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**SUPPORTING INFORMATION**

# Diastereoselective Synthesis of *α*-(Aminomethyl)-*γ*-Butyrolactones via a Catalyst-free Aminolactonization

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## Experimental Procedures



## Characterization Data



## $^{1}$H and $^{13}$C NMR Spectra

## General Supporting Information

All reagents were purchased from Sigma-Aldrich, Fisher-Acros, Strem Chemical, or Alfa-Aesar, and were used without further purification unless otherwise noted. All solvents were distilled prior to use unless otherwise noted: DCM and Pentanes from $CaH_2$, Toluene from Na, and $Et_2O$ and THF from Na/Benzophenone. All reactions were performed at room temperature and under a nitrogen atmosphere in either flame or oven-dried glassware unless otherwise noted. All TLC analysis was performed using 60Å, Glass-backed Thin-Layer Chromatography Plates (250 µm thickness, F-254 indicator). All solvent systems are given as volumetric ratios. Flash chromatography was performed using 230-400 mesh, 60Å pore diameter flash chromatography gel. All chromatography elutions were gradient in nature, eluting first with hexanes, followed by incorporating more polar solvents as appropriate. Any volatile products were eluted with appropriate mixtures of $Et_2O$ and pentanes. $^{1}$H, $^{2}$H, and $^{13}$C spectra were recorded at room temperature, on Varian INOVA 300 MHz, Bruker ARX400, or Bruker DRX500 spectrometers. Chemical shifts (δ values) are reported in parts per million, and are referenced to either the deuterated residual solvent peak, or to tetramethylsilane. $^{2}$H are referenced to a 1 : 1 $CHCl_3$ / $CDCl_3$ mixture at 7.26 ppm. Data are reported as: δ value, multiplicity, and integration, (s=singlet, d=doublet, t=triplet, q=quartet, p=pentet, h=hextet, g=heptet, br=broad). $^{1}$H NMR was used as a measurement of the diastereomeric ratios of aminolactonization products, and were made by comparing the relative integration values of either the *α* or *γ* protons of the respective diastereomers.

## General Procedure for the Morita-Baylis-Hillman Reaction

Into a round bottom flask charged with a stirbar was added 1.0 equiv. aldehyde, followed by 2.0 equiv. methyl acrylate and 0.5 equiv. DABCO. The reaction mixture was stirred until judged complete by TLC, then was partitioned between 1.0 M acetic acid and $CH_2Cl_2$. The organic layer was set aside, and the residual product was extracted from the aqueous layer with an additional portion of $CH_2Cl_2$. The combined organic layers were washed with deionized water then brine, then concentrated and purified via column chromatography.

## General Procedure for the Allylic Brominative $S_N2'$ Reaction

Into a round bottom flask charged with a magnetic stirbar was added 1 equiv. MBH adduct, followed by 3 equiv. 33 wt % HBr (in HOAc). The solution was vigorously stirred until judged complete by TLC, then was poured into a 1 : 1 (volumetric) mixture of deionized water and $CH_2Cl_2$. The organic layer was separated, then the residual product was extracted from the aqueous layer with an additional portion of $CH_2Cl_2$. The combined organic layers were washed with deionized water then brine, then were dried with $Na_2SO_4$, filtered, concentrated, and purified via column chromatography.

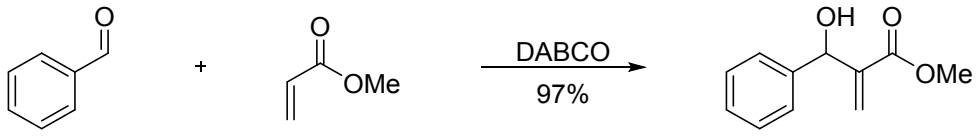
## General Procedure for the Indium-Promoted Allylation of Electrophiles

Into a round bottom flask charged with a magnetic stirbar was added 1.0 equiv. allylic bromide. This material was suspended in deionized water to produce a 1.0 M suspension. 1.5 volumetric equiv. of THF (w/respect to $H_2O$) were then added with vigorous stirring, followed by 1.5 equiv. electrophile and 1.3 equiv. (1.1 equiv, for brominated allylic bromides) indium powder. The reaction mixture was stirred for 12 hours, then was partitioned between EtOAc and deionized water. After separating the organic layer, the residual product was extracted with multiple portions (as necessary) of ethyl acetate. The combined organic layers was washed with brine, dried with $Na_2SO_4$, filtered, concentrated, and purified via column chromatography.

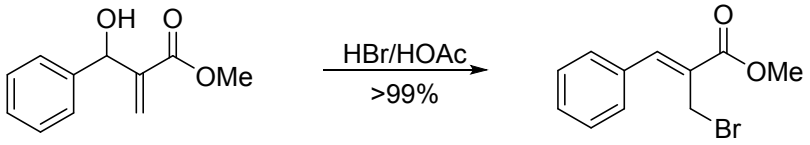
## General Procedure for Aminolactonization Reactions

Into a round bottom flask containing a stirbar and butanoate ester (1.0 equiv.) was added enough ethanol to produce a 0.1 M solution (with respect to the butanoate ester), followed by piperidine (2.0 equiv.). The reaction mixture was then stirred until deemed complete by TLC analysis (usually a period of less than 3 hours). A small aliquot was removed from the reaction mixture for the determination of the diastereomeric ratio by $^{1}$H NMR analysis. The stirbar was then removed from the reaction mixture, and rinsed with a small amount of diethyl ether. The mixture was subsequently concentrated to remove all volatiles. If necessary, the crude product was purified via column chromatography.

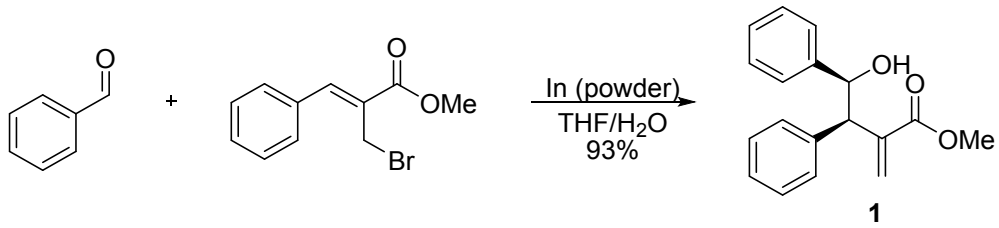
## Preparation of Butanoate Ester 1




**Methyl 2-((hydroxy)phenylmethyl)prop-2-enoate**. Benzaldehyde was distilled prior to use. $R_f$ = 0.28, 75 : 25 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.37-7.27 (m, 5H), 6.33 (s, 1H), 5.85 (s, 1H), 5.54 (s, 1H), 3.69 (s, 3H), 3.31 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.7, 141.9, 141.2, 128.3, 127.7, 126.6, 125.9, 73.0, 51.9. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 193.1, found 193.0.



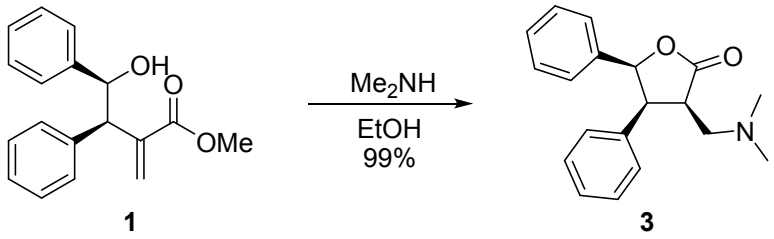

**Methyl (2*Z*)-2-(bromomethyl)-3-phenylprop-2-enoate**. $R_f$ = 0.56, 75 : 25 = Hex : EtOAc, stain = Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.82 (s, 1H), 7.57 (d, J = 7.2 Hz, 2H), 7.47-7.39 (m, 3H), 4.39 (s, 2H), 3.87 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.6, 142.9, 134.2, 129.6, 128.9, 128.6, 52.5, 26.8. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 277.0, found 276.8.




**1**

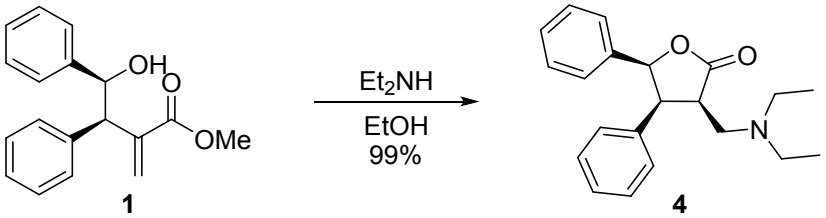
**Methyl *syn*-4-hydroxy-2-methylene-3,4-diphenylbutanoate** (**1**). Benzaldehyde was distilled prior to use. $R_f$ = 0.38, 75 : 25 = Hex : EtOAc, stain = $I_2$, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.30-7.21 (m, 10H), 6.21 (s, 1H), 5.78 (s, 1H), 5.22 (d, J = 8.0 Hz, 1H), 4.29 (d, J = 8.0 Hz, 1H), 3.52 (s, 3H), 2.16 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.9, 142.1, 141.0, 138.6, 129.2, 128.5, 128.2, 127.7, 127.2, 127.0, 126.9, 75.7, 54.2, 51.9. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 295.1, found 295.3.

## Aminolactonization of Butanoate Ester 1 With Different Amine Substrates



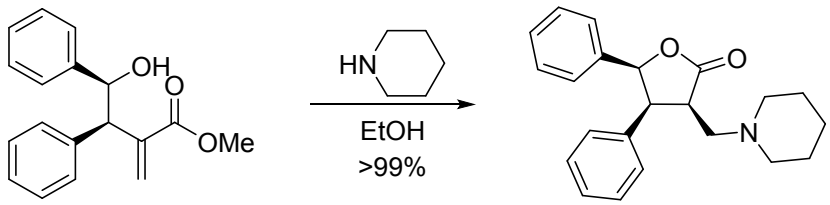

**1** **3**

**(±)-(2,3-*cis*,2,4-*cis*)-2-((dimethylamino)methyl)-3,4-diphenylbutano-4-lactone** (**3**). Dimethylamine was introduced as a 2.0 M solution in THF. 99 : 1 = dr; 99% yield of *cis*,*cis*-product. $R_f$ = 0.29, 95 : 5 = EtOAc : MeOH, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.06-6.97 (d, J = 34.3 Hz, 8H), 6.81 (dd, J = 7.4, 2.0 Hz, 2H), 5.78 (d, J = 5.1 Hz, 1H), 4.02 (dd, J = 7.5, 5.2 Hz, 1H), 3.32-3.27 (m, 1H), 2.61 (dd, J = 13.2, 3.8 Hz, 1H), 2.18 (dd, J = 13.2, 8.8 Hz, 1H), 2.07 (s, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.5, 135.6, 134.4, 129.3, 128.1, 127.9, 127.3, 127.1, 125.3, 83.0, 55.4, 51.7, 46.1, 45.5. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 296.2, found 296.3.



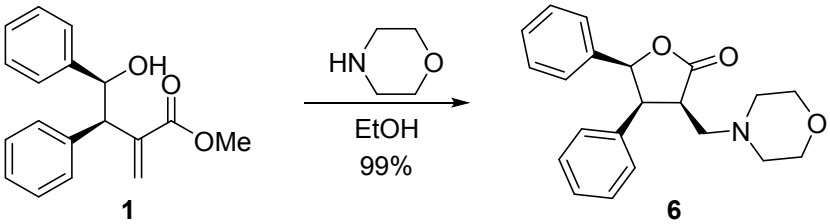

**1** **4**

**(2,3-*cis*,2,4-*cis*)-2-((diethylamino)methyl)-3,4-diphenylbutano-4-lactone** (**4**). 99 : 1 = dr; 99% yield of *cis*,*cis*-product. $R_f$ = 0.13, 50 : 50 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.10-7.02 (m, 8H), 6.87 (m, 2H), 5.82 (d, J = 5.0 Hz, 1H), 4.05 (m, 1H), 3.40 (m, 1H), 2.89 (dd, J = 13.7, 3.6 Hz, 1H), 2.49-2.29 (m, 5H), 0.80 (t, J = 7.1 Hz, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 178.0, 135.8, 134.7, 129.4, 128.0, 127.8, 127.3, 127.0, 125.3, 83.1, 51.9, 48.8, 46.9, 46.0, 11.5. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 324.2, found 324.1.



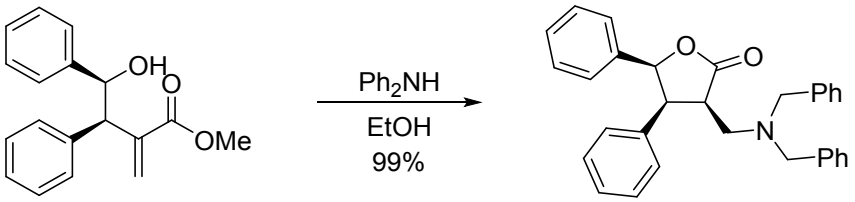

**1** **5**

**(2,3-*trans*,2,4-*cis*)-3,4-diphenyl-2-((piperidin-1-yl)methyl)butano-4-lactone** (**5**). Piperidine was distilled prior to use. 99 : 1 = dr; >99% yield of *cis*,*cis*-product. $R_f$ = 0.18, 70 : 30 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.12-7.02 (m, 8H), 6.89 (d, J = 7.8 Hz, 2H), 5.83 (d, J = 5.2 Hz, 1H), 4.10 (dd, J = 7.6, 5.2 Hz, 1H), 3.44 (td, J = 8.5, 3.8 Hz, 1H), 2.74 (dd, J = 13.3, 3.8 Hz, 1H), 2.37 (m, 2H), 2.20 (dd, J = 13.3, 8.8 Hz, 1H), 2.08 (m, 2H), 1.53-1.35 (m, 6H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 177.8, 135.8, 134.7, 129.4, 127.9, 127.8, 127.2, 1267.0, 125.3, 82.9, 54.7, 54.4, 52.0, 45.9, 26.0, 24.1. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 336.2, found 336.2.



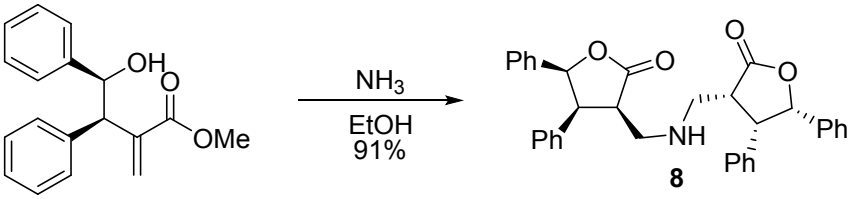

**1** **6**

**(2,3-*cis*,2,4-*cis*)-2-((morpholin-4-yl)methyl)-3,4-diphenylbutano-4-lactone** (**6**). 99 : 1 = dr; 99% yield of *cis*,*cis*-product. $R_f$ = 0.58, 50 : 50 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.13-7.02 (m, 8H), 6.90 (d, J = 7.8 Hz, 2H), 5.86 (d, J = 5.2 Hz, 1H), 4.10 (dd, J = 7.6, 5.2 Hz, 1H), 3.61 (m, 4H), 3.44 (m, 1H), 2.76 (dd, J = 13.3, 4.0 Hz, 1H), 2.44 (m, 2H), 2.22 (dd, J = 13.3, 9.3 Hz, 1H), 2.11 (m, 2H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 177.3, 135.5, 134.3, 129.2, 127.8, 127.7, 125.1, 82.8, 66.8, 54.2, 53.2, 51.5, 45.3. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 338.2, found 338.2.



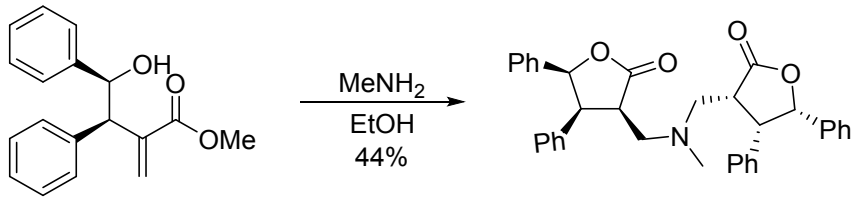

**1** **7**

**(2,3-*cis*,2,4-*cis*)-3,4-diphenyl-2-((dibenzylamino)methyl)butano-4-lactone** (**7**). 99 : 1 = dr; 99% yield of *cis*,*cis*-product. $R_f$ = 0.61, 70 : 30 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.27-6.98 (m, 18H), 6.77 (m, 2H), 5.62 (d, J = 5.1 Hz, 1H), 3.84 (dd, J = 7.4, 5.2 Hz, 1H), 3.54-3.34 (m, 4H), 3.29 (m, 1H), 2.94 (dd, J = 13.6, 3.9 Hz, 1H), 2.67 (dd, J = 13.6, 9.7 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.6, 138.9, 135.6, 134.4, 129.1, 128.7, 128.2, 128.1, 127.8, 127.3, 127.1, 126.9, 125.3, 83.1, 58.9, 51.7, 51.1, 46.4. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 448.2, found 448.2.



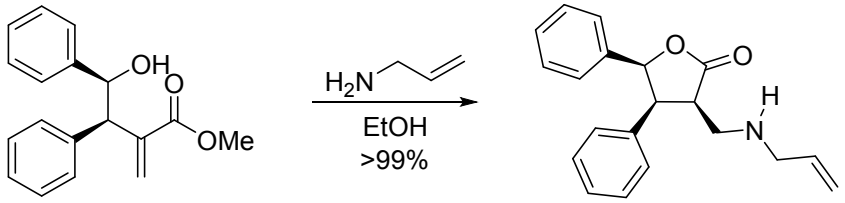

**8**

**(±)-*N*,*N*-bis(((2,3-*cis*,2,4-*cis*)-3,4-diphenylbutano-4-lactone-2-yl)methyl)amine** (**8**). Ammonia was introduced as a 33 wt% aqueous solution. 92 : 8 = dr; 91% yield of *cis*,*cis*-product. $R_f$ = 0.35, 70 : 30 = Hex : EtOAc, stain = Dragendorff-Munier, Ninhydrin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.14-7.04 (m, 16H), 6.84 (m, 4H), 5.78 (t, J = 4.6 Hz, 2H), 3.93 (dd, J = 7.7, 5.3 Hz, 1H), 3.85 (dd, J = 7.7, 5.3 Hz, 1H), 3.27 (q, J = 7.5 Hz, 1H), 3.19 (q, J = 7.5 Hz, 1H), 2.85 (dd, J = 12.7, 6.3 Hz, 1H), 2.77 (dd, J = 12.5, 6.0 Hz, 1H), 2.41 (dd, J = 12.6, 8.4 Hz, 1H), 2.32 (dd, J = 12.7, 7.7 Hz, 1H), 1.75 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.6, 177.4, 135.4, 134.2, 134.1, 129.2, 129.1, 128.3, 128.2, 128.1, 127.9, 127.8, 127.4, 125.3, 83.1, 83.0, 50.9, 50.8, 47.0, 46.9, 45.7, 45.6. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 518.2, found 518.3; for $[M+Na]^+$ 540.2, found 540.2.




**1** **9**

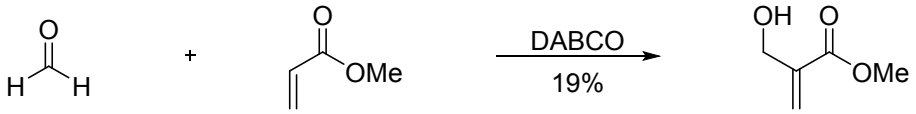
**(±)-*N*-methyl-*N*,*N*-bis(((2,3-*cis*,2,4-*cis*)-3,4-diphenylbutano-4-lactone-2-yl)methyl)amine** (**9**)**.** Methylamine was introduced as a 2.0 M solution in THF. 99 : 1 = dr; 44% yield of *cis*,*cis*-product. $R_f$ = 0.34, 60 : 40 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.27-7.16 (m, 16H), 6.97 (m, 4H), 5.75 (d, J = 5.2 Hz, 1H), 5.67 (d, J = 5.1 Hz, 1H), 3.85 (dd, J = 7.6, 5.3 Hz, 1H), 3.73 (dd, J = 7.3, 5.3 Hz, 1H), 3.04 (m, 1H), 2.94 (m, 2H), 2.74 (m, 2H), 2.56 (dd, J = 13.3, 10.7 Hz, 1H), 2.34 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.6, 177.1, 135.5, 134.8, 134.7, 129.4, 129.2, 128.2, 128.1, 127.9, 127.3, 127.27, 127.2, 125.2, 83.0, 82.8, 53.1, 52.8, 51.7, 51.0, 45.7, 45.0, 43.0. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 532.2, found 532.3; for $[M+Na]^+$ 554.2, found 554.3.



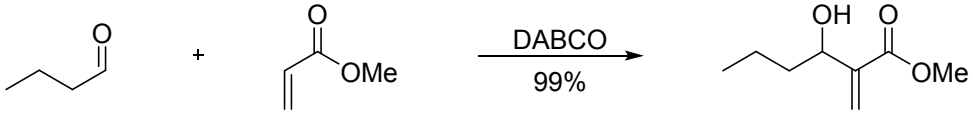

**1** **10**

**(2,3-*cis*,2,4-*cis*)-2-((allylamino)methyl)-3,4-diphenylbutano-4-lactone** (**10**). 99 : 1 = dr; >99% yield of *cis*,*cis*-product. $R_f$ = 0.28, 95 : 5 = EtOAc : MeOH, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.12-7.06 (m, 8H), 6.91 (m, 2H), 5.86 (d, J = 5.3 Hz, 1H), 5.72 (ddt, J = 16.5, 11.1, 5.9 Hz, 1H), 5.07-4.99 (m, 2H), 4.04 (m, 1H), 3.45 (q, J = 7.1 Hz, 1H), 3.17-3.03 (m, 2H), 2.89 (dd, J = 12.4, 6.7 Hz, 1H), 2.48 (dd, J = 12.4, 7.5 Hz, 1H), 2.02 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.9, 136.1, 135.5, 134.2, 129.1, 128.3, 128.0, 127.5, 127.4, 125.3, 116.2, 83.2, 52.3, 51.1, 47.4, 45.6. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 308.2, found 308.2.

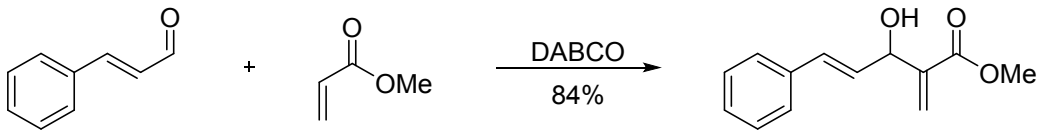
## Preparation of Monosubstituted Butanoate Esters



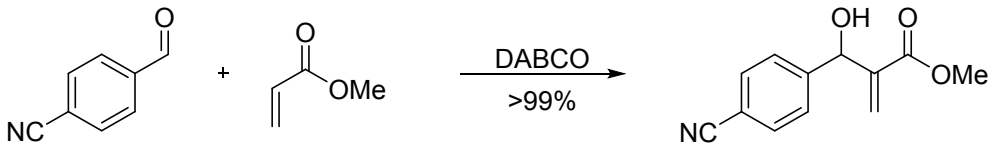

**Methyl 2-(hydroxymethyl)prop-2-enoate.** Formalin (13.4 M) was used as a formaldehyde source. $R_f$ = 0.28, 70 : 30 = Hex : EtOAc, stain = $I_2$, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 6.26 (s, 1H), 5.87 (s, 1H), 4.32 (s, 2H), 3.78 (s, 3H), 3.46 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.9, 139.5, 125.5, 61.8, 51.9. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 117.1, found 117.2.



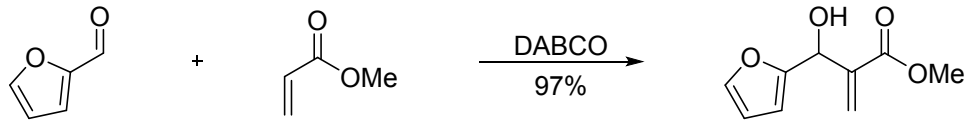

**Methyl 3-hydroxy-2-methylenehexanoate**. $R_f$ = 0.39, 75 : 25 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 6.23 (s, 1H), 5.80 (s, 1H), 4.41 (t, J = 6.4 Hz, 1H), 3.79 (s, 3H), 2.63 (s, 1H), 1.63 (m, 2H), 1.51-1.32 (m, 2H), 0.94 (t, J = 7.6 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 167.1, 142.5, 124.9, 71.5, 51.9, 38.4, 19.1, 13.9. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 159.1, found 159.1; for $[M+K]^+$ 197.1, found 197.2.



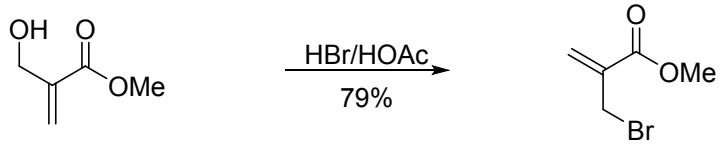

**Methyl (4*E*)-3-hydroxy-2-methylene-5-phenylpent-4-enoate**. $R_f$ = 0.31, 75 : 25 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.41-7.22 (m, 5H), 6.66 (d, J = 16.0 Hz, 1H), 6.32-6.27 (dd, J = 16.0, 6.1 Hz, 1H), 6.29 (s, 1H), 5.92 (s, 1H), 5.13 (t, J = 6.1 Hz, 1H), 3.79 (s, 3H), 3.02 (d, J = 6.1 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.4, 141.4, 136.3, 130.9, 129.2, 128.3, 127.5, 126.4, 125.3, 71.0, 51.7. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 219.1, found 219.1; for $[M+Na]^+$ 241.1, found 241.1; for $[M+K]^+$ 257.1, found 257.2.



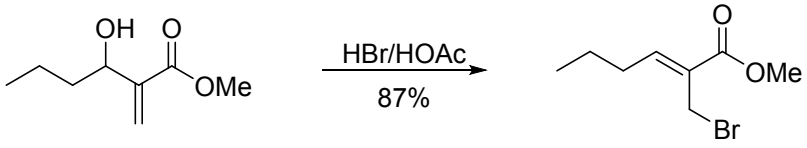

**Methyl 2-((4-cyanophenyl)(hydroxy)methyl)prop-2-enoate**. $R_f$ = 0.20, 75 : 25 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), 6.38 (s, 1H), 5.88 (s, 1H), 5.58 (s, 1H), 3.73, (s, 3H), 3.47 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.4, 146.8, 141.1, 132.2, 127.3, 127.1, 118.7, 111.5, 72.7, 52.2. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+Na]^+$ 240.1, found 240.2.



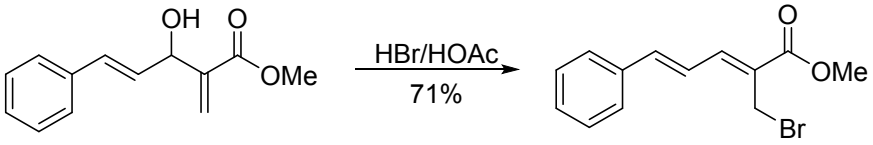

**Methyl 2-((furan-2-yl)hydroxymethyl)prop-2-enoate**. Furan-2-carbaldehyde was distilled prior to use. $R_f$ = 0.23, 75 : 25 = Hex : EtOAc, stain = Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.33 (s, 1H), 6.36 (s, 1H), 6.29 (s, 1H), 6.20 (s, 1H), 5.97 (s, 1H), 5.57 (d, J = 6.1 Hz, 1H), 3.86 (s, 1H), 3.69 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.5, 154.3, 142.3, 139.7, 126.6, 110.4, 107.2, 66.5, 52.0. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+Na]^+$ 205.0, found 205.1; for $[M+K]^+$ 221.0, found 221.2.



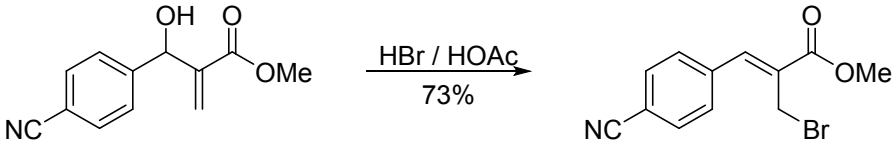

**Methyl 2-(bromomethyl)prop-2-enoate**. $R_f$ = 0.69, 70 : 30 = Hex : EtOAc, stain = $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 6.34 (s, 1H), 5.97 (s, 1H), 4.19 (s, 2H), 3.82 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.3, 137.3, 129.3, 52.3, 29.3. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+Na]^+$ 200.9, found 200.8.



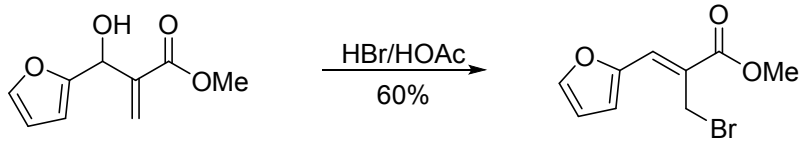

**Methyl (2*Z*)-2-(bromomethyl)hex-2-enoate**. $R_f$ = 0.71, 75 : 25 = Hex : EtOAc, stain = PMA, $I_2$, Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 6.97 (dd, J = 8.1, 7.3 Hz, 1H), 4.24 (s, 2H), 3.78 (s, 3H), 2.29 (m, 2H), 1.55 (h, J = 7.4 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.4, 147.7, 129.1, 51.6, 30.4, 23.9, 21.1, 13.5. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 221.0, found 221.0; for $[M+Na]^+$ 243.0, found 243.0; for $[M+K]^+$ 259.0, found 259.0.



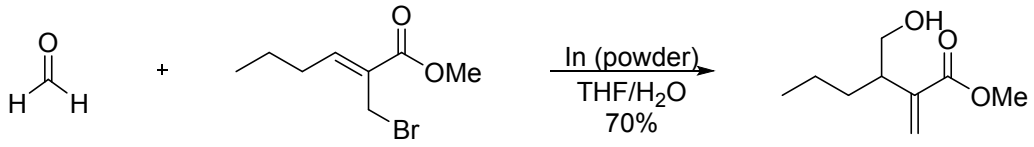

**Methyl (2*Z*,4*E*)-2-(bromomethyl)-5-phenylpenta-2,4-dienoate**. $R_f$ = 0.56, 75 : 25 = Hex : EtOAc, stain = Vanillin, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.46 (dd, J = 13.7, 9.3 Hz, 3H), 7.32 (m, 3H), 7.08 (dd, J = 15.1, 11.7 Hz, 1H), 6.93 (d, J = 15.2 Hz, 1H), 4.43 (s, 2H), 3.78 (s, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 165.9, 142.5, 142.4, 135.5, 129.3, 128.6, 127.3, 126.6, 122.1, 51.9, 24.7. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 281.0, found 281.1; for $[M+Na]^+$ 303.0, found 303.1.



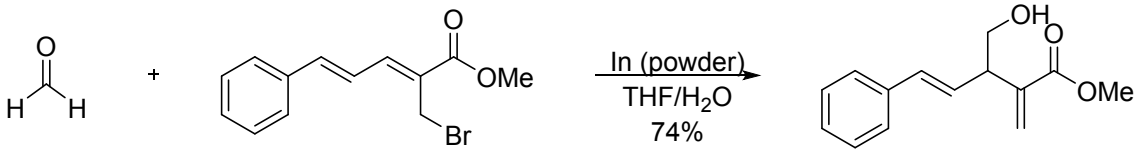

**Methyl *Z*-2-(bromomethyl)-3-(4-cyanophenyl)prop-2-enoate**. $R_f$ = 0.38, 75 : 25 = Hex : EtOAc, stain = Vanillin, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.80 (s, 1H), 7.77 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.2 Hz, 2H), 4.32 (s, 2H), 3.91 (s, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 165.8, 140.3, 138.6, 132.6, 131.4, 129.9, 118.3, 112.9, 52.8, 25.5. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 302.0, found 301.6.



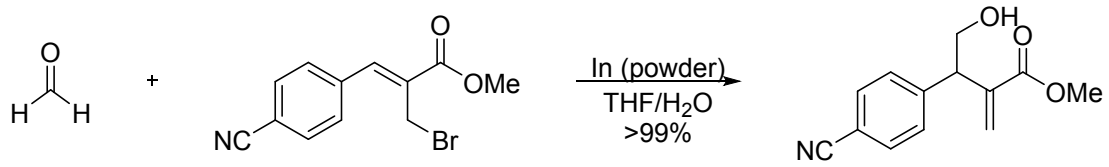

**Methyl (2*Z*)-2-(bromomethyl)-3-(furan-2-yl)prop-2-enoate**. $R_f$ = 0.51, 75 : 25 = Hex : EtOAc, stain = Vanillin, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 1.8 Hz, 1H), 7.50 (s, 1H), 6.84 (d, J = 3.5 Hz, 1H), 6.57 (dd, J = 3.5, 1.8 Hz, 1H), 4.71 (s, 2H), 3.85 (s, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 166.7, 150.3, 146.2, 128.3, 124.1, 118.7, 112.7, 52.4, 26.7. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 245.0, found 245.0; for $[M+Na]^+$ 267.0, found 267.0.



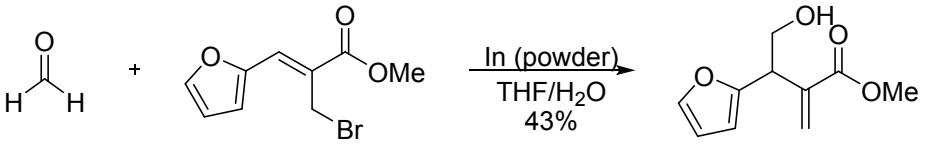

**Methyl 3-(hydroxymethyl)-2-methylenehexanoate**. Formalin (13.4 M) was used as a formaldehyde source. $R_f$ = 0.32, 70 : 30 = Hex : EtOAc, stain = $I_2$, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 6.29 (s, 1H), 5.62 (s, 1H), 3.75 (s, 3H), 3.62 (qd, J = 11.8, 7.9 Hz, 2H), 2.91 (s, 1H), 2.77 (m, 1H), 1.61-141 (m, 2H), 1.29 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 168.0, 141.3, 125.7, 65.2, 51.8, 43.4, 32.3, 20.2, 14.0. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 173.1, found 173.0.



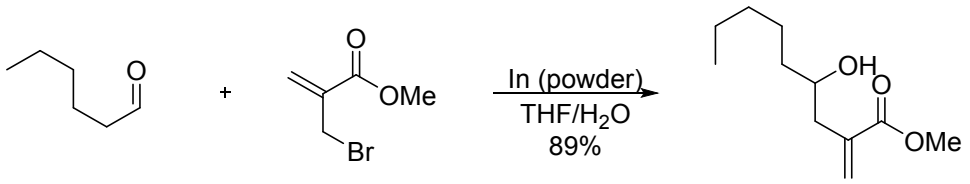

**Methyl (4*E*)-3-(hydroxymethyl)-2-methylene-5-phenylpent-4-enoate**. Formalin (13.4 M) was used as a formaldehyde source. $R_f$ = 0.28, 70 : 30 = Hex : EtOAc, stain = $I_2$, *p*-Anis., Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.36-7.19 (m, 5H), 6.51 (d, J = 15.9 Hz, 1H), 6.33 (s, 1H), 6.24 (dd, J = 16.0, 8.1 Hz, 1H), 5.71 (s, 1H), 3.86-3.77 (m, 2H), 3.75 (s, 3H), 3.63 (m, 1H), 2.30 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 167.4, 140.3, 137.0, 132.6, 128.6, 128.1, 127.6, 126.5, 126.3, 64.8, 52.1, 47.4. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 255.1, found 255.1.



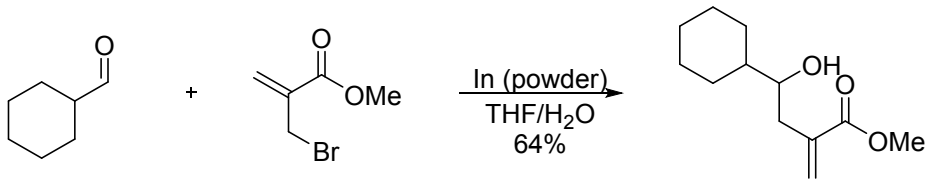

**Methyl 3-(4-cyanophenyl)-4-hydroxy-2-methylenebutanoate**. Formalin (13.4 M) was used as a formaldehyde source. $R_f$ = 0.18, 70 : 30 = Hex : EtOAc, stain = $I_2$, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 8.3 Hz, 2H), 7.39 (d, J = 8.3 Hz, 2H), 6.46 (s, 1H), 5.76 (s, 1H), 4.14 (t, J = 6.7 Hz, 1H), 4.02-3.92 (m, 2H), 3.69 (s, 3H), 2.39 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.8, 145.8, 139.5, 132.3, 129.2, 126.8, 118.8, 110.7, 64.3, 52.2, 48.9. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 232.1, found 232.1.



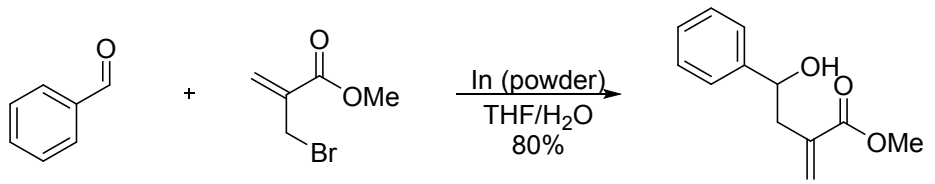

**Methyl 3-(furan-2-yl)-4-hydroxy-2-methylenebutanoate**. Formalin (13.4 M) was used as a formaldehyde source. $R_f$ = 0.28, 70 : 30 = Hex : EtOAc, stain = $I_2$, *p*-Anis., Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.36 (s, 1H), 6.38 (s, 1H), 6.33 (m, 1H), 6.20 (d, J = 3.2 Hz, 1H), 5.68 (s, 1H), 4.25 (t, J = 6.4 Hz, 1H), 3.96 (d, J = 6.2 Hz, 2H), 3.77 (s, 3H), 2.19 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 167.2, 153.5, 142.0, 138.4, 127.6, 110.4, 107.2, 64.0, 52.3, 43.2. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 219.1, found 219.1.



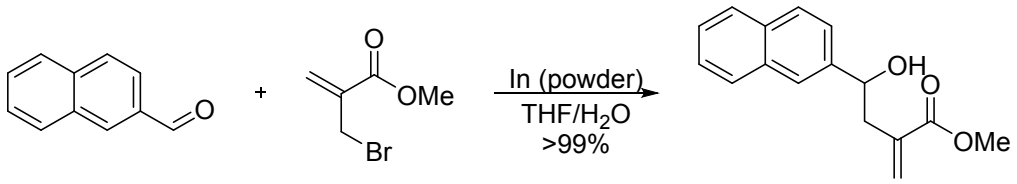

**Methyl 4-hydroxy-2-methylenenonanoate**. $R_f$ = 0.17, 85 : 15 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 6.24 (s, 1H), 5.67 (s, 1H), 3.76 (s, 3H), 3.73 (m, 1H), 2.63 (s, 1H), 2.56 (dd, J = 13.9, 3.7 Hz, 1H), 2.33 (dd, J = 13.9, 8.3 Hz, 1H), 1.46-1.30 (m, 8H), 0.89 (t, J = 6.7 Hz, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 168.2, 137.6, 127.7, 70.4, 52.0, 40.4, 37.2, 31.9, 25.4, 22.7, 14.1. Mass: LRMS (ESI+) *m/z* calcd for $[M+K]^+$ 239.2, found 239.2.




**Methyl 4-cyclohexyl-4-hydroxy-2-methylenebutanoate**. $R_f$ = 0.25, 85 : 15 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 6.23 (s, 1H), 5.67 (s, 1H), 3.75 (s, 3H), 3.47 (m, 1H), 2.61 (dd, J = 14.0, 2.1 Hz, 1H), 2.43 (s, 1H), 2.28 (dd, J = 14.0, 9.4 Hz, 1H), 1.87-1.65 (m, 5H), 1.40-1.00 (m, 6H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 168.1, 138.1, 127.3, 74.6, 51.9, 43.7, 37.3, 29.0, 27.8, 26.5, 26.2, 26.1. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 235.1, found 235.1.



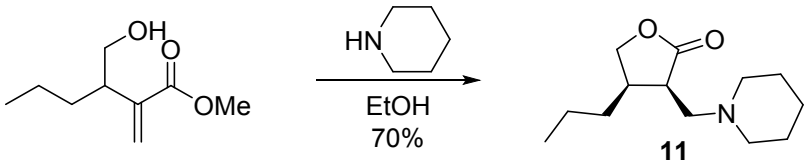

**Methyl 4-hydroxy-2-methylene-4-phenylbutanoate**. Benzaldehyde was distilled prior to use. $R_f$ = 0.33, 70 : 30 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.31-7.22 (m, 5H), 6.17 (s, 1H), 5.53 (s, 1H), 4.80 (m, 1H), 3.69 (s, 3H), 3.21 (s, 1H), 2.71 (dd, J = 14.0, 4.5 Hz, 1H), 2.63 (dd, J = 14.0, 8.2 Hz, 1H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 168.0, 143.9, 136.7, 128.3, 128.2, 127.3, 125.7, 72.8, 52.0, 42.2. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 207.1, found 207.1.



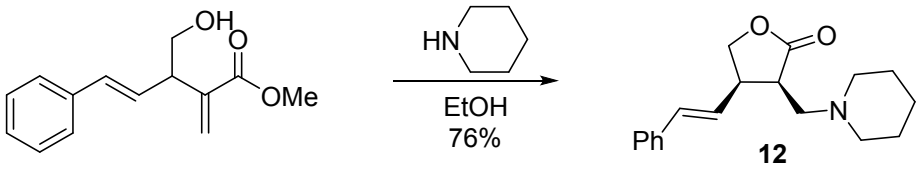

**Methyl 4-hydroxy-2-methylene-4-(naphthalen-2-yl)butanoate**. $R_f$ = 0.31, 70 : 30 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.74 (m, 4H), 7.40 (m, 3H), 6.14 (s, 1H), 5.50 (s, 1H), 4.95 (dd, J = 8.0, 4.5 Hz, 1H), 3.64 (s, 3H), 3.36 (s, 1H), 2.80-2.65 (m, 2H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 168.1,

141.4, 136.6, 133.2, 132.8, 128.4, 128.0, 127.9, 127.6, 126.0, 125.7, 124.4, 124.0, 72.9, 52.0, 42.2. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 257.1, found 257.2; for $[M+Na]^+$ 279.1, found 279.1.

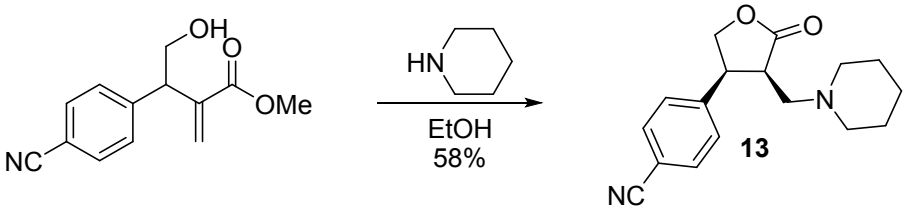
## Aminolactonization of Monosubstituted Butanoate Esters



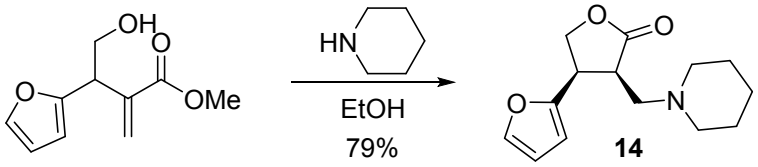

**(2,3-*cis*)-2-((piperidin-1-yl)methyl) -3-propylbutano-4-lactone** (**11**). Piperidine was distilled prior to use. 74 : 26 = dr; 70% yield of *cis*-product. $R_f$ = 0.21, 95 : 5 = EtOAc : MeOH, stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 4.41 (t, J = 8.7 Hz, 1H), 3.85 (t, J = 8.5 Hz, 1H), 2.68 (dd, J = 12.9, 4.8 Hz, 1H), 2.55 (dd, J = 13.0, 7.6 Hz, 1H), 2.49-2.30 (m, 6H), 1.72 (m, 1H), 1.55 (m, 4H), 1.41 (m, 2H), 1.34 (m, 3H), 0.94 (t, J = 7.0 Hz, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 179.1, 71.9, 58.3, 54.8, 44.1, 39.8, 35.0, 25.9, 24.1, 20.2, 14.1. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 226.2, found 226.3.



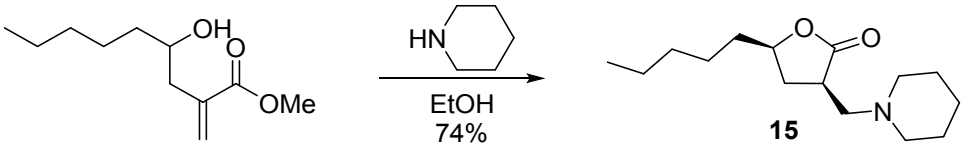

**(2,3-*cis*)-3-((1*E*)-2-phenyleth-1-en-1-yl)-2-((piperidin-1-yl)methyl)butano-4-lactone** (**12**). Piperidine was distilled prior to use. 79 : 21 = dr; 76% yield of *cis*-product. $R_f$ = 0.33, 95 : 5 = EtOAc : MeOH, stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.37-7.23 (m, 5H), 6.54 (d, J = 15.8 Hz, 1H), 6.13 (dd, J = 15.8, 8.2 Hz, 1H), 4.45 (dd, J = 9.1, 8.0 Hz, 1H), 4.02 (t, J = 9.2 Hz, 1H), 3.32 (p, J = 8.8 Hz, 1H), 2.76-2.56 (m, 3H), 2.40 (m, 4H), 1.50 (m, 4H), 1.38 (m, 2H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 178.2, 136.5, 132.7, 128.6, 127.8, 127.2, 126.2, 70.4, 57.1, 54.9, 44.7, 43.7, 26.0, 24.1. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 286.2, found 286.3.



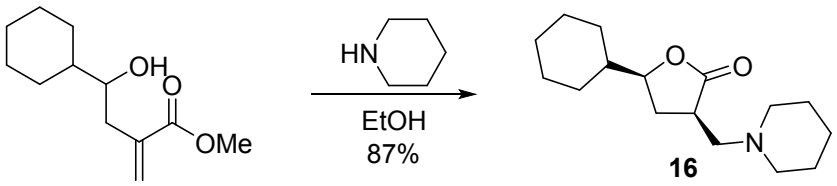

**(2,3-*cis*)-3-(4-cyanophenyl)-2-((piperidin-1-yl)methyl)butano-4-lactone** (**13**). Piperidine was distilled prior to use. 79 : 21 = dr; 58% yield of *cis*-product. $R_f$ = 0.48, 95 : 5 = EtOAc : MeOH, stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 8.1 Hz, 2H), 4.64 (t, J = 8.8 Hz, 1H), 4.24 (t, J = 9.1 Hz, 1H), 3.81 (q, J = 9.0 Hz, 1H), 2.91 (td, J = 9.0, 5.0 Hz, 1H), 2.65 (m, 2H), 2.25 (m, 4H), 1.41-1.23 (m, J = 70.2 Hz, 6H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 177.2, 145.4, 132.5, 128.4, 118.5, 111.0, 71.8, 57.9, 54.5, 46.1, 45.9, 25.7, 23.9. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 285.2, found 285.4.



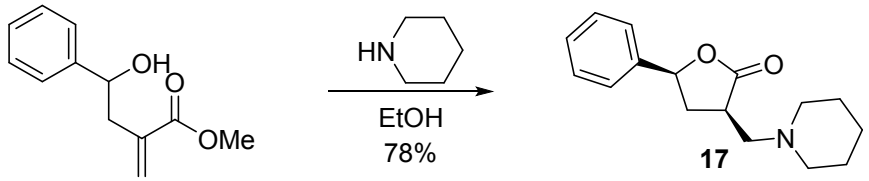

**(2,3-*cis*)-3-(furan-2-yl)-2-((piperidin-1-yl)methyl)butano-4-lactone** (**14**). Piperidine was distilled prior to use. 91 : 9 = dr; 79% yield of *cis*-product. $R_f$ = 0.23, 95 : 5 = EtOAc : MeOH, stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.37 (s, 1H), 6.33 (m, 1H), 6.20 (m, 1H), 4.53 (t, J = 8.6 Hz, 1H), 4.28 (t, J = 8.8 Hz, 1H), 3.85 (m, 1H), 2.95 (m, 1H), 2.71 (m, 2H), 2.34 (m, 4H), 1.45 (m, 4H), 1.36 (m, 2H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 177.8, 152.3, 142.2, 110.5, 106.9, 69.8, 57.2, 55.0, 44.0, 39.0, 26.1, 24.2. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 250.1, found 250.3.



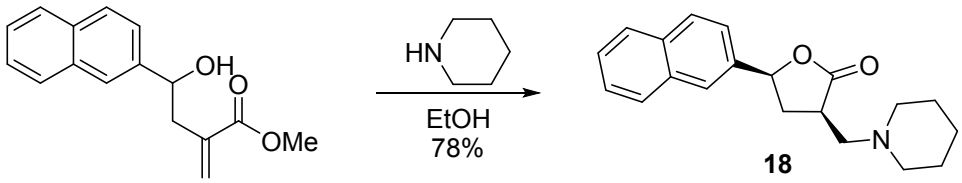

**(2,4-*cis*)-2-((piperidin-1-yl)methyl)nonano-4-lactone** (**15**). Piperidine was distilled prior to use. 86 : 14 = dr; 74% yield of *cis*-product. $R_f$ = 0.46, 20 : 20 : 20 : 40 = $CHCl_3$ : $Et_2O$ : EtOAc : Hex w/ 3% $NH_3$ (30%, aq.), stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 4.38 (m, 1H), 2.87 (m, 2H), 2.58-2.38 (m, 6H), 1.73 (m, 2H), 1.60 (m, 6H), 1.45 (m, 4H), 1.33 (m, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 178.2, 79.1, 59.2, 54.5, 39.6, 35.4, 35.0, 31.4, 25.6, 24.8, 24.0, 22.4, 13.9. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 254.2, found 254.4.




**(2,4-*cis*)-4-cyclohexyl-2-((piperidin-1-yl)methyl)butano-4-lactone** (**16**). Piperidine was distilled prior to use. 87 : 13 = dr; 87% yield of *cis*-product. $R_f$ = 0.46, 20 : 20 : 20 : 40 = $CHCl_3$ : $Et_2O$ : EtOAc : Hex w/ 3% $NH_3$ (30%, aq.), stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 4.08 (ddd, J = 10.5, 7.7, 5.5 Hz, 1H), 2.82 (m, 2H), 2.44 (m, 4H), 2.34 (m, 2H), 1.97 (d, J = 12.7 Hz, 1H), 1.80-0.96 (m, 19H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 178.3, 83.1, 59.3, 54.6, 42.6, 39.6, 32.8, 29.2, 27.6, 26.2, 25.9, 25.6, 25.5, 24.2. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 266.2, found 266.4.

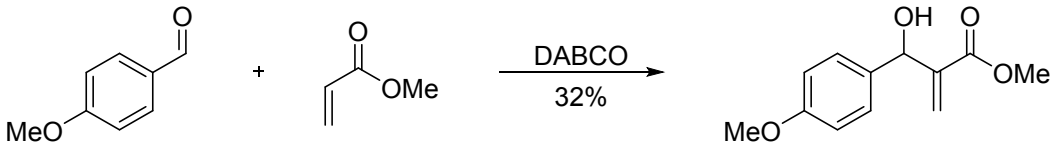



**(2,4-*cis*)-4-phenyl-2-((piperidin-1-yl)methyl)butano-4-lactone** (**17**). Piperidine was distilled prior to use. 83 : 17 = dr; 78% yield of *cis*-product. $R_f$ = 0.33, 20 : 20 : 20 : 40 = $CHCl_3$ :d $Et_2O$ : EtOAc : Hex w/ 3% $NH_3$ (30%, aq.), stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.35 (m, 5H), 5.37 (dd, J = 10.6, 5.8 Hz, 1H), 3.00 (m, 1H), 2.90 (dd, J = 12.9, 4.1 Hz, 1H), 2.83 (m, 1H), 2.55 (dd, J = 12.9, 8.8 Hz, 1H), 2.47 (m, 2H), 2.39 (m, 2H), 2.07 (q, J = 11.9 Hz, 1H), 1.57 (m, 4H), 1.42 (m, 2H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 178.0, 139.2, 128.7, 128.5, 125.6, 79.7, 59.0, 54.7, 40.3, 37.7, 25.9, 24.1. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 260.2, found 260.3.

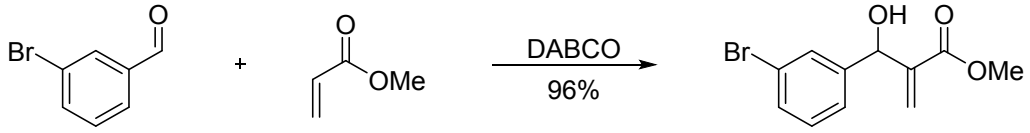



**(2,4-*cis*)-4-(naphtha-2-yl)-2-((piperidin-1-yl)methyl)butano-4-lactone** (**18**). Piperidine was distilled prior to use. 84 : 16 = dr; 78% yield of *cis*-product. $R_f$ = 0.33, 20 : 20 : 20 : 40 = $CHCl_3$ : $Et_2O$ : EtOAc : Hex w/ 3% $NH_3$ (30%, aq.), stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.82 (m, 4H), 7.45 (m, 3H), 5.48 (dd, J = 10.4, 6.0 Hz, 1H), 2.98 (m, 1H), 2.87 (dd, J = 13.0, 4.1 Hz, 1H), 2.80 (m, 1H), 2.54 (dd, J = 12.9, 8.7 Hz, 1H), 2.43 (m, 2H), 2.34 (m, 2H), 2.14 (q, J = 12.7 Hz, 1H), 1.52 (m, 4H), 1.40 (m, 2H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 178.0, 136.7, 133.3, 133.2, 128.7, 128.0, 127.8, 126.5, 126.4, 124.6, 123.2, 79.7, 59.1, 54.8, 40.4, 37.4, 26.1, 24.2. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 310.2, found 310.4.

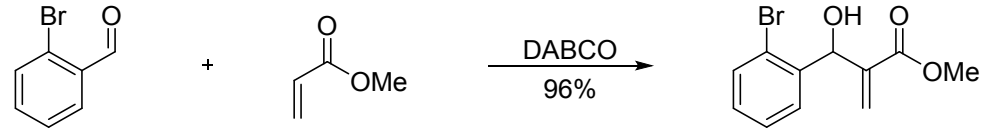
## Preparation of Aminolactonization Substrates



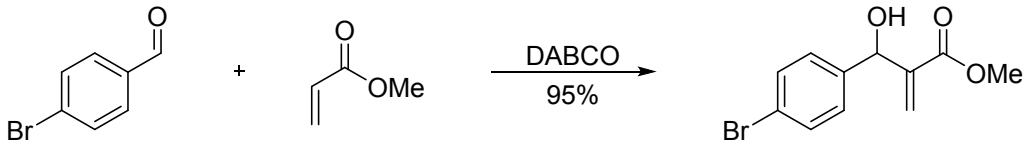

**Methyl 2-((hydroxy)(4-methoxyphenyl)methyl)prop-2-enoate**. 4-Methylbenzaldehyde was distilled prior to use. $R_f$ = 0.24, 75 : 25 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.29 (s, 1H), 5.87 (s, 1H), 5.48 (d, *J* = 4.4 Hz, 1H), 3.75 (s, 3H), 3.67 (s, 3H), 3.31 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.7, 159.2, 142.4, 133.6, 128.0, 125.3, 113.8, 72.4, 55.2, 51.9. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 223.1, found 222.9.



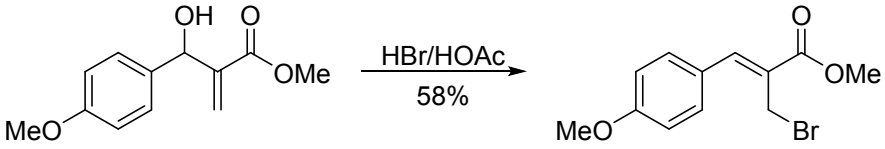

**Methyl 2-((hydroxy)(3-bromophenyl)methyl)prop-2-enoate**. $R_f$ = 0.32, 75 : 25 = Hex : EtOAc, stain = Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.51 (s, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.28 (d, J = 7.7 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 6.34 (s, 1H), 5.84 (s, 1H), 5.48 (d, J = 5.7 Hz, 1H), 3.71 (s, 3H), 3.36 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.5, 143.7, 141.4, 130.8, 129.9, 129.6, 126.6, 125.2, 122.5, 72.5, 52.1. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+K]^+$ 309.0, found 309.0.



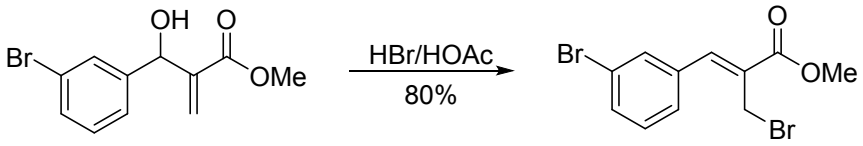

**Methyl 2-((hydroxy)(2-bromophenyl)methyl)prop-2-enoate**. $R_f$ = 0.35, 75 : 25 = Hex : EtOAc, stain = Vanillin, $KMnO_4$. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.9 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 6.34 (s, 1H), 5.93 (s, 1H), 5.57 (s, 1H), 3.77 (s, 3H), 3.43 (s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 167.1, 140.7, 139.9, 132.8, 129.4, 128.5, 127.7, 127.2, 123.2, 71.5, 52.2. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+Na]^+$ 283.0, found 283.0.



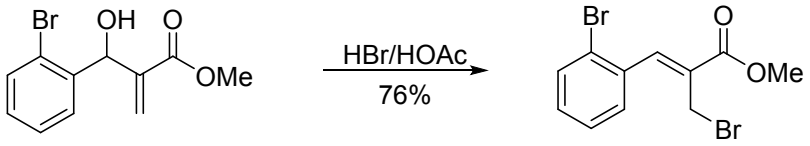

**Methyl 2-((hydroxy)(4-bromophenyl)methyl)prop-2-enoate**. $R_f$ = 0.31, 75 : 25 = Hex : EtOAc, stain = Vanillin, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.41 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 8.4 Hz, 2H), 6.29 (s, 1H), 5.84 (s, 1H), 5.43 (d, J = 5.3 Hz, 1H), 3.70 (d, J = 5.4 Hz, 1H), 3.65 (s, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 166.4, 141.7, 140.4, 131.4, 128.4, 126.0, 121.6, 72.1, 51.9. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 271.0, found 271.1.



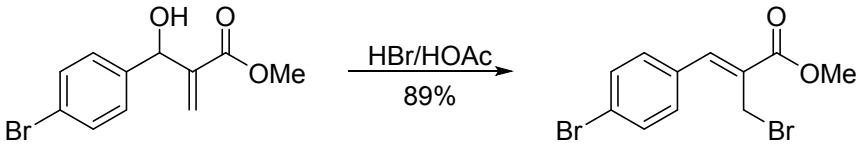

**Methyl (2*Z*)-2-(bromomethyl)-3-(4-methoxyphenyl)prop-2-enoate**. $R_f$ = 0.45, 75 : 25 = Hex : EtOAc, stain = Vanillin, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 1H), 7.55 (d, J = 8.8 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 4.42 (s, 2H), 3.84 (s, 3H), 3.82 (s, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): 13C NMR (101 MHz, CDCl3) δ 166.8, 160.8, 142.9, 132.0, 126.6, 126.0, 114.4, 55.3, 52.3, 27.6. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 307.0, found 307.0.



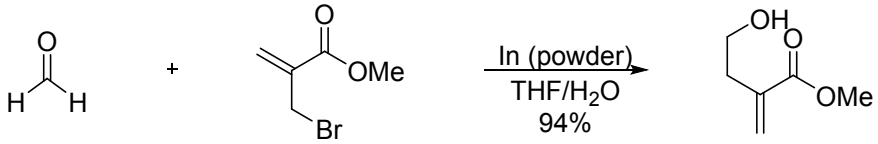

**Methyl (2*Z*)-2-(bromomethyl)-3-(3-bromophenyl)prop-2-enoate**. $R_f$ = 0.45, 80 : 20 = Hex : EtOAc, stain = PMA, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.72 (s, 1H), 7.68 (s, 1H), 7.52 (m, 2H), 7.33 (t, J = 7.9 Hz, 1H), 4.33 (s, 2H), 3.88 (s, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): 13C NMR (101 MHz, CDCl3) δ 166.2, 141.0, 136.2, 132.5, 132.3, 130.4, 130.0, 127.9, 122.9, 52.6, 26.1. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 354.9, found 354.9.



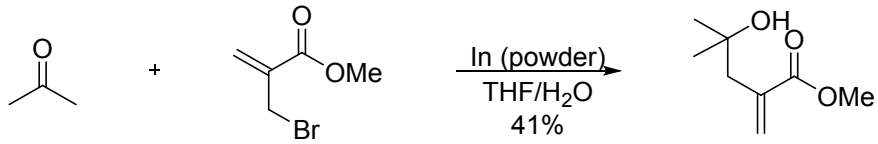

**Methyl (2*Z*)-2-(bromomethyl)-3-(2-bromophenyl)prop-2-enoate**. $R_f$ = 0.63, 80 : 20 = Hex : EtOAc, stain = PMA, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.85 (s, 1H), 7.66 (dd, J = 18.7, 7.8 Hz, 2H), 7.42 (t, J = 7.6 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 4.24 (s, 2H), 3.90 (s, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 166.1, 141.7, 134.7, 133.1, 130.7, 130.3, 129.7, 127.7, 124.5, 52.7, 26.3. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 332.9, found 333.1; for $[M+K]^+$ 370.9, found 370.8.



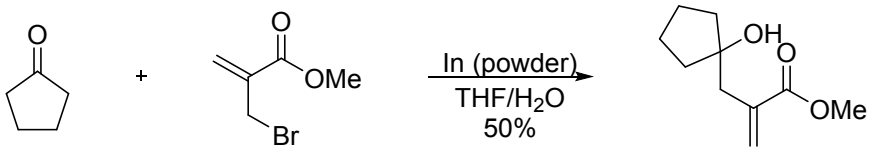

**Methyl (2*Z*)-2-(bromomethyl)-3-(4-bromophenyl)prop-2-enoate**. $R_f$ = 0.53, 75 : 25 = Hex : EtOAc, stain = PMA, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.70 (s, 1H), 7.55 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 8.5 Hz, 2H), 4.33 (s, 2H), 3.86 (s, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$): 13C NMR (101 MHz, CDCl3) δ 166.0, 141.3, 132.8, 132.0, 131.0, 129.0, 123.9, 52.4, 26.3. Mass: LRMS (ESI+) *m/z* calcd for $[M+K]^+$ 370.9, found 370.4.



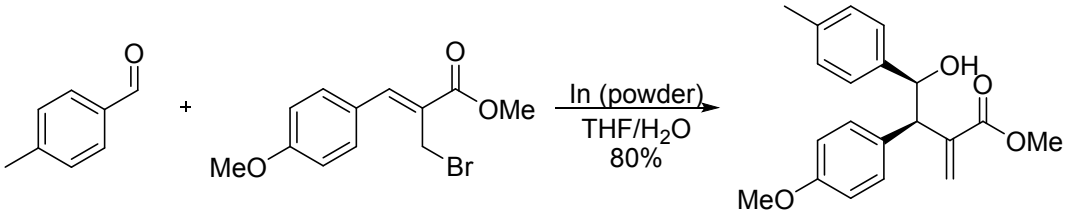

**Methyl 4-hydroxy-2-methylenebutanoate**. Formalin (13.4 M) was used as a formaldehyde source. $R_f$ = 0.19, 70 : 30 = Hex : EtOAc, stain = $I_2$, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 6.25 (s, 1H), 5.68 (s, 1H), 3.77 (s, 3H), 3.75 (t, J = 6.3 Hz, 2H), 2.58 (t, J = 6.3 Hz, 2H), 2.55 (s, 1H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 167.7, 137.2, 127.2, 61.3, 51.9, 35.4. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 131.1, found 131.1.



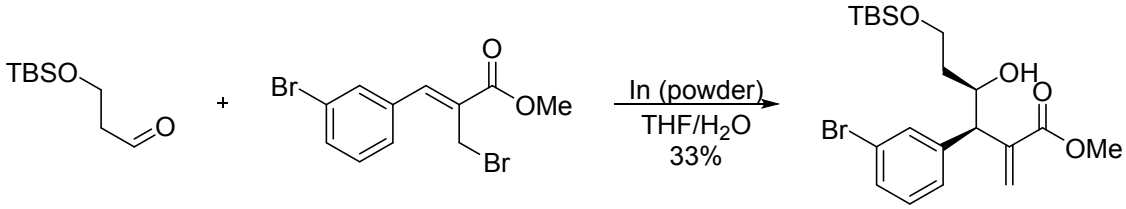

**Methyl 4-hydroxy-4,4-dimethyl-2-methylenebutanoate**. $R_f$ = 0.36, 70 : 30 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 6.29 (s, 1H), 5.65 (s, 1H), 3.78 (s, 3H), 2.74 (s, 1H), 2.55 (s, 2H), 1.21 (s, 6H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 169.1, 137.1, 128.8, 70.2, 52.2, 45.3, 29.3. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 159.1, found 159.2.



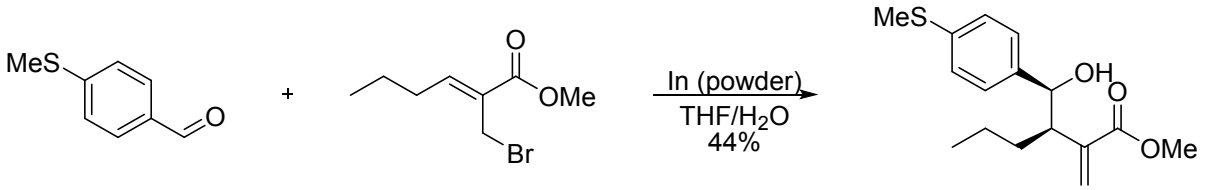

**Methyl 2-((1-hydroxycyclopentyl)methyl)prop-2-enoate**. $R_f$ = 0.30, 80 : 20 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 6.26 (s, 1H), 5.68 (s, 1H), 3.78 (s, 3H), 3.78 (s, 1H) 2.65 (s, 2H), 1.82-1.55 (m, 8H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 169.2, 137.6, 128.3, 81.4, 52.2, 42.9, 39.4, 23.4. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 185.1, found 185.2; for $[M+Na]^+$ 207.1, found 207.2.



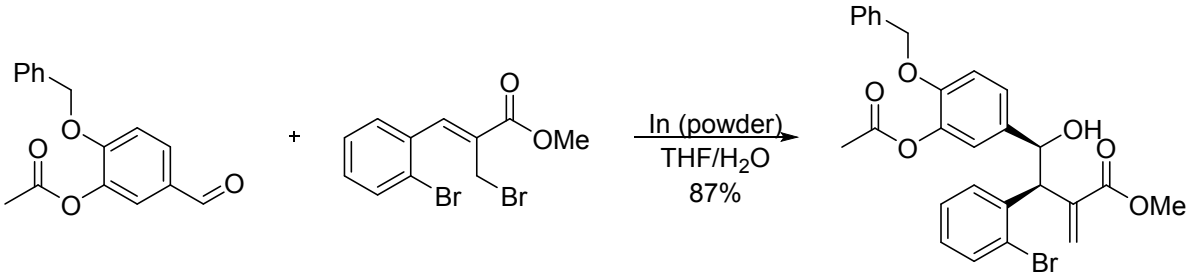

**Methyl *syn*-4-hydroxy-3-(4-methoxyphenyl)-2-methylene-4-(4-methylphenyl)butanoate**. 4-Methylbenzaldehyde was distilled prior to use. $R_f$ = 0.43, 70 : 30 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.21 (d, J = 8.7 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 7.9 Hz, 2H), 6.81 (d, J = 8.7 Hz, 2H), 6.18 (s, 1H), 5.75 (s, 1H), 5.12 (d, J = 7.8 Hz, 1H), 4.21 (d, J = 7.9 Hz, 1H), 3.73 (s, 3H), 3.52 (s, 3H), 2.29 (s, 3H), 2.22 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 167.0, 158.6, 141.4, 139.3, 137.2, 130.6, 130.2, 128.8, 126.9, 126.3, 113.8, 75.5, 55.1, 53.3, 51.8, 21.1. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 349.1, found 349.2.



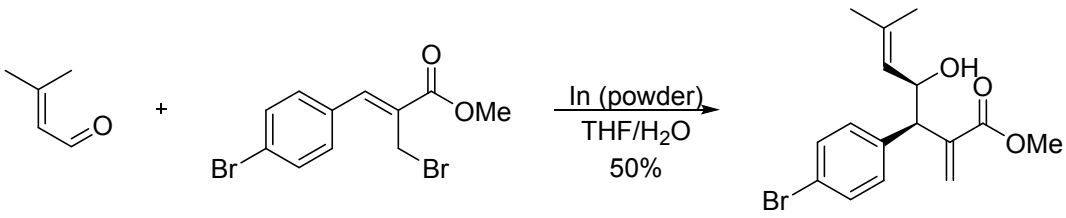

**Methyl *syn*-3-(3-bromophenyl)-6-(*t*-butyldimethylsilyloxy)-4-hydroxy-2-methylenehexanoate**. An additional 63% of unprotected product was obtained from this reaction. $R_f$ = 0.63, 40 : 60 = Hex : EtOAc, stain = $I_2$, 2,4-DNP, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.49 (s, 1H), 7.31 (dd, J = 12.3, 7.0 Hz, 2H), 7.14 (t, J = 7.8 Hz, 1H), 6.35 (s, 1H), 5.85 (s, 1H), 4.38 (t, J = 8.0 Hz, 1H), 3.89-3.78 (m, 3H), 3.67 (s, 3H), 3.24 (s, 1H), 1.70 (m, 1H), 1.57 (m, 1H), 0.87 (s, 9H), 0.04 (s & s, J = 2.9 Hz, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 167.1, 142.1, 141.2, 132.3, 129.9, 129.8, 128.2, 126.8, 122.4, 72.4, 62.3, 52.3, 52.1, 37.0, 25.9, 25.8, 18.2, -5.5. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 465.1, found 465.3.



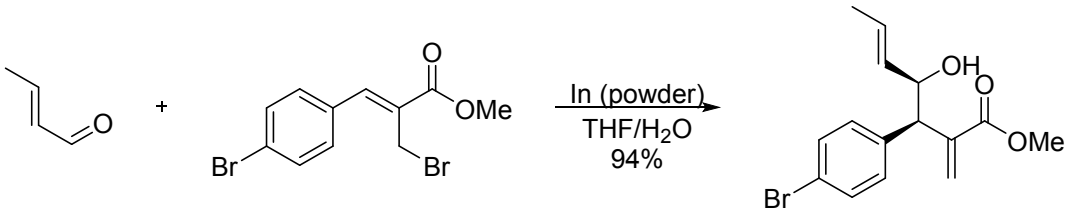

**Methyl *syn*-3-((hydroxyl)(4-methylthiophenyl)methyl)2-methylenehexanoate**. $R_f$ = 0.43, 75 : 25 = Hex : EtOAc, stain = $I_2$, *p*-Anis., Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.22 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 8.6 Hz, 2H), 6.22 (s, 1H), 5.42 (s, 1H), 4.79 (d, J = 4.5 Hz, 1H), 3.73 (s, 3H), 2.95 (dt, J = 9.9, 4.6 Hz, 1H), 2.85 (s, 1H), 2.47 (s, 3H), 1.63-1.45 (m, 2H), 1.30-1.20 (m, 1H), 1.14-1.05 (m, 1H), 0.82 (t, J = 7.3 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 168.5, 140.3, 139.6, 137.0, 127.2, 127.1, 126.2, 76.0, 52.1, 49.0, 29.8, 20.5, 15.9, 14.0. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 295.1, found 295.3.




**Methyl *syn*-4-(3-acetoxy-4-(benzyloxy)phenyl)-3-(2-bromophenyl)-4-hydroxy-2-methylenebutanoate**. $R_f$ = 0.37, 70 : 30 = Hex : EtOAc, stain = $I_2$, *p*-Anis., $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, J = 7.8 Hz, 1H), 7.47 (d, J = 7.9 Hz, 1H), 7.39 (m, J = 7.2 Hz, 2H), 7.31 (t, J = 7.3 Hz, 2H), 7.25 (t, J = 7.4 Hz, 2H), 7.03 (t, J = 8.2 Hz, 1H), 6.73 (m, J = 10.3 Hz, 3H), 6.24 (s, 1H), 5.70 (s, 1H), 5.19 (m, 1H), 5.06 (s, 2H), 4.75 (d, J = 7.1 Hz, 1H), 3.72 (s, 3H), 3.49 (s, 3H), 2.51 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.6, 149.2, 147.4, 140.1, 138.1, 137.0, 135.2, 132.9, 130.2, 128.3, 128.1, 127.9, 127.6, 127.1, 126.9, 126.8, 119.1, 113.4, 110.5, 74.8, 70.8, 55.7, 52.3, 51.7. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+Na]^+$ 547.1, found 547.5

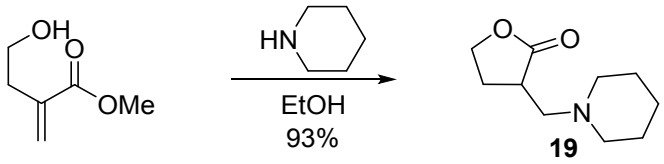



**Methyl *syn*-3-(4-bromophenyl)-4-hydroxy-6-methyl-2-methylenehept-5-enoate**. $R_f$ = 0.28, 75 : 25 = Hex : EtOAc, stain = $I_2$, *p*-Anis., Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 7.0 Hz, 2H), 7.05 (d, J = 7.0 Hz, 2H), 6.34 (s, 1H), 5.87 (dd, J = 15.2, 6.4 Hz, 1H), 5.58 (s, 1H), 5.51 (d, J = 15.5 Hz, 1H), 4.56 (s, 1H), 3.66 (s, 3H), 2.42 (s, 1H), 1.28 (s, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.8, 142.3, 140.5, 140.1, 131.4, 129.9, 126.8, 126.2, 120.3, 70.5, 51.8, 48.1, 29.7, 29.6. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+K]^+$ 377.2, found 377.0.



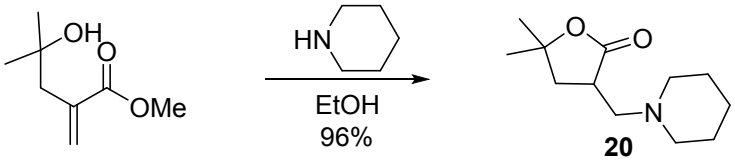

**Methyl *syn*- (5*E*)-3-(4-bromophenyl)-4-hydroxy-2-methylenehept-5-enoate**. $R_f$ = 0.56, 70 : 30 = Hex : EtOAc, stain = $I_2$, *p*-Anis., $KMnO_4$. $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.41 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 6.33 (s, 1H), 5.79 (s, 1H), 5.67 (dd, J = 15.3, 6.6 Hz, 1H), 5.42 (ddd, J = 15.3, 7.3, 1.6 Hz, 1H), 4.55 (t, J = 7.2 Hz, 1H), 3.91 (d, J = 7.2 Hz, 1H), 3.65 (s, 3H), 2.01 (d, J = 1.7 Hz, 1H), 1.65 (d, J = 6.4, 1.2 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 167.0, 140.8, 138.1, 131.8, 131.3, 131.0, 128.7, 126.9, 120.8, 73.8, 52.2, 52.0, 17.7. Mass: LRMS (ESI+) *m/z* calcd for $[M+K]^+$ 363.0, found 363.3.

## Aminolactonization of Example Substrates




**19**

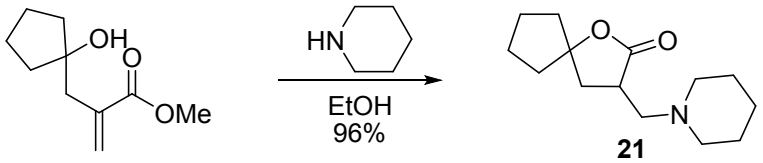
**2-((piperidin-1-yl)methyl)butano-4-lactone** (**19**). Piperidine was distilled prior to use. $R_f$ = 0.13, 10 : 90 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 4.36 (m, 1H), 4.22 (q, J = 8.7 Hz, 1H), 2.84-2.69 (m, 2H), 2.54-2.30 (m, 6H), 2.17 (M, 1H), 1.57 (m, 4H), 1.43 (m, 2H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 178.9, 66.7, 59.0, 54.6, 38.0, 28.1, 25.8, 24.1. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 184.1, found 184.3.




**20**

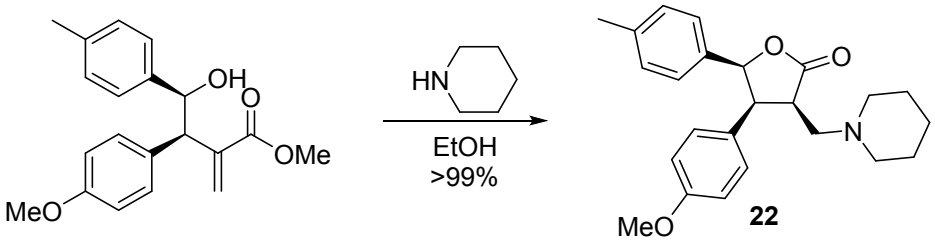
**4,4-dimethyl-2-((piperidin-1-yl)methyl)butano-4-lactone** (**20**). Piperidine was distilled prior to use. $R_f$ = 0.13, 100% EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 3.00 (s, 1H), 2.86 (dd, J = 12.8, 4.0 Hz, 1H), 2.52-2.28 (m, 6H), 1.94 (t, J = 11.9 Hz, 1H), 1.56 (m, 4H), 1.47 (s, 3H), 1.43 (m,

2H), 1.39 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 178.1, 82.7, 59.7, 54.7, 41.2, 39.7, 29.0, 27.3, 25.9, 24.2. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 212.2, found 212.3.



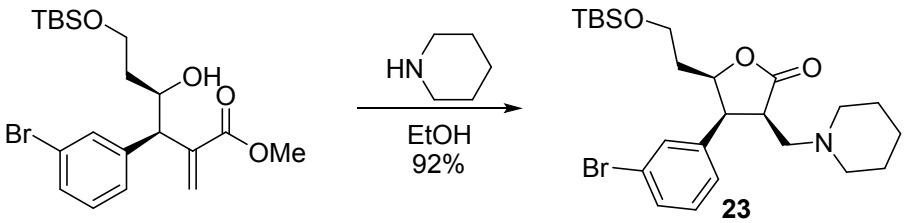

**21**

**3-((piperidin-1-yl)methyl)-1-oxaspiro[4.4]nonan-2-one** (**21**). Piperidine was distilled prior to use. $R_f$ = 0.13, 95 : 5 = EtOAc : MeOH, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.92 (m, 1H), 2.85 (dd, J = 12.7, 4.1 Hz, 1H), 2.48 (m, 3H), 2.37 (m, 3H), 2.13 (m, 1H), 2.03 (m, 1H), 1.94 (m, 1H), 1.85-1.42 (m, 12H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 178.1, 93.1, 59.6, 54.7, 40.0, 38.9, 38.6, 25.9, 24.2, 24.1, 23.6. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 238.2, found 238.3.




**22**

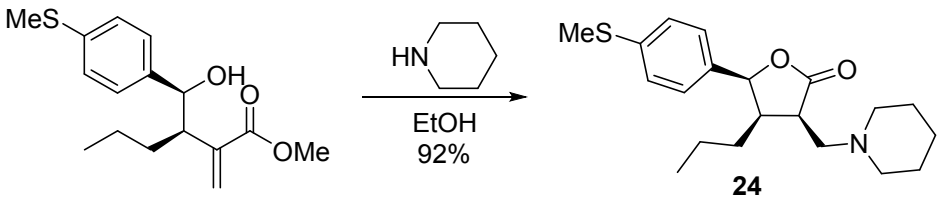
**(2,3-*cis*,2,4-*cis*)-3-(4-methoxyphenyl)-4-(4-methylphenyl)-2-((piperidin-1-yl)methyl)butano-4-lactone** (**22**). Piperidine was distilled prior to use. 99 : 1 = dr; >99% yield of *cis*,*cis*-product. $R_f$ = 0.21, 10 : 90 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.00 (d, J = 7.9 Hz, 2H), 6.92 (d, J = 7.9 Hz, 2H), 6.82 (d, J = 8.3 Hz, 2H), 6.58 (d, J = 8.3 Hz, 2H), 5.76 (d, J = 5.0 Hz, 1H), 4.03 (m, 1H), 3.61 (s, 3H), 3.38 (m, 1H), 2.70 (dd, J = 13.2, 3.1 Hz, 1H), 2.37 (m, 2H), 2.19 (m, 1H), 2.16 (s, 3H), 2.09 (m, 2H), 1.49 (m, 4H), 1.36 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.9, 158.2, 136.6, 132.8, 130.4, 128.6, 126.7, 125.6, 125.3, 113.2, 83.1, 54.8, 54.6, 54.3, 51.2, 46.9, 46.1, 26.6, 26.0, 24.7, 24.1, 20.9. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+Na]^+$ 380.2, found 380.4.




**23**

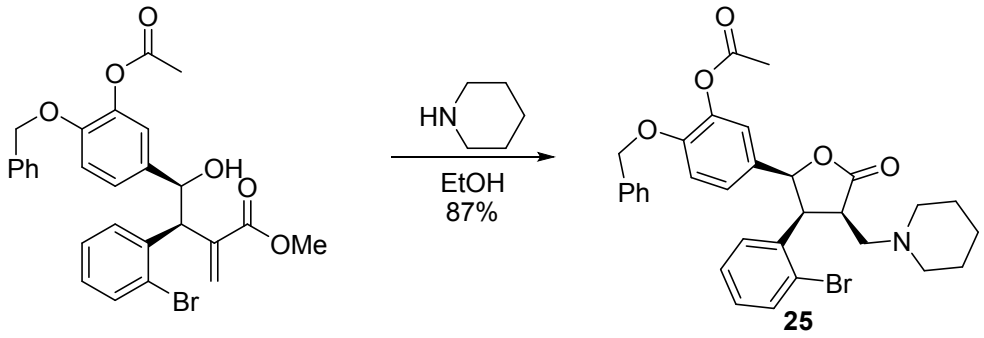
**(2,3-*cis*,2,4-*cis*)-3-(3-bromophenyl)-6-(*t*-butyldimethylsilyloxy)-2-((piperidin-1-yl)methyl)hexano-4-lactone** (**23**). Piperidine was distilled prior to use. 93 : 7 = dr; 92% yield of *cis*,*cis*-product. $R_f$ = 0.11, 70 : 30 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.40 (m, 1H), 7.26 (s,

1H), 7.16 (t, J = 7.9 Hz, 1H), 7.01 (d, J = 7.7 Hz, 1H), 4.85 (dt, J = 9.2, 4.6 Hz, 1H), 3.71-3.59 (m, 3H), 3.27 (m, 1H), 2.59 (dd, J = 13.3, 4.0 Hz, 1H), 2.34 (m, 2H), 2.04 (dd, J = 14.1, 8.8 Hz, 1H), 1.97 (m, 2H), 1.69 (m, 1H), 1.53-1.35 (m, 8H), 0.87 (s, 9H), 0.02 (s, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.7, 138.0, 133.0, 130.6, 129.8, 127.6, 122.5, 79.1, 59.2, 54.3, 54.2, 49.6, 45.3, 34.1, 25.9, 24.2, 18.3, -5.4. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 496.2, found 496.4.



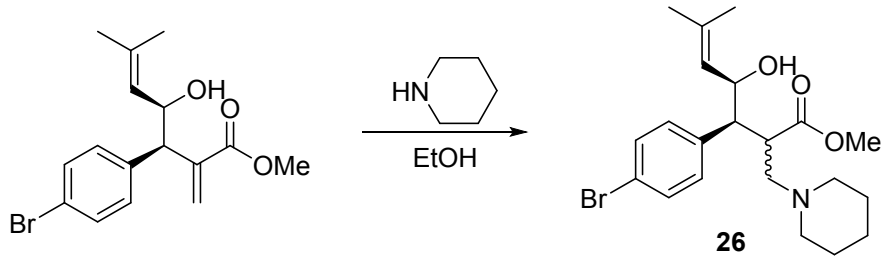

**24**

**(2,3-*cis*,2,4-*cis*)-4-(4-(methylthio)phenyl)-2-((piperidin-1-yl)methyl)-3-propylbutano-4-lactone** (**24**). Piperidine was distilled prior to use. 92 : 8 = dr; 92% yield of *cis*,*cis*-product. $R_f$ = 0.12, 50 : 50 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.23 (m, 4H), 5.47 (d, J = 4.6 Hz, 1H), m.12 (s, 1H), 2.81-2.64 (m, 2H), 2.46 (s, 3H), 2.48-2.39 (m, 1H), 2.32 (m, 2H), 1.55 (m, 4H), 1.42 (m, 2H), 1.16 (m, 2H), 0.92 (m, 1H), 0.77 (m, 1H), 0.61 (t, J = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.5, 137.9, 132.8, 126.0, 125.7, 82.3, 54.3, 54.1, 44.2, 43.5, 25.8, 25.6, 24.1, 19.9, 15.3, 14.0. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 348.2, found 348.4.



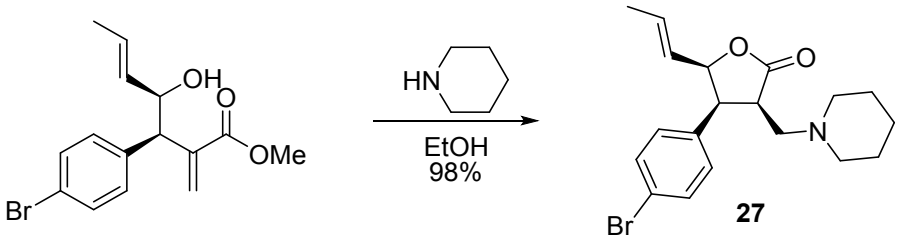

**25**

**(2,3-*cis*,2,4-*cis*)-4-(3-acetoxy-4-benzyloxyphenyl)-3-(2-bromophenyl)-2-((piperidin-1-yl)methyl)butano-4-lactone** (**25**). Piperidine was distilled prior to use. 99 : 1 = dr; >99% yield of *cis*,*cis*-product. $R_f$ = 0.41, 95 : 5 = EtOAc : MeOH, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.39-7.26 (m, 7H), 7.04 (t, J = 7.3, Hz, 1H), 6.92 (d, J = 7.7 Hz, 2H), 6.72 (d, J = 7.6 Hz, 1H), 6.66 (d, J = 8.3 Hz, 1H), 6.58 (s, 1H), 5.81 (d, J = 5.6 Hz, 1H), 5.00 (s, 2H), 4.83 (dd, J = 7.9, 5.8 Hz, 1H), 3.71 (s, 3H), 3.49 (m, 1H), 2.73 (dd, J = 13.3, 4.3 Hz, 1H), 2.34 (m, 2H), 2.23 (dd, J = 13.2, 9.6 Hz, 1H), 1.98 (dt, J = 10.6, 5.2 Hz, 2H), 1.49 (m, 4H), 1.34 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.8, 149.0, 147.1, 136.8, 134.7, 132.9, 129.0, 128.4, 128.3, 127.7, 127.2, 126.7, 126.6, 117.7, 113.3, 108.8, 82.4, 70.7, 55.7, 54.4, 54.2, 49.0, 45.2, 25.8, 24.2. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 578.2, found 578.5.



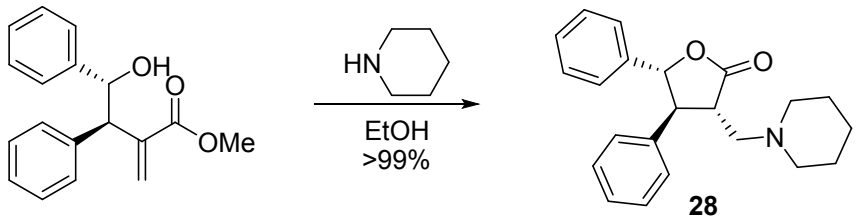

**26**

**Methyl (3,4-*cis*)-3-(4-bromophenyl)-4-hydroxy-6-methyl-2-((piperidin-1-yl)methyl)hept-5-enoate** (**26**). Piperidine was distilled prior to use. $R_f$ = 0.25, 90 : 10 = EtOAc : MeOH, stain = Dragendorff-Munier, $KMnO_4$. Major product: $^1$H NMR (300 MHz, $CDCl_3$): δ 7.43 (d, J = 8.2 Hz, 2H), 7.05 (d, J = 8.2 Hz, 2H), 5.77-5.60 (m, 2H), 3.65 (s, 3H), 3.38 (m, 1H), 3.01 (td, J = 10.6, 4.3 Hz, 1H), 2.54 (t, J = 11.6 Hz, 1H), 2.34 (m, 2H), 2.13 (m, 2H), 1.99 (dd, J = 12.2, 4.2 Hz, 1H), 1.45 (m, 4H), 1.34 (m, 2H), 1.24 (d, J = 4.3 Hz, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 174.7, 140.9, 139.9, 131.9, 129.5, 127.0, 120.5, 70.5, 59.7, 54.4, 51.4, 49.8, 49.6, 29.8, 26.1, 24.3. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+Na]^+$ 414.1, found 414.4.




**27**

**(2,3-*cis*,2,4-*cis*)-5*E*-3-(4-bromophenyl)-2-((piperidin-1-yl)methyl)hept-5-en-4-lactone** (**27**). Piperidine was distilled prior to use. 98 : 2 = dr; 98% yield of *cis*,*cis*-product. $R_f$ = 0.21, 95 : 5 = EtOAc : MeOH, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 8.5 Hz, 2H), 6.97 (d, J = 8.6 Hz, 2H), 5.86 (dq, J = 13.4, 6.5 Hz, 1H), 5.16 (dd, J = 15.0, 8.0 Hz, 1H), 5.04 (dd, J = 8.0, 5.0 Hz, 1H), 3.70 (dd, J = 7.5, 5.0 Hz, 1H), 3.25 (m, 1H), 2.61 (dd, J = 13.2, 3.9 Hz, 1H), 2.35 (m, 2H), 2.03 (m, 3H), 1.60 (d, J = 6.6 Hz, 3H), 1.47 (m, 4H), 1.38 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.6, 134.6, 133.0, 131.4, 131.1, 125.1, 121.2, 83.1, 54.3, 54.2, 50.6, 45.3, 26.0, 24.2, 17.8. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 378.1, found 378.3.

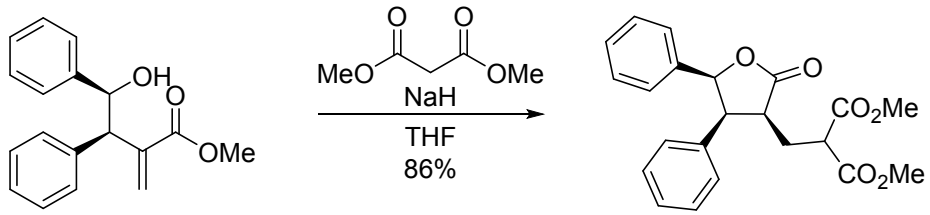



**28**

**(2,3-*trans*,2,4-*cis*)-2-((piperidin-1-yl)methyl)-3,4-diphenylbutano-4-lactone** (**28**): Piperidine was distilled prior to use. The starting material was prepared according to the method of Ramachandran and co-workers.[1] 99 : 1 = dr; >99% yield of *cis*,*cis*-product. $R_f$ = 0.36, 70 : 30 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.35-7.15 (m, 6H), 7.15 (m, 4H), 5.38 (d, J = 9.7 Hz, 1H), 3.57 (dd, J = 11.3, 9.7 Hz, 1H), 3.10 (dt, J = 11.3, 5.8 Hz, 1H), 2.70 (dd, J = 5.7, 3.1 Hz, 2H), 2.23 (m, 4H), 1.28 (m, 6H). $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 177.2, 138.2, 138.0, 128.8, 128.5, 128.4, 128.1, 127.5, 125.7, 85.7, 57.1, 54.9, 54.8, 47.9, 25.9, 24.1. Mass: LRMS (ESI+) *m/z* calcd for $[M+H]^+$ 336.2, found 336.2.

[1]Ramachandran, P. V.; Garner, G.; Pratihar, D. *Org. Lett.* **2007**, *9*, 4753.

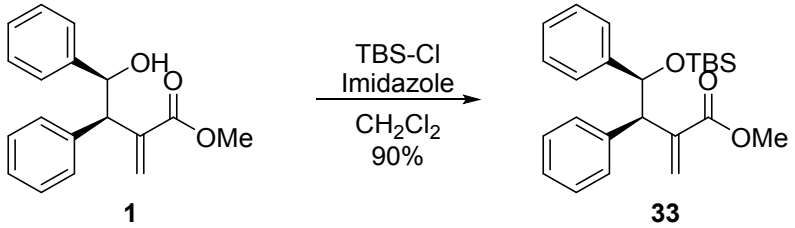
## Related Domino Reaction




**1** **31**

**(2,3-*cis*,2,4-*cis*)-2-(2,2-bis(methoxycarbonyl)ethyl)-3,4-diphenylbutano-4-lactone** (**31**): Into a round bottom flask charged with a stirbar, sodium hydride (1.01 eq.), and THF (0.1 M with respect to dimethyl malonate) was added dimethyl malonate dropwise over 10 minutes at 0 °C. After stirring for 30 minutes, a 1.0 M solution of **1** in THF was then added in one portion. After the reaction was complete, $(NH_4)_2SO_4$ (sat., aq.) was added to quench, and the organic product was extracted with ethyl acetate. The crude product was purified via column chromatography to furnish **31**. 99 : 1 = dr; >99% yield of *cis*,*cis*-product. $R_f$ = 0.36, 70 : 30 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.14-7.00 (m, 8H), 6.86 (m, 2H), 5.82 (d, J = 5.2 Hz, 1H), 3.99 (dd, J = 7.6, 5.3 Hz, 1H), 3.71 (s, 3H), 3.67 (s, 3H), 3.32 (q, J = 7.3 Hz, 1H), 2.24 (dt, J = 14.4, 7.2 Hz, 1H), 1.88 (dt, J = 14.9, 7.6 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 177.6, 169.2, 169.1, 135.3, 133.7, 129.0, 128.3, 127.8, 127.5, 127.3, 125.2, 82.8, 52.6, 52.6, 51.8, 48.8, 43.8, 25.2.

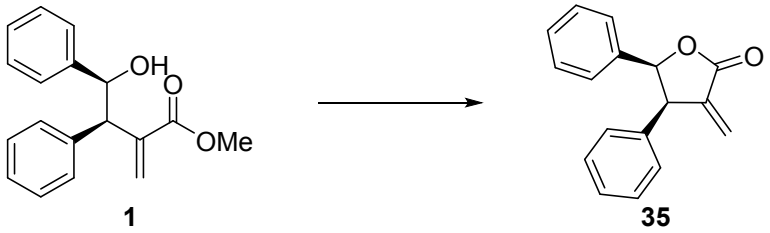
## Preparation of 33 (TBS-Protected Derivative of 1)




**1** **33**

**Methyl *syn*-4-(*t*-butyldimethylsilyloxy)-2-methylene-3,4-diphenylbutanoate** (**33**). Into a 15 mL round bottom flask charged with a stirbar was added 1.0 equiv. **1**. This material was then dissolved in $CH_2Cl_2$ to produce a 0.05 M solution. Added to this solution were 5.5 equiv. imidazole, followed by 5.4 equiv. *t*-butyldimethylsilyl chloride. The opaque solution was then stirred for 12 hrs, then was partitioned between $CH_2Cl_2$ and deionized water. The organic layer was then directly filtered through $Na_2SO_4$ and concentrated. The crude product was then purified via column chromatography to furnish **33**. $R_f$ = 0.46, 85 : 15 = Hex : EtOAc, stain = $I_2$, Vanillin, $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.37-7.15 (m, 10H), 6.20 (s, 1H), 5.68 (s, 1H), 5.21 (d, J = 7.4 Hz, 1H), 4.22 (d, J = 7.4 Hz, 1H), 3.60 (s, 3H), 0.69 (s, 9H), -0.23 (s, 3H), -0.38 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): 13C NMR (101 MHz, CDCl3) δ 167.3, 143.3, 140.9, 139.9, 129.8, 127.8, 127.7, 127.2, 126.5, 55.7, 51.8, 25.6, 17.9, -4.7, -5.5. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 419.2, found 419.3; for $[M+K]^+$ 435.2, found 435.3.

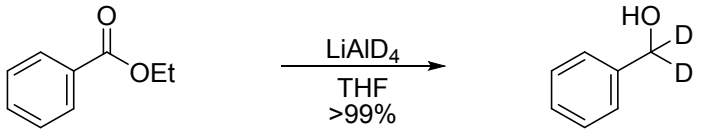
## Lactone 35



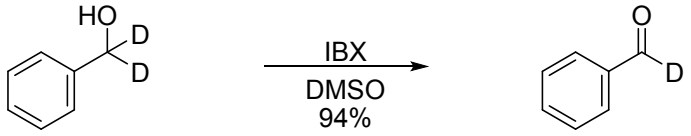

**1** **35**

***cis*-2-methylene-3,4-diphenylbutano-4-lactone** (**35**)**.** Triethylamine was distilled over KOH prior to use. $R_f$ = 0.44, 75 : 25 = Hex : EtOAc, stain = $I_2$, *p*-Anis., $KMnO_4$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.09-7.04 (d, 6H), 6.83 (m, 2H), 6.74 (m, 2H), 6.51 (d, J = 2.7 Hz, 1H), 5.83 (d, J = 8.3 Hz, 1H), 5.55 (d, J = 2.7 Hz, 1H), 4.67 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 170.8, 138.0, 136.3, 136.2, 129.3, 128.2, 127.9, 127.8, 127.3, 125.9, 124.8, 82.6, 51.9. Mass: LRMS (ESI+) *m/z* calcd for $[M+Na]^+$ 273.1, found 273.50

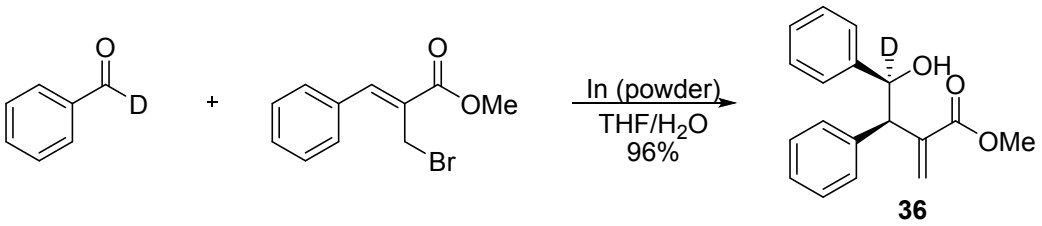
## Preparation of 36 (*γ*-Deuterio Derivative of 5)




**1,1-dideuterio-1-phenylmethanol**. A 250 mL round bottom flask was charged with a stirbar, 5 g ethyl benzoate, and 83 mL THF. After cooling to 0 °C, 890 mg (21.2 mmol, 0.65 equiv.) lithium aluminum deuteride were added. The reaction mixture was then stirred for 10 minutes, whereafter the cold bath was removed. The mixture was then heated to reflux for 12 hours. After cooling the reaction mixture to 0 °C, 25 mL saturated aqueous ammonium sulfate were added slowly to the mixture, followed by 10 mL 2.5 M NaOH (aq.) and 10 mL saturated aqueous Rochelle's Salt. After stirring for 3 hours, the product was extracted from the mixture with ethyl acetate, then dried with $Na_2SO_4$ to furnish 3.66 g (100%) pure 1,1-dideuterio-1-phenylmethanol. TLC information for product was identified by comparison with diprotiobenzyl alcohol. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.25 (m, 5H), 3.38 (s, 1H). $^2$H NMR (46 MHz, $CDCl_3$) δ 4.45. $^{13}$C NMR (101 MHz, $CDCl_3$): δ 140.8, 128.4, 127.4, 127.0, 64.1 (p).

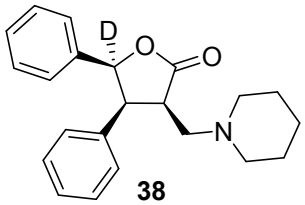



**1-deuteriobenzaldehyde.** Into a 200 mL round bottom flask that had been charged with a stirbar was added 3.4 g (30.9 mmol, 1.0 equiv.) 1,1-dideuterio-1-phenylmethanol, followed by 85 mL dimethyl sulfoxide. After adding 9.5 g (33.9 mmol, 1.1 equiv.) IBX, the suspension was stirred for 3 hours, after which time 50 mL deionized water were added at 0 °C. The suspension was then filtered, and the filtrand was washed four times with 100 mL portions of $CH_2Cl_2$. The combined organic volumes were then washed with three 250 mL portions of deionized water. The organic mixture was then filtered directly through $Na_2SO_4$ then concentrated to provide 3.12 g (94%) 1-deuteriobenzaldehyde. TLC information for product was identified by comparison with protiobenzaldehyde. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.88 (d, J = 8.2 Hz, 2H), 7.64 (t, J = 8.1 Hz, 1H), 7.53 (t, J = 7.3 Hz, 2H). $^2$H NMR (46 MHz, $CDCl_3$) δ 10.0. $^{13}$C NMR (75 MHz, $CDCl_3$): δ 191.8 (t) 136.0, 134.2, 129.3, 128.7.




**36**

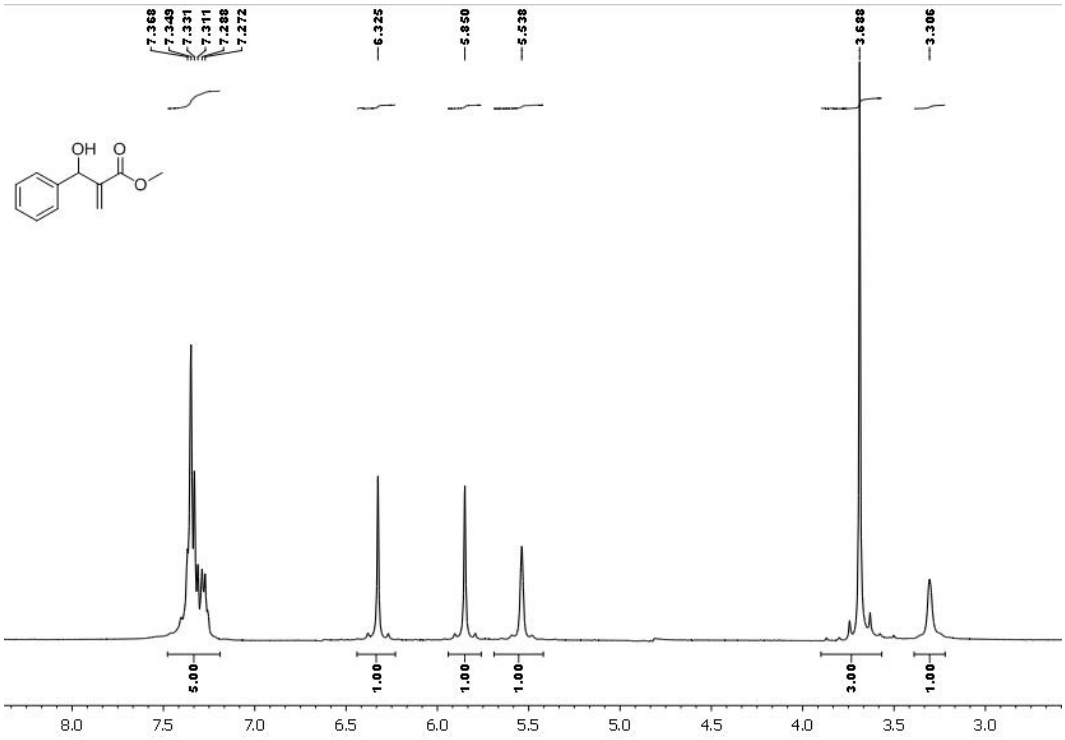
**Methyl *syn*-4-deuterio-4-hydroxy-2-methylene-3,4-diphenylbutanoate** (**36**): $R_f$ = 0.38, 75 : 25 = Hex : EtOAc, stain = $I_2$, $KMnO_4$. $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.30-7.21 (m, 10H), 6.21 (s, 1H), 5.78 (s, 1H), 4.29 (s, 1H), 3.52 (s, 3H), 2.38 (s, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 166.9, 142.1, 141.0, 138.7, 129.2, 128.3, 128.1, 127.6, 127.2, 127.0, 126.9, 126.8 75.0 (t, $J_{CD}$ = 16.5 Hz), 54.0, 51.8. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+Na]^+$ 306.1, found 306.1.



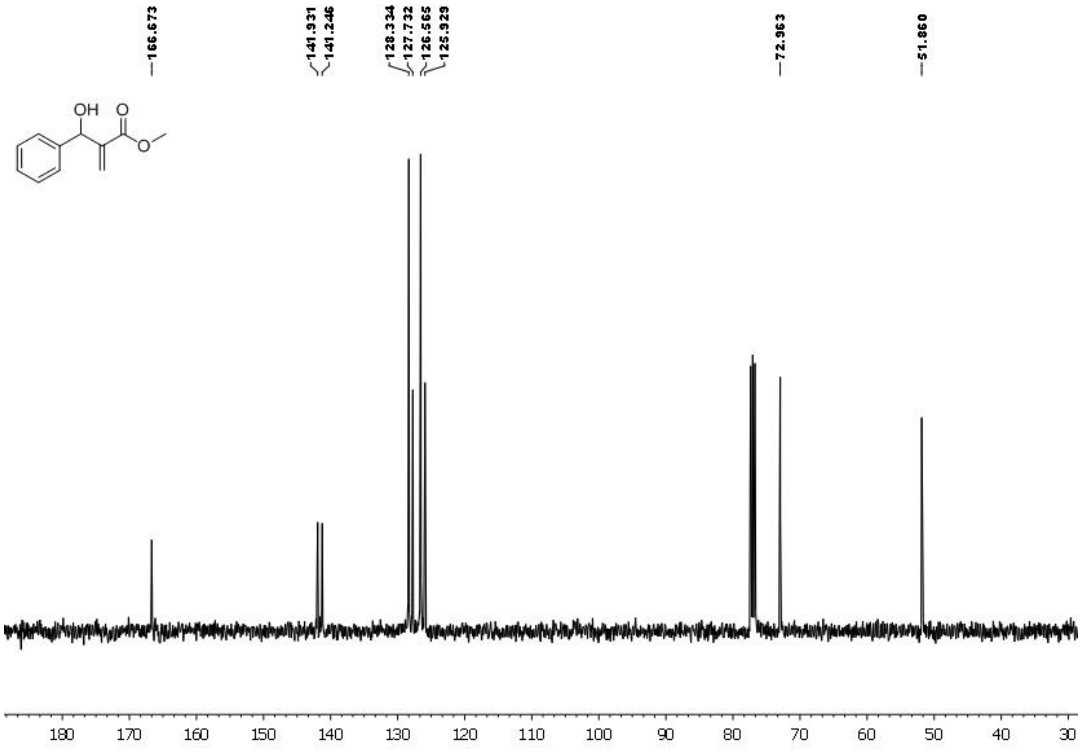

**38**

**(2,3-*cis*,2,4-*cis*)-4-deuterio-3,4-diphenyl-2-((piperidin-1-yl)methyl)butano-4-lactone** (**38**). $R_f$ = 0.18, 70 : 30 = Hex : EtOAc, stain = Dragendorff-Munier, $KMnO_4$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.13-6.88 (m, 10H), 4.09 (d, J = 7.5 Hz, 1H), 3.43 (m, 1H), 2.73 (dd, J = 13.3, 3.8 Hz, 1H), 2.37 (m, 2H), 2.19 (dd, J = 13.4, 8.9 Hz, 1H), 2.06 (m, 2H), 1.48 (m, 4H), 1.36 (m, 2H). $^2H$ NMR (46 MHz, $CDCl_3$) δ 5.81. $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 177.8, 135.8, 134.7, 129.4, 127.9, 127.8, 127.2, 126.9, 125.3, 82.5 (t), 54.7, 54.3, 51.8, 45.8, 26.0, 24.1. Mass: LRMS (ESI+) *m*/*z* calcd for $[M+H]^+$ 337.2, found 337.2; for $[M+Na]^+$ 359.2, found 359.3.

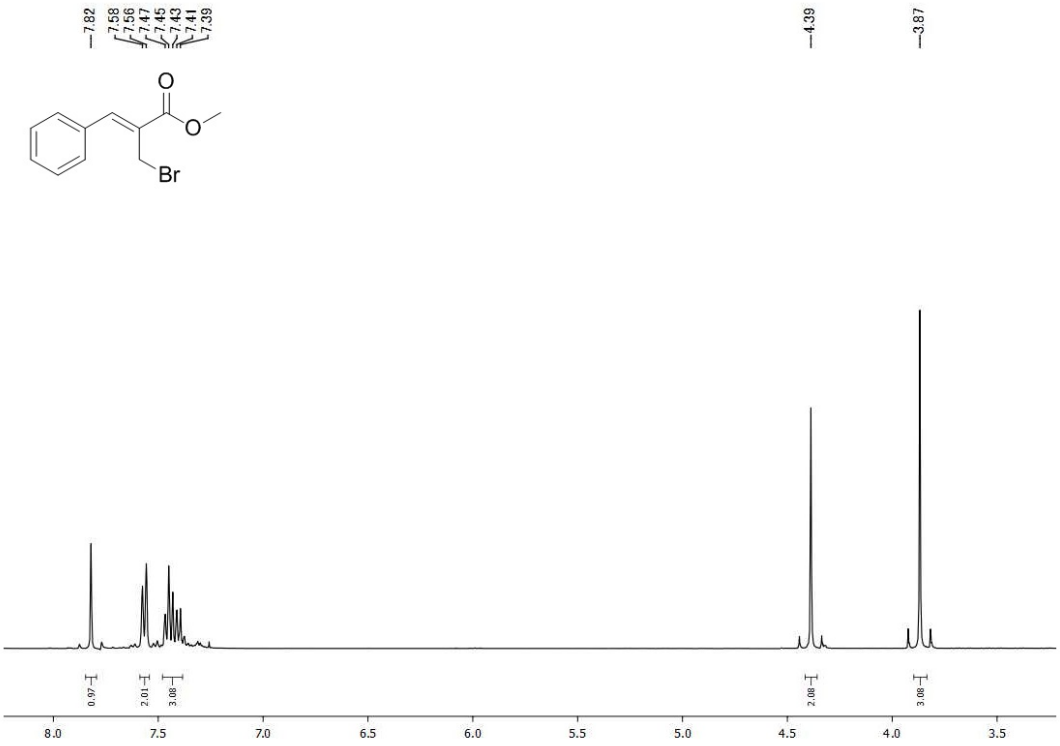
**NMR Spectra Associated with the Preparation of Butanoate Ester 1**



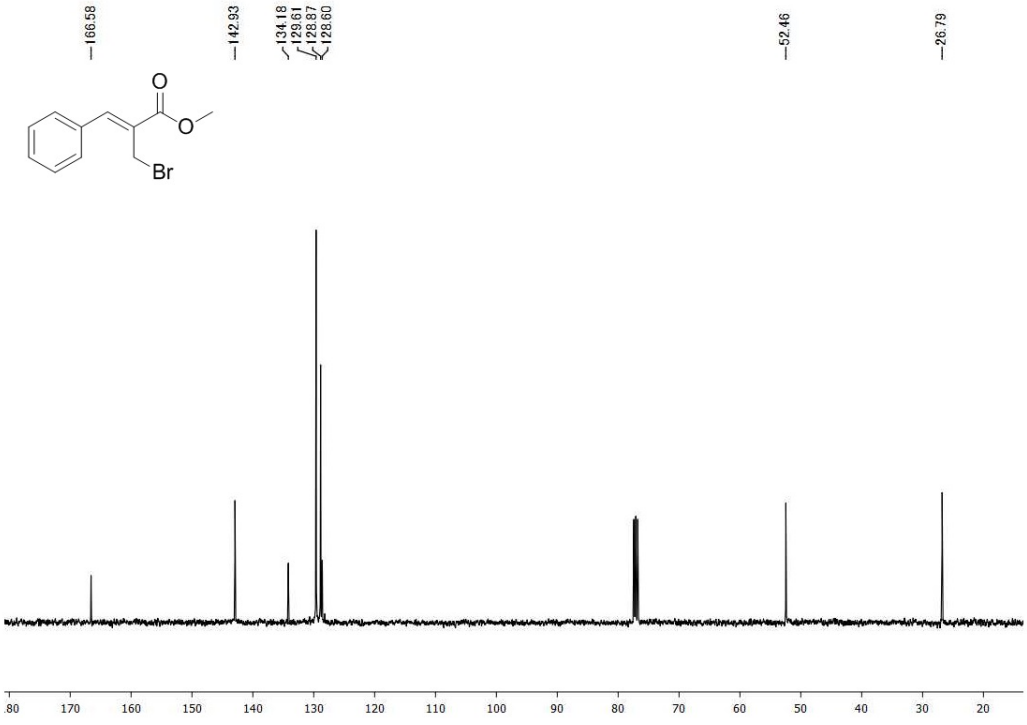

$^{1}$H NMR spectrum of methyl 2-((hydroxy)phenylmethyl)prop-2-enoate.



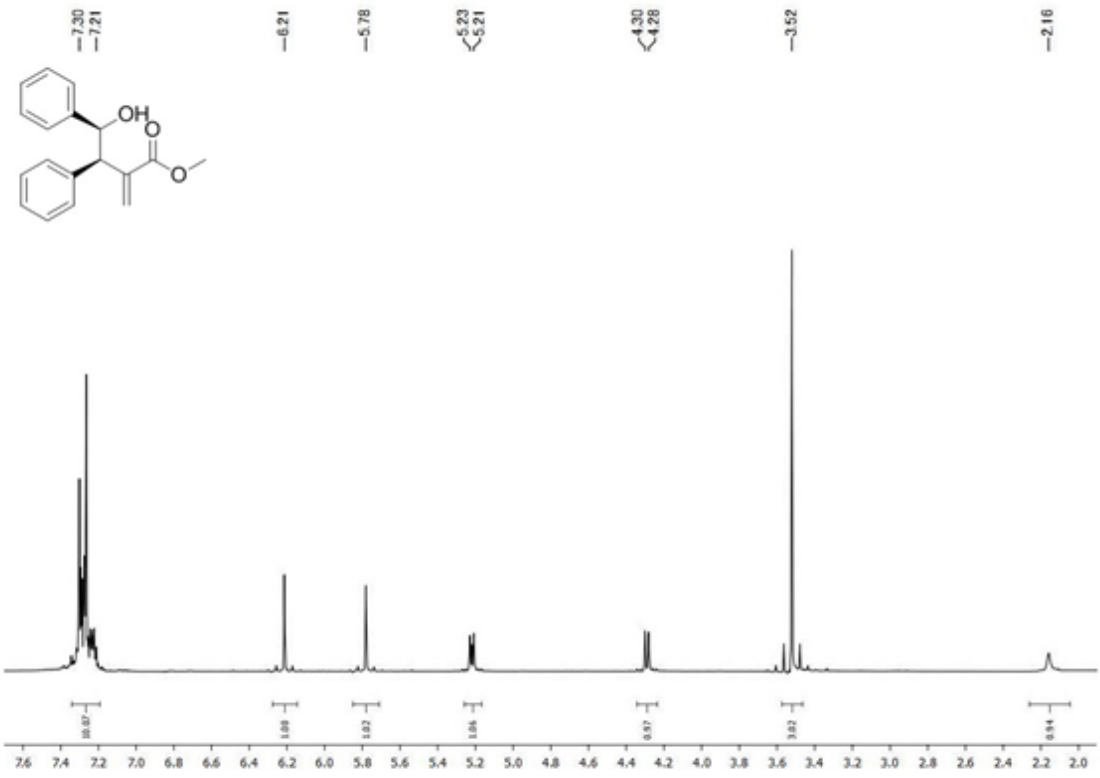

$^{13}$C NMR spectrum of methyl 2-((hydroxy)phenylmethyl)prop-2-enoate.



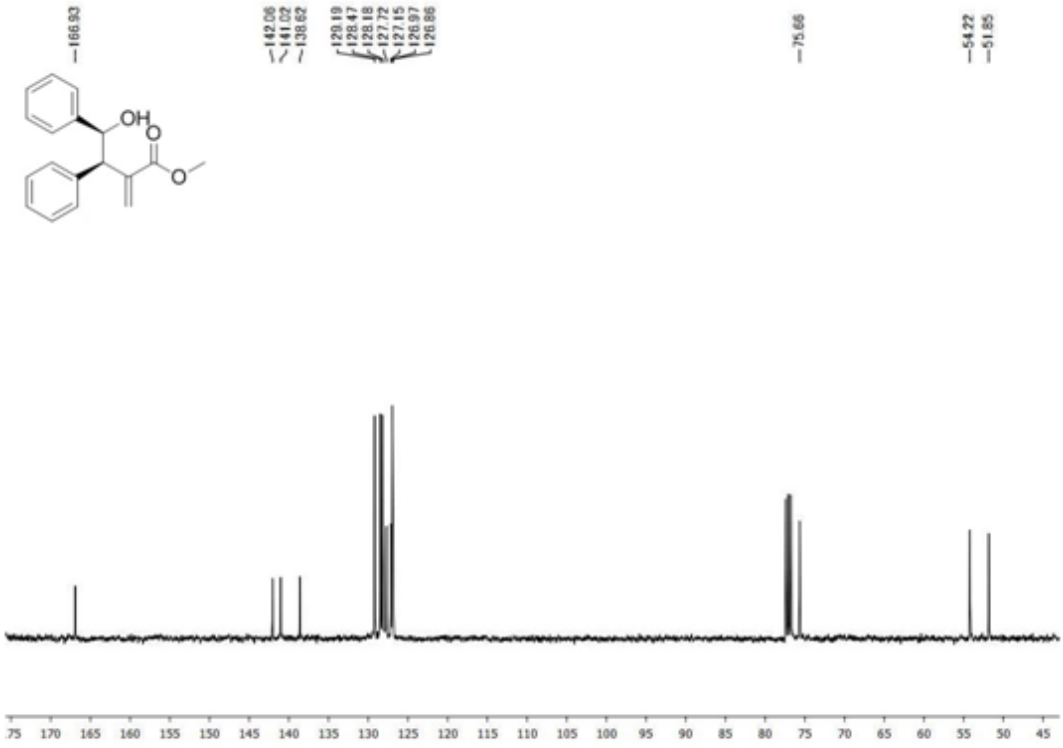

$^{1}$H NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-phenylprop-2-enoate.




$^{13}$C NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-phenylprop-2-enoate.

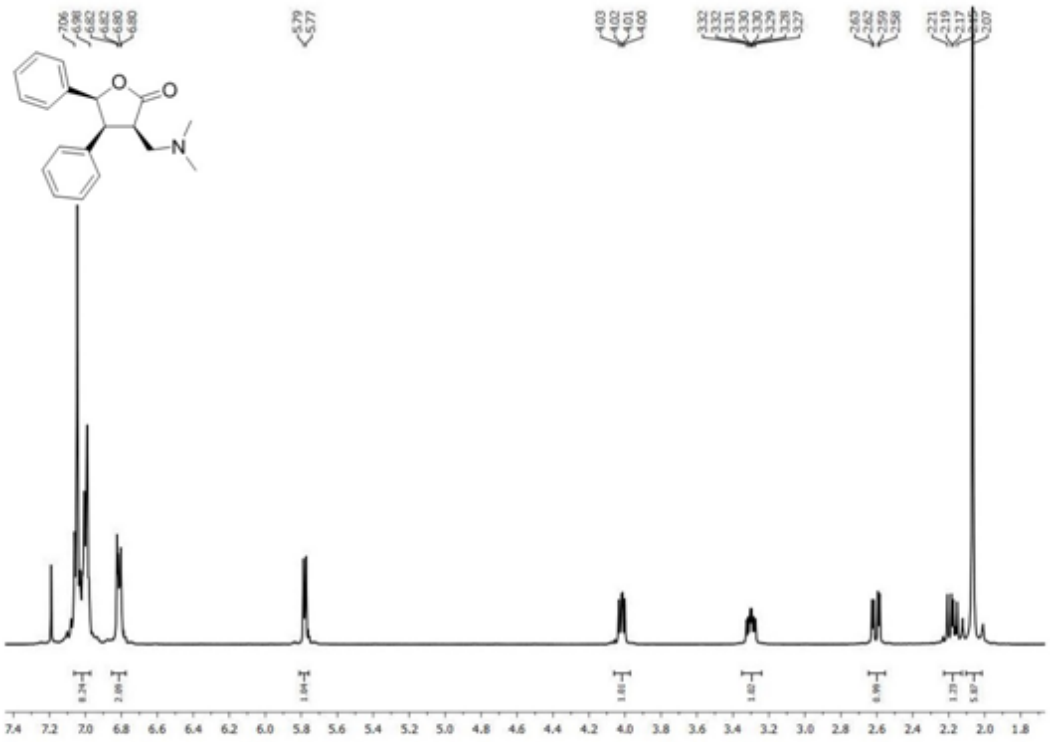



$^{1}$H NMR spectrum of **1**.

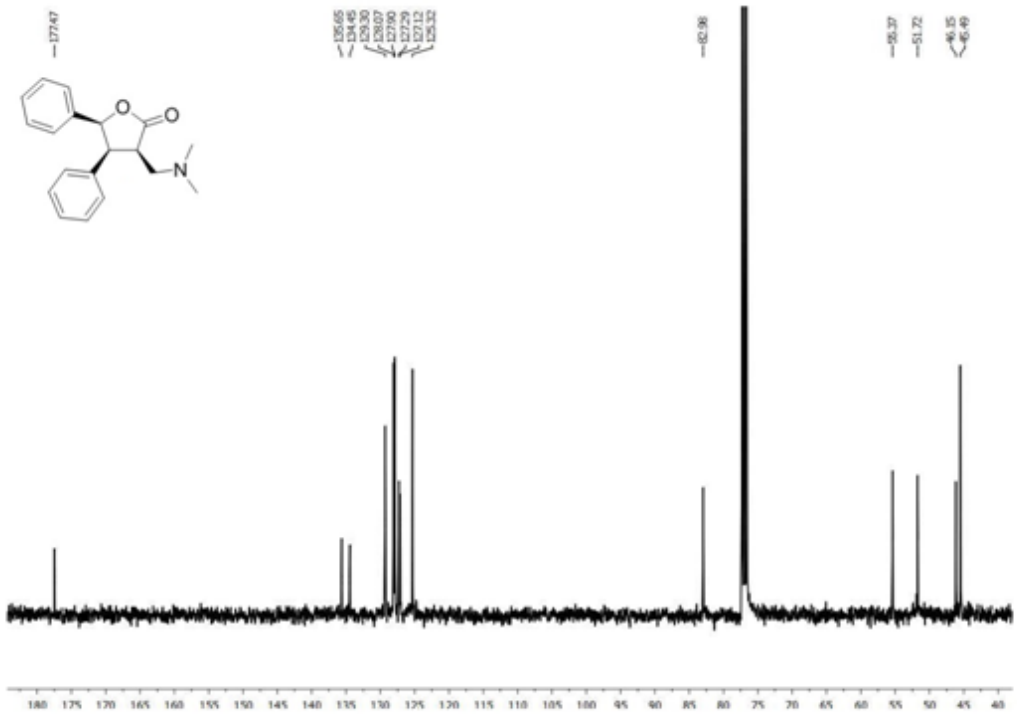



$^{13}$C NMR spectrum of **1**.

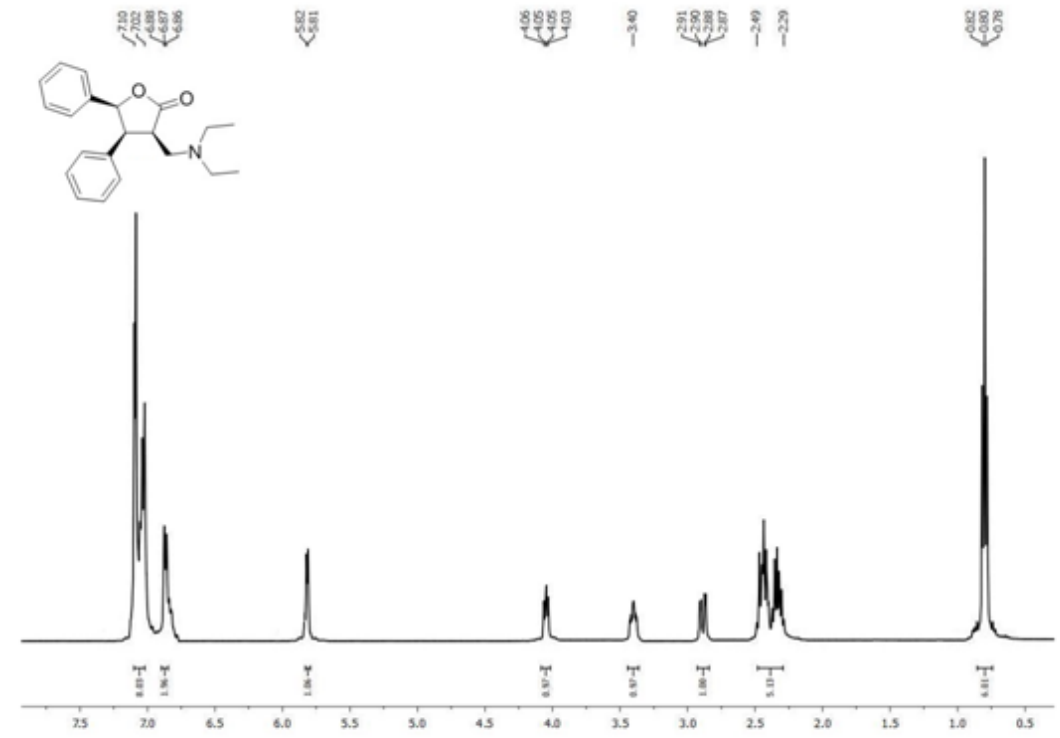
**NMR Spectra of Aminated Derivatives of 1**



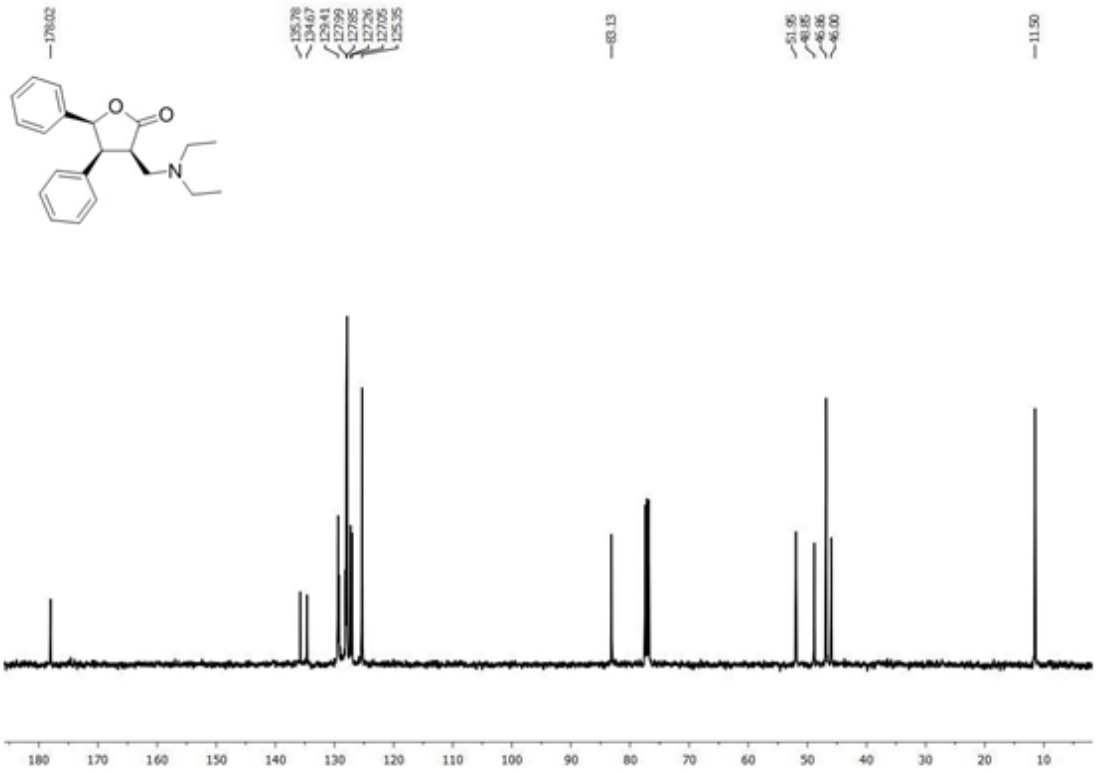
$^{1}$H NMR spectrum of **3**.



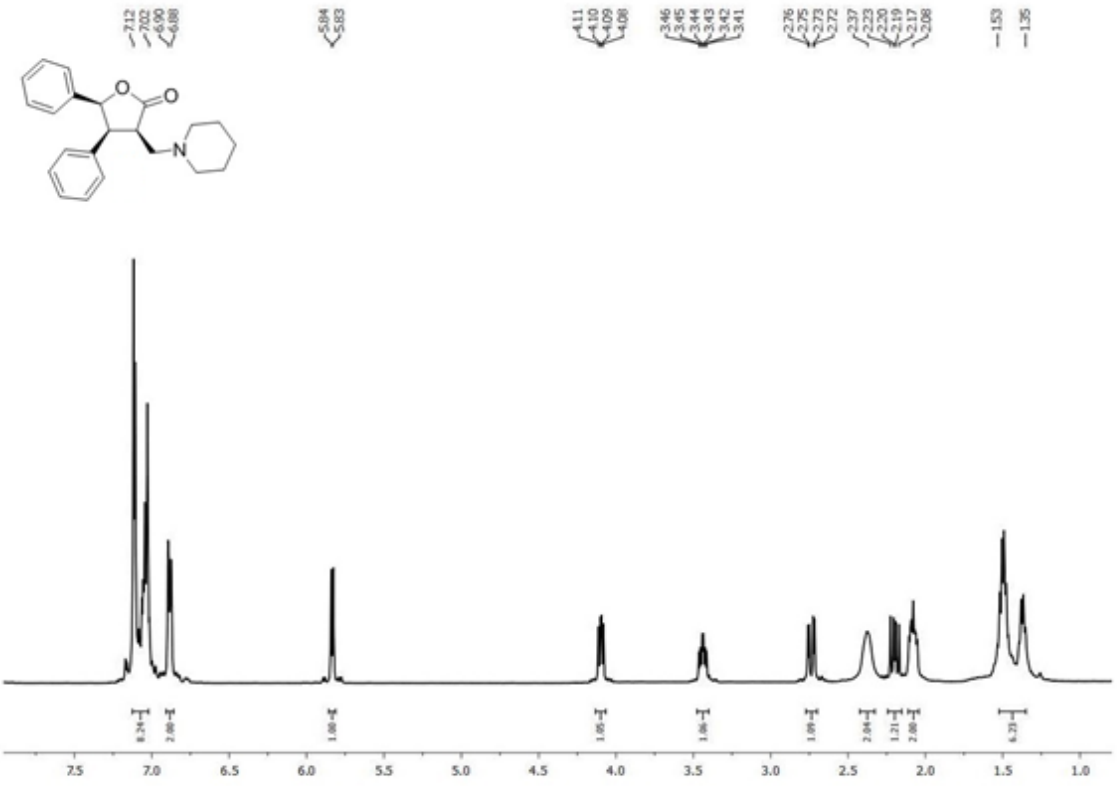
$^{13}$C NMR spectrum of **3**.



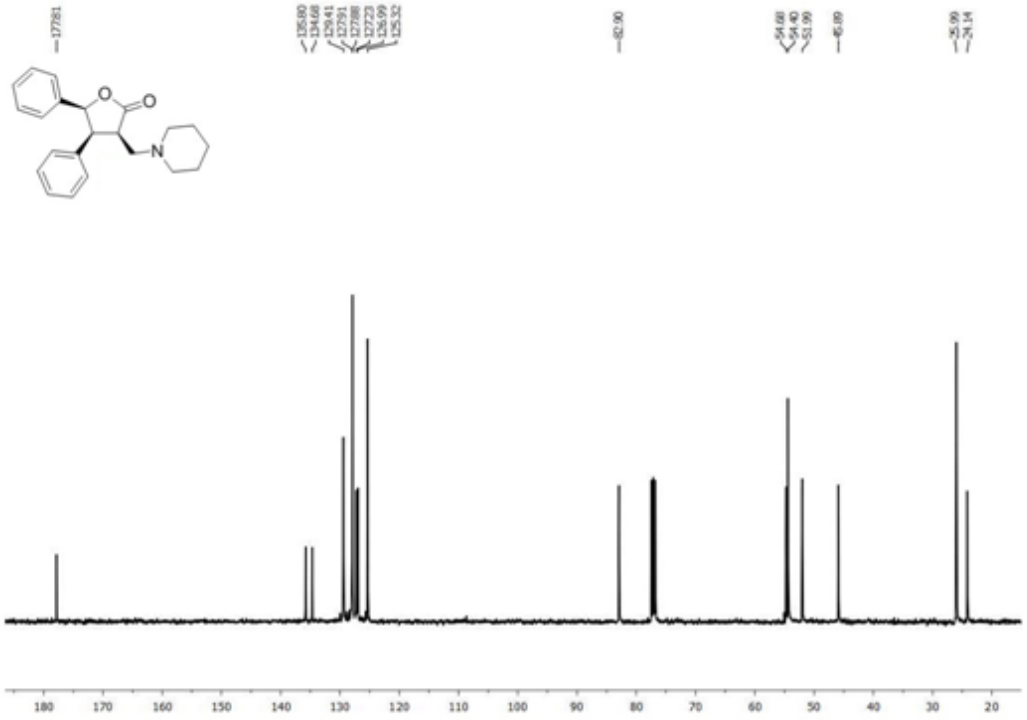
$^{1}$H NMR spectrum of **4**.



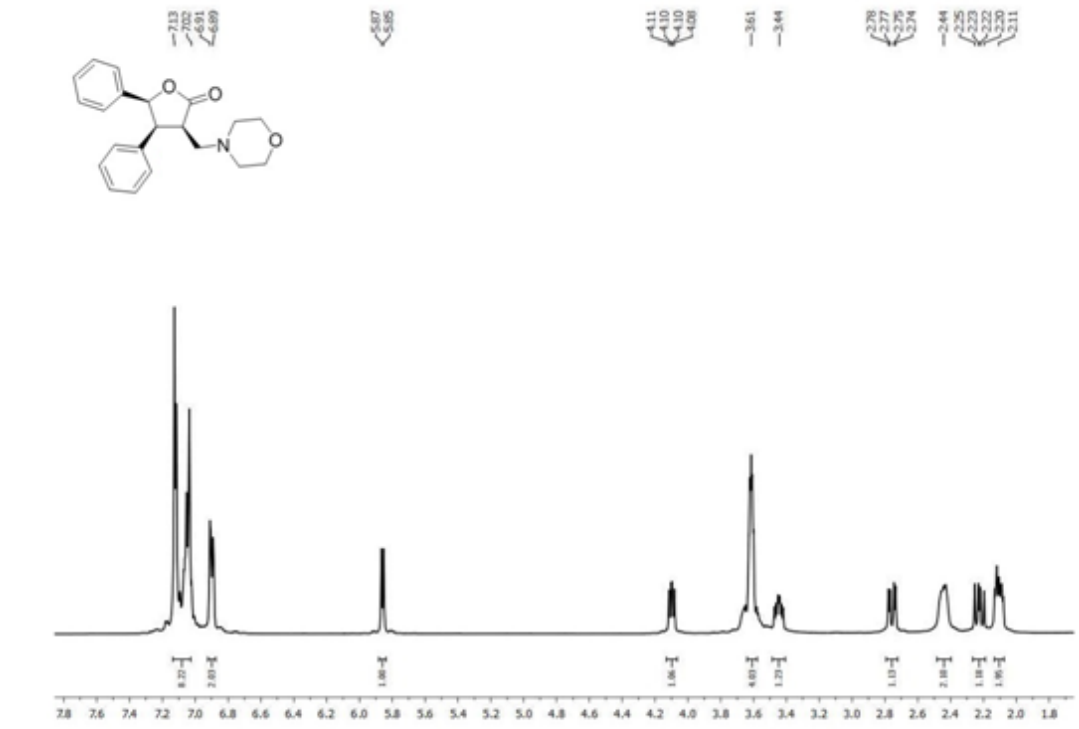
$^{13}$C NMR spectrum of **4**.



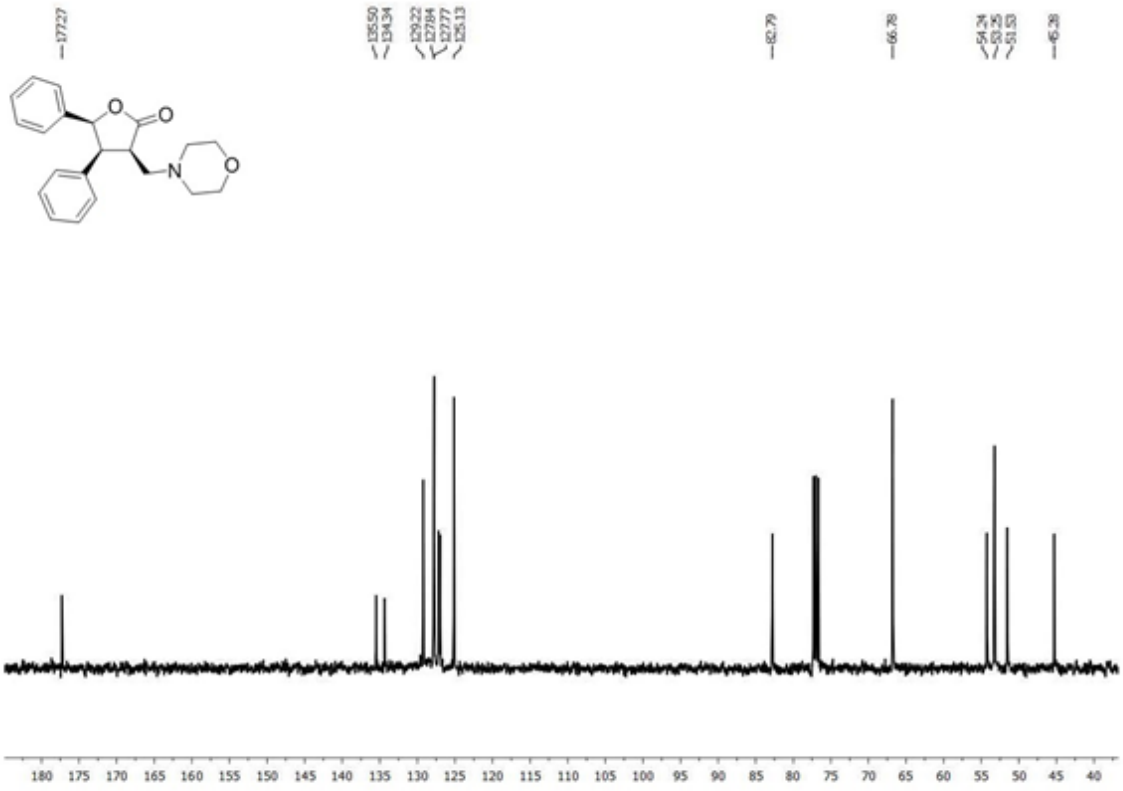
$^{1}$H NMR spectrum of **5**.



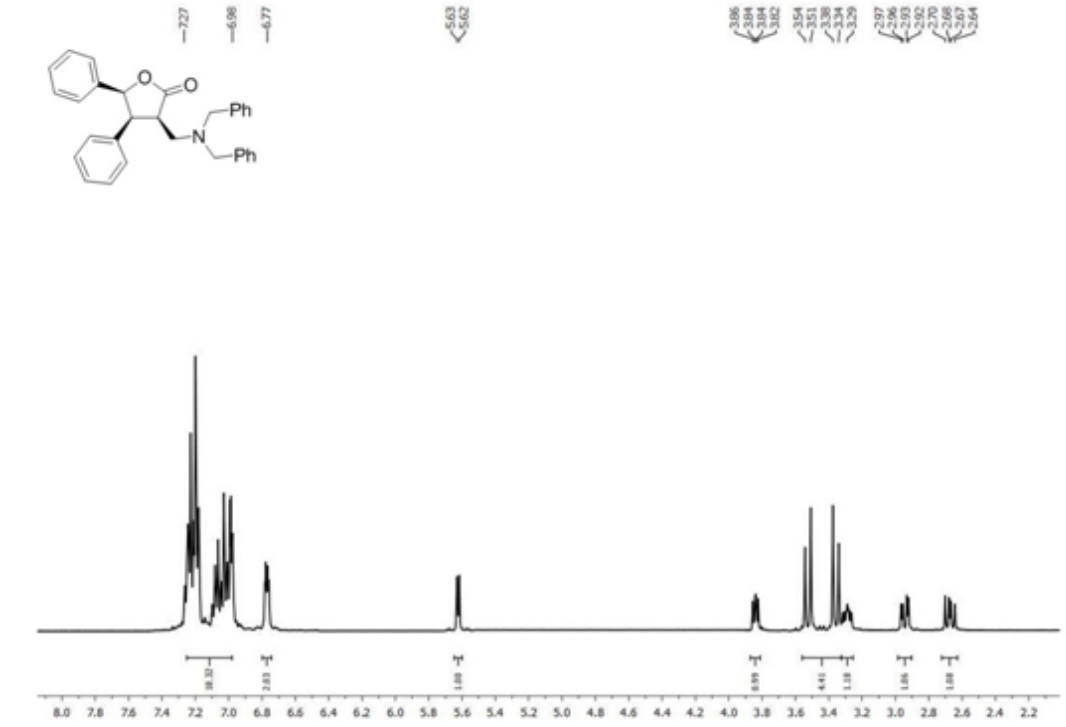
$^{13}$C NMR spectrum of **5**.



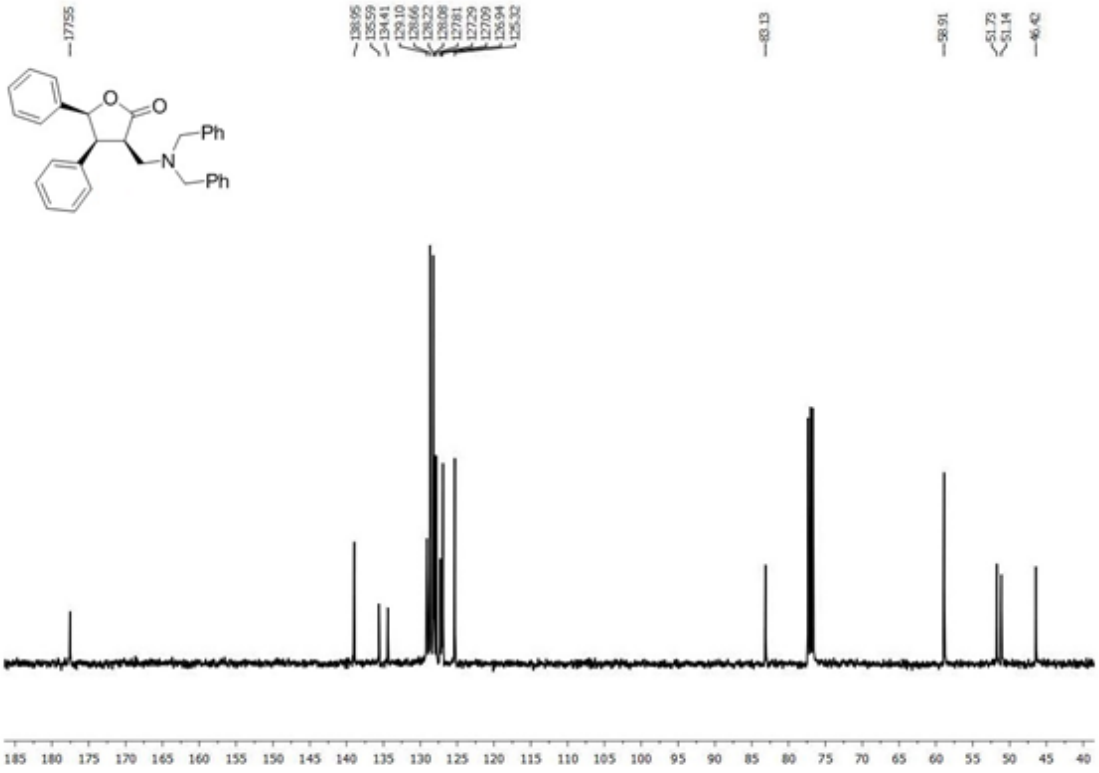
$^{1}$H NMR spectrum of **6**.



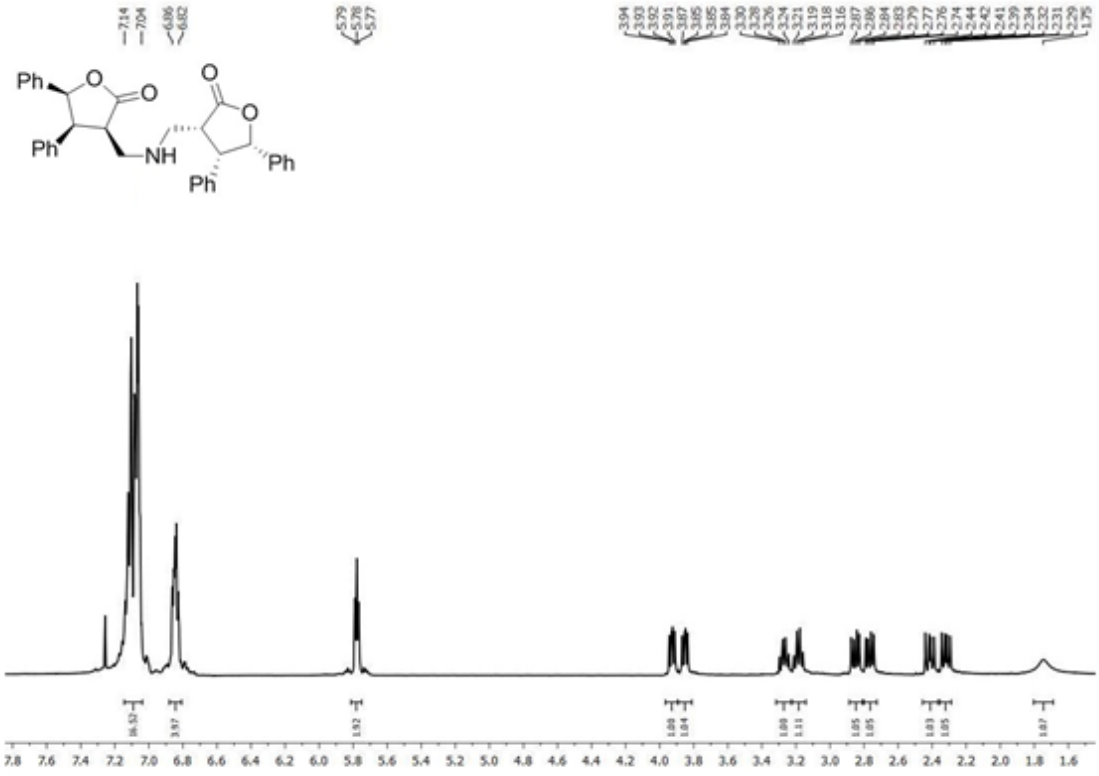
$^{13}$C NMR spectrum of **6**.



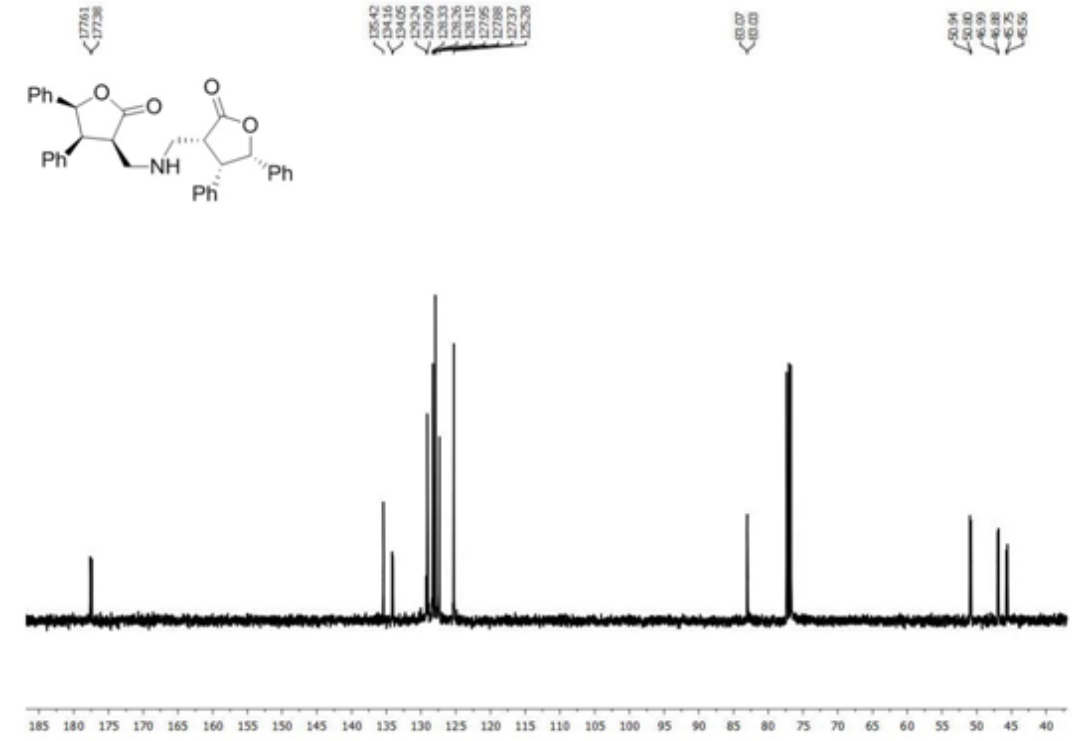

$^{1}$H NMR spectrum of **7**.



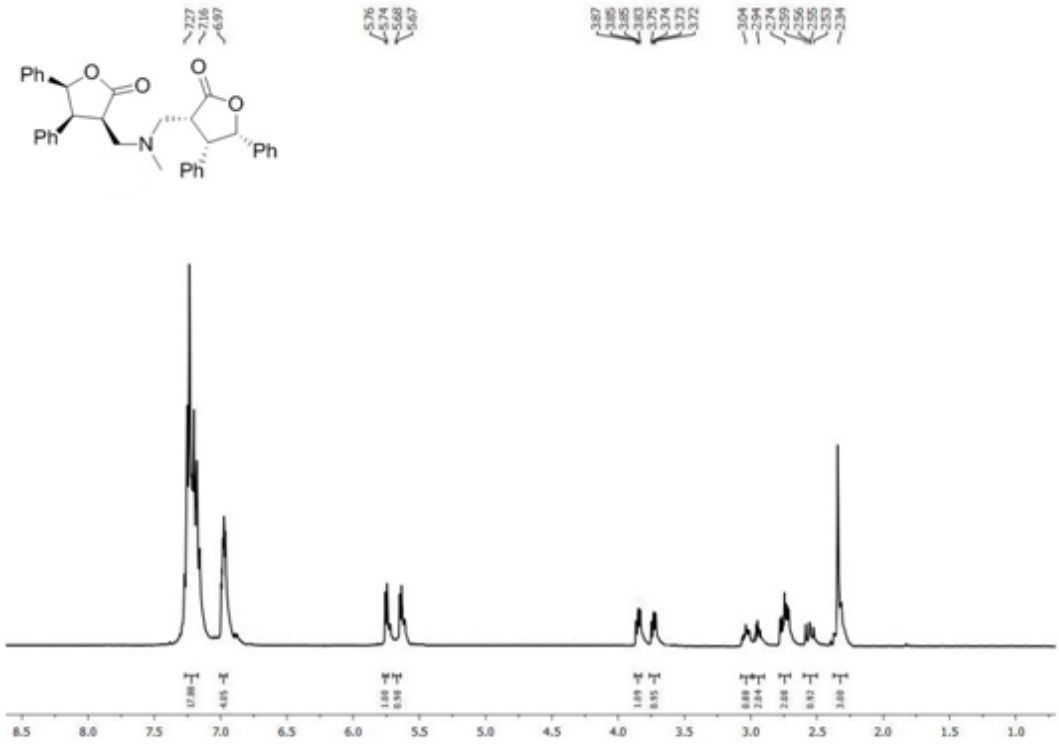

$^{13}$C NMR spectrum of **7**.



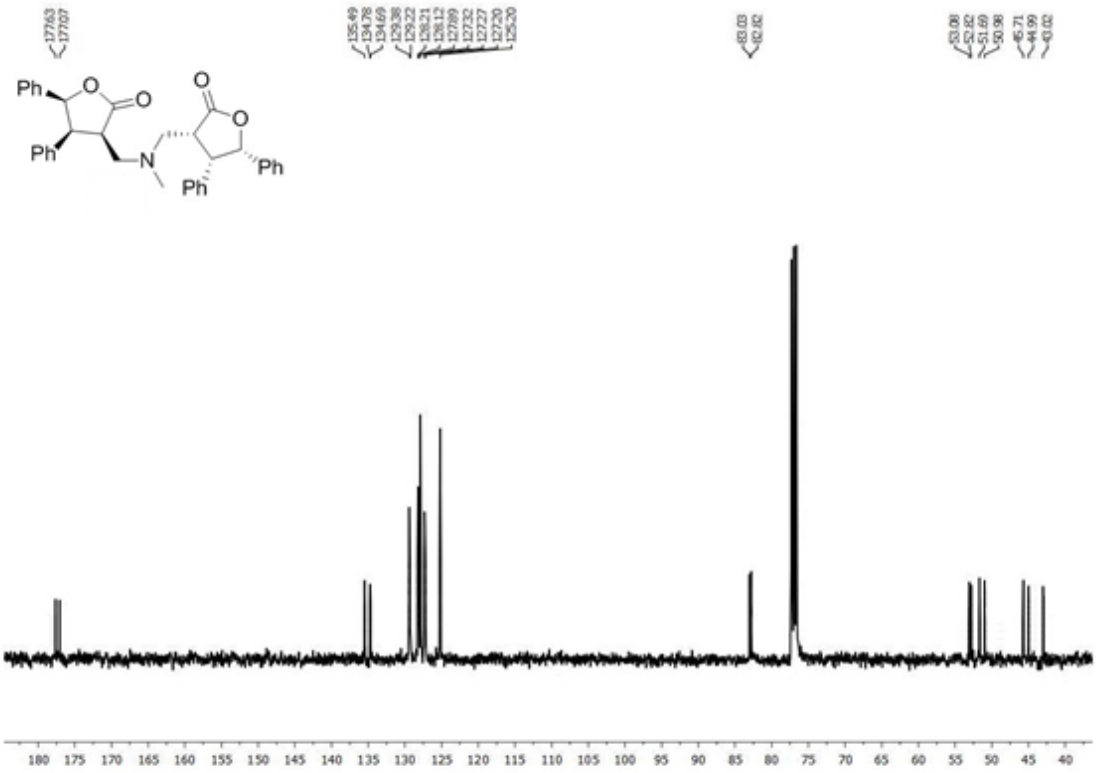

$^{1}$H NMR spectrum of **8**.



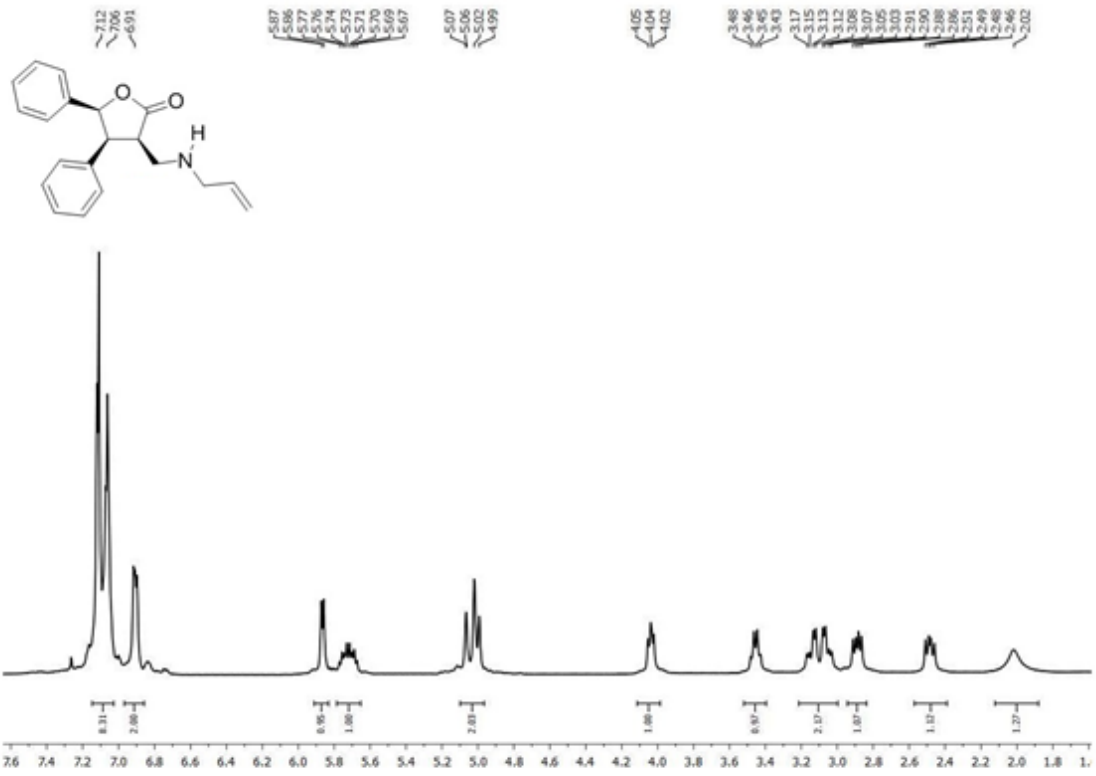

$^{13}$C NMR spectrum of **8**.



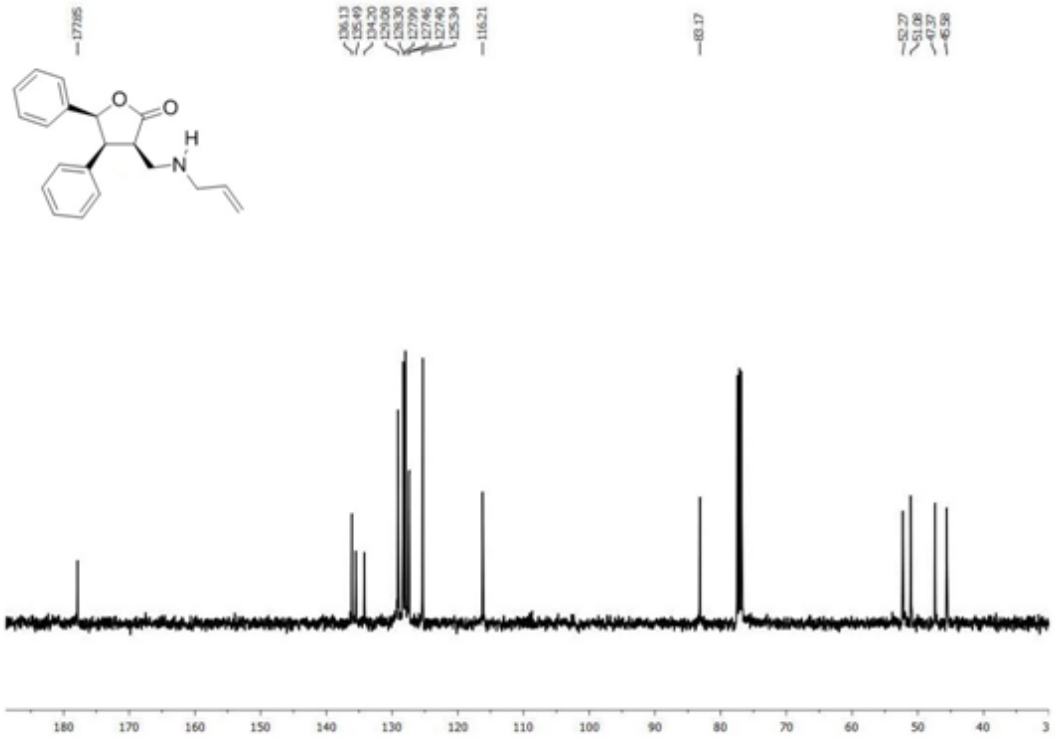
$^{1}$H NMR spectrum of **9**.



$^{13}$C NMR spectrum of **9**.

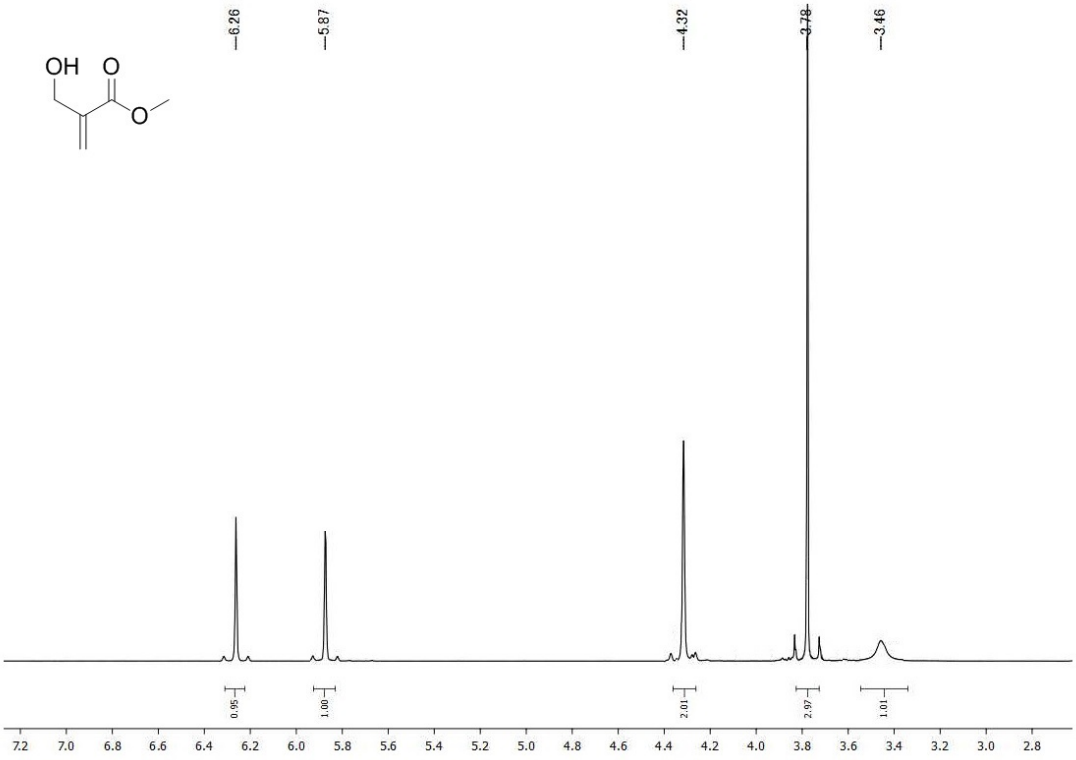


$^{1}$H NMR spectrum of **10**.

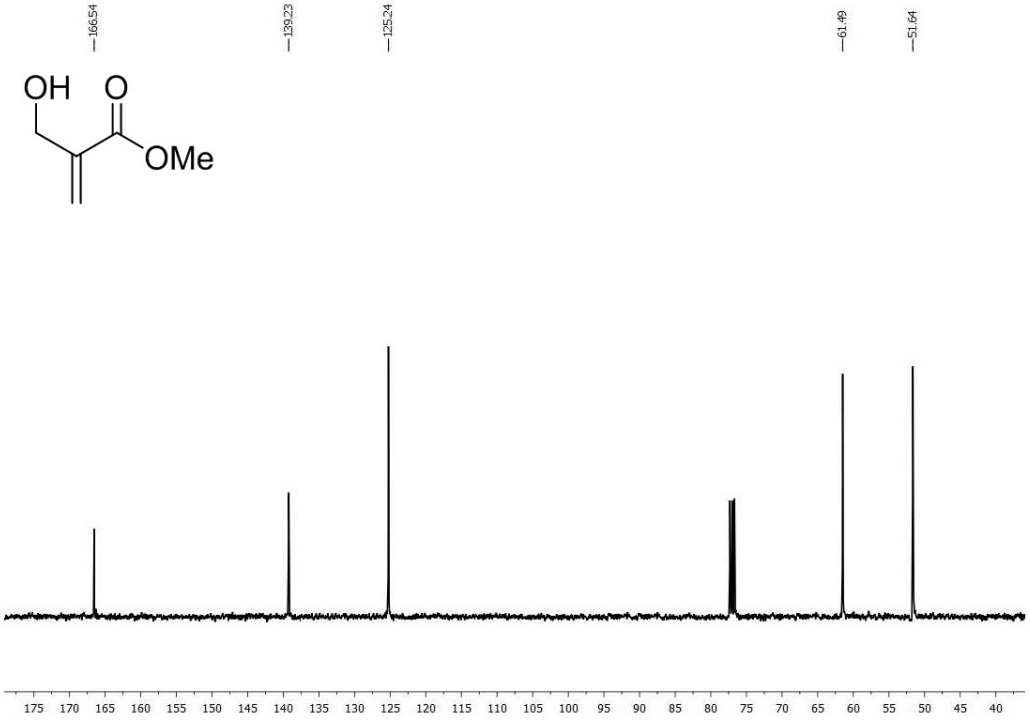


$^{13}$C NMR spectrum of **10**.

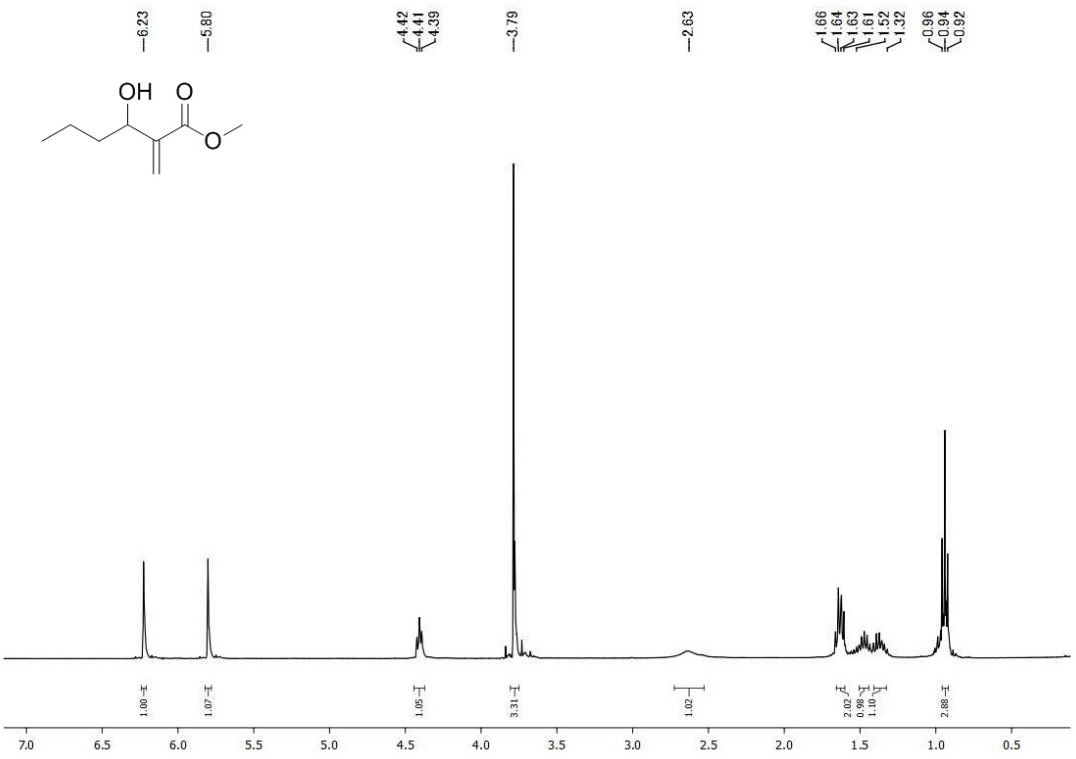
**NMR Spectra Associated with the Preparation of Monosubstituted Butanoate Esters**



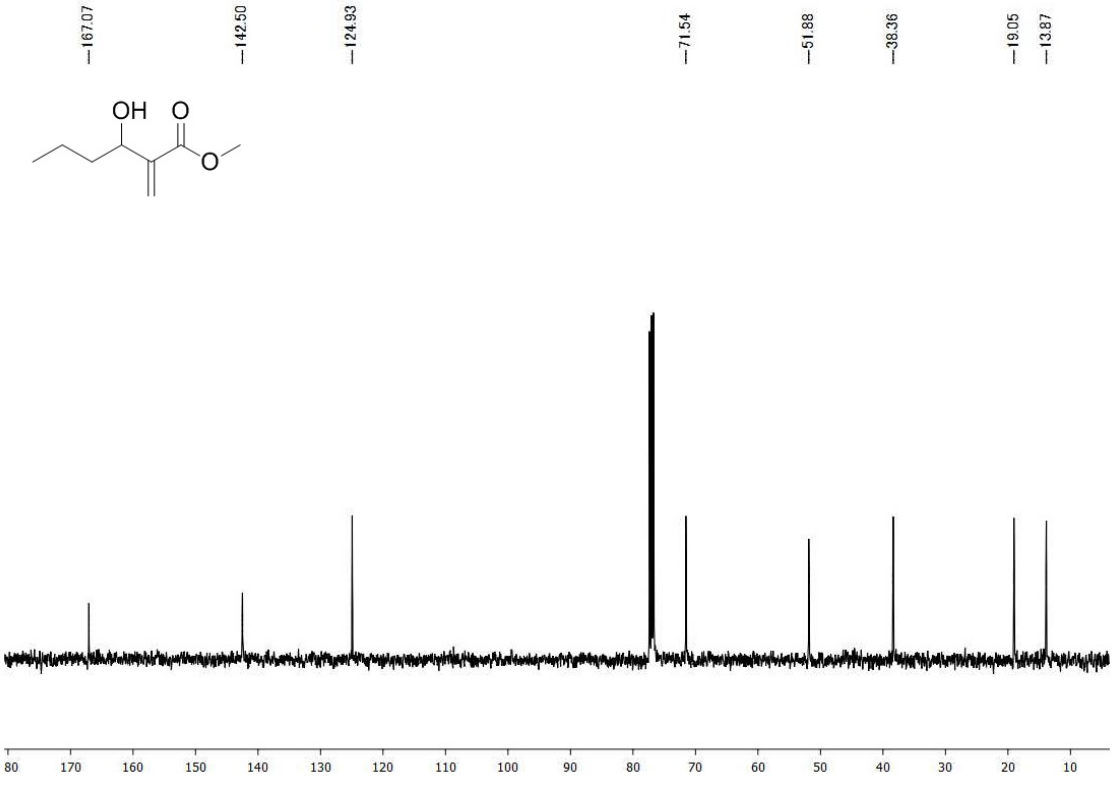

$^{1}$H NMR spectrum of methyl 2-(hydroxymethyl)prop-2-enoate.



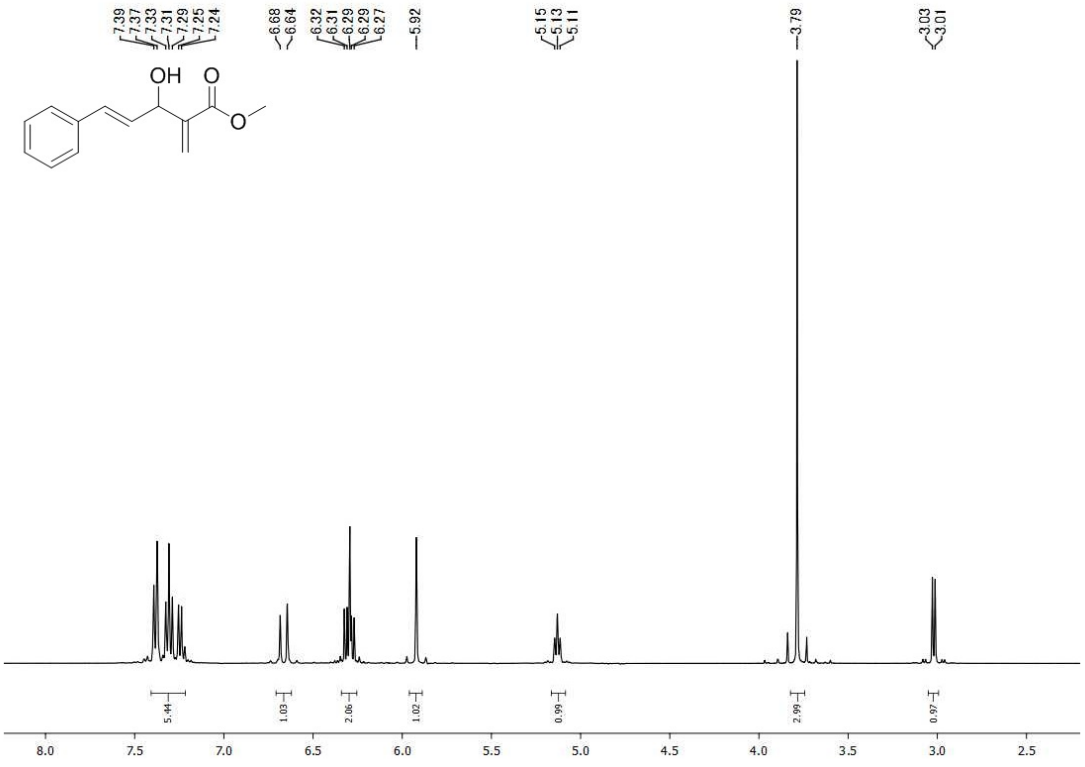

$^{13}$C NMR spectrum of methyl 2-(hydroxymethyl)prop-2-enoate.



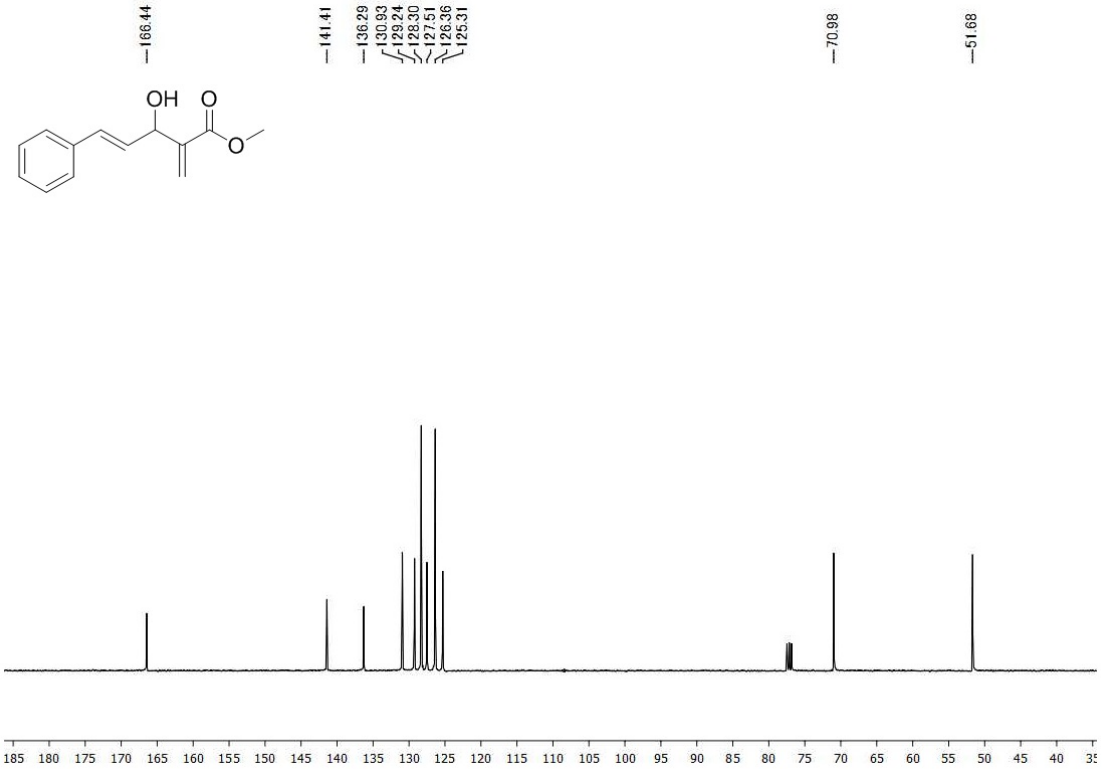

$^{1}$H NMR spectrum of methyl 3-hydroxy-2-methylenehexanoate.



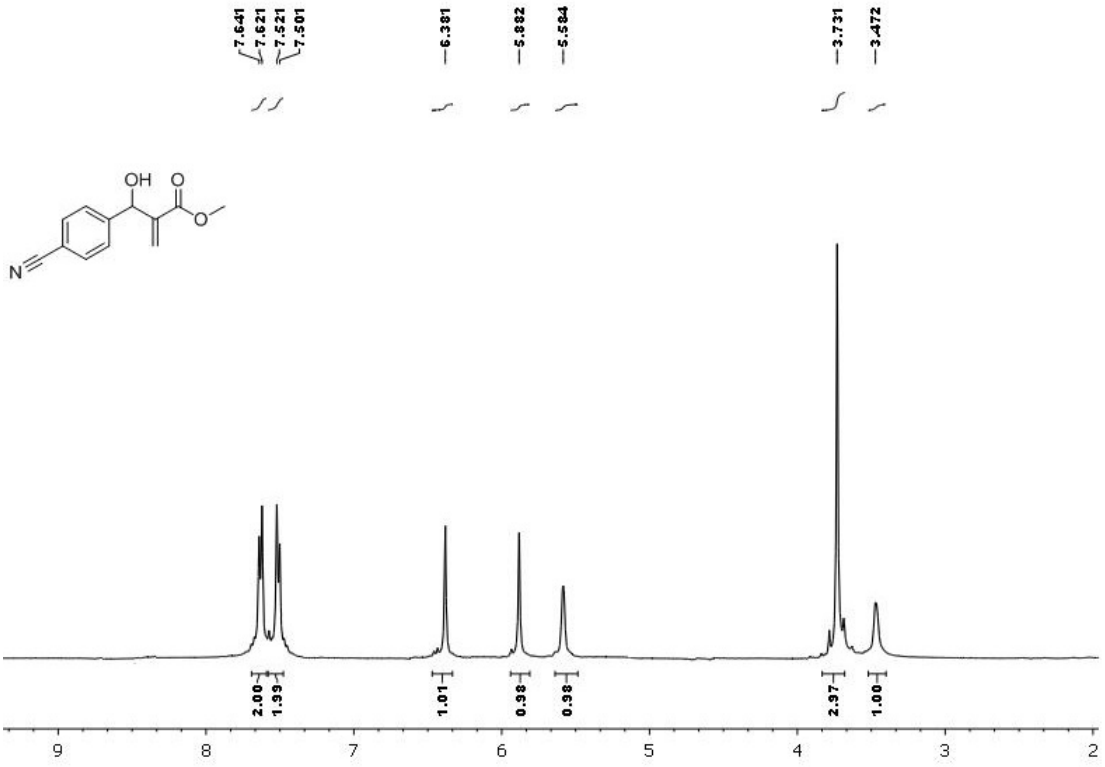

$^{13}$C NMR spectrum of methyl 3-hydroxy-2-methylenehexanoate.



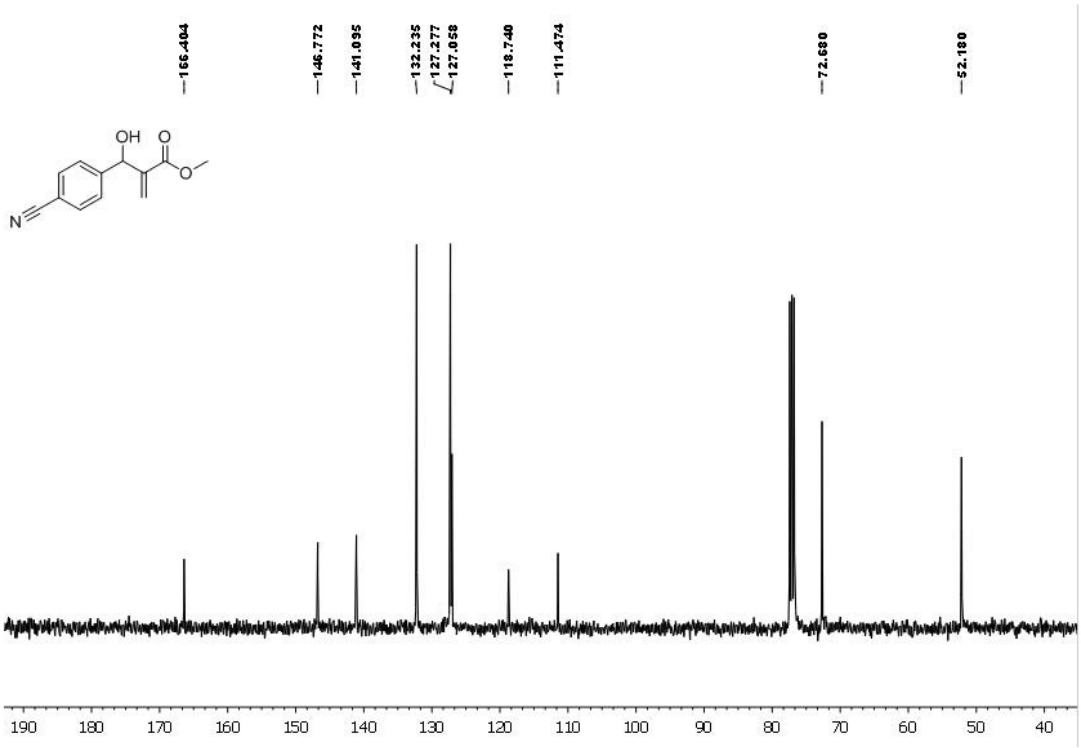

$^{1}$H NMR spectrum of methyl (4*E*)-3-hydroxy-2-methylene-5-phenylpent-4-enoate.



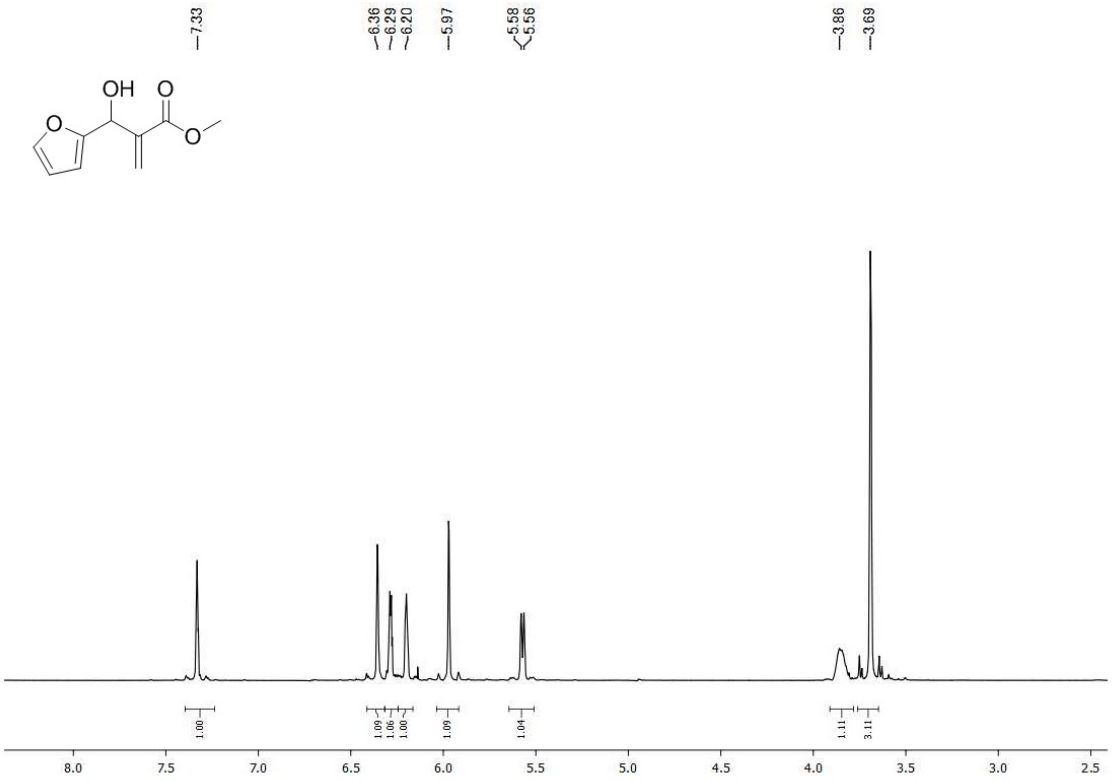

$^{13}$C NMR spectrum of methyl (4*E*)-3-hydroxy-2-methylene-5-phenylpent-4-enoate.



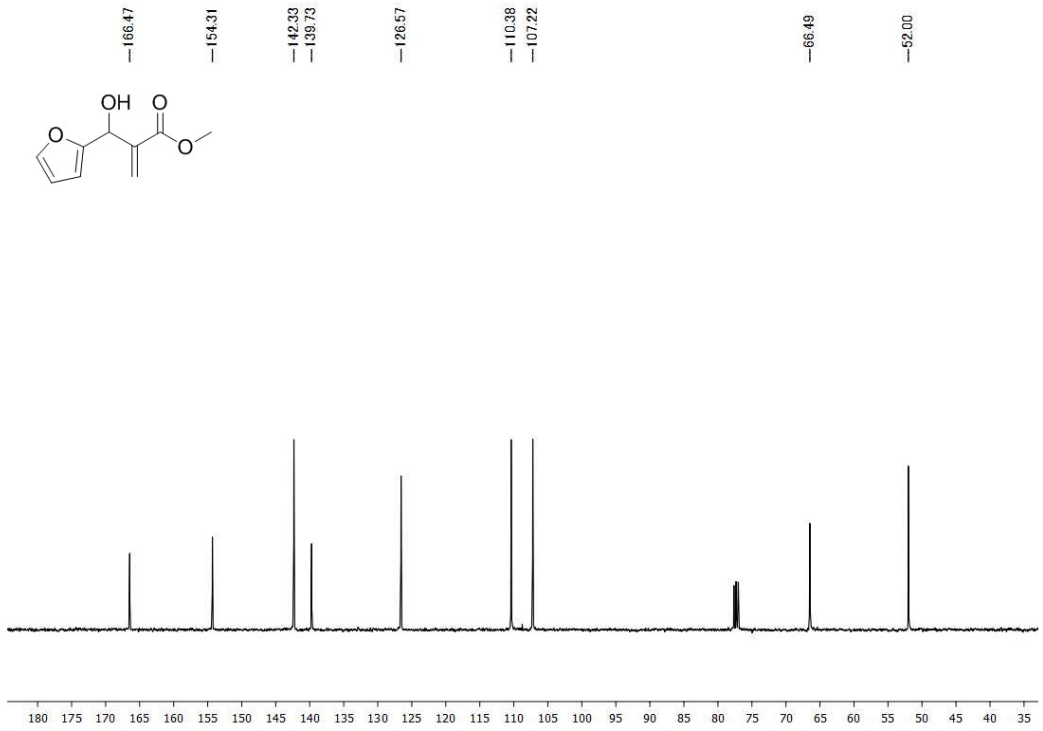

$^{1}$H NMR spectrum of methyl 2-((4-cyanophenyl)(hydroxy)methyl)prop-2-enoate.



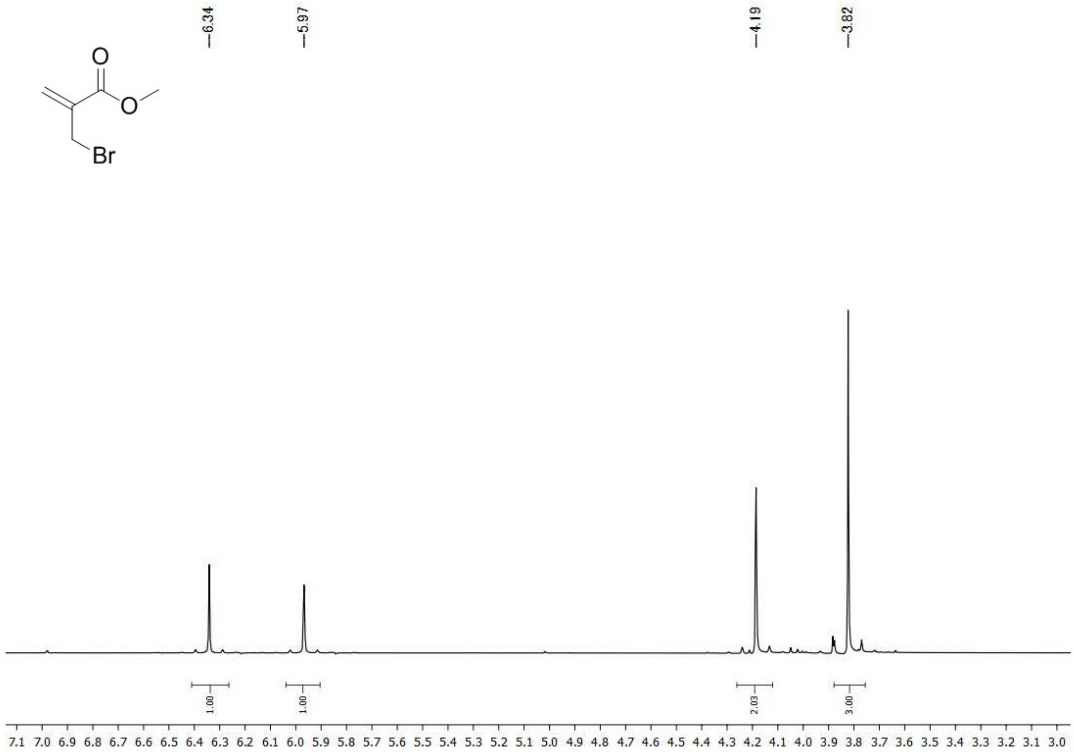

$^{13}$C NMR spectrum of methyl 2-((4-cyanophenyl)(hydroxy)methyl)prop-2-enoate.



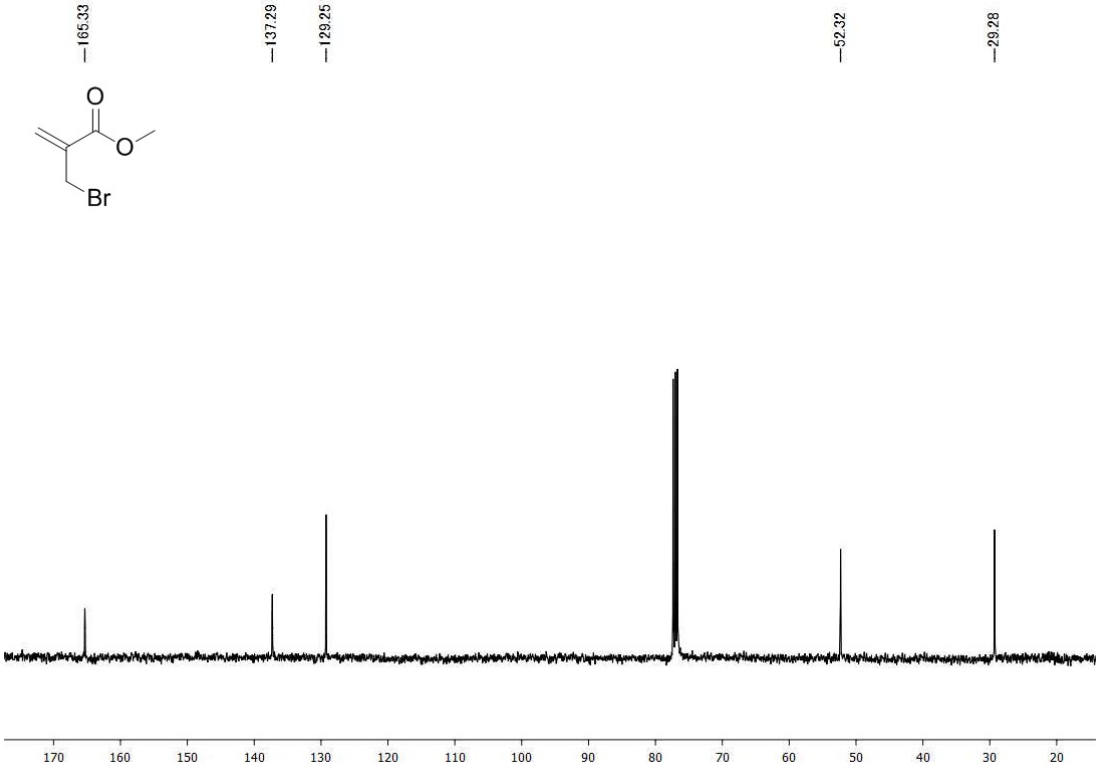

$^{1}$H NMR spectrum of methyl 2-((furan-2-yl)hydroxymethyl)prop-2-enoate.



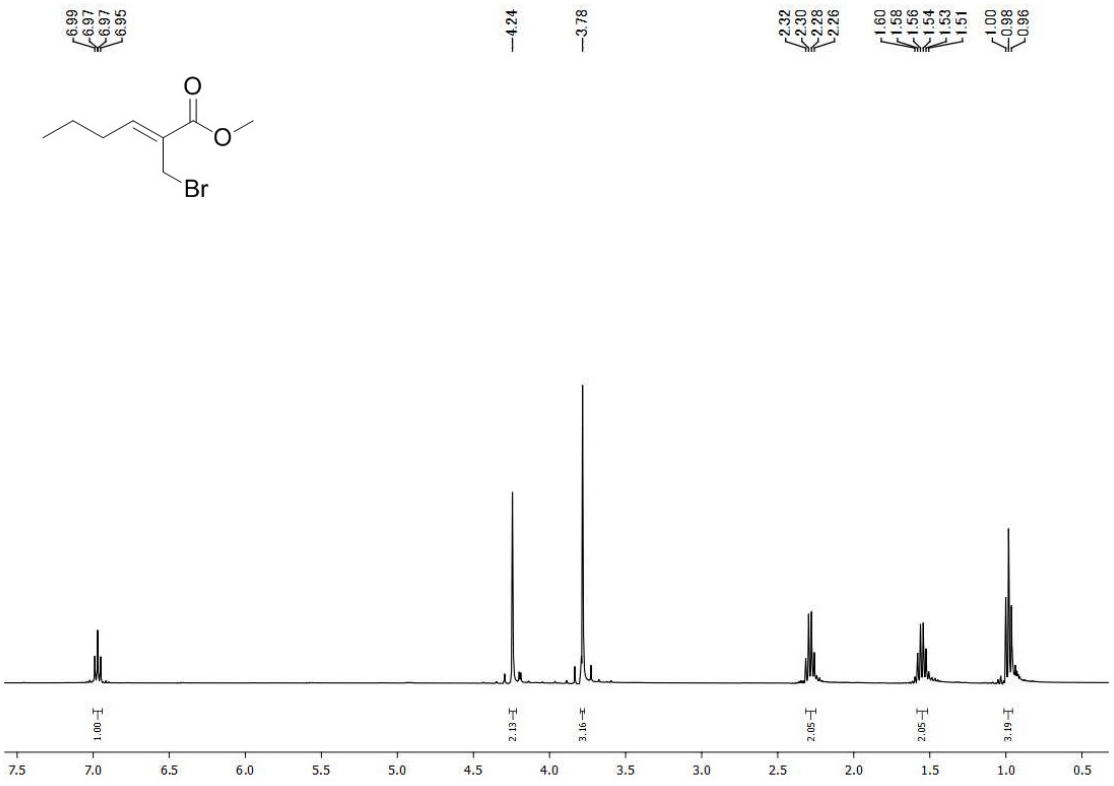

$^{13}$C NMR spectrum of methyl 2-((furan-2-yl)hydroxymethyl)prop-2-enoate.



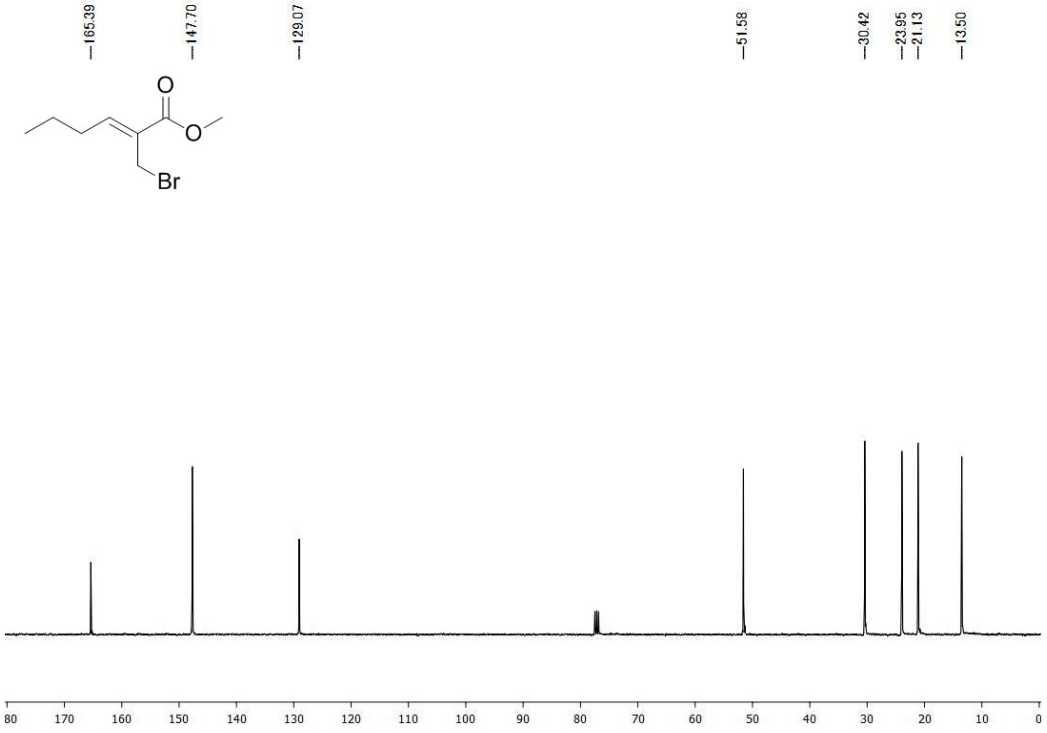

$^{1}$H NMR spectrum of methyl 2-(bromomethyl)prop-2-enoate.



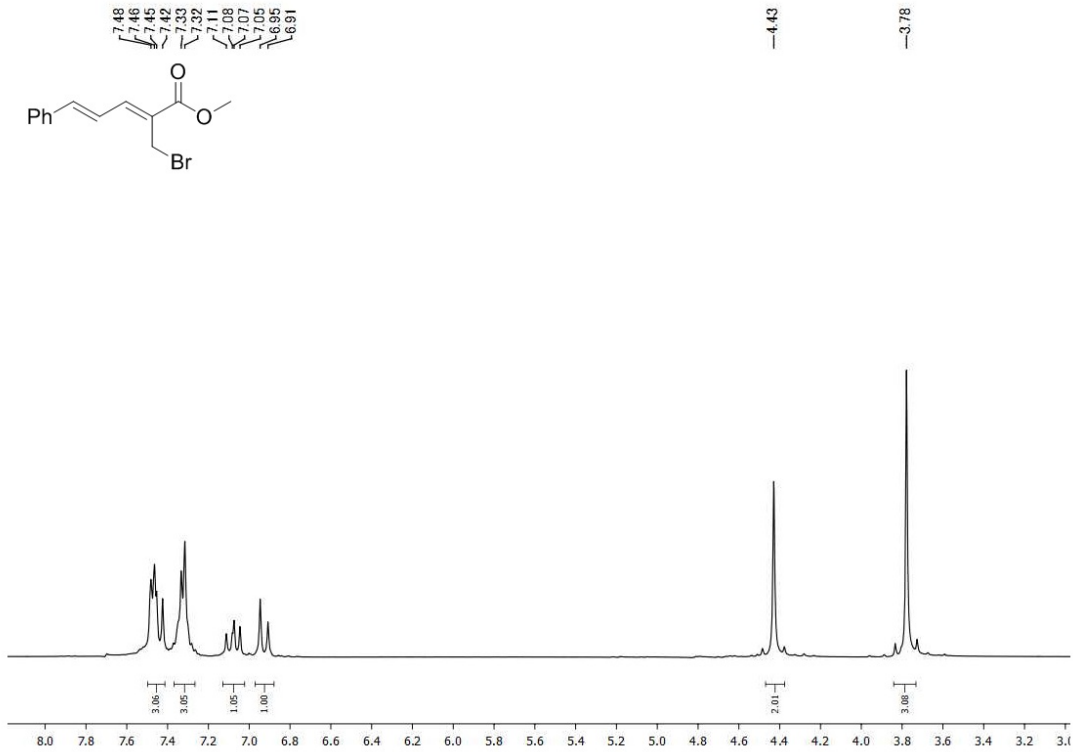

$^{13}$C NMR spectrum of methyl 2-(bromomethyl)prop-2-enoate.



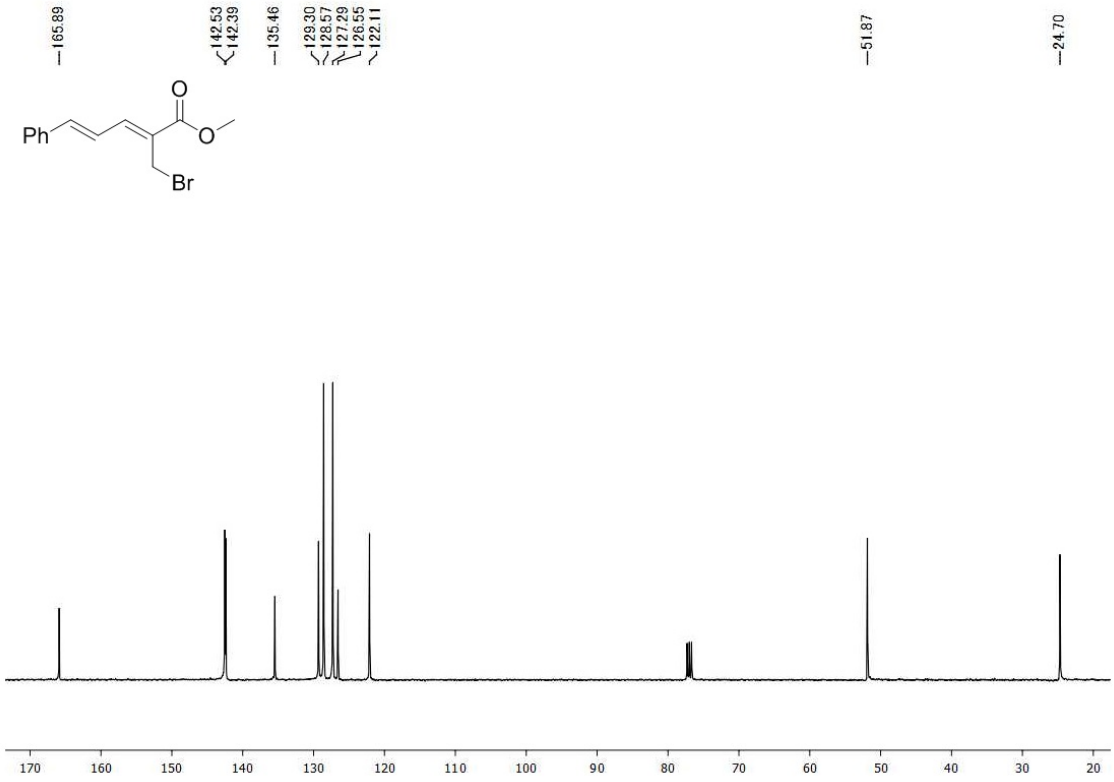

$^{1}$H NMR spectrum of methyl (2*Z*)-2-(bromomethyl)hex-2-enoate.



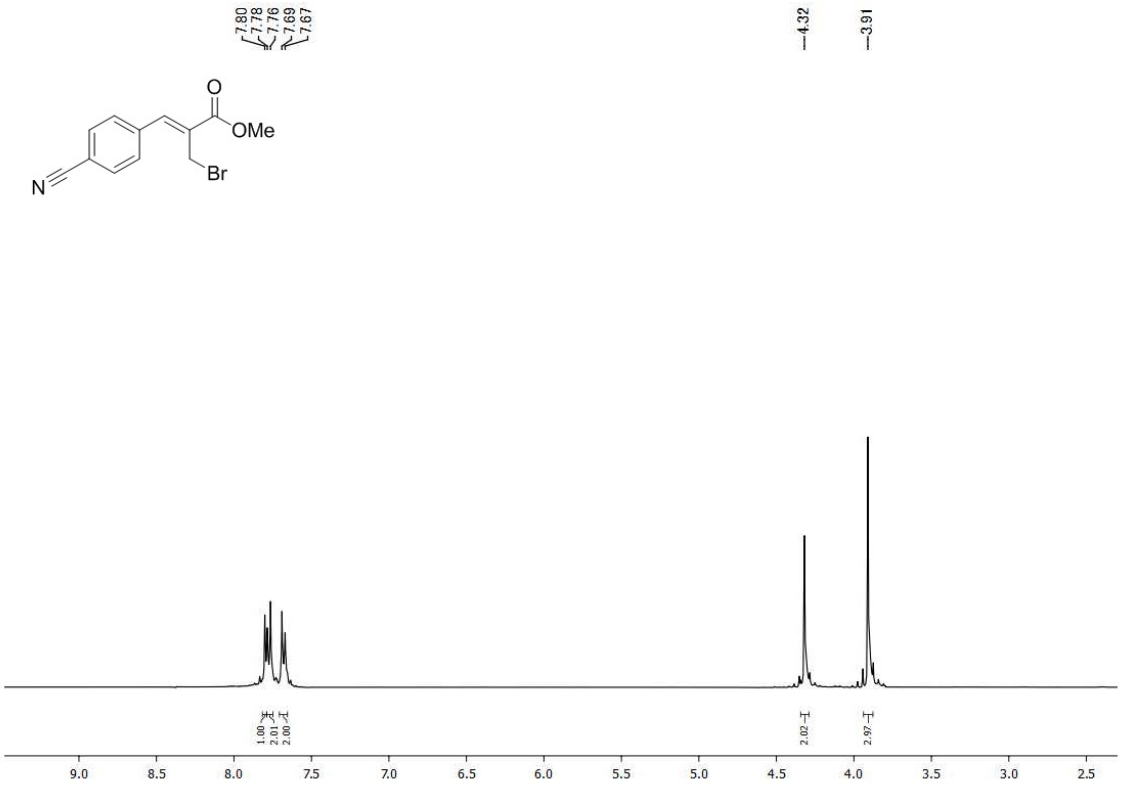

$^{13}$C NMR spectrum of methyl (2*Z*)-2-(bromomethyl)hex-2-enoate.



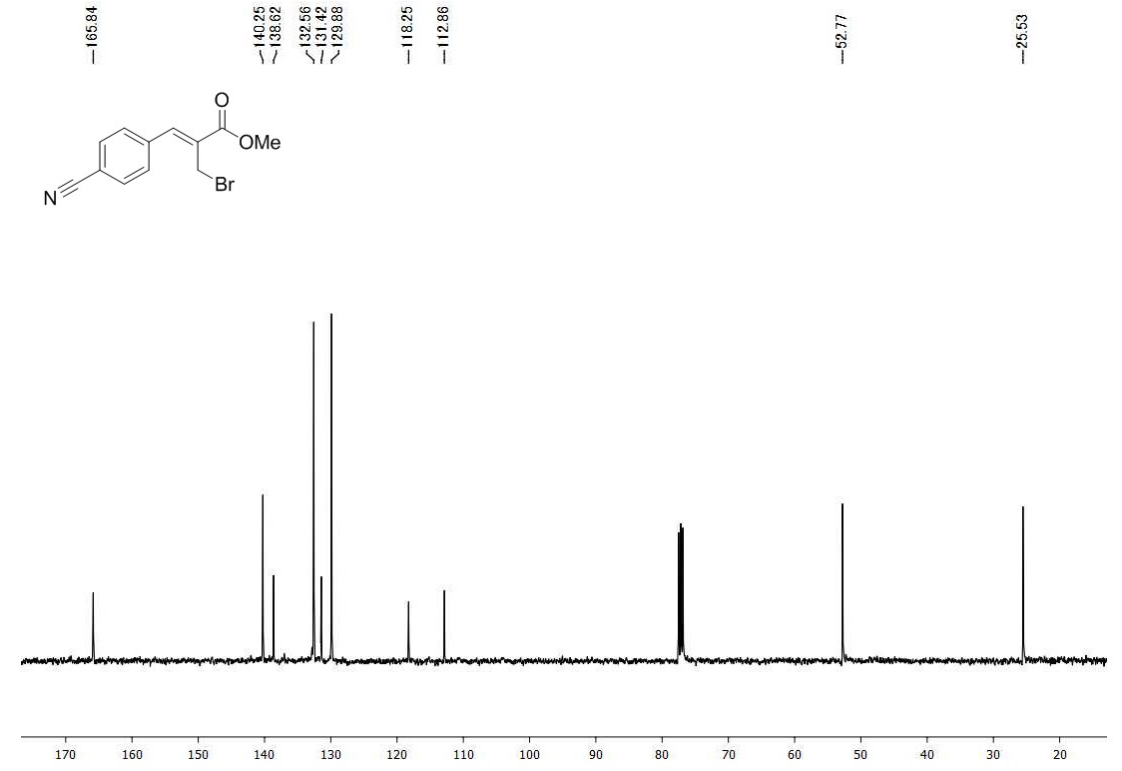

$^{1}$H NMR spectrum of methyl (2*Z*,4*E*)-2-(bromomethyl)-5-phenylpenta-2,4-dienoate.



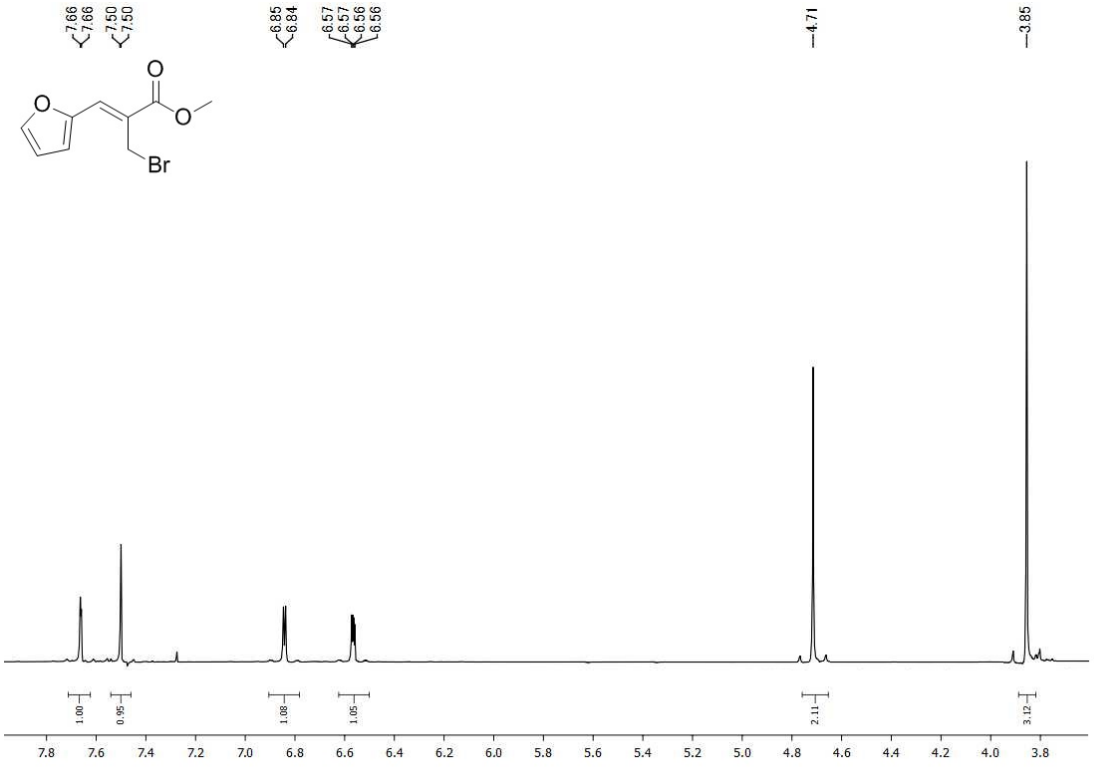

$^{13}$C NMR spectrum of methyl (2*Z*,4*E*)-2-(bromomethyl)-5-phenylpenta-2,4-dienoate.



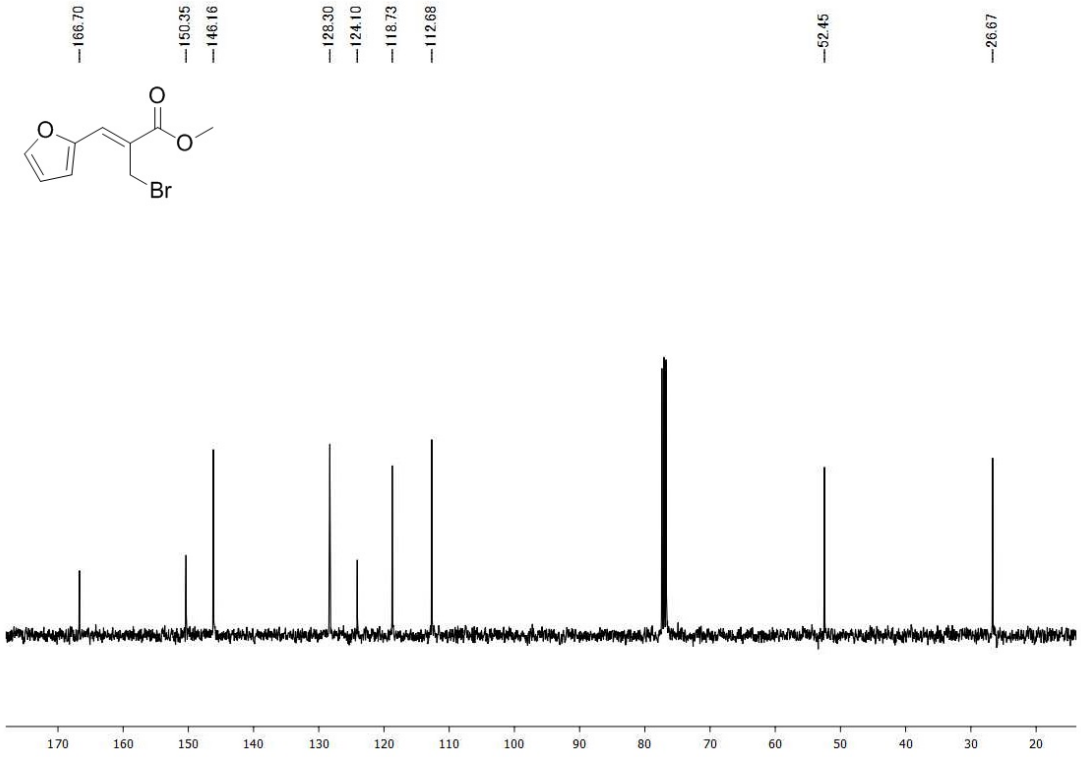

$^{1}$H NMR spectrum of methyl *Z*-2-(bromomethyl)-3-(4-cyanophenyl)prop-2-enoate.



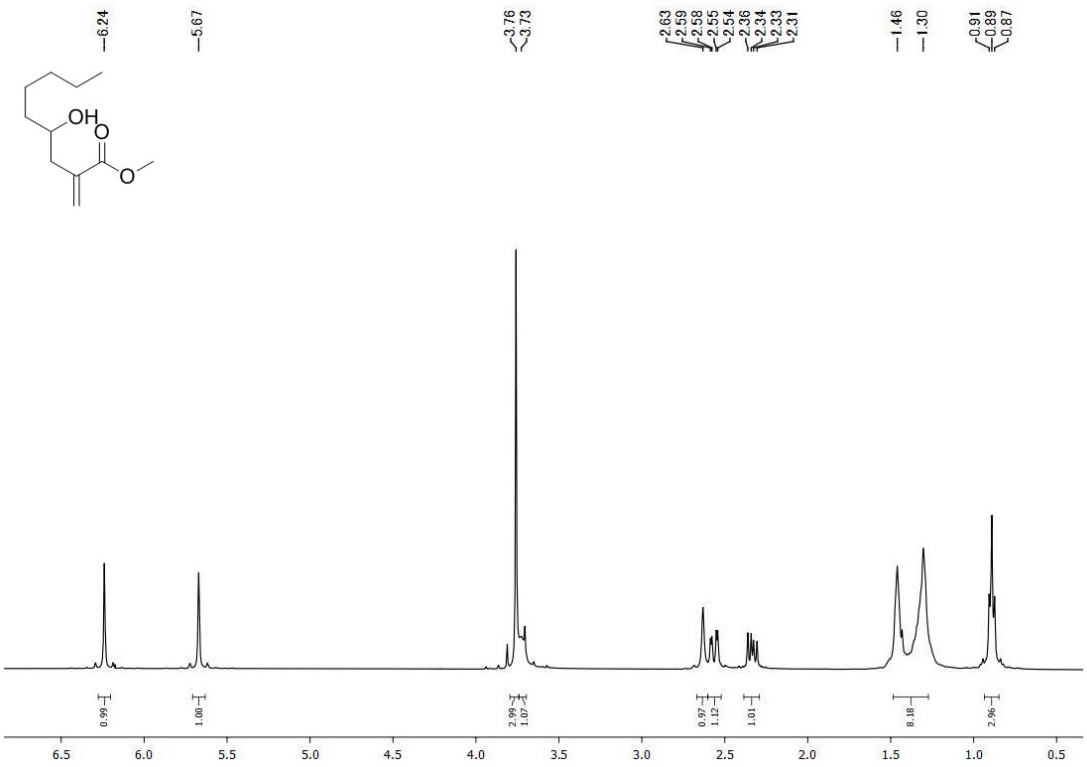

$^{13}$C NMR spectrum of methyl *Z*-2-(bromomethyl)-3-(4-cyanophenyl)prop-2-enoate.



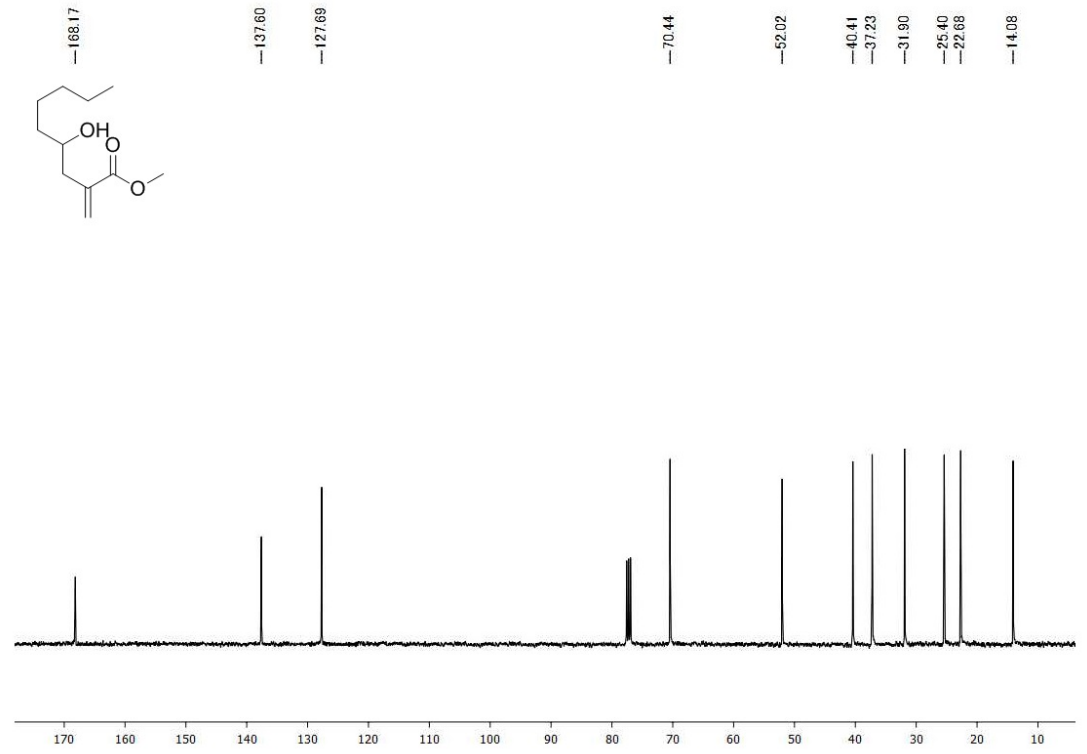

$^{1}$H NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-(furan-2-yl)prop-2-enoate.



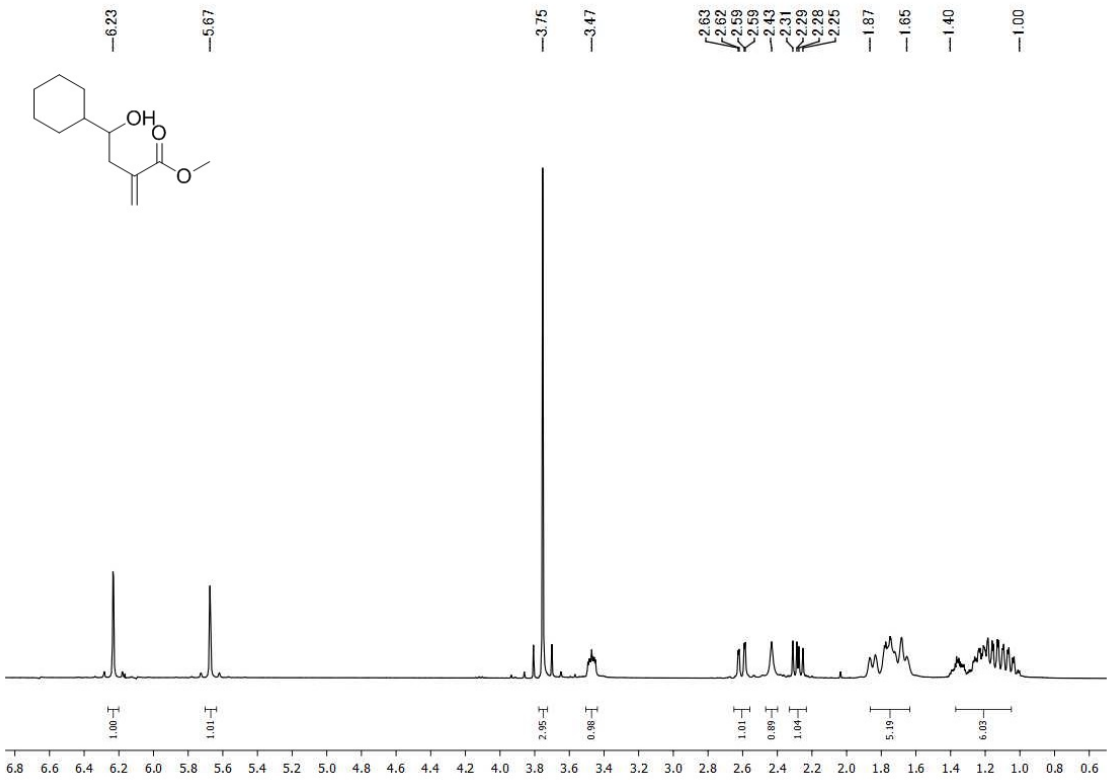

$^{13}$C NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-(furan-2-yl)prop-2-enoate.



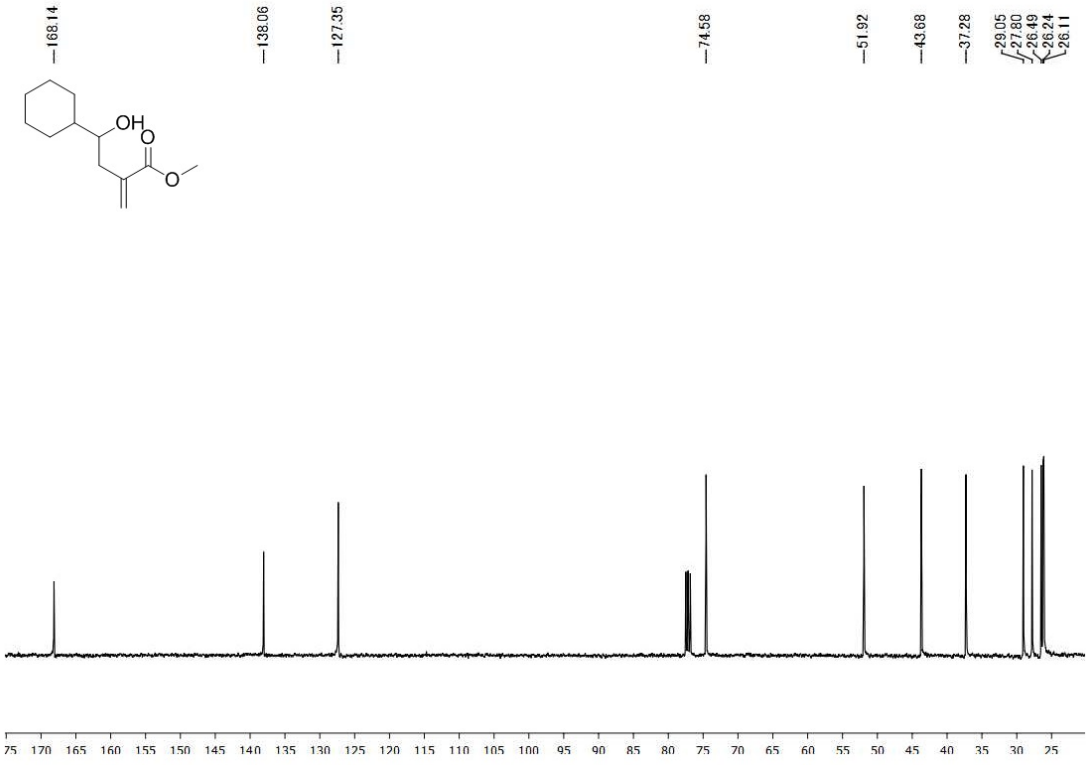

$^{1}$H NMR spectrum of methyl 4-hydroxy-2-methylenenonanoate.



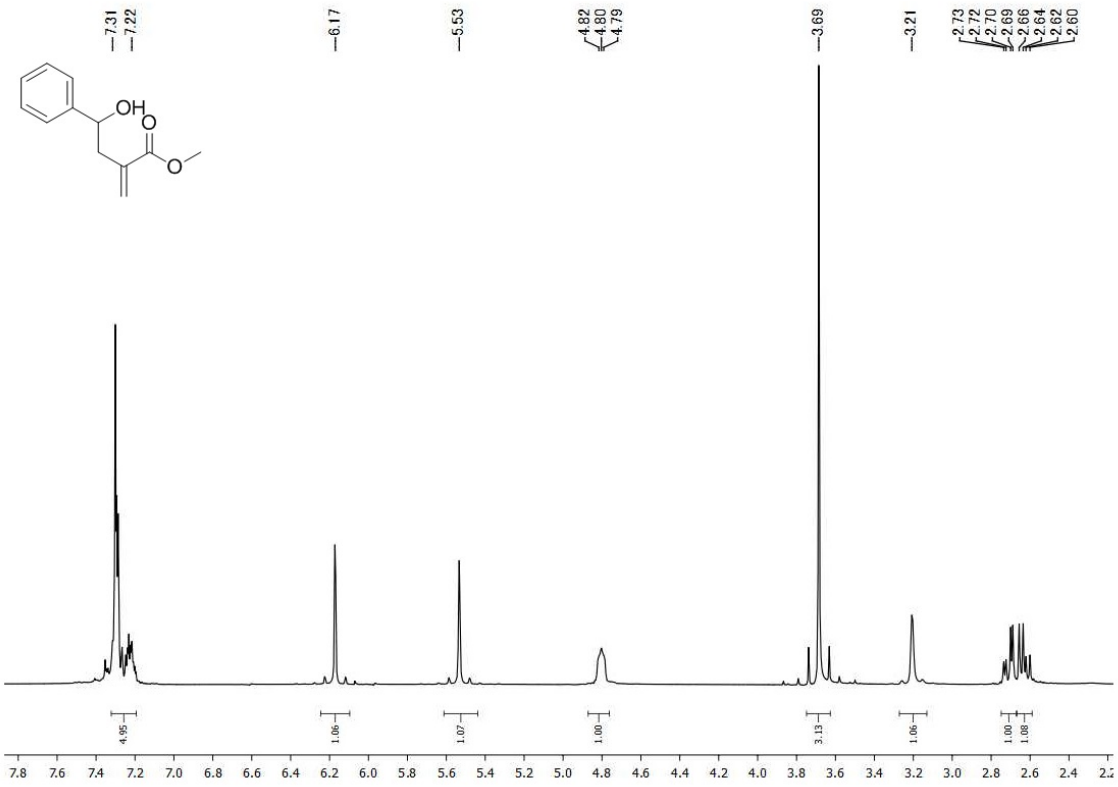

$^{13}$C NMR spectrum of methyl 4-hydroxy-2-methylenenonanoate.



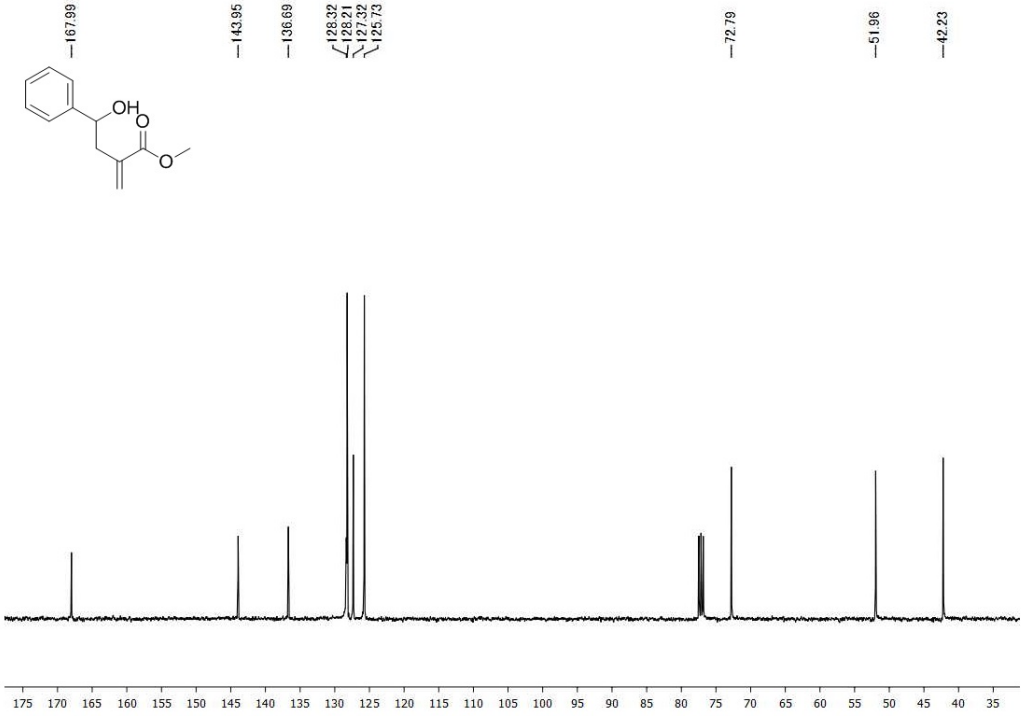

$^{1}$H NMR spectrum of methyl 4-cyclohexyl-4-hydroxy-2-methylenebutanoate.



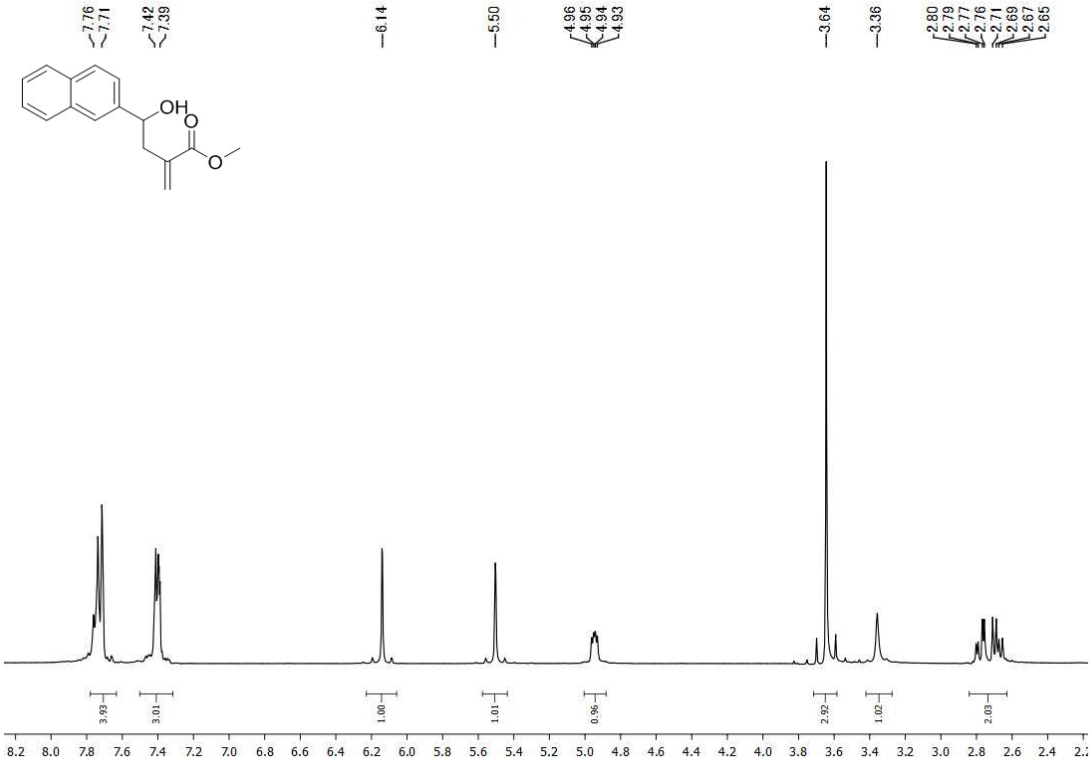

$^{13}$C NMR spectrum of methyl 4-cyclohexyl-4-hydroxy-2-methylenebutanoate.



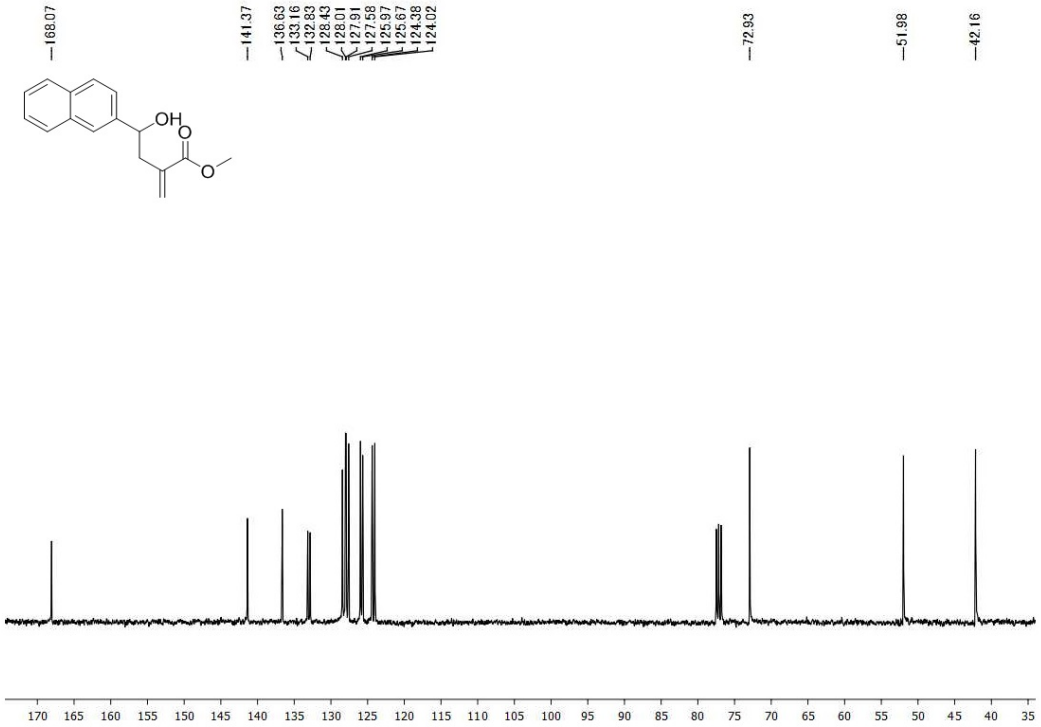

$^{1}$H NMR spectrum of methyl 4-hydroxy-2-methylene-4-phenylbutanoate.



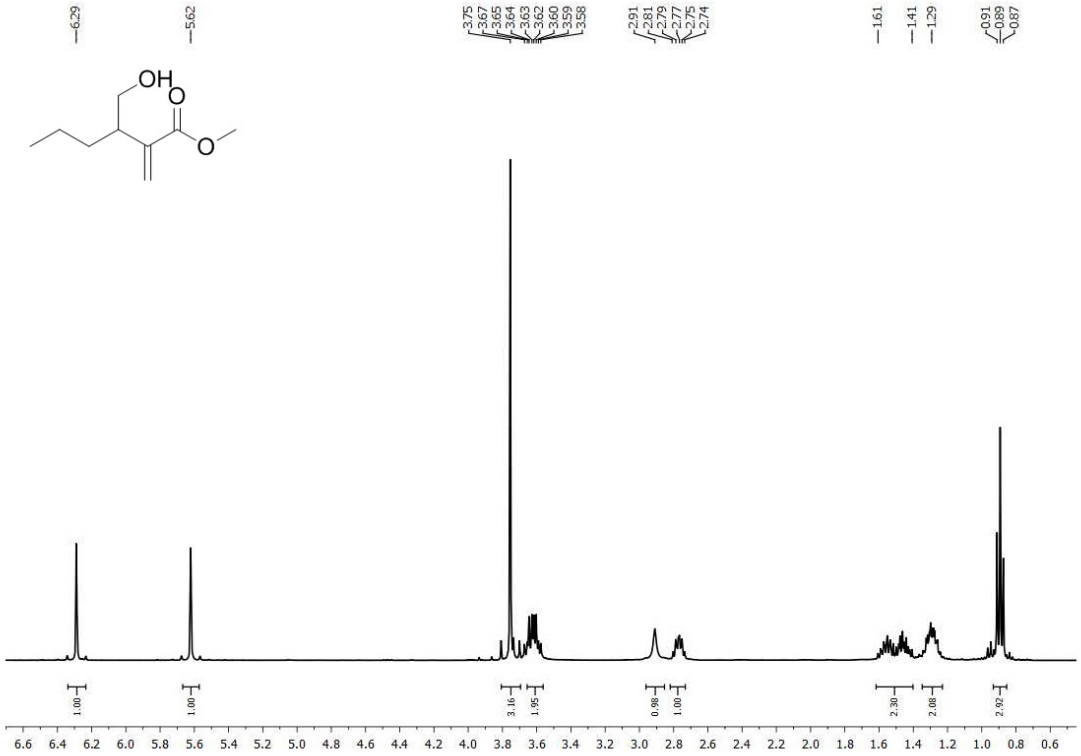

$^{13}$C NMR spectrum of methyl 4-hydroxy-2-methylene-4-phenylbutanoate.



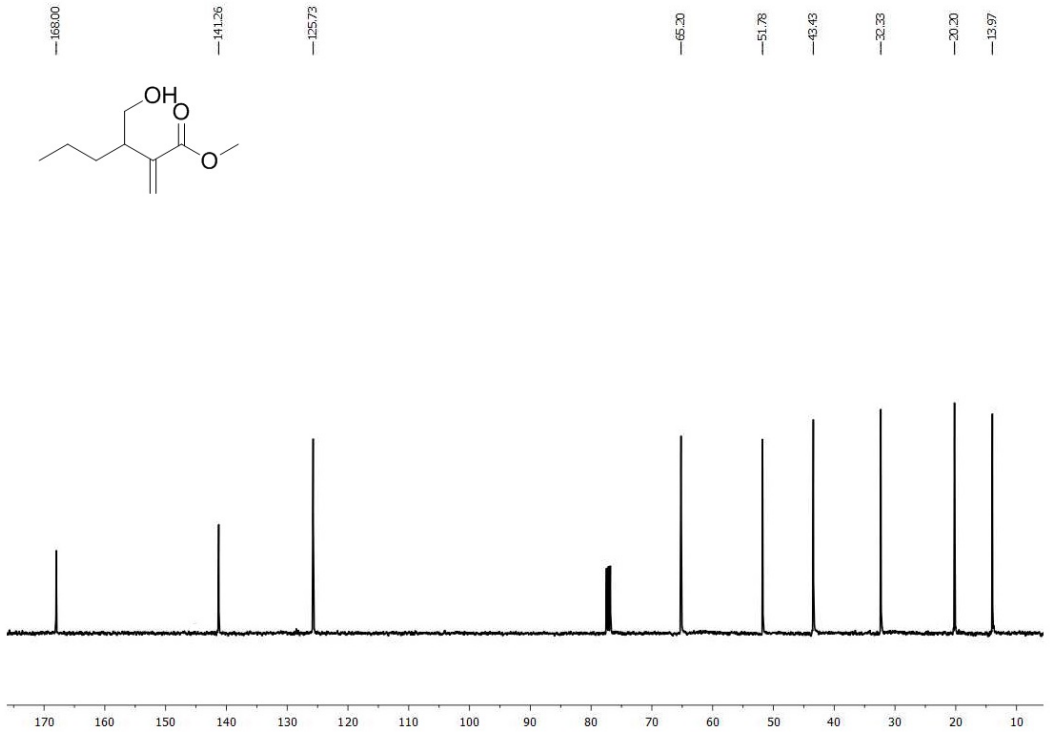

$^{1}$H NMR spectrum of methyl 4-hydroxy-2-methylene-4-(naphthalen-2-yl)butanoate.



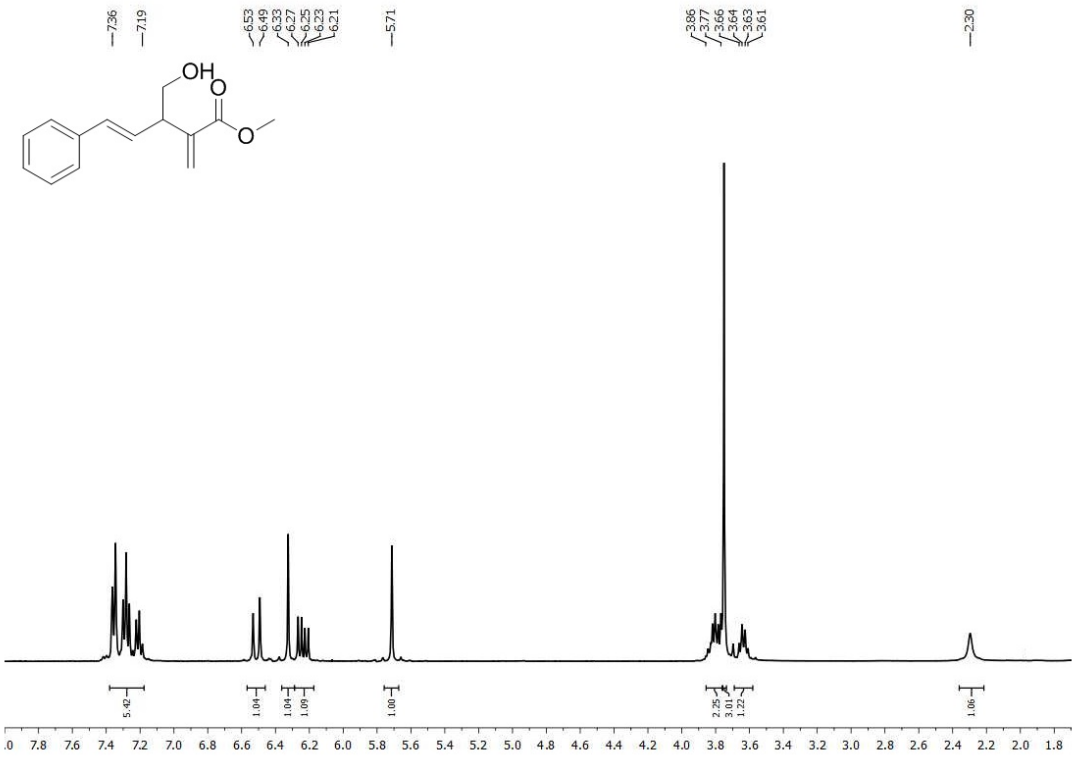

$^{13}$C NMR spectrum of methyl 4-hydroxy-2-methylene-4-(naphthalen-2-yl)butanoate.



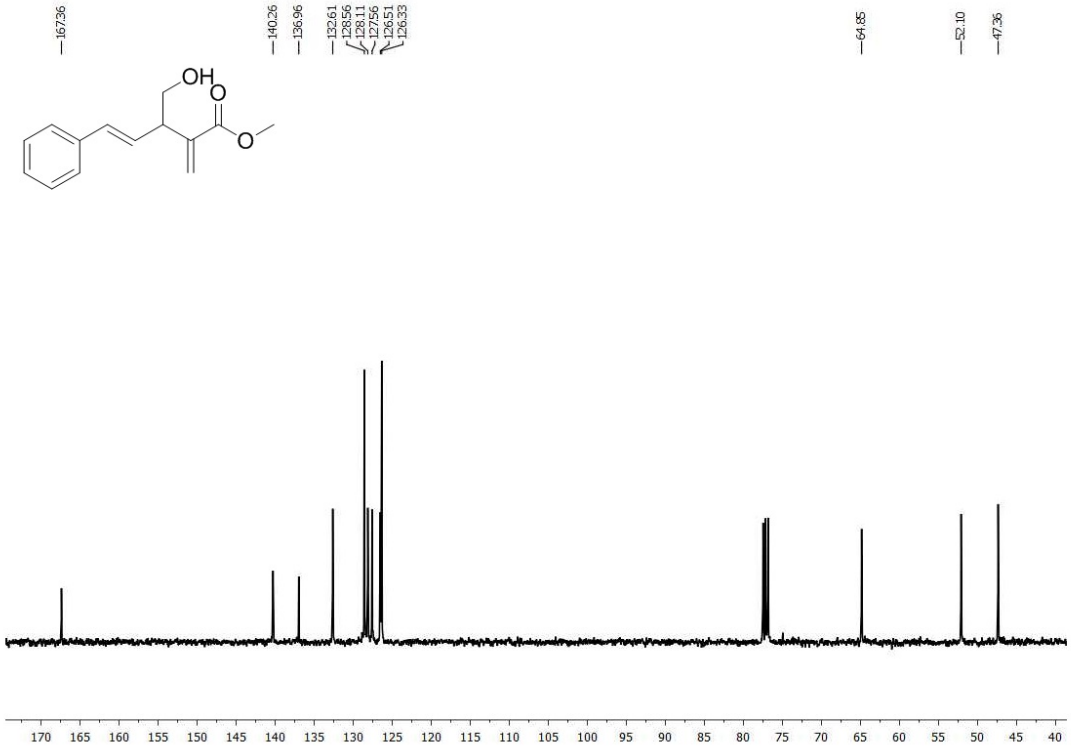

$^{1}$H NMR spectrum of methyl 3-(hydroxymethyl)-2-methylenehexanoate.



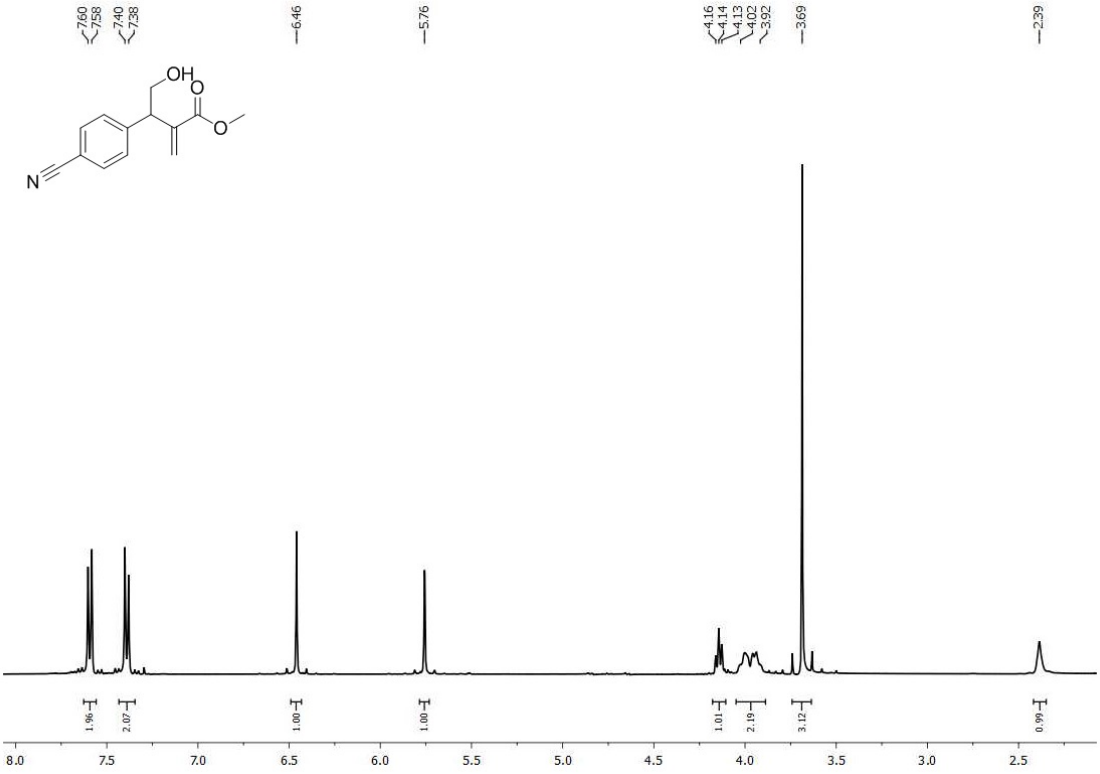

$^{13}$C NMR spectrum of methyl 3-(hydroxymethyl)-2-methylenehexanoate.



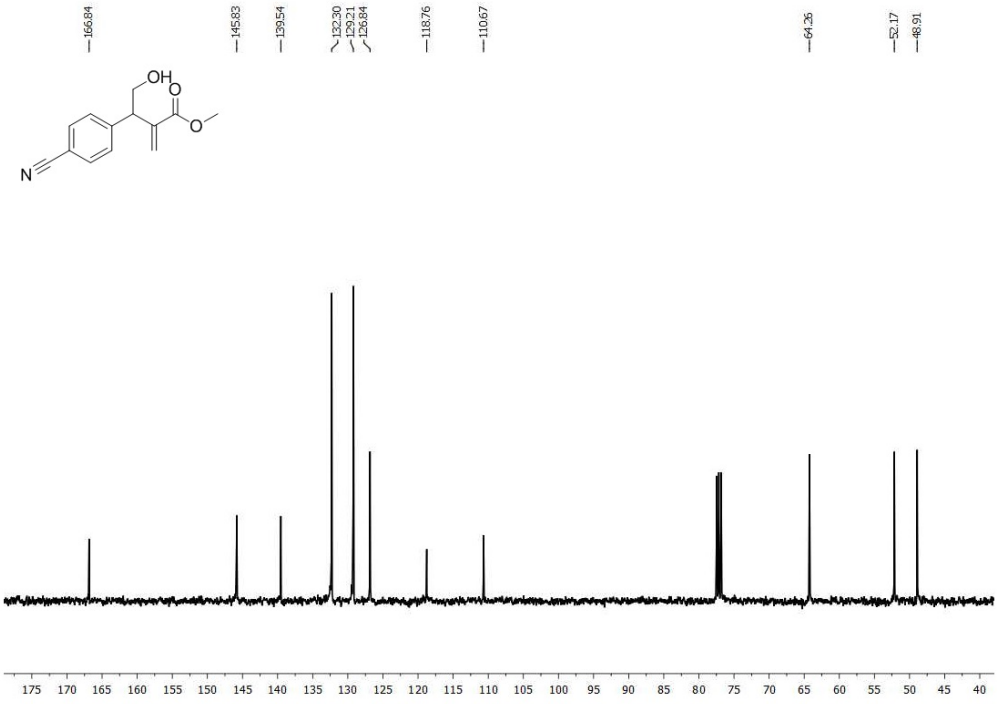

$^{1}$H NMR spectrum of methyl (4*E*)-3-(hydroxymethyl)-2-methylene-5-phenylpent-4-enoate.



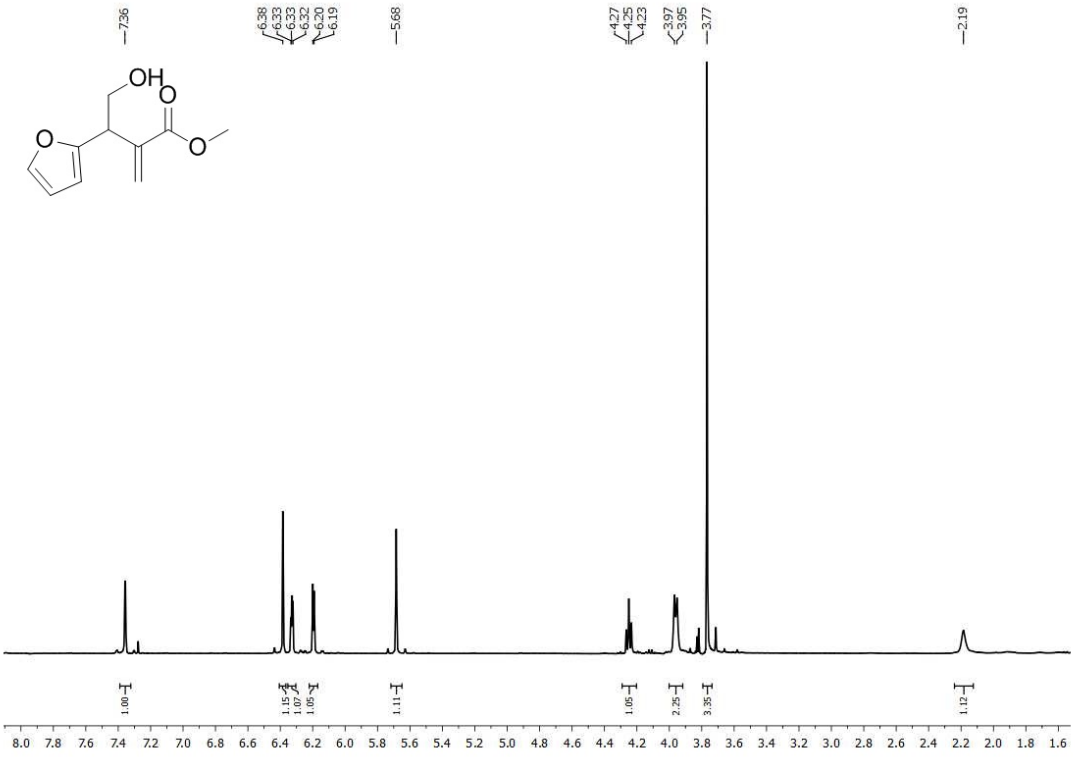

$^{13}$C NMR spectrum of methyl (4*E*)-3-(hydroxymethyl)-2-methylene-5-phenylpent-4-enoate.



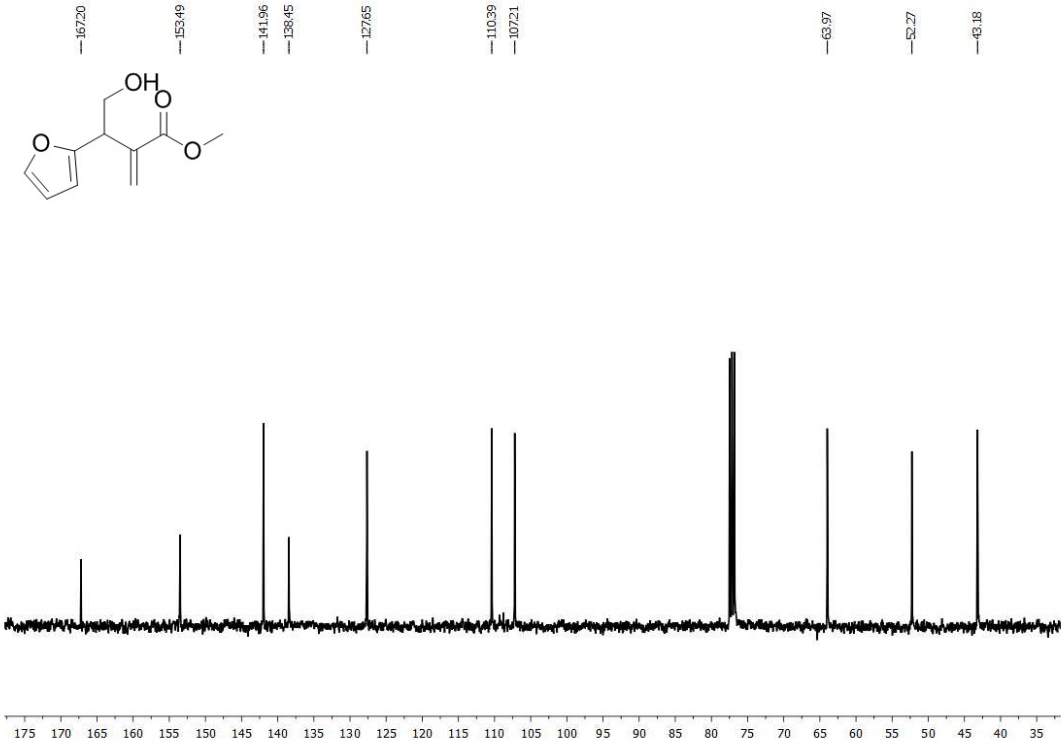

$^{1}$H NMR spectrum of methyl 3-(4-cyanophenyl)-4-hydroxy-2-methylenebutanoate.




$^{13}$C NMR spectrum of methyl 3-(4-cyanophenyl)-4-hydroxy-2-methylenebutanoate.

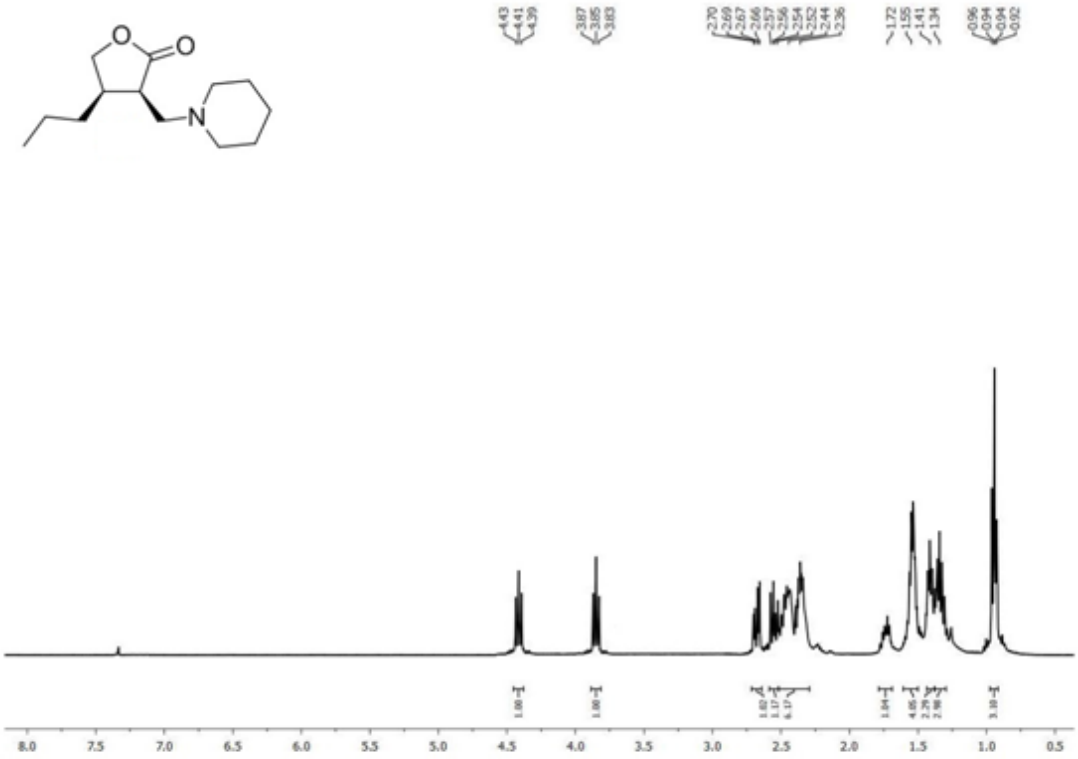



$^{1}$H NMR spectrum of methyl 3-(furan-2-yl)-4-hydroxy-2-methylenebutanoate.

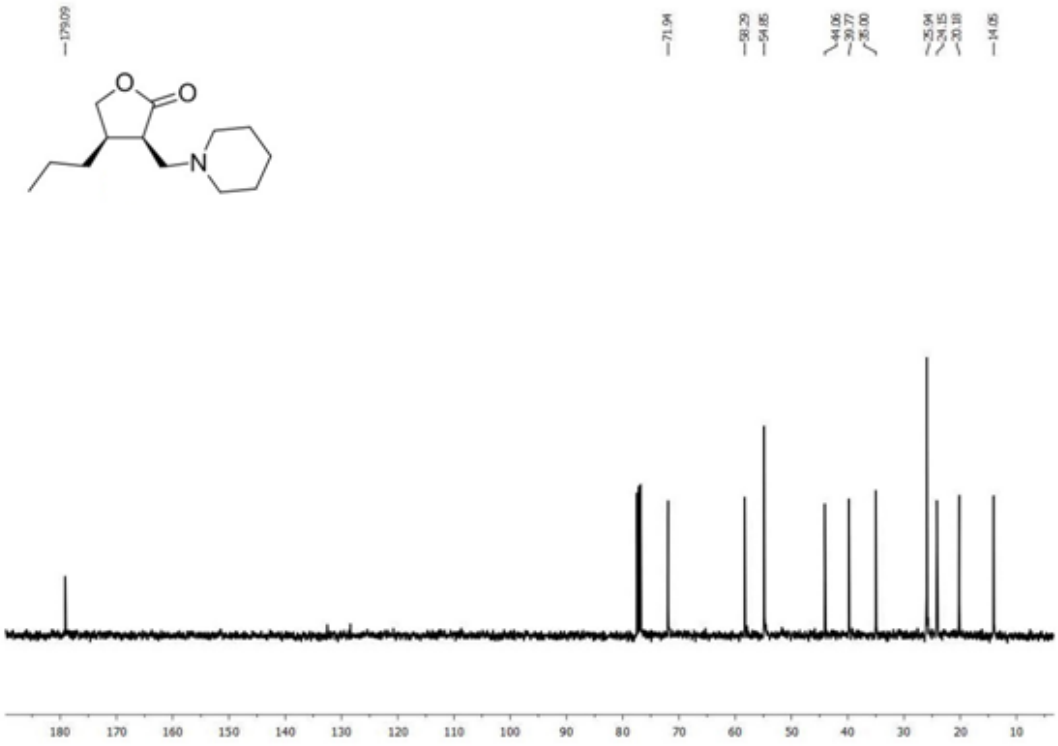



$^{13}$C NMR spectrum of methyl 3-(furan-2-yl)-4-hydroxy-2-methylenebutanoate.

**NMR Spectra of *cis*-Aminolactones**

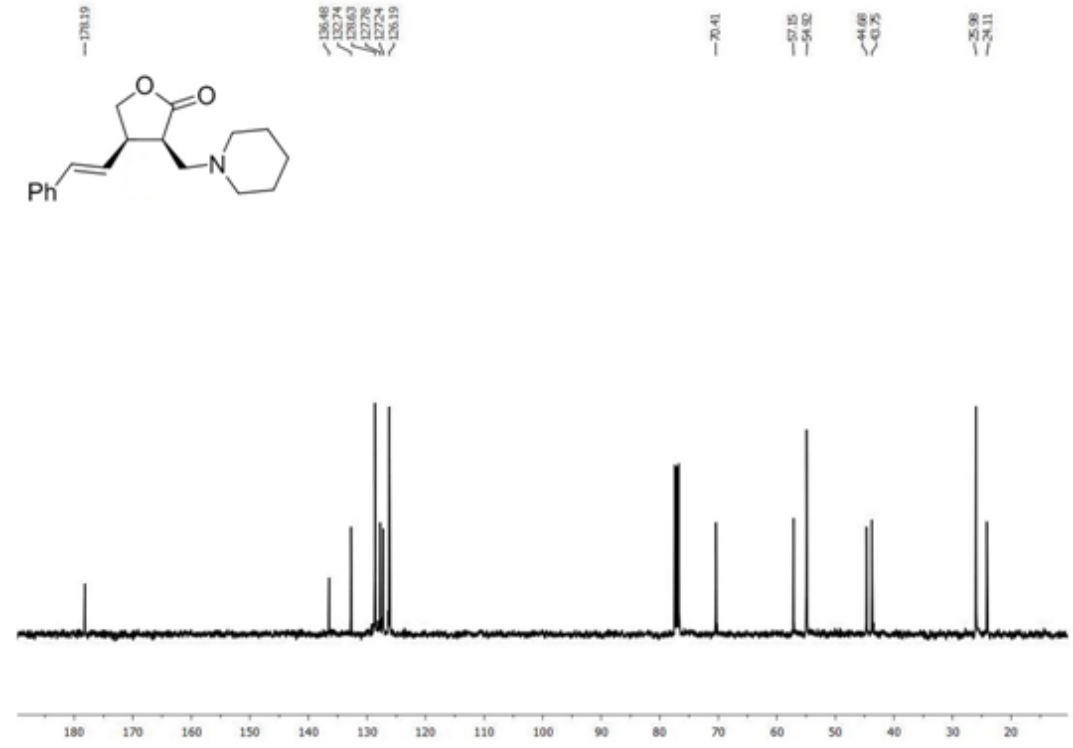


$^{1}$H NMR spectrum of **11**.

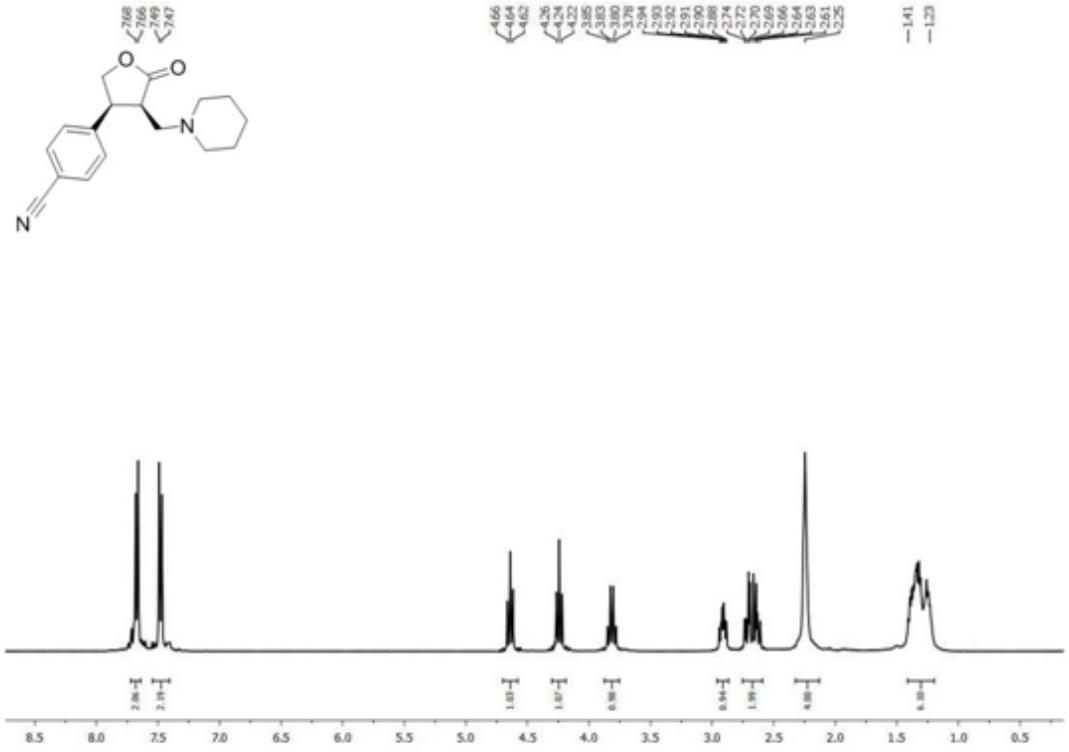


$^{13}$C NMR spectrum of **11**.

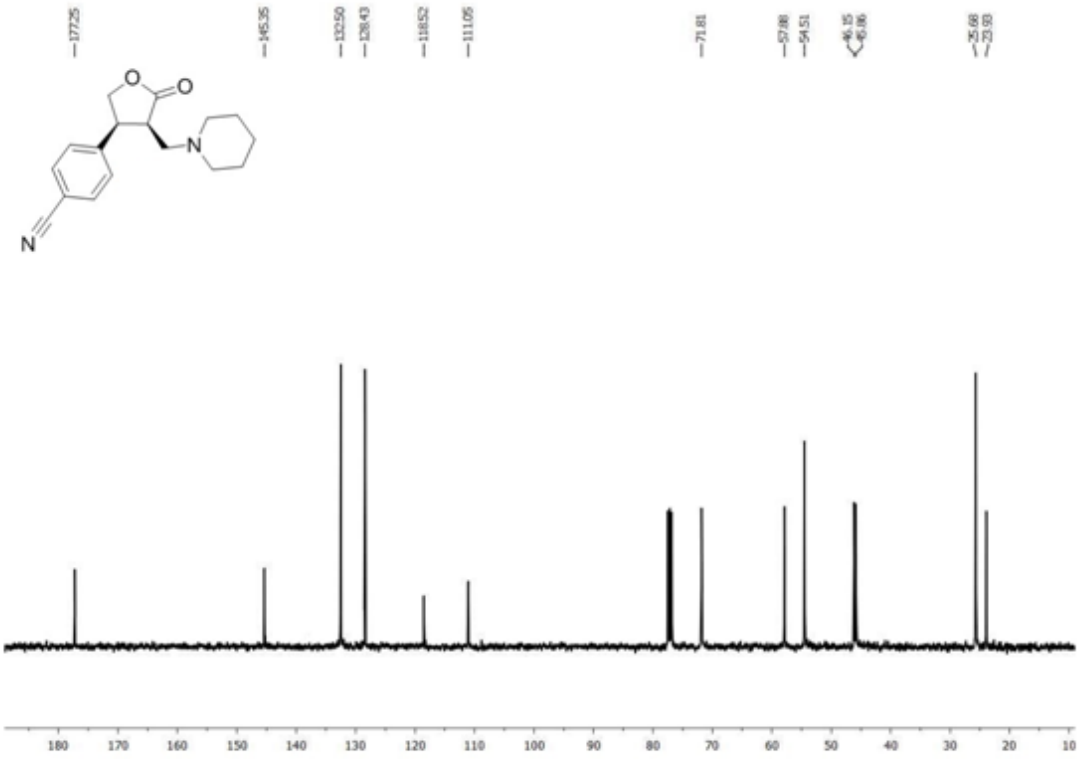

$^{1}$H NMR spectrum of **12**.



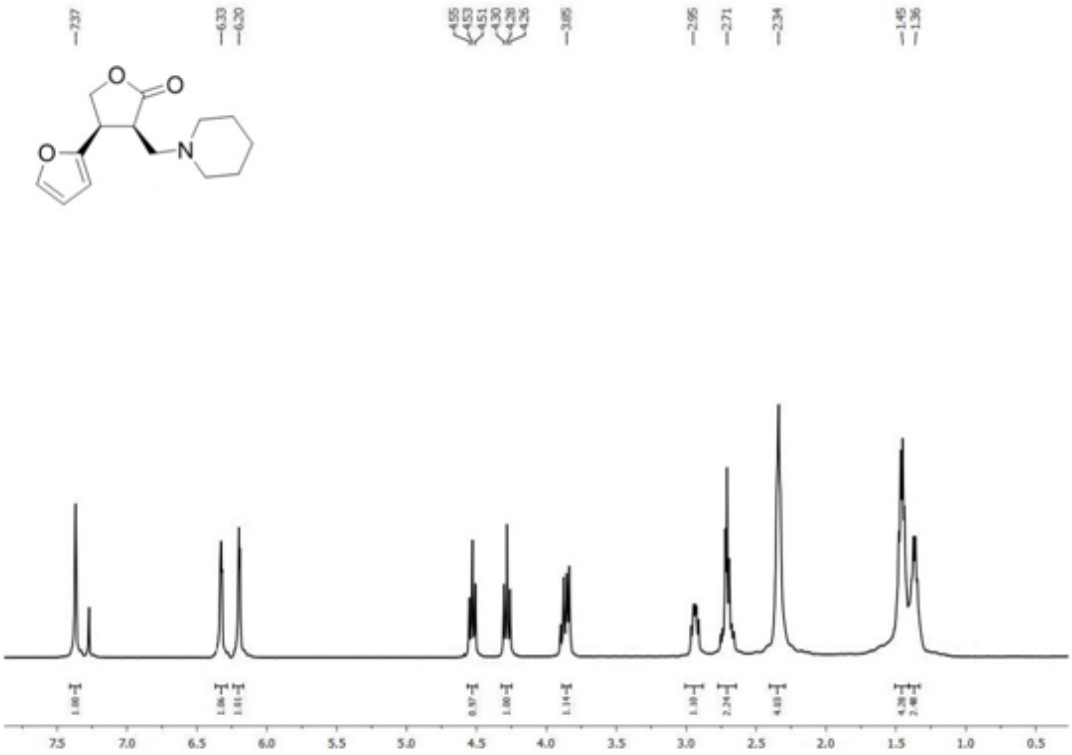

$^{13}$C NMR spectrum of **12**.



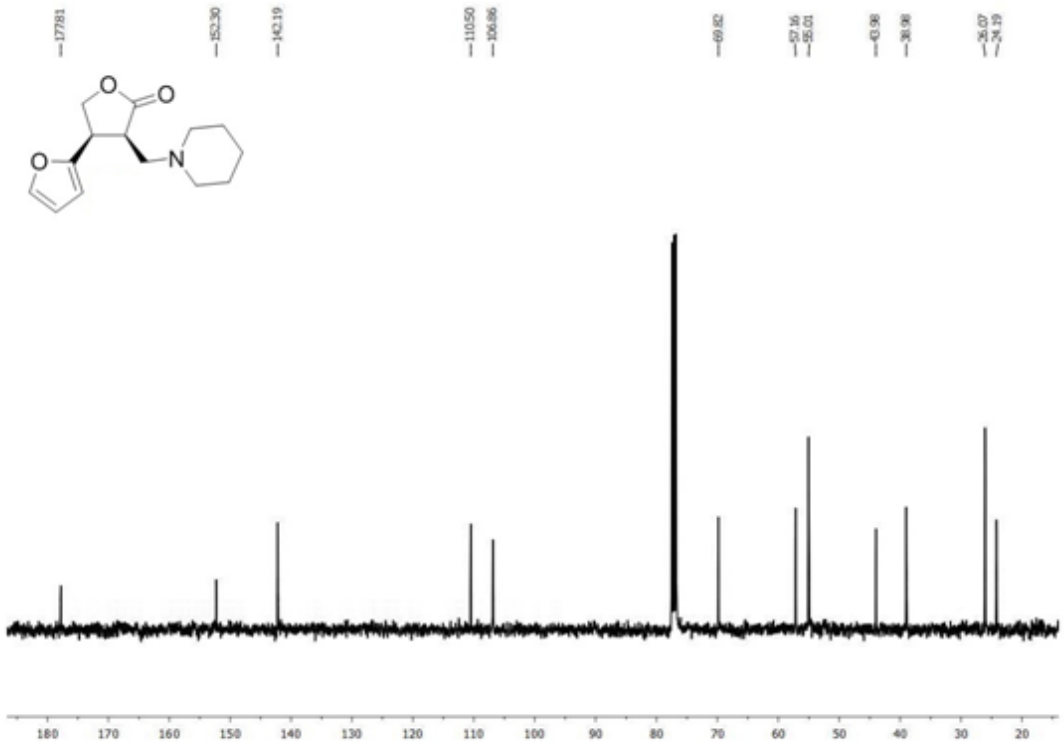
$^{1}$H NMR spectrum of **13**.



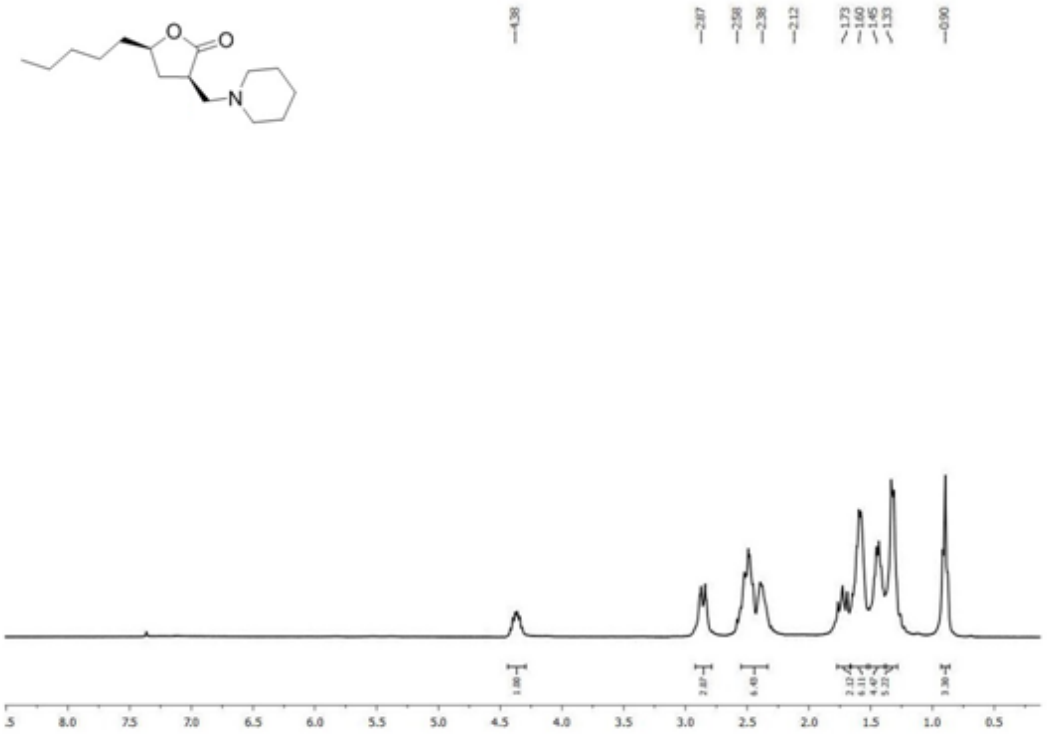
$^{13}$C NMR spectrum of **13**.



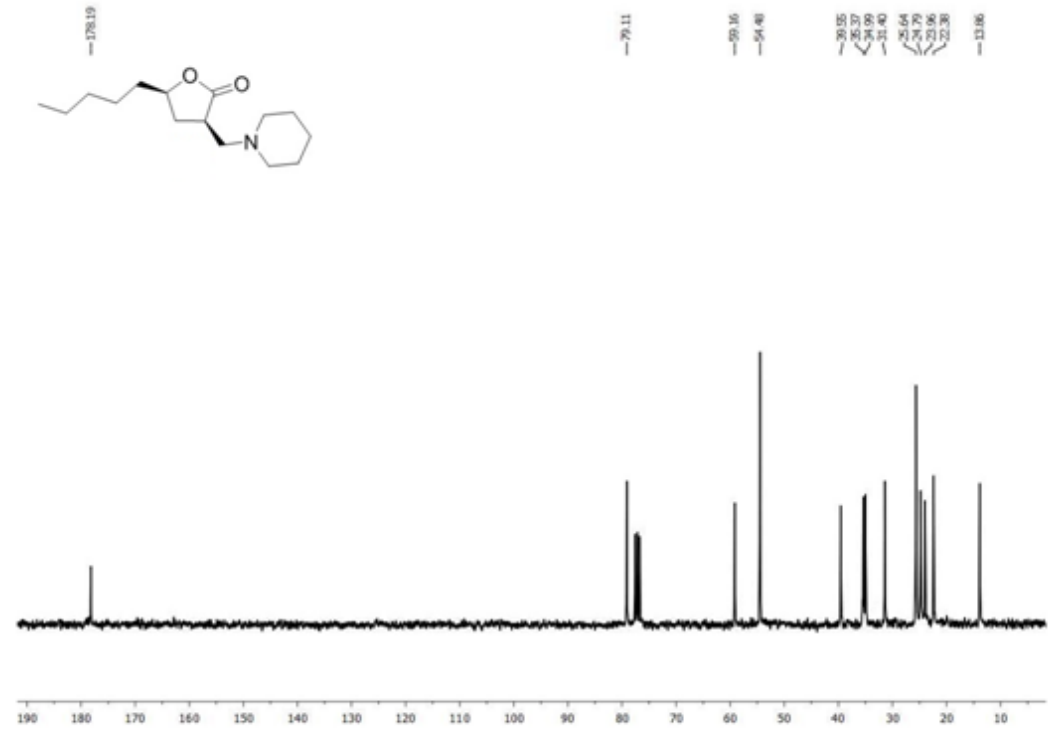
$^{1}$H NMR spectrum of **14**.



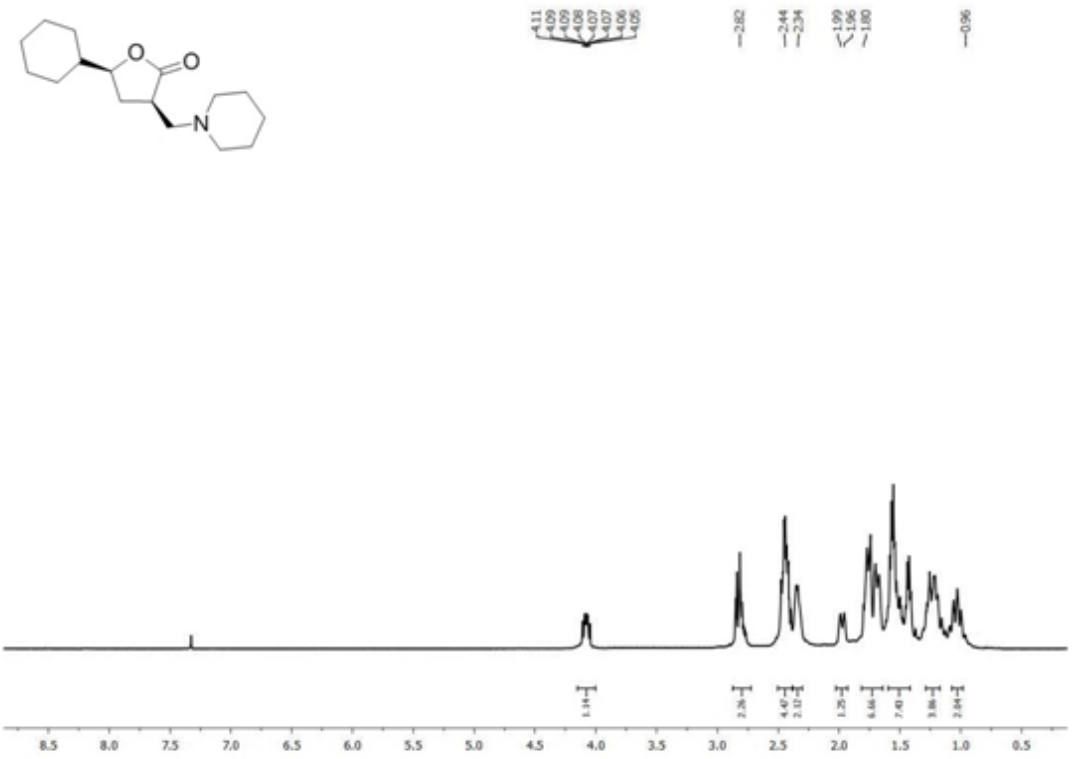
$^{13}$C NMR spectrum of **14**.



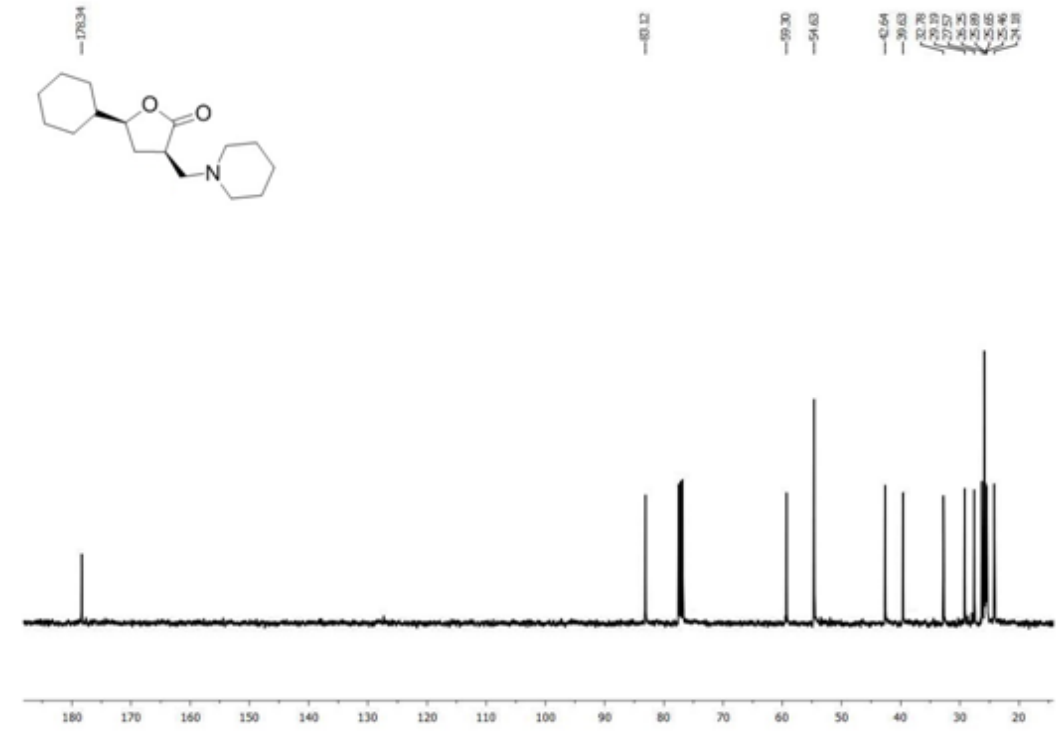
$^{1}$H NMR spectrum of **15**.



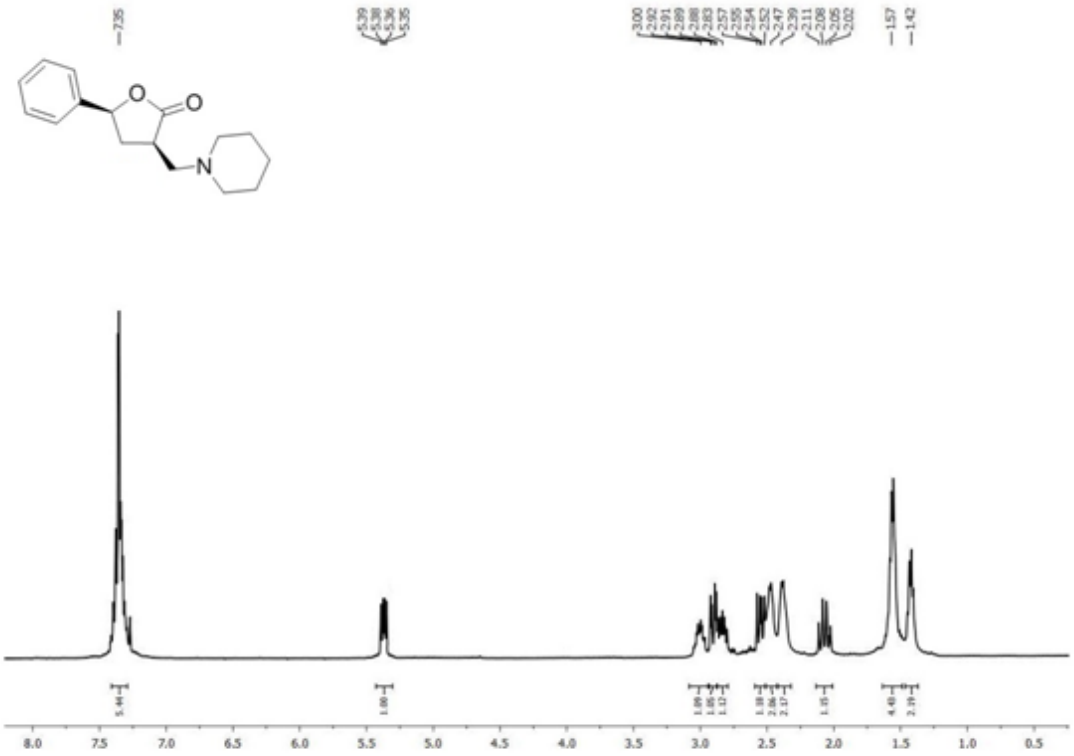
$^{13}$C NMR spectrum of **15**.



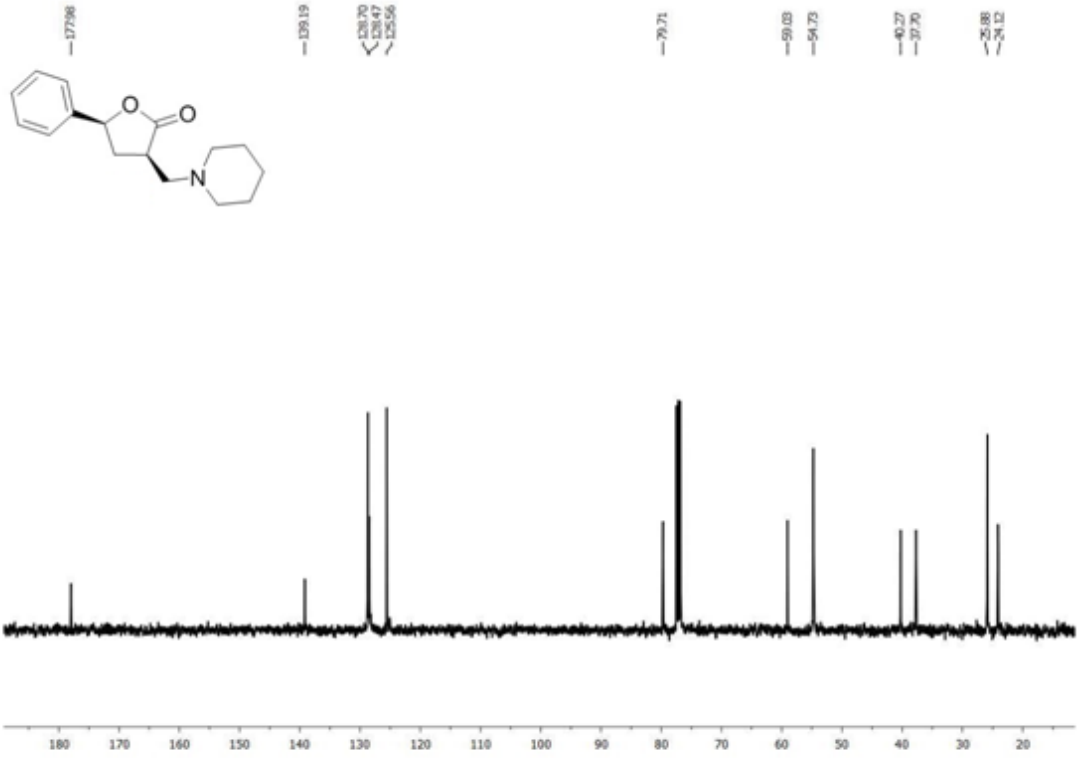
$^{1}$H NMR spectrum of **16**.



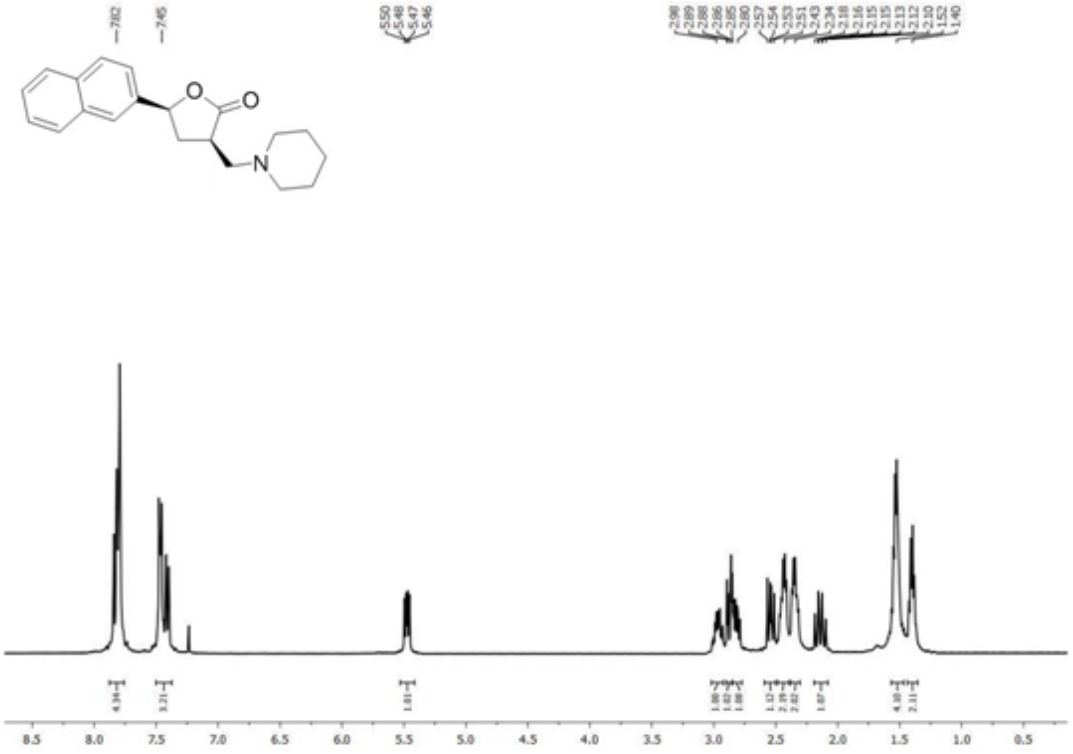
$^{13}$C NMR spectrum of **16**.



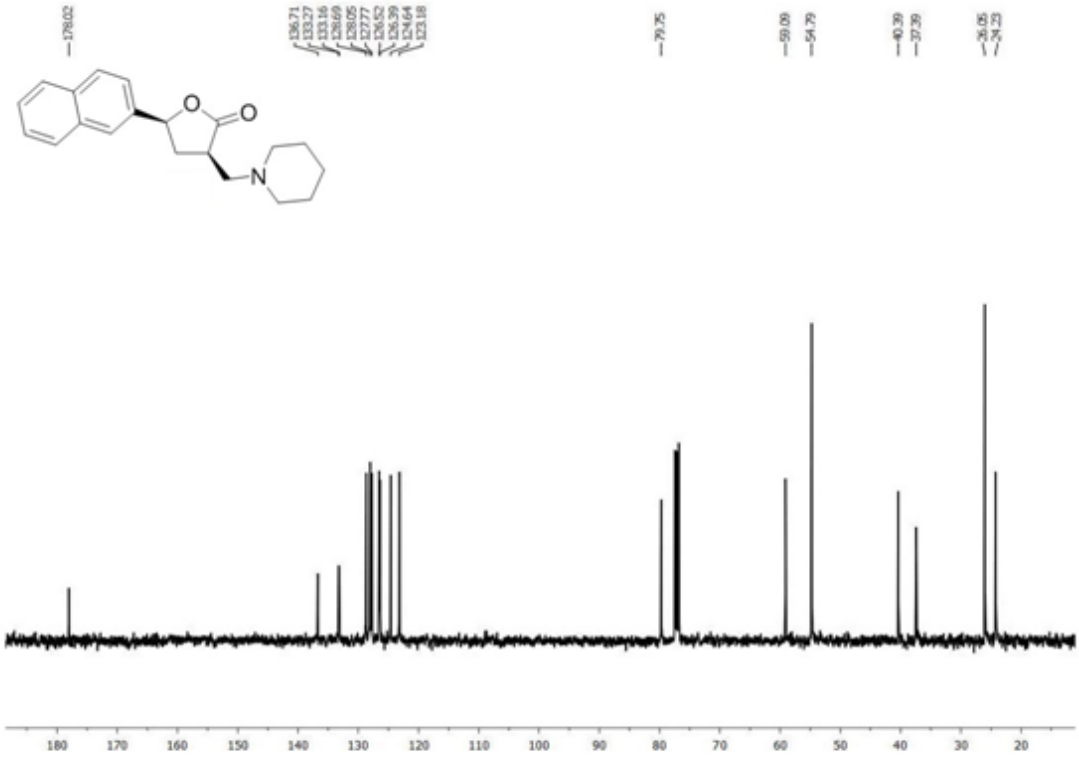
$^{1}$H NMR spectrum of **17**.



$^{13}$C NMR spectrum of **17**.

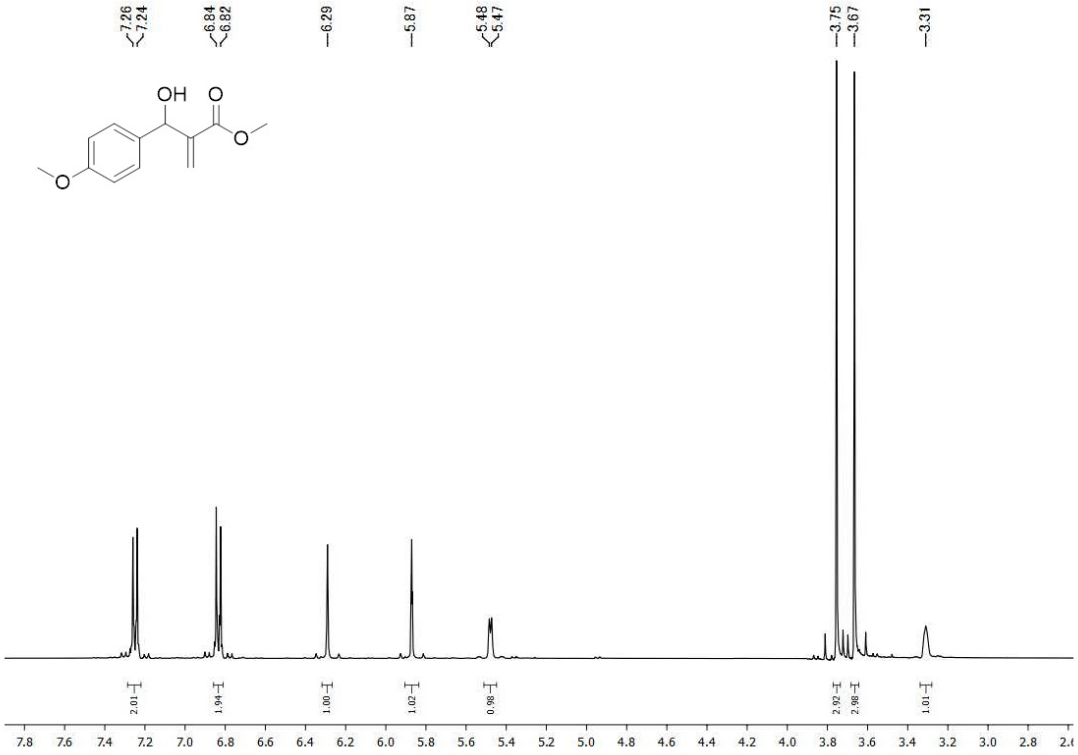


$^{1}$H NMR spectrum of **18**.

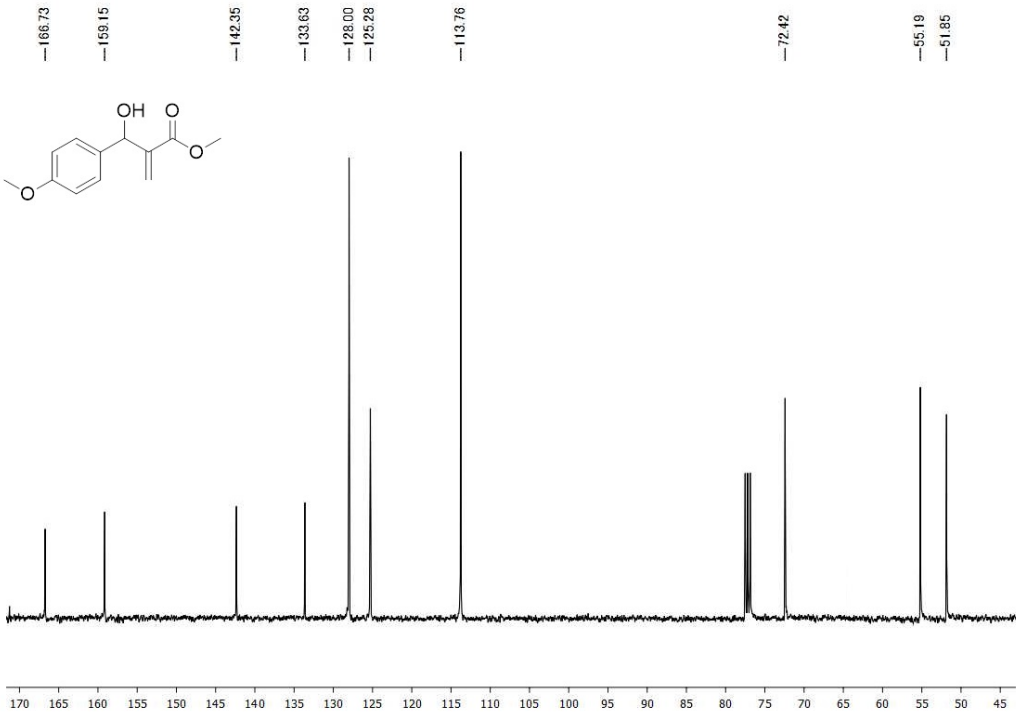


$^{13}$C NMR spectrum of **18**.

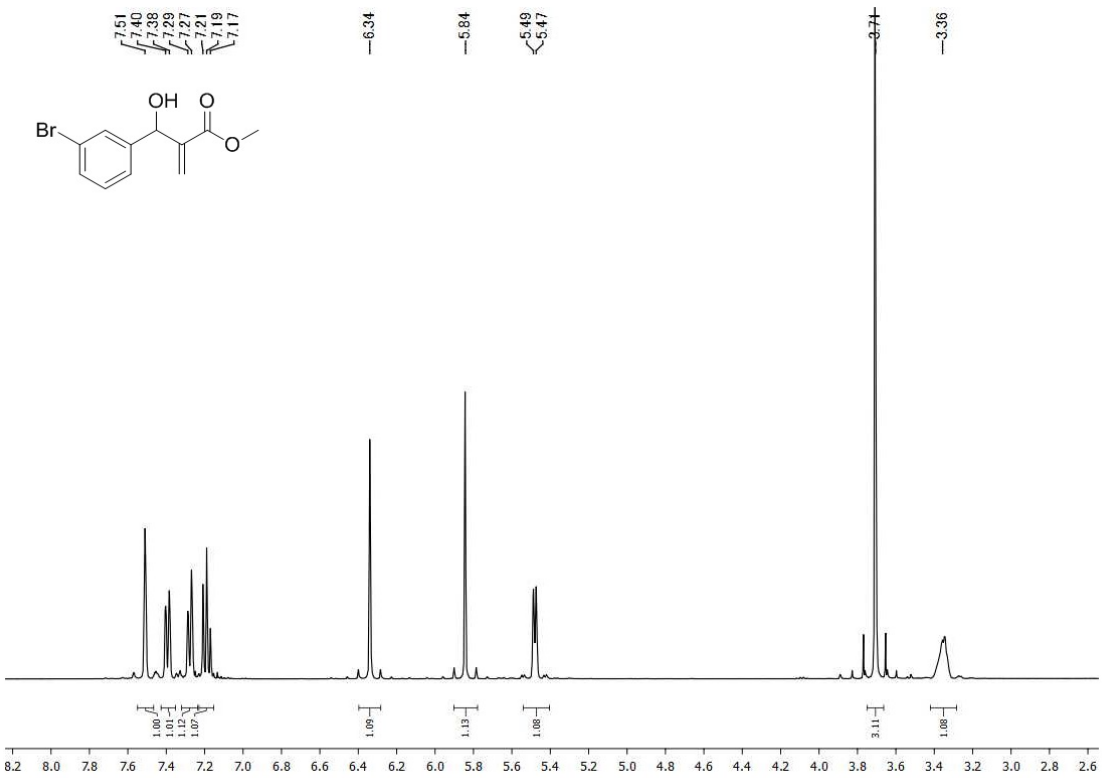
**NMR Spectra Associated with the Preparation of Aminolactonization Substrates**



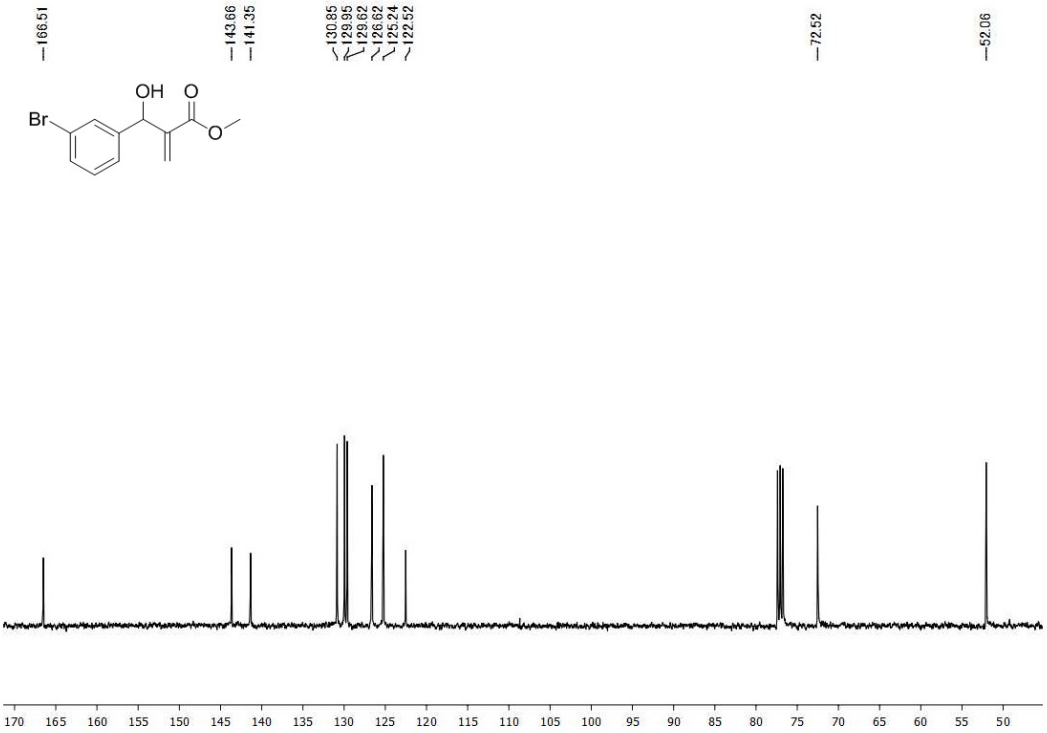

$^{1}$H NMR spectrum of methyl 2-((hydroxy)(4-methoxyphenyl)methyl)prop-2-enoate.



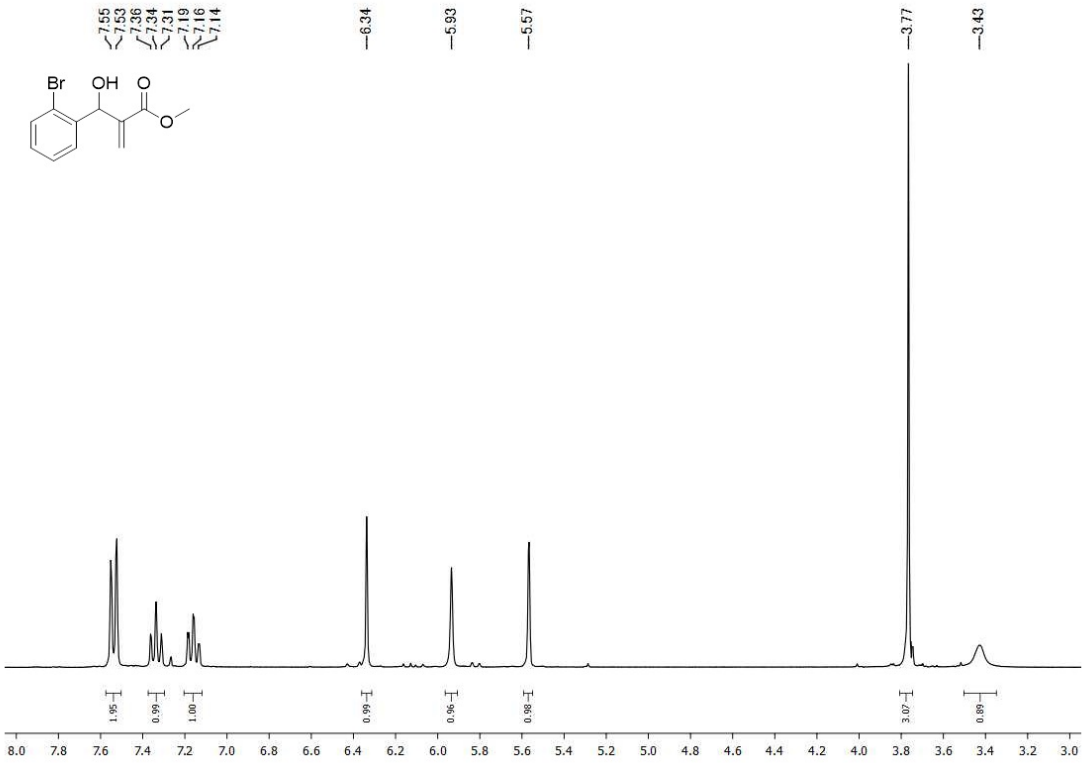

$^{13}$C NMR spectrum of methyl 2-((hydroxy)(4-methoxyphenyl)methyl)prop-2-enoate.



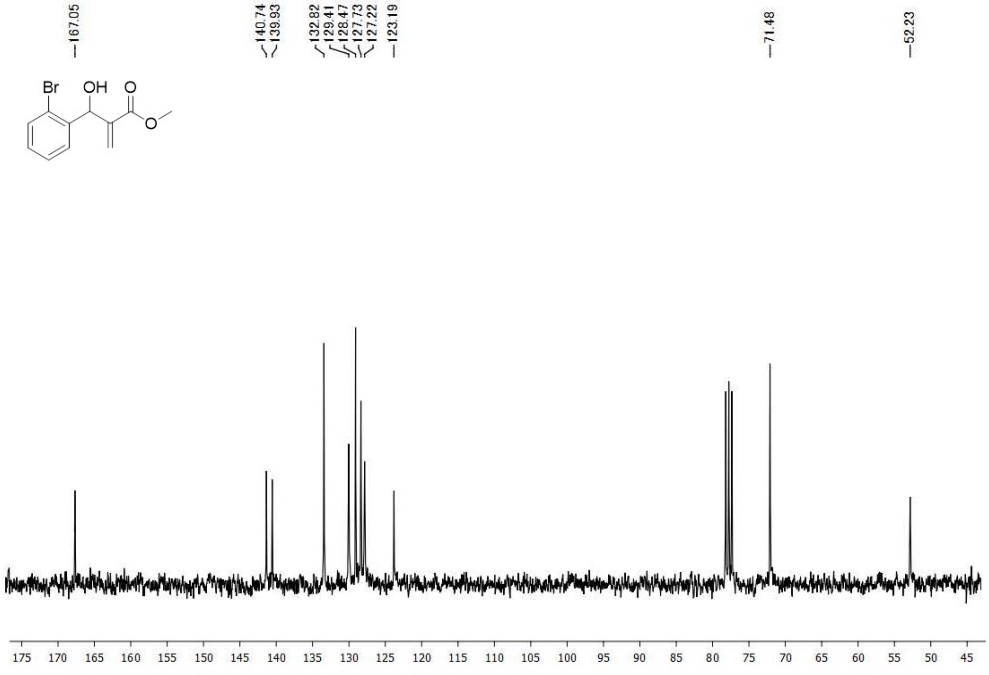

$^{1}$H NMR spectrum of methyl 2-((hydroxy)(3-bromophenyl)methyl)prop-2-enoate.



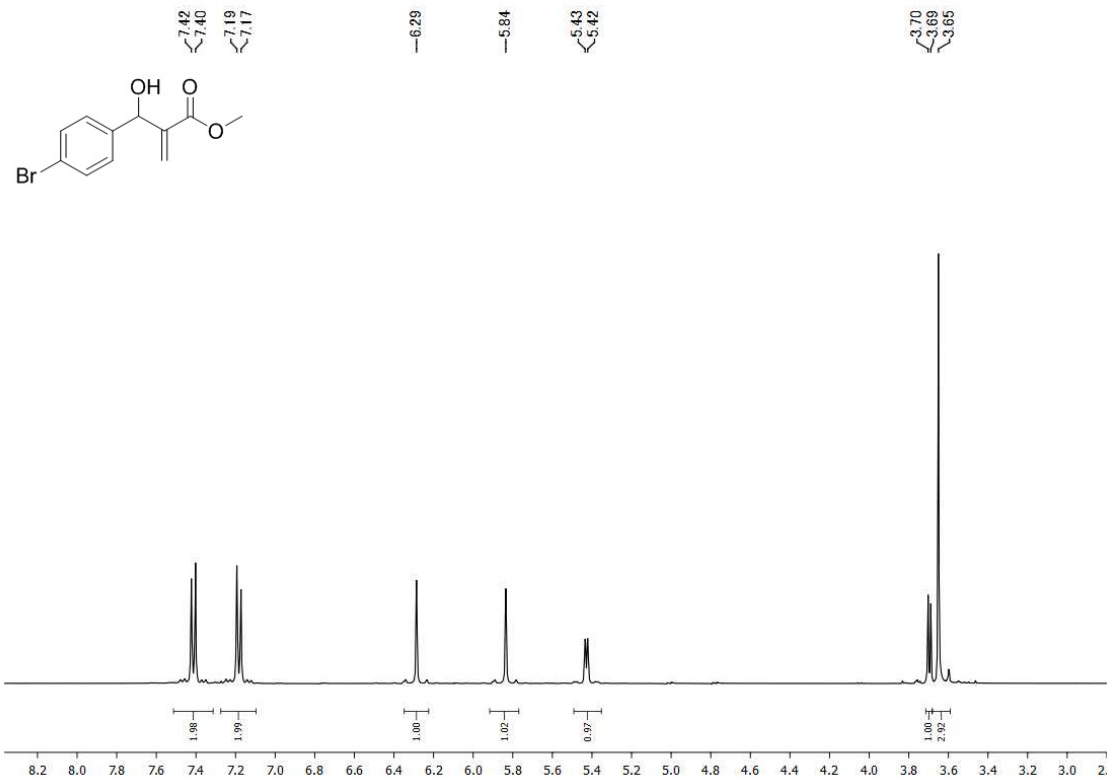

$^{13}$C NMR spectrum of methyl 2-((hydroxy)(3-bromophenyl)methyl)prop-2-enoate.



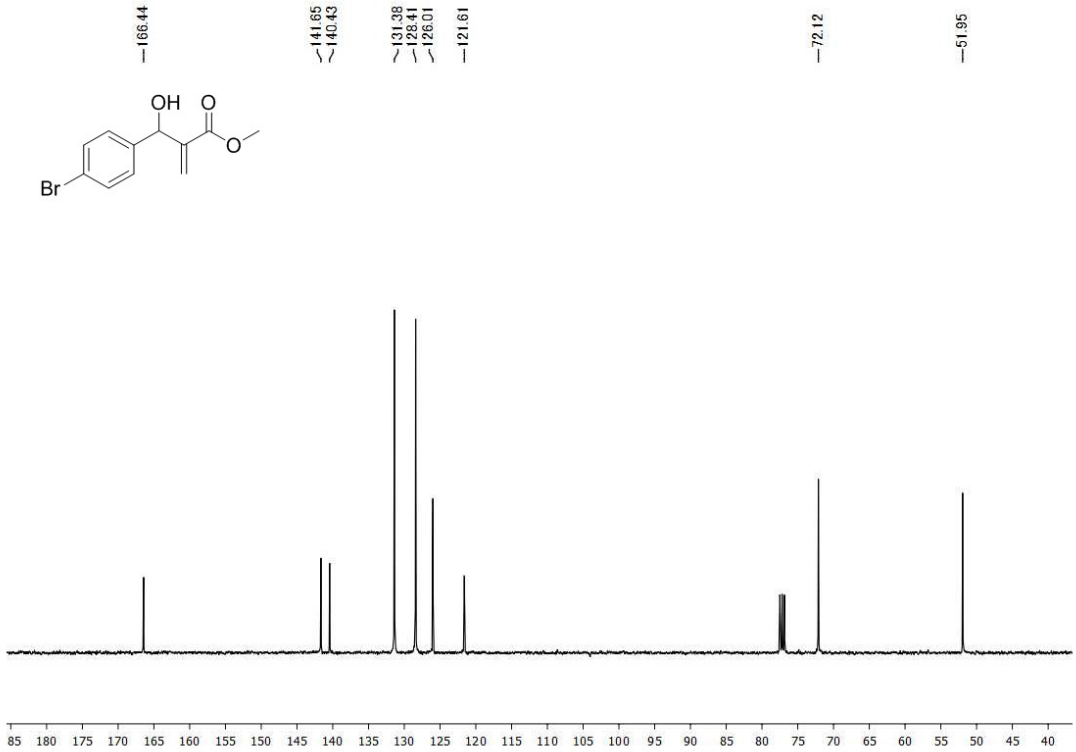

$^{1}$H NMR spectrum of methyl 2-((hydroxy)(2-bromophenyl)methyl)prop-2-enoate.



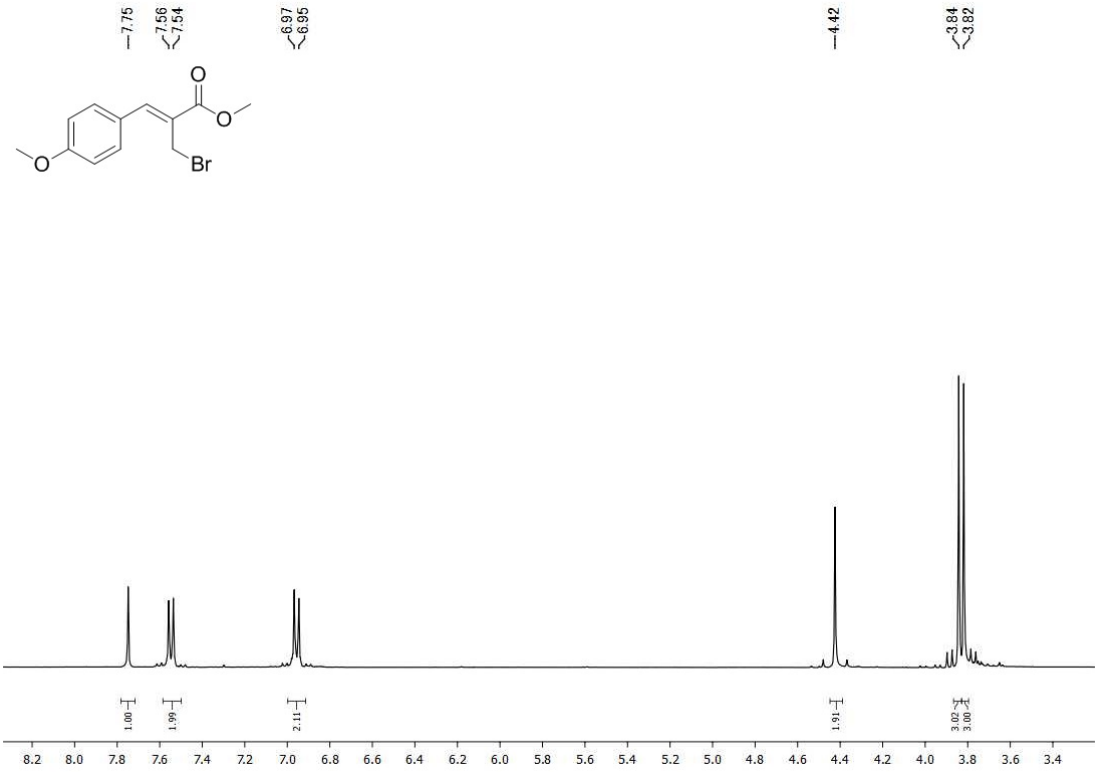

$^{13}$C NMR spectrum of methyl 2-((hydroxy)(2-bromophenyl)methyl)prop-2-enoate.



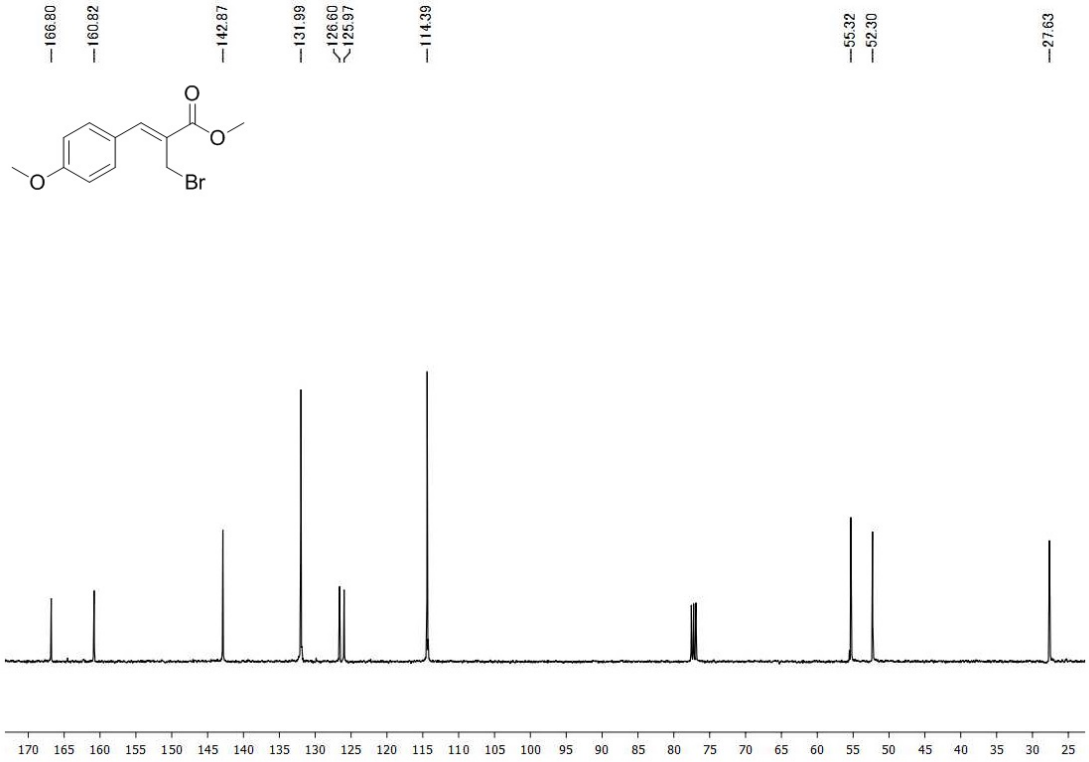

$^{1}$H NMR spectrum of methyl 2-((hydroxy)(4-bromophenyl)methyl)prop-2-enoate.



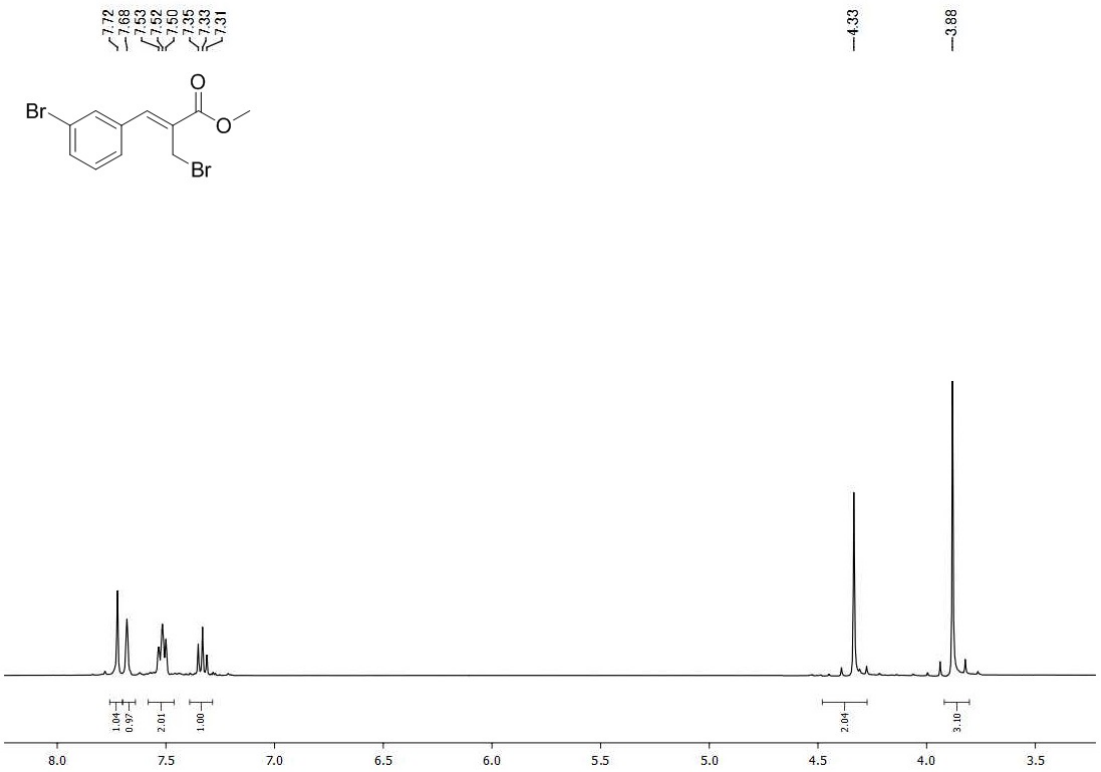

$^{13}$C NMR spectrum of methyl 2-((hydroxy)(4-bromophenyl)methyl)prop-2-enoate.



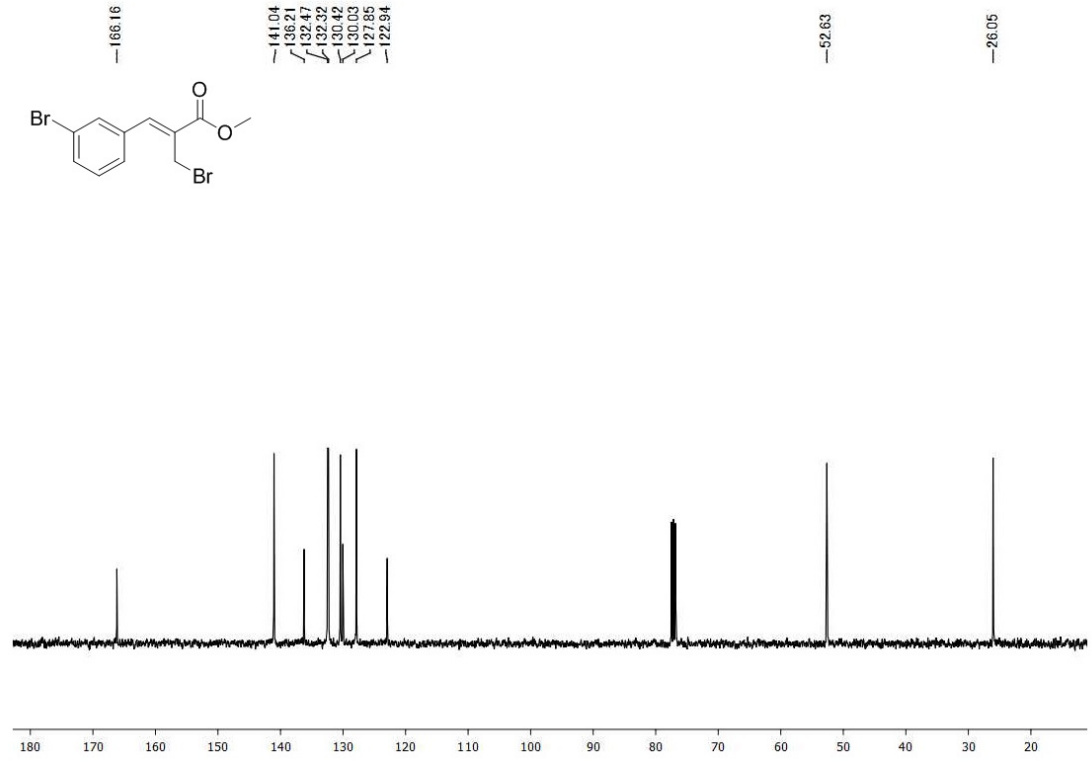

$^{1}$H NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-(4-methoxyphenyl)prop-2-enoate.



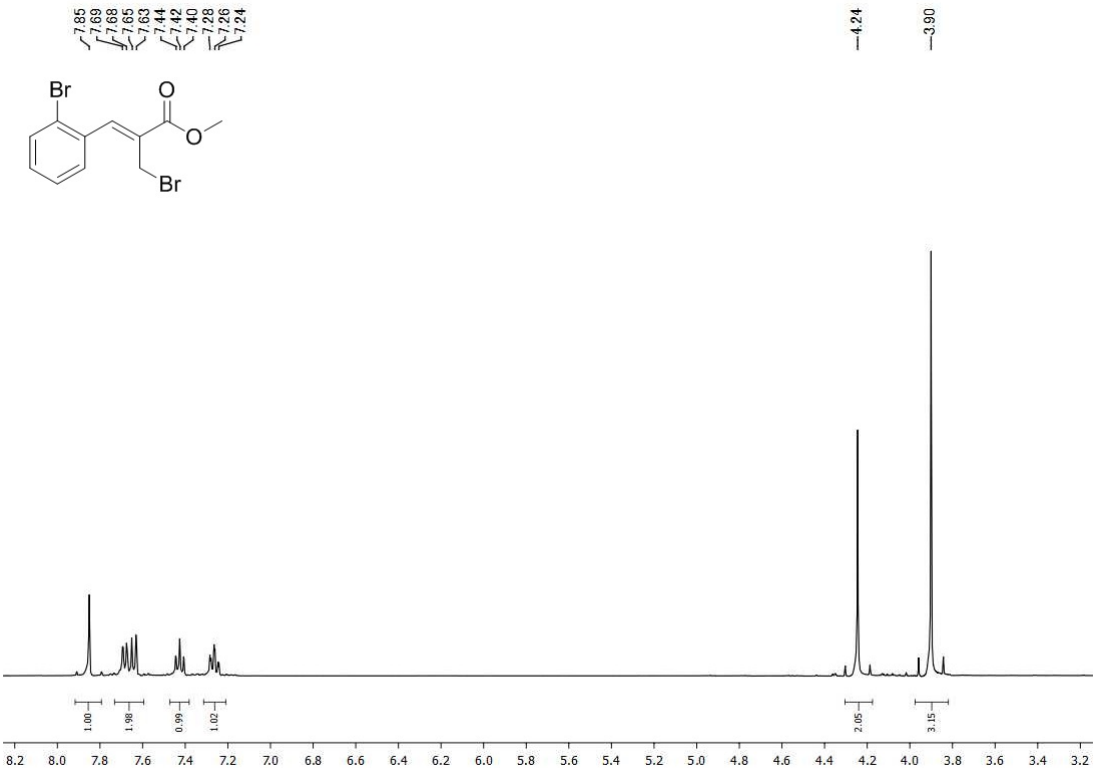

$^{13}$C NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-(4-methoxyphenyl)prop-2-enoate.



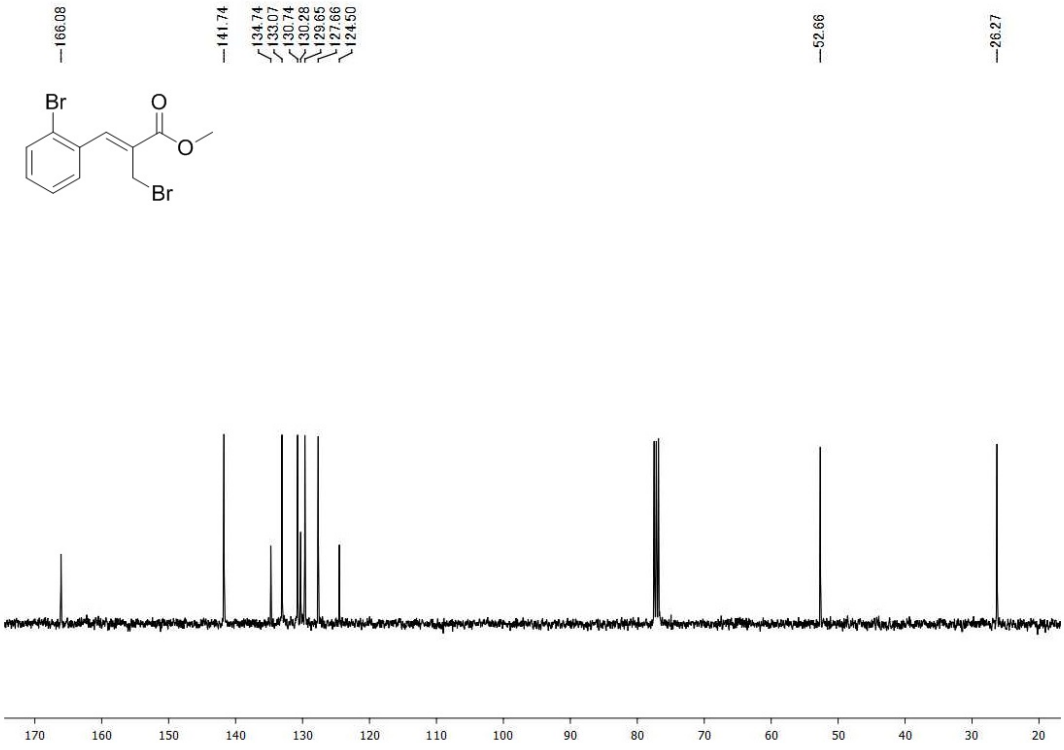

$^{1}$H NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-(3-bromophenyl)prop-2-enoate.



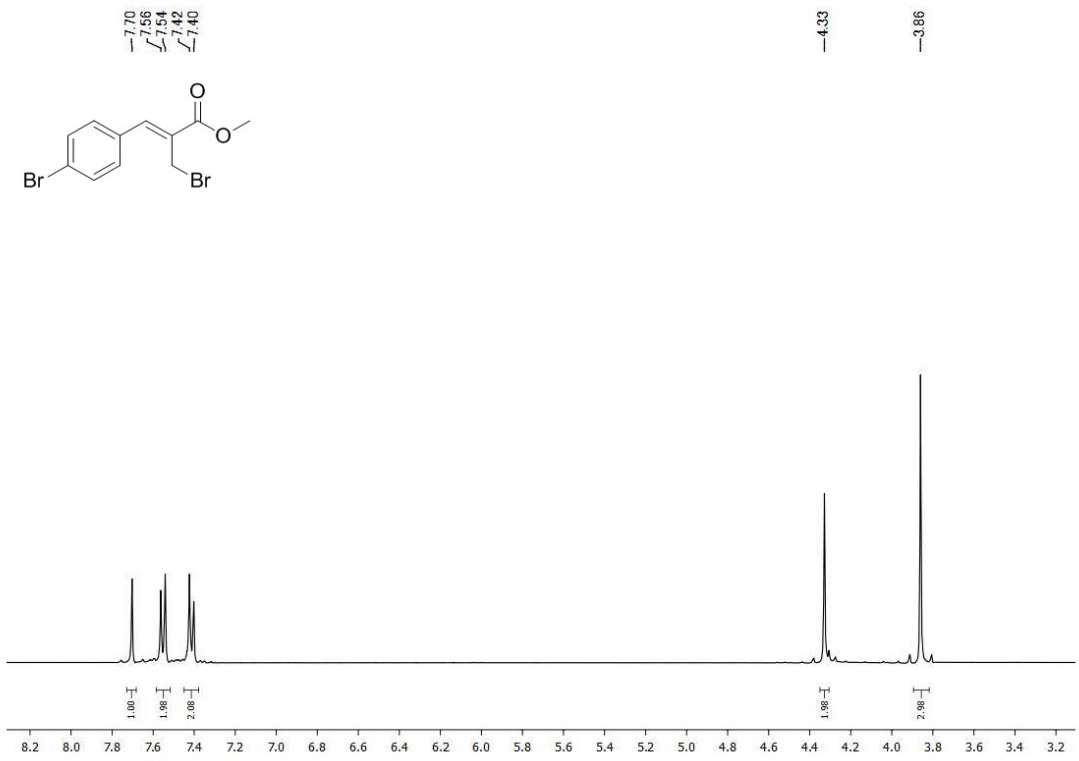

$^{13}$C NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-(3-bromophenyl)prop-2-enoate.



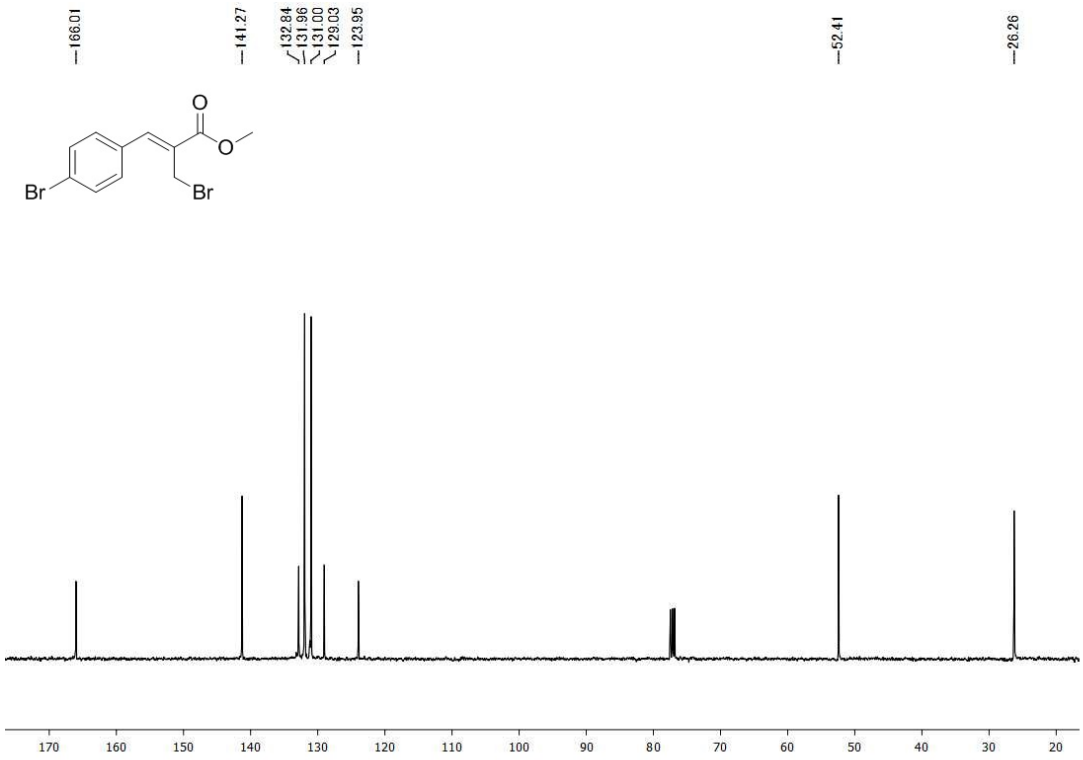

$^{1}$H NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-(2-bromophenyl)prop-2-enoate.



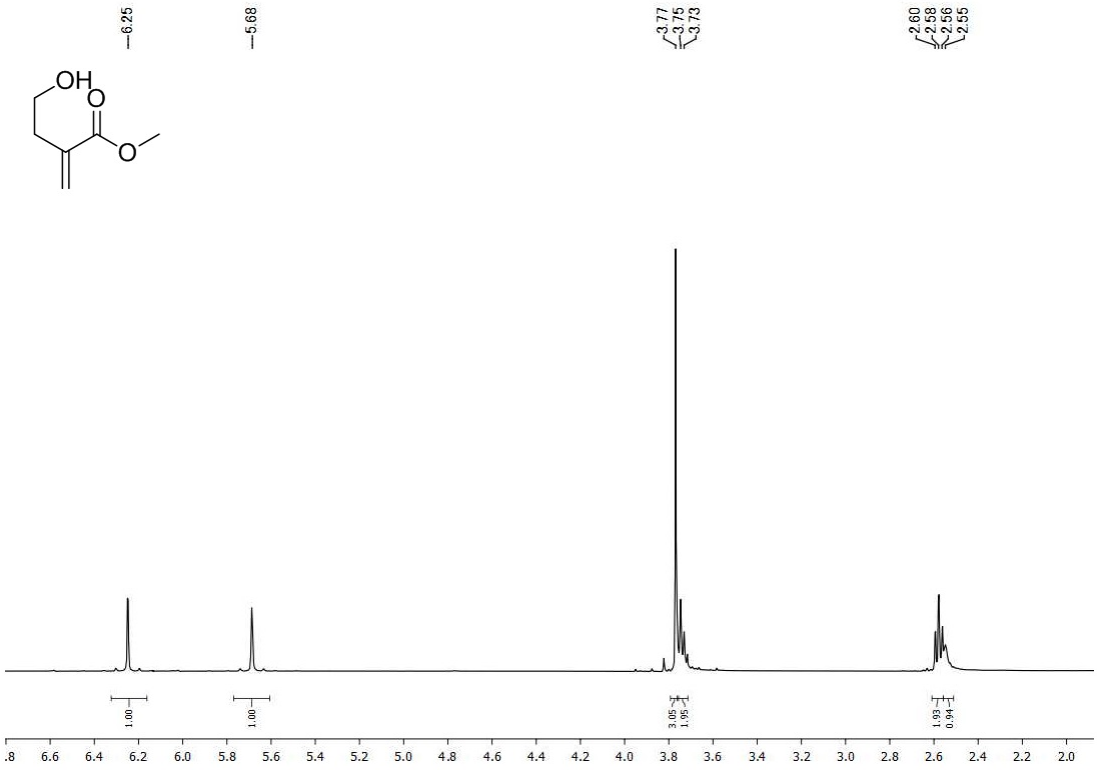

$^{13}$C NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-(2-bromophenyl)prop-2-enoate.



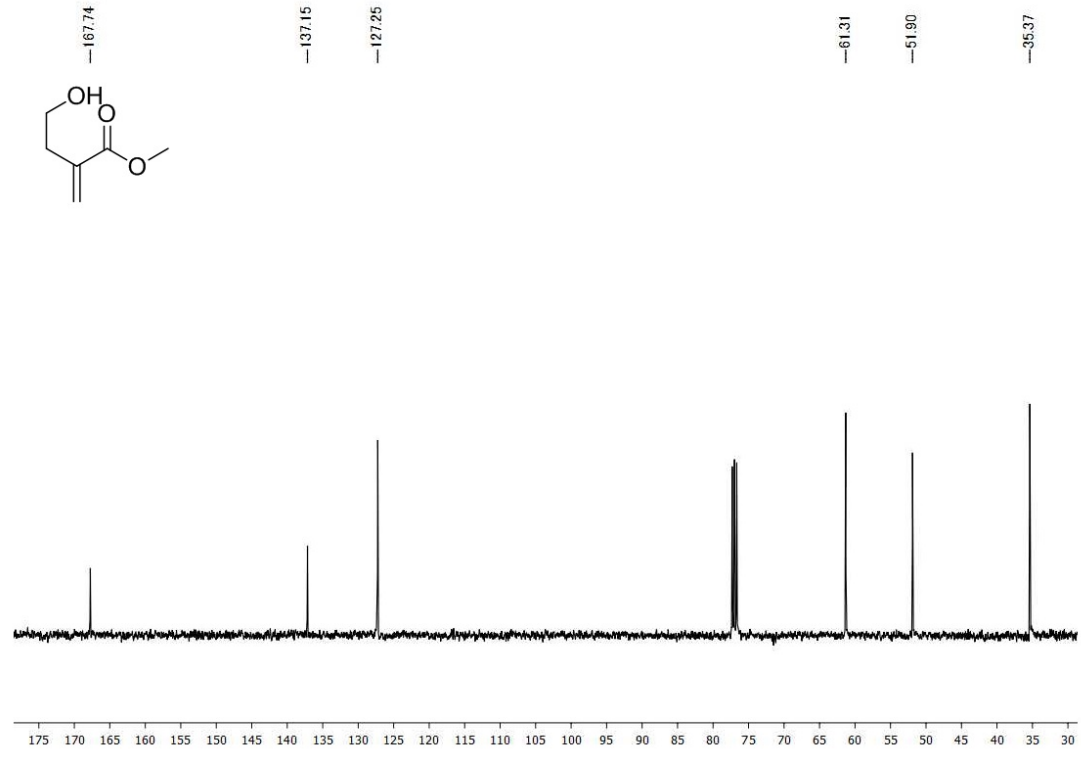

$^{1}$H NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-(4-bromophenyl)prop-2-enoate.



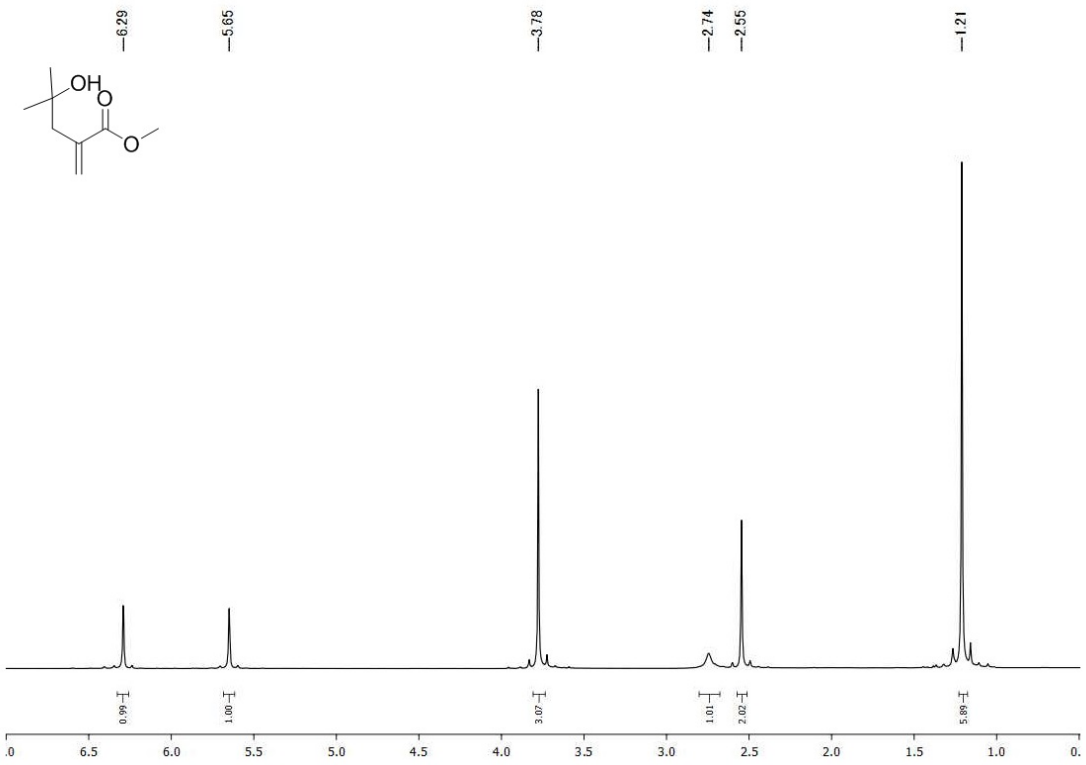

$^{13}$C NMR spectrum of methyl (2*Z*)-2-(bromomethyl)-3-(4-bromophenyl)prop-2-enoate.



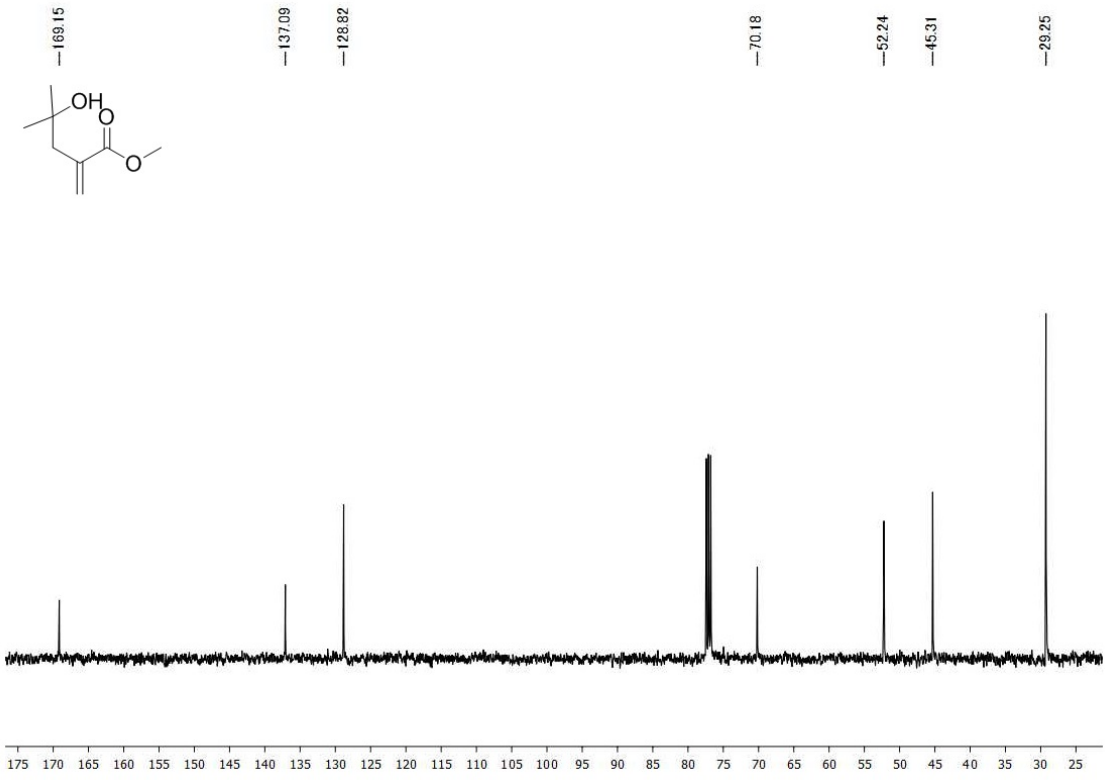

$^{1}$H NMR spectrum of methyl 4-hydroxy-2-methylenebutanoate.



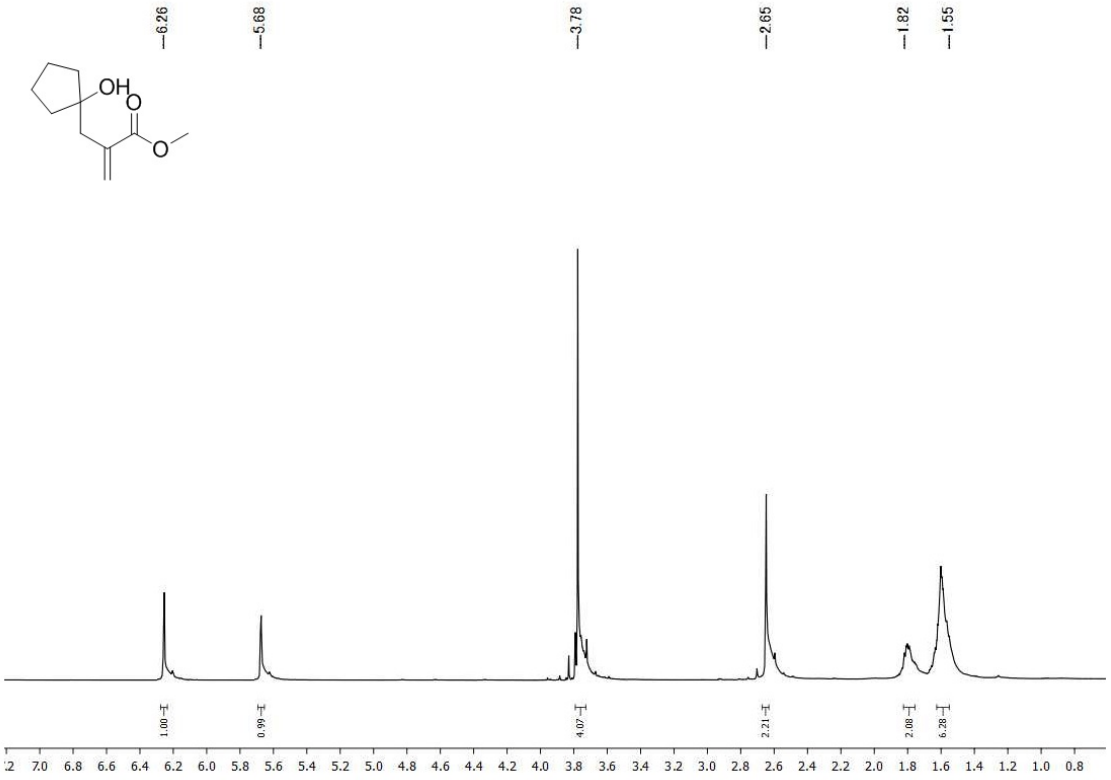

$^{13}$C NMR spectrum of methyl 4-hydroxy-2-methylenebutanoate.




$^{1}$H NMR spectrum of methyl 4-hydroxy-4,4-dimethyl-2-methylenebutanoate.

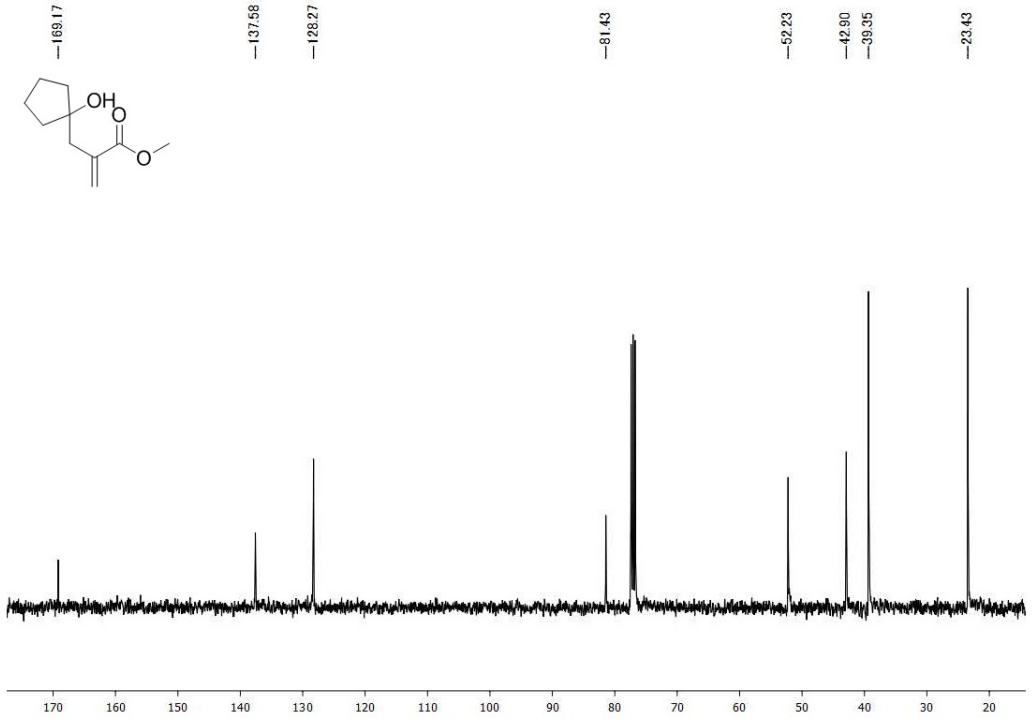



$^{13}$C NMR spectrum of methyl 4-hydroxy-4,4-dimethyl-2-methylenebutanoate.

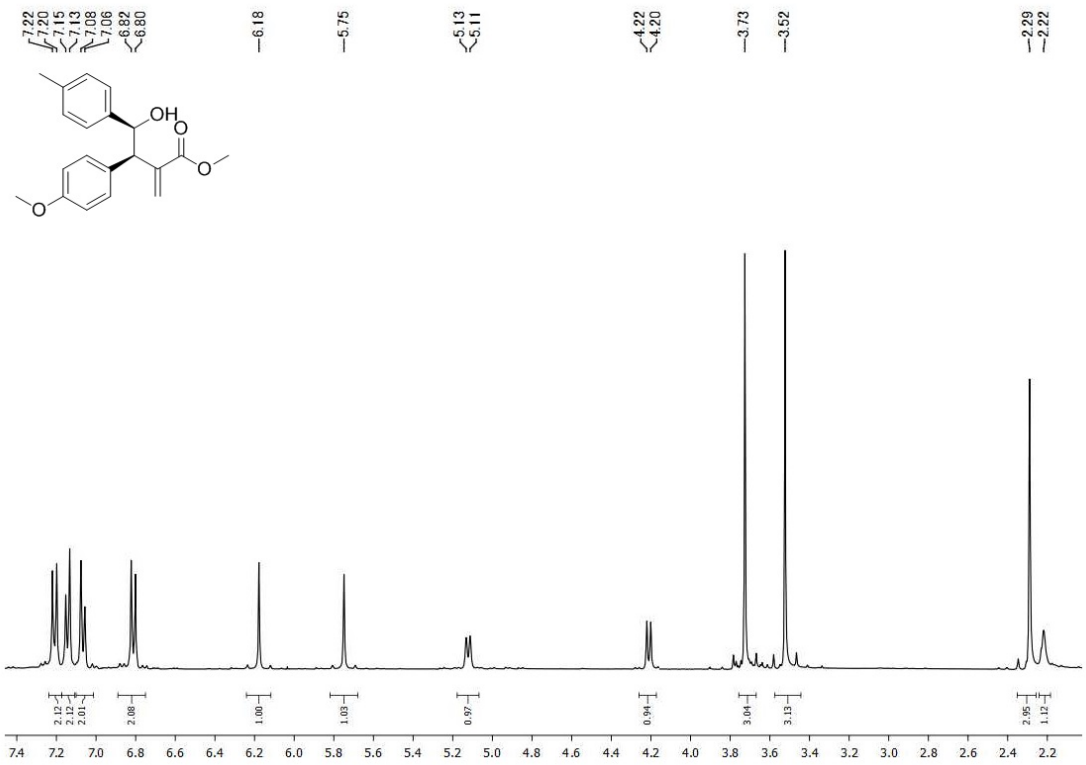



$^{1}$H NMR spectrum of methyl 2-((1-hydroxycyclopentyl)methyl)prop-2-enoate.

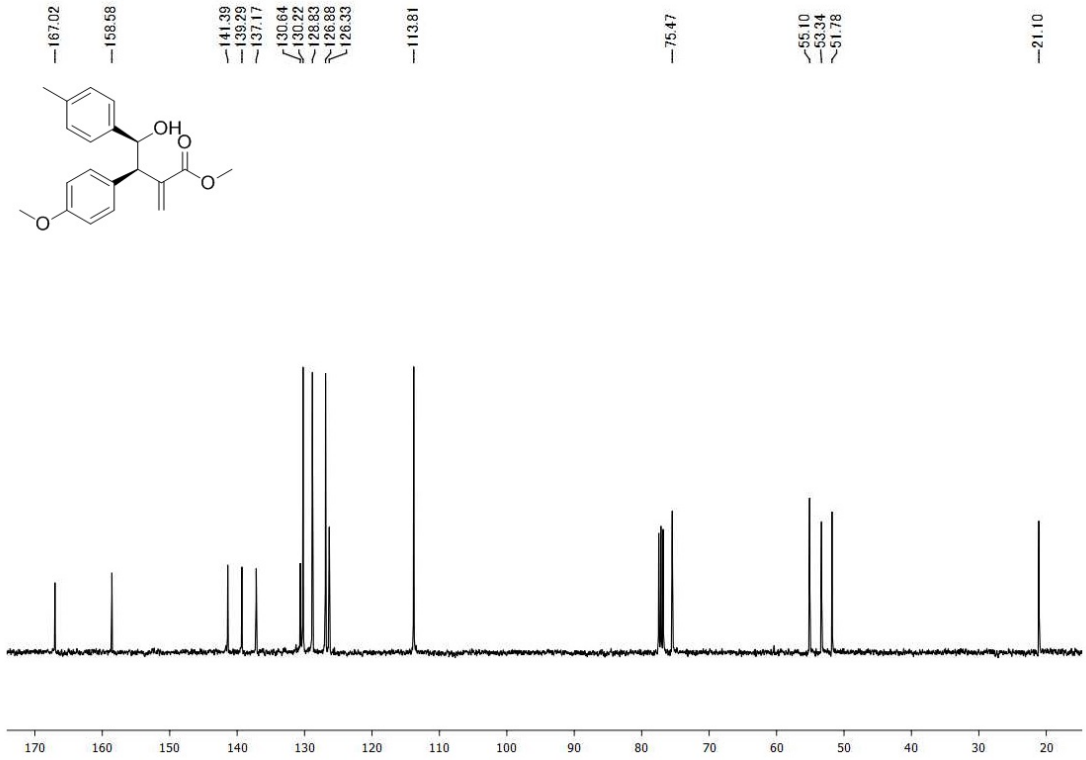
-



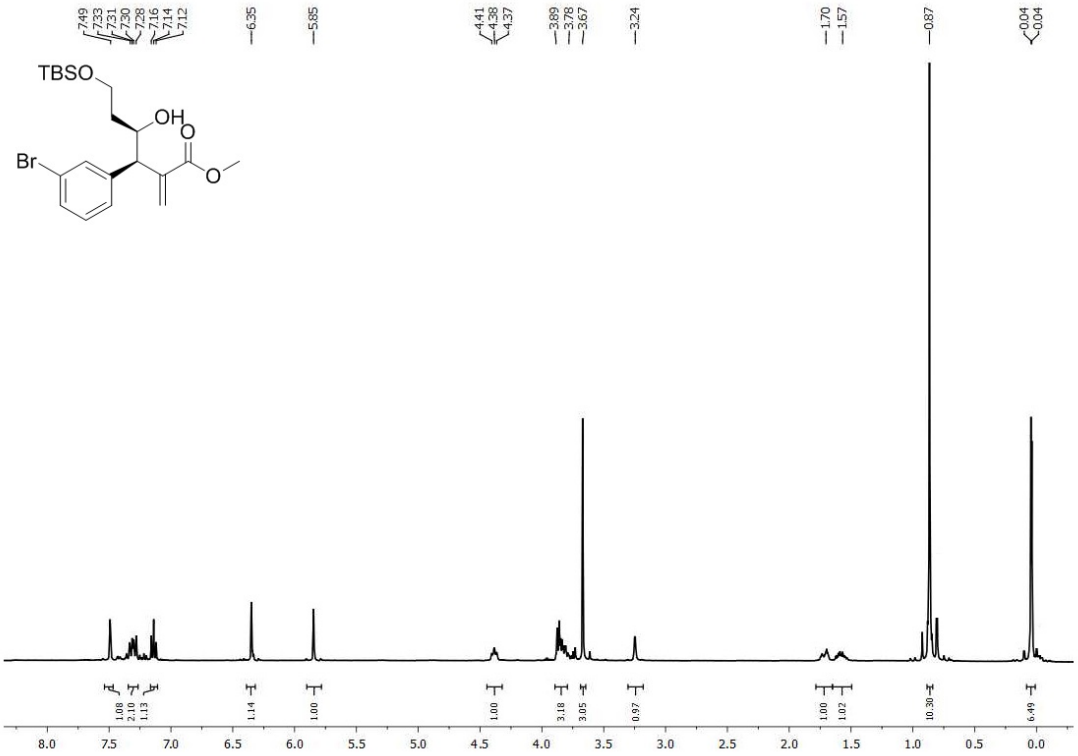

$^{13}$C NMR spectrum of methyl 2-((1-hydroxycyclopentyl)methyl)prop-2-enoate.



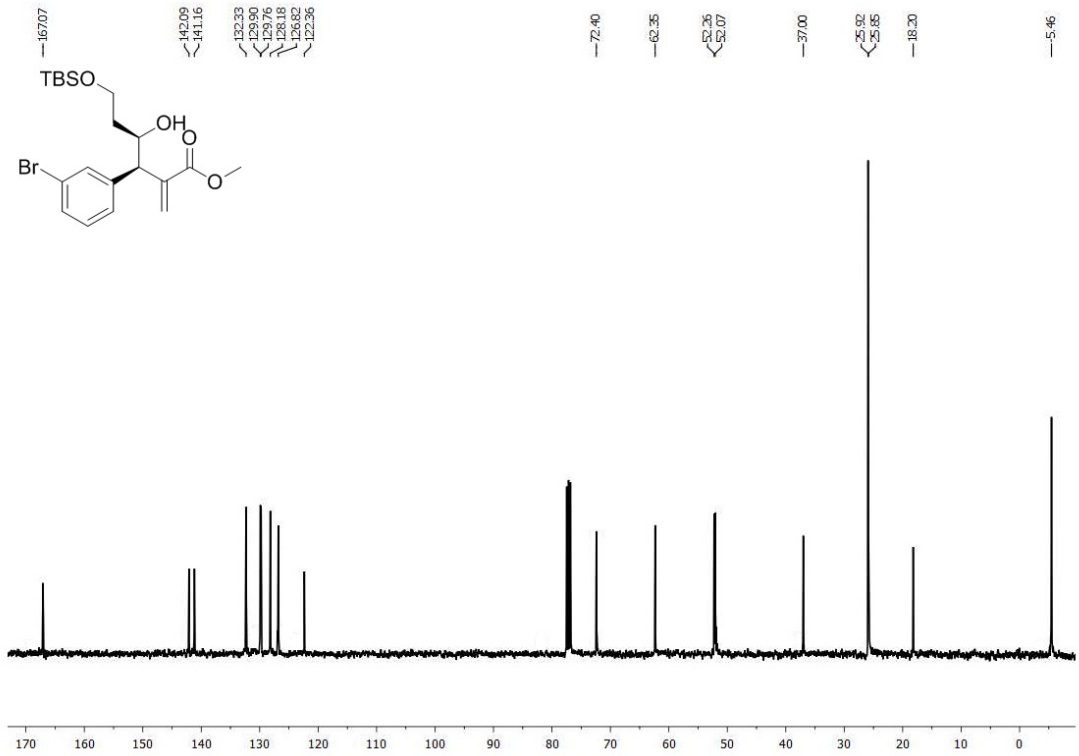

$^{1}$H NMR spectrum of methyl *syn*-4-hydroxy-3-(4-methoxyphenyl)-2-methylene-4-(4-methylphenyl)butanoate.



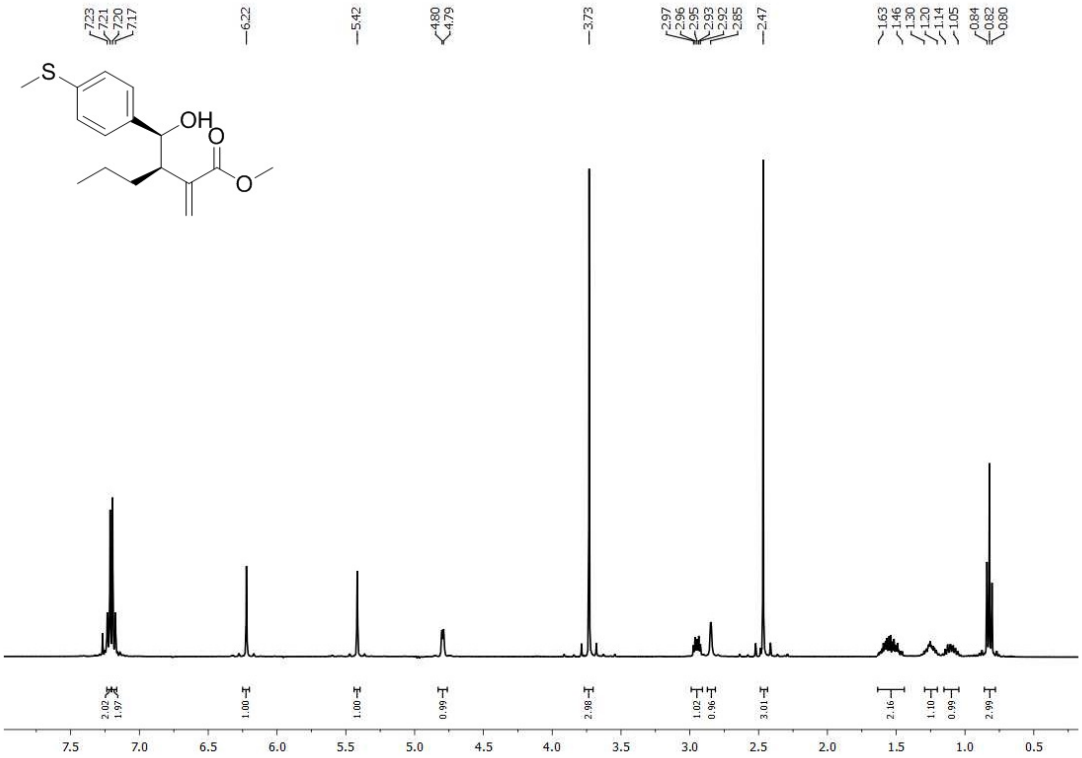

$^{13}$C NMR spectrum of methyl *syn*-4-hydroxy-3-(4-methoxyphenyl)-2-methylene-4-(4-methylphenyl)butanoate.



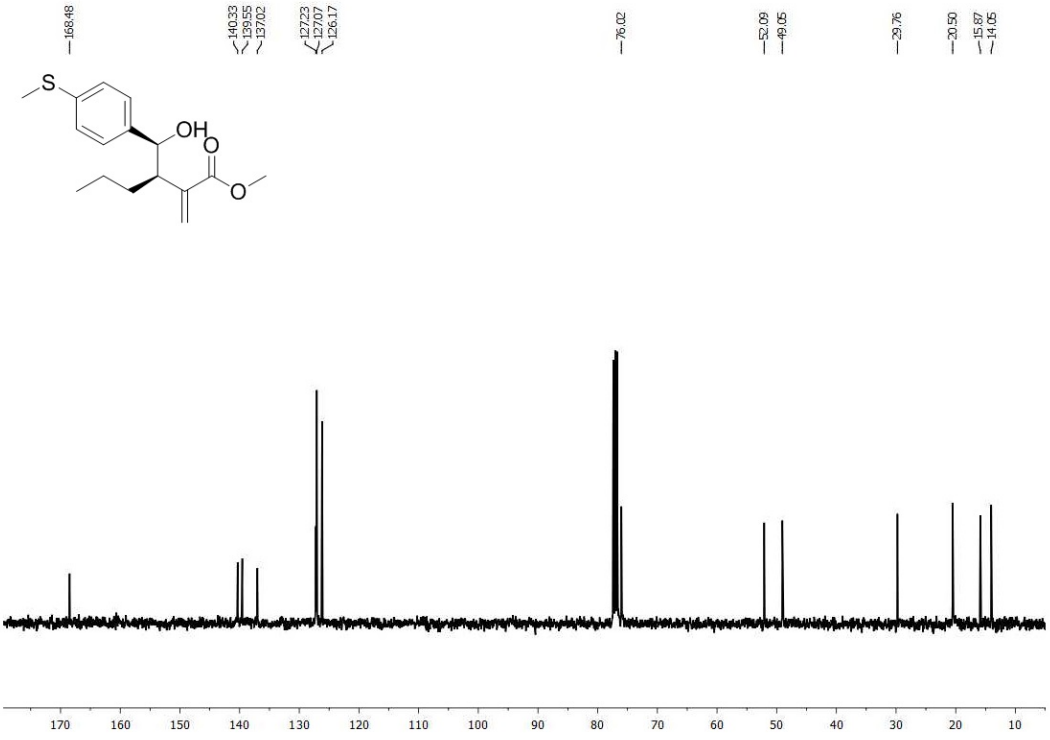

$^{1}$H NMR spectrum of methyl *syn*-3-(3-bromophenyl)-6-(*t*-butyldimethylsilyloxy)-4-hydroxy-2-methylenehexanoate.



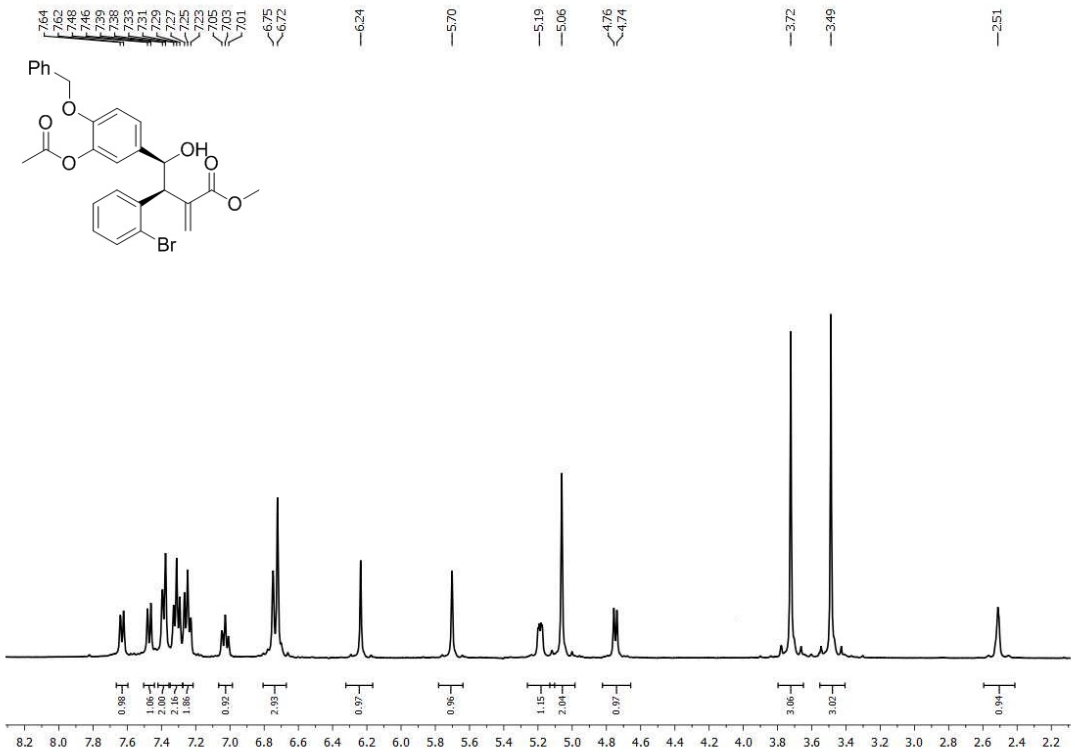

$^{13}$C NMR spectrum of methyl *syn*-3-(3-bromophenyl)-6-(*t*-butyldimethylsilyloxy)-4-hydroxy-2-methylenehexanoate.



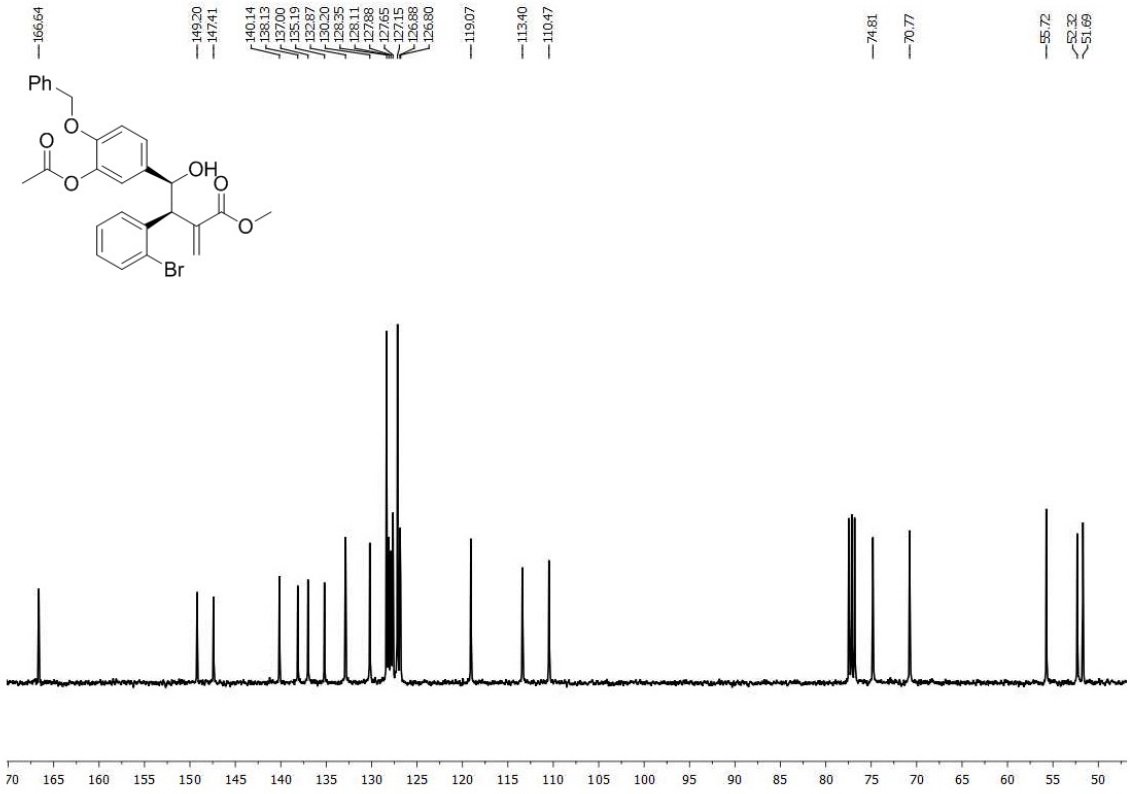

$^{1}$H NMR spectrum of methyl *syn*-3-((hydroxyl)(4-methylthiophenyl)methyl)2-methylenehexanoate.



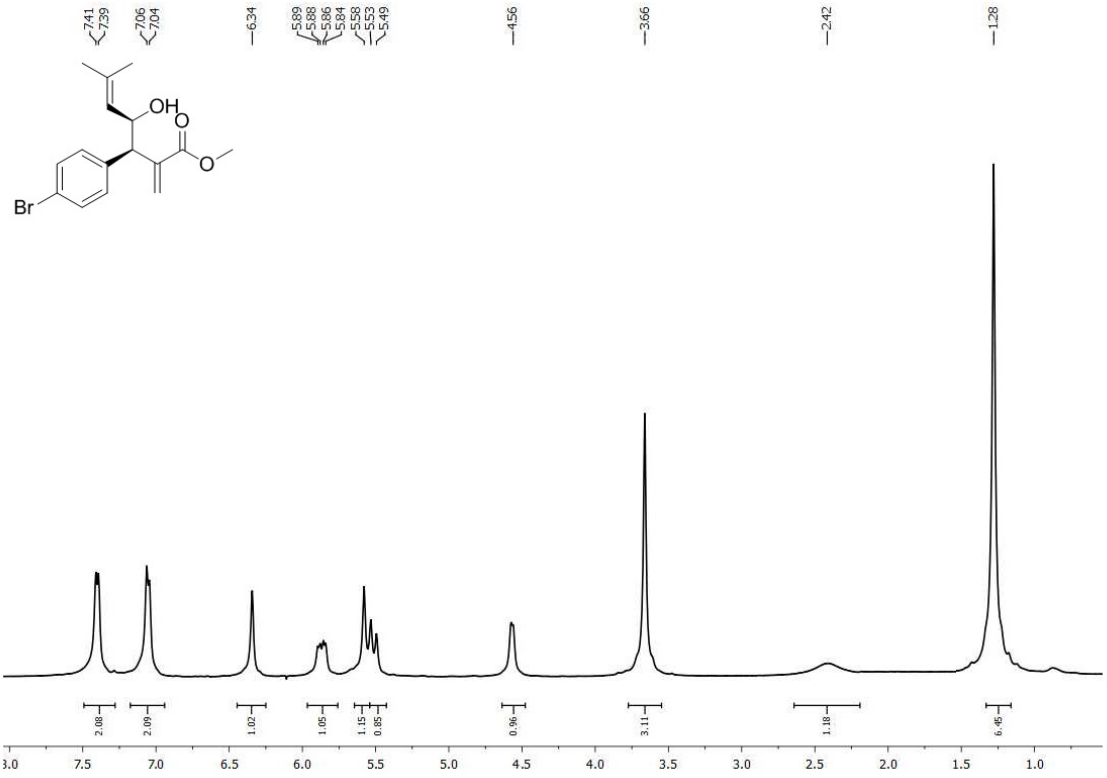

$^{13}$C NMR spectrum of methyl *syn*-3-((hydroxyl)(4-methylthiophenyl)methyl)2-methylenehexanoate.



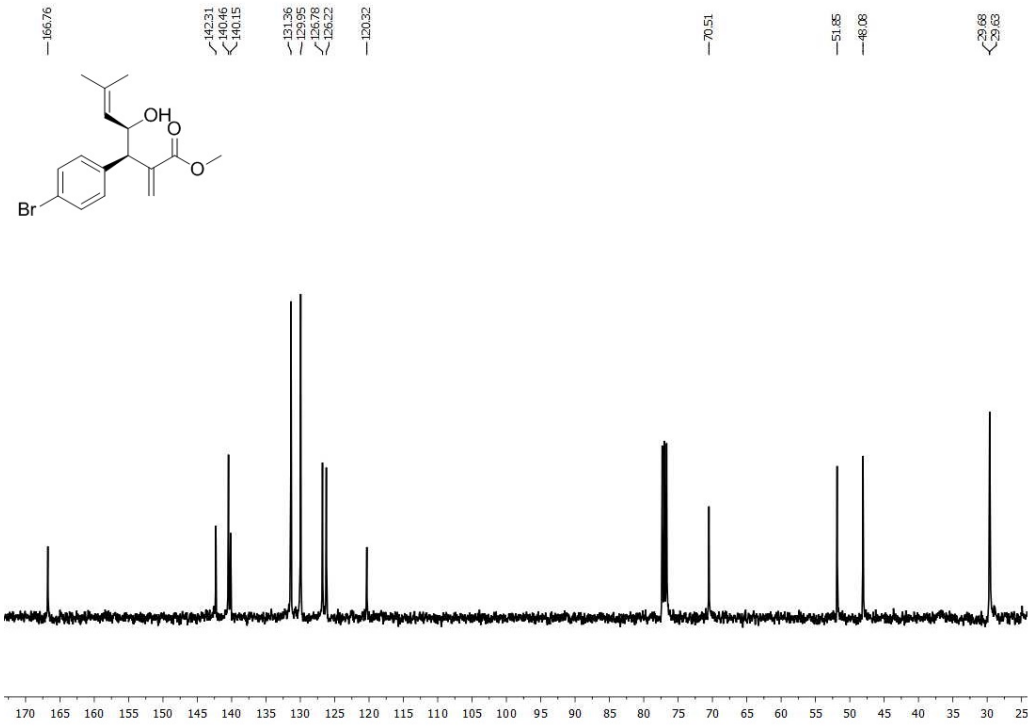

$^{1}$H NMR spectrum of methyl *syn*-4-(3-acetoxy-4-(benzyloxy)phenyl)-3-(2-bromophenyl)-4-hydroxy-2-methylenebutanoate.



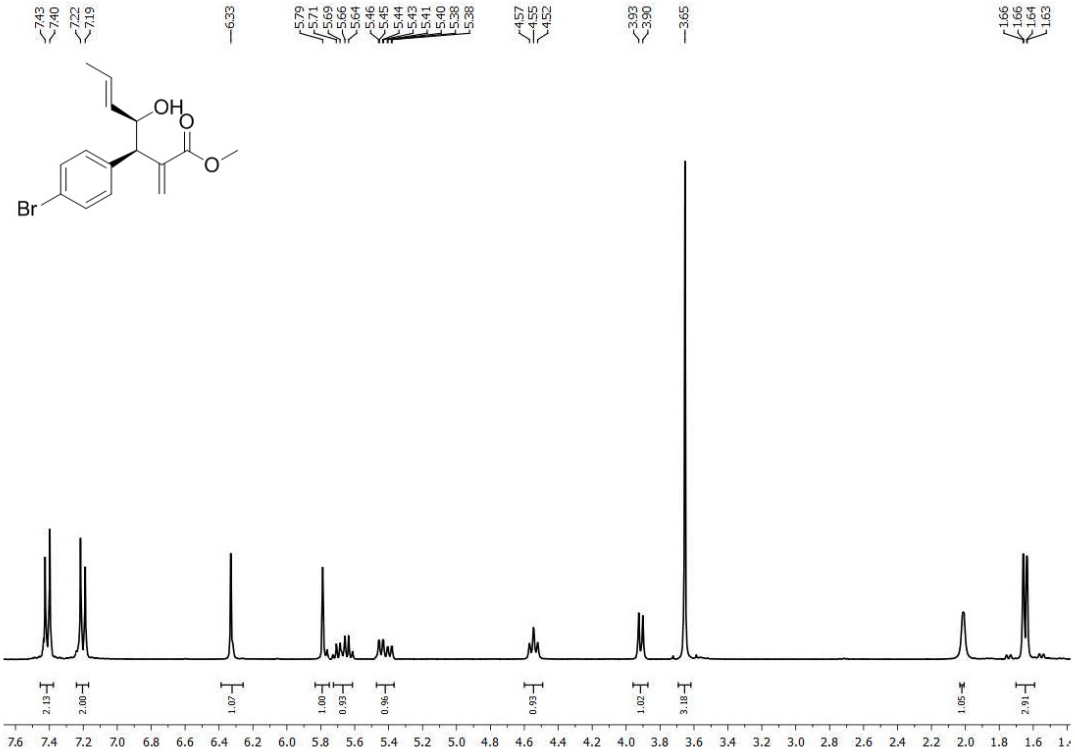

$^{13}$C NMR spectrum of methyl *syn*-4-(3-acetoxy-4-(benzyloxy)phenyl)-3-(2-bromophenyl)-4-hydroxy-2-methylenebutanoate.



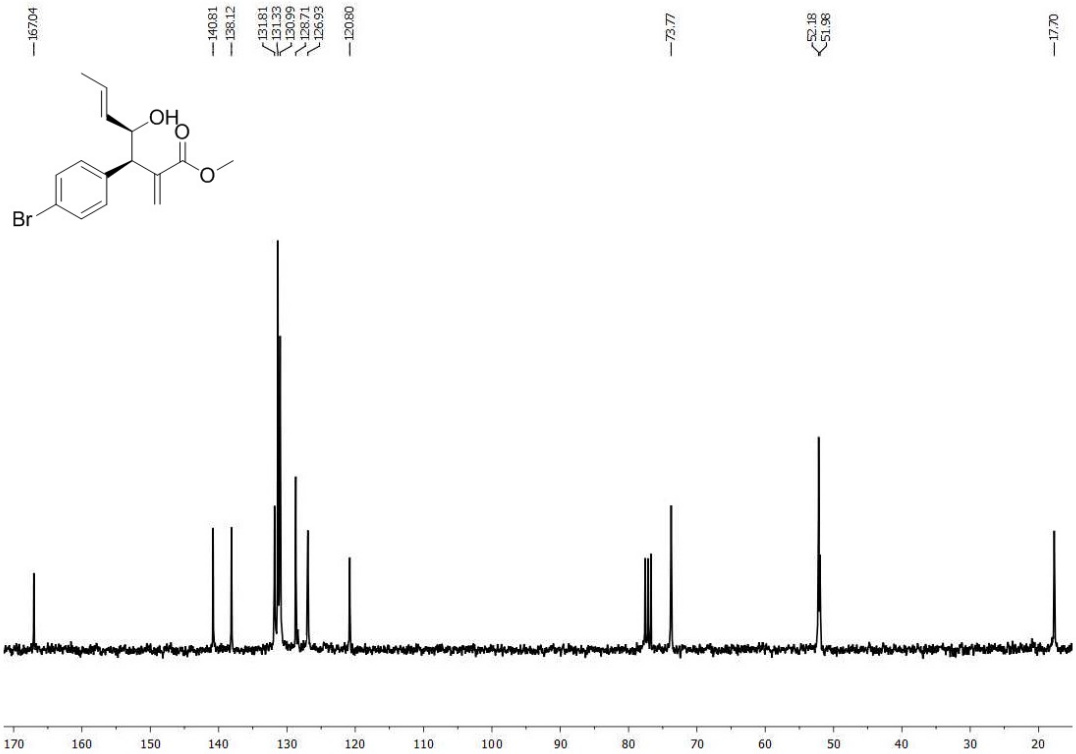

$^{1}$H NMR spectrum of methyl *syn*-3-(4-bromophenyl)-4-hydroxy-6-methyl-2-methylenehept-5-enoate.




$^{13}$C NMR spectrum of methyl *syn*-3-(4-bromophenyl)-4-hydroxy-6-methyl-2-methylenehept-5-enoate.

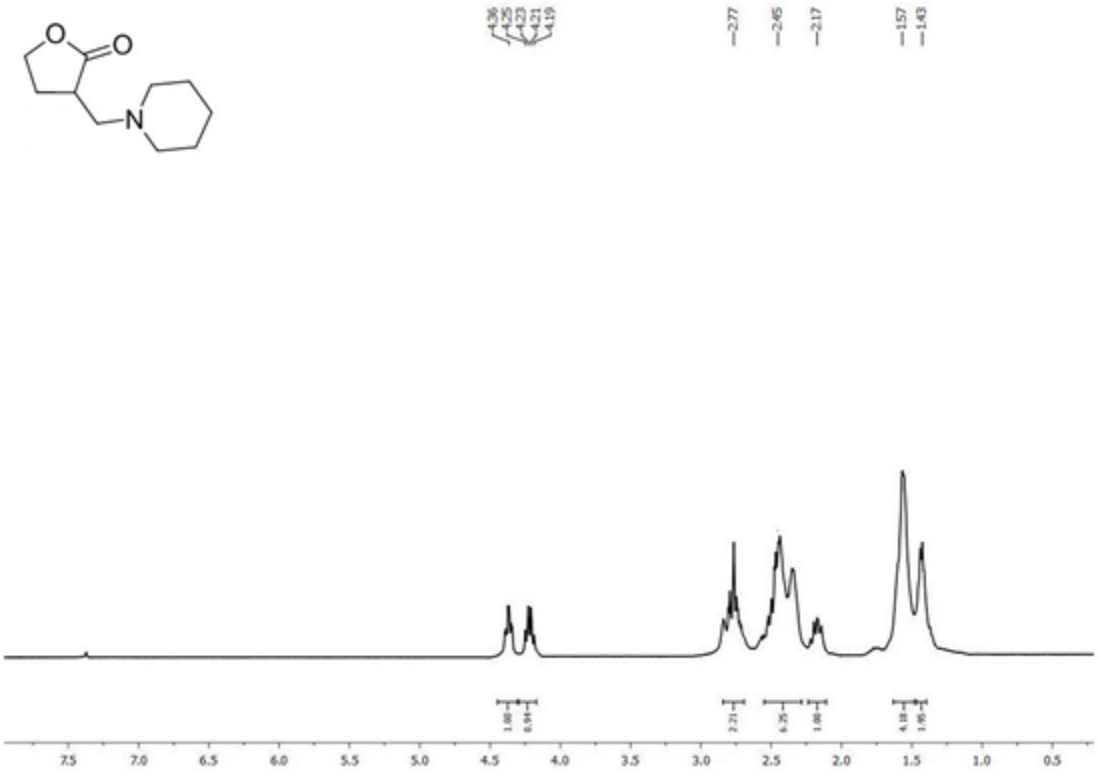



$^{3}$H NMR spectrum of methyl *syn*- (5*E*)-3-(4-bromophenyl)-4-hydroxy-2-methylenehept-5-enoate.

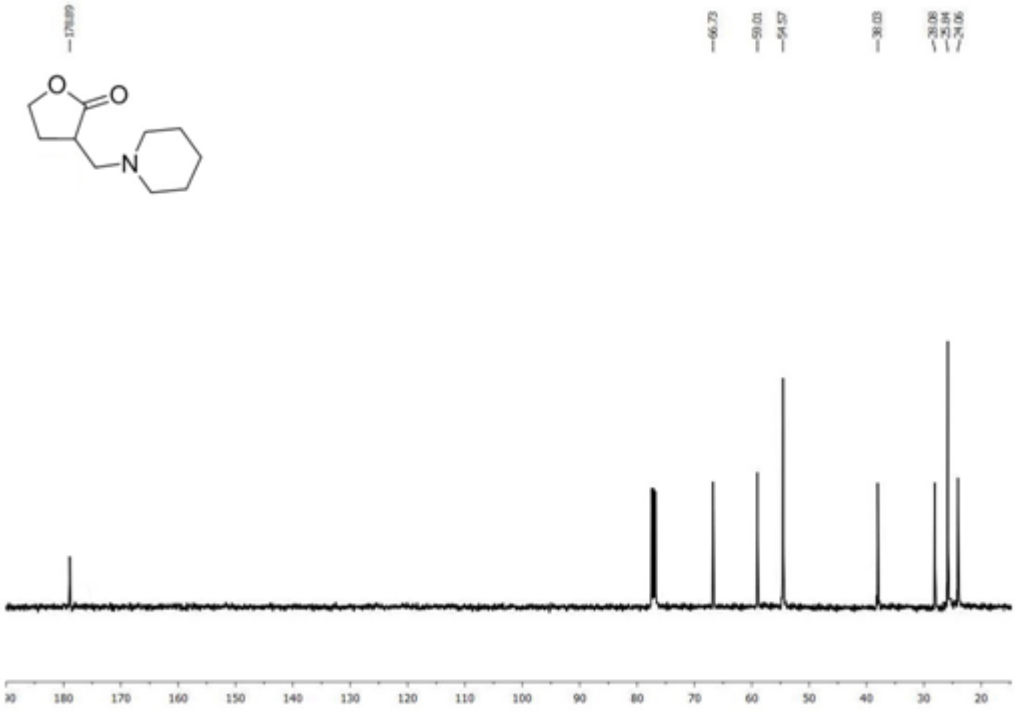



$^{13}$C NMR spectrum of methyl *syn*- (5*E*)-3-(4-bromophenyl)-4-hydroxy-2-methylenehept-5-enoate.

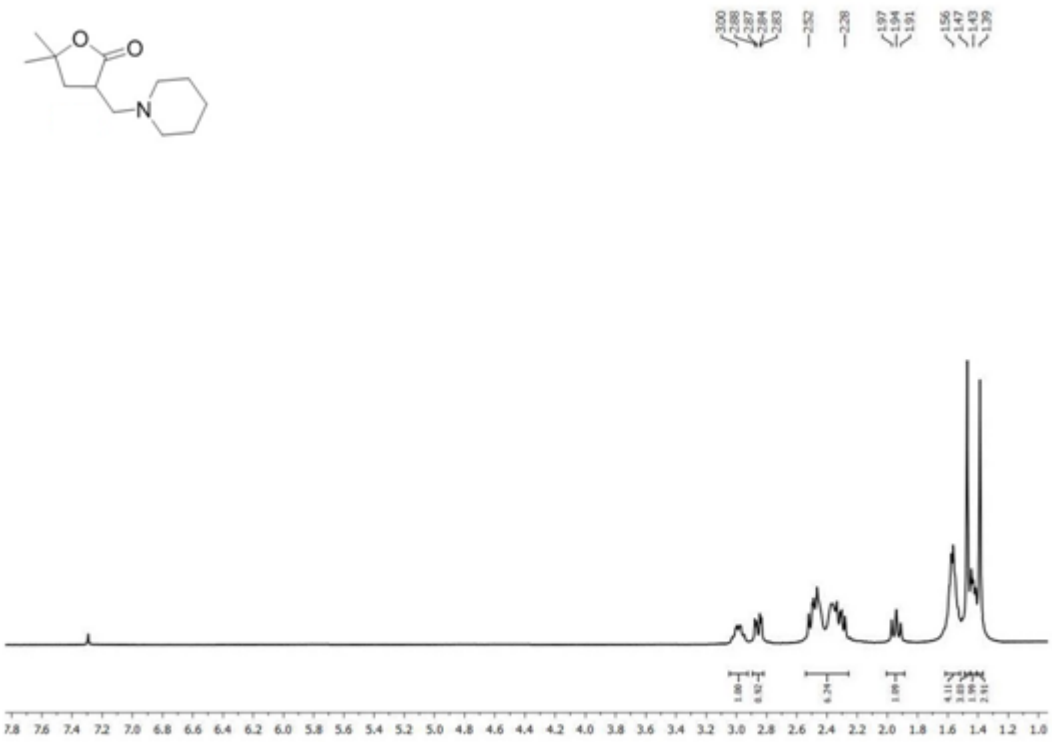
**NMR Spectra of Aminated Lactones 19-28**



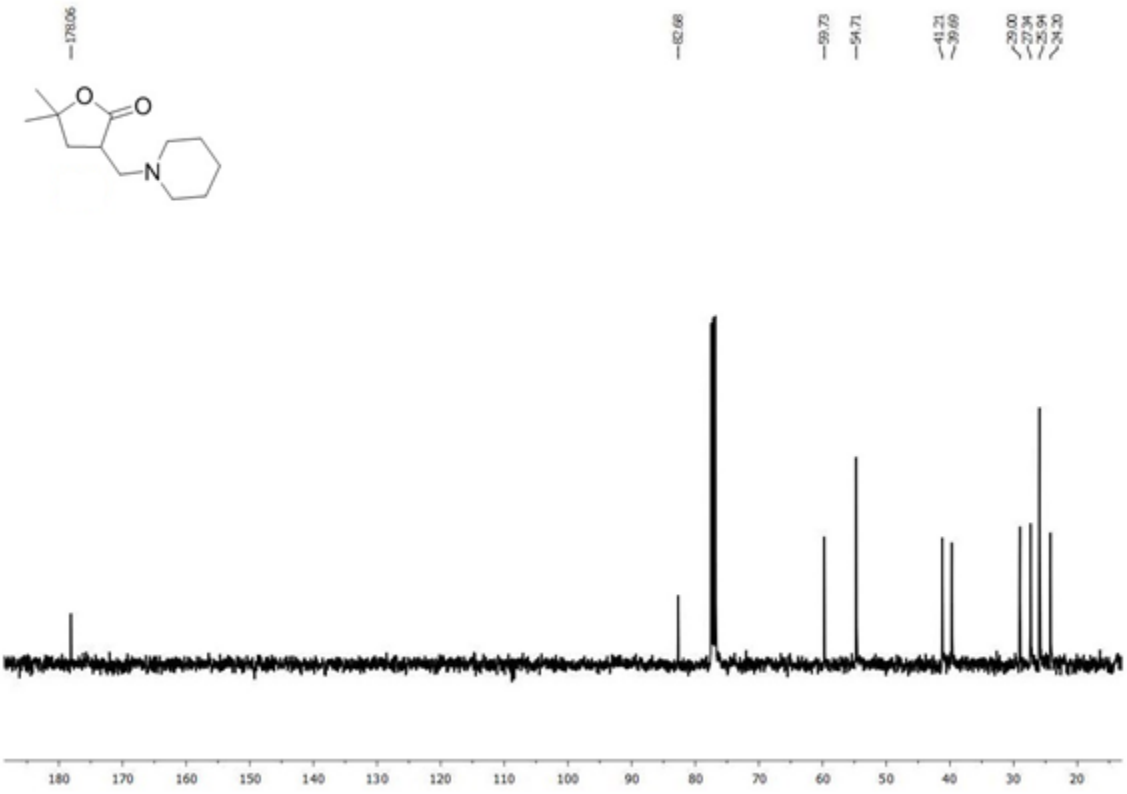
$^{1}$H NMR spectrum of **19**.



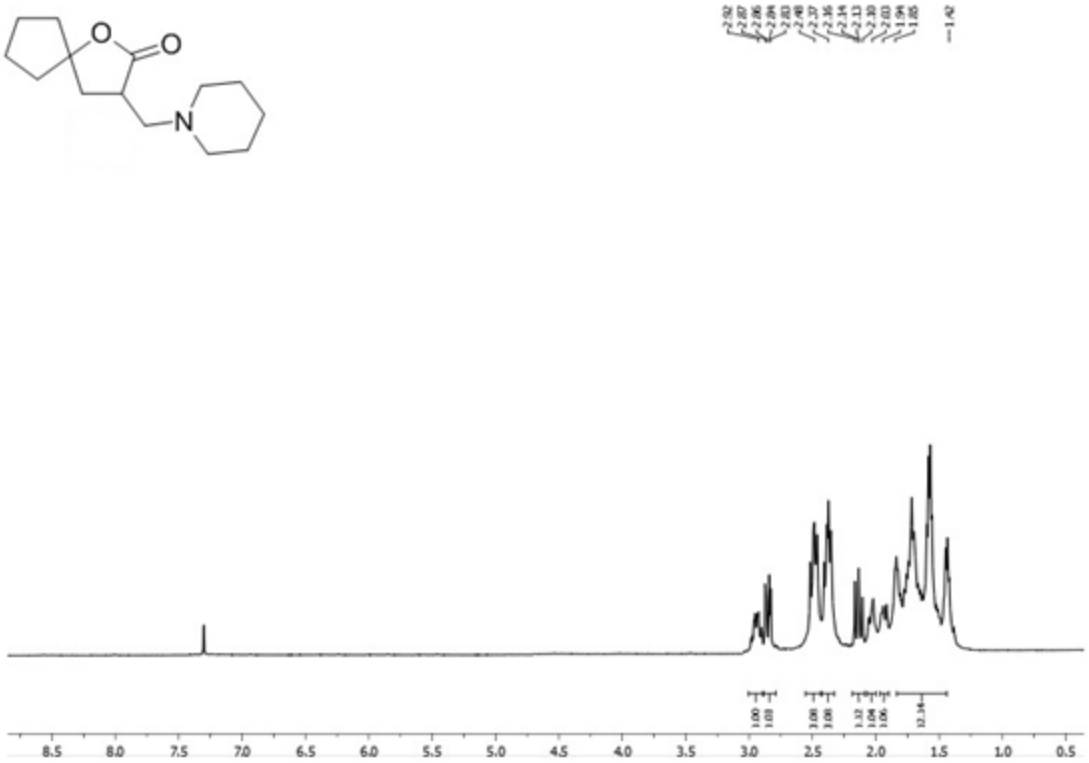
$^{13}$C NMR spectrum of **19**.



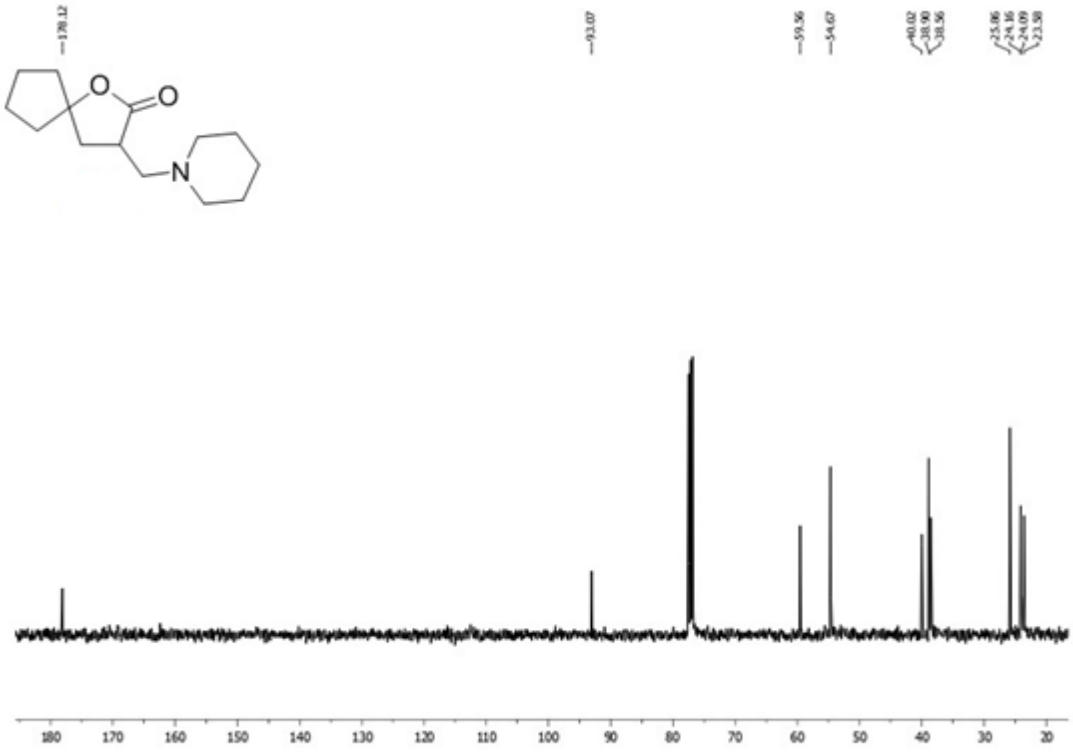
$^{1}$H NMR spectrum of **20**.



$^{13}$C NMR spectrum of **20**.

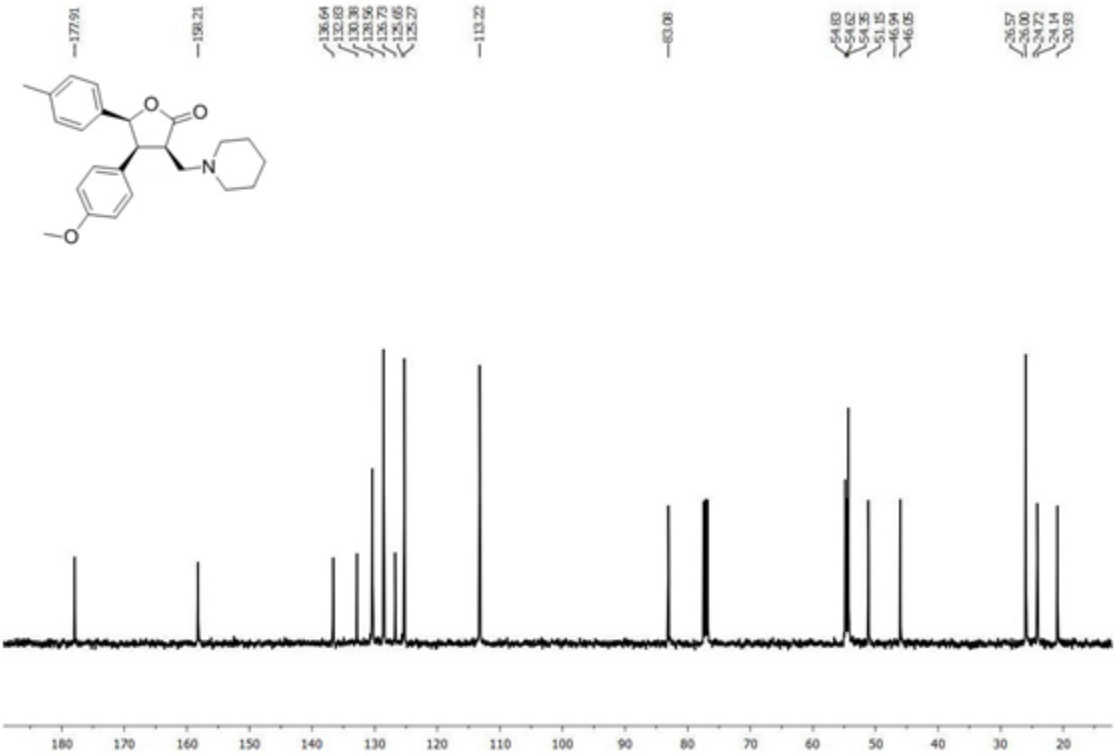


$^{1}$H NMR spectrum of **21**.

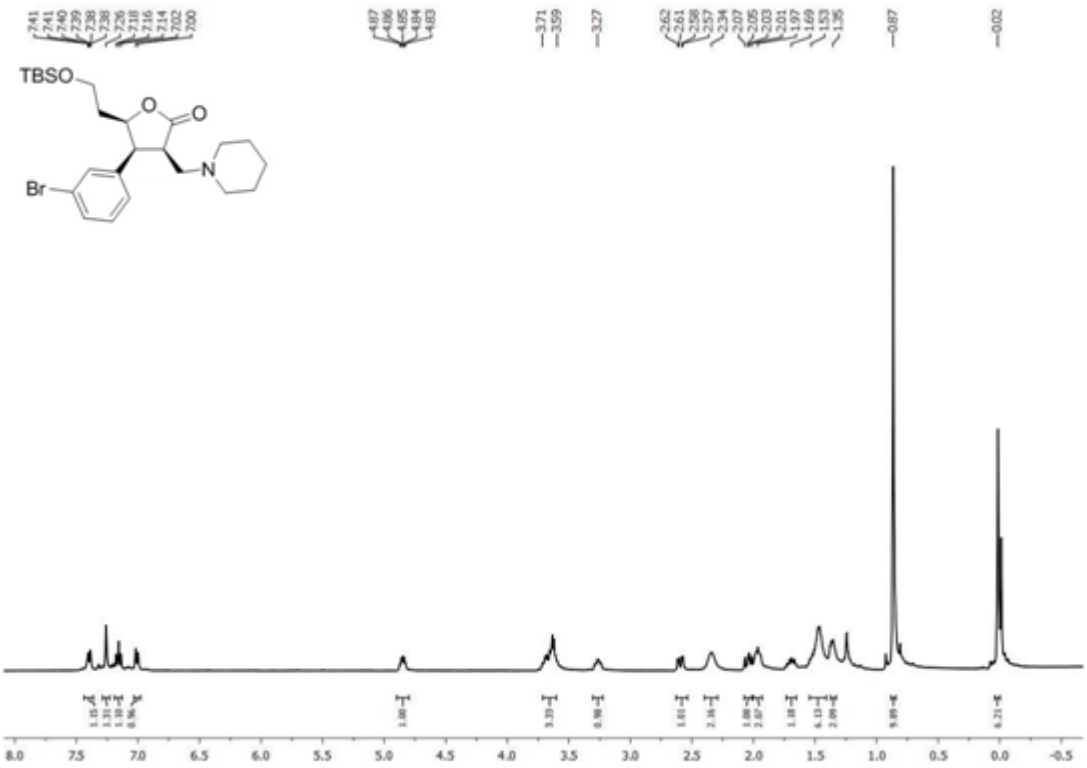


$^{13}$C NMR spectrum of **21**.

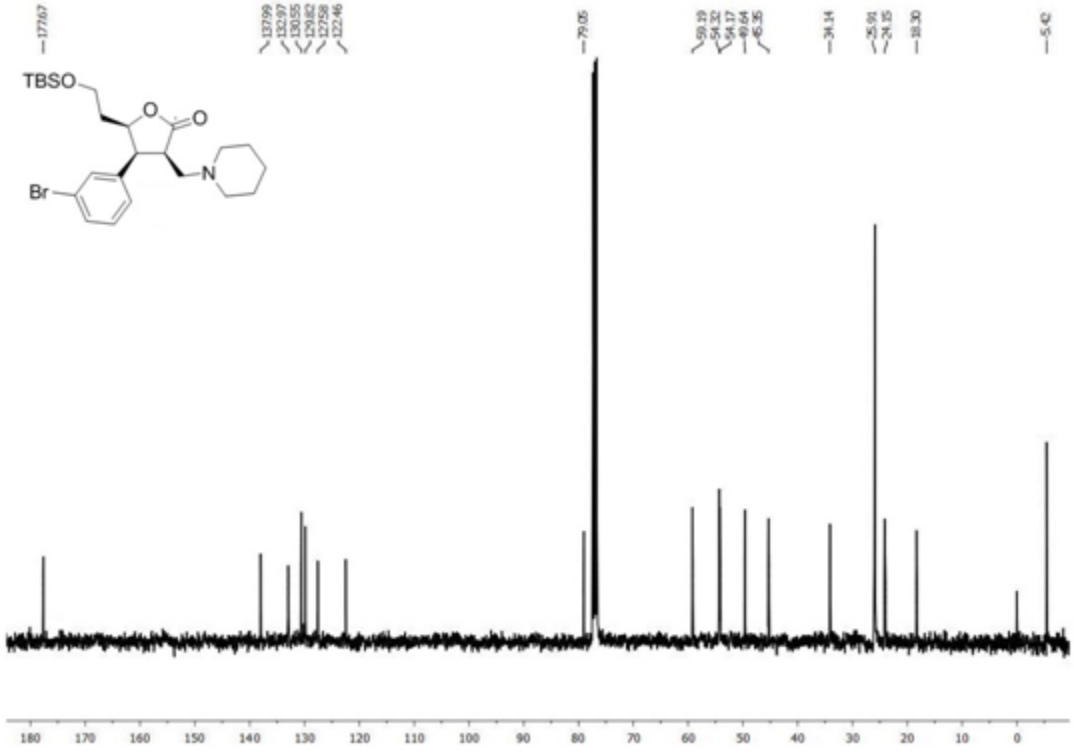
$^{1}$H NMR spectrum of **22**.



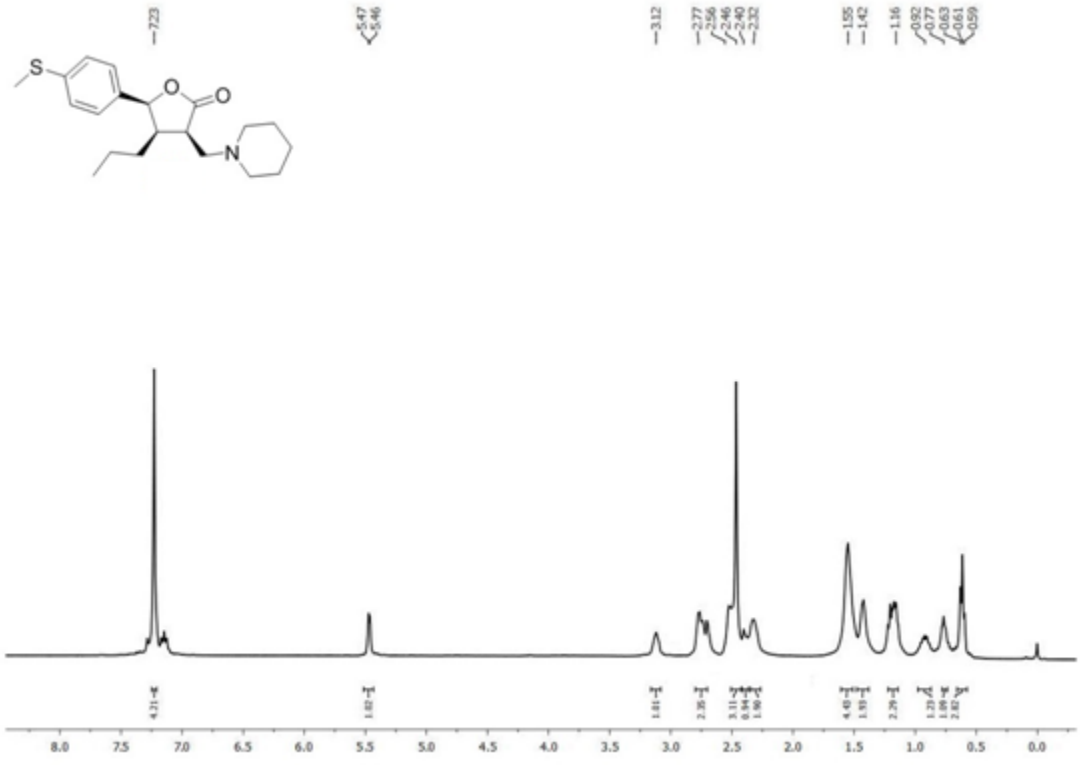
$^{13}$C NMR spectrum of **22**.



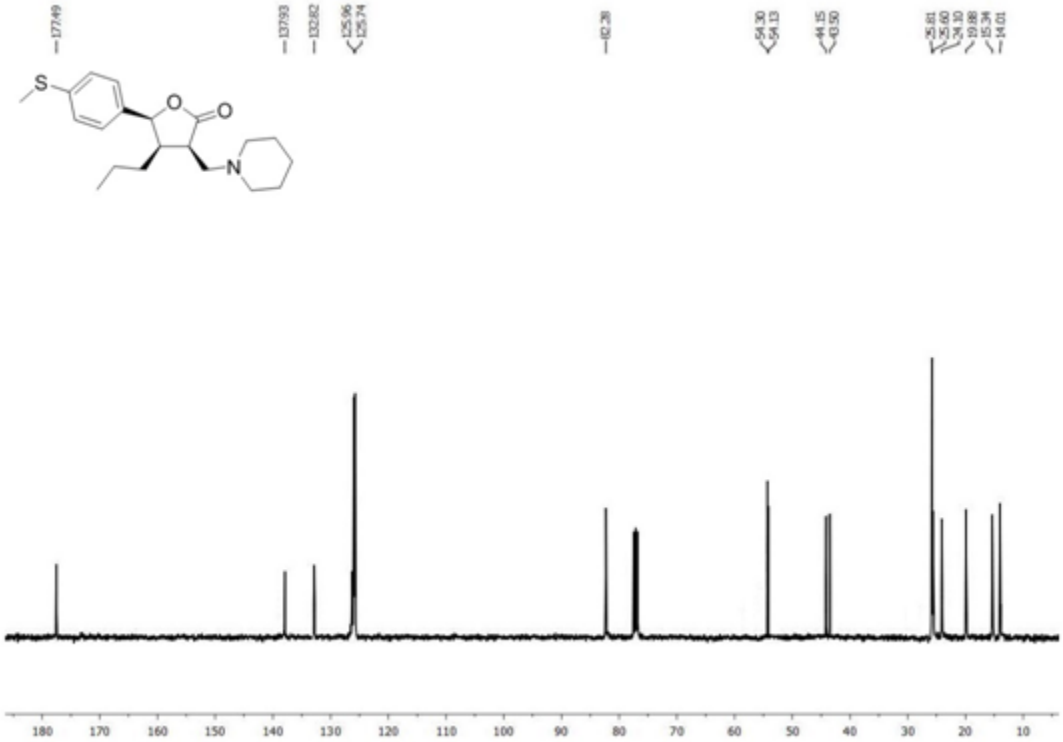

$^{1}$H NMR spectrum of **23**.



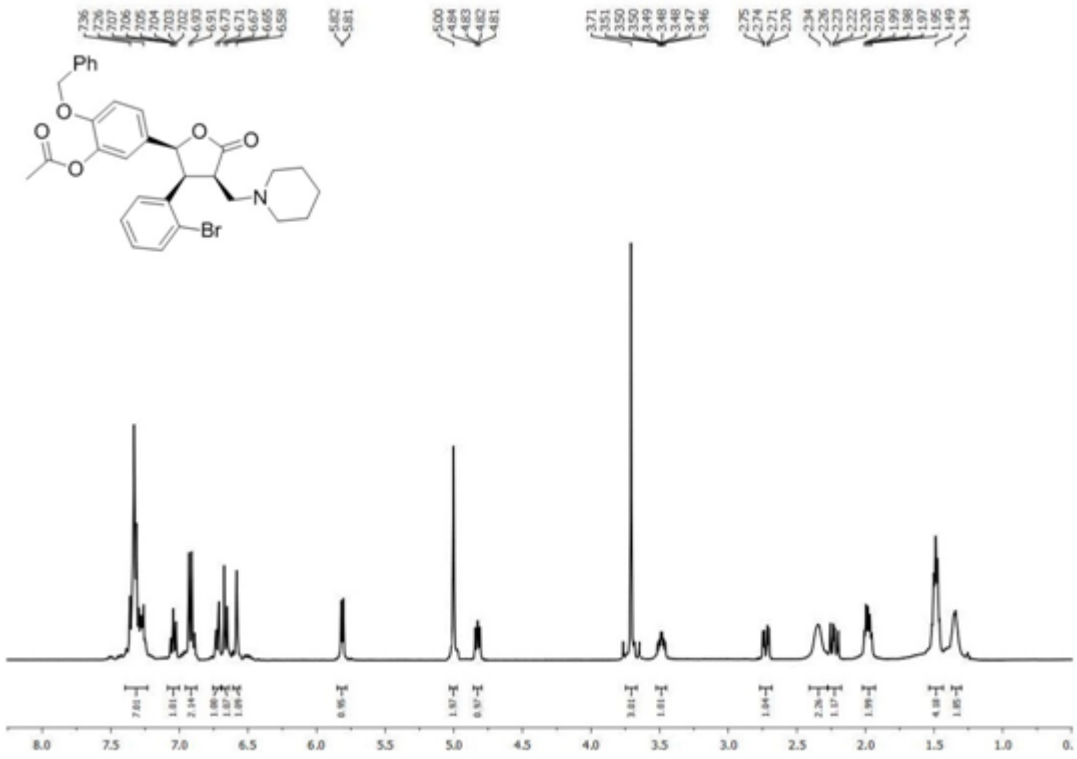

$^{13}$C NMR spectrum of **23**.



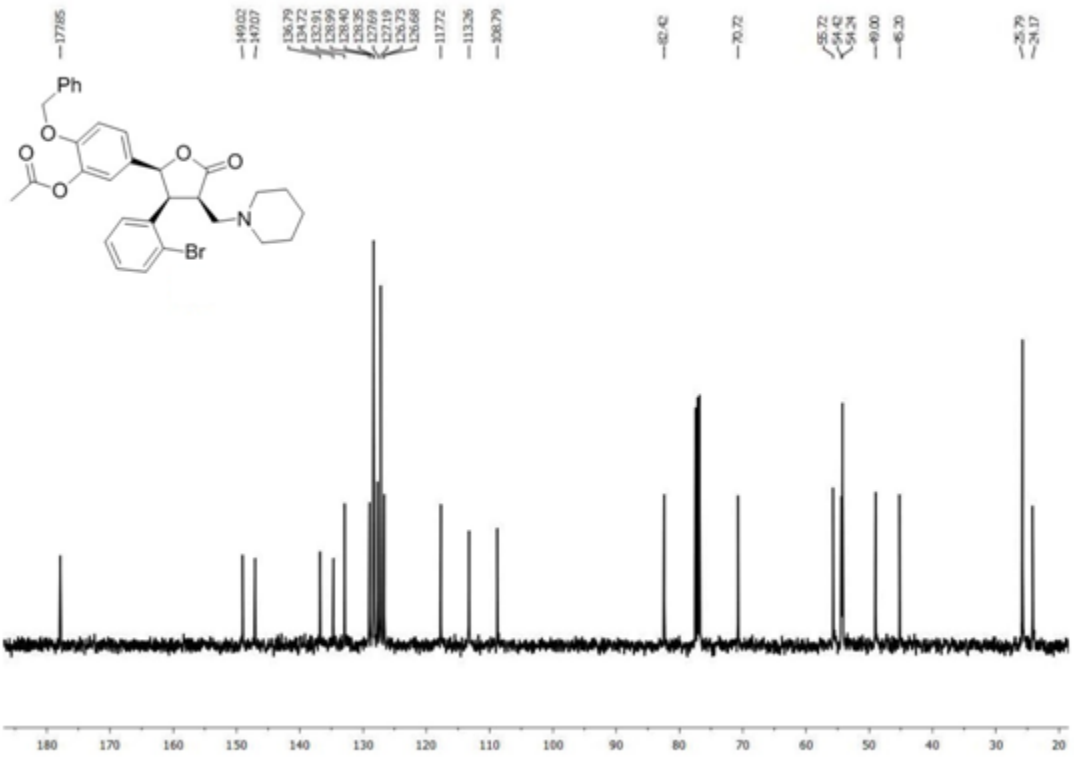
$^{1}$H NMR spectrum of **24**.



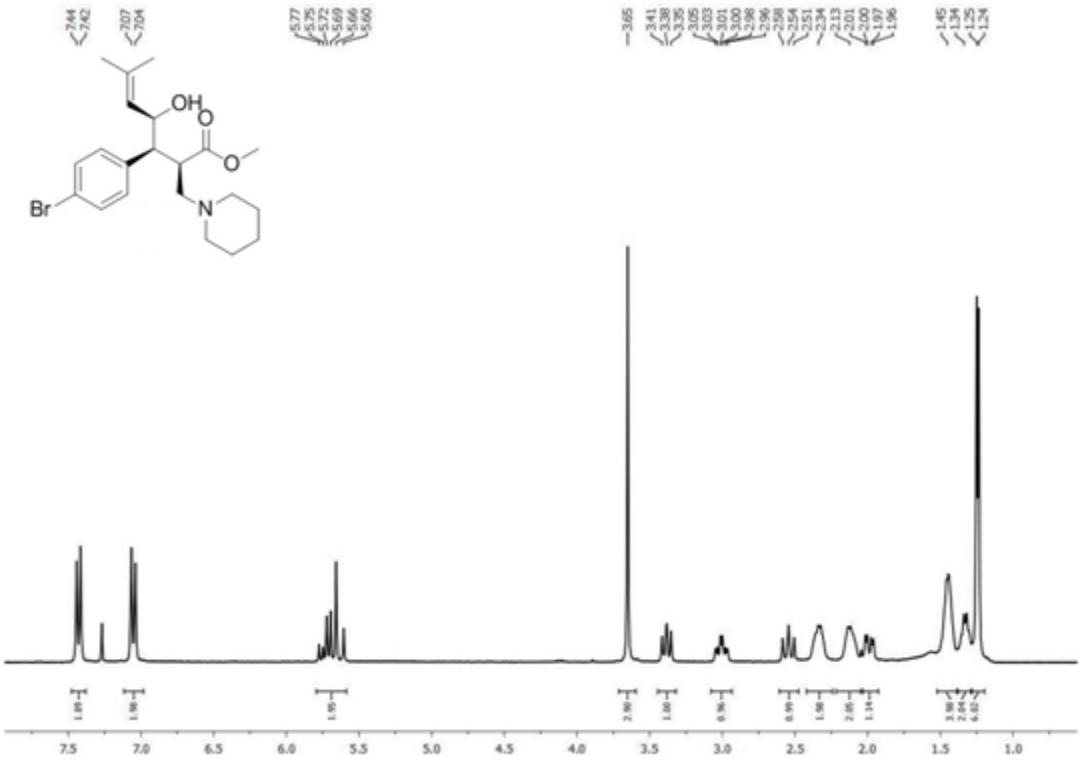
$^{13}$C NMR spectrum of **24**.



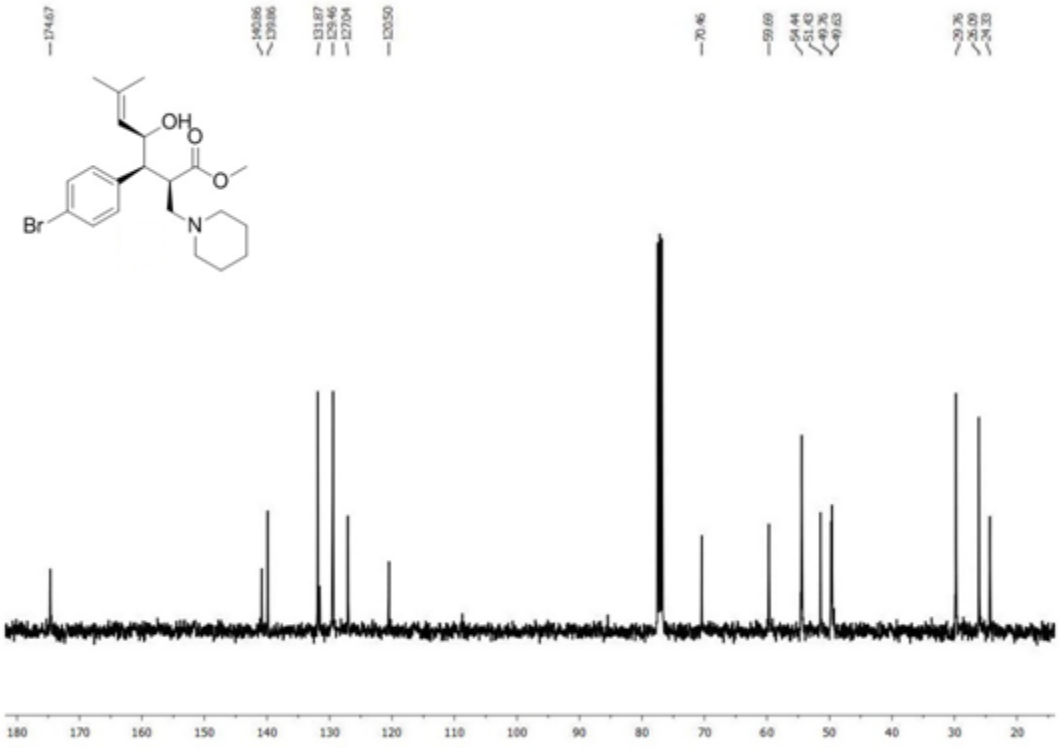

$^{1}$H NMR spectrum of **25**.



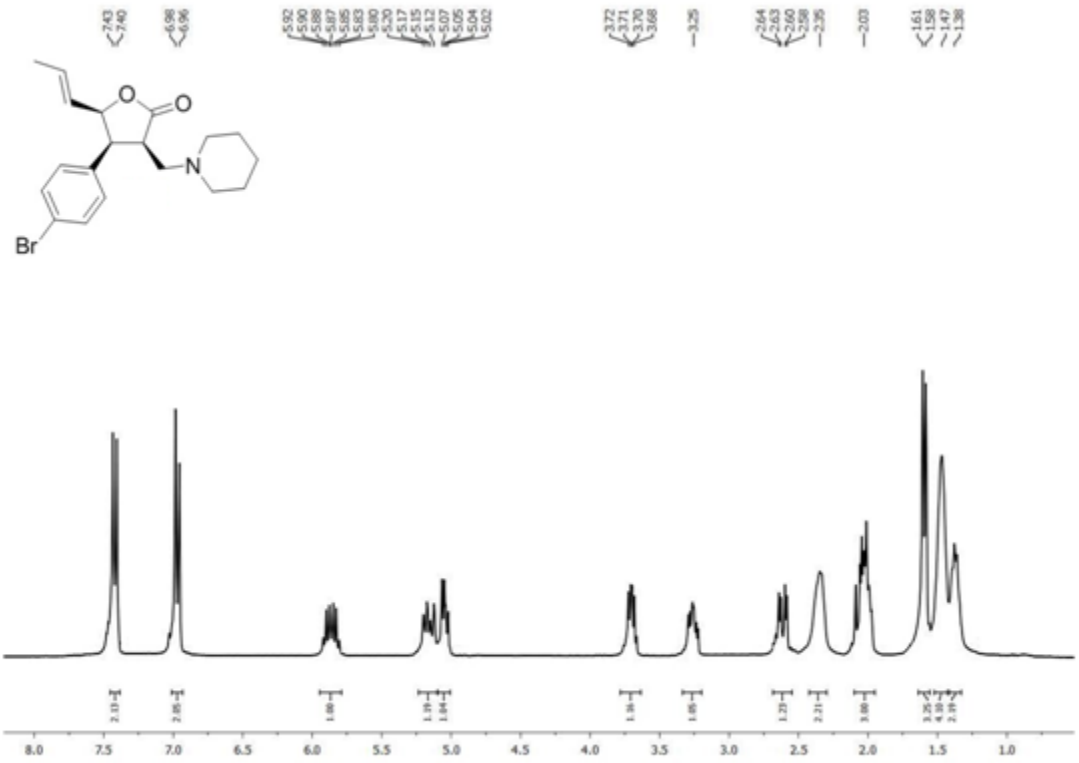

$^{13}$C NMR spectrum of **25**.



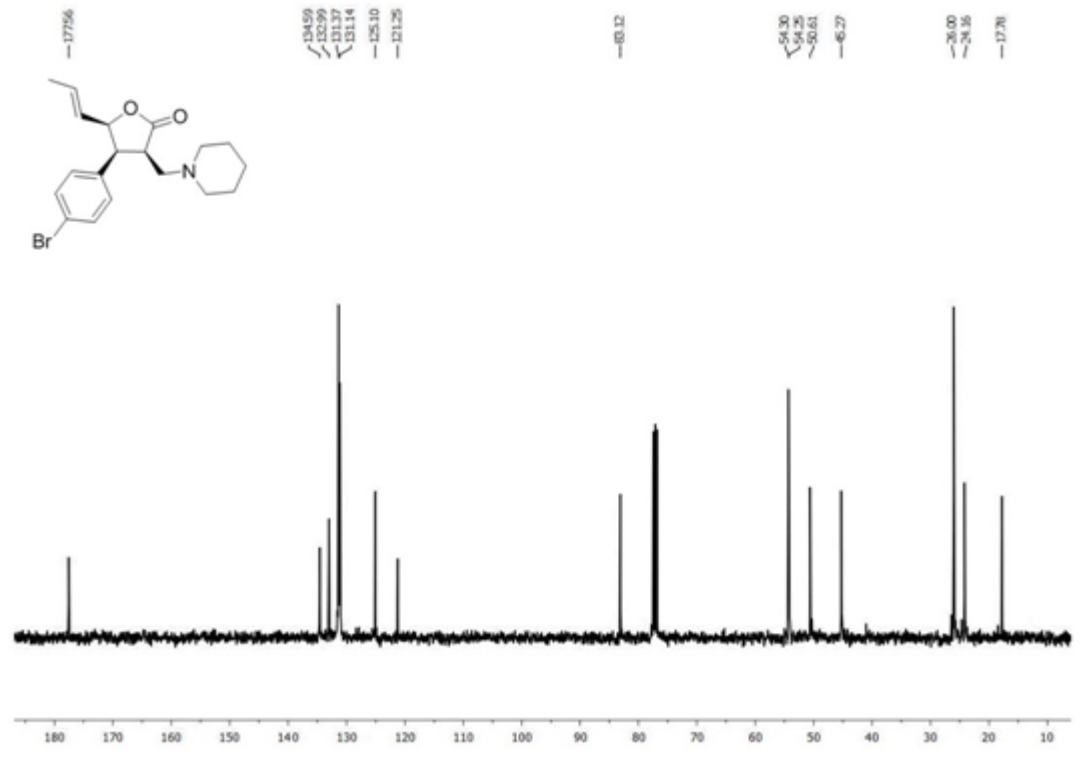

$^{1}$H NMR spectrum of **26**.




$^{13}$C NMR spectrum of **26**.

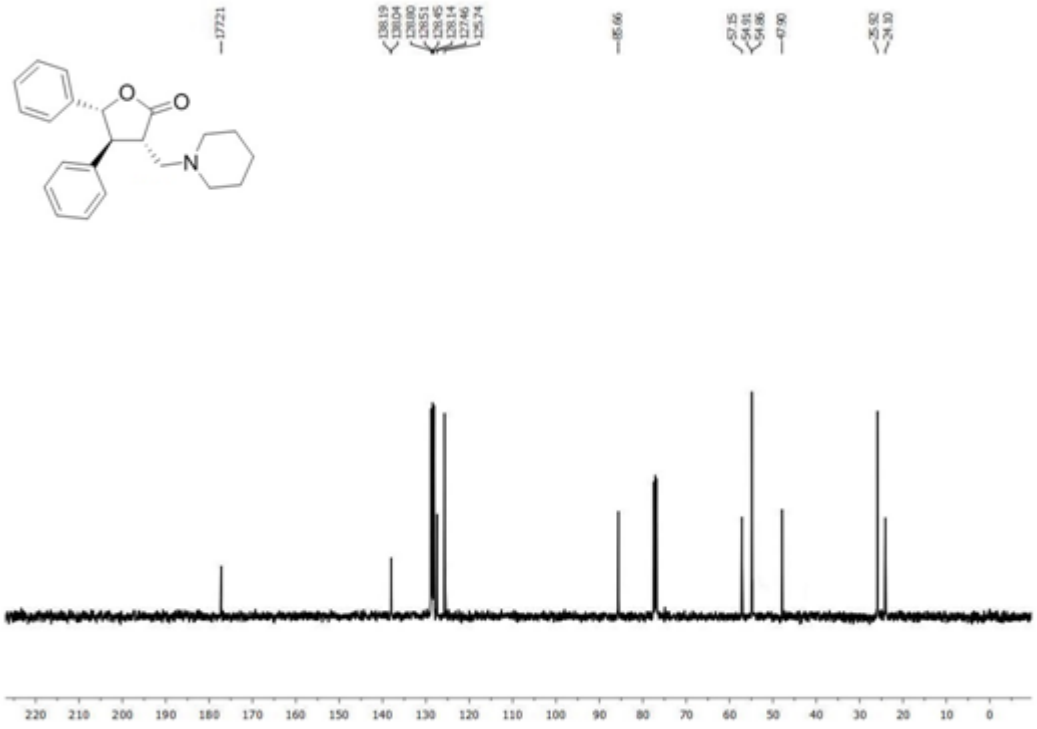



$^{1}$H NMR spectrum of **27**.



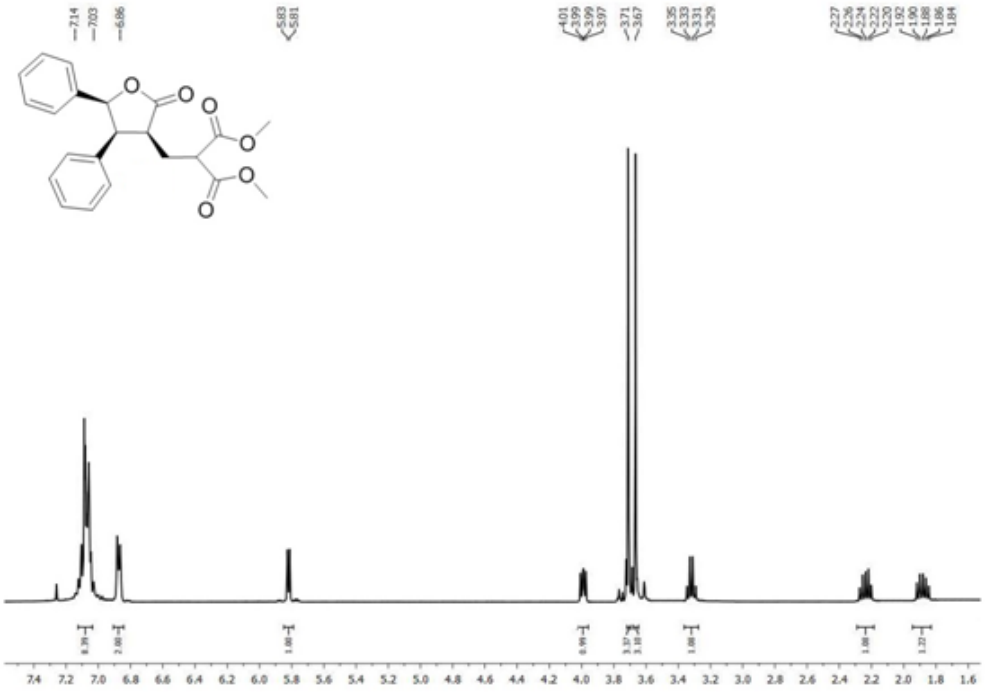

$^{13}$C NMR spectrum of **27**.

$^{1}$H NMR spectrum of **28**.

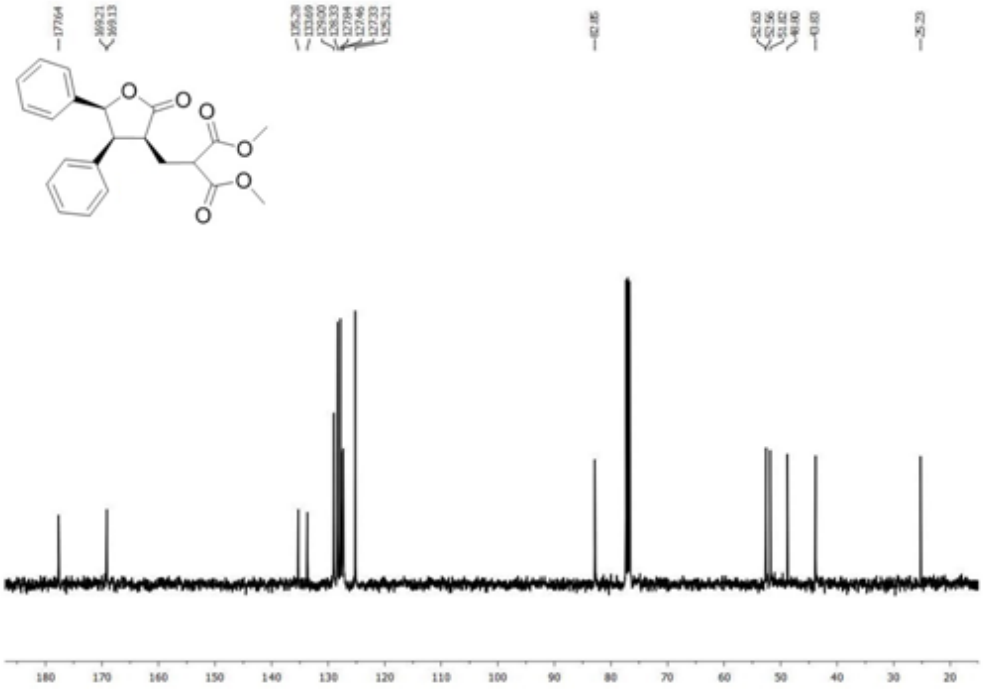


$^{13}$C NMR spectrum of **28**.

**NMR Spectra of Related Domino Reaction**

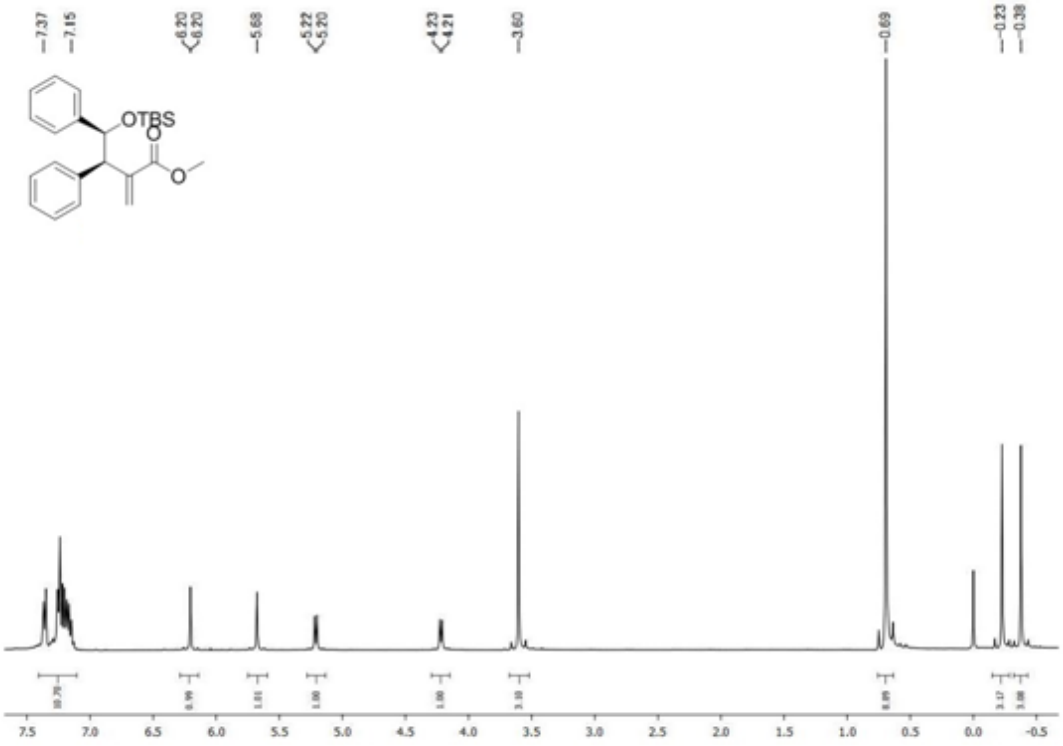


$^{1}$H NMR spectrum of **31**.

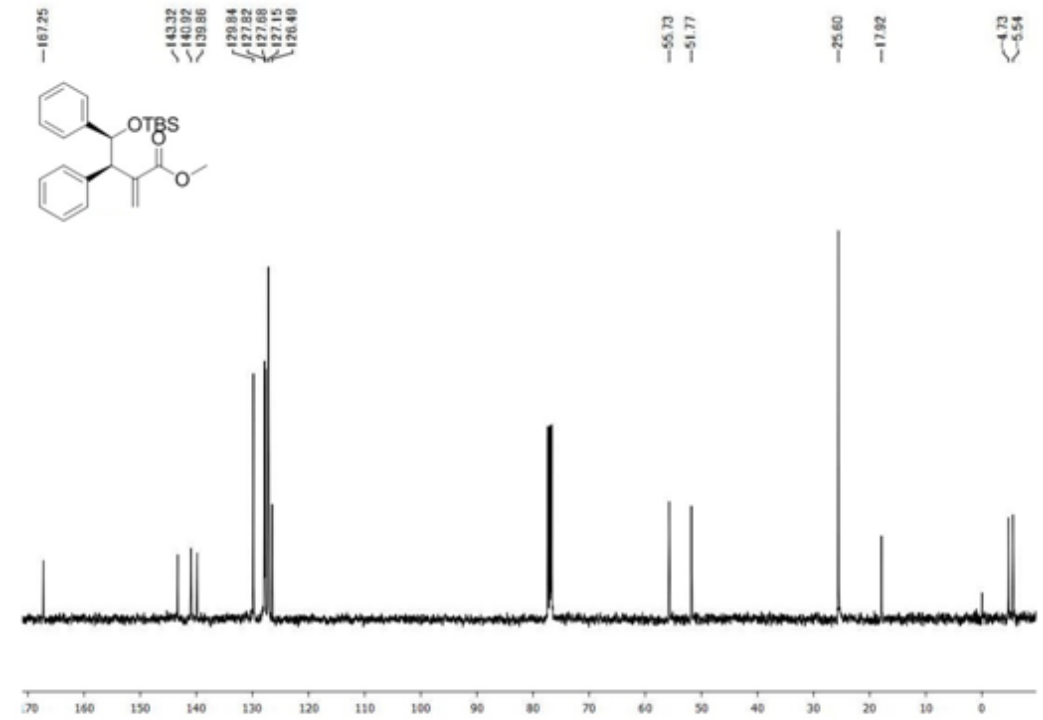


$^{13}$C NMR spectrum of **31**.

**NMR Spectra of 33**

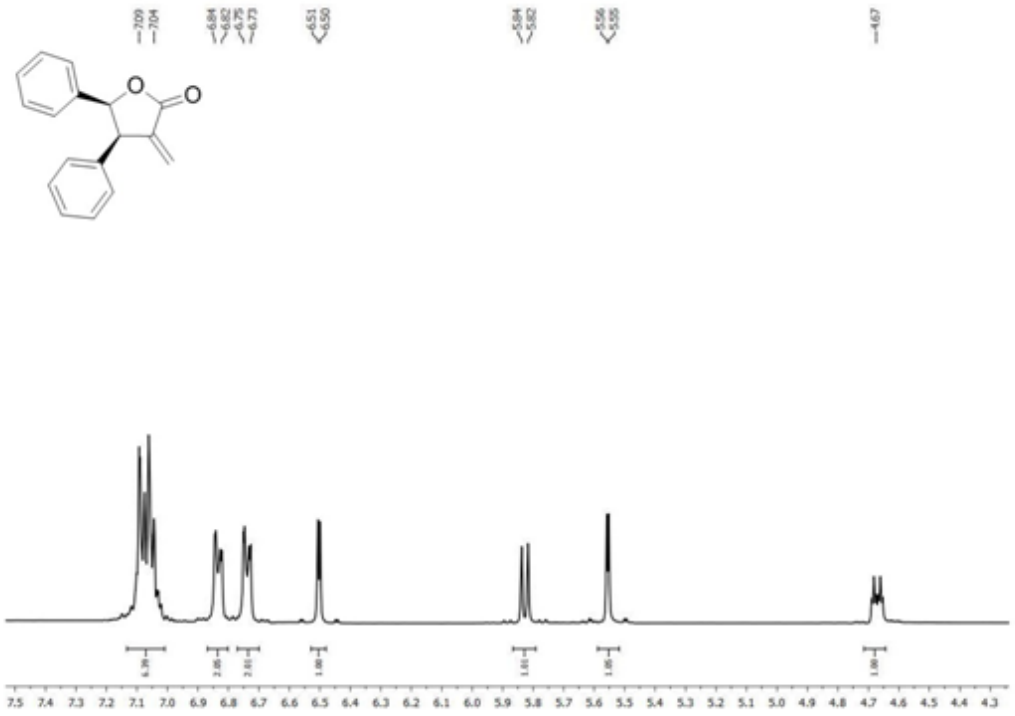



$^{1}$H NMR spectrum of **33**.

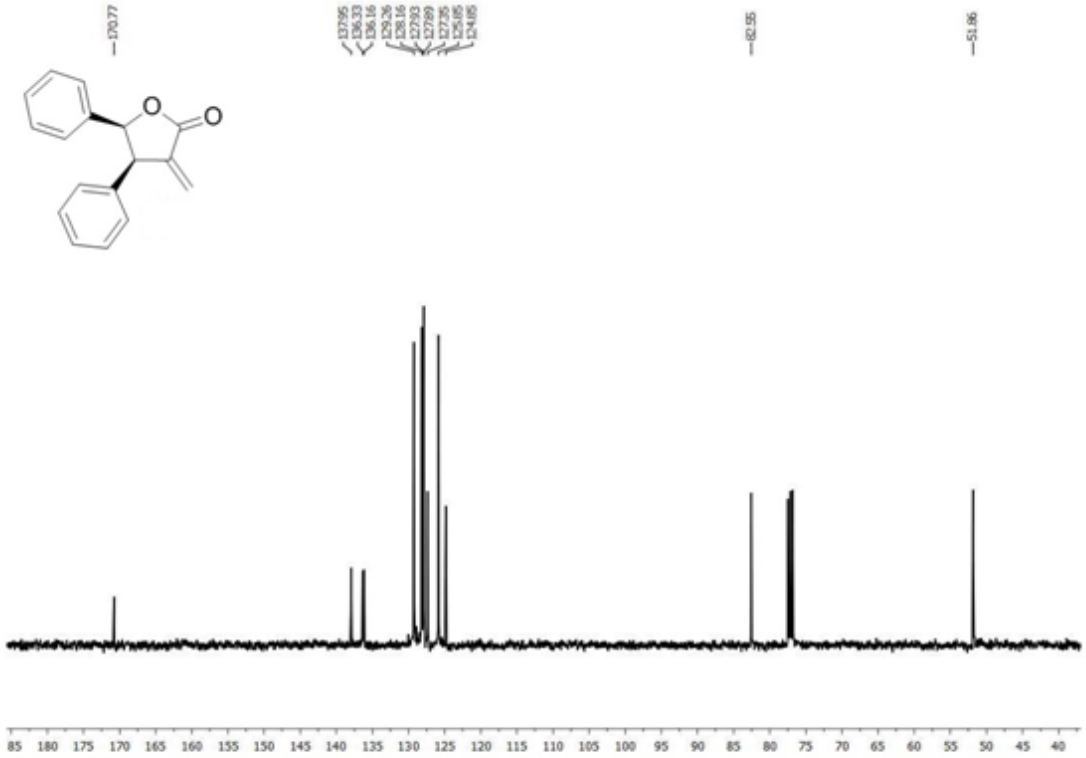



$^{13}$C NMR spectrum of **33**.

**NMR Spectra of Lactone 35**

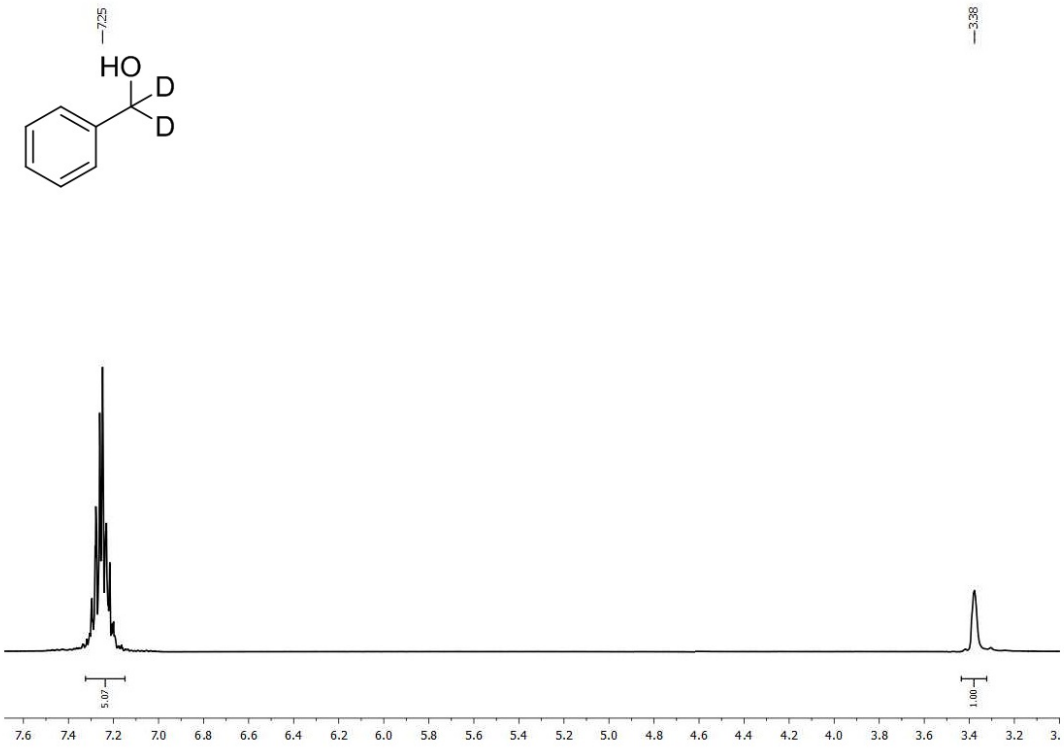


$^{1}$H NMR spectrum of **35**.

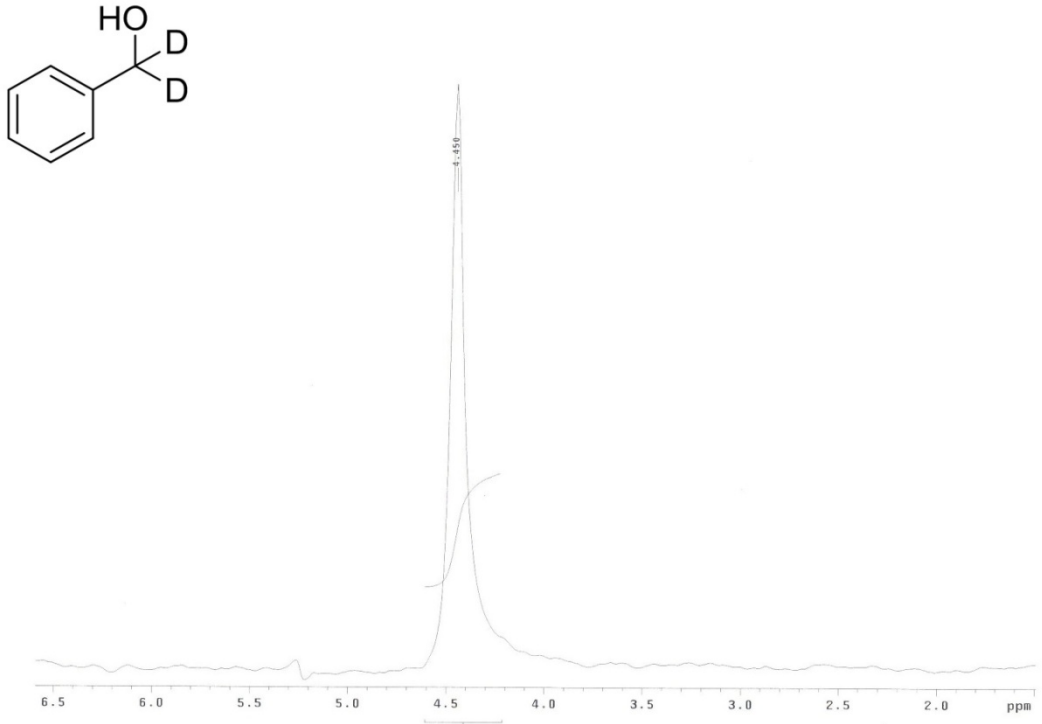


$^{13}$C NMR spectrum of **35**.

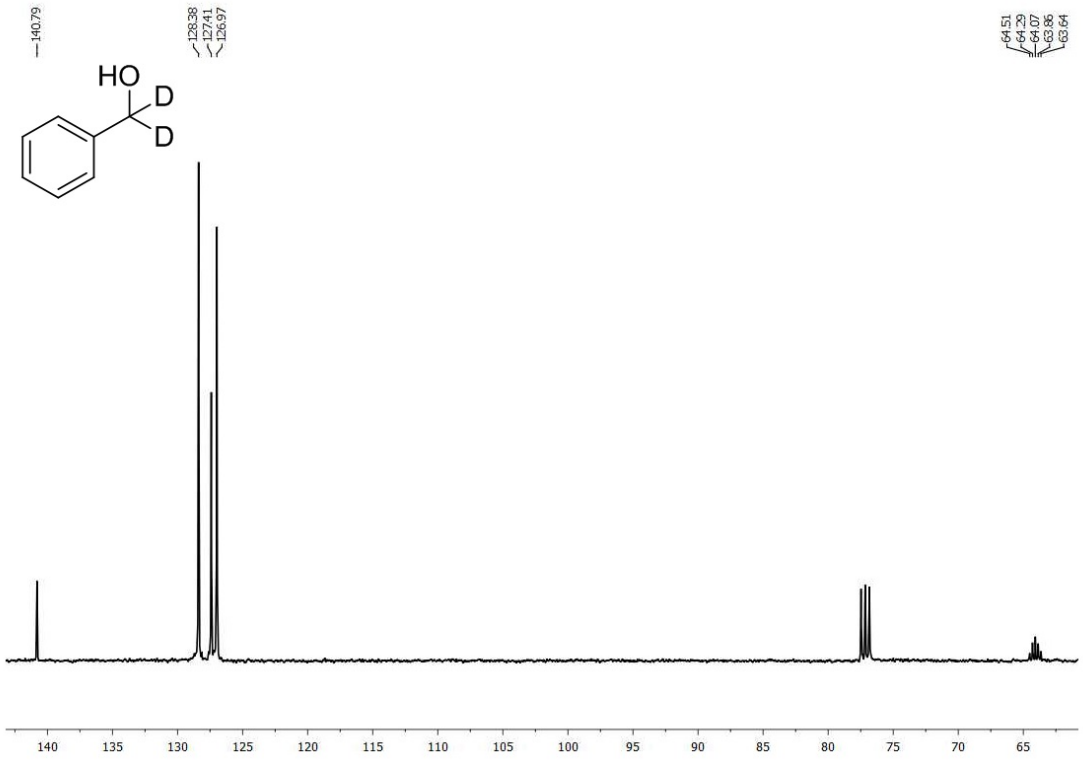
**NMR Spectra Associated with the Preparation of 38**



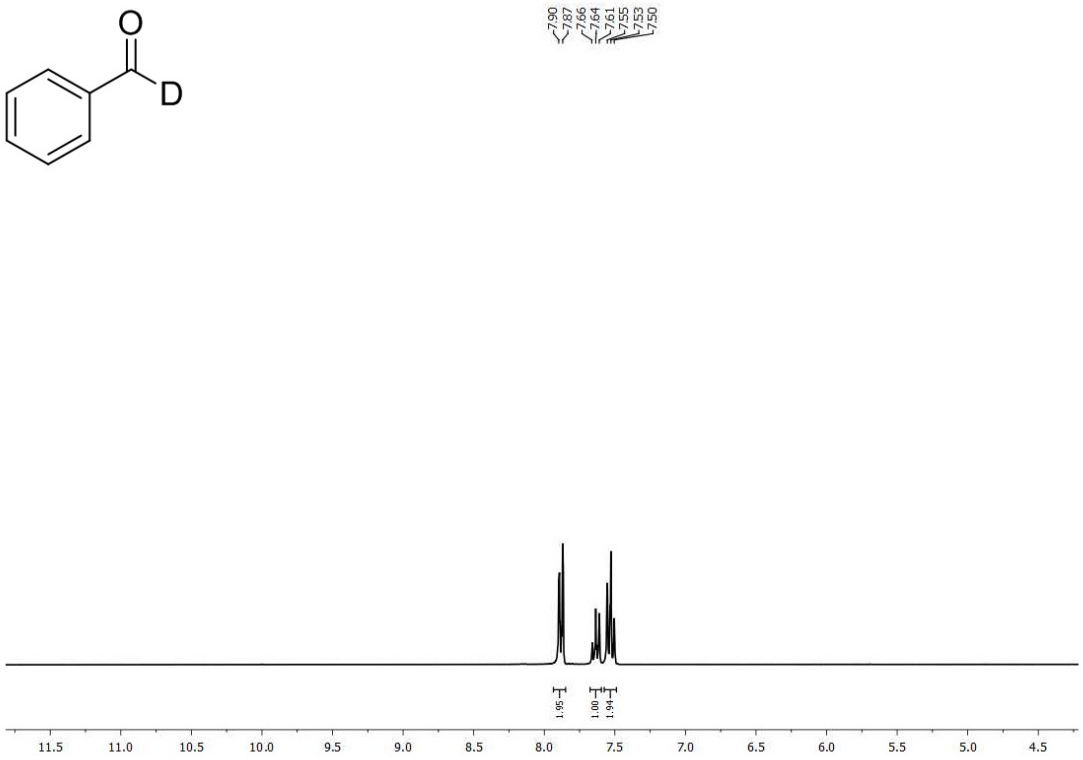

$^{1}$H NMR spectrum of 1,1-dideuterio-1-phenylmethanol.



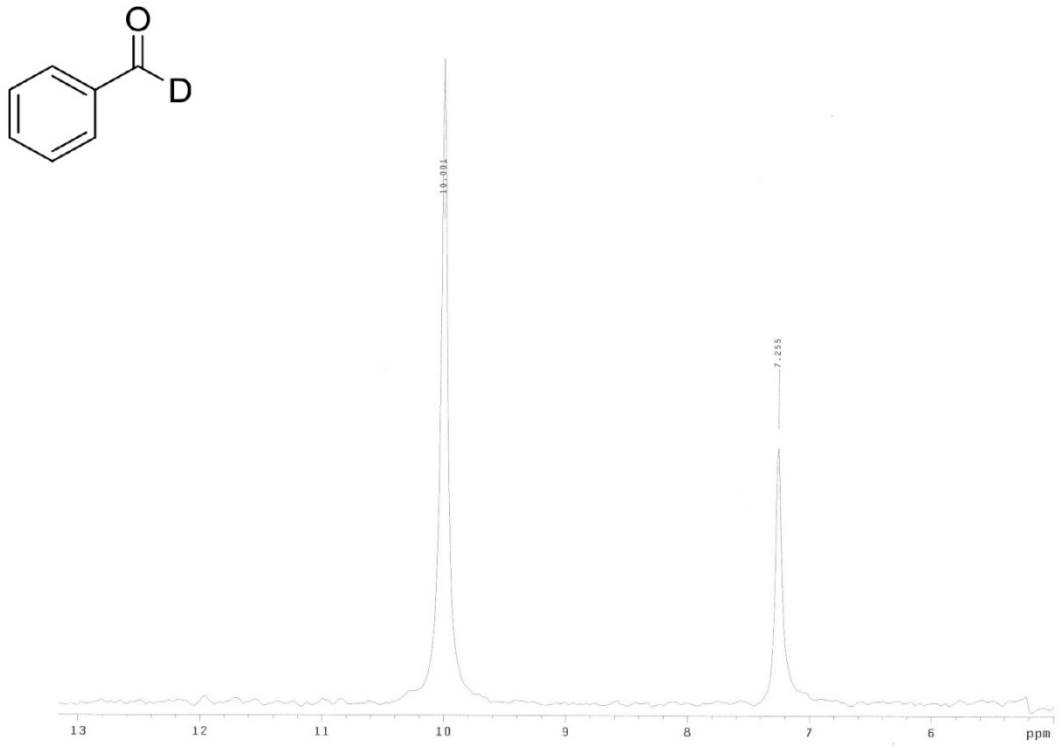

$^{2}$H NMR spectrum of 1,1-dideuterio-1-phenylmethanol.



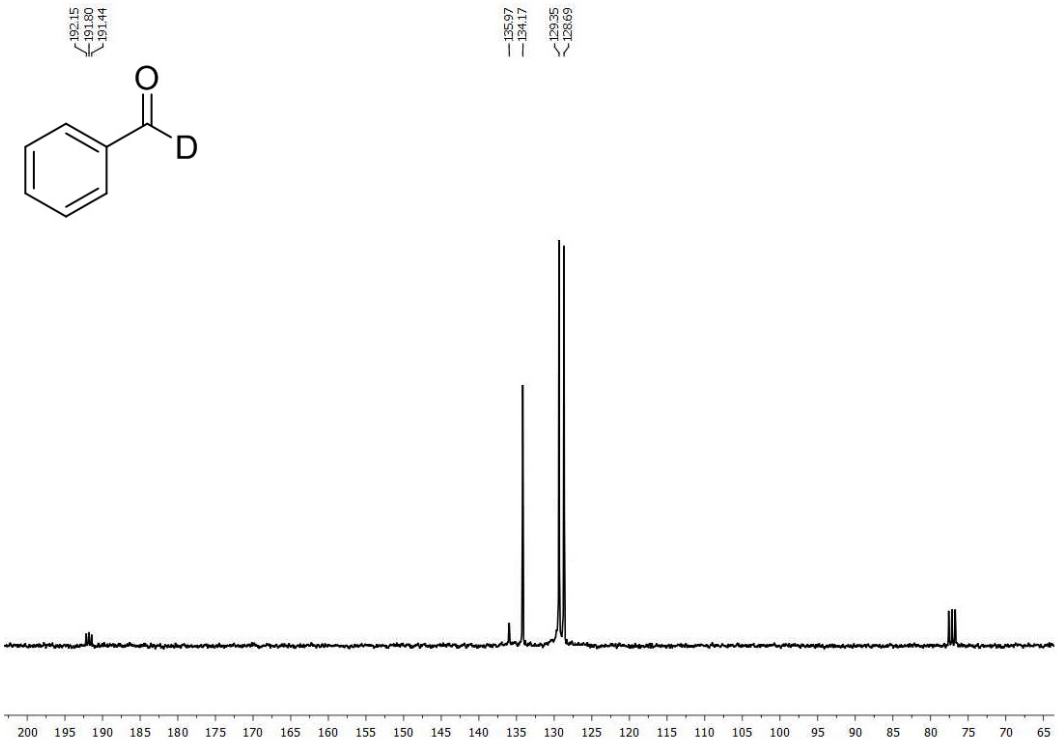

$^{13}$C NMR spectrum of 1,1-dideuterio-1-phenylmethanol.



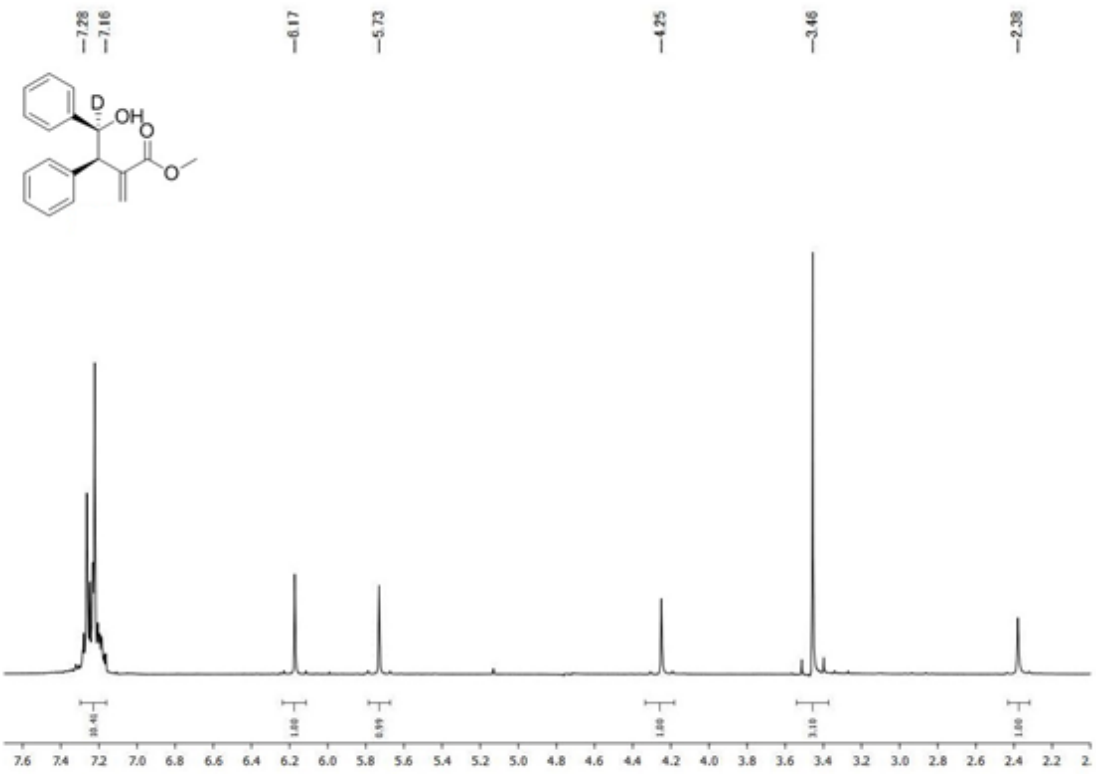

$^{1}$H NMR spectrum of 1-deuteriobenzaldehyde.



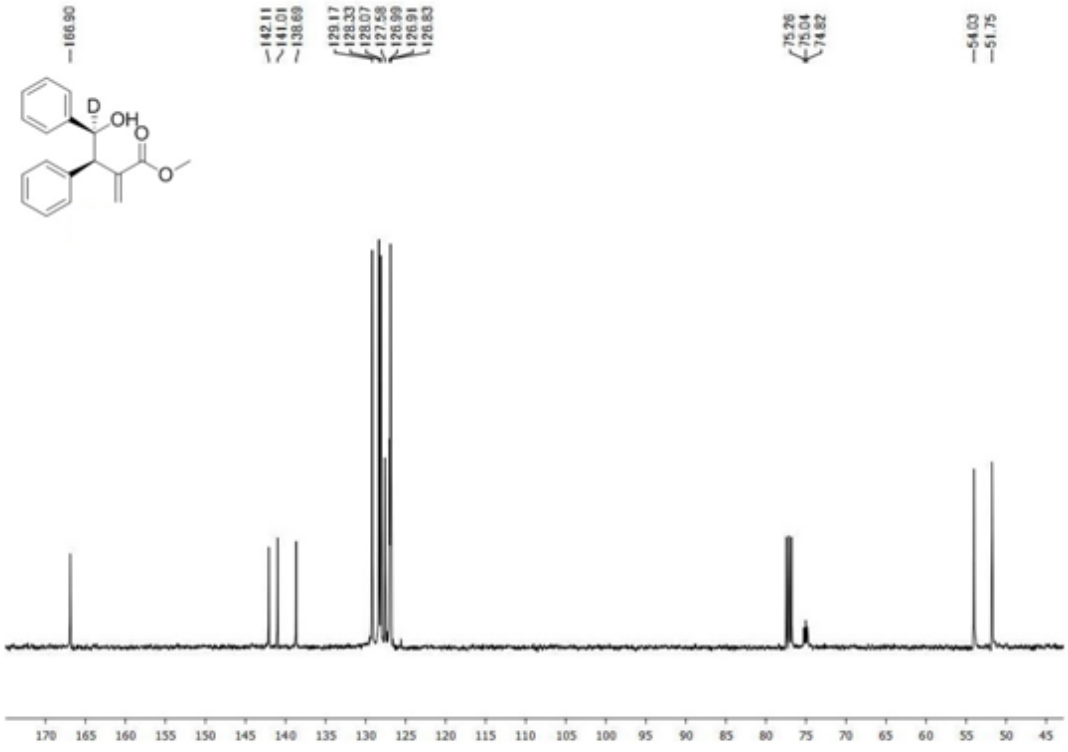

$^{2}$H NMR spectrum of 1-deuteriobenzaldehyde.



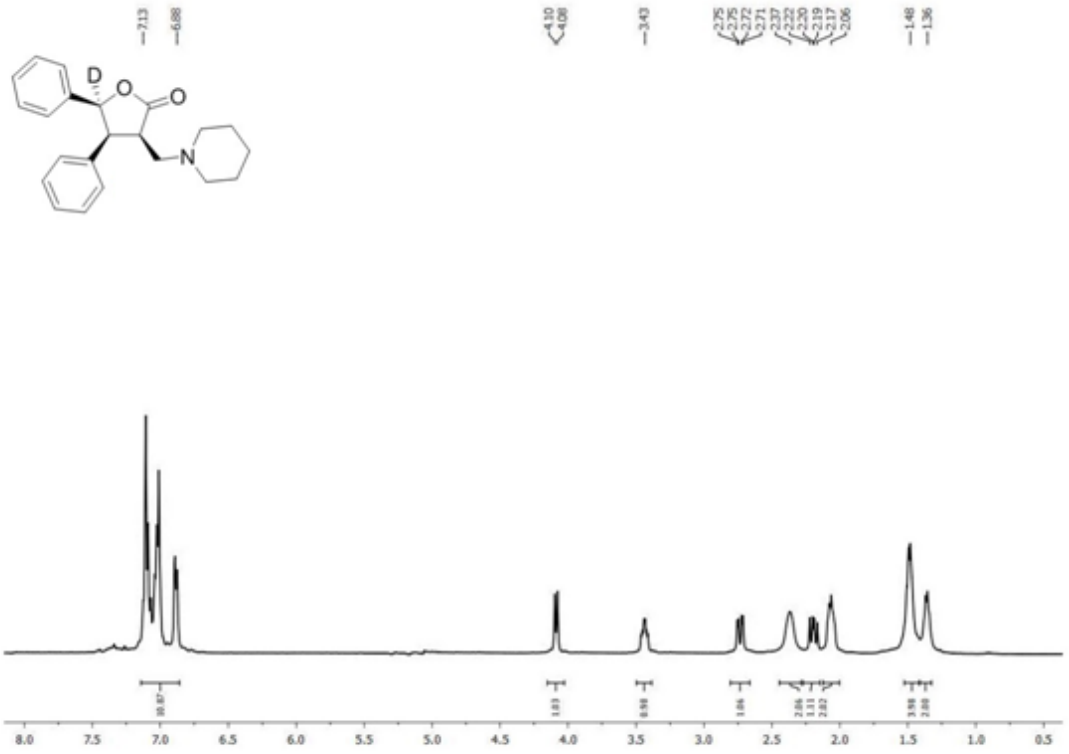

$^{13}$C NMR spectrum of 1-deuteriobenzaldehyde.



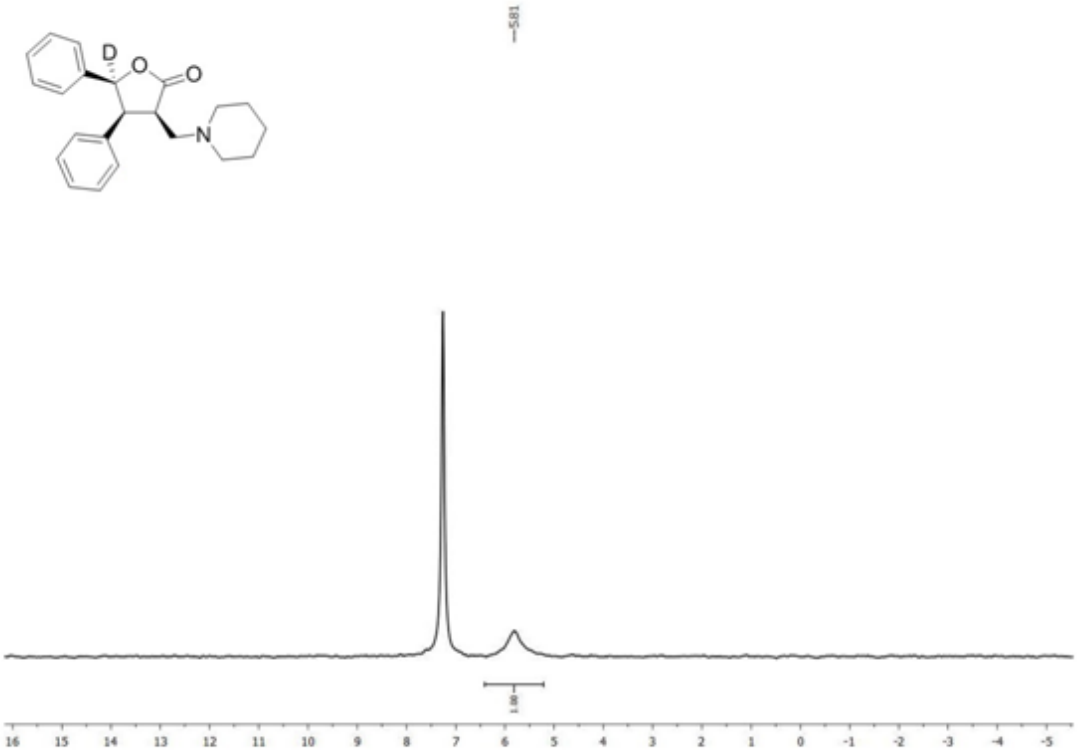

$^{1}$H NMR spectrum of **36**.



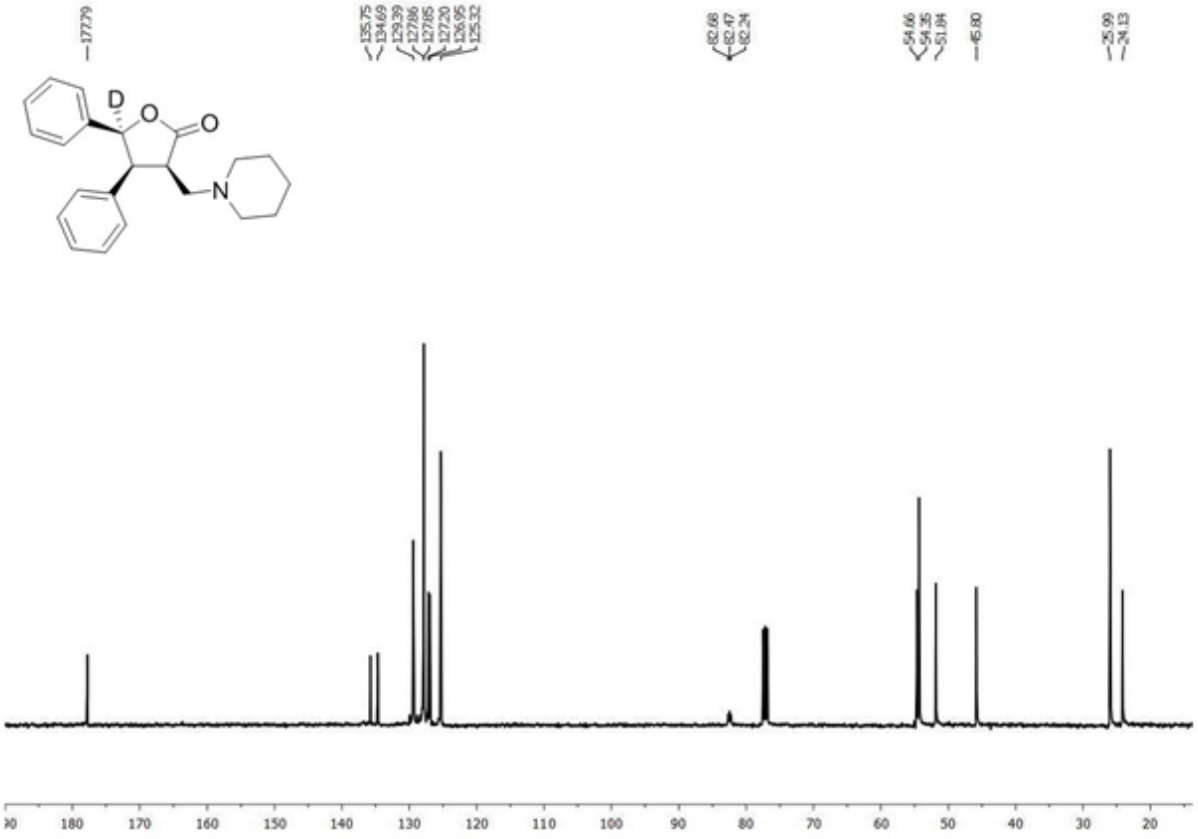

$^{13}$C NMR spectrum of **36**.




$^{1}$H NMR spectrum of **38**.




$^{2}$H NMR spectrum of **38**.




$^{13}$C NMR spectrum of **38**.

## Postulation for Predicting the Stereochemistry

The *γ*-substituted butanoates possess A-1,3 strain in the geometrically optimized transition state of pathway **B** (Figure 1). Consequently, **A**, leading to the *cis*-diastereomer, is favored. In the case of β-substituted butanoates (Figure 1b), transannular, *syn*-butanyl interactions destabilize **D**, favoring instead the *cis*-producing pathway **C**, which has no such destabilizing interactions.[13] As dialkyl A-1,3 interactions are typically more energetically demanding than *syn*-butanyl interactions, a higher *cis*-selectivity would be predicted for the aminolactonization of *γ*-substituted butanoates than for β-substituted ones; this is in accord with our observations (*γ*-substituted examples, average dr = 85:15; β-substituted examples, average dr = 81:19). For *syn*-β,*γ*-disubstututed lactones, increased A-1,3 interactions destabilize **F** (relative to **B**), promoting the formation of the *cis*,*cis*-diastereomer through pathway **E**. With *anti*-β,*γ*-disubstututed lactones, an A-1,3 interaction (similar to **B**), and possible gauche interaction between the allylic methylene and β-substituent would destabilize pathway **H**, favouring *anti*,*anti*-producing pathway **G** (Figure 1d).

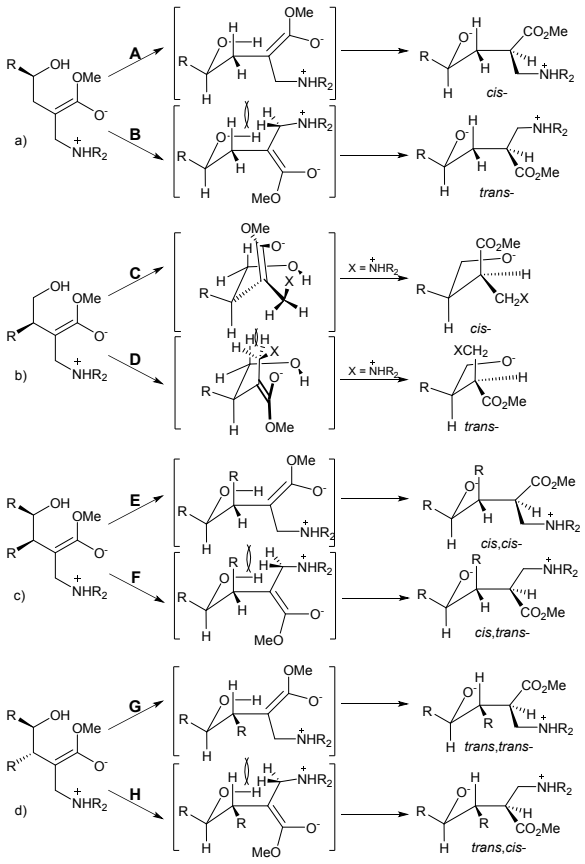



**Figure 1** Predicted stereochemical outcome for substituted butanoates