 233.12850.

1-(4-((tert-Butyldimethylsilyloxy)phenyl)-5-phenylpent-1-yn-3-ol (12): Prepared according to general procedure S_A (see the Supporting Information). ^1H NMR (CDCl_3 , 600 MHz): δ = 7.32 (d, J = 8.6 Hz, 2H), 7.31–7.28 (m, 2H), 7.26–7.24 (m, 2H), 7.22–7.19 (m, 1H), 6.79 (d, J = 8.6 Hz, 2H), 4.59 (brt, J = 5.5 Hz, 1H), 2.86 (t, J = 7.5 Hz, 2H), 2.14–2.08 (m, 2H), 1.96 (brs, 1H), 0.98 (s, 9H), 0.20 ppm (s, 6H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 156.2, 141.5, 133.3, 128.7, 128.6, 126.1, 120.3, 115.4, 88.6, 85.4, 62.5, 39.5, 31.6, 25.8, 18.3, –4.3 ppm; IR (film) $\tilde{\nu}$ = 3650, 3007, 2944, 2293 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{23}\text{H}_{30}\text{O}_2\text{Si}$: 366.20096 [M]; found: 366.20131.

Daphenone (13):^[21] Prepared according to general procedure A; ^1H NMR (CDCl_3 , 600 MHz): δ = 7.85 (d, J = 8.8 Hz, 2H), 7.29 (m, 2H), 7.21 (m, 3H), 7.07 (dt, J = 15.3, 6.8 Hz, 1H), 6.89 (d, J = 8.8 Hz, 2H), 6.88 (dt, J = 15.3, 1.3 Hz, 1H), 6.44 (brs, 1H), 2.84 (t, J = 7.5 Hz, 2H), 2.64 ppm (m, 2H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 189.7, 160.4, 148.1, 141.0, 131.4, 130.6, 128.6, 128.5, 126.30, 126.26, 115.5, 34.69, 34.63 ppm; IR (film) $\tilde{\nu}$ = 2954, 2926, 2856, 1737 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{17}\text{H}_{16}\text{O}_2$: 252.11448 [M]; found: 252.11537.

Silver-catalyzed substitution of propargylic alcohols

General procedure B (preparation of compounds 17 and 22): AgNTf_2 (1 mol %) and nucleophile (2 equiv) were added to a solution of propargylic alcohol in toluene (10 mL g^{-1}) and the solution stirred magnetically at room temperature until the starting material had disappeared (TLC) or at 60°C overnight. The reaction was quenched with aq. NaHCO_3 and the organic phase extracted with diethyl ether. The combined organic phases were washed with brine, dried (MgSO_4) and concentrated in vacuo. The residue was purified by flash column chromatography to give **17**.

1-Methoxy-4-(1-methoxyhept-2-yn-1-yl)benzene (17a):^[38] ^1H NMR (CDCl_3 , 600 MHz): δ = 7.42 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 5.02 (brt, J = 1.9 Hz, 1H), 3.81 (s, 3H), 3.37 (s, 3H), 2.29 (td, J = 7.2, 1.9 Hz, 2H), 1.56–1.51 (m, 2H), 1.47–1.40 (m, 2H), 0.92 ppm (t, J = 7.3 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 159.7, 131.5, 128.9, 113.8, 88.5, 77.8, 72.9, 55.5, 55.4, 30.9, 22.1, 18.7, 13.7 ppm; HRMS (EI): m/z : calcd for $\text{C}_{15}\text{H}_{20}\text{O}_2$: 232.14578 [M]; 232.14620.

2-(3-(Cyclohex-1-en-1-yl)-1-methoxyprop-2-yn-1-yl)-5-methylthiophene (17b): ^1H NMR (CDCl_3 , 600 MHz): δ = 6.94 (d, J = 3.4 Hz, 1H), 6.60 (m, 1H), 6.19 (m, 1H), 5.37 (s, 1H), 3.39 (s, 3H), 2.46 (s, 3H), 2.19–2.14 (m, 2H), 2.12–2.08 (m, 2H), 1.66–1.61 (m, 2H), 1.61–1.55 ppm (m, 2H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 141.1, 139.9, 136.0, 126.5, 124.6, 120.1, 89.0, 83.3, 68.8, 55.0, 29.2, 25.7, 22.3, 21.5, 15.6 ppm; IR (film) $\tilde{\nu}$ = 3007, 2958, 2238 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{15}\text{H}_{18}\text{OS}$: 246.10729 [M]; found: 246.10810.

1-(1-(Benzyloxy)hept-2-yn-1-yl)-4-methoxybenzene (17c): ^1H NMR (CDCl_3 , 600 MHz): δ = 7.45 (d, J = 8.6 Hz, 2H), 7.39–7.33 (m, 4H), 7.28 (m, 1H), 6.89 (d, J = 8.6 Hz, 2H), 5.16 (brt, J = 1.9 Hz, 1H), 4.65 (d, J = 11.7 Hz, 1H), 4.62 (d, J = 11.7 Hz, 1H), 3.81 (s, 3H), 2.31 (td, J = 7.1, 1.9 Hz, 2H), 1.55 (appqn, J = 7.4 Hz, 2H), 1.45 (appsx, J = 7.4 Hz, 2H), 0.93 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 159.6, 138.2, 131.6, 129.0, 128.5, 128.2, 127.7, 113.8, 88.6, 78.0, 70.4, 69.6, 55.4, 30.9, 22.1, 18.7, 13.8 ppm; IR (film) $\tilde{\nu}$ = 2958, 2933, 2872, 2230 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{21}\text{H}_{24}\text{O}_2$: 308.17708 [M]; found: 308.17794.

2-(1-(4-Methoxyphenyl)hept-2-yn-1-yl)furan (17d): ^1H NMR (CDCl_3 , 600 MHz): δ = 7.32 (d, J = 8.7, 2H), 7.30 (m, 1H), 6.86 (d, J = 8.7 Hz, 2H), 6.28 (brdd, J = 3.2, 1.9 Hz, 1H), 6.16 (brdt, J = 3.2, 0.9 Hz, 1H), 4.96 (brt, J = 2.2 Hz, 1H), 3.79 (s, 3H), 2.26 (td, J = 7.1, 2.2 Hz, 2H), 1.52 (appqn, J = 7.4 Hz, 2H), 1.43 (appsx, J = 7.4 Hz, 2H), 0.91 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 158.8, 155.1, 142.1, 131.8, 128.9, 114.0, 110.3, 106.1, 84.2, 78.2, 55.4, 36.6, 31.1, 22.1, 18.7, 13.8 ppm; IR (film) $\tilde{\nu}$ = 2957, 2930, 2871, 2265, 1607 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{18}\text{H}_{20}\text{O}_2$: 268.14577 [M]; found: 268.14630.

2-(1-(4-Methoxyphenyl)hept-2-yn-1-yl)-5-methylfuran (17e): ^1H NMR (CDCl_3 , 600 MHz): δ = 7.32 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.02 (brd, J = 2.9 Hz, 1H), 5.86 (brdd, J = 2.9, 1.1 Hz, 1H), 4.91 (brs, 1H), 3.79 (s, 3H), 2.26 (td, J = 7.1, 2.2 Hz, 2H), 2.23 (s, 3H), 1.53 (appqn, J = 7.4 Hz, 2H), 1.43 (appsx, J = 7.4 Hz, 2H), 0.92 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 158.7, 153.2, 151.7, 132.1, 128.9, 113.9, 106.8, 106.2, 84.0, 78.5, 55.4, 36.6, 31.1, 22.1, 18.7, 13.77, 13.76 ppm; IR (film) $\tilde{\nu}$ = 2956, 2932, 2871, 2837, 2249, 1609 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{19}\text{H}_{22}\text{O}_2$: 282.16142 [M]; found: 282.16170.

3-(1-(4-Methoxyphenyl)hept-2-yn-1-yl)pentane-2,4-dione (17f): ^1H NMR (CDCl_3 , 600 MHz): δ = 7.23 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 4.36 (dt, J = 10.8, 2.3 Hz, 1H), 4.05 (d, J = 10.8 Hz, 1H), 3.78 (s, 3H), 2.30 (s, 3H), 2.16 (td, J = 7.1, 2.3 Hz, 2H), 1.89 (s, 3H), 1.47–1.41 (m, 2H), 1.35 (appsx, J = 7.4 Hz, 2H), 0.88 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 202.31, 202.29, 158.9, 130.9, 129.1, 114.2, 85.3, 79.0, 76.4, 55.4, 37.1, 31.4, 30.9, 28.6, 22.0, 18.5, 13.7 ppm; IR (film) $\tilde{\nu}$ = 2957, 2928, 2871, 2160, 1700 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{19}\text{H}_{24}\text{O}_3$: 300.17200 [M]; found: 300.17241.

1-(Dec-1-en-5-yn-4-yl)-4-methoxybenzene (17g):^[28c] ^1H NMR (CDCl_3 , 600 MHz): δ = 7.27 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 5.86 (m, 1H), 5.07 (m, 2H), 3.79 (s, 3H), 3.68 (m, 1H), 2.45 (appt, J = 7.0 Hz, 2H), 2.25 (td, J = 7.0, 2.3 Hz, 2H), 1.51 (m, 2H), 1.42 (appsx, J = 7.4 Hz, 2H), 0.92 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 158.4, 136.0, 134.2, 128.5, 116.3, 113.9, 84.0, 81.5, 55.4, 43.3, 37.6, 31.3,

22.1, 18.7, 13.8 ppm; IR (film) $\tilde{\nu}$ =2958, 2933, 2873, 2250, 1641 cm^{-1} ; HRMS (CI): m/z : calcd for $\text{C}_{17}\text{H}_{22}\text{O}$: 243.17489 [$M+H$]; found: 243.17533.

***t*-Butyl (1-(4-methoxyphenyl)hept-2-yn-1-yl)carbamate (17h):** ^1H NMR (CDCl_3 , 600 MHz): δ =7.41 (brd, J =8.7 Hz, 2H), 6.86 (d, J =8.7 Hz, 2H), 5.57 (brs, 1H), 4.96 (brs, 1H), 3.80 (s, 3H), 2.24 (td, J =7.1, 2.1 Hz, 2H), 1.50 (appqn, J =7.4 Hz, 2H), 1.44 (s, 9H), 1.40 (appsx, J =7.4 Hz, 2H), 0.91 ppm (t, J =7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =159.2, 154.9, 132.6, 128.2, 113.9, 85.3, 80.0, 78.6, 55.4, 46.0, 30.8, 28.5, 22.1, 18.6, 13.7 ppm; IR (film) $\tilde{\nu}$ =3351, 2959, 2933, 2870, 2250, 1699 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{19}\text{H}_{27}\text{O}_3\text{N}$: 340.1889 [$M+Na$]; found: 340.1881.

N-(1-(4-Methoxyphenyl)hept-2-yn-1-yl)-4-methylbenzenesulfonamide (17i): ^1H NMR (CDCl_3 , 600 MHz): δ =7.76 (brd, J =8.1 Hz, 2H), 7.37 (d, J =8.8 Hz, 2H), 7.28 (brd, J =8.1 Hz, 2H), 6.82 (d, J =8.8 Hz, 2H), 5.24 (brdt, J =8.8, 2.1 Hz, 1H), 4.79 (brd, J =8.8 Hz, 1H), 3.78 (s, 3H), 2.42 (s, 3H), 1.96 (td, J =7.0, 2.1 Hz, 2H), 1.30–1.22 (m, 4H), 0.85 ppm (t, J =7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =159.6, 143.3, 137.7, 130.4, 129.5, 128.7, 127.6, 114.0, 87.4, 76.9, 55.4, 49.1, 30.5, 22.0, 21.7, 18.3, 13.7 ppm; IR (film) $\tilde{\nu}$ =3270, 2958, 2933, 2872, 2251 cm^{-1} ; HRMS (ES): m/z : calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_3\text{S}$: 394.1453 [$M+Na$]; found: 394.1446.

4,4'-(Oxybis(hept-2-yne-1,1-diyl))bis(methoxybenzene) (17j): Mixture of diastereoisomers A and B, crude ratio of A/B was 1.3:1. **A:** ^1H NMR (CDCl_3 , 600 MHz): δ =7.47 (d, J =8.7 Hz, 4H), 6.86 (d, J =8.7 Hz, 4H), 5.53 (brt, J =1.9 Hz, 2H), 3.79 (s, 6H), 2.32 (td, J =7.2, 1.9 Hz, 4H), 1.55 (m, 4H), 1.45 (appsx, J =7.4 Hz, 4H), 0.93 (t, J =7.4 Hz, 6H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =159.5, 131.8, 129.2, 113.7, 88.5, 78.1, 69.2, 57.4, 30.9, 22.1, 18.7, 13.8 ppm; **B:** ^1H NMR (CDCl_3 , 600 MHz): δ =7.41 (d, J =8.7 Hz, 4H), 6.88 (d, J =8.7 Hz, 4H), 5.14 (brt, J =1.9 Hz, 2H), 3.8 (s, 6H), 2.26 (td, J =7.2, 1.9 Hz, 4H), 1.54–1.49 (m, 4H), 1.41 (appsx, J =7.4 Hz, 4H), 0.91 ppm (t, J =7.4 Hz, 6H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =159.7, 131.5, 129.4, 113.9, 88.3, 78.4, 68.5, 55.4, 30.8, 22.2, 18.8, 13.8 ppm; IR (film) $\tilde{\nu}$ =2956, 2932, 2871, 2238 cm^{-1} ; HRMS (ES): m/z : calcd for $\text{C}_{28}\text{H}_{38}\text{O}_3$: 419.2586 [$M+H$]; 419.2600.

Attempted Meyer-Schuster rearrangement of terminal alkynes

Reaction of **18** using contaminated gold catalyst^[24] according to general procedure A gave a 1:5 mixture of **19** and **20**, respectively. Reaction of **18** using a different batch of gold catalyst gave a mixture of compounds **19** and **21**.

(E)-3-(4-Methoxyphenyl)acrylaldehyde (19): ^1H NMR (CDCl_3 , 600 MHz): δ =9.65 (d, J =7.6 Hz, 1H), 7.53 (d, J =8.8 Hz, 2H), 7.43 (d, J =15.8 Hz, 1H), 6.95 (d, J =8.8 Hz, 2H), 6.62 (dd, J =15.8, 7.6 Hz, 1H), 3.86 ppm (s, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =193.9, 162.3, 152.9, 127.9, 126.9, 126.7, 114.7, 55.64 ppm.

1-Methoxy-1-(4-methoxyphenyl)propan-2-one (20):^[39] Reaction of **22** according to general procedure A with an uncontaminated batch of gold catalyst gave **20** as the sole product. ^1H NMR (CDCl_3 , 600 MHz): δ =7.29 (d, J =8.5 Hz, 2H), 6.91 (d, J =8.5 Hz, 2H), 4.61 (s, 1H), 3.81 (s, 3H), 3.35 (s, 3H), 2.10 ppm (s, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =206.8, 160.1, 130.5, 128.5, 114.4, 89.0, 57.1, 55.4, 25.4 ppm; IR (film) $\tilde{\nu}$ =3002, 2937, 2909, 1716 cm^{-1} .

1-Hydroxy-1-(4-methoxyphenyl)propan-2-one (21): General procedure A: ^1H NMR (CDCl_3 , 600 MHz): δ =7.23 (d, J =8.9 Hz, 2H), 6.91 (d, J =8.9 Hz, 2H), 5.05 (brd, J =3.5 Hz, 1H), 4.24 (brd, J =3.5 Hz, 1H), 3.81 (s, 3H), 2.07 ppm (s, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =207.5, 160.0, 130.1, 128.8, 114.5, 79.7, 55.4, 25.4 ppm; IR (film) $\tilde{\nu}$ =3465, 3055, 2988, 1712 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{10}\text{H}_{12}\text{O}_3$: 180.07810 [M]; found: 180.07883.

1-Methoxy-4-(1-methoxyprop-2-yn-1-yl)benzene (22): Prepared according to general procedure B. ^1H NMR (CDCl_3 , 600 MHz): δ =7.44 (d, J =8.7 Hz, 2H), 6.91 (d, J =8.7 Hz, 2H), 5.04 (brd, J =2.1 Hz, 1H), 3.81 (s, 3H), 3.42 (s, 3H), 2.65 ppm (brd, J =2.1 Hz, 1H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =159.9, 130.3, 128.9, 114.0, 81.6, 75.7, 72.5, 55.8, 55.4 ppm; IR (film) $\tilde{\nu}$ =2995, 2936, 2904, 2174 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{11}\text{H}_{12}\text{O}_2$: 176.08318 [M]; found: 176.08350.

One-pot syntheses of β -substituted ketones 30–33

Compounds **30a–d** have previously been reported.^[14]

General procedure C (preparation of compounds 31–33): [$\text{Ph}_3\text{PAuNTf}_2$] $\cdot\text{PhMe}$ (1 mol %) and alcohol (2 equiv) or 4-methoxyphenylboronic acid (0.2 equiv) were added to a solution of propargylic alcohol in toluene (10 mL g^{-1}) and the solution stirred magnetically at room temperature until starting material had disappeared (TLC). After this time nucleophile (2 equiv) was added to the solution and it was stirred overnight at room temperature. The solvent was removed in vacuo and the crude product purified by column chromatography to give the β -substituted ketone.

1-(Benzyloxy)hexan-3-one (31a): ^1H NMR (CDCl_3 , 600 MHz): δ =7.36–7.25 (m, 5H), 4.51 (s, 2H), 3.74 (t, J =6.3 Hz, 2H), 2.69 (t, J =6.3 Hz, 2H), 2.43 (t, J =7.3 Hz, 2H), 1.59 (appsx, J =7.4 Hz, 2H), 0.91 ppm (t, J =7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =209.6, 138.2, 128.5, 127.81, 127.77, 73.4, 65.5, 45.5, 43.0, 17.1, 13.8 ppm; IR (film) $\tilde{\nu}$ =2963, 2935, 2875, 1712 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{19}\text{O}_2$: 207.13850 [$M+H$]; found: 207.13812.

1-Isopropoxyhexan-3-one (31b): ^1H NMR (CDCl_3 , 600 MHz): δ =3.62 (t, J =6.5 Hz, 2H), 3.51 (septet, J =6.1 Hz, 2H), 2.58 (t, J =6.5 Hz, 2H), 2.37 (t, J =7.4 Hz, 2H), 1.60 (appsx, J =7.4 Hz, 2H), 1.08 (d, J =6.1 Hz, 6H), 0.86 ppm (t, J =7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =209.9, 71.8, 63.2, 45.4, 43.2, 22.1, 17.1, 13.8 ppm; IR (film) $\tilde{\nu}$ =2966, 2935, 2875, 1710 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_9\text{H}_{19}\text{O}_2$: 159.13850 [$M+H$]; found: 159.13881.

1-(Diethylamino)hexan-3-one (32a): ^1H NMR (CDCl_3 , 600 MHz): δ =2.74 (t, J =7.5 Hz, 2H), 2.55 (t, J =7.5 Hz, 2H), 2.50 (q, J =7.3 Hz, 4H), 2.40 (t, J =7.3 Hz, 2H), 1.59 (appsx, J =7.4 Hz, 2H), 1.01 (t, J =7.3 Hz, 6H), 0.91 ppm (t, J =7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =210.9, 47.4, 47.0, 45.3, 40.5, 17.3, 13.9, 11.8 ppm; IR (film) $\tilde{\nu}$ =2968, 2928, 2856, 1709 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{10}\text{H}_{21}\text{ON}$: 171.16177 [M]; found: 171.16234.

1-(Dibenzylamino)hexan-3-one (32b): ^1H NMR (CDCl_3 , 600 MHz): δ =7.33–7.22 (m, 10H), 3.55 (s, 4H), 2.76 (t, J =7.2 Hz, 2H), 2.56 (t, J =7.2 Hz, 2H), 2.23 (t, J =7.4 Hz, 2H), 1.53 (appsx, J =7.4 Hz, 2H), 0.85 ppm (t, J =7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =210.6, 139.5, 129.0, 128.3, 127.1, 58.4, 48.7, 44.6, 41.0, 17.2, 13.8 ppm; IR (film) $\tilde{\nu}$ =2961, 2932, 2874, 1708 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{20}\text{H}_{25}\text{NO}$: 295.19307 [M]; found: 295.19352.

1-Morpholinohexan-3-one (32c): ^1H NMR (CDCl_3 , 600 MHz): δ =3.68 (brt, J =4.6 Hz, 4H), 2.67–2.55 (m, 4H), 2.42 (brs, 4H), 2.40 (t, J =7.4 Hz, 2H), 1.60 (appsx, J =7.4 Hz, 2H), 0.90 ppm (t, J =7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =209.9, 67.0, 53.7, 53.2, 45.1, 40.1, 17.2, 13.8 ppm; IR (film) $\tilde{\nu}$ =2960, 2855, 2809, 1709 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{10}\text{H}_{20}\text{O}_2\text{N}$: 186.14940 [M]; found: 186.15011.

1-(4-Methylpiperazin-1-yl)hexan-3-one (32d): ^1H NMR (CDCl_3 , 600 MHz): δ =2.65 (t, J =7.1 Hz, 2H), 2.58 (t, J =7.1, 2H), 2.39 (t, J =7.4 Hz, 2H), 2.26 (s, 3H), 2.71–2.20 (m, 8H), 1.58 (appsx, J =7.4 Hz, 2H), 0.89 ppm (t, J =7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =210.2, 55.2, 53.1, 52.8, 46.1, 45.1, 40.4, 17.3, 13.9 ppm; IR (film) $\tilde{\nu}$ =2961, 2936, 2876, 2794, 1711 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{11}\text{H}_{22}\text{ON}_2$: 198.17266 [M]; found: 198.17302.

1-(1,2,3,4-Tetrahydroisoquinolin-2-yl)hexan-3-one (32e): ^1H NMR (CDCl_3 , 600 MHz): δ =7.13–7.07 (m, 3H), 7.01 (m, 1H), 3.63 (brs, 2H), 2.89 (brt, J =6.0 Hz, 2H), 2.84 (t, J =7.3 Hz, 2H), 2.74 (t, J =6.0 Hz, 2H), 2.71 (t, J =7.3 Hz, 2H), 2.44 (t, J =7.4 Hz, 2H), 1.61 (appsx, J =7.4 Hz, 2H), 0.91 ppm (t, J =7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =210.2, 134.5, 134.2, 128.7, 126.7, 126.3, 125.8, 56.2, 52.7, 51.1, 45.2, 40.8, 29.2, 17.3, 13.9 ppm; IR (film) $\tilde{\nu}$ =2960, 2931, 2874, 1709 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{15}\text{H}_{22}\text{ON}$: 232.1701 [M]; found: 232.1707.

1-(Methyl(phenyl)amino)hexan-3-one (32f): ^1H NMR (CDCl_3 , 600 MHz): δ =7.24 (m, 2H), 6.71 (m, 3H), 3.64 (t, J =6.9 Hz, 2H), 2.92 (brs, 3H), 2.67 (t, J =6.9 Hz, 2H), 2.38 (t, J =7.4 Hz, 2H), 1.63–1.54 (2H, m, CH_2), 0.89 ppm (t, J =7.4 Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): δ =210.5, 129.4, 128.7, 116.7, 112.5, 47.5, 45.6, 39.4, 38.6, 17.2, 13.8 ppm; IR (film) $\tilde{\nu}$ =2963, 2951, 2810, 1710 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{19}\text{ON}$: 205.14612 [M]; found: 205.14639.

1-Hexylsulfanylhexan-3-one (33a):^[40] ^1H NMR (CDCl_3 , 600 MHz): δ =2.73 (m, 2H), 2.68 (m, 2H), 2.50 (t, J =7.5 Hz, 2H), 2.40 (t, J =7.5 Hz,

2H), 1.65–1.53 (m, 4H), 1.39–1.22 (m, 6H), 0.91 (t, $J=7.2$ Hz, 3H), 0.88 ppm (t, $J=7.0$ Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): $\delta=209.5$, 45.1, 42.9, 32.6, 31.5, 29.7, 28.7, 25.9, 22.7, 17.3, 14.2, 13.8 ppm; IR (film) $\tilde{\nu}=2958$, 2926, 2857, 1710 cm^{-1} .

1-(Phenylthio)hexan-3-one (33b):^[41] ^1H NMR (CDCl_3 , 600 MHz): $\delta=7.35$ – 7.32 (m, 2H), 7.31–7.27 (m, 2H), 7.21–7.18 (m, 1H), 3.14 (t, $J=7.4$ Hz, 2H), 2.72 (t, $J=7.4$ Hz, 2H), 2.37 (t, $J=7.4$ Hz, 2H), 1.55 (m, 2H), 0.90 ppm (t, $J=7.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz): $\delta=209.2$, 135.9, 129.5, 129.1, 126.4, 45.1, 42.2, 27.6, 17.3, 13.8 ppm; IR (film) $\tilde{\nu}=2961$, 2933, 2875, 1710 cm^{-1} .

Acknowledgements

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