Supporting Information

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

Xiao Liu, Lingjuan Zhang, Xianxiu Xu,* Shan Wang, Ling Pan, Qian Zhang and Qun Liu*

Department of Chemistry, Northeast Normal University, Changchun 130024, People's Republic of China

xuxx677@nenu.edu.cn; liuqun@nenu.edu.cn

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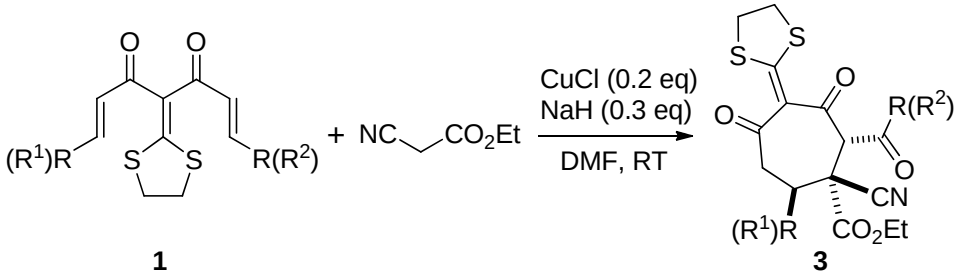
I. General Information

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).

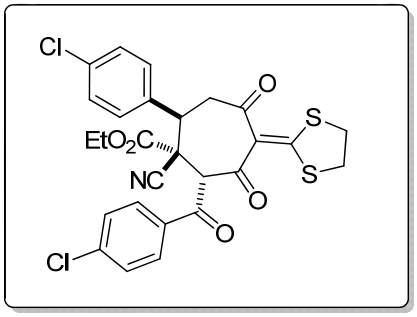
II. Synthetic procedures and analytical data of Compounds **3**



1 **3**

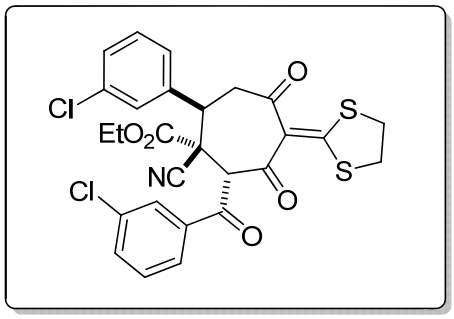
General procedure (**taking 3a as an example**):

To the solution of **1a** (R = 4-ClC_6H_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.

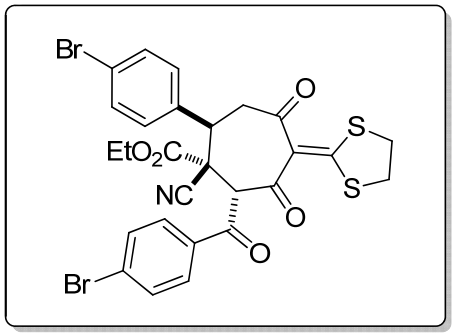
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.23(t, J = 7.0 Hz, 3H), 3.19 (d, J = 19.0 Hz, 1H), 3.27-3.37 (m, 2H), 3.50-3.56 (m, 2H), 3.70 (dd, J_1 = 19.0 Hz, J_2 = 7.5 Hz, 1H), 3.83 (d, J = 12.0 Hz, 1H), 4.20 (dd, J_1 = 10.5 Hz, J_2 = 3.5 Hz, 1H), 4.32 (dd, J_1 = 10.5 Hz, J_2 = 3.5 Hz, 1H), 5.17 (s, 1H), 7.18 (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, $CDCl_3$): δ 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 $C_{27}H_{22}Cl_2NO_5S_2^+$, ([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.

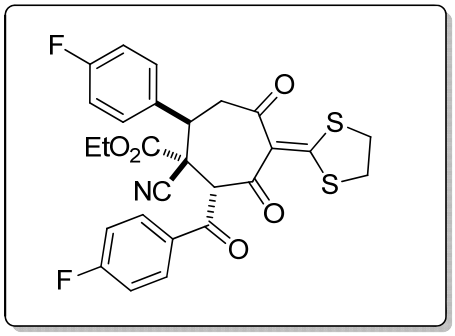
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.22 (t, J = 7.0 Hz, 3H), 3.23 (d, J = 19.0 Hz, 1H), 3.28-3.36 (m, 2H), 3.51-3.57 (m, 2H), 3.72 (dd, J_1 = 19.0 Hz, J_2 = 7.0 Hz, 1H), 3.83 (d, J = 11.5 Hz, 1H), 4.24-4.33 (m, 2H), 5.20 (s, 1H), 7.19 (d, J = 8.5 Hz, 2H), 7.34 (s, 1H), 7.37 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.76 (s, 1H).**^{13}C NMR** (125 MHz, $CDCl_3$): δ 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) Calcd for $C_{27}H_{22}Cl_2NO_5S_2^+$, ($[M + H]^+$) 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.

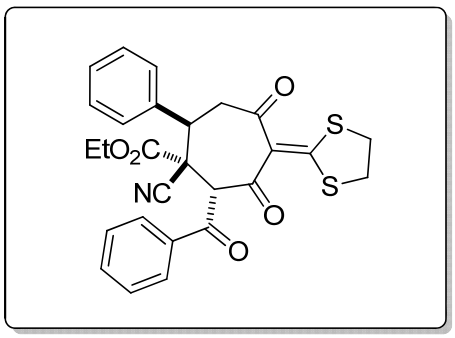
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.21 (t, J = 7.5 Hz, 3H), 3.17 (d, J = 19.0 Hz, 1H), 3.25-3.35 (m, 2H), 3.49-3.55 (m, 2H), 3.68 (dd, J_1 = 19.5 Hz, J_2 = 7.5 Hz, 1H), 3.80 (d, J = 12.0 Hz, 1H), 4.15-4.21 (m, 1H), 4.28-4.34 (m, 1H), 5.15 (s, 1H), 7.10 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.5 Hz, 2H), 7.58 (d, J = 8.5 Hz, 2H).**^{13}C NMR** (125 MHz, $CDCl_3$): δ 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) Calcd for $C_{27}H_{22}Br_2NO_5S_2^+$, ($[M + H]^+$) 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.

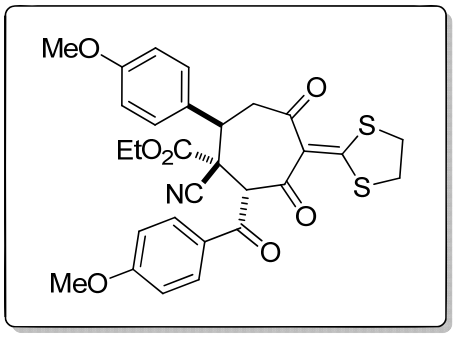
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.21 (t, J = 7.5 Hz, 3H), 3.21 (d, J = 19.0 Hz, 1H), 3.28-3.34 (m, 2H), 3.50-3.56 (m, 2H), 3.70 (dd, J_1 = 19.0 Hz, J_2 = 7.0 Hz, 1H), 3.85 (d, J

= 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).**^{13}C NMR** (125 MHz, $CDCl_3$): δ 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) Calcd for $C_{27}H_{22}F_2NO_5S_2^+$, ($[M + H]^+$) 542.0902. Found 542.0908.



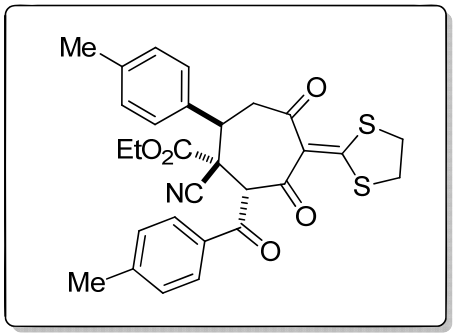
3e, Ethyl 2-benzoyl-1-cyano-4-(1, 3-dithiolan-2-ylidene)-3, 5-dioxo-7-Phenylcycloheptanecarboxylate.Yellow solid. m.p. 230–231^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.18 (t, J = 7.0 Hz, 3H), 3.24-3.30 (m, 3H), 3.48-3.53 (m, 2H), 3.75 (dd, J_1 = 19.0 Hz, J_2 = 7.0 Hz, 1H), 3.86 (d, 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, J = 7.5 Hz, 3H), 7.55 (t, J = 7.5 Hz, 1H), 7.74 (d, J = 7.5 Hz, 2H).**^{13}C NMR** (125 MHz, $CDCl_3$): δ 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) Calcd for $C_{27}H_{24}NO_5S_2^+$, ($[M + H]^+$) 506.1090. Found 506.1099.



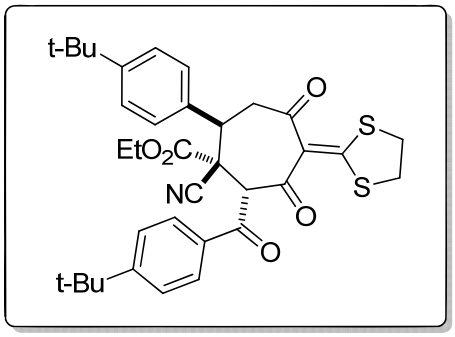
3f, Ethyl 1-cyano-4-(1, 3-dithiolan-2-ylidene)-2-(4-methoxybenzoyl)-7-(4-methoxyphenyl)-3, 5-dioxocycloheptanecarboxylate.Yellow solid. m.p. 278–279^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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 $C_{29}H_{28}NO_7S_2^+$, ($[M + H]^+$) 566.1302. Found 566.1299.

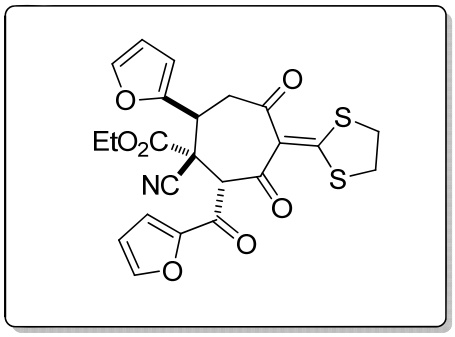


3g, Ethyl 1-cyano-4-(1, 3-dithiolan-2-ylidene)-2-(4-methylbenzoyl)-3, 5-dioxo-7-(p-tolyl)cycloheptanecarboxylate.Yellow solid. m.p.186–187^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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 $C_{29}H_{28}NO_5S_2^+$, ($[M + H]^+$) 534.1403. Found 534.1411.



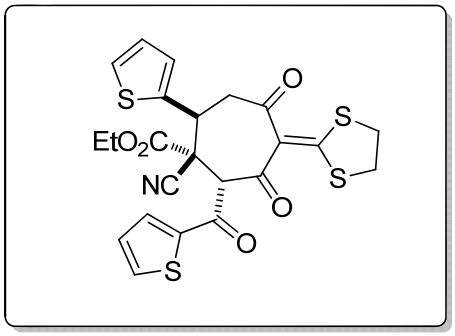
3h, Ethyl 2-(4-(tert-butyl) benzoyl)-7-(4-(tert-butyl) phenyl)-1-cyano-4-(1, 3-dithiolan-2-ylidene)-3, 5-dioxocycloheptanecarboxylate.Yellow solid. m.p. 198–199°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.12 (t, J = 7.5 Hz, 3H), 1.29 (s, 9H), 1.30 (s, 9H), 3.22 (d, J = 18.5 Hz, 2H), 3.28-3.33 (m, 1H), 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, $CDCl_3$): δ 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 $C_{35}H_{40}NO_5S_2^+$, ($[M + H]^+$) 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.

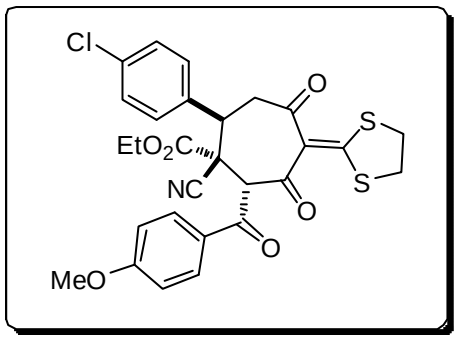
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.32 (t, J = 7.0 Hz, 3H), 3.28 (d, J = 19.5 Hz, 1H), 3.24-3.33 (m, 2H), 3.49-3.54 (m, 2H), 3.58 (dd, J_1 = 19.5 Hz, J_2 = 7.5 Hz, 1H), 4.02 (d, J = 12.0 Hz, 1H), 4.36 (dd, J_1 = 14.0 Hz, J_2 = 7.0 Hz, 2H), 5.10 (s, 1H), 6.32 (d, J = 3.0 Hz, 1H), 6.36-6.38 (m, 1H), 6.53-6.55 (m, 1H), 7.28 (d, J = 3.0 Hz, 1H), 7.39 (s, 1H), 7.48 (s, 1H).**^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.7, 37.0, 37.8, 40.8, 43.1, 51.8, 62.1, 63.2, 108.7,

110.6, 113.0, 116.4, 118.4, 124.7, 142.8, 146.8, 150.1, 151.0, 166.9, 180.0, 183.7, 189.6, 195.3. **HRMS** (ESI-TOF) Calcd for $C_{23}H_{20}NO_7S_2^+$, ($[M + H]^+$) 486.0676. Found 486.0682.



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.

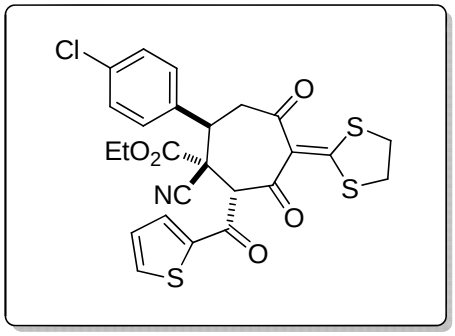
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.17 (t, J = 7.0 Hz, 3H), 3.25 (d, J = 20.0 Hz, 1H), 3.20-3.30 (m, 2H), 3.43-3.48 (m, 2H), 3.65 (dd, J_1 = 19.5 Hz, J_2 = 7.5 Hz, 1H), 4.11 (d, J = 11.5 Hz, 1H), 4.18-4.23 (m, 1H), 4.25-4.30 (m, 1H), 5.02 (s, 1H), 6.94 (t, J = 4.0 Hz, 1H), 6.98 (d, J = 3.0 Hz, 1H), 7.00 (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, $CDCl_3$): δ 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) Calcd for $C_{23}H_{20}NO_5S_4^+$, ($[M + H]^+$) 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.

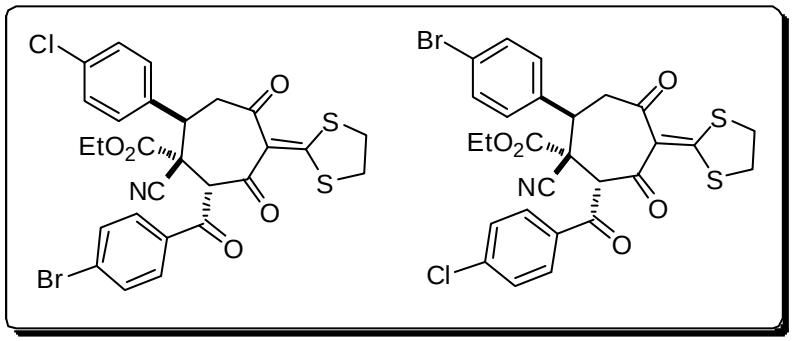
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.22 (t, J = 7.5 Hz, 3H), 3.18 (d, J = 19.0 Hz, 1H),

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, $CDCl_3$): δ 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) Calcd for $C_{28}H_{25}ClNO_6S_2^+$, ($[M + H]^+$) 570.0806. Found 570.0800.



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^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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) Calcd for $C_{25}H_{21}ClNO_5S_3^+$, ($[M + H]^+$) 546.0265. Found 546.0258.



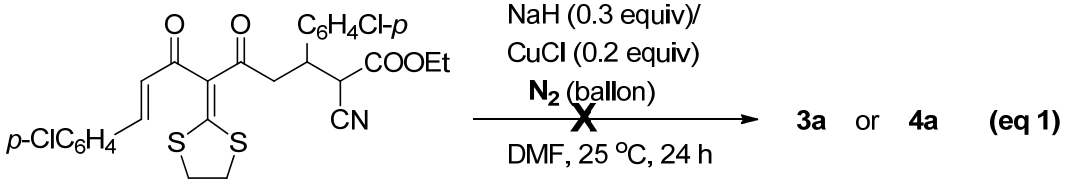
3m, Ethyl 2-(4-bromobenzoyl)-7-(4-chlorophenyl)-1-cyano-4-(1, 3-dithiolan -2-ylidene)-3, 5-dioxocycloheptanecarboxylate.

3m', Ethyl 7-(4-bromophenyl)-2-(4-chlorobenzoyl)-1-cyano-4-(1,3-dithiolan -2-ylidene)-3, 5-dioxocycloheptanecarboxylate.

3m/ **3m'** = 1.0/1.0.Yellow solid. m.p. 239–240°C. **^{1}H NMR** (500 MHz, $CDCl_3$): 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, J_1 = 19.5 Hz, J_2 = 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).**^{13}C NMR** (125 MHz, $CDCl_3$): 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 $C_{27}H_{22}BrClNO_5S_2^+$, ($[M + H]^+$) 617.9806. Found 617.9809.

III. Control Reactions

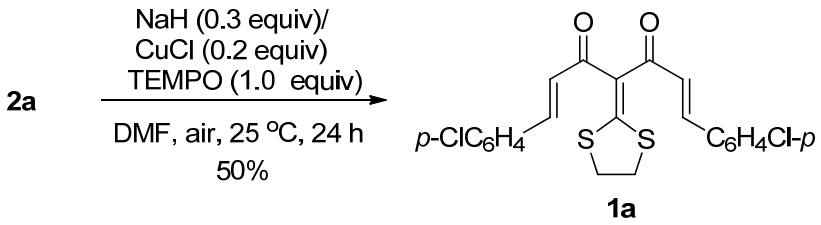
All reactions were carried out in oven- or flame-dried glassware at 25 °C.



2a

Procedure:

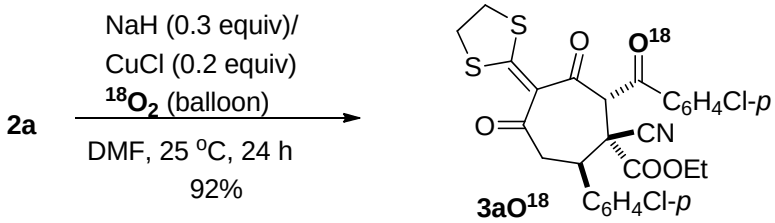
The reaction was carried out under N_2 atmosphere. To a stirring suspension of **2a** (280 mg, 0.5 mmol) in anhydrous DMF (2.5 mL) was added 60% NaH (6 mg, 0.15 mmol) and CuCl (10 mg, 0.1 mmol). After 24 hours of continues agitation, 15 mL water was added to quench the reaction. The product extracted with ethyl acetate (15 mL × 3) and the organic phase was washed with water (15 mL ×3), dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude product was a complex mixture without **3a** or **4a**.



(eq 2)

Procedure:

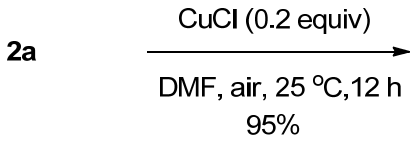
The reaction was carried out under air atmosphere. To a stirring suspension of **2a** (280 mg, 0.5 mmol) in anhydrous DMF (2.5 mL) was added 60% NaH (6 mg, 0.15 mmol), CuCl (10 mg, 0.1 mmol) and 2,2,6,6-Tetramethylpiperidine (71 mg, 0.5 mmol). After 24 hours of continues agitation, 15 mL water was added 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 $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, EtOAc/PE = 1: 10) to give **1a** (110 mg, 50%).



(eq 3)

Procedure:

The reaction was carried out under $^{18}O_2$ 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 $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, EtOAc/PE = 1: 10) to give **3aO^{18}** (264 mg, 92%, 0.46 mmol). The product **3aO^{18}** was analyzed by mass spectroscopy, and the molecular ion at [M + H^+] = 576 proves incorporation of one ^{18}O atoms.



(eq 4)

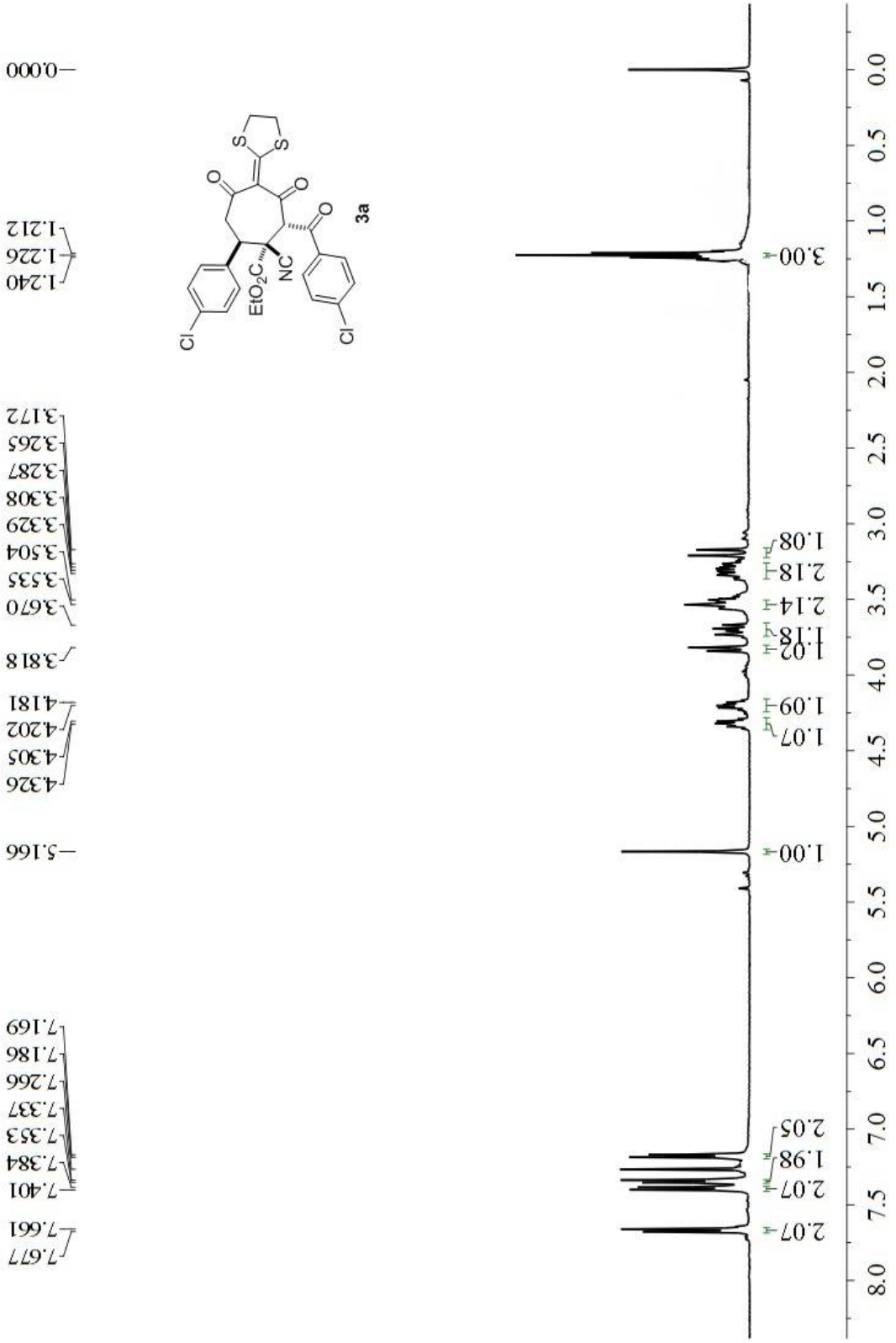
Procedure:

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 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 $MgSO_4$ 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).

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 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 $MgSO_4$ 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**



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129.231
129.760
140.544
167.087
184.212
190.098
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124.615
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129.231
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129.760
132.965
134.820
135.418
140.544
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Cl
Cl
NC
EtO2C
O
O
O
S
S

3b
Cl
EtO2C
NC
Cl
S
S
O
O
O
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2.06
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1.00
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3b
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Cl
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O
S
S
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100
80
60
40
20
0

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O
O
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EtO2C

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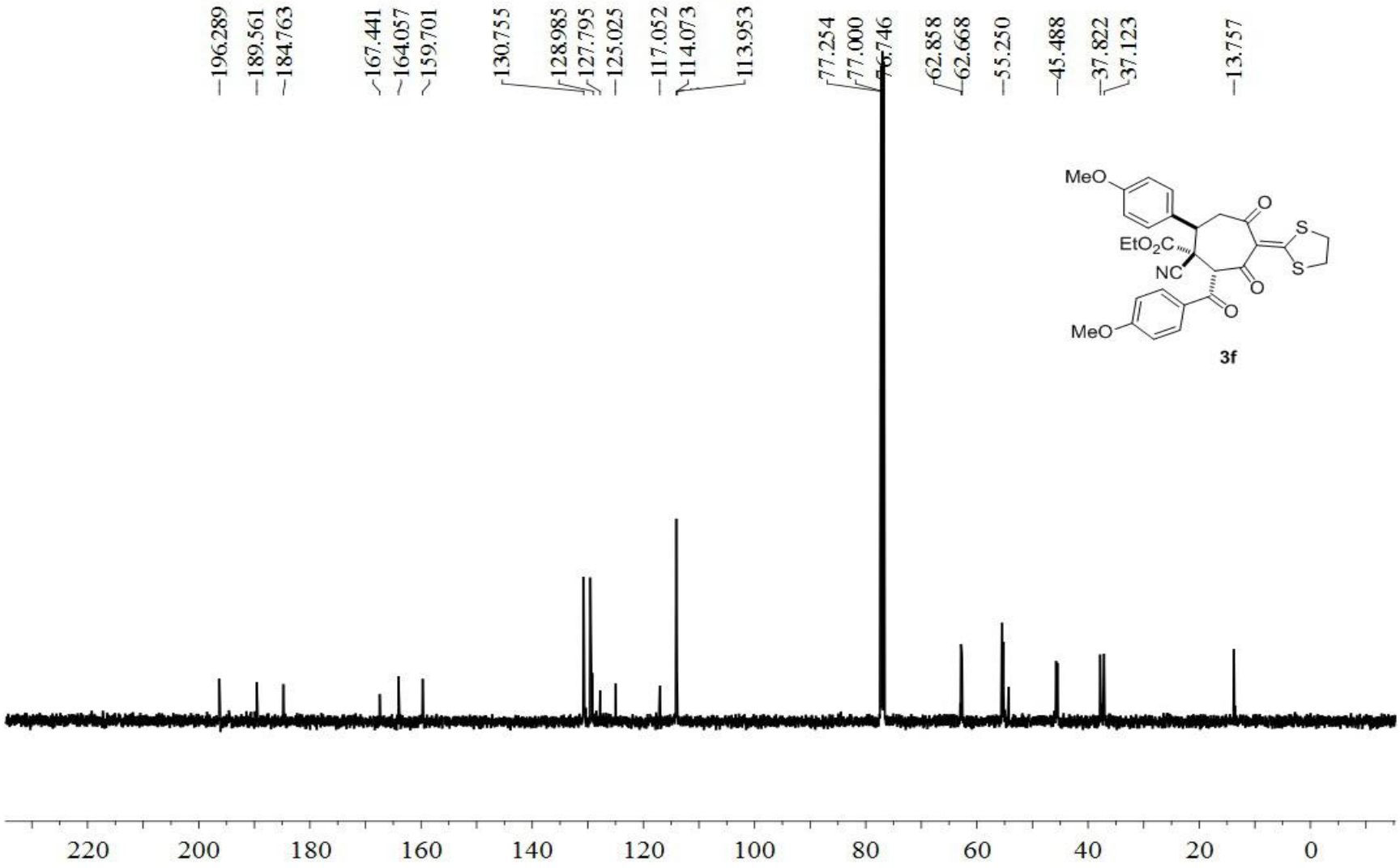
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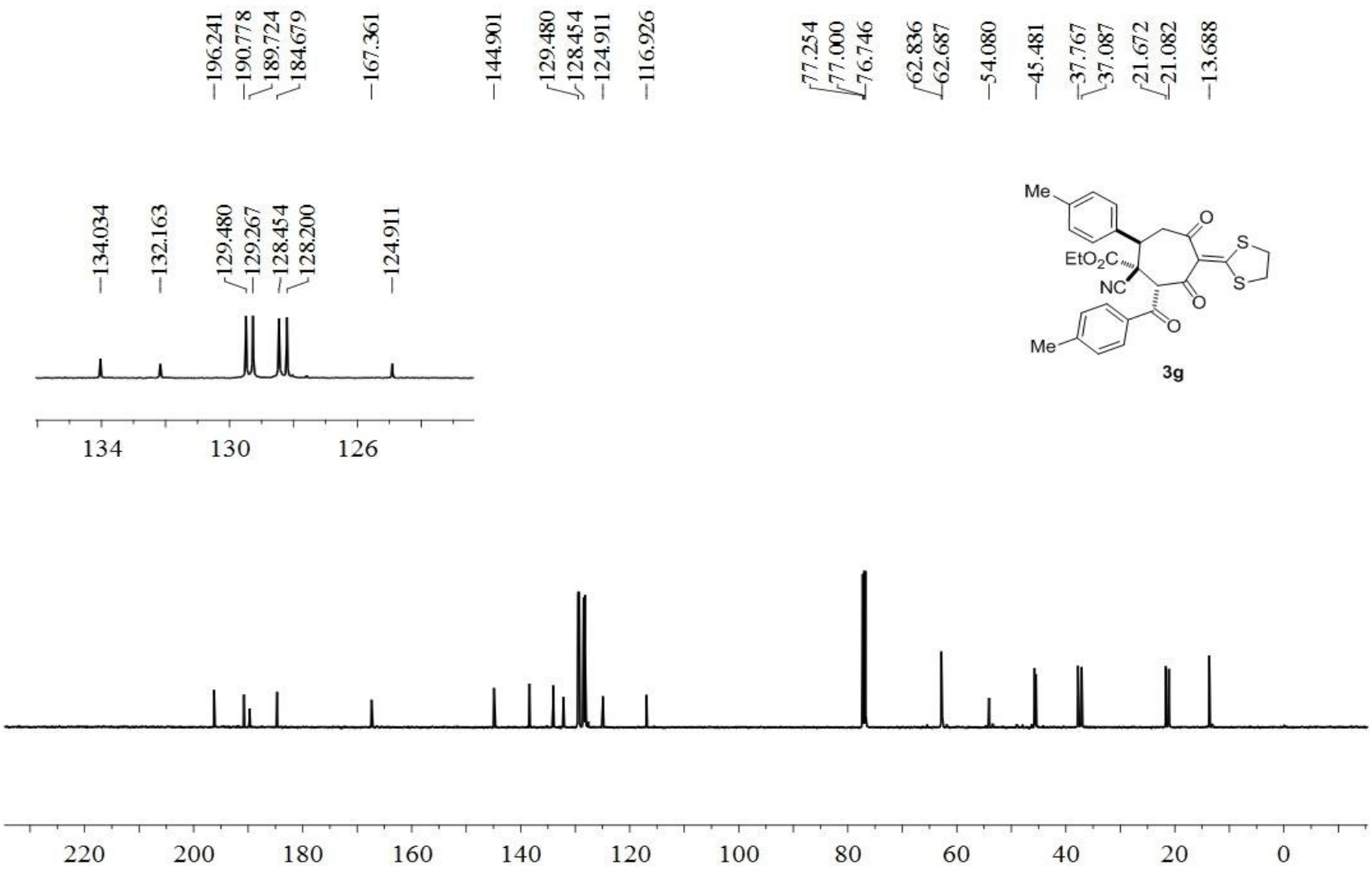
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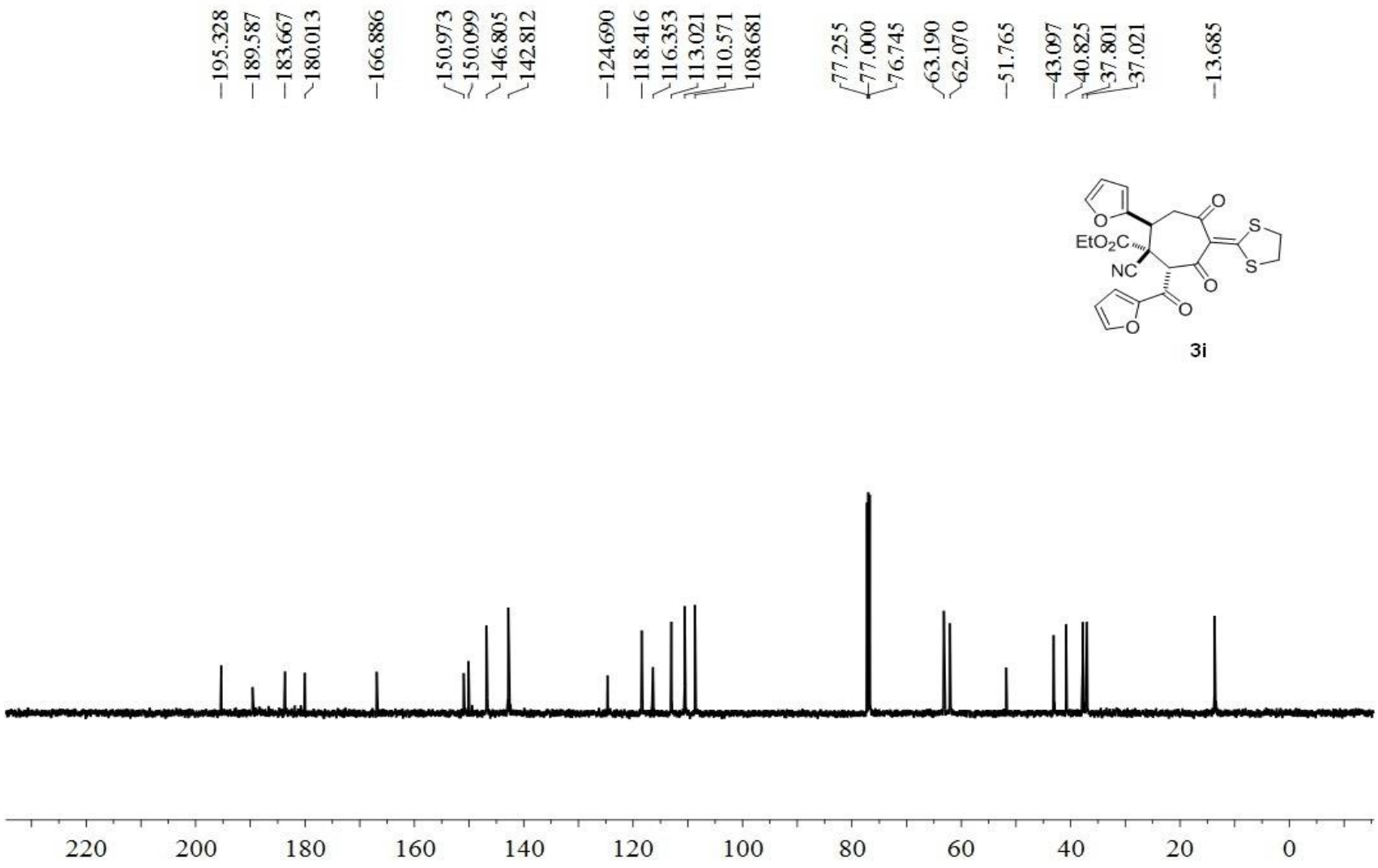
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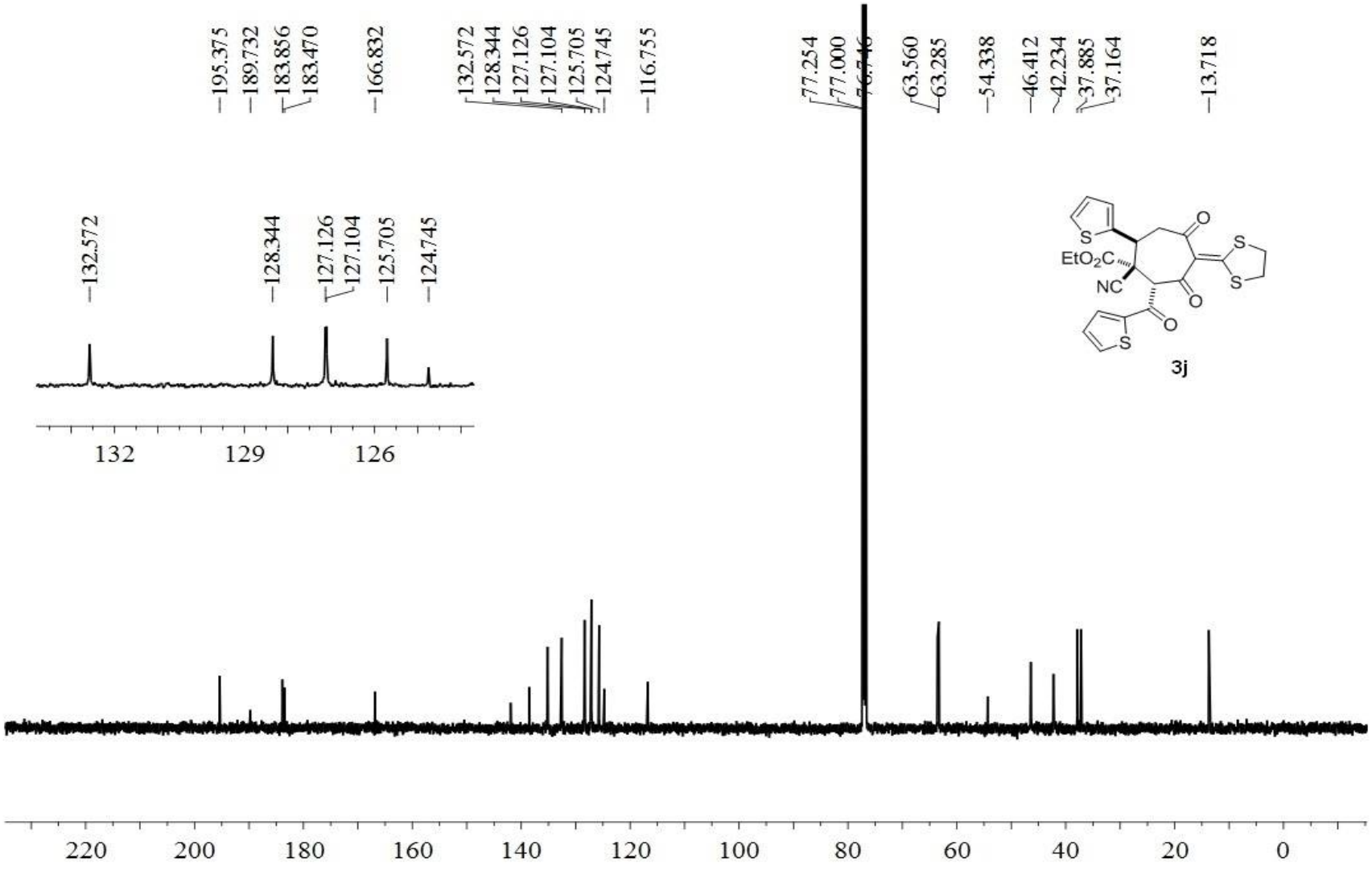
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124.745
132
129
126
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200
180
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140
120
100
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60
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20
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3k
Cl
EtO2C
NC
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EtO2C
NC
MeO
S
S
O
O
O
0
20
40
60
80
100
120
140
160
180
200
220

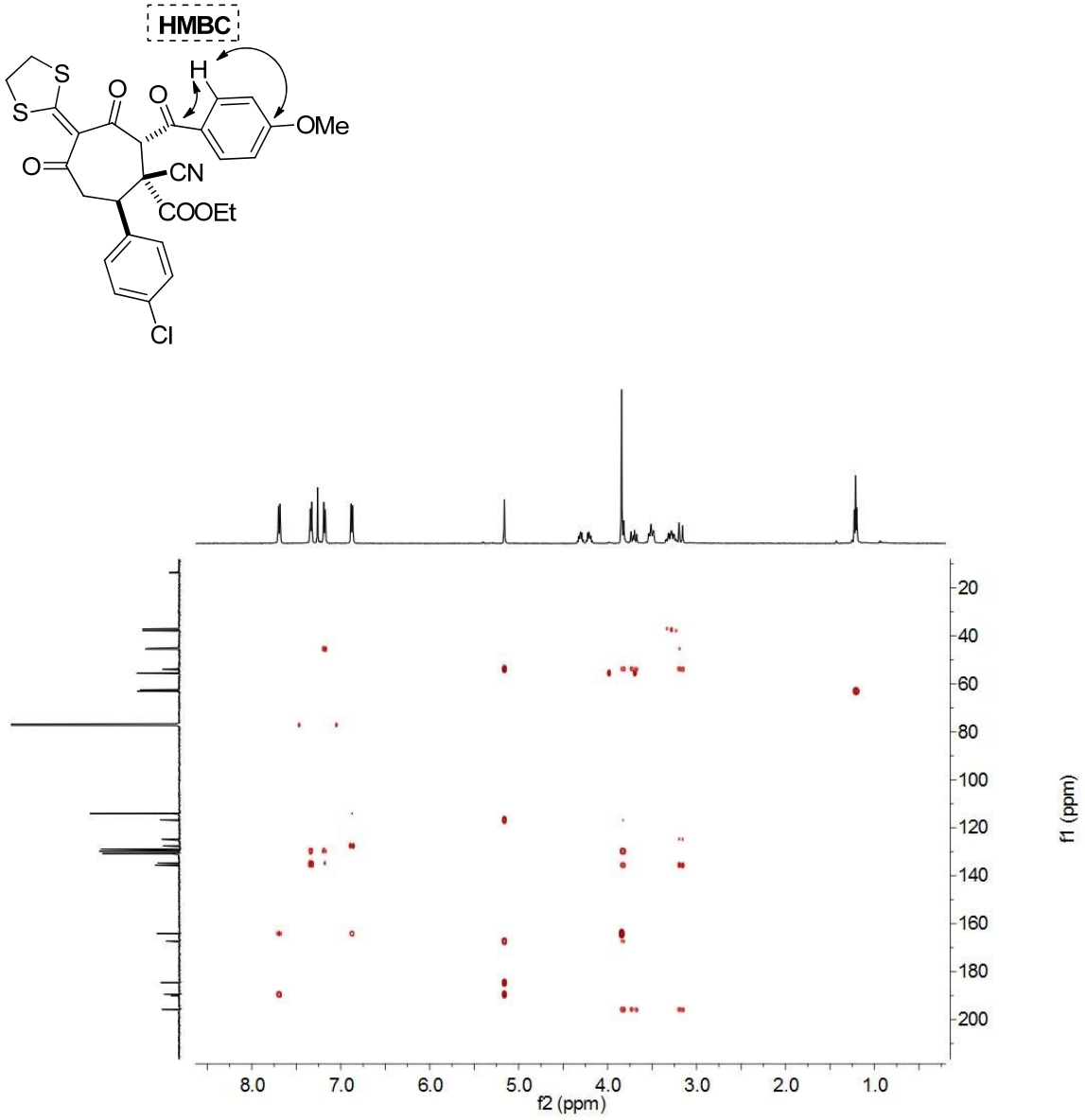
7.682
7.672
7.350
7.333
7.265
7.191
7.174
7.088
7.079
7.070
5.091
4.297
4.283
4.232
4.214
3.553
3.532
3.509
3.353
3.311
3.297
3.287
3.276
3.202
3.164
1.225
1.211
1.196
0.070
0.000
1.08
1.11
1.97
2.04
1.02
1.00
1.11
1.12
1.03
1.14
2.06
2.01
1.12
3.20
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Cl
NC
EtO2C
O
O
O
S
S
S
3l

13.332
13.749
37.197
37.855
45.212
53.821
63.242
63.603
76.746
77.000
77.254
116.508
124.848
128.348
132.587
141.880
166.862
183.625
184.066
190.135
195.474
3l
Cl
EtO2C
NC
O
S
0
20
40
60
80
100
120
140
160
180
200
220

3m
3m'
Br
Cl
EtO2C
NC
S
O

3m'
3m
135.931
135.423
134.746
132.093
131.849
130.028
129.171
128.893
124.587
122.944
195.495
195.459
190.708
190.391
190.160
184.229
167.055
135.423
133.355
132.150
130.028
129.694
128.893
122.944
116.584
77.254
77.000
76.745
63.136
62.697
53.689
45.101
37.840
37.199
13.721

V. ^{1}H-^{1}H NOESY spectrum of **3k**

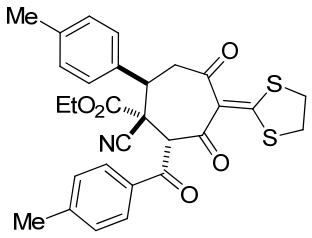


VI. Crystal data and OPTEP drawing of compound **3g**

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 (λ = 0.71073 Å) radiation with a ω 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:



3g

Crystal data:

Empirical formula	$C_{29}H_{27}NO_5S_2$
Formula weight	574.03
Crystal system	Monoclinic
Space group	$P2_1/n$
a (Å)	24.428(4)
b (Å)	12.340(2)
c (Å)	22.946(4)
α (deg)	90
β (deg)	92.211(2)
γ (deg)	90
Volume ($Å^3$)	1455.56(7)
Z	4
Calculated density (mg/m^3)	1.416
Absorption coefficient (mm^{-1})	0.250
F(000)	640
Theta range for data collection (deg)	2.27 to 25.12
Reflections collected/unique	5691/2554
Goodness-of-fit on F^2	1.025
Final R indices [$I > 2\sigma(I)$]	R1=0.0665, WR2 =0.1800
R indices (all data)	R1=0.0808, WR2 =0.2036