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Gold-Catalyzed Conversion of Aryl- and Alkyl-Substituted 1-(*o*-Aminophenyl)-2-propyn-1-ones to the Corresponding 2-Substituted 4-Quinolones

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Keywords: Synthetic methods / Homogeneous catalysis / Hydroamination / Gold / Density functional calculations

Gold-catalyzed cyclization of alkyl- or aryl-substituted 1-(*o*-aminophenyl)-2-propyn-1-ones to the corresponding 2-substituted 4-quinolones was studied with various gold salts and complexes. Screening of the different catalysts showed highest performance with cationic Au^{I} species. In particular PPh_3AuNTf_2 complex was the most efficient catalyst. Relative to classic quinolone synthesis that requires harsh cyclocondensation conditions, the current method offers a mild and atom-economic alternative. Mechanistically, DFT studies at TPSS-D3/def2-TZVP level suggest that gold operates in an alkynophilic manner rather than through conjugative carbonyl activation.

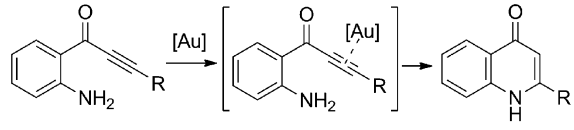
Introduction

Nitrogen-containing heterocycles are recurrent structural motifs in bioactive molecules.[1] Amongst the numerous scaffolds, 4-quinolone is featured in many commonly used antibiotics such as fluoroquinolones,[2] with proven effects as antimalarial,[3] anticancer,[4,5] antiviral[6] and antidiabetic[7] agents.

Various synthetic routes towards 4-quinolones have been developed[8] and approaches based on cyclocondensation, such as the Niementowski,[9] Conrad–Limpach[10] and Camps cyclizations,[11] are widely employed. The major shortcoming in these methods is the required harsh reaction conditions, which rely on the use of high temperatures and/or strong bases that dramatically limit the scope of these reactions. Hence, new methodologies based on milder reaction conditions are actively sought. Recent developments in transition-metal catalysis have opened a few viable routes mediated by Cu and Pd species.[11,12] The role of the transition metal is generally to activate an aryl–halide bond to promote the coupling of the aryl carbon with either a carbonyl carbon or an amine.[13,14]

During the last decade, gold catalysis has shown its supremacy in activations of unsaturated C–C bonds towards various nucleophiles.[15] One valuable invention has been the syntheses of nitrogen heterocycles through gold-catalyzed hydroamination of internal alkynes, allenes and alkenes with primary and secondary amines as expedient nucleophiles.[16] Pioneering work in this area was reported by Utimoto and co-workers, who successfully accomplished the cycloisomerization of aminoalkynes to form tetrahydropyridines by $NaAuCl_4$ catalysis.[17] Since then many N-heterocycles with various ring sizes and degrees of saturation have been prepared through intramolecular hydroamination upon development of new gold catalytic methods.[18]

In connection with our previous reports on the cyclization reaction of 2-alkynylanilines to indoles by homogeneous cationic Au^{III} catalysis[19] and heterogeneous Au/C catalysis,[20] we envisaged that a similar Au-catalyzed approach could be applied to the synthesis of 4-quinolones by using 2-acetylic ketones of anilines as precursors (Scheme 1). Further support to our hypothesis is provided by some recent reports on hydroamination reactions catalyzed by gold species. In particular, Gong at al. have developed a direct conversion of *o*-(2-propynyl)anilines into tetrahydroquinolines catalyzed by both Au^{I} and Au^{III} catalysts,[21] whereas Gouault et al. recently used Au^{I} salts in the hydroamination step for the cyclization of asymmetric *N*-*tert*-butoxycarbonyl (Boc) β-aminoynones into chiral *N*-Boc-substituted pyridones.[22] Herein we report the catalytic activity of several gold derivatives towards the synthesis of 2-substituted 4-quinolones (Scheme 1). Conditions, optimization and scope of the reaction are thoroughly explored, together with computational evidence on the direct alkyne activation by the gold species during the catalytic cycle.



Scheme 1. Envisaged gold-catalyzed synthesis of 2-substituted 4-quinolones.

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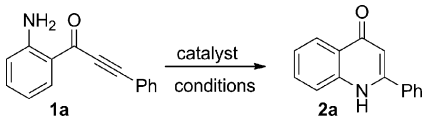
Results and Discussion

Initial screening of the catalysts was carried out on model phenyl-substituted 2-alkynylaniline **1a** (Table 1). Both the Au catalyst supported on carbon (see the Exp. Sect.) and the homogeneous auric acid catalysis in ethanol turned out to be inactive even at high temperatures (Table 1, Entries 1, 2 and 3). A change of solvent to MeCN gave slight conversion to product **2a** at room temp. (Table 1, Entry 4), but did not improve at elevated temperatures (Table 1, Entry 5). By mimicking Arcadi indole synthesis conditions,[23] (Au^{III}-catalyzed annulation of 2-alkynylanilines) gave a better result with $KAuCl_4$, which was inactive in EtOH at room temp., but provided some conversion when heated at 70 °C (Table 1, Entries 6 and 7), with isolated yields reaching 61%. Correspondingly, no yield or only poor outcomes were obtained when the reaction was performed in MeCN at room temp. or 70 °C, respectively (Table 1, Entries 8–9).

Table 1. Screening of catalyst and reaction conditions with precursor **1a**.[a]



1a 2a

Entry	Catalyst	Catalyst loading [mol-%]	Solvent	*T* [°C]	Isolated yield [%]
1	Au/C	10	toluene	90	–
2	$HAuCl_4 \cdot 3H_2O$	10	EtOH	r.t.	–
3	$HAuCl_4 \cdot 3H_2O$	10	EtOH	70	–
4	$HAuCl_4 \cdot 3H_2O$	5	MeCN	r.t.	7
5	$HAuCl_4 \cdot 3H_2O$	10	MeCN	70	–
6	$KAuCl_4$	10	EtOH	r.t.	–
7	$KAuCl_4$	10	EtOH	70	61
8	$KAuCl_4$	10	MeCN	r.t.	–
9	$KAuCl_4$	10	MeCN	70	5
10	$PtCl_2$	5	MeCN	r.t.	2
11	$PtCl_2$	5	CH_2Cl_2	r.t.	3
12	$PtCl_2$	5	toluene	90	17
13[b]	IMes-$AuNTf_2$[d]	5	CH_2Cl_2	r.t.	40
14	IMes-$AuNTf_2$	5	MeCN	r.t.	51
15	IMes-$AuNTf_2$	8	MeCN	60	66
16	PPh_3AuNTf_2	5	CH_2Cl_2	r.t.	20
17[c]	PPh_3AuNTf_2	5	MeCN	r.t.	80
18	**PPh_3AuNTf_2**	**5**	**MeCN**	**r.t.**	**96**

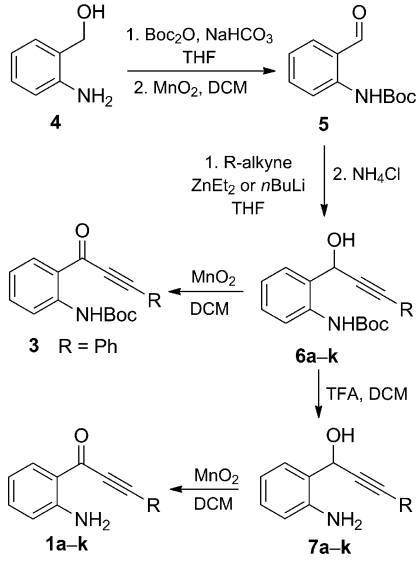
[a] The concentration in reactions was 0.1 M and reaction time was 24 h. [b] Reaction time 5 h. [c] Reaction time 8 h. [d] IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene.

In the wake of the reported analogy to gold catalysts, platinum-based π-acid catalysts have been applied in various alkyne activations for nucleophiles.[24] We tested platinum(II) dichloride salt and although mildly active, yields remained poor even after prolonged heating at 90 °C (Table 1, Entries 10–12).

When cationic Au^I complexes were employed, a significant increase in overall performance was observed. The Au N-heterocyclic carbene (NHC) complex, IMes-$AuNTf_2$, gave fair yields in CH_2Cl_2 and MeCN after 24 h at room temp., whereas the reaction progressed to 40% conversion within 5 h at room temp. (Table 1, Entries 13 and 14). A increase in temperature to 60 °C increased the yield to 66% in MeCN (Table 1, Entry 15). The corresponding phosphine complex, PPh_3AuNTf_2, was the best-performing catalyst. However, its catalytic activity was poor in CH_2Cl_2 (Table 1, Entry 16). The change of solvent to MeCN dramatically improved the yield to 80% and 96%, after 8 and 24 h, respectively, when reactions were performed at room temperature (Table 1, Entries 17 and 18).

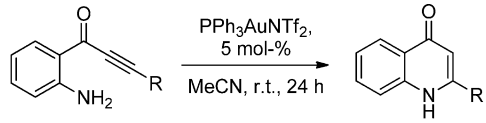
The observed performance differences of the phosphine and NHC carbene ligand in cationic Au^I catalysts in CH_2Cl_2 and MeCN can be rationalized in view of recent work by Hammond, Xu and co-workers, that showed environmental effects, such as solvent, critically affect Au^I disproportionation and consequently catalytic activity.[25] Although catalyst stability is enhanced in the presence of σ-donors, such as MeCN, catalytic activity diminishes. In our systems this likely explains the slow but steady catalysis by Au^I with phosphine ligands in MeCN. In contrast, catalyst decomposition becomes a limiting factor for experiments performed in CH_2Cl_2.

With the optimized conditions in hand, we investigated the scope of the reaction by varying the alkyne substituent. Various substrates were prepared according to the synthetic routes described in Scheme 2, and results for the 4-quinolone synthesis are presented in Table 2. 2-Aryl-4-quinolones including both electron-withdrawing and donating substituents could be isolated with excellent yields (Table 2, Entries 1–4). Similarly, straight chain alkyl substitution gave high yields (Table 2, Entry 5). To our disappointment cyclization did not take place at all with a simple TMS-protected substrate (Table 2, Entry 6), whereas the unprotected derivative underwent oligomerization to tar even in the absence of catalyst.

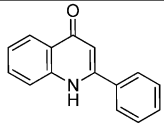
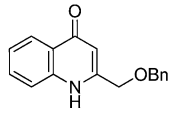
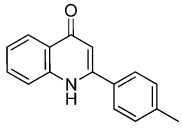
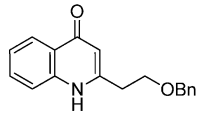
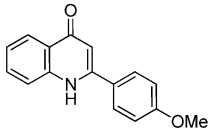
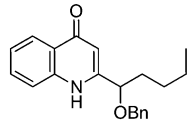
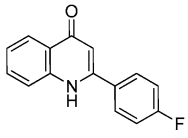
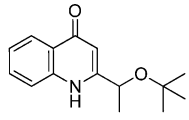
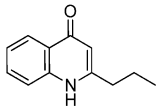
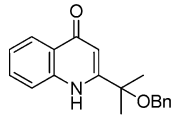
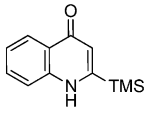


Scheme 2. Synthetic pathways towards substrates **1a**–**1k** and **3**.

Table 2. Gold-catalysed synthesis of 2-substituted 4-quinolones.[a]



1a–k **2a–k**

Entry	Product	Isolated yield [%]	Entry	Product	Isolated yield [%]
1	**2a** 	96	7	**2g** 	33
2	**2b** 	93	8	**2h** 	58
3	**2c** 	95	9	**2i** 	42
4	**2d** 	88	10	**2j** 	26
5	**2e** 	89	11	**2k** 	19
6	**2f** 	–			

[a] The concentration of reactions was 0.1 M.

Studies of various aliphatic branched-chain ethers revealed that oxygen and bulkiness in the vicinity of the alkyne result in lower yields (Table 2, Entries 7–11). Benzyl ether at the α-position gives 33% isolated yield, whereas the yield is almost doubled (58%) for the corresponding ether at the β-position (Table 2, Entries 7 and 8). Branching at the alkyne α-carbon leads to poor yields; for benzyl ether combined with a butyl chain the yield is 42%, whereas it decreases to 26% for *tert*-butyl ether combined with methyl substitution. A further decrease in yield (19%) is found with a combination of dimethyl and benzyl ether substitution (Table 2, Entry 11).

For analysis of *N*-Boc-protected aliphatic amines used by Gouault et al., we also decided to run catalytic tests with *N*-Boc-functionalized **3** as a substrate (see Supporting Information, Table S1). The course of the reaction was quite unexpected. The cationic catalysts showed no or poor activity, whereas conversion to Boc-free product **2a** took place at best with 15 mol-% auric acid loading in EtOH at 70 °C with 68% isolated yield. This is somewhat surprising given that direct use of Boc-free starting material under the same reaction conditions did not lead to any conversion (Table 1, Entry 3). We propose that the activity of auric acid originates from the combination of two actions: it catalyzes Boc removal, and the Boc moiety chelates the ligand-free gold prior to its cleavage. These possibilities will be studied in our future work.

To provide some theoretical insights into the reaction mechanism, we performed DFT calculations at TPSS-D3/def2-TZVP level with COSMO solvation model for acetonitrile.[26] Important scalar relativistic effects for gold were taken into account by using a small-core ECP from the same basis set.[27,28] Structures related to either Au coordination or alkyne activation and leading to cyclization were also taken into account. At first, we studied different coordination modes between gold and the functional groups of

substrate **1a**, i.e. amine, carbonyl and alkyne (Figure 1). The respective computations were done for three different Au species: $AuCl_3$, dimethylimidazole-coordinated (NHC) and PMe_3-coordinated cationic Au^I. Ground-state coordination energies were also calculated by using PPh_3 as ligand. The energy gap between amine- and alkyne-coordinated structures (**1-[Au]** and **3-[Au]**) justify the approximation of PMe_3 as a model system.[29]

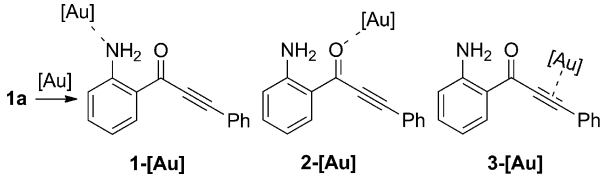


Figure 1. Different coordination modes of gold catalyst to substrate **1a**.

Figure 2 shows that cationic Au species have quite similar energy profiles, i.e. NHC- and PMe_3-coordinated gold complexes, whereas $AuCl_3$ displays some different features. Overall, amine-gold coordination was found to be the preferred binding mode between the studied substrates and Au species. Notably, binding between the amine and $AuCl_3$ is more exothermic relative to alkyne coordination. For the cationic Au species, the coordination on the carbonyl is slightly more endothermic, ca. 1 kcal/mol, whereas the Au–alkyne bonding lies at 2.8 and 4.2 kcal/mol higher energy level, respectively. For these species direct alkyne activation for cyclization has similar energy barriers being ca. 13 kcal/mol. In addition to the highly exothermic amine binding of $AuCl_3$ species its transition state for cyclization through alkyne coordination is only 6.6 kcal/mol higher than the coordination itself. Notably, the energy of related cyclized intermediate **4-[Au]** is drops by –14.5 kcal/mol. Alternative conjugated addition reaction pathways, i.e. activation of the alkyne through carbonyl coordination (**2-[Au]**), was studied with PMe_3-liganded Au complex and proved to be unlikely because the activation energy barrier was remarkably high (30.3 kcal/mol relative to **1-[Au]**).

Close inspection of the transition-state structures in Figure 3 reveals that the bond forming C–N distance is distinctly longer for the $AuCl_3$ complex (2.77 Å) than that for the cationic species (ca. 2.4 Å). One could expect that the long bond-forming distance, together with a low-energy cyclization barrier after the alkyne coordination step would

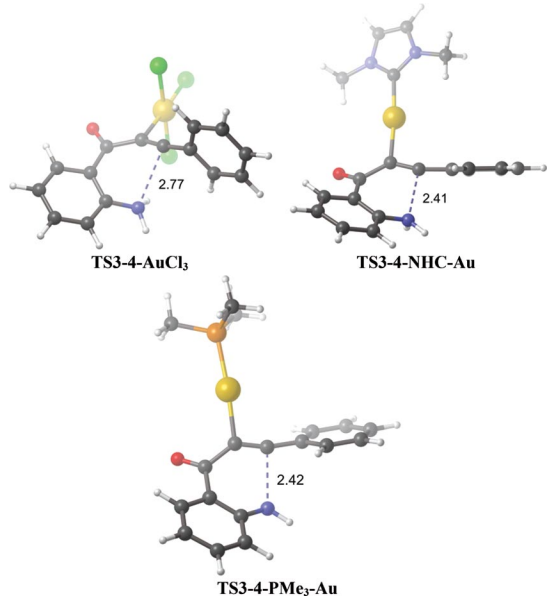


Figure 3. TPSS-D3/def2-TZVP optimised transition states **TS3–4-[Au]**.

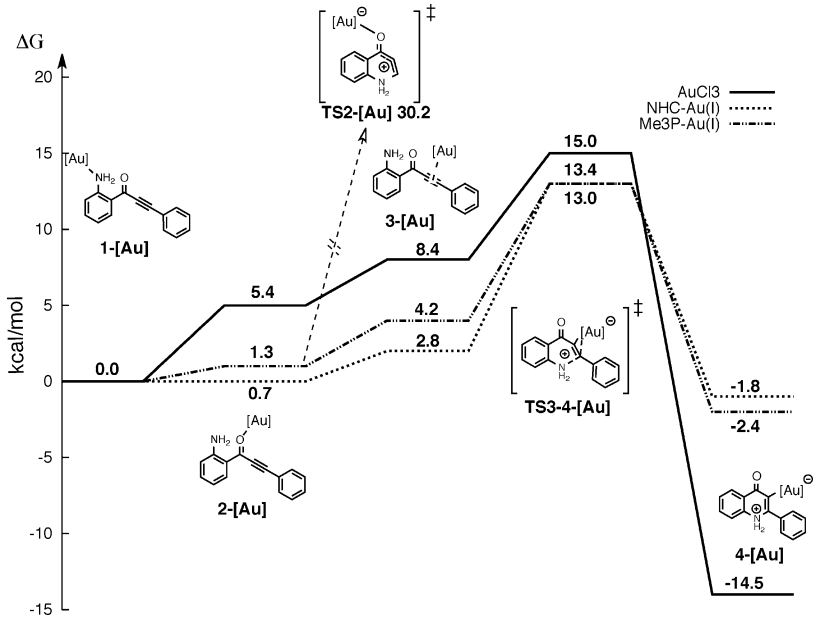


Figure 2. Reaction profile for the cyclisation reaction of **1a** including different Au complexes according to TPSS-D3/def2-TZVP computations in MeCN.

result in facile reactivity for $AuCl_3$ catalysis. Yet, experimentally its performance was rather poor relative to cationic Au^I complexes. This cannot be fully explained by the slightly higher global energy barrier of $AuCl_3$, (ca. 2.0 kcal/mol), than that of the cationic complexes. Single-point energies computed at PW6B95-D3/def2-TZVPP level on TPSS-D3 geometries showed similar behavior (see Supporting Information).[30] We presume that the reason behind the poor experimental performance of Au^{III} lies in the catalyst decomposition over the course of the reaction as suggested by the observed gold mirrors in the catalytic experiments. The tighter amine–$AuCl_3$ coordination might lead to inhibition and also some decomposition through a redox mechanism of the gold catalyst.

Conclusions

We have developed a gold-catalyzed route to the synthesis of 2-substituted 4-quinolones from aryl- and alkyl-substituted aniline-2-propynones. The reaction takes place with a cationic Au^I catalyst at ambient temperature and products can be isolated with high yields. DFT analysis suggests that the cyclization step in the reaction proceeds through direct gold activation of the alkyne rather than through conjugation of the carbonyl group. Our experimental and computational results are in agreement on the major role of the deactivation of the catalyst during the reaction, which explains the observed sluggish catalytic performance of $AuCl_3$.

Experimental Section

General Remarks: Unless otherwise specified, all commercial materials were used as received without further purification. Dry tetrahydrofuran (THF) was taken directly from VAC Solvent Purifier. Reactions that involved the use of air- and moisture-sensitive materials were carried out in an atmosphere of dry argon by using Schlenk techniques. PPh_3AuNTf_2 was purchased from Sigma–Aldrich. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded with a Varian Mercury 300. ^1H spectra were referenced to tetramethylsilane (TMS, 0.0 ppm) or to dimethyl sulfoxide (DMSO; δ =2.50 ppm) and are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Chemical shifts of the $^{13}C\{^1H\}$ NMR spectra were measured relative to $CDCl_3$ (δ = 77.16 ppm) or to DMSO (δ = 39.52 ppm). HRMS data was acquired with a JEOL JMS-700 instrument in EI ionization mode. Column chromatographic purifications were performed with Merck Silica gel 60 (230–400 mesh). Thin layer chromatography was performed with TLC Silica gel 60 F_{256} plates.

General Procedure for Gold-Catalyzed Cyclization Reactions Leading to 2a–2k: Compound **6** (0.06–0.13 mmol) was dissolved in MeCN (c = 0.1 M). PPh_3AuNTf_2 (5 mol-%) was added and the mixture was mixed at room temperature for 24 h. The solvent was evaporated and the product was purified by flash chromatography with CH_2Cl_2 and methanol (20:1) as eluent.

2-Phenyl-quinolin-4(1*H*)-one (2a): The general procedure afforded 26.1 mg (96%) of the desired product. ^1H NMR (300 MHz, DMSO): δ = 11.73 (s, 1 H), 8.12 (dd, J = 8.1, 1.3 Hz, 1 H), 7.88–7.81 (m, 2 H), 7.78 (d, J = 8.2 Hz, 1 H), 7.67 (ddd, J = 8.4, 7.0, 1.5 Hz, 1 H), 7.62–7.55 (m, 3 H), 7.38–7.30 (m, 1 H), 6.36 (s, 1 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 176.94, 150.10, 134.29, 131.76, 130.41, 128.98, 127.40, 124.80, 124.68, 123.28, 118.79, 107.27 ppm. HRMS (EI^+): calcd. for $[C_{15}H_{11}NO]^+$ m/z 221.0841; found 221.0839.

2-(4-Methylphenyl)quinolin-4(1*H*)-one (2b): The general procedure afforded 30.6 mg (96%) of the desired product. ^1H NMR (300 MHz, DMSO): δ = 11.64 (s, 1 H), 8.10 (dd, J = 8.1, 1.3 Hz, 1 H), 7.81–7.71 (m, 1 H), 7.66 (ddd, J = 8.4, 6.9, 1.5 Hz, 1 H), 7.39 (d, J = 7.9 Hz, 1 H), 7.33 (ddd, J = 8.0, 7.0, 1.1 Hz, 1 H), 6.32 (s, 1 H), 2.40 (s, 3 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 176.92, 149.90, 140.50, 140.33, 131.71, 131.27, 129.53, 127.21, 124.85, 124.69, 123.15, 118.66, 106.91, 20.88 ppm. HRMS (EI^+): calcd. for $[C_{16}H_{13}NO]^+$ m/z 235.0997; found 235.0995.

2-(4-Methoxyphenyl)quinolin-4(1*H*)-one (2c): The general procedure afforded 31.6 mg (95%) of the desired product. ^1H NMR (300 MHz, DMSO): δ = 11.58 (s, 1 H), 8.09 (dd, J = 8.0, 1.0 Hz, 1 H), 7.86–7.73 (m, 3 H), 7.70–7.61 (m, 1 H), 7.32 (t, J = 7.1 Hz, 1 H), 7.13 (d, J = 8.8 Hz, 2 H), 6.30 (s, 1 H), 3.85 (s, 3 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 176.84, 161.03, 149.65, 140.48, 131.63, 128.82, 126.22, 124.78, 124.67, 123.07, 118.58, 114.38, 106.49, 55.43 ppm. HRMS (EI^+): calcd. for $[C_{16}H_{13}NO_2]^+$ m/z 251.0946; found 251.0955.

2-(4-Fluorophenyl)quinolin-4(1*H*)-one (2d): The general procedure afforded 24.8 mg (88%) of the desired product. ^1H NMR (300 MHz, DMSO): δ = 11.72 (s, 1 H), 8.10 (d, J = 8.0 Hz, 1 H), 7.91 (dd, J = 7.7, 5.9 Hz, 2 H), 7.76 (d, J = 8.2 Hz, 1 H), 7.67 (t, J = 7.6 Hz, 1 H), 7.42 (t, J = 8.7 Hz, 2 H), 7.34 (t, J = 7.4 Hz, 1 H), 6.35 (s, 1 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 164.99, 161.70, 149.11, 140.58, 131.75, 130.78, 129.89, 129.77, 128.64, 124.63, 123.29, 118.85, 116.07, 115.78, 107.24 ppm. HRMS (EI^+): calcd. for $[C_{15}H_{10}FNO]^+$ m/z 239.0746; found 239.0737.

2-Propylquinolin-4(1*H*)-one (2e): The general procedure afforded 24.8 mg (89%) of the desired product. ^1H NMR (300 MHz, DMSO): δ = 11.49 (s, 1 H), 11.49 (s, 1 H), 8.05 (dd, J = 8.1, 1.3 Hz, 1 H), 8.05 (dd, J = 8.1, 1.3 Hz, 1 H), 7.60 (ddd, J = 8.2, 6.8, 1.4 Hz, 1 H), 7.60 (ddd, J = 8.2, 6.8, 1.4 Hz, 1 H), 7.53 (dd, J = 7.7, 0.5 Hz, 1 H), 7.53 (dd, J = 7.7, 0.5 Hz, 1 H), 7.30–7.23 (m, 1 H), 7.31–7.23 (m, 1 H), 5.93 (s, 1 H), 2.59–2.53 (m, 2 H), 1.84–1.55 (m, 2 H), 0.93 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 176.80, 153.31, 140.15, 131.39, 124.73, 124.60, 122.68, 117.86, 107.67, 35.13, 21.65, 13.37 ppm. HRMS (EI^+): calcd. for $[C_{12}H_{13}NO]^+$ m/z 187.0997; found 187.0999.

2-[(Benzyloxy)methyl]quinolin-4(1*H*)-one (2g): The general procedure afforded 11.2 mg (33%) of the desired product. ^1H NMR (300 MHz, DMSO): δ = 11.65 (s, 1 H), 8.07 (d, J = 8.1 Hz, 1 H), 7.63 (d, J = 3.6 Hz, 2 H), 7.34 (dd, J = 28.1, 8.7 Hz, 6 H), 6.10 (s, 1 H), 4.61 (s, 2 H), 4.54 (s, 2 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 176.97, 149.13, 140.15, 137.64, 131.68, 128.31, 127.72, 125.01, 124.79, 122.95, 118.25, 107.14, 71.94, 68.32 ppm. HRMS (EI^+): calcd. for $[C_{17}H_{15}NO_2]^+$ m/z 265.1103; found 265.1113.

2-[(Benzyloxy)ethyl]quinolin-4(1*H*)-one (2h): The general procedure afforded 11.7 mg (58%) of the desired product. ^1H NMR (300 MHz, DMSO): δ = 10.36 (s, 1 H), 7.59 (dd, J = 13.4, 10.3 Hz, 2 H), 7.41–7.22 (m, 9 H), 7.03 (t, J = 7.3 Hz, 2 H), 6.93 (d, J = 7.8 Hz, 1 H), 6.31 (s, 1 H), 4.50 (s, 3 H), 3.54 (t, J = 6.4 Hz, 3 H), 2.59 (td, J = 6.4, 1.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 150.62, 138.22, 135.68, 129.45, 128.21, 127.40, 124.57, 122.63, 119.52, 114.10, 87.12, 76.12, 71.69, 67.90, 67.37, 19.46 ppm. HRMS (EI^+): calcd. for $[C_{18}H_{17}NO_2]^+$ m/z 279.1259; found 279.1258.

2-[1-(Benzyloxy)pentyl]quinolin-4(1*H*)-one (2i): The general procedure afforded 8.1 mg (42%) of the desired product. ^{1}H NMR (300 MHz, DMSO): δ = 11.54 (s, 1 H), 8.06 (d, J = 7.3 Hz, 1 H), 7.70 (d, J = 8.2 Hz, 1 H), 7.66–7.59 (m, 1 H), 7.59–7.47 (m, 2 H), 7.38–7.26 (m, 7 H), 6.08 (s, 1 H), 4.52 (d, J = 11.9 Hz, 1 H), 4.39 (d, J = 11.9 Hz, 1 H), 4.33 (dd, J = 7.8, 5.6 Hz, 1 H), 1.97–1.67 (m, 2 H), 1.30 (m, 4 H), 0.84 (t, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 176.92, 152.70, 140.27, 137.81, 131.59, 128.24, 127.75, 127.62, 125.16, 124.73, 122.97, 118.46, 106.79, 78.48, 70.59, 34.82, 27.20, 21.82, 13.83 ppm. HRMS (EI$^+$): calcd. for $[C_{21}H_{23}NO_2]^+$ m/z 321.1729; found 321.1738.

2-[1-(*tert*-Butoxy)ethyl]quinolin-4(1*H*)-one (2j): The general procedure afforded 6.2 mg (19%) of the desired product. ^{1}H NMR (300 MHz, DMSO): δ = 11.18 (s, 1 H), 8.04 (d, J = 7.7 Hz, 1 H), 7.83 (d, J = 8.0 Hz, 1 H), 7.74–7.52 (m, 2 H), 7.44–7.22 (m, 5 H), 6.12 (s, 1 H), 4.30 (s, 2 H), 1.62 (s, 6 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 177.20, 155.17, 140.38, 138.47, 131.69, 128.79, 128.14, 127.71, 127.33, 124.55, 122.89, 118.69, 106.33, 75.97, 65.23, 25.93 ppm. HRMS (EI$^+$): calcd. for $[C_{19}H_{19}NO_2]^+$ m/z 293.1416; found 293.1420.

2-[2-(Benzyloxy)propan-2-yl]quinolin-4(1*H*)-one (2k): The general procedure afforded 14.0 mg (26%) of the desired product. ^{1}H NMR (300 MHz, DMSO): δ = 11.36 (s, 1 H), 8.04 (d, J = 8.1 Hz, 1 H), 7.73 (d, J = 8.3 Hz, 1 H), 7.61 (ddd, J = 8.4, 1.4, 0.7 Hz, 1 H), 7.28 (t, J = 7.5 Hz, 1 H), 6.10 (s, 1 H), 4.68 (q, J = 6.5 Hz, 1 H), 1.38 (d, J = 6.5 Hz, 3 H), 1.16 (s, 9 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 176.95, 157.00, 140.05, 131.38, 125.02, 124.65, 122.83, 118.48, 105.01, 74.77, 67.12, 27.79, 24.04 ppm. HRMS (EI$^+$): calcd. for $[C_{15}H_{19}NO_2]^+$ m/z 245.1416; found 245.1409.

***tert*-Butyl [2-(3-Phenylpropioloyl)phenyl]carbamate (3):** Compound **6a** (26.0 mg, 0.08 mmol) was dissolved in CH_2Cl_2 (5 mL). MnO_2 (85%, 35.0 mg, 0.4 mmol) was added and the mixture was mixed for 5 h at room temperature. The mixture was filtered through silica and the solvents evaporated to afford 25.9 mg (99%) of the desired product. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.78 (s, 1 H), 8.50 (d, J = 8.6 Hz, 1 H), 8.36 (d, J = 7.9 Hz, 1 H), 7.68 (d, J = 7.9 Hz, 1 H), 7.57 (t, J = 7.9 Hz, 1 H), 7.49 (d, J = 7.6 Hz, 1 H), 7.43 (t, J = 7.7 Hz, 1 H), 7.10 (t, J = 7.6 Hz, 1 H), 1.55 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 180.70, 153.12, 142.95, 135.96, 134.69, 133.14, 131.03, 128.86, 121.88, 121.26, 120.18, 118.91, 94.27, 87.24, 80.97, 28.45 ppm. HRMS (EI$^+$): calcd. for $[C_{20}H_{19}NO_3]^+$ m/z 321.1365; found 321.1377.

***tert*-Butyl (2-Formylphenyl)carbamate (5):** 2-Aminobenzylic alcohol (**4**, 330.0 mg, 2.7 mmol) was dissolved in THF (20 mL). Boc anhydride (830.0 mg, 3.80 mmol) and $NaHCO_3$ (500.0 mg, 5.95 mmol) was added to the solution. After mixing the solution at room temperature for 42 h the solvent was evaporated. The obtained oil was dissolved in CH_2Cl_2 (40 mL). MnO_2 (activated 85%, 1.39 g, 13.5 mmol) was added to the solution. The mixture was mixed at room temperature for 24 h. MnO_2 was filtered and the solvent evaporated. Purification of the crude mixture by column chromatography with *n*-hexane and ethyl acetate (5:1) as eluent afforded 551.4 mg (93%) of the desired product. Spectral data was found to match literature values. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.39 (s, 1 H), 9.90 (s, 1 H), 8.46 (d, J = 8.5 Hz, 1 H), 7.62 (dd, J = 7.7, 1.6 Hz, 1 H), 7.60–7.53 (m, 1 H), 7.13 (td, J = 7.5, 1.0 Hz, 1 H), 1.54 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.12, 153.01, 141.94, 136.19, 136.06, 121.61, 121.36, 118.38, 81.07, 28.42 ppm.

General Procedure for Attaching Aromatic Acetylenes (Procedure A): Acetylene (1.13 mmol) was dissolved in dry THF (5 mL) under argon in a flame-dried Schlenk flask. $ZnEt_2$ (1.0 M in hexanes, 1.13 mL, 1.13 mmol) was added dropwise to the solution. The mixture was mixed at room temperature for 30 min. Compound **5** (100.0 mg, 0.45 mmol) was dissolved in dry THF (4 mL) and added dropwise to the flask. The mixture was mixed at room temperature for 24 h. NH_4Cl (aq, 5 mL) was added to the mixture and the crude product was extracted with ethyl acetate. The product was purified by flash chromatography with *n*-hexane and ethyl acetate (3:1) as eluent.

General Procedure for Attaching Alkylacetylenes (Procedure B): Acetylene (1.13 mmol) was dissolved in dry THF (5 mL) under argon in a flame-dried Schlenk flask. *n*BuLi (2.5 M in hexanes, 0.45 mL, 1.13 mmol) was added dropwise to the solution. The mixture was mixed at room temperature for 30 min. Compound **3** (100.0 mg, 0.45 mmol) was dissolved in dry THF (4 mL) and added dropwise to the flask. The mixture was mixed at room temperature for 24 h. NH_4Cl (aq, 5 mL) was added to the mixture and the crude product was extracted with ethyl acetate. The product was purified by flash chromatography with *n*-hexane and ethyl acetate (3:1) as eluent.

***tert*-Butyl [2-(1-Hydroxy-3-phenylprop-2-yn-1-yl)phenyl]carbamate (6a):** Following general procedure A afforded 126.3 mg (92%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.86 (d, J = 8.1 Hz, 1 H), 7.68 (s, 1 H), 7.56 (dd, J = 7.7, 1.6 Hz, 1 H), 7.50–7.44 (m, 2 H), 7.37–7.27 (m, 3 H), 7.07 (td, J = 7.5, 1.2 Hz, 1 H), 5.71 (s, 1 H), 3.15 (s, 1 H), 1.50 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 180.58, 153.01, 142.86, 135.88, 134.61, 133.06, 130.97, 128.79, 121.78, 121.20, 120.06, 118.82, 94.21, 87.17, 80.86, 28.37 ppm. HRMS (EI$^+$): calcd. for $[C_{20}H_{21}NO_3]^+$ m/z 323.1521; found 323.1532.

***tert*-Butyl {2-[1-Hydroxy-3-(*p*-tolyl)prop-2-yn-1-yl]phenyl}carbamate (6b):** Following general procedure A afforded 122.7 mg (91%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.85 (d, J = 8.0 Hz, 1 H), 7.75 (s, 1 H), 7.51 (dd, J = 7.6, 1.3 Hz, 1 H), 7.34 (d, J = 8.1 Hz, 2 H), 7.32–7.25 (m, 1 H), 7.08 (d, J = 7.9 Hz, 2 H), 7.03 (td, J = 7.6, 1.1 Hz, 1 H), 5.65 (s, 1 H), 3.52 (s, 1 H), 2.32 (s, 3 H), 1.48 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.56, 138.87, 137.00, 131.72, 129.36, 129.06, 127.98, 123.43, 122.12, 119.23, 87.91, 86.45, 80.58, 63.75, 28.37, 21.50 ppm. HRMS (EI$^+$): calcd. for $[C_{21}H_{23}NO_3]^+$ m/z 337.1678; found 337.1689.

***tert*-Butyl {2-[1-Hydroxy-3-(4-methoxyphenyl)prop-2-yn-1-yl]phenyl}carbamate (6c):** Following general procedure A afforded 105.7 mg (88%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87 (d, J = 8.1 Hz, 1 H), 7.72 (s, 1 H), 7.54 (dd, J = 7.7, 1.4 Hz, 1 H), 7.45–7.35 (m, 1 H), 7.31 (td, J = 8.1, 1.5 Hz, 1 H), 7.05 (td, J = 7.5, 1.2 Hz, 1 H), 6.82 (d, J = 8.9 Hz, 1 H), 5.68 (s, 1 H), 3.78 (s, 1 H), 1.50 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.98, 153.56, 137.09, 133.36, 129.45, 128.02, 123.47, 122.16, 114.39, 114.02, 87.92, 85.74, 80.62, 63.89, 55.37, 28.44 ppm. HRMS (EI$^+$): calcd. for $[C_{21}H_{23}NO_4]^+$ m/z 353.1627; found 353.1642.

***tert*-Butyl {2-[3-(4-Fluorophenyl)-1-hydroxyprop-2-yn-1-yl]phenyl}carbamate (6d):** Following general procedure A afforded 77.3 mg (62%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.85 (d, J = 8.0 Hz, 1 H), 7.64 (s, 1 H), 7.53 (dd, J = 7.7, 1.3 Hz, 1 H), 7.49–7.39 (m, 3 H), 7.33 (td, J = 8.0, 1.5 Hz, 1 H), 7.17–6.89 (m, 3 H), 5.69 (d, J = 4.9 Hz, 1 H), 3.15 (d, J = 5.3 Hz, 1 H), 1.49 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.46, 161.14, 153.65, 136.98, 133.86, 133.75, 129.54, 129.42, 128.01, 123.64, 122.42, 118.44, 115.82, 115.53, 86.92, 86.66, 80.74, 63.77, 28.41 ppm. HRMS (EI$^+$): calcd. for $[C_{20}H_{20}FNO_3]^+$ m/z 341.1427; found 341.1420.

***tert*-Butyl [2-(1-Hydroxyhex-2-yn-1-yl)phenyl]carbamate (6e):** Following general procedure B afforded 75.1 mg (62%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.86 (d, J = 8.1 Hz, 1 H), 7.69 (s, 1 H), 7.47 (dd, J = 7.7, 1.4 Hz, 1 H), 7.33–7.25 (m, 1 H), 7.03 (td, J = 7.5, 1.2 Hz, 1 H), 5.46 (s, 1 H), 2.99 (s, 1 H), 2.25 (td, J = 7.1, 2.0 Hz, 2 H), 1.57 (dd, J = 14.5, 7.3 Hz, 2 H), 1.51 (s, 9 H), 1.00 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.45, 137.03, 129.48, 129.26, 127.79, 123.22, 121.81, 88.91, 80.47, 78.41, 63.52, 28.42, 22.03, 20.88, 13.61 ppm. HRMS (EI$^+$): calcd. for $[C_{17}H_{23}NO_3]^+$ m/z 289.1678; found 289.1680.

***tert*-Butyl {2-[1-Hydroxy-3-(trimethylsilyl)prop-2-yn-1-yl]phenyl}carbamate (6f):** Following general procedure B afforded 58.0 mg (54%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.86 (d, J = 8.2 Hz, 1 H), 7.60 (s, 1 H), 7.47 (dd, J = 7.6, 1.4 Hz, 1 H), 7.38–7.26 (m, 1 H), 7.05 (td, J = 7.6, 1.1 Hz, 1 H), 5.46 (s, 1 H), 3.03 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.47, 137.03, 129.51, 128.89, 128.01, 123.45, 122.02, 103.26, 93.12, 80.61, 63.66, 28.47, –0.11 ppm. HRMS (EI$^+$): calcd. for $[C_{17}H_{25}NO_3Si]^+$ m/z 319.1604; found 319.1611.

***tert*-Butyl {2-[4-(Benzyloxy)-1-hydroxybut-2-yn-1-yl]phenyl}carbamate (6g):** Following general procedure B afforded 130.7 mg (78%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.84 (d, J = 8.1 Hz, 1 H), 7.63 (s, 1 H), 7.48 (dd, J = 7.6, 1.5 Hz, 1 H), 7.40–7.18 (m, 6 H), 7.04 (td, J = 7.5, 1.2 Hz, 1 H), 5.52 (s, 1 H), 4.58 (s, 2 H), 4.23 (d, J = 1.8 Hz, 2 H), 3.37 (s, 1 H), 1.49 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.54, 136.98, 129.49, 129.05, 128.52, 128.21, 128.02, 127.84, 126.66, 123.50, 122.19, 84.75, 83.80, 80.66, 71.80, 63.20, 57.40, 28.41 ppm. HRMS (EI$^+$): calcd. for $[C_{22}H_{25}NO_4]^+$ m/z 367.1784; found 367.1782.

***tert*-Butyl {2-[5-(Benzyloxy)-1-hydroxypent-2-yn-1-yl]phenyl}carbamate (6h):** Following general procedure B afforded 62.4 mg (38%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.85 (d, J = 8.1 Hz, 1 H), 7.65 (s, 1 H), 7.54–7.45 (m, 1 H), 7.39–7.20 (m, 1 H), 7.01 (td, J = 7.5, 1.1 Hz, 1 H), 5.43 (d, J = 15.1 Hz, 1 H), 4.52 (s, 1 H), 3.67–3.53 (m, 1 H), 3.11 (s, 1 H), 2.57 (ddd, J = 11.6, 6.8, 1.6 Hz, 1 H), 1.50 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.49, 137.96, 137.07, 129.34, 128.53, 128.28, 127.80, 126.72, 123.36, 122.04, 85.61, 80.50, 79.49, 73.06, 68.26, 64.74, 63.34, 28.47, 20.36 ppm. HRMS (EI$^+$): calcd. for $[C_{23}H_{27}NO_4]^+$ m/z 381.1940; found 381.1959.

***tert*-Butyl {2-[4-(Benzyloxy)-1-hydroxyoct-2-yn-1-yl]phenyl}carbamate (6i):** Following general procedure B afforded 68.2 mg (36%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87 (d, J = 8.0 Hz, 1 H), 7.64 (d, J = 3.2 Hz, 1 H), 7.58–7.44 (m, 1 H), 7.42–7.19 (m, 6 H), 7.04 (td, J = 7.5, 1.2 Hz, 1 H), 5.54 (s, 1 H), 4.77 (dd, J = 11.8, 3.3 Hz, 1 H), 4.50 (dd, J = 11.8, 2.4 Hz, 1 H), 4.22–4.12 (m, 1 H), 3.14 (s, 1 H), 1.89–1.69 (m, 2 H), 1.49 (s, 9 H), 1.47–1.19 (m, 4 H), 0.89 (t, J = 6.7 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.46, 137.93, 137.07, 129.50, 129.09, 128.66, 128.44, 128.08, 127.79, 126.71, 123.40, 122.00, 87.31, 83.92, 80.64, 70.79, 68.89, 63.23, 35.47, 28.43, 27.56, 22.44, 14.06 ppm. HRMS (EI$^+$): calcd. for $[C_{26}H_{33}NO_4]^+$ m/z 423.2410; found 423.2413.

***tert*-Butyl {2-[4-(*tert*-Butoxy)-1-hydroxypent-2-yn-1-yl]phenyl}carbamate (6j):** Following general procedure B afforded 94.6 mg (57%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88 (d, J = 8.1 Hz, 1 H), 7.60 (s, 1 H), 7.44 (dd, J = 7.7, 1.4 Hz, 1 H), 7.36–7.17 (m, 6 H), 7.02 (td, J = 7.5, 1.1 Hz, 1 H), 5.49 (s, 1 H), 4.62 (s, 2 H), 2.92 (s, 1 H), 1.57 (d, J = 1.8 Hz, 6 H), 1.49 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.40, 138.95, 137.07, 129.56, 129.00, 128.41, 127.87, 127.78, 127.51, 123.41, 121.97, 90.34, 82.48, 80.66, 70.85, 66.80, 63.30, 29.01, 28.94, 28.46 ppm. HRMS (EI$^+$): calcd. for $[C_{24}H_{29}NO_4]^+$ m/z 395.2097; found 395.2108.

***tert*-Butyl {2-[4-(Benzyloxy)-1-hydroxy-4-methylpent-2-yn-1-yl]-phenyl}carbamate (6k):** Compound **4k** reacted according to general procedure B afforded 121.5 mg (76%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88 (d, J = 8.1 Hz, 1 H), 7.72 (s, 1 H), 7.44 (t, J = 6.2 Hz, 1 H), 7.33–7.25 (m, 1 H), 7.02 (t, J = 7.5 Hz, 1 H), 5.50 (s, 1 H), 4.36 (q, J = 6.6 Hz, 1 H), 3.33 (s, 1 H), 1.50 (s, 9 H), 1.41 (dd, J = 6.6, 3.9 Hz, 3 H), 1.24 (d, J = 5.9 Hz, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.35, 137.10, 129.29, 128.87, 127.81, 123.13, 121.66, 90.98, 81.31, 81.27, 80.44, 75.07, 63.30, 57.85, 28.44, 28.21, 24.29 ppm. HRMS (EI$^+$): calcd. for $[C_{20}H_{29}NO_4]^+$ m/z 347.2097; found 347.2103.

General Procedure for the Boc-Deprotection Reaction Leading to 7a–7k: Compound **6** was dissolved in CH_2Cl_2 (10 mL). Trifluoroacetic acid (0.4 mL) was added dropwise to the solution. The solution was mixed at room temperature for 15 min. Water (15 mL) was added and mixture was extracted with CH_2Cl_2. The product was purified by flash chromatography with *n*-hexane and ethyl acetate (3:1) as eluent.

1-(2-Aminophenyl)-3-phenylprop-2-yn-1-ol (7a): Following the general procedure afforded 79.4 mg (91%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.45 (s, 2 H), 7.52–7.45 (m, 2 H), 7.42–7.27 (m, 5 H), 7.11 (td, J = 7.6, 1.0 Hz, 1 H), 6.97 (d, J = 7.9 Hz, 1 H), 6.31 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.01, 135.09, 132.13, 130.07, 129.35, 128.47, 124.97, 123.82, 121.55, 119.00, 114.90, 89.27, 82.93, 69.91 ppm. HRMS (EI$^+$): calcd. for $[C_{15}H_{13}NO]^+$ m/z 223.0997; found 223.0995.

1-(2-Aminophenyl)-3-(*p*-tolyl)prop-2-yn-1-ol (7b): Following the general procedure afforded 68.2 mg (81%) of the desired product. ^{1}H NMR (300 MHz, DMSO): δ = 10.46 (s, 2 H), 7.45–7.29 (m, 4 H), 7.20 (d, J = 7.9 Hz, 2 H), 7.10 (t, J = 7.5 Hz, 1 H), 6.97 (d, J = 7.9 Hz, 1 H), 6.59 (s, 1 H), 2.31 (s, 3 H), 1.91 (s, 1 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 150.57, 139.44, 135.77, 131.60, 129.67, 129.41, 124.69, 122.88, 119.14, 117.71, 114.31, 87.76, 83.77, 68.14, 21.03 ppm. HRMS (EI$^+$): calcd. for $[C_{16}H_{15}NO]^+$ m/z 237.1154; found 237.1147.

1-(2-Aminophenyl)-3-(4-methoxyphenyl)prop-2-yn-1-ol (7c): Following the general procedure afforded 66.6 mg (88%) of the desired product. ^{1}H NMR (300 MHz, DMSO): δ = 10.44 (s, 2 H), 7.47–7.37 (m, 3 H), 7.33 (td, J = 7.7, 1.3 Hz, 1 H), 7.09 (td, J = 7.5, 1.0 Hz, 1 H), 7.02–6.89 (m, 3 H), 6.57 (s, 1 H), 3.77 (s, 3 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 160.06, 150.62, 135.76, 133.37, 129.62, 124.69, 122.85, 119.25, 114.42, 114.28, 112.58, 87.78, 83.00, 68.23, 55.29 ppm. HRMS (EI$^+$): calcd. for $[C_{16}H_{15}NO_2]^+$ m/z 253.1103; found 253.1108.

1-(2-Aminophenyl)-3-(4-fluorophenyl)prop-2-yn-1-ol (7d): Following the general procedure afforded 47.4 mg (87%) of the desired product. ^{1}H NMR (300 MHz, DMSO): δ = 10.47 (s, 1 H), 7.56 (dd, J = 8.2, 5.6 Hz, 2 H), 7.41 (d, J = 7.5 Hz, 1 H), 7.34 (t, J = 7.7 Hz, 1 H), 7.24 (t, J = 8.6 Hz, 2 H), 7.10 (t, J = 7.5 Hz, 1 H), 6.97 (d, J = 7.9 Hz, 1 H), 6.61 (s, 1 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 164.09, 160.79, 150.49, 135.76, 134.22, 134.11, 129.71, 124.71, 122.89, 118.95, 117.19, 116.23, 115.93, 114.31, 86.54, 84.16, 68.04 ppm. HRMS (EI$^+$): calcd. for $[C_{15}H_{12}FNO]^+$ m/z 241.0903; found 241.0897.

1-(2-Aminophenyl)hex-2-yn-1-ol (7e): Following the general procedure afforded 41.3 mg (84%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.52 (s, 1 H), 7.36–7.24 (m, 2 H), 7.08 (t, J = 7.5 Hz, 1 H), 6.93 (d, J = 7.7 Hz, 1 H), 6.06 (s, 1 H), 2.26 (td, J = 7.0, 2.1 Hz, 2 H), 1.64–1.50 (m, 2 H), 0.99 (t, J = 7.4 Hz, 3

H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.34, 135.05, 129.78, 124.80, 123.59, 119.60, 114.75, 90.77, 74.53, 69.80, 21.77, 20.84, 13.51 ppm. HRMS (EI$^+$): calcd. for $[C_{12}H_{15}NO]^+$ *m*/*z* 189.1154; found 189.1160.

1-(2-Aminophenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (7f): Following the general procedure afforded 30.9 mg (75%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.17 (s, 1 H), 7.40–7.25 (m, 1 H), 7.11 (td, *J* = 7.6, 1.0 Hz, 1 H), 6.91 (d, *J* = 7.9 Hz, 1 H), 6.08 (s, 1 H), 0.21 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.85, 135.10, 130.04, 125.06, 123.81, 118.77, 114.72, 98.27, 95.40, 69.74, –0.25 ppm. HRMS (EI$^+$): calcd. for $[C_{12}H_{15}NOSi]^+$ *m*/*z* 217.0923; found 219.1073.

1-(2-Aminophenyl)-4-(benzyloxy)but-2-yn-1-ol (7g): Following the general procedure afforded 76.4 mg (90%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.46 (s, 1 H), 7.42–7.17 (m, 7 H), 7.08 (t, *J* = 7.5 Hz, 1 H), 6.93 (d, *J* = 7.9 Hz, 1 H), 6.11 (s, 1 H), 4.57 (d, *J* = 1.2 Hz, 2 H), 4.25 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.09, 134.86, 130.08, 128.55, 128.22, 128.06, 124.78, 123.81, 118.61, 114.92, 85.70, 80.71, 71.89, 69.31, 57.25 ppm. HRMS (EI$^+$): calcd. for $[C_{17}H_{17}NO_2]^+$ *m*/*z* 267.1259; found 267.1254.

1-(2-Aminophenyl)-5-(benzyloxy)pent-2-yn-1-ol (7h): The Boc protection was cleaved by using the general procedure. The product was not purified at this stage. After checking the ^{1}H NMR spectra the crude product was dissolved in CH_2Cl_2 and oxidized according to the general procedure.

1-(2-Aminophenyl)-4-(benzyloxy)oct-2-yn-1-ol (7i): Following the general procedure afforded 21.4 mg (62%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.25 (s, 1 H), 7.42–7.23 (m, 7 H), 7.19–7.02 (m, 1 H), 6.93 (d, *J* = 7.8 Hz, 1 H), 6.14 (s, 1 H), 4.76 (dd, *J* = 11.7, 8.3 Hz, 1 H), 4.48 (dd, *J* = 11.7, 5.5 Hz, 1 H), 4.18 (td, *J* = 6.6, 1.2 Hz, 1 H), 1.77 (dq, *J* = 13.5, 6.8 Hz, 2 H), 1.55–1.19 (m, 6 H), 0.88 (td, *J* = 7.2, 3.0 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.90, 137.80, 135.06, 130.10, 128.51, 128.13, 127.87, 124.89, 123.84, 119.01, 114.80, 89.17, 79.88, 70.91, 69.46, 68.77, 35.26, 27.51, 22.45, 14.06 ppm. HRMS (EI$^+$): calcd. for $[C_{21}H_{25}NO_2]^+$ *m*/*z* 323.1885; found 323.1877.

1-(2-Aminophenyl)-4-(*tert*-butoxy)pent-2-yn-1-ol (7j): Following the general procedure afforded 41.3 mg (77%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.52 (s, 1 H), 7.29 (t, *J* = 7.7 Hz, 2 H), 7.08 (t, *J* = 7.5 Hz, 1 H), 6.94 (d, *J* = 8.0 Hz, 1 H), 6.09 (s, 1 H), 4.37 (q, *J* = 6.4 Hz, 1 H), 1.41 (d, *J* = 6.7 Hz, 3 H), 1.23 (d, *J* = 7.5 Hz, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.13, 135.00, 129.87, 124.78, 123.62, 118.96, 114.73, 92.95, 75.09, 69.47, 57.69, 28.15, 24.01 ppm. HRMS (EI$^+$): calcd. for $[C_{15}H_{21}NO_2]^+$ *m*/*z* 247.1572; found 247.1581.

1-(2-Aminophenyl)-4-(benzyloxy)-4-methylpent-2-yn-1-ol (7k): Following the general procedure afforded 33.3 mg (52%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.26 (s, 1 H), 7.41–7.17 (m, 7 H), 7.08 (td, *J* = 7.6, 0.9 Hz, 1 H), 6.91 (dd, *J* = 8.2, 0.8 Hz, 1 H), 6.12 (s, 1 H), 4.60 (s, 2 H), 2.16 (s, 1 H), 1.58 (s, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.90, 138.73, 135.04, 130.06, 128.41, 127.82, 127.54, 124.82, 123.81, 118.96, 114.77, 92.11, 78.37, 70.80, 69.42, 66.90, 28.77 ppm. HRMS (EI$^+$): calcd. for $[C_{24}H_{29}NO_4]^+$ *m*/*z* 295.1572; found 295.1571.

General Procedure for the Oxidation of the Alcohols 8a–8k: Compound **7** was dissolved in CH_2Cl_2 (10 mL). MnO_2 (5 equiv.) was added to the solution. The mixture was mixed for 5 h. The oxidant was filtered and the solvent evaporated. The product was purified by flash chromatography with *n*-hexane and ethyl acetate (5:1) as eluent.

1-(2-Aminophenyl)-3-phenylprop-2-yn-1-one (8a): Following the general procedure afforded 69.1 mg (90%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (dd, *J* = 8.1, 1.2 Hz, 1 H), 7.68–7.61 (m, 2 H), 7.48–7.35 (m, 3 H), 7.29 (ddd, *J* = 8.5, 7.0, 1.6 Hz, 1 H), 6.71 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1 H), 6.66 (d, *J* = 8.4 Hz, 1 H), 6.40 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.52, 151.20, 135.38, 134.50, 132.84, 130.44, 128.66, 120.61, 118.92, 116.87, 116.16, 92.36, 87.22 ppm. HRMS (EI$^+$): calcd. for $[C_{15}H_{11}NO]^+$ *m*/*z* 221.0841; found 221.0842.

1-(2-Aminophenyl)-3-(*p*-tolyl)prop-2-yn-1-one (8b): Following the general procedure afforded 58.2 mg (90%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.18 (dd, *J* = 8.1, 1.3 Hz, 1 H), 7.59–7.51 (m, 2 H), 7.31 (ddd, *J* = 8.5, 7.1, 1.6 Hz, 1 H), 7.21 (dd, *J* = 8.5, 0.6 Hz, 2 H), 6.72 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1 H), 6.66 (dd, *J* = 8.3, 0.6 Hz, 1 H), 6.35 (s, 2 H), 2.40 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.61, 151.15, 141.06, 135.24, 134.48, 132.84, 129.44, 118.95, 117.46, 116.84, 116.09, 92.95, 87.02, 21.76 ppm. HRMS (EI$^+$): calcd. for $[C_{16}H_{13}NO]^+$ *m*/*z* 235.0997; found 235.1001.

1-(2-Aminophenyl)-3-(4-methoxyphenyl)prop-2-yn-1-one (8c): Following the general procedure afforded 44.8 mg (80%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (dd, *J* = 8.1, 1.5 Hz, 1 H), 7.69–7.53 (m, 2 H), 7.30 (ddd, *J* = 8.4, 7.1, 1.6 Hz, 1 H), 6.98–6.83 (m, 2 H), 6.71 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1 H), 6.65 (dd, *J* = 8.3, 0.5 Hz, 1 H), 6.37 (s, 2 H), 3.83 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.74, 161.48, 151.10, 135.19, 134.85, 134.50, 119.07, 116.87, 116.15, 114.43, 112.47, 93.38, 87.02, 55.50 ppm. HRMS (EI$^+$): calcd. for $[C_{16}H_{13}NO_2]^+$ *m*/*z* 251.0946; found 251.0949.

1-(2-Aminophenyl)-3-(4-fluorophenyl)prop-2-yn-1-one (8d): Following the general procedure afforded 40.3 mg (86%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14 (dd, *J* = 8.1, 1.6 Hz, 1 H), 7.71–7.59 (m, 2 H), 7.31 (ddd, *J* = 8.5, 7.0, 1.6 Hz, 1 H), 7.16–7.04 (m, 2 H), 6.79–6.62 (m, 2 H), 6.38 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.43, 165.56, 162.21, 151.23, 135.47, 135.18, 135.06, 134.47, 118.90, 116.92, 116.37, 116.24, 116.07, 91.30, 87.12 ppm. HRMS (EI$^+$): calcd. for $[C_{15}H_{10}FNO]^+$ *m*/*z* 239.0746; found 239.0737.

1-(2-Aminophenyl)hex-2-yn-1-one (8e): Following the general procedure afforded 30.9 mg (76%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (dd, *J* = 8.1, 1.5 Hz, 1 H), 7.27 (ddd, *J* = 8.5, 7.1, 1.6 Hz, 1 H), 6.67 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1 H), 6.62 (dd, *J* = 8.5, 0.8 Hz, 1 H), 6.31 (s, 2 H), 2.46 (t, *J* = 7.0 Hz, 2 H), 1.76–1.62 (m, 2 H), 1.07 (t, *J* = 7.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 180.02, 151.06, 135.11, 134.72, 118.97, 116.77, 116.06, 95.70, 80.10, 21.56, 21.26, 13.73 ppm. HRMS (EI$^+$): calcd. for $[C_{12}H_{13}NO]^+$ *m*/*z* 187.0997; found 187.0999.

1-(2-Aminophenyl)-3-(trimethylsilyl)prop-2-yn-1-one (8f): Following the general procedure afforded 26.4 mg (89%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (dd, *J* = 8.1, 1.6 Hz, 1 H), 7.35–7.23 (m, 1 H), 6.69 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1 H), 6.63 (dd, *J* = 8.4, 0.8 Hz, 1 H), 6.32 (s, 2 H), 0.30 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.21, 151.26, 135.47, 134.77, 118.68, 116.79, 116.23, 101.33, 99.40, –0.46 ppm. HRMS (EI$^+$): calcd. for $[C_{12}H_{15}NOSi]^+$ *m*/*z* 217.0923; found 217.0912.

1-(2-Aminophenyl)-4-(benzyloxy)but-2-yn-1-one (8g): Following the general procedure afforded 41.5 mg (63%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04 (dd, *J* = 8.1, 1.6 Hz, 1 H), 7.44–7.20 (m, 6 H), 6.75–6.58 (m, 2 H), 6.34 (s, 2 H), 4.68 (s, 2 H), 4.43 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.87, 151.24, 136.99, 135.55, 134.59, 128.64, 128.26, 128.20, 118.46, 116.82,

116.23, 89.27, 84.56, 72.23, 57.35 ppm. HRMS (EI^+): calcd. for $[C_{17}H_{15}NO_2]^+$ *m/z* 265.1103; found 265.1092.

1-(2-Aminophenyl)-5-(benzyloxy)pent-2-yn-1-one (8h): Following the general procedure afforded 20.3 mg (44%) of the desired product, yield was calculated from the amount of **6h**. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.08 (dd, J = 8.3, 1.1 Hz, 1 H), 7.41–7.19 (m, 3 H), 6.62 (t, J = 7.8 Hz, 1 H), 6.29 (s, 1 H), 4.59 (s, 1 H), 3.72 (t, J = 6.7 Hz, 1 H), 2.78 (t, J = 6.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.71, 151.07, 137.96, 135.25, 134.87, 128.60, 127.91, 127.83, 118.90, 116.74, 116.16, 92.22, 80.57, 73.27, 67.58, 20.86 ppm. HRMS (EI^+): calcd. for $[C_{18}H_{17}NO_2]^+$ *m/z* 279.1259; found 279.1261.

1-(2-Aminophenyl)-4-(benzyloxy)oct-2-yn-1-one (8i): Following the general procedure afforded 21.4 mg (83%) of the desired product. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.05 (d, J = 6.6 Hz, 1 H), 7.46–7.20 (m, 7 H), 6.75–6.58 (m, 2 H), 6.33 (s, 2 H), 4.87 (d, J = 11.7 Hz, 1 H), 4.58 (d, J = 11.7 Hz, 1 H), 4.35 (t, J = 6.6 Hz, 1 H), 1.97–1.82 (m, 2 H), 1.62–1.44 (m, 2 H), 1.35 (dd, J = 14.9, 7.2 Hz, 2 H), 0.92 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.18, 151.23, 137.66, 135.50, 134.60, 128.59, 128.16, 128.00, 118.73, 116.86, 116.26, 92.63, 83.97, 71.33, 68.94, 35.11, 27.57, 22.49, 14.06 ppm. HRMS (EI^+): calcd. for $[C_{21}H_{23}NO_2]^+$ *m/z* 321.1729; found 321.1743.

1-(2-Aminophenyl)-4-(*tert*-butoxy)pent-2-yn-1-one (8j): Following the general procedure afforded 36.2 mg (91%) of the desired product. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.05 (dd, J = 8.1, 0.7 Hz, 1 H), 7.28 (ddd, J = 8.5, 7.1, 1.6 Hz, 1 H), 6.73–6.59 (m, 2 H), 6.35 (s, 2 H), 4.52 (q, J = 6.7 Hz, 1 H), 1.50 (d, J = 6.7 Hz, 3 H), 1.30 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.43, 151.13, 135.27, 134.60, 118.70, 116.75, 116.04, 96.35, 81.65, 75.26, 57.81, 28.17, 23.64 ppm. HRMS (EI^+): calcd. for $[C_{15}H_{19}NO_2]^+$ *m/z* 245.1416; found 245.1422.

1-(2-Aminophenyl)-4-(benzyloxy)-4-methylpent-2-yn-1-one (8k): Following the general procedure afforded 24.9 mg (80%) of the desired product. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.00 (dd, J = 8.3, 1.5 Hz, 1 H), 7.45–7.19 (m, 6 H), 6.70–6.54 (m, 2 H), 6.33 (s, 2 H), 4.72 (s, 2 H), 1.68 (s, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.24, 151.22, 138.56, 135.47, 134.49, 128.52, 127.83, 127.69, 118.70, 116.87, 116.22, 95.21, 82.55, 71.03, 67.29, 28.54 ppm. HRMS (EI^+): calcd. for $[C_{19}H_{19}NO_2]^+$ *m/z* 293.1416; found 293.1420.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra, catalysis of *N*-Boc-protected substrate, computational details including *XYZ* parameters of computed structures.

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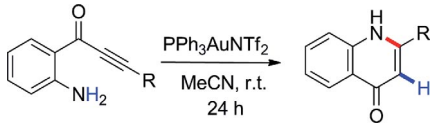
Gold Catalysis



R = alkyl, aryl

10 examples
up to 96% yield

A mild and atom-economic gold-catalyzed route from aryl- and alkyl-substituted 1-(*o*-aminophenyl)-2-propyn-1-ones to form 2-substituted 4-quinolones has been developed. Cationic gold(I) catalysts were found to be most efficient in direct alkyne activation for hydroamination reactions.

Keywords: Synthetic methods / Homogeneous catalysis / Hydroamination / Gold / Density functional calculations

