Allylic C–H Alkynylation via Copper-Photocatalyzed Cross-Dehydrogenative Coupling

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Abstract
An efficient, novel photocatalyzed allylic-alkynylation methodology via copper-based cross-dehydrogenative coupling (CDC) is described. Different types of 1,4-enyne compounds were synthesized in one step at room temperature using copper(I) terpyridyl complex as photocatalyst/initiator. This procedure is an improvement and to some extent complementary to previously reported thermal CDC methods. Preliminary investigations on the reaction mechanism are also presented.

Key words C–C bond, copper catalyst, C–H functionalization, photocatalyst, allylic-alkynylation, 1,4-enyne

The search for more efficient and ‘environmentally friendlier’ processes is one of the major tasks to be accomplished by chemists, in response to the growing society’s concern about pollution, energy, and resources. Therefore, the development of new catalytic strategies of high selectivity, low energy demand, and reduced waste are of paramount importance. Among these strategies, photocatalysis has been in the spotlight during the last decades.1 Remarkably, among the plethora of reported photocatalyzed reactions, allylic functionalization represents only a small fraction, in spite of the ubiquity of the allylic moiety in natural products and pharmaceuticals.2 In a pioneering report, Reiser developed the first photocatalyzed allylation of α-halocarbonsyls with allyltributylstannane using homoleptic [Cu(dpa)2] as photosensitizer.3 Later on, the same group improved the reaction scope by using allylsilanes and heteroleptic copper(I) complexes having longer excited state lifetimes and stronger reductive capabilities (Scheme 1 A).4 Alkylation of allyl sulfones by aryl radicals generated from diaryliodonium salts using [Cu(dpp)2]PF6 as photocatalyst was reported by Ollivier in 2013 (Scheme 1 B).5 Two years later, MacMillan reported a more benign approach towards allylic C–H functionalizations avoiding the use of stoichiometric amounts of oxidant, leading to the direct arylation of allylic C–H bonds under mild conditions (Scheme 1 C).6 An important drawback of this methodology is that it relies on the use of expensive iridium photosensitizers.

Scheme 1 Recent examples of photocatalyzed allylic functionalizations; dap: 2,9-bis(4-methoxyphenyl)-1,10-phenanthroline; dpp: 2,9-diphenyl-1,10-phenanthroline; py: 2-phenylpyridine.

Very recently, we reported the alkynylation of underivatized allylic substrates under oxidative conditions using terminal alkynes.7 This is an example of a thermal cross-dehydrogenative coupling (CDC) reaction, which can be described as the coupling of a pre-nucleophile and a pre-electrophile, both devoid of leaving groups.8 CDC reactions
have been thoroughly studied in the last decade\(^9\) and several photocatalyzed CDC processes either using a sacrificial oxidant or a proton reductant have been reported.\(^10\) In most cases (thermal and photocatalyzed), the derivatization takes place at sp\(^3\) carbons adjacent to nitrogen, and allylic substrates have been neglected. Herein, we combine for the first time the advantages of CDC and photocatalysis for the alkylation of allylic substrates, using a Cu(I) terpyridine complex as photocatalyst and tert-butyl hydroperoxide (TBHP) as sacrificial oxidant at room temperature (Scheme 1, D).

We began our investigation on the photocatalyzed CDC between phenylacetylene (1a) and cyclohexene (2a) as model reactants using white light (xenon lamp, \(\lambda = 300–700 \text{ nm}\)) at room temperature (23–26 °C) (Scheme 2). We employed the reaction conditions from our previous report\(^7\) (except the reaction temperature) using DTBP as oxidant and terpyridine ligand \(L_1\) (Table 1). Terpyridines are important chelating ligands in many applications spawning from supramolecular\(^11\) and macromolecular chemistry to luminescent devices\(^12\) and photoelectrical cells.\(^13\) However, the low photoabsorption and quantum yield of metallic mono- and bis-terpyridyl complexes compared to their bipyridine analogues has discouraged their application as photoredox catalysts in organic synthesis.\(^14\) Furthermore, most of the studied copper terpyridine complexes are of Cu(II),\(^14a,15\) with only few Cu(I) examples.\(^16,17\) Under these conditions, only 10% of the desired product 3a was obtained (Table 1, entry 1). No product was detected without the copper complex or the oxidant (entries 2 and 3). Having 1a as the sole ligand (entry 4) was not effective in our case, in contrast to previous reports on Sonogashira-type photoinduced coupling reactions.\(^18\) Using TBHP instead of DTBP was sufficient to increase the yield to 55% (entry 5). Motivated by this observation, different oxidants were tested, but no product was produced (entries 6–10). By lowering the amount of oxidant, a decreased yield was observed (entry 11, 41%). The addition of an excess of \(L_1\) (1.5 and 2 equiv relative to Cu) resulted in an increase of product yield (entries 12 and 13, 61 and 60%, respectively). An increased excess of 2a was also beneficial, giving 3a in 72% (entry 14). Conversely, further increase on the amount of 2a or oxidant showed to be detrimental (entries 15 and 16). At this stage, we turned our attention to the role of the ligand, for which different terpyridine derivatives \(L_2-L_4\), 4,7-diphenyl-1,10-phenanthroline (L6), and 2,6-bis(1H-benzo[d]imidazo[2,1-\(y\)]pyridine (L7), were tested. In all cases, either lower conversion or no reaction was observed (Table S1, SI).

**Table 1** Screening of Optimal Reaction Conditions\(^a\)

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<tr>
<th>Entry</th>
<th>2a (equiv)</th>
<th>X (mol%)</th>
<th>Y (mol%)</th>
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<th>Solvent</th>
<th>3a Yield (%)(^b)</th>
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\(^a\) Reaction conditions: 1a (0.5 mmol), tert-butyl hydroperoxide (TBHP) solution in decane 5.5 M, DTBP (di-tert-butylperoxide), DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone), BPO (benzoyl peroxide), temperature was kept at 24–26 °C by flowing dry air through the reactor.

\(^b\) GC-MS yield; nd: not detected.

\(^c\) TBHP: 1 equiv.

\(^d\) TBHP: 3 equiv.

\(^e\) TBHP: 3 equiv.

\(^f\) \(\lambda = 400–700 \text{ nm}\).

\(^g\) With isolated CuI-L1.

\(^h\) With 5 mol% [Cu(CF\(_3\)SO\(_3\))]\(_2\).
Moreover, we tested the effect of different light sources, including LED strips and household bulbs. To our delight all tested light sources were able to produce the desired product, however, only in moderate yields (Table S1, SI). By removing the UV radiation of the Xenon light source, that is, using only visible light ($\lambda_{\text{exc}} = 420–600$ nm), a yield of 54% was obtained (Table 1, entry 17). This decrease can be due to the reduction of the light intensity resulting from the use of the long pass filter. We also investigated the solvent effect (entries 18–23) and found that MeCN gives the best results (entry 19, 78%). Interestingly, coupling by-products resulting from a reaction between 1a with DMF and THF were produced. The nature of the copper species was briefly investigated. By using the isolated complex [CuI-L1] (see SI) as catalyst, very similar results were obtained as when it is produced in situ (entry 24, 70%). Interestingly, and contrary to what we observed under thermal conditions, using CuII instead of CuI resulted in 30% yield of 3a (entry 25). Importantly, high selectivity towards the allylic alkynylation product was achieved in all cases, in strong contrast to the results under thermal conditions. There, a variety of by-products were always present, for instance the Glaser coupling product of 1a being practically unavoidable. In this case, only the CDC product 3 is produced.

Once we have identified a suitable set of reaction conditions, we proceeded with the investigations on the substrate scope. In general, all phenylacetylene derivatives 1 tested produced the CDC products with 2a in moderate to good yields (Scheme 3, 3a–p). The highest yield was obtained for the electronically enriched 1-ethyl-4-methoxy-2-methylbenzene (1n) (90% of 3n), while the lowest was obtained for the electron-poor 1-ethyl-4-fluorobenzene (1d) (44% of 3d). Interestingly, halogenated substrates 1b–f gave satisfactory results in spite of their propensity to form radical species by reacting with analogous catalysts.21 Importantly, the presence of reactive functionalities like thiophene and phenol did not inhibit the product formation (3o and 3p, respectively). The presence of a carboxyl moiety at position 1 of the allyl substrate 2q resulted in complete reaction inhibition, while the methyl-substituted

Scheme 3 Substrate scope for the photocatalyzed allylic alkynylation reaction. Isolated yields are reported. * Determined by GC-MS.
analogue produced the desired product 3r in moderate yield (53%). Under the same conditions, cyclopentene and cycloheptene produced exclusively the expected products 3s and 3t in 80% and 49% yield, respectively. Unfortunately, the regioselectivity was not controlled in the case of cyclooctene, producing a mixture of isomers 3u. The lack of regioselectivity for 3u and the high regioselectivity for 3s are in strong contrast with the thermal method where the complete opposite behavior was observed.\(^7\) The difference in selectivity between the two sets of conditions (thermal vs photoinduced) relays on the stability and reactivity of the metal-allyl intermediates 6 and 8, common to both mechanism, but that can undergo different side reactions (like thermal isomerization) before the product-forming step (vide infra). Moreover, the use of open-chain allylic substrates or a not-conjugated alkyne did not yield the desired products 3v and 3w or 3x, respectively. We believe that for the former, it is due to unintended photooxidation of the substrates while for the latter, due the lower acidity of the alkyne. The thermal method, on the other hand, was effective for the coupling of both alkylic and open-chain substrates. This makes, to some extent, the two approaches effective for the coupling of both alkylic and open-chain substrates. This hypothesis has to be supported by experimental data (current being collected in our laboratories). Preliminary photoluminescence quenching experiments (\(\lambda_{ex} = 317\) nm) for complex Cu-L1 with the three different substrates showed that only the peroxide (TBHP) is capable of effectively quenching the excited state emission of the copper complex. This suggests that, as expected, the photoexcited copper catalyzes the peroxide splitting, presumably by single electron transfer (SET) during the irradiation period (Figures S5 to S7, SI).

The addition of an excess of the radical-trapping reagent TEMPO only resulted in a decrease on the reaction yield to 56%, also in strong contrast to the use if DTBP under thermal conditions where the addition of the scavenger resulted in complete inhibition of the reaction.\(^7\) Under thermal conditions, the main open-shell species formed by the peroxide decomposition showed to be methyl radicals, which were presumably also responsible for the hydrogen abstraction at the alkylic substrate. In the present case, the methyl radical seems to play only a minor role, if any (a very small amount of methylated TEMPO was detected. See Figure S8, SI).

Although a detailed reaction mechanism cannot be proposed with the available data, based in our preliminary observations and our previous report,\(^7\) we anticipate that the reaction pathway might be as depicted in Scheme 4. After photon absorption, the excited copper species [CuI]\(^+\) shall react with TBHP via SET to produce the oxidized complex copper(II) 5, which shall be feasible considering the enhanced reductive power of photoexcited copper complexes (for instance, [Cu(XyBnta)(dppb)]\(^+\)) is a very strong photoreductant: \(E^\circ_{\text{red}} = -2.40\) V vs. SCE in THF; XyBnta: N-[2-(1-benzyl-1H-1,2,3-triazol-4-yl)phenyl]-2,6-dimethylaniline; dppb: 1,2-bis(diphenylphosphanyl)benzene).\(^23\) The radicals resulting from the peroxide splitting can then abstract a hydrogen from the allyl substrate 2, to yield an open-shell species 4 that shall react quickly with complex 5\(^24\) to produce a transient copper(III) intermediate 6.\(^25\) Under the re-
action condition it is expected that organocuprates 7 are formed from 1.26 Finally, ligand exchange between 6 and 7 followed by reductive elimination from 8 shall regenerate the copper(1) catalyst and lead to the cross-coupling product 3.

In conclusion, we have developed a new photocatalytic method for the synthesis of substituted 1,4-ynes via cross-dehydrogenative coupling of undervatized cyclic alkenes and terminal alkynes under very mild conditions. This methodology poses a dramatic improvement over our previous reports under thermal conditions and, to some extent, is complementary to it on the substrate scope. Moreover, the use of copper complex as photocatalyst/photoinitiator at room temperature for this reaction poses an attractive alternative to previous CDC methodologies relying on precious metals. Further investigations on the underlying reaction mechanism, the role and nature of the photocatalyst and the application of this methodology in asymmetric allylic functionalization are currently under investigation and will be the subject of a later report.

Chemicals, reagents, and solvents were purchased from commercial suppliers and used without further purification. The ligands L2, L3, and L4 were synthesized following reported procedures.27 TLC was performed on silica HSGF254 plates. 1H and 13C NMR spectra were recorded in CDCl3 using a Bruker Avance 300 spectrometer with a QNP probe head (1H: 300 MHz, 13C: 75 MHz) or Bruker Avance 400 (1H: 400 MHz, 13C: 100 MHz). The calibration of the spectra were carried out on referenced with residual solvent shifts (CDCl3, 1H = 7.26, 13C = 77.16) and were reported as parts per million relative to SiMe4. The NMR data matched with the previous report.28 GC analysis was performed on Hewlett-Packard 6890 Series. Samples were dissolved in DCM and sampled in to the GC column. The chromatogram peak ratios of the (cyclonexene-2-en-1-ylethynyl)benzene (3a) and internal standard naphthalene (AE/AS) were used for calibration (exemplary calibration curve in Figure S9, SI). The GC-yields were calculated with the corresponding calibration curve with naphthalene as an internal standard. Asahi Spectra Max-303 Xenon Light Source was used.

Allylic C–H Alkylation; General Procedure

In an oven-dried glass Schlenk tube equipped with a stirring bar, Cu(MeCN)4PF6 and ligand L1 were mixed under argon. The tube was evacuated and carefully refilled with argon three times. Then anhydrous MeCN (2.0 mL) was injected into the tube through a syringe. After stirring for 15 min at rt, TBHP, a 20-fold excess of the allyl substrate 2, and the corresponding alkyne 1 were subsequently injected into the reaction tube. The reaction was then irradiated with white light (Xenon lamp, 300–700 nm) for 24 h (9 cm was the distance between the light source and the Schlenk tube) while keeping the temperature (23–26 °C) by a stream of dry air. After stirring for 24 h, H2O was added and the product was extracted with DCM (3 × 50 mL). The pure product 3 was obtained by flash column chromatography on silica gel. Importantly, most of the obtained compounds were found to be unstable in solution under bench conditions, most probably due to polymerization.

1-(Cyclohex-2-en-1-ylethynyl)benzene (3a)

Following the general procedure, using Cu(MeCN)4PF6 (7.9 mg, 0.02 mmol), ligand L1 (7 mg, 0.02 mmol), cyclohexene (2a; 663 mg, 8.07 mmol), 1-ethyl-1-fluorobenzene (1a; 50 mg, 0.40 mmol), and TBHP (72 mg, 0.8 mmol), the pure product was obtained by flash column chromatography on silica gel with Pentane as eluent; colorless oil; yield: 46 mg (57%, 0.22 mmol); Rf = 0.7.

1H NMR (400 MHz, CDCl3): δ = 7.43–7.37 (m, 1 H), 7.21–7.18 (m, 3 H), 5.74–5.68 (m, 1 H), 5.65 (ddt, J = 10.0, 3.5, 1.8 Hz, 1 H), 3.22 (ddp, J = 7.6, 5.1, 2.6 Hz, 1 H), 1.98–1.87 (m, 3 H), 1.81–1.69 (m, 2 H), 1.59–1.49 (m, 1 H).

1C NMR (101 MHz, CDCl3): δ = 131.8, 128.3, 128.2, 127.7, 127.2, 93.0, 80.4, 29.5, 28.1, 24.8, 20.8.

The NMR data matched with the previous report.28 MS: m/z calculated for C14H14 [M + H]+: 182.10900; found: 182.10905.

1-(Cyclohex-2-en-1-ylethynyl)-2-fluorobenzene (3b)

Following the general procedure, using Cu(MeCN)4PF6 (8.3 mg, 0.024 mmol), ligand L1 (8 mg, 0.02 mmol), cyclohexene (2a; 670 mg, 8.07 mmol), 1-ethyl-1-fluorobenzene (1b; 50 mg, 0.40 mmol), and TBHP (72 mg, 0.8 mmol), the pure product was obtained by flash column chromatography on silica gel with Et2O/pentane (5:95) as eluent; colorless oil; yield: 45 mg (57%, 0.22 mmol); Rf = 0.7.

1H NMR (300 MHz, CDCl3): δ = 6.67–6.70 (m, 1 H), 6.85–6.87 (m, 1 H), 5.89–5.82 (m, 1 H), 5.73–5.66 (m, 1 H), 3.28 (td, J = 5.7, 2.4 Hz, 1 H), 1.97–1.81 (m, 4 H), 1.79–1.72 (m, 1 H), 1.45–1.35 (m, 1 H).

1C NMR (75 MHz, CDCl3): δ = 166.8, 161.5, 133.5, 129.0, 128.1, 127.8, 127.4, 126.8, 13.27, 115.2, 98.4, 74.3, 29.2, 28.4, 24.6, 20.5.

1F NMR (282 MHz, CDCl3): δ = –110.4.

MS: m/z calculated for C14H13F [M + H]+: 200.09958; found: 200.09983.

1-(Cyclohex-2-en-1-ylethynyl)-3-fluorobenzene (3c)

Following the general procedure, using Cu(MeCN)4PF6 (8.1 mg, 0.02 mmol), ligand L1 (8 mg, 0.02 mmol), cyclohexene (2a; 670 mg, 8.07 mmol), 1-ethyl1-2-fluorobenzene (1b; 50 mg, 0.40 mmol), and TBHP (72 mg, 0.8 mmol), the pure product was obtained by flash column chromatography on silica gel with Et2O/pentane (2:98) as eluent; colorless oil; yield: 36 mg (47%, 0.19 mmol); Rf = 0.8.

1H NMR (400 MHz, CDCl3): δ = 7.24–7.18 (m, 2 H), 6.84–6.78 (m, 2 H), 6.76–6.70 (m, 1 H), 5.84 (ddt, J = 10.1, 3.6, 2.1 Hz, 1 H), 5.75–5.69 (m, 1 H), 3.24 (td, J = 5.7, 2.5 Hz, 1 H), 1.90–1.81 (m, 4 H), 1.80–1.71 (m, 1 H), 1.48–1.37 (m, 1 H).

1C NMR (101 MHz, CDCl3): δ = 163.8, 161.4, 129.7, 128.0, 127.8, 127.5, 126.8, 118.4, 114.7, 94.1, 79.7, 29.2, 28.1, 24.6, 20.6.


1-(Cyclohex-2-en-1-ylethynyl)-4-fluorobenzene (3d)

Following the general procedure, using Cu(MeCN)4PF6 (8.1 mg, 0.02 mmol), ligand L1 (8 mg, 0.02 mmol), cyclohexene (2a; 670 mg, 8.07 mmol), 1-ethyl-4-ethynylbenzene (1d; 50 mg, 0.40 mmol), and TBHP (72 mg, 0.8 mmol), the pure product was obtained by flash column chromatography on silica gel with Et2O/pentane (2:98) as eluent; colorless oil; yield: 38 mg (47%, 0.19 mmol); Rf = 0.8.

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(72 mg, 0.8 mmol), the pure product was obtained by flash column chromatography on silica gel with EtO/pentane (5:95) as eluent; colorless oil; yield: 35 mg (44%, 0.18 mmol); Rf = 0.7.

1H NMR (400 MHz, CCl3D): δ = 7.38 (dd, J = 8.9, 5.4 Hz, 2 H), 6.99–6.94 (m, 2 H), 5.79 (dd, J = 9.3, 2.5, 2.1 Hz, 1 H), 5.71 (dd, J = 9.9, 3.5, 2.0 Hz, 1 H), 5.32 (ddp, J = 7.9, 5.4, 2.6 Hz, 1 H), 2.06–2.01 (m, 2 H), 2.00–1.94 (m, 1 H), 1.90–1.82 (m, 1 H), 1.82–1.75 (m, 1 H), 1.66–1.55 (m, 1 H).

13C NMR (101 MHz, CCl3D): δ = 163.5, 161.0, 133.6, 133.5, 128.3, 127.0, 120.1, 115.6, 115.4, 92.6, 79.4, 29.5, 28.1, 24.8, 20.8.

1F NMR (282 MHz, CCl3D): δ = −112.0.

1-Chloro-4-(cyclohex-2-en-1-ylethynyl)benzene (3e)

Following the general procedure, using Cu(MeCN)4PF6 (7 mg, 0.018 mmol), ligand L1 (6.1 mg, 0.018 mmol), cyclohexene (2a; 590 mg, 7.2 mmol), and TBHP (64 mg, 0.71 mmol), the pure product was obtained by flash column chromatography on silica gel with pentane as eluent; colorless oil; yield: 55 mg (70%, 0.25 mmol); Rf = 0.76.

1H NMR (300 MHz, CDCl3): δ = 7.27 (d, J = 8.7 Hz, 2 H), 7.18 (d, J = 8.8 Hz, 2 H), 5.77–5.70 (m, 1 H), 5.65 (ddt, J = 10.0, 3.7, 1.9 Hz, 1 H), 3.22 (ddp, J = 7.6, 5.2, 2.4 Hz, 1 H), 1.99–1.87 (m, 3 H), 1.79–1.68 (m, 2 H), 1.61–1.51 (m, 1 H).

13C NMR (75 MHz, CDCl3): δ = 133.6, 133.0, 128.6, 128.4, 126.9, 122.5, 94.0, 79.4, 29.4, 28.1, 24.8, 20.7.

1-Bromo-4-(cyclohex-2-en-1-ylethynyl)benzene (3f)

Following the general procedure, using Cu(MeCN)4PF6 (5.5 mg, 0.013 mmol), ligand L1 (5.1 mg, 0.013 mmol), cyclohexene (2a; 445 mg, 5.4 mmol), 1-bromo-4-ethylbenzene (1f; 50 mg, 0.27 mmol), and TBHP (94 mg, 0.54 mmol), the pure product was obtained by flash column chromatography on silica gel with pentane as eluent; colorless oil; yield: 46 mg (65%, 0.18 mmol); Rf = 0.54.

1H NMR (300 MHz, CDCl3): δ = 7.40 (d, J = 8.6 Hz, 2 H), 7.27–7.24 (m, 2 H), 5.82–5.75 (m, 1 H), 5.71 (dd, J = 7.9, 4.2, 2.5 Hz, 1 H), 3.28 (ddp, J = 7.6, 5.1, 2.4 Hz, 1 H), 2.05–2.00 (m, 2 H), 1.87 (ddd, J = 14.1, 6.2, 2.9 Hz, 1 H), 1.82–1.73 (m, 1 H), 1.67–1.58 (m, 1 H).

13C NMR (75 MHz, CDCl3): δ = 133.2, 131.5, 128.4, 126.8, 123.0, 121.8, 94.3, 79.5, 29.4, 28.1, 24.8, 20.7.

1-(Cyclohex-2-en-1-ylethynyl)-2-methoxybenzene (3g)

Following the general procedure, using Cu(MeCN)4PF6 (7.1 mg, 0.018 mmol), ligand L1 (6.1 mg, 0.018 mmol), cyclohexene (2a; 603 mg, 7.3 mmol), 1-ethyl-2-methoxybenzene (1g; 50 mg, 0.37 mmol), and TBHP (66 mg, 0.73 mmol), the pure product was obtained by flash column chromatography on silica gel with EtO/pentane (1:30) as eluent; colorless oil; yield: 42 mg (52%, 0.21 mmol); Rf = 0.6.

1H NMR (400 MHz, CCl3D): δ = 7.39 (d, J = 9.3 Hz, 1 H), 7.23 (dd, J = 8.3, 1.8, 1 Hz, 1 H), 6.88 (dd, J = 7.5, 1.1 Hz, 1 H), 6.84 (d, J = 8.7 Hz, 1 H), 5.77 (d, J = 14.1 Hz, 2 H), 3.86 (s, 3 H), 3.43–3.34 (m, 1 H), 2.06–1.98 (m, 3 H), 1.91 (ddd, J = 13.2, 5.7, 2.5 Hz, 1 H), 1.87–1.80 (m, 1 H), 1.67–1.57 (m, 1 H).

13C NMR (101 MHz, CCl3D): δ = 159.9, 133.8, 129.0, 128.0, 127.3, 120.4, 113.1, 110.7, 97.2, 76.5, 55.9, 29.5, 28.4, 24.8, 20.8.


1-(Cyclohex-2-en-1-ylethynyl)-3-methoxybenzene (3h)

Following the general procedure, using Cu(MeCN)4PF6 (7.1 mg, 0.018 mmol), ligand L1 (6.1 mg, 0.018 mmol), cyclohexene (2a; 603 mg, 7.3 mmol), 1-ethyl-3-methoxybenzene (1h; 50 mg, 0.37 mmol), and TBHP (66 mg, 0.73 mmol), the pure product was obtained by flash column chromatography on silica gel with EtO/pentane (1:99) as eluent; colorless oil; yield: 46 mg (54%, 0.21 mmol); Rf = 0.7.

1H NMR (300 MHz, CDCl3): δ = 7.72–7.16 (m, 1 H), 7.04–7.00 (m, 2 H), 6.96 (dd, J = 2.6, 1.4 Hz, 1 H), 6.86–6.81 (m, 1 H), 5.83–5.77 (m, 1 H), 5.74 (dd, J = 9.9, 3.0, 1.6 Hz, 1 H), 3.79 (s, 3 H), 3.35–3.27 (m, 1 H), 2.07–1.95 (m, 3 H), 1.90 (ddd, J = 13.2, 5.6, 2.4 Hz, 1 H), 1.85–1.79 (m, 1 H), 1.69–1.57 (m, 1 H).

13C NMR (75 MHz, CDCl3): δ = 159.3, 129.3, 128.2, 127.1, 125.0, 124.3, 116.5, 114.4, 92.8, 80.3, 77.2, 55.3, 29.5, 28.1, 24.8, 20.8.

MS: m/z = 212 (100), 197 (65), 184 (45), 165 (41), 131 (74), 118 (57).

1\(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 137.0, 134.9, 132.4, 129.3, 128.5, 128.0, 127.4, 123.5, 96.7, 79.5, 77.2, 29.7, 28.3, 24.8, 20.9, 20.8, 20.3.

1-Butyl-4-(cyclohex-2-en-1-ylethynyl)benzene (3I)

Following the general procedure, using Cu(MeCN)\(_4\)PF\(_6\) (5.8 mg, 0.015 mmol), ligand L1 (5.2 mg, 0.015 mmol), cyclohexene (2a; 500 mg, 6 mmol), 1-butyl-4-ethylbenzene (1I; 50 mg, 0.3 mmol), and TBHP (55 mg, 0.61 mmol), the pure product was obtained by flash column chromatography on silica gel using pentane as eluent; colorless oil; yield: 51 mg (71%, 0.21 mmol); R\(_f\) = 0.52.

1H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.36\) (d, \(J = 4.1\) Hz, 1 H), 7.22 (d, \(J = 3.0\) Hz, 1 H), 7.09–7.07 (m, 1 H), 5.78 (ddt, \(J = 9.1, 3.5, 2.1\) Hz, 1 H), 5.72 (ddt, \(J = 9.9, 3.5, 1.9\) Hz, 1 H), 3.28 (ddp, \(J = 7.8, 5.4, 2.8\) Hz, 1 H), 2.05–1.94 (m, 3 H), 1.91–1.83 (m, 1 H), 1.82–1.75 (m, 1 H), 1.66–1.57 (m, 1 H).

1\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta = 130.2, 128.2, 127.8, 127.1, 125.0, 122.9, 92.5, 77.6, 77.2, 76.7, 75.4, 29.4, 28.1, 24.8, 20.8.

2-(cyclohex-2-en-1-ylethynyl)phenol (3P)

Following the general procedure, using Cu(MeCN)\(_4\)PF\(_6\) (7.8 mg, 0.021 mmol), ligand L1 (6.7 mg, 0.021 mmol), cyclohexene (2a; 810 mg, 8.04 mmol), 2-ethylphenol (1P; 50 mg, 0.4 mmol), and TBHP (72 mg, 0.8 mmol), the pure product was obtained by flash column chromatography on silica gel using pentane/EtOAc (8:2) as eluent; colorless oil; yield: 45 mg (56%, 0.22 mmol); R\(_f\) = 0.6.

Note: Extensive drying of the product under high vacuum leads to decomposition of the product.

1H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.14\) (t, \(J = 7.9\) Hz, 1 H), 6.98 (d, \(J = 7.7\) Hz, 1 H), 6.89–6.86 (m, 1 H), 6.75 (dd, \(J = 8.1, 3.5\) Hz, 1 H), 5.82–5.75 (m, 1 H), 5.74–5.67 (m, 1 H), 3.28 (pt, \(J = 6.0, 3.2\) Hz, 1 H), 2.07–2.00 (m, 2 H), 1.96 (dd, \(J = 11.3, 4.0\) Hz, 1 H), 1.92–1.83 (m, 1 H), 1.83–1.72 (m, 1 H), 1.67–1.55 (m, 1 H).

1\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta = 155.3, 129.6, 128.3, 127.1, 125.3, 124.5, 118.5, 115.2, 93.2, 80.1, 77.2, 29.4, 28.1, 24.8, 20.8.

[3-Methylcyclohex-2-en-1-ylethynyl]benzene (3r)

Following the general procedure, using Cu(MeCN)\(_4\)PF\(_6\) (9.2 mg, 0.024 mmol), ligand L1 (8.4 mg, 0.024 mmol), 1-methylcyclohex-1-ene (2e; 923 mg, 9.6 mmol), phenylacetylene (1a; 50 mg, 0.48 mmol), and TBHP (86 mg, 0.96 mmol), the pure product was obtained by flash column chromatography on silica gel using pentane as eluent; colorless oil; yield: 50 mg (53%, 0.25 mmol); R\(_f\) = 0.8.

1H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.39–7.35\) (m, 2 H), 7.23–7.20 (m, 3 H), 5.42 (dh, \(J = 3.0, 1.5\) Hz, 1 H), 3.24 (dd, \(J = 7.4, 5.5, 4.1, 2.1\) Hz, 1 H), 1.89 (dd, \(J = 10.9, 6.1, 2.8\) Hz, 3 H), 1.85–1.77 (m, 1 H), 1.75–1.67 (m, 1 H), 1.65 (dd, \(J = 2.2, 1.8, 0.8\) Hz, 3 H), 1.57 (dddd, \(J = 9.0, 4.8, 2.6\) Hz, 1 H).

1\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta = 135.5, 131.7, 128.2, 127.6, 124.1, 121.2, 93.5, 80.2, 77.2, 29.8, 29.3, 28.4, 23.9, 21.2.

(Cyclopent-2-1-en-1-ylethynyl)benzene (3s)

Following the general procedure, using Cu(MeCN)\(_4\)PF\(_6\) (9.2 mg, 0.024 mmol), ligand L1 (8.4 mg, 0.024 mmol), cyclopentene (2b; 653 mg, 9.6 mmol), phenylacetylene (1a; 50 mg, 0.48 mmol), and TBHP (86 mg, 0.96 mmol), the pure product was obtained by flash column chromatography on silica gel using EtOAc/pentane (0.5:99.5) as eluent; colorless oil; yield: 65 mg (80%, 0.38 mmol); R\(_f\) = 0.8.

Note: Extensive drying of the product under high vacuum leads to decomposition of the product.

1H NMR (300 MHz, CDCl\(_3\)): \(\delta = 7.35–7.31\) (m, 2 H), 7.21–7.17 (m, 3 H), 5.81–5.76 (m, 1 H), 5.71–5.65 (m, 1 H), 3.64 (dddt, \(J = 9.2, 7.1, 4.6, 2.3\) Hz, 1 H), 2.47–2.38 (m, 1 H), 2.36–2.29 (m, 1 H), 2.22–2.21 (m, 1 H), 1.93–1.88 (m, 1 H).

1\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta = 132.3, 132.0, 131.8, 131.4, 128.4, 128.3, 127.7, 124.2, 92.8, 80.8, 77.2, 36.7, 32.2, 31.9, 26.0.

MS: \(m/z\) = 167 (100), 153 (53), 141 (11), 128 (8), 115 (16).
3-[(Phenylethynyl)cyclohept-1-ene (3t)]
Following the general procedure, using Cu[MeCN]4PF6 (9.5 mg, 0.024 mmol), ligand L1 (8.4 mg, 0.024 mmol), cycloheptene (2c; 941 mg, 9.6 mmol), phenylacetylene (1a; 50 mg, 0.48 mmol), and TBHP (86 mg, 0.96 mmol), the pure product was obtained by flash column chromatography on silica gel using Et2O/pentane (1:99) as eluent; colorless oil; yield: 50 mg (49%, 0.25 mmol); Rf = 0.8.

1H NMR (300 MHz, CDCl3): δ = 7.40–7.36 (m, 2 H), 7.26–7.23 (m, 3 H), 5.85–5.82 (m, 2 H), 3.50–3.43 (m, 1 H), 2.30–2.18 (m, 1 H), 2.05 (dddd, J = 13.6, 10.1, 6.8, 3.2 Hz, 2 H), 1.94–1.86 (m, 1 H), 1.81–1.68 (m, 2 H), 1.55 (ddt, J = 15.7, 8.9, 3.2 Hz, 2 H).

13C NMR (75 MHz, CDCl3): δ = 131.7, 131.1, 130.2, 128.3, 127.7, 124.1, 93.7, 80.9, 77.2, 33.8, 32.6, 29.7, 28.5, 26.9.

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References