

Silver Triflate and *N*-Heterocyclic Carbene Co-Catalyzed Reaction of *N'*-(2-Alkynylbenzylidene)hydrazide, Methanol with α,β -Unsaturated Aldehyde

Zhiyuan Chen,[†] Xingxin Yu,[†] and Jie Wu^{*,†,‡}

[†]*Department of Chemistry, Fudan University, 220 Handan Road, Shanghai 200433, China, and*

[‡]*State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry,*

Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

jie_wu@fudan.edu.cn

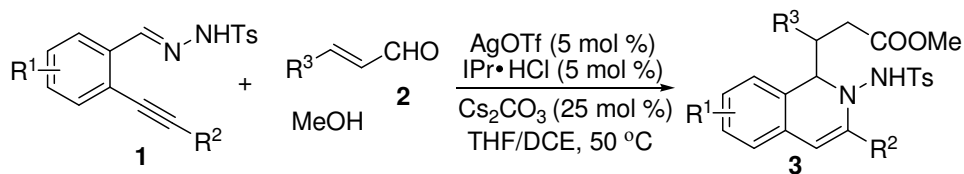
Supporting Information

1. General experimental methods (S2)
2. General experimental procedure and characterization data (S2-S11).
3. ¹H and ¹³C NMR spectra of compound **3** (S12-S45).
4. X-ray ORTEP illustration of 2-amino-1,2-dihydroisoquinoline **3m** (S46).

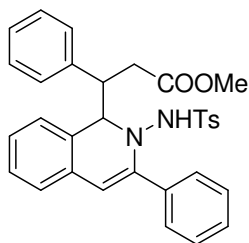
General experimental methods:

All reactions were performed in reaction tubes under nitrogen atmosphere. 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. Commercial reagents and solvents were used as received. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale.

General procedure for silver triflate and N-heterocyclic carbene co-catalyzed reaction of N'-(2-alkynylbenzylidene)hydrazide, methanol, with α,β-unsaturated aldehyde.



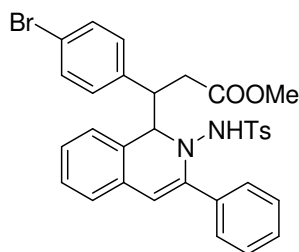
A mixture of *N'*-(2-alkynylbenzylidene)hydrazide **1** (0.2 mmol) and AgOTf (5 mol %) in DCE (1.0 mL) was stirred at 50 °C for 1 hour. Subsequently, α,β-unsaturated aldehyde **2** (0.24 mmol, 1.2 equiv), IPr•HCl (5 mol %), Cs₂CO₃ (25 mol %), and THF (1.8 mL), MeOH (0.2 mL) were added, and the mixture was stirred at 50 °C for a period of time. After completion of the reaction as indicated by TLC, the solvent was removed under vacuum, and the residue obtained was purified by flash chromatography column on silica gel (eluting with PE: EA = 1:4) to provide the desired product **3**.



Methyl

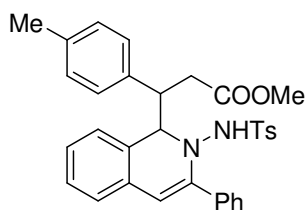
3-(2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)-3-phenylpropanoate **3a**

Yield: 94%; ^1H NMR (400 MHz, CDCl_3): 7.41-7.27 (m, 7H), 7.18-7.10 (m, 3H), 7.04-6.96 (m, 2H), 6.90-6.82 (m, 4H), 6.45 (d, $J = 7.80$ Hz, 2H), 6.02 (s, 1H), 6.00-5.94 (br, 1H), 5.07 (d, $J = 11.0$ Hz, 1H), 3.35 (s, 3H), 3.33-3.20 (m, 1H), 2.57-2.54 (dd, $^1J = 9.16$ Hz, $^2J = 5.48$ Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.6, 38.4, 44.7, 51.5, 70.0, 124.9, 126.4, 126.6, 127.3, 127.5, 127.8, 128.2, 128.4, 128.7, 128.8, 128.9, 129.1, 130.4, 131.9, 134.4, 134.9, 141.4, 143.8, 172.0; HRMS calcd. for $\text{C}_{32}\text{H}_{30}\text{N}_2\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 561.1824, found 561.1856.



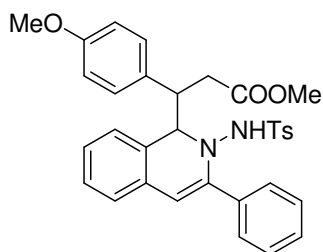
Methyl 3-(4-bromophenyl)-3-(2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)propanoate **3b**

Yield: 78%; ^1H NMR (400 MHz, CDCl_3): δ 7.51-7.47 (m, 2H), 7.36-7.29 (m, 2H), 7.21-7.11 (m, 5H), 6.97-6.86 (m, 6H), 6.46 (d, $J = 7.32$ Hz, 2H), 6.16 (s, 1H), 6.05-6.00 (br, 1H), 5.05 (d, $J = 10.6$ Hz, 1H), 3.37 (s, 3H), 3.23-3.17 (m, 1H), 2.57-2.51 (dd, $^1J = 9.64$ Hz, $^2J = 4.16$ Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.6, 38.2, 44.4, 51.6, 69.8, 120.9, 125.1, 125.1, 126.8, 127.2, 127.7, 127.9, 128.0, 128.2, 128.4, 129.1, 130.3, 130.8, 131.6, 134.2, 134.7, 140.4, 143.9, 171.7; HRMS calcd for $\text{C}_{32}\text{H}_{29}\text{BrN}_2\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 639.0929, found 639.0931.



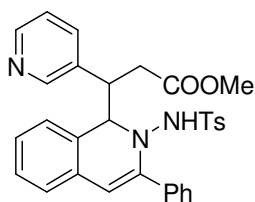
Methyl 3-(2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)-3-*p*-tolylpropanoate **3c**

Yield: 66%; ^1H NMR (400 MHz, CDCl_3): δ 7.33-7.27 (m, 2H), 7.22-7.18 (m, 4H), 7.16-7.11 (m, 3H), 7.06-6.72 (m, 2H), 6.90-6.83 (m, 4H), 6.51 (d, $J = 7.80$ Hz, 2H), 6.04 (s, 1H), 6.03-5.92 (br, 1H), 5.01 (d, $J = 10.5$ Hz, 1H), 3.34 (s, 3H), 3.26-3.20 (m, 1H), 2.52-2.47 (dd, $^1J = 9.64$ Hz, $^2J = 4.16$ Hz, 2H), 2.42 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.3, 21.6, 38.3, 44.1, 51.4, 70.1, 124.8, 126.3, 126.4, 127.5, 127.6, 127.7, 128.1, 128.4, 128.7, 128.9, 129.1, 129.4, 130.3, 131.9, 134.4, 134.8, 136.8, 138.2, 143.8, 172.0; HRMS calcd. for $\text{C}_{33}\text{H}_{32}\text{N}_2\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 575.1980, found 575.1982.



Methyl 3-(4-methoxyphenyl)-3-(2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)propanoate **3d**

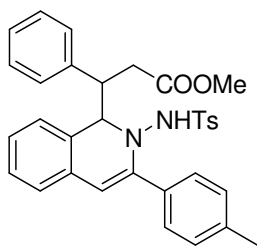
Yield: 70%; ^1H NMR (400 MHz, CDCl_3): δ 7.34-7.22 (m, 4H), 7.18-7.11 (m, 3H), 7.05-6.84 (m, 8H), 6.53 (d, $J = 7.32$ Hz, 2H), 6.08 (s, 1H), 5.98-5.90 (br, 1H), 5.00 (d, $J = 10.5$ Hz, 1H), 3.87 (s, 3H), 3.35 (s, 3H), 3.26-3.20 (m, 1H), 2.52-2.47 (dd, $^1J = 10.1$ Hz, $^2J = 4.12$ Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.6, 38.4, 43.8, 51.4, 55.4, 70.1, 114.0, 124.8, 126.3, 126.4, 127.5, 127.7, 127.8, 128.1, 128.3, 128.5, 128.8, 129.1, 129.8, 130.4, 131.8, 133.1, 134.4, 134.8, 143.8, 158.7, 172.1; HRMS calcd. for $\text{C}_{33}\text{H}_{32}\text{N}_2\text{O}_5\text{S}$ $[\text{M}+\text{Na}]^+$: 591.1930, found 591.1961.



methyl

3-(2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)-3-(pyridin-3-yl)propanoate **3e**

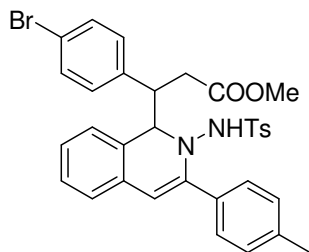
Yield: 83%. ^1H NMR (400 MHz, CDCl_3): 8.55 (d, $J = 4.12$ Hz, 1H), 8.46 (s, 1H), 7.70 (d, $J = 9.68$ Hz, 1H), 7.38-7.27 (m, 4H), 7.24-7.10 (m, 3H), 7.02-6.94 (m, 2H), 6.90-6.87 (m, 4H), 6.52 (d, $J = 7.32$ Hz, 2H), 6.30-6.00 (br, 1H), 5.14 (d, $J = 10.52$ Hz, 1H), 3.39 (s, 3H), 3.28-3.24 (m, 1H), 2.61 (d, $J = 7.32$ Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.6, 38.0, 42.8, 51.6, 69.8, 123.4, 125.2, 126.4, 126.9, 127.1, 127.6, 128.0, 128.1, 128.3, 128.9, 129.1, 130.2, 130.3, 131.6, 134.3, 135.0, 136.3, 136.8, 143.8, 148.3, 150.5, 171.6; HRMS calcd. for $\text{C}_{31}\text{H}_{29}\text{N}_3\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 562.1776, found 562.1781.



Methyl 3-(2-(4-methylphenylsulfonamido)-3-*p*-tolyl-1,2-dihydroisoquinolin-1-yl)-3-phenylpropanoate **3f**

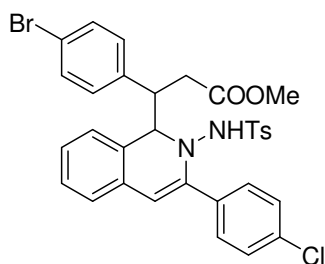
Yield: 66%; ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.27 (m, 7H), 7.17-7.12 (m, 2H), 6.90-6.85 (m, 4H), 6.80-6.78 (m, 2H), 6.34 (d, $J = 6.88$ Hz, 2H), 6.02 (s, 1H), 6.00-5.94 (br, 1H), 5.04 (d, $J = 10.5$ Hz, 1H), 3.34 (s, 3H), 3.28-3.23 (m, 1H), 2.57-2.53 (dd, $^1J = 9.16$ Hz, $^2J = 5.48$ Hz, 2H), 2.37 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.2, 21.6, 38.4, 44.7, 51.4, 69.8, 124.8, 126.2, 127.2, 127.4, 127.5, 127.7, 128.3, 128.4, 128.5, 128.7, 128.8, 128.9, 129.0, 130.4, 131.5, 132.1,

134.8, 138.2, 141.4, 143.8, 172.0; HRMS calcd. for $C_{33}H_{32}N_2O_4S [M+Na]^+$: 575.1980, found 575.1926.



Methyl 3-(4-bromophenyl)-3-(2-(4-methylphenylsulfonamido)-3-*p*-tolyl-1,2-dihydroisoquinolin-1-yl)propanoate **3g**

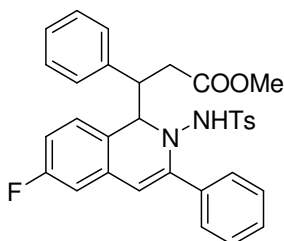
Yield: 53%; 1H NMR (400 MHz, $CDCl_3$): δ 7.52-7.49 (m, 2H), 7.36-7.28 (m, 2H), 7.21-7.16 (m, 4H), 6.92-6.85 (m, 4H), 6.81-6.77 (m, 2H), 6.35 (d, $J = 7.80$ Hz, 2H), 6.11 (s, 1H), 6.10-5.99 (br, 1H), 5.03 (d, $J = 11.0$ Hz, 1H), 3.37 (s, 3H), 3.21-3.17 (m, 1H), 2.56-2.52 (dd, $^1J = 9.64$ Hz, $^2J = 3.68$ Hz, 2H), 2.38 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3, 21.7, 38.3, 44.4, 51.6, 69.7, 120.9, 125.1, 126.6, 127.2, 127.8, 128.0, 128.5, 128.6, 129.0, 130.2, 130.8, 131.4, 131.6, 131.8, 134.7, 138.3, 140.4, 143.9, 171.8; HRMS calcd. for $C_{33}H_{31}BrN_2O_4S [M+Na]^+$: 653.1086, found 653.1072.



Methyl 3-(4-bromophenyl)-3-(3-(4-chlorophenyl)-2-(4-methylphenylsulfonamido)-1,2-dihydroisoquinolin-1-yl)propanoate **3h**

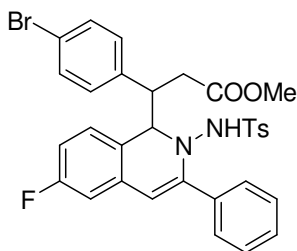
Yield: 82%; 1H NMR (400 MHz, $CDCl_3$): δ 7.51-7.47 (m, 2H), 7.36-7.29 (m, 2H), 7.22-7.15 (m, 4H), 6.96-6.85 (m, 6H), 6.41 (d, $J = 8.24$ Hz, 2H), 6.13 (s, 1H), 6.12-5.90 (br, 1H), 5.01 (d, $J = 10.5$ Hz, 1H), 3.36 (s, 3H), 3.18-3.07 (m, 1H), 2.58-2.54 (dd, $^1J = 12.84$ Hz, $^2J = 7.36$ Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ

21.6, 38.4, 44.6, 51.6, 69.9, 120.9, 125.4, 127.1, 127.8, 128.1, 128.2, 128.4, 128.5, 128.7, 129.1, 129.3, 130.2, 130.8, 131.2, 131.6, 133.0, 133.9, 134.7, 140.3, 144.2, 171.7; HRMS calcd. for $C_{32}H_{28}BrClN_2O_4S$ $[M+Na]^+$: 673.0539, found 673.0552.



Methyl 3-(6-fluoro-2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)-3-phenylpropanoate **3i**

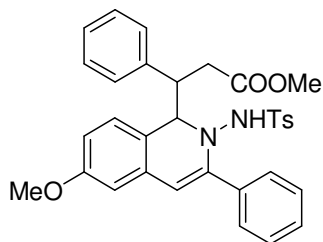
Yield: 64%; 1H NMR (400 MHz, $CDCl_3$): 7.42-7.25 (m, 5H), 7.17-7.08 (m, 2H), 7.02-7.6.96 (m, 3H), 6.92-6.83 (m, 5H), 6.44 (d, $J = 7.32$ Hz, 2H), 6.05 (s, 1H), 5.85 (br, 1H), 5.07 (d, $J = 10.5$ Hz, 1H), 3.37 (s, 3H), 3.32-3.26 (m, 1H), 2.54-2.51 (dd, $^1J = 9.16$ Hz, $^2J = 5.48$ Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 38.1, 44.7, 51.5, 69.6, 110.8 (d, $^2J_{CF} = 22.9$ Hz), 112.9 (d, $^2J_{CF} = 22.9$ Hz), 126.1, 127.4, 127.6, 127.8, 128.3, 128.5, 128.6, 128.7, 128.8, 129.1, 133.8, 133.9, 134.7, 141.1, 142.1, 144.0, 162.5 (d, $^1J_{CF} = 243.1$ Hz), 171.8. HRMS calcd. for $C_{32}H_{29}FN_2O_4S$ $[M+Na]^+$: 579.1730, found 579.1748.



Methyl 3-(4-bromophenyl)-3-(6-fluoro-2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)propanoate **3j**

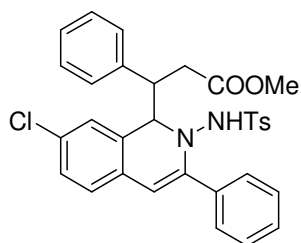
Yield: 65%; 1H NMR (400 MHz, $CDCl_3$): δ 7.52-7.48 (m, 2H), 7.20-7.09 (m, 4H), 7.04-6.97 (m, 3H), 6.94-6.85 (m, 5H), 6.45 (d, $J = 7.32$ Hz, 2H), 6.21 (s, 1H), 5.98-5.89 (br, 1H), 5.06 (d, $J = 10.6$ Hz, 1H), 3.39 (s, 3H), 3.25-3.18 (m, 1H),

2.54-2.49 (dd, $^1J = 8.28$ Hz, $^2J = 2.32$ Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.6, 37.9, 44.5, 51.6, 69.4, 111.1 (d, $^2J_{\text{CF}} = 25.8$ Hz), 113.3, (d, $^2J_{\text{CF}} = 22.9$ Hz), 121.1, 126.0, 127.3, 128.0, 128.3, 128.6, 128.8, 128.9, 129.2, 130.6, 131.7, 133.6, 133.7, 134.7, 140.1, 142.1, 144.1, 162.5 (d, $^1J_{\text{CF}} = 243.1$ Hz), 171.6; HRMS calcd. for $\text{C}_{32}\text{H}_{28}\text{BrFN}_2\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 657.0835, found 657.0873.



Methyl 3-(6-methoxy-2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)-3-phenylpropanoate **3k**

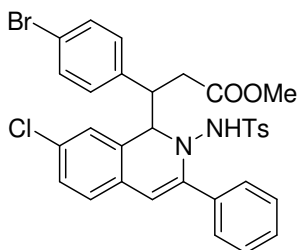
Yield: 55%; ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.32 (m, 5H), 7.15-7.11 (m, 1H), 7.05-6.96 (m, 3H), 6.93-6.88 (m, 4H), 6.86-6.83 (m, 1H), 6.72-6.70 (m, 1H), 6.48 (d, $J = 7.80$ Hz, 2H), 6.00 (s, 1H), 6.00-5.84 (br, 1H), 5.00 (d, $J = 11.0$ Hz, 1H), 3.88 (s, 3H), 3.36 (s, 3H), 3.28-3.24 (m, 1H), 2.56-2.52 (dd, $^1J = 9.16$ Hz, $^2J = 2.72$ Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.6, 38.4, 45.0, 51.5, 55.4, 69.5, 109.6, 112.1, 123.2, 127.3, 127.6, 127.8, 128.2, 128.4, 128.7, 128.8, 128.9, 129.1, 133.1, 134.4, 134.9, 141.4, 143.8, 159.3, 172.0; HRMS calcd. for $\text{C}_{33}\text{H}_{32}\text{N}_2\text{O}_5\text{S}$ $[\text{M}+\text{Na}]^+$: 591.1930, found 591.1939.



Methyl 3-(7-chloro-2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)-3-phenylpropanoate **3l**

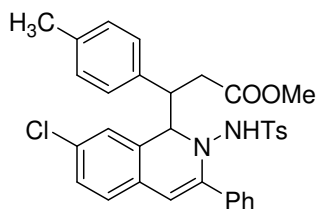
Yield: 65%; ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.26 (m, 6H), 7.18-7.07 (m, 2H),

7.04-6.96 (m, 3H), 6.94-6.91 (m, 4H), 6.51 (d, $J = 7.36$ Hz, 2H), 6.12 (s, 1H), 5.95 (br, 1H), 4.92 (d, $J = 10.8$ Hz, 1H), 3.39 (s, 3H), 3.30-3.25 (m, 1H), 2.53 (d, $J = 7.60$ Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.6, 38.0, 44.4, 51.5, 69.6, 125.7, 126.9, 127.4, 127.5, 127.7, 127.8, 128.2, 128.3, 128.6, 128.7, 129.1, 130.5, 131.5, 131.6, 134.0, 134.7, 140.9, 141.4, 144.0, 171.7; HRMS calcd for $\text{C}_{32}\text{H}_{29}\text{ClN}_2\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 595.1434, found 595.1477.



Methyl 3-(4-bromophenyl)-3-(7-chloro-2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)propanoate **3m**

Yield: 92%; ^1H NMR (400 MHz, CDCl_3): δ 7.49-7.46 (m, 2H), 7.30-7.28 (m, 1H), 7.18-7.09 (m, 4H), 7.04-6.99 (m, 3H), 6.96-6.91 (m, 4H), 6.51 (d, $J = 7.36$ Hz, 2H), 6.31 (s, 1H), 6.04-5.97 (br, 1H), 4.92 (d, $J = 10.6$ Hz, 1H), 3.40 (s, 3H), 3.22-3.18 (m, 1H), 2.54-2.51 (d, $J = 7.32$ Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.7, 37.9, 44.3, 51.6, 69.5, 121.1, 126.1, 127.1, 127.3, 127.9, 128.3, 128.5, 129.2, 130.3, 130.6, 131.7, 131.8, 131.9, 133.9, 134.8, 139.9, 141.4, 144.1, 171.6; HRMS calcd. for $\text{C}_{32}\text{H}_{28}\text{BrClN}_2\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 673.0539, found 673.0536.

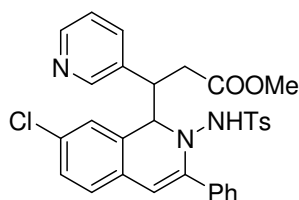


methyl

3-(7-chloro-2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)-3-*p*-tolylpropanoate **3n**

Yield: 75%; ^1H NMR (400 MHz, CDCl_3): 7.29-7.24 (m, 1H), 7.22-7.15 (m, 5H),

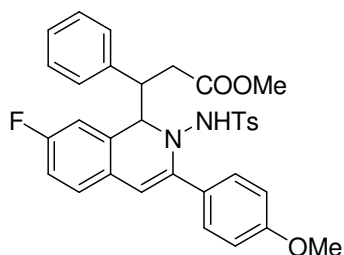
7.10-7.03 (m, 3H), 6.98-6.90 (m, 5H), 6.58 (s, 1H), 6.56 (s, 1H), 6.08 (s, 1H), 5.93-5.91 (br, 1H), 4.86 (d, $J = 10.56$ Hz, 1H), 3.38 (s, 3H), 3.26-3.22 (m, 1H), 2.48 (d, $J = 5.26$ Hz, 2H), 2.42 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.3, 21.7, 38.1, 43.9, 51.6, 69.9, 125.8, 126.9, 127.7, 127.8, 127.9, 128.3, 128.4, 128.6, 129.3, 129.6, 130.6, 131.4, 131.6, 134.2, 134.8, 137.1, 137.8, 141.6, 144.1, 171.9; HRMS calcd. for $\text{C}_{33}\text{H}_{31}\text{ClN}_2\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 609.1591, found 609.1599.



Methyl

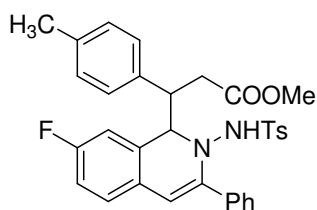
3-(7-chloro-2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)-3-(pyridin-3-yl)propanoate **3o**

Yield: 77%; ^1H NMR (400 MHz, CDCl_3): 8.47 (d, $J = 3.68$ Hz, 1H), 8.44 (d, $J = 1.84$ Hz, 1H), 7.62 (d, $J = 7.80$ Hz, 1H), 7.31-7.23 (m, 2H), 7.17-7.08 (m, 3H), 7.05-6.96 (m, 3H), 6.96-6.91 (m, 4H), 6.57 (m, 2H), 6.14-6.00 (br, 1H), 5.01 (d, $J = 10.08$ Hz, 1H), 3.41 (s, 3H), 3.26-3.23 (m, 1H), 2.62-2.56 (m, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.6, 37.6, 42.7, 51.7, 69.5, 123.5, 126.1, 127.2, 127.4, 128.1, 128.2, 128.3, 128.6, 129.3, 129.4, 130.2, 131.6, 132.1, 134.0, 135.1, 136.3, 136.5, 141.3, 144.0, 148.4, 150.2, 171.5; HRMS calcd. for $\text{C}_{31}\text{H}_{28}\text{ClN}_3\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 596.1387, found 596.1398.



Methyl 3-(7-fluoro-3-(4-methoxyphenyl)-2-(4-methylphenylsulfonamido)-1,2-dihydroisoquinolin-1-yl)-3-phenylpropanoate **3p**

Yield: 54%; ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.29 (m, 5H), 7.17-7.08 (m, 1H), 6.98-6.88 (m, 5H), 6.85-6.82 (m, 1H), 6.56-6.51 (m, 2H), 6.41-6.35 (m, 2H), 6.05-6.01 (br, 1H), 5.89-5.78 (br, 1H), 5.03 (d, $J = 11.0$ Hz, 1H), 3.76 (s, 3H), 3.36 (s, 3H), 3.31-3.24 (m, 1H), 2.58-2.48(m, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.6, 38.1, 44.5, 51.5, 55.3, 69.5, 69.6, 110.8 (d, $^2J_{CF} = 22.8$ Hz), 112.5 (d, $^2J_{CF} = 22.8$ Hz), 113.2, 125.9, 126.4, 126.7, 127.4, 128.3, 128.5, 128.6, 128.8, 129.0, 129.1, 134.1, 134.7, 141.2, 141.9, 143.9, 159.9, 162.4 (d, $^1J_{CF} = 243.1$ Hz), 171.9; HRMS calcd. for $\text{C}_{33}\text{H}_{31}\text{FN}_2\text{O}_5\text{S}$ $[\text{M}+\text{Na}]^+$: 609.1835, found 609.1837.



Methyl

3-(7-fluoro-2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl)-3-*p*-tolylpropanoate **3q**

Yield: 68%; ^1H NMR (400 MHz, CDCl_3): 7.23-7.18 (m, 4H), 7.16-7.10 (m, 2H), 7.05-6.98 (m, 3H), 6.94-6.90 (m, 4H), 6.79 (dd, $^1J = 2.28$ Hz, $^2J = 8.72$ Hz, 1H), 6.51 (d, $J = 7.36$ Hz, 1H), 6.08 (s, 1H), 5.94-5.92 (br, 1H), 4.95 (d, $J = 10.96$ Hz, 1H), 3.38 (s, 3H), 3.29-3.21 (m, 1H), 2.53-2.51 (dd, $^1J = 5.48$ Hz, $^2J = 8.725.48$ Hz, 2H), 2.41 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.2, 21.5, 38.1, 44.0, 51.4, 69.7, 114.1 (d, $^2J = 22.9$ Hz), 114.6, (d, $^2J = 21.9$ Hz), 125.9, 126.0, 127.4, 127.7, 128.1, 128.2, 128.6, 129.0, 129.4, 132.1, 132.2, 134.2, 134.8, 136.9, 137.7, 140.3, 143.9, 161.5 (d, $^1J = 245.0$ Hz), 171.8; HRMS calcd. for $\text{C}_{33}\text{H}_{31}\text{FN}_2\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 593.1886, found 593.1897.

