Convenient and Practical Alkynylation of Heteronucleophiles with Copper Acetylides

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Dedicated to Prof. François Couty on the occasion of his 50th birthday

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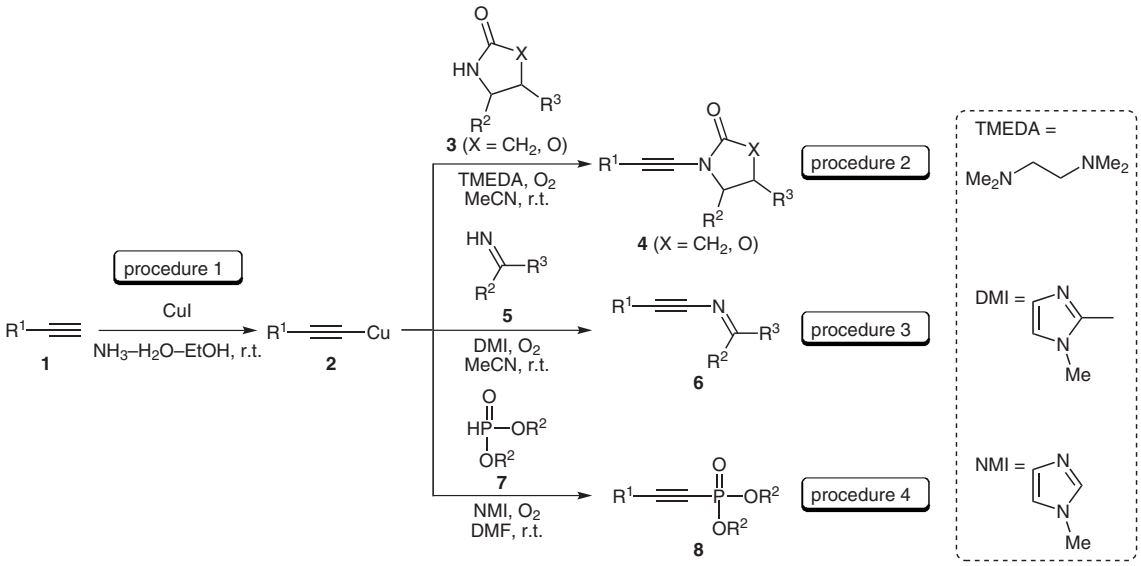
Abstract: Copper acetylides, readily available reagents which are characterized by their lack of reactivity, can be simply activated by oxidation with oxygen in the presence of simple nitrogen ligands such as TMEDA or imidazole derivatives. Upon activation, these nucleophilic species undergo a formal umpolung and can transfer their alkyne subunit to a wide range of heteronucleophiles, including amides, oxazolidinones, imines, and dialkyl phosphites. This alkynylation, which provides one of the most practical entry to useful building blocks such as ynamides, ynimines, and alkynylphosphonates, proceeds under especially mild conditions and can be easily performed on a multigram scale.

Key words: copper acetylides, alkynylation, ynamides, ynimines, alkynylphosphonates



Scheme 1 Alkynylation of heteronucleophiles with copper acetylides: a convenient and practical synthesis of ynamides, ynimines, and alkynylphosphonates

Hetero-substituted alkynes definitely represent the most useful and versatile class of alkynes.[1–4] The strong polarization of the triple bond due to the presence of the heteroatom allows these compounds to undergo highly efficient, regio- and stereoselective transformations. Among these building blocks, nitrogen- and phosphorus-substituted alkynes are emerging as key synthetic intermediates in chemical synthesis, where their use for the development of new reactions have resulted in the appearance of new synthetic paradigms, and also in medicinal chemistry and material sciences.

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As a result of this increased interest for these building blocks, there is a strong demand for the development of efficient, robust, and reliable methods for their synthesis, which has definitely become a hot topic in modern organic chemistry. Indeed, a lot of efforts have been recently devoted to the design of straightforward processes that would allow for an easy synthesis of nitrogen- (namely ynamides)[5] and phosphorus-substituted[6] alkynes. Despite the excellent results obtained with these reactions, they, however, often require heating and/or the presence of a base – which are not always compatible with the sensitivity of the products – and the slow addition of one reagent. In addition, they sometimes rely on catalysts or reagents that are not readily available and their use on large scales can be problematic.

To address these limitations, we have recently reported a new approach to nitrogen- and phosphorus-substituted alkynes based on the use of readily available reagents, copper acetylides **2**.[7] These reagents are easily and conveniently prepared by simple addition of terminal alkynes **1** to a solution of copper iodide in a mixture of aqueous ammonia and ethanol followed by filtration of the copper acetylides **2**, which immediately precipitate from the reaction mixture (Scheme 1).

One of the main characteristic features of these polymeric reagents is their total lack of reactivity. Unlike other organocopper reagents, they are indeed remarkably stable to acids and air, and their reactions with electrophiles are especially sluggish (their hydrolysis, which typically requires heating in concentrated hydrochloric acid, is quite representative of their low reactivity). We have recently found that they can, however, be readily activated by oxidation with molecular oxygen in the presence of simple nitrogen ligands such as *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) or imidazole derivatives, which results in an umpolung of their reactivity.[8] Under these conditions, they can indeed react with various nitrogen and phosphorus nucleophiles and therefore act as remarkably practical and efficient alkynylating agents.[9] This strategy could notably be used for the development of efficient entries to ynamides, ynimines, and alkynylphosphonates (Scheme 1), which can be readily obtained by oxidative alkynylation of amides/carbamates, imines, and dialkyl phosphites, respectively, with copper acetylides.

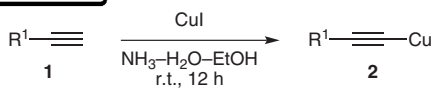
Scope and Limitations

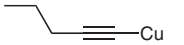
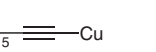
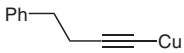
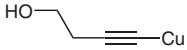
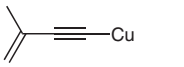
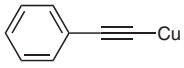
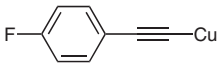
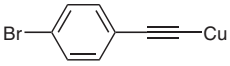
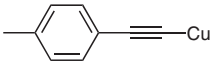
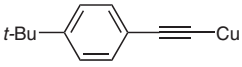
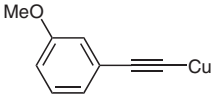
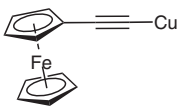
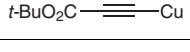
Apart from phenylethynylcopper, which is commercially available, other copper acetylides are readily prepared by modification of previously reported procedures.[10] Upon addition of a terminal alkyne to a solution of copper(I) iodide in a mixture of aqueous ammonia and ethanol, a yellow precipitate starts to appear almost instantaneously (Scheme 1, procedure 1). After 12 hours at room temperature to ensure full metalation of the starting alkyne, the copper acetylide – which is totally insoluble in all organic solvents evaluated – is collected by simple filtration, successively washed with aqueous ammonia, water, ethanol, and diethyl ether, and the resulting bright yellow polymeric copper acetylide is finally dried under high vacuum. These bench-stable reagents can be stored at room temperature without specific precautions, can be kept for years without noticeable degradation, and – contrary to certain preconceived ideas – are not explosive at all (in opposition to copper carbide and bis-copper acetylides).[11]

Due to the operational simplicity, the reaction can be easily performed on a multigram scale and representative copper acetylides that can be obtained according to procedure 1 are shown in Table 1. The reaction is compatible with alkyl- (Table 1, entries 1–4), alkenyl- (entry 5), and aryl-substituted (entries 6–12) alkynes as well as conjugated ones such as *tert*-butyl propiolate (entry 13). As a

Table 1 Preparation of Copper Acetylides[a]

procedure 1



Entry	Copper acetylide **2**		Yield (%)[b]	Isolated mass
1	**2a**		86	11.2 g
2	**2b**		84	7.3 g
3	**2c**		90	3.2 g
4	**2d**		55	1.5 g
5	**2e**		54	1.4 g
6	**2f**		87	13.9 g
7	**2g**		79	3.0 g
8	**2h**		91	1.1 g
9	**2i**		98	16.5 g
10	**2j**		78	1.8 g
11	**2k**		94	7.2 g
12	**2l**		97	1.3 g
13	**2m**		76	2.3 g

[a] Conditions: alkyne (1 equiv), CuI (2 equiv).
[b] Isolated yield of pure product.

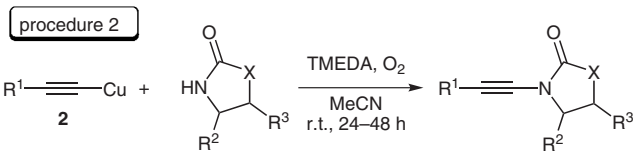
note, more complex copper acetylides that might not be compatible with the use of ethanol and/or ammonia can be prepared by an alternative procedure based on the reaction of the corresponding terminal alkyne with copper(I) iodide in the presence of potassium carbonate at room temperature in DMF.[9a]

Table 2 illustrates the ability of these reagents to transfer their alkyne group to various nitrogen nucleophiles such as γ-lactam and oxazolidin-2-ones **3** (Scheme 1, procedure 2). Previous optimization of the alkynylation of these nucleophiles with copper acetylides **2** led to conditions involving TMEDA as the ligand in the presence of molecular oxygen (balloon) in acetonitrile at room temperature until complete disappearance of the copper acetylide (which is characterized by complete dissolution to a deep blue homogeneous reaction mixture after 24–48 h).[9a] This reaction has advantages over previously reported ones of being especially practical (reagent grade acetonitrile and reagents, room temperature, self-indicating reaction which changes color upon completion, no workup required) and conveniently performed on a multigram scale.

The reaction readily proceeds regardless the nature of the copper acetylide, and nitrogen nucleophiles such as γ-lactams (Table 2, entries 1–7) and oxazolidin-2-ones (entries 8–10) are typically transformed to the corresponding ynamides **4** in good to excellent yields. Copper acetylides can also be used for the alkynylation of chiral oxazolidinones, yielding the corresponding chiral ynamides such as **4k** with good efficiency (entry 11), provided, however, that there is no bulky substituent α to the nitrogen atom. Interestingly, the presence of an aromatic bromide such as in **4e** is compatible with the alkynylation, which provides a starting point for further functionalization. A limitation was, however, found in the reactivity of less reactive amides such as *N*-methylacetamide and δ-valerolactam, which showed no reactivity under the reaction conditions. As a note, an excess (4 equiv) of the nitrogen nucleophile is used in typical procedure 2. A useful yield of **4d** (61%) is also obtained with a single equivalent of γ-lactam, even if a higher amount of dimerization of the starting copper acetylide is observed in this case.

Besides lactams and oxazolidin-2-ones, imines **5** can also be used as nucleophiles and their alkynylation with copper acetylides is also quite efficient, especially when the high sensitivity of the ynimines **6** formed is taken into consideration (Scheme 1, procedure 3). Representative examples from Table 3 show typical ynimines **6** that can be obtained using the oxidative alkynylation with copper acetylides. The procedure is quite similar to the one involving lactams and oxazolidinones, the only difference being the use of 1,2-dimethylimidazole (DMI) as the ligand.[9b] Diaryl- (Table 3, entry 1) and arylalkylynimines (entries 2–4) can be obtained with similar efficiency, mixtures of *E*- and *Z*-isomers being formed in the latter cases.

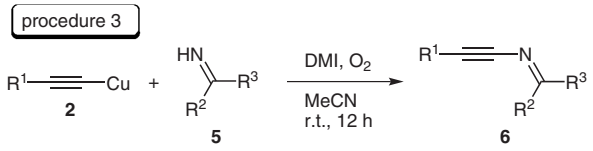
Table 2 Synthesis of Ynamides by Alkynylation of γ-Lactam and Oxazolidin-2-ones with Copper Acetylides[a]

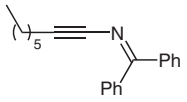
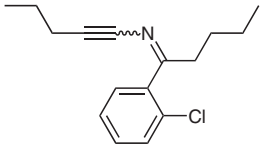
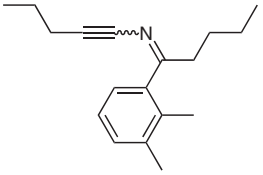
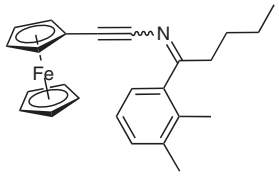


Entry	Ynamide **4**	Yield (%)[b]	Isolated mass
1	**4a**	82	12.4 g
2	**4b**	92	1.9 g
3	**4c**	77	0.3 g
4	**4d**	70	3.9 g
5	**4e**	61	1.0 g
6	**4f**	77	0.3 g
7	**4g**	60	0.3 g
8	**4h**	91	2.0 g
9	**4i**	54	0.2 g
10	**4j**	75	0.3 g
11	**4k**	72	0.4 g

[a] Conditions: copper acetylide (1 equiv), lactam or oxazolidinone (4 equiv), TMEDA (1 equiv).
[b] Isolated yield of pure product.

Table 3 Synthesis of Ynimines by Alkynylation of Imines with Copper Acetylides[a]

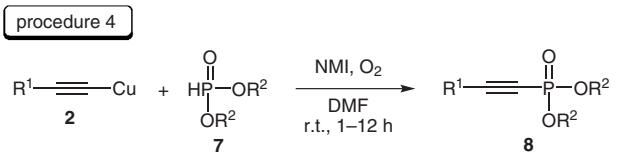


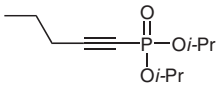
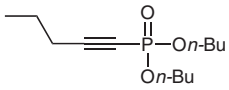
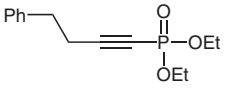
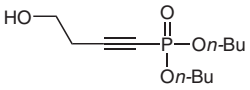
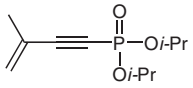
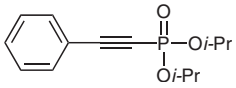
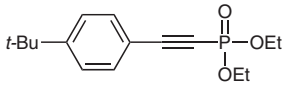
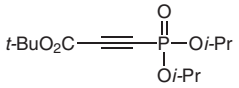
Entry	Ynimine **6**	Yield (%)[b]	Isolated mass
1	**6a** 	57	0.2 g
2	**6b**  *Z*/*E* = 50:50	69	0.2 g
3	**6c**  *Z*/*E* = 40:60	75	1.5 g
4	**6d**  *Z*/*E* = 38:62	62	0.2 g

[a] Conditions: copper acetylide (1 equiv), imine (4 equiv), 1,2-dimethylimidazole (2 equiv).
[b] Isolated yield of pure product.

In Table 4, the ability to perform a remarkably clean alkynylation of dialkyl phosphites **7** yielding to the corresponding alkynylphosphonates **8** is demonstrated (procedure 4), which further highlights the generality of the alkynylation of heteronucleophiles with copper acetylides. This procedure requires the use of DMF as the solvent and *N*-methylimidazole (NMI) as the ligand, which allows for a clean and fast alkynylation of a wide range of dialkyl phosphites.[9a] Alkyl- (Table 4, entries 1–4) and aryl-substituted (entries 6 and 7) alkynylphosphonates can conveniently be prepared using the corresponding copper acetylides as well as alkenyl- (entry 5) and carboxy-substituted (entry 8) ones.

Table 4 Synthesis of Alkynylphosphonates by Alkynylation of Dialkyl Phosphites with Copper Acetylides[a]



Entry	Alkynylphosphonate **8**	Yield (%)[b]	Isolated mass
1	**8a** 	92	16.0 g
2	**8b** 	92	4.8 g
3	**8c** 	96	0.5 g
4	**8d** 	96	1.0 g
5	**8e** 	88	0.4 g
6	**8f** 	97	2.6 g
7	**8g** 	96	0.5 g
8	**8h** 	48	0.3 g

[a] Conditions: copper acetylide (1 equiv), dialkyl phosphite (4 equiv), 1-methylimidazole (2 equiv).
[b] Isolated yield of pure product.

Summary

In summary, we have reported efficient and especially practical procedures for the alkynylation of nitrogen and phosphorus nucleophiles based on the alkynylation with readily available, bench-stable copper acetylides. Ynamides, ynimines, and alkynylphosphonates can be readily obtained at room temperature with the utmost operational simplicity by the means of these procedures, which can be easily performed on multigram scales. From a practical point of view, these 'practical synthetic procedures' have many advantages including the use of user-friendly conditions (room temperature, simple activation with a balloon of oxygen, self-indicating reaction mixture, which turns from a yellow heterogeneous suspension to a

homogeneous deep blue or deep green solution upon completion), the use of reagent grade solvents and reagents, easy purifications, and they do not rely on expensive ligands.

Procedures

All solvents and starting materials were purchased from commercial suppliers and used without further purification. Petroleum ether (PE) used refers to the fraction boiling in the 40–60 °C range. Reactions were magnetically stirred. Flash chromatography was performed with silica gel 60 (particle size 35–70 μm) supplied by SDS. Yields refer to chromatographically and spectroscopically pure compounds. ^{1}H NMR spectra were recorded using an internal deuterium lock at ambient temperature on a Bruker 300 MHz spectrometer. Internal references of δ_H 7.26 was used for $CDCl_3$. Data are presented as follows: chemical shift (in ppm on the δ scale relative to Me_4Si at 0 ppm), multiplicity (standard abbreviations), coupling constant (*J*, in Hz), and integration. Resonances that are either partially or fully obscured are denoted obscured (obs). ^{13}C NMR spectra were recorded at 75 MHz. Internal reference of δ_C 77.16 ppm was used for $CDCl_3$. ^{31}P and ^{19}F NMR spectra were recorded at 121/161 and 377 MHz, respectively. Optical rotations were recorded on a Perkin Elmer 341 polarimeter at 589 nm and reported as follows: $[\alpha]_D^{20}$, concentration (*c* in g/100 mL), and solvent. Melting points were recorded on a Büchi B-545. IR spectra were recorded on a Nicolet iS 10 (SMART iTR diamond ATR) spectrophotometer. High-resolution mass spectra were obtained on a Waters Xevo Qtof spectrometer. Elemental analyses were obtained by combustion analysis (for C, H, N) and by inductively coupled plasma atomic emission spectroscopy (for Cu).

Preparation of Copper Acetylides; Procedure 1

To a solution of CuI (3.8 g, 20.0 mmol) in a mixture of NH_4OH (28% NH_3 solution, 50 mL) and EtOH (30 mL) was added the alkyne **1** (10.0 mmol) dropwise. The deep blue reaction mixture was stirred overnight at r.t. under argon and the yellow precipitate was collected by filtration and successively washed with NH_4OH (10% NH_3 solution, 3 × 50 mL), H_2O (3 × 50 mL), EtOH (3 × 50 mL), and Et_2O (3 × 50 mL). The bright yellow solid was then dried under high vacuum overnight to afford the desired polymeric copper acetylide **2**, which was used without further purification.

Alkynylation of γ-Lactam and Oxazolidin-2-ones with Copper Acetylide; Procedure 2

A 5 mL round-bottomed flask was successively charged with the nitrogen nucleophile **3** (8.0 mmol), the copper acetylide **2** (2.0 mmol), and MeCN (4 mL). The resulting bright yellow slurry was then treated with TMEDA (300 μL, 2.0 mmol) and the reaction mixture was vigorously stirred at r.t. and under an atmosphere of O_2 (balloon). After complete disappearance of the alkynylcopper reagent (complete dissolution to a deep blue homogeneous reaction mixture: typically 24–48 h), the crude reaction mixture was concentrated under vacuum, and the residue was finally purified by flash chromatography over silica gel to afford the desired ynamide **4**.

Alkynylation of Imines with Copper Acetylide; Procedure 3

A 10 mL round-bottomed flask was successively charged with the imine **5** (8.0 mmol), the copper acetylide **2** (2.0 mmol), and MeCN (8 mL). The resulting bright yellow slurry was then treated with 1,2-dimethylimidazole (384 mg, 4.0 mmol) and the reaction mixture was vigorously stirred at r.t. and under an atmosphere of O_2 (balloon). After complete disappearance of the alkynylcopper reagent (complete dissolution to a deep green homogeneous reaction mixture: typically 12 h), the crude reaction mixture was concentrated under vacuum and the residue was finally purified by flash chromatography over triethylamine-deactivated silica gel to afford the desired ynimine **6**.

Alkynylation of Dialkyl Phosphites with Copper Acetylide; Procedure 4

A 5 mL round-bottomed flask was successively charged with dialkyl phosphite **7** (8.0 mmol), the copper acetylide **2** (2.0 mmol), and DMF (4 mL). The resulting bright yellow slurry was then treated with *N*-methylimidazole (315 μL, 4.0 mmol) and the reaction mixture was vigorously stirred at r.t. and under an atmosphere of O_2 (balloon). After complete disappearance of the alkynylcopper reagent (complete dissolution to a deep blue homogeneous reaction mixture: typically 1–12 h), the reaction was diluted with an aqueous mixture of sat. aq NH_4Cl and 28% NH_4OH (1:1 solution, 20 mL) and extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The crude residue was finally purified by flash chromatography over silica gel to give the desired alkynylphosphonate **8**.

Pent-1-yn-1-ylcopper (2a)

Prepared according to procedure 1 from pent-1-yne (9.9 mL, 100.0 mmol) and a solution of CuI (38.1 g, 200.0 mmol) in a mixture of NH_4OH (28% NH_3 solution, 500 mL) and EtOH (300 mL); yield: 11.2 g (86.0 mmol, 86%); bright yellow solid.

Anal. Calcd for C_5H_7Cu: C, 45.96; H, 5.40; Cu, 47.94. Found: C, 45.36; H, 5.26; Cu, 48.64.

Oct-1-yn-1-ylcopper (2b)

Prepared according to procedure 1 from oct-1-yne (7.4 mL, 50 mmol) and a solution of CuI (19.0 g, 100.0 mmol) in a mixture of NH_4OH (28% NH_3 solution, 250 mL) and EtOH (150 mL); yield: 7.3 g (42.0 mmol, 84%); bright yellow solid.

Anal. Calcd for $C_8H_{13}Cu$: C, 55.63; H, 7.59; Cu, 36.79. Found: C, 55.31; H, 7.29; Cu, 36.69.

4-Phenylbut-1-yn-1-ylcopper (2c)

Prepared according to procedure 1 from 4-phenylbut-1-yne (2.6 mL, 18.5 mmol) and a solution of CuI (7.1 g, 37.2 mmol) in a mixture of NH_4OH (28% NH_3 solution, 100 mL) and EtOH (60 mL); yield: 3.2 g (16.6 mmol, 90%); bright yellow solid.

Anal. Calcd for $C_{10}H_9Cu$: C, 62.32; H, 4.71; Cu, 32.97. Found: C, 62.10; H, 4.76; Cu, 33.21.

4-Hydroxybut-1-yn-1-ylcopper (2d)

Prepared according to procedure 1 from but-3-yn-1-ol (1.6 mL, 21.1 mmol) and a solution of CuI (8.1 g, 42.5 mmol) in a mixture of NH_4OH (28% NH_3 solution, 100 mL) and EtOH (30 mL); yield: 1.54 g (11.6 mmol, 55%); bright yellow solid.

Anal. Calcd for C_4H_5CuO: C, 36.22; H, 3.80; Cu, 47.91. Found: C, 35.92; H, 3.62; Cu, 48.15.

3-Methylbut-3-en-1-yn-1-ylcopper (2e)

Prepared according to procedure 1 from 2-methylbut-1-en-3-yne (1.9 mL, 20.0 mmol) and a solution of CuI (7.6 g, 40.0 mmol) in a mixture of NH_4OH (28% NH_3 solution, 100 mL) and EtOH (60 mL); yield: 1.4 g (10.9 mmol, 54%); bright yellow solid.

Anal. Calcd for C_5H_5Cu: C, 46.68; H, 3.92; Cu, 49.40. Found: C, 46.67; H, 3.86; Cu, 48.31.

Phenylethynylcopper (2f)

Prepared according to procedure 1 from phenylacetylene (10.7 mL, 97.4 mmol) and a solution of CuI (37.3 g, 195.8 mmol) in a mixture of NH_4OH (28% NH_3 solution, 500 mL) and EtOH (300 mL); yield: 13.9 g (84.4 mmol, 87%); bright yellow solid.

Anal. Calcd for C_8H_5Cu: C, 58.35; H, 3.06; Cu, 38.59. Found: C, 58.02; H, 3.08; Cu, 37.99.

(4-Fluorophenyl)ethynylcopper (2g)

Prepared according to procedure 1 from (4-fluorophenyl)ethyne (2.4 mL, 20.9 mmol) and a solution of CuI (8.0 g, 42.0 mmol) in a mixture of NH_4OH (28% NH_3 solution, 100 mL) and EtOH (60 mL); yield: 3.0 g (16.4 mmol, 79%); bright yellow solid.

Anal. Calcd for C_8H_4FCu: C, 52.60; H, 2.21; Cu, 34.79. Found: C, 52.01; H, 2.19; Cu, 35.13.

(4-Bromophenyl)ethynylcopper (2h)
Prepared according to procedure 1 from (4-bromophenyl)ethyne (884 mg, 4.9 mmol) and a solution of CuI (1.9 g, 10.0 mmol) in a mixture of NH_4OH (28% NH_3 solution, 25 mL) and EtOH (15 mL); yield: 1.1 g (4.5 mmol, 91%); bright yellow solid.

Anal. Calcd for C_8H_4BrCu: C, 39.45; H, 1.66; Cu, 26.09. Found: C, 40.34; H, 1.76; Cu, 25.19.

4-Tolylethynylcopper (2i)
Prepared according to procedure 1 from 4-tolylethyne (12.0 mL, 94.6 mmol) and a solution of CuI (36.2 g, 190.0 mmol) in a mixture of NH_4OH (28% NH_3 solution, 500 mL) and EtOH (300 mL); yield: 16.5 g (92.3 mmol, 98%); bright yellow solid.

Anal. Calcd for C_9H_7Cu: C, 60.49; H, 3.95; Cu, 35.56. Found: 61.03; H, 4.21; Cu, 36.02.

(4-*tert*-Butylphenyl)ethynylcopper (2j)
Prepared according to procedure 1 from (4-*tert*-butylphenyl)ethyne (1.9 mL, 10.5 mmol) and a solution of CuI (4.0 g, 21.0 mmol) in a mixture of NH_4OH (28% NH_3 solution, 50 mL) and EtOH (30 mL); yield: 1.8 g (8.2 mmol, 78%); bright yellow solid.

Anal. Calcd for $C_{12}H_{13}Cu$: C, 65.28; H, 5.94; Cu, 28.78. Found: C, 64.28; H, 5.84; Cu, 28.01.

(3-Methoxyphenyl)ethynylcopper (2k)
Prepared according to procedure 1 from (3-methoxyphenyl)ethyne (5.0 mL, 39.3 mmol) and a solution of CuI (15.0 g, 78.8 mmol) in a mixture of NH_4OH (28% NH_3 solution, 200 mL) and EtOH (120 mL); yield: 7.2 g (37.0 mmol, 94%); bright yellow solid.

Anal. Calcd for C_9H_7CuO: C, 55.52; H, 3.62; Cu, 32.64. Found: C, 55.37; H, 3.40; Cu, 31.98.

Ferrocenylethynylcopper (2l)
Prepared according to procedure 1 from ethynylferrocene (1.0 g, 4.8 mmol) and a solution of CuI (1.8 g, 9.6 mmol) in a mixture of NH_4OH (28% NH_3 solution, 25 mL) and EtOH (15 mL); yield: 1.3 g (4.7 mmol, 97%); bright orange solid.

Anal. Calcd for $C_{12}H_9CuFe$: C, 52.87; H, 3.33; Cu, 23.31. Found: C, 53.02; H, 3.18; Cu, 22.97.

(*tert*-Butoxycarbonyl)ethynylcopper (2m)
Prepared according to procedure 1 from *tert*-butyl propiolate (2.2 mL, 16.0 mmol) and a solution of CuI (6.1 g, 32.0 mmol) in a mixture of NH_4OH (28% NH_3 solution, 160 mL) and EtOH (50 mL); yield: 2.3 g (12.2 mmol, 76%); bright orange solid.

Anal. Calcd for $C_7H_9CuO_2$: C, 44.56; H, 4.81; Cu, 33.68. Found: C, 44.79; H, 4.67; Cu, 33.21.

1-(Pent-1-yn-1-yl)pyrrolidin-2-one (4a)
Prepared according to procedure 2 from pent-1-yn-1-ylcopper (**2a**; 13.1 g, 100.2 mmol), pyrrolidin-2-one (30.5 mL, 401.4 mmol), and TMEDA (15.0 mL, 100.0 mmol) in MeCN (200 mL). Purified by flash column chromatography (PE–EtOAc, 50:50); yield: 12.4 g (82.0 mmol, 82%); pale yellow oil.

IR (ATR): 2963, 2261, 1716, 1390, 1298, 1211, 1089, 639 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.60 (t, *J* = 7.5 Hz, 2 H), 2.36 (t, *J* = 8.1 Hz, 2 H), 2.25 (t, *J* = 7.2 Hz, 2 H), 2.10–1.95 (m, 2 H), 1.53–1.46 (m, 2 H), 0.92 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.1, 72.4, 71.5, 50.1, 29.6, 22.3, 20.5, 18.6, 13.4.

HRMS (ESI): *m*/*z* calcd for $C_9H_{14}NO$ $[M + H]^+$: 152.1076; found: 152.1075.

1-(Oct-1-yn-1-yl)pyrrolidin-2-one (4b)
Prepared according to procedure 2 from oct-1-yn-1-ylcopper (**2b**; 1.85 g, 10.7 mmol), pyrrolidin-2-one (3.3 mL, 43.4 mmol), and TMEDA (1.6 mL, 10.7 mmol) in MeCN (20 mL). Purified by flash column chromatography (PE–EtOAc, 50:50); yield: 1.9 g (9.8 mmol, 92%); pale yellow oil.

IR (ATR): 2930, 2857, 2260, 1719, 1399, 1367, 1297, 1218, 1169, 1091, 813, 756 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.57 (t, *J* = 7.4 Hz, 2 H), 2.33 (t, *J* = 8.1 Hz, 2 H), 2.23 (t, *J* = 7.2 Hz, 2 H), 2.02 (app quint, *J* = 7.6 Hz, 2 H), 1.44 (app quint, *J* = 7.2 Hz, 2 H), 1.36–1.12 (m, 6 H), 0.80 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.0, 72.5, 71.3, 50.0, 31.3, 29.5, 28.8, 28.5, 22.4, 18.6, 18.5, 14.0.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{20}NO$ $[M + H]^+$: 194.1545; found: 194.1542.

Characterization data were consistent with those reported in the literature.[12]

1-(4-Phenylbut-1-yn-1-yl)pyrrolidin-2-one (4c)
Prepared according to procedure 2 from 4-phenylbut-1-yn-1-ylcopper (**2c**; 386 mg, 2.0 mmol), pyrrolidin-2-one (610 μL, 8.0 mmol), and TMEDA (300 μL, 2.0 mmol) in MeCN (4 mL). Purified by flash column chromatography (cyclohexane–EtOAc, 60:40); yield: 330 mg (1.5 mmol, 77%); orange solid; mp 51 °C.

IR (ATR): 2257, 1708, 1453, 1394, 1219, 1196, 751, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.17 (m, 5 H), 3.36 (t, *J* = 7.2 Hz, 2 H), 2.86 (t, *J* = 7.8 Hz, 2 H), 2.62 (t, *J* = 7.2 Hz, 2 H), 2.41 (t, *J* = 8.4 Hz, 2 H), 2.09 (quint, *J* = 7.2 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.2, 140.8, 128.6, 128.5, 126.4, 72.2, 72.0, 50.1, 35.5, 29.7, 21.0, 18.8.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{16}NO$ $[M + H]^+$: 214.1232; found: 214.1233.

Characterization data were consistent with those reported in the literature.[13]

1-(Phenylethynyl)pyrrolidin-2-one (4d)
Prepared according to procedure 2 from phenylethynylcopper (**2f**; 5.0 g, 30.4 mmol), pyrrolidin-2-one (9.2 mL, 121.1 mmol), and TMEDA (4.6 mL, 30.7 mmol) in MeCN (60 mL). Purified by flash column chromatography (PE–EtOAc, 50:50); yield: 3.9 g (21.1 mmol, 70%); pale yellow solid; mp 52 °C.

IR (ATR): 2243, 1717, 1488, 1392, 1198, 1150, 757, 696, 647 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.38 (m, 2 H), 7.30–7.23 (m, 3 H), 3.76 (t, *J* = 7.3 Hz, 2 H), 2.46 (t, *J* = 8.0 Hz, 2 H), 2.15 (app quint, *J* = 7.8 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.9, 131.6, 128.3, 128.0, 122.7, 80.5, 72.7, 50.2, 29.8, 19.0.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{12}NO$ $[M + H]^+$: 186.0919; found: 186.0921.

Characterization data were consistent with those reported in the literature.[5c]

1-(4-Bromophenylethynyl)pyrrolidin-2-one (4e)
Prepared according to procedure 2 from (4-bromophenyl)ethynylcopper (**2h**; 1.5 g, 6.2 mmol), pyrrolidin-2-one (1.9 mL, 25.0 mmol), and TMEDA (930 μL, 6.2 mmol) in MeCN (12 mL). Purified by flash column chromatography (PE–EtOAc, 60:40); yield: 992 mg (3.8 mmol, 61%); white solid; mp 88 °C.

IR (ATR): 2986, 2900, 2237, 1720, 1400, 1207, 1144, 1073 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 10.2 Hz, 2 H), 7.25 (d, *J* = 9.0 Hz, 2 H), 3.72 (t, *J* = 7.2 Hz, 2 H), 2.43 (t, *J* = 8.4 Hz, 2 H), 2.18–2.07 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.1, 133.2, 131.8, 122.3, 121.9, 81.8, 72.0, 50.3, 30.0, 19.2.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{11}BrNO$ $[M + H]^+$: 264.0029; found: 264.0024.

1-(4-Tolylethynyl)pyrrolidin-2-one (4f)
Prepared according to procedure 2 from 4-tolylethynylcopper (**2i**; 357 mg, 2.0 mmol), pyrrolidin-2-one (610 μL, 8.0 mmol), and TMEDA (300 μL, 2.0 mmol) in MeCN (4 mL). Purified by flash column chromatography (cyclohexane–EtOAc, 60:40); yield: 306 mg (1.5 mmol, 77%); white solid; mp 115 °C.

IR (ATR): 2246, 1713, 1402, 1233, 1199, 1150, 813 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 8.1 Hz, 2 H), 7.10 (d, *J* = 7.8 Hz, 2 H), 3.77 (t, *J* = 7.2 Hz, 2 H), 2.48 (t, *J* = 8.4 Hz, 2 H), 2.32 (s, 3 H), 2.16 (app quint, *J* = 7.8 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.9, 138.1, 131.6, 129.1, 119.6, 79.8, 72.7, 50.3, 29.8, 21.6, 19.0.

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{14}NO$ $[M + H]^+$: 200.1075; found: 200.1077.

Characterization data were consistent with those reported in the literature.[14]

1-(3-Methoxyphenylethynyl)pyrrolidin-2-one (4g)
Prepared according to procedure 2 from (3-methoxyphenyl)ethynylcopper (**2k**; 390 mg, 2.0 mmol), pyrrolidin-2-one (610 μL, 8.0 mmol), and TMEDA (300 μL, 2.0 mmol) in MeCN (4 mL). Purified by flash column chromatography (cyclohexane–EtOAc, 60:40); yield: 260 mg (1.2 mmol, 60%); orange oil.

IR (ATR): 2962, 2247, 1596, 1574, 1424, 1392, 1197, 1135, 1034, 784, 689 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17 (t, *J* = 7.8 Hz, 1 H), 7.01 (d, *J* = 7.5 Hz, 1 H), 6.95 (s, 1 H), 6.82 (d, *J* = 8.4 Hz, 1 H), 3.76 (s, 3 H), 3.75 (obs t, *J* = 7.5 Hz, 2 H), 2.45 (t, *J* = 8.1 Hz, 2 H), 2.18 (app quint, *J* = 7.8 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.7, 159.2, 129.2, 123.9, 123.6, 116.1, 114.5, 80.4, 72.5, 55.2, 50.1, 29.6, 18.8.

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{14}NO_2$ $[M + H]^+$: 216.1025; found: 216.1024.

3-(Oct-1-yn-1-yl)oxazolidin-2-one (4h)
Prepared according to procedure 2 from oct-1-yn-1-ylcopper (**2b**; 1.9 g, 11.2 mmol), oxazolidin-2-one (3.9 g, 44.8 mmol), and TMEDA (1.7 mL, 11.3 mmol) in MeCN (22 mL). Purified by flash column chromatography (PE–EtOAc, 60:40); yield: 2.0 g (10.2 mmol, 91%); pale yellow oil.

IR (ATR): 2929, 2858, 2269, 1767, 1415, 1301, 1206, 1115, 1035, 976, 751 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.39 (dd, *J* = 9.1, 7.7 Hz, 2 H), 3.86 (dd, *J* = 9.3, 7.8 Hz, 2 H), 2.28 (t, *J* = 7.0 Hz, 2 H), 1.72–1.17 (m, 8 H), 0.87 (t, *J* = 6.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.8, 71.3, 70.1, 62.9, 47.1, 31.4, 28.8, 28.6, 22.6, 18.5, 14.1.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{18}NO_2$ $[M + H]^+$: 196.1338; found: 196.1341.

Characterization data were consistent with those reported in the literature.[15]

3-(4-Fluorophenylethynyl)oxazolidin-2-one (4i)
Prepared according to procedure 2 from (4-fluorophenyl)ethynylcopper (**2g**; 365 mg, 2.0 mmol), oxazolidin-2-one (696 mg, 8.0 mmol), and TMEDA (300 μL, 2.0 mmol) in MeCN (4 mL). Purified by flash column chromatography (cyclohexane–EtOAc, 60:40); yield: 221 mg (1.1 mmol, 54%); white solid; mp 114 °C.

IR (ATR): 2268, 1754, 1416, 1208, 1195, 1165, 1091, 835, 744 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.38 (m, 2 H), 7.04–6.95 (m, 2 H), 4.48 (dd, *J* = 9.3, 7.7 Hz, 2 H), 4.00 (dd, *J* = 9.3, 7.7 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.6 (d, *J* = 248 Hz), 156.0, 133.8 (d, *J* = 8.4 Hz), 118.3 (d, *J* = 3.5 Hz), 115.7 (d, *J* = 21.9 Hz), 78.7, 70.3, 63.2, 47.1.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –114.1 (s, 1 F).

HRMS (ESI): *m*/*z* calcd for $C_{11}H_9FNO_2$ $[M + H]^+$: 206.0617; found: 206.0618.

Characterization data were consistent with those reported in the literature.[16]

3-(4-Tolylethynyl)oxazolidin-2-one (4j)
Prepared according to procedure 2 from 4-tolylethynylcopper (**2i**; 357 mg, 2 mmol), oxazolidin-2-one (696 mg, 8 mmol), and TMEDA (300 μL, 2 mmol) in MeCN (4 mL). Purified by flash column chromatography (cyclohexane–EtOAc, 60:40); yield: 304 mg (1.5 mmol, 75%); white solid; mp 123 °C.

IR (ATR): 2263, 1752, 1417, 1217, 1199, 1164, 1031, 818, 746, 707 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 8.1 Hz, 2 H), 7.11 (d, *J* = 7.8 Hz, 2 H), 4.47 (dd, *J* = 9.3, 7.7 Hz, 2 H), 3.99 (dd, *J* = 9.3, 7.7 Hz, 2 H), 2.34 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.1, 138.5, 131.7, 129.2, 119.0, 78.4, 71.4, 63.1, 47.2, 21.6.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{12}NO_2$ $[M + H]^+$: 202.0868; found: 202.0870.

Characterization data were consistent with those reported in the literature.[5f]

(4*S*,5*R*)-4-Methyl-3-(oct-1-yn-1-yl)-5-phenyloxazolidin-2-one (4k)
Prepared according to procedure 2 from oct-1-yn-1-ylcopper (**2b**; 340 mg, 2.0 mmol), (4*S*,5*R*)-4-methyl-5-phenyloxazolidin-2-one (1.42 g, 8.0 mmol), and TMEDA (300 μL, 2.0 mmol) in MeCN (4 mL). Purified by flash column chromatography (PE–EtOAc, 90:10); yield: 411 mg (1.45 mmol, 72%); sticky colorless oil; $[\alpha]_D^{20}$ –6 (*c* 1.0, $CHCl_3$).

IR (ATR): 2931, 2253, 1760, 1405, 1188, 1125 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.34 (m, 3 H), 7.27–7.23 (m, 2 H), 5.68 (d, *J* = 8.1 Hz, 1 H), 4.29 (dq, *J* = 8.1, 6.6 Hz, 1 H), 2.31 (t, *J* = 6.9 Hz, 2 H), 1.57–1.47 (m, 2 H), 1.41–1.26 (m, 6 H), 0.90 (t, *J* = 6.6 Hz, 3 H), 0.87 (t, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.1, 134.2, 128.9, 128.7, 126.0, 79.5, 72.3, 69.1, 58.1, 31.3, 28.8, 28.6, 22.6, 18.5, 14.8, 14.0.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{24}NO_2$ $[M + H]^+$: 286.1807; found: 286.1809.

***N*-(Diphenylmethylene)oct-1-yn-1-amine (6a)**
Prepared according to procedure 3 from oct-1-yn-1-ylcopper (**2b**; 173 mg, 1.00 mmol), diphenylmethanimine (670 μL, 4.00 mmol), and 1,2-dimethylimidazole (175 μL, 1.97 mmol) in MeCN (4 mL). Purified by flash column chromatography [on triethylamine-deactivated silica gel, PE–Et_2O (95:5). Note: the column had to be run quickly as the compound is rather sensitive to silica gel]; yield: 165 mg (0.57 mmol, 57%); pale orange oil.

IR (ATR): 2919, 2848, 2246, 1661, 1444, 1313, 1274, 761, 692, 638 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 7.5 Hz, 2 H), 7.48–7.44 (m, 6 H), 7.40–7.35 (m, 2 H), 2.43 (t, *J* = 6.8 Hz, 2 H), 1.45–140 (m, 2 H), 1.31–1.23 (m, 6 H), 0.88 (t, *J* = 9.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.2, 138.2, 136.5, 131.2, 129.6, 129.2, 128.6, 128.3, 128.0, 96.5, 83.7, 31.5, 29.1, 28.4, 22.6, 20.3, 14.2.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{24}N$ $[M + H]^+$: 290.1909; found: 290.1902.

_N_-[1-(2-Chlorophenyl)pentylidene]pent-1-yn-1-amine (6b)
Obtained as a mixture of *Z*- and *E*-isomers in a 50:50 ratio. Prepared according to procedure 3 from pent-1-yn-1-ylcopper (**2a**; 131 mg, 1.00 mmol), 1-(2-chlorophenyl)pentan-1-imine (783 mg, 4.00 mmol), and 1,2-dimethylimidazole (175 μL, 1.97 mmol) in MeCN (4 mL). Purified by flash column chromatography [on triethylamine-deactivated silica gel, PE–Et_2O (95:5). Note: the column had to be run quickly as the compound is rather sensitive to silica gel]; yield: 180 mg (0.69 mmol, 69%); pale yellow oil.

IR (ATR): 2958, 2929, 2866, 2207, 1590, 1467, 1429, 1340, 1182, 1033, 745.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.39 and 7.17–7.13 (m, 1 H, stereoisomers), 7.36–7.27 (m, 3 H), 3.06 and 2.72 (t, *J* = 7.5 Hz, t, *J* = 7.4 Hz, 2 H, stereoisomers), 2.57 and 2.24 (t, *J* = 6.9 Hz, t, *J* = 6.8 Hz 2 H, stereoisomers), 1.68–1.61 (m, 2 H), 1.52–1.28 (m, 4 H), 1.06 and 0.73 (t, *J* = 7.3 Hz, t, *J* = 7.3 Hz, 3 H, stereoisomers), 0.92 and 0.89 (t, *J* = 7.3 Hz, t, *J* = 7.2 Hz, 3 H, stereoisomers).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 184.3 and 181.8 (stereoisomers), 138.8 and 138.7 (stereoisomers), 131.7, 130.3, 130.0, 129.8, 129.7, 129.6 and 127.7 (stereoisomers), 126.7 and 126.6 (stereoisomers), 96.3 and 90.1 (stereoisomers), 82.1 and 81.4 (stereoisomers), 39.8 and 36.4 (stereoisomers), 28.1 and 27.9 (stereoisomers), 22.7, 22.6, 22.4, 22.3, 22.1 and 21.5 (stereoisomers) 13.9, 13.7, 13.6 and 13.1 (stereoisomers).

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{21}ClN$ $[M + H]^+$: 262.1363; found: 262.1365.

_N_-[1-(2,3-Dimethylphenyl)pentylidene]pentyn-1-yn-1-amine (6c)
Obtained as a mixture of *Z*- and *E*-isomers in a 40:60 ratio. Prepared according to procedure 3 from pent-1-yn-1-ylcopper (**2a**; 1.0 g, 7.6 mmol), 1-(2,3-dimethylphenyl)pentan-1-imine (5.8 g, 30.6 mmol), and 1,2-dimethylimidazole (1.35 mL, 15.2 mmol) in MeCN (30 mL). Purified by flash column chromatography [on triethylamine-deactivated silica gel, PE–Et_2O (95:5). Note: the column had to be run quickly as the compound is rather sensitive to silica gel]; yield: 1.45 g (5.7 mmol, 75%); pale yellow oil.

IR (ATR): 2958, 2929, 2871, 2361, 2341, 1597, 1456, 1378, 1337, 1274, 1177, 1087, 1017, 989, 784, 749, 722 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (major) = 7.17–7.06 (m, 2 H), 6.90–6.86 (m, 1 H), 2.65 (t, *J* = 7.5 Hz, 2 H), 2.29 (s, 3 H), 2.22 (t, *J* = 6.8 Hz, 2 H), 2.13 (s, 3 H), 1.66–1.58 (m, 2 H), 1.56–1.26 (m, 4 H), 0.91 (t, *J* = 7.3 Hz, 3 H), 0.69 (t, *J* = 7.3 Hz, 3 H); δ (minor) = 7.17–7.06 (m, 3 H), 2.92 (t, *J* = 7.6 Hz, 2 H), 2.55 (t, *J* = 6.9 Hz, 2 H), 2.13 (s, 3 H), 2.25 (s, 3 H), 1.66–1.58 (m, 2 H), 1.56–1.26 (m, 4 H), 1.05 (t, *J* = 7.3 Hz, 3 H), 0.89 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ (major) = 186.2, 140.2, 137.3, 132.7, 130.0, 125.5, 123.2, 88.8, 82.7, 41.1, 28.1, 22.7, 22.6, 21.7, 20.4, 16.6, 14.0, 13.1; δ (minor) = 187.1, 140.0, 137.8, 134.2, 130.5, 125.4, 125.3, 94.1, 81.8, 38.1, 28.3, 23.0, 22.9, 22.2, 20.6, 16.9, 13.9, 13.7.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{26}N$ $[M + H]^+$: 256.2065; found: 256.2065.

_N_-[1-(2,3-Dimethylphenyl)pentylidene](ferrocenylethynyl)-1-amine (6d)
Obtained as a mixture of *Z*- and *E*-isomers in a 38:62 ratio. Prepared according to procedure 3 from ferrocenylethynylcopper (**2l**; 273 g, 1.00 mmol), 1-(2,3-dimethylphenyl)pentan-1-imine (757 m g, 4.00 mmol), and 1,2-dimethylimidazole (175 μL, 1.97 mmol) in MeCN (4 mL). Purified by flash column chromatography [on triethylamine-deactivated silica gel, PE–EtOAc (90:10). Note: the column had to be run quickly as the compound is rather sensitive to silica gel]; yield: 246 mg (0.62 mmol, 62%); pale orange oil.

IR (ATR): 2955, 2927, 2870, 2361, 2341, 2189, 1576, 1456, 1411, 1383, 1264, 1105, 1069, 1023, 1000, 887, 816, 782, 752, 724, 492 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (major) = 7.24–7.12 (m, 2 H), 6.99 (d, *J* = 7.1 Hz, 1 H), 4.16 (s, 2 H), 4.14 (s, 2 H), 4.02 (s, 5 H), 2.74 (t, *J* = 7.6 Hz, 2 H), 2.41 (s, 3 H), 2.27 (s, 3 H), 1.70 (app quint, *J* = 7.5 Hz, 2 H), 1.46 (app sext, *J* = 7.4 Hz, 2 H), 0.98 (t, *J* = 7.3 Hz, 3 H); δ (minor) = 7.24–7.12 (m, 3 H), 4.49 (s, 2 H), 4.30 (s, 2 H), 4.27 (s, 5 H), 3.03 (t, *J* = 7.7 Hz, 2 H), 2.35 (s, 6 H), 1.63 (app quint, *J* = 7.5 Hz, 2 H), 1.46 (app sext, *J* = 7.4 Hz, 2 H), 1.00 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (major) = 185.8, 140.5, 137.2, 132.7, 130.2, 125.6, 123.1, 87.6, 87.1, 71.1, 69.8, 68.6, 66.6, 41.0, 28.1, 22.6, 20.4, 16.7, 14.0; δ (minor) = 185.7, 139.9, 137.9, 134.3, 130.7, 125.4, 125.3, 93.2, 86.4, 71.4, 69.9, 69.0, 66.8, 38.4, 28.4, 23.0, 20.6, 17.0, 13.9.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{27}FeN$ $[M]^+$: 397.1493; found: 397.1509.

Diisopropyl (Pent-1-yn-1-yl)phosphonate (8a)
Prepared according to procedure 4 from pent-1-yn-1-ylcopper (**2a**; 9.8 g, 75.0 mmol), diisopropyl phosphite (50.3 mL, 300.0 mmol), and *N*-methylimidazole (12.0 mL, 150.5 mmol) in DMF (150 mL). Purified by flash column chromatography (pentane–EtOAc, 50:50); yield: 16.0 g (68.9 mmol, 92%); colorless oil.

IR (ATR): 2982, 2205, 1385, 1255, 981 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.67–4.60 (m, 2 H), 2.24 (td, *J* = 6.9 Hz and $J_{H,P}$ = 4.2 Hz, 2 H), 1.53 (tq, *J* = 7.5, 7.2 Hz, 2 H), 1.28 (d, *J* = 7.2 Hz, 12 H), 0.93 (t, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 102.1 (d, $J_{C,P}$ = 52.5 Hz), 72.2 (d, $J_{C,P}$ = 300.0 Hz), 72.0 (d, $J_{C,P}$ = 5.3 Hz), 24.4 (d, $J_{C,P}$ = 4.5 Hz), 23.7 (d, $J_{C,P}$ = 4.8 Hz), 21.3, 21.2, 13.3.

^{31}P NMR (121 MHz, $CDCl_3$): δ = –8.7.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{22}O_3P$ $[M + H]^+$: 233.1307; found: 233.1305.

Dibutyl (Pent-1-yn-1-yl)phosphonate (8b)
Prepared according to procedure 4 from pent-1-yn-1-ylcopper (**2a**; 2.6 g, 20.0 mmol), dibutyl phosphite (15.7 mL, 80.0 mmol), and *N*-methylimidazole (3.2 mL, 4.0 mmol) in DMF (40 mL). Purified by flash column chromatography (cyclohexane–EtOAc, 60:40); yield: 4.8 g (18.4 mmol, 92%); pale yellow oil.

IR (ATR): 2961, 2204, 1272, 1063, 1022, 992, 794 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.05 (app q, *J* = 7.6 Hz, 4 H), 2.30 (td, *J* = 7.0 Hz and $J_{H,P}$ = 4.3 Hz, 2 H), 1.73–1.52 (m, 6 H), 1.41 (app sext, *J* = 7.6 Hz, 4 H), 1.00 (t, *J* = 7.3 Hz, 3 H), 0.92 (t, *J* = 7.6 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 103.0 (d, $J_{C,P}$ = 52.4 Hz), 70.7 (d, $J_{C,P}$ = 300.6 Hz), 66.7 (d, $J_{C,P}$ = 5.6 Hz), 32.3 (d, $J_{C,P}$ = 7.3 Hz), 21.2 (d, $J_{C,P}$ = 4.4 Hz), 21.1 (d, $J_{C,P}$ = 2.3 Hz), 18.8, 13.7, 13.5.

^{31}P NMR (161 MHz, $CDCl_3$): δ = –5.1.

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{26}O_3P$ $[M + H]^+$: 261.1620; found: 261.1617.

Diethyl (4-Phenylbut-1-yn-1-yl)phosphonate (8c)
Prepared according to procedure 4 from 4-phenylbut-1-yn-1-ylcopper (**2c**; 385 mg, 2.0 mmol), diethyl phosphite (1.0 mL, 8.0 mmol), and *N*-methylimidazole (320 μL, 4.0 mmol) in DMF (4 mL). Purified by flash column chromatography (cyclohexane–EtOAc, 50:50); yield: 513 mg (1.93 mmol, 96%); pale yellow oil.

IR (ATR): 2984, 2204, 1262, 1022, 974, 752 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29–7.22 (m, 2 H), 7.21–7.13 (m, 3 H), 4.08–3.95 (m, 4 H), 2.84 (t, *J* = 7.3 Hz, 2 H), 2.60 (td, *J* = 7.3 Hz and $J_{H,P}$ = 4.3 Hz, 2 H), 1.27 (t, *J* = 7.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.3, 128.4, 128.3, 126.6, 101.9 (d, $J_{C,P}$ = 52.1 Hz), 71.2 (d, $J_{C,P}$ = 298.6 Hz), 62.9 (d, $J_{C,P}$ = 5.4 Hz), 33.5 (d, $J_{C,P}$ = 2.1 Hz), 21.2 (d, $J_{C,P}$ = 4.5 Hz), 16.0 (d, $J_{C,P}$ = 7.2 Hz).

^{31}P NMR (161 MHz, $CDCl_3$): δ = –5.8.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{20}O_3P$ $[M + H]^+$: 267.1150; found: 267.1147.

Dibutyl (4-Hydroxybut-1-yn-1-yl)phosphonate (8d)
Prepared according to procedure 4 from 4-hydroxybut-1-yn-1-ylcopper (**2d**; 530 mg, 4.0 mmol), dibutyl phosphite (3.1 mL, 16.0 mmol), and *N*-methylimidazole (640 μL, 8.0 mmol) in DMF (8 mL). Purified by flash column chromatography (cyclohexane–EtOAc, 10:90); yield: 1.0 g (3.81 mmol, 96%); colorless oil.

IR (ATR): 2961, 2206, 1250, 1058, 1023, 731 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.06 (app q, *J* = 7.3 Hz, 4 H), 3.79 (t, *J* = 6.4 Hz, 2 H), 2.74 (br s, 1 H), 2.61 (td, *J* = 7.3 Hz and $J_{H,P}$ = 4.4 Hz, 2 H), 1.68 (app quint, *J* = 6.9 Hz, 4 H), 1.42 (app sext, *J* = 7.7 Hz, 4 H), 0.93 (t, *J* = 7.4 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 100.9 (d, $J_{C,P}$ = 52.6 Hz), 71.1 (d, $J_{C,P}$ = 300.1 Hz), 66.8 (d, $J_{C,P}$ = 6.0 Hz), 59.7, 32.1 (d, $J_{C,P}$ = 7.2 Hz), 23.4 (d, $J_{C,P}$ = 4.3 Hz), 18.6, 13.5.

^{31}P NMR (161 MHz, $CDCl_3$): δ = –5.4.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{24}O_4P$ $[M + H]^+$: 263.1412; found: 263.1355.

Diisopropyl (3-Methylbut-3-en-1-yn-1-yl)phosphonate (8e)
Prepared according to procedure 4 from 3-methylbut-3-en-1-yn-1-ylcopper (**2e**; 257 mg, 2.0 mmol), diisopropyl phosphite (1.35 mL, 8.0 mmol), and *N*-methylimidazole (320 μL, 4.0 mmol) in DMF (4 mL). Purified by flash column chromatography (pentane–EtOAc, 60:40); yield: 405 mg (1.75 mmol, 88%); colorless oil.

IR (ATR): 2979, 2182, 1377, 1258, 983 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.45 (br s, 1 H), 5.39 (br s, 1 H), 4.67–4.59 (m, 2 H), 1.81 (s, 3 H), 1.26 (d, *J* = 6.3 Hz, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 127.5, 124.5, 99.3 (d, $J_{C,P}$ = 51.8 Hz), 78.8 (d, $J_{C,P}$ = 300.0 Hz), 72.2 (d, $J_{C,P}$ = 6.0 Hz), 23.9 (d, $J_{C,P}$ = 4.5 Hz), 23.7 (d, $J_{C,P}$ = 4.8 Hz), 22.1.

^{31}P NMR (121 MHz, $CDCl_3$): δ = –8.6.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{20}O_3P$ $[M + H]^+$: 231.1150; found: 231.1145.

Diisopropyl Phenylethynylphosphonate (8f)
Prepared according to procedure 4 from phenylethynylcopper (**2f**; 1.7 g, 10.3 mmol), diisopropyl phosphite (6.9 mL, 41.1 mmol), and *N*-methylimidazole (1.6 mL, 20.1 mmol) in DMF (20 mL). Purified by flash column chromatography (pentane–EtOAc, 50:50); yield: 2.65 g (9.95 mmol, 97%); colorless oil.

IR (ATR): 2981, 2186, 1386, 1261, 988, 851, 758 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (d, *J* = 7.0 Hz, 2 H), 7.46–7.31 (m, 3 H), 4.88–4.71 (m, 2 H), 1.38 (d, *J* = 6.3 Hz, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 132.6 (d, $J_{C,P}$ = 2.5 Hz), 130.6, 128.6, 119.7 (d, $J_{C,P}$ = 35.9 Hz), 98.2 (d, $J_{C,P}$ = 52.5 Hz), 79.9 (d, $J_{C,P}$ = 296.7 Hz), 72.4 (d, $J_{C,P}$ = 5.5 Hz), 24.0 (d, $J_{C,P}$ = 4.5 Hz), 23.7 (d, $J_{C,P}$ = 4.8 Hz).

^{31}P NMR (161 MHz, $CDCl_3$): δ = –8.0.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{20}O_3P$ $[M + H]^+$: 267.1150; found: 267.1147.

Characterization data were consistent with those reported in the literature.[6d]

Diethyl (4-*tert*-Butylphenylethynyl)phosphonate (8g)
Prepared according to procedure 4 from (4-*tert*-butylphenyl)ethynylcopper (**2j**; 442 mg, 2.0 mmol), diethyl phosphite (1.0 mL, 8.0 mmol), and *N*-methylimidazole (320 μL, 4.0 mmol) in DMF (4 mL). Purified by flash column chromatography (cyclohexane–EtOAc, 50:50); yield: 563 mg (1.91 mmol, 96%); colorless oil.

IR (ATR): 2965, 2185, 1264, 1023, 974, 865, 755 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 8.4 Hz, 2 H), 7.38 (d, *J* = 8.5 Hz, 2 H), 4.22 (m, 4 H), 1.40 (t, *J* = 7.0 Hz, 6 H), 1.31 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.8, 132.9 (d, $J_{C,P}$ = 2.4 Hz), 126.0, 116.8 (d, $J_{C,P}$ = 5.6 Hz), 100.0 (d, $J_{C,P}$ = 52.9 Hz), 78.1 (d, $J_{C,P}$ = 298.7 Hz), 63.5 (d, $J_{C,P}$ = 5.4 Hz), 35.4, 31.2, 16.5 (d, $J_{C,P}$ = 6.9 Hz).

^{31}P NMR (121 MHz, $CDCl_3$): δ = –5.1.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{23}O_3P$ + Na $[M + Na]^+$: 317.1283; found: 317.1280.

Characterization data were consistent with those reported in the literature.[17]

Diisopropyl (*tert*-Butoxycarbonylethynyl)phosphonate (8h)
Prepared according to procedure 4 from (*tert*-butoxycarbonyl)ethynylcopper (**2m**; 377 mg, 2.0 mmol), diisopropyl phosphite (1.35 mL, 8.0 mmol), and *N*-methylimidazole (320 μL, 4.0 mmol) in DMF (4 mL). Purified by flash column chromatography (pentane–EtOAc, 50:50); yield: 279 mg (0.96 mmol, 48%); brownish orange oil.

IR (ATR): 2975, 1708, 1369, 1255, 1151, 983 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.67–4.60 (m, 2 H), 1.38 (s, 9 H), 1.26 (d, *J* = 6.3 Hz, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.6, 87.4 (d, $J_{C,P}$ = 45.8 Hz), 85.4, 74.0 (d, $J_{C,P}$ = 285.0 Hz), 73.4 (d, $J_{C,P}$ = 5.3 Hz), 28.0, 23.9 (d, $J_{C,P}$ = 4.5 Hz), 23.6 (d, $J_{C,P}$ = 4.9 Hz).

^{31}P NMR (121 MHz, $CDCl_3$): δ = –11.6.

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{24}O_5P$ $[M + H]^+$: 291.1361; found: 291.1359.

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