JOC The Journal of Organic Chemistry

Note

Iridium(III)-Catalysed Alkynylation of 2-(Hetero)arylquinazolin-4-one Scaffolds via C–H Bond Activation

Rajendra Shankarrao Rohokale, Rupali G Kalshetti, and Chepuri V. Ramana

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b02738 • Publication Date (Web): 28 Jan 2019

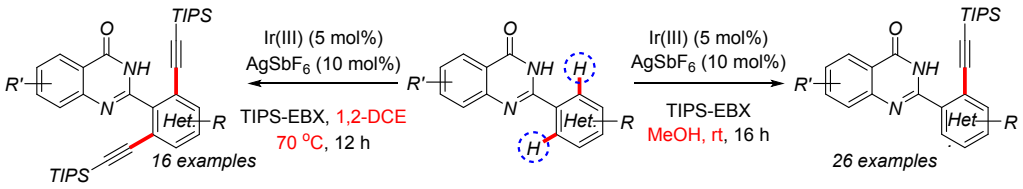
ACS Publications

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Iridium(III)-Catalysed Alkynylation of 2-(Hetero)arylquinazolin-4-one Scaffolds *via* C–H Bond Activation

Rajendra S. Rohokale,[a] * Rupali G. Kalshetti[a,b] and Chepuri V. Ramana[a,b]

[a]CSIR–National Chemical Laboratory, Division of Organic Chemistry
Dr. Homi Bhabha Road, Pune–411008, India
[b]Academy of Scientific and Innovative Research, New Delhi-110025, India

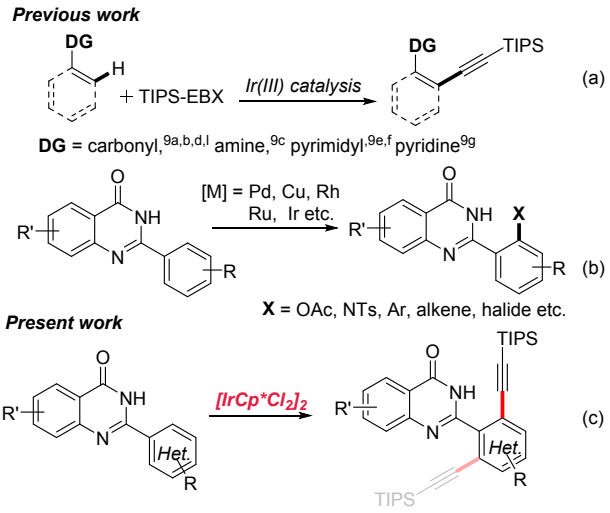


ABSTRACT: The directed C–H alkynylation of 2-(hetero)arylquinazolin-4-ones has been explored with the ethynylbenziodoxolone reagent TIPS-EBX employing an Ir(III)-catalyst. Complementary conditions for either monoalkynylation or dialkynylation have been developed. Also demonstrated is the broad scope of this reaction and the compatibility of various functional groups such as -F, -Cl, -Br, -CF_3, -OMe, -NO_2 and alkyl etc.

"Alkyne" is a unique functional group in organic synthesis that allows the introduction of a wide range of carbon and/or hetero atom centred functional groups that can be easily transformed into carbo-/heterocycles of varying ring sizes.[1] There are several methods based on either functional group manipulation or cross-coupling reactions to construct or introduce an alkyne unit. In recent years, there has been tremendous interest in the catalytic alkynylation of C–H bonds to avoid pre-functionalization of the reacting substrates.[2] Indeed, the direct/directed alkynylation of sp^2 C–H bonds is considered as a reliable alternative to Sonogashira coupling.[3,4] The directed alkynylation reactions occupy a special role in this regard as they are regioselective and can be conducted even at room temperature.[4] A variety of functional groups such as amine, amide, anilide, imine, ester, carboxylic acid, various heterocycles, hydroxyl and ketone groups have been employed as directing groups for directed C–H bond alkynylations. The alkyne sources employed in this pursuit include terminal alkynes,[5] haloalkynes,[6] borane alkynes,[7] and alkynylated hypervalent iodine reagents.[8] There are various inorganic metal complexes (Pd, Ru, Rh, Ir, Co etc.) that have been employed for the different types of C–H bond- (sp^3, sp^2 and sp) activation processes. Amongst these, iridium complexes occupy a special place due to the high reactivity of the Ir(III) species toward C–H bond cleavage.[9] Coming to the Ir(III)-catalyzed

directed alkynylations using EBX-based reagents (Scheme 1a),[9a–9g] the Jiang, Zeng, Li and Xie groups reported respectively the carbonyl/carboxylate and pyrimidine directed *ortho* C−H alkynylation of (hetero)aryl rings. The selective terminal alkynylation of 2-vinylanilines has been reported by the Nachtsheim group. Li and co-workers on the other hand, documented an Ir-catalyzed pyridine directed alkynylation of pendant aryls units of N^1-aryl-7-azaindol derivatives using TIPS-EBX. Very recently, Zhao and co-workers reported the selective *ortho*-alkynylation of Cbz-protected benzylamines employing bromoalkynes as the electrophilic alkynylating agents.

As part of our ongoing program on C–H activation functionalization at ambient temperatures employing [Ir]-complexes,[10] the directed alkynylation of 2-arylquinazolinones has been undertaken considering the fact that quinazolin-4-one is a privileged structural unit widely found in natural products and in some approved/investigational drug candidates.[11] Anticancer drugs like erlotinib, gefitinib and prazosin, which have been employed for curing high blood pressure, anxiety and panic disorder are representative quinazolin-4-one based marketed drugs.



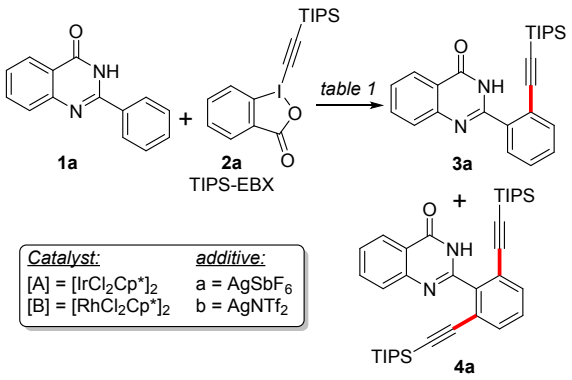
Scheme 1: Transition-metal catalyzed alkynylation reactions

The directed C–H functionalization of the pendant aryl ring in the 2-arylquinazolin-4-one core has been well explored.[12] C–H amination,[13] arylation,[14] alkenylation[15] and cross dehydrogenative coupling[16] with acrylates and aceotxylation[17] have been documented using [Pd], [Ru], [Rh] and [Cu]-complexes (Scheme 1b). Coming to the reports with [Ir]-complexes, there are very few in this regard. The mono-/bis-sulfamidation of the aryl ring in 2-arylquinazolin-4-one using sulfonyl azides was recently reported by Cui and co-workers

and the reactions were carried out at elevated temperatures.[13e] This compilation on C–H functionalization of 2-arylquinazolin-4-ones revealed that the corresponding directed alkynylation *via* C–H bond functionalization on these scaffolds is missing. This prompted us to conduct explorations in this direction.

In this context, the preliminary experiments were conducted employing 2-phenylquinazolin-4-one **1a** (0.05 mmol) and TIPS-EBX **2** (0.06 mmol) as substrates and $[IrCp^*Cl_2]_2$ (5 mol%) and $AgSbF_6$ (10 mol%) as the catalyst system. Initially, different solvents were screened to see the feasibility of the proposed alkynylation. As shown in Table 1, the reaction outcome seems to be solvent dependent. When conducted in CH_3CN at rt, the reaction was sluggish and gave monoalkynylated quinazolin-4-one **3a** (21%) along with dialkynylated quinazolin-4-one **4a** (10%) (Table 1, entry 1). The products yield was improved when we switched to other aprotic polar solvents such as THF and dioxane. However, both mono- and dialkynylated products were obtained in varying proportions (Table 1, entries 2-3). Interestingly, when the reactions were conducted in protic solvents such as methanol, ethanol and trifluroethanol at room temperature (Table 1, entries 4-8), the dialkynylated product was not observed and the monoalkynylated product was obtained in varying yields. It was found that methanol was a good choice of solvent for this reaction, giving **3a** in 89% isolated yield (entry 4). At this juncture, to check the possibility of carrying out the dialkynylation exclusively, the reactions were conducted using 2.5 equiv of TIPS-EBX (with respect to **1a**) and different non-polar solvents such as toluene, dichloromethane and dichloroethane were screened at different temperatures. As shown in Table 1, the best results were obtained in dichloroethane at 70 °C, resulting in the dialkynylated product **4a** in 94% isolated yield (entry 14). Control experiments revealed that the presence of the Ir-complex is essential and that under similar conditions, the Rh(III) complex performed poorly (entries 15–17).

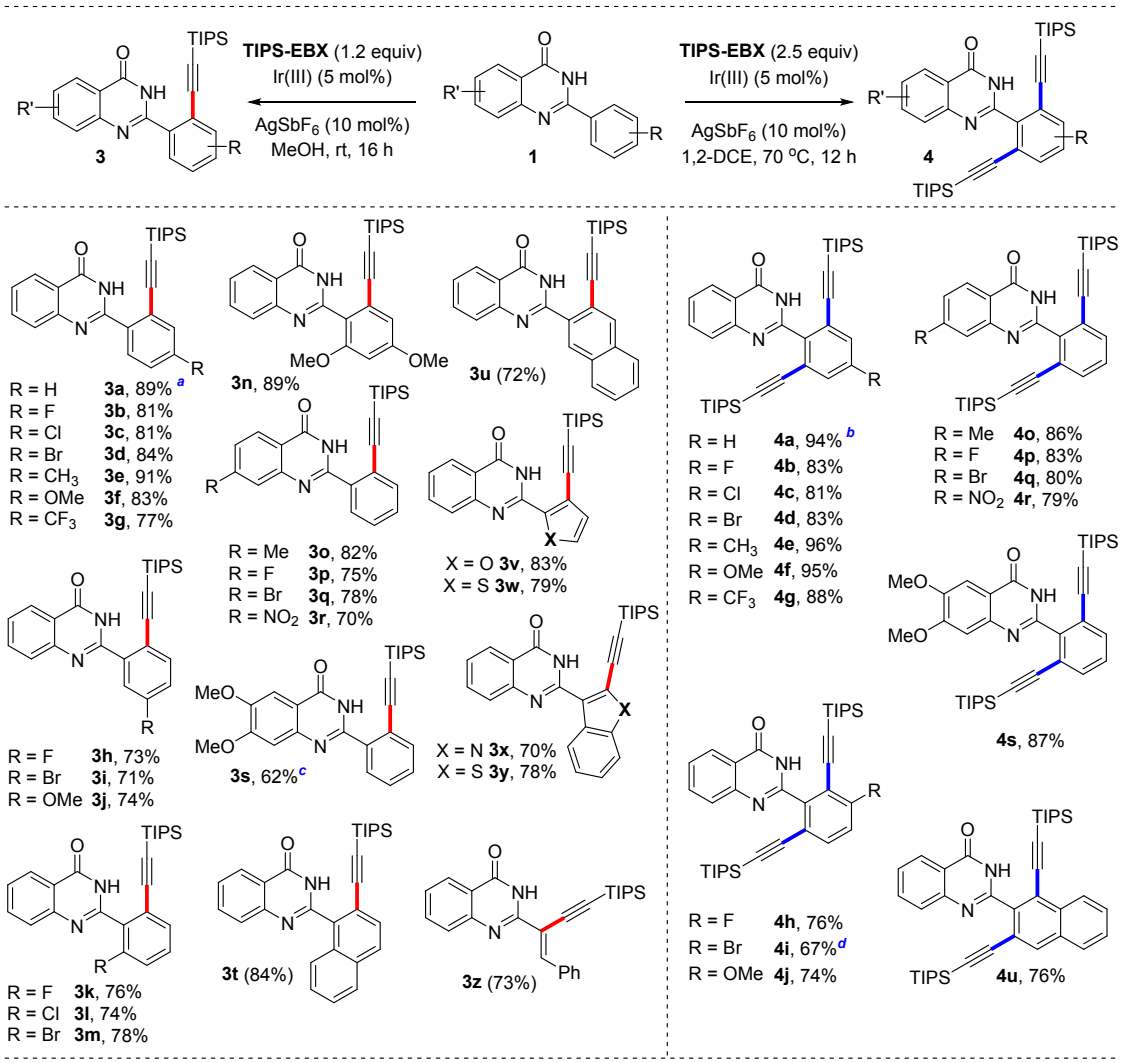
Table 1: Optimization studies[a]



entry	catalyst/ additive		solvent	temp. (°C) time (h)	yield[b] (%)	
					3a	**4a**
1	[A]/a		CH_3CN	rt/16	21	10
2	[A]/a		THF	rt/12	42	8
3	[A]/a		Dioxane	rt/16	44	trace
4	[A]/a		**MeOH**	**rt/16**	**89**	**trace**
5	[A]/a		EtOH	rt/16	52	trace
6	[A]/a		HFIP	rt/16	36	trace
7	[A]/a		TFE	rt/16	30	trace
8	[A]/a		Toluene	rt/16	35	12
9	[A]/a		DCM	rt/16	38	22
10	[B]/a		DCE	rt/16	27	trace
11	[A]/b		DCE	rt/16	18	43
12	[A]/a		MeOH	70/12	20	53
13	[A]/a		DCM	70/12	12	62
14	[A]/a		**DCE**	**70/12**	**--**	**94**
15	[B]/a		DCE	70/12	12	40
16	[B]/b		DCE	70/12	8	32
17	[B]/b		DCE	70/12	trace	28[c]
18	[A]/b		DCE	70/12	8	68
19	[A]/b		DCE	70/12	24	38[c]

[a]Reaction conditions: for entries 1-10: 0.05 mmol of **1a**, 0.06 mmol of **2a**, 5 mol % of catalyst, 10 mol % of additive, dry solvent (1.0 mL), 16 h; for entries 12-19: 0.05 mmol of **1a**, 0.125 mmol of **2a**, 5 mol % of $[IrCp^*Cl_2]_2$, 10 mol % of additives, dry solvent (1.0 mL), 12 h. [b]Isolated yields. [c]NaOAc (1.2 eq.) was used.

Having the complementary conditions for the selective mono- or dialkynylation in hand, we proceeded to explore the scope of the current transformations employing diverse 2-(hetero)arylquinazolin-4-one scaffolds (Scheme 2). Initially, we examined the scope of substituents on the *para*-position (F, Cl, Br, Me, OMe, CF_3; respectively **1b**–**1g**), the *meta*-position (F, Br, OMe; respectively **1h**–**1j**), The selective mono-/dialkynylation of these substrates **1b**–**1j** proceeded smoothly with **2** under optimised conditions and provided the corresponding monoalkynylated products **3b**–**3j** (73–91%) and dialkynylated products **4b**–**4j** (67–96%) in good to excellent yields. The catalytic *ortho*-C–H alkynylation was not affected by the steric hindrance of another *ortho*-substitution (**1k**–**1m)** Even when methoxy groups were placed at the *ortho*- and *para*-positions, the alkynylation reaction proceeded smoothly and provided the corresponding product **3n** in 89% yield.



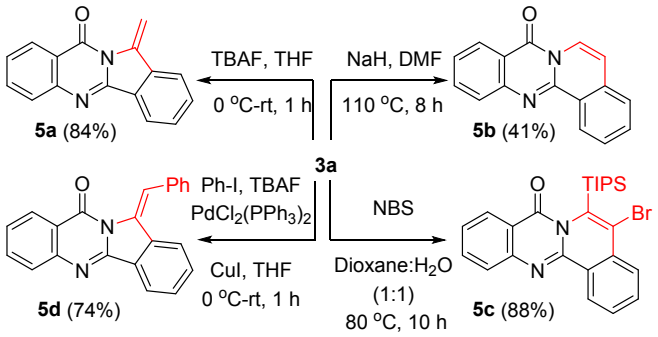
Scheme 2: Ir(III)-catalysed C–H mono/dialkynylation of 2-(hetero)arylquinazolin-4-one scaffolds; [a]82% on 1 g scale; [b]92% on 1 g scale; [c]14% of **4s** was isolated; [d]12% of **3i** was isolated

Next, we examined the scope of substituents on the aryl ring of the quinazolin-4-one core by employing the C7–(Me, F, Br or NO_2) substituted 2-phenylquinazolin-4-ones **1o**–**1r**. In all the cases, the mono- and dialkynylation with **2** proceeded smoothly and provided the corresponding monoalkynylated products **3o**–**3r** (70–82%) and dialkynylated products **4o**–**4r** (79–86%) in very good yields. However, the monoalkynylation of 6,7-dimethoxy-2-phenylquinazolin-4(3*H*)-one (**1s**) gave the corresponding monoalkynylated product **3s** in 62% yield, along with the dialkynylated product **4s** in 14% yield.

The scope of the alkynylation reaction has been further examined by employing quinazolin-4-ones **1t**–**1z** having C2-napthyl and heteroaryl substituents. In case of 2-(1-napthyl)

quinazolin-4(3*H*)-one (**1t**), the alkynylation happened as expected at the C2 of the naphthyl ring and gave the corresponding product **3t** in 84% yield. On the other hand, in case of the isomeric 2-(2-napthyl) quinazolin-4(3*H*)-one (**1u**), the monoalkynylation took place selectively at the C3 position instead of C1, resulting in the product **3u**. This site selectivity seems to originating from steric hindrance by the fused aromatic ring. The dialkynylation of **1u** is also facile giving the 1,3-dialkynylated product **4u** in 76% yield. Coming to the alkynylation of 2-heteroaryl quinazolin-4-ones such as (2-furanyl; **1v**), (2-thiophenyl; **1w**), (3-indolyl; **1x**) and (3-benzothiophenyl; **1y**), under the standard reaction conditions, the alkynylation with **2** proceeded smoothly and gave the products **3v**–**3y** in good yields (70–83%). However, 2-(2-pyridyl)quinazolin-4-none was found to be intact under these reaction conditions, suggesting the possible formation of a stable *N*,*N*'-bidentate iridium complex which seems to inhibit further reactions. Interestingly, when (*E*)-2-styrylquinazolin-4(3*H*)-one (**1z**) was employed as a substrate, under the standard reaction conditions, the alkynylation with **2** proceeded selectively at the *β*-carbon of the styrene and gave **3z** in 73% yield. To have a substrate for exploring the synthetic utility, the mono- and dialkynylation of 2-phenylquinazolin-4(3*H*)-one **1a** has been carried out on 1 g scale using 5 mol % of the iridium complex. The reactions proceeded smoothly to afford **3a** (1.5 g) and **4a** (2.3 g) in 82% and 92% yields respectively.

The possibility of using R-EBX (R = *n*-octyl or phenyl) has been examined under both mono and dialkylation conditions. At room temperature both substrates are intact and when heated the R-EBX is undergoing an internal redox process resulting in the 2-oxo-2-(*n*-octyl or phenyl)ethyl 2-iodobenzoate derivatives (See Scheme S1, SI).

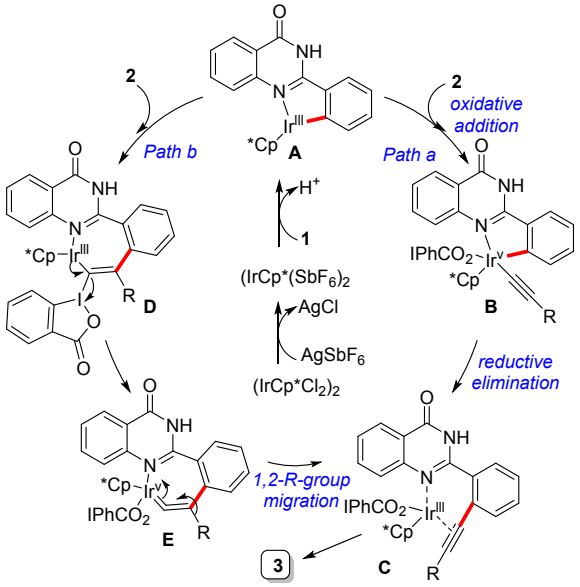


Scheme 3: Synthetic utility of **3a**

Next, the synthetic utility of alkyne **3a** (Scheme 3) was demonstrated by subjecting it to cycloisomerization employing tetra-*n*-butylammonium fluoride (TBAF) and sodium hydride (NaH) in DMF to obtain the complementary 5-*exo*-dig and 6-*endo*-dig cyclised

products **5a** and **5b** with simultaneous TIPS deprotection respectively in 84% and 41% yield. On the other hand, the electrophilic 6-*endo*-dig bromocyclization of compound **3a** with *N*-bromosuccinimide (NBS) resulted in the formation of **5c** in 88% yield and the one-pot desilylation with TBAF and [Pd]-catalyzed Sonogashira/hydroamination afforded cyclised product **5d** in 74% yield.

Next, control experiments have been carried out to understand the course of the reaction in general and the complementary mono vs. dialkynylation. Deuterium labelling experiments employing CD_3OD (10% in *ortho*-position of the phenyl group under heating in DCE and no labelling when carried out in CD_3OD at rt) revealed that the C−H bond cleavage was a reversible process (see SI, Schemes S3 and S4). When the reaction was carried out in the presence of **2** (Scheme S5, SI), no deuterium incorporation was observed in the recovered **1a**, indicating that the alkynylation process proceeds faster than the deuteration. As expected, the competitive reaction of an equimolar amount of **1h** (3-flurophenyl), **1j** (3-methoxphenyl) and **2** under standard conditions gave **3h** in 21% and **3j** in 68% isolated yield respectively (1:3.2 ratio) indicating that electron-rich phenyl groups undergo alkynylation faster (See Scheme S6, SI).



Scheme 4: Mechanistic Proposal.

Based upon the previous reports,[18–21] we propose the following tentative mechanistic pathway (Scheme 4). The catalytic cycle starts with the formation of the monomeric $IrCp^*(SbF_6)_2$ complex, upon reaction of the dimeric iridium complex with $AgSbF_6$. This undergoes a coordinative C–H insertion with 2-arylquinazolin-4-one **1**, resulting in the cyclometalated Ir(III)-complex **A**.[18] There are two possible pathways proposed for the

transfer of the alkyne group from the TIPS-EBX to the aryl ring. In one path, the involvement of an intermediate Ir(V) species occurs *via* the oxidative addition resulting in the alkynyl-Ir(V) species **B**, which undergoes a reductive elimination, generating the key Ir(III)-alkyne intermediate **C** (path a). [2b, 19] In another path, the complexation of the intermediate **A** with the alkyne unit TIPS-EBX followed by a regioselective migratory insertion of alkyne results in the intermediate **D** which, upon the α-elimination of 2-iodobenzoic acid, results in the iridium vinylidene species **E**.[2h,20,21b] The intermediate **E** then undergoes a concerted R group-migration followed by elimination, resulting in intermediate **C,** a species that is common in both the pathways a and b. Finally, the alkynylated product **3** and the active Ir(III)-species are generated by the dissociation of alkyne from **C** by complexing with 2-arylquinazolin-4-one **1**, which undergoes a C–H insertion to continue the catalytic cycle.

In conclusion, [Ir]-catalysed *ortho*-alkynylation of 2-(hetero)arylquinazolin-4-ones with TIPS-EBX has been established. In methanol, selective monoalkynylation has been observed at room temperature. On the other hand, the dialkynylation could be conducted by switching to 1,2-dichloroethane as a solvent and conducting the reaction at 70 °C. A wide-range of mono-/dialkynylated quinazolin-4-ones have been synthesized in good to excellent yields. Considering the ease of functionalizing the alkyne groups and the importance of the quinazolin-4-one scaffold in new drug discovery programs, this late stage alkynylation provides an attractive handle to synthesise molecules of therapeutic interest.

EXPERIMENTAL SECTION:

General Information:

The reactions were carried out in anhydrous solvents under argon atmosphere in oven–dried glassware. All anhydrous solvents were distilled prior to use: dichloromethane, DCE and CH_3CN from CaH_2; methanol from Mg cake; THF on Na/benzophenone. Commercial reagents were used without any purification. Column chromatography was carried out by using silica gel (60–120, 100–200, 230–400 mesh). ^1H and ^{13}C NMR chemical shifts are reported in ppm relative to chloroform-D (δ = 7.26) or TMS and coupling constants (J) are reported in hertz (Hz). The following abbreviations have been used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, sxt = sextet, hept = septet, m = multiplet, b = broad. High Resolution Mass Spectra (HRMS) were recorded on a Q Exactive Hybrid Quadrupole Orbitrap Mass Spectrometer, where the mass analyser used for analysis is orbitrap. Melting points were recorded on a digital microscopic melting apparatus and

uncorrected. Infrared spectra were recorded on an ATR and only major peaks are reported in cm^{-1}. All starting quinazolin-2-ones[21a] and ethynyl benziodoxolones[21b] were prepared according to well–known literature procedures.

General procedure for iridium catalyzed C–H monoalkynylation of quinazolin-2-ones: To a screw capped vial with a spinvane triangular–shaped Teflon stir bar were added aryl quinqzolinone (0.2 mmol), TIPS-EBX (0.24 mmol), $[IrCp^*Cl_2]_2$ (5 mol%, 8 mg), $AgSbF_6$ (10 mol%, 7 mg), and methanol (3 mL) under air. The reaction mixture was stirred at room temperature for 16 h. After completion, the reaction mixture was diluted with CH_2Cl_2 and washed with sat. $NaHCO_3$ followed by brine, dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude was purified by column chromatography (5:1 petroleum ether/EtOAc) to afford monoalkynylated quinazolin-2-ones **3**.

General procedure for iridium catalyzed C–H dialkynylation of quinazolin-2-ones: To a screw capped vial with a spinvane triangular shaped teflon stir bar were added quinazolin-4-one (0.2 mmol), TIPS-EBX (0.5 mmol), $[IrCp^*Cl_2]_2$ (5 mol%, 8 mg), $AgSbF_6$ (10 mol%, 7 mg) and 1,2-dichloroethane (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After completion, the reaction mixture was diluted with CH_2Cl_2 and washed with sat. $NaHCO_3$ followed by brine, dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude was purified by column chromatography (9:1 petroleum ether/EtOAc) to afford dilalkynylated quinazolin-4-ones **4**.

2-(2-((Triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3a).

The product was obtained as white solid; Yield: 72 mg (89%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 146–147 °C; IR(neat) ν_{max}: 3022, 2944, 2142, 2863, 2150, 1671, 1563, 1368, 1213, 881, 769, 675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.76 (s, 1H), 8.34–8.23 (m, 2H), 7.84–7.72 (m, 2H), 7.69–7.57 (m, 1H), 7.54–7.45 (m, 3H), 1.38–0.99 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4 (s), 151.2 (s), 149.1 (s), 134.8 (d), 134.5 (d), 133.7 (s), 130.8 (d), 130.0 (d), 129.2 (d), 128.0 (d), 127.0 (d), 126.5 (d), 121.4 (s), 120.6 (s), 104.1 (s), 100.4 (s), 18.6 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{31}N_2OSi$ 403.2200, found 403.2206.

2-(4-Fluoro-2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3b).

The product was obtained as white solid; Yield: 68 mg (81%). R_f: 0.4 (5:1 petroleum ether/EtOAc) Mp: 154–155 °C; IR(neat) ν_{max}: 2944, 2861, 2155, 1655, 1462, 1370, 1223, 876, 768, 637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.71 (s, 1H), 8.42–8.10 (m, 2H), 7.85–

7.71 (m, 2H), 7.59–7.43 (m, 1H), 7.32 (dd, J = 8.7, 2.6 Hz, 1H), 7.22 (ddd, J = 8.9, 7.8, 2.7 Hz, 1H), 1.30–1.06 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.6 (ds, $^1J_{C–F}$ = 253.7 Hz), 161.3 (s), 150.3 (s), 149.0 (s), 134.6 (d), 132.6 (dd, $^3J_{C-F}$ = 9.2 Hz), 130.0 (ds, $^4J_{C-F}$ = 2.9 Hz), 128.0 (d), 127.1 (d), 126.5 (d), 122.6 (ds, $^3J_{C-F}$ = 10.1 Hz), 121.3 (s), 121.2 (dd, $^2J_{C-F}$ = 23.6 Hz), 117.1 (dd, $^2J_{C-F}$ = 21.6 Hz), 102.9 (s), 102.1 (s), 18.6 (q, 6C), 11.1 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{30}FN_2OSi$ 421.2106, found 421.2110.

2-(4-Chloro-2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3c).

The product was obtained as white solid; Yield: 70 mg (81%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 151–152 °C; IR(neat) ν_{max}: 2948, 2860, 2152, 1670, 1463, 1368, 1228, 860, 732, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.77 (s, 1H), 8.29 (dd, J = 8.2, 3.2 Hz, 2H), 7.79 (d, J = 3.8 Hz, 2H), 7.61 (d, J = 2.0 Hz, 1H), 7.49 (ddd, J = 8.6, 6.5, 2.9 Hz, 2H), 1.35–1.04 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.3 (s), 150.2 (s), 149.0 (s), 137.0 (s), 134.7 (d), 134.2 (d), 131.9 (s), 131.5 (d), 129.6 (d), 128.0 (d), 127.2 (d), 126.5 (d), 121.9 (s), 121.4 (s), 102.8 (s), 102.3 (s), 18.6 (q, 6C), 11.1 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for, $C_{25}H_{30}ClN_2OSi$ 437.1810 found 437.1816.

2-(4-Bromo-2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3d).

The product was obtained as white solid; Yield: 80 mg (84%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 153–154 °C; IR(neat) ν_{max}: 3281, 2938, 2862, 2146, 1691, 1467, 1372, 1213, 880, 727, 634 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.71 (s, 1H), 8.30 (dt, J = 7.9, 1.1 Hz, 1H), 8.23 (d, J = 8.6 Hz, 1H), 7.89–7.74 (m, 3H), 7.64 (dd, J = 8.6, 2.1 Hz, 1H), 7.57–7.41 (m, 1H), 1.26–0.93 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.2 (s), 150.2 (s), 149.0 (s), 137.1 (d), 134.7 (d), 132.6 (d), 132.3 (s), 131.5 (d), 128.1 (d), 127.2 (d), 126.5 (d), 125.2 (s), 122.1 (s), 121.4 (s), 102.7 (s), 102.5 (s), 18.6 (q, 6C), 11.1 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{30}BrN_2OSi$ 481.1305, found 481.1312.

2-(4-Methyl-2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3e).

The product was obtained as white solid; Yield: 76 mg (91%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 149–150 °C; IR(neat) ν_{max}: 2944, 2861, 2158, 1680, 1571, 1463, 1369, 1222, 840, 710, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.79 (s, 1H), 8.30 (d, J = 7.7 Hz, 1H), 8.23 (d, J = 8.2 Hz, 1H), 7.86–7.64 (m, 2H), 7.54–7.39 (m, 2H), 7.31 (dd, J = 8.2, 1.0 Hz, 1H), 2.41 (s, 3H), 1.76–0.81 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4 (s), 151.2 (s), 149.2 (s), 141.4 (s), 135.2 (d), 134.5 (d), 130.7 (s), 130.3 (d), 130.0 (d), 128.0 (d),

126.7 (d), 126.5 (d), 121.3 (s), 120.2 (s), 104.5 (s), 100.1 (s), 21.1 (q), 18.7 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{26}H_{33}N_2OSi$ 417.2357, found 417.2362.

2-(4-Methoxy-2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3f).

The product was obtained as white solid; Yield: 72 mg (83%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 150–151 °C; IR(neat) ν_{max}: 2937, 2859, 2143, 1685, 1578, 1460, 1370, 1226, 726, 664 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.81 (s, 1H), 8.32 (d, J = 8.9 Hz, 1H), 8.30–8.26 (m, 1H), 7.79–7.72 (m, 2H), 7.45 (ddd, J = 8.2, 6.0, 2.3 Hz, 1H), 7.09 (d, J = 2.6 Hz, 1H), 7.04 (dd, J = 8.9, 2.7 Hz, 1H), 3.89 (s, 3H), 1.29–1.10 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4 (s), 161.3 (s), 150.9 (s), 149.3 (s), 134.46 (d), 132.0 (d), 127.8 (d), 126.6 (d), 126.5 (d), 125.9 (s), 121.6 (s), 121.2 (s), 119.3 (d), 115.8 (d), 104.2 (s), 100.6 (s), 55.6 (q), 18.7 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{26}H_{33}N_2O_2Si$ 433.2306, found 433.2310.

2-(4-(Trifluoromethyl)-2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3g).

The product was obtained as white solid; Yield: 74 mg (77%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 169–170 °C; IR(neat) ν_{max}: 2922, 2862, 2140, 1668, 1564, 1464, 1330, 1120, 899, 774, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.78 (s, 1H), 8.42 (d, J = 8.3 Hz, 1H), 8.31 (d, J = 8.0 Hz, 1H), 7.86 (s, 1H), 7.84–7.77 (m, 2H), 7.74 (dd, J = 8.3, 1.3 Hz, 1H), 7.58–7.47 (m, 1H), 1.46–0.86 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.3 (s), 149.9 (s), 148.8 (s), 136.8 (s), 134.8 (d), 133.0 (qs, $^2J_{C\text{-}F}$ = 33.8 Hz), 131.43 (qd, $^3J_{C\text{-}F}$ = 11.0 Hz), 130.8 (d), 128.2 (d), 127.5 (d), 126.6 (d), 125.6 (qd, $^3J_{C\text{-}F}$ = 10.3 Hz), 124.5 (qs, $^1J_{C\text{-}F}$ = 273.0 Hz), 121.5 (ds, $^4J_{C\text{-}F}$ = 2.9 Hz), 121.5 (s), 107.5 (s), 102.6 (s), 18.6 (q, 6C), 11.1 (d, 3C). HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{26}H_{30}F_3N_2OSi$ 471.2074, found 471.2081.

2-(5-Fluoro-2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3h).

The product was obtained as white solid; Yield: 62 mg (73%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 136–137 °C; IR(neat) ν_{max}: 3296, 2943, 2862, 2150, 1685, 1554, 1462, 1285, 844, 721, 672 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.86 (s, 1H), 8.30 (d, J = 7.9 Hz, 1H), 8.07 (d, J = 7.9 Hz, 1H), 7.89–7.71 (m, 2H), 7.57–7.40 (m, 2H), 7.36–7.20 (m, 1H), 1.31–1.02 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.2 (ds, $^1J_{C\text{-}F}$ = 252.7 Hz), 161.4 (s), 150.2 (s), 148.9 (s), 135.5 (s), 134.7 (d), 130.0 (dd, $^3J_{C\text{-}F}$ = 8.7 Hz), 128.1 (d), 127.2 (d), 126.5 (d), 125.5 (dd, $^4J_{C\text{-}F}$ = 3.4 Hz), 121.4 (s), 117.8 (dd, $^2J_{C\text{-}F}$ = 21.8 Hz), 110.0 (ds, $^2J_{C\text{-}F}$ = 18.8 Hz), 107.2 (s), 96.5 (s), 18.6 (q, 6C), 11.1 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{30}FN_2OSi$ 421.2106, found 421.2107.

2-(5-Bromo-2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3i).

The product was obtained as white solid; Yield: 68 mg (71%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 164–165 °C; IR(neat) ν_{max}: 3024, 2939, 2861, 2152, 1665, 1603, 1465, 1291, 878, 767, 658 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.82 (s, 1H), 8.51 (d, J = 2.1 Hz, 1H), 8.31 (d, J = 7.7 Hz, 1H), 7.86–7.75 (m, 2H), 7.61 (dd, J = 8.3, 2.1 Hz, 1H), 7.54–7.48 (m, 2H), 1.23–1.18 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.3 (s), 149.7 (s), 148.9 (s), 136.0 (d), 134.9 (s), 134.7 (d), 133.9 (d), 132.9 (d), 128.6 (d), 127.32 (d), 126.5 (d), 123.6 (s), 121.4 (s), 119.3 (s), 103.2 (s), 102.2 (s), 18.6 (q, 6C), 11.1 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{30}BrN_2OSi$ 481.1305, found 481.1313.

2-(5-Methoxy-2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3j).

The product was obtained as white solid; Yield: 64 mg (74%). R_f: 0.6 (5:1 petroleum ether/EtOAc) Mp: 122–123 °C; IR(neat) ν_{max}: 2938, 2862, 2150, 1664, 1591, 1463, 1241, 1025, 877, 773, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.00 (s, 1H), 8.30 (d, J = 7.9 Hz, 1H), 7.84–7.74 (m, 3H), 7.56 (d, J = 8.6 Hz, 1H), 7.48 (t, J = 7.3 Hz, 1H), 7.01 (dd, J = 8.6, 2.5 Hz, 1H), 3.91 (s, 3H), 1.22–1.01 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.6 (s), 160.0 (s), 151.1 (s), 149.1 (s), 136.3 (d), 135.1 (s), 134.5 (d), 128.0 (d), 127.0 (d), 126.5 (d), 121.4 (s), 117.8 (d), 114.1 (d), 112.9 (s), 104.2 (s), 98.4 (s), 55.7 (q), 18.6 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{26}H_{33}N_2O_2Si$ 433.2306, found 433.2311.

2-(2-Fluoro-6-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3k).

The product was obtained as white solid; Yield: 62 mg (76%). R_f: 0.4 (5:1 petroleum ether/EtOAc) Mp: 153–154 °C; IR(neat) ν_{max}: 2941, 2863, 2154, 1665, 1467, 1371, 1221, 871, 761, 648 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.33 (s, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.91–7.71 (m, 2H), 7.52 (ddd, J = 8.1, 4.8, 3.5 Hz, 1H), 7.47–7.37 (m, 2H), 7.24–7.11 (m, 1H), 0.97–0.74 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.3 (s), 159.9 (ds, $^1J_{C\text{-}F}$ = 251.2 Hz), 148.9 (s), 147.6 (s), 134.6 (d), 131.7 (dd, $^3J_{C\text{-}F}$ = 9.2 Hz), 129.3 (dd, $^4J_{C\text{-}F}$ = 3.3 Hz), 128.1 (d), 127.4 (d), 126.4 (d), 125.0 (s), 124.6 (ds, $^2J_{C\text{-}F}$ = 16.4 Hz), 121.4 (s), 116.4 (dd, $^2J_{C\text{-}F}$ = 21.6 Hz), 102.2 (ds, $^4J_{C\text{-}F}$ = 3.8 Hz), 97.9 (s), 18.4 (q, 6C), 11.0 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{30}FN_2OSi$ 421.2106, found 421.2107.

2-(2-Chloro-6-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3l).

The product was obtained as white solid; Yield: 64 mg (74%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 184–185 °C; IR(neat) ν_{max}: 2943, 2864, 2153, 1670, 1462, 1379, 1228,

860, 738, 661 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.47 (s, 1H), 8.23 (d, J = 8.1 Hz, 1H), 7.86–7.68 (m, 2H), 7.57–7.48 (m, 2H), 7.46 (dd, J = 8.2, 1.3 Hz, 1H), 7.43–7.34 (m, 1H), 0.87–0.80 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.6 (s), 150.2 (s), 148.9 (s), 135.6 (s), 134.6 (d), 133.1 (s), 131.4 (d), 130.9 (d), 129.7 (d), 128.1 (d), 127.4 (d), 126.3 (d), 125.2 (s), 121.4 (s), 102.3 (s), 97.8 (s), 18.3 (q, 6C), 10.9 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for, $C_{25}H_{30}ClN_2OSi$ 437.1810 found 437.1814.

2-(2-Bromo-6-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3m).

The product was obtained as white solid; Yield: 75 mg (78%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 194–195 °C; IR(neat) ν_{max}: 3222, 2940, 2862, 2148, 1666, 1468, 1370, 1220, 882, 730, 636 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.26 (dd, J = 8.4, 4.5 Hz, 1H), 7.79 (d, J = 3.6 Hz, 2H), 7.64 (d, J = 8.1 Hz, 1H), 7.58 (dd, J = 7.8, 1.1 Hz, 1H), 7.55–7.49 (m, 1H), 7.32 (t, J = 8.0 Hz, 1H), 1.04–0.71 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.9 (s), 151.1 (s), 148.8 (s), 137.4 (s), 134.6 (d), 132.8 (d), 131.9 (d), 131.1 (d), 128.1 (d), 127.4 (d), 126.4 (d), 125.2 (s), 121.8 (s), 121.5 (s), 102.2 (s), 98.0 (s), 18.4 (q, 6C), 11.0 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{30}BrN_2OSi$ 481.1305, found 481.1309.

2-(2,4-Dimethoxy-6-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3n).

The product was obtained as white solid; Yield: 82 mg (89%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 129–130 °C; IR(neat) ν_{max}: 2922, 2860, 2145, 1671, 1596, 1387, 1216, 1021, 861, 734, 643 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.3 (s, 1H), 8.55 (d, J = 7.9 Hz, 1H), 8.20 (s, 1H), 8.11–7.97 (m, 2H), 7.72 (ddd, J = 8.2, 6.7, 1.6 Hz, 1H), 7.51 (s, 1H), 4.29 (s, 3H), 4.23 (s, 3H), 1.58–1.31 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4 (s), 150.9 (s), 150.7 (s), 150.0 (s), 149.2 (s), 134.5 (d), 127.8 (d), 126.7 (d), 126.6 (s), 126.5 (d), 121.2 (s), 116.2 (d), 113.2 (s), 112.1 (d), 104.5 (s), 99.5 (s), 56.2 (q), 56.2 (q), 18.7 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{35}N_2O_3Si$ 463.2411, found 463.2419.

7-Methyl-2-(2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3o).

The product was obtained as white solid; Yield: 68 mg (82%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 118–119 °C; IR(neat) ν_{max}: 2935, 2859, 2155, 1655, 1610, 1456, 1216, 880, 791, 666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.59 (s, 1H), 8.29 (dd, J = 7.4, 1.5 Hz, 1H), 8.19 (d, J = 8.1 Hz, 1H), 7.65 (dd, J = 7.1, 1.6 Hz, 1H), 7.60 (s, 1H), 7.55–7.45 (m, 2H), 7.31 (d, J = 8.1 Hz, 1H), 2.52 (s, 3H), 1.49–0.76 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)

δ 161.2 (s), 151.2 (s), 149.3 (s), 145.5 (s), 134.8 (d), 133.7 (s), 130.68 (d), 130.0 (d), 129.2 (d), 128.5 (d), 127.8 (d), 126.3 (d), 120.5 (s), 119.0 (s), 104.2 (s), 100.5 (s), 21.9 (q), 18.6 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{26}H_{33}N_2OSi$ 417.2357, found 417.2352.

7-Fluoro-2-(2-((triisopropylsilyl)ethynyl)phenyl)quinazolin4(3*H*)-one(3p).

The product was obtained as white solid; Yield: 63 mg (75%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 121–122 °C; IR(neat) ν_{max}: 3283, 2944, 2861, 2143, 1687, 1576, 1373, 1285, 879, 765, 676 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.92 (brs, 1H), 8.33–8.17 (m, 2H), 7.69–7.56 (m, 1H), 7.54–7.48 (m, 2H), 7.43 (d, J = 9.7 Hz, 1H), 7.24–7.13 (m, 1H), 1.31–0.84 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.7 (ds, $^1J_{C\text{-}F}$ = 254.2 Hz), 160.7 (s,), 152.4 (s), 151.3 (ds, $^3J_{C\text{-}F}$ = 13.2 Hz), 134.9 (d), 133.3 (ds, $^4J_{C\text{-}F}$ = 3.1 Hz), 131.0 (d), 130.0 (d), 129.2 (d), 129.1 (dd, $^3J_{C\text{–}F}$ = 11.0 Hz), 120.7 (s), 118.1 (s,), 115.7 (dd, $^2J_{C\text{–}F}$ = 23.6 Hz), 113.3 (dd, $^2J_{C\text{–}F}$ = 21.8 Hz), 104.1 (s), 100.7 (s), 18.6 (q, 6C), 11.2 (d, 3C); ^{19}F NMR (377 MHz, $CDCl_3$) δ –103.2.; HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{30}FN_2OSi$ 421.2106, found 421.2100.

7-Bromo-2-(2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3q).

The product was obtained as white solid; Yield: 75 mg (78%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 124–125 °C; IR(neat) ν_{max}: 3308, 2941, 2143, 2864, 1689, 1587, 1462, 1234, 880, 769, 659 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.86 (s, 1H), 8.31 (d, J = 8.1 Hz, 1H), 8.14 (d, J = 8.5 Hz, 1H), 7.98 (d, J = 1.8 Hz, 1H), 7.70–7.62 (m, 1H), 7.58 (dd, J = 8.5, 1.9 Hz, 1H), 7.56–7.45 (m, 2H), 1.56–0.89 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.8 (s), 152.2 (s), 150.1 (s), 135.0 (d), 133.0 (s), 131.1 (d), 130.8 (d), 130.3 (d), 130.1 (d), 129.3 (d), 129.3 (s), 127.9 (d), 120.5 (s), 120.2 (s), 104.1 (s), 101.1 (s), 18.6 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{30}BrN_2OSi$ 481.1305, found 481.1298.

7-Nitro-2-(2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3r).

The product was obtained as yellow solid; Yield: 62 mg (70%). R_f: 0.4 (5:1 petroleum ether/EtOAc) Mp: 147–148 °C; IR(neat) ν_{max}: 3261, 2933, 2862, 2150, 1702, 1576, 1347, 1228, 880, 731, 676 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 11.16 (s, 1H), 8.64 (d, J = 2.1 Hz, 1H), 8.46 (d, J = 8.7 Hz, 1H), 8.44–8.39 (m, 1H), 8.24 (dd, J = 8.7, 2.1 Hz, 1H), 7.73–7.66 (m, 1H), 7.62–7.43 (m, 2H), 1.26–1.03 (m, 21H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 160.1 (s), 153.0 (s, 2C), 151.8 (s), 149.7 (s), 135.2 (d), 132.2 (s), 131.6 (d), 130.2 (d), 129.5 (d),

128.4 (d), 125.5 (s), 123.6 (d), 120.5 (d), 104.0 (s), 101.8 (s), 18.6 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{30}N_3O_3Si$ 448.2051, found 448.2047.

6,7-Dimethoxy-2-(2-((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (3s).

The product was obtained as white solid; Yield: 58 mg (62%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 129–130 °C; IR(neat) ν_{max}: 2942, 2861, 2148, 1656, 1569, 1385, 1269, 1218, 1080, 980, 878, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.65 (s, 1H), 8.33 (dd, J = 7.6, 1.5 Hz, 1H), 7.70–7.66 (m, 2H), 7.57–7.48 (m, 2H), 7.29 (s, 1H), 4.06 (s, 3H), 4.04 (s, 3H), 1.33–1.10 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.7 (s), 155.1 (s), 149.9 (s), 149.3 (s), 145.4 (s), 134.9 (d), 133.5 (s), 130.6 (d), 129.7 (d), 129.3 (d), 120.3 (s), 114.7 (s), 108.5 (d), 105.5 (d), 104.3 (s), 100.5 (s), 56.4 (q), 56.3 (q), 18.7 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{35}N_2O_3Si$ 463.2411, found 463.2408.

2-(2-((Triisopropylsilyl)ethynyl)naphthalen-1yl)quinazolin-4(3*H*)-one (3t).

The product was obtained as yellow solid; Yield: 76 mg (84%). R_f: 0.6 (5:1 petroleum ether/EtOAc) Mp: 202–203 °C; IR(neat) ν_{max}: 2943, 2858, 2142, 1662, 1466, 1371, 1221, 880, 768, 670, 634 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 8.29 (d, J = 7.5 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.86 (d, J = 7.5 Hz, 1H), 7.84–7.79 (m, 2H), 7.76 (d, J = 8.8 Hz, 1H), 7.63 (d, J = 8.5 Hz, 1H), 7.58–7.45 (m, 3H), 1.06–0.78 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.0 (s), 151.6 (s), 149.0 (s), 134.7 (d), 134.5 (s), 132.9 (s), 130.7 (s), 130.2 (d), 128.7 (d), 128.3 (d), 128.1 (d), 128.0 (d), 127.3 (d), 127.2 (d), 126.4 (d), 124.9 (d), 121.5 (s), 121.0 (s), 103.9 (s), 97.9 (s), 18.4 (q, 6C), 11.0 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{29}H_{33}N_2OSi$ 453.2357, found 453.2361.

2-(3-((Triisopropylsilyl)ethynyl)naphthalen-2-yl)quinazolin-4(3*H*)-one (3u).

The product was obtained as white solid; Yield: 64 mg (72%). R_f: 0.6 (5:1 petroleum ether/EtOAc) Mp: 194–195 °C; IR(neat) ν_{max}: 2941, 2861, 2148, 1665, 1602, 1462, 1370, 1224, 880, 763, 668, 639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.76 (s, 1H), 8.73 (s, 1H), 8.31 (d, J = 7.8 Hz, 1H), 8.17 (s, 1H), 7.97 (d, J = 7.1 Hz, 1H), 7.86 (d, J = 7.9 Hz, 2H), 7.83–7.74 (m, 1H), 7.65–7.53 (m, 2H), 7.50 (t, J = 7.4 Hz, 1H), 1.22–1.09 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.5 (s), 151.6 (s), 149.3 (s), 135.3 (d), 134.3 (d), 133.6 (s), 132.5 (s), 130.8 (d), 130.3 (s), 129.0 (d), 128.5 (d), 128.0 (d), 127.9 (d), 127.4 (d), 126.9 (d), 126.5 (d), 121.3 (s), 117.0 (s), 104.5 (s), 99.1 (s), 18.7 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{29}H_{33}N_2OSi$ 453.2357, found 453.2355.

2-(3-((Triisopropylsilyl)ethynyl)furan-2-yl)quinazolin-4(3*H*)-one (3v).

The product was obtained as yellow solid; Yield: 64 mg (83%). R_f: 0.6 (5:1 petroleum ether/EtOAc) Mp: 148–149 °C; IR(neat) ν_{max}: 2924, 2858, 2139, 1655, 1370, 1211, 881, 748, 642 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1H), 8.29 (dd, J = 8.0, 1.1 Hz, 1H), 7.84 (dd, J = 8.2, 0.7 Hz, 1H), 7.77 (ddd, J = 8.3, 7.1, 1.6 Hz, 1H), 7.62 (d, J = 1.9 Hz, 1H), 7.48 (ddd, J = 8.1, 7.1, 1.2 Hz, 1H), 6.66 (d, J = 1.9 Hz, 1H), 1.31–1.13 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.7 (s), 148.7 (s), 146.7 (s), 145.2 (d), 143.0 (s), 134.8 (d), 128.1 (d), 127.2 (d), 126.7 (d), 121.8 (s), 115.6 (d), 110.4 (s), 103.9 (s), 96.9 (s), 18.8 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{29}N_2O_2Si$ 393.1993, found 393.1995.

2-(3-((Triisopropylsilyl)ethynyl)thiophen-2-yl)quinazolin-4(3*H*)-one (3w).

The product was obtained as yellow solid; Yield: 64 mg (79%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 136–137 °C; IR(neat) ν_{max}: 2944, 2861, 2141, 1689, 1464, 1348, 1212, 769, 710, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.03 (s, 1H), 8.28 (d, J = 7.9 Hz, 1H), 7.82–7.61 (m, 2H), 7.49–7.41 (m, 2H), 7.18 (d, J = 5.1 Hz, 1H), 1.36–1.12 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.9 (s), 148.9 (s), 146.8 (s), 138.5 (s), 134.6 (d), 132.5 (d), 129.8 (d), 127.6 (d), 126.7 (d), 126.6 (d), 121.6 (s), 121.2 (s), 102.3 (s), 100.4 (s), 18.7 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{29}N_2OSSi$ 409.1764, found 409.1765.

2-(2-((Triisopropylsilyl)ethynyl)-1*H*-indol-3-yl)quinazolin-4(3*H*)-one (3x).

The product was obtained as yellow solid; Yield: 60 mg (70%). R_f: 0.5 (5:1 petroleum ether/EtOAc) Mp: 209–210 °C; IR(neat) ν_{max}: 3254, 2937, 2862, 2139, 1661, 1584, 1418, 1235, 874, 718, 674 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.52 (brs, 1H), 8.89 (d, J = 7.4 Hz, 1H), 8.70 (brs, 1H), 8.30 (dd, J = 7.9, 1.1 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.76 (ddd, J = 8.3, 7.1, 1.6 Hz, 1H), 7.43 (ddd, J = 8.1, 7.2, 1.2 Hz, 1H), 7.40–7.31 (m, 3H), 1.36–1.11 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.6 (s), 149.9 (s), 148.5 (s), 135.8 (s), 134.4 (d), 127.9 (d), 126.5 (d), 126.0 (d), 125.6 (s), 125.5 (d), 123.9 (d), 122.7 (d), 121.3 (s), 118.4 (s), 113.4 (s), 110.8 (d), 105.9 (s), 96.8 (s), 18.7 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{32}N_3OSi$ 442.2309, found 442.2305.

2-(2-((Triisopropylsilyl)ethynyl)benzo[b]thiophen-3-yl)quinazolin-4(3*H*)-one (3y).

The product was obtained as yellow solid; Yield: 72 mg (78%). R_f: 0.6 (5:1 petroleum ether/EtOAc) Mp: 170–171 °C; IR(neat) ν_{max}: 2930, 2861, 2133, 1664, 1594, 1457, 885, 765,

684, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 1H), 9.00 (d, J = 7.9 Hz, 1H), 8.34 (d, J = 7.9 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.83–7.75 (m, 2H), 7.54–7.45 (m, 3H), 1.51–1.06 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.2 (s), 149.0 (s), 147.4 (s), 139.2 (s), 136.7 (s), 134.6 (d), 130.1 (s), 128.2 (d), 127.2 (d), 126.8 (d), 126.6 (d), 126.6 (d), 125.9 (d), 124.8 (s), 121.7 (ds, 2C), 108.9 (s), 97.7 (s), 18.7 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{31}N_2OSSi$ 459.1921, found 459.1916.

(*Z*)-2-(1-Phenyl-4-(triisopropylsilyl)but-1-en-3-yn-2-yl)quinazolin-4(3*H*)-one (3z).

The product was obtained as yellow thick liquid; Yield: 62 mg (73%). R_f: 0.6 (5:1 petroleum ether/EtOAc) IR(neat) ν_{max}: 3308, 2941, 2864, 1689, 1587, 1462, 1234, 880, 769, 659, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 11.33 (s, 1H), 8.30 (d, J = 7.9 Hz, 1H), 7.80 (d, J = 8.0 Hz, 2H), 7.79–7.71 (m, 2H), 7.52–7.42 (m, 4H), 7.12 (s, 1H), 1.46–1.09 (m, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.0 (s), 150.2 (s), 149.2 (s), 136.9 (s), 134.6 (d), 129.9 (d), 129.0 (s), 128.8 (d, 2C), 127.8 (d), 127.4 (d), 127.24 (d), 126.9 (d, 2C), 126.7 (d), 121.8 (s), 109.5 (s), 102.9 (s), 18.7 (q, 6C), 11.2 (d, 3C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{33}N_2OSi$ 429.2357, found 429.2356.

2-(2,6-Bis((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (4a).

The product was obtained as white solid; Yield: 110 mg (94%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp. 188–189 °C; IR(neat) ν_{max}: 2943, 2862, 2148, 1666, 1459, 1370, 1224, 880, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.28 (d, J = 7.9 Hz, 1H), 7.75 (dd, J = 4.6, 1.2 Hz, 2H), 7.58–7.54 (m, 2H), 7.52–7.48 (m, 1H), 7.40 (dd, J = 8.3, 7.4 Hz, 1H), 0.86 (s, 42H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4 (s), 151.2 (s), 148.9 (s), 138.9 (s), 134.4 (d), 132.7 (d, 2C), 129.8 (d), 128.1 (d), 127.1 (d), 126.2 (d), 123.3 (s, 2C), 121.6 (s), 102.6 (s, 2C), 97.2 (s, 2C), 18.3 (q, 12C),11.0 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{36}H_{51}N_2OSi_2$ 583.3534, found 583.3543.

2-(4-Fluoro-2,6-bis((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (4b).

The product was obtained as white solid; Yield: 100 mg (83%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp: 168–169 °C. IR(neat) ν_{max}: 2942, 2863, 2149, 1668, 1464, 1369, 1223, 996, 878, 662 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.26 (s, 1H), 8.27 (d, J = 7.7 Hz, 1H), 7.88–7.65 (m, 2H), 7.52–7.48 (m, 1H), 7.26 (d, J = 8.6 Hz, 2H), 0.85 (s, 42H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.4 (ds, $^1J_{C\text{-}F}$ = 251.7 Hz), 161.6 (s), 150.5 (s), 148.9 (s), 135.5 (ds, $^4J_{C\text{-}F}$ = 3.4 Hz), 134.4 (d), 128.1 (d), 127.3 (d), 126.2 (d), 125.4 (ds, $^3J_{C\text{-}F}$ = 10.9 Hz, 2C), 121.6 (s), 119.7 (dd, $^2J_{C\text{-}F}$ = 23.3 Hz, 2C), 101.5 (ds, $^4J_{C\text{-}F}$ = 3.0 Hz, 2C), 98.7 (s, 2C), 18.3 (q,

12C), 10.9 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{36}H_{50}FN_2OSi_2$ 601.3440, found 601.3449.

2-(4-Chloro-2,6-bis((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (4c).

The product was obtained as white solid; Yield: 100 mg (81%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp: 185–186 °C; IR(neat) ν_{max}: 2942, 2863, 2152, 1664, 1498, 1369, 1212, 999, 772, 662 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.27 (d, J = 7.7 Hz, 1H), 7.82–7.71 (m, 2H), 7.54 (s, 2H), 7.53–7.48 (m, 1H), 0.86 (s, 42H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4 (s), 150.3 (s), 148.8 (s), 137.2 (s), 135.8 (s), 134.4 (d), 132.4 (d, 2C), 128.1 (d), 127.3 (d), 126.2 (d), 124.8 (s, 2C), 121.6 (s), 101.3 (s, 2C), 98.9 (s, 2C), 18.3 (q, 12 C), 10.9 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{36}H_{50}ClN_2OSi_2$ 617.3145, found 617.3153.

2-(4-Bromo-2,6-bis((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (4d).

The product was obtained as white solid; Yield: 110 mg (83%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp: 181–182 °C; IR(neat) ν_{max}: 2942, 2862, 2152, 1667, 1464, 1369, 1213, 939, 773, 670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.27 (d, J = 7.8 Hz, 1H), 7.79–7.72 (m, 2H), 7.69 (s, 2H), 7.53–7.49 (m, 1H), 0.86 (s, 42H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4 (s), 150.4 (s), 148.8 (s), 137.7 (s), 135.2 (d, 2C), 134.5 (d), 128.1(d), 127.3 (d), 126.2 (d), 124.9 (s, 2C), 123.6 (s), 121.6 (s), 101.2 (s, 2C), 99.1 (s, 2C), 18.3 (q, 12C), 10.9 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{36}H_{50}BrN_2OSi_2$ 661.2640, found 661.2643.

2-(4-Methyl-2,6-bis((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (4e).

The product was obtained as white solid; Yield: 114 mg (96%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp: 190–191 °C. IR(neat) ν_{max}: 2970, 2862, 2144, 1668, 1438, 1369, 1212, 901, 653 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.27 (d, J = 7.8 Hz, 1H), 7.74 (d, J = 3.8 Hz, 2H), 7.48 (m, 1H), 7.37 (s, 2H), 2.37 (s, 3H), 0.86 (s, 42H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.8 (s), 151.2 (s), 148.9 (s), 140.1 (s), 136.2 (s), 134.3 (d), 133.3 (d, 2C), 128.1 (d), 127.0 (d), 126.1 (d), 123.0 (s, 2C), 121.6 (s), 102.8 (s, 2C), 96.5 (s, 2C), 20.93 (q), 18.3 (q, 12C), 10.9 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{37}H_{53}N_2OSi_2$ 597.3691, found 597.3702.

2-(4-Methoxy-2,6-bis((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (4f).

The product was obtained as white solid; Yield: 116 mg (95%). R_f: 0.8 (9:1 petroleum ether/EtOAc) Mp: 183–184 °C; IR(neat) ν_{max}: 2940, 2862, 2144, 1669, 1496, 1369, 1222, 880, 670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.27 (d, J = 7.9 Hz, 1H), 7.74 (dd, J = 4.6, 1.0 Hz, 2H), 7.54–7.40 (m, 1H), 7.05 (s, 2H), 3.86 (s, 3H), 0.86 (s, 42H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.6 (s), 160.1 (s), 151.1 (s), 149.0 (s), 134.3 (d), 131.9 (s), 128.1 (d), 127.0 (d), 126.1 (d), 124.5 (s, 2C), 121.5 (s), 118.3 (d, 2C), 102.7 (s, 2C), 96.8 (s, 2C), 55.8 (q), 18.3 (q, 12C), 10.9 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{37}H_{53}N_2O_2Si_2$ 613.3640, found 613.3649.

2-(4-(Trifluoromethyl)-2,6-bis((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (4g).

The product was obtained as white solid; Yield: 114 mg (88%). R_f: 0.8 (9:1 petroleum ether/EtOAc) Mp: 186–187 °C; IR(neat) ν_{max}: 2942, 2860, 2156, 1670, 1496, 1373, 1232, 950, 880, 674 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.44 (s, 1H), 8.26 (d, J = 7.9 Hz, 1H), 8.10–7.63 (m, 4H), 7.53–7.49 (m, 1H), 0.86 (s, 42H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.5 (s), 150.1 (s), 148.8 (s), 141.7 (s), 134.5 (d), 132.5 (qs, $^2J_{C\text{-}F}$ = 33.3 Hz), 129.0 (qd, $^3J_{C\text{-}F}$ = 3.6 Hz, 2C), 128.1 (d), 127.4 (d), 126.2 (d), 124.5 (s, 2C), 122.9 (qs, $^1J_{C\text{-}F}$ = 273.2 Hz), 121.7 (s), 101.2 (s, 2C), 99.6 (s, 2C), 18.3 (q, 12C), 10.9 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{37}H_{50}F_3N_2OSi_2$ 651.3408, found 651.3420.

2-(3-Fluoro-2,6-bis((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (4h).

The product was obtained as white solid; Yield: 91 mg (76%). R_f: 0.6 (9:1 petroleum ether/EtOAc) Mp: 178–179 °C; IR(neat) ν_{max}: 2933, 2861, 2140, 1667, 1463, 1370, 1226, 881, 773, 674 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.29 (d, J = 7.9 Hz, 1H), 7.81–7.68 (m, 2H), 7.56–7.48 (m, 2H), 7.18 (t, J = 8.5 Hz, 1H), 0.87 (d, 42H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163. 9 (ds, $^1J_{C\text{-}F}$ = 257.4 Hz), 161.4 (s), 149.9 (s), 148.8 (s), 140.6 (s), 134.5 (d), 134.1 (dd, $^3J_{C\text{-}F}$ = 8.4 Hz), 128.2 (d), 127.4 (d), 126.2 (d), 121.6 (s), 119.3 (ds, $^4J_{C\text{-}F}$ = 4.0 Hz), 117.4 (dd, $^2J_{C\text{-}F}$ = 21.9 Hz), 112.7 (ds, $^2J_{C\text{-}F}$ = 18.49 Hz), 103.6 (s), 101.7 (s), 96.8 (s), 95.5 (s), 18.3 (dq, $^4J_{C\text{-}F}$ = 2.6 Hz, 12C), 11.0 (dd, $^4J_{C\text{-}F}$ = 4.6 Hz, 6C)^{19}F NMR (376 MHz, $CDCl_3$) δ –105.4.; HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{36}H_{50}FN_2OSi_2$ 601.3440, found 601.3452.

2-(3-Bromo-2,6-bis((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (4i).

The product was obtained as white solid; Yield: 88 mg (67%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp: 184–185 °C; IR(neat) ν_{max}: 2940, 2863, 2148, 1681, 1463, 1371, 1209,

991, 879, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.27 (d, J = 7.5 Hz, 1H), 7.78–7.72 (m, 2H), 7.68 (d, J = 8.6 Hz, 1H), 7.51 (ddd, J = 8.2, 6.1, 2.2 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 0.91–0.74 (m, 42H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.5 (s), 150.7 (s), 148.9 (s), 140.5 (s), 134.5 (d), 134.0 (d), 132.9 (d), 128.2 (d), 127.4 (d), 126.3 (d), 122.3 (s), 121.8 (s), 103.5 (s), 101.8 (s), 100.9 (s, 2C), 98.5 (s, 2C), 18.4 (q, 6C), 18.3 (q, 6C), 11.0 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{36}H_{50}BrN_2OSi_2$ 661.2640, found 661.2640.

2-(3-Methoxy-2,6-bis((triisopropylsilyl)ethynyl)phenyl)quinazolin-4(3*H*)-one (4j).

The product was obtained as white solid; Yield: 86 mg (74%). R_f: 0.8 (9:1 petroleum ether/EtOAc) Mp: 169–170 °C; IR(neat) ν_{max}: 2942, 2863, 2133, 1669, 1496, 1370, 1232, 880, 670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.27 (d, J = 7.9 Hz, 1H), 7.76–7.73 (m, 2H), 7.61–7.35 (m, 2H), 6.94 (d, J = 8.7 Hz, 1H), 3.91 (s, 3H), 0.86 (s, 21H), 0.84 (s, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4 (s), 160.9 (s), 151.0 (s), 149.0 (s), 140.4 (s), 134.3 (d), 134.0 (d), 128.1 (d), 127.1 (d), 126.1 (d), 121.6 (s), 115.1 (s), 113.1 (s), 112.3 (d), 102.6 (s), 101.8 (s), 98.5 (s), 94.6 (s), 56.4 (q), 18.4 (q, 12C), 10.9 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{37}H_{53}N_2O_2Si_2$ 613.3640, found 613.3640.

2-(2,6-Bis((triisopropylsilyl)ethynyl)phenyl)-7-methylquinazolin-4(3*H*)-one (4o).

The product was obtained as white solid; Yield: 102 mg (86%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp: 202–203 °C; IR(neat) ν_{max}: 2941, 2862, 2141, 1657, 1453, 1370, 1224, 985, 879, 667 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.15 (d, J = 8.1 Hz, 1H), 7.61–7.55 (m, 3H), 7.39 (t, J = 7.8 Hz, 1H), 7.31 (d, J = 8.1 Hz, 1H), 2.49 (s, 3H), 0.87 (s, 42H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 161.3 (s), 151.1 (s), 149.0 (s), 145.2 (s), 138.9 (s), 132.7 (d, 2C), 129.6 (d), 128.6 (d), 128.0 (d), 126.0 (d), 123.3 (s, 2C), 119.2 (s), 102.6 (s, 2C), 97.1 (s, 2C), 21.9 (q), 18.3 (q, 12C), 11.0 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{37}H_{53}N_2OSi_2$ 597.3691, found 597.3684.

2-(2,6-Bis((triisopropylsilyl)ethynyl)phenyl)-7-fluoroquinazolin-4(3*H*)-one (4p).

The product was obtained as white solid; Yield: 99 mg (83%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp: 203–204 °C; IR(neat) ν_{max}: 2940, 2863, 2145, 1663, 1608, 1452, 1370, 1225, 985, 877, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCL_3$) δ 9.35 (s, 1H), 8.28 (dd, J = 8.7, 6.2 Hz, 1H), 7.56 (d, J = 7.8 Hz, 2H), 7.44–7.36 (m, 2H), 7.21 (td, J = 8.6, 2.3 Hz, 1H), 0.87 (s, 42H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.5 (ds, $^1J_{C-F}$ = 254.3 Hz), 160.9 (s), 152.7 (s), 151.2 (ds, $^3J_{C-F}$ = 13.1 Hz), 138.5 (s), 132.7 (d, 2C), 130.0 (d), 128.9 (dd, $^3J_{C-F}$ = 10.6 Hz), 123.2 (s, 2C), 118.3 (s), 115.8 (dd, $^2J_{C-F}$ = 23.6 Hz), 113.4 (dd, $^2J_{C-F}$ = 22.1 Hz), 102.5 (s,

2C), 97.4 (s, 2C), 18.3 (q, 12C), 10.9 (d, 6C); ^{19}F NMR (376 MHz, $CDCl_3$) δ –103.1.; HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{36}H_{50}FN_2OSi_2$ 601.3440, found 601.3450.

2-(2,6-Bis((triisopropylsilyl)ethynyl)phenyl)-7-bromoquinazolin-4(3*H*)-one (4q).

The product was obtained as white solid; Yield: 106 mg (80%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp: 202–203 °C; IR(neat) ν_{max}: 2941, 2862, 2145, 1661, 1596, 1445, 1370, 1225, 986, 881, 670 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.13 (d, J = 8.5 Hz, 1H), 7.93 (d, J = 1.8 Hz, 1H), 7.61 (dd, J = 8.5, 1.9 Hz, 1H), 7.57 (d, J = 7.9 Hz, 2H), 7.45–7.38 (m, 1H), 0.89 (s, 42H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.8 (s), 152.5 (s), 149.9 (s), 138.4 (s), 132.8 (d, 2C), 130.9 (d), 130.5 (d), 130.0 (d), 129.0 (s), 127.6 (d), 123.2 (s, 2C), 120.5 (s), 102.4 (s, 2C), 97.5 (s, 2C), 18.4 (q, 12C), 10.9 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{36}H_{50}BrN_2OSi_2$ 661.2640, found 661.2637.

2-(2,6-Bis((triisopropylsilyl)ethynyl)phenyl)-7-nitroquinazolin-4(3*H*)-one (4r).

The product was obtained as yellow solid; Yield: 98 mg (79%). R_f: 0.6 (9:1 petroleum ether/EtOAc) Mp: 212–213 °C; IR(neat) ν_{max}: 2941, 2862, 2155, 1667, 1606, 1534, 1453, 1346, 1228, 985, 880, 668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (brs, 1H), 8.59 (d, J = 1.8 Hz, 1H), 8.42 (d, J = 8.7 Hz, 1H), 8.26 (dd, J = 8.7, 2.0 Hz, 1H), 7.59 (d, J = 7.8 Hz, 2H), 7.45 (t, J = 7.8 Hz, 1H), 0.86 (s, 42H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.4 (s), 153.7 (s), 151.6 (s), 149.6 (s), 137.9 (s), 132.9 (d, 2C), 130.3 (d), 128.1 (d), 125.7 (s), 123.6 (d), 123.1 (s, 2C), 120.8 (d), 102.4 (s, 2C), 97.7 (s, 2C), 18.3 (q, 12C), 10.9 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{36}H_{50}N_3O_3Si_2$ 628.3385, found 628.3372.

2-(2,6-Bis((triisopropylsilyl)ethynyl)phenyl)-6,7-dimethoxyquinazolin-4(3*H*)-one (4s).

The product was obtained as white solid; Yield: 112 mg (87%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp: 193–194 °C; IR(neat) ν_{max}: 2940, 2862, 2138, 1647, 1608, 1457, 1385, 1269, 1213, 1093, 980, 878, 666 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (s, 1H), 7.60 (s, 1H), 7.54 (d, J = 7.8 Hz, 2H), 7.38 (t, J = 7.8 Hz, 1H), 7.19 (s, 1H), 4.01 (s, 3H), 3.95 (s, 3H), 0.88 (s, 42H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.1 (s), 154.8 (s), 149.9 (s), 149.3 (s), 145.3 (s), 138.8 (s), 132.7 (d, 2C), 129.7 (d), 123.3 (s, 2C), 114.9 (s), 108.7 (d), 105.1 (d), 102.7 (s, 2C), 97.0 (s, 2C), 56.4 (q), 56.2 (q), 18.4 (q, 12C), 11.0 (d, 6C); HRMS (ESI–TOF) m/z: $[M]^+$ calcd for $C_{38}H_{54}N_2O_3Si_2$ 642.3667, found 642.3647.

2-(1,3-Bis((triisopropylsilyl)ethynyl)naphthalen-2-yl)quinazolin-4(3*H*)-one (4u).

The product was obtained as white solid; Yield: 96 mg (76%). R_f: 0.7 (9:1 petroleum ether/EtOAc) Mp: 204–205 °C; IR(neat) ν_{max}: 2936, 2862, 2141, 1665, 1606, 1463, 1371, 1023, 881, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.40 (d, J = 8.1 Hz, 1H), 8.29 (d, J = 7.8 Hz, 1H), 8.10 (s, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.81–7.71 (m, 2H), 7.67–7.55 (m, 2H), 7.53–7.45 (m, 1H), 0.92 (s, 21H), 0.88 (s, 21H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.5 (s), 151.6 (s), 149.0 (s), 136.6 (s), 134.3 (d), 133.3 (d), 133.0 (s), 132.6 (s), 128.6 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.1 (d), 126.8 (d), 126.2 (d), 121.7 (s), 121.7 (s), 119.4 (s), 103.1 (s), 100.7 (s), 96.4 (s, 2C), 18.4 (q, 6C), 18.3 (q, 6C), 11.0 (d, 6C); HRMS (ESI–TOF) m/z: $[M + H]^+$ calcd for $C_{40}H_{53}N_2OSi_2$ 633.3691, found 633.3682.

12-Methyleneisoindolo[1,2-b]quinazolin-10(12*H*)-one (5a): To a solution of TIPS-alkyne **3a** (81 mg, 0.2 mmol) in THF (1 mL) was added TBAF (0.24 mL, 0.24 mmol) at 0 °C. After addition, the solution was warmed up to room temperature and stirred for another 1h and quenched with water, extracted with ethyl acetate (3×10 mL). The combined organic layers were dried over Na_2SO_4. The volatile compounds were removed in vacuo and the residue was subjected to column chromatography on silica gel to afford **5a** (42 mg; 84%). Colorless solid; R_f: 0.5 (5:1 petroleum ether/EtOAc); Mp: 280–282 °C; IR (neat) ν_{max}: 2921, 2552, 1669, 1650, 1602, 1468, 1334, 873, 768, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, J = 7.8 Hz, 1H), 8.17 (d, J = 7.4 Hz, 1H), 7.90–7.76 (m, 3H), 7.63 (dt, J = 22.0, 7.3 Hz, 2H), 7.52 (t, J = 7.3 Hz, 1H), 7.07 (s, 1H), 5.94 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.8 (s), 151.8 (s), 147.6 (s), 139.7 (s), 135.6 (s), 134.4 (d), 132.4 (d), 130.2 (d), 129.9 (s), 127.6 (d), 127.1 (d), 126.8 (d), 123.0 (d), 121.4 (s), 120.3 (d), 101.8 (t); HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{11}ON_2$ 247.0866, found 247.0865.

8*H*-Isoquinolino[1,2-b]quinazolin-8-one (5b): To a solution of TIPS-alkyne **3a** (81 mg, 0.2 mmol) in dry DMF (1.5 mL) was added NaH (60%) (4.8 mg, 0.2 mmol) at room temperature. The solution was heated at 80 °C for 10h and then extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was subjected to column chromatography on silica gel to afford **5b** (20 mg 41%). yellow solid; R_f: 0.7 (5:1 petroleum /EtOAc); Mp: 167–169 °C (168–170 °C)[22]; ^1H NMR (400 MHz, $CDCl_3$) δ 9.10 (d, J = 8.0 Hz, 1H), 8.67 (d, J = 7.8 Hz, 1H), 8.48 (d, J = 7.9 Hz, 1H), 7.89 (dt, J = 15.0, 7.5 Hz, 2H), 7.77–7.72 (m, 1H), 7.67 (dd, J = 12.8, 7.5 Hz, 2H), 7.53 (t, J = 7.0 Hz, 1H), 7.05 (d, J = 7.8 Hz, 1H); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.5 (s), 147.6 (s), 146.2 (s), 134.8 (d), 132.9 (s), 132.2 (d, 2C), 128.5 (d), 127.6 (d), 127.3 (d), 127.3 (d), 126.5 (d), 125.8 (d), 122.0 (s), 117.8 (s), 113.2 (d); LC-MS (ESI) m/z: 247 $[M+H]^+$.

5-Bromo-6-(triisopropylsilyl)-8*H*-isoquinolino[1,2-b]quinazolin-8-one (5c): To a solution of TIPS-alkyne **3a** (81 mg, 0.2 mmol) in dioxane:water (1:1) (1.5 mL) was added NBS (53 mg, 0.3 mmol) at room temperature. The solution was heated at 80 °C for 10h and then extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was subjected to column chromatography on silica gel to afford **5c** (85 mg; 88%). yellow solid; R_f: 0.3 (5:1 petroleum /EtOAc); Mp: 180–182 °C; IR (neat) ν_{max}: 2948, 2667, 1676, 1598, 1564, 1466, 1367, 879, 749, 665 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 7.8 Hz, 1H), 8.18 (d, J = 7.5 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.74–7.62 (m, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 7.32 (d, J = 8.4 Hz, 1H), 1.84–1.74 (m, 3H), 1.31 (brs, 18H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 170.1 (s), 160.0 (s), 145.1 (s), 138.4 (s), 136.7 (s), 132.8 (d), 131.8 (d), 130.5 (s), 129.9 (d), 128.5 (d), 125.3 (d), 124.6 (d), 121.9 (d), 121.1 (d), 120.0 (s), 119.9 (s), 19.4 (q, 6C), 14.2 (d, 3C); HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{30}ON_2{}^{81}BrSi$ 483.1285, found 483.1292.

(*E*)-12-Benzylideneisoindolo[1,2-b]quinazolin-10(12*H*)-one (5d): In oven dried Schlenk tube was charged with TIPS-alkyne **3a** (81 mg, 0.2 mmol), aryl iodide (49 mg, 0.24 mmol), $PdCl_2(PPh)_3$ (14 mg, 10 mol%), CuI (11.4 mg, 30 mol%) in sequence. The Schlenk tube was vacuumed and backfilled with nitrogen for three times followed by adding anhydrous THF (1 ml). TBAF (0.4 mL, 1M in THF) was added into the solution at 0 °C and under the protection of nitrogen through syringe and then the Schenk tube was closed tightly. After warming up to room temperature and stirring for 1 h, water was added and the resulting mixture was extracted with dichloromethane (2×20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was subjected to column chromatography on silica gel to afford **5d** (48 mg; 74%) as yellow solid.R_f: 0.7 (5:1 petroleum /EtOAc); Mp: 184−186 °C (184−185 °C)[23]; ^1H NMR (500 MHz, $CDCl_3$) δ 9.15 (s, 1 H) 8.48 (dd, J = 8.01, 1.14 Hz, 1 H) 8.20 (d, J = 7.63 Hz, 1 H) 7.83–7.88 (m, 1 H) 7.77–7.83 (m, 1 H) 7.49–7.56 (m, 4 H) 7.46–7.49 (m, 2H) 7.41–7.46 (m, 1H) 7.33–7.38 (m, 1 H) 7.27–7.30 (d, J= 8.0 Hz, 1 H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 161.3 (s), 151.4 (s), 147.5 (s), 135.3 (s, 2C), 134.4 (s), 134.3 (d), 131.9 (d), 130.7 (s), 129.6 (d), 129.0 (d, 2C), 128.8 (d, 2C), 128.2 (d), 127.5 (d), 127.2 (d), 126.6 (d), 123.8 (d), 123.2 (d), 122.9 (d), 121.5 (s); HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{15}N_2O$ 323.1179, found 323.1179.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website http://pubs.acs.org. • ^{1}H and ^{13}C NMR spectra of all new compounds (PDF)

AUTHOR INFORMATION:

Corresponding Author

*E-mail: rajunipune@gmail.com, rs.rohokale@ncl.res.in

ORCID

Rajendra S. Rohokale: 0000-0001-8083-0466

Chepuri V. Ramana: 0000-0001-5801-311X

Notes

The authors declare no competing financial interest

ACKNOWLEDGMENT:

R. S. R. is thankful to the Science and Engineering Research Board (SERB), New Delhi for the National Postdoctoral Fellowship (PDF/2016/001476) and R. G. K is thankful to the CSIR, New Delhi for the award of a Senior Research Fellowship (SRF).

REFERENCE:

1. (a) Trost, B. M.; Li, C.-J. Modern Alkyne Chemistry: Catalytic and Atom-Economic Transformations; Wiley: New York, **2014**. (b) Stang, P. J.; Diederich, F. Modern Acetylene Chemistry; Wiley: New York, **2008**. (c) Diederich, F.; Stang, P. J.; Tykwinski, R. R. Acetylene Chemistry; Wiley: New York, **2005**. (d) Schobert, H. Production of Acetylene and Acetylene-based Chemicals from Coal. *Chem. Rev.* **2014**, *114*, 1743–1760. (e) Trotus, I.-T.; Zimmermann, T.; Schuth, F. Catalytic Reactions of Acetylene: A Feedstock for the Chemical Industry Revisited. *Chem. Rev.* **2014**, *114*, 1761–1782. (f) Chinchilla, R.; Najera, C. Chemicals from Alkynes with Palladium Catalysts. *Chem. Rev.* **2014**, *114*, 1783–1826. (g) Boyarskiy, V. P.; Ryabukhin, D. S.; Bokach, N. A.; Vasilyev, A. V. Alkenylation of Arenes and Heteroarenes with Alkynes. *Chem. Rev.* **2016**, *116*, 5894–5986.

2. For selected examples of C–H alkynylation: (a) Caspers, L. D.; Nachtsheim, B. J. Directing-Group-mediated C–H Alkynylations. *Chem. Asian J.* **2018**, *13*, 1231–1247 and references cited therein. (b) Xie, F.; Qi, Z.; Yu, S.; Li, X. Rh(III)- and Ir(III)-Catalyzed C–H Alkynylation of Arenes under Chelation Assistance. *J. Am. Chem. Soc.* **2014**, *136*, 4780–4787. (c) Dudnik, A. S.; Gevorgyan, V. Formal Inverse

Sonogashira Reaction: Direct Alkynylation of Arenes and Heterocycles with Alkynyl Halides. *Angew. Chem., Int. Ed.* **2010**, *49*, 2096–2098.

3. (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. A convenient synthesis of acetylenes: catalytic substitutions of acetylenic hydrogen with bromoalkenes, iodoarenes and bromopyridines. *Tetrahedron Lett*. **1975**, *16*, 4467–4470. (b) Meijere, A. d.; Diederich, F. *Metal-catalyzed cross–coupling reactions*, 2nd, completely rev. and enl. ed., Wiley-VCH, Weinheim, **2004**. (c) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. Palladium-Catalyzed Cross-Coupling Reactions in Total Synthesis. *Angew. Chem., Int. Ed*. **2005**, *44*, 4442–4489. (d) Plenio, H. Catalysts for the Sonogashira Coupling-The Crownless Again Shall Be King. *Angew. Chem., Int. Ed*. **2008**, *47*, 6954–6956. (e) Chinchilla, R.; Nájera, C. Recent advances in Sonogashira reactions. *Chem. Soc. Rev*. **2011**, *40*, 5084–5121.

4. (a) Negishi, E.; Anastasia, L. Palladium–Catalyzed Alkynylation. *Chem. Rev*. **2003**, *103*, 1979–2018. (b) Weng, Y.; Cheng, B.; He, C.; Lei, A. Rational Design of a Palladium-Catalyzed Csp–Csp Cross-Coupling Reaction Inspired by Kinetic Studies. *Angew. Chem., Int. Ed*. **2012**, *51*, 9547–9551. (c) Wang, M.; Wang, Z.; Shang. M.; Dai. H. Transition Metal Catalyzed C–H Alkynylation. *Chin. J. Org. Chem*. **2015**, *35*, 570–577. (d) Li, C.-J. The Development of Catalytic Nucleophilic Additions of Terminal Alkynes in Water. *Acc. Chem. Res*. **2010**, *43*, 581–590. (e) For recent reviews on transition metal catalyzed C–H bond functionalization by the use of diverse directing groups, see: Zhang, M.; Zhang, Y.; Jie, X.; Zhao, H.; Li, G.; Su, W. Recent advances in directed C–H functionalizations using monodentate nitrogen-based directing groups. *Org. Chem. Front.* **2014**, *1*, 843–895.

5. Selected examples for alkynylation using terminal alkyne reagents: (a) Liu, W.; Li, L.; Li, C.-J. Empowering a transition-metal-free coupling between alkyne and alkyl iodide with light in water. *Nat. Commun*. **2015**, *6*, 6526. (b) Yi, J.; Lu, X.; Sun, Y.-Y.; Xiao, B.; Liu, L. Nickel-Catalyzed Sonogashira Reactions of Non-activated Secondary Alkyl Bromides and Iodides. *Angew. Chem., Int. Ed*. **2013**, *52*, 12409–12413. (c) Eckhardt, M.; Fu, G. C. The First Applications of Carbene Ligands in Cross-Couplings of Alkyl Electrophiles: Sonogashira Reactions of Unactivated Alkyl Bromides and Iodides. *J. Am. Chem. Soc*. **2003**, *125*, 13642–13643. (d) Tang, S.; Liu,Y.; Gao, X.; Wang, P.; Huang, P.; Lei, A. Multi-Metal-Catalyzed Oxidative Radical Alkynylation with Terminal Alkynes: A New Strategy for C(sp^3)–C(sp) Bond

Formation *J. Am. Chem. Soc.* **2018**, *140*, 6006–6013. (e) Wu, X.-X.; Liu, A.; Xu, S.; He, J.; Sun, W.; Chen, S. Palladium-Catalyzed Domino Cyclization/Alkylation of Terminal Alkynes: Synthesis of Alkynyl-Functionalized Azaindoline Derivatives. *Org. Lett.* **2018**, *20*, 1538–1541. (f) Luo, F.-X.; Cao, Z.-C.; Zhao, H.-W.; Wang, D.; Zhang, Y.-F.; Xu, X.; Shi, Z.-J. Nickel-Catalyzed Oxidative Coupling of Unactivated C(sp^3)–H Bonds in Aliphatic Amides with Terminal Alkynes. *Organometallics* **2017**, *36*, 18–21.

6. Selected examples for alkynylation using haloalkyne reagents: (a) Seregin, I. V.; Ryabova, V.; Gevorgyan, V. Direct Palladium-Catalyzed Alkynylation of *N*-Fused Heterocycles. *J. Am. Chem. Soc.* **2007**, *129*, 7742–7743. (b) Tobisu, M.; Ano, Y.; Chatani, N. Palladium-Catalyzed Direct Alkynylation of C–H Bonds in Benzenes. *Org. Lett.* **2009**, *11*, 3250–3252. (c) Ano, Y.; Tobisu, M.; Chatani, N. Palladium-Catalyzed Direct *ortho*–Alkynylation of Aromatic Carboxylic Acid Derivatives. *Org. Lett.* **2012**, *14*, 354–357.

7. Selected examples for alkynylation using boron alkyne reagent: (a) Bertolini, F.; Woodward, S. Rapid 1,4-Alkynylation of Acyclic Enones Using K[F_3BCCR]. *Synlett* **2009**, *1*, 51–54. (b) Molander, G. A.; Traister, K. M. Pd-Catalyzed Alkynylation of 2-Chloroacetates and 2-Chloroacetamides with Potassium Alkynyltrifluoroborates. *Org. Lett.* **2013,** *15*, 5052–5055. (c) Molander, G. A.; Katona, B.W.; Machrouhi, F. Development of the Suzuki-Miyaura Cross-Coupling Reaction: Use of Air-Stable Potassium Alkynyltrifluoroborates in Aryl Alkynylations. *J. Org. Chem.* **2002**, *67*, 8416–8423.

8. For reviews and highlight articles on reactions of hypervalent iodine reagents: (a) Brand, J. P.; Waser, J. Electrophilic alkynylation: the dark side of acetylene chemistry. *Chem. Soc. Rev.* **2012**, *41*, 4165–4179. (b) Li, Y.; Hari, D. P.; Vita, V. M.; Waser J. Cyclic Hypervalent Iodine Reagents for Atom-Transfer Reactions: Beyond Trifluoromethylation. *Angew. Chem., Int. Ed.* **2016**, *55*, 4436–4454. (c) Waser, J. Benziodoxol(on)e Reagents as Tools in Organic Synthesis: The Background behind the Discovery at the Laboratory of Catalysis and Organic Synthesis. *Synlett* **2016**, *27*, 2761–2773. (d) Kaschel, J.; Werz, D. B. Ethynyl Benziodoxolone (EBX): Installing Alkynes the Reversed Way. *Angew. Chem., Int. Ed.* **2015**, *54*, 8876–8878.

9. For selected examples of $[Cp^*IrCl_2]_2$-catalyzed C–H activation, see: (a) Li, X.; Wu, G.; Liu, X.; Zhu, Z.; Huo, Y.; Jiang, H. Regioselective C−H Bond Alkynylation of Carbonyl Compounds through Ir(III) Catalysis. *J. Org. Chem.* **2017**, *82*, 13003−13011. (b) Chen, C.; Liu, P.; Tang, J.; Deng, G.; Zeng, X. Iridium-Catalyzed, Weakly Coordination-Assisted *Ortho*-Alkynylation of (Hetero)aromatic Carboxylic Acids without Cyclization. *Org. Lett.* **2017**, *19*, 2474−2477. (c) Caspers, L. D.; Finkbeiner, P.; Nachtsheim, B. J. Direct Electrophilic C–H Alkynylation of Unprotected 2-Vinylanilines. *Chem. -Eur. J.* **2017**, *23*, 2748–2752. (d) Li, G.; Hu, J.; Zeng, R.; Shi, D-Q.; Zhao, Y. Direct *ortho*-Selective C–H Functionalization of Carboxybenzyl-Protected Arylalkylamines via Ir(III)-Catalyzed C−H Activation. *Org. Lett.* **2018**, *20*, 2454−2458. (e) Wu, Y.; Yang, Y.; Zhou, B.; Li, Y. Iridium(III)-Catalyzed C-7 Selective C–H Alkynylation of Indolines at Room Temperature. *J. Org. Chem.* **2015**, *80*, 1946−1951. (f) Tang, G.-D.; Pan, C.-L.; Xie, F. Ir(III)-catalyzed C–H alkynylation of arenes under chelation assistance. *Org. Biomol. Chem.* **2016**, *14*, 2898–2904. (g) Liu, B.; Wang, X.; Ge, Z.; Li, R. Regioselective Ir(III)-catalyzed C–H alkynylation directed by 7-azaindoles. *Org. Biomol. Chem.* **2016**, *14*, 2944-2949. (h) Pan, S.; Shibata, T. Recent Advances in Iridium-Catalyzed Alkylation of C–H and N–H Bonds. *ACS Catal.* **2013**, *3*, 704–712. (i) Ryu, J.; Kwak, J.; Shin, K.; Lee, D.; Chang, S. Ir(III)-Catalyzed Mild C–H Amidation of Arenes and Alkenes: An Efficient Usage of Acyl Azides as the Nitrogen Source. *J. Am. Chem. Soc*. **2013**, *135*, 12861. (j) Kang, T.; Kim, Y.; Lee, D.; Wang, Z.; Chang, S. Iridium-Catalyzed Intermolecular Amidation of sp^3 C–H Bonds: Late-Stage Functionalization of an Unactivated Methyl Group. *J. Am. Chem. Soc.* **2014**, *136*, 4141–4144. (k) Zhou, T.; Li, L.; Li, B.; Song, H.; Wang, B. Ir(III)-Catalyzed Oxidative Coupling of NH Isoquinolones with Benzoquinone. *Org. Lett*. **2015**, *17*, 4204–4207. (l) Wu, G.; Ouyang, W.; Chen, Q.; Huo, Y.; Li, X. Cross-dehydrogenative alkynylation of sulfonamides and amides with terminal alkynes via Ir(III) catalysis. *Org. Chem. Front. 2018, DOI:10.1039/C8QO01105B*.

10. (a) Phatake, R. S.; Patel, P.; Ramana, C. V. Ir(III)-Catalyzed Synthesis of Isoquinoline *N*-Oxides from Aryloxime and α–Diazocarbonyl Compounds. *Org. Lett.* **2016**, *18*, 292–295. (b) Phatake, R. S.; Patel, P.; Ramana, C. V. Ir(III)-Catalyzed Carbenoid Functionalization of Benzamides: Synthesis of *N*-Methoxyisoquinolinediones and *N*-Methoxyisoquinolinones. *Org. Lett.* **2016**, *18*, 2828–2831.

11. (a) Gundla, R.; Kazemi, R.; Sanam, R.; Muttineni, R.; Sarma, J. A. R. P.; Dayam, R.; Neamati, N. Discovery of Novel Small-Molecule Inhibitors of Human Epidermal Growth Factor Receptor-2: Combined Ligand and Target-Based Approach. *J. Med. Chem.* **2008**, *51*, 3367–3377. (b) Campbell, S. F.; Davey, M. J.; Hardstone, J. D.; Lewis, B. N.; Palmer, M. J. 2,4-Diamino-6,7-dimethoxyquinazolines. 2-[4-(1,4-Benzodioxan-2-ylcarbonyl)piperazin-1-yl] derivatives as α_1 Adrenoceptor Antagonists and Antihypertensive agents. *J. Med. Chem.* **1987**, *30*, 49–57. (c) Rudolph, J.; Esler, W. P.; O'Connor, S.; Coish, P. D. G.; Wickens, P. L.; Brands, M.; Bierer, D. E.; Bloomquist, B. T.; Bondar, G.; Chen, L.; Chuang, C. Y.; Claus, T. H.; Fathi, Z.; Fu, W.; Khire, U. R.; Kristie, J. A.; Liu, X. G.; Lowe, D. B.; McClure, A. C.; Michels, M.; Ortiz, A. A.; Ramsden, P. D.; Schoenleber, R. W.; Shelekhin, T. E.; Vakalopoulos, A.; Tang, W.; Wang, L.; Yi, L.; Gardell, S. J.; Livingston, J. N.; Sweet, L. J.; Bullock, W. H. Quinazolinone Derivatives as Orally Available Ghrelin Receptor Antagonists for the Treatment of Diabetes and Obesity. *J. Med. Chem.* **2007**, *50*, 5202–5216.

12. (a) Gupta, P. K.; Yadav, N.; Jaiswal, S.; Asad, M.; Kant, R.; Hajela, K. Palladium-Catalyzed Synthesis of Phenanthridine/Benzoxazine-Fused Quinazolinones by Intramolecular C–H Bond Activation. *Chem. -Eur. J.* **2015**, *21*, 13210–13215. (b) Dabiri, M.; Lehi, N. F.; Movahed, S. K.; and Khavasi, H. R. Pd-Catalyzed regioselective C–H halogenation of quinazolinones and benzoxazinones. *Org. Biomol. Chem.* **2017**, *15*, 6264–6268. (c) Lingayya, R.; Vellakkaran, M.; Nagaiah, K.; Nanubolu, J. Rhodium(II)-Catalyzed Carbenoid Insertion of *N*-Tosylhydrazones into Amide N–H Bonds: An Efficient Approach to N^3-Benzyl/Alkyl-2-arylquinazolinones. *Adv. Synth. Catal.* **2016**, *358*, 81–89. (d) Lu, H.; Yang, Q.; Zhou, Y.; Guo, Y.; Deng, Z.; Ding, Q.; Peng, Y. Cross-coupling/annulations of quinazolones with alkynes for access to fused polycyclic heteroarenes under mild conditions. *Org. Biomol. Chem.* **2014**, *12*, 758–764. (e) Wei, L.-S.; He, G.-X.; Kong, X.-F.; Pan, C.-X.; Mo, D.-L.; Su, G.-F. Gold(III)-Catalyzed Selective Cyclization of Alkynyl Quinazolinone-Tethered Pyrroles: Synthesis of Fused Quinazolinone Scaffolds. *J. Org. Chem.* **2018**, *83*, 6719–6727.

13. (a) Yang, W.; Chen, J.; Huang, X.; Ding, J.; Liu, M.; Wu, H. Pd-Catalyzed Intramolecular Aerobic Oxidative C–H Amination of 2-Aryl-3-(arylamino)quinazolinones: Synthesis of Fluorescent Indazolo[3,2-*b*]quinazolinones.

Org. Lett. **2014**, *16*, 5418–5421. (b) Banerji, B.; Bera, S.; Chatterjee, S.; Killi, S. K.; Adhikary, S. Regioselective Synthesis of Quinazolinone-/Phenanthridine Fused Heteropolycycles by Pd-Catalyzed Direct Intramolecular Aerobic Oxidative C–H Amination from Aromatic Strained Amides. *Chem. -Eur. J.* **2016**, *22*, 3506–3512. (c) Banerjee, A.; Subramanian, P.; Kaliappan, K. P. Copper-Catalyzed Cascade Amination Route to *N*-Aryl Benzimidazoquinazolinones. *J. Org. Chem.* **2016**, *81*, 10424–10432. (d) Zhang, C.; Zhou, Y.; Deng, Z.; Chen, X.; Peng, Y. Rhodium-Catalyzed Regioselective Direct C–H Amidation of 2,4-Diarylquinazoline with Sulfonyl Azides: An Example of Steric Hindrance Regulated Mono- and Diamidation Selectivity. *Eur. J. Org. Chem.* **2015**, 1735–1744. (e) Feng, Y.; Li, Y.; Yu, Y.; Wang, L.; Cui, X. Iridium-catalysed direct sulfamidation of quinazolinones. *RSC Adv.* **2018**, *8*, 8450–8454.

14. (a) Yu, Y.; Yue, Y.; Wang, D.; Li, X.; Chen, C.; Peng, J. Modular Synthesis of Quinazolinone-Fused Phenanthridinones by a Palladium-Catalyzed Cascade C–H/N–H Arylation Process. *Synthesis* **2016**, *48*, 3941–3950. (b) Laclef, S.; Harari, M.; Godeau, J.; Schmitz-Afonso, I.; Bischoff, L.; Hoarau, C.; Levacher, V.; Fruit, C.; Besson, T. Ligand-Free Pd-Catalyzed and Copper-Assisted C–H Arylation of Quinazolin-4-ones with Aryl Iodides under Microwave Heating. *Org. Lett.* **2015**, *17*, 1700–1703. (c) Godeau, J.; Harari, M.; Laclef, S.; Deau, E.; Fruit, C.; Besson, T. Cu/Pd-Catalyzed C2–H Arylation of Quinazolin-4(3*H*)-ones with (Hetero)aryl Halides. *Eur. J. Org. Chem.* **2015**, 7705–7717. (d) Lee, J. B.; Kang, M. E.; Kim, J.; Lee, C. Y.; Kee, J.-M.; Myung, K.; Park, J.-U.; Hong, S. Y. Direct diversification of unmasked quinazolin-4(3*H*)-ones through orthogonal reactivity modulation. *Chem. Commun.* **2017**, *53*, 10394–10397. (e) Garad, D. N.; Viveki, A. B.; Mhaske, S. B. Pd-Catalyzed Regioselective Mono-Arylation: Quinazolinone as the Inherent Directing Group for C(sp^2)–H Activation. *J. Org. Chem.* **2017**, *82*, 6366–6372.

15. (a) Zheng, Y.; Song, W.-B.; Zhang, S.-W.; Xuan, L.-J. Ruthenium-catalyzed oxidative coupling of 2-aryl-4-quinazolinones with olefins: synthesis of pyrrolo[2,1-*b*]quinazolin-9(1*H*)-one motifs. *Org. Biomol. Chem.* **2015**, *13*, 6474–6478. (b) Viveki, A. B.; Mhaske, S. B. Ruthenium-Catalyzed Regioselective Alkenylation/Tandem Hydroamidative Cyclization of Unmasked Quinazolinones Using Terminal Alkynes. *J. Org. Chem.* **2018**, *83*, 8906–8913.

16. Jiang, X.; Yang, Q.; Yuan, J.; Deng, Z.; Mao, X.; Peng, Y.; Yu, C. Rhodium-catalyzed tandem C–H activation and aza-Michael addition of 2-arylquinazolin-4-ones with acrylates for the synthesis of pyrrolo[2,1-*b*]quinazolin-9(1*H*)-one derivatives. *Tetrahedron* **2016**, *72*, 1238–1243.

17. Reddy, B. V. S.; Narasimhulu, G.; Umadevi, N.; Yadav, J. S. Quinazolinone-Directed C–H Activation: A Novel Strategy for the Acetoxylation-Methoxylation of the Arenes. *Synlett* **2012**, *23*, 1364–1370.

18. (a) Li, L.; Brennessel, W. W.; Jones, W. D. C–H Activation of Phenyl Imines and 2-Phenylpyridines with $[Cp^*MCl_2]_2$ (M = Ir, Rh): Regioselectivity, Kinetics, and Mechanism. *Organometallics* **2009**, *28*, 3492–3500. (b) Li, L.; Brennessel, W. W.; Jones, W. D. An Efficient Low-Temperature Route to Polycyclic Isoquinoline Salt Synthesis via C–H Activation with $[Cp^*MCl_2]_2$ (M = Rh, Ir). *J. Am. Chem. Soc.* **2008**, *130*, 12414–12419.

19. Li, Y.; Xie, F.; Li, X. Formal Gold- and Rhodium-Catalyzed Regiodivergent C–H Alkynylation of 2-Pyridones. *J. Org. Chem.* **2016**, *81*, 715–722.

20. Finkbeiner, P.; Kloeckner, U.; Nachtsheim, B. J. OH-Directed Alkynylation of 2-Vinylphenols with Ethynyl Benziodoxolones: A Fast Access to Terminal 1,3-Enynes. *Angew. Chem., Int. Ed.* **2015**, *54*, 4949–4952.

21. (a) For the synthesis of starting materials see: supporting information. (b) Brand, J. P.; Chevalley, C.; Scopelliti, R.; Waser, J. Ethynyl Benziodoxolones for the Direct Alkynylation of Heterocycles: Structural Requirement, Improved Procedure for Pyrroles, and Insights into the Mechanism. *Chem. -Eur. J.* **2012**, *18*, 5655–5666. (c) Sun, J.; Tan, Q.; Yang, W.; Liu, B.; Xu, B. Copper-Catalyzed Aerobic Oxidative Annulation and Carbon-Carbon Bond Cleavage of Arylacetamides: Domino Synthesis of Fused Quinazolinones. *Adv. Synth. Catal.* **2014**, *356*, 388–394.

22. Rao, D. N.; Rasheed, S.; Das, P. Palladium/Silver Synergistic Catalysis in Direct Aerobic Carbonylation of C(sp2)–H Bonds Using DMF as a Carbon Source: Synthesis of Pyrido-Fused Quinazolinones and Phenanthridinones. *Org. Lett*. **2016**, *18*, 3142−3145.

23. Liu, J. -Q.; Ma, Y. -G.; Zhang, M. -M.; Wang, X. -S. Consecutive Sonogashira Coupling and Hydroamination Cyclization for the Synthesis of Isoindolo[1,2-

b]quinazolin-10(12*H*)-ones Catalyzed by CuI/L-Proline. *J. Org. Chem.* **2017**, *82*, 4918−4923.