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# Cu-Catalyzed Cascade Annulation of Alkynols with 2-Azidobenzaldehydes: Access to 6*H*-Isochromeno[4,3-*c*]quinoline

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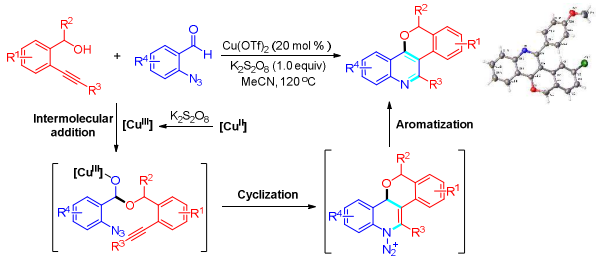



**Abstract:** A copper-catalyzed cascade reaction of alkynols and 2-azidobenzaldehydes has been achieved, giving 6*H*-isochromeno[4,3-*c*]quinoline in yields of 40 to 81%. This reaction provides a novel, concise strategy for rapidly constructing compounds with fused *N*- and *O*-containing heterocycles. In contrast to previously reported reactions of alkynols in which the first step is intramolecular cycloisomerization, the first step in this novel reaction of alkynols is entropically unfavorable intermolecular addition. The resulting hemiacetal intermediate then undergoes intramolecular cyclization and aromatization to afford the product.

Quinoline alkaloids have attracted extensive attention due to their useful biological activities and interesting properties.[1] Of particular interest are pyrano[3,2-*c*]quinoline derivatives, which are present in several biologically active molecules.[2] For example, 5-phenyl-pyrano[3,2-*c*]quinoline-6-chlorotacrine hybrid **I** can inhibit acetylcholinesterase (AChE) as well as butyrylcholinesterase (BChE).[2e] Molecule **II**, extracted from a strain of *Chaetomium funicola*, inhibits metallo-β-lactamases.[2f] Distomadine **III**, isolated from the New Zealand ascidian *Pseudodistoma aureum*, exhibits mild antifungal activity (Fig. 1).[2g]

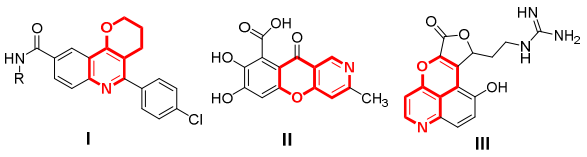


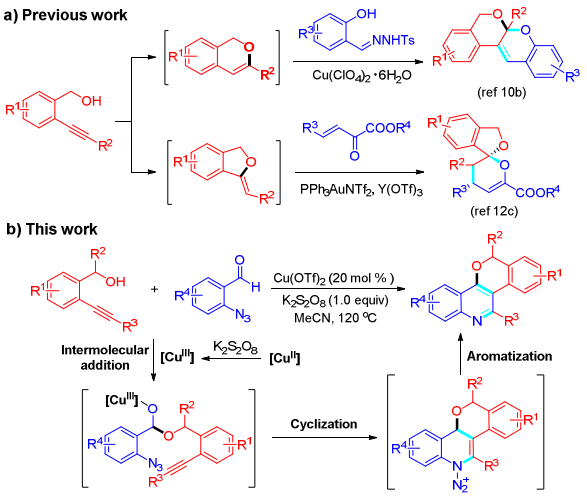

**Figure 1.** Biologically active molecules containing a pyrano[3,2-*c*]quinoline motif.

Several groups have made extensive efforts to synthesize pyrano[3,2-*c*]quinoline derivatives efficiently, and most of the syntheses reported so far require multiple steps because of the difficulty in simultaneously constructing pyridine and pyran rings. Recently, Flynn and co-workers generated these compounds via $I_2$-catalyzed cyclization of N-(*o*-alkynolphenyl)imines.[3] Wang and co-workers generated them via thermolysis of 1-isocyanato-2-(5-methoxypent-1-yn-1-yl)benzene, but this method requires harsh conditions and gives only low yield (9%).[4a] Therefore, more concise and efficient synthetic routes to pyrano[3,2-*c*]quinoline derivatives are needed.

One approach to developing such syntheses may lie in transition metal-catalyzed cascade transformation of alkynols. Such transformations are useful for constructing

O-containing heterocyclic compounds, including natural products and drugs.[5-13] Most of these reactions are catalyzed by tungsten,[6] gold,[7] platinum,[8] palladium,[9] and copper catalysts.[10] The typical approach is to subject alkynols to intramolecular cycloisomerization in order to yield highly reactive *endo*- or *exo*-cyclic enol ether intermediates. These intermediates subsequently undergo diverse transformations such as Prins-type cyclization[11], Diels-Alder reaction,[12] and Povarov reaction.[13] Since this approach usually involves addition to a C=C bond of *endo*- or *exo*-cyclic enol ethers, the resulting derivatives are limited to those having *endo*- or *exo*-cyclic enol ethers as the basic skeleton (Scheme 1a).[14] It is possible that other types of intermediates and therefore products can be generated by subjecting alkynols to intermolecular reactions with other types of reactants. However, intermolecular addition of alkynols is entropically unfavorable, making this approach challenging.

**Scheme 1.** Cascade reactions of alkynols

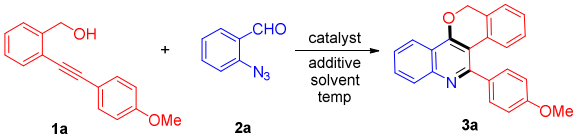



Here we report a copper-catalyzed cascade annulation of alkynols with 2-azidobenzaldehydes, in which the first step is the entropically unfavorable intermolecular addition of a hydroxyl group to the aldehyde group. This

unprecedented reaction provides a concise method for constructing the 6*H*-isochromeno[4,3-*c*]quinoline skeleton in moderate to good yields. The reaction combines intermolecular addition, intramolecular cyclization and aromatization in a single operation (Scheme 1b). This new strategy avoids intramolecular cycloisomerization of internal alkynols and connects two substrates in the first step to promote subsequent tandem annulation.

As shown in Table 1, our study started with the $Cu(OTf)_2$-mediated reaction of internal alkynol **1a** with 2-azidobenzaldehyde **2a** at 80 $^oC$ in acetonitrile. Using 0.2 equiv of $Cu(OTf)_2$ gave the corresponding product **3a** in 10% isolated yield (entry 1). Then we screened various reaction conditions to optimize the catalytic process. The solvents toluene, DMF, and THF were ineffective for this reaction (entries 2-4). Screening of additives showed that $K_2S_2O_8$ substantially improved yield from 10% to 59% (entry 5). Lowering catalyst load to 0.1 equiv or increasing the dosage of $K_2S_2O_8$ to 2 equiv was ineffective (entries 6 and 7). Reversing the ratio of **1a** : **2a** to 1.2 : 1 made the reaction more efficient, affording product in 74% yield (entry 8), which was increased to 81% by raising the temperature to 120 $^oC$ (entry 9). Decreasing additive loading to 20 mol% reduced the yield from 81% to 40% (entry 10). The catalysts $Sc(OTf)_3$, AgOTf, and $In(OTf)_3$ gave product **3a** in yields of 55-62% (entries 11-13). No product was detected using $Cu(OAc)_2$, demonstrating the importance of the trifluoromethanesulfonic anion in the reaction (entry 14). Other oxidizing agents did not deliver better results than $K_2S_2O_8$ (entries 15-17).

**Table 1.** Optimization of reaction conditions.[a]



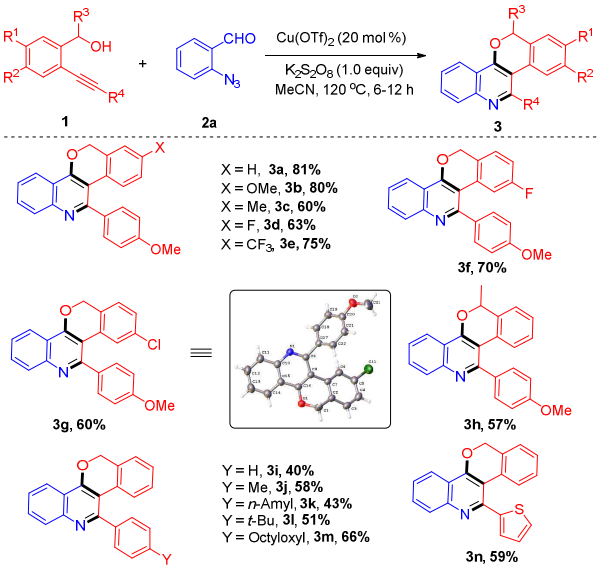

| entry | catalyst | additive | solvent | temp (°C) | yield (%)[b] |
|---|---|---|---|---|---|
| 1 | $Cu(OTf)_2$ | - | MeCN | 80 | 10 |
| 2 | $Cu(OTf)_2$ | - | Toluene | 80 | 0 |
| 3 | $Cu(OTf)_2$ | - | DMF | 80 | 0 |
| 4 | $Cu(OTf)_2$ | - | THF | 80 | 0 |
| 5 | $Cu(OTf)_2$ | $K_2S_2O_8$ | MeCN | 80 | 59 |
| 6[c] | $Cu(OTf)_2$ | $K_2S_2O_8$ | MeCN | 80 | 40 |
| 7[d] | $Cu(OTf)_2$ | $K_2S_2O_8$ | MeCN | 80 | 47 |
| 8[e] | $Cu(OTf)_2$ | $K_2S_2O_8$ | MeCN | 80 | 74 |
| 9[e] | $Cu(OTf)_2$ | $K_2S_2O_8$ | MeCN | 120 | 81 |
| 10[e,f] | $Cu(OTf)_2$ | $K_2S_2O_8$ | MeCN | 120 | 40 |
| 11[e] | $Sc(OTf)_3$ | $K_2S_2O_8$ | MeCN | 120 | 60 |
| 12[e] | AgOTf | $K_2S_2O_8$ | MeCN | 120 | 55 |
| 13[e] | $In(OTf)_3$ | $K_2S_2O_8$ | MeCN | 120 | 62 |
| 14[e] | $Cu(OAc)_2$ | $K_2S_2O_8$ | MeCN | 120 | 0 |
| 15[e] | $Cu(OTf)_2$ | $(NH_4)_2S_2O_8$ | MeCN | 120 | 64 |
| 16[e] | $Cu(OTf)_2$ | DDQ | MeCN | 120 | trace |
| 17[e] | $Cu(OTf)_2$ | $Cu(OAc)_2$ | MeCN | 120 | 0 |
| 18[e] | $Cu(OTf)_2$ | BQ | MeCN | 120 | trace |
| 19[e] | $Cu(OTf)_2$ | *t*-BuOOH | MeCN | 120 | 21 |

[a]Reactions were performed in sealed tubes containing **1a** (0.2 mmol), **2a** (0.24 mmol), catalyst (0.04 mmol), additive (0.2 mmol), and solvent (2 mL) under Ar, unless noted otherwise. [b]Isolated yield. [c]$K_2S_2O_8$ (0.4 mmol) was used. [d]$Cu(OTf)_2$ (0.02 mmol) was used. [e]**1a** (0.24 mmol) and **2a** (0.2 mmol) were used. [f]$K_2S_2O_8$ (0.04 mmol) was used.

Using the optimized conditions for this cascade reaction, we evaluated the substrate scope. First we examined the ability of various substituted alkynols **1** to react with 2-azidobenzaldehyde (Scheme 2). A substrate carrying a methoxyl group at the $R^1$ position reacted smoothly, generating **3b** in 80% yield. Placing Me and F at the $R^1$ position hampered the reaction slightly, generating **3c** in 60% yield and **3d** in 63% yield. Placing the electron-withdrawing group $CF_3$ at the same position efficiently

generated product **3e** in 75% yield. Internal alkynols bearing F and Cl at the $R^2$ position also participated in the reaction, generating product **3f** in 70% yield and **3g** in 60% yield. The structure of product **3g** was confirmed by single-crystal X-ray diffraction analysis (see Supporting Information). A substrate with Me at the $R^3$ position gave the product **3h** in 57% yield.

**Scheme 2. Scope of Alkynols 1**[a]

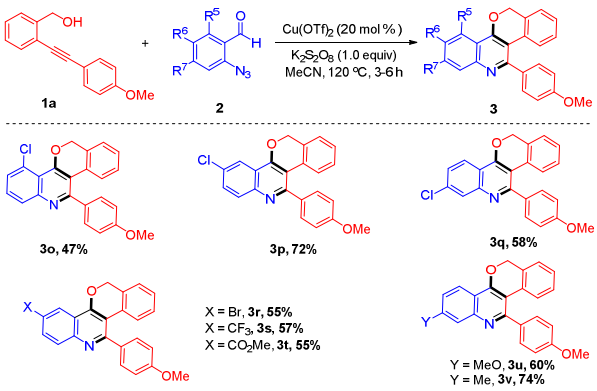



[a]Reactions were conducted at 120 °C for 6-12 h using **1** (0.24 mmol), **2a** (0.2 mmol), $Cu(OTf)_2$ (0.04 mmol), $K_2S_2O_8$ (0.2 mmol), and acetonitrile (2 mL). Isolated yields are shown.

The reaction also proceeded with (2-(phenylethynyl)phenyl)methanol, giving **3i** in 40% yield. These results illustrate the importance of an electron-donating group at the $R^4$ position. Using (2-(*p*-tolylethynyl)phenyl)methanol led to **3j** in 58% yield; 4-pentylphenyl alkynols also reacted, though the corresponding product **3k** was generated in only 43% yield. The substrates 4-(*tert*-butyl) and 4-octyloxy alkynols generated **3l** in 51% yield and **3m** in 66% yield. An alkynol containing the

heterocyclic thiophenyl group afforded **3n** in 59% yield. Note that alkynol substituted with alkyl group such as (2-(hex-1-yn-1-yl)phenyl)methanol ($R^4$ = butyl) did not reacted with **2a** under standard conditions.

**Scheme 3. Scope of 2-Azidobenzaldehyde 2**[a]



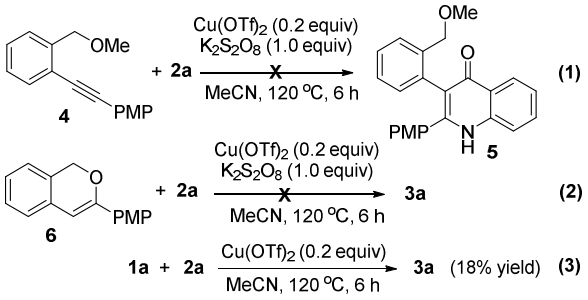

[a]Reactions were conducted at 120 °C for 3-6 h using **1a** (0.24 mmol), **2** (0.2 mmol), $Cu(OTf)_2$ (0.04 mmol), $K_2S_2O_8$ (0.2 mmol), and acetonitrile (2 mL). Isolated yields are shown.

To explore the full scope of the reaction, we examined the ability of 2-azidobenzaldehyde to react with internal alkynol **1** (Scheme 3). The substrate 2-azidobenzaldehyde with Cl groups at the $R^5$, $R^6$ or $R^7$ position afforded products **3o-3q** in 47-72% yields. Substrates carrying Br at the $R^6$ position generated **3r** in 55% yield. Placing the electron-withdrawing groups $CF_3$ or methyl ester at the same position provided **3s** in 57% yield and **3t** in 55% yield. Placing the electron-donating groups OMe or Me at the $R^7$ position afforded **3u** in 60% yield and **3v** in 74% yield.

We performed some experiments to clarify the mechanism of this cascade reaction (Scheme 4). Firstly, the reaction of **4** and **2a** was carried out but no reaction proceeded (eq 1), which expelled the possibility of the rearrangement of **2a** to imino ketene and

the following formal [4+2] cycloaddition to form the product **5**. The standard reaction of **1a** and **2a** in the presence of 1 equiv. of 2,4,6-tri-tert-butylphenol produced **3a** in 62% yield, which expelled the possibility of radical process for this reaction.

**Scheme 4. Mechanistic Investigations**




Next, we reacted **1a** under standard conditions and obtained the cycloisomerization product **6** only in 8% yield, whereas we observed no product when we reacted **2a** with the *endo*-cyclic enol ether **6** under the same conditions (eq 2). This demonstrates that the reaction proceeds via intermolecular alkynol cyclization, rather than intramolecular cycloisomerization. Moreover, the control reaction of **1a** and **2a** under standard reaction conditions without $K_2S_2O_8$ only gave **3a** in 18% yield (eq 3), indicating that $Cu(OTf)_2$ was not the active catalyst for this reaction. Similarly, the Lewis acid $AlCl_3$ and Brønsted acid HOTf were also tested as the catalysts in this reaction, 15% and 20% yields were obtained respectively, illustrating conventional acids can promote this reaction although not so effecitive. Lewis acid $ZnCl_2$ (20 mol%) was also tested with 1 equiv. $K_2S_2O_8$ and the product **3a** was obtained in 30% yield.

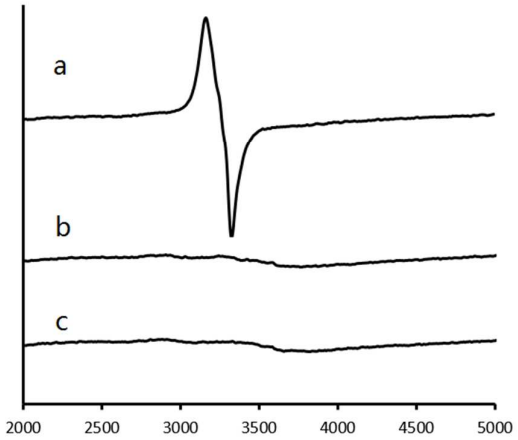
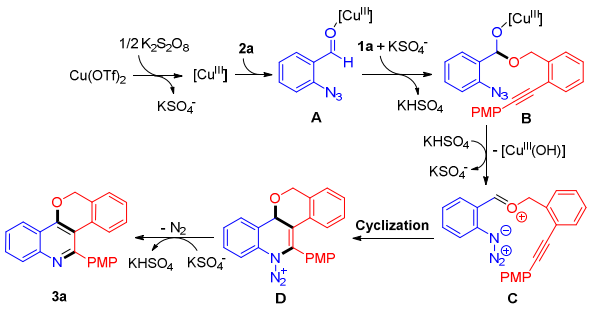



**Figure 2.** Line a: $Cu(OTf)_2$ (0.02 mmol) in MeCN at 120 $^oC$ for 1 h. Line b: $Cu(OTf)_2$ (0.02 mmol) and $K_2S_2O_8$ (0.1 mmol) in MeCN at 120 $^oC$ for 1 h. Line c: **1a** (0.12 mmol) and **2a** (0.1 mmol) was reacted at 120 $^oC$ for 1 h with $Cu(OTf)_2$ (0.02 mmol) and $K_2S_2O_8$ (0.1 mmol) in MeCN.

To clarify the active catalyst and the role of $K_2S_2O_8$ in the cascade reaction (Figure 2), we explored control experiments monitored by electron paramagnetic resonance (EPR). When $Cu(OTf)_2$ was stirred in MeCN at 120 $^oC$ for 1 h, the EPR signal of Cu(II) could be clearly seen (Fig. 2, line a). However, when the mixture of $Cu(OTf)_2$ and excess $K_2S_2O_8$ was stirred at the same condition, the signal of Cu(II) disappeared, suggesting that Cu(II) species was oxidized to Cu(III) (Fig. 2, line b). Next, under standard conditions to form **3a**, an EPR spectra line c similar to line b was obtained, indicating that Cu(III) species may be the active catalyst for this cascade reaction (Fig. 2, line c).

**Scheme 5. Proposed Mechanism**




On the basis of these mechanistic studies, we propose a tentative mechanism for this copper-promoted cascade reaction of internal alkynol and 2-azidobenzaldehyde to generate 6*H*-isochromeno[4,3-*c*]quinoline (Scheme 5). Firstly, with the oxidization of $K_2S_2O_8$, Cu(II) was transformed into Cu(III). Then coordination between the carbonyl of **2a** and Cu(III) (**A**) enhances electrophilicity of the aldehyde. Next the hydroxyl group adds to the electro-deficient aldehyde, producing unstable intermediate **B**. Acidic conditions convert **B** into **C**, and subsequent intramolecular cyclization of **C** generates intermediate **D**, which undergoes aromatization to form the product **3a.**

In summary, we have developed a new copper-catalyzed cascade annulation of alkynol and 2-azidobenzaldehyde to give 6*H*-isochromeno[4,3-*c*]quinoline in moderate to good yields. The first step in this novel approach is entropically unfavorable intermolecular addition, instead of conventional intramolecular cycloisomerization. The resulting hemiacetal intermediate undergoes intramolecular cyclization and aromatization to afford the product. This new strategy may allow the development of new cascade reactions involving alkynols, as well as the straightforward construction of highly diverse heterocyclic skeletons.

**Experimental Section**

All manipulations were carried out under a nitrogen or argon atmosphere using standard Schlenk techniques, unless otherwise stated. Solvents were distilled under nitrogen from sodium-benzophenone (THF, toluene, dioxane) or calcium hydride (MeCN, $CH_3NO_2$, DMF, DCE). Other chemicals were obtained from commercial sources, and were used without further purification. The alkynols[15] and s2-azidobenzaldehydes[16] were prepared according to the literature methods. Chemical shifts (δ, ppm) in the $^1H$ NMR spectra were recorded using TMS as internal standard. Chemical shifts in $^{13}C\{^1H\}$ NMR spectra were internally referenced to $CDCl_3$ (δ = 77.16 ppm). EPR spectra were recorded on a Bruker BioSpin GmbH spectrometer. The sample was taken out into a thin small tube and then detected by EPR spectrometer at indicated temperature and parameters.

**General procedure for the ERP analysis.**

After 1 h, the solution sample was taken out into a small tube and then analyzed by EPR. EPR spectra was recorded at room temperature on EPR spectrometer operated at 9.870 GHz. Typical spectrometer parameters are shown as follows, sweep width: 3000G; center field sets: 3500G; time constant: 163.84 ms; sweep time: 41.943 s; modulation amplitude: 4.0 G; modulation frequency: 100 kHz; receiver gain: 7.1 x $10^4$; microwave power: 2.016 mW.

**Typical Experimental Procedure for 3 (3a as an example).**

To a mixture of internal alkynol **1a** (57.12 mg, 0.24 mmol) and 2-azidobenzaldehyde **2a** (29.4 mg, 0.2 mmol) in $CH_3CN$ (2 mL) was added the copper(II) trifluoromethanesulfonate (14.4 mg, 0.04mmol), $K_2S_2O_8$ (54 mg, 0.2 mmol)

under Ar. The reaction mixture was stirred at 120 $^{o}$C for 6 hours and the progress was monitored using TLC detection. After completion of present reaction, the solvent was extracted with ethyl acetate. The combined organic layers were washed with $H_2O$, $NH_4Cl$ and brine, dried over $MgSO_4$, filtrated, and evaporated. After that the crude product was passed through flash column chromatography on silica gel to afford the desired products **3a.**

*11-(4-Methoxyphenyl)-6H-isochromeno[4,3-c]quinoline* (**3a**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3a** was obtained in 81% yield (55 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.10 (d, $J$ = 8.28 Hz, 1H), 7.98 (d, $J$ = 8.40 Hz, 1H), 7.58-7.62 (m, 3H), 7.38-7.41 (m, 1H), 7.09-7.17 (m, 2H), 6.94-6.98 (m, 1H), 6.88 (d, $J$ =8.76 Hz, 2H), 6.84 (d, $J$ =7.92 Hz, 1H), 5.24 (s, 2H), 3.78 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 160.3, 159.3, 157.6, 148.0, 134.0, 131.1, 130.5, 130.4, 129.6, 129.1, 128.0, 127.1, 126.5, 125.8, 124.9, 121.9, 119.4, 114.2, 112.9, 69.8, 55.5; HRMS (EI, TOF): caled for $C_{24}H_{19}NO_3^{+}$ $[M]^{+}$: 369.1365, found: 369.1366.

*8-Methoxy-11-(4-methoxyphenyl)-6H-isochromeno[4,3-c]quinoline* (**3b**). The compound was prepared from (5-methoxy-2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3b** was obtained in 80% yield (59 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl

acetate 5:1 v/v); $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.16 (d, $J$ = 8.24 Hz, 1H), 8.04 (d, $J$ = 8.44 Hz, 1H), 7.64-7.67 (m, 3H), 7.46 (t, $J$ = 7.88 Hz, 1H), 6.96 (d, $J$ = 8.64 Hz, 2H), 6.82 (d, $J$ =8.76 Hz, 1H), 6.76 (d, $J$ =2.56 Hz, 1H), 6.59 (dd, $J_1$ =8.76 Hz, $J_2$ =2.60 Hz, 1H), 5.28 (s, 2H), 3.87 (s, 3H), 3.79 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 160.2, 158.8, 158.2, 157.1, 147.5, 134.0, 132.2, 130.9, 129.8, 128.9, 127.9, 125.7, 122.0, 121.6, 119.4, 114.1, 113.4, 112.9, 110.4, 69.7, 55.4, 55.3; HRMS (EI, TOF): caled for $C_{24}H_{19}NO_3^+$ $[M]^+$: 369.1365, found: 369.1366.

*11-(4-Methoxyphenyl)-8-methyl-6H-isochromeno[4,3-c]quinoline* (**3c**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)-5-methylphenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3c** was obtained in 60% yield (42 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.17 (dd, $J_1$ = 8.28 Hz, $J_2$ = 0.80 Hz, 1H), 8.04 (d, $J$ = 8.36 Hz, 1H), 7.64-7.69 (m, 3H), 7.45-7.49 (m, 1H), 7.04 (s,, 1H), 6.96 (d, $J$ =8.72 Hz, 2H), 6.86 (d, $J$ =8.12 Hz, 1H), 6.79 (d, $J$ =8.12 Hz, 1H), 5.29 (s, 2H), 3.87 (s, 3H), 2.34 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$160.2, 158.9, 157.4, 147.8, 137.0, 134.1, 131.0, 130.5, 130.0, 128.9, 128.7, 126.7, 126.4, 125.7, 125.5, 121.7, 119.4, 114.1, 112.9, 69.5, 55.4, 21.1; HRMS (EI, TOF): caled for $C_{24}H_{19}NO_2^+$ $[M]^+$: 353.1416, found: 353.1409.

*8-Fluoro-11-(4-methoxyphenyl)-6H-isochromeno[4,3-c]quinoline* (**3d**). The compound was prepared from (5-fluoro-2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azidobenzaldehyde

following the general procedure. The product **3d** was obtained in 63% yield (45 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.17 (dd, $J_1$ = 8.24 Hz, $J_2$ = 0.64 Hz, 1H), 8.05 (d, $J$ = 8.40 Hz, 1H), 7.66-7.70 (m, 1H), 7.64 (d, $J$ = 8.68 Hz, 2H), 7.48 (t, $J$ = 7.60 Hz, 1H), 6.97 (d, $J$ = 8.72 Hz, 2H), 6.94 (d, $J$ =2.56 Hz, 1H), 6.89 (d, $J$ = 5.36 Hz, 1H), 6.87 (d, $J$ = 5.36 Hz, 1H), 5.29 (s, 2H), 3.87 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 162.9, 160.5, 160.3, 158.7, 157.2, 147.9, 133.7, 132.6, 132.5, 131.0, 130.3, 129.0, 128.4, 128.3, 125.9, 125.7, 125.6, 121.7, 119.2, 115.1, 114.9, 114.2, 112.3, 112.0, 111.8, 69.2, 55.4; HRMS (EI, TOF): caled for $C_{23}H_{16}FNO_2^+$ $[M]^+$: 357.1165, found: 357.1164.

*11-(4-Methoxyphenyl)-8-(trifluoromethyl)-6H-isochromeno[4,3-c]quinoline* (**3e**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)-5-(trifluoromethyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3e** was obtained in 75% yield (61 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.19 (d, $J$ = 7.60 Hz, 1H), 8.07 (d, $J$ = 8.40 Hz, 1H), 7.72 (t, $J$ = 7.00 Hz, 1H), 7.64 (d, $J$ =8.68 Hz, 2H), 7.48-7.52 (m, 2H), 7.30 (d, $J$ = 8.24 Hz, 1H), 7.01 (d, $J$ = 8.52 Hz, 1H), 6.98 (d, $J$ =8.68 Hz, 2H), 5.37 (s, 2H), 3.88 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 106.6, 160.1, 157.5, 148.3, 133.3, 133.2, 131.1, 131.0, 130.6, 129.1, 126.6, 126.1, 125.0, 124.9, 122.0, 121.9, 121.9, 119.4, 114.4, 111.9, 69.4, 55.5; HRMS (EI, TOF): caled for $C_{24}H_{16}F_3NO_2^+$ $[M]^+$: 407.1133, found: 407.1131.

*9-Fluoro-11-(4-methoxyphenyl)-6H-isochromeno[4,3-c]quinoline* (**3f**). The compound was prepared from (4-fluoro-2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3f** was obtained in 70% yield (50 mg) as a yellow solid after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); Mp: 150-152 $^{o}$C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.19 (d, $J$ = 8.20 Hz, 1H), 8.06 (d, $J$ = 8.40 Hz, 1H), 7.70 (t, $J$ = 7.60 Hz,, 1H), 7.66 (d, $J$ = 8.40 Hz, 2H), 7.49 (t, $J$ = 7.16 Hz,, 1H), 7.19-7.22 (m, 1H), 6.99 (d, $J$ =8.44 Hz, 2H), 6.88-6.93 (m, 1H), 6.60 (dd, $J_1$ = 10.88 Hz, $J_2$ = 2.40 Hz, 1H), 5.30 (s, 2H), 3.88 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 163.6, 161.2, 160.5, 159.4, 157.4, 148.1, 133.2, 131.7, 131.6, 131.0, 130.7, 129.1, 126.3, 126.2, 125.9, 121.9, 119.1, 114.3, 114.1, 113.8, 113.5, 113.2, 112.1, 112.0, 69.2, 55.4; HRMS (EI, TOF): caled for $C_{23}H_{16}FNO_2^+$ $[M]^+$: 357.1165, found: 357.1167.

*9-Chloro-11-(4-methoxyphenyl)-6H-isochromeno[4,3-c]quinoline* (**3g**). The compound was prepared from (4-chloro-2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3g** was obtained in 60% yield (45 mg) as a yellow solid after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); Mp: 173-176 $^{o}$C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.20 (dd, $J_1$ = 8.28 Hz, $J_2$ = 0.80 Hz, 1H), 8.08 (d, $J$ = 8.40 Hz, 1H), 7.73 (t, $J$ = 7.60 Hz, 1H), 7.67 (d, $J$ = 8.76 Hz, 2H), 7.49-7.54 (m, 1H), 7.20 (d, $J$ = 1.04 Hz, 2H), 7.02 (d, $J$ =8.76 Hz, 2H), 6.87 (s, 1H), 5.32 (s, 2H), 3.91 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$

160.6, 159.6, 157.4, 148.3, 133.9, 133.3, 131.4, 131.0, 130.7, 129.2, 128.6, 127.0, 126.5, 126.1, 125.9, 121.9, 119.2, 114.4, 111.9, 69.2, 55.6; HRMS (EI, TOF): caled for $C_{23}H_{16}ClNO_2^+$ $[M]^+$: 373.0870, found: 373.0866.

*11-(4-Methoxyphenyl)-6-methyl-6H-isochromeno[4,3-c]quinoline* (**3h**). The compound was prepared from 1-(2-((4-methoxyphenyl)ethynyl)phenyl)ethan-1-ol and 2-azidobenzaldehyde following the general procedure. The product **3h** was obtained in 57% yield (40 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^1$H NMR (400 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 8.21 (d, $J$ = 7.96 Hz, 1H), 8.05 (d, $J$ = 8.32 Hz, 1H), 7.66-7.70 (m, 3H), 7.49-7.46 (m, 1H), 7.22-7.25 (m, 2H), 7.02-7.06 (m, 1H), 6.94-6.98 (m, 3H), 5.45 (q, $J$ = 6.56 Hz, 2H), 3.84 (s, 3H). 1.87 (d, $J$ = 6.56 Hz, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^o$C): 160.3, 158.2, 157.4, 148.0, 134.8, 134.1, 131.1, 130.3, 129.0, 128.9, 127.6, 127.3, 126.8, 125.7, 123.6, 121.9, 119.7, 114.2, 112.7, 75.2, 55.5, 18.9; HRMS (EI, TOF): caled for $C_{24}H_{19}NO_2^+$ $[M]^+$: 353.1416, found: 353.1415.

*1-Phenyl-6H-isochromeno[4,3-c]quinoline* (**3i**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3i** was obtained in 40% yield (25 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 25:1 v/v); $^1$H NMR (400 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 8.21 (dd, $J_1$ = 8.24 Hz, $J_2$ = 0.76 Hz, 1H), 8.08 (d, $J$ = 8.44 Hz, 1H), 7.68-7.73 (m, 3H), 7.48-7.52 (m, 1H), 7.43-7.45 (m, 3H), 7.18-7.23 (m, 2H), 6.99-7.03 (m, 1H), 6.82 (d, $J$ = 7.92 Hz, 1H), 5.35 (s, 2H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 159.3, 157.9, 147.9, 141.5, 130.5, 130.3,

129.6, 129.3, 129.2, 128.8, 128.7, 127.9, 127.1, 126.6, 125.9, 124.8, 121.8, 119.5, 113.0, 69.8; HRMS (EI, TOF): caled for $C_{22}H_{15}NO^{+}$ $[M]^{+}$: 309.1154, found: 309.1150.

*11-(p-Tolyl)-6H-isochromeno[4,3-c]quinoline* (**3j**). The compound was prepared from (2-(p-tolylethynyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3j** was obtained in 58% yield (37 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.19 (d, $J$ = 8.00 Hz, 1H), 8.06 (d, $J$ = 8.44 Hz, 1H), 7.66-7.70 (m, 1H), 7.61 (d, $J$ = 8.00 Hz, 2H), 7.46-7.50 (m, 1H), 7.17-7.23 (m, 4H), 7.01-7.05 (m, 1H), 6.89 (d, $J$ = 7.92 Hz, 1H), 5.33 (s, 2H), 2.42 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 159.2, 157.9, 147.9, 138.8, 138.6, 130.5, 130.3, 129.6, 129.5, 129.4, 129.1, 127.9, 127.1, 126.6, 125.9, 124.9, 121.8, 119.4, 113.0, 69.8, 21.5; HRMS (EI, TOF): caled for $C_{23}H_{17}NO^{+}$ $[M]^{+}$: 323.1310, found: 323.1312.

*1-(4-Ethylphenyl)-6H-isochromeno[4,3-c]quinoline* (**3k**). The compound was prepared from (2-((4-pentylphenyl)ethynyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3k** was obtained in 43% yield (33 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.20 (d, $J$ = 8.28 Hz, 1H), 8.07 (d, $J$ = 8.44 Hz, 1H), 7.69 (t, $J$ = 7.60 Hz, 1H), 7.62 (d, $J$ =8.04 Hz, 2H), 7.48 (t, $J$ = 7.56 Hz, 1H), 7.17-7.23 (m, 4H), 7.01 (t, $J$ = 7.32 Hz, 1H),6.86 (d, $J$ =8.00 Hz, 1H), 5.33 (s, 2H), 2.67 (t, $J$ = 7.48 Hz, 2H), 1.61-1.68 (m, 2H), 1.32-1.35 (m, 4H), 0.90 (t, $J$ = 6.76 Hz, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 159.2, 158.1, 148.0, 143.8, 138.8, 130.5, 130.3, 129.6, 129.5, 129.2, 128.9, 127.9,

127.1, 126.6, 125.9, 124.9, 121.8, 119.5, 113.1, 69.8, 35.8, 31.5, 31.1, 22.6, 14.2; HRMS (EI, TOF): caled for $C_{27}H_{25}NO^+$ $[M]^+$: 379.1936, found: 379.1935.

*11-(4-(tert-Butyl)phenyl)-6H-isochromeno[4,3-c]quinoline* (**3l**). The compound was prepared from (2-((4-(tert-butyl)phenyl)ethynyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3l** was obtained in 51% yield (37 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^1$H NMR (400 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 8.16 (dd, $J_1$ = 8.28 Hz, $J_2$ = 0.80 Hz, 1H), 8.07 (d, $J$ = 8.40 Hz, 1H), 7.63-7.70 (m, 3H), 7.44-7.50 (m, 3H), 7.17-7.24 (m, 2H), 7.00-7.04 (m, 1H), 6.90 (d, $J$ =7.92 Hz, 1H), 5.34 (s, 2H), 1.36 (s, 9H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 159.2, 157.9, 151.9, 147.9, 138.5, 130.4, 130.2, 129.4, 129.2, 129.1, 127.9, 127.0, 126.6, 125.8, 125.6, 124.8, 121.8, 119.4, 112.9, 69.7, 34.8, 31.4; HRMS (EI, TOF): caled for $C_{26}H_{23}NO^+$ $[M]^+$: 365.1780, found: 365.1779.

*11-(4-(Octyloxy)phenyl)-6H-isochromeno[4,3-c]quinoline* (**3m**). The compound was prepared from (2-((4-(octyloxy)phenyl)ethynyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3m** was obtained in 66% yield (58 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^1$H NMR (400 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 8.18 (d, $J$ = 8.28 Hz, 1H), 8.05 (d, $J$ = 8.44 Hz, 1H), 7.65-7.70 (m, 3H), 7.45-7.49 (m, 1H), 7.17-7.22 (m, 2H), 7.02-7.06 (m, 1H), 6.92-6.96 (m, 3H), 5.32 (s, 2H), 4.01 (t, $J$ = 6.64 Hz, 2H), 1.81 (m, 2H), 1.47 (m, 2H), 1.33 (m, 8H), 0.89 (t, $J$ = 6.84 Hz, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 159.9, 159.2, 157.6, 147.9, 133.7, 131.0, 130.4,

130.3, 129.6, 128.9, 127.9, 127.0, 126.5, 125.7, 124.8, 121.8, 119.3, 114.7, 112.9, 69.7, 68.1, 53.5, 31.8, 29.4, 29.3, 26.1, 22.7, 14.1; HRMS (EI, TOF): caled for $C_{30}H_{31}NO_2^+$ $[M]^+$: 437.2355, found: 437.2358.

*11-(Thiophen-2-yl)-6H-isochromeno[4,3-c]quinoline* (**3n**). The compound was prepared from (2-(thiophen-2-ylethynyl)phenyl)methanol and 2-azidobenzaldehyde following the general procedure. The product **3n** was obtained in 59% yield (37 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v). $^1$H NMR (400 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 8.16 (d, $J$ = 8.24 Hz, 1H), 8.02 (d, $J$ = 8.44 Hz, 1H), 7.66-7.70 (m, 1H), 7.45-7.49 (m, 2H), 7.37 (dd, $J_1$ = 3.60 Hz, $J_2$ = 0.96 Hz,1H), 7.32 (d, $J$ = 7.92 Hz, 1H), 7.27 (m, 2H), 7.14-7.16 (m, 1H), 7.03-7.05 (m, 1H), 5.32 (s, 2H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 159.3, 150.9, 148.1, 144.2, 130.6, 130.5, 129.3, 129.1, 129.0, 128.1, 127.9, 127.6, 127.5, 126.2, 126.1, 125.1, 121.8, 119.5, 113.1, 69.9; HRMS (EI, TOF): caled for $C_{20}H_{13}NOS^+$ $[M]^+$: 315.0718, found: 315.0719.

*4-Chloro-11-(4-methoxyphenyl)-6H-isochromeno[4,3-c]quinoline* (**3o**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azido-6-chlorobenzaldehyde following the general procedure. The product **3o** was obtained in 47% yield (35 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v). $^1$H NMR (400 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 7.96 (dd, $J_1$ = 7.72 Hz, $J_2$ = 1.84 Hz, 1H), 7.66 (d, $J$ = 8.68 Hz, 2H), 7.49-7.51 (m, 2H), 7.24-7.25 (m, 2H), 7.03-7.07 (m, 1H), 6.91-6.96 (m, 3H), 5.32 (s, 2H), 3.87 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^o$C): $\delta$ 160.5, 159.9, 159.7, 149.8, 133.3, 131.2,

130.6, 129.4, 129.2, 129.1, 128.7, 128.6, 127.9, 127.3, 126.8, 124.7, 117.5, 114.3, 114.1, 69.5, 55.4; HRMS (EI, TOF): caled for $C_{23}H_{16}ClNO_2^+$ $[M]^+$: 373.0870, found: 373.0871.

*3-Chloro-11-(4-methoxyphenyl)-6H-isochromeno[4,3-c]quinoline* (**3p**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azido-5-chlorobenzaldehyde following the general procedure. The product **3p** was obtained in 72% yield (54 mg) as a yellow solid after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v). Mp: 183-186 $^oC$; $^1H$ NMR (400 MHz, $CDCl_3$, 25 $^oC$): $\delta$ 8.16 (d, $J$ = 2.24 Hz, 1H), 7.97 (d, $J$ = 8.96 Hz, 1H), 7.66 (d, $J$ = 8.76 Hz, 2H), 7.61 (dd, $J_1$ =8.96 Hz, $J_2$ =2.40 Hz, 1H), 7.22-7.24 (m, 2H), 7.04-7.08 (m, 1H), 6.96 (d, $J$ = 8.76 Hz, 2H),6.93 (d, $J$ =8.12 Hz, 1H), 5.37 (s, 2H), 3.88 (s, 3H); $^{13}C$ NMR (100.6 MHz, $CDCl_3$, 25 $^oC$): $\delta$ 160.4, 158.3, 157.7, 146.3, 133.6, 131.5, 131.1, 130.7, 130.4, 129.2, 128.1, 127.4, 126.5, 124.9, 120.9, 120.1, 114.2, 113.6, 69.8, 55.4; HRMS (EI, TOF): caled for $C_{23}H_{16}ClNO_2^+$ $[M]^+$: 373.0870, found: 373.0867.

*2-Chloro-11-(4-methoxyphenyl)-6H-isochromeno[4,3-c]quinoline* (**3q**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azido-5-chlorobenzaldehyde following the general procedure. The product **3q** was obtained in 58% yield (43 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^1H$ NMR (400 MHz, $CDCl_3$, 25 $^oC$): $\delta$ 8.11 (d, $J$ = 8.84 Hz, 1H), 8.05 (d, $J$ = 1.92 Hz, 1H), 7.66 (d, $J$ = 8.76 Hz, 2H), 7.41 (dd, $J_1$ = 8.80 Hz, $J_2$ = 2.00 Hz, 1H), 7.21-7.23 (m, 2H), 7.03-7.07 (m, 1H), 6.96 (d, $J$ = 8.76

Hz, 2H), 6.92 (d, $J$ = 7.92 Hz, 1H), 5.33 (s, 2H), 3.88 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 160.5, 159.2, 158.6, 148.4, 136.1, 133.5, 131.1, 130.3, 129.2, 128.1, 128.0, 127.3, 126.6, 126.4, 124.9, 123.3, 117.7, 114.1, 113.1, 69.8, 55.4; HRMS (EI, TOF): caled for $C_{23}H_{16}ClNO_2^+$ $[M]^+$: 373.0870, found: 373.0868.

*3-Bromo-11-(4-methoxyphenyl)-6H-isochromeno[4,3-c]quinoline* (**3r**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azido-5-bromobenzaldehyde following the general procedure. The product **3r** was obtained in 56% yield (46 mg) as a yellow solid after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v). Mp: 143-146 $^{o}$C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.34 (s, 1H), 7.91 (d, $J$ = 8.84 Hz, 1H), 7.73 (d, $J$ = 8.80 Hz, 1H), 7.66 (d, $J$ = 8.24 Hz, 2H), 7.23 (d, $J$ =6.60 Hz, 2H), 7.06 (t, $J$ = 6.48 Hz, 1H), 6.96 (d, $J$ = 8.36 Hz, 2H), 6.93 (d, $J$ = 8.08 Hz, 1H), 5.33 (s, 2H), 3.88 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 160.6, 158.3, 157.9, 146.6, 133.7, 131.2, 130.9, 130.5, 129.2, 128.2, 127.6, 126.6, 125.1, 124.4, 120.6, 119.7, 114.3, 113.7, 69.9, 55.5; HRMS (EI, TOF): caled for $C_{23}H_{16}BrNO_2^+$ $[M]^+$: 417.0364, found: 417.0365.

*11-(4-Methoxyphenyl)-3-(trifluoromethyl)-6H-isochromeno[4,3-c]quinoline* (**3s**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azido-5-(trifluoromethyl)benzaldehyde following the general procedure. The product **3s** was obtained in 57% yield (46 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^{1}$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.35 (s, 1H), 8.28 (d, $J$ = 8.68 Hz, 1H), 7.68 (d, $J$ = 8.72 Hz, 2H), 7.63 (dd, $J_1$ =8.68 Hz, $J_2$ =1.44 Hz, 1H), 7.24-7.25 (m, 2H), 7.05-7.09 (m, 1H),

6.95-6.99 (m, 3H), 5.36 (s, 2H), 3.88 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 160.6, 158.9, 158.8, 146.9, 133.4, 132.0, 131.7, 131.1, 130.4, 129.0, 128.2, 127.7, 128.6, 128.7, 128.6, 125.1, 123.2, 121.3, 121.2, 121.1, 114.4, 114.2, 69.9, 55.4; HRMS (EI, TOF): caled for $C_{24}H_{16}F_3NO_2^+$ $[M]^+$: 407.1133, found: 407.1131.

*Methyl 11-(4-methoxyphenyl)-6H-isochromeno[4,3-c]quinoline-3-carboxylate* (**3t**).The compound was prepared from (2-((4-methoxyphenyl)ethynyl)phenyl)methanol and methyl 4-azido-3-formylbenzoate following the general procedure. The product **3t** was obtained in 55% yield (63 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^1$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C) δ 8.94 (s, 1H), 8.26 (d, $J$ = 8.84 Hz, 1H), 8.06 (d, $J$ = 8.92 Hz, 1H), 7.70 (d, $J$ = 8.36 Hz, 2H), 7.22 (d, $J$ =7.20 Hz, 2H), 7.07 (t, $J$ = 6.96 Hz, 1H), 6.94-6.98 (m, 3H), 5.37 (s, 2H), 3.99 (s, 3H), 3.88 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): 166.9, 160.7, 160.2, 159.7, 138.8, 136.0, 131.3, 130.4, 130.0, 129.3, 129.2, 128.2, 127.6, 127.2, 126.5, 125.4, 125.1, 118.8, 114.3, 113.6, 69.9, 55.5, 52.5; HRMS (EI, TOF): caled for $C_{25}H_{19}NO_4^+$ $[M]^+$: 397.1314, found: 397.1310.

*2-Thoxy-11-(4-methoxyphenyl)-6H-isochromeno[4,3-c]quinoline* (**3u**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azido-4-methoxybenzaldehyde fTollowing the general procedure. The product **3u** was obtained in 60% yield (44 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 5:1 v/v); $^1$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.07 (d, $J$ = 9.08 Hz, 1H), 7.65 (d, $J$ = 8.68 Hz, 2H), 7.40 (d, $J$ = 2.40 Hz, 1H),

7.15-7.23 (m, 2H), 7.11 (d, $J$ = 9.08 Hz, 1H), 7.01-7.05 (m, 1H), 6.96 (d, $J$ = 8.68 Hz, 2H), 6.89 (d, $J$ = 8.12 Hz, 1H), 5.30 (s, 2H), 3.95 (s, 3H), 3.87 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 161.6, 160.2, 159.4, 157.9, 149.8, 133.9, 133.0, 130.9, 130.2, 129.7, 127.9, 126.7, 126.3, 124.9, 123.1, 118.6, 114.1, 113.9, 111.5, 107.3, 69.7, 55.6, 55.4; HRMS (EI, TOF): caled for $C_{24}H_{19}NO_3^+$ $[M]^+$: 369.1365, found: 369.1364.

*11-(4-Ethoxyphenyl)-2-methyl-6H-isochromeno[4,3-c]quinoline* (**3v**). The compound was prepared from (2-((4-methoxyphenyl)ethynyl)phenyl)methanol and 2-azido-4-methylbenzaldehyde following the general procedure. The product **3v** was obtained in 74% yield (52 mg) as a yellow foam after column chromatography (eluent = petroleum ether/ethyl acetate 10:1 v/v); $^1$H NMR (400 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 8.06 (d, $J$ = 8.40 Hz, 1H), 7.84 (s, 1H), 7.66 (d, $J$ = 8.72 Hz, 2H), 7.30 (dd, $J_1$ =8.44 Hz, $J_2$ =1.24 Hz, 1H), 7.16-7.23 (m, 2H), 7.03 (t, $J$ = 8.08 Hz, 1H), 6.95 (d, $J$ = 8.68 Hz, 2H), 6.90 (d, $J$ =7.92 Hz, 1H), 5.30 (s, 2H), 3.87 (s, 3H), 2.54 (s, 3H); $^{13}$C NMR (100.6 MHz, $CDCl_3$, 25 $^{o}$C): $\delta$ 160.2, 159.3, 157.5, 148.2, 140.7, 134.0, 131.1, 130.3, 129.7, 128.1, 127.9, 126.8, 126.4, 142.8, 121.5, 117.2, 114.0, 112.2, 69.7, 55.4, 21.9; HRMS (EI, TOF): caled for $C_{24}H_{19}NO_2^+$ $[M]^+$: 353.1416, found: 353.1411.

**Supporting Information**

The copies of $^1$H NMR, $^{13}$C NMR spectra of products (PDF), crystallographic data for **3g** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.T

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