Supporting Information

Generation of ArS-substituted Flavone Derivatives via Using Aryl Thiols as Sulfenylating Agents

Wannian Zhao, Ping Xie, Zhaogang Bian, Aihua Zhou, Haibo Ge, Ben Niu, and Yingcai Ding

Pharmacy School, Jiangsu University, Xuefu Road 301, Zhenjiang City, Jiangsu, China, 212013,
Scientific Information Research Institute, Jiangsu University (Library)
Department of Chemistry and Chemical Biology, Indiana University Purdue University Indianapolis, Indianapolis IN 46202 (USA)

ahz@ujs.edu.cn

Table of contents

General experimental procedures ................................................................. S1
Experimental data for compounds 3a-q ......................................................... S1-7
$^1$H NMR and $^{13}$C NMR spectra of compounds ............................................. S8-39
General experimental procedures

All reactions were carried out in sealed tubes; stirring was achieved with an oven-dried magnetic stirring bar. Solvents were purified by standard methods unless otherwise noted. Commercially available reagents were purchased from Aladdin Company in China and used throughout without further purification other than those detailed below. Flash column chromatography was performed on silica gel (200-300 mesh). All reactions were monitored by TLC analysis. Deuterated solvents were purchased from Cambridge Isotope laboratories. $^1$H- and $^{13}$C-NMR spectra were recorded on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz respectively. HRMS spectrometry (LC-HRMS) was recorded on a LXQ Spectrometer (Thermo Scientific) operating on ESI-TOF (MeOH as a solvent). Flavones derivatives were synthesized according to the literature.

General procedure for the syntheses of compounds 3a-q

Flavone 1a (0.5 mmol, 1.0 equiv.) was added to a dried sealed tube with DMF (0.5 mL), followed by the addition of NH$_4$I (2.0 equiv.) and aryl thiol (1.2 equiv.). The mixture was stirred at 135 °C. After 15 h, the reaction was cooled down to room temperature, diluted with ethyl acetate, washed with brine, dried over anhydrous Na$_2$SO$_4$ and concentrated under vacuum. The residue was purified by flash chromatography (Petroleum ether: EtOAc =15:1) on silica gel to give the desired product 3a as a colorless oil in an 86% yield. The same procedure was applied to the production of other compounds 3b-q.

3-(p-Tolylthio)-4H-chromen-4-one (3a)

\[ \text{FTIR} : 3075, 2923, 2359, 1647, 1464, 1114, 758 \text{ cm}^{-1}; \]

\[ ^1\text{H-NMR} \text{ (CDCl}_3, 400 \text{ MHz}): \]
δ 8.26 (dd, J=8.0, 1.6 Hz, 1H), 8.07 (s, 1H), 7.72-7.68 (m, 1H), 7.49-7.42 (m, 2H), 7.37 (d, J=8.0 Hz, 2H), 7.13 (d, J=8.0 Hz, 2H), 2.33 (s, 3H); **13C-NMR** (CDCl₃, 100 MHz): δ 175.1, 156.3, 156.2, 137.6, 133.9, 131.0, 130.1, 129.8, 126.4, 125.4, 123.6, 121.1, 118.1, 21.1; **HRMS** (ESI-TOF) m/z calculated for C₁₆H₁₂NaO₂S⁺ 291.0450 (M+Na)⁺, found 291.0447.

3-(Phenylthio)-4H-chromen-4-one (3b)

![3-(Phenylthio)-4H-chromen-4-one (3b)](base64_encoded_image)

**FTIR** : 3058, 2925, 1653, 1612, 1464, 1309, 1113, 760 cm⁻¹; **1H-NMR** (CDCl₃, 400 MHz): δ 8.28 (dd, J=8.0, 1.6 Hz, 1H), 8.18 (s, 1H), 7.74-7.70 (m, 1H), 7.51-7.40 (m, 4H), 7.33-7.22 (m, 3H); **13C-NMR** (CDCl₃, 100 MHz): δ 175.1, 157.4, 156.4, 134.0, 129.9, 129.2, 127.1, 126.5, 125.8, 123.7, 120.0, 118.2; **HRMS** (ESI-TOF) m/z calculated for C₁₅H₁₀NaO₂S⁺ 277.0294 (M+Na)⁺, found 277.0296.

3-((4-((tert-Butyl)phenyl)thio)-4H-chromen-4-one (3c)

![3-((4-((tert-Butyl)phenyl)thio)-4H-chromen-4-one (3c)](base64_encoded_image)

**FTIR** : 3070, 2963, 1649, 1611, 1560, 1462, 1115, 846, 764 cm⁻¹; **1H-NMR** (CDCl₃, 400 MHz): δ 8.27 (dd, J=8.0, 1.2 Hz, 1H), 8.09 (s, 1H), 7.73-7.68 (s, 1H), 7.49-7.43 (m, 2H), 7.40-7.33 (m, 4H), 1.30 (s, 9H); **13C-NMR** (CDCl₃, 100 MHz): δ 175.2, 156.6, 156.3, 150.7, 133.9, 130.5, 130.0, 126.7, 126.4, 126.3, 125.7, 123.6, 118.1, 34.6, 31.2; **HRMS** (ESI-TOF) m/z calculated for C₁₉H₁₈NaO₂S⁺ 333.0920 (M+Na)⁺, found 333.0917.

3-((4-Bromophenyl)thio)-4H-chromen-4-one (3d)
FTIR : 3061, 2925, 1641, 1086, 901, 798 cm\(^{-1}\); \(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta\) 8.26 (dd, \(J=7.2, 4.8\) Hz, 2H), 7.76-7.71 (m, 1H), 7.52-7.45 (m, 2H), 7.41 (dd, \(J=6.8, 2.0\) Hz, 2H), 7.26 (dd, \(J=8.8, 6.8\) Hz, 2H); \(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): \(\delta\) 174.9, 158.1, 156.4, 134.2, 133.6, 132.2, 131.0, 126.5, 126.0, 123.7, 121.0, 119.0, 118.2; HRMS (ESI-TOF) m/z calculated for C\(_{15}\)H\(_9\)BrNaO\(_2\)S\(^+\) 354.9399 (M+Na)\(^+\), found 354.9394.

3-((4-Chlorophenyl)thio)-4H-chromen-4-one (3e)

FTIR : 3051, 1648, 1478, 1465, 1313, 1091, 827, 758 cm\(^{-1}\); \(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta\) 8.25 (m, 2H), 7.75-7.71 (m, 1H), 7.52-7.45 (m, 2H), 7.35-7.25 (m, 4H); \(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): \(\delta\) 175.0, 157.9, 156.4, 134.2, 133.1, 132.8, 130.9, 129.3, 126.5, 125.9, 123.7, 119.2, 118.2; HRMS (ESI-TOF) m/z calculated for C\(_{15}\)H\(_9\)ClNaO\(_2\)S\(^+\) 310.9904 (M+Na)\(^+\), found 310.9894.

3-((4-Fluorophenyl)thio)-4H-chromen-4-one (3f)

FTIR : 3053, 2361, 1645, 1491, 1465, 1222, 829, 758 cm\(^{-1}\); \(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta\) 8.24 (dd, \(J=8.0, 1.2\) Hz, 1H), 8.16 (s, 1H), 7.73-7.69 (m, 1H), 7.49-7.43 (m, 4H), 7.01 (t, \(J=8.8\) Hz, 2H); \(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): \(\delta\) 175.1, 163.6, 161.1, 156.9, 156.3, 134.1, 132.9, 132.8, 128.8, 126.4, 125.8, 123.7, 120.5, 118.2, 116.5, 116.2; HRMS (ESI-TOF) m/z calculated for C\(_{15}\)H\(_9\)FNaO\(_2\)S\(^+\) 295.0199 (M+Na)\(^+\), found 295.0205.
3-((4-Chlorophenyl)thio)-6-methyl-4H-chromen-4-one (3g)

\[
\text{FTIR: } 3053, 2922, 1639, 1478, 1311, 1091, 812, 789 \text{ cm}^{-1}; \quad \text{\textsuperscript{1}H-NMR (CDCl}_3, 400 \text{ MHz): } \delta 8.24 (s, 1H), 8.03 (d, J=1.2 \text{ Hz, } 1H), 7.53 (dd, J=8.4, 2.0 \text{ Hz, } 1H), 7.40 (d, J=8.8 \text{ Hz, } 1H), 7.33-7.22 (m, 4H), 2.47 (s, 3H); \quad \text{\textsuperscript{13}C-NMR (CDCl}_3, 100 \text{ MHz): } \delta 175.1, 158.1, 154.7, 136.1, 135.4, 133.1, 132.9, 130.7, 129.2, 125.7, 123.4, 118.8, 118.0, 21.0; \quad \text{HRMS (ESI-TOF) m/z calculated for } C_{16}H_{11}ClNaO_2S^+ 325.0060 (M+Na)^+, \text{ found 325.0049.}
\]

3-\((p\text{-Tolylthio})\)-4H-benzo[\text{h}]chromen-4-one (3h)

\[
\text{FTIR: } 3057, 2920, 2361, 1650, 1633, 1384, 1113, 886, 765 \text{ cm}^{-1}; \quad \text{\textsuperscript{1}H-NMR (CDCl}_3, 400 \text{ MHz): } \delta 8.40 (d, J=8.0 \text{ Hz, } 1H), 8.16 (d, J=8.8 \text{ Hz, } 1H), 8.08 (s, 1H), 7.91 (d, J=7.6 \text{ Hz, } 1H), 7.77-7.64 (m, 3H), 7.43 (d, J=8.0 \text{ Hz, } 2H), 7.16 (d, J=8.0 \text{ Hz, } 2H), 2.35 (s, 3H); \quad \text{\textsuperscript{13}C-NMR (CDCl}_3, 100 \text{ MHz): } \delta 174.8, 154.3, 153.7, 138.0, 135.8, 131.7, 130.2, 129.5, 129.1, 128.1, 127.3, 125.7, 123.8, 123.4, 122.2, 121.0, 119.6, 21.2; \quad \text{HRMS (ESI-TOF) m/z calculated for } C_{20}H_{14}NaO_2S^+ 341.0607 (M+Na)^+, \text{ found 341.0603.}
\]

6-Chloro-3-(phenylthio)-4H-chromen-4-one (3i)

\[
\text{FTIR: } 3068, 2925, 2360, 1653, 1466, 1303, 1122, 918, 821, 755 \text{ cm}^{-1}; \quad \text{\textsuperscript{1}H-NMR (CDCl}_3, 400 \text{ MHz): } \delta 8.22 (d, J = 2.6 \text{ Hz, } 1H), 8.12 (s, 1H), 7.65 (dd, J=9.2, 2.8 \text{ Hz, } 1H), 7.47-7.40 (m, 3H), 7.34-7.25 (m, 3H); \quad \text{\textsuperscript{13}C-NMR (CDCl}_3, 100 \text{ MHz): } \delta 174.0,
157.0, 154.7, 134.2, 133.4, 131.7, 130.3, 129.3, 127.5, 125.7, 124.5, 120.5, 120.0; HRMS (ESI-TOF) m/z calculated for C_{15}H_{9}ClNaO_{2}S^{+} 310.9904 (M+Na)^{+}, found 310.9914.

6-Chloro-7-methyl-3-(p-tolylthio)-4H-chromen-4-one (3j)

\[ \text{FTIR : 3060, 2924, 1651, 1412, 1097, 899, 786 cm}^{-1}; \text{ } ^1\text{H-NMR (CDCl}_3, 400 \text{ MHz): } \delta 8.19 (s, 1H), 7.98 (s, 1H), 7.35 (d, J=8.0 Hz, 3H), 7.13 (d, J=8.0 Hz, 2H), 2.51 (s, 3H), 2.33 (s, 3H); ^{13}\text{C-NMR (CDCl}_3, 100 \text{ MHz): } \delta 174.0, 155.9, 154.6, 143.3, 137.8, 132.3, 131.2, 130.1, 129.5, 122.5, 121.2, 119.9, 21.1, 20.9; \text{HRMS (ESI-TOF) m/z calculated for C}_{17}\text{H}_{13}\text{ClNaO}_{2}\text{S}^{+} 339.0217 (M+Na)^{+}, \text{found 339.0213.} \]

8-Bromo-6-methyl-3-(phenylthio)-4H-chromen-4-one (3k)

\[ \text{FTIR : 3054, 2925, 2360, 1660, 1463, 1299, 1090, 785, 691 cm}^{-1}; \text{ } ^1\text{H-NMR (CDCl}_3, 400 \text{ MHz): } \delta 8.11 (s, 1H), 7.98 (d, J=1.2 Hz, 1H), 7.75 (d, J=2.0 Hz, 1H), 7.43 (dd, J=3.6, 1.6 Hz, 2H), 7.34-7.24 (m, 3H), 2.45 (s, 3H); ^{13}\text{C-NMR (CDCl}_3, 100 \text{ MHz): } \delta 174.5, 156.4, 151.2, 138.5, 136.8, 133.2, 130.5, 129.3, 127.5, 125.3, 124.3, 120.8, 111.2, 20.8; \text{HRMS (ESI-TOF) m/z calculated for C}_{16}\text{H}_{11}\text{BrNaO}_{2}\text{S}^{+} 368.9555 (M+Na)^{+}, \text{found 368.9553.} \]

3-((4-Chlorophenyl)thio)-4-oxo-4H-chromene-6-carbonitrile (3l)

\[ \text{FTIR : 3054, 2924, 2361, 1654, 1475, 1313, 815, 670 cm}^{-1}; \text{ } ^1\text{H-NMR (CDCl}_3, 400 \text{ MHz): } \delta 8.11 (s, 1H), 7.98 (d, J=1.2 Hz, 1H), 7.75 (d, J=2.0 Hz, 1H), 7.43 (dd, J=3.6, 1.6 Hz, 2H), 7.34-7.24 (m, 3H), 2.45 (s, 3H); ^{13}\text{C-NMR (CDCl}_3, 100 \text{ MHz): } \delta 174.5, 156.4, 151.2, 138.5, 136.8, 133.2, 130.5, 129.3, 127.5, 125.3, 124.3, 120.8, 111.2, 20.8; \text{HRMS (ESI-TOF) m/z calculated for C}_{16}\text{H}_{11}\text{BrNaO}_{2}\text{S}^{+} 368.9555 (M+Na)^{+}, \text{found 368.9553.} \]
6-Nitro-3-(phenylthio)-4H-chromen-4-one (3m)

\[
\begin{align*}
\text{FTIR:} & \quad 3061, 2342, 1655, 1524, 1346, 1105, 835, 738 \text{ cm}^{-1}; \\
\text{\textsuperscript{1}H-NMR (CDCl}_3, 400 MHz): & \quad \delta 9.11 (d, J=2.8 Hz, 1H), 8.52 (dd, J=9.2, 2.8 Hz, 1H), 8.04 (s, 1H), 7.60 (d, J=9.2 Hz, 1H), 7.48 (dd, J=8.0, 1.6 Hz, 2H), 7.38-7.32 (m, 3H); \\
\text{\textsuperscript{13}C-NMR (CDCl}_3, 100 MHz): & \quad \delta 173.6, 159.0, 155.7, 145.0, 132.1, 131.4, 129.5, 128.2, 128.1, 123.4, 123.2, 122.7, 120.0; \\
\text{HRMS (ESI-TOF) m/z calculated for C}_{15}{H}_{9}N{NaO}_{3}S^+ & \quad 322.0144 (M+Na)^+, \text{ found 322.0143}. 
\end{align*}
\]

6-Bromo-3-(phenylthio)-4H-chromen-4-one (3n)

\[
\begin{align*}
\text{FTIR:} & \quad 3058, 2923, 1652, 1548, 1462, 1121, 908, 818, 735 \text{ cm}^{-1}; \\
\text{\textsuperscript{1}H-NMR (CDCl}_3, 400 MHz): & \quad \delta 8.38 (d, J=2.4 Hz, 1H), 8.12 (s, 1H), 7.78 (q, J=2.4, 1H), 7.43-7.38 (m, 3H), 7.34-7.24 (m, 3H); \\
\text{\textsuperscript{13}C-NMR (CDCl}_3, 100 MHz): & \quad \delta 173.8, 157.0, 155.1, 137.0, 133.4, 130.3, 129.3, 129.0, 127.5, 124.8, 120.6, 120.2, 119.2; \\
\text{HRMS (ESI-TOF) m/z calculated for C}_{15}{H}_{9}Br{NaO}_{3}S^+ & \quad 354.9399 (M+Na)^+, \text{ found 354.9394}. 
\end{align*}
\]

6-Bromo-3-((p-tolylthio)-4H-chromen-4-one (3o)
**2-Methyl-3-(phenylthio)-4H-chromen-4-one (3q)**

**FTIR** : 3050, 2924, 1647, 1465, 1120, 982, 764, 691 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz): δ 8.23 (dd, $J$=8.0, 1.6 Hz, 1H), 7.71-7.67 (m, 1H), 7.47-7.40 (m, 2H), 7.28-7.22 (m, 4H), 7.17-7.12 (m, 1H), 2.74 (s, 3H); ¹³C-NMR (CDCl₃, 100 MHz): δ 175.3, 171.5, 155.6, 135.7, 133.8, 129.3, 129.0, 127.5, 126.6, 126.0, 125.5, 122.9, 117.7, 115.3, 20.8; HRMS (ESI-TOF) m/z calculated for C₁₆H₁₂NaO₂S⁺ 291.0450 (M+Na)⁺, found 291.0451.