A palladium-catalyzed tandem reaction of 2-alkynylbenzenesulfonamides with 2-(2-bromoarylidene)cyclobutanones

Xinxing Gong, a Hongguang Xia, b,* and Jie Wu a,c,*

a Department of Chemistry, Fudan University, 220 Handan Road, Shanghai 200433, China
b Department of Biochemistry and Molecular Biology, Zhejiang University School of Medicine, Hangzhou 310058, China
c State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

jie_wu@fudan.edu.cn

Supporting Information

1. General experimental methods (S2).
2. General experimental procedure and characterization data (S2-S9).
3. 1H and 13C NMR spectra of compounds 3 (S10-S39).
General experimental methods:

Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63μm, 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 at 25–35°C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale. $^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$ on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values are quoted in ppm and coupling constants quoted in Hz. High resolution mass spectrometry (HRMS) spectra were obtained on a micrOTOF II Instrument.

General experimental procedure for the palladium-catalyzed reaction of 2-alkynylbenzenesulfonamides 1 with 2-(2-bromobenzylidene)cyclobutanones 2

\[
\text{2-(2-Bromobenzylidene)cyclobutanone 2 (0.24 mmol) was added to a mixture of 2-alkynylbenzenesulfonamide 1 (0.20 mmol), Pd(OAc)$_2$ (5 mol %), PCy$_3$ (10 mol %), and K$_2$CO$_3$ (2.0 equiv) in 1,4-dioxane (2.0 mL) under N$_2$ atmosphere, and the suspension was heated to 80 °C. After the conversion was completed as indicated by TLC, the solvent was evaporated under reduced pressure. The residue was purified directly by flash column chromatograph to give the corresponding product 3.}
\]
6-Methyl-15-phenyl-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazonin-7(6H)-one 5,5-dioxide (3a). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.01 (d, $J$ = 7.8 Hz, 1H), 7.86 (d, $J$ = 8.2 Hz, 1H), 7.71 (s, 1H), 7.52-7.47 (m, 2H), 7.39-7.32 (m, 3H), 7.28-7.25 (m, 2H), 7.22-7.17 (m, 3H), 7.01-7.00 (m, 1H), 3.17-3.08 (m, 3H), 2.73-2.53 (m, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 172.6, 140.8, 139.0, 138.2, 135.4, 133.8, 133.1, 132.3, 131.8, 130.9, 130.4, 128.5, 128.4, 127.9, 127.5, 127.1, 126.9, 126.5, 126.3, 37.3, 32.0, 29.6. HRMS (ESI) calcd for C$_{26}$H$_{22}$NO$_3$S$: 428.1315 (M + H$^+$), found: 428.1310.

6,13-Dimethyl-15-phenyl-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazonin-7(6H)-one 5,5-dioxide (3b). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.00 (d, $J$ = 7.9 Hz, 1H), 7.76 (d, $J$ = 8.32 Hz, 1H), 7.65 (s, 1H), 7.39-7.32 (m, 3H), 7.29-7.25 (m, 2H), 7.22-7.16 (m, 4H), 7.00 (m, 1H), 3.17-3.04 (m, 3H), 2.69-2.53 (m, 4H), 2.37 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 172.7, 140.9, 138.4, 137.5, 136.1, 135.4, 133.7, 132.2, 132.0, 131.4, 131.0, 130.4, 128.8, 128.4, 128.3, 127.8, 127.4, 127.1, 126.9, 125.7, 37.2, 31.9, 29.8, 21.9. HRMS (ESI) calcd for C$_{27}$H$_{24}$NO$_3$S$: 442.1471 (M + H$^+$), found: 442.1461.

6,12-Dimethyl-15-(p-tolyl)-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazonin-7(6H)-one 5,5-dioxide (3c). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.00 (d, $J$ = 7.3 Hz, 1H), 7.74 (d, $J$ = 8.2 Hz, 1H), 7.53 (s, 1H), 7.39-7.32 (m, 3H), 7.29-7.25 (m, 2H), 7.22-7.17 (m, 3H), 7.01-7.00 (m, 1H), 3.17-3.08 (m, 3H), 2.73-2.53 (m, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 172.7, 140.9, 138.4, 137.5, 136.1, 135.4, 133.7, 132.2, 132.0, 131.4, 131.0, 130.4, 128.8, 128.4, 128.3, 127.8, 127.4, 127.1, 126.9, 125.7, 37.2, 31.9, 29.8, 21.9. HRMS (ESI) calcd for C$_{27}$H$_{24}$NO$_3$S$: 442.1471 (M + H$^+$), found: 442.1461.
ne 5,5-dioxide (3c). ¹H NMR (400 MHz, CDCl₃): δ 8.00 (d, J = 7.6 Hz, 1H), 7.74 (d, J = 8.3 Hz, 1H), 7.63 (s, 1H), 7.38-7.31 (m, 3H), 7.24 (s, 1H), 7.17-7.15 (m, 1H), 7.05-6.99 (m, 4H) 3.16-3.00 (m, 3H), 2.66-2.51 (m, 4H), 2.36 (s, 3H), 2.27 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 172.7, 140.9, 138.5, 136.3, 136.0, 135.4, 135.2, 133.7, 132.3, 132.2, 131.4, 130.9, 130.3, 129.0, 128.7, 127.9, 127.8, 127.4, 125.8, 37.2, 31.8, 29.9, 21.9, 21.2. HRMS (ESI) calcd for C₂₈H₂₆NO₃S: 456.1628 (M + H⁺), found: 456.1625.

![Image](image-url)

12,13-Dimethoxy-6-methyl-15-phenyl-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazin-7(6H)-one 5,5-dioxide (3d). ¹H NMR (400 MHz, CDCl₃): δ 8.00 (d, J = 7.7 Hz, 1H), 7.55 (s, 1H), 7.39-7.25 (m, 4H), 7.22-7.15 (m, 4H), 7.00 (d, J = 7.2 Hz, 1H), 6.75 (s, 1H), 4.03 (s, 3H), 3.69 (s, 3H), 3.11 (s, 3H), 2.71-2.52 (s, 4H). ¹³C NMR (100 MHz, CDCl₃): δ 172.7, 149.9, 149.6, 138.5, 137.7, 133.8, 133.5, 132.2, 130.7, 130.4, 129.1, 128.5, 128.3, 128.2, 127.8, 127.4, 127.2, 126.9, 126.7, 105.9, 105.6, 55.9, 55.5, 37.2, 31.9, 29.8. HRMS (ESI) calcd for C₂₈H₂₆NO₅S: 488.1526 (M + H⁺), found: 488.1524.

![Image](image-url)

12-Fluoro-6-methyl-15-phenyl-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazonin-7(6 H)-one 5,5-dioxide (3e). ¹H NMR (400 MHz, CDCl₃): δ 8.00 (d, J = 7.8 Hz, 1H), 7.64 (s, 1H), 7.50-7.46 (m, 2H), 7.39-7.33 (m, 2H), 7.31-7.26 (m, 2H), 7.20-7.11 (m, 4H), 7.00 (m, 1H), 3.16-3.14 (m, 3H), 2.79 (s, 3H), 2.50 (s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 172.4, 161.0 (d, Jₜₙ = 246.0 Hz), 139.1, 138.6, 137.2, 134.8, 134.1 (d, Jₜₙ = 9.3 Hz), 133.8, 132.4, 130.8, 130.3, 129.7, 129.6, 128.8, 128.6, 128.4, 127.9, 127.2, 127.1, 116.4 (d, Jₜₙ = 24.8 Hz), 110.5 (d, Jₜₙ = 20.4 Hz), 37.3, 32.1, 29.5. HRMS (ESI) calcd
for C_{26}H_{21}FNO_{3}S^+: 446.1221 (M + H\(^+\)), found: 446.1202.

2-Chloro-6-methyl-15-phenyl-8,9-dihydrobenzo[h]naptho[2,3-f][1,2]thiazonin-7(6H)-one 5,5-dioxide (3f). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.93 (d, \(J = 8.7\) Hz, 1H), 7.86 (d, \(J = 8.1\) Hz, 1H), 7.72 (s, 1H), 7.53-7.47 (m, 2H), 7.40-7.38 (m, 1H), 7.36-7.31 (m, 2H), 7.25-7.17 (m, 4H), 7.02 (m, 1H), 3.22-3.10 (m, 3H), 2.73-2.54 (m, 4H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 172.4, 139.3, 138.5, 137.8, 134.2, 133.7, 133.3, 131.7, 130.8, 130.2, 129.5, 128.6, 128.5, 128.1, 127.5, 127.4, 127.3, 126.9, 126.8, 126.4, 37.3, 32.2, 29.7. HRMS (ESI) calcd for C_{26}H_{21}ClNO_{3}S^+: 462.0925 (M + H\(^+\)), found: 462.0923.

2-Methoxy-6-methyl-15-phenyl-8,9-dihydrobenzo[h]naptho[2,3-f][1,2]thiazinon-7(6H)-one 5,5-dioxide (3g). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.90 (d, \(J = 9.0\) Hz, 1H), 7.86 (d, \(J = 8.2\) Hz, 1H), 7.71 (s, 1H), 7.50-7.48 (m, 2H), 7.38-7.34 (m, 1H), 7.29-7.21 (m, 5H), 6.85-6.82 (m, 1H), 6.45 (m, 1H), 3.64 (s, 3H), 3.19-3.17 (m, 3H), 2.82-2.54 (s, 4H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 172.7, 161.9, 139.9, 138.8, 138.4, 135.6, 133.2, 131.7, 130.9, 130.5, 130.1, 128.5, 127.7, 127.5, 127.0, 126.9, 126.5, 126.2, 118.3, 114.4, 55.5, 37.5, 32.2, 29.6. HRMS (ESI) calcd for C_{27}H_{24}NO_{4}S^+: 458.1421 (M + H\(^+\)), found: 458.1419.
6-Methyl-15-(p-tolyl)-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazonin-7(6H)-one 5,5-dioxide (3h). $^1$H NMR (400 MHz, CDCl$_3$): δ 8.01 (d, J = 7.8 Hz, 1H), 7.85-7.83 (m, 1H), 7.68 (s, 1H), 7.50-7.46 (m, 2H), 7.39-7.31 (m, 3H), 7.15-7.14 (m, 1H), 7.05-6.99 (m, 4H), 3.18-3.04 (m, 3H), 2.69-2.52 (s, 4H), 2.27 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 172.6, 140.9, 139.1, 137.5, 136.5, 135.4, 135.1, 133.7, 133.1, 132.3, 132.0, 130.8, 130.3, 129.0, 128.4, 127.9, 127.8, 127.5, 126.9, 126.4, 126.2, 37.3, 31.9, 29.7, 21.1. HRMS (ESI) calcd for C$_{27}$H$_{24}$NO$_3$S$^+$: 442.1471 (M + H$^+$), found: 442.1468.

2-Chloro-12,13-dimethoxy-6-methyl-15-phenyl-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazonin-7(6H)-one 5,5-dioxide (3l). $^1$H NMR (400 MHz, CDCl$_3$): δ 7.94 (d, J = 8.7 Hz, 1H), 7.56 (s, 1H), 7.34-7.31 (m, 2H), 7.26 (s, 1H), 7.23-7.18 (m, 3H), 7.15 (s, 1H), 7.01 (m, 1H), 6.74 (s, 1H), 4.03 (s, 3H), 3.70 (s, 3H), 3.15-3.07 (m, 3H), 2.70-2.55 (m, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 172.6, 150.1, 149.7, 139.4, 138.4, 138.2, 137.8, 133.7, 132.3, 130.6, 130.2, 129.4, 129.3, 128.6, 128.4, 127.4, 127.2, 126.7, 105.9, 105.6, 55.9, 55.6, 37.3, 32.1, 29.6. HRMS (ESI) calcd for C$_{28}$H$_{25}$ClNO$_5$S$^+$: 522.1136 (M + H$^+$), found: 522.1116.
15-(4-Chlorophenyl)-2,6-dimethyl-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazonin-7(6H)-one 5,5-dioxide (3j). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.90-7.85 (m, 2H), 7.71 (s, 1H), 7.53-7.49 (m, 1H), 7.43-7.36 (m, 2H), 7.28-7.18 (m, 4H), 7.13-7.11 (m, 1H), 6.79 (s, 1H), 3.18-3.11 (m, 3H), 2.75-2.55 (m, 4H), 2.24 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 172.6, 143.5, 137.6, 136.9, 135.7, 134.1, 133.1, 133.0, 132.2, 131.8, 131.6, 129.4, 128.6, 128.1, 127.6, 127.3, 126.5, 126.4, 37.3, 32.0, 29.6, 21.1. HRMS (ESI) calcd for C$_{27}$H$_{23}$ClNO$_3$S$: 476.1082 (M + H$^+$), found: 476.1077.

12,13-Dimethoxy-6-methyl-15-(p-tolyl)-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazonin-7(6H)-one 5,5-dioxide (3k). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.03 (d, J = 7.6 Hz, 1H), 7.54 (s, 1H), 7.40-7.34 (m, 2H), 7.15 (s, 2H), 7.08 (s, 2H), 7.01 (d, J = 7.6 Hz, 2H), 6.80 (s, 1H), 4.04 (s, 3H), 3.72 (s, 3H), 3.16-3.05 (m, 3H), 2.69-2.52 (m, 4H), 2.29 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 172.8, 149.9, 149.5, 137.7, 136.4, 135.4, 133.8, 133.5, 132.2, 130.5, 130.2, 129.1, 128.3, 127.9, 127.7, 127.6, 126.6, 105.9, 105.8, 55.9, 55.6, 37.2, 31.9, 29.7, 21.1. HRMS (ESI) calcd for C$_{29}$H$_{28}$NO$_5$S$: 502.1683 (M + H$^+$), found: 502.1672.
12-Fluoro-2-methoxy-6-methyl-15-phenyl-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazonin-7(6H)-one 5,5-dioxide (3i). $^1$H NMR (400 MHz, CDCl$_3$): δ 7.90 (d, $J = 8.8$ Hz, 1H), 7.65 (s, 1H), 7.51-7.45 (m, 2H), 7.30 (s, 1H), 7.25-7.22 (m, 4H), 7.12 (t, $J = 7.9$ Hz, 1H), 6.84 (d, $J = 7.5$ Hz, 1H), 6.44 (s, 1H), 3.65 (s, 3H), 3.17 (m, 3H), 2.88-2.52 (m, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 172.5, 162.0, 161.0 (d, $^{1}J_{CF} = 250.0$ Hz), 138.9, 138.2, 134.2 (d, $^{3}J_{CF} = 9.4$ Hz), 130.7, 130.4, 130.1, 129.7 (d, $^{3}J_{CF} = 8.9$ Hz), 129.4, 128.8, 128.6, 127.2, 127.1, 126.8, 122.4, 118.4, 116.3 (d, $^{2}J_{CF} = 24.9$ Hz), 114.5, 110.4 (d, $^{2}J_{CF} = 20.5$ Hz), 55.5, 37.4, 32.2, 29.1. HRMS (ESI) calcd for C$_{27}$H$_{23}$FNO$_{4}$S$: 476.1326$ (M + H$^+$), found: 476.1316.

15-(4-Chlorophenyl)-12-fluoro-2,6-dimethyl-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazonin-7(6H)-one 5,5-dioxide (3m). $^1$H NMR (400 MHz, CDCl$_3$): δ 7.88 (d, $J = 8.3$ Hz, 1H), 7.65 (s, 1H), 7.48-7.40 (m, 2H), 7.28-7.26 (m, 1H), 7.22-7.17 (m, 3H), 7.16-7.10 (m, 2H), 6.78 (s, 1H), 3.19-3.12 (m, 3H), 2.82-2.49 (m, 4H), 2.24 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 172.4, 162.2, 159.7, 143.6, 137.7, 136.7, 135.2, 134.2, 134.0, 133.2, 132.0, 131.7, 129.5, 129.3 (d, $^{3}J_{CF} = 8.8$ Hz), 128.7, 128.6, 128.2, 127.4, 116.6 (d, $^{2}J_{CF} = 24.9$ Hz), 110.6 (d, $^{2}J_{CF} = 20.6$ Hz), 37.3, 32.1, 29.7, 21.1. HRMS (ESI) calcd for C$_{27}$H$_{22}$ClFNO$_{4}$S$: 494.0987$ (M + H$^+$), found: 494.0987.
15-Cyclopropyl-6-methyl-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazin-7(6H)-one 5,5-dioxide (3n). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.59 (d, $J = 8.0$ Hz, 1H), 8.21 (s, 1H), 7.81-7.79 (m, 1H), 7.66-7.60 (m, 3H), 7.56-7.49 (m, 2H), 7.28-7.25 (m, 1H), 3.04 (s, 3H), 2.51-2.02 (m, 4H), 1.26 (s, 1H), 0.95 (s, 1H), 0.52-0.45 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 172.7, 140.2, 136.2, 133.3, 133.2, 133.0, 132.7, 128.8, 128.6, 128.0, 126.3, 126.0, 125.5, 37.5, 31.9, 29.7, 13.0, 9.5, 7.4. HRMS (ESI) calcd for C$_{23}$H$_{22}$NO$_3$S$^+$: 392.1315 (M + H$^+$), found: 392.1308.

6-Benzyl-15-phenyl-8,9-dihydrobenzo[h]naphtho[2,3-f][1,2]thiazin-7(6H)-one 5,5-dioxide (3o). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.95 (s, 1H), 7.88 (d, $J = 7.9$ Hz, 1H), 7.75 (s, 1H), 7.53-7.50 (m, 2H), 7.40-7.36 (m, 2H), 7.32-7.30 (m, 2H), 7.26-7.16 (m, 9H), 7.02-7.00 (m, 1H), 4.34 (s, 2H), 3.19-2.95 (m, 3H), 2.59-2.56 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 172.6, 141.1, 139.2, 138.2, 136.8, 135.3, 133.6, 133.2, 132.4, 131.9, 131.0, 130.5, 128.7, 128.5, 128.3, 128.3, 127.7, 127.5, 127.3, 127.2, 127.0, 126.6, 126.4, 49.7, 37.5, 30.1. HRMS (ESI) calcd for C$_{32}$H$_{26}$NO$_3$S$^+$: 504.1628 (M + H$^+$), found: 504.1623.