Copper-mediated cascade radical cyclization of olefins with naphthalenyl iododifluoromethyl ketones

Peng Peng,[a] Guo-zhi Huang,[a] Ying-xin Sun,[a] Xing Wang,[a] Jing-jing Wu*[a] and Fan-hong Wu*[a]

[a] School of Chemical and Environmental Engineering, Shanghai Institute of Technology, Shanghai 201418, China

[b] Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

E-mail: wujj@sit.edu.cn

-Supporting Information-

1. General procedures.

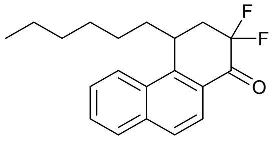
All reactions were carried out under argon atmosphere. All reagents were commercially available and used without further purification unless indicated otherwise. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by thin layer chromatorgraphy (TLC) carried out on GF254 plates (0.25 mm layer thickness) using UV light as visualizing agent. Flash chromatography was performed with 400-500 mesh silica gels.

All NMR spectra were recorded on a Bruker Avance 500 (resonance frequencies 500 MHz for ^{1}H and 125 MHz for ^{13}C) equipped with a 5 mm inverse broadband probe head with z-gradients at 295.8 K with standard Bruker pulse programs. The samples were dissolved in 0.6 ml $CDCl_3$ (99.8% D.TMS). Chemical shifts were given in values of δ^H and δ_C referenced to residual solvent signals (δ_H 7.26 for ^{1}H, δ_C 77.0 for ^{13}C in $CDCl_3$). The ^{19}F NMR spectra were obtained using a 500 spectrometer (470 MHz) using trifluorotoluene as external standard. High resolution mass spectra (HRMS) were recorded on P-SIMS-Gly of Bruker Daltonics Inc. using ESI-TOF (electrospray ionization-time of flight).

2. The procedure for preparation of Compoud 3.

To a solution of 2-iodo-2,2-difluoroacetophenones **1** (1 mmol, 1.0 equiv.) in DMF (2mL) was added alkene **2** (1mmol, 1.0 equiv.), copper (1 mmol, 1.0 equiv.). The mixture was stirred at 120°C under N_2 protection for 1h. The reaction was quenched with water (10mL), and extracted with ethyl acetate (3 x 10mL), the combined organic layers were dried over anhydrous sodium sulfate and the solvent was evaporated in vacuo to give the crude product, which was purified carefully by column chromatography, eluting Petroleum ether/Ethyl acetate (50:1, 40:1) to afford the product **3** as yellow oil (32-70%).

(**3a**) **2,2-difluoro-4-hexyl-3,4-dihydrophenanthren-1(*2H*)-one**



3a

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-2-yl)ethan-1-one (**1a**) with 1-octene (**2a**), and purified by flash column chromatography as white solid (221.0 mg, 70% yield).

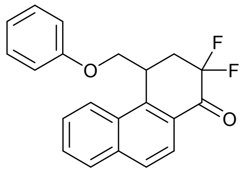
δH (500 MHz, $CDCl_3$, Me_4Si) 8.10(2H, t, *J*=5.0Hz), 7.90(1H, d, *J* = 10.0Hz), 7.82(1H, d, *J*=10.0 Hz), 7.66 (2H, m), 3.89 (1H, d, *J* = 5.0 Hz), 2.97(1H, t, *J* = 15.0 Hz), 2.56 (1H, m), 1.84(2H, dd, *J* = 10.0,5.0 Hz), 1.73 (1H, m), 1.53(1H, m), 1.37 (6H, m), 0.90(3H, d, *J* = 5.0 Hz).

δF (470 MHz, $CDCl_3$) -98.4(1F, d, *J* = 285.0 Hz), -102.8(1F, d, *J* = 285.0 Hz).

δC (125 MHz, $CDCl_3$) 185.7(t, *J* = 25.0 Hz), 147.9, 136.8, 130.1, 129.4(d, *J* = 5.0Hz), 128.4, 127.5, 125.0, 123.2, 113.0(t, *J* = 246.3 Hz), 36.1(d, *J* = 3.8Hz), 33.9(t, *J* = 21.3 Hz), 33.4(d, *J* = 10.0 Hz), 31.7, 29.1, 28.0, 22.6, 14.1.

HRMS (EI-TOF) calculated $[M]^+$ for $C_{20}H_{22}F_2O$ 316.1639, found 316.1638.

(**3b**) 2,2-difluoro-4-(phenoxymethyl)-3,4-dihydrophenanthren-1(*2H*)-one



3b

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-2-yl)ethan-1-one (**1a**) with (allyloxy)benzene (**2b**), and purified by flash column chromatography as yellow oil (226.5 mg, 67% yield).

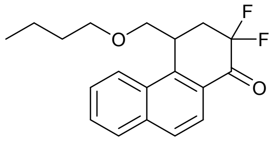
δH (500 MHz, $CDCl_3$, Me_4Si) 8.23(1H, d, *J* = 10.0 Hz), 8.16(1H, d, *J* = 10.0 Hz), 7.92(2H, dd, *J* = 10.0,5.0 Hz), 7.67(2H, m), 7.26(2H, t, *J* = 10.0 Hz), 6.96(1H, t, *J* = 10.0 Hz), 6.88(2H, d, *J* = 5.0 Hz), 4.45(1H, s), 4.26(2H, m), 3.35(1H, t, *J* = 15.0 Hz), 2.68 (1H, m).

δF (470 MHz, $CDCl_3$) -97.8(1F, d, *J* = 285.0 Hz), -104.6(1F, d, *J* = 285.0 Hz).

δC NMR (125 MHz, $CDCl_3$) 185.3(t, *J* = 25.0 Hz), 158.4, 141.5, 136.7, 130.5, 129.6, 129.4(d, *J* = 5.0 Hz), 127.9, 125.0, 123.3, 121.4, 114.7, 112.9(t, *J* = 242.5 Hz), 69.9, 34.1(d, *J* = 10.0 Hz), 33.3(t, *J* = 21.3 Hz).

HRMS (EI-TOF) calculated $[M]^+$ for $C_{21}H_{16}F_2O_2$ 338.1118 , found 338.1119.

(**3c**) 4-(butoxymethyl)-2,2-difluoro-3,4-dihydrophenanthren-1(*2H*)-one



3c

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-2-yl)ethan-1-one (**1a**) with 1-(allyloxy)butane (**2c**), and purified by flash column chromatography as yellow oil (190.8 mg, 60% yield).

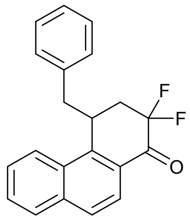
δH (500 MHz, $CDCl_3$, Me_4Si) 8.24(1H, d, *J* = 5.0 Hz), 8.13(1H, d, *J* = 5.0Hz), 7.91(1H, d, *J* = 2.0 Hz), 7.86(2H, d, *J* = 2.0 Hz, 7.67(2H, m), 4.22(1H, s), 3.80(1H, d, *J* = 10.0 Hz), 3.64(1H, td, *J* = 10.0, 2.0 Hz), 2.48 (1H, m), 3.24(1H, t, *J* = 15.0 Hz), 2.56 (1H, m), 1.60(2H, td, *J* = 15.0, 5.0 Hz), 1.42(2H, td, *J* = 15.0, 5.0 Hz), 0.94(3H, t, *J* = 5.0 Hz).

δF (470 MHz, $CDCl_3$) -97.8(1F, d, *J* = 286.9 Hz), -104.0(1F, d, *J* = 286.9 Hz).

δC (125 MHz, $CDCl_3$) 185.5(t, *J*=36.8 Hz), 142.6, 136.6, 130.6, 129.2(t, *J*=26.3 Hz), 127.6, 125.2, 123.2, 112.9(t, *J*=248.8 Hz), 72.9(d, *J*=3.8 Hz), 71.2, 34.5(d, *J*=10.0 Hz), 33.2(t, *J*=21.5 Hz), 19.3, 13.9.

HRMS (EI-TOF) calculated $[M]^+$ for $C_{19}H_{20}F_2O_2$ 318.1431 , found 318.1432.

(**3d**) 4-benzyl-2,2-difluoro-3,4-dihydrophenanthren-1(*2H*)-one



3d

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-2-yl)ethan-1-one (**1a**) with allylbenzene (**2d**), and purified by flash column chromatography as yellow oil (206.0 mg, 64% yield).

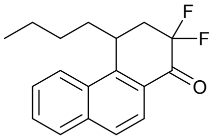
δH (500 MHz, $CDCl_3$, Me_4Si) 8.32(1H, d, *J* = 10.0 Hz), 8.17(1H, d, *J* = 5.0 Hz), 7.93(1H, t, *J* = 5.0 Hz), 7.87(1H, d, *J* = 10.0 Hz), 7.71(m, 2H), 7.42(4H, d, *J* = 5.0 Hz), 7.31(m, 1H), 4.18(1H, d, *J* = 10.0 Hz), 3.28(1H, d, *J* = 15.0 Hz), 2.97(1H, m), 2.77(1H, t, *J* = 15.0 Hz), 2.42(1H,m).

δF (470 MHz, $CDCl_3$) -96.7(1F, d, *J* = 289.8 Hz), -103.5(1F, d, *J* = 289.8 Hz).

δC (125 MHz, $CDCl_3$) 185.5(t, *J*=25.0 Hz), 146.0, 139.1, 136.9, 130.0, 129.5(d, *J*=17.5 Hz), 128.9(d, *J*=6.3 Hz), 127.8, 127.0, 124.8, 123.3, 113.1(t, *J*=245.0 Hz), 41.5(d, *J*=3.8 Hz), 35.6(d, *J*=10.0 Hz), 33.2(t, *J*=20.0 Hz).

HRMS (EI-TOF) calculated $[M]^+$ for $C_{21}H_{16}F_2O$ 322.1169 , found 322.1170.

(**3e**) **4-butyl-2,2-difluoro-3,4-dihydrophenanthren-1(*2H*)-one**



3e

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-2-yl)ethan-1-one (**1a**) with 1-Hexene (**2e**), and purified by flash column chromatography as yellow oil (149.8 mg, 52% yield).

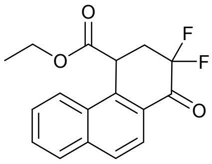
δH (500 MHz, $CDCl_3$, Me_4Si) 8.10(2H, t, *J* = 5.0 Hz), 7.90(1H, d, *J* = 5.0 Hz), 7.82(1H, d, *J* = 5.0 Hz), 7.67(2H, m), 3.88(1H, s), 2.96(1H, t, *J* = 10.0 Hz), 2.56(1H, m), 1.84(2H, d, *J* = 10.0 Hz), 1.54(1H, m), 1.40(2H, m), 0.95(3H, t, *J* = 10.0 Hz).

δF (470 MHz, $CDCl_3$) δ=-98.4(d, *J*= 357.2 Hz, 1F), -102.8(d, *J*=357.2 Hz, 1F).

δC (125 MHz, $CDCl_3$), δ=185.7(t, *J*=26.3 Hz), 147.8, 136.8, 130.1, 129.3(d, *J*=2.5 Hz), 128.4, 127.5, 125.0, 123.2, 113.0(t, *J*=243.8 Hz), 35.8(d, *J*=3.8 Hz), 34.0(t, *J*=21.3 Hz), 33.4(d, *J*=10.0 Hz), 30.2, 22.5, 14.0.

HRMS (EI-TOF) calculated $[M]^+$ $C_{18}H_{18}F_2O$ for 288.1326 , found 288.1325

(**3f**) **Methyl-2,2-difluoro-1-oxo-1,2,3,4-tetrahydrophenanthrene-4-carboxylate**



3f

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-2-yl)ethan-1-one (**1a**) with ethyl acrylate (**2f**), and purified by flash column chromatography as white solid (191.5 mg, 63% yield).

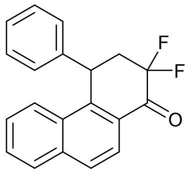
δH (500 MHz, $CDCl_3$, Me_4Si) 8.13(1H, d, *J* = 10.0 Hz), 7.91(3H, t, *J* = 7.0 Hz), 7.65(2H, m), 4.82(1H, d, *J* = 5.5 Hz), 4.17(2H, dd, *J* = 14.0,7.0 Hz), 3.33(1H, m), 2.84(2H, m), 1.16 (3H, t, *J* = 7.0 Hz).

δF (470 MHz, $CDCl_3$) -105.0(1F, d, *J* = 277.3 Hz), -109.6(1F, d, *J* = 277.3 Hz).

δC (125 MHz, $CDCl_3$), δ=184.7(t, *J*=25.0 Hz), 171.1, 138.5, 136.5, 131.2, 129.7, 129.5, 129.2, 127.9, 124.7, 122.9, 112.3(t, *J*=250.0 Hz), 62.1, 39.9(d, *J*=8.8 Hz), 35.7(t, *J*=23.8 Hz), 13.9.

HRMS (EI-TOF) calculated [M]$^+$ for $C_{17}H_{14}F_2O_3$ 304.0911 , found 304.0913.

(**3g**) **2,2-difluoro-4-phenyl-3,4-dihydrophenanthren-1(*2H*)-one**



3g

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-2-yl)ethan-1-one (**1a**) with styrene (**2g**), and purified by flash column chromatography as yellow oil (163.2 mg, 53% yield).

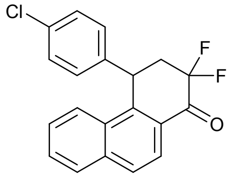
δH (500 MHz, $CDCl_3$, Me_4Si) 8.24(1H, d, *J* = 10.0 Hz), 7.94(1H, d, *J* = 10.0 Hz), 7.89(1H, d, *J* = 10.0 Hz), 7.79(1H, d, *J* = 10.0 Hz), 7.58(1H, t, *J* = 10.0 Hz), 7.40(1H, m), 7.22(3H, m), 7.00(2H, d, *J* = 10.0 Hz), 5.28(1H, m), 3.02(2H, m).

δF (470 MHz, $CDCl_3$) -102.3(1F, d, *J* = 343.1 Hz), -107.6(1F, d, *J* = 343.1 Hz).

δC (125 MHz, $CDCl_3$) 185.7(t, *J*=25.0 Hz), 143.4, 142.9, 136.8, 130.8, 129.3(d, *J*=8.8 Hz), 129.0, 128.8, 127.9(d, *J*=1.3 Hz), 127.5, 127.0, 126.5, 122.9, 112.5(t, *J*=247.5 Hz), 40.2(t, *J*=20.0 Hz), 39.9(d, *J*=8.8 Hz).

HRMS (EI-TOF) calculated [M]$^+$ $C_{20}H_{14}F_2O$ for 308.1013 , found 308.1014.

(**3h**) **4-(4-chlorophenyl)-2,2-difluoro-3,4-dihydrophenanthren-1(*2H*)-one**



3h

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-2-yl)ethan-1-one (**1a**) with 1-chloro-4-vinylbenzene (**2h**), and purified by flash column chromatography as yellow oil (193.4 mg, 58% yield).

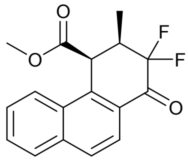
δH (500 MHz, $CDCl_3$, Me_4Si) 8.15(1H, d, *J* = 10.0 Hz), 7.87(1H, d, *J* = 10.0 Hz), 7.82(1H, d, *J* = 10.0 Hz), 7.65(1H, d, *J* = 5.0 Hz), 7.52(1H, m), 7.35(1H, m), 7.12(2H, d, *J* = 10.0 Hz), 6.82(2H, d, *J* = 10.0 Hz), 7.21(2H, d, *J* = 10.0 Hz), 6.94(2H, d, *J* = 5.0 Hz), 5.18(1H, m), 2.91(2H, m).

δF (470 MHz, $CDCl_3$) -101.8(1F, d, *J* = 347.8 Hz), -106.9(1F, d, *J* = 347.8 Hz).

δC (125 MHz, $CDCl_3$) 185.4(t, *J*=25.0 Hz), 142.1, 141.8, 136.8, 132.9,129.6, 129.4(d, *J*=8.8 Hz), 129.1(d, *J*=18.8 Hz), 127.7, 126.2, 123.0, 112.4(t, *J*=246.3 Hz), 53.4, 40.0(t, *J*=21.3 Hz), 39.2(d, *J*=7.5 Hz).

HRMS (EI-TOF) calculated [M]$^+$ for $C_{20}H_{13}F_2OCl$ 342.0623 , found 342.0622.

(3i) Methyl-2,2-difluoro-3-methyl-1-oxo-1,2,3,4-tetrahydrophenanthrene-4-carboxylate



3i

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-2-yl)ethan-1-one (**1a**) with methyl crotonate (**2i**), and purified by flash column chromatography as yellow oil (133.8mg, 44% yield).

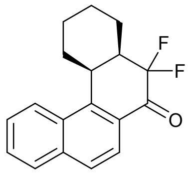
δH (500 MHz, $CDCl_3$, Me_4Si) 8.14(1H, d, *J* = 10.0 Hz), 7.92(3H, t, *J* = 10.0 Hz), 7.66(2H, m), 4.59(1H, t, *J* = 5.0 Hz), 3.68(1H, s), 3.50(1H, m), 1.28(3H, d, *J* = 10.0 Hz).

δF (470 MHz, $CDCl_3$) -106.0(1F, d, *J* = 338.4 Hz), -119.2(1F, d, *J* = 338.4 Hz).

δC (125 MHz, $CDCl_3$) 184.6(t, *J*=26.3 Hz), 172.0, 136.7, 136.6, 131.8, 129.6, 129.3(d, *J*=8.8 Hz), 127.9, 124.5, 122.7, 114.2(t, *J*=243.8 Hz), 53.0(d, *J*=1.3 Hz), 47.8(d, *J*=6.3 Hz), 40.5(t, *J*=21.3 Hz), 13.5(d, J=7.5 Hz).

HRMS (EI-TOF) calculated $[M]^+$ $C_{17}H_{14}F_2O_3$ for 304.0911 , found 304.0909.

(3j) **5,5-difluoro-1,3,4,4a,5,12c-hexahydrobenzo[c]phenanthren-6(*2H*)-one**



3j

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-2-yl)ethan-1-one (**1a**) with methyl crotonate (**2i**), and purified by flash column chromatography as yellow oil (134.4 mg, 47% yield).

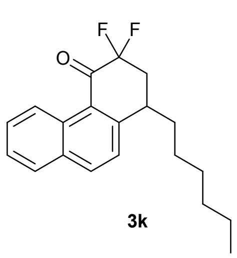
δH (500 MHz, $CDCl_3$, Me_4Si) 8.05(2H, d, *J* = 10.0 Hz, 5Hz), 7.82(1H, m), 7.74(1H, d, *J* = 10.0 Hz), 7.57(2H, m), 3.72(1H, m), 2.65(1H, m), 2.47(1H,m), 2.11(1H, d, *J* = 10.0 Hz), 1.91(1H, d, *J* = 10.0 Hz), 1.78(1H, m), 1.70(3H, d, *J* = 10.0 Hz), 1.60(1H, m).

δF (470 MHz, $CDCl_3$) -103.1(1F, d, *J* = 352.5 Hz), -112.7(1F, d, *J* = 338.4 Hz).

δC (125 MHz, $CDCl_3$) 185.8(t, *J*=25.0 Hz), 147.8, 136.7, 130.0, 129.3(d, *J*=5.0 Hz), 128.4, 127.4, 125.1, 123.3, 115.3(t, *J*=247.5 Hz), 39.9(t, *J*=20.0 Hz), 37.3(d, *J*=8.8 Hz), 26.2, 24.2, 22.2(d, *J*=5.0 Hz).

HRMS (EI-TOF) calculated $[M]^+$: $C_{18}H_{16}F_2O$ for 286.1169, found 286.1168.

(3k) **3,3-difluoro-1-hexyl-2,3-dihydrophenanthren-4(*1H*)-one**



3k

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-1-yl)ethan-1-one (**1b**) with 1-octene (**2a**), and purified by flash column chromatography as yellow oil (116.9 mg, 37% yield).

δH (500 MHz, $CDCl_3$, Me_4Si) 9.31(1H, t, *J* = 10.0 Hz), 8.04(1H, d, *J* = 10.0 Hz), 7.84(1H, d, *J* = 10.0

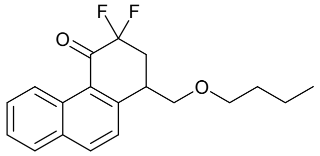
Hz), 7.68(1H, t, *J* = 5.0 Hz), 7.55(1H, t, *J* = 5.0 Hz), 7.41(1H, d, *J* = 10.0 Hz), 3.32(1H, s), 2.63 (2H, m), 1.83(2H, d, *J* = 5.0 Hz), 1.32(8H, d, *J* = 25.0 Hz), 0.88(3H, s).

δF (470 MHz, CDCl$_3$) -102.2(1F, d, *J* = 338.4 Hz), -103.0(1F, , *J* = 338.4 Hz).

δC (125 MHz, CDCl$_3$) 187.1(t, *J* = 25.0 Hz), 150.1, 136.1, 132.6, 131.5, 129.7, 128.5, 126.8, 126.2, 125.9, 124.4, 113.7(t, *J* = 245.0 Hz), 37.2(t, *J* = 3.8 Hz), 36.8, 35.1(t, *J* = 21.3 Hz), 31.7, 29.2, 27.0, 22.6, 14.1.

HRMS (EI-TOF) calculated [M]$^+$ for C$_{20}$H$_{22}$F$_2$O 316.1639, found 316.1638.

(3l)butoxy-3,3-difluoro-2,3-dihydrophenanthren-4(*1H*)-one



3l

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-1-yl)ethan-1-one (**1b**) with 1-Octene (**2a**), and purified by flash column chromatography as yellow oil (111.3 mg, 35% yield).

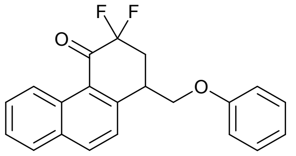
δH (500 MHz, CDCl$_3$, Me$_4$Si) δ=8.32(d, *J*=10.0Hz, 1H), 8.05(d, *J*=10.0Hz, 1H), 7.85(d, *J*=10.0 Hz, 1H), 7.69(t, *J*=10.0 Hz, 1H), 7.57(t, *J*=10.0 Hz, 1H), 7.51(d, *J*=10.0 Hz, 1H), 4.22(s, 1H), 3.74(m, 2H), 3.59(t, *J*=5.0 Hz, 1H), 3.47(td, *J*=15.0, 5.0 Hz, 2H), 2.74(m, 2H), 1.56 (m, 2H), 1.36(td, *J*=15.0,10.0 Hz, 2H), 0.91(t, *J*=10.0 Hz, 3H).

δF (470 MHz, CDCl$_3$) δ= -102.6(d, *J*= 338.4 Hz, 1F), -104.3(d, *J*=333.7 Hz, 1F).

δC (125 MHz, CDCl$_3$), δ=186.8(t, *J*=25.0 Hz), 146.3, 136.0, 132.8, 131.5, 129.7, 128.5, 126.9, 126.3, 126.0, 113.6(t, *J*=246.3 Hz), 74.1(d, *J*=1.3 Hz), 71.3, 53.4, 38.0(dd, *J*=6.3, 2.5 Hz), 33.7(t, *J*=22.5 Hz), 31.6, 19.3, 13.9.

HRMS (EI-TOF) calculated [M]$^+$ for C$_{19}$H$_{20}$F$_2$O$_2$ 318.1431 , found 318.1432.

(3m)3,3-difluoro-1-(phenoxymethyl)-2,3-dihydrophenanthren-4(*1H*)-one



3m

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-1-yl)ethan-1-one (**1b**) with (allyloxy)benzene (**2b**), and purified by flash column chromatography as yellow oil (125.1 mg, 37% yield).

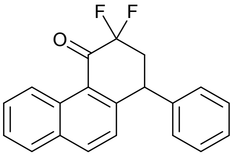
δH (500 MHz, CDCl$_3$, Me$_4$Si) 9.33(1H, d, *J* = 10.0 Hz), 8.05(1H, d, *J* = 10.0 Hz), 7.84(1H, d, *J* = 10.0 Hz), 7.68(1H, t, *J* = 8.0 Hz), 7.56(1H, t, *J* = 7.5 Hz), 7.51 (1H, d, *J* = 6.5 Hz), 7.27(2H, t, *J* = 8.0 Hz), 6.96(1H, t, *J* = 7.0 Hz), 6.88(1H, d, *J* = 8.0 Hz), 4.29(2H, m), 3.80(1H, t, *J* = 5.0 Hz), 2.84(2H, m).

δF (470 MHz, CDCl$_3$) -102.4(1F, d, *J* = 329.0Hz), -104.4(1F, d, *J* = 333.7 Hz).

δC (125 MHz, CDCl$_3$) 186.7(t, *J* = 25.0 Hz), 158.3, 145.2, 136.4, 133.0, 131.5, 129.9, 129.7, 128.6, 127.2, 126.3, 125.8, 121.5, 114.7, 114.0(t, *J* = 246.0 Hz), 70.9, 37.6(dd, *J* = 6.3, 5.0 Hz), 33.8(t, *J* = 22.5 Hz).

HRMS (EI-TOF) calculated [M]$^+$ for $C_{21}H_{16}F_2O_2$ 338.1118 , found 338.1119.

(3n) **3,3-difluoro-1-phenyl-2,3-dihydrophenanthren-4(*1H*)-one**



3n

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-1-yl)ethan-1-one (**1b**) with styrene (**2g**), and purified by flash column chromatography as yellow oil (175.6 mg, 57% yield).

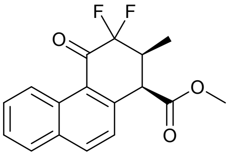
δH (500 MHz, $CDCl_3$, Me_4Si) 9.31(1H, d, J = 10.0 Hz), 7.75(1H, d, J = 8.5 Hz), 7.67(1H, d, J = 8.0 Hz), 7.58(1H, t, J = 8.0 Hz), 7.44(1H, t, J = 7.5 Hz, 7.22(3H, m), 7.03(2H, d, J = 7.0 Hz), 6.86(1H, d, J = 8.5 Hz), 4.53(1H, dd, J = 10.5, 5.5 Hz), 2.86(1H, m), 2.55(1H, m).

δF (470 MHz, $CDCl_3$) -108.3(1F, d, J= 324.3Hz), -110.0(1F, d, J = 329.0 Hz).

δC (125 MHz, $CDCl_3$) 186.9(t, J = 25.0 Hz), 148.4, 142.9, 136.0, 132.7, 131.3, 129.9, 129.3, 128.8, 128.6, 127.7, 127.1, 127.0, 126.3, 113.3(t, J = 250.0 Hz), 43.59(dd, J = 7.5, 2.5 Hz), 40.7(t, J = 22.5 Hz).

HRMS (EI-TOF) calculated [M]$^+$ for $C_{20}H_{14}F_2O$ 308.1013 , found 308.1012.

(3o) **methyl 3,3-difluoro-2-methyl-4-oxo-1,2,3,4-tetrahydrophenanthrene-1-carboxylate**



3o

The title compound was prepared according to the general procedure described above by the reaction between 2,2-difluoro-2-iodo-1-(naphthalen-1-yl)ethan-1-one (**1b**) with methyl crotonate (**2i**), and purified by flash column chromatography as yellow oil (103.4 mg, 34% yield).

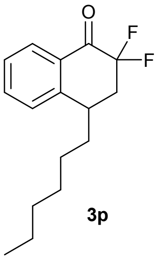
δH (500 MHz, $CDCl_3$, Me_4Si) 9.27(1H, d, J = 10.0 Hz), 8.99(1H, d, J = 10.0 Hz), 7.79(1H, d, J = 8.0 Hz), 7.64(1H, t, J = 8.0 Hz), 7.52(1H, t, J = 7.0 Hz), 7.23 (1H, d, J = 8.5 Hz), 4.06(1H, d, J = 8.5 Hz), 3.76(3H, s), 3.06(1H, m), 1.26(3H, d, J = 7.0 Hz).

δF (470 MHz, $CDCl_3$) -116.7(1F, d, J = 324.3Hz), -120.4(1F, d, J = 319.6 Hz).

δC (125 MHz, $CDCl_3$) 186.2(t, J = 25.0 Hz), 171.8, 140.9, 136.5, 133.0, 131.4, 130.1, 129.6, 127.3, 126.3, 125.0, 114.0(t, J = 250.0 Hz), 52.9, 51.8(d, J = 5.0 Hz), 39.3(t, J = 22.5 Hz), 11.2(t, J = 2.5 Hz).

HRMS (EI-TOF) calculated [M]$^+$ for $C_{17}H_{14}F_2O_3$ for 304.0911 , found 304.0909.

(3p) **2,2-difluoro-4-hexyl-3,4-dihydronaphthalen-1(*2H*)-one**



3p

The title compound was prepared according to the general procedure described above by the reaction between 2-iodo-2,2-difluoroacetophenone (**1c)** with 1-octene (**2a**), and purified by flash column chromatography as yellow oil (87.8 mg, 33% yield).

δH (500 MHz, $CDCl_3$, Me_4Si) 8.12(1H, d, *J* = 10.0 Hz), 7.63(1H, t, *J* = 5.0 Hz), 7.87(1H, t, *J* = 10.0 Hz), 7.41(2H, m), 3.24(1H, m), 2.64(1H, m), 2.43(1H, m), 1.59(1H, s), 1.48(1H, m), 1.35(6H, m), 0.90(3H, t, *J* = 6.5 H).

δF (470 MHz, $CDCl_3$) -105.1(1F, d, *J* = 277.3 Hz), -106.5(1F, d, *J* = 277.3 H).

δC (125 MHz, $CDCl_3$) 185.6(t, *J* = 25.0 Hz), 147.0, 135.1, 129.7, 128.8, 127.9, 127.4, 113.6(t, *J* = 250.0 Hz), 36.2(t, *J* = 20.0 Hz), 35.6(t, *J* = 5.0 Hz), 35.3, 29.2, 26.6, 22.7, 14.1.

HRMS (EI-TOF) calculated $[M]^+$ for $C_{16}H_{20}F_2O$ 266.1482 , found 266.1481.

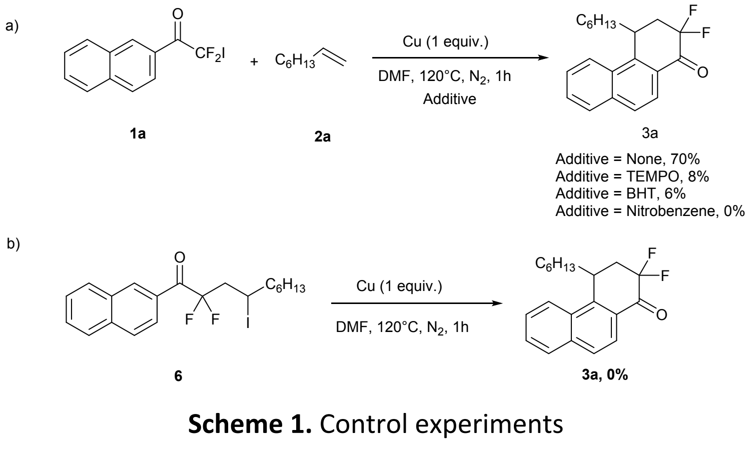
3. The reaction of other naphthalenyl halodifluoromethyl ketones with 1-octene

To a solution of 2-halo-2,2-difluoroacetophenones (1 mmol, 1.0 equiv.) in DMF (2mL) was added alkene **2a** (1mmol, 1.0 equiv.), copper (1 mmol, 1.0 equiv.), $AgNO_3$ (1 mmol, 1.0 equiv.). The mixture was stirred at 120°C under N_2 protection for 1h. The reaction was quenched with water (10mL), and extracted with ethyl acetate (3 x 10mL), the combined organic layers were dried over anhydrous sodium sulfate and the solvent was evaporated in vacuo to give the crude product, which was purified carefully by column chromatography, eluting Petroleum ether/Ethyl acetate (50:1, 40:1) to afford the product **3** as yellow oil (75% yield, halo = Br; 54% yield, halo = Cl).

4. Studies on Reaction Mechanism

4.1 Control experiment

We added the radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) to this cyclization reaction under standard conditions and found that the reaction was suppressed. Similarly, when butylated hydroxytoluene (BHT) and nitrobenzene were subjected to the standard reaction system respectively, the yield of the desired cyclic product **3a** was declined sharply (Scheme 1a). These results indicated that the reaction might undergo a tandem radical addition and cyclization process. Then, the addition compound **6** was prepared and used to perform the intramolecular cyclization in the presence of copper under standard condition. However, the desired product **3a** was not obtained (Scheme 1b),



Scheme 1. Control experiments

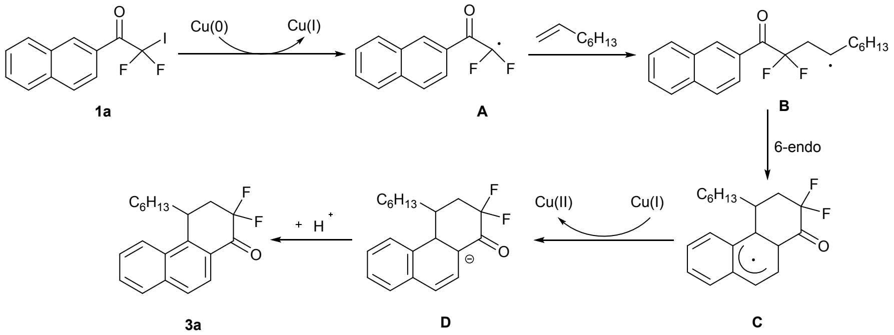
4.2 Computational Methods

We employed the DFT method with M06-2X hybrid meta-GGA functional as default to describe the all molecules.1,2 It is well-known that B3LYP functional has many shortcomings,3 such as (1) it systematically underestimates activation barrier heights of transition states (TSs), and (2) it is not enough to treat medium-range VDW interactions, for example, aromatic-aromatic stacking energies. Recently, Zhao et al. developed new density functionals, called M06-class, for a variety of databases.4-6 The M06-2X is a hybrid meta functional and has excellent performances for accurately predicting main-group thermochemistry, electronic excitation energies, and aromatic-aromatic stacking interactions. This functional could be considered to describe the noncovalent interactions as reliably as the Møller-Plesset second-order perturbation theory (MP2) with the affordable computational costs for very large systems.

During structural optimization, molecular structures were allowed to relax. The frequency calculations were performed at the same level of theory. The 6-31G(d,p) basis set was employed for O, C, F, and H atoms and LANL2DZ effective core potential basis set was used for Cu and I atoms. Single-point energy calculations were carried out at the M06-2X/6-311++G(2d,2p) levels using the abovementioned M06-2X/6-31G(d,p) optimized structures in order to obtain more reliable interaction energies. A polarized continuum model (PCM-SMD) was utilized to simulated the solvent effect of n,n-DiMethylFormamide (DMF). Unless otherwise mentioned, the Gibbs free energies are used at the M06-2X/6-311++G(2d,2p) level in DMF solution. All the calculations were performed using the Gaussian 09 code.7

4.3 Description of Reaction Mechanism

As given in Figure 1, the **A** can be formed from **1a** by Cu catalyst and need the energy of 258.58 kJ/mol. Furthermore, the B can be obtained by a dimerization step and are energetically favorable due to a large exothermic step (-163.87 kJ/mol). The **B** radical will experience a cyclization step and two intermediates, **C** and **D**, are produced. The **C** is further reduced by losing an electron to produce **E** (250.90 kJ/mol), followed by a deprotonation step (414.53 kJ/mol). The main product **3a** is finally formed. All molecular structures are shown in Figure 2.



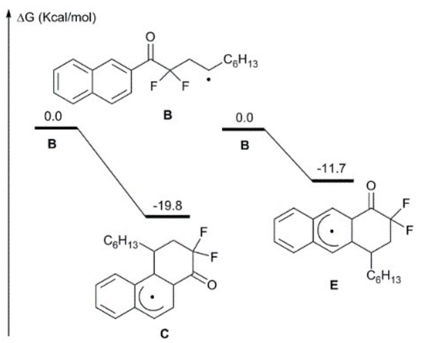
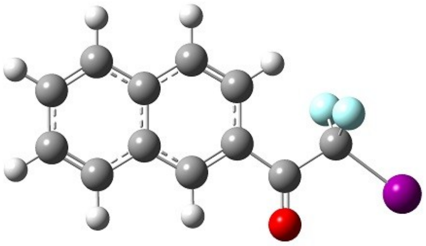
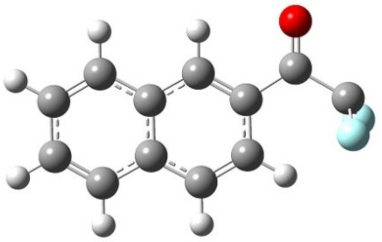


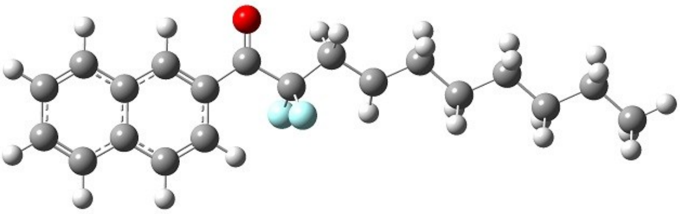
Figure 1. Plausible copper oxidation quenching mechanism for the formation of **3a**



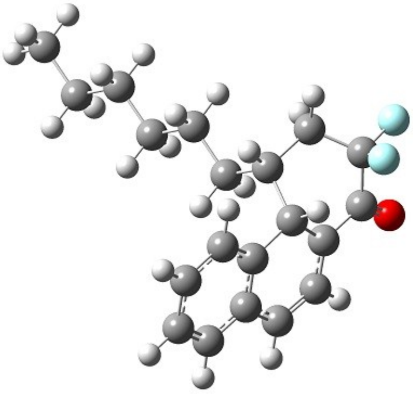
1a



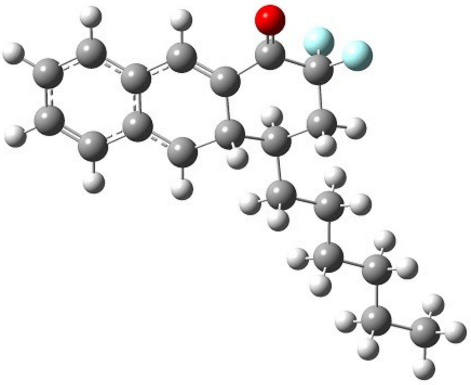
A



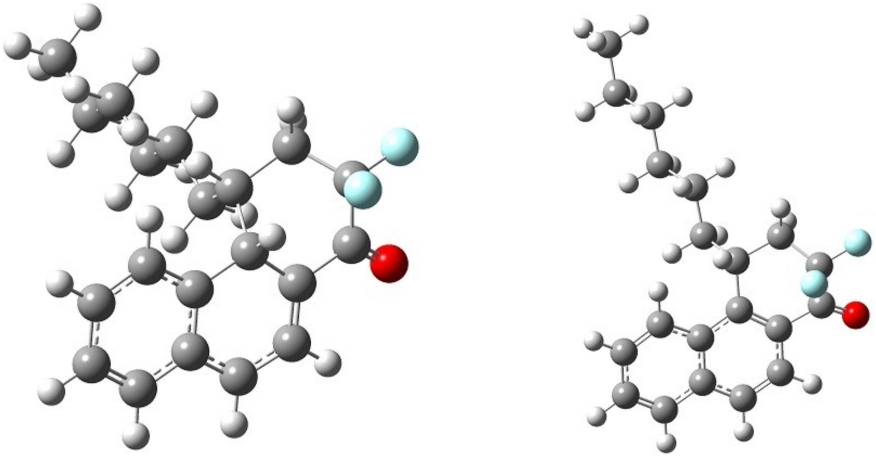
B



C



D



E **3a**

Figure 2. The optimized structures of **1a**, **A**-**E**, **3a** molecules at the level of M06-2X/6-31G(d,p).

5. X-Ray Data Collection and Structure Refinement Details

X-Ray data for compound **3a**

A good quality single crystal of size 0.20 x 0.16 x 0.13 mm^3, was selected under a polarizing microscope and was mounted on a glass fiber for data collection. Single crystal X-ray data for compound **3a** were collected on the Rigaku Kappa 3 circle diffractometer equipped with the AFC12 goniometer and enhanced sensitivity (HG) Saturn724+ CCD detector in the 4x4 bin mode using the monochromated Mo-Kα radiation generated from the microfocus sealed tube MicroMax-003 X-ray generator equipped with specially designed confocal multilayer optics. Data collection was performed using ω-scans of 0.5° steps at 296(2) K. Cell determination, data collection and data reduction was performed using the Rigaku CrystalClear-SM Expert 2.1 b24[1]software. Structure solution and refinement were performed by using SHELX-97[2]. Refinement of coordinates and anisotropic thermal parameters of non-hydrogen atoms were carried out by the full-matrix least-squares method. The hydrogen atoms attached to carbon atoms were generated with idealized geometries and isotropically refined using a riding model.

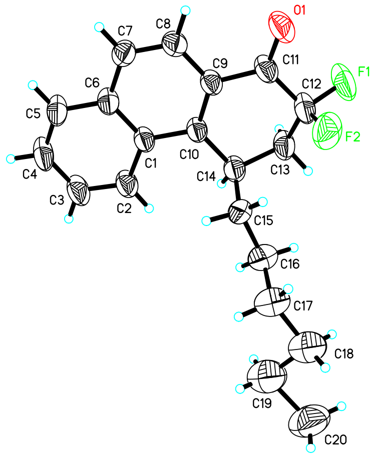


Figure 3. ORTEP diagram drawn with 30% ellipsoid probability for non-H atoms of the

crystallographic structure of compound 3a determined at 296 K.

Crystallization: Crystal of compound 3a was grown from the solvents PE + EA by slow evaporation method.

Table 1. Crystal data and structure refinement for 3a.

Compound	**3a**
Empirical formula	$C_{20}H_{22}F_2O$
Formula weight	316.37
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a = 10.0026(6) Å α= 90°.
	b = 25.7449(14) Å β= 103.519(2)°
	c = 7.0051(4) Å γ = 90°.
Volume	1753.94(17) $Å^3$
Z	4
Density (calculated)	1.198 Mg/m^3
Absorption coefficient	0.086 mm^{-1}
F(000)	672
Crystal size	0.20 x 0.16 x 0.13 mm^3
Theta range for data collection	2.625 to 24.997°.
Index ranges	-11<=h<=11, -30<=k<=30, -8<=l<=8
Reflections collected	8890
Independent reflections	3050 [R(int) = 0.0404]
Completeness to theta = 25.242°	96.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6097
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3050 / 72 / 265
Goodness-of-fit on F^2	1.033
Final R indices [I>2sigma(I)]	R1 = 0.0747, wR2 = 0.2071
R indices (all data)	R1 = 0.1057, wR2 = 0.2380
Largest diff. peak and hole	0.201 and -0.203 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for 3a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
F(2)	8762(2)	6173(1)	14961(3)	137(1)
F(1)	9505(2)	6957(1)	14960(3)	139(1)
O(1)	7677(2)	6947(1)	17144(3)	122(1)
C(1)	4002(2)	6669(1)	11512(3)	69(1)
C(10)	5445(2)	6653(1)	12456(3)	67(1)
C(6)	3058(2)	6869(1)	12550(4)	73(1)
C(9)	5845(2)	6828(1)	14372(3)	70(1)
C(2)	3477(3)	6505(1)	9561(4)	91(1)
C(8)	4884(3)	7020(1)	15378(4)	84(1)
C(5)	1648(3)	6903(1)	11590(5)	91(1)
C(7)	3533(3)	7039(1)	14499(4)	84(1)
C(13)	7896(3)	6688(2)	12161(4)	94(1)
C(14)	6466(2)	6450(1)	11366(4)	83(1)
C(11)	7298(3)	6826(1)	15436(4)	82(1)
C(12)	8359(3)	6658(1)	14326(5)	91(1)
C(4)	1189(3)	6743(2)	9727(5)	106(1)
C(3)	2105(3)	6542(2)	8696(5)	108(1)
C(15)	6484(8)	5867(3)	11265(19)	100(2)
C(16)	7131(8)	5699(3)	9525(13)	126(2)
C(17)	7229(10)	5106(3)	9546(16)	157(2)
C(18)	8184(13)	4847(6)	8257(17)	180(3)
C(19)	7130(13)	4807(7)	6329(19)	196(3)
C(20)	8280(16)	4481(5)	5330(20)	198(4)
C(15')	6460(30)	5848(7)	11420(50)	202(5)
C(16')	7410(20)	5503(8)	10550(20)	208(4)
C(17')	6711(19)	5339(9)	8560(20)	214(4)
C(18')	7680(20)	5057(6)	7360(20)	225(4)
C(19')	7850(20)	4504(6)	6970(20)	234(4)
C(20')	6780(20)	4439(7)	4990(20)	245(5)

_

Table 3. Bond lengths [Å] and angles [°] for 3a.

F(2)-C(12)	1.355(4)
F(1)-C(12)	1.365(3)
O(1)-C(11)	1.209(3)
C(1)-C(2)	1.410(4)
C(1)-C(6)	1.416(4)
C(1)-C(10)	1.441(3)
C(10)-C(9)	1.384(3)
C(10)-C(14)	1.504(4)
C(6)-C(7)	1.406(4)
C(6)-C(5)	1.416(4)
C(9)-C(8)	1.406(4)
C(9)-C(11)	1.470(3)
C(2)-C(3)	1.368(4)
C(2)-H(2)	0.9300
C(8)-C(7)	1.349(4)
C(8)-H(8)	0.9300
C(5)-C(4)	1.342(4)
C(5)-H(5)	0.9300
C(7)-H(7)	0.9300
C(13)-C(12)	1.481(4)
C(13)-C(14)	1.535(4)
C(13)-H(13A)	0.9700
C(13)-H(13B)	0.9700
C(14)-C(15)	1.502(8)
C(14)-C(15')	1.550(17)
C(14)-H(14)	0.9800
C(11)-C(12)	1.518(4)
C(4)-C(3)	1.392(5)
C(4)-H(4)	0.9300
C(3)-H(3)	0.9300
C(15)-C(16)	1.569(10)
C(15)-H(15A)	0.9700
C(15)-H(15B)	0.9700

C(16)-C(17)	1.528(10)
C(16)-H(16A)	0.9700
C(16)-H(16B)	0.9700
C(17)-C(18)	1.605(12)
C(17)-H(17A)	0.9700
C(17)-H(17B)	0.9700
C(18)-C(19)	1.510(14)
C(18)-H(18A)	0.9700
C(18)-H(18B)	0.9700
C(19)-C(20)	1.700(14)
C(19)-H(19A)	0.9700
C(19)-H(19B)	0.9700
C(20)-H(20A)	0.9600
C(20)-H(20B)	0.9600
C(20)-H(20C)	0.9600
C(15')-C(16')	1.531(17)
C(15')-H(15C)	0.9700
C(15')-H(15D)	0.9700
C(16')-C(17')	1.473(15)
C(16')-H(16C)	0.9700
C(16')-H(16D)	0.9700
C(17')-C(18')	1.594(15)
C(17')-H(17C)	0.9700
C(17')-H(17D)	0.9700
C(18')-C(19')	1.466(15)
C(18')-H(18C)	0.9700
C(18')-H(18D)	0.9700
C(19')-C(20')	1.551(15)
C(19')-H(19C)	0.9700
C(19')-H(19D)	0.9700
C(20')-H(20D)	0.9600
C(20')-H(20E)	0.9600
C(20')-H(20F)	0.9600

C(2)-C(1)-C(6)	117.7(2)
C(2)-C(1)-C(10)	122.9(2)
C(6)-C(1)-C(10)	119.4(2)
C(9)-C(10)-C(1)	117.8(2)

C(9)-C(10)-C(14)	122.0(2)
C(1)-C(10)-C(14)	120.2(2)
C(7)-C(6)-C(5)	121.0(3)
C(7)-C(6)-C(1)	119.8(2)
C(5)-C(6)-C(1)	119.2(2)
C(10)-C(9)-C(8)	121.6(2)
C(10)-C(9)-C(11)	121.2(2)
C(8)-C(9)-C(11)	117.2(2)
C(3)-C(2)-C(1)	121.1(3)
C(3)-C(2)-H(2)	119.5
C(1)-C(2)-H(2)	119.5
C(7)-C(8)-C(9)	120.9(2)
C(7)-C(8)-H(8)	119.6
C(9)-C(8)-H(8)	119.6
C(4)-C(5)-C(6)	121.3(3)
C(4)-C(5)-H(5)	119.4
C(6)-C(5)-H(5)	119.4
C(8)-C(7)-C(6)	120.4(3)
C(8)-C(7)-H(7)	119.8
C(6)-C(7)-H(7)	119.8
C(12)-C(13)-C(14)	113.1(2)
C(12)-C(13)-H(13A)	108.9
C(14)-C(13)-H(13A)	108.9
C(12)-C(13)-H(13B)	108.9
C(14)-C(13)-H(13B)	108.9
H(13A)-C(13)-H(13B)	107.8
C(15)-C(14)-C(10)	112.8(4)
C(15)-C(14)-C(13)	113.2(4)
C(10)-C(14)-C(13)	111.3(2)
C(10)-C(14)-C(15')	109.1(9)
C(13)-C(14)-C(15')	113.3(11)
C(15)-C(14)-H(14)	106.3
C(10)-C(14)-H(14)	106.3
C(13)-C(14)-H(14)	106.3
O(1)-C(11)-C(9)	123.0(3)
O(1)-C(11)-C(12)	119.1(2)
C(9)-C(11)-C(12)	117.9(2)
F(2)-C(12)-F(1)	104.5(2)

F(2)-C(12)-C(13)	112.4(3)
F(1)-C(12)-C(13)	110.0(3)
F(2)-C(12)-C(11)	106.5(3)
F(1)-C(12)-C(11)	107.9(3)
C(13)-C(12)-C(11)	114.9(2)
C(5)-C(4)-C(3)	120.1(3)
C(5)-C(4)-H(4)	120.0
C(3)-C(4)-H(4)	120.0
C(2)-C(3)-C(4)	120.7(3)
C(2)-C(3)-H(3)	119.7
C(4)-C(3)-H(3)	119.7
C(14)-C(15)-C(16)	109.0(6)
C(14)-C(15)-H(15A)	109.9
C(16)-C(15)-H(15A)	109.9
C(14)-C(15)-H(15B)	109.9
C(16)-C(15)-H(15B)	109.9
H(15A)-C(15)-H(15B)	108.3
C(17)-C(16)-C(15)	107.8(7)
C(17)-C(16)-H(16A)	110.1
C(15)-C(16)-H(16A)	110.1
C(17)-C(16)-H(16B)	110.1
C(15)-C(16)-H(16B)	110.1
H(16A)-C(16)-H(16B)	108.5
C(16)-C(17)-C(18)	117.0(8)
C(16)-C(17)-H(17A)	108.0
C(18)-C(17)-H(17A)	108.0
C(16)-C(17)-H(17B)	108.0
C(18)-C(17)-H(17B)	108.0
H(17A)-C(17)-H(17B)	107.3
C(19)-C(18)-C(17)	98.6(9)
C(19)-C(18)-H(18A)	112.1
C(17)-C(18)-H(18A)	112.1
C(19)-C(18)-H(18B)	112.1
C(17)-C(18)-H(18B)	112.1
H(18A)-C(18)-H(18B)	109.7
C(18)-C(19)-C(20)	90.2(9)
C(18)-C(19)-H(19A)	113.6
C(20)-C(19)-H(19A)	113.6

C(18)-C(19)-H(19B)	113.6
C(20)-C(19)-H(19B)	113.6
H(19A)-C(19)-H(19B)	110.9
C(19)-C(20)-H(20A)	109.5
C(19)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(19)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(16')-C(15')-C(14)	124.4(18)
C(16')-C(15')-H(15C)	106.2
C(14)-C(15')-H(15C)	106.2
C(16')-C(15')-H(15D)	106.2
C(14)-C(15')-H(15D)	106.2
H(15C)-C(15')-H(15D)	106.4
C(17')-C(16')-C(15')	110.0(19)
C(17')-C(16')-H(16C)	109.7
C(15')-C(16')-H(16C)	109.7
C(17')-C(16')-H(16D)	109.7
C(15')-C(16')-H(16D)	109.7
H(16C)-C(16')-H(16D)	108.2
C(16')-C(17')-C(18')	114.5(14)
C(16')-C(17')-H(17C)	108.6
C(18')-C(17')-H(17C)	108.6
C(16')-C(17')-H(17D)	108.6
C(18')-C(17')-H(17D)	108.6
H(17C)-C(17')-H(17D)	107.6
C(19')-C(18')-C(17')	130.8(19)
C(19')-C(18')-H(18C)	104.6
C(17')-C(18')-H(18C)	104.6
C(19')-C(18')-H(18D)	104.6
C(17')-C(18')-H(18D)	104.6
H(18C)-C(18')-H(18D)	105.7
C(18')-C(19')-C(20')	100.6(13)
C(18')-C(19')-H(19C)	111.7
C(20')-C(19')-H(19C)	111.7
C(18')-C(19')-H(19D)	111.7
C(20')-C(19')-H(19D)	111.7

H(19C)-C(19')-H(19D)	109.4
C(19')-C(20')-H(20D)	109.5
C(19')-C(20')-H(20E)	109.5
H(20D)-C(20')-H(20E)	109.5
C(19')-C(20')-H(20F)	109.5
H(20D)-C(20')-H(20F)	109.5
H(20E)-C(20')-H(20F)	109.5

Table 4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for 3a.

The anisotropic displacement factor exponent takes the form: $-2\pi^2[\,h^2 a^{*2}U^{11} + \dots + 2hk\,a^{*}b^{*}U^{12}\,]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
F(2)	114(2)	162(2)	124(2)	20(1)	5(1)	52(1)
F(1)	63(1)	231(3)	114(2)	-10(1)	1(1)	-42(1)
O(1)	78(1)	200(3)	74(1)	-19(1)	-11(1)	-2(1)
C(1)	52(1)	96(2)	57(1)	2(1)	7(1)	-6(1)
C(10)	52(1)	89(2)	57(1)	4(1)	8(1)	-2(1)
C(6)	55(1)	98(2)	66(2)	8(1)	12(1)	-4(1)
C(9)	58(1)	93(2)	56(1)	2(1)	5(1)	-2(1)
C(2)	62(2)	144(3)	63(2)	-10(2)	6(1)	-7(2)
C(8)	74(2)	116(2)	60(2)	-9(1)	10(1)	-1(2)
C(5)	50(1)	138(3)	84(2)	11(2)	15(1)	0(1)
C(7)	67(2)	114(2)	73(2)	-5(2)	21(1)	6(1)
C(13)	56(2)	142(3)	83(2)	1(2)	17(1)	-4(2)
C(14)	58(2)	125(2)	64(2)	-8(2)	11(1)	-2(1)
C(11)	66(2)	112(2)	61(2)	3(1)	-3(1)	-6(1)
C(12)	53(2)	126(3)	86(2)	7(2)	0(1)	-5(2)
C(4)	50(2)	170(3)	90(2)	15(2)	0(2)	-11(2)
C(3)	67(2)	178(3)	68(2)	-9(2)	-3(1)	-16(2)
C(15)	66(3)	112(4)	127(4)	-46(3)	33(3)	-5(3)
C(16)	111(3)	131(4)	141(4)	-47(3)	39(3)	4(3)
C(17)	154(4)	151(4)	166(4)	-57(4)	37(3)	13(3)
C(18)	184(5)	164(5)	184(5)	-54(5)	27(4)	21(4)
C(19)	206(6)	180(6)	192(6)	-47(5)	28(5)	22(5)
C(20)	229(8)	197(8)	179(7)	-54(6)	65(7)	40(7)
C(15')	235(10)	186(8)	168(8)	-67(7)	16(7)	64(8)
C(16')	244(10)	192(8)	172(7)	-66(7)	16(7)	61(7)
C(17')	256(9)	197(7)	171(7)	-60(6)	14(6)	58(7)
C(18')	272(9)	202(7)	178(7)	-56(6)	7(6)	54(7)
C(19')	280(10)	209(7)	189(7)	-47(6)	5(7)	52(7)
C(20')	295(12)	206(9)	204(9)	-45(8)	-4(9)	33(9)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 3a.

	x	y	z	U(eq)
H(2)	40736369	8850109		
H(8)	51857134	16666101		
H(5)	10287038	12263109		
H(7)	29117166	15185100		
H(13A)	85556508	11579112		
H(13B)	78787049	11761112		
H(14)	61556573	1001099		
H(4)	2596767	9124127		
H(3)	17816432	7406129		
H(15A)	55555733	11058120		
H(15B)	70235727	12490120		
H(16A)	65595817	8286151		
H(16B)	80385850	9683151		
H(17A)	63074968	9095188		
H(17B)	75654996	10897188		
H(18A)	89485070	8161216		
H(18B)	85274510	8758216		
H(19A)	68595140	5714235		
H(19B)	63304602	6406235		
H(20A)	91964589	5960298		
H(20B)	81054555	3954298		
H(20C)	81894114	5524298		
H(15C)	66175753	12798242		
H(15D)	55325741	10809242		
H(16C)	82455692	10509250		
H(16D)	76755199	11375250		
H(17C)	63075643	7823257		
H(17D)	59675106	8644257		
H(18C)	74425216	6071270		

H(18D)	85965178	7968270
H(19C)	76374286	7992281
H(19D)	87764429	6844281
H(20D)	60344677	4942368
H(20E)	64354089	4886368
H(20F)	72094509	3930368

_

Table 6. Torsion angles [°] for 3a.

C(2)-C(1)-C(10)-C(9)	179.5(3)
C(6)-C(1)-C(10)-C(9)	0.9(4)
C(2)-C(1)-C(10)-C(14)	-0.5(4)
C(6)-C(1)-C(10)-C(14)	-179.0(3)
C(2)-C(1)-C(6)-C(7)	-179.8(3)
C(10)-C(1)-C(6)-C(7)	-1.2(4)
C(2)-C(1)-C(6)-C(5)	-1.0(4)
C(10)-C(1)-C(6)-C(5)	177.6(3)
C(1)-C(10)-C(9)-C(8)	-0.3(4)
C(14)-C(10)-C(9)-C(8)	179.7(3)
C(1)-C(10)-C(9)-C(11)	-179.8(2)
C(14)-C(10)-C(9)-C(11)	0.2(4)
C(6)-C(1)-C(2)-C(3)	0.7(5)
C(10)-C(1)-C(2)-C(3)	-177.9(3)
C(10)-C(9)-C(8)-C(7)	-0.1(4)
C(11)-C(9)-C(8)-C(7)	179.4(3)
C(7)-C(6)-C(5)-C(4)	179.6(3)
C(1)-C(6)-C(5)-C(4)	0.9(5)
C(9)-C(8)-C(7)-C(6)	-0.1(5)
C(5)-C(6)-C(7)-C(8)	-177.9(3)
C(1)-C(6)-C(7)-C(8)	0.8(4)
C(9)-C(10)-C(14)-C(15)	102.0(6)
C(1)-C(10)-C(14)-C(15)	-78.0(6)
C(9)-C(10)-C(14)-C(13)	-26.5(4)
C(1)-C(10)-C(14)-C(13)	153.5(3)
C(9)-C(10)-C(14)-C(15')	99.3(13)
C(1)-C(10)-C(14)-C(15')	-80.7(13)
C(12)-C(13)-C(14)-C(15)	-79.0(6)

C(12)-C(13)-C(14)-C(10)	49.4(4)
C(12)-C(13)-C(14)-C(15')	-74.1(12)
C(10)-C(9)-C(11)-O(1)	-175.5(3)
C(8)-C(9)-C(11)-O(1)	4.9(4)
C(10)-C(9)-C(11)-C(12)	3.9(4)
C(8)-C(9)-C(11)-C(12)	-175.6(3)
C(14)-C(13)-C(12)-F(2)	75.2(3)
C(14)-C(13)-C(12)-F(1)	-168.8(3)
C(14)-C(13)-C(12)-C(11)	-46.8(4)
O(1)-C(11)-C(12)-F(2)	74.4(4)
C(9)-C(11)-C(12)-F(2)	-105.1(3)
O(1)-C(11)-C(12)-F(1)	-37.2(4)
C(9)-C(11)-C(12)-F(1)	143.3(3)
O(1)-C(11)-C(12)-C(13)	-160.4(3)
C(9)-C(11)-C(12)-C(13)	20.1(4)
C(6)-C(5)-C(4)-C(3)	-0.3(5)
C(1)-C(2)-C(3)-C(4)	-0.1(6)
C(5)-C(4)-C(3)-C(2)	-0.1(6)
C(10)-C(14)-C(15)-C(16)	159.5(5)
C(13)-C(14)-C(15)-C(16)	-73.0(8)
C(15')-C(14)-C(15)-C(16)	-165(18)
C(14)-C(15)-C(16)-C(17)	176.1(8)
C(15)-C(16)-C(17)-C(18)	-165.4(8)
C(16)-C(17)-C(18)-C(19)	-87.6(14)
C(17)-C(18)-C(19)-C(20)	-174.6(10)
C(15)-C(14)-C(15')-C(16')	37(16)
C(10)-C(14)-C(15')-C(16')	-177(2)
C(13)-C(14)-C(15')-C(16')	-53(3)
C(14)-C(15')-C(16')-C(17')	-95(3)
C(15')-C(16')-C(17')-C(18')	170.3(16)
C(16')-C(17')-C(18')-C(19')	101(3)
C(17')-C(18')-C(19')-C(20')	92(2)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for 3a [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)

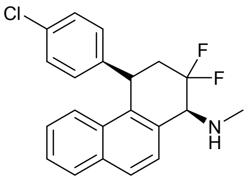
C(13)-H(13B)...O(1)#1	0.97	2.61	3.520(5)	156.3
C(13)-H(13B)...O(1)#1	0.97	2.61	3.520(5)	156.3

Symmetry transformations used to generate equivalent atoms:
#1 x,-y+3/2,z-1/2

6. The transformation reactions of *gem*-difluorodihydrophenanthrenones.

6.1 The procedure for preparation of **9** 4-(4-chlorophenyl)-2,2-difluoro-N-methyl-1,2,3,4-tetrahydrophenanthren-1-amine.

To a solution of 4-(4-chlorophenyl)-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one **3h** (1 mmol, 1.0 equiv.) in MeOH (5mL) was added CH_3NH_2 (25% in EtOH, 10 mmol, 10.0 equiv.), $Na(CN)BH_3$ (1.25 mmol, 1.25 equiv.), $ZnCl_2$ (1 mmol, 1.0 equiv.) . The mixture was stirred at rt under N2 protection overnight. The solvent was evaporated in vacuo, and extracted with DCM (3 x 20mL), the combined organic layers were dried over anhydrous sodium sulfate and the solvent was evaporated in vacuo to give the crude product, which was purified carefully by column chromatography, eluting Petroleum ether/Ethyl acetate (100:1, 80:1) to afford the product **9** as yellow oil(125.3 mg, 35% yield).

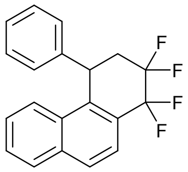


9

δH (500 MHz, $CDCl_3$, Me_4Si) 7.81(2H, t, J = 10.0 Hz), 7.56(2H, dd, J = 20.0, 5.0 Hz), 7.39 (1H, t, J = 10.0 Hz), 7.27(1H, d, J = 5.0 Hz), 7.18(2H, t, J = 5.0 Hz), 6.97(2H, d, J = 5.0 Hz), 4.91(1H, t, J = 9.0 Hz), 4.02(1H, t, J = 9.0 Hz), 2.71(5H, m).
δF (470 MHz, $CDCl_3$) -98.7(1F, m), -107.2(1F, m).
δC (125 MHz, $CDCl_3$) 144.7, 133.7, 132.0, 131.3, 128.9(d, J = 12.5 Hz), 128.6(d, J = 12.5 Hz), 127.5, 126.3, 125.8, 125.5, 63.3(dd, J = 27.5, 22.5 Hz), 41.1(t, J = 5.0 Hz), 37.6(t, J = 21.3 Hz), 36.2, 1.0.
HRMS (EI-TOF) calculated $[M]^+$ for $C_{21}H_{18}F_2NCl$ 358.1168, found 358.1168.

6.2 The procedure for preparation of **10** 1,1,2,2-tetrafluoro-4-phenyl-1,2,3,4-tetrahydrophenanthrene

To a solution of 4-(4-chlorophenyl)-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one **3h** (1 mmol, 1.0 equiv.) in DCM (5mL) was added DAST (15 mmol, 15.0 equiv.). The mixture was stirred at 30°C under N_2 protection overnight. The solvent was added to the 50mL sat. $NaHCO_3$(aq), then extracted with DCM (3 x 20mL), the combined organic layers were dried over anhydrous sodium sulfate and the solvent was evaporated in vacuo to give the crude product, which was purified carefully by column chromatography, eluting Petroleum ether/Ethyl acetate (100:1) to afford the product **10** as yellow oil(282.4 mg, 80% yield).



10

δH (500 MHz, CDCl$_3$, Me$_4$Si) 8.01(1H, d, *J* = 10.0 Hz), 7.91(2H, d, *J* = 10.0 Hz), 7.70 (1H, d, *J* = 10.0 Hz), 7.52(1H, t, *J* = 10.0 Hz), 7.36(1H, t, *J* = 10.0 Hz), 7.27(2H, t, *J* = 5.0 Hz), 7.23(1H, t, *J* = 10.0 Hz), 7.03(2H, d, *J* = 10.0 Hz), 5.15(1H, s), 3.08(1H, m), 2.74(1H, m).

δF NMR (470 MHz, CDCl$_3$) -105.4(1F, ddd, *J* = 23.5, 18.8, 9.4 Hz), -110.1(1F, d, *J* = 23.5, 18.8, 9.4 Hz), -118.0(1F, ddd, *J* = 23.5, 14.1, 4.7 Hz), -118.7(1F, ddd, *J* = 23.5, 14.1, 4.7 Hz).

δC NMR (125 MHz, CDCl$_3$) 144.8, 135.0, 134.0(t, *J* = 6.3 Hz), 130.6, 130.0, 128.9(d, *J* = 13.8 Hz), 127.7, 127.4, 126.9(d, *J* = 16.3 Hz), 126.1, 121.5(t, *J* = 3.8 Hz), 115.9(t, *J* = 26.3 Hz), 113.0(t, *J* = 27.5 Hz), 40.8(d, *J* = 3.8 Hz), 37.3(t, *J* = 20.0 Hz) ppm.

HRMS (EI-TOF) calculated [M]$^+$ for C$_{20}$H$_{14}$F$_4$ 353.0923, found 353.0929.

References

1 Y. Zhao and D. G. Truhlar, *Theor. Chem. Acc.* 2008, **120**, 215.

2 A. K. Rappé, C. J. Casewit, K. S. Colwell,W. A. Goddard III and W. M. Skiff, *J. Am. Chem. Soc*. 1992, **114**, 10024.

3 Y. Zhao and D. G. Truhlar, *Acc. Chem. Res.* 2008, **41**, 157.

4 Y. Zhao and D. G. Truhlar, *J. Chem. Phys.* 2006, **125**, 194101.

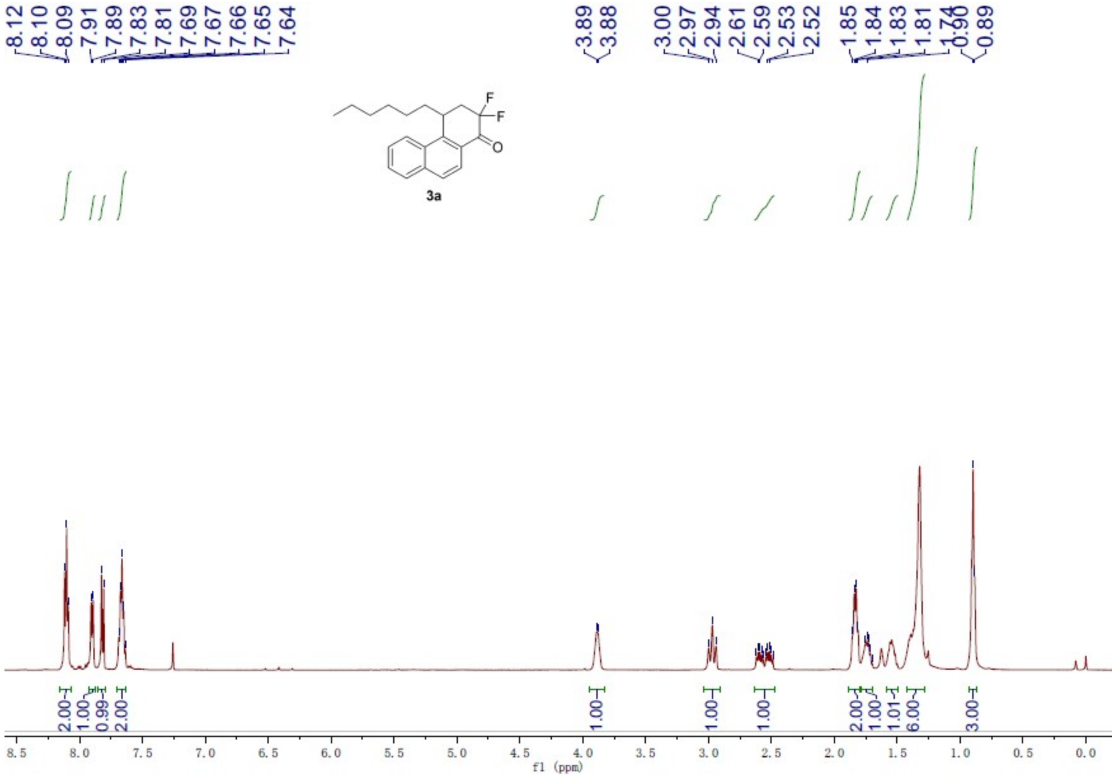
5 Y. Zhao and D. G. Truhlar, *J. Phys. Chem. A.* 2006, **110**, 13126.

6 Y. Zhao, N. E. Schultz and D. G. Truhlar, *J. Chem. Theory Comput.* 2006, **2**, 364.

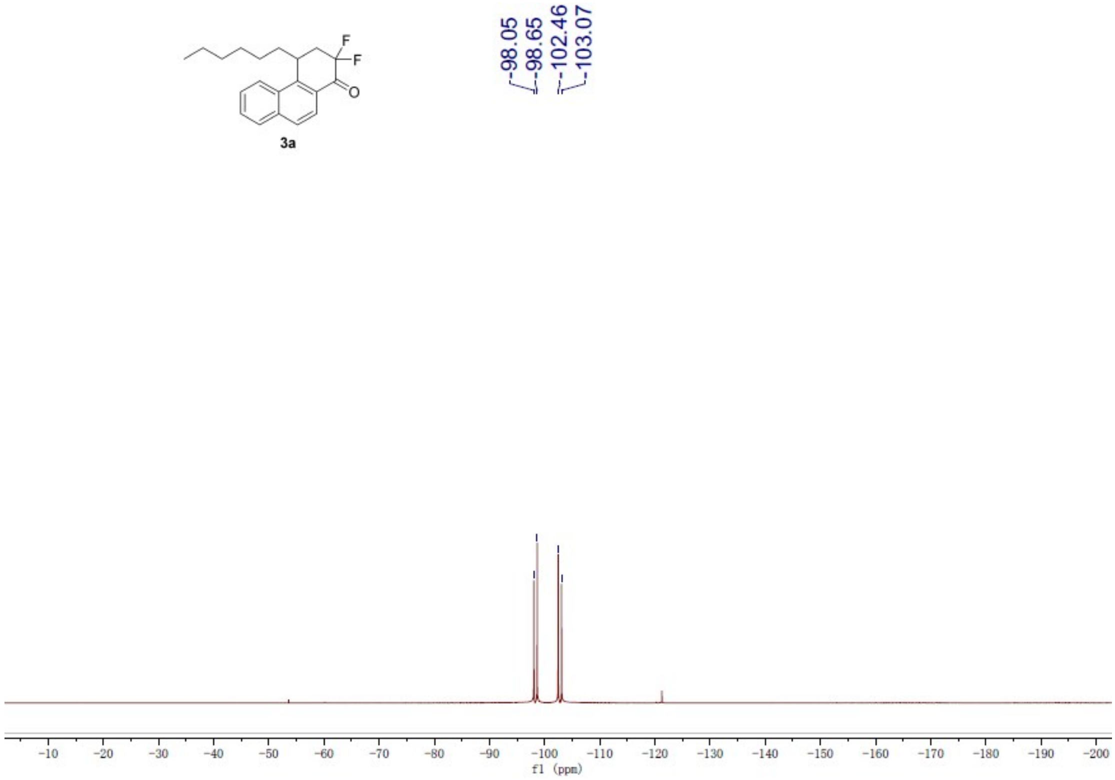
7 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci and G. A. Petersson, Gaussian 09, revision A.01; Gaussian, Inc.: Wallingford, CT, **2009**.

7. Spectral data

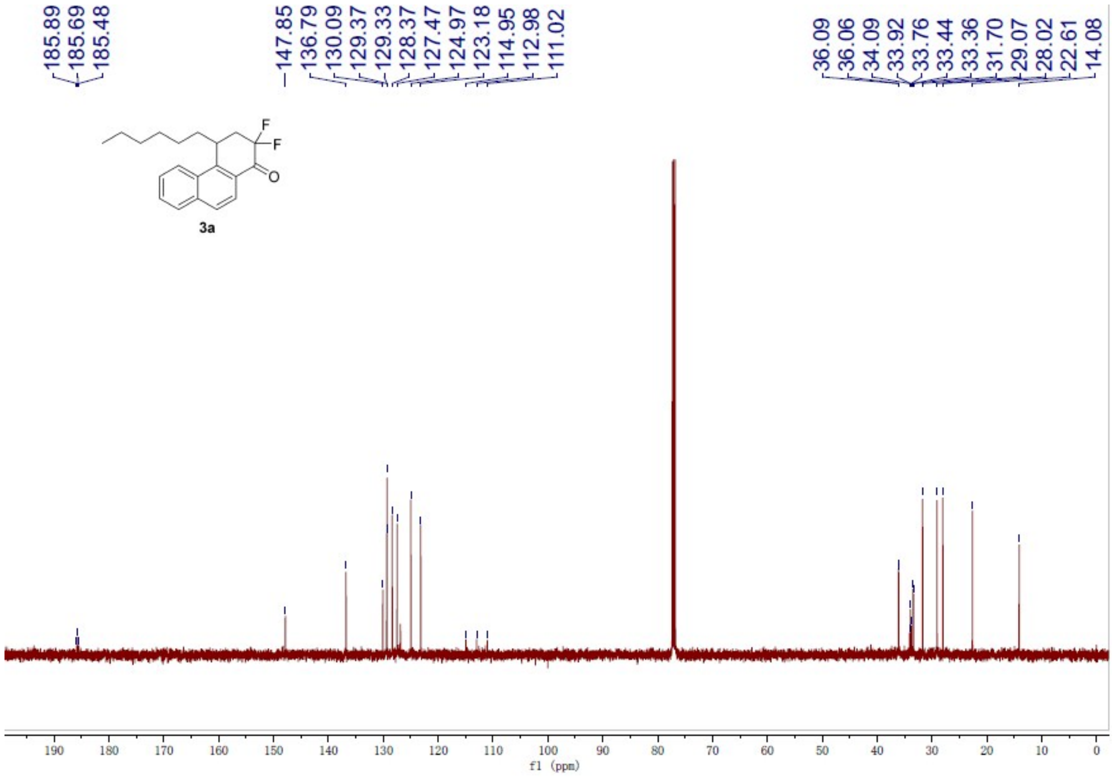
^{1}H NMR spectrum of 2,2-difluoro-4-hexyl-3,4-dihydrophenanthren-1(2H)-one(**3a**)



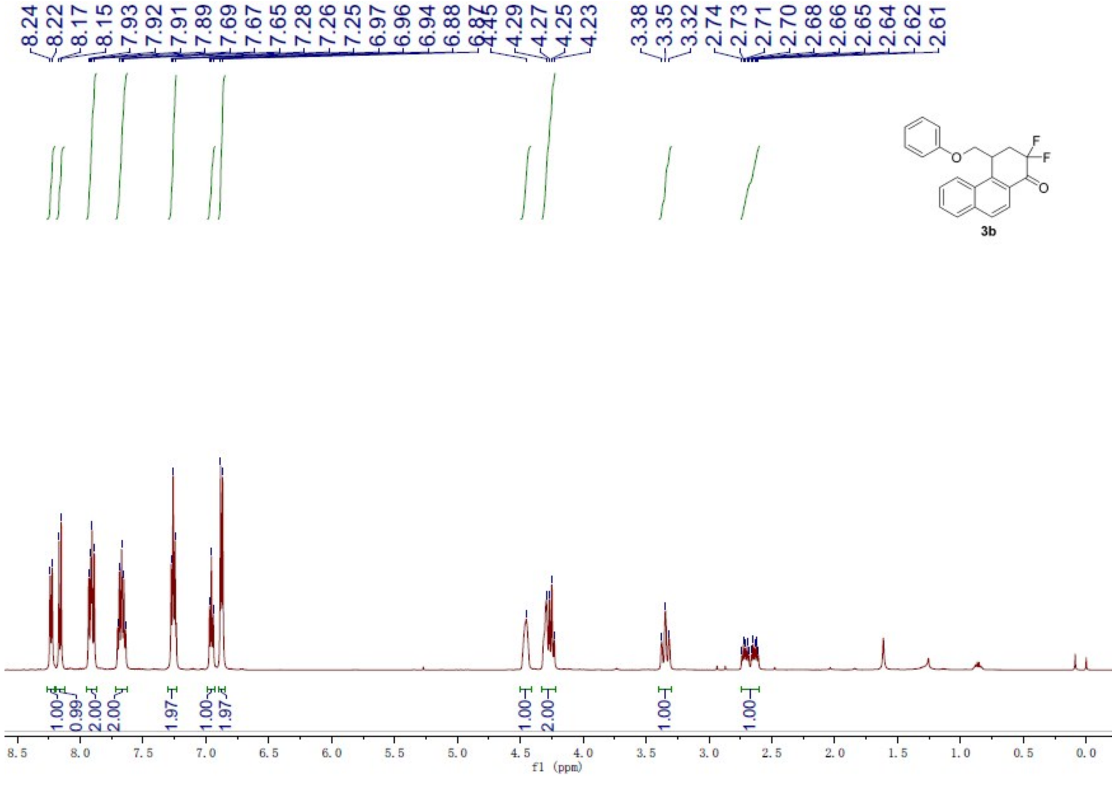
^{19}F NMR spectrum of 2,2-difluoro-4-hexyl-3,4-dihydrophenanthren-1(2H)-one(**3a**)



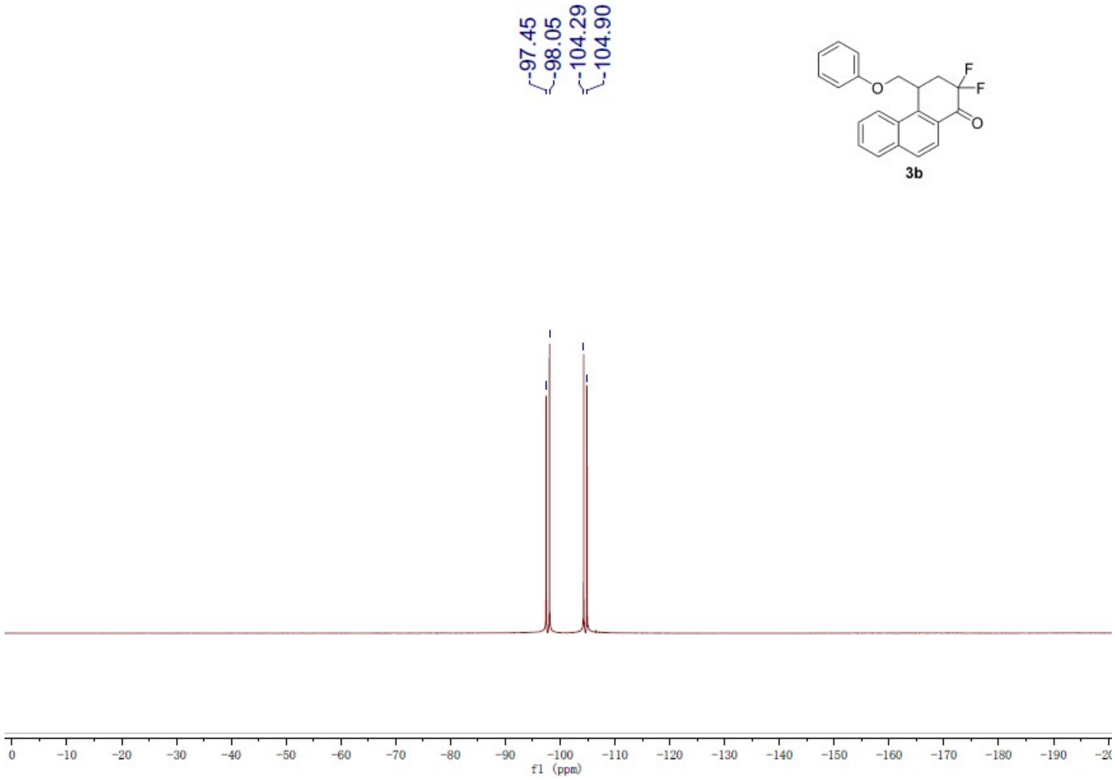
^{13}C NMR spectrum of 2,2-difluoro-4-hexyl-3,4-dihydrophenanthren-1(2H)-one(**3a**)



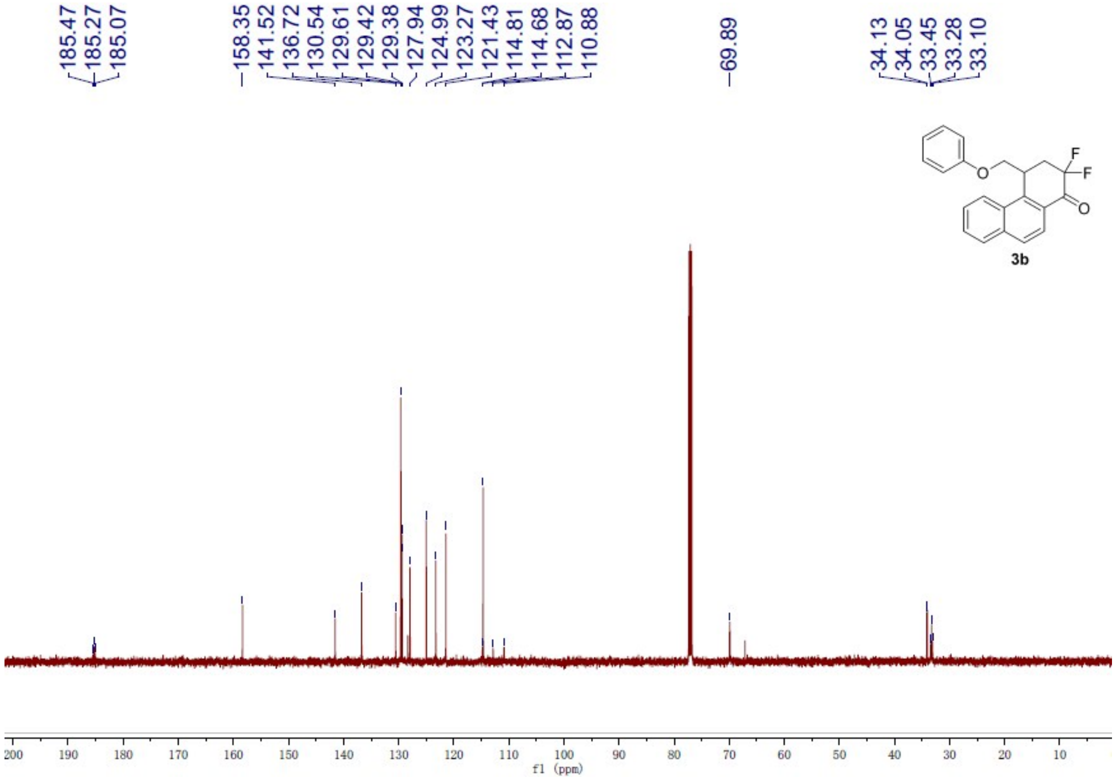
^{1}H NMR spectrum of 2,2-difluoro-4-(phenoxymethyl)-3,4-dihydrophenanthren-1(2H)-one(**3b**)



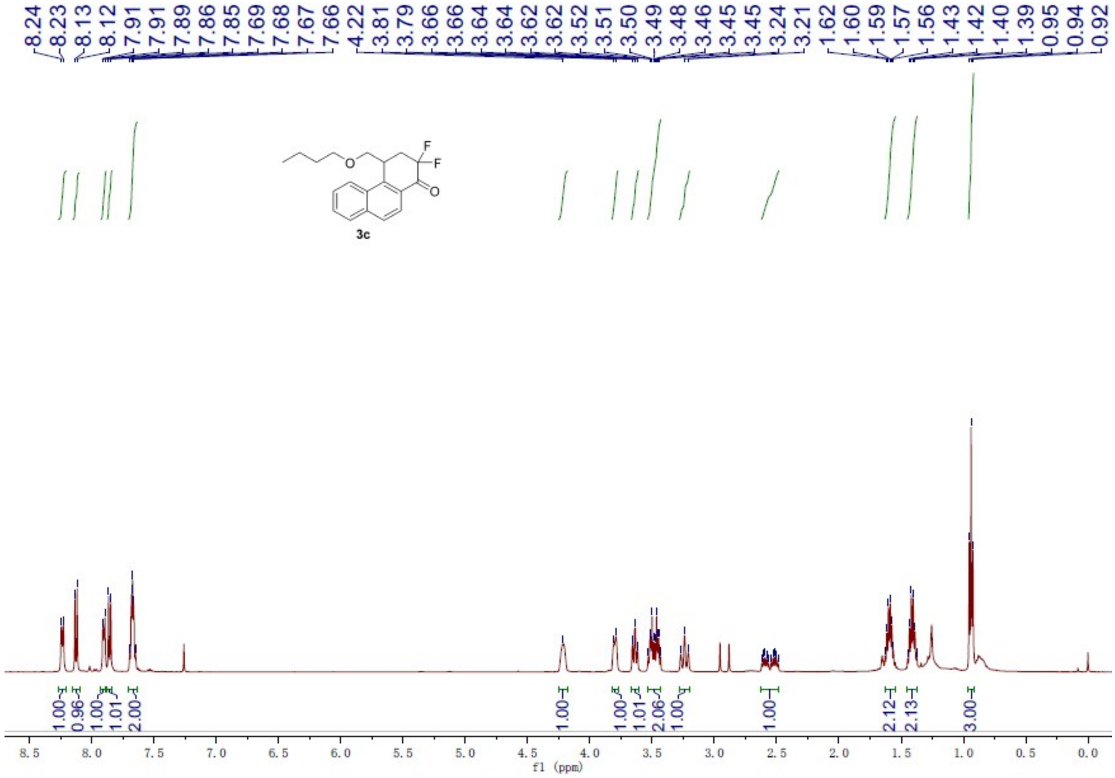
^{19}F NMR spectrum of 2,2-difluoro-4-(phenoxymethyl)-3,4-dihydrophenanthren-1(2H)-one(**3b**)



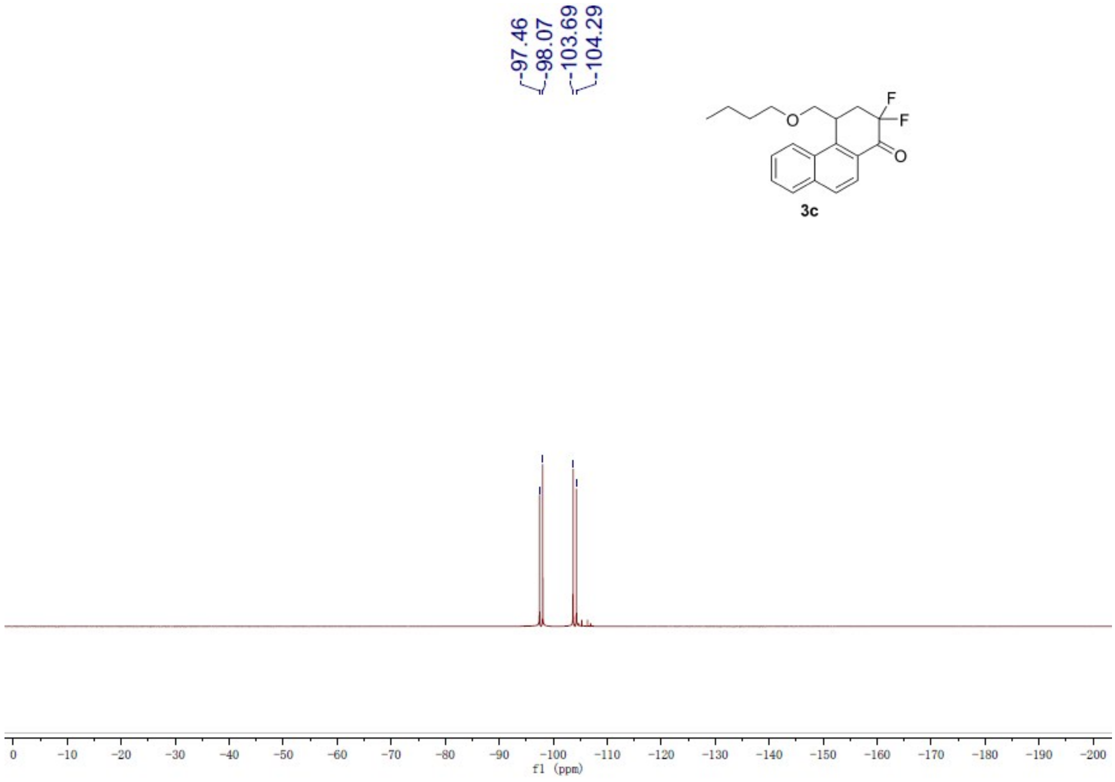
^{13}C NMR spectrum of 2,2-difluoro-4-(phenoxymethyl)-3,4-dihydrophenanthren-1(2H)-one(**3b**)



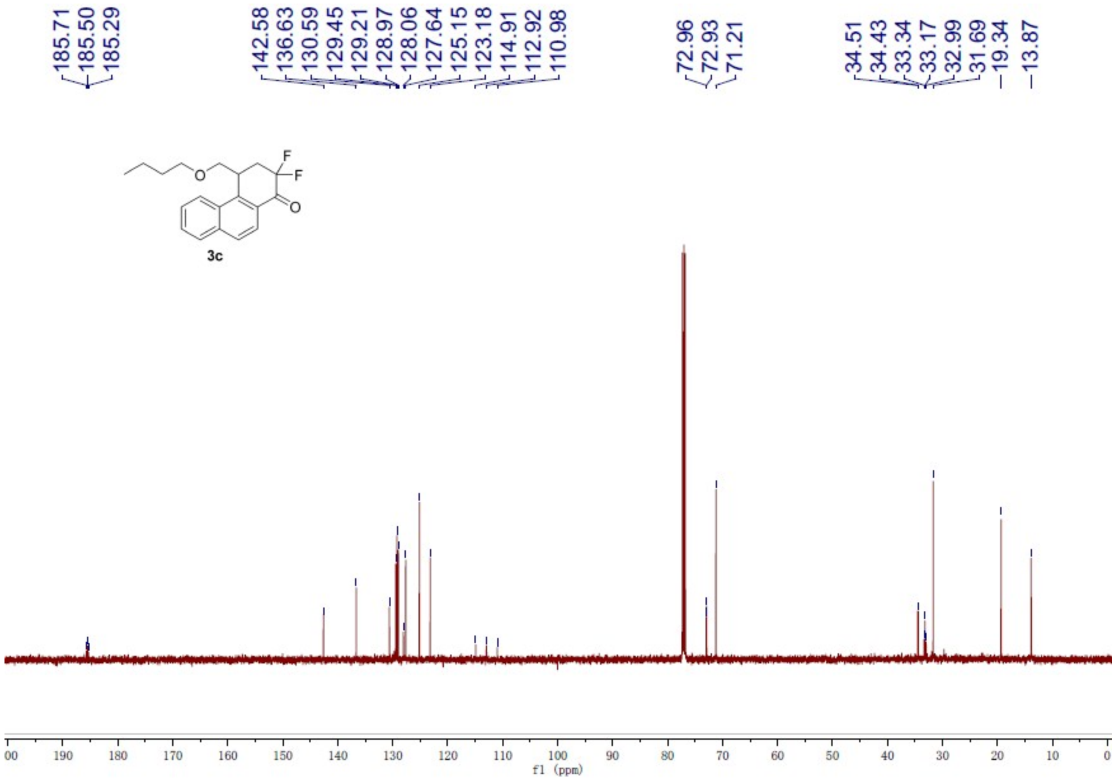
^{1}H NMR spectrum of 4-(butoxymethyl)-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3c**)



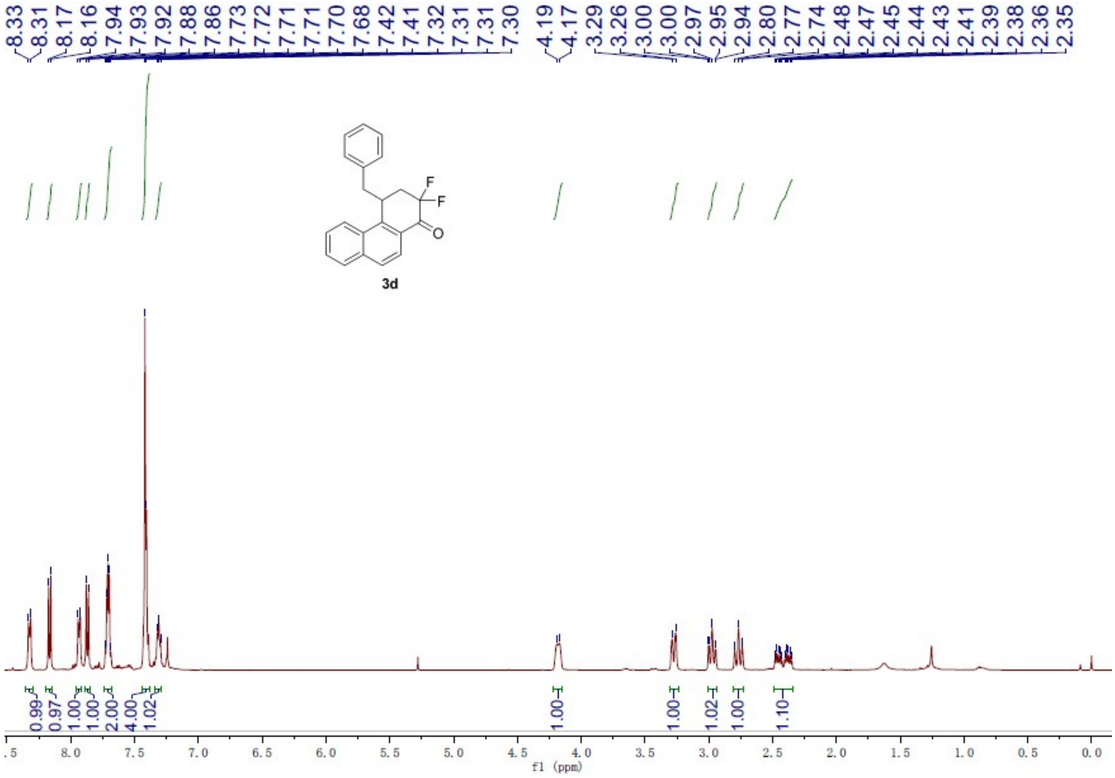
^{19}F NMR spectrum of 4-(butoxymethyl)-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3c**)



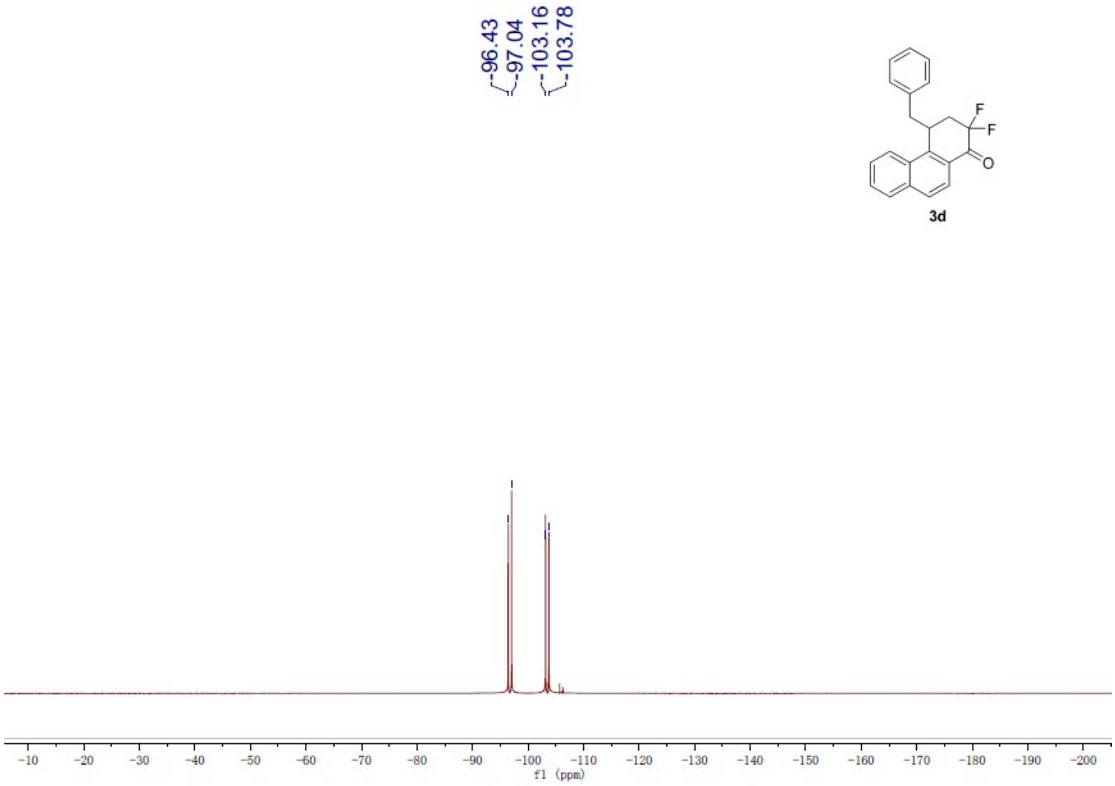
^{13}C NMR spectrum of 4-(butoxymethyl)-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3c**)



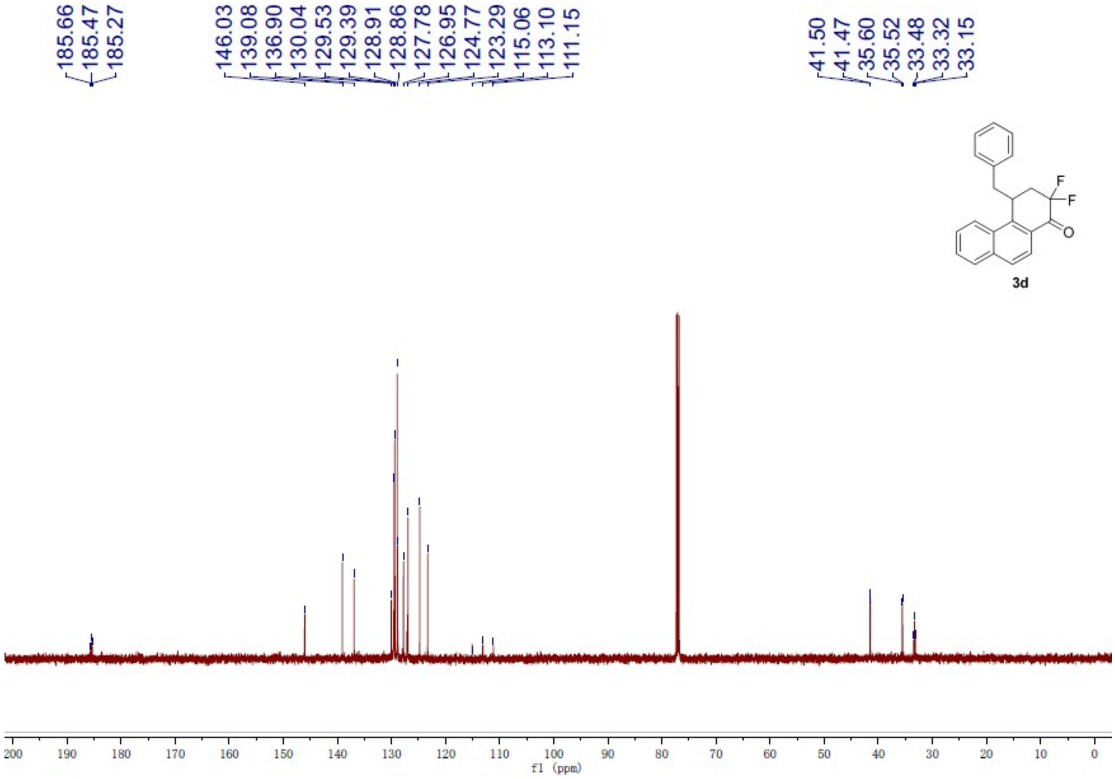
^{1}H NMR spectrum of 4-benzyl-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3d**)



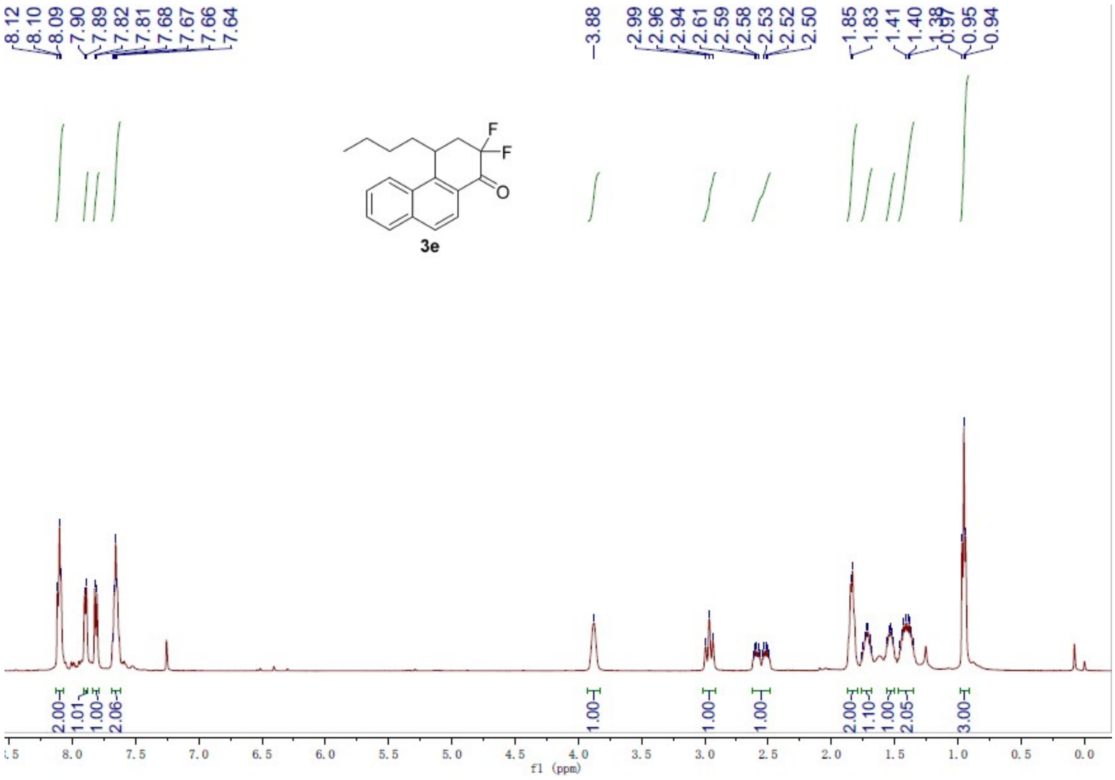
^{19}F NMR spectrum of 4-benzyl-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3d**)



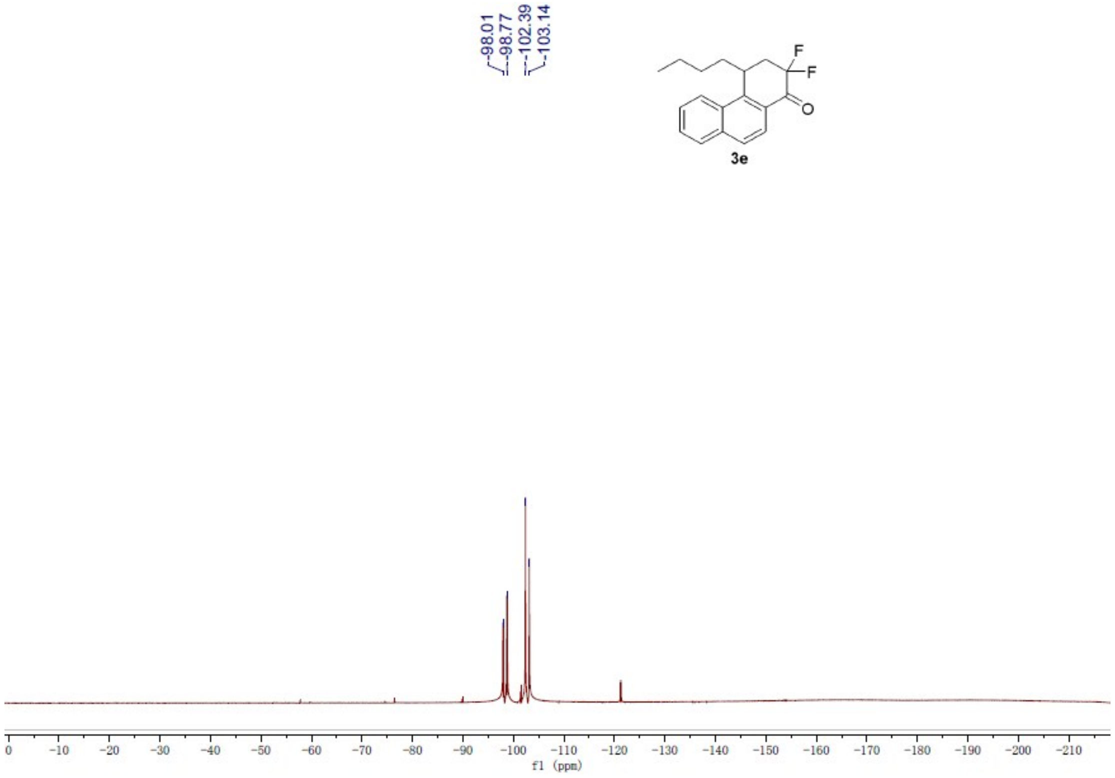
^{13}C NMR spectrum of 4-benzyl-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3d**)



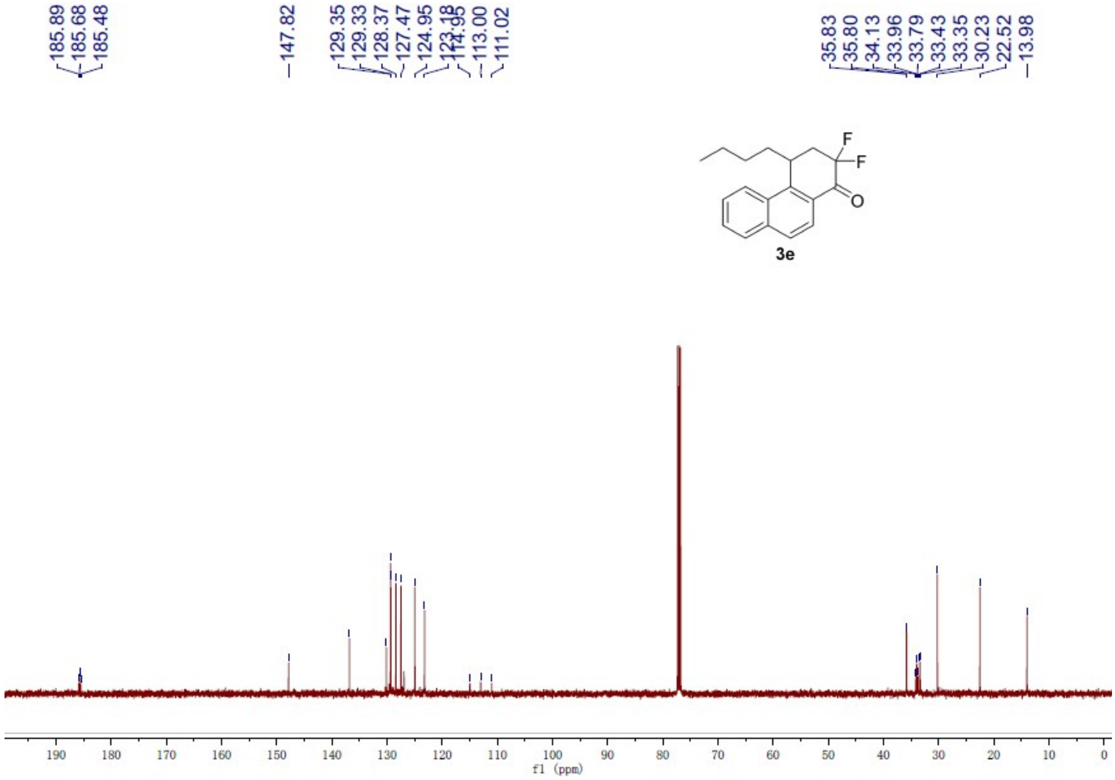
^{1}H NMR spectrum of 4-butyl-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3e**)



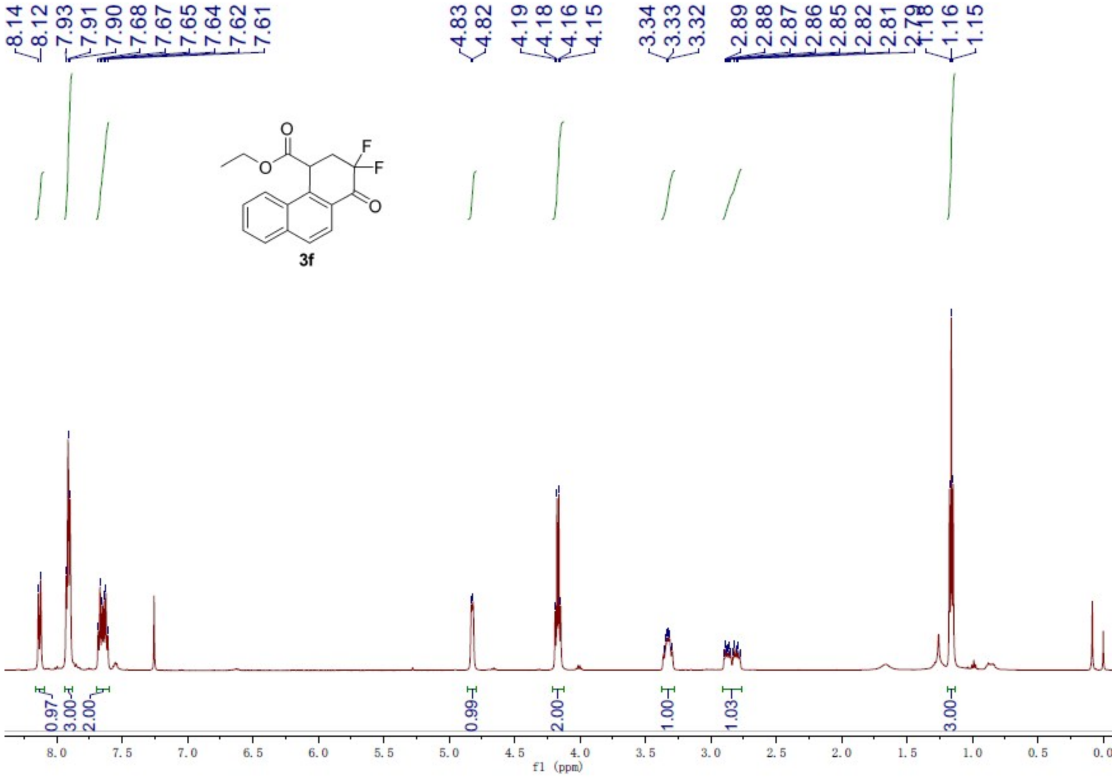
^{19}F NMR spectrum of 4-butyl-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one (**3e**)



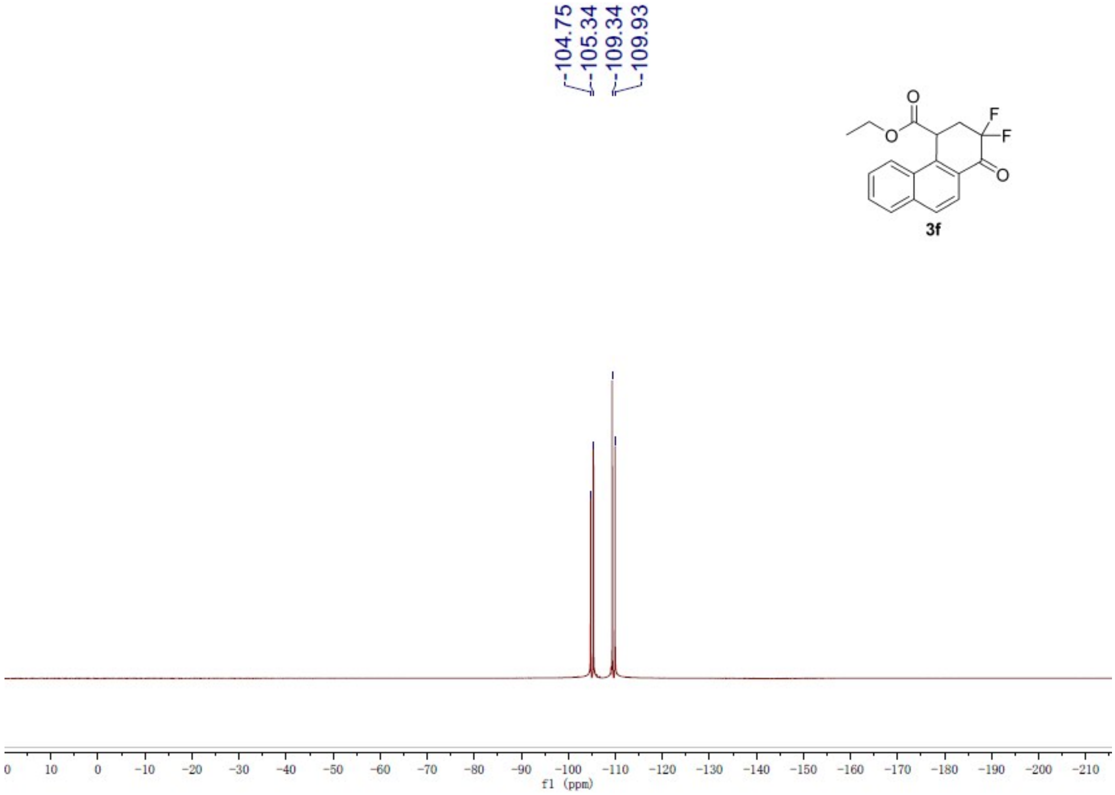
^{13}C NMR spectrum of 4-butyl-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3e**)



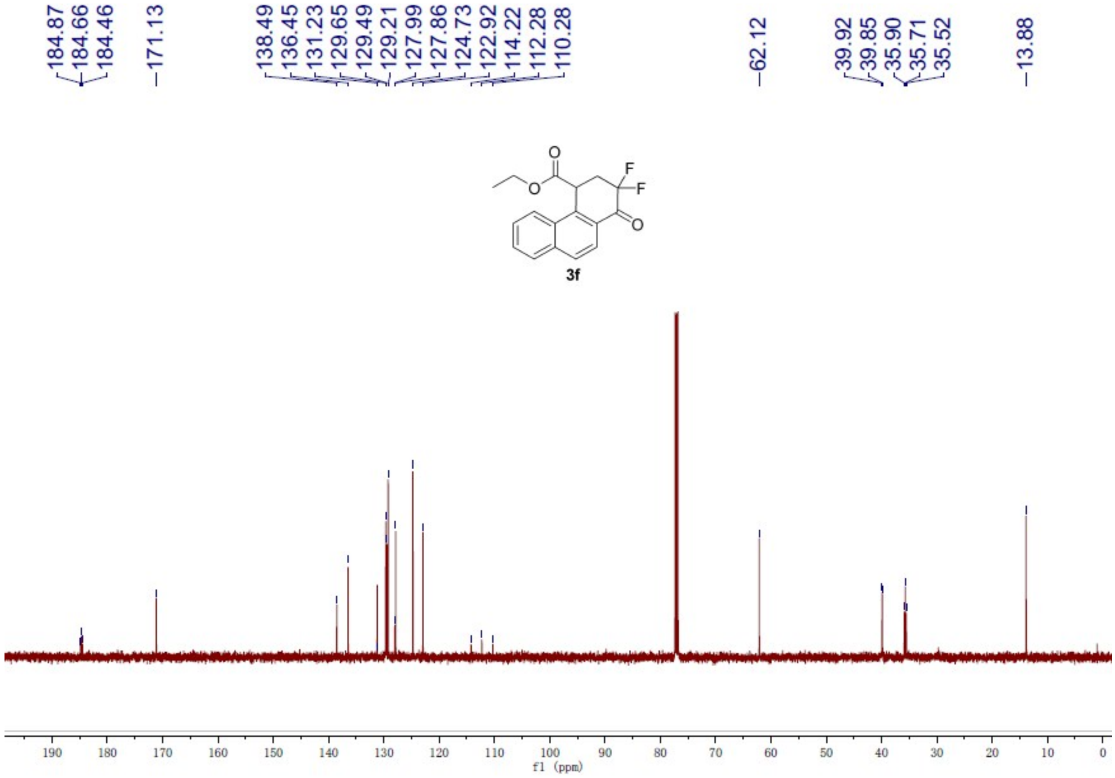
^{1}H NMR spectrum of Methyl-2,2-difluoro-1-oxo-1,2,3,4-tetrahydrophenanthrene-4-carboxylate(**3f**)



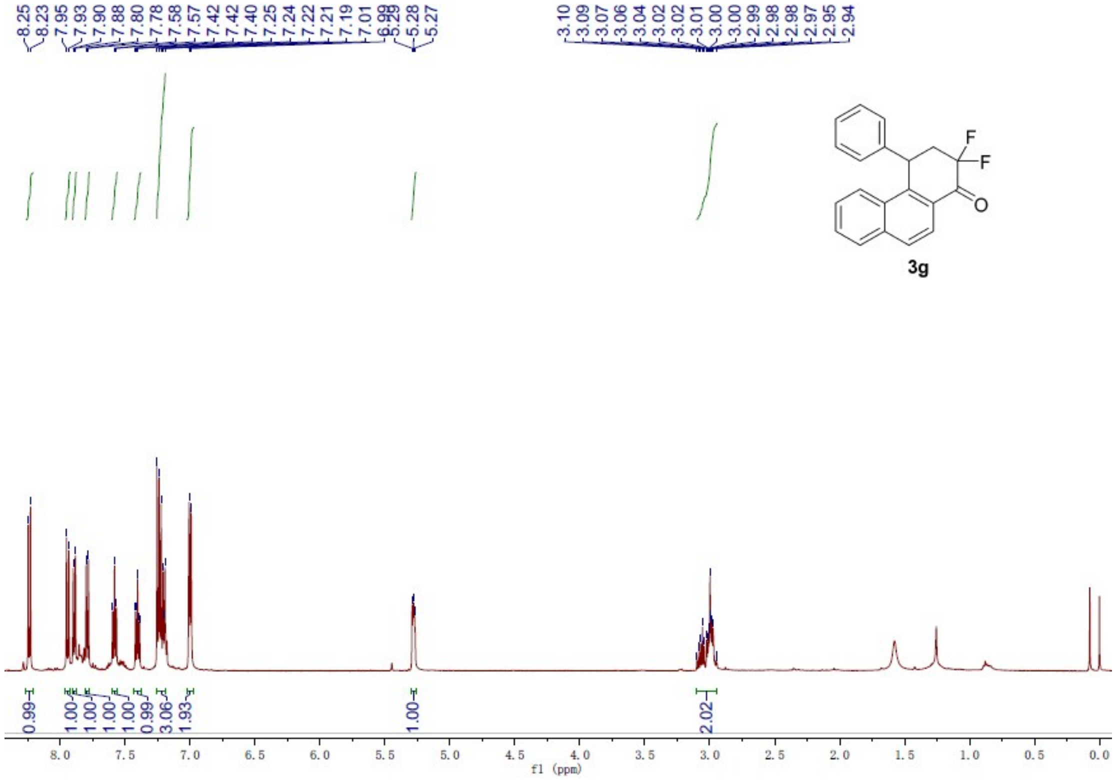
^{19}F NMR spectrum of Methyl-2,2-difluoro-1-oxo-1,2,3,4-tetrahydrophenanthrene-4-carboxylate(**3f**)



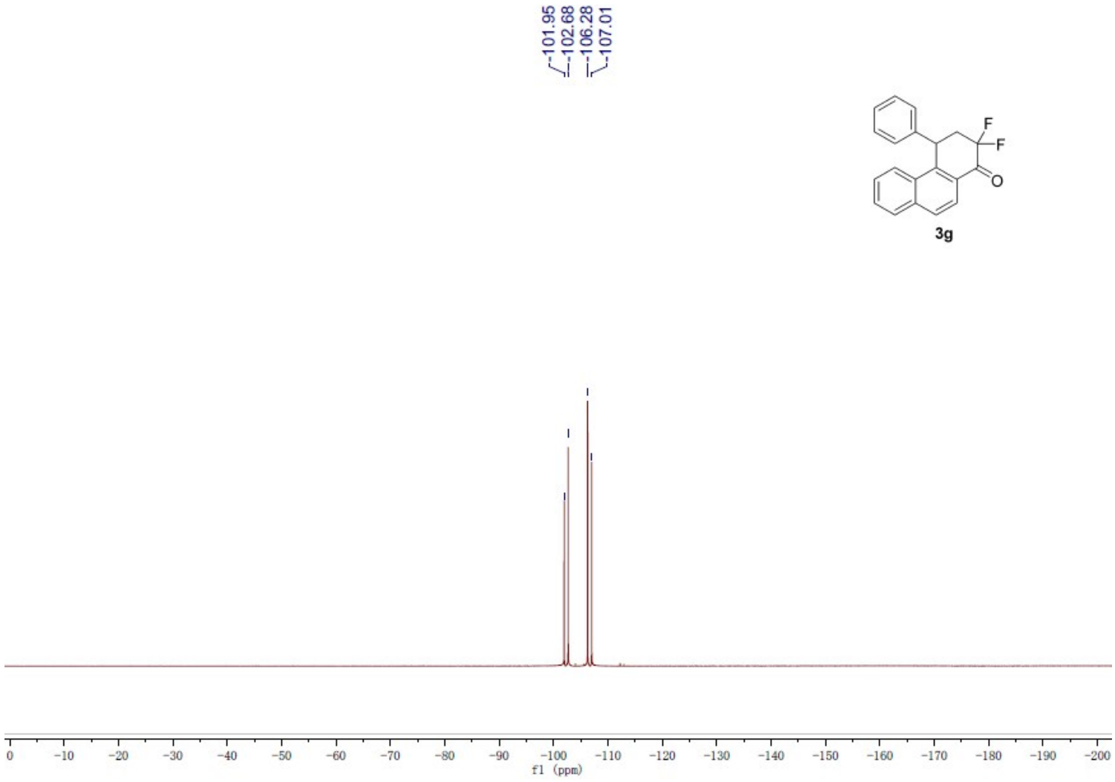
^{13}C NMR spectrum of Methyl-2,2-difluoro-1-oxo-1,2,3,4-tetrahydrophenanthrene-4-carboxylate(**3f**)



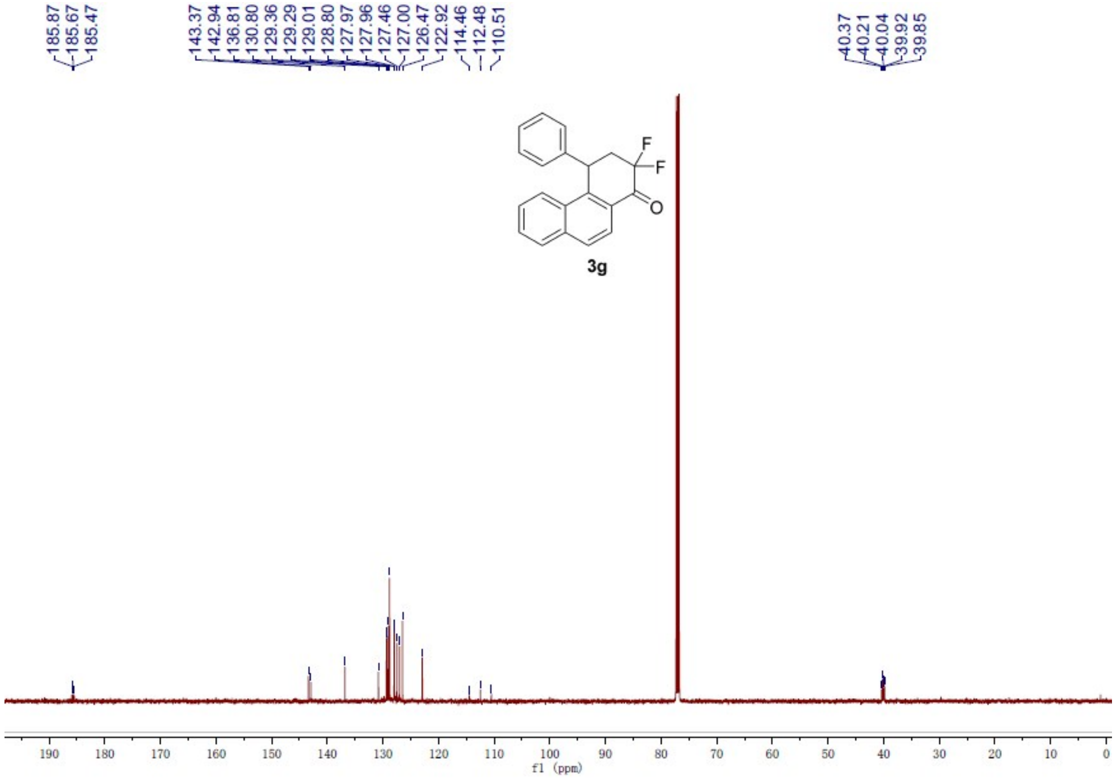
^{1}H NMR spectrum of 2,2-difluoro-4-phenyl-3,4-dihydrophenanthren-1(2H)-one(**3g**)



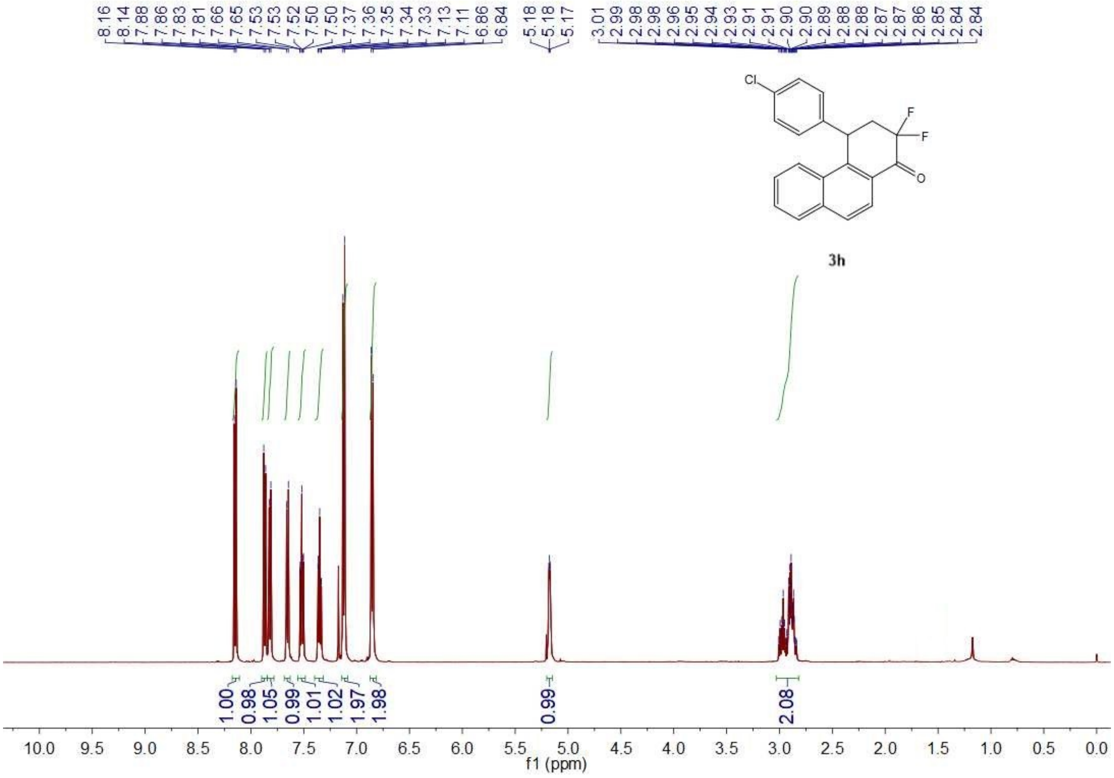
^{19}F NMR spectrum of 2,2-difluoro-4-phenyl-3,4-dihydrophenanthren-1(2H)-one(**3g**)



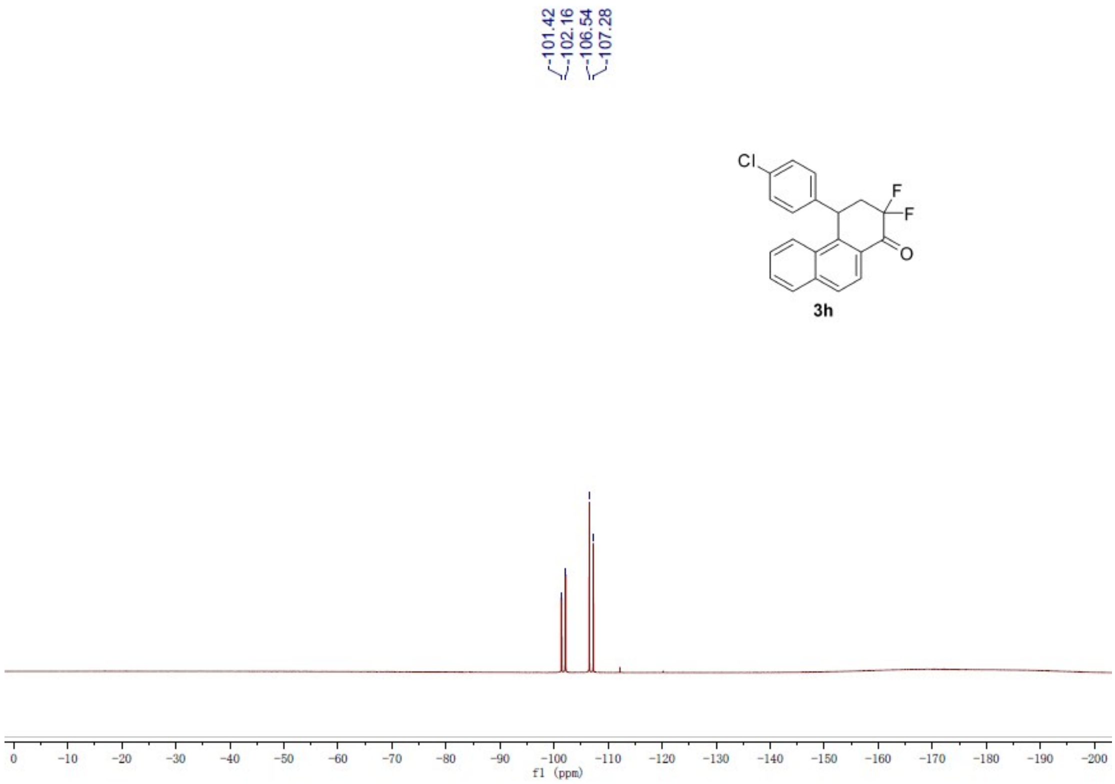
^{13}C NMR spectrum of 2,2-difluoro-4-phenyl-3,4-dihydrophenanthren-1(2H)-one(**3g**)



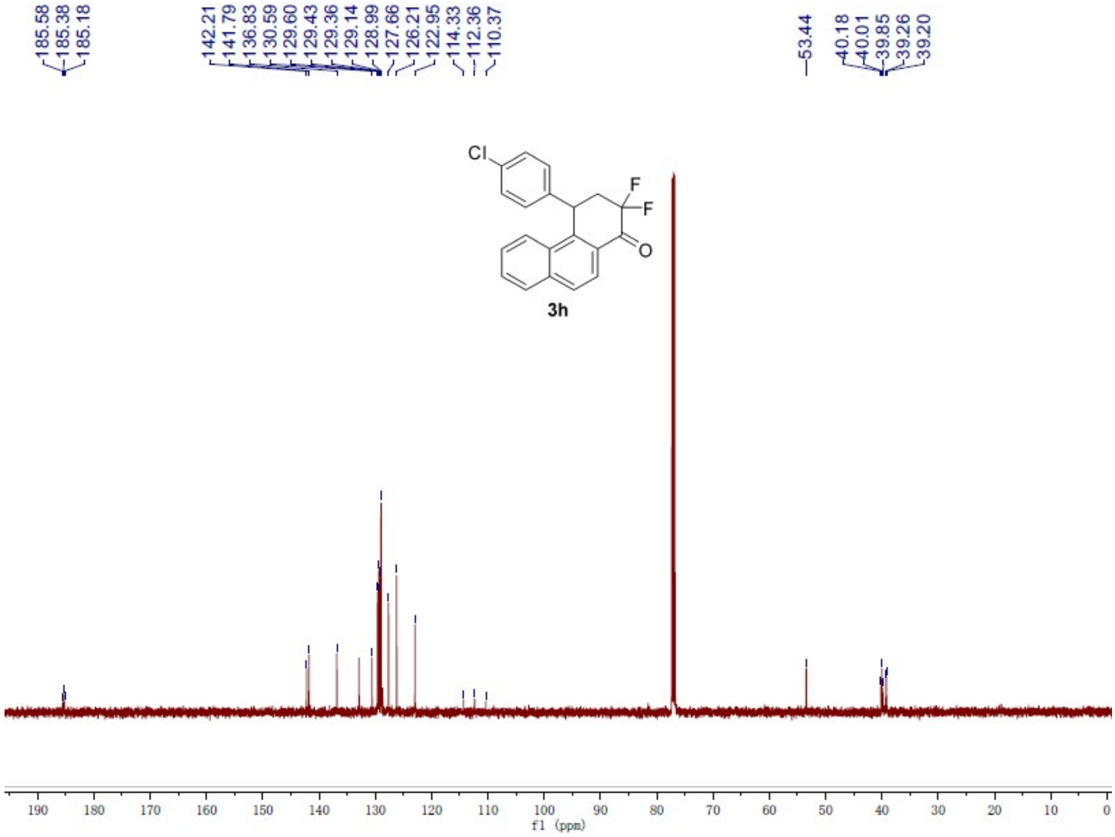
^{1}H NMR spectrum of 4-(4-chlorophenyl)-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3h**)



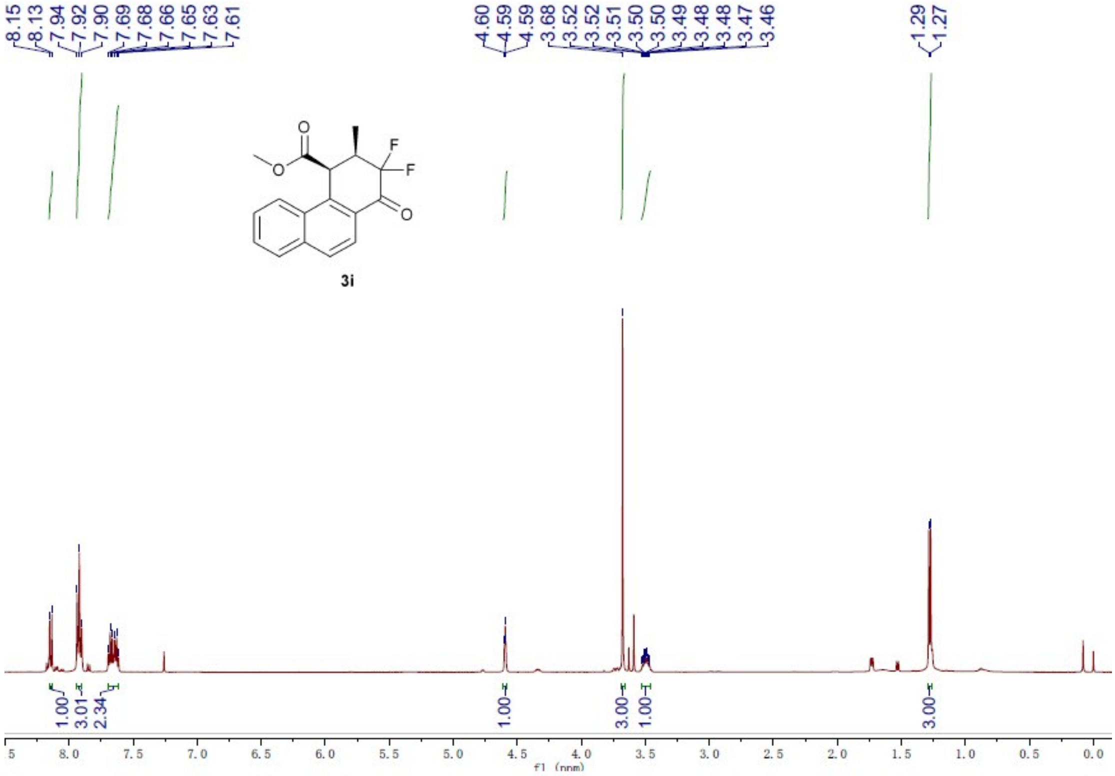
^{19}F NMR spectrum of 4-(4-chlorophenyl)-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3h**)



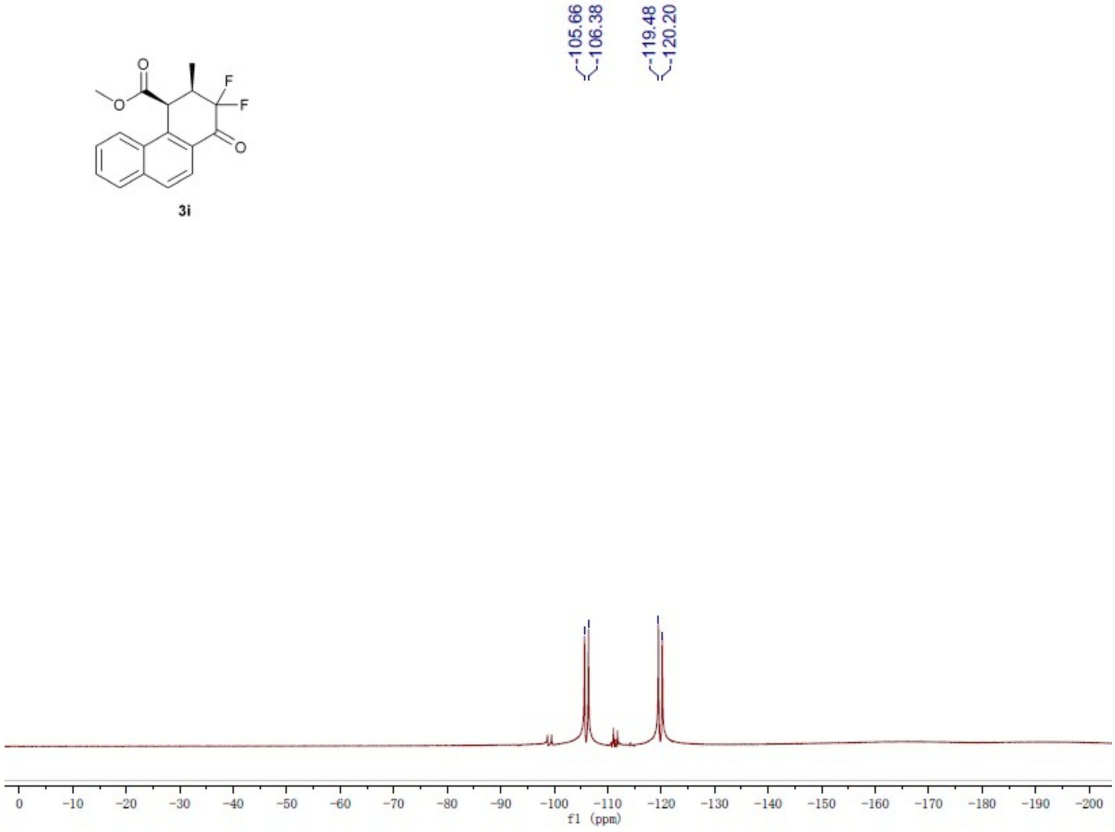
^{13}C NMR spectrum of 4-(4-chlorophenyl)-2,2-difluoro-3,4-dihydrophenanthren-1(2H)-one(**3h**)



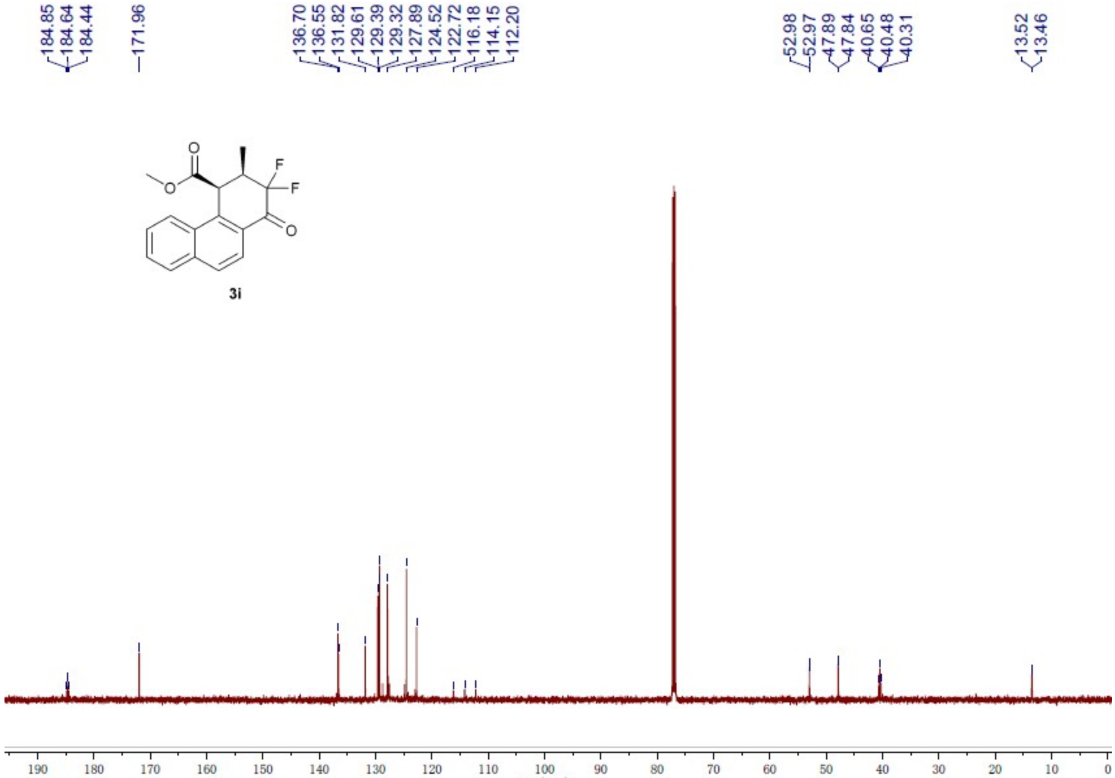
^1H NMR spectrum of Methyl-2,2-difluoro-3-methyl-1-oxo-1,2,3,4-tetrahydrophenanthrene-4-carboxylate(**3i**)



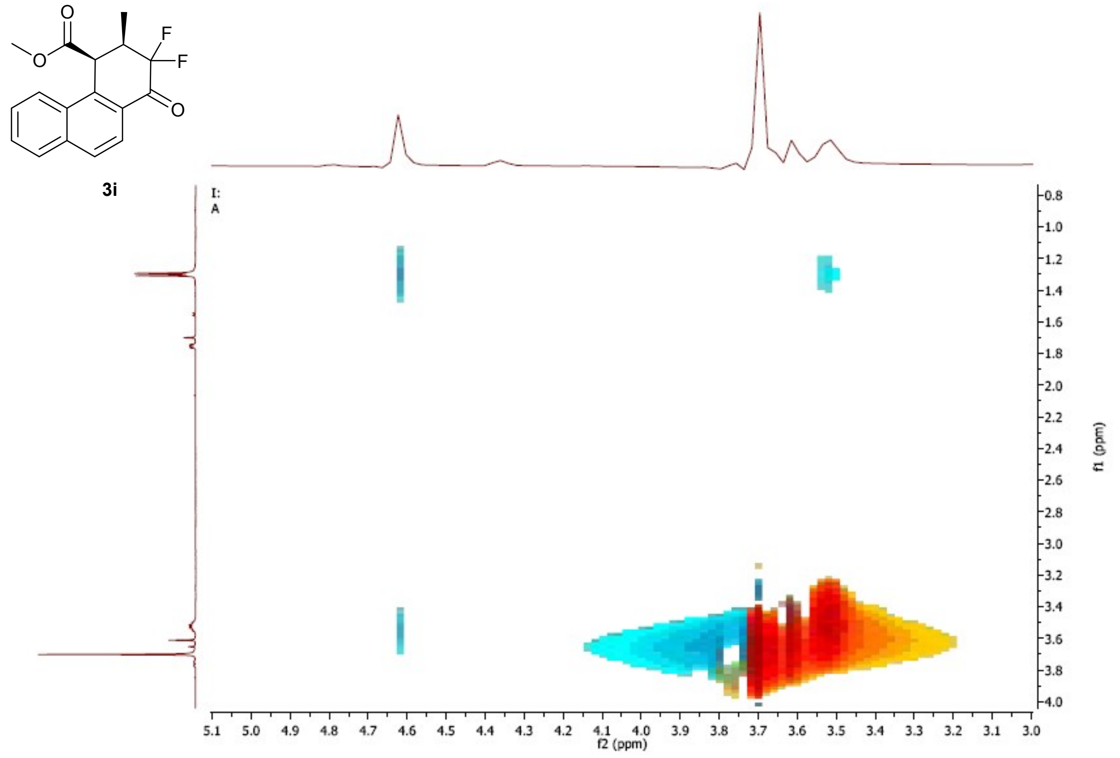
^{19}F NMR spectrum of Methyl-2,2-difluoro-3-methyl-1-oxo-1,2,3,4-tetrahydrophenanthrene-4-carboxylate(**3i**)



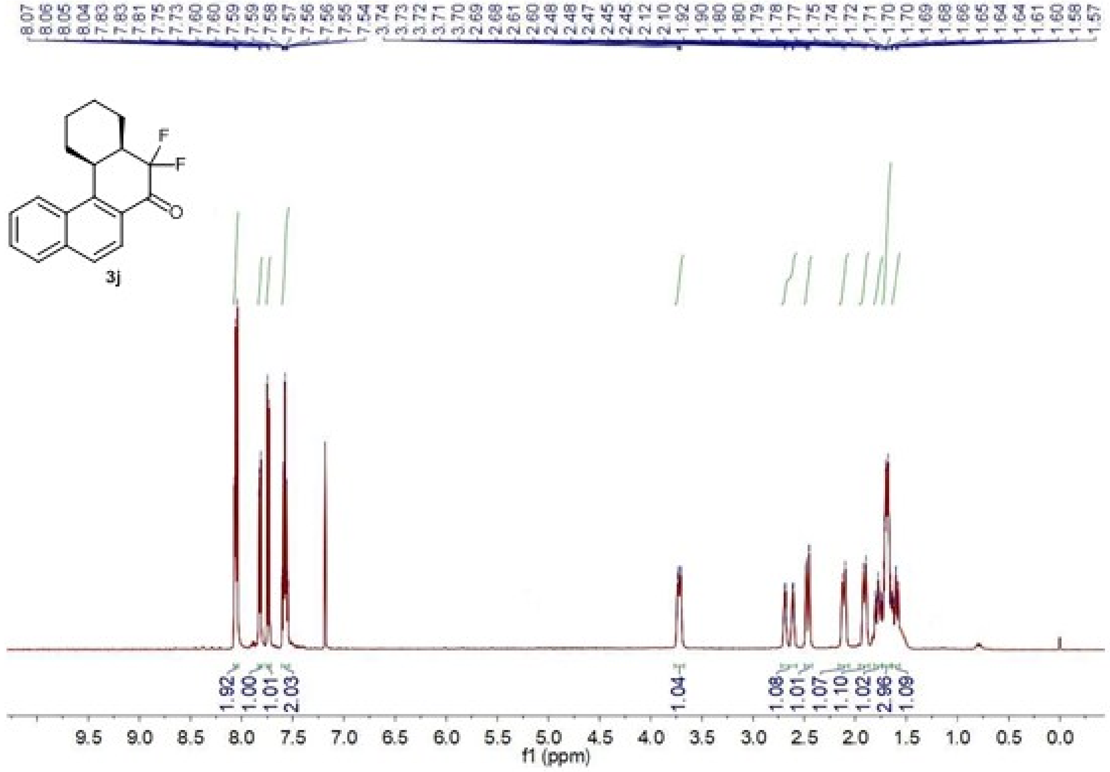
^{13}C NMR spectrum of Methyl-2,2-difluoro-3-methyl-1-oxo-1,2,3,4-tetrahydrophenanthrene-4-carboxylate(**3i**)



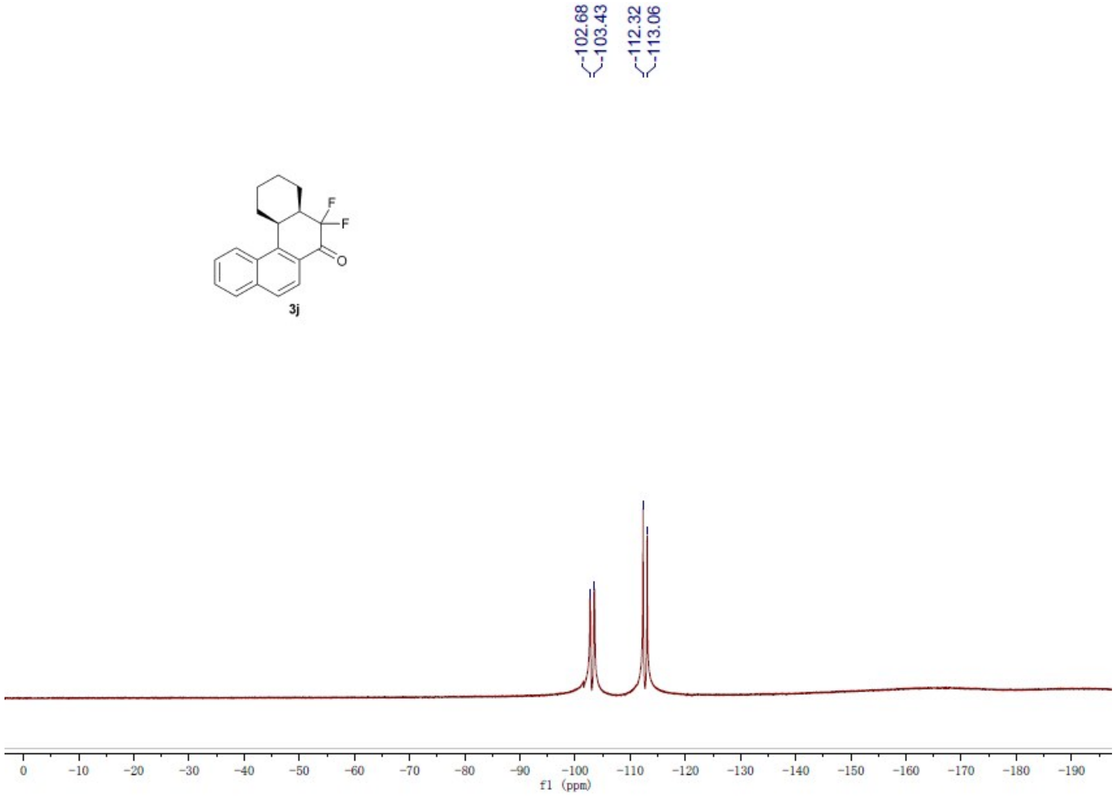
The NOESY spectrum of Methyl-2,2-difluoro-3-methyl-1-oxo-1,2,3,4-tetrahydrophenanthrene-4-carboxylate(**3i**)



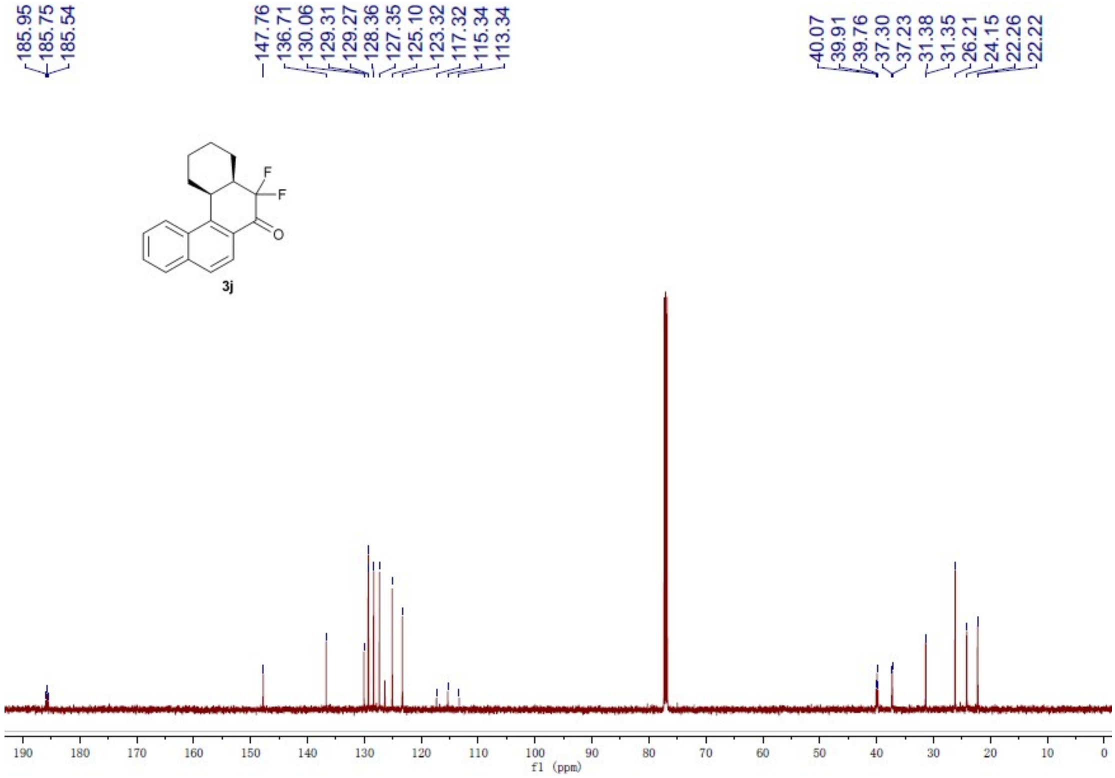
^{1}H NMR spectrum of 5,5-difluoro-1,3,4,4a,5,12c-hexahydrobenzo[c]phenanthren-6(2H)-one(**3j**)



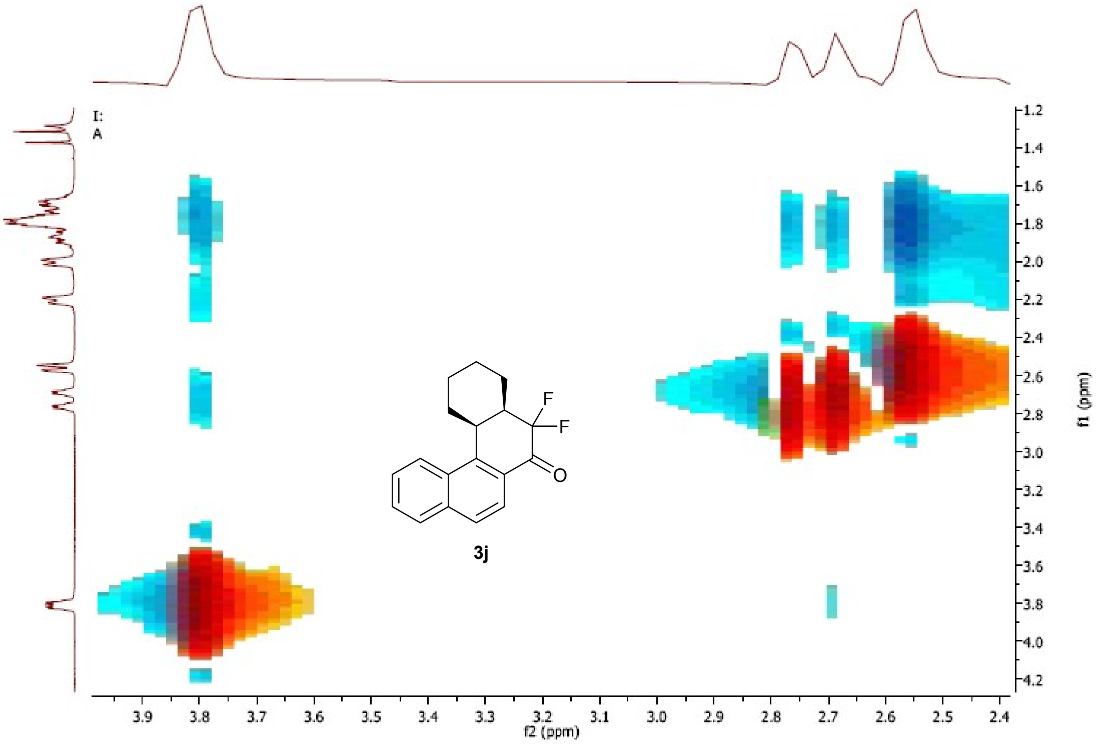
^{19}F NMR spectrum of 5,5-difluoro-1,3,4,4a,5,12c-hexahydrobenzo[c]phenanthren-6(2H)-one(**3j**)



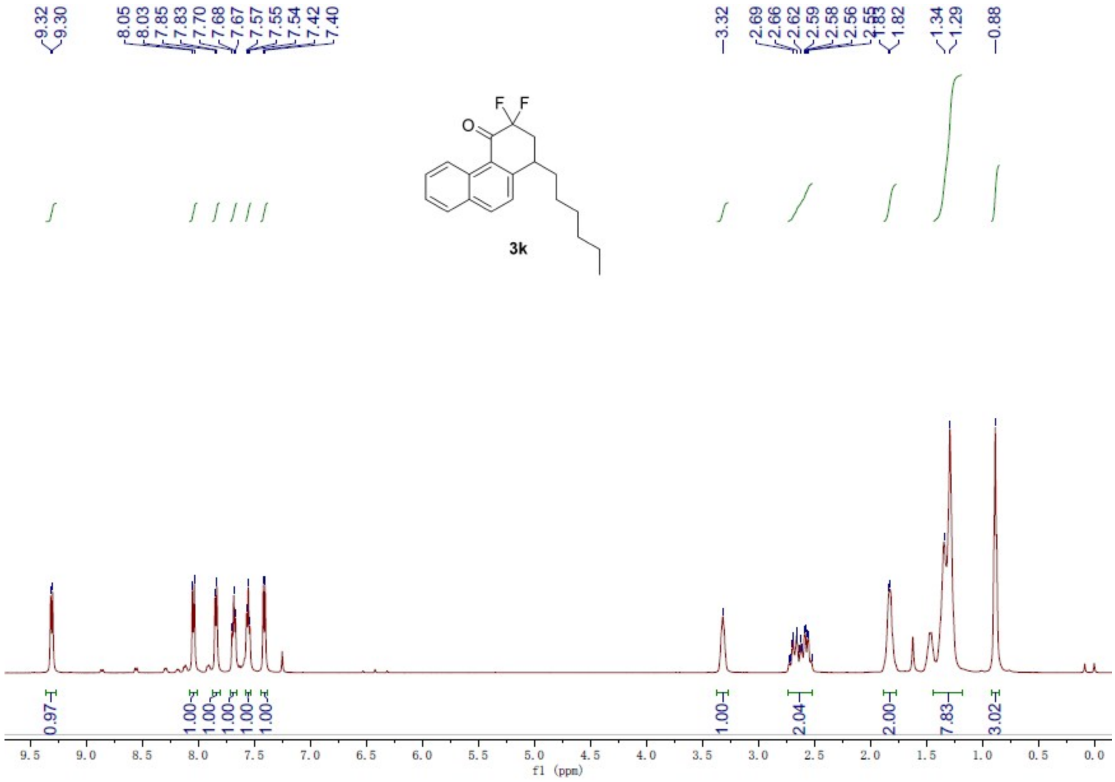
^{13}C NMR spectrum of 5,5-difluoro-1,3,4,4a,5,12c-hexahydrobenzo[c]phenanthren-6(2H)-one(**3j**)



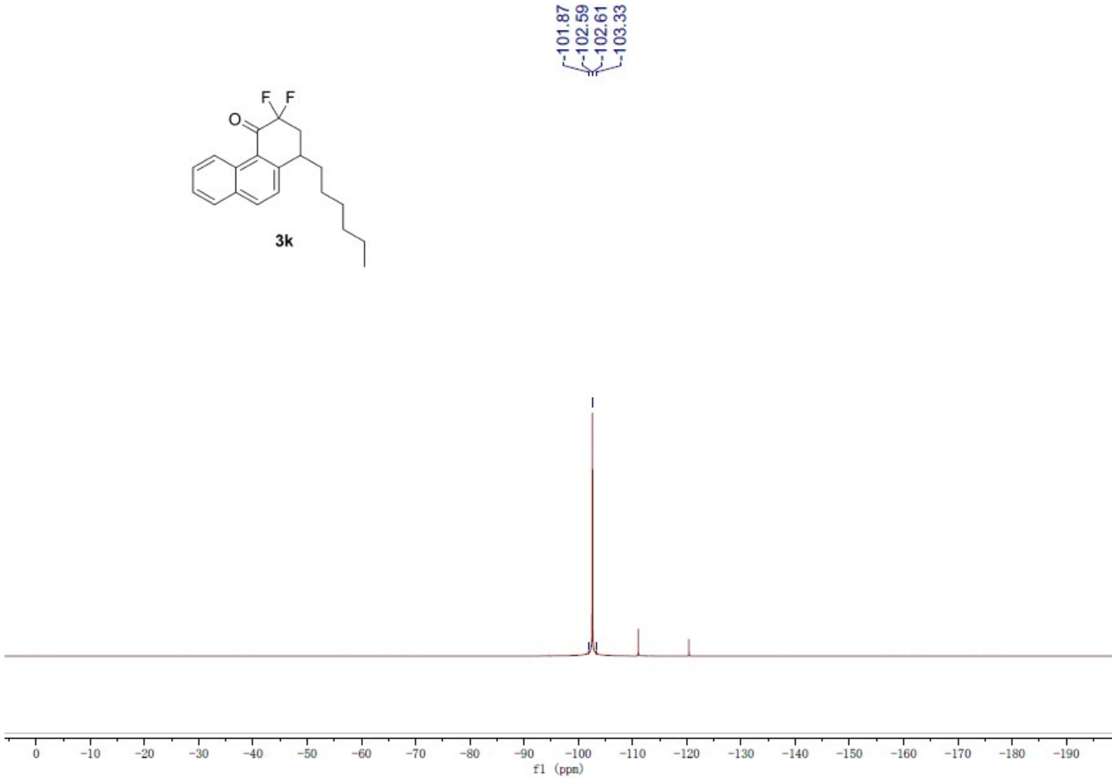
The NOESY spectrum of 5,5-difluoro-1,3,4,4a,5,12c-hexahydrobenzo[c]phenanthren-6(2H)-one (**3j**)



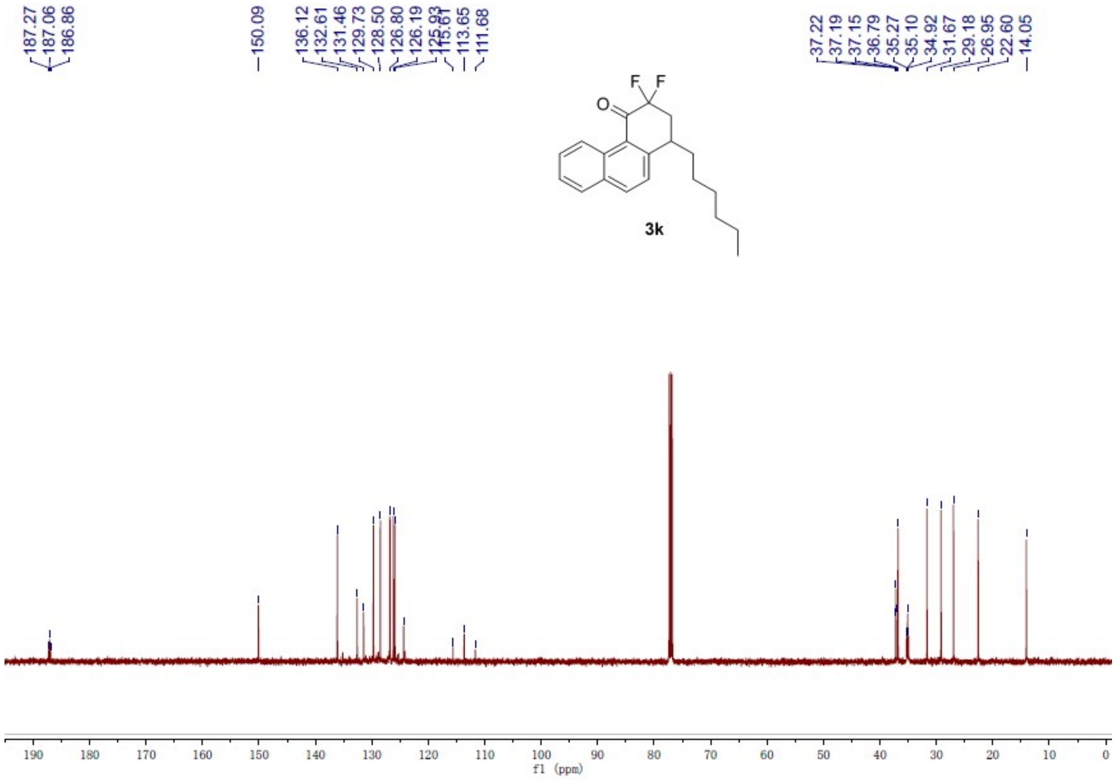
^{1}H NMR spectrum of 3,3-difluoro-1-hexyl-2,3-dihydrophenanthren-4(1H)-one(**3k**)



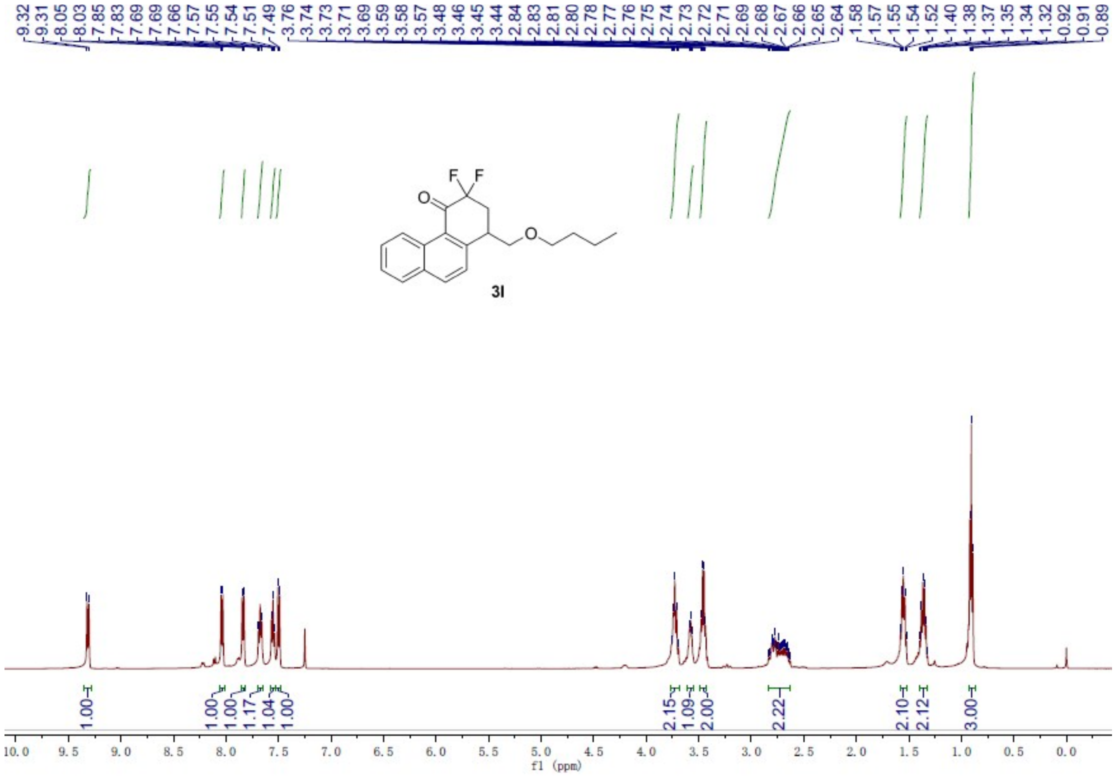
^{19}F NMR spectrum of 3,3-difluoro-1-hexyl-2,3-dihydrophenanthren-4(1H)-one(**3k**)



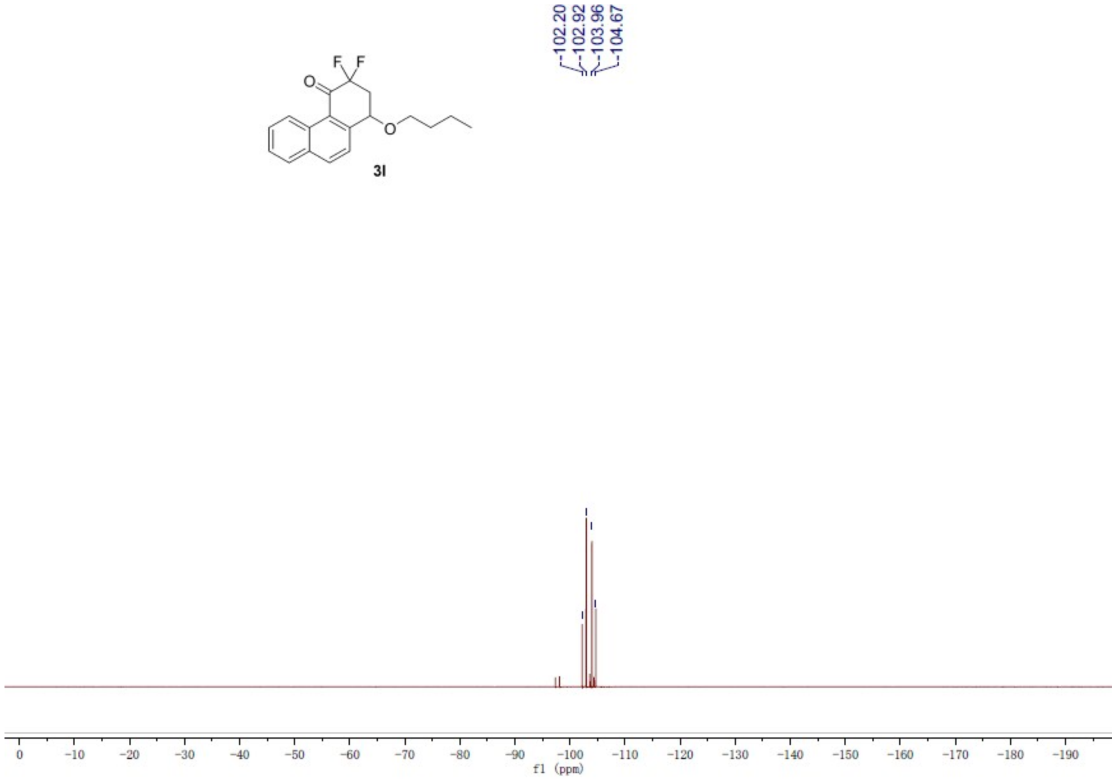
^{13}C NMR spectrum of 3,3-difluoro-1-hexyl-2,3-dihydrophenanthren-4(1H)-one(**3k**)



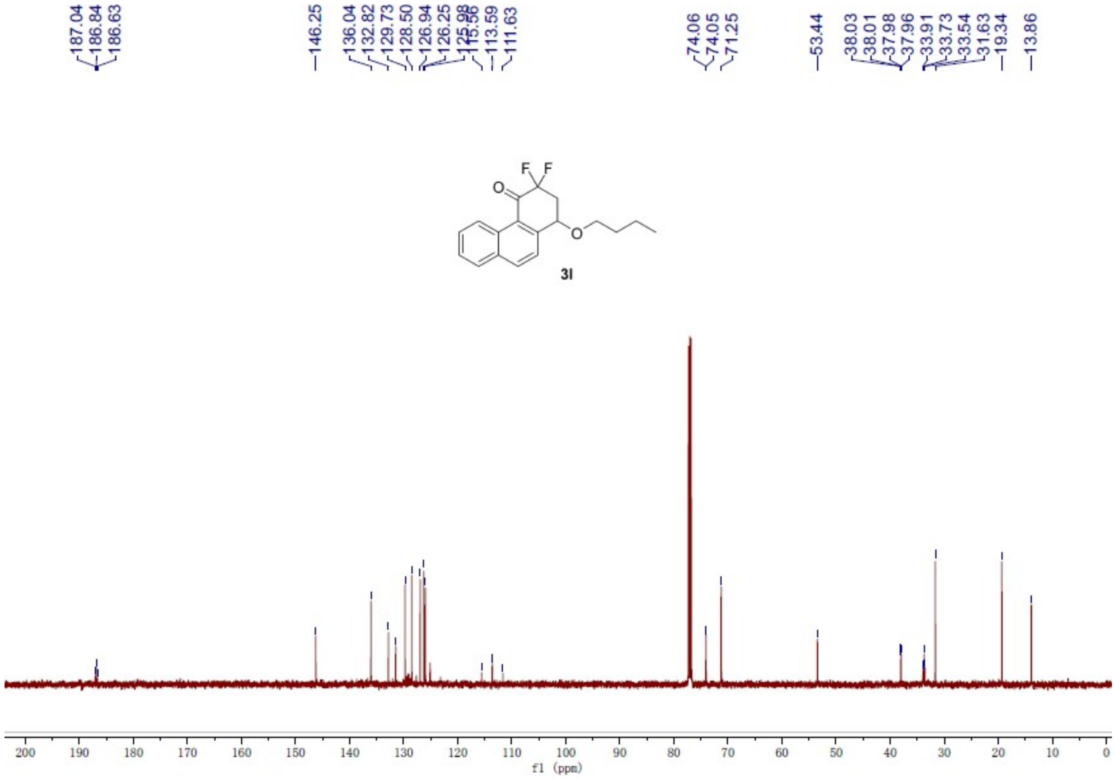
^{1}H NMR spectrum of butoxy-3,3-difluoro-2,3-dihydrophenanthren-4(1H)-one(**3l**)



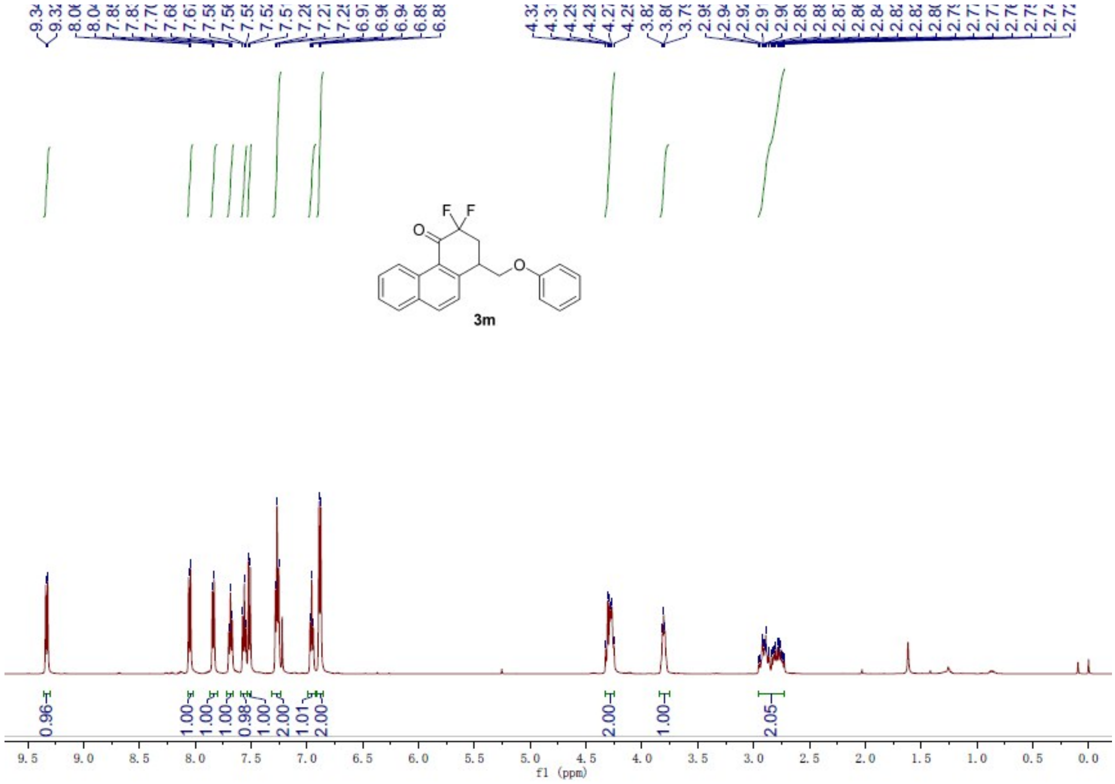
^{19}F NMR spectrum of butoxy-3,3-difluoro-2,3-dihydrophenanthren-4(1H)-one(**3l**)



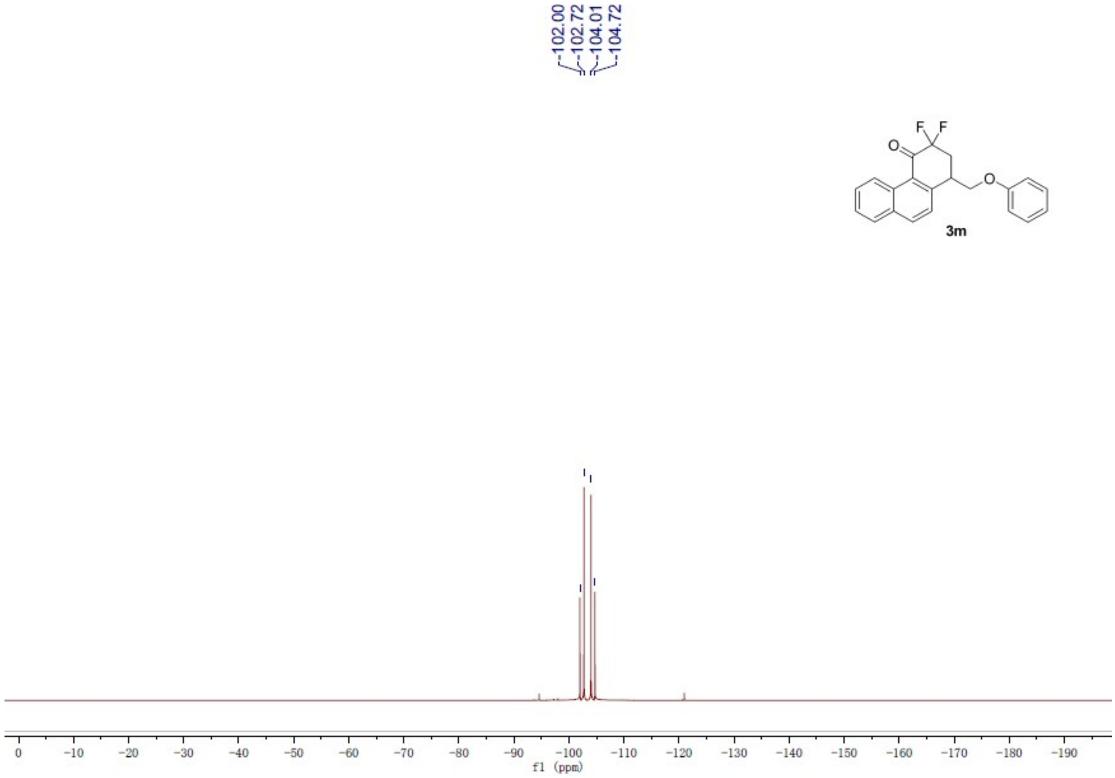
^{13}C NMR spectrum of butoxy-3,3-difluoro-2,3-dihydrophenanthren-4(1H)-one(**3l**)



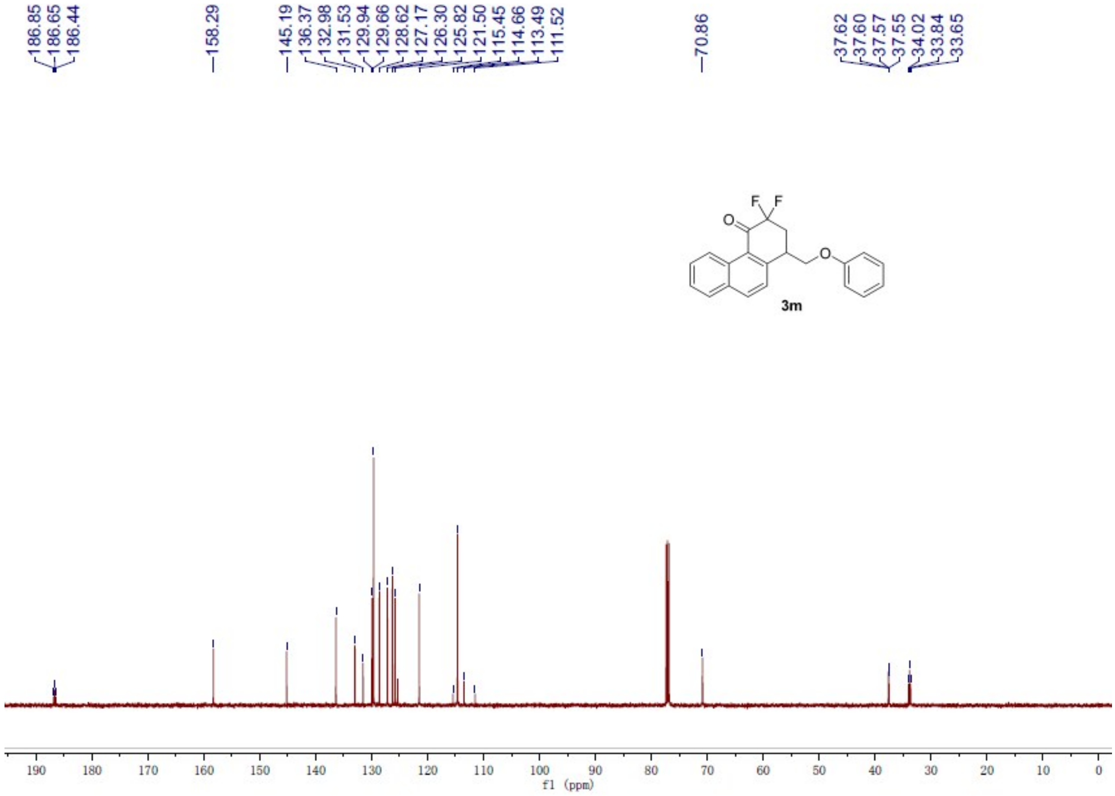
^{1}H NMR spectrum of 3,3-difluoro-1-(phenoxymethyl)-2,3-dihydrophenanthren-4(1H)-one(**3m**)



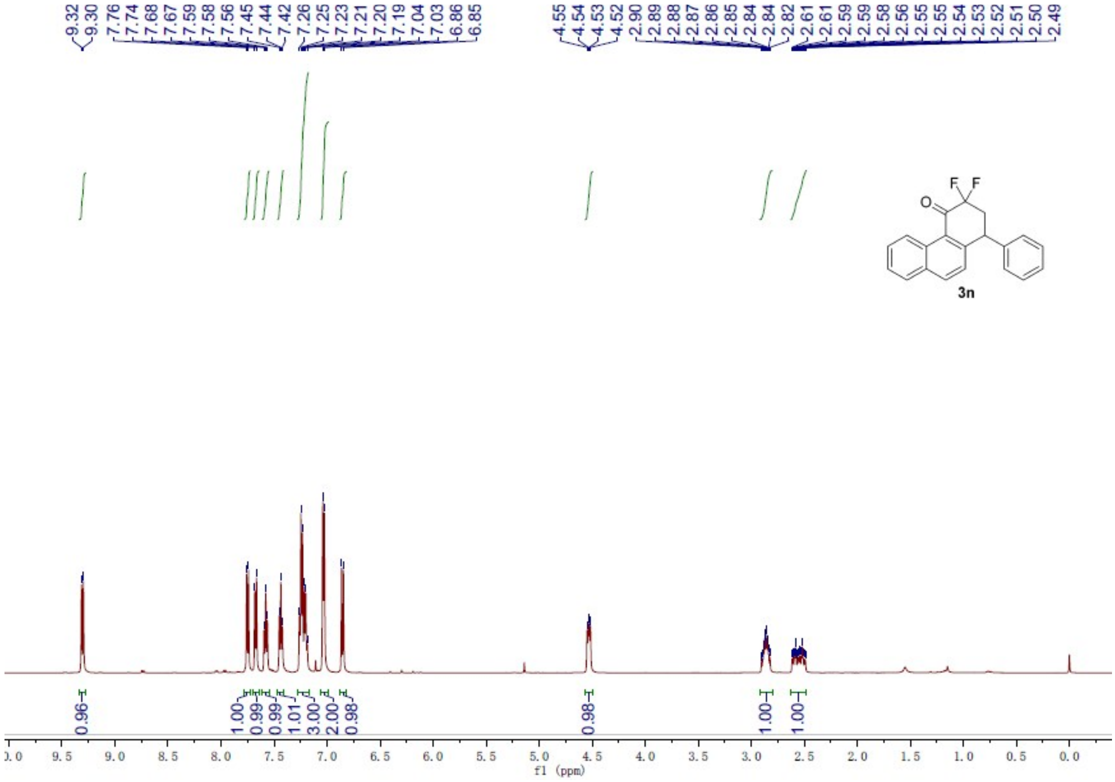
^{19}F NMR spectrum of 3,3-difluoro-1-(phenoxymethyl)-2,3-dihydrophenanthren-4(1H)-one(**3m**)



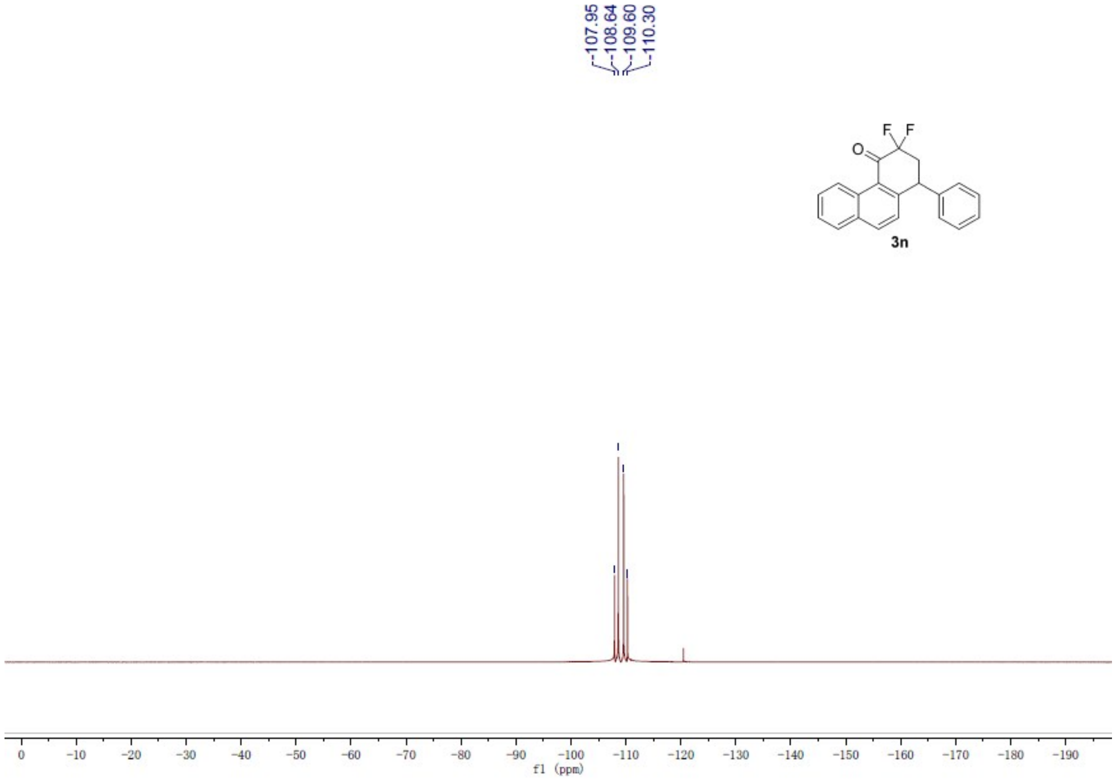
^{13}C NMR spectrum of 3,3-difluoro-1-(phenoxymethyl)-2,3-dihydrophenanthren-4(1H)-one(**3m**)



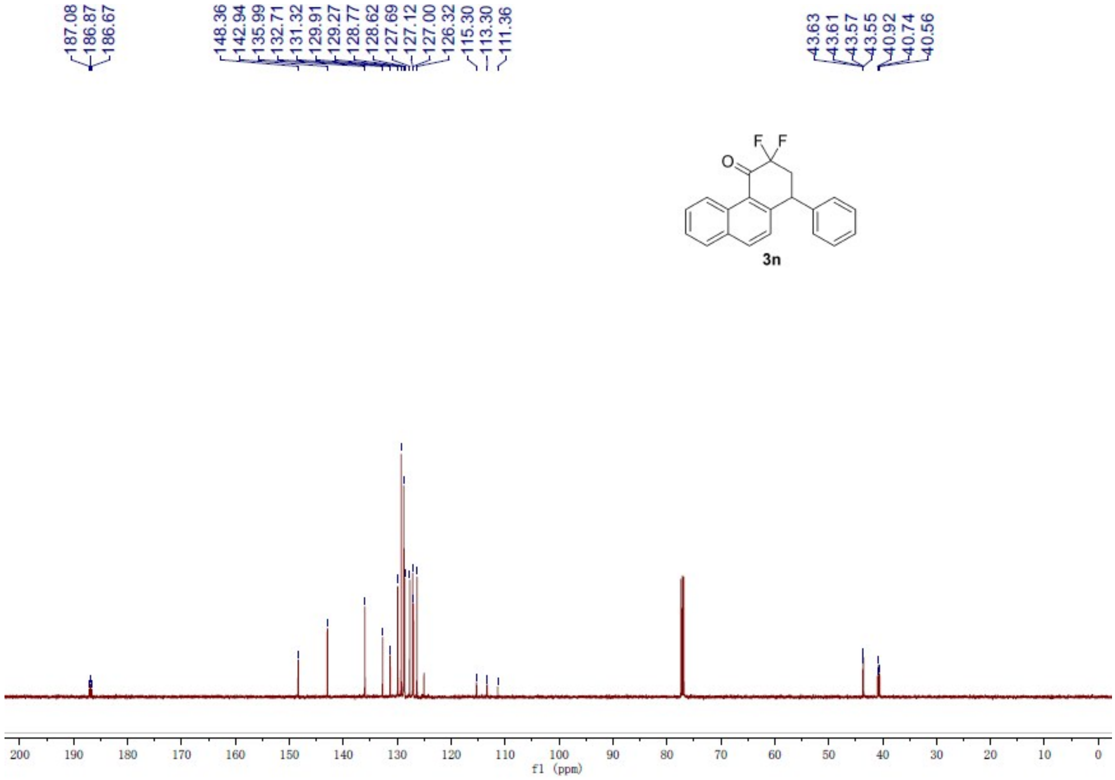
^{1}H NMR spectrum of 3,3-difluoro-1-phenyl-2,3-dihydrophenanthren-4(1H)-one(**3n**)



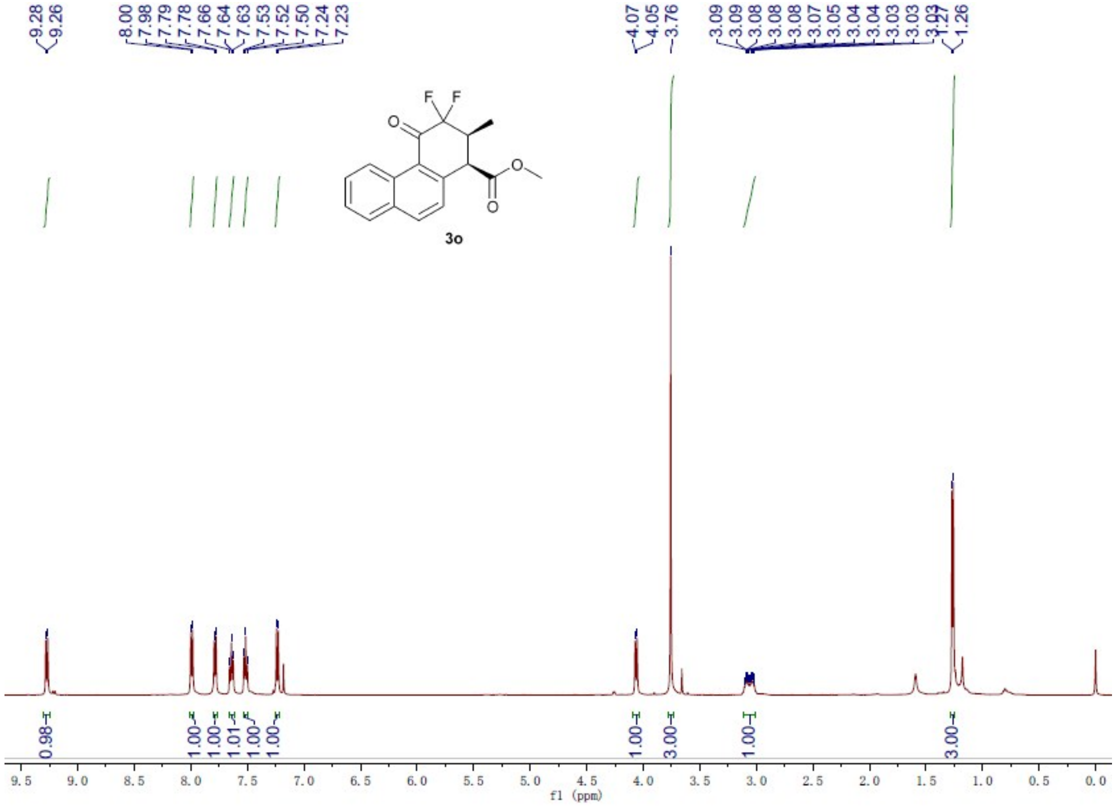
^{19}F NMR spectrum of 3,3-difluoro-1-phenyl-2,3-dihydrophenanthren-4(1H)-one(**3n**)



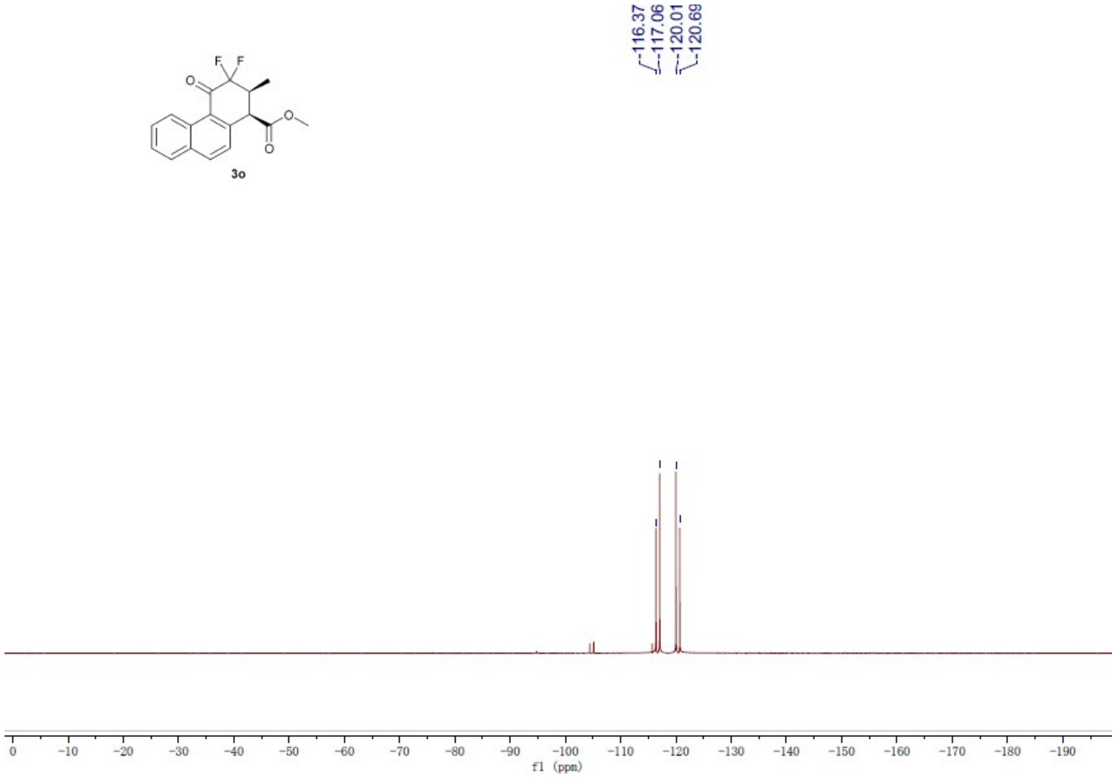
^{13}C NMR spectrum of 3,3-difluoro-1-phenyl-2,3-dihydrophenanthren-4(1H)-one(**3n**)



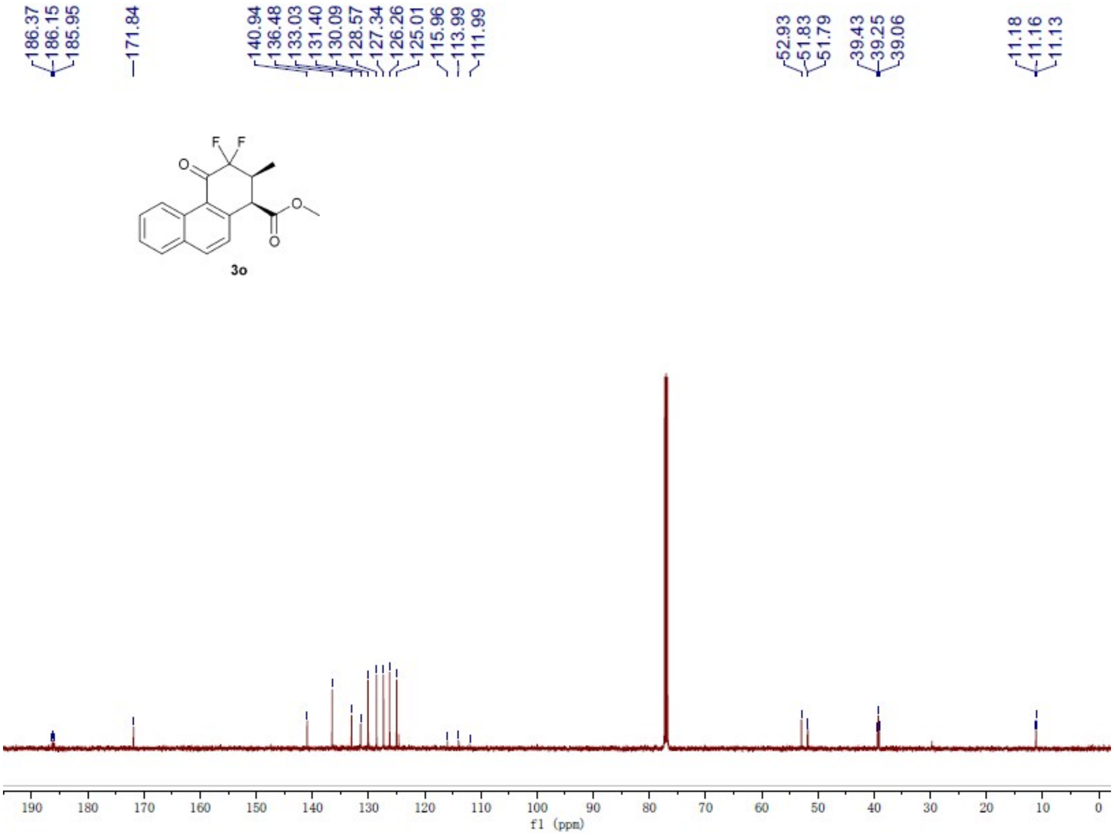
^{1}H NMR spectrum of methyl 3,3-difluoro-2-methyl-4-oxo-1,2,3,4-tetrahydrophenanthrene-1-carboxylate(**3o**)



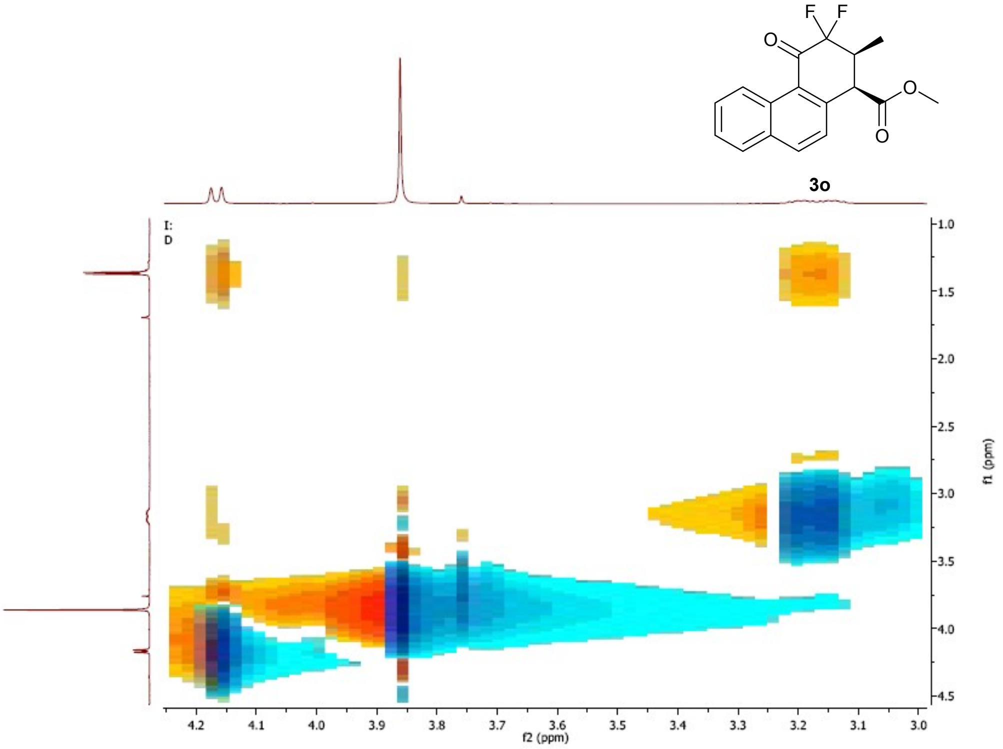
^{19}F NMR spectrum of methyl 3,3-difluoro-2-methyl-4-oxo-1,2,3,4-tetrahydrophenanthrene-1-carboxylate(**3o**)



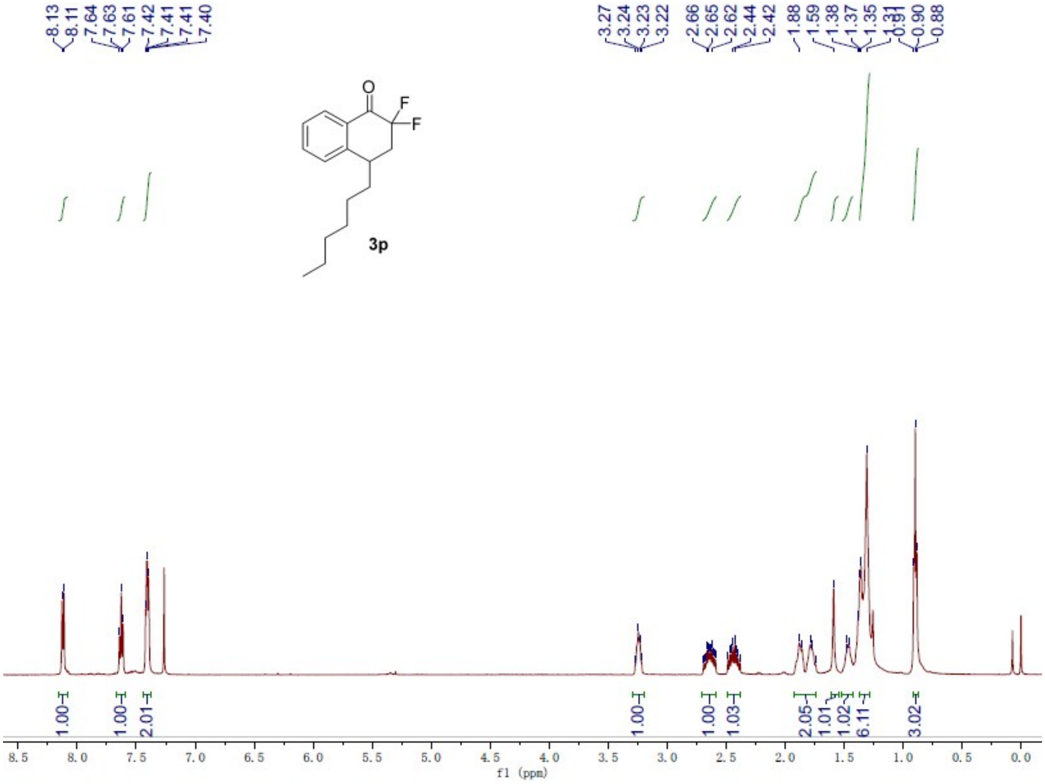
^{13}C NMR spectrum of methyl 3,3-difluoro-2-methyl-4-oxo-1,2,3,4-tetrahydrophenanthrene-1-carboxylate(**3o**)



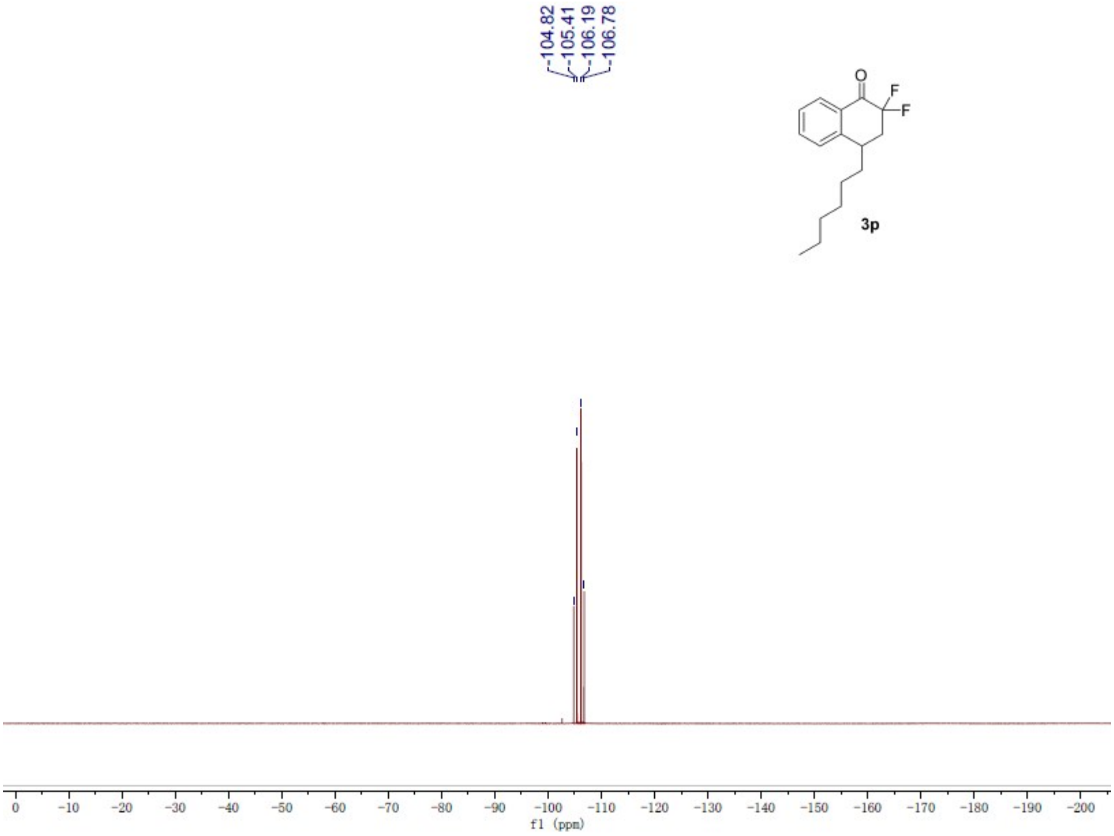
The NOESY spectrum of methyl 3,3-difluoro-2-methyl-4-oxo-1,2,3,4-tetrahydrophenanthrene-1-carboxylate(**3o**)



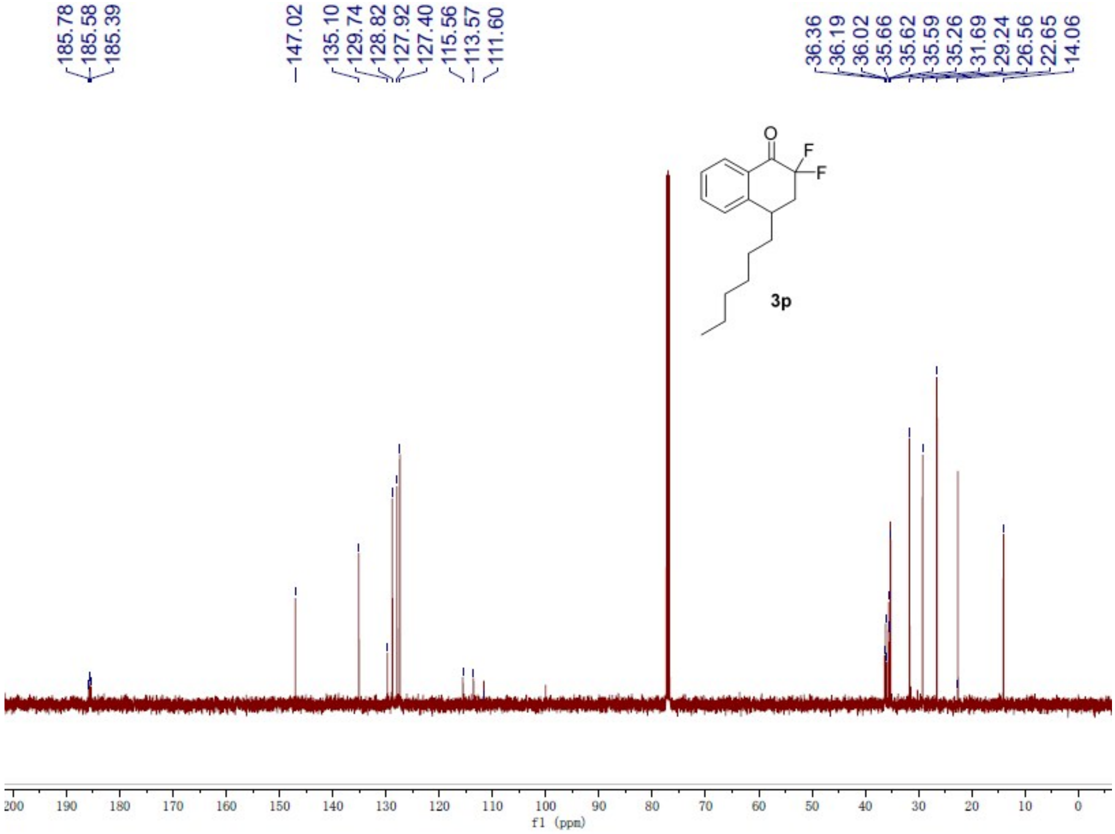
^{1}H NMR spectrum of 2,2-difluoro-4-hexyl-3,4-dihydronaphthalen-1(2H)-one(**3p**)



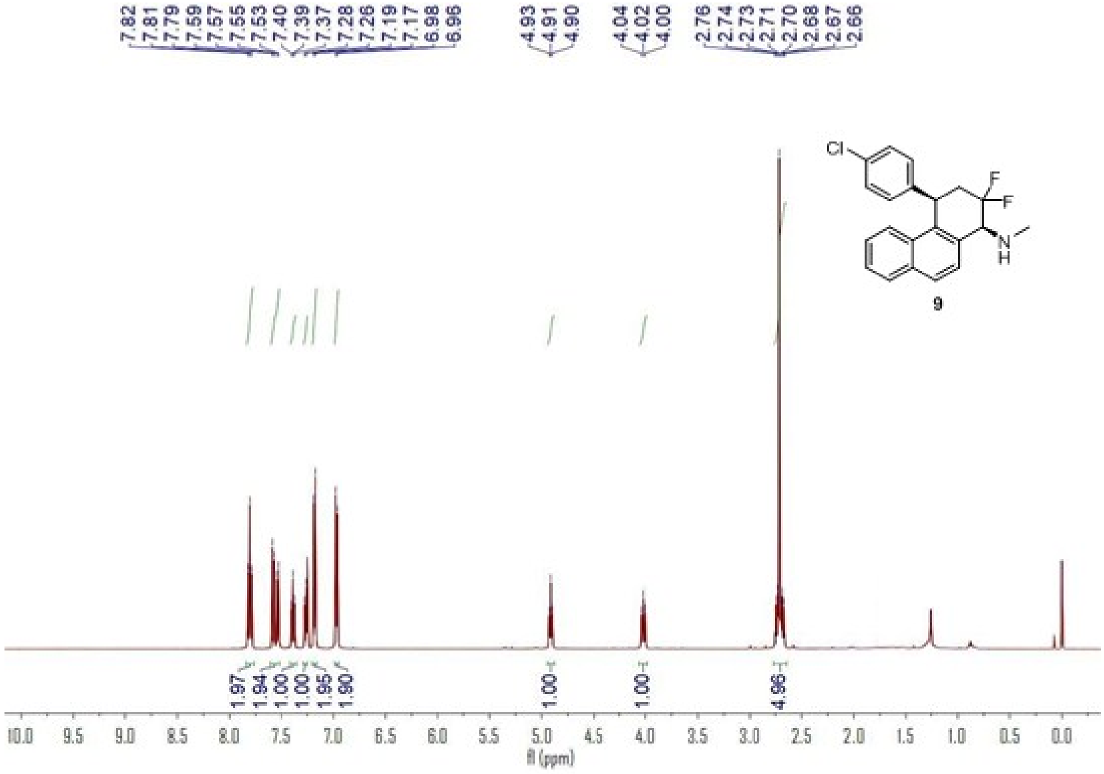
^{19}F NMR spectrum of 2,2-difluoro-4-hexyl-3,4-dihydronaphthalen-1(2H)-one(**3p**)



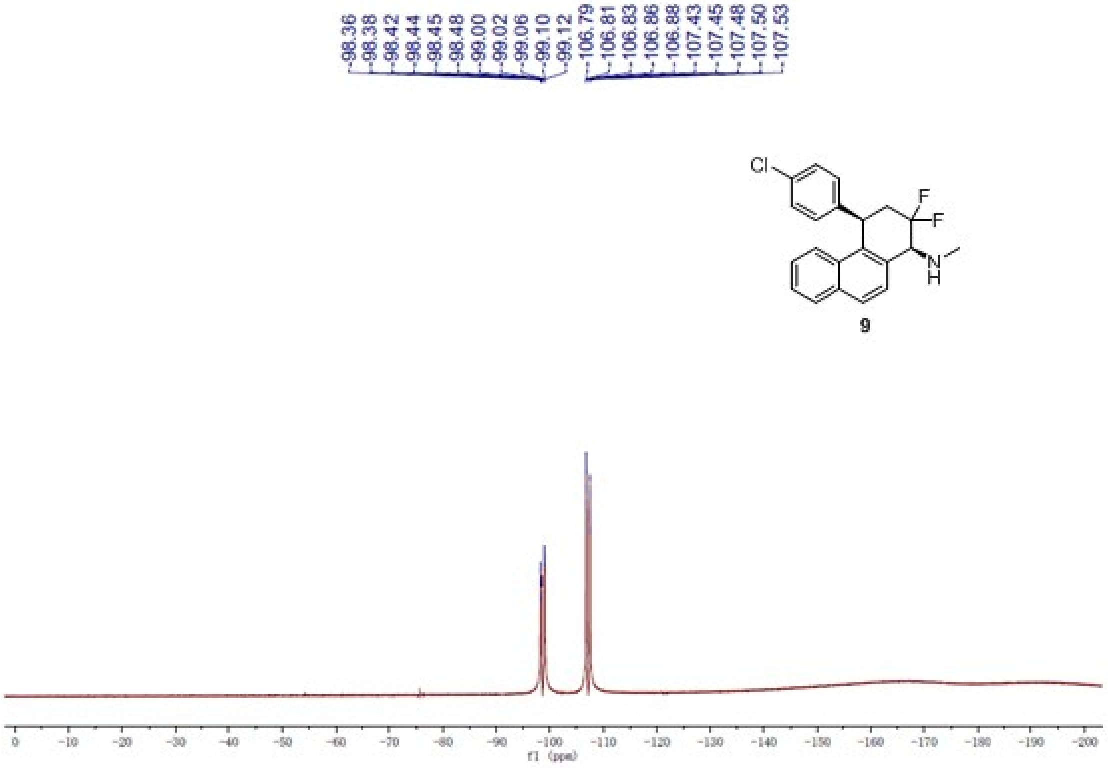
^{13}C NMR spectrum of 2,2-difluoro-4-hexyl-3,4-dihydronaphthalen-1(2H)-one(**3p**)



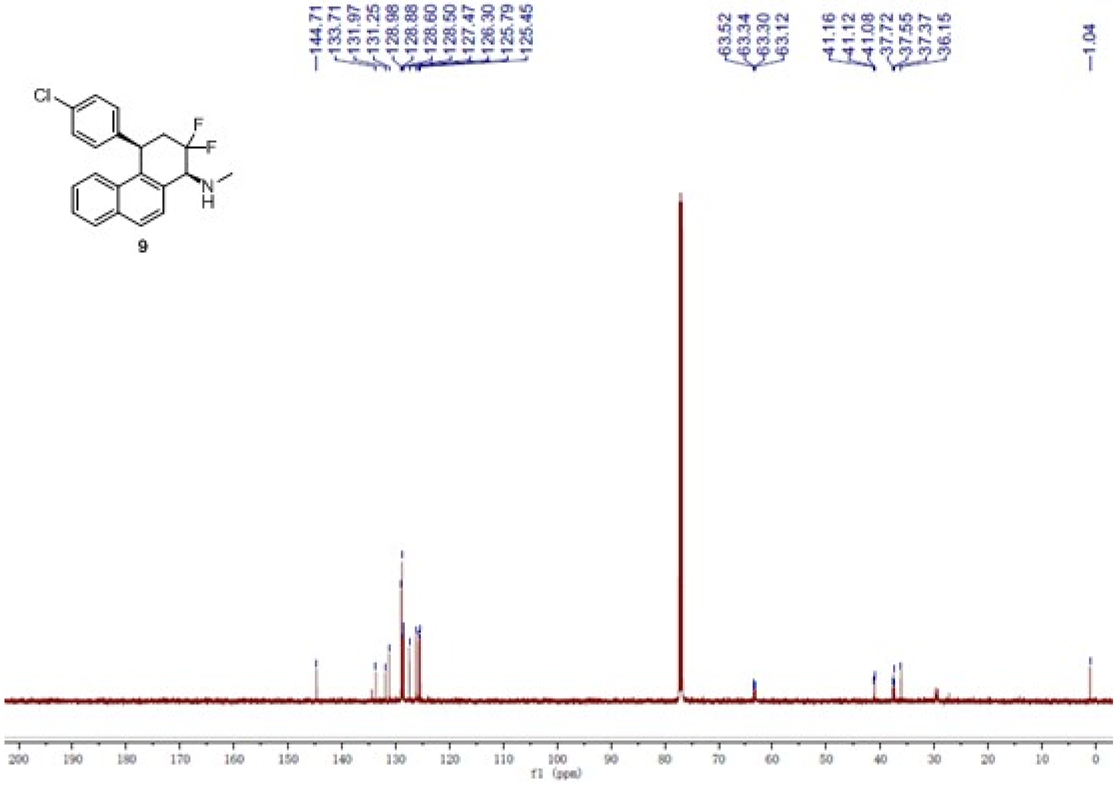
^{1}H NMR spectrum of 4-(4-chlorophenyl)-2,2-difluoro-N-methyl-1,2,3,4-tetrahydrophenanthren-1-amine(**9**)



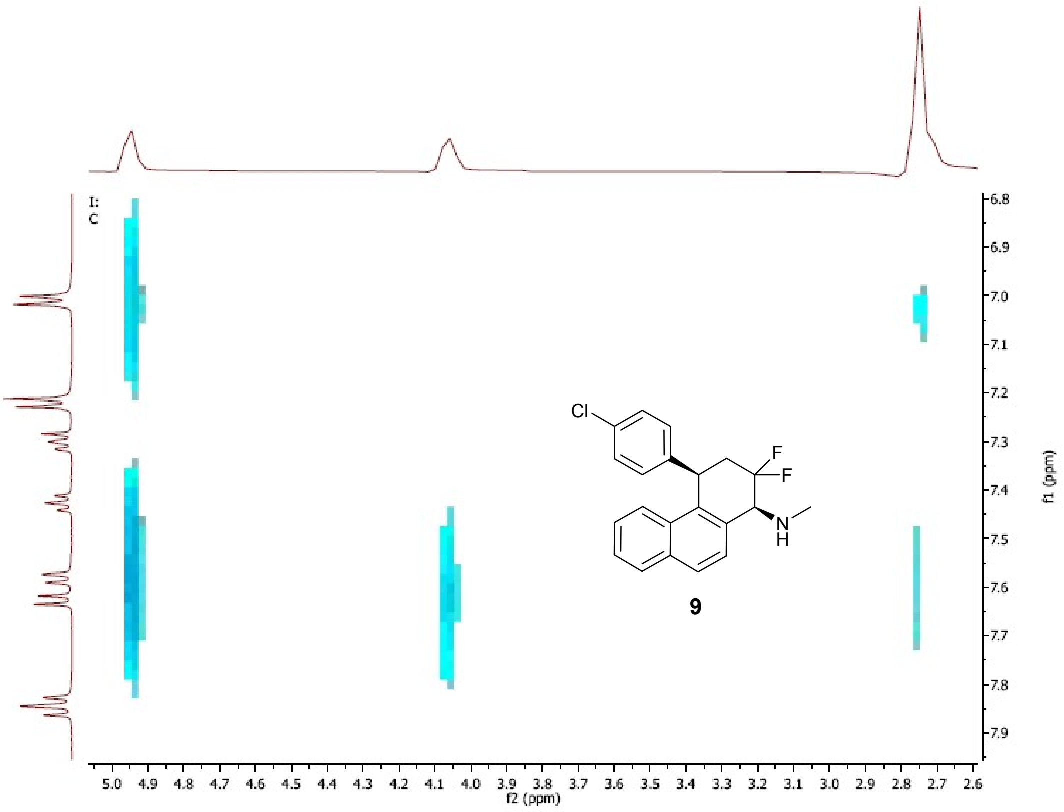
^{19}F NMR spectrum of 4-(4-chlorophenyl)-2,2-difluoro-N-methyl-1,2,3,4-tetrahydrophenanthren-1-amine(**9**)



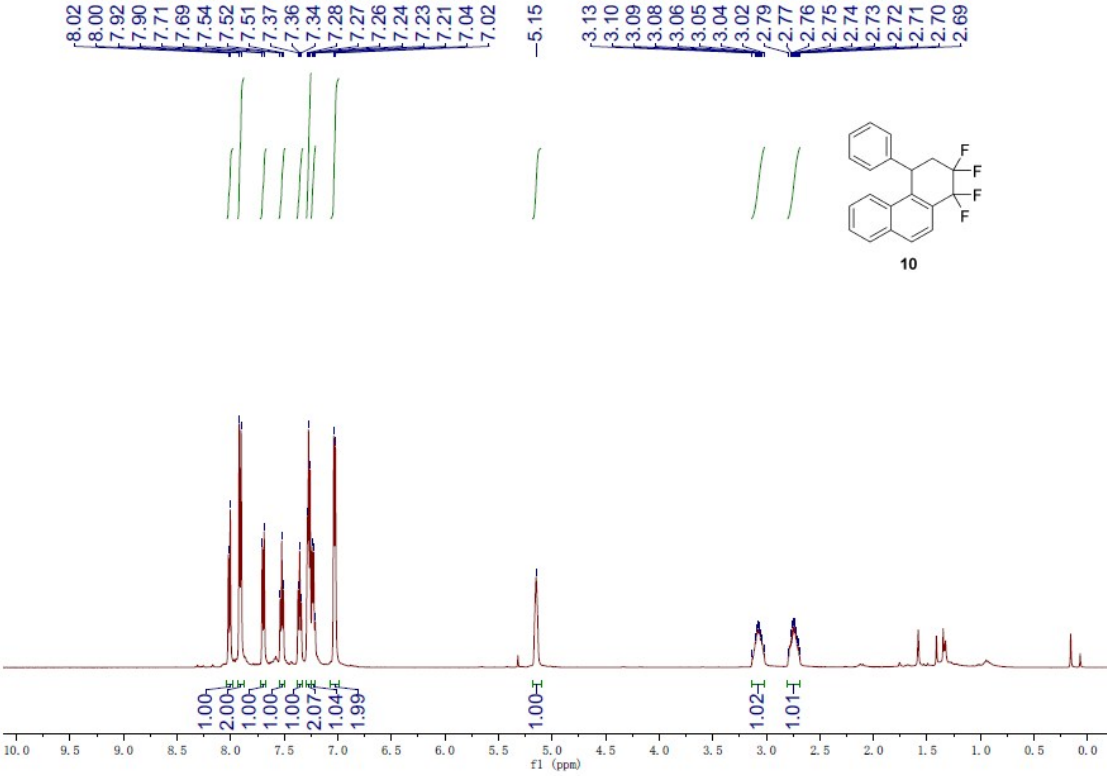
^{13}C NMR spectrum of 4-(4-chlorophenyl)-2,2-difluoro-N-methyl-1,2,3,4-tetrahydrophenanthren-1-amine(**9**)



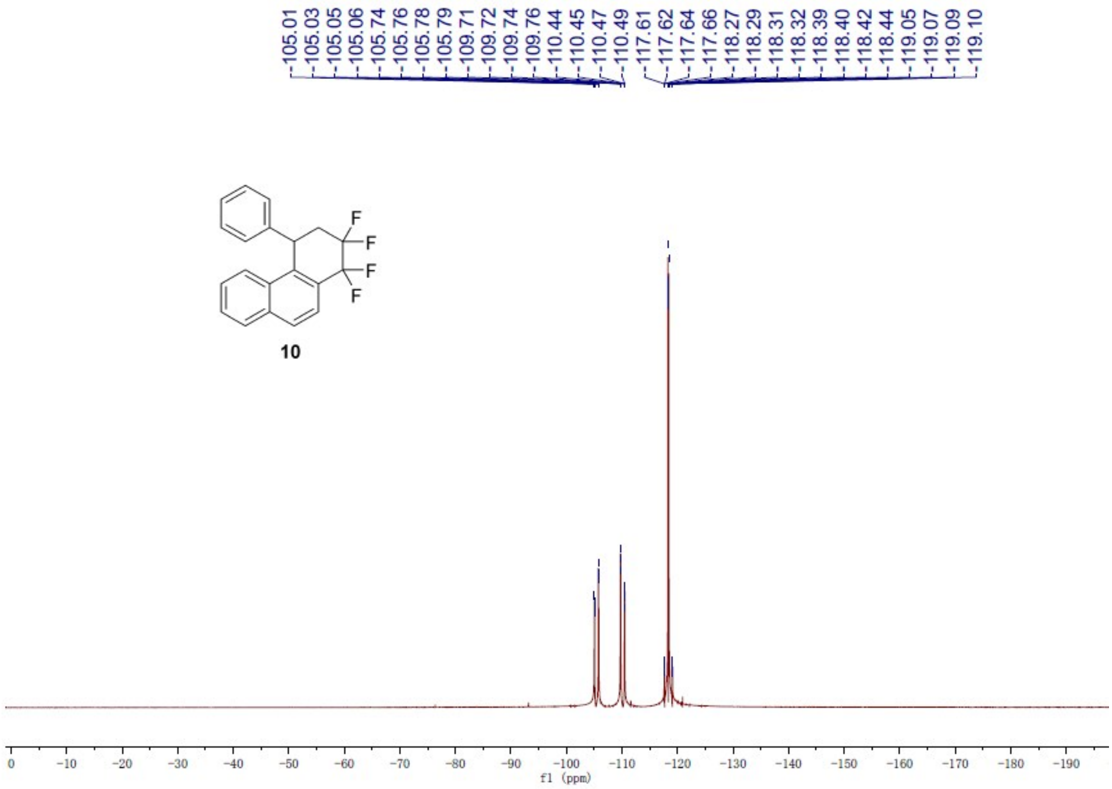
The NOESY spectrum of 4-(4-chlorophenyl)-2,2-difluoro-N-methyl-1,2,3,4-tetrahydrophenanthren-1-amine(**9**)



^{1}H NMR spectrum of 1,1,2,2-tetrafluoro-4-phenyl-1,2,3,4-tetrahydrophenanthrene(**10**)



^{19}F NMR spectrum of 1,1,2,2-tetrafluoro-4-phenyl-1,2,3,4-tetrahydrophenanthrene(**10**)



^{13}C NMR spectrum of 1,1,2,2-tetrafluoro-4-phenyl-1,2,3,4-tetrahydrophenanthrene(**10**)