Supporting Information

Aerobic Copper-Catalyzed Oxidative [6C+1C] Annulation: An Efficient Route to Seven-Membered Carbocycles**

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Table of Contents

I. General Information .................................................................S2
II. Synthetic procedures and analytical data of Compounds 3 ..................S2
III. Control Reactions ..................................................................S10
IV. Copies of $^1$H NMR and $^{13}$C NMR spectra of compound 3 ..........S13
V. $^1$H-$^1$H NOESY spectrum of 3k ............................................S39
VI. Crystal data and OPTEP drawing of compound 3g ......................S39
I. General Information

All reagents were purchased from commercial sources and used without further purification, unless otherwise indicated. $N, N$-Dimethylformamide (DMF) was dried over calcium hydride and distilled before use. All reactions were carried out in oven-dried flasks and monitored by TLC, which was performed on precoated aluminum sheets of silica gel 60 (F254). The products were purified by flash column chromatography on silica gel (300–400 mesh). Melting points were uncorrected. The $^1$H NMR and $^{13}$C NMR spectra were determined at 25ºC on a 500 MHz and 125 MHz, respectively, and TMS as internal standard. All chemical shifts are given in ppm. High-resolution mass spectra (HRMS) were obtained using a Bruker microTOF II focus spectrometer (ESI).

II. Synthetic procedures and analytical data of Compounds 3

General procedure (taking 3a as an example):

To the solution of 1a ($R = 4$-$\text{ClC}_6\text{H}_4$, 223.5 mg, 0.5 mmol) and ethyl 2-cyanoacetate (0.064 mL, 0.6 mmol) in anhydrous DMF (3 mL) was added NaH (60%, 6 mg, 0.15 mmol) and CuCl (10 mg, 0.1 mmol) at room temperature, then the reaction mixture was stirring under air atmosphere. After 1a was consumed as indicated by TLC, the resulting mixture was poured into water (30 mL) and extracted with ethyl acetate (15 mL × 3). The combined organic phase was washed with water (15 mL × 3), dried over anhydrous MgSO$_4$ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, EtOAc/PE = 1: 10) to give 3a (244 mg, 85%, 0.425 mmol) as a yellow solid.
3a. Ethyl 2-(4-chlorobenzoyl)-7-(4-chlorophenyl)-1-cyano-4-(1, 3-dithiolan-2-ylidene)-3, 5-dioxocycloheptanecarboxylate. Yellow solid. m.p. 239–240°C.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.23(t, $J = 7.0$ Hz, 3H), 3.19 (d, $J = 19.0$ Hz, 1H), 3.27-3.37 (m, 2H), 3.50-3.56 (m, 2H), 3.70 (dd, $J_1 = 19.0$ Hz, $J_2 = 7.5$ Hz, 1H), 3.83 (d, $J = 12.0$ Hz, 1H), 4.20 (dd, $J_1 = 10.5$ Hz, $J_2 = 3.5$ Hz, 1H), 4.32 (dd, $J_1 = 10.5$ Hz, $J_2 = 3.5$ Hz, 1H), 5.17 (s, 1H), 7.18 (d, $J = 8.5$ Hz, 2H), 7.55 (d, $J = 8.0$ Hz, 2H), 7.39(d, $J = 8.5$ Hz, 2H), 7.67 (d, $J = 8.0$ Hz, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 13.7, 37.2, 37.9, 45.2, 45.5, 53.8, 62.8, 63.2, 116.6, 124.6, 128.9, 129.2, 129.7, 129.8, 133.0, 134.8, 135.4, 140.5, 167.1, 184.2, 190.1, 190.8, 195.5. HRMS (ESI-TOF) Calcd for C$_{27}$H$_{22}$Cl$_2$NO$_5$S$_2$, ([M + H]$^+$) 574.0311. Found 574.0307.

3b. Ethyl 2-(3-chlorobenzoyl)-7-(3-chlorophenyl)-1-cyano-4-(1, 3-dithiolan-2-ylidene)-3, 5-dioxocycloheptanecarboxylate. Yellow solid. m.p. 224–225°C.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.22 (t, $J = 7.0$ Hz, 3H), 3.23 (d, $J = 19.0$ Hz, 1H), 3.28-3.36 (m, 2H), 3.51-3.57 (m, 2H), 3.72 (dd, $J_1 = 19.0$ Hz, $J_2 = 7.0$ Hz, 1H), 3.83 (d, $J = 11.5$ Hz, 1H), 4.24-4.33 (m, 2H), 5.20 (s, 1H), 7.19 (d, $J = 8.5$ Hz, 2H), 7.34 (s, 1H), 7.37 (d, $J = 8.0$ Hz, 2H), 7.53 (d, $J = 8.0$ Hz, 1H), 7.56 (d, $J = 8.0$ Hz, 1H), 7.76 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 13.8, 37.3, 37.8, 45.0, 45.8, 53.7, 62.9, 63.3, 116.5,
124.7, 126.3, 126.4, 128.5, 128.8, 128.9, 130.1, 133.9, 134.4, 135.2, 136.2, 138.8, 167.0, 184.3, 190.3, 190.8, 195.2. HRMS (ESI-TOF) Caled for C_{27}H_{22}Cl_{2}NO_{5}S_{2}^{+}, ([M + H]^+) 574.0311. Found 574.0313.

3c, Ethyl 2-(4-bromobenzoyl)-7-(4-bromophenyl)-1-cyano-4-(1,3-dithiolan-2-ylidene)-3,5-dioxocycloheptanecarboxylate. Yellow solid. m.p. 227–228°C.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.21 (t, $J = 7.5$ Hz, 3H), 3.17 (d, $J = 19.0$ Hz, 1H), 3.25-3.35 (m, 2H), 3.49-3.55 (m, 2H), 3.68 (dd, $J_1 = 19.5$ Hz, $J_2 = 7.5$ Hz, 1H), 3.80 (d, $J = 12.0$ Hz, 1H), 4.15-4.21 (m, 1H), 4.28-4.34 (m, 1H), 5.15 (s, 1H), 7.10 (d, $J = 8.0$ Hz, 2H), 7.48 (d, $J = 8.5$ Hz, 2H), 7.54 (d, $J = 8.5$ Hz, 2H), 7.58 (d, $J = 8.5$ Hz, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 13.8, 37.3, 37.9, 45.2, 45.7, 53.8, 62.8, 63.2, 116.6, 123.0, 124.7, 129.4, 129.7, 130.1, 131.9, 132.2, 133.5, 136.0, 167.0, 184.2, 190.3, 190.7, 195.5. HRMS (ESI-TOF) Caled for C$_{27}$H$_{22}$Br$_2$NO$_5$S$_2$^{+}, ([M + H]^+) 661.9301. Found 661.9298.

3d, Ethyl 1-cyano-4-(1,3-dithiolan-2-ylidene)-2-(4-fluorobenzoyl)-7-(4-fluorophenyl)-3,5-dioxocycloheptanecarboxylate. Yellow solid. m.p. 229–230°C.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.21 (t, $J = 7.5$ Hz, 3H), 3.21 (d, $J = 19.0$ Hz, 1H), 3.28-3.34 (m, 2H), 3.50-3.56 (m, 2H), 3.70 (dd, $J_1 = 19.0$ Hz, $J_2 = 7.0$ Hz, 1H), 3.85 (d, $J$...
= 12.0 Hz, 1H), 4.17-4.23 (m, 1H), 4.28-4.33 (m, 1H), 5.16 (s, 1H), 7.06-7.09 (m, 4H),
7.22-7.24 (m, 2H), 7.74-7.77 (m, 2H).\^1^3C\ NMR\ (125 MHz, CDCl\textsubscript{3}): \^\delta\ 13.7, 37.2, 37.9,
45.5, 54.0, 62.8, 63.1, 115.7, 115.8, 116.1, 116.2, 116.7, 124.7, 130.1, 130.2, 131.0, 131.1,
132.8, 161.8, 163.8, 165.1, 167.1, 184.3, 189.6, 190.5, 195.7. \HRMS\ (ESI-TOF) Caled
for \text{C}_{27}\text{H}_{22}\text{F}_{2}\text{NO}_{5}\text{S}_{2}^+, ([M + H]^+) 542.0902. Found 542.0908.

\textbf{3e}, Ethyl 2-benzoyle-1-cyano-4-(1, 3-dithiolan-2-ylidene)-3, 5-dioxo-7-
Phenylcycloheptanecarboxylate. Yellow solid. m.p. 230–231°C.

\textbf{1H NMR} (500 MHz, CDCl\textsubscript{3}): \^\delta\ 1.18 (t, \textit{J} = 7.0 Hz, 3H), 3.24-3.30 (m, 3H), 3.48-3.53 (m,
2H), 3.75 (dd, \textit{J\textsubscript{1}} = 19.0 Hz, \textit{J\textsubscript{2}} = 7.0 Hz, 1H), 3.86 (d, \textit{J} = 12.0 Hz, 1H), 4.19-4.24 (m,
1H), 4.26-4.33 (m, 1H), 5.23 (s, 1H), 7.24-7.26 (m, 1H), 7.35-7.36 (m, 3H), 7.42 (t, \textit{J} =
7.5 Hz, 3H), 7.55 (t, \textit{J} = 7.5 Hz, 1H), 7.74 (d, \textit{J} = 7.5 Hz, 2H).\^1^3C\ NMR\ (125 MHz,
CDCl\textsubscript{3}): \^\delta\ 13.7, 37.1, 37.8, 45.4, 46.2, 54.0, 62.8, 63.0, 116.9, 124.9, 128.3, 128.4, 128.7,
128.9, 133.9, 134.7, 137.0, 167.3, 184.5, 190.0, 191.2, 196.1. \HRMS\ (ESI-TOF) Caled
for \text{C}_{27}\text{H}_{24}\text{NO}_{5}\text{S}_{2}^+, ([M + H]^+) 506.1090. Found 506.1099.

\textbf{3f}, Ethyl 1-cyano-4-(1, 3-dithiolan-2-ylidene)-2-(4-methoxybenzoyl)-7-
(4-methoxyphenyl)-3, 5-dioxocycloheptanecarboxylate. Yellow solid. m.p. 278–279°C.
$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.21 (t, $J$ = 7.0 Hz, 3H), 3.20 (d, $J$ = 19.0 Hz, 1H), 3.24-3.31 (m, 2H), 3.47-3.50 (m, 2H), 3.71 (dd, $J_1$ = 19.0 Hz, $J_2$ = 7.0 Hz, 1H), 3.80 (s, 3H), 3.83 (d, $J$ = 12.5 Hz, 1H), 3.84 (s, 3H), 4.18-4.24 (m, 1H), 4.27-4.33 (m, 1H), 5.17 (s, 1H), 6.86-6.88 (m, 4H), 7.16 (d, $J$ = 9.0 Hz, 2H), 7.70 (d, $J$ = 9.0 Hz, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 13.8, 37.1, 37.8, 45.5, 45.7, 54.3, 55.3, 55.5, 62.7, 62.9, 114.0, 114.1, 117.1, 125.0, 127.8, 129.0, 129.2, 129.6, 130.8, 159.7, 164.1, 167.4, 184.8, 189.6, 196.3. HRMS (ESI-TOF) Calcd for C$_{29}$H$_{28}$NO$_7$S$_2$ $^+$, ([M + H]$^+$) 566.1302. Found 566.1299.

![Chemical Structure](image)

3g. Ethyl 1-cyano-4-(1, 3-dithiolan-2-ylidene)-2-(4-methylbenzoyl)-3, 5-dioxo-7-(p-tolyl)cycloheptanecarboxylate. Yellow solid. m.p. 186–187°C. 

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.20 (t, $J$ = 7.0 Hz, 3H), 2.34 (s, 3H), 2.37 (s, 3H), 3.22 (d, $J$ = 19.0 Hz, 1H), 3.25-3.32 (m, 2H), 3.46-3.52 (m, 2H), 3.73 (dd, $J_1$ = 19.0 Hz, $J_2$ = 7.0 Hz, 1H), 3.81 (d, $J$ = 11.5 Hz, 1H), 4.18-4.24 (m, 1H), 4.27-4.33 (m, 1H), 5.23 (s, 1H), 7.12 (d, $J$ = 7.5 Hz, 2H), 7.15 (d, $J$ = 7.5 Hz, 2H), 7.19 (d, $J$ = 8.0 Hz, 2H), 7.64 (d, $J$ = 8.0 Hz, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 13.7, 21.1, 21.7, 37.1, 37.8, 45.5, 45.7, 54.1, 62.7, 62.8, 116.9, 124.9, 128.2, 128.5, 129.3, 129.5, 132.2, 134.0, 138.4, 144.9, 167.4, 184.7, 189.7, 190.8, 196.2. HRMS (ESI-TOF) Calcd for C$_{29}$H$_{28}$NO$_5$S$_2$ $^+$, ([M + H]$^+$) 534.1403. Found 534.1411.
3h, Ethyl 2-(4-(tert-butyl) benzoyl)-7-(4-(tert-butyl) phenyl)-1-cyano-4-(1, 3-dithiolan-2-ylidene)-3, 5-dioxocycloheptanecarboxylate. Yellow solid. m.p. 198–199°C. 

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.12 (t, $J = 7.5$ Hz, 3H), 1.29 (s, 9H), 1.30 (s, 9H), 3.22 (d, $J = 18.5$ Hz, 2H), 3.28-3.33 (m, 1H), 3.46-3.50 (m, 2H), 3.74 (dd, $J_1 = 17.5$ Hz, $J_2 = 6.5$ Hz, 1H), 3.83 (d, $J = 12.0$ Hz, 1H), 4.22-4.28 (m, 2H), 5.27-5.29 (m, 1H), 7.17 (d, $J = 8.0$ Hz, 2H), 7.36 (d, $J = 8.5$ Hz, 2H), 7.41 (d, $J = 8.0$ Hz, 2H), 7.70 (d, $J = 8.0$ Hz, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 13.5, 30.9, 31.1, 34.4, 35.1, 37.0, 37.8, 45.3, 45.7, 54.0, 62.6 (2), 116.9, 124.8, 125.4, 125.7, 128.0, 128.3, 131.9, 133.9, 151.4, 157.6, 167.3, 184.6, 189.6, 190.8, 196.3. HRMS (ESI-TOF) Calcd for C$_{35}$H$_{40}$NO$_5$S$_2$ $^+$, ([M + H]$^+$) 618.2342. Found 618.2350.

3i, Ethyl 1-cyano-4-(1, 3-dithiolan-2-ylidene)-2-(furan-2-carbonyl)-7-(furan-2-yl)-3, 5-dioxocycloheptanecarboxylate. Yellow solid. m.p. 247–248°C.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.32 (t, $J = 7.0$ Hz, 3H), 3.28 (d, $J = 19.5$ Hz, 1H), 3.24-3.33 (m, 2H), 3.49-3.54 (m, 2H), 3.58 (dd, $J_1 = 19.5$ Hz, $J_2 = 7.5$ Hz, 1H), 4.02 (d, $J = 12.0$ Hz, 1H), 4.36 (dd, $J_1 = 14.0$ Hz, $J_2 = 7.0$ Hz, 2H), 5.10 (s, 1H), 6.32 (d, $J = 3.0$ Hz, 1H), 6.36-6.38 (m, 1H), 6.53-6.55 (m, 1H), 7.28 (d, $J = 3.0$ Hz, 1H), 7.39 (s, 1H), 7.48 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 13.7, 37.0, 37.8, 40.8, 43.1, 51.8, 62.1, 63.2, 108.7,
3j, Ethyl 1-cyano-4-(1, 3-dithiolan-2-ylidene)-3, 5-dioxo-7-(thiophen-2-yl)-2-(thiophene-2-carbonyl)cycloheptanecarboxylate. Yellow solid. m.p. 245–246°C.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.17 (t, $J = 7.0$ Hz, 3H), 3.25 (d, $J = 20.0$ Hz, 1H), 3.20-3.30 (m, 2H), 3.43-3.48 (m, 2H), 3.65 (dd, $J_1 = 19.5$ Hz, $J_2 = 7.5$ Hz, 1H), 4.11 (d, $J = 11.5$ Hz, 1H), 4.18-4.23 (m, 1H), 4.25-4.30 (m, 1H), 5.02 (s, 1H), 6.94 (t, $J = 4.0$ Hz, 1H), 6.98 (d, $J = 3.0$ Hz, 1H), 7.00 (t, $J = 4.5$ Hz, 1H), 7.21 (d, $J = 5.0$ Hz, 1H), 7.34 (d, $J = 4.0$ Hz, 1H), 7.60 (d, $J = 4.5$ Hz, 1H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 13.7, 37.2, 37.9, 42.2, 46.4, 54.3, 63.3, 63.6, 116.8, 124.7, 125.7, 127.1 (2), 128.3, 132.6, 135.2, 138.5, 141.9, 166.8, 183.5, 183.9, 189.7, 195.4. HRMS (ESI-TOF) Caled for C$_{23}$H$_{20}$NO$_5$S$_4^+$, ([M + H]$^+$) 518.0219. Found 518.0230.

3k, Ethyl 2-(4-chlorobenzoyl)-1-cyano-4-(1, 3-dithiolan-2-ylidene)-7-(4-methoxyphenyl)-3, 5-dioxocycloheptanecarboxylate. Yellow solid. m.p. 285–286°C.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.22 (t, $J = 7.5$ Hz, 3H), 3.18 (d, $J = 19.0$ Hz, 1H),
3.23-3.35 (m, 2H), 3.48-3.54 (m, 2H), 3.71 (dd, $J_1 = 19.0$ Hz, $J_2 = 7.0$ Hz, 1H), 3.83 (d, $J = 11.5$ Hz, 1H), 3.85 (s, 3H), 4.18-4.24 (m, 1H), 4.28-4.34 (m, 1H), 5.17 (s, 1H), 6.88 (d, $J = 8.5$ Hz, 2H), 7.18 (d, $J = 8.5$ Hz, 2H), 7.34 (d, $J = 8.5$ Hz, 2H), 7.70 (d, $J = 8.5$ Hz, 2H).$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 13.8, 37.1, 37.8, 45.3, 45.5, 53.9, 55.5, 62.5, 63.1, 114.1, 116.7, 124.8, 127.6, 128.9, 129.8, 130.8, 134.7, 135.6, 164.1, 167.3, 184.6, 189.4, 190.1, 195.7. HRMS (ESI-TOF) Calced for C$_{28}$H$_{25}$ClNO$_6$S$_2^+$, ([M + H]$^+$) 570.0806. Found 570.0800.

![Chemical Structure](image1.png)

3l, Ethyl 7-(4-chlorophenyl)-1-cyano-4-(1,3-dithiolan-2-ylidene)-3,5-dioxo-2-(thiophene-2-carbonyl)cycloheptanecarboxylate. Yellow solid. m.p. 253–254°C.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.21 (t, $J = 7.5$ Hz, 3H), 3.18 (d, $J = 19.0$ Hz, 1H), 3.28-3.33 (m, 2H), 3.51-3.55 (m, 2H), 3.69 (dd, $J_1 = 19.5$ Hz, $J_2 = 7.0$ Hz, 1H), 3.84 (d, $J = 11.5$ Hz, 1H), 4.19-4.23 (m, 1H), 4.28-4.32 (m, 1H), 5.09 (s, 1H), 7.08 (t, $J = 4.5$ Hz, 1H), 7.18 (d, $J = 8.5$ Hz, 2H), 7.34 (d, $J = 8.5$ Hz, 2H), 7.41 (d, $J = 3.5$ Hz, 1H), 7.68 (d, $J = 5.0$ Hz, 1H).$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 13.7, 37.2, 37.9, 45.2, 45.6, 53.8, 63.2, 63.6, 116.5, 124.8, 128.3, 128.9, 129.8, 132.6, 134.8, 135.2, 135.4, 141.9, 166.9, 183.6, 184.1, 190.1, 195.5. HRMS (ESI-TOF) Calced for C$_{25}$H$_{21}$ClNO$_5$S$_3^+$, ([M + H]$^+$) 546.0265. Found 546.0258.
**3m**, Ethyl 2-(4-bromobenzoyl)-7-(4-chlorophenyl)-1-cyano-4-(1,3-dithiolane-2-ylidene)-3,5-dioxocycloheptanecarboxylate.

**3m′**, Ethyl 7-(4-bromophenyl)-2-(4-chlorobenzoyl)-1-cyano-4-(1,3-dithiolane-2-ylidene)-3,5-dioxocycloheptanecarboxylate.

**3m/3m′ = 1.0/1.0.** Yellow solid. m.p. 239–240°C. **1H NMR** (500 MHz, CDCl3): δ 1.22 (t, J = 7.0 Hz, 3H), 1.26 (t, J = 7.5 Hz, 3H), 3.16–3.20 (m, 2H), 3.26–3.33 (m, 4H), 3.50–3.54 (m, 4H), 3.70 (dd, J1 = 19.5 Hz, J2 = 7.5 Hz, 2H), 3.80–3.84 (m, 2H), 4.16–4.23 (m, 2H), 4.29–4.34 (m, 2H), 5.18 (s, 1H), 5.19 (s, 1H), 7.11 (d, J = 8.5 Hz, 2H), 7.17 (d, J = 8.5 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 7.49 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 7.60 (d, J = 8.5 Hz, 2H), 7.68 (d, J = 8.5 Hz, 2H). **13C NMR** (125 MHz, CDCl3): δ 13.7, 37.2, 37.8, 45.1, 45.2, 45.5, 45.6, 53.7, 53.8, 62.6, 62.7, 63.1, 116.6, 122.9, 124.6, 128.9, 129.2, 129.6, 129.7, 130.0, 131.8, 132.2, 132.9, 133.4, 134.7, 135.4, 135.9, 140.5, 167.1, 184.2, 190.2, 190.4, 190.7 (2), 195.4, 195.5. **HRMS** (ESI-TOF) Calcd for C27H22BrClNO5S2+, ([M + H]+) 617.9806. Found 617.9809.

### III. Control Reactions

All reactions were carried out in oven- or flame-dried glassware at 25 °C.

![Control Reactions Diagram](image)

**Procedure:**

The reaction was carried out under N2 atmosphere. To a stirring suspension of 2a (280 mg, 0.5 mmol) in anhydrous DMF (2.5 mL) was added 60% NaH (6 mg, 0.15 mmol) and CuCl (10 mg, 0.1 mmol). After 24 hours of continues agitation, 15 mL water was added to quench the reaction. The product extracted with ethyl acetate (15 mL × 3) and the organic phase was washed with water (15 mL × 3), dried over anhydrous MgSO4 and concentrated in vacuo. The crude product was a complex mixture without 3a or 4a.
Procedure:
The reaction was carried out under air atmosphere. To a stirring suspension of 2a (280 mg, 0.5 mmol) in anhydrous DMF (2.5 mL) was added 60% NaH (6 mg, 0.15 mmol), CuCl (10 mg, 0.1 mmol) and 2,2,6,6-Tetramethylpiperidine (71 mg, 0.5 mmol). After 24 hours of continues agitation, 15 mL water was added to quench the reaction. The product extracted with ethyl acetate (15 mL × 3) and the organic phase was washed with water (15 mL × 3), dried over anhydrous MgSO₄ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, EtOAc/PE = 1: 10) to give 1a (110 mg, 50%).

Procedure:
The reaction was carried out under ¹⁸O₂ atmosphere. To a stirring suspension of 2a (280 mg, 0.5 mmol) in anhydrous DMF (2.5 mL) was added 60% NaH (6 mg, 0.15 mmol), CuCl (10 mg, 0.1 mmol). After 24 hours of continues agitation, 15 mL water was added to quench the reaction. The product extracted with ethyl acetate (15 mL × 3) and the organic phase was washed with water (15 mL × 3), dried over anhydrous MgSO₄ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, EtOAc/PE = 1: 10) to give 3aO¹⁸ (264 mg, 92%, 0.46 mmol). The product 3aO¹⁸ was analyzed by mass spectroscopy, and the molecular ion at [M + H⁺] = 576 proves incorporation of one ¹⁸O atoms.
Procedure:
The reaction was carried out under air atmosphere. To a stirring suspension of $2a$ (280 mg, 0.5 mmol) in anhydrous DMF (2.5 mL) was added CuCl (10 mg, 0.1 mmol). After 24 hours of continuous agitation, 15 mL water was added to quench the reaction. The product extracted with ethyl acetate (15 mL × 3) and the organic phase was washed with water (15 mL × 3), dried over anhydrous MgSO$_4$ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, EtOAc/PE = 1: 10) to give $3a$ (273 mg, 95%, 0.48 mmol).

\[
\begin{align*}
2a & \xrightarrow{\text{CuCl (0.2 equiv)} \quad \text{TEMPO (1.0 equiv)}} 3a \\
\text{DMF, air, } 25^\circ\text{C, 24 h} & \quad 20\%
\end{align*}
\]

Procedure:
The reaction was carried out under air atmosphere. To a stirring suspension of $2a$ (280 mg, 0.5 mmol) in anhydrous DMF (2.5 mL) was added CuCl (10 mg, 0.1 mmol) and 2,2,6,6-Tetramethylpiperidine (71 mg, 0.5 mmol). After 24 hours of continuous agitation, 15 mL water was added to quench the reaction. The product extracted with ethyl acetate (15 mL × 3) and the organic phase was washed with water (15 mL × 3), dried over anhydrous MgSO$_4$ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, EtOAc/PE = 1: 10) to give $3a$ (58 mg, 20%, 0.10 mmol).
IV. Copies of $^1$H NMR and $^{13}$C NMR spectra of compound 3
V. $^1$H-$^1$H NOESY spectrum of 3k

VI. Crystal data and OPTEP drawing of compound 3g

Single-crystal X-ray diffraction data was collected at room temperature on a Oxford Diffraction Gemini R Ultra diffractometer, the X-ray generator using Mo-Kα ($\lambda = 0.71073$ Å) radiation with a $\omega$ scan technique. The crystal structures were solved by direct method of SHELXS-97$^3$ and refined by full-matrix least-squares techniques using the SHELXL-97 program. Non-hydrogen atoms were refined anisotropic. CCDC deposition
number: 971669 (3g). Data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

ORTEP drawing:

![ORTEP drawing](image)

Crystal data:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{29}H_{27}NO_{5}S_{2}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>574.03</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P2_{1}/n</td>
</tr>
<tr>
<td>a (Å)</td>
<td>24.428(4)</td>
</tr>
<tr>
<td>b (Å)</td>
<td>12.340(2)</td>
</tr>
<tr>
<td>c (Å)</td>
<td>22.946(4)</td>
</tr>
<tr>
<td>α (deg)</td>
<td>90</td>
</tr>
<tr>
<td>β (deg)</td>
<td>92.211(2)</td>
</tr>
<tr>
<td>γ (deg)</td>
<td>90</td>
</tr>
<tr>
<td>Volume (Å^3)</td>
<td>1455.56(7)</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Calculated density (mg/m^3)</td>
<td>1.416</td>
</tr>
<tr>
<td>Absorption coefficient (mm^{-1})</td>
<td>0.250</td>
</tr>
<tr>
<td>F(000)</td>
<td>640</td>
</tr>
<tr>
<td>Theta range for data collection (deg)</td>
<td>2.27 to 25.12</td>
</tr>
<tr>
<td>Reflections collected/unique</td>
<td>5691/2554</td>
</tr>
<tr>
<td>Goodness-of-fit on F^2</td>
<td>1.025</td>
</tr>
<tr>
<td>Final R indices [I &gt; 2σ(I)]</td>
<td>R1=0.0665, WR2=0.1800</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>R1=0.0808, WR2=0.2036</td>
</tr>
</tbody>
</table>