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A Molecular Oxygen-Promoted General and Site-Specific Alkylation with Organoboronic Acid

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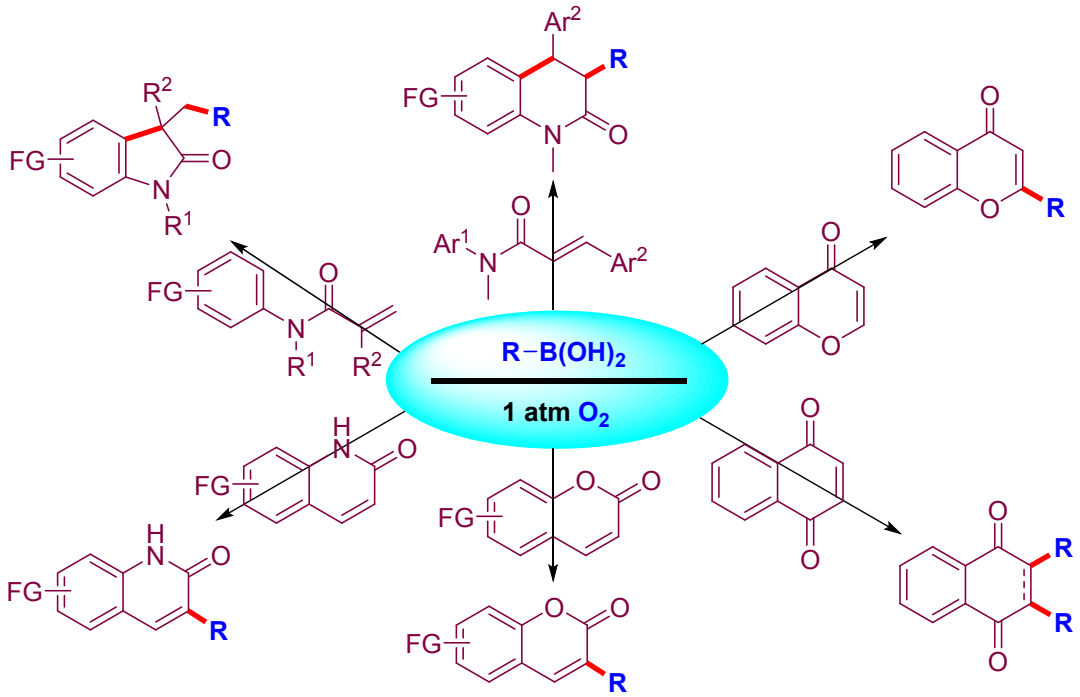


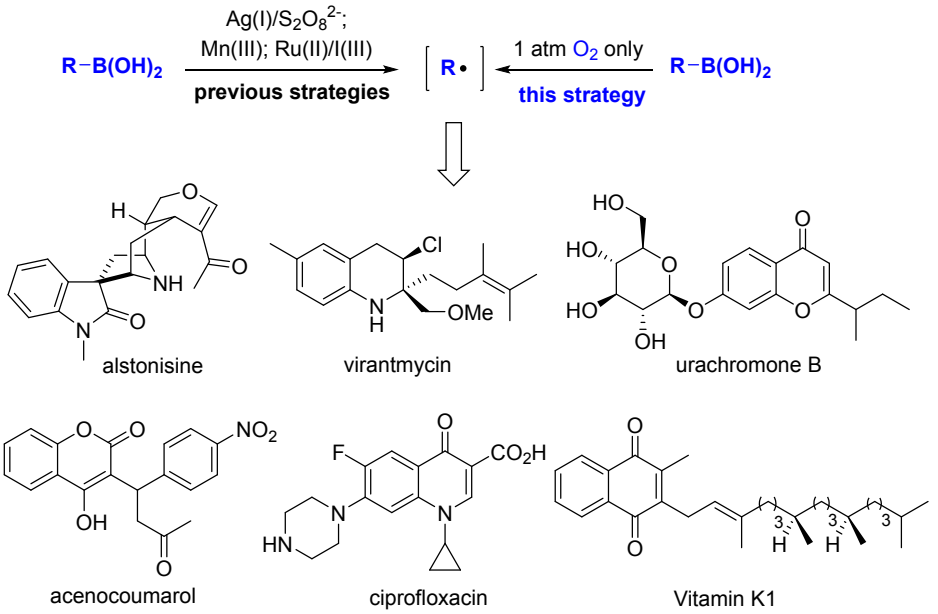
● 42 examples ● 43-90% yields ● metal-free ● chemical oxidant-free ● site-specific

Abstract: A general alkylating method using organoboronic acid under 1 atm. of oxygen is developed. It allows a facile access to a wide range of functionalized molecules with privileged scaffolds in drugs and natural products such as oxindoles, quinolinones, chromones, naphthoquinones, coumarins, and quinolones. In contrast to previous alkylation approaches that generally requiring transition-metal catalysis and stoichiometric chemical oxidant, the present strategy features metal-free, molecular oxygen as the terminal oxidant and site-specificity.

INTRODUCTION

Combustion of triethylborane could produce a beautiful green flame, which was considered as the first report on reaction of organoborane with molecular oxygen by

Frankland in 1860.[1] Studies on free radical chemistry of organoborane sprang up till one century later. Since then authoxidation of trialkylborane has become one of the most important initiating system for free radical reactions.[2] As carbon-centered radical precursors, trialkylboranes[3] and organotrifluoroborates[4] have been widely utilized to form C-C bonds. In contrast, more stable organoboronic acids are rarely used as a radical source. The reaction of molecular oxygen with boronic acid was firstly reported by Davies and Roberts in 1966.[5] They found that optically pure 1-phenylethylboronic acid was oxidized to racemic peroxides by oxygen. And then they suggested the autoxidation of organoborane would undergo a radical-chain process. Fifty-four years later, a facile Ag(I)/$S_2O_8^{2-}$-mediated Minisci-type C-C formation by using R(Ar)-$B(OH)_2$ was demonstrated by Baran and co-workers.[6] Subsequently, Chatani[7] and Rodríguez[8] achieved convenient alkylation of isonitrile and arene with alkylboronic acid by stoichiometric Mn(III), respectively. In 2013, an efficient (sp^3)C-H arylation with arylboronic acid by Ni(II)/DTBP was developed by Lei.[9] Two years later, Antonchick and Bering found that hot DMSO could enable aryl boronic acid to realize arylation of quinoline *N*-oxide.[10] Recently, an effective Ru(II)/hypervalent iodine-triggered photoredox alkylation of heterocycle using alkylboronic acids was explored by Chen.[11] Very recently, we realized a first O_2-promoted heteroaromatic C-H alkylation by using boronic acids.[12] Herein, we wish to report a molecular oxygen-mediated radical alkylation and/or alkylarylation of activated alkenes with organoboronic acids (Scheme 1). It could allow a general, metal-free and stoichiometric chemical oxidant-free access to structurally diverse heterocycles such as alkylated oxindoles,[13] 3,4-dihydroquinolin-2(1*H*)-ones,[14] chromones, coumarins, quinolones, and naphthoquinones.[15] These molecules are well-known as biologically active compounds with privileged scaffolds for library design and drug discovery (Scheme 1).[16] To the best of our knowledge, this work represents the first applicable alkylation and/or alkylarylation of alkenes by using organoboronic acids and O_2.



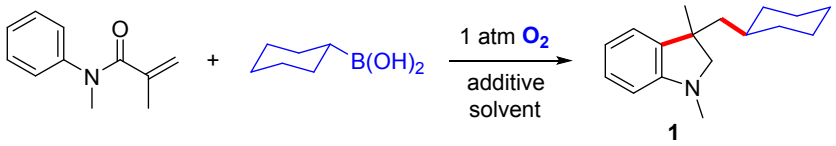
Scheme 1. Alkyl Radical Generation Using Alkylboronic Acid as Precursor and Relevant Biologically Active Molecules.

RESULTS AND DISCUSSION

Molecular oxygen based oxidation[17] and transformations[18] represent the most clean and sustainable processes. As our continuous endeavors for developing highly efficient radical synthetic methods,[19] we found that reaction of alkylboronic acid with O_2 could afford alkyl radical by heating.[12] Then we began to envision whether it could realize a general C-C bond formating method. In order to test this hypothesis, radical addition/cyclization cascade reaction of *N*-arylacrylamide with $RB(OH)_2$ was initially carried out to optimize the reaction conditions (Table 1). We found that additive, solvent and temperature are important to this system. Firstly, a series of solvents were screened (entries 1-7). To our delight, the desired product **1** was isolated in an excellent yield in a mixed solvent (entry 7). Next, we evaluated the effect of the acid additive (entries 10-12). The products were obtained in 50% yield without TFA and 47% yield without any acids. The yield increased to 62% by addition of 1 equivalent of TFA. The results indicate that acids could promote this process. Subsequently, we examined the effect of temperature for this transformation (entries 13 and 14). As a result, the reactions under 80°C and 100°C gave the corresponding products in 47% and 65% yields, respectively. Finally, we observed that a decreased yield of **1** was obtained by decreasing the amount of boronic acid (entry 15). No reaction occurred

under nitrogen atmosphere (entry 16).

Table 1. Optimization of the Reaction Conditions[a]



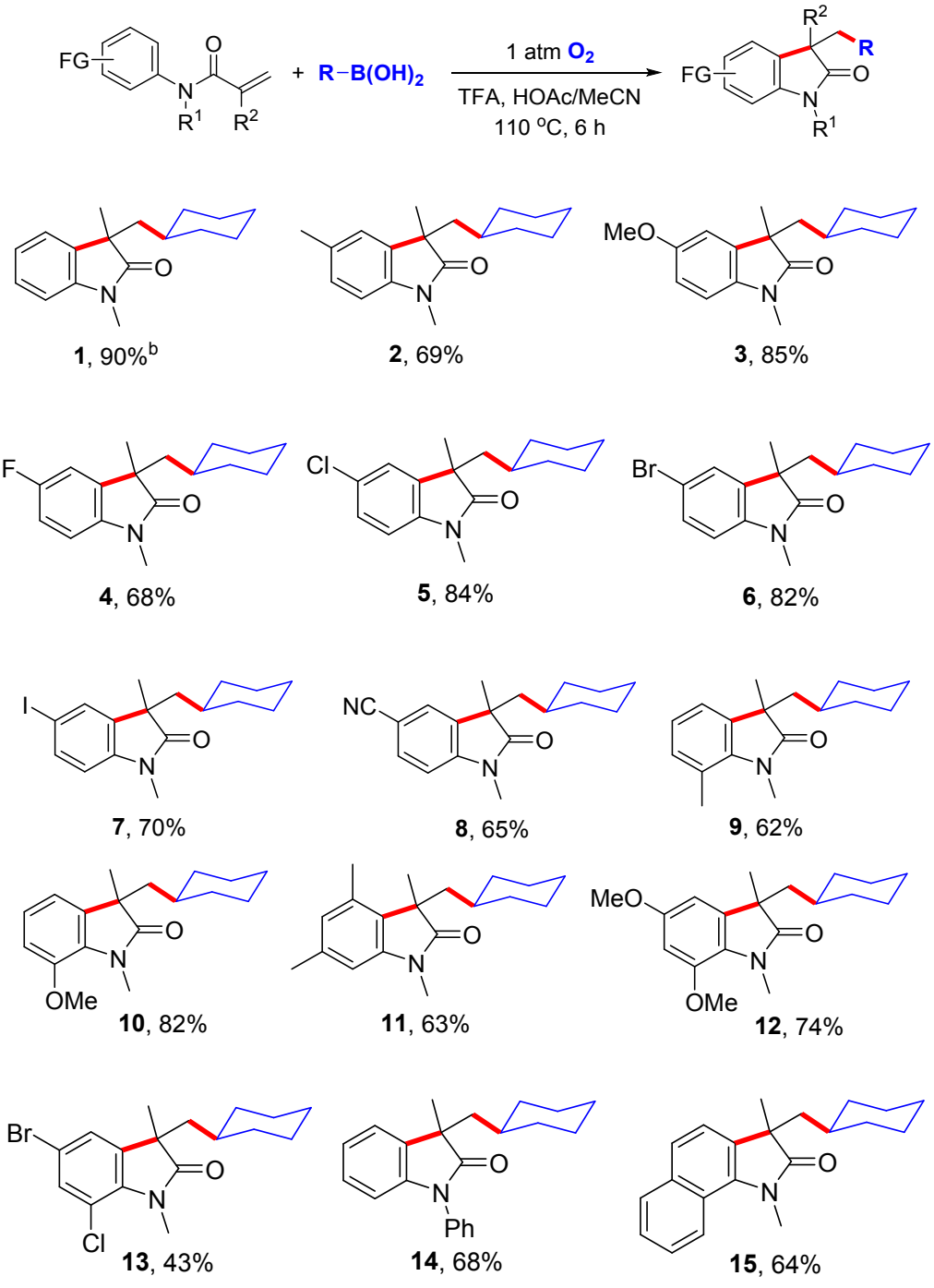
entry	additive (equiv)	solvent (mL)	T (°C)	yield (%)[b]
1	TFA (2)	DCE (0.5)	110	52
2	TFA (2)	*t*-BuOH (0.5)	110	35
3	TFA (2)	EtOH (0.5)	110	40
4	TFA (2)	CH_3CN (0.5)	110	69
5	TFA (2)	EtOH/DCE (0.25/0.25)	110	82
6	TFA (2)	HOAc/DCE (0.25/0.25)	110	79
7	**TFA (2)**	**HOAc/CH_3CN (0.25/0.25)**	**110**	**90**
8	TFA (2)	HOAc/CH_3CN (0.2/0.2)	110	77
9	TFA (2)	HOAc/CH_3CN (0.3/0.3)	110	82
10	-	HOAc/CH_3CN (0.25/0.25)	110	50
11	-	CH_3CN (0.5)	110	47
12	TFA (1)	HOAc/CH_3CN (0.25/0.25)	110	62
13	TFA (2)	HOAc/CH_3CN (0.25/0.25)	80	47
14	TFA (2)	HOAc/CH_3CN (0.25/0.25)	100	65
15[c]	TFA (2)	HOAc/CH_3CN (0.25/0.25)	100	76
16[d]	TFA (2)	HOAc/CH_3CN (0.25/0.25)	110	0

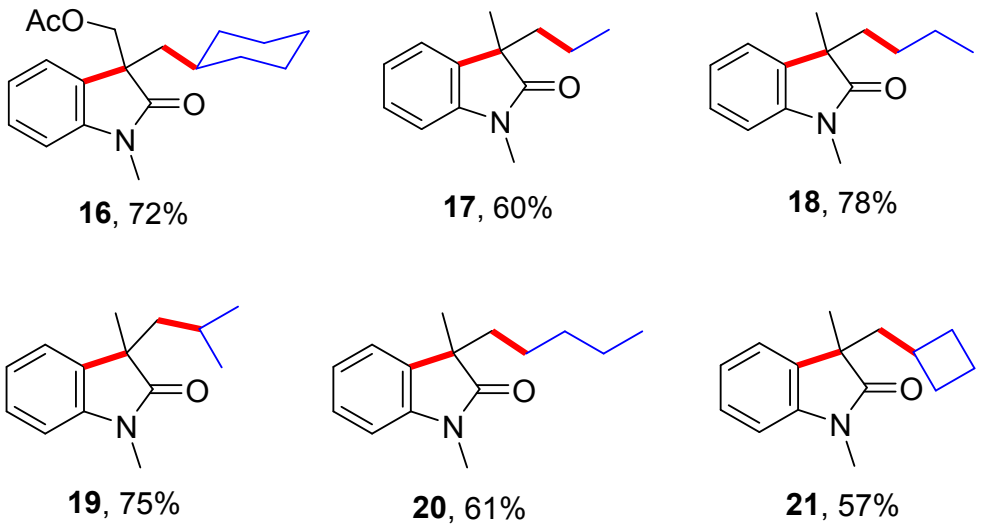
[a] Reaction conditions: *N*-methyl-*N*-phenylmethacrylamide (0.2 mmol, 1 equiv), cyclohexylboronic acid (1 mmol, 5 equiv), 1 atm O_2 (oxygen bag), 6 h, unless otherwise noted. [b] Isolated yields. [c] cyclohexylboronic acid (0.8 mmol, 4 equiv). [d] N_2 instead of O_2.

With the above informations in hand, we then start to investigate the substrate scope. It can be seen from Scheme 2 that a wide range of *N*-arylacrylamides and alkyl boronic acids could afford the corresponding oxindoles in moderate to high yields. Both electron-donating and electron-withdrawing groups as well as halogens (F, Cl, Br, and I) on the aromatic core in *N*-arylacrylamides gave the desired products in good yields (**2**-**13**). Poly-substituents at *ortho*-, *meta*-, and *para*-position of

N-arylacrylamides also led to acceptable yield of the oxindoles, which indicated that the steric effect was not remarkable. Furthermore, *N*,*N*-diphenylmethacrylamide, *N*-methyl-*N*-(naphthalen-1-yl)methacrylamide, and 2-(methyl(phenyl)carbamoyl)allyl acetate afforded the corresponding products in good yields (**14-16**). Finally, an array of alkylboronic acids were evaluated (**17-21**). And we found that both linear and cyclic alkyl boronic acids gave the desired oxindoles in moderate to good yields.

Scheme 2. O_2-Promoted Alkylarylation of alkenes with Alkyl Boronic Acids.[a]



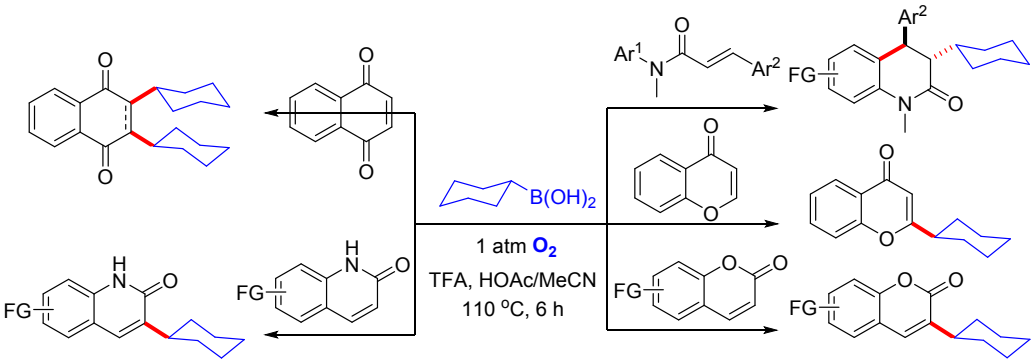


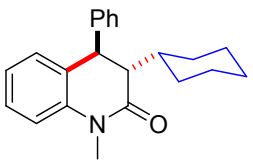
[a] Reaction conditions: N-arylacrylamide (0.2 mmol, 1 equiv), alkyl boronic acid (5 equiv, 1 mmol), TFA (2 equiv, 0.4 mmol), HOAc (0.25 mL), CH_3CN (0.25 mL), 1 atm O_2 (oxygen bag), 110°C (measured temperature of the oil bath), 6 h, unless otherwise noted. [b] Isolated yields.

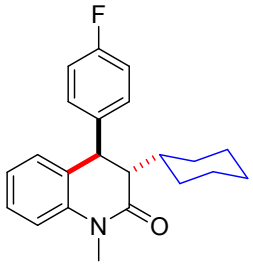
Next, various kinds of molecules containing activated C=C double bonds were evaluated under the typical reaction conditions (Scheme 3). First, a series of N-methyl-N-arylcinnamamides were found to be effective substrates, and the corresponding alkylated 3,4-dihydroquinolin-2(1H)-ones were smoothly obtained via this radical addition/cyclization cascade strategy (**22-27**). It is noteworthy that the chemoselectivities are extremely high. Only anti-isomers of 3-cyclohexyl-1-methyl-4-aryl-3,4-dihydroquinolin-2(1H)-ones were observed, which should be due to the radical stability and steric effect. Then several chromones were examined. As a result, site-specific alkylated chromones (**28-30**) were isolated in 45-53% yields. The relatively nucleophilic alkyl radical trends to attack the electron-deficient C2 position, which might be responsible for the site-selectivity. Subsequently, an array of coumarins and quinolones were examined to be also amenable to this system. The desired 3-alkyl-2H-chromen-2-ones as well as 3-alkyl quinolin-2(1H)-ones were facilely synthesized in moderate to good yields (**31-39**). Gratifyingly, site-specific alkylation occurred at C3 position, which should be due to the generation of more stable benzyl radical intermediate. Finally, dialkylation products were obtained with 1,4-naphthoquinones (**40-42**). Interestingly, naphthalene-1,4-dione and 2-methylnaphthalene-1,4-dione afforded dialkyl addition

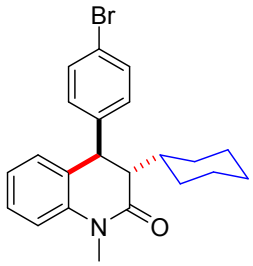
products (**40** and **41**) while 2-chloronaphthalene-1,4-dione gave the addition/elimination dialkyl 1,4-naphthoquinone (**42**). Overall, diverse alkyl heterocycles could be synthesized by this protocol.

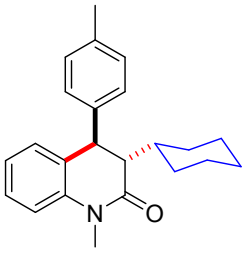
Scheme 3. O_2-Promoted Alkylarylation and/or alkylation of activated alkenes with Alkyl Boronic Acids.[a]

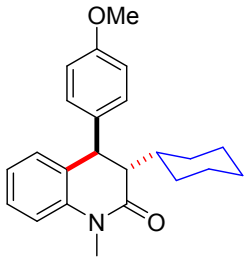


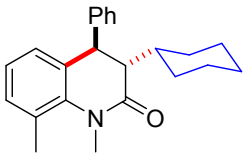

22, 47%[b,c]

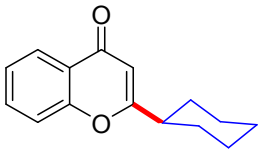

23, 67%[c]

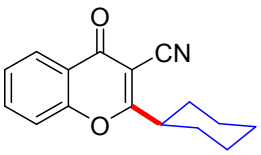

24, 73%[c]

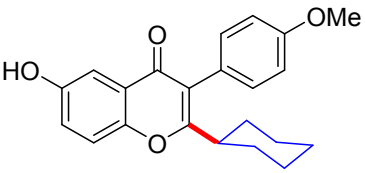

25, 63%[c]

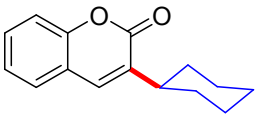

26, 57%[c]

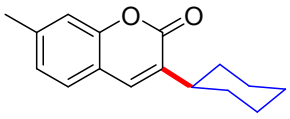

27, 51%[c]

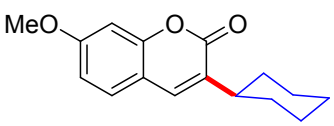

28, 46%

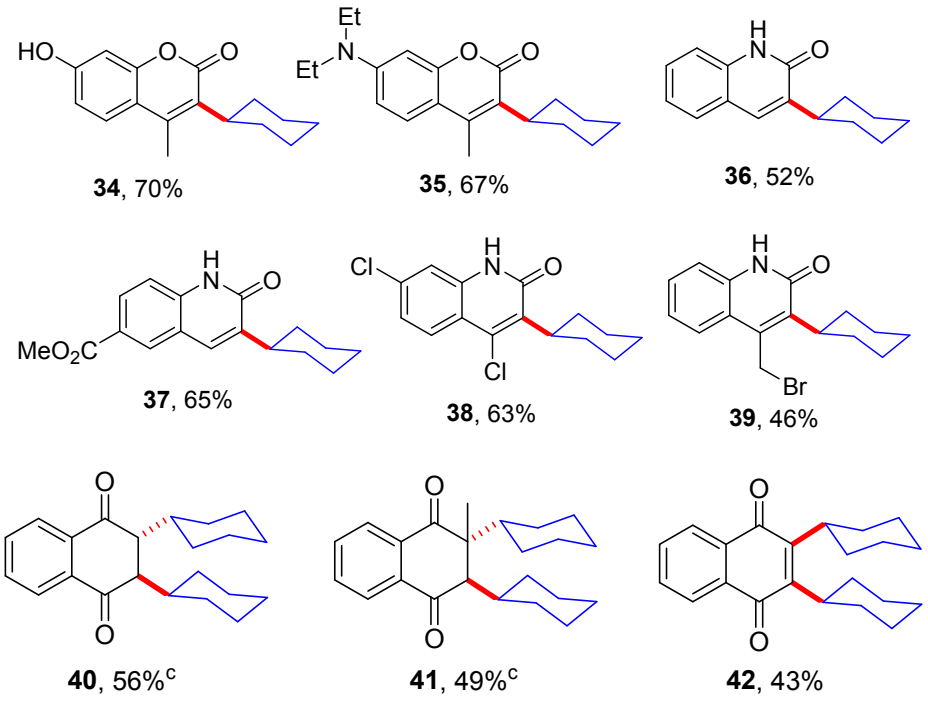

29, 53%


30, 45%


31, 66%


32, 65%

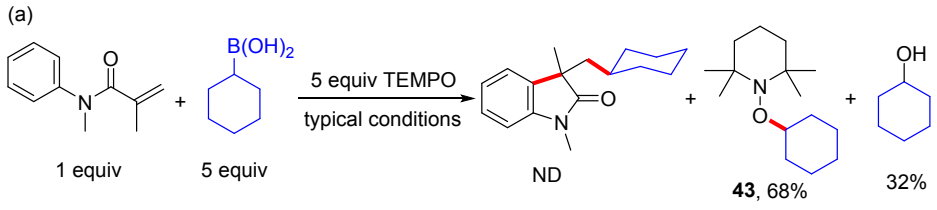

33, 62%

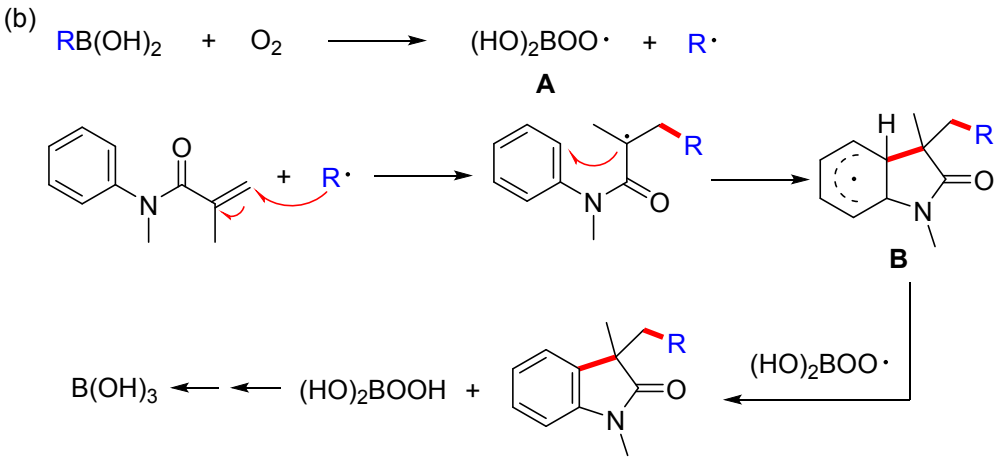


[a] Reaction conditions: substrate (0.2 mmol, 1 equiv), cyclohexylboronic acid (5 equiv, 1 mmol), TFA (2 equiv, 0.4 mmol), HOAc (0.25 mL), CH_3CN (0.25 mL), 1 atm O_2 (oxygen bag), 110°C (measured temperature of the oil bath), 6 h, unless otherwise noted. [b] Isolated yields. [c] Only trans isomers were observed.

As demonstrated in Scheme 4a, radical scavenger TEMPO was introduced into the reaction of N-arylacrylamide with cyclohexylboronic acid. No alkylated oxindole was observed, but 1-(cyclohexyloxy)-2,2,6,6-tetramethylpiperidine (**43**) was isolated as a radical trapping adduct in 68% yield. In addition, 32% yield of cyclohexanol was isolated. In accordance with the experimental results and literatures precedent, a plausible mechanism was proposed in Scheme 4b.[2, 20] Initially, reaction of boronic acid with molecular oxygen would afford radical **A** and alkyl radical. Addition of alkyl radical to alkene followed by cyclization would give radical **B**. Then hydrogen-atom transfer (HAT) from **B** to **A** would form the product and peroxyboronic acid, which would lead to boric acid finally.

Scheme 4. Radical trap experiment and proposed mechanism.





CONCLUSIONS

In summary, we demonstrated a molecular oxygen-mediated alkylation and/or alkylarylation of activated alkenes via autoxidation of alkylboronic acid. By simply heating organoboronic acid under 1 atm. of oxygen, diverse functionalized heterocycles such as oxindoles, quinolinones, chromones, coumarins and quinolones can be efficiently synthesized. This strategy features metal-free, stoichiometric chemical oxidant free, and high chemoselectivity. Furthermore, alphatic boronic acids were used as the alkyl radical donors, which is far more stable and safer than other organoboranes. Hence, the present alkylation strategy would be expected to become a general C-C bond constructing strategy and would find wide applications in synthetic organic chemistry.

EXPERIMENTAL SECTION

General Information: All chemicals were commercially available and used as received without further purification. Reactions were monitored by thin-layer chromatography (TLC). ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded at 400, 100, and 375 MHz, respectively. Chemical shifts (δ) are given relative to internal TMS. The NMR data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constant J (Hz), and integration. HRMS spectra (ESI-TOF) were recorded in CH_2Cl_2 or acetonitrile.

Typical Experimental Procedure for the Synthesis of 1-42.

A mixture of *N*-methyl-*N*-phenylmethacrylamide (1 equiv., 0.20 mmol), TFA (2 equiv., 0.40 mmol), cyclohexylboronic acid (5 equiv., 1 mmol) was dissolved in a solution of acetic acid (0.25 mL) and acetonitrile (0.25 mL). The reaction vial was purged with O_2 for three times and then the reaction mixture was refluxing at 110°C (measured temperature of the oil bath) for 6 hours. After the reaction finished, the solvent was removed under reduced pressure, and purified by flash chromatography on silica gel to afford the desired product.

A scaled-up experimental procedure: A mixture of *N*-methyl-*N*-phenylmethacrylamide (1 equiv., 8 mmol, 1.40 g), TFA (2 equiv., 16 mmol, 1.82 g), cyclohexylboronic acid (5 equiv., 40 mmol, 7.17 g) was dissolved in a solution of acetic acid (10 mL) and acetonitrile (10 mL). The reaction vial was purged with O_2 for three times and then the reaction mixture was refluxing at 110°C (measured temperature of the oil bath) for 6 hours. After the reaction finished, the solvent was removed under reduced pressure, and purified by flash chromatography on silica gel to afford the desired product (1.74 g, isolated yield: 84%).

3-(cyclohexylmethyl)-1,3-dimethylindolin-2-one ***(1)***.[19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 90%, 46.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 – 7.24 (m, 1H), 7.16 (d, J = 6.8 Hz, 1H), 7.05 (t, J = 7.2 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 3.22 (s, 3H), 1.93 (dd, J = 14.0, 6.8 Hz, 1H), 1.72 (dd, J = 14.0, 5.2 Hz, 1H), 1.53 – 1.45 (m, 3H), 1.36 – 1.19 (m, 5H), 1.02 – 0.70 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.1, 143.1, 134.4, 127.5, 122.7, 122.3, 107.9, 47.8, 45.4, 34.7, 34.5, 33.5, 26.2, 26.1, 26.1, 26.0. MS (EI, m/z): 257(9.5), 161 (100), 160(32.8), 55(8.3).

3-(cyclohexylmethyl)-1,3,5-trimethylindolin-2-one ***(2)***.[19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 69%, 37.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (d, J = 8.0 Hz, 1H), 6.96 (s, 1H), 6.72 (d, J = 8.0 Hz, 1H), 3.19 (s, 3H), 2.35 (s, 3H), 1.91 (dd, J = 14.0, 6.8 Hz, 1H), 1.69 (dd, J = 14.0, 5.2 Hz, 1H), 1.52 – 1.46 (m, 3H), 1.36 – 1.21 (m, 5H), 1.00 – 0.91 (m, 4H), 0.88 – 0.73 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.1, 140.7, 134.5, 131.7, 127.7, 123.5, 107.6, 47.9, 45.4, 34.7, 34.5, 33.5, 26.2, 26.1, 26.0,

21.2. MS (EI, m/z): 271(10.4), 176 (14.1), 175(100), 40(24.2).

3-(cyclohexylmethyl)-5-methoxy-1,3-dimethylindolin-2-one（***3***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 85%, 51.5mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.79 – 6.72 (m, 3H), 3.81 (s,3H), 3.19 (s, 3H), 1.92 (dd, J = 14.0, 7.2 Hz, 1H), 1.68 (dd, J = 14.0, 5.2 Hz, 1H), 1.52 – 1.46 (m, 3H), 1.36 – 1.21 (m, 5H), 1.05 – 0.71 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.7, 160.5(d, J=955), 139.0, 136.3, 113.8 (d, J=93.6), 111.0 (d, J=96.8), 108.3 (d, J=32.4), 55.8, 48.3, 45.4, 34.7, 34.4, 33.5, 26.3, 26.1, 26.0. MS (EI, m/z): 287(21.4), 191 (100), 190(33.6), 176(11.0).

3-(cyclohexylmethyl)-5-fluoro-1,3-dimethylindolin-2-one（***4***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 68%, 37.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95 (td, J = 9.2, 2.4 Hz, 1H), 6.90 (dd, J = 8.0, 2.4 Hz, 1H), 6.75 (dd, J = 8.4, 4.0 Hz, 1H), 3.20 (s, 3H), 1.93 (dd, J = 14.0, 6.8 Hz, 1H), 1.68 (dd, J = 14.0, 5.2 Hz, 1H), 1.53 – 1.47 (m, 3H), 1.35 – 1.19 (m, 5H), 1.03 – 0.88 (m, 4H), 0.86 – 0.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.7, 160.5, 158.1, 139.0, 136.3, 113.8, 113.5, 111.0, 110.7, 108.3, 108.2, 48.4, 45.4, 34.7, 34.4, 33.5, 26.3, 26.1, 26.0, 26.0. MS (EI, m/z): 275(7.1), 179 (100), 178(30.2), 40(14.0).

5-chloro-3-(cyclohexylmethyl)-1,3-dimethylindolin-2-one（***5***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 84%, 48.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (dd, J = 8.4, 2.0 Hz, 1H), 7.12 (d, J = 2.0 Hz, 1H), 6.75 (d, J = 8.4 Hz, 1H), 3.19 (s, 3H), 1.92 (dd, J = 14.0, 7.2 Hz, 1H), 1.69 (dd, J = 14.0, 5.2 Hz, 1H), 1.52 – 1.47 (m, 3H), 1.32 – 1.20 (m, 5H), 1.02 – 0.88 (m, 4H), 0.86 – 0.71 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.5, 141.7, 136.2, 127.7, 127.5, 123.2, 108.8, 48.1, 45.3, 34.7, 34.4, 33.4, 26.3, 26.1, 26.0, 25.9. MS (EI, m/z): 291(8.2), 197 (32.0), 195(100), 55(15.4).

5-bromo-3-(cyclohexylmethyl)-1,3-dimethylindolin-2-one（***6***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 82%, 54.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (dd, J = 8.4, 2.0 Hz, 1H), 7.25 (d, J = 1.6 Hz, 1H), 6.71 (d, J = 8.4 Hz, 1H), 3.18 (s, 3H), 1.92 (dd, J = 14.0,

7.2 Hz, 1H), 1.68 (dd, J = 14.0, 5.2 Hz, 1H), 1.52 – 1.47 (m, 3H), 1.32 – 1.20 (m, 5H), 1.05 – 0.88 (m, 4H), 0.86 – 0.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.4, 142.2, 136.6, 130.4, 125.9, 115.1, 109.4, 48.1, 45.3, 34.7, 34.4, 33.4, 26.3, 26.1, 26.0, 25.9. MS (EI, m/z): 335(8.0), 239 (100), 130(12.4), 55(26.9).

3-(cyclohexylmethyl)-5-iodo-1,3-dimethylindolin-2-one （***7***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 70%, 51.7 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (dd, J = 8.4, 2.0 Hz, 1H), 7.42 (d, J = 2.0 Hz, 1H), 6.62 (d, J = 8.0 Hz, 1H), 3.18 (s, 3H), 1.91 (dd, J = 14.0, 6.8 Hz, 1H), 1.68 (dd, J = 14.4, 5.2 Hz, 1H), 1.50 – 1.47 (m, 3H), 1.32 – 1.20 (m, 5H), 1.06 – 0.70 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.2, 142.9, 136.9, 136.4, 131.5, 110.0, 84.9, 47.9, 45.3, 34.7, 34.4, 33.4, 26.2, 26.1, 26.0, 25.9. MS (EI, m/z): 383(8.9), 287 (100), 160(14.7), 55(24.1).

3-(cyclohexylmethyl)-1,3-dimethyl-2-oxoindoline-5-carbonitrile （***8***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 65%, 34.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, J = 8.0, 1.6 Hz, 1H), 7.39 (d, J = 1.6 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 3.23 (s, 3H), 1.95 (dd, J = 14.4, 6.8 Hz, 1H), 1.73 (dd, J = 14.4, 4.9 Hz, 1H), 1.52 – 1.46(m, 3H), 1.32 (s, 3H), 1.26 – 1.17 (m, 2H), 1.00 – 0.76 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.6, 146.9, 135.4, 133.0, 126.0, 119.3, 108.3, 105.3, 47.6, 45.1, 34.7, 34.3, 33.3, 26.4, 25.9, 25.9, 25.8. MS (EI, m/z): 282(4.9), 186 (100), 55(15.0), 40(51.1)

3-(cyclohexylmethyl)-1,3,7-trimethylindolin-2-one （***9***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 62%, 33.6 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 – 6.91 (m, 3H), 3.49 (s, 3H), 2.59 (s, 3H), 1.91 (dd, J = 14.0, 6.8 Hz, 1H), 1.68 (dd, J = 14.0, 5.2 Hz, 1H), 1.53 – 1.46 (m, 3H), 1.38 – 1.20 (m, 5H), 1.03 – 0.69 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.9, 140.9, 135.1, 131.2, 122.2, 120.6, 119.5, 47.1, 45.6, 34.6, 34.5, 33.5, 29.5, 26.6, 26.1, 26.1, 26.0, 19.1. MS (EI, m/z): 271(7.5), 176 (13.2), 175(100), 40(43.8).

3-(cyclohexylmethyl)-7-methoxy-1,3-dimethylindolin-2-one （***10***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate =

20/1, Yield: 82%, 44.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (t, J = 7.2 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 6.77 (dd, J = 7.6, 0.8 Hz, 1H), 3.86 (s, 3H), 3.48 (s, 3H), 1.90 (dd, J = 14.0, 6.8 Hz, 1H), 1.68 (dd, J = 14.0, 5.2 Hz, 1H), 1.53 – 1.46 (m, 3H), 1.39 – 1.21 (m, 5H), 1.01 – 0.70 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.3, 145.3, 136.2, 130.9, 122.8, 115.5, 111.4, 55.9, 47.9, 45.5, 34.7, 34.4, 33.5, 29.4, 26.5, 26.1, 26.0. MS (EI, m/z): 287(10.1), 191 (100), 176(7.7), 40(29.5).

3-(cyclohexylmethyl)-1,3,4,6-tetramethylindolin-2-one（***11***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 63%, 35.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.63 (s, 1H), 6.51 (s, 1H), 3.17 (s, 3H), 2.34 (s, 3H), 2.30 (s, 3H), 1.93 (d, J = 3.6 Hz, 2H), 1.50 – 1.45 (m, 3H), 1.34 (s, 3H), 1.30 – 1.22 (m, 2H), 1.02 – 0.75 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.6, 143.4, 137.3, 133.8, 128.0, 125.4, 106.7, 48.4, 43.8, 35.1, 34.1, 33.0, 26.2, 26.1, 25.9, 24.2, 21.5, 18.1. MS (EI, m/z): 285(4.6), 189 (100), 188(66.5), 173(10.0).

3-(cyclohexylmethyl)-5,7-dimethoxy-1,3-dimethylindolin-2-one（***12***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 74%, 46.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$):δ 6.41 (d, J = 2.0 Hz, 1H), 6.35 (d, J = 2.4 Hz, 1H), 3.84 (s, 3H), 3.80 (s, 3H), 3.43 (s, 3H), 1.89 (dd, J = 14.0, 6.8 Hz, 1H), 1.64 (dd, J = 14.0, 5.2 Hz, 1H), 1.53 – 1.47 (m, 3H), 1.40 – 1.23 (m, 5H), 1.06 – 0.70 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.0, 156.5, 145.8, 136.8, 124.5, 100.8, 98.7, 55.9, 55.8, 48.5, 45.5, 34.6, 34.4, 33.4, 29.3, 26.5, 26.1, 26.0 .MS (EI, m/z): 317(25.1), 221 (100), 206(18.6), 55(8.9).

5-bromo-7-chloro-3-(cyclohexylmethyl)-1,3-dimethylindolin-2-one（***13***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 43%, 31.7 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (dd, J = 2.0, 0.4 Hz, 1H), 7.26 (s, 1H), 7.03 (d, J = 2.0 Hz, 1H), 1.92 (dt, J = 14.0, 7.2 Hz, 1H), 1.66 (dd, J = 14.0, 5.2 Hz, 1H), 1.54 – 1.48 (m, 1H), 1.28 (s, 1H), 1.24 – 1.20 (m, 1H), 1.02 – 0.76 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.8, 139.2, 138.8, 132.4, 128.1, 122.2, 102.2, 47.9, 45.5, 34.5, 34.4, 33.3, 29.7, 26.6, 26.0, 25.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{17}H_{21}BrClNOH$ 370.0568, found 370.0566.

3-(cyclohexylmethyl)-3-methyl-1-phenylindolin-2-one （***14***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 68%, 43.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (t, J = 8.0 Hz, 2H), 7.41 – 7.38 (m, 3H), 7.25 – 7.16 (m, 2H), 7.09 (t, J = 7.2 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 2.03 (dd, J = 14.0, 7.2 Hz, 1H), 1.80 (dd, J = 14.0, 5.2 Hz, 1H), 1.56 – 1.50 (m, 3H), 1.44 (s, 3H), 1.29 (d, J = 12.4 Hz, 1H), 1.14 – 0.75 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.4, 143.0, 134.8, 134.2, 129.5, 127.8, 127.4, 126.4, 123.0, 122.8, 109.3, 47.9, 45.8, 34.9, 34.4, 33.6, 26.4, 26.2, 26.1, 26.0. MS (EI, m/z): 319(7.3), 223 (100), 194(7.0), 40(39.0).

3-(cyclohexylmethyl)-1,3-dimethyl-1,3-dihydro-2H-benzo[g]indol-2-one（***15***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 64%, 39.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J = 8.0 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.44 – 7.38 (m, 2H), 6.94 (d, J = 7.2 Hz, 1H), 3.53 (s, 3H), 2.41 (dd, J = 14.0, 7.6 Hz, 1H), 1.87 (dd, J = 14.0, 4.8 Hz, 1H), 1.63 (s, 3H), 1.45 – 1.18 (m, 5H), 1.14 – 0.72 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 138.5, 136.9, 133.3, 126.8, 126.2, 125.6, 123.1, 122.3, 119.6, 108.0, 51.0, 46.5, 34.8, 34.5, 33.3, 32.9, 29.6, 26.2, 26.1. MS (EI, m/z): 307(8.6), 211 (100), 182(32.6), 55(8.6).

(3-(cyclohexylmethyl)-1-methyl-2-oxoindolin-3-yl)methyl acetate（***16***）. [19c] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 72%, 45.4mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (td, J = 7.6, 1.2 Hz, 1H), 7.18 (d, J = 7.2 Hz, 1H), 7.05 (t, J = 7.2 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 4.43 (d, J = 10.8 Hz, 1H), 4.08 (d, J = 10.8 Hz, 1H), 3.23 (s, 3H), 1.87 (dd, J = 14.0, 7.2 Hz, 1H), 1.82 (s, 3H), 1.76 (dd, J = 14.0, 5.2 Hz, 1H), 1.52 – 1.42 (m, 3H), 1.33 (d, J = 13.2 Hz, 1H), 1.25 – 1.20 (m, 1H), 1.05 – 0.71 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.0, 170.3, 144.0, 129.8, 128.3, 123.6, 122.4, 107.9, 68.4, 51.9, 40.2, 34.4, 34.0, 33.5, 26.3, 26.0, 25.9, 20.5. MS (EI, m/z): 315(6.6), 159 (100), 130(7.5), 40(17.3).

1,3-dimethyl-3-propylindolin-2-one（***17***）. [13] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 60%, 24.4

mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (td, *J* = 6.8, 1.2 Hz, 1H), 7.17 (dd, *J* = 7.2, 0.8 Hz, 1H), 7.06 (td, *J* = 7.6, 1.2 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 3.21 (s, 3H), 1.84–1.91 (m, 1H), 1.74 – 1.66 (m, 1H), 1.35 (s, 3H), 1.04 – 0.96 (m, 1H), 0.90 – 0.82 (m, 1H), 0.77 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.9, 143.3, 134.3, 127.5, 122.5, 122.4, 107.8, 48.5, 40.8, 26.0, 23.7, 17.8, 14.1. MS (EI, m/z): 203(30.5), 161 (100), 160(94.2), 40(58.4).

3-butyl-1,3-dimethylindolin-2-one（***18***）. [13] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 78%, 33.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 – 7.24(m, 1H), 7.16 (d, *J* = 7.2 Hz, 1H), 7.06 (t, *J* = 7.2 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 3.21 (s, 3H), 1.89 (td, *J* = 13.2, 4.8 Hz, 1H), 1.72 (td, *J* = 12.8, 4.4 Hz, 1H), 1.34 (s, 3H), 1.13–1.22 (m, 2H), 0.92–0.98 (m, 1H), 0.84 – 0.80 (m, 1H), 0.77 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.0, 143.2, 134.2, 127.5, 122.8, 122.2, 107.8, 48.2, 46.0, 33.9, 33.5, 32.2, 27.1, 27.0, 26.3, 26.1, 25.6, 25.1, 24.9. MS (EI, m/z): 217(27.8), 161 (100), 160(83.4), 132(14.3).

3-isobutyl-1,3-dimethylindolin-2-one（***19***）. [13] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 75%, 32.6 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (td, *J* = 7.2, 1.2 Hz, 1H), 7.15 – 7.12 (m, 1H), 7.04 (td, *J* = 7.2, 0.8 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 3.19 (s, 3H), 1.92 (dd, *J* = 13.6, 7.6 Hz, 1H), 1.74 (dd, *J* = 13.6, 5.2 Hz, 1H), 1.30 (s, 3H), 1.23 (dt, *J* = 12, 6.4 Hz, 1H), 0.63 (d, *J* = 6.4 Hz, 3H), 0.58 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.0, 143.1, 134.1, 127.5, 122.7, 122.3, 107.9, 48.0, 46.7, 26.1, 26.1, 25.5, 24.1, 22.8. MS (EI, m/z): 217(19.6), 161 (100), 160(74.9), 132(11.6).

1,3-dimethyl-3-pentylindolin-2-one（***20***）. [13] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 61%, 28.2 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (td, *J* = 7.6, 1.2 Hz, 1H), 7.16 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.06 (td, *J* = 7.2, 0.8 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 3.19 (s, 3H), 1.87 (ddd, *J* = 13.2, 12.4, 4.8 Hz, 1H), 1.75 – 1.67 (m, 1H), 1.34 (s, 3H), 1.17 – 1.10(m, 4H), 1.02 – 0.92 (m, 1H), 0.86 – 0.80 (m, 1H), 0.77 (dd, *J* = 6.8, 2.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.1, 143.3, 134.3, 127.5, 122.4, 122.3, 107.8, 48.4,

38.45, 31.9, 26.0, 24.0, 23.7, 22.3, 13.9. MS (EI, m/z): 231(20.0), 161 (100), 160(67.4), 132(10.4).

3-(cyclobutylmethyl)-1,3-dimethylindolin-2-one（***21***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 57%, 26.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$)：δ 7.27 – 7.23 (m, 1H), 7.17 – 7.14 (m, 1H), 7.04 (td, *J* = 7.6, 1.2 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 3.19 (s, 3H), 2.04 (dd, *J* = 12.4, 6.0 Hz, 1H), 1.85 (dd, *J* = 13.2, 6.8 Hz, 1H), 1.72 – 1.67 (m, 1H), 1.65 – 1.53 (m, 4H), 1.47 – 1.36 (m, 2H), 1.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.8, 143.2, 134.1, 127.5, 122.8, 122.2, 107.7, 47.9, 45.5, 32.9, 29.4, 28.8, 26.1, 23.9, 18.8. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{15}H_{19}NOH$ 230.1539, found 230.1537.

3-cyclohexyl-1-methyl-4-phenyl-3,4-dihydroquinolin-2(1H)-one（***22***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1, Yield: 47%, 30.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (m, 1H), 7.19 (dt, *J* = 13.2, 7.6 Hz, 4H), 7.10 – 7.04 (m, 2H), 6.96 (d, *J* = 7.6 Hz, 2H), 4.22 (s, 1H), 3.36 (s, 3H), 2.67 (d, *J* = 8.8 Hz, 1H), 1.92 (d, *J* = 10.0 Hz, 1H), 1.69 (d, *J* = 10.8 Hz, 2H), 1.58 (s, 2H), 1.49 – 0.84 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 142.3, 140.0, 129.6, 128.7, 128.0, 127.0, 126.6, 123.2, 114.8, 55.6, 44.4, 37.6, 31.4, 31.1, 29.4, 26.1, 26.1, 25.9. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{22}H_{25}NOH$ 320.2009, found 320.2007.

3-cyclohexyl-4-(4-fluorophenyl)-1-methyl-3,4-dihydroquinolin-2(1H)-one（***23***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1, Yield: 67%, 45.2 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 – 7.30 (m, 1H), 7.23 – 7.14 (m, 1H), 7.10 – 7.03 (m, 2H), 6.94 – 6.86 (m, 4H), 4.19 (s, 1H), 3.35 (s, 3H), 2.63 (dd, *J* = 9.2, 1.6 Hz, 1H), 1.91 (d, *J* = 9.6 Hz, 1H), 1.79 – 1.64 (m, 2H), 1.56 (d, *J* = 11.6 Hz, 2H), 1.44 – 0.93 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 162.7, 160.3, 139.9, 137.9, 129.5, 128.6 (d, J=31.4), 128.1, 126.4, 123.3, 115.5, 115.3, 114.9, 55.7, 43.6, 37.5, 31.3, 31.0, 29.4, 26.1, 25.9. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{22}H_{24}FNOH$ 338.1915, found 338.1909.

4-(4-bromophenyl)-3-cyclohexyl-1-methyl-3,4-dihydroquinolin-2(1H)-one （***24***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1, Yield: 73%, 58.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.29 (m, 3H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.07 (dd, *J* = 7.4, 6.4 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 4.16 (s, 1H), 3.35 (s, 3H), 2.61 (d, *J* = 8.8 Hz, 1H), 1.90 (d, *J* = 10.8 Hz, 1H), 1.79 – 1.50 (m, 5H), 1.38 – 1.02 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 141.2, 139.9, 131.7, 129.5, 128.8, 128.3, 126.0, 123.3, 120.5, 114.9, 55.5, 43.8, 37.5, 31.3, 31.0, 29.5, 26.0, 25.9. HRMS (ESI-TOF) m/z: ［M+H］$^{+}$ Calculated for $C_{22}H_{24}BrNOH$ 398.1114, found 398.1112.

3-cyclohexyl-1-methyl-4-(p-tolyl)-3,4-dihydroquinolin-2(1H)-one （***25***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1, Yield: 63%, 42.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (t, *J* = 6.8 Hz, 1H), 7.18 (d, *J* = 6.8 Hz, 1H), 7.10 – 6.99 (m, 4H), 6.85 (d, *J* = 7.6 Hz, 2H), 4.18 (s, 1H), 3.36 (s, 3H), 2.65 (d, *J* = 8.4 Hz, 1H), 2.25 (s, 3H), 1.92 (d, *J* = 10.0 Hz, 1H), 1.69 (m, 2H), 1.56 (d, *J* = 12.4 Hz, 2H), 1.41 – 1.02 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 134.0, 139.2, 136.1, 129.5, 129.3, 127.9, 126.9, 126.9, 123.2, 114.8, 55.6, 44.0, 37.6, 31.4, 31.1, 29.4, 26.1, 25.9, 20.9. HRMS (ESI-TOF) m/z: ［M+H］$^{+}$ Calculated for $C_{23}H_{27}NOH$ 334.2165, found 334.2162.

3-cyclohexyl-4-(4-methoxyphenyl)-1-methyl-3,4-dihydroquinolin-2(1H)-one（***26***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1, Yield: 57%, 39.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (td, *J* = 8.0, 1.6 Hz, 1H), 7.18 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.06 (dd, *J* = 6.8, 4 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.75 (d, *J* = 8.8 Hz, 2H), 4.16 (s, 1H), 3.73 (s, 3H), 3.35 (s, 3H), 2.64 (dd, *J* = 9.2, 1.6 Hz, 1H), 1.91 (d, *J* = 10.4 Hz, 1H), 1.69 (m, 2H), 1.56 (d, *J* = 12.4 Hz, 2H), 1.20 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 158.1, 139.9, 134.2, 129.5, 128.0, 127.9, 127.0, 123.2, 114.8, 114.0, 55.7, 55.2, 43.5, 37.5, 31.4, 31.1, 29.5, 26.1, 25.9. HRMS (ESI-TOF) m/z: ［M+H］$^{+}$ Calculated for $C_{23}H_{27}NO_2H$ 350.2115, found 350.2111.

3-cyclohexyl-1,8-dimethyl-4-phenyl-3,4-dihydroquinolin-2(1H)-one （***27***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl

acetate = 10/1, Yield: 51%, 34.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, *J* = 7.6 Hz, 2H), 7.17 (dd, *J* = 7.2, 1.2 Hz, 2H), 7.07 – 7.02 (m, 2H), 7.02 – 6.97 (m, 2H), 4.13 (s, 1H), 3.23 (s, 3H), 2.67 (dd, *J* = 9.6, 1.6 Hz, 1H), 2.40 (s, 3H), 1.85 (d, *J* = 8.8 Hz, 1H), 1.71 – 1.54 (m, 4H), 1.35 – 0.92 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 151.1, 141.6, 141.2, 141.2, 131.6, 129.8, 128.6, 127.7, 127.2, 127.0, 126.6, 124.5, 56.9, 44.8, 36.4, 35.8, 31.6, 31.0, 26.1, 25.9, 25.8, 20.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{23}H_{27}NOH$ 334.2165, found 334.2162.

3-cyclohexyl-4H-chromen-4-one（***28***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 46%, 21.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 – 8.09 (m, 1H), 7.71 – 7.56 (m, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H) , 6.19 (s, 1H), 2.53 (t, *J* = 11.6 Hz, 1H), 2.03 (d, *J* = 12.4 Hz, 2H), 1.82 (m, 3H), 1.59 – 1.25 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.8, 173.5, 156.4, 133.4, 125.6, 124.8, 123.7, 117.8, 107.8, 42.8, 30.4, 25.8, 25.7. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{16}O_2H$ 229.1221, found 229.1223.

2-cyclohexyl-4-oxo-4H-chromene-3-carbonitrile（***29***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1, Yield: 53%, 26.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (dd, J = 8.0, 1.2 Hz, 1H), 7.83 – 7.69 (m, 1H), 7.49 (dd, J = 13.2, 7.6 Hz, 2H), 3.15 (tt, J = 12.0, 3.2 Hz, 1H), 2.10 – 1.87 (m, 4H), 1.84 – 1.67 (m, 3H), 1.53 – 1.26 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.0, 173.7, 155.4, 134.8, 126.6, 126.1, 122.3, 118.0, 113.1, 98.8, 43.6, 29.6, 25.4, 25.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{16}H_{15}NO_2H$ 254.1176, found 254.1180.

2-cyclohexyl-6-hydroxy-3-(4-methoxyphenyl)-4H-chromen-4-one（***30***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1, Yield: 45%, 31.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 – 7.81 (m, 2H), 7.14 (d, J = 8.8 Hz, 1H), 6.96 (dd, J = 6.0, 3.6 Hz, 3H), 6.72 (dd, J = 8.4, 2.0 Hz, 1H), 5.45 (s, 1H), 3.89 (s, 3H), 3.01 (tt, J = 12.0, 3.6 Hz, 1H), 1.90 (d, J = 12.8 Hz, 2H), 1.83 – 1.77 (m, 2H), 1.71 (dd, J = 12.4, 3.2 Hz, 2H), 1.35 – 1.17 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.0, 167.4, 163.5, 154.3, 153.6, 131.9, 131.7, 121.5,

120.6, 115.1, 113.6, 112.2, 98.1, 55.5, 37.4, 31.2, 26.1, 25.7. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{22}H_{22}O_4H$ 351.1591, found 351.1600.

3-cyclohexyl-2H-chromen-2-one（***31***）.[15] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 66%, 30.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (t, *J* =6.8 Hz, 3H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 6.8 Hz, 1H), 2.81 (t, *J* = 12.0 Hz, 1H), 2.01 (d, *J* = 11.6 Hz, 2H), 1.84 (m, 3H), 1.48 (m, 12.8 Hz, 2H), 1.38 – 1.27 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 152.6, 136.3, 134.8, 130.4, 127.3, 124.1, 119.6, 116.3, 38.1, 32.1, 26.5, 26.1. MS (EI, m/z): 115(47.8), 160 (86.4), 172(96.8), 228(100).

3-cyclohexyl-7-methyl-2H-chromen-2-one（***32***）. [15] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 65%,31.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (s, 1H), 7.26 – 7.21 (m, 2H), 7.18 (d, *J* = 8.4 Hz, 1H), 2.76 (m, 1H), 2.38 (s, 3H), 1.96 (d, *J* = 12.0 Hz, 2H), 1.88 – 1.73 (m, 3H), 1.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 150.7, 136.3, 134.6, 133.7, 131.4, 127.1, 119.3, 115.9, 38.0, 32.1, 26.5, 26.1, 20.8. MS (EI, m/z): 128(25.3), 174 (88.6), 186(88.2), 242(100).

3-cyclohexyl-7-methoxy-2H-chromen-2-one（***33***）. [15] A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 62%, 32.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (s, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 6.80 (m, 2H), 3.84 (s, 3H), 2.71 (t, *J* = 12.0 Hz, 1H), 1.94 (d, *J* = 11.6 Hz, 2H), 1.82 (d, *J* = 13.2 Hz, 2H), 1.75 (d, *J* = 12.8 Hz, 1H), 1.49 – 1.19 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 161.6, 154.2, 136.4, 131.0, 128.1, 113.2, 112.2, 100.2, 55.6, 37.9, 32.1, 26.5, 26.1. MS (EI, m/z): 77(15.2), 177 (100), 189(70.4), 258(67.2).

3-cyclohexyl-7-hydroxy-4-methyl-2H-chromen-2-one（***34***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1, Yield: 70%, 36.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.94 (s, 1H), 7.51 (d, *J* = 8.8 Hz, 1H), 7.11 (d, *J* = 2.4 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.4 Hz, 1H), 2.87 (t, *J* = 12.0 Hz, 1H), 2.43 (s, 3H), 2.16 (dd, *J* = 13.2, 10.0 Hz, 2H), 1.83 (d, *J* = 4.8 Hz, 2H), 1.70 (s, 1H), 1.55 (d, *J* = 12.4 Hz, 2H), 1.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2,

159.2, 153.3, 147.6, 126.2, 126.1, 113.9, 113.4, 102.7, 39.5, 29.2, 26.9, 25.7, 15.0. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{16}H_{18}O_3H$ 259.1329, found 259.1325.

3-cyclohexyl-7-(diethylamino)-4-methyl-2H-chromen-2-one（***35***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 67%, 41.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 9.2 Hz, 1H), 6.55 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.44 (d, *J* = 2.8 Hz, 1H), 3.37 (q, *J* = 7.2 Hz, 4H), 2.80 (t, *J* = 12.0 Hz, 1H), 2.35 (s, 3H), 2.25 – 2.09 (m, 2H), 1.89 – 1.77 (m, 2H), 1.67 (d, *J* = 4.0 Hz, 1H), 1.52 (d, *J* = 12.8 Hz, 2H), 1.31 (t, *J* = 6.4 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2, 154.5, 149.2, 146.1, 125.5, 123.9, 109.7, 108.1, 97.1, 44.6, 39.3, 29.3, 27.0, 25.7, 14.5, 12.4. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{20}H_{27}NO_2H$ 314.2115, found 314.2110.

3-cyclohexylquinolin-2(1H)-one（***36***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 52%, 23.6 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.80 (s, 1H), 7.60 (s, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 3.05 (t, J = 11.6 Hz, 1H), 2.04 (d, J = 11.6 Hz, 2H), 1.90 (d, J = 12.8 Hz, 2H), 1.62 – 1.48 (m, 2H), 1.46 – 1.25 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8, 139.2, 137.0, 134.3, 129.2, 127.2, 122.2, 120.4, 115.4, 37.1, 32.6, 26.7, 26.4. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{15}H_{17}NOH$ 228.1383, found 228.1387.

methyl 3-cyclohexyl-2-oxo-1,2-dihydroquinoline-6-carboxylate（***37***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1, Yield: 65%, 37.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.23 (s, 1H), 8.26 (d, J = 1.2 Hz, 1H), 8.10 (dd, J = 8.4, 1.6 Hz, 1H), 7.62 (s, 1H), 7.41 (d, J = 8.8 Hz, 1H), 3.94 (s, 3H), 2.99 (t, J = 11.6 Hz, 1H), 1.99 (d, J = 12.0 Hz, 2H), 1.87 (d, J = 12.8 Hz, 2H), 1.50 (dd, J = 25.6, 12.8 Hz, 2H), 1.40 – 1.22 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 164.2, 140.0, 134.6, 130.0, 129.7, 124.2, 119.8, 115.5, 52.2, 37.2, 32.4, 26.7, 26.3. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{17}H_{19}NO_3H$ 286.1438, found 286.1447).

4,7-dichloro-3-cyclohexylquinolin-2(1H)-one （***38***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1, Yield: 63%, 37.2 mg). ^{1}H NMR (400 MHz, DMSO): δ 11.16 (s, 1H), 7.03 (d, J = 8.8 Hz, 1H), 6.50 (d, J = 2.0 Hz, 1H), 6.44 (dd, J = 8.8, 2.0 Hz, 1H), 2.39 (t, J = 11.6 Hz, 1H), 1.49 – 1.26 (m, 2H), 0.94 (d, J = 12.4 Hz, 2H), 0.65 (d, J = 12.8 Hz, 2H), 0.54 – 0.34 (m, 4H). ^{13}C NMR (100 MHz, DMSO): δ 160.5, 139.8, 138.2, 135.8, 135.5, 127.5, 122.9, 117.2, 114.6, 28.3, 26.4, 25.9. HRMS (ESI-TOF) m/z: [M+H]$^{+}$ Calculated for $C_{15}H_{15}Cl_2NOH$ 296.0603, found 296.0613.

4-(bromomethyl)-3-cyclohexylquinolin-2(1H)-one （***39***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 46%, 29.3mg). ^{1}H NMR (400 MHz, $CDCl_3$):δ 11.75 (s, 1H), 7.75 – 7.69 (m, 1H), 7.47 – 7.41 (m, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.23 – 7.14 (m, 1H), 2.54 (s, 2H), 2.38 (d, J = 4.4 Hz, 1H), 1.88 (d, J = 6.0 Hz, 2H), 1.76 (s, 2H), 1.61 (d, J = 12.8 Hz, 2H), 1.40 (t, J = 8.2 Hz, 3H), 1.26 (t, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 142.6, 137.0, 135.0, 129.0, 124.5, 121.9, 121.2, 115.5, 33.6, 29.4, 27.3, 26.2, 15.2. HRMS (ESI-TOF) m/z: [M+H]$^{+}$ Calculated for $C_{16}H_{18}BrNOH$ 320.0645, found 320.0649.

2,3-dicyclohexyl-2,3-dihydronaphthalene-1,4-dione（***40***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 100/1, Yield: 56%, 36.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (dd, J = 6.0, 3.6 Hz, 2H), 7.72 (dd, J =6.0, 3.6 Hz, 2H), 2.82 (d, J = 8.4 Hz, 2H), 1.87 (d, J = 12.4 Hz, 2H), 1.70 – 1.55 (m, 6H), 1.50 – 1.37 (m, 4H), 1.18 – 0.92 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.9, 134.6, 134.2, 126.5, 58.1, 40.4, 31.6, 31.0, 26.0, 25.9, 25.9. HRMS (ESI-TOF) m/z: [M+H]$^{+}$ Calculated for $C_{22}H_{28}O_2H$ 325.2162, found 325.2172.

2,3-dicyclohexyl-2-methyl-2,3-dihydronaphthalene-1,4-dione（***41***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 100/1, Yield: 49%, 33.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 – 7.94 (m, 1H), 7.90 – 7.86 (m, 1H), 7.70 – 7.64 (m, 2H), 2.78 (d, J = 2.0 Hz, 1H), 2.24 (d, J = 11.6 Hz, 1H), 2.15 (t, J = 11.6 Hz, 1H), 1.88 – 1.61 (m, 6H), 1.55 – 1.42 (m, 4H), 1.41 – 1.12 (m, 6H), 1.11 (s, 3H), 1.08 – 0.84 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.1,

199.4, 135.9, 135.1, 134.0, 133.3, 126.6, 125.5, 64.3, 52.2, 39.7, 36.7, 32.8, 31.6, 30.1, 29.2, 27.0, 26.9, 26.9, 26.8, 26.8, 26.3, 25.6, 21.9. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{23}H_{30}O_2H$ 339.2319, found 339.2328.

2,3-dicyclohexylnaphthalene-1,4-dione（***42***）. A colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, Yield: 43%, 27.7 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, J = 6.0, 3.6 Hz, 2H), 7.65 (dd, J = 6.0, 3.6 Hz, 2H), 3.07 (t, J = 11.6 Hz, 2H), 2.09 – 2.00 (m, 4H), 1.91 – 1.72 (m, 6H), 1.60 (d, J = 12.4 Hz, 4H), 1.35 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ185.9, 150.8, 133.0, 132.5, 125.9, 39.7, 30.5, 27.1, 25.9. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{22}H_{26}O_2H$ 323.2006, found 323.2016.

1-(cyclohexyloxy)-2,2,6,6-tetramethylpiperidine ***(43)***. A mixture of *N*-methyl-*N*-phenylmethacrylamide (1 equiv., 0.20 mmol), TFA (2 equiv., 0.40 mmol), cyclohexylboronic acid (5 equiv., 1 mmol) and TEMPO (5 eq, 1 mmol) was dissolved in a solution of acetic acid (0.25 mL) and acetonitrile (0.25 mL). The reaction vial was purged with O_2 for three times and then the reaction mixture was reflux at 110^{o}C (measured temperature of the oil bath) for 6 hours. After the reaction finished, the solvent was removed under reduced pressure, and purified by flash chromatography on silica gel to afford cyclohexanol and **43** as a colorless oil (petroleum ether/ethyl acetate =60/1- 20/1, Yield: 68%, 32.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.16 – 3.02 (m, 1H), 2.05 (dd, *J* = 9.6, 4.2 Hz, 2H), 1.73 (d, *J* = 2.8 Hz, 2H), 1.53 (d, *J* = 5.2 Hz, 6H), 1.45 (s, 4H), 1.21 (t, *J* = 10.0 Hz, 4H), 1.12 (s, 13H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 81.7, 59.6, 40.3, 32.9, 26.0, 25.1, 17.3. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for $C_{15}H_{29}NOH$ 240.2322, found 240.2330.

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Notes

The authors declare no competing financial interest.

Supporting Information

Experimental procedures, mechanistic studies, and characterization and spectral data. This material is available free of charge via the Internet at **http://pubs.acs.org**.

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