Supplementary Information

Regiospecific α-methylene functionalisation of tertiary amines with alkynes via
Au-catalysed concerted one-proton/two-electron transfer to O₂

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Supplementary Methods

Instruments and Reagents: Gas chromatography (GC) analyses were performed on a Shimadzu GC-2014 instrument with a flame ionization detector (FID) equipped with a TC-5 capillary column. GC-mass spectrometry (MS) spectra were recorded on a Shimadzu GCMS-QP2010 instrument equipped with an InertCap5 capillary column at an ionization voltage of 70 eV. Liquid-state $^1$H, $^{13}$C, and $^{19}$F NMR spectra were recorded on a JEOL JNM-ECA 500 instrument. $^1$H and $^{13}$C NMR spectra were collected at 500.16 and 125.77 MHz, respectively. $^1$H and $^{13}$C NMR spectra were calibrated by tetramethylsilane (TMS) as the internal standard ($\delta = 0$ ppm) or the solvent peak ($^1$H NMR using toluene-$d_8$: $\delta = 7.01$ ppm, $^{13}$C NMR using toluene-$d_8$: $\delta = 20.43$ ppm, CDCl$_3$: $\delta = 77.16$ ppm). $^{19}$F NMR was measured at 470.62 MHz with benzotrifluoride as an external standard ($\delta = -63.72$ ppm). The desired products were isolated using Biotage Isolera. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) analyses were performed on a Shimadzu ICPS-8100 instrument. Transmission electron microscopy (TEM) measurements were performed on JEOL JEM-2000EX II. TEM samples were prepared by placing a drop of the suspension with EtOH on carbon-coated Cu grids and dried in vacuo. X-ray diffraction (XRD) patterns were recorded using a Rigaku SmartLab instrument under Cu K$\alpha$ radiation (45 kV, 200 mA). X-ray photoelectron spectroscopy (XPS) measurements were carried out on a ULVAC-PHI PHI5000 VersaProbe instrument using the Al K$\alpha$ radiation ($h\nu = 1486.6$ eV). Infrared (IR) spectra were measured on Jasco FT/IR-4100 using KBr disks. Elemental analyses for C, H, and N were performed on Elementar vario MICRO cube. Pd supported on Al$_2$O$_3$ (Pd/Al$_2$O$_3$. Pd: 5wt%, Lot. No. 237-020410, N.E. CHEMCAT), Pt supported on Al$_2$O$_3$ (Pt/Al$_2$O$_3$. Pt: 5wt%, Lot. No. 137-90020, N.E. CHEMCAT), Ru supported on Al$_2$O$_3$ (Ru/Al$_2$O$_3$, Ru: 5wt%, Lot. No. 437-000050, N.E. CHEMCAT), Mg$_6$Al$_2$(OH)$_{16}$(CO$_3$)$_4$·4H$_2$O (layered double hydroxide: LDH) (47 m$^2$ g$^{-1}$, Cat. No. Tomita-AD 500, Tomita Pharmaceutical), Ca$_{10}$(PO$_4$)$_6$(OH)$_2$ (hydroxyapatite: HAP) (11 m$^2$ g$^{-1}$, Cat. No. 011-14882, FUJIFILM Wako), ZnO (7 m$^2$ g$^{-1}$ after calcination at 600 °C for 2 h, Cat. No. 265-00971, FUJIFILM Wako), CeO$_2$ (45 m$^2$ g$^{-1}$ after calcination at 600 °C for 2 h, Cat. No. 544841-25G, Sigma-Aldrich), ZrO$_2$ (48 m$^2$ g$^{-1}$ after calcination at 600 °C for 2 h, Cat. No. JRC-ZRO-6, Catalysis Society of Japan), Al$_2$O$_3$ (183 m$^2$ g$^{-1}$ after calcination at 600 °C for 2 h, Cat. No. KHS-24, Sumitomo Chemical), and TiO$_2$ (66 m$^2$ g$^{-1}$ after calcination at 600 °C for 2 h, Cat. No. ST-01, Ishihara Sangyo Kaisha) were commercially available. Solvents, substrates, and metal sources were obtained from Kanto Chemical, Tokyo Chemical Industry, FUJIFILM Wako, Sigma-Aldrich, or Alfa Aesar (reagent grade). Several substrates were purified by Kugelrohr distillation just before use.
**Leaching Test:** To establish whether the observed catalysis of the α-methylene-selective alkynylation of 1a with 2a was heterogeneous in nature and was affected by Au/HAP — and not by metal species leaching from Au/HAP into the reaction solution — Au/HAP was removed from the reaction mixture by hot filtration 2 h after the initiation of the reaction under the optimized conditions; the reaction was then carried forward with the filtrate under the same optimized conditions (Supplementary Fig. 4). Removal of the catalyst caused the production of 2a to cease immediately, and the yield of 3aa did not change at the end of the specified 24 h. In order to measure the amount of metals leached into solution, the filtrate in which the reaction had been carried out for 24 h was evaporated to dryness *in vacuo*, and the residue obtained was treated with concentrated aqua regia (1 mL), and sonicated. The amounts of Au and Ca in the filtrate were then determined by ICP-AES after the solution was filtered off and moved into a 10 mL volumetric flask. The results indicated that gold and calcium were hardly detected in the reaction mixture (Au: 0.30% and Ca: 0.054% of Au and Ca used for the reaction, respectively). Therefore, the observed catalysis of Au/HAP for this reaction was confirmed to be truly heterogeneous. On the other hand, in the filtrate, a substantial amount of Zn species was detected by ICP-AES (27% of Zn used for the reaction), which was consistent with the role of Zn species as the homogeneous cocatalyst for nucleophilic addition.

**Reuse Test:** After the reaction, Au/HAP was retrieved from the reaction mixture by simple filtration using an Omnipore membrane filter. The retrieved catalyst was washed with CH₃CN (20 mL for every 100 mg of Au/HAP), and dried *in vacuo*. The catalyst thus retrieved was utilized to conduct reuse experiments. Consequently, Au/HAP can be reused at least twice for the reaction of 1a and 2a without lowering the yields of 3aa as of 24 h, although the reaction rate appeared to decrease as the number of reuses increased (Supplementary Table 3 and Supplementary Fig. 5). FT-IR spectra showed no obvious difference between fresh Au/HAP and the used Au/HAP (Supplementary Fig. 6). XRD patterns of the used Au/HAP indicated that the structure of HAP had not changed after the reaction, whereas the gold nanoparticle size had increased slightly (Supplementary Fig. 7). In fact, TEM images of the used catalysts shown in Supplementary Fig. 8 clarified the aggregation of Au nanoparticles after the reactions (mean diameter of before use: 5.1 nm, mean diameter after the 1st use: 9.0 nm, mean diameter after the 3rd use: 10.5 nm). Furthermore, the presence of Zn species in the used Au/HAP was confirmed by XPS (Supplementary Fig. 9). Considering these evidences, the apparent progressive deactivation of the catalyst as a consequence of reuse is likely the result of an increase in the size of the gold nanoparticle and/or of the attachment of Zn species onto Au/HAP.
**O₂ Pressure Dependence on Production Rates:** Experiments of O₂ pressure dependence on production rates of 3aa were carried out as follows. Into a schlenk flask, an internal standard (biphenyl, 0.1 mmol), substrates (1a: 0.5 mmol, 2a: 0.5 mmol), Au/HAP (100 mg, 1.5 mol%), ZnBr₂ (10 mol%), and PhCF₃ solvent (2 mL) were added. After the flask and the solution were degassed by freeze-pump-thaw cycling, the reaction started under an atmosphere of O₂/N₂ mixed gas balloon with controlled O₂ partial pressures using flow meters. The solutions sampled every 10 min for 40 min were analyzed by GC.

**Use of Deuterated Amine HCl Salts (Example: Kinetic Isotope Effect Using 1a-d₄):** 1-Methylpiperidine-2,2-d₂ (1a-d₂) and 1-methylpiperidine-2,2,2,2-d₄ (1a-d₄) were synthesized as the HCl salts, thus, before the use of them, neutralization using NaOH in H₂O or NaOD in D₂O, extraction with solvent used for reactions, dehydration, and filtration were conducted. As a typical procedure of using the deuterated amines, an experiment of kinetic isotope effects using 1a-d₄ on the present α-alkynylation with 2a was shown below. First, the HCl salt of 1a-d₄ (0.3 mmol) was added into a vial. Then, into the vial, an aqueous solution of 2M NaOH (150 µL) and PhCF₃ (0.5 mL×3) were added to extract 1a-d₄ in the PhCF₃. The collected extraction solution was dried over Na₂SO₄ (100 mg). Then, filtration of the solids and washing with PhCF₃ (0.25 mL) gave the solution of 1a-d₄. After the addition of 2a (1 mmol) and biphenyl (0.1 mmol) to the solution, GC analysis was performed to check the initial amount of 1a-d₄ and 2a. Into a Pyrex glass test tube, ZnBr₂ (5 mol% to 2a), Au/HAP (Au: 0.8 mol% to 2a), a Teflon-coated magnetic stir bar, and the prepared solution (containing 1a-d₄, 2a, and biphenyl) were added. The mixture was stirred at 95 °C under an open air (1 atm). The solutions sampled every 10 min for 40 min were analyzed by GC to determine the yields of 3aa-d₃. As for the counterpart (1a), an HCl salt of 1a was used in the same manner, and the production rate of 3aa was determined.

**DFT Calculations:** All calculations were performed using the Gaussian 16 Rev B.01 or Rev. C software. Geometry optimizations and single-point energy calculations were conducted using the B3LYP functional or M06 functional with SDD basis sets for Au and 6-31G(d,p) basis sets for the other elements. For the spin multiplicity, all structures were calculated as the singlet state. All thermodynamic data were calculated at the standard state (25 °C and 1 atm).

**Synthesis of N-methyl tertiary amines:** The N-methyldamines described below were prepared by reductive amination according to literature procedures. In particular, a secondary amine (10 mmol) was added into the mixture of a formaldehyde solution (37%, 40 mmol) and formic acid (40 mmol) at
room temperature. After the resulting mixture was refluxed for 24 h and cooled to room temperature, it was added to an aqueous solution of NaOH (2 M, 50 mL) and extracted with diethyl ether. The organic layers were washed with brine and dried over K$_2$CO$_3$. After the filtration of K$_2$CO$_3$, the solvent was evaporated under reduced pressure, and the residue was purified by distillation, affording the desired $N$-methylamine.

1c (CAS No. 1192-95-6)

1-methylazepane (1c): $^1$H NMR (500 MHz CDCl$_3$, TMS): $\delta$ 1.59–1.69 (m, 8H), 2.35 (s, 3H), 2.53–2.56 (m, 4H). MS (70 eV, EI): $m/z$ (%): 113 (51) [M$^+$], 112 (28), 98 (14), 85 (8), 84 (100), 71 (34), 70 (34), 58 (27), 57 (46), 56 (5), 55 (7).

1e (CAS No. 1612-65-3)

2-methyl-1,2,3,4-tetrahydroisoquinoline (1f): $^1$H NMR (500 MHz CDCl$_3$, TMS): $\delta$ 2.45 (s, 3H), 2.68 (t, $J = 6.0$ Hz, 2H), 2.92 (t, $J = 6.0$ Hz, 2H), 3.58 (s, 2H), 7.00–7.02 (m, 1H), 7.09–7.14 (m, 3H). MS (70 eV, EI): $m/z$ (%): 147 (45) [M$^+$], 146 (100), 144 (11), 131 (7), 115 (6), 105 (8), 104 (55), 103 (16), 78 (16), 77 (11), 73 (6), 51 (5).

Synthesis of $trans-N,N$-dimethyl-1-(2-phenylcyclopropyl)methanamine (1s): The amine substrate of a radical clock for HAT (1q) was synthesized referring to literature procedures.$^{88}$ $trans$-2-Phenylcyclopropene-1-carboxylic acid (2.5 mmol), 4-dimethylaminopyridine (0.25 mmol), dry dichloromethane (8 mL), dimethylamine (5 mmol, 2M THF solution), and Et$_3$N (2.5 mmol) were successively added into a Schlenk flask. After cooling the solution to 0 °C, EDAC-HCl (3 mmol, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride) was added and stirred for 2 h at 0 °C. Then, the reaction solution was additionally stirred for 24 h at room temperature. The resulting solution was extracted with EtOAc (30 mL) and sat. citric acid aqueous solution (50 mL) followed by sat. NaHCO$_3$ aqueous solution (2×25 mL) and deionized water (30 mL). After drying the organic layer using Na$_2$SO$_4$ and evaporating the organic solvent in vacuo, the crude product was subjected to column chromatography on silica gel using EtOAc/hexane = 4/6 as an eluent, affording $trans-N,N$-dimethyl-2-phenylcyclopropane-1-carboxamide (0.261 g). Then, all the amides were added at 0 °C to a Schlenk flask containing LiAlH$_4$ (4 mmol) and dry THF (15 mL). After stirring the solution for 2 h, the reaction was quenched by deionized water and 2M NaOH aqueous solution. After filtration of
white solids with celite, washing by dry THF (10 mL), and drying on Na₂SO₄, the solution was evaporated in vacuo to afford the desired product, trans-N,N-dimethyl-1-(2-phenylcyclopropyl) methanamine (1s) (96.4 mg).

(CAS No. 5279-83-4)

trans-N,N-dimethyl-2-phenylcyclopropane-1-carboxamide: ¹H NMR (500 MHz CDCl₃, TMS): δ 1.25–1.30 (m, 1H), 1.62–1.66 (m, 1H), 1.97–2.01 (m, 1H), 2.46–2.50 (m, 1H), 2.99 (s, 3H), 3.13 (s, 3H), 7.11–7.13 (m, 2H), 7.18–7.21 (m, 1H), 7.26–7.29 (m, 2H). MS (70 eV, EI): m/z (%): 189 (53) [M⁺], 145 (20). 144 (34), 127 (26), 117 (56), 116 (32), 115 (52), 98 (12), 91 (26), 72 (100), 68 (26), 65 (11).

1s (CAS No. 16583-42-9)

trans-N,N-dimethyl-1-(2-phenylcyclopropyl) methanamine (1s): ¹H NMR (500 MHz CDCl₃, TMS): δ 0.81–0.85 (m, 1H), 0.95–0.99 (m, 1H), 1.19–1.26 (m, 1H), 1.67–1.70 (m, 1H), 2.28 (dd, J = 12.6 and 6.3 Hz, 1H), 2.29 (s, 6H), 2.40 (dd, J = 12.6 and 6.3 Hz, 1H), 7.05–7.07 (m, 2H), 7.12–7.15 (m, 1H), 7.23–7.26 (m, 2H). MS (70 eV, EI): m/z (%): 175 (2) [M⁺], 134 (13), 129 (7), 115 (7), 91 (12), 84 (10), 71 (79), 58 (100), 56 (12).

Synthesis of ethyl 1-(diethylamino)cyclopropane-1-carboxylate (1t): According to the reference,⁵⁹ ethyl 1-(diethylamino)cyclopropane-1-carboxylate (1t) was synthesized as follows. Into a brown vial (volume: ~20 mL), K₂CO₃ (1.8 g, 13.1 mmol), 1-aminocyclopropanecarboxylic acid ethyl ester hydrochloride (0.36 g, 2.2 mmol), CH₃CN solvent (10 mL), and EtI (1.2 g, 7.9 mmol) were added and stirred at room temperature for 84 h. The resulting slurry was filtrated and washed with diethyl ether (15 mL). The solvent of the filtrate was evaporated, and then the residue was subjected to column chromatography on amine-modified silica gel using hexane/EtOAc = 9/1 as an eluent. After the column chromatography, evaporation of the desired fractions afforded 1t (82.2 mg).
**ethyl 1-(diethylamino)cyclopropane-1-carboxylate (1t):** ¹H NMR (500 MHz CDCl₃, TMS): δ 0.97 (dd, J = 7.3 and 4.0 Hz, 2H), 1.03 (t, J = 7.3 Hz, 6H), 1.25 (t, J = 7.3 Hz, 3H), 1.27 (dd, J = 7.5 and 4.0 Hz, 2H), 2.88 (q, J = 7.3 Hz, 4H), 4.11 (q, J = 7.1 Hz, 2H). ¹³C–¹H NMR (125 MHz, CDCl₃, TMS): δ 14.3, 15.4, 19.1, 45.1, 47.8, 60.1, 175.1. MS (70 eV, EI): m/z (%): 185 (9) [M⁺], 170 (8), 157 (7), 156 (66), 142 (7), 128 (8), 112 (33), 98 (5), 96 (6), 85 (7), 84 (100), 83 (8), 82 (13), 73 (11), 70 (8), 68 (11), 57 (6), 56 (100), 55 (20), 54 (28).

**Synthesis of 1-methylpiperidine-2,2-d₂ (1a-d₂):** By referring to the previous report, ¹-methylpiperidine-2,2-d₂ (1a-d₂) was synthesized as the corresponding HCl salt through amide reduction. 1-Methylpiperidin-2-one (2 mmol) was added at 0 °C to a Schlenk flask containing LiAlD₄ (6 mmol) and dry THF (20 mL). After stirring the solution for 2 h, the reaction was quenched by deionized water and 2M NaOH aqueous solution. After filtration of white solids with celite and washing by dry THF (10 mL), the filtrate was dried over K₂CO₃ and Na₂SO₄ overnight. After filtration and partial evaporation, an aqueous solution of 1M HCl (5 mL) was added to the solution. The resulting solution was evaporated in vacuo using azeotrope with toluene several times to afford the desired HCl salt (193.2 mg). ¹H NMR of 1a-d₂ was measured in toluene-d₈ after treatment with NaOD/D₂O (40wt%) and filtration, determining the deuteration ratio (>95%).

1a-d₂ (CAS No. 695-72-7)

**1-methylpiperidine-2,2-d₄ (1a-d₄):** ¹H NMR (500 MHz, toluene-d₈): δ 1.23–1.31 (m, 2H), 1.47–1.52 (m, 4H), 2.09 (s, 3H), 2.10–2.22 (m, 2H).

**Synthesis of 1-methylpiperidine-2,2,2,2-d₄ (1a-d₄):** After N-methylglutarimide synthesis, reduction of the imide with LiAlD₄ afforded 1-methylpiperidine-2,2,2,2-d₄ (1a-d₄) as follows. Glutarimide (1 g), K₂CO₃ (2.1 g), and CH₃I (2.13 g) were mixed in dry acetone (20 mL). Then, the reactions slurry was stirred under reflux for 24 h. After cooling, filtration, and evaporation of acetone, the residue was subjected to column chromatography on silica gel with an eluent of hexane/EtOAc = 6/4, affording N-methylglutarimide (0.77 g). Then, the imide (2 mmol) was added at 0 °C to a Schlenk flask containing LiAlD₄ (6 mmol) and dry diethyl ether (15 mL). After stirring the solution for 19 h,
the reaction was quenched by deionized water and 2M NaOH aqueous solution. After filtration of white solids and washing by dry diethyl ether, the filtrate was dried over Na₂SO₄. After filtration, an aqueous solution of 12M HCl (0.2 mL) was added to the solution with stirring. The resulting solution was evaporated in vacuo using azeotrope with toluene several times to afford the desired HCl salt (94.9 mg). ¹H NMR of 1a-d₄ was measured in toluene-d₈ after treatment with NaOD/D₂O (40wt%) and filtration, determining the deuteration ratio (>95%).

(N-methylglutarimide: ¹H NMR (500 MHz, CDCl₃): δ 1.96 (quin, J = 6.5 Hz, 2H), 2.67 (t, J = 6.5 Hz, 4H), 3.14 (s, 3H). MS (70 eV, EI): m/z (%): 128 (7), 127 (100) [M⁺], 99 (10), 98 (27), 71 (17), 70 (29), 58 (12), 56 (6), 55 (19).

1a-d₄ (CAS No. 25077-25-2)

1-methylpiperidine-2,2,2,2-d₄ (1a-d₄): ¹H NMR (500 MHz, toluene-d₈): δ 1.22–1.34 (m, 2H), 1.48 (t, J = 5.9 Hz, 4H), 2.09 (s, 3H).

Synthesis of phenylacetylene-d (2a-d): In the following manner referred to the previous report,¹¹ phenylacetylene-d (2a-d) was synthesized. Into a Pyrex glass test tube, phenylacetylene (3 mmol) and D₂O (5 mL) were added. After purging the air in the test tube with Ar, the mixture was stirred at room temperature for about 3 days. The resulting mixture was extracted by dichloromethane three times and dried over Na₂SO₄. After removing Na₂SO₄ by filtration, evaporation of the solvents gave the desired 2a-d (120 mg) (deuteration ratio: 98%, determined by ¹H NMR).

2a-d (CAS No. 3240-11-7)

phenylacetylene-d (2a-d): ¹H NMR (500 MHz, CDCl₃): δ 7.30–7.37 (m, 3H), 7.47–7.52 (m, 2H).
Spectral Data:

3aa (CAS No. 51498-55-6)

1-methyl-2-(phenylethynyl)piperidine (3aa): 78% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.47–1.52 (m, 1H), 1.55–1.75 (m, 3H), 1.81–1.93 (m, 2H), 2.35–2.41 (m, 1H), 2.41 (s, 3H), 2.62–2.68 (m, 1H), 3.55 (brs, 1H), 7.27–7.32 (m, 3H), 7.42–7.46 (m, 2H). $^{13}$C–{$^1$H} NMR (125 MHz, CDCl$_3$, TMS): $\delta$20.9, 25.9, 31.9, 44.6, 52.1, 54.8, 86.2, 87.6, 123.5, 128.0, 128.3, 131.8. MS (70 eV, EI): $m/z$ (%): 199 (44) [$M^+$], 198 (54), 184 (11), 171 (23), 170 (100), 157 (22), 156 (16), 143 (11), 142 (36), 128 (28), 127 (14), 122 (25), 116 (15), 115 (44), 102 (13), 94 (11), 79 (10). Anal. Calcd. for C$_{14}$H$_{17}$N·0.25H$_2$O: C, 82.57; H, 8.66; N, 6.87. Found: C, 82.97; H, 8.49; N, 6.85.

3ab

2-((4-chlorophenyl)ethynyl)-1-methylpiperidine (3ab): 77% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.47–1.50 (m, 1H), 1.55–1.73 (m, 3H), 1.80–1.93 (m, 2H), 2.34–2.42 (m, 1H), 2.39 (s, 3H), 2.61–2.65 (m, 1H), 3.53 (brs, 1H), 7.26–7.28 (m, 2H), 7.35–7.38 (m, 2H). $^{13}$C–{$^1$H} NMR (125 MHz, CDCl$_3$, TMS): $\delta$21.0, 25.8, 31.9, 44.6, 52.3, 54.8, 85.0, 88.7, 122.0, 128.6, 133.0, 134.0. MS (70 eV, EI): $m/z$ (%): 235 (17), 234 (26) [$M^+$], 233 (50), 232 (60), 218 (12), 206 (35), 205 (23), 204 (100), 191 (24), 190 (13), 178 (12), 177 (10), 176 (28), 162 (15), 149 (23), 127 (21), 126 (12), 122 (32), 115 (33), 113 (11), 96 (12), 94 (15). Anal. Calcd. for C$_{14}$H$_{16}$NCl: C, 71.94; H, 6.90; N, 5.99. Found: C, 71.54; H, 6.77; N, 5.91.

3ac

2-((3-chlorophenyl)ethynyl)-1-methylpiperidine (3ac): 77% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.48–1.53 (m, 1H), 1.55–1.71 (m, 3H), 1.80–1.93 (m, 2H), 2.36–2.44 (m, 1H), 2.40 (s, 3H), 2.60–2.64 (m, 1H), 3.56 (brs, 1H), 7.21–7.33 (m, 3H), 7.42–
7.43 (m, 1H). $^{13}$C–$^{1}$H NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 20.9, 25.8, 31.8, 44.6, 52.1, 54.7, 84.9, 89.0, 125.2, 128.3, 129.6, 129.9, 131.7, 134.1. MS (70 eV, EI): $m/z$ (%): 235 (13), 234 (21) [M$^+$], 233 (41), 232 (47), 218 (11), 206 (35), 205 (24), 204 (100), 191 (20), 190 (10), 178 (11), 176 (27), 162 (13), 149 (21), 127 (20), 126 (10), 122 (36), 115 (31), 113 (10), 96 (12), 94 (18). Anal. Calcd. for C$_{14}$H$_{16}$NCl·0.1H$_2$O: C, 71.39; H, 6.93; N, 5.95. Found: C, 71.52; H, 6.71; N, 5.88.

3ad

2-((2-chlorophenyl)ethynyl)-1-methylpiperidine (3ad): 87% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.50–1.55 (m, 1H), 1.56–1.78 (m, 3H), 1.86–1.94 (m, 2H), 2.39–2.47 (m, 1H), 2.43 (s, 3H), 2.65–2.70 (m, 1H), 3.68 (bbrs, 1H), 7.18–7.24 (m, 2H), 7.38–7.40 (m, 1H), 7.47–7.48 (m, 1H). $^{13}$C–$^{1}$H NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 20.6, 25.8, 31.7, 44.5, 51.7, 54.7, 83.1, 93.1, 123.4, 126.4, 129.0, 129.3, 133.4, 136.0. MS (70 eV, EI): $m/z$ (%): 235 (18), 234 (24) [M$^+$], 233 (54), 232 (52), 218 (12), 206 (36), 205 (24), 204 (100), 198 (24), 191 (23), 178 (12), 176 (29), 170 (11), 162 (15), 151 (11), 149 (24), 142 (10), 127 (23), 126 (12), 122 (43), 115 (36), 114 (10), 113 (12), 96 (14), 94 (16). Anal. Calcd. for C$_{14}$H$_{16}$NCl·0.1H$_2$O: C, 71.39; H, 6.93; N, 5.95. Found: C, 71.36; H, 6.55; N, 5.89.

3ae

2-((4-bromophenyl)ethynyl)-1-methylpiperidine (3ae): 82% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.47–1.50 (m, 1H), 1.55–1.72 (m, 3H), 1.79–1.92 (m, 2H), 2.34–2.42 (m, 1H), 2.39 (s, 3H), 2.61–2.64 (m, 1H), 3.52 (bbrs, 1H), 7.28–7.31 (m, 2H), 7.41–7.47 (m, 2H). $^{13}$C–$^{1}$H NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 21.0, 25.8, 31.8, 44.5, 52.2, 54.8, 85.1, 88.9, 122.1, 122.4, 131.5, 133.2. MS (70 eV, EI): $m/z$ (%): 279 (53), 278 (66) [M$^+$], 277 (53), 276 (69), 251 (33), 250 (96), 249 (25), 248 (100), 237 (26), 235 (27), 222 (28), 220 (27), 169 (45), 127 (36), 126 (23), 122 (65), 115 (58), 114 (21), 113 (21), 94 (28). Anal. Calcd. for C$_{14}$H$_{16}$NBr: C, 60.45; H, 5.80; N, 5.03. Found: C, 60.09; H, 5.52; N, 5.00.
2-((4-fluorophenyl)ethynyl)-1-methylpiperidine \((3af)\): 64% isolated yield (eluent: hexane/EtOAc = 6/4). \(^1\)H NMR (500 MHz, CDCl\(_3\), TMS): \(\delta 1.47–1.50 (m, 1H), 1.54–1.73 (m, 3H), 1.80–1.93 (m, 2H), 2.34–2.41 (m, 1H), 2.40 (s, 3H), 2.61–2.64 (m, 1H), 3.52 (brs, 1H), 6.97–7.01 (m, 2H), 7.39–7.43 (m, 2H). \(^{13}\)C–\(^1\)H NMR (125 MHz, CDCl\(_3\), TMS): \(\delta 21.0, 25.8, 31.9, 44.5, 52.2, 54.8, 85.0, 87.2, 115.5 (d, \(J = 22.8\) Hz), 119.5 (d, \(J = 3.6\) Hz), 133.6 (d, \(J = 8.4\) Hz), 162.3 (d, \(J = 248.3\) Hz). \(^19\)F NMR (470 MHz, CDCl\(_3\)): \(\delta -112.92\). MS (70 eV, EI): \(m/z\) (%): 217 (52) \([M^+]\), 216 (61), 202 (12), 189 (23), 188 (100), 175 (24), 174 (16), 161 (12), 160 (36), 146 (30), 145 (12), 134 (15), 133 (50), 122 (22), 120 (15), 94 (15), 88 (12). Anal. Calcd. for C\(_{14}\)H\(_{16}\)NF·0.35H\(_2\)O: C, 75.21; H, 7.53; N, 6.26. Found: C, 75.08; H, 7.09; N, 6.21.

\[ \text{3ag} \]

1-methyl-2-(phenylethynyl)piperidine \((3ag)\): 76% isolated yield (eluent: hexane/EtOAc = 8/2). \(^1\)H NMR (500 MHz, CDCl\(_3\), TMS): \(\delta 1.46–1.49 (m, 1H), 1.54–1.76 (m, 3H), 1.79–1.89 (m, 2H), 2.33–2.41 (m, 1H), 2.40 (s, 3H), 2.63–2.67 (m, 1H), 3.51 (brs, 1H), 3.80 (s, 3H), 6.81–6.84 (m, 2H), 7.36–7.39 (m, 2H). \(^{13}\)C–\(^1\)H NMR (125 MHz, CDCl\(_3\), TMS): \(\delta 21.1, 25.9, 32.1, 44.6, 52.3, 54.9, 55.4, 85.9, 86.1, 113.9, 115.7, 133.2, 159.4. MS (70 eV, EI): \(m/z\) (%): 230 (14), 229 (87) \([M^+]\), 228 (100), 214 (32), 201 (21), 200 (88), 187 (17), 186 (29), 172 (55), 159 (14), 158 (51), 157 (11), 145 (21), 144 (12), 143(12), 130 (14), 128 (10), 122 (31), 115 (23), 94 (14), 89 (11). Anal. Calcd. for C\(_{15}\)H\(_{19}\)NO: C, 78.56; H, 8.35; N, 6.11. Found: C, 77.92; H, 8.38; N, 5.95.

\[ \text{3ah} \]

1-methyl-2-(\(p\)-tolylethynyl)piperidine \((3ah)\): 82% isolated yield (eluent: hexane/EtOAc = 6/4). \(^1\)H NMR (500 MHz, CDCl\(_3\), TMS): \(\delta 1.46–1.49 (m, 1H), 1.54–1.74 (m, 3H), 1.80–1.92 (m, 2H), 2.34 (s, 3H), 2.35–2.43 (m, 1H), 2.40 (s, 3H), 2.63–2.67 (m, 1H), 3.54 (brs, 1H), 7.10–7.11 (m, 2H), 7.33–
7.34 (m, 2H). $^{13}$C–{$^1$H} NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 21.0, 21.5, 25.8, 31.9, 44.5, 52.1, 54.8, 86.2, 86.7, 120.4, 129.1, 131.7, 138.0. MS (70 eV, El): $m/z$ (%): 213 (64) [$M^+$], 212 (71), 198 (19), 185 (25), 184 (100), 177 (24), 170 (25), 157 (12), 156 (57), 142 (20), 141 (22), 129 (28), 128 (20), 122 (30), 115 (30), 94 (11), 86 (14). Anal. Calcd. for C$_{13}$H$_{19}$N·0.15H$_2$O: C, 83.40; H, 9.01; N, 6.48. Found: C, 83.29; H, 8.79; N, 6.38.

3ai

1-methyl-2-((4-(trifluoromethyl)phenyl)ethynyl)piperidine (3ai): 72% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.49–1.52 (m, 1H), 1.56–1.73 (m, 3H), 1.82–1.95 (m, 2H), 2.34–2.42 (m, 1H), 2.41 (s, 3H), 2.62–2.65 (m, 1H), 3.56 (brs, 1H), 7.52–7.57 (m, 4H). $^{13}$C–{$^1$H} NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 21.0, 25.8, 31.8, 44.6, 52.2, 54.8, 84.9, 90.5, 124.1 (q, $J = 272.3$ Hz), 125.2–125.3 (m), 127.3, 129.8 (q, $J = 129.8$ Hz), 132.0. $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ –65.4. MS (70 eV, El): $m/z$ (%): 267 (39) [$M^+$], 266 (47), 252 (11), 239 (26), 238 (100), 225 (20), 224 (11), 210 (27), 183 (17), 127 (11), 122 (17), 115 (11), 94 (11). Anal. Calcd. for C$_{15}$H$_{16}$F$_3$N: C, 67.40; H, 6.03; N, 5.24. Found: C, 67.11; H, 5.80; N, 5.15.

3aj

4-((1-methylpiperidin-2-yl)ethynyl)benzonitrile (3aj): 66% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.49–1.54 (m, 1H), 1.56–1.71 (m, 3H), 1.81–1.94 (m, 2H), 2.36–2.44 (m, 1H), 2.40 (s, 3H), 2.60–2.64 (m, 1H), 3.57 (brs, 1H), 7.51–7.53 (m, 2H), 7.59–7.61 (m, 2H). $^{13}$C–{$^1$H} NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 20.9, 25.7, 31.6, 44.5, 52.1, 54.8, 84.7, 92.7, 111.3, 118.6, 128.4, 132.0, 132.3. MS (70 eV, El): $m/z$ (%): 224 (37) [$M^+$], 223 (44), 209 (11), 196 (23), 195 (100), 182 (20), 181 (13), 167 (29), 153 (18), 141 (13), 140 (34), 127 (15), 122 (20), 94 (12). Anal. Calcd. for C$_{15}$H$_{16}$N$_2$·0.2H$_2$O: C, 79.05; H, 7.25; N, 12.29. Found: C, 79.18; H, 7.10; N, 12.25.
3ak

**1-methyl-2-((4-nitrophenyl)ethyl)piperidine (3ak)**: 61% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.51–1.55 (m, 1H), 1.57–1.72 (m, 3H), 1.82–1.96 (m, 2H), 2.37–2.45 (m, 1H), 2.41 (s, 3H), 2.61–2.65 (m, 1H), 3.59 (brs, 1H), 7.57–7.59 (m, 2H), 8.17–8.19 (m, 2H). $^{13}$C–$^1$H NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 20.9, 25.7, 31.6, 44.6, 52.1, 54.9, 84.6, 93.8, 123.6, 130.4, 132.5, 146.9. MS (70 eV, EI): m/z (%): 244 (48) [M$^+$], 243 (49), 229 (13), 216 (27), 215 (100), 202 (13), 197 (20), 187 (23), 169 (29), 141 (21), 128 (11), 127 (11), 122 (25), 115 (30), 114 (10), 94 (16). Anal. Calcd. for C$_{14}$H$_{16}$N$_2$O$_2$·0.1H$_2$O: C, 68.33; H, 6.64; N, 11.38. Found: C, 68.18; H, 6.45; N, 11.32.

3al

**1-methyl-2-(thiophen-3-ylethynyl)piperidine (3al)**: 66% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.46–1.49 (m, 1H), 1.55–1.73 (m, 3H), 1.79–1.92 (m, 2H), 2.39 (s, 3H), 2.32–2.40 (m, 1H), 2.62–2.65 (m, 1H), 3.52 (brs, 1H), 7.11 (dd, $J$ = 5.2 and 1.2 Hz, 1H), 7.25 (dd, $J$ = 5.2 and 2.9 Hz, 1H), 7.40 (dd, $J$ = 2.9 and 1.2 Hz, 1H). $^{13}$C–$^1$H NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 21.0, 25.8, 31.9, 44.6, 52.2, 54.9, 81.1, 87.2, 122.4, 125.2, 128.2, 130.2. MS (70 eV, EI): m/z (%): 206 (11), 205 (59) [M$^+$], 204 (69), 190 (12), 177 (30), 176 (100), 163 (26), 162 (22), 149 (13), 148 (53), 135 (12), 134 (27), 122 (26), 121 (34), 108 (11), 94 (13), 82 (15). Anal. Calcd. for C$_{12}$H$_{15}$NS·0.1H$_2$O: C, 69.59; H, 7.40; N, 6.76. Found: C, 69.32; H, 7.13; N, 6.64.

3am

**2-(cyclohex-1-en-1-ylethynyl)-1-methylpiperidine (3am)**: 74% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.42–1.46 (m, 1H), 1.51–1.68 (m, 7H), 1.71–1.86 (m, 2H), 2.06–2.15 (m, 4H), 2.29–2.37 (m, 1H), 2.33 (s, 3H), 2.56–2.59 (m, 1H), 3.43 (brs, 1H), 6.06–6.09 (m, 1H). $^{13}$C–$^1$H NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 20.9, 21.6, 22.4, 25.6, 25.8, 29.7,
32.0, 44.4, 52.0, 54.7, 84.5, 87.9, 120.7, 134.0. MS (70 eV, EI): m/z (%): 204 (14), 203 (100) [M+], 202 (93), 188 (32), 175 (21), 174 (76), 161 (23), 160 (54), 148 (11), 147 (22), 146 (97), 134 (17), 133 (13), 132 (37), 131 (21), 122 (53), 120 (18), 111 (19), 118 (31), 114 (32), 115 (19), 105 (16), 104 (10), 103 (12), 98 (12), 96 (13), 94 (24), 91 (46), 82 (12), 81 (16), 80 (15), 79 (23), 78 (14), 77 (27), 70 (19), 68 (11), 67 (11), 65 (18), 55 (11), 51 (12). Anal. Calcd. for C14H21N·0.25H2O: C, 80.91; H, 10.43; N, 6.74. Found: C, 80.96; H, 10.11; N, 6.66.

3an

1-((1-methylpiperidin-2-yl)ethynyl)cyclohexan-1-ol (3an): 30% isolated yield (eluent: EtOAc). 1H NMR (500 MHz, CDCl3, TMS): δ 1.18–1.28 (m, 1H), 1.42–1.48 (m, 1H), 1.52–1.95 (m, 14H), 2.32 (s, 3H), 2.31–2.39 (m, 1H), 2.54–2.57 (m, 1H), 2.85 (brs, 1H). 13C–{1H} NMR (125 MHz, CDCl3, TMS): δ 20.8, 23.7, 25.3, 25.6, 31.8, 40.4, 44.4, 51.8, 54.1, 68.8, 81.7, 90.0. MS (70 eV, EI): m/z (%): 221 (20) [M+], 220 (22), 178 (14), 150 (13), 125 (10), 124 (100), 122 (52), 108 (14), 98 (21), 96 (21), 95 (12), 94 (30), 82 (12), 81 (13), 80 (12), 79 (11), 70 (21), 66 (15), 55 (20). Anal. Calcd. for C14H23NO·0.5H2O: C, 73.00; H, 10.50; N, 6.08. Found: C, 72.7; H, 10.08; N, 6.04.

3ao

1-methyl-2-(oct-1-yn-1-yl)piperidine (3ao): 26% isolated yield (eluent: hexane/EtOAc = 6/4). 1H NMR (500 MHz, CDCl3, TMS): δ 0.89 (t, J = 7.1 Hz, 3H), 1.27–1.35 (m, 4H), 1.38–1.44 (m, 3H), 1.48–1.72 (m, 6H), 1.77–1.83 (m, 1H), 2.22 (td, J = 7.0 and 1.9 Hz, 2H), 2.32 (s, 3H), 2.28–2.36 (m, 1H), 2.57–2.60 (m, 1H), 2.92 (brs, 1H). 13C–{1H} NMR (125 MHz, CDCl3, TMS): δ 14.2, 18.8, 21.0, 22.7, 25.9, 28.6, 29.2, 31.4, 32.4, 44.4, 52.2, 54.5, 77.9, 86.0. MS (70 eV, EI): m/z (%): 207 (26) [M+], 206 (48), 192 (19), 178 (21), 164 (19), 151 (12), 150 (100), 137 (69), 136 (49), 134 (14), 124 (18), 123 (12), 122 (84), 120 (10), 110 (14), 109 (24), 108 (57), 107 (13), 98 (24), 96 (38), 95 (22), 94 (62), 93 (16), 91 (18), 84 (11), 82 (27), 81 (20), 80 (19), 79 (26), 77 (19), 70 (25), 68 (13), 67 (20), 65 (14), 57 (14), 55 (23), 53 (15). Anal. Calcd. for C14H25N·0.25H2O: C, 79.37; H, 12.13; N, 6.61. Found: C, 79.28; H, 11.92; N, 6.34.
3ba (CAS No. 87143-80-4)

1-methyl-2-(phenylethynyl)pyrrolidine: 49% isolated yield (eluent: hexane/EtOAc = 8/2). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.78–1.85 (m, 1H), 1.91–2.06 (m, 2H), 2.17–2.23 (m, 1H), 2.38–2.43 (m, 1H), 2.49 (s, 3H), 2.94 (td, $J = 8.8$ and 4.0 Hz, 1H), 3.32 (t, $J = 7.1$ Hz, 1H), 7.27–7.30 (m, 3H), 7.41–7.45 (m, 2H). $^{13}$C–{$^1$H} NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 22.6, 32.4, 40.1, 55.0, 57.2, 84.3, 89.0, 123.4, 128.0 128.3, 131.8. MS (70 eV, EI): m/z (%): 186 (6), 185 (47) [M$^+$], 184 (100), 170 (5), 158 (6), 157 (45), 156 (36), 143 (8), 142 (24), 141 (8), 129 (13), 128 (16), 127 (10), 116 (14), 115 (42), 114 (12), 113 (6), 108 (37), 102 (6), 89 (5), 84 (6), 82 (6), 77 (8), 63 (8), 55 (8), 51 (5).

3ca (CAS No. 125038-93-9)

1-methyl-2-(phenylethynyl)azepane: 48% isolated yield (eluent: hexane/EtOAc = 8/2). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.63–1.72 (m, 5H), 1.82–2.06 (m, 3H), 2.49 (s, 3H), 2.58–2.63 (m, 1H), 2.76–2.81 (m, 1H), 3.82 (dd, $J = 6.7$ and 4.2 Hz, 1H), 7.27–7.32 (m, 3H), 7.42–7.47 (m, 2H). $^{13}$C–{$^1$H} NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 23.8, 26.9, 28.0, 34.3, 45.3, 53.6, 57.2, 86.0, 88.3, 123.7, 127.9, 128.4, 131.8. MS (70 eV, EI): m/z (%): 213 (49) [M$^+$], 212 (19), 198 (12), 184 (33), 171 (21), 170 (100), 157 (30), 156 (19), 142 (23), 141 (14), 129 (13), 128 (19), 127 (11), 116 (13), 115 (53), 114 (11), 102 (11), 94 (19).

3da

(trans-1-methyl-2-(phenylethynyl)piperidin-4-yl)methanol: 55% isolated yield (eluent: EtOAc). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.30 (qd, $J = 12.0$ and 5.0 Hz, 1H, NCH$_2$CH$_2$H$_2$), 1.56 (td, $J = 13.1$ and 4.4 Hz, 1H, NCH$_2$CH$_2$H$_2$), 1.72–1.76 (m, 1H, NCH$_2$CH$_2$H$_2$), 1.92–2.01 (m, 2H, NCH$_2$CH$_2$H$_2$, OCH$_2$CH), 2.38 (s, 3H, CH$_3$), 2.57 (td, $J = 11.9$ and 2.9 Hz, 1H, NCH$_2$CH$_2$H$_2$), 2.60–2.70 (m, 2H, NCH$_2$CH$_2$H$_2$, OH), 3.49 (d, $J = 6.7$ Hz, 2H, OCH$_2$), 3.93 (dd, $J = 4.2$ and 2.7 Hz, 1H, NCH$_2$), 7.28–7.32 (m, 3H), 7.41–7.46 (m, 2H). $^{13}$C–{$^1$H} NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 28.8, 33.7, 34.0, 43.9, 49.4, 53.3,
67.6, 86.0, 87.4, 123.3, 128.1, 128.3, 131.8. MS (70 eV, EI): m/z (%): 229 (34) [M+], 228 (65), 198 (45), 171 (27), 170 (100), 157 (38), 156 (26), 155 (31), 153 (29), 152 (46), 142 (50), 129 (26), 128 (54), 127 (31), 116 (23), 115 (73), 102 (22), 96 (36), 94 (21), 77 (24). Anal. Calcd. for C15H19NO·0.5H2O: C, 75.59; H, 8.46; N, 5.88. Found: C, 75.72; H, 8.23; N, 5.80.

3ea (CAS No. 1356845-31-2)

2-methyl-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline: 29% isolated yield (eluent: hexane/EtOAc = 8/2). 1H NMR (500 MHz, CDCl3, TMS): δ 2.63 (s, 3H), 2.68–2.74 (m, 1H), 2.88–3.12 (m, 3H), 4.70 (s, 1H), 7.11–7.14 (m, 1H), 7.16–7.20 (m, 2H), 7.26–7.29 (m, 3H), 7.34–7.38 (m, 1H), 7.40–7.44 (m, 2H). 13C–1H NMR (125 MHz, CDCl3, TMS): δ 28.9, 43.9, 48.8, 57.1, 86.4, 87.6, 123.3, 126.0, 127.1, 127.8, 128.2, 128.3, 129.0, 131.9, 133.6, 135.3. MS (70 eV, EI): m/z (%): 248 (9), 247 (57) [M+], 246 (100), 205 (6), 204 (34), 203 (30), 202 (31), 170 (21), 146 (5), 144 (10), 115 (11), 103 (5), 101 (7), 77 (6).

3fa

1-ethyl-2-(phenylethynyl)piperidine: 65% isolated yield (eluent: hexane/EtOAc = 8/2). 1H NMR (500 MHz, CDCl3, TMS): δ 1.11 (t, J = 7.2 Hz, 3H), 1.53–1.76 (m, 4H), 1.83–1.89 (m, 2H), 2.52–2.66 (m, 4H), 3.85 (brs, 1H), 7.28–7.32 (m, 3H), 7.42–7.46 (m, 2H). 13C–1H NMR (125 MHz, CDCl3, TMS): δ 12.3, 21.1, 25.9, 31.6, 49.1, 50.1, 51.7, 86.4, 87.3, 123.6, 127.19, 128.3, 131.8. MS (70 eV, EI): m/z (%): 213 (50) [M+], 212 (36), 198 (61), 185 (24), 184 (100), 170 (10), 156 (39), 142 (10), 141 (12), 136 (12), 129 (16), 128 (49), 127 (13), 116 (11), 115 (58), 108 (10), 102 (12), 77 (11), 70 (12), 56 (22). Anal. Calcd. for C15H10N·0.1H2O: C, 83.75; H, 9.00; N, 6.51. Found: C, 83.58; H, 8.91; N, 6.41.
3ga

1-cyclohexyl-2-(phenylethynyl)piperidine: 63% isolated yield (eluent: hexane/EtOAc = 9/1). $^1$H NMR (500 MHz, CDCl$_3$, TMS): δ 1.09–1.32 (m, 5H), 1.48–1.90 (m, 9H), 1.99–2.08 (m, 2H), 2.50–2.62 (m, 2H), 2.72–2.76 (m, 1H), 4.02 (t, $J$ = 4.2 Hz, 1H), 7.27–7.32 (m, 3H), 7.40–7.45 (m, 2H). $^{13}$C–$^1$H NMR (125 MHz, CDCl$_3$, TMS): δ 21.5, 26.0, 26.3, 28.9, 31.1, 32.4, 45.3, 49.5, 61.3, 86.1, 88.8, 123.8, 127.8, 128.3, 131.7. MS (70 eV, EI): m/z (%): 267 (28) [M$^+$], 266 (12), 238 (18), 224 (25), 211 (37), 210 (41), 190 (18), 184 (17), 156 (12), 141 (13), 135 (11), 134 (100), 128 (27), 115 (20), 55 (18). Anal. Calcd. for C$_{19}$H$_{25}$N·0.1H$_2$O: C, 84.77; H, 9.43; N, 5.20. Found: C, 84.86; H, 9.40; N, 5.14.

3ha (CAS No. 479543-27-6)

benzyl-2-(phenylethynyl)piperidine: 72% isolated yield (eluent: hexane/EtOAc = 9/1). $^1$H NMR (500 MHz, CDCl$_3$, TMS): δ 1.52–1.64 (m, 3H), 1.69–1.77 (m, 1H), 1.80–1.86 (m, 2H), 2.51–2.54 (m, 1H), 2.61–2.64 (m, 1H), 3.61–3.80 (m, 3H), 7.23–7.26 (m, 1H), 7.29–7.35 (m, 5H), 7.38–7.41 (m, 2H), 7.47–7.51 (m, 2H).MS (70 eV, EI): m/z (%): 276 (12), 275 (56) [M$^+$], 274 (39), 248 (10), 247 (13), 246 (31), 198 (21), 185 (11), 184 (73), 156 (16), 142 (12), 129 (19), 128 (49), 115 (38), 91 (100), 65 (18).

3ia

ethyl 3-(2-(phenylethynyl)piperidin-1-yl)propanoate: 50% isolated yield (eluent: hexane/EtOAc = 8/2). $^1$H NMR (500 MHz, CDCl$_3$, TMS): δ 1.26 (t, $J$ = 7.2 Hz, 3H), 1.51–1.75 (m, 4H), 1.79–1.89 (m, 2H), 2.50–2.63 (m, 4H), 2.85–2.89 (m, 2H), 3.81–3.85 (m, 1H), 4.14 (q, $J$ = 7.2 Hz, 2H), 7.28–7.32 (m, 3H), 7.42–7.46 (m, 2H). $^{13}$C–$^1$H NMR (125 MHz, CDCl$_3$, TMS): δ 14.4, 20.8, 25.9, 31.6, 32.9, 49.1, 51.8, 52.3, 60.4, 86.6, 87.1, 123.5, 128.0, 128.3, 131.8, 172.8. MS (70 eV, EI): m/z (%):285 (3)
3ja

3-(2-(phenylethynyl)piperidin-1-yl)propanenitrile: 48% isolated yield (eluent: hexane/EtOAc = 8/2). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.52–1.75 (m, 4H), 1.83–1.90 (m, 2H), 2.54 (t, $J = 7.2$ Hz, 2H), 2.57 (t, $J = 4.0$ Hz, 1H), 2.63–2.68 (m, 1H), 2.79–2.91 (m, 2H), 3.81 (t, $J = 4.0$ Hz, 1H), 7.28–7.33 (m, 3H), 7.41–7.45 (m, 2H). $^{13}$C–$^1$H NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 16.4, 20.6, 25.7, 31.5, 49.1, 51.7, 52.4, 86.5, 86.8, 119.1, 123.1, 128.3, 128.4, 131.8. MS (70 eV, EI): $m/z$ (%): 238 (4) [$M^+$], 237 (6), 209 (6), 199 (17), 198 (100), 184 (7), 170 (5), 156 (12), 155 (10), 142 (8), 141 (10), 129 (9), 128 (26), 127 (9), 116 (5), 115 (37), 102 (8), 91 (9), 77 (7), 70 (19), 55 (6), 54 (9). Anal. Calcd. for C$_{16}$H$_{18}$N$_2$: C, 80.63; H, 7.61; N, 11.75. Found: C, 80.35; H, 7.58; N, 11.67.

3ka

$N,N$-dimethyl-1-phenyldec-1-yn-3-amine: 53% isolated yield (eluent: hexane/EtOAc = 8/2). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 0.88 (t, $J = 7.2$ Hz, 3H), 1.28–1.74 (m, 12H), 2.32 (s, 6H), 3.51 (dd, $J = 8.5$ and 6.5 Hz, 1H), 7.27–7.32 (m, 3H), 7.42–7.46 (m, 2H). $^{13}$C–$^1$H NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 14.2, 22.8, 26.9, 29.4, 29.5, 32.0, 34.1, 41.6, 46.5, 58.4, 86.1, 87.2, 123.6, 128.0, 128.4, 131.9. MS (70 eV, EI): $m/z$ (%): 257 (0.1) [$M^+$], 159 (13), 158 (100), 129 (1), 128 (3), 127 (1), 116 (2), 115 (22), 102 (1), 91 (2), 89 (1), 84 (2), 55 (1). Anal. Calcd. for C$_{18}$H$_{27}$N·0.25H$_2$O: C, 82.54; H, 10.58; N, 5.35. Found: C, 82.28; H, 10.37; N, 5.16.
3la (CAS No. 153396-40-8)

N,N-diethyl-4-phenylbut-3-yn-2-amine: 27% isolated yield (eluent: hexane/EtOAc = 9/1). \(^1\)H NMR (500 MHz, CDCl$_3$, TMS): \(\delta\) 1.11 (t, \(J = 7.1\) Hz, 6H), 1.42 (d, \(J = 7.1\) Hz, 3H), 2.48–2.56 (m, 2H), 2.71–2.78 (m, 2H), 3.90 (q, \(J = 7.1\) Hz, 1H), 7.27–7.31 (m, 3H), 7.39–7.43 (m, 2H). \(^{13}\)C–\(^1\)H NMR (125 MHz, CDCl$_3$, TMS): \(\delta\) 13.8, 20.2, 44.8, 48.4, 84.2, 89.6, 123.6, 127.9, 128.3, 131.8. MS (70 eV, EI): \(m/\varepsilon\) (%): 201 (3) \([M^+]\), 187 (15), 186 (100), 130 (6), 129 (36), 128 (25), 127 (11), 115 (18), 103 (5), 77 (7), 58 (6), 56 (7).

3ma (CAS No. 131381-49-1)

N,N-dimethyl-1-(phenylethynyl)cyclohexan-1-amine: 64% isolated yield (eluent: hexane/EtOAc = 4/6). \(^1\)H NMR (500 MHz, CDCl$_3$, TMS): \(\delta\) 1.19–1.27 (m, 1H), 1.44–1.49 (m, 2H), 1.59–1.75 (m, 5H), 2.05–2.11 (m, 2H), 2.36 (s, 6H), 7.27–7.32 (m, 3H), 7.42–7.47 (m, 2H). \(^{13}\)C–\(^1\)H NMR (125 MHz, CDCl$_3$, TMS): \(\delta\) 23.2, 25.7, 36.5, 39.5, 59.9, 86.5, 89.5, 123.8, 127.9, 128.3, 131.9. MS (70 eV, EI): \(m/\varepsilon\) (%): 227 (20) \([M^+]\), 212 (31), 198 (11), 185 (16), 184 (100), 170 (17), 150 (13), 142 (10), 141 (30), 128 (11), 115 (24). Anal. Calcd. for C$_{16}$H$_{21}$N·0.1H$_2$O: C, 83.86; H, 9.32; N, 6.11. Found: C, 83.86; H, 8.88; N, 5.65.

3na

N-(3-chloropropyl)-N-ethyl-4-phenylbut-3-yn-2-amine: 28% isolated yield (eluent: hexane/EtOAc = 9/1). \(^1\)H NMR (500 MHz, CDCl$_3$, TMS): \(\delta\) 1.10 (t, \(J = 7.2\) Hz, 3H), 1.40 (d, \(J = 7.1\) Hz, 3H), 1.87–2.00 (m, 2H), 2.49–2.60 (m, 2H), 2.64–2.71 (m, 1H), 2.76–2.84 (m, 1H), 3.59–3.68 (m, 2H), 3.90 (q, \(J = 7.1\) Hz, 1H), 7.27–7.31 (m, 3H), 7.39–7.44 (m, 2H). \(^{13}\)C–\(^1\)H NMR (125 MHz, CDCl$_3$, TMS): \(\delta\) 14.0, 20.5, 31.7, 43.5, 45.7, 47.6, 48.7, 84.2, 89.5, 123.6, 128.0, 128.4, 131.8. MS (70 eV, EI): \(m/\varepsilon\) (%): 249 (3) \([M^+]\), 237 (5), 236 (34), 235 (17), 234 (100), 186 (17), 130 (11), 129 (78), 128 (36), 127
(15), 115 (16), 103 (5), 77 (8), 58 (11), 56 (5). Anal. Calcd. for C$_{15}$H$_{20}$ClN: C, 72.13; H, 8.07; N, 5.61. Found: C, 72.62; H, 7.82; N, 5.33.

3oa

*trans*-ethyl 1-methyl-6-(phenylethynyl)piperidine-2-carboxylate, *cis*-ethyl 1-methyl-6-(phenylethynyl)piperidine-2-carboxylate: *trans*-isomer: 39% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.29 (t, $J = 7.1$ Hz, 3H), 1.60–1.70 (m, 2H), 1.77–1.91 (m, 3H), 1.94–2.01 (m, 1H), 2.40 (s, 3H), 3.26 (dd, $J = 10.6$ and 3.0 Hz, 1H), 4.01 (t, $J = 3.6$ Hz, 1H), 4.22 (q, $J = 7.1$ Hz, 2H), 7.29–7.33 (m, 3H), 7.43–7.47 (m, 2H). $^{13}$C–$^1$H NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 14.4, 19.3, 30.0, 30.7, 41.8, 53.8, 60.9, 63.1, 86.1, 87.5, 123.2, 128.2, 128.4, 131.9, 173.8. MS (70 eV, El): m/z (%): 271 (2) [M$^+$], 199 (15), 198 (100), 170 (6), 169 (6), 167 (10), 142 (8), 141 (38), 128 (8), 115 (19), 102 (5), 96 (45), 91 (6), 85 (9). Anal. Calcd. for C$_{17}$H$_{21}$NO$_2$: C, 75.25; H, 7.80; N, 5.16. Found: C, 75.52; H, 7.45; N, 4.93. *cis*-isomer: 5% isolated yield (eluent: hexane/EtOAc = 6/4). $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.29 (t, $J = 7.1$ Hz, 3H), 1.35–1.47 (m, 1H), 1.70–1.80 (m, 1H), 1.84–1.94 (m, 3H), 2.00–2.08 (m, 1H), 2.50 (s, 3H), 2.77 (dd, $J = 11.5$ and 2.7 Hz, 1H), 3.02 (dd, $J = 11.1$ and 3.1 Hz, 1H), 4.24 (qd, $J = 7.1$ and 1.0 Hz, 2H), 7.27–7.30 (m, 3H), 7.39–7.42 (m, 2H). $^{13}$C–$^1$H NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 14.4, 23.5, 29.8, 32.7, 42.5, 56.9, 61.0, 69.0, 84.4, 89.4, 123.4, 128.2, 128.3, 131.7, 173.2. MS (70 eV, El): m/z (%): 271 (1) [M$^+$], 199 (16), 198 (100), 167 (9), 142 (7), 141 (36), 128 (7), 115 (17), 96 (35), 85 (6).

3pa

*trans*-3-(1-methyl-5-(phenylethynyl)pyrrolidin-2-yl)pyridine, *cis*-3-(1-methyl-5-(phenylethynyl)pyrrolidin-2-yl)pyridine, 3-(1-methyl-2-(phenylethynyl)pyrrolidin-2-yl)pyridine: 32% isolated yield in total (eluent: hexane/EtOAc = 4/6) (the ratio determined by $^1$H NMR: *trans*-isomer/*cis*-isomer/regio-isomer = 77/18/5). Anal. Calcd. for C$_{18}$H$_{18}$N$_2$: 0.1H$_2$O: C, 81.84; H, 6.94; N, 10.60. Found: C, 81.57; H, 6.80; N, 10.50. *trans*-isomer: $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 1.71–1.79 (m, 1H), 2.07 (ddddd, $J = 12.3$, 9.2, 3.4 and 1.2 Hz, 1H), 2.29 (s, 3H), 2.31–2.39
(m, 1H), 2.43–2.53 (m, 1H), 3.63 (dd, J = 8.8 and 7.1 Hz, 1H), 4.27 (d, J = 6.5 Hz, 1H), 7.25–7.36 (m, 4H), 7.44–7.49 (m, 2H), 7.70 (dt, J = 7.8 and 1.8 Hz, 1H), 8.51 (dd, J = 4.8 and 1.7 Hz, 1H), 8.57 (d, J = 1.9 Hz, 1H). \(^{13}\)C–\(^{1}\)H NMR (125 MHz, CDCl\(_3\), TMS): \(\delta\) 31.0, 33.9, 36.5, 57.0, 64.9, 86.5, 87.5, 123.3, 123.7, 128.1, 128.4, 131.9, 135.1, 139.3, 148.8, 149.7. MS (70 eV, EI): \(m/z\) (%): 263 (10), 262 (60) [M\(^+\)], 261 (100), 234 (27), 233 (42), 219 (12), 193 (12), 185 (27), 184 (37), 156 (13), 155 (23), 142 (26), 129 (32), 128 (16), 119 (10), 118 (18), 115 (21). cis-isomer: \(^{1}\)H NMR (500 MHz, CDCl\(_3\), TMS): \(\delta\) 1.77–1.87 (m, 1H), 2.10–2.29 (m, 3H), 2.30 (s, 3H), 3.22–3.27 (m, 1H), 3.31–3.37 (m, 1H), 7.26–7.34 (m, 4H), 7.45–7.49 (m, 2H), 7.79 (dt, J = 7.8 and 2.0 Hz, 1H), 8.52 (dd, J = 4.8 and 1.7 Hz, 1H), 8.56 (d, J = 1.9 Hz, 1H). \(^{13}\)C–\(^{1}\)H NMR (125 MHz, CDCl\(_3\), TMS): \(\delta\) 73.69, 100, 84.4, 89.2, 90.7, 113.8, 123.6, 128.0, 128.3, 131.8, 158.2, 162.2, 204.6. MS (70 eV, EI): \(m/z\) (%): 262 (12) [M\(^+\)], 261 (9), 233 (10), 185 (18), 184 (100), 115 (6).

\[\text{3qa}\]

**4-(2-(phenylethynyl)pyrrolidin-1-yl)-1-(2,4,6-trimethoxyphenyl)butan-1-one**: 12% isolated yield (eluent: EtOAc). \(^{1}\)H NMR (500 MHz, CDCl\(_3\), TMS): \(\delta\) 1.75–2.04 (m, 5H), 2.12–2.23 (m, 1H), 2.43–2.55 (m, 2H), 2.73–2.91 (m, 4H), 3.54–3.61 (m, 1H), 3.74 (s, 6H), 3.80 (s, 3H), 6.07 (s, 2H), 7.26–7.30 (m, 3H), 7.39–7.43 (m, 2H). \(^{13}\)C–\(^{1}\)H NMR (125 MHz, CDCl\(_3\), TMS): \(\delta\) 22.3, 23.2, 32.0, 43.2, 51.9, 53.2, 55.3, 55.5, 55.9, 84.4, 89.2, 90.7, 113.8, 123.6, 128.0, 128.3, 131.8, 158.2, 162.2, 204.6. MS (70 eV, EI): \(m/z\) (%): 407 (3) [M\(^+\)], 376 (16), 213 (17), 212 (100), 210 (12), 198 (23), 197 (40), 196 (73), 195 (75), 170 (34), 169 (25), 156 (10), 153 (10), 152 (12), 137 (11), 129 (10), 128 (22), 120 (17), 115 (17), 102 (12). Anal. Calcd. for C\(_{23}\)H\(_{29}\)NO\(_4\): C, 73.69; H, 7.17; N, 3.44. Found: C, 73.33; H, 6.68; N, 3.21.
3ra

1-(2-((4-chlorophenyl)(phenyl)methoxy)ethyl)-2-(phenylethynyl)piperidine: 17% isolated yield (eluent: hexane/EtOAc = 8/2 (1st), toluene/EtOAc = 9/1 (2nd)). \( ^1H \) NMR (500 MHz, CDCl\(_3\), TMS): \( \delta \) 1.50–1.76 (m, 4H), 1.81–1.88 (m, 2H), 2.54–2.70 (m, 2H), 2.79–2.89 (m, 2H), 3.56–3.66 (m, 2H), 3.82–3.86 (m, 1H), 5.37 (s, 1H), 7.22–7.35 (m, 12H), 7.41–7.46 (m, 2H). \( ^13C\)–\{\( ^1H \)\} NMR (125 MHz, CDCl\(_3\), TMS): \( \delta \) 20.7, 25.8, 31.5, 49.8, 52.8, 55.8, 67.3, 83.1, 86.4, 87.4, 123.5, 127.0, 127.6, 127.9, 128.2, 128.4, 128.45, 131.7, 133.1, 141.0, 141.9. MS (70 eV, EI): \( m/z \) (%): 431 (7), 430 (6), 429 (19) \([M^+\]\), 229 (17), 228 (100), 212 (13), 210 (6), 202 (6), 201 (37), 200 (7), 185 (8), 184 (7), 182 (8), 170 (6), 169 (7), 168 (9), 167 (17), 166 (19), 165 (20), 122 (16), 91 (23), 79 (5). Anal. Calcd. for C\(_{28}\)H\(_{28}\)ClNO: C, 78.21; H, 6.56; N, 3.26. Found: C, 78.20; H, 6.46; N, 3.27.

3sa

(S\(^*\))-N,N-dimethyl-3-phenyl-1-(trans-2-phenylcyclopropyl)prop-2-yn-1-amine, \( (R^*\))-N,N-dimethyl-3-phenyl-1-(trans-2-phenylcyclopropyl)prop-2-yn-1-amine: major diastereoisomer: 25% isolated yield (eluent: hexane/EtOAc = 9/1). \( ^1H \) NMR (500 MHz, CDCl\(_3\), TMS): \( \delta \) 1.03–1.07 (m, 1H), 1.25–1.30 (m, 1H), 1.44–1.50 (m, 1H), 1.97–2.00 (m, 1H), 2.40 (s, 6H), 3.77 (d, \( J = 5.2 \) Hz, 1H), 7.06–7.20 (m, 3H), 7.24–7.28 (m, 2H), 7.30–7.36 (m, 3H), 7.44–7.48 (m, 2H). \( ^13C\)–\{\( ^1H \)\} NMR (125 MHz, CDCl\(_3\), TMS): \( \delta \) 14.3, 20.5, 25.0, 42.1, 60.9, 84.1, 87.0, 123.2, 125.7, 126.1, 128.3, 128.43, 128.45, 132.0, 142.7. MS (70 eV, EI): \( m/z \) (%): 275 (10) \([M^+\]\), 274 (16), 215 (17), 171 (45), 170 (46), 159 (14), 158 (100), 134 (25), 115 (54), 71 (20). Anal. Calcd. for C\(_{20}\)H\(_{21}\)N\( \cdot 0.25\)H\(_2\)O: C, 85.82; H, 7.74; N, 5.00. Found: C, 86.11; H, 7.82; N, 4.66. minor diastereoisomer: 8% isolated yield (eluent: hexane/EtOAc = 9/1). \( ^1H \) NMR (500 MHz, CDCl\(_3\), TMS): \( \delta \) 0.97–1.01 (m, 1H), 1.09–1.13 (m, 1H), 1.39–1.44 (m, 1H), 2.11–2.15 (m, 1H), 2.39 (s, 6H), 3.83 (d, \( J = 5.0 \) Hz, 1H), 7.12–7.17 (m, 3H), 7.25–7.28 (m, 2H), 7.30–7.34 (m, 3H), 7.43–7.48 (m, 2H). \( ^13C\)–\{\( ^1H \)\} NMR (125 MHz, CDCl\(_3\), TMS): \( \delta \) 12.7, 21.2, 25.1, 42.0,
61.1, 83.7, 87.2, 122.8, 123.2, 125.8, 126.3, 128.3, 128.5, 132.0, 142.5. MS (70 eV, EI): m/z (%): 275 (3) [M+], 274 (3), 215 (17), 171 (42), 170 (33), 159 (13), 158 (100), 134 (30), 115 (50), 71 (49).

3ta

**ethyl 1-(ethyl(4-phenylbut-3-yn-2-yl)amino)cyclopropane-1-carboxylate:** 6% isolated yield (eluent: hexane/EtOAc = 19/1 (1st), dichloromethane (2nd)). \(^1\)H NMR (500 MHz, CDCl₃, TMS): \(\delta\) 1.13 (t, \(J = 7.3\) Hz, 3H), 1.09–1.21 (m, 2H), 1.23 (t, \(J = 7.3\) Hz, 3H), 1.28–1.40 (m, 2H), 1.42 (d, \(J = 6.9\) Hz, 3H), 2.98–3.15 (m, 2H), 4.07–4.18 (m, 3H), 7.26–7.30 (m, 3H), 7.38–7.40 (m, 2H). \(^13\)C–\(^1\)H NMR (125 MHz, CDCl₃, TMS): \(\delta\) 14.3, 16.2, 18.8, 19.5, 23.1, 44.7, 46.1, 50.5, 60.5, 83.5, 91.7, 123.8, 127.6, 128.2, 131.4, 175.4. MS (70 eV, EI): m/z (%): 285 (1) [M+], 270 (32), 256 (10), 212 (44), 170 (51), 156 (13), 142 (13), 141 (12), 129 (70), 128 (100), 127 (40), 115 (23), 103 (10), 84 (18), 82 (13), 77 (16), 73 (16), 70 (13), 56 (53), 55 (19), 54 (23).

3ua

**4-methyl-3-(phenylethynyl)morpholine:** 11% GC yield. MS (70 eV, EI): m/z (%): 201 (60) [M+], 173 (15), 172 (19), 171 (15), 170 (90), 156 (14), 144 (20), 143 (34), 142 (100), 129 (13), 128 (46), 127 (30), 116 (35), 115 (70), 102 (35), 99 (17), 98 (37), 77 (10), 76 (13), 63 (13), 51 (12).
### Supplementary Tables

**Supplementary Table 1.** Comparison of this work with previous main reports on oxidative α-methylene C–H functionalisations of tertiary amines except for benzylic amines, N-protected amines, and symmetric amines.

| Reference | Nucleophile or Reaction | Demonstrated tertiary amine substrate type applicable to α-methylene selective functionalization (number of the substrates) | α-Methylene selectivity | Reaction intermediate |
|-----------|-------------------------|-----------------------------------------------------------------------------------------------------------------|------------------------|----------------------|
|           |                         |                                                                                                                | vs Methyl              | vs Methylene         | vs Methine          |
| this work | alkyl                   | linear, cyclic, unsymmetrical (17)                                                                             | methylene              | cyclic methylene     | methylene          |
| S12       | silylalkyne              | cyclic (4)                                                                                                      | cyclic methylene       | cyclic methylene     | —                   |
| S13       | alkyne                  | linear, cyclic (3) (low yields: 8–16%)                                                                          | cyclic methylene       | —                    | methylene           |
| S14       | iodoalkyne              | cyclic (1)                                                                                                      | methyl                 | cyclic methylene     | —                   |
| S15       | dicyanobenzene          | cyclic (4)                                                                                                      | —                      | cyclic methylene     | methylene           |
| S16       | cyclization             | cyclic (4) (minor α-methine oxidation)                                                                         | —                      | cyclic methylene     | methylene           |
| S17       | aryl isocyanate         | cyclic (3) (minor α-methyl oxidation)                                                                          | cyclic methylene       | —                    | methylene           |
| S18       | ketone                  | cyclic (1)                                                                                                      | cyclic methylene       | —                    | —                   |
| S19       | cyclization             | cyclic, unsymmetrical (6)                                                                                       | methyl                 | cyclic methylene     | methylene           |
| S20       | bromoalkene             | cyclic (4)                                                                                                      | cyclic methylene       | both                 | —                   |
| S21       | bromobenzene            | cyclic (1) (exceptional substrate)                                                                            | both                   | —                    | methylene           |
| S22       | alkene                  | linear, cyclic, unsymmetrical (20) (Curtin–Hammet principle)                                                   | methylene              | both                 | methine             |
| S23       | NaCN                    | linear, cyclic (12) (minor α- linear methylene oxidation)                                                        | both                   | cyclic methylene     | methylene           |
| S16       | NaCN                    | cyclic (3) (minor α-methyl oxidation)                                                                           | cyclic methylene       | cyclic methylene     | —                   |
| S24       | NaCN                    | linear, cyclic, unsymmetrical (8) (minor α-methyl, linear methylene oxidation)                                 | cyclic methylene       | cyclic methylene     | methylene           |
| S25       | oxygenation             | cyclic, unsymmetrical (3)                                                                                      | cyclic methylene       | —                    | —                   |
| S26       | oxygenation             | cyclic, unsymmetrical (20)                                                                                     | cyclic methylene       | cyclic methylene     | —                   |
| S27       | oxygenation             | linear, cyclic (11)                                                                                            | methylene              | cyclic methylene     | —                   |
| S13       | oxygenation             | linear, cyclic (7)                                                                                            | methylene              | cyclic methylene     | —                   |
Supplementary Table 2. The effect that different supports and Zn cocatalysts have on the yield of the α-methylene-selective alkynylation of 1-methylpiperidine (1a) with phenylacetylene (2a). a

![Chemical structure and reaction scheme]

| Entry | Catalyst | Cocatalyst | Yield [%] | 3aa | 4aa | 5a |
|-------|----------|------------|-----------|-----|-----|----|
| 1     | Au/HAP   | ZnBr\(_2\) | 57        | <1  | <1  | <1 |
| 2     | Au/HAP   | ZnF\(_2\)  | 23        | <1  | <1  | <1 |
| 3     | Au/HAP   | Zn(OAc)\(_2\)
\(2\)H\(_2\)O | 12        | <1  | <1  | <1 |
| 4     | Au/HAP   | Zn(acac)\(_2\) | 7         | <1  | <1  | <1 |
| 5     | Au/HAP   | ZnI\(_2\)  | 1         | <1  | <1  | <1 |
| 6     | Au/ZrO\(_2\) | ZnBr\(_2\) | 40        | <1  | <1  | <1 |
| 7     | Au/CeO\(_2\) | ZnBr\(_2\) | 36        | <1  | <1  | <1 |
| 8     | Au/LDH   | ZnBr\(_2\) | <1        | <1  | <1  | <1 |
| 9     | —        | —          | <1        | <1  | <1  | <1 |

aReaction conditions: 1a (0.5 mmol), 2a (0.5 mmol), Au/support (1.5 mol%), Zn cocatalyst (10 mol%), PhCF\(_3\) (2 mL), 95 °C, \(\text{O}_2\) (1 atm), 20 h. Yields were determined by gas chromatography analysis using biphenyl as an internal standard. —: none.
Supplementary Table 3. The effect that different solvents have on the yield of the α-methylene-selective alkylation of 1-methylpiperidine (1a) with phenylacetylene (2a).a

![Chemical structure](attachment:ChemStructure.png)

| Entry | Solvent   | Yield [%] |
|-------|-----------|-----------|
|       |           | 3aa | 4aa | 5a |
| 1     | PhCF₃     | 73  | <1  | <1 |
| 2     | Toluene   | 83  | <1  | <1 |
| 3     | PhCl      | 72  | <1  | <1 |
| 4     | Mesitylene| 68  | <1  | <1 |
| 5     | 1,4-Dioxane| 68 | <1  | <1 |
| 6     | BuOAc     | 53  | <1  | <1 |
| 7     | DMF       | 8   | <1  | 4  |
| 8     | DMA       | 6   | <1  | 4  |

*aReaction conditions: 1a (1 mmol), 2a (0.5 mmol), Au/HAP (Au: 1.5 mol%), ZnBr₂ (10 mol%), solvent (2 mL), 95 °C, O₂ (1 atm), 20 h. Yields were determined by gas chromatography (GC) analysis using biphenyl as an internal standard. BuOAc: butyl acetate; DMF: N,N-dimethylformamide; DMA: N,N-dimethylacetamide.
**Supplementary Table 4.** Catalyst reuse tests conducted on the α-methylene-selective alkynylation of 1-methylpiperidine (1a) with phenylacetylene (2a).a

![Chemical structure](image)

| Entry | Catalyst          | Yield [%] |   |   |
|-------|-------------------|-----------|---|---|
|       |                   | 3aa       | 4aa | 5a |
| 1     | Fresh             | 82        | <1  | <1 |
| 2     | 1st reuse         | 82        | <1  | <1 |
| 3     | 2nd reuse         | 78        | <1  | <1 |

*aReaction conditions: 1a (1 mmol), 2a (0.5 mmol), Au/HAP (100 mg, Au: 1.5 mol%), ZnBr₂ (10 mol%), toluene (2 mL), 95 °C, O₂ (1 atm), 24 h. Yields were determined by gas chromatography analysis using biphenyl as internal standard. The average values calculated over 8, 5, and 3 runs are reported for entries 1, 2, and 3, respectively.
Supplementary Table 5. Optimization of reaction conditions for α-methine alkynylation of N,N-dimethylcyclohexylamine (1m) with 2a.

| Entry | 2a [eq.] | ZnBr₂ [mol%] | MS-4A [mg] | Conv. of 1m [%] | Yield [%] | 3ma | 4ma | 5a | 6a |
|-------|----------|---------------|-------------|-----------------|------------|-----|-----|----|----|
| 1     | 2        | 20            | 0           | 89              | 12         | 1   | 3   | 19 |
| 2     | 4        | 20            | 0           | 77              | 16         | 1   | 1   | 11 |
| 3     | 6        | 20            | 0           | 87              | 23         | 1   | 1   | 7  |
| 4     | 6        | 40            | 0           | 99              | 35         | <1  | <1  | 10 |
| 5     | 6        | 20            | 100         | 72              | 28         | 1   | <1  | <1 |
| 6     | 6        | 20            | 200         | 84              | 52         | 1   | <1  | <1 |
| 7     | 6        | 20            | 300         | 97              | 84         | <1  | <1  | <1 |
| 8     | 6        | 40            | 300         | 73              | 39         | <1  | 1   | <1 |

*aReaction conditions: 1m (0.3 mmol), 2a (0.6, 1.2, or 1.8 mmol), Au/HAP (100 mg, Au: 2.5 mol%), ZnBr₂ (20 or 40 mol%), MS-4A (0, 100, 200, or 300 mg), toluene (2 mL), 95 °C, O₂ (1 atm), 24 h. Conversions and yields were determined by gas chromatography analysis using biphenyl as internal standard. MS-4A = molecular sieves 4A.*
**Supplementary Table 6.** Comparison of 1a conversions with/without 2a and/or ZnBr₂.a

![Chemical reaction diagram](image)

| Entry | 2a [eq.] | ZnBr₂ [mol%] | Conv. of 1a [%] | Yield [%] |
|-------|----------|--------------|----------------|-----------|
| 1     | 0        | 0            | 18             | <1        |
| 2     | 0        | 10           | 26             | <1        |
| 3     | 1        | 0            | 36             | <1        |
| 4     | 1        | 10           | 77             | <1        |

*aReaction conditions: 1a (0.5 mmol), 2a (0 or 0.5 mmol), Au/HAP (Au: 1.5 mol%), ZnBr₂ (0 or 10 mol%), PhCF₃ (2 mL), 95 °C, O₂ (1 atm), 20 h. Conversions and yields were determined by gas chromatography using biphenyl as an internal standard.*
Supplementary Figures

**Path A**
\[
\begin{align*}
\text{R}_1\text{N}^+\text{R}_3 & \xrightarrow{\text{SET}} \text{R}_1\text{N}^+\text{R}_3^- \xrightarrow{-\text{H}^+} \text{R}_1\text{N}^+\text{R}_3^- \xrightarrow{\text{SET}} \text{R}_1\text{N}^+\text{R}_3
\end{align*}
\]

**Path B**
\[
\begin{align*}
\text{R}_1\text{N}^+\text{R}_3 & \xrightarrow{\text{HAT}} \text{R}_1\text{N}^+\text{R}_3^- \xrightarrow{\text{SET}} \text{R}_1\text{N}^+\text{R}_3
\end{align*}
\]

**Path C**
\[
\begin{align*}
\text{R}_1\text{N}^+\text{R}_3 & \xrightarrow{\text{SET}} \text{R}_1\text{N}^+\text{R}_3^- \xrightarrow{\text{HAT}} \text{R}_1\text{N}^+\text{R}_3
\end{align*}
\]

**Path D**
\[
\begin{align*}
\text{R}_1\text{N}^+\text{R}_3 & \xrightarrow{\text{Oxidation}} \text{R}_1\text{N}^+\text{R}_3^- \xrightarrow{\text{Polonovski–Potier Reaction}} \text{R}_1\text{N}^+\text{R}_3
\end{align*}
\]

**Path E**
\[
\begin{align*}
\text{R}_1\text{N}^+\text{R}_3 & \xrightarrow{\beta\text{-Hydride Elimination}} \text{R}_1\text{N}^+\text{R}_3
\end{align*}
\]

**Supplementary Fig. 1** Proposed paths of amine oxidation to iminium cations based on previous reports; path A: single-electron-transfer (SET)/deprotonation/SET, path B: hydrogen-atom-transfer (HAT)/SET, path C: SET/HAT, path D: amine oxidation to amine oxides followed by Polonovski–Potier reaction, and path E: β-hydride elimination.
Supplementary Fig. 2 TEM images and nanoparticle size distributions of (a) Au/HAP (mean diameter: 5.1 nm, $\sigma = 1.7$ nm) and (b) Au/TiO$_2$ (mean diameter: 4.3 nm, $\sigma = 1.0$ nm). The size distributions were determined using 200 particles.
**Supplementary Fig. 3** X-ray photoelectron spectra around Au 4f components: (a) Au/HAP, (b) Au/ZnO, (c) Au/Al₂O₃, and (d) Au/ZrO₂. Black lines and blue broken lines indicate the deconvoluted signals and the sum of these lines. Red dotted lines indicate the data plots. The binding energies were calibrated by using the C Is signal at 284.8 eV.
**Supplementary Fig. 3 (continued)** X-ray photoelectron spectra around Au 4f components: (e) Au/TiO$_2$, (f) Au/CeO$_2$, and (g) Au/LDH. Black lines and blue broken lines indicate the deconvoluted signals and the sum of these lines. Red dotted lines indicate the data plots. The binding energies were calibrated by using the C 1s signal at 284.8 eV.
Supplementary Fig. 4 Influence of the mid-reaction removal by hot filtration of catalyst Au/HAP on the profile of the reaction of 1-methylpiperidine (1a) with phenylacetylene (2a) to produce 1-methyl-2-(phenylethynyl)piperidine (3aa) (verification of heterogeneous catalysis). Reaction conditions: 1a (1 mmol), 2a (0.5 mmol), Au/HAP (100 mg), ZnBr$_2$ (10 mol%), toluene (2 mL), 95 °C, O$_2$ (1 atm). Yields were determined by gas chromatography analysis using biphenyl as internal standard.

Supplementary Fig. 5 Reaction profiles obtained for catalyst reuse tests. Reaction conditions: 1-methylpiperidine (1a, 1 mmol), phenylacetylene (2a, 0.5 mmol), Au/HAP (100 mg), ZnBr$_2$ (10 mol%), toluene (2 mL), 95 °C, O$_2$ (1 atm). Yields were determined by gas chromatography analysis using biphenyl as internal standard.
Supplementary Fig. 6 FT-IR spectra of (a) Au/HAP retrieved after the 1st use, and (b) fresh Au/HAP.

Supplementary Fig. 7 X-ray diffraction (XRD) patterns of (a) Au/HAP retrieved after the 1st use, and (b) fresh Au/HAP.
Supplementary Fig. 8 TEM images and nanoparticle size distributions of (a) Au/HAP retrieved after the 1st use (mean diameter: 9.0 nm, $\sigma = 3.2$ nm) and (b) Au/HAP retrieved after the 3rd use (mean diameter: 10.5 nm, $\sigma = 4.3$ nm). The size distributions were determined using 200 particles.
Supplementary Fig. 9 X-ray photoelectron spectra of Au/HAP retrieved after the 1st use around the Au 4f region. Black lines and blue broken lines indicate the deconvoluted signals and the sum of these lines. Red dotted lines indicate the data plots. The binding energies were calibrated by using the C 1s signal at 284.8 eV.

Supplementary Fig. 10 Limitation of amine substrate scope. Yields were determined by GC or 1H NMR analysis. Reaction conditions: 1 (1 mmol), 2a (0.5 mmol), Au/HAP (100 mg, Au: 1.5 mol%), ZnBr₂ (11 mg, 10 mol%), PhCF₃ (2 mL), 95 °C, O₂ (1 atm), 24 h. Toluene (2 mL). 1 (0.3 mmol), 2a (0.6 mmol), Au/HAP (160 mg, 4 mol%), ZnBr₂ (13 mg, 20 mol%). 2a (1.8 mmol), MS-4A (300 mg).
Supplementary Fig. 11 The effect of a radical scavenger (1 mmol, 1 equivalent with respect to 1a) on the α-methylene-selective alkynylation of 1-methylpiperidine with phenylacetylene. The reaction conditions were the same as those described in Supplementary Fig. 4. GC-determined yields of 1-methyl-2-(phenylethynyl)piperidine (3aa) are shown in the vertical axis. BHT: 2,6-di-tert-butyl-4-methylphenol.

Supplementary Fig. 12 Ring-opening reactions of radical clocks (a) 1s or (b) 1t when HAT or SET of the amines occurs, respectively.
Supplementary Fig. 13 DFT scan calculation using Gaussian about ring-opening reactions of the corresponding (a) carbon-centered radical species and (b) iminium cation species derived from 1s, respectively.
Reactions to obtain an $\alpha$-methylene alkynylated product (3ua) with 2a using the present hybrid catalytic system comprising Au/HAP and ZnBr$_2$ starting from (a) 4-methylmorpholine (1u) or (b) 4-methylmorpholine $N$-oxide (1u'). Reaction conditions are indicated in the figure, and the yields were determined by GC using biphenyl as internal standard.
Supplementary Fig. 15 GC-MS patterns obtained by selected ion monitoring mode for m/z = 96–103 to detect the deuterium scrambling using several substrates under the reaction conditions indicated in Fig. 2b: (a) 1a-d2, (b) 1a-d2 after the reaction only with Au/HAP, (c) 1a, (d) 1a after the reaction with NaBD4 and Au/HAP, and (e) 1a after the reaction with D2O and Au/HAP.
**Supplementary Fig. 16** $^1$H NMR spectra to detect the deuterium scrambling using several substrates and toluene-$d_8$ solvent under the reaction conditions indicated in Fig. 2b: (a) the spectra of $\text{1a-d}_2$ before/after the reaction only with Au/HAP, (b) the spectra of $\text{1a}$ before/after the reaction with NaBD$_4$ and Au/HAP, and (c) the spectra of $\text{1a}$ before/after the reaction with D$_2$O and Au/HAP, recorded at $\sim$25 °C in toluene-$d_8$ at 500 MHz.
Supplementary Fig. 17 ¹³C NMR spectra to detect the deuterium scrambling using several substrates and toluene-⁶ solvent under the reaction conditions indicated in Fig. 2b: (a) the spectra of 1a-d₂ before/after the reaction only with Au/HAP, (b) the spectra of 1a before/after the reaction with NaBD₄ and Au/HAP, and (c) the spectra of 1a before/after the reaction with D₂O and Au/HAP, recorded at ~25 °C in toluene-⁶ at 126 MHz.
Supplementary Fig. 18 α-Alkynylation of 1a with 2a in the presence of Au/HAP without any cocatalysts under an Ar atmosphere. Reaction conditions are indicated in the figure, and the yields were determined by GC using biphenyl as internal standard.

Supplementary Fig. 19 The dependence of the initial condensation of 1a (0.1 mM, 0.15 mM, 0.2 mM, or 0.25 mM) on 3aa production rate using the present hybrid catalytic system comprising Au/HAP and ZnBr₂. Reaction conditions: 1a (0.2, 0.3, 0.4, or 0.5 mmol), 2a (1 mmol), Au/HAP (0.8 mol% to 2a), ZnBr₂ (5 mol% to 2a), PhCF₃ (2 mL), 95 °C, open air (1 atm). Yields were determined by gas chromatography analysis using biphenyl as an internal standard. The data plots are average values of 2 runs, and the error bars calculated from 2 runs show the maximum/minimum values of the respective yields.
Supplementary Fig. 20 The dependence of the initial condensation of 2a (0.1 mM, 0.15 mM, 0.2 mM, or 0.25 mM) on 3aa production rate using the present hybrid catalytic system comprising Au/HAP and ZnBr₂. Reaction conditions: 1a (1 mmol), 2a (0.2, 0.3, 0.4, or 0.5 mmol), Au/HAP (0.8 mol% to 1a), ZnBr₂ (5 mol% to 1a), PhCF₃ (2 mL), 95 °C, open air (1 atm). Yields were determined by gas chromatography analysis using biphenyl as an internal standard. The data plots are average values of 2 runs, and the error bars calculated from 2 runs show the maximum/minimum values of the respective yields.
The dependence of O\textsubscript{2} partial pressure (0.1 atm, 0.2 atm, 0.3 atm, 0.5 atm, 0.8 atm, or 1 atm) on 3aa production rate from 1a and 2a using the present hybrid catalytic system comprising Au/HAP and ZnBr\textsubscript{2}. Reaction conditions: 1a (0.5 mmol), 2a (0.5 mmol), Au/HAP (1.5 mol%), ZnBr\textsubscript{2} (10 mol%), PhCF\textsubscript{3} (2 mL), 95 °C. Yields were determined by gas chromatography analysis using biphenyl as an internal standard.

**Supplementary Fig. 21**
**Supplementary Fig. 22** Kinetic isotope effect on α-alkynylation with 2a in the presence of Au/HAP and ZnBr₂ using 1a or 1a-\(d_4\) as an amine substrate, respectively. Reaction conditions are indicated in Fig. 2e, and the yields were determined by GC using biphenyl as internal standard.

**Supplementary Fig. 23** Kinetic isotope effect investigation on α-alkynylation of 1a in the presence of Au/HAP and ZnBr₂ using 2a or 2a-\(d\) as an alkyne substrate, respectively. Reaction conditions are indicated in this figure, and the yields were determined by GC using biphenyl as internal standard. GC-MS spectra were recorded in scan mode, and deuteriation ratios of each sampling were approximately estimated from the relative intensity of \(m/z = 103\) based on those of 2a and 2a-\(d\) (D: 98%) and from the relative intensity of \(m/z = 200\) based on those of 3aa and 3aa-\(d_2\) (D: 13% and 76%).
**Supplementary Fig. 24** GC-MS patterns of 2a obtained by scan mode for m/z = 101–105 to detect the deuterium scrambling using 2a-d as an alkyne substrate under the reaction conditions indicated in Supplementary Fig. 23: (a) 2a and (b) 2a-d (D: 98% determined by $^1$H NMR). (c) 10 min, (d) 20 min, (e) 30 min, and (f) 40 min after the reaction started.
Supplementary Fig. 25 GC-MS patterns of 3aa obtained by scan mode for m/z = 197–203 to detect the deuterium scrambling using 2a-d as an alkyne substrate or D₂O as an additive under the reaction conditions indicated in Supplementary Fig. 23 or 28: (a) 3aa, (b) 3aa-β-d₂ (D: 13% determined by ¹H NMR) isolated 24 h after the reaction using 2a-d as an alkyne substrate, (c) 3aa-β-d₂ (D: 76% determined by ¹H NMR) isolated 25 h after the reaction using D₂O as an additive. (d) 10 min, (e) 20 min, (f) 30 min, and (g) 40 min after the reaction using 2a-d as an alkyne substrate started.
Supplementary Fig. 26 GC-MS patterns of 1a obtained by selected ion monitoring mode for m/z = 97–103 to detect the deuterium scrambling using 2a-d as an alkyne substrate under the reaction conditions indicated in Supplementary Fig. 23: (a) 1a, (b) 10 min, (c) 20 min, (d) 30 min, and (e) 40 min after the reaction started.
Supplementary Fig. 27 Proposed mechanism of the corresponding iminium cations and enamine formation by aerobic oxidation of 1a in the presence of Au nanoparticle catalysts.
Supplementary Fig. 28 (a) β-Deuterated propargylic amine synthesis. Reaction conditions are indicated in this figure, and the yield was determined by isolation. The deuteration ratio was determined by $^1$H NMR, (b) $^1$H NMR, (c) $^2$H NMR, and (d) $^{13}$C NMR spectra of the isolated 3aa-β-$d_2$. recorded at ~25 °C in CDCl$_3$ at 500 MHz, 77 MHz, and 126 MHz, respectively.
**Supplementary Fig. 29** Kinetic isotope effect investigation on α-alkynylation of 1a in the presence of Au/HAP and ZnBr₂ using 2a as an alkyne substrate with H₂O or D₂O, respectively. Reaction conditions are indicated in this figure, and the yields were determined by GC using biphenyl as internal standard. GC-MS spectra were recorded in scan or selected ion monitoring mode, and deuteration ratios of each sampling were approximately estimated from the relative intensity of m/z = 103 or 200.
Supplementary Fig. 30 Kinetic isotope effect on α-alkynylation with 2a in the presence of Au/HAP and ZnBr₂ using 1a-d₂ as an amine substrate. Reaction conditions are indicated in the figure, and the isolated yield of 3aa is shown (GC yield determined using biphenyl as internal standard is also 58%). The shown kinetic isotope effect was calculated from the ¹H NMR spectrum of isolated 3aa at the lower side, recorded at ~25 °C in CDCl₃ at 500 MHz.
**The present α-alkynylation of tertiary amines**

\[
\text{N} + \text{Ph} = \text{H} \rightarrow \text{N} = \text{Ph} + \text{N} = \text{Ph} \quad r.r. >99\% : <1\%
\]

\[
\Delta G^\circ = 9.73 \text{ kcal/mol} \\
K = 7.3 \times 10^{-8} \\
>99\% : <1\%
\]

**DFT calculation**

\[
\Delta G^\circ \text{ vs } \quad \Delta G^\circ \text{ vs }
\]

\[
\text{N} + \text{Ph} = \text{H} \rightarrow \text{N} = \text{Ph} + \text{N} = \text{Ph} \quad r.r. 96\% : 4\%
\]

\[
\Delta G^\circ = 1.45 \text{ kcal/mol} \\
K = 8.6 \times 10^{-2} \\
96\% : 4\%
\]

\[
\text{N} + \text{Ph} = \text{H} \rightarrow \text{N} = \text{Ph} + \text{N} = \text{Ph} \quad r.r. >99\% : <1\%
\]

\[
\Delta G^\circ = 5.71 \text{ kcal/mol} \\
K = 1.5 \times 10^{4} \\
<1\% : >99\%
\]

\[
\text{N} + \text{Ph} = \text{H} \rightarrow \text{N} = \text{Ph} + \text{N} = \text{Ph} \quad r.r. >99\% : <1\%
\]

\[
\Delta G^\circ = 0.10 \text{ kcal/mol} \\
K = 1.2 \\
63\% : 37\%
\]

_Supplementary Fig. 31_ Comparison of regioselectivity to Au/HAP and ZnBr\(_2\)-catalyzed α-alkynylation of several selected tertiary amines (shown in Table 3) with Gibbs free energy difference given by DFT calculation between iminium cations derived from dehydrogenation at the cyclic methylene positions and the counterparts. Equilibrium constants (\(K\)) were calculated from \(\Delta G^\circ = -RT\ln K (T = 298.15 \text{ K})\). The number of \(α\)-C–H bonds of amines was taken into consideration on the shown ratios of iminium cations based on DFT calculation.
Supplementary Fig. 32 Optimized structures of (a) Au\textsubscript{20} cluster with no charge, the corresponding iminium cation of 1a, and (b) Au\textsubscript{20} cluster adsorbed by the corresponding iminium cation of 1a based on DFT calculation. The Au\textsubscript{20} cluster model was constructed by referring to our previous report\textsuperscript{S28}. Although three types of initial adsorbed structures were investigated (adsorption site A, B, or C of Au\textsubscript{20} cluster shown in this figure (a)), all the structures converged to the adsorbed structure at the site C as shown in this figure (b). The adsorption energy was calculated based on Gibbs energies of Au\textsubscript{20} cluster, the corresponding iminium cation of 1a, and Au\textsubscript{20} cluster adsorbed by the corresponding iminium cation of 1a in this figure.
Supplementary Fig. 33. $^1$H NMR and $^{13}$C NMR of 3aa, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 34. $^1$H NMR and $^{13}$C NMR of 3ab, recorded at $\sim$25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 35. $^1$H NMR and $^{13}$C NMR of 3ac, recorded at $\sim$25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 36. $^1$H NMR and $^{13}$C NMR of 3ad, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 37. $^1$H NMR and $^{13}$C NMR of 3ae, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 38. $^1$H NMR and $^{13}$C NMR of 3af, recorded at -25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 39. $^1$H NMR and $^{13}$C NMR of 3ag, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 40. $^1$H NMR and $^{13}$C NMR of 3ah, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 41. $^1$H NMR and $^{13}$C NMR of 3ai, recorded at ~25 °C in CDCl₃ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 42. $^1$H NMR and $^{13}$C NMR of 3aj, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 43. ¹H NMR and ¹³C NMR of 3ak, recorded at ~25 °C in CDCl₃ at 500 MHz and 126 MHz, respectively.
**Supplementary Fig. 44.** $^1$H NMR and $^{13}$C NMR of 3a1, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 45. $^1$H NMR and $^{13}$C NMR of 3am, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 46. $^1$H NMR and $^{13}$C NMR of 3an, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 47. $^1$H NMR and $^{13}$C NMR of 3ao, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 48. $^{1}$H NMR and $^{13}$C NMR of 3ba, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 49. $^1$H NMR and $^{13}$C NMR of 3ca, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
**Supplementary Fig. 50.** $^1$H NMR and $^{13}$C NMR of 3da, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 51. $^1$H–$^1$H COSY of 3da, recorded at ~25 °C in CDCl$_3$ at 500 MHz.
Supplementary Fig. 52. $^1$H NMR and $^{13}$C NMR of 3ea, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 53. $^1$H NMR and $^{13}$C NMR of 3fa, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 54. $^1$H NMR and $^{13}$C NMR of 3ga, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 55. $^1$H NMR and $^{13}$C NMR of 3ha, recorded at $\sim$25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 56. $^1$H NMR and $^{13}$C NMR of 3ia, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 57. $^1$H NMR and $^{13}$C NMR of 3ja, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 58. $^1$H NMR and $^{13}$C NMR of 3ka, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 59. $^1$H NMR and $^{13}$C NMR of 3la, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 60. $^1$H NMR and $^{13}$C NMR of 3ma, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 61. $^1$H NMR and $^{13}$C NMR of 3na, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 62. $^1$H NMR and $^{13}$C NMR of 3oa (trans), recorded at -25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 63. $^1$H NMR and $^{13}$C NMR of 3oa (cis), recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 64. ^1^H NMR and ^1^C NMR of 3pa (trans), recorded at ~25 °C in CDCl₃ at 500 MHz and 126 MHz, respectively. Eluent: hexane/EtOAc = 4/6 (1st), hexane/EtOAc = 3/7 (2nd).
Supplementary Fig. 65. $^1$H NMR and $^{13}$C NMR of 3pa (cis), recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively. Eluent: hexane/EtOAc = 4/6 (1st), hexane/EtOAc = 3/7 (2nd).
Supplementary Fig. 66. $^1$H NMR and $^{13}$C NMR of 4pa, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively. Eluent: hexane/EtOAc = 4/6 (1st), hexane/EtOAc = 3/7 (2nd). Peaks of the regio-isomer were picked up from the mixture of trans/cis/regio-isomers.
Supplementary Fig. 67. $^1$H NMR and $^{13}$C NMR of 3qa, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 68. $^1$H–$^1$H COSY of 3qa, recorded at ~25 °C in CDCl$_3$ at 500 MHz.
Supplementary Fig. 69. $^1$H NMR and $^{13}$C NMR of 3ra, recorded at ~25 °C in CDCl₃ at 500 MHz and 126 MHz, respectively.
**Supplementary Fig. 70.** $^1$H NMR and $^{13}$C NMR of $3\text{sa}$ (major diastereoisomer), recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 71. $^1$H NMR and $^{13}$C NMR of 3sa (minor diastereoisomer), recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
Supplementary Fig. 72. $^1$H NMR and $^{13}$C NMR of 3ta, recorded at ~25 °C in CDCl$_3$ at 500 MHz and 126 MHz, respectively.
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