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Lewis Acid Promoted Oxonium Ion Driven Carboamination of Alkynes for the Synthesis of 4-Alkoxy Quinolines

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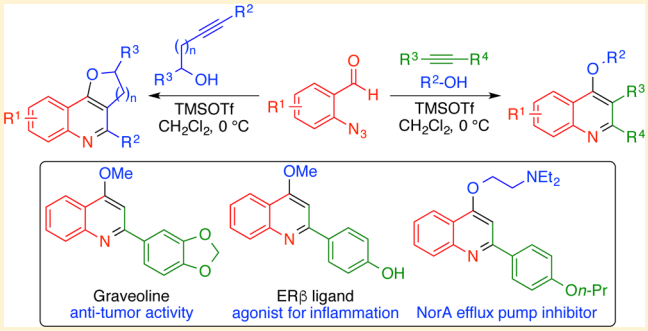
Supporting Information

ABSTRACT: Lewis acid mediated multisegment coupling cascade is designed for the synthesis of densely substituted 4-alkoxy quinolines via an oxonium ion triggered alkyne carboamination sequence involving C−C and C−N bond formations. Cyclic ether fused-quinolines could also be accessed using this fast, operationally simple, high yielding, chemoselective and functional group tolerant method. Versatility and utility of this methodology is demonstrated by postfunctionalization of products obtained and its use in synthesis of potent drug molecules.



INTRODUCTION

Polysubstituted quinoline moiety is an integral part of many natural products and agrochemicals.[1a−f] It is the backbone of several potent drugs and pharmaceuticals exhibiting a diverse range of activities such as antimalarial, schistosomiasis and antifungal.[1g−i] Among these, 4-alkoxy quinolines are quite prevalent pharmacophores (Figure 1). For example, graveoline (**1**) shows antitumor activity, whereas ERβ ligand **2** possessing 4-alkoxy quinoline core acts as selective agonist in treating inflammation. On the other hand, quinoline derivative **3** is used as a neuroprotective drug, 4-ethoxy quinoline (**4**) shows IGF-1R inhibition activity, and 7-PPyQ (**5**) is an antiproliferative drug. Quinoline derivative **6** is found to be an efficient NorA efflux pump inhibitor.[2] Apart from the classical methods, recent years have seen emergence of not only transition metal-mediated transformations but also metal-free approaches for the synthesis of quinolines.[3−5] Interestingly, while significant progress has been made on the synthesis of substituted quinolines, methods giving direct access to 4- alkoxy quinolines are typically fraught with multistep transformations resulting in lower yields.[6] Moreover, there are only scattered reports on the synthesis of cyclic ether fused quinolines.[7] Given the biological activity of the 4-alkoxy quinoline derivatives, a general, concise and efficient synthesis of these scaffolds is highly desirable. Herein we disclose a simple and scalable multisegment cascade coupling strategy for the synthesis of diversely substituted 4-alkoxy quinolines as well as cyclic ether-fused quinoline derivatives.

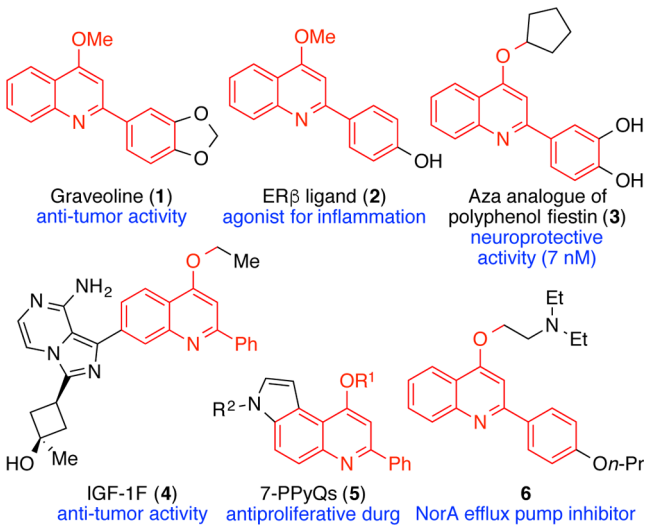


Figure 1. Biologically active 4-alkoxy quinoline pharmacophores.

RESULTS AND DISCUSSION

Transition metal catalyzed carboamination of alkynes for the simultaneous formation of C−C and C−N bonds has attracted considerable attention in recent times.[8] These studies have opened new avenues for the synthesis of nitrogen heterocycles, providing impetus for the development of transition metal-free carboamination reactions, which are amenable to cascade processes. In a program directed at developing methods for synthesis of various functionalized heterocycles, we envisioned an oxoniumion driven carboamination of alkynes for the synthesis of 4-alkoxy quinolines (Scheme 1).[9] We anticipated that treating the azido aldehyde **7** with the alcohol **8** in the presence of a Lewis/Brønsted acid would generate an oxonium ion, which upon reaction with alkyne **9** would form new intermediate vinyl cation forming C−C bond. This vinyl cation

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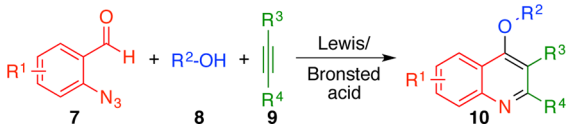
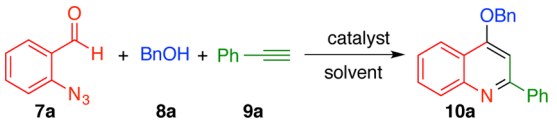
Scheme 1. Proposed Synthesis of 4-Alkoxy Quinolines 10



would be further trapped by azide in an intramolecular fashion followed by a 1,4-elimination of H^+ and N_2 from this intermediate leading to the 4-alkoxy quinoline **10**.

To test the feasibility of the proposed hypothesis, cyclization of azido aldehyde **7a** with benzyl alcohol (**8a**) and phenylacetylene (**9a**) was attempted using TMSOTf (1 equiv) as a Lewis acid in CH_2Cl_2 as solvent. Gratifyingly, the reaction proceeded smoothly to give the desired 4-benzyloxy quinoline **10a** in excellent yield (Table 1, entry 1). Various other Lewis as

Table 1. Optimization of 4-Alkoxy Quinoline Synthesis[a]



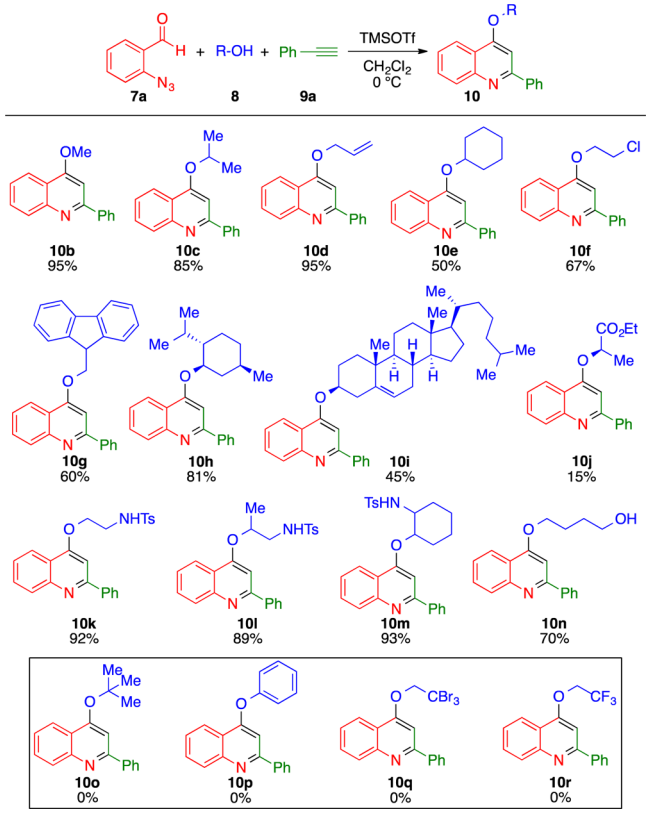
entry	acid	equiv	solvent	temp (°C)	time (h)	yield (%)[b]
1	**TMSOTf**	**1**	**CH_2Cl_2**	**0**	**0.25**	**78 (78)**[c]
2	$In(OTf)_3$	1	CH_2Cl_2	0–rt	17	77 (77)[c]
3	$Sc(OTf)_3$	1	CH_2Cl_2	0	17	74
4	$Cu(OTf)_2$	1	CH_2Cl_2	rt	18	–[d]
5	$Zn(OTf)_2$	1	CH_2Cl_2	rt	18	–[d]
6	TMSOTf	1	CH_3CN	0–rt	18	–[d]
7	$In(OTf)_3$	1	$(CH_2Cl)_2$	0	2	69
8	$Sc(OTf)_3$	1	$(CH_2Cl)_2$	0	2	70[c]
9	$FeCl_3$	1	CH_2Cl_2	rt	18	44
10	$TiCl_4$	1	CH_2Cl_2	rt	20	54
11	$AlCl_3$	1	CH_2Cl_2	rt	18	43
12	$BF_3{\cdot}OEt_2$	1	CH_2Cl_2	0–rt	20	32
13	TMSOTf	0.5	CH_2Cl_2	0	18	30
14	$Sc(OTf)_3$	0.2	CH_2Cl_2	rt–40	12	25
15	$In(OTf)_3$	0.2	CH_2Cl_2	rt–40	18	12
16	TfOH	1	CH_2Cl_2	0	18	40

[a]All the reactions were carried out with azido aldehyde **7a** (1.0 equiv), phenylacetylene **9a** (1.0 equiv) and benzyl alcohol **8a** (1.0 equiv). [b]Yield was determined on the basis of ^1H NMR using trimethoxybenzene as internal standard. [c]Isolated yield. [d]Starting material was recovered.

well as Brønsted acids were screened for optimizing the reaction. $In(OTf)_3$ and $Sc(OTf)_3$ were found to give the quinoline product **10a** in comparable yield, albeit with longer reaction time (Table 1, entries 2–3). Milder Lewis acids like $Cu(OTf)_2$ and $Zn(OTf)_2$ failed to give the quinoline **10a**, with complete recovery of starting compounds (Table 1, entries 4–5). Lewis acids such as $FeCl_3$, $TiCl_4$, $AlCl_3$ and $BF_3{\cdot}OEt_2$ furnished the quinoline **10a** in moderate yield (Table 1, entries 9–12). TfOH too was found to promote the reaction, however in lower yield (Table 1, entry 16). Reaction did not proceed at all in acetonitrile as a solvent (Table 1, entry 6), whereas $(CH_2Cl)_2$ proved to be an inferior solvent (Table 1, entries 7–8). In order to make the process economical, we tried to reduce the catalyst loading. However, it led to sluggish reactions and significant amounts of starting materials were recovered back (Table 1, entries 13–15). After all this screening, TMSOTf (1 equiv) in CH_2Cl_2 at 0 °C was identified as optimal condition to carry out the synthesis of quinolines **10**.

The scope and limitation of this three component, "one-pot" cascade cyclization process for the synthesis of various 4-alkoxy quinoline derivatives **10** was studied in detail. The reaction was found to work efficiently with a broad range of aldehydes **7**, alcohols **8** and alkynes **9**. The azido aldehyde **7a** and phenylacetylene (**9a**) reacted with alcohols such as MeOH (**8b**), isopropanol (**8c**) and allyl alcohol (**8d**) to furnish the corresponding quinolines **10b–d** in excellent yields (Scheme 2). Use of cyclohexanol (**8e**), 2-chloroethanol (**8f**) and 9-

Scheme 2. Alcohol Substrate Scope



fluorenylmethanol (**8g**) resulted in slightly diminished yield of quinolines **10e–g**. D-(−)-Menthol (**8h**) and cholesterol (**8i**) also gave the quinolines **10h–i** in 85% and 45%, respectively. Ethyl (*S*)-lactate (**8j**) reacted with azido aldehyde **7a** and phenylacetylene (**9a**) leading to the quinoline **10j** in poor yield along with formation of the 2-phenylquinolin-4-ol (**11**) as the major product. Formation of the latter is perhaps an outcome of an elimination reaction under the strongly acidic conditions employed. *N*-Tosyl amino alcohols **8k–m** also participated in the reaction efficiently furnishing corresponding quinolines **10k–m** in excellent yields exhibiting high chemoselectivity. Interestingly, using 1,4-butanediol (**8n**) as an alcohol variant afforded only quinoline **10n** with no trace of *bis*-quinoline derivative even on using excess amounts of azido aldehyde (**7a**), phenylacetylene (**9a**) or TMSOTf. Anticipating that basicity of quinoline could be the reason for inefficiency of the second quinoline formation step, we also attempted this reaction by adding stoichiometric amount of TFA in addition to two equivalents of TMSOTf, albeit without much success.

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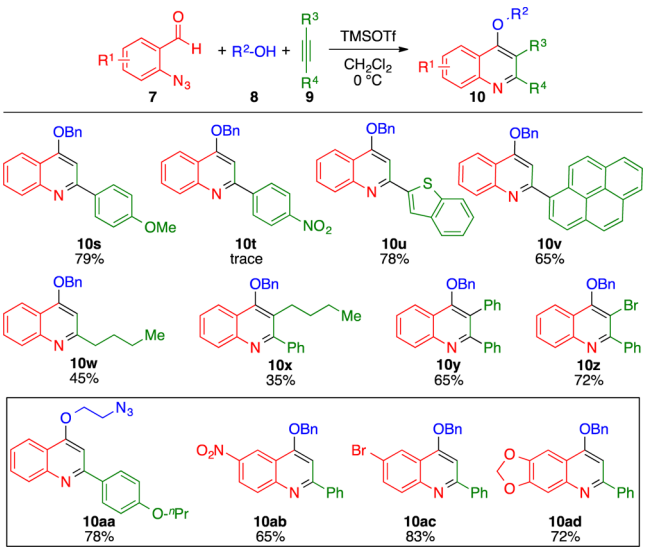
It is also pertinent to mention that *tert*-butyl alcohol (**8o**) led to extensive decomposition, while phenol (**8p**) 2,2,2-tribromoethanol (**8q**) and 2,2,2-trifluoroethanol (**8r**) failed to give the desired quinolines **10o−r**. In all the cases, the structure and regioselectivity of the quinoline products was established on the basis of their spectral data. It was further unambiguously confirmed in the cases of quinolines **10g**, **10i** and **10k** by single crystal X-ray diffraction studies.[10]

The multisegment coupling strategy for the synthesis of quinolines **10** was further explored by changing the alkynes **9** and azido aldehydes **7**. While *p*-methoxyphenyl acetylene (**9b**) participated in the reaction with azido aldehyde (**7a**) furnishing the quinolines **10s** in good yield, *p*-nitrophenyl acetylene (**9c**) gave the product **10t** in only trace amounts (Scheme 3). This is

Scheme 3. Alkyne and Azidoaldehyde Substrate Scope



due to the presence of strong electron withdrawing nitro group on the aromatic ring that destabilizes the vinyl carbocation intermediate thus slowing this reaction. Heteroaryl substituted alkyne **9d**, pyrene substituted alkyne **9e** as well as 1-hexyne **9f** gave the corresponding quinolines **10u−w**. Even internal alkynes **9g−h** were found to be good reaction partners in this synthesis furnishing the quinolines **10x−y**, respectively, in good to moderate yields. Formation of the **10x** can be rationalized as follows: the nucleophilic attack of unsymmetrical alkyne onto the oxonium ion may occur in two different ways. In one approach it forms secondary vinyl carbocataion and in other it forms secondary as well as benzylic carbocataion, which is more stabilized hence leading to the formation of **10x** as the product. Interestingly, alkynyl bromide **9i** also participated in this transformation giving rise to trisubstituted quinoline **10z**. When 2-azidoethanol (**8s**) was reacted with azido aldehyde **7a** and alkyne **9j**, the quinoline **10aa** was formed in good yield, clearly indicating that only the azide conjugated with aryl aldehyde moiety participates in this reaction.

Finally, scope of differently substituted azido aldehydes **7b−d** was tested by reacting these under optimized conditions with phenylacetylene (**9a**) and benzyl alcohol (**8a**) and it was observed that irrespective of the nature of group linked to the aryl moiety quinolines **10ab-ad** were obtained in good to excellent yield. Structures and regioselectivity of the products were unambiguously confirmed by single crystal X-ray diffraction studies on quinoline derivatives **10s** and **10z**.[10]

In order to demonstrate the versatility of the established protocol, synthesis of cyclic ether-fused quinolines employing alcohol tethered alkynes was planned next. Toward this, alkynol **12a** was treated with azido aldehyde **7a** using optimized condition (1 equiv of TMSOTf in CH_2Cl_2 at 0 °C), which to our delight led to the furoquinoline **13a** in quantitative yield (Scheme 4). The reaction was found to be very general and a variety of alkyl and aryl group-substituted alkynols **12b−k** participated in the reaction with azido aldehyde **7a** furnishing the corresponding furoquinolines **13b−k** in excellent yields. It is pertinent to mention here that alkynols **12l−n** bearing alkyne, vinyl chloride and enyne functionality, respectively, were tolerated under the reaction conditions employed and corresponding furoquinolines **13l−n** were obtained in good yield. The diol **12o** also worked albeit giving only monoquinoline derivative **13o**. The alkynols **12p−s** reacted with azido aldehyde **7a** giving almost quantitatively, the pyranoquinolines **13p−s**. Even the oxepinoquinoline **13t** could be obtained efficiently using the alkynol **12t**. Azido aldehyde variant **7d** bearing acetal moiety was also smoothly transformed to the furoquinoline **13u**. The structures of the quinolines **13l** and **13q** were unambiguously confirmed by single crystal X-ray diffraction studies.[10]

To examine robustness of this multisegment coupling cascade, we devised a synthesis of sugar-derived quinoline. Thus, known alkynol **14** synthesized from D-glucal[11] was reacted with azido aldehyde **7a** under the optimized reaction conditions to furnish the *bis*-cyclic ether-fused quinoline **15**, a variant of conformationally constrained *C*-aryl sugar derivatives (Scheme 5).[12]

After successfully establishing scope of the reaction, based on our mechanistic hypothesis, we reasoned that this multisegment, cascade coupling for the synthesis of quinolines can be further extrapolated in two ways. In the first approach, we planned to explore the in situ synthesis of alkynol followed by its further reaction for accessing quinoline. This approach required extrapolation of the one pot sequence by incorporating an additional C−C bond formation process to this multisegment cascade. To test the hypothesis, alkynal **16** was subjected to reaction with allyltributyltin (**17**) and $BF_3{\cdot}OEt_2$ in CH_2Cl_2 at 0 °C. After the complete consumption of aldehyde **16** (TLC control), azido aldehyde **7a** was added to reaction mixture to obtain the quinoline **18** in good overall yield (Scheme 6).[13] In the second approach, the azido aldehyde **7a** was allylated using allyltributyltin (**17**) and $BF_3{\cdot}OEt_2$ in CH_2Cl_2 at 0 °C; phenylacetylene (**9a**) was added and it was refluxed to furnish the quinoline **19** in moderate yield.

Versatility of the obtained alkoxy quinolines was demonstrated by converting these into functionalized scaffolds. The bromoquinoline **10z** was found to be a good partner in Suzuki coupling and furnished the quinoline **10ae** upon reaction with $PhB(OH)_2$ (**20**) in the presence of catalytic amounts of $Pd(PPh_3)_2Cl_2$ (Scheme 7). Fascinatingly, the quinoline **13a** when treated with $[Ph_2I]BF_4$ **21** and $Pd(OAc)_2$ in AcOH at 120 °C participated in selective C−H activation at the *ortho* position of the phenyl substituent leading to the quinoline **22** in moderate yield.[14] Selective reduction of quinoline **13a** was attempted in two directions. Catalytic hydrogenation using 10% Pd/C furnished the densely substituted pyridine derivative **23**.[10] Alternatively, tetrahydroquinoline **24** was obtained as the major product with excellent diastereoselectivity when quinoline **13a** was subjected to reduction using $NiCl_2$ and $NaBH_4$.

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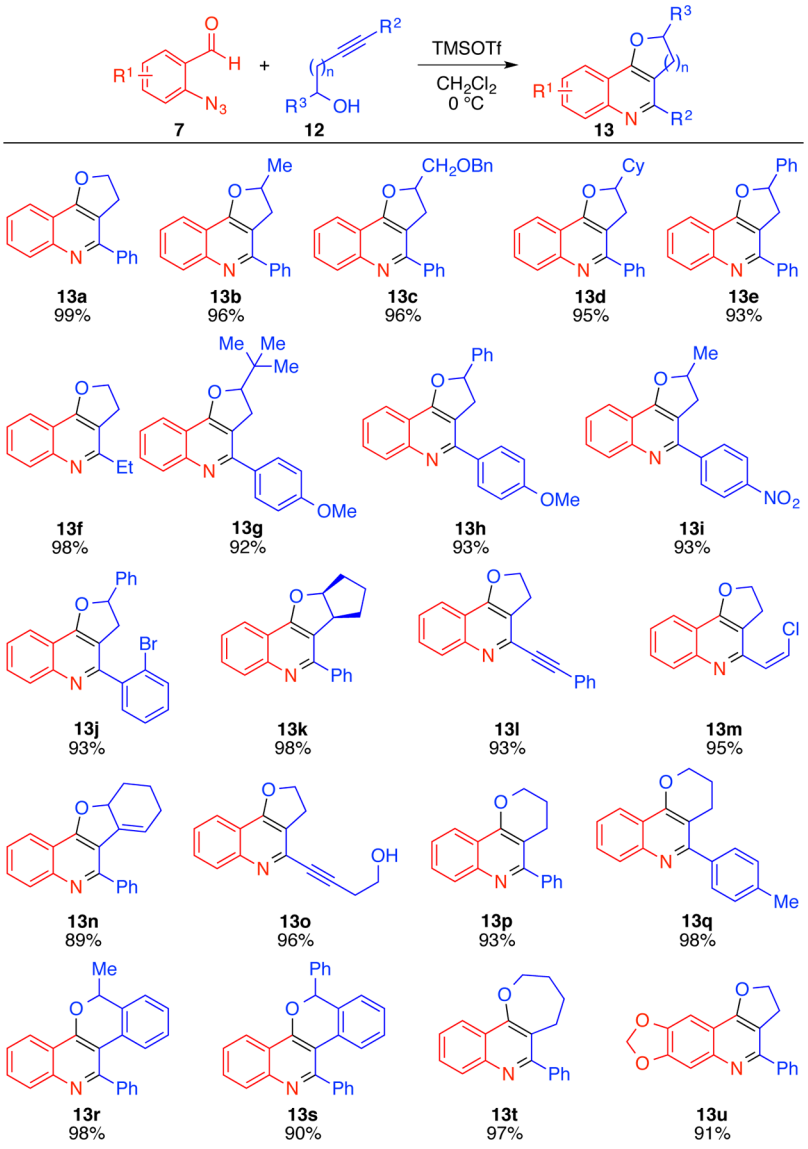
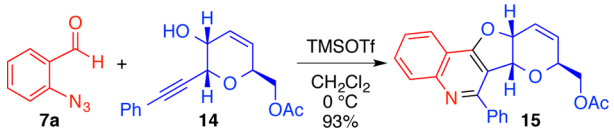
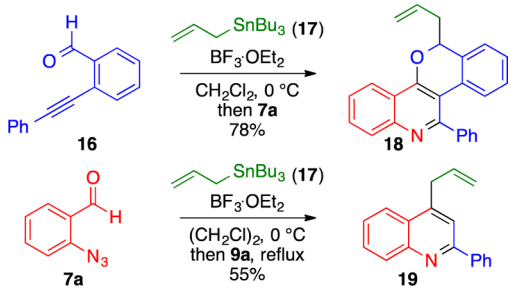
Scheme 4. Synthesis of Cyclic Ether-Fused Quinolines



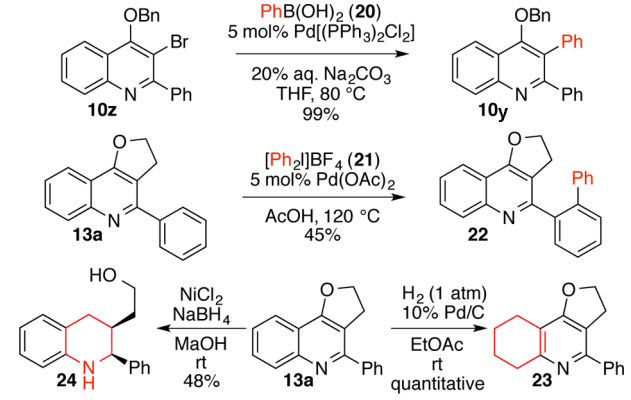
Scheme 5. Synthesis of Sugar-Derived Quinoline



Scheme 6. "One-Pot" Synthesis of Functionalized Quinolines



Scheme 7. Functionalization of Quinolines



Finally, utility of this quinoline synthesis was exemplified in a new approach for efficient assembly of natural products and drug molecules. A single step, divergent synthesis of graveoline (**1**) and the drug candidate **6** could be accomplished starting from the azido aldehyde **7a** with appropriate alcohol **8** and

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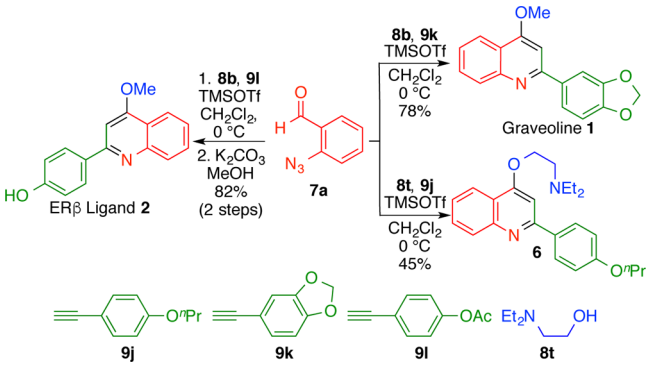
alkyne **9** (Scheme 8). Similarly, ERβ ligand (**2**) could be accessed in excellent overall yields from the azido aldehyde **7a**

Scheme 8. Total Synthesis of Natural Product and Drug Molecules



employing an addition deprotection step. These are shortest and most efficient syntheses of these molecules reported until date.[15]

CONCLUSIONS

In conclusion, we have developed a metal free, Lewis acid mediated multisegment, cascade coupling approach for the synthesis of diversely substituted quinolines. Versatility of the method was demonstrated by its use in the synthesis of cyclic ether-fused and sugar-fused quinoline derivatives. In all, the approach employed not only worked efficiently with short reaction spans but also allowed for sequencing of the multiple cascades. We have also shown that the protocol gave a rapid access to biologically active natural products and drug molecules. Further functionalization of the quinolines has opened up interesting possibilities.

EXPERIMENTAL SECTION

General Experimental Methods. Melting points are recorded using sigma melting point apparatus in capillary tubes and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded either on 400 or 500 MHz spectrometer. The chemical shifts (δ ppm) are reported in the standard fashion with reference to either internal tetramethylsilane or residual solvent peak. The coupling constants are reported in Hz. In the ^{13}C{^{1}H}NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording the DEPT-135 experiment, and is given in parentheses.

All commercial reagents were used as such without any further purification. All other alkyne and alkynols were prepared using well established protocols involving either Sonogashira coupling reaction or opening of epoxide with lithium anion of appropriate phenylacetylene.

General Procedure of Intermolecular Multisegment Coupling Reaction for Synthesis of 4-Alkoxy Quinoline Derivatives 10. *4-(Benzyloxy)-2-phenylquinoline (**10a**).* To a magnetically stirred solution of azido aldehyde **7a** (50 mg, 0.340 mmol), benzyl alcohol **8a** (35 μL, 0.340 mmol) and phenyl acetylene **9a** (34 μL, 0.340 mmol) in dry CH_2Cl_2 (8.0 mL) was added dropwise TMSOTf (65 μL, 0.340 mmol) at 0 °C. Reaction was monitored by TLC, quenched with saturated aq. solution of $NaHCO_3$ upon completion, extracted with CH_2Cl_2 (3 × 5 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc–petroleum ether (2:98) as eluent furnished 4-alkoxy quinoline **10a** (72 mg, 78%) as a colorless liquid; IR (neat) 3060, 3033, 2929, 1593, 1556, 1507, 1494, 1422, 1379, 1353, 1224, 1181, 1108, 982, 918, 839, 766, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dd, J = 8.4, 0.4 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 8.14–8.12 (m, 2H), 7.57–7.71 (m, 1H), 7.56–7.52 (m, 4H), 7.51–7.41 (m, 5H), 7.25 (s, 1H), 5.34 (s, 2H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$, DEPT) δ 161.9 (C), 158.7 (C), 149.1 (C), 140.1 (C), 135.8 (C), 130.1 (CH), 129.9 (CH), 129.1 (CH), 128.8 (4 × CH), 128.9 (CH), 127.6 (2 × CH), 127.5 (2 × CH), 125.5 (CH), 121.9 (CH), 120.5 (C), 99.8 (CH), 70.2 (CH_2); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd. for $C_{22}H_{18}NO$ 312.1381, found 312.1386.

*4-Methoxy-2-phenylquinoline (**10b**).*[16] Reaction of azido aldehyde **7a** (73 mg, 0.5 mmol), methanol **8b** (22 μL, 0.5 mmol) and phenyl acetylene **9a** (55 μL, 0.5 mmol) with TMSOTf (91 μL, 0.5 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **9a** followed by purification on a silica gel column using ethyl acetate–petroleum ether (3:97) as eluent furnished the 4-alkoxy quinoline **10a** (111 mg, 95%) as white solid; mp 66–68 °C; IR (neat) 3020, 2975, 1594, 1559, 1510, 1447, 1421, 1379, 1216, 1161, 1115, 760, 701, 669 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23–8.17 (m, 1H), 8.17–8.08 (m, 3H), 7.72 (ddd, J = 8.4, 6.9, 1.51 Hz, 1H), 7.57–7.44 (m, 4H), 7.18 (s, 1H), 4.12 (d, J = 1.5 Hz, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$, DEPT) δ 163.1 (C), 158.9 (C), 149.1 (C), 140.3 (C), 130.2 (CH), 129.5 (CH), 129.1 (CH), 128.9 (2 × CH), 127.7 (2 × CH), 125.6 (CH), 121.8 (CH), 120.5 (C), 98.2 (CH), 55.8 (CH_3); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd. for $C_{16}H_{14}NO$ 236.1070, found 236.1069.

*4-Isopropoxy-2-phenylquinoline (**10c**).*[17] Reaction of azido aldehyde **7a** (75 mg, 0.5 mmol), isopropyl alcohol **8c** (40 μL, 0.5 mmol) and phenyl acetylene **9a** (55 μL, 0.5 mmol) with TMSOTf (91 μL, 0.5 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate–petroleum ether (3:97) as eluent furnished the 4-alkoxy quinoline **10c** (134 mg, 85%) as a white solid; mp 94–96 °C; IR (neat) 2981, 2934, 1591, 1508, 1494, 1446, 1381, 1221, 1113, 947, 760, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, J = 8.2, 1.0 Hz, 1H), 8.13–8.06 (m, 3 H), 7.73–7.68 (m, 1H), 7.56–7.44 (m, 4H), 7.16 (s, 1H), 4.95 (sept, J = 6.0 Hz, 1H), 1.53 (d, J = 6.0 Hz, 6H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$, DEPT) δ 161.2 (C), 158.9 (C), 149.6 (C), 140.7 (C), 129.9 (CH), 129.2 (CH), 128.8 (2 × CH), 128.7 (CH), 127.7 (2 × CH), 125.2 (CH), 122.1 (CH), 121.1 (C), 99.4 (CH), 70.7 (CH), 21.9 (2 × CH_3); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd. for $C_{18}H_{18}NO$ 264.1383, found 264.1381.

*4-(Allyloxy)-2-phenylquinoline (**10d**).* Reaction of azido aldehyde **6a** (50 mg, 0.34 mmol), allyl alcohol **7d** (31 μL, 0.342 mmol) and phenyl acetylene **9a** (45 μL, 0.34 mmol) with TMSOTf (61 μL, 0.34 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate–petroleum ether (3:97) as eluent furnished the 4-alkoxy quinoline **10d** (63 mg, 78%) as a yellow liquid; IR (neat) 3052, 2926, 1566, 1463, 1370, 1227, 1170, 1006, 678, 669 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.1 Hz, 1H), 8.17–8.14 (m, 2H), 8.03 (dd, J = 8.1, 0.8 Hz, 1H), 7.74 (s, 1H), 7.72–7.20 (m, 1H), 7.56–7.51 (m, 3H), 7.48–7.46 (m, 1H), 6.19–6.09 (m, 1H), 5.24–5.16 (m, 2H), 3.91 (dd, J = 6.4, 0.4 Hz, 2H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$, DEPT) δ 161.8 (C), 158.8 (C), 149.3 (C), 140.4 (C), 132.2 (CH), 130.1 (CH), 129.4 (CH), 129.2 (CH), 128.8 (2 × CH), 127.6 (2 × CH), 125.5 (CH), 121.8 (CH), 120.5 (C), 118.5 (CH_2), 99.1 (CH), 69.1 (CH_2); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd. for $C_{18}H_{16}NO$ 262.1266, found 262.1264.

*4-(Cyclohexyloxy)-2-phenylquinoline (**10e**).* Reaction of azido aldehyde **7a** (73 mg, 0.5 mmol), cyclohexanol **8e** (52 μL, 0.5 mmol) and phenyl acetylene **9a** (55 μL, 0.5 mmol) with TMSOTf (91 μL, 0.5 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate–petroleum ether (3:97) as eluent furnished the 4-alkoxy quinoline **10e** (75 mg, 50%) as a yellow viscous liquid; IR (neat) 3020, 2975, 1594,1559, 1510, 1360, 1216, 1115, 900, 758, 678 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28–8.22 (d, J = 8.2, 1H), 8.14–8.06 (m, 3H), 7.74–7.67 (m, 1H), 7.56–7.44 (m, 4H), 7.17 (s, 1H), 4.72 (tt, J = 7.9, 3.7 Hz, 1H), 2.10 (td, J = 7.7, 3.5 Hz, 2H), 1.96–1.86 (m, 2H), 1.86–1.75 (m, 2H), 1.68–1.58 (m, 1H), 1.58–1.42 (m, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 161.1 (C), 158.6 (C), 149.6 (C), 140.7 (C), 132.9 (CH), 129.9 (CH), 129.2 (2 × CH), 128.8 (2 × CH), 127.7 (CH), 125.2 (CH), 122.1 (CH), 121.3 (C),

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99.6 (CH), 75.5 (CH), 31.3 (2 × CH_2), 25.6 (2 × CH_2), 23.5 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{21}H_{22}NO$ 304.1696, found 304.1694.

*4-(2-Chloroethoxy)-2-phenylquinoline (**10f**).* Reaction of azido aldehyde **7a** (73 mg, 0.5 mmol), 2-chloro ethanol **8f** (35 μL, 0.5 mmol) and phenyl acetylene **9a** (55 μL, 0.5 mmol) with TMSOTf (91 μL, 0.5 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (3:97) as eluent furnished the 4-alkoxy quinoline **10f** (95 mg, 67%) as a white solid; mp 90−92 °C; IR (neat) 3062, 3034, 2962, 1594, 1510, 1424, 1359, 1223, 1160, 1115, 1020, 927, 836, 768, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 8.2 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H), 8.11−8.06 (m, 2H), 7.77−7.68 (m, 1H), 7.57−7.44 (m, 4H), 7.13 (s, 1H), 4.58−4.46 (t, J = 5.6 Hz, 2H), 4.00 (t, J = 5.6 Hz, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 161.5 (C), 158.8 (C), 149.3 (C), 104.2 (C), 130.3 (C), 129.5 (CH), 129.3 (CH), 128.9 (2 × CH), 127.7 (2 × CH), 125.8 (CH), 121.8 (CH), 120.3 (C), 98.7 (CH), 68.2 (CH_2), 41.6 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{17}H_{15}ClNO$, 284.0837 found 284.0836.

*4-((9H-Fluoren-9-yl)oxy)-2-phenylquinoline (**10g**).* Reaction of azido aldehyde **7a** (73 mg, 0.5 mmol), alcohol **8g** (100 mg, 0.5 mmol) and phenyl acetylene **9a** (55 μL, 0.5 mmol) with TMSOTf (91 μL, 0.5 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (3:97) as eluent furnished the 4-alkoxy quinoline **10g** (120 mg, 60%) as a white solid; mp 150−154 °C; IR (neat) 3020, 2978, 1594, 1510, 1425, 1355, 1216, 1112, 928, 758, 670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.44−8.37 (m, 1H), 8.17 (d, J = 8.2 Hz, 1H), 8.10−8.03 (m, 2H), 7.89−7.75 (m, 5H), 7.64−7.58 (m, 1H), 7.52−7.42 (m, 5H), 7.40−7.34 (m, 2H), 7.15 (s, 1H), 4.64 (t, J = 7.2 Hz, 1H), 4.53 (d, J = 7.2 Hz, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 162.1 (C), 158.9 (C), 149.3 (C), 143.8 (2 × C), 141.5 (C), 140.2 (C), 135.9 (C), 130.2 (CH), 129.4 (2 × CH), 128.9 (2 × CH), 128.2 (2 × CH), 127.7 (2 × CH), 127.4 (2 × CH), 125.8 (CH), 125.4 (2 × CH), 121.7 (CH), 120.4 (C), 120.3 (2 × CH), 98.8 (CH), 71.2 (CH_2), 47.4 (CH); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{29}H_{22}NO$ 400.1696, found 400.1696.

*4-(((1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl)oxy)-2-phenylquinoline (**10h**).* Reaction of azido aldehyde **7a** (50 mg, 0.34 mmol), (1*R*,2*S*,5*R*)-(−)-menthol **8h** (64 mg, 0.34 mmol) and phenyl acetylene **9a** (55 μL, 0.34 mmol) with TMSOTf (70 μL, 0.34 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (2:98) as eluent furnished the 4-alkoxy quinoline **10h** (96 mg, 78%) as a sticky solid; $[\alpha]_D^{25}$ −180.884 (*c* 0.500, $CHCl_3$); IR (neat) 2952, 2926, 1466, 1453, 1350, 1217, 1180, 1016, 698, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.4 Hz, 1H), 8.13 (t, J = 8.4 Hz, 3H), 7.74−7.70 (m, 1H), 7.56 (t, J = 7.6 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.21 (s, 1H), 4.49 (td, J = 10.4, 4.0 Hz, 2H), 2.37−2.34 (m, 1H), 2.26 (quind, J = 6.8, 2.0 Hz, 1H), 1.85−1.75 (m, 3H), 1.67−1.58 (m, 1H), 1.29−1.22 (m, 2H), 0.99 (dd, J = 6.4, 5.6 Hz, 6H), 0.83 (d, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 161.5 (C), 159.1 (C), 149.6 (C), 140.8 (C), 129.9 (CH), 129.3 (CH), 129.2 (2 × CH), 128.8 (CH), 127.8 (2 × CH), 125.2 (CH), 122.1 (CH), 121.2 (C), 98.9 (CH), 77.9 (CH), 48.1 (CH), 39.7 (CH_2), 34.5 (CH_2), 31.5 (CH), 26.6 (CH), 24.0 (CH_2), 22.2 (CH_3), 20.8 (CH_3), 17.1 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{25}H_{30}NO$ 360.2322, found 360.2321.

*4-(((3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)-2-phenylquinoline (**10i**).* Reaction of azido aldehyde **7a** (45 mg, 0.306 mmol), cholesterol **10i** (114 mg, 0.306 mmol) and phenyl acetylene **9a** (40 μL, 0.306 mmol) with TMSOTf (55 μL, 0.306 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (2:98) as eluent furnished the 4-alkoxy quinoline **10i** (80 mg, 45%) as a white solid; mp 170−172 °C; $[\alpha]_D^{25}$ −35.618 (*c* 1.00, $CHCl_3$); IR (neat) 3013, 2494, 1590, 1559, 1467, 1423, 1397, 1216, 1109, 1066, 999, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 8.2 Hz, 1H), 8.16−8.04 (m, 3H), 7.74−7.65 (m, 1H), 7.57−7.42 (m, 4H), 7.17 (s, 1H), 5.48 (d, J = 4.77 Hz, 1H), 4.61−4.46(m, 1H), 2.72−2.55 (m, 2H), 2.20 (d, J = 12.5 Hz, 1H), 2.11−1.96 (m, 3H), 1.95−1.79 (m, 2H), 1.67−1.45 (m, 6H), 1.45−1.21(m, 6H), 1.21−1.10 (m, 12H), 0.94 (d, J = 6.4 Hz, 3H), 0.91−0.82 (m, 6H), 0.71 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 161.2 (C), 158.9 (C), 149.6 (C), 140.7 (C), 139.9 (C), 130.1 (CH), 129.3 (CH), 128.9 (2 × CH), 127.8 (2 × CH), 125.3 (CH), 123.2 (CH), 122.1 (CH), 121.1 (C), 118.2 (CH), 99.5 (CH), 76.8 (CH), 56.9 (CH), 56.3 (CH), 50.3 (CH), 42.5 (C), 39.9 (CH_2), 39.7 (CH_2), 38.5 (CH_2), 37.2 (CH_2), 37.03 (C), 36.3 (CH_2), 35.9 (CH), 32.1 (CH_2), 32.0 (CH), 28.4 (CH_2), 28.2 (CH), 28.0 (CH_2), 24.4 (CH_2), 23.9 (CH_2), 22.9 (C), 22.7 (CH_3), 21.2 (CH_2), 19.6 (CH_3), 18.9 (CH_3), 12.0 (2 × CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{42}H_{56}NO$ 590.4356, found 590.4358.

*Ethyl (S)-2-((2-phenylquinolin-4-yl)oxy)propanoate (**10j**).* Reaction of azido aldehyde **7a** (50 mg, 0.34 mmol), (−)-Ethyl L-lactate **10j** (42 μL, 0.34 mmol) and phenyl acetylene **9a** (44 μL, 0.34 mmol) with TMSOTf (65 μL, 0.34 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (2:98) as eluent furnished the 4-alkoxy quinoline **10j** (17 mg, 15%) as a brown color sticky liquid; $[\alpha]_D^{25}$ −2.712 (*c* 0.500, $CHCl_3$); IR (neat) 3060, 3017, 2984, 2926, 2851, 1749, 1594, 1558, 1494, 1423, 1367, 1216, 1113, 698, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 8.5 Hz, 1H), 8.12 (d, J = 8.5 Hz, 1H), 8.04 (d, J = 7.0 Hz, 2H), 7.72 (t, J = 7.5 Hz, 1H), 7.15 (dd, J = 7.5, 0.0 Hz, 3H), 7.46 (d, J = 7.0 Hz, 1H), 7.05 (s, 1H), 5.10 (q, J = 6.5 Hz, 1H), 4.29−4.22 (m, 2H), 1.81 (d, J = 7.0 Hz, 3H), 1.25 (t, J = 6.0 Hz, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 171.3 (C), 163.9 (C), 158.6 (C), 147.5 (C), 140.1 (C), 130.4 (CH), 129.5 (CH), 129.2 (CH), 128.9 (2 × CH), 127.7 (2 × CH), 125.7 (CH), 122.1 (CH), 120.4 (C), 99.2 (CH), 73.1 (CH), 61.8 (CH_2), 18.5 (CH_3), 14.3 (CH_3); HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd. for $C_{20}H_{19}NNaO_3$ 344.1257, found 344.1250.

*4-Methyl-N-(2-((2-phenylquinolin-4-yl)oxy)ethyl)-benzenesulfonamide (**10k**).* Reaction of azido aldehyde **7a** (50 mg, 0.34 mmol), aminoalcohol **10k** (81 mg, 0.374 mmol) and phenyl acetylene **9a** (50 μL, 0.34 mmol) with TMSOTf (70 μL, 0.34 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (50:50) as eluent furnished the 4-alkoxy quinoline **10k** (131 mg, 92%) as a white solid; mp 165−167 °C; IR (neat) 3353, 2934, 2873, 1617, 1592, 1509, 1357, 1223, 1112, 1065, 912, 769, 732, 699 cm^{-1}; ^1H NMR (500 MHz, CD_3OD + $CDCl_3$) δ 8.01 (t, J = 7.5 Hz, 2H), 7.91 (d, J = 8.0 Hz, 2H), 7.68−7.63 (m, 3H), 7.47−7.39 (m, 4H), 7.12 (d, J = 8.0 Hz, 2H), 6.94 (s, 1H), 4.21 (t, J = 5.5 Hz, 2H), 3.44 (d, J = 5.5 Hz, 2H), 2.25 (s, 3H); $^{13}C\{^1H\}$NMR (125 MHz, CD_3OD + $CDCl_3$, DEPT) δ 161.5 (C), 159.0 (C), 148.1 (C), 142.8 (C), 139.4 (C), 137.2 (C), 129.8 (CH), 130.0 (2 × CH), 128.9 (CH), 128.1 (2 × CH), 127.2 (2 × CH), 126.1 (2 × CH), 124.9 (2 × CH), 121.4 (CH), 119.7 (C), 98.7 (CH), 66.4 (CH_2), 41.3 (CH_2), 20.2 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{24}H_{23}N_2O_3S$ 419.1424, found 419.1424.

*4−4-Methyl-N-(1-((2-phenylquinolin-4-yl)oxy)propan-2-yl)-benzenesulfonamide (**10l**).* Reaction of azido aldehyde **7a** (100 mg, 0.675 mmol), aminoalcohol **8l** (155 mg, 0.675 mmol) and phenyl acetylene **9a** (90 μL, 0.675 mmol) with TMSOTf (125 μL, 0.675 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (50:50) as eluent furnished the 4-alkoxy quinoline **1ol** (263 mg, 89%) as a sticky solid; IR (neat) 3383, 2924, 2863, 1627, 1582, 1519, 1367, 1224, 1115, 1067, 915, 768, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.8 Hz, 1H), 8.09−8.01 (m, 3H), 7.64 (d, J = 8.0 Hz, 2H), 7.52−7.47 (m, 3H), 7.45−7.39 (m, 2H), 7.06 (d, J = 8.0 Hz, 2H), 6.99 (s, 1H), 5.53 (bs, 1H), 4.80−4.72 (m, 1H), 3.38−3.27 (m, 2H), 2.24 (s, 3H), 1.39 (d, J = 6.0 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 160.4 (C), 158.6 (C), 149.4 (C), 143.7 (C), 140.1 (C), 137.1 (C), 130.2 (CH), 129.8 (2 × CH), 129.4 (CH), 129.2 (CH), 128.9 (2 × CH), 127.6 (2 × CH), 126.9 (2 × CH), 125.5 (CH), 121.7 (CH), 120.6 (C), 99.4

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(CH), 72.8 (CH_2), 47.7 (CH_2), 21.5 (CH_3), 17.1 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{25}H_{25}N_2O_3S$ 433.1580, found 433.1577.

4-Methyl-N-((1R,2R*)-2-((2-phenylquinolin-4-yl)oxy)cyclohexyl)-benzenesulfon-amide (**10m**).* Reaction of azido aldehyde **7a** (80 mg, 0.544 mmol), aminoalcohol **10m** (146 mg, 0.544 mmol) and phenyl acetylene **9a** (75 μL, 0.544 mmol) with TMSOTf (140 μL, 0.544 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (50:50) as eluent furnished the 4-alkoxy quinoline **10m** (241 mg, 93%) as a white solid; mp 215−217 °C; IR (neat) 3274, 3060, 2914, 2861, 1616, 1591, 1493, 1320, 1223, 1155, 1109, 1091, 908, 762, 697, 664, 571, 549 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 7.8 Hz, 2H), 8.06 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.5 Hz, 1H), 7.68−7.62 (m, 3H), 7.52 (t, J = 7.5 Hz, 2H), 7.45 (d, J = 7.0 Hz, 1H), 7.37 (d, J = 7.5 Hz, 1H), 7.22 (s, 1H), 6.98 (d, J = 7.8 Hz, 2H), 5.48 (d, J = 6.5 Hz, 1H), 4.60 (br s, 1H), 3.55 (d, J = 6.5 Hz, 1H), 2.42 (s, 3H), 2.16−2.09 (m, 2H), 1.78 (br s, 1H), 1.61 (br s, 2H), 1.42−1.41 (m, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 160.5 (C), 158.8 (C), 149.5 (C), 143.4 (C), 140.3 (C), 137.5 (C), 130.0 (CH), 129.7 (2 × CH), 129.4 (CH), 129.2 (CH), 128.9 (2 × CH), 127.7 (2 × CH), 126.9 (2 × CH), 125.2 (CH), 120.0 (CH), 120.9 (C), 99.6 (CH), 76.8 (CH), 53.9 (CH), 30.4 (CH_2), 28.3 (CH_2), 22.6 (CH_2), 22.1 (CH_2), 21.5 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{28}H_{29}N_2O_3S$ 473.1893, found 473.1880.

*4-((2-Phenylquinolin-4-yl)oxy)butan-1-ol (**10n**).* Reaction of azido aldehyde **7a** (163 mg, 1.109 mmol), butan-1,4-diol **8n** (50 mg, 0.554 mmol) and phenyl acetylene **9a** (150 μL, 1.36 mmol) with TMSOTf (200 μL, 1.109 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (50:50) as eluent furnished the 4-alkoxy quinoline **10n** (102 mg, 70%) as a yellow solid; mp 85−87 °C; IR (neat) 3420, 3062, 3030, 2955, 2927, 2869, 1596, 1567, 1507, 1424, 1358, 1211, 1113, 1025, 869, 765, 735, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.16 (dd, J = 9.5, 1.0 Hz, 1H), 8.12 (d, J = 9.5 Hz, 1H), 8.06−8.05 (m, 2H), 7.69 (td, J = 6.5, 0.5 Hz, 1H), 7.51−7.48 (m, 2H), 7.46−7.42 (m, 2H), 7.48 (s, 1H), 4.22 (t, J = 6.5 Hz, 2H), 3.72 (t, J = 6.5 Hz, 2H), 2.04−1.97 (m, 2H), 2.51 (s, 1H), 1.82−1.77 (m, 2H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 162.2 (C), 159.0 (C), 149.1 (C), 140.3 (C), 130.1 (CH), 129.9 (CH), 128.9 (CH), 128.8 (2 × CH), 127.7 (2 × CH), 125.4 (CH), 121.8 (CH), 120.5 (C), 98.8 (CH), 68.2 (CH_2), 62.2 (CH_2), 29.9 (CH_2), 25.6 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{19}H_{20}NO_2$ 294.1489, found 294.1481.

*(Benzyloxy)-2-(4-methoxyphenyl)quinoline (**10s**).* Reaction of azido aldehyde **7a** (133 mg, 0.908 mmol), benzyl alcohol **8a** (140 μL, 0.908 mmol) and alkyne **9b** (120 mg, 0.908 mmol) with TMSOTf (195 μL, 0.908 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (4:96) as eluent furnished the 4-alkoxy quinoline **10s** (248 mg, 79%) as a white solid; mp 118−120 °C; IR (neat) 3019, 2984, 2907, 1734, 1594, 1502, 1374, 1249, 1216, 1046, 757, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.0 Hz, 1H), 8.15 (d, J = 8.0 Hz, 1H), 8.09 (d, J = 8.4 Hz, 2H), 7.71 (t, J = 7.6 Hz, 1H), 7.54 (d, J = 7.2 Hz, 2H), 7.48−7.41 (m, 4H), 7.16 (s, 1H), 7.04 (d, J = 8.4 Hz, 2H), 5.27 (s, 2H), 3.85 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 161.6 (C), 160.7 (C), 158.1 (C), 149.2 (C), 135.9 (C), 132.6 (CH), 129.9 (CH), 128.9 (CH), 128.8 (2 × CH), 128.7 (2 × CH), 128.2 (CH), 127.4 (2 × CH), 125.0 (CH), 121.7 (CH), 120.2 (C), 114.1 (2 × CH), 98.5 (CH), 70.0 (CH_2), 55.7 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{23}H_{20}NO_2$ 342.1489, found 342.1485.

*4-(4-Methoxyquinolin-2-yl)phenyl acetate (**10t**).* Reaction of azido aldehyde **7a** (100 mg, 0.68 mmol), methanol **8b** (28 μL, 0.68 mmol) and acetate protected alkyne **9c** (158 mg, 0.68 mmol) with TMSOTf (123 μL, 0.68 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (4:96) as eluent furnished the 4-alkoxy quinoline **10t** (175 mg, 88%) as a yellow sticky solid; IR (neat) 2952, 2936, 1468, 1459, 1357, 1218, 1182, 1017, 688, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16−8.09 (m, 4H), 7.70 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.26−7.24 (m, 2H), 7.12 (s, 1H), 4.06 (s, 3H), 2.33 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 169.4 (C), 162.9 (C), 157.8 (C), 151.7 (C), 149.1 (C), 138.0 (C), 130.1 (CH), 129.1 (CH), 128.8 (2 × CH), 125.5 (CH), 121.9 (2 × CH), 121.7 (CH), 120.4 (C), 97.8 (CH), 55,7 (CH_3), 21.2 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{18}H_{16}NO_3$ 294.1125, found 294.1123.

*2-(Benzo[b]thiophen-2-yl)-4-(benzyloxy)quinoline (**10u**).* Reaction of azido aldehyde **7a** (50 mg, 0.316 mmol), benzyl alcohol **8a** (55 μL, 0.316 mmol) and alkyne **9d** (46 mg, 0.316 mmol) with TMSOTf (65 μL, 0.316 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (3:97) as eluent furnished the 4-alkoxy quinoline **10u** (90 mg, 78%) as a yellow solid; mp 143−145 °C; IR (neat) 3018, 1617, 1591, 1560, 1425, 1365, 1215, 1109, 825, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.0 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.91−7.89 (m, 1H), 7.87 (s, 1H), 7.81−7.79 (m, 1H), 7.01 (t, J = 7.4 Hz, 1H), 7.58−7.56 (m, 2H), 7.51−7.43 (m, 4H), 7.38−7.36 (m, 2H), 7.23 (s, 1H), 5.33 (s, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 161.6 (C), 153.2 (C), 149.1 (C), 145.9 (C), 141.1 (C), 140.4 (C), 135.8 (C), 130.3 (CH), 128.9 (CH), 128.8 (2 × CH), 128.5 (CH), 127.6 (2 × CH), 125.7 (CH), 125.3 (CH), 124.5 (CH), 124.3 (CH), 122.6 (CH), 122.1 (CH), 121.7 (CH), 120.9 (C), 97.7 (CH), 70.4 (CH_2); HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd. for $C_{24}H_{17}NNaOS$ 390.0923, found 390.0928.

*4-(benzyloxy)-2-(pyren-1-yl)quinoline (**10v**).* Reaction of azido aldehyde **7a** (59 mg, 0.397 mmol), benzyl alcohol **8a** (42 μL, 0.397 mmol) and pyrene alkyne **9e** (90 mg, 0.397 mmol) with TMSOTf (72 μL, 0.397 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (2:98) as eluent furnished the 4-alkoxy quinoline **10v** (110 mg, 62%) as a white sticky solid; IR (neat) 3052, 2826, 1476, 1473, 1390, 1237, 1220, 1036, 658, 628 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 8.4 Hz, 1H), 8.31−8.18 (m, 6H), 8.13 (s, 2H), 8.05−8.01 (m, 2H), 7.81 (t, J = 8.0 Hz, 1H), 7.61 (t, J = 8.0 Hz, 1H), 7.52 (d, J = 7.2 Hz, 2H), 7.45 (q, J = 8.0 Hz, 4H), 5.36 (s, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 161.3 (C), 160.8 (C), 149.3 (C), 136.5 (C), 135.8 (C), 131.9 (C), 131.5 (C), 131.0 (C), 130.4 (CH), 129.3 (CH), 128.9 (CH), 128.8 (C), 128.5 (CH), 128.2 (2 × CH), 128.1 (CH), 127.6 (3 × CH), 127.5 (CH), 126.2 (CH), 125.9 (CH), 125.5 (CH), 125.3 (CH), 125.2 (C), 124.9 (CH), 124.9 (C), 125.9 (C), 122.1 (CH), 120.4 (C), 104.3 (CH), 70.5 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{32}H_{22}NO$ 436.1696, found 436.1697.

*4-(Benzyloxy)-2-butylquinoline (**10w**).* Reaction of azido aldehyde **7a** (75 mg, 0.51 mmol), benzyl alcohol **8a** (60 μL, 0.51 mmol) and hexyne **9f** (90 μL, 0.765 mmol) with TMSOTf (74 μL, 0.51 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (2:98) as eluent furnished the 4-alkoxy quinoline **10w** (68 mg, 45%) as a sticky solid; IR (neat) 2852, 3018, 1592, 1557, 1493, 1445, 1422, 1338, 1215, 1160, 759, 668, 549 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.1 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H), 8.67 (t, J = 8.1 Hz, 1H), 7.52−7.25 (m, 6H), 6.72 (s, 1H), 5.23 (s, 2H), 2.93 (t, J = 8.0 Hz, 2H), 1.80−1.72 (m, 2H), 1.44−1.38 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 164.2 (C), 161.9 (C), 141.1 (C), 135.7 (C), 135.7 (CH), 128.8 (CH), 128.5 (CH), 128.4 (2 × CH), 127.6 (CH), 127.5 (2 × CH), 125.5 (CH), 117.6 (C), 101.06 (CH), 70.3 (CH_2), 39.1 (CH_2), 32.2 (CH_2), 22.6 (CH_2), 14.1 (CH_3); HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd. for $C_{20}H_{21}NNaO$ 314.1515, found 314.1513.

*4-(Benzyloxy)-3-butyl-2-phenylquinoline (**10x**).* Reaction of azido aldehyde **7a** (74.2 mg, 0.5 mmol), benzyl alcohol **8a** (50 μL, 0.5 mmol) and alkyne **9g** (98 mg, 0.6 mmol) with TMSOTf (92 μL, 0.5 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (2:98) as eluent furnished the 4-alkoxy quinoline **10x** (64 mg, 35%) as a pale yellow liquid; IR (neat) 3019,

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2952, 2936, 1476, 1433, 1310, 1257, 1160, 1006, 658, 618 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, J = 8.3 Hz, 1H), 8.09 (dd, J = 8.3, 0.76 Hz, 1H), 7.68 (ddd, J = 8.4, 6.9, 1.45 Hz, 1H), 7.59−7.51 (m, 5H), 7.51−7.39 (m, 6H), 5.18 (s, 2H), 2.81−2.70 (m, 2H), 1.46−1.35 (m, 2H), 1.23−1.11 (m, 2H), 0.73 (t, J = 7.40 Hz, 3H); $^{13}C\{^1H\}$NMR (126 MHz, $CDCl_3$, DEPT) δ 162.8 (C), 160.8 (C), 148.2 (C), 141.3 (C), 136.9 (C), 129.9 (CH), 129.2 (CH), 128.8 (2 × CH), 128.7 (2 × CH), 128.5 (CH), 128.3 (2 × CH), 128.2 (CH), 127.8 (2 × CH), 126.6 (C), 126.3 (CH), 123.1 (C), 121.9 (CH), 76.8 (CH_2), 32.4 (CH_2), 26.8 (CH_2), 22.9 (CH_2), 13.7 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{26}H_{26}NO$ 368.2009, found 368.2009.

*4-(Benzyloxy)-2,3-diphenylquinoline (**10y**).* Reaction of azido aldehyde **7a** (60 mg, 0.408 mmol), benzyl alcohol **8a** (50 μL, 0.489 mmol) and alkyne **9h** (72 mg, 0.408 mmol) with TMSOTf (75 μL, 0.408 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (2:98) as eluent furnished the 4-alkoxy quinoline **10y** (90 mg, 65%) as a colorless liquid; IR (neat) 2930, 1585, 1508, 1489, 1415, 1110, 939, 844, 762, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.24 (t, J = 7.0 Hz, 2H), 7.78 (t, J = 7.5 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.41−7.26 (m, 13H), 7.13−7.12 (m, 2H), 4.60 (s, 2H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 160.8 (C), 160.4 (C), 149.9 (C), 140.6 (C), 136.4 (C), 135.6 (C), 131.4 (2 × CH), 130.1 (CH), 130.0 (2 × CH), 129.7 (CH), 128.6 (2 × CH), 128.5 (2 × CH), 128.4 (CH), 128.3 (2 × CH), 127.9 (CH), 127.8 (2 × CH), 127.4 (CH), 126.6 (CH), 126.2 (C), 123.2 (C), 122.6 (CH), 75.8 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{28}H_{22}NO$ 388.1696, found 388.1691.

*4-(Benzyloxy)-3-bromo-2-phenylquinoline (**10z**).* Reaction of azido aldehyde **7a** (120 mg, 0.816 mmol), benzyl alcohol **8a** (85 μL, 0.816 mmol) and bromo alkyne **9i** (147.8 mg, 0.816 mmol) with TMSOTf (148 μL, 0.816 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (2:98) as eluent furnished the 4-alkoxy quinoline **10z** (187 mg, 72%) as a white solid; mp 122−125 °C; IR (neat) 3115, 2826, 1566, 1553, 1450, 1317, 1080, 1016, 678, 628 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.4 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.76−7.71 (m, 3H), 7.61 (d, J = 7.2 Hz, 2H), 7.57−7.39 (m, 7H), 5.28 (s, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 160.5 (C), 160.4 (C), 148.3 (C), 140.4 (C), 136.2 (C), 130.1 (CH), 129.8 (CH), 129.5 (2 × CH), 128.9 (CH), 128.8 (2 × CH), 128.8 (2 × CH), 128.5 (2 × CH), 128.1 (CH), 127.2 (CH), 124.1 (C), 122.1 (CH), 110.9 (C), 76.3 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{22}H_{17}BrNO$ 390.0488, found 390.0485.

*4-(2-Azidoethoxy)-2-(4-propoxyphenyl)quinoline (**10aa**).* Reaction of azido aldehyde **7a** (70 mg, 0.476 mmol), azido alcohol **8o** (45 mg, 0.476 mmol) and alkyne **9j** (76 mg, 0.476 mmol) with TMSOTf (86 μL, 0.476 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **9a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (4:96) as eluent furnished the 4-alkoxy quinoline **10aa** (83 mg, 50%) as yellow liquid; IR (neat) 2854, 2928, 2233, 1465, 1455, 1352, 1218, 1186, 1017, 697, 665 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, J = 8.5 Hz, 1H), 8.15 (s, 1H), 8.06 (d, J = 9.0 Hz, 2H), 7.72 (td, J = 8.5, 1.0 Hz, 1H), 7.48 9(t, J = 7.5 Hz, 1H), 7.10 (s, 1H), 7.01 (d, J = 8.5 Hz, 2H), 4.45 (t, J = 5.0 Hz, 2H), 3.99 (t, J = 6.5 Hz, 2H), 3.78 (t, 5.0 Hz, 2H), 1.88−1.81 (m, 2H), 1.07 (t, J = 7.5 Hz, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 161.8 (C), 160.7 (C), 158.2 (2 × C), 130.5 (CH), 128.7 (C), 129.1 (CH), 125.6 (CH), 121.8 (CH), 119.9 (C), 114.9 (3 × CH), 98.2 (CH), 69.8 (CH_2), 67.6 (CH_2), 50.3 (CH_2), 22.7 (CH_2), 10.6 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{20}H_{21}N_4O_2$ 349.1659, found 349.1658.

*4-(Benzyloxy)-6-nitro-2-phenylquinoline (**10ab**).* Reaction of azido aldehyde **6b** (100 mg, 0.52 mmol), benzyl alcohol **8a** (55 μL, 0.52 mmol) and phenyl acetylene **9a** (57 μL, 0.52 mmol) with TMSOTf (94 μL, 0.52 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (3:97) as eluent furnished the 4-alkoxy quinoline **10ab** (120 mg, 83%) as a yellow sticky solid; IR (neat) 3153, 2834, 2863, 1627, 1492, 1409, 1367, 1253, 1122, 1015, 914, 768, 734, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.16 (d, J = 2.0 Hz, 1H), 8.43 (m, 1H), 8.17 (d, J = 9.2 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.56−7.41 (m, 8H), 7.36 (s, 1H), 5.43 (s, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 163.1 (C), 162.4 (C), 151.6 (C), 144.7 (C), 139.2 (C), 134.9 (C), 131.8 (CH), 130.4 (CH), 129.1 (2 × CH), 129.1 (CH), 128.9 (2 × CH), 127.8 (2 × CH), 127.7 (2 × CH), 119.7 (CH), 119.6 (CH), 100.5 (CH), 71.1 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{22}H_{17}N_2O_3$ 357.1234, found 357.1235.

*4-(Benzyloxy)-6-bromo-2-phenylquinoline (**10ac**).* Reaction of azido aldehyde **7c** (100 mg, 0.442 mmol), benzyl alcohol **8a** (46 μL, 0.442 mmol) and phenyl acetylene **9a** (49 μL, 0.442 mmol) with TMSOTf (80 μL, 0.442 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (3:97) as eluent furnished the 4-alkoxy quinoline **10ac** (143 mg, 83%) as a white sticky solid; IR (neat) 3053, 2954, 2843, 1607, 1592, 1519, 1357, 1243, 1122, 1015, 918, 777, 731, 649 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, J = 2.5 Hz, 1H), 8.08−8.06 (m, 2H), 7.98 (d, J = 6.5 Hz, 1H), 7.76 (dd, J = 7.2, 2.5 Hz, 1H), 7.54−7.51 (m, 4H), 7.49−7.46 (m, 3H), 7.43−7.40 (m, 1H), 7.25 (s, 1H), 5.34 (s, 2H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 161.0 (C), 159.1 (C), 147.8 (C), 139.8 (C), 135.5 (C), 131.0 (CH), 129.7 (CH), 129.0 (CH), 128.9 (2 × CH), 128.7 (2 × CH), 127.8 (CH), 127.7 (2 × CH), 127.6 (2 × CH), 124.4 (CH), 121.7 (C), 119.4 (C), 99.8 (CH), 70.6 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{22}H_{17}BrNO$ 390.0488, found 390.0486.

*8-(Benzyloxy)-6-phenyl-[1,3]dioxolo[4,5-g]quinoline (**10ad**).* Reaction of azido aldehyde **7d** (70 mg, 0.366 mmol), benzyl alcohol **8a** (55 μL, 0.366 mmol) and phenyl acetylene **9a** (50 μL, 0.366 mmol) with TMSOTf (75 μL, 0.366 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (3:97) as eluent furnished the 4-alkoxy quinoline **10ad** (110 mg, 83%) as a white solid; mp 108−110 °C; IR (neat) 3133, 2984, 2863, 1627, 1542, 1519, 1347, 1323, 1212, 1165, 932, 759, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 7.2 Hz, 2H), 7.53−7.35 (m, 10H), 7.15 (s, 1H), 6.07 (s, 2H), 5.31 (s, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 161.2 (C), 156.9 (C), 151.0 (C), 147.5 (C), 147.2 (C), 140.2 (C), 136.0 (C), 129.5 (CH), 128.8 (2 × CH), 128.8 (2 × CH), 128.4 (CH), 127.6 (2 × CH), 127.4 (2 × CH), 116.4 (C), 105.9 (CH), 101.7 (CH_2), 98.5 (CH), 97.9 (CH), 70.2 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{23}H_{18}NO_3$ 356.1281, found 356.1290.

*2-Phenylquinolin-4-ol (**11**).*[18] Reaction of azido aldehyde **7a** (50 mg, 0.34 mmol), (−)-Ethyl L-lactate **8j** (42 μL, 0.34 mmol) and phenyl acetylene **9a** (44 μL, 0.34 mmol) with TMSOTf (65 μL, 0.34 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (50:50) as eluent furnished the 4-alkoxy quinoline **11** (50 mg, 65%) as a white solid; mp 205−207 °C; IR (neat) 3533, 2952, 2926, 1466, 1453, 1350, 1217, 1180 cm^{-1}; ^1H NMR (500 MHz, Acetone-d_6) δ 8.34 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.5 Hz, 1H), 7.69−7.64 (m, 3H), 7.51−7.42 (m, 3H), 7.26 (t, J = 7.5 Hz, 1H), 6.65 (s, 1H); $^{13}C\{^1H\}$NMR (125 MHz, Acetone-d_6, DEPT) δ 179.2 (C), 134.8 (C), 133.1 (CH), 131.5 (2 × CH), 129.9 (2 × CH), 128.4 (CH), 126.1 (C), 125.6 (CH), 124.7 (C), 123.2 (CH), 119.5 (C), 118.1 (CH), 108.7 (CH); HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd. for $C_{15}H_{11}NaNO$ 244.0733, found 244.0728.

General Procedure of Intramolecular Reaction for Synthesis of Cyclic Ether-Fused Quinoline Derivatives. *4-Phenyl-2, 3-dihydrofuro[3,2-c]quinoline (**13a**).*[19] To a magnetically stirred solution of azido aldehyde **7a** (70 mg, 0.476 mmol), alkynol **12a** (70 mg, 0.476 mmol) in dry CH_2Cl_2 (8.0 mL) was added dropwise TMSOTf (85 μL, 0.476 mmol) at 0 °C. Reaction was monitored by TLC, quenched with saturated aq. solution of $NaHCO_3$ upon completion, extracted with CH_2Cl_2 (3 × 5 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc−petroleum ether as eluent furnished 4-alkoxy quinoline **13a** (117 mg, 99%) as a white solid; mp 64−66 °C; IR (neat) 3052, 2926, 1566, 1473, 1360, 1207,

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1190, 1006, 688, 658 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.86 (d, J = 7.5 Hz, 2H), 7.63 (t, J = 7.5 Hz, 1H), 7.47 (d, J = 7.5 Hz, 2H), 7.41 (d, J = 7.5 Hz, 2H), 4.71 (t, J = 9.0 Hz, 2H), 3.39 (t, J = 9.0 Hz, 2H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 164.2 (C), 155.3 (C), 149.0 (C), 139.7 (C), 129.6 (CH), 129.1 (CH), 128.7 (CH), 128.4 (2 × CH), 128.2 (2 × CH), 125.2 (CH), 121.3 (CH), 115.9 (C), 115.0 (C), 72.9 (CH_2), 29.9 (CH_2); HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd. for $C_{17}H_{13}NNaO$ 270.0899, found 270.0877.

*2-Methyl-4-phenyl-2,3-dihydrofuro[3,2-c]quinoline (**13b**).* Reaction of azido aldehyde **7a** (64 mg, 0.436 mmol), alkynol **12b** (70 mg, 0.436 mmol) with TMSOTf (80 μL, 0.436 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13b** (109 mg, 96%) as a white solid; mp 68−70 °C; IR (neat) 3059, 2975, 2927, 2857, 1630, 1592, 1554, 1505,, 703, 674 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.13 (dd, J = 8.5, 1.0 Hz, 1H), 7.96 (dd, J = 8.5, 1.0 Hz, 1H), 7.91−7.89 (m, 2H), 7.68−7.64 (m, 1H), 7.52−7.48 (m, 2H), 7.46−7.42 (m, 2H), 5.25−5.18 (m, 1H), 3.66 (dd, J = 15.0, 9.5 Hz, 1H), 3.15 (dd, J = 15.0, 7.5 Hz, 1H), 1.58 (d, J = 6.0 Hz, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 163.6 (C), 155.6 (C), 149.3 (C), 140.6 (C), 129.6 (CH), 129.3 (CH), 128.8 (CH), 128.5 (2 × CH), 128.3 (2 × CH), 125.3 (CH), 121.5 (CH), 116.1 (C), 114.9 (C), 82.1 (CH), 37.5 (CH_2), 22.1 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{18}H_{16}NO$ 262.1226, found 262.1228.

*2-((Benzyloxy)methyl)-4-phenyl-2,3-dihydrofuro[3,2-c]quinoline (**13c**).* Reaction of azido aldehyde **7a** (70 mg, 0.476 mmol), alkynol **12c** (152 mg, 0.476 mmol) with TMSOTf (87 μL, 0.476 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13c** (168 mg, 96%) as a pale yellow liquid; IR (neat) 3063, 2926, 1466, 1453, 1350, 1217, 1180, 1016, 698, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.1 Hz, 1H), 7.99 (d, J = 7.4 Hz, 1H), 7.90 (d, J = 7.4 Hz, 2H), 7.27−7.68 (m, 1H), 7.52−7.45 (m, 4H), 7.32−7.26 (m, 5H), 5.32 (bs, 1H), 4.63 (AB, J = 12.4, 5.6 Hz, 2H), 3.83−3.75 (m, 2H), 3.66−3.59 (m, 1H), 3.39 (dd, J = 15.2, 6.8 Hz, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 164.0 (C), 155.5 (C), 149.1 (C), 139.6 (C), 137.8 (C), 129.9 (CH), 129.1 (CH), 129.0 (CH), 128.7 (2 × CH), 128.6 (2 × CH), 128.5 (2 × CH), 127.9 (CH), 127.9 (2 × CH), 125.6 (CH), 121.6 (CH), 116.0 (C), 114.8 (C), 84.2 (CH), 73.7 (CH_2), 71.7 (CH_2), 32.6 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{25}H_{22}NO_2$ 368.1645, found 368.1644.

*2-Cyclohexyl-4-phenyl-2,3-dihydrofuro[3,2-c]quinoline (**13d**).* Reaction of azido aldehyde **7a** (45 mg, 0.306 mmol), alkynol **12d** (70 mg, 0.306 mmol) with TMSOTf (58 μL, 0.306 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13d** (95 mg, 95%) as a white solid; mp 122−125 °C; IR (neat) 3022, 2936, 1456, 1433, 1356, 1267, 1160, 1026, 698, 666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 8.5 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 8.5 Hz, 2H), 7.65 (td, J = 7.0, 1.5 Hz, 1H), 7.51 (t, J = 7.5, Hz, 2H), 7.44 (td, J = 7.0, 1.5 Hz, 2H), 4.81 (dd, J = 16.2, 7.2 Hz, 1H), 3.53 (dd, J = 15.5, 9.0 Hz, 1H), 3.29 (dd, J = 15.5, 9.0 Hz, 1H), 2.05 (d, J = 13.0 Hz, 1H), 1.81−1.71 (m, 5H), 1.33−1.28 (m, 3H), 1.27−1.13 (m, 2H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 163.9 (C), 155.6 (C), 149.3 (C), 140.2 (C), 129.6 (CH), 129.3 (CH), 128.6 (2 × CH), 128.4 (3 × CH), 125.2 (CH), 121.6 (CH), 115.9 (C), 115.2 (C), 89.9 (CH), 43.3 (CH), 33.4 (CH_2), 28.5 (CH_2), 28.2 (CH_2), 26.4 (CH_2), 25.9 (CH_2), 25.7 (CH_2); HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd. for $C_{23}H_{23}NNaO$ 352.1672, found 352.1675.

*2,4-Diphenyl-2,3-dihydrofuro[3,2-c]quinoline (**13e**).* Reaction of azido aldehyde **7a** (42 mg, 0.288 mmol), alkynol **12e** (69 mg, 0.288 mmol) with TMSOTf (80 μL, 0.288 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13e** (97 mg, 93%) as a white solid; mp 130−132 °C; IR (neat) 3013, 2986, 1456, 1443, 1360, 1277, 1160, 1026, 678, 658 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.49−7.37 (m, 7H), 7.30 (d, J = 8.0 Hz, 2H), 6.11 (t, J = 8.5 Hz, 1H), 3.76 (dd, J = 8.5, 7.5 Hz, 1H), 3.45 (dd, J = 8.5, 7.5 Hz, 1H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 163.0 (C), 156.4 (C), 149.2 (C), 141.1 (C), 141.0 (C), 132.9 (CH), 130.6 (CH), 130.1 (CH), 129.9 (CH), 129.5 (CH), 128.9 (2 × CH), 128.6 (CH), 127.7 (CH), 125.9 (CH), 125.9 (2 × CH), 121.8 (CH), 121.7 (CH), 116.5 (C), 116.2 (C), 86.7 (CH), 37.5 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{23}H_{18}NO$ 324.1383, found 324.1382.

*4-Ethyl-2,3-dihydrofuro[3,2-c]quinoline (**13f**).* Reaction of azido aldehyde **7a** (84 mg, 0.641 mmol), alkynol **12f** (63 mg, 0.641 mmol) with TMSOTf (116 μL, 0.641 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13f** (126 mg, 98%) as a yellow liquid; IR (neat) 3013, 2998, 1566, 1463, 1370, 1237, 1120, 1036, 679, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.59 (t, J = 7.2 Hz, 1H), 7.38 (t, J = 7.2 Hz, 1H), 4.82 (t, J = 8.8 Hz, 2H), 3.31 (t, J = 10.4 Hz, 2H), 2.86 (q, J = 7.6 Hz, 2H), 1.34 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 163.4 (C), 160.8 (C), 149.1 (C), 129.4 (CH), 128.5 (CH), 124.8 (CH), 121.4 (CH), 115.9 (C), 115.4 (C), 73.1 (CH_2), 30.3 (CH_2), 28.2 (CH_2), 12.9 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{13}H_{14}NO$ 200.1070, found 200.1072.

*2-(tert-Butyl)-4-(4-methoxyphenyl)-2,3-dihydrofuro[3,2-c]-quinoline (**13g**).* Reaction of azido aldehyde **7a** (42 mg, 0.288 mmol), alkynol **12g** (67 mg, 0.288 mmol) with TMSOTf (52 μL, 0.288 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13g** (88 mg, 92%) as a white solid; mp 140−142 °C; IR (neat) 2999, 2986, 1476, 1433, 1310, 1207, 1090, 1036, 678, 658 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.8 Hz, 1H), 7.97 (dd, J = 8.0, 0.8 Hz, 1H), 7.90 (dd, J = 6.8, 2.0 Hz, 2H), 7.67−7.63 (m, 1H), 7.46−7.42 (m, 1H), 7.04 (dd, J = 6.8, 2.0 Hz, 2H), 4.81 (t, J = 8.8 Hz, 1H), 3.88 (s, 3H), 3.47 (dd, J = 15.6, 10.0 Hz, 1H), 3.32 (dd, J = 15.6, 8.6 Hz, 1H), 1.04 (s, 9H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 164.3 (C), 160.4 (C), 155.0 (C), 150.0 (C), 132.4(C), 129.9 (2 × CH), 129.8 (CH), 128.9 (CH), 125.0 (CH), 121.6 (CH), 115.7 (C), 114.9 (C), 114.1 (2 × CH), 93.4 (CH), 55.5 (CH), 34.8 (C), 31.5 (CH_2), 25.1 (3 × CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{22}H_{24}NO_2$ 334.1820, found 334.1821.

*4-(4-Methoxyphenyl)-2-phenyl-2,3-dihydrofuro[3,2-c]quinoline (**13h**).* Reaction of azido aldehyde **7a** (67 mg, 0.455 mmol), alkynol **12h** (115 mg, 0.455 mmol) with TMSOTf (85 μL, 0.455 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13h** (155 mg, 93%) as a white solid; mp 152−154 °C; IR (neat) 3092, 2966, 1557, 1456, 1423, 1320, 1207, 1190, 1006, 658, 648 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 8.5 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 2H), 7.68 (t, J = 7.5 Hz, 1H), 7.48−7.44 (m, 3H), 7.40 (t, J = 7.5 Hz, 2H), 7.35−7.33 (m, 1H), 7.01 (d, J = 8.0 Hz, 2H), 6.04 (dd, J = 8.0, 0.0 Hz, 1H), 4.40 (dd, J = 15.0, 9.5 Hz, 1H), 3.86 (s, 3H), 3.58 (dd, J = 15.0, 8.0 Hz, 1H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 163.6 (C), 160.3 (C), 155.1 (C), 149.5 (C), 141.3 (C), 132.5 (C), 129.8 (3 × CH), 129.3 (CH), 128.9 (2 × CH), 128.5 (CH), 125.8 (2 × CH), 125.3 (CH), 121.6 (CH), 115.8 (C), 114.1 (C), 114.0 (2 × CH), 86.1 (CH), 55.4 (CH_3), 39.3 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{24}H_{20}NO_2$ 354.1489, found 354.1481.

*2-Methyl-4-(4-nitrophenyl)-2,3-dihydrofuro[3,2-c]quinoline (**13i**).* Reaction of azido aldehyde **7a** (57 mg, 0.389 mmol), alkynol **13i** (80 mg, 0.389 mmol) with TMSOTf (75 μL, 0.389 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13i** (110 mg, 93%) as a white sticky solid; IR (neat) 2952, 2936, 1456, 1423, 1390, 1297, 1150, 1026, 688, 648 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.34−8.32 (m, 2H),

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8.10−8.07 (m, 3H), 7.97 (dd, J = 8.5 Hz, 1H), 7.71−7.67 (m, 1H), 7.51−7.48 (m, 1H), 5.32−5.25 (m, 1H), 3.69 (dd, J = 15.0, 9.0 Hz, 1H), 3.18 (J = 15.0, 7.5 Hz, 1H), 1.62 (d, J = 6.5 Hz, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 164.3 (C), 152.8 (C), 149.3 (C), 148.0 (C), 146.1 (C), 130.2 (CH), 129.5 (CH), 129.3 (2 × CH), 126.2 (CH), 123.8 (2 × CH), 121.7 (CH), 116.4 (C), 115.2 (C), 82.4 (CH), 37.5 (CH_2), 22.1 (CH_3); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd. for $C_{18}H_{15}N_2O_3$ 307.1038, found 307.1036.

*4-(2-Bromophenyl)-2-phenyl-2,3-dihydrofuro[3,2-c]quinoline (**13j**).* Reaction of azido aldehyde **7a** (50 mg, 0.332 mmol), alkynol **12j** (100 mg, 0.332 mmol) with TMSOTf (60 μL, 0.332 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13j** (124 mg, 93%) as a white solid; mp 168−170 °C; IR (neat) 3012, 2986, 1416, 1403, 1360, 1207, 1120, 1006, 678, 658 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.50−7.37 (m, 7H), 7.30 (t, J = 8.0 Hz, 1H), 6.11 (t, J = 8.5 Hz, 1H), 3.76 (dd, J = 15.5, 10.0 Hz, 1H), 3.35 (dd, J = 15.5, 7.0 Hz, 1H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 163.0 (C), 156.4 (C), 149.2 (C), 141.1 (C), 141.0 (C), 132.9 (CH), 130.6 (CH), 130.1 (CH), 129.9 (CH), 129.5 (CH), 128.9 (2 × CH), 128.6 (CH), 127.7 (CH), 125.9 (CH), 125.9 (2 × CH), 121.9 (C), 121.7 (CH), 116.5 (C), 116.2 (C), 86.7 (CH), 37.5 (CH_2); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd. for $C_{23}H_{17}BrNO$ 402.0488, found 402.0489.

(6bS,9aS*)-6-Phenyl-6b,8,9,9a-tetrahydro-7H-cyclopenta[4,5]furo[3,2-c]quinoline (**13k**).* Reaction of azido aldehyde **7a** (63 mg, 0.429 mmol), alkynol **12k** (80 mg, 0.429 mmol) with TMSOTf (80 μL, 0.429 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13k** (121 mg, 98%) as a white solid; mp 86−88 °C; IR (neat) 3056, 2960, 1630, 1591, 1556, 1398, 1328, 1300, 1205, 1156, 1091, 1022, 991, 913, 760, 736, 700, 673 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 8.5, 1.0 Hz, 1H), 7.97 (dd, J = 8.5, 1.0 Hz, 1H), 7.91 (d, J = 7.0 Hz, 2H), 7.67−7.63 (m, 1H), 7.49 (t, J = 8.0 Hz, 2H), 7.45−7.42 (m, 2H), 5.52 (t, J = 6.5 Hz, 1H), 4.34−4.31 (m, 1H), 2.18 (dd, J = 11.6, 4.5 Hz, 1H), 1.87−1.81 (m, 1H), 1.75−1.68 (m, 1H), 1.61−1.56 (m, 1H), 1.53−1.49 (m, 1H), 1.42−1.39 (m, 1H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 164.2 (C), 156.1 (C), 149.1 (C), 139.7 (C), 129.5 (CH), 129.2 (CH), 128.6 (CH), 128.5 (2 × CH), 128.4 (2 × CH), 125.2 (CH), 121.7 (CH), 118.9 (C), 115.7 (C), 95.5 (CH), 46.4 (CH), 35.2 (CH_2), 33.4 (CH_2), 23.4 (CH_2); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd. for $C_{20}H_{17}NNaO$ 310.1202, found 310.1201.

*4-(Phenylethynyl)-2,3-dihydrofuro[3,2-c]quinoline (**13l**).* Reaction of azido aldehyde **7a** (60 mg, 0.411 mmol), alkynol **12l** (70 mg, 0.411 mmol) with TMSOTf (90 μL, 0.411 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13l** (108 mg, 93%) as a white solid; mp 135−137 °C; IR (neat) 2984, 2102, 1466, 1383, 1263, 1037, 1027, 978, 877, 758, 608 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.61−7.56 (m, 3H), 7.37 (t, J = 7.6 Hz, 1H), 77.31−7.28 (m, 3H), 4.76 (t, J = 9.2 Hz, 2H), 3.38 (t, J = 9.2 Hz, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 163.2 (C), 149.2 (C), 140.2 (C), 132.1 (2 × CH), 129.8 (CH), 129.1 (CH), 128.9 (CH), 128.4 (2 × CH), 125.9 (CH), 122.1 (C), 121.2 (CH), 119.6 (C), 116.2 (C), 92.2 (C), 87.3 (C), 73.2 (CH_2), 28.6 (CH_2); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd. for $C_{19}H_{14}NO$ 272.1070, found 272.1069.

*(Z)-4-(2-Chlorovinyl)-2,3-dihydrofuro[3,2-c]quinoline (**13m**).* Reaction of azido aldehyde **7a** (68 mg, 0.467 mmol), alkynol **12m** (60 mg, 0.467 mmol) with TMSOTf (101 μL, 0.467 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13m** (102 mg, 95%) as a white solid; mp 88−90 °C; IR (neat) 3092, 2929, 1566, 1453, 1390, 1207, 1120, 1026, 688, 658 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 7.43 (t, J = 8.0 Hz, 1H), 6.92 (d, J = 8.0 Hz, 1H), 6.54 (d, J = 8.0 Hz, 1H), 4.84 (t, J = 8.8 Hz, 2H), 3.37 (t, J = 8.8 Hz, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 164.0 (C), 150.7 (C), 148.9 (C), 129.8 (CH), 129.1 (CH), 128.7 (CH), 125.8 (CH), 122.8 (CH), 121.4 (CH), 116.9 (C), 116.0 (C), 73.3 (CH_2), 28.6 (CH_2); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd. for $C_{13}H_{11}ClNO$ 232.0534, found 232.0532.

*6-Phenyl-8,9,10,10a-tetrahydrobenzofuro[3,2-c]quinoline (**13n**).* Reaction of azido aldehyde **7a** (74 mg, 0.504 mmol), alkynol **13n** (100 mg, 0.504 mmol) with TMSOTf (109 μL, 0.504 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13n** (135 mg, 89%) as a brown liquid; IR (neat) 3033, 3013, 2953, 1677, 1590, 1267, 1459, 1356, 1222, 1191, 678, 658 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.8 Hz, 1H), 7.98 (d, J = 8.8 Hz, 1H), 7.85 (dd, J = 8.1, 1.6 Hz, 1H), 7.62 (td, J = 8.1, 1.2 Hz, 2H), 7.50−7.41 (m, 4H), 5.44 (dd, J = 6.8, 3.6 Hz, 1H), 5.31−5.27 (m, 1H), 2.52−2.48 (m, 1H), 2.19−2.12 (m, 1H), 2.10−2.01 (m, 1H), 1.92−1.89 (m, 1H), 1.76−1.66 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 165.6 (C), 155.2 (C), 148.9 (C), 139.5 (C), 136.0 (C), 130.1 (CH), 129.4 (CH), 128.9 (CH), 128.8 (2 × CH), 128.4 (2 × CH), 125.5 (CH), 121.5 (CH), 118.7 (CH), 116.3 (C), 115.22 (C), 85.3 (CH), 27.5 (CH_2), 24.7 (CH_2), 19.2 (CH_2); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd. for $C_{21}H_{17}NNaO$ 322.1202, found 322.1200.

*4-(2,3-Dihydrofuro[3,2-c]quinolin-4-yl)but-3-yn-1-ol (**13o**).* Reaction of azido aldehyde **7a** (127 mg, 0.868 mmol), alkynol **12o** (60 mg, 0.343 mmol) with TMSOTf (235 μL, 1.302 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13o** (100 mg, 96%) as a white solid; mp 203−205 °C; IR (neat) 3058, 3093, 2952, 2826, 1566, 1473, 1310, 1207, 1190, 1026, 688, 678 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.45 (AB, J = 17.6, 8.4 Hz, 2H), 7.69 (t, J = 7.2 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 4.88 (t, J = 8.8 Hz, 2H), 3.64 (t, J = 6.4 Hz, 2H), 3.37 (t, J = 8.4 Hz, 2H), 2.65 (t, J = 6.4 Hz, 2H); $^{13}C\{^1H\}$NMR (100 MHz, DMSO-d_6, DEPT) δ 162.5 (C), 148.6 (C), 140.3 (C), 129.9 (CH), 128.5 (CH), 126.1 (CH), 121.0 (CH), 120.1 (C), 115.5 (C), 92.1 (C), 79.8 (C), 73.4 (CH_2), 59.6 (CH_2), 28.2 (CH_2), 23.2 (CH_2); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd. for $C_{15}H_{13}NNaO$ 262.0838, found 262.0837.

*5-Phenyl-3,4-dihydro-2H-pyrano[3,2-c]quinoline (**13p**).*[19] Reaction of azido aldehyde **7a** (90 mg, 0.624 mmol), alkynol **12p** (100 mg, 0.624 mmol) with TMSOTf (112 μL, 0.624 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13p** (158 mg, 97%) as a white solid; mp 83−85 °C; IR (neat) 3052, 2976, 1456, 1423, 1310, 1207, 1180, 1026, 688, 658 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, J = 8.4, 0.8 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.66−7.62 (m, 1H), 7.59−7.57 (m, 2H) 7.48−7.41 (m, 4H), 4.40 (t, J = 5.2 Hz, 2H), 2.72 (t, J = 6.4 Hz, 2H), 2.00−1.94 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 160.8 (C), 157.3 (C), 147.2 (C), 140.5 (C), 129.1 (CH), 128.9 (CH), 128.7 (2 × CH), 128.2 (2 × CH), 128.1 (CH), 125.3 (CH), 121.2 (CH), 119.9 (C), 110.6 (C), 66.9 (CH_2), 23.8 (CH_2), 21.8 (CH_2); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd. for $C_{18}H_{16}NO$ 262.1226, found 22.1224.

*5-(p-Tolyl)-3,4-dihydro-2H-pyrano[3,2-c]quinoline (**13q**).*[19] Reaction of azido aldehyde **7a** (89 mg, 0.605 mmol), alkynol **12q** (106 mg, 0.605 mmol) with TMSOTf (109 μL, 0.605 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13q** (162 mg, 97%) as a white solid; mp 105−107 °C; IR (neat) 2949, 1613, 1587, 1492, 1409, 1373, 1352, 1324, 1272, 1215, 1158, 1134, 1116, 985, 934, 863, 827, 756, 665 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, J = 8.4, 1.2 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.65−7.61 (m, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.46−7.43 (m, 1H), 7.27 (d, J = 8.0 Hz, 2H), 4.40 (t, J = 5.2 Hz, 2H), 2.74 (t, J = 6.0 Hz, 2H), 2.42 (s, 3H), 2.01−1.97 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 160.8 (C), 157.3 (C),

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147.2 (C), 137.9 (C), 137.5 (C), 129.1 (CH), 128.9 (3 × CH), 128.7 (2 × CH), 125.2 (CH), 121.2 (CH), 119.9 (C), 110.6 (C), 66.9 (CH_2), 23.8 (CH_2), 21.8 (CH_2), 21.3 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{19}H_{18}NO$ 276.1383, found 276.1381.

*6-Methyl-11-phenyl-6H-isochromeno[4,3-c]quinoline (**13r**).* Reaction of azido aldehyde **7a** (84 mg, 0.571 mmol), alkynol **12r** (127 mg, 0.571 mmol) with TMSOTf (103 μL, 0.571 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13r** (160 mg, 98%) as a white solid; mp 148−150 °C; IR (neat) 3099, 2976, 2911, 1670, 1590, 1460, 1352, 688, 588 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (dd, J = 8.8, 0.8 Hz, 1H), 8.12 (d, J = 6.8 Hz, 1H), 7.75−7.7.68 (m, 3H), 7.53−7.49 (m, 1H), 7.47−7.01 (m, 3H), 7.03−6.86 (m, 3H), 6.87 (d, J = 8.0 Hz, 1H), 5.46 (q, J = 6.8 Hz, 1H), 1.86 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 158.2 (C), 157.7 (C), 147.9 (C), 141.5 (C), 134.9 (C), 130.3 (CH), 129.7 (2 × CH), 129.1 (CH), 128.8 (CH), 128.8 (2 × CH), 128.6 (C), 127.5 (CH), 127.3 (CH), 126.9 (CH), 125.9 (CH), 123.6 (CH), 121.9 (CH), 119.8 (C), 112.8 (C), 75.2 (CH), 18.9 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{23}H_{18}NO$ 324.1388, found 324. 1385.

*6,11-Diphenyl-6H-isochromeno[4,3-c]quinoline (**13s**).* Reaction of azido aldehyde **7a** (45 mg, 0.305 mmol), alkynol **12s** (87 mg, 0.305 mmol) with TMSOTf (55 μL, 0.305 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13s** (105 mg, 90%) as a pale yellow liquid; IR (neat) 3016, 2924, 2854, 1672, 1588, 1564, 1494, 1481, 1405, 1385, 1285, 1207, 1154, 1099, 1061, 976, 940, 910, 757, 734, 704, 650 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 8.5 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.72−7.70 (m, 3H), 7.55−7.52 (m, 3H), 7.51−7.47 (m 2H), 7.44−7.39 (m, 4H), 7.21 (t, J = 7.0 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 7.01−6.95 (m, 2H), 6.46 (s, 1H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 157.7 (C), 148.1 (C), 141.5 (C), 138.4 (C), 133.3 (C), 130.4 (CH), 129.6 (2 × CH), 129.3 (CH), 129.2 (CH), 129.1 (C), 128.9 (2 × CH), 128.8 (2 × CH), 128.6 (C), 127.9 (CH), 127.9 (3 × CH), 127.2 (CH), 126.9 (CH), 126.1 (2 × CH), 112.0 (CH), 119.9 (C), 113.3 (C), 80.6 (CH); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{28}H_{20}NO$ 386.1539, found 386.1527.

*6-Phenyl-2,3,4,5-tetrahydrooxepino[3,2-c]quinoline (**13t**).* Reaction of azido aldehyde **7a** (70 mg, 0.401 mmol), alkynol **12t** (59 mg, 0.401 mmol) with TMSOTf (75 μL, 0.401 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13t** (105 mg, 96%) as a white solid; mp 98−100 °C; IR (neat) 3057, 2928, 2855, 1614, 1584, 1487, 1405, 1361, 1225, 1108, 1084, 1049, 971, 767, 709, 578 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.69−7.66 (m, 1H), 7.57−7.50 (m, 3H), 7.48−7.41 (m, 3H), 4.38 (t, J = 7.0 Hz, 2H), 2.91 (dd, J = 7.0, 2.0 Hz, 2H), 2.14−2.09 (m, 2H), 1.85−1.79 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 164.1 (C), 162.1 (C), 147.5 (C), 141.2 (C), 129.3 (CH), 129.1 (CH), 128.9 (2 × CH), 128.4 (CH), 128.3 (2 × CH), 126.0 (CH), 122.8 (C), 122.6 (C), 121.8 (CH), 73.5 (CH_2), 31.2 (CH_2), 29.5 (CH_2), 20.0 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{19}H_{18}NO$ 276.1383, found 276.1384.

*4-Phenyl-2,3-dihydro-[1,3]dioxolo[4,5-g]furo[3,2-c]quinoline (**13u**).* Reaction of azido aldehyde **7b** (70 mg, 0.366 mmol), alkynol **12a** (60 mg, 0.366 mmol) with TMSOTf (75 μL, 0.402 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **13u** (83 mg, 96%) as a white solid; mp 145−147 °C; IR (neat) 3032, 2976, 1456, 1463, 1350, 1227, 1190, 1016, 698, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.6 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.41−7.38 (m, 2H), 7.11 (s, 1H), 6.02 (s, 2H), 4.73 (t, J = 8.8 Hz, 2H), 3.44 (t, J = 8.8 Hz, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 163.7 (C), 153.0 (C), 150.8 (C), 147.3 (C), 146.9 (C), 139.9 (C), 128.5 (2 × CH), 128.1 (2 × CH), 114.1 (C), 111.6 (C), 105.9 (2 × CH), 101.5 (CH_2), 96.8 (CH), 72.7 (CH_2), 30.0 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{18}H_{14}NO_3$ 292.0968, found 292.0965.

*((6bR,10aR)-6-Phenyl-6b,10a-dihydro-8H-pyrano[2′,3′:4,5]furo-[3,2-c]quinolin-8-yl)methyl acetate (**15**).* Reaction of azido aldehyde **7a** (32 mg, 0.22 mmol), alkynol **14** (60 mg, 0.22 mmol) with TMSOTf (40 μL, 0.22 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the quinoline **13a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (5:95) as eluent furnished the quinoline **15** (79 mg, 96%) as a white sticky solid; IR (neat) 2952, 2956, 1456, 1433, 1320, 1227, 1190, 678, 658 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 7.2 Hz, 1H), 8.14 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 7.52−7.44 (m, 4H), 6.43−6.39 (m, 1H), 6.23 (dd, J = 10.6, 7.6 Hz, 1H), 5.55 (d, J = 4.8 Hz, 1H), 4.89 (t, J = 4.8 Hz, 1H), 4.53 (d, J = 4.4 Hz, 1H), 4.23 (d, J = 5.6 Hz, 2H), 2.1 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 170.7 (C), 165.7 (C), 156.8 (C), 150.0 (C), 139.3 (C), 132.0 (CH), 130.8 (CH), 129.5 (CH), 129.2 (CH), 129.1 (2 × CH), 128.5 (2 × CH), 125.7 (CH), 122.5 (CH), 121.9 (CH), 116.2 (C), 115.2 (C), 77.1 (CH), 70.7 (CH), 70.0 (CH), 62 9 (CH_2), 21.0 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{23}H_{20}NO_4$ 374.1387, found 374.1390.

*6-Allyl-11-phenyl-6H-isochromeno[4,3-c]quinoline (**18**).* To an ice-cold solution of alkynal **16** (100 mg, 0.485 mmol) and allyltributyltin **17** (165 μL, 0.533 mmol) in dry CH_2Cl_2 (8 mL) at 0 °C was added $BF_3{\cdot}OEt_2$ (120 μL, 0.970 mmol). After complete consumption of alkynal **16** (TLC control) was added azido aldehyde **7a** (60 mg, 0.485 mmol) and reaction mixture was stirred at same temperature. Reaction was monitored by TLC, quenched with saturated aq. solution of $NaHCO_3$ upon completion, extracted with CH_2Cl_2 (3 × 5 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc−petroleum ether (3:97) as eluent furnished 4-allyl quinoline **18** (132 mg, 78%) as a brown color liquid; IR (neat) 3016, 2926, 2857, 1631, 1592, 1508, 1406, 1215, 1086, 915, 758, 701, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.24 (dd, J = 8.0, 0.5 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.72−7.69 (m, 3H), 7.51 (td, J = 7.0, 1.0 Hz, 1H), 7.48−7.46 (m, 3H), 7.20 (d, J = 4.5 Hz, 2H), 7.02−6.98 (m, 1H), 6.87 (d, J = 8.0 Hz, 1H) 6.07−5.98 (m, 1H), 5.43 (dd, J = 8.5, 5.0 Hz, 1H), 5.20−5.14 (m, 2H), 2.97−2.91 (m, 1H), 3.01−2.91 (m, 1H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 157.6 (C), 157.3 (C), 147.9 (C), 141.5 (C), 133.5 (C), 133.2 (CH), 130.4 (CH), 129.6 (2 × CH), 129.0 (CH), 128.8 (2 × CH), 128.7 (CH), 128.2 (C), 127.6 (CH), 127.2 (CH), 127.1 (CH), 126.0 (CH), 124.7 (CH), 121.9 (CH_2), 119.9 (C), 118.5 (CH), 112.7 (C), 78.6 (CH), 37.7 (CH_2); HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd. for $C_{25}H_{19}NNaO$ 372.1359, found 372.1358.

*4-Allyl-3-phenylquinoline (**19**).* To an ice-cold solution of azido aldehyde **7a** (60 mg, 0.408 mmol) and allyltributyltin **17** (151 μL, 1.068 mmol) in dry $(CH_2Cl)_2$ (8 mL) at 0 °C was added $BF_3{\cdot}OEt_2$ (100 μL, 1.15 mmol). After complete consumption of azido aldehyde **7a** (TLC control) was added phenyl acetylene **9a** (55 μL, 0.443 mmol) and reaction mixture was refluxed at 50 °C. Reaction was monitored by TLC, quenched with saturated aq. solution of $NaHCO_3$ upon completion, extracted with CH_2Cl_2 (3 × 5 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc−petroleum ether (2:98) as eluent furnished 4-allyl quinoline **19** (55 mg, 55%) as a brown color liquid; IR (neat) 3053, 2934, 2873, 1617, 1592, 1509, 1357, 1223, 1112, 1065, 912, 769, 732, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.1 Hz, 1H), 8.17−8.14 (m, 2H), 8.03 (dd, J = 8.1, 0.8 Hz, 1H), 7.74 (s, 1H), 7.72−7.20 (m, 1H), 7.56−7.51 (m, 3H), 7.48−7.46 (m, 1H), 6.19−6.09 (m, 1H), 5.24−5.16 (m, 2H), 3.91 (dd, J = 6.4, 0.4 Hz, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 157.3 (C), 148.4 (C), 146.8 (C), 139.8 (C), 135.2 (CH), 130.5 (CH), 129.5 (CH), 129.4 (CH), 128.9 (2 × CH), 127.7 (2 × CH), 126.6 (C), 126.3 (CH), 123.6 (CH), 119.2 (CH), 117.9 (CH_2), 36.8 (CH_2); HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd. for $C_{18}H_{15}NNa$ 268.1097, found 268.1096.

*4-(Benzyloxy)-2,3-diphenylquinoline (**10ae**).* To a solution of 3-bromo quinoline **10z** (60 mg, 0.153 mmol) in THF (4 mL) were

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added $Pd[(PPh_3)_2Cl_2]$ (6 mg, 5 mol %), phenyl boronic acid **20** (29 mg, 0.234 mmol) and 2 M aq. Solution of Na_2CO_3 (1.5 mL) under inert atmosphere. The reaction mixture was stirred at 40 °C for 1 h. Then water was added to reaction mixture and extracted with EtOAc (3 × 10 mL). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc−petroleum ether as eluent furnished 4-alkoxy quinoline **10ae** (55 mg, 99%) as a colorless liquid.

*4-([1,1′-Biphenyl]-2-yl)-2,3-dihydrofuro[3,2-c]quinoline (**22**).* To a stirred solution of **13a** (50 mg, 0.202 mmol) in AcOH (2 mL) was added diphenyl tetrafluoro borate **21** (89 mg, 0.242 mmol) was added $Pd(OAc)_2$ (3 mg, 0.0101 mmol) and was heated for 45 h at 120 °C in a Teflon capped tube. Reaction was filtered with Celite pad, diluted with CH_2Cl_2 (5 mL), neutralized with with saturated aq. solution of $NaHCO_3$, extracted with CH_2Cl_2 (3 × 5 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc−petroleum ether (5:95) as eluent furnished 4-alkoxy quinoline **22** (30 mg, 45%) as brown liquid; IR (neat) 3016, 2926, 2857, 1631, 1592, 1508, 1406, 1215, 1086, 915, 758, 701, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 8.5 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.69 (dd, J = 7.5, 1.5 Hz, 1H), 7.62 (d, J = 7.5 Hz, 1H), 7.52−7.51 (m, 2H), 7.45−7.46 (m, 2H), 7.25−7.23 (m, 2H), 7.19−7.14 (m, 3H), 4.49 (t, J = 9.0 Hz, 2H), 2.52 (t, J = 9.0 Hz, 2H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 163.6 (C), 157.8 (C), 156.5 (C), 148.9 (C), 140.1 (C), 140.3 (C), 130.8 (CH), 130.1 (C), 129.6 (CH), 129.3 (2 × CH), 129.2 (CH), 128.3 (2 × CH), 127.8 (CH), 127.2 (CH), 125.6 (CH), 121.5 (CH), 117.4 (CH), 116.0 (C), 115.6 (CH), 73.3 (CH_2), 28.5 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{23}H_{18}NO$ 324.1388, found 324.1388.

*4-Phenyl-2,3,6,7,8,9-hexahydrofuro[3,2-c]quinoline (**23**).* 10% Pd−C (5 mg) was added to a solution of the quinoline **13a** (50.0 mg, 0.23 mmol) in EtOAc (5 mL). The reaction mixture was stirred 5 days at rt in an atmosphere of hydrogen created by evacuative displacement of air by hydrogen (balloon) and then the catalyst was filtered off through a Celite pad. Evaporation of the solvent afforded the pyridine **23** (50.0 mg, 99%) as a colorless solid; IR (neat) 3016, 2926, 2857, 1631, 1592, 1508, 1406, 1215, 1086, 915, 758, 701, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 12.6 HZ, 2H), 7.43 (t, J = 12.Hz, 2H), 7.34−7.33 (m, 1H), 4.63 (t, J = 8.8 Hz, 2H), 3.36 (t, J = 8.8 Hz, 2H), 2.93 (t, J = 6.4 Hz, 2H), 2.66 (t, J = 6.4 Hz, 2H), 1.92−1.86 (m, 2H), 1.84−1.78 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 165.9 (C), 157.7 (C), 151.2 (C), 139.9 (C), 128.5 (2 × CH), 128.1 (CH), 127.9 (2 × CH), 117.6 (C), 114.2 (C), 727.7 (CH_2), 32.6 (CH_2), 29.4 (CH_2), 23.3 (CH_2), 22.3 (CH_2), 22.2 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{17}H_{18}NO$ 252.1383, found 252. 1381.

2-((2S,3S*)-2-Phenyl-1,2,3,4-tetrahydroquinolin-3-yl)ethan-1-ol (**24**).* To a well stirred solution of quinoline **13a** (50.0 mg, 0.23 mmol) in MeOH (15 mL) was added $NiCl_2$ (315 mg, 2.424 mmol) and $NaBH_4$ (545 mg, 14.372 mmol). After complete consumption of starting material, reaction mixture was diluted with H_2O, extracted with CH_2Cl_2 (3 × 5 mL), dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc−petroleum ether (50:50) as eluent furnished tetrahydroquinoline **24** (22 mg, 48%) as a brown color liquid; IR (neat) 3356, 3323, 3036, 2946, 2858, 1661, 1572, 1518, 1405, 1225, 1096, 925, 768, 721, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35−7.25 (m, 5H), 7.06−7.00 (m, 2H), 6.67 (td, J = 7.2, 0.8 Hz, 1H), 6.57 (d, J = 7.6 Hz, 1H), 4.58 (d, J = 3.6 Hz, 1H), 3.67−3.62 (m, 1H), 3.61−3.45 (m, 1H), 2.98 (dd, J = 16.4, 4.8 Hz, 1H), 2.66−2.60 (m, 1H), 2.38−2.26 (m, 1H), 1.61−1.53 (m, 1H), 1.35−1.29 (m, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 144.3 (C), 142.7 (C), 129.8 (CH), 128.4 (2 × CH), 1127.4 (CH), 127.2 (3 × CH), 119.8 (C), 117.4 (CH), 114.0 (CH), 61.0 (CH_2), 58.9 (CH), 33.9 (CH), 31.9 (CH_2), 30.6 (CH_2); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{17}H_{20}NO$ 254.1539, found 254.1538.

*Total Synthesis of Graveoline (**1**).*[20] Reaction of azido aldehyde **7a** (100 mg, 0.684 mmol), methanol **8b** (30 μL, 0.752 mmol) and piperonal derived alkyne **9k** (100 mg, 0.684 mmol) with TMSOTf (130 μL, 0.684 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (4:96) as eluent furnished the Graveoline **1** (150 mg, 79%) as a yellow solid; mp 100−102 °C; IR (neat) 3096, 3012, 2999, 2892, 1677, 1557, 1222, 1011, 698, 678 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.13 (dd, J = 8.5, 1.0 Hz, 1H), 8.06 (d, J = 8.5 Hz, 1H), 7.70−7.66 (m, 2H), 7.60 (dd, J = 8.5, 1.5 Hz, 1H), 7.47−7.43 (m, 1H), 7.06 (s, 1H), 6.93 (d, J = 8.0 Hz, 1H), 6.02 (s, 2H), 4.07 (s, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 162.8 (C), 158.2 (C), 149.1 (C), 148.8 (C), 148.4 (C), 134.8 (C), 130.0 (CH), 129.1 (CH), 125.3 (CH), 121.7 (CH), 121.6 (CH), 120.4 (C), 108.4 (CH), 108.1 (CH), 101.4 (CH_2), 97.6 (CH), 55.7 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{17}H_{14}NO_3$ 280.0968, found 280.0963.

Synthesis of ERβ Ligand 2. *4-(4-Methoxyquinolin-2-yl)phenyl acetate (**2a**).* Reaction of azido aldehyde **7a** (100 mg, 0.68 mmol), methanol **8b** (28 μL, 0.68 mmol) and acetate protected alkyne **9l** (158 mg, 0.68 mmol) with TMSOTf (123 μL, 0.68 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (4:96) as eluent furnished the 4-alkoxy quinoline **2a** (175 mg, 88%) as a yellow liquid; IR (neat) 3022, 2986, 1446, 1423, 1370, 1227, 1190, 1026, 658, 638 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16−8.09 (m, 4H), 7.70 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.26−7.24 (m, 2H), 7.12 (s, 1H), 4.06 (s, 3H), 2.33 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$, DEPT) δ 169.4 (C), 162.9 (C), 157.8 (C), 151.7 (C), 149.1 (C), 138.0 (C), 130.1 (CH), 129.1 (CH), 128.8 (2 × CH), 125.5 (CH), 121.9 (2 × CH), 121.7 (CH), 120.4 (C), 97.8 (CH), 55,7 (CH_3), 21.2 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{18}H_{16}NO_3$ 294.1125, found 294.1122.

*ERβ Ligand (**2**).*[21] To a stirred solution of 4-methoxy quinoline **2a** (50 mg, 0.170 mmol) in dry MeOH (6 mL), at 0 °C K_2CO_3 (24 mg, 0.170 mmol) was added. After complete consumption starting material reaction mixtured evaporate, diluted with EtOAc and washed with H_2O, dried over anhydrous Na_2SO_4. Evaporation of the solvent furnished pure ERβ ligand **2** (33 mg, 78%) as a yellow sticky solid; IR (neat) 3372, 3049, 2926, 1595, 1497, 1475, 1453, 1360, 1270, 1180, 1016, 810, 698, 668 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 9.86 (s, 1H), 8.16 (d, J = 8.4 Hz, 2H), 8.08 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H) 7.49−7.45 (m, 2H), 6.92 (d, J = 7.2 Hz, 2H) 4.13 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, DMSO-d_6, DEPT) δ 162.2 (C), 159.1 (C), 157.5 (C), 148.2 (C), 130.0 (CH), 129.9 (CH), 128.9 (2 × CH), 128.5 (C), 125.0 (CH), 121.3 (CH), 119.5 (C), 115.4 (2 × CH), 97.5 (CH), 56.1 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{16}H_{14}NO_2$ 252.1019, found 252.1017.

*N,N-Diethyl-2-((2-(4-propoxyphenyl)quinolin-4-yl)oxy)ethan-1-amine (**6**).*[21] Reaction of azido aldehyde **7a** (70 mg, 0.476 mmol), aminoethanol **8t** (60 mg, 0.476 mmol) and alkyne **9j** (114 mg, 0.476 mmol) with TMSOTf (86 μL, 0.476 mmol) in dry CH_2Cl_2 (8.0 mL) at 0 °C as described for the 4-alkoxy quinoline **10a** followed by purification on a silica gel column using ethyl acetate−petroleum ether (4:96) as eluent furnished the 4-alkoxy quinoline **6** (85 mg, 45%) as a brown color liquid; IR (neat) 2952, 2956, 1496, 1453, 1320, 1297, 1190, 1066, 678, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 8.5 Hz, 3H), 7.69−7.66 (m, 1H), 7.46−7.42 (m, 1H), 7.15 (s, 1H), 7.02 (d, J = 8.5 Hz, 2H), 4.35 (t, J = 6.0 Hz, 2H), 3.99 (t, J = 7.0 Hz, 2H), 3.08 (t, J = 6.0 Hz, 2H), 2.72 (q, J = 7. 0 Hz, 4H), 1.91−1.81 (m, 2H), 1.13 (t, J = 7.5 Hz, 6H), 1.07 9t J = 7.5 Hz, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$, DEPT) δ 160.4 (C), 158.6 (C), 149.4 (C), 143.7 (C), 140.1 (C), 137.1 (C), 130.2 (CH), 129.8 (2 × CH), 129.4 (CH), 129.2 (CH), 128.9 (2 × CH), 127.6 (2 × CH), 126.9 (2 × CH), 125.5 (CH), 121.7 (CH), 120.6 (C), 99.4 (CH), 72.8 (CH_2), 47.7 (CH_2), 21.5 (CH_3), 17.1 (CH_3); HRMS (ESI-TOF) m/z $[M + H]^+$ calcd. for $C_{24}H_{31}N_2O_2$ 379.2380, found 379.2384.

■ ASSOCIATED CONTENT

Supporting Information

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NMR spectra of products (PDF)
X-ray diffraction data (CIF files) of products (ZIP)

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Notes

The authors declare the following competing financial interest(s): A patent application (Indian Patent Application No.: 201621041730 dated December 6, 2016) has been filed based on the studies described in this manuscript.

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Schemes 2 and 7 were revised and the name of compound **10v** was corrected in the Experimental Section, the correct version reposted on February 8, 2017.

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