Supplementary Material

Enantioselective synthesis of the side-chain acid of homoharringtonine and harringtonine from the same γ-butyrolactone intermediate

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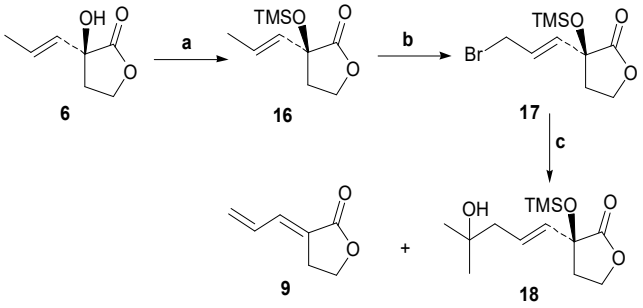
Verification experiment about Barbier coupling

For testing and verifying if the coordination of Zn cation to hydroxyl was the main reason of dehydroxylation during Barbier coupling, the liberated hydroxyl of **6** was protected through the action of TMSOTf and Et_3N, and bromide **17** was prepared in 83% yield over two steps (Scheme **3**).However, byproduct **9** still was produced in approximately 20% yields, while **18** in 65% yields.



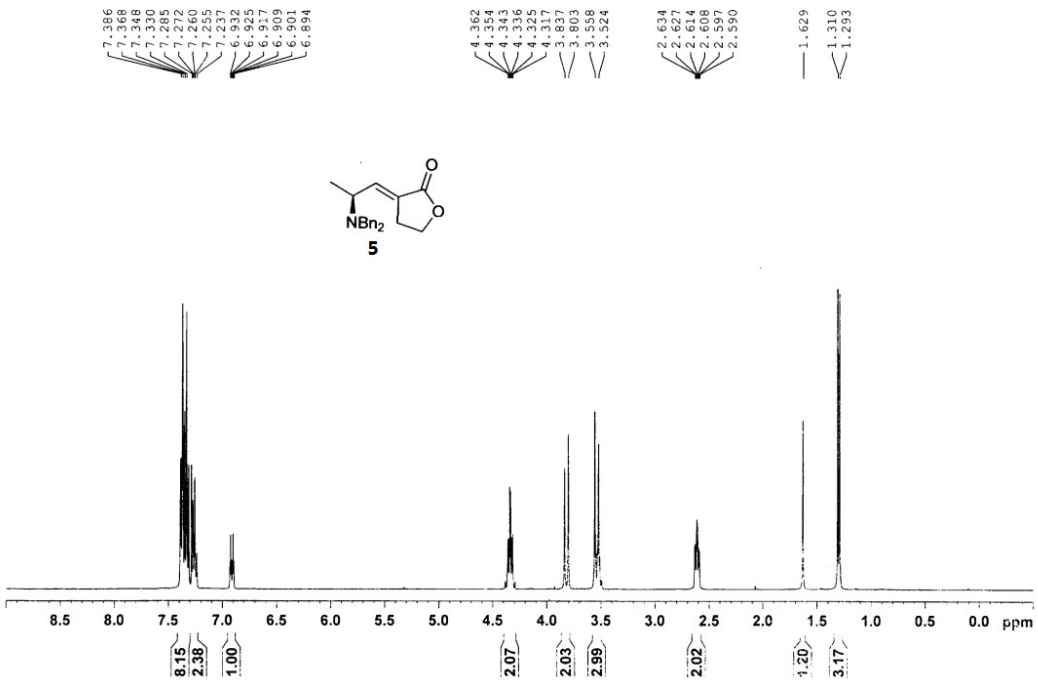
Scheme 3. Efforts to improve Barbier reaction. Reagents and conditions: (**a**) TMSOTf, Et_3N, CH_2Cl_2, 0 °C, 98%; (**b**)NBS, $(PhCO)_2O_2$, CCl_4, reflux, 85%; (**c**) Acetone, Zn, aq.NH_4Cl-DMF, r.t., 65%.

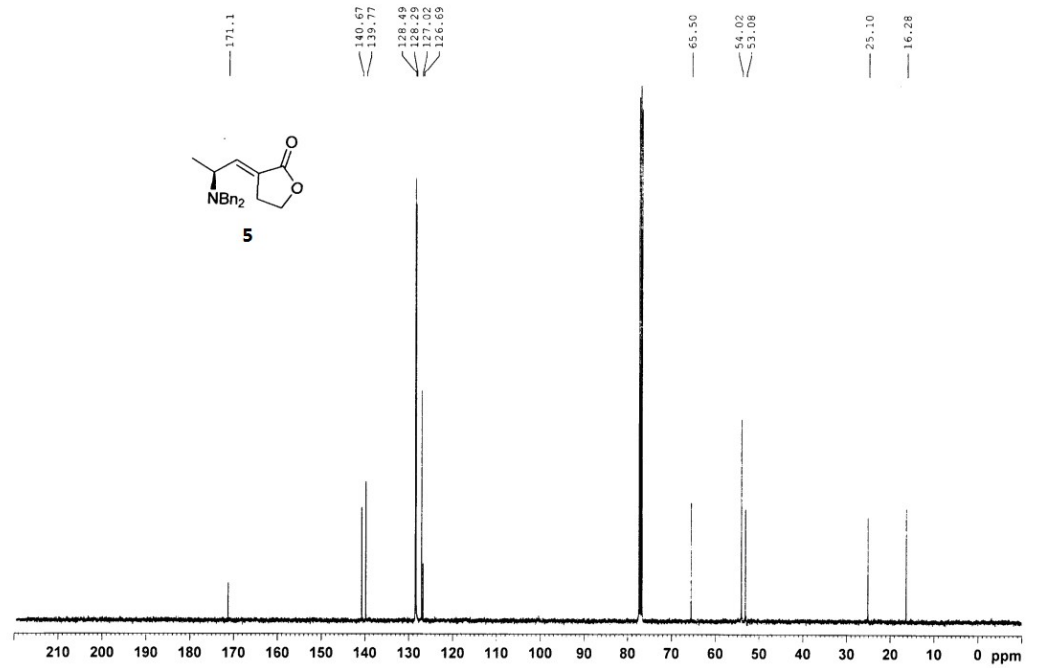
(*S*, *E*)-3-(Prop-1-en-1-yl)-3-((trimethylsilyl)oxy)dihydrofuran-2(3*H*)-one (16): To a solution of allyl alcohol **6** (420 mg, 2.955 mmol) and Et_3N (0.54 mL, 3.842 mmol) in dry CH_2Cl_2 (18 mL) was added TMSOTf (0.70 mL, 3.842 mmol) at 0 °C. Then the reaction mixture was allowed to reach room temperature and the resulting mixture was stirred at this temperature for 30 min. The mixture was extracted with CH_2Cl_2 (3 × 30 mL), washed with saturated brine (2 × 10 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (petroleum ether − EtOAc 30:1) to give **16** (621 mg, 98%) as a colorless liquid. IR (KBr) 1786 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.82 (dq, *J* = 19.4, 6.5 Hz, 1H), 5.65−5.61 (m, 1H), 4.36−4.31 (m, 1H), 4.15−4.09 (m, 1H), 2.45−2.35 (m, 2H), 1.76 (dd, *J* = 6.5, 1.4 Hz, 3H), 0.16 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4(C), 129.6 (CH), 129.1 (CH), 76.9 (C), 64.8 (CH_2), 38.0 (CH_2), 18.0 (CH_3), 2.1(3CH_3); HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{10}H_{18}O_3SiNa$, 237.0923, found 237.0925.

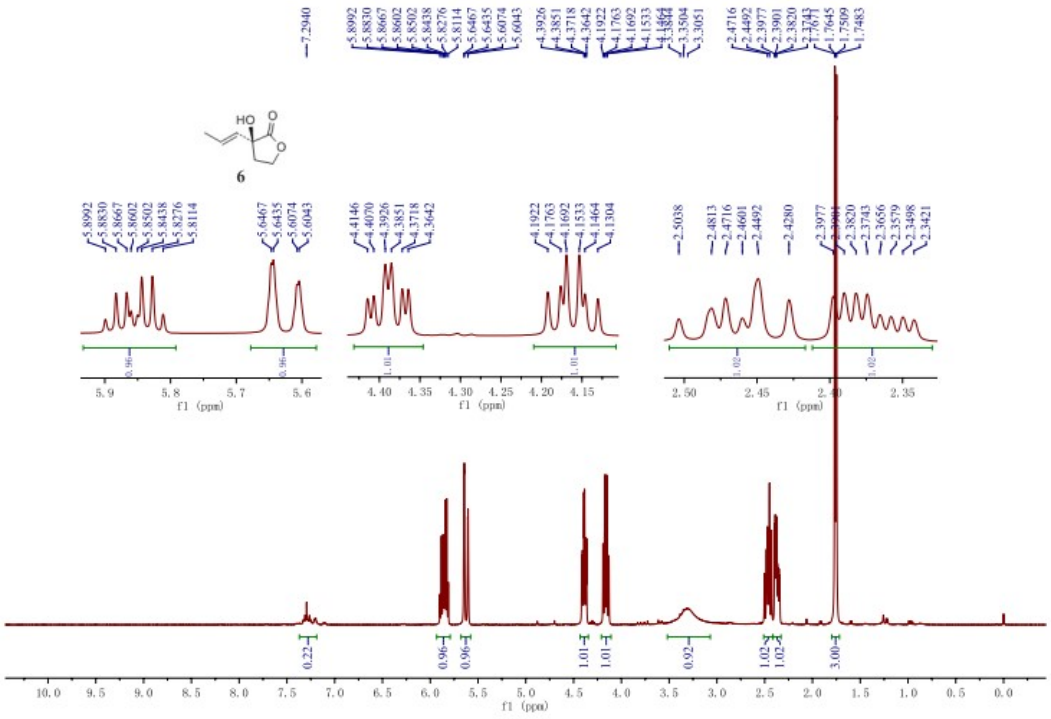
(*S*, *E*)-3-(3-Bromoprop-1-en-1-yl)-3-((trimethylsilyl)oxy)dihydrofuran-2(3*H*)-one (17): To a solution of **16** (693 mg, 3.233 mmol) in dry CCl_4 (8 mL) was added *N*-bromosuccinimide (633 mg, 3.557 mmol) and benzoyl peroxide (39 mg, 0.162 mmol). The reaction was stirred under reflux. After the reaction was complete, the suspension was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography on silica gel (petroleum ether − EtOAc, 20:1) to give **17** (807 mg, 85%) as a pale-yellow oil. IR (KBr) 3441, 1782 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.07−6.00 (m, 1H), 5.91 (d, *J* = 15.5 Hz, 1H), 4.41− 4.36 (m, 1H), 4.22−4.16 (m, 1H), 3.97 (dd, *J* = 7.2, 0.6 Hz, 2H), 2.48−2.36 (m, 2H), 0.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6 (C), 132.98 (CH), 129.04 (CH), 76.4 (C), 65.02 (CH_2), 38.04 (CH_2), 31.08 (CH_2), 2.0 (3CH_3); HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{10}H_{17}O_3BrSiNa$, 315.0028, found 315.0027.

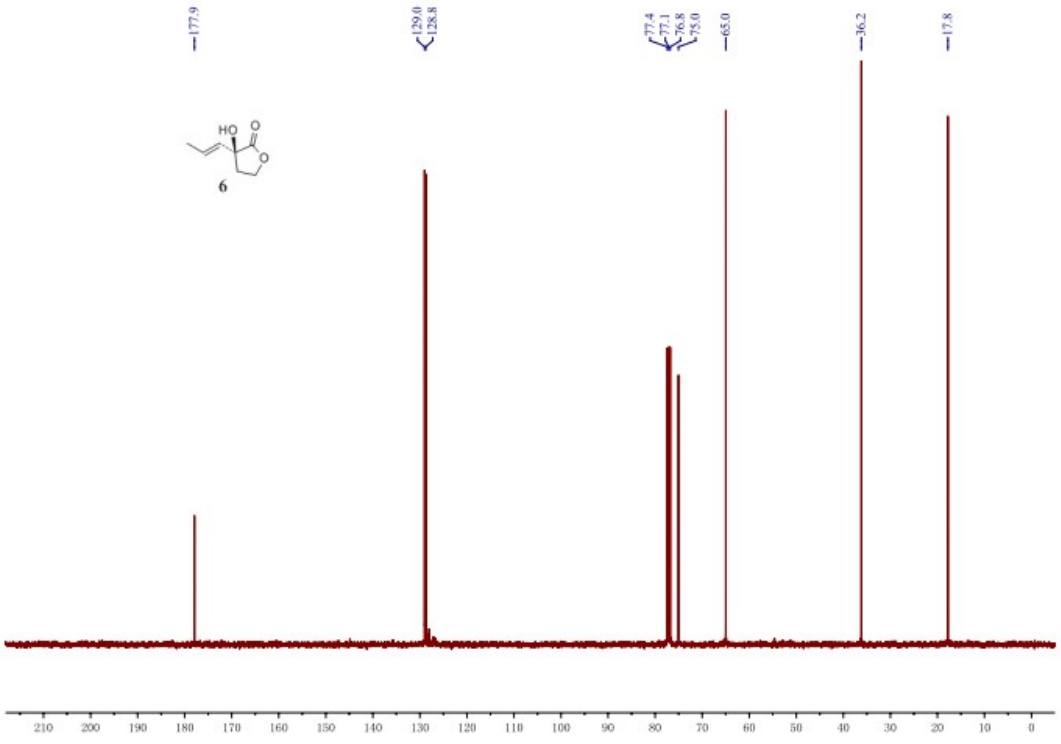
(*S*, *E*)-3-(4-Hydroxy-4-methylpent-1-en-1-yl)-3-((trimethylsilyl)oxy)dihydrofuran-2(3 *H*)-one

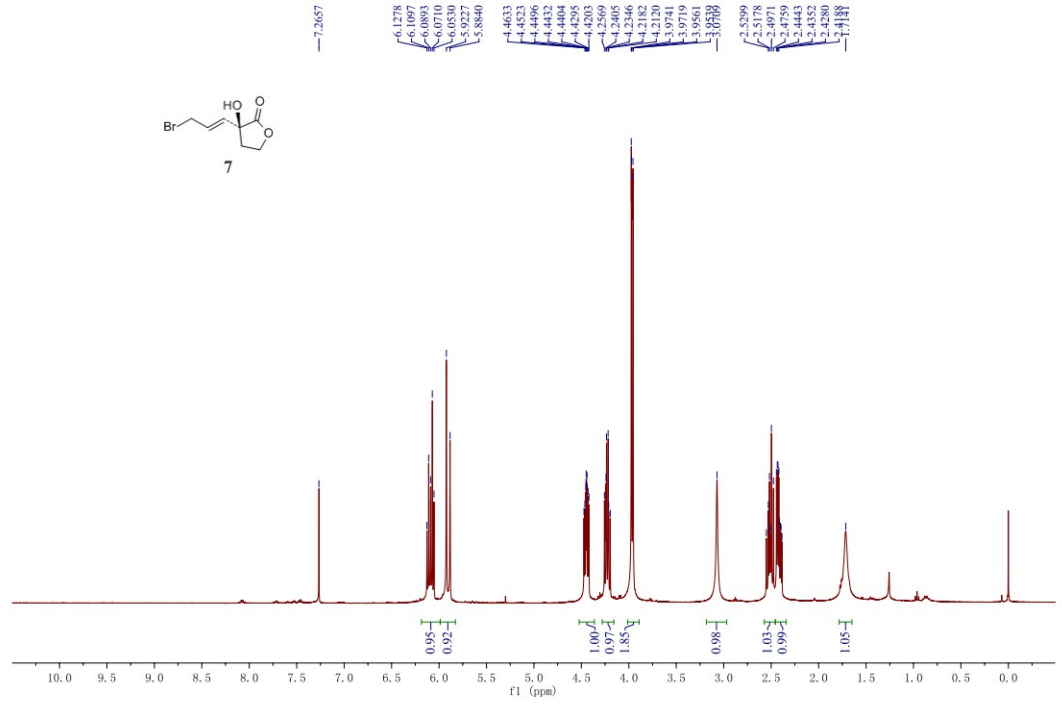
(18): The experimental procedure was as the same as that described for the preparation of **8** from bromide **7**. The compound **18** (661 mg, 65 %) was obtained as a colorless oil. IR (KBr): 3439, 1735, 1654, 1637, 1618 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89−5.81 (m, 1H), 5.67 (d, *J* = 15.8 Hz, 1H), 4.36−4.31 (m, 1H), 4.16–4.10 (m, 1H), 2.44−2.35 (m, 2H), 2.25 (d, *J* = 7.3 Hz, 2H), 1.20 (d, *J* = 2.6 Hz, 6H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1 (C), 131.7 (CH), 129.3 (CH), 76.7, 70.6, 64.7, 46.6 (CH_2), 37.9 (CH_2), 29.2 (CH_3), 29.3 (CH_3), 1.8 (CH_3); HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{13}H_{24}O_4SiNa$ 295.1342, found 295.1340.

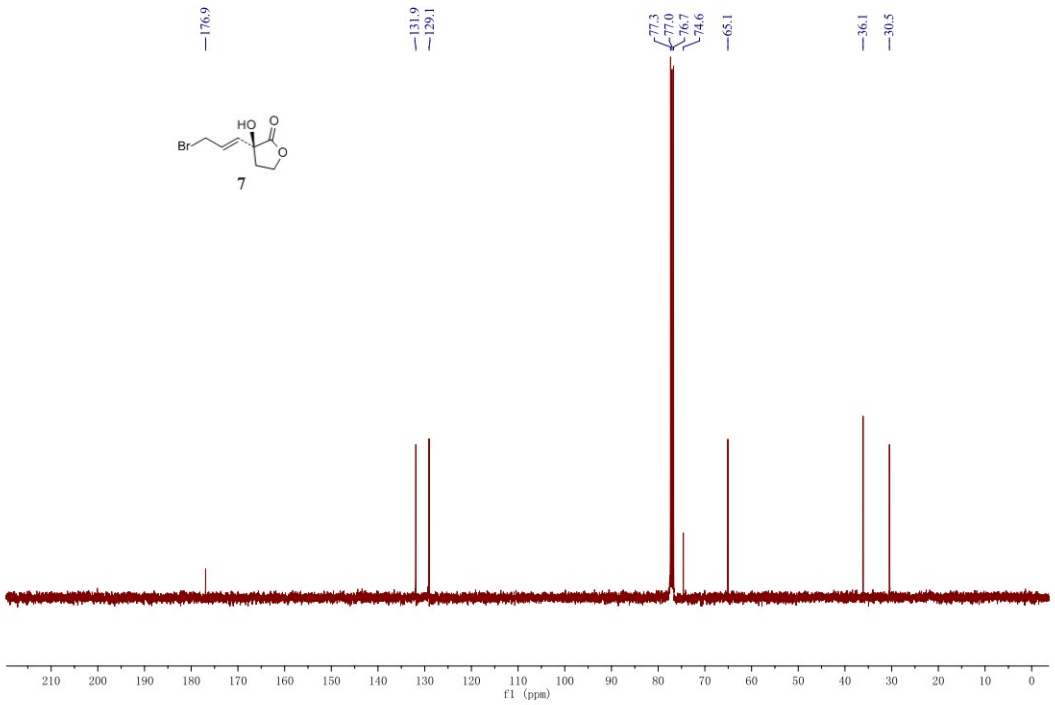


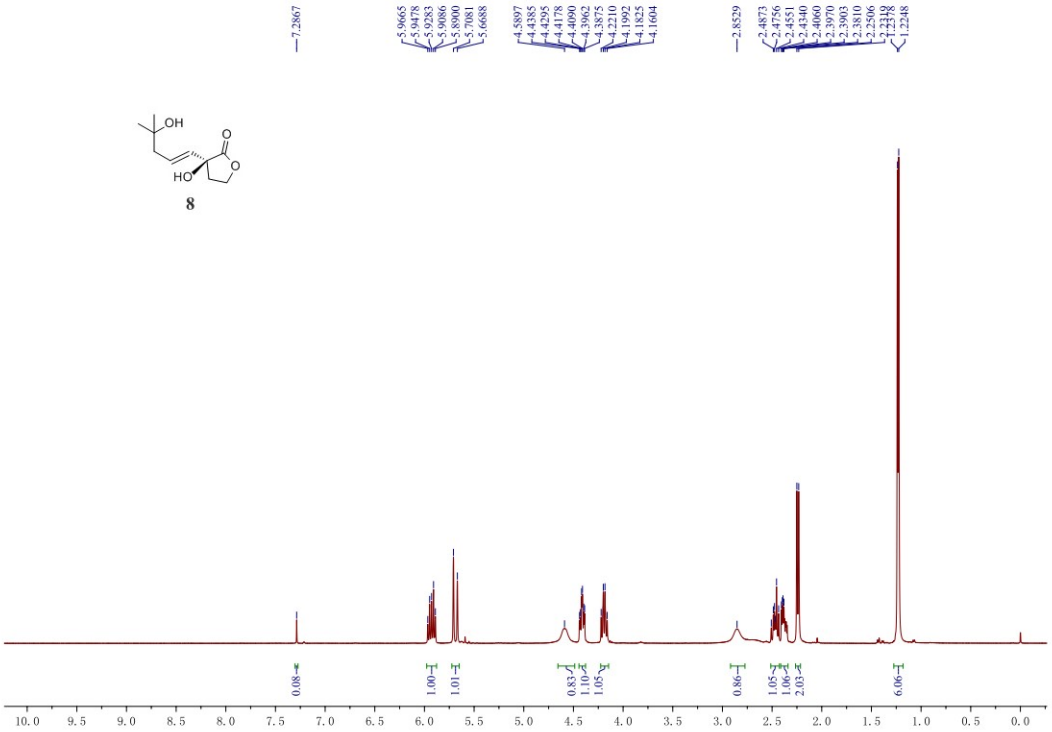


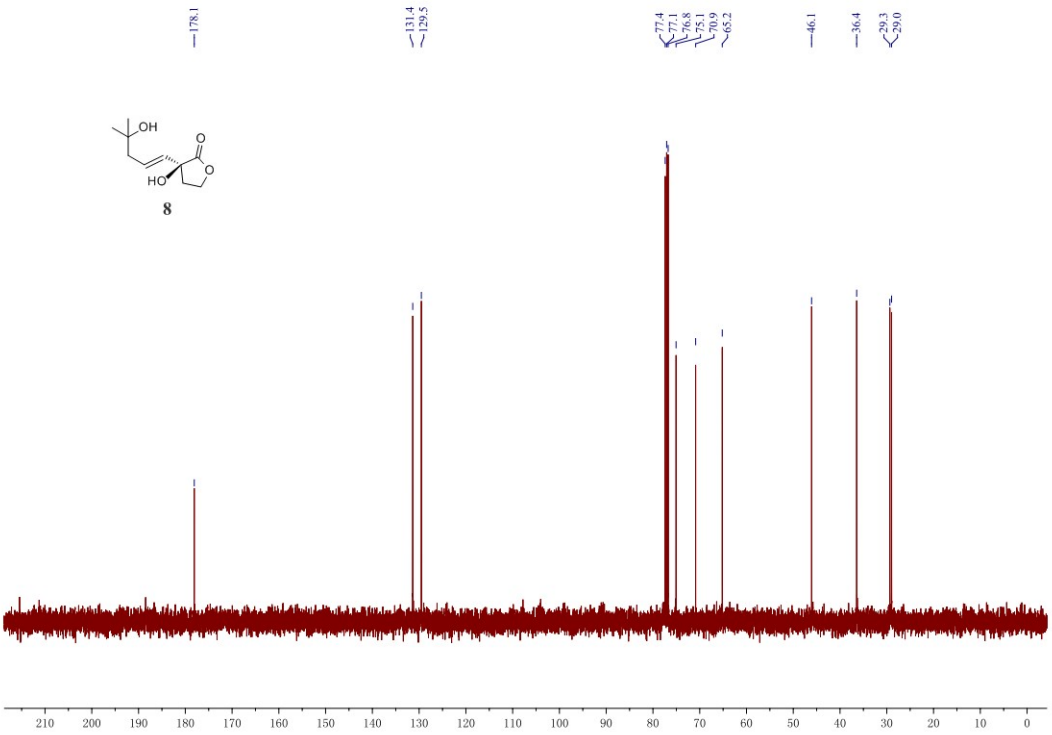


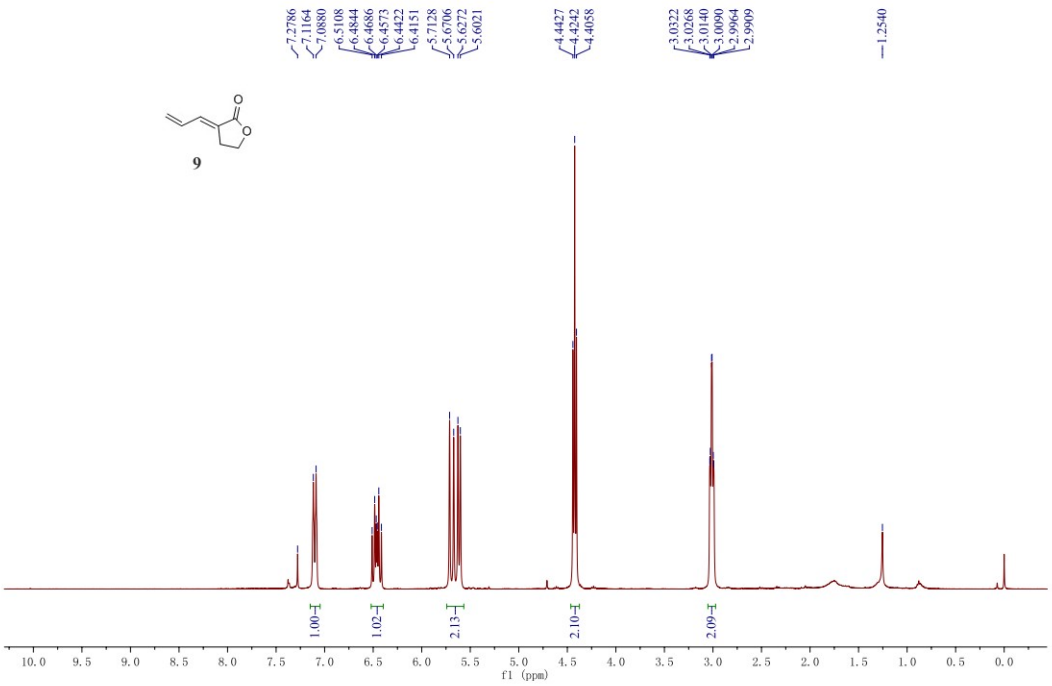


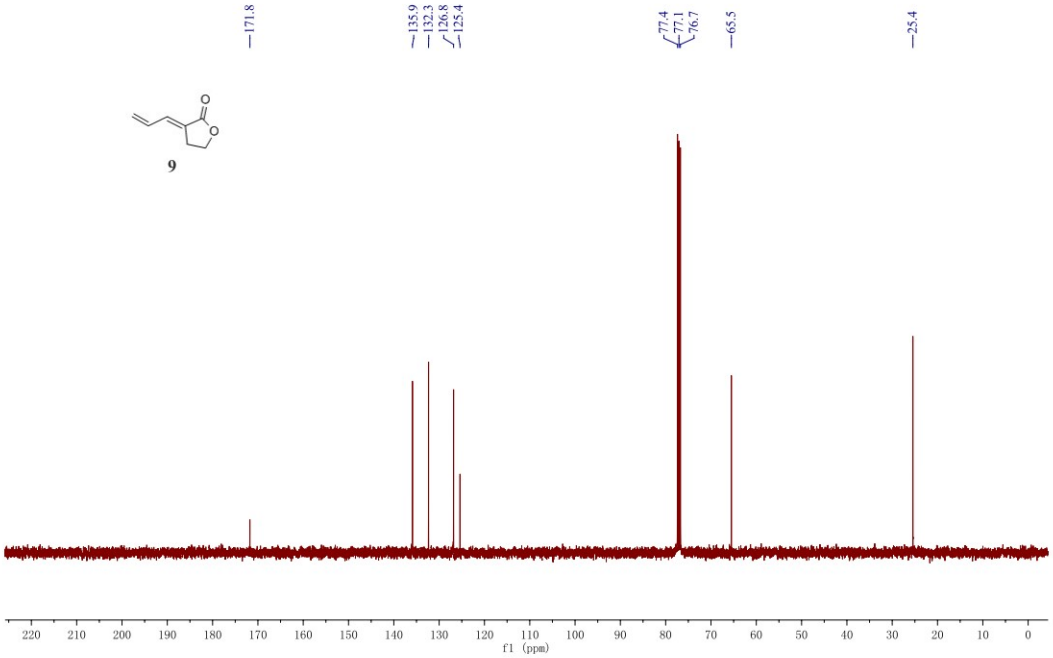


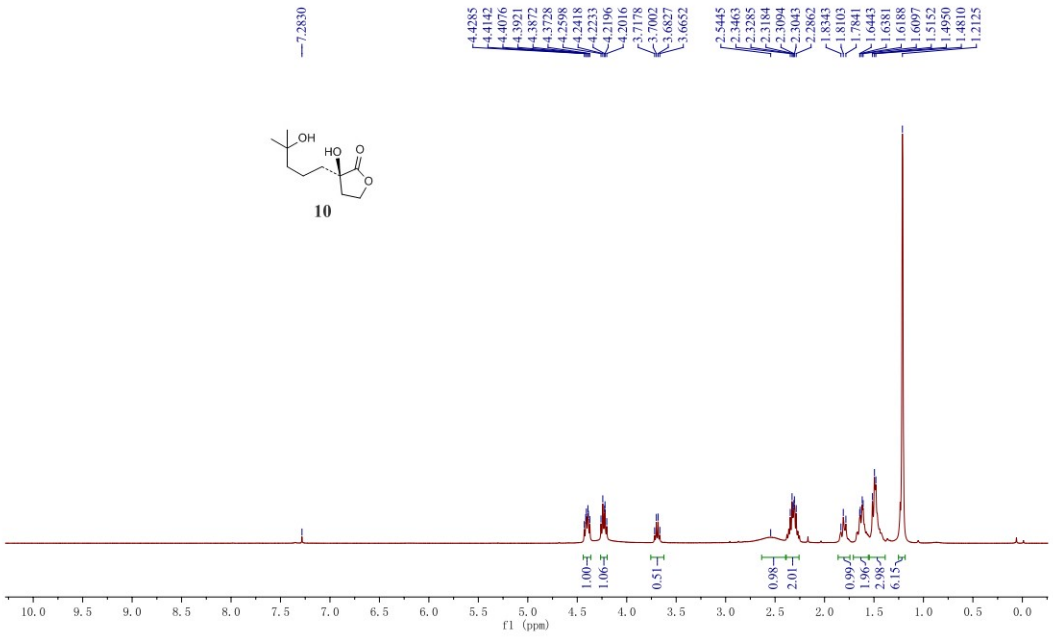


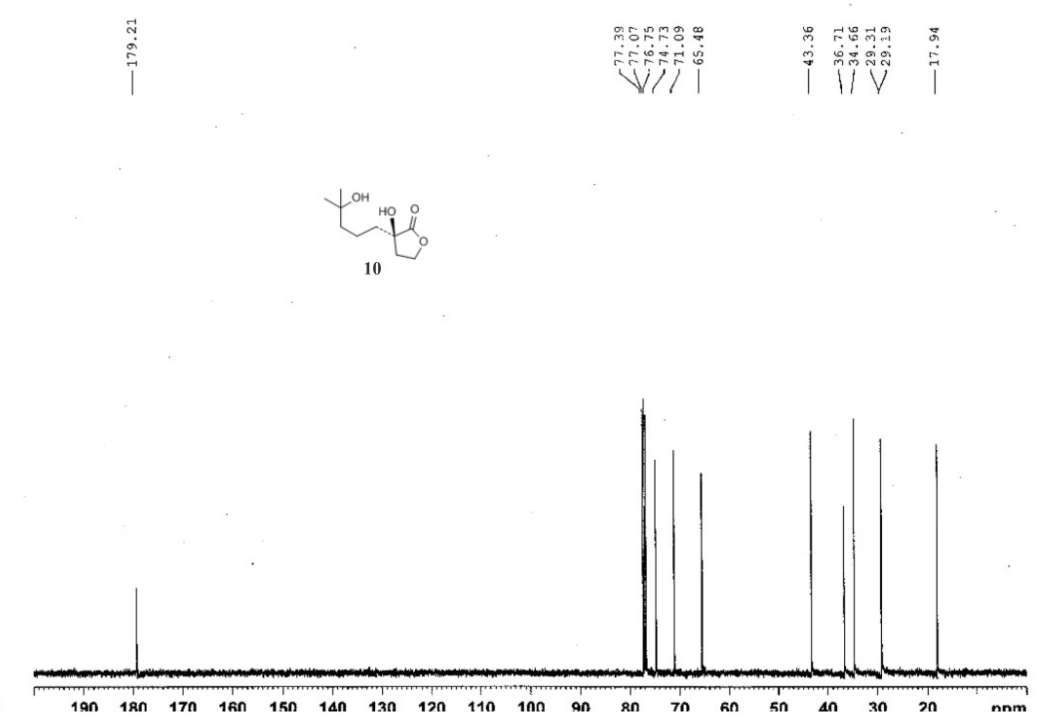


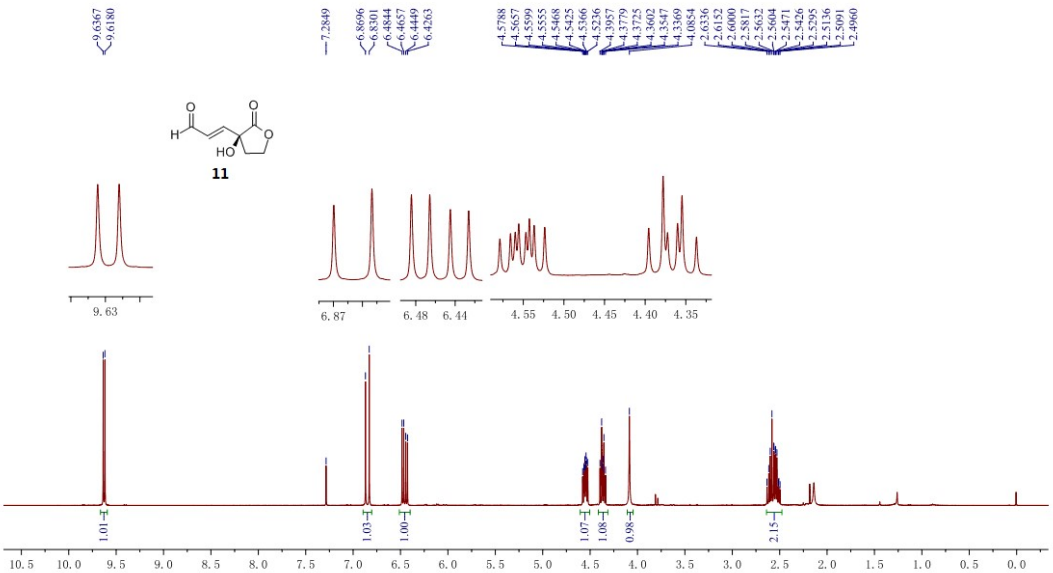


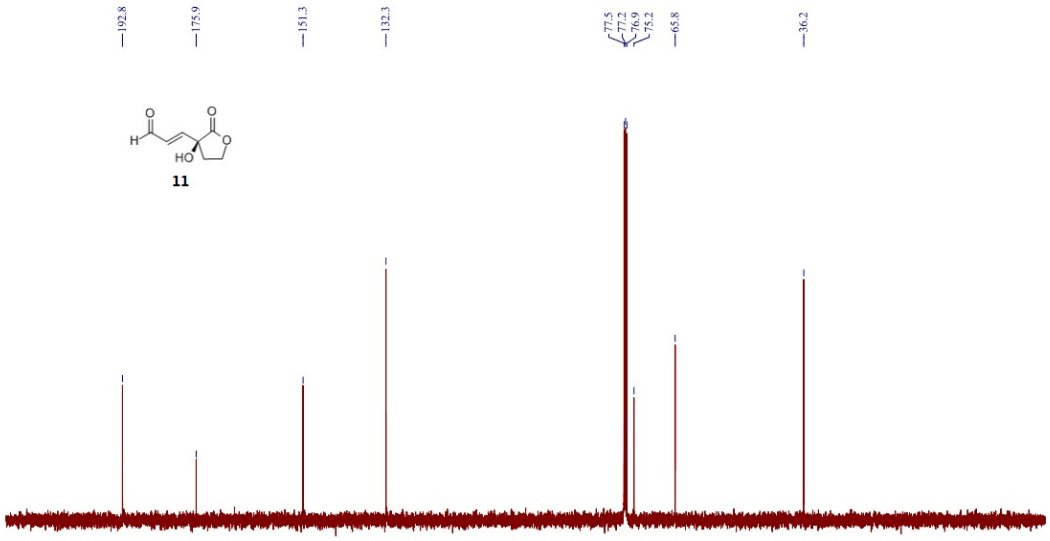


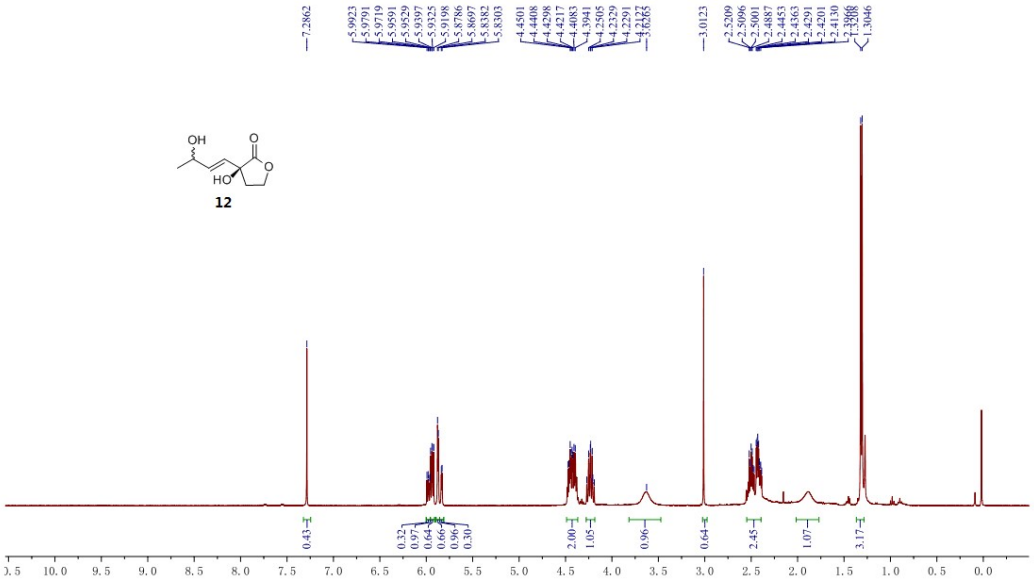


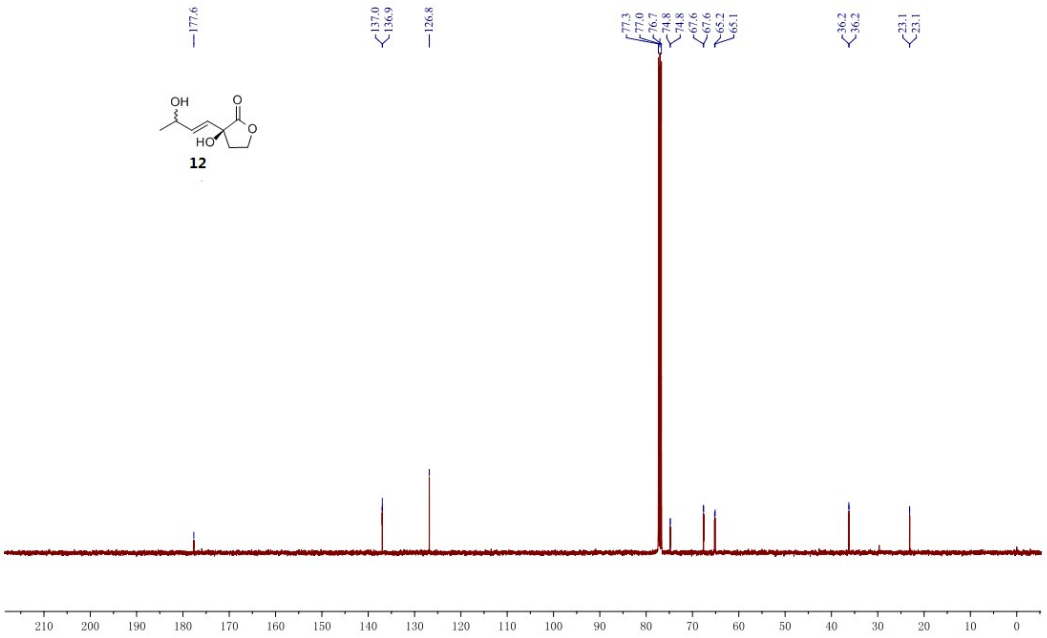


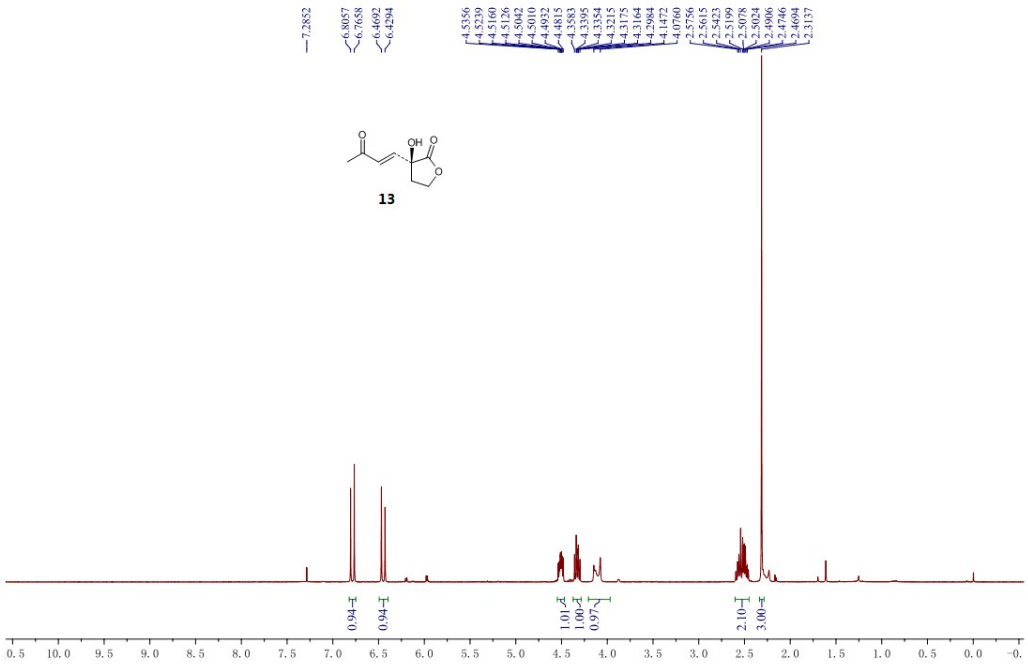


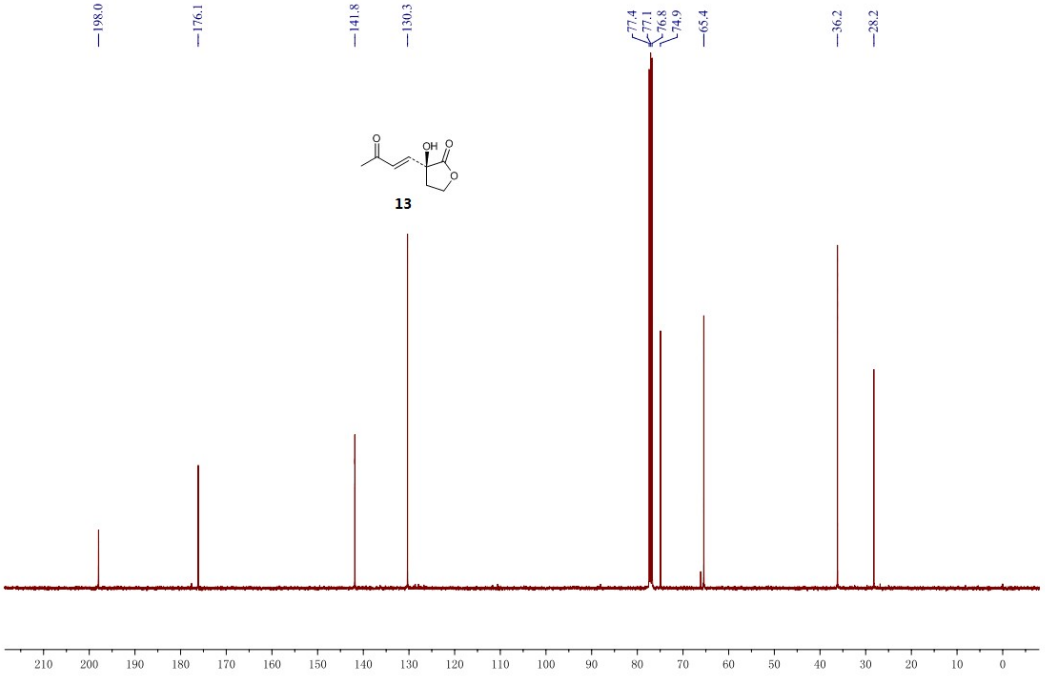


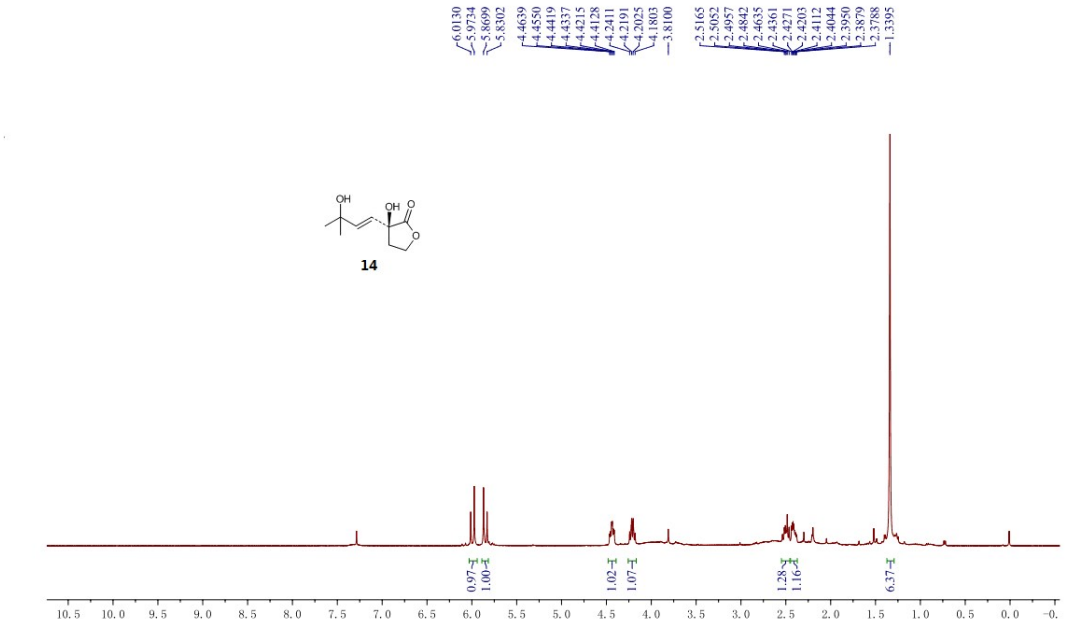


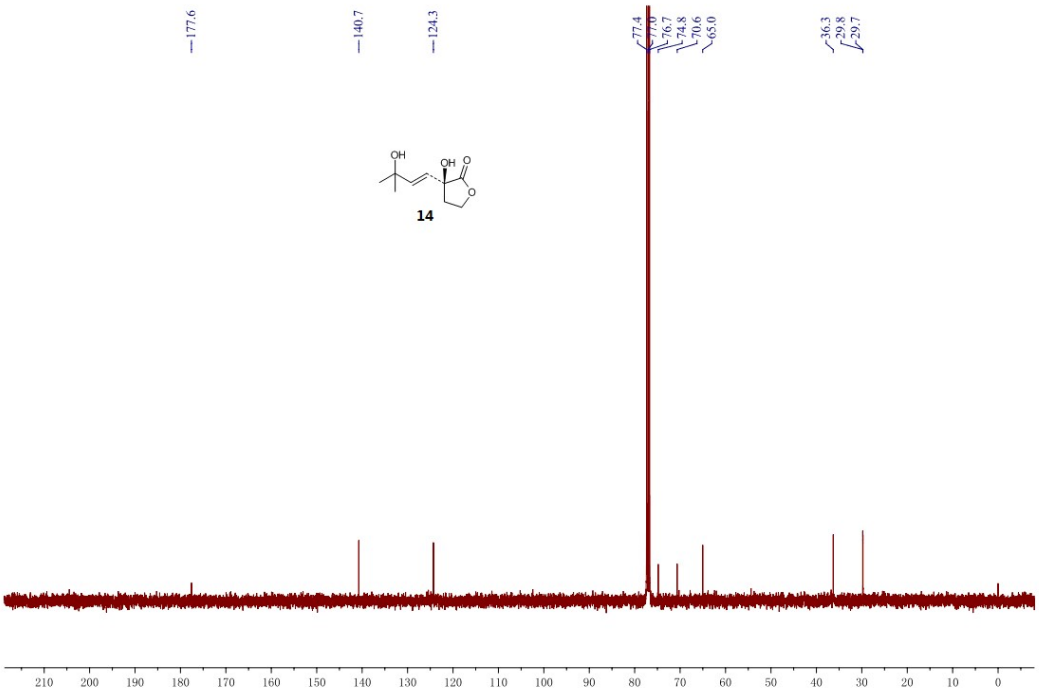


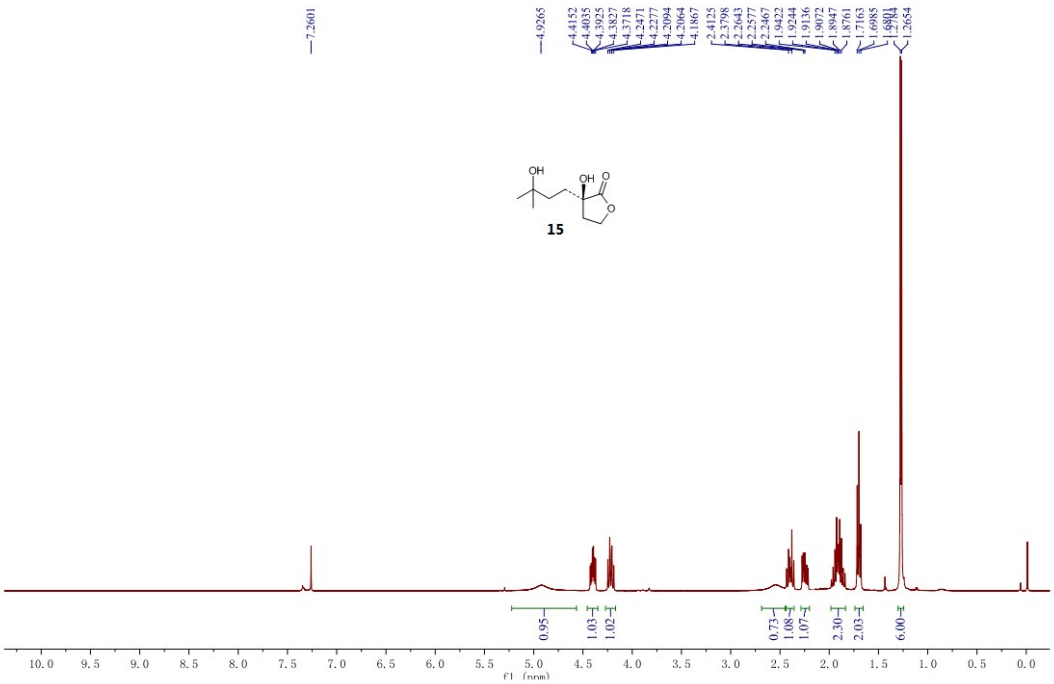


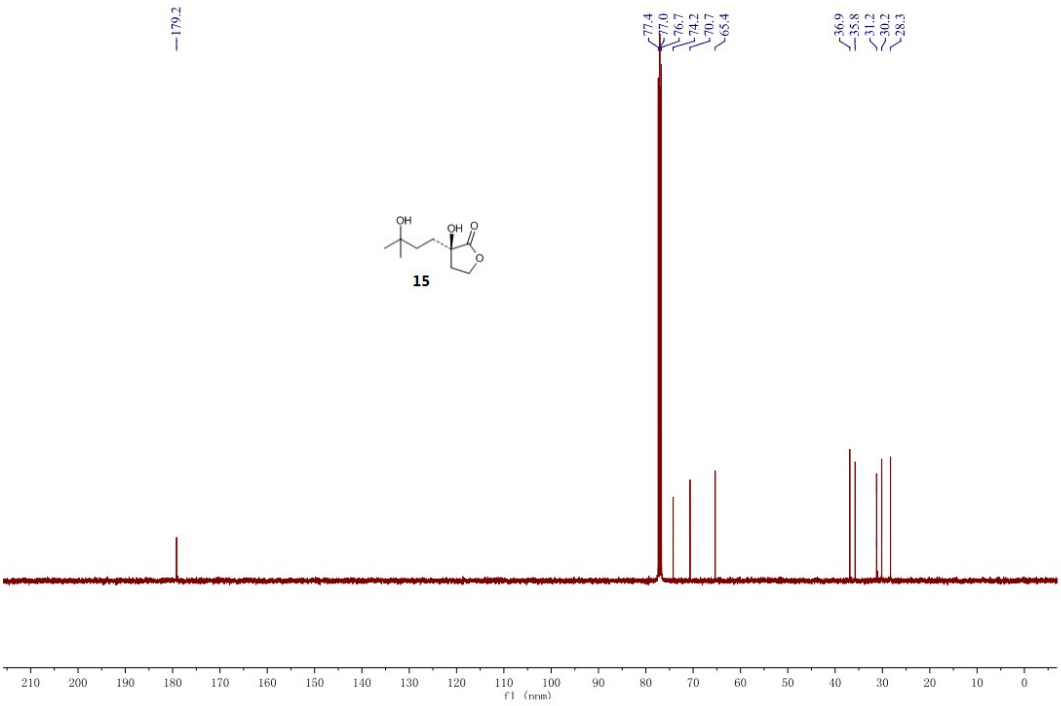


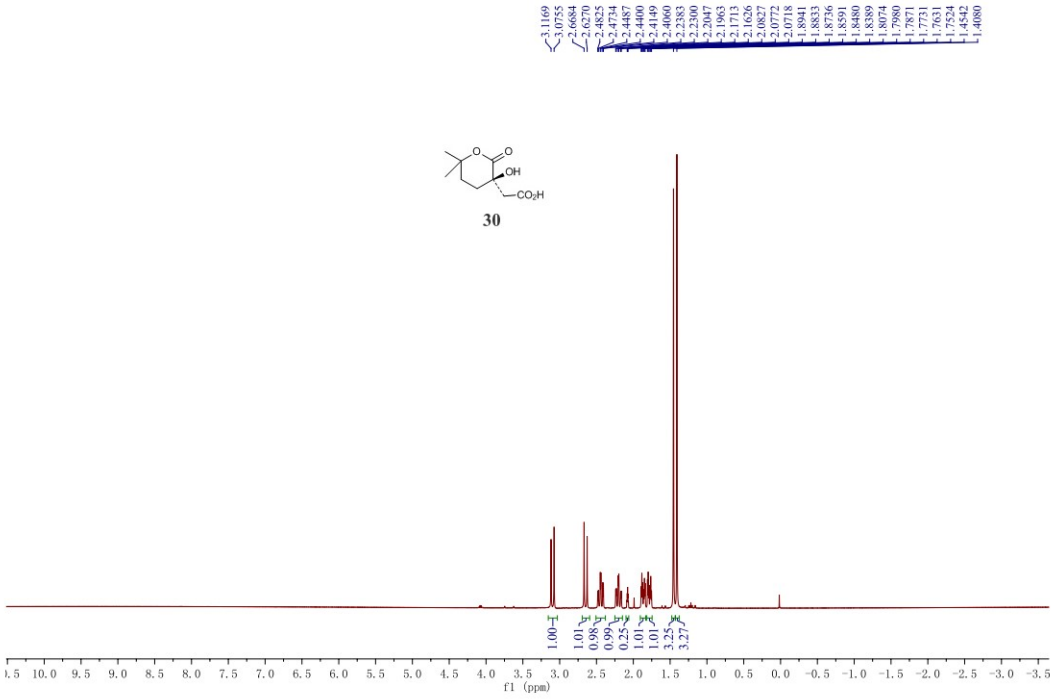


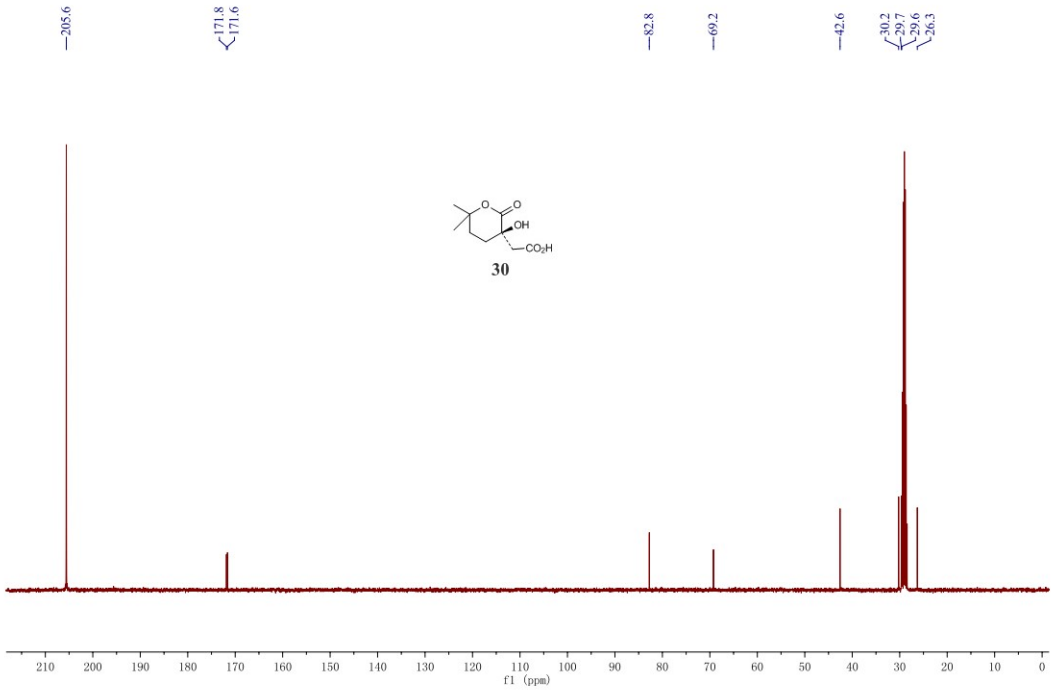












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