Tandem Nickel-Catalyzed Dimerization/(4+2) Cycloaddition of Terminal Alkynes with Four-Membered Ring Ketones

Manuel Barday, Eva Nicolas, Bradley Higginson, François Delmotte, Martin Appelmans, Christophe Aïssa

Abstract Controlling the behavior of terminal alkynes in metal-catalyzed intermolecular tandem reactions is a formidable challenge despite the potential advantage offered by these strategies in modern synthesis. Herein, we describe that a nickel catalyst enables a tandem process involving the rapid dimerization of terminal alkynes into 1,3-enynes and the cycloaddition of these intermediates with an azetidinone, an oxetanone or benzocyclobutenones. Significantly, the slow or sequential addition of reagents and catalysts is not required to orchestrate their reactivity. These results are in stark contrast with previous cycloadditions of terminal alkynes with strained four-membered ring substrates, which previously led to oligomerization or cyclotrimerization, except in the case of tert-butylacetylene.

Multicomponent reactions are extremely efficient for rapid molecular assembly;[1] however, controlling the reactivity of terminal alkynes in purely intermolecular metalcatalyzed multicomponent reactions with other π-components remains very challenging. Indeed, complex mixtures of products are often formed in the intermolecular cycloadditions of two untethered terminal alkynes with another π-component,[2] even if remarkable progress has been made on this specific class of metal-catalyzed reactions.[3] Among these precedents, pioneering work by Saito enabled the selective cycloaddition of two terminal alkynes and an electron-poor alkylidenecyclopropane with concomitant carbon–carbon bond (C–C) cleavage (Scheme 1, A).[4] Significantly,although impressive advances have been made on metal-catalyzed C–C bond activation,[5] the intermolecular nickel-catalyzed (4+2) cycloadditions of terminal alkynes with cyclobutanones,[6] cyclobutenones,[7] benzocyclobutenones,[8] azetidin-3-ones and oxetan-3-ones[9] are notoriously problematic and lead to oligomerization or cyclotrimerization products (Scheme 1, B, path a). A notable exception is the cycloaddition of tert-butylacetylene with Bocprotected azetidin-3-one (Boc = tert-butoxycarbonyl) (Scheme 1, B, path b),[9b] where the rate of otherwise uncontrolled oligomerization is presumably decreased by the size of the alkyne substituent. In contrast to these precedents, we report herein a remarkable three-component tandem reaction that affords pyridinones, pyranones, and naphthols, after the rapid nickel-catalyzed head-to-head dimerization of terminal alkynes[10,11] followed by the regioselective nickel-catalyzed (4+2) cycloaddition of the 1,3-enynes thus formed with an azetidinone, an oxetanone (Scheme 1, B, path c) or benzocyclobutenones (Scheme 1, B, path d). Importantly, we demonstrate that a slow or sequential addition of the reagents is not required to maintain the remarkable selectivity and efficiency of this tandem process. In continuation of our efforts to explore and develop the scope of the nickel-catalyzed (4+2) cycloaddition of alkynes with azetidin-3-one **1a**,[9a,9e–g] we examined the reaction of this substrate with trimethylsilylacetylene (**2a**) and obtained a very complex mixture of products. However, we were able to isolate traces of **3aa**, the product of an unprecedented head-to-head dimerization/(4+2) cycloaddition tandem process (Scheme 2). After further optimization, we found that adding 1a to a mixture of the active catalyst and the 1,3-enyne formed after brief

treatment of an excess of **2a** with $Ni(cod)_2$ and PPh_3 in a 1:3 ratio (method A) led to **3aa** in 56% yield. Inspired by Ogoshi's study of the head-to-head dimerization of terminal alkynes,[11] we were able to improve the yield of **3aa** to 75% by using a combination of 10 mol% $Ni(cod)_2$ and $PtBu_3$ in a 1:1 ratio before adding **1a** and 30 mol% of PPh_3 (method B). It is noteworthy that the (4+2) cyclization did not occur in the absence of PPh_3. Significantly, we also observed the positive effect induced by the addition of $PtBu_3$ in reactions where all reagents and catalysts were simply mixed and were all present at the start of the reaction (Scheme 3, methods C and D,). Using less than 4.4 equivalents of the alkyne or using 20 mol% of PPh_3 instead of 30 mol% led to inferior yields of the desired product.

When examining the generality of the tandem reaction of azetidinone **1a** with alkynes **2a–d** under method D, where all the reagents and the catalyst were added in one portion, we observed the formation of silylated cycloadducts **3ab–ad** in good yields (Scheme 4), which suggests that high performance in this tandem process does not generally require the slow or sequential addition of the reagents. Hence, the reactions of oxetanone **1b** with alkynes **2a–d** under the same conditions gave **3ba–bd** in similar fashion. However, the reaction of bulky triisopropylacetylene **2e** with **1a** gave 85% of the trans 1,3-enyne that resulted from its head-to-head dimerization, alongside 68% of recovered 1a and without any trace of the expected cycloadduct **3ae** [R = $Si(iPr)_3$]. When we attempted to use method C, where $PtBu_3$ was absent from the mixture, **2e** underwent direct cycloaddition with **1a** to give **4** in 55% yield. This result agrees with the Ni-catalyzed (4+2) cycloaddition of **1a** and tert-butylacetylene reported previously.[9b]

Moreover, we observed that the beneficial effect of added $PtBu^3$ was verified in most cases with **1a** for methods A and B (Table 1, entries 1–4) and led to an increase in yieldby 7–19%. Conversely, the effect of added $PtBu_3$ on the tandem dimerization/(4+2) cycloaddition process with oxetanone **1b** was less predictable. Thus, contrary effects were observed with some alkynes (entries 5 and 6), whereas almost no effect was observed for others (entries 7 and 8).
Moreover, the beneficial effect of added PtBu3 was also visible in methods C and D, where all reagents and catalystswere present at the start of the reaction. Thus, the average yields of isolated products **3** obtained via method D were increased by 4–19% when compared to the yields obtained by applying method C (Table 1, entries 1, 2, 4 and 6–8), whereas the yields were essentially the same in both methods for **3ac** (entry 3) and 3ba (entry 5). Significantly, comparing the average yields of products **3** for methods A (62%) and C (60%) on the one hand, and B (69%) and D (69%) on the other hand, confirms that the orchestration of the dimerization of terminal silylated alkynes and the (4+2) cycloaddition of the resulting 1,3-enynes with **1a** and **1b** in the presence of a nickel catalyst does not require the slow or sequential addition of the reagents.

Although arylacetylenes are ideal substrates for Ogoshi's $Ni/PtBu_3$-catalyzed head-to-head dimerization into 1,3-enynes,[11] we did not examine their reactivity in the present study because our previous studies established that the resulting 1,3-enynes would not insert into the C(sp2)–C(sp3) bond of **1a** or **1b** in a regioselective manner.[9a] Conversely, terminal alkynes substituted with an alkyl chain would lead to 1,3-enynes that are more amenable to regioselective insertion

into four-membered ring ketones,[9e] but these terminal alkynes underwent dimerization in only low yields under Ogoshi's optimized conditions due to oligomerization.[11] Nevertheless, we attempted the tandem dimerization/(4+2) cycloaddition of 1-hexyne (**2f**) with **1a** and were delighted to isolate compound **3af** in 31% yield (Scheme 5), which is a remarkable result in view of the challenges associated with the selective dimerization of the terminal alkyne **2f** and of the instability of **3af**.[12] Methods A–C gave inferior yields.

With the dimerization/(4+2) cycloaddition tandem process established in the case of azetidinone **1a** and oxetanone **1b**, we decided to explore the reactivity of other four-membered ring ketones (Scheme 6, A). Although cyclobutanone **5** and cyclobutenone **6** failed to give the expected results, benzocyclobutenone **7** and alkynes **2a**–**c** underwent the tandem dimerization/(4+2) cycloaddition after modification of method B, whereby a temperature of 100 °C was required for the cycloaddition (Scheme 6, B). Under these conditions, the reaction of **2a** led to a mixture of products **10a**–**12a** in a combined 51% yield. The formation of **11a** could be explained by known thermal [1,3]-carbon-to-oxygen Brook rearrangement of **10a**,[13] whereas cleavage of the O–Si bond in **11a** would lead to **12a**. In agreement with this scenario, more robust silicon groups increased the **10**/**11**/**12** ratio in favor of products **10** and **11**, and the reactions of **2b** and **2c** led to mixtures of **10b**/**11b** and **10c**/**11c** in combined yields of 51% and 58%, respectively. In addition, the mixture of products **10c** and **11c** was easily resolved into a single product by performing a desilylation on the crude mixture to give **12c** in 52% yield (Scheme 6, C). The protocol could also be applied to benzocyclobutenones **8** and **9** using **2a** as the alkyne to give products **13** and **14**, respectively, in synthetically useful yields after two steps. Importantly, we could perform the tandem reaction by simply adding all the reagents and catalysts in one portion and heating the mixture at 100 °C, with only a slight decrease of the combined yield of isolated products **10b** and **11b** being observed (Scheme 6, D). The cleavage of the C(sp2)–C(sp2) bond of the four-membered ring that was observed in the reactions of compounds **7**–**9**, as opposed to the cleavage of the C(sp2)–C(sp3) bond,[8,14] is likely controlled by minimization of steric hindrance, in agreement with a report that appeared during the preparation of this manuscript.[15] The excellent selectivity of the dimerization/(4+2) cycloaddition tandem process demonstrated above may be explained by the much faster formation of 1,3-enynes as compared to other reactions of the terminal alkynes. Thus, sampling the reaction of azetidinone **1a** with alkyne **2b** under the conditions used in either method C or method D (i.e., no sequential addition) after only 5 minutes showed that most of **2b** had already dimerized into the expected *trans* 1,3-enyne,16 whereas **1a** was mostly intact and only traces of **3ab** could be observed by ^{1}H NMR spectroscopy.

Using $^{31}P\{^{1}H\}$ NMR spectroscopy, we found that mixing $Ni(cod)_2$, P*t*Bu_3, and PPh_3 in a 1:1:3 ratio in toluene-d_8 at room temperature for five minutes left P*t*Bu3 as free ligand, whereas the main nickel-phosphine complexes were $[Ni(cod)(PPh_3)_2]$17 and $[Ni(PPh_3)_4]$.[18] Heating this mixture at 60 °C for one hour converted a small portion of these complexes into [Ni(P*t*Bu3)2] and $[Ni(PPh_3)(P$*t*$Bu_3)]$, but free P*t*Bu_3 was still a major constituent of the mixture, in agreement with its facile dissociation.[19,20] The large ^{2}JP–P coupling constant of 210 Hz observed for the partially unresolved doublet at 122 ppm and ascribed to $[Ni(PPh_3)(PtBu_3)]$ is in agreement with a trans configuration of the phosphine ligands. Several of these complexes can serve as a

reservoir for the active catalyst of each stage of the tandem reaction, but previous DFT calculations suggest that monophosphine complexes initiate the dimerization of the terminal alkyne[21] and the oxidative addition of the metal into the C–C bond of **1a** and **1b** in the presence of an alkyne.[22] Thus, [Ni($PtBu_3$)] could serve as an active catalyst in the very rapid first stage of the tandem process to give the intermediate 1,3-enyne after head-to-head dimerization, as proposed previously (Scheme 7).[11] However, no cycloaddition was observed when a mixture of **1a** and 1,3-enyne **15** was treated with a catalytic amount of $Ni(cod)_2$ and $PtBu_3$, whereas a $Ni(cod)_2$/PPh_3 mixture led to the formation of **3aa** in 80% yield (Scheme 8), which suggests that although [Ni($PtBu_3$)] may be the active catalyst for the dimerization of terminal alkynes,[11] it is not the active catalyst for the second stage of the tandem process. Thus, [Ni(1,3-enyne)(PPh_3)$_2$] (**A**) might be more active in that stage.[22] Hence, after rapid formation of the 1,3-enyne,[11] a plausible mechanism would involve a sequence comprised of the following steps: (i) conversion of [Ni(cod)(PPh_3)$_2$] into **A**, (ii) replacement of one PPh_3 by **1** or **7–9** to give **B**, (iii) oxidative addition into the C(sp2)–C(sp3) bond of the four-membered ring ketone to give **C**, (iv) insertion of the triple bond of the coordinated 1,3-enyne to give either **D** or **E**, and (v) reductive elimination to regenerate **A** in the presence of excess PPh_3 and liberation of products **3** and **10–14**.

In summary, we have demonstrated that terminal alkynes undergo a nickel-catalyzed three-component tandem of two reactions consisting of their stereoselective head-to-head dimerization into 1,3-enynes and the (4+2) cycloadditions of these compounds with an azetidinone, an oxetanone or benzocyclobutenones. The orchestration of the two catalytic cycles without recourse to slow or sequential addition of the reagents and catalysts is made possible by the rapid dimerization of the terminal alkynes prior to the cycloaddition.

Otherwise noted, all reactions were carried out in flame-dried glassware under dry nitrogen atmosphere. The solvents were purified with the solvent purification system Pure Solv MD-6 (THF, Et_2O, CH_2Cl_2). Toluene was purchased from Acros (99.85%, Extra Dry over Molecular Sieve, AcroSeal™). Temperature cited for reactions are oil bath temperatures. Flash chromatography: Merck silica gel 60 (230-400 mesh). NMR: Spectra were recorded on a Bruker DRX 500 in $CDCl_3$; chemical shifts (δ) are given in ppm. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δC = 77.0 ppm; residual $CHCl_3$ in $CDCl_3$: δH = 7.26 ppm); apparent splitting patterns are designated using the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), quint. (quintuplet), sept. (septuplet), m (multiplet), br (broad), and the appropriate combinations. The regiochemistry of the cycloaddition products was established by either HMBC or nOe experiments. The NMR spectra of **3aa**–**3ad**, **4**, and **3af** were recorded at 40 °C with a relaxation delay of 4 seconds in order to obtain optimum resolution, which was otherwise poor at room temperature due to slow conformer equilibration. Acquisition time was limited to 5 hours to prevent decomposition. IR: PerkinElmer Spectrum 100 FT-IR spectrometer. The intensity of the peaks is indicated by w (weak), m (medium), and s (strong). HRMS determined at the University of Liverpool on micromass LCT mass spectrometer (ESI) and Trio-1000 or Agilent QTOF 7200 mass spectrometers (CI). Melting points: Griffin melting point apparatus (not corrected). Elemental analyses: ThermoFisher Flash Smart (University of Liverpool). Compounds **1b**, **2a**, **2b**, **2e** and

2f are commercially available. All commercially available reagents were used as received. Compounds **1a**,[23] **2c**,[24] **2d**,[25] **7**,[26] **8**,[26] **9**,[27] and **15**[11] were prepared according to the literature.

Nickel-catalyzed cycloadditions of ketones 1a and 1b with terminal alkynes 2a–2f

Method A

Inside an argon-filled glovebox, a Teflon-screw flame-dried Schlenk flask equipped with a small stirrer bar was charged with $Ni(cod)_2$ (6.1 mg, 0.022 mmol, 0.1 equiv). Then, outside the glovebox and under N_2, PPh_3 (17.4 mg, 0.066 mmol, 0.3 equiv) was added, followed by toluene (0.2 mL). The mixture was stirred at room temperature for 5 minutes before toluene (0.2 mL) and **2a** (137 µL, 0.96 mmol, 4.4 equiv) were added. The mixture was stirred at 60 °C for 20 minutes. Then, the mixture was cooled to room temperature and a solution of **1a** (38 mg, 0.22 mmol, 1 equiv) in toluene (0.6 mL) was added. The tube was sealed and the mixture was stirred at 60 °C for 17 h. At room temperature, the mixture was filtered over a short plug of silica and all volatiles were removed in vacuo. Purification by flash chromatography on silica gel (petroleum ether/ethyl acetate = 98:2 to 95:5) afforded compound **3aa** as a pale-yellow oil.

Method B

Inside an argon-filled glovebox, a Teflon-screw flame-dried Schlenk flask equipped with a small stirrer bar was charged with $Ni(cod)_2$ (6.1 mg, 0.022 mmol, 0.1 equiv) and P*t*-Bu_3 (4.4 mg, 0.022 mmol, 0.1 equiv). Then, outside the glovebox and under N_2, toluene (0.2 mL) was added and the mixture was stirred at room temperature for 5 minutes before toluene (0.2 mL) and **2a** (137 µL, 0.96 mmol, 4.4 equiv) were added. The mixture was stirred at 60 °C for 10 minutes. Then, the mixture was cooled to room temperature and PPh_3 (17.4 mg, 0.066 mmol, 0.3 equiv) was added, followed by a solution of **1a** (38 mg, 0.22 mmol, 1 equiv) in toluene (0.6 mL). The remaining of the procedure is identical to that described in method A.

Method C

Inside an argon-filled glovebox, a Teflon-screw flame-dried Schlenk flask equipped with a small stirrer bar was charged with $Ni(cod)_2$ (6.1 mg, 0.022 mmol, 0.1 equiv). Then, outside the glovebox and under N_2, PPh_3 (17.4 mg, 0.066 mmol, 0.3 equiv) was added, followed by toluene (0.2 mL). The mixture was stirred at room temperature for 5 minutes before a solution of **1a** (38 mg, 0.22 mmol, 1 equiv) and **2a** (137 µL, 0.96 mmol, 4.4 equiv) in toluene (0.8 mL) was added. The tube was sealed and the mixture was stirred at 60 °C for 17 h. At room temperature, the mixture was filtered over a short plug of silica and all volatiles were removed in vacuo. Purification by flash chromatography is identical to that described in method A.

Method D

The procedure is identical to that describe for method C except that P*t*-Bu_3 (4.4 mg, 0.022 mmol, 0.1 equiv) is added inside an argon-filled glovebox to the teflon-screw flame-dried Schlenk flask equipped with a small stirrer bar and charged with $Ni(cod)_2$ (6.1 mg, 0.022 mmol, 0.1 equiv).

***tert*-butyl (*E*)-3-oxo-4-(trimethylsilyl)-5-(2-(trimethylsilyl)vinyl)-3,6-dihydropyridine-1(*2H*)-carboxylate (3aa)**

This compound was obtained from **1a** (38 mg, 0.22 mmol, 1 equiv) and **2a** (137 µL, 0.96 mmol, 4.4 equiv) according to method D. Flash chromatography afforded **3aa** as pale-yellow oil (run 1: 46 mg, 57%; run 2: 46 mg, 57%, R_f = 0.30 in petroleum ether/ethyl acetate = 9:1).

FT-IR (neat): 2971 (m), 1699 (s), 1660 (s), 1535 (w), 1410 (m), 1393 (m), 1365 (s), 1246 (s), 1216 (m), 1159 (s), 1110 (m), 1066 (m), 986 (w), 947 (w), 905 (w), 866 (s), 839 (s), 765 (m), 734 (m), 694 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 7.00 (d, *J* = 19.2 Hz, 1H), 6.64–6.40 (br s, 1H), 4.33 (s, 2H), 4.01 (s, 2H), 1.48 (s, 9H), 0.27 (s, 9H), 0.14 (s, 9H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 198.3, 160.6 (br), 154.2, 141.5, 139.9 (br), 137.8, 80.6, 51.7 (br), 43.2 (br), 28.2 (3C), 1.4 (3C), -1.7 (3C).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{33}NNaO_3Si_2$: 390.1891; found: 390.1901.

***tert*-butyl (*E*)-3-oxo-4-(triethylsilyl)-5-(2-(triethylsilyl)vinyl)-3,6-dihydropyridine-1(*2H*)-carboxylate (3ab)**

This compound was obtained from **1a** (38 mg, 0.22 mmol, 1 equiv) and **2b** (173 µL, 0.96 mmol, 4.4 equiv) according to method D. Flash chromatography afforded **3ab** as pale-yellow oil (run 1: 74 mg, 74%; run 2: 75 mg, 75%, R_f = 0.3 in petroleum ether/ethyl acetate = 95:5).

FT-IR (neat): 2955 (m), 2909 (m), 2876 (m), 1665 (s), 1531 (w), 1455 (w), 1412 (m), 1393 (m), 1367 (m), 1241 (m), 1158 (s), 1066 (m), 1056 (m), 1005 (m), 960 (w), 908 (m), 858 (w), 794 (m), 723 (s) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 6.95 (d, *J* = 19.3 Hz, 1H), 6.54–6.37 (br m, 1H), 4.38–4.22 (br s, 2H), 3.98 (s, 2H), 1.43 (s, 9H), 0.91 (t, *J* = 7.9 Hz, 9H), 0.87 (t, *J* = 8.2 Hz, 9H), 0.75 (q, *J* = 7.1 Hz, 6H), 0.60 (q, *J* = 7.7 Hz, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 198.9, 161.6 (br), 154.4, 142.8, 136.9 (br), 136.0, 80.7, 52.0, 43.3 (br), 28.2 (3C), 7.5 (3C), 7.1 (3C), 5.3 (3C), 3.2 (3C).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{45}NNaO_3Si_2$: 474.2830; found: 474.2843.

***tert*-butyl (*E*)-4-(dimethyl(phenyl)silyl)-5-(2-(dimethyl(phenyl)silyl)vinyl)-3-oxo-3,6-dihydropyridine-1(*2H*)-carboxylate (3ac)**

This compound was obtained from **1a** (38 mg, 0.22 mmol, 1 equiv) and **2c** (155 mg, 0.96 mmol, 4.4 equiv) according to method D. Flash chromatography afforded **3ac** as pale-yellow oil (run 1: 85 mg, 79%; run 2: 82 mg, 76%, R_f = 0.45 in petroleum ether/ethyl acetate = 9:1).

FT-IR (neat): 3066 (w), 2956 (w), 1698 (s), 1660 (s), 1531 (m), 1427 (m), 1365 (s), 1246 (s), 1158 (s), 1113 (s), 984 (m), 908 (m), 840 (s), 777 (m), 731 (m), 700 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 7.54-7.49 (m, 2H), 7.43-7.32 (m, 8H), 6.86 (d, *J* = 19.1, 1H), 6.77–6.47 (br m, 1H), 4.39 (s, 2H), 4.10 (s, 2H), 1.53 (s, 9H), 0.51 (s, 6H), 0.25 (s, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 198.3, 161.2 (br), 154.2, 143.0, 139.1, 138.1 (br), 136.8, 136.7, 133.7 (2C), 133.6 (2C), 129.2, 128.8, 127.83 (2C), 127.80 (2C), 80.7, 51.8 (br), 43.2 (br), 28.2 (3C), -0.1 (2C), -3.3 (2C).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{37}NNaO_3Si_2$: 514.2204; found: 514.2207.

***tert*-butyl (*E*)-4-(benzyldimethylsilyl)-5-(2-(benzyldimethylsilyl)vinyl)-3-oxo-3,6-dihydropyridine-1(*2H*)-carboxylate (3ad)**

This compound was obtained from **1a** (38 mg, 0.22 mmol, 1 equiv) and **2d** (168 mg, 0.96 mmol, 4.4 equiv) according to method D. Flash chromatography afforded **3ad** as pale-yellow oil (run 1: 74 mg, 65%; run 2: 86 mg, 75%, R_f = 0.45 in petroleum ether/ethyl acetate = 9:1).

FT-IR (neat): 2973 (m), 2901 (m), 1697 (s), 1657 (s), 1599 (w), 1534 (w), 1492 (m), 1451 (w), 1410 (m), 1366 (m), 1246 (s), 1206 (m), 1154 (s), 1115 (w), 1056 (m), 984 (w), 906 (m), 826 (s), 793 (w), 762 (w), 729 (s), 697 (s) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 7.22 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.5 Hz, 2H), 7.09 (t, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.97 (t, *J* = 8.2 Hz, 4H), 6.61 (d, *J* = 19.2 Hz, 1H), 6.51–6.36 (br s, 1H), 4.26–4.21 (br s, 2H), 4.07 (s, 2H), 2.36 (s, 2H), 2.13 (s, 2H), 1.52 (s, 9H), 0.23 (s, 6H), 0.06 (s, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 198.6, 161.6 (br), 154.2, 142.3, 139.6, 138.9 (br), 138.3, 136.6, 128.2 (4C), 128.1 (4C), 124.3, 124.1, 80.8, 51.7 (br), 43.3 (br), 28.3 (3C), 26.3, 25.5, -0.1 (2C), -3.7 (2C).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{30}H_{41}NNaO_3Si_2$: 542.2517; found: 542.2532.

***tert*-butyl (*E*)-4-butyl-5-(hex-1-en-1-yl)-3-oxo-3,6-dihydropyridine-1(*2H*)-carboxylate (3af)**

This compound was obtained from **1a** (38 mg, 0.22 mmol, 1 equiv) and **2f** (110 µL, 0.96 mmol, 4.4 equiv) according to method D. Flash chromatography afforded **3af** as pale-yellow oil (23 mg, 31%, R_f = 0.40 in petroleum ether/ethyl acetate = 9:1). This compound is not stable and peaks indicative of decomposition appeared in the in the ^{13}C spectrum during the long acquisition required to see the broad signals.

FT-IR (neat): 2957 (m), 2929 (m), 2860 (w), 1699 (s), 1668 (s), 1628 (m), 1422 (m), 1367 (s), 1279 (m), 1243 (m), 1163 (s), 1136 (m), 964 (w), 906 (w), 857 (w), 766 (w), 732 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 6.49 (d, *J* = 15.9 Hz, 1H), 6.33–6.16 (br s, 1H), 4.35 (s, 2H), 4.07 (s, 2H), 2.46-2.38 (m, 2H), 2.25 (q, *J* = 7.1 Hz, 2H), 1.50–1.41 (m, 2H), 1.48 (s, 9H), 1.41-1.28 (m, 6H), 0.96–0.88 (m, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 193.6, 154.3, 147.3 (br), 139.6 (br), 133.8, 125.5, 80.8, 51.5 (br), 42.8 (br), 33.5, 31.7, 30.9, 28.3 (3C), 23.7, 22.7, 22.1, 13.8, 13.7.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{33}NNaO_3$: 358.2353; found: 358.2358.

(*E*)-4-(trimethylsilyl)-5-(2-(trimethylsilyl)vinyl)-*2H*-pyran-3(*6H*)-one (3ba)

This compound was obtained from **1b** (14 µL, 0.22 mmol, 1 equiv) and **2a** (137 µL, 0.96 mmol, 4.4 equiv) according to method D. Flash chromatography afforded **3ba** as pale-yellow oil (run 1: 31 mg, 51%; run 2: 34 mg, 57%, R_f = 0.40 in petroleum ether/ethyl acetate = 95:5).

FT-IR (neat): 2955 (m), 1665 (s), 1531 (w), 1423 (w), 1284 (m), 1248 (m), 1217 (m), 1122 (m), 1046 (m), 987 (w), 941 (w), 838 (s), 763 (w), 727 (w), 691 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 6.98 (d, *J* = 19.4 Hz, 1H), 6.33 (d, *J* = 19.5 Hz, 1H), 4.48 (s, 2H), 4.06 (s, 2H), 0.28 (s, 9H), 0.14 (s, 9H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 199.2, 161.7, 140.8, 139.9, 136.6, 71.9, 65.6, 1.4 (3C), -1.6 (3C).

Anal. Calcd for $C_{13}H_{24}O_2Si_2$: C, 58.15; H, 9.01. Found: C, 58.68; H, 9.33.

(*E*)-4-(triethylsilyl)-5-(2-(triethylsilyl)vinyl)-*2H*-pyran-3(*6H*)-one (3bb)

This compound was obtained from **1b** (14 µL, 0.22 mmol, 1 equiv) and **2b** (173 µL, 0.96 mmol, 4.4 equiv) according to method D. Flash chromatography afforded **3bb** as pale-yellow oil (run 1: 62 mg, 80%; run 2: 60 mg, 77%, R_f = 0.35 in petroleum ether/ethyl acetate = 95:5).

FT-IR (neat): 2953 (m), 2875 (m), 1668 (s), 1527 (m), 1458 (m), 1415 (m), 1279 (m), 1235 (m), 1154 (m), 1003 (s), 793 (w), 732 (s) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.97 (d, *J* = 19.4 Hz, 1H), 6.30 (d, *J* = 19.5 Hz, 1H), 4.50 (s, 2H), 4.07 (s, 2H), 0.95 (t, *J* = 8.0 Hz, 9H), 0.93 (t, *J* = 7.9 Hz, 9H), 0.81 (q, *J* = 7.8 Hz, 6H), 0.64 (q, *J* = 8.1 Hz, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 199.7, 162.7, 142.2, 136.8, 134.6, 71.9, 65.6, 7.6 (3C), 7.2 (3C), 5.2 (3C), 3.1 (3C).

Anal. Calcd for $C_{19}H_{36}O_2Si_2$: C, 64.71; H, 10.29. Found: C, 64.69; H, 10.35.

(*E*)-4-(dimethyl(phenyl)silyl)-5-(2-(dimethyl(phenyl)silyl)vinyl)-*2H*-pyran-3(*6H*)-one (3bc)

This compound was obtained from **1b** (14 µL, 0.22 mmol, 1 equiv) and **2c** (155 mg, 0.96 mmol, 4.4 equiv) according to method D. Flash chromatography afforded **3bc** as pale-yellow oil (run 1: 65 mg, 75%; run 2: 60 mg, 70%, R_f = 0.22 in petroleum ether/ethyl acetate = 95:5).

FT-IR (neat): 3069 (w), 2959 (w), 2817 (w), 1663 (s), 1527 (m), 1427 (m), 1283 (m), 1248 (m), 1218 (w), 1191 (w), 1112 (s), 1045 (w), 984 (m), 938 (w), 909 (w), 829 (s), 813 (s), 776 (m), 730 (s), 699 (s) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.55-7.48 (m, 2H), 7.42-7.31 (m 8H), 6.79 (d, *J* = 19.4 Hz, 1H), 6.34 (d, *J* = 19.3 Hz, 1H), 4.49 (s, 2H), 4.11 (s, 2H), 0.50 (s, 6H), 0.21 (s, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 199.2, 162.3, 142.3, 139.1, 138.0, 136.8, 135.6, 133.8 (2C), 133.7 (2C), 129.4, 129.0, 128.0 (2C), 127.9 (2C), 71.9, 65.6, -0.2 (2C), -3.3 (2C).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{28}NaO_2Si_2$: 415.1520; found: 415.1530.

(*E*)-4-(benzyldimethylsilyl)-5-(2-(benzyldimethylsilyl)vinyl)-*2H*-pyran-3(*6H*)-one (3bd)

This compound was obtained from **1b** (14 µL, 0.22 mmol, 1 equiv) and **2d** (168 mg, 0.96 mmol, 4.4 equiv) according to method D. Flash chromatography afforded **3bd** as pale-yellow oil (run 1: 64 mg, 69%; run 2: 56 mg, 60%, R_f = 0.22 in petroleum ether/ethyl acetate = 95:5).

FT-IR (neat): 3024 (w), 2955 (w), 1661 (s), 1599 (m), 1530 (m), 1492 (m), 1451 (w), 1285 (m), 1249 (m), 1205 (m), 1153 (m), 1123 (m), 1055 (m), 985 (m), 941 (w), 906 (w), 835 (vs), 763 (m), 733 (m), 699 (s) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.21 (t, *J* = 7.6 Hz, 2H), 7.17 (t, *J* = 7.5 Hz, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.05 (t, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 4H), 6.55 (d, *J* = 19.4 Hz, 1H), 6.15 (t, *J* = 19.4 Hz, 1H), 4.40 (s, 2H), 4.10 (s, 2H), 2.35 (s, 2H), 2.11 (s, 2H), 0.21 (s, 6H), 0.04 (s, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 199.3, 162.7, 141.5, 139.7, 139.0, 138.1, 135.2, 128.3 (4C), 128.12 (2C), 128.09 (2C), 124.3, 124.1, 71.8, 65.7, 26.3, 25.5, -0.3 (2C), -3.8 (2C).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{25}H_{32}NaO_2Si_2$: 443.1833; found: 443.1841.

***tert*-butyl 3-oxo-5-(triisopropylsilyl)-3,6-dihydropyridine-1(*2H*)-carboxylate (4)**

This compound was obtained from **1a** (38 mg, 0.22 mmol, 1 equiv) and **2e** (220 µL, 0.96 mmol, 4.4 equiv) according to method C. Flash chromatography afforded **4** as pale-yellow paste (9.4 mg, 55%, R_f = 0.50 in petroleum ether/ethyl acetate = 9:1).

FT-IR (neat): 2945 (m), 2857 (m), 1686 (vs),1458 (w), 1417 (m), 1392 (w), 1366 (m), 1235 (m), 1161 (s), 1109 (m), 1071 (w), 1024 (m), 956 (w), 901 (w), 882 (m), 808 (w), 765 (w), 733 (m), 678 (w) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.31 (s, 1H), 4.22 (s, 2H), 4.07 (s, 2H), 1.43 (s, 9H), 1.23 (sept, *J* = 7.5 Hz, 3H), 1.06 (d, *J* = 7.4 Hz, 18H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 192.1, 161.9 (br)/160.7 (br),* 153.9, 135.9 (br), 80.7, 52.0 (br)/51.6 (br),* 46.0 (br), 28.2 (3C), 18.4 (6C), 10.6 (3C). The signals highlighted with a star (*) are pair of resonances for two rotamers.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{35}NNaO_3Si$: 376.2278; found: 376.2280.

Nickel-catalyzed cycloaddition of ketone 7 with terminal alkyne 2a

Inside an argon-filled glovebox, a teflon-screw flame-dried Schlenk flask equipped with a small stirrer bar was charged with $Ni(cod)_2$ (6.1 mg, 0.022 mmol, 0.1 equiv) and P*t*-Bu_3 (4.4 mg, 0.022 mmol, 0.1 equiv). Then, outside the glovebox and under N_2, toluene (0.2 mL) was added and the mixture was stirred 5 minutes at room temperature before toluene (0.2 mL) and **2a** (137 µL, 0.96 mmol, 4.4 equiv) were added. The mixture was stirred at 60 °C for 10 minutes. Then, the mixture was cooled down to room temperature and PPh_3 (17.4 mg, 0.066 mmol, 0.3 equiv) was added, followed by a solution of **7** (33 mg, 0.22 mmol, 1 equiv) in toluene (0.6 mL). The tube was sealed and the mixture was stirred at 100 °C for 17 h. At room temperature, the mixture was filtered over a short plug of silica and all volatiles were removed *in vacuo*. Purification by flash chromatography on silica gel (petroleum ether/ethyl acetate = 98:2 to 95:5) afforded compound **10a** (3 mg, 7%), **11a** (7 mg, 9%) and **12a** (21 mg, 35%). Only the major compound **12a** was fully characterised whilst the minor compounds **10a** and **11a** were characterised by ^{1}H NMR data.

(*E*)-8-methoxy-2-(trimethylsilyl)-3-(2-(trimethylsilyl)vinyl)naphthalen-1-ol (10a)

Yellow paste, R_f = 0.59 in petroleum ether/ethyl acetate = 95:5.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.73 (s, 1H), 7.36 (d, *J* = 7.5 Hz, 1H) , 7.30 (d, *J* = 18.5 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 6.30 (d, *J* = 18.7 Hz, 1H), 4.05 (s, 3H), 0.41 (s, 9H), 0.18 (s, 9H).

(*E*)-((8-methoxy-3-(2-(trimethylsilyl)vinyl)naphthalen-1-yl)oxy)trimethylsilane (11a)

This product contains traces of **10a**. Yellow paste, R_f = 0.70 in petroleum ether/ethyl acetate = 95:5.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39 (s, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 6.99 (s, 1H), 6.93 (d, *J* = 19.0 Hz, 1H), 6.75 (d, *J* = 7.5 Hz, 1H), 6.51 (d, *J* = 19.0 Hz, 1H), 3.92 (s, 3H), 0.29 (s, 9H), 0.19 (s, 9H).

(*E*)-8-methoxy-3-(2-(trimethylsilyl)vinyl)naphthalen-1-ol (12a)

Yellow paste, R_f = 0.35 in petroleum ether/ethyl acetate = 95:5.

FT-IR (neat): 3408 (m), 2952 (m), 1637 (m), 1599 (m), 1573 (m), 1508 (w), 1449 (w), 1381 (s), 1305 (w), 1282 (m), 1244 (m), 1202 (w), 1189 (w), 1170 (w), 1155 (w), 1087 (s), 1059 (w), 984 (m), 965 (w), 863 (s), 836 (s), 810 (m), 744 (m), 726 (w), 692 (w) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.25 (s, 1H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.32-7.25 (m, 2H), 7.08 (s, 1H), 6.94 (d, *J* = 19.1 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.58 (d, *J* = 19.1 Hz, 1H), 4.04 (s, 3H), 0.19 (s, 9H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 156.1, 154.6, 143.2, 137.8, 136.9, 130.7, 126.0, 122.2, 118.2, 114.9, 107.2, 104.1, 56.1, -1.2 (3C).

HRMS (CI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{21}O_2Si$: 273.1305; found: 273.1314.

Nickel-catalyzed cycloaddition of ketone 7 with terminal alkyne 2b

The procedure described for the preparation of **10a**–**12a** was applied to **7** (33 mg, 0.22 mmol, 1 equiv) and **2b** (173 µL, 0.96 mmol, 4.4 equiv). Flash chromatography afforded **10b** (12 mg, 13%) and **11b** (36 mg, 38%). Only the major compound **11b** was fully characterised whilst the minor compound **10b** was characterised by NMR data. Note: **10b** was isolated with traces of unknown impurities and was characterised only by ^{1}H and ^{13}C NMR.

(*E*)-8-methoxy-2-(triethylsilyl)-3-(2-(triethylsilyl)vinyl)naphthalen-1-ol (10b)

Yellow paste. R_f = 0.57 in petroleum ether/ethyl acetate = 95:5.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.71 (s, 1H), 7.40-7.36 (m, 2H), 7.33 (d, *J* = 18.9 Hz, 1H), 7.28 (d, *J* = 7.9 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 6.31 (d, *J* = 18.8 Hz, 1H), 4.05 (s, 3H), 1.02 (t, *J* = 8.1 Hz, 9H), 0.97 (s, 15H), 0.70 (q, *J* = 7.8 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.6, 155.8, 148.0, 146.2, 137.2, 127.9, 126.2, 121.8, 116.6, 115.2, 113.6, 103.9, 56.1, 8.0 (3C), 7.5 (3C), 6.1 (3C), 3.5 (3C).

(*E*)-((8-methoxy-3-(2-(triethylsilyl)vinyl)naphthalen-1-yl)oxy)triethylsilane (11b)

Yellow paste. R_f = 0.70 in petroleum ether/ethyl acetate = 95:5.

FT-IR (neat): 3369 (m), 3067 (w), 2953 (w), 2853 (w), 1620 (w), 1572 (m), 1478 (w), 1452 (m), 1427 (m), 1348 (s), 1298 (w), 1246 (m), 1229 (m), 1114 (m), 1088 (s), 1064 (m), 1016 (w), 987 (w), 972 (w), 816 (s), 776 (m), 752 (m), 729 (s), 698 (s) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.37 (s, 1H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 6.99 (s, 1H), 6.96 (d, *J* = 19.1 Hz, 1H), 6.75 (d, *J* = 7.5 Hz, 1H), 6.45 (d, *J* = 19.1 Hz, 1H), 3.91 (s, 3H), 1.03 (dt, *J* = 7.5, 1.5 Hz, 18H), 0.84 (q, *J* = 7.9 Hz, 6H), 0.71 (q, *J* = 7.9 Hz, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 157.0, 152.6, 144.5, 137.6, 136.5, 126.3 (2C),* 121.0, 120.3, 119.5, 112.7, 105.4, 55.4, 7.4 (3C), 6.7 (3C), 5.1 (3C), 3.6 (3C). The signal highlighted with a star (*) is an overlap of two resonances, as determined by HSQC.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{41}O_2Si_2$: 429.2645; found: 429.2640.

Nickel-catalyzed cycloaddition of ketone 7 with terminal alkyne 2c

The procedure described for the preparation of **10a**–**12a** was applied to **7** (33 mg, 0.22 mmol, 1 equiv) and **2c** (155 mg, 0.96 mmol, 4.4 equiv). Flash chromatography afforded **10c** (40 mg, 39%) and **11c** (20 mg, 19%). Only the major compound **10c** was fully characterised whilst the minor compound **11c** was characterised by ^{1}H NMR and HMRS data.

(*E*)-2-(dimethyl(phenyl)silyl)-3-(2-(dimethyl(phenyl)silyl)vinyl)-8-methoxynaphthalen-1-ol (10c)

Yellow paste. R_f = 0.47 in petroleum ether/ethyl acetate = 95:5.

FT-IR (neat): 3369 (m), 3067 (w), 2953 (w), 2853 (w), 1620 (w), 1572 (m), 1478 (w), 1452 (m), 1427 (m), 1348 (s), 1298 (w), 1246 (m), 1229 (m), 1114 (m), 1088 (s), 1064 (m), 1016 (w), 987 (w), 972 (w), 816 (s), 776 (m), 752 (m), 729 (s), 698 (s) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.77 (s, 1H), 7.57-7.53 (m, 2H), 7.52-7.48 (m, 2H), 7.46 (s, 1H), 7.40-7.27 (m, 8H), 7.21 (d, *J* = 18.8 Hz, 1H), 6.74 (d, *J* = 7.5 Hz, 1H), 6.41 (d, *J* = 18.7 Hz, 1H), 4.03 (s, 3H), 0.64 (s, 6H), 0.30 (s, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 160.7, 155.9, 148.2, 145.0, 141.4, 138.7, 137.5, 133.9 (2C), 133.6 (2C), 128.9, 128.8, 128.4, 127.7 (2C), 127.6 (2C), 126.5, 121.9, 116.7, 115.2, 113.8, 104.1, 56.0, 2.1 (2C), -2.7 (2C).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{32}NaO_2Si_2$: 491.1833; found: 491.1827.

(*E*)-(2-(4-((dimethyl(phenyl)silyl)oxy)-5-methoxynaphthalen-2-yl)vinyl)dimethyl(phenyl)silane (11c)

Yellow paste. R_f = 0.60 in petroleum ether/ethyl acetate = 95:5.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.74-7.69 (m, 2H), 7.60-7.55 (m, 2H), 7.43-7.38 (m, 5H), 7.37-7.27 (m, 4H), 6.92 (d, *J* = 19.1 Hz, 1H), 6.89 (d, *J* = 1.7 Hz, 1H), 6.74 (dd, *J* = 7.3, 1.2 Hz, 1H), 6.38 (d, *J* = 19.0 Hz, 1H), 3.79 (s, 3H), 0.52 (s, 6H), 0.43 (s, 6H).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{32}NaO_2Si_2$: 491.1833; found: 491.1826.

Two-step synthesis of compound 12c.

The procedure described for the preparation of **10a**–**12a** was applied to **7** (65 mg, 0.44 mmol, 1 equiv) and **2c** (310 mg, 1.94 mmol, 4.4 equiv). After evaporation of all volatiles the crude residue was dissolved in dry THF (4.4 mL) and TBAF•3H_2O (0.42 g, 1.3 mmol, 3 equiv) was added at 0 °C. The mixture was stirred at room temperature for 1h. Then, water was added and the mixture was extracted 3 times with diethyl ether (3 X 10 mL). The combined organic layer was washed with water, brine, was dried over $MgSO_4$ and concentrated. Purification by flash chromatography (petroleum ether/ethyl acetate = 98:2 to 95:5) afforded compound **12c** (77 mg, 52%).

(*E*)-3-(2-(dimethyl(phenyl)silyl)vinyl)-8-methoxynaphthalen-1-ol (12c)

Brown amorphous solid. R_f = 0.23 in petroleum ether/ethyl acetate = 95:5.

FT-IR (neat): 3401 (m), 2954 (m), 2844 (w), 1698 (w), 1631 (m), 1610 (m), 1598 (m), 1573 (m), 1508 (w), 1448 (w), 1427 (w), 1381 (s), 1305 (w), 1282 (m), 1239 (m), 1202 (w), 1189 (w), 1170 (w), 1156 (w), 1113 (m), 1086 (s), 1060 (m), 985 (m), 965 (w), 908 (w) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.26 (s, 1H), 7.64-7.59 (m, 2H), 7.42-7.38 (m, 4H), 7.32 (d, *J* = 7.7 Hz, 1H), 7.31-7.29 (m, 1H), 7.11 (s, 1H), 7.02 (d, *J* = 19.1 Hz, 1H), 6.78 (d, *J* = 7.7 Hz, 1H), 6.71 (d, *J* = 19.1 Hz, 1H), 4.08 (s, 3H), 0.48 (s, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 156.1, 154.6, 144.9, 138.5, 137.6, 136.8, 133.9 (3C), 129.1, 128.2, 127.8, 126.1, 122.2, 118.4, 115.0, 107.2, 104.3, 56.1, 2.5 (2C).

HRMS (CI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{23}O_2Si$: 335.1467; found: 335.1476.

Two-step synthesis of compound 13

The procedure described for the preparation of **12c** was applied to **8** (39 mg, 0.22 mmol, 1 equiv) and **2a** (156 µL, 1.14 mmol, 5 equiv). The procedure was modified by applying a temperature of 120 °C after sealing the teflon-screw flame-dried Schlenk flask. Purification by flash chromatography (petroleum ether/ethyl acetate = 98:2 to 95:5) afforded compound **13** (16 mg, 24%).

(*E*)-6,8-dimethoxy-3-(2-(trimethylsilyl)vinyl)naphthalen-1-ol (13)

Orange solid. R_f = 0.27 in petroleum ether/ethyl acetate = 15:1.

Mp 107–108 °C.

FT-IR (neat): 3354 (m), 2997 (w), 2953 (m), 1619 (s), 1512 (w), 1475 (m), 1456 (m), 1395 (s), 1373 (s), 1304 (m), 1271 (w), 1246 (s), 1210 (s), 1199 (m), 1186 (m), 1155 (s), 1117 (s), 1047 (s), 981 (s), 934 (m), 861 (s), 830 (s), 818 (s), 806 (s) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.05 (s, 1H), 7.16 (d, *J* = 1.5 Hz, 1H), 6.92 (d, *J* = 1.4 Hz, 1H), 6.90 (d, *J* = 19.0 Hz, 1H), 6.70 (d, *J* = 2.2 Hz, 1H), 6.56 (d, *J* = 19.1 Hz, 1H), 6.42 (d, *J* = 2.2 Hz, 1H), 4.00 (s, 3H), 3.89 (s, 3H), 0.48 (s, 6H), 0.18, (s, 9H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 157.9, 157.1, 154.7, 143.3, 138.3, 137.5, 130.5, 117.3, 110.5, 105.4, 99.8, 97.7, 56.1, 55.3, -1.3 (3C).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{23}O_3Si$: 303.1416; found: 303.1427.

Two-step synthesis of compound 14

The procedure described for the preparation of **13** was applied to **9** (39 mg, 0.22 mmol, 1 equiv) and **2a** (156 µL, 1.14 mmol, 5 equiv). Purification by flash chromatography (petroleum ether/ethyl acetate = 20:1 to 17:1) afforded compound **14** (18 mg, 27%).

(*E*)-5,8-dimethoxy-3-(2-(trimethylsilyl)vinyl)naphthalen-1-ol (14)

Orange solid. R_f = 0.20 in petroleum ether/ethyl acetate = 15:1.

Mp 108–114 °C.

FT-IR (neat): 3386 (m), 2998 (w), 2951 (m), 2898 (w), 2838 (m), 1633 (w), 1622 (s), 1514 (s), 1452 (s), 1390 (s), 1320 (w), 1304 (w), 1243 (s), 1200 (m), 1183 (m), 1093 (s), 1054 (s), 996 (s), 971 (m), 864 (s), 835 (s), 802 (s) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.38 (s, 1H), 7.69 (d, *J* = 1.5 Hz, 1H), 7.11 (d, *J* = 1.6 Hz, 1H) 6.97 (d, *J* = 19.1 Hz, 1H), 6.65 (d, *J* = 8.5 Hz, 1H), 6.63 (d, *J* = 8.5 Hz, 1H), 6.58 (d, *J* = 19.1 Hz, 1H), 4.00 (s, 3H), 3.95 (s, 3H), 0.17 (s, 9H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 154.5, 150.5, 150.0, 143.6, 137.4, 130.2, 128.4, 115.3, 112.4, 108.0, 103.5, 103.4, 55.2, 55.7, -1.3 (3C).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{234}O_3Si$: 303.1416; found: 303.1424.

Reactions of 2b and 7 according to method D

Method D was applied to **2b** (0.13 mL, 0.96 mmol, 4.4 equiv) and **7** (33 mg, 0.22 mmol, 1 equiv) except that the temperature was set at 100 °C. After separation by flash chromatography, **10b** (9 mg, 10 %) and **11b** (29 mg, 31%) were obtained as yellow pastes.

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Supporting Information

YES (this text will be updated with links prior to publication)

Primary Data

NO (this text will be deleted prior to publication)

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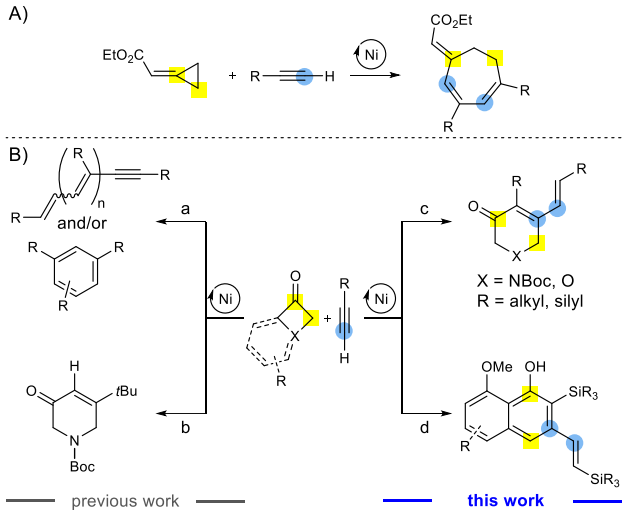
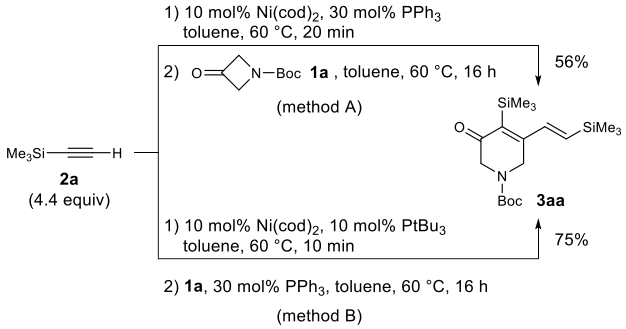
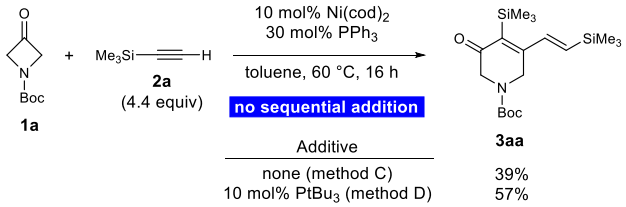


Scheme 1. (A) Nickel-catalyzed (3+2+2) cycloaddition of terminal alkynes and an alkylidenecyclopropane. (B) Nickel-catalyzed reactions of terminal alkynes and four-membered ring ketones.



Scheme 2. Tandem nickel-catalyzed dimerization/(4+2) cycloaddition by sequential addition of alkyne **2a** and azetidinone **1a**. Yields are for isolated products and are averages of duplicated experiments; cod: cyclooctadiene.

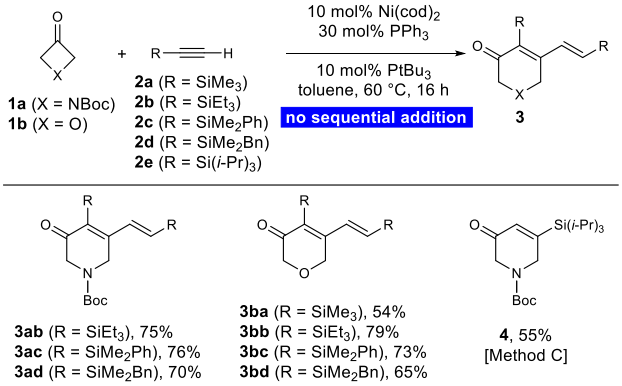


Scheme 3. Tandem nickel-catalyzed dimerization/(4+2) cycloaddition without sequential addition of alkyne **2a** and azetidinone **1a**. Yields are for isolated products and are averages of duplicated experiments; cod: cyclooctadiene.

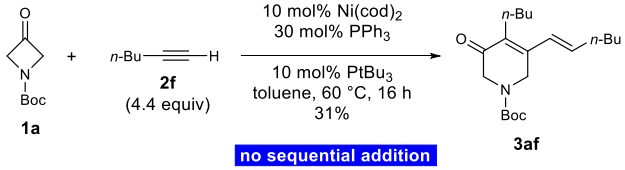
Table 1 Comparison of yields obtained by following methods A–D.[a]

entry	product	Yield obtained by following methods A–D			
		A	B	C	D
1	**3aa**	56%	75%	39%	57%
2	**3ab**	66%	76%	70%	75%
3	**3ac**	74%	81%	76%	76%
4	**3ad**	56%	72%	62%	70%
5	**3ba**	52%	72%	52%	54%
6	**3bb**	82%	72%	69%	79%
7	**3bc**	56%	54%	69%	73%
8	**3bd**	56%	53%	46%	65%

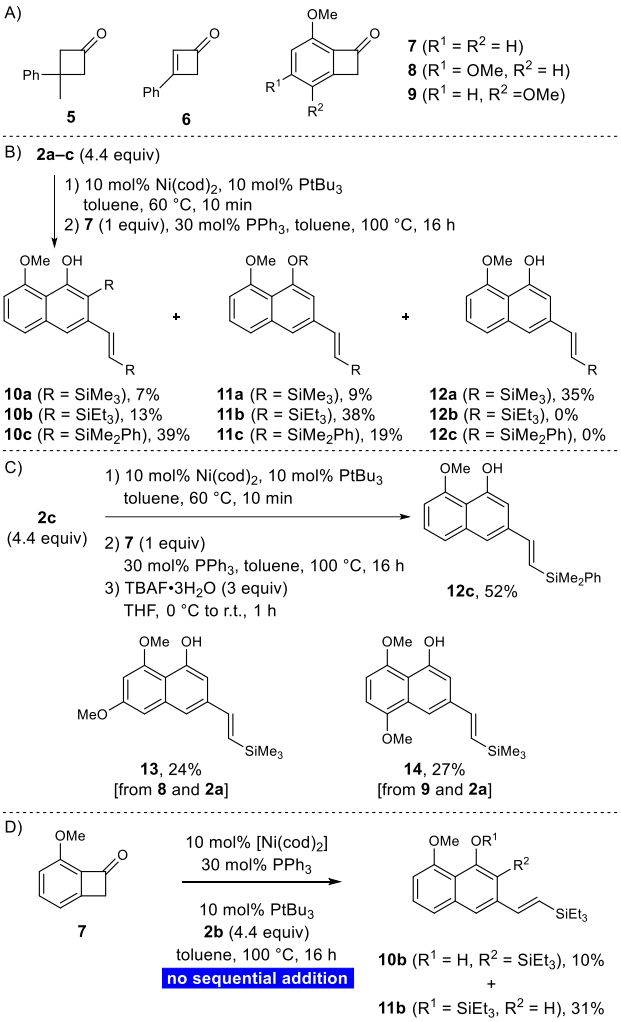
[a] Yield of isolated product as average of two experiments.



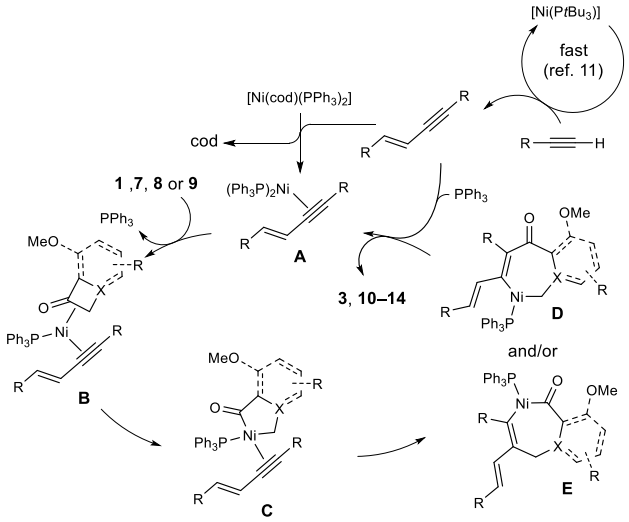
Scheme 4. Tandem nickel-catalyzed dimerization/(4+2) cycloaddition of silylated alkynes and azetidinone **1a** or oxetanone **1b**. All yields are for isolated products, and all are averages of duplicated experiments except for **4**. Reaction conducted with **1** (0.22 mmol, 1 equiv), **2** (4.4 equiv), $Ni(cod)_2$ (0.1 equiv), $PtBu_3$ (0.1 equiv), and PPh_3 (0.3 equiv) in toluene (1 mL). Yields of isolated product as averages of two experiments.



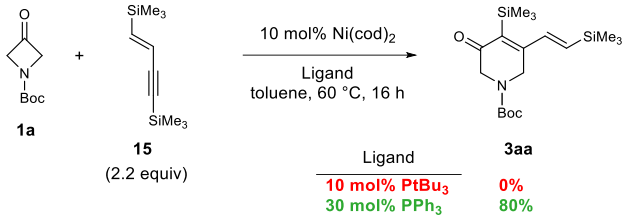
Scheme 5. Tandem nickel-catalyzed dimerization/(4+2) cycloaddition of 1-hexyne (**2f**) and azetidinone **1a**. Yield of isolated products as averages of duplicated experiments; cod: cyclooctadiene.



Scheme 6. (A) Structures of the examined four-membered-ring ketones. (B) Tandem nickel-catalyzed dimerization/(4+2) cycloaddition of alkynes **2a–c** and benzocyclobutenone 7. (C) Reactions of **2c** + **7**, **2a** + **8**, and **2a** + **9**, followed by desilylation. (D) Tandem nickel-catalyzed dimerization/(4+2) cycloaddition without sequential addition; TBAF: tetrabutylammonium fluoride; THF: tetrahydrofuran.



Scheme 7. Proposed mechanism.



Scheme 8. Control reactions; cod: cyclooctadiene