$AgNO_3$-Catalyzed Decarboxylative Cross-coupling Reaction: An Approach to Coenzyme Q

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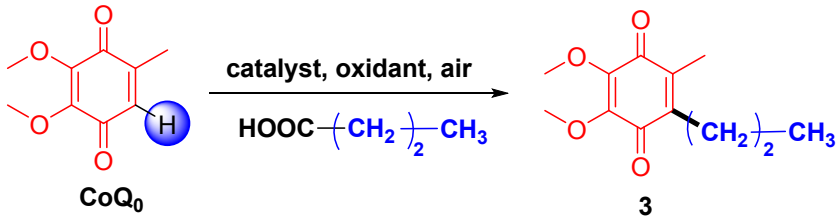
Experimental Procedures

All reactions were monitored by TLC (SiO_2, petrol ether/EtOAc 5:1), Melting points were measured on Melting Point M-565 (BUCHI). NMR and mass spectra were recorded on a Bruker Avanc III-HD 400 NMR and a TripleTOF Mass spectrometers, respectively. All reagents: e.g. Potassium Persulfate ($K_2S_2O_8$), Ammonium persulphate ($(NH_4)_2S_2O_8$) were purchased from Adamas, P. R. China, and used without further purification.

Table 1. Control experiments



Entry	Oxidant	Catalyst	Solvent	Yield (%)
1	$K_2S_2O_8$	Ag_2CO_3	CH_3CN	10
2	$K_2S_2O_8$	Ag_2O	CH_3CN	8
3	$K_2S_2O_8$	AgOAc	CH_3CN	14
4	$(NH_4)_2S_2O_8$	$AgNO_3$	CH_3CN	25
5	H_2O_2	$AgNO_3$	CH_3CN	0
6	TBHP	$AgNO_3$	CH_3CN	trace
7	TBPB	$AgNO_3$	CH_3CN	12
8	DTBP	$AgNO_3$	CH_3CN	trace
9	TBPB	$Bi(OTf)_3$	CH_3CN	0
10	TBPB	$Cu(OAc)_2$	CH_3CN	trace
11	TBPB	$Pd(OAc)_2$	CH_3CN	trace

Reaction Conditions: **CoQ_0** (0.02 mol), butanoic acid (1.2 equiv), Catalyst 40%, Oxidant 2 equiv (DTBP: *di*-tertbutyl peroxide. TBHP＝*tert*-butyl hydroperoxide, TBPB＝*tert*-butyl peroxybenzoate). 80 °C, 4h

Synthesis of CoQ compounds

To a solution of Coenzyme Q_0 (3.64 g, 0.02 mol) and carboxylic acids (0.03mol) in acetonitrile 80 mL was added $AgNO_3$ (1.35 g, 8 mmol). The mixture was heated to 80 °C and a solution of $K_2S_2O_8$ (10.81 g, 0.04 mol) in distilled water 80 mL was added dropwise over 2 h, then the reaction mixture was stirred for another 2 h, with TLC monitoring unitil the starting material was consumed. The resulting mixture was cooled and extracted with CH_2Cl_2. The organic layer was washed with water, then dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatograph on silica gel (PE/EtOAc= 5:1) to give CoQ compounds.

Compound **3**, red oil;

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 2.45 (t, 2H, *J* = 8.0 Hz, CH_2), 2.02 (s, 3H, CH_3), 1.39-1.49 (m, 2H, CH_2), 0.96 (t, *J* = 8.0 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 184.7 (C=O), 184.2 (C=O), 144.3, 144.2, 142.8, 138.9, 61.2(O**C**H_3), 28.3, 22.1, 14.3, 11.9 (**C**H_3).

Compound **4**, red oil;

^{1}H NMR (400 MHz, $CDCl_3$) δ4.00 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 2.45 (t, 2H, *J* = 8.0 Hz, CH_2), 2.01 (s, 3H, CH_3), 1.15-1.45 (m, 14H, CH_2), 0.88 (t, *J* = 8.0 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 184.7 (C=O), 184.2 (C=O), 144.3, 144.2, 143.1, 138.6, 61.2 (O**C**H_3), 31.9, 29.8, 29.5, 29.4, 29.3, 28.7, 26.4, 22.7, 14.1, 11.9 (**C**H_3).

Compound **5**, red oil[1];

^{1}H NMR (400MHz, $CDCl_3$) δ 3.91 (s, 6H, OCH_3), 3.55 (t, *J* = 8.0Hz, 2H, CH_2OH), 2.52 (s, 1H, OH), 2.36 (t, *J* = 8.0Hz, 2H), 2.00 (s, 3H, CH_3), 1.48(t, *J* = 8.0Hz, 2H), 1.10-1.45 (m, 14H).

^{13}CNMR (100MHz, $(CD_3)_2CO$) δ 184.5 (C=O), 183.9 (C=O), 144.0, 142.8(2C), 138.5, 62.6(O**C**H_3), 60.9(O**C**H_3), 32.5, 29.6, 29.2, 29.1, 29.0, 28.5, 26.2, 25.5, 11.7 (**C**H_3).

Idebenone (compound **6**), red solid, m.p. 53-55 °C (Lit. [2] 52-54 °C).

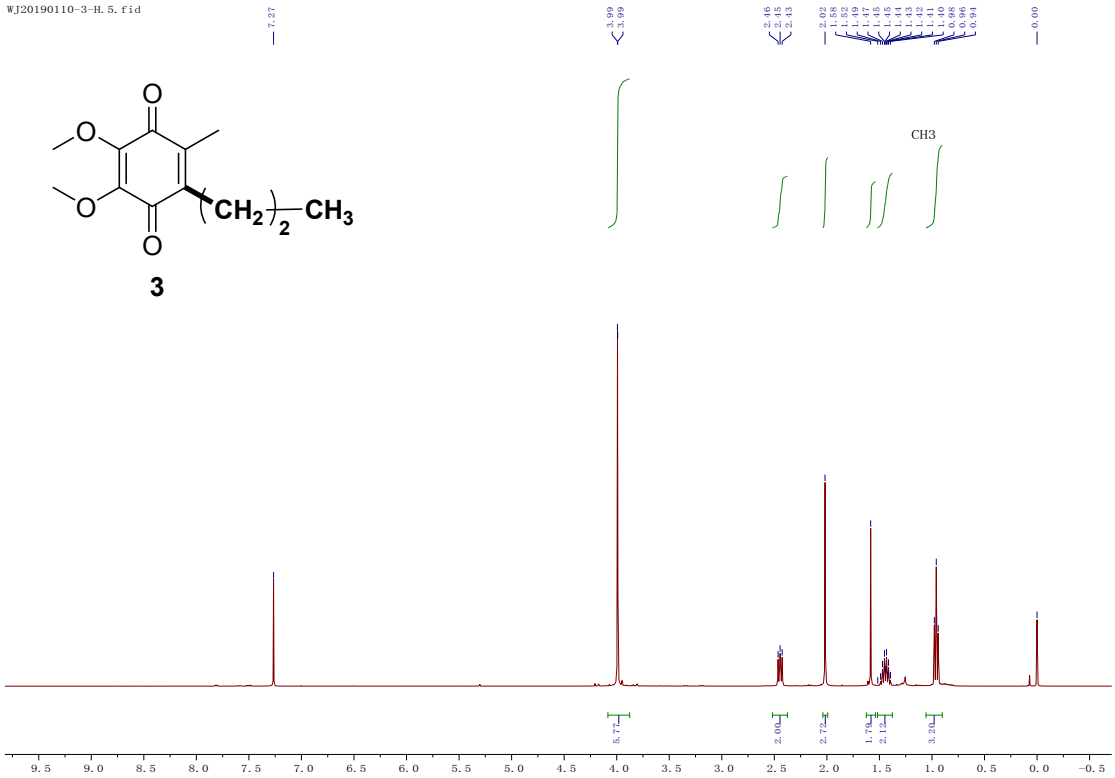
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (s, 3H, OCH_3),3.99 (s,3H, OCH_3), 3.62-3.66 (m, 2H, CH_2), 2.45 (t, 2H, *J* = 8.0 Hz, CH_2), 2.01 (s, 3H, CH_3), 1.61 (s,1H,OH), 1.59-1.52 (m, 2H), 1.42-1.22 (m, 14H);

^{13}CNMR (100 MHz, $CDCl_3$) δ 184.7 (C=O), 184.2 (C=O), 144.3, 144.2, 143.1, 138.7, 63.1(O**C**H_3), 61.2(O**C**H_3), 32.8, 29.8, 29.5, 29.4, 29.3,28.7, 26.4 , 25.7, 11.9 (**C**H_3).

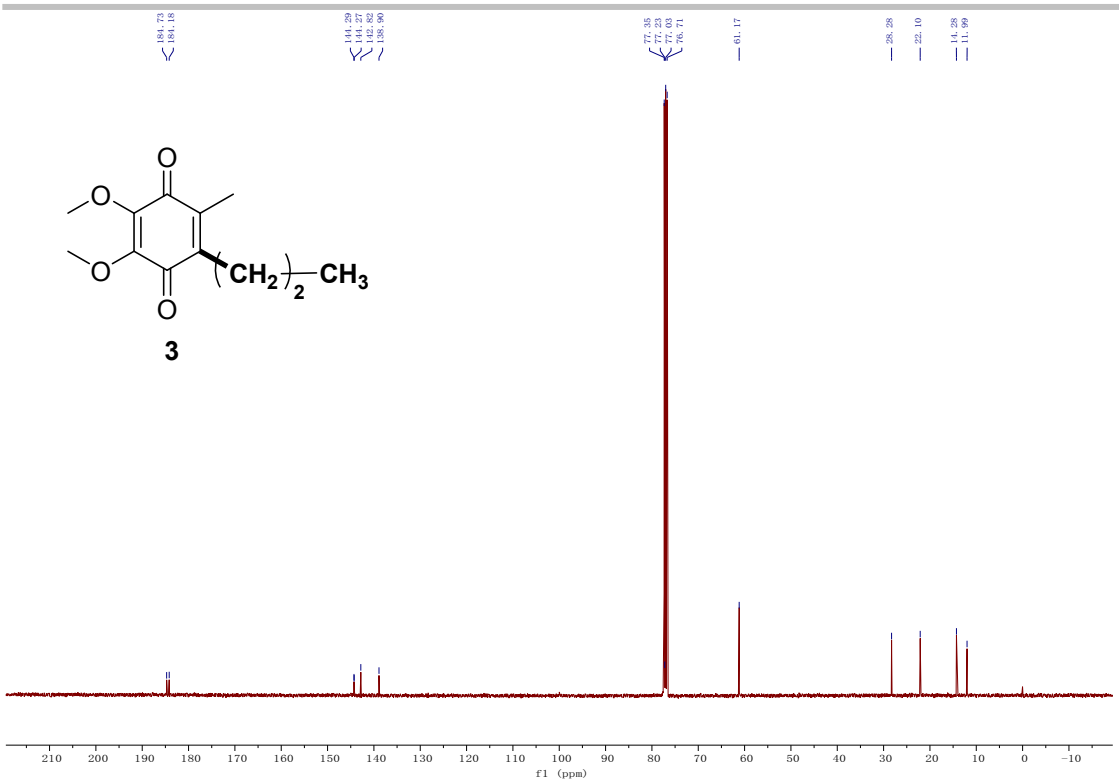
References

[1] J. Wang, S. Li, T. Yang and J. Yang, European Journal of Medicinal Chemistry, 2014, 86, 710-713

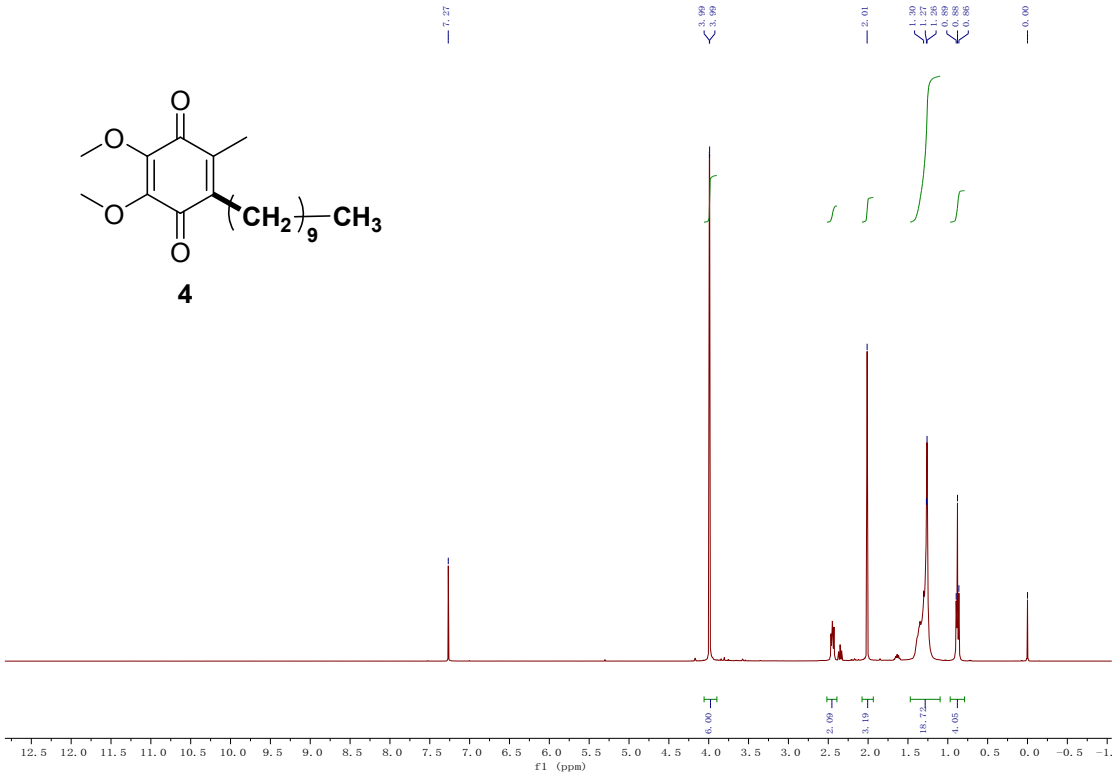
[2] J. Wang, S. Li, T. Yang and J. Yang, Tetrahedron, 2014, 70, 9029-9032.



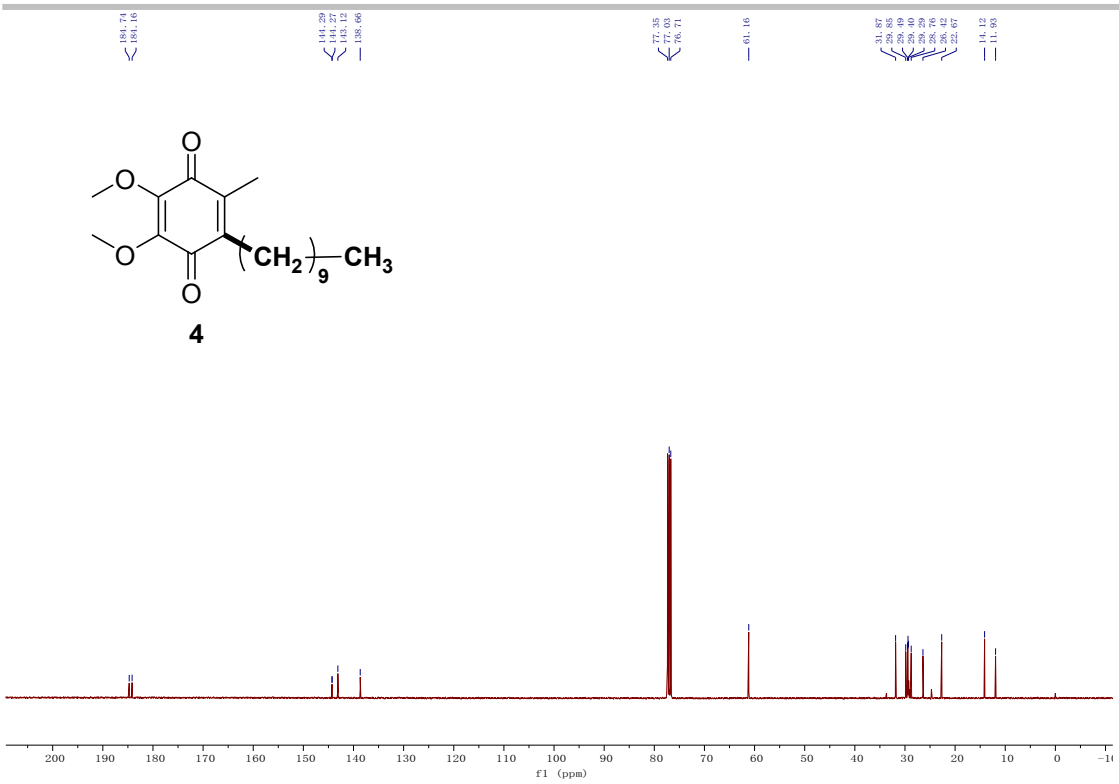
^{1}H NMR spectrum of compound **3**



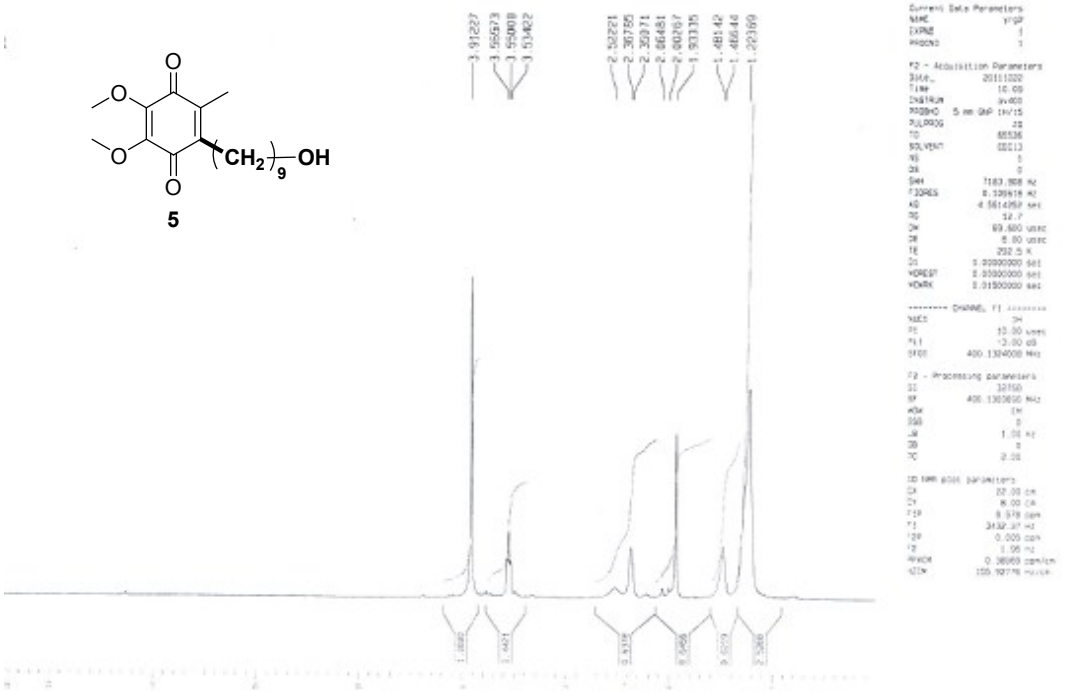
^{13}C NMR spectrum of compound **3**



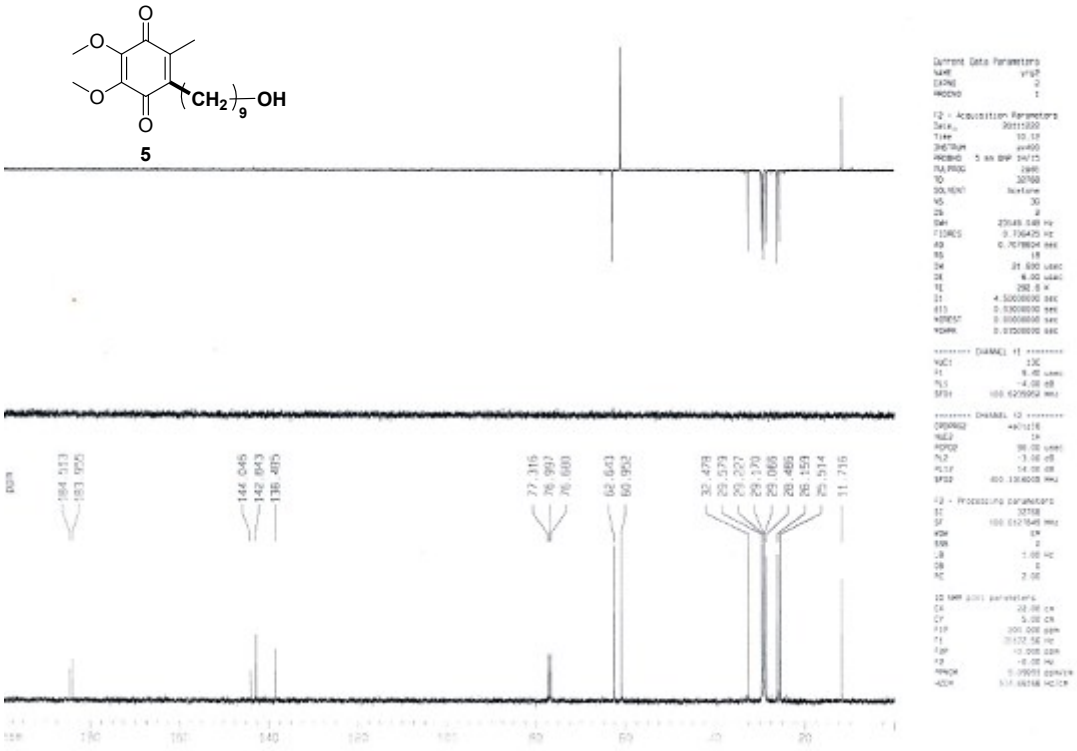
^{1}H NMR spectrum of compound **4**



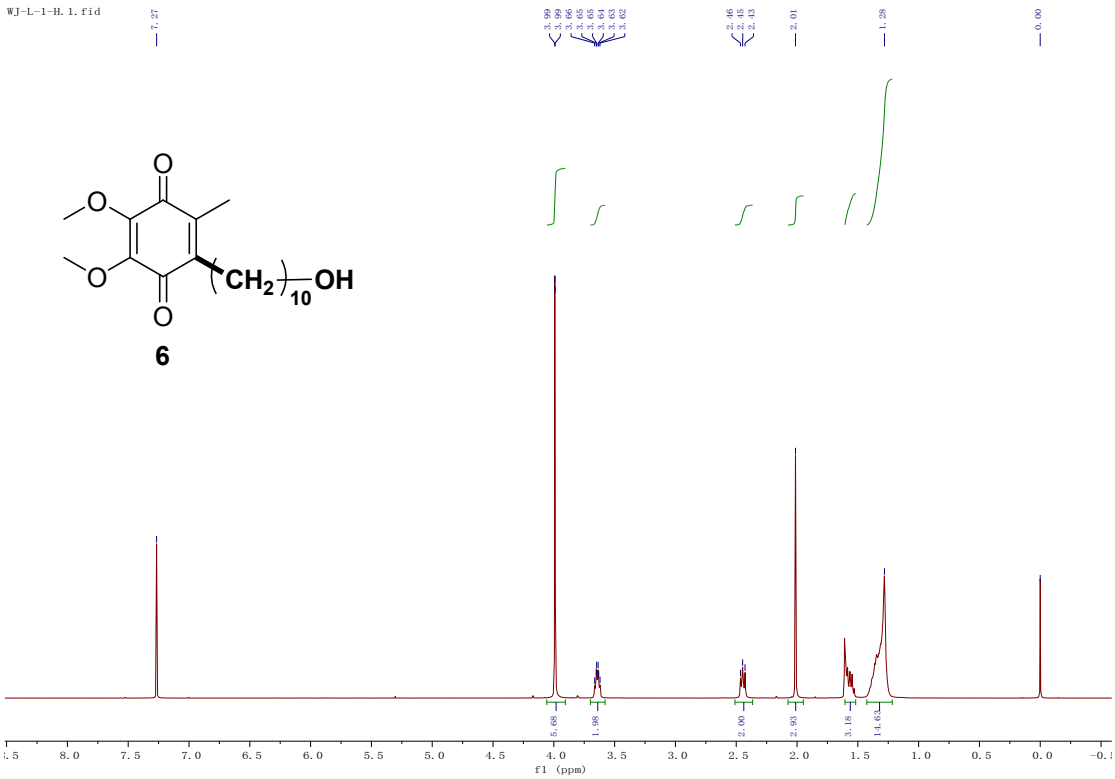
^{13}C NMR spectrum of compound **4**



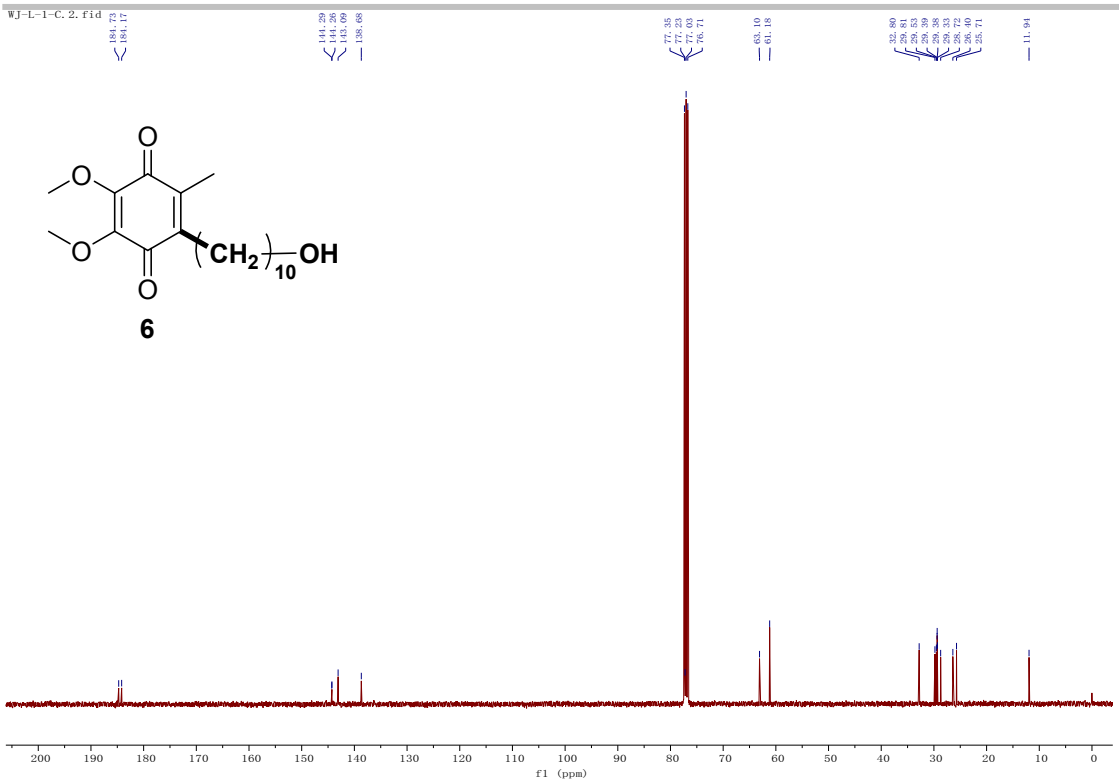
^{1}H NMR spectrum of compound **5**



^{13}C NMR spectrum of compound **5**



^{1}H NMR spectrum of **idebenone (6)**



^{13}C NMR spectrum of **idebenone (6)**