



Cite this: *RSC Adv.*, 2021, 11, 31152

Received 21st August 2021
Accepted 1st September 2021

DOI: 10.1039/d1ra06330h

rsc.li/rsc-advances

A simple and efficient copper-catalyzed three-component reaction to synthesize (Z)-1,2-dihydro-2-iminoquinolines†

Xiai Luo,^{abc} Yu Zhao,^a Susu Tao,^a Zhong-Tao Yang,^{ab} Hui Luo^{*abd}
and Weiguang Yang^{ID *abd}

An operationally simple synthesis of (Z)-1,2-dihydro-2-iminoquinolines that proceeds under mild conditions is achieved by copper-catalyzed reaction of 1-(2-aminophenyl)ethan-1-ones, sulfonyl azides and terminal ynones. In particular, the reaction goes through a base-free CuAAC/ring-opening process to obtain the Z-configured products due to hydrogen bonding.

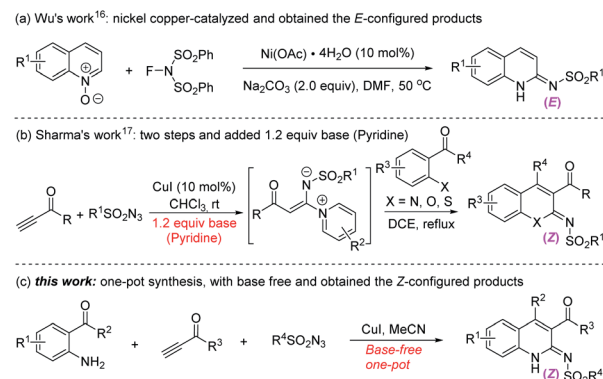
Nitrogen-containing polyheterocycles are present in a wide variety of bioactive natural products¹ and biological molecules that may be good drug candidates.² Specifically, quinoline-based compounds represent a medicinally and pharmaceutically important class of heterocyclic motifs that are found as the core structural skeletons in a variety of potential candidates.³ 2-Aminoquinolines are found to be antagonists for the hormone 1-receptor (MCH1-R),⁴ as targets for JNK phosphorylation,⁵ as potent and selective neuronal nitric oxide synthase inhibitors,⁶ and as new inhibitors of protein kinase CK2.⁷ Therefore, the development of novel methods for the synthesis of these quinoline derivatives is important in the field of synthetic organic and pharmaceutical chemistry.

In the past few years, utilizing the annulation reactions of Cu,⁸ Pd,⁹ Ni,¹⁰ Ag,¹¹ Ru,¹² and a few other catalysts^{13–15} have provided attractive and valuable routes for the construction of 2-aminoquinolines. As an isomer of 2-aminoquinolines, the synthesis of 2-iminoquinoline skeletons has still rarely been investigated. To the best of our knowledge, only two examples of the nickel¹⁶ or copper-catalyzed¹⁷ cascade reaction have been developed, leading to 2-iminoquinolines. However, these two examples have been limited to the use of a base or obtained the E-configured products (Scheme 1a and b).

Previous studies reported on the copper-catalyzed multi-component reactions (MCRs) of sulfonyl azides and terminal

alkynes with other components that generated N-heterocycles and related compounds (CuAAC/ring-opening reaction),^{18,19} and have also been used in the synthesis of 2-aminoquinolines²⁰ and 2-iminoquinolines.¹⁷ However, the reaction was generally carried out under strong basic conditions. This limited the application of some substrates, such as terminal ynones, which would undergo self-condensation under the basic conditions.²¹ Thus, neutral or weak acidic conditions have been developed in our previous study, and the terminal ynones were successfully used in the CuAAC/ring-opening reaction to form highly active intermediate α -acyl-N-sulfonyl ketenimines.²² Herein, we report the base-free copper-catalyzed reaction of 1-(2-aminophenyl)ethan-1-ones, sulfonyl azides and terminal alkynes, leading to Z-configured 2-iminoquinolines (Scheme 1c).

Our investigations began with an examination of the synthesis of the parent and previously unreported system, N-(3-acetyl-4-methylquinolin-2(1H)-ylidene)-4-methylbenzene sulfonamide (**4a**), from 1-(2-aminophenyl)ethan-1-one (**1a**), but-3-yn-2-one (**2a**) and p-tosyl azide (**3a**). Initial screenings involved using CuI as a catalyst in a range of standard solvents. These



Scheme 1 Synthesis of 2-iminoquinolines.

^aGuangdong Key Laboratory for Research and Development of Natural Drugs, The Marine Biomedical Research Institute, Guangdong Medical University, Zhanjiang, 524023, China. E-mail: luohui@gdmu.edu.cn; 09ywg@163.com

^bThe Marine Biomedical Research Institute of Guangdong Zhanjiang, Zhanjiang, Guangdong, 524023, China

^cDepartment of Pharmacy, Hunan University of Medicine, Huaihua, 418000, China

^dSouthern Marine Science and Engineering Guangdong Laboratory (Zhanjiang), Zhanjiang, Guangdong, 524023, China

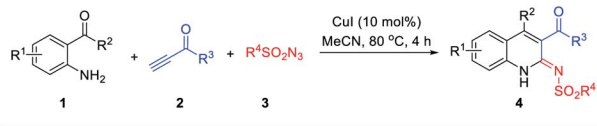
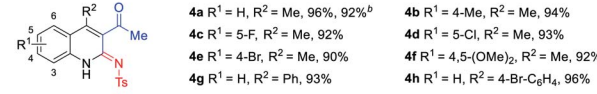
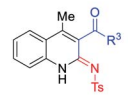
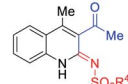
† Electronic supplementary information (ESI) available. CCDC 2092343, 2092351 and 2092350. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1ra06330h



screenings revealed that the desired conversion could be achieved in many solvents (Table 1, entries 1–9), with MeCN delivering product **4a** in highest yield (96%). The other solvents gave comparable yields, such as DCE, toluene, THF and 1,4-dioxane, while DMSO and DMF gave the lowest yield of **4a** at 20% and 46%, respectively. Thus, the optimal solvent was determined to be MeCN. Encouraged by this promising result, a variety of catalysts were screened. Among the copper catalysts used, most Cu-catalysts exhibited high catalytic reactivity in this reaction, whether it was Cu^I-catalysts or Cu^{II}-catalysts (Table 1, entries 10–14). Other catalysts, such as AgOAc, failed to produce the desired product (Table 1, entries 15). Lastly, the effect of temperature was evaluated. Screening results revealed that a reaction temperature above or below 80 °C decreased the reaction yield and produced side-products (Table 1, entries 16 and 17).

With optimized reaction conditions for the formation of the “parent reaction” having been defined, the capacity of these to affect the coupling of a range of different substrates was investigated. As shown in Table 2, the electron effects of the substituents R¹ had slight influences for the substrates **1**. For example, substrates bearing a 4-Me, 5-F, 4-Br and 4,5-(OMe)₂ group were examined, and 90–96% yields of **4a–4f** were isolated. The substrates R² bearing the –Ph and 4-Br–C₆H₄ group also can obtain **4g–4h** in good yield. Next, the scope and limitation of the substrate terminal ynones **2** were tested. When R³ was employed by the *n*-pentyl, isopropyl, –Ph, –OMe, –OEt and –O^t-Bu groups, it provided the corresponding iminoquinoline derivatives **4i–4n**

Table 2 Substrate scopes^a

			
1	2	3	4
			
4a R ¹ = H, R ² = Me, 96%, 92% ^b 4b R ¹ = 4-Me, R ² = Me, 94% 4c R ¹ = 5-F, R ² = Me, 92% 4d R ¹ = 5-Cl, R ² = Me, 93% 4e R ¹ = 4-Br, R ² = Me, 90% 4f R ¹ = 4,5-(OMe) ₂ , R ² = Me, 92% 4g R ¹ = H, R ² = Ph, 93% 4h R ¹ = H, R ² = 4-Br-C ₆ H ₄ , 96%			
			
4i R ³ = <i>n</i> -C ₅ H ₁₁ , 95% 4j R ³ = <i>i</i> -Pr, 94% 4k R ³ = Ph, 94% 4l R ³ = OMe, 92% 4m R ³ = OEt, 93% 4n R ³ = O ^t -Bu, 95%			
			
4o R ⁴ = Me, 96% 4p R ⁴ = Et, 93% 4q R ⁴ = <i>n</i> -Pr, 95% 4r R ⁴ = <i>n</i> -Bu, 92% 4s R ⁴ = Bn, 90% 4t R ⁴ = 4-Cl-C ₆ H ₄ , 95% 4u R ⁴ = 4-Br-C ₆ H ₄ , 95% 4v R ⁴ = 4-OMe-C ₆ H ₄ , 97%			

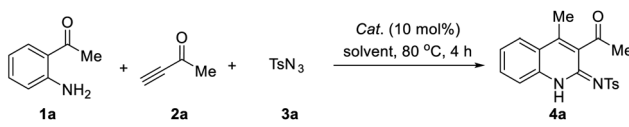
^a Unless otherwise noted, the reaction conditions were as follows: **1** (0.5 mmol), CuI (10 mol%) in the MeCN (3 mL) was added **2** (1.5 equiv.), **3** (1.5 equiv.) with stirring at 80 °C for 4 h. ^b Gram-scale synthesis of compound **4a**: magnify by 10 times.

in good yields of 92–95%. It is noteworthy that the substrate sulfonyl azides also showed slight influences for the reaction. The R⁴ changed for aliphatic or aromatic substituents also can smoothly give the anticipated products (**4o–4v**) in excellent yields. From the above experimental results, this reaction is easy to operate and highly efficient.

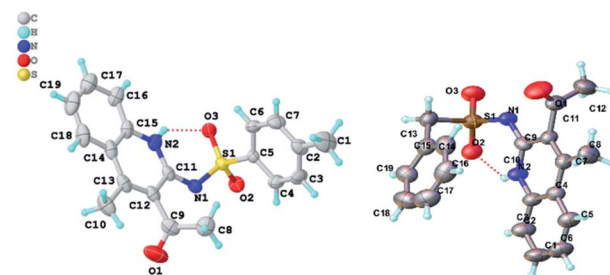
Except for **4m**, none of the products 1,2-dihydro-2-iminoquinolines **4a–4v** have been reported previously, which were subject to full spectroscopic characterization (see ESI for details[†]) and the derived data were in complete accordance with the assigned structures. Furthermore, **4a** and **4s** were confirmed by single-crystal X-ray analysis (Fig. 1). These analyses revealed that both incorporate Z-configured imine residues due to the hydrogen bonding (Fig. 1, the red dotted line). Thus, it has been assumed that all the other products formed during the course of this study possess the same geometry about the C=N bond.

In order to further explain the effect of hydrogen bonding on the spatial structure of products, we synthesized N1 substituted product **4w** through 1-(2-(methylamino)phenyl)ethan-1-one (**1i**), but-3-yn-2-one (**2a**) and *p*-tosyl azide (**3a**) under the standard

Table 1 Optimization of the catalytic conditions^a

			
Entry	Cat.	Solvent	Yield ^b (%) 4a
1	CuI	CHCl ₃	72
2	CuI	DCE	81
3	CuI	Toluene	79
4	CuI	MeCN	96
5	CuI	THF	85
6	CuI	1,4-Dioxane	94
7	CuI	DMSO	20
8	CuI	DMF	46
9	CuI	EtOH	40
10	CuCl	MeCN	88
11	CuBr	MeCN	84
12	CuBr ₂	MeCN	78
13	Cu(OAc) ₂	MeCN	80
14	Cu(OTf) ₂	MeCN	22
15	AgOAc	MeCN	nd ^c
16	CuI	MeCN	90 ^d
17	CuI	MeCN	86 ^e

^a Reaction conditions: **1a** (0.5 mmol), cat. (10 mol%) in the solvent (3 mL) was added **2a** (1.5 equiv.) and **3a** (1.5 equiv.) stirring at 80 °C for 4 h. ^b Isolated yields. ^c nd = not detected the target product. ^d The reaction temperature was 70 °C. ^e The temperature was 90 °C.

Fig. 1 Single-crystal X-ray analysis of **4a** (CCDC 2092343) and **4s** (CCDC 2092351).

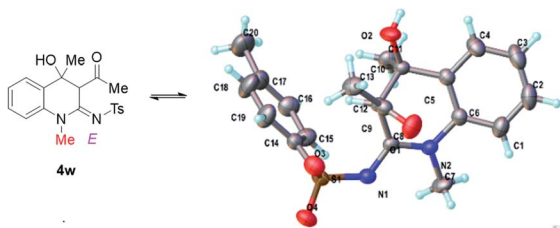
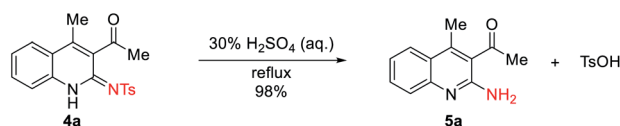


Fig. 2 Single-crystal X-ray analysis of **4w** (CCDC 2092350).



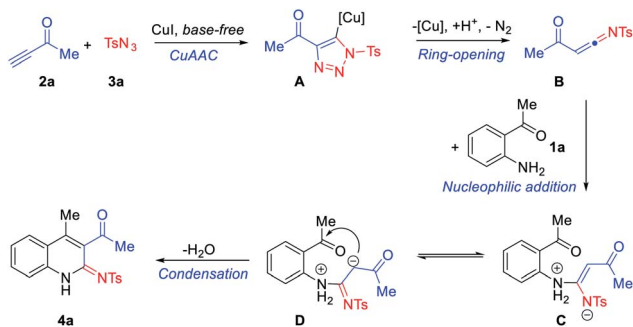
Scheme 2 Hydrolysis of 2-iminoquinolines.

condition. The single crystal analyses revealed that the product **4w** gave the *E*-configured imine residues without the hydrogen bonding (Fig. 2).

Products **4a–4v** are all relatively stable species that survive chromatographic purification under conventional conditions. However, the 2-iminoquinolines skeletons were easy hydrolysis to 2-aminoquinolines. For example, upon treatment with 1.5 equivalents of 30% H_2SO_4 in water under reflux for 6 h, compound **4a** is converted into 2-iminoquinolines product **5a** of yield 98% (Scheme 2).

A possible reaction pathway for the formation of *N*-(3-acetyl-4-methylquinolin-2(1*H*)-ylidene)-4-methylbenzenesulfonamide (**4a**) from precursors **1a**, **2a** and **3a** is shown in Scheme 3. Thus, in keeping with earlier proposals,²² substrates **2a** and **3a** are expected to react in the presence of the copper(i) catalyst, so as to form the metallated triazole **A** that fragments with the accompanying loss of nitrogen to form a highly active intermediate, α -acyl-*N*-sulfonyl ketenimine **B**. Then, **B** is captured by **1a** to generate the adduct **C**, which can transfer to the isomer **D** that undergoes aldol condensation to deliver the observed product **4a**.

In summary, we have developed an operationally simple and effective means for preparing (*Z*)-1,2-dihydro-2-iminoquinolines from a mixture of the corresponding 1-(2-aminophenyl)ethan-1-ones, sulfonyl azides and terminal ynones through the base-free



Scheme 3 Plausible reaction mechanism.

CuAAC/ring-opening process, and obtain the *Z*-configured products. This methodology is quite flexible and offers the capacity to generate forms of the title products that will be particularly useful in, for example, building more 2-iminoquinolines block facility.

Experimental

General

All melting points were determined on a Yanaco melting point apparatus and were uncorrected. IR spectra were recorded as KBr pellets on a Nicolet FT-IR 5DX spectrometer. All spectra of ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on a Bruker AVANCE NEO 400 MHz spectrometer in $\text{DMSO}-d_6$ or CDCl_3 (otherwise as indicated), with TMS used as an internal reference and the *J* values are given in Hz. HRMS were obtained on a Thermo Scientific Q Exactive Focus Orbitrap LC-MS/MS spectrometer. All 1-(2-aminophenyl)ethan-1-ones (**1a–1i**, see ESI Section 1†) were prepared by purchase, terminal ynones (**2a–2g**, see ESI Section 1†) were prepared by purchase or literature methods,²³ and sulfonyl azides (**3a–3i**, see ESI Section 1†) were prepared by literature methods.²⁴

Preparation and characterizations of compounds **4a–4w** and **5a**

(Z)-N-(3-Acetyl-4-methylquinolin-2(1*H*)-ylidene)-4-methylbenzenesulfonamide (4a**).** To a solution of 1-(2-aminophenyl)ethanone (**1a**, 67.6 mg, 0.5 mmol), CuI (9.5 mg, 0.05 mmol) in MeCN (1.5 mL) was added. Then, the mixture but-3-yn-2-one (**2a**, 51.0 mg, 0.75 mmol), TsN_3 (**3a**, 147.8 mg, 0.75 mmol) in MeCN (1.5 mL) was added. After the reaction was stirred at 80 °C for 4 h and cooled to room temperature, the solvent was removed by evaporating in vacuum. The residue was purified by flash chromatography [silica gel, 20% EtOAc in petroleum ether (60–90 °C)] to give 170 mg (96%) of product **4a** as a white solid, m.p. 195.5–196.8 °C. IR (KBr) ν 3462, 3267, 1705, 1615, 1592, 1366, 1138 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.93 (s, 1H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.40–7.36 (m, 2H), 7.23 (t, *J* = 8.0 Hz, 2H), 2.47 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 201.7, 150.5, 145.1, 142.5, 139.7, 134.8, 132.4, 131.9, 129.1 (2C), 125.7 (2C), 125.1, 124.8, 121.1, 117.0, 31.3, 21.2, 15.5; HRMS (ESI) *m/z* calcd for $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_3\text{S}^+$ [*M* + *H*] $^+$ 355.11108, found 355.11041.

The products **4b–4w** were prepared by the similar procedure.

(Z)-N-(3-Acetyl-4,7-dimethylquinolin-2(1*H*)-ylidene)-4-methylbenzenesulfonamide (4b**).** 173 mg (94%), white solid, m.p. 233.8–234.4 °C. IR (KBr) ν 3450, 3240, 1701, 1609, 1520, 1350, 1134 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.90 (s, 1H), 7.80 (d, *J* = 6.8 Hz, 2H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.26–7.17 (m, 4H), 2.47 (s, 6H), 2.40 (s, 3H), 2.36 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 202.1, 150.8, 145.3, 143.3, 142.5, 139.9, 135.2, 131.6, 129.3 (2C), 126.5, 125.9 (2C), 125.0, 119.2, 117.0, 31.5, 21.6, 21.4, 15.6; HRMS (ESI) *m/z* calcd for $\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}_3\text{S}^+$ [*M* + *H*] $^+$ 369.12674, found 369.12601.

(Z)-N-(3-Acetyl-6-fluoro-4-methylquinolin-2(1*H*)-ylidene)-4-methylbenzenesulfonamide (4c**).** 171 mg (92%), white solid,



m.p. 184.1–186.4 °C. IR (KBr) ν 3240, 3190, 1709, 1609, 1416, 1350, 1130, 1072 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 12.02 (s, 1H), 7.82 (d, J = 8.0 Hz, 2H), 7.45 (td, J = 9.2 Hz, 2.4 Hz, 2H), 7.38 (td, J = 8.8 Hz, 2.8 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 2.49 (s, 3H), 2.40 (s, 3H), 2.39 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 202.6, 159.2 (d, J = 244.6 Hz), 150.5, 144.1 (d, J = 3.6 Hz), 142.8, 139.6, 133.6, 131.7, 129.3 (2C), 125.9 (2C), 122.4 (d, J = 8.4 Hz), 120.4 (d, J = 24.7 Hz), 119.1, 110.5 (d, J = 23.6 Hz), 31.4, 21.4, 15.8; HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{18}\text{FN}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 373.10167, found 373.10077.

(Z)-N-(3-Acetyl-6-chloro-4-methylquinolin-2(1H)-ylidene)-4-methylbenzenesulfonamide (4d). 181 mg (93%), white solid, m.p. 204.2–205.9 °C. IR (KBr) ν 3466, 3198, 1709, 1617, 1589, 1531, 1350, 1134 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.90 (s, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 1.0 Hz, 1H), 7.47 (dd, J = 8.8 Hz, 1.0 Hz, 1H), 7.30 (d, J = 8.8 Hz, 1H), 7.16 (d, J = 8.4 Hz, 2H), 2.39 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 201.4, 150.5, 143.8, 142.8, 139.5, 133.6, 132.1, 130.4, 129.3 (2C), 125.9 (2C), 124.6, 122.3, 118.7, 31.3, 21.4, 15.7; HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{18}\text{ClN}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 389.07212, found 389.07147.

(Z)-N-(3-Acetyl-7-bromo-4-methylquinolin-2(1H)-ylidene)-4-methyl benzenesulfonamide (4e). 195 mg (90%), white solid, m.p. 261.2–263.7 °C. IR (KBr) ν 3401, 3252, 1618, 1524, 1346, 1138 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, $\text{DMSO}-d_6$) δ 11.94 (s, 1H), 8.42 (s, 1H), 7.88 (d, J = 8.8 Hz, 1H), 7.81 (d, J = 8.0 Hz, 2H), 7.62 (dd, J = 8.8 Hz, 1.6 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 2.35 (s, 6H), 2.31 (s, 3H), 2.31 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, $\text{DMSO}-d_6$) δ 202.3, 150.1, 145.2, 143.0, 140.4, 137.0, 133.1, 130.0 (2C), 128.3, 127.9, 126.3 (2C), 125.6, 121.4, 120.6, 31.6, 21.5, 15.9; HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{18}\text{BrN}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 433.02160, found 433.02118.

(Z)-N-(3-Acetyl-6,7-dimethoxy-4-methylquinolin-2(1H)-ylidene)-4-methylbenzenesulfonamide (4f). 191 mg (92%), white solid, m.p. 128.2–130.0 °C. IR (KBr) ν 3437, 3248, 1609, 1520, 1423, 1334, 1269 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 12.04 (s, 1H), 7.76 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.01 (s, 1H), 6.92 (s, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 2.41 (s, 3H), 2.35 (s, 3H), 2.29 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 202.3, 153.6, 149.9, 147.4, 144.8, 142.2, 140.2, 131.5, 129.9, 129.1 (2C), 125.6 (2C), 115.1, 104.6, 99.1, 56.4, 56.1, 31.5, 21.2, 15.9; HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_5\text{S}^+$ $[\text{M} + \text{H}]^+$ 415.13221, found 415.13144.

(Z)-N-(3-Acetyl-4-phenylquinolin-2(1H)-ylidene)-4-methylbenzenesulfonamide (4g). 194 mg (93%), white solid, m.p. 228.9–229.4 °C. IR (KBr) ν 3421, 3252, 1713, 1623, 1362, 1284, 1134 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 12.12 (s, 1H), 7.86 (d, J = 6.8 Hz, 2H), 7.63 (t, J = 8.0 Hz, 1H), 7.48–7.44 (m, 4H), 7.28–7.26 (m, 6H), 2.39 (s, 3H), 2.19 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 200.2, 150.8, 148.6, 142.8, 139.8, 135.6, 133.2, 132.1 (2C), 129.6, 129.3 (2C), 128.9 (2C), 128.6 (2C), 127.8, 126.4, 126.0, 124.8, 121.3, 116.9, 31.5, 21.5; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{21}\text{N}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 417.12674, found 417.12585.

(Z)-N-(3-Acetyl-4-(4-bromophenyl)quinolin-2(1H)-ylidene)-4-methyl benzenesulfonamide (4h). 238 mg (96%), white solid, m.p. 243.9–244.5 °C. IR (KBr) ν 3451, 3152, 1709, 1618, 1528, 1366, 1288, 1134 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.92 (s, 1H), 7.64 (d, J = 7.6 Hz, 2H), 7.45–7.40 (m, 3H), 7.25 (d, J =

8.0 Hz, 1H), 7.06 (d, J = 7.2 Hz, 4H), 6.96 (d, J = 8.0 Hz, 2H), 2.19 (s, 3H), 2.01 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 199.9, 150.6, 147.4, 142.8, 139.6, 135.6, 133.3, 132.3, 132.1, 131.9 (2C), 130.6 (2C), 129.3 (2C), 127.5, 126.0 (2C), 124.9, 123.8, 120.9, 117.0, 31.5, 21.4; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{20}\text{BrN}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 495.03725, found 495.03677.

(Z)-N-(3-Hexanoyl-4-methylquinolin-2(1H)-ylidene)-4-methylbenzene sulfonamide (4i). 194 mg (95%), white solid, m.p. 141.3–142.1 °C. IR (KBr) ν 3461, 3275, 1622, 1531, 1369, 1138, 1084 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.92 (s, 1H), 7.78 (t, J = 8.0 Hz, 3H), 7.60 (t, J = 7.6 Hz, 1H), 7.39–7.34 (m, 2H), 7.22 (d, J = 8.4 Hz, 2H), 2.70 (t, J = 7.2 Hz, 2H), 2.39 (s, 3H), 2.36 (s, 3H), 1.64–1.57 (m, 2H), 1.27–1.19 (m, 4H), 0.85 (t, J = 6.8 Hz, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 204.5, 150.8, 145.1, 142.6, 139.8, 135.0, 132.6, 131.9, 129.2 (2C), 125.9 (2C), 125.1, 124.8, 121.3, 117.2, 43.7, 31.1, 23.1, 22.4, 21.4, 15.7, 13.9; HRMS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{27}\text{N}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 411.17369, found 411.17322.

(Z)-N-(3-Isobutyryl-4-methylquinolin-2(1H)-ylidene)-4-methylbenzene sulfonamide (4j). 180 mg (94%), white solid, m.p. 155.9–156.7 °C. IR (KBr) ν 3263, 2970, 1701, 1624, 1531, 1369, 1281, 1138 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.93 (s, 1H), 7.79 (d, J = 8.0 Hz, 3H), 7.62 (t, J = 7.6 Hz, 1H), 7.38 (t, J = 8.4 Hz, 2H), 7.23 (d, J = 9.3 Hz, 2H), 2.40 (s, 3H), 2.37 (s, 3H), 1.12 (s, 3H), 1.10 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 208.5, 151.1, 145.9, 142.6, 139.8, 135.1, 132.2, 131.9, 129.3 (2C), 125.9 (2C), 125.2, 124.8, 121.4, 117.2, 41.1, 21.4, 17.9 (2C), 16.2; HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 383.14239, found 383.14163.

(Z)-N-(3-Benzoyl-4-methylquinolin-2(1H)-ylidene)-4-methylbenzene sulfonamide (4k). 196 mg (94%), white solid, m.p. 239.1–241.2 °C. IR (KBr) ν 3433, 3271, 1674, 1621, 1531, 1369, 1146 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.99 (s, 1H), 7.82–7.66 (m, 4H), 7.49–7.34 (m, 7H), 7.06 (s, 2H), 2.40 (s, 3H), 2.33 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 194.0, 151.4, 146.9, 142.2, 139.8, 136.5, 135.5, 133.6, 132.1, 130.6, 129.1 (2C), 129.0 (2C), 128.7 (2C), 125.8 (2C), 125.1, 124.9, 121.4, 117.3, 21.4, 16.1; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{21}\text{N}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 417.12674, found 417.12601.

Methyl (Z)-4-methyl-2-(tosylimino)-1,2-dihydroquinoline-3-carboxylate (4l). 170 mg (92%), white solid, m.p. 190.1–192.0 °C. IR (KBr) ν 3360, 2959, 1748, 1622, 1592, 1369, 1138 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.87 (s, 1H), 7.82 (d, J = 6.4 Hz, 2H), 7.73 (d, J = 8.0 Hz, 1H), 7.58 (t, J = 8.0 Hz, 1H), 7.36–7.29 (m, 2H), 7.21 (d, J = 8.0 Hz, 2H), 3.90 (s, 3H), 2.44 (s, 3H), 2.33 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 165.8, 150.7, 146.4, 142.4, 140.0, 135.0, 132.2, 129.1 (2C), 126.1, 125.8, 125.0, 124.9 (2C), 120.6, 117.1, 52.7, 21.3, 16.4; HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_4\text{S}^+$ $[\text{M} + \text{H}]^+$ 371.10600, found 371.10532.

Ethyl (Z)-4-methyl-2-(tosylimino)-1,2-dihydroquinoline-3-carboxylate (4m). 179 mg (93%), white solid, m.p. 144.5–146.4 °C (lit⁷ 146–147 °C). $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.84 (s, 1H), 7.78 (d, J = 7.6 Hz, 2H), 7.70 (d, J = 8.0 Hz, 1H), 7.53 (td, J = 8.0 Hz, 1.2 Hz, 1H), 7.32–7.26 (m, 2H), 7.15 (d, J = 8.4 Hz, 2H), 4.34–4.29 (m, 2H), 2.42 (s, 3H), 2.29 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 165.4, 150.7, 146.2, 142.5,



140.0, 135.2, 132.1, 129.1 (4C), 126.0, 125.1, 124.9, 120.9, 117.2, 61.9, 21.4, 16.4, 14.0.

Tert-butyl (Z)-4-methyl-2-(tosylimino)-1,2-dihydroquinoline-3-carboxylate (4n). 196 mg (95%), white solid, m.p. 134.8–136.6 °C. IR (KBr) ν 3460, 3283, 2978, 1732, 1624, 1582, 1285, 1146 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.80 (s, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.4 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.32–7.25 (m, 2H), 7.19–7.16 (m, 2H), 2.43 (s, 3H), 2.30 (s, 3H), 1.45 (s, 9H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 164.5, 150.9, 145.1, 142.4, 140.3, 135.2, 131.8, 129.1 (2C), 127.5, 126.0 (2C), 125.1, 124.7, 121.1, 117.1, 28.0 (3C), 21.4, 16.1; HRMS (ESI) m/z calcd for $\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}_4\text{S}^+$ $[\text{M} + \text{H}]^+$ 413.15295, found 413.15222.

(Z)-N-(3-Acetyl-4-methylquinolin-2(1H)-ylidene)methane sulfonamide (4o). 134 mg (96%), white solid, m.p. 151.1–153.0 °C. IR (KBr) ν 3256, 3210, 1705, 1628, 1601, 1531, 1366, 1096 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.65 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.54 (td, J = 8.0 Hz, 1.2 Hz, 1H), 7.32 (td, J = 8.0 Hz, 0.8 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 2.99 (s, 3H), 2.48 (s, 3H), 2.37 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 202.0, 150.7, 144.9, 134.9, 132.2, 131.8, 125.0, 124.7, 121.0, 117.1, 42.5, 31.3, 15.6; HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{15}\text{N}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 277.06524, found 277.06476.

(Z)-N-(3-Acetyl-4-methylquinolin-2(1H)-ylidene)ethane sulfonamide (4p). 136 mg (93%), white solid, m.p. 155.4–156.7 °C. IR (KBr) ν 3485, 3256, 1709, 1671, 1605, 1273, 1096 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.69 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.53 (td, J = 7.2 Hz, 0.4 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 7.24 (d, J = 8.4 Hz, 1H), 3.07–3.02 (m, 2H), 2.48 (s, 3H), 2.37 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 201.9, 151.3, 144.6, 134.9, 132.2, 131.8, 125.0, 124.6, 120.9, 117.0, 49.0, 31.3, 15.5, 8.11; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{17}\text{N}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 293.09543, found 293.09485.

(Z)-N-(3-Acetyl-4-methylquinolin-2(1H)-ylidene)propane-1-sulfonamide (4q). 146 mg (95%), white solid, m.p. 121.6–123.3 °C. IR (KBr) ν 3280, 3206, 1710, 1631, 1596, 1377, 1261 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.70 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 3.02–2.98 (m, 2H), 2.48 (s, 3H), 2.37 (s, 3H), 1.84–1.74 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 202.0, 151.1, 144.6, 134.9, 132.3, 131.8, 125.0, 124.6, 120.9, 117.0, 56.4, 31.3, 17.2, 15.5, 12.8; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_3\text{S}^-$ $[\text{M} - \text{H}]^-$ 305.09653, found 305.09616.

(Z)-N-(3-Acetyl-4-methylquinolin-2(1H)-ylidene)butane-1-sulfonamide (4r). 147 mg (92%), white solid, m.p. 95.4–96.8 °C. IR (KBr) ν 3183, 2959, 1709, 1638, 1531, 1366, 1088 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.70 (s, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 3.05–3.01 (m, 2H), 2.49 (s, 3H), 2.38 (s, 3H), 1.78–1.70 (m, 2H), 1.41–1.31 (m, 2H), 0.83 (t, J = 7.2 Hz, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 202.0, 151.2, 144.6, 135.0, 132.2, 131.8, 125.1, 124.6, 121.0, 117.1, 54.5, 31.4, 25.4, 21.3, 15.6, 13.4; HRMS (ESI) m/z calcd for $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 321.12674, found 321.12637.

(Z)-N-(3-Acetyl-4-methylquinolin-2(1H)-ylidene)-1-phenylmethane sulfonamide (4s). 159 mg (90%), white solid, m.p. 154.3–156.2 °C. IR (KBr) ν 3458, 3240, 1709, 1621, 1585, 1528, 1361, 1288 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.37 (s,

1H), 7.72 (d, J = 8.0 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.38 (d, J = 7.6 Hz, 2H), 7.32 (t, J = 7.6 Hz, 1H), 7.18 (t, J = 7.6 Hz, 2H), 7.06–7.03 (m, 2H), 4.13 (s, 2H), 2.51 (s, 3H), 2.40 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 202.0, 152.0, 144.7, 134.6, 132.1, 131.7, 130.9 (2C), 129.4, 128.2 (3C), 124.9, 124.7, 120.9, 116.9, 60.7, 31.5, 15.6; HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 355.11108, found 355.11072.

(Z)-N-(3-Acetyl-4-methylquinolin-2(1H)-ylidene)-4-chlorobenzene sulfonamide (4t). 178 mg (95%), white solid, m.p. 228.0–228.9 °C. IR (KBr) ν 3462, 3275, 1618, 1369, 1277, 1138, 1080 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.86 (s, 1H), 7.78 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 7.6 Hz, 1H), 7.57 (td, J = 7.6 Hz, 0.8 Hz, 1H), 7.36–7.31 (m, 4H), 2.41 (s, 3H), 2.37 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 201.8, 150.8, 145.6, 141.2, 138.2, 134.9, 132.5, 132.1, 128.9 (2C), 127.4 (2C), 125.2, 125.1, 121.4, 117.3, 31.5, 15.7; HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{16}\text{ClN}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 375.05647, found 375.05569.

(Z)-N-(3-Acetyl-4-methylquinolin-2(1H)-ylidene)-4-bromobenzene sulfonamide (4u). 199 mg (95%), white solid, m.p. 247.2–248.5 °C. IR (KBr) ν 3421, 3275, 1705, 1630, 1531, 1372, 1142 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.87 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.4 Hz, 2H), 7.58 (td, J = 4.0 Hz, 1.2 Hz, 1H), 7.50 (d, J = 8.4 Hz, 2H), 7.34 (t, J = 8.4 Hz, 2H), 2.41 (s, 3H), 2.38 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 201.8, 150.8, 145.6, 141.8, 135.0, 132.6, 132.2, 131.9 (2C), 127.5 (2C), 126.8, 125.2, 125.1, 121.4, 117.4, 31.5, 15.8; HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{16}\text{BrN}_2\text{O}_3\text{S}^+$ $[\text{M} + \text{H}]^+$ 419.00595, found 419.00549.

(Z)-N-(3-Acetyl-4-methylquinolin-2(1H)-ylidene)-4-methoxybenzenesulfonamide (4v). 180 mg (97%), white solid, m.p. 190.6–191.5 °C. IR (KBr) ν 3414, 3352, 1709, 1628, 1535, 1366, 1254, 1134 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 11.93 (s, 1H), 7.85 (d, J = 8.4 Hz, 2H), 7.79 (d, J = 8.0 Hz, 1H), 7.62 (td, J = 8.0 Hz, 0.8 Hz, 1H), 7.38 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 9.2 Hz, 2H), 3.81 (s, 3H), 2.47 (s, 3H), 2.42 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 202.0, 162.4, 150.6, 145.0, 135.1, 134.6, 132.7, 132.0, 128.0 (2C), 125.2, 124.8, 121.3, 117.2, 113.9 (2C), 55.5, 31.5, 15.7; HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_4\text{S}^+$ $[\text{M} + \text{H}]^+$ 371.10600, found 371.10535.

(E)-N-(3-Acetyl-4-hydroxy-1,4-dimethyl-3,4-dihydroquinolin-2(1H)-ylidene)-4-methylbenzenesulfonamide (4w). 145 mg (75%), white solid, m.p. 211.1–211.5 °C. IR (KBr) ν 3448, 2974, 1713, 1535, 1273, 1142, 1084 cm^{-1} ; $\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ 7.88 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 7.2 Hz, 1H), 7.32 (d, J = 7.6 Hz, 3H), 7.19 (t, J = 7.6 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 5.06 (s, 1H), 4.34 (s, 1H), 3.52 (s, 3H), 2.43 (s, 3H), 2.23 (s, 3H), 1.38 (s, 3H); $\{^{13}\text{C}\}$ NMR (100 MHz, CDCl_3) δ 205.1, 161.9, 143.0, 139.9, 136.5, 134.1, 129.4 (2C), 128.7, 126.6 (2C), 125.6, 124.1, 116.4, 71.5, 60.4, 33.6, 30.9, 28.1, 21.5; HRMS (ESI) m/z calcd for $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_4\text{S}^+$ $[\text{M} + \text{H}]^+$ 387.13730, found 387.13651.

1-(2-Amino-4-methylquinolin-3-yl)ethanone (5a). A solution of *N*-(3-acetyl-4-methylquinolin-2(1H)-ylidene)-4-methylbenzene sulfonamide (4a, 70.8 mg, 0.2 mmol) in 30% H_2SO_4 (3 mL) was refluxed for 6 h. Then, the pH of the mixture was adjusted to 9–10 with saturated K_2CO_3 after cooling to room temperature. The product was extracted with DCM, the aqueous layer was extracted with 3 \times 20 mL DCM, and the organic phases were combined and dried with anhydrous MgSO_4 . Then, the solvent



was removed by evaporating in vacuum. The residue was purified by flash chromatography [silica gel, 30% EtOAc in petroleum ether (60–90 °C)] to give 39 mg (98%) of product **5a** as a white solid, m.p. 154.0–154.5 °C. IR (KBr) ν 3448, 3125, 2924, 1690, 1663, 1601, 1420, 1223 cm⁻¹; ¹H} NMR (400 MHz, CDCl₃) δ 7.77 (d, J = 8.0 Hz, 1H), 7.58–7.50 (m, 2H), 7.24 (t, J = 7.2 Hz, 2H), 5.09 (s, 2H), 2.54 (s, 3H), 2.353 (s, 3H); ¹³C} NMR (100 MHz, CDCl₃) δ 206.3, 152.7, 147.2, 142.2, 130.7, 126.4, 124.0, 123.9, 123.3, 123.2, 32.6, 16.4; HRMS (ESI) m/z calcd for C₁₂H₁₃N₂O⁺ [M + H]⁺ 201.10224, found 201.10193.

All NMR spectra: please see ESI Section 3.†

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Financial support was provided by the Foundation and Applied Basic Research Fund project of Guangdong Province of China (2019A1515110918); Medical Scientific Research Foundation of Guangdong Province (A2021037 and A2020202); Discipline Construction Project of Guangdong Medical University (4SG21004G); Funds for PhD researchers of Guangdong Medical University in 2021; and the Science and technology program of Guangdong Province (2019B090905011).

Notes and references

- (a) L. Chen, Z. Deng and C. Zhao, *ACS Chem. Biol.*, 2021, **16**, 559; (b) G. E. Chambers, A. E. Sayan and R. C. D. Brown, *Nat. Prod. Rep.*, 2021, DOI: 10.1039/D0NP00096E; (c) S. Bhambhani, K. R. Kondhare and A. P. Giri, *Molecules*, 2021, **26**, 3374; (d) A. Wang, P. Li, P. Han, G. Gu, T. Shan, D. Lai and L. Zhou, *Nat. Prod. Res.*, 2021, **35**, 272; (e) M. A. Cinelli and A. D. Jones, *Molecules*, 2021, **26**, 2629; (f) S. Asamizu, *Biosci., Biotechnol., Biochem.*, 2017, **81**, 871; (g) A. K. Chattopadhyay and S. Hanessian, *Chem. Rev.*, 2017, **117**, 4104; (h) J. F. Hu, H. Fan, J. Xiong and S. B. Wu, *Chem. Rev.*, 2011, **111**, 5465; (i) A. Padwa, *Chem. Soc. Rev.*, 2009, **38**, 3072; (j) H. Fan, J. Peng, M. T. Hamann and J. F. Hu, *Chem. Rev.*, 2008, **108**, 264.
- (a) H. M. Hgel, N. H. de Silva, A. Siddiqui, E. Blanch and A. Lingham, *Bioorg. Med. Chem.*, 2021, **43**, 116270; (b) D. N. Huang, F. F. Wu, A. H. Zhang, H. Sun and X. J. Wang, *Pharmacol. Res.*, 2021, **169**, 105667; (c) M. Ghanbari-Movahed, T. Kaceli, A. Mondal, M. H. Farzaei and A. Bishayee, *Biomedicines*, 2021, **9**, 480; (d) F. S. Youssef and J. Simal-Gandara, *Biomedicines*, 2021, **9**, 485.
- (a) A. Martorana, G. La Monica and A. Lauria, *Molecules*, 2020, **25**, 4279; (b) X. Nqoro, N. Tobeka and B. A. Aderibigbe, *Molecules*, 2017, **22**, 2268; (c) S. Vandekerckhove and M. D'hooghe, *Bioorg. Med. Chem.*, 2015, **23**, 5098; (d) P. Wadhwa, P. Jain, S. Rudrawar and H. R. A. Jadhav, *Curr. Drug Discovery Technol.*, 2018, **15**, 2.
- R. J. DeVita, *Curr. Top. Med. Chem.*, 2007, **7**, 1433.
- M. Zhu, D. Gong and A. Mouse, *Med. Sci. Monit.*, 2020, **26**, e920989.
- M. A. Cinelli, H. Li, G. Chreifi, P. Martásek, L. J. Roman, T. L. Poulos and R. B. Silverman, *J. Med. Chem.*, 2014, **57**, 1513.
- A. R. Syniugin, O. V. Ostrynska, M. O. Chekanov, G. P. Volynets, S. A. Starosyla, V. G. Bdzhola and S. M. Yarmoluk, *J. Enzyme Inhib. Med. Chem.*, 2016, **31**, 160.
- (a) Z. Chen and D. Ma, *Org. Lett.*, 2019, **21**, 6874; (b) C. Wu, X. Qin, A. M. P. Moeljadi, H. Hirao and J. S. Zhou, *Angew. Chem., Int. Ed. Engl.*, 2019, **58**, 2705; (c) Y. Liang, H. Jiang, Z. Tan and M. Zhang, *Chem. Commun.*, 2018, **54**, 10096; (d) A. Behera, P. Sau, A. K. Sahoo and B. K. Patel, *J. Org. Chem.*, 2018, **83**, 11218.
- (a) T. N. Ansari, A. Taussat, A. H. Clark, M. Nachtegaal, S. Plummer, F. Gallou and S. Handa, *ACS Catal.*, 2019, **9**, 10389; (b) W. Wu, M. Li, J. Zheng, W. Hu, C. Li and H. Jiang, *Chem. Commun.*, 2018, **54**, 6855.
- (a) R. T. McGuire, A. A. Yadav and M. Stradiotto, *Angew. Chem., Int. Ed. Engl.*, 2021, **60**, 4080; (b) R. T. McGuire, C. M. Simon, A. A. Yadav, M. J. Ferguson and M. Stradiotto, *Angew. Chem., Int. Ed. Engl.*, 2020, **59**, 8952.
- (a) M. Li, S. Fang, J. Zheng, H. Jiang and W. Wu, *Org. Lett.*, 2019, **21**, 8439; (b) R. Yi, X. Li and B. Wan, *Adv. Synth. Catal.*, 2018, **360**, 875.
- (a) B. C. Roy, S. Debnath, K. Chakrabarti, B. Paul, M. Maji and S. Kundu, *Org. Chem. Front.*, 2018, **5**, 1008; (b) M. Maji, K. Chakrabarti, B. Paul, B. C. Roy and S. Kundu, *Adv. Synth. Catal.*, 2018, **360**, 722.
- C. Zhou, T. Lei, X. Z. Wei, C. Ye, Z. Liu, B. Chen, C. H. Tung and L. Z. Wu, *J. Am. Chem. Soc.*, 2020, **142**, 16805.
- K. Das, A. Mondal, D. Pal and D. Srimani, *Org. Lett.*, 2019, **21**, 3223.
- S. Shee, K. Ganguli, K. Jana and S. Kundu, *Chem. Commun.*, 2018, **54**, 6883.
- S. Han, X. Gao, Q. Wu, J. Li, D. Zou, Y. Wu and Y. Wu, *Org. Chem. Front.*, 2019, **6**, 830.
- N. P. Massaro, A. Chatterji and I. Sharma, *J. Org. Chem.*, 2019, **84**, 13676.
- (a) S. Bahadorikhalili, M. Divar, T. Damghani, F. Moeini, S. Ghassamipour, A. Iraj, M. A. Miller, B. Larijani and M. Mahdavi, *J. Organomet. Chem.*, 2021, **939**, 121773; (b) S. H. Kim, S. H. Park, J. H. Choi and S. Chang, *Chem.-Asian J.*, 2011, **6**, 2618; (c) I. Bae, H. Han and S. Chang, *J. Am. Chem. Soc.*, 2005, **127**, 2038; (d) S. H. Cho, E. J. Yoo, I. Bae and S. Chang, *J. Am. Chem. Soc.*, 2005, **127**, 16046.
- For examples of relevant recent work see: (a) Y. Zhao, Z. Zhou, L. Liu, M. Chen, W. Yang, Q. Chen, M. G. Gardiner and M. G. Banwell, *J. Org. Chem.*, 2021, **86**, 9155; (b) Y. Zhao, Z. Zhou, M. Chen and W. Yang, *Molecules*, 2021, **26**, 3700; (c) W. Yang, Y. Zhao, Z. Zhou, L. Li, L. Cui and H. Luo, *RSC Adv.*, 2021, **11**, 8701; (d) C.-G. Wang, R. Wu, T.-P. Li, T. Jia, Y. Li, D. Fang, X. Chen, Y. Gao, H.-L. Ni, P. Hu, B.-Q. Wang and P. Cao, *Org. Lett.*, 2020, **22**, 3234; (e) N. P. Massaro, A. Chatterji and I. Sharma, *J. Org. Chem.*, 2019, **84**, 13676; (f) L. Xu, T. Zhou, M. Liao, R. Hu and B. Z. Tang, *ACS Macro Lett.*,



- 2019, **8**, 101; (g) S. Guo, P. Dong, Y. Chen, X. Feng and X. Liu, *Angew. Chem., Int. Ed.*, 2018, **57**, 16852; (h) K. Kacprzak, I. Skiera, M. Piasecka and Z. Paryzek, *Chem. Rev.*, 2016, **116**, 5689.
- 20 B. Reichart, G. Guedes de la Cruz, K. Zangger, C. O. Kappe and T. Glasnov, *Adv. Synth. Catal.*, 2016, **358**, 50.
- 21 (a) C. Nájera, L. K. Sydnes and M. Yus, *Chem. Rev.*, 2019, **119**, 11110; (b) M. Nallagangula and K. Namitharan, *Org. Lett.*, 2017, **19**, 3536; (c) C. Shao, Q. Zhang and G. Cheng, *Eur. J. Org. Chem.*, 2013, 6443; (d) P. V. Ramachandran, M. T. Rudd and M. V. R. Reddy, *Tetrahedron Lett.*, 2005, **46**, 2547.
- 22 (a) Y. Zhao, L. Li, Z. Zhou, M. Chen, W. Yang and H. Luo, *Org. Biomol. Chem.*, 2021, **19**, 3868; (b) W. Yang, D. Huang, X. Zeng, J. Zhang, X. Wang and Y. Hu, *Tetrahedron*, 2019, **75**, 381; (c) W. Yang, D. Huang, X. Zeng, D. Luo, X. Wang and Y. Hu, *Chem. Commun.*, 2018, **54**, 8222.
- 23 D. Chernyak, S. B. Gadamsetty and V. Gevorgyan, *Org. Lett.*, 2008, **10**, 2307.
- 24 D. Das and R. Samanta, *Adv. Synth. Catal.*, 2018, **360**, 379.

