# Metal-Free Radical Cyclization of Vinyl Isocyanides with Alkanes: Synthesis of 1-Alkylisoquinolines 

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Abstract A metal-free radical cyclization reaction of vinyl isocyanides with alkanes is developed, allowing convenient access to a diverse range of potentially valuable 1-alkylisoquinolines. The methodology is simple and efficient, demonstrating excellent functional group tolerance and broad substrate scope. A mechanism involving a radical process is supported by kinetic isotope effect and radical inhibition studies.

Key words metal-free, radical cyclization reaction, vinyl isocyanides, alkanes, 1-alkylisoquinolines

The isoquinoline skeleton has been found in a large variety of natural products, bioactive molecules and pharma-
ceutical drugs. ${ }^{1}$ Bischler-Napieralski, Pomeranz-Fritsch and ety of natural products, bioactive molecules and pharma-
ceutical drugs. ${ }^{1}$ Bischler-Napieralski, Pomeranz-Fritsch and Pictet-Spengler reactions are traditional approaches for the synthesis of isoquinolines, but which suffer from the disadvantage of harsh reaction conditions. ${ }^{2}$ Consequently, the development of efficient syntheses of multisubstituted isoquinolines under mild conditions is significant.

In recent years, the functionalization of $\mathrm{C}-\mathrm{H}$ bonds to form C-C bonds has generated interest from the scientific community. ${ }^{3}$ Isocyanides, as uniquely versatile building blocks, can be employed to directly construct heterocycles with high efficiency. ${ }^{4}$ Under certain reaction conditions, processes in which the C-H bonds of alkanes can be functionalized via a radical pathway have been widely recogtionalized via a radical pathway have been widely recog-
nized. ${ }^{5}$ However, the cyclization of isocyanides with simple alkanes is scarcely reported. In 2014, Cheng and Liu developed an elegant new protocol for the modular synthesis of phenanthridines by using a free-radical cascade cyclization of biphenyl isocyanides with simple alkanes (Scheme 1). ${ }^{6}$ In 2017, we developed a microwave-assisted protocol for the synthesis of hydroxy-containing isoquinolines that involved



37 examples up to $89 \%$ yield synthesis of hydroxy-containing isoquinolines thatinvolved
a metal-free radical cyclization reaction of vinyl isocyanides with alcohols, requiring $30 \mathrm{~mol} \%$ of 1,8 -diazabicyclo-[5.4.0]undec-7-ene (DBU) to obtain the highest yields. ${ }^{4 n}$ Cheng and Liu's reports, along with our previous work, led us to reason that the reaction of vinyl isocyanides with simple alkanes would concisely synthesize different 1-alkylisoquinolines via a radical pathway. To the best of our knowledge, the synthesis of 1 -alkylisoquinolines by using easily accessible vinyl isocyanides in reactions with various alkanes has never been reported. The process would involve the formation of two $\mathrm{C}-\mathrm{C}$ bonds in one step (Scheme 1 ). This approach is amenable for the introduction of a wide range of alkyl and (hetero)aryl groups at the C1-position of


Scheme 1 Strategies for the preparation of 1-alkylisoquinolines
the isoquinoline. The methodology is very simple and efficient, demonstrating excellent functional group tolerance and broad substrate scope.

Initially, the reaction of methyl 2-isocyano-3,3-diphenylacrylate ( $\mathbf{1 a}$ ) with cyclohexane was chosen as a model system for optimization of the reaction conditions (Table 1).

Initiated by benzoyl peroxide (BPO), the desired product, methyl 1-cyclohexyl-4-phenylisoquinoline-3-carboxylate (2a), was obtained in 64\% yield (Table 1, entry 7). Dicumyl peroxide (DCP), potassium persulfate $\left(\mathrm{K}_{2} \mathrm{~S}_{2} \mathrm{O}_{8}\right)$, sodium persulfate $\left(\mathrm{Na}_{2} \mathrm{~S}_{2} \mathrm{O}_{8}\right)$, ammonium persulfate $\left[\left(\mathrm{NH}_{4}\right)_{2} \mathrm{~S}_{2} \mathrm{O}_{8}\right]$, iodobenzene diacetate $\left[\mathrm{PhI}(\mathrm{OAc})_{2}\right]$ and tert-
butyl peroxybenzoate (TBPB) as radical initiators proved less efficient than BPO (entries 1-7). In addition, it was found that the yield could be increased to $68 \%$ by using 30 $\mathrm{mol} \%$ of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base (entry 8). Raising the reaction temperature to $120^{\circ} \mathrm{C}$ resulted in a slightly decreased production of $\mathbf{2 a}$ (entry 9 ). On increasing the volume of cyclohexane to 5 mL , the yield of product 2a increased dramatically to $85 \%$ (entry 10). Lowering the reaction temperature to $80^{\circ} \mathrm{C}$ or changing the amount of radical initiator resulted in slightly decreased yields of 2a (entries 11-13). Optimization studies of the amount of DBU demonstrated that $30 \mathrm{~mol} \%$ of DBU was more efficient than $20 \mathrm{~mol} \%$ and $40 \mathrm{~mol} \%$ (entries 10,14


Scheme 2 Scope of the cyclization of substrate 1a with alkanes. Reagents and conditions: 1 a ( 0.2 mmol, 1 equiv), BPO ( 0.4 mmol, 2 equiv), DBU ( $30 \mathrm{~mol} \%, 0.06 \mathrm{mmol}$ ), alkane ( 5 mL ) (as solvent), $100^{\circ} \mathrm{C}, 2 \mathrm{~h}$, argon atmosphere. Yields are those of isolated products.

Table 1 Optimization of the Reaction Conditions ${ }^{\text {a }}$


| Entry | Oxidant (equiv) | Base (mol\%) | Solvent (mL) | Temp ( ${ }^{\circ} \mathrm{C}$ ) | Yield $(\%)^{b}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | DCP (2) | - | 2 | 100 | trace |
| 2 | $\mathrm{K}_{2} \mathrm{~S}_{2} \mathrm{O}_{8}$ (2) | - | 2 | 100 | trace |
| 3 | $\mathrm{Na}_{2} \mathrm{~S}_{2} \mathrm{O}_{8}(2)$ | - | 2 | 100 | trace |
| 4 | $\left(\mathrm{NH}_{4}\right)_{2} \mathrm{~S}_{2} \mathrm{O}_{8}(2)$ | - | 2 | 100 | trace |
| 5 | $\mathrm{PhI}(\mathrm{OAc})_{2}$ (2) | - | 2 | 100 | trace |
| 6 | TBPB (2) | - | 2 | 100 | 49 |
| 7 | BPO (2) | - | 2 | 100 | 64 |
| 8 | BPO (2) | DBU (30) | 2 | 100 | 68 |
| 9 | BPO (2) | DBU (30) | 2 | 120 | 65 |
| 10 | BPO (2) | DBU (30) | 5 | 100 | 85 |
| 11 | BPO (2) | DBU (30) | 5 | 80 | 53 |
| 12 | BPO (3) | DBU (30) | 5 | 100 | 75 |
| 13 | BPO (1.5) | DBU (30) | 5 | 100 | 68 |
| 14 | BPO (2) | DBU (20) | 5 | 100 | 73 |
| 15 | BPO (2) | DBU (40) | 5 | 100 | 69 |
| 16 | - | DBU (30) | 5 | 100 | trace |
| $17^{\text {c }}$ | BPO (2) | DBU (30) | 5 | 100 | 75 |
| 18 | BPO (2) | 2,2'-bipy (30) | 5 | 100 | 79 |
| 19 | BPO (2) | $\mathrm{Et}_{3} \mathrm{~N}$ (30) | 5 | 100 | 82 |
| 20 | BPO (2) | DABCO (30) | 5 | 100 | 63 |
| 21 | BPO (2) | $\mathrm{K}_{2} \mathrm{CO}_{3}(30)$ | 5 | 100 | 66 |
| $22^{\text {d }}$ | BPO (2) | DBU (30) | 5 | 100 | 84 |

${ }^{\text {a }}$ Reaction conditions: methyl 2-isocyano-3,3-diphenylacrylate (1a) (0.2 mmol, 1 equiv), radical initiator ( $0.4 \mathrm{mmol}, 2$ equiv), cyclohexane (as solvent), $100^{\circ} \mathrm{C}, 2 \mathrm{~h}$, under argon; unless otherwise noted.
${ }^{\mathrm{b}}$ Yield of isolated product.
${ }^{\text {c }}$ Reaction at $100^{\circ} \mathrm{C}$ for 1 h .
${ }^{\text {d }}$ Substrate 1 a (2 mmol) for 2 h .
and 15). Only a trace amount of the product was observed without BPO (entry 16). Shortening the reaction time to 1 hour resulted in a decrease in the yield of product $\mathbf{2 a}$ to $75 \%$ (entry 17). Two organic bases (2,2'-bipyridine, $\mathrm{Et}_{3} \mathrm{~N}$ ) were applied for this reaction, however, both gave slightly decreased yields compared to DBU (entries 18 and 19). Other bases including 1,4-diazabicyclo[2.2.2]octane (DABCO) and potassium carbonate $\left(\mathrm{K}_{2} \mathrm{CO}_{3}\right)$ proved less efficient than DBU



Scheme 3 Scope of the vinyl isocyanides. Reagents and conditions: isocyanide 1 ( $0.2 \mathrm{mmol}, 1$ equiv), BPO ( $0.4 \mathrm{mmol}, 2$ equiv), DBU ( $30 \mathrm{~mol} \%$, 0.06 mmol ), cyclohexane ( 5 mL ) (as solvent), $100^{\circ} \mathrm{C}$, argon atmosphere. Yields are those of isolated products.
(entries 20 and 21). To confirm the practicality of this method, we performed a larger scale reaction ( $1 \mathbf{a}, 2 \mathrm{mmol}$ ) and isolated product $\mathbf{2 a}$ in $84 \%$ yield (entry 22 ).

With optimized reaction conditions in hand, we next examined the scope of the alkanes in the cyclization reaction with 1a. It can be seen from Scheme 2 that cyclohexane, cyclopentane, cycloheptane and cyclooctane underwent cyclization with 1a to give the desired products 2a-d in good yields. Other alkanes such as toluene, phenylethane, 4-ethylpyridine, 3-ethylpyridine and 2-ethylpyridine gave the products $\mathbf{2 g}-\mathbf{k}$ in moderate yields. 2,2-Dimethylbutane and 2-ethylpyrazine gave the expected products $\mathbf{2 e}$ and $\mathbf{2 l}$ in low yields. It was noticed that the reaction of 3-methylpentane also proceeded smoothly, but with moderate regioselectivity to afford products $\mathbf{2 f}$ and $\mathbf{2 f}^{\prime}$.

Subsequently, we used a variety of vinyl isocyanides in the reaction with cyclohexane under the standardized conditions (Scheme 3). The reactions of diaryl ketone derived vinyl isocyanides with cyclohexane proceeded well and the corresponding isoquinolines 3a-g were isolated in yields of $70-85 \%$. The electronic properties of the substituents on both benzene rings did not affect the reaction. Reactions of substrates with differently substituted aromatic rings also proceeded smoothly, with the isoquinolines $\mathbf{3 f}, \mathbf{g}$ being isolated in good yields and with good regioselectivities. Furthermore, aliphatic aryl ketone derived vinyl isocyanides participated quite well in this reaction, affording the corresponding products $\mathbf{3 h}-\mathbf{p}$ in yields of $50-83 \%$. However, lower yields of the corresponding isoquinolines 3q-t were ob-
tained for aryl aldehyde derived vinyl isocyanides compared to those derived from ketones. It was observed that when a meta-substituent was present on the phenyl moiety of the aryl aldehyde derived vinyl isocyanide, the products 3t and 3t' were obtained in a non-regioselective manner. Substrates with ethyl ester or amide substituents at the terminal position of the vinyl group also worked well in this reaction to afford isoquinolines $\mathbf{3 u} \mathbf{u} \mathbf{w}$.

To investigate the reaction mechanism, a series of competing kinetic isotope effect (KIE) experiments were carried out (Scheme 4). A significant KIE was found with the ratio of 4.9:1 $\left(k_{\mathrm{H}} / k_{\mathrm{D}}\right)$ in the experiment conducted between 1a, cyclohexane and $\left[\mathrm{D}_{12}\right]$-cyclohexane. The result showed that cleavage of the $\mathrm{C}\left(\mathrm{sp}^{3}\right)-\mathrm{H}$ bonds to form alkane radicals may be involved in the rate-determining step of this procedure. On the other hand, no kinetic isotope effects $\left(k_{\mathrm{H}} / k_{\mathrm{D}}=\right.$ 1:1) were observed in the intermolecular experiment $\mathbf{1 a} /\left[\mathrm{D}_{10}\right]-\mathbf{1 a}$. This proved that the reaction proceeded through a free-radical substitution. ${ }^{7}$ Next, it was found that the reaction was suppressed remarkably when the scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was added, the trapping product $\mathbf{4}$ being detected by mass spectrometry (Scheme 5). This observation further supports the reaction proceeding via a radical process.

Based on these observations, a plausible reaction mechanism has been proposed (Scheme 6). Firstly, the homolytic cleavage of BPO forms benzoyl radicals, which abstract a proton from cyclohexane to form cyclohexanyl radical I. Next, intermediate II was obtained by a radical addition



Scheme 5 Radical inhibition studies
process, followed by intramolecular radical cyclization to yield radical III. A proton is then abstracted from intermediate III by a benzoyl radical to from isoquinoline 2a. Meanwhile, DBU as base can promote the conversion of radical III in radical anion IV, which is oxidized by BPO to form 2a. ${ }^{4}$

In summary, a metal-free tandem oxidative cyclization reaction of vinyl isocyanides with alkanes to synthesize 1alkylisoquinolines in moderate to good yields has been developed. The present method offers a unique strategy for the convenient preparation of pharmacologically interesting isoquinolines with excellent functional group tolerance and broad substrate scope. This approach is amenable for the introduction of a wide range of alkyl and (hetero)aryl moieties onto the isoquinoline framework.

Purchased reagents were used without further purification. The vinyl isocyanide substrates were prepared following literature methods. ${ }^{4 d-f}$ All reactions were carried out under an argon atmosphere. Column
chromatography was performed using Rushan Taiyang Desiccant Co., Ltd. silica gel (200-300 mesh). Melting points were recorded by thermal analysis method based on a WRS-1B digital instrument. ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR spectra were recorded on Varian 400 MHz and Bruker 600 MHz spectrometers, respectively. ESI-HRMS (high-resolution mass spectrometry) spectra were obtained on an AB SCIEX TRIPLE TOF 5600+ mass spectrometer.

## Isoquinolines 2 and 3; General Procedure

A sealed tube was charged with the vinyl isocyanide $\mathbf{1}(0.2 \mathrm{mmol}, 1$ equiv), DBU ( $30 \mathrm{~mol} \%, 0.06 \mathrm{mmol}$ ), BPO ( $0.4 \mathrm{mmol}, 2$ equiv) and the alkane ( 5 mL ). The reaction tube was charged with argon three times and the mixture then stirred at $100^{\circ} \mathrm{C}$ for 2 h . EtOAc ( 10 mL ) and saturated $\mathrm{NaHCO}_{3}$ solution ( 10 mL ) were added, the organic layer was separated and the aqueous phase was extracted with EtOAc ( $2 \times 10$ $\mathrm{mL})$. The combined organic layers were washed with $\mathrm{H}_{2} \mathrm{O}(2 \times 10 \mathrm{~mL})$ and brine $(1 \times 10 \mathrm{~mL})$, then dried over anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$. The solvent was removed and the resulting residue purified by silica gel column chromatography to afford the desired product $\mathbf{2}$ or $\mathbf{3}$.

Methyl 1-Cyclohexyl-4-phenylisoquinoline-3-carboxylate (2a)
Product 2a ( $58.4 \mathrm{mg}, 85 \%$ ) was obtained as a white solid after purification by column chromatography (PE/EtOAc, 99:1).
Mp 136.1-138.5 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=8.31(\mathrm{~d}, \mathrm{~J}=8.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.69-7.57(\mathrm{~m}, 3$ H), 7.52-7.42 (m, 3 H ), 7.35 (d, $J=6.5 \mathrm{~Hz}, 2 \mathrm{H}$ ), 3.66 ( $\mathrm{s}, 3 \mathrm{H}$ ), 3.60 (d, J = $11.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.05(\mathrm{~d}, J=10.1 \mathrm{~Hz}, 2 \mathrm{H}), 2.01-1.90(\mathrm{~m}, 4 \mathrm{H}), 1.83(\mathrm{~d}, J=$ $12.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.56(\mathrm{q}, J=12.9 \mathrm{~Hz}, 2 \mathrm{H}), 1.42(\mathrm{dd}, J=25.2,12.7 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.7,164.5,140.8,135.8,135.2$, $130.6,129.34,129.31,127.5,127.3,127.1,126.6,126.0,124.1,51.5$, 41.2, 31.7, 26.2, 25.5.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{23} \mathrm{H}_{24} \mathrm{NO}_{2}$ : 346.1802; found: 346.1807.


Scheme 6 A plausible mechanism

## Methyl 1-Cyclopentyl-4-phenylisoquinoline-3-carboxylate (2b)

Product $\mathbf{2 b}$ ( $54.4 \mathrm{mg}, 82 \%$ ) was obtained as a colorless oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.33(\mathrm{~d}, J=7.9 \mathrm{~Hz}, 1 \mathrm{H}), 7.64(\mathrm{dd}, J=$ $17.4,8.2 \mathrm{~Hz}, 3 \mathrm{H}), 7.47$ (d, J = $7.3 \mathrm{~Hz}, 3 \mathrm{H}$ ), 7.34 (d, $J=6.8 \mathrm{~Hz}, 2 \mathrm{H}$ ), 4.06 (quin, $J=7.9 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.66 (s, 3 H ), 2.20 (s, 4 H ), 1.94 (s, 2 H ), 1.79 (d, $J=4.5 \mathrm{~Hz}, 2 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.7,163.5,140.4,135.8,135.2$, 130.8, 129.4, 129.3, 127.5, 127.3, 127.1, 126.8, 126.4, 124.6, 51.5, 42.8, 31.9, 25.4.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{22} \mathrm{H}_{22} \mathrm{NO}_{2}$ : 332.1645; found: 332.1652.

## Methyl 1-Cycloheptyl-4-phenylisoquinoline-3-carboxylate (2c)

Product $\mathbf{2 c}$ ( $63.7 \mathrm{mg}, 89 \%$ ) was obtained as a colorless oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 99: 1$ ).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.29(\mathrm{~d}, J=8.5 \mathrm{~Hz}, 1 \mathrm{H}), 7.65(\mathrm{dd}, J=7.0$, $5.8 \mathrm{~Hz}, 2 \mathrm{H}), 7.60(\mathrm{dd}, J=8.3,6.0 \mathrm{~Hz}, 1 \mathrm{H}), 7.52-7.41(\mathrm{~m}, 3 \mathrm{H}), 7.35(\mathrm{~d}$, $J=6.5 \mathrm{~Hz}, 2 \mathrm{H}), 3.79(\mathrm{dq}, J=13.8,6.9 \mathrm{~Hz}, 1 \mathrm{H}), 3.65(\mathrm{~s}, 3 \mathrm{H}), 2.12$ (dd, $J=10.5,5.4 \mathrm{~Hz}, 4 \mathrm{H}), 1.99-1.91$ (m, 2 H$), 1.82-1.67$ (m, 6 H ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.2,166.3,141.1,136.3,135.7$, $130.9,129.7,128.0,127.7,127.6,127.0,126.1,124.7,52.0,43.5,34.1$, 28.0, 27.4.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{24} \mathrm{H}_{26} \mathrm{NO}_{2}$ : 360.1958 ; found: 360.1963.

## Methyl 1-Cyclooctyl-4-phenylisoquinoline-3-carboxylate (2d)

Product $\mathbf{2 d}$ ( $61.0 \mathrm{mg}, 82 \%$ ) was obtained as a light yellow oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 99: 1$ ).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.30(\mathrm{~s}, 1 \mathrm{H}), 7.63(\mathrm{~d}, \mathrm{~J}=17.6 \mathrm{~Hz}, 3 \mathrm{H})$, 7.47 (s, 3 H), 7.35 (s, 2 H), $3.90(\mathrm{~s}, 1 \mathrm{H}), 3.66$ (s, 3 H), 2.17 (s, 2 H ), 2.09 (s, 2 H ), 1.92 ( $\mathrm{s}, 2 \mathrm{H}$ ), 1.73 ( $\mathrm{s}, 8 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.3,166.1,140.2,135.4,135.0$, 130.0, 128.9, 127.1, 126.8, 126.7, 126.2, 125.3, 123.9, 51.1, 31.9, 28.7, 25.8, 25.7, 25.3.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{25} \mathrm{H}_{28} \mathrm{NO}_{2}$ : 374.2115; found: 374.2123.

Methyl 1-(3,3-Dimethylbutan-2-yl)-4-phenylisoquinoline-3-carboxylate (2e)
Product $\mathbf{2 e}$ ( $22.0 \mathrm{mg}, 32 \%$ ) was obtained as a colorless oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 99: 1$ ).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.39(\mathrm{~d}, J=8.1 \mathrm{~Hz}, 1 \mathrm{H}), 7.61(\mathrm{dt}, J=$ $13.5,7.0 \mathrm{~Hz}, 3 \mathrm{H}), 7.52-7.41$ (m, 3 H ), 7.37 (d, J = $6.1 \mathrm{~Hz}, 2 \mathrm{H}$ ), 3.77 (dt, $J=25.8,12.9 \mathrm{~Hz}, 1 \mathrm{H}), 3.67(\mathrm{~s}, 3 \mathrm{H}), 1.48-1.43(\mathrm{~m}, 3 \mathrm{H}), 1.02(\mathrm{~d}, J=23.2$ $\mathrm{Hz}, 9 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.7,164.0,140.3,135.8,135.0$, 130.1, 129.4, 129.1, 127.6, 127.5, 127.1, 127.0, 126.5, 124.7. 51.5, 43.1, 34.5, 27.9, 27.7, 15.4.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{23} \mathrm{H}_{26} \mathrm{NO}_{2}$ : 348.1958 ; found: 348.1960.

Methyl 1-(3-Methylpentan-2-yl)-4-phenylisoquinoline-3-carboxylate (2f)
Product $\mathbf{2 f}$ ( $12.1 \mathrm{mg}, 17 \%$ ) was obtained as a white solid after purification by column chromatography (PE/EtOAc, 99:1).

Mp 60.5-62.9 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=8.31(\mathrm{~d}, J=7.1 \mathrm{~Hz}, 1 \mathrm{H}), 7.64(\mathrm{dd}, J=$ $18.7,8.0 \mathrm{~Hz}, 3 \mathrm{H}$ ), 7.47 ( $\mathrm{s}, 3 \mathrm{H}$ ), 7.41-7.30 (m, 2 H ), 4.82 ( $\mathrm{s}, 1 \mathrm{H}$ ), 3.65 ( $\mathrm{s}, 3 \mathrm{H}$ ), $2.15(\mathrm{~s}, 1 \mathrm{H}), 1.74(\mathrm{~s}, 2 \mathrm{H}), 1.43(\mathrm{t}, J=7.5 \mathrm{~Hz}, 3 \mathrm{H}), 0.91$ (ddd, $J=$ $34.7,23.5,6.5 \mathrm{~Hz}, 6 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.4,165.6,165.4,141.5,141.4$, 136.4, 135.8, 130.8, 130.0, 129.9, 128.2, 128.1, 127.80, 127.78, 127.4, 127.2, 127.1, 124.9, 124.8, 52.1, 41.6, 40.9, 39.3, 28.5, 25.6, 17.9, 17.3, 15.9, 15.5, 11.9, 11.1.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{23} \mathrm{H}_{26} \mathrm{NO}_{2}$ : 348.1958 ; found: 348.1966.

## Methyl 1-(3-Methylpentan-3-yl)-4-phenylisoquinoline-3-carboxylate (2f')

Product 2f' $\mathbf{~}^{\prime} 23.9 \mathrm{mg}, 34 \%$ ) was obtained as a white solid after purification by column chromatography (PE/EtOAc, 99:1).
Mp 94.2-95.8 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=8.63(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 1 \mathrm{H}), 7.72-7.64(\mathrm{~m}, 1$ H), 7.58 (dd, $J=13.8,7.4 \mathrm{~Hz}, 2 \mathrm{H}), 7.52-7.44(\mathrm{~m}, 3 \mathrm{H}), 7.35(\mathrm{~d}, J=6.5$ $\mathrm{Hz}, 2 \mathrm{H}$ ), 3.66 ( $\mathrm{s}, 3 \mathrm{H}$ ), 2.35 (dq, $J=14.6,7.4 \mathrm{~Hz}, 2 \mathrm{H}$ ), 2.01 (dq, $J=14.6$, $7.4 \mathrm{~Hz}, 2 \mathrm{H}), 1.63(\mathrm{~s}, 3 \mathrm{H}), 0.74(\mathrm{t}, J=7.4 \mathrm{~Hz}, 6 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.3,164.8,140.0,136.6,136.5$, $131.5,130.0,129.2,128.1,127.8,127.7,127.4,126.9,126.1,52.1,47.8$, 34.2, 25.6, 9.2.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{23} \mathrm{H}_{26} \mathrm{NO}_{2}$ : 348.1958 ; found: 348.1966.

## Methyl 1-Benzyl-4-phenylisoquinoline-3-carboxylate (2g)

Product $\mathbf{2 g}$ ( $32.1 \mathrm{mg}, 45 \%$ ) was obtained as a light yellow oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 49: 1$ ).
${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.21(\mathrm{~d}, \mathrm{~J}=5.0 \mathrm{~Hz}, 1 \mathrm{H}), 7.63(\mathrm{~d}, J=4.9$ $\mathrm{Hz}, 1 \mathrm{H}), 7.58(\mathrm{~d}, J=8.1 \mathrm{~Hz}, 2 \mathrm{H}), 7.49(\mathrm{t}, J=6.8 \mathrm{~Hz}, 3 \mathrm{H}), 7.39-7.32(\mathrm{~m}$, $4 \mathrm{H}), 7.27(\mathrm{t}, J=7.3 \mathrm{~Hz}, 2 \mathrm{H}), 7.19(\mathrm{t}, \mathrm{J}=7.2 \mathrm{~Hz}, 1 \mathrm{H}), 4.80(\mathrm{~s}, 2 \mathrm{H}), 3.72$ ( $\mathrm{s}, 3 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.1,159.1,140.3,138.4,135.6$, $135.5,132.4,129.8,129.2,128.0,127.8,127.6,127.3,127.0,126.6$, 125.8, 125.4, 51.8, 41.7, 29.1.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{24} \mathrm{H}_{20} \mathrm{NO}_{2}$ : 354.1489; found: 354.1491.

## Methyl 4-Phenyl-1-(1-phenylethyl)isoquinoline-3-carboxylate

 (2h)Product $\mathbf{2 h}$ ( $45.2 \mathrm{mg}, 62 \%$ ) was obtained as a light yellow oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.26-8.19(\mathrm{~m}, 1 \mathrm{H}), 7.61(\mathrm{dd}, J=6.3,2.7$ $\mathrm{Hz}, 1 \mathrm{H}$ ), 7.52 (dd, $J=6.5,3.1 \mathrm{~Hz}, 2 \mathrm{H}$ ), 7.48 (d, $J=7.1 \mathrm{~Hz}, 2 \mathrm{H}), 7.37$ (dd, $J=17.0,7.6 \mathrm{~Hz}, 5 \mathrm{H}$ ), 7.27 (t, $J=7.7 \mathrm{~Hz}, 2 \mathrm{H}$ ), 7.15 (dd, $J=15.6,7.8$ $\mathrm{Hz}, 1 \mathrm{H}), 5.09(\mathrm{q}, J=6.9 \mathrm{~Hz}, 1 \mathrm{H}), 3.69(\mathrm{~d}, J=6.4 \mathrm{~Hz}, 3 \mathrm{H}), 1.90(\mathrm{~d}, J=6.9$ $\mathrm{Hz}, 3 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.5,162.4,145.8,141.4,136.5$, 136.2, 132.2, 130.2, 130.1, 130.0, 129.3, 128.8, 128.7, 128.4, 128.3, 128.2, 128.1, 127.9, 127.3, 126.5, 125.5, 52.4, 44.0, 29.9, 22.1.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{25} \mathrm{H}_{22} \mathrm{NO}_{2}$ : 368.1645 ; found: 368.1649.

Methyl 4-Phenyl-1-[1-(pyridin-4-yl)ethyl]isoquinoline-3-carboxylate (2i)
Product 2 ( $32.6 \mathrm{mg}, 44 \%$ ) was obtained as a light yellow oil after purification by column chromatography (PE/EtOAc, 9:1).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.52(\mathrm{~s}, 2 \mathrm{H}), 8.12(\mathrm{dd}, J=6.1,3.3 \mathrm{~Hz}, 1$ H), 7.69-7.63 (m, 1 H ), 7.59 (dd, $J=6.5,3.1 \mathrm{~Hz}, 2 \mathrm{H}$ ), $7.53-7.46$ (m, 3 H), 7.39 (d, $J=5.2 \mathrm{~Hz}, 2 \mathrm{H}$ ), $7.35(\mathrm{t}, J=7.8 \mathrm{~Hz}, 2 \mathrm{H}), 5.10(\mathrm{q}, J=6.9 \mathrm{~Hz}, 1$ H), 3.69 ( $\mathrm{s}, 3 \mathrm{H}$ ), 1.91 (d, $J=7.0 \mathrm{~Hz}, 3 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.3,159.7,154.7,148.3,140.7$, 135.5, 135.3, 131.9, 129.7, 129.3, 129.1, 127.8, 127.6, 127.4, 126.8, 126.2, 123.9, 122.8, 51.6, 42.4, 29.1, 20.6.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{24} \mathrm{H}_{21} \mathrm{~N}_{2} \mathrm{O}_{2}$ : 369.1598; found: 369.1601.

## Methyl 4-Phenyl-1-[1-(pyridin-3-yl)ethyl]isoquinoline-3-carboxylate ( 2 j )

Product $\mathbf{2 j}$ ( $29.5 \mathrm{mg}, 40 \%$ ) was obtained as a light yellow oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 9: 1$ ).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.81(\mathrm{~s}, 1 \mathrm{H}), 8.48(\mathrm{~s}, 1 \mathrm{H}), 8.22(\mathrm{~d}, \mathrm{~J}=$ $7.7 \mathrm{~Hz}, 1 \mathrm{H}), 7.86(\mathrm{~d}, J=7.2 \mathrm{~Hz}, 1 \mathrm{H}), 7.68-7.56(\mathrm{~m}, 3 \mathrm{H}), 7.48(\mathrm{~s}, 3 \mathrm{H})$, 7.33 (d, J = $5.9 \mathrm{~Hz}, 2 \mathrm{H}), 7.28(\mathrm{~s}, 1 \mathrm{H}), 5.17(\mathrm{~d}, J=6.7 \mathrm{~Hz}, 1 \mathrm{H}), 3.68(\mathrm{~s}, 3$ H), 1.90 (d, $J=6.9 \mathrm{~Hz}, 3 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.4,160.1,148.0,146.6,135.5$, 135.4, 131.7, 129.7, 129.3, 129.1, 127.9, 127.6, 127.4, 126.8, 126.1, 123.9, 51.6, 40.0, 29.1, 21.3.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{24} \mathrm{H}_{21} \mathrm{~N}_{2} \mathrm{O}_{2}$ : 369.1598; found: 369.1603.

## Methyl 4-Phenyl-1-[1-(pyridin-2-yl)ethyl]isoquinoline-3-carbox-

 ylate ( 2 k )Product $\mathbf{2 k}$ ( $31.6 \mathrm{mg}, 43 \%$ ) was obtained as a light yellow oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 9: 1$ ).
${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.57(\mathrm{~d}, J=4.3 \mathrm{~Hz}, 1 \mathrm{H}), 8.42(\mathrm{~d}, J=8.0$ $\mathrm{Hz}, 1 \mathrm{H}), 7.64-7.54(\mathrm{~m}, 4 \mathrm{H}), 7.48(\mathrm{~d}, J=6.7 \mathrm{~Hz}, 3 \mathrm{H}), 7.35(\mathrm{~d}, J=6.6 \mathrm{~Hz}$, $3 \mathrm{H}), 7.15(\mathrm{~d}, J=5.7 \mathrm{~Hz}, 1 \mathrm{H}), 5.40(\mathrm{~d}, J=6.1 \mathrm{~Hz}, 1 \mathrm{H}), 3.69(\mathrm{~s}, 3 \mathrm{H}), 1.95$ (d, $J=7.0 \mathrm{~Hz}, 3 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.6,140.6,135.6,135.4,131.7$, $129.5,129.3,129.2,127.7,127.6,127.5,127.3,126.8,126.4,125.1$, 121.0, 51.5, 29.1, 19.7.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{24} \mathrm{H}_{21} \mathrm{~N}_{2} \mathrm{O}_{2}$ : 369.1598; found: 369.1603.

Methyl 4-Phenyl-1-[1-(pyrazin-2-yl)ethyl]isoquinoline-3-carboxylate (21)
Product $2 \mathbf{l}$ ( $20.1 \mathrm{mg}, 27 \%$ ) was obtained as a brown oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 9: 1$ ).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.73(\mathrm{~s}, 1 \mathrm{H}), 8.53(\mathrm{~s}, 1 \mathrm{H}), 8.42(\mathrm{~s}, 1 \mathrm{H})$, $8.33(\mathrm{~d}, J=7.9 \mathrm{~Hz}, 1 \mathrm{H}), 7.62(\mathrm{~d}, J=11.9 \mathrm{~Hz}, 2 \mathrm{H}), 7.47(\mathrm{t}, J=9.9 \mathrm{~Hz}, 4$ H), 7.34 (d, $J=7.2 \mathrm{~Hz}, 2 \mathrm{H}$ ), $5.47-5.36(\mathrm{~m}, 1 \mathrm{H}), 3.68(\mathrm{~s}, 3 \mathrm{H}), 2.00(\mathrm{~d}, J=$ $6.9 \mathrm{~Hz}, 3 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.2,159.7,159.0,144.2,142.8$, 141.6, 140.5, 135.6, 135.4, 132.7, 132.0, 129.7, 129.3, 129.1, 127.9, 127.6, 127.4, 126.7, 124.5, 51.6, 44.0, 29.1, 19.4.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{23} \mathrm{H}_{20} \mathrm{~N}_{3} \mathrm{O}_{2}$ : 370.1550; found: 370.1553.

## Methyl 1-Cyclohexyl-7-fluoro-4-(4-fluorophenyl)isoquinoline-3-

 carboxylate (3a)Product $\mathbf{3 a}$ ( $57.9 \mathrm{mg}, 76 \%$ ) was obtained as a colorless oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 99: 1$ ).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=7.86(\mathrm{~d}, J=10.0 \mathrm{~Hz}, 1 \mathrm{H}), 7.63-7.54(\mathrm{~m}$, $1 \mathrm{H}), 7.36(\mathrm{t}, J=8.5 \mathrm{~Hz}, 1 \mathrm{H}), 7.30-7.24(\mathrm{~m}, 2 \mathrm{H}), 7.15(\mathrm{dd}, J=8.4,7.0$ $\mathrm{Hz}, 2 \mathrm{H}), 3.66(\mathrm{~d}, J=1.4 \mathrm{~Hz}, 3 \mathrm{H}), 3.42(\mathrm{t}, J=10.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.98(\mathrm{~d}, J=$ $11.8 \mathrm{~Hz}, 2 \mathrm{H}), 1.90(\mathrm{t}, J=12.8 \mathrm{~Hz}, 4 \mathrm{H}), 1.80(\mathrm{~d}, J=11.3 \mathrm{~Hz}, 1 \mathrm{H}), 1.59-$ $1.50(\mathrm{~m}, 2 \mathrm{H}), 1.39(\mathrm{t}, \mathrm{J}=12.1 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C} \operatorname{NMR}\left(151 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=167.8,164.5(\mathrm{~d}, J=5.3 \mathrm{~Hz}), 162.4(\mathrm{~d}, \mathrm{~J}=$ $247.6 \mathrm{~Hz}), 161.5(\mathrm{~d}, J=250.8 \mathrm{~Hz}), 140.9,132.8,131.9,131.4(\mathrm{~d}, J=7.9$ $\mathrm{Hz}), 130.0,129.7(\mathrm{~d}, J=8.6 \mathrm{~Hz}), 127.6(\mathrm{~d}, J=8.0 \mathrm{~Hz}), 120.2(\mathrm{~d}, J=24.8$ $\mathrm{Hz}), 115.2(\mathrm{~d}, J=21.6 \mathrm{~Hz}), 108.5(\mathrm{~d}, J=21.6 \mathrm{~Hz}), 52.1,41.9,32.0,26.6$, 25.9.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{23} \mathrm{H}_{22} \mathrm{~F}_{2} \mathrm{NO}_{2}$ : 382.1613; found: 382.1615.

Methyl 7-Chloro-4-(4-chlorophenyl)-1-cyclohexylisoquinoline-3carboxylate (3b)
Product $\mathbf{3 b}$ ( $62.1 \mathrm{mg}, 75 \%$ ) was obtained as a white solid after purification by column chromatography (PE/EtOAc, 99:1).
Mp 147.4-149.1 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=8.25(\mathrm{~s}, 1 \mathrm{H}), 7.58-7.51(\mathrm{~m}, 2 \mathrm{H}), 7.46$ (d, $J=8.1 \mathrm{~Hz}, 2 \mathrm{H}$ ), 7.25 (d, $J=8.1 \mathrm{~Hz}, 2 \mathrm{H}), 3.70(\mathrm{~s}, 3 \mathrm{H}), 3.50(\mathrm{dd}, J=$ $14.7,7.1 \mathrm{~Hz}, 1 \mathrm{H}), 2.02-1.90(\mathrm{~m}, 6 \mathrm{H}), 1.83(\mathrm{~d}, \mathrm{~J}=12.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.56$ (dd, $J=23.4,10.6 \mathrm{~Hz}, 2 \mathrm{H}$ ), 1.42 ( $\mathrm{s}, 1 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.8,164.8,141.6,134.5,134.4$, 134.3, 134.2, 131.3, 131.2, 130.0, 128.8, 128.7. 127.4, 124.0, 52.4, 41.9, 32.4, 27.0, 26.7, 26.1.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{23} \mathrm{H}_{22} \mathrm{Cl}_{2} \mathrm{NO}_{2}$ : 414.1022; found: 414.1023.

Methyl 7-Bromo-4-(4-bromophenyl)-1-cyclohexylisoquinoline-3carboxylate (3c)
Product $\mathbf{3 c}$ ( $70.2 \mathrm{mg}, 70 \%$ ) was obtained as a colorless oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.34(\mathrm{~s}, 1 \mathrm{H}), 7.59(\mathrm{~d}, J=9.0 \mathrm{~Hz}, 1 \mathrm{H})$, $7.53(\mathrm{~d}, J=8.2 \mathrm{~Hz}, 2 \mathrm{H}), 7.37(\mathrm{~d}, J=9.0 \mathrm{~Hz}, 1 \mathrm{H}), 7.11(\mathrm{~d}, J=8.2 \mathrm{~Hz}, 2 \mathrm{H})$, $3.62(\mathrm{~s}, 3 \mathrm{H}), 3.41(\mathrm{dd}, J=15.0,7.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.91(\mathrm{~d}, J=14.1 \mathrm{~Hz}, 4 \mathrm{H})$, $1.83(\mathrm{~d}, J=13.6 \mathrm{~Hz}, 2 \mathrm{H}), 1.73(\mathrm{~s}, 1 \mathrm{H}), 1.48(\mathrm{~d}, J=12.7 \mathrm{~Hz}, 2 \mathrm{H}), 1.35(\mathrm{~d}$, $J=9.7 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.1,164.1,140.9,134.2,133.6$, 133.0, 130.93, 130.86, 129.4, 128.1, 127.0, 126.6, 122.1, 121.7, 51.7, 41.1, 31.7, 26.3, 26.0, 25.4.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{23} \mathrm{H}_{22}{ }^{79} \mathrm{Br}^{81} \mathrm{BrNO}_{2}$ : 503.9993; found: 503.9995.

## Methyl 1-Cyclohexyl-7-methyl-4-(p-tolyl)isoquinoline-3-carboxylate (3d)

Product $\mathbf{3 d}$ ( $61.2 \mathrm{mg}, 82 \%$ ) was obtained as a colorless oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.03(\mathrm{~s}, 1 \mathrm{H}), 7.56(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 1 \mathrm{H})$, $7.41(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 1 \mathrm{H}), 7.27(\mathrm{~d}, J=7.7 \mathrm{~Hz}, 2 \mathrm{H}), 7.21(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 2 \mathrm{H})$, $3.68(\mathrm{~s}, 3 \mathrm{H}), 3.57(\mathrm{t}, J=11.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.57(\mathrm{~s}, 3 \mathrm{H}), 2.44(\mathrm{~s}, 3 \mathrm{H}), 2.04-$ $1.88(\mathrm{~m}, 6 \mathrm{H}), 1.82(\mathrm{~d}, J=12.4 \mathrm{~Hz}, 1 \mathrm{H}), 1.56(\mathrm{q}, J=13.1 \mathrm{~Hz}, 2 \mathrm{H}), 1.43$ $(\mathrm{t}, J=12.6 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.9,163.5,139.9,137.3,136.7$, 133.6, 133.0, 131.4, 130.7, 129.1, 128.3, 126.5, 126.2, 123.0, 51.5, 41.0, 31.7, 26.2, 25.5, 20.8.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{25} \mathrm{H}_{28} \mathrm{NO}_{2}: 374.2115$; found: 374.2118.

## Methyl 1-Cyclohexyl-7-methoxy-4-(4-methoxyphenyl)isoquino-line-3-carboxylate (3e)

Product 3 e ( $62.9 \mathrm{mg}, 78 \%$ ) was obtained as a white solid after purification by column chromatography (PE/EtOAc, 99:1).
Mp 128.7-130.4 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=7.60(\mathrm{~d}, J=9.2 \mathrm{~Hz}, 1 \mathrm{H}), 7.51(\mathrm{~d}, \mathrm{~J}=1.7$ Hz, 1 H), 7.29-7.21 (m, 3 H ), 7.00 (d, J = $8.5 \mathrm{~Hz}, 2 \mathrm{H}$ ), 3.98 (s, 3 H ), 3.88 ( $\mathrm{s}, 3 \mathrm{H}), 3.69(\mathrm{~s}, 3 \mathrm{H}), 3.48(\mathrm{t}, \mathrm{J}=11.1 \mathrm{~Hz}, 1 \mathrm{H}), 2.04(\mathrm{~d}, J=10.7 \mathrm{~Hz}, 2 \mathrm{H})$, 1.94 (dd, $J=21.8,12.2 \mathrm{~Hz}, 4 \mathrm{H}), 1.82(\mathrm{~d}, J=12.2 \mathrm{~Hz}, 1 \mathrm{H}), 1.55(\mathrm{q}, J=$ $13.2 \mathrm{~Hz}, 2 \mathrm{H}), 1.48-1.38$ (m, 1 H ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.3,162.8,159.0,158.8,139.6$, $131.3,131.0,130.8,128.8,128.6,127.9,121.6,113.5,103.2,55.3,55.1$, 51.9, 41.8, 31.9, 26.7, 26.0.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{25} \mathrm{H}_{28} \mathrm{NO}_{4}$ : 406.2013; found: 406.2016.

## Methyl 1-Cyclohexyl-7-fluoro-4-(4-methoxyphenyl)isoquinoline-

 3-carboxylate (3f)Product $\mathbf{3 f}$ ( $55.8 \mathrm{mg}, 71 \%$ ) was obtained as a brown oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=7.82(\mathrm{~d}, J=10.2 \mathrm{~Hz}, 1 \mathrm{H}), 7.66(\mathrm{dd}, J=$ $9.1,5.8 \mathrm{~Hz}, 1 \mathrm{H}), 7.32(\mathrm{t}, \mathrm{J}=8.6 \mathrm{~Hz}, 1 \mathrm{H}), 7.20(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 2 \mathrm{H}), 6.96$ (d, $J=8.3 \mathrm{~Hz}, 2 \mathrm{H}), 3.83(\mathrm{~s}, 3 \mathrm{H}), 3.64(\mathrm{~s}, 3 \mathrm{H}), 3.39(\mathrm{t}, J=11.0 \mathrm{~Hz}, 1 \mathrm{H})$, $2.01-1.81(\mathrm{~m}, 6 \mathrm{H}), 1.76(\mathrm{~d}, \mathrm{~J}=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.57-1.42(\mathrm{~m}, 2 \mathrm{H}), 1.40-$ 1.31 (m, 1 H ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.3,163.1(\mathrm{~d}, \mathrm{~J}=5.3 \mathrm{~Hz}), 160.5(\mathrm{~d}, \mathrm{~J}=$ $250.2 \mathrm{~Hz}), 158.3,140.4,132.2,130.0,129.6,129.1(\mathrm{~d}, J=8.6 \mathrm{~Hz})$, $127.0,126.7(\mathrm{~d}, J=8.0 \mathrm{~Hz}), 119.1(\mathrm{~d}, J=24.8 \mathrm{~Hz}), 112.7,107.5(\mathrm{~d}, J=$ $21.6 \mathrm{~Hz}), 54.2,51.2,40.9,28.7,28.5,25.7,25.0$.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{24} \mathrm{H}_{25} \mathrm{FNO}_{3}$ : 394.1813; found: 394.1816.

## Methyl 1-Cyclohexyl-4-(4-fluorophenyl)-7-methoxyisoquinoline-3-carboxylate (3g)

Product 3 g ( $10.1 \mathrm{mg}, 13 \%$ ) was obtained as a colorless oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=7.45(\mathrm{~d}, \mathrm{~J}=10.2 \mathrm{~Hz}, 2 \mathrm{H}), 7.22(\mathrm{~s}, 3 \mathrm{H})$, 7.11 (s, 2 H ), 3.94 ( s, 3 H ), 3.63 ( s, 3 H ), 3.40 (d, J = $26.3 \mathrm{~Hz}, 1 \mathrm{H}$ ), 2.03$1.86(\mathrm{~m}, 6 \mathrm{H}), 1.77(\mathrm{~d}, J=11.5 \mathrm{~Hz}, 1 \mathrm{H}), 1.50(\mathrm{~d}, J=12.7 \mathrm{~Hz}, 2 \mathrm{H}), 1.38$ ( $\mathrm{t}, \mathrm{J}=11.8 \mathrm{~Hz}, 1 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.5,162.9,161.8(\mathrm{~d}, J=246.9 \mathrm{~Hz})$, $158.5,138.7,132.0,130.8$ (d, $J=7.9 \mathrm{~Hz}$ ), 130.6, 130.2, 128.1, 127.5, $121.5,114.6(\mathrm{~d}, \mathrm{~J}=21.4 \mathrm{~Hz}), 102.8,54.9,51.5,41.3,31.5,29.1,26.2$, 25.5.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{24} \mathrm{H}_{25} \mathrm{FNO}_{3}$ : 394.1813; found: 394.1817.

## Methyl 1-Cyclohexyl-4-methylisoquinoline-3-carboxylate (3h)

Product $\mathbf{3 h}$ ( $47.0 \mathrm{mg}, 80 \%$ ) was obtained as a white solid after purification by column chromatography (PE/EtOAc, 99:1).
Mp 74.1-75.6 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.26(\mathrm{~d}, J=8.3 \mathrm{~Hz}, 1 \mathrm{H}), 8.11(\mathrm{~d}, J=8.4$ $\mathrm{Hz}, 1 \mathrm{H}), 7.74(\mathrm{t}, J=7.5 \mathrm{~Hz}, 1 \mathrm{H}), 7.65(\mathrm{t}, J=7.5 \mathrm{~Hz}, 1 \mathrm{H}), 4.02(\mathrm{~s}, 3 \mathrm{H})$, $3.52(\mathrm{t}, \mathrm{J}=11.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.76(\mathrm{~s}, 3 \mathrm{H}), 2.00-1.85(\mathrm{~m}, 6 \mathrm{H}), 1.80(\mathrm{~d}, \mathrm{~J}=$ $13.0 \mathrm{~Hz}, 1 \mathrm{H}$ ), 1.52 (dd, $J=25.2,12.4 \mathrm{~Hz}, 2 \mathrm{H}), 1.44-1.36(\mathrm{~m}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.2,162.7,140.7,135.6,129.2$, 127.0, 125.9, 125.4, 124.5, 124.2, 51.8, 41.0, 31.7, 26.2, 25.5, 13.6, 13.5.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{18} \mathrm{H}_{22} \mathrm{NO}_{2}$ : 284.1645; found: 284.1649.

Methyl 1-Cyclohexyl-7-methoxy-4-methylisoquinoline-3-carboxylate (3i)
Product 3 i ( 40.1 mg , 64\%) was obtained as a colorless oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.04(\mathrm{~d}, J=9.2 \mathrm{~Hz}, 1 \mathrm{H}), 7.47(\mathrm{~s}, 1 \mathrm{H})$, 7.38 (d, J = $9.0 \mathrm{~Hz}, 1 \mathrm{H}$ ), 4.00 ( $\mathrm{s}, 3 \mathrm{H}$ ), 3.98 ( $\mathrm{s}, 3 \mathrm{H}$ ), 3.40 (t, J = $9.9 \mathrm{~Hz}, 1$ H), $2.76(\mathrm{~s}, 3 \mathrm{H}), 2.03-1.83(\mathrm{~m}, 6 \mathrm{H}), 1.80(\mathrm{~d}, J=12.9 \mathrm{~Hz}, 1 \mathrm{H}), 1.51$ (dd, $J=24.1,11.5 \mathrm{~Hz}, 2 \mathrm{H}), 1.45-1.35(\mathrm{~m}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.2,161.0,158.2,138.6,130.8$, $127.4,126.2,126.1,121.0,103.3,54.8,51.8,41.1,31.4,29.1,26.2$, 25.5, 13.7.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{19} \mathrm{H}_{24} \mathrm{NO}_{3}$ : 314.1751; found: 314.1755.

Methyl 1-Cyclohexyl-4,7-dimethylisoquinoline-3-carboxylate (3j)
Product 3j ( $42.7 \mathrm{mg}, 72 \%$ ) was obtained as a white solid after purification by column chromatography (PE/EtOAc, 99:1).
Mp 112.8-115.9 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.00(\mathrm{~d}, J=9.2 \mathrm{~Hz}, 2 \mathrm{H}), 7.56(\mathrm{~d}, J=8.3$ $\mathrm{Hz}, 1 \mathrm{H}$ ), 4.01 ( $\mathrm{s}, 3 \mathrm{H}$ ), $3.50(\mathrm{t}, \mathrm{J}=9.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.75(\mathrm{~s}, 3 \mathrm{H}), 2.59(\mathrm{~s}, 3$ H), 1.98-1.87 (m, 5 H$), 1.86-1.73(\mathrm{~m}, 2 \mathrm{H}), 1.53(\mathrm{~d}, J=12.3 \mathrm{~Hz}, 2 \mathrm{H})$, 1.46-1.35 (m, 1 H ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.3,162.0,140.0,137.1,133.7$, 131.3, 126.1, 125.6, 124.2, 123.5, 51.8, 40.8, 31.7, 29.1, 26.2, 25.5, 21.4, 13.6.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{19} \mathrm{H}_{24} \mathrm{NO}_{2}$ : 298.1802; found: 298.1803.

Methyl 1-Cyclohexyl-7-fluoro-4-methylisoquinoline-3-carboxylate (3k)
Product 3k ( $42.4 \mathrm{mg}, 70 \%$ ) was obtained as a white solid after purification by column chromatography (PE/EtOAc, 99:1).

Mp 81.9-82.6 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=8.14$ (dd, $J=9.3,5.6 \mathrm{~Hz}, 1 \mathrm{H}$ ), 7.84 (d, $J=10.3 \mathrm{~Hz}, 1 \mathrm{H}), 7.52(\mathrm{t}, J=7.5 \mathrm{~Hz}, 1 \mathrm{H}), 4.05-3.99(\mathrm{~m}, 3 \mathrm{H}), 3.37(\mathrm{~s}, 1$
H), 2.81-2.74 (m, 3 H ), 1.94 ( s, 4 H ), 1.86 ( $\mathrm{s}, 1 \mathrm{H}), 1.83$ ( $\mathrm{s}, 2 \mathrm{H}), 1.51$ (d, $J=12.5 \mathrm{~Hz}, 2 \mathrm{H}), 1.41(\mathrm{~d}, J=12.6 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.0,162.1(\mathrm{~d}, J=5.1 \mathrm{~Hz}), 160.9(\mathrm{~d}, J=$ $249.9 \mathrm{~Hz}), 140.3,132.6,127.1(\mathrm{~d}, \mathrm{~J}=8.8 \mathrm{~Hz}), 125.5,119.4(\mathrm{~d}, J=24.8$ $\mathrm{Hz}), 108.4(\mathrm{~d}, \mathrm{~J}=21.3 \mathrm{~Hz}), 51.8,41.2,31.5,29.1,26.1,25.4,13.7$.
HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{18} \mathrm{H}_{21} \mathrm{FNO}_{2}$ : 302.1551; found: 302.1558.

Methyl 1-Cyclohexyl-4-methyl-7-(trifluoromethyl)isoquinoline-3-carboxylate (31)
Product 31 ( $55.5 \mathrm{mg}, 79 \%$ ) was obtained as a white solid after purification by column chromatography (PE/EtOAc, 99:1).

Mp 122.7-124.3 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.51(\mathrm{~s}, 1 \mathrm{H}), 8.24(\mathrm{~d}, J=8.8 \mathrm{~Hz}, 1 \mathrm{H})$, 7.91 (d, $J=8.7 \mathrm{~Hz}, 1 \mathrm{H}), 4.03(\mathrm{~s}, 3 \mathrm{H}), 3.54(\mathrm{~d}, J=10.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.77(\mathrm{~s}$, $3 \mathrm{H}), 1.93(\mathrm{~d}, J=9.8 \mathrm{~Hz}, 5 \mathrm{H}), 1.87-1.78(\mathrm{~m}, 2 \mathrm{H}), 1.55(\mathrm{~d}, J=12.2 \mathrm{~Hz}, 2$ H), 1.45-1.34 (m, 1 H$)$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.4,164.4,143.4,137.8,129.4(\mathrm{q}, \mathrm{J}=$ 32.6 Hz ), 126.2, 125.6, 125.5, 123.9 ( $\mathrm{q}, J=272.7 \mathrm{~Hz}), 122.8,52.7,41.6$, 32.4, 29.7, 26.6, 26.0, 14.3, 14.1.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{19} \mathrm{H}_{21} \mathrm{~F}_{3} \mathrm{NO}_{2}$ : 352.1519; found: 352.1522 .

## Methyl 1,4-Dicyclohexylisoquinoline-3-carboxylate (3m)

Product 3 m ( $58.6 \mathrm{mg}, 83 \%$ ) was obtained as a brown oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=8.33(\mathrm{~s}, 1 \mathrm{H}), 8.26(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 1 \mathrm{H})$, $7.69(\mathrm{t}, J=7.3 \mathrm{~Hz}, 1 \mathrm{H}), 7.60(\mathrm{t}, J=7.4 \mathrm{~Hz}, 1 \mathrm{H}), 4.01(\mathrm{~d}, J=5.1 \mathrm{~Hz}, 3 \mathrm{H})$, $3.49(\mathrm{~d}, J=8.9 \mathrm{~Hz}, 1 \mathrm{H}), 3.20(\mathrm{~s}, 1 \mathrm{H}), 1.96(\mathrm{t}, J=29.5 \mathrm{~Hz}, 9 \mathrm{H}), 1.82$ (dd, $J=25.5,13.5 \mathrm{~Hz}, 4 \mathrm{H}), 1.55-1.32(\mathrm{~m}, 7 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=169.7,162.9,142.2,134.6,130.4$, 128.6, 126.2, 124.9, 51.8, 40.9, 31.7, 31.2, 29.1, 26.9, 26.2, 25.6, 25.5.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{23} \mathrm{H}_{30} \mathrm{NO}_{2}$ : 352.2271; found: 352.2274.

Methyl 1-Cyclohexyl-4-isopropylisoquinoline-3-carboxylate (3n) Product 3n ( $42.7 \mathrm{mg}, 69 \%$ ) was obtained as a light yellow oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 99: 1$ ).
${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.28(\mathrm{t}, \mathrm{J}=7.6 \mathrm{~Hz}, 2 \mathrm{H}), 7.69(\mathrm{t}, J=7.7$ $\mathrm{Hz}, 1 \mathrm{H}), 7.60(\mathrm{t}, J=7.6 \mathrm{~Hz}, 1 \mathrm{H}), 4.00(\mathrm{~s}, 3 \mathrm{H}), 3.63(\mathrm{dt}, J=14.3,7.1 \mathrm{~Hz}$, $1 \mathrm{H}), 3.50(\mathrm{dd}, J=15.3,7.3 \mathrm{~Hz}, 1 \mathrm{H}), 1.97-1.83(\mathrm{~m}, 6 \mathrm{H}), 1.79(\mathrm{~d}, \mathrm{~J}=$ $13.1 \mathrm{~Hz}, 1 \mathrm{H}), 1.55(\mathrm{~s}, 3 \mathrm{H}), 1.53(\mathrm{~s}, 3 \mathrm{H}), 1.47(\mathrm{~d}, J=12.6 \mathrm{~Hz}, 2 \mathrm{H}), 1.38$ ( $\mathrm{t}, J=12.6 \mathrm{~Hz}, 1 \mathrm{H}$ ).
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=169.9,163.5,142.4,134.7$, 132.1, 129.0, 126.8, 126.7, 125.5, 125.2, 52.3, 41.4, 32.1, 29.4, 26.6, 26.0, 21.9.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{20} \mathrm{H}_{26} \mathrm{NO}_{2}$ : 312.1958; found: 312.1963.

## Methyl 1-Cyclohexyl-5,6-dihydro-4H-benzo[de]isoquinoline-3carboxylate (30)

Product 30 ( $31.1 \mathrm{mg}, 50 \%$ ) was obtained as a light yellow oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 99: 1$ ).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.08(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 1 \mathrm{H}), 7.55(\mathrm{~d}, J=7.8$ $\mathrm{Hz}, 1 \mathrm{H}), 7.46(\mathrm{~s}, 1 \mathrm{H}), 3.99(\mathrm{~s}, 3 \mathrm{H}), 3.59(\mathrm{~d}, \mathrm{~J}=69.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.32(\mathrm{~s}, 2$ H), 3.08 (s, 2 H$), 2.04(\mathrm{~s}, 2 \mathrm{H}), 2.00-1.87(\mathrm{~m}, 6 \mathrm{H}), 1.79(\mathrm{~d}, J=11.6 \mathrm{~Hz}, 1$ H), $1.51(\mathrm{~d}, J=13.1 \mathrm{~Hz}, 2 \mathrm{H}), 1.39(\mathrm{~d}, J=12.9 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=162.3,137.4,132.8,129.1,129.0$, 127.5, 127.2, 126.4, 122.1, 51.7, 41.2, 31.6, 30.1, 29.1, 26.8, 26.2, 25.5, 22.1, 13.5.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{20} \mathrm{H}_{24} \mathrm{NO}_{2}$ : 310.1802; found: 310.1804.

## Methyl 1-Cyclohexyl-8-methoxy-4-methylbenzo[ $h$ ]isoquinoline-3-carboxylate (3p)

Product $\mathbf{3 p}$ ( $44.0 \mathrm{mg}, 61 \%$ ) was obtained as a yellow solid after purification by column chromatography (PE/EtOAc, 99:1).
Mp 136.2-139.0 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.49(\mathrm{~d}, J=8.9 \mathrm{~Hz}, 1 \mathrm{H}), 7.93(\mathrm{~d}, J=9.0$ $\mathrm{Hz}, 1 \mathrm{H}), 7.86(\mathrm{~d}, J=9.0 \mathrm{~Hz}, 1 \mathrm{H}), 7.32(\mathrm{~d}, J=9.8 \mathrm{~Hz}, 2 \mathrm{H}), 4.03(\mathrm{~s}, 3 \mathrm{H})$, $3.99(\mathrm{~s}, 3 \mathrm{H}), 3.76(\mathrm{t}, \mathrm{J}=10.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.78(\mathrm{~s}, 3 \mathrm{H}), 2.08(\mathrm{~d}, \mathrm{~J}=10.6 \mathrm{~Hz}$, $2 \mathrm{H}), 1.96(\mathrm{~d}, J=15.4 \mathrm{~Hz}, 4 \mathrm{H}), 1.80(\mathrm{~s}, 1 \mathrm{H}), 1.49(\mathrm{~d}, J=7.5 \mathrm{~Hz}, 3 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=168.4,160.9,158.2,141.6,135.7$, $134.9,130.6,129.0,125.1,124.8,123.5,122.2,116.8,108.7,55.3,52.3$, 44.9, 33.0, 29.5, 26.6, 25.9, 14.4.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{23} \mathrm{H}_{26} \mathrm{NO}_{3}$ : 364.1907; found: 364.1911.

## Methyl 1-Cyclohexylisoquinoline-3-carboxylate (3q)

Product $\mathbf{3 q}(27.5 \mathrm{mg}, 51 \%)$ was obtained as a yellow solid after purification by column chromatography (PE/EtOAc, 99:1).
Mp 114.0-115.6 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.40(\mathrm{~s}, 1 \mathrm{H}), 8.28(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 1 \mathrm{H})$, $7.94(\mathrm{~d}, J=5.1 \mathrm{~Hz}, 1 \mathrm{H}), 7.78-7.68(\mathrm{~m}, 2 \mathrm{H}), 4.02(\mathrm{~d}, J=3.4 \mathrm{~Hz}, 3 \mathrm{H})$, $3.58(\mathrm{~s}, 1 \mathrm{H}), 2.01-1.91(\mathrm{~m}, 6 \mathrm{H}), 1.81(\mathrm{~d}, J=12.4 \mathrm{~Hz}, 1 \mathrm{H}), 1.54(\mathrm{~d}, J=$ $12.5 \mathrm{~Hz}, 2 \mathrm{H}), 1.41(\mathrm{~d}, \mathrm{~J}=9.9 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR (151 MHz, $\mathrm{CDCl}_{3}$ ): $\delta=166.1,165.5,139.8,135.4,129.6$, 128.5, 127.1, 124.4, 121.9, 52.1, 41.5, 31.6, 29.1, 26.1, 25.4.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{17} \mathrm{H}_{20} \mathrm{NO}_{2}$ : 270.1489; found: 270.1491.

Methyl 1-Cyclohexyl-5-methoxyisoquinoline-3-carboxylate (3r)
Product 3r ( 30.0 mg , 50\%) was obtained as a yellow oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.79(\mathrm{~s}, 1 \mathrm{H}), 7.80(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 1 \mathrm{H})$, $7.60(\mathrm{t}, J=7.9 \mathrm{~Hz}, 1 \mathrm{H}), 7.02(\mathrm{~d}, J=7.6 \mathrm{~Hz}, 1 \mathrm{H}), 4.02(\mathrm{~s}, 6 \mathrm{H}), 3.52(\mathrm{t}, J=$ $10.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.00-1.91(\mathrm{~m}, 5 \mathrm{H}), 1.88-1.76(\mathrm{~m}, 2 \mathrm{H}), 1.52(\mathrm{~d}, \mathrm{~J}=13.0$ $\mathrm{Hz}, 2 \mathrm{H}), 1.40(\mathrm{~d}, J=12.2 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=166.6,166.3,157.4,140.2,138.6$, $130.2,121.8,121.1,120.3,108.8,55.6,52.4,45.8,32.8,29.5,27.0$, 26.1.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{18} \mathrm{H}_{22} \mathrm{NO}_{3}$ : 300.1594; found: 300.1597.

Methyl 1-Cyclohexyl-7-methoxyisoquinoline-3-carboxylate (3s)
Product 3s ( $29.8 \mathrm{mg}, 50 \%$ ) was obtained as a light yellow oil after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 99: 1$ ).
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=8.34(\mathrm{~s}, 1 \mathrm{H}), 7.85(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 1 \mathrm{H})$, $7.48(\mathrm{~s}, 1 \mathrm{H}), 7.38(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 1 \mathrm{H}), 4.00(\mathrm{~s}, 3 \mathrm{H}), 3.99(\mathrm{~s}, 3 \mathrm{H}), 3.45(\mathrm{~s}$, $1 \mathrm{H}), 2.04-1.92(\mathrm{~m}, 6 \mathrm{H}), 1.81(\mathrm{~d}, J=11.2 \mathrm{~Hz}, 1 \mathrm{H}), 1.53(\mathrm{~d}, J=12.5 \mathrm{~Hz}$, $2 \mathrm{H}), 1.41(\mathrm{~d}, \mathrm{~J}=12.0 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR (151 MHz, $\mathrm{CDCl}_{3}$ ): $\delta=166.8,164.0,159.8,138.7,131.1$, $130.4,128.9,122.11,122.07,114.1,103.4,55.2,52.4,41.9,31.8,29.5$, 26.6, 26.2, 25.9.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{18} \mathrm{H}_{22} \mathrm{NO}_{3}$ : 300.1594; found: 300.1596.

Methyl 1-Cyclohexyl-6-methoxyisoquinoline-3-carboxylate (3t)
Product 3t ( $21.0 \mathrm{mg}, 28 \%$ ) was obtained as a yellow oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=8.31(\mathrm{~s}, 1 \mathrm{H}), 8.17(\mathrm{~d}, J=9.2 \mathrm{~Hz}, 1 \mathrm{H})$, $7.31(\mathrm{~d}, \mathrm{~J}=9.2 \mathrm{~Hz}, 1 \mathrm{H}), 7.19(\mathrm{~s}, 1 \mathrm{H}), 4.02(\mathrm{~s}, 3 \mathrm{H}), 3.96(\mathrm{~s}, 3 \mathrm{H}), 3.51(\mathrm{~s}$, $1 \mathrm{H}), 1.99-1.90(\mathrm{~m}, 6 \mathrm{H}), 1.80(\mathrm{~d}, J=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.52(\mathrm{~d}, J=12.7 \mathrm{~Hz}$, $2 \mathrm{H}), 1.41(\mathrm{~d}, J=13.0 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=166.8,165.3,160.4,141.0,138.1$, $126.6,123.2,121.6,121.4,106.3,55.4,52.5,41.9,32.0,29.5,26.6$, 25.9.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{18} \mathrm{H}_{22} \mathrm{NO}_{3}: 300.1594$; found: 300.1597.

## Methyl 1-Cyclohexyl-8-methoxyisoquinoline-3-carboxylate (3t')

Product 3t' $21.0 \mathrm{mg}, 35 \%$ ) was obtained as a yellow solid after purification by column chromatography (PE/EtOAc, 99:1).
Mp 111.5-113.2 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.25(\mathrm{~s}, 1 \mathrm{H}), 7.56(\mathrm{t}, J=7.9 \mathrm{~Hz}, 1 \mathrm{H})$, $7.44(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 1 \mathrm{H}), 7.01(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.03(\mathrm{~d}, J=11.3 \mathrm{~Hz}, 1$ H), 3.99 (s, 3 H ), 3.98 (d, $J=1.0 \mathrm{~Hz}, 3 \mathrm{H}$ ), 1.98 (d, $J=12.4 \mathrm{~Hz}, 2 \mathrm{H}), 1.88$ (d, $J=12.5 \mathrm{~Hz}, 2 \mathrm{H}$ ), $1.77(\mathrm{dd}, J=25.8,12.5 \mathrm{~Hz}, 3 \mathrm{H}), 1.45(\mathrm{dd}, J=25.8$, $13.1 \mathrm{~Hz}, 2 \mathrm{H}), 1.34(\mathrm{~d}, J=12.3 \mathrm{~Hz}, 1 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=166.7,165.2,156.0,139.9,129.0$, 128.3, 116.6, 116.4, 107.4, 55.6, 52.4, 42.1, 32.0, 29.5, 26.6, 25.9.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{18} \mathrm{H}_{22} \mathrm{NO}_{3}: 300.1594$; found: 300.1597.

## Ethyl 1-Cyclohexyl-4-phenylisoquinoline-3-carboxylate (3u)

Product $\mathbf{3 u}(61.0 \mathrm{mg}, 85 \%)$ was obtained as a white solid after purification by column chromatography ( $\mathrm{PE} / \mathrm{EtOAc}, 99: 1$ ).
Mp 95.9-97.5 ${ }^{\circ} \mathrm{C}$.
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.30(\mathrm{~s}, 1 \mathrm{H}), 7.63(\mathrm{~d}, \mathrm{~J}=13.4 \mathrm{~Hz}, 3 \mathrm{H})$, $7.46(\mathrm{~s}, 3 \mathrm{H}), 7.36(\mathrm{~s}, 2 \mathrm{H}), 4.09(\mathrm{~d}, \mathrm{~J}=5.6 \mathrm{~Hz}, 2 \mathrm{H}), 3.61(\mathrm{~s}, 1 \mathrm{H}), 2.03(\mathrm{~s}$, $2 \mathrm{H}), 1.96(\mathrm{~d}, J=11.3 \mathrm{~Hz}, 4 \mathrm{H}), 1.82(\mathrm{~d}, J=9.5 \mathrm{~Hz}, 1 \mathrm{H}), 1.55(\mathrm{~d}, J=12.1$ $\mathrm{Hz}, 2 \mathrm{H}), 1.43(\mathrm{t}, \mathrm{J}=11.7 \mathrm{~Hz}, 1 \mathrm{H}), 0.93(\mathrm{~s}, 3 \mathrm{H})$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.5,164.5,141.3,136.0,135.1$, $130.0,129.5,129.3,127.5,127.12,127.10,126.4,125.9,124.1,60.4$, 41.2, 31.7, 26.2, 25.5, 13.0.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{24} \mathrm{H}_{26} \mathrm{NO}_{2}: 360.1958$; found: 360.1961.

## (1-Cyclohexyl-4-phenylisoquinolin-3-yl)(pyrrolidin-1-yl)methanone (3v)

Product $3 v$ ( $61.5 \mathrm{mg}, 80 \%$ ) was obtained as a light yellow oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.28(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 1 \mathrm{H}), 7.72(\mathrm{~d}, J=7.8$ $\mathrm{Hz}, 1 \mathrm{H}), 7.63-7.54(\mathrm{~m}, 2 \mathrm{H}), 7.47-7.38(\mathrm{~m}, 5 \mathrm{H}), 3.59(\mathrm{t}, J=10.3 \mathrm{~Hz}, 1$ H), $3.42(\mathrm{t}, J=6.7 \mathrm{~Hz}, 2 \mathrm{H}), 3.14(\mathrm{t}, J=6.4 \mathrm{~Hz}, 2 \mathrm{H}), 1.95(\mathrm{dd}, J=25.5$, $12.6 \mathrm{~Hz}, 6 \mathrm{H}), 1.82-1.66(\mathrm{~m}, 5 \mathrm{H}), 1.53(\mathrm{dd}, J=25.6,12.5 \mathrm{~Hz}, 2 \mathrm{H})$, 1.44-1.35 (m, 1 H ).
${ }^{13} \mathrm{C}$ NMR (151 MHz, $\mathrm{CDCl}_{3}$ ): $\delta=168.1,165.3,146.8,135.9,135.7$, 130.6, 130.0, 128.4, 128.1, 127.6, 127.2, 126.6, 126.0, 124.9, 47.7, 45.3, 41.9, 32.7, 29.9, 27.0, 26.4, 26.0, 24.5.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{26} \mathrm{H}_{29} \mathrm{~N}_{2} \mathrm{O}$ : 385.2274; found: 385.2280 .

## (1-Cyclohexyl-4-phenylisoquinolin-3-yl)(piperidin-1-yl)methanone (3w)

Product 3w ( $67.1 \mathrm{mg}, 84 \%$ ) was obtained as a light yellow oil after purification by column chromatography (PE/EtOAc, 99:1).
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=8.27(\mathrm{~d}, J=7.9 \mathrm{~Hz}, 1 \mathrm{H}), 7.70(\mathrm{~d}, J=7.7$ Hz, 1 H), 7.63-7.55 (m, 2 H ), 7.45 (s, 5 H ), 3.60 (d, J=10.5 Hz, 1 H ), $3.54(\mathrm{~d}, J=4.9 \mathrm{~Hz}, 2 \mathrm{H}), 3.05(\mathrm{~s}, 2 \mathrm{H}), 2.01-1.87(\mathrm{~m}, 6 \mathrm{H}), 1.80(\mathrm{~d}, J=$ $12.0 \mathrm{~Hz}, 1 \mathrm{H}$ ), 1.53 (dd, $J=26.1,9.2 \mathrm{~Hz}, 5 \mathrm{H}), 1.45-1.33$ (m, 4 H$)$.
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta=167.4,164.5,145.3,135.0,134.8$, $130.0,129.2,127.6,127.3,126.7,126.3,125.8,125.1,124.0,46.9,41.5$, 41.0, 31.8, 29.1, 26.2, 25.6, 25.4, 24.7, 23.9.

HRMS (ESI): $m / z[M+H]^{+}$calcd for $\mathrm{C}_{27} \mathrm{H}_{31} \mathrm{~N}_{2} \mathrm{O}$ : 399.2431; found: 399.2435.

## The Kinetic Isotope Effect Study between Cyclohexane and [ $D_{12}$ ]Cyclohexane

A sealed tube was charged with 1a ( $0.2 \mathrm{mmol}, 1$ equiv), DBU (30 $\mathrm{mol} \%, 0.06 \mathrm{mmol})$, BPO ( 0.4 mmol , 2 equiv), cyclohexane ( 2.5 mL ) and [ $\mathrm{D}_{12}$ ]-cyclohexane ( 2.5 mL ). The reaction tube was charged with argon three times and the mixture then stirred at $100^{\circ} \mathrm{C}$ for 2 h . EtOAc $(10 \mathrm{~mL})$ and saturated $\mathrm{NaHCO}_{3}$ solution $(10 \mathrm{~mL})$ were added, the organic layer was separated and the aqueous phase was extracted with $\operatorname{EtOAc}(2 \times 10 \mathrm{~mL})$. The combined organic layers were washed with $\mathrm{H}_{2} \mathrm{O}(2 \times 10 \mathrm{~mL})$ and brine $(1 \times 10 \mathrm{~mL})$, then dried over anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$. The solvent was removed and the residue was purified by silica gel column chromatography (PE/EtOAc, 99:1) to afford a mixture of products $\mathbf{2 a}$ and $\mathbf{2 a} \mathbf{a}^{\prime}(54.9 \mathrm{mg}, 78 \%)$.
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDC}_{3}$ ): $\delta=8.32(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 1 \mathrm{H}), 7.62$ (dt, $J=$ $14.6,7.2 \mathrm{~Hz}, 3 \mathrm{H}), 7.53-7.42(\mathrm{~m}, 3 \mathrm{H}), 7.35(\mathrm{~d}, \mathrm{~J}=6.9 \mathrm{~Hz}, 2 \mathrm{H}), 3.66(\mathrm{~s}, 3$ H), $3.60(\mathrm{~d}, J=11.3 \mathrm{~Hz}, 0.83 \mathrm{H}), 2.05(\mathrm{~d}, J=10.0 \mathrm{~Hz}, 2 \mathrm{H}), 2.02-1.90(\mathrm{~m}$, $4 \mathrm{H}), 1.83(\mathrm{~d}, J=12.2 \mathrm{~Hz}, 1 \mathrm{H}), 1.56(\mathrm{q}, J=12.9 \mathrm{~Hz}, 2 \mathrm{H}), 1.44(\mathrm{t}, J=12.6$ Hz, 1 H).

## The Kinetic Isotope Effect Study between 1a and [ $\mathrm{D}_{\mathbf{1 0}}$ ]-1a

A sealed tube was charged with $\left[D_{10}\right]-1 \mathbf{a}(0.1 \mathrm{mmol}, 0.5$ equiv), $\mathbf{1 a}$ ( 0.1 $\mathrm{mmol}, 0.5$ equiv), DBU ( $30 \mathrm{~mol} \%, 0.06 \mathrm{mmol}$ ), BPO ( $0.4 \mathrm{mmol}, 2$ equiv) and cyclohexane ( 5 mL ). The reaction tube was charged with argon three times and the mixture then stirred at $100^{\circ} \mathrm{C}$ for 2 h . EtOAc (10 mL ) and saturated $\mathrm{NaHCO}_{3}$ solution ( 10 mL ) were added, the organic layer was separated and the aqueous phase was extracted with EtOAc $(2 \times 10 \mathrm{~mL})$. The combined organic layers were washed with $\mathrm{H}_{2} \mathrm{O}$ $(2 \times 10 \mathrm{~mL})$ and brine $(1 \times 10 \mathrm{~mL})$, then dried over anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$. The solvent was removed and the residue was purified by silica gel column chromatography (PE/EtOAc, 99:1) to afford a mixture of products 2a and 2a" ( $58.8 \mathrm{mg}, 84 \%$ ).
${ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta=8.32(\mathrm{~d}, J=8.1 \mathrm{~Hz}, 1 \mathrm{H}), 7.61(\mathrm{dd}, J=$ $16.4,9.4 \mathrm{~Hz}, 3 \mathrm{H}), 7.48(\mathrm{~d}, J=6.9 \mathrm{~Hz}, 3 \mathrm{H}), 7.35(\mathrm{~d}, J=6.8 \mathrm{~Hz}, 2 \mathrm{H}), 3.66$ (s, 6 H), 3.61 (d, $J=9.6 \mathrm{~Hz}, 2 \mathrm{H}), 2.05(\mathrm{~d}, J=9.9 \mathrm{~Hz}, 4 \mathrm{H}), 1.96(\mathrm{~d}, J=$ $11.5 \mathrm{~Hz}, 8 \mathrm{H}), 1.83(\mathrm{~d}, J=11.8 \mathrm{~Hz}, 2 \mathrm{H}), 1.56(\mathrm{q}, J=12.5 \mathrm{~Hz}, 4 \mathrm{H}), 1.44$ ( $\mathrm{t}, J=12.4 \mathrm{~Hz}, 2 \mathrm{H}$ ).

## Radical Inhibition Studies

A sealed tube was charged with $1 \mathbf{1 a}$ ( 0.2 mmol , 1 equiv), DBU (30 $\mathrm{mol} \%, 0.06 \mathrm{mmol}$ ), BPO ( $0.4 \mathrm{mmol}, 2$ equiv), TEMPO ( $0.8 \mathrm{mmol}, 4$ equiv) and cyclohexane ( 5 mL ). The reaction tube was charged with argon three times and the mixture then stirred at $100^{\circ} \mathrm{C}$ for 2 h . The mixture was then subjected to analysis by mass spectrometry (ESI, positive mode). Almost no 2a was observed.
LCMS (ESI) for 4: $m / z[M+H]^{+}$calcd for $\mathrm{C}_{15} \mathrm{H}_{29} \mathrm{NO}$ : 240.2; found: 240.3.

Synthesis
D. Xue et al.

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## Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610661.

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