Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c9ob01395d

Preparation of isoquinazolines *via* metal-free [4 + 2] cycloaddition of ynamides with nitriles†

Hao Wu,‡[a] Yu Liu,‡[a] Ming-xing He,[a] Hao Wen,[a] Wei Cao,[a] Ping Chen*[a] and Yu Tang *[a,b]

Received 20th June 2019,
Accepted 15th August 2019

DOI: 10.1039/c9ob01395d

rsc.li/obc

TfOH-mediated [4 + 2] cycloaddition of ynamides with nitriles to construct 1,2-dihydroquinazolines is realized by a direct reaction in moderate to excellent yields (up to 93%) in a stereospecific manner. A rapid and efficient strategy has been employed for the syntheses of alkyl-substituted 1,2-dihydroquinazoline derivatives, and it exhibits good functional group tolerance, has a short reaction time, shows excellent diastereoselectivity, and is a simple and high-yielding reaction.

Introduction

Quinazoline alkaloid is an important scaffold ubiquitously present in many natural products, agrochemicals and other pharmaceutically active ingredients.[1] Its diverse pharmacological activities such as anticancer, antifungal and anti-hypertensive activities have attracted extensive attention.[2] In particular, quinazolines represent a relevant class of derivatives that have been studied as potent pan-KIT mutant kinase inhibitors, transmembrane voltage-gated sodium channel $Na_v1.7$ inhibitors, and potent inhibitors lipid kinase phosphoinositide-3-kinases (PI3Ks) (Fig. 1).[3]

Because of the great demand for quinazolines and their derivatives, a multitude of synthetic methods have been developed.[4] Ynamides, owing to their special reactivity, are regarded as extremely prominent and versatile N-containing building blocks in numerous organic reactions.[5] The cycloaddition reaction of ynamides is the most widely used method for the construction of various heterocyclic compounds. Herein [4 + 2] cycloaddition of ynamides and nitriles has been extensively studied to prepare N-containing compounds.[6] The Maulide group reported TfOH-mediated regioselective formal [4 + 2] cycloaddition of ynamides and nitriles for the synthesis of isoquinoline products.[6e] The Skrydstrup group further developed [4 + 2] cycloaddition of ynamides with imines to form isoquinoline derivatives.[6f] Recently, considerable heterocyclic compounds have been synthesized by a catalytic [2 + 2 + 2] cycloaddition reaction between ynamides and nitriles.[7] Our group reported the syntheses of 4-aminopyrimidine and δ-carboline derivatives *via* TfOH-mediated [2 + 2 + 2] cycloaddition of ynamides and nitriles and a direct metal-free protocol for the synthesis of quinazolines from common *N*-alkyl-*N*′-arylamidine under photoredox conditions (Scheme 1).[8,4c] Herein, we report the syntheses of 1,2-dihydroquinazoline derivatives through TfOH-mediated regioselective [4 + 2] cycloadditions between various ynamides and nitriles.

Results and discussion

Our initial attempt to obtain 1,2-dihydroquinazoline **3a** involved using starting material **1a** (0.125 mmol), benzonitrile **2a** (0.125 mmol) and 4 Å MS in the presence of TfOH (0.125 mmol) in CH_2Cl_2 under N_2 at −40 °C. Delightfully, the expected product **3a** was obtained in a yield of 78% within 1 minute (Table 1, entry 1). Afterward, we examined different Brønsted acids such as HPF_6 and Tf_2NH and Lewis acids including $BF_3{\cdot}Et_2O$, $Fe(OTf)_3$, AgOTf and $Sc(OTf)_3$, but these acids were not able to improve the reaction (entries 2 and 4–7), even with a prolonged reaction time of more than 24 h. Notably, Tf_2NH could also facilitate this reaction affording the

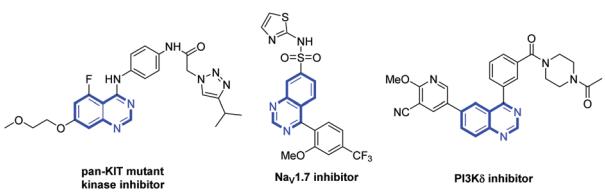
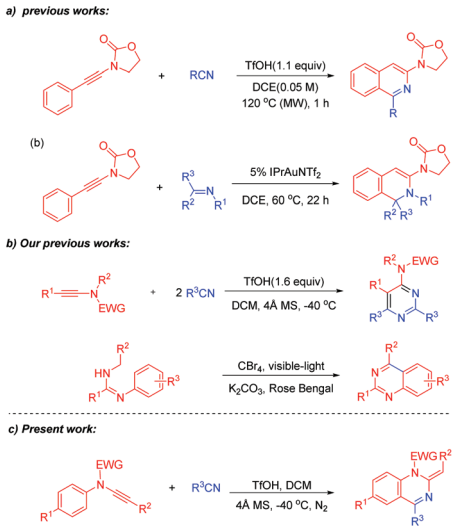


Fig. 1 Important quinazoline bioactive molecules.

[a]*Key Laboratory of Marine Drugs, Chinese Ministry of Education, School of Medicine and Pharmacy, Ocean University of China, Yushan Road, Qingdao, 266003, P. R. China. E-mail: tangyu@ouc.edu.cn, chenping8315@126.com*
[b]*Laboratory for Marine Drugs and Bioproducts Qingdao National Laboratory for Marine Science and Technology Qingdao, 266237, P. R. China*

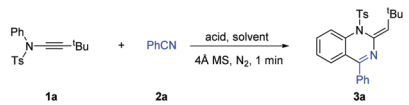
† Electronic supplementary information (ESI) available: Optimization of the reaction conditions and NMR spectra of the target compounds. CCDC 1904657. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c9ob01395d

‡ These authors contributed equally.



Scheme 1 Cycloadditions between ynamides and nitriles.

Table 1 Optimization studies[a,b,c]



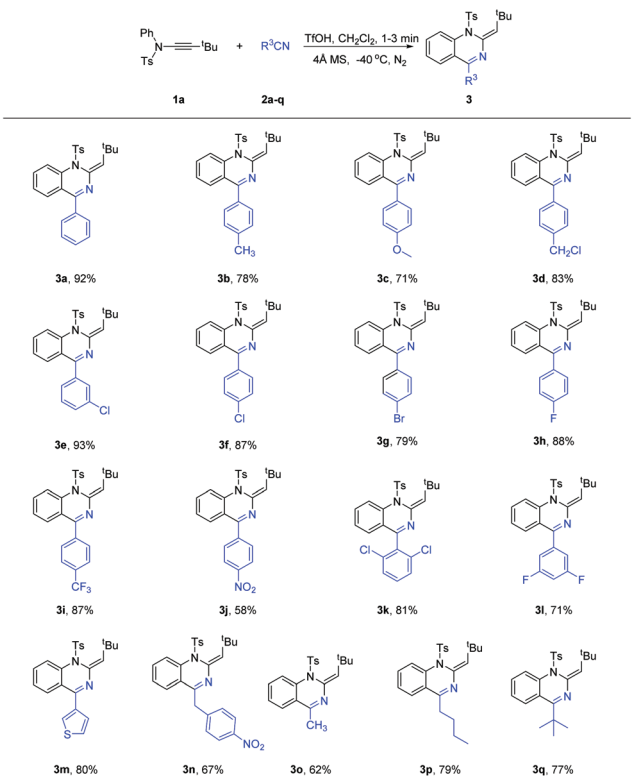
1a 2a 3a

Entry	Acid (eq.)	**1a** (eq.)	*T* (°C)	Solvent	Yield (%)
1	TfOH (1.0)	1.0	−40	CH_2Cl_2	78
2	$BF_3{\cdot}Et_2O$ (1.0)	1.0	−40	CH_2Cl_2	—
3	Tf_2NH (1.0)	1.0	−40	CH_2Cl_2	45
4[d]	HPF_6 (1.0)	1.0	−40	CH_2Cl_2	Trace
5[e]	$Fe(OTf)_3$ (1.0)	1.0	−40	CH_2Cl_2	—
6[e]	AgOTf (1.0)	1.0	−40	CH_2Cl_2	—
7[e]	$Sc(OTf)_3$ (1.0)	1.0	−40	CH_2Cl_2	—
8	TfOH (1.0)	1.0	r.t.	CH_2Cl_2	64
9	TfOH (1.0)	1.0	−40	DCE	71
10	TfOH (1.0)	1.0	−40	Toluene	72
11	TfOH (1.0)	1.0	−40	THF	Decomposed
12	TfOH (1.0)	1.0	−40	DMF	Trace
13	TfOH (1.5)	1.0	−40	CH_2Cl_2	76
14	TfOH (0.8)	0.8	−40	CH_2Cl_2	74
15	**TfOH (1.2)**	**1.2**	**−40**	**CH_2Cl_2**	**92**
16[f]	TfOH (1.2)	1.2	−40	CH_2Cl_2	89
17[g]	TfOH (1.2)	1.2	−40	CH_2Cl_2	87

[a] Unless noted otherwise, all reactions were conducted using ynamide **1a**, benzonitrile **2a** (0.125 mmol), 4 Å MS and acid in 2 mL of solvent under a N_2 atmosphere. [b] Isolated yield. [c] Time (within 1 min). [d] Time (0.5 h). [e] Time (over 24 h). [f] Under an air atmosphere. [g] CH_2Cl_2 (4 mL) was added.

product in 45% yield (entry 3). Furthermore, attempts to increase the reaction temperature to room temperature resulted in a lower yield (entry 8). The solvent effect was also examined. DCE and toluene exhibited less efficiency (entries 9 and 10), and there were no desired products obtained in other solvents, such as THF and DMF (entries 11 and 12). Interestingly, we found that the yield could not be improved by increasing the acid loading to 1.5 equivalents (entry 13). Moreover, the impact of ynamide **1a** loading and concentrations on the reaction was then investigated, and 1.2 equivalents of **1a** were identified as the optimal loading, which furnished **3a** in the highest yield (entries 14, 15 and 17). The yield of product **3a** was slightly reduced under an air atmosphere (entry 16).

Scheme 2 depicts nitriles **2a–q** which were compatible with our cycloaddition. To our delight, various functionalities on the aromatic rings were compatible, giving the corresponding products in good to excellent yields (**3a–3l**). For the 4-substituted benzonitriles **2b–d**, bearing electron-donating groups (for example, OMe, Me and CH_2Cl), the corresponding products **3b–d** were obtained in 78%, 71% and 83% yields, respectively. A group of halogen atoms, including fluorine, chloride, and bromide (**3e–3h**), were compatible to produce satisfactory outcomes, which provide valuable opportunities for further late-stage derivatizations. Electron-withdrawing groups were well tolerated to afford the expected products smoothly. Strong electron-withdrawing groups, such as trifluoromethyl and nitro groups, also gave good results (**3i** and **3j**). Additionally, disubstituted substrates were well-tolerated (**3k** and **3l**). For 3-thienylnitrile and 4-nitrophenylnitrile, the resulting products **3m** and **3n** were obtained in 80% and 67% yields. This method was also compatible with the aliphatic nitriles (**3o–3q**), thus yielding the desired isoquinazolines **3o**, **3p** and **3q**, respectively, in 62%–79% yields.

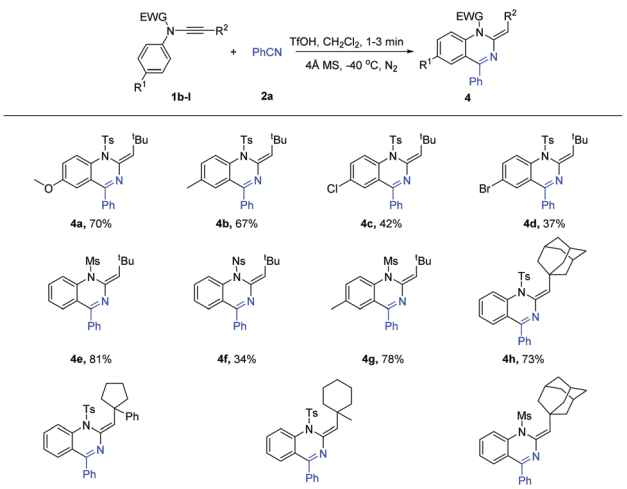


Scheme 2 Cycloaddition of ynamide **1a** with various nitriles. Unless noted otherwise, all reactions were carried out using ynamide **1a** (0.15 mmol), nitriles **2** (0.125 mmol), TfOH (0.15 mmol) and 4 Å MS in 2 mL of solvent under a N_2 atmosphere. Isolated yield.

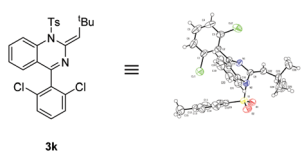
After exploring the scope of nitriles, the other reaction partner, the ynamides were then probed. The results are depicted in Scheme 3. Functional groups such as OMe, Me, Cl and Br presented good compatibility (**4a–4d**). For example, **4b** was generated from **1c** in 67% yield. Additionally, ynamide incorporating the electron-withdrawing sulfonyl group (*e.g.*, Ns) tended to decrease its reactivity (**4f**). Besides, the *tert*-butyl-like-substituted substrates **1i–1l** also undergo cycloaddition, producing the corresponding products **4h–4k** in good yields.

The structures of all [4 + 2] cyclization products **3** and **4** were determined by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HR MS. In addition, the absolute configuration of **3k** was confirmed by X-ray single-crystal analysis (Scheme 4).

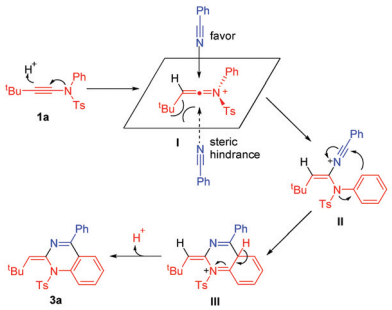
According to the above experimental results, a plausible mechanism is elucidated (Scheme 5).[6a,8,9] Ynamide **1a** was activated by TfOH to form keteniminium ion **I**. The benzonitrile attacked keteniminium ion **I** to obtain intermediate **II**, and subsequently **II** was cyclized by 6-*endo-dig* cyclization to obtain intermediate **III**. Finally, **3a** was formed through β-elimination. When the benzonitrile attacked intermediate **I**, the steric hindrance effect of the *tert*-butyl was detrimental to the subsurface attack of the benzonitrile, whereas the steric hindrance effect of the hydrogen atom was low, which was favorable for the attack of the benzonitrile from the surface (hydrogen atom side) to obtain the Z-type product **3a**.



Scheme 3 Cycloaddition of benzonitrile with ynamides. Unless noted otherwise, all reactions were carried out using ynamide **1a** (50 mg, 1.2 eq.), benzonitrile **2a** (1 eq.), TfOH (1.2 eq.) and 4 Å MS in 2 mL of solvent under a N_2 atmosphere. Isolated yield.



Scheme 4 X-ray single-crystal structure of **3k**.



Scheme 5 Proposed mechanism.

Conclusions

In summary, we have developed a direct approach for the preparation of isoquinazolines, by the treatment of ynamides and nitriles in the presence of TfOH. Accordingly a possible accompanying mechanism of the reaction is proposed. This strategy may show promise in the synthesis of useful pharmaceuticals and bioactive molecules. Additionally, this methodology is environmentally friendly and atom economical, because of using inexpensive and non-toxic TfOH instead of the metal-catalyzed pathway. We anticipate that the ynamides will continue to be explored and utilized.

Experimental section

General experimental method

Unless otherwise noted, all reactions were performed in flame-dried glassware under air. Solvents were distilled prior to use. Reagents were commercially available and used as purchased unless otherwise noted. Chromatographic separations were performed using a Kangbino 48–75 Å SiO_2. ^{1}H and ^{13}C NMR spectra were obtained on 400 MHz or 500 MHz spectrometers using $CDCl_3$ with TMS or a residual solvent as the standard unless otherwise noted. Melting points were determined using melting point apparatus and were uncorrected/calibrated. TLC analysis was performed using Kangbino glass-backed plates (60 Å, 250 μm) and visualized using UV and iodine stains. High-resolution mass spectra were obtained using a Thermo Fisher Exactive APCI-orbitrap spectrometer.

Substrate preparation

General procedure 1 for the syntheses of ynamides (1a–1h).[10a] To a flask were added $CuCl_2{\cdot}H_2O$ (20 mol%), benzenesulfonamide (5.0 eq.) and Na_2CO_3 (2.0 eq.). The reaction flask was purged with oxygen for 15 min. A solution of pyridine (2.0 eq.) in dry toluene (0.2 M) was added. A balloon filled with oxygen was connected to the flask and the flask was heated at 70 °C. After 15 min, a solution of 3,3-dimethylbut-1-yne (1.0 eq.) in dry toluene (0.2 M) was added over 4 h using a dropping funnel. Upon completion, the reaction mixture was cooled to room temperature and diluted with EtOAc and filtered through Celite, and the filtrate was concentrated in vacuum. The

residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate.

General procedure 2 for the syntheses of ynamides (1i–1l).[10a–d] Step 1: $LiAlH_4$ (2.0 eq.) was suspended in THF at 0 °C, and then the carboxylic acid (1.0 eq.) dissolved in THF was added dropwise within 15 minutes. The resulting suspension was refluxed overnight. The reaction mixture was quenched with water at 0 °C and treated with (5%) aq. HCl. The aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The product was used without further purification in the next step.

Step 2: Pyridinium chlorochromate (1.2 eq.) and moderate silica gel were combined and ground with a mortar and pestle until a fine, light-orange powder resulted. The powder was transferred into a flask and suspended in DCM, and then alcohol (1.0 eq.) was added *via* a syringe, and the resulting mixture was stirred overnight at room temperature. The mixture was filtered through Celite, and the filter pad was washed with DCM. The solvent was evaporated under the reduced pressure. The residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate.

Step 3: CBr_4 (2.0 eq.) and PPh_3 (4.0 eq.) were stirred at 0 °C in DCM, and then aldehyde (1.0 eq.) was added dropwise to the reaction mixture at 0 °C. The ice bath was removed, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was quenched with pentane and filtered through Celite, and then the organic layers were washed with sat. aq. NaCl and dried over $MgSO_4$ and the solvent was removed under reduced pressure. This product was used without further purification directly in the next reaction.

Step 4: To a stirred solution of dibromide (1.0 eq.) in DMSO was added Cs_2CO_3 (2.5 eq.). The reaction mixture was stirred for 12 h at 115 °C. Upon completion, the reaction mixture was cooled to room temperature and diluted with pentane and filtered through Celite and the layers were separated, and the organic layers were washed with sat. aq. NaCl and dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was used without further purification in the next step.

Step 5: To a flask were added $CuCl_2{\cdot}H_2O$ (20 mol%), sulfonamide (5.0 eq.) and Na_2CO_3 (2.0 eq.), and then the reaction flask was purged with oxygen for 15 min. A solution of pyridine (2.0 eq.) in dry toluene (0.2 M) was added. A balloon filled with oxygen was connected to the flask and the flask was heated at 70 °C. After 15 min, a solution of alkyne (1.0 eq.) in dry toluene (0.2 M) was added over 4 h using a dropping funnel. After this addition, the reaction mixture was allowed to cool to room temperature. Upon completion, the reaction mixture was cooled to room temperature and diluted with EtOAc and filtered through Celite, and the filtrate was concentrated in vacuum. The residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate.

*N-(3,3-Dimethylbut-1-yn-1-yl)-4-methyl-N-phenylbenzenesulfonamide (**1a**).* Following the general procedure 1; purified by using silica gel column chromatography (13.1 g, 71%); white solid; mp: 75–76 °C; R_f = 0.55 (PE/EA = 90 : 10); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 8.3 Hz, 2H), 7.34–7.23 (m, 7H), 2.44 (s, 3H), 1.24 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$)δ 144.6, 139.5, 132.7, 129.1, 128.8, 128.4, 127.7, 125.9, 78.5, 73.1, 31.0, 27.5, 21.7; HRMS (APCI–orbitrap) m/z: calcd for $C_{19}H_{22}NO_2S$ $[M + H]^+$ 328.1366, found 328.1363.

*N-(3,3-Dimethylbut-1-yn-1-yl)-N-phenylmethanesulfonamide (**1b**).* Following the general procedure 1; purified by using silica gel column chromatography (1.09 g, 34%); white solid; mp: 86–87 °C; R_f = 0.5 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.48 (m, 2H), 7.43–7.37 (m, 2H), 7.35–7.29 (m, 1H), 3.05 (s, 3H),1.28 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 139.3, 129.4, 128.0, 125.3, 79.2, 72.4, 35.8, 31.1, 27.7; HRMS (APCI–orbitrap) m/z: calcd for $C_{13}H_{18}NO_2S$ $[M + H]^+$ 252.1053, found 252.1054.

*N-(3,3-Dimethylbut-1-yn-1-yl)-4-nitro-N-phenylbenzenesulfon-amide (**1c**).* Following the general procedure 1; purified by using silica gel column chromatography (604 mg, 15%); pale yellow solid; mp: 144–146 °C; R_f = 0.55 (PE/EA = 95 : 5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 8.8 Hz, 2H), 7.83 (d, J = 8.8 Hz, 2H), 7.38–31 (m, 3H), 7.24–7.19 (m, 2H), 1.24 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.8, 140.9, 138.8, 129.6, 129.3, 128.6, 125.9, 123.9, 79.4, 72.2, 31.0, 27.6; HRMS (APCI–orbitrap) m/z: calcd for $C_{18}H_{19}N_2O_4S$ $[M + H]^+$ 359.1060, found 359.1060.

*N-(3,3-Dimethylbut-1-yn-1-yl)-4-methyl-N-(p-tolyl)benzenesul-fonamide (**1d**).* Following the general procedure 1; purified by using silica gel column chromatography (837 mg, 21%); white solid; mp: 90–91 °C; R_f = 0.5 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.53 (m, 2H), 7.28–7.24 (m, 2H), 7.10 (s, 4H), 2.44 (s, 3H), 2.34 (s, 3H), 1.22 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 144.6, 138.0, 137.0, 132.8, 129.6, 129.2, 128.5, 126.1, 78.1, 73.4, 31.1, 27.6, 21.8, 21.2; HRMS (APCI–orbitrap) m/z: calcd for $C_{20}H_{24}NO_2S$ $[M + H]^+$ 342.1522, found 342.1521.

*N-(3,3-Dimethylbut-1-yn-1-yl)-N-(p-tolyl)methanesulfonamide (**1e**).* Following the general procedure 1; purified by using silica gel column chromatography (1.12 g, 25%); white solid; mp: 78–79 °C; R_f = 0.45 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.34 (m, 2H), 7.22–7.18 (m, 2H), 3.03 (s, 3H), 2.36 (s, 3H), 1.27 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.2, 136.8, 130.0, 125.4, 78.7, 72.7, 35.6, 31.1, 27.7, 21.1; HRMS (APCI–orbitrap) m/z: calcd for $C_{14}H_{20}NO_2S$ $[M + H]^+$ 266.1209, found 266.1209.

*N-(3,3-Dimethylbut-1-yn-1-yl)-N-(4-methoxyphenyl)-4-methyl-benzenesulfonamide (**1f**).* Following the general procedure 1; purified by using silica gel column chromatography (1.93 g, 19%); white solid; mp: 96–97 °C; R_f = 0.45 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.52 (m, 2H), 7.29–7.25 (d, J = 7.9 Hz, 3H), 7.13–7.08 (m, 2H), 6.83–6.78 (m, 2H), 3.80 (s, 3H), 2.45 (s, 3H), 1.22 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.2, 144.6, 132.7, 132.3, 129.2, 128.6, 127.7, 114.1, 77.9, 73.6, 55.6, 31.1, 27.6, 21.8; HRMS (APCI–orbitrap) m/z: calcd for $C_{20}H_{24}NO_3S$ $[M + H]^+$ 358.1471, found 358.1471.

*N-(4-Chlorophenyl)-N-(3,3-dimethylbut-1-yn-1-yl)-4-methyl-benzenesulfonamide (**1g**).* Following the general procedure 1; puri-

fied by using silica gel column chromatography (1.64 g, 28%); white solid; mp: 98–99 °C; R_f = 0.6 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.52 (m, 2H), 7.30–7.25 (m, 4H), 7.20–7.16 (m, 2H), 2.44 (s, 3H), 1.23 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 145.0, 138.2, 133.6, 132.5, 129.4, 129.1, 128.5, 127.2, 79.1, 72.8, 31.1, 27.6, 21.8; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{19}H_{21}ClNO_2S$ $[M + H]^+$ 362.0976, found 362.0975.

*N-(4-Bromophenyl)-N-(3,3-dimethylbut-1-yn-1-yl)-4-methyl-benzenesulfonamide (**1h**).* Following the general procedure 1; purified by using silica gel column chromatography (2.07 g, 17%); white solid; mp: 112–114 °C; R_f = 0.55 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.52 (m, 2H), 7.45–7.40 (m, 2H), 7.30–7.25 (m, 2H), 7.14–7.10 (m, 2H), 2.44 (s, 3H),1.22 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 145.0, 138.7, 132.5, 132.1, 129.4, 128.5, 127.5, 121.6, 79.1, 72.7, 31.0, 27.6, 21.8; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{19}H_{21}BrNO_2S$ $[M + H]^+$ 406.0471, found 406.0472.

*N-(((1S,3S)-Adamantan-1-yl)ethynyl)-4-methyl-N-phenyl-benzenesulfonamide (**1i**).* Following the general procedure 2; purified by using silica gel column chromatography (1.15 g, 28%); white solid; mp: 110–112 °C; R_f = 0.4 (PE/EA = 95 : 5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.52 (m, 2H), 7.33–7.22 (m, 7H), 2.44 (s, 3H), 1.95 (s, 3H), 1.88–1.83 (m, 6H), 1.73–1.63 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 144.7, 139.6, 132.7, 129.3, 128.9, 128.5, 127.8, 126.0, 78.4, 73.5, 43.0, 36.4, 29.7, 28.1, 21.8; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{25}H_{28}NO_2S$ $[M + H]^+$ 406.1835, found 406.1834.

*N-(((1S,3S)-Adamantan-1-yl)ethynyl)-N-phenylmethanesulfon-amide (**1j**).* Following the general procedure 2; purified by using silica gel column chromatography (441 mg, 12%); white solid; mp: 111–112 °C; R_f = 0.35 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.48 (m, 2H), 7.42–7.37 (m, 2H), 7.34–7.29 (m, 1H), 3.05 (s, 3H), 1.97 (s, 3H), 1.94–189 (m, 6H), 1.74–1.65 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 139.3, 129.3, 127.9, 125.3, 79.1, 72.8, 43.0, 36.4, 35.7, 29.8, 28.1; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{19}H_{24}NO_2S$ $[M + H]^+$ 330.1522, found 330.1523.

*4-Methyl-N-phenyl-N-((1-phenylcyclopentyl)ethynyl)benzene-sulfonamide (**1k**).* Following the general procedure 2; purified by using silica gel column chromatography (829 mg, 34%); colorless oil; R_f = 0.45 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.44 (m, 4H), 7.32–7.15 (m, 10H), 2.40 (s, 3H), 2.23–2.14 (m, 2H), 2.04–1.75 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 145.4, 144.8, 139.5, 132.9, 129.4, 129.1, 128.4, 128.3, 128.0, 126.5, 126.4, 126.0, 76.6, 76.4, 47.5, 42.3, 24.4, 21.8; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{26}H_{26}NO_2S$ $[M + H]^+$ 416.1679, found 416.1679.

*4-Methyl-N-((1-methylcyclohexyl)ethynyl)-N-phenylbenzenesulfonamide (**1l**).* Following the general procedure 2; purified by using silica gel column chromatography (1.22 g, 20%); colorless oil; R_f = 0.6 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.52 (m, 2H), 7.34–7.22 (m, 7H), 2.43 (s, 3H), 1.73–1.50 (m, 7H), 1.23–1.07 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 144.7, 139.7, 132.9, 129.3, 129.0, 128.4, 127.8, 126.0, 76.7, 75.3, 39.6, 32.9, 30.5, 25.9, 23.5, 21.8; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{22}H_{26}NO_2S$ $[M + H]^+$ 368.1679, found 368.1680.

General procedure A for TfOH-mediated reaction of ynamide (1a) with various nitriles (2a–2q). To a suspension of ynamide (**1a**) (50.0 mg, 0.15 mmol, 1.2 eq.), nitriles (0.125 mmol, 1 eq.) and 4 Å MS in dry CH_2Cl_2 (2 mL), TfOH was added dropwise (13.5 μl, 0.15 mmol, 1.2 eq.) *via* a syringe pump at −40 °C under a nitrogen atmosphere. Then, the reaction was monitored by TLC. When the reaction appeared to be complete, saturated aq. $NaHCO_3$ was added to the mixture and the resulting mixture was extracted with DCM (2 × 10 ml). The organic layers were washed with sat. aq. NaCl and dried over Na_2SO_4. Filtration and concentration of the mixture *in vacuo* afforded the crude product that was purified by flash silica gel column chromatography (gradient eluent: EtOAc/petroleum ether) to obtain the corresponding products.

*(Z)-2-(2,2-Dimethylpropylidene)-4-phenyl-1-tosyl-1,2-dihydroquinazoline (**3a**).* Following the general procedure A; purified by using silica gel column chromatography (49.9 mg, 91%); white solid; mp: 118–119 °C; R_f = 0.4 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.6 Hz, 1H), 7.58–7.51 (m, 1H), 7.39–7.19 (m, 6H), 7.14–7.09 (m, 1H), 7.05–7.00 (m, 2H), 6.87 (d, J = 8.0 Hz, 2H), 5.99 (s, 1H), 2.18 (s, 3H), 1.36 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.0, 144.0, 142.4, 139.1, 135.6, 134.39, 134.37, 131.7, 129.8, 129.1, 129.0, 128.4, 127.9, 127.1, 126.8, 126.7, 126.3, 34.2, 30.4, 21.4; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{26}H_{27}N_2O_2S$ $[M + H]^+$ 431.1788, found 431.1788.

*(Z)-2-(2,2-Dimethylpropylidene)-4-(p-tolyl)-1-tosyl-1,2-dihydroquinazoline (**3b**).* Following the general procedure A; purified by using silica gel column chromatography (44.1 mg, 78%); white solid; mp: 123–124 °C; R_f = 0.4 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.9 Hz, 1H), 7.58–7.51 (m, 1H), 7.27–7.20 (m, 3H), 7.16–7.06 (m, 3H), 6.94 (d, J = 8.0 Hz, 2H), 6.88 (d, J = 8.0 Hz, 2H), 5.98 (s, 1H), 2.37 (s, 3H), 2.19 (s, 3H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.9, 143.9, 142.1, 139.9, 139.2, 134.4, 132.8, 131.6, 129.02, 128.99, 128.6, 128.5, 128.4, 127.2, 126.8, 126.6, 126.4, 34.2, 30.4, 21.5, 21.4; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{27}H_{29}N_2O_2S$ $[M + H]^+$ 445.1944, found 445.1942.

*(Z)-2-(2,2-Dimethylpropylidene)-4-(4-methoxyphenyl)-1-tosyl-1,2-dihydroquinazoline (**3c**).* Following the general procedure A; purified by using silica gel column chromatography (41.6 mg, 71%); white solid; mp: 145–147 °C; R_f = 0.25 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.0 Hz, 1H), 7.59–7.52 (m, 1H), 7.24 (d, J = 8.2 Hz, 3H), 7.18–7.13 (m, 1H), 7.03 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.0 Hz, 2H), 6.81 (d, J = 8.7 Hz, 2H), 5.96 (s, 1H), 3.84 (s, 3H), 2.19 (s, 3H), 1.36 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.9, 159.5, 143.8, 141.7, 139.2, 134.4, 131.6, 130.6, 129.0, 128.4, 128.1, 127.2, 126.8, 126.6, 126.5, 113.2, 55.5, 34.1, 30.4, 21.5; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{27}H_{29}N_2O_3S$ $[M + H]^+$ 461.1893, found 461.1888.

*(Z)-4-(4-(Chloromethyl)phenyl)-2-(2,2-dimethylpropylidene)-1-tosyl-1,2-dihydroquinazoline (**3d**).* Following the general procedure A; purified by using silica gel column chromatography (43.2 mg, 83%); white solid; mp: 142–143 °C; R_f = 0.4 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.0 Hz, 1H), 7.60–7.54 (t, J = 7.6 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.28–7.21 (m, 3H), 7.12 (d, J = 7.7 Hz, 1H), 7.06 (d, J = 8.0 Hz, 2H), 6.88

(d, J = 8.1 Hz, 2H), 6.00 (s, 1H), 4.60 (s, 2H), 2.19 (s, 3H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.3, 144.0, 142.8, 139.1, 139.0, 135.6, 134.4, 134.3, 131.8, 129.4, 129.1, 128.4, 128.1, 126.93, 126.91, 126.8, 126.1, 45.8, 34.2, 30.4, 21.5; HRMS (APCI–orbitrap) m/z: calcd for $C_{27}H_{28}ClN_2O_2S$ $[M + H]^+$ 479.1555, found 479.1551.

*(Z)-4-(3-Chlorophenyl)-2-(2,2-dimethylpropylidene)-1-tosyl-1,2-dihydroquinazoline (**3e**).* Following the general procedure A; purified by using silica gel column chromatography (55.0 mg, 93%); white solid; mp: 138–139 °C; R_f = 0.6 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.0 Hz, 1H), 7.61–7.51 (m, 1H), 7.35 (d, J = 7.9 Hz, 1H), 7.30–7.18 (m, 4H), 7.12–7.00 (m, 2H), 6.96–6.84 (m, 3H), 6.02 (s, 1H), 2.24 (s, 3H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.6, 144.3, 143.4, 139.1, 137.4, 134.3, 134.2, 133.8, 132.0, 129.8, 129.5, 129.1, 129.0, 128.4, 127.1, 127.0, 126.7, 125.9, 34.3, 30.3, 21.5; HRMS (APCI–orbitrap) m/z: calcd for $C_{26}H_{26}ClN_2O_2S$ $[M + H]^+$ 465.1398, found 465.1396.

*(Z)-4-(4-Chlorophenyl)-2-(2,2-dimethylpropylidene)-1-tosyl-1,2-dihydroquinazoline (**3f**).* Following the general procedure A; purified by using silica gel column chromatography (51.4 mg, 87%); white solid; mp: 143–144 °C; R_f = 0.4 (PE/EA = 90 : 10); ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, J = 8.1 Hz, 1H), 7.59–7.54 (m, 1H), 7.29–7.21 (m, 5H), 7.09 (d, J = 7.8 Hz, 1H), 7.00 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.1 Hz, 2H), 6.00 (s, 1H), 2.20 (s, 3H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 158.6, 143.8, 142.9, 139.1, 135.8, 134.4, 131.8, 130.2, 128.9, 128.4, 128.1, 126.9, 126.7, 126.6, 125.9, 34.1, 30.3, 21.4; HRMS (APCI–orbitrap) m/z: calcd for $C_{26}H_{26}ClN_2O_2S$ $[M + H]^+$ 465.1398, found 465.1396.

*(Z)-4-(4-Bromophenyl)-2-(2,2-dimethylpropylidene)-1-tosyl-1,2-dihydroquinazoline (**3g**).* Following the general procedure A; purified by using silica gel column chromatography (51.1 mg, 79%); white solid; mp: 148–149 °C; R_f = 0.55 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.0 Hz, 1H), 7.61–7.54 (m, 1H), 7.43 (d, J = 8.4 Hz, 2H), 7.29–7.20 (m, 4H), 7.11–7.06 (m, 1H), 6.96–6.87 (m, 4H), 6.00 (s, 1H), 2.21 (s, 3H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.8, 144.0, 143.1, 139.2, 134.5, 134.4, 134.2, 131.9, 131.1, 130.6, 129.0, 128.5, 127.0, 126.8, 125.9, 124.2, 34.3, 30.3, 21.5; HRMS (APCI–orbitrap) m/z: calcd for $C_{26}H_{26}BrN_2O_2S$ $[M + H]^+$ 509.0893, found 509.0892.

*(Z)-2-(2,2-Dimethylpropylidene)-4-(4-fluorophenyl)-1-tosyl-1,2-dihydroquinazoline (**3h**).* Following the general procedure A; purified by using silica gel column chromatography (50.2 mg, 88%); white solid; mp: 128–129 °C; R_f = 0.4 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 7.88–7.84 (m, 1H), 7.60–7.54 (m, 1H), 7.28–7.22 (m, 4H), 7.12–7.03 (m, 3H), 7.02–6.95 (m, 2H), 6.91–6.87 (m, 2H), 5.99 (s, 1H), 2.20 (s, 3H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.7 (d, J = 248.8 Hz), 158.9, 143.9, 142.6, 139.2, 134.4, 134.2, 131.9, 131.7 (d, J = 3.0 Hz), 131.0, 130.9, 129.0, 128.5, 126.9, 126.8 (d, J = 5.3 Hz), 126.1, 115.0 (d, J = 21.5 Hz), 34.2, 30.4, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ −110.53. HRMS (APCI–orbitrap) m/z: calcd for $C_{26}H_{26}FN_2O_2S$ $[M + H]^+$ 449.1694, found 449.1690.

*(Z)-2-(2,2-Dimethylpropylidene)-1-tosyl-4-(4-(trifluoromethyl)-phenyl)-1,2-dihydroquinazoline (**3i**).* Following the general procedure A; purified by using silica gel column chromatography (55.2 mg, 87%); white solid; mp: 123–124 °C; R_f = 0.4 (PE/EA = 90 : 10); ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 8.1 Hz, 1H), 7.61–7.54 (m, 3H), 7.29–7.23 (m, 3H), 7.18 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 7.8 Hz, 1H), 6.90 (d, J = 8.3 Hz, 2H), 6.05 (s, 1H), 2.19 (s, 3H), 1.38 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 158.4, 143.9, 143.6, 139.1, 138.9 (d, J = 1.1 Hz), 134.4, 134.1, 132.0, 131.5 (q, J = 32.4 Hz), 129.22, 129.0, 128.4, 127.0, 126.8, 126.4, 125.7, 124.8(q, J = 3.8 Hz), 123.9(d, J = 270.9 Hz), 34.2, 30.2, 21.3; ^{19}F NMR (470 MHz, $CDCl_3$) δ −62.80. HRMS (APCI–orbitrap) m/z: calcd for $C_{27}H_{26}F_3N_2O_2S$ $[M + H]^+$ 499.1662, found 499.1658.

*(Z)-2-(2,2-Dimethylpropylidene)-4-(4-nitrophenyl)-1-tosyl-1,2-dihydroquina zoline (**3j**).* Following the general procedure A; purified by using silica gel column chromatography (35.1 mg, 58%); pale yellow solid; mp: 151–152 °C; R_f = 0.45 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.7 Hz, 2H), 7.89 (d, J = 7.7 Hz, 1H), 7.65–7.59 (m, 1H), 7.31–7.21 (m, 5H), 7.04 (d, J = 7.7 Hz, 1H), 6.91 (d, J = 8.0 Hz, 2H), 6.09 (s, 1H), 2.22 (s, 3H), 1.38 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.7, 148.5, 144.7, 144.1, 141.6, 139.1, 134.4, 134.2, 132.3, 129.9, 129.1, 128.5, 127.2, 127.1, 126.2, 125.6, 123.2, 34.4, 30.3, 21.5; HRMS (APCI–orbitrap) m/z: calcd for $C_{26}H_{26}N_3O_4S$ $[M + H]^+$ 476.1639, found 476.1636.

*(Z)-4-(2,6-Dichlorophenyl)-2-(2,2-dimethylpropylidene)-1-tosyl-1,2-dihydroquina zoline (**3k**).* Following the general procedure A; purified by using silica gel column chromatography (51.4 mg, 81%); white solid; mp: 183–185 °C; R_f = 0.3 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.1 Hz, 1H), 7.57–7.51 (m, 1H), 7.41 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.0 Hz, 1H), 7.27–7.21 (m, 1H), 7.20–7.13 (m, 2H), 7.05 (d, J = 8.1 Hz, 2H), 6.70 (d, J = 7.7 Hz, 1H), 6.03 (s, 1H), 2.31 (s, 3H), 1.38 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.8, 144.2, 143.4, 138.1, 136.2, 135.9, 134.0, 133.8, 133.7, 132.2, 130.6, 129.8, 128.6, 128.5, 127.7, 126.7, 125.9, 125.4, 124.3, 34.4, 30.1, 21.5; HRMS (APCI–orbitrap) m/z: calcd for $C_{26}H_{25}Cl_2N_2O_2S$ $[M + H]^+$ 499.1008, found 499.1006.

*(Z)-4-(3,5-Difluorophenyl)-2-(2,2-dimethylpropylidene)-1-tosyl-1,2-dihydroquina zoline (**3l**).* Following the general procedure A; purified by using silica gel column chromatography (42.2 mg, 71%); white solid; mp: 171–172 °C; R_f = 0.45 (PE/EA = 90 : 10); ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 8.0 Hz, 1H), 7.62–7.57 (m, 1H), 7.31–7.25 (m, 1H), 7.22 (d, J = 8.2 Hz, 2H), 7.09 (d, J = 7.8 Hz, 1H), 6.93 (d, J = 8.3 Hz, 2H), 6.86–6.80 (m, 1H), 6.57–6.51 (m, 2H), 6.03 (s, 1H), 2.24 (s, 3H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 162.5 (d, J = 247.9 Hz), 162.4 (d, J = 247.9 Hz), 157.6 (t, J = 2.9 Hz), 144.3, 143.9, 139.0, 138.8 (t, J = 8.8 Hz), 134.2, 134.0, 132.1, 129.0, 128.4, 127.0, 126.9, 126.3, 125.6, 111.9 (d, J = 7.5 Hz), 111.7 (d, J = 7.5 Hz), 105.2, 104.9 (t, J = 25.3 Hz), 34.2, 30.2, 21.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ −109.26. HRMS (APCI–orbitrap) m/z: calcd for $C_{26}H_{25}F_2N_2O_2S$ $[M + H]^+$ 467.1599, found 467.1599.

*(Z)-2-(2,2-Dimethylpropylidene)-4-(thiophen-3-yl)-1-tosyl-1,2-dihydroquinazoline (**3m**).* Following the general procedure A; purified by using silica gel column chromatography (44.4 mg, 80%); colorless oil; R_f = 0.4 (PE/EA = 90 : 10); ^1H NMR

(400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.0 Hz, 1H), 7.61–7.54 (m, 1H), 7.36–7.28 (m, 2H), 7.28–7.23 (m, 2H), 7.20 (d, J = 8.2 Hz, 2H), 7.10 (s, 1H), 7.07–7.03 (m, 1H), 6.85 (d, J = 8.0 Hz, 2H), 5.96 (s, 1H), 2.17 (s, 3H), 1.36 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.2, 143.9, 142.2, 139.1, 137.6, 134.2, 134.1, 131.8, 128.9, 128.4, 128.0, 127.6, 126.9, 126.7, 126.6, 125.3, 34.2, 30.4, 21.5; HRMS (APCI–orbitrap) m/z: calcd for $C_{24}H_{25}N_2O_2S_2$ $[M + H]^+$ 437.1352, found 437.1356.

*(Z)-2-(2,2-Dimethylpropylidene)-4-(4-nitrobenzyl)-1-tosyl-1,2-dihydroquinazoline (**3n**).* Following the general procedure A; purified by using silica gel column chromatography (41.7 mg, 67%); pale yellow solid; mp: 137–138 °C; R_f = 0.25 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.5 Hz, 2H), 7.84 (d, J = 8.0 Hz, 1H), 7.57–7.51 (m, 1H), 7.29–7.16 (m, 4H), 7.10 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H), 5.85 (s, 1H), 3.74 (d, J = 16.0 Hz, 1H), 3.53 (d, J = 16.0 Hz, 1H), 2.37 (s, 3H), 1.33 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.7, 146.9, 144.2, 144.1, 142.2, 138.4, 135.0, 133.6, 132.2, 129.9, 129.1, 128.4, 127.1, 126.5, 125.6, 124.5, 123.7, 39.8, 34.1, 30.2, 21.7; HRMS (APCI–orbitrap) m/z: calcd for $C_{27}H_{28}N_3O_4S$ $[M + H]^+$ 490.1795, found 490.1793.

*(Z)-2-(2,2-Dimethylpropylidene)-4-methyl-1-tosyl-1,2-dihydroquinazoline (**3o**).* Following the general procedure A; purified by using silica gel column chromatography (29.1 mg, 62%); white solid; mp: 121–122 °C; R_f = 0.3 (PE/EA = 80 : 20); ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.0 Hz, 1H), 7.55–7.50 (m, 1H), 7.33–7.26 (m, 1H), 7.26–7.21 (m, 1H), 7.18 (d, J = 8.2 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 5.79 (s, 1H), 2.32 (s, 3H), 1.81 (s, 3H), 1.32 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.4, 143.9, 140.7, 138.0, 134.3, 134.2, 131.7, 128.8, 128.4, 127.1, 126.9, 126.5, 124.6, 33.9, 30.4, 21.6, 20.6; HRMS (APCI–orbitrap) m/z: calcd for $C_{21}H_{25}N_2O_2S$ $[M + H]^+$ 369.1631, found 369.1628.

*(Z)-4-Butyl-2-(2,2-dimethylpropylidene)-1-tosyl-1,2-dihydro-quinazoline (**3p**).* Following the general procedure A; purified by using silica gel column chromatography (37.1 mg, 71%); white solid; mp: 96–97 °C; R_f = 0.45 (PE/EA = 90 : 10); ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.0 Hz, 1H), 7.54–7.49 (m, 1H), 7.32–7.25 (m, 2H), 7.20 (d, J = 8.2 Hz, 2H), 7.02 (d, J = 8.2 Hz, 2H), 5.80 (s, 1H), 2.34–2.25 (m, 4H), 2.15–2.07 (m, 1H), 1.32 (s, 9H), 1.29–1.18 (m, 2H), 1.09–0.95 (m, 2H), 0.86 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 143.7, 140.3, 138.1, 134.9, 131.3, 128.9, 128.2, 126.8, 126.4, 126.2, 124.3, 33.8, 33.5, 30.3, 28.4, 22.8, 21.4, 14.0; HRMS (APCI–orbitrap) m/z: calcd for $C_{24}H_{31}N_2O_2S$ $[M + H]^+$ 411.2101, found 411.2099.

*(Z)-4-(tert-Butyl)-2-(2,2-dimethylpropylidene)-1-tosyl-1,2-di-hydroquinazoline (**3q**).* Following the general procedure A; purified by using silica gel column chromatography (40.2 mg, 77%); white solid; mp: 130–131 °C; R_f = 0.65 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 7.86–7.81 (m, 1H), 7.63–7.58 (m, 1H), 7.50–7.44 (m, 1H), 7.30–7.21 (m, 3H), 7.03 (d, J = 8.0 Hz, 2H), 5.74 (s, 1H), 2.29 (s, 3H), 1.32 (s, 9H), 0.97 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.4, 143.9, 139.1, 138.9, 135.5, 134.3, 130.5, 129.2, 128.4, 126.8, 126.2, 125.9, 125.3, 37.9, 33.8, 30.4, 29.2, 21.4; HRMS (APCI–orbitrap) m/z: calcd for $C_{24}H_{31}N_2O_2S$ $[M + H]^+$ 411.2101, found 411.2099.

General procedure B for TfOH-mediated reaction of ynamides (1b–1k) with benzonitrile. To a suspension of ynamide (50.0 mg, 1.2 eq.), benzonitrile (1.0 eq.) and 4 Å MS in dry CH_2Cl_2 (2 ml), TfOH was added dropwise (1.2 eq.) *via* a syringe pump at −40 °C under a nitrogen atmosphere. Then, the reaction was monitored by TLC. When the reaction appeared to be complete, saturated aq. $NaHCO_3$ was added to the mixture and the resulting mixture was extracted with DCM (2 × 10 ml). The organic layers were washed with sat. aq. NaCl and dried over Na_2SO_4. Filtration and concentration of the mixture *in vacuo* afforded the crude product that was purified by flash silica gel column chromatography (gradient eluent: EtOAc/petroleum ether) to obtain the corresponding products.

*(Z)-2-(2,2-Dimethylpropylidene)-6-methoxy-4-phenyl-1-tosyl-1,2-dihydroquinazoline (**4a**).* Following the general procedure B; purified by using silica gel column chromatography (37.6 mg, 70%); white solid; mp: 135–136 °C; R_f = 0.3 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.8 Hz, 1H), 7.40–7.34 (m, 1H), 7.28 (m, 4H), 7.10 (m, 1H), 7.05 (d, J = 7.2 Hz, 2H), 6.90 (d, J = 8.0 Hz, 2H), 6.62 (d, J = 2.7 Hz, 1H), 5.99 (s, 1H), 3.73 (s, 3H), 2.19 (s, 3H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.7, 157.9, 143.9, 142.4, 135.5, 134.6, 134.3, 132.0, 129.8, 129.1, 128.9, 128.5, 128.0, 127.9, 127.1, 117.2, 112.1, 55.7, 34.2, 30.4, 21.4; HRMS (APCI–orbitrap) m/z: calcd for $C_{27}H_{29}N_2O_3S$ $[M + H]^+$ 461.1893, found 461.1891.

*(Z)-2-(2,2-Dimethylpropylidene)-6-methyl-4-phenyl-1-tosyl-1,2-dihydroquinazoline (**4b**).* Following the general procedure B; purified by using silica gel column chromatography (36.3 mg, 67%); white solid; mp: 148–149 °C; R_f = 0.3 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.2 Hz, 1H), 7.40–7.34 (m, 2H), 7.33–7.23 (m, 4H), 7.06–7.02 (m, 2H), 6.93–6.87 (m, 3H), 5.97 (s, 1H), 2.30 (s, 3H), 2.19 (s, 3H), 1.36 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.0, 143.8, 142.2, 136.7, 135.7, 134.5, 134.5, 132.5, 129.7, 129.0, 129.0, 128.5, 127.9, 127.3, 126.6, 126.1, 34.2, 30.4, 21.4, 21.3; HRMS (APCI–orbitrap) m/z: calcd for $C_{27}H_{29}N_2O_2S$ $[M + H]^+$ 445.1944, found 445.1942.

*(Z)-6-Chloro-2-(2,2-dimethylpropylidene)-4-phenyl-1-tosyl-1,2-dihydroquinazoline (**4c**).* Following the general procedure B; purified by using silica gel column chromatography (22.5 mg, 42%); white solid; mp: 142–143 °C; R_f = 0.65 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.6 Hz, 1H), 7.54–7.48 (m, 1H), 7.42–7.36 (m, 1H), 7.34–7.23 (m, 4H), 7.25 (d, J = 7.9 Hz, 3H), 7.10 (d, J = 2.1 Hz, 1H), 7.01 (d, J = 7.2 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 6.01 (s, 1H), 2.19 (s, 3H), 1.35 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.7, 144.3, 143.4, 137.6, 135.0, 134.2, 134.0, 132.5, 131.7, 130.0, 129.2, 128.8, 128.4, 128.3, 128.1, 127.4, 126.8, 34.3, 30.3, 21.5; HRMS (APCI–orbitrap) m/z: calcd for $C_{26}H_{26}ClN_2O_2S$ $[M + H]^+$ 465.1398, found 465.1396.

*(Z)-6-Bromo-2-(2,2-dimethylpropylidene)-4-phenyl-1-tosyl-1,2-dihydroquinazoline (**4d**).* Following the general procedure B; purified by using silica gel column chromatography (19.3 mg, 37%); white solid; mp: 142–143 °C; R_f = 0.65 (PE/EA = 90 : 10); ^1H NMR (400 MHz, $CDCl_3$) δ 7.75–7.65 (m, 2H), 7.43–7.37 (m, 1H), 7.35–7.24 (m, 5H), 7.03 (d, J = 7.3 Hz, 2H), 6.93 (d, J = 8.0 Hz, 2H), 6.03 (s, 1H), 2.21 (s, 3H), 1.36 (s, 9H); $^{13}C\{^1H\}$

NMR (100 MHz, $CDCl_3$) δ 158.6, 144.3, 143.5, 138.2, 134.9, 134.7, 134.1, 133.8, 130.1, 129.8, 129.3, 128.9, 128.6, 128.4, 128.1, 127.7, 120.4, 34.3, 30.3, 21.5; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{26}H_{26}BrN_2O_2S$ $[M + H]^+$ 509.0893, found 509.0891.

*(Z)-2-(2,2-Dimethylpropylidene)-1-(methylsulfonyl)-4-phenyl-1,2-dihydroquinazoline (**4e**).* Following the general procedure B; purified by using silica gel column chromatography (47.6 mg, 81%); white solid; mp: 144–145 °C; R_f = 0.3 (PE/EA = 90 : 10); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75–7.70 (m, 3H), 7.59–7.54 (m, 1H), 7.52–7.46 (m, 4H), 7.37–7.33 (m, 1H), 6.01 (s, 1H), 2.64 (s, 3H), 1.30 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 160.4, 142.3, 139.4, 135.9, 133.6, 132.1, 130.3, 128.9, 128.6, 127.6, 127.0, 126.6, 125.3, 37.1, 34.1, 30.1; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{20}H_{23}N_2O_2S$ $[M + H]^+$ 355.1475, found 355.1476.

*(Z)-2-(2,2-Dimethylpropylidene)-1-((4-nitrophenyl)sulfonyl)-4-phenyl-1,2-dihydroquinazoline (**4f**).* Following the general procedure B; purified by using silica gel column chromatography (18.2 mg, 34%); white solid; mp: 154–156 °C; R_f = 0.45 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92–7.85 (m, 3H), 7.66–7.59 (m, 1H), 7.56 (d, *J* = 8.8 Hz, 2H), 7.40–7.30 (m, 2H), 7.29–7.20 (m, 3H), 7.05 (d, *J* = 7.3 Hz, 2H), 6.05 (s, 1H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.9, 150.2, 143.2, 143.0, 138.3, 134.87, 133.5, 132.2, 130.5, 129.7, 128.8, 128.6, 128.2, 127.4, 126.8, 126.0, 123.5, 34.3, 30.3; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{25}H_{24}N_3O_4S$ $[M + H]^+$ 462.1482, found 462.1480.

*(Z)-2-(2,2-Dimethylpropylidene)-6-methyl-1-(methylsulfonyl)-4-phenyl-1,2-dihydroquinazoline (**4g**).* Following the general procedure B; purified by using silica gel column chromatography (45.1 mg, 78%); white solid; mp: 136–137 °C; R_f = 0.25 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.70 (m, 2H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.53–7.47 (m, 3H), 7.40–7.35 (m, 1H), 7.26 (s, 1H), 5.99 (s, 1H), 2.63 (s, 3H), 2.36 (s, 3H), 1.29 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.6, 142.1, 137.2, 137.1, 136.1, 133.9, 133.0, 130.3, 129.0, 128.7, 127.9, 126.4, 125.2, 37.0, 34.2, 30.2, 21.3; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{21}H_{25}N_2O_2S$ $[M + H]^+$ 369.1631, found 369.1629.

*(Z)-2-((Adamantan-1-yl)-methylene)-4-phenyl-1-tosyl-1,2-dihydroquinazoline (**4h**).* Following the general procedure B; purified by using silica gel column chromatography (37.0 mg, 73%); white solid; mp: 141–143 °C; R_f = 0.5 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87–7.84 (m, 1H), 7.60–7.54 (m, 1H), 7.40–7.34 (m, 1H), 7.32–7.21 (m, 6H), 7.15–7.11 (m, 1H), 7.06–7.02 (m, 2H), 6.90–6.86 (m, 2H), 5.80 (s, 1H), 2.18 (s, 3H), 2.12 (d, *J* = 12.1 Hz, 3H), 2.08–2.03 (s, 3H), 1.94 (d, *J* = 12.2 Hz, 3H), 1.76 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.8, 143.9, 143.0, 139.2, 135.6, 134.4, 134.1, 131.7, 129.7, 129.1, 129.0, 128.4, 127.9, 127.1, 126.9, 126.7, 126.3, 42.0, 36.9, 36.5, 28.5, 21.4; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{32}H_{33}N_2O_2S$ $[M + H]^+$ 509.2257, found 509.2254.

*(Z)-4-Phenyl-2-((1-phenylcyclopentyl)methylene)-1-tosyl-1,2-dihydroquinazoline (**4i**).* Following the general procedure B; purified by using silica gel column chromatography (39.5 mg, 76%); white solid; mp: 143–145 °C; R_f = 0.3 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.41 (m, 2H), 7.38–7.33 (m, 2H), 7.30–7.21 (m, 6H), 7.15–7.08 (m, 3H), 7.03–6.95 (m, 4H), 6.81 (d, *J* = 8.0 Hz, 2H), 6.38 (s, 1H), 2.65–2.56 (m, 1H), 2.48–2.39 (m, 1H), 2.34–2.25 (m, 1H), 2.18–2.06 (m, 4H), 1.93–1.76 (m, 3H), 1.68–1.54 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 156.0, 146.7, 143.7, 141.6, 138.3, 135.5, 135.5, 134.5, 131.2, 129.8, 129.0, 128.9, 128.3, 127.9, 127.4, 126.7, 126.4, 126.0, 125.6, 52.8, 42.7, 37.9, 23.4, 23.2, 21.4; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{33}H_{31}N_2O_2S$ $[M + H]^+$ 519.2101, found 519.2098.

*(Z)-2-((1-Methylcyclohexyl)methylene)-4-phenyl-1-tosyl-1,2-dihydroquinazoline (**4j**).* Following the general procedure B; purified by using silica gel column chromatography (45.9 mg, 86%); colorless oil; R_f = 0.45 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84–7.81 (m, 1H), 7.58–7.53 (m, 1H), 7.40–7.35 (m, 1H), 7.33–7.22 (m, 6H), 7.15–7.11 (m, 1H), 7.07–7.02 (m, 2H), 6.91–6.86 (m, 2H), 5.95 (s, 1H), 2.37–2.25 (m, 1H), 2.20 (s, 3H), 1.82–1.74 (m, 1H), 1.58–1.46 (m, 4H), 1.43 (m, 7H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.7, 144.0, 141.8, 139.0, 135.5, 135.2, 134.3, 131.7, 129.8, 129.1, 129.0, 128.5, 127.9, 127.3, 127.1, 126.8, 126.3, 41.3, 37.6, 36.0, 27.5, 26.3, 23.1, 22.7, 21.5; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{29}H_{31}N_2O_2S$ $[M + H]^+$ 471.2101, found 471.2097.

*(Z)-2-((Adamantan-1-yl)methylene)-1-(methyl-sulfonyl)-4-phenyl-1,2-dihydroquinazoline (**4k**).* Following the general procedure B; purified by using silica gel column chromatography (39.1 mg, 74%); white solid; mp: 103–104 °C; R_f = 0.25 (PE/EA = 90 : 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75–7.70 (m, 3H), 7.60–7.54 (m, 1H), 7.52–7.45 (m, 4H), 7.38–7.32 (m, 1H), 5.81 (s, 1H), 2.63 (s, 3H), 2.08–1.98 (m, 6H), 1.85 (d, *J* = 11.9 Hz, 3H), 1.72 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.3, 142.9, 139.6, 136.0, 133.5, 132.2, 130.4, 129.0, 128.7, 127.6, 127.1, 126.7, 125.4, 41.8, 37.1, 36.8, 36.5, 28.5; HRMS (APCI–orbitrap) *m*/*z*: calcd for $C_{26}H_{29}N_2O_2S$ $[M + H]^+$ 433.1944, found 433.1941.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We thank the Key R&D Project of Shandong Province (2018GSF118022) and the National Natural Science Foundation of China (21772181, 21572154, 81803344), and the NSFC-Shandong Joint Fund for Marine Science Research Centers (U1606403) for financial support. The Fundamental Research Funds for the Central Universities (201612013) and Qingdao Scientific and Technological Innovation Center for Marine Biomedicine Development Grant (2017-CXZX01-1-1) are also gratefully acknowledged.

Notes and references

1 (*a*) M. Moloudizargari, P. Mikaili, S. Aghajanshakeri, M. H. Asghari and J. Shayegh, *Pharmacogn. Rev.*, 2013, 7, 199–212; (*b*) B. Avula, S. Begum, S. Ahmed,

M. I. Choudhary and I. A. Khan, *Pharmazie*, 2008, **63**, 20–22; (*c*) U. A. Kshirsagar, *Org. Biomol. Chem.*, 2015, **13**, 9336–9352; (*d*) F. Dumitrascu and M. M. Popa, *ARKIVOC*, 2014, **2014**, 428–452; (*e*) D. He, M.-L. Wang, S.-Y. Zhao, Y.-S. Shu, H.-L. Zeng, C. Xiao, C. Lu and Y.-Y. Liu, *Fitoterapia*, 2017, **119**, 136–149; (*f*) X.-F. Shang, S. L. Morris Natschke, Y.-Q. Liu, X. Guo, X.-S. Xu, M. Goto, J.-C. Li, G.-Z. Yang and K.-H. Lee, *Med. Res. Rev.*, 2018, **38**, 775–828; (*g*) X.-F. Shang, S. L. Morris Natschke, Y.-Q. Liu, X. Guo, X.-S. Xu, M. Goto, J.-C. Li, G.-Z. Yang and K.-H. Lee, *Med. Res. Rev.*, 2018, **38**, 1614–1660; (*h*) O. O. Ajani, D. V. Aderohunmu, E. N. Umeokoro and A. O. Olomieja, *Bangladesh J. Pharmacol.*, 2016, **11**, 716–733.

2 (*a*) D. Giardin, D. Martarelli, G. Sagratini, P. Angeli, D. Ballinari, U. Gulini, C. Melchiorre, E. Poggesi and P. Pompei, *J. Med. Chem.*, 2009, **52**, 4951–4954; (*b*) I. Khan, A. Ibrar, N. Abbas and A. Saeed, *Eur. J. Med. Chem.*, 2014, **76**, 193–244; (*c*) G. Grover and S. G. Kini, *Eur. J. Med. Chem.*, 2006, **41**, 256–262; (*d*) L. F. Kuyper, D. P. Baccanari, M. L. Jones, R. N. Hunter, R. L. Tansik, S. S. Joyner, C. M. Boytos, S. K. Rudolph, V. Knick, H. R. Wilson, J. M. Caddell, H. S. Friedman, J. C. W. Comley and J. N. Stables, *J. Med. Chem.*, 1996, **39**, 892–903; (*e*) K. S. Jain, J. B. Bariwal, M. K. Kathiravan, M. S. Phoujdar, R. S. Sahne, B. S. Chauhan, A. K. Shah and M. R. Yadav, *Bioorg. Med. Chem.*, 2008, **16**, 4759–4800.

3 (*a*) J. G. Kettle, R. Anjum, E. Barry, D. Bhavsar, C. Brown, S. Boyd, A. Campbell, K. Goldberg, M. Grondine, S. Guichard, C. J. Hardy, T. Hunt, R. D. O. Jones, X.-W. Li, O. Moleva, D. Ogg, R. C. Overman, M. J. Packer, S. Pearson, M. Schimpl, W. Shao, A. Smith, J. M. Smith, D. Stead, S. Stokes, M. Tucker and Y. Ye, *J. Med. Chem.*, 2018, **61**, 8797–8810; (*b*) M. M. Weiss, T. A. Dineen, I. E. Marx, S. Altmann, A. Boezio, H. Bregman, M. Chu-Moyer, E. F. DiMauro, E. F. Bojic, R. S. Foti, H. Gao, R. Graceffa, H. Gunaydin, A. Guzman-Perez, H.-B. Huang, L.-Y. Huang, M. Jarosh, T. Kornecook, C. R. Kreiman, J. Ligutti, D. S. La, M.-J. Lin, D. Liu, B. D. Moyer, H. N. Nguyen, E. A. Peterson, P. E. Rose, K. Taborn, B. D. Youngblood, V. Yu and R. T. Fremeau Jr., *J. Med. Chem.*, 2017, **60**, 5969–5989; (*c*) K. Hoegenauer, N. Soldermann, F. Stauffer, P. Furet, N. Graveleau, A. B. Smith, C. Hebach, G. J. Hollingworth, I. Lewis, S. Gutmann, G. Rummel, M. Knapp, R. M. Wolf, J. Blanz, R. Feifel, C. Burkhart and F. Zécri, *ACS Med. Chem. Lett.*, 2016, **7**, 762–767.

4 (*a*) I. Khan, S. Zaib, S. Batool, N. Abbas, Z. Ashraf, J. Iqbal and A. Saeed, *Bioorg. Med. Chem.*, 2016, **24**, 2361–2381; (*b*) P.-Y. Chung, Z.-X. Bian, H.-Y. Pun, D. Chan, A. S.-C. Chan, C.-H. Chui, J. C.-O. Tang and K.-H. Lam, *Future Med. Chem.*, 2015, **7**, 947–967; (*c*) Z. Zhang, M. Wang, C.-F. Zhang, Z.-X. Zhang, J.-M. Lu and F. Wang, *Chem. Commun.*, 2015, **51**, 9205–9207; (*d*) X.-Q. Yu, L.-Q. Gao, L.-N. Jia, Y. Yamamoto and M. Bao, *J. Org. Chem.*, 2018, **83**, 10352–10358; (*e*) Z.-C. Shen, P. Yang and Y. Tang, *J. Org. Chem.*, 2016, **81**, 309–317.

5 (*a*) X.-N. Wang, H.-S. Yeom, C.-F. Li, S.-Z. He, Z.-X. Ma, B. L. Kedrowski and R. P. Hsung, *Acc. Chem. Res.*, 2014, **47**, 560–578; (*b*) K. A. DeKorver, H. Li, A. G. Lohse, R. Hayashi, Z. Lu, Y. Zhang and R. P. Hsung, *Chem. Rev.*, 2010, **110**, 5064–5106; (*c*) G. Evano, A. Coste and K. Jouvin, *Angew. Chem., Int. Ed.*, 2010, **49**, 2840–2859; (*d*) R. H. Dodd and K. Cariou, *Chem. – Eur. J.*, 2018, **24**, 2297–2304; (*e*) F. Pan, C. Shu and L.-W. Ye, *Org. Biomol. Chem.*, 2016, **14**, 9456–9465; (*f*) Y. Minko, M. Pasco, L. Lercher, M. Botoshansky and I. Marek, *Nature*, 2012, **490**, 522–526.

6 (*a*) T.-J. Meng, R.-X. Chen, L.-T. Liu, T. Wang, X.-M. Liu and W.-X. Zhao, *Chin. J. Org. Chem.*, 2015, **35**, 2108–2113; (*b*) J. Xue, E.-H. Gao, X.-N. Wang and J.-B. Chang, *Org. Lett.*, 2018, **20**, 6055–6058; (*c*) N. D. Rode, A. Arcadi, A. D. Nicola, F. Marinelli and V. Michelet, *Org. Lett.*, 2018, **20**, 5103–5106; (*d*) H.-X. Liu, Y.-Y. Yang, J. Wu, X.-N. Wang and J.-B. Chang, *Chem. Commun.*, 2016, **52**, 6801–6804; (*e*) L.-G. Xie, S. Niyomchon, A. J. Mota, L. González and N. Maulide, *Nat. Commun.*, 2016, **7**, 10914–10922; (*f*) Z. Xin, S. Kramer, J. Overgaard and T. Skrydstrup, *Chem. – Eur. J.*, 2014, **20**, 7926–7930.

7 (*a*) J.-Y. Zhang, Q.-S. Zhang, B. Xia, J. Wu, X.-N. Wang and J.-B. Chang, *Org. Lett.*, 2016, **18**, 3390–3393; (*b*) S. N. Karad and R.-S. Liu, *Angew. Chem., Int. Ed.*, 2014, **53**, 9072–9076; (*c*) H. O. Kyung, G. K. Jin and K. P. Jin, *Org. Lett.*, 2017, **19**, 3994–3997; (*d*) D.-Y. Liu, Q. Nie and M.-Z. Cai, *Tetrahedron*, 2018, **74**, 3020–3029; (*e*) P. Garcia, S. Moulin, Y. Miclo, D. Leboeuf, V. Gandon, C. Aubert and M. Malacria, *Chem. – Eur. J.*, 2009, **15**, 2129–2139; (*f*) P. Garcia, Y. Evanno, P. George, M. Sevrin, G. Ricci, M. Malacria, C. Aubert and V. Gandon, *Org. Lett.*, 2011, **13**, 2030–2033; (*g*) Y. Wang, L.-J. Song, X.-H. Zhang and J.-W. Sun, *Angew. Chem., Int. Ed.*, 2016, **55**, 9704–9708; (*h*) H.-S. Liang, S.-W. Bi, Y.-X. Liu, Y.-N. Tang and C.-C. Liu, *Org. Biomol. Chem.*, 2016, **14**, 2637–2644; (*i*) G.-N. Wang, X. You, Y. Gan and Y.-H. Liu, *Org. Lett.*, 2017, **19**, 110–113.

8 (*a*) P. Chen, C.-X. Song, W.-S. Wang, X.-L. Yu and Y. Tang, *RSC Adv.*, 2016, **6**, 80055–80058; (*b*) W.-S. Wang, P. Chen and Y. Tang, *Tetrahedron*, 2017, **73**, 2731–2739; (*c*) H. Wen, W. Cao, Y. Liu, L. Wang, P. Chen and Y. Tang, *J. Org. Chem.*, 2018, **83**, 13308–13324.

9 (*a*) W. Cao, P. Chen, L. Wang, H. Wen, Yu. Liu, W.-S. Wang and Y. Tang, *Org. Lett.*, 2018, **20**, 4507–4511; (*b*) B. Peng, X.-L. Huang, L.-G. Xie and N. Maulide, *Angew. Chem., Int. Ed.*, 2014, **53**, 8718–8721.

10 (*a*) T. Hamada, X. Ye and S. S. Stahl, *J. Am. Chem. Soc.*, 2008, **130**, 833–835; (*b*) T. A. Dineen, K. Chen, A. C. Cheng, K. Derakhchan, O. Epstein, J. Esmay, D. Hickman, C. E. Kreiman, I. E. Marx, R. C. Wahl, P. H. Wen, M. M. Weiss, D. A. Whittington, S. Wood, R. T. Fremeau, R. D. White and V. F. Patel, *J. Med. Chem.*, 2014, **57**, 9811–9831; (*c*) K. Domino, C. Veryser, B. A. Wahlqvist, C. Gaardbo, K. T. Neumann, K. Daasbjerg, W. M. D. Borggraeve and T. Skrydstrup, *Angew. Chem., Int. Ed.*, 2018, **57**, 6858–6862; (*d*) M. Zhao, C.-X. Kuang, Q. Yang and X.-Z. Cheng, *Tetrahedron Lett.*, 2011, **52**, 992–994.