Diversity-Oriented Approach to 1,2-Dihydroisoquinolin-3(4H)-imines via Copper(I)-Catalyzed Reaction of (E)-2-Ethynylphenylchalcone, Sulfonyl Azide, and Amine

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Supporting Information

1. General experimental methods (S2)
2. Conditions optimization, general experimental procedure, and characterization data (S2-S16)
3. $^1$H and $^{13}$C NMR spectra of compound 4 (S17-S38)
General experimental methods:

Unless otherwise stated, all commercial reagents and solvents were used without additional purification. All reactions were performed in reaction tubes under N₂. The Flash column chromatography was performed using silica gel (60-Å pore size, 32-63 µm, standard grade). Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr (house vacuum) at 25-35°C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane (TMS) on the δ scale.

X-ray Crystallographic Analysis. Suitable crystals were selected under a microscope. Data collections were performed on a Bruker SMART APEX (at 293K) diffractometer with CCD area detector using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The determination of crystal class and unit cell was carried out by SMART program package. The raw frame data were processed using SAINT (SAINTPlus Data Reduction and Correction Program v. 6.02 a; Bruker AXS: Madison, WI, 2000.) and SADABS (Sheldrick, G. M. SADABS, A Program for Empirical Absorption Correction; University of Göttingen: Göttingen, Germany, 1998.) to yield the reflection data file. The structure was solved by using SHELXTL program (Sheldrick, G. M. SHELXL-97, Program for the Refinement of Crystal Structures; University of Göttingen: Göttingen, Germany, 1997.). Refinement was performed on F² anisotropically by the full-matrix least-squares method for all the non-hydrogen atoms. Hydrogen atoms were placed at the calculated positions and included in the structure calculation without further refinement of the parameters. The residual electron densities were of no chemical significance. CCDC 815165 (compound 4a), contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44)-1223-336033; or deposit@ccdc.cam.ac.uk).
Table 1 Initial studies for the copper-catalyzed three-component reaction of (E)-2-ethynylphenylchalcone 1a, tosyl azide 2a, and p-anisidine 3a.

![Chemical structure](image)

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$^a$ Isolated yield based on (E)-2-ethynylphenylchalcone 1a.
General procedure for the synthesis of 1,2-dihydroisoquinolin-3(4H)-imine s via a copper(I)-catalyzed reaction of (E)-2-ethynylphenylchalcone, sulfonyl azide, and amine.

A solution of 2-ethynylphenylchalcone 1 (0.20 mmol) in anhydrous THF (0.5 mL) was added a mixture of sulfonyl azide 2 (0.24 mmol, 1.2 equiv), amine 3 (0.22 mmol, 1.1 equiv) and CuCl (0.01 mmol, 5 mol %) in THF (0.5 mL) at room temperature under N₂ atmosphere. Subsequently triethylamine (43 μL, 0.30 mmol, 1.5 equiv) was slowly added by a syringe. The resulting suspension was stirred at room temperature for about 12hs and the reaction might become clear as a dark yellow solution. After completion of the reaction as indicated by TLC, the reaction mixture was concentrated in vacuum. The crude residue was purified by flash column chromatograph (EtOAc/n-hexane, 1:3) to give the desired product 4 as a light yellow solid.
N-(2-(4-Methoxyphenyl)-1-(2-(4-methoxyphenyl)-2-oxoethyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4a

Yield: 92%; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.75-7.73 (m, 2H), 7.64-7.62 (m, 2H), 7.37-7.28 (m, 3H), 7.25-7.15 (m, 5H), 6.92-6.85 (m, 4H), 5.55-5.52 (m, 1H), 5.04 (d, \(J = 19.60\) Hz, 1H), 4.25 (d, \(J = 19.60\) Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.55-3.44 (m, 2H), 2.36 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 21.4, 34.2, 42.6, 55.5, 55.57, 62.3, 113.8, 114.6, 126.0, 126.2, 127.2, 128.0, 128.41, 128.47, 128.9, 129.4, 129.8, 130.3, 134.3, 134.39, 140.8, 141.8, 138.9, 163.9, 165.4, 194.3; HRMS calcd. for C\(_{32}\)H\(_{31}\)N\(_2\)O\(_5\)S\(^+\)[M+H]\(^+\): 555.1954, found 555.1950.

N-(1-(2-(4-Chlorophenyl)-2-oxoethyl)-2-(4-methoxyphenyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4b

Yield: 80%; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.68-7.66 (m, 2H), 7.61-7.59 (m, 2H), 7.35-7.29 (m, 5H), 7.24-7.16 (m, 1H), 7.14-7.13 (m, 4H), 6.90-6.88 (m, 2H), 5.51-5.48 (m, 1H), 5.02 (d, \(J = 20.0\) Hz, 1H), 4.25 (d, \(J = 20.0\) Hz, 1H), 3.81 (s, 3H), 3.54-3.45 (m, 2H), 2.34 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 21.3, 34.1, 43.0, 55.5, 62.1, 114.6, 126.0, 126.1, 127.2, 128.1, 128.4, 128.5, 128.9, 129.0, 129.3, 129.8, 134.0, 134.2, 134.5, 140.1, 140.7, 141.8, 158.9, 165.3, 194.8; HRMS calcd. for C\(_{31}\)H\(_{28}\)ClN\(_2\)O\(_4\)S\(^+\)[M+H]\(^+\): 559.1458, found 559.1478.
N-(1-(2-(4-Bromophenyl)-2-oxoethyl)-2-(4-methoxyphenyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4c
Yield: 81%; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.61-7.58 (m, 4H), 7.52-7.50 (m, 2H), 7.33-7.29 (m, 3H), 7.24-7.21 (m, 1H), 7.16-7.13 (m, 4H), 6.89-6.88 (m, 2H), 5.50-5.48 (m, 1H), 5.01 (d, $J$ = 16.0 Hz, 1H), 4.25 (d, $J$ = 16.0 Hz, 1H), 3.80 (s, 3H), 3.54-3.44 (m, 2H), 2.34 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.3, 34.1, 43.0, 55.5, 62.1, 114.6, 126.0, 126.1, 127.2, 128.1, 128.4, 128.5, 128.9, 129.4, 129.8, 130.9, 132.0, 134.0, 134.2, 134.9, 140.7, 141.8, 158.9, 165.3, 195.0; HRMS calcd. for C$_{31}$H$_{28}$BrN$_2$O$_4$S$^+$ [M+H]$^+$: 603.0953, found 603.0971.

N-(6-Methoxy-2-(4-methoxyphenyl)-1-(2-(4-methoxyphenyl)-2-oxoethyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4d
Yield: 94%; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.72-7.70 (m, 2H), 7.61-7.60 (m, 2H), 7.24-7.23 (m, 1H), 7.16-7.12 (m, 4H), 6.88-6.87 (m, 2H), 6.84-6.79 (m, 3H), 6.74-6.72 (m, 1H), 5.46-5.44 (m, 1H), 4.96 (d, $J$ = 16.0 Hz, 1H), 4.24 (d, $J$ = 16.0 Hz, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.76 (s, 3H), 3.50-3.39 (m, 2H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.3, 34.4, 42.7, 55.3, 55.5, 62.0, 112.4, 113.4, 113.8, 114.5, 125.9, 126.4, 127.4, 128.4, 128.9, 129.4, 130.3, 131.1, 134.4, 140.8, 141.7, 158.9, 159.5, 163.8, 165.2, 194.6; HRMS calcd. for C$_{33}$H$_{33}$N$_2$O$_6$S$^+$ [M+H]$^+$: 585.2059, found 585.2068.
**N-(6,7-Dimethoxy-2-(4-methoxyphenyl)-1-(2-(4-methoxyphenyl)-2-oxoethyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4e**

Yield: 87%; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.73-7.71 (m, 2H), 7.61-7.59 (m, 2H), 7.18-7.11 (m, 5H), 6.89-6.82 (m, 4H), 6.75 (s, 1H), 5.44-5.42 (m, 1H), 4.93 (d, $J = 16.4$ Hz, 1H), 4.20 (d, $J = 16.0$ Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 3.796 (s, 3H), 3.790 (s, 3H), 3.51-3.39 (m, 2H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.3, 33.6, 42.9, 55.48, 55.49, 56.00, 56.01, 62.2, 109.4, 110.5, 113.8, 114.5, 121.6, 125.9, 126.2, 128.4, 128.9, 129.5, 130.3, 134.3, 140.8, 141.7, 147.9, 149.0, 158.9, 163.8, 165.5, 194.8; HRMS calcd. for C$_{34}$H$_{35}$N$_2$O$_7$S$^+$ [M+H]$^+$: 615.2165, found 615.2168.

**N-(7-Fluoro-2-(4-methoxyphenyl)-1-(2-(4-methoxyphenyl)-2-oxoethyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4f**

Yield: 85%; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.76-7.74 (m, 2H), 7.60-7.59 (m, 2H), 7.23-7.20 (m, 1H), 7.15-7.11 (m, 5H), 6.98-6.94 (m, 1H), 6.88-6.83 (m, 4H), 5.49-5.44 (m, 1H), 5.00 (d, $J = 16.0$ Hz, 1H), 4.21(d, $J = 16.0$ Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.56-3.44 (m, 2H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.3, 33.5, 42.3, 55.4, 55.5, 61.9, 113.3, 113.5, 113.8, 114.6, 115.3, 115.5, 125.5, 125.9, 126.2, 126.3, 128.4, 128.9, 129.2, 129.5, 129.6, 130.3, 134.1, 136.2, 136.3, 140.7, 141.8, 159.0, 160.5, 162.5, 163.9, 165.2, 194.1; HRMS calcd. for C$_{32}$H$_{29}$FN$_2$NaO$_5$S$^+$ [M+Na]$^+$: 595.1679, found 595.1680.
N-(7-Chloro-2-(4-methoxyphenyl)-1-(2-(4-methoxyphenyl)-2-oxoethyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4g
Yield: 91%; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.76-7.74 (m, 2H), 7.60-7.58 (m, 2H), 7.39 (d, $J = 1.60$ Hz, 1H), 7.25-7.12 (m, 6H), 6.89-6.84 (m, 4H), 5.48-5.45 (m, 1H), 4.99 (d, $J = 16.0$ Hz, 1H), 4.22 (d, $J = 16.0$ Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.54-3.44 (m, 2H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.3, 33.6, 42.3, 55.4, 55.5, 61.7, 113.8, 114.6, 125.9, 126.3, 128.3, 128.4, 128.5, 128.9, 129.1, 129.2, 130.3, 132.9, 134.0, 136.0, 140.6, 141.8, 159.0, 163.9, 164.9, 194.0; HRMS calcd. for C$_{32}$H$_{29}$ClN$_2$NaO$_5$S$^+$ [M+Na]$^+$: 611.1383, found 611.1408.

N-(2-(4-Methoxyphenyl)-1-(2-oxopentyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4h
Yield: 76%; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.72-7.70 (m, 2H), 7.28-7.16 (m, 8H), 6.85-6.83 (m, 2H), 5.41 (s, 1H), 4.98 (d, $J = 2.40$ Hz, 1H), 3.76 (s, 3H), 3.62 (s, 1H), 2.43-2.35 (m, 5H), 1.66-1.58 (m, 1H), 1.43-1.40 (m, 1H), 1.29-1.22 (m, 2H), 0.85 (t, $J = 5.60$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 14.2, 16.2, 21.4, 42.5, 43.6, 55.4, 63.9, 75.0, 114.3, 121.6, 126.2, 126.3, 126.7, 127.8, 128.2, 129.1, 129.5, 133.2, 134.2, 138.8, 140.7, 142.1, 158.6, 168.3; HRMS calcd. for C$_{28}$H$_{31}$N$_2$O$_4$S$^+$ [M+H]$^+$: 491.2005, found 491.2001.
N-(2-(4-Methoxyphenyl)-1-(2-(4-methoxyphenyl)-2-oxoethyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)benzenesulfonamide **4i**

Yield: 90%; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.73-7.71 (m, 4H), 7.43-7.31 (m, 5H), 7.25-7.24 (m, 1H), 7.21-7.14 (m, 3H), 6.88-6.86 (m, 2H), 6.83-6.81 (m, 2H), 5.52-5.50 (m, 1H), 5.00 (d, \(J = 16.0\) Hz, 1H), 4.27 (d, \(J = 16.0\) Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.53-3.43 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 34.2, 42.5, 55.5, 55.52, 62.4, 113.8, 114.6, 125.9, 126.2, 126.3, 127.2, 127.9, 128.3, 128.4, 128.6, 129.3, 129.7, 130.3, 131.3, 134.2, 143.6, 158.9, 163.8, 165.5, 194.3; HRMS calcd. for C\(_{31}\)H\(_{29}\)N\(_2\)O\(_5\)S\(^+\)[M+H\(^+\)]: 541.1797, found 541.1801.

N-(2-(4-Methoxyphenyl)-1-(2-(4-methoxyphenyl)-2-oxoethyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-nitrobenzenesulfonamide **4j**

Yield: 93%; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.15-8.13 (m, 2H), 7.85-7.83 (m, 2H), 7.72-7.71 (m, 2H), 7.35-7.22 (m, 4H), 7.16-7.14 (m, 2H), 6.91-6.82 (m, 4H), 5.53-5.51 (m, 1H), 4.94 (d, \(J = 16.0\) Hz, 1H), 4.34 (d, \(J = 16.0\) Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.54-3.45 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 34.5, 42.3, 55.5, 62.5, 113.8, 114.7, 123.6, 126.1, 127.2, 127.4, 127.9, 128.2, 128.5, 129.2, 130.3, 133.8,
133.9, 149.1, 149.2, 159.2, 163.9, 166.0, 194.2; HRMS calcd. for C$_{31}$H$_{27}$N$_3$NaO$_7$S$^+$, [M+Na]$^+$: 608.1467, found 608.1478.

![Structure of compound 4k](image)

**N-(2-(4-Methoxyphenyl)-1-(2-(4-methoxyphenyl)-2-oxoethyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)methanesulfonamide 4k**

Yield: 98%; 1H NMR (400 MHz, CDCl$_3$): δ 7.73-7.71 (m, 2H), 7.32-7.16 (m, 6H), 6.92-6.90 (m, 2H), 6.86-6.83 (m, 2H), 5.49-5.47 (m, 1H), 4.91 (d, J = 16.0 Hz, 1H), 4.21 (d, J = 16.0 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.51-3.41 (m, 2H), 2.84 (s, 3H); 13C NMR (100 MHz, CDCl$_3$): δ 34.2, 42.6, 43.3, 55.4, 55.5, 62.3, 113.8, 114.5, 126.1, 126.8, 127.1, 127.9, 128.3, 128.4, 129.4, 129.7, 130.3, 134.3, 158.8, 163.8, 165.2, 194.3; HRMS calcd. for C$_{26}$H$_{26}$N$_2$NaO$_5$S$^+$, [M+Na]$^+$: 501.1460, found 501.1465.

![Structure of compound 4l](image)

**N-(1-(2-(4-Methoxyphenyl)-2-oxoethyl)-2-p-tolyl-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4l**

Yield: 97%; 1H NMR (400 MHz, CDCl$_3$): δ 7.72-7.70 (m, 2H), 7.61-7.59 (m, 2H), 7.34 (d, J = 6.00 Hz, 1H), 7.26-7.25 (m, 1H), 7.20-7.14 (m, 4H), 7.12-7.10 (m, 4H), 6.82-6.80 (m, 2H), 5.53-5.51 (m, 1H), 5.01 (d, J = 16.00 Hz, 1H), 4.26 (d, J = 16.00 Hz, 1H), 3.78 (s, 3H), 3.54-3.43 (m, 2H), 2.33 (s, 3H), 2.31 (s, 3H); 13C NMR (100 MHz, CDCl$_3$): δ 21.4, 21.6, 34.4, 42.7, 55.7, 62.4, 114.0, 126.2, 126.5, 127.2, 127.3, 128.1, 128.5, 129.2, 129.4, 130.0, 130.2, 130.5, 134.5, 138.1, 139.2, 141.0, 142.0,
164.0, 165.6, 194.6; HRMS calcd. for C_{32}H_{31}N_{2}O_{4}S\(^{+}\) [M+H]\(^{+}\): 539.2005, found 539.2019.

\[
\text{N-(1-(2-(4-Methoxyphenyl)-2-oxoethyl)-2-phenyl-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4m}
\]

Yield: 77%; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.75-7.73\) (m, 2H), 7.61-7.59 (m, 2H), 7.43-7.33 (m, 5H), 7.31-7.24 (m, 4H), 7.14-7.11 (m, 2H), 6.86-6.84 (m, 2H), 5.60-5.57 (m, 1H), 5.05 (d, \(J = 20.00\) Hz, 1H), 4.31 (d, \(J = 20.00\) Hz, 1H), 3.83 (s, 3H), 3.59-3.46 (m, 2H), 2.34 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 21.4, 34.2, 42.6, 55.5, 62.1, 113.8, 126.0, 126.3, 127.2, 127.4, 128.0, 128.1, 128.4, 128.9, 129.3, 129.5, 129.8, 130.3, 134.3, 140.7, 141.7, 141.8, 163.9, 165.3, 194.3; HRMS calcd. for C\(_{31}\)H\(_{29}\)N\(_2\)O\(_4\)S\(^{+}\) [M+H]\(^{+}\): 525.1848, found 525.1847.

\[
\text{N-(2-(4-Bromophenyl)-1-(2-(4-methoxyphenyl)-2-oxoethyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4n}
\]

Yield: 94%; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.73-7.71\) (m, 2H), 7.64-7.62 (m, 2H), 7.57-7.56 (m, 2H), 7.39-7.35 (m, 3H), 7.30-7.12 (m, 5H), 6.84-6.82 (m, 2H), 5.60-5.57 (m, 1H), 5.05 (d, \(J = 15.60\) Hz, 1H), 4.28 (d, \(J = 16.00\) Hz, 1H), 3.81 (s, 3H), 3.52-3.47 (m, 2H), 2.34 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 21.3, 34.0, 42.5, 55.4, 61.9, 113.7, 121.7, 125.9, 126.1, 127.2, 127.9, 128.4, 129.0, 129.1, 129.2, 129.5, 130.3, 132.5, 134.1, 140.2, 140.5, 142.0, 163.8, 165.3, 194.2; HRMS calcd. for...
C$_{31}$H$_{28}$BrN$_2$O$_4$S$^+$ [M+H]$^+$: 603.0953, found 603.0946.

\[
\text{OMe} \quad \begin{array}{c}
\text{Br} \\
\text{N} \\
\text{CF}_3 \\
\text{NTs} \\
\text{N} \\
\text{OMe}
\end{array}
\]

\[ \text{N-(1-(2-(4-Methoxyphenyl)-2-oxoethyl)-2-(4-(trifluoromethyl)phenyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4o} \]
Yield: 72%; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.78-7.74 (m, 2H), 7.69-7.65 (m, 2H), 7.61-7.58 (m, 2H), 7.44-7.39 (m, 3H), 7.34-7.32 (m, 2H), 7.29-7.25 (m, 1H), 7.18-7.16 (m, 2H), 6.88-6.85 (m, 2H), 5.63-5.60 (m, 1H), 5.07 (d, $J = 20.00$ Hz, 1H), 4.32 (d, $J = 19.60$ Hz, 1H), 3.85 (s, 3H), 3.60-3.45 (m, 2H), 2.37 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.6, 34.4, 42.9, 55.7, 62.0, 114.0, 126.1, 126.4, 126.6, 126.7, 126.83, 128.86, 127.6, 128.3, 128.8, 129.3, 129.7, 130.6, 134.3, 140.4, 142.5, 145.0, 164.1, 165.6, 194.3; HRMS calcd. for C$_{32}$H$_{28}$F$_3$N$_2$O$_4$S$^+$ [M+H]$^+$: 593.1722, found 593.1729.

\[
\begin{array}{c}
\text{OMe} \\
\text{O} \\
\text{N} \\
\text{COOEt} \\
\text{NTs} \\
\text{N}
\end{array}
\]

\[ \text{Ethyl 4-(1-(2-(4-methoxyphenyl)-2-oxoethyl)-3-(tosylimino)-3,4-dihydroisoquinolin-2(1H)-yl)benzoate 4p} \]
Yield: 65%; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.24-8.21 (m, 2H), 7.76-7.73 (m, 2H), 7.62-7.60 (m, 2H), 7.46-7.43 (m, 2H), 7.40-7.37 (m, 1H), 7.34-7.28 (m, 3H), 7.20-7.17 (m, 2H), 6.87-6.85 (m, 2H), 5.67-5.64 (m, 1H), 5.09 (d, $J = 20.0$ Hz, 1H), 4.31 (d, $J = 20.0$ Hz, 1H), 3.90-3.84 (m, 5H), 3.52-3.50 (m, 2H), 2.37 (s, 3H), 1.41-1.25 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 14.5, 21.6, 34.4, 42.9, 55.7, 61.5,
62.0, 114.0, 126.1, 126.4, 127.5, 127.6, 128.3, 128.7, 129.3, 129.4, 129.8, 130.1, 130.5, 130.9, 134.4, 142.3, 145.8, 164.1, 165.5, 165.9, 194.3; HRMS calcd. for C_{34}H_{32}N_{2}NaO_{6}S \ ^{+} [M+Na]^{+}: 619.1879, found 619.1896.

\[
\text{OMe} \\
\begin{array}{c}
\text{O} \\
\text{N} \\
\text{NTs}
\end{array}
\]

\[\text{N-(1-(2-(4-Methoxyphenyl)-2-oxoethyl)-2-(4-nitrophenyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4q}\]

Yield: 54%; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \delta 8.07-8.05 (m, 2H), 7.74-7.72 (m, 2H), 7.61-7.59 (m, 2H), 7.39-7.30 (m, 6H), 7.16-7.14 (m, 2H), 6.85-6.83 (m, 2H), 5.62-5.59 (m, 1H), 5.07 (d, J = 20.00 Hz, 1H), 4.30 (d, J = 20.00 Hz, 1H), 3.82 (s, 3H), 3.57-3.44 (m, 2H), 2.35 (s, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \delta 21.5, 34.2, 46.0, 55.6, 61.8, 113.9, 124.7, 126.0, 127.0, 127.6, 128.2, 128.5, 128.7, 129.2, 129.4, 130.4, 130.8, 134.1, 139.9, 142.5, 146.6, 147.4, 164.1, 165.4, 193.9; HRMS calcd. for C_{31}H_{27}N_{3}NaO_{6}S \ ^{+} [M+Na]^{+}: 592.1518, found 592.1539.

\[
\text{OMe} \\
\begin{array}{c}
\text{O} \\
\text{N} \\
\text{NTs}
\end{array}
\]

\[\text{N-(2-(2,6-Diethylphenyl)-1-(2-(4-methoxyphenyl)-2-oxoethyl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4r}\]

Yield: 78%; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \delta 7.73-7.71 (m, 2H), 7.53-7.51 (m, 2H), 7.33-7.28 (m, 4H), 7.21-7.17 (m, 3H), 7.11-7.09 (m, 2H), 6.86-6.83 (m, 2H), 5.31-5.28 (m, 1H), 5.06 (d, J = 19.20 Hz, 1H), 4.35 (d, J = 19.20 Hz, 1H), 3.82 (s, 3H), 3.61-3.36 (m, 2H), 2.57-2.46 (m, 2H), 2.32 (s, 3H), 2.29-2.23 (m, 2H), 1.15 (t, J = 7.60 Hz, 3H), 1.03 (t, J = 7.60 Hz, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \delta 14.2, 14.4,
21.4, 24.2, 24.3, 34.0, 41.8, 55.5, 62.0, 113.9, 125.9, 126.0, 126.2, 127.3, 127.4, 128.1,
128.4, 128.6, 128.9, 129.4, 129.8, 130.2, 134.9, 138.4, 139.7, 140.6, 140.8, 141.7,
163.8, 165.2, 194.3; HRMS calcd. for C_{35}H_{37}N_{2}O_{4}S [M+H]^+: 581.2474, found
581.2473.

\[
\text{\begin{tikzpicture}
\node[draw, circle] at (0,0) (o) {O};
\node[draw, rectangle, fill=none] at (-1,2) (a) {O};
\node[draw, rectangle, fill=none] at (-2,4) (b) {NTs};
\node[draw, rectangle, fill=none] at (-2,-2) (c) {NTs};
\node[draw, rectangle, fill=none] at (-1,-4) (d) {OMe};
\node[draw, rectangle, fill=none] at (-2,0) (e) {N};
\node[draw, rectangle, fill=none] at (-1,0) (f) {N};
\node[draw, rectangle, fill=none] at (-2,-2) (g) {N};
\node[draw, rectangle, fill=none] at (2,0) (h) {N};
\node[draw, rectangle, fill=none] at (2,-2) (i) {N};
\node[draw, rectangle, fill=none] at (2,0) (j) {NTs};
\node[draw, rectangle, fill=none] at (2,-2) (k) {OMe};
\node[draw, rectangle, fill=none] at (0,4) (l) {O};
\node[draw, rectangle, fill=none] at (0,-4) (m) {O};
\end{tikzpicture}}
\]

\[N-(2-\text{tert}-\text{butyl}-1-(2-(4-\text{methoxyphenyl})-2-\text{oxoethyl})-1,2-\text{dihydroisoquinolin}-3(4H)-\text{ylidene})-4-\text{methylbenzenesulfonamide 4s}\]

Yield: 96%; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 8.04-8.01 (m, 2H), 7.93-7.70 (m, 4H),
7.41-7.36 (m, 2H), 7.28-7.24 (m, 2H), 6.98-6.95 (m, 2H), 5.29-5.08 (d, 1H), 4.42-4.28
(m, 2H), 3.87 (s, 3H), 3.73-3.71 (m, 2H), 2.41-2.37 (m, 3H), 1.23-1.19 (d, 9H); \(^{13}\)C
NMR (100 MHz, CDCl\(_3\)): \(\delta 21.8, 28.0, 28.2, 38.8, 38.9, 53.9, 55.8, 55.9, 114.2, 114.3,
125.8, 126.4, 128.4, 128.7, 128.8, 129.2, 129.3, 129.4, 129.5, 130.7, 131.0, 131.1,
131.30, 131.34, 132.2, 133.1, 135.3, 137.4, 140.2, 140.4, 140.9, 142.2, 142.3, 163.8,
164.2, 164.3, 165.1, 188.5, 190.5; HRMS calcd. for C\(_{29}\)H\(_{33}\)N\(_2\)O\(_4\)S\(^+\) [M+H]\(^+\): 505.2161,
found 505.2171.

\[
\text{\begin{tikzpicture}
\node[draw, circle] at (0,0) (o) {O};
\node[draw, rectangle, fill=none] at (-1,2) (a) {O};
\node[draw, rectangle, fill=none] at (-2,4) (b) {NTs};
\node[draw, rectangle, fill=none] at (-2,-2) (c) {NTs};
\node[draw, rectangle, fill=none] at (-1,-4) (d) {OMe};
\node[draw, rectangle, fill=none] at (-2,0) (e) {N};
\node[draw, rectangle, fill=none] at (-1,0) (f) {N};
\node[draw, rectangle, fill=none] at (-2,-2) (g) {N};
\node[draw, rectangle, fill=none] at (2,0) (h) {N};
\node[draw, rectangle, fill=none] at (2,-2) (i) {N};
\node[draw, rectangle, fill=none] at (2,0) (j) {NTs};
\node[draw, rectangle, fill=none] at (2,-2) (k) {OMe};
\node[draw, rectangle, fill=none] at (0,4) (l) {O};
\node[draw, rectangle, fill=none] at (0,-4) (m) {O};
\end{tikzpicture}}
\]

\[N-(2-\text{Benzyl}-1-(2-(4-\text{methoxyphenyl})-2-\text{oxoethyl})-1,2-\text{dihydroisoquinolin}-3(4H)-\text{ylidene})-4-\text{methylbenzenesulfonamide 4t}\]

Yield: 98%; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.81-7.75 (m, 4H), 7.29-7.18 (m, 11H),
6.89-6.87 (m, 2H), 5.37-5.30 (m, 2H), 5.05 (d, \(J = 19.60 \text{ Hz}, 1H), 4.97 (d, \(J = 14.80
\text{ Hz}, 1H), 4.12-4.06 (m, 1H), 3.84 (s, 3H), 3.40-3.25 (m, 2H), 2.39 (s, 3H); \(^{13}\)C NMR
(100 MHz, CDCl$_3$): $\delta$ 22.4, 34.7, 44.3, 52.8, 58.4, 114.8, 126.7, 127.1, 128.2, 128.8, 128.9, 129.2, 129.7, 130.1, 130.2, 130.4, 131.3, 135.9, 136.3, 141.7, 143.0, 164.9, 166.1, 195.5; HRMS calcd. for C$_{32}$H$_{31}$N$_2$O$_4$S$^+$ [M+H]$^+$: 539.2005, found 539.2029.

\[ N\text{-}(1-(2-(4-Methoxyphenyl)-2-oxoethyl)-2-octyl-1,2-dihydroisoquinolin-3(4H)-yliden)e)-4-methylbenzenesulfonamide 4u \]

Yield: 82%; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.85-7.83 (m, 2H), 7.80-7.78 (m, 2H), 7.31-7.17 (m, 6H), 6.88-6.87 (m, 2H), 5.29-5.27 (m, 1H), 4.94 (d, $J = 16.0$ Hz, 1H), 4.09-4.06 (m, 1H), 3.97 (d, $J = 15.6$ Hz 1H), 3.83 (s, 3H), 3.41-3.26 (m, 2H), 3.08-3.05 (m, 1H), 2.39 (s, 3H), 1.56-1.55 (m, 1H), 1.26-1.17 (m, 11H), 0.85 (t, $J = 5.60$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 14.4, 21.8, 22.9, 27.0, 27.2, 29.2, 32.0, 34.0, 43.7, 49.7, 55.8, 58.5, 114.2, 126.2, 126.4, 127.5, 128.1, 128.5, 129.4, 129.5, 130.1, 130.7, 135.2, 141.3, 142.2, 164.3, 164.6, 195.1; HRMS calcd. for C$_{33}$H$_{41}$N$_2$O$_4$S$^+$ [M+H]$^+$: 561.2787, found 561.2772.

\[ N\text{-}(1-(2-(4-Methoxyphenyl)-2-oxoethyl)-2-(piperidin-1-yl)-1,2-dihydroisoquinolin-3(4H)-ylidene)-4-methylbenzenesulfonamide 4v \]

Yield: 86%; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.87-7.85 (m, 4H), 7.27-7.15 (m, 6H), 6.90-6.88 (m, 2H), 4.72 (d, $J = 15.60$ Hz, 1H), 4.18 (d, $J = 15.60$ Hz, 1H), 3.84-3.81 (m, 4H), 3.53-3.39 (m, 3H), 2.86-2.81 (m, 2H), 2.41-2.37 (m, 4H), 1.64-1.37 (m, 6H);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.4, 23.5, 26.5, 34.8, 42.9, 55.5, 62.5, 113.8, 125.5, 126.1, 126.3, 127.0, 127.5, 128.0, 129.1, 129.3, 129.5, 130.4, 134.5, 141.1, 142.0, 163.0, 163.7, 194.7; HRMS calcd. for C$_{30}$H$_{34}$N$_3$O$_4$S$^+$ [M+H]$^+$: 532.2270, found 532.2289.