Supporting Information

Decarboxylative C_{sp}^3-C_{sp}^3 Coupling for Benzylation of Unstabilized Ketone Enolates: Synthesis of *p*-(Acylethyl)phenols

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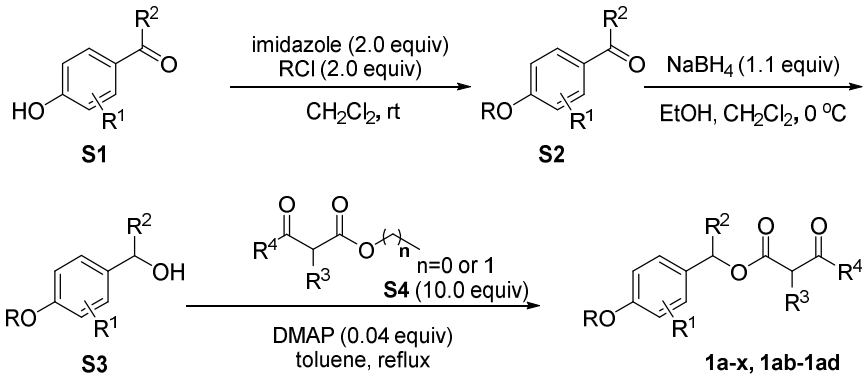
I. General Information

All chemicals were purchased commercially, and used without further purification unless otherwise noted. All reactions were carried out under room temperature unless otherwise noted. Toluene, tetrahydrofuran, and ether were distilled from sodium. 1,2-Dichloroethane and acetonitrile were distilled from calcium hydride. Flash column chromatography was performed on Tsingdao silica gel (60, particle size 0.040–0.063 mm). Thin-layer chromatography (TLC) was carried out on 0.25 mm Huanghai silica gel plates (HSGF-254) and visualized by exposure to UV light (254 nm) and/or $KMnO_4$ (aq.) was used as revealing system. ^1H and ^{13}C NMR Spectra were registered on Bruker spectrometers (300, 400 or 500 MHz for ^1H NMR; 75, 100 or 125 MHz for ^{13}C NMR). Chemical shifts were reported in δ units by assigning $CHCl_3$ [^1H δ = 7.26, ^{13}C δ = 77.36] or TMS [^1H δ = 0.00, ^{13}C δ = 0.00] resonance. Data for ^1H NMR spectra were reported as following: chemical shift (δ/ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.), coupling constant (*J*/Hz) and integration. Data for ^{13}C NMR spectra were reported in terms of the chemical shift. IR spectra were recorded on a Shimadzu IRPrestige-21 and were reported in terms of frequency of absorption (cm^{-1}). High-resolution mass spectrometry (HRMS) was conducted on Bruker Apex IV RTMS. Gas chromatograph mass spectrometer (GC-MS) was performed on Agilent 6890N-5975. X-ray diffraction was performed on Rigaku Saturn 70 CCD diffractometer using graphite monochromated Cu-Kα radiation at a temperature of 100 ±1 K. Crystallographic data were obtained from Oxford diffraction single crystal X-ray diffractometer (Gemini S Ultra).

II. Experimental Procedure

General procedure for preparation of *β*–ketoester (1a-x, 1ab-1ad):

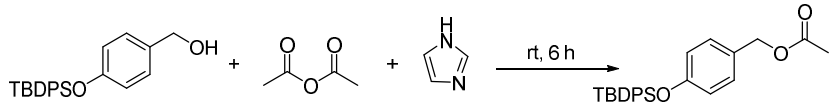


R = silyl group, DMAP = 4-dimethylaminopyridine

To a solution of *para*- or *ortho*-hydroxybenzaldehyde (16.4 mmol) in CH_2Cl_2 (50 mL), imidazole (2.23 g, 32.8 mmol, 2.0 equiv) was dissolved under N_2. After being stirred at room temperature for 3 h, RCl (32.8 mmol, 2.0 equiv) was added. The resulting mixture was stirred overnight and quenched with water. The aqueous phase was extracted with CH_2Cl_2 (50 mL × 3). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated at reduced pressure. Purification of the residue by flash chromatography (hexanes/EtOAc = 200:1 to 50:1) afforded **S2** as a pale yellow oil.

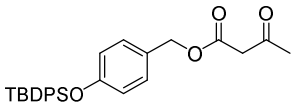
In an oven-dried round-bottomed flask, aldehyde **S2** (11.0 mmol) was dissolved in freshly distilled CH_2Cl_2 (50 mL) at 0 °C. Then a solution of $NaBH_4$ (0.458 g, 12.1 mmol, 1.1 equiv) in EtOH (20 mL) was added. The mixture was stirred vigorously for 45 min at 0 °C. Then the reaction was quenched with water. The aqueous phase was extracted by CH_2Cl_2 (50 mL × 3). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated at reduced pressure. The residue was purified by column chromatography (silica gel, hexanes/EtOAc = 50:1 to 20:1) to afford **S3**.

To a stirred solution of **S3** (4.14 mmol) and DMAP (20.8 mg, 0.17 mmol, 0.04 equiv) in toluene (40 mL) was added *β*–ketoester **S4** (41.4 mmol, 10.0 equiv) [2] under N_2. The resulting solution was refluxed for 1 to 3 days before being concentrated under reduced pressure. Then water was added to the residue and the aqueous phase was extracted with EtOAc (50 mL × 5). The combined organic phases were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated at reduced pressure. Then vacuum distillation was applied to remove the remaining ethyl acetoacetate. The residue was purified by column chromatography (silica gel, hexanes/EtOAc = 60:1 to 20:1) to afford **1**.



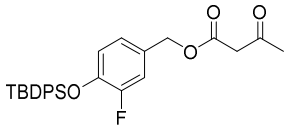
S3' **1aa**

Preparation of 1aa:[3] Substrate **S3'** was prepared according to the procedure described above. To a mixture of **S3'** (1.0 g, 2.76 mmol) and imidazole (15.0 mg, 0.22 mmol, 0.08 equiv) was added acetic anhydride (564 mg, 5.52 mmol, 2.0 equiv). The mixture was stirred overnight. Then the residue was purified by column chromatography (silica gel, hexanes/EtOAc = 30:1) to afford **1aa** (0.12 g, 61%) as a pale yellow solid.



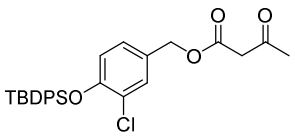
1a

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl 3-oxobutanoate (1a): 0.777 g (34% yield for 3 steps, crystalline solid), mp. 38–46 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.0, 1.3 Hz, 4H), 7.44–7.42 (m, 2H), 7.39–7.36 (m, 4H), 7.11 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 8.5 Hz, 2H), 5.05 (s, 2H), 3.45 (s, 2H), 2.21 (s, 3H), 1.12 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.3, 166.9, 155.9, 135.5, 132.7, 129.9, 129.9, 127.8, 119.8, 119.7, 66.9, 50.1, 30.0, 26.5, 19.4. IR (KBr) 3072, 3050, 2959, 2932, 2893, 2858, 1962, 1890, 1746, 1720, 1610, 1515, 1429, 1361, 1314, 1257, 1170, 1149, 1113, 918, 823, 744, 702, 612, 502 cm^{-1}. HRMS (ESI) calculated for $C_{27}H_{30}O_4NaSi$ $(M + Na)^+$: 469.1811, found: 469.1806.



1b

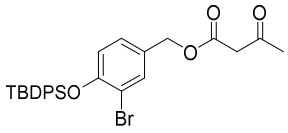
4-((*tert*-Butyldiphenylsilyl)oxy)-3-fluorobenzyl 3-oxobutanoate (1b): 0.189 g (26% yield for 3 steps, pale yellow oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 8.0, 1.2 Hz, 4H), 7.47–7.41 (m, 2H), 7.38 (t, *J* = 7.2 Hz, 4H), 7.06 (dd, *J* = 11.1, 2.0 Hz, 1H), 6.75 (d, *J* = 8.3 Hz, 1H), 6.61 (t, *J* = 8.4 Hz, 1H), 5.02 (s, 2H), 3.46 (s, 2H), 2.22 (s, 3H), 1.14 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.2, 166.8, 154.5 (d, *J* = 245), 143.6 (d, *J* = 12.5), 135.4, 132.4, 130.1, 128.7 (d, *J* = 6.25), 127.8, 124.1 (d, *J* = 3.75), 121.3 (*d*, *J* = 1.25), 116.7 (d, *J* = 18.75), 66.3, 50.0, 30.1, 26.5, 19.6. IR (KBr) 3013, 2960, 2933, 2894, 2858, 2375, 2346, 2311, 1734, 1715, 1517, 1362, 1301, 1260, 1224, 1148, 1124, 1115, 908, 897, 821, 701 cm^{-1}. HRMS (ESI) calculated for $C_{27}H_{29}FNaO_4Si$ $(M + Na)^+$: 487.1717, found: 487.1711.



1c

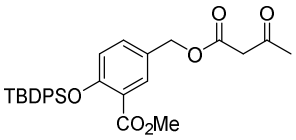
4-((*tert*-Butyldiphenylsilyl) oxy)-3-chlorobenzyl 3-oxobutanoate (1c): 1.15 g (19% yield for 3 steps, yellow oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 8.0, 1.3 Hz, 4H), 7.46–7.43 (m, 2H), 7.38 (m, 5H), 6.81 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.47 (d, *J*

= 8.4 Hz, 1H), 5.00 (s, 2H), 3.45 (s, 2H), 2.22 (s, 3H), 1.13 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.0, 166.7, 151.5, 135.4, 134.8, 132.2, 130.4, 130.1, 127.8, 127.5, 125.1, 120.0, 66.1, 50.0, 30.0, 26.4, 19.7. IR (KBr) 3052, 2959, 2933, 2894, 2860, 1739, 1722, 1717, 1645, 1606, 1501, 1429, 1293, 1263, 1149, 1114, 1060, 929, 822, 701, 502 cm^{-1}. HRMS (ESI) calculated for $C_{27}H_{29}ClNaO_4Si$ $(M + Na)^+$: 503.1421, found: 503.1417.



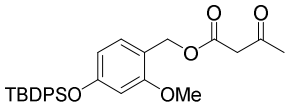
1d

3-Bromo-4-((*tert*-butyldiphenylsilyl)oxy)benzyl 3-oxobutanoate (1d): 0. 25 g (25% yield for 3 steps, pale yellow oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.1 Hz, 4H), 7.57 (d, *J* = 1.8 Hz, 1H), 7.44 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 4H), 6.85 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.44 (d, *J* = 8.4 Hz, 1H), 5.00 (s, 2H), 3.46 (s, 2H), 2.22 (s, 3H), 1.15 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.1, 166.8, 152.5, 135.4, 133.5, 132.0, 130.1, 129.1, 128.3, 127.9, 119.7, 114.6, 66.0, 50.0, 30.0, 26.4, 19.7. IR (KBr) 3015, 2954, 2928, 2856, 1674, 1615, 1596, 1516, 1506, 1456, 1394, 1262, 1221, 1173, 1108, 1082, 1031, 1012, 827 cm^{-1}. HRMS (ESI) calculated for $C_{27}H_{29}BrNaO_4Si$ $(M + Na)^+$: 547.0916, found: 547.0912.



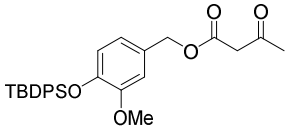
1e

Methyl 2-((*tert*-butyldiphenylsilyl)oxy)-5-(((3-oxobutanoyl)oxy)methyl)benzoate (1e): 1.25 g (45% yield for 3 steps, yellow oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 2.4 Hz, 1H), 7.73 (dd, *J* = 8.0, 1.3 Hz, 4H), 7.45–7.40 (m, 2H), 7.38 (t, *J* = 7.2 Hz, 4H), 7.03 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.47 (d, *J* = 10 Hz, 1H), 5.04 (s, 2H), 3.91 (s, 3H), 3.45 (s, 2H), 2.21 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.2, 167.0, 166.8, 155.0, 135.4, 132.9, 132.1, 131.8, 130.1, 127.9, 127.4, 122.3, 120.8, 66.3, 52.0, 50.0, 30.0, 26.1, 19.5. IR (KBr) 2953, 2932, 2894, 2856, 1714, 1616, 1498, 1429, 1326, 1260, 1206, 1147, 1114, 1083, 923, 702, 501 cm^{-1}. HRMS (ESI) calculated for $C_{29}H_{32}NaO_6Si$ $(M + Na)^+$: 527.1866, found: 527.1862



1f

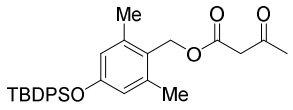
4-((*tert*-Butyldiphenylsilyl)oxy)-2-methoxybenzyl 3-oxobutanoate (1f): 1.52 g (24% yield for 3 steps, pale yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.9, 1.5 Hz, 4H), 7.49–7.33 (m, 6H), 7.03 (d, *J* = 8.2 Hz, 1H), 6.35 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.29 (d, *J* = 2.2 Hz, 1H), 5.09 (s, 2H), 3.52 (s, 3H), 3.43 (s, 2H), 2.22 (s, 3H), 1.13 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.6, 167.1, 158.5, 157.4, 135.4, 132.6, 131.2, 129.9, 127.8, 115.9, 111.3, 103.1, 62.6, 55.1, 50.1, 29.9, 26.5, 19.4. IR (KBr) 3073, 3050, 3015, 2959, 2933, 2893, 2859, 1723, 1714, 1609, 1587, 1511, 1464, 1428, 1362, 1296, 1218, 1166, 1114, 1036, 982, 857, 839, 822, 701, 501 cm^{-1}. HRMS (ESI) calculated for $C_{28}H_{32}NaO_5Si$ $(M + Na)^+$: 499.1917, found: 499.1911.



1g

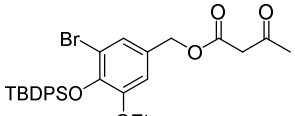
4-((*tert*-Butyldiphenylsilyl)oxy)-3-methoxybenzyl 3-oxobutanoate (1g): 1.10g (33% yield for 3 steps, pale yellow oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.0, 1.4 Hz, 4H), 7.43–7.37 (m, 2H), 7.34 (dd, *J* = 11.3, 4.3 Hz, 4H), 6.78 (d, *J* = 1.8

Hz, 1H), 6.70–6.62 (m, 2H), 5.04 (s, 2H), 3.59 (s, 3H), 3.46 (s, 2H), 2.21 (s, 3H), 1.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.3, 166.9, 150.5, 145.3, 135.3, 133.4, 129.6, 128.3, 127.5, 121.1, 120.0, 112.8, 67.2, 55.4, 50.1, 30.1, 26.6, 19.7. IR (KBr) 3073, 3050, 2999, 2958, 2932, 2894, 2858, 1962, 1755, 1709, 1606, 1589, 1506, 1451, 1428, 1361, 1039, 937, 905, 822, 745, 704, 681, 611, 501 cm^{-1}. HRMS (ESI) calculated for $C_{28}H_{32}NaO_5Si$ (M + Na)$^+$: 499.1917, found: 499.1912.



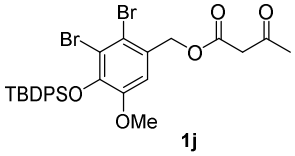
1h

4-((*tert*-Butyldiphenylsilyl)oxy)-2,6-dimethylbenzyl 3-oxobutanoate (1h): 1.62 g (49%, pale yellow solid), mp. 81–84 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79–7.70 (m, 4H), 7.48–7.42 (m, 2H), 7.39 (dd, *J* = 8.4, 5.8 Hz, 4H), 6.52–6.43 (m, 2H), 5.19–5.10 (m, 2H), 3.45 (d, *J* = 1.7 Hz, 2H), 2.22 (s, 3H), 2.21–2.17 (m, 6H), 1.14–1.09 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.4, 167.3, 155.6, 139.7, 135.5, 132.9, 129.9, 127.7, 124.1, 119.3, 61.9, 50.1, 30.0, 26.5, 19.5, 19.5. IR (KBr) 3048, 2959, 2931, 2859, 1744, 1718, 1602, 1488, 1315, 1155, 1113, 1045, 862, 846, 702, 502 cm^{-1} HRMS (ESI) calculated for: $C_{29}H_{34}NaO_4Si$ (M + Na)$^+$: 497.2124, found: 497.2117.



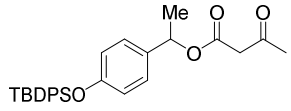
1i

3-Bromo-4-((*tert*-butyldiphenylsilyl)oxy)-5-ethoxybenzyl 3-oxobutanoate (1i): 1.02 g (22% yield for 3 steps, white solid), mp. 86–89 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 7.9, 1.5 Hz, 4H), 7.41–7.29 (m, 6H), 7.17 (d, *J* = 2.0 Hz, 1H), 6.53 (d, *J* = 2 Hz, 1H), 5.02 (s, 2H), 3.49 (s, 2H), 3.26 (q, *J* = 7.0 Hz, 2H), 2.23 (s, 3H), 1.11 (s, 9H), 0.34–0.25(m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.2, 166.7, 149.2, 142.4, 134.4, 129.1, 128.6, 127.1, 124.5, 114.3, 111.0, 89.5, 66.4, 63.2, 49.9, 30.1, 26.2, 20.1, 12.7. IR (KBr) 3072, 3051, 2960, 2931, 2892, 2857, 1748, 1718, 1570, 1492, 1429, 1321, 1267, 1148, 1116, 1049, 922, 744, 702, 678, 504 cm^{-1}.HRMS (ESI) calculated for $C_{29}H_{33}BrNaO_5Si$ (M + Na)$^+$: 591.1178, found: 591.1174.



1j

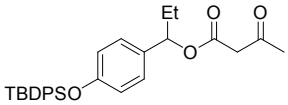
2,3-Dibromo-4-((*tert*-butyldiphenylsilyl)oxy)-5-methoxybenzyl 3-oxobutanoate (1j): 2.0 g (49% yield for 3 steps, yellow solid), mp. 77–87 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.64 (m, 4H), 7.35 (m, 6H), 6.67 (s, 1H), 5.20 (s, 2H), 3.50 (s, 2H), 2.82 (s, 3H), 2.24 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1, 166.5, 148.6, 143.8, 134.2, 134.0, 129.1, 128.2, 127.2, 118.5, 116.8, 111.9, 67.7, 54.0, 49.8, 30.2, 26.4, 20.2. IR (KBr) 3072, 2960, 2932, 2856, 1749, 1718, 1553, 1471, 1314, 1263, 1147, 1105, 976, 923, 852, 822, 702, 505 cm^{-1}. HRMS (ESI) calculated for $C_{28}H_{30}Br_2NaO_5Si$ (M + Na)$^+$: 655.0127, found: 655.0120.



1k

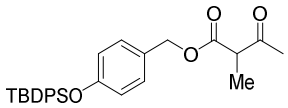
1-(4-((*tert*-Butyldiphenylsilyl)oxy)phenyl)ethyl 3-oxobutanoate (1k): 0.295 g (9% yield for 3 steps, white solid), mp. 65–68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (m, 4H), 7.47–7.41 (m, 2H), 7.37 (m, 4H), 7.14–7.06 (m, 2H), 6.78–6.70 (m, 2H), 5.86 (q, *J* = 6.6 Hz, 1H), 3.41 (s, 2H), 2.18 (s, 3H), 1.51 (d, *J* = 6.6 Hz, 3H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.4, 166.3, 155.4, 135.4, 133.1, 132.7, 129.8, 127.7, 127.3, 119.5, 73.1, 50.3, 29.9, 26.4, 21.5, 19.3. IR (KBr) 3072, 3052, 2960, 2932, 2858, 1740, 1718, 1610, 1513, 1259, 1172, 1150, 1114, 1058, 998, 920, 836, 823, 701, 504 cm^{-1}. HRMS (ESI)

calculated for $C_{28}H_{32}NaO_4Si$ $(M + Na)^+$: 483.1968, found: 483.1965.



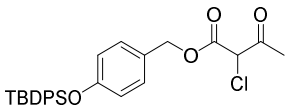
1l

1-(4-((*tert*-Butyldiphenylsilyl)oxy)phenyl)propyl 3-oxobutanoate (1l)： 1.31 g (44% yield for 3 steps, white solid), mp. 55–57 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74–7.65 (m, 4H), 7.45–7.39 (m, 2H), 7.39–7.32 (m, 4H), 7.07–7.01 (m, 2H), 6.75–6.69 (m, 2H), 5.60 (t, *J* = 7.0 Hz, 1H), 3.40 (s, 2H), 2.16 (s, 3H), 1.95–1.81 (m, 1H), 1.81–1.68 (m, 1H), 1.09 (s, 9H), 0.82 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.35, 166.43, 155.47, 135.53, 132.90, 132.22, 129.91, 127.81, 127.76, 119.64, 76.76, 50.48, 29.88, 28.82, 26.54, 19.46, 9.85. IR (KBr) 2964, 2933, 1739, 1718, 1609, 1512, 1429, 1362, 1256, 1189, 1171, 1152, 1113, 918, 823, 744, 702, 612, 538, 504 cm^{-1}. HRMS (ESI) calculated for $C_{29}H_{34}NaO_4Si$ $(M + Na)^+$: 497.2124, found: 497.2118.



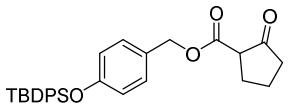
1m

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl 2-methyl-3-oxobutanoate (1m): 1.79 g (75% yield for 3 steps, white solid), mp. 39–45 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.69 (m, 4H), 7.47–7.40 (m, 2H), 7.40–7.34 (m, 4H), 7.11–7.06 (m, 2H), 6.78–6.73 (m, 2H), 5.04 (d, *J* = 1.4 Hz, 2H), 3.49 (q, *J* = 7.2 Hz, 1H), 2.13 (s, 3H), 1.33 (d, *J* = 7.2 Hz, 3H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.3, 170.3, 155.7, 135.4, 132.6, 129.9, 129.7, 129.2, 127.7, 119.7, 66.8, 53.5, 28.2, 26.4, 19.3, 12.6. IR (KBr) 2959, 2933, 1741, 1716, 1610, 1513, 1428, 1260, 1193, 1170, 1113, 917, 823, 744, 701, 502 cm^{-1}. HRMS (ESI) calculated for $C_{28}H_{32}NaO_4Si$ $(M + Na)^+$: 483.1968, found: 483.1961.



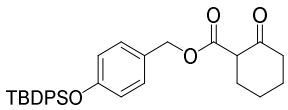
1n

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl 2-chloro-3-oxobutanoate (1n): 0.27 g (11% yield for 3 steps, pale yellow solid)，mp. 46–53 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.67 (m, 4H), 7.46–7.40 (m, 2H), 7.37 (dd, *J* = 11.2, 4.3 Hz, 4H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.78–6.71 (m, 2H), 5.12 (d, *J* = 2.5 Hz, 2H), 4.75 (s, 1H), 2.26 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 164.7, 156.0, 135.4, 132.5, 130.0, 129.9, 127.7, 126.8, 119.8, 68.4, 61.3, 26.4, 26.0, 19.3. IR (KBr) 3071, 3049, 2959, 2932, 2893, 2859, 1730, 1610, 1513, 1261, 1169, 1113, 917, 822, 743, 701, 502 cm^{-1}. HRMS (ESI) calculated for $C_{27}H_{29}ClNaO_4Si$ $(M + Na)^+$: 503.1421, found: 503.1424.



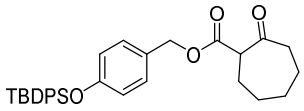
1o

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl 2-oxocyclopentane-1-carboxylate (1o): 0.94 g (52%, pink solid), mp. 85–90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.0, 1.4 Hz, 4H), 7.43 (m, 2H), 7.40–7.33 (m, 4H), 7.09 (d, *J* = 8.6 Hz, 2H), 6.74 (d, *J* = 8.6 Hz, 2H), 5.04 (d, *J* = 2.5 Hz, 2H), 3.16 (t, *J* = 8.9 Hz, 1H), 2.35–2.20 (m, 4H), 2.18–2.04 (m, 1H), 1.91–1.77 (m, 1H), 1.09 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.0, 169.2, 155.6, 135.4, 132.6, 129.8, 129.5, 127.9, 127.7, 119.6, 66.8, 54.6, 37.9, 27.3, 26.4, 20.8, 19.3. IR (KBr) 3072, 3051, 2960, 2932, 2890, 2859, 1756, 1726, 1610, 1512, 1257, 1114, 918, 823, 701, 502 cm^{-1}. HRMS (ESI) calculated for $C_{29}H_{32}NaO_4Si$ $(M + Na)^+$: 495.1968, found: 495.1965.



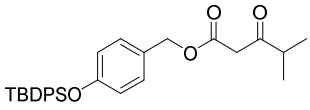
1p

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl 2-oxocyclohexane-1-carboxylate (1p): 0.96 g (48% yield for 3 steps, pale yellow solid), mp. 56–59 °C. ^{1}H NMR (300 MHz, $CDCl_3$) for the major δ 7.81–7.70 (m, 4H), 7.51–7.34 (m, 6H), 7.14 (d, *J* = 8.5 Hz, 2H), 6.79 (d, *J* = 8.5 Hz, 2H), 5.09 (s, 2H), 2.41–2.04 (m, 4H), 2.04–1.75 (m, 1H), 1.65 (m, 4H), 1.14 (s, 9H).); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.1, 172.4, 172.3, 169.8, 155.6, 155.6, 155.5, 135.4, 132.7, 129.9, 129.7, 129.2, 128.5, 127.8, 119.7, 119.6, 97.7, 66.6, 65.4, 57.2, 41.5, 29.9, 29.1, 27.0, 26.4, 23.2, 22.3, 22.3, 21.8, 19.4. IR (KBr) 3071, 3050, 2934, 2859, 1653, 1610, 1512, 1428, 1295, 1255, 1217, 1078, 918, 822, 700, 501 cm^{-1}. HRMS (ESI) calculated for $C_{30}H_{34}NaO_4Si$ $(M + Na)^+$: 509.2124, found: 509.2117.



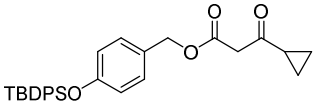
1q

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl 2-oxocycloheptane-1-carboxylate (1q): 0.046 g (47% yield for 3 steps, pale yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.68 (s, 1H, enol), 7.74–7.67 (m, 4H), 7.50–7.38 (m, 2H), 7.40–7.33 (m, 4H), 7.12–7.05 (m, 2H), 6.78–6.71 (m, 2H), 5.04 (s, 1H, enol), 5.02 (s, 1H), 3.75–3.50 (m, 1H), 2.70–2.30 (m, 3H), 2.15–1.75 (m, 4H), 1.73–1.50 (m, 1H), 1.49–1.37 (m, 2H), 1.10 (d, *J* = 1.8 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.7, 179.8, 170.3, 155.6, 135.4, 132.7, 132.6, 129.8, 129.6, 129.1, 127.9, 127.7, 119.6, 119.5, 66.5, 65.6, 58.8, 43.0, 35.3, 31.8, 29.5, 27.8, 27.4, 27.2, 26.4, 24.5, 24.2, 24.2, 19.3. IR (KBr) 3073, 3050, 2933, 2895, 2859, 1734, 1700, 1609, 1502, 1429, 1363, 1261, 1214, 1170, 1114, 1060, 1008, 924, 873, 823, 745, 671, 492 cm^{-1}. HRMS (ESI) calculated for $C_{31}H_{36}NaO_4Si$ $(M + Na)^+$, 523.2281, found: 523.2275.



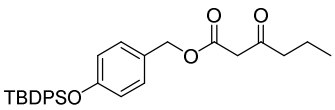
1r

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl 4-methyl-3-oxopentanoate (1r): 0.315 g (23% yield for 3 steps, pale yellow oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73–7.69 (m, 4H), 7.45–7.40 (m, 2H), 7.36 (dd, *J* = 11.2, 4.3 Hz, 4H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.74 (d, *J* = 8.6 Hz, 2H), 5.03 (s, 2H), 3.49 (s, 2H), 2.67 (m, 1H), 1.14–1.07 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.3, 167.2, 155.8, 135.4, 132.7, 129.9, 129.8, 129.7, 127.8, 119.7, 66.9, 47.1, 41.1, 26.5, 19.4, 17.8. IR (KBr) 3072, 3051, 2964, 2933, 2892, 2860, 1961, 1755, 1738, 1706, 1609, 1511, 1472, 1464, 1429, 1306, 1274, 1170, 1153, 1114, 1107, 1071, 918, 822, 744, 702, 612, 501 cm^{-1}.HRMS (ESI) calculated for $C_{29}H_{34}NaO_4Si$ $(M + Na)^+$: 497.2124, found: 497.2115.



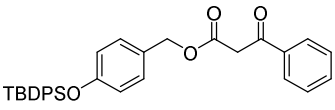
1s

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl 3-cyclopropyl-3-oxopropanoate (1s): 0.423 g (36% yield for 3 steps, pale yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.0, 1.4 Hz, 4H), 7.47–7.40 (m, 2H), 7.40–7.33 (m, 4H), 7.11–7.09 (m, 2H), 6.78–6.72 (m, 2H), 5.05 (s, 2H), 3.57 (s, 2H), 2.10–1.90 (m, 1H), 1.10 (s, 9H), 1.09–1.04 (m, 2H) 0.92–0.85 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 198.4, 167.0, 155.8, 135.4, 132.7, 129.9, 129.8, 127.8, 119.7, 66.8, 50.0, 26.4, 20.7, 19.4, 11.7. IR (KBr) 3072, 3050, 2959, 2932, 2859, 1743, 1701, 1610, 1513, 1428, 1257, 1114, 918, 823, 701, 612, 502 cm^{-1}. HRMS (ESI) calculated for $C_{29}H_{32}NaO_4Si$ $(M + Na)^+$: 495.1968, found: 495.1961.



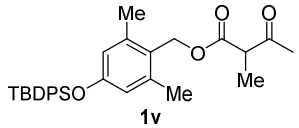
1t

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl 3-oxohexanoate (1t): 0.23 g (12% yield for 3 steps, pale yellow oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 8.0, 1.4 Hz, 4H), 7.46–7.41 (m, 2H), 7.37 (dd, *J* = 11.2, 4.3 Hz, 4H), 7.12–7.07 (m, 2H), 6.77–6.73 (m, 2H), 5.04 (s, 2H), 3.43 (s, 2H), 2.46 (t, *J* = 7.3 Hz, 2H), 1.59 (m, 2H), 1.10 (s, 9H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.6, 167.1, 155.8, 135.4, 132.7, 129.9, 129.9, 127.8, 127.7, 119.7, 66.9, 49.3, 44.8, 26.5, 19.4, 16.9, 13.5. IR (KBr) 3073, 3051, 2962, 2933, 2875, 2859, 1961, 1890, 1713, 1610, 1511, 1473, 1428, 1362, 1257, 1225, 1171, 1152, 1113, 1069, 919, 822, 701, 502 cm^{-1}. HRMS (ESI) calculated for $C_{29}H_{34}NaO_4Si$ $(M + Na)^+$: 497.2124, found: 497.2119.



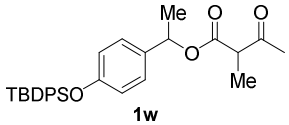
1u

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl 3-oxo-3-phenylpropanoate (1u): 0.528 g (20% yield for 3 steps, white solid), mp. 61–82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): a mixture of **1u** and its enol isomer (4:1) **1u**: 7.71 (m, 5H), 7.47–7.40 (m, 5H), 7.40–7.32 (m, 5H), 7.04 (d, *J* = 8.6 Hz, 2H), 6.74–6.68 (m, 2H), 5.05 (s, 2H), 3.99 (s, 2H), 1.09 (s, 9H). Enol: δ 12.50 (s, 1H), 7.89 (m, 8H), 7.75 (m, 2H), 7.56 (m, 4H), 7.50–7.30 (m, 1H), 7.14 (d, *J* = 8.6 Hz, 2H), 6.77 (d, *J* = 8.6 Hz, 2H), 5.68 (s, 1H), 5.11 (s, 2H), 1.09 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 167.3, 155.6, 135.8, 135.4, 133.6, 132.6, 129.8, 129.7, 128.6, 128.4, 127.7, 125.9, 119.6, 119.6, 66.9, 45.9, 26.4, 19.3. IR (KBr) 3072, 3052, 2959, 2932, 2859, 1735, 1685, 1611, 1513, 1428, 1261, 1187, 1114, 975, 918, 823, 745, 701, 502 cm^{-1}. HRMS (ESI) calculated for $C_{32}H_{32}NaO_4Si$ $(M + Na)^+$: 531.1968, found: 531.1960.



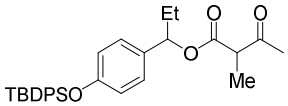
1v

4-((*tert*-Butyldiphenylsilyl)oxy)-2,6-dimethylbenzyl 2-methyl-3-oxobutanoate (1v): white solid, mp. 77–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75–7.67 (m, 4H), 7.42 (dd, *J* = 5.1, 3.7 Hz, 2H), 7.40–7.33 (m, 4H), 6.44 (s, 2H), 5.12 (s, 2H), 3.48 (q, *J* = 7.2 Hz, 1H), 2.16 (s, 6H), 2.14 (s, 3H), 1.32 (d, *J* = 7.2 Hz, 3H), 1.09 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.32, 170.68, 155.63, 139.63, 135.50, 133.02, 129.87, 127.72, 124.27, 119.38, 61.87, 53.64, 28.17, 26.57, 19.52, 12.72, 0.98. IR (KBr) 1707, 1601, 1474, 1428, 1363, 1315, 1261, 1236, 1193, 1155, 1114, 1045, 845, 701, 502 cm^{-1}. HRMS (ESI) calculated for $C_{30}H_{36}NaO_4Si$ $(M + Na)^+$: 511.2281, found: 511.2277.



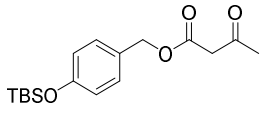
1w

1-(4-((*tert*-Butyldiphenylsilyl)oxy)phenyl)ethyl 2-methyl-3-oxobutanoate (**1w**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76–7.69 (m, 4H), 7.47–7.41 (m, 2H), 7.41–7.33 (m, 4H), 7.09 (d, *J* = 8.6 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 5.85 (q, *J* = 6.5 Hz, 1H), 3.45 (qd, *J* = 7.1, 2.5 Hz, 1H), 2.15 (s, 1.5 H), 2.04 (s, 1.5 H), 1.50 (dd, *J* = 6.6, 4.2 Hz, 3H), 1.31 (dd, *J* = 7.1, 1.0 Hz, 3H), 1.11 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.45, 203.33, 169.73, 169.69, 155.40, 135.44, 133.20, 133.14, 132.71, 132.67, 129.89, 127.74, 127.36, 127.33, 119.59, 119.58, 73.04, 53.88, 53.79, 28.33, 28.05, 26.44, 21.45, 19.38, 12.52, 12.49. IR (KBr) 3072, 3050, 2981, 2958, 2933, 2859, 1740, 1716, 1610, 1513, 1361, 1259, 1197, 1173, 1113, 1058, 919, 835, 701, 503 cm^{-1}. HRMS (ESI) calculated for $C_{29}H_{34}O_4NaSi$ $(M+Na)^+$, 497.2124, found: 497.2120.



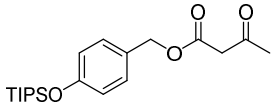
1x

1-(4-((*tert*-Butyldiphenylsilyl)oxy)phenyl)propyl 2-methyl-3-oxobutanoate (1x): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74–7.68 (m, 4H), 7.46–7.40 (m, 2H), 7.36 (ddd, *J* = 6.8, 6.4, 2.7 Hz, 4H), 7.08–7.01 (m, 2H), 6.76–6.71 (m, 2H), 5.60 (t, *J* = 7.0 Hz, 1H), 3.45 (q, *J* = 7.1 Hz, 1H), 2.12 (s, 1.5H), 2.01 (s, 1.5H), 1.94–1.83 (m, 1H), 1.77–1.70 (m, 1H), 1.29 (d, *J* = 7.1 Hz, 3H), 1.10 (s, 9H), 0.86–0.80 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.33, 203.22, 169.88, 169.80, 155.47, 135.54, 135.52, 134.81, 132.92, 132.87, 132.30, 132.22, 129.92, 127.79, 127.75, 127.74, 127.34, 119.69, 119.67, 119.54, 78.28, 78.22, 53.98, 53.97, 29.53, 28.82, 28.75, 28.33, 27.98, 26.59, 26.54, 19.45, 12.60, 12.55, 9.90, 9.86. IR (KBr) 3072, 3051, 2963, 2933, 2893, 2859, 1740, 1735, 1716, 1609, 1512, 1473, 1428, 1392, 1378, 1361, 1257, 1196, 1172, 1113, 1078, 1040, 917, 834, 823, 743, 702, 612, 503 cm^{-1}. HRMS (ESI) calculated for $C_{30}H_{36}O_4NaSi$ $(M + Na)^+$: 511.2281, found: 511.2278.



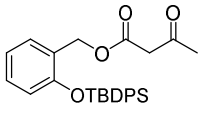
1a$_1$

4-((*tert*-Butyldimethylsilyl)oxy)benzyl 3-oxobutanoate (1a$_1$): 0.15 g (10% yield for 3 steps, crystalline solid), mp. 30–33 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.5 Hz, 2H), 6.84–6.79 (m, 2H), 5.10 (s, 2H), 3.47 (s, 2H), 2.23 (s, 3H), 0.98 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 166.9, 155.9, 130.0, 127.9, 120.0, 66.9, 50.0, 30.0, 25.5, 18.1, -4.5. IR (KBr) 3035, 2956, 2930, 2886, 2858, 1740, 1715, 1610, 1512, 1260, 1149, 1029, 1005, 964, 913, 839, 780, 690 cm^{-1}. HRMS (ESI) calculated for $C_{17}H_{26}NaO_4Si$ $(M + Na)^+$: 345.1498, found: 345.1491.



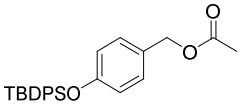
1a$_2$

4-((Triisopropylsilyl)oxy)benzyl 3-oxobutanoate (1a$_2$): 1.51 g (35% yield for 3 steps, colorless liquid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 5.09 (s, 2H), 3.46 (s, 2H), 2.21 (s, 3H), 1.35–1.15 (m, 3H), 1.13–0.96 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 166.9, 156.3, 130.0, 127.5, 119.8, 66.9, 50.0, 29.9, 17.8, 12.5. IR (KBr) 2946, 1748, 1715, 1610, 1507, 1458, 1268, 1236, 1169, 1152, 963, 912, 883, 688 cm^{-1}. HRMS (ESI) calculated for $C_{20}H_{32}NaO_4Si$ $(M + Na)^+$: 387.1968, found: 387.1962.



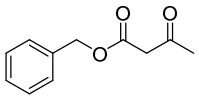
5a

2-((*tert*-Butyldiphenylsilyl)oxy)benzyl 3-oxobutanoate (5a): 1.23 g (25% yield for 3 steps, pale yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77–7.65 (m, 4H), 7.47–7.30 (m, 7H), 6.95–6.81 (m, 2H), 6.45 (d, *J* = 7.7 Hz, 1H), 5.40 (s, 2H), 3.47 (s, *J* = 2.9 Hz, 2H), 2.26 (s, *J* = 1.8 Hz, 3H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 167.0, 153.8, 135.2, 132.2, 130.4, 129.9, 129.4, 127.8, 125.1, 120.9, 118.8, 63.3, 49.9, 30.0, 26.3, 19.4. IR (KBr) 3073, 2958, 2933, 2893, 2860, 1750, 1645, 1602, 1586, 1506, 1456, 1363, 1269, 1115, 1029, 926, 823, 758, 701, 615, 502 cm^{-1}. HRMS (ESI) calculated for $C_{27}H_{30}NaO_4Si$ $(M + Na)^+$: 469.1811, found: 469.1806.



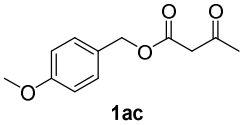
1aa

4-((*tert*-Butyldiphenylsilyl)oxy)benzyl acetate (1aa): 0.676 g (61% yield for 1 step, pale yellow solid), mp. 51–53 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 8.0, 1.4 Hz, 4H), 7.47–7.42 (m, 2H), 7.42–7.36 (m, 4H), 7.12 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 4.99 (s, 2H), 2.07 (s, 3H), 1.13 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 155.7, 135.5, 132.8, 129.9, 129.7, 128.4, 127.8, 119.7, 66.1, 26.5, 21.0, 19.4. IR (KBr) 3072, 3050, 2959, 2933, 2859, 1740, 1610, 1513, 1429, 1254, 1114, 1025, 918, 822, 701, 612, 502 cm^{-1}. HRMS (ESI) calculated for $C_{25}H_{28}O_3NaSi$ $(M + Na)^+$, 427.1705, found: 427.1697.



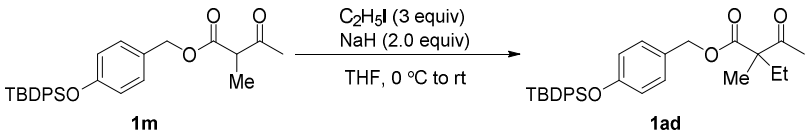
1ab

Benzyl 3-oxobutanoate (1ab): 1.33 g (75% yield for 1 step, pale yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 5H), 5.18 (s, 2H), 3.50 (s, 2H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 166.8, 135.1, 128.5, 128.4, 128.3, 67.0, 49.9, 30.1. IR (KBr) 2940, 1753, 1713, 1456, 1410, 1362, 1316, 1267, 1149, 1029, 968, 751, 699, 541 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{12}NaO_3$ $(M + Na)^+$: 215.0684, found: 215.0682.



1ac

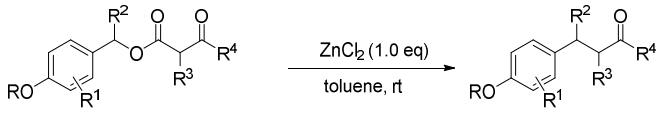
4-Methoxybenzyl 3-oxobutanoate (1ac): 1.50 g (47% yield for 1 step, pale yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.6 Hz, 2H), 6.92–6.84 (m, 2H), 5.10 (s, 2H), 3.79 (s, 3H), 3.46 (s, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 166.9, 159.7, 130.1, 127.3, 113.9, 66.8, 55.2, 50.0, 30.0. IR (KBr) 2959, 2838, 1746, 1714, 1614, 1516, 1464, 1374, 1248, 1174, 1150, 1032, 963, 824, 564, 540 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{14}NaO_4$ $(M + Na)^+$: 245.0790, found: 245.0789.



1m **1ad**

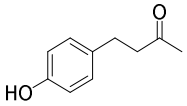
4-((*tert*-butyldiphenylsilyl)oxy)benzyl 2-ethyl-2-methyl-3-oxobutanoate (1ad): To a suspension of NaH (6.2 mg, 0.25 mmol, 2.3 equiv) in THF (2 mL) at 0 °C was added *β*–ketoester **1m** (50 mg, 0.11 mmol). After being stirred at 0 °C for 40 min, iodoethane (51.5 mg, 0.33 mmol, 3 equiv) was added and then the reaction was gradually warmed to room temperature. When the substrate disappeared (monitored by TLC), the reaction was quenched with saturated $NaHCO_3$ (aq) and diluted with ethyl acetate (5 mL) and water (5 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate twice. The combined organic layers were washed with water, brine, dried over Na_2SO_4 and concentrated at reduced pressure. Purification of the residue by flash chromaytography (silica gel, hexanes/EtOAc = 200:1 to 60:1) afforded **1ad** as pale yellow oil (24.6 mg, 46%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.0, 1.3 Hz, 4H), 7.42 (dd, *J* = 5.1, 3.7 Hz, 2H), 7.36 (dd, *J* = 11.3, 4.3 Hz, 4H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.76–6.70 (m, 2H), 5.03 (d, *J* = 2.1 Hz, 2H), 1.97 (s, 3H), 1.90 (dt, *J* = 15.1, 7.5 Hz, 1H), 1.77 (dq, *J* = 14.9, 7.5 Hz, 1H), 1.28 (s, 3H), 1.10 (s, 9H), 0.76 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.48, 172.82, 155.82, 135.49, 132.77, 129.94, 129.85, 128.01, 127.77, 119.80, 66.67, 60.09, 27.68, 26.51, 26.07, 19.45, 18.17, 8.49. IR (KBr) 3073, 3049, 2962, 2933, 2890, 2859, 1961, 1889, 1714, 1700, 1609, 1512, 1473, 1458, 1361, 1251, 1141, 1114, 1056, 1008, 916, 822 cm^{-1}. HRMS (ESI) calculated for $C_{30}H_{36}O_4NaSi$ $(M + Na)^+$: 511.2281, found: 511.2275.

III. Benzylation of the Unstabilized Ketone Enolates



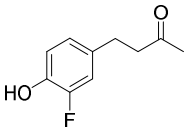
1 **2**

General procedure A: To a 10 mL round-bottomed flask placed with a stirred solution of *β*–ketoester **1** (0.2 mmol) and $ZnCl_2$ (27.3 mg, 0.2 mmol, 1.0 equiv) in toluene (2 mL), TBAF (1M in THF, 0.2 mmol, 1.0 equiv) was added via micro-syringe. After being stirred for 45 min or longer time (monitored by TLC) at room temperature, the reaction mixture was quenched with water. The aqueous phase was extracted with EtOAc (3 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated with silica gel. Then the mixture was purified by column chromatography (silica gel, hexanes/EtOAc = 4:1) to afford compound **2**.



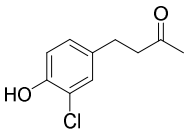
2a

4-(4-Hydroxyphenyl) butan-2-one (2a): Prepared according to general procedure A. Reaction run on a 0.1 mmol scale. *β*–Ketoester **1a** afforded **2a** in 82% yield (13.4 mg, colorless crystalline solid), mp. 51–72 °C; *β*–ketoester **1a1** (50 mg, 0.155 mmol) afforded target compound **2a** in 66% yield (16.8 mg), and *β*–ketoester **1a2** (36.5 mg, 0.1 mmol) afforded target compound **2a** in 70% yield (11.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, *J* = 8.5 Hz, 2H), 6.75 (d, *J* = 8.5 Hz, 2H), 5.30 (s, 1H), 2.88–2.76 (m, 2H), 2.75–2.70 (m, 2H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.7, 153.9, 132.8, 129.3, 115.2, 45.3, 30.0, 28.8. IR (KBr) 3322, 3020, 2923, 1696, 1615, 1596, 1516, 1447, 1368, 1232, 1172, 822, 541 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_{11}O_2$ (M - H)$^-$:163.0759, found: 163.0765.



2b

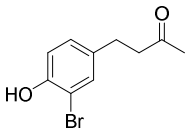
4-(3-Fluoro-4-hydroxyphenyl) butan-2-one (2b): Following procedure A, compound **2b** was obtained in 62% yield (22.5 mg, pale yellow crystalline solid), mp. 83–87 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92–6.85 (m, 2H), 6.82 (d, *J* = 8.2 Hz, 1H), 2.81 (t, *J* = 7.3 Hz, 2H), 2.72 (t, *J* = 7.3 Hz, 2H), 2.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.0, 151.8 (d, *J* = 236.2), 141.8 (d, *J* = 13.7), 133.8 (d, *J* = 5.0), 124.4 (d, *J* = 3.7), 117.2 (d, *J* = 2.5), 115.4 (d, *J* = 17.5), 45.0, 30.1, 28.7. IR (KBr) 3286, 3093, 2953, 2923, 1693, 1601, 1445, 1375, 1201, 1115, 827, 732 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_{10}FO_2$ (M - H)$^-$: 181.0665, found: 181.0668.



2c

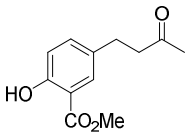
4-(3-Chloro-4-hydroxyphenyl) butan-2-one (2c): Prepared according to general procedure A. Reaction run on a 0.1 mmol scale. Compound **2c** was obtained in 63% yield (12.5 mg, pale yellow solid), mp. 53–59 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 2.0 Hz, 1H), 6.99 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.92 (d, *J* = 8.3 Hz, 1H), 5.47 (s, 1H), 2.84–2.78 (m, 2H), 2.75–2.66 (m, 2H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.5, 149.5, 134.1, 128.5, 128.2, 119.5, 116.0, 44.9, 30.0, 28.4. IR (KBr) 3292, 2951, 2929, 2856, 1704, 1506, 1340, 1289, 1222, 1182, 1166, 1056, 816, 747 cm^{-1}. HRMS (ESI) calculated for

$C_{10}H_{10}ClO_2$ (M - H)$^-$: 197.0369, found: 197.0378.



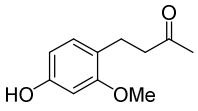
2d

4-(3-Bromo-4-hydroxyphenyl) butan-2-one (2d): Following procedure A, compound **2d** was obtained in 66% yield (32.0 mg, pale yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 2.1 Hz, 1H), 7.03 (dd, J = 8.3, 2.1 Hz, 1H), 6.92 (d, J = 8.3 Hz, 1H), 5.46 (s, 1H), 2.84–2.78 (m, 2H), 2.75–2.67 (m, 2H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.5, 150.5, 134.6, 131.5, 129.0, 115.9, 109.9, 45.0, 30.0, 28.3. IR (KBr) 3452, 2986, 2960, 2920, 2850, 1694, 1652, 1087, 809 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_{10}BrO_2$ (M - H)$^-$: 240.9864, found: 240.9871.



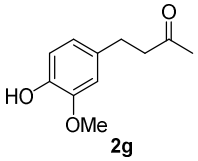
2e

Methyl 2-hydroxy-5-(3-oxobutyl) benzoate (2e): Following procedure A, compound **2e** was obtained in 58% yield (24.9 mg, pale yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.60 (s, 1H), 7.65 (d, J = 2.2 Hz, 1H), 7.28 (dd, J = 8.5, 2.3 Hz, 1H), 6.90 (d, J = 8.5 Hz, 1H), 3.94 (s, 3H), 2.86–2.78 (m, 2H), 2.76–2.69 (m, 2H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.6, 170.3, 159.9, 135.8, 131.5, 129.0, 117.5, 112.0, 52.1, 45.0, 30.0, 28.5. IR (KBr) 3162, 3026, 2923, 2852, 1714, 1679, 1674, 1615, 1600, 1493, 1452, 1442, 1354, 1298, 1254, 1157, 1091, 1028, 973, 908, 759, 699 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{13}O_4$ (M - H)$^-$: 221.0814, found: 221.0817.



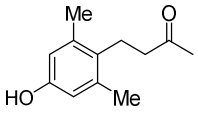
2f

4-(4-Hydroxy-2-methoxyphenyl) butan-2-one (2f): Following procedure A, compound **2f** was obtained in 63% yield (24.3 mg, pale yellow solid), mp. 106–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (d, J = 8.1 Hz, 1H), 6.39 (d, J = 2.4 Hz, 1H), 6.32 (dd, J = 8.1, 2.4 Hz, 1H), 5.60 (s, 1H), 3.76 (s, 3H), 2.86–2.74 (m, 2H), 2.74–2.63 (m, 2H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.7, 158.3, 155.4, 130.2, 120.9, 106.5, 98.8, 55.1, 43.9, 29.8, 24.3. IR (KBr) 3432, 2976, 2924, 2849, 2012, 1988, 1696, 1617, 1597, 1437, 1396, 1239, 1160, 1036, 955, 846, 645 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{13}O_3$ (M - H)$^-$: 193.0865, found: 193.0869.



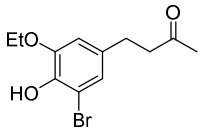
2g

4-(4-Hydroxy-3-methoxyphenyl) butan-2-one (2g): Following procedure A, compound **2g** was obtained in 70% yield (27.1 mg, pale yellow solid), mp. 40–41 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.82 (d, J = 8.0 Hz, 1H), 6.69 (d, J = 1.8 Hz, 1H), 6.66 (dd, J = 8.0, 1.9 Hz, 1H), 5.49 (s, 1H), 3.87 (s, 3H), 2.82 (t, J = 7.5 Hz, 2H), 2.72 (t, J = 7.3 Hz, 2H), 2.13 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.1, 146.4, 143.9, 132.9, 120.7, 114.3, 111.0, 55.8, 45.5, 30.1, 29.4. IR (KBr) 3387, 2923, 2850, 2380, 2252, 1602, 1707, 1680, 1602, 1507, 1266, 1151, 1120, 1030, 916, 809, 791 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{13}O_3$ (M - H)$^-$: Exact Mass: 193.0865, found: 193.0875.



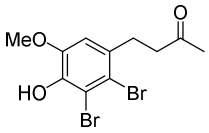
2h

4-(4-Hydroxy-2,6-dimethylphenyl) butan-2-one (2h): Following procedure A, compound **2h** was obtained in 95% yield (36.5 mg, crystalline solid). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.51 (s, 2H), 2.82 (dd, *J* = 9.6, 7.0 Hz, 2H), 2.55 (dd, *J* = 9.5, 7.1 Hz, 2H), 2.25 (s, 6H), 2.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.7, 153.3, 137.6, 129.7, 114.9, 43.0, 29.9, 22.9, 19.8. IR (KBr) 3255, 2970, 2954, 2860, 1749, 1685, 1473, 1355, 1312, 1263, 1238, 1219, 1199, 1154, 1142, 1027, 879, 854, 748 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{15}O_2$ (M - H)$^-$: 191.1072, found: 191.1077.



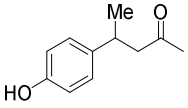
2i

4-(3-Bromo-5-ethoxy-4-hydroxyphenyl) butan-2-one (2i): Following procedure A, compound **2i** was obtained in 48% yield (27.4 mg, pale yellow solid), mp. 76–81 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (d, *J* = 1.8 Hz, 1H), 6.63 (d, *J* = 1.8 Hz, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 2.81–2.74 (m, 2H), 2.74–2.67 (m, 2H), 2.12 (s, 3H), 1.43 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.6, 146.2, 141.4, 133.6, 123.8, 111.2, 107.7, 64.9, 45.0, 30.0, 28.9, 14.7. IR (KBr) 3434, 3055, 2921, 2851, 1710, 1583, 1499, 1428, 1396, 1362, 1273, 1184, 1160, 1136, 1112, 1046, 897, 826, 744 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{14}BrO_3$ (M - H)$^-$: 285.0126, found: 285.0129.



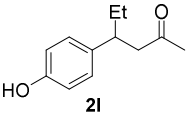
2j

4-(2,3-Dibromo-4-hydroxy-5-methoxyphenyl) butan-2-one (2j): Following procedure A, after being stirred for 4 h, TBAF (40 uL, 0.04 mmol, 0.2 equiv) was added to the reaction mixture, 2.5 days was used before another TBAF (20 uL, 0.02 mmol, 0.1 equiv) was added again. Finally compound **2j** was obtained in 51% yield (35.7 mg, pale yellow solid), mp. 140–146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (s, 1H), 3.88 (s, 3H), 3.01 (t, *J* = 7.4 Hz, 2H), 2.76 (t, *J* = 7.4 Hz, 2H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.5, 145.9, 142.8, 133.0, 117.2, 112.1, 111.8, 56.3, 43.3, 31.6, 29.9. IR (KBr) 3247, 3188, 3092, 2983, 2940, 2850, 1693, 1595, 1442, 1345, 1278, 1245, 1192, 1168, 1062, 1050, 982, 848 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{11}Br_2O_3$ (M - H)$^-$: 348.9075, found: 348.9078.



2k

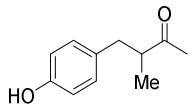
4-(4-Hydroxyphenyl) pentan-2-one (2k): Following procedure A, compound **2k** was obtained in 98% yield (34.9 mg, pale yellow solid), mp. 77–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07–6.98 (m, 2H), 6.78–6.70 (m, 2H), 3.26–3.18 (m, 1H), 2.73 (dd, *J* = 15.9, 7.3 Hz, 1H), 2.63 (dd, *J* = 16.0, 7.4 Hz, 1H), 2.06 (s, 3H), 1.23 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.5, 154.3, 137.5, 127.6, 115.4, 52.2, 34.8, 30.4, 22.2. IR (KBr) 3274, 2962, 2929, 2873, 2486, 1707, 1613, 1595, 1517, 1446, 1364, 1263, 1225, 1174, 833, 749, 548 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{13}O_2$ (M - H)$^-$: 177.0916, found 177.0920.



2l

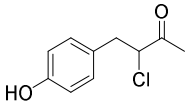
4-(4-Hydroxyphenyl)hexan-2-one (2l): Following procedure A, compound **2l** was obtained in 76% yield (29.3 mg, pale yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04–6.97 (m, 2H), 6.76–6.68 (m, 2H), 3.02–2.88 (m, 1H), 2.70 (d, *J* = 7.4 Hz, 2H), 2.02 (s, 3H), 1.70-1.45 (m, 2H), 0.77 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.55, 154.23, 135.73, 128.47, 115.29, 50.75, 42.38, 30.56, 29.59, 11.90. IR (KBr) 3383, 2963, 2931, 2875, 1696, 1615, 1595, 1516, 1456, 1363, 1244, 1174,

1014, 965, 834, 551 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{16}O_2Na$ $(M + Na)^+$: 215.1048, foumd: 215.1042.



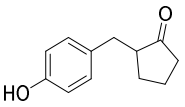
2m

4-(4-Hydroxyphenyl)-3-methylbutan-2-one (2m): Following procedure A, compound **2m** was obtained in 90% yield (32.2 mg, pale yellow oil). ^1H NMR (400 MHz, $CDCl_3$) δ 6.98 (d, J = 8.4 Hz, 2H), 6.74 (d, J = 8.4 Hz, 2H), 2.99–2.70 (m, 2H), 2.60–2.40 (m, 1H), 2.08 (s, 3H), 1.08 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.7, 154.4, 131.0, 129.8, 115.3, 49.0, 38.1, 28.8, 16.1. IR (KBr) 3327, 3054, 2968, 2934, 2571, 1702, 1654, 1595, 1517, 1457, 1265, 1171, 833, 745 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{13}O_2$ $(M - H)^-$: 177.0916, found: 177.0921.



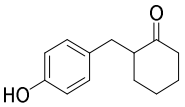
2n

3-Chloro-4-(4-hydroxyphenyl) butan-2-one (2n): Following procedure A, compound **2n** was obtained in 93% yield (36.8 mg, yellow solid). ^1H NMR (500 MHz, $CDCl_3$) δ 7.08 (d, J = 8.5 Hz, 2H), 6.77 (d, J = 8.5 Hz, 2H), 4.35 (dd, J = 7.7, 6.5 Hz, 1H), 3.25 (dd, J = 14.4, 6.4 Hz, 1H), 3.02 (dd, J = 14.3, 7.8 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 154.8, 130.6, 128.1, 115.5, 63.9, 39.0, 26.8. IR (KBr) 3385, 2925, 1714, 1613, 1516, 1359, 1265, 1224, 1174, 913, 824, 743 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_{10}ClO_2$ $(M - H)^-$: 197.0369, found: 197.0375.



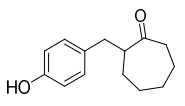
2o

2-(4-Hydroxybenzyl) cyclopentan-1-one (2o): Following procedure A, compound **2o** was obtained in 99% yield (37.7 mg, pale yellow solid), mp. 85–90 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.06–6.94 (m, 2H), 6.81–6.69 (m, 2H), 3.03 (dd, J = 14.0, 4.3 Hz, 1H), 2.51 (dd, J = 14.0, 9.2 Hz, 1H), 2.40–2.23 (m, 2H), 2.16–1.99 (m, 2H), 1.99–1.84 (m, 1H), 1.75–1.60 (m, 1H), 1.58-1.52 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 221.3, 154.2, 131.4, 129.9, 115.2, 51.1, 38.3, 34.5, 28.8, 20.4. IR (KBr) 3336, 2963, 2877, 1718, 1614, 1515, 1448, 1363, 1264, 1230, 1160, 1014, 1002, 924, 825, 577, 473 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{13}O_2$ $(M - H)^-$: 189.0916, found: 189.0916.



2p

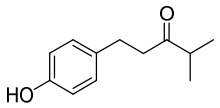
2-(4-hydroxybenzyl) cyclohexan-1-one (2p): Following procedure A, compound **2p** was obtained in 89% yield (36.4 mg, pale yellow solid), mp. 92–96 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, J = 8.5 Hz, 2H), 6.76 (d, J = 8.5 Hz, 2H), 3.12 (dd, J = 14.0, 5.1 Hz, 1H), 2.56–2.47 (m, 1H), 2.47–2.26 (m, 3H), 2.10–1.98 (m, 2H), 1.86–1.78 (m, 1H), 1.74–1.51 (m, 2H), 1.41–1.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.1, 154.1, 131.7, 130.0, 115.1, 52.6, 42.0, 34.5, 33.3, 28.0, 24.8. IR (KBr) 3362, 2937, 2860, 1694, 1685, 1614, 1595, 1516, 1447, 1362, 1313, 1264, 1226, 1128, 835, 748, 557 cm^{-1}. HRMS (ESI) calculated for $C_{13}H_{15}O_2$ $(M - H)^-$: 203.1072, found: 203.1078.



2q

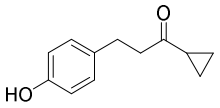
2-(4-Hydroxybenzyl) cycloheptan-1-one (2q): Following procedure A, compound **2q** was obtained in 77% yield (34.3 mg,

pale yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, *J* = 8.4 Hz, 2H), 6.73 (d, *J* = 8.5 Hz, 2H), 2.96 (dd, *J* = 13.8, 6.2 Hz, 1H), 2.85–2.70 (m, 1H), 2.51 (dd, *J* = 13.8, 7.9 Hz, 1H), 2.45 (dd, *J* = 9.5, 4.5 Hz, 2H), 1.93–1.72 (m, 4H), 1.70–1.48 (m, 1H), 1.36–1.24 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 217.0, 154.2, 131.3, 130.0, 115.1, 53.9, 43.0, 37.1, 30.3, 29.2, 28.4, 24.2. IR (KBr) 3292, 3013, 2925, 2854, 1672, 1613, 1595, 1517, 1457, 1374, 1228, 1171, 1015, 936, 835, 554 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_{17}O_2$ (M - H)$^-$: 217.1229, found: 217.1235.



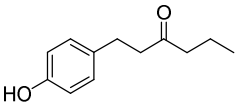
2r

1-(4-Hydroxyphenyl)-4-methylpentan-3-one (2r): Following procedure A, compound **2r** was obtained in 70% yield (26.9 mg, pale yellow oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.5 Hz, 2H), 2.84–2.78 (m, 2H), 2.75–2.70 (m, 2H), 2.62–2.51 (m, 1H), 1.06 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.6, 154.1, 133.1, 129.4, 115.3, 42.2, 41.0, 29.0, 18.1. IR (KBr) 3357, 2970, 2929, 1696, 1516, 1448, 1363, 1262, 1222, 1104, 1071, 827, 749 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{15}O_2$ (M - H)$^-$: 191.1072, found: 191.1076.



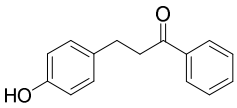
2s

1-Cyclopropyl-3-(4-hydroxyphenyl) propan-1-one (2s): Following procedure A, compound **2s** was obtained in 68% yield (25.8 mg, pale yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06–6.99 (m, 2H), 6.78–6.71 (m, 2H), 2.85 (s, 4H), 1.96–1.88 (m, 1H), 1.05–0.99 (m, 2H), 0.90–0.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.3, 154.2, 132.6, 129.2, 115.3, 45.1, 29.1, 20.6, 10.9. IR (KBr) 3334, 3014, 2954, 2928, 2806, 1674, 1615, 1596, 1516, 1456, 1393, 1262, 1222, 1173, 1108, 1082, 1031, 1012, 903, 828, 705 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{13}O_2$ (M - H)$^-$: 189.0916, found: 189.0921.



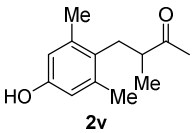
2t

1-(4-Hydroxyphenyl) hexan-3-one (2t): Following procedure A, compound **2t** was obtained in 72% yield (27.7 mg, colorless oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (d, *J* = 8.1 Hz, 2H), 6.74 (d, *J* = 8.1 Hz, 2H), 2.82 (t, *J* = 7.5 Hz, 2H), 2.68 (t, *J* = 7.5 Hz, 2H), 2.35 (t, *J* = 7.3 Hz, 2H), 1.60–1.56 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.4, 154.1, 132.9, 129.3, 115.3, 45.0, 44.5, 28.9, 17.2, 13.7. IR (KBr) 3448, 2963, 2932, 1693, 1614, 1517, 1449, 1374, 1265, 1226, 1173, 1072, 824, 704, 539 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{15}O_2$ (M - H)$^-$: 191.1072, found: 191.1078.



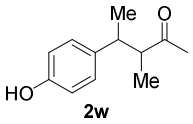
2u

3-(4-Hydroxyphenyl)-1-phenylpropan-1-one (2u): Following procedure A, after being stirred for 9 hours, TBAF (40 uL, 0.04 mmol, 0.2 equiv) was added, additional 4 days was needed to achieve the full conversion of the substrate. Finally compound **2u** was obtained in 81% yield (36.4 mg, pale yellow solid), mp. 115–117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00–7.91 (m, 2H), 7.59–7.53 (m, 1H), 7.45 (dd, *J* = 10.5, 4.7 Hz, 2H), 7.20–6.90 (m, 2H), 6.82–6.74 (m, 2H), 3.27 (t, *J* = 7.6 Hz, 2H), 3.00 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 153.9, 136.7, 133.9, 129.4, 128.5, 128.0, 115.3, 40.6, 29.2. IR (KBr) 3420 3065, 3034, 2961, 2923, 2894, 2853, 1676, 1595, 1447, 1290, 1202, 972, 811, 745, 689, 547 cm^{-1}. HRMS (ESI) calculated for $C_{15}H_{13}O_2$ (M - H)$^-$: 225.0916, found: 225.0916.



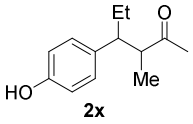
2v

4-(4-Hydroxy-2,6-dimethylphenyl)-3-methylbutan-2-one (2v): Following procedure A, reaction run on a 0.15 mmol scale compound **2v** was obtained in 70 % yield (22.2 mg, pale yellow oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.52 (s, 2H), 4.87 (s, 1H), 2.89 (dd, *J* = 14.0, 6.2 Hz, 1H), 2.84–2.75 (m, 1H), 2.62 (dd, *J* = 14.0, 8.5 Hz, 1H), 2.26 (s, 6H), 2.07 (s, 3H), 1.06 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.98, 153.44, 138.23, 128.68, 115.13, 46.97, 31.73, 29.26, 20.40, 15.83. IR (KBr) 3366, 2967, 2930, 1696, 1594, 1457, 1308, 1276, 1216, 1196, 1142, 1028, 856, 749 cm^{-1}. HRMS (ESI) calculated for $C_{13}H_{18}NaO_2$ $(M + Na)^+$: 229.1204, found: 229.1206.



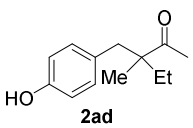
2w

4-(4-Hydroxyphenyl)-3-methylpentan-2-one (2w): Following procedure A, compound **2w** was obtained in a total yield of 70% (26.4 mg, pale yellow oil). Major (*anti*-**2w**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 5.01 (s, 1H), 2.86 (dq, *J* = 9.9, 6.9 Hz, 1H), 2.65 (dq, *J* = 9.9, 6.9 Hz, 1H), 2.18 (s, 3H), 1.17 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.18, 154.15, 136.70, 128.59, 115.31, 54.27, 41.92, 29.11, 20.64, 15.78. Minor (*syn*-**2w**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, *J* = 8.5 Hz, 2H), 6.74 (d, *J* = 8.6 Hz, 2H), 4.92 (s, 1H), 2.94 (dt, *J* = 14.1, 7.1 Hz, 1H), 2.73 (dq, *J* = 13.8, 6.9 Hz, 1H), 1.88 (s, 3H), 1.21 (d, *J* = 7.0 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.79, 153.91, 137.42, 128.30, 115.19, 54.00, 41.17, 29.28, 18.17, 13.82. IR (KBr) 3332, 2964, 2925, 2874, 2850, 1696, 1690, 1516, 1456, 1363, 1275, 1260, 1231, 1174, 1072, 835, 764, 749 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{16}O_2Na$ $(M + Na)^+$: 215.1048, found: 215.1041.



2x

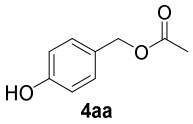
4-(4-Hydroxyphenyl)-3-methylhexan-2-one (2x): Following procedure A, compound **2w** was obtained in a total yield of 72% (29.7 mg, pale yellow oil). Major (*anti*-**2x**): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.98 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 5.17 (s, 1H), 2.74–2.66 (m, 1H), 2.62 (td, *J* = 10.3, 3.8 Hz, 1H), 2.18 (s, 3H), 1.60–1.52 (m, 1H), 1.52–1.44 (m, 1H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.68 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.51, 154.20, 134.15, 129.37, 115.27, 53.32, 49.64, 29.02, 27.56, 15.58, 12.13. Minor (*syn*-**2x**): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (d, *J* = 8.5 Hz, 2H), 6.76–6.71 (m, 2H), 4.88 (s, 1H), 2.77 (dq, *J* = 13.7, 6.8 Hz, 1H), 2.65–2.58 (m, 1H), 1.83 (s, 3H), 1.80 (ddd, *J* = 13.6, 7.4, 3.7 Hz, 1H), 1.46 (ddd, *J* = 13.5, 11.1, 7.2 Hz, 1H), 1.14 (d, *J* = 6.9 Hz, 3H), 0.70 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.69, 154.03, 135.14, 129.27, 115.25, 53.28, 49.22, 29.23, 24.89, 14.50, 11.67. IR (KBr) 3334, 2965, 2932, 2875, 1703, 1694, 1615, 1595, 1516, 1456, 1358, 1244, 1175, 1135, 1105, 1079, 834 cm^{-1}. HRMS (ESI) calculated for $C_{13}H_{18}O_2Na$ $(M + Na)^+$: 229.1204, found: 229.1200.



2ad

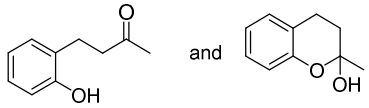
3-(4-Hydroxybenzyl)-3-methylpentan-2-one (2ad): Following procedure A, only trace amounts of compound **2ad** was obtained. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 8.5 Hz, 2H), 2.87 (d, *J* = 13.7 Hz, 1H), 2.61 (d, *J* = 13.7 Hz, 1H), 2.07 (s, 3H), 1.76 – 1.71 (m, 1H), 1.46 – 1.42 (m, 1H), 1.05 (s, 3H), 0.83 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125

MHz, $CDCl_3$) δ 213.78, 154.11, 131.31, 129.96, 114.90, 52.66, 43.11, 31.10, 26.64, 20.29, 8.90. IR (KBr) 3351, 2921, 2855, 1732, 1682, 1558, 1472 cm^{-1}. HRMS (ESI) calculated for $C_{13}H_{17}O_2$ (M - H)$^-$: 205.1229, found: 205.1240.



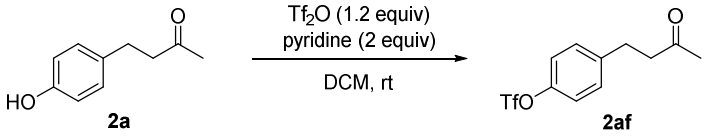
4aa

4-Hydroxybenzyl acetate (4aa): Following procedure A, compound **4aa** was obtained in a yield of 56% (18.7 mg, pale yellow oil). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.21 (m, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 5.45 (s, 1H), 5.03 (s, 2H), 2.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 155.8, 130.3, 128.0, 115.4, 66.2, 21.0. IR (KBr) 3356, 1718, 1616, 1517, 1362, 1264, 1233, 1171, 1027, 828 cm^{-1}. HRMS (ESI) calculated for $C_9H_{10}O_3Na$ (M + Na)$^+$: 189.0528, found: 189.0522.



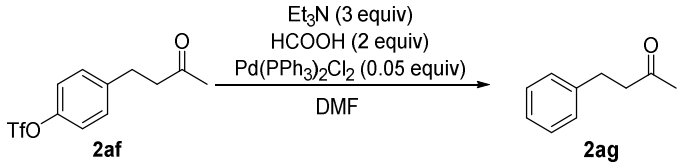
5b **5c**

4-(2-Hydroxyphenyl) butan-2-one (5b) and 2-methylchroman-2-ol (5c): Following procedure A, compound **5b** and **5c** was obtained in a total yield of 58% (19.2 mg, pale yellow oil, 5b:5c = 2.1:1). Spectrum data matches that reported in the literature[4]. HRMS (ESI) calculated for $C_{10}H_{11}O_2$ (M - H)$^-$: 163.0759, found: 163.0765.



2a **2af**

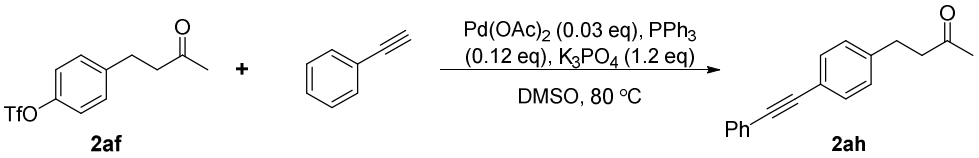
4-(3-Oxobutyl)phenyl trifluoromethanesulfonate (2af): To a solution of **2a** (31.9 mg, 0.19 mmol) in DCM was added pyridine (30.1 mg, 0.38 mmol, 2 equiv). The mixture was cooled to 0 °C before Tf_2O (65.8 mg, 0.23 mmol, 1.2 equiv) was added dropwise. The reaction was monitored by TLC until substrate was disappeared. Then the reaction mixture was diluted with Et_2O, quenched with 10% aqueous HCl and washed with saturated $NaHCO_3$. Then the organic phase was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by flash chromatography (silica gel, hexanes/EtOAc = 6:1) afforded **2af** (51.9 mg, 92 % yield, pale yellow liquid). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H), 2.90 (d, *J* = 7.5 Hz, 2H), 2.77 (d, *J* = 7.5 Hz, 2H), 2.14 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.92, 147.95, 141.72, 130.11, 121.26, 120.03 (d, *J* = 319 Hz), 44.61, 29.97, 28.86. IR (KBr) 1718, 1506, 1419, 1363, 1250, 1216, 1141, 1017, 889, 824, 719, 697, 639, 608, 501 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{11}F_3NaO_4S$ (M + Na)$^+$: 319.0228, found: 319.0224.



2af **2ag**

4-Phenylbutan-2-one (2ag)[5]: To a mixture of **2af** (52.6 mg, 0.178 mmol), Et_3N (54.0 mg, 0.533 mmol, 3 equiv) and $Pd(PPh_3)_2Cl_2$ (6.3 mg, 0.0089 mmol, 0.05 equiv) in anhydrous DMF was added formic acid (16.4 mg, 0.356 mmol, 2 equiv) in one portion. Then the mixture was warmed to 110 °C until **2af** was disappeared (monitored by TLC). The reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated at reduced pressure. The residue was further purified by column chromatography (silica

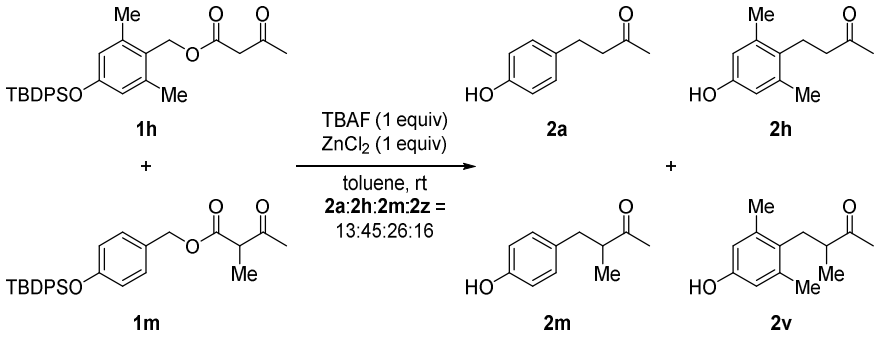
gel, hexanes/EtOAc = 50:1 to 20:1) to afford compound **2ag** as pink liquid in 75% yield (19.7 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.24 (m, 2H), 7.19 (t, *J* = 6.4 Hz, 3H), 2.94–2.86 (m, 2H), 2.76 (dd, *J* = 11.2, 4.3 Hz, 2H), 2.14 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.98, 140.93, 128.45, 128.24, 126.06, 45.14, 30.04, 29.67. IR (KBr) 3062, 3028, 2925, 1718, 1603, 1496, 1453, 1409, 1358, 1162 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_{13}O$ (M + H)$^+$: 149.0966, found: 149.0963.



2af **2ah**

4-(4-(Phenylethynyl)phenyl)butan-2-one (2ah)[6]: A solution of **2af** (30 mg, 0.1 mmol), phenylacetylene (15.3 mg, 0.15 mmol, 1.5 equiv), $Pd(OAc)_2$ (0.67 mg, 0.003 mmol, 0.03 equiv), PPh_3 (3.15 mg, 0.012 mmol, 0.12 equiv) and K_3PO_4 (25.5 mg, 0.12 mmol, 1.2 equiv) in dry DMSO (0.2 mL) was degassed by four freeze-thaw cycles. The mixture began to be stirred at 80 °C until **2af** was disappeared (monitored by TLC). Water was added and the mixture was extracted with diethyl ether. Then the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated at reduced pressure. The residue was further purified by column chromatography (silica gel, hexanes/EtOAc = 100:1 to 60:1) to afford **2ah** (18.5 mg, yellow oil) in 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.4, 1.9 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 6.9 Hz, 3H), 7.17 (d, *J* = 8.1 Hz, 2H). 2.91 (dd, *J* = 9.2, 5.8 Hz, 2H), 2.77 (t, *J* = 7.5 Hz, 2H), 2.15 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.42, 141.41, 132.10, 131.74, 131.56, 128.35, 128.30, 128.13, 121.11, 89.30, 89.07, 44.80, 30.04, 29.64. IR (KBr) 3079, 3031, 2954, 2916, 2849, 1714, 1706, 1669, 1653, 1559, 1539, 1520, 1507, 1490, 1472, 1457, 1418, 1339, 1260, 755, 418 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{17}O$ (M + H)$^+$: 249.1279, found: 249.1273.

IV. Crossover Reaction



General procedures for crossover reaction: To a 5 mL oven-dried round-bottomed flask placed with a solution of *β*–ketoester **1h** (47.4 mg, 0.1 mmol), *β*–ketoester **1m** (46.1 mg, 0.1 mmol, 1.0 equiv) and $ZnCl_2$ (27.3 mg, 0.2 mmol, 2.0 equiv) in toluene (2.0 mL), TBAF (200 uL, 1M in THF, 2.0 equiv) was added via micro-syringe. The mixture was stirred at room temperature until *β*–ketoester **1m** and **1h** disappeared. Then the reaction was quenched with H_2O. The aqueous phase was extracted with EtOAc and the combined organic phases were dried over anhydrous Na_2SO_4. The residue was evaporated under reduced pressure and purified by column chromatography (silica gel, hexanes/EtOAc = 4:1). A mixture of **2a**, **2h**, **2m** and **2v** were detected by HRMS, the relative proportion was detected by GC-MS, using biphenyl as an internal standard.

V. ^{1}H and ^{13}C NMR Spectra

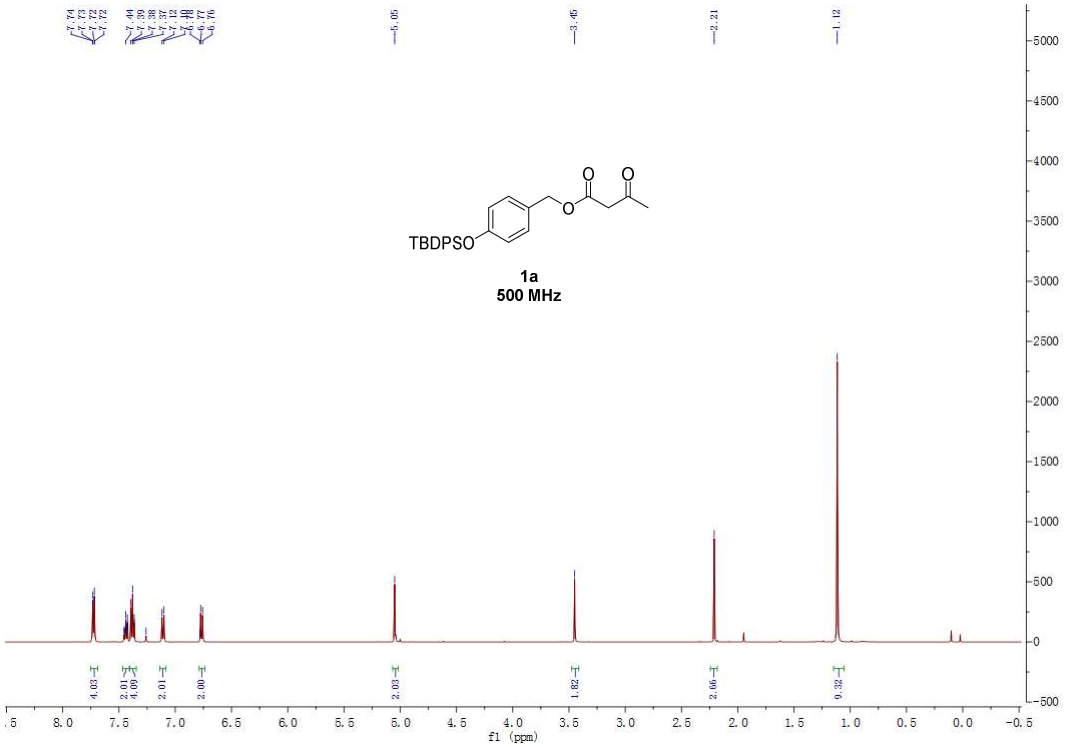


Fig. S1. ^{1}H NMR Spectrum of 1a (500 MHz, $CDCl_3$).

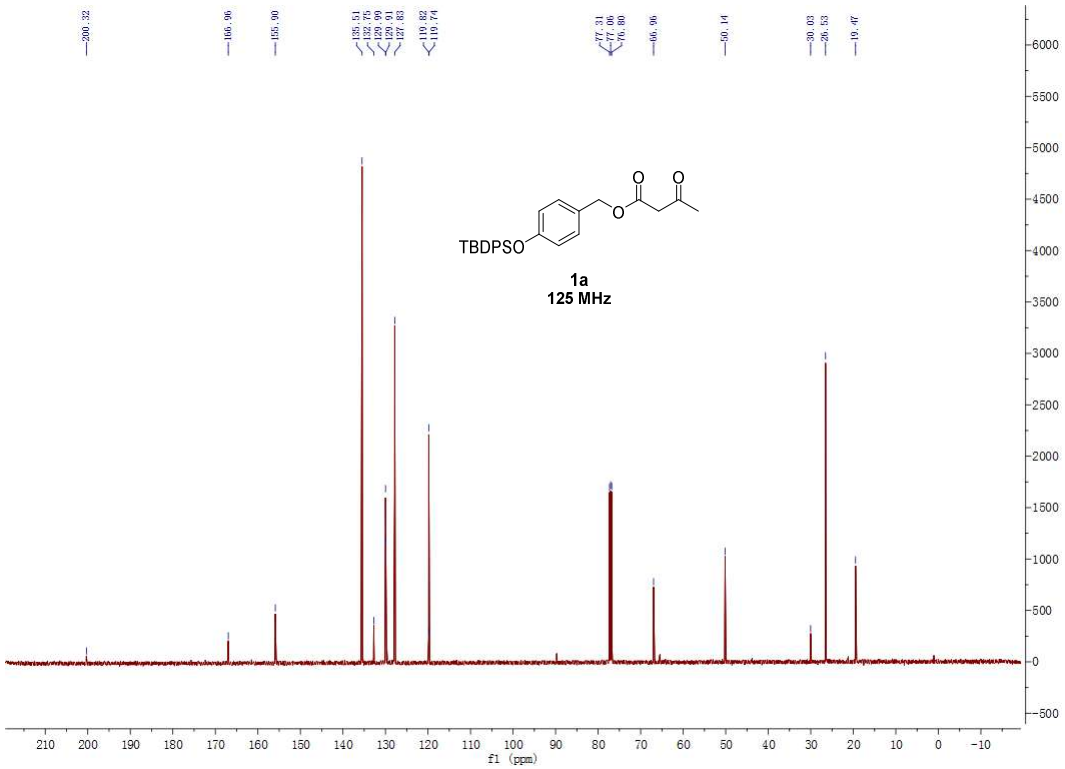


Fig. S2. ^{13}C NMR Spectrum of 1a (125 MHz, $CDCl_3$).

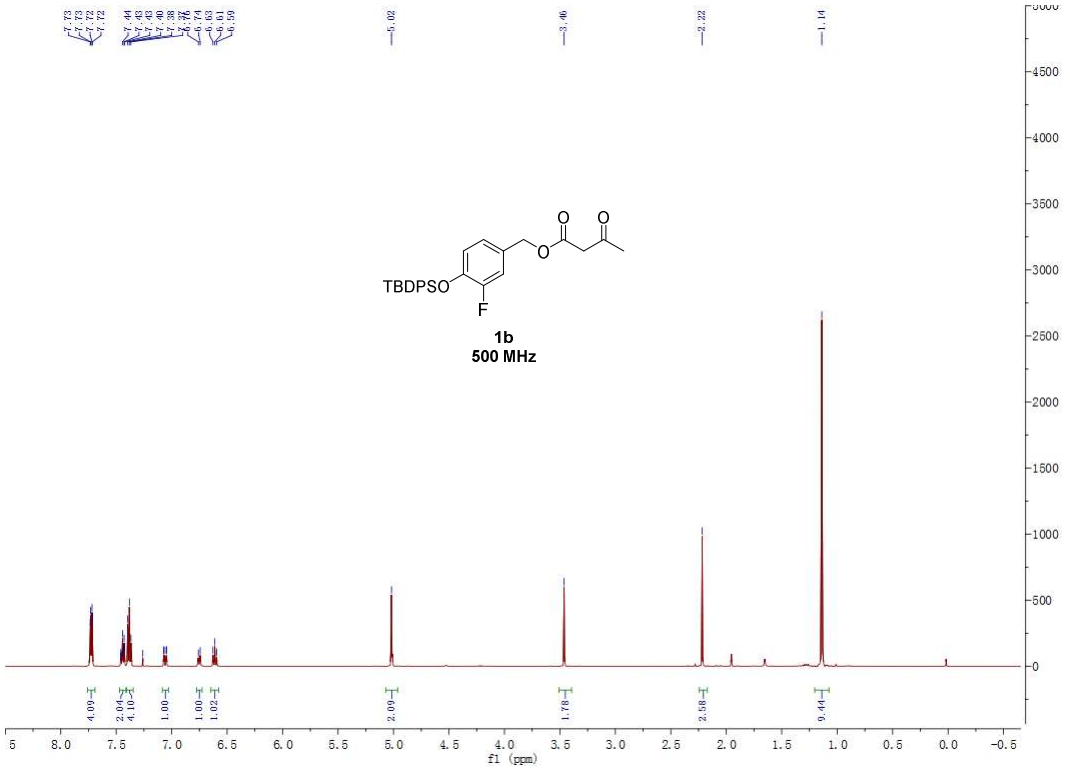


Fig. S3. ^{1}H NMR Spectrum of 1b (500 MHz, $CDCl_3$).

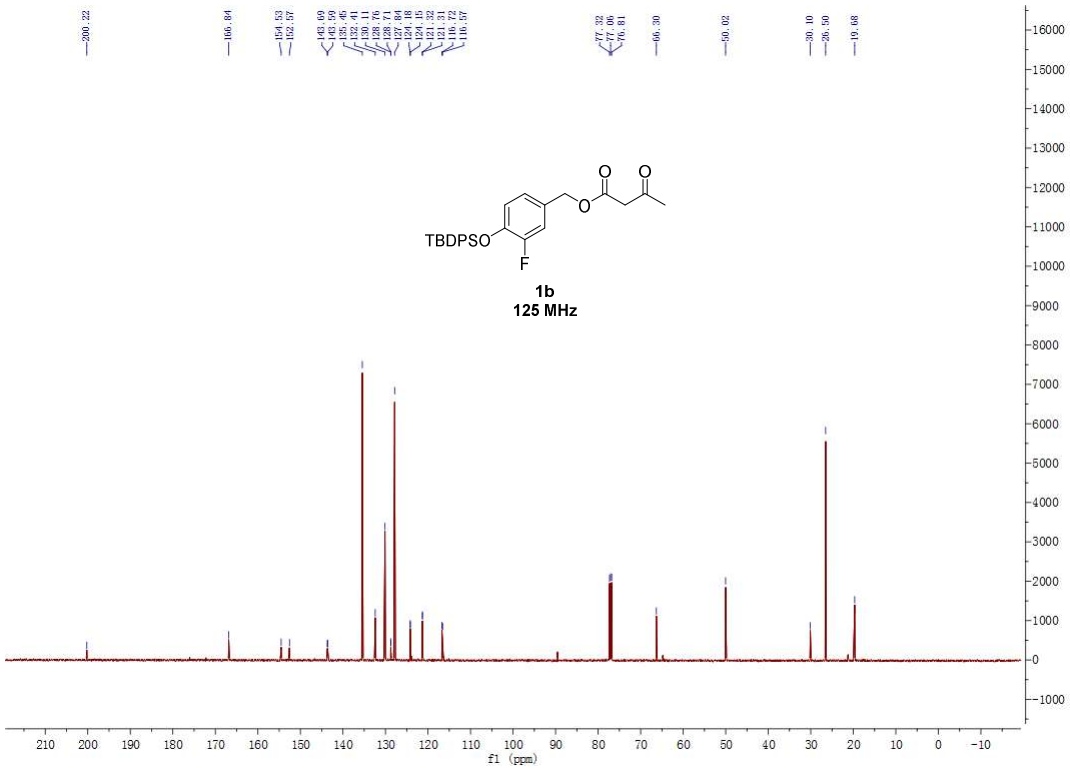


Fig. S4. ^{13}C NMR Spectrum of 1b (125 MHz, $CDCl_3$).

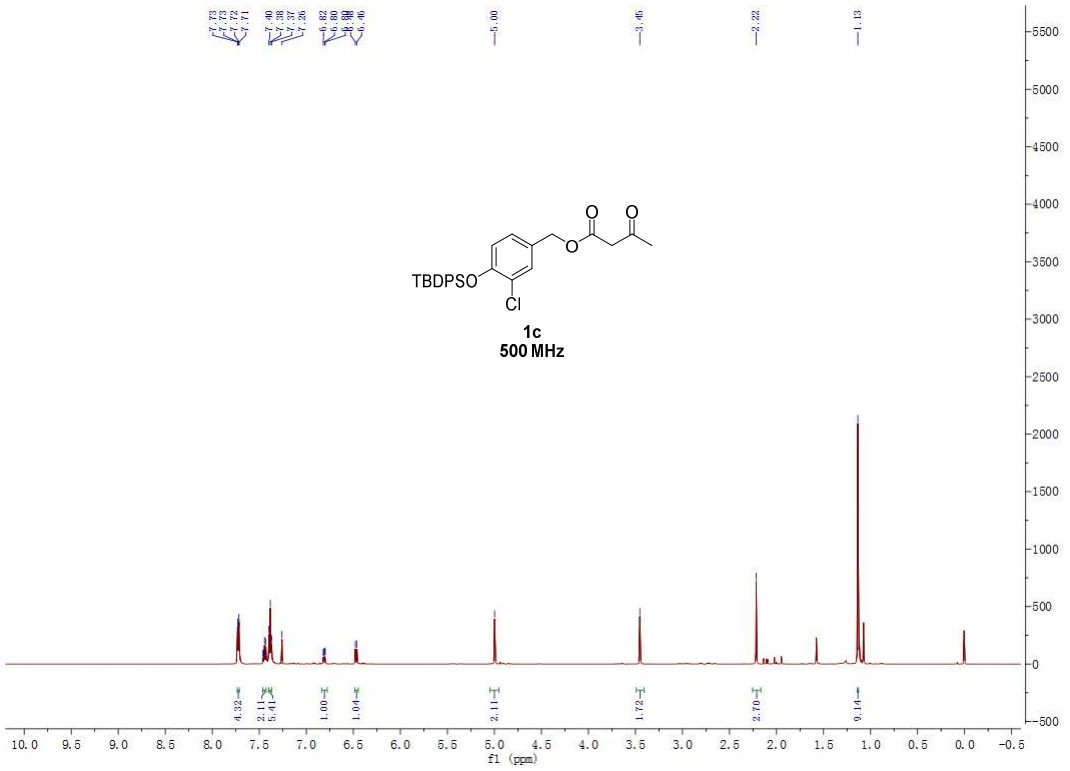


Fig. S5. ^{1}H NMR Spectrum of 1c (500 MHz, $CDCl_3$).

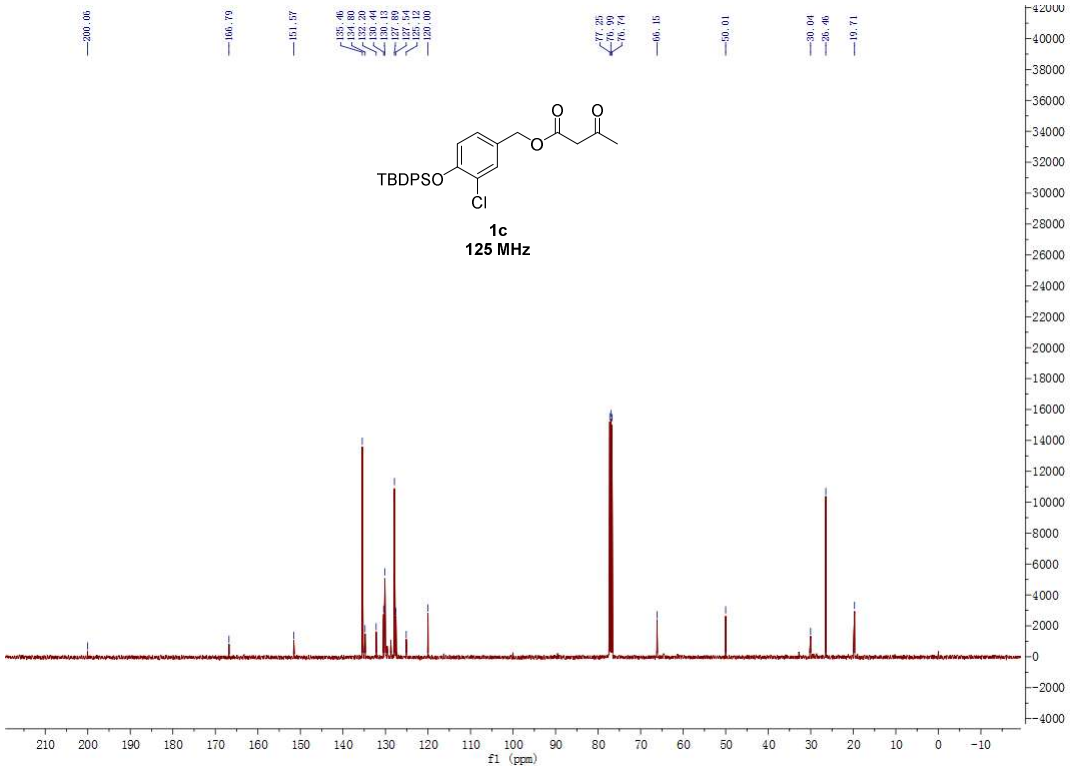


Fig. S6. ^{13}C NMR Spectrum of 1c (125 MHz, $CDCl_3$).

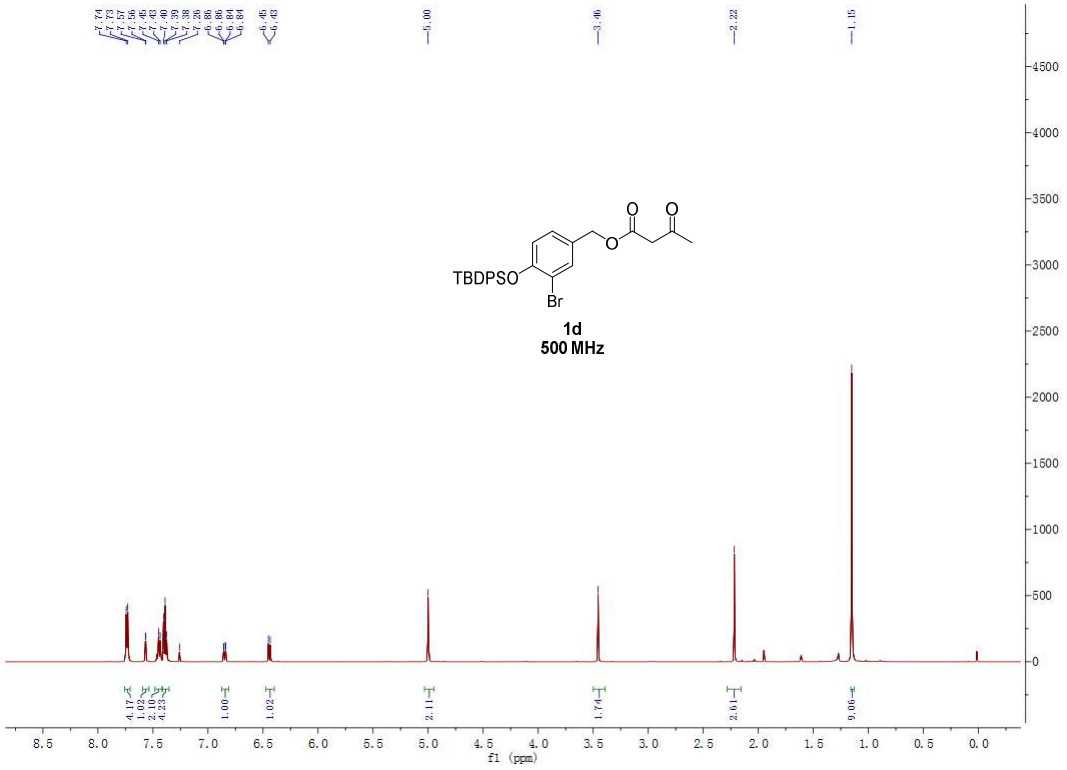


Fig. S7. ^{1}H NMR Spectrum of 1d (500 MHz, $CDCl_3$).

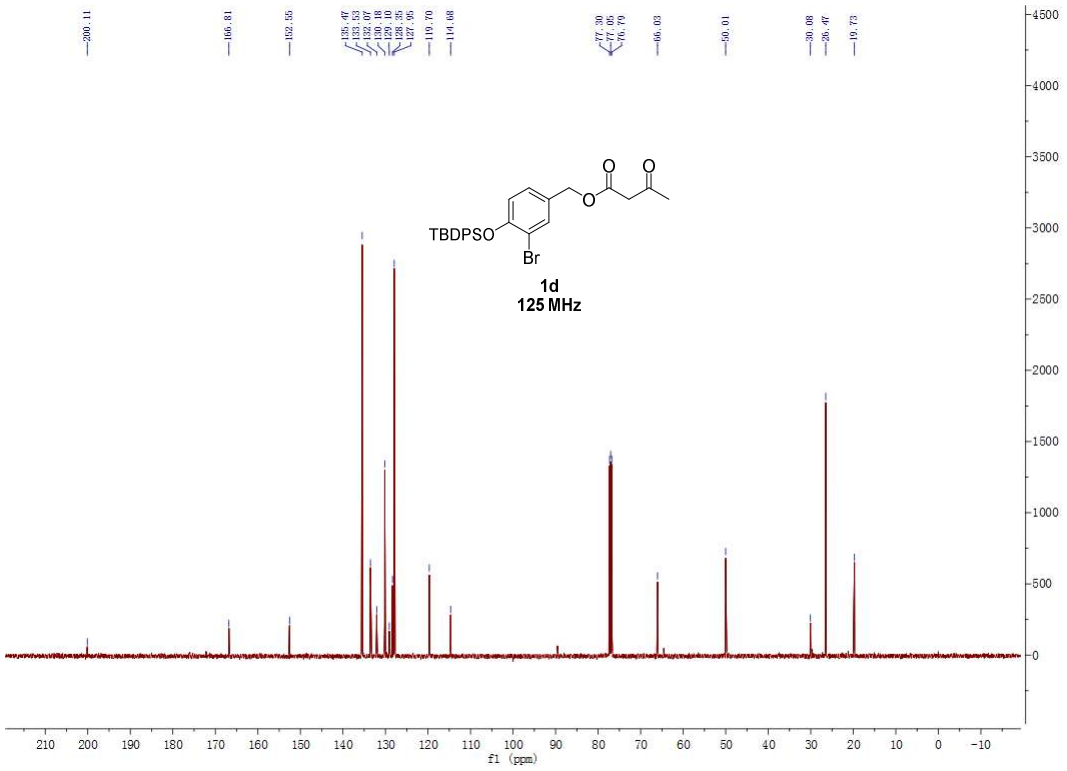


Fig. S8. ^{13}C NMR Spectrum of 1d (125 MHz, $CDCl_3$).

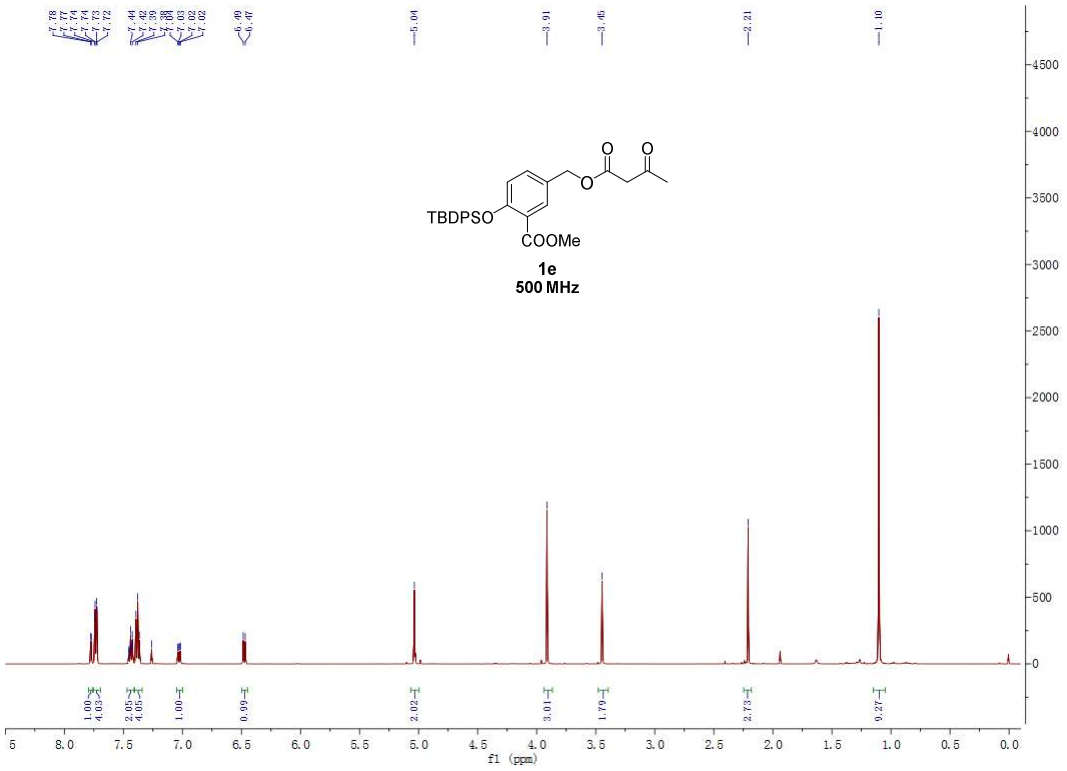


Fig. S9. ^{1}H NMR Spectrum of 1e (500 MHz, $CDCl_3$).

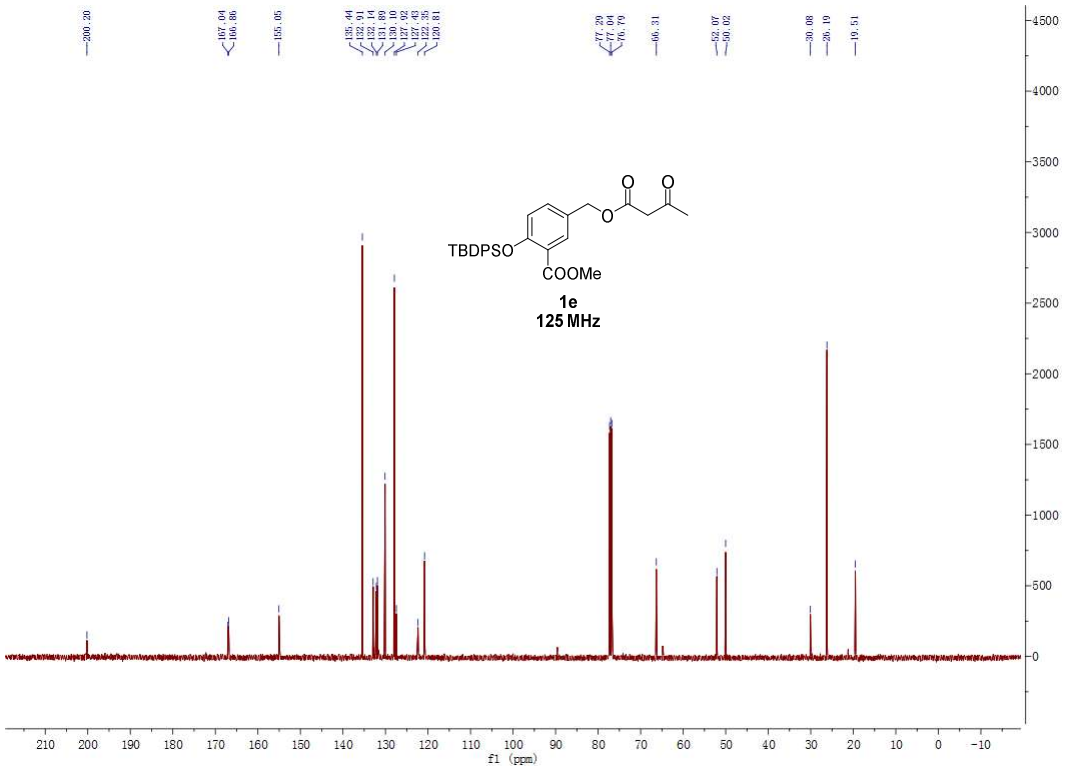


Fig. S10. ^{13}C NMR Spectrum of 1e (125 MHz, $CDCl_3$).

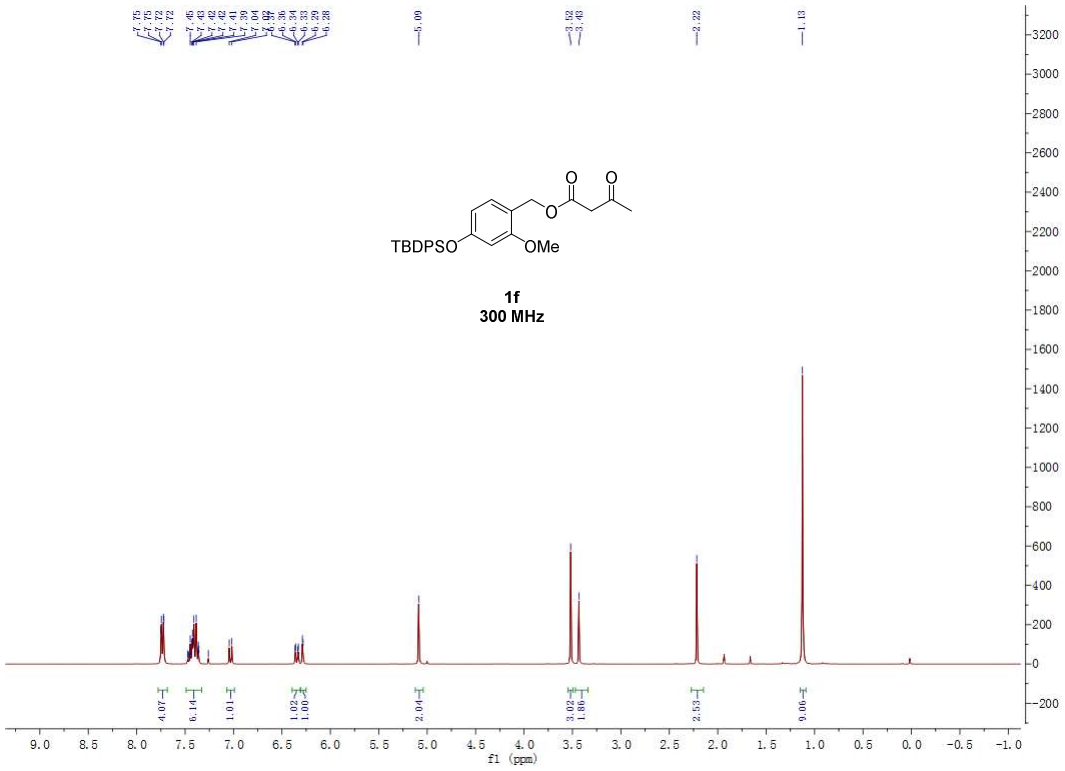


Fig. S11. ^{1}H NMR Spectrum of 1f (300 MHz, $CDCl_3$).

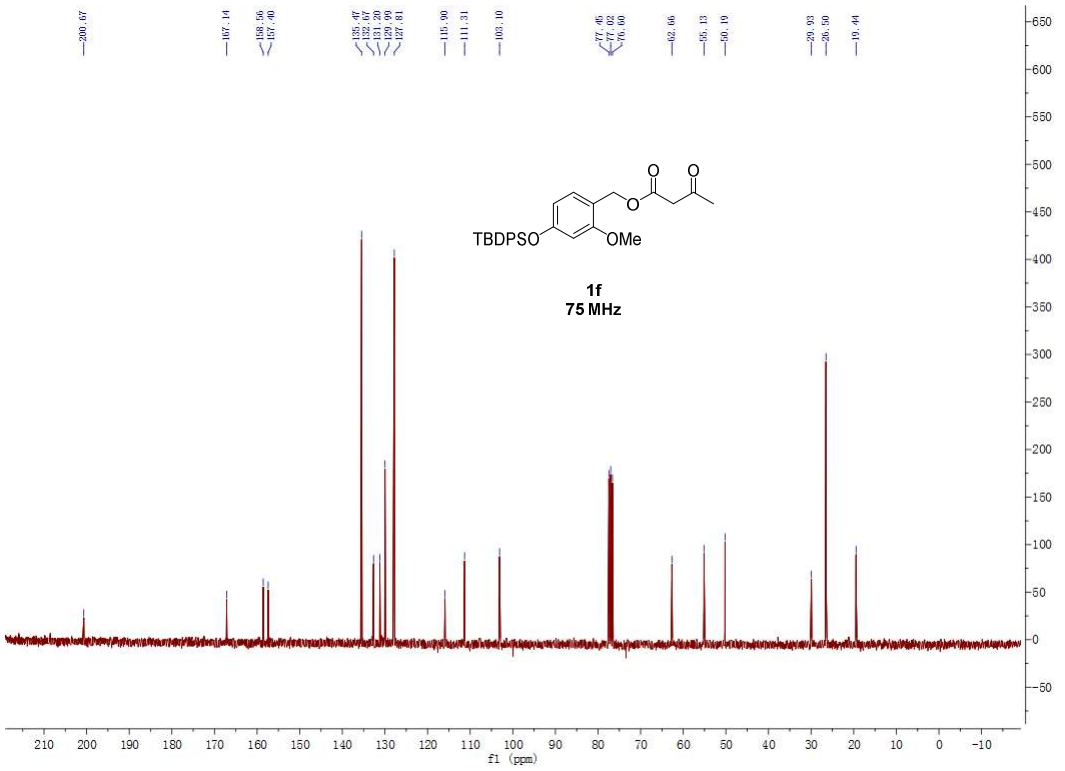


Fig. S12. ^{13}C NMR Spectrum of 1f (75 MHz, $CDCl_3$).

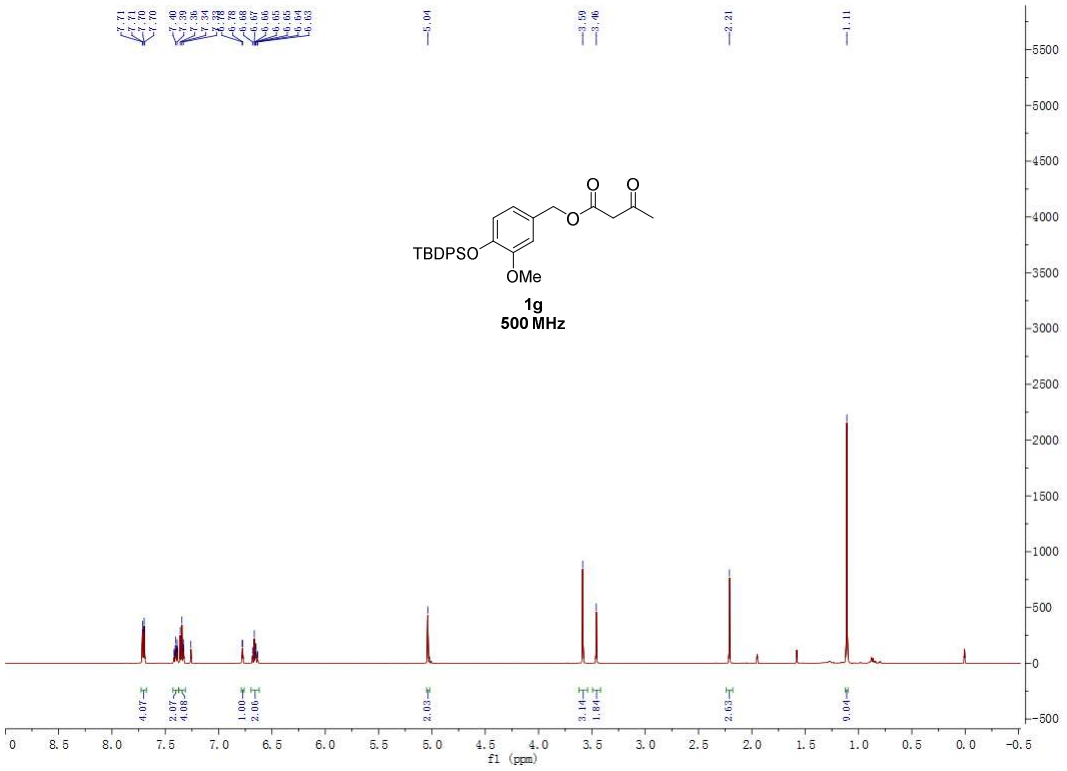


Fig. S13. ^{1}H NMR Spectrum of 1g (500 MHz, $CDCl_3$).

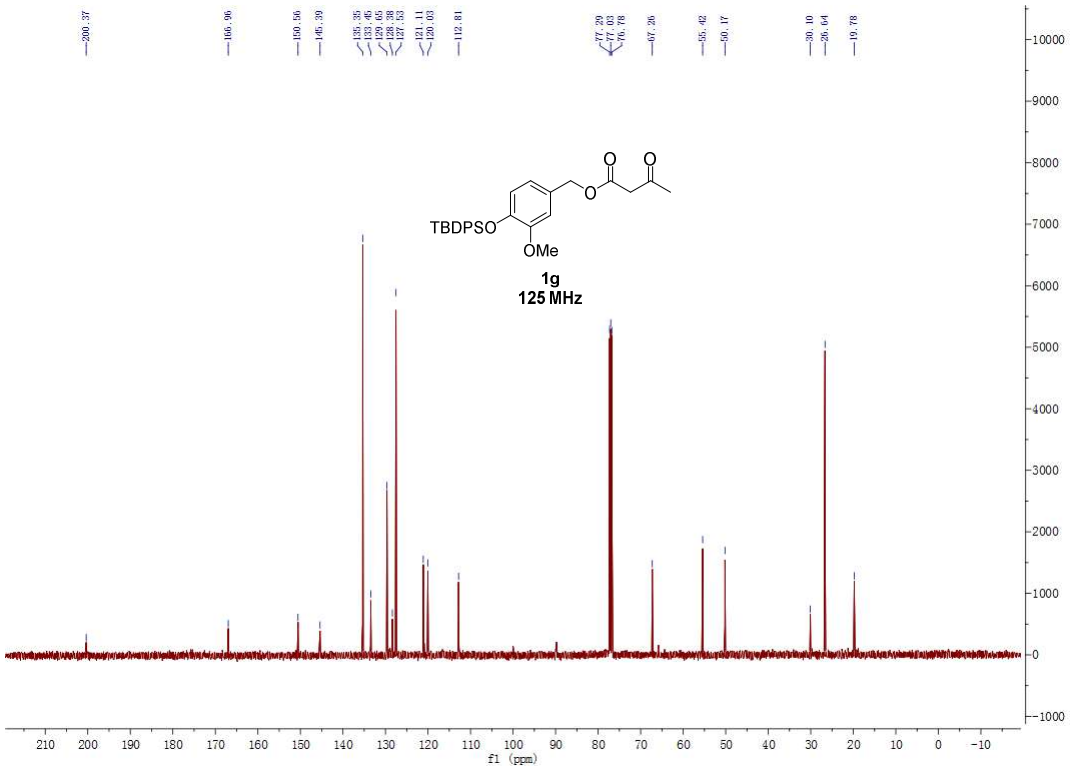


Fig. S14. ^{13}C NMR Spectrum of 1g (125 MHz, $CDCl_3$).

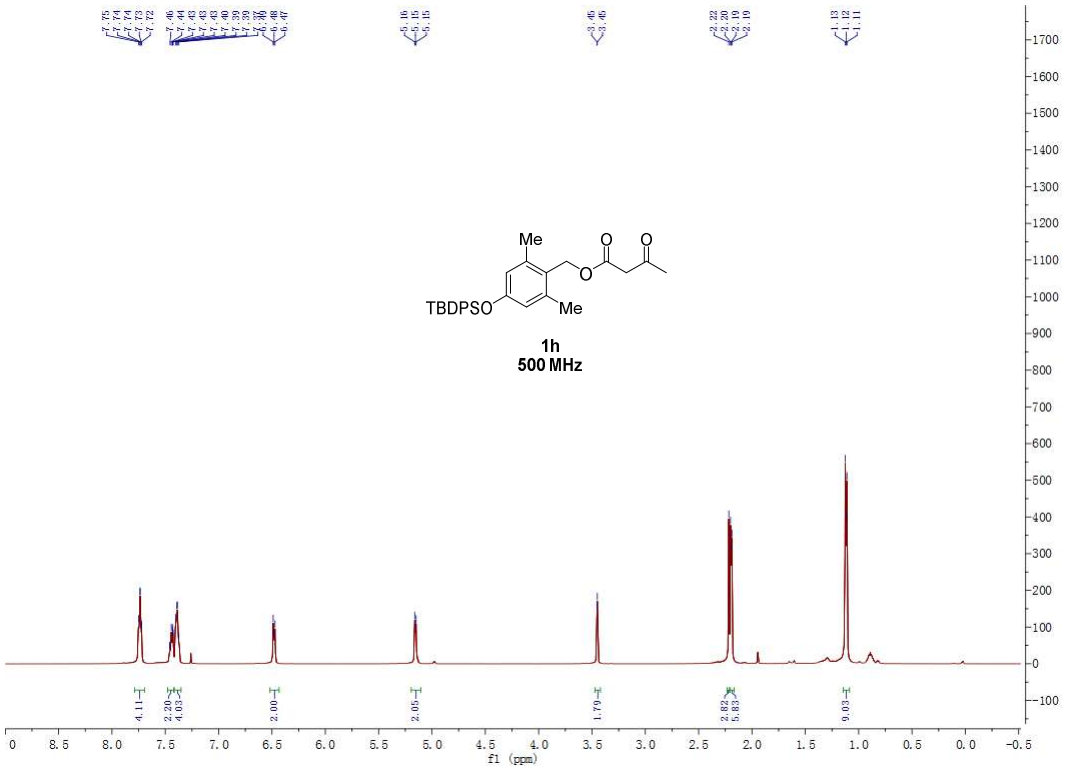


Fig. S15. ^{1}H NMR Spectrum of 1h (500 MHz, $CDCl_3$).

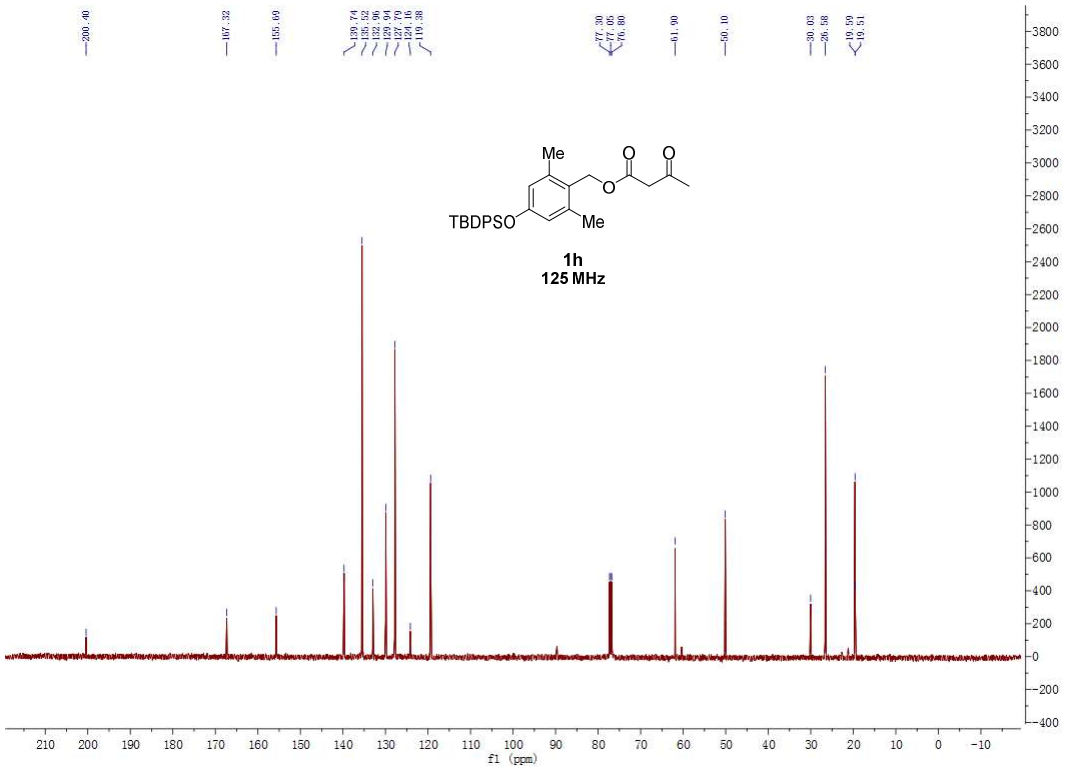


Fig. S16. ^{13}C NMR Spectrum of 1h (125 MHz, $CDCl_3$).

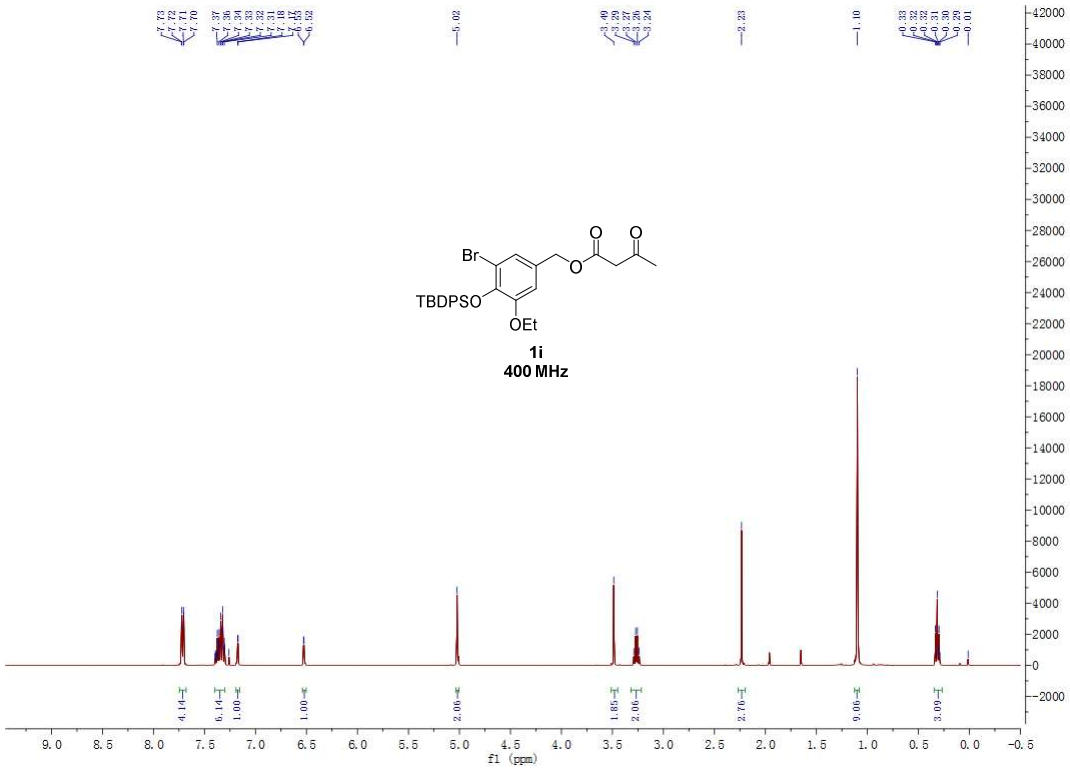


Fig. S17. ^{1}H NMR Spectrum of 1i (400 MHz, $CDCl_3$).

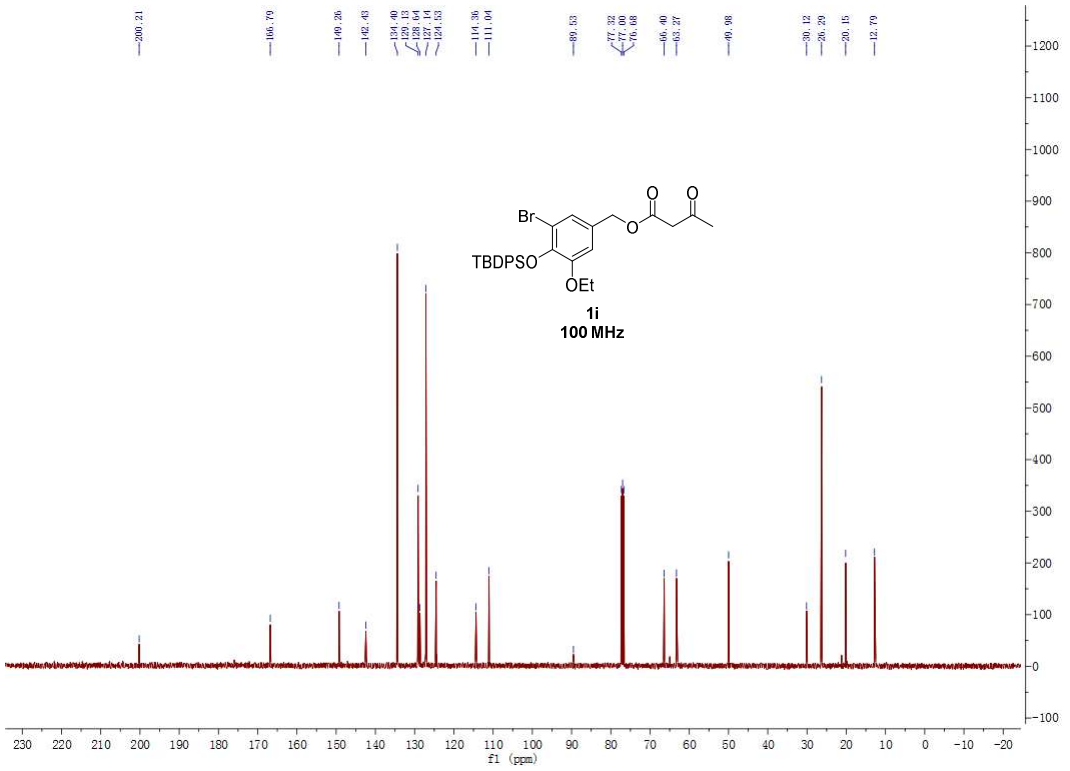


Fig. S18. ^{13}C NMR Spectrum of 1i (100 MHz, $CDCl_3$).

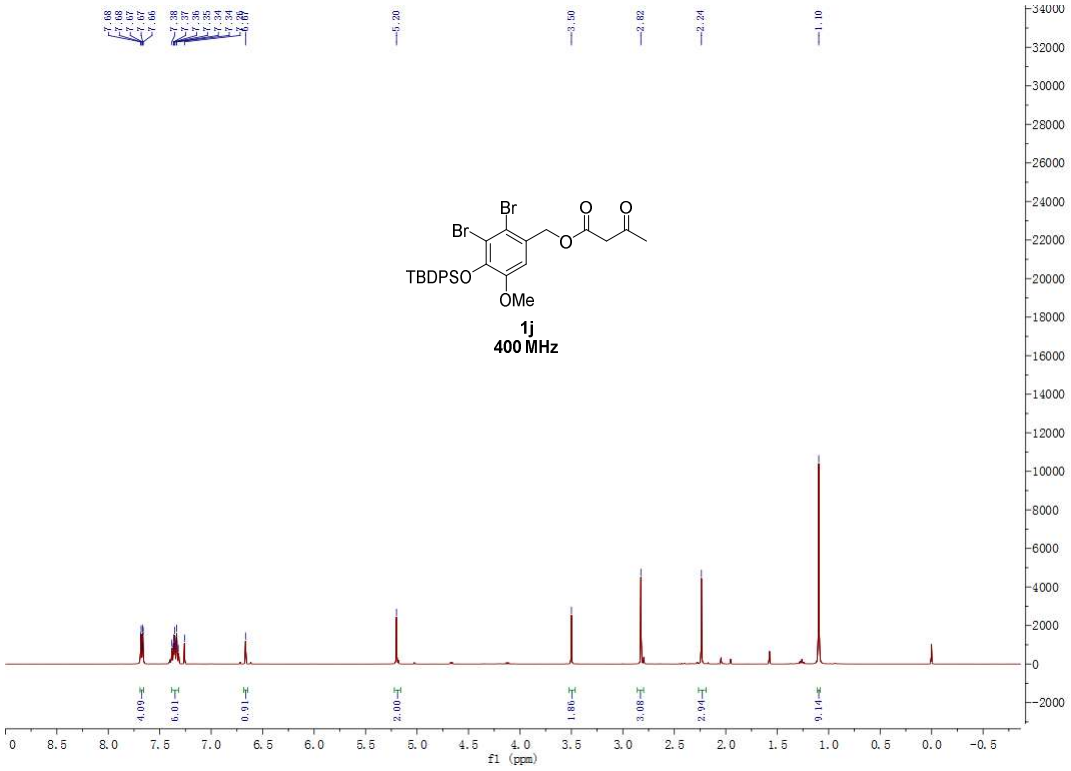


Fig. S19. ^{1}H NMR Spectrum of 1j (400 MHz, $CDCl_3$).

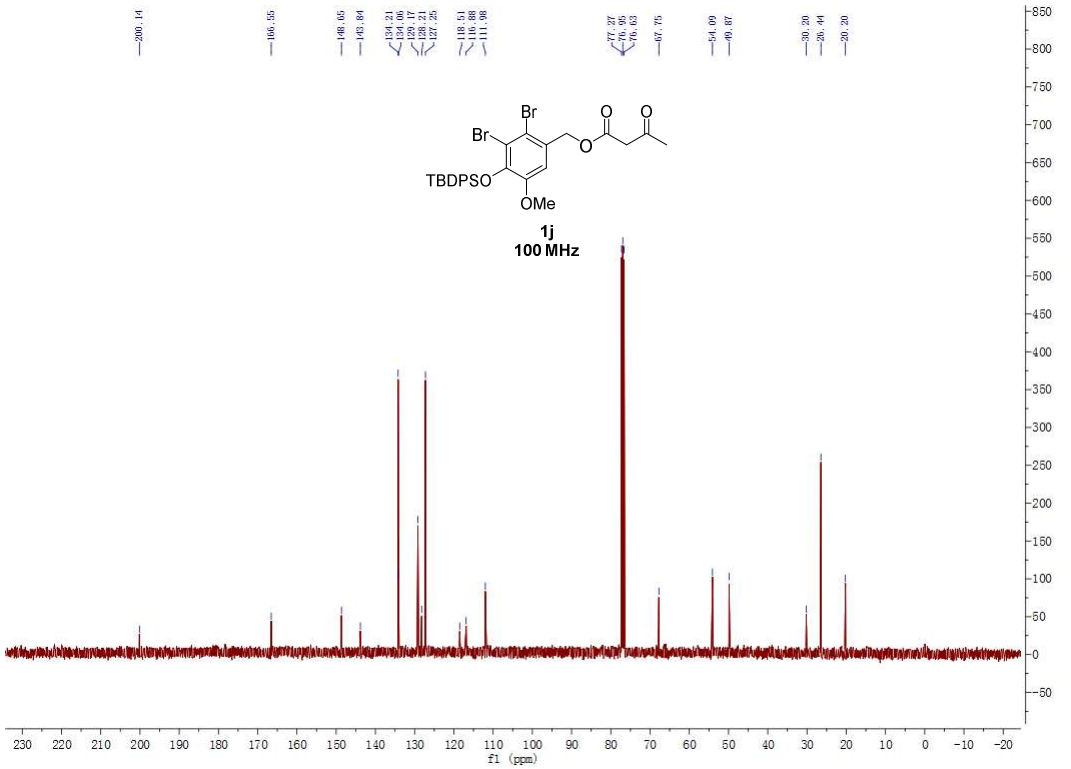


Fig. S20. ^{13}C NMR Spectrum of 1j (100 MHz, $CDCl_3$).

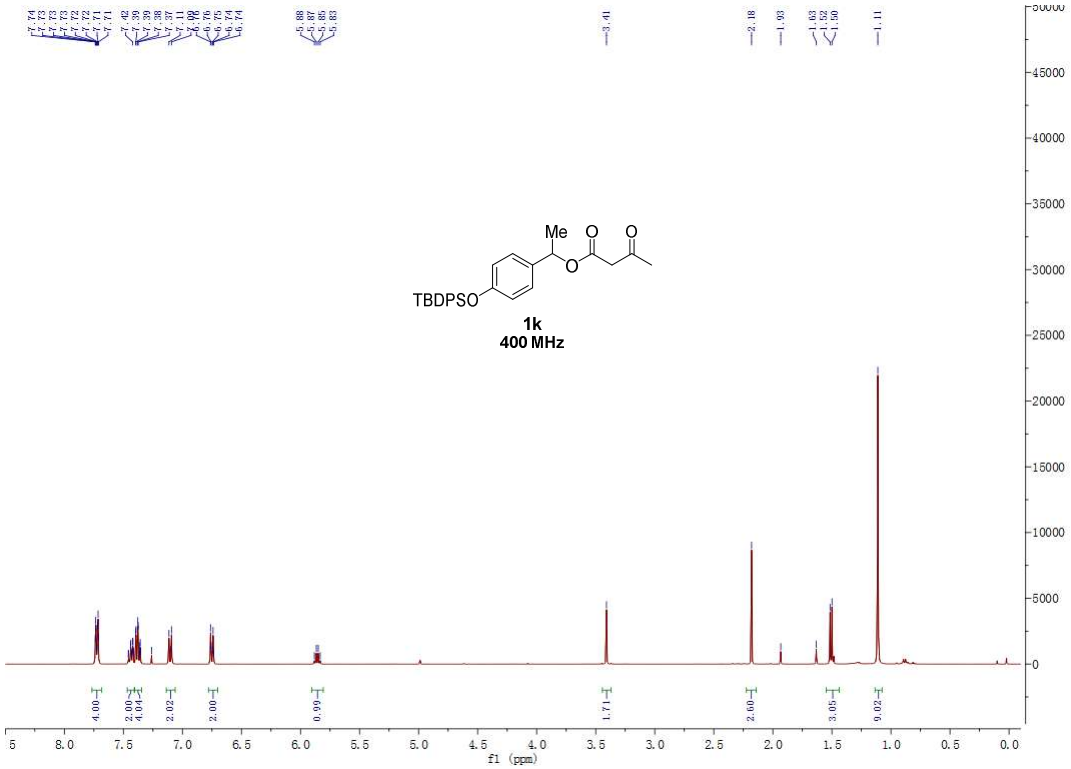


Fig. S21. ^{1}H NMR Spectrum of 1k (400 MHz, $CDCl_3$).

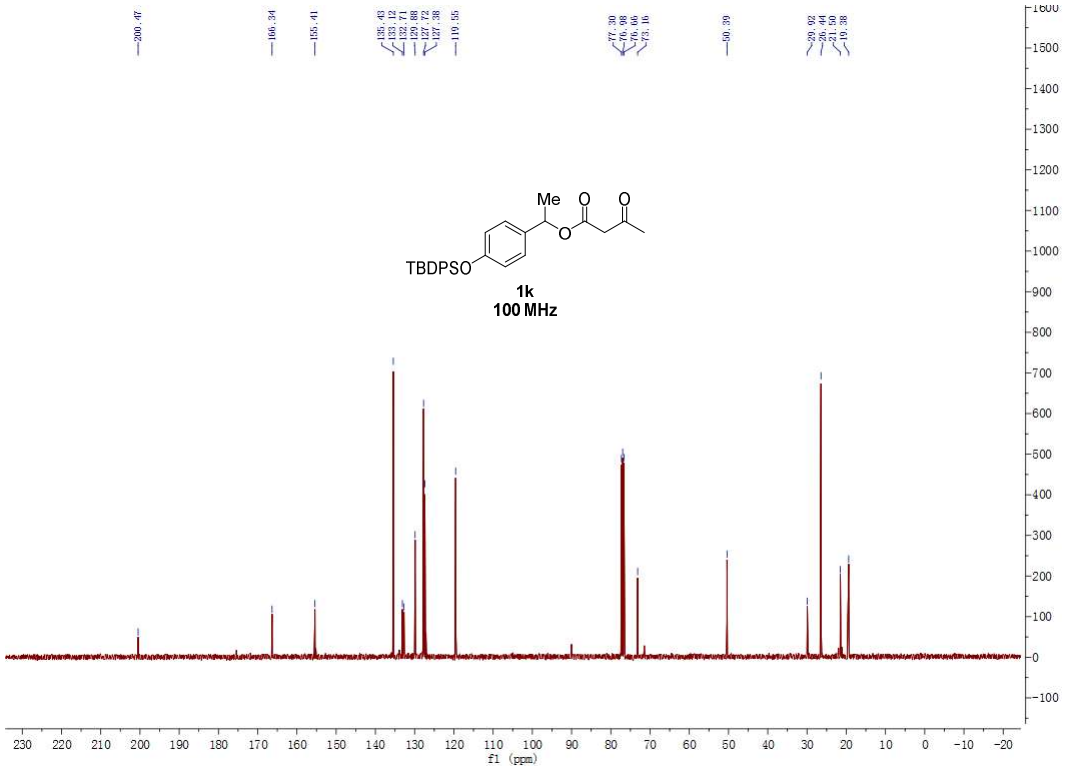


Fig. S22. ^{13}C NMR Spectrum of 1k (100 MHz, $CDCl_3$).

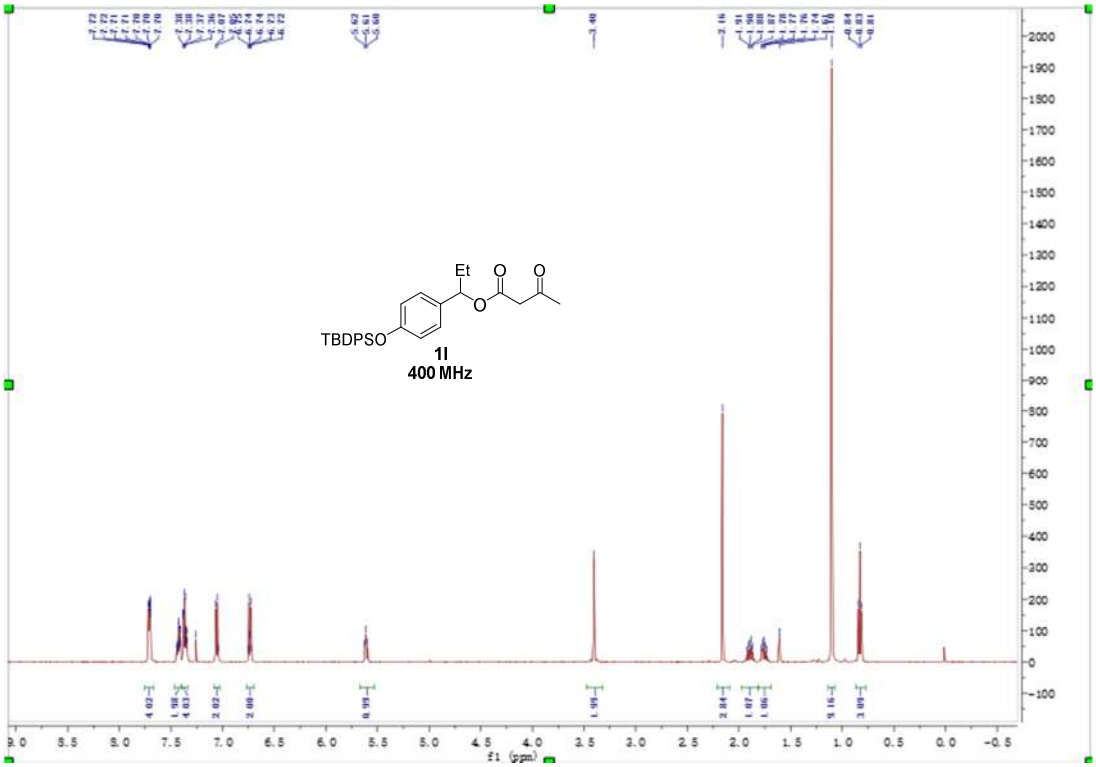


Fig. S23. ^{1}H NMR Spectrum of 1l (400 MHz, $CDCl_3$).

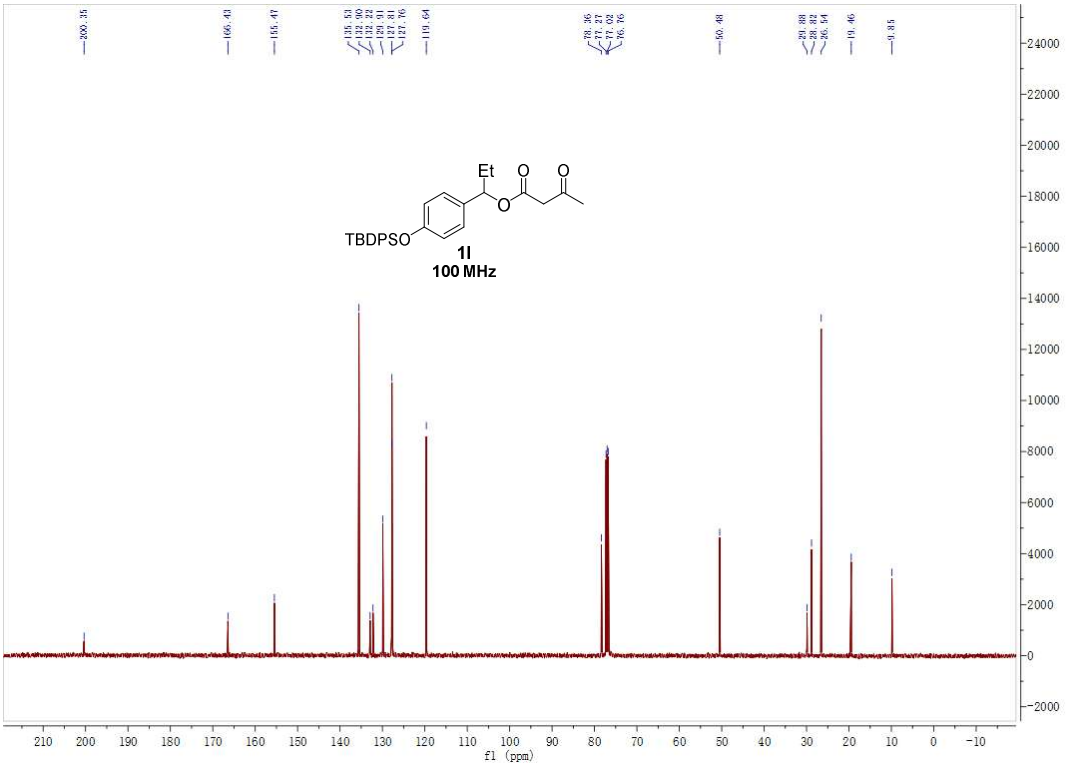


Fig. S24. ^{13}C NMR Spectrum of 1l (100 MHz, $CDCl_3$).

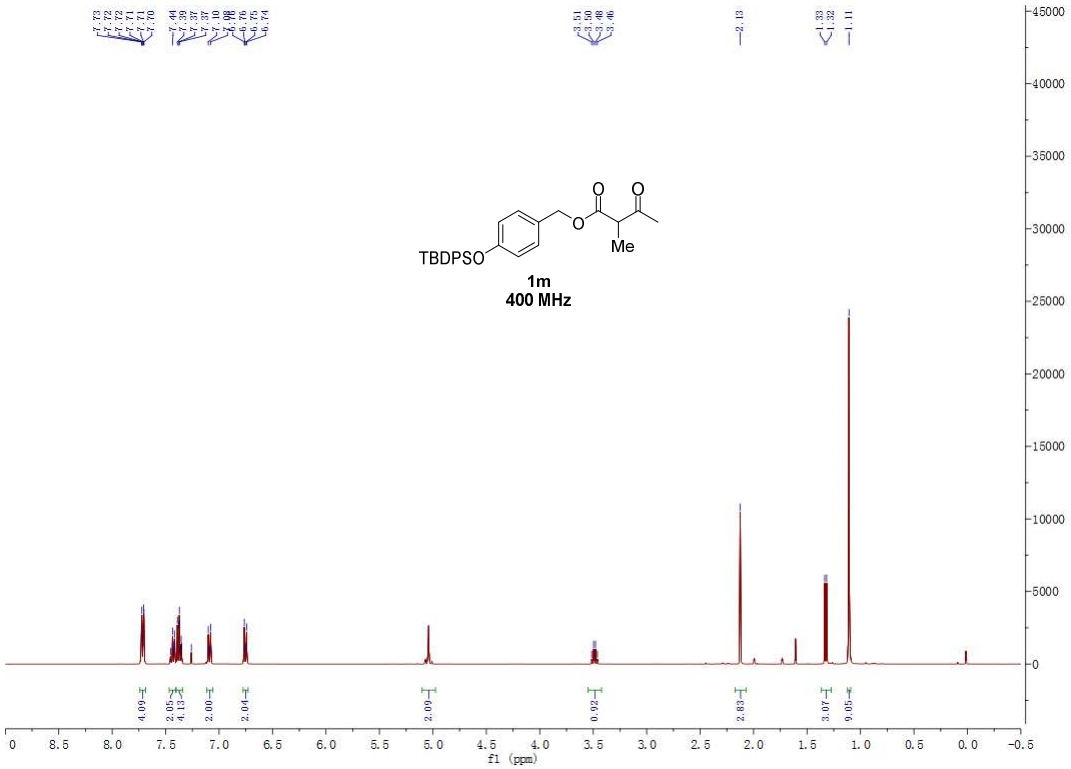


Fig. S25. ^{1}H NMR Spectrum of 1m (400 MHz, $CDCl_3$).

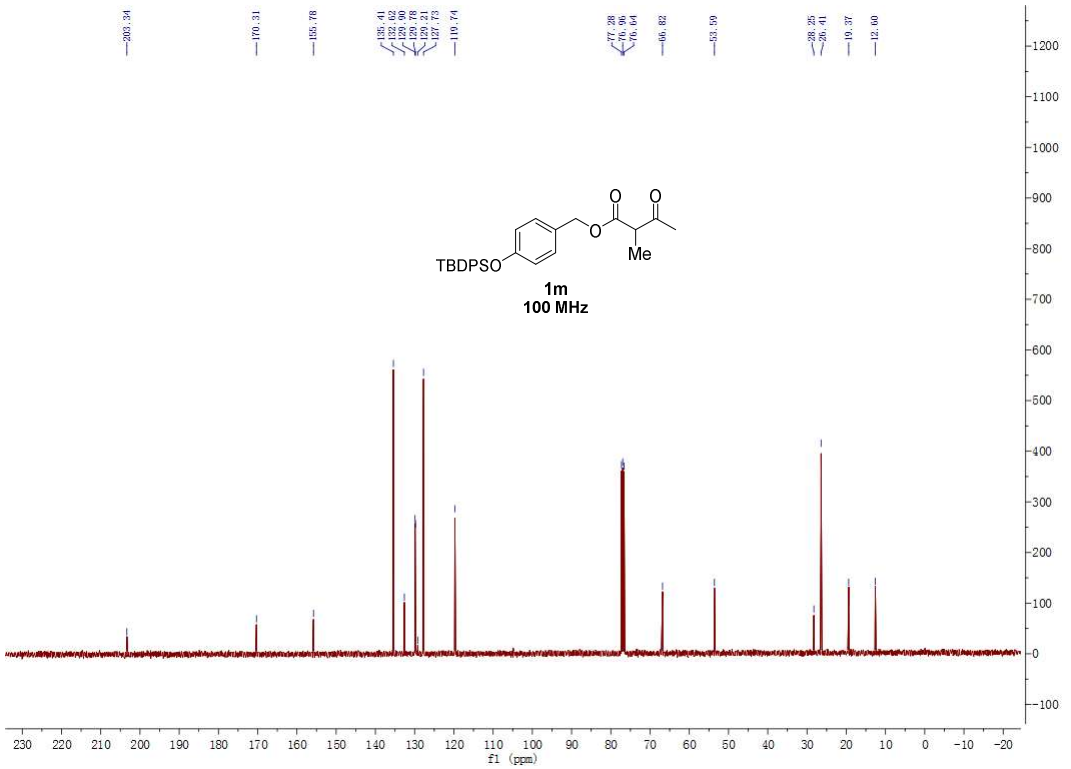


Fig. S26. ^{13}C NMR Spectrum of 1m (100 MHz, $CDCl_3$).

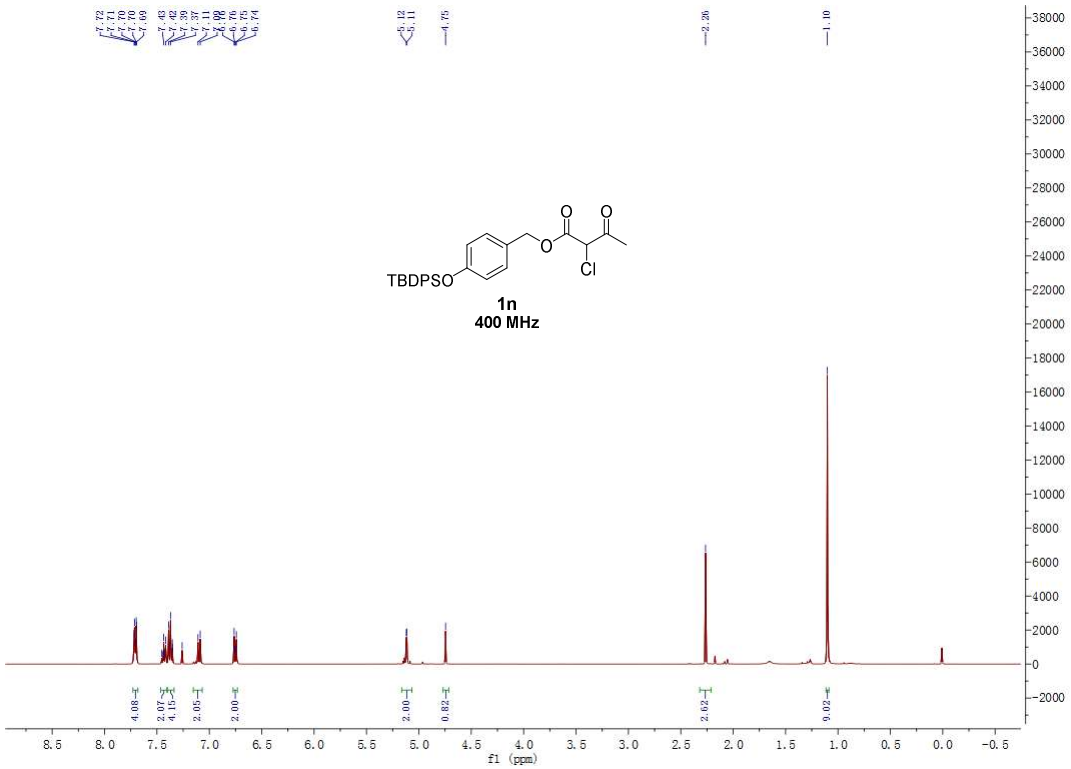


Fig. S27. ^{1}H NMR Spectrum of 1n (400 MHz, $CDCl_3$).

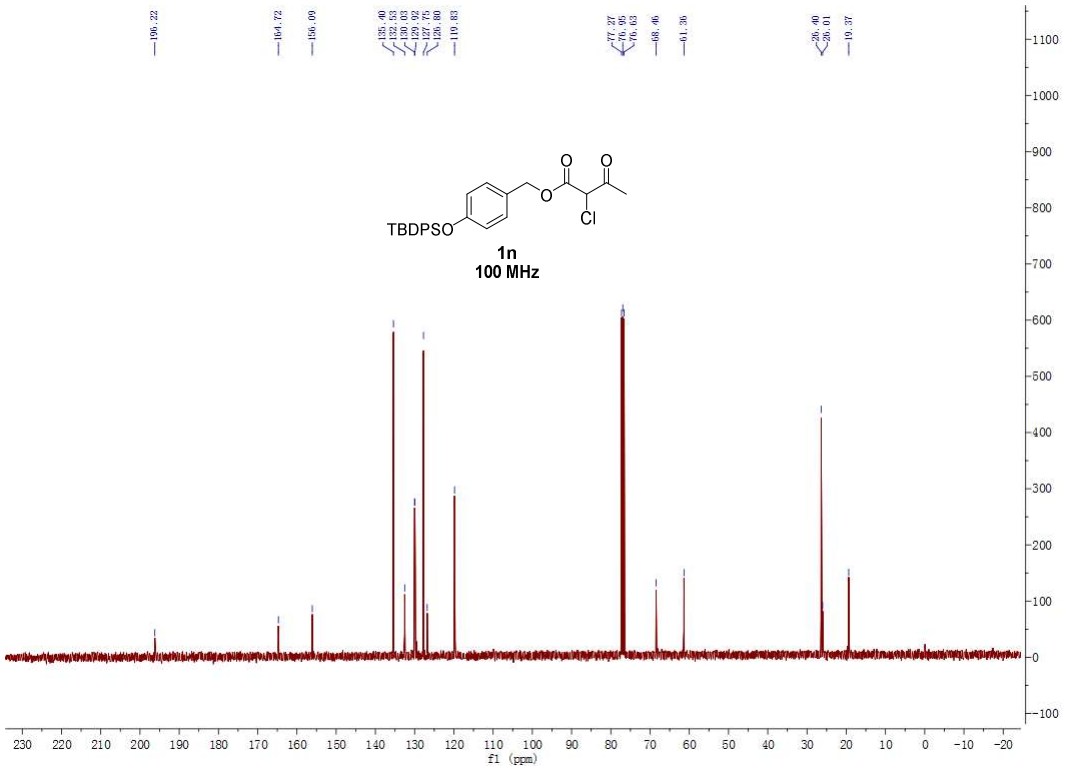


Fig. S28. ^{13}C NMR Spectrum of 1n (100 MHz, $CDCl_3$).

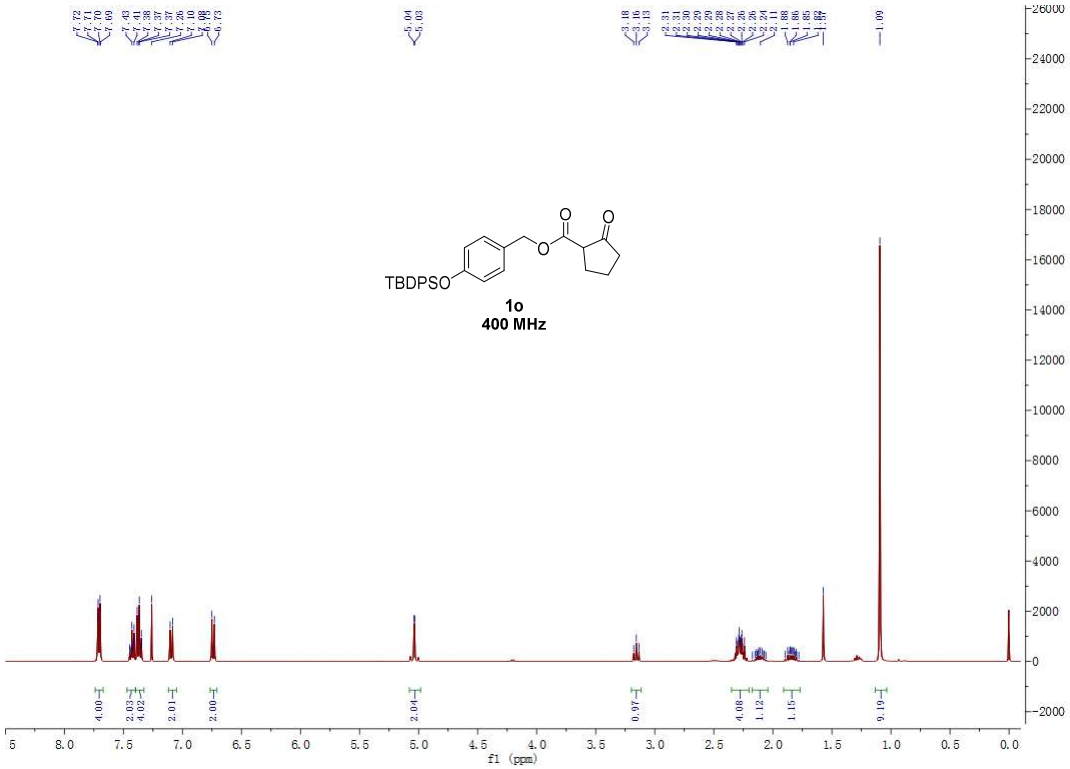


Fig. S29. ^{1}H NMR Spectrum of 1o (400 MHz, $CDCl_3$).

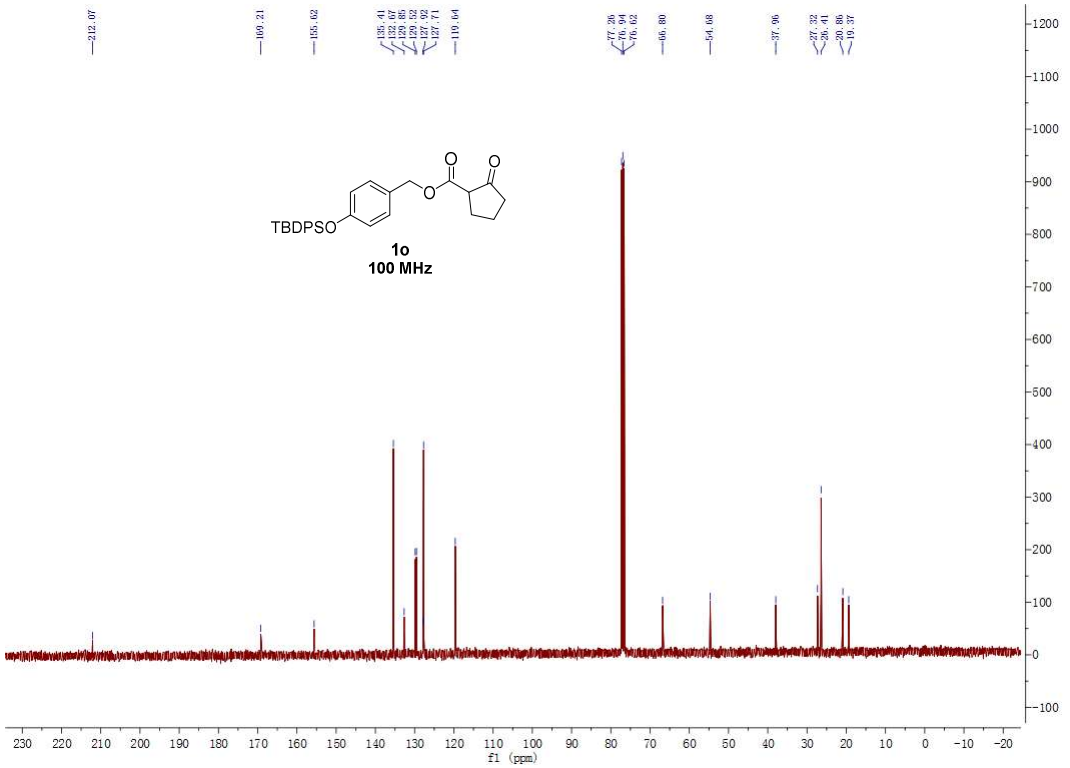


Fig. S30. ^{13}C NMR Spectrum of 1o (100 MHz, $CDCl_3$).

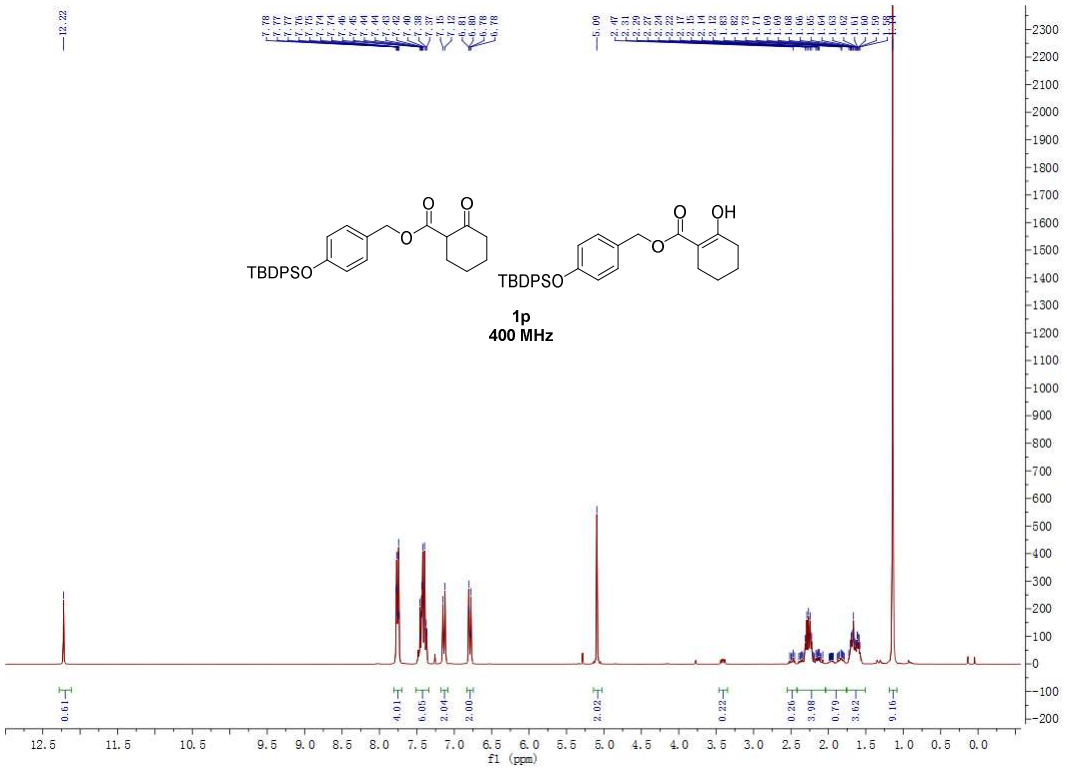


Fig. S31. ^{1}H NMR Spectrum of 1p (400 MHz, $CDCl_3$).

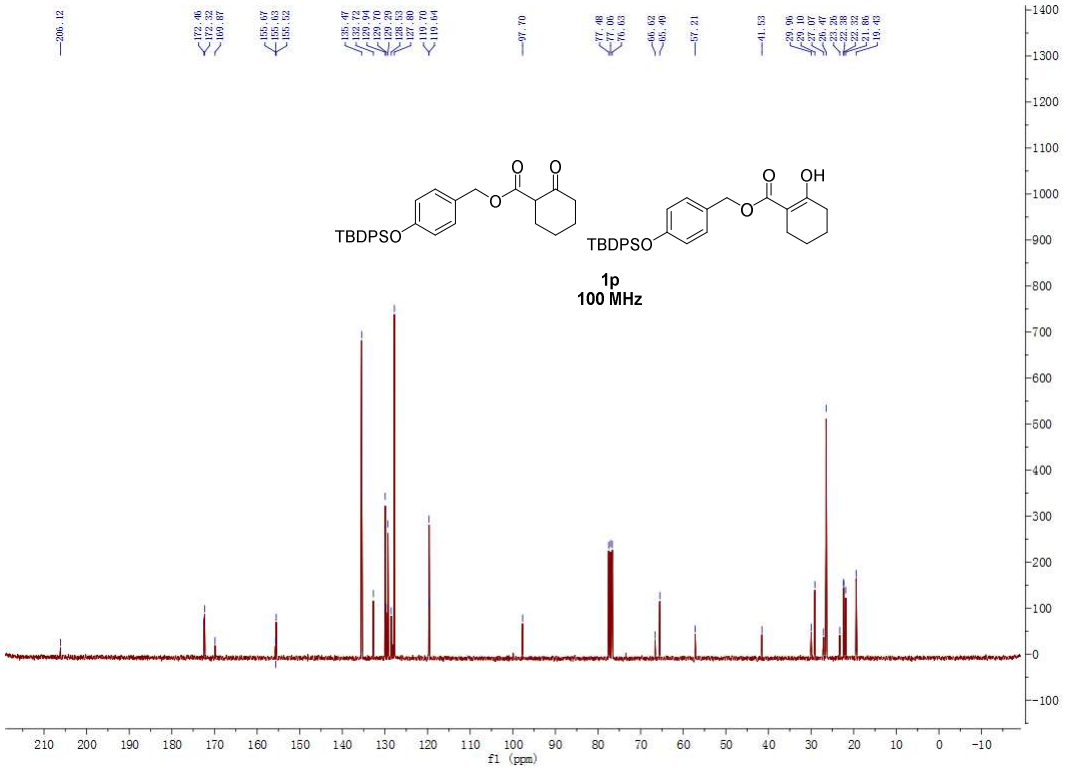


Fig. S32. ^{13}C NMR Spectrum of 1p (100 MHz, $CDCl_3$).

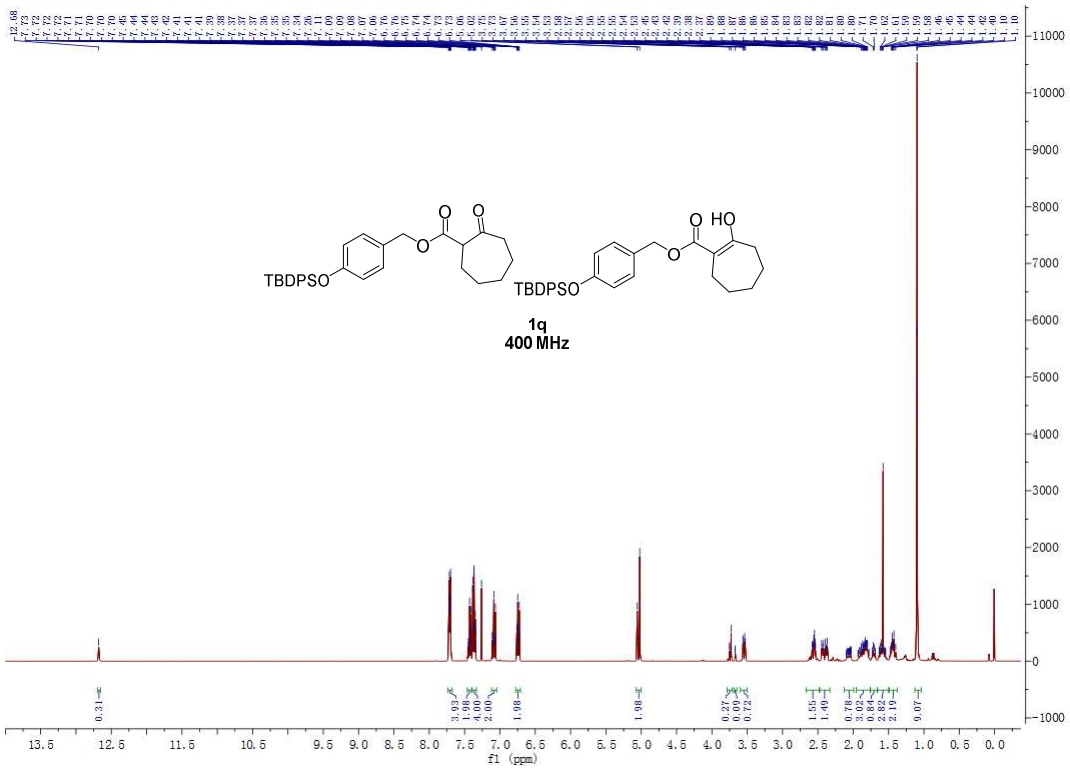


Fig. S33. ^{1}H NMR Spectrum of 1q (400 MHz, $CDCl_3$).

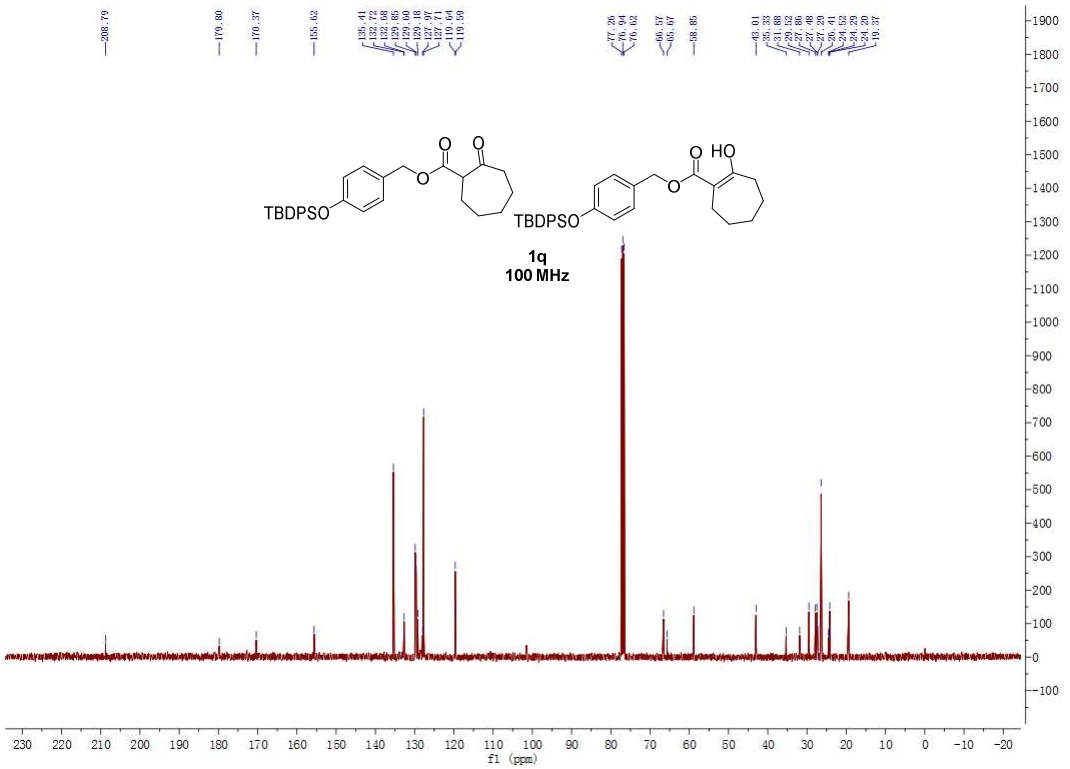


Fig. S34. ^{13}C NMR Spectrum of 1q (100 MHz, $CDCl_3$).

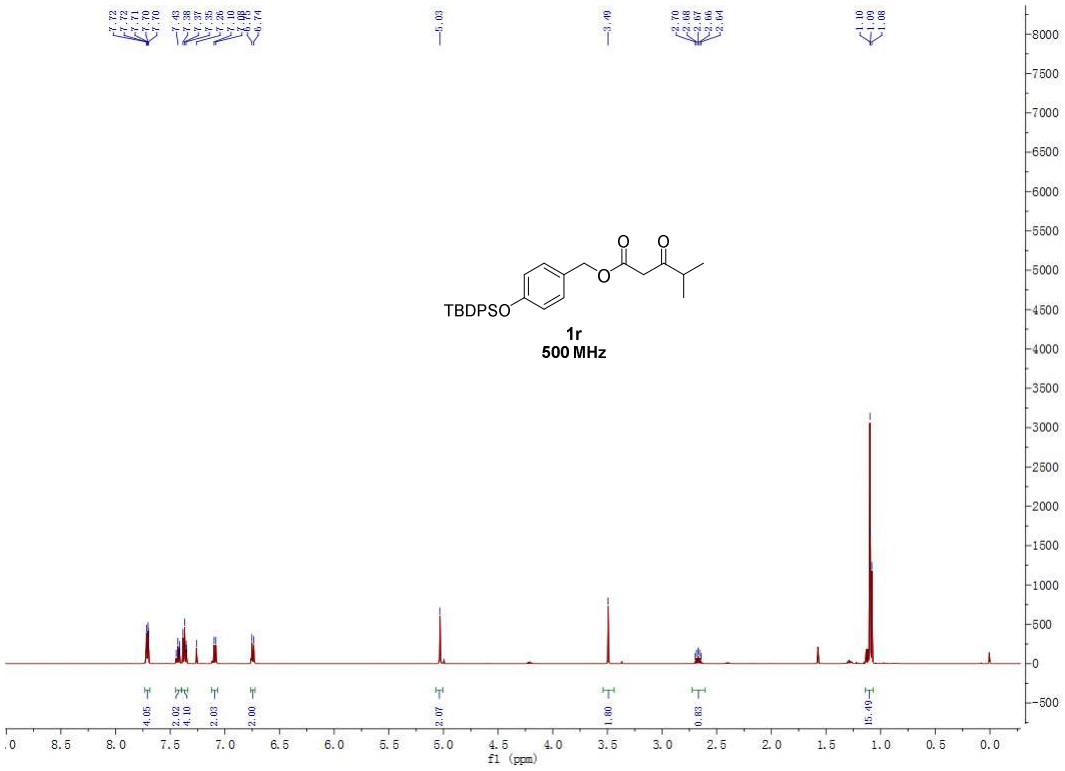


Fig. S35. ^{1}H NMR Spectrum of 1r (500 MHz, $CDCl_3$).

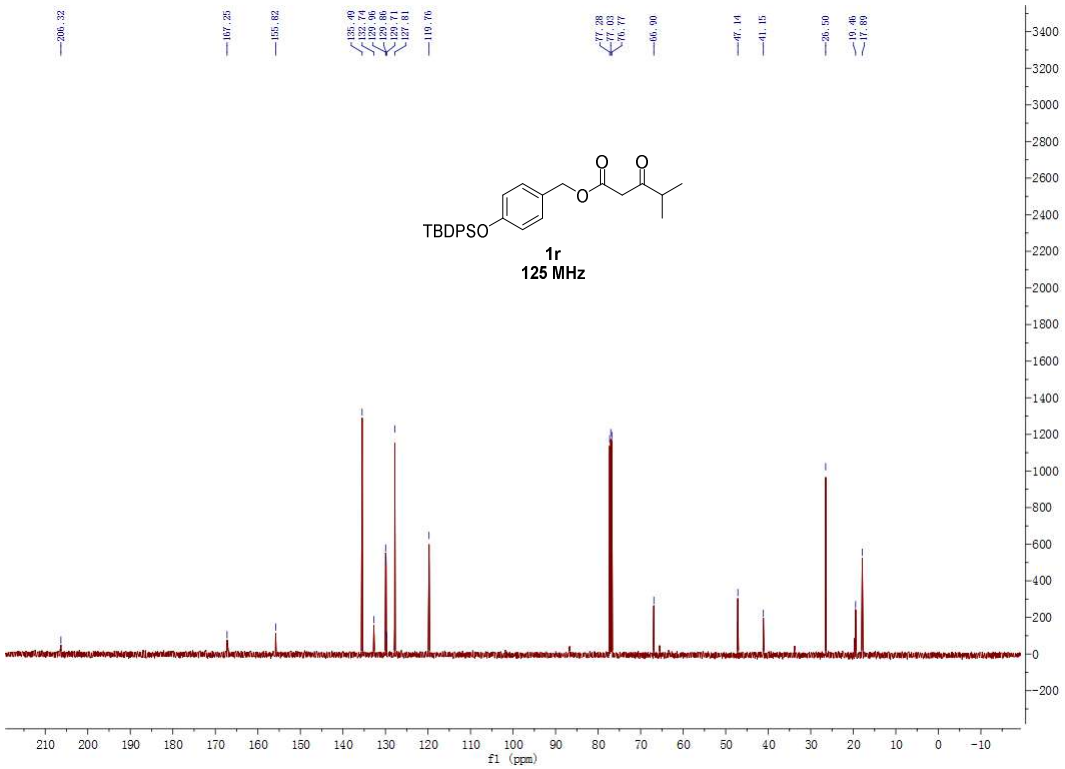


Fig. S36. ^{13}C NMR Spectrum of 1r (125 MHz, $CDCl_3$).

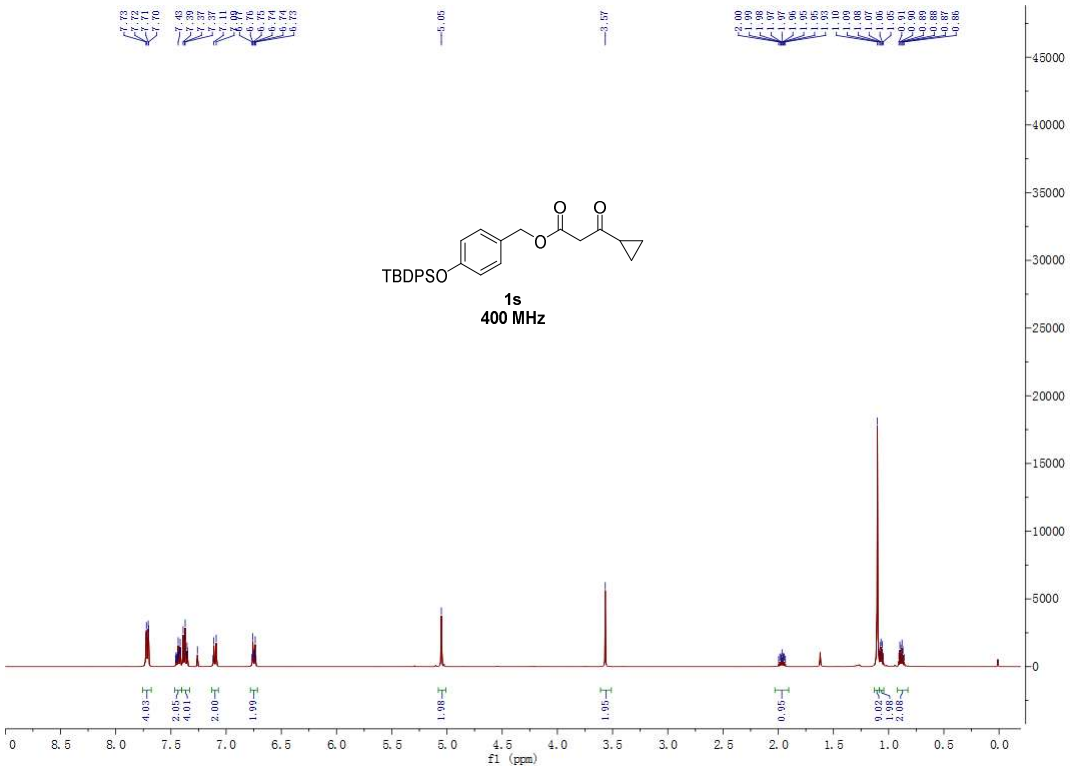


Fig. S37. ^{1}H NMR Spectrum of 1s (400 MHz, $CDCl_3$).

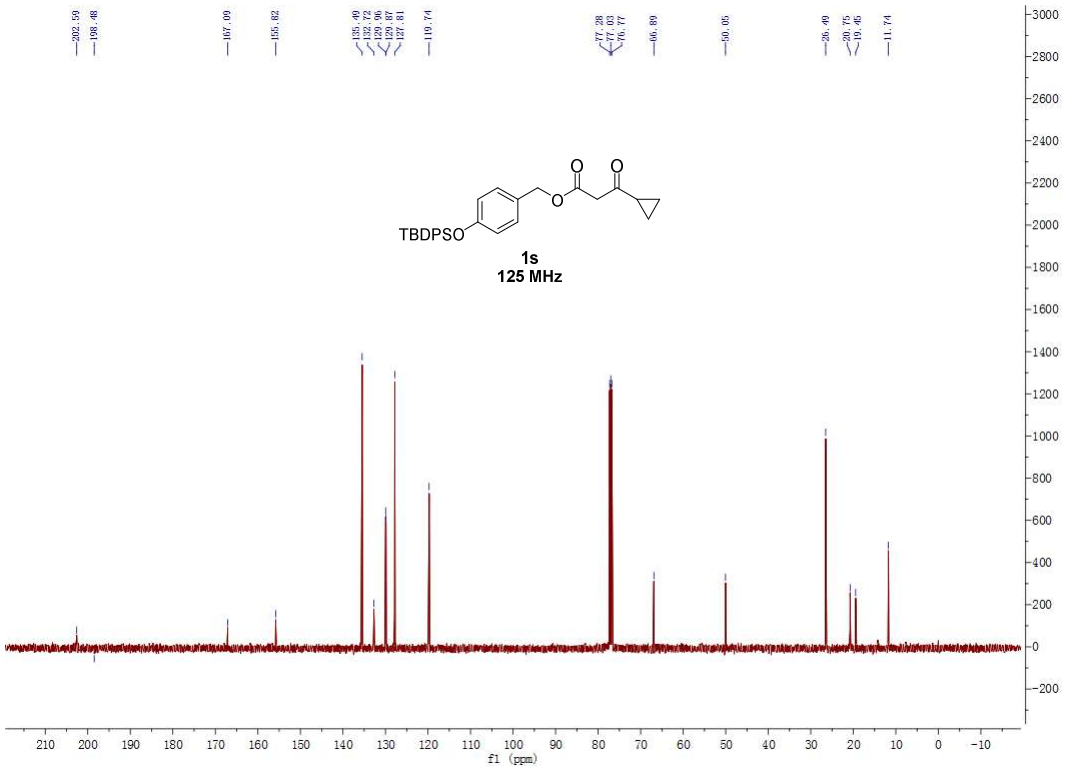


Fig. S38. ^{13}C NMR Spectrum of 1s (125 MHz, $CDCl_3$).

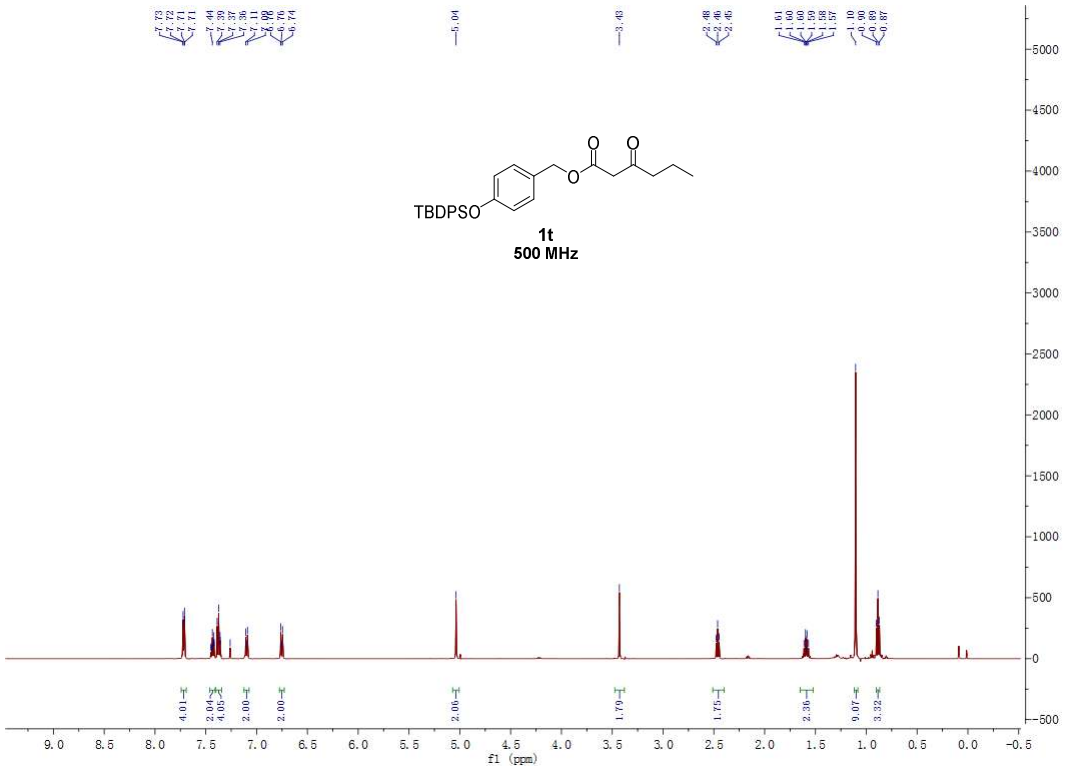


Fig. S39. ^{1}H NMR Spectrum of 1t (500 MHz, $CDCl_3$).

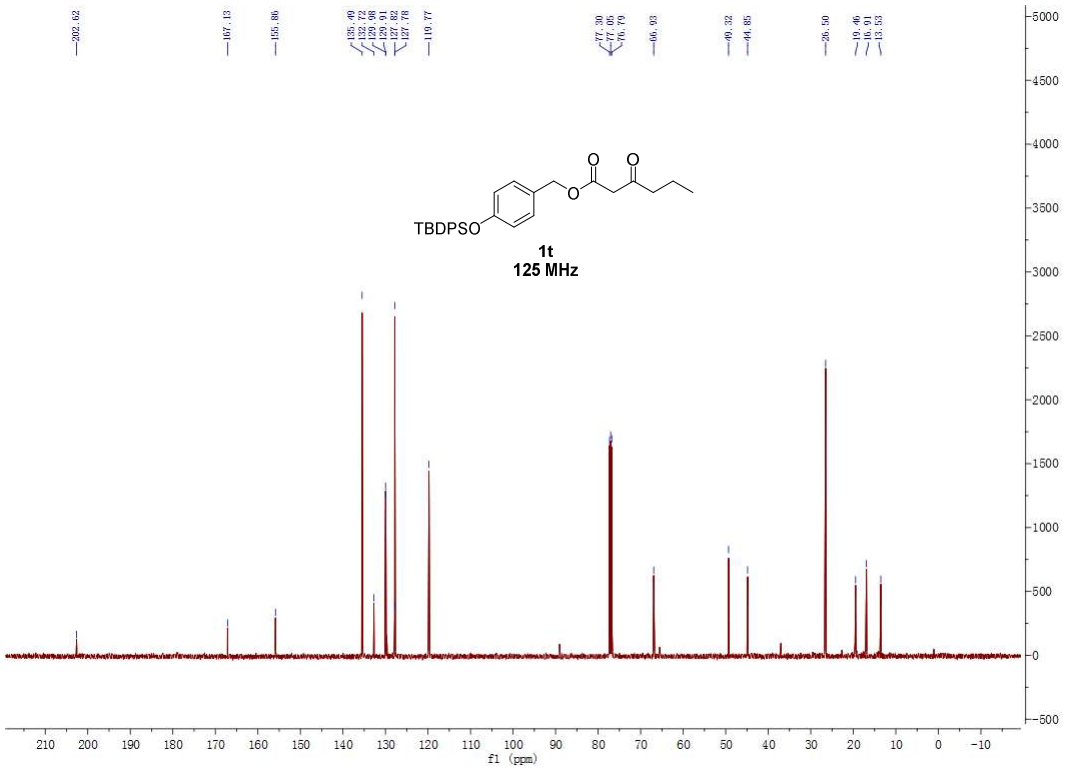


Fig. S40. ^{13}C NMR Spectrum of 1t (125 MHz, $CDCl_3$).

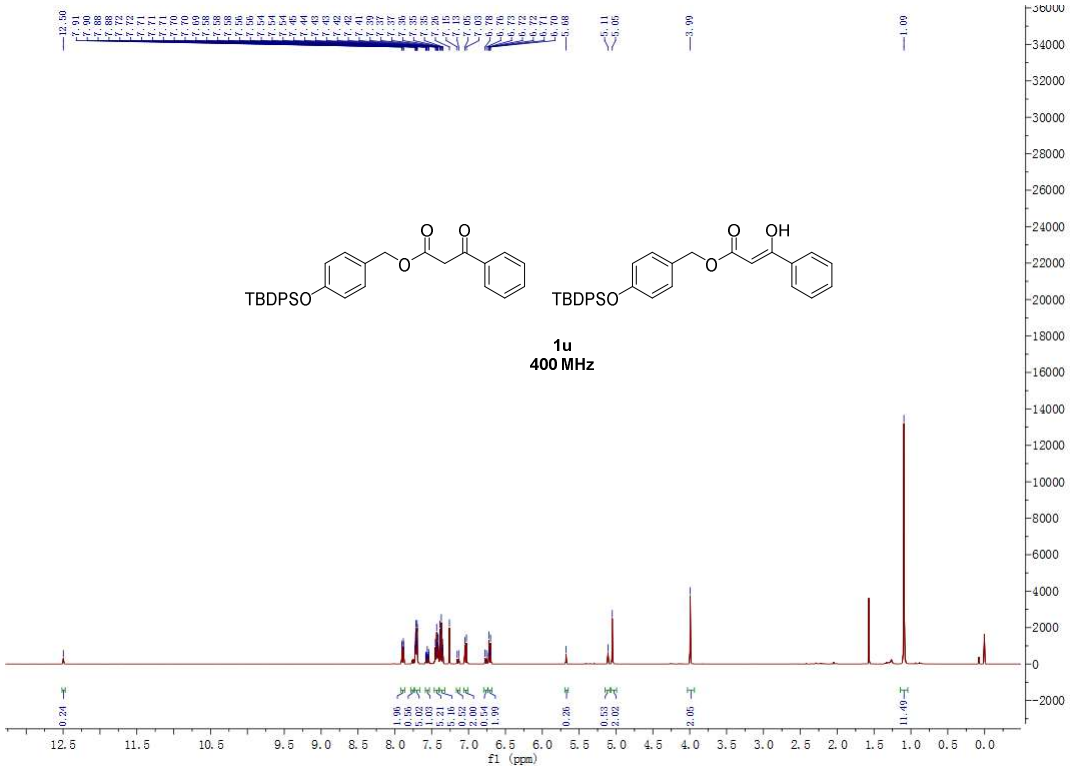


Fig. S41. ^{1}H NMR Spectrum of 1u (400 MHz, $CDCl_3$).

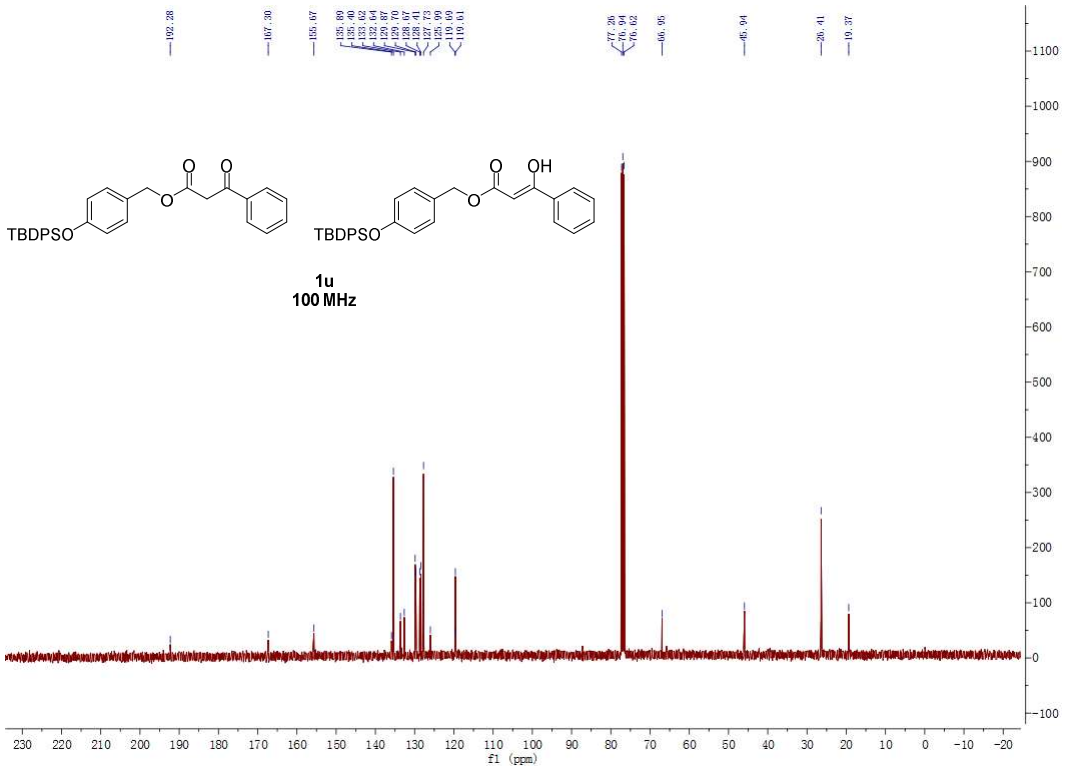


Fig. S42. ^{13}C NMR Spectrum of 1u (100 MHz, $CDCl_3$).

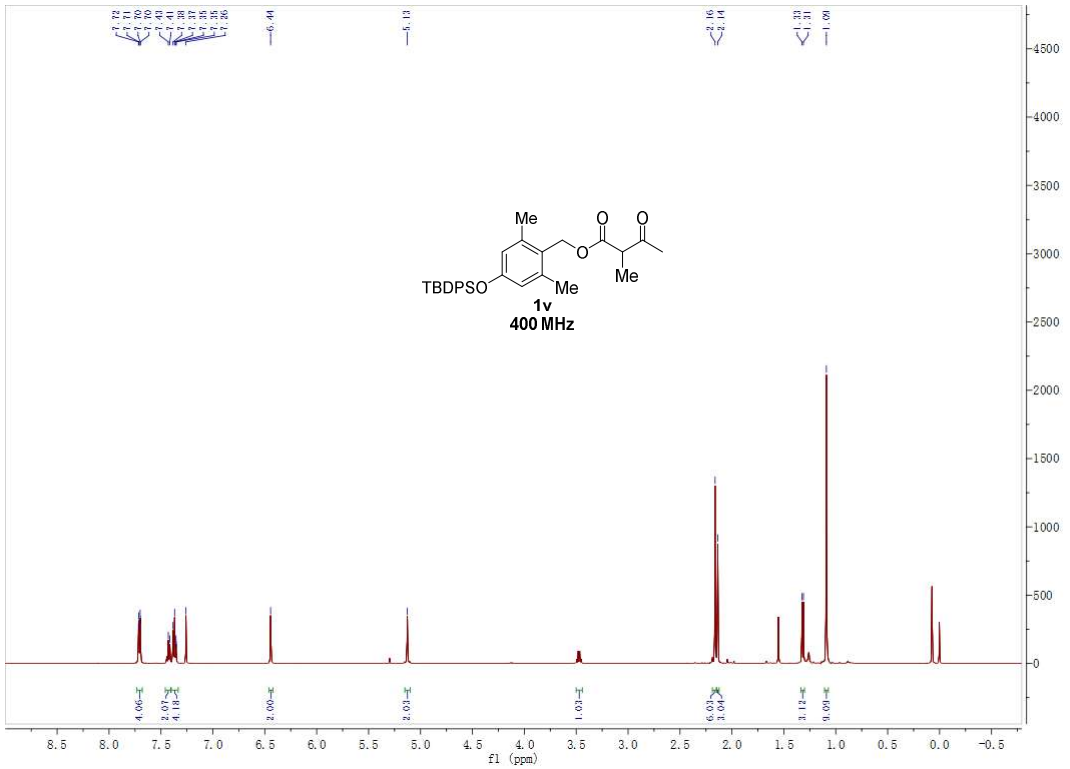


Fig. S43. ^{1}H NMR Spectrum of 1v (400 MHz, $CDCl_3$).

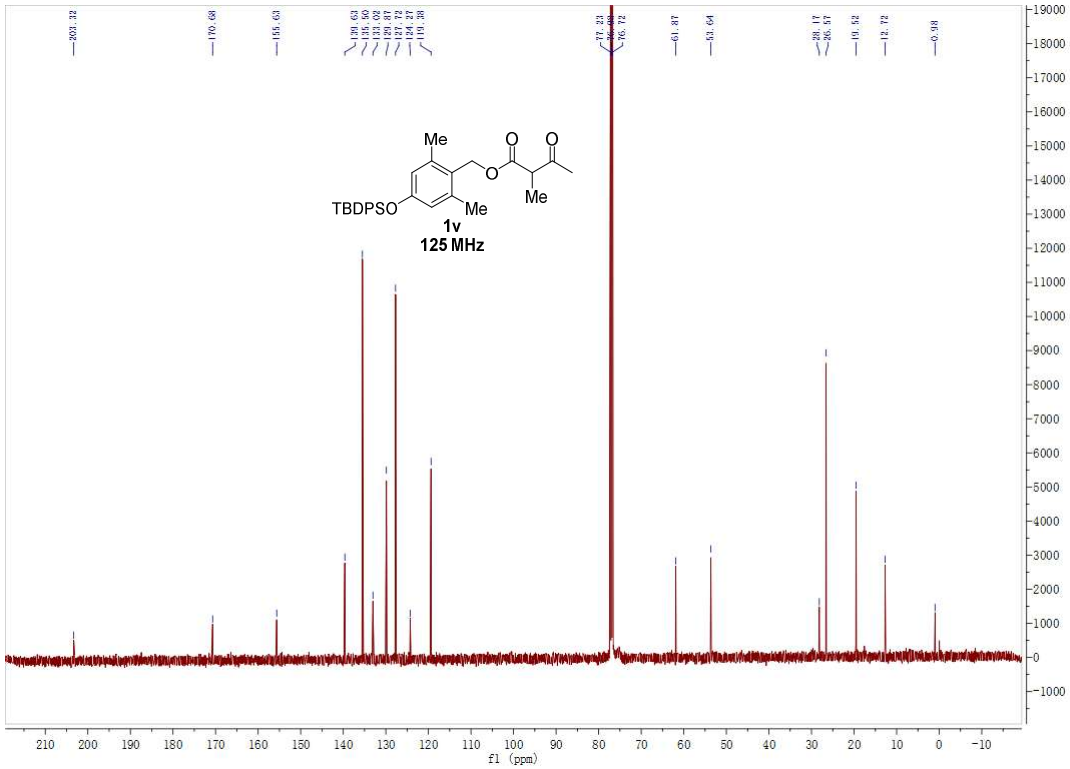


Fig. S44. ^{13}C NMR Spectrum of 1v (125 MHz, $CDCl_3$).

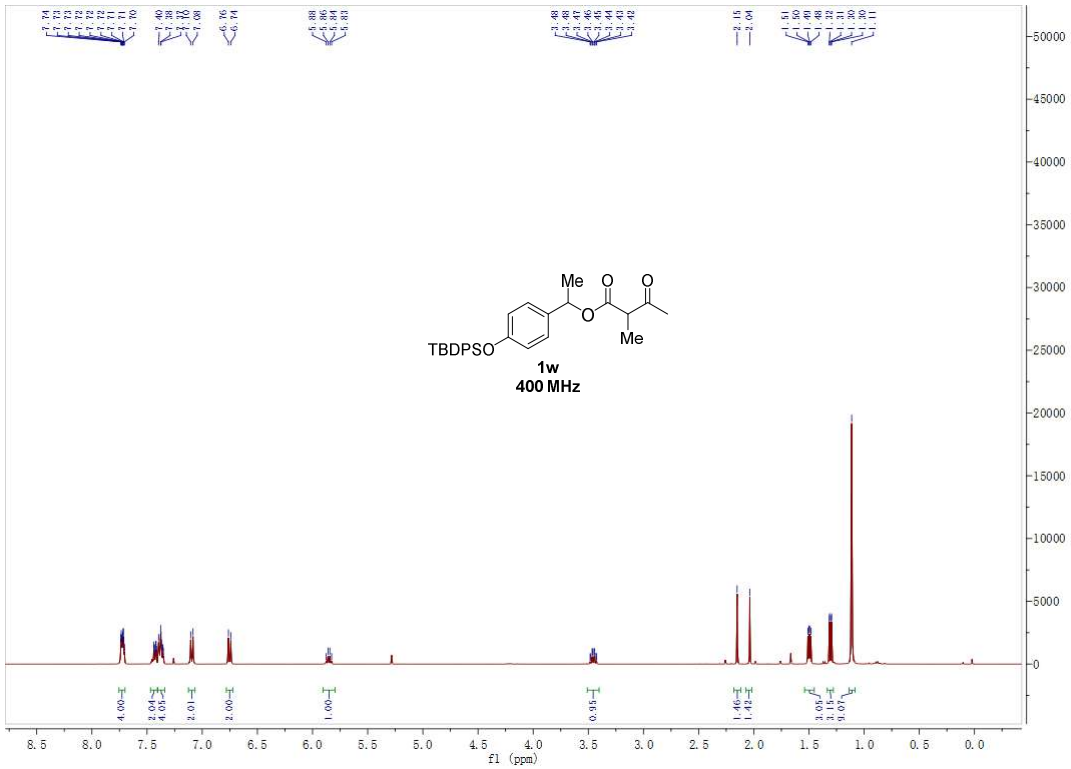


Fig. S45. ^{1}H NMR Spectrum of 1w (400 MHz, $CDCl_3$).

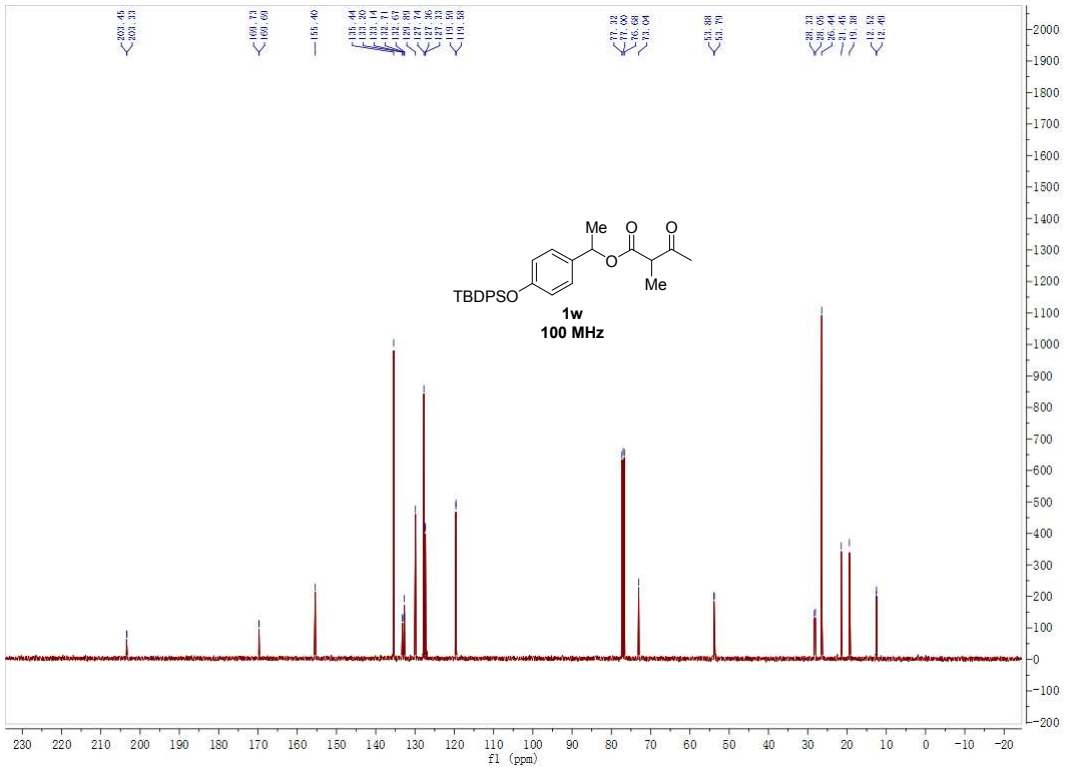


Fig. S46. ^{13}C NMR Spectrum of 1w (100 MHz, $CDCl_3$).

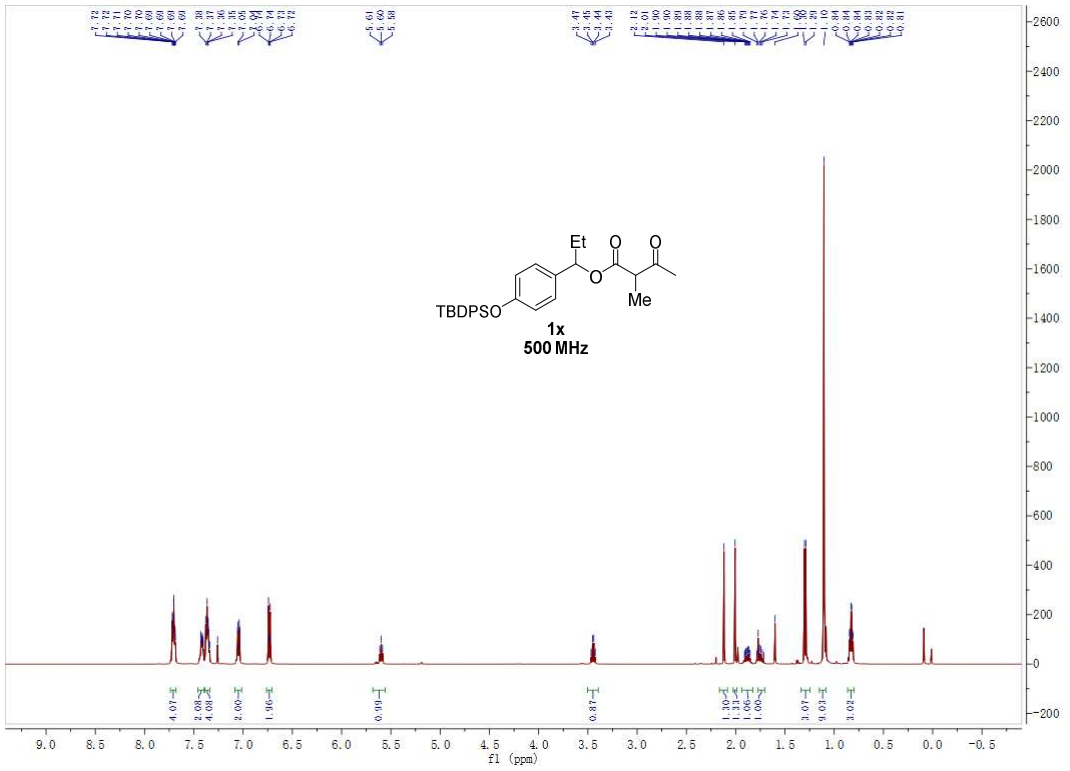


Fig. S47. ^{1}H NMR Spectrum of 1x (500 MHz, $CDCl_3$).

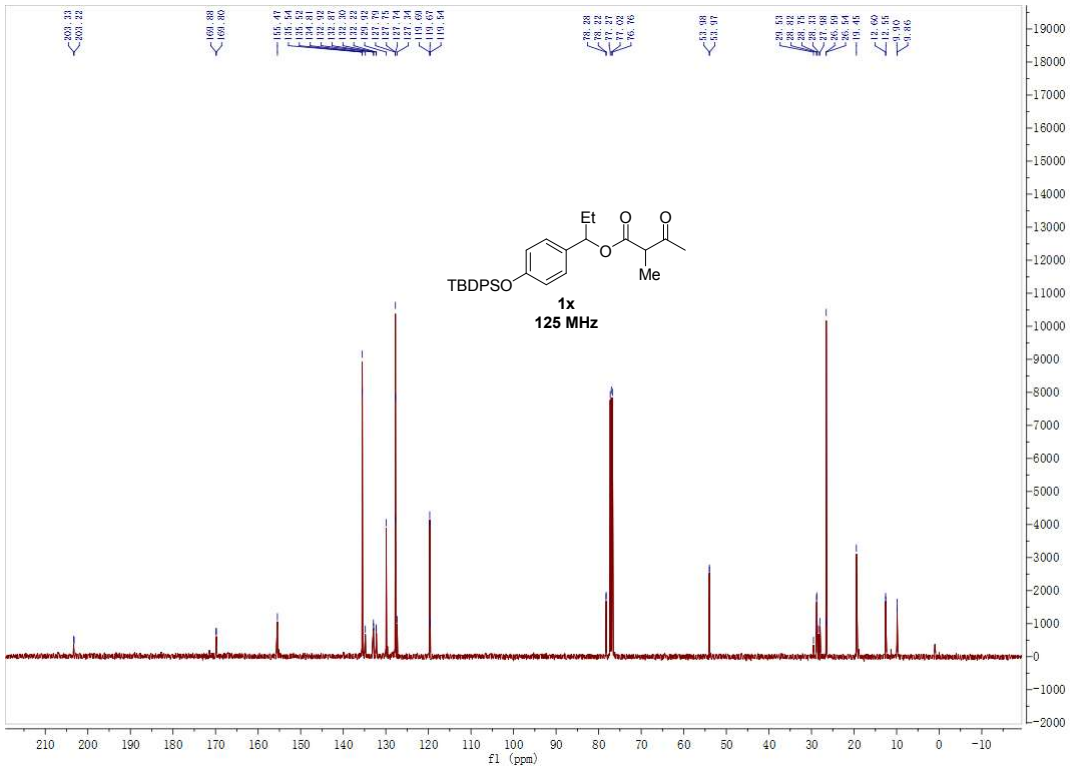


Fig. S48. ^{13}C NMR Spectrum of 1x (125 MHz, $CDCl_3$).

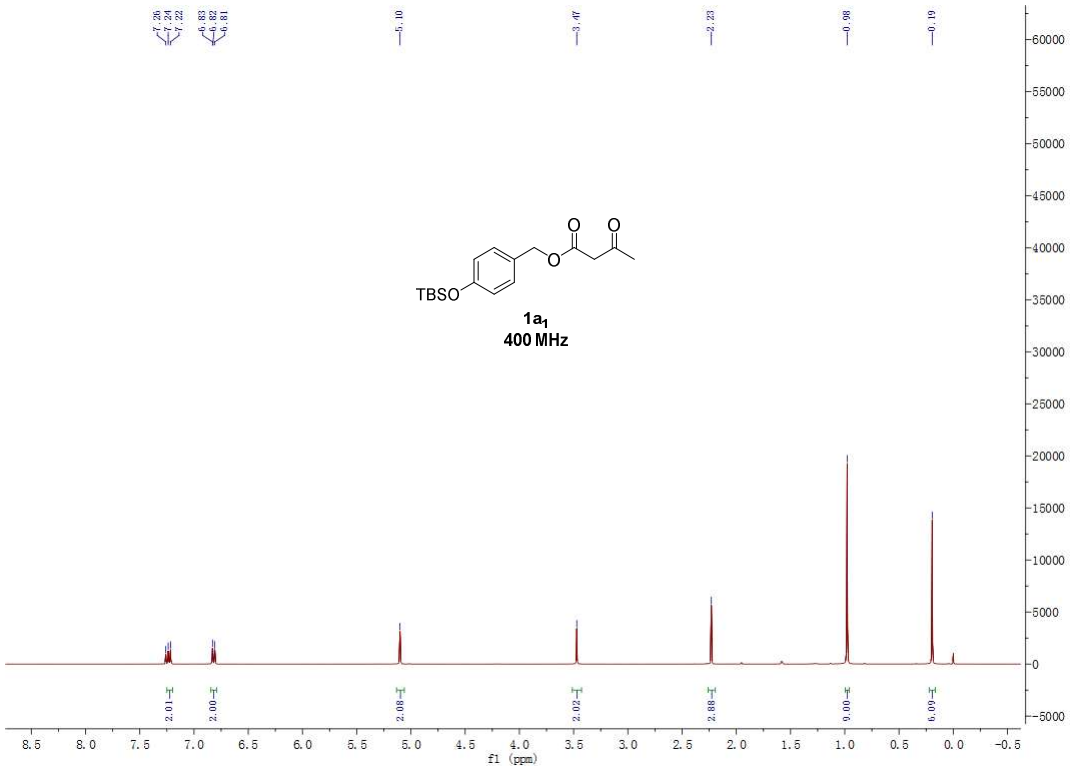


Fig. S49. ^{1}H NMR Spectrum of 1a$_1$ (400 MHz, CDCl$_3$).

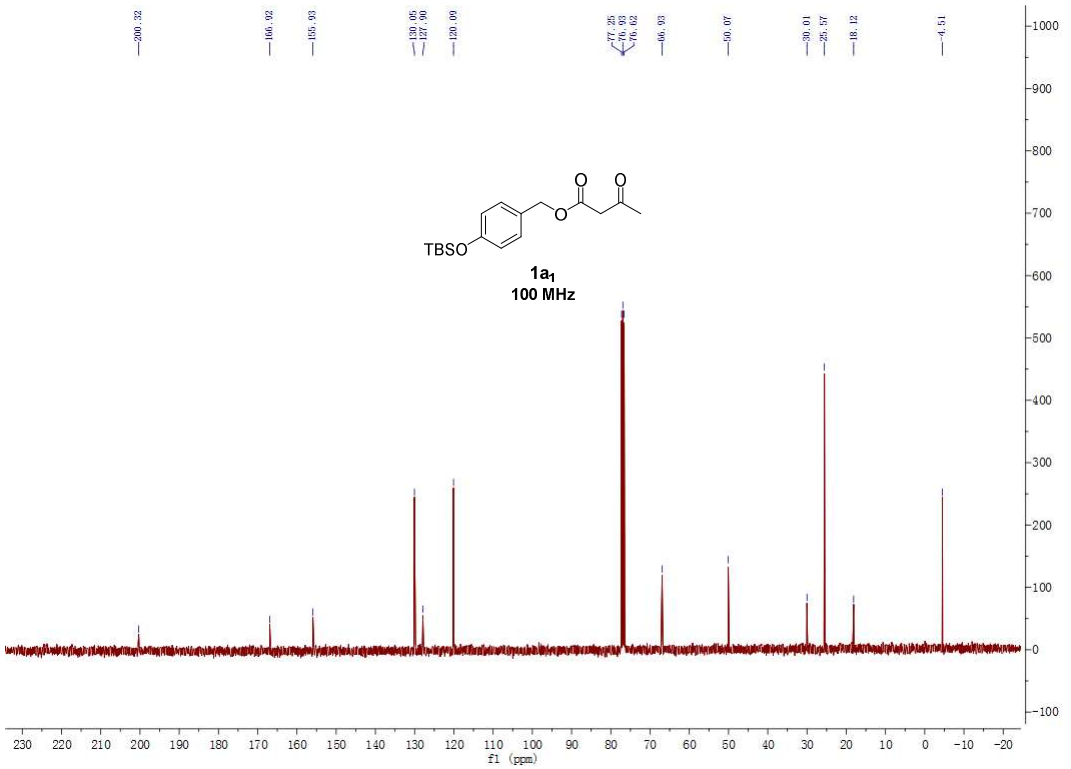


Fig. S50. ^{13}C NMR Spectrum of 1a$_1$ (100 MHz, CDCl$_3$).

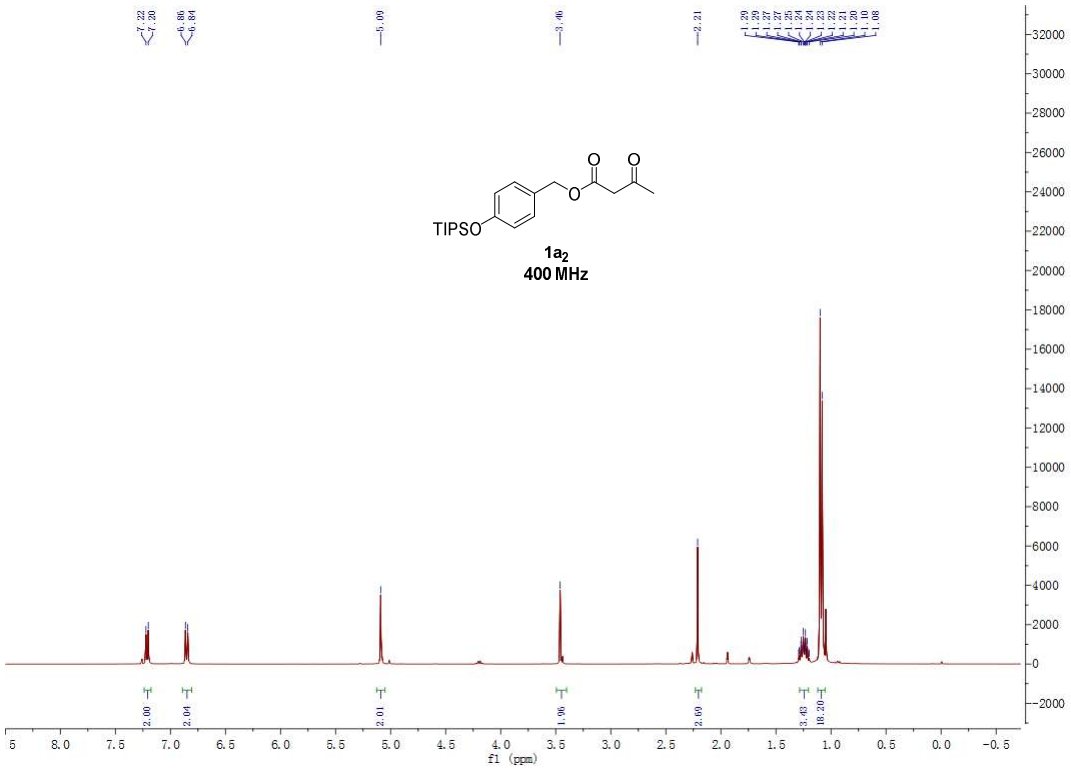


Fig. S51. ^{1}H NMR Spectrum of 1a$_2$ (400 MHz, CDCl$_3$).

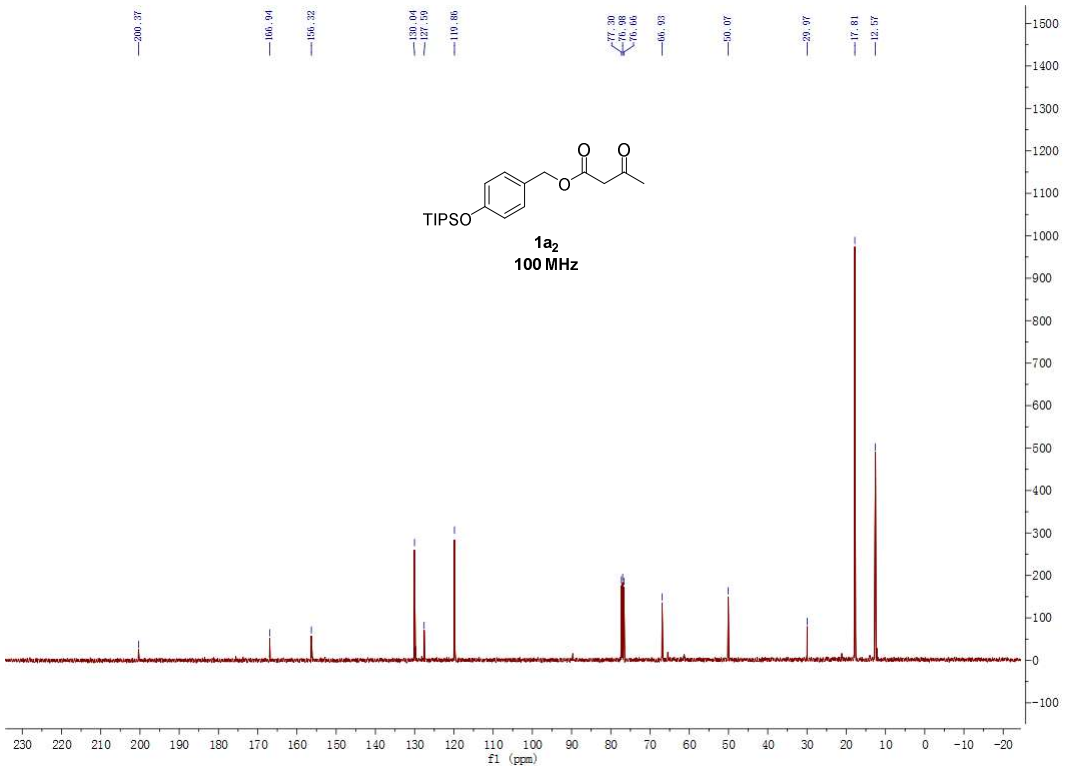


Fig. S52. ^{13}C NMR Spectrum of 1a$_2$ (100 MHz, CDCl$_3$).

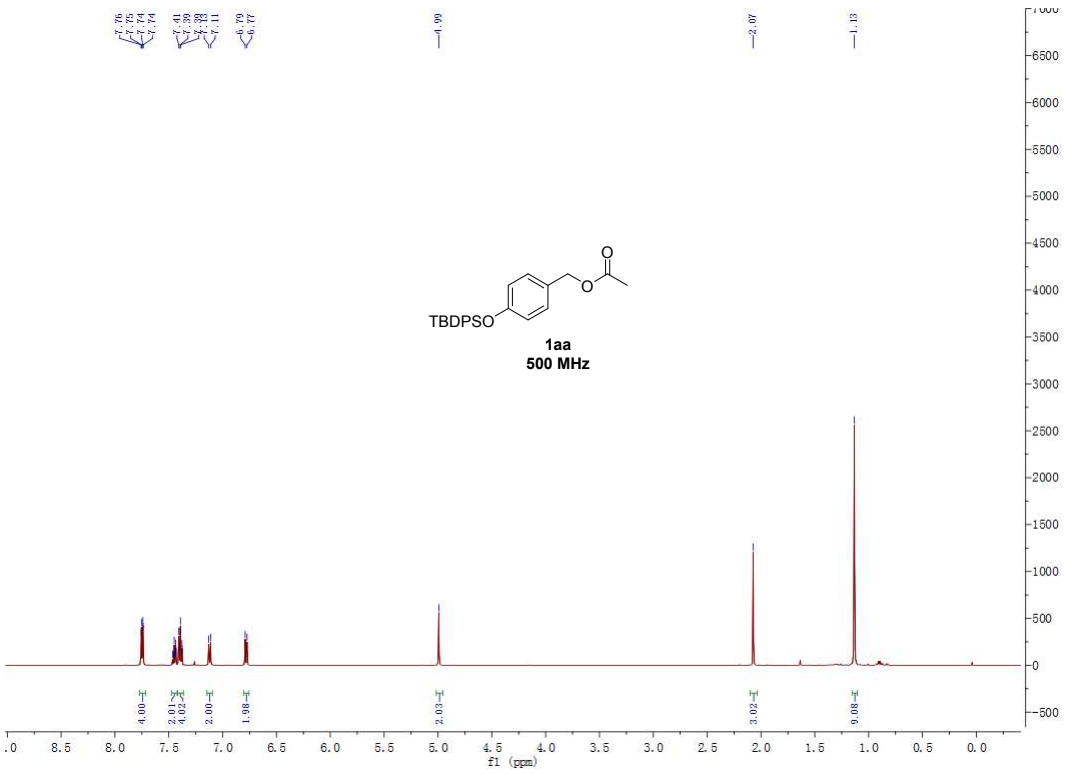


Fig. S53. ^{1}H NMR Spectrum of 1aa (500 MHz, $CDCl_3$).

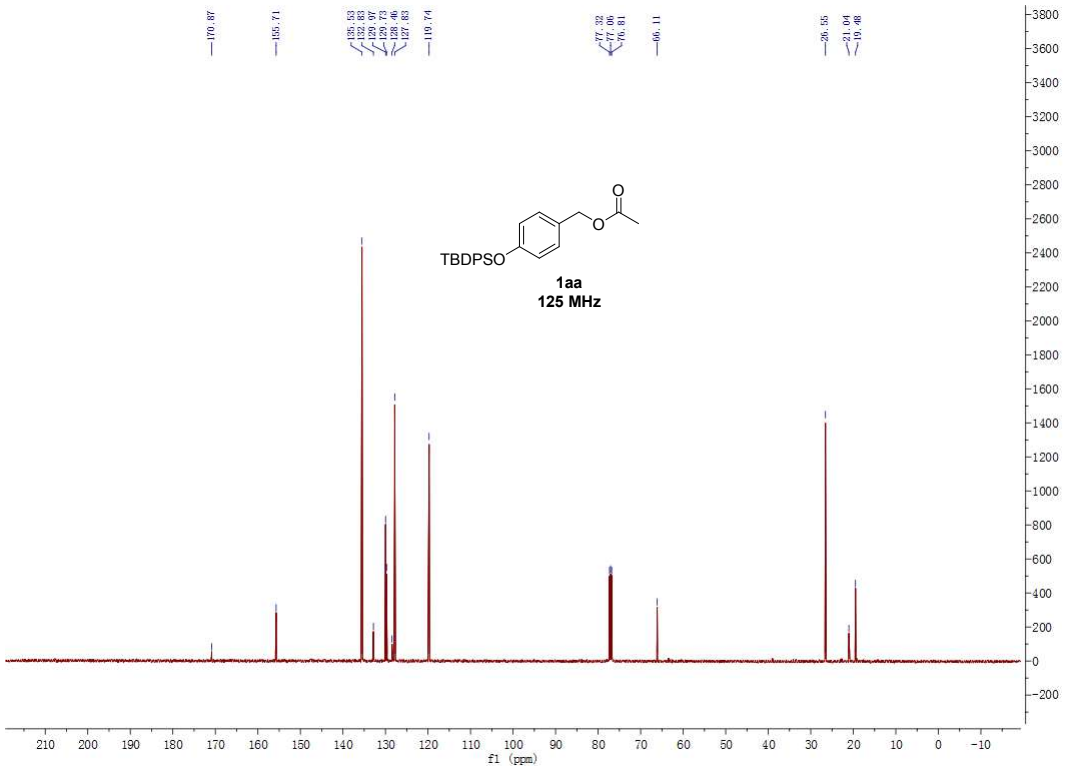


Fig. S54. ^{13}C NMR Spectrum of 1w (125 MHz, $CDCl_3$).

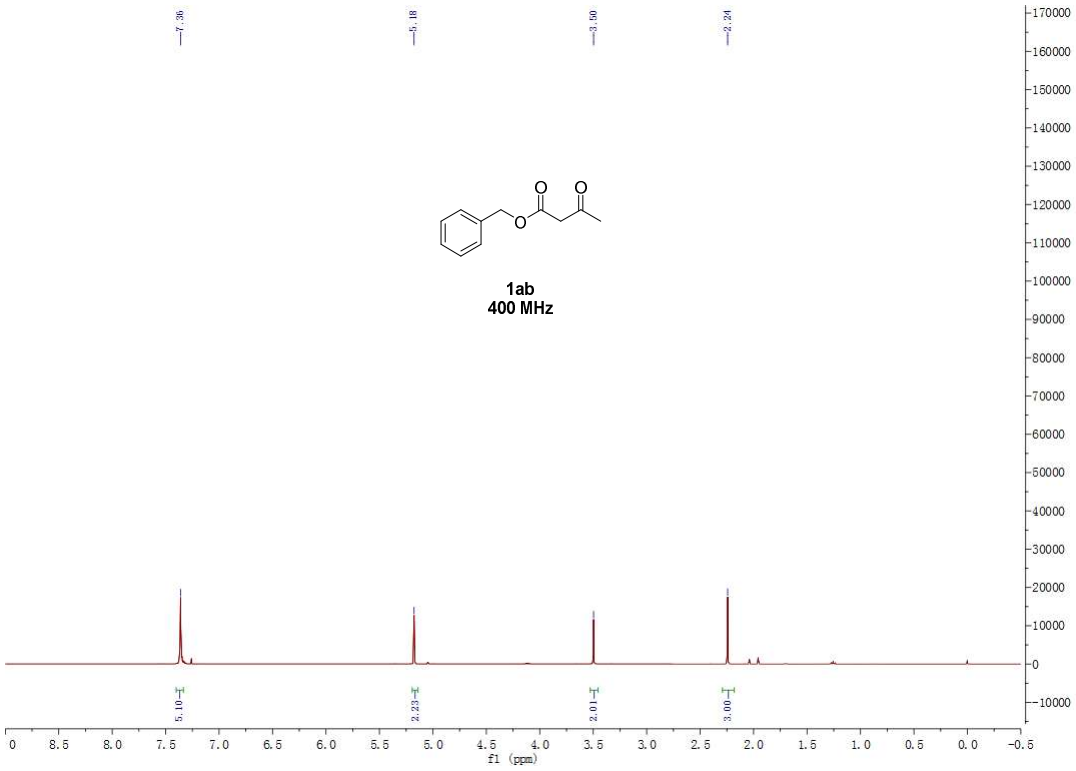


Fig. S55. ^{1}H NMR Spectrum of 1ab (400 MHz, $CDCl_3$).

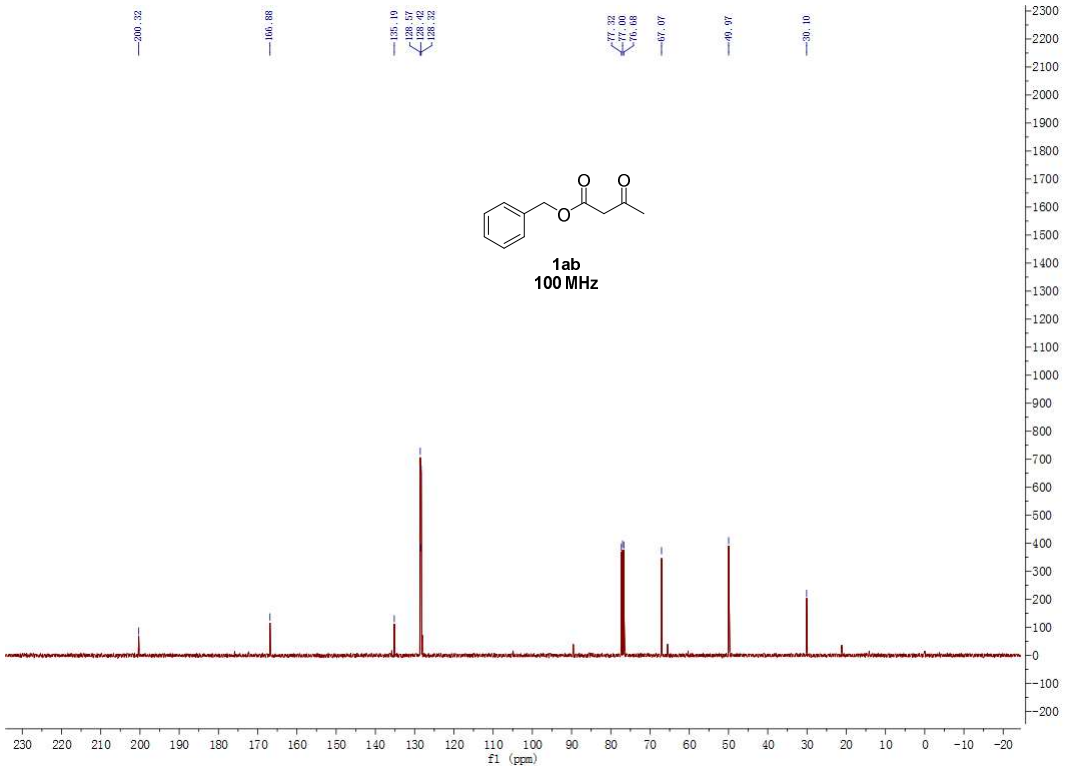


Fig. S56. ^{13}C NMR Spectrum of 1ab (100 MHz, $CDCl_3$).

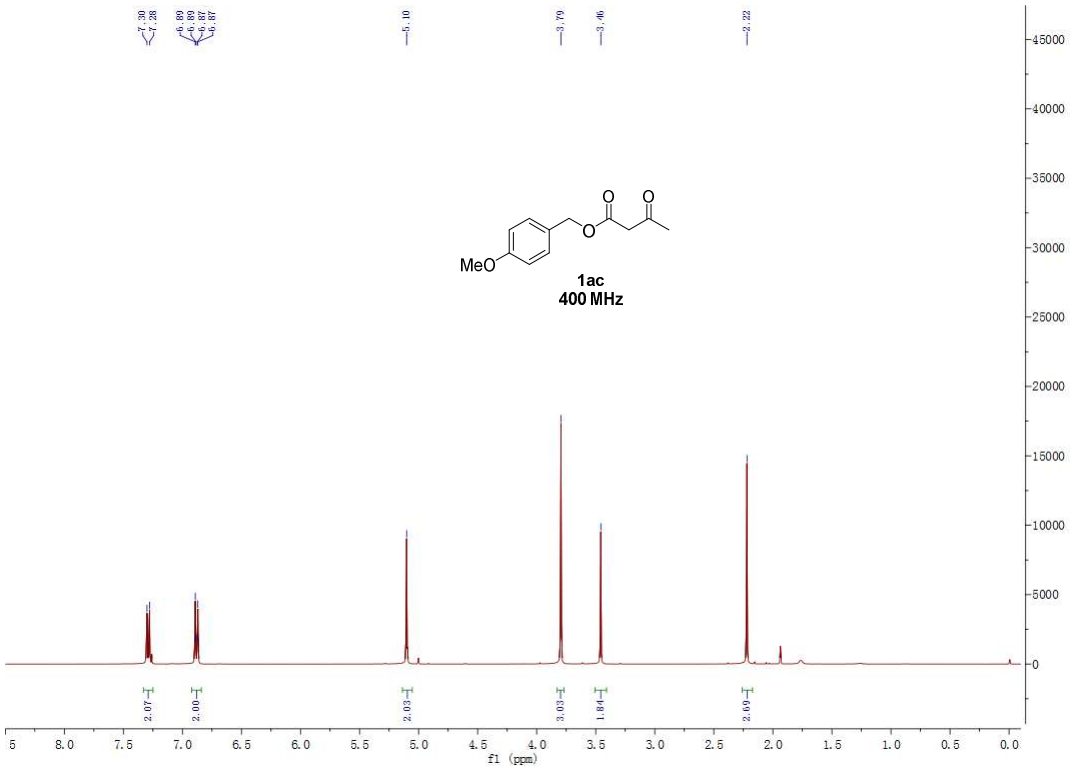


Fig. S57. ^{1}H NMR Spectrum of 1ac (400 MHz, $CDCl_3$).

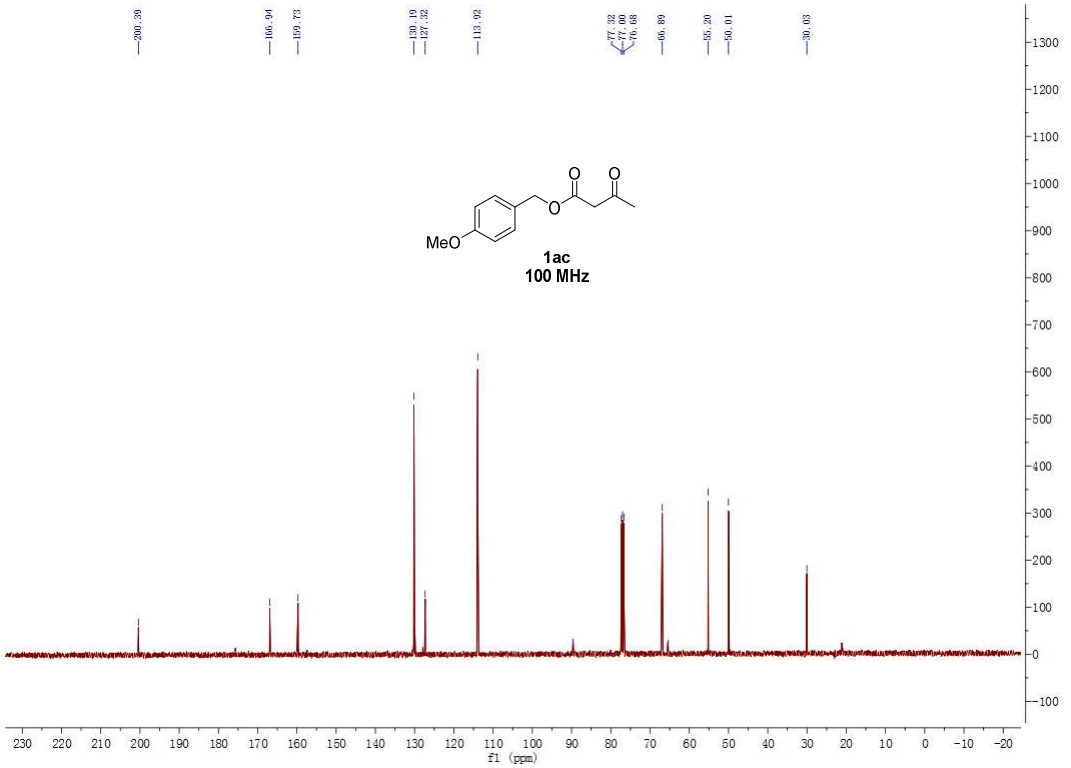


Fig. S58. ^{13}C NMR Spectrum of 1ac (100 MHz, $CDCl_3$).

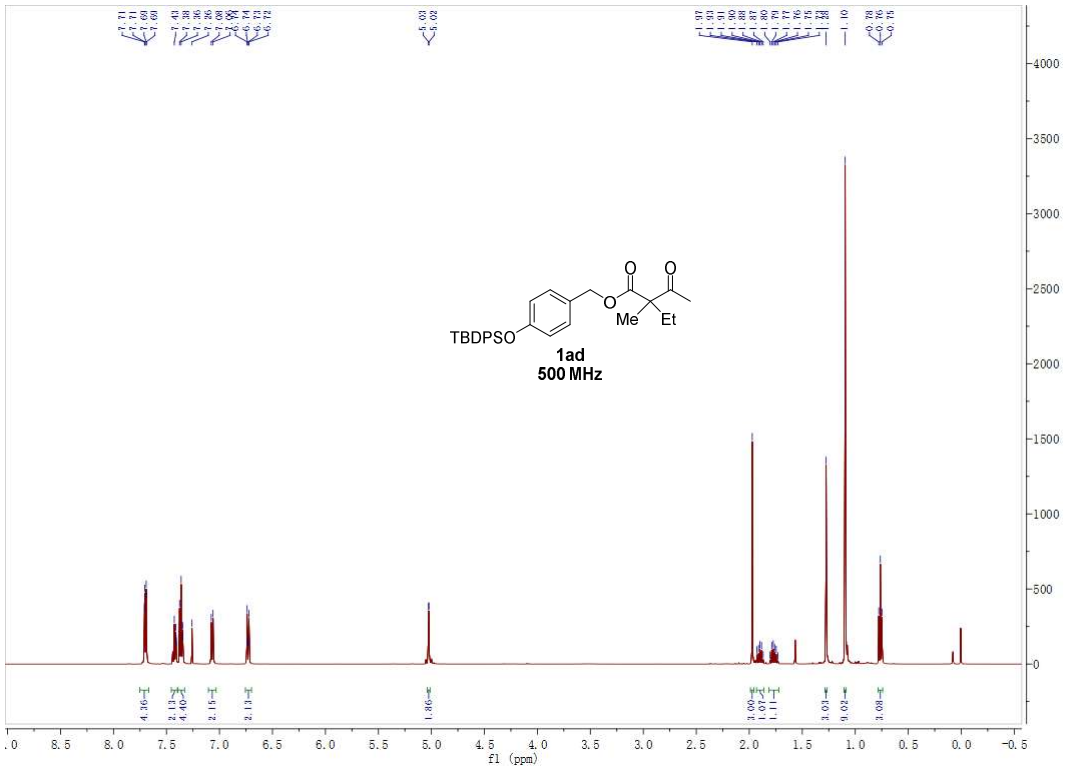


Fig. S59. ^{1}H NMR Spectrum of 1ad (500 MHz, $CDCl_3$).

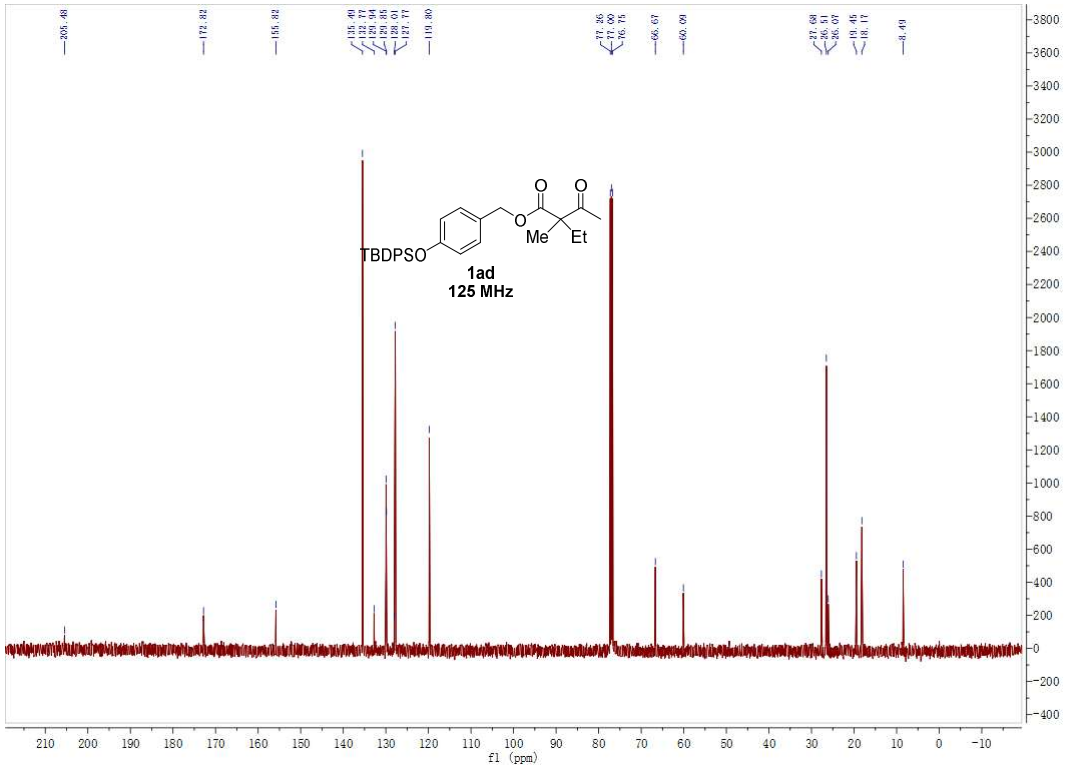


Fig. S60. ^{13}C NMR Spectrum of 1ad (125 MHz, $CDCl_3$).

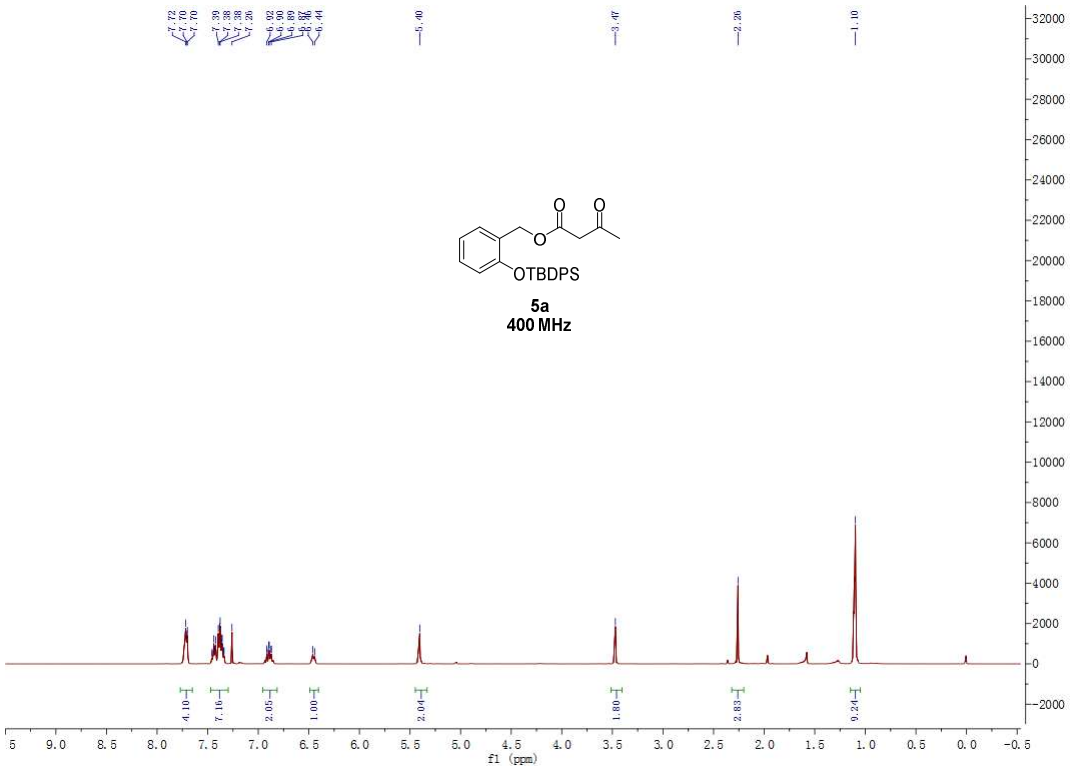


Fig. S61. ^{1}H NMR Spectrum of 5a (400 MHz, $CDCl_3$).

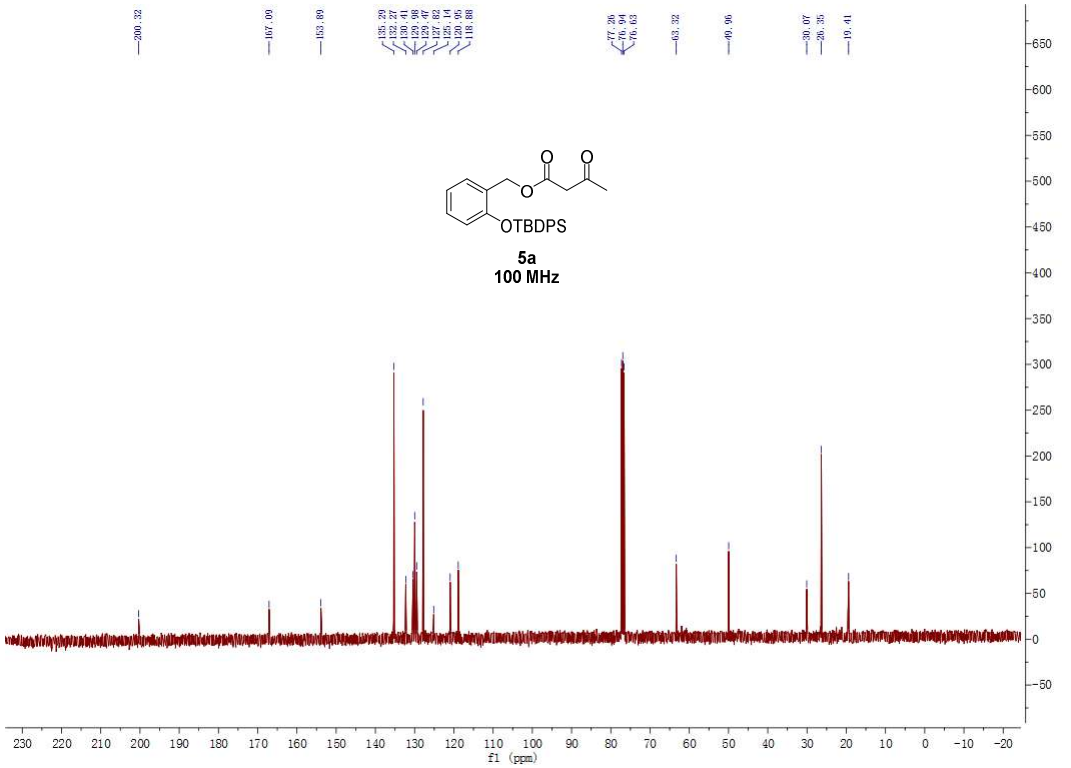


Fig. S62. ^{13}C NMR Spectrum of 5a (100 MHz, $CDCl_3$).

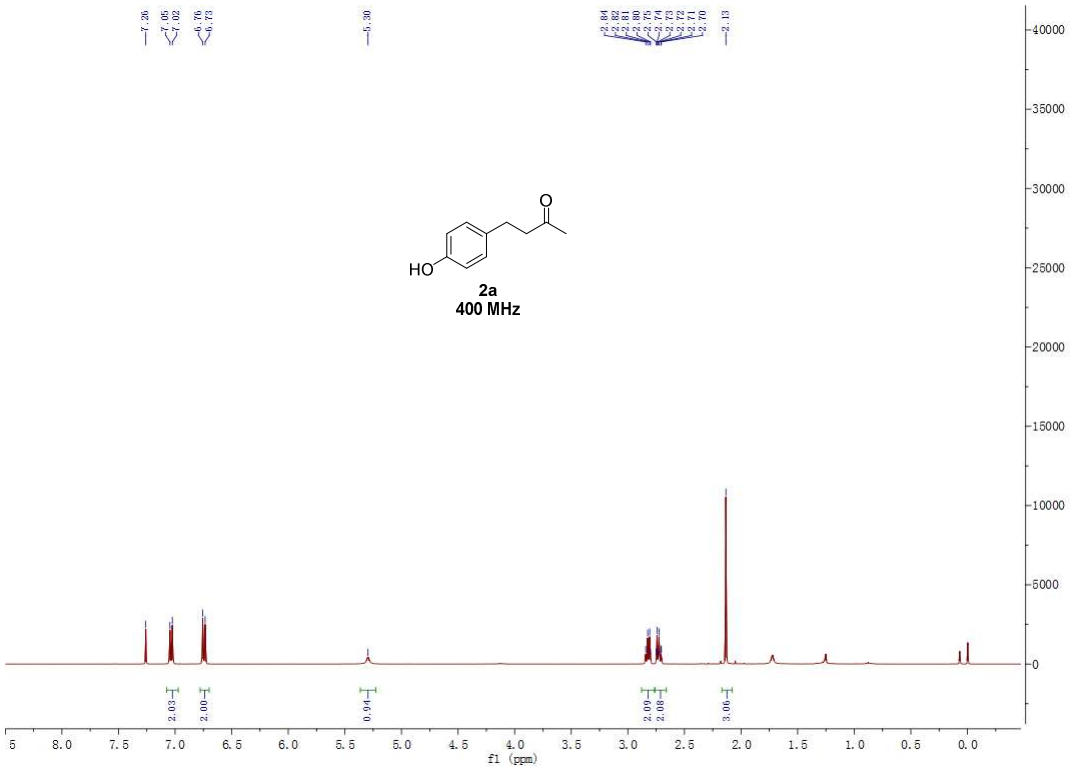


Fig. S63. ^{1}H NMR Spectrum of 2a (400 MHz, $CDCl_3$).

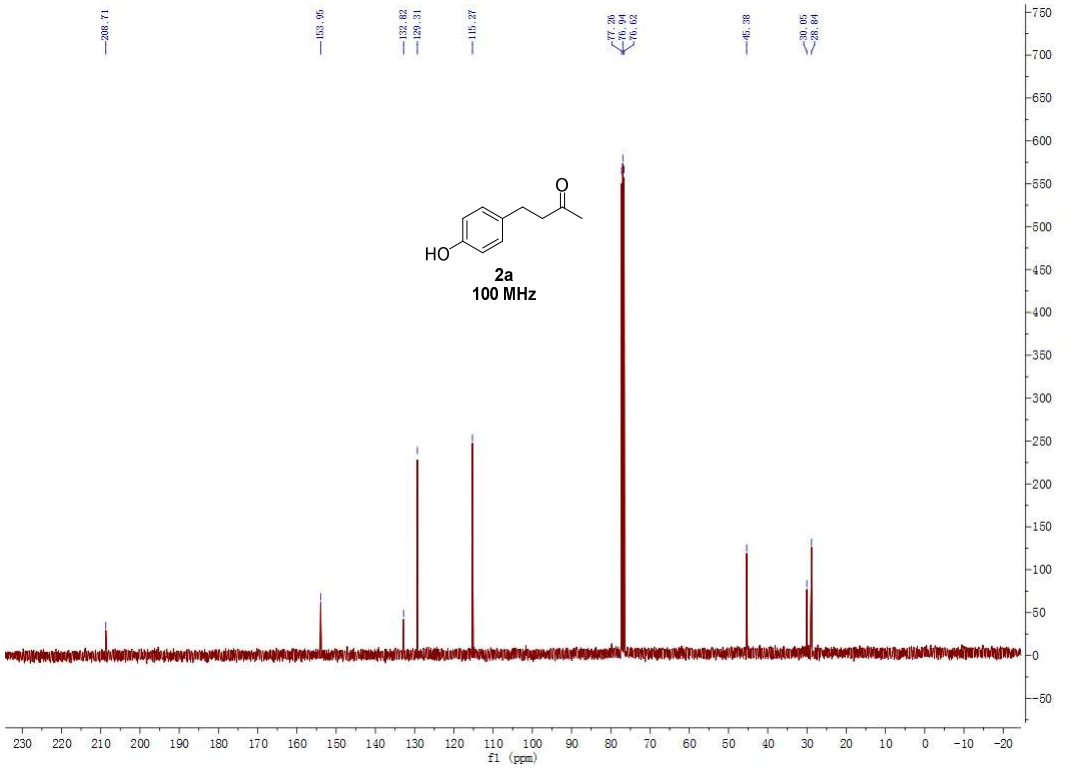


Fig. S64. ^{13}C NMR Spectrum of 2a (100 MHz, $CDCl_3$).

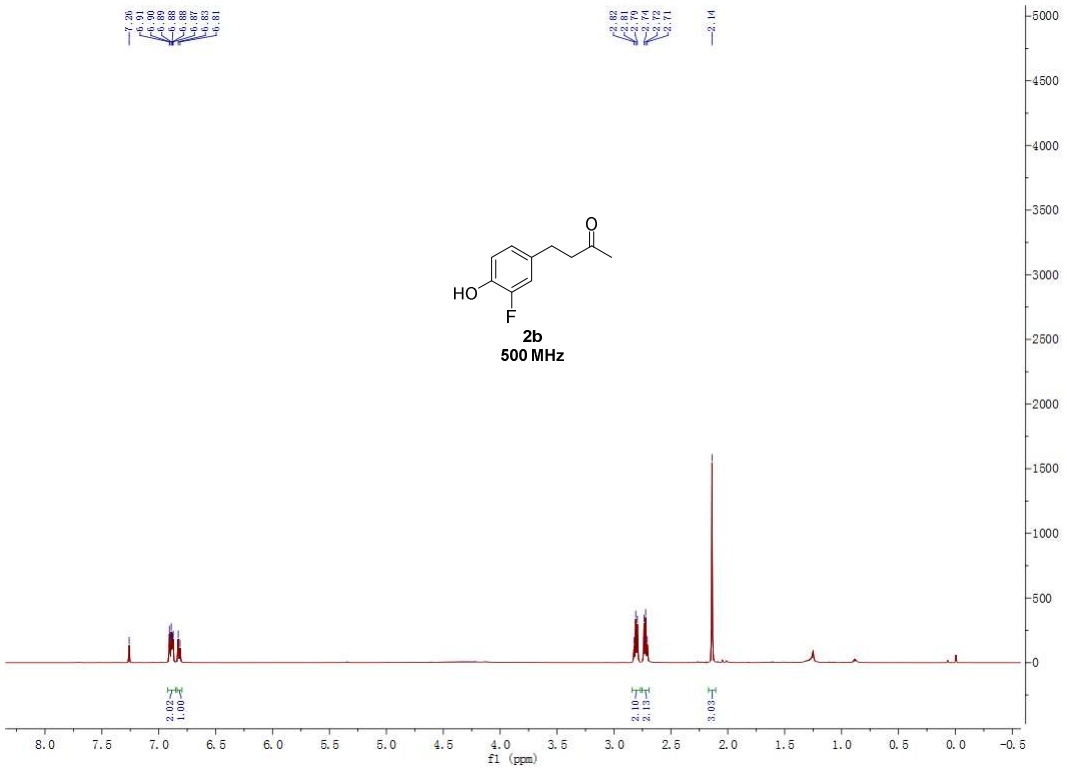


Fig. S65. ^{1}H NMR Spectrum of 2b (500 MHz, $CDCl_3$).

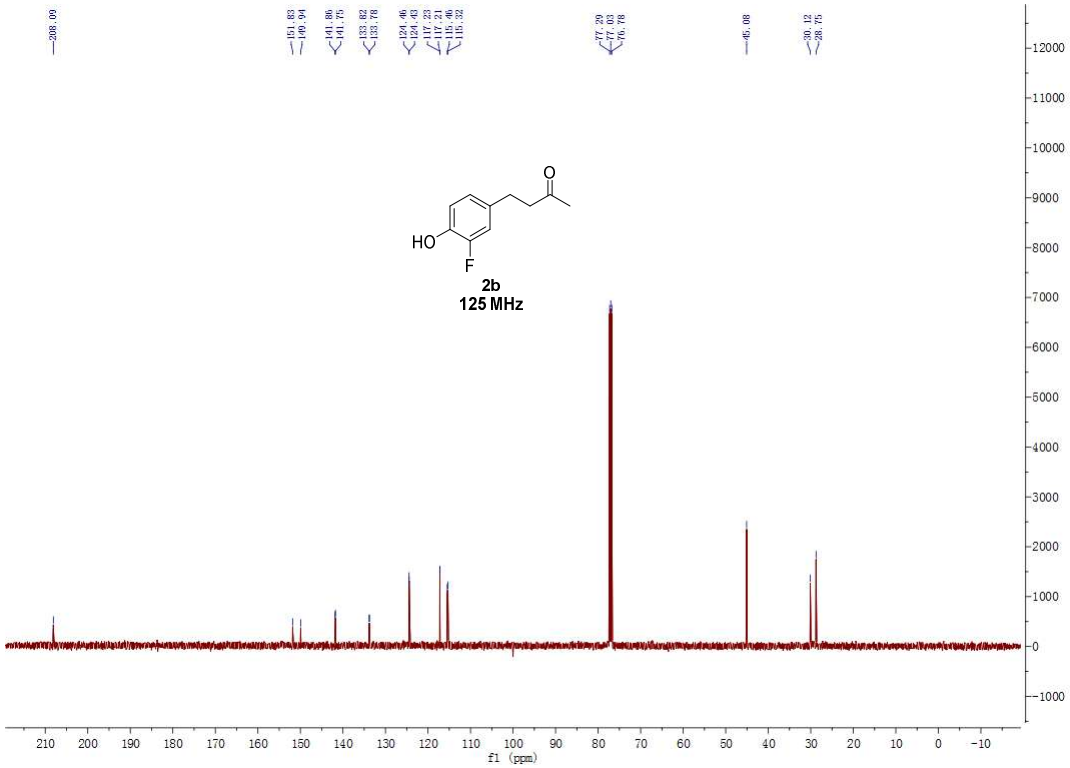


Fig. S66. ^{13}C NMR Spectrum of 2b (125 MHz, $CDCl_3$).

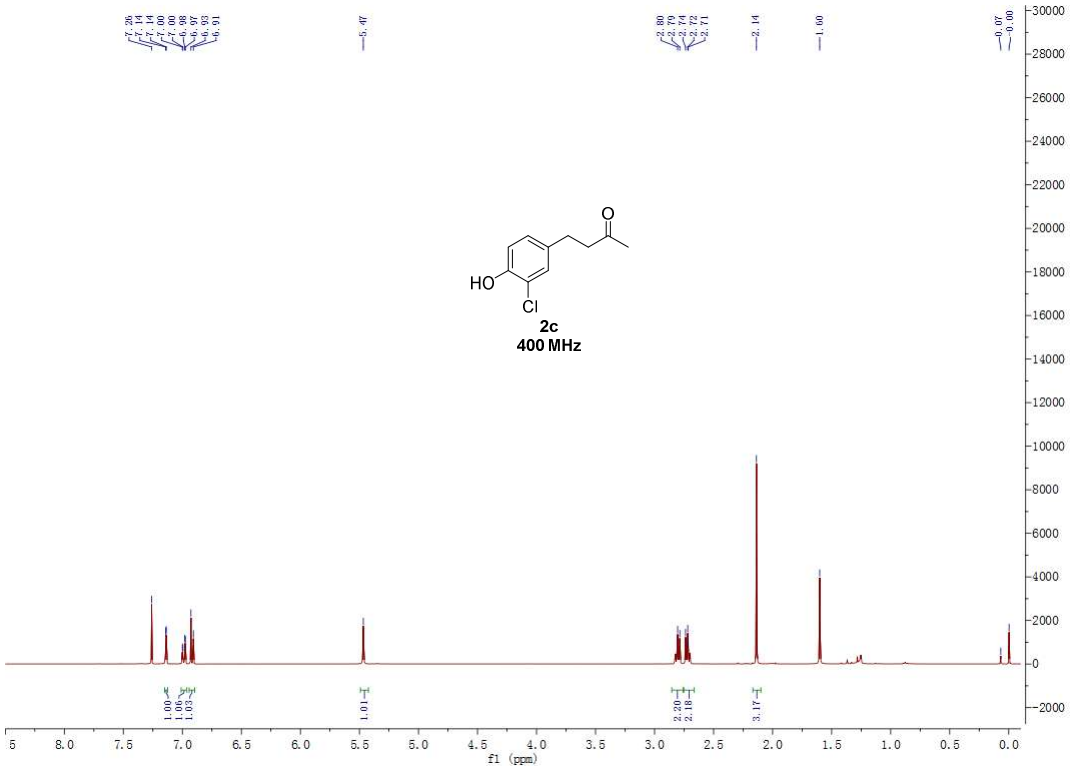


Fig. S67. ^{1}H NMR Spectrum of 2c (400 MHz, $CDCl_3$).

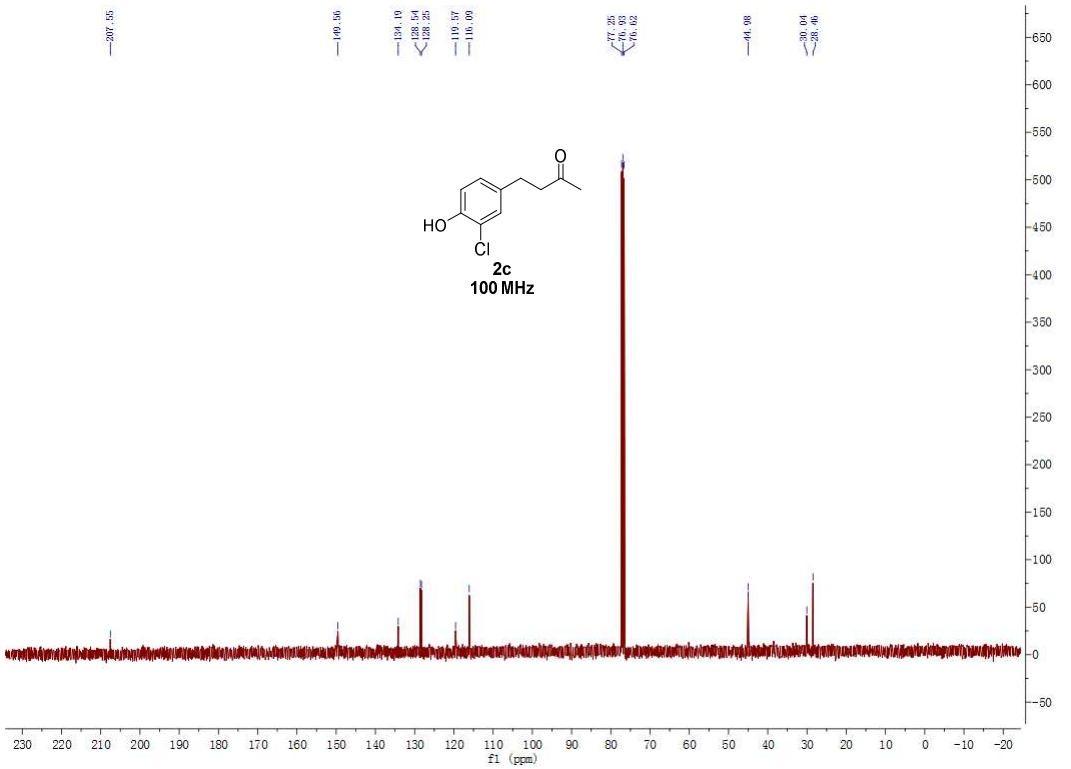


Fig. S68. ^{13}C NMR Spectrum of 2c (100 MHz, $CDCl_3$).

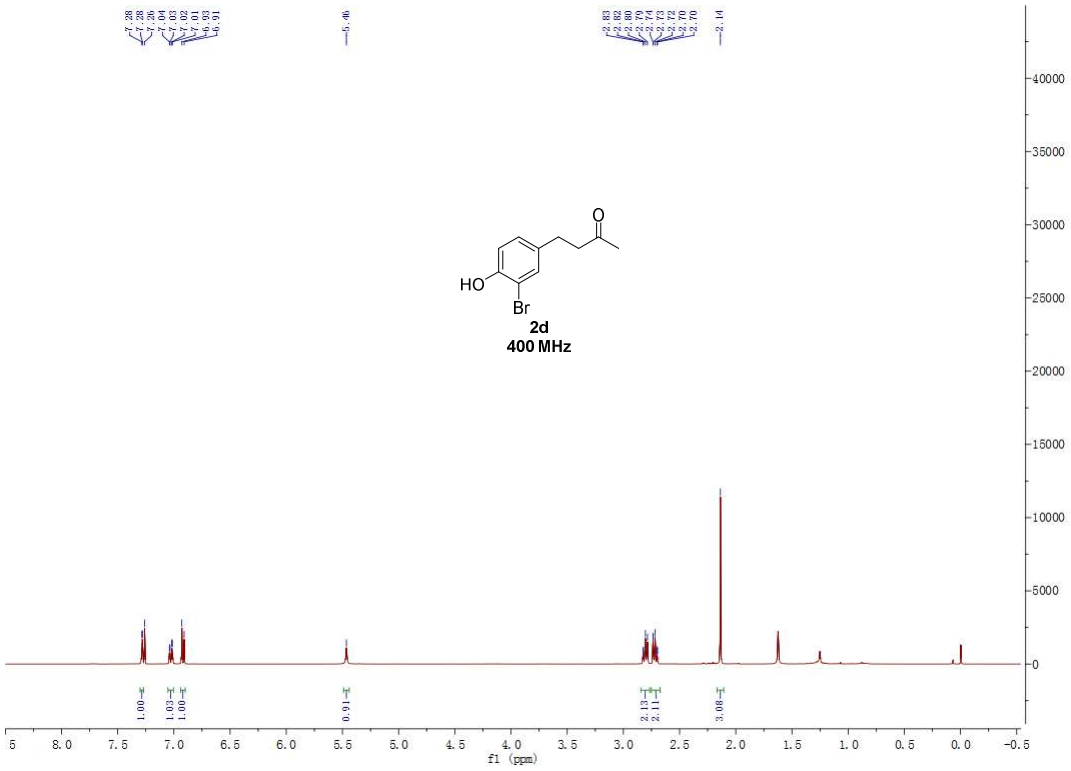


Fig. S69. ^{1}H NMR Spectrum of 2d (400 MHz, $CDCl_3$).

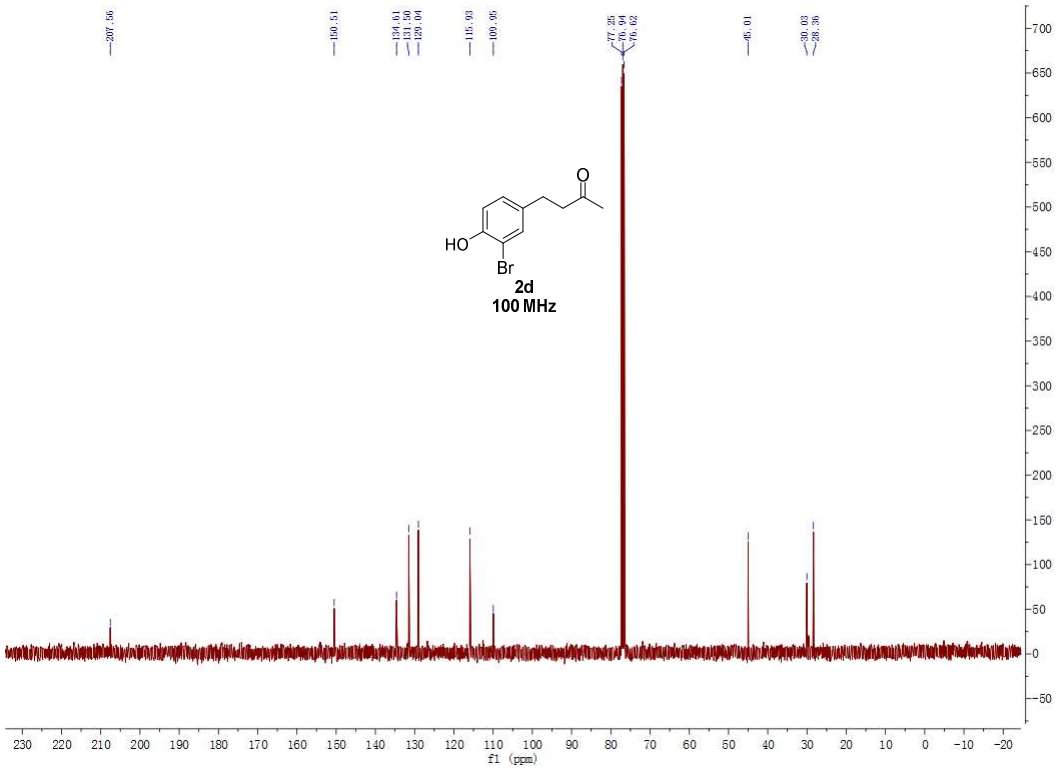


Fig. S70. ^{13}C NMR Spectrum of 2d (100 MHz, $CDCl_3$).

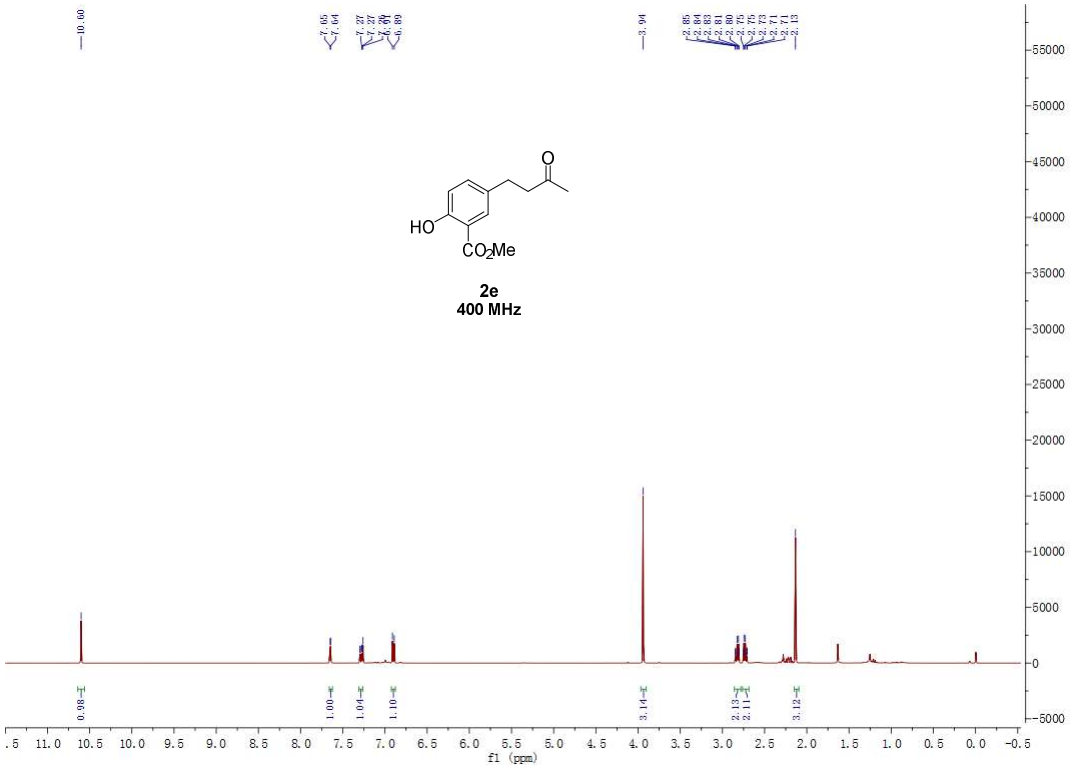


Fig. S71. ^{1}H NMR Spectrum of 2e (400 MHz, $CDCl_3$).

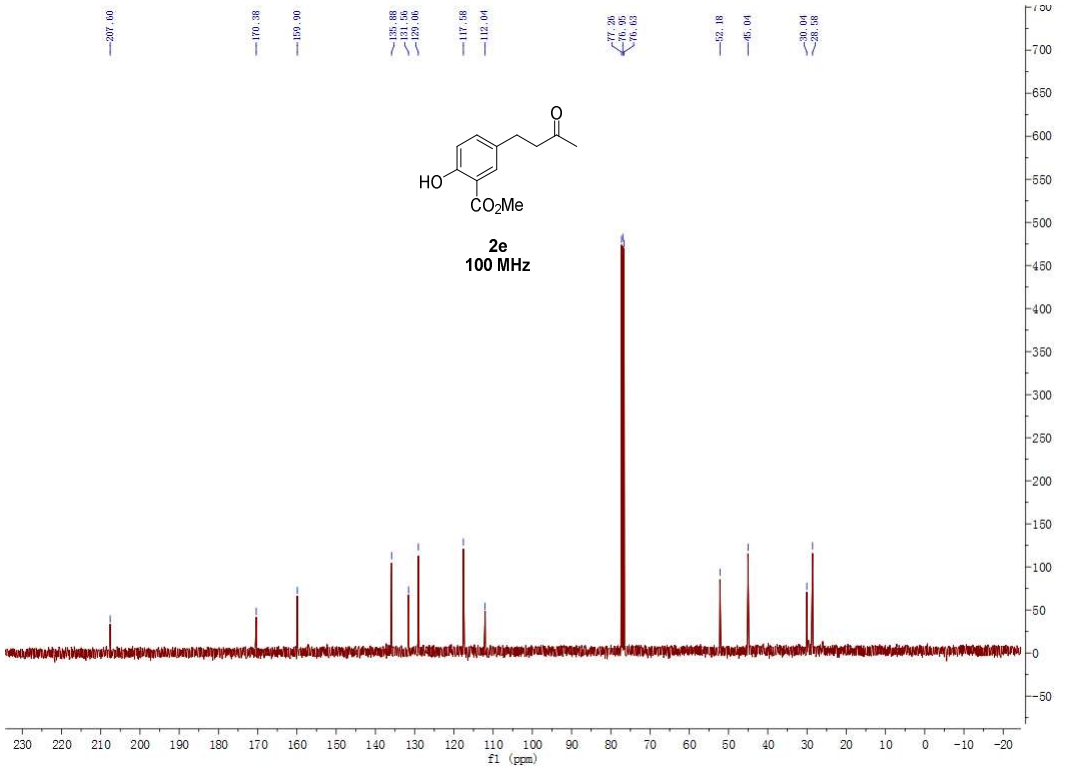


Fig. S72. ^{13}C NMR Spectrum of 2e (100 MHz, $CDCl_3$).

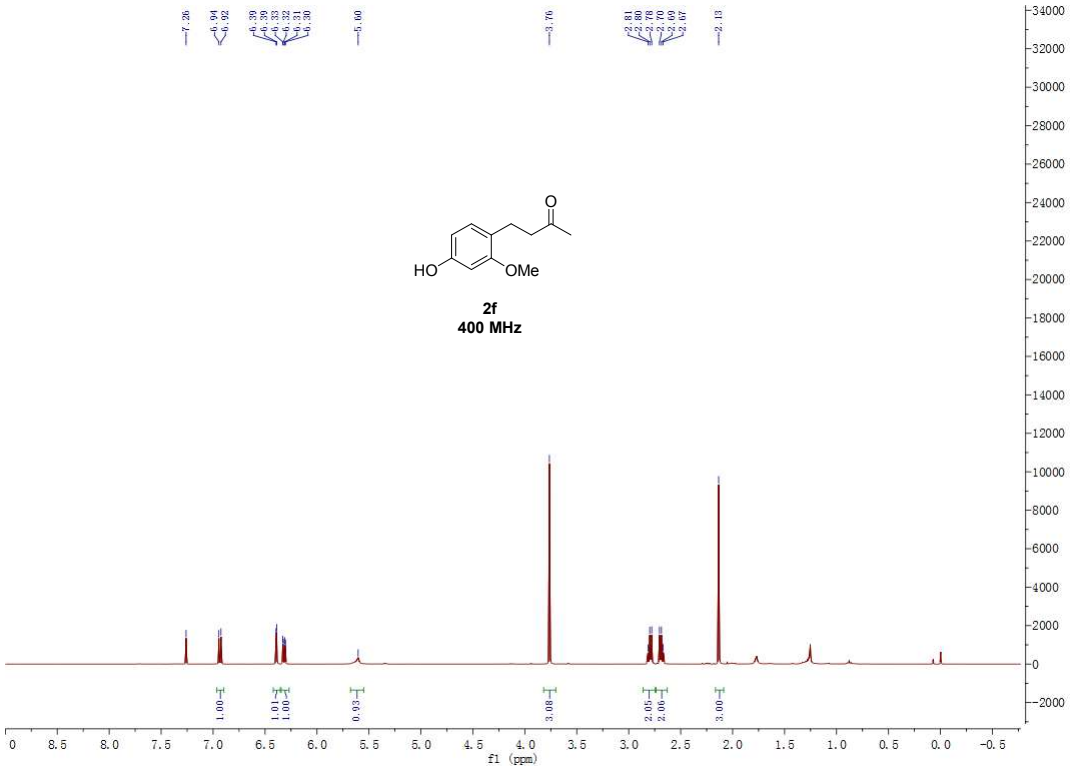


Fig. S73. ^{1}H NMR Spectrum of 2f (400 MHz, $CDCl_3$).

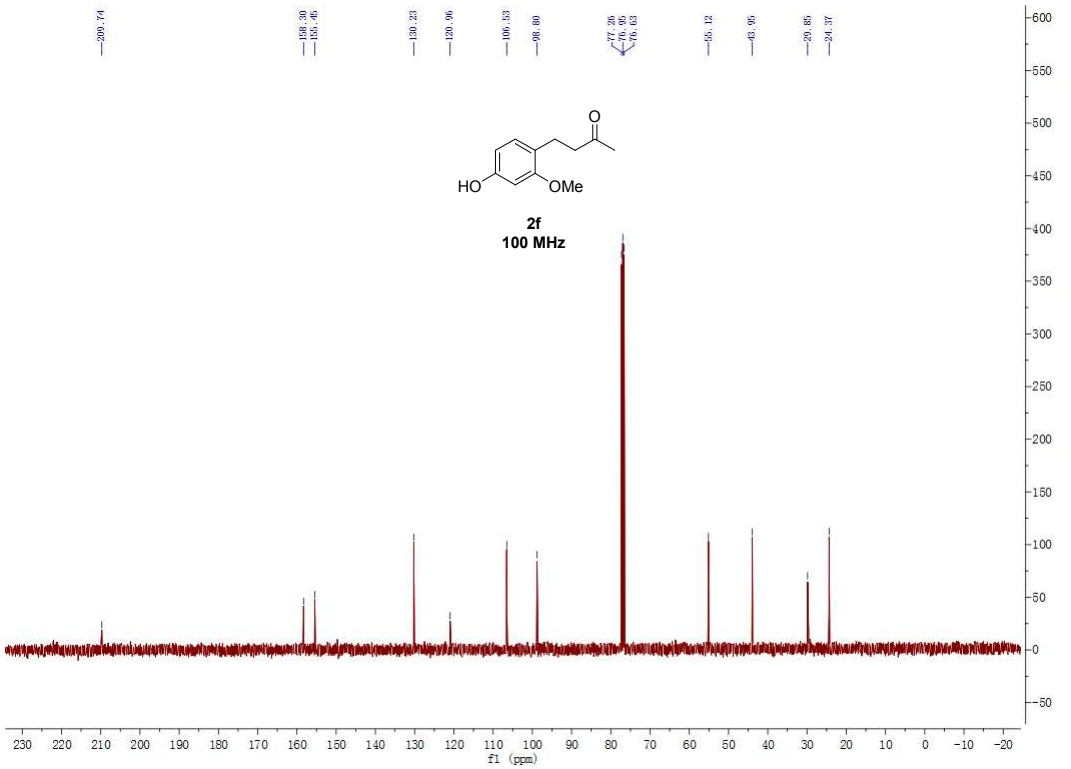


Fig. S74. ^{13}C NMR Spectrum of 2f (100 MHz, $CDCl_3$).

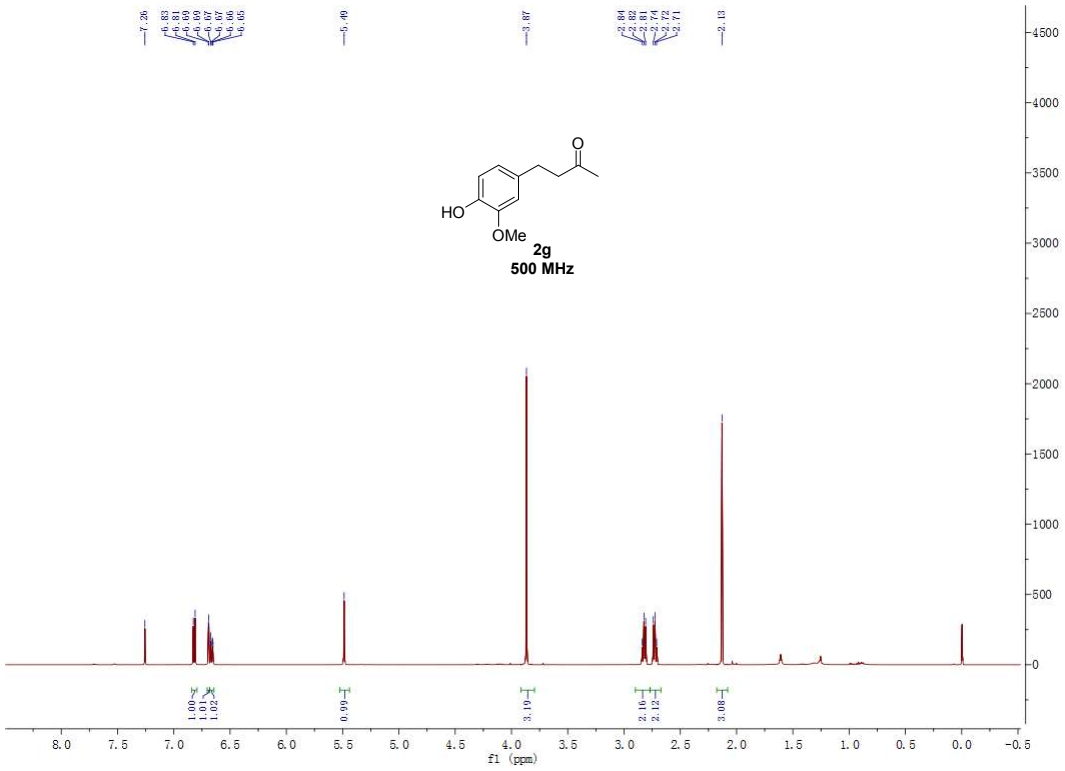


Fig. S75. ^{1}H NMR Spectrum of 2g (500 MHz, $CDCl_3$).

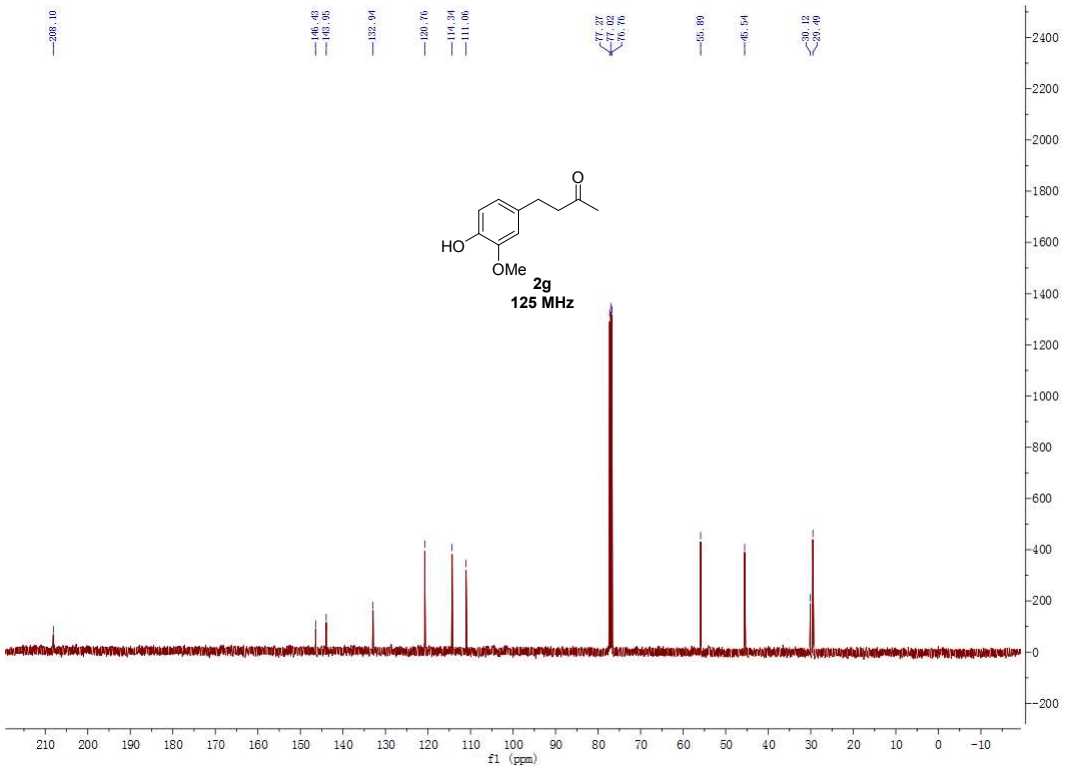


Fig. S76. ^{13}C NMR Spectrum of 2g (125 MHz, $CDCl_3$).

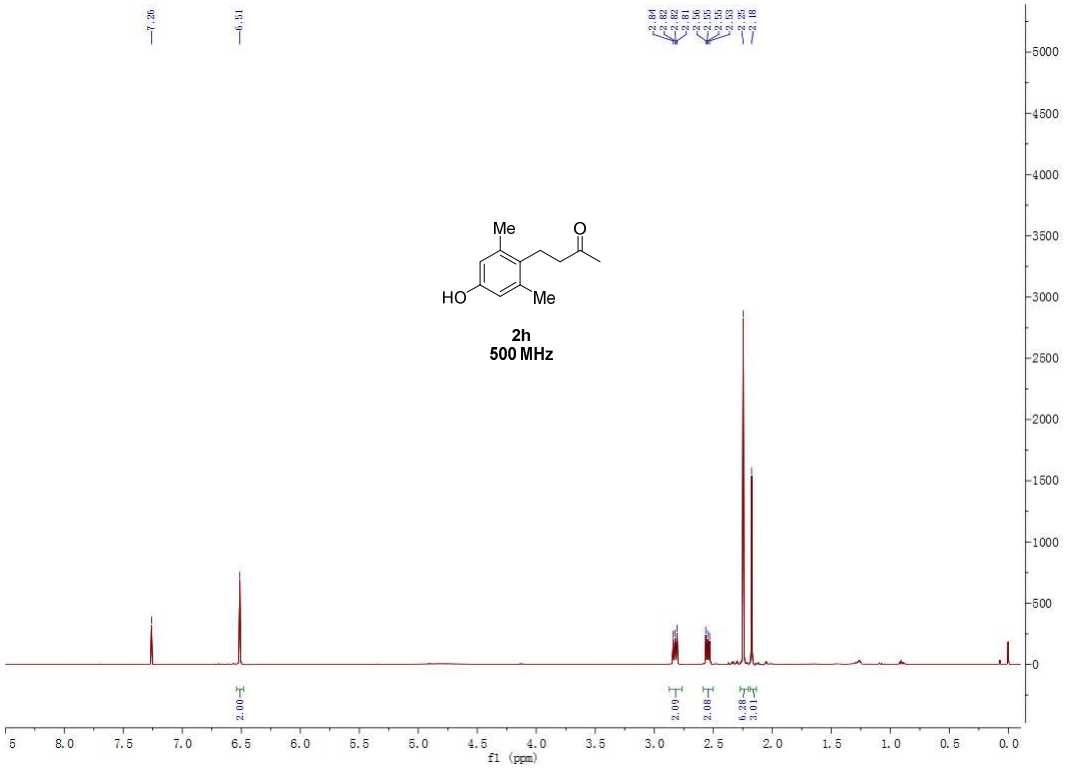


Fig. S77. ^{1}H NMR Spectrum of 2h (500 MHz, $CDCl_3$).

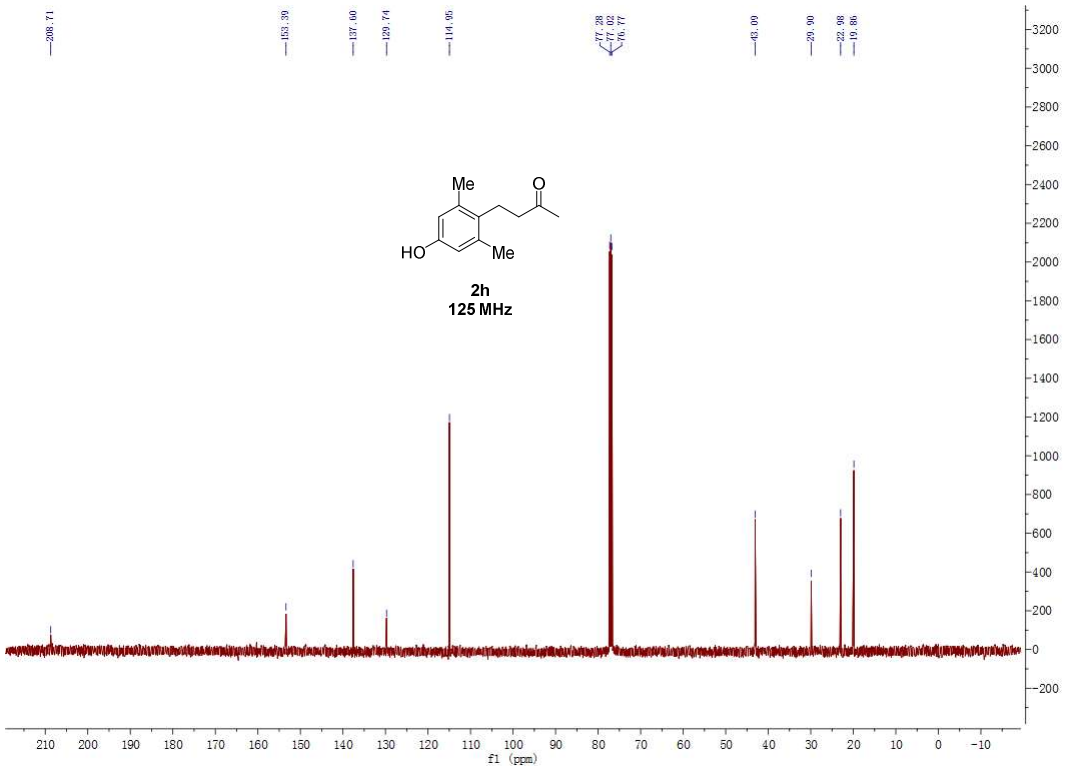


Fig. S78. ^{13}C NMR Spectrum of 2h (125 MHz, $CDCl_3$).

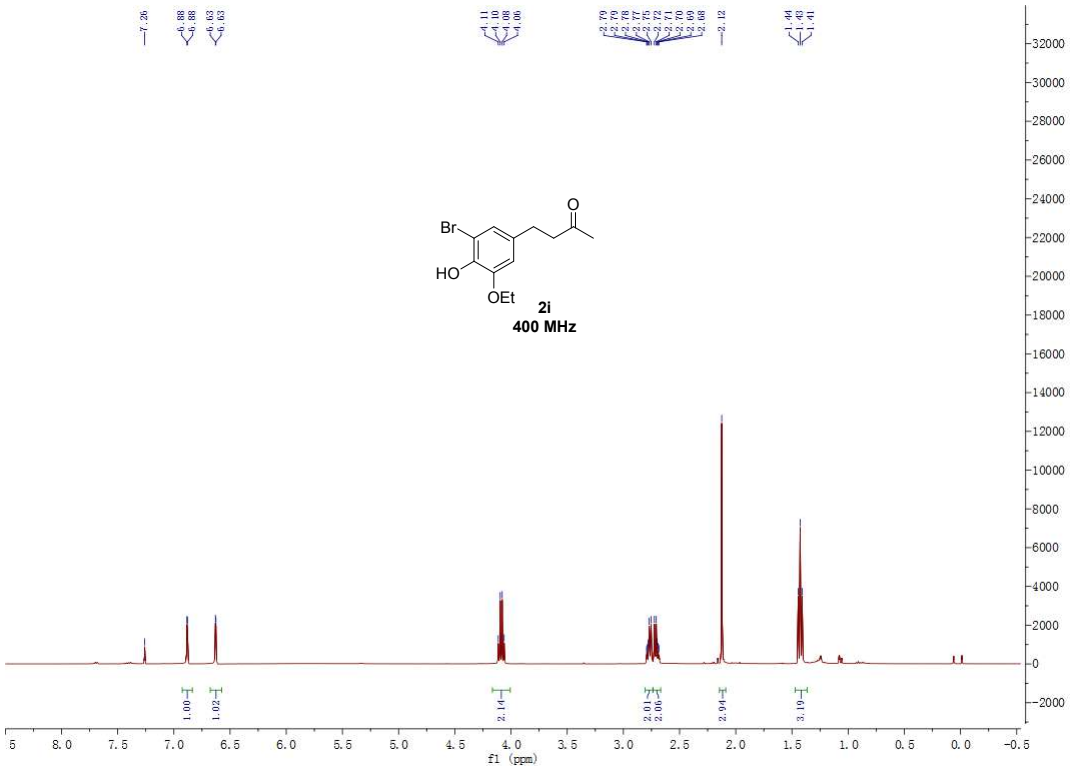


Fig. S79. ^{1}H NMR Spectrum of 2i (400 MHz, $CDCl_3$).

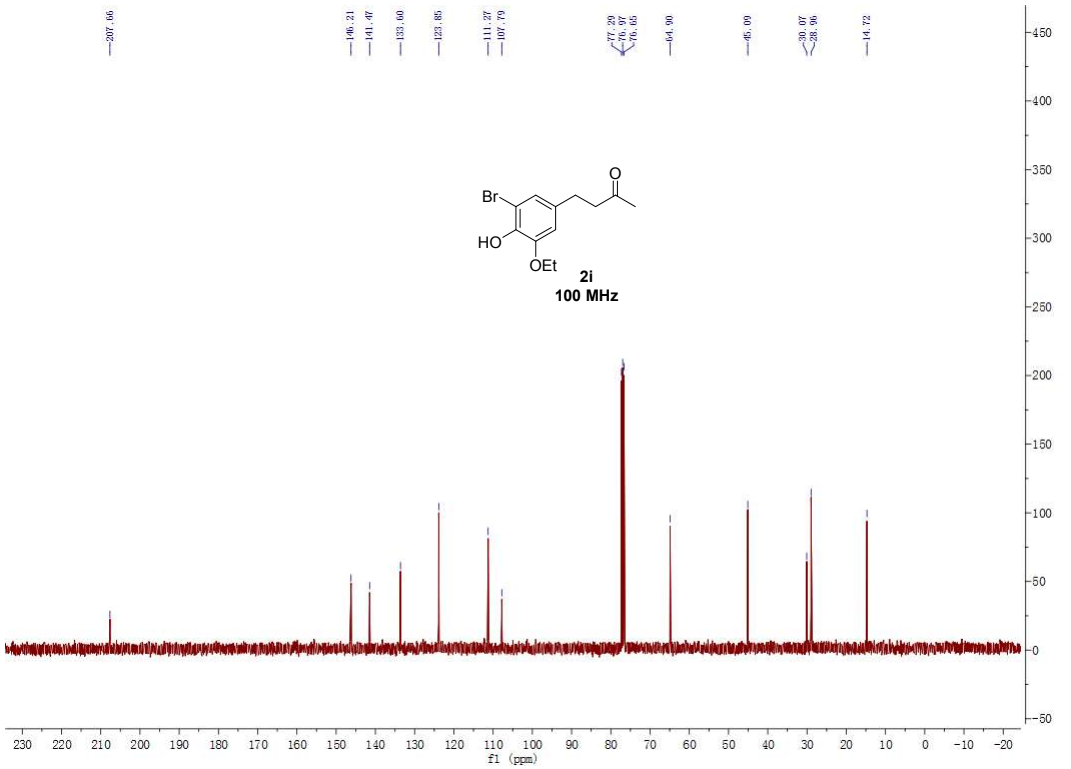


Fig. S80. ^{13}C NMR Spectrum of 2i (100 MHz, $CDCl_3$).

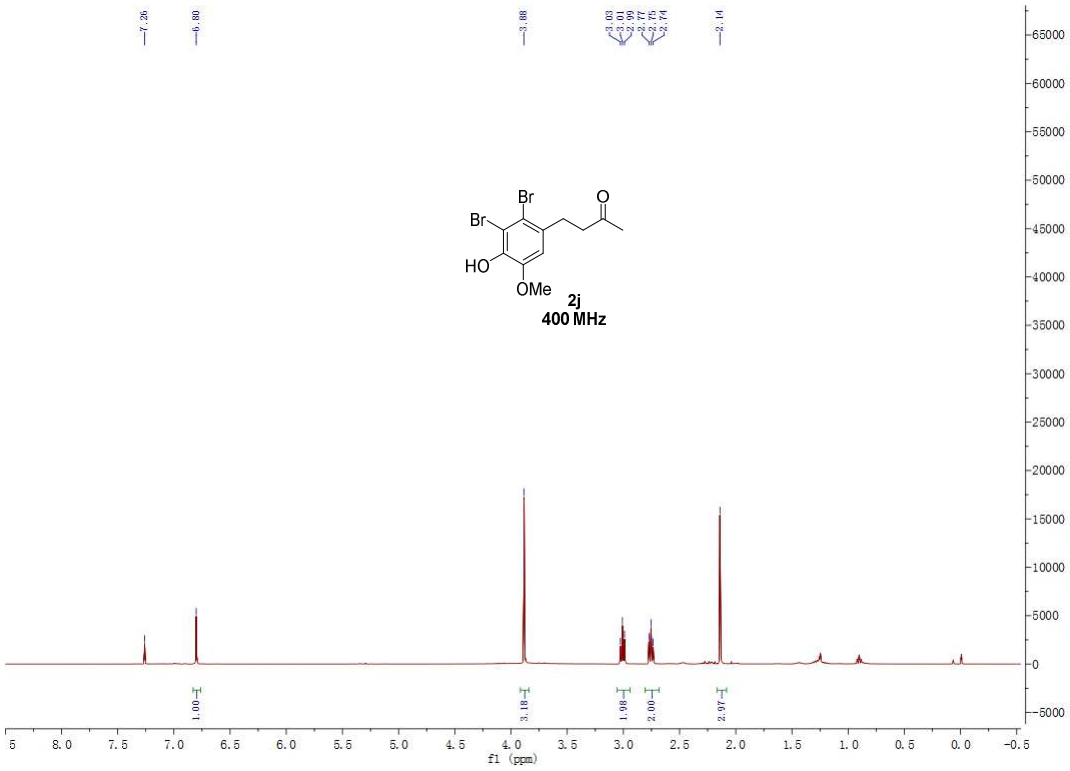


Fig. S81. ^{1}H NMR Spectrum of 2j (400 MHz, $CDCl_3$).

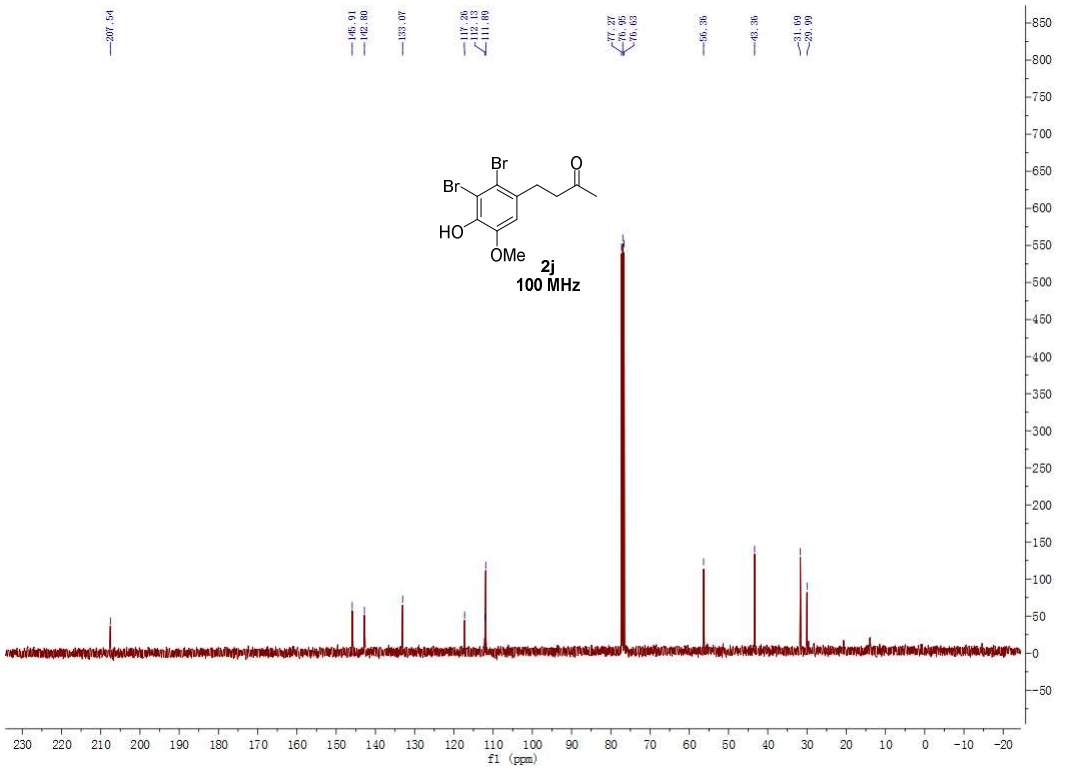


Fig. S82. ^{13}C NMR Spectrum of 2j (100 MHz, $CDCl_3$).

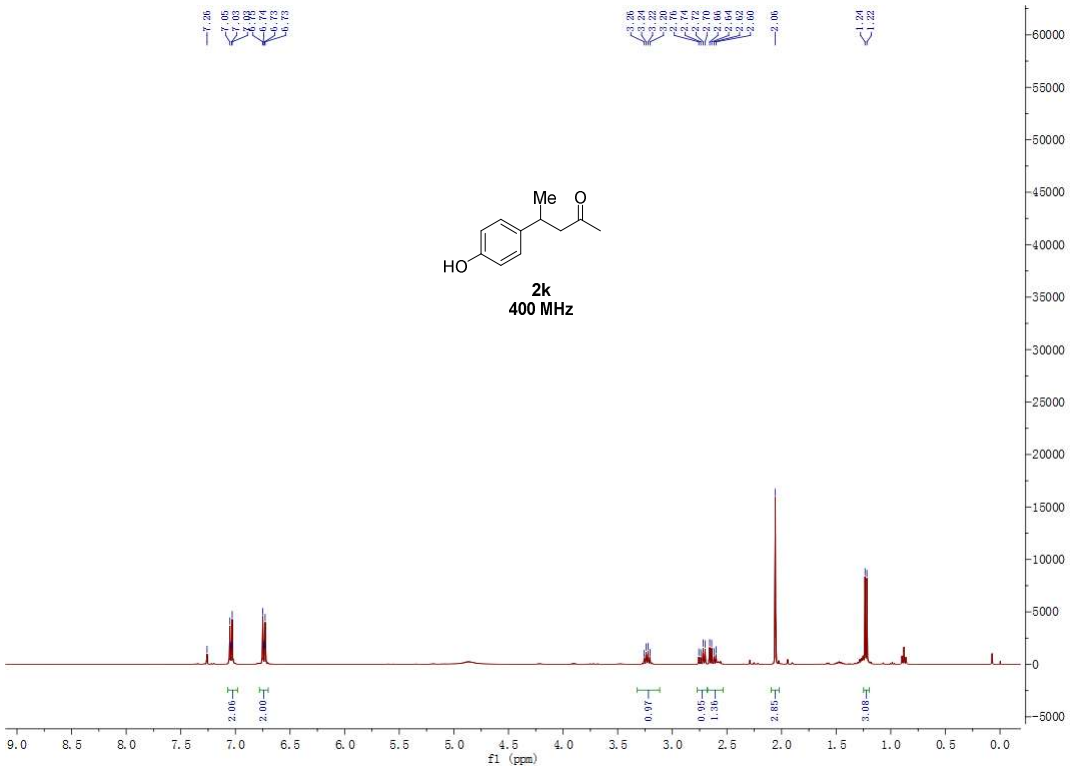


Fig. S83. ^{1}H NMR Spectrum of 2k (400 MHz, $CDCl_3$).

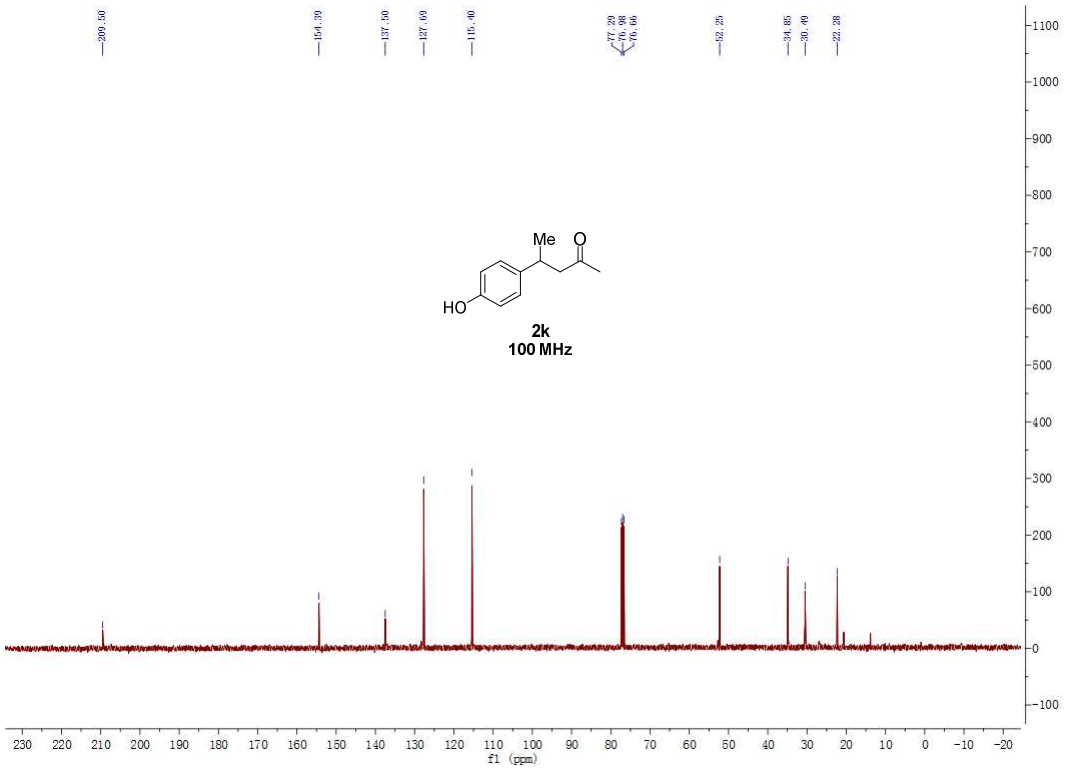


Fig. S84. ^{13}C NMR Spectrum of 2k (100 MHz, $CDCl_3$).

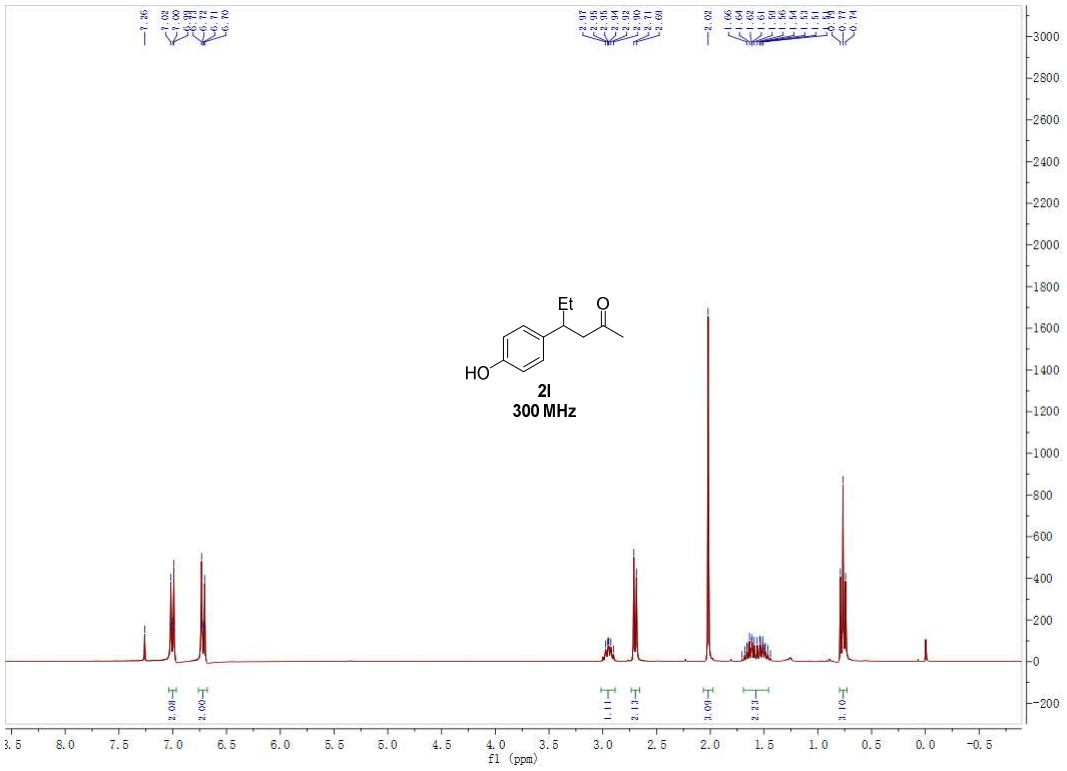


Fig. S85. ^{1}H NMR Spectrum of 2l (300 MHz, $CDCl_3$).

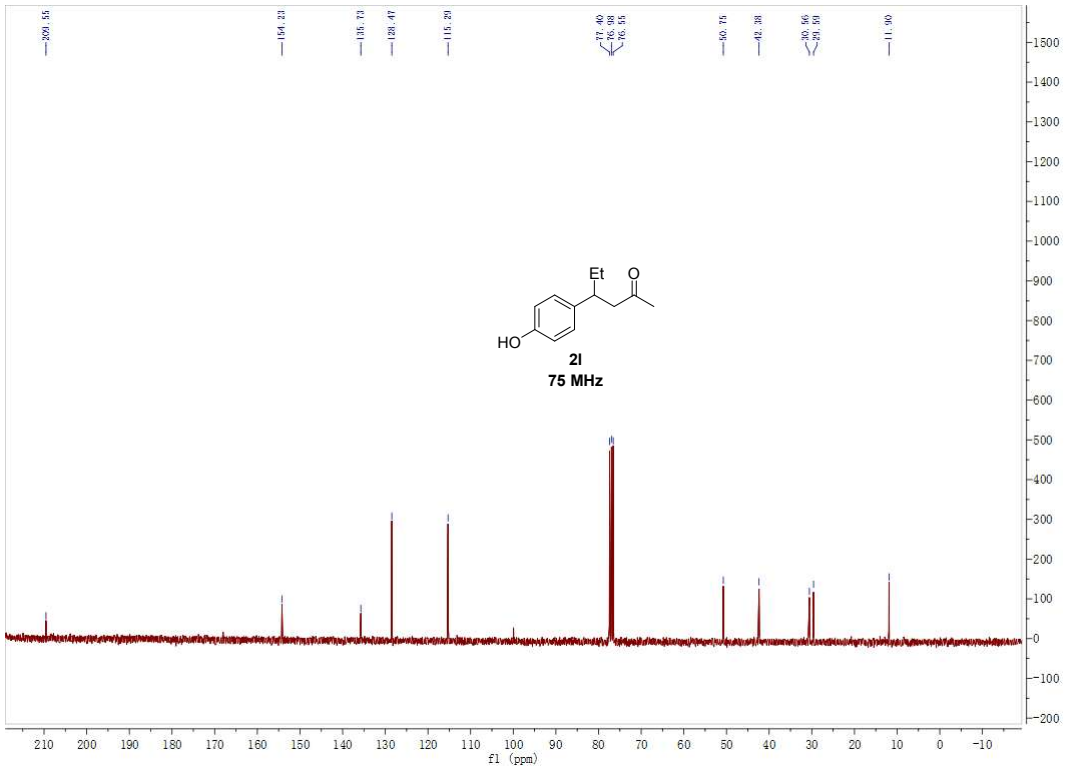


Fig. S86. ^{13}C NMR Spectrum of 2l (75 MHz, $CDCl_3$).

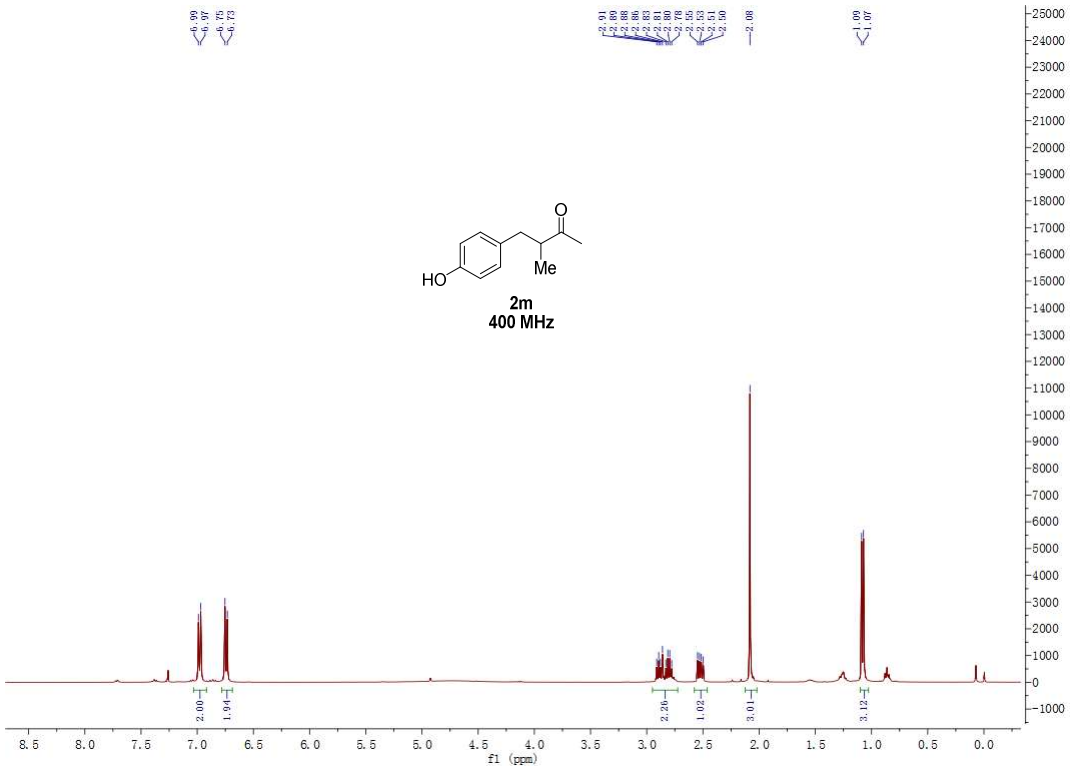


Fig. S87. ^{1}H NMR Spectrum of 2m (400 MHz, $CDCl_3$).

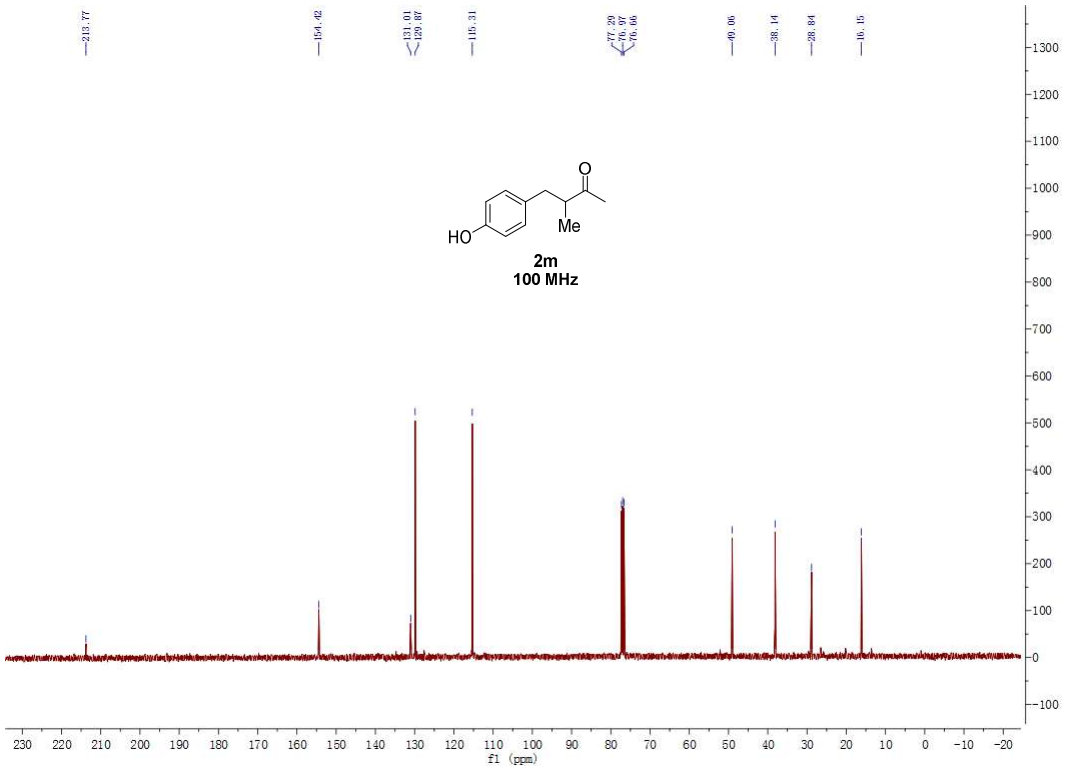


Fig. S88. ^{13}C NMR Spectrum of 2m (100 MHz, $CDCl_3$).

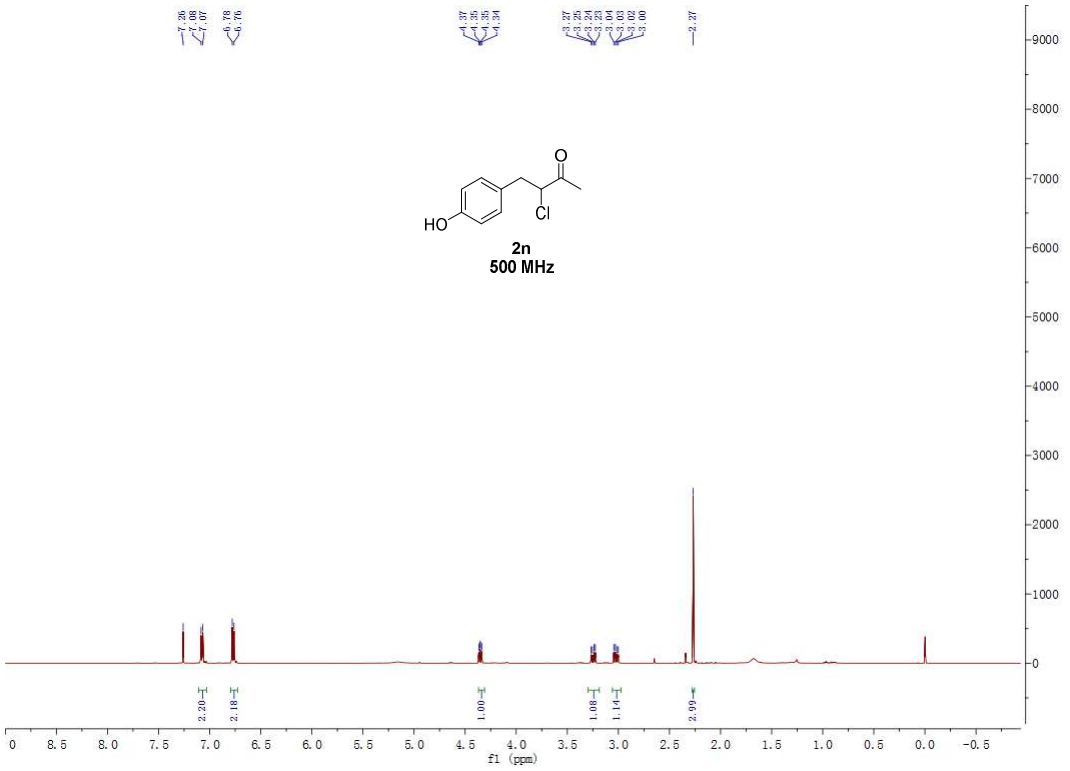


Fig. S89. ^{1}H NMR Spectrum of 2n (500 MHz, $CDCl_3$).

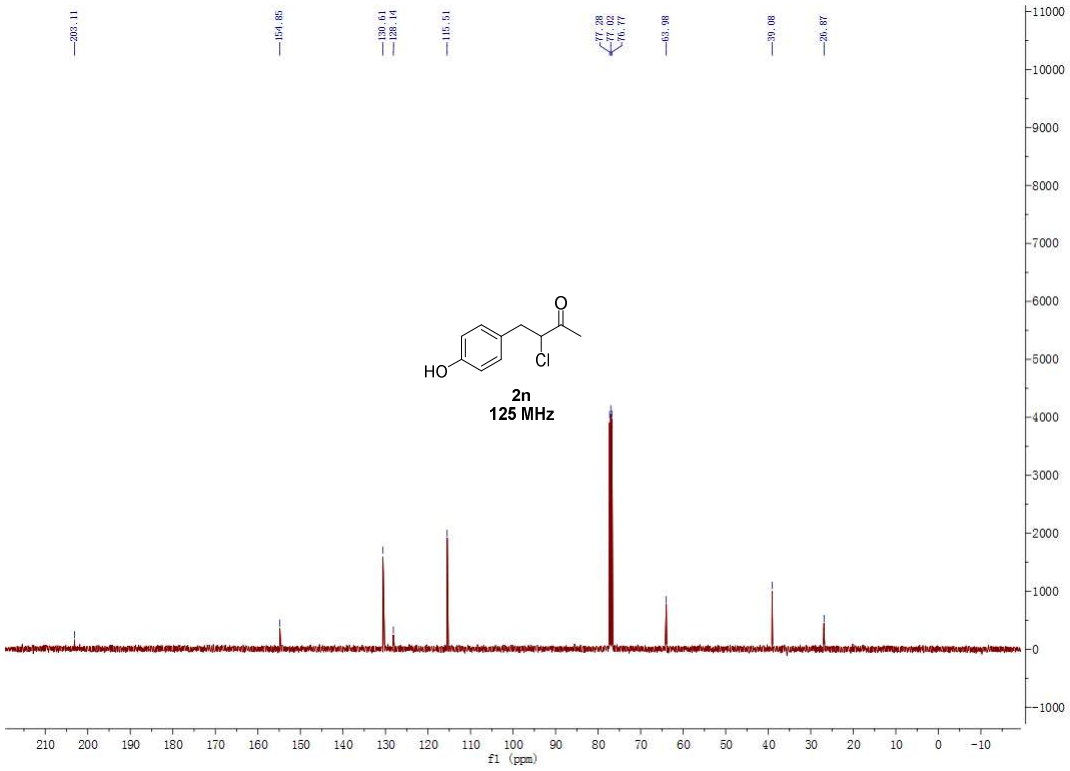


Fig. S90. ^{13}C NMR Spectrum of 2n (125 MHz, $CDCl_3$).

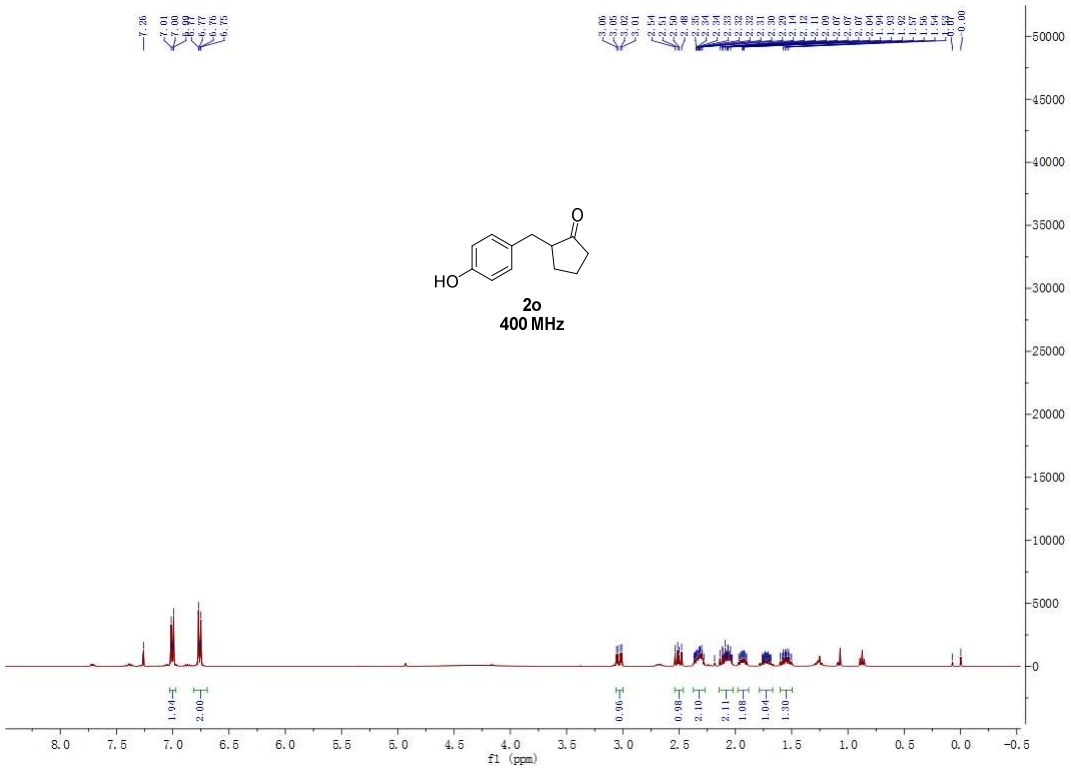


Fig. S91. ^{1}H NMR Spectrum of 2o (400 MHz, $CDCl_3$).

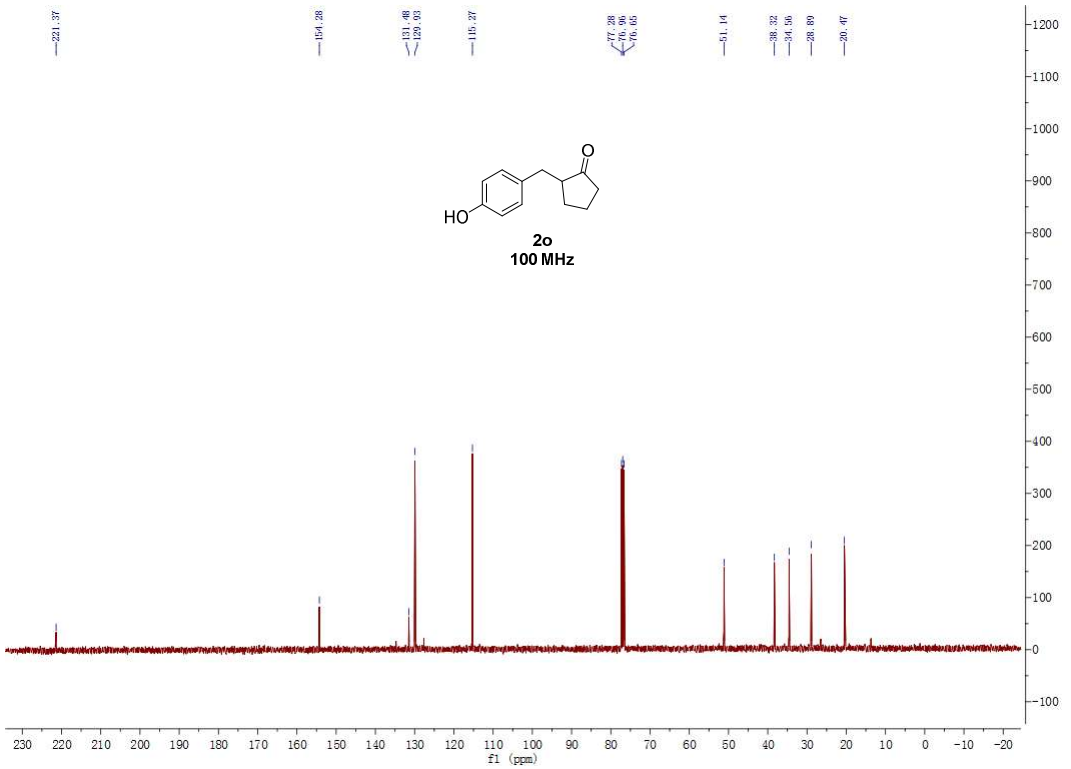


Fig. S92. ^{13}C NMR Spectrum of 2o (100 MHz, $CDCl_3$).

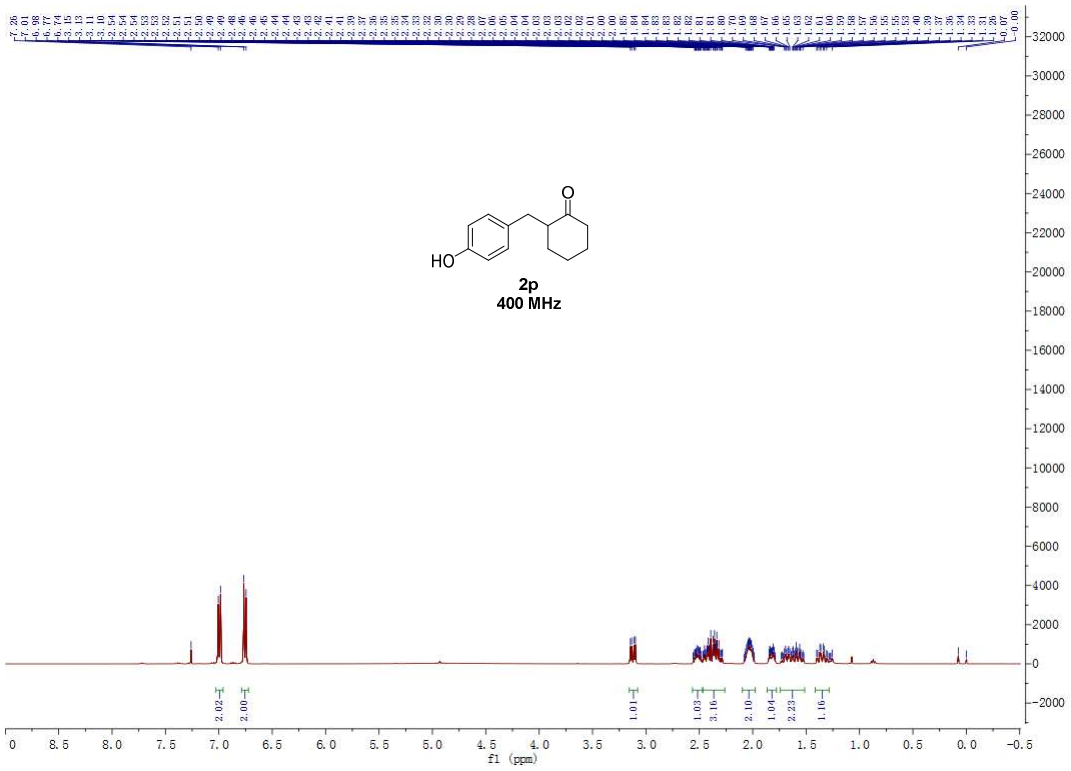


Fig. S93. ^{1}H NMR Spectrum of 2p (400 MHz, $CDCl_3$).

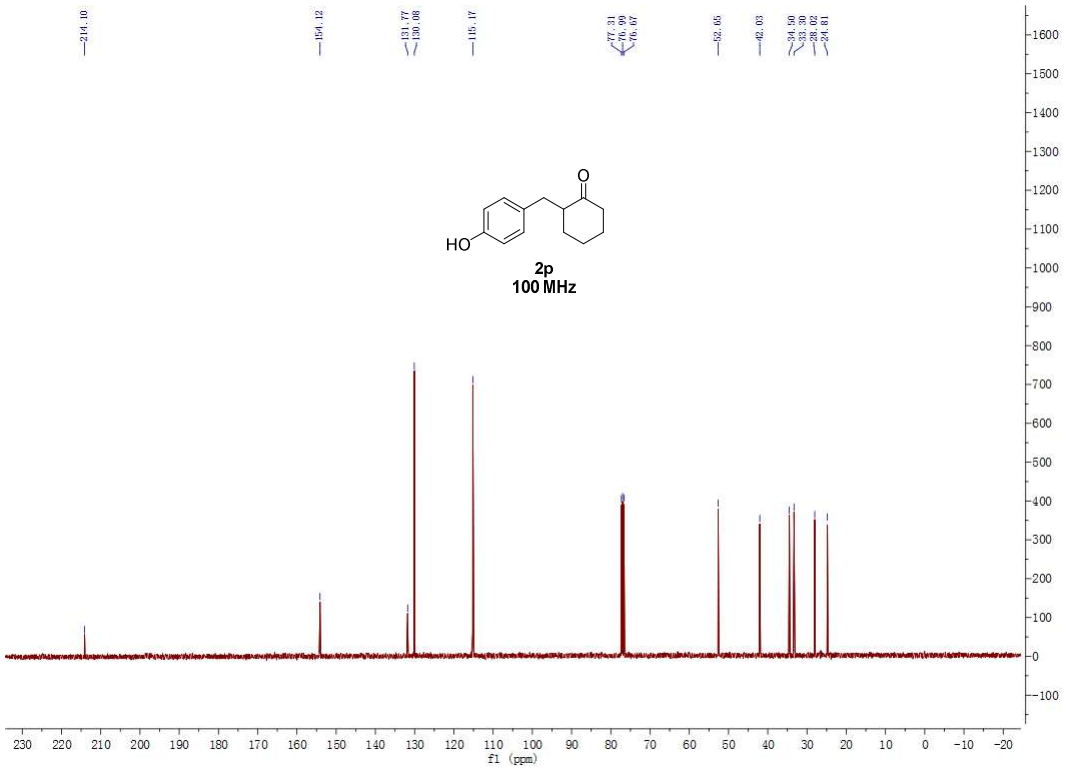


Fig. S94. ^{13}C NMR Spectrum of 2p (100 MHz, $CDCl_3$).

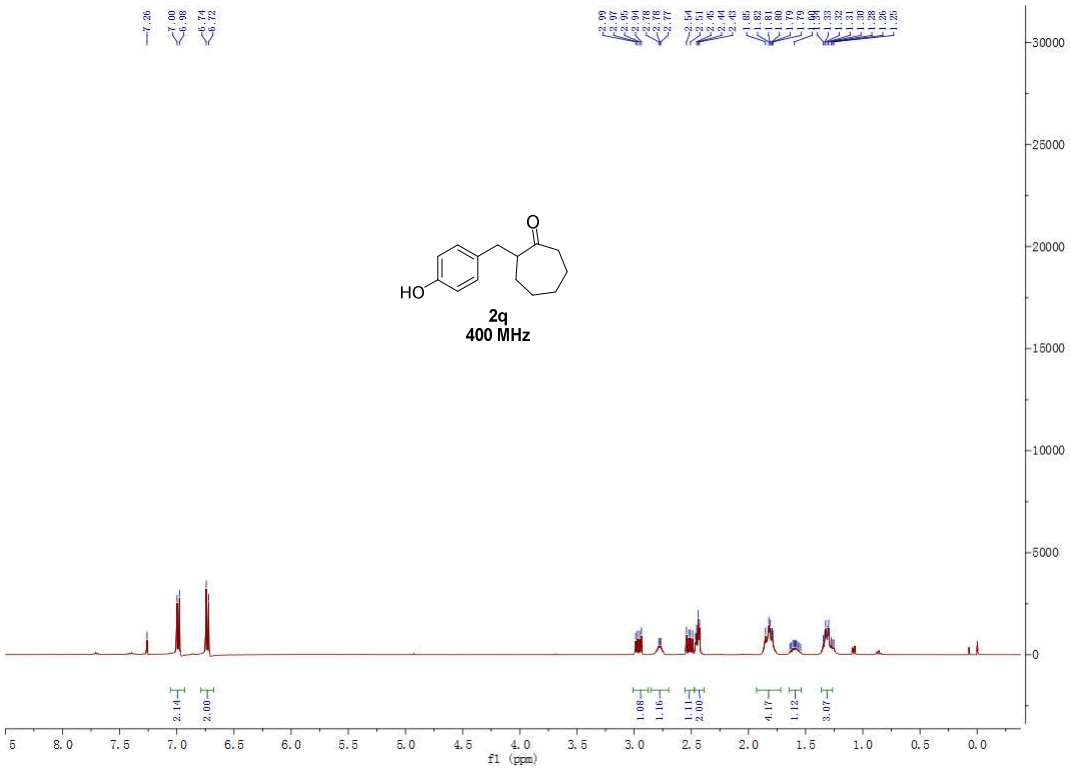


Fig. S95. ^{1}H NMR Spectrum of 2q (400 MHz, $CDCl_3$).

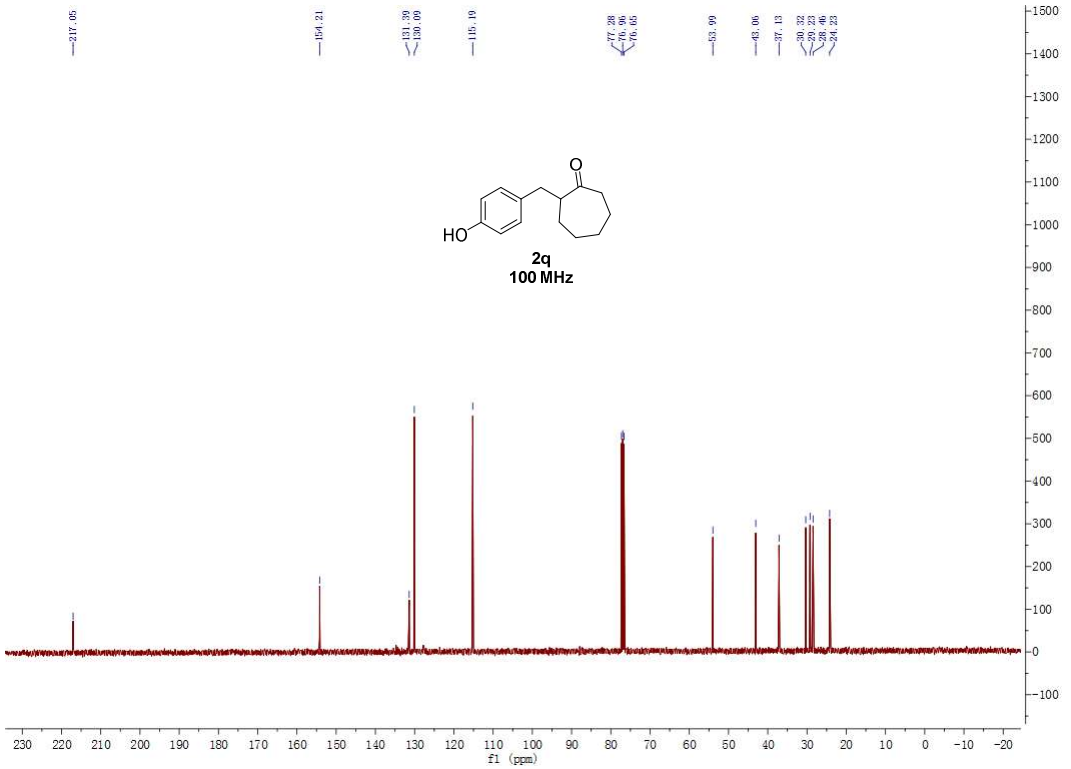


Fig. S96. ^{13}C NMR Spectrum of 2q (100 MHz, $CDCl_3$).

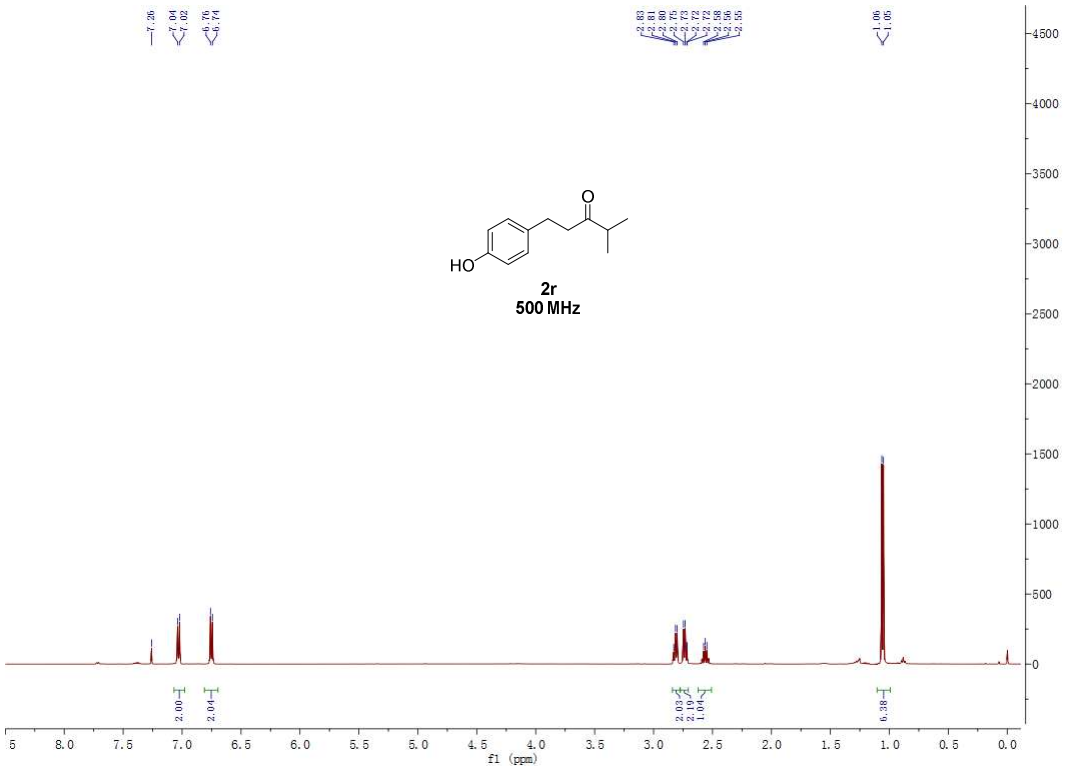


Fig. S97. ^{1}H NMR Spectrum of 2r (500 MHz, $CDCl_3$).

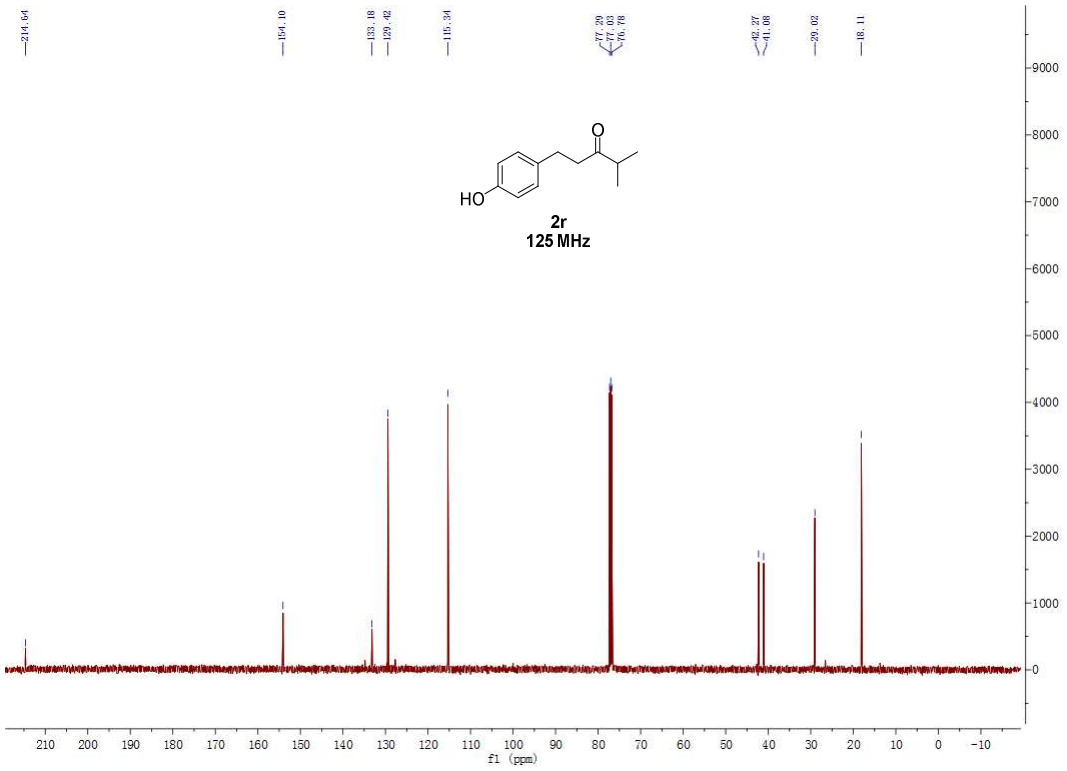


Fig. S98. ^{13}C NMR Spectrum of 2r (125 MHz, $CDCl_3$).

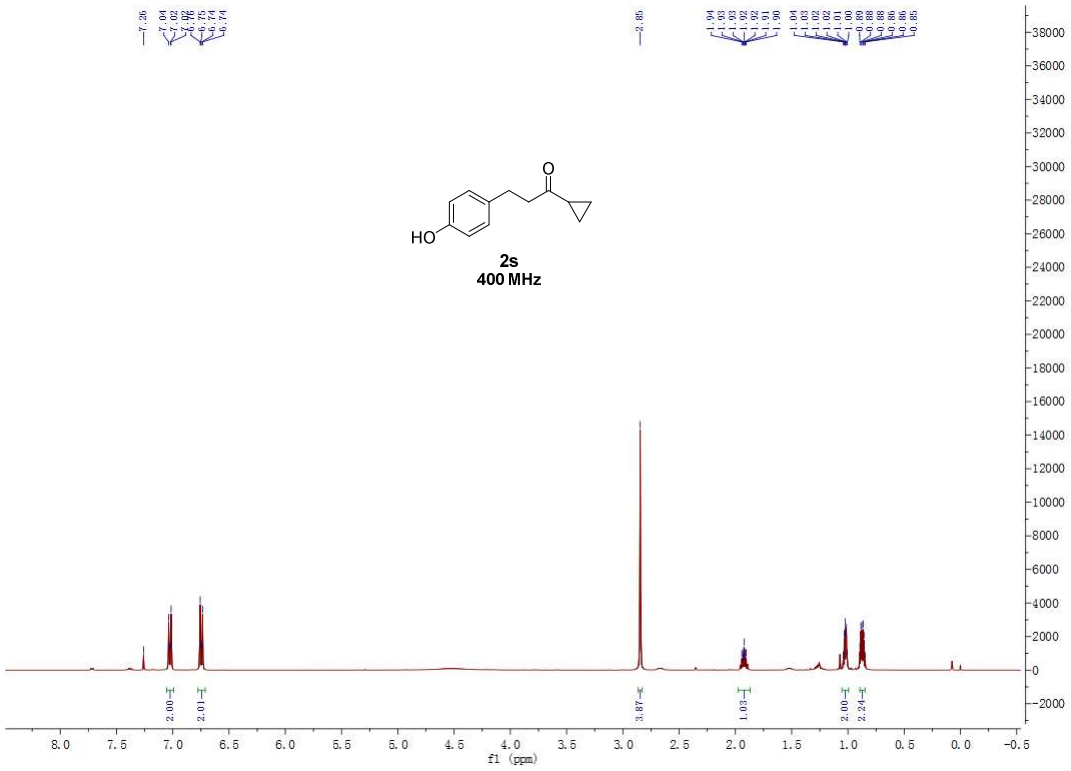


Fig. S99. ^{1}H NMR Spectrum of 2s (400 MHz, $CDCl_3$).

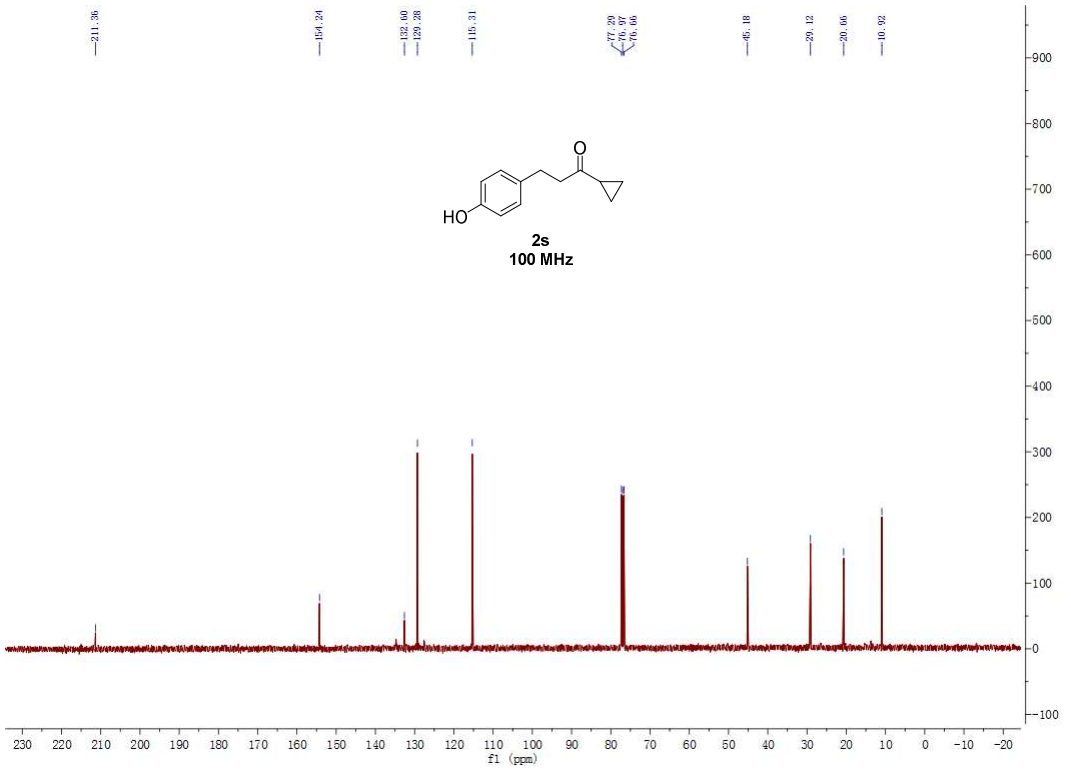


Fig. S100. ^{13}C NMR Spectrum of 2s (100 MHz, $CDCl_3$).

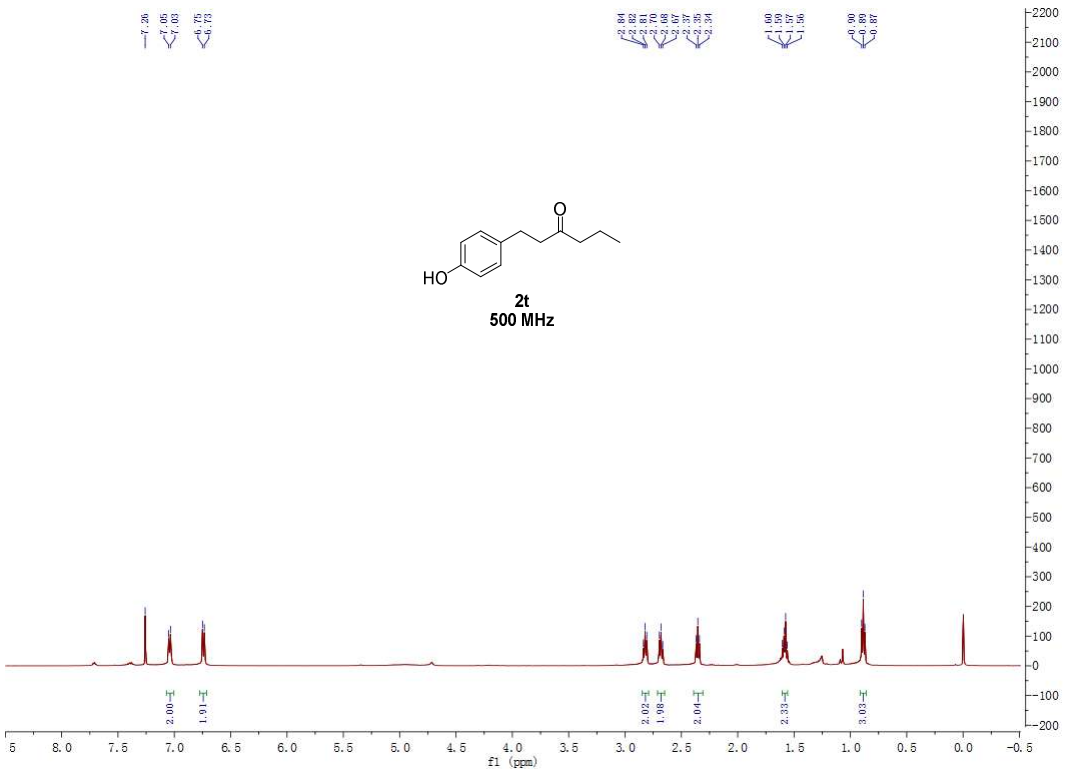


Fig. S101. ^{1}H NMR Spectrum of 2t (500 MHz, $CDCl_3$).

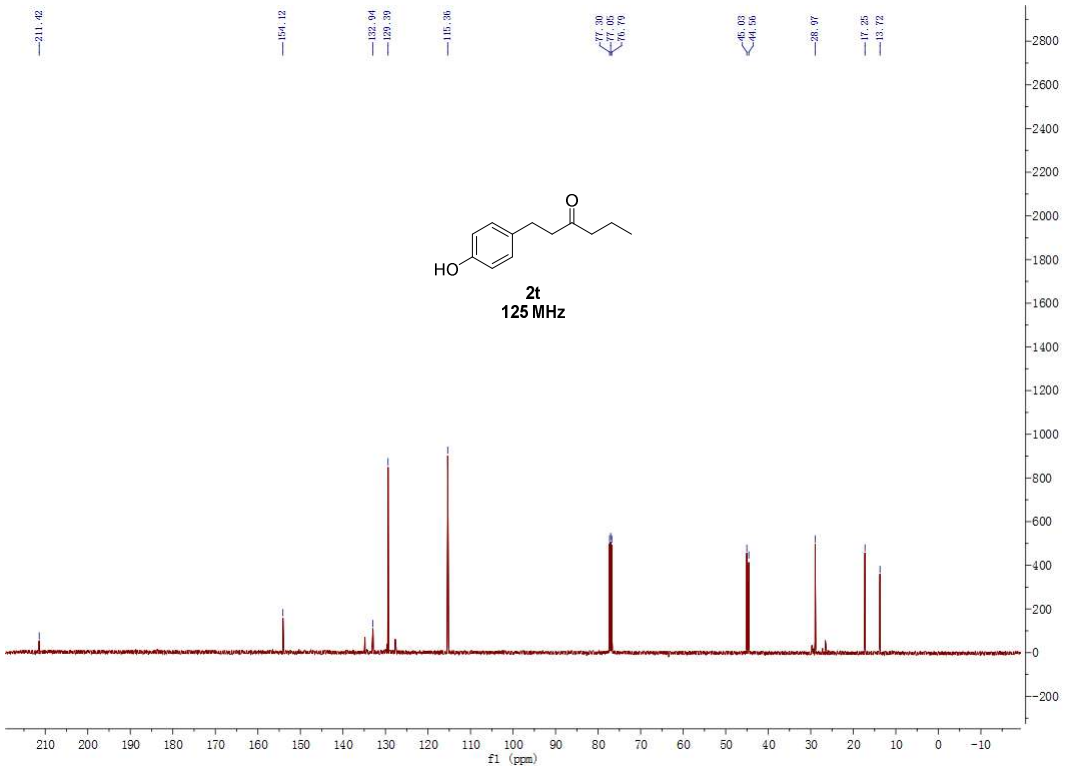


Fig. S102. ^{13}C NMR Spectrum of 2t (125 MHz, $CDCl_3$).

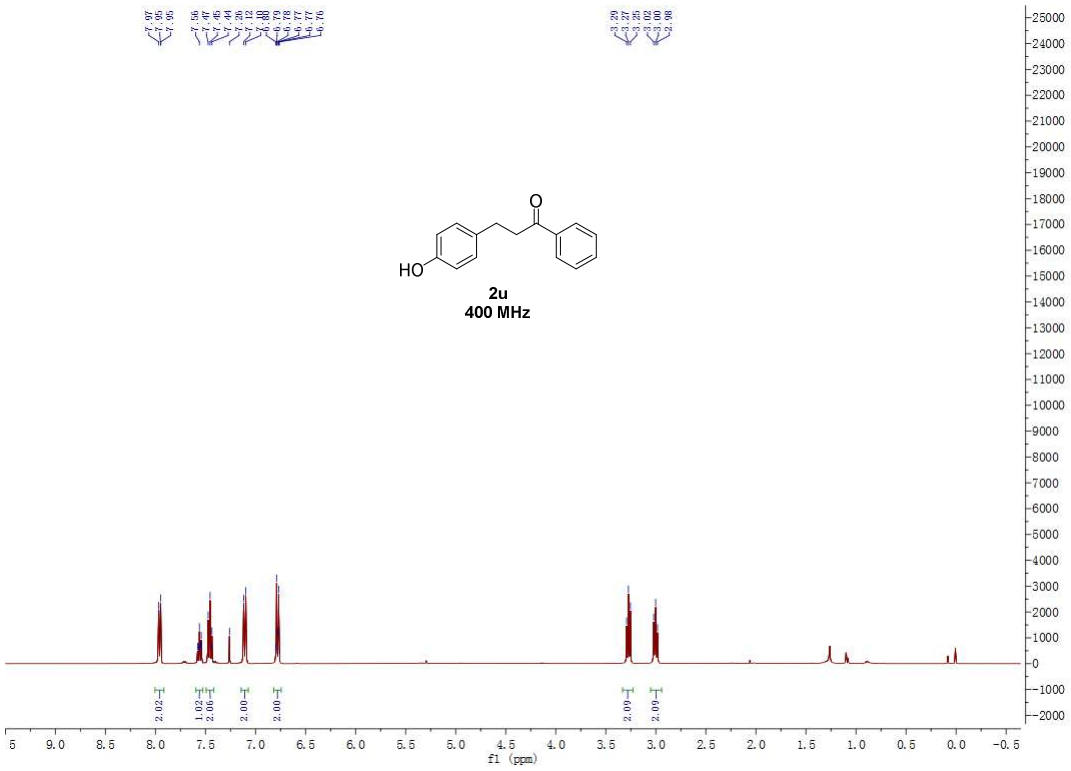


Fig. S103. ^{1}H NMR Spectrum of 2u (400 MHz, $CDCl_3$).

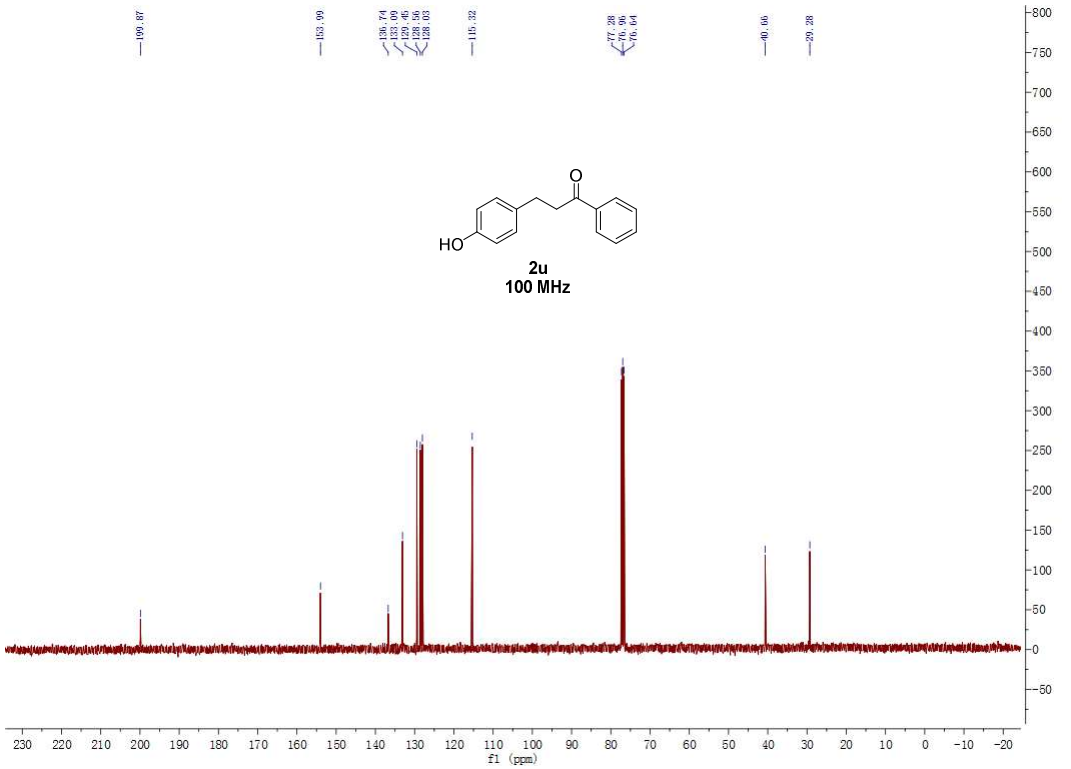


Fig. S104. ^{13}C NMR Spectrum of 2u (100 MHz, $CDCl_3$).

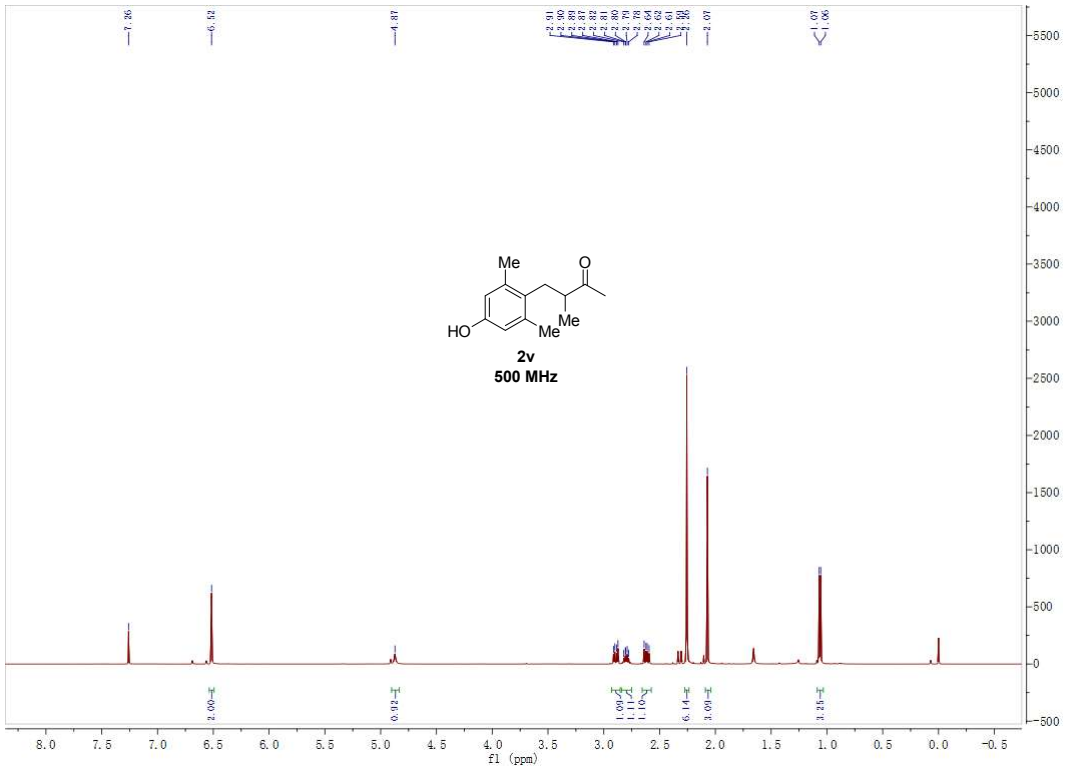


Fig. S105. ^{1}H NMR Spectrum of 2v (500 MHz, $CDCl_3$).

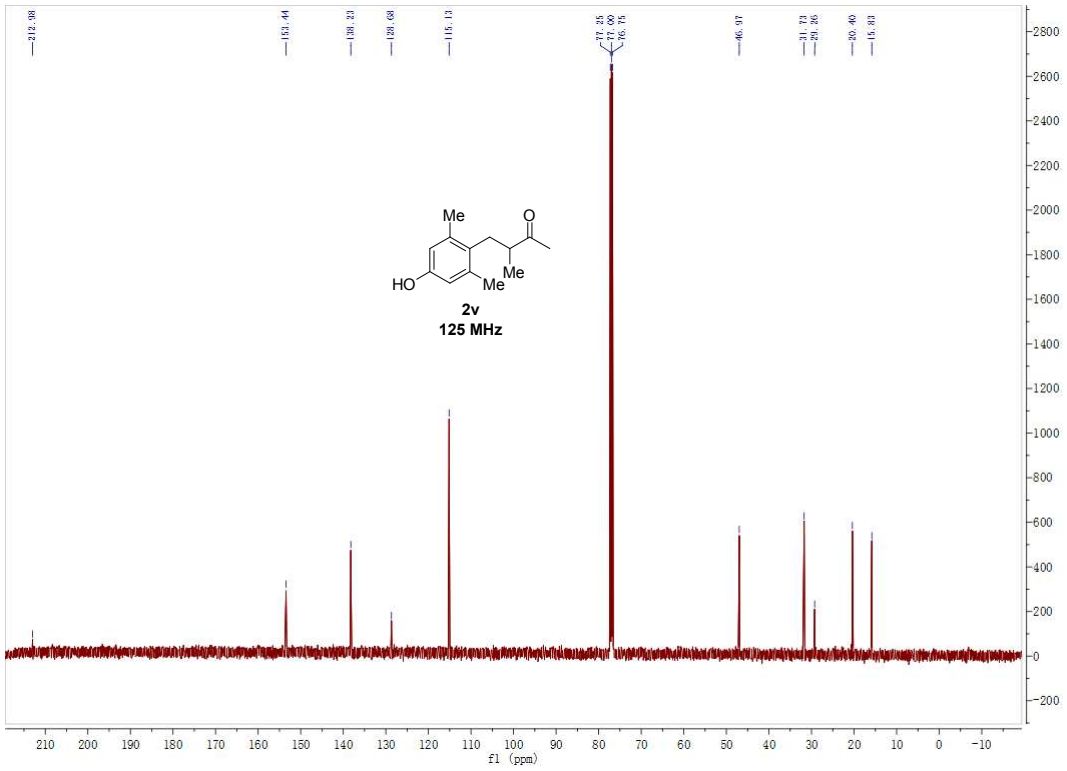


Fig. S106. ^{13}C NMR Spectrum of 2v (125 MHz, $CDCl_3$).

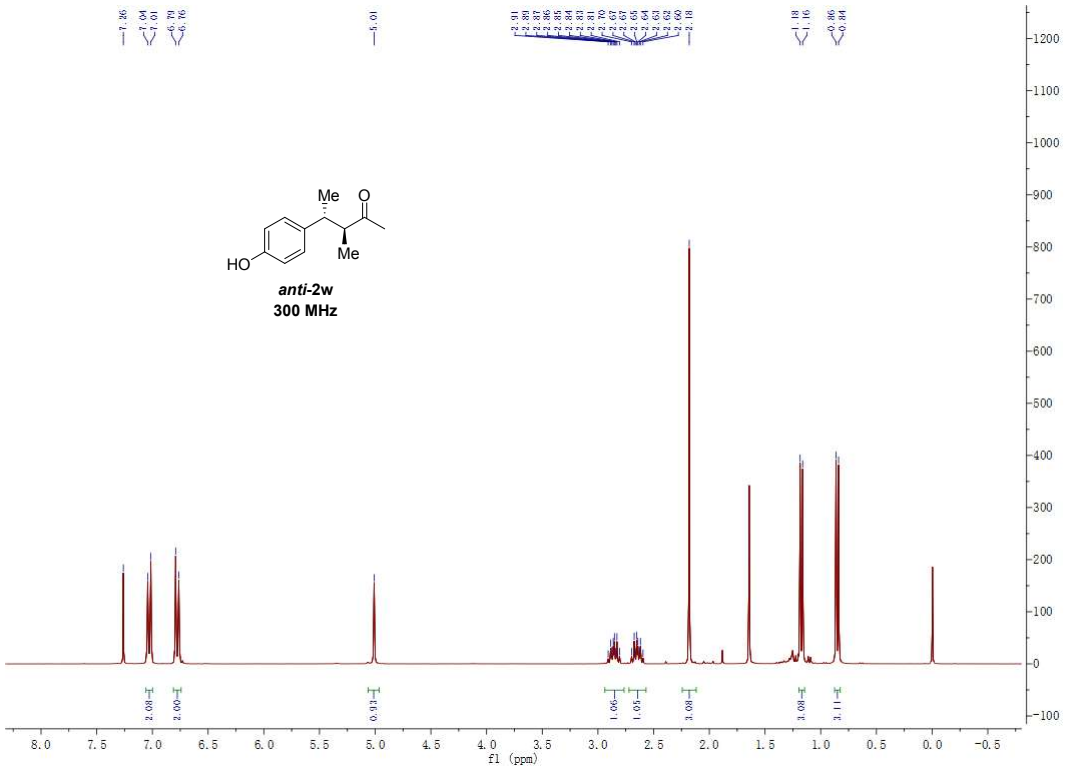


Fig. S107. ^{1}H NMR Spectrum of 2w (major) (300 MHz, $CDCl_3$).

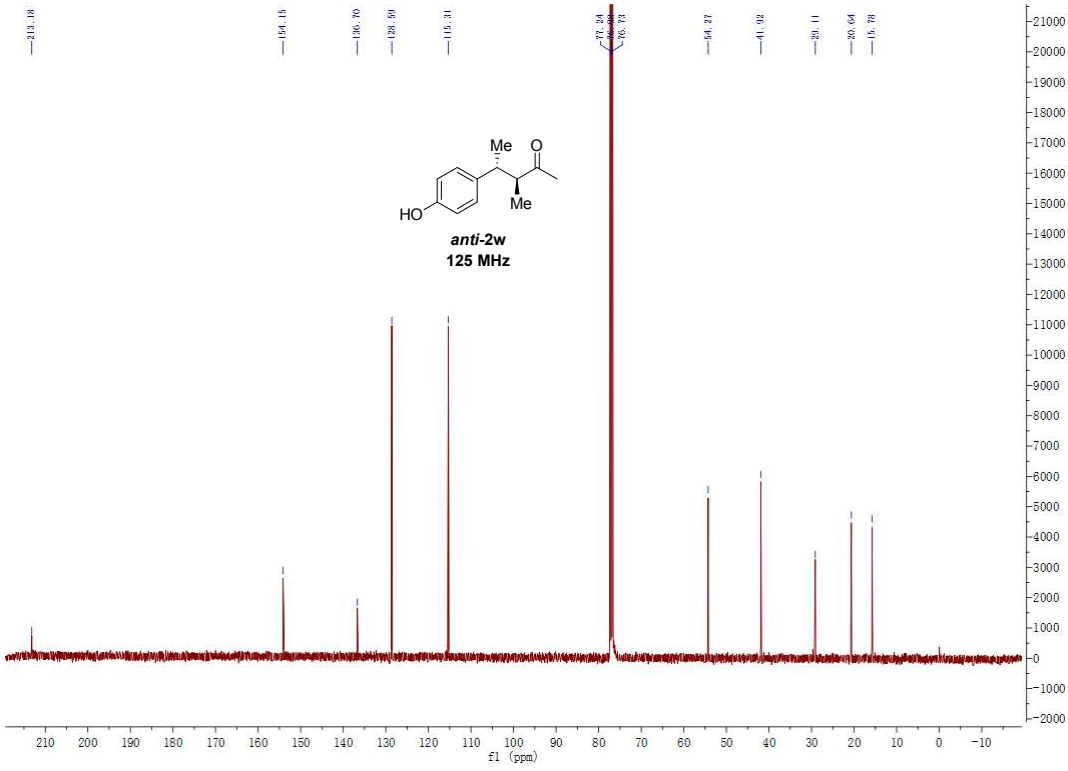


Fig. S108. ^{13}C NMR Spectrum of 2w (major) (125 MHz, $CDCl_3$).

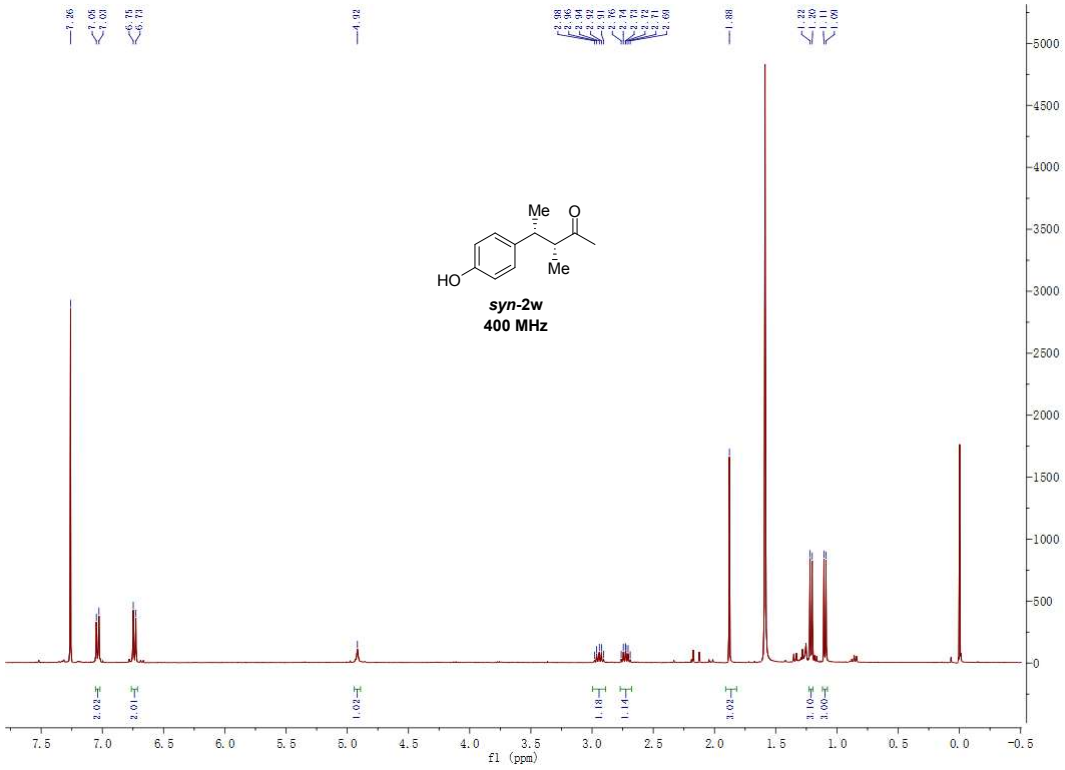


Fig. S109. ^{1}H NMR Spectrum of 2w (minor) (400 MHz, $CDCl_3$).

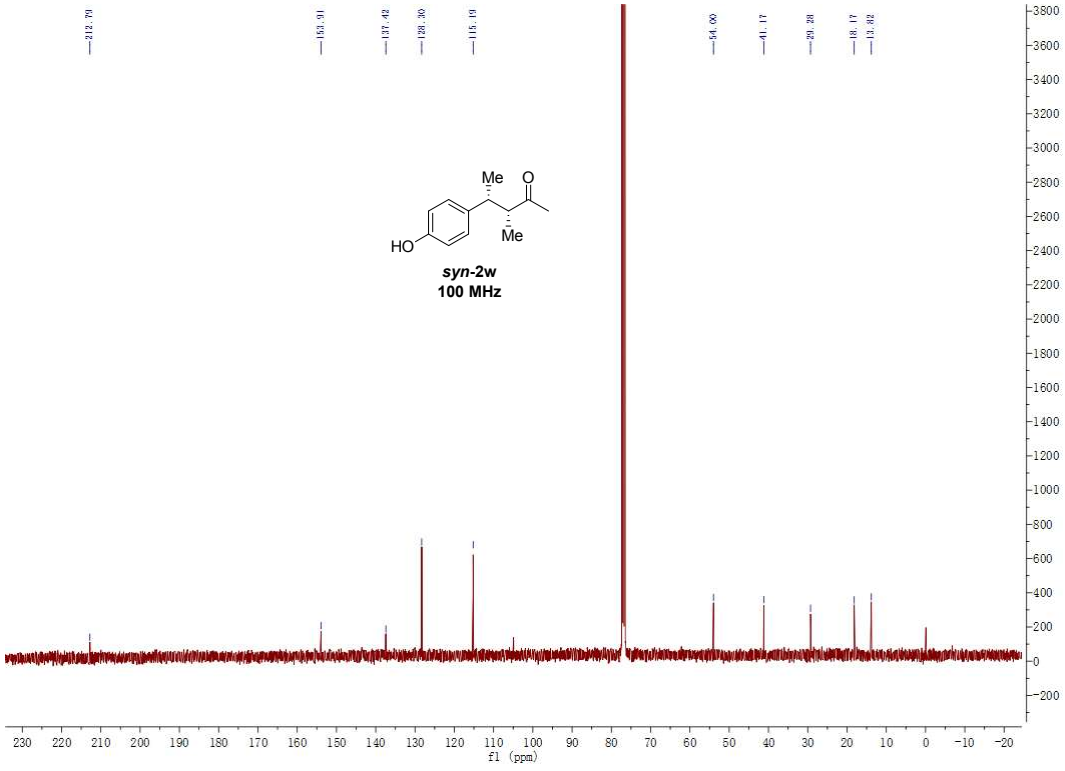


Fig. S110. ^{13}C NMR Spectrum of 2w (minor) (100 MHz, $CDCl_3$).

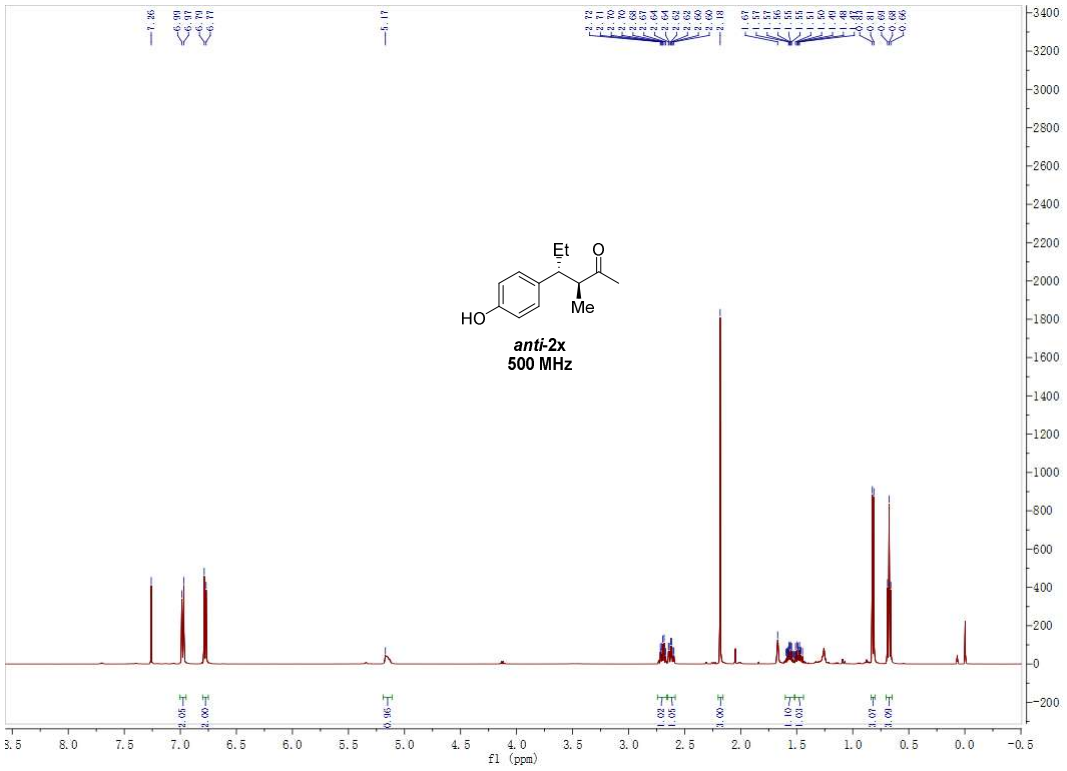


Fig. S111. ^{1}H NMR Spectrum of 2x (major) (500 MHz, $CDCl_3$).

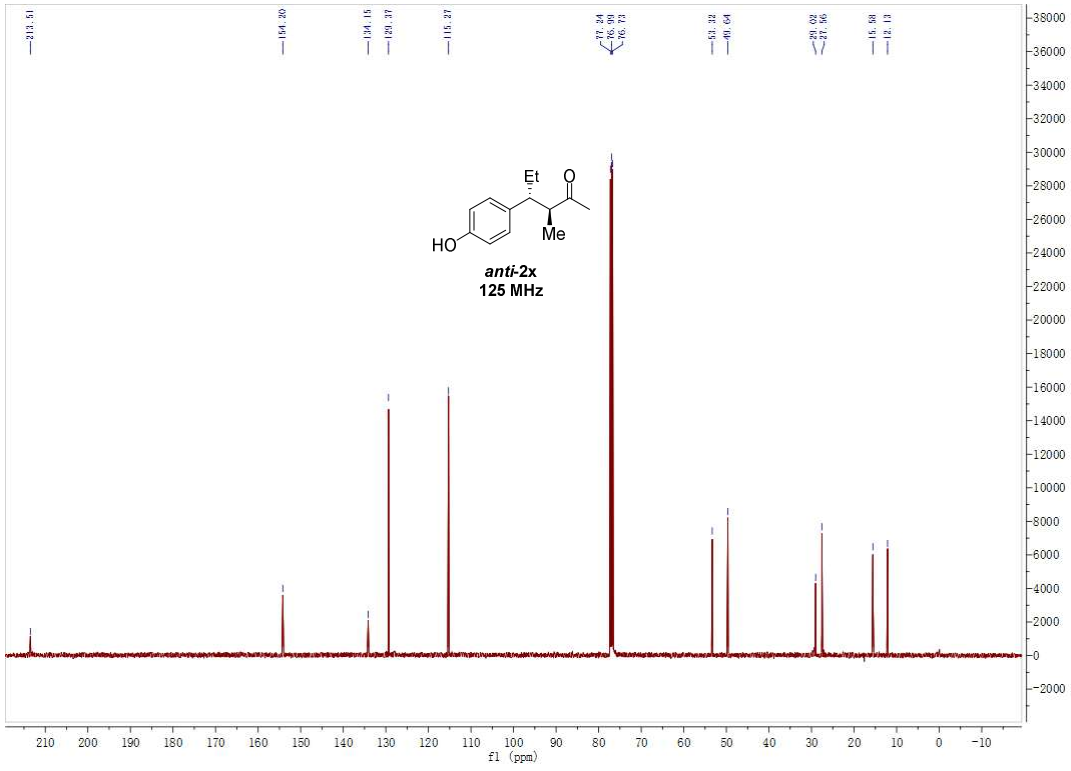


Fig. S112. ^{13}C NMR Spectrum of 2x (major) (125 MHz, $CDCl_3$).

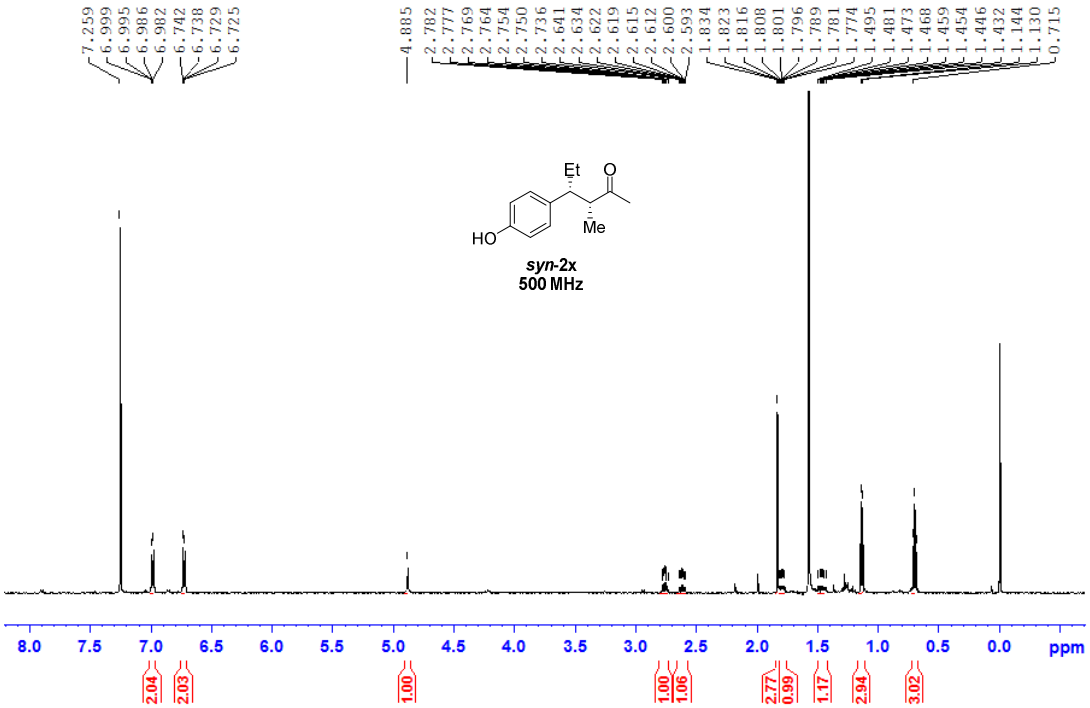


Fig. S113. ^{1}H NMR Spectrum of 2x (minor) (500 MHz, $CDCl_3$).

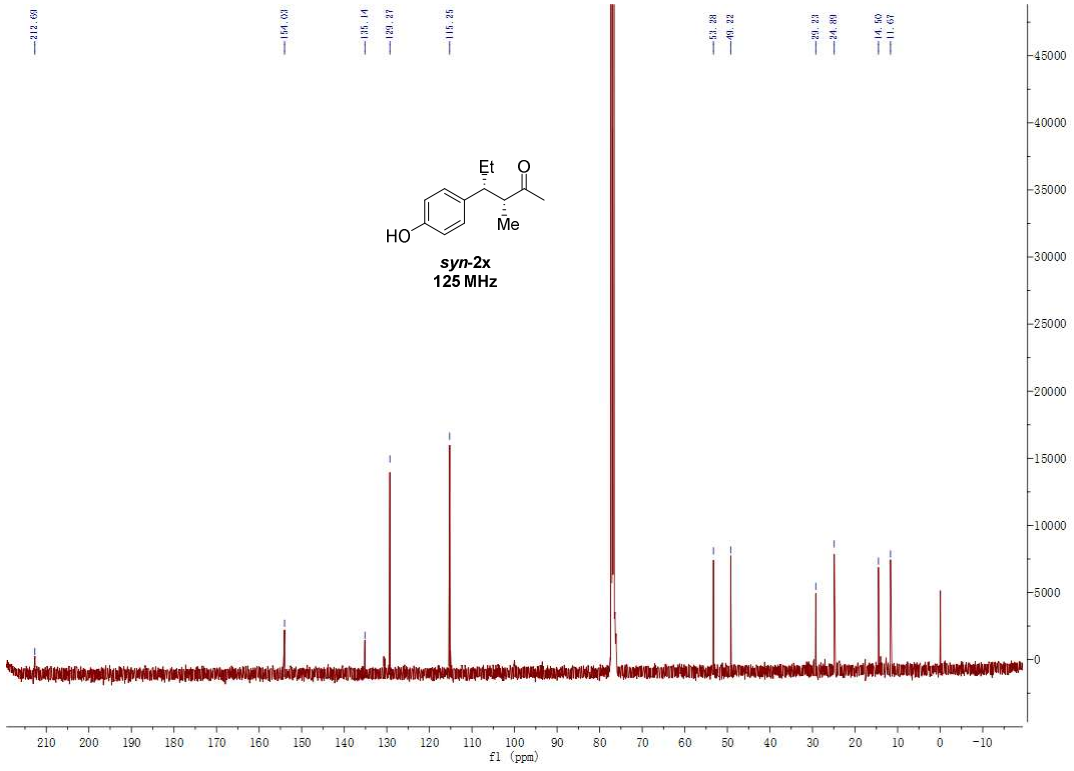


Fig. S114. ^{1}H NMR Spectrum of 2x (minor) (125 MHz, $CDCl_3$).

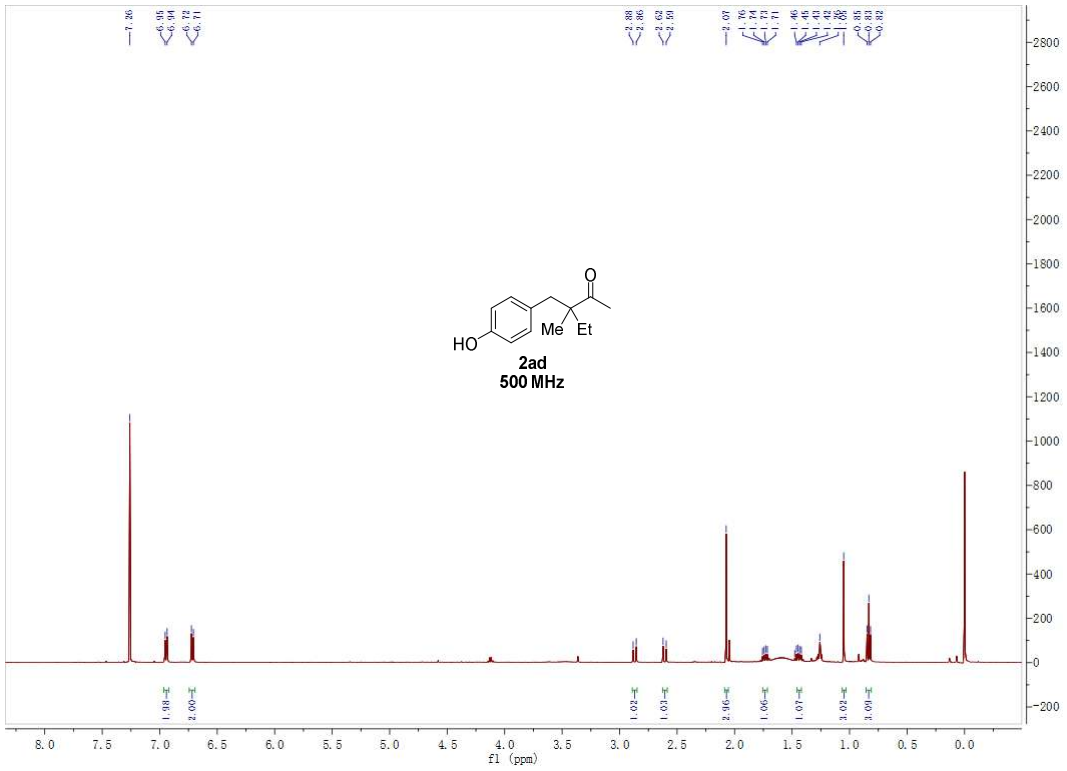


Fig. S115. ^{1}H NMR Spectrum of 2ad (500 MHz, $CDCl_3$).

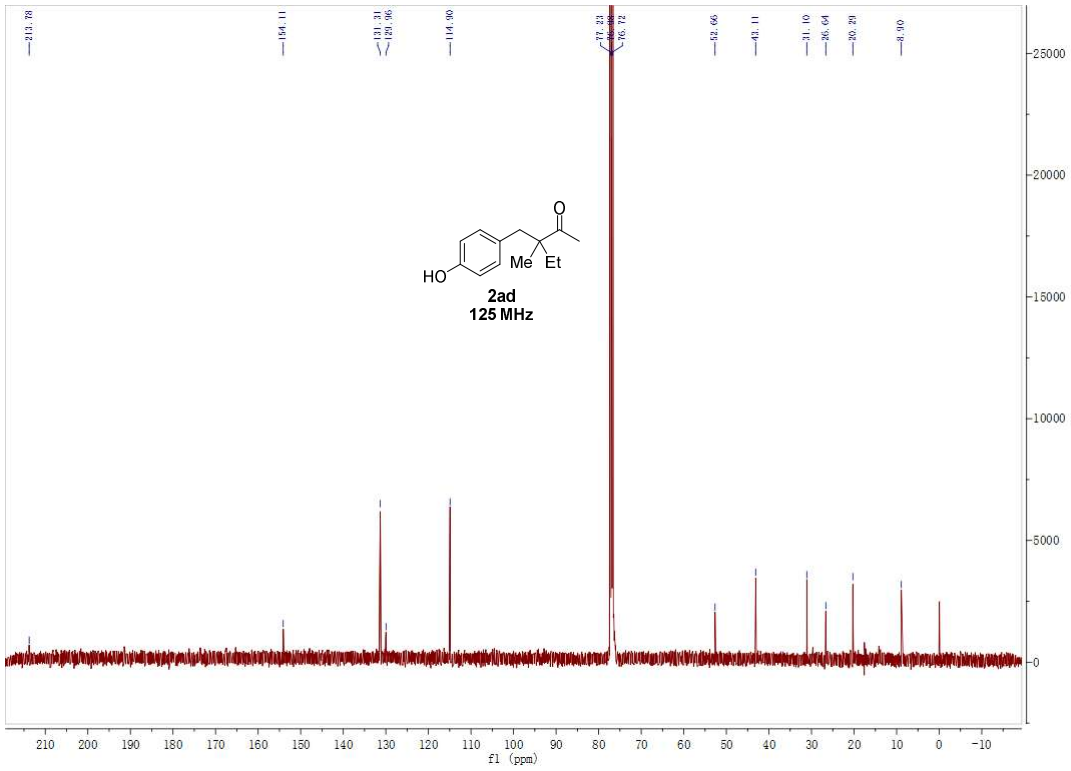


Fig. S116. ^{13}C NMR Spectrum of 2ad (125 MHz, $CDCl_3$).

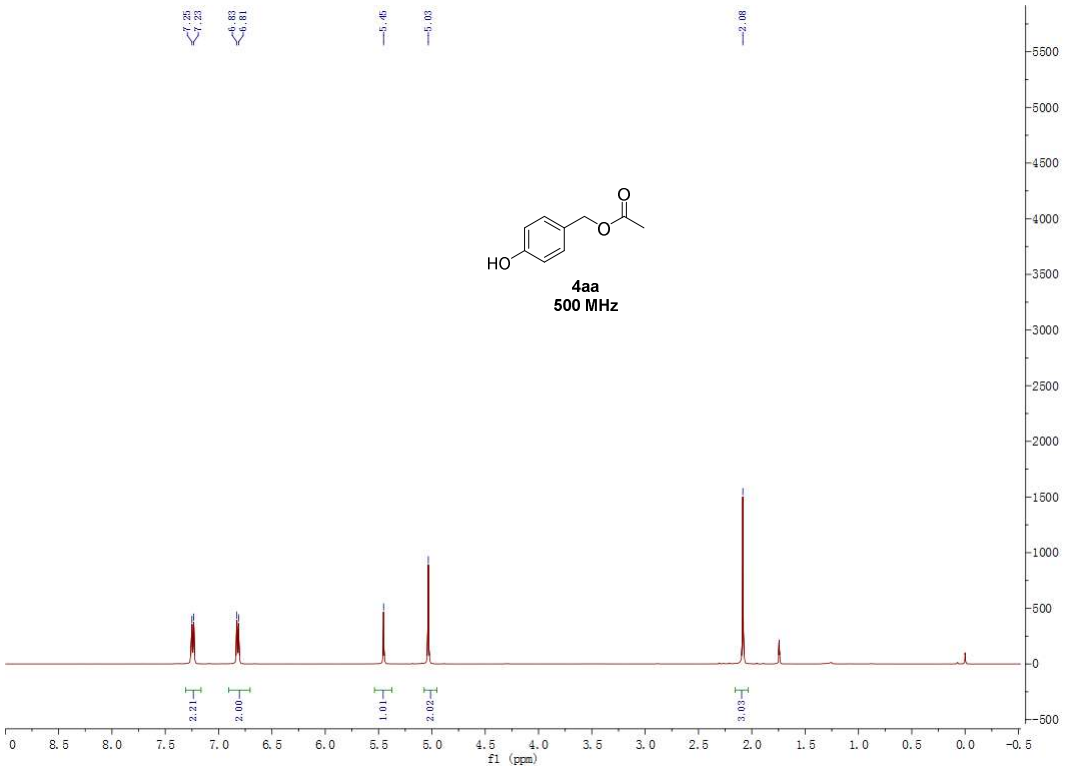


Fig. S117. ^{1}H NMR Spectrum of 4aa (500 MHz, $CDCl_3$).

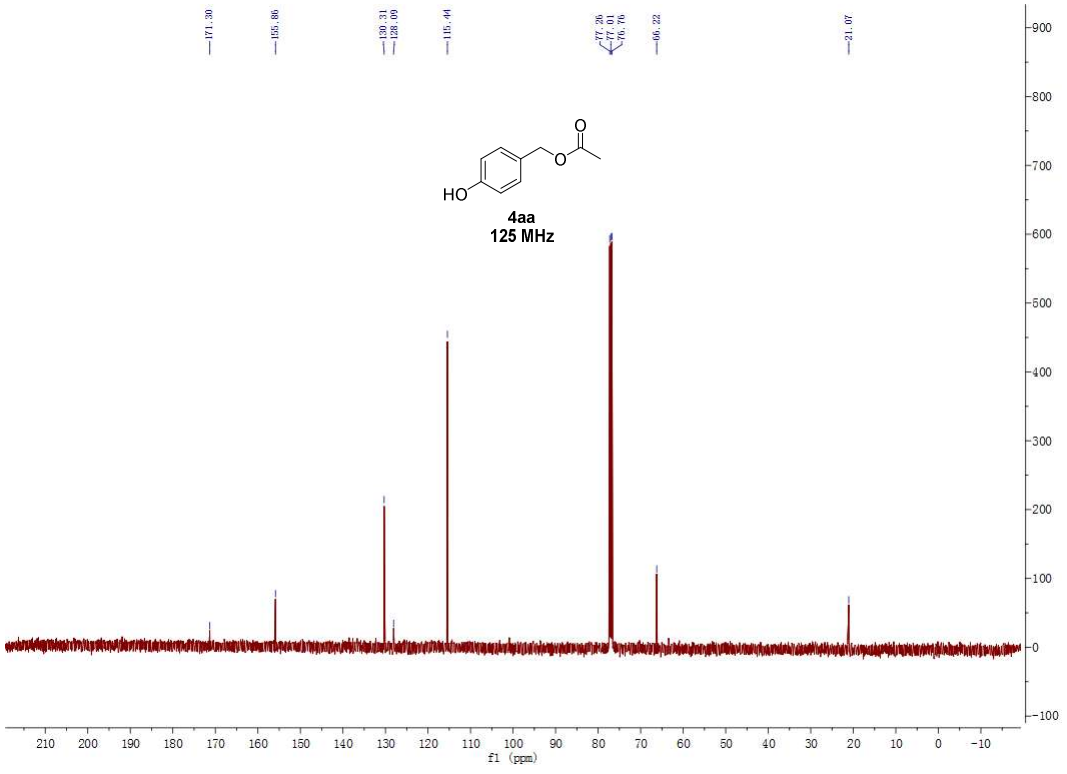


Fig. S118. ^{13}C NMR Spectrum of 4aa (125 MHz, $CDCl_3$).

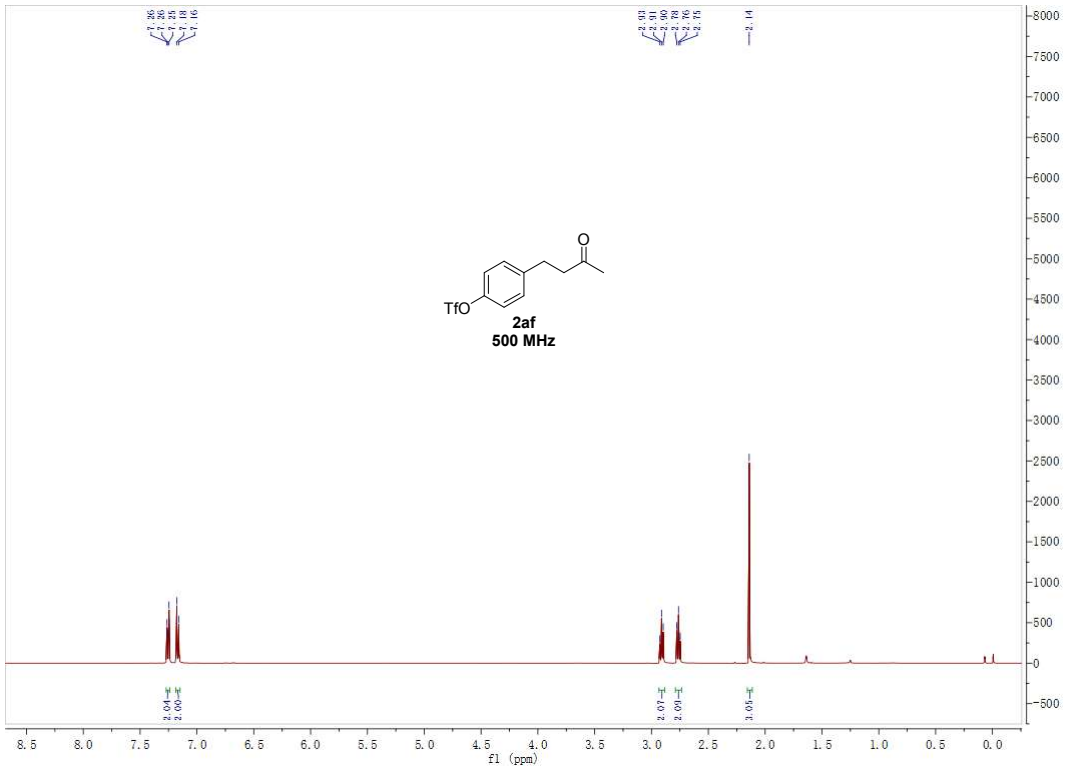


Fig. S119. ^{1}H NMR Spectrum of 2af (500 MHz, $CDCl_3$).

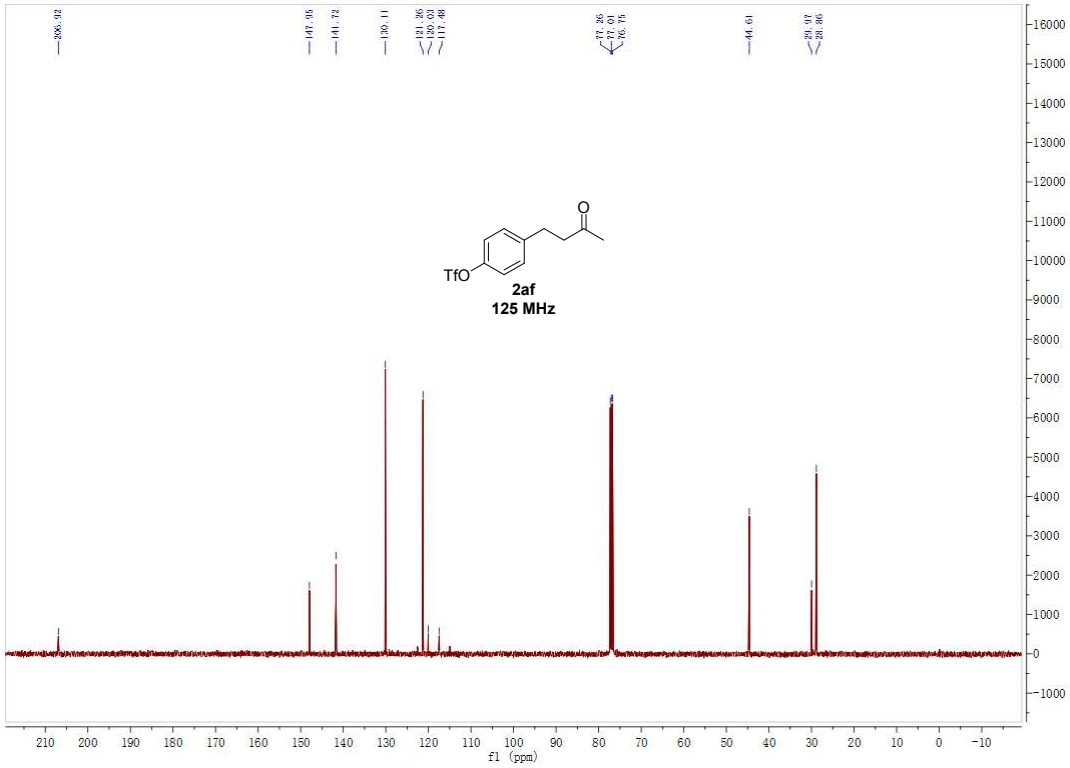


Fig. S120. ^{13}C NMR Spectrum of 2af (125 MHz, $CDCl_3$).

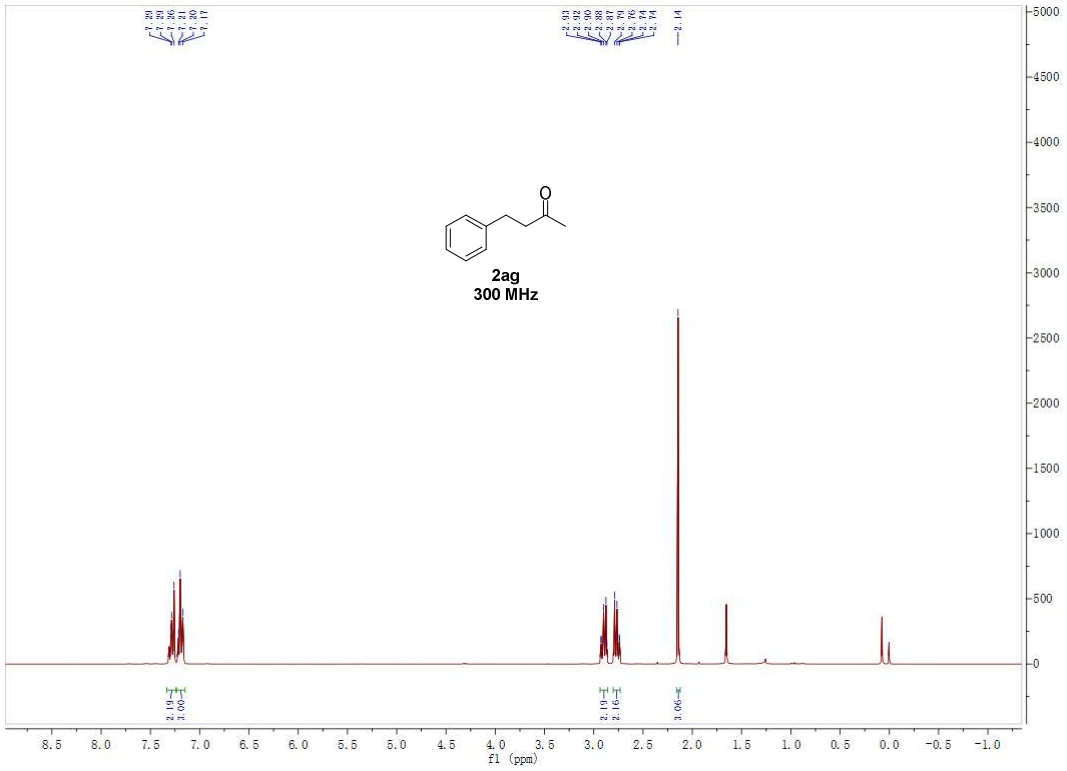


Fig. S121. ^{1}H NMR Spectrum of 2ag (300 MHz, $CDCl_3$).

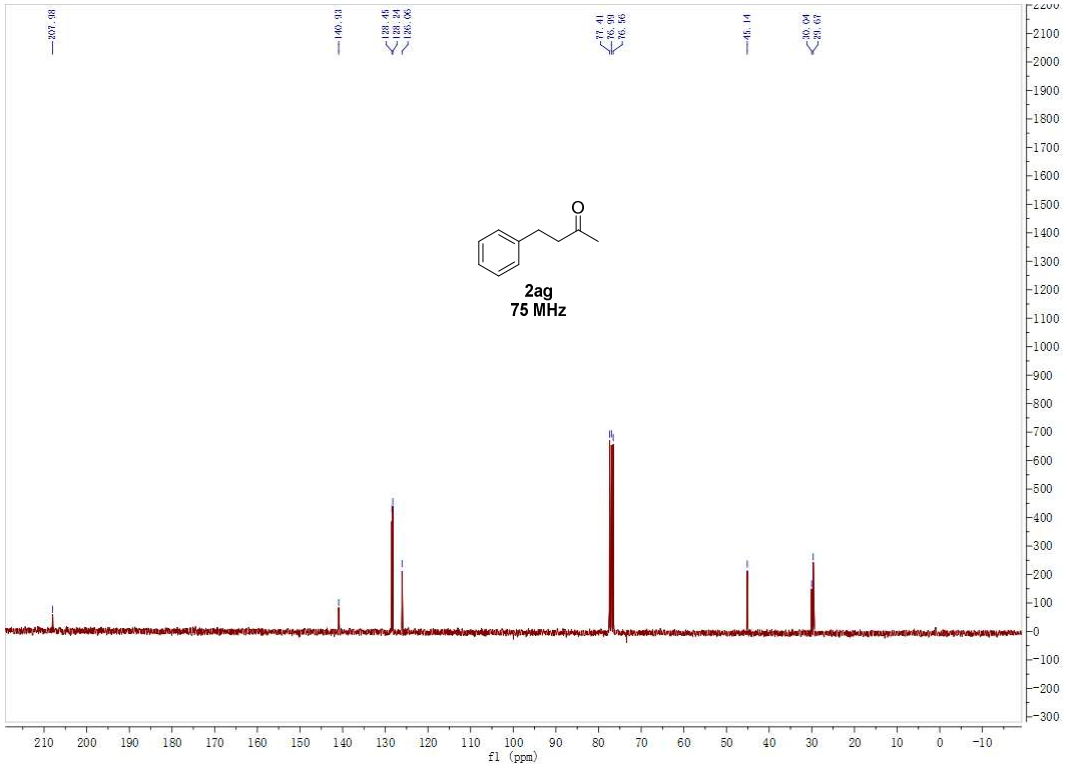


Fig. S122. ^{13}C NMR Spectrum of 2ag (75 MHz, $CDCl_3$).

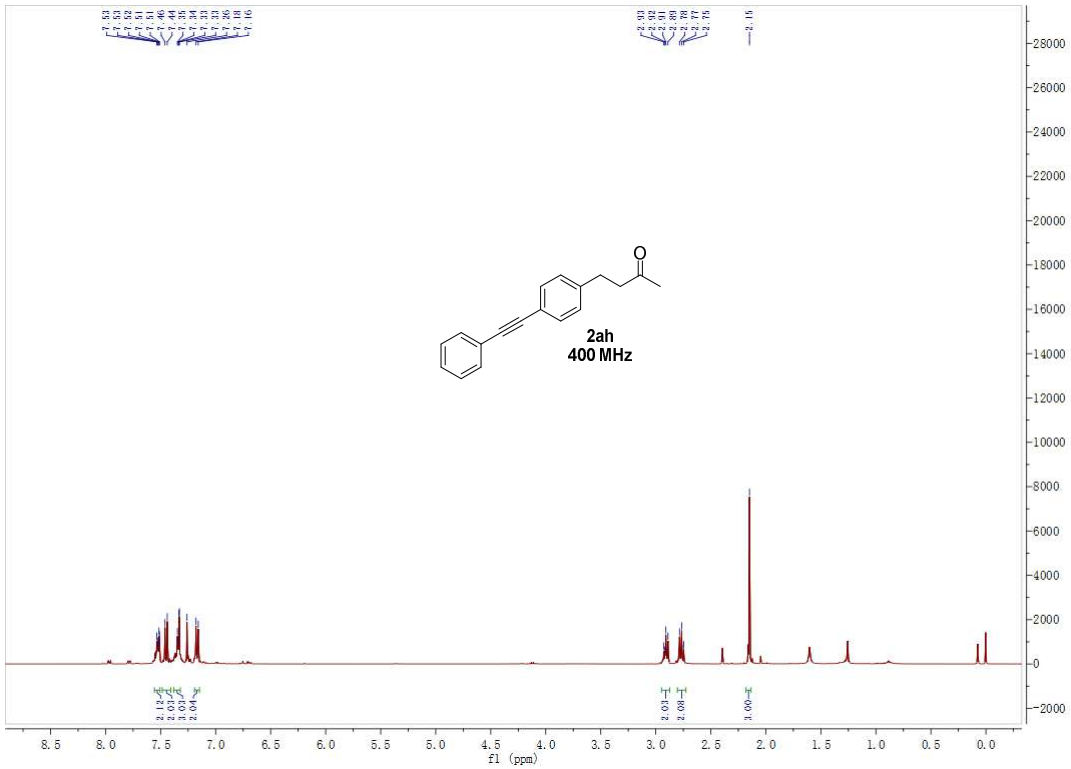


Fig. S123. ^{1}H NMR Spectrum of 2ah (400 MHz, $CDCl_3$).

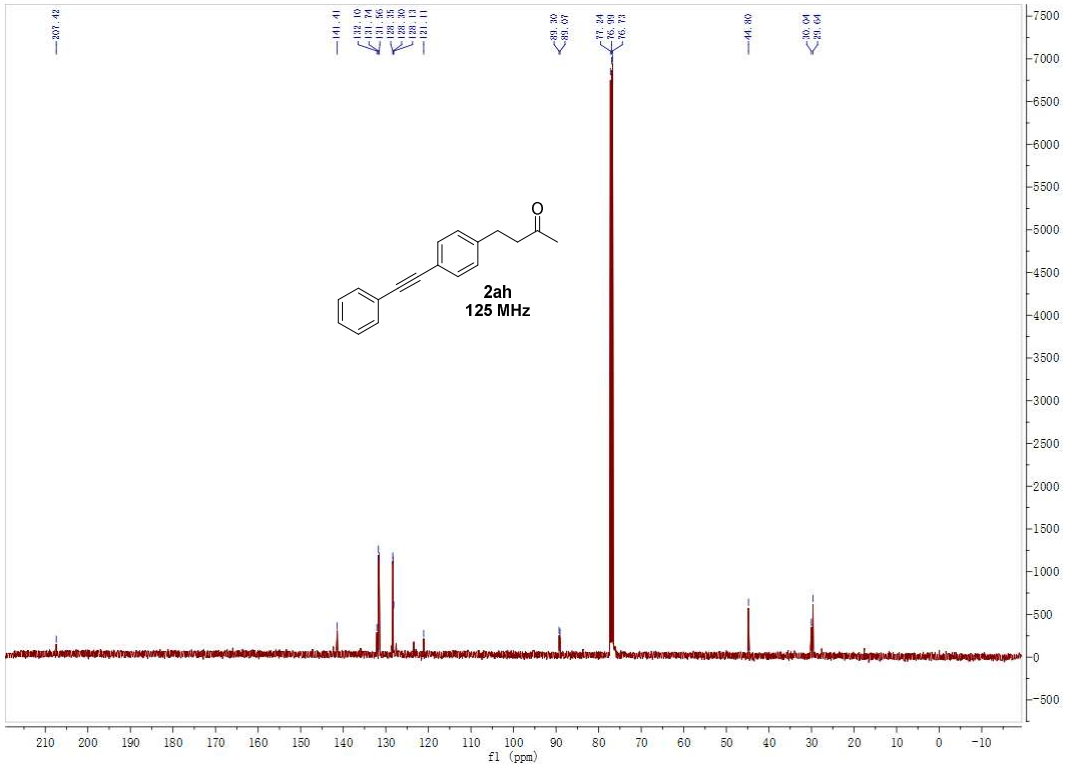


Fig. S124. ^{13}C NMR Spectrum of 2ah (500 MHz, $CDCl_3$).

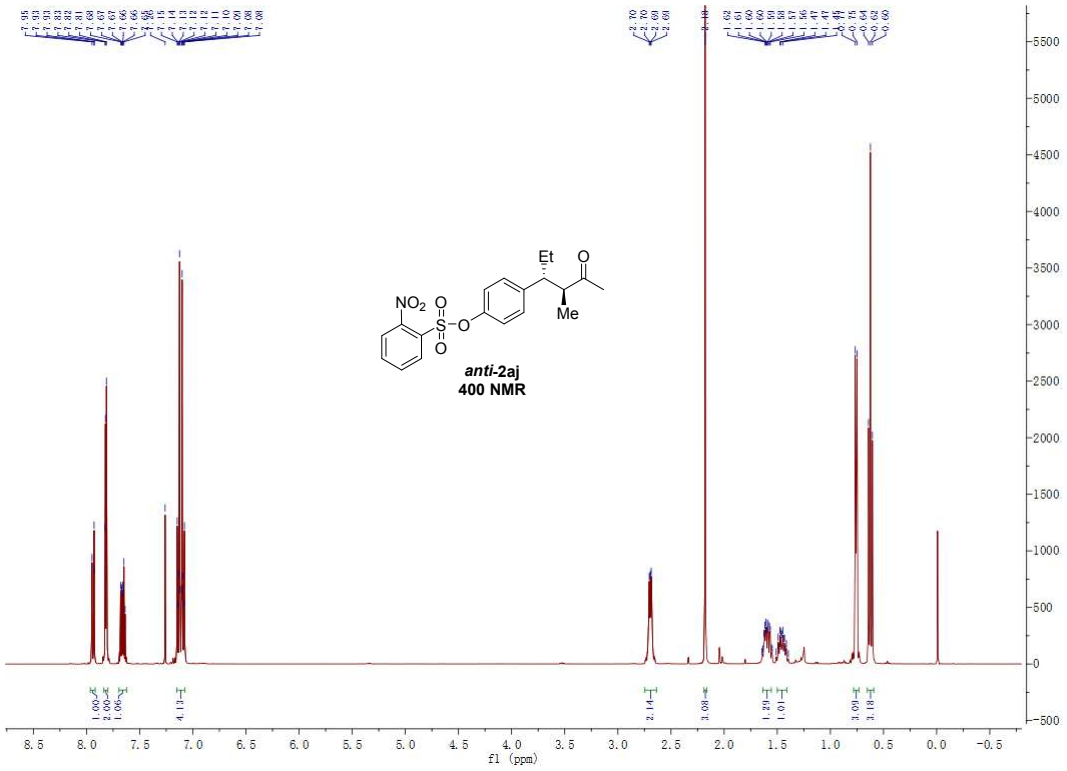


Fig. S125. ^{1}H NMR Spectrum of 2aj (400 MHz, $CDCl_3$).

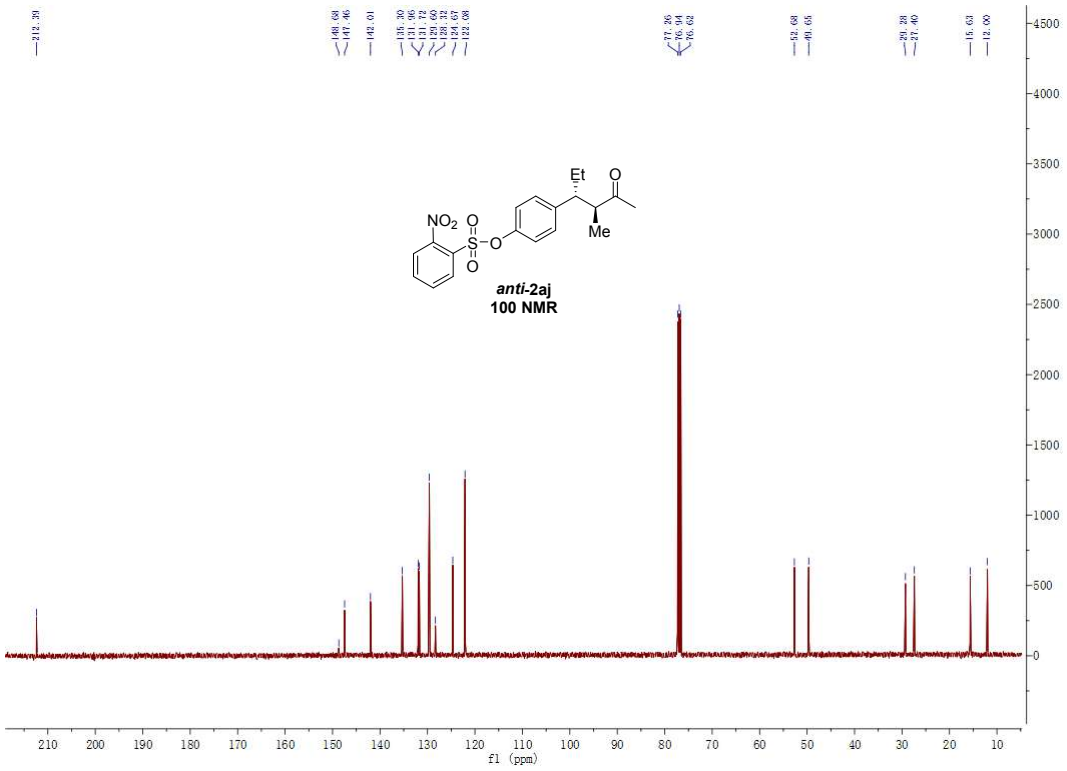


Fig. S126. ^{13}C NMR Spectrum of 2aj (100 MHz, $CDCl_3$).

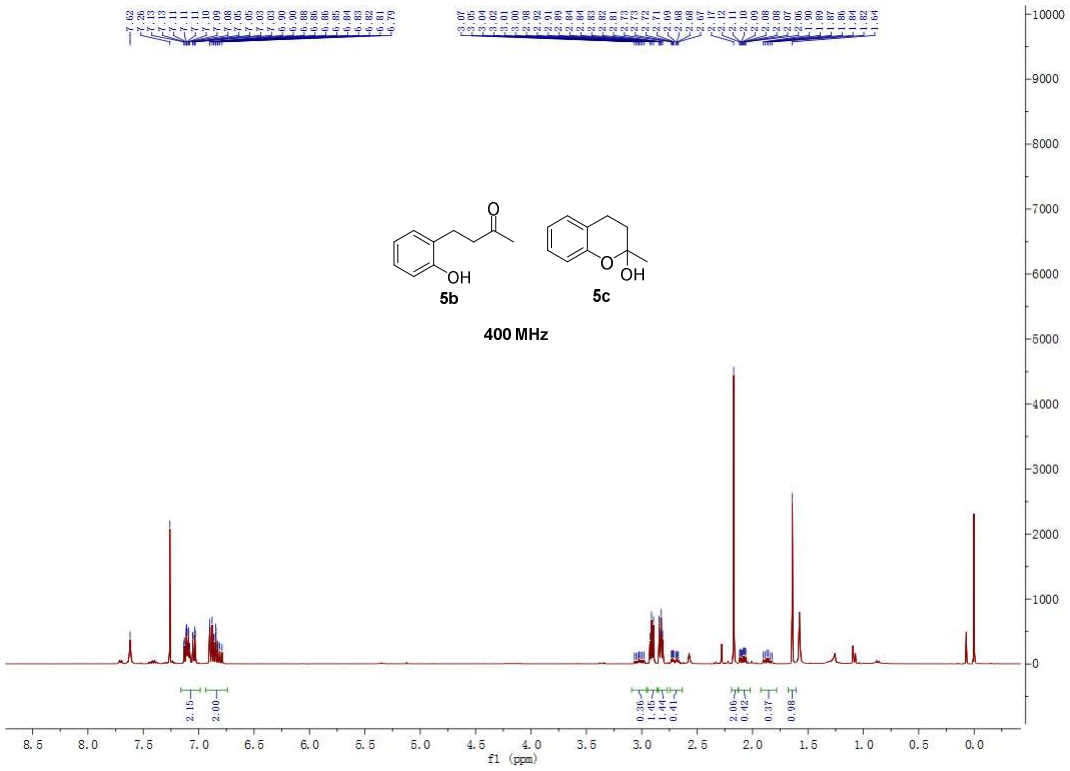
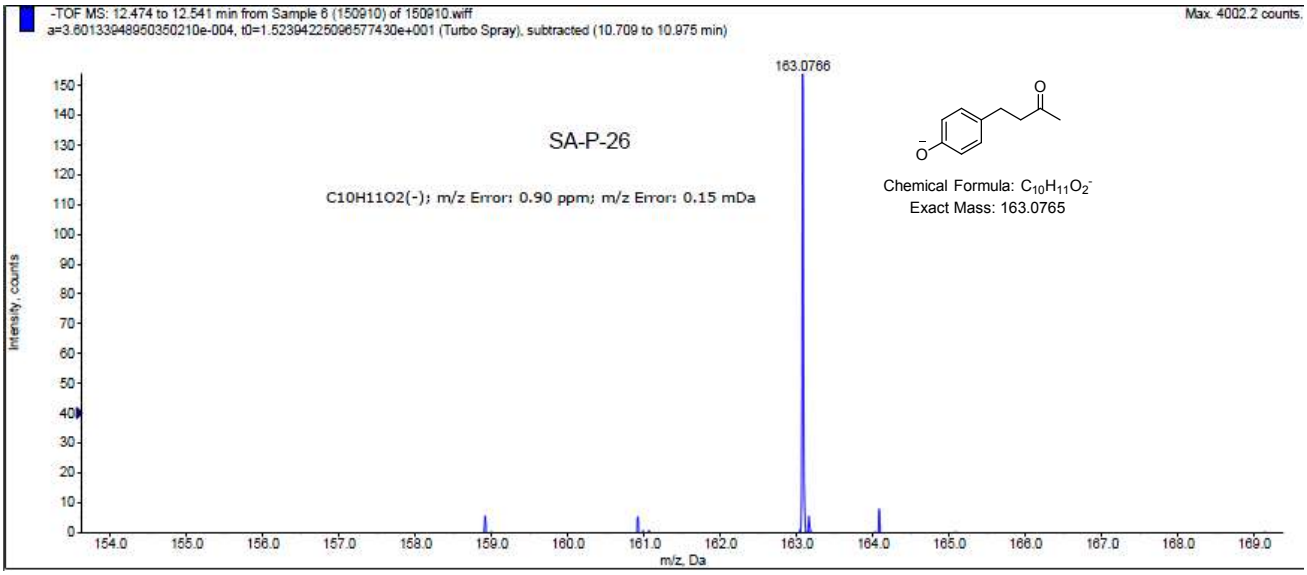
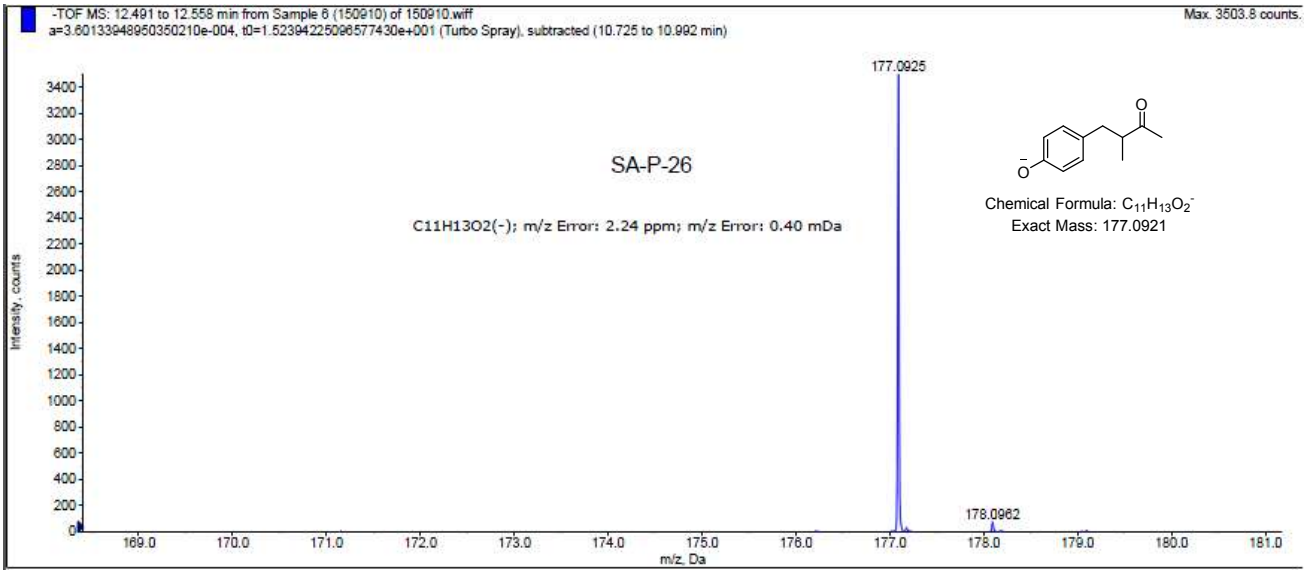
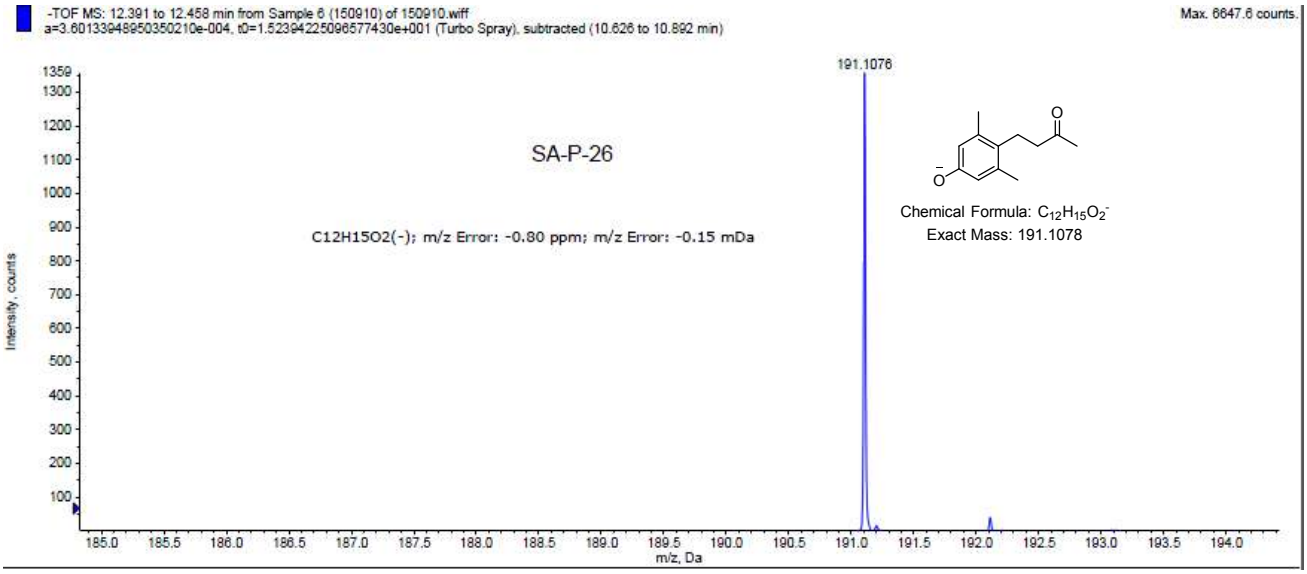


Fig. S127. ^{1}H NMR Spectrum of 5b and 5c (400 MHz, $CDCl_3$).

VI. HRMS and GC-MS Spectra of the Crossover Reaction Products




-TOF MS: 12.491 to 12.558 min from Sample 6 (150910) of 150910.wiff
a=3.60133948950350210e-004, t0=1.52394225096577430e+001 (Turbo Spray), subtracted (10.725 to 10.992 min)
Max. 3503.8 counts.
177.0925
178.0962
SA-P-26
C11H13O2(-); m/z Error: 2.24 ppm; m/z Error: 0.40 mDa
Chemical Formula: C11H13O2-
Exact Mass: 177.0921
Intensity, counts
m/z, Da


-TOF MS: 12.391 to 12.458 min from Sample 6 (150910) of 150910.wiff
a=3.60133948950350210e-004, t0=1.52394225096577430e+001 (Turbo Spray), subtracted (10.626 to 10.892 min)
Max. 6647.6 counts.
191.1076
SA-P-26
C12H15O2(-); m/z Error: -0.80 ppm; m/z Error: -0.15 mDa
Chemical Formula: C12H15O2-
Exact Mass: 191.1078
Intensity, counts
m/z, Da

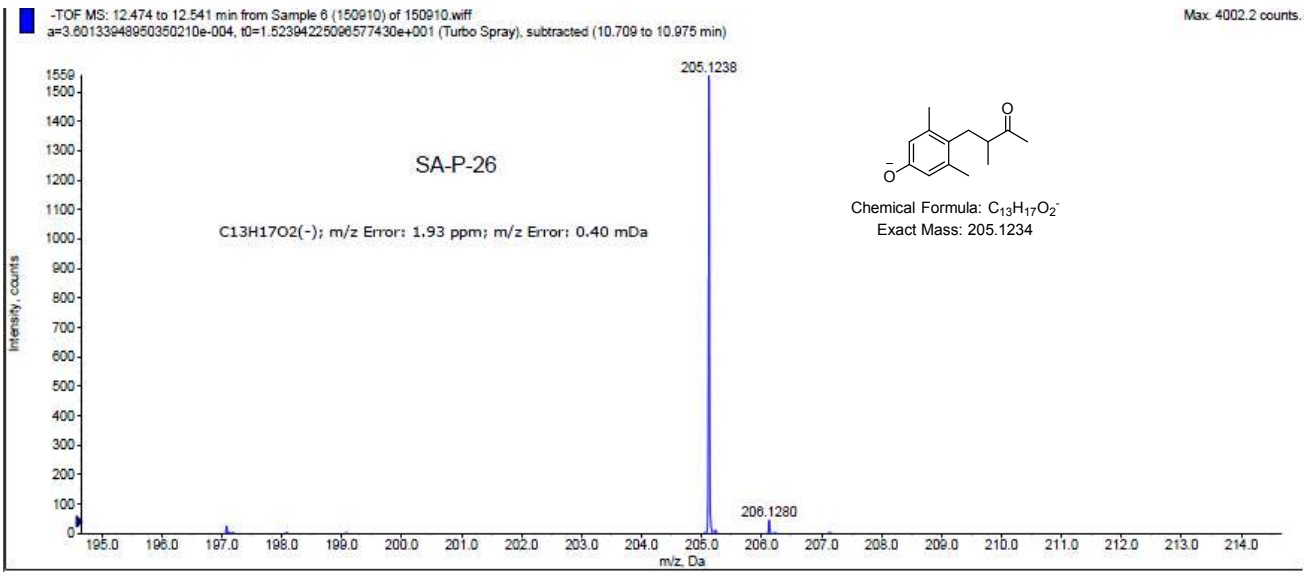

-TOF MS: 12.474 to 12.541 min from Sample 6 (150910) of 150910.wiff
a=3.60133948950350210e-004, t0=1.52394225096577430e+001 (Turbo Spray), subtracted (10.709 to 10.975 min)
Max. 4002.2 counts.
205.1238
206.1280
SA-P-26
C13H17O2(-); m/z Error: 1.93 ppm; m/z Error: 0.40 mDa
Chemical Formula: C13H17O2-
Exact Mass: 205.1234
Intensity, counts
m/z, Da

Fig. S128. HRMS Spectra of the Crossover Reaction Products.

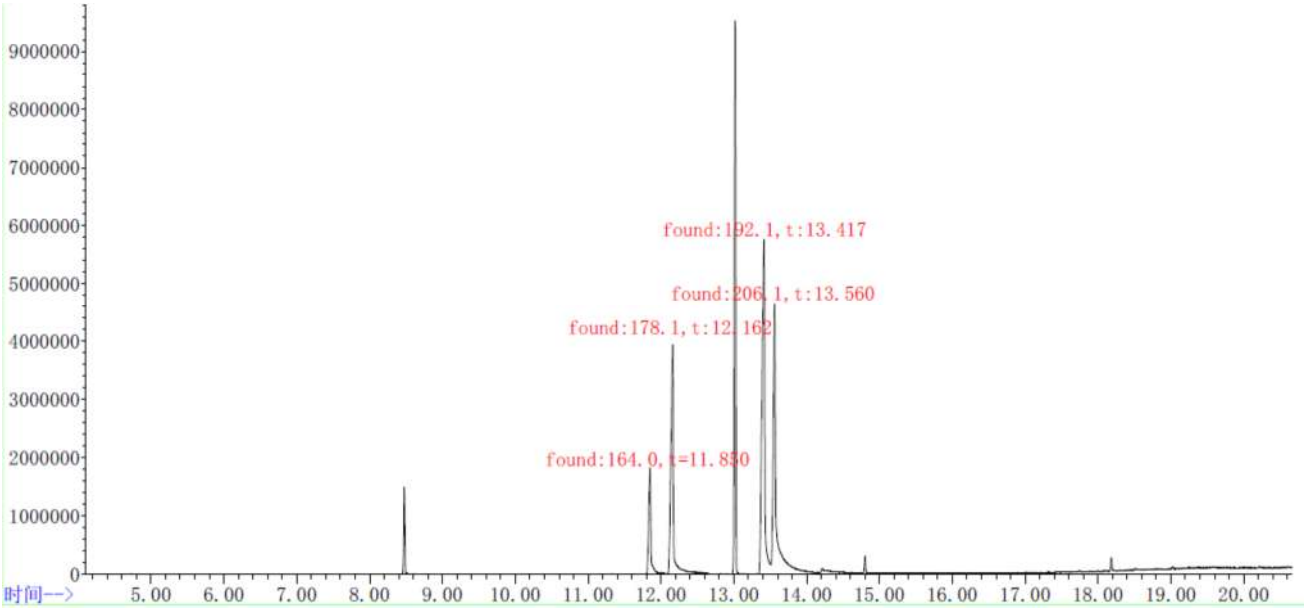


Fig. S129. GC-MS Spectrum of the Crossover Reaction Products.

VII. Standard GC-MS Spectra of the Crossover Reaction Products

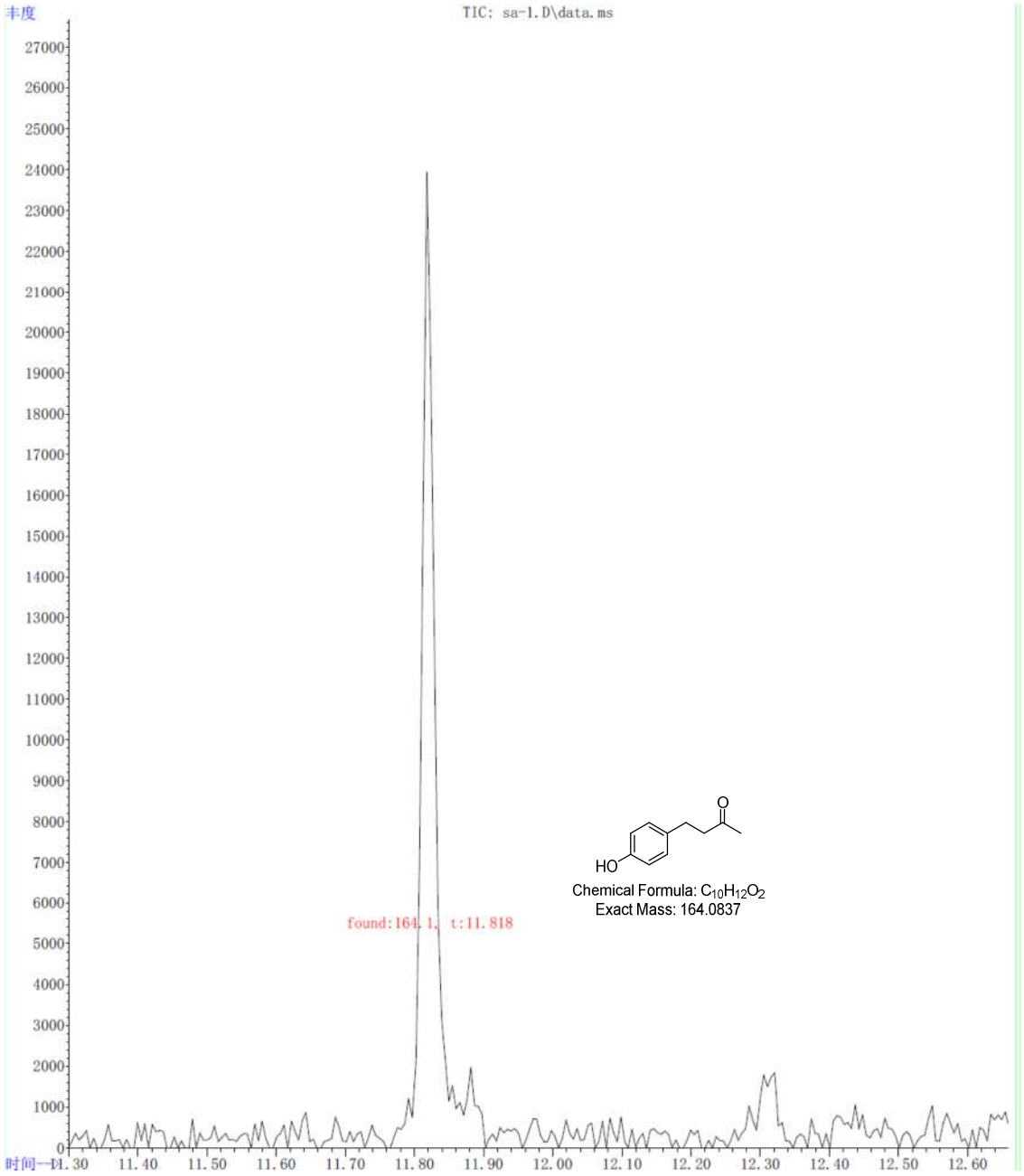


Fig. S130. Standard GC-MS Spectrum of the Crossover Reaction Product 2a.

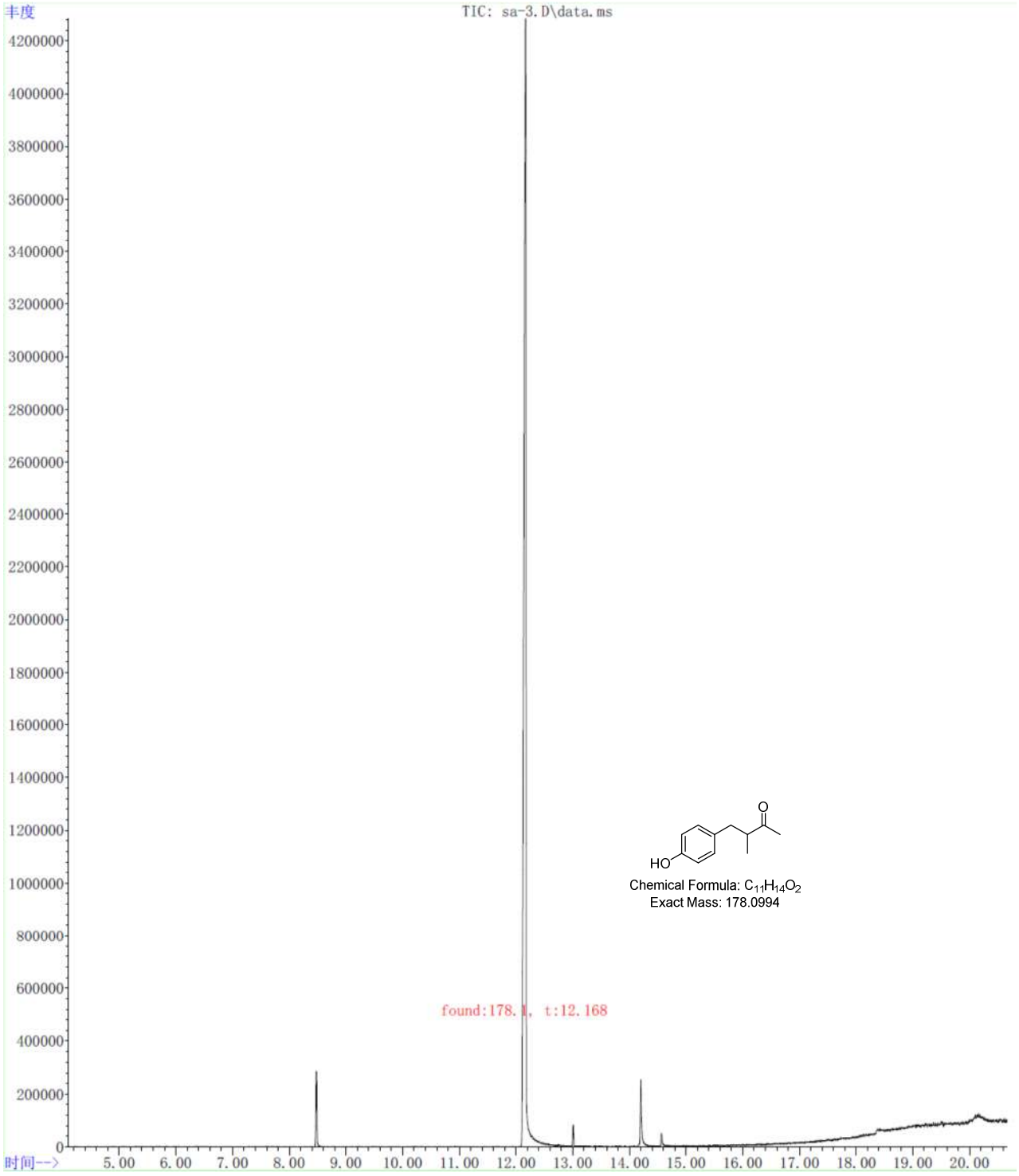


Fig. S131. Standard GC-MS Spectrum of the Crossover Reaction Product 2m.

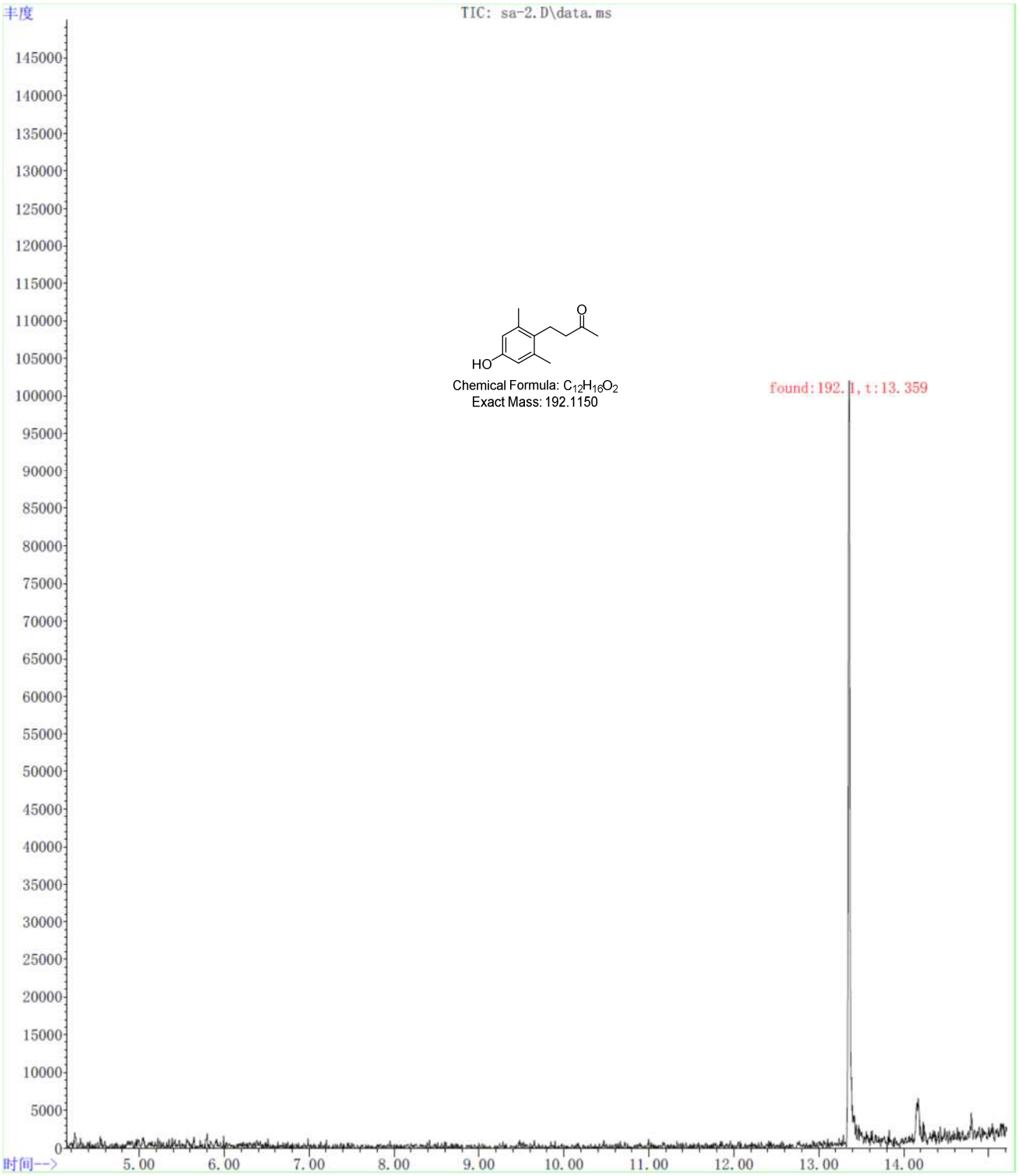


Fig. S132. Standard GC-MS Spectrum of the Crossover Reaction Product 2h.

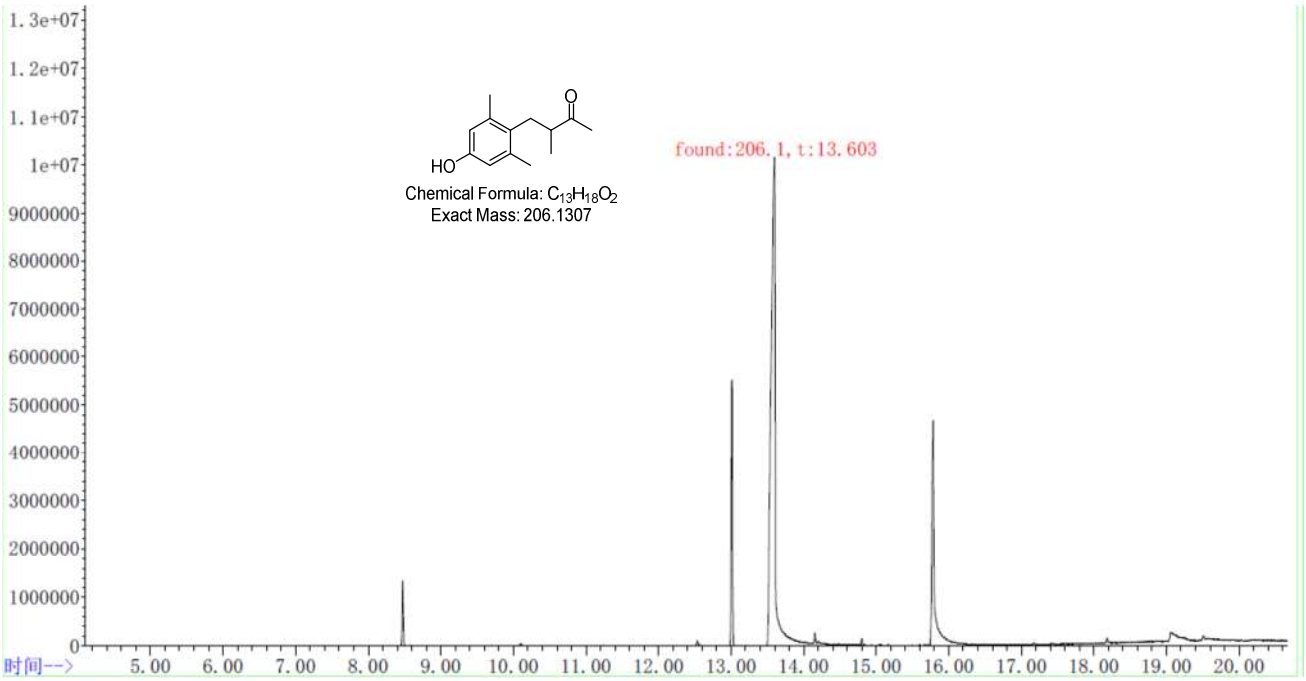
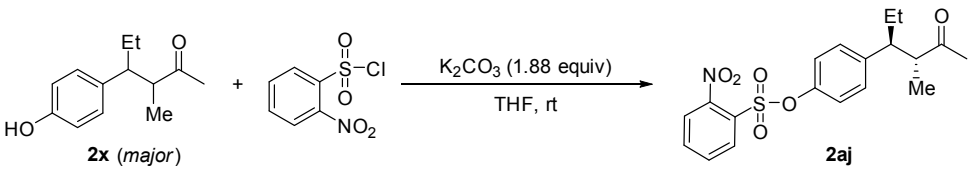


Fig. S133. Standard GC-MS Spectrum of the Crossover Reaction Product 2z.

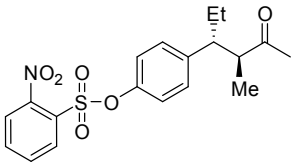
VIII. Determination of the Stereochemistry of the Major Diastereomer of 2x



4-(4-methyl-5-oxohexan-3-yl)phenyl 2-nitrobenzenesulfonate (2aj): To a solution of the major diastereomer of **2x** (28.2 mg, 0.137 mmol) in THF (1 mL) was added K_2CO_3 (35.6 mg, 0.258 mmol, 1.88 equiv) in one portion. The resulting mixture was cooled to 0 °C, and 2-nitrobenzenesulfonyl chloride (13.5 mg, 0.06 mmol, 1.01 equiv) was added slowly. The mixture was stirred at room temperature until **2x** was disappeared (monitored by TLC). Ethyl acetate was added and the two-phase mixture was separated. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and concentrated at reduced pressure. The residue was further purified by column chromatography (silica gel, hexanes/EtOAc = 5:1) to afford **2aj** (37.5 mg, colorless crystal) in 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.91 (m, 1H), 7.84–7.79 (m, 2H), 7.69–7.62 (m, 1H), 7.15–7.07 (m, 4H), 2.70 (dd, J = 4.6, 2.7 Hz, 2H), 2.18 (s, 3H), 1.63–1.56 (m, 1H), 1.45 (ddq, J = 14.5, 10.3, 7.3 Hz, 1H), 0.76 (d, J = 6.6 Hz, 3H), 0.62 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.39, 148.68, 147.46, 142.01, 135.30, 131.96, 131.72, 129.60, 128.32, 124.67, 122.08, 52.68, 49.65, 29.28, 27.40, 15.63, 12.00. HRMS (ESI) calculated for $C_{19}H_{21}NO_6SNa$ $(M + Na)^+$: 414.0987, found: 414.0976.

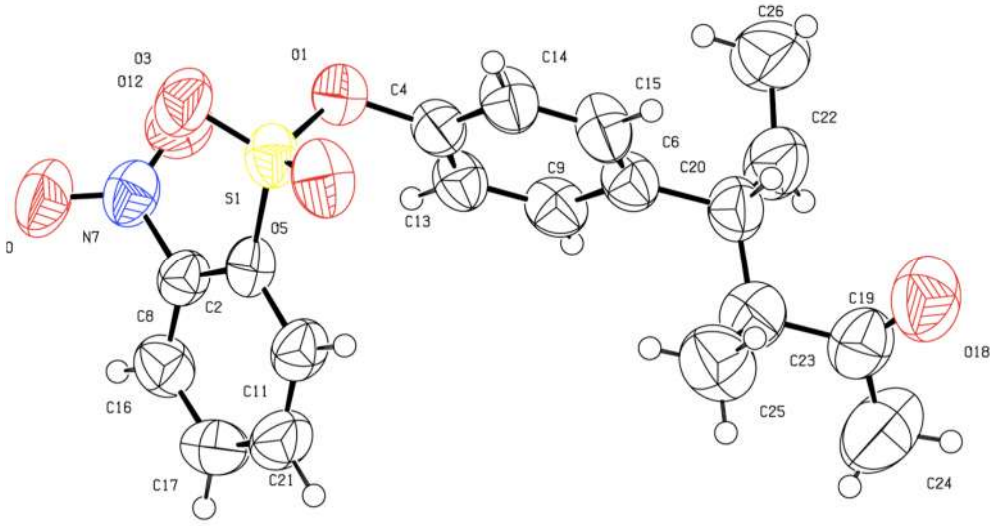
Control experiment conducted in the absence of 2-nitrobenzenesulfonyl chloride resulted in the starting material ***2x*** *remained (determined by ^{1}H-NMR after purification), thereby confirming that epimerization won't take place under the reaction conditions.*

Crystal Structure of 2aj



2aj

(CCDC number: 1486135 **)**



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